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Diaminohexopyranosides as Ligands in Half-Sandwich Ruthenium(II), Rhodium(III), and Iridium(III) Complexes

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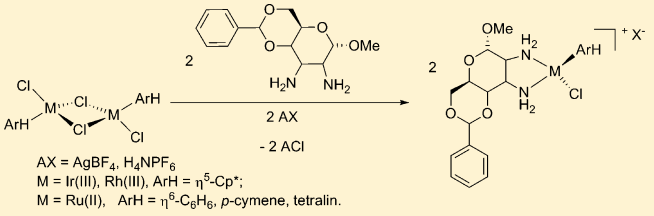
Supporting Information

ABSTRACT: The syntheses of methyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-hexopyranosides of glucose, mannose, gulose, and talose and methyl 2-amino-4,6-benzylidene-2,3-dideoxy-3-tosylamido-α-D-glucopyranoside are exhaustively presented, as well as their application as ligands in half-sandwich ruthenium(II), rhodium(III), and iridium(III) complexes. The complex formation occurs highly diastereoselectively, creating a stereogenic metal center. The molecular structures of the ligands and their complexes were investigated by X-ray structure analysis, NMR spectroscopy, polarimetry, and DFT methods. The diamino monosaccharide complexes have been subjected to antitumor activity studies. In vitro tests of a few ruthenium complexes against different cancer cell types showed antiproliferative activities 4−10 times lower than that of cisplatin.



INTRODUCTION

Carbohydrate coordination compounds have been studied for more than 100 years.[1] Early investigations were mainly focused on pharmaceutical,[2a,b] physiological,[2c−g] and technical[2h] applications.

However, the first molecular structure of a transition-metal carbohydrate complex, an alkoxy sugar dimolybdate, was published in 1981.[3a] Four years later the first organometallic transition-metal sugar compound was synthesized, a carbohydrate pentacarbonyl manganese complex containing a metal−carbon σ bond.[3b] Cyclopentadienyl titanium and zirconium compounds with alkoxy sugar ligands were investigated with respect to their application as antitumor agents,[4a] as chiral reagents,[4b] or in catalysis.[4c]

Transition-metal complexes with ligands derived from amino sugars have attracted a great deal of interest since 1986.[5,6] Ruffo et al.[7a] and others[7b] reported transition-metal complexes of 2,3-diamino-2,3-dideoxyhexopyranosides and their application in asymmetric catalysis. Due to their high costs and laborious preparation, 2,3-diamino-2,3-dideoxyhexopyranosides and their derivatives were model compounds for analogous oligo- or polycarbohydrates rather than promising ligands in applied chemistry. Catalytic studies with chitosane as auxiliary ligand have demonstrated the large potential of polysaccharides in asymmetric reactions.[8a] In 2012 Fontaine et al. published a modified chitosan with a protecting group in a C6 position and its use as a polyligand in the synthesis of η^6-cymeneruthenium(II) complexes. Transfer hydrogenation of acetophenone with 2-propanol and sodium 2-propanolate catalyzed by the obtained polycomplex yielded (*S*)-1-phenylethanol with an enantiomeric excess up to 72%.[8b]

Half-sandwich complexes of ruthenium, rhodium, and iridium with chelating nitrogen ligands were effectively used in catalyses such as water oxidation,[9a] intramolecular hydroamination of alkynes,[9b] Diels−Alder reactions,[9c] asymmetric Michael addition reactions,[9d] asymmetric hydrogenation,[9e] and transfer hydrogenation[9f,g] reactions of ketones and imines.

The first pharmaceutical use of carbohydrate coordination compounds dates back to the early 20th century. Long before the discovery of the cytostatic effect of platinum compounds starting in 1965 by Rosenberg,[10a,b] aurothioglucose, a polymeric coordination compound of 1-deoxy-1-thio-β-D-glucose and gold(I) cations, was prescribed for rheumatism.[2a] In 1972 Sutton and others synthesized its replacement, auranofin ((2,3,4,6-tetraacetyl-1-deoxy-1-thiolato-β-D-glucose)(triethylphosphane)gold(I)).[2b]

Twenty years after the ascent of cisplatin[10b] research on transition-metal sugar complexes with cytostatic properties was carried out. In the beginning monoaminocarbohydrate platinum(II) complexes were synthesized.[5a] While the first diamino carbohydrate complex of a transition metal was reported in 1966 by Guthrie, wherein nickel(II) ions were chelated by 2,3-diamino-2,3-dideoxyhexopyranosides comparable to the case for ethylenediamine,[11a] various diamino carbohydrate complexes analogous to cisplatin and its derivatives have been synthesized since 1986 which demonstrated antitumor activity similar to that of platinum(II) reagents.[11b] Low toxicity and high selectivity turn diamino carbohydrate chelating ligands into encouraging auxiliaries in platinum-containing compounds for medical purposes.

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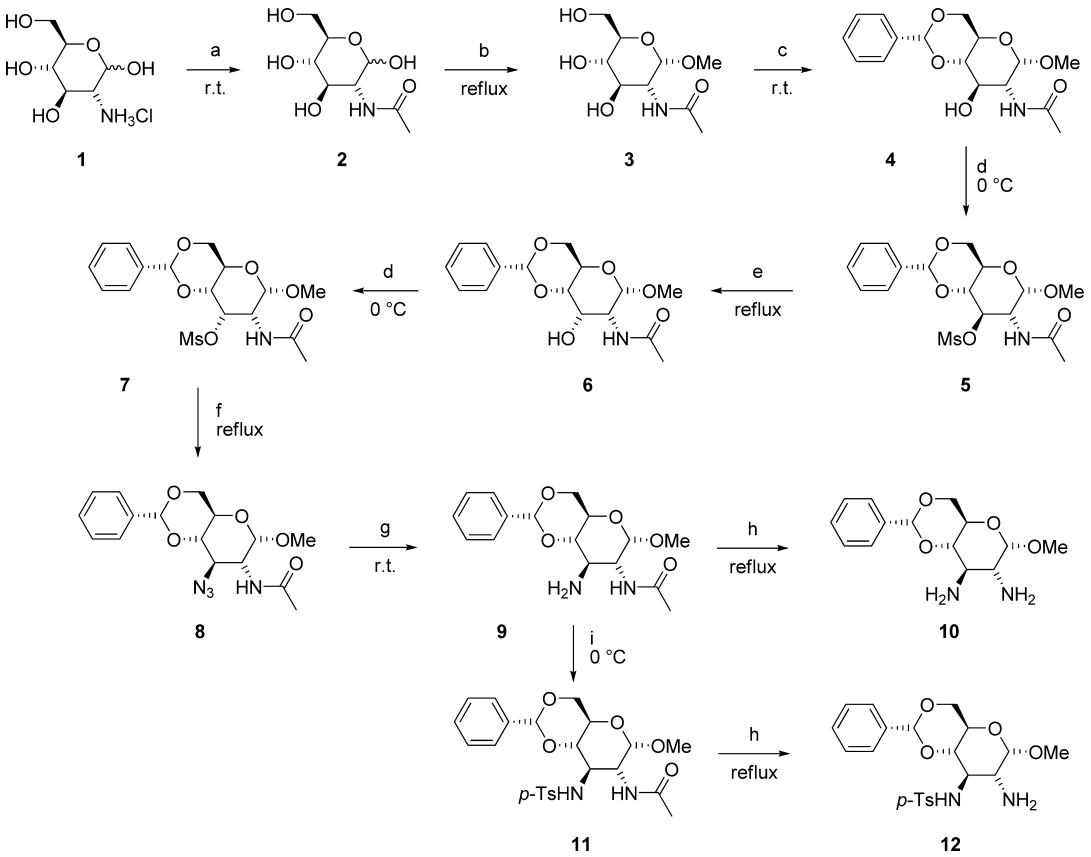
Scheme 1. Synthesis of Methyl 2,3-Diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranoside (10) and Methyl 2-Amino-4,6-*O*-benzylidene-2,3-dideoxy-3-tosylamido-α-D-glucopyranoside (12)[a]



[a]Legend: (a) (1) sodium methanolate in methanol, (2) acetic anhydride;[16a−c,i,j] (b) Amberlite IR120H$^+$ in methanol;[16a−c,i,j] (c) benzaldehyde dimethylacetal and tetrafluoridoboric acid in *N*,*N*-dimethylformamide;[16l] (d) methanesulfonyl chloride in pyridine;[16a,b,k] (e) sodium acetate in 2-methoxyethanol and water;[16a,b,k] (f) sodium azide in *N*,*N*-dimethylformamide and 1,4-dioxane;[16a,b,k] (g) normal atmospheric pressure of H_2 and Pd(C) in methanol;[16a,b,k] (h) potassium hydroxide in ethanol;[16c] (i) *p*-tosyl chloride in dichloromethane and pyridine.

Trigonal platinum(0) complexes with carbohydrate-derived diimine ligands were reported with respect to antitumor application.[5b] Yano and Mikata linked pyranosides to diamine ligands chelating platinum(II). Their idea was to create antitumor reagents which are more specific toward cancer cells utilizing the faster metabolism and, thus, greater carbohydrate uptake of the degenerated cells. The new sugar complexes could compete with cisplatin in in vitro tests.[11c] Möker and Thiem reported similar *cis*-diamminemalonato-platinum(II) complexes linked to D-glucose in 2009. The antitumor activity of these compounds was comparable to that of carboplatin.[11d]

A galactal complex of a hydridocarbonylruthenium cluster showed high activity against chronic myelogical leukemia and other types of cancer cells comparable to the effects of cisplatin.[12] Currently, pentamethyl-η^5-cyclopentadienyliridium-(III) and -rhodium(III),[13a−c] η^6-areneruthenium(II) half-sandwich,[13d−g] and octahedral iridium(III),[14] rhodium(III),[14] and ruthenium(II)[15] complexes are the focus of antitumor research, with the objective that other metals might tackle the cancer cells, as the *cis*-Pt complexes are becoming too inactive. Another aspect is the search for less toxic complexes.[13a]

With this publication we wish to describe the synthesis and molecular structure of methyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-hexopyranoside ligands and their pentamethyl-η^5-cyclopentadienylrhodium(III), -iridium(III), and η^6-areneruthenium(II) complexes. Furthermore, we will present results from antiproliferative studies of the carbohydrate complexes with different cancer cell types. In further publications the novel complexes will be applied as precatalysts in catalytic hydrogenation reactions.

RESULTS AND DISCUSSION

Synthesis of the Hexopyranoside Ligands. The synthesis of 2,3-diamino-2,3-dideoxy-D-glucopyranosides has already been reported.[16a−h] The introduction of the benzylidene protecting group yielding **4** was carried out by means of tetrafluoridoboric acid. This procedure was also applied in the synthesis of **20**.[16l] Tosylation of **9** and subsequent cleavage of the acetyl amido group led to the formerly unknown methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-tosylamido-α-D-glucopyranoside (**12**; Scheme 1).

The synthesis of 2,3-diamino-2,3-dideoxy-D-manno-pyranosides has been reported as well,[16h,m−p] though not in as detailed and coherent a manner as for the 2,3-diamino-2,3-dideoxy-D-glucopyranosides. For example, there is no detailed description for the subsequent reduction of the azide functions to amino groups. Guthrie used a hydrogenation reaction with Adams' catalyst,[16n,o] while Ruffo and co-workers applied the Staudinger reaction pathway.[5c] The subsequent reduction of both azide

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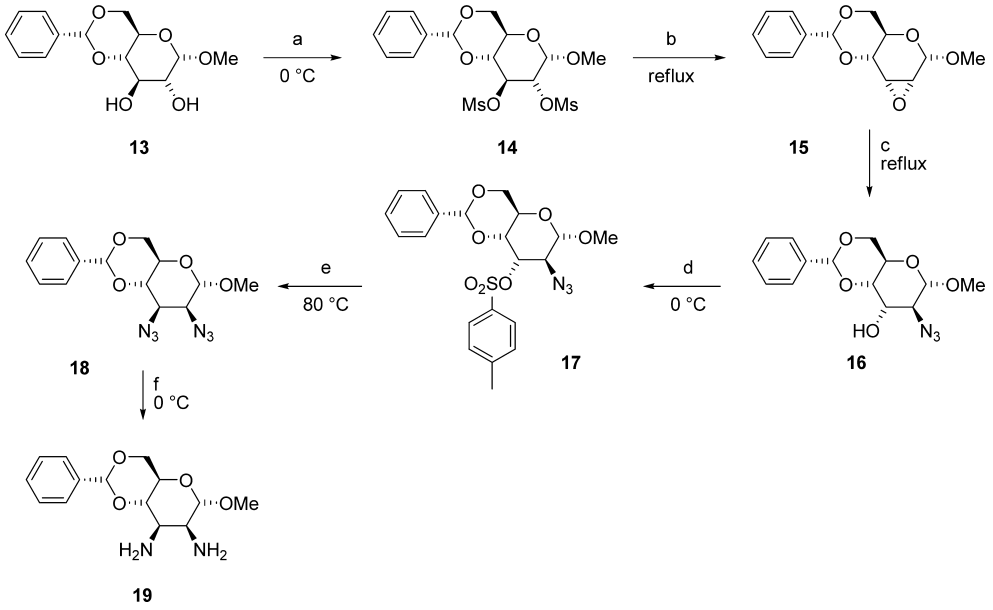
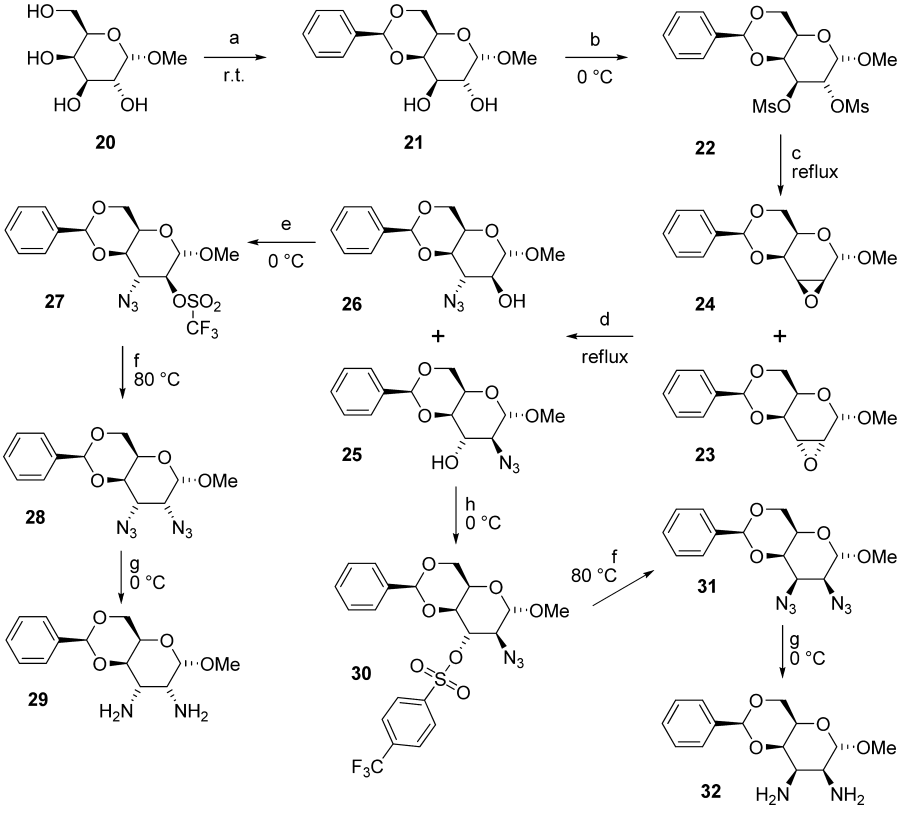
Scheme 2. Synthesis of Methyl 2,3-Diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside (19)[a]



[a]Legend: (a) methanesulfonyl chloride in pyridine;[16n,o,q] (b) sodium methanolate in methanol;[16n,o,q] (c) sodium azide and ammonium chloride in 2-methoxyethanol and water;[16n,o] (d) *p*-tosyl chloride and 4-(*N*,*N*-dimethylamino)pyridine in dichloromethane and pyridine;[16r] (e) sodium azide in *N*,*N*-dimethylformamide and 1,4-dioxane; (f) lithium alanate in tetrahydrofuran.

Scheme 3. Synthesis of Methyl 2,3-Diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-gulopyranoside (29) and Methyl 2,3-Diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-talopyranoside (32)[a]



[a]Legend: (a) benzaldehyde dimethylacetal and tetrafluoridoboric acid in *N*,*N*-dimethylformamide;[16l] (b) methanesulfonyl chloride in pyridine; (c) [16q]sodium methanolate in methanol; (d) sodium azide and ammonium chloride in 2-methoxyethanol and water;[16u] (e) triflic anhydride and 4-(*N*,*N*-dimethylamino)pyridine in dichloromethane and pyridine; (f) trimethylsilyl azide and tetra-*n*-butylammonium fluoride in tetrahydrofuran; (g) lithium alanate in tetrahydrofuran; (h) *p*-trifluoromethanebenzenesulfonyl chloride and 4-(*N*,*N*-dimethylamino)pyridine in dichloromethane and pyridine

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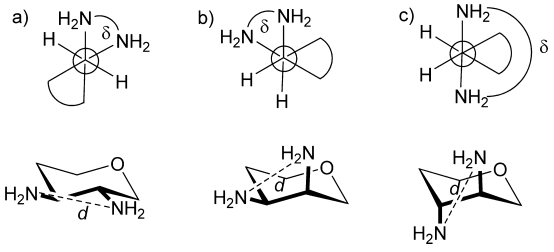
groups by means of lithium alanate was demonstrated to be the most efficient procedure for the syntheses of **19** (Scheme 2) and of **29** and **32** (Scheme 3). The formation of 2,3-diamino-2,3-dideoxy-D-gulopyranosides[16e] has been reported similarly to the synthesis outlined here, but the methyl D-gulopyranoside was merely characterized as its diacetylamide, as was the case for all of the 2,3-diamino-2,3-dideoxy-D-hexopyranosides before 1986. Moreover, 2,3-diamino-2,3-dideoxy-D-talopyranosides have yet been entirely prepared on the basis of a strategy involving nitro monosaccharides.[16t]

The anhydroguloside **23** and the anhydrotaloside **24**, respectively, were converted to the 2-azidoidopyranoside **25** and the 3-azidoidopyranoside **26**, respectively.[16u] The mixture was separated by chromatographic methods.

Esterification of **26** with triflic anhydride gave the sulfonate **27**, which was converted to the 2,3-diazidogulopyranoside **28** by means of trimethylsilyl azide and tetra-*n*-butylammonium fluoride. Common leaving groups were not suitable for the inversion of **25** at the C3 position. Thus, **25** was esterificated with *p*-trifluoromethanebenzenesulfonyl chloride, producing sulfonate **30**, which was not fully characterized. Substitution of the sulfonate with trimethylsilyl azide and tetra-*n*-butylammonium fluoride yielded the 2,3-diazidotalopyranoside **31**.

Chart 1. Dihedral Angles (δ) Defined by the Planes N2−C2−C3 and C2−C3−N3 and Distances (d) between Two Equatorially Arranged (a), One Equatorially and One Axially Arranged (b), and Two Axially Arranged Amino Groups (c) in 2,3-Diamino-2,3-dideoxy-D-hexopyranosides



Structural Discussion of Methyl 2,3-Diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-hexopyranosides. The capability of the chelating coordination mode of the four 2,3-diamino-2,3-dideoxy-D-hexopyranosides depends on the dihedral angle δ defined by the planes N2−C2−C3 and C2−C3−N3. When the dihedral angle δ includes two equatorially arranged amino groups (Chart 1a) or one equatorially and one axially arranged amino group (Chart 1b), δ roughly amounts to 60°, whereas δ is close to 180° (Chart 1c) when the planes include two axially arranged amino groups, which then are not suitable for a chelating coordination. For that purpose carbohydrate ligands with amino substituents in orientation (a) such as glucose (or galactose) and (b) such as mannose or talose were prepared. A similar orientation of the substituents is given in gulose (and allose), where both amino groups are inverted in comparison to the arrangement in Chart 1b. Thus, a ligand with a gulose backbone was also synthesized. Closely related to the dihedral angle is the nonbonding N2,N3 distance d.

Unfortunately, suitable crystals for an X-ray structure determination could only be obtained for 2,3-diazidomannopyranoside **18** and 2,3-diazidotalopyranoside **31** (molecular structures are given in Figure S1.1 and crystallographic data in Table S1.1 in the Supporting Information). Therefore, the molecular structures of the diaminopyranosides **10**, **19**, **29**, and **32** as well as those of the diazidopyranosides **18**, **28**, and **31** were calculated by DFT methods[17] (Table 1). The reliability of the molecular structures calculated by DFT methods can be evaluated by comparison of the molecular structures obtained by means of X-ray structure determination as well as DFT calculations for **18** and **31**.

For compounds **18** and **31** the N2,N3 distances d obtained from X-ray structure analysis correspond with those derived from DFT calculations, while the dihedral angle δ differs significantly by about 10°, which may be due to interactions in the crystal packing. Overall the structural data derived from DFT calculations (of both functionals BP86 and B3LYP) correlate well with those from single-crystal X-ray structure analysis. Hence, structural data originating from DFT calculations using the hybrid functional B3LYP was used to draw the molecular structures of **10**, **19**, **28**, **29**, and **32** (Figure S5.1 in the Supporting Information).

The dihedral angle δ of compound **10** (gluco) was calculated to be 62.6° (B3LYP). The corresponding dihedral angles of **19** (manno), **29** (gulo) and **32** (talo) were calculated to be 50.1, 49.8, and 53.4°, respectively. The N2,N3 distances d of the 2,3-diaminopyranosides increase with an increasing number of axially arranged substituents in the order 288 pm (**10**), 291 pm (**19**), 293 pm (**29**), and 295 pm (**32**).

Table 1. Dihedral Angles δ and Nonbonding N2,N3 Distance d in Methyl 2,3-Diamino- (10, 19, 29, 32) and 2,3-Diazido-2,3-dideoxy-D-hexopyranosides (18, 28, 31) Derived from X-ray Structure Determinations and DFT Calculations

	X-ray structure analysis		selected structural data obtained from DFT calculation[a] (functional BP86)		DFT calculation[a] (functional B3LYP)	
compound	δ (deg)[b]	d (pm)	δ (deg)[b]	d (pm)	δ (deg)[b]	d (pm)
10 (gluco)			62.3	287	62.6	288
18 (manno)	56.07(22)	283.3(3)[c]	46.4	284[c]	45.8	284[c]
19 (manno)			49.6	290	50.1	291
28 (gulo)			61.3	297[c]	60.6	295[c]
29 (gulo)			49.7	293	49.8	293
31 (talo)	63.68(22)	299.0(3)[c]	54.1	301[c]	53.6	300[c]
32 (talo)			53.3	296	53.4	295

[a]Structural data obtained by calculations using DFT methods from Orca 2.9, functionals BP86 and B3LYP, and basis sets TZV for H and TZV(2d2p) for main-group elements.[17] [b]Dihedral angle δ defined by the planes N2−C2−C3 and C2−C3−N3. [c]Distances d between N2 at C2 and N3 at C3.

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For compounds **10**, **19**, and **32** the single-point energies of the optimized structures with constrained dihedral angles δ were calculated for ±10−15° from optimum (Figure 1). The

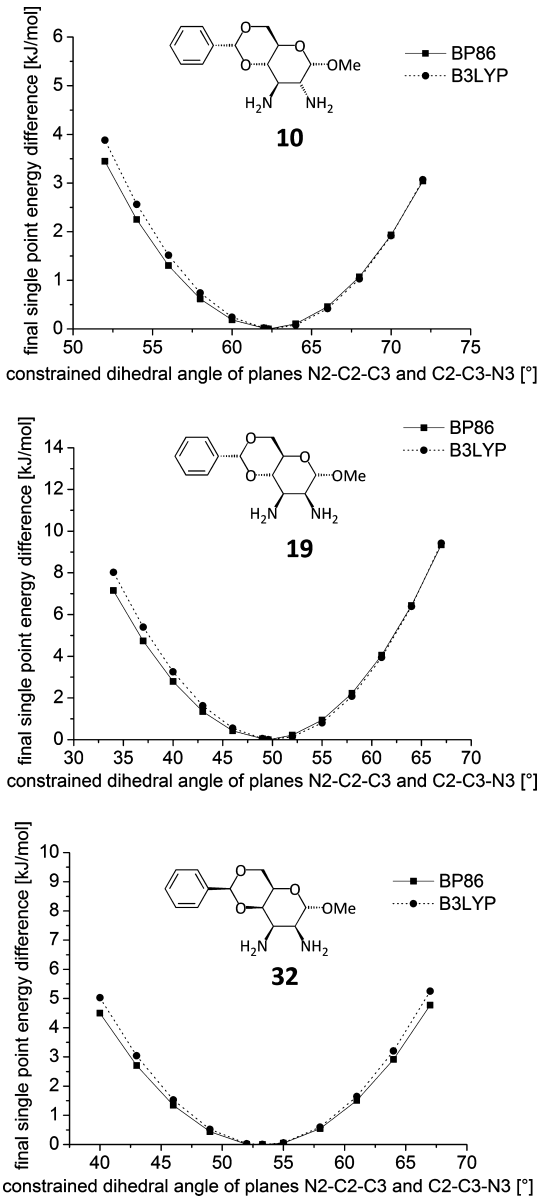

Figure 1. DFT calculated energy barriers (final single-point energy) of the dihedral angles δ of methyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranoside (**10**), methyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-mannopyranoside (**19**), and methyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-talopyranoside (**32**) (Orca 2.9, functionals BP86 and B3LYP, basis sets TZV for H and TZV(2d2p) for main-group elements).[17]

ability of the two amino groups to adopt a chelating coordination mode at different metal centers was examined: for all ligands (**10**, **19** and **32**) low energy barriers of about 3 kJ/mol were calculated for the deviations of the dihedral angles ±10° from optimum. With deviations of ±5° the energy barrier even decreased to 1 kJ/mol (Table 2).

Hence, the DFT calculations confirmed a certain flexibility of the amino functions of the 2,3-diaminohexopyranosides, which makes them capable to chelate metal atoms of different sizes, as long as the metal atoms are not extraordinarily small (as Ti^{4+} cations)[18a] or large (as Hg^{2+} cations).[18b] Therefore, an easy coordination of middle and late transition metals can be expected, and it is not surprising that coordination compounds of the metals with cis-coordinated 1,2-disubstituted ethylenediamine-type ligands (*N*,*N*-en-type ligands) (Table 3) possess dihedral angles defined by the planes N1−C1−C2 and C1−C2−N2 comparable to those of ligands **10**, **19**, **29**, and **32** (Table 1).[18c−g]

Synthesis and Structure of the Half-Sandwich Ruthenium, Rhodium, and Iridium Complexes. The first monomeric η^5-cyclopentadienylrhodium(III) and -iridium(III) and η^6-areneruthenium(II) complexes were reported by *Maitlis* et al.[19a,b] in 1969 and Zelonka and Baird[19c,d] in 1972, respectively. With the dimeric species $[\{M(ArH)Cl\}_2(\mu\text{-}Cl)_2]$ (**33$_a$**, M = Ir, ArH = Cp*; **33$_b$**:, M = Rh, ArH = Cp*; **33$_c$**, M = Ru: ArH = benzene; **33$_d$**, M = Ru, ArH = *p*-cymene; **33$_e$**, M = Ru, ArH = tetralin) as starting material, the monomeric compounds were obtained by addition of the chelating ligand and substitution of one chlorido ligand per metal center.[19e] Hence, silver or ammonium salts were used, depending on the solubility of the resulting complex. Complexes with high solubility were favorably prepared in dichloromethane with silver salts,[19f] whereas complexes with low solubility were synthesized in methanol with ammonium salts (Scheme 4).[19g]

Thus, the iridium(III) complex **34** with ligand **10** (gluco) and rhodium(III) complexes **35**, **39**, **42**, **43**, and **46** and ruthenium(II) complexes **36**-**38**, **40**, **41**, **44**, **45**, **47**, and **48** were synthesized (Scheme 4).

Compounds **34**−**48** were fully characterized by NMR spectroscopy, elemental analysis, polarization angle, and (if needed) high-resolution mass spectrometry. Compounds **34**, **35**, **39**, **42**, and **46** were crystallized, and their molecular structures were determined by X-ray crystallography. The complexes demonstrate the expected structures. The absolute configuration at the metal centers of **34**, **35** (gluco), and **46** (talo) is *T*-4-*S*, while the configuration of **42** (gulo) is *T*-4-*R*, when the geometries of these piano-stool complexes are considered as (pseudo)tetrahedral (Figure 2; stereodescriptor [*T*-4-*R*/*S*] with *T*-4 denoting tetrahedral and *R*/*S* absolute configuration following the CIP rules). The configurations at the metal centers in the solid-state structures are in accordance with the configuration in liquid solution identified by the NMR

Table 2. Energy Barriers (kJ/mol) for the Deviations from the Optimal Dihedral Angles δ Calculated by DFT Methods

	deviation							
	−10°		−5°		+5°		+10°	
compound	BP86	B3LYP	BP86	B3LYP	BP86	B3LYP	BP86	B3LYP
10 (gluco)	3.4	3.6	0.9	1.0	0.8	0.8	3.2	3.2
19 (manno)	2.9	3.4	0.8	1.1	0.8	0.7	3.2	2.9
32 (talo)	2.5	2.9	0.7	0.8	0.7	0.8	2.5	2.9

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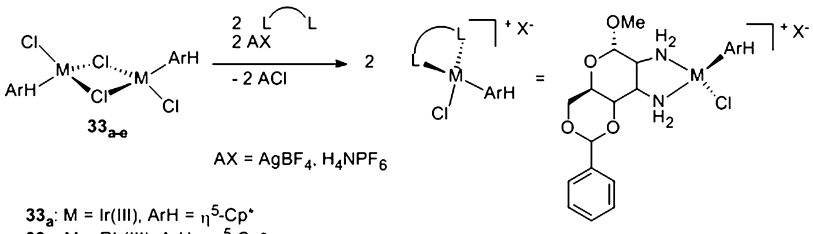
Table 3. Dihedral Angles Defined by the Planes N1−C1−C2 und C1−C2−N2 of Transition Metals with Cis-Coordinated *N,N*-en-Type Ligands and Chlorido Ligands

metal center	*cis-N,N* ligand	dihedral angle (planes N1−C1−C2 and C1−C2−N2) (deg)
Ru^{2+a}	*cis,cis*-dach[b]	48.71(56)[18c]
Pt^{2+}	*cis,trans*-dach[b]	51.55(6)[18d]
Pt^{2+}	*cis,cis*-dach[b]	50.87(60)[18e]
Pt^{2+}	methyl 2,3-diamino-2,3-dideoxy-α-D-mannopyranoside	49.57(113)[18f,g]

[a]1,4-Bis(diphenylphosphino)butane (dppb) as an additional neutral ligand. [b]dach: 1,2-diaminocyclohexane.

Scheme 4. Synthesis of Compounds 34−48



33_a: M = Ir(III), ArH = η^5-Cp*
33_b: M = Rh(III), ArH = η^5-Cp*
33_c: M = Ru(II), ArH = η^6-C_6H_6
33_d: M = Ru(II), ArH = η^6-*p*-cymene
33_e: M = Ru(II), ArH = η^6-tetralin.

[*T*-4-*S*] (LL = **10**)
34: gluco, M = Ir, ArH = Cp*, X = BF_4
35: gluco, M = Rh, ArH = Cp*, X = BF_4
36: gluco, M = Ru, ArH = benzene, X = BF_4
37: gluco, M = Ru, ArH = *p*-cymene, X = BF_4
38: gluco, M = Ru, ArH = tetralin, X = BF_4
[*T*-4-*R*] + [*T*-4-*S*] (LL = **19**)
39: manno, M = Rh, ArH = Cp*, X = BF_4
40: manno, M = Ru, ArH = *p*-cymene, X = BF_4
41: manno, M = Ru, ArH = tetralin, X = BF_4
[*T*-4-*R*] (LL = **29**)
42, **43**: gulo, M = Rh, ArH = Cp*, X = BF_4 (**42**), PF_6 (**43**)
44: gulo, M = Ru, ArH = *p*-cymene, X = BF_4
45: gulo, M = Ru, ArH = tetralin, X = PF_6
[*T*-4-*S*] (LL = **32**)
46: talo, M = Rh, ArH = Cp*, X = BF_4
47: talo, M = Ru, ArH = *p*-cymene, X = BF_4
48: talo, M = Ru, ArH = tetralin, X = BF_4

spectra of complexes **34**−**38** with ligand **10** (gluco), complexes **42**−**45** with ligand **29** (gulo), and complexes **46**−**48** with ligand **32** (talo), which reveal only one diastereomer for each compound in dichloromethane at room temperature. The asymmetric unit of **34** and **35** contains one molecule of diethyl ether per two cationic complexes, which was treated as a diffuse contribution to the total electron density. Crystals of **42** contain acetone and those of **46** dichloromethane, but their structures were solved including the solvent molecules. All compounds except for **39** crystallize in the space group $P2_12_12_1$ with R1 = 0.0513 (**34**), 0.0556 (**35**), 0.0560 (**42**), 0.0292 (**46**). The mannopyranoside complex **39** was found as a diastereomeric mixture with a ratio of roughly 1:1 for *T*-4-*R*/*T*-4-*S* in liquid solution (dichloromethane) at room temperature. However, the molecular structure in the solid state demonstrates the configuration *T*-4-*R* (R1 = 0.0379). A crystal for the molecular structure determination of **39** was obtained from a chloride-containing batch, and the compound crystallized with a mixture of the anions tetrafluoridoborate and chloride in the ratio 2:1. The space group is $P2_1$, and the asymmetric unit contains one molecule of water and three cationic complexes. Partially cocrystallized dichloromethane was treated as a diffuse contribution to the total electron density of the data sets (crystallographic data in Table S1.2 in the Supporting Information).

The experimentally determined bond lengths between the metals and the chlorido ligands as well as the nitrogen atoms of the carbohydrate ligands in **34**, **35**, **39**, **42**, and **46** are in quite good accordance with the molecular structure optimization by DFT[17] calculations for these compounds. The bond lengths between ligand atoms and the iridium atom in **34** are insignificantly larger than the bond lengths between ligand atoms and the rhodium atom in **35** (Table 4). This is not unexpected, since the ionic radius of Ir(III) is very much the same as that for Rh(III).[20]

The crystal structures of **35**, **39**, **42**, and **46** indicate intra- and intermolecular attractive interactions (Figure S1.2 in the Supporting Information). For the crystal structures of **35** (ligand **10**, gluco) and **39** (ligand **19**, manno) an intermolecular face-to-face stacking mode of the aromatic Cp* ligand of one cationic complex and the phenyl group of the neighboring complex is observed, which is displaced slightly parallel (the intermolecular distances between related carbon atoms are about 360 pm). This stacking feature is responsible for the pillard alignment of the complexes in the crystalline state of **35** and **39** (Figure S1.2). A column stacking mode of the complexes in the crystalline state is also observed for compound **42** (ligand **29**, gulo), but in contrast to the case for **35** and **39** the column structure in **42** is the result of an intermolecular edge-to-face order of the methyl hydrogen atoms of the Cp* ligand of one complex and the aromatic plane of the phenyl group of the next molecule (Figure S1.2; the intermolecular distances between related carbon atoms are about 360 pm).

The structures of complexes **35**, **39**, and **42** are different from that of **46** (ligand **32**, talo), where an intramolecular attractive edge-to-face interaction is located between the phenyl ring of the sugar ligand and the Cp* ring of the same complex (the distances between the nearest methyl carbon atom of the Cp* ring and the phenyl carbon atoms are estimated to be about 350 pm). In addition, the back side of the phenyl ring of one complex is arranged in an intermolecular face-to-face mode to the next complex displaced in a slightly parallel manner. The distances of related carbon atoms of the two rings are about 340−400 pm. This creates a staircaselike arrangement of the interacting complexes in the crystal (Figure S1.2 in the Supporting Information). All measured distances are in accordance with the distances assumed for π interactions.[21]

Similarly to **39** the mannopyranoside complexes **40** and **41** were obtained as diastereomeric mixtures in the ratio [*T*-4-*R*]:[*T*-4-*S*] 1:3 for **40** and [*T*-4-*R*]:[*T*-4-*S*] 1:2 for **41**. The assignment of the NMR signals of the [*T*-4-*R*] and [*T*-4-*S*] diastereomers of **39** and **40** (Figure 3) was accomplished by comparison of the NMR spectra and the calculated molecular

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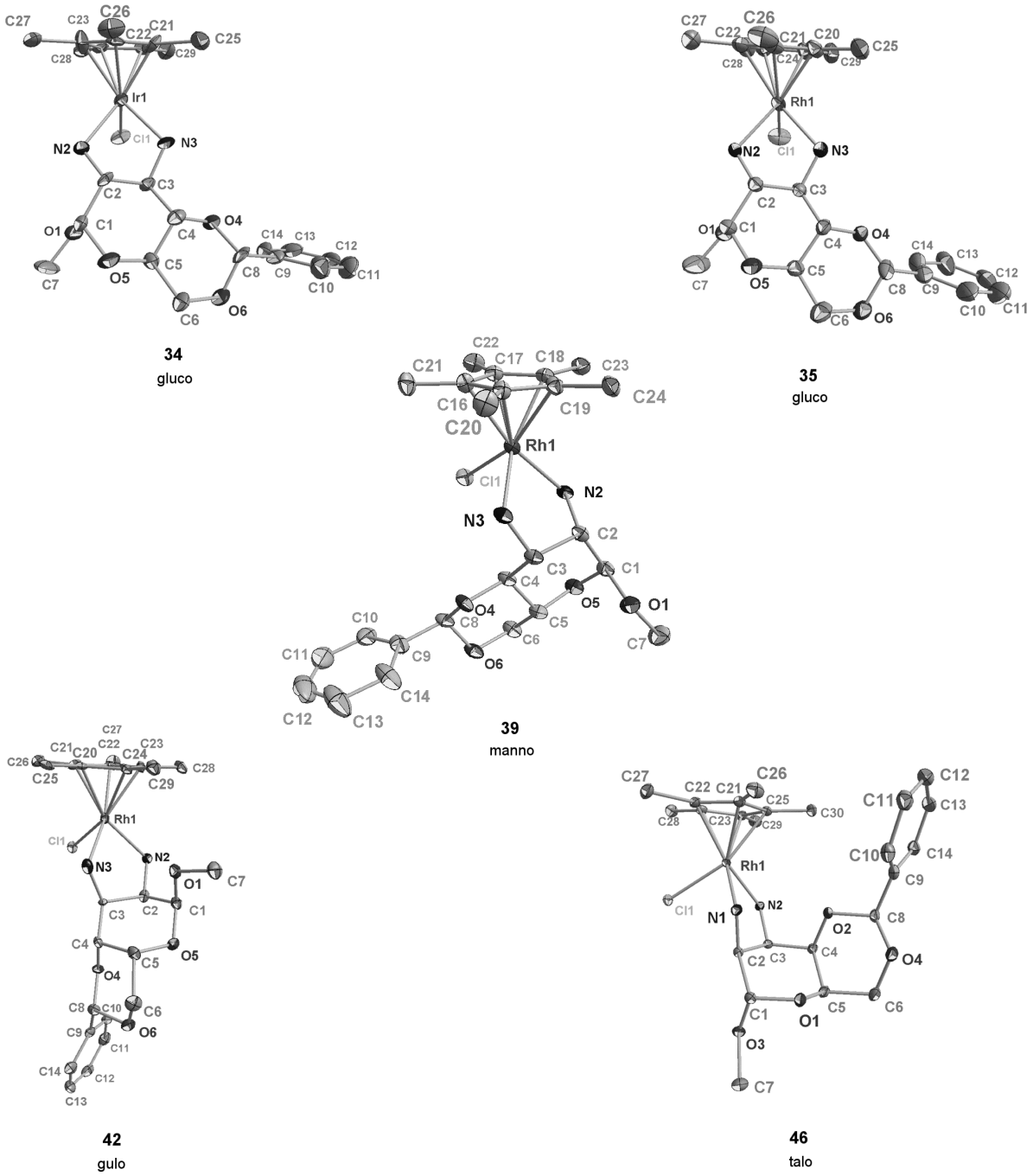

Figure 2. Molecular structures of **34** ($P2_12_12_1$, R1 = 0.0513), **35** ($P2_12_12_1$, R1 = 0.0556), **39** ($P2_1$, R1 = 0.0379), **42** ($P2_12_12_1$, R1 = 0.0560), and **46** ($P2_12_12_1$, R1 = 0.0292) derived from X-ray structure determination. The complexes are positively charged. Hydrogen atoms, cocrystallized solvent molecules, and counterions are omitted for clarity.

structures of the diastereomers. The protons of the alkyl groups of the arene ligands are facing the sugar ligand protons. Thus, the diastereomers are identified by through-space coupling of the arene protons with the particular ligand protons (NOE contacts in Figure 3). The similarity of their proton NMR spectra implies the same assignment of the proton signals for **40** and **41**, respectively.

The specific polarization angles of compounds **34**−**38** and **42**−**48** were measured (Table 5). Compounds **39**−**41** (ligand **19**) are diastereomeric mixtures (*T*-4-*R* and *T*-4-*S* configuration); thus, their polarization angles are omitted.

The similarity of the polarization angles of **34**−**38** (ligand **10**) leads to the conclusion that these complexes adopt the same configuration at the metal atom in liquid solution at room temperature. The absolute configuration of compound **37** was confirmed as *T*-4-*S* in liquid solution by NMR spectra (Figure 3) and was the same as that obtained from X-ray structure determinations for **34** and **35**.

For the complexes **46**−**48** (ligand **32**) the *T*-4-*S* configuration is stabilized by the intramolecular attractive edge-to-face interactions between the protons of the arene ligand and the phenyl ring of the sugar ligand, in agreement with the DFT calculations of **46**. In this edge-to-face arrangement the Cp*

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Table 4. Dihedral Angles δ, Nonbonding N2,N3 Distances d, and Selected Bond Lengths of 34 (Ir), 35 (Rh), 39 (Rh), 42 (Rh), and 46 (Rh) Derived from X-ray Structure Determination and Corresponding DFT Optimized Structures[17]

			bond length (pm; M = Ir/Rh)		
compound	δ^a (deg)	d^b (pm)	M−N2	M−N3	M−Cl
[*T*-4-*S*]-**34** (Ir, gluco)	59.88(78)	273.5(10)	217.0(7)	216.4(7)	241.2(2)
	58.23(90)	273.7(11)	216.0(8)	215.8(7)	241.4(2)
[*T*-4-*S*]-**35** (Rh, gluco)	56.27(32)	274.80(41)	214.5(3)	214.3(3)	241.65(10)
	58.83(42)	275.28(74)	214.7(4)	213.2(3)	241.76(10)
[*T*-4-*R*]-**35**^{c} (Rh, gluco)	57.4 (DFT)	279 (DFT)	220 (DFT)	218 (DFT)	242 (DFT)
[*T*-4-*S*]-**35**^{c} (Rh, gluco)	56.7 (DFT)	279 (DFT)	219 (DFT)	219 (DFT)	241 (DFT)
[*T*-4-*R*]-**39** (Rh, manno)	50.14(24)	272.4(3)	216.1(2)	215.46(19)	241.97(6)
	46.73(25)	272.49(30)	215.9(2)	215.4(2)	242.27(7)
	49.77(25)	273.98(26)	215.2(2)	214.5(2)	239.36(7))
[*T*-4-*R*]-**39**^{c} (Rh, manno)	48.7 (DFT)	277 (DFT)	218 (DFT)	219 (DFT)	241 (DFT)
[*T*-4-*S*]-**39**^{c} (Rh, manno)	53.4 (DFT)	279 (DFT)	220 (DFT)	218 (DFT)	242 (DFT)
[*T*-4-*R*]-**42** (Rh, gulo)	44.21(50)	275.8(6)	216.0(4)	213.5(4)	244.4(1)
[*T*-4-*R*]-**42**^{c} (Rh, gulo)	50.2 (DFT)	277 (DFT)	221 (DFT)	220 (DFT)	240 (DFT)
[*T*-4-*S*]-**42**^{c} (Rh, gulo)	41.5 (DFT)	268 (DFT)	221 (DFT)	218 (DFT)	240 (DFT)
[*T*-4-*S*]-**46** (Rh, talo)	45.35(14)	272.53(17)	216.87(12)	214.3(3)	242.30(3)
[*T*-4-*R*]-**46**^{c} (Rh, talo)	43.1 (DFT)	268 (DFT)	218 (DFT)	222 (DFT)	239 (DFT)
[*T*-4-*S*]-**46**^{c} (Rh, talo)	49.9 (DFT)	276 (DFT)	219 (DFT)	222 (DFT)	242 (DFT)

^{a}Dihedral angle defined by the planes N2−C2−C3 and C2−C3−N3. ^{b}Nonbonding N^2,N^3 distance. ^{c}Structural data obtained by calculation using DFT methods by Orca 2.8, functional BP86, and basis sets TZV for H, TZV(2d2p) for main-group elements, and TZV(2d2fg,3p2df) for transition elements.[17]

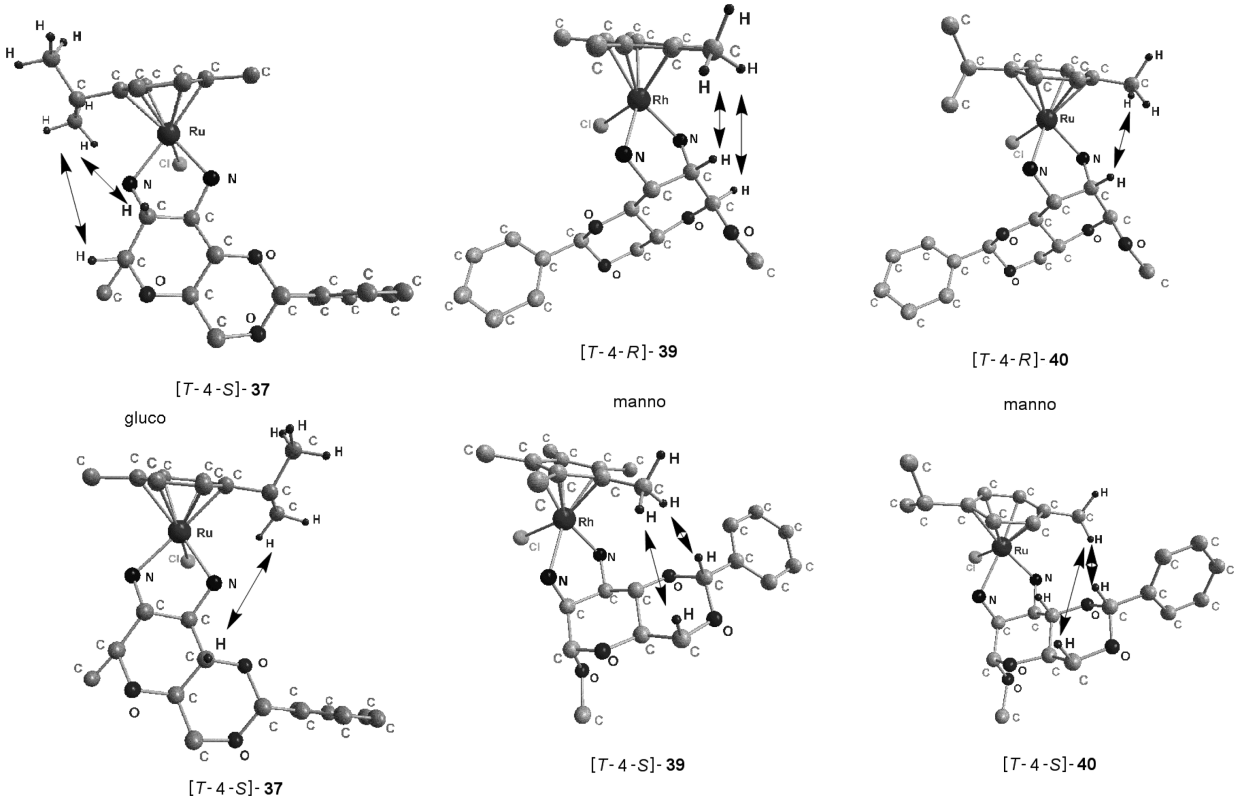

Figure 3. DFT calculated molecular structures of [*T*-4-*S*]-**37**, [*T*-4-*R*]-**39**, [*T*-4-*S*]-**39**, [*T*-4-*R*]-**40**, and [*T*-4-*S*]-**40** with observed NOE contacts (see arrows) (Orca 2.8, functionals BP86 and DefBas-4, basis sets TZV for H, TZV(2d2p) for main group elements, and TZV(2d2fg,3p2df) for transition elements).[17] The complexes are positively charged. Hydrogen atoms, except for those which demonstrate NOE effects, and counterions are omitted for clarity.

protons are located in the shielding area of the benzene ring, which shifts the signals of the protons of the Cp* ligand to high field (see **46**).[22] In contrast, **42** (ligand **29**) should have the absolute configuration *T*-4-*R*, which was confirmed for the related complex **45** in solution by NOE contacts between the methoxy group of the sugar ligand and the protons of the substituents of the arene ligand. As expected for this configuration, the proton NMR signals of the phenyl ring of

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Table 5. Specific Polarization Angles ($[\alpha]_{25\,°C}^{589\,nm}$ (deg)) of the Cationic Complexes 34−38 and 42−48

compound [absolute configuration]	transition metal	arene ligand[a]	polarization angle (deg) (solvent)
methyl 4,6-*O*-benzylidene-α-D-glucopyranoside			+110.4 (tcm)[d,23a]
benzyl 2,3-diamino-4,6-*O*-benzylidene-2,3-dideoxy-α-D-glucopyranoside			+95 (MeOH)[16a,b]
34 [*T*-4-*S*][b]	Ir(III)	Cp*	−51 (dcm)[e]
35 [*T*-4-*S*][b]	Rh(III)	Cp*	−37 (dcm)[e]
36 [*T*-4-*S*][b]	Ru(II)	C_6H_6	−43 (dcm)[e]
37 [*T*-4-*S*][b]	Ru(II)	Cy	−48 (dcm)[e]
38 [*T*-4-*S*][b]	Ru(II)	Tet	−74 (dcm)[e]
methyl 4,6-*O*-benzylidene-α-D-gulopyranoside			+79.8 (tcm)[d,23b]
29			+85 (dcm)[e]
42 [*T*-4-*R*][b]	Rh(III)	Cp*	+135 (acetone)
43 [*T*-4-*R*][c]	Rh(III)	Cp*	+75 (acetone)
43 [*T*-4-*R*][c]	Rh(III)	Cp*	+135 (dcm)[e]
44 [*T*-4-*R*][b]	Ru(II)	Cy	+106 (dcm)[e]
44 [*T*-4-*R*][b]	Ru(II)	Cy	+114 (acetone)
45 [*T*-4-*R*][c]	Ru(II)	Tet	+133 (acetone)
methyl 4,6-*O*-benzylidene-α-D-talopyranoside			+80.4 (tcm)[d,23c]
32			+82 (dcm)[e]
46 [*T*-4-*S*][b]	Rh(III)	Cp*	+56 (dcm)[e]
47 [*T*-4-*S*][b]	Ru(II)	Cy	+56 (dcm)[e]
48 [*T*-4-*S*][b]	Ru(II)	Tet	+52 (dcm)[e]

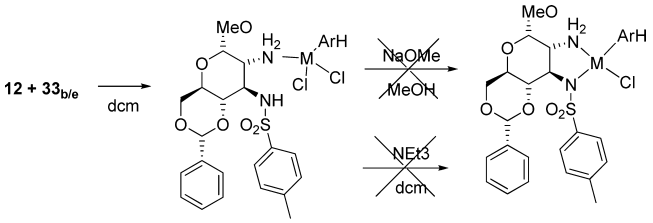
[a]Cp* = pentamethyl-η^5-cyclopentadienyl, C_6H_6 = η^6-benzene, Cy = η^6-*p*-cymene, Tet = η^6-tetralin. [b]Counterion tetrafluoridoborate. [c]Counterion hexafluoridophosphate. [d]tcm = trichloromethane. [e]dcm = dichloromethane.

the sugar ligand are poorly separated due to the distal position of the phenyl ring relative to the arene ligand. Unfortunately, the determination of the polarization angles is hampered by the insufficient solubility of complexes **42**−**45** with the ligand **29** (gulo). Therefore, data from those analytes suffer from large errors, which may explain the high variance of the measured values from measurements in different solvents. The methyl 4,6-*O*-benzylidene-α-D-pyranosides[23] and benzyl[16a,b] or methyl 2,3-diamino-4,6-*O*-benzylidene-α-D-pyranosides of each sugar backbone show polarization angles similar to those demonstrated for the gluco-, gulo-, and talopyranosides.

Though the complexes of ligands **29** (gulo) and **32** (talo) illustrate polarization angles similar to those of their diamino pyranoside congeners, a large difference is observed between the polarization angles of α-D-glucopyranosides and those for the complexes of the corresponding diaminoglucopyranoside **10**. However, the *T*-4-*S* configuration seems to have a tendency for a negative shift in the polarization angle while the polarization angles of **42**−**45** (*T*-4-*R*) are somewhat larger than those of the gulopyranosides. Hence, the configuration *T*-4-*R* has a tendency for a positive shift in the polarization angle, which is opposite to the effect of *T*-4-*S*, as expected.

Final Synthetic Strategy Regarding the Grade of Inequivalence of the Binding Groups of the Ligands. The synthesized ligands and complexes were designated as precursors in Noyori-type transfer hydrogenation. However, the usual concept, to prevent two identical active sides in the catalyst, is to discriminate the (two) amino groups. This is usually achieved by sulfonylation of one amino group in the final step of the ligand synthesis.[24] In the case of chemically unequal amino groups the *p*-toluenesulfonylation reaction could not be conclusively executed with regard to the formation of regioisomers. Therefore, methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-*N*-*p*-toluenesulfonylamido-α-D-glucopyranoside (**12**) was synthesized from **9**. Two complexes were produced on the basis of ligand **12** (Scheme 5): dichlorido-η^1-(methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-*p*-tosylamido-α-D-glucopyranoside)-η^6-(1′,2′,3′,4′-tetrahydronaphthalene)-ruthenium(II) (**51**) and dichlorido-η^1-(methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-*p*-tosylamido-α-D-glucopyranoside)-pentamethyl-η^5-cyclopentadienylrhodium(III) (**52**).

Scheme 5. Synthesis of Compounds 51 and 52



51: M = Ru(II); ArH = η^6-1,2,3,4-tetraline
52: M = Rh(III); ArH = η^5-Cp*

Compounds **51** and **52** were obtained by stirring the ligand and complex precursor in dichloromethane (Scheme 5). The ligand binds to the metal by the amino group at C2. A chelating coordination might be achieved by deprotonation of the *p*-tosylamido group at C3. However, under basic conditions (sodium methanolate, triethylamine) degradation of the ligand took place. Therefore, only the η^1 complexes were obtained. The complexes were characterized by NMR spectroscopy, elemental analysis, polarization angle, and mass spectrometry.

Antitumor Activity Studies. Due to the recent results with iridium(III), rhodium(III), and ruthenium(II) half-sandwich complexes in antitumor applications,[13] the effect of the novel complexes **34**−**48** on three cancer cell lines was tested. In contrast to complexes with conventional organic ligands sugar complexes might provide less toxicity while preserving the cytostatic activity of related complexes. Metabolic interaction of the sugar ligand could increase the specificity of the complexes toward cancer cells. Thus, an antitumor agent with a higher therapeutic index might be obtained.

The cytotoxicity testing with the three adherent cell lines was carried out by an antiproliferation assay based on the staining of cells with crystal violet, following a method that was described earlier.[25a,b] The adherent cell lines originated from cervical (SISO), pancreas (DAN-G), and lung (LCLC-103H) cancers. In primary screening (see Table S4 in the Supporting Information) the *T*/*C* values of complexes **34** and **37** (ligand **10**, gluco), **40** and **41** (ligand **19**, manno), **44**−**46** (ligand **29**, gulo), and **46**−**48** (ligand **32**, talo) were examined. Of all of these complexes the Ru derivatives **40**, **41**, and **48** displayed the most promising *T*/*C* values.

Therefore, these three Ru(II) compounds were tested in a secondary screening, wherein their IC_{50} values were determined (Table 6). This demonstrated that especially η^6-tetralin ruthenium complex **41** with the mannopyranoside ligand **19** has antiproliferative activity against the cell lines SISO and LCLC-103H that is 4−10 times lower than that of cisplatin.[25d]

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Table 6. Secondary Screening of Selected Substances: IC_{50} Values

	IC_{50} (μM, am[a]) ($\pm$sd[b])		
compound	DAN-G	SISO	LCLC-103H
40 (Ru, manno)	26.9[c]	5.54(1.95)[d]	12.5(2.8)[d]
41 (Ru, manno)	28.5(13.9)[d]	2.79(0.31)[d]	4.39(3.20)[d]
48 (Ru, talo)	-[e]	32.5(32.8)[d]	20.2[c]
cisplatin[f]	0.53(0.07)[f]	0.24(0.05)[f]	1.1(0.4)[f]

[a]Arithmetic mean. [b]Standard deviation from three assays. [c]From two assays. [d]From three assays. [e]Not determined. [f]From ref 25d.

CONCLUSION AND OUTLOOK

One amino-tosylamido- and four diaminocarbohydrate ligands were synthesized and characterized. DFT calculations indicate a considerable flexibility of the dihedral angle of the diamino ligands, which makes the amino functions capable of chelating most transition metals. These ligands will be applied in further transition-metal complexes, which is beyond the scope of this publication.

With these ligands the synthesis of the half-sandwich ruthenium(II), rhodium(III), and iridium(III) diamino sugar complexes was feasible. The structures of these 17 new complexes, including their configuration at the metal center, were determined in the crystalline phase by X-ray crystallography and in liquid solution by NMR spectroscopy and polarimetry. The pseudotetrahedral complexes formed with high diastereoselectivity, illustrating a stereogenic metal atom: with the gluco- and talopyranoses **10** and **32**, respectively, a *T*-4-*S* configuration, for the gulopyranose **29** a *T*-4-*R* configuration, and for complexes with the mannopyranose ligand **19** diastereomeric mixtures are obtained. The origin of the diastereoselectivity of the complex formation will be examined by epimerization studies and further DFT calculations.

Moreover, the new half-sandwich ruthenium, rhodium, and iridium diamino sugar complexes will be applied as catalyst precursors in Noyori-type transfer hydrogenation.

The antiproliferative properties of the majority of the new complexes were examined. Compounds **40** and **41** show IC values 4−10 times larger than those of cisplatin toward different cancer cell types.

EXPERIMENTAL SECTION

General Considerations. All the manipulations of air-sensitive compounds were carried out under a nitrogen atmosphere using the standard Schlenk techniques.[26a] The solvents were dried and distilled prior to use by literature methods.[26b,c] ^{1}H and ^{13}C NMR spectra (DEPTQ/APT) were recorded on a Bruker Fourier 300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) and/or on a Bruker Avance 400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) at room temperature, and the chemical shift values refer to acetone-d_6 (δ(^{1}H), 2.05 ppm; δ(^{13}C), 29.84 ppm),[26d] dmso-d_6 (δ(^{1}H), 2.50 ppm; δ(^{13}C), 39.52 ppm),[26d] $CDCl_3$ (δ(^{1}H), 7.26 ppm; δ(^{13}C), 77.16 ppm),[26d] D_3CCN (δ(^{1}H), 1.94 ppm; δ (^{13}C), 1.32 ppm),[26d] CD_2Cl_2 (δ(^{1}H), 5.32 ppm; δ (^{13}C), 54.00 ppm),[26e] and $Cl_2DCCDCl_2$ (δ(^{1}H), 5.91 ppm).[26f] For the assignment of the proton signals various 2D-NMR methods were carried out (^{1}H−^{1}H-COSY, HSQC, HMBC, TOCSY, NOESY, ^{15}N-HSQC). Elemental analyses were carried out by the central elemental analysis section of the Department of Chemistry at the University of Hamburg. Air-sensitive compounds were analyzed on an Elementar Vario EL III instrument, and nonsensitive compounds were analyzed on a Carlo Erba EA 1108 CHNS-O instrument. EI-MS and ESI-HRMS measurements were carried out by the MS section of the Institute of Organic Chemistry of the University of Hamburg with a Finnigan MAT 311 A instrument at 70 eV (EI-MS) and a Agilent Technologies 6224 TOF LC-MS instrument (ESI-HRMS). UV/vis spectra were recorded in dichloromethane on a Varian Cary 5E UV/vis-NIR spectrometer. Polarization angles were measured with an A. Krüss Optronic GmbH P8000T polarimeter. The specific polarization angles were determined by known methods.[26g] Column chromatography was performed on silica gel 60 (70−230 mesh) from Merck and Macherey & Nagel. All chemical reagents were purchased from commercial sources and used as received (for example μ-dichloridobis[chloridopentamethyl-η^5-cyclopentadienyliridium(III)] (**33$_a$**) from Acros; 99%) unless otherwise indicated, except for 4-trifluoromethylbenzenesulfonyl chloride,[26h,i] μ-dichlorido-bis[chlorido-pentamethyl-η^5-cyclopentadienylrhodium(III)] (**33$_b$**),[19a,b] μ-dichloridobis[chlorido-η^6-benzeneruthenium(II)] (**33$_c$**),[19c] μ-dichloridobis[chlorido-η^6-*p*-cymeneruthenium(II)] (**33$_d$**),[26j] and μ-dichloridobis[chlorido-η^6-(1,2,3,4-tetrahydronaphthalene)ruthenium(II)] (**33$_e$**),[26k] which were synthesized by literature procedures. The synthesis of the organic compounds is described in the Supporting Information (section S2).

DFT Studies. Orca 2.8 and 2.9[17a] were used for DFT calculations. The functional BP86[17b] and the hybrid functional B3LYP[13c] were applied for structure optimization of the organic structures with DefBas-3 basis sets (basis sets: H, Ahlrichs-TZV; main-group elements, Ahlrichs-TZV(2d2p)).[17d,e] For structure optimization of the organometallic complexes the functional BP86[17b] with DefBas-4 basis sets (basis sets: H, Ahlrichs-TZV; main-group elements, Ahlrichs-TZV(2d2p); second-row transition elements, Ahlrichs-TZV-(2d2fg,3p2df))[17d−f] was used. Usually some constraints were used for optimization such as (commands) TightOpt, SlowConv, Grid4, NoFinalGrid, and Decontract, and when problems with negative frequencies arose, additional constraints were added as needed such as (commands) Grid6, Grid7, TightSCF, VerySlowConv, VerytightSCF, and ExtremeSCF. All minima were verified to have no negative frequencies (under −50 cm^{-1}). For optimization of crowded organometallic structures a van der Waals correction (VDW06) was used.[17g] In the case of compounds **10**, **19**, and **32** single-point energies were calculated for optimized structures with constraint dihedral angles defined by the planes N2−C2−C3 and C2−C3−N3 for examination of the progress of the potential for deviating dihedral angles (from the minimum structure). The explanation of the used commands is given in the user manual of Orca 2.9 (OrcaManual 2.9).[17h] The resulting xyz files, free energies, and single-point energies as well as the command files are deposited in the Supporting Information (S5).

X-ray Crystallographic Studies. Colorless crystals were grown from **18**, **25**, **26**, and **31** by evaporation of the solvent at normal pressure and room temperature from a mixture of trichloromethane, *n*-hexane, and petroleum. Yellow and orange-yellow crystals were obtained from **34**, **35**, **39**, **42**, and **46** by recrystallization from dichloromethane and diethyl ether at −20 °C and in the case of **42** by recrystallization from acetone and *n*-heptane (room temperature). The X-ray single-crystal structures were determined on a Bruker SMART CCD diffractometer with Mo Kα radiation (λ = 71.073 pm); programs used SAINT,[26l] SADABS,[26m] XPREP,[26n] SHELXS-97,[26o] SHELXL-97,[26p] and CrySalis^{Pro}.[26q] The diffuse contribution to the total electron density generated by partially cocrystallized solvent molecules in the data sets of **34**, **35**, and **39** was treated by the subprogram sqeeze from the program Platon.[26r] The crystallographic data tables are deposited in the Supporting Information (S1).

In Vitro Cytotoxicity Studies..[25a−c] The microtiter plate method used for testing of antiproliferative properties is based on crystal violet staining of cells and has been described in detail elsewhere.[25a,b] All of the cells were obtained from the German Collection of Microorganisms and Cell Cultures (DSMZ) (Braunschweig, FRG) and cultured at 37 °C under a humidified atmosphere of 5% CO_2/air in RPMI-1640 culture medium supplemented with 10% fetal calf serum and the antibiotics streptomycin and benzylpenicillin. Stock solutions of compounds were prepared in DMSO and diluted 1000-fold with cell culture medium (RPMI medium + 10% fetal calf serum) for testing. The cells were seeded out (500−1000 cells/well in 100 mL) 24 h before testing, and drug treatment took place for 96 h. Cell

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growth was stopped after 96 h by the addition of a 1% glutaraldehyde solution. The cells were later stained with a 0.02% crystal violet solution in water. Excess dye was washed out with water, and cell-bound dye was taken back into solution with a 70% ethanol/water mixture.

The optical density of the crystal violet was determined at λ 570 nm with an Anthos 2010 microtiter plate reader. For IC_{50} determinations, all substances were tested at three serially diluted concentrations. The corrected T/C values ($(T/C)_{corr}$) for each concentration were calculated with the equation

$$(T/C)_{corr}\ (\%) = (OD_T - OD_{C,0})/(OD_C - OD_{C,0}A) \times 100$$

where T is the optical density at λ 570 nm (OD_{570}) of the treated cells after 96 h of treatment time, OD_C is the OD_{570} value of the untreated cells after 96 h of growth without substance, and $OD_{C,0}$ is the OD_{570} value of the cells at the time of treatment (i.e., 96 h before T and C). Linear regression analysis of the log concentration versus $(T/C)_{corr}$ plots was used to estimate the concentration of substance that caused $(T/C)_{corr}$ = 50% (IC_{50}). The T/C values from the primary screening are deposited in the Supporting Information (S4).

General Procedure for the Synthesis of Monocationic Complexes by Means of Silver Tetrafluoridoborate. The complex precursor **33**$_a$ (141 mg, 0.18 mmol), **10** (99 mg, 0.35 mmol), and silver tetrafluoridoborate (69 mg, 0.35 mmol) were stirred in dichloromethane (15 mL) in the absence of light for 4 h. Then, the solution was filtered, reduced to a few milliliters (just before precipitation of the product), covered with a layer of diethyl ether, and cooled in a refrigerator (−20 °C). The yellow precipitate of **34** (229 mg, 0.31 mmol; 89% yield) was washed with diethyl ether and then dried under vacuum.

*[T-4-S]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-glucopyranoside)pentamethyl-η^5-cyclopentadienyliridium(III) Tetrafluoridoborate (**34**).* Yellow powder. [α](dichloromethane, 25 °C, 589 nm) = −51°. Anal. Found: C, 40.64; H, 5.35; N, 3.88. Calcd for $C_{52}H_{80}B_2Cl_2F_8Ir_2N_4O_9$ (X-ray: 2[$C_{24}H_{35}ClIrN_2O_4$]BF_4·$C_4H_{10}O$): C, 40.71; H, 5.26; N, 3.65; the compound contains 1/2 equiv of diethyl ether. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.52−7.47 (m, 2 H, H-2′), 7.40−7.35 (m, 3 H, H-3′, H-4′), 5.63 (s, 1 H, H-7), 5.12 (d, $^3J_{1,2}$ = 3.3 Hz, 1 H, H-1), 5.05 (m, 1 H, Ha-N-2), 4.66 (m, 1 H, Ha-N-3), 4.26 (dd, 1 H, Ha-6), 3.95−3.84 (m, 2 H, H-4, Hb-N-3), 3.81−3.69 (m, 2 H, Hb-6, Hb-N-2), 3.64 (ddd, 1 H, H-5), 3.48 (s, 3 H, OCH_3), 3.34 (m, 1 H, H-3), 2.93 (m, 1 H, H-2), 1.76 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (shifts from HSQC, CD_2Cl_2): δ 129.3 (C4′), 128.5 (C3′), 126.9 (C2′), 102.3 (C7), 99.1 (C1), 80.1 (C4), 69.0 (C6), 64.2 (C5), 60.6 (C2), 56.0 (C3), 55.8 (OCH_3), 9.3 ($C_5(CH_3)_5$) ppm.

*[T-4-S]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-glucopyranoside)pentamethyl-η^5-cyclopentadienylrhodium(III) Tetrafluoridoborate (**35**; 84% Yield).* Orange-yellow powder. [α](dichloromethane, 25 °C, 589 nm) = −37°. Anal. Found: C, 45.64; H, 6.16; N, 4.28. Calcd for $C_{52}H_{80}B_2Cl_2F_8Rh_2N_4O_9$ (X-ray: 2[$C_{24}H_{35}ClN_2O_4Rh$]BF_4·$C_4H_{10}O$): C, 46.07; H, 5.95; N, 4.13; the compound contains 1/2 equiv of diethyl ether. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.51−7.46 (m, 2 H, H-2′), 7.39−7.35 (m, 3 H, H-3′, H-4′), 5.61 (s, 1 H, H-7), 5.04 (d, $^3J_{1,2}$ = 3.0 Hz, 1 H, H-1), 4.38 (m, 1 H, Ha-N-2), 4.25−4.13 (m, 2 H, Ha-6, Ha-N-3), 3.88 (dd, 1 H, H-4), 3.74 (dd, 1 H, Hb-6), 3.61−3.47 (m, 2 H, H-5, Hb-N-3), 3.45 (s, 3 H, OCH_3), 3.28 (m, 1 H, Hb-N-2), 3.10 (m, 1 H, H-3), 2.97 (m, 1 H, H-2), 1.78 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (shifts from HSQC, CD_2Cl_2): δ 129.3 (C4′), 128.5 (C3′), 126.8 (C2′), 102.4 (C7), 99.1 (C1), 81.0 (C4), 68.9 (C6), 63.8 (C5), 58.8 (C2), 55.9 (OCH_3), 54.8 (C3), 9.1 ($C_5(CH_3)_5$) ppm.

*[T-4-S]-η^6-Benzenechlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-glucopyranoside)ruthenium(II) Tetrafluoridoborate (**36**; 88% Yield).* Yellow powder. [α](dichloromethane, 25 °C, 589 nm) = −43°. Anal. Found: C, 41.65; H, 4.83; N, 4.94. Calcd for $C_{20}H_{26}BClF_4N_2O_4Ru$: C, 41.29; H, 4.50; N, 4.82. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.48−7.43 (m, 2 H, H-2′), 7.40−7.34 (m, 3 H, H-3′, H-4′), 5.90 (m, 1 H, Ha-N-2), 5.79 (s, 6 H, C_6H_6), 5.56 (s, 1 H, H-7), 5.31 (m, 1 H, Ha-N-3), 5.00 (d, 1 H, H-1), 4.20 (dd, $^3J_{6a,5}$ = 4.8 Hz, $^2J_{6a,6b}$ = 10.2 Hz, 1 H, Ha-6), 3.76−3.64 (m, 3 H, H-4, Hb-6, Hb-N-3), 3.52 (ddd, $^3J_{5,6a}$ = 4.8 Hz, ^3J = 14.5 Hz, 1 H, H-5), 3.41 (s, 3 H, OCH_3), 3.02−2.89 (m, 2 H, H-2, Hb-N-2), 2.73 (m, 1 H, H-3) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.2 (C4′), 128.2 (C3′), 126.3 (C2′), 101.7 (C7), 98.3 (C1), 83.4 (C_6H_6), 80.3 (C4), 68.5 (C6), 63.2 (C5), 59.9 (C2), 55.4 (OCH_3), 53.6 (C3) ppm.

*[T-4-S]-Chlorido-η^6-p-cymene(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-glucopyranoside)ruthenium(II) Tetrafluoridoborate (**37**; 85% Yield).* Yellow powder. [α (dichloromethane, 25 °C, 589 nm) = −48°. Anal. Found: C, 45.55; H, 5.42; N, 4.65. Calcd for $C_{24}H_{34}BClF_4N_2O_4Ru$: C, 45.19; H, 5.37; N, 4.39. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.50−7.44 (m, 2 H, H-2′), 7.40−7.35 (m, 3 H, H-3′, H-4′), 5.73, 5.67, 5.55, 5.51 (m, 4 H, H-2″, H-3″, H-5″, H-6″), 5.59 (s, 1 H, H-7), 5.31 (m, 1 H, Ha-N-2), 5.04 (d, 1 H, H-1), 4.83 (m, 1 H, Ha-N-3), 4.22 (dd, $^3J_{6a,5}$ = 4.8 Hz, $^2J_{6a,6b}$ = 10.2 Hz, 1 H, Ha-6), 3.80−3.69 (m, 2 H, H-4, Hb-6), 3.59−3.51 (m, 2 H, H-5, Hb-N-3), 3.43 (s, 3 H, OCH_3), 3.02 (m, 1 H, Hb-N-2), 2.97−2.85 (m, 2 H, H-2, $CH(CH_3)_2$), 2.79 (m, 1 H, H-3), 2.30 (s, 3 H, CH_3), 1.31, 1.29 (m, 6 H, $CH(CH_3)_2$) ppm. ^{1}H NMR (400 MHz, dmso-d_6): δ 7.54−7.45 (m, 2 H, H-2′), 7.41−7.34 (m, 3 H, H-3′, H-4′), 6.58 (m, 1 H, Ha-N-2), 5.81 (m, 1 H, Ha-N-3), 5.65 (s, 1 H, H-7), 5.59, 5.49 (m, 4 H, H-2″, H-3″, H-5″, H-6″), 5.38 (m, 1 H, Hb-N-3), 4.85 (d, 1 H, H-1), 4.22 (dd, 1 H, Ha-6), 3.76 (m, 1 H, Hb-6), 3.61 (dd, 1 H, H-4), 3.41−3.29 (m, 4 H, OCH_3, H-5 [3.36 {s, 3 H, OCH_3}]), 2.86 (m, 1 H, $CH(CH_3)_2$), 2.77 (m, 1 H, Hb-N-2), 2.50−2.31 (m, 2 H, H-2, H-3), 2.18 (s, 3 H, CH_3), 1.22, 1.20 (m, 6 H, $CH(CH_3)_2$) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.7 (C4′), 128.7 (C3′), 126.9 (C2′), 102.4 (C7), 98.8 (C1), 83.8, 83.3, 80.9, 80.7 (C2″, C3″, C5″, C6″), 80.8 (C4), 69.0 (C6), 63.7 (C5), 60.2 (C2), 55.9 (OCH_3), 54.1 (C3), 31.3 ($CH(CH_3)_2$), 23.2, 22.5 ($CH(CH_3)_2$), 18.4 (CH_3) ppm. ^{13}C NMR (100 MHz, dmso-d_6): δ 137.3 (C1′), 129.0 (C4′), 128.1 (C3′), 126.4 (C2′), 104.5 (C4″), 100.8 (C7), 98.0 (C1), 95.8 (C1″), 81.1, 80.8, 80.1 (C2″, C3″, C5″, C6″), 80.8 (C4), 67.6 (C6), 63.0 (C5), 59.6 (C2), 55.2 (OCH_3), 52.9 (C3), 30.0 ($CH(CH_3)_2$), 22.7, 21.6 ($CH(CH_3)_2$), 17.4 (CH_3) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, dmso-d_6; NH_3, δ_N 0 ppm, calcd): δ 4.4 (N-2), −0.1 (N-3) ppm.

*[T-4-S]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-glucopyranoside)-η^6-(1″,2″,3″,4″-tetrahydronaphthalene)ruthenium(II) Tetrafluoridoborate (**38**; 82% Yield).* Yellow powder. [α](dichloromethane, 25 °C, 589 nm) = −74°. Anal. Found: C, 44.70; H, 5.15; N, 3.99. Calcd for $C_{48}H_{66}B_2Cl_2F_8N_4O_9Ru$ (NMR: 2[$C_{24}H_{32}ClN_2O_4Ru$]BF_4·H_2O): C, 44.70; H, 5.16 N, 4.34; the compound contains 1/2 equiv of water. HRMS (esi): m/z 549.1126 (100%, $[M]^+$, calcd 549.1094). ^{1}H NMR (300 MHz, CD_2Cl_2): 7.50−7.44 (m, 2 H, H-2′), 7.39−7.33 (m, 3 H, H-3′, H-4′), 5.78−5.42 (m, 6 H, H-7, H-5″, H-6″, H-7″, H-8″, Ha-N-2), 5.19 (m, 1 H, Ha-N-3), 4.99 (d, 1 H, H-1), 4.14 (dd, $^3J_{6a,5}$ = 4.8 Hz, $^2J_{6a,6b}$ = 10.3 Hz, 1 H, Ha-6), 3.75−3.65 (m, 2 H, H-4, Hb-6), 3.57−3.48 (m, 1 H, H-5), 3.42 (s, 3 H, OCH_3), 3.37 (m, 1 H, Hb-N-3), 2.98−2.42 (m, 7 H, H-2, H-3, H-1″, H-4″, Hb-N-2), 2.01−1.65 (m, 4 H, H-2″, H-3″) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.1 (C4′), 128.2 (C3′), 126.4 (C2′), 101.9 (C7), 98.5 (C1), 82.7, 82.4, 80.4, 80.3 (C5″, C6″, C7″, C8″), 79.4 (C4), 68.5 (C6), 63.2 (C5), 55.4 (OCH_3), 60.2, 53.4 (C2, C3), 26.8, 26.4 (C1″, C4″), 21.5, 21.4 (C2″, C3″) ppm.

*[T-4-R]- and [T-4-S]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-mannopyranoside)pentamethyl-η^5-cyclopentadienylrhodium(III) Tetrafluoridoborate (**39**; Ratio ca. 1:1; 87% Yield).* Orange-yellow powder. Anal. Found: C, 44.71; H, 5.60; N, 4.09. Calcd for $C_{24}H_{35}BClF_4N_2O_4Rh$: C, 44.99; H, 5.51; N, 4.37.

Data for [*T*-4-*R*] are as follows. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.55−7.29 (m, 5 H, H-2′, H-3′, H-4′), 5.50 (s, 1 H, H-7), 4.95 (d, 1 H, H-1), 4.69 (m, 1 H, Ha-N-2), 4.26 (dd, 1 H, H-4), 4.15 (dd, 1 H, Ha-6), 4.09 (m, 1 H, Ha-N-3), 3.87 (m, 1 H, H-5), 3.81 (m, 1 H, Hb-N-3), 3.69 (m, 1 H, Hb-6), 3.63 (m, 1 H, H-3), 3.39 (s, 3 H, OCH_3), 3.27 (m, 1 H, H-2), 3.22 (m, 1 H, Hb-N-2), 1.75 (m, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (100 MHz, shifts partially from HSQC, CD_2Cl_2): δ 130.1 (C4′), 129.0 (C3′), 126.9 (C2′), 102.7 (C7), 100.5 (C1), 74.2 (C4), 69.2 (C6), 63.0 (C5), 61.6 (C2), 56.0 (OCH_3), 53.7 (C3), 9.2 ($C_5(CH_3)_5$) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, CD_2Cl_2; NH_3, δ_N 0 ppm, calcd): δ 14.2 (N-2), 10.7 (N-3) ppm.

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Data for [*T*-4-*S*] are as follows. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.55−7.29 (m, 5 H, H-2′, H-3′, H-4′), 5.63 (s, 1 H, H-7), 4.86 (d, 1 H, H-1), 4.50 (m, 1 H, Ha-N-3), 4.33 (dd, 1 H, Ha-6), 3.97 (dd, 1 H, Hb-6), 3.71 (m, 1 H, Ha-N-2), 3.70 (m, 1 H, H-5), 3.55 (m, 1 H, Hb-N-2), 3.53 (m, 1 H, H-2), 3.43 (m, 1 H, Hb-N-3), 3.40 (dd, 1 H, H-4), 3.38 (s, 3 H, OCH_3), 3.28 (m, 1 H, H-3), 1.80 (m, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (100 MHz, shifts partially from HSQC, CD_2Cl_2): δ 129.8 (C4′), 128.8 (C3′), 126.7 (C2′), 102.9 (C7), 99.9 (C1), 75.5 (C4), 69.1 (C6), 63.3 (C5), 56.8 (C3), 56.2 (OCH_3), 55.2 (C2), 9.7 ($C_5(CH_3)_5$) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, CD_2Cl_2; NH_3, δ_N 0 ppm, calcd): δ 12.7 (N-2), 5.3 (N-3) ppm.

*[T-4-R]- and [T-4-S]-Chlorido-η^6-p-cymene(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-mannopyranoside)ruthenium-(II)Tetrafluoridoborate (**40**; Ratio ca. 1:3; 82% Yield).* Yellow powder. Anal. Found: C, 44.99; H, 5.38; N, 4.17. Calcd for $C_{24}H_{34}BClF_4N_2O_4Ru$: C, 45.19; H, 5.37; N, 4.39.

Data for [*T*-4-*R*] are as follows. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.52−7.32 (m, 5 H, H-2′, H-3′, H-4′), 6.04−5.41 (m, 6 H, H-2″, H-3″, H-5″, H-6″, Ha-N-2, Ha-N-3), 5.42 (s, 1 H, H-7), 4.94 (d, 1 H, H-1), 4.17 (dd, 1 H, Ha-6), 3.99 (m, 1 H, H-4), 3.73 (m, 1 H, H-5), 3.63 (m, 1 H, Hb-6), 3.60−3.48 (m, 1 H, H-3), 3.40−3.27 (m, 2 H, H-2, Hb-N-3), 3.33 (s, 3 H, OCH_3), 3.06−2.86 (m, 2 H, Hb-N-2, C*H*$(CH_3)_2$), 2.26 (s, 3 H, CH_3), 1.36−1.24 (m, 6 H, CH(C*H*$_3)_2$) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ 129.8 (C4′), 128.7 (C3′), 126.8 (C2′), 102.5 (C7), 100.3 (C1), 84.8, 83.8, 83.0, 80.1 (C2″, C3″, C5″, C6″), 74.2 (C4), 69.1 (C6), 63.3 (C5), 62.7 (C2), 55.9 (OCH_3), 53.1 (C3), 31.1 ($CH(CH_3)_2$), 23.2, 22.4 ($CH(CH_3)_2$), 18.2 (CH_3) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, CD_2Cl_2; NH_3, δ_N 0 ppm, calcd): δ 5.7 (N-2), −4.8 (N-3) ppm.

Data for [*T*-4-*S*] are as follows. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.52−7.32 (m, 5 H, H-2′, H-3′, H-4′), 6.04−5.41 (m, 5 H, H-2″, H-3″, H-5″, H-6″, Ha-N-3), 5.71 (s, 1 H, H-7), 4.82 (d, 1 H, H-1), 4.71 (m, 1 H, Ha-N-2), 4.26 (dd, 1 H, H-6a), 4.10 (dd, 1 H, H-6b), 3.83 (m, 1 H, H-5), 3.64 (dd, 1 H, H-4), 3.60−3.48 (m, 2 H, H−N-2b, H−N-3b), 3.40−3.27 (m, 1 H, H-2), 3.36 (s, 3 H, OCH_3), 3.06−2.86 (m, 2 H, H-3, C*H*$(CH_3)_2$), 2.21 (s, 3 H, CH_3), 1.36−1.24 (m, 6 H, CH(C*H*$_3)_2$) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2): δ 137.4 (C1′), 130.0 (C4′), 129.0 (C3′), 126.7 (C2′), 104.8 (C4″), 102.5 (C7), 99.3 (C1), 97.7 (C1″), 87.6, 81.8, 80.5, 80.2 (C2″, C3″, C5″, C6″), 74.4 (C4), 68.5 (C6), 63.2 (C5), 56.4 (C3), 56.0 (OCH_3), 55.0 (C2), 31.6 ($CH(CH_3)_2$), 23.9, 21.7 ($CH(CH_3)_2$), 18.9 (CH_3) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, CD_2Cl_2; NH_3, δ_N 0 ppm, calcd): δ 4.2 (N-2), −1.3 (N-3) ppm.

*[T-4-R]- and [T-4-S]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-mannopyranoside)-η^6-(1″,2″,3″,4″-tetrahydronaphthalene)ruthenium(II) Tetrafluoridoborate (**41**; Ratio ca. 1:2; 82% Yield).* Yellow powder. Anal. Found: C, 44.85; H, 5.21; N, 4.34. Calcd for $C_{48}H_{66}B_2Cl_2F_8N_4O_9Ru$ (NMR: 2[$C_{24}H_{32}ClN_2O_4Ru$]-BF_4·H_2O): C, 44.70; H, 5.16 N, 4.34; the compound contains 1/2 equiv of water.

Data for [*T*-4-*R*] are as follows. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.60−7.30 (m, 5 H, H-2′, H-3′, H-4′), 6.18 (m, 1 H, Ha-N-3), 6.01 (m, 1 H, Ha-N-2), 5.93−5.26 (m, 4 H, H-5″, H-6″, H-7″, H-8″), 5.44 (s, 1 H, H-7), 4.92 (d, 1 H, H-1), 4.29−4.08 (m, 1 H, Ha-6), 4.02 (m, 1 H, H-4), 3.87−3.60 (m, 2 H, H-5, Hb-6), 3.58−3.23 (m, 2 H, H-2, H-3), 3.29 (s, 3 H, OCH_3), 3.16−2.46 (m, 6 H, H-1″, H-4″, Hb-N-2, Hb-N-3), 1.98−1.62 (m, 4 H, H-2″, H-3″) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.2 (C4′), 128.2 (C3′), 126.3 (C2′), 102.0 (C7), 98.8 (C1), 83.5, 82.3, 80.3 (C5″, C6″, C7″, C8″), 73.8 (C4), 68.6 (C6), 62.8 (C5), 62.4, (C2), 55.2 (OCH_3), 52.4 (C3), 27.0, 26.2 (C1″, C4″), 21.5 (C2″, C3″) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, CD_2Cl_2; NH_3, δ_N 0 ppm, calcd): δ 4.0 (N-2), −6.0 (N-3) ppm.

Data for [*T*-4-*S*] are as follows. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.60−7.30 (m, 5 H, H-2′, H-3′, H-4′), 5.93−5.26 (m, 5 H, H-5″, H-6″, H-7″, H-8″, Ha-N-3), 5.78 (s, 1 H, H-7), 4.84 (d, 1 H, H-1), 4.77 (m, 1 H, Ha-N-2), 4.29−4.08 (m, 2 H, H-6), 3.87−3.60 (m, 3 H, H-4, H-5, Hb-N-3), 3.58−3.23 (m, 2 H, H-2, Hb-N-2), 3.36 (s, 3 H, OCH_3), 3.16−2.46 (m, 5 H, H-3, H-1″, H-4″), 1.98−1.62 (m, 4 H, H-2″, H-3″) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.4 (C4′), 128.4 (C3′), 126.4 (C2′), 102.0 (C7), 100.0 (C1), 84.4, 81.0, 79.8 (C5″, C6″, C7″, C8″), 74.1 (C4), 68.0 (C6), 62.7 (C5), 56.0 (C3), 55.4 (OCH_3), 54.6 (C2), 27.0, 26.3 (C1″, C4″), 21.5 (C2″, C3″) ppm. ^{15}N NMR (shifts from ^{15}N HSQC, CD_2Cl_2; NH_3, δ_N 0 ppm, calcd): δ 2.7 (N-2), −1.2 (N-3) ppm.

*[T-4-R]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-gulopyranoside)pentamethyl-η^5-cyclopentadienyl-rhodium(III) Tetrafluoridoborate (**42**; 58% Yield).* The crude product was extracted from the reaction residue with hot 1,2-dichloroethane due to its low solubility. Orange-yellow powder. [α](dichloromethane, 25 °C, 589 nm) = 135°. Anal. Found: C, 42.26; H, 5.03; N, 3.58. Calcd for $C_{26}H_{39}BCl_3F_4N_2O_4Rh$ (X-ray: [$C_{24}H_{35}ClN_2O_4Rh$]BF_4·$C_2H_4Cl_2$): C, 42.22; H, 5.31; N, 3.79; the compound contains 1 equiv of 1,2-dichloroethane. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.45−7.31 (m, 5 H, H-2′, H-3′, H-4′), 5.56 (s, 1 H, H-7), 4.95 (d, 1 H, H-1), 4.30−4.17 (m, 3 H, H-4, H-6), 4.02 (m, 1 H, H-5), 3.60−3.38 (m, 5 H, H-2, H-3, OCH_3 {3.55 [s, 3 H, OCH_3], 3.43 [m, 1 H, H-2]}), 1.75 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{1}H NMR (300 MHz, acetone-d_6): δ 7.45−7.30 (m, 5 H, H-2′, H-3′, H-4′), 5.63 (s, 1 H, H-7), 5.02 (d, 1 H, H-1), 4.90−4.52 (m, 3 H, H−N), 4.30 (dd, 1 H, H-4), 4.20 (m, 2 H, H-6), 4.10 (m, 1 H, H-5), 3.65−3.48 (m, 5 H, H-3, OCH_3, H−N {3.61 [s, 3 H, OCH_3]}), 3.43 (m, 1 H, H-2), 1.81 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (shifts from HSQC, acetone-d_6): δ 128.8 (C3′), 127.0 (C2′), 101.6 (C7), 99.2 (C1), 75.7 (C4), 71.0 (C3), 69.6 (C6), 55.6 (OCH_3), 50.6 (C2), 9.2 ($C_5(CH_3)_5$) ppm. UV/vis (dichloromethane λ_{max} (ε [M^{-1} cm^{-1}]): 369 (1423) nm.

*[T-4-R]-Chlorido-η^6-p-cymene(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-gulopyranoside)ruthenium(II) Tetrafluoridoborate (**44**; 81% Yield).* Yellow powder. [α](dichloromethane, 25 °C, 589 nm) = 106°. [α](acetone, 25 °C, 589 nm) = 114°. Anal. Found: C, 45.25; H, 5.48; N, 4.33. Calcd for $C_{24}H_{34}BClF_4N_2O_4Ru$: C, 45.19; H, 5.37; N, 4.39. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.45−7.36 (m, 2 H, H-2′), 7.33−7.23 (m, 3 H, H-3′, H-4′), 5.72−5.19 (m, 6 H, H-7, H-2″, H-3″, H-5″, H-6″, Ha-N-2), 4.98 (d, 1 H, H-1), 4.93 (m, 1 H, H-aN-3), 4.32−3.89 (m, 5 H, H-4, H-5, H-6, Hb-N-3), 3.52 (s, 3 H, OCH_3), 3.49 (m, 1 H, Hb-N-2), 3.20 (m, 1 H, H-2), 3.09 (m, 1 H, H-3), 2.78 (m, 1 H, C*H*$(CH_3)_2$), 2.15 (s, 3 H, CH_3), 1.20 (dd, 6 H, CH(C*H*$_3)_2$) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.3 (C4′), 128.4 (C3′), 126.3 (C2′), 101.2 (C7), 98.1 (C1), 85.5, 83.0, 80.1. 79.9 (C2″, C3″, C5″, C6″), 73.9 (C4), 69.2 (C6), 58.2 (C5), 55.4 (OCH_3), 54.6 (C3), 49.8 (C2), 30.8 (*C*H$(CH_3)_2$), 22.8, 22.1 ($CH(CH_3)_2$), 17.9 (CH_3) ppm.

*[T-4-S]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-talopyranoside)pentamethyl-η^5-cyclopentadienyl-rhodium(III) Tetrafluoridoborate (**46**; 80% Yield).* Orange-yellow powder. [α](dichloromethane, 25 °C, 589 nm) = 56°. Anal. Found: C, 44.76; H, 5.65; N, 4.68. Calcd for $C_{24}H_{35}BClF_4N_2O_4Rh$: C, 44.99; H, 5.51; N, 4.37. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.68−7.60 (m, 2 H, H-2′), 7.48−7.40 (m, 3 H, H-3′, H-4′), 5.68 (s, 1 H, H-7), 4.89 (d, 1 H, H-1), 4.57−4.48 (m, 2 H, H-4, Ha-N-3), 4.23 (dd, 1 H, Ha-6), 4.13 (dd, 1 H, Hb-6), 3.80 (m, 1 H, Ha-N-2), 3.63 (m, 1 H, H-5), 3.62−3.50 (m, 2 H, H-2, Hb-N-3), 3.44−3.36 (m, 1 H, H-3), 3.35 (s, 3 H, OCH_3), 3.24 (m, 1 H, Hb-N-2), 1.37 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 130.0 (C4′), 128.7 (C3′), 127.8 (C2′), 103.3 (C7), 100.6 (C1), 73.4 (C4), 69.4 (C6), 62.4 (C5), 55.2 (OCH_3), 53.8 (C2), 49.2 (C3), 8.5 ($C_5(CH_3)_5$) ppm. UV/vis (dichloromethane λ_{max} (ε [M^{-1} cm^{-1}]): 376 (2587) nm.

*[T-4-S]-Chlorido-η^6-p-cymene(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-talopyranoside)ruthenium(II) Tetrafluoridoborate (**47**; 85% Yield).* Yellow powder. [α](dichloromethane, 25 °C, 589 nm) = 56°. Anal. Found: C, 45.42; H, 5.50; N, 4.24. Calcd for $C_{24}H_{34}BClF_4N_2O_4Ru$: C, 45.19; H, 5.37; N, 4.39. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.84−7.77 (m, 2 H, H-2′), 7.56−7.41 (m, 3 H, H-3′, H-4′), 5.72 (s, 1 H, H-7), 5.66 (m, 1 H, Ha-N-2), 5.49, 5.05, 4.69, 4.30 (m, 4 H, H-2″, H-3″, H-5″, H-6″), 4.92 (d, 1 H, H-1), 4.59 (m, 1 H, Ha-N-3), 4.51 (dd, 1 H, H-4), 4.26 (dd, 1 H, Ha-6), 4.14 (dd, 1 H, Hb-6), 3.71 (m, 1 H, Hb-N-3), 3.60 (m, 1 H, H-5), 3.40 (m, 1 H, Hb-N-2), 3.35 (s, 3 H, H-7), 3.21 (m, 1 H, H-2), 2.97 (m, 1 H, H-3), 2.69 (m, 1 H, C*H*$(CH_3)_2$), 1.91 (s, 3 H, CH_3), 1.19 (m, 6 H, CH(C*H*$_3)_2$) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 130.4 (C4′), 129.2 (C3′), 127.4 (C2′), 102.2 (C7), 100.0 (C1), 85.0, 82.8, 81.4, 80.3 (C2″, C3″, C5″,

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C6″), 72.9 (C4), 69.6 (C6), 62.6 (C5), 55.7 (OCH_3), 53.7 (C3), 50.2 (C2), 31.1 ($CH(CH_3)_2$), 22.9, 22.7 ($CH(CH_3)_2$), 18.0 (CH_3) ppm.

*[T-4-5]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-talopyranoside)-η⁶-(1″,2″,3″,4″-tetrahydronaphthalene)-ruthenium(II) Tetrafluoridoborate (**48**; 79% Yield).* Yellow powder. [α](dichloromethane, 25 °C, 589 nm) = −52°. Anal. Found: C, 44.82; H, 5.20; N, 4.36. Calcd for $C_{48}H_{66}B_2Cl_2F_8N_4O_9Ru$ (NMR: 2-$[C_{24}H_{32}ClN_2O_4Ru]BF_4{\cdot}H_2O$): C, 44.70; H, 5.16 N, 4.34; the compound contains 1/2 equiv of water. HRMS (ESI): *m/z* 549.1105 (100%, $[M]^+$, calcd 549.1094). ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.81−7.74 (m, 2 H, H-2′), 7.55−7.41 (m, 3 H, H-3′, H-4′), 5.91 (m, 1 H, Ha-N-2), 5.72 (s, 1 H, H-7), 5.16, 5.08, 5.00, 3.94 (m, 4 H, H-5″, H-6″, H-7″, H-8″), 4.86 (d, 1 H, H-1), 4.80 (m, 1 H, Ha-N-3), 4.51 (dd, 1 H, H-4), 4.26 (dd, 1 H, Ha-6), 4.13 (dd, 1 H, Hb-6), 3.59 (m, 1 H, H-5), 3.36 (s, 3 H, OCH_3), 3.32−2.98 (m, 4 H, H-2, H-3, Hb-N-2, Hb-N-3), 2.92−2.24, 1.97−1.61 (m, 8 H, H-1″, H-2″, H-3″, H-4″) ppm. ^{1}H NMR (300 MHz, acetone-d_6): δ 7.90−7.80 (m, 2 H, H-2′), 7.56−7.43 (m, 3 H, H-3′, H-4′), 6.34 (m, 1 H, Ha-N-3), 5.71 (s, 1 H, H-7), 5.28−4.39 (m, 6 H, H-4, H-5″, H-6″, H-7″, H-8″, Ha-N-2), 5.00 (d, 1 H, H-1), 4.22 (m, 2 H, H-6), 4.08 (m, 1 H, Hb-N-3), 3.70 (m, 1 H, H-5), 3.42−3.31 (m, 1 H, H-3), 3.35 (s, 3 H, OCH_3), 3.04−2.68, 2.51−2.31 (m, 6 H, H-2, H-1″, H-4″, Hb-N-2), 1.88−1.56 (m, 4 H, H-2″, H-3″) ppm. ^{13}C NMR (75 MHz, acetone-d_6): δ 130.3 (C4′), 129.3 (C3′), 127.9 (C2′), 102.6 (C7), 100.5 (C1), 84.4, 82.2, 81.7, 80.8 (C5″, C6″, C7″, C8″), 73.7 (C4), 69.8 (C6), 63.0 (C5), 55.3 (OCH_3), 54.1 (C2), 50.7 (C3), 26.6 (C1″, C4″), 22.0, 21. Nine (C2″, C3″) ppm.

General Procedure for the Synthesis of Monocationic Complexes by Means of Ammonium Hexafluoridophosphate. Complex precursor **33$_b$** (47 mg, 0.076 mmol), ligand **28** (43 mg, 0.15 mmol), and ammonium hexafluoridophosphate (25 mg, 0.15 mmol) were heated with stirring in methanol (15 mL) to reflux until a clear solution was obtained (1 h). The solution was reduced to a few milliliters (just after the start of precipitation) and cooled in a refrigerator (−20 °C). The yellow precipitate of **43** (58 mg, 0.083 mmol; 54% yield) was washed with a few milliliters of cold methanol and with diethyl ether and then dried under vacuum.

*[T-4-R]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-gulopyranoside)pentamethyl-η⁵-cyclopentadienyl-rhodium(III) Hexafluoridophosphate (**43**).* Orange-yellow powder. [α](dichloromethane, 25 °C, 589 nm) = 135°. [α](acetone, 25 °C, 589 nm) = 75°. Anal. Found: C, 40.46; H, 5.06; N, 3.80. Calcd for $C_{24}H_{37}ClF_6N_2O_5PRh$ (NMR: $[C_{24}H_{35}ClN_2O_4Rh]PF_6{\cdot}H_2O$): C, 40.21; H, 5.20; N, 3.91; the compound contains 1 equiv of water. HRMS (ESI): *m/z* 553.1352 (100%, $[M]^+$, calcd 553.1340). ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.45−7.31 (m, 5 H, H-2′, H-3′, H-4′), 5.54 (s, 1 H, H-7), 4.93 (d, 1 H, H-1), 4.30−4.07 (m, 4 H, H-4, Ha-6, Hb-6, H−N), 3.95 (m, 1 H, H-5), 3.64−3.50 (m, 5 H, H-3, H-7, H−N {3.51 [s, 3 H, OCH_3]}), 3.47−3.38 (m, 2 H, H-2, H−N), 3.18 (m, 1 H, H−N), 1.71 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{1}H NMR (300 MHz, $NCCD_3$): δ 7.45−7.31 (m, 5 H, H-2′, H-3′, H-4′), 5.63 (s, 1 H, H-7), 4.99 (d, 1 H, H-1), 4.72 (m, 2 H, H−N-3), 4.60 (m, 1 H, Ha-N-2), 4.34−4.15 (m, 4-H, H-3, H-4, H-6), 4.11 (m, 1 H, H-5), 3.63−3.51 (m, 1 H, Hb-N-2), 3.56 (s, 3 H, OCH_3), 3.42 (m, 1 H, H-2), 1.80 (s, 15 H, $C_5(CH_3)_5$) ppm. ^{13}C NMR (75 MHz, $NCCD_3$): δ 129.4 (C4′), 128.6 (C3′), 126.7 (C2′), 101.2 (C7), 98.9 (C1), 75.5 (C4), 69.3 (C6), 58.9 (C5), 55.6, 55.3, 50.1 (C2, C3, OCH_3), 9.0 ($C_5(CH_3)_5$) ppm.

*[T-4-R]-Chlorido(methyl 2,3-diamino-4,6-O-benzylidene-2,3-dideoxy-α-D-gulopyranoside)-η⁶-(1″,2″,3″,4″-tetrahydro-naphthalene)ruthenium(II) Hexafluoridophosphate (**45**; 94% Yield).* Yellow powder. [α](acetone, 25 °C, 589 nm) = 133°. [α](dimethyl sulfoxide, 25 °C, 589 nm) = 115°. Anal. Found: C, 41.64; H, 4.69; N, 3.94. Calcd for $C_{24}H_{32}ClF_6N_2O_4PRu$: C, 41.54; H, 4.65; N, 4.04. ^{1}H NMR (300 MHz, $NCCD_3$): δ 7.43−7.30 (m, 5 H, H-2′, H-3′, H-4′), 6.18 (m, 1 H, Ha-N-2), 5.87 (m, 1 H, Ha-N-3), 5.81−5.45 (m, 5 H, H-7, H-5″, H-6″, H-7″, H-8″), 4.91 (d, 1 H, H-1), 4.67 (m, 1 H, Hb-N-3), 4.30 (dd, 1 H, H-4), 4.21 (m, 2 H, H-6), 4.10−3.99 (m, 2 H, H-5, Hb-N-2 {4.03 [m, 1 H, H-5]}), 3.55 (s, 3 H, OCH_3), 3.31 (m, 1 H, H-2), 3.15 (m, 1 H, H-3), 2.98−2.77, 2.68−2.50 (m, 4 H, H-1″, H-4″), 1.94−1.66 (m, 4 H, H-2″, H-3″) ppm. ^{1}H NMR (300 MHz, dmso-d_6): δ 7.36 (m, 5 H, H-2′, H-3′, H-4′), 6.35 (m, 1 H, Ha-N-2), 5.75−5.24 (m, 6 H, H-7, H-5″, H-6″, H-7″, H-8″, Ha-N-3), 5.15 (m, 1 H, Hb-N-3), 4.72 (d, 1 H, H-1), 4.28−4.04 (m, 4 H, H-4, H-6, Hb-N-2), 3.92 (m, 1 H, H-5), 3.34 (s, 3 H, OCH_3), 3.30−2.68 (m, 4 H, H-2, H-3, H-1″, H-4″), 2.59−2.37 (m, 2 H, H-1″, H-4″), 1.90−1.55 (m, 4 H, H-2″, H-3″) ppm. ^{13}C NMR (75 MHz, dmso-d_6): δ 129.3 (C4′), 128.5 (C3′), 126.4 (C2′), 100.2 (C7), 97.8 (C1), 83.5, 82.0, 80.7, 80.5 (C5″, C6″, C7″, C8″), 73.7 (C4), 68.8 (C6), 58.4 (C5), 55.2 (OCH_3), 54.6 (C2), 50.1 (C3), 26.2, 26.1 (C1″, C4″), 21.6, 21.5 (C2″, C3″) ppm.

General Procedure for the Synthesis of Uncharged η¹-Amino Complexes. The complex precursor **33$_e$** (35.8 mg, 0.059 mmol) and the ligand **12** (51.2 mg, 0.12 mmol) were stirred in dichloromethane (10 mL) for 2 h. The solution was filtered, reduced to a few milliliters (just before precipitation of the product), covered with a layer of *n*-hexane, and cooled in a refrigerator (−20 °C). The orange precipitate of **51** (79 mg, 0.11 mmol; 91%) was washed with diethyl ether and then dried under vacuum.

*Dichlorido-η¹-(methyl 2-amino-4,6-O-benzylidene-2,3-dideoxy-3-tosylamido-α-D-glucopyranoside)-η⁶-(1″,2″,3″,4″-tetrahydro-naphthalene)ruthenium(II) (**51**).* Orange powder. [α]-(dichloromethane, 25 °C, 589 nm) = −13°. Anal. Found: C, 49.87; H, 5.23; N, 3.71; S; 3.83. Calcd for $C_{62}H_{78}Cl_4N_4O_{13}Ru_2S_2$ {2[$C_{31}H_{38}Cl_2N_2O_6RuS$]·$H_2O$}: C, 49.80; H, 5.26; N, 3.75; S, 4.29; the compound contains 1/2 equiv of water. HRMS (ESI): *m/z* 703.1167 (2%, $[M - Cl]^+$, calcd 703.1183), 667.1409 (18%, $[M - Cl - HCl]^+$, calcd 667.1416). ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.68, 6.91 (AA′BB′, 4 H, H-2′, H-3′), 7.42−7.23, 7.12 (m, 6 H, H-2″, H-3″, H-4″), 6.54 (s, 1 H, H−N-3), 5.74−5.25 (m, 6 H, H-7, H-5‴, H-6‴, H-7‴, H-8‴, Ha-N-2), 5.02 (d, 1 H, H-1), 4.08 (dd, 1 H, H-6a), 3.70−3.43 (m, 4 H, H-3, H-5, Hb-6, Hb-N-2), 3.36 (s, 3 H, OCH_3), 3.36−2.96, 2.48 (m, 6 H, H-2, H-4, H-1‴, H-4‴), 2.23 (s, 3 H, $(CO)CH_3$), 1.97, 1.75 (m, 4 H, H-2‴, H-3‴) ppm. ^{1}H NMR (300 MHz, 1,1,2,2-tetrachlorethane-d_2): δ 7.66, 6.90 (AA′BB′, 4 H, H-2′, H-3′), 7.40−7.23, 7.07 (m, 5 H, H-2″, H-3″, H-4″), 6.34 (s, 1 H, H−N-3), 5.63, 5.40 (m, 4 H, H-5‴, H-6‴, H-7‴, H-8‴), 5.38−5.30 (m, 1 H, H-3) 5.26 (s, 1 H, H-7), 5.00 (d, 1 H, H-1), 4.10 (dd, 1 H, Ha-6), 3.77−3.50 (m, 4 H, H-5, Hb-6, H−N-2), 3.36 (s, 3 H, OCH_3), 3.41−2.93 (m, 2 H, H-2, H-4), 3.13−2.94, 2.51−2.28 (m, 4 H, H-1‴, H-4‴), 2.24 (s, 3 H, $(CO)CH_3$), 2.06−1.91, 1.79−1.63 (m, 4 H, H-2‴, H-3‴) ppm. ^{13}C NMR (shifts from HSQC, 1,1,2,2-tetrachlorethane-d_2): δ 129.3, 127.3 (C2′, C3′), 127.9 (C3″), 126.5 (C2″), 101.8 (C7), 98.8 (C1), 83.4, 82.7, 79.4, 74.2 (C5‴, C6‴, C7‴, C8‴), 68.5 (C6), 63.6 (C5), 55.1 (OCH_3), 26.5 (C1‴, C4‴), 21.7 ($(CO)CH_3$), 21.3 (C2‴, C3‴) ppm.

*Dichlorido-η¹-(methyl 2-amino-4,6-O-benzylidene-2,3-dideoxy-3-tosylamido-α-D-glucopyranoside)pentamethyl-η⁵-cyclopenta-dienylrhodium(III) (**52**; 93% Yield).* Orange powder. [α]-(dichloromethane, 25 °C, 589 nm) = −11°. Anal. Found: C, 50.14; H, 5.59; N, 3.88; S; 3.82. Calcd for $C_{31}H_{41}Cl_2N_2O_6RhS$: C, 50.08; H, 5.56; N, 3.77; S, 4.31. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.63, 6.89 (AA′BB′, 4 H, H-9, H-10), 7.39−7.25, 7.08 (m, 5 H, H-15, H-16, H-17), 6.18 (m, 1 H, H−N-3), 5.30 (s, 1 H, H-13), 5.13 (d, 1 H, H-1), 4.08 (dd, 1 H, Ha-6), 3.69−3.56 (m, 2 H, H-5, Hb-6), 3.53−3.41 (m, 4 H, H-3, H-4, H−N-2), 3.37 (s, 3 H, OCH_3), 3.21 (dd, 1 H, H-2), 2.23 (s, 3 H, $(CO)CH_3$), 1.71 (s, 15 H, H-18) ppm. ^{13}C NMR (75 MHz, CD_2Cl_2): δ 129.2, 127.4 (C2′, C3′), 128.7 (C4″), 127.8 (C3″), 126.3 (C2″), 101.7 (C7), 98.5 (C1), 78.4 (C4), 68.5 (C6), 63.8 (C5), 56.5 (C2), 55.6 (C3), 54.6 (OCH_3), 21.3 ($(CO)CH_3$), 9.0 ($C_5(CH_3)_5$) ppm.

■ ASSOCIATED CONTENT

Supporting Information

Text, tables, figures, and CIF and xyz files giving crystallographic data for **18**, **25**, **26**, **32**, **34**, **35**, **39**, **42** and **46**, molecular structures of **18** and **31**, crystal packing of **35**, **39**, **42**, and **46**, synthesis of the organic compounds, additional NMR spectroscopic data of the complexes, *T*/*C* values from primary screening of the complexes, molecular structures of **10**, **19**, **28**, **29** and **32**, and data derived from DFT calculations. This

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material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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