Carbohydrate Complexes of Platinum-Group Metals

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Received March 9, 2000

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I. Introduction

Biosynthesis of carbohydrates is a basic process of life and quantitatively the most important one. Monosaccharides are fundamental biomolecules in that they are the building blocks of polysaccharides. They are the constitutional parts of complex lipids (glycolipids) and proteins (glycoproteins). They are also building blocks of nucleotides and, hence, of nucleic acids and of the chemical ADP/ATP energy-storage system. Thus, carbohydrates exert a wide range of functions in living organisms, and due to the wide distribution of metals and their complex functions for all forms of life, metal−carbohydrate interactions are a key for understanding bioinorganic chemistry, and the study of complexation of carbohydrates to metals is one of the main objectives of carbohydrate coordination chemistry.

From a coordination chemistry perspective, carbohydrates are abundantly functionalized with weak donor sites. Water is an effective competitive donor for nonfunctionalized carbohydrates. Thus, the coordination behavior in water and in noncompetitive organic solvents may be totally different. On the other hand, carbohydrates properly functionalized with Lewis-basic substituents ("anchoring" groups) may form highly stable complexes with practically all metals. Many carbohydrates easily undergo redox processes. Facile oxidation can abrogate metal binding, particularly so with high oxidation state transition metals.

Due to the manifold donor sites of nearly equivalent oxygen atoms and due to equilibria between several isomers, saccharides are, in general, very versatile, "chameleon"-like ligands. Simple aldoses, for example, may exist in aqueous solution as acyclic aldehydes and the corresponding hydrates, as α- and β-pranoses, and as α- and β-furanoses (Scheme 1). The aldehyde, pyranoses, and furanoses are constitutional isomers, whereas α and β anomers represent stereoisomers. Constitutional and stereoisomeric ratios vary with structure. For example, the pentoses D-arabinose, D-lyxose, D-ribose, and D-xylose were found (D_2O; 28 °C) in relative abundance of 0.8−7.4%/

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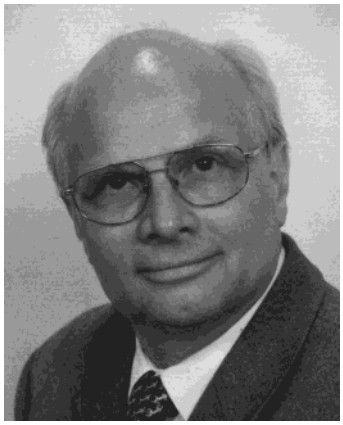
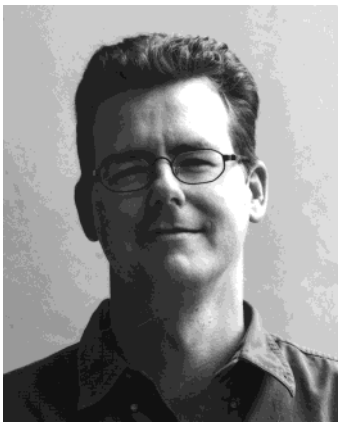
10.1021/cr9903050 CCC: $35.00
Published on Web 10/21/2000



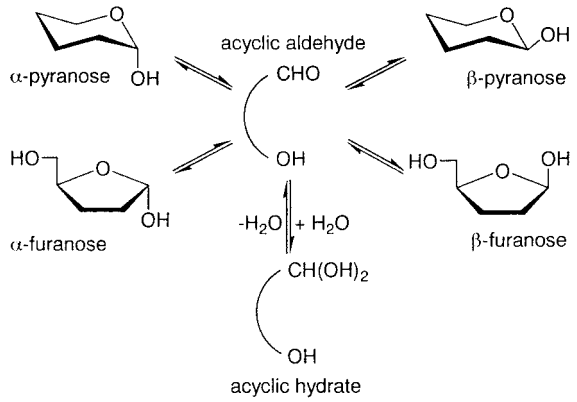
Dirk Steinborn, born in Berlin, Germany (1946), studied Chemistry at the Humboldt-Universität zu Berlin and obtained his Ph.D. degree in Chemistry (Dr. rer. nat.) in 1974 from the Technische Hochschule Leuna-Merseburg with an organometallic thesis under the direction of Rudolf Taube. From 1981 to 1983 he worked in chemical industry. In 1984, he received his Dr. sc. nat. degree with work on nitrogen-functionalized alkylmetal compounds and the electronic influence of organo ligands. This was followed in 1985 by a Facultas docendi, after which he was appointed (in 1987) to a Hochschuldozent of the Technische Hochschule Leuna-Merseburg. In the same year he was awarded the Friedrich-Wöhler-Prize. In 1992 he was appointed Full Professor for Inorganic Chemistry at the Martin-Luther-Universität Halle-Wittenberg. His research interests are in the area of organometallic chemistry, complex catalysis, and bioinorganic chemistry.



Henrik Junicke, born in Luckenwalde, Germany (1970), received his chemical education at the Technische Hochschule Leuna-Merseburg and at the Martin-Luther-Universität Halle-Wittenberg. He obtained his Ph.D. degree in Chemistry (Dr. rer. nat.) in 1999 with a thesis on the synthesis and characterization of the first platinum(IV) carbohydrate complexes under the direction of Dirk Steinborn. He is currently a Postdoctoral Fellow of the Akademie der Naturforscher Leopoldina in the research group of Jacqueline K. Barton at the California Institute of Technology studying novel cyclometalated rhodium complexes for selective recognition of base-pair mismatches in DNA fragments.

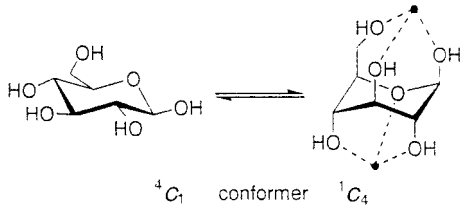
0.6−13.2% α-/β-furanose, 20.2−70.8%/26.9−62.0% α-/β-pyranose, 0.06−0.10% hydrate, and 0.01−0.04% aldehyde.[1] Furthermore, different conformers of furanose and pyranose rings may render totally different modes for metal binding. An illustrative example is β-D-glucopyranose, the main isomer of D-glucose in aqueous solution (62% at 31 °C). In its most stable form ($^4C_1$ conformer), all hydroxyl groups are equatorial and there is no way for *facial* coordination to a metal. By flipping into the less stable $^1C_4$ conformer, two syn−axial hydroxyl groups and the exocyclic hydroxyl group or the pyranose oxygen atom, respectively, provide opportunities for *facial*

Scheme 1



(adapted from [1])

Scheme 2

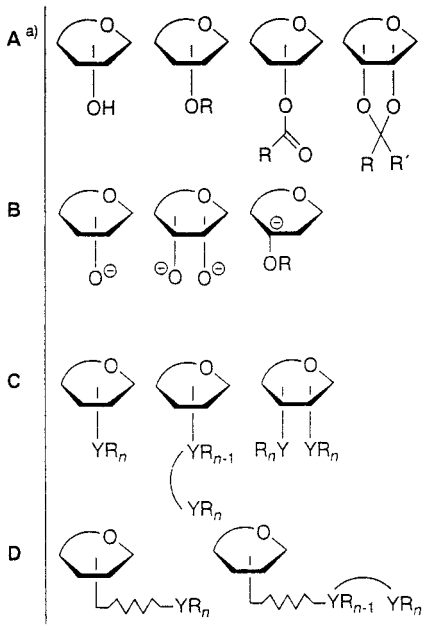


coordination (Scheme 2). Further examples of diversity in coordination modes due to ring flipping are cyclohexane-based polyamino−polyalcohol ligands. Thus, one chair form of 1,3,5-triamino-1,3,5-trideoxy-*cis*-inositol (taci) is *facial*-N_3- and *facial*-N_2O-binding and the other one *facial*-O_3- and *facial*-O_2N-binding.[2]

The relative ratio of isomers of saccharides may be strongly affected by complex formation, and less stable forms may be "frozen" in complexes. Furthermore, formation of chelate complexes offers a means of making inherently flexible saccharides more rigid. Such is the case with furanoses. Thus, for further development of carbohydrate coordination chemistry, it is necessary to determine the coordination modes of carbohydrates. This is a challenge, particularly for transition-metal complexes, because single crystals suitable for X-ray diffraction measurements are difficult to obtain and conventional NMR spectroscopic measurements are not able to discern the coordination mode in many cases. The full repertoire of modern spectroscopic methods such as multinuclear and two-dimensional NMR spectroscopy, relaxation measurements and NOE experiments, FT-IR and Raman spectroscopies, and single-crystal X-ray measurements are necessary to characterize coordination modes of carbohydrates. This is the case both in solution and in the solid state.

For platinum-group metals, "simple" nonfunctionalized carbohydrates are unique weak ligands. The same holds for alkylated, acylated, and acetal-protected carbohydrates (Chart 1, **A**). Here we assume these carbohydrates to be nonfunctionalized. There are, however, several strategies to increase donor capability. Stronger binding anionic carbohydrate ligands are obtained either by deprotonation of one or two hydroxyl groups or by formation of carbohydrate carbanions (Chart 1, **B**). Analogous "abiotic" ligands are alcoholato/diolato ligands and

Chart 1



a) Schematically, further substituents are omitted.

oxygen-functionalized alkyl/cycloalkyl ligands, respectively. Functionalization of carbohydrates with ligating ("anchoring") groups leads to stronger binding ligands. Examples are given in Chart 1 (**C**). Due to the dominant coordination ability of the anchoring groups, in many cases such complexes behave similarly to those with corresponding carbohydrate-free (abiotic) ligands. Furthermore, ligating groups can be bound via a spacer to carbohydrates (Chart 1, **D**).

Carbohydrates are naturally occurring enantiomeric pure compounds ("chiral pool"). Thus, apart from the biological area, carbohydrate−metal interactions are of interest in metal-assisted or metal-catalyzed enantioselective synthesis. Because platinum-group metals play an important role in homogeneous catalysis, carbohydrate complexes of these metals are of special interest.

Starting in 1966,[3] several reviews describing sugar−metal complexes were published, among them the "classics" from Angyal.[4] Recent reviews by Verchère and co-workers[5] and by Alekseev and co-workers[6] discuss carbohydrate−metal complexes in solution and complexes of natural carbohydrates with metal cations, respectively. Piarulli and Floriani[7] and Gyurcsik and Nagy[8] reviewed mainly carbohydrate complexes of transition metals. The present review is directed to carbohydrate complexes of platinum-group metals where coordination−chemical aspects of isolated and well-characterized complexes are brought into focus. Complexes with ligands that contain carbohydrate moieties remote from the ligator atoms (Chart 1, **D**) are not considered. Complexes with more complex bioligands having integral carbohydrate moieties such as nucleosides and nucleotides and medical and pharmaceutical aspects, as especially important for platinum complexes with respect to their cytotoxic and antitumor properties, are not discussed as well.[9]

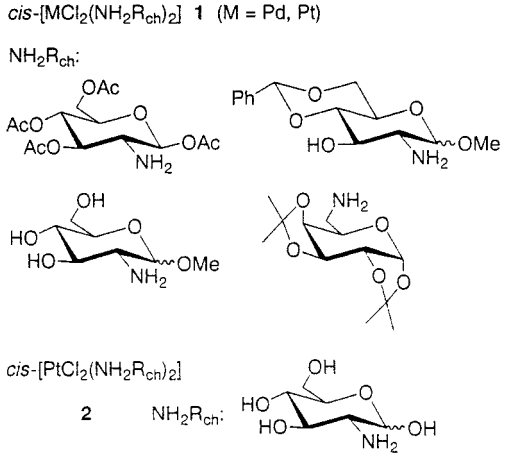
II. Carbohydrate Ligands with Donor Groups

A. *N*-Binding Substituents

1. Monodentate N-Donor Ligands

Aminomonosaccharides with protected 1-OH groups react with potassium tetrachloroplatinate to give *cis*-[$MCl_2(NH_2R_{ch})_2$] (**1**, M = Pt). Similar reactions carried out with *trans*-[$PdCl_2(PhCN)_2$] or $Na_2[PdCl_4]$ yield the corresponding palladium complexes (**1**, M = Pd) (Chart 2).[10] Protection of the hemiacetal moiety

Chart 2



prevents reduction to metallic platinum or palladium. With D-glucosamine, an aminosugar with a nonprotected hemiacetal moiety, $K_2[PtCl_4]$ reacts in water at room temperature to give metallic platinum as main product. Alternatively, at lower temperature (5 °C), the expected cis complex **2** was obtained (Chart 2).[11]

The Schiff base of tetra-*O*-acetyl-D-glucosamine R_{ch}−N=CH−Ar reacts in aqueous methanol with $K_2[PtCl_4]$ to effect hydrolysis of the benzylidene group, yielding the monosubstituted ionic complex **3** as main product (Scheme 3). This occurs not only when the substrates are in a 1:1 ratio, but also when a 2:1 ratio exists. Furthermore, *cis*- and *trans*-bis(tetraacetylglucosamine) complexes **4** and **5**, respectively, and a small quantity of *trans*-bis(benzylidene-*N*-glucosamin) complex **6** were isolated. The proposed intermediates en route to these complexes are shown in Scheme 3. The formation of **6** and the nonstereospecific reaction (formation of cis *and* trans complexes **4**/**5**) indicate that Schiff-base hydrolysis proceeds after metal coordination. The formation of the monosubstituted complex **3** and unusual stereochemistry of reaction is discussed in terms of the sterically bulky Schiff-base ligand. All complexes were, however, only identified by microanalysis, IR spectroscopy, and measurement of electric conductivity.[11]

Diamino- and triamino-substituted sucrose-based ligands react with amminetrichloroplatinate(II) in 1:2 and 1:3 stoichiometry, respectively, yielding bis- and tris(platinum) complexes **7** and **8**, respectively (Chart 3). These are cisplatin-type complexes in which *cis*-$PtCl_2(NH_3)$ units are monodentately *N*-coordinated to the disaccharide such that it acts as a bridging ligand.[12] The constitutions of these complexes were

Scheme 3

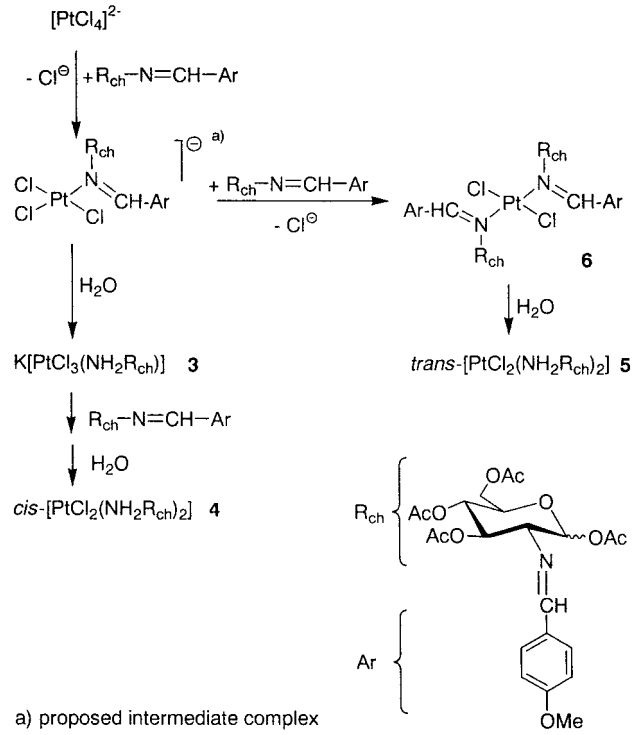
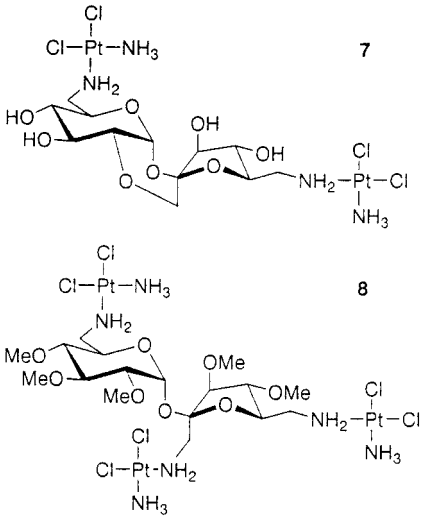


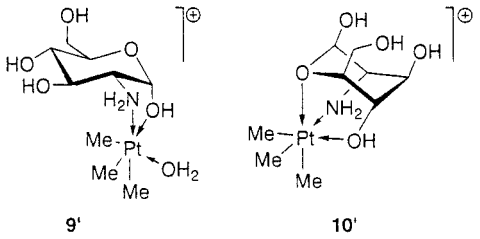
Chart 3



established by two-dimensional NMR spectroscopic investigations.

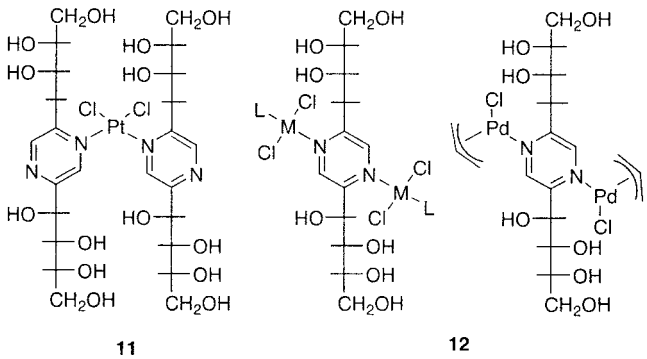
$[PtMe_3(H_2O)_3]^+$ (obtained by dissolving $[\{PtMe_3(H_2O)_2\}_2SO_4]$[13] in water) reacts in water with 2-amino-2-deoxy-α-D-glucose (D-glucosamine, NH_2R_{ch}) to give the complex $[PtMe_3(NH_2R_{ch})]_2SO_4$ (**9**).[14] To prevent precipitation of undesired $[\{PtMe_3(OH)\}_4]$, dilute concentrations are employed. ^1H, ^{13}C, and ^{195}Pt NMR measurements show that in aqueous solutions glucosamine is bound in bidentate fashion through the nitrogen atom and the anomeric hydroxyl group. Due to the $^4C_1$ geometry of the pyranose ring, no further donor atom is in a chelating position and the coordination sphere of platinum is completed by an aqua ligand (Chart 4, **9′**). Furthermore, glucosamine was found to react in acetone in a heterogenic reaction with tris(acetone)trimethylplatinum(IV) tetrafluoroborate, $[PtMe_3(Me_2CO)_3]BF_4$, yielding complex $[PtMe_3(NH_2R_{ch})]BF_4$ (**10**).[15] NMR measurements in acetone show that the pyranose ring is in its $^1C_4$ conformation and that Pt coordination involves N2, O4, and the cyclic oxygen (Chart 4, **10′**). ESI mass spectra verify the constitution. Although glucosamine is a reducing carbohydrate, no reduction of platinum(IV) was observed.

Chart 4



Deoxyfructosazine, a pyrazine derivative formed via Schiff-base condensation of D-glucosamine, reacts with $K_2[PtCl_4]$ in 2:1 stoichiometry yielding the bis(deoxyfructosazine) complex **11** (Chart 5). The di-

Chart 5



M	L	M	L
Pd	PEt_3, PBu_3	Rh, Ir	η^5-C_5Me_5
Pt	PBu_3	Ru	η^6-$MeC_6H_4(iPr)$

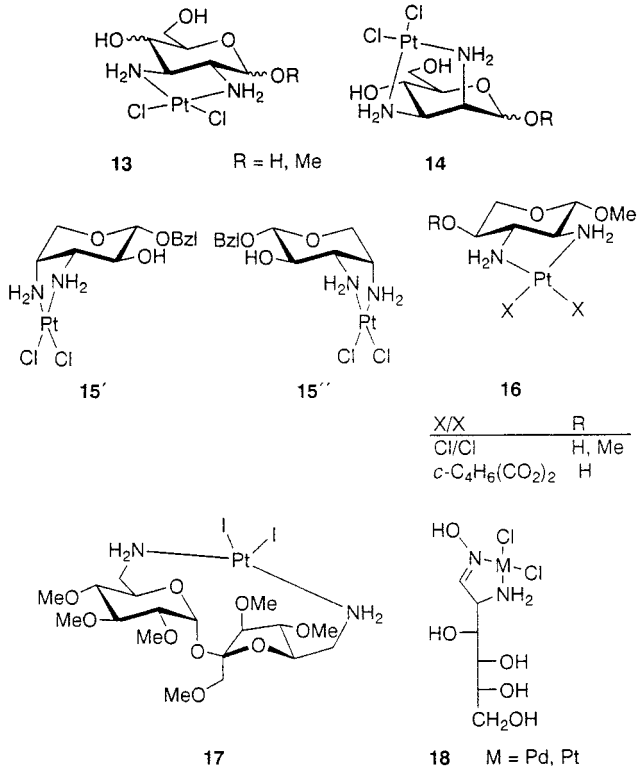
nuclear complexes $[\{MCl(\mu\text{-}Cl)L\}_2]$ (M = Pd, L = PEt_3, PBu_3; M = Pt, L = PBu_3; M = Rh, Ir, L = η^5-C_5Me_5; M = Ru, L = η^6-$MeC_6H_4(iPr)$) and $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)\}_2]$ react with deoxyfructosazine in 1:1 stoichiometry with cleavage the chloro bridges yielding complexes **12** which contain bridging deoxyfructosazine ligands. The constitutional makeup of complexes was established by NMR (^1H, ^{31}P) and IR spectroscopy.[16]

2. Bidentate N,N-Donor Ligands

2,3-Diamino- and 3,4-diaminoaldoses react with $K_2[PtCl_4]$ in aqueous solution to give cisplatin-type diamino sugar complexes of the form **13** (glucose and galactose derivatives), **14** (mannose derivatives), **15′**/**15″** (D-/L-arabinose derivatives), and **16** (X = Cl; L-xylose derivatives) (Chart 6).[17,18]

Among the complexes **13**/**14** are those with nonprotected hemiacetal units. In complexes **13**−**16**, the diamino sugar ligands adopt the pyranose form and can be regarded as ethylenediamine ligands with a carbohydrate backbone. In complexes **13**, the two amino groups have equatorial orientation with respect to the pyranose ring, which lies in the same plane as that around the platinum atom. In com-

Chart 6



plexes **14** and **15**, the two amino groups have axial and equatorial orientations, respectively. Therefore, the pyranose ring is in a nearly perpendicular orientation with respect to the coordination plane around the platinum atom. This was revealed by X-ray structure analysis of the methyl 2,3-diamino-2,3-dideoxy-α-D-mannopyranoside complex **14** (R = Me) (Figure 1).[17b] Absorption and circular dichroism spectra are as expected for complexes with *trans*- and *cis*-1,2-diaminocyclohexane-type ligands, respectively.[17] The conformation of pyranose rings in the D-arabinose and L-xylofuranose complexes **15′** and **16**, respectively, was determined to be $^1C_4$. The reaction of complex **16** (X = Cl, R = H) with the dipotassium salt of cyclobutane-1,1-dicarboxylic acid affords a carboplatin homologue complex (**16**, X/X = *c*-$C_4H_6(CO_2)_2$, R = H) whose structure was definitively ascertained by single-crystal X-ray diffraction analysis.[18]

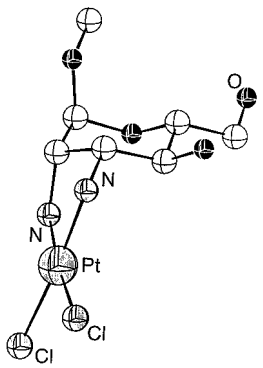


Figure 1. Molecular structure of complex **14**·H_2O (R = Me, α anomer) (Water molecule is not shown; H atoms are omitted).[17b]

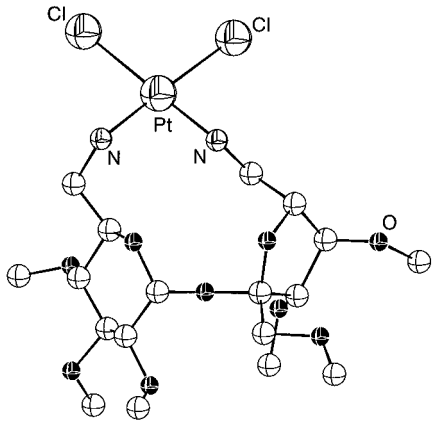


Figure 2. Molecular structure of complex **17**·H_2O·Me_2CO (Solvate molecules are not shown; H atoms are omitted).[12]

Permethylated 6,6′-diamino-6,6′-dideoxysucrose reacts with $[PtI_4]^{2-}$ in a molar ratio of 1:1 yielding complex **17** (Chart 6) where the disaccharide acts as a chelating *N*,*N*-ligand. The molecular structure of **17** exhibits a 12-membered trioxa−diaza−platina cyclic structure (Figure 2).[12] Complex **17** was converted into the oxalato, malonato, and cyclopropylmalonato complex by treating aqueous solutions of **17** with $AgNO_3$ and the disodium salts of the requisite diacids.

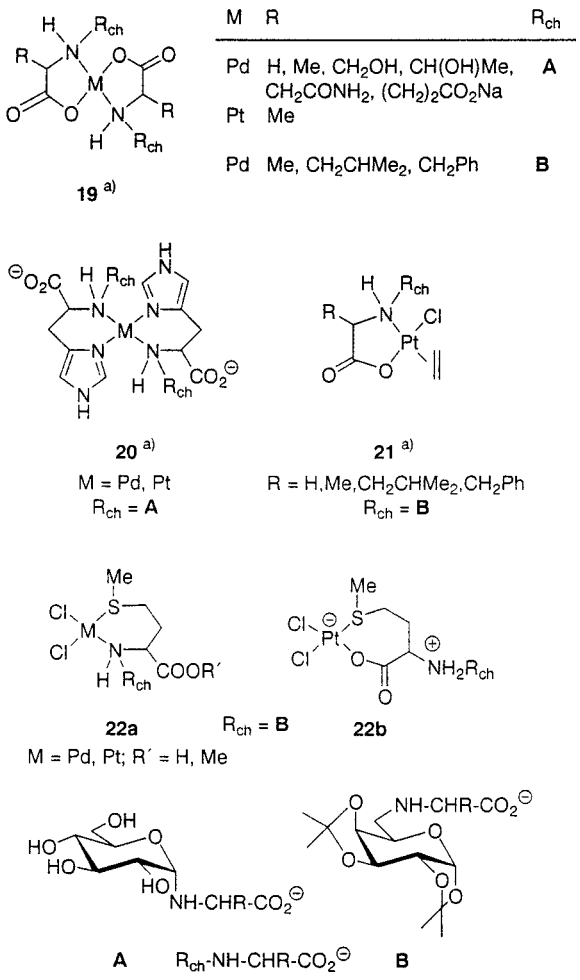
2-Amino-2-deoxy-D-glucoseoxime reacts with tetrachloroplatinate and -palladate to give amino-oxime complexes **18** (Chart 6).[19] The ν(CN) stretching vibrations are at 1678 (M = Pd) and 1652 cm^{-1} (M = Pt), respectively, revealing that the amino-oxime ligand is present in its chain form. Signals of the free ligand in ^1H NMR spectra of solutions of complexes in dimethyl sulfoxide show that a partial dissociation of amino-oxime ligands takes place. Poorly characterized are corresponding complexes with glucoseoxime/glucoseoximato ligands having only one strong donor site.[19]

3. N-Donor Ligands with Additional Functionality

Aminosugars in which the amino groups are part of an amino acid act as negatively charged bidentate *N*,*O*-ligands in most cases. Thus, sodium salts of *N*-glycosides derived from glucose and α-amino acids (glycine, alanine, serine, threonine, asparagine) (Chart 7, **A**) react with $Na_2[PdCl_4]$ in a 2:1 ratio to give complexes **19**.[20] The *N*-glycoside of glutamic acid ($^-O_2C-(CH_2)_2-CH(NHR_{ch})-CO_2^-$) acts also as a *N*,*O*-chelate ligand, whereas the *N*-glycoside of histidine ($C_3H_3N_2-CH_2-CH(NHR_{ch})-CO_2^-$) acts as a *N*,*N*-chelate ligand yielding complexes of types **19** and **20**, respectively. Reactions of $K_2[PtCl_4]$ with *N*-glycosides of alanine and histidine afforded analogous complexes of types **19** and **20**, respectively. The coordination modes of ligands were derived exclusively from IR spectroscopic investigations (especially via coordination-induced shifts of CO_2 bands). Thus, cis/trans structure (configuration index *SP*-4-1 as given in Chart 7 vs *SP*-4-2) remains speculative.

Similarly, anions of *N*-(1,2:3,4-di-*O*-isopropylidene-6-deoxy-α-D-glactopyranos-6-yl)-α-amino acids (alanine, leucine, phenylalanine) (Chart 7, **B**) react with $Na_2[PdCl_4]$ yielding inner-complexes **19** (Chart 7).[21]

Chart 7



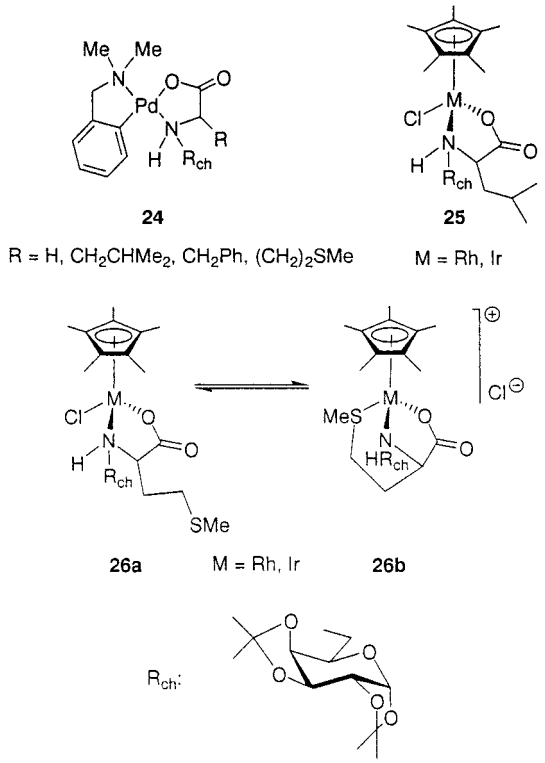
a) *cis/trans* structure tentative

^{1}H NMR spectra exhibit that only one isomer is formed. The same reactions performed with Zeise's salt result in formation of complexes **21**.[21] ^{1}H NMR spectra reveal that in all cases a minimum of two isomers (cis/trans isomers and/or diastereomers) are formed. In the case of the phenylalaninato complex, evidence was found for a dynamic equilibrium between complex and free ethylene.

Reactions of the galactopyranosyl-substituted methionine with $[MCl_4]^{2-}$ (M = Pd, Pt) give complexes **22** (R′ = H).[21] As shown by X-ray crystallography, the palladium complex benefits from N and S coordination (**22a**). In accordance with this, an intense absorption for the free COOH group at 1730 cm^{-1} was found. The platinum complex **22** (M = Pt, R′ = H) possesses two IR bands at 1650 and 1735 cm^{-1} pointing to the presence of *N*,*S*- and *S*,*O*-coordinated ligands (**22a** vs **22b**). From the intensities it was determined that the *S*,*O* isomer **22b** is preferred. Enhanced solubility for such complexes can be obtained using the methyl ester MeS−$(CH_2)_2$−CH(NHR_{ch})−COOMe to afford complexes **22a** (R′ = Me). The ligands are *N*,*S*-coordinated with nitrogen and sulfur as stereogenic centers. ^{1}H NMR spectra show that in the palladium case two of four diastereomers are obtained. Alternatively, using platinum as the metal center yields all four diastereomers. Reactions of $[MCl_4]^{2-}$ with galactopyranosyl-substituted methyl esters of amino acids without donor functionality in the side chain result in complexes $[MCl_2(NHR_{ch}$−CHR−COOMe$)_2]$ (**23**; M = Pd, R = H, Me, CH_2-$CHMe_2$, CH_2Ph; M = Pt, R = H, Me, CH_2CHMe_2).[21] From spectroscopic investigations (IR, ^{1}H NMR), it can only be derived that the ligands seem to be monodentately *N*-bound.

Reactions of diisopropylidene-protected galactopyranos-6-yl-substituted aminocarboxylates with chloro-bridged complexes $[\{Pd(o\text{-}C_6H_4CH_2NMe_2\text{-}C,N)(\mu\text{-}Cl)\}_2]$ and $[\{M(\eta^5\text{-}C_5Me_5)Cl(\mu\text{-}Cl)\}_2]$ (M = Rh, Ir) result in cleavage of the M−Cl−M bridges yielding complexes **24**−**26** (Scheme 4).[21] ^{1}H NMR spectra of complexes

Scheme 4



24 show that only one of two possible diastereomers is formed. X-ray diffractions of the methionine and phenylalanine derivatives exhibit the *SP*-4-4 configuration as shown in Scheme 4 and make unambiguously clear that the methionine sulfur atom is not coordinated to palladium. In complexes **25**, the leucinato ligands are *N*,*O*-coordinated with metal and nitrogen are asymmetric. Of the four possible diastereomers, three iridium, and four rhodium complexes were observed by ^{13}C NMR spectroscopy. ^{1}H and ^{13}C NMR spectra of complexes **26** in $CDCl_3$ exhibit the presence of neutral complexes with bidentately *N*,*O*-coordinated methioninato ligands (**26a**) and of cationic complexes with tridentately *N*,*O*,*S*-coordinated methioninato ligands (**26b**) in a ratio of about 5:6 (Rh) and 7:10 (Ir). The structural characterization reveals that the iridium complex crystallizes with a tridentately *N*,*O*,*S*-coordinated ligand (Figure 3). In the unit cell, two of the four diastereoisomers are present in a ratio of 3:1.[21]

D-Glucose reacts with amino acids (glycine, β-alanine) to afford Amadori compounds (1-(*N*-amino

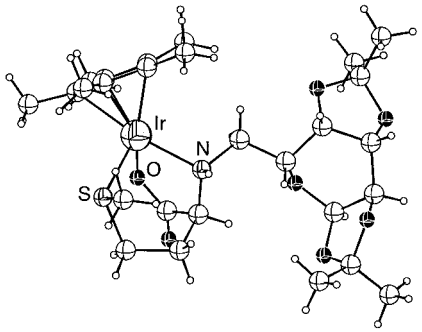
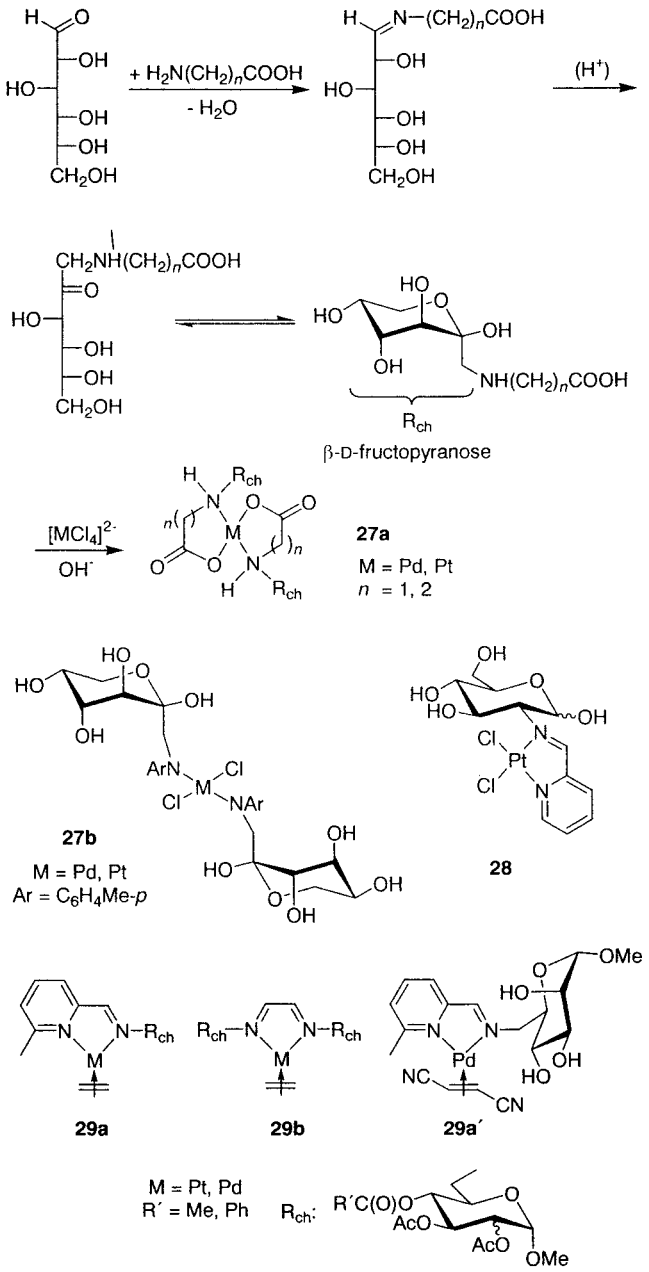


Figure 3. Molecular structure of the cation of complex **26b** (M = Ir) (One of the two symmetry independent molecule is shown).[21]

acid)-1-deoxy-D-fructose). In aqueous solution, these exist primarily as β-pyranose (Scheme 5). Sodium salts of these compounds react with tetrachloropalladate and -platinate yielding inner-complexes **27a**

Scheme 5



where the ligands are bidentately *N*,*O*-coordinated.[20] The Amadori adduct prepared from D-glucose and *p*-toluidine affords complexes **27b** with monodentately *N*-bound ligands. IR spectra of complexes **27** indicate that the Amadori-type ligands are present mainly in their pyranose form. The unusual trans structure of complexes **27b** was derived from IR spectra where only one absorption in the M−Cl region was found. As for complexes **19**, the cis/trans structure of complexes **27a** remains tentative.

Pyridin-2-ylmethylene-D-glucosamine, a carbohydrate-derivative Schiff-base ligand with an additional *N*-donor site, reacts with $K_2[PtCl_4]$ in aqueous solution yielding a mixture of products from which the neutral complex **28** was isolated (Scheme 5).[22] The bidentate *N*,*N*-coordination of the ligand was established by IR spectroscopy. Treatment of complex **28** with weakly acidified water (pH ca. 6) effects hydrolysis of the Schiff base probably yielding a complex with *N*-coordinated D-glucosamine ligand.

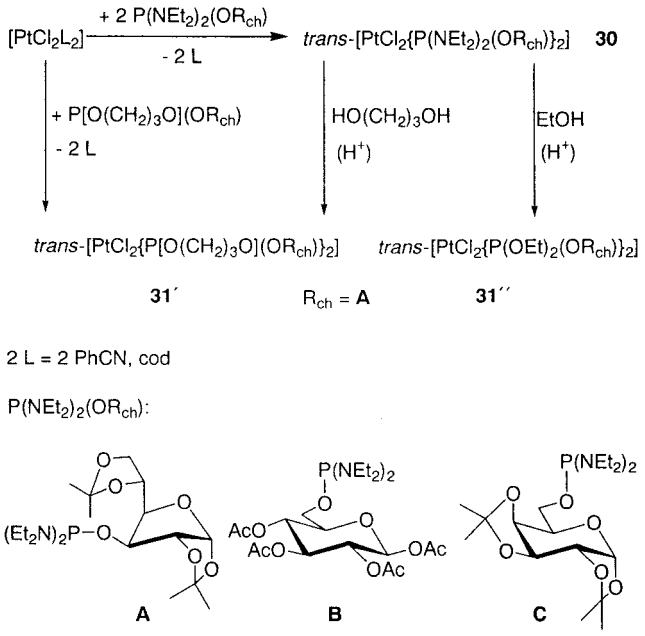
Three-coordinate platinum(0) and palladium(0) complexes **29** with carbohydrate-dervied *N*,*N*-chelate ligands and electron-withdrawing olefin ligands were synthesized (Scheme 5). The *N*,*N*-chelate induces enantioselectivity in the coordination of prochiral olefins. Furthermore, the ability to promote stereoselective stoichiometric processes is assessed. Deprotection of the alcoholic function in **29a** (M = Pd, olefin = fumarodinitrile) resulted in complex **29a′**, which was characterized by X-ray crystallography.[23]

B. *P*-Binding Substituents

1. Phosphite, Thiophosphite, and Phosphinite Donors

Bis(diethylamido)phosphite-substituted carbohydrates **A**−**C** (Scheme 6) react with bis(benzonitrile)- or cyclooctadienedichloroplatinum(II) yielding *trans*-$[PtCl_2\{P(NEt_2)_2(OR_{ch})\}_2]$ (**30**) (Scheme 6). With ethyl alcohol or propane-1,3-diol in the presence of trifluoroacetic acid, complexes **31** are formed with

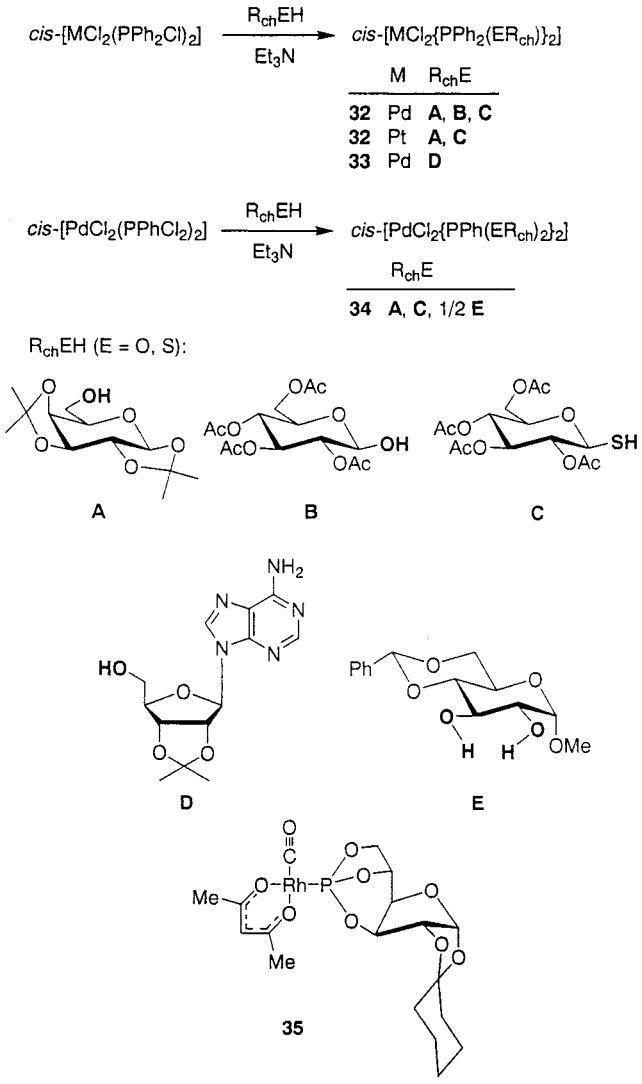
Scheme 6



cleavage of the amido groups. The 1,3,2-dioxaphosphorinane complex **31′** was also obtained directly from [$PtCl_2$(cod)] and 3-(trimethylenephosphite)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose.[24]

To circumvent the − possibly difficult − syntheses of "free" phosphite-substituted carbohydrate ligands, carbohydrates with OH or SH groups can be reacted with chlorophosphine−metal complexes in the presence of amines (Scheme 7).[25] In this manner, not only

Scheme 7

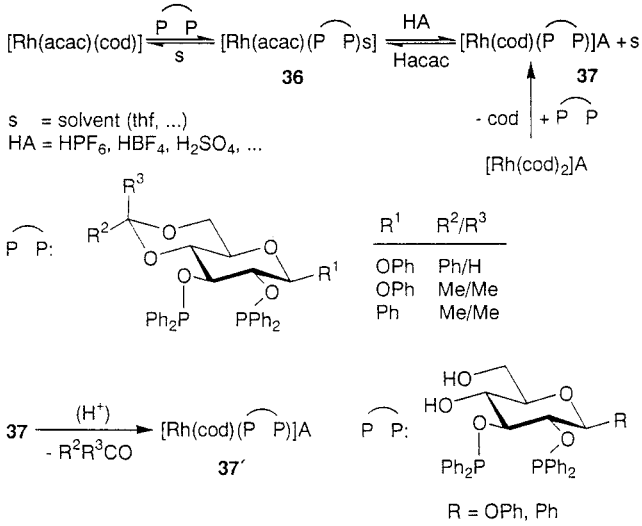


can complexes with phosphite-functionalized monosaccharides **(32)** be obtained but also a palladium complex with a phosphite-modified nucleoside (**33**) is possible. Corresponding reactions with [$PdCl_2$-($PPhCl_2$)$_2$] afforded complexes of the form **34** containing two sugar groups attached to each phosphorus atom or with λ^3-dioxaphospholane ligands when the carbohydrate has two neighboring hydroxyl groups.

The rhodium(I) complex **35** (Scheme 7) having a bicyclic phosphite ligand with a carbohydrate backbone (1,2-*O*-cyclohexylidene-α-D-glucofuranose) reacts much more easily with nucleophiles (water, alcohol) than the free ligand. The X-ray structure analysis reveals the rhodium to be square-planar coordinated. The geometry of the ligand is not changed markedly upon coordination.[26]

Alkylidene-protected 2,3-bis(*O*-diphenylphosphino)-glucopyranosides react with [Rh(acac)(cod)] yielding neutral complexes **36**, which are in equilibrium with the cationic complexes **37** in the presence of acids (HA) with weakly coordinating anions (Scheme 8).

Scheme 8



Complexes of type **37** are also obtained by reactions of bis(cyclooctadiene) complexes [$Rh(cod)_2$]A with carbohydrate-derived diphosphinites.[27,28] Acid-catalyzed cleavage of the alkylidene moiety affords the unprotected complexes **37′**. Such rhodium complexes were fully characterized by NMR spectroscopy[29] and X-ray crystallographies of complex **37** (P P = phenyl 2,3-bis(*O*-diphenylphosphino)-β-D-glucopyranoside, A = BF_4) (Figure 4) and of the analogous norbornadiene

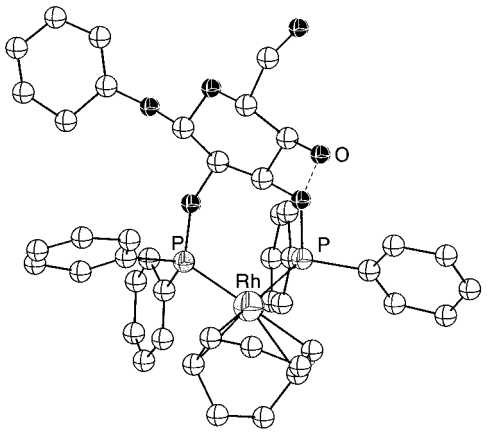
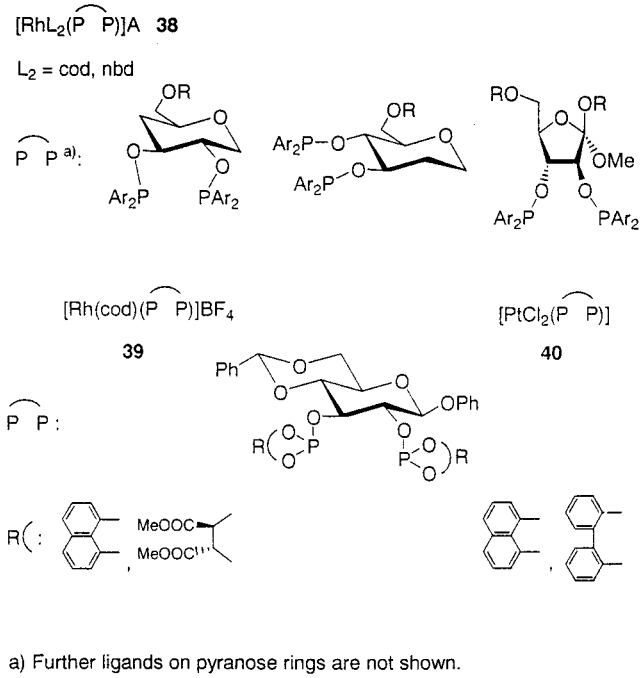


Figure 4. Molecular structure of the cation of [Rh(cod)-(P P)]BF_4 (P P = phenyl 2,3-bis(*O*-diphenylphosphino)-β-D-glucopyranoside) (**37**) (H atoms are omitted).[30a]

complex.[30] The pyranose rings and the seven-membered rhodacycles adopt chair and distorted boat conformations, respectively.

The chelate ligands in complexes **37/38** can be regarded as 1,2-bis(phosphinite)ethane ligands with a carbohydrate backbone. Similarly, a great variety of analogous rhodium complexes [RhL_2(P P)]A (L_2 = cod, nbd; A = BF_4, SbF_6, OTf) (**38**) with carbohydrate-derived $Ar_2P-O-C-C-O-PAr_2$ ligands (Ar = phenyl, substituted phenyls) have been prepared from

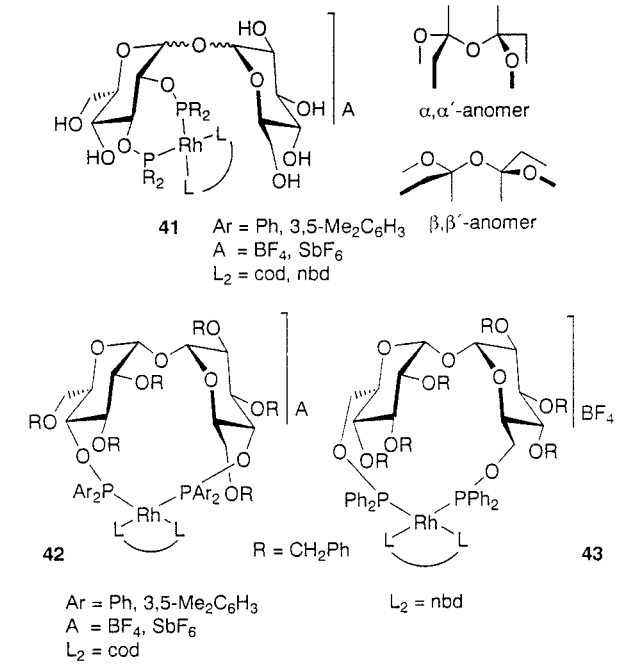
Chart 8



cationic complexes $[RhL_4]A$ (Chart 8).[28] From reactions of carbohydrate-derived diphosphite ligands with $[Rh(cod)_2]BF_4$ and $[PtCl_2(cod)]$, complexes **39** and **40** could be isolated (Chart 8).[31]

Analogous complexes from α,α′- and *β*,*β*′-trehalose **41** were also described (Chart 9).[32] Due to the free

Chart 9

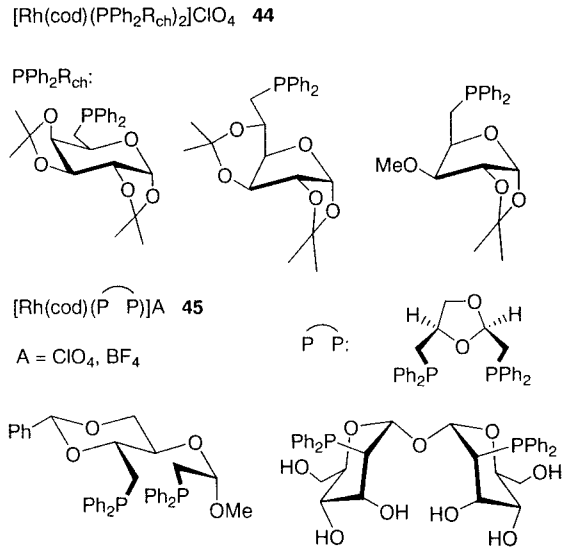


hydroxyl groups, they are water-soluble. 4,4′- and 6,6′-diphosphinite-substituted α,α′-trehalose derivatives form cationic complexes **42** and **43**, respectively, having 14-membered rhodacycles.[32a] From ^{31}P NMR spectra, their C_2-symmetric nature is evident. Most likely, there is coordination of benzyloxy groups to rhodium that is strongly dependent on temperature.

2. Phosphine Donors

Analogous to phosphite/phosphinite complexes, cationic rhodium complexes with galactopyranose-, glucofuranose-, and xylofuranose-derived monophosphine ligands (**44**) and diphosphine ligands (**45**) are well-known (Chart 10).[33]

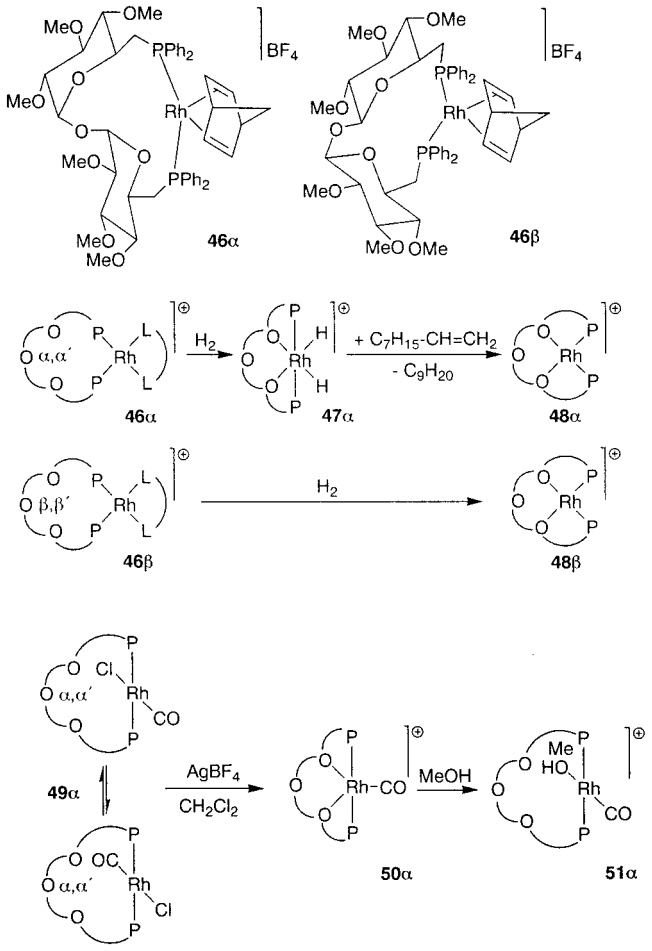
Chart 10



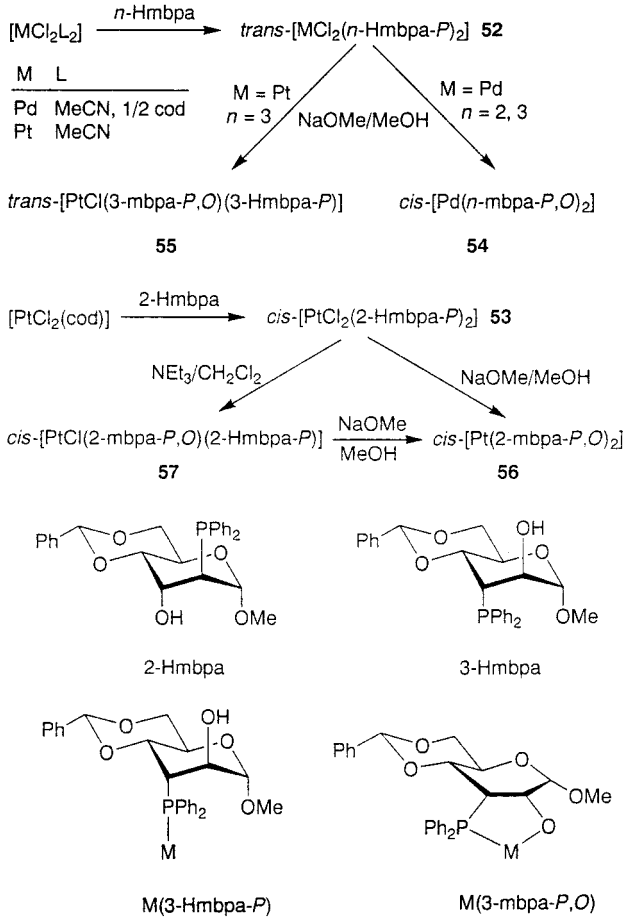
Reactions of 6,6′-diphosphine-substituted α,α′- and *β*,*β*′-trehaloses with $[Rh(nbd)_2]BF_4$ afford complexes **46**α/*β* with 12-membered rhodacycles and *cis-P,P*-arrangement. Treatment of the α,α′-trehalose complex **46**α with H_2 results in formation of the dihydrido complex **47**α (*trans-P,P* structure) that yields with non-1-ene complex **48**α (*cis-P,P* structure). In contrast, *β*,*β*′-trehalose-derived complex **46***β* reacts with H_2 directly to complex **48***β*, without the intervention of an observable dihydrido complex (Scheme 9).[34] The coordination patterns were derived from NMR studies. Analogous reactions with $[\{Rh(\mu\text{-}Cl)(CO)_2\}_2]$ lead to mononuclear carbonyl−chloro complexes **49**α/*β*. The α,α-anomer **49**α shows a dynamic NMR behavior and reacts with $AgBF_4$ yielding complexes **50**α and **51**α with a *trans-P,P*-arrangement (Scheme 9). Otherwise, the *β*,*β*-anomer **49***β* does not show such a dynamic as **49**α and the complexes of type **50***β* and **51***β* are rather unstable. Overall, the α,α-anomer shows more propensity for *trans-P,P*-complexation than the *β*,*β*-anomer.[34]

Platinum(II) and palladium(II) complexes with phosphine-substituted carbohydrate ligands were prepared from the reaction of $[MCl_2L_2]$ (M = Pd, Pt, L = MeCN, $^1/_2$ cod) with diphenylphosphino-substituted altropyranosides *n*-Hmbpa (*n* = 2, 3) (Scheme 10).[35,36] Starting from $[MCl_2(MeCN)_2]$ (M = Pd, Pt), the trans complexes *trans*-$[MCl_2(n\text{-Hmbpa-}P)_2]$ (**52**, M = Pd, Pt; *n* = 2, 3) were obtained. The same complexes are obtained when $[PdCl_2(cod)]$ is used as substrate, whereas the reaction of $[PtCl_2(cod)]$ with 2-Hmbpa affords *cis*-$[PtCl_2(2\text{-Hmbpa-}P)_2]$ (**53**). *P*-coordination of ligands and the stereochemistry of complexes were shown by extended NMR studies and in the case of *trans*-$[MCl_2(3\text{-Hmbpa-}P)_2]$ (**52**, M = Pd, Pt) (Figure 5) also by X-ray crystallography.[35a,36] In

Scheme 9



Scheme 10



the solid state, both complexes exhibit crystallographically imposed C_2 symmetry. The apparent deviations from the ideal square-planar complex geometries (P−M−P′ 165.4(1)°/165.4(2)°, Cl−M−Cl′ 174.1(1)°/174.6(2)°; M = Pd/Pt) can be primarily attributed to the overcrowding caused by the bulky phosphine ligands, although trans to each other.

The palladium complexes **52** both with 2- and 3-Hmbpa ligands were found to react with NaOMe in MeOH, yielding under deprotonation of the 3-OH and 2-OH group, respectively, inner-complexes **54** with *P,O*-chelating ligands (Scheme 10). NMR studies reveal a cis arrangement of the two ligands. In the case of platinum, the trans complexes **52** are more stable to base and only *trans*-[$PtCl_2$(3-Hmbpa-*P*)$_2$] reacts with NaOMe/MeOH yielding complex **55** in which only one Hmbpa ligand is deprotonated. Treatment of the cis complex **53** with NaOMe/MeOH results in formation of the inner-complex **56** analogous to those (**54**) of palladium. The weaker base NEt_3 reacts with **53** to deprotonate only one 2-Hmbpa ligand. The resulting complex **57** can be further deprotonated with NaOMe/MeOH to give **56**.[35b,36]

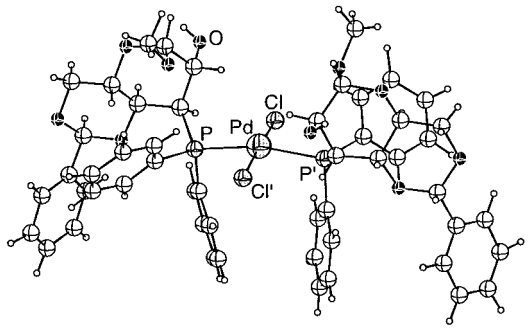


Figure 5. Molecular structure of *trans*-[$PdCl_2$(3-Hmbpa-*P*)$_2$] (**52**) (M = Pd).[36]

The coordination mode of inner-complexes **54**−**57** is worth noting because in the free ligand the diphenylphosphino and the neighboring hydroxyl group are in axial positions which are fixed by the 4,6-*O*-benzylidene ring. To coordinate to metal simultaneously, the phosphorus- and oxygen-donor atoms must twist close to each other resulting in significant conformational change of the altropyranose rings. These adopt a distorted boat conformation in complexes as shown in Figure 6 for *cis*-[Pt(2-mbpa-*P,O*)$_2$] (**56**).[35b] The bow atoms are C(2) and C(5). Conformational changes of the altropyranoside ligand upon complexation are most evident when considering the torsion angles P−C(2)−C(3)−O(3)/P′−C(2′)−C(3′)−O(3′). In the free ligand, these angles are 180° (ideal value), but in the complexed form (**56**), these angles are −34°/−58°. Thus, metal binding induces severe altropyranoside distortion.

The bis(alkoxo) complex **56** reacts with excess acetic acid to afford cleavage of the Pt−O bond yielding *cis*-[Pt(OAc)(2-mpba-*P,O*)(2-Hmbpa-*P*)]. Treatment with perchloric acid results in cleavage of the benzylidene groups yielding *cis*-[Pt(2-mpa-*P,O*)$_2$] (2-Hmpa = methyl 2-deoxy-2-(diphenylphosphino)-α-D-

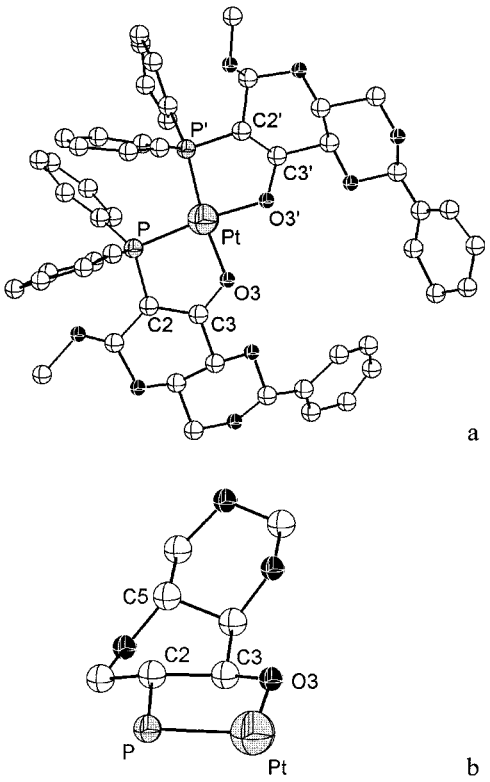


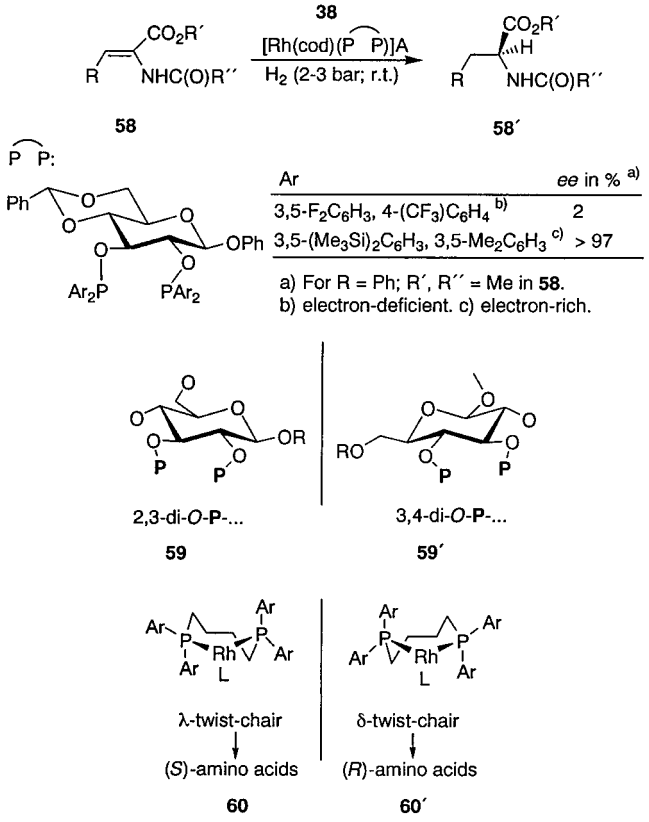
Figure 6. (a) Molecular structure of *cis*-[Pt(2-mbpa-*P*,*O*)$_2$]·3H$_2$O (**56**·3H$_2$O) (Water molecules are not shown; H atoms are omitted).[35b] (b) Structural detail showing the distortion of one of the two altropyranoside rings.

altropyranoside). Platin complexes **53**, **56**, and **57** exhibit antitumor activity. This, coupled with the established acid lability of **56**, prompted the elaboration of such complexes with hemilabile ligands. This concept is well-known in homogeneous catalysis.[37] From such a scaffold, novel agents for molecular medicine could be envisoned.[35b]

3. P-Binding Carbohydrate Ligands in Asymmetric Catalysis

Rhodium complexes with *P*-binding carbohydrate ligands are chiral in the carbohydrate backbone. Many of them, either prepared as definite substances (see Schemes 8 and 9 and Charts 8−10) or prepared in situ, are potent catalysts for enantioselective reactions, especially for asymmetric hydrogenation of olefins.[38] Phosphinite rhodium complexes with carbohydrate backbones were extensively used for hydrogenation of dehydroamino acid derivatives (Scheme 11).[28,39,40,48] On the basis of [Rh(acac)(cod)]/phenyl 4,6-*O*-benzylidene-2,3-bis(*O*-diphenylphosphino)-*β*-D-glucopyranoside (see Scheme 8), a commercial process for the production of L-DOPA (ee > 90%) has been developed in Isis-Chemie Zwickau (Selke, Pracejus 1978).[41] Immobilization of catalysts on styrene−divinylbenzene ion exchangers[42] or on silica-based cation exchangers[43] results in enhanced enantioselectivity. The water-soluble diphosphinite complexes **41** (Chart 9) allow one to perform the hydrogenation in water and in aqueous biphasic systems;[32] enantioselectivities up to 98% ee were found with a catalyst based on *β*,*β*′-trehalose.[32b] Micellar systems are a further perspective for diphosphinite-based complexes.[32c,44,45] In water and in the presence of sodium dodecyl sulfate, enantioselectivities up to 99.9% ee were obtained with type **41** catalysts.[32b]

Scheme 11



Systematic studies of hydrogenation of dehydroamino acid derivatives **58** with cationic rhodium(I) complexes of type **38** as catalysts (Scheme 11) reveal two things. First, the best substrates are aromatic and heteroaromatic dehydroamino acid derivatives, whereas the synthesis of aliphatic amino acids has serious limitations. Second, easily removable *N*-protecting groups (such as *N*-(benzyloxycarbonyl)) can survive the rhodium-catalyzed hydrogenation.[28] As the example in Scheme 11 demonstrates, the aryl substituents of the chelating phosphorus atoms have a remarkable electronic effect on the enantioselectivity. The origin of this remains speculative: assuming a kinetically controlled enantioselectivity, it is possible that the electron density at rhodium (which depends on *P*-aryl substituents) strongly influences the reactivity pattern of the major and minor diastereomeric transition states. In such a scenario it is wholly possible that the minor product formed between the cationic rhodium complex **38** and the prochiral olefin **58** corresponds to the more reactive of the two diastereomers. Notably, this argument bodes well for the likely reaction pathway since oxidative H_2 addition is the rate-determining step.[28,46] PHIP-NMR experiments (parahydrogen-induced polarization) provided evidence for the intermediate dihydrido rhodium complex.[47]

There is a pseudoenantiomeric relation between 2,3- and 3,4-disubstituted D-glucopyranosides (cf. **59**/**59**′). Hydrogenation of α-(*N*-acylamino)acrylic acid

derivatives using Rh complexes with **59**-type ligands affords (*S*)-amino acids. The use of Rh complexes with **59′**-type ligands allows ready access to (*R*)-amino acid derivatives. This demonstrates that product enantioselectivity depends only on the local chirality, i.e., on the chirality of the carbons to which the chelating phosphorus atoms are attached. Thus, both enantiomeric amino acids can be obtained with catalysts based on readily available D-glucopyranoside ligands.[28,48] Analogous results were obtained with catalysts based on α,α-trehalose derivatives (2,2′- versus 3,3′-bis(diphenylphosphinite) substitution).[49]

The conformation of seven-membered cationic rhodium chelates **60** and **60′** (Scheme 11) is critical for the enantioselective recognition and the subsequent hydrogenation of prochiral olefins. In both conformers there is an asymmetric, alternating axial−equatorial array of *P*-aryl groups. This arrangement seems to be more stable when all pyranoside substituents are equatorially arranged. Importantly, enantioselectivities of greater than 90% ee require all pyranoside substituents to be in equatorial positions.[28,45b,50]

Rhodium complexes with phosphine- and phosphinite-derived carbohydrate ligands have been used for asymmetric hydrogenation of prochiral imines.[51] Furthermore, *P*-binding carbohydrates have been used as cocatalysts in rhodium- and platinum-catalyzed asymmetric hydroformylation of olefins,[31,52] in nickel- and palladium-catalyzed asymmetric Grignard cross-coupling reactions,[53] in palladium-catalyzed allylic alkylation reactions,[54] as well as in Heck and Suzuki coupling reactions.[55]

C. *S*-Binding and *Se*-Binding Substituents

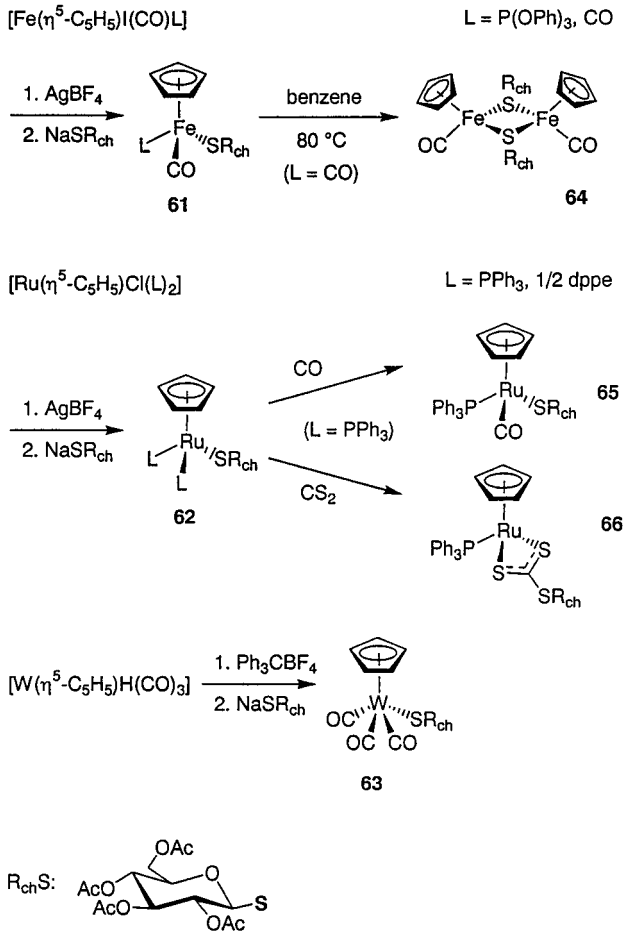
1. Thiolato and Selenolato Ligands

Substitution of OH groups in carbohydrates by SH or SeH groups affords carbohydrates which can be easily deprotonated to give thiolato and selenolato ligands, respectively. Such complexes with platinum-group metals M were obtained (i) by reaction of $R_{ch}E^-$ with L_xM-Cl or L_xM^+ (E = S, Se), (ii) by oxidative addition of $R_{ch}E-ER_{ch}$ to lower valent metal complexes L_xM, or (iii) by reaction of L_xM-OMe with R_{ch}-EH.

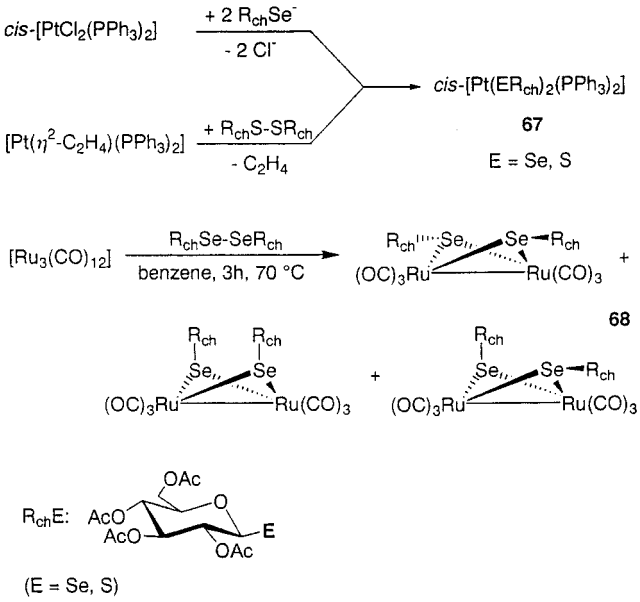
The sodium salt of the acetyl-protected β-D-thioglucopyranose reacts with cationic cyclopentadienyl−carbonyl complexes of Fe, Ru, and W (prepared in situ) to give thioglucopyranosato-*S* complexes **61**−**63** (Scheme 12).[56] Thermolysis of the iron complex **61** (L = CO) results in formation of the dinuclear complex **64**, which is isomerically pure in solution. The ruthenium complex **62** (L = PPh_3) reacts with CO with substitution of PPh_3 and with CS_2 with insertion yielding complexes **65** and **66**, respectively. All complexes were identified by NMR (^1H, ^{13}C) and IR spectroscopies. As expected, NMR spectra of complexes with asymmetrically substituted metal atoms (**61**, L = $P(OPh)_3$; **65**) show the formation of two diastereomers.

The reaction of *cis*-$[PtCl_2(PPh_3)_2]$ with 2 equiv of in-situ-prepared anion of acetylated 1-seleno-β-D-glucose affords the bis(selenoglucopyranosato-*Se*)-platinum complex **67** (Scheme 13).[57] The corresponding thiolato complex was obtained by oxidative addition of the acetylated bis(glucopyranosyl)disulfide to $[Pt(\eta^2-C_2H_4)(PPh_3)_2]$.[58] The cis geometries of the two complexes **67** were established by IR spectroscopy. The oxidative addition of the acetylated bis-(glucopyranosyl)diselenide to $[Ru_3(CO)_{12}]$ yields the dinuclear complex **68** with two bridging selenoglucopyranosato−*Se* ligands (Scheme 13).[57] Due to the

Scheme 12



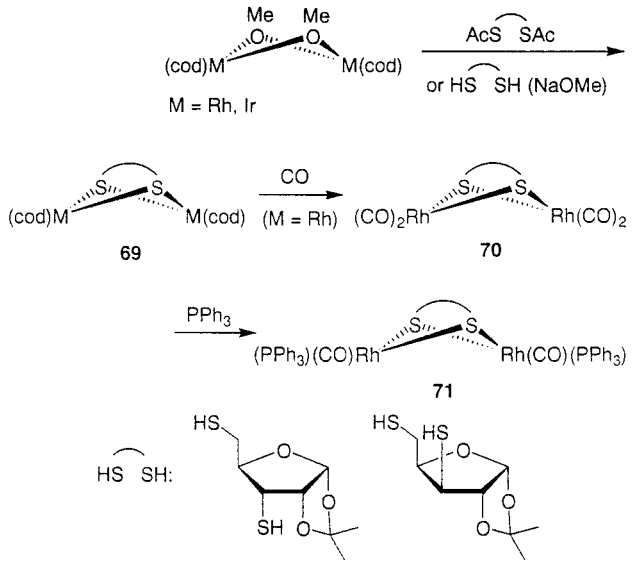
Scheme 13



butterfly structure of **68**, the different orientations of the selenoglucopyranosyl substituents give rise to three isomers. Triplication of all carbohydrate signals in ^{13}C NMR spectrum reveals that in solution all three isomers occur.

Dithiolato ligands with a backbone derived from ribofuranose and xylofuranose, respectively, which can be regarded as substituted propane-1,3-dithiolato ligands, form complexes with rhodium(I) and iridium(I) (Scheme 14).[59] Reaction of [{M(μ-OMe)(cod)}$_2$] (M = Rh, Ir) with the bis(thioacetate) or bis(thiol) carbohydrates in the presence of NaOMe yields dithiolato complexes **69**. FAB mass spectra suggest that the complexes are dinuclear. The rhodium complexes react with carbon monoxide to give the tetracarbonyl complexes **70**. These in turn can react with 2 equiv of triphenylphosphine to form mixed dinuclear carbonyl−phosphine complexes **71**. The IR spectra suggest that these complexes are present in the solid state as the trans isomers only. Alternately, ^{31}P NMR spectroscopy confirms the presence of cis and trans isomers in solution (CD_2Cl_2). DFT calculations for carbonyl complexes **70**[59] reveal bent double square-planar structures (dihedral angles between the coordination planes, 127−129°) with Rh···Rh distances of 3.25−3.30 Å. These distances are outside the typically accepted range for Rh···Rh interactions. The complex with the xylofuranose dithiolato ligand occurs in two conformers. In the more stable conformer (ΔE = −6.6 kcal/mol), the furanose ring oxygen atom lies directly above one of the rhodium atoms. The Rh···O distance of 2.98 Å suggests a weak interaction that could explain an unusual downfield shift for the anomeric proton upon complexation.

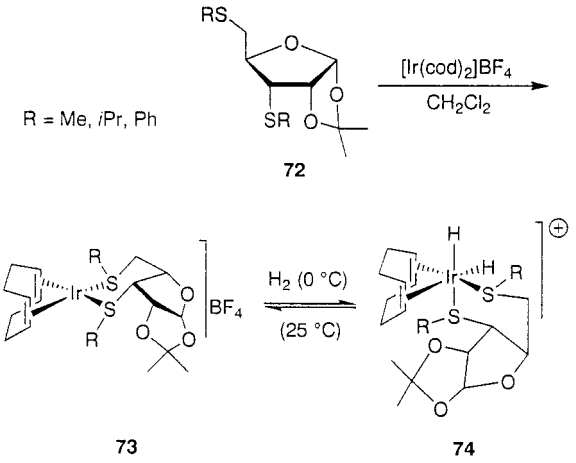
Scheme 14



2. Thioether and Other S-Donor Ligands

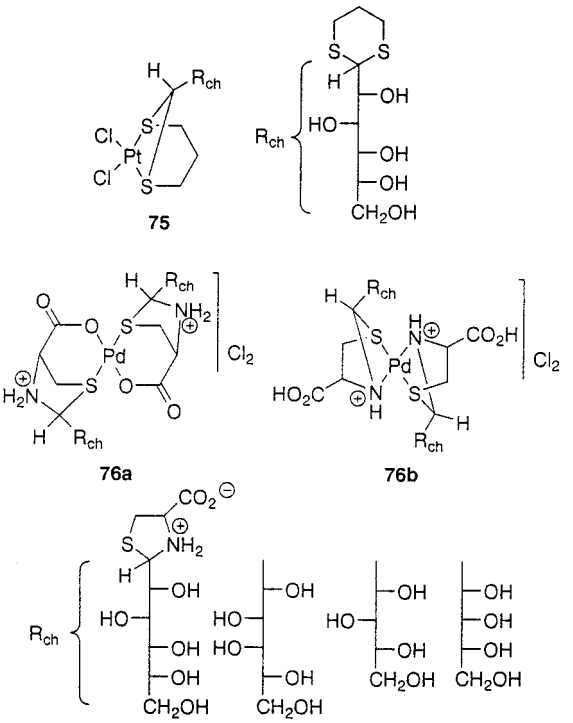
1,2-*O*-Isopropylidene-3,5-bis(alkyl/arylthio)-α-D-(+)-ribofuranoses **72** can act as di(thioether) chelate ligands. They react with [Ir(cod)$_2$]BF$_4$ to displace one cyclooctadiene ligand, yielding cationic complexes **73** (Scheme 15).[60] Coordination to iridium generates two stereogenic centers. NMR measurements indicate that the reactions are highly diastereoselective. For complex **73** (R = Me), NMR studies (including NOE experiments) in combination with molecular modeling show that the dithiairidacyclohexane ring has a twist−chair conformation with a (*S*,*R*) dithioether configuration. Complexes **73** react in CD_2Cl_2 solution with H_2 at 0 °C to give the corresponding *cis*-dihydridoiridium(III) complexes **74** (characterized by NMR spectroscopy in solution). At 25 °C, hydrogen is cleaved off and the parent complexes **73** are recovered. Complexes **73** were tested in the asymmetric hydrogenation of acrylic acid derivatives (room temperature, 1 bar of H_2), providing enantioselectivities of up to 62% ee.[60]

Scheme 15



D-Glucose trimethylene mercaptal, a carbohydrate derivative of 1,3-dithiane, is a soft ligand and reacts with $K_2[PtCl_4]$ to produce complex **75** (Chart 11).[19] The condensation products of D-glucose, D-galactose, D-xylose, and D-ribose with L-cysteine are thiazolidine

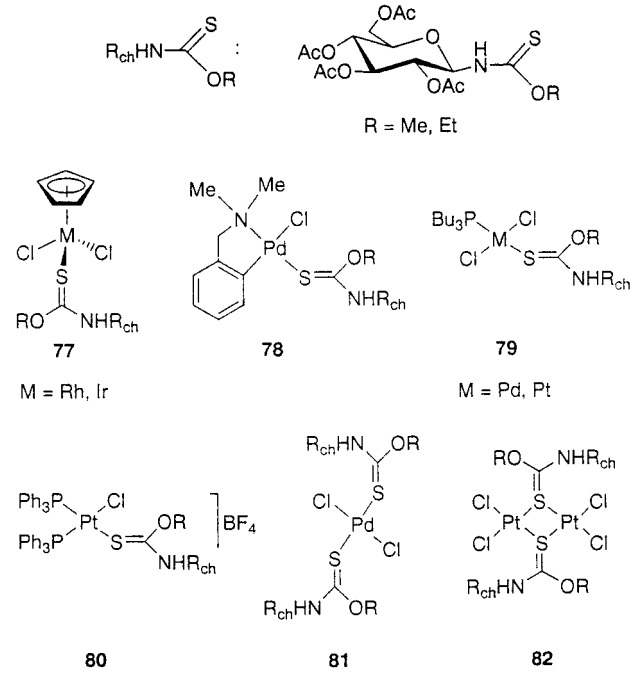
Chart 11



derivatives with a betaine structure. These react with $Na_2[PdCl_4]$ in methanol yielding complexes **76**.[61] IR investigations show two $\nu_{as}(CO_2)$ bands, intense at 1610 and weaker at 1720 cm^{-1}, indicating the presence of two isomeric complexes with *S*,*O*- (**76a**) and *S*,*N*-coordinated ligands (**76b**), respectively. The major isomers are complexes **76a** (Chart 11).[61]

Thiocarbonic acid derivatives have proved to be useful ligands for platinum-group metals. Acetylated *N*-(β-D-glucopyranosyl)thiocarbamate esters (prepared from alcohols and acetylated glucopyranosylisothiocyanate) react with chloro-bridged dinuclear complexes $[\{M(\eta^5\text{-}C_5Me_5)Cl(\mu\text{-}Cl)\}_2]$ (M = Rh, Ir), $[\{Pd(o\text{-}C_6H_4CH_2NMe_2\text{-}C,N)(\mu\text{-}Cl)\}_2]$, $[\{MCl(\mu\text{-}Cl)(P\text{-}Bu_3)\}_2]$ (M = Pd, Pt), and $[Pt(\mu\text{-}Cl)(PPh_3)_2\}_2](BF_4)_2$ with cleavage of the M−Cl−M bridges yielding complexes **77**−**80** with thiocarbamate ester ligands (Chart 12).[62] Tetrachloropalladate and -platinate

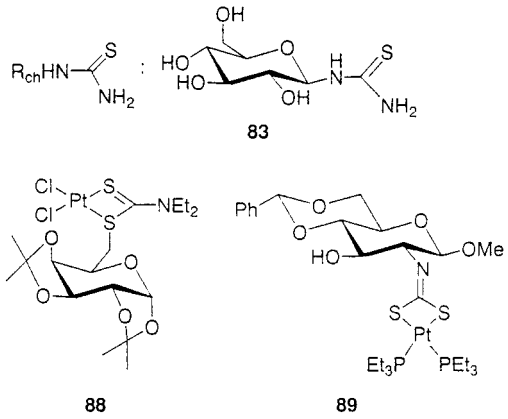
Chart 12



were found to react, yielding the mononuclear palladium complexes **81** and the bridged dinuclear platinum complexes **82**, respectively. Sulfur coordination was established by IR spectroscopic investigations exhibiting coordination-induced shifts of ν(CN) and ν(CS) to higher and lower wavenumbers, respectively. Further support comes from ^1H NMR spectroscopic investigations. The stereochemistry of complexes **78** and **81** and the formulation of **82** with sulfur-bridged ligands were deduced from analogous complexes without carbohydrate functionalization.

As with thiocarbamate esters, β-D-glucopyranosylthiourea **83** (Chart 13) (prepared from ammonia and glucopyranosylisothiocyanate) reacts with $[\{M(\eta^5\text{-}C_5Me_5)Cl(\mu\text{-}Cl)\}_2]$ (M = Rh, Ir), $[\{Pd(o\text{-}C_6H_4CH_2NMe_2\text{-}C,N)(\mu\text{-}Cl)\}_2]$, and $[\{PdCl(\mu\text{-}Cl)(PEt_3)\}_2]$. Cleavage of the chloro bridges affords thiourea complexes $[M(\eta^5\text{-}C_5Me_5)Cl_2\{R_{ch}NH{-}C(S){-}NH_2\}]$ (**84**, M = Rh, Ir), $[Pd(o\text{-}C_6H_4CH_2NMe_2\text{-}C,N)Cl\{R_{ch}NH{-}C(S){-}NH_2\}]$ (**85**), and $[PdCl_2(PEt_3)\{R_{ch}NH{-}C(S){-}NH_2\}]$ (**86**), re-

Chart 13



spectively. From $[MCl_4]^{2-}$ (M = Pd, Pt), mononuclear bis(thiourea) complexes $[MCl_2\{R_{ch}NH{-}C(S){-}NH_2\}_2]$ (**87**) were obtained.[62] The IR spectra of complexes **84**−**86** might be indicative for *N*-coordinated thiourea ligands. The coordination geometries in complexes **87** is unknown.

The reaction of $K_2[PtCl_4]$ with *N*,*N*-diethyldithiocarbamoyl-substituted α-D-galactopyranose in water/ethanol affords the platinum complex **88** (Chart 13). The X-ray structure analysis shows the dithiocarbamoyl group to be bidentately *S*,*S*-coordinated to platinum (Pt−S 2.233(2), 2.268(2) Å) (Figure 7).[63] The

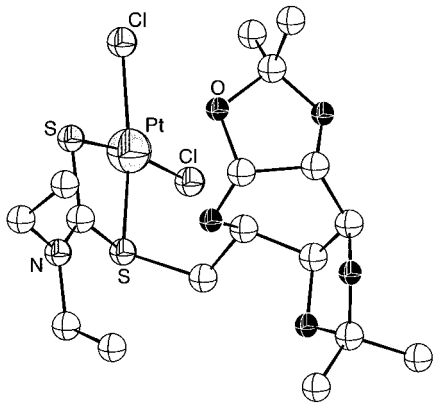
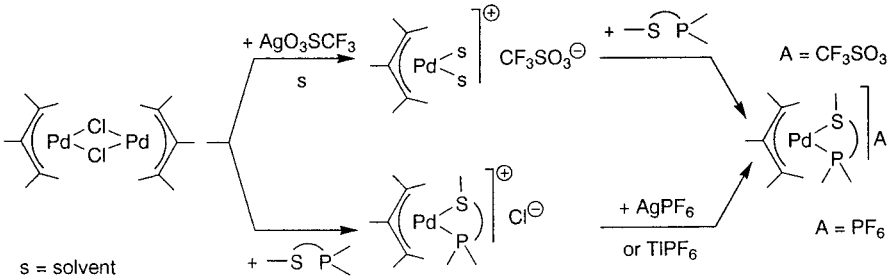


Figure 7. Molecular structure of complex **88**·Me_2CO (Acetone molecule is not shown; H atoms are omitted).[63]

$PtCl_2(S_2C{-}NC_2)$ unit is approximately planar; this and the bond distances within the S_2CN unit (C−N 1.28(1) Å, C−S 1.69(1)/1.80(1) Å) indicate a delocalization of π electrons. The pyranosyl ring has a skew−boat conformation. Furthermore, platinum complex **89** (Chart 13) with carbohydrate-substituted dithiocarbimato ligand was prepared in a one-pot-reaction from *cis*-$[PtCl_2(PEt_3)_2]$, 1-*O*-methyl-2-amino-2-deoxy-4,6-benzylidene-α,β-D-glucopyranoside and CS_2 in the presence of NEt_3.[58] The bidentate *S*,*S*-coordination was established by IR and NMR (^1H, ^{31}P) spectroscopy.

Palladium complexes **90**−**95** with *S*,*P*-ligands based on β-D-thioglucose tetraacetate were obtained either by ligand substitution starting from $[PdCl_2(MeCN)_2]$[64] and $[Pd(C_6H_4R'\text{-}p)X(tmeda)]$ (X = Br, I),[65] respectively, or from dinuclear palladium allyl complexes as shown in Scheme 16.[64,66,67] X-ray crystal-structure

Scheme 16



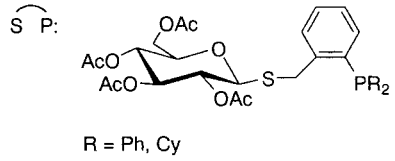
[Pd(η^3-allyl)(S PR_2)]A

η^3-allyl	R	A	
η^3-C_3H_5	Ph	PF_6, CF_3SO_3	**92**
η^3-PhCHCHCHPh	Ph, Cy	PF_6	**93**
η^3-$C_{19}H_{29}O_2$ [a)]	Ph	PF_6	**94**

a) $C_{19}H_{29}O_2$: allyl derived from 3,17-dioxo-4-androstene.

[$PdCl_2$(S PPh_2)] **90**

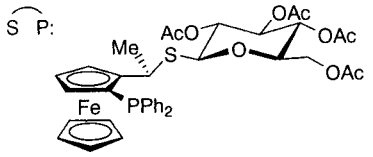
[Pd(C_6H_4R'-*p*)X(S PPh_2)] **91**
(R′ = MeO, Me, H, CF_3, ...; X = Br, I)



R = Ph, Cy

A

[Pd(η^3-PhCHCHCHPh)(S P)]CF_3SO_3 **95**



B

analyses of complexes **92** (A = PF_6)[64] and **95** (Figure 8)[66] show unambiguously the bidentate *S*,*P*-coordination of the ligands. The diphenylallyl ligand in **95** is strongly rotated such that the terminal C3 carbon trans to the *P*-donor is found ca. 0.85(3) Å below the coordination plane. This is to avoid unfavorable steric interactions with the large sugar moiety (Figure 8). NMR experiments of the diphenylallyl complexes **93** and **95**[64,68] demonstrated that in $CDCl_3$ solution at least two diastereomeric exo/endo complexes exist (exo/endo refers to the position of the central allyl proton with respect to the sugar moiety). For complex **93** (R = Cy), a syn−anti isomerization of the 1,3-diphenylallyl ligand was found.

Carbohydrate-derived *S*,*P*-ligands are also capable of forming Pd(0) complexes **96** with strongly electron-withdrawing olefin ligands (Scheme 17).[69] The X-ray crystal-structure analysis of the benzoquinone complex **96** (X = −CH=CH−) exhibits a η^2-coordinated benzoquinone ligand whose placement relative to the other ligands is shown in the sketch in Scheme 17. There are interesting dynamics in solution; in complex **96** (X = −CH=CH−), the benzoquinone dissociates and then recombines, whereas in **96** (X = $-CH_2-$), a rotation of cyclopent-4-ene-1,3-dione without dissociation was found.

Reactions of [Rh(acac)(cod)] with carbohydrate-derived *S*,*P*-ligands in the presence of HBF_4 afforded complexes **97** (Chart 14).[70] Their identities were confirmed by NMR spectroscopy and FAB mass spectrometry. The magnitudes of the Rh−P coupling constants and CD spectra reveal that the ligands are coordinated in a bidentate manner.

In analogy to the palladium complexes with *S*,*P*-donor ligands (see Scheme 16), complexes **98** and **99** with *S*,*N*-oxazoline−thioglucose ligands were prepared starting from [PdMe(Cl)(cod)] or from palladium allyl complexes [{Pd(η^3-PhCHCHCHPh)(μ-Cl)}$_2$] (Chart 15).[71] The diasteromeric structure (configuration index *SP*-4-2) of complexes **98** (R = Ac; R′ = *i*Pr, Ph) has been derived by X-ray crystallography.[71a] The allyl complexes **99** exist in $CDCl_3$ solution as a mixture of (syn/syn) exo and endo diastereomeric complexes (exo/endo refers to the position of the central allyl proton with respect to the oxazoline substituent R′) that interconvert via allyl rotation.

Palladium complexes with chiral *S*,*P*- and *S*,*N*-ligands were used as precatalysts in enantioselective allylic alkylations according to Scheme 18. In general, the prochiral allyl acetate is oxidatively added to a chiral Pd(0) complex to afford a cationic η^3-allyl Pd(II) complex. This complex is then attacked, in the rate-determining step, by the nucleophile Nu^-. The alkylation of *rac*-1,3-diphenylallyl acetate (R = Ph) with dimethyl malonate (Nu^- = $(MeO_2C)_2CH^-$) affords, in the presence of *S*,*P*-coligands, the *R* enantiomer (precatalyst **92**/**93** (R = Cy), ca. 64/53% ee; precatalyst **95**, ca. 88% ee). In the presence of *S*,*N*-coligands, the *S* enantiomer is formed (precatalyst **99**, ca. 90−97% ee). Using type **99** complexes having instead of the sugar moiety at sulfur an *S*-cyclohexyl

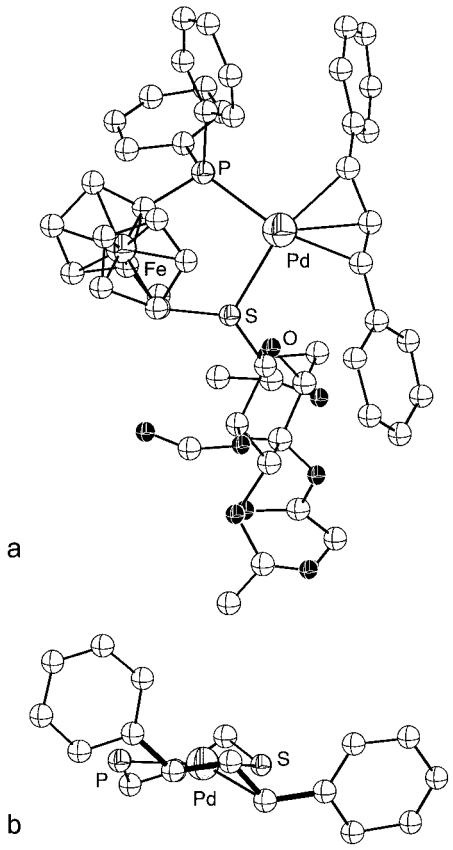
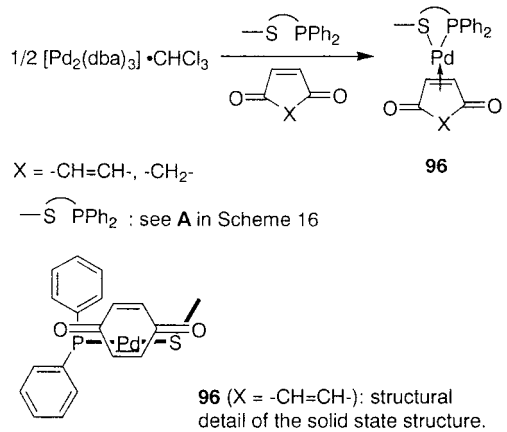


Figure 8. (a) Molecular structure of [Pd(η^3-PhCHCH-CHPh)(S⁀P)]CF_3SO_3·2$CHCl_3$ (**95**·2$CHCl_3$) (Anion and solvate molecules are not shown; H atoms are omitted). (b) Structural detail showing the coordination of the 1,3-diphenylallyl ligand with respect to the six-membered palladacycle.[66]

Scheme 17



donor, the enantiomeric excess is much lower (ca. 75%), indicating that the sugar moiety plays an important role. The enantioselectivity can be explained in terms of the preferential attack at the terminal allyl carbon pseudo-trans to the donor with the stronger trans effect (P in *S,P*-ligands and S in *S,N*-ligands). A different reactivity of exo and endo isomers as well as an equilibrium between them also plays a role. Thus, the depleted diastereomer can be rapidly reformed, and there is not necessarily a correlation between observed enantiomeric excess and population of the diastereomers in solution.[64,66,68,71b,72] Palladium-catalyzed asymmetric allylic substitution reactions were also performed with *P,N*-chelate ligands based on carbohydrate-derived phosphine- and phosphinite-oxazolines.[73]

Chart 14

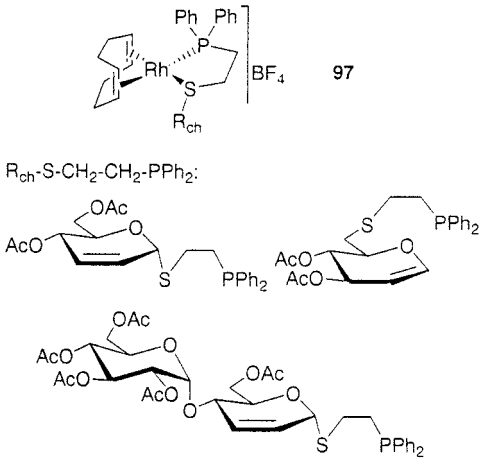
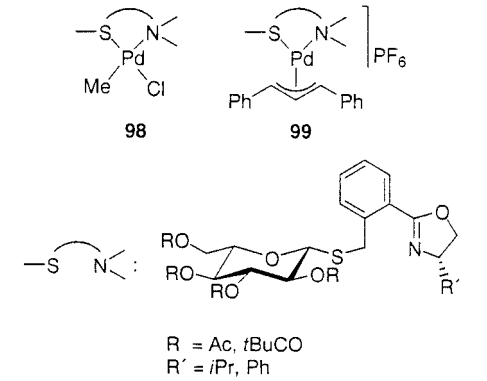
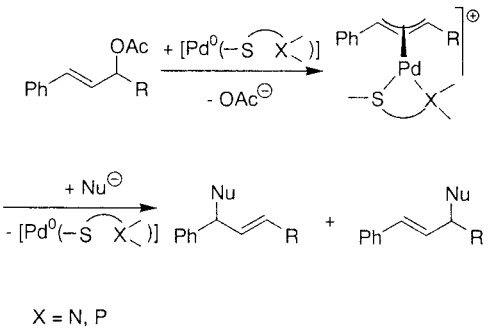


Chart 15



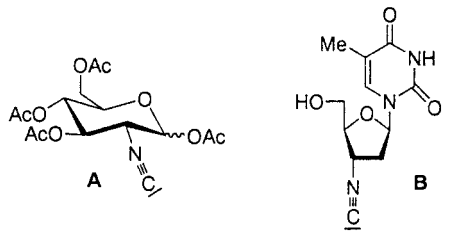
Scheme 18



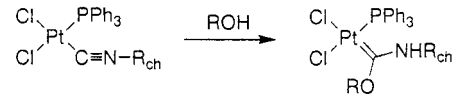
D. *C*-Binding Substituents

As with simple isocyanide ligands CNR (R = alkyl, aryl), platinum-group metal complexes with carbohydrate-substituted isocyanides CNR_{ch} were synthesized.[74a] Both anomers of tetra-*O*-acetyl-2-deoxy-2-isocyano-D-glucopyranose R_{ch}−N≡C (A) (Chart 16) react with dinuclear complexes [{M(η^5-C_5Me_5)Cl(μ-Cl)}$_2$] (M = Rh, Ir), [{PtCl(μ-Cl)(PPh_3)}$_2$], and [Pt(μ-Cl)(PPh_3)$_2$}$_2$](BF_4)$_2$ with cleavage of the chloro bridges yielding complexes **100**−**102** (Chart 16). Reactions with palladium and platinum dichloride afford *cis*-dichlorobis(isocyanoglucopyranose) complexes **103**. The stereochemistry of complexes **100**−**103** was determined from IR and NMR spectroscopic investi-

Chart 16

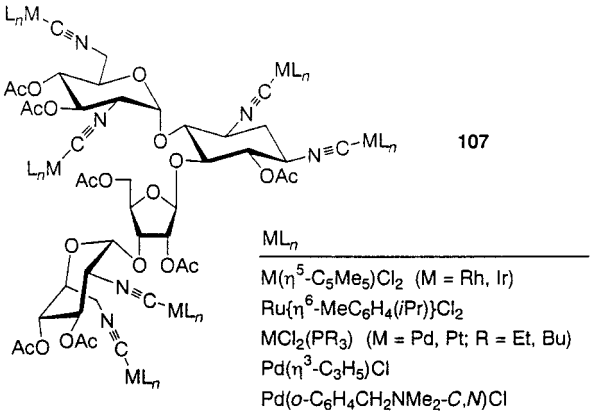


		R_{ch}—N≡C|
$[M(\eta^5\text{-}C_5Me_5)Cl_2(CNR_{ch})]$ (M = Rh, Ir)	100	A, B
$[PtCl_2(CNR_{ch})(PR_3)]$	101	A (R = Ph), B (R = Bu)
trans-$[PtCl(CNR_{ch})(PPh_3)_2]BF_4$	102	A, B
cis-$[MCl_2(CNR_{ch})_2]$ (M = Pd, Pt)	103	A
$[PdCl_2(CNR_{ch})(PEt_3)]$	105	B
$[PdCl(o\text{-}C_6H_4CH_2NMe_2\text{-}C,N)(CNR_{ch})]$	106	B



101 104

R = Me, Et; R_{ch}—N≡C\| : A



107

ML_n
$M(\eta^5\text{-}C_5Me_5)Cl_2$ (M = Rh, Ir)
$Ru\{\eta^6\text{-}MeC_6H_4(iPr)\}Cl_2$
$MCl_2(PR_3)$ (M = Pd, Pt; R = Et, Bu)
$Pd(\eta^3\text{-}C_3H_5)Cl$
$Pd(o\text{-}C_6H_4CH_2NMe_2\text{-}C,N)Cl$

gations. Coordination-induced shifts of ν(CN) to higher wavenumbers is much greater in Pd^{II}/Pt^{II} complexes **101**−**103** than in Rh^{III}/Ir^{III} complexes **100**, pointing to a substantial contribution of π back-donation in M−C bonds within complexes **100**. The molecular structure of $[Ir(\eta^5\text{-}C_5Me_5)Cl_2(CNR^{\alpha}_{ch})]$ (**100**) exhibits a nearly linear Ir−C−N (177(3)°) and a more bent C−N−C bond (169(2)°) as typical for isocyanide complexes.[74a]

The platinum complexes **101** add alcohols to give neutral carbohydrate-derivative carbene platinum complexes **104** (Chart 16).[74a] The ^{31}P NMR spectrum of carbene complex **104** with C(OMe)−NHR^{β}_{ch} ligand is consistent with the presence of two rotamers.

As with the isocyanoglucopyranose **A**, complexes of type **100**−**102** with the isocyano-substituted nucleoside **B** have been prepared. Analogously, the palladium complexes **105** and **106** were obtained (Chart 16).[74b] The hexaisocyanide of the acetyl-protected amino glycoside neomycin-B forms hexanuclear metal complexes **107**.[74c] FAB mass spectra of the rhodium complex and of the 2-(*N*,*N*-dimethylaminomethyl)phenylpalladium complex show [M^+ − Cl] as the ions of highest mass.

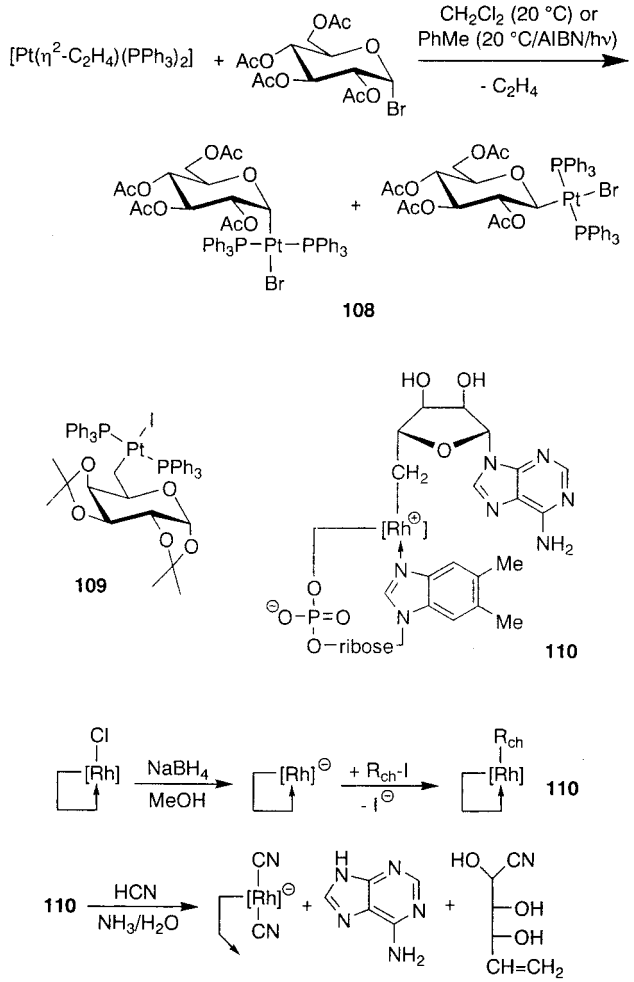
III. Carbohydrate Ligands without Donor Groups

A. Anionic Carbohydrate Ligands

1. Carbohydrate Carbanions

Peracetylated α-D-glucopyranosylbromide reacts with $[Pt(\eta^2\text{-}C_2H_4)(PPh_3)_2]$ in methylene chloride in an oxidative addition reaction to give the platinum(II) complex **108** bearing a σ-bonded carbohydrate carbanion (Scheme 19).[58] The reaction proceeds with

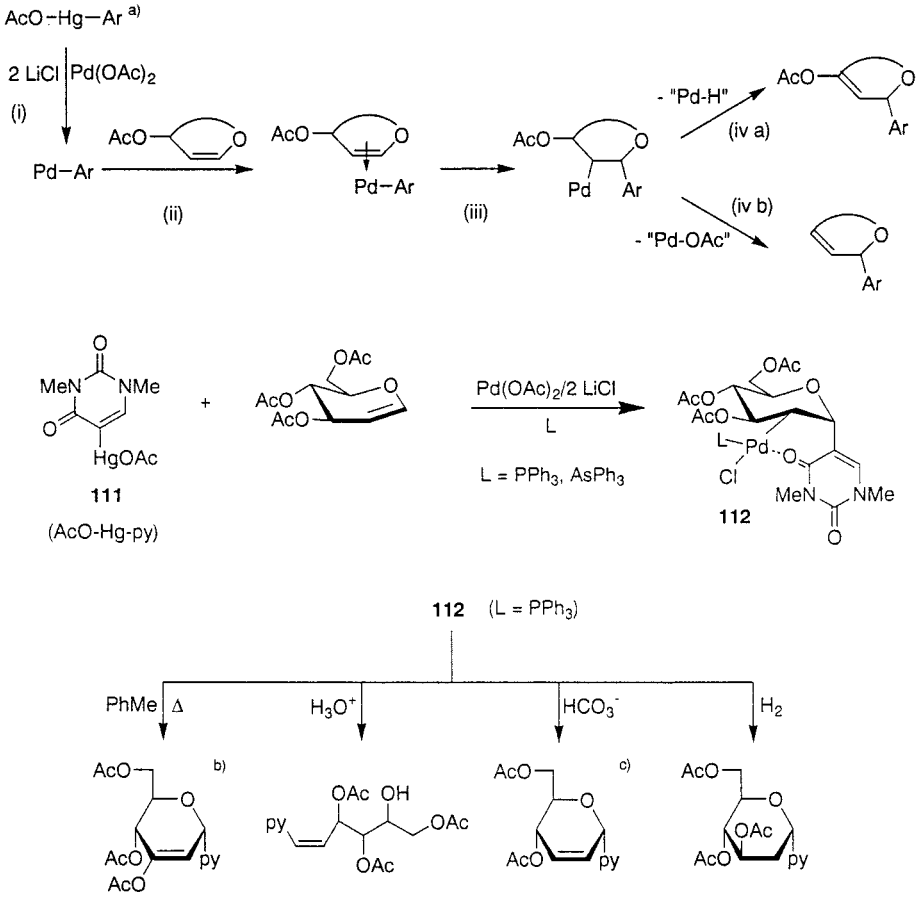
Scheme 19



racemization at C1 yielding α- and β-anomers in a ratio of 47:53. In toluene the reaction proceeds only in the presence of azobis(isobutyrylnitrile) (AIBN) with UV irradiation. This coupled with the racemization at C1 points to a radical mechanism for the oxidative addition. Analogously, isopropylidene-protected 6-deoxy-6-iodo-α-D-galactopyranose reacts with $[Pt(\eta^2\text{-}C_2H_4)(PPh_3)_2]$ in toluene (without AIBN and UV irradiation) to give the σ-organoplatinum complex **109**. In solution, both complexes slowly decompose yielding $[PtX_2(PPh_3)_2]$ (X = Br, I). The trans structure of complexes **108** and **109** was determined by NMR spectroscopy.

The rhodium analogue of coenzyme B_{12}, 5′-deoxy-5′-adenosylrhodibalamin **110** (the equatorial corrinoid ligand is symbolized by square brackets), was

Scheme 20



a) Ar = aryl, heterocyclic, ...; ligand sphere on palladium is not shown.
b) Type iv a reaction. c) Type iv b reaction.

obtained in the reaction of the rhodium(I) complex with 5′-iodo-5′-deoxyadenosine as shown in Scheme 19.[75a] This complex was also obtained when *Propionibacterium shermanii* was grown in the absence of cobalt with chloro- or aquarhodibalamin as precursors. In the presence of HCN, both the axial base (5,6-dimethylbenzimidazole) and the organo group is cleaved from **110** to give dicyanorhodibalamin, adenine, and the cyanhydrin of D-erythro-2,3-dihydroxypent-4-enal. In the same reaction with the analogous methyl complex, the benzimidazole ligand is selectively cleaved off. Thus, the Rh−C bond in **110** is more susceptible to cyanide than that of the corresponding methyl complex. Electrophoretic behavior shows that at pH 2.5 a protonation of **110** takes place without cleavage of the organo group. An anti-vitamin B_{12} effect of these rhodium complexes was observed in both bacteria and human cells.[75]

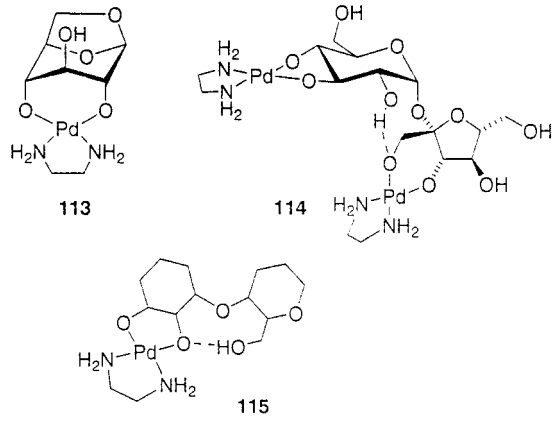
Facile syntheses of *C*-glycosides and *C*-nucleosides are based on palladium-mediated or -catalyzed coupling reactions of 1,2-unsaturated carbohydrates (glycals) with organopalladium reagents (Scheme 20).[76] These coupling reactions involve four steps: (i) formation of the organopalladium reagent from a precursor compound (this might be an organomercurial), (ii) π complex formation with the glycal double bond, (iii) insertion of the double bond into the Pd−C bond, and (iv) product formation by β-elimination.

The reaction of (1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)mercuric acetate **111** with 3,4,6-tri-*O*-acetyl-D-glucal mediated by $Pd(OAc)_2$/LiCl requires addition of PPh_3 or $AsPh_3$ to give stable glucopyranosylpalladium complexes **112**. These were fully characterized by NMR, IR, and UV spectroscopies as well as by FAB mass spectrometry (Scheme 20).[77] The reaction is stereospecific: the glycal ring is attacked by the intermediate pyrimidinedion-5-ylpalladium reagent from the face opposite the allylic (C3) substituent. Complexes **112** belong to the small class of stable σ-organopalladium complexes with *cis*-β-hydrogen atoms. The origin of stability is thought to lie in the conformational rigidity of the system (carbohydrate backbone and oxygen coordination of the pyrimidinedione).[77b] Complex **112** (L = PPh_3) reacts very selectively in refluxing toluene with (syn) β-hydride elimination. Alternately, with H_3O^+ and HCO_3^-, in water anti elimination of Pd^{II}/alkoxide and Pd^{II}/acetate occurs. Additionally, hydrogenolysis of the Pd−C bond is readily achieved (Scheme 20).[77a,78]

2. Carbohydrate Diolato Ligands

Strong alkaline aqueous solutions of $[Pd(OH)_2(en)]$ react with 1 equiv of 1,6-anhydro-β-D-glucose (levoglucosan) and $^1/_2$ equiv of sucrose to give palladium complexes **113** and **114**, respectively (Chart 17).[79] X-ray diffraction of complex **113**·H_2O shows that

Chart 17



levoglucosan acts as a 1,3-diolato ligand by bonding through O2 and O4. Due to formation of the six-membered dioxapallada chelate, the pyranose chair is distorted toward a boat conformation. The structural characterization of complex **114**·11H_2O (Figure 9) reveals a 4-fold deprotonated sucrose ligand. The

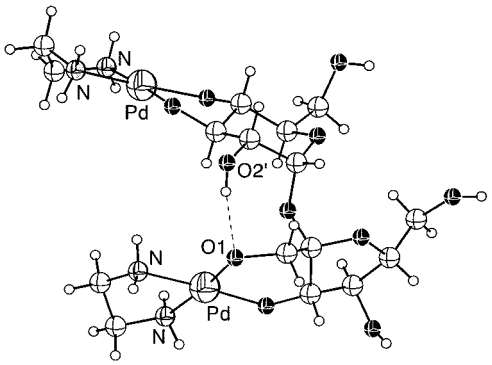


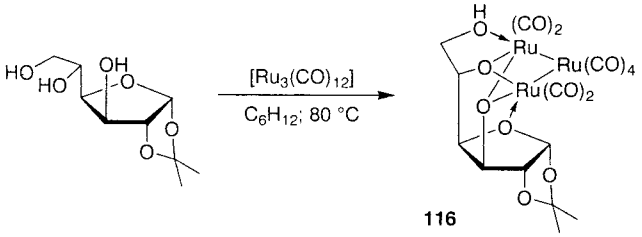
Figure 9. Molecular structure of complex **114**·11H_2O (Solvate molecules are not shown).[79b]

Pd(en) entities are bound to 1,2- (through O3′ and O4′ of the glucose moiety) and 1,3- (through O1 and O3 of the fructose moiety) diolate groups forming five- and six-membered dioxapallada chelate rings. The conformation of the disaccharide ligand is fixed by an intramolecular O2′−H···O1 hydrogen bond (O···O 2.657(6) Å). Compared with the uncomplexed sucrose (O···O 2.788 Å[80]), this hydrogen bond is strengthened by deprotonation of the acceptor and by fixing the direction of the O−H vector. Furthermore, in both complexes a network of hydrogen bonds including water molecules was found with O···O distances between 2.63 and 2.86 Å.

As ^{13}C NMR measurements show, the pattern of metal-binding sites found in the crystalline state of sucrose complex **114** is not the only possibility. In aqueous solutions, coordination through O4 and O6 of the fructofuranoside and through O2′ and O3′ of the glucopyranosyl unit may also occur.[79b] Aqueous solutions of [Pd(OH)$_2$(en)] provide a coordinating solvent for cellulose.[79,81] Cellulose samples of any degree of polymerization are dissolved. The maximum amount of cellulose dissolved in a given quantity of [Pd(OH)$_2$(en)] is in accord with 1:1 complexation (1 Pd per anhydroglucose monomer). DFT calculations on a truncated metalated cellulose complex **115**·4H_2O (Chart 17) show geometrical parameters of the minimum-energy structure close to those of the corresponding structural unit in **114**·11H_2O.[79b]

The ruthenium cluster [$Ru_3(CO)_{12}$] reacts with 1,2-*O*-isopropylidene-α-D-glucofuranose forming complex **116** (yield 40%) in which two deprotonated hydroxyl groups bridge two ruthenium centers (Scheme 21).[82]

Scheme 21



X-ray crystal-structure analysis of **116**·H_2O shows that there is no bond between these two ruthenium atoms (Ru···Ru 3.002 Å; Ru−O av. 2.146 Å) (Figure 10). Furthermore, the furanose oxygen atom and the

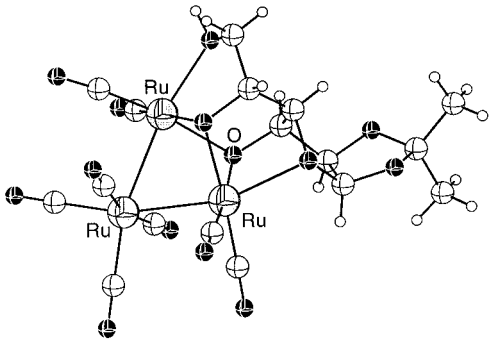


Figure 10. Molecular structure of [$Ru_3(CO)_8$L]·H_2O (H_2L = 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) (**116**·H_2O) (Water molecule is not shown).[82]

hydroxyl group at C6 are coordinated at ruthenium (2.256/2.377 Å). Starting from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, the same complex was obtained, although in lower yields (<25%). Complex **116** was used as precatalyst for hydrogenation reactions.

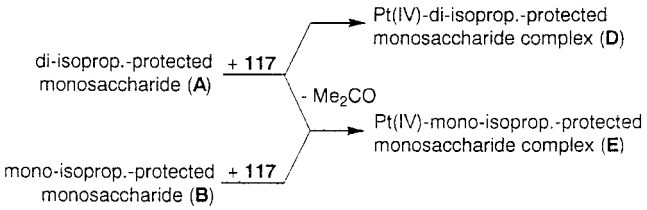
B. Neutral Carbohydrate Ligands

1. Platinum(IV) Complexes with Monoprotected Carbohydrate Ligands

The trimethylplatinum(IV) cation has three free coordination sites at its disposal for facially coordinating tridentate carbohydrate ligands. The tris(acetone) complex with BF_4^- as a weakly coordinating anion, [$PtMe_3(Me_2CO)_3$]BF_4 (**117**), is monomeric in the solid state[83] and quite soluble in acetone, a weakly donating solvent. Complex **117** reacts with di-*O*-isopropylidene-protected monosaccharides (**A**) in anhydrous acetone with or without the loss of an isopropylidene group to give platinum(IV) complexes with mono- (**E**) or di- (**D**) isopropylidene-protected carbohydrate ligands. Type **E** complexes can also be obtained directly from the monoprotected carbohydrates (**B**) (Scheme 22).

Corresponding reactions are shown in Scheme 23. Reactions **118A** → **118E** and **119A** → **119E** are

Scheme 22



accompanied by the cleavage of one isopropylidene group, with the platinum coordinating to the liberated hydroxyl groups and to a third hydroxyl group or oxygen donor if functionalized monosaccharides are used (coordination mode, 3 × OH or 2 × OH + O_{ester}). Reactions **118B** → **118E** and **120B** → **120E** proceed without the loss of a protecting group. In the α-D-xylofuranose complex **120E**, the carbohydrate ligand coordinates via its two OH groups, presumably since these are the strongest donor sites. The ring oxygen of the furanose also participates in metal binding (coordination mode, 2 × OH + O_{ring}).[84]

During the complex formation (Scheme 23), one of the two isopropylidene groups is lost as acetone, presumably due to the presence of trace amounts of water in the reaction mixture. This reaction is platinum-promoted as shown in the conversion **118A** → **118E** (L = 1,2-*O*-isopropylidene-α-D-glucofuranose). Adding water to the reaction mixture immediately effects cleavage of L from the complex and formation of $[PtMe_3(H_2O)_3]BF_4$. No further cleavage of the isopropylidene group from nonreacted L′ (1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose) takes place. Significantly, with an excess of L′, the isopropylidene group of the surplus sugar is not cleaved.[84a]

The rate constants for the hydrolysis reactions **118A** → **118E** and **119A** → **119E** (Scheme 23) point to an initial monodentate coordination of the ligand L′ through the functional group at C3 (**118**) and C1 (**119**), respectively. Hydrolysis is facilitated by the coordination of water (the resulting acidity of water is estimated to increase by as much as 13 orders of magnitude[85]), which positions the proton donor near the acetal oxygen of the protecting group (Chart 18, intermediate **A**). Alternatively, an additional coordination of L′ through the acetal oxygen of the protecting group (Chart 18, intermediate **B**) could occur, resulting in enhanced electrophilicity of the acetal carbon. In the latter case, both effects may play a role (Chart 18, intermediate **B′**). The importance of the precoordination of L′ through the functional group at C3 can be derived from the order of reactivity: (i) the weakest donor groups on C3 (OSO_2Me, OCOMe) react more slowly than those with stronger donating hydroxyl groups and (ii) 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (precoordination would be possible through C1−OH, which would not position platinum near a acetal oxygen) does not react with $[PtMe_3(Me_2CO)_3]BF_4$ (**117**).[84b]

The very weak coordination of the ether oxygen of the acetoxy substituent at C3 in complex **118E** (L = 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose) is evident in the reaction shown in Scheme 24.[86] In wet

Scheme 23

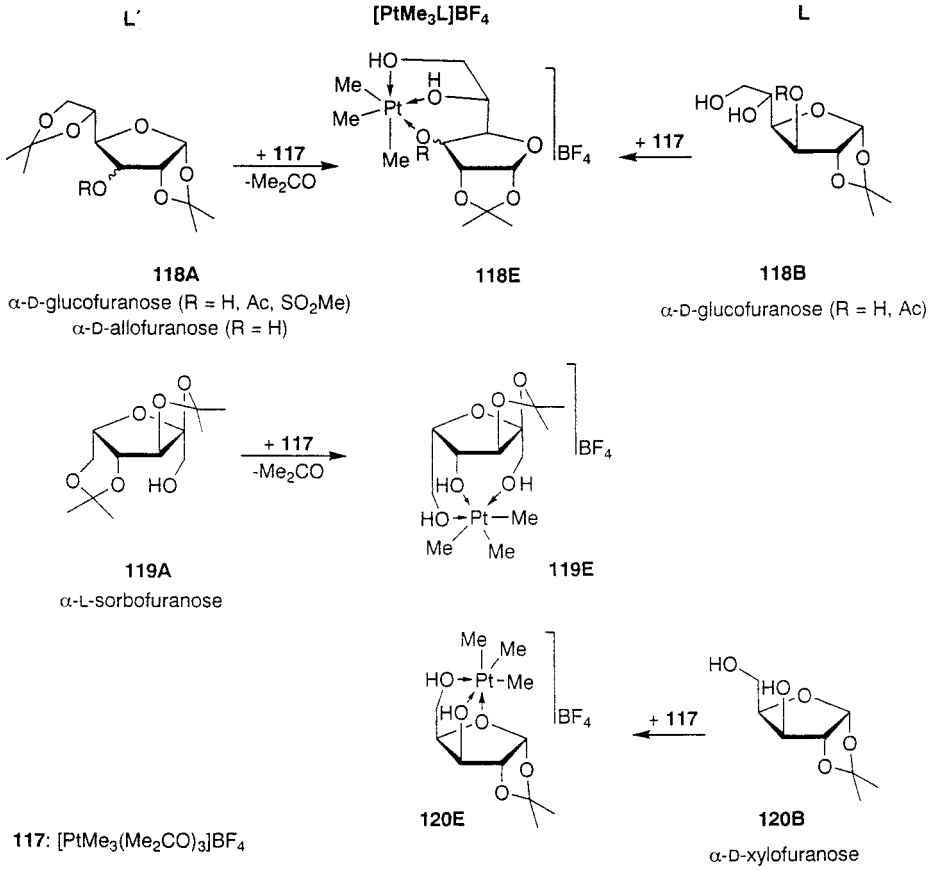
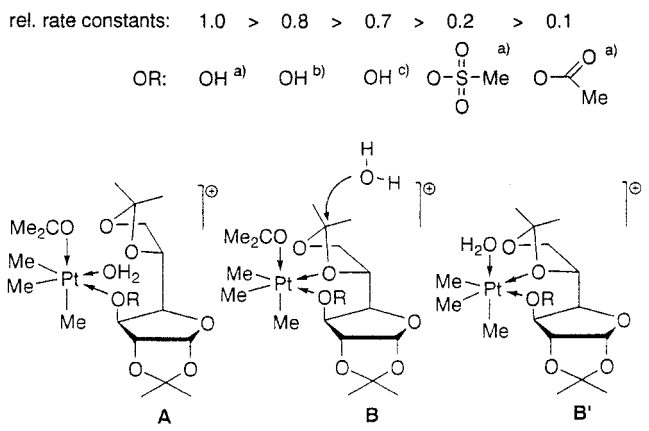
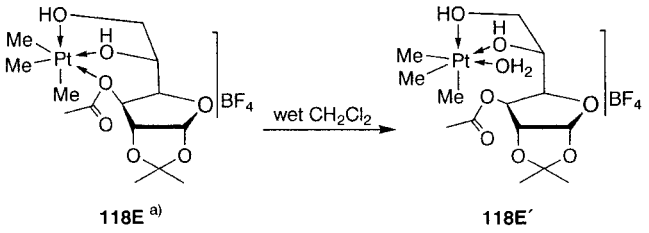


Chart 18



a) α-D-glucofuranoses **118**. b) α-L-sorbofuranose **119** (precoordination via C1-OH). c) α-D-allofuranose **118**.

Scheme 24



a) cf. Scheme 23 (**118E**, R = Ac)

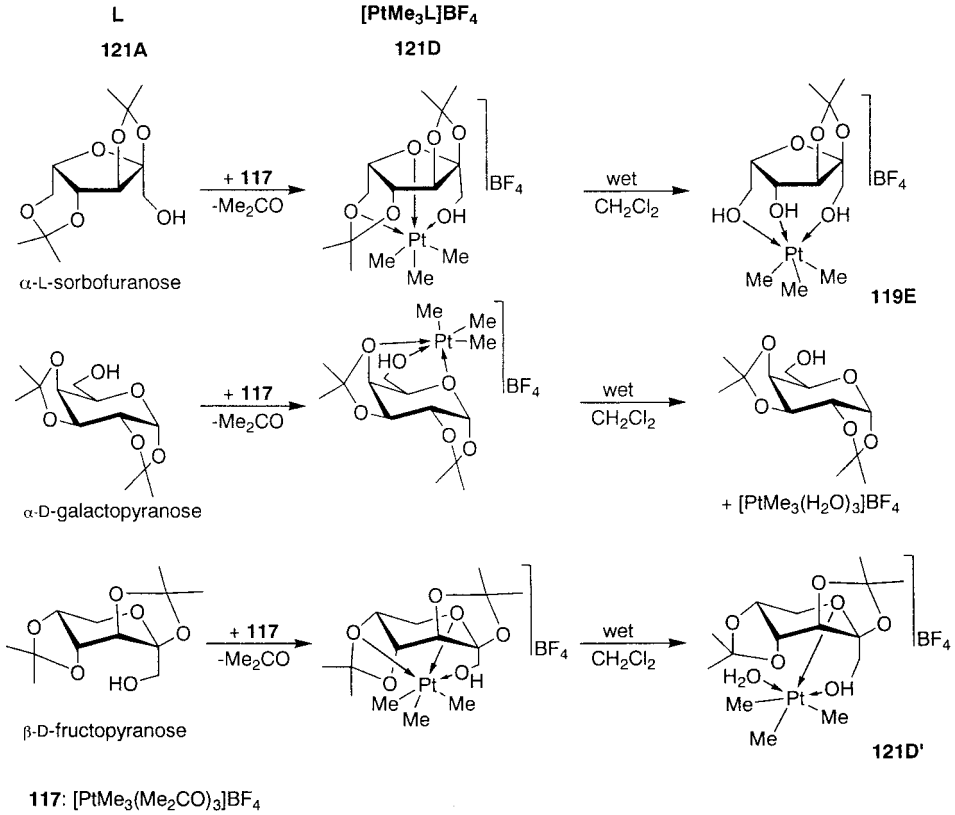
methylene chloride, the weakest of the three oxygen donors is replaced by the stronger donating aqua ligand forming complex **118E′**·H_2O. In this complex, the carbohydrate ligand is only bidentately bound through two OH groups (coordination mode, 2 × OH). Interestingly, this coordination is so stable that the carbohydrate ligand is not cleaved off by the additional water molecule present in the complex.[86]

2. Platinum Complexes with Diprotected Carbohydrate Ligands

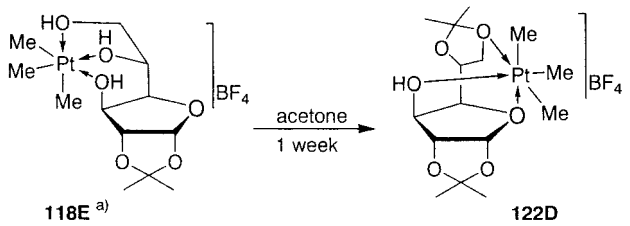
The di-*O*-isopropylidene-protected monosaccharides may also react with the tris(acetone)platinum complex **117** without accompanying cleavage of an isopropylidene protecting group (Scheme 25). In complexes **121D**, the carbohydrate ligands coordinate through one hydroxyl group and two weaker donors, namely, the ring oxygen of the furanose or pyranose ring and an acetal oxygen of an isopropylidene group (coordination mode, 1 × OH + O_{ring} + O_{acetal}).

Complexes **121D** are highly air- and moisture-sensitive. In wet methylene chloride, the sorbofuranose complex reacts with the loss of one isopropylidene group to give complex **119E** (L = 2,3-*O*-isopropylidene-α-L-sorbofuranose), in which the carbohydrate ligand coordinates via three hydroxyl groups. In contrast, dissolving the galactopyranose complex in wet methylene chloride results in the cleavage of the carbohydrate ligand without cleavage of a protecting group. Dissolution of the fructopyranose complex in wet methylene chloride yields complex **121D′** in which the ligated acetal oxygen atom of the isopropylidene group is replaced by an aqua ligand without deprotection of the carbohydrate. Thus, complex **121D′** exhibits a unique coordination mode (1 × OH + 1 × O_{ring}): the carbohydrate ligand is exclusively bidentately coordinated via a relatively strong OH donor and a weaker pyranose oxygen.[84b]

Scheme 25



Scheme 26



118E [a] **122D**

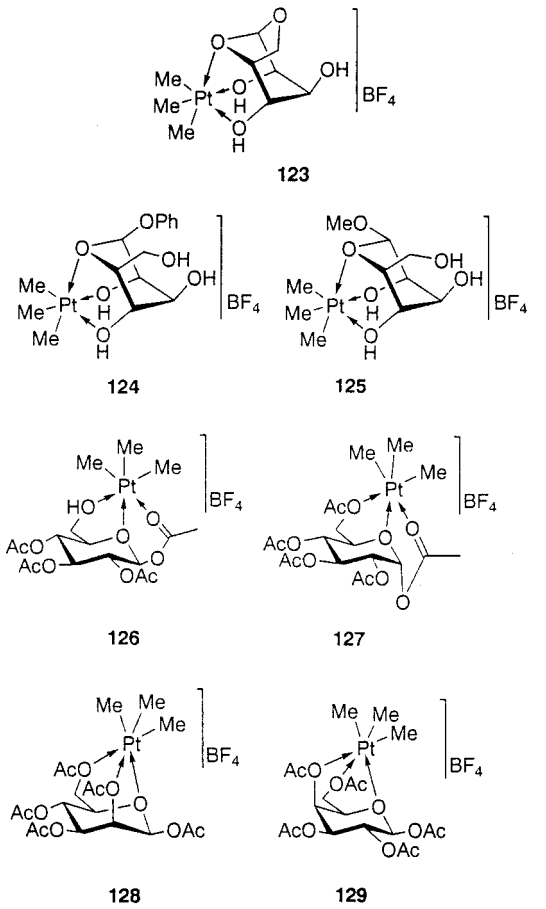
a) cf. Scheme 23 (**118E**, R = H)

As demonstrated in Scheme 26, platinum-promoted isopropylidenation represents a route to prepare platinum(IV) complex **122D** with a diprotected carbohydrate ligand. The coordination mode ($1 \times OH + 1 \times O_{ring} + 1 \times O_{acetal}$) is the same as that shown in complexes **121D**.[84b]

3. Platinum Complexes with Glucopyranoside and Acetylated Carbohydrate Ligands

Reactions of 1,6-anhydro-β-D-glucopyranose, 1-phenyl-β-D-glucopyranoside, and 1-methyl-α-D-glucopyranoside with the tris(acetone)platinum complex **117** afforded in moderate to good yields (40−81%) carbohydrate platinum complexes **123**−**125** in which the ligands are coordinated through two OH groups and the oxygen atom of the pyranose ring (Chart 19). The pyranoses are present in their unfavored $^1C_4$ ring geometry to provide relatively strong donating tridentate ligands (coordination mode, $2 \times OH + 1 \times O_{ring}$).[83]

Chart 19



123

124 **125**

126 **127**

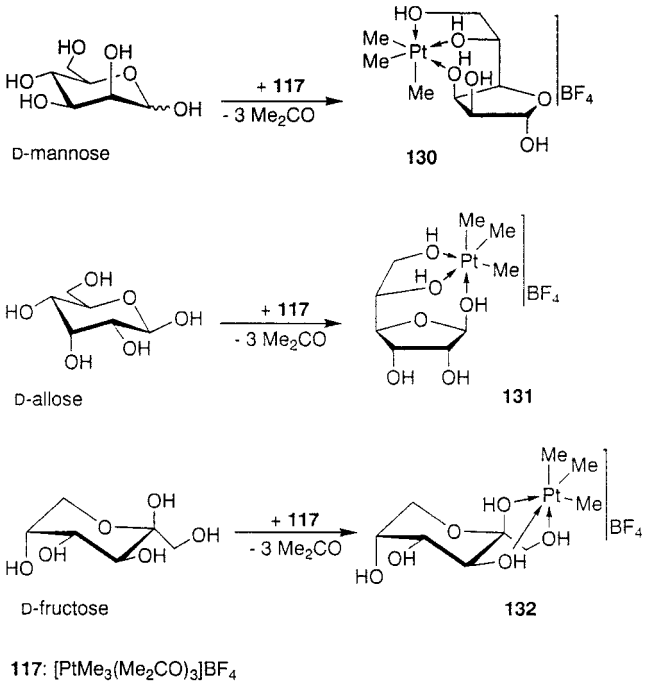
128 **129**

In 1,2,3,4-tetraacetyl-β-D-glucopyranose and in the peracetylated α-D-gluco-, β-D-manno-, and β-D-galactopyranoses, the $^4C_1$ conformation is preferred due to the space-demanding acetoxy groups. These carbohydrates were found to react with $[PtMe_3(Me_2CO)_3]BF_4$ (**117**) in acetone, yielding complexes **126**−**129** (Chart 19). NMR spectroscopic investigations show that in all these complexes the pyranose rings are present in their $^4C_1$ conformations. In complex **126**, the carbohydrate is coordinated through the hydroxyl group (the strongest donor site available), the pyranose ring oxygen atom, and the acetyl oxygen atom of the acetoxy substituent at C1 (coordination mode, $1 \times OH + 1 \times O_{ring} + 1 \times O_{ester/C(\mathbf{O})OR}$). The carbohydrate ligands in the other complexes **127**−**129** are coordinated through three relatively weakly donating oxygen atoms, namely, $1 \times O_{ring} + 1 \times O_{ester/C(O)\mathbf{O}R} + 1 \times O_{ester/C(\mathbf{O})OR}$ (**127**) and $1 \times O_{ring} + 2 \times O_{ester/C(O)\mathbf{O}R}$ (**128**, **129**), respectively.[87]

4. Platinum Complexes with Nonprotected Carbohydrate Ligands

Although nonprotected monosaccharides $C_6H_{12}O_6$ are insoluble in acetone, D-mannose, D-allose, and D-fructose react with complex **117** within 24 h to give carbohydrate complexes **130**−**132** (Scheme 27). Man-

Scheme 27



D-mannose **130**

D-allose **131**

D-fructose **132**

117: $[PtMe_3(Me_2CO)_3]BF_4$

nose and allose convert into furanoses upon complexation with *fac*-$[PtMe_3]^+$ moiety, through which sufficently strong coordination with three hydroxyl groups ($3 \times OH$) is achieved, namely, the two exocyclic hydroxyl groups at C5 and C6 and the hydroxyl group at C3 (**130**) and at C1 (**131**), respectively. Obviously, D-mannose and D-allose are not good *facial*-binding tridentate ligands in their pyranose forms. Addition of water to complexes **130** and **131** generates $[PtMe_3(H_2O)_3]BF_4$ and cleaves the carbohydrate ligands which in turn revert rapidly into the more thermodynamically stable pyranoses.

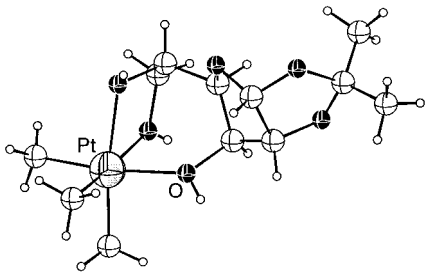


Figure 11. Molecular structure of the cation of $[PtMe_3L]BF_4$ (**118E**, L = 1,2-*O*-isopropylidene-α-D-glucofuranose).[84a]

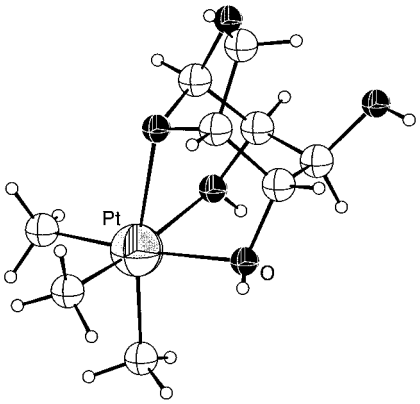


Figure 12. Molecular structure of the cation of $[PtMe_3L]BF_4$ (**123**, L = 1,6-anhydro-*β*-D-glucopyranose).[83]

Using the same reaction conditions to obtain **130**−**132**, D-glucose and D-galactose do not give complexes but rather reduction of platinum occurs.[88]

5. Characterization of Carbohydrate Platinum(IV) Complexes

All carbohydrate trimethylplatinum(IV) complexes **118**−**132** were isolated as white air- and moisture-sensitive powders or colorless crystals. These have been fully characterized by microanalysis and ^1H, ^{13}C, and ^{195}Pt NMR spectroscopy. The identities of complexes $[PtMe_3L]BF_4$ (**118E**, L = 1,2-*O*-isopropylidene-α-D-glucofuranose;[84a] **119E**, L = 2,3-*O*-isopropylidene-α-L-sorbofuranose;[84b] **123**, L = 1,6-anhydro-*β*-D-glucopyranose),[83] $[PtMe_3L(H_2O)]BF_4$ (**121D′**, L = 2,3;4,5-di-*O*-isopropylidene-*β*-D-fructopyranose),[84b] and $[PtMe_3L(H_2O)]BF_4 \cdot H_2O$ (**118E′**·H_2O, L = 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose)[86] were also confirmed by single-crystal X-ray diffraction analyses (see Figures 11−13 as examples). In the crystal structures of these complexes, there are strong cation−anion interactions via O−H···F hydrogen bonds. These might be essential for the marked tendency of these complexes to crystallize, which is unusual for carbohydrate−metal complexes. The facial coordination of the carbohydrate ligands in complexes **118E**, **119E**, and **123** results in bicyclic systems with 1,3,2-dioxaplatina rings. Especially in complexes **118E** and **123**, these systems are not free from angle strain; two of the three O−Pt−O angles are distinctly smaller (73.6(2)°−78.6(4)°) than 90°. The O−Pt−O angles in the 1,3,2-dioxaplatinacyclopentane rings of the complexes with bidentately coordinated carbohydrate ligands are 75.3(4)° (**121D′**) and 75.5(3)° (**118E′**·H_2O), respectively, pointing to marked ring strain. The reduced donor capability of the acetal oxygen atom versus the hydroxyl oxygen atoms in complex **123** is evident from the corresponding Pt−O bond lengths (2.288(4) vs 2.246(5)/2.248(5) Å).

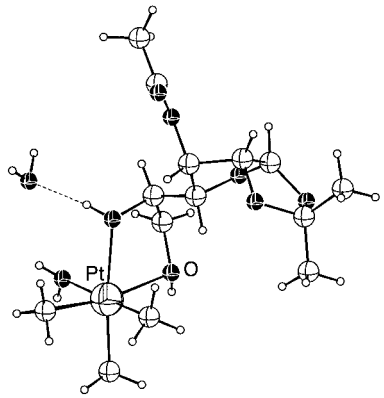


Figure 13. Molecular structure of the cation of $[PtMe_3L(H_2O)]BF_4 \cdot H_2O$ (**118E′**·H_2O, L = 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose).[86]

For the wide range of coordination modes of neutral nonfunctionalized carbohydrate ligands to platinum(IV), the following order of donor ability was derived: 3 × OH > 2 × OH + 1 × O > 1 × OH + 2 × O > 3 × O (O = O_{ring}, O_{ester}, O_{acetal}).[84b,87] As a consequence of the very weak donor characteristics of neutral carbohydrate ligands, coordination-induced NMR shifts are small in platinum(IV) complexes and ^{13}C chemical shifts are unreliable diagnostic probes of the coordination of the carbohydrate ligands. Useful information, however, was obtained from $^1H-^1H$ coupling constants as well as from $^{13}C-^{13}C$ and $^{13}C-^1H$ coupling constants which were readily measured in complexes with site-specific ^{13}C-labeled monosaccharide ligands (**118E**, L = 1,2-*O*-isopropylidene-α-D-glucofuranose; **130**, **131**). Evaluation of the $^{13}C-^{13}C$ couplings ^1J(C5,C6), ^2J(C4,C6), and ^3J(C3,C6) together with additional information from $^3J_{CH}$ and $^3J_{HH}$ allowed identification of the conformations of the exocyclic fragments $-C^5H(OH)-C^6H_2OH$ and their positions relative to the furanose rings. Finally, ^{13}C-labeling proved to be a powerful tool unambiguously to assign the coordination modes of the carbohydrate ligands in acetone solution.[84b,88a] Further support for the constitution of these complexes and the coordination mode of the carbohydrate ligands comes from ESI-MS analyses where, in nearly all cases, the mass peaks of the molecular cations $[PtMe_3L]^+$ (L = carbohydrate) were detected. The fragmentation of the isolated parent ions with isopropylidene-protected carbohydrate ligands proceeds either by loss of acetone or by reductive elimination of two methyl ligands from the platinum(IV) cation. This allows identification of the coordination mode.[83,84b]

IV. Sugar Alcohol and Sugar Acid Ligands

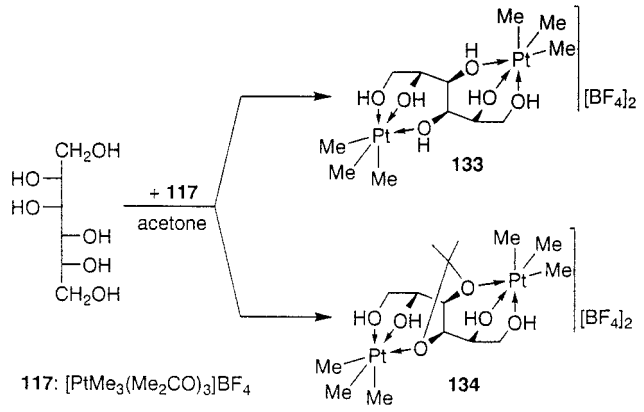
A. Sugar Alcohol Ligands

1. Sugar Alcohols without Donor Groups

Synthesis and characterization by single-crystal X-ray analysis of a platinum(II) complex with the most simple vicinal diol, $[Pt(HOCH_2-CH_2OH)\{1,2-$

$(PMePh)_2C_6H_4$-*P*,*P*'}]$(CF_3SO_3)_2$,[89] demonstrates that complexes of platinum-group metals with sugar alcohols are accessible. Thus, $[PtMe_3(Me_2CO)_3]BF_4$ (**117**) reacts with D-mannitol in acetone in a heterogeneous reaction yielding the expected bis(trimethylplatinum) complex **133** and complex **134**. The latter bears an isopropylidene protecting group whose formation is platinum-promoted (Scheme 28).[88b] As

Scheme 28

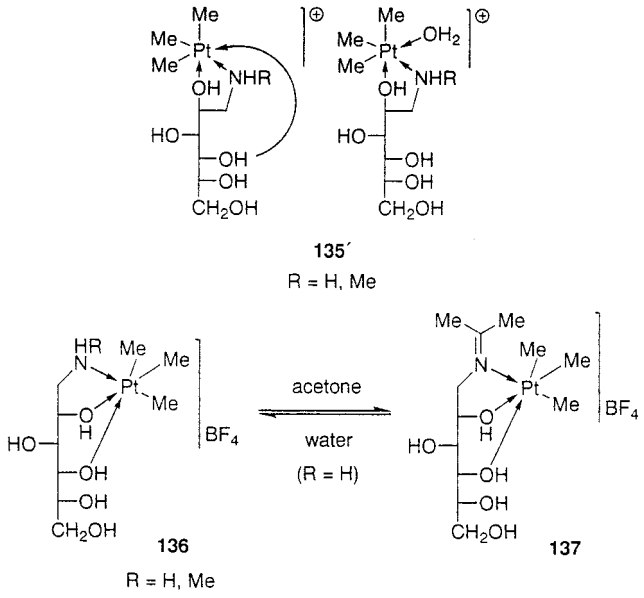


NMR spectroscopic investigations (^1H, ^{13}C, ^{195}Pt) show, the complexes are highly symmetric and the two platinum centers are bound via O1, O2, O4 and O3, O5, O6, respectively.

2. Sugar Alcohols with Donor Groups

As with 2-amino-2-deoxy-α-D-glucose (see Chart 4), $[\{PtMe_3(H_2O)_2\}_2SO_4]$ reacts in dilute aqueous solution with 1-amino- and 1-(*N*-methylamino)-1-deoxy-D-glucitol to give aminoglucitol complexes $[PtMe_3L]_2SO_4$ (**135**).[14] NMR spectroscopic investigations show that in aqueous solutions (**135′**, see Scheme 29) the

Scheme 29

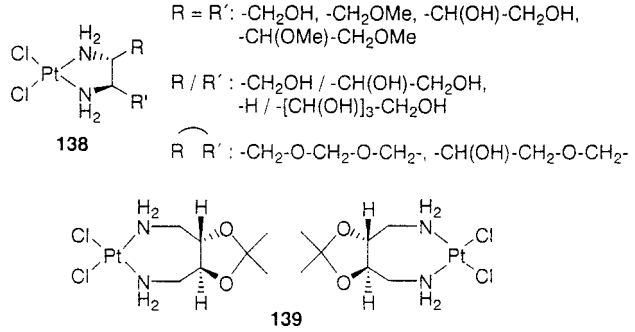


carbohydrate ligand is coordinated to platinum through the nitrogen atom and most likely through hydroxyl group at C2. The coordination sphere of platinum may be completed by the hydroxyl group at C4 or by an aqua ligand.

1-(*N*-Methylamino)-1-deoxy-D-glucitol was found to react in acetone with $[PtMe_3(Me_2CO)_3]BF_4$ (**117**), yielding the analogous complex $[PtMe_3L]BF_4$ (**136**, R = Me) (Scheme 29). In contrast to this, the reaction with 1-amino-1-deoxy-D-glucitol affords the glucoseimine complex **137**. Schiff-base formation proceeds most likely by a platinum-promoted mechanism. In water, the imino group is lost forming complex **136** (R = H). The reaction is thus reversible. As for complexes **135**, instead of the C4−OH completing the Pt coordination sphere, solvent (acetone, water) may be coordinated.[15]

Substitution of two vicinal hydroxyl groups in alditols by amino groups results in substituted ethylenediamine ligands that readily form cisplatin-type complexes in reaction with $K_2[PtCl_4]$. Thus, complexes **138** with stereochemically defined diamino−dideoxy−alditols have been prepared. In the same way, complexes with *O*-methylated and methylene-protected alditols were obtained (Chart 20).[18,19,90]

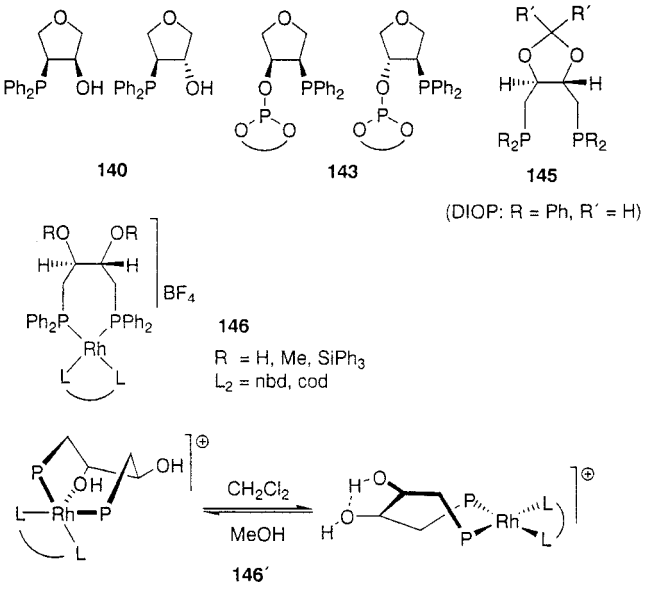
Chart 20



Complexes **138** with R = R′ are C_2 symmetrical. The molecular structure of complex **138**·H_2O (R = R′ = CH(OH)−CH_2OH) was determined by single-crystal X-ray analysis.[90d] Substitution of terminal hydroxyl groups in threitol by amino groups affords 1,4-diaminobutane-type ligands. Reactions of the 2,3-*O*-isopropylidene-protected derivatives with $K_2[PtCl_4]$ in aqueous solution resulted in formation of the enantiomeric pair of complexes **139** (Chart 20).[90c] Antitumor activity of the cisplatin-type complexes and their molecular interaction with nucleotides and DNA have been investigated.

Related to sugar alcohols are ligands derived from phosphorus-substituted tetrahydrofuranols and 1,3-dioxolanes. Some representatives are shown in Scheme 30. *cis*- and *trans*-3-diphenylphosphino-4-hydroxytetrahydrofuran (**140**) form mononuclear and dinuclear rhodium cyclooctadiene complexes [Rh(cod)(*cis*-P⌒O)]BF_4 (**141**) and [{Rh(cod)(*μ-trans*-P⌒O)}$_2$]$(BF_4)_2$ (**142**) (P⌒O = **140**), respectively.[91] Rhodium complexes with chiral 3-phosphine-4-phosphite−tetrahydrofuran ligands **143**, $[Rh(CO)_2(P⌒P)]^+$ (**144**, P⌒P = **143**), were prepared by reaction of $[Rh(acac)(CO)_2]$ with the diastereomeric pair of ligands **143**. Surprisingly, in asymmetric hydroformylation reactions, the isolated complexes **144** are poorer catalysts than the in situ mixtures $[Rh(acac)(CO)_2]$/**143**.[92] DIOP-type ligands **145**, among them water-soluble and polymer-

Scheme 30



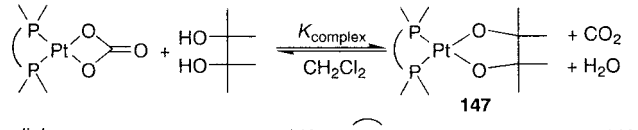
bound derivatives, were extensively used in rhodium-, palladium-, and ruthenium-catalyzed enantioselective hydrogenation, hydroformylation, hydrosilylation, and hydrocyanation reactions.[38,44,93]

Analogous to DIOP, 1,4-bis(diphenylphosphino)-butane-2,3-diols form rhodium complexes [Rh(Ph_2-PCH_2−CH(OR)−CH(OR)−CH_2PPh_2-*P,P′*)L_2]BF_4 (L_2 = cod, nbd) (**146**). Single-crystal X-ray analyses of complexes **146′** (R = H, L_2 = nbd) and **146″** (R = Me, L_2 = cod) revealed a key issue. In the **146′** case, a strong interaction between one of the enantiotopic hydroxyl groups with rhodium (Rh···O 2.396 Å) was found (Scheme 30).[94] ^{31}P NMR experiments made clear that in solution this interaction is strongly dependent on the solvent and the ligands L. Tripodal *P,P,O*-coordination was found in CD_3OD but not in CD_2Cl_2 (see Scheme 30) and with ligands L_2 = norbornadiene, (*Z*)-*N*-acetylaminocinnamate but not with L = MeOH.[95] In asymmetric hydrogenation reactions, complex **146′** proved to be less active but afforded higher enantioselectivities than those observed with **146″**. These observations could be rationalized by the hemilabile coordinating OH group (tripodal *P,P,O*- vs bidentate *P,P*-coordination).[94,95,96]

3. Diolato Ligands

Treatment of bis(phosphine)carbonatoplatinum(II) complexes[97] with polyols containing at least one vicinal diol moiety gives equilibrium conversion to the corresponding diolato complexes **147** (Scheme 31). Product formation can usually be driven to completion by utilizing a modest excess of diol and argon purge.[98] In this manner, many type **147** dppp complexes derived from diols (ethane-1,2-diol, propane-1,2-diol, D- and *meso*-butane-2,3-diol, *cis*- and *trans*-cyclohexane-1,2-diol, pinacol, phenylethane-1,2-diol, 3-methoxypropane-1,2-diol), triols (glycerol, butane-1,2,4-triol), and alditols (erythritol, DL-threitol, ribitol, xylitol, galactitol, D-mannitol) were prepared. This route is superior to the synthesis of diolato complexes via alcohol exchange reaction from diols with [Pt-$(OR)_2L_2$] (L = *P*-donor; R = alkyl). These bis(alcoholato) complexes are water-sensitive and readily undergo β-hydrogen elimination resulting in limited stability at room temperature. Conversley, the carbonato complexes are stable to air and water at room temperature.

Scheme 31



diol	rel *K*
2,2-dimethylpropane-1,3-diol	ca 1
pinacol	100
trans-cyclohexane-1,2-diol	100
meso-butane-2,3-diol	300
D-butane-2,3-diol	700
cis-cyclohexane-1,2-diol	700
propane-1,2-diol	800
ethane-1,2-diol	1000
phenylethane-1,2-diol	8000

P P	rel *K*
2 PPh_3	300
Cy_2P-$(CH_2)_2$-PCy_2	500
Ph_2P-$(CH_2)_3$-PPh_2 (dppp)	1000
$(p\text{-tol})_2P$-$(CH_2)_3$-$P(p\text{-tol})_2$	3000
Ph_2P-$(CH_2)_2$-PPh_2 (dppe)	8000
Ph_2P-CH=CH-PPh_2	20000

rel *K*: Relative complexation constants (K_{cmplx}) as a function of diol (for dppp as reference phosphine; *K* = 1000 for ethanediol) and of phosphine (for ethanediol as reference diol; *K* = 1000 for dppp complex), respectively.[98]

The solid-state structure of the D-mannitolato-O^3,O^4 complex **147** was determined by X-ray crystallography (Figure 14a).[98] The five-membered PtO_2C_2 ring exhibits a twist conformation with two axially disposed dihydroxyethyl substituents (Figure 14b). The striking feature of the structure is the formation of strong intramolecular hydrogen-bonding interactions as shown in Figure 14c (O1···O3 2.66(2) Å, O4···O5 2.65(2) Å, O3···O6 2.65(2) Å). The conformation of complexes **147** in solution was studied by

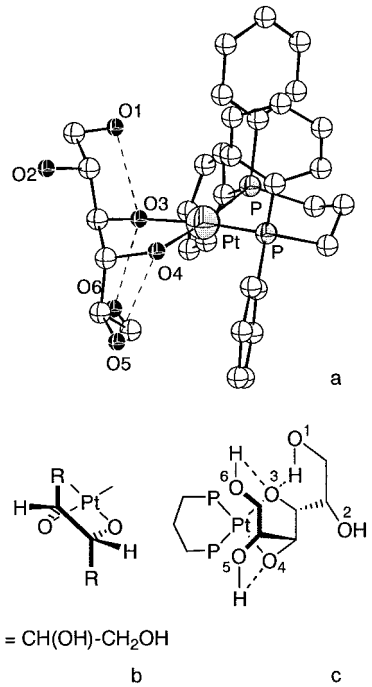
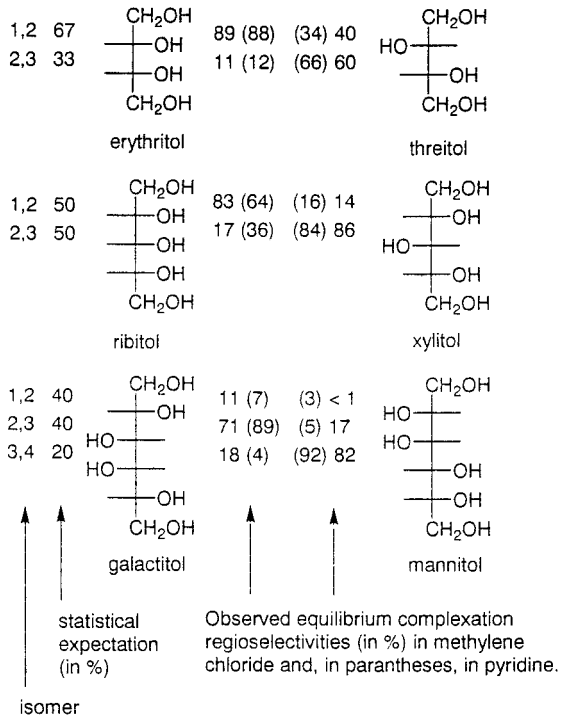


Figure 14. (a) Molecular structure of bis(diphenylphosphino)propane-(3,4-D-mannitolato)platinum (**147**·CH_2Cl_2) (Methylene chloride is not shown; H atoms are omitted).[98] (b) Illustration of the 1,3,2-dioxaplatinacyclopentane ring and substituent geometry.[98] (c) Schematic of X-ray structure showing intramolecular O−H···O hydrogen bonds.[99]

NMR spectroscopy (^{1}H, ^{13}C, ^{31}P, ^{195}Pt) using Karplus-type dihedral angle dependencies.[98,99] From this it follows that strong hydrogen bonds are the predominant feature of these complexes in solution.

From (intermolecular) competition experiments, relative diol complexation constants were determined as a function of both the diol and the phosphine ligands (Scheme 31). 1,2-Diol chelation is favored over 1,3-diol chelation by 2−3 orders of magnitude (first entry in Scheme 31). Complexation of polyols provides an intramolecular selectivity competition (Chart 21).[98,99] In polyols, complexation is favored at

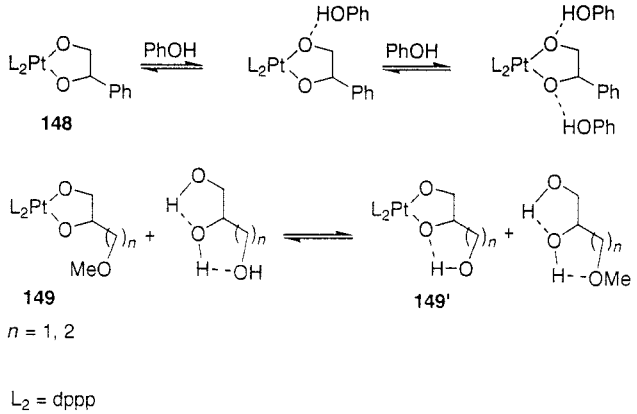
Chart 21



threo versus erythro diol units (preference for ax/ax over ax/eq substitution in 1,3,2-dioxaplatinacyclopentane rings, see Figure 14b). When an internal threo linkage is not available, complexation occurs preferentially at the terminal nonstereogenic diol. Furthermore, complexation is favored in positions that lead to preferential dihydroxyethyl versus hydroxymethyl side chains of the metallacycle. These preferences reflect stabilization by (intramolecular) hydrogen bonds as shown in Figure 14c, which can be formed with axial hydroxyalkyl substituents. Importantly, these interactions are stronger when large hydrogen-bonded rings (more linear O−H···O bonds) are formed.[99] Substituents without hydroxyl groups (methyl, *tert*-butyl, phenyl) on the 1,3,2-dioxaplatinacyclopentane scaffold favor equatorial placement as opposed to axial placement.

Thermodynamic data for intermolecular hydrogen-bonding association of 1 and 2 equiv of phenol with phenylethane-1,2-diolato complex **148** and for competitive coordination exchange reactions with complexes **149** in methylene chloride and pyridine (Scheme 32) provide the basis for understanding the role of hydrogen bonding in determining the complexation properties of alditols to $(P\frown P)Pt^{II}$.[99] The

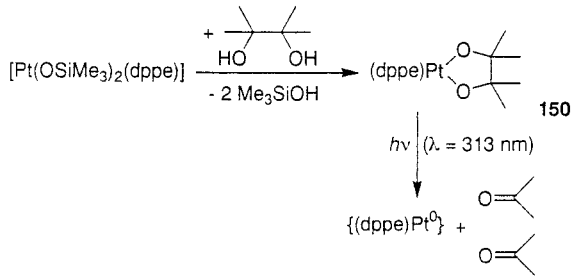
Scheme 32



regioselectivities for alditol complexation may depend on solvent (Chart 21). When all hydroxyl groups are involved in intramolecular hydrogen bonds, the isomer ratios are generally independent of solvent. Regioisomers having hydroxyl groups that are geometrically precluded from participating in intramolecular hydrogen bonding form new *inter*molecular hydrogen bonds to pyridine. This leads to lower energies for these isomers relative to those not capable of such interactions. Thus, regioselectivity may be dictated by choice of solvent.[99]

Glycolato complexes **150** were prepared from vicinal diols (ethane-1,2-diol, propane-1,2-diol, hexane-1,2-diol, dodecane-1,2-diol, pinacol, 1,2:5,6-di-*O*-isopropylidenemannitol) and $[Pt(OSiMe_3)_2(dppe)]$ in good yields (Scheme 33).[100] Due to the high stability

Scheme 33

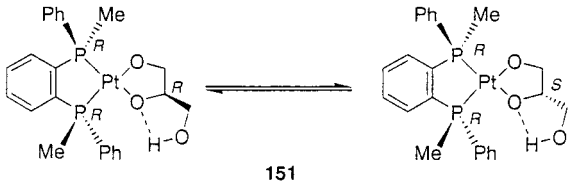


of $[Pt(OSiMe_3)_2(dppe)]$, this procedure offers an alternative to the carbonate route depicted in Scheme 31. Complexes **150** are thermally robust and relatively stable toward both air and water. Photolysis results in [2 + 2 + 2] redox cycloreversion with formation of aldehydes/ketones. Evidence for the $(dppe)Pt^0$ intermediate was provided by trapping experiments utilizing ethylene, H_2, or dppe which gave $[Pt(\eta^2\text{-}C_2H_4)(dppe)]$, $[PtH_2(dppe)]$, or $[Pt(dppe)_2]$, respectively. Carrying out the reactions in the presence of H_2, no hydrogenation of aldehydes or ketones takes place. When a hydrogenation catalyst ($[RuH_2(PPh_3)_4]$) is added, hydrogenation takes place as shown in the reaction with the 1,2:5,6-di-*O*-isopropylidenemannitolato-O^3,O^4 complex yielding 1,2-*O*-isopropylideneglycerol in 84% yield. This may be considered as a first step for the development of a catalytic cycle for effecting hydrocracking of carbohydrate C−C bonds.[100]

Glycerolato-O^1,O^2-platinum(II) complexes can be used as chiral glycerol synthons. Thus, the complex

(*R**,*R**)-(±)-[Pt(OMe)$_2${1,2-(PMePh)$_2$C$_6$H$_4$}] (asterisked sterochemical descriptors are used here for racemates) in benzene/methanol reacts with 1 equiv of glycerol to give a solution of diastereoisomeric glycerolato complexes **151** with 3:2 diastereoselectivity (Scheme 34).[101] By NMR spectroscopy, a relatively small concentration of the non-hydrogen-bonded forms of the diastereoisomers (not shown in Scheme 34) was also detected. In a typical second-order asymmetric transformation, a pure diastereoisomer (95% of substance), namely, [(*R**,*R**),(*R**)]-(±)-(**151**)·2MeOH, crystallizes from solution. Upon dissolution in CD_2Cl_2, the bis(methanol) solvate rearranges with redistribution of glycerolato ligands (even at −90 °C) into a 3:2 equilibrium mixture of diastereoisomers. This interconversion may occur via intermolecular (by redistribution of glycerolato ligands) or intramolecular (by site exchange of the terminal oxygen atoms) interactions. The solid-state structure of [(*R**,*R**),(*R**)]-(±)-(**151**)·2MeOH shows centrosymmetric dimers via hydrogen bridges (O···O 2.666(8) Å) between asymmetric monomers of opposite helicity (Figure 15). The enantiomers of **151** (prepared from (*R*,*R*)-(+)- and (*S*,*S*)-(−)-[Pt(OMe)$_2${1,2-(PMePh)$_2$-C$_6$H$_4$}], respectively) have considerable potential for asymmetric synthesis.[101]

Scheme 34



Only one enantiomer of each diastereoisomer is shown.

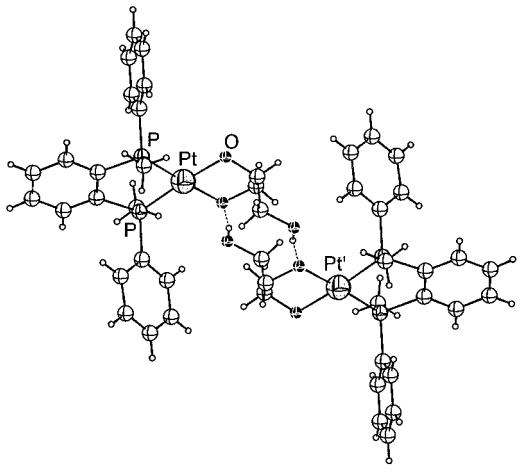


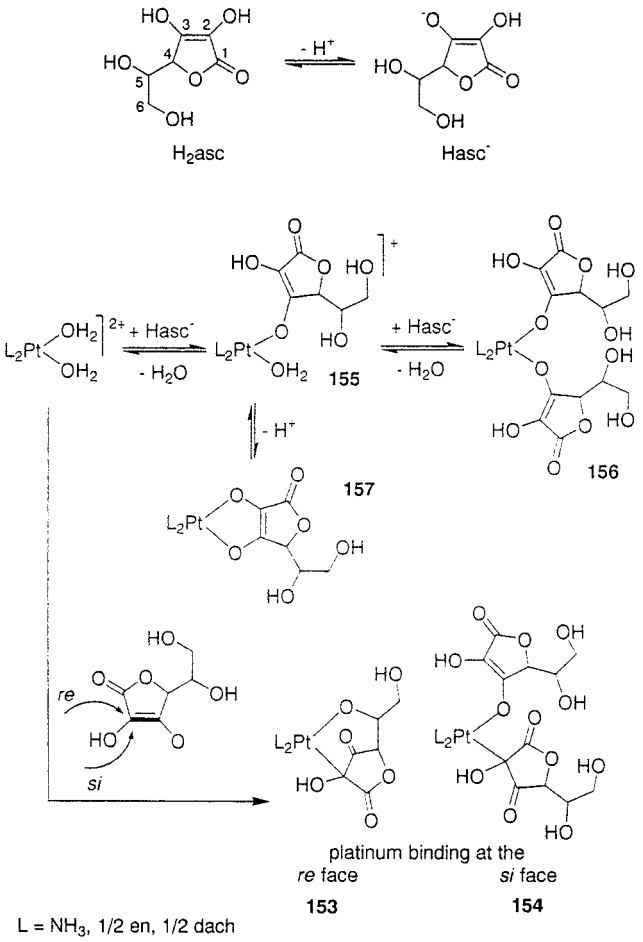
Figure 15. Molecular structure of [(*R**,*R**),(R*)]-(±)-(**151**)·2MeOH showing dimer formation in the solid state (Solvate molecules are not shown).[101]

As with 1,6-anhydro-β-D-glucose and sucrose (see Chart 17), anhydroerythriol reacts with strong alkaline aqueous solutions of [Pd(OH)$_2$L$_2$] (L$_2$ = en, bpy) to give *meso*-oxolane-3,4-diolatopalladium complexes [Pd(C$_4$H$_6$O$_3$-*O*,*O*')L$_2$] (C$_4$H$_6$O$_3$-*O*,*O*' = *meso*-oxolane-3,4-diolato(2−)-κ^2*O*,*O*'; L$_2$ = en, bpy) (**152**). The crystal structure analyses of **152**·*n*H$_2$O (L$_2$ = en, *n* = 4; L$_2$ = bpy, *n* = 6.5) show the expected square-planar geometry at Pd with a chelating diolato(2−) ligand.[79b,102] Similarly, *cis*-[Pt(OH)$_2$(NH$_3$)$_2$] reacts with D-mannitol yielding a 2:1 complex with a mannitolato(4−) ligand that is symmetrically coordinated to two Pt(NH$_3$)$_2$ units probably by vicinal diolate units.[103]

B. Sugar Acid Ligands

Acidity of L-ascorbic acid (H$_2$asc; vitamin C), the lactone version of a sugar acid, is based on its enediol structure (Scheme 35). Diaminediaquaplatinum(II) complexes *cis*-[Pt(NH$_2$R)$_2$(H$_2$O)$_2$](NO$_3$)$_2$ (2NH$_2$R = 2NH$_3$, en, dach) react with ascorbic acid or sodium ascorbate in aqueous solutions yielding diamineplatinum(II) ascorbato complexes. The chemistry is quite complex, with the distribution of products being a function of amine ligands, reagent stoichiometry, pH, and time.[104]

Scheme 35



The reaction of *cis*-[Pt(*cis*-dach)(H$_2$O)$_2$](NO$_3$)$_2$ with sodium ascorbate affords three major products, namely, two isomeric forms of a monoascorbato complex [Pt(asc-*C*^{2},*O*^{5})(*cis*-dach)]·3H$_2$O (**153**/**153′**) and a bis(ascorbato) complex [Pt(Hasc-*C*^{2})(Hasc-*O*^{3})(*cis*-dach)]·2H$_2$O (**154**). The bis(ascorbato) complex is less stable and slowly converts in aqueous solution to the mixture of complexes **153**/**153′** and ascorbic acid. The structure of **153** (L = *cis*-dach) was unequivocally confirmed by single-crystal X-ray analysis (Figure

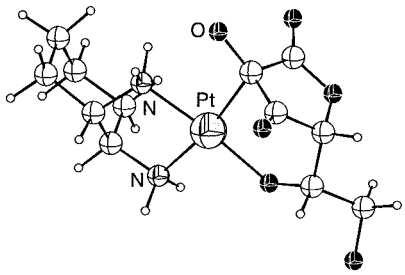


Figure 16. Molecular structure of [Pt(asc-C^2,O^5)(*cis*-dach)]·$3H_2O$ (**153**) (OH protons and water are not shown).[104a]

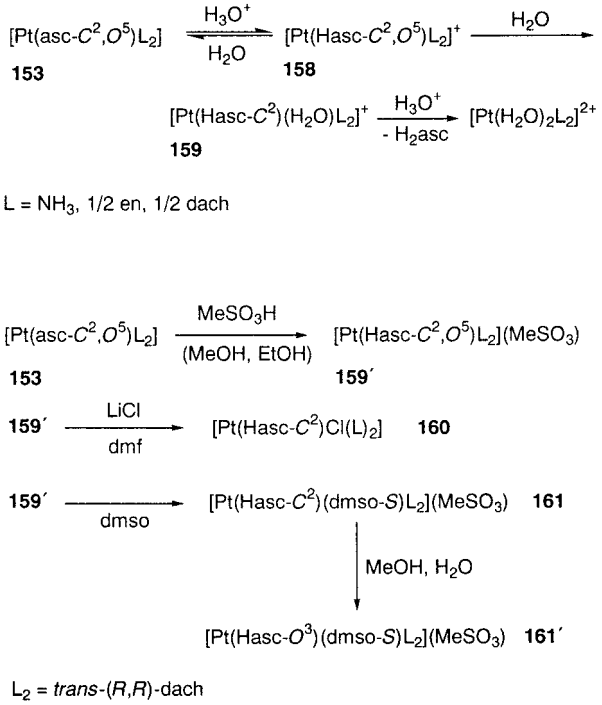
16).[104a] The dianionic ascorbato ligand is bound to platinum through C2 and the deprotonated O5. Thus, the ligands (asc-C^2,O^5) and (Hasc-C^2) can be viewed as carbon-bound α-hydroxy-β-diketonato ligands. Such bonding has been observed in a number of acetylacetonato platinum complexes.[105] As expected, the organo group exerts a greater trans influence than the alcoholate group. Thus, the Pt−N bond distance trans to C2 is 0.05(1) Å longer than the corresponding bond length trans to O5. In accordance with this, quantum chemical calculations of model complexes reveal dissociation energies $Pt-N_{trans-O} > Pt-N_{trans-C}$ and Pt−C > Pt−O.[104b] As X-ray analyses show, the corresponding *trans*-dach complex [Pt(asc-C^2,O^5)(*trans*-dach)]·$3H_2O$[106] and the diammine complex [Pt(asc-C^2,O^5)$(NH_3)_2$]·$2H_2O$[107] have analogous structures.

Further insight into diamineplatinum(II) ascorbato complexes came from time-dependent ^{195}Pt and ^{13}C NMR investigations of the reaction between [Pt([1,2-$^{15}N_2$]en)$(H_2O)_2$]$(NO_3)_2$ with sodium ascorbate (Scheme 35).[104c] During the initial stage of the reaction (t < 1 h), mainly oxygen-bound ascorbato complexes are formed. Two complexes of the ascorbate monoanion ([Hasc-O^3]$^-$ **155/156**) and one of the ascorbate dianion ([asc-O^2,O^3]$^{2-}$ **157**) are of particular interest. The reaction ultimately produces two carbon−oxygen-bound complexes, namely, [Pt(asc-C^2,O^5)([1,2-$^{15}N_2$]-en)] (**153**) and [Pt(Hasc-C^2)(Hasc-O^3)([1,2-$^{15}N_2$]en)] (**154**), which are analogous to the *cis*-dach complexes described above. Platinum can bind to the prochiral C2-carbon atom from either the *re* or *si* face of the ascorbate ring (Scheme 35). When the platinum binds to the *re* face, the hydroxyl group at O5 is properly positioned for ring closure, resulting in the formation of the asc-C^2,O^5-chelate complexes **153**. However, when the platinum binds to C2 through the opposite face (*si* face), ring closure is not possible since the exocyclic $C^5H(OH)-C^6H_2OH$ chain is positioned away from the metal on the oppsite side of the ascorbate ring. Since ring closure is geometrically prohibited, the remaining binding site on platinum, which contains a reactive aqua ligand, is available for further reaction with a second ascorbate anion. Thus, when excess sodium ascorbate is present, bis(ascorbato) complexes **154** are readily generated.

Further support for these mechanisms comes from analogous investigations with $^{15}NH_3$, *trans*-*R*,*R*-dach, and *trans*-*S*,*S*-dach ligands resulting in complexes *cis*-[Pt(asc-C^2,O^5)$(NH_2R)_2$]·nH_2O ($2NH_2R$ = *trans*-*R*,*R*-dach, n = 3; $2NH_2R$ = *trans*-*S*,*S*-dach, n = 2; $NH_2R = {}^{15}NH_3$, n = 2).[104c] The reaction between *cis*-[Pt$(OH)_2(PMe_3)_2$] and ascorbic acid afforded *cis*-[Pt(asc-O^2,O^3)$(PMe_3)_2$]·$2H_2O$ (**157′**) as final product. The binding of the ascorbato ligand through O^2 and O^3 as in type **157** complexes was shown by X-ray crystallography.[106a]

In the absence of a nucleophile, chelate complexes **153** are protonated by acids at the O5 site of the ascorbato ligand yielding complexes **158** with protonated chelate Hasc-C^2,O^5-ligands (Scheme 36).[108]

Scheme 36



Furthermore, hydrolysis takes place yielding ring-opened complexes **159** and diaqua complexes with cleavage of H_2asc. When the protonation reaction was conducted with the use of methanesulfonic acid in dry alcohols, the protonated chelate complex **159′** was isolated. With nucleophiles, in nonaqueous solution the ring-opened complexes **160** and **161** were obtained and could be characterized by NMR spectroscopy (Scheme 36). Both complexes are unstable in aqueous solution; the chloro complex **160** undergoes ring closure, reforming the chelate complex **153** and the C^2-bound dimethyl sulfoxide complex **161** isomerizes yielding the O^3-bound complex **161′**.[108]

Bis(ascorbato)-1,2-diaminocyclohexaneplatinum complexes were tested for their antitumor activity.[109] Iproplatin, [$PtCl_2(OH)_2(NH_2iPr)_2$], a prodrug for the treatment of a variety of cancers, is reduced by ascorbic acid yielding stoichiometric amounts of Pt(II) and dehydroascorbic acid. Intermediates are platinum−ascorbate complexes and a long-lived ascorbate radical.[110] Ascorbatoruthenium(III) complexes were characterized mostly in solution: Ru(III) forms stable ascorbato complex [Ru(asc)$(NH_3)_5$](O_3SCF_3), presumably with *O*-bound ascorbato ligands.[111] Furthermore, it was shown that $[RuCl_2(H_2O)_4]^+$ reacts with L-ascorbic acid, yielding a 1:1 ascorbatoruthenium(III) complex that undergoes an inner-sphere electron transfer.[112] The Ru(III)−EDTA−H_2asc−O_2

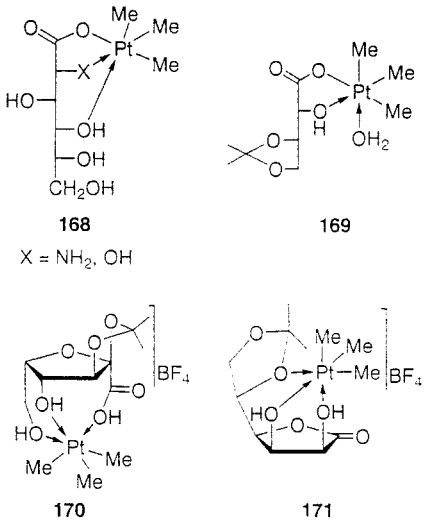
and Ru(III)−EDTA−H_2asc−H_2O_2 systems catalyze effectively the oxidation or oxygenation of a variety of organic substrates and are formally analogous to monooxygenase and peroxidase activity, respectively. Examples are hydroxylation of cyclohexane, toluene, or cyclohexanol,[113] epoxidation of olefins,[113c,e,114] and oxidation of ascorbic acid.[115]

A great variety of carboxylatoplatinum complexes have been synthesized and antitumor activities studied. Cisplatin-type complexes $[Pt(O_2CR_{ch})_2L_2]$ (**162**) (L = NH_3, $^1/_2$ dach, ...) with sugar acids $R_{ch}CO_2H$ as the anionic leaving groups have been synthesized via conventional methodes, such as reactions (i) of $[PtL_2(H_2O)_2]^{2+}$ with MO_2CR_{ch} (M = Na, K), (ii) of $[PtCl_2L_2]$ with AgO_2CR_{ch} or $Ag_2SO_4/Ba(O_2CR_{ch})_2$, and (iii) of [Pt(OOC−COO)L_2] with $Ca(O_2CR_{ch})_2$. Complexes from all three major types of sugar acids are known, namely, from aldonic acids (gluconate, tetra-*O*-acetylgluconate, hexahydroxyheptanoate)[116,117,118] and uronic acids (glucuronate, galacturonate, tetra-*O*-acetylglucuronate).[116,119,120,121,122] Aldaric acids $HO_2C-(CHOH)_{n-2}-CO_2H$ form 1:1 complexes $[Pt(O_2C-R_{ch}-CO_2)L_2]$ (**163**) (saccharate, mucate, tartrate) and 2:1 complexes $[Pt(O_2C-R_{ch}-CO_2H)_2L_2]$ (**164**) (saccharate, saccharatolactone).[118,119,120f,123] From IR and ^{1}H NMR measurements, it was determined that the sugar coordination occurs monodentately via the negatively charged carboxylate oxygen atom in trans complexes *trans*-$[Pt(O_2CR_{ch})_2(NH_3)_2]$ (**165′**) and bidentately in *cis*-$[Pt(O_2CR_{ch})(NH_3)_2](O_2CR_{ch})$ (**165″**) (HO_2CR_{ch}, glucuronic acid, gluconic acid) through carboxylate oxygen atoms or through one carboxylate oxygen atom and pyranose ring oxygen atom (glucuronate anion) and α-hydroxy group (gluconate anion), respectively, forming five-membered chelate rings.[116b]

Dinuclear carboxylatorhodium(II) complexes $[Rh_2(O_2CR_{ch})_4L_2]$ (**166**) (O_2CR_{ch} = glucuronate, ketogluconate; L = H_2O, cyclophosphamide) were prepared and tested for cytotoxicity.[124] The solvate-free gluconate complex $[Rh_2(O_2CR_{ch})_4]$ (**167**) (O_2CR_{ch} = gluconate) was used as a catalyst in enantioselective cyclopropanation reactions.[125] Polarographic and spectrophotometric investigations showed that in basic solution ruthenium(III) forms with gluconate ion a 1:1 complex. This could not be isolated in the solid state, so the exact formula and structure are still unknown. The complex is sufficiently stable to keep Ru(III) in solution in the presence of 2 M NaOH.[126] Furthermore, it has been shown that Os(VI), Os(IV), and Os(III) are strongly complexed by sodium gluconate in alkaline solutions.[127] Reactions of K[Os(OAc)$_3O_2$] with glucose in acetic acid result in carbohydrate polymers (molecular weight 10^4−10^5 g/mol) containing 10−40% osmium in an average oxidation state +4.[128] OsO_2 moieties might be bound to glucose and/or gluconate units. These polymers are polydisperse anionic polyelectrolytes and serve as potential antiarthritic drugs.

Reactions of $[PtMe_3(H_2O)_3]^+$ with stoichiometric amounts of sodium salts of D-gluconic and 2-amino-2-deoxy-D-gluconic acid and with calcium *O*-isopropylidene-D-threonate result in neutral platinum(IV) complexes $[PtMe_3L]$ (**168**) (L = gluconate/aminogluconate) and $[PtMe_3L(H_2O)]$ (**169**) (L = threonate),

Chart 22



respectively (Chart 22).[14] NMR spectroscopic investigations (^{1}H, ^{13}C, ^{195}Pt) reveal that the ligands are deprotonated sugar acids. In aqueous solutions, the gluconato ligands are tridentately coordinated as shown in Chart 22. Alternatively, a bidentate binding mode is possible by replacement of the C4−OH with water.

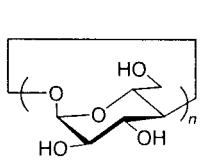
Reactions of tris(acetone)trimethylplatinum(IV) tetrafluoroborate **117** with 2,3-*O*-isopropylidene-2-keto-L-gulonic acid and 5,6-*O*-isopropylidene-D-gulono-1,4-lactone in acetone afford complexes **170** and **171**, respectively (Chart 22).[84b] The coordination modes of the carbohydrate ligands were derived from NMR spectroscopic investigations. In complex **170** the carboxyl group is not deprotonated upon complexation to platinum(IV). In contrast to all other cationic carbohydrate complexes $[PtMe_3L]^+$ (L = carbohydrate), complex **170** did not show any signal in ESI-MS analysis, due most likely to facile deprotonation of the highly acidic carboxylic group yielding a neutral nondetectable complex.

V. Cyclodextrin Complexes

A. Inclusion Compounds

Cyclodextrins are cyclic oligosaccharides with 1,4-linked glucopyranoside building blocks (generally 6−8) that exist in $^4C_1$ chair conformation (Chart 23).

Chart 23



	n	*d* in Å	cavity *V* in Å^3
α	6	4.7-5.3	174
β	7	6.0-6.5	262
γ	8	7.5-8.3	427

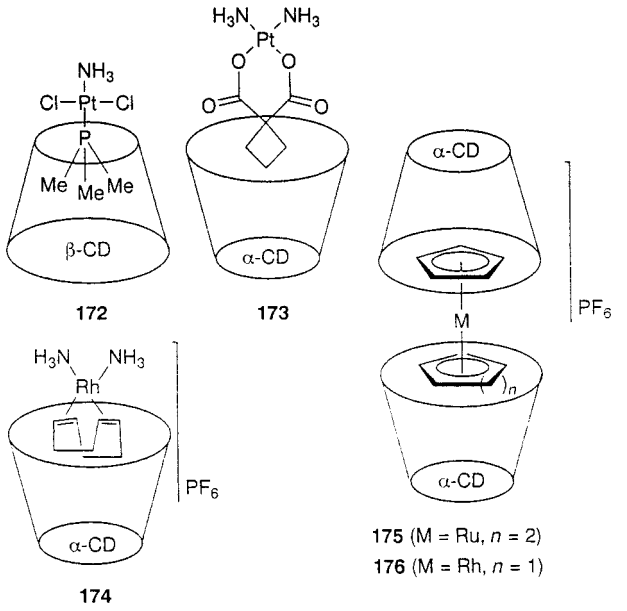
d - internal diameter
V - volume

The structures resemble hollow truncated cones (tori) and exhibit approximate C_n symmetry (n = 6−8). The large internal diameters of the cavities allow the formation of inclusion compounds in which the cyclodextrins act as molecular receptors (hosts) that bind substrates (guests), forming host−guest com-

plexes or supramolecular species. Functionalization of cyclodextrins with donor groups leads to ligands that can form a multitude of complexes.[129]

Several inclusion compounds of cyclodextrins with platinum-group metal complexes as guests were characterized by single-crystal X-ray diffraction (Chart 24). In the solid state, all these complexes are

Chart 24



hydrates and thus possess a network of hydrogen bonds. Apart from the β-CD complex **172**, the guest molecules penetrate into the broad side of the cyclodextrin torus.

The structure of $[PtCl_2(NH_3)(PMe_3)]\cdot(\beta\text{-CD})\cdot 5.5H_2O$ (**172**) is strongly disorded, and the schematic drawing in Chart 24 is valid for only 57% of the molecules.[130] The platinum complex penetrates into the β-CD molecule with its PMe_3 ligand. There are no notable host−guest contacts. In the 1:1 adduct of carboplatin with α-cyclodextrin, $[Pt\{c\text{-}C_4H_6(COO)_2\}(NH_3)_2]\cdot(\alpha\text{-CD})\cdot 5.5H_2O$ (**173**), the cyclobutane ring of the cyclobutane-1,1-dicarboxylato ligand penetrates into α-cyclodextrin.[131] The adduct is stabilized by two N−H···O hydrogen bonds between the ammine hydrogen atoms and oxygen atoms of hydroxyl groups of this host cyclodextrin molecule (N···O 2.94, 3.14 Å). Surprisingly, perhaps, there are no (intramolecular) hydrogen bonds between the carbonyl oxygen atoms of the carboxylato ligand and hydroxyl groups of this host cyclodextrin molecule but only intermolecular ones to other cyclodextrin molecules.

In the solid-state structure of the 1:1 adduct $[Rh(cod)(NH_3)_2]PF_6\cdot(\alpha\text{-CD})\cdot 6H_2O$ (**174**), the cyclooctadiene ligand adopts a boat conformation (Figure 17).[131b,132] One of the two $-CH_2-CH_2-$ units of the cod ligand penetrates into the cyclodextrin cavity. Four N···O distances between 3.24 and 3.46 Å point to a stabilization of the adduct by intramolecular N−H···O hydrogen bonds. α-Cyclodextrin forms 2:1 inclusion compounds with $[Ru(\eta^5\text{-}C_5H_5)(\eta^6\text{-}C_6H_6)]PF_6\cdot 2(\alpha\text{-CD})\cdot 8H_2O$ (**175**)[133] and $[Rh(\eta^5\text{-}C_5H_5)_2]PF_6\cdot 2(\alpha\text{-CD})\cdot 8H_2O$ (**176**).[134] The host molecules are arranged head-to-head to form a dimer. The cations are encapsulated within the cavity of the dimer, while the PF_6 anions are located outsight the cavities. The guest cations are tilted against the mean planes of oxygen atoms of the 12 secondary hydroxyl groups of α-CD molecules by angles of 36° (**175**) and 42/43° (**176**), respectively. The structure of the rhodicinium cation appears to be unaffected by inclusion into the cyclodextrin cavity.

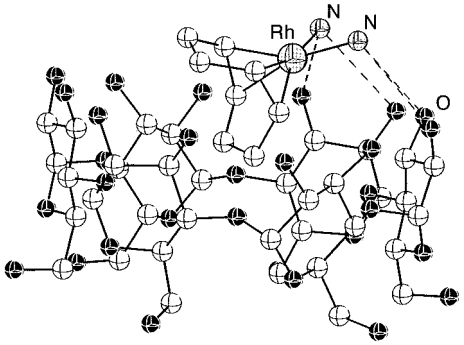


Figure 17. Molecular structure of $[Rh(cod)(NH_3)_2]PF_6\cdot(\alpha\text{-CD})\cdot 6H_2O$ (**174**) (Anion and water are not shown; H atoms are omitted).[131b,132] N−H···O hydrogen bonds (N···O 3.24−3.46 Å) are shown as dashed lines.

Apart from these structurally characterized complexes, it has been shown that cyclodextrins and their *O*-methylated derivatives can form inclusion complexes, both in the solid state and in solution, with a wide range of platinum-group metal complexes. Guest molecules are sandwich and half-sandwich complexes (analogues to complexes **175**/**176**),[133,134,135] $[PtCl_2(NH_3)(PEt_3)]$ (analogue to complex **172**)[130] and $[RhL_2(L')_2]PF_6$ (L_2 = cod, nbd; L′ = NH_3, $^1/_2$en) (analogues to complex **174**).[131b,132] Furthermore, β- and γ-cyclodextrin form 2:1 (CD:guest) inclusion compounds with dimeric complexes $[\{Rh(\mu\text{-}X)L_2\}_2]$ (L_2 = cod, nbd; X = Cl, Br, I) (**177**) and 1:1 inclusion compounds with the monomeric complexes $[PtX_2(cod)]$ (X = Cl, Br, I) (**178**).[136] A 1:1 inclusion complex of β-cyclodextrin and $[Rh(\eta^5\text{-}C_5H_5)(nbd')]$ (nbd′ = 2-formylnorbornadiene) (**179**) was obtained.[137] Separation of racemates of planar−chiral cyclopentadienyl rhodium complexes into enantiomers by liquid chromatography using aqueous β-cyclodextrin as a mobile phase is an example for chiral recognition of metal complexes due to formation of inclusion compounds.[138] The dimeric complexes $[\{Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}X)\}_2]$ (X = Cl, Br, I) (**180**) and the analogous crotyl and 2-methylallyl complexes (X = Cl) form 1:1 inclusion compounds with β- and/or γ-cyclodextrin.[139]

In all cases, the formation of inclusion compounds proved to be strongly dependent on the size and shape of the guest molecules. The topology of these inclusion compounds was most precisely determined by single-crystal X-ray diffraction but was also obtained in solution from NMR and induced circular dichroism measurements. Formation of inclusion compounds may alter the properties of the guest complexes. For instance, inclusion of $[Ru(\eta^5\text{-}C_5H_5)_2]$ in β-cyclodextrin prevents oxidation of ruthenocene by iodine.[135b,135c] Cyclodextrins can affect the kinetics or even change the reaction mechanism (outer-sphere vs inner-sphere) of electron-transfer reactions.[140] Furthermore, they can influence photophysical prop-

erties.[141] The thermal stability may be increased at inclusion ([{Rh(μ-Cl)(cod)}$_2$] T_{dec} ca. 200 °C; [{Rh(μ-Cl)(cod)}$_2$]·2(β-CD) T_{dec} ca. 275 °C).[136b] In general, cyclodextrin adducts have been prepared in water and inclusion of complexes results in increased water-solubility. An increase in water-solubility can improve the uptake of hydrophobic drugs. This was the motivation for inclusion of the antitumor active rhodium(II) α-methylcinnamate within β-cyclodextrin[142] and also for formulations of cisplatin-type complexes with cyclodextrins.[131b,143]

Owing to the ability of forming water-soluble inclusion compounds with organic molecules, cyclodextrins can be used as inverse-phase-transfer catalysts by improving the mass transfer of organic substrates between organic and aqueous layers.[44] Biphasic olefin oxidation (Wacker oxidation),[144] hydroformylation,[144e,145] hydrocarboxylation reactions,[144e,146] cleavage of allylic carbonates,[147] and hydrogenation of aldehydes,[148] ketones (in THF),[149] and α-keto esters (in MeOH/H_2O)[150] were described using water-soluble palladium, rhodium, or ruthenium catalysts. In an analogous manner, a solid-phase catalyst (Pd/C) was used for reduction of bromoanisols to hydrocarbons.[151] To improve the efficiency of inverse-phase-transfer catalysts, OR-substituted (R = Me, Ac, CH_2-CH_2-OH, $CH_2-CH(Me)-OH$, ...) cyclodextrins were also used. Substrate selectivity was achieved according to the shape/size concept (cyclodextrin cavity vs substrate). Product selectivity may also result from inclusion of the substrate. Thus, *n*/iso ratios in hydroformylation and -carboxylation reactions are effected by means of cyclodextrins.

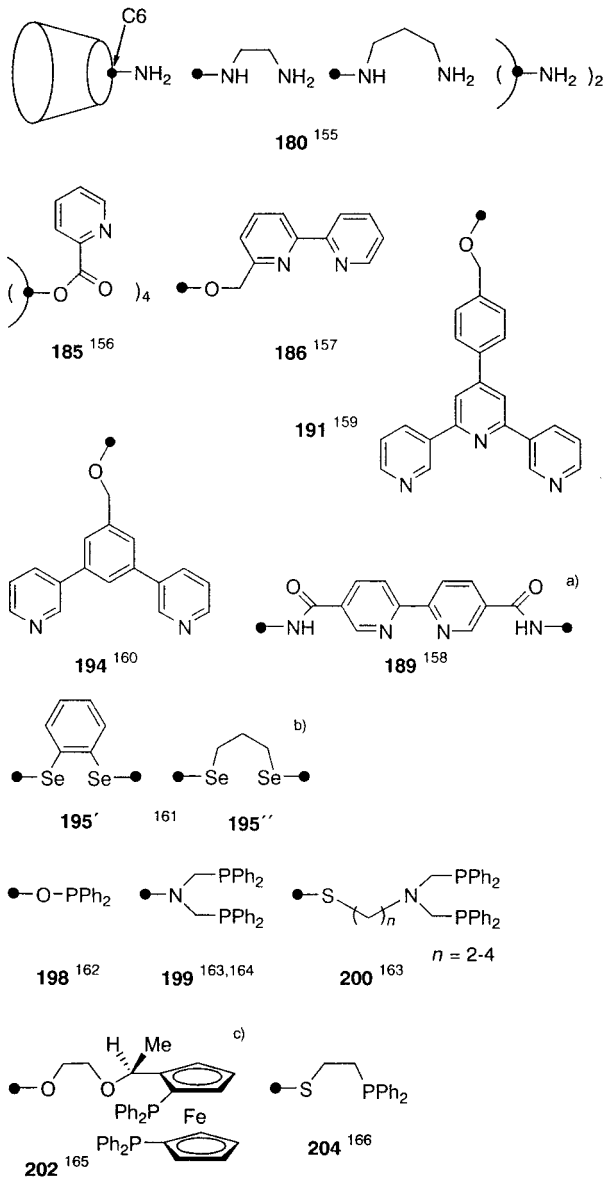
Platinum inclusion compounds of type **178** as well as [$PtMe_2$(cod)] and [$PtMe_3(\eta^5-C_5H_5)$] are hydrosilylation catalysts and were used in "command-cure" applications. The addition−cure reaction is a well-known industrial process for cross-linking silicones. A curable formulation is one with a long work-life at ambient temperature and rapid cure time at elevated temperature.[152b] Surprisingly, the palladium analogue, [$PdCl_2$(cod)]·(β-CD) (**179**), proved to be a good command-cure catalyst whereas the guest complex [$PdCl_2$(cod)] lacking cyclodextrin was not active in the hydrosilylation reaction.[152] Palladium colloids stabilized by β-cyclodextrin act as an artificial heterogeneous catalyst for CO_2/HCO_3^- reduction to formate which mimics enzyme activities.[153] β-Cyclodextrin−epichlorhydrin copolymers deposited with noble metals have been used as enantioselective heterogeneous catalysts.[154]

B. Cyclodextrins with Donor Groups

An overwiew of cyclodextrins with anchoring groups is given in Chart 25. In most cases the anchoring group is bound directly or via a spacer to one of the C6 carbon atoms located on the narrow side of the torus. These chemically modified cyclodextrins can be covalently bound to metals. From the amine ligands **180**, platinum(II) complexes of the types [$PtCl_2$(β/γ-CD-NH_2)(NH_3)] (**181**), [$PtCl_2$(β/γ-CD-en)] (**182**), and [$PtCl_2${β-CD-NH$(CH_2)_3NH_2$}] (**183**) were synthesized, characterized (^{1}H, ^{13}C, and ^{195}Pt NMR, FAB MS, UV−vis), and tested for their cytotoxic and antitumor activities.[155] The X-ray crystal-structure analysis of *cis*-[$PtCl_2${β-CD(NH_2)$_2$}]·13H_2O (**184**) (Figure 18) reveals that the complexation with platinum induces a distortion of the cyclodextrin cavity. The O−H···O hydrogen bridges around the functionalized units on the broader side of the torus are significantly weakened (O···O 3.08−3.46 vs 2.74−2.84 Å).[155b]

6^A,6^B,6^D,6^E-Tetra-*O*-nicotinyl-substituted permethylated α-cyclodextrin **185** has two pairs of preferentially *cis*-coordinating pyridyl ligands. It reacts with *cis*-[$PtCl_2$(MeCN)$_2$] to yield a bis(*cis*-$PtCl_2$)cyclodextrin complex as revealed by ^{1}H NMR investigations.[156] 2,2′-Bipyridine-functionalized permethylated β-cyclodextrin (β-CD-bpy) **186** reacts with [$RuCl_2$(bpy)$_2$] and [{M(η^5-C_5Me_5)Cl(μ-Cl)}$_2$] (M = Rh, Ir) to yield complexes [Ru(bpy)$_2$(β-CD-bpy)]Cl_2 (**187**) and [M(η^5-C_5Me_5)Cl(β-CD-bpy)]Cl (M = Rh, Ir) (**188**), respec-

Chart 25



References refer to complexes with the ligands shown.
a) 3,3′-bridged dimer. b) 6,6′- and 2,2'-bridged dimer.
c) Functionalization at C2.

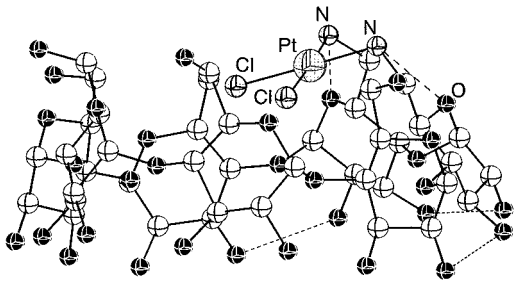


Figure 18. Molecular structure of $[PtCl_2\{\beta\text{-CD}(NH_2)_2\}]\cdot 13H_2O$ (**184**) (Water is not shown; H atoms are omitted).[155b] N−H···O hydrogen bonds (N···O 2.96/3.09 Å) and weakened O−H···O hydrogen bonds (O···O 3.08−3.46 Å) are shown as dashed lines.

tively. Importantly, these molecules are interesting candidates by which to investigate electron and/or photon transfer between an encapsulated guest molecule and an active metal center.[157] The bipyridine-functionalized cyclodextrin dimer **189** (based on a silylated β-cyclodextrin) readily forms a rhodium complex, $[Rh(\eta^5\text{-}C_5Me_5)Cl(\mathbf{189})]Cl$ (**190**).[158] From terpyridine-functionalized cyclodextrin **191** were prepared ruthenium(II) complexes $[Ru(\beta\text{-CD-ttp})L_3](PF_6)_2$ (**192**) (β-CD-ttp = **191** with permethylated β-CD; L_3 = terpyridine, *p*-tolylterpyridine). The luminescence of complexes **192** responds to guest binding.[159] An efficient route for the preparation of $[Ru(\beta\text{-CD-dpp})L_3]PF_6$ (**193**) (β-CD-dpp = cyclometalated **194**; L_3 = *p*-tolylterpyridine) allowed the investigation of these complexes as photoactive receptor units.[160]

Organoselenium-bridged bis(β-cyclodextrin) **195′** reacts with $PdCl_2$ and $K_2[PtCl_6]$ yielding 1:1 complexes $[PdCl_2(\beta\text{-CD}-Se-C_6H_4-Se-\beta\text{-CD-}Se,Se')]\cdot 11H_2O$ (**196**) and $K_2[PtCl_6]\cdot(\beta\text{-CD}-Se-C_6H_4-Se-\beta\text{-CD})\cdot 10H_2O$ (**197**), respectively. Conductivity measurements indicate that the corresponding platinum(IV) complex with the 6,6′-trimethylenediseleno-bridged dimer has a 2:1 stoichiometry (**195″**:Pt) whereas the 2,2′-bridged dimer **195″** has a strict 1:1 stoichiometry.[161] Due to dual hydrophobic cavities in close vicinity to one and other, both free ligands and their platinum complexes show cooperative binding capabilities for guest molecules. This was demonstrated using a number of fluorescent dyes.

Cyclodextrins with *P*-binding substituents were mainly used as catalyst components in homogeneous catalytic reactions. Generally, catalysts with cyclodextrin-modified ligands may exhibit substrate selectivities due to inclusion of substrates in cyclodextrin cavities. Such catalysts are particularly powerful tools in phase-transfer catalysis. Hydroformylation and hydrogenation reactions of olefins with Rh/**198**,[162] Rh/**199**,[163] and Rh/**200**[163] have also proved to be substrate selective in biphasic systems. Investigations on reduction of halo−nitro aromatic compounds by β-cyclodextrin-modified catalysts M/**199** (M = Rh, Ir, Pd, Pt, Ru) in biphasic systems showed that the platinum catalysts $[PtCl_2(cod)]$/**199** are the most active and selective ones, resulting in the chemoselective formation of halo−aniline derivatives.[164] In these processes it has to be assumed that catalytically active species are metal complexes with cyclodextrin-modified ligands. Palladium and rhodium complexes with phosphine-functionalized cyclodextrins, $[PdCl_2(\beta\text{-CD-}PP)]$ (**201**)[165] (β-CD-*PP* = **202** based on heptakis(2,6-di-*O*-methyl)-β-cyclodextrin) and $[Rh(nbd)(\beta\text{-CD-}PS)]BF_4$ (**203**)[166] (β-CD-*PS* = **204** based on β-cyclodextrin), have been synthesized and characterized by NMR spectroscopy and FAB mass spectrometry.

The well-defined hydrophobic cavities of cyclodextrins are the basis not only for molecular but also for chiral recognition of substrates. Due to the reversibility of binding of substrates, cyclodextrins are ideal host compounds to carry out reactions under topochemical control and for substrate-sensitive catalytic processes. Coordination of cyclodextrins via donor groups to metal catalysts brings the cavities in close vicinity to the catalytic centers. This mimics metalloenzymes and is a promising development toward supramolecular catalysts for highly active and selective enantioselective reactions.

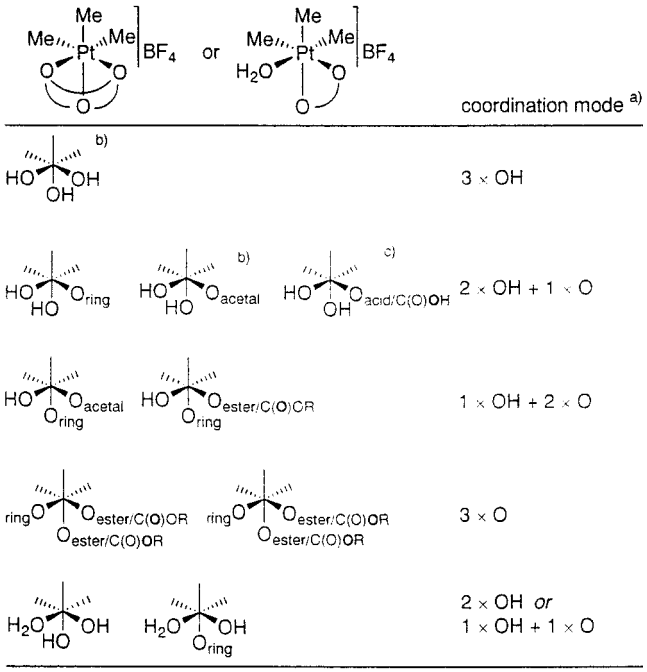
VI. Conclusion

Coordination chemistry of platinum-group metals with carbohydrate ligands bearing Lewis-basic substituents is strongly dominated by these "anchoring" groups. In general, these moieties are much stronger donor ligands than the remaining oxygen-donor sites of the carbohydrate. These may give rise to further coordination forming chelate complexes. Thus, donor-substituted carbohydrates behave − in many aspects − similarly to analogous ligands without carbohydrate backbones. From a coordination chemical viewpoint, close analogies were also found between anionic carbohydrate ligands obtained by deprotonation of one or two hydroxyl groups or of a sugar acid and corresponding alcoholato, diolato, or carboxylato ligands, respectively, without carbohydrate backbones.

Nonfunctionalized neutral carbohydrate ligands are unique, and their highly versatile coordination behavior is documentated best in trimethylplatinum(IV) complexes (Chart 26). Although they are weak donors, pyranoses, furanoses, and acyclic carbohydrates can be bound to platinum(IV), a high oxidation state transition metal. The carbohydrates are neither oxidized by platinum(IV) nor deprotonated upon complexation, although the latter often occurs using metals in high oxidation states. Importantly, platinum-promoted cleavage or formation of isopropylidene protection groups and Schiff bases can occur depending on steric conditions.

Apart from the primary coordination sphere, the high steric demand of carbohydrate moieties and their conformational rigidity have a pronounced influence on stability and reactivity of carbohydrate complexes. This seems to be especially significant for organometallic carbohydrate ligands. Furthermore, the inherent chirality of naturally abundant carbohydrates, their biocompatibility, the "fine-tuning" of conformations and coordination behavior via hydrogen bonds, and enhanced solubility of carbohydrate derivative complexes may play an outstanding role for applications of carbohydrate complexes as catalysts in homogeneous catalytic reactions or in medicine and pharmacology. The deeper understanding

Chart 26



a) O: O_{ring}, O_{ester}, O_{acetal}.

b) Also for sugar alcohols. c) Sugar acids.

of metal coordination modes for carbohydrates and applications of influencing configuration and conformation of carbohydrate ligands in metal complexes is an integral concept in bioinorganic chemistry. Applications to medicine and pharmacology as well as to both synthetic and enzyme mimicry catalysis are readily envisioned based on the current states of carbohydrate platinum coordination chemistry. Indeed, it is likely to be in these areas that the next frontier of metal carbohydrate chemistry lies.

VII. Abbrevations

Ac	acetyl
Ar	aryl
Bzl	benzyl
CD	cyclodextrin
cod	cycloocta-1,5-diene
dach	1,2-diaminocyclohexane
dba	dibenzylideneacetone
DIOP	2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane
HA	HBF_4, HPF_6, ... (A = weakly coordinating anion)
H_2asc	L-ascorbic acid
n-Hmbpa	4,6-*O*-benzylidene-*n*-deoxy-*n*-(diphenylphosphino)-α-D-altropyranoside (*n* = 2, 3)
nbd	bicyclo[2.2.1]hepta-2,5-diene (norbornadiene)
Nu	nucleophile
R	alkyl, aryl, H
R_{ch}−OH	carbohydrate
YR_n	NR_2, PR_2, OR, SR, ...

VIII. Acknowledgments

The work of our own group described herein has been supported by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie*. We acknowledge Dr. Gerlach and Ms. Lettau (University Halle) for their help in providing the literature survey. The authors also thank Dr. Rajski (California Institute of Technology) for critical reading the manuscript.

IX. References

(1) Drew, K. N.; Zajicek, J.; Bondo, G.; Bose, B.; Serianni, A. S. *Carbohydr. Res.* **1998**, *307*, 199.
(2) Hegetschweiler, K. *Chem. Soc. Rev.* **1999**, *28*, 239.
(3) Rendleman Jr., J. A. *Adv. Carbohydr. Chem.* **1966**, *21*, 209.
(4) (a) Angyal, S. J. *Pure Appl. Chem.* **1973**, *35*, 131. (b) Angyal, S. J. *Chem. Soc. Rev.* **1980**, *9*, 415. (c) Angyal, S. J. *Adv. Carbohydr. Chem. Biochem.* **1989**, *47*, 1.
(5) Verchère, J.-F.; Chapelle, S.; Xin, F.; Crans, D. C. *Prog. Inorg. Chem.* **1998**, *47*, 837.
(6) Alekseev, Yu. E.; Garnovskii, A. D.; Zhdanov, Yu. A. *Usp. Khim.* **1998**, *67*, 723.
(7) Piarulli, U.; Floriani, C. *Prog. Inorg. Chem.* **1997**, *45*, 393.
(8) Gyurcsik, B.; Nagy, L. *Coord. Chem. Rev.* **2000**, *203*, 81.
(9) (a) Bruhn, S. L., Toney, J. H.; Lippard, S. J. *Prog. Inorg. Chem.* **1990**, *38*, 477. (b) *Metal Complexes in Cancer Chemotherapy*; Keppler B. K., Ed.; VCH: Weinheim, 1993. (c) *Molecular Aspects of Anticancer Drug−DNA Interactions*; Neidle, S., Waring, M., Eds.; Macmillan: Basingstoke, 1993; Vol. 1. (d) Yano, S.; Otsuka, M. *Met. Ions Biol. Syst.* **1996**, *32*, 27. (e) *Cisplatin: Chemistry and Biochemistry of a Leading Anticancer Drug*; Lippert, B., Ed.; WILEY−VCH: Weinheim, 1999. (f) Kozelka, J.; Legendre, F.; Reeder, F.; Chottard, J.-C. *Coord. Chem. Rev.* **1999**, *190−192*, 61.
(10) Thiel, G.; Beck, W. *Z. Naturforsch.* **1983**, *38b*, 1081.
(11) Kuduk-Jaworska, J.; Jezowska-Trzebiatowska, B. *Inorg. Chim. Acta* **1986**, *123*, 209.
(12) Sachinvala, N. D.; Chen, H.; Niemczura, W. P.; Furusawa, E.; Cramer, R. E., Rupp, J. J.; Ganjian, I. *J. Med. Chem.* **1993**, *36*, 1791.
(13) Junicke, H.; Bruhn, C.; Müller, T.; Steinborn, D. *Z. Anorg. Allg. Chem.* **1999**, *625*, 2149.
(14) Junicke, H.; Arendt, Y.; Steinborn, D. *Inorg. Chim. Acta* **2000**, *304*, 224.
(15) Junicke, H.; Kasyan, G.; Steinborn, D. Unpublished results.
(16) Krawielitzki, S.; Beck, W. *Z. Anorg. Allg. Chem.* **1998**, *624*, 1718.
(17) (a) Tsubomura, T.; Ogawa, M.; Yano, S.; Kobayashi, K.; Sakurai, T.; Yoshikawa, S. *Inorg. Chem.* **1990**, *29*, 2622. (b) Tsubomura, T.; Yano, S.; Kobayashi, K.; Sakurai, T.; Yoshikawa, S. *J. Chem. Soc., Chem. Commun.* **1986**, 459.
(18) Hanessian, S.; Wang, J. *Can. J. Chem.* **1993**, *71*, 886.
(19) Nagel, Y.; Beck, W. *Z. Naturforsch.* **1986**, *41b*, 1447.
(20) Chen, J.; Pill, T.; Beck, W. *Z. Naturforsch.* **1989**, *44b*, 459.
(21) Zhou, Y.; Wagner, B.; Polborn, K.; Sünkel, K.; Beck, W. *Z. Naturforsch.* **1994**, *49b*, 1193.
(22) Kuduk-Jaworska, J. *Trans. Met. Chem.* **1994**, *19*, 296.
(23) (a) Ferrara, M. L.; Orabona, I.; Ruffo, F.; Funicello, M., Panunzi, A. *Organometallics* **1998**, *17*, 3832. (b) Ferrara, M. L.; Giordano, F.; Orabona, I.; Panunzi, A.; Ruffo, F. *Eur. J. Inorg. Chem.* **1999**, 1939.
(24) Nifant'ev, E. E.; Chechegoeva, E. V.; Zhelyaev, V. M. *Dokl. Akad. Nauk SSSR* **1986**, *287*, 874.
(25) Lednor, P. W.; Beck, W.; Thiel, G. *Inorg. Chim. Acta* **1976**, *20*, L11.
(26) Koroteev, M. P.; Prozorovskii, A. E.; Teleshev, A. T.; Shishin, A. V.; Nifant′ev, E. E. *Zh. Strukt. Khim.* **1992**, *33*, 121.
(27) Selke, R. *J. Organomet. Chem.* **1989**, *370*, 241.
(28) RajanBabu, T. V.; Ayers, T. A.; Halliday, G. A.; You, K. K.; Calabrese, J. C. *J. Org. Chem.* **1997**, *62*, 6012.
(29) Michalik, M.; Freier, T.; Schwarze, M.; Selke, R. *Magn. Reson. Chem.* **1995**, *33*, 835.
(30) (a) Kempe, R.; Schwarze, M.; Selke, R. *Z. Kristallogr.−New Cryst. Struct.* **1995**, *210*, 555. (b) Kempe, R.; Spannenberg, A.; Heller, D. *Z. Kristallogr.−New Cryst. Struct.* **1998**, *213*, 631.
(31) Kadyrov, R.; Heller, D.; Selke, R. *Tetrahedron: Asymmetry* **1998**, *9*, 329.
(32) (a) Shin, S.; RajanBabu, T. V. *Org. Lett.* **1999**, *1*, 1229. (b) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 5593. (c) Yonehara, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 9381.
(33) (a) Lafont, D.; Sinou, D.; Descotes, G. *J. Organomet. Chem.* **1979**, *169*, 87. (b) Yonehara, K.; Hashizume, T.; Ohe, K.; Uemura, S. *Tetrahedron: Asymmetry* **1999**, *10*, 4029.
(34) Brown, J. M.; Cook, S. J.; Kent, A. G. *Tetrahedron* **1986**, *42*, 5097.
(35) (a) Shi, J.-C.; Zheng, Y.; Wu, D.-X.; Huang, X.-Y.; Liu, Q.-T.; Kang, B.-S. *Inorg. Chim. Acta* **1999**, *290*, 121. (b) Shi, J.-C.; Yueng, C.-H.; Wu, D.-X.; Liu, Q.-T.; Kang, B.-S. *Organometallics* **1999**, *18*, 3796.

(36) Shi, J.-C.; Wu, D.-X.; Weng, T.-B.; Hong, M.-C.; Liu, Q.-T.; Kang, B.-S.; Lu, S.-J.; Wang, H.-Q. *J. Chem. Soc., Dalton Trans.* **1996**, 2911.
(37) Bader, A.; Lindner, E. *Coord. Chem. Rev.* **1991**, *108*, 27.
(38) *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; VCH: Weinheim, 1996; Vols. 1−2.
(39) (a) Selke, R. *J. Organomet. Chem.* **1989**, *370*, 249. (b) Selke, R.; Facklam, C.; Foken, H.; Heller, D. *Tetrahedron: Asymmetry* **1993**, *4*, 369. (c) Berens, U.; Fischer, C.; Selke, R. *Tetrahedron: Asymmetry* **1995**, *6*, 1105. (d) Heller, D.; Kortus, K.; Selke, R. *Liebigs Ann.* **1995**, 575. (e) Heller, D.; Borns, S.; Baumann, W.; Selke, R. *Chem. Ber.* **1996**, *129*, 85.
(40) (a) Li, C.; Bernet, B.; Vasella, A.; Broger, E. A.; Meili, A. *Carbohydr. Res.* **1991**, 149. (b) Gilbertson, S. R., Chang C.-W. T. *J. Org. Chem.* **1995**, *60*, 6226.
(41) Vocke, W.; Hänel, R.; Flöther, F.-U. *Chem. Techn.* **1987**, *39*, 123.
(42) (a) Selke, R. *J. Mol. Catal.* **1986**, *37*, 227. (b) Selke, R.; Häupke, K.; Krause, H. W. *J. Mol. Catal.* **1989**, *56*, 315.
(43) Selke, R.; Čapka, M. *J. Mol. Catal.* **1990**, *63*, 319.
(44) *Aqueous-Phase Organometallic Catalysis*; Cornils, B.; Herrmann, W. A., Eds.; WILEY−VCH: Weinheim, 1998.
(45) (a) Kumar, A.; Oehme, G.; Roque, J. P.; Schwarze, M.; Selke, R. *Angew. Chem.* **1994**, *106*, 2272. (b) Selke, R.; Ohff, M.; Riepe, A. *Tetrahedron* **1996**, *52*, 15079.
(46) (a) RajanBabu, T. V.; Radetich, B.; You, K. K.; Ayers, T. A.; Casalnuovo, A. L.; Calabrese, J. C. *J. Org. Chem.* **1999**, *64*, 3429. (b) RajanBabu, T. V.; Casalnuovo, A. L.; Ayers, T. A. *Adv. Catal. Proc.* **1997**, *2*, 1.
(47) (a) Harthun, A.; Selke, R.; Bargon, J. *Angew. Chem.* **1996**, *108*, 2666. (b) Harthun, A.; Kadyrov, R.; Selke, R.; Bargon, J. *Angew. Chem.* **1997**, *109*, 1155.
(48) RajanBabu, T. V.; Ayers, T. A.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 4101.
(49) Yonehara, K.; Hashizume, T.; Ohe, K.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1967.
(50) Selke, R.; Schwarze, M.; Baudisch, H.; Grassert, I.; Michalik, M.; Oehme, G.; Stoll, N.; Costisella, B. *J. Mol. Catal.* **1993**, *84*, 223.
(51) Tararov, V. I.; Kadyrov, R.; Riermeier, T. H.; Holz, J.; Börner, A. *Tetrahedron: Asymmetry* **1999**, *10*, 4009.
(52) (a) Brown, J. M.; Cook, S. J.; Khan, R. *Tetrahedron* **1986**, *42*, 5105. (b) RajanBabu, T. V.; Ayers, T. A. *Tetrahedron Lett.* **1994**, *35*, 4295. (c) Buisman, G. J. H.; Martin, M. E.; Vos, E. J.; Klootwijk, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Tetrahedron: Asymmetry* **1995**, *6*, 719.
(53) Iida, A.; Yamashita, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2365.
(54) (a) Nomura, N.; Mermet-Bouvier, Y. C.; RajanBabu, T. V. *Synlett* **1996**, 745. (b) Clyne, D. S.; Mermet-Bouvier, Y. C.; Nomura, N.; RajanBabu, T. V. *J. Org. Chem.* **1999**, *64*, 7601.
(55) Beller, M.; Krauter, J. G. E.; Zapf, A. *Angew. Chem.* **1997**, *109*, 793.
(56) Zhou, Y.; Beck, W. *J. Organomet. Chem.* **1994**, *479*, 217.
(57) Pill, T.; Breu, W.; Wagner, H.; Beck, W. *Chem. Ber.* **1991**, *124*, 713.
(58) Nagel, Y.; Beck, W. *Z. Naturforsch.* **1985**, *40b*, 1181.
(59) Pàmies, O.; Net, G.; Ruiz, A.; Bo, C.; Poblet, J. M.; Claver, C. *J. Organomet. Chem.* **1999**, *586*, 125.
(60) Pàmies, O.; Diéguez, M.; Net, G.; Ruiz, A.; Claver, C. *J. Chem. Soc., Dalton Trans.* **1999**, 3439.
(61) Chen, J.; Pill, T.; Beck, W. *Z. Naturforsch.* **1990**, *45b*, 404.
(62) Pill, T.; Beck, W. *Z. Naturforsch.* **1993**, *48b*, 1461.
(63) Julien, P. R.; Ronco, G.; Lemay, C.; Khodadad, P.; Rodier, N. *Acta Crystallogr.* **1991**, *C47*, 29.
(64) Barbaro, P.; Currao, A.; Herrmann, J.; Nesper, R.; Pregosin, P. S.; Salzmann, R. *Organometallics* **1996**, *15*, 1879.
(65) Tschoerner, M.; Pregosin, P. S. *Inorg. Chim. Acta* **1999**, *290*, 95.
(66) Albinati, A.; Pregosin, P. S.; Wick, K. *Organometallics* **1996**, *15*, 2419.
(67) Drommi, D.; Nesper, R.; Pregosin, P. S., Trabesinger, G.; Zürcher, F. *Organometallics* **1997**, *16*, 4268.
(68) Pregosin, P. S.; Trabesinger, G. *J. Chem. Soc., Dalton Trans.* **1998**, 727.
(69) Tschoerner, M.; Trabesinger, G.; Albinati, A.; Pregosin, P. S. *Organometallics* **1997**, *16*, 3447.
(70) Borwitzky, A.; Schareina, T.; Paetzold, E.; Oehme, G. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1996**, *114*, 115.
(71) (a) Boog-Wick, K.; Pregosin, P. S.; Wörle, M.; Albinati, A. *Helv. Chim. Acta* **1998**, *81*, 1622. (b) Boog-Wick, K.; Pregosin, P. S.; Trabesinger, G. *Organometallics* **1998**, *17*, 3254.
(72) (a) Togni, A.; Burckhardt, U.; Gramlich, V.; Pregosin, P. S.; Salzmann, R. *J. Am. Chem. Soc.* **1996**, *118*, 1031. (b) Selvakumar, K.; Valentini, M.; Pregosin, P. S.; Albinati, A. *Organometallics* **1999**, *18*, 4591.
(73) (a) Gläser, B.; Kunz, H. *Synlett* **1998**, 53. (b) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *Chem. Commun.* **1999**, 415. (c) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 9374.
(74) (a) Pill, T.; Polborn, K.; Beck, W. *Chem. Ber.* **1990**, *123*, 11. (b) Pill, T.; Polborn, K.; Kleinschmidt, A.; Erfle, V.; Breu, W.; Wagner, H.; Beck, W. *Chem. Ber.* **1991**, *124*, 1541. (c) Krawielitzki, S.; Beck, W. *Chem. Ber./Recl.* **1997**, *130*, 1659.
(75) (a) Koppenhagen, V. B.; Elsenhans, B.; Wagner, F.; Pfiffner, J. J. *J. Biol. Chem.* **1974**, *249*, 6532. (b) Elsenhans, B.; Rosenberg, I. H. *Biochemistry* **1984**, *23*, 805. (c) Carmel, R.; Koppenhagen, V. B. *Arch. Biochem. Biophys.* **1977**, *184*, 135.
(76) (a) Arai, I.; Lee, T. D.; Hanna, R., Daves Jr., G. D. *Organometallics*, **1982**, *1*, 742. (b) Hacksell, U.; Daves Jr., G. D. *Organometallics* **1983**, *2*, 772. (c) Daves Jr., G. D.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433. (d) Daves Jr., G. D. *Acc. Chem. Res.* **1990**, *23*, 201.
(77) (a) Arai, I.; Daves Jr., G. D. *J. Am. Chem. Soc.* **1981**, *103*, 7683. (b) Hacksell, U.; Kalinkoski, H. T.; Barofsky, D. F.; Daves Jr., G. D. *Acta Chem. Scand.* **1985**, *B 39*, 469.
(78) Cheng, J. C.-Y.; Daves Jr., G. D. *J. Org. Chem.* **1987**, *52*, 3083.
(79) (a) Kettenbach, G.; Klüfers, P.; Mayer, P. *Macromol. Symp.* **1997**, *120*, 291. (b) Ahlrichs, R.; Ballauff, M.; Eichkorn, K.; Hanemann, O.; Kettenbach, G.; Klüfers, P. *Chem. Eur. J.* **1998**, *4*, 835.
(80) Hynes, R. C.; Le Page, Y. *J. Appl. Crystallogr.* **1991**, *24*, 352.
(81) Burger, J.; Kettenbach, G.; Klüfers, P. *Macromol. Symp.* **1995**, *99*, 113.
(82) Bhaduri, S.; Sapre, N.; Khwaja, H.; Jones, P. G. *J. Organomet. Chem.* **1992**, *426*, C12.
(83) Junicke, H.; Bruhn, C.; Ströhl, D.; Kluge, R.; Steinborn, D. *Inorg. Chem.* **1998**, *37*, 4603.
(84) (a) Steinborn, D.; Junicke, H.; Bruhn, C. *Angew. Chem.* **1997**, *109*, 2803. (b) Junicke, H.; Bruhn, C.; Kluge, R.; Serianni, A. S.; Steinborn, D. *J. Am. Chem. Soc.* **1999**, *121*, 6232.
(85) van Eldik, R. *Adv. Inorg. Bioinorg. Mech.* **1984**, *3*, 275.
(86) Junicke, H.; Bruhn, C.; Wagner, C.; Steinborn, D. *Chem. Heterocycl. Compd.* **1999**, 1119.
(87) Junicke, H.; Kluge, R.; Steinborn, D. *J. Inorg. Biochem.* **2000**, *81*, 43.
(88) (a) Junicke, H.; Serianni, A. S.; Steinborn, D. *J. Org. Chem.* **2000**, *65*, 4153. (b) Junicke, H. Ph.D. Thesis, University Halle 1999.
(89) Appelt, A.; Ariaratnam, V.; Willis, A. C.; Wild, S. B. *Tetrahedron: Asymmetry* **1990**, *1*, 9.
(90) (a) Okamoto, K.; Behnam, V.; Gauthier, J.-Y.; Hanessian, S.; Theophanides, T. *Inorg. Chim. Acta* **1986**, *123*, L1. (b) Okamoto, K.; Behnam, V.; Viet, M. T. P.; Polissiou, M.; Gauthier, J.-Y.; Hanessian, S.; Theophanides, T. *Inorg. Chim. Acta* **1986**, *123*, L3. (c) Haines, A. H.; Morley, C.; Murrer, B. A. *J. Med. Chem.* **1989**, *32*, 742. (d) Hanessian, S.; Gauthier, J.-Y.; Okamoto, K.; Beauchamp, A. L.; Theophanides, T. *Can. J. Chem.* **1993**, *71*, 880.
(91) Börner, A.; Kless, A.; Holz, J.; Baumann, W.; Tillack, A., Kadyrov, R. *J. Organomet. Chem.* **1995**, *490*, 213.
(92) Kless, A.; Holz, J.; Heller, D.; Kadyrov, R.; Selke, R.; Fischer, C.; Börner, A. *Tetrahedron: Asymmetry* **1996**, *7*, 33.
(93) (a) Stille, J. K.; Fritschel, S. J.; Takaishi, N.; Masuda, T.; Imai, H.; Bertelo, C. A. *Ann. N.Y. Acad. Sci.* **1980**, 35. (b) Genet, J. P.; Mallart, S.; Pinel, C.; Juge, S.; Laffitte, J. A. *Tetrahedron: Asymmetry* **1991**, *2*, 43. (c) Fache, F.; Gamez, P.; Nour, F.; Lemaire, M. *J. Mol. Catal.* **1993**, *85*, 131. (d) Genêt, J. P.; Pinel, C.; Ratovelomanana-Vidal, V.; Mallart, S.; Pfister, X.; Caño De Andrade, M. C.; Laffitte, J. A. *Tetrahedron: Asymmetry* **1994**, *5*, 665. (e) Genêt, J. P.; Pinel, C.; Ratovelomanana-Vidal, V.; Mallart, S.; Pfister, X.; Bischoff, L.; Caño De Andrade, M. C.; Darses, S.; Galopin, C.; Laffitte, J. A. *Tetrahedron: Asymmetry* **1994**, *5*, 675. (f) Berens, U.; Selke, R. *Tetrahedron: Asymmetry* **1996**, *7*, 2055. (g) Selke, R.; Holz, J.; Riepe, A.; Börner, A. *Chem. Eur. J.* **1998**, *4*, 769.
(94) Borns, S.; Kadyrov, R.; Heller, D.; Baumann, W.; Spannenberg, A.; Kempe, R.; Holz, J.; Börner, A. *Eur. J. Inorg. Chem.* **1998**, 1291.
(95) Borns, S.; Kadyrov, R.; Heller, D.; Baumann, W.; Holz, J.; Börner, A. *Tetrahedron: Asymmetry* **1999**, *10*, 1425.
(96) (a) Börner, A.; Kless, A.; Kempe, R.; Heller, D.; Holz, J.; Baumann, W. *Chem. Ber.* **1995**, *128*, 767. (b) Heller, D.; Holz, J.; Borns, S.; Spannenberg, A.; Kempe, R.; Schmidt, U.; Börner, A. *Tetrahedron: Asymmetry* **1997**, *8*, 213. (c) Bühl, M.; Baumann, W.; Kadyrov, R.; Börner, A. *Helv. Chim. Acta* **1999**, *82*, 811.
(97) Andrews, M. A.; Gould, G. L.; Klooster, W. T.; Koenig, K. S.; Voss, E. J. *Inorg. Chem.* **1996**, *35*, 5478.
(98) Andrews, M. A.; Voss, E. J.; Gould, G. L.; Klooster, W. T.; Koetzle, T. F. *J. Am. Chem. Soc.* **1994**, *116*, 5730.
(99) Andrews, M. A.; Cook, G. K.; Shriver, Z. H. *Inorg. Chem.* **1997**, *36*, 5832.
(100) Andrews, M. A.; Gould, G. L. *Organometallics*, **1991**, *10*, 387.
(101) Appelt, A.; Willis, A. C.; Wild, S. B. *J. Chem. Soc., Chem. Commun.* **1988**, 938.
(102) Achternbosch, M.; Klüfers, P. *Acta Crystallogr.* **1994**, *C50*, 175.
(103) Eshaque, M.; McKay, M. J.; Theophanides, T. *J. Clin. Hematol. Oncol.* **1977**, *7*, 338.
(104) (a) Hollis, L. S.; Amundsen, A. R.; Stern, E. W. *J. Am. Chem. Soc.* **1985**, *107*, 274. (b) Basch, H.; Krauss, M.; Stevens, W. J.

Inorg. Chem. **1986**, *25*, 4777. (c) Hollis, L. S.; Stern, E. W.; Amundsen, A. R.; Miller, A. V.; Doran, S. L. *J. Am. Chem. Soc.* **1987**, *109*, 3596.
(105) Roundhill, D. M. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, 1987; Vol 5, p 351.
(106) (a) Yuge, H.; Miyamoto, T. K. *Chem. Lett.* **1996**, 375. (b) Yuge, H.; Miyamoto, T. K. *Acta Crystallogr.* **1996**, *C52*, 3002.
(107) Huang, Z. X.; Qiu, Z.; Cheng, M. Q.; Li, X. J. *Chin. Chem. Lett.* **1991**, *2*, 121.
(108) Hollis, L. S.; Stern, E. W. *Inorg. Chem.* **1988**, *27*, 2826.
(109) (a) Hacker, M. P.; Khokhar, A. R.; Brown, D. B.; McCormack, J. J.; Krakoff, I. H. *Cancer Res.* **1985**, *45*, 4748. (b) Sakai, K.; Yamane, Y. *Biomed. Res. Trace Elem.* **1990**, *1*, 59.
(110) Bose, R. N.; Weaver, E. L. *J. Chem. Soc., Dalton Trans.* **1997**, 1797.
(111) Bryan, D. M.; Pell, S. D.; Kumar, R.; Clarke, M. J.; Rodriguez, V.; Sherban, M.; Charkoudian, J. *J. Am. Chem. Soc.* **1988**, *110*, 1498.
(112) Taqui Khan, M. M.; Shukla, R. S. *Inorg. Chim. Acta* **1988**, *149*, 89.
(113) (a) Taqui Khan, M. M.; Shukla, R. S.*J. Mol. Catal.* **1988**, *44*, 73. (b) Taqui Khan, M. M.; Shukla, R. S. *J. Mol. Catal.* **1988**, *45*, 25. (c) Taqui Khan, M. M.; Shukla, R. S.; Prakash Rao, A. *Inorg. Chem.* **1989**, *28*, 452. (d) Taqui Khan, M. M.; Shukla, R. S. *J. Mol. Catal.* **1989**, *54*, 45. (e) Taqui Khan, M. M.; Shukla, R. S. *J. Mol. Catal.* **1992**, *71*, 157.
(114) Taqui Khan, M. M.; Shukla, R. S. *J. Mol. Catal.* **1992**, *72*, 361.
(115) Taqui Khan, M. M.; Shukla, R. S. *J. Mol. Catal.* **1986**, *37*, 269.
(116) (a) Okamoto, K.; Noji, M.; Tashiro, T.; Kidani, Y. *Chem. Pharm. Bull.* **1981**, *29*, 929. (b) Tajmir-Riahi, H. A. *Biophys. Chem.* **1987**, *27*, 243. (c) Noji, M.; Hanai, M.; Ohmori, T.; Tashiro, T.; Suzuki, K.; Kidani, Y. *Chem. Pharm. Bull.* **1988**, *36*, 3439.
(117) Craciunescu, D.; Molina, C.; Carvajal, R. M.; Doadrio Lopez, A.; Berger, M.; Ghirvu, C. *An. Real Acad. Farm.* **1986**, *52*, 45.
(118) Schwartz, P.; Meischen, S. J.; Gale, G. R.; Atkins, L. M.; Smith, A. B.; Walker Jr., E. M. *Cancer Treat. Rep.* **1977**, *61*, 1519.
(119) Khokhar, A. R.; Hacker, M. P. *Inorg. Chim. Acta* **1991**, *179*, 289.
(120) (a) Noji, M.; Okamoto, K.; Kidani, Y. *J. Med. Chem.* **1981**, *24*, 508. (b) Noji, M.; Achiwa, K.; Kondo, A.; Kidani, Y. *Chem. Lett.* **1982**, 1757. (c) Matsumoto, N.; Sekimizu, K.; Horikoshi, M.; Ohtsuki, M.; Kidani, Y.; Natori, S. *Cancer Res.* **1983**, *43*, 4338. (d) Noji, M.; Gohchi, Y.; Kidani, Y. *Chem.-Biol. Interact.* **1984**, *51*, 37. (e) Kidani, Y.; Achiwa, K.; Ono, H.; Tomatsu, K.; Zaikokuji, K.; Noji, M.; Tashiro, T. *J. Clin. Hematol. Oncol.* **1985**, *15*, 35. (f) Kidani, Y. *Trends Inorg. Chem.* **1990**, *1*, 107.
(121) Das Sarma, B.; Daley, S. K.; Elespuru, R. K. *Chem.-Biol. Interact.* **1983**, *46*, 219.
(122) (a) Kidani, Y.; Noji, M.; Tsukagoshi, S.; Tashiro, T. *Gann* **1978**, *69*, 263. (b) Kidani, Y.; Okamoto, K., Noji, M.; Tashiro, T. *Gann* **1978**, *69*, 863. (c) Kidani, Y.; Noji, M.; Tashiro, T. *Gann* **1980**, *71*, 637. (d) Mesa-Valle, C. M.; Craciunescu, D.; Parrondo-Iglesias, E.; Osuna, A. *Arzneim.-Forsch./Drug Res.* **1989**, *39*, 838.
(123) (a) Noji, M.; Suzuki, K.; Tashsiro, T.; Suzuki, M.; Harada, K.-I.; Masuda, K.; Kidani, Y. *Chem. Pharm. Bull.* **1987**, *35*, 221. (b) Hrubiško, M.; Kysela, B.; Kuliffay, P. *Neoplasma*, **1989**, *36*, 401.
(124) de Souza Gil, E.; de Almeida Gonçalves, M. I.; Ferreira, E. I.; Zyngier, S. B.; Najjar, R. *Met.-Based Drugs* **1999**, *6*, 19.
(125) Brunner, H.; Kluschanzoff, H.; Wutz, K. *Bull. Soc. Chim. Belg.* **1989**, *98*, 63.
(126) Sawyer, D. T.; George, R. S.; Bagger, J. B. *J. Am. Chem. Soc.* **1959**, *81*, 5893.
(127) Sawyer, D. T.; Tinti, D. S. *Inorg. Chem.* **1963**, *2*, 796.
(128) (a) Hinckley, C. C.; Ostenburg, P. S.; Roth, W. J. *Polyhedron* **1982**, *1*, 335. (b) Hinckley, C. C.; Bemiller, J. N.; Strack, L. E.; Russel, L. D. *ACS Symp. Ser.* **1983**, *209*, 421.
(129) (a) Wenz, G. *Angew. Chem.* **1994**, *106*, 851. (b) D'Souza, V. T.; Lipkowitz, K. B. *Chem. Rev.* **1998**, *98*, 1741. (c) Szejtli, J. *Chem. Rev.* **1998**, *98*, 1743.
(130) Alston, D. R.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J.; Zarzycki, R. *Angew. Chem.* **1988**, *100*, 1215.
(131) (a) Alston, D. R.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1602. (b) Alston, D. R.; Ashton, P. R.; Lilley, T. H.; Stoddart, J. F.; Zarzycki, R. *Carbohydr. Res.* **1989**, *192*, 259.
(132) Alston, D. R.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem.* **1985**, *97*, 771.
(133) Meister, G.; Stoeckli-Evans, H.; Süss-Fink, G. *J. Organomet. Chem.* **1993**, *453*, 249.
(134) Klingert, B.; Rihs, G. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1991**, *10*, 255.
(135) (a) Sokolov, V. I. *Metalloorg. Khim.* **1988**, *1*, 25. (b) Sokolov, V. I.; Blyumenfel'd, A. L.; Narankiewicz, Z.; Nefedova, M. N.; Mamed'yarova, I. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1991**, 2165. (c) Narankiewicz, Z.; Alexander, A. L.; Bondareva, L.; Mamedyarova, I. A.; Nefedova, M. N.; Sokolov, V. I. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1991**, *11*, 233. (d) Klingert, B.; Rihs, G. *J. Chem. Soc., Dalton Trans.* **1991**, 2749. (e) Sokolov, V. I.; Bondareva, V. L.; Shustov, G. V. *Metalloorg. Khim.* **1991**, *4*, 697.
(136) (a) Harada, A.; Takahashi, S. *J. Chem. Soc., Chem. Commun.* **1986**, 1229. (b) Harada, A.; Yamamoto, S.; Takahashi, S. *Organometallics* **1989**, *8*, 2560.
(137) Sokolov, V. I.; Bondareva, V. L.; Chizhevskii, I. T.; Reutov, O. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987**, *7*, 1689.
(138) Morimoto, Y.; Ando, K.; Uno, M.; Takahashi, S. *Chem. Lett.* **1996**, 887.
(139) Harada, A.; Takeuchi, M.; Takahashi, S. *Chem. Lett.* **1986**, 1893.
(140) (a) Imonigie, J. A.; Macartney, D. H. *Inorg. Chem.* **1993**, *32*, 1007. (b) Robinson, E, A.; Earley, J. E. *Inorg. Chem.* **1999**, *38*, 4128.
(141) Cline III, J. I.; Dressick, W. J.; Demas, J. N.; DeGraff, B. A. *J. Phys. Chem.* **1985**, *89*, 94.
(142) Sinisterra, R. D.; Najjar, R.; Alves, O. L.; Santos, P. S.; Alves de Carvalho, C. A.; Conde da Silva, A. L. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1995**, *22*, 91.
(143) (a) Alston, D. R.; Lilley, T. H.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1600. (b) Brunner, H.; Hankofer, P.; Treittinger, B. *Chem. Ber.* **1990**, *123*, 1029. (c) Tanaka, M.; Kuwahara, E.; Shimizu, T.; Chikazawa, H.; Hisada, S.; Takahashi, N. *Biol. Pharm. Bull.* **1999**, *22*, 521. (d) Ferruti, P.; Ranucci, E.; Trotta, F.; Gianasi, E.; Evagorou, E. G.; Wasil, M.; Wilson, G.; Duncan, R. *Macromol. Chem. Phys.* **1999**, *200*, 1644.
(144) (a) Zahalka, H. A.; Januszkiewicz, K.; Alper, H. *J. Mol. Catal.* **1986**, *35*, 249. (b) Monflier, E.; Blouet, E.; Barbaux, Y.; Mortreux, A. *Angew. Chem.* **1994**, *106*, 2183. (c) Monflier, E.; Tilloy, S.; Fremy, G.; Barbaux, Y.; Mortreux, A. *Tetrahedron Lett.* **1995**, *36*, 387. (d) Monflier, E.; Tilloy, S.; Blouet, E.; Barbaux, Y.; Mortreux, A. *J. Mol. Catal. A: Chem.* **1996**, *109*, 27. (e) Tilloy, S.; Bertoux, F.; Mortreux, A.; Monflier, E. *Catal. Today* **1999**, *48*, 245.
(145) (a) Anderson, J. R.; Campi, E. M.; Jackson, W. R. *Catal. Lett.* **1991**, *9*, 55. (b) Monflier, E.; Tilloy, S.; Fremy, G.; Castanet, Y.; Mortreux, A. *Tetrahedron Lett.* **1995**, *36*, 9481. (c) Monflier, E.; Fremy, G.; Castanet, Y.; Mortreux, A. *Angew. Chem.* **1995**, *107*, 2450.
(146) Monflier, E.; Tilloy, S.; Bertoux, F.; Castanet, Y.; Mortreux, A. *New J. Chem.* **1997**, *21*, 857.
(147) Lacroix, T.; Bricout, H.; Tilloy, S.; Monflier E. *Eur. J. Org. Chem.* **1999**, 3127.
(148) Monflier, E.; Tilloy, S.; Castanet, Y.; Mortreux, A. *Tetrahedron Lett.* **1998**, *39*, 2959.
(149) Zahalka, H. A.; Alper, H. *Organometallics* **1986**, *5*, 1909.
(150) (a) Pinel, C.; Gendreau-Diaz, N.; Lemaire, M. *Chem. Ind. (Dekker)* **1996**, *68*, 385. (b) Pinel, C.; Gendreau-Diaz, N.; Bréhéret, A.; Lemaire, M. *J. Mol. Catal. A: Chem.* **1996**, *112*, L157.
(151) Shimizu, S.; Sasaki, Y.; Hirai, C. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 176.
(152) (a) Lewis, L. N.; Sumpter, C. A.; Davis, M. *J. Inorg. Organomet. Polym.* **1995**, *5*, 377. (b) Lewis, L. N.; Sumpter, C. A.; Stein, J. *J. Inorg. Organomet. Polym.* **1996**, *6*, 123. (c) Lewis, L. N.; Sumpter, C. A. J. *Mol. Catal. A: Chem.* **1996**, *104*, 293.
(153) Willner, I.; Mandler, D. *J. Am. Chem. Soc.* **1989**, *111*, 1330.
(154) Smith, G. V.; Cheng, J.; Song, R. *Chem. Ind. (Dekker)* **1996**, *68*, 479.
(155) (a) Cucinotta, V.; Mangano, A.; Nobile, G.; Santoro, A. M.; Vecchio, G. *J. Inorg. Biochem.* **1993,** *52*, 183. (b) Cucinotta, V.; Grasso, G.; Pedotti, S.; Rizzarelli, E.; Vecchio, G.; Di Blasio, B.; Isernia, C.; Saviano, M.; Pedone, C. *Inorg. Chem.* **1996**, *35*, 7535. (c) Matsumoto, K.; Noguchi, Y.; Yoshida, N. *Inorg. Chim. Acta* **1998**, *272*, 162.
(156) Ling, C.-C.; Miocque, M.; Coleman, A. W. *J. Coord. Chem.* **1993**, *28*, 313.
(157) (a) Brügger. N.; Deschenaux, R.; Ruch, T.; Ziessel, R. *Tetrahedron Lett.* **1992**, *33*, 3871. (b) Deschenaux, R.; Ruch, T.; Deschenaux, P.-F.; Juris, A.; Ziessel, R. *Helv. Chim. Acta* **1995**, *78*, 619.
(158) Venema, F.; Baselier, C. M.; van Dienst, E.; Ruël, B. H. M.; Feiters, M. C.; Engbersen, J. F. J.; Reinhoudt, D. N.; Nolte, R. J. M. *Tetrahedron Lett.* **1994**, *35*, 1773.
(159) Weidner, S.; Pikramenou, Z. *Chem. Commun.* **1998**, 1473.
(160) Chavarot, M.; Pikramenou, Z. *Tetrahedron Lett.* **1999**, *40*, 6865.
(161) (a) Liu, Y.; Li, B.; Wada, T.; Inoue, Y. *Supramol. Chem.* **1999**, *10*, 279. (b) Liu, Y.; You, C.-C.; Chen, Y.; Wada, T.; Inoue, Y. *J. Org. Chem.* **1999**, *64*, 7781.
(162) Deshpande, R. M.; Fukuoka, A.; Ichikawa, M. *Chem. Lett.* **1999**, 13.
(163) Reetz, M. T.; Waldvogel, S. R. *Angew. Chem.* **1997**, *109*, 870.
(164) Reetz, M. T.; Frömbgen, C. *Synthesis* **1999**, 1555.
(165) Sawamura, M.; Kitayama, K.; Ito, Y. *Tetrahedron: Asymmetry* **1993**, *4*, 1829.
(166) Reetz, M. T.; Rudolph, J. *Tetrahedron: Asymmetry* **1993**, *4*, 2405.

CR9903050