Inorg. Chem. **2007**, *46*, 4326–4335

Studies Directed to Understanding the Structure of Chitosan–Metal Complexes: Investigations of Mono- and Disaccharide Models with Platinum(II) Group Metals

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Received January 4, 2007

X-ray and NMR experiments were performed with simple chitosan models based on glucosamine monosaccharides and disaccharides to understand the binding properties and structures of the complexes formed between this polysaccharide and platinum(II) metals. Subjection of the glucosamine derivatives with $[PdCl_2(PhCN)_2]$ provided *trans*-diamine complexes which upon further treatment with excess $(NH_4)PF_6$ generated complexes possessing two 5-membered chelate rings involving the C2-amine and the C3-hydroxyl group of the two individual glucosamine units.

Introduction

The complexation between carbohydrates and metal ions is of increasing interest as such interactions owing to their important functions in a variety of biological systems involving structural support in membrane systems, cell−cell adhesion, and transmission of nerve impulses.[1] Apart from the biological area, metal−carbohydrate interactions have also been exploited in metal-catalyzed enantioselective synthesis, as carbohydrates represent enantiomerically pure compounds isolated from the chiral pool.[2] From a coordination chemistry perspective, carbohydrates are functionalized with a sequence of weakly chelating donor sites. The high content of hydroxyl groups can result in the formation of a potpourri of configurational isomers upon complexation, where some of these are in conformational and configurational equilibrium as a consequence of the low-energy barrier between the isomers.[3] These concerns which are inherent to the specific metal−carbohydrate complexes complicates isolation and characterization and is a main contributor to why this field has been largely unexplored.[4] Carbohydrate derivatives containing other functionalities such as amides, amines, and carboxylic groups contribute to stronger metal ion complexation.[5] Chitosan is a long chained linear polysaccharide comprised of random units of glucosamine and its *N*-acetyl derivative, with a high abundance of free amine groups (Figure 1a). It is derived from the basic hydrolysis of the *N*-acetyl glucosamine polymer, chitin, representing the second most abundant biopolymer in nature after cellulose.[6] Due to the strong complexation abilities of the amine groups with metal ions, chitosan has by large been investigated as an absorption material for recovering valuable metal ions from industrial effluents.[7] The high physical and chemical versatility of chitosan has promoted an increasing interest for heterogeneous chitosan-supported catalysis.[8] It is desirable to have inexpensive and easily accessible catalysts using ligands that have the potential to overcome the disadvantages of catalyst sensitivity to environmental concerns as well as being air stable. Chiral materials such

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10.1021/ic070016r CCC: $37.00
Published on Web 04/20/2007

as chitosan could even enhance enantioselectivities in catalytic reactions.[9]

The interaction between this biopolymer and a transition-metal ion has been disputed, and several mechanisms have been proposed. The current stuctures proposed involve (a) a complex comprised of one amine group per bound metal and (b) a bridging model which involves a metal complexed to two amine groups from either the same or an opposite chain (Figure 1b).[8] It is though commonly accepted that the amine sites are the main reactive groups for metal ion absorption but that the high content of hydroxyl groups may also contribute to binding with the metal ions, for example, the hydroxyl group in the C-3 position in close proximity to the amine group or the hydroxyl groups of the vicinal glucosamine unit toward the reducing end could additionally be contributing to metal ion absorption.[10] The physical and chemical properties of such complexes nevertheless complicate analyses by conventional methods like NMR and X-ray. Kramareva et al. have investigated a series of chitosan complexes with palladium(II).[11] In this work, a structure of a complex between palladium(II) chloride and chitosan formed via a coprecipitation method was proposed based on a FTIR study. The palladium(II) metal ion is bound tetravalently to chitosan via complexation to two amine groups and two hydroxy groups of the adjacent glucosamine units. This is a reasonable assumption considering the preferred conformation of β-(1→4)-linked glucose and glucosamine units where the C6-OH is in close proximity to the C2′-nitrogen.[12] In an attempt to clarify whether these results represent a true picture of the Pd(II)·chitosan complexes, we have investigated the structures of palladium and platinum salts with glucosamine derivatives as mono- and disaccharides in solution using NMR spectroscopy as the key technique, the outcome of which are presented below. Our results lead to the proposal of an alternative complex formed between chitosan and the platinum(II) group metals.

Results and Discussions

Synthesis of the Mono- and Disaccharide Ligands. In an effort to clarify the coordination mode of chitosan with platinum group metals, different monosaccharides and disaccharides of glucosamine were synthesized. A study with such sugars not only would bring to light valuable information concerning the metal binding properties of the individual carbohydrate units but also provide a simple model for examining the possible role of the vicinal sugar in metal complexation. With respect to the monosaccharides, both methyl 2-amino-2-deoxy-β-D-glucopyranoside (**1**, Me-GlcN), representing the simplest binding unit of chitosan as well as the 3,4,6-tri-*O*-acetyl derivative **2** (Me-AcGlcN), were prepared. Inclusion of the triacetate **2** for this investigation was made under the assumption that this sugar only possesses one coordination site due to the absence of the free hydroxyl groups and therefore respresents a monodentate ligand for Pd or Pt for comparison with the unprotected ligand **1**. In addition, this triactylated glucosamine derivative readily dissolves in a range of organic solvents.

Both the glucosamine derivatives **1** and **2** were prepared in a straightforward procedure from readily available D-glucosamine·HCl (Scheme 1).[13] Formation of the α-glycosyl bromide in acetyl bromide, followed by a glycosylation step with MeOH, provided Me-AcGlcN (**2**) with a free amino group in a 41% yield for the two steps. The acetyl groups were conveniently removed by treatment with a catalytic amount of NaOMe in MeOH. Purification by ion-exchange chromatography then provided Me-GlcN (**1**) in a 95% yield.

In order to determine the influence of a vicinal sugar moiety in the coordination of the metal ion, the disaccharide **3** (Scheme 2) was prepared as a model of chitosan. This disaccharide was constructed with glucose rather than glucosamine in the reducing end to prevent possible complications arising from the participation of an additional amine functionality in the complexation studies with the transition-metal ions.

For further investigation of the postulated participation of the C6-OH in the chelation of metal ions, the synthesis of the analogous 6-deoxy disaccharide **4** (Scheme 2) was also performed. The disaccharide ligands **3** and **4** were synthesized as illustrated in Scheme 2. The glycosylation steps were performed between the PNZ-amine protected glycosyl donor, imidate **5**,[14,15] and the two partially protected methyl α-D-

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(15) PNZ = *p*-nitrobenzyloxycarbonyl.

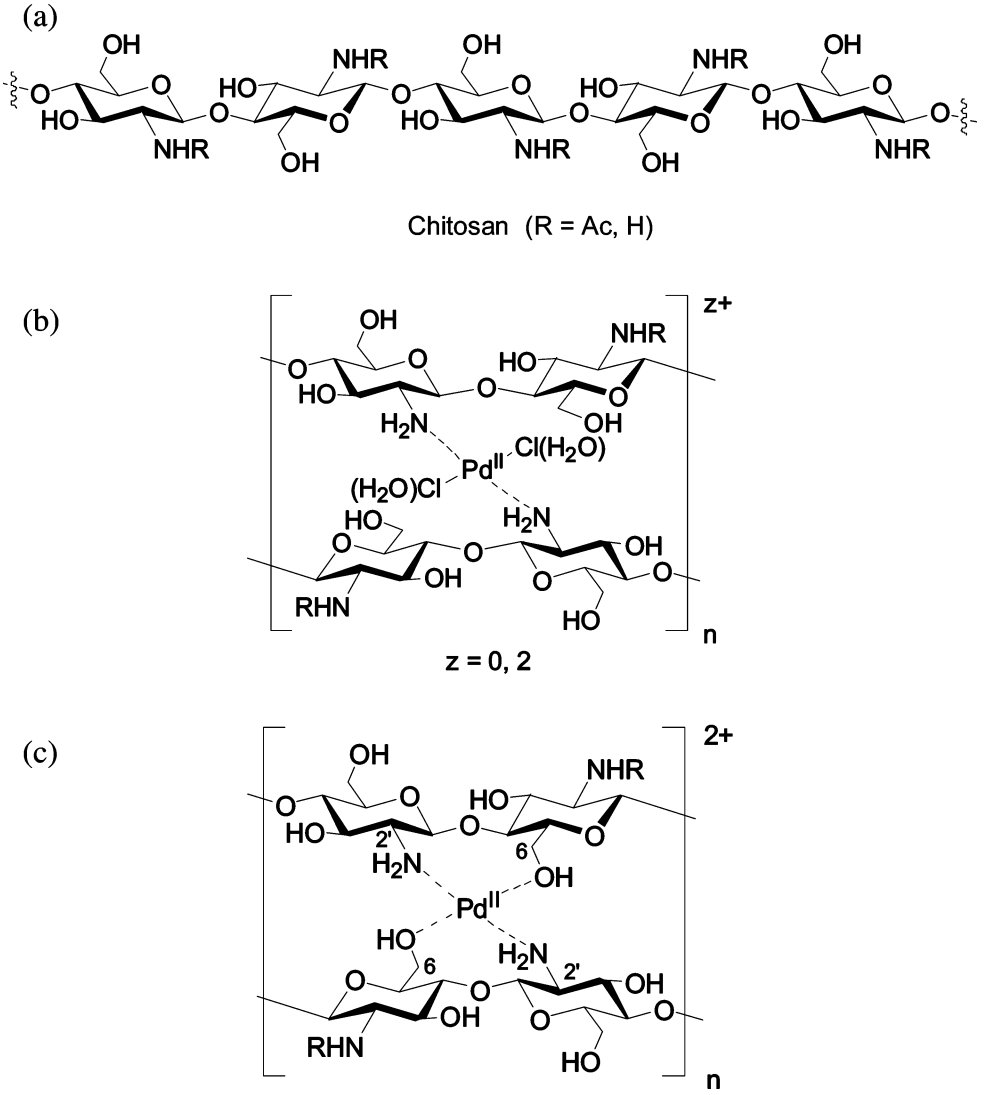

Figure 1. (a) Chitosan, (b) bridging model with the palladium(II) center complexed to two amine groups from opposing chitosan chains, and (c) proposed chitosan complex with palladium(II) as reported by Kramareva et al.[11]

glucopyranoside derivatives **6** and **7**.[16] These coupling partners were readily obtained in few steps from D-glucosamine·HCl and methyl α-D-glucopyranoside, respectively. Treatment of imidate **5** with either acceptor **6** or **7** under Schmidt's conditions using BF_3·Et_2O as the Lewis acid promoter afforded the β-disaccharides **8** and **9** containing a β-(1→4) linkage in good yields and high β-selectivities.[17] The deprotected disaccharide **3** was obtained from simple deacetylation using Zemplén conditions to the triol **10** followed by hydrogenation with Pd/C and hydrogen under acidic conditions. Alternatively, attempted hydrogenolysis of **9** with Pd/C and H_2 under nonacidic conditions interestingly cleaved the PNZ group selectively affording the amine **11** with the benzyl groups intact. Nevertheless, deacetylation to **12** followed by a second hydrogenolysis step in the presence of acetic acid led smoothly to the 6-deoxy disaccharide **4**.

Complexation Studies with Me-AcGlcN (2). Treatment of $[PdCl_2(PhCN)_2]$, which is solely comprised of the *trans*-isomer,[18] with Me-AcGlcN (**2**) in a molar ratio of 1:2 in dichloromethane furnished instantaneously the yellow complex *trans*-$[PdCl_2$(Me-AcGlcN$)_2]$ (**13**) by replacement of the weakly coordinated benzonitriles (Scheme 3). Changing the ratio to 1:1 does not affect the coordination mode of the ligand in solution and led to a 1:1 mixture of **13** and the free substrate. The metal·sugar complex could be purified by chromatography on silica gel and isolated in a yield of 91%. Additionally, **13** is air-stable and can be stored at room temperature for several months without decomposition.

^{1}H chemical shifts for the free ligand and the complex **13** are listed for comparison in Table 1. The ^{1}H NMR spectrum of **13** in $CDCl_3$ reveals only one set of 13 magnetically nonequivalent protons, indicating a close symmetrical arrangement of the two glucosamine units around the palladium(II) metal. A broadening of the resonances correspond-

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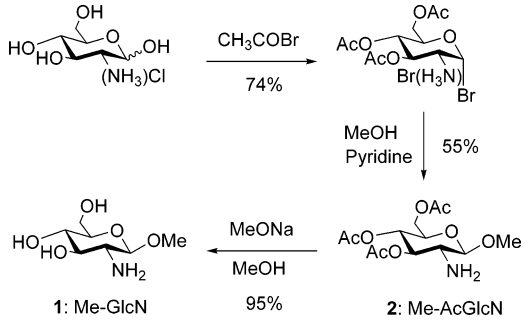
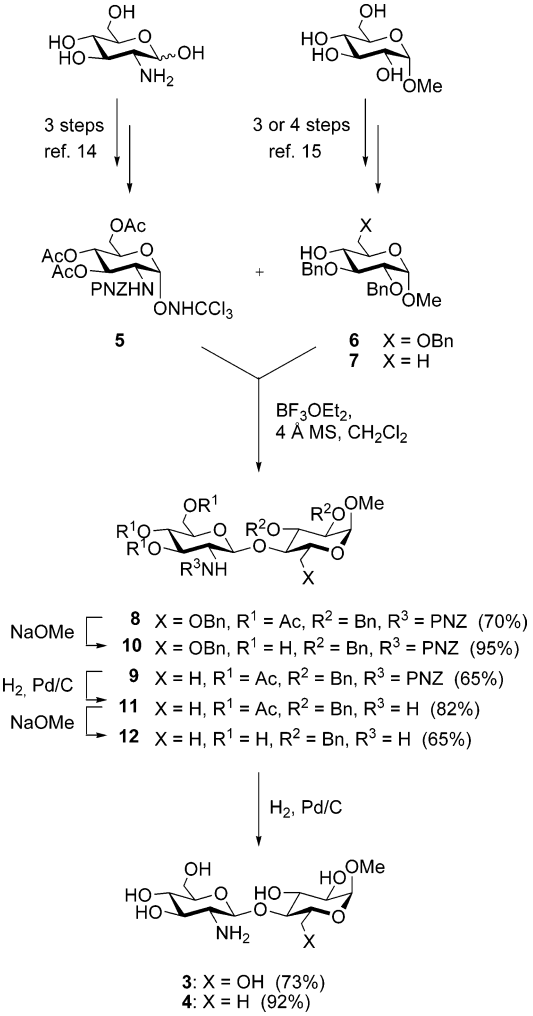
Scheme 1. Synthesis of the Glucosamine Derivatives **1** and **2**



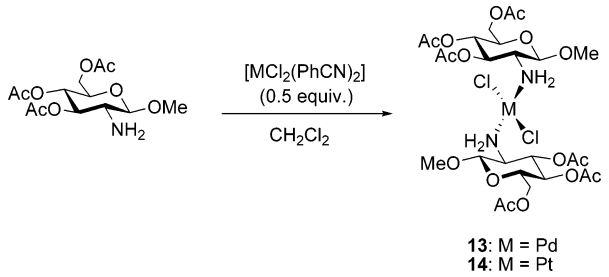
Scheme 2. Synthesis of the Disaccharides **3** and **4**



ing to H-1 and H-3 is observed which nevertheless suggests a slight difference in nature of the these ring protons between the two metal bound sugar units. Comparison of the NMR data of the free ligand and the complex reveals coordination induced shifts.

Upon complexation the two diastereotopic amine protons give rise to two resonances in the ^{1}H NMR spectrum, undoubtedly because of a slow inversion at the nitrogen when the amine group is coordinated to the metal center. The chemical shifts for both protons are downfield compared to the free ligand which is attributed to the formation of a Pd−N bond. Similar changes in chemical shifts have been reported

Scheme 3. Formation of Pd and Pt Complexes **13** and **14** with Me-AcGlcN (**2**)



by Georgiadis et al. for the platinum complex of 2-desoxystreptamine.[19]

The ring protons in close proximity of the coordination site display significant deshielding in the ^{1}H NMR spectrum. The induced shifts of $\Delta\delta$(H) = 0.81 and 1.65 ppm for H-1 and H-3, respectively, are considerably different from the changes of a comparable palladium complex with 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine reported by Beck, where the induced shifts of H-1 and H-3 are equal in magnitude.[20] The noteworthy deshielding of the H-3 ring proton can be attributed to the arrangement of the acetyl group at C3 in close proximity to the plane of the Pd(II) complex. This arrangement is supported by X-ray analysis (vide infra). Furthermore an upfield shift ($\Delta\delta$(H) = −0.31 ppm) of the H-2 was also observed for the complex **13**. A similar change in chemical shift was not observed for the complex reported by Beck, due to coalescence of the resonances of the ring protons.[20]

A similar complexation study was performed in DMSO-d_6 in order to examine the influence of a polar coordinating solvent on the complexation of **2** with [$PdCl_2(PhCN)_2$], although it was anticipated not to be without problems as the decomposition of amino palladium complexes in DMSO by ligand to solvent exchange has previously been reported.[21] Indeed, the NMR data in DMSO-d_6 was complicated by the appearance of three Pd complexes **13a**−**c** in the ratio of 5:9:2 apart from the free ligand (Table 1). Displacement of one ligand affords a complex with only one glucosamine unit, which is expected to account for one set of signals in the ^{1}H NMR. Another set of signals is undoubtedly the *trans*-complex. Palladium(II) complexes are known to preferably adapt the *trans*-configuration in the case of monoamine-based ligands,[21] whereas the literature reveals only limited examples of *cis*-isomers.[22] Furthermore, the steric bulk of the glucosamine moiety would disfavor the more sterically congested *cis*-isomer. Accordingly the remaining signals could arise from rotamers of the *trans*-complex in conjunction with

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Table 1. ^{1}H NMR Data for Complexes **2**, **13**, and **14**[a]

compd	H-1	H-2	H-3	H-4	H-5	H-6a and 6b	NH	solvent
2	4.16	2.90	5.01	4.97	3.68	4.29, 4.12	1.39	$CDCl_3$
2	4.28 (7.9)	2.62 (10.0)	4.92 (9.6)	4.76 (10.0)	3.80 (5.0)	4.17 (12.2), 3.99 (2.3)		$(CD_3)_2SO$[b]
13	4.97 (8.4)	2.59	6.66	5.02 (8.6, 9.7)	4.28	4.38 (3.9, 12.3), 4.17 (1.8, 12.3)	3.39 (4.6, 10.7), 3.22 (10.7)	$CDCl_3$
13a[c]	4.63 (8.0)	2.78 (10.1)	5.36 (9.1)	4.73 (10.0)	3.78 (4.6)	4.20 (12.5), 4.02 (2.4)	3.69 (7.0, 11.3), 3.56 (4.0)	$(CD_3)_2SO$[b]
13b[c]	4.58 (8.2)	3.03 (10.2)	5.27 (9.3)	4.72 (10.0)	3.73 (4.3)	4.20 (12.5), 4.02 (2.4)	4.45 (7.3, 10.7), 4.19 (6.5)	$(CD_3)_2SO$[b]
13c[c]	4.70	3.12	5.23 (9.2)	4.77 (10.2)	3.85 (4.5)	4.20, 3.99	4.30, 4.24	$(CD_3)_2SO$[b]
14	4.90 (9.9)	2.62 (4.7, 10.1)	6.58 (9.1)	4.92 (8.4)		4.49, 3.42		$CDCl_3$

[a] Chemical shifts (δ) in ppm. Coupling constants (J) in Hertz. [b] ^{1}H NMR spectrum measured at 600 MHz. [c] Three different palladium(II) complexes were observed in DMSO.

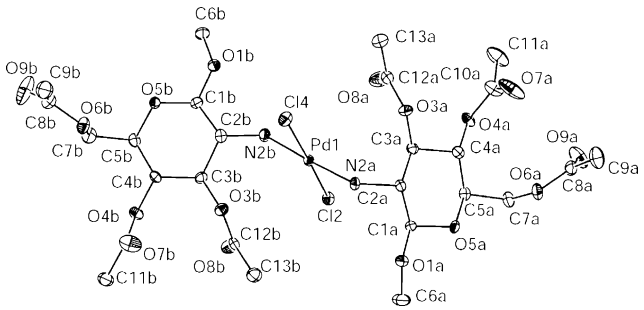

Figure 2. ORTEP representation of the complex *trans*-[$PdCl_2$(Me-AcGlcN)$_2$] (**13**) at the 50% probability level. Important bond lengths: Cl2−Pd1 2.3061(8), Cl4−Pd1 2.2953(8), Pd1−N2B 2.061(3), Pd1−N2A 2.067(3).

other complex studies in DMSO.[23] Although each glucosamine ligand has two relatively small chlorido ligands in the *cis*-position as well as the fact that different rotamers were not observed in $CDCl_3$ could argue against this possibility. Alternatively, this set of signals could be ascribed to a complex obtained by the partial solvolysis of the *trans*-complex with release of a chloride ion. Interestingly, the coupling constants of the amino protons of the two major compounds are distinct, indicating a different orientation of the glucosamine moiety relative to the plane of the palladium complex (Table 1).

Attempts to grow crystals suitable for X-ray structural analysis of complex **13** in various traditional solvent systems employing the vapor diffusion technique afforded only fine powders of the material. However, crystallization from DMSO produced suitable crystals upon standing at room temperature. The X-ray data reveal that the two glucosamine derivatives lie on opposite sides of the palladium center and that each of the two glucosamine units adopts the expected chair conformation with the methoxy group in an equatorial position (Figure 2). Furthermore, the two glucosamine units are shown to be crystallographically independent, and therefore no symmetry is displayed in the complex. This is reflected in the distance between the metal center to H-3 of the two glucosamine units, measured to 2.983 Å and 4.103 Å, respectively. The square planar geometry about Pd is slightly distorted, with N−Pd−Cl angles of 90.89(8)°, 86.32(7)°, 96.14(7)°, and 86.66(8)°, whereas the Pd−Cl and Pd−N distances (av 2.301 Å and 2.065 Å, respectively) have normal values. Interestingly, the complex exhibits two dangling or very weakly interacting oxygen atoms of the acetyl group in C-3 position of the sugar in the apical positions of the square planar complex, at 3.23 Å and 3.54 Å from the metal center.[24] In view of the structural results obtained, it is likely that the quasi-octahedral stereochemistry of the complex accounts for the significant chemical shift change of H-3. In comparison, the Pd(II) complex presented by Beck has two acetyl groups approximately in the same distance of the amino group which brings competition between the two groups giving rise to changes in chemical shift which are similar in value.[20]

The analogous Pt complex was prepared from [$PtCl_2$-$(PhCN)_2$], a pale yellow salt composed of a mixture of two isomers. Me-AcGlcN (**2**) reacts with [$PtCl_2(PhCN)_2$] in a molar ratio of 2:1 affording a pale yellow powder after column chromatography. Ligand exchange of Pt is slow compared to Pd, and higher temperature and longer reaction times are required. The product consists of two different complexes where the predominant component **14** displays similar coordinatively induced chemical shifts in the ^{1}H NMR spectrum as for the Pd *trans*-complex. The minor component could be the *cis*-isomer, but this has not been verified. Additional structural support for the major isomer was discerned from the solid-state structure of the Pt complex determined by single-crystal X-ray diffraction, where it was found to be isomorphous with the analogous Pd complex.[25] The acetyl groups at the C3-positions are situated apically to the Pt center providing a distorted pseudooctahedral stereochemistry with the angles of N−Pt−Cl being 91.51(16)°, 85.79(14)°, 96.24(14)°, and 86.46(16)°. The distances of the two C3-oxygens to the Pt center are 3.310 Å and 3.580 Å, respectively.

Complexation Studies with Me-GlcN (1). The free hydroxyl groups of Me-GlcN provide means of additional coordination sites on the monosaccharide and thereby rigidity of the inherently flexible complex. Upon mixing **1** with [$PdCl_2(PhCN)_2$] in a molar ratio of 2:1 in MeOH-d_4 two

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(25) Crystallographic data for compound **14** are found in the Supporting Information.

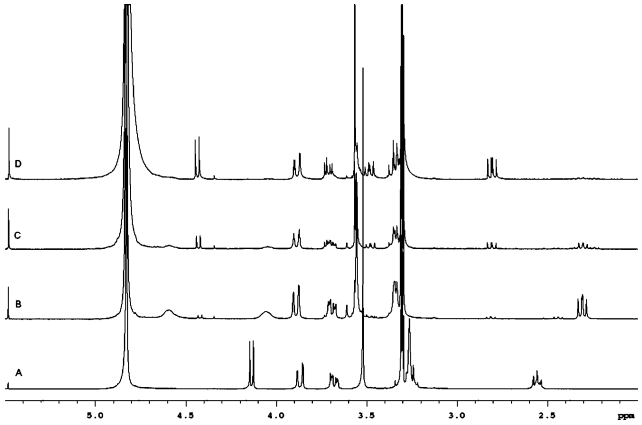
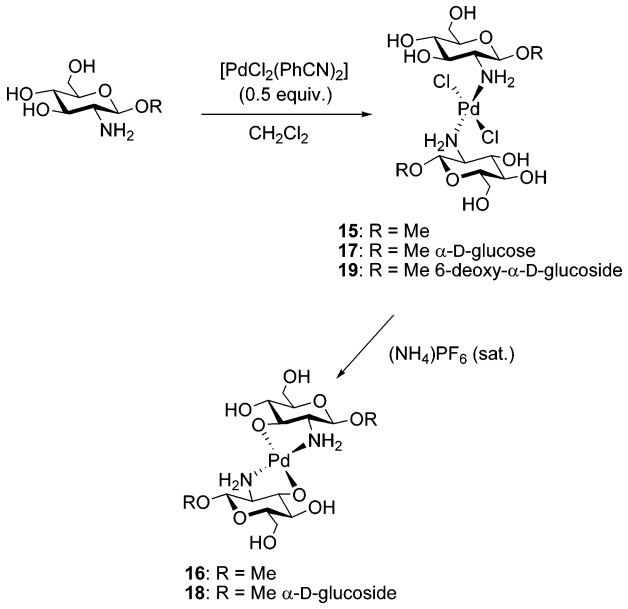


Figure 3. Complexation studies with Me-GlcN (**1**) by ^{1}H NMR spectroscopy in MeOH-d_4: spectrum A, Me-GlcN (**1**); spectrum B, Me-GlcN and $[PdCl_2(PhCN)_2]$ (0.5 equiv); spectrum C, Me-GlcN, $[PdCl_2(PhCN)_2]$ (0.5 equiv) and $(NH_4)PF_6$ (1 equiv), 1 h; and spectrum D, Me-GlcN, $[PdCl_2(PhCN)_2]$ (0.5 equiv) and $(NH_4)PF_6$ (5 equiv), 24 h.

Scheme 4. Formation of the Pd complexes **15**−**19**



complexes detectable by NMR spectroscopy were rapidly formed (Figure 3). $[PdCl_2(PhCN)_2]$ is practically insoluble in MeOH but readily dissolves in the presence of Me-GlcN, indicating complexation of the sugar ligand. In contrast to Me-AcGlcN (**2**), the complexes prepared with the glucosamine units possessing free hydroxyl groups could not be purified by column chromatography. Therefore, the spectroscopic data were measured directly on the complexes formed in solution. ^{1}H chemical shifts for the free ligand and the complexes **15** and **16** (Scheme 4) are listed in Table 2 for comparison. Proton signals were observed in the aromatic region that are consistent with uncoordinated PhCN, which also substantiates complex formation between the metal and the sugar. The free PhCN is not believed to have an influence on the spectroscopic data of the complexes, and the signals corresponding to PhCN are therefore omitted.

The main peaks are presumed to originate from the *trans*-isomer **15** (Scheme 4). The changes in the chemical shifts of H-1 and H-3 upon complexation are $\Delta\delta(H) = 0.49$ and 0.81 ppm, respectively, whereas H-2 is upfield shifted ($\Delta\delta(H) = -0.35$ ppm). The δ values of the minor complex are significantly displaced with respect to the *trans*-complex and the free ligand, and, interestingly, the δ value of H-2 is shifted downfield, whereas for H-1 and H-3 the change is upfield in comparison to the presumed *trans*-isomer **15**. Furthermore, the latter two signals of the minor complex sharpen, insinuating an increased rigidity of the complex. The remaining ring protons are only slightly affected by coordination. These observations can possibly be rationalized by coordination of the Pd(II) center to the C3-OH groups with the formation of either a cationic or a neutral complex **16**. The molecular structure of this complex exhibits a five-membered *N*,*O*-chelate cycle fused to the pyranose ring where the coordinating groups occupy an equatorial orientation. A similar type of coordination has been reported by Yoshikawa and co-workers for a diequatorial vicinal diamino sugar.[26] The ratio between the two complexes **15** and **16** (or the cationic species) does not change upon standing in solution. Further support for the formation of a complex with two bidentate bound sugars was obtained upon subjection of the mixture with a large excess of $(NH_4)PF_6$ overnight. In this way only a single complex, corresponding to the minor component in solution, was detected in the ^{1}H NMR spectrum (Figure 3). Two types of coordination between the Pd(II) center and the C3-hydroxyl groups are possible. Simple abstraction of the chloride with $(NH_4)PF_6$ from the metal center and metal coordination of the C3-hydroxyl group would lead to a cationic complex. Halide abstraction from Pd(II) complexes using $(NH_4)PF_6$ to afford air-stable cationic species is well-known in the literature. On the other hand, deprotonation of the C3-OH and loss of HCl generate a better electron donating ligand for coordination, affording a neutral Pd(II) alkoxide species as represented in structure **16** (Scheme 3). Although it was not possible to obtain suitable crystals of the complex for a structural confirmation, we assume that the *trans*-configuration of the nitrogen atoms on the metal center has been conserved. Unfortunately, attempts to produce the same type of complex with Pt led only to a complex mixture of compounds according to the ^{1}H NMR spectrum, and no further investigation of these compounds was continued.

Table 2. ^{1}H NMR Data for Compounds **1**, **15**, and **16**[a]

compd	**1**	**15**	**16**
H-1	4.12 (d, 8.0)	4.61 (bs)	4.44 (d, 8.4)
H-2	2.55 (dd, 8.0, 9.2)	2.30 (dd, 8.4, 10.0)	2.81 (dd, 8.4, 10.6)
H-3	3.26	4.07 (bs)	3.48 (dd, 8.2, 10.6)
H-4	3.24 (t, 9.4)	3.32	3.34
H-5	3.26	3.32	3.31
H-6_a	3.87 (dd, 1.6, 12.1)	3.89 (dd, 1.2, 11.1)	3.88 (dd, 2.1, 11.9)
H-6_b	3.68	3.69	3.71 (dd, 5.0, 11.9)
Me	3.52 (s)	3.55 (s)	

[a] ^{1}H NMR spectra are recorded in $CDCl_3$ at 400 MHz. Chemical shifts (δ) in ppm. Coupling constants (J) in Hertz.

Complexation Studies with the Disaccharides 3 and 4. The manifold of donor sites of nearly equivalent oxygen

(26) Tsubomura, T.; Yano, S.; Kobayashi, K.; Sakurai, T.; Yoshikawa, S. *J. Chem. Soc., Chem. Commun.* **1986**, 459−460.

Table 3. ^{1}H NMR Data for Compounds **3**, **4**, and **17**−**19**[a]

compd	**3**	**17**	**18**	**4**	**19**
H-1′	4.37 (d, 8.1)	4.84 (bs)	4.77 (d, 8.5)	4.33 (d, 8.0)	4.81 (8.4)
H-2′	2.62 (dd, 9.6)	2.50	2.99 (dd, 10.5)	2.65 (dd, 9.4)	2.48 (dd, 9.9)
H-3′	3.29 (dd, 9.1)	4.03 (bs)	3.53 (dd, 9.5)	3.26 (dd, ≈ 9)	4.04
H-4′	3.25 (dd, 9.1)	3.33	3.37	3.29	3.33
H-5′	3.35 (m)	3.40	3.40 (1.6)	3.35	3.38
H-6′	3.67 (dd, 6.0, 11.9), 3.89 (dd, 2.1, 11.8)	3.64 (dd, 6.6, 11.9), 3.91 (dd, 1.8, 11.8)	3.89 (dd, 12.2), 3.70 (dd, 5.0)	3.66 (6.1), 3.89 (2.2, 11.8)	3.62 (dd, 6.8, 11.7), 3.92 (dd, 1.8, 11.7)
H-1	4.66 (d, 3.7)	4.66 (3.7)	4.68 (d, 3.8)	4.59 (d, 3.8)	4.59 (d, 3.6)
H-2	3.45 (dd, 9.6)	3.44 (dd, 9.6)	3.46 (dd, 9.4)	3.45 (dd, 9.7)	3.44 (dd, 9.7)
H-3	3.74 (dd, 8.6)	3.80	3.78	3.66 (dd, 8.5)	3.74
H-4	3.56 (dd, 9.9)	3.66	3.74 (9.5)	3.18 (dd, 9.5)	3.35
H-5	3.65 (m)	3.67	3.67 (3.3)	3.75	3.77 (dd, 9.5)
H-6	3.78 (dd, 2.3, 12.2), 3.83 (dd, 3.9, 12.2)	3.88, 3.88 (bs)	3.80, 3.76	1.31 (d, 6.2)	1.35 (d, 5.3)
Me	3.40 (s)	3.40 (s)	3.40 (s)	3.38 (s)	3.38 (s)

[a] ^{1}H NMR spectra are recorded in $CDCl_3$ at 600 MHz. Chemical shifts (δ) in ppm. Coupling constants (J) in Hertz.

Table 4. ^{13}C NMR Data for Compounds **3**, **4**, and **17**−**19**[a]

compd	**3**	**17**	**18**	**4**	**19**
C-1′	104.3	101.0 (3.3)	99.1 (5.2)	104.6	100.6 (4)
C-2′	58.2	61.5 (−3.3)	56.9 (1.3)	58.3	61.7 (−3.4)
C-3′	77.4	75.8 (1.6)	73.6 (3.8)	77.2	75.7 (1.5)
C-4′	71.3	71.5 (−0.2)	71.2 (−0.1)	71.4	71.5 (−0.1)
C-5′	78.1	78.1 (0)	78.3 (−0.2)	78.1	78.1 (0)
C-6′	62.2	62.3 (−0.1)	61.6 (0.6)	62.3	62.3 (0)
C-1	100.8	100.8 (0)	100.7 (0.1)	100.6	100.6 (0)
C-2	73.1	73.0 (0.1)	73.1 (0)	73.2	73.1 (0.1)
C-3	73.2	73.2 (0)	72.9 (0.3)	73.0	72.9 (0.1)
C-4	80.4	80.4 (0)	78.6 (1.8)	86.6	85.5 (1.1)
C-5	71.7	71.4 (−0.3)	71.1 (0.6)	66.8	66.6 (−0.2)
C-6	61.6	62.7 (−1.1)	62.0 (−0.4)	18.2	18.9 (−0.7)
Me	55.4	55.4 (0)	55.4 (0)	55.3	55.3

[a] ^{1}H NMR spectra are recorded in $CDCl_3$ at 600 MHz. Chemical shifts (δ) in ppm. Coupling constants (J) in Hertz. Values in parentheses refer to the change in chemical shift with respect to the free ligand.

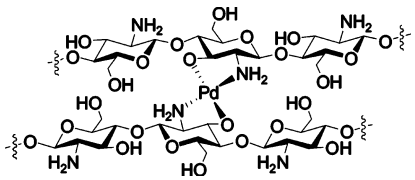


Figure 4. Proposed model chitosan complex with palladium(II).

atoms of the disaccharide **3** can inevitably contribute to the formation of several isomers upon complexation with the Pd(II) salt. When treated with $[PdCl_2(PhCN)_2]$, the disaccharide **3** forms two similar types of complexes as for Me-GlcN under the same conditions (Scheme 4). The chemical shifts of the major complex **17** in the ^{1}H and ^{13}C NMR spectra are compared with the free ligand in Tables 3 and 4, respectively. The shifts are mainly observed for the ring protons of the glucosamine unit in the immediate vicinity of the palladium center, indicating that only the amine functionality contributes to complexation of the metal. The downfield shift of H-1′ and H-3′ ($\Delta\delta$(H) = 0.47 and 0.74 ppm) is comparable to the palladium complex of the monosaccharide, although the upfield shift of H-2′ ($\Delta\delta$(H) = −0.12 ppm) is less significant. Interestingly, a slight broadening of the signals from the H-6_a and H-6_b were observed, which can be attributed to a close proximity of the two protons to the metal center. However, only small chemical shifts of 0.1 and 0.05 ppm are exhibited for these protons implying that there is no coordination of the palladium center to the 6-OH. The presumed coordination mode is supported by the ^{13}C NMR data of the complex where only the carbon atoms in the vicinity of the palladium center are affected, which includes C-6 (−1.1 ppm) (Table 4).

Treatment of the metal complex in solution with excess of $(NH_4)PF_6$ leads only to a single compound corresponding to the minor complex **18** that display a considerable chemical shift change for H-3′ as observed with Me-GlcN. Furthermore, sharpening of the H-3′resonance was displayed. The C6 now exhibits basically the same resonance as for the free ligand ($\Delta\delta$(C) = −0.4 ppm). On the basis of these spectroscopic data, coordination between the C3′-hydroxyl group and the palladium center is again assumed. Additional support for this coordination mode with the disaccharide **3** was obtained subjecting the C6-deoxy disaccharide **4** with $[PdCl_2(PhCN)_2]$under similar conditions. The resulting complex **19** revealed the same coordination-induced changes in chemical shifts as with **17** in the ^{1}H and ^{13}C NMR spectra as depicted in Tables 3 and 4. Despite the lack of the of C6-OH group, a small effect upon coordination is observed for H-6 and C-6 which are comparable to those observed for complex **17**.

These observations undoubtedly confirm that the C6-OH of the adjacent sugar does not participate in coordination of the palladium atom under the given conditions.

Structure of the Chitosan·Pd(II) Complexes in Relationship to Earlier Studies. The question then remains as to the nature of the complexes formed upon treatment of the polysaccharide, chitosan, with Pd(II) salts, and whether the above study may be used to compare directly with the structure of the Pd(II)·chitosan complexes proposed by Kramareva and co-workers.[11] The protocol adapted by these authors relies on the coprecipitation of an acidic solution (0.1 M HCl) of 80% deacetylated chitosan and $PdCl_2$ (2% w) by treatment with an aqueous sodium hydroxide solution (0.5 M). It is reasonable to assume that complexation of the palladium(II) salts under the acidic conditions could lead to the formation of a *trans*-complex as was the case for the compounds **15**, **17**, and **19**. Whereas Kramareva et al.[11] suggest that the neighboring C6-hydroxyl group is also

Table 5. Crystallographic Data of Me-AcGlcN Complexes

	trans-[Pd(Me-AcGlcN)$_2$Cl$_2$]	*trans*-[Pt(Me-AcGlcN)$_2$Cl$_2$]
abbreviation	**13**	**14**
emp formula	$C_{26}H_{42}Cl_2N_2O_{16}Pd$	$C_{26}H_{42}Cl_2N_2O_{16}Pt$
formula wt	815.92	904.61
cryst system	monoclinic	monoclinic
space group	*C*2	*C*2
a (Å)	36.298 (3)	36.9313 (10)
b (Å)	5.4644 (4)	5.5130 (2)
c (Å)	17.3189 (10)	17.4561 (6)
β (deg)	94.004 (2)	94.2051 (10)
V (Å^3)	3426.7 (4)	3544.5 (2)
Z	4	4
temp (K)	100 (2)	293 (2)
D_{calcd} (g·cm^{-3})	1.582	1.695
$2\theta_{max}$(deg)	58.9	42.79
obsd data	9603	5041
R($I>2\sigma$)	0.0434	0.0292
R_w (all)	0.0718	0.0507
GOF	0.987	1.019
residue (e Å^{-3})		
max.	0.791	0.377
min.	−0.652	−0.556

involved in the metal complexation forming a 9-membered chelate (Figure 1c), it seems more likely that under the basic conditions employed for the precipitation of the metal bound polysaccharide that deprotonation occurs leading to the formation of a Pd(II) alkoxide. Yet, our results with the monosaccharide and disaccharide ligand models **1**, **3**, and **4** do not support the interaction of the C6-hydroxyl from the adjacent sugar unit with the metal center. Moreover, chloride abstraction leads to a thermodynamically more stable 5-membered chelate involving the C3-hydroxyl group of the same sugar unit. Even though there is a *trans*-relationship between the two protons at the junction of the 5-membered ring chelate with the sugar ring, ring strain is not an issue due to the long O−Pd and N−Pd bonds. We therefore propose a new model for these chitosan·palladium(II) complexes as illustrated in Figure 4, which involves two antiparallel chitosan strands forming 5-membered ring chelates with two glucosamine units.

Conclusions

We have performed a series of experiments with simple chitosan models based on glucosamine to understand the binding properties and structure of the complexes formed between this polysaccharide and platinum(II) metals. Our results based on both ^{1}H and ^{13}C NMR spectroscopic investigations with these complexes suggest that two 5-membered chelate rings are formed involving the C2-amine and the C3-hydroxyl group of the two individual glucosamine units and that a *trans*-relationship is obtained between the two amine groups. We have found no indication for the involvement of a 9-membered chelate which engages the C6-hydroxyl group of the connecting sugar units in the direction of the reducing end as recently described by Kramareva and co-workers. Further studies are now being performed with the chitosan·palladium(II) complexes in order to confirm the above results.

Experimental Section

General Methods. NMR spectra were measured in $CDCl_3$ or MeOH-d_4 either operating at 400 or 600 MHz for ^{1}H and 100 or 150.9 MHz for ^{13}C. Chemical shifts are expressed in parts per million (ppm) downfield from internal TMS standards as positive values. Reagent [$PdCl_2(PhCN)_2$]and [$PtCl_2(PhCN)_2$]was prepared according to the literature method.[18] Methyl 2-amino-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (**2**) was prepared as reported.[13] The ^{1}H NMR spectra of most disaccharides containing the PNZ moiety gave broad peaks due to rotamers which make assignments difficult. Therefore the spectra was recorded at 75 °C. To make sure the compound did not decompose at this temperature, ^{1}H NMR was recorded at 26 °C before and after the experiment.

Methyl 2-Amino-2-deoxy-β-D-glucopyranoside (1). To a suspension of 786.6 mg (2.46 mmol) of **2** in 20 mL of dry MeOH cooled to 0 °C was added a catalytic amount of NaOMe in MeOH. The reaction mixture was stirred for several hours. The reaction was followed by TLC using EtOAc as a solvent. To the solution was added 20 mL of Amberlite IR 120 H^+ (washed with MeOH and H_2O before use). The mixture was stirred for 2 h. The Amberlite was filtered off and washed with water. The product was eluted with NH_4OH (5%) to afford a 95% yield of **1** as a pale yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (d, 1H J = 8.0 Hz), 3.87 (dd, 1H, J = 1.6, 12.1 Hz), 3.71−3.66 (m, 1H), 3.52 (s 3H), 3.35 (s, 1H), 3.28−3.21 (m, 3H), 2.58−2.52 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 105.7, 78.1, 77.6, 71.8, 62.7, 58.3, 57.3. HRMS (ES+) *m*/*z* (M + H) $C_7H_{16}NO_5$ calc 194.1028 measured 194.1027.

General Procedure for Formation of Glycosidic Linkage. Under an argon atmosphere 1.1 equiv of the alcohol and 1 equiv of the trichloroimidate **5** were added to a round bottomed flask with 4 Å molecular sieves. Dry CH_2Cl_2 was added, and the reaction vessel was cooled to 0 °C. After 15 min of stirring 0.5 equiv of BF_3·OEt_2 was added to the reaction mixture followed by stirring for an additional 5 h, while the reaction temperature was slowly increased to 20 °C. $CHCl_3$ was added and the organic phase was washed twice with a saturated solution of $NaHCO_3$ and brine. The combined aqueous solutions were extracted with $CHCl_3$. The organic phases was combined, dried with Na_2SO_4, and concentrated in vacuo. The resulting residue was further purified by silica chromatography.

Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-*p*-nitrobenzyloxycarbonylamino-β-D-glucopyranosyl-(1→4)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (8). Compound **8** was obtained from **6** (2.0 g, 4.32 mmol) and **5** (2.4 g, 3.85 mmol) in 20 mL of dry CH_2Cl_2 according to the general procedure for formation of the glycosidic linkage. The crude product was purified by silica gel chromatography eluting with EtOAc/pentane (7:12) to yield **8** (2.4 g, 70%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 75 °C) δ 8.17 (d, 2H, J = 8.8 Hz), 7.45−7.19 (m, 17H), 5.13 (s, 2H), 4.95−4.91 (m, 3H), 4.79 (d, 1H, J = 11.5 Hz), 4.69 (dd, 1H, J = 2.0, 12.1 Hz), 4.62 (d, 1H, J = 3.5 Hz), 4.58 (d, 1H, J = 11.9 Hz), 4.53 (bd, 1H, J = 7.2 Hz), 4.43 (d, 1H, J = 12.1 Hz), 4.35 (bs, 1H), 4.09 (dd, 1H, J = 4.7, 12.3 Hz), 3.91 (dd, 1H, J = 2.7, 12.3 Hz), 3.87−3.82 (m, 2H), 3.67−3.64 (m, 2H), 3.55−3.46 (m, 3H), 3.42−3.36 (m, 2H), 3.37 (s, 3H), 1.99 (s, 3H), 1.93 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.6, 169.6, 155.3, 147.8, 144.1, 139.7, 138.4, 137.6, 129.1 (2C), 128.9 (2C), 128.6 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 127.4 (2C), 123.9 (2C), 100.5, 98.6, 80.3, 79.2, 77.5, 75.2, 73.8, 73.6, 72.7, 71.5, 69.6, 68.7 ,67.9, 65.4, 62.0, 56.8, 55.7, 20.8 (3C). HRMS (ES+) *m*/*z* (M + Na) $C_{48}H_{54}N_2NaO_{17}$ calc 953.3320, measured 953.3325.

Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-*p*-nitrobenzyloxycarbonylamino-β-D-glucopyranosyl-(1→4)-6-deoxy-2,4-di-*O*-benzyl-α-D-glucopyranoside (9). Compound **9** was obtained from **7** (0.76 g, 2.11 mmol) and **5** (1.20 g, 0.92 mmol) according to the general procedure for formation of glycosidic linkages. The crude product was purified by silica gel chromatography eluting with EtOAc/pentane (1:4) to yield **9** (1.04 g, 65%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 75 °C) δ 8.19 (d, 2H, J = 8.4 Hz), 7.47 (d, 2H, J = 8.4 Hz), 7.36−7.22 (m, 10H), 5.18 (t, 1H, J = 10.2 Hz), 5.16 (s, 2H), 4.98 (t, 1H, J = 9.8 Hz), 4.94 (d, 1H, J = 11.9 Hz), 4.88 (d, 1H, J = 11.9 Hz), 4.92−4.86 (m, 1H), 4.74 (d, 1H, J = 9.0 Hz), 4.66 (d, 1H, J = 12.1 Hz), 4.58 (d, 1H, J = 11.9 Hz), 4.55 (d, 1H, J = 3.7 Hz), 4.07 (dd, 1H, J = 4.5, 12.3 Hz), 3.93 (dd, 1H, J = 2.7, 12.3 Hz), 3.90 (t, 1H, J = 9.2 Hz), 3.71 (dq, 1H, J = 6.3, 9.6 Hz), 3.55−3.43 (m, 3H), 3.36 (dd, 1H, J = 9.0, 9.4 Hz), 3.35 (s, 3H), 1.97 (s, 3H), 1.96 (s, 3H), 1.94 (s, 3H), 1.13 (d, 3H, J = 6.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.8, 169.6, 155.4, 147.9, 143.8, 139.6, 138.2, 128.6, 128.5, 128.4, 128.3, 128.1, 127.4, 126.8, 123.9, 100.8, 97.9, 83.5, 80.2, 80.1, 74.7, 73.4, 72.4, 71.9, 68.4, 66.0, 65.6, 61.9, 57.5, 55.4, 20.9, 20.8 (2C), 18.1. HRMS (ES+) m/z (M + Na) $C_{14}H_{48}N_2NaO_{16}$ calc 847.2902, measured 847.2898.

Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-amino-β-D-glucopyranosyl-(1→4)-6-deoxy-2,4-di-*O*-benzyl-α-D-glucopyranoside (11). To a solution of 821.3 mg of **9** (0.99 mmol) in 15 mL of ethyl acetate under an inert atmosphere was added a catalytic amount of Pd/C 10%. The reaction flask was flushed with H_2. The reaction mixture was stirred overnight and filtered through a pad of Celite. After removal of the organic solvent in vacuo the crude product was purified by silica gel chromatography eluting with a gradient of EtOAc/pentane (1:1 to 3:2) to yield **11** (516 mg, 82%) as a pale yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.20 (m, 10H), 5.02−4.92 (m, 4H), 4.85 (d, 1H, J = 11.3 Hz), 4.72 (d, 1H, J = 12.1 Hz), 4.59 (d, 1H, J = 12.1 Hz), 4.53−4.49 (m, 2H), 4.16 (dd, 1H, J = 4.5, 12.1 Hz), 3.92 (dd, 1H, J = 2.3, 12.1 Hz), 3.87 (t, 1H, J = 9.2 Hz), 3.82−3.73 (m, 1H), 3.55−3.44 (m, 3H), 3.37 (s, 3H), 2.92 (dd, 1H, J = 7.8, 9.8 Hz), 2.06 (s, 3H), 1.98 (s, 3H), 1.96 (s, 3H), 1.60 (bs, 2H), 1.34 (d, 1H, J = 6.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 (2C), 169.7, 139.3, 138.1, 128.3, 128.1, 128.0, 127.8, 127.2, 103.4, 97.8, 82.8, 79.6 (2C), 75.3, 74.9, 73.3, 71.7, 68.6, 66.1, 62.1, 56.5, 55.1, 20.7, 20.6 (2C), 18.3. HRMS (ES+) m/z (M + Na) $C_{33}H_{43}NNaO_{12}$ calc 668.2683, measured 668.2726.

General Procedure for Deacetylation. To a solution of the protected disaccharide in a mixture of CH_2Cl_2 and MeOH was added a catalytic amount of NaOMe in MeOH. The reaction mixture was stirred for 2.5 h at room temperature. Amberlite IR 120$^+$ was added in small amounts while the solution was being stirred until the pH of the solution was neutral. The mixture was filtered, and the organic solvents were removed in vacuo. The residue was purified by silica gel chromatography.

Methyl 2-Deoxy-2-*p*-nitrobenzyloxycarbonylamino-β-D-glucopyranosyl-(1→4)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (10). Compound **10** was obtained from **8** (2.5 g, 2.68 mmol) according to the general procedure for deacetylation. The crude product was purified by silica gel chromatography eluting with $CHCl_3$/MeOH (9:1) to yield **10** (2.06 g, 95%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 75°) δ 8.16 (d, 2H, J = 8.5 Hz), 7.44 (d, 2H, J = 8.5 Hz), 7.36−7.20 (m, 15H), 5.16−5.13 (m, 2H), 4.84 (s, 2H), 4.73 (d, 1H, J = 12.1 Hz), 4.64 (d, 1H, J = 12.1 Hz), 4.67−4.58 (m, 2H), 4.49−4.41 (m, 2H), 3.87 (t, 1H, J = 9.0 Hz), 3.83−3.64 (m, 4H), 3.58 (dd, 1H, J = 3.1, 10.8 Hz), 3.49 (dd, 1H, J = 3.7, 9.4 Hz), 3.46−3.33 (m, 3H), 3.36 (s, 3H), 3.32−3.24 (m, 1H), 3.16−3.11 (m, 1H), 1.5 (bs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 147.6, 144.4, 138.2, 138.0, 137.7, 128.7, 128.6, 128.4, 128.2, 128.1, 123.8, 100.3, 98.2, 80.5, 79.2, 77.6, 76.7, 76.4, 75.6, 74.6, 73.6, 71.4, 70.1, 68.1, 65.2, 61.8, 58.4, 55.5. HRMS (ES+) m/z (M + Na) $C_{42}H_{48}N_2NaO_{14}$ calc 827.3003, measured 827.3073.

Methyl 2-Deoxy-2-amino-β-D-glucopyranosyl-(1→4)-6-deoxy-2,4-di-*O*-benzyl-α-D-glucopyranoside (12). Compound **12** was obtained from **11** (246.0 mg, 0.39 mmol) according to the general procedure for deacetylation. The crude product was purified by silica gel chromatography eluting with $CHCl_3$/MeOH (9:1) to yield **12** (132.1 mg, 65%) as a pale yellow glassy oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.25 (m, 10H), 4.92 (d, 1H, J = 10.3 Hz), 4.86−4.60 (m, 7H), 4.44 (d, 1H, J = 7.8 Hz), 3.85−3.72 (m, 3H), 3.55−3.46 (m, 3H), 3.37 (s, 3H), 3.35−3.16 (m, 4H), 2.67 (dd, 1H, J = 8.0, 9.6 Hz), 1.33 (d, 3H, J = 6.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4 (2C), 127.6, 127.3, 127.1, 126.9, 126.7, 101.4, 96.6, 79.5, 79.2, 78.8, 76.7, 75.4, 75.0, 71.9, 70.2, 65.7, 61.0, 57.2, 53.3, 16.6. HRMS (ES+) m/z (M + Na) $C_{27}H_{37}NNaO_9$ calc 542.2366, measured 542.2372.

General Procedure for Hydrogenation under Acidic Conditions. The deacetylated disaccharide was dissolved in a mixture of H_2O, AcOH, and THF under a nitrogen atmosphere. 10% Pd/C was added, and the reaction flask was flushed three times with H_2 using a balloon. The reaction mixture was stirred for 20 h and filtered through a pad of Celite. Amberlite IR 120 H^+ (washed with MeOH and H_2O before use) was added to absorb the disaccharide, and the mixture was stirred for 1.5 h at room temperature. The Amberlite resin was filtered off and washed with water. The product was eluted with NH_4OH 5%. No further purification was necessary.

Methyl 2-Amino-2-deoxy-β-D-glucopyranosyl-(1→4)-α-D-glucopyranoside (3) Compound **3** was obtained from **10** (231.2 mg, 0.356 mmol) according to the general procedure for hydrogenation to yield 92.6 mg (73%) of a white foam. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.66 (d, 1H, J = 3.7 Hz), 4.37 (d, 1H, J = 8.1 Hz), 3.89 (dd, 1H, J = 2.1, 11.8 Hz), 3.83 (dd, 1H, J = 3.9, 12.2 Hz), 3.78 (dd, 1H, J = 2.3, 12.2 Hz), 3.74 (dd, 1H, J = 8.6, 9.6 Hz), 3.67 (dd, 1H, J = 6.0, 11.9 Hz), 3.65 (m), 3.56 (dd, 1H, J = 9.6, 9.9 Hz), 3.45 (dd, 1H, J = 3.7, 9.6 Hz), 3.40 (s, 3H), 3.35 (m), 3.29 (dd, 1H, J = 9.1, 9.6 Hz), 3.25 (t, 1H, J = 9.1 Hz), 2.62 (dd, 1H, J = 8.1, 9.6 Hz). ^{13}C NMR (100 MHz, CDCl3) δ 104.3, 100.8, 80.4, 78.1, 77.4, 73.2, 73.1, 71.7, 71.3, 62.2, 61.6, 58.2, 55.4. HRMS (ES+) m/z (M + Na) $C_{13}H_{25}NNaO_{10}$ calc 378.1376, measured 378.1372.

Methyl 2-Amino-2-deoxy-β-D-glucopyranosyl-(1→4)-6-deoxy-α-D-glucopyranoside (4). Compound **4** was obtained from **12** (132 mg, 0.25 mmol) according to the general procedure for hydrogenation under acidic conditions to yield 80 mg (92%) of a pale yellow foam. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.59 (d, 1H, J = 3.8 Hz), 4.33 (d, 1H, J = 8.0 Hz), 3.89 (dd, J = 2.2, 11.8 Hz), 3.75 (m, 1H), 3.66 (dd, 1H, J = 9.5, 9.7 Hz), 3.66 (dd, 1H, J = 6.1, 11.8 Hz), 3.45 (dd, 1H, J = 3.8, 9.7 Hz), 3.38 (s, 3H), 3.35 (m, 1H), 3.29 (m, 1H), 3.26 (m, 1H), 3.18 (t, 1H, J = 9.5 Hz), 2.65 (dd, 1H, J = 8.0, 9.4 Hz), 1.31 (d, 3H, J = 6.2 Hz). ^{13}C NMR (100 MHz, CDCl3) δ 104.6, 100.6, 86.6, 78.1, 77.2, 73.2, 73.0, 71.4, 66.8, 62.3, 58.3, 18.2. HRMS (ES+) m/z (M + Na) $C_{13}H_{25}NNaO_9$ calc 362.1427, measured 362.1425.

$PdCl_2$(Me-AcGlcN)$_2$ (13). A solution of 2 equiv of **2** (84.5 mg, 0.26 mmol) in 2 mL of CH_2Cl_2 was added to 1 equiv of [$PdCl_2$-($PhCN)_2$] (50.8 mg, 0.13 mmol) in a sample vial. The complex **13** was then isolated by removal of the solvent to a minimum volume after 10 min. The solution was directly applied to a column of silica gel, and the product was eluted with EtAc/pentane (6:4) to yield **13** (91%) as an air-stable, orange-yellow amorphous solid. ^{1}H NMR

(400 MHz, $CDCl_3$) δ 6.66 (t, 1H, $J = 8.4$ Hz), 5.02 (dd, 1H, $J = 8.6, 9.7$ Hz), 4.97 (d, 1H, $J = 8.4$ Hz), 4.38 (dd, 1H, $J = 3.9, 12.3$ Hz), 4.28 (m, 1H), 4.17 (dd, 1H, $J = 1.8, 12.3$ Hz), 3.39 (dd, 1H, $J = 4.6, 10.7$ Hz), 3.22 (d, 1H, $J = 10.7$ Hz), 2.59 (m, 1H), 3.53 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.8, 170.2, 100.1, 73.8, 71.2, 69.8, 62.2, 58.2, 56.8, 22.0, 20.8 (2C). MALDI TOF analysis showed a signal at 778.8 *m*/*z* corresponding to $[PdCl(Me\text{-}AcGlcN)_2]^+$ and 743.8 *m*/*z* corresponding to $[Pd(Me\text{-}AcGlcN)_2]^{2+}$.

$PtCl_2$(Me-AcGlcN)$_2$ (14). A solution of 2 equiv of **2** (140 mg, 0.44 mmol) in 2 mL of CH_2Cl_2 was added to 1 equiv of $[PtCl_2(PhCN)_2]$ (103.3 mg, 0.22 mmol) in a sample vial and sealed with a screw cap. The yellow solution was stirred for 2 days at 40 °C. The complex **14** was then isolated by removal of the solvent to a minimum volume after 10 min. The solution was directly applied to a column of silica gel, and the product was eluted with EtAc/pentane (4:6) to yield a mixture of two isomers (91%) as an yellow amorphous solid. The major isomer: ^1H NMR (400 MHz, $CDCl_3$, 20 °C) δ 6.72 (dd ,1H, $J = 9.2, 9.9$ Hz), 5.02 (dd, 1H, $J = 8.8, 9.2$ Hz), 5.01 (d, 1H, $J = 8.2$ Hz), 4.38 (dd, 1H, $J = 3.7, 12.3$ Hz), 4.30−4.24 (m, 1H), 4.20 (bs, 2H), 4.19−4.13 (m, 1H), 3.52 (s, 3H), 2.72 (dd, 1H, $J = 8.2, 9.9$ Hz), 2.08 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.6, 74.3, 71.0, 69.9, 62.3, 59.8, 56.5, 21.9, 20.9, 20.9. MALDI TOF analysis showed a signal at 868.8 *m*/*z* corresponding to $[PtCl(Me\text{-}AcGlcN)_2]^+$ and 833.8 *m*/*z* corresponding to $[Pt(Me\text{-}AcGlcN)_2]^{2+}$. CCDC 628689 (Pd) and CCDC 628690 (Pt) contains the Supporting Information crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif or by e-mailing data_request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, U.K.; fax +44 1223 336033.

General Procedure for Formation of Complexes 15−19. A solution of 2 equiv of the amino sugar in MeOH-d_4 was added to 1 equiv of $[PdCl_2(PhCN)_2]$ to afford complexes (**15**, **17**, and **19**) as the major products. The addition of excess $(NH_4)PF_6$ (5 equiv) to the solution containing the complexes **15** and **17** then afforded the principal complexes **16** and **18**, respectively.

X-ray Structures. Single-crystal diffraction data (Table 5) was collected using needlelike crystals of **13** and **14**. The data were collected on a CCD-based Bruker X8Apex2 diffractometer equipped with graphite-monochromated Mo Kα radiation and an Oxford Cryosystems cooling device. Integration and Lp-correction was performed using Saint+,[27] and an empirical absorption correction was done using SADABS.[28] The crystal structures were solved using direct methods from SHELXS-97,[29] and least-squares refinement to convergence was done with SHELXL-97.[29] All non-H atoms were refined with anisotropic atomic displacement parameters (adp). All hydrogen atoms were refined in a riding model and assigned an adp 20% larger than the equivalent isotropic motion of their parent atoms.

Acknowledgment. The authors are grateful to Dr. Jacob Overgaard for the X-ray crystallographic analysis. Furthermore we are indebted to the Ministry of Science and Technology, the University of Aarhus, and the Carlsberg Foundation for generous financial support.

Supporting Information Available: Crystallographic data in CIF format for complexes **13** and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

IC070016R

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