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Short Note

(2-Deoxy-2-{[2-(2-pyridinyl-κ*N*)-4-thiazolecarbonyl-κN^3]amino}-α-D-glucopyranose) dichloropalladium(II) Methanol Solvate

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Abstract: A novel palladium(II) complex with a glycoconjugated 2-(2-pyridyl)thiazole ligand was synthesized. Single-crystal X-ray analysis revealed a packing structure that may be stabilized by hydrogen bonding between sugar moieties and between methanol (crystal solvent) and a sugar moiety.

Keywords: palladium complex; sugar; pyridylthiazole; X-ray structure analysis; hydrogen bonding

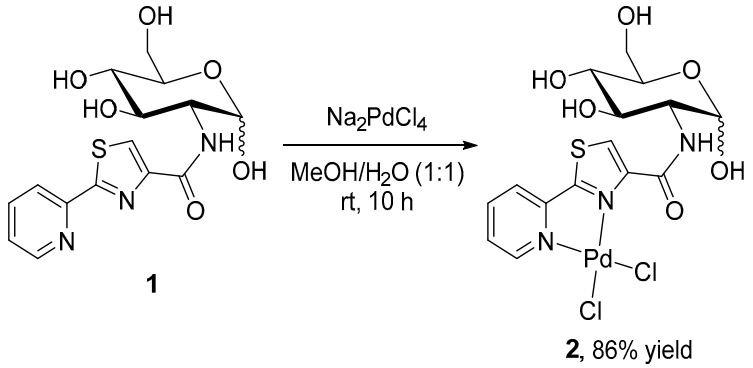
1. Introduction

Glycoconjugated transition-metal complexes have played an important role in bioinorganic and biomedicinal chemistry [1–4]. In the context of our recent research on complexes of group 10 metals with sugar-conjugated ligands as antitumor metallo-drugs [5,6], we have synthesized a novel glycoconjugated palladium complex and have successfully determined its crystal structure.

2. Results and Discussion

Glycoconjugated 2-(2-pyridyl)thiazole ligand **1** was synthesized by the condensation of 2-(2-pyridinyl)-4-thiazolecarboxylic acid [7] with glucosamine in the presence of 1-[3-dimethylaminopropyl]-3-ethylcarbodiimide (EDC) and 1-hydroxybenzotriazole (HOBT). Then, the reaction of **1** with sodium tetrachloropalladate(II) (Na_2PdCl_4) in a mixed MeOH/H_2O solvent afforded the desired glycoconjugated palladium(II) complex **2** in an 86% yield (Scheme 1).

The structure of complex **2** has been determined unambiguously by single-crystal X-ray analysis (Figure 1) to show a distorted square planar geometry about the Pd(II) atom. The Pd–N (2.024(10) and 2.028(9) Å) and Pd–Cl (2.283(3) and 2.288(3) Å) bond distances are within the range reported for the structurally related palladium(II) bipyridine complexes [8,9]. In addition, a hydrogen bond was observed between the hydroxyl proton (H2) of the D-glucopyranose moiety and methanol (crystal solvent), and the O2···O7 distance is 2.737(12) Å.



Scheme 1. Synthesis of the glycoconjugated palladium(II) complex **2**.

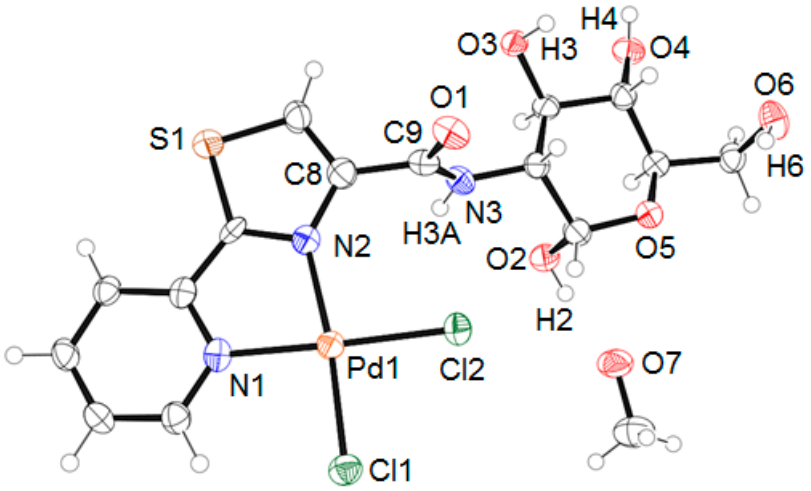


Figure 1. Crystal structure of **2**·MeOH with numbered atoms. Ellipsoids are shown at the 50% probability level. Hydrogen atoms were added automatically except for H2, H3, H4, H6, and H3A. The absolute configuration of complex **2** were established by the structure determination of the D-glucopyranose moiety of known absolute configuration and confirmed by anomalous-dispersion effects in diffraction measurements on the crystal. Selected interatomic distances (Å) and angles (deg): Pd1–N1, 2.028(9); Pd1–N2, 2.024(10); Pd1–Cl1, 2.283(3); Pd1–Cl2, 2.288(3); O1–C9, 1.238(13); N3–C9, 1.327(14); O2···O7, 2.737(12); N1–Pd1–N2, 81.1(4); N1–Pd1–Cl1, 92.8(3); N2–Pd1–Cl1, 173.9(3); N1–Pd1–Cl2, 177.6(3); N2–Pd1–Cl2, 96.6(3); Cl1–Pd1–Cl2, 89.53(12); O1–C9–N3, 125.3(11); O1–C9–C8, 118.9(11); N3–C9–C8, 115.6(11).

Figure 2 shows that intermolecular hydrogen-bonding interactions were present between the D-glucopyranose moieties and between methanol and the D-glucopyranose moiety, resulting in the formation of two-dimensional (2D) molecular networks. The selected interatomic distances and angles for hydrogen bonds found in the molecules are shown as follows: 0.85(3) Å (O2–H2), 1.89(4) Å (O2–H2···O7), 2.737(12) Å, and 171(15)° (O2–H2···O7); 0.83(3) Å (O3–H3), 2.09(7) Å (O3–H3···$O3^{i}$), 2.848(7) Å, and 151(12)° (O3–H3 ··· $O3^{i}$); 0.84(3) Å ($O4^{i}$–$H4^{i}$), 1.89(5) Å ($O4^{i}$–$H4^{i}$···O1 = C9), 2.691(11) Å, and 161(14)° ($O4^{i}$–$H4^{i}$···O1); 0.84(3) Å (O6–H6), 1.96(10) Å (O6–H6···$O4^{ii}$), 2.659(13) Å, and 140(14)° (O6–H6···$O4^{ii}$). Symmetry operators: (i) $-1/2 + X, 3/2 - Y, 1 - Z$; (ii) $-1 + X, Y, Z$.

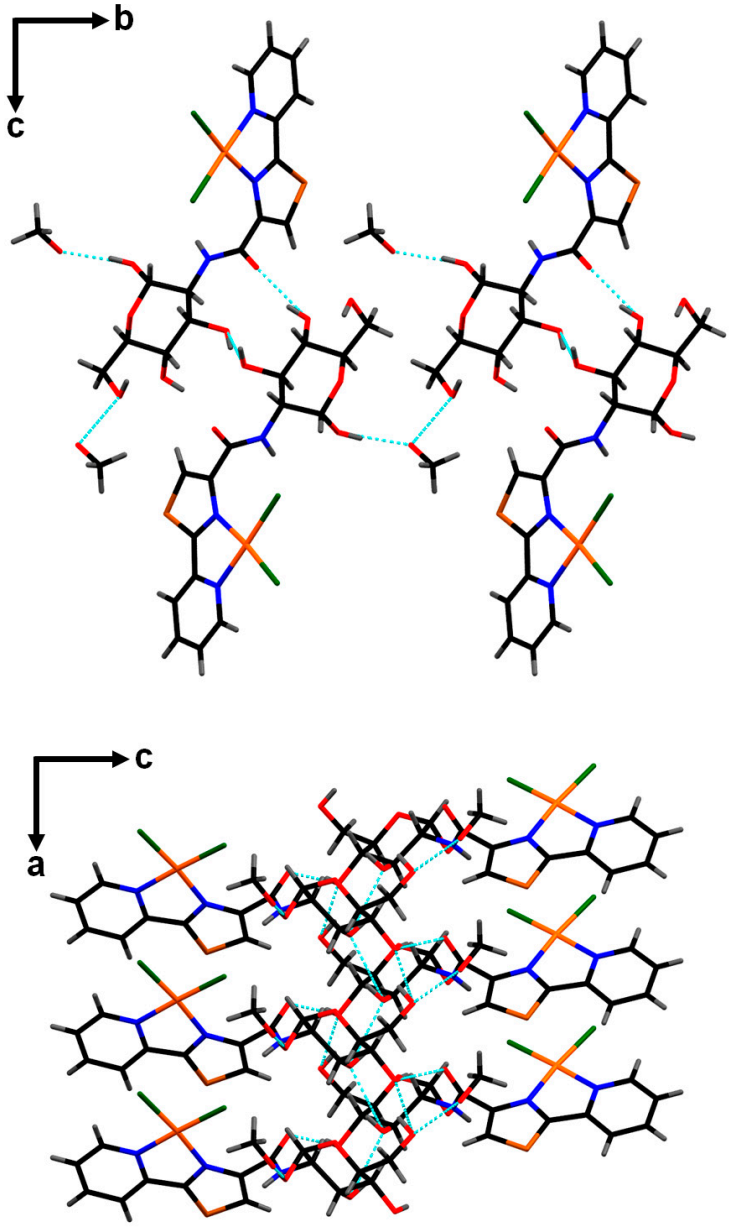


Figure 2. Crystal packing of **2**·MeOH viewed along the *a*-axis (**top**) and *b*-axis (**bottom**). Hydrogen bonds are represented by the dotted blue lines.

3. Materials and Methods

3.1. General

All reagents and solvents were purchased from chemical companies and used without further purification. ^{1}H (400 MHz) and ^{13}C{^{1}H} (100 MHz) NMR spectra were recorded on a JEOL ECX-400 spectrometer (JEOL, Tokyo, Japan). Chemical shifts are reported in δ, referenced to residual ^{1}H and ^{13}C signals of *N*,*N*-dimethylformamide-d_7 (DMF-d_7) as an internal standard. The IR spectrum was recorded on a JASCO FT/TR-8900 spectrometer (JASCO, Tokyo, Japan).

3.2. Synthesis of Glycoconjugated Palladium(II) Complex **2**

A mixture of 2-(2-pyridinyl)-4-thiazolecarboxylic acid (430 mg, 2.0 mmol), D-(+)-glucosamine hydrochloride (481 mg, 2.2 mmol), EDC (448 mg, 2.9 mmol) and HOBT (324 mg, 2.4 mmol) in DMF

(16 mL) was stirred at room temperature for 1 h. The resulting mixture was evaporated in vacuo, and the residue was washed with Et_2O and then dissolved in EtOH. The solution was filtered, and the filtrate was evaporated in vacuo to afford glycoconjugated 2-(2-pyridyl)thiazole ligand **1** (163 mg, 21% yield) as yellow solid. Then, Na_2PdCl_4 (58.9 mg, 0.2 mmol) and **1** (75.8 mg, 0.2 mmol) were stirred in a mixed MeOH/H_2O (1:1) solvent (30 mL) at room temperature for 10 h. The resulting suspension was filtered to obtain **2** (93.0 mg, 86% yield) as pale yellow powder. Mp 247–250 °C (decomp.); ^{1}H NMR (DMF-d_7, 400 MHz) δ 9.15 (d, *J* = 4.8 Hz, 1H), 8.51 (d, *J* = 7.2 Hz, 1H), 8.43 (td, *J* = 8.0, 1.2 Hz, 1H), 8.36 (s, 1H), 8.34 (s, 1H), 7.90 (ddd, *J* = 7.6, 5.6, 1.6 Hz, 1H), 6.75 (d, *J* = 3.6 Hz, 1H), 5.46 (t, *J* = 3.8 Hz, 1H), 5.06 (d, *J* = 3.6 Hz, 1H), 4.73 (br, 1H), 4.46 (br, 1H), 4.00 (td, *J* = 10, 2.5 Hz, 1H), 3.88–3.78 (m, 3H), 3.73–3.59 (m, 1H), 3.46–3.38 (m, 1H); ^{13}C{^{1}H} (DMF-d_7, 100 MHz) δ 169.9, 161.6, 153.4, 152.5, 150.8, 142.6, 128.3, 125.7, 125.3, 92.1, 73.5, 72.9, 72.8, 63.1, 56.6; IR (cm^{-1}) 3245, 3117, 2924, 1647, 1539, 1506, 1309, 1095, 1037, 779; Anal. Calcd for $C_{16}H_{21}Cl_2N_3O_7Pd$: C, 33.32; H, 3.67; N, 7.29. Found: C, 33.01; H, 3.58; N, 7.63.

3.3. X-ray Diffraction Studies

An X-ray crystallographic measurement was carried out on a Rigaku RAXIS-RAPID diffractometer (Rigaku, Tokyo, Japan) with Mo Kα radiation at 123 K. Of 28,532 reflections collected, 3712 were unique (R_{int} = 0.1634). An empirical absorption correction was applied, which resulted in transmission factors ranging from 0.283 to 0.987. The data were corrected for Lorentz and polarization effects. The structure of **2**·MeOH was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined using the riding model. All calculations were performed with the *CrystalStructure* [10] crystallographic software package except for refinements, which was performed using SHELXL Version 2016/6 [11]. Hydrogen atoms were added automatically except for H2, H3, H4, H6, and H3A. The hydrogen atom of hydroxyl group of methanol was not included in the refinements. The absolute configuration of complex **2** were established by the structure determination of the D-glucopyranose moiety of known absolute configuration and confirmed by anomalous-dispersion effects in diffraction measurements on the crystal. Although the present results provide a marginal dataset, the acceptable structure model has been achieved.

Crystallographic data: formula weight = 575.71; orthorhombic; space group $P2_12_12_1$; *a* = 4.9453(3) Å, *b* = 12.1389(8) Å, *c* = 34.058(2) Å; *V* = 2044.5(2) Å^3; *Z* = 4; ρ_{calcd} = 1.870 g·cm^{-3}; total reflections collected = 28,532; *GOF* = 1.050; R_1 = 0.0657; wR_2 = 0.1224. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre (CCDC-1567381). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk).

Supplementary Materials: The following are available online: http://www.mdpi.com/1422-8599/2017/4/M959 Figure S1: ^{1}H-NMR spectrum (DMF-d_7, 400 MHz) of **2**; Figure S2: ^{13}C{^{1}H}-NMR spectrum (DMF-d_7, 400 MHz) of **2**.

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Author Contributions: S.K., A.N., Y.S., and A.O. performed research; S.K., K.K., and S.Y. analyzed X-ray data. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

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