Sugar ligands in organotitanium complexes

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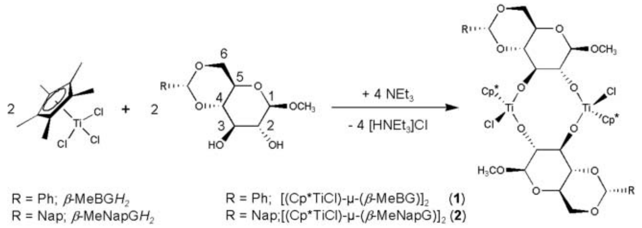
Using ligands derived from D-glucose, dinuclear organotitanium compounds with interesting structural features were synthesized.

Despite their advantageous properties, monosaccharide derived ligands have been rarely applied in the synthesis of organometallic compounds and thus little is known about their coordination capabilities. Most of the established monosaccharide–metal complexes are based on late transition metals such as Rh, Pd, Pt.[1] Among early transition metals, monosaccharide complexes containing Ti and Zr are of importance.[2] Although the information pertaining to their metal–ligand binding sites is scarce, both late and early transition metal complexes of modified monosaccharides have been successfully applied as chiral reagents and catalysts in stereoselective synthesis.[3]

Within this research topic we are interested in the coordination ability of glucopyranosides and the use of these complexes in stereoselective synthesis. In particular, we are investigating the 2- and 3-positions of glucopyranosides as coordination sites for organometallic complexes of early transition metals such as Ti and Zr. We are looking to determine whether the torsion angle between the *trans* orientated oxygen functions of C2 and C3 of a glucopyranosidato ligand can either build a mononuclear chelating complex or a bridging coordination to two Ti atoms, forming a dinuclear complex.

Methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (β-MeBGH_2) and methyl (4,6-*O*-β-naphthyl-2′-methylidene)-β-D-glucopyranoside (β-MeNapGH_2) were used as ligand precursors and were easily obtained from methyl β-D-glucopyranoside. In a previously published paper we discussed the structural data of β-MeBGH_2.[4] Therein it was determined that the chelating capability of the oxygen atoms O2 and O3 are dependent upon the dihedral angle O2–C2–C3–O3. Using this ligand we were able to obtain a triethylammonium zirconate with two glucopyranoside units acting as 2,3-diolato ligands which demonstrate a bridging and chelating coordination mode. Titanium complexes could be synthesized in a similar fashion (Scheme 1). The reaction of β-MeBGH_2 or β-MeNapGH_2 with Cp*$TiCl_3$ (Cp* = pentamethylcyclopentadienyl) in the presence of NEt_3 yielded dinuclear titanium complexes **1** and **2** with the two glucopyranoside units acting as 2,3-diolato ligands.†

The chemistry pertaining to these compounds proved to be quite challenging. Appropriate solvents, reaction conditions and chemical ratios are crucial for the successful synthesis of these titanium monosaccharide complexes. By means of NMR spectroscopy an indication of two additional products could be observed. However, the low stability of the two additional products hampers their isolation and thus more thorough characterization. The compounds **1** and **2** could be isolated through recrystallization.[5]



Scheme 1 Synthesis of the monosaccharide titanium complexes.§

Although both complexes crystallize in orthorhombic space groups,‡ there exist differences in the molecular geometries of **1** and **2**. The molecular geometry of **1** (Fig. 1) deviates slightly from the C_2 symmetry found in solution by means of NMR spectroscopy and crystallizes in the space group $P2_12_12_1$ with four formula units per unit cell. The symmetry of **2** (Fig. 2) in the crystalline state, however, confirms the C_2 symmetry found in solution, with **2** crystallizing in the space group $P2_12_12$ with two formula units per unit cell. Both complexes are dinuclear, with each Ti atom containing a Cp* ligand and terminally bound Cl ligand. The Ti atoms are bridged *via* the 2,3-diolato functions of the glucopyranosidato ligands and thus build a central ten-membered ring. In contrast to comparable complexes with ten-membered dizirconium rings, no dynamic behavior is found in solution leading to an intermediate tricyclic ring system.[8] Each of the titanium centers consists of twelve d-electrons and demonstrates a large degree of Lewis acidity.

A unique feature of these compounds is the V-shaped cavity formed through the monosaccharide ligands and the position of the benzylidene (naphthyl-2′-methylidene) protecting groups of the

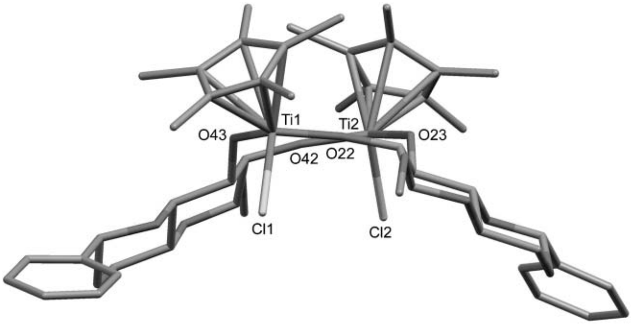


Fig. 1 Molecular structure of [(Cp*TiCl)-μ-(β-MeBG)]₂ (**1**).[6]

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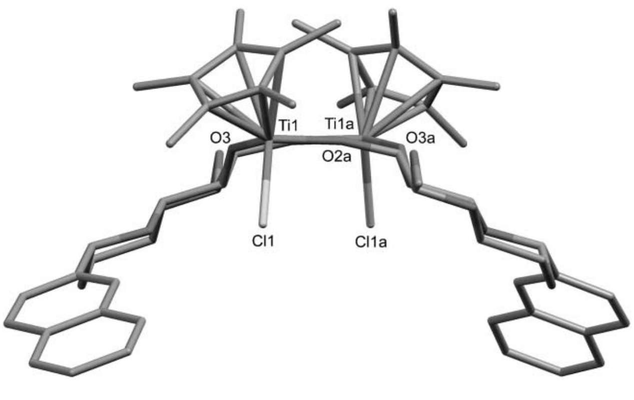

Fig. 2 Molecular structure of $[(Cp^*TiCl)\text{-}\mu\text{-}(\beta\text{-MeNapG})]_2$ (**2**).[7]

carbohydrate ligands. The opening of the cavity is approximately 1.3 nm wide. The two chloro ligands project into this cavity, a peculiarity which makes these ligands easily accessible for further reactions. It is plausible that the exchange of a chloro ligand for a transferable group, along with the pronounced Lewis acidity of these complexes, can lead to a new reagent for stereoselective induction. These properties could make these compounds advantageous for stereoselective, catalytic hetero Diels–Alder reactions[9] and hydroaminations.[10] We are currently studying these applications.

Using these 2,3-glucopyranosidato ligands, we were solely able to obtain complexes with a 1,6-dititana ten-membered ring. Within the class of compounds utilizing monosaccharide ligands, there are no other known complexes in which the Ti atoms are included in a ring system. In fact, there is only one known and structurally characterized 1,2-diolato mononuclear titanium complex, 1,1-bis cyclopentadienyl-3,4-diphenyl titana dioxolane.[11] In terms of dinuclear complexes, the only other structurally characterized Cp*Ti complex with 1,2-diolato ligands is $[Cp^*TiCl(\mu\text{-}\eta^1,\eta^1\text{-}2\text{-}CF_3\text{-dpbd})]_2$.[12] A key difference between this published complex and our glucopyranosidato complexes is the relative positioning of the ligands with respect to the 1,6-dititana ten-membered ring. Whereas the Cp* and Cl ligands of the literature complex have a *trans* orientation with respect to the ten-membered ring, we have been able to confirm a *cis* orientation of the ligands, which leads to the C_2-symmetrical V-shaped cavity.

In conclusion, we were able to synthesize dinuclear titanium complexes with naturally occurring glucopyranosides as chiral ligands. By means of X-ray structure analysis, we confirmed a molecular structure in which the two chloro ligands project into a well-defined cavity. In **2** a C_2 symmetrical geometry was even determined by means of X-ray structure determination. This unique cavity and its symmetry together with the pronounced Lewis acidity of the metal centers are very promising as a reaction site for stereoselective bond formation.

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Notes and references

† **Experimental**: All experiments were carried out under a purified nitrogen atmosphere using standard Schlenk techniques. All solvents were vigorously dried and freshly distilled under nitrogen. NMR: Bruker AVANCE 400. *J* values are given in Hz. Elemental analysis: Heraeus CHN-O-Rapid, Zentrale Elementanalytik, Fachbereich Chemie, Universität Hamburg. β-MeBG*H*$_2$, β-MeNapG*H*$_2$[13] and Cp^*TiCl_3[14] were synthesized according to the literature.

$[(Cp^*TiCl)\text{-}\mu\text{-}(\beta\text{-MeBG})]_2$ (1): A solution of Cp^*TiCl_3 (295 mg, 1.02 mmol) in dichloromethane (20 mL) was added to β-MeBG*H*$_2$ (284 mg, 1.02 mmol) dissolved in dichloromethane (10 mL). NEt_3 (690 μL, 5 mmol) in dichloromethane (10 mL) was added dropwise. The reaction mixture was refluxed for 15 h. The solvent was removed *in vacuo* and the remaining solid was suspended in toluene. The undissolved $[Et_3NH]Cl$ was filtered off and the filtrate was evaporated to dryness. The yellow solid was suspended in hot hexane and filtered (346 mg, 68%). X-ray quality crystals were obtained by dissolving the yellow solid in minimal amounts of toluene and allowing pentane to diffuse into the solution.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 2.10$ (s, 15H, Cp*), 3.26 (dd, $^3J_{H4,H5} = 9.2$ Hz, 1H, 4-H), 3.40 (ddd, $^3J_{H5,H6eq} = 5.1$ Hz, 1H, 5-H), 3.51 (s, 3H, OCH_3), 3.69 (dd, $^2J_{H6ax,H6eq} = 10.2$ Hz, 1H, 6ax-H), 4.08 (dd, $^3J_{H2,H1} = 7.7$ Hz, $^3J_{H2,H3} = 8.3$ Hz, 1H, 2-H), 4.31 (dd, $^3J_{H6eq,H5} = 5.1$ Hz, 1H, 6eq-H), 4.53 (d, 1H, 1-H), 4.87 (dd, $^3J_{H3,H4} = 8.8$ Hz, 1H, 3-H), 5.44 (s, 1H, 7-H), 7.34–7.40 (m, 3H, $Ph_{\mathit{ortho}\text{-H}/\mathit{para}\text{-H}}$), 7.58–7.64 (m, 2H, $Ph_{\mathit{meta}\text{-H}}$). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 12.4$ (C_{Cp^*prim}), 54.8 (OCH_3), 63.7 (C5), 67.1 (C6), 80.6 (C4), 84.8 (C3), 86.9 (C2), 99.6 (C7), 101.5 (C1), 124.6, 126.3, 126.6, 126.8 (C_{phenyl}), 135.6 (C8). $[\alpha]_{589}{}^{20}$ −54 (c 0.18 in CH_2Cl_2). Elemental analysis: Found: C, 59.1; H, 7.0; N, 0.2. Calc. for $C_{48}H_{62}Cl_2O_{12}Ti_2\cdot([NEt_3H]Cl)_{0.18}$: C, 58.7; H, 6.6; N, 0.3%.[15]

$[(Cp^*TiCl)\text{-}\mu\text{-}(\beta\text{-MeNapG})]_2$ (2): Following a procedure similar to that described for the preparation of **1**, a solution of Cp^*TiCl_3 (370 mg, 1.28 mmol) in dichloromethane (15 mL) was added to β-MeNapG*H*$_2$ (425 mg, 1.28 mmol) dissolved in dichloromethane (15 mL). NEt_3 (850 μL, 6.14 mmol) in dichloromethane (10 mL) was added dropwise. Compound **2** was obtained as a yellow solid (489 mg, 35%). X-ray quality crystals were obtained as yellow needles by suspending the resulting solid in dichloromethane, heating to form clear solution and subsequent cooling.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 2.13$ (s, 15H, Cp*), 3.35 (dd, $^3J_{H4,H5} = 8.9$ Hz, 1H, 4-H), 3.43 (ddd, $^3J_{H5,H6eq} = 5.0$ Hz, 1H, 5-H), 3.56 (s, 3H, OCH_3), 3.76-3-73 (m 1H, 6ax-H), 4.14 (dd, $^3J_{H2,H3} = 8.2$ Hz, 1H, 2-H), 4.38-4-32 (m 1H, 6eq-H), 4.69 (d, $^3J_{H1,H2} = 7.7$ Hz, 1H, 1-H), 4.95 (dd, $^3J_{H3,H4} = 8.8$ Hz, 1H, 3-H), 5.62 (s, 1H, 7-H), 7.46-7.51 (m, 1H, 7′-H), 7.63-7.66 (m, 2H, 3′-H, 5′-H), 7.81-7.87 (m, 2H, 4′-H, 6′-H), 7.97-7.98 (m, 1H, 8′-H), 8.27 (s, 1H, 1′-H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 11.8$, 11.9, 12.2 (C_{Cp^*prim}), 57.6 (OCH_3), 66.4 (C5), 68.8 (C6), 80.7 (C4), 87.6 (C3), 88.5 (C2), 102.1 (C7), 104.2 (C1), 123.7, 124.0, 125.7, 125.8, 126.2, 126.3, 126.4, 126.5 ($C_{naphthyl}$), 134.7 (C2′). $[\alpha]_{546}{}^{20}$ −15 (c 0.12 in CH_2Cl_2). Elemental analysis: Found: C, 60.5; H, 6.2. Calc. for $C_{56}H_{66}Cl_2O_{12}Ti_2$: C, 61.3; H, 6.1%.

‡ CCDC reference numbers 274863 (**1**) and 275215 (**2**). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b508851h

§ Numbering in the glucopyranoside corresponds to the NMR characterization.

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5 Compound **1** crystallizes from toluene/hexane as yellow blocks. The small size of the crystals, and thus their weak diffracting power, make X-ray structure determination difficult. As a result, the R_{int} value is high (0.35) and only the heavier atoms Ti and Cl could be refined anisotropically. In contrast, compound **2** was recrystallized from dichloromethane as yellow needles. These crystals were more suitable for X-ray structure analysis ($R_{\mathrm{int}} = 0.08$).

6 **Crystal data for 1.** $C_{55}H_{70}Cl_2O_{12}Ti_2$, $M = 1089.81$, orthorhombic, $a = 820.3(7)$, $b = 2161.3(17)$, $c = 3049(3)$ pm, $U = 5.41(1)$ nm^3, $T = 153(2)$ K, space group $P2_12_12_1$, $Z = 4$, $\mu(\text{Mo-K}\alpha) = 0.454$ mm^{-1}, 32757 reflections measured, 5036 unique ($R_{\mathrm{int}} = 0.3488$) which were used in all calculations. The final R was 0.0581 and $wR(F^2)$ was 0.1159 (all data). Atom numbering corresponds to CIF file‡.

7 **Crystal data for 2.** $C_{30}H_{36}Cl_5O_6Ti$, $M = 717.74$, orthorhombic, $a = 1484.15(9)$, $b = 2532.03(16)$, $c = 804.38(5)$ pm, $U = 3.0228(3)$ nm^3, $T = 153(2)$ K, space group $P2_12_12$, $Z = 2$, $\mu(\text{Mo-K}\alpha) = 0.385$ mm^{-1}, 36490 reflections measured, 6875 unique ($R_{\mathrm{int}} = 0.0846$) which were used in all calculations. The final R was 0.0625 and $wR(F^2)$ was 0.1786 (all data). Atom numbering corresponds to CIF file‡.

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15 ^{1}H NMR spectrum shows traces of [NEt$_3$H]Cl which could not be removed by filtration.