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Stereocontrol by a Pair of Epimeric Sugar-Derived Ligands of the Coordination Sphere of Copper(II) Complexes

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A pair of novel C3-epimeric sugar-derived ligands (*glycoligands*) with a neutral N_4O donor set was synthesized. Copper(II) complexes of both ligands were obtained and characterized by X-ray crystallography. Cyclic voltammetry, electron paramagnetic resonance, and UV–vis spectroscopies showed similar electronic properties. Mirror-image CD spectra were obtained for the Cu^{II} d−d band, indicating an enantiomeric character of the coordination sphere, which has been rationalized structurally. This example shows the possible predetermination of stereochemistry for complexes by ligands based on a glycoscaffold.

The diastereoselective synthesis of metal complexes with chiral ligands[1,2] is an important and rapidly expanding research subject with applications in asymmetric catalysis,[3] supramolecular chemistry[2,4] and biological recognition.[5] Chirality is often ultimately derived from the use of compounds naturally occurring such as derivatives of terpenes,[2,6] amino acids,[7] or carbohydrates.[8−10]

It is of interest to fine-tune the stereochemistry of the metal environment by the controlled modulation of the complex stereogenic elements,[11] including stereogenic atoms, edge configurations,[12] conformations of chelate cycles, and helical folding of ligand(s). The ligands used in such strategies should present restrained conformational freedom. This ensures that the stereochemical changes in the ligand backbone induce a predictable change of the stereochemistry of the coordination sphere. Moreover, it would be an asset if the ligands were easily synthetically modified. Both characteristics are accessible in the field of glycochemistry, and carbohydrates are thus promising scaffolds for such applications. We have recently designed and studied a series of *glycocomplexes*[13] derived from functionalized monosaccharide platforms and investigated the influence of the sugar scaffold of some hexadentate *glycoligands* on the stereochemistry of the chelating site.[10] We now report the synthesis and structural and spectroscopic characterizations of a pair of copper(II) complexes with two pentadentate N_4O pentofuranose-derived ligands. The ligands are based on conformationally constrained bicyclic *xylo*- or *ribo*-1,2-*O*-isopropylidenefurano-scaffolds[14] and differ only by the absolute

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(1) Knight, P. D.; Scott, P. *Coord. Chem. Rev.* **2003**, *242*, 125–143. von Zelewsky, A. *Coord. Chem. Rev.* **1999**, *190–192*, 811–825. von Zelewsky, A.; Mamula, O. *J. Chem. Soc., Dalton Trans.* **2000**, 219–231. Knof, U.; von Zelewsky, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 302–322.

(2) Mamula, O.; von Zelewsky, A. *Coord. Chem. Rev.* **2003**, *242*, 87–95.

(3) Diéguez, M.; Pàmies, O.; Ruiz, A.; Diaz, Y.; Castillón, S.; Claver, C. *Coord. Chem. Rev.* **2004**, *248*, 2165–2192. Jacobsen, E. N., Wu, M. H., Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; *Comprehensive Asymmetric Catalysis*, Vol. II; Springer: Berlin, 1999; pp 649–677. Pfaltz, A.; Drury, W. J. *Proc. Natl. Acad. Sci.* **2004**, *101*, 5723–5726.

(4) Lehn, J.-M. *Supramolecular Chemistry*; Wiley: New York, 1995.

(5) Betschinger, F.; Libman, J.; Felder, C. E.; Shanzer, A. *Chirality* **1998**, *10*, 396–404. Dayan, I.; Libman, J.; Agi, Y.; Shanzer, A. *Inorg. Chem.* **1993**, *32*, 1467–1475. Tor, Y.; Libman, J.; Shanzer, A. *J. Am. Chem. Soc.* **1987**, *109*, 6518–6519.

(6) Hayoz, P.; Zelewski, A. v.; Stoeckli-Evans, H. *J. Am. Chem. Soc.* **1993**, *115*, 5111–5114.

(7) Pessoa, J. C.; Correia, I.; Galvao, A.; Gameiro, A.; Felix, V.; Fiuza, E. *Dalton Trans.* **2005**, *231*, 2–2321. Telfer, S. G.; Bernardinelli, G.; Williams, A. F. *Dalton Trans.* **2003**, 435–440. Telfer, S. G.; Bernardinelli, G.; Williams, A. F. *Chem. Commun.* **2001**, 1498–1499. Seitz, M.; Kaiser, A.; Stempfhuber, S.; Zabel, M.; Reiser, O. *Inorg. Chem.* **2005**, *44*, 4630–4636. (e) Seitz, M.; Stempfhuber, S.; Zabel, M.; Schütz, M.; Reiser, O. *Angew. Chem., Int. Ed.* **2004**, *44*, 242–245.

(8) Mikata, Y.; Sugai, Y.; Obata, M.; Harada, M.; Yano, S. *Inorg. Chem.* **2006**, *45*, 1543–1551. Mikata, Y.; Sugai, Y.; Yano, S. *Inorg. Chem.* **2004**, *43*, 4778–4780.

(9) Constable, E. C.; Frantz, R.; Housecroft, C. E.; Lacour, J.; Mahmood, A. *Inorg. Chem.* **2004**, *43*, 4817–4919.

(10) Cisnetti, F.; Guillot, R.; Pelosi, G.; Desmadril, M.; Policar, C. *Dalton Trans.* **2007**, 1473–1476.

(11) von Zelewsky, A. *Stereochemistry of Coordination Compounds*; Wiley: New York, 1996.

(12) Brorson, M.; Damhus, T.; Schäffer, C. E. *Inorg. Chem.* **1983**, *22*, 1569–1573.

(13) Bellot, F.; Hardré, R.; Pelosi, G.; Thérisod, M.; Policar, C. *Chem. Commun.* **2005**, 5414–5416. Charron, G.; Bellot, F.; Cisnetti, F.; Pelosi, G.; Rebilly, J.-N.; Rivière, E.; Barra, A.-L.; Mallah, T.; Policar, C. *Chem. Eur. J.* **2007**, *13*, 2774–2782. Cisnetti, F.; Guillot, R.; Thérisod, M.; Policar, C. *Acta Crystallogr.* **2007**, *C63*, m201–m203.

(14) Houseknecht, J. B.; McCarren, P. R.; Lowary, T. L.; Hadad, C. M. *J. Am. Chem. Soc.* **2001**, *123*, 8811–8824. Plavec, J.; Tong, W.; Chattopadhyaya, J. *J. Am. Chem. Soc.* **2001**, *115*, 9734–9746.

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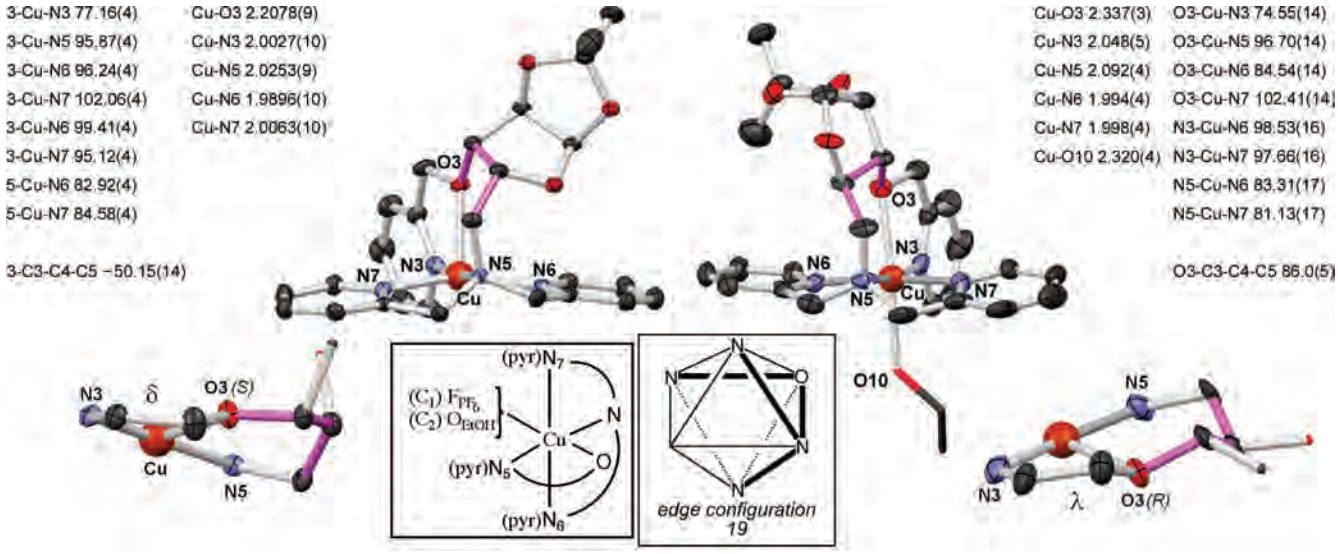


Figure 1. (Left) [Cu(**L1**)](PF$_6$)$_2$ (**C1**): X-ray structure, selected bond lengths and angles, and focus on the chirality elements (below). (Right) [Cu(**L2**)(EtOH)](PF$_6$)$_2$ (**C2**): X-ray structure, selected bond lengths and angles, and focus on the chirality elements (below). Ellipsoids are drawn at the 60% probability level. O3−C3−C4−C5 are highlighted in violet. H atoms and PF_6^- anions are omitted. Insets: schematic view of the coordination sphere and edge configuration for both complexes.

configuration of the C3 atom. We show in the following that this stereochemical difference in the ligands generates pseudoenantiomeric complexes.

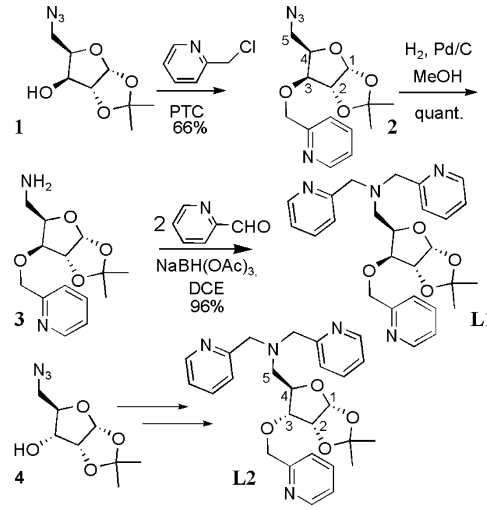
L1 (5-amino-5-deoxy-1,2-*O*-isopropylidene-5-*N*,*N*-di-2-picolyl-3-*O*-2-picolyl-α-D-xylofuranose) and **L2** (its *ribo* epimer) were obtained through three synthetic steps from published synthons, the *xylo*-azido alcohol **1**[15] for **L1** and its *ribo* epimer **4** for **L2** (Scheme 1). The synthesis of **L1** consisted of picolylation by a phase-transfer-catalysis (PTC) procedure[10,16] followed by azide reduction (amine **3**). The final step was the reductive amination of **3** with 2-pyridinecarboxaldehyde using NaBH(OAc)$_3$ as the reductant.[17]

The copper(II) complexes of **L1** and **L2** were obtained by reacting equimolar amounts of the ligands and copper(II) nitrate trihydrate in an ethanolic solution. Precipitation was observed upon the addition of NH_4PF_6. The hexafluorophosphate salts **C1** and **C2** of both complexes were redissolved with acetone and crystallized by slow evaporation, yielding X-ray-suitable crystals. The structures of both complexes have been solved (Figure 1).

The complexes crystallize in the noncentrosymmetric space group $P2_12_12_1$.[18] The pentadentate ligands adopt the same edge configurations (19 in the Damhus nomenclature;[11,12] see Figure 1) with a meridional dipicolylamine moiety (N5, N6, and N7). In the structure of **C1**, the Cu atom is pentacoordinate (square-based pyramidal geometry, with a τ parameter[19] of 0.258). A hexafluorophosphate anion shows a weak interaction [Cu···F 2.8934(10) Å] with the atoms of the coordination sphere. In the structure of **C2**, the Cu atom achieves hexacoordination through the binding of a solvent molecule. Cremer−Pople ring-puckering analysis[20] indicates that the furanose rings of **L1** and **L2** are in $^3T_4$ and $^OT_4$ conformations, respectively. Analysis of the coordination bond distances indicates Cu−O3 > Cu−N$_i$; i.e., the ether moiety is a weak axial ligand.

Upon chelation, O3 becomes a stereogenic atom[8] and the five-membered metallacycle defined by Cu, O3, and N3 displays conformational chirality. The appropriate Cahn−Ingold−Prelog descriptors for the O3 atoms and the conformational chirality descriptors δ/λ for the cycle are the opposite in the two complexes; that is, *S*, δ for **C1**; *R*, λ for **C2** (see Figure 1). Because the edge configuration is the same

Scheme 1. Synthetic pathway to **L1** (PTC = Phase Transfer Catalysis)[a]



[a] Conditions: H_2O/toluene, NaOH, ^{t}amyl-OH, NBu_4HSO_4, DCE = 1,2-dichloroethane). **L2** was obtained similarly (see the Supporting Information for experimental details). Numbering of the carbohydrate carbons is shown.

(15) Yamashita, M.; Takahashi, C.; Seo, K. *Heterocycles* **1993**, *36*, 651–654.
(16) Szeja, W.; Fokt, I.; Grynckiewicz, G. *Recl. Trav. Chim. Pays-Bas* **1989**, *108*, 224–226.
(17) Abdel-Magid, A. F.; Mehrman, S. J. *Org. Process Res. Dev.* **2006**, *10*, 971–1031.
(18) See Supporting Information(Table S2) for crystallographic details.
(19) Addison, A. W.; Rao, T. N.; Reedijk, J.; Rijn, J. V.; Verschoor, G. V. *J. Chem. Soc., Dalton Trans.* **1984**, 1349–1356.
(20) Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.

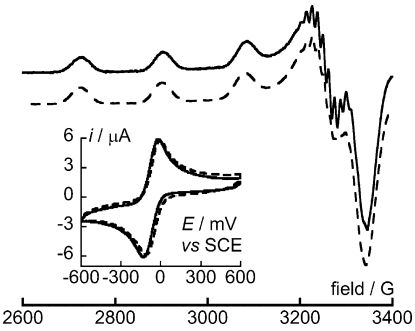


Figure 2. Copper(II) complex of **L1**: continuous line. Copper(II) complex of **L2**: dashed line. X-band EPR spectra (frozen 1:1 toluene/acetone solutions, concentration = 10^{-3} mol L^{-1}, T = 100 K). Inset: CV (concentration = 3.3×10^{-4} mol L^{-1} in 2:1 ethanol/acetone with 3.3×10^{-2} mol L^{-1} $LiClO_4$ as the supporting electrolyte). See the Supporting Information for EPR simulations (Figures S1 and S2) and for further experimental details.

Table 1. EPR and CV Data for the Copper(II) Complexes of **L1** and **L2**

	$g_\perp{}^a$	$g_\parallel{}^a$	$A_\parallel{}^{a,b}$	$A_{Niso}{}^{a,b}$	$E_p{}^{ac}$	$E_p{}^{cc}$	$E_{1/2}{}^c$
C1	2.057	2.239	549	33.5	−26	−134	−80
C2	2.056	2.242	547	36.5	−7	−108	−58

[a] Parameters were obtained by simulation[22] with *XSophe*.[23] [b] Unit: MHz. [c] Unit: mV vs SCE.

in both complexes, these stereochemical descriptors are determined by the sign of the O3−C3−C4−C5 dihedral angle (φ_6; see Figure 1). Because the bicyclic furano-scaffolds are conformationally constrained with the bulky substituents of C4 near their most favorable equatorial position,[14] the difference in the absolute configuration of C3 results in opposite signs for the respective O3−C3−C4−C5 dihedral angles (φ_6): in **C1**, O3 ends up axial with $\varphi_6 < 0$, whereas in **C2**, O3 is equatorial and $\varphi_6 > 0$.

The electronic properties of the copper(II) complexes were studied by three techniques insensitive to chirality. Electron paramagnetic resonance (EPR) and cyclic voltammetry (CV; Figure 2 and Table 1) as well as visible spectroscopy (Figure 3 and Table 1) were recorded for solutions of redissolved crystals of **C1** and **C2**.

EPR and visible data of the complexes in solution are consistent with a weak tetragonal field[21] as expected from the X-ray structures (similar edge configuration).[22] The similar spectra and voltammograms indicate similar coordination spheres for **C1** and **C2** in solution, probably with a coordinated solvent molecule as in the structure of **C2**.

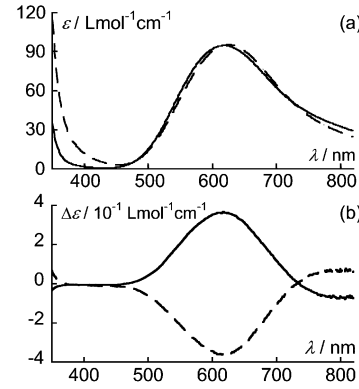


Figure 3. Visible and CD spectra of copper(II) complexes of **L1** (continuous line) and **L2** (dashed line) in 1:1 ethanol/acetone. Concentration: 10^{-2} mol L^{-1}.

The CD spectra of solutions of **C1** and **C2** were recorded in the region of Cu^{II} d−d transitions and showed a mirror-image pattern (Figure 3 and Table S1 in the Supporting Information), typical of enantiomers.[24]

The observation of a pair of mirror-image CD signals as well as the very similar physical properties (see above) for the copper(II) complexes of **L1** and **L2** indicate a pseudo-enantiomeric nature of the coordination environments in solution. This type of behavior has already been observed by Mikata et al.[8] in the case of glycoconjugate copper(II) complexes. In the latter case, however, only one atom of the sugar is bound to the metal: the sugar acts as a chiral appendage to the ligand. In the present case, the furanose ring is fused to the six-membered chelate ring and, thus, its stereochemistry acts directly on the conformation of the chelate ring. In **C1** and **C2**, the two ligands show the same edge configuration, which is not inherently chiral (see the inset in Figure 1). The stereogenic elements of the complexes have been described above: they are controlled by the sign of φ_6, which derives from the C3 configuration.

The results described in this Communication show the interest of using pentadentate ligands derived from sugars in stereoselective complexation reactions. We have demonstrated that a pair of diastereomeric carbohydrate-derived ligands varying only by the absolute configuration of C3 ensured a predetermination of the chirality of the derived copper(II) complexes, with a stereoselective transfer of chirality from the ligand to the metal complex.

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Supporting Information Available: Synthetic procedures for **L1**, **L2**, and their copper(II) complexes, X-ray diffraction data, and superimpositions of experimental/simulated EPR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) Hathaway, B., Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: New York, 1987; pp 533–750.
(22) The EPR spectra could be simulated (see the Supporting Information, Figures S1 and S2). The hypefine coupling seen in $g_\perp$ could be reproduced by an interaction with four equivalent N atoms. This unambiguously indicates that four N atoms are in plane, with O_{ether} being axial. In other words, the edge configuration in solution is the same as that in the solid state.
(23) Griffin, M.; Muys, A.; Noble, C.; Wang, D.; Eldershaw, C.; Gates, K. E.; Burrage, K.; Hanson, G. R. *Mol. Phys. Rep.* **1999**, *26*, 60–84.
(24) Rodger, A.; Nordén, B. *Circular Dichroism and Linear Dichroism*; Oxford Chemistry Masters Series; Oxford University Press: Oxford, U.K., 1997.