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Induction of Chirality into Metal Complexes by Boronic Acid-Sugar Interactions

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Abstract: By sonication in MeOH *N-m*-(phenylboronic acid)-2,2'-bipyridine-5-carboxylamide easily formed its bidentate boronate sugar ligands. Solutions of the corresponding Cu(I) and Fe(II) complexes showed opposite CD effects for the D and the L form of the sugar. The stoichiometry of the metal complexes was determined by Job plots and by mass spectrometry. A macrocyclic structure, that includes ten cycles, is proposed as the most probable CD-active species.

Polyimine ligands such as bipyridine, terpyridine or phenanthroline have been used to generate metal complexes with many transition metals.[1] Depending on the properties of the metal and the polyimine ligand it is possible to create a diversity of structures, for example, helical[2] and dendritic structures,[3] that often show chirality. From the chiral pool amino acids, terpenes and sugars have been used as chiral auxiliares for the formation of metal complexes. Until now sugars were only used to influence the constitution of the complex after its formation.[4] Here a new alternate way is demonstrated, that is the connection of the sugar to a metal chelating agent followed by the transformation of the resulting ligands into the corresponding metal complexes. Sugars are very suitable for the molecular design of chiral supramolecules because of their well known formation of heterocycles with boronic acids.[5] Depending on the chain length of the sugar, its cyclic constitution (e.g. furanose or pyranose structure), the absolute configuration (D or L form) and the different ratio of boronic acid to sugar, an immense variety of new ligands is possible.

To connect the phenylboronic acid and the 2,2'-bipyridine an amide bond (**2**) was chosen, which is more rigid than an ester or an ether bond.[6] Amide **2** was mixed with the D and L form of xylose, threitol and arabinose in a ratio of 2:1. After sonication of these mixtures in MeOH the corresponding saccharide/bipyridine bidentate boronate ester (**3D,L**; **4D,L**; **5D,L**; Scheme1), one sugar and two boronic acid units were linked by cyclic esters and formed a precipitate.[7,8] ^{1}H NMR data for xylose, arabinose[9] and threitol[10] (based on X-ray crystal structure analysis) boronic esters are available. Xylofuranose and the boronic acid were connected by one six-membered and one five-membered heterocycle (**3D,L**). Arabinopyranose forms five-membered ring heterocycles (**5D,L**) in opposite to the six-membered rings of the threitol-framework (**4D,L**) (Scheme 1, right).

The reaction was also tried with the D and L isomers of lyxose, ribose, fucose, 3-methyl-*O*- D-glucose and pentaerythritol. All of these saccharides contain four free hydroxyl-groups. Therefore it

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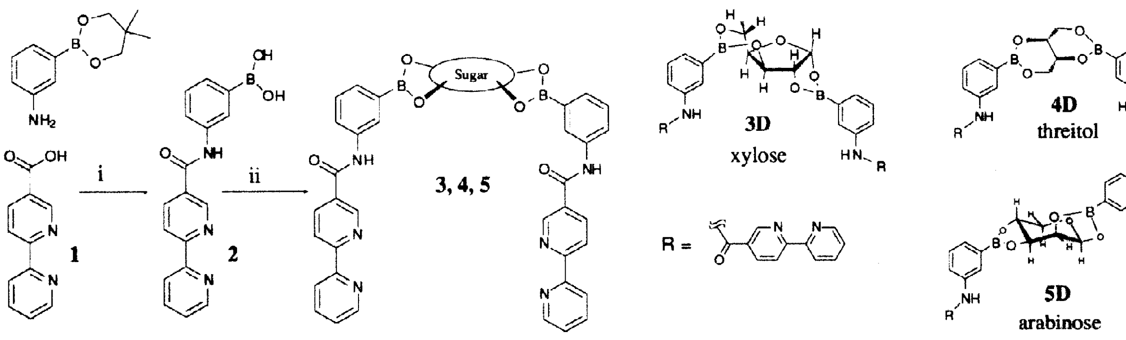
was expected, that in a possible bidentate boronate complex all hydroxyl-groups should be esterified and its solubility should be similar to the examples mentioned above. The reaction failed to give a precipitate with fucose, ribose and 3-methyl-*O*-D-glucose. Pentaerythritol and lyxose produced solid, which was analyzed by mass spectrometry. Additionally ^{1}H NMR signals of the symmetrical pentaerythritol were in agreement with the proposed structure of the polyol. An explanation of the different behavior of the sugars is ascribed to the different tendency to form an unique product. Like cited before xylose formed preferably the furanose, arabinose the pyranose and threitol the six membered bicyclic structure: this means that an unique compound resulted, so that the solubility product was exceeded.



Scheme 1 i) $SOCl_2$; 50-60%; ii) sonication in MeOH with the D and L form of xylose. Threitol and arabinose lead to the bidentate boronates **3D, 3L, 4D, 4L** and **5D, 5L**; 40-80%.

To generate the chiral metal complexes, a suspension of the enantiomers (**D** or **L** form) was sonicated in MeOH with Fe(II) Cl_2 in a ratio of 1:1. MeOH was used because all six ligands (**3D,L**; **4D,L**; **5D,L**) were formed and stable in this solvent. After sonication a red suspension was obtained. UV/VIS Spectra showed in the visible region an absorption (due to the MLCT of a $Fe(bpy)_x$ λ_{max} = 545 nm) and the CD band was opposite for each D and L sugar-containing enantiomer. A similar result was found by use of the threitol ligands **4D** and **4L**. The arabinose complex did not show any effect in the CD spectra. A possible explanation for this behavior might be fast decomposition of the complex after its Fe(II) complex formation. The composition of these complexes was determined both by Job plots and by SI mass spectral analysis.

The Job plots for all complexes (**Fe · 3D,L**; **Fe · 4D,L**; **Fe · 5D,L**) were similar: the value was close to 0.5. A value of 0.5 indicates a 1:1 complex of ligand and iron(II), that is containing two chlorine counterions.[11] Determination of the red solutions by mass spectrometry (using SIMS mode) showed a strong indication for a 1:1 complex of metal and ligand for **Fe · 3** [MS (SIMS) m/z = 843 (M+H $^+$, 2 %), 808 (M-Cl+H $^+$, 2 %)] and **Fe · 4** [MS (SIMS) m/z = 779 (M-Cl $^+$, 5.5 %), 743 (M-2Cl $^+$, 6.5%)]. The CD effect can be explained by an induced chirality of the sugar into the metal-bipyridine complex moiety. MM2-calculations [12] also supported a structure, where two chlorine counter ions were in a *trans* position, whereas the formation of a *cis* complex is unfavored.

The copper complexes (**Cu·3D,L**; **Cu·4D,L** and **Cu·5D,L**) were synthesized in acetonitrile with $Cu(I)(CH_3CN)_4ClO_4$[13] as reagent. The resulting solutions showed CD activity (Fig.1). Mass spectra proved the 1:1 stoichiometry for **Cu·3** [MS (SIMS) m/z = 779 ($M-ClO_4^+$, 6 %)] and **Cu·4** [MS (SIMS) m/z = 751 ($M-ClO_4^+$, 4 %)]. By comparison with literature data the following proposals (Table 1.) can be made for the helicity of these complexes.[14]

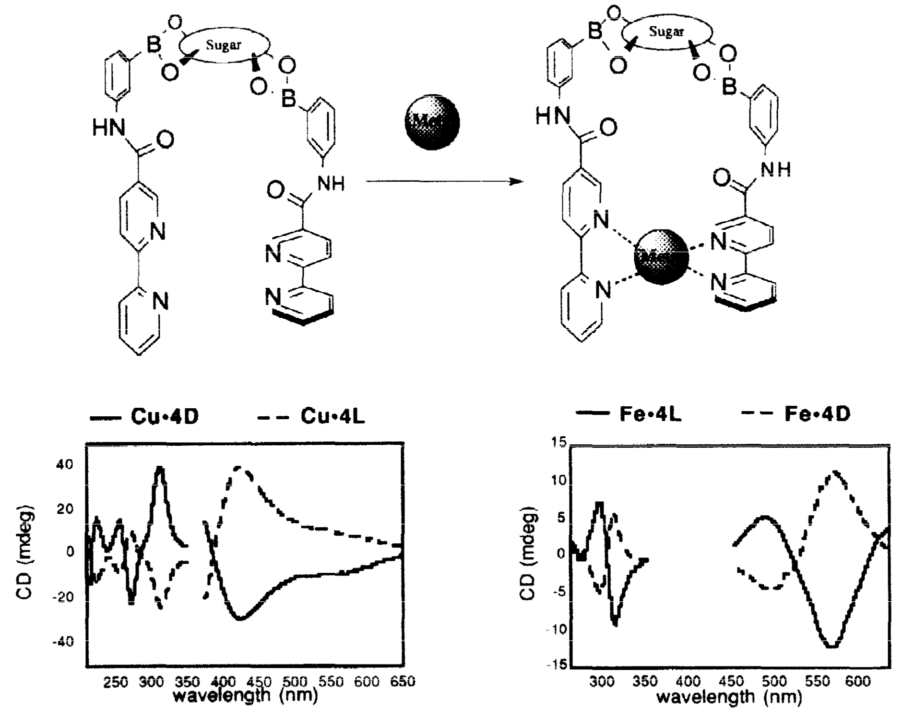


Fig. 1. Top: 1:1 metal complexes were detected by mass spectrometry; Bottom: CD spectra of the solutions of **Cu·4D,L** and **Fe·4D,L**; for xylose a similar result was obtained; for arabinose only the Cu(I) complex showed CD activity.

Table 1. Helicity of the 1:1 complexes proposed from the CD sign of the MLCT region.

For xylose (**Cu·3**)	D = Plus, L = Minus (λ_{max} = 450 nm, CD = 12 mdeg)
For threitol (**Cu·4**)	D = Plus, L = Minus (λ_{max} = 415 nm, CD = 40 mdeg)
For arabinose (**Cu·5**)	D = Minus, L = Plus (λ_{max} = 505 nm, CD = 500 mdeg).[14]

In summary, three pairs of enantiomeric bipyridine-phenylboronic acid sugar ligands (**3D,L**; **4D,L**; **5D,L**) have been characterized. Solutions of the corresponding Fe(II) (**Fe·3D,L**; **Fe·4D,L**) and Cu(I) (**Cu·3D,L**; **Cu·4D,L**) complexes of threitol and xylose showed CD activity in the metal to ligand charge transfer absorption. Arabinose boronate **5** showed CD activity only in combination with Cu(I) (**Cu·**

5D,L). Mass spectra and in addition Job plots for the Fe(II) complexes supported the 1:1 stoichiometry of these metal containing macrocycles.

This study demonstrated that sugars are useful as efficient auxiliaries for chiral coordination compounds. We believe that this concept is applicable to chiral molecular recognition by metal complexes.

References and Notes

1. a) Lehn, J.-M. *Supramolecular Chemistry* VCH, Weinheim **1995**; b) Zelewsky, A. V. *Coordination Compounds in Supramolecular Chemistry* Wiley, Chichester **1996**.
2. a) Williams, A. *Chem. Eur. J.*, **1997**, *3*, 15-16; b) Constable, E. C.; Kulke, T.; Neuburger, M.; Zehnder, M. *Chem. Commun.*, **1997**, 489-490; c) Charbonniere, L. J.; Williams, A. F.; Frey, U.; Merbach, A. E.; Kamalprija, P.; Schaad, O. *J. Am. Chem. Soc.*, **1997**, *119*, 2488-2496.
3. Newcome, G. R.; Moorefield, C.; Voegtle, F. *Dendritic Molecules - Concepts*Synthesis*Perspectives* VCH, Weinheim **1996**.
4. Chirality of 2,2'-bipyridine complexes can be influenced by a) terpene frameworks: Hayoz, P.; Zelewsky, A. V.; Stoeckli-Evans, H. *J. Am. Chem. Soc.*, **1993**, *115*, 5111-5114; b) boronic acid sugar template interaction: Mizuno, T.; Takeuchi, M.; Hamachi, I.; Nakashima, K.; Shinkai, S. *Chem. Commun.*, **1997**, 1793-1794; c) amino acids: Weizman, H.; Libman, J.; Shanzer, A. *J. Am. Chem. Soc.*, **1998**, *120*, 2188-2189.
5. a) Lorand, J. P.; Edwards, J. D. *J. Org. Chem.*, **1959**, *24*, 769-770; b) James, T. D.; Sandanayake, S. K. R. A.; Shinkai, S. *Nature*, **1995**, *374*, 375.
6. 5-Methyl-2,2'-bipyridine was synthesized according to Kroehnke, F. *Synthesis*, **1976**, 1-24; the methylgroup was oxidized by $KMnO_4$ to receive **1**, that was transformed to the amide **2**; a similar connection is described by Yam, W.-W.; Kai, A.S.F. *Chem. Commun.*, **1998**, 109-110.
7. Precipitation occured mainly in form of gels; additional information about organic gelators: Yoza, K.; Ono, Y.; Yoshihara, K.; Akao, T.; Shinmori, H.; Takeuchi, M.; Shinkai, S. Reinhoudt, D.N. *Chem. Commun.*, **1998**, 109-110.
8. **3 D**,**3 L**, **4 D**, **4 L**, **5 D** and **5L** were characterized and assigned definitely and will be published in a full paper.
9. a) Wood P. J.; Siddiqui, I. R. *Carbohydr. Res.*, **1974**, *32*, 97-104; b) Norrild, J. C.; Eggert, H. *J. Am. Chem. Soc.*, **1995**, *117*, 1481-1484.
10. Ishi-i, T.; Nakashima, K.; Shinkai, S. *Tetrahedron*, **1998**, *54*, 8679-8686.
11. a) Complexes of the composition $Fe(II)bpy_2X_2$ (X = SCN) were described by Driver, R.; Walker, W. R. *Aust. J. Chem.*, **1967**, *20*, 1376-1383.
12. Models were calculated with the Chem3D implanted MM2 module on a Mac Intosh Power PC.
13. Hathaway, B. J.; Holah, D. G.; Postlethwaite, J. D. *J. Chem. Soc.*, **1961**, 3215-3218.
14. a) Woods, C. R.; Benaglia, M.; Cozzi, F.; Siegel, J. S. *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 1830-1833; b) Yamamoto, M.; Takeuchi, M.; Shinkai, S. *Tetrahedron Lett.*, **1998**, *39*, 1189-1192; c) Nabeshima, T.; Inaba, T.; Furukawa, N.; Hosoya, T.; Yano, Y. *Inorg. Chem.*, **1993**, *32*, 1407-1416.