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Diastereoselective Self-Assembly of Double- and Triple-Stranded Helicates from a D-Isomannide Derivative

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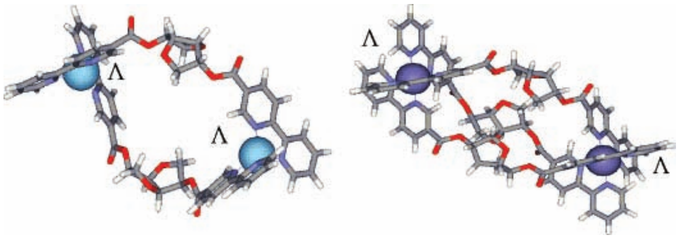
ABSTRACT



Difunctionalization of D-isomannide yielded a bis(bipyridine) ligand bearing four stereogenic centers whose diastereoselective self-assembly to enantiomerically pure dinuclear helicates upon coordination to different metal ions was investigated by NMR and CD spectroscopic as well as ESI mass spectrometric methods.

The diastereoselective formation of self-assembled helicates[1−5] from chiral ligands and suitable metal ions has seen a tremendous development in recent years. Our approach aims at the formation of self-assembled helical metal complexes from C_2-symmetric ligands that have cavities with inwardly directed functionalities. We were able to show that dinuclear double- and triple-stranded helical metallosupramolecular aggregates of bis(bipyridine) ligands prepared from substituted C_2-symmetric building blocks as enantiopure 1,1′-binaphthyls (BINOLs) or even racemic Tröger's base derivatives can be formed through self-assembly processes in a diastereoselective manner.[6] In order to broaden this scope and to show that our concept is more general, we were

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(1) Reviews: (a) Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Chem. Rev.* **1997**, *97*, 2005. (b) Albrecht, M. *Chem. Soc. Rev.* **1998**, *27*, 281. (c) von Zelewsky, A. *Coord. Chem. Rev.* **1999**, *190−192*, 811. (d) Knof, U.; von Zelewsky, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 302. (e) von Zelewsky, A.; Mamula, O. *J. Chem. Soc., Dalton Trans.* **2000**, 219. (f) Albrecht, M. *Chem. Eur. J.* **2000**, *6*, 3485. (g) Albrecht, M. *Chem. Rev.* **2001**, *101*, 3457. (h) Mamula, O.; von Zelewsky, A. *Coord. Chem. Rev.* **2003**, *242*, 87.

(2) Selected examples for the diastereoselective formation of helicates with 2,2′-bipyridines: (a) Zarges, W.; Hall, J.; Lehn, J.-M.; Bolm, C. *Helv. Chim. Acta* **1991**, *74*, 1843. (b) Mamula, O.; Monlien, F. J.; Porquet, A.; Hopfgartner, G.; Merbach, A. E.; von Zelewsky, A. *Chem. Eur. J.* **2001**, *7*, 533. (c) Mamula, O.; von Zelewsky, A.; Brodard, P.; Schläpfer, C.-W.; Bernardinelli, G.; Stoeckli-Evans, H. *Chem. Eur. J.* **2005**, *11*, 3049. (d) Woods, C. R.; Benaglia, M.; Cozzi, F.; Siegel, J. S. *Angew. Chem., Int. Ed.* **1996**, *35*, 1830. (e) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Woods, C. R.; Siegel, J. S. *Eur. J. Org. Chem.* **2001**, 173. (f) Baum, G.; Constable, E. C.; Fenske, D.; Housecroft, C. E.; Kulke, T. *Chem. Commun.* **1999**, 195. (g) Prabaharan, R.; Fletcher, N. C.; Nieuwenhuyzen, M. *J. Chem. Soc., Dalton Trans.* **2002**, 602. (h) Prabaharan, R.; Fletcher, N. C. *Inorg. Chim. Acta* **2003**, *355*, 449. (i) Telfer, S. G.; Tajima, N.; Kuroda, R. *J. Am. Chem. Soc.* **2004**, *126*, 1408.

(3) Selected examples for the diastereoselective formation of helicates with ter- and quaterpyridines: (a) Baum, G.; Constable, E. C.; Fenske, D.; Housecroft, E.; Kulke, T.; Neuburger, M.; Zehnder, M. *J. Chem. Soc., Dalton Trans.* **2000**, 945. (b) Baum, G.; Constable, E. C.; Fenske, D.; Housecroft, C. E.; Kulke, T. *Chem. Eur. J.* **1999**, *5*, 1862.

(4) Selected examples for the diastereoselective formation of helicates with oxazolines and pyridylmethanimines: (a) Provent, C.; Rivara-Minten, E.; Hewage, S.; Brunner, G.; Williams, A. F. *Chem. Eur. J.* **1999**, *5*, 3487. (b) van Stein, G. C.; van Koten, G.; Vrieze, K.; Brevard, C.; Spek, A. L. *J. Am. Chem. Soc.* **1984**, *106*, 4486. (c) Masood, M. A.; Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int Ed.* **1998**, *37*, 928. (d) Amendola, V.; Fabbrizzi, L.; Mangano, C.; Pallavicini, P.; Roboli, E.; Zema, M. *Inorg. Chem.* **2000**, *39*, 5803. (e) Hamblin, J.; Childs, L. J.; Alcock, N. W.; Hannon, M. J. *J. Chem. Soc., Dalton Trans.* **2002**, 164. See also ref 2i.

(5) Selected examples for the diastereoselective formation of helicates with catechols: (a) Kersting, B.; Meyer, M.; Powers, R. E.; Raymond, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 7221. (b) Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 996. (c) Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int Ed.* **1998**, *37*, 932. (d) Albrecht, M. *Synlett* **1996**, 565. (e) Albrecht, M.; Janser, I.; Fleischhauer, J.; Wang, Y.; Raabe, G.; Fröhlich, R. *Mendeleev Commun.* **2004**, 250.

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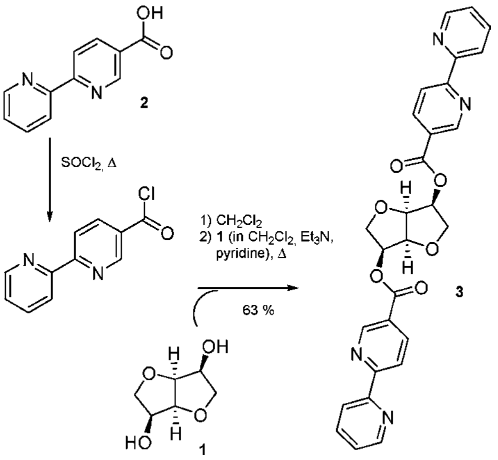
looking for another readily available, V-shaped and chiral building block that can be easily used for our purposes. Such a compound is D-isomannide (1,4:3,6-dianhydro-D-mannitol, (**1**)) which bears four stereogenic centers and can easily be difunctionalized via its two OH-functions which point toward the concavity of the bicyclic architecture.

D-Isomannide was first described in 1882 by Fauconnier,[7] but its structure was not elucidated until 1946.[8] D-Isomannide or its derivatives have been used as chiral auxiliaries,[9] in asymmetric catalysis,[10] for the self-assembly of [2]catenanes,[11] and the construction of crown ether derivatives for the recognition of ammonium salts;[12] very recently, the photoswitching behavior of a diazobenzene analogue has been investigated.[13] Additionally, 4-pyridyl-substituted ligands have been prepared from D-isomannide and D-isosorbide that form triple-stranded coordination networks of helical shape with $HgCl_2$.[14]

Esterification of **1** with in situ generated 2,2′-bipyridine-5-carbonyl chloride was performed which yielded bis(bipyridine) ligand **3** in 63% (Scheme 1).

Scheme 1. Synthesis of Bis(bipyridine) Ligand **3** from D-Isomannide (**1**) and 2,2′-Bipyridine-5-carboxylic Acid (**2**)



The coordination behavior of **3** toward transition metal ions such as silver(I), copper(I), zinc(II), and iron(II) was at first investigated by ^1H NMR spectroscopic means. Whereas Ag^+ and Cu^+ typically prefer a tetrahedral geometry that gives rise to double-stranded helicates and the application of Fe^{2+} usually provides the formation of triple-stranded complexes due to octahedral coordination of these metal ions, the use of Zn^{2+} may result in both species due to its "chameleon" character.[15] Upon addition of the metal salts to **3**, characteristic color changes for bipyridine complexes of Ag^+, Cu^+, and Fe^{2+} could be observed, whereas the solution of the Zn^{2+}-aggregate remained colorless.

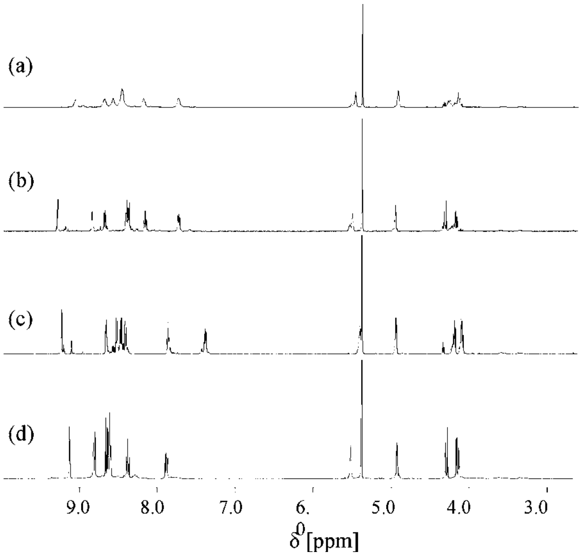


Figure 1. ^1H NMR complexation studies of **3** in CD_2Cl_2/CD_3CN (3:1). (a) **3** + $[Cu(CH_3CN)_4]BF_4$ (1:1). (b) **3** + $[Ag(CH_3CN)_2]BF_4$ (1:1). (c) **3**. (d) **3** + $[Zn(BF_4)_2]\cdot 6.5\ H_2O$ (1:1).

The ^1H NMR spectra (Figure 1) indicated the successful formation of metal complexes with **3**. Although the hydrogen atoms of the aggregates formed with Cu^+ and also with Fe^{2+} (dinuclear $[Fe_2\mathbf{3}_3](SO_4)_2$ was formed from 3:2 mixtures of **3** and Fe^{2+} salt in a mixture of dichloromethane-d_2 and DMSO-d_6, thus it is not displayed in Figure 1) gave rise to relatively broad signals, it is evident that almost all signals are significantly shifted compared to that of the free ligand (Figure 1c).

However, the addition of Ag^+ and Zn^{2+} in equimolar amounts results in well-resolved spectra with only one set of sharp signals in each case and indicates the formation of a double-stranded Zn^{2+}-complex with, respectively, a coordination number of four and a tetrahedral geometry in this case. These observations refer to the formation of discrete dinuclear helicates and exclude the formation of oligomeric or polymeric species which could also be proven by ESI

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(6) (a) Lützen, A.; Hapke, M.; Griep-Raming, J.; Haase, D.; Saak, W. *Angew. Chem., Int. Ed.* **2002**, *41*, 2086. (b) Schalley, C. A.; Lützen, A.; Albrecht, M. *Chem. Eur. J.* **2004**, *10*, 1072. (c) Kiehne, U.; Weilandt, T.; Lützen, A. *Org. Lett.* **2007**, *9*, 1283.

(7) Fauconnier, A. C. R. *Acad. Sci.* **1882**, *95*, 991.

(8) Hockett, R. C.; Fletcher, H. G., Jr.; Sheffield, E. L.; Goepp, R. M., Jr.; Soltzberg, S. *J. Am. Chem. Soc.* **1946**, *68*, 930.

(9) (a) Loupy, A.; Monteux, D. A. *Tetrahedron* **2002**, *58*, 1541. (b) Sano, S.; Teranishi, R.; Nakano, F.; In, K.; Takeshige, H.; Ishii, T.; Shiro, M.; Nagao, Y. *Heterocycles* **2003**, *59*, 793.

(10) (a) De Coster, G.; Vandyck, K.; Van der Eycken, E.; Van der Eycken, J.; Elseviers, M.; Roper, H. *Tetrahedron: Asymmetry* **2002**, *13*, 1673. (b) Carcedo, C.; Dervisi, A.; Fallis, I. A.; Ooi, L.; Malik, K. M. A. *Chem. Commun.* **2004**, 1236. (c) Dervisi, A.; Carcedo, C.; Ooi, L.-l. *Adv. Catal. Synth.* **2006**, *348*, 175.

(11) Ashton, P. R.; Heiss, A. M.; Pasini, D.; Raymo, F. M.; Shipway, A. N.; Stoddart, J. F.; Spencer, N. *Eur. J. Org.* **1999**, 995.

(12) (a) Metcalfe, J. C.; Stoddart, J. F.; Jones, G.; Crawshaw, T. H.; Quick, A.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1981**, 430. (b) Metcalfe, J. C.; Stoddart, J. F.; Jones, G.; Crawshaw, T. H.; Gavuzzo, E.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1981**, 432.

(13) Alam, Z.; Yoshioka, T.; Ogata, T.; Nonaka, T.; Kurihara, S. *Chem. Eur. J.* **2007**, *13*, 2641.

(14) Grosshans, P.; Jouaiti, A.; Bulach, V.; Planeix, J.-M.; Hosseini, M. W.; Nicoud, J.-F. *Chem. Commun.* **2003**, 1336.

(15) Sigel, H.; Martin, R. B. *Chem. Soc. Rev.* **1994**, *23*, 83.

mass spectrometric experiments because only signals of the intact helicates and fragments resulting from them could be detected, which is representatively shown for $[Ag_2\mathbf{3}_2](BF_4)_2$ in Figure 2. The same results could be found for double-stranded $[Cu_2\mathbf{3}_2](BF_4)_2$ and $[Zn_2\mathbf{3}_2](BF_4)_4$ and triple-stranded $[Fe_2\mathbf{3}_3](BF_4)_4$, respectively. However, the formed complexes appear not to be very stable under these conditions because the main peaks can be attributed to the fragments $[M_1\mathbf{3}_1]^{n+}$ or $[M_1\mathbf{3}_2]^{n+}$ in all cases ($M = Cu, Zn, Fe$; $n = 1$ or 2).

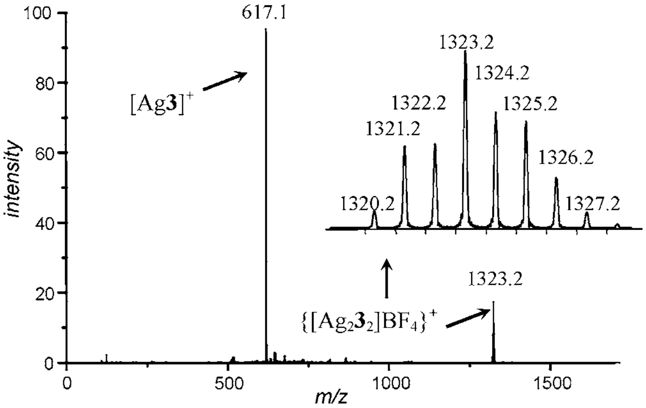

Figure 2. Positive ESI MS of a solution of $[Ag_2\mathbf{3}_2](BF_4)_2$ in dichloromethane.

Due to the fact that the ^1H NMR spectra of the complexes show the same number of proton signals as for free enantiopure ligand **3**, one can exclude the formation of (Δ,Λ)- or (Λ,Δ)-configured "*meso*"-helicates, which should result in the double amount of signals due to the lower symmetry of the newly formed aggregates. The fact that both halves of the ligand are still magnetically equivalent is only feasible when architectures with equally configured metal centers are formed. Since the two possible helicates with (Δ,Δ)- or (Λ,Λ)-configuration are diastereomers, however, it is very unlikely that all of the proton signals of those complexes should be isochronic by coincidence. Therefore, one can conclude that the self-assembly processes are indeed completely diastereoselective yielding D_{2d}- or D_{3d}-symmetrical helicates with equally configured metal centers.

An additional indication for the formation of chiral complexes is their optical rotation which was determined by polarimetry. The complexes possess the same absolute sense of rotation as **3**, but have significantly larger values.

To elucidate the stereochemistry of the complexes, ^1H NMR ROESY experiments were carried out with the double-stranded complexes $[Ag_2\mathbf{3}_2](BF_4)_2$ and $[Zn_2\mathbf{3}_2](BF_4)_4$, which allow an assignment of the relative orientation of the bipyridine core and the isomannide backbone. As Figure 3 shows representatively for $[Zn_2\mathbf{3}_2](BF_4)_4$, clear evidence points toward a (Λ,Λ)-configuration in both cases: ROE contacts of bipyridine proton H-6 to H-1*endo* and H-2 of the isomannide bicyclic structure can be observed. This would not be possible in case of (Δ,Δ)-configured helicates because the distances are too far. Similar results were obtained for $[Ag_2\mathbf{3}_2](BF_4)_2$.

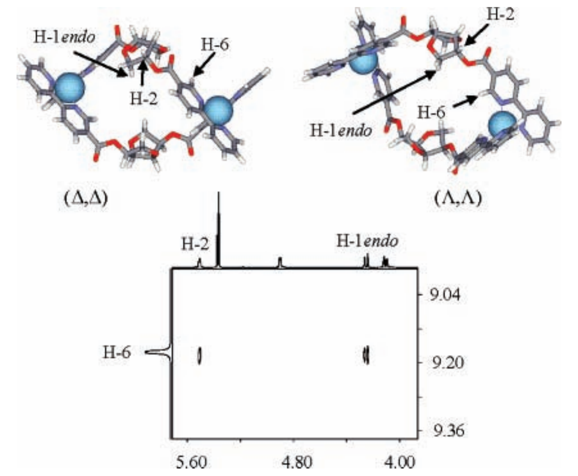

Figure 3. PM3-TM-minimized structures of (Δ,Δ)-$[Zn_2\mathbf{3}_2]^{4+}$ (left) and (Λ,Λ)-$[Zn_2\mathbf{3}_2]^{4+}$ (right) and extensions of the relevant area of the recorded gs-2D-ROESY-NMR-spectra (in CD_2Cl_2/CD_3CN (3:1), 298 K).

CD spectroscopy is a powerful chirooptical spectroscopic method and has been widely used in the last years to elucidate the stereochemistry of chiral bipyridine transition metal complexes.[16] Assignments of the absolute configuration of such helical systems can be derived from the sign of ligand-centered (lc) $\pi-\pi^*$-transitions around 300−340 nm in most cases. Especially in case of copper(I) complexes it can also be derived from the sign of metal-to-ligand-charge-transfer bands (mlct) around 400−550 nm in the CD spectrum.[1c,d,h,2,3,16−18] Besides the assignment of the absolute configuration by local Δ- or Λ-descriptors for each metal ion of the complex, the turn of the helix can also be used to assign either a *P*- (plus/clockwise) or an *M*-conformation (minus/counter-clockwise) to each complex. According to the *oriented line* reference system,[19,20] a Δ-configuration of the metal centers always corresponds to a *P* helix.[16] A *P*-handedness has been proposed for complexes displaying positive signs for the bands of the characteristic regions mentioned above.[1c,d,h,2,3,16−18] However, the exciton model gives Δ- and Λ-orientations (and as a result a *P* and *M* screw) of the helices arising from *skew line* convention. In double-stranded helicates, the ligands are almost perpendicular to each other, and in fact, i.e., an *M*-conformation can be adressed to either a Δ- or Λ-configuration of the metal centers, depending on the distortion being either less than or greater than 90°.[16,21] As a result, the CD spectra should

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(16) Ziegler, M.; von Zelewsky, A. *Coord. Chem. Rev.* **1998**, *177*, 257.

(17) (a) Telfer, S. G.; Kuroda, R.; Sato, T. *Chem. Commun.* **2003**, 1064. See also ref 2i.

(18) Amendola, V.; Fabbrizzi, L.; Mangano, C.; Pallavicini, P.; Roboli, E.; Zema, M. *Inorg. Chem.* **2000**, *39*, 5803.

(19) Damhus, T.; Schaeffer, C. E. *Inorg. Chem.* **1983**, *22*, 2406.

(20) von Zelewsky, A. *Stereochemistry of Coordination Compounds*; John Wiley & Sons: Chichester, 1996.

(21) This is not a problem for triple-stranded complexes because the angle between two exciton-coupled ligands will always be less than 90°.

be interpreted in terms of the absolute configurations of the individual metal centers rather than the overall helicity of the assemblies, and it should always be stated which reference system was used for the determination of the absolute configuration to prevent misunderstandings.

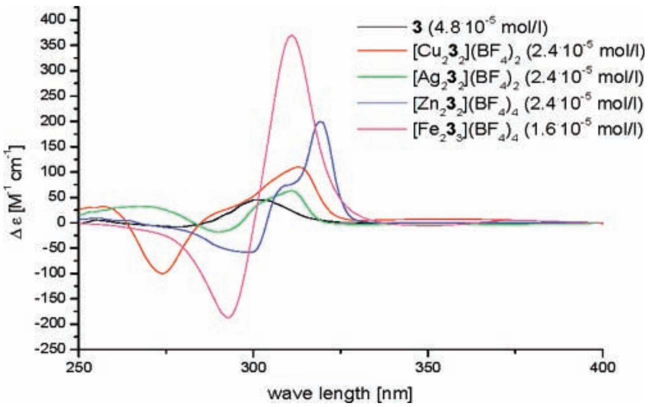

Figure 4. CD spectra of **3**, [Ag_2**3**$_2$](BF_4)$_2$, [Cu_2**3**$_2$](BF_4)$_2$, [Zn_2**3**$_2$](BF_4)$_4$, and [Fe_2**3**$_3$](BF_4)$_4$.

Figure 4 shows the CD spectra of **3** and its metal complexes in the lc region. In general, intensities of the aggregates are much higher than of the free ligand **3**. All complexes show a CD activity in the relevant lc region. The observed absorptions can be assigned to two coupled exciton $\pi-\pi^*$-transitions of two chromophoric bipyridine units which are coordinated to the same metal ion.

Those absorptions are largest for the triple-stranded Fe^{2+}-helicate ($\Delta\epsilon_{310} = +370$ M^{-1} cm^{-1}) and smallest for the double-stranded dinuclear Ag^+-complex ($\Delta\epsilon_{310} = +64$ M^{-1} cm^{-1}). The positive exciton couplet observed for the Fe^{2+}-complex of **3** clearly corresponds to a Λ-configuration of the Fe^{2+}-centers as observed for many Fe^{2+}−bipyridine complexes before.[2b,d,e,g−i,22] The mlct region shows an additional characteristic band for (Λ,Λ)-[Fe_2**3**$_3$] ($\Delta\epsilon_{514} = +3.4$ M^{-1} cm^{-1}, see Supporting Information).

All absorptions for the double-stranded complexes show a positive sign which generally is characteristic for a *P*-helicity as mentioned above. If these transitions are attributed to $\pi-\pi^*$-transitions and exciton coupling is assumed, the metal centers bear a local (Λ,Λ)-configuration (according to *skew line* convention) which could be observed for similar examples.[16,23]

These results are in full agreement with the conclusions that could be drawn from the interpretation of the ^{1}H NMR ROESY spectra and are also consistent with the findings of Hosseini et al., who also attributed a *P* (and a (Λ,Λ)-)-conformation to a triple-stranded helix formed by an isomannide derivative and $HgCl_2$ via crystal structure analysis.[14] Interestingly, the mlct bands of the CD spectrum of the Cu^+-helicate (see Supporting Information) gave initially unexpected results due to a maximum ($\Delta\epsilon_{450} = +1$ M^{-1} cm^{-1}) and a minimum ($\Delta\epsilon_{415} = -2.5$ M^{-1} cm^{-1}) in the characteristic region. Usually, only one maximum (or minimum) can be observed which has the same sign as the absorptions in the lc region. However, this observation is in agreement with a related case of a metal coordination compound derived from an enantiopure ligand that has been reported by Fabbrizzi,[18] where the signs of the absorption maxima of the lc and mlct region of copper(I)-helicates contradicted each other. Nevertheless, the lc regions for all complexes clearly indicate a (Λ,Λ)-configuration of the metal ions that could also be confirmed by X-ray crystal analysis in Fabbrizzis case as we could confirm the assignment by NMR studies.

In conclusion, we have demonstrated that C_2-symmetric D-isomannide derivative **3**, which bears four stereogenic centers, forms enantiomerically pure D_{2d}- or D_{3d}-symmetrical dinuclear double- and triple-stranded complexes of helical shape with metal ions as Ag^+, Cu^+, Zn^{2+}, and Fe^{2+} in a diastereoselective manner. Thus, we could show that the concept of diastereoselective self-assembly of dinuclear helicates could also be applied to nonaromatic dissymmetric core skeletons and rather flexible linkers such as ester groups. The stereochemistry of the aggregates could be independently determined by ^{1}H NMR ROESY and CD spectroscopic techniques. In all cases (Λ,Λ)-configured helicates are formed. We are currently broadening the scope of D-isomannide-based ligands and investigating the ability of these chiral helicates for the molecular recognition of chiral guests.

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Supporting Information Available: Experimental and spectroscopic data for **3** and its metal complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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[22] It should be noted, however, that there is scope for competing exciton-coupling effects in these systems, because a couplet in this region may also be attributed to a mononuclear Fe^{2+}-species (but also Λ-configured) because Δϵ-values for those are generally only slightly smaller than the ones observed for dinuclear helicates.(see refs 2i and 16).

[23] (a) Mamula, O.; von Zelewsky, A.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 290. (b) Constable, E. C.; Kulke, T.; Baum, G.; Fenske, D. *Chem. Commun.* **1997**, 2043.