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# Stereochemically Stable Double-Helicate Dinuclear Complexes of Bis(dipyrromethene)s: A Chiroptical Study

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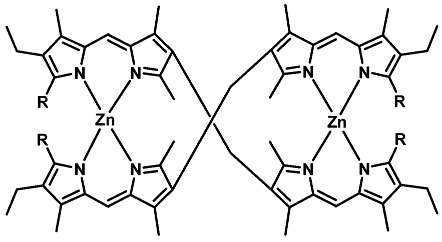
Dipyrromethenes are fully conjugated, planar bipyrrolic units that have attracted recent attention as ligands in supramolecular self-assembly.[1] N-Deprotonated dipyrromethenes act as ligands on cationic metal centers. The resulting complexes are neutral and can often be purified by chromatography in contrast to bipyridyl and catechol complexes that bear the charge of the metal cation involved.[2] Recent reports using dipyrromethenes with appendages containing acetylenyl, thiol, or pyridyl functionality have shown rod-like, polymeric, hexagonal, and other crystalline frameworks to form via self-assembly.[3]

Carefully designed bis(dipyrromethene)s self-assemble into discrete complexes of helical mononuclear, dinuclear, and trinuclear architectures,[1,4] depending on the length of the spacer that joins the two dipyrromethene units. As part of our work with chiral bis(dipyrromethene) complexes, we herein report the first synthesis, isolation, and chiroptical studies of enantiopure bis(dipyrromethene) ligands and their stereochemically stable, double-helicate complexes.

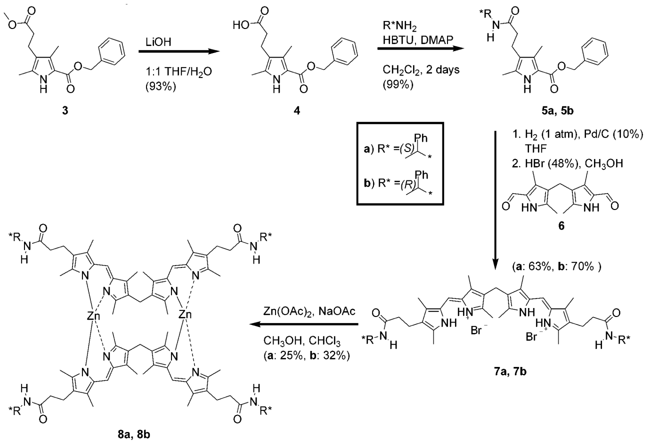
Methylene-, ethylene-, and propylene-linked bis(dipyrromethene)s form, with divalent metal cations, helical complexes with a structural formula $L_2M_2$, illustrated by the complexes **1**[1a] and **2**[5] in Figure 1. Until now, only racemic mixtures of enantiomeric helicates have been formed, as identified by X-ray crystallography[1a] and confirmed by chiral lanthanide shift $^1H$ NMR spectroscopy.[6] Neither of these techniques enabled the stereochemical stability of the helix to be determined. The *M* and *P* helical zinc(II) complexes formed from homochiral bis(dipyrromethene) ligands are related to each other as diastereoisomers, and therefore the complexation process is potentially diastereoselective. However, separation of these diastereomeric helices necessitates stereochemical stability, that is, the absence of helix sense interconversion. Stereogenic centers have previously been used as chiral auxiliaries to induce helix formation in a particular sense (i.e., helical diastereoselectivity).[7] Reichardt et al. have reported on a number of helical polymethine dyes,[8] and Lightner et al. have shown that bilirubin and other dipyrrinone structures adopt either *M* or *P* helical conformations according to the absolute stereochemistry of remote stereogenic centers.[9] Similarly, Mizutani et al. have shown that zinc(II) bilinones may be formed diastereoselectively through the induction of helicity by the point chirality in homochiral precursors.[10] Although homochiral dipyrromethene ligands have been used to form optically active fluorescent boron dipyrromethene (BODIPY) dyes,[11] there are no reports of such homochiral ligands being used in the formation of helical complexes. To the best of our knowledge, homochiral bis(dipyrromethene) ligands and/or the corresponding complexes have not previously been reported.



**1)** R=H
**2)** R=Me

***Figure 1.*** Symmetric zinc(II) bis(dipyrromethene) helicate.

***Scheme 1.*** Synthesis of the Zinc(II) Bis(dipyrromethene) Helicates Bearing Homochiral Amide Substituents



To establish the stereochemical stability of double-helical dinuclear bis(dipyrromethene) complexes and to examine the potential for diastereoselective helicate formation, we have synthesized bis(dipyrromethene) ligands that contain chiral amide substituents at the two termini of the linear tetrapyrrolic molecules (Scheme 1). Benzyl 3,5-dimethyl-4-propionic acid-pyrrole-2-carboxylate (**4**) was prepared by the hydrolysis of benzyl 4-(2′-methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate (**3**)[12] using lithium hydroxide. The incorporation of the chiral substituent into the ligand was achieved by coupling a homochiral amine (1-phenylethylamine) with **4** using *O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU). The chiral amide-substituted pyrrole (**5**) was then coupled to 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane (**6**)[1b] to form the hydrobromide salt of the bis(dipyrromethene) (**7a** and **7b**). The zinc(II) complexes (**8a** and **8b**) were obtained by stirring a solution of the bis(dipyrromethene) ligands with zinc acetate and sodium acetate, followed by extraction and routine workup and full characterization.

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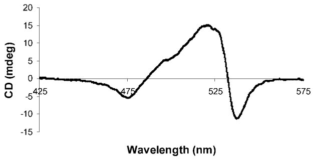

*Figure 2.* CD spectrum for the unresolved mixture of **8a**.

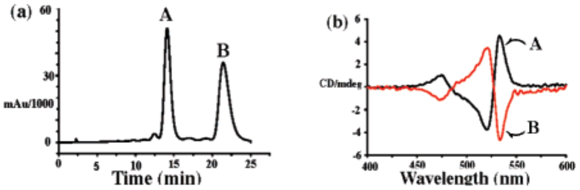

*Figure 3.* (a) UV−vis trace for the chiral HPLC analysis of **8a**. (b) CD spectra for the two isomers (A and B) resolved by chiral HPLC.

Circular dichroism (CD) spectra were recorded for samples **8a** and **8b** (Figure 2). In each case, the presence of a measurable ellipticity in the unresolved samples suggested that the reactions had indeed proceeded with some diastereoselectivity. Encouragingly, the two enantiomeric ligands (**8a** and **8b**) gave rise to zinc complexes that had opposite circular dichroisms, suggesting that the *R* and *S* chiral centers were inducing opposite senses of helicity, as anticipated. However, $^1$H and $^{13}$C NMR spectroscopic studies indicated an approximate 1:1 mixture of diastereomeric helicates in each case. The CD is directly related to the molar absorptivity of the complexes, and this was measured to be in the order of $10^6$ L mol$^{-1}$ dm$^{-1}$. Consequently, a small diastereomeric excess of one helicate over the other would manifest itself as a relatively large CD activity.

Chiral HPLC analysis[13] of **8a** and **8b** showed two major peaks at 534 nm (Figure 3a) that displayed opposite circular dichroisms both using an internal HPLC-CD detector operating at 220 nm and then following isolation of the two major peaks and full CD analysis (Figure 3b). Isomer A shows a positive Cotton effect at 470 nm and a negative Cotton effect at 520 nm (with exciton coupling), leading to its tentative assignment as the *M* helix and isomer B as the *P* helix.[14]

To eliminate the possibility that the CD activity was a result of *induced* exciton coupling[14] between the phenyl ring of the homochiral amide substituent and the dipyrromethene units, an achiral bis(dipyrromethene) ligand was complexed to form the per-alkyl bis(dipyrromethene) zinc(II) complex **2** (Figure 1). Chiral HPLC analysis of **2** again resolved two major peaks with opposing CD couplets. In the absence of other chromophores in **2**, the observed chiroptical properties of the compounds must arise from the stereochemically stable helical, and thus chiral, dipyrromethene units within the complex. Using the molar ellipticities of the two chiral HPLC-resolved zinc(II) bis(dipyrromethene) helices A and B, the total molar ellipticity of the unresolved mixture, and the molar absorptivities of the unresolved mixtures, we calculated diastereomeric excesses for each of the mixtures **8a** and **8b**. The calculated diastereomeric excesses were low: 8% for **8a** and 2% for **8b**. As enantiomeric homochiral ligands **7a** and **7b** were used to prepare the mixtures **8a** and **8b**, respectively, the diastereomeric excesses should be equal for the two samples. The observed discrepancy between these two values is presumably a consequence of the low concentrations used in the CD studies (HPLC fractions) and the fact that unresolved mixtures were used to measure the required molar absorptivities.

These results represent the first diastereoselective dipyrromethene complexation reactions. Additionally, we have shown that double-helicate dinuclear bis(dipyrromethene) complexes are stereochemically stable. This indicates that stereochemical inversion around the zinc center is not taking place. Having shown that diastereoselective bis(dipyrromethene) complexes reactions are feasible and that the *M* and *P* helices of the complexes are isolable, our current work is being directed toward improving the diastereoselectivity of dipyrromethene complexation reactions by expanding the repertoire of homochiral dipyrromethene ligands for double-helicate dinuclear bis(dipyrromethene) complexes.

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**Supporting Information Available:** Procedures for the preparation of **4**−**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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