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Dinuclear Zinc(II) Double-Helicates of Homochirally Substituted Bis(dipyrromethene)s

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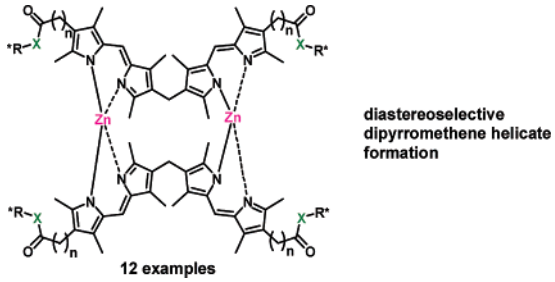

A series of bis(dipyrromethene)s substituted with aromatic amide and aliphatic ester homochiral auxiliaries have been prepared and complexed with zinc(II) ions to form double-helical dinuclear complexes. CD analysis of the crude complexes revealed that the helicates formed in a diastereoselective manner. The helicates have been resolved into their constituent *M* and *P* helices by HPLC, indicating that the helical sense of the complexes is stable to racemization.

Introduction

Self-assembling[1] helicates have consistently been of interest in the field of supramolecular science.[2] As an example, oligopyridines, as well as 2,2′-bipyridyl (bipy), 1,10-phenanthroline (phen), 2,2′:6′,2″-terpyridyl (terpy), and 2,2′:6′,2″:6″:2‴-quaterpyridine derivatives, have proven very popular ligands for the synthesis of helicates.[3] Other ligands that are useful in self-assembly processes include the fully conjugated bipyrrolic class of molecules known as dipyrromethenes. These molecules, an example of which is shown in Figure 1, are, structurally, half of a porphyrin ring. It is for this reason that they were originally prepared as synthetic precursors to porphyrins and other cyclic tetrapyrroles.[4] Dipyrromethenes are generally stored and handled as their hydrobromide salts, although those that bear electron-withdrawing substituents in the 5-position are stable in their free-base form.[5]

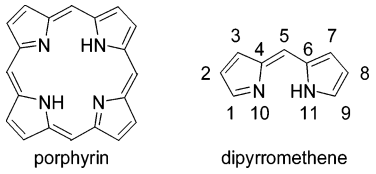

FIGURE 1. Structural comparison of a porphyrin and a dipyrromethene.

It was soon discovered that deprotonated monoanionic dipyrromethenes form complexes with a wide variety of metal ions.[6] These metal complexes were originally of great interest as efficient templates in the synthesis of cyclic tetrapyrroles[4] and have been isolated as byproducts of the Rothemund synthesis of arylporphyrins.[7,8] Thereafter, the significance of dipyrromethenes in the study of coordination chemistry became apparent. The steric

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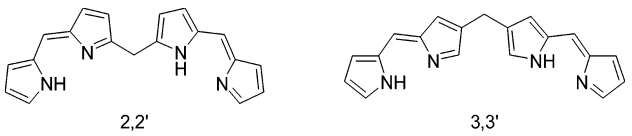

FIGURE 2. Structures of 2,2′- and 3,3′-bis(dipyrromethene)s.

interactions between 1,9-substituents of two dipyrromethenes coordinated to the same metal, even those as small as hydrogens, of the dipyrromethenes[9] were found to distort the geometry of coordination about the metal ions. As such, even those metal(II) ions for which square planarity is usually the preferred geometry adopt pseudotetrahedral coordination geometry with dipyrromethene ligands.[10,11] An advantage to the use of dipyrromethenes is that their metal complexes often do not require counterions since the ligands are charged, therefore resulting in less disorder in their crystal structures and the ability to be purified by standard chromatographic methods. Although dipyrromethenes are known to readily form complexes with many different metal ions under mild conditions, contemporarily the most common complexes are those of boron difluoride. Dipyrromethene complexes of this type are known as bodipy dyes. Fluorescent bodipy dyes have found extensive use in optical[12] and biological applications due to their high absorption and emission, stability, pH independence, highly tunable optical properties, and high functionalizability and because many are commercially available.[13] Recent research has shown that the fluorescence quantum efficiencies of transition-metal complexes of dipyrromethenes, which under similar conditions are significantly lower than those of bodipy dyes, can be made higher by the judicious choice of subsituents.[14]

Improved procedures for the synthesis of dipyrromethenes bearing aryl substituents in the 5-position[5,15] have created a renewal of interest in dipyrromethene metal complex chemistry.[16−18] Bis(dipyrromethene)s provide access to a variety of metal complex architectures, including helices and double helices. As shown in Figure 2, the two dipyrromethene units of bis(dipyrromethene)s may be connected through the 2,2′- or the 3,3′-positions. Linkage through the 2,2′-positions by a methylene group is historically the most common connection due to the use of these structures in the syntheses of corroles.[19] More recently, linkage through the 3,3′-positions has become more common, as such skeletons are facile to prepare and give interesting structures upon complexation.[20−23] A recent publication reports the synthesis of non-symmetrical 2,3′-bis(dipyrromethene)s and their zinc(II) complexation products.[24] The first example of a 2,2′-bis(dipyrromethene) forming a double helicate with metal ions was reported for cobalt(II) in 1966,[25] although X-ray crystal structure data was not obtained until 1980 for a zinc(II) complex of a similar ligand.[26] The metal-to-ligand ratio of the complexation product of 2,2′-bis(dipyrromethene)s is highly dependent upon the structure of the ligand and the solvent that is employed for the complexation reaction. For reaction with the same ligand, cobalt(II) has been shown to form 1:1 monomeric helical complexes in ethanol and 2:2 dimeric helicates when the reaction is conducted in methanol.[25] Similar products were obtained for the products of copper(II) complexation of a 2,2′-bis(dipyrromethene) in which the two dipyrromethene units were directly attached at the 2,2′-position without a spacer.[27] In general, those metal ions for which a square planar coordination geometry is preferred, such as nickel(II), copper(II), and palladium(II), yield monomeric helical complexes with dipyrromethenes,[28−30] while metal ions for which tetrahedral geometry is the preferred mode of coordination, such as cobalt(II) and zinc(II), yield dinuclear dimeric double helicates.[25,26,29−31]

Interest in bis(dipyrromethene) helicates for use in supramolecular chemistry was shown in 1998 with the report of a series of cobalt(II) and zinc(II) complexes in which the length of the 2,2′-spacer was varied.[32] This was followed by reports of 3,3′-bis(dipyrromethene)s which demonstrated that the metal-to-ligand ratio in the complexation products of these ligands was highly dependent upon the length of the 3,3′-spacer.[21,23] Monomeric cobalt(II) and zinc(II) complexes were formed when the spacer was six or more carbons in length, dimeric when the spacer was one to three carbons in length, and trimeric,[23] with a metal-to-ligand ratio of 3:3, when there was no spacer and the two dipyrromethene units were directly bonded to each other. Several other reports regarding the synthesis and structure of dinuclear zinc(II) complexes,[33−35] nickel(II) complexes,[36] and cobalt(II) complexes[35] of 3,3′-

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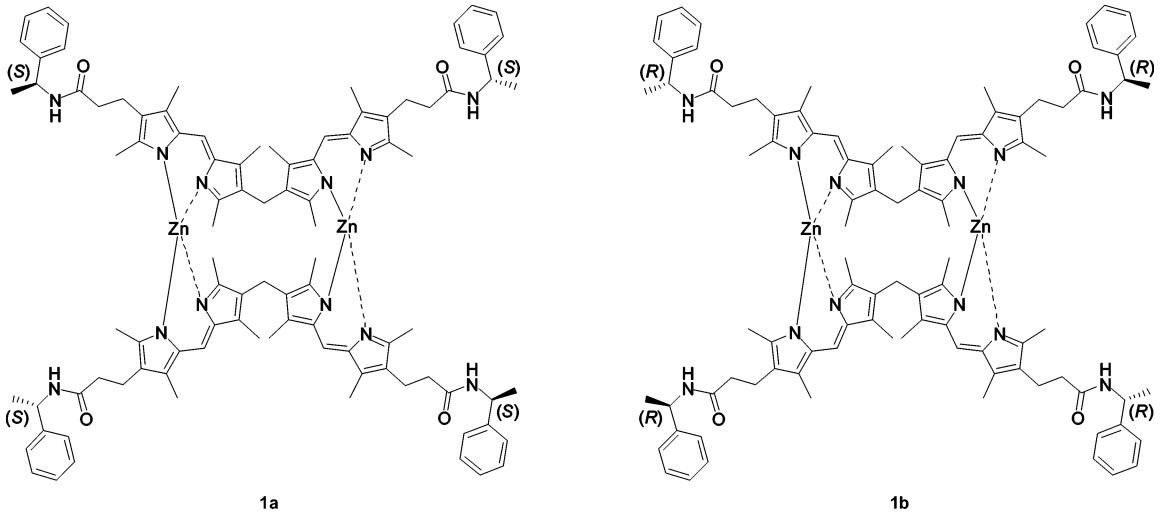

FIGURE 3. Homochirally substituted bis(dipyrromethene) zinc(II) helicates.

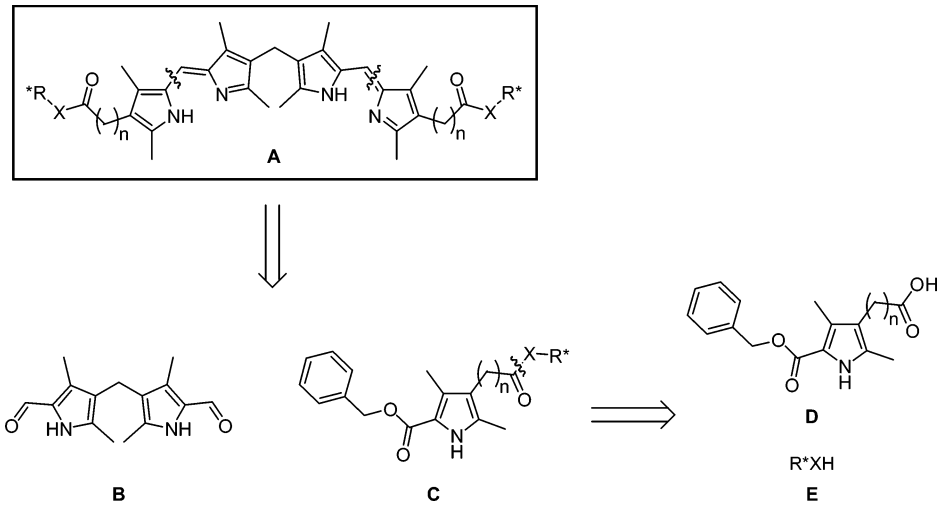

FIGURE 4. Disconnection strategy for the synthesis of homochirally substituted bis(dipyrromethene)s.

bis(dipyrromethene)s have been published. Helical 3,3′-bis(dipyrromethene) complexes of zinc(II) have since been studied by ^{1}H NMR spectroscopy and shown to form as a racemic mixture of *M* and *P* helices.[22] A resolution of the *M* and *P* helices of a 1:1 nickel(II) 2,2′-bis(dipyrromethene) complex was achieved in 2001 by MPLC using a chiral column.[37] Circular dichroism (CD) analysis showed that the helical enantiomers did not racemize, even with prolonged heating.[37]

BINOL- and tartrate-linked bis(dipyrromethene) ligands give excellent diastereoselectivity for the formation of mononuclear helicates.[41] In a previously published report, it was demonstrated that dinuclear, double-stranded helical zinc(II) complexes of homochirally substituted 3,3′-bis(dipyrromethene)s **1a** and **1b** (Figure 3) form diastereoselectively.[38] The helicates were shown to be sufficiently stereochemically stable to allow isolation of the *M* and *P* helices by chiral HPLC. In this paper, the diastereoselective complexation of a range of bis(dipyrromethene) ligands homochirally appended with amides and esters is demonstrated, and the influence of the chiral auxiliary is discussed.

Results and Discussion

Figure 4 shows a disconnection strategy for the synthesis of bis(dipyrromethene)s substituted with terminal homochiral amides or esters. This strategy allows for a range of homochiral moieties to be incorporated, as well as for varying the length of the spacer between the dipyrromethene unit and the auxiliary. It was anticipated that access to such a variety of skeletons would enable the scope of the effect of the auxiliary type and position upon the diastereoselectivity of complexation to be fully studied.

Although the molecule **A** in Figure 4 is symmetric, each dipyrromethene unit therein is asymmetric. The synthesis of asymmetric dipyrromethenes is most effectively accomplished by the condensation reaction of (appropri-

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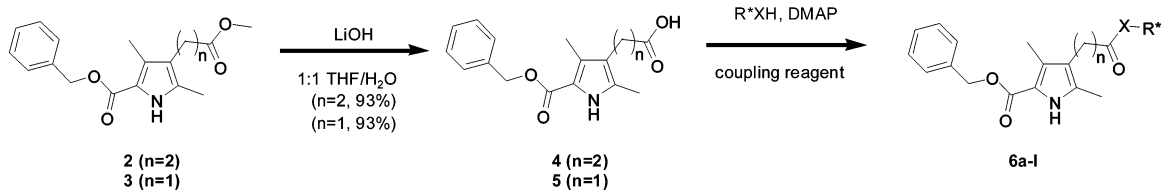
SCHEME 1. Synthesis of the Homochiral Substituted Pyrrole Amides and Esters

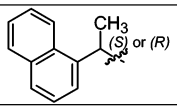
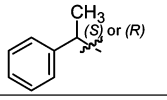
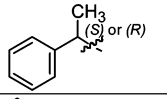
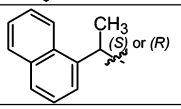
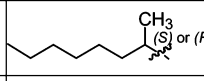
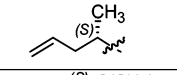
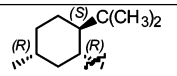


ately substituted) 2-formylpyrroles (**B**) with pyrroles that are unsubstituted in the α-position. These α-unsubstituted pyrroles, also known as α-free, can be prepared in situ by decarboxylation of the corresponding α-carboxylic acid derivative, which in turn is easily prepared by hydrogenolysis of the benzyl ester derivative (**C**), synthesized on large scales via Knorr-type reactions. The bis(dipyrromethene) ligands can be formed by coupling 2 equiv of the α-free derivative of homochirally substituted pyrroles with 1 equiv of a diformyldipyrromethane.[39] The homochiral substituents can be incorporated into the pyrrole by the use of amide and ester derivatives of a pyrrole carboxylic acid (**D**) and homochiral amines and esters (**E**).

The homochiral substituents were incorporated into the bis(dipyrromethene)s early in the synthesis by attaching the chiral auxiliaries to 2-benzyl carboxylate pyrroles that would later be transformed into α-free pyrroles for incorporation into dipyrromethenes. Chemoselective hydrolysis of the methyl ester functional group in benzyl 4-(2-methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate[40] (**2**) using aqueous lithium hydroxide provided benzyl 3,5-dimethyl-4-(propanoic acid)pyrrole-2-carboxylate (**4**)[38] (Scheme 1). Similarly, benzyl 4-(ethanoic acid)-3,5-dimethylpyrrole-2-carboxylate (**5**) was prepared by hydrolysis of benzyl 4-(methoxycarbonylmethyl)-3,5-dimethylpyrrole-2-carboxylate (**3**).[41]

The carboxylic acid functionality of pyrroles **4** and **5** provided excellent handles for the incorporation of homochiral auxiliaries through the synthesis of chiral amides and esters. Amides were prepared by the coupling of optically pure chiral amines with **4** or **5** with *O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU) or a combination of *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC·HCl) and 1-hydroxybenzotriazol hydrate (HOBT). Likewise, esters were prepared by the coupling of optically pure chiral alcohols. For coupling reactions involving **4**, dichloromethane was used as a solvent and HBTU as a coupling reagent, providing high yields of the desired products. The pyrrole carboxylic acid **5** is sparingly soluble in dichloromethane, so tetrahydrofuran was used as the solvent for coupling reactions of this compound. For the preparation of amides from **5**, HBTU was utilized as the coupling reagent while for the preparation of esters from **5** EDC·HCl/HOBT provided higher product yields. In preliminary work, *N*,*N*′-dicyclohexylcarbodiimide (DCC) was used as the coupling reagent in the synthesis of amides **6e**−**h**. However, unsatisfactory results were obtained, and the *N*-acylurea side product **7** (Figure 5) dominated.[42] The products **6a**−**l** were obtained following workup suited to removal of the coupling reagent and subsequent column chromatography. The yields of products **6a**−**l** are listed in Table 1.

TABLE 1. Yields for the Synthesis of Pyrrole Derivatives 6a−l

6[a]	n	X	R*	Yield (%)[b]
a, b	2	NH		72
c, d	2	NBn		95
e, f	1	NH		89
g, h	1	NH		68
i, j	1	O		39
k	1	O		44
l	1	O		54

[a] **6a**,**c**,**e**,**g**,**i** have (*S*) absolute stereochemistry. [b] Averaged yields for the two enantiomers.

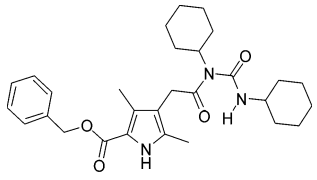


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FIGURE 5. *N*-Acylurea side product obtained from the use of DCC.

The bis(dipyrromethene)s ligands were prepared in two synthetic steps from the homochiral auxiliary-bearing pyrroles **6a**−**l**. Hydrogenolysis of the benzyl group from compounds **6a**−**l** at atmospheric pressure using palladium on carbon as a catalyst provided the α-carboxylic acid required for preparation of the dipyrromethene (Scheme 2). Monitoring of the reactions by TLC was necessary so as to avoid hydrogenolysis of the benzyl substituents of the aliphatic amides or esters, rather than just the pyrrole α-benzyl ester as required. In the case of **6k**, hydrogenation of the pentene substituent occurred in addition to the hydrogenolysis of the pyrrole α-benzyl ester. The bis(dipyrromethene)s were synthesized by coupling the homochiral amide or ester pyrrole-2-car-

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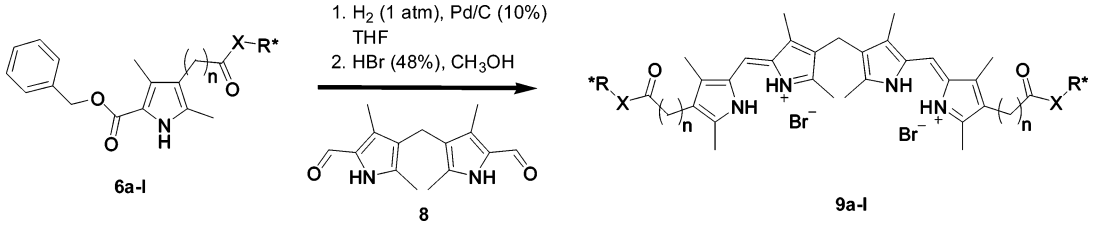
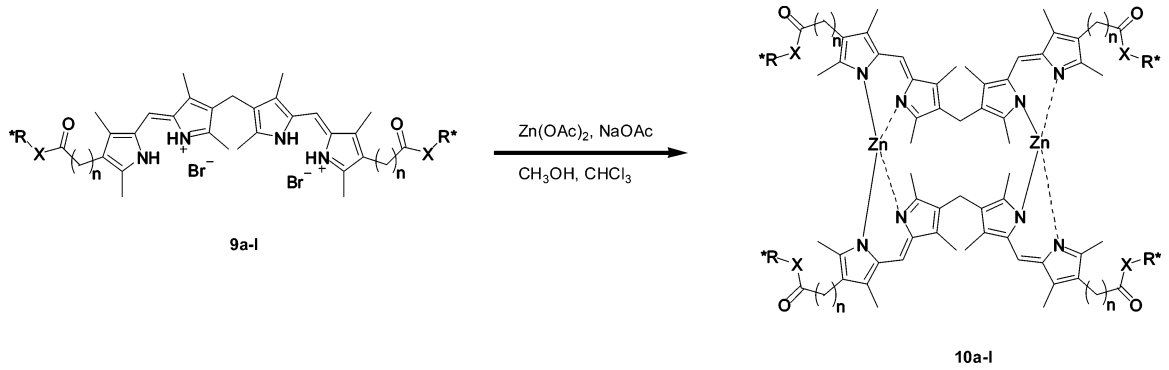
SCHEME 2. Synthesis of the Bis(dipyrromethene) Hydrobromide Salts Bearing Homochiral Substituents



SCHEME 3. Synthesis of the Zinc(II) Bis(dipyrromethene) Helicates Bearing Homochiral Substituents



boxylic acid with 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane[33] (**8**) in the presence of hydrobromic acid yielding the hydrobromide salts of the homochirally substituted bis(dipyrromethene)s (**9a**−**l**). Salts **9a**−**l** were isolated by precipitation either during the reaction or from minimal dichloromethane by the addition of diethyl ether or hexanes, followed by filtration. The poor solubility of the amide-containing ligands was overcome by the incorporation of a third substituent on the amide nitrogen center, as **9c** and **9d** were much more soluble than **9a** and **9b** in the solvents tested. The propanoic derivatives **9a**,**b** were generally more soluble than their ethanoic counterparts **9e**−**h**. The ester-containing ligands **9i**−**l** were all quite soluble in conventional solvents. However, it should be noted that complete dissolution of the bis(dipyrromethene) hydrobromide salt is not necessary to effect complexation of the ligand to zinc(II) ions.

The preparation of zinc(II) complexes **10a**−**l** was accomplished by the addition of a solution of excess zinc acetate and sodium acetate in methanol to a solution of the ligand in chloroform (Scheme 3) using a procedure modified from literature.[23] Those ligands that were only sparingly soluble in chloroform and were suspensions rather than solutions in chloroform at the beginning of the reaction were seen to dissolve as complexation proceeded. The formation of zinc(II) complexes of dipyrromethenes is easily monitored by analysis of the visible absorbance spectrum of the reaction mixture. Upon complexation the wavelength of maximum absorbance (λ_{max}) generally undergoes a bathochromic shift of approximately 20 nm. This shift of λ_{max} is usually observable by visual inspection, with the reaction mixture changing color from orange to fuscia over the course of the complexation reaction. The diastereomeric helicate products are obtained in good yield as a mixture through routine workup involving extraction and precipitation from minimal dichloromethane by the addition of diethyl ether. The zinc complexes are generally stable to silica flash chromatography and this technique can be used for purification, if necessary, although separation of *M* and *P* helical diastereoisomers was not achieved using this procedure. However, some decomposition was observed for compounds **1a**,**b**, **10a**,**b**, and **10e**−**h** during attempted separations of diastereoisomers using silica chromatography. As **1a**,**b**, **10a**,**b**, and **10e**−**h** are secondary amides this observed decomposition suggests that the decomposition is facilitated by primary amides. Deuterium exchange was observed by ^{1}H NMR spectroscopy for these amide hydrogens upon the addition of deuterated water on the time scale of less than 24 h and also in deuterated chloroform in less than 4 days.

Mass spectrometry confirmed the formation of dinuclear complexes with the stoichiometry M_2L_2, rather than monomers or oligomers. The presence of two sources of chirality, one fixed (the auxiliary) and one variable (the helix), gives rise to two possible diastereoisomers. Circular dichroism (CD) spectra were recorded for each diastereomeric mixture of helicates **10a**−**l**. Every sample exhibits a measurable ellipticity, which indicates that there exists an excess of one diastereoisomer over the other in the mixtures. As anticipated, the ellipticities are opposite for helicates resulting from enantiomeric ligands. Since the absolute stereochemistry of the auxiliary is fixed, the diastereomeric excess must arise from the preferential generation of one helical sense over the other in the complexation process. The activity observed in the CD experiments arises from $\pi \rightarrow \pi^*$ transitions in the dipyrromethene unit of the ligand.[43] CD activity from induced exciton coupling of a dipyrromethene unit with an aromatic ring of the homochiral amide substituents on the zinc(II) bis(dipyrromethene) helicate has been ruled out by previous studies.[38] Chiral HPLC[44] analysis has been performed upon several of these samples (**10a**−**d**). Similar to the analysis of compounds **1a** and **1b**, these samples displayed two major peaks monitored at 534 nm.

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(44) Kubota, T.; Yamamoto, C.; Okamoto, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3703−3712.

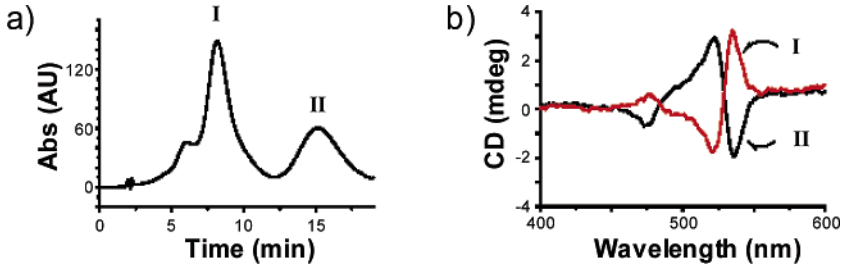

FIGURE 6. (a) Chiral HPLC resolution of **10a**; (b) CD spectra of the resolved *M* (I) and *P* (II) helices of **10a**.

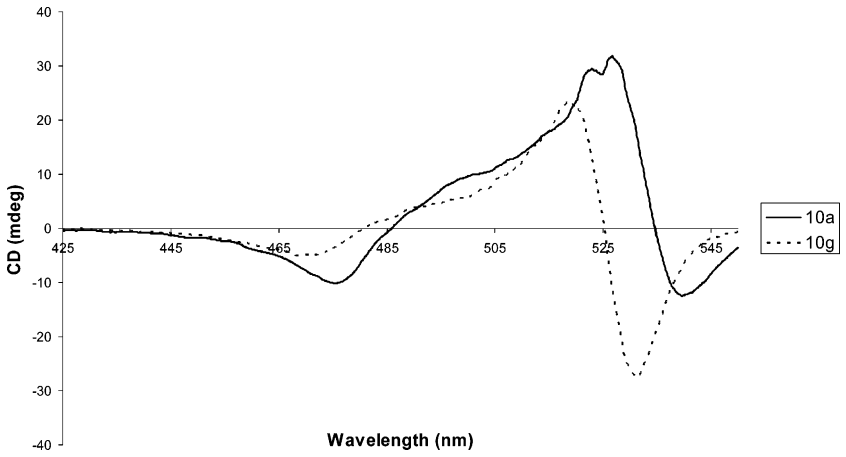

FIGURE 7. CD spectra of equimolar solutions of the diastereomeric mixtures for **10a** and **10g**.

CD spectra were recorded for the isolated contents of these two major peaks from each HPLC resolution. These resolved compounds displayed opposite and approximately equal CD spectra, supporting their identification as the resolved *M* and *P* helicates. The chiral HPLC elution profile and the CD spectra of the resolved helices of **10a** are shown in Figure 6. Isomers that show a positive Cotton effect at the lower wavelength (~470 nm) and a negative Cotton effect with exciton coupling at the higher wavelength (~520 nm) are assigned as the *M* helix and those with an opposite CD spectrum as the *P* helix.[45] Thus, isomer I in Figure 6 was identified as the *M* helix, and II the *P* helix, of **10a**. Our work with BINOL-linked bis(dipyrromethene) complexes that form monomeric helicates has confirmed this assignment via X-ray crystallography.[41]

The generation and isolation of single helicates of dipyrromethene complexes is contingent upon the stereochemical stability of the helices. Disassociation of the metal complexes and the resulting scrambling of ligands is a mechanism by which the chirality of the helical sense might be racemized if the bis(dipyrromethene)s are labile on the zinc(II) centers. To investigate the stability of the helicity established during the formation of these complexes, an equimolar solution of two different zinc helicates (**1b** and **10d**) in toluene was heated to reflux for 24 h, and alternately, an equimolar solution of the helicates in dichloromethane was stirred at room temperature for 24 h. Analysis of the reaction mixtures using MALDI-MS revealed no apparent ligand exchange between the two compounds, as observed by the lack of any compound of intermediate mass, as would be present if ligand scrambling had occurred. The mass spectrum of the reaction mixture showed only peaks associated with the two starting zinc helicates (Supporting Information). This study suggests that the bis(dipyrromethene) ligands are non-labile on zinc(II) metal centers under neutral conditions. Racemization of the chiral sense of the helices might also occur by a mechanism of inversion of the stereochemistry about the metal ion center. Further investigations involving time-dependent CD studies will be conducted to further investigate the non-inversion of stereochemistry at the chiral metal center.

As can be seen by comparison of the CD spectra of the diastereomeric mixtures of **10a** and **10g**, where only the length of the pyrrole-auxiliary spacer changes (Figure 7), the magnitudes of the circular dichroisms are similar. This demonstrates that, somewhat surprisingly, the length of the spacer between the dipyrromethene unit and the chiral auxiliary does not significantly affect the diastereoselectivity of the complexation reaction. By comparing the molar ellipticity values of their diastereomeric mixtures, the zinc(II) complexes of the ester bis(dipyrromethene) derivatives **(10i−l)** likely formed with similar diastereoselectivity to the amide derivatives. Again, this is somewhat unexpected as free rotation about the O-carbonyl bond, and thus greater number of degrees of freedom for the esters by which to minimize steric crowding, was predicted to induce lower stereoselectivity than the amides which show a slow rotation as evidenced by the diastereotopic relationship between the methylene protons of the ethanoate and propanoate linkers in ^{1}H NMR spectra of these complexes.

In considering both the spacer length and the functionality of the auxiliary, it is apparent from NMR spec-

(45) Boiadjiev, S. E.; Lightner, D. A. *Tetrahedron: Asymmetry* **1999**, *10*, 2535−2550.

troscopy that low diastereoselectivities are obtained with the skeletons discussed herein and so the differences in stereochemical induction for the various substituents are small. The modest diastereoselectivity observed in the synthesis of zinc helicates **10a**−**d** show that the terminal homochiral auxiliaries are too removed from the metal center to induce efficient stereoselectivity during the formation of the helicate. Nevertheless, the CD activity observed for these reaction mixtures was the first unequivocal evidence that stereochemical induction was feasible. Isolation of the *M* and *P* helices of compounds **10a**−**d** show that the helical chirality of zinc(II) complexes of bis(dipyrromethene)s is stable. Having established that induction is feasible, current work involves the development of increased stereoselectivity of bis(dipyrromethene) helicate formation by the incorporation of homochiral auxiliaries, such as optically pure binol and dimethyltartrate as template spacers joining two dipyrromethene units.[41]

Conclusions

Similar to the previously reported compounds **1a** and **1b**, the formation of zinc(II) helical complexes of a series of homochirally substituted bis(dipyrromethene)s (**10a**−**l**) is diastereoselective. These Zn(II) dipyrromethene helicates form diastereoselectivly due to the inclusion of homochiral auxiliaries in the ligand. The auxiliaries are attached through either ester or amide bonds, and the retrosynthetic strategy allows for the incorporation of a wide range of auxiliaries and homochiral spacers/linkers through well-documented coupling and functional group manipulation. With success in diastereoselectively forming dipyrromethene helicates, the synthesis of dipyrromethenes bearing homochirality in close proximity to the chiral metal centers is ongoing. The results presented herein strongly suggest that the Zn(II) center is stereochemically stable in dipyrromethene helicates, and this unusual behavior[46−48] is being further investigated for dipyrromethenes with other connectivities. Currently, conditions for HPLC separation of the *M* and *P* helices for each of compounds **10e**−**l** are being elucidated, after which an extended study of the stereochemical stability of bis(dipyrromethene) double-helicates with a variety of metal ions will be conducted.

Experimental Section

Benzyl 3,5-Dimethyl-4-[(*S* or *R*)-2-(1-naphthylethylcarbamoyl)ethyl]-1*H*-pyrrole-2-carboxylate (6a or 6b). Under dry conditions and using nitrogen gas as an inert atmosphere, benzyl 3,5-dimethyl-4-(propanoic acid)pyrrole-2-carboxylate (**4**) (2.0 g, 6.6 mmol) was dissolved in dry dichloromethane (50 mL) in a dry two-neck 250 mL round-bottom flask with stirring. To this was added 4-(*N*,*N*′-dimethylamino)-pyridine (DMAP) (0.81 g, 6.6 mmol). The resulting solution was cooled to 0 °C by suspension in an ice bath. At this lowered temperature, (*S*)-(−)-1-(1-naphthyl)-α-ethylamine (to prepare **6a**) or (*R*)-(+)-1-(1-naphthyl)-α-ethylamine (to prepare **6b**) (1.1 mL, 1.2 g, 6.7 mol) was added slowly dropwise by syringe. The resulting solution was stirred, and after 30 s a light pink solid began to form. At this time, additional dry dichloromethane (20 mL) was added, followed by *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU) (2.5 g, 6.6 mmol). The mixture stirred, eventually warming to room temperature, for 2 days. The reaction mixture was then filtered, concentrated, washed twice with 5% (w/vol) aqueous hydrochloric acid solution, washed with brine, and concentrated by rotary evaporation. Purification by chromatography using silica and 30% (v/v) ethyl acetate in hexanes as the eluent gave the product as a white solid (2.2 g, 72%) (sol: chloroform, methanol, dimethyl sulfoxide; sp. sol: dichloromethane, acetone, ethyl acetate, ethanol; insol: water, diethyl ether, hexanes): R_f 0.28 (silica, 40% ethyl acetate 60% hexanes); mp 189−190 °C; ^{1}H NMR: δ (250 MHz, $CDCl_3$) 1.58 (3H, d, J = 7.0 Hz), 2.06 (3H, s), 2.25 (3H, s), 2.27 (2H, t, J = 7.3 Hz), 2.72 (2H, t, J = 7.0 Hz), 5.29 (2H, s), 5.50 (1H, d, J = 7.6 Hz), 5.82−5.93 (1H, m), 7.29−7.51 (9H, m), 7.75 (1H, d, J = 7.9 Hz), 7.83 (1H, d, J = 8.1 Hz), 8.03 (1H, d, J = 7.3 Hz), 7.97 (1H, br s); ^{13}C{^{1}H} NMR δ (126 MHz, $CDCl_3$) 10.9, 11.6, 20.4, 21.1, 37.7, 44.9, 65.7, 116.9, 120.6, 122.7, 123.6, 125.4, 126.0, 126.7, 128.3, 128.5, 128.8, 129.0, 130.5, 131.2, 134.1, 136.8, 138.6, 162.0, 171.4; EI-HRMS calcd 454.2256 for $C_{29}H_{30}N_2O_3$, found 454.2266 (**6a**) and 454.2243 (**6b**).

Benzyl 3,5-Dimethyl-4-[2-(1,3-dicyclohexylureido)-2-oxoethyl]-1*H*-pyrrole-2-carboxylate (7): (sol: chloroform, methanol; sp. sol: dichloromethane, acetone; insol: water, diethyl ether, hexanes); R_f 0.79 (silica, 60% ethyl acetate 40% hexanes); mp 156−159 °C; ^{1}H NMR δ (500 MHz, $CDCl_3$) 1.12−1.37 (12H, m) 1.58−1.81 (4H, m), 1.92−1.95 (4H, m), 2.16 (3H, s, Ar-CH_3), 2.25 (3H, s), 3.53 (2H, s), 3.65−3.67 (1H, m), 3.93−3.97 (1H, m), 5.28 (2H, s), 7.18 (1H, br s), 7.31−7.40 (5H, m), 9.06 (1H, br s); ^{13}C{^{1}H} NMR δ (126 MHz, $CDCl_3$) 11.1, 11.8, 24.9, 25.5, 25.6, 26.5, 31.1, 32.1, 32.9, 49.9, 56.7, 65.6, 115.1, 117.0, 128.1, 128.2, 128.7, 131.7, 136.7, 154.2, 161.6, 172.5; EI+ calcd 493.3 for $C_{29}H_{39}N_3O_4$, 516.3 $(M + Na)^+$.

Bis{3-[(*S* or *R*)-2-(1-naphthylethylcarbamoyl)ethyl]-2,2′,4,4′-tetramethyldipyrromethene} Hydrobromide Salt (9a or 9b). To a mixture of benzyl 3,5-dimethyl-4-[(*S*)-2-(1-naphthylethylcarbamoyl)ethyl]-1*H*-pyrrole-2-carboxylate (**6a**) (to prepare **9a**) or benzyl 3,5-dimethyl-4-[(*R*)-2-(1-naphthylethylcarbamoyl)ethyl]-1*H*-pyrrole-2-carboxylate (**6b**) (to prepare **9b**) (0.56 g, 1.24 mmol) and a catalytic amount of 10 mol % palladium on activated carbon (0.011 g) in a 100 mL round-bottom flask was added tetrahydrofuran (25 mL). Hydrogenolysis of the benzyl ester was achieved using an enclosed hydrogenation apparatus. After the mixture was purged with hydrogen gas, the mixture was stirred for 16 h. The mixture was then filtered through a plug of Celite to remove the catalyst. The filtrate was collected in a 100 mL round-bottom flask and diluted with methanol (5 mL). At this time, 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane (**8**) (0.16 g, 0.62 mmol) was added, followed by the addition of 48% (w/v) hydrobromic acid (0.40 mL). The reaction immediately turned from a light brown suspension to a very dark red homogeneous solution. The reaction was stirred for 20 min, dried with anhydrous sodium sulfate, filtered, and concentrated to a dark red liquid by rotary evaporation. To this dark red liquid was added just enough chloroform to form a homogeneous solution, and then diethyl ether was added to give a precipitate, which was collected by filtration and rinsed with more diethyl ether to give the product as a dark orange powder (0.45 g, 71%) (sol: methanol, dimethyl sulfoxide; sp. sol: chloroform, dichloromethane, ethanol, acetone, ethyl acetate; insol: water, diethyl ether, hexanes): mp >250 °C dec; ^{1}H NMR δ (500 MHz, DMSO-d_6) 1.42 (6H, d, J = 7.2 Hz), 2.23 (6H, s), 2.30 (6H, s), 2.34−2.36 (4H, t, J = 6.9 Hz), 2.43 (6H, s), 2.46 (6H, s), 2.62−2.72 (4H, m), 3.73 (2H, s), 5.62−5.68 (2H, m), 7.32−7.38 (4H, m), 7.35 (2H, d, J = 7.7 Hz), 7.46 (2H, t, J = 7.5 Hz), 7.52 (2H, t, J = 7.2 Hz), 7.75 (2H, d, J = 8.2 Hz), 7.89 (2H, d, J = 7.7 Hz), 8.05 (2H, d, J = 8.2 Hz), 8.41 (2H, d, J = 7.7 Hz), 12.16 (2H, br s), 12.20 (2H, br s); ^{13}C{^{1}H} NMR δ (126 MHz,

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DMSO-d_6) 10.4, 10.4, 13.4, 13.4, 19.3, 20.1, 22.1, 35.3, 44.4, 121.4, 122.6, 122.7, 123.6, 125.8, 126.6, 127.6, 128.6, 129.1, 130.7, 140.8, 142.9, 144.5, 152.4, 152.7, 155.2, 155.3, 170.6; ESI+ found 863.5 $(M - 2HBr)^+$ (**9a**) and 863.5 $(M - 2HBr)^+$ (**9b**); $\lambda_{max}(CH_2Cl_2)$ 505 nm, 462 nm; $\epsilon_{505}(CH_2Cl_2)$ 2.37×10^7 L mol^{-1} dm^{-1}; $[\Theta]_{502}(CH_2Cl_2) = -30473$ deg cm^2 dmol^{-1}.

Zinc(II) Di(bis{3-[(*S*)-2-(1-naphthylethylcarbamoyl)-ethyl]-2,2′,4,4′-tetramethyldipyrromethene}) (10a). In a 50 mL round-bottom flask, bis{3-[(*S*)-2-(1-naphthylethylcarbamoyl)ethyl]-2,2′,4,4′-tetramethyldipyrromethene} hydrobromide salt (**9a**) (0.11 g, 0.11 mmol) was combined with chloroform (5 mL). In a 10 mL Erlenmeyer flask were combined zinc acetate dihydrate (0.12 g, 0.54 mmol), sodium acetate trihydrate (0.074 g, 0.54 mmol), and methanol (5 mL). The acetate solution in methanol was added to the bis(dipyrromethene) solution in chloroform via a pipet. The mixture was stirred for 20 min. The resulting dark purple solution was washed with distilled water, dried with sodium sulfate, filtered, and placed on a rotary evaporator to concentrate. A minimal amount of dichloromethane was added, followed by hexanes to precipitate the product as a fuscia-colored powder (0.076 g, 75%) (sol: chloroform, dichloromethane; sp. sol: methanol, ethanol, acetone, ethyl acetate; insol: water, diethyl ether, hexanes): mp >250 °C dec; ^{1}H NMR δ (250 MHz, $CDCl_3$) 1.38 (12H, d, J = 4.5 Hz), 1.48−1.55 (12H, m), 1.89 (12H, d, J = 7.0 Hz), 2.10 (12H, d, J = 2.0 Hz), 2.13−2.28 (20H, m), 2.60−2.69 (8H, m), 3.41 (4H, br s), 5.63−5.72 (4H, m), 5.77−5.90 (4H, m), 6.86 (4H, d, J = 3.3 Hz), 7.31−7.54 (20H, m), 7.71−7.85 (4H, m), 7.97−8.08 (4H, m); ^{13}C{^{1}H} NMR δ (126 MHz, $CDCl_3$) 21.0, 21.3, 22.9, 37.34, 44.7, 44.8, 121.0, 122.6, 122.6, 123.6, 125.4, 125.5, 125.6, 126.0, 126.7, 128.4, 128.9, 131.3, 134.1, 135.4, 137.3, 138.6, 155.5, 171.6; APCI+ found 1857.6 $(M + 6H)^+$ λ_{max} (95% CH_3OH, 5% CH_2Cl_2) 525 nm, 478 nm; ϵ_{525} (95% CH_3OH, 5% CH_2Cl_2) 2.30×10^6 L mol^{-1} dm^{-1}; $[\Theta]_{475}$-(95% CH_3OH, 5% CH_2Cl_2) = −153238 deg cm^2 dmol^{-1}, $[\Theta]_{527}$ = +386884 deg cm^2 dmol^{-1}, $[\Theta]_{540}$ = −134389 deg cm^2 dmol^{-1}.

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Supporting Information Available: Synthetic procedures and characterization data for **6c**−**l**, **9c**−**l**, and **10b**−**l**, conditions for HPLC resolutions of **10a**−**d**, and the MALDI-mass spectra for the **1b** and **10d** ligand scrambling experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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