

Nuclear Magnetic Resonance Studies of Helical Dipyrromethene–Zinc Complexes

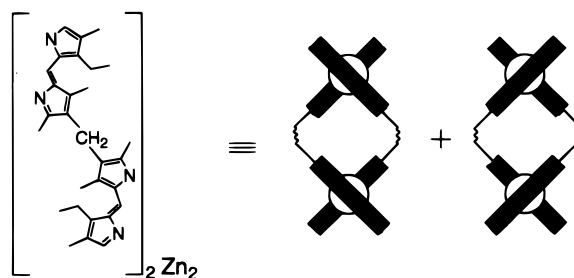
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ABSTRACT



Analysis of helical chirality within dinuclear dipyrromethene–Zn(II) complexes has been achieved with the use of ¹H NMR spectroscopy. The use of AgFOD and chiral lanthanide shift reagents gives fully resolved resonances attributable to two diastereomeric helical complexes.

Given the range of synthetic helical structures now known, recent efforts have been directed toward the analysis of optical and chiral properties of helical structures. For example, Mizutani has studied the effects of helical chirality control in zinc–bilinone monomers¹ and dimers² using CD and ¹H NMR. Similarly, Lightner³ has used CD to investigate the influence of intramolecular hydrogen bonding upon helically chiral bilirubin analogues. The stability of dextro- and levorotatory iron(II) bis(terpyridyl) helical complexes has been demonstrated using CD by Sauvage and Keene,⁴ while Constable⁵ has investigated diastereoselective formation of enantiomeric (M) and (P) double helicates by dicopper(I) complexation of chiral 2,2':6'2''-terpyridines by

¹H NMR and specific optical rotation measurements. Additionally, Wang⁶ has studied the stability toward racemization of helically twisted σ -terphenyl helicene analogues using optical rotation and CD. With the exception of studies involving diastereomeric helices containing chiral auxiliaries, the purity of helical compounds has not been studied by ¹H NMR since the two helical enantiomers would, of course, have identical spectra.

Although CD and specific optical rotation methods can reveal extremely useful information concerning enantiomerically/helically pure molecules, both of these methods give the summative effect representative of both optical isomers present in a nonenantiomerically pure sample. It is only by comparison with a sample of unequivocal enantiomeric purity that useful correlation of optical purity can be drawn. Ideally, a method of simultaneously observing both helical enantiomers is required. We herein report our preliminary use of silver(I)–lanthanide(III) shift reagents for the ¹H NMR analysis of helical structures containing aromatic moieties.

(1) Mizutani, T.; Yagi, S.; Morinaga, T.; Nomura, T.; Takagishi, T.; Kitagawa, S.; Ogoshi, H. *J. Am. Chem. Soc.* **1999**, *121*, 754–759.

(2) Yagi, S.; Sakai, N.; Yamada, R.; Takahashi, H.; Mizutani, T.; Takagishi, T.; Kitagawa, S.; Ogoshi, H. *J. Chem. Soc., Chem. Commun.* **1999**, 911–912.

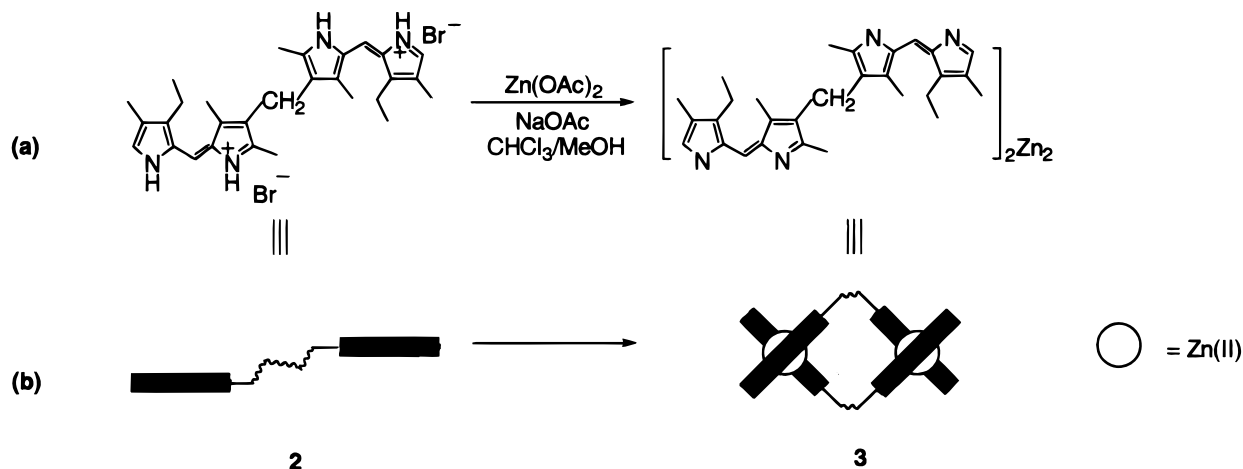
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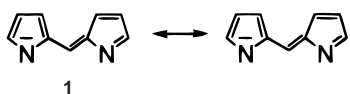
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(6) Ping Gao, J.; Sheng Meng, X.; Bender, T. P.; MacKinnon, S.; Grand, V.; Yuan Wang, Z. *J. Chem. Soc., Chem. Commun.* **1999**, 1281–1282.

Scheme 1



Our ongoing studies⁷ involve the design and synthesis of dipyrrromethene–zinc complexes using self-assembly.⁸ Dipyrrromethenes **1** are fully conjugated flat bipyrrrolic mono-



anionic structures and are excellent ligands for chelation with metal ions. This paper reports our studies involving the use of dinuclear complex **3**⁹ which is formed by complexation of ligand **2**¹⁰ to $\text{Zn}(\text{II})$ (Scheme 1a).¹¹ We have shown that similar α -linked bis(dipyrrromethene) complexes crystallize in a binuclear helical arrangement^{7b} and X-ray analysis confirmed the helical structure of **3**, as denoted in Scheme 1b.¹¹ Helix **3** is obviously formed as a racemic mixture of (M) and (P) helices, since no asymmetric induction operates during the self-assembly process. We wished to simultaneously observe the two helical enantiomers of complex **3** to both confirm the inherent chirality and develop a new

method with which to investigate helical chirality control for future studies.

Mixed silver(I)–lanthanide(III) binuclear shift reagents with chiral ligands can be useful for determining the enantiomeric excess of chiral alkenes, alkynes, allenes, and arenes.¹² The silver cation binds to soft Lewis bases (such as double bonds), while the paramagnetic lanthanide induces shifts in the NMR spectrum of the donor compound. In effect, the silver cation acts as a bridge between the double bond and the lanthanide shift reagent. The chiral–chiral interaction of the molecule studied and the lanthanide ligands results in signal splitting due to the existence of dynamic diastereoisomers under fast exchange conditions and different shift consequences for each diastereoisomer.

A partial ^1H 200 MHz NMR spectrum of complex **3** is shown in Figure 1a.¹³ The signals at 7.06 and 6.93 ppm are due to the α - and meso-hydrogens respectively, as deter-

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(9) To a stirred solution of ligand **2** (100 mg, 0.17 mmol) in CHCl_3 (1 mL) at room temperature was added a solution of $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ (182 mg, 0.83 mmol) and $\text{NaOAc} \cdot 3\text{H}_2\text{O}$ (113 mg, 0.83 mmol) in MeOH (1 mL). The reaction mixture was stirred for 30 min and the solvents then removed in vacuo. CH_2Cl_2 (10 mL) and water (10 mL) were then added; the organic layer was then separated, washed with water (10 mL), and then dried over MgSO_4 . Filtration through a short plug of silica gel eluting with CH_2Cl_2 and then 1:10 MeOH: CH_2Cl_2 , and removal of the solvents in vacuo gave **3** as an orange powder with a green metallic lustre (80 mg, 96%), mp (decomp) >230 °C; UV–vis $\lambda_{\text{max}}(\text{CH}_2\text{Cl}_2)/\text{nm}$ 522 (11, ϵ 220 000), 474 (4); $\delta_{\text{H}}(400 \text{ MHz}; \text{CDCl}_3)$ 1.15 (3H, t, $J = 7.6$), 1.38 (3H, s), 1.97 (3H, s), 2.18 (3H, s), 2.61 (2H, q, $J = 7.6$), 3.36 (1H, s), 6.93 (1H, s), 7.06 (1H, s); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 9.88 (CH_3), 10.00 (CH_3), 15.23 (CH_3), 16.50 (CH_3), 18.07 (CH_2), 20.44 (CH_2), 122.09 (CH), 122.78, 126.81, 135.77, 136.60, 138.02, 142.03, 146.03, (CH), 160.17; m/z EI 1008 (M^+ , 100%), 504 (M^{2+} , 22) (Found: M^+ , 1008.4102. $\text{C}_{58}\text{H}_{68}\text{N}_8\text{Zn}_2 \cdot 1.5\text{H}_2\text{O}$ requires 1008.4107). Anal. Calcd for $\text{C}_{58}\text{H}_{68}\text{N}_8\text{Zn}_2 \cdot 1.5\text{H}_2\text{O}$: C, 67.63; H, 6.46; N, 10.88. Found: C, 67.32; H, 6.61; N, 10.73.

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(11) Thompson, A.; Dolphin, D. Manuscript in preparation (full paper).

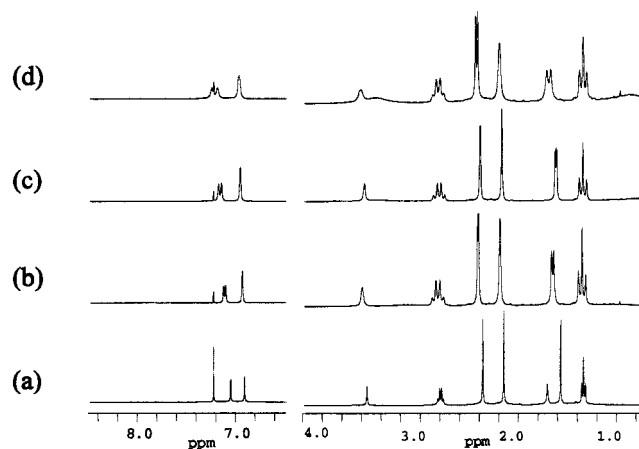


Figure 1. ^1H NMR 200 MHz spectra¹³ in CDCl_3 of (a) **3**, (b) 0.035 M **3**, 0.035 M AgFOD and 0.035 M $\text{Eu}(\text{tfc})_3$, (c) 0.07 M **3**, 0.035 M AgFOD and 0.035 M $\text{Eu}(\text{tfc})_3$, and (d) 0.07 M **3**, 0.07 M AgFOD and 0.07 M $\text{Eu}(\text{tfc})_3$.

mined by NOE experiments.¹¹ Figure 1b shows the spectrum when 0.035 M each of **3**, AgFOD [(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)silver] and Eu(tfc)₃ [tris-(trifluoromethylhydroxymethylene)-(+)-camphorate europium] were measured in CDCl₃. Encouragingly, slight signal separation ($\Delta\delta_\alpha$ 0.02 ppm at α -position) and downfield shifting was observed. Reasoning that increased concentrations would favor the trimolecular association process, we increased the concentration of **3** to 0.07 M (effective molarity of dipyrromethene ligand 0.28 M, as there are four equivalent dipyrromethene units present within **3**), and $\Delta\delta_\alpha$ increased to 0.03 ppm (Figure 1c). Increasing the concentration of all components to 0.07 M as shown in Figure 1d resulted in increased downfield shifting and splitting ($\Delta\delta_\alpha$ 0.05 ppm).¹⁴ Two signals due to methyl groups are also slightly resolved under these conditions.

After useful concentration conditions for these experiments were identified, the chiral lanthanide shift reagent was varied. The use of Eu(hfc)₃ [tris(3-(heptafluoropropylhydroxymethylene)europium)-(+)-camphorate] or Yb(hfc)₃ with AgFOD did not result in increased $\Delta\delta$ values, while Pr(tfc)₃ and Pr(hfc)₃ gave no signal separation, although line broadening and signal shifting were observed. Fortunately, Yb(tfc)₃ with AgFOD and complex **3**, all at 0.07 M, gave $\Delta\delta_\alpha$ 0.20 ppm, as shown in Figure 2b, accompanied by

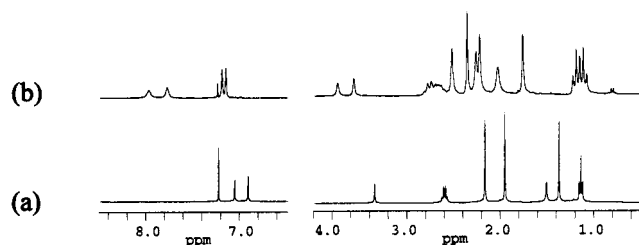


Figure 2. ¹H NMR 200 MHz spectra¹³ in CDCl₃ of (a) **3**, (b) 0.07 M **3**, 0.07 M AgFOD, and 0.07 M Yb(tfc)₃.

significant splitting and shifting in other areas of the spectrum.

Yb(III) chelates have previously been observed to give larger downfield shifts than Eu(III) reagents.^{12a} This is crucial to our work, since Figure 2b shows that the separated α -signals are both shifted sufficiently downfield to be

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(13) To the required amounts of **3**, AgFOD, and lanthanide shift reagent was added the appropriate volume of dry degassed CDCl₃. The mixture was agitated for 2 min and then filtered through glass wool into a NMR tube. The samples were prepared in the dark, and all spectra were recorded immediately after preparation. The concentrations indicated represent the upper possible limits based upon the amount of the reagents used, since some insoluble material was removed in most cases.

(14) Line broadening was observed upon addition of paramagnetic shift reagents to sample **3** and this effect prevented the use of higher reagent concentrations. As expected, line broadening was increased at higher fields and so although initial screening experiments were performed using a Bruker WH-400 instrument, the most useful information obtained, and that reported herein, was obtained using a Bruker AC-200 instrument.

completely removed from the solvent CHCl₃ signal. Importantly, baseline separation of the split signals is complete, allowing for accurate individual integration of the resolved signals. For Figure 2b, the signals at 7.98 and 7.78 ppm integrate to a ratio of 1.00:1.05 respectively, while the signals at 3.76 and 3.59 ppm integrate to a ratio of 1.00:1.06. This confirms the presence of equal populations of the enantiomeric species in the racemic sample of **3** and validates the integration method.

In the absence of AgFOD, no signal shifting or splitting was observed. In the presence of achiral Yb(III) compounds YbFOD and Yb(tmhd)₃ [tris(2,2,6,6-tetramethyl-3,5-heptanedionato)ytterbium], instead of Yb(tfc)₃, signal splitting was not observed. The results of these control experiments confirm the existence of a dipyrromethene–Ag(I)–Yb(III) “sandwich”, with a chiral–chiral interaction between the dipyrromethene complex and the chiral ligands of the Yb(III) reagent.

It is evident that the two sets of signals seen in Figure 2b are due to the presence of diastereomeric dipyrromethene–Ag(I)–Yb(III) structures under dynamic equilibrium, indicative of the two enantiomeric helices of **3**. To determine whether the two helices of **3** interconvert in solution a ¹H 2D EXSY experiment¹⁵ was performed under the same conditions as those used to obtain the spectrum shown in Figure 2b. Cross signals were not observed between any of the signals, indicating that the diastereomeric structures, and hence the enantiomeric helices of **3**, do not interconvert under the experimental conditions.¹⁶ Over a period of 2 h, decomposition of the Ag(I) reagent was seen to slowly occur by deposition of Ag(s) on the inside of the NMR tube, accompanied by slow upfield shifting and a decrease in separation of all signals. Eventually the signals due to pure **3**, as shown in Figure 1a, were returned. This effect necessitated the employment of rapid experiments and prevented the use of investigative variable-temperature NMR spectroscopy since the rate of decomposition increased with temperature.

Silver–aromatic bond strengths and stabilities are very dependent upon steric factors, with the silver cation preferentially occupying a complexation site furthest removed from steric encumbrances.¹⁷ This presumably accounts for our observations of largest shifting and splitting of the signal due to the α -hydrogens for the AgFOD/Yb(tfc)₃ experiments. The exact nature of the dipyrromethene–silver(I)–

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(16) The ¹H 2D EXSY experiments using a Bruker AMX-500 instrument gave no observable cross-peaks (positive phase cross-peaks would be indicative of interconversion).¹⁵ The pulse sequence used is identical to that used for ¹H 2D NOESY experiments, but negative cross-peaks due to atoms linked through space were not observed since the number of scans (4 or 8) was insufficient. The 2D EXSY spectrum shows the slow degradation of the Ag(I) reagent over time by slight upfield “smearing” of the split signals. Nevertheless, no evidence of cross-peaks was observed under the experimental conditions. Mixing times of 0.4 and 0.8 s were used. A wide range of mixing times were not used in the 2DEXSY experiments (to probe a large range of exchange rates), although our observations were confirmed by NOEDIFF experiments which showed no sign of interconversion occurring.

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ytterbium(III) association is currently under investigation, as is the precise stability of the (M) and (P) helices of complex **3**.

In conclusion, we have reported the use of silver(I)–chiral lanthanide shift reagents to analyze the helical distribution of dipyrromethene complexes. By using this strategy, integration of the resolved signals reveals the helical enantiomeric ratio of the sample, which will prove to be extremely useful in future work involving the analysis of helical enantiomeric excesses. This approach should be applicable

to a wide range of helical compounds containing olefinic or aromatic moieties, thus circumventing the need for optically pure samples for comparative purposes.

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