LETTER

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The selective formation of neutral, heteroleptic zinc(II) complexes *via* self-discrimination of chiral bisoxazoline racemates and pseudoracemates†

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The reversible metal-directed multi-component self-assembly of chiral bisoxazolines proceeds with a high level of chiral self-discrimination and thus defines a simple strategy for the preparation of neutral, heteroleptic zinc(II) complexes.

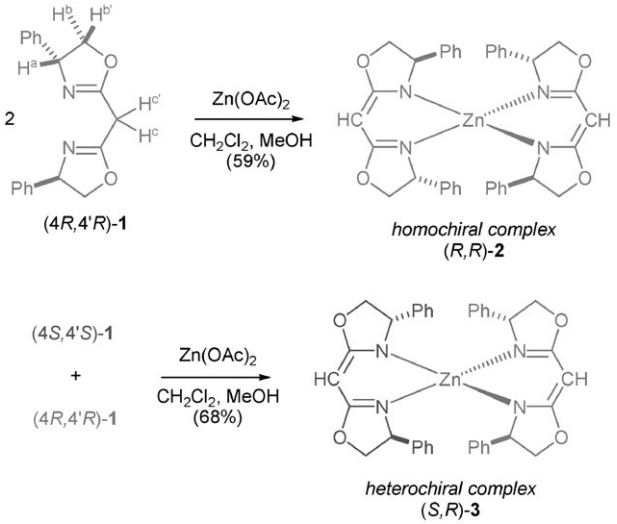
Developing strategies to predictably connect different subunits under reversible conditions is important for programming the multi-component self-assembly of supramolecules,[1] particularly as it relates to the design of functional materials such as catalysts,[2] sensors, and molecular machines. Two approaches are often employed to direct multi-component self-assembly:[3] self-recognition[4] or self-discrimination.[5] These are typically reduced to practice by constructing pairs of complementary hydrogen-bonding motifs[6] or pairs of ligands possessing complementary steric or electronic motifs to bias their assembly.[7] We are interested in exploiting metal-directed multi-component self-assembly for the formation of chiral, heteroleptic complexes in the design of new heterobimetallic asymmetric catalyst systems.[8]

Schmittel and co-workers have paired unhindered 1,10-phenanthrolines with sterically encumbered ones for the very successful self-assembly of cationic, heteroleptic copper(I) and silver(I) complexes.[9] We have explored an alternative approach to prepare neutral, heteroleptic zinc(II) complexes, using the complementary chirality of bisoxazoline (box) ligands to direct their assembly. Chiral ligands have been widely used to control metal-centered and helical chirality in self-assembled metal complexes and in some cases to direct self-sorting.[10]

The neutral, homochiral complex (*R,R*)-**2** is formed by stirring 2 equiv. of (4*R*,4′*R*)-**1** with $Zn(OAc)_2$ (Scheme 1).‡ $Zn(OAc)_2$ serves a dual role in the reaction, simultaneously delivering the metal center and the required base. However, when a racemic mixture of box ligands [*i.e.*, 1 equiv. each of (4*S*,4′*S*)-**1** and (4*R*,4′*R*)-**1**] is combined with $Zn(OAc)_2$, three complexes can form: the homochiral complexes (*S,S*)- and (*R,R*)-**2** (*i.e.*, chiral self-recognition) and/or the heterochiral complex (*S,R*)-**3** (*i.e.*, chiral self-discrimination). The tetrahedral coordination geometry of zinc(II) strongly favors self-discrimination in this case: only the neutral, heterochiral complex (*S,R*)-**3** is observed.

Fig. 1 compares the 3.3–5.3 ppm region of the 600 MHz ^{1}H NMR spectrum ($CDCl_3$) for the free box ligand **1** to those of the heterochiral [(*S,R*)-**3**] and homochiral [(*R,R*)-**2**] complexes. Overall, the spectra show that the homochiral and heterochiral complexes are distinctly different in solution, and at the level of NMR detection, the combination of (4*S*,4′*S*)-**1** and (4*R*,4′*R*)-**1** with $Zn(OAc)_2$ affords exclusively the heterochiral complex. Of particular note in the spectrum of (*S,R*)-**3** is the dramatic upfield shift for the hydrogen on the phenyl-bearing carbon of the dihydrooxazole ring (H^a; see structure **1**, Scheme 1). It is highly shielded in the heterochiral complex relative to the free ligand or homochiral complex. In addition, it is worth noting the resonances for (*R,R*)-**2** are somewhat broadened, indicative of possible dynamic behavior.

The neutral, heterochiral zinc complexes are proving to be quite remarkable compounds. Complexation is reversible in the presence of a proton source; for example, adding another (*R*)- or (*S*)-box derivative leads to rapid substitution, while a mixture of homochiral complexes rapidly disproportionates to the heterochiral complex (Scheme 2) as judged by ^{1}H NMR.[11] The complexes are typically freely soluble in a variety of



Scheme 1 Synthetic scheme of the facile preparation of neutral $(box)_2Zn$ complexes.

† Electronic supplementary information (ESI) available: full experimental details for complexes (*S,S*)-**2**, (*S,R*)-**3** and **6**, including structure determination procedures and ^{1}H and ^{13}C NMR spectra (plus NMR spectra of the free ligands); preparation procedure for (*R,R*)-**5**. See http://www.rsc.org/suppdata/nj/b4/b413439g/

‡ Both the homochiral complex **2** [colorless solid; mp 185–186 °C (with decomposition)] and the heterochiral complex (*S,R*)-**3** [colorless solid; mp 271–276 °C (with decomposition)] form quantitatively and are obtained as solids upon removal of CH_2Cl_2 and trituration; the yields given in Scheme 1 largely reflect mechanical losses.

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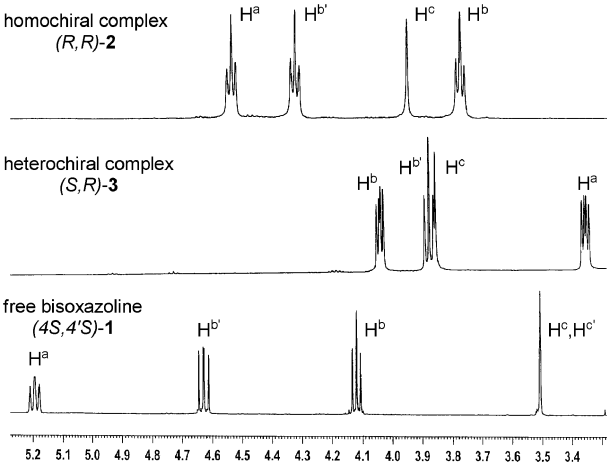


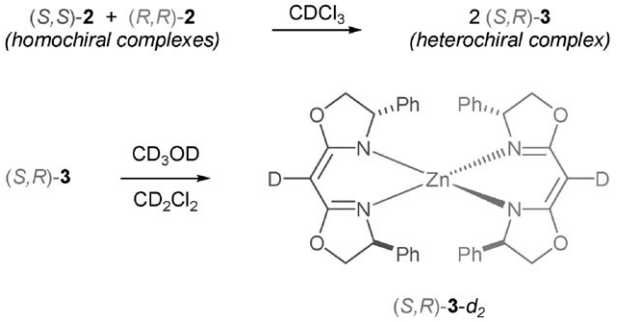
Fig. 1 The 3.3–5.3 ppm region of the 600 MHz ^{1}H NMR spectrum ($CDCl_3$) for the free box ligand (4*S*,4′*S*)-**1**, the homochiral complex (*R*,*R*)-**2** and the heterochiral complex (*S*,*R*)-**3**. See structure **1** for the identities of H^a–H^c; assignments are based on decoupling and NOE experiments.

moderately polar organic solvents (*e.g.*, CH_2Cl_2, $CHCl_3$, THF, and toluene) and partially soluble in methanol. They are stable toward water but insoluble. However, the complexes are not completely inert toward protic solvents as evidenced, for example, by rapid H/D exchange. Adding CD_3OD to a solution of (*S*,*R*)-**3** (CD_2Cl_2) shows complete H/D exchange within the time the NMR spectrum can be recorded.

Box-metal complexes have been widely investigated due to their successful use in asymmetric catalysis and the observation of nonlinear effects.[12] Both homochiral and heterochiral cationic complexes have been reported by others, including a tetrahedral zinc complex from isopropylidene box derivatives,[13] and several octahedral complexes derived from box[14] or pybox[15] ligands. The crystal structure of one neutral, homochiral complex has been reported.[16] To better understand the factors favoring self-discrimination over self-recognition, we grew crystals of (*S*,*R*)-**3** and (*S*,*S*)-**2** and determined their structures by X-ray analysis (Fig. 2).§

The heterochiral complex (*S*,*R*)-**3** exhibits near-perfect tetrahedral coordination while the homochiral complex (*S*,*S*)-**2**, for which there are two closely related conformers in the unit cell, distorts from tetrahedral coordination to minimize steric interactions between the phenyl substituents of the two box ligands. Otherwise, the selected bond lengths and angles summarized in Table 1 show little variation between the two complexes. The crystal structures are consistent with the NMR data, particularly the positioning of the phenyl groups in the heterochiral

§ CCDC reference numbers 245214–245216. See http://www.rsc.org/suppdata/nj/b4/b413439g/ for crystallographic data in .cif or other electronic format. Crystal data for compound (*S*,*S*)-**2**: $C_{38}H_{34}N_4O_4Zn$, orthorhombic, a = 10.2844(5), b = 16.5841(8), c = 75.389(4) Å, U = 12 858(1) Å^3, T = 100(2) K, space group $C2221$ (no. 20), Z = 16, μ(MoKα) = 0.812 mm^{-1}, 60 061 reflections measured, 13 131 unique (R_{int} = 0.0519). The final R_1 and wR_2 were 0.0524 and 0.1037 for 12 539 reflections with $I > 2\sigma(I)$. Crystal data for compound (*S*,*R*)-**3**: $C_{38}H_{34}N_4O_4Zn$, monoclinic, data were reduced and the cell determined *via* the software MARXDS (MarResearch), a = 17.205(3), b = 10.733(2), c = 18.407(4) Å, β = 105.98(3) °, U = 3267.7(11) Å^3, T = 298(2) K, space group $P21/c$ (no. 14), Z = 4, μ(MoKα) = 0.799 mm^{-1}, 16 914 reflections measured, 5045 unique (R_{int} = 0.335). The final R_1 and wR_2 were 0.0549 and 0.1408 for 4114 reflections with $I > 2\sigma(I)$. Crystal data for compound **6**: $C_{92}H_{78}N_{10}O_8Zn_2$, triclinic, a = 10.7889(6), b = 10.8866(6), c = 17.2241(9) Å, α = 73.146 (1)°, β = 88.623(1)°, γ = 86.943(1)°, U = 1933.3(2) Å^3, T = 100(2) K, space group $P1$ (no. 1), Z = 1, μ(MoKα) = 0.687 mm^{-1}, 23 488 reflections measured, 17 235 unique (R_{int} = 0.0164). The final R_1 and wR_2 were 0.0378 and 0.0903 for 16 737 reflections with $I > 2\sigma(I)$.



Scheme 2 Facile disproportionation of a mixture of homochiral complexes and H/D exchange of the heterochiral (*S*,*R*)-**3**.

complex (*S*,*R*)-**3** so as to shield the hydrogen on the phenyl-bearing carbon of the dihydrooxazole ring (H^a).

Heterochiral complexes such as (*S*,*R*)-**3** are meso by inversion symmetry and hence achiral. Nevertheless, the process of chiral self-discrimination is inherently one of heteroleptic self-assembly (*i.e.*, non-identical groups bond to the metal) and should not be restricted to pairs of enantiomers. Pseudo-enantiomers could combine similarly to afford complexes lacking a center of inversion. To illustrate the idea and its potential versatility for preparing chiral, heteroleptic complexes, the pseudo-racemic combination (4*S*,4′*S*)-**4** and (4*R*,4′*R*)-**5** was used to prepare the mixed cyano/benzyl-substituted complex **6** (Fig. 3). The heteroleptic complex forms exclusively as judged by NMR. In spite of the complementary chirality of the box moieties, complex **6** lacks inversion symmetry and is chiral, for example, exhibiting a large optical rotation, $[\alpha]_D = -203°$ (c = 0.75, CH_2Cl_2).

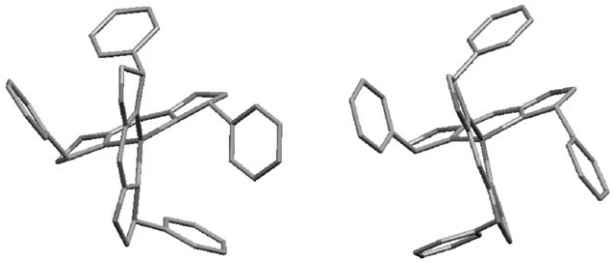


Fig. 2 The crystal structures of (*S*,*S*)-**2** (left) and (*S*,*R*)-**3** (right).

Table 1 Selected bond lengths (Å) and angles (°) in (*S*,*S*)-**2** and (*S*,*R*)-**3**

	(*S*,*S*)-**2** (conformer a)[a]	(*S*,*S*)-**2** (conformer b)[a]	(*S*,*R*)-**3**
N1–Zn–N2	93.83	93.99	94.21
N3–Zn–N4	95.05	92.34	93.56
Zn–N1	1.988(3)	2.005(3)	1.971(3)
Zn–N2	1.967(3)	1.948(3)	1.973(3)
Zn–N3	1.999(3)	2.018(3)	1.975(3)
Zn–N4	1.965(3)	1.968(3)	1.976(3)
N1–C3	1.310(5)	1.295(5)	1.303(4)
N2–C5	1.313(5)	1.323(5)	1.311(5)
N3–C10	1.303(5)	1.304(5)	1.316(4)
N4–C12	1.305(5)	1.306(5)	1.292(4)
C3–C4	1.394(6)	1.398(6)	1.392(5)
C4–C5	1.396(6)	1.387(6)	1.386(6)
C10–C11	1.403(6)	1.402(6)	1.371(5)
C11–C12	1.393(7)	1.388(6)	1.396(6)

[a] Two conformers of (*S*,*S*)-**2** are present in the unit cell.

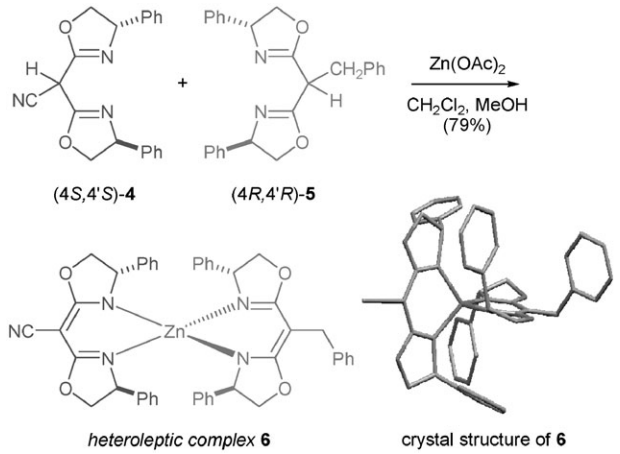


Fig. 3 Preparation and crystal structure of heteroleptic complex **6**.

In summary, chiral self-discrimination of box ligands directs the multi-component self-assembly of neutral, heteroleptic zinc(II) complexes. Complexes prepared *via* chiral self-recognition are usually homoleptic and highly symmetric, a limitation for the design of functional materials. The self-assembly of pseudo-racemates with chiral self-discrimination could be used to overcome this limitation. The approach described should be readily extended to a variety of other metal ions and chiral ligands. Further studies are in progress.

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