

Diastereoselective formation and optical activity of an M_4L_6 cage complex

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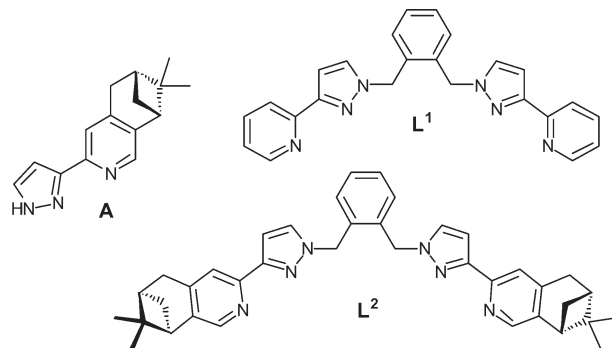
A chiral bridging ligand affords a single diastereoisomer of tetrahedral M_4L_6 cage complex in which the optical rotation of each ligand is increased by a factor of 5 on coordination.

Since Werner first proposed the chiral tris-chelate structure for six-coordinate complexes with bidentate chelating ligands¹ it has been apparent that combination of achiral metal and ligand components can generate chiral assemblies. In the absence of any chiral auxiliary the complex formation is necessarily racemic, and resolution post-synthesis is necessary to separate the stereoisomers. Interest in this phenomenon increased enormously in the 1980s and 1990s with the advent of extensive series of polynuclear helical complexes in which long (achiral) ligand strands were organised into helical configurations on coordination to labile metal ions.² Measurement of the chiroptical properties of the helicates requires either resolution³ (which is only worth doing if the helicate is kinetically inert enough not to racemise quickly) or the use of a chiral auxiliary to induce formation of only one stereoisomer in the helix.^{4–6} This could be either a chiral counter-ion, which biases the helicate towards one enantiomer *via* differential ion-pairing,⁴ or a chiral substituent on the ligand.^{5–7} This latter approach has been widely adopted in recent years, in particular by the groups of von Zelewsky⁵ and Constable,^{6,7} who have prepared oligopyridine ligands containing chiral substituents such as pinene or terpene units. Assembly of such chiral ligands around metal ions to give helical arrays proceeds with high diastereoselectivity, such that the chirality of the ligand substituent controls the sense of helical chirality in the complex. Isolation of enantiopure helical assemblies in this way has allowed the study of their chiroptical properties; the molar optical rotations of such helical assemblies are much higher than those of the ligands alone, and can be of the same order as those of organic helicenes.⁸

We report here the extension of this principle to the diastereoselective formation of a M_4L_6 tetrahedral cage. Such cages, in which a six-coordinate metal ion is located at each vertex and a bis-bidentate bridging ligand spans each edge, have been extensively studied by the groups of Raymond^{9,10} and Saalfrank,¹¹ and indeed Raymond and co-workers have resolved some of these and demonstrated that they racemise extremely slowly due to the strong mechanical interlocking of the components.¹⁰ We described

a while ago the (racemic) cage complexes $[M_4(L^1)_6]X_8$ [$M = Co(II), Zn(II)$; $X = BF_4^-, ClO_4^-$] in which one of the tetrahedral counterions is trapped in the cage cavity and actually acts as a template for assembly of the metal/ligand cage around it.¹² A notable feature of these is that all four metal centres have the same optical configuration, and all six ligands have the same sense of helical twist along the edges of the tetrahedron, such that each complex molecule has *T* symmetry. An enantiopure example would therefore be expected to show very strong optical activity, from the combination of the twelve pinene groups present in the ligands, and the additional helical chirality in the ligands induced by coordination to give the cage.

The chiral pyridyl-pyrazole derivative **A** (Scheme 1) was prepared as described earlier,¹³ the pyridyl group bears a pinene group fused to positions C⁴ and C⁵. This chiral structural motif forms the basis of the well-known 'CHIRAGEN' ligands of von Zelewsky and co-workers.⁵ Reaction of this with 1,2-bis(bromomethyl)benzene† in the same way as used for **L**¹ resulted in formation of the new ligand **L**² in good yield.¹² Reaction of **L**² with Co(II) acetate or Zn(II) acetate in MeOH (3 : 2 molar ratio) followed by precipitation of the complexes with the templating anions BF_4^- or ClO_4^- afforded the cage complexes $[M_4(L^2)_6](BF_4)_8$ [$M = Co(II), Zn(II)$] in good yield. Electrospray mass spectra confirmed formation of the cage complexes, indicating that the pinene substituents have not interfered in any way with cage formation. ¹H NMR spectra were consistent with the presence of a single diastereoisomer of *T* symmetry, in which all ligands are equivalent and each ligand has twofold symmetry. In particular, in the ¹H NMR spectrum of $[Co_4(L^2)_6](BF_4)_8$ the paramagnetism of the cage shifts the peaks over the range +86 to –103 ppm,¹² with 16 signals being observed as required and no evidence for the alternate diastereoisomer.



Scheme 1 Ligands discussed in this paper.

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The crystal structure of $[\text{Zn}_4(\text{L}^2)_6](\text{BF}_4)_8$ is shown in Figs. 1 and 2.‡ The complex cation has non-crystallographic T symmetry, with a tetrafluoroborate anion encapsulated in the centre, and crystallises in the chiral space group $C2$. It will be apparent from the view down one of the threefold axes that the direction in which the ligands are twisted arises from minimisation of steric interactions between the peripheral pinene groups, and that this controls the overall assembly of the cage. Coordination to the $\text{Zn}(\text{II})$ ions has resulted in all six ligands adopting the same helically twisted conformation, with substantial twists (in the same sense) between the two near-planar pyridyl-pyrazole units and the central phenyl spacer.

To see the consequent chiral amplification effect we compared the specific rotation α_D of the ligand L^2 and the cage $[\text{Zn}_4(\text{L}^2)_6](\text{BF}_4)_8$ using 589 nm light in a standard 1 dm polarimeter cell, with CH_2Cl_2 as solvent in each case. For L^2 the value of α_D is -74° ; for $[\text{Zn}_4(\text{L}^2)_6](\text{BF}_4)_8$ it is -300° . These are based on sample concentrations expressed in g cm^{-3} ; for a meaningful comparison these need converting to molar values, which are -432° for the free ligand and -13400° for the complex.¹⁴ Thus the complex, containing six ligands, has an optical rotation per mole of > 30 times

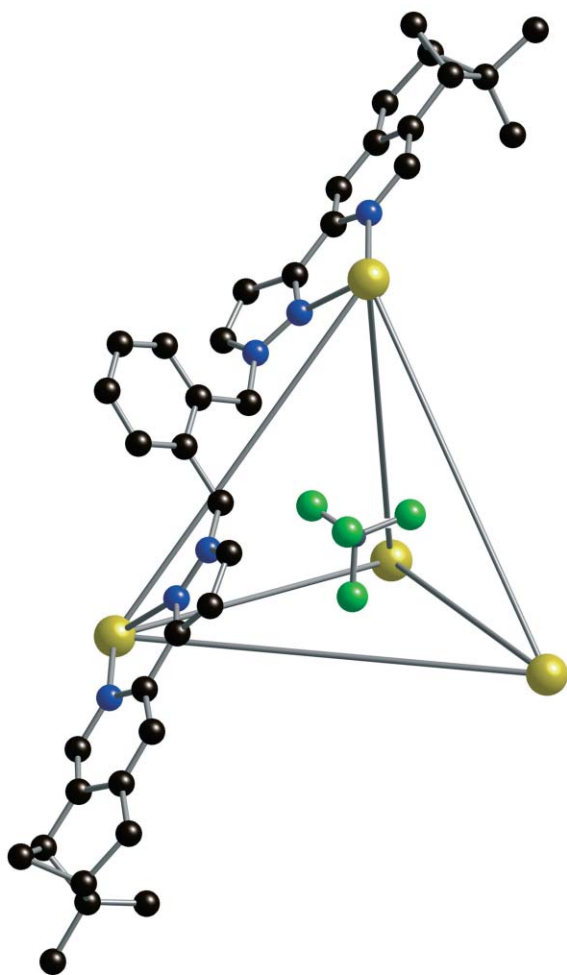


Fig. 1 Structure of $[\text{Zn}_4(\text{L}^2)_6](\text{BF}_4)_8$ showing only the metal cage, the encapsulated anion, and one of the bridging ligands. Zn-N distances lie in the range 2.11–2.27 Å; the $\text{Zn}\cdots\text{Zn}$ distances are all 9.85 Å.

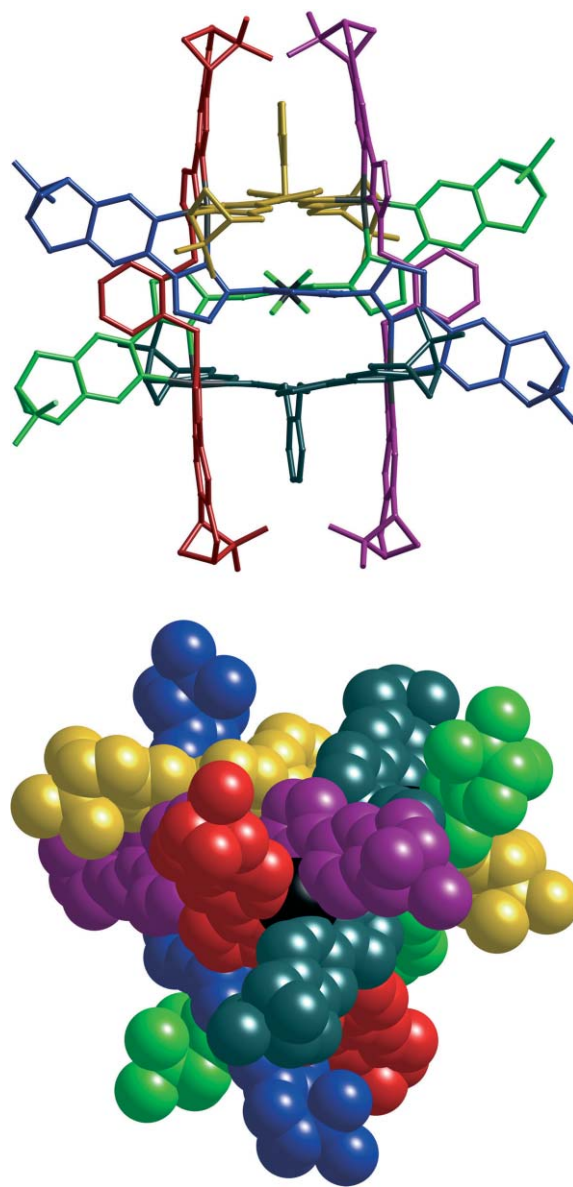


Fig. 2 Two views of the structure of the cage complex $[\text{Zn}_4(\text{L}^2)_6](\text{BF}_4)_8$. The upper one shows all six ligands (coloured separately), the stacking between them, and the encapsulated anion; the lower picture is a space-filling view looking down one of the C_3 axes.

that of the free ligand, *i.e.* a fivefold increase in optical rotation between a set of six free ligands and a set of six coordinated ligands, arising from the conformational changes associated with diastereoselective formation of the cage. In other words, $> 80\%$ of the optical rotation arises from the chirality of the cage superstructure with $< 20\%$ coming from the pinene groups.¹⁵ The molar rotation value is large in absolute terms, comparable to those of organic helicenes⁸ and the resolved trefoil knot.¹⁶

In conclusion, diastereoselective formation of a coordination cage has been achieved using a chiral bridging ligand, resulting in substantial chiral amplification associated with adoption by all of the ligands of a helical conformation upon binding. Extension of this principle to larger cages (M_4L_6 tetrahedra,¹⁷ M_8L_{12} cubes¹⁸ and $\text{M}_{12}\text{L}_{18}$ truncated tetrahedra¹⁹) based on similar ligands is in progress; these will be of interest not only for their chiroptical

properties but the possibility of stereoselectivity in the host–guest chemistry associated with their large central cavities.

Notes and references

† **Preparation of ligand L².** A mixture of 1,2-bis(bromomethyl)benzene (1.50 g, 6.28 mmol), 5-(2'-pinene-[4',5']-pyridyl)pyrazole A (1.5 g, 6.28 mmol), aqueous NaOH (10 M, 15 cm³), toluene (80 cm³) and Bu₄NOH (40% aqueous solution, 3 drops) was stirred at 60 °C for 30 min. The mixture was diluted with H₂O (60 cm³) and the organic layer separated, dried over MgSO₄ and concentrated before purification by alumina column (5% THF/dichloromethane) to give L² as an off-white solid (Yield: 1.6 g, 88%). ¹H NMR (250 MHz, CDCl₃): δ 8.14 ppm (2H, s, pyridyl H⁶), 7.75 (2H, s, pyridyl H⁵), 7.33–7.09 (6H, m, pyrazolyl H³ and 4 × Ph), 6.89 (2H, d, J 2.4, pyrazolyl H⁴), 5.45 (4H, s, CH₂), 3.01–2.96 (4H, m, pyridyl-4-CH₂), 2.82 (2H, t, J 5.5, CH-CH₂-CH), 2.68 (2H, dt, J 9.5, J 5.5, CH-CH₂-CH), 2.32–2.24 (2H, m, pyridyl-4-CH₂-CH), 1.40 (6H, s, CH₃), 1.21 (2H, d, J 9.5, pyridyl-5-CH). EIMS: m/z 580 (M⁺), 341. Found: C, 77.8%; H, 6.9%; N, 13.8%. Required for C₃₈H₄₀N₆·(H₂O)_{0.5}: C, 77.3%; H, 7.0%; N, 14.2%. **Preparations of complexes.** A mixture of L² and M(BF₄)₂ (M = Co, Zn) in a 3 : 2 molar ratio in MeCN was stirred for 5 minutes and the product precipitated by addition of diethyl ether; after filtration the solid product was recrystallised from CH₂Cl₂/Pr₂O. Data for [Zn₄(L²)₆][BF₄]₈ (M): m/z 1392.7 {(M – 3BF₄)³⁺}, 1022.9 {(M – 4BF₄)⁴⁺}, 801.2 {(M – 5BF₄)⁵⁺}, 653.0 {(M – 6BF₄)⁶⁺}, 545.6 {(M – 7BF₄)⁷⁺}. Data for [Co₄(L²)₆][BF₄]₈ (M): m/z 2119.6 {(M – 2BF₄)²⁺}, 1384.2 {(M – 3BF₄)³⁺}, 1016.4 {(M – 4BF₄)⁴⁺}, 795.8 {(M – 5BF₄)⁵⁺}, 543.8 {(M – 7BF₄)⁷⁺}. ¹H NMR (400 MHz, CD₃CN): δ 86.2(sh), 75.6(br), 71.8(sh), 51.9(sh), 31.6(sh), 20.0(sh), 7.6(sh), 2.0(sh), 1.9(sh), 1.2(sh), –1.4(sh), –3.0(sh), –9.0(sh), –10.0(sh), –64.9(sh), –102.6(br) [sh = sharp; br = broad]. Satisfactory C,H,N analytical data were obtained for both complexes.

‡ **Crystallography.** A small crystal of [Zn₄(L²)₆][BF₄]₈ (CH₂Cl₂)₁₁ (0.3 × 0.2 × 0.1 mm) was mounted on a Bruker-PROTEUM diffractometer at 100K. Formula: C₂₃₉H₂₆₂B₈Cl₂₂F₃₂N₃₆Zn₄; formula weight 5374.71; monoclinic, C₂; a = 32.3394(5), b = 22.8698(4), c = 22.8658(6) Å; β = 134.9860(10)°; V = 11961.1(4) Å³; Z = 2; ρ = 1.492 g cm⁻³; μ(Cu-Kα) = 3.454 mm⁻¹; λ = 1.54184 Å. Refinement of 1513 parameters with 41 restraints converged at R₁ = 0.1096 [selected data with I > 2σ(I)], wR₂ = 0.2948 (all data). The Flack parameter is 0.04(3). The complex cation lies on a twofold axis with half of the molecule in the asymmetric unit.²⁰ CCDC 277409. See <http://dx.doi.org/10.1039/b509239f> for crystallographic data in CIF or other electronic format.

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- 20 PLATON points out that this unit cell can be transformed to a higher-symmetry cubic cell in I23 (with a = b = c = 22.87 Å). The structure can be solved and refined to a similar R₁ value in this space group, with one metal ion (on a C₃ axis) and one half of one ligand in the asymmetric unit. However the anions and lattice solvent molecules are more significantly disordered, and most importantly the Flack parameter increases from 0.04(3) to 0.34(3). We therefore prefer the solution in C₂.