Guest-induced Assembly of a Chiral [2 + 2] Metallomacrocycle

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A chiral metallomacrocycle, assembled from two zinc(II) ions and two strands of ligand **L**^{1}, and stabilized by inclusion of *o*-dimethoxybenzene in the cavity, is characterized by NMR spectroscopy.

The use of metal ions in the controlled assembly of single, double and triple helices is now well established.[1] In contrast, the use of metal ions in the assembly of macrocyclic complexes with selective recognition properties has received little attention.[2] We have recently reported the synthesis of a series of bisbipyridyl ligands, containing 2-oxapropyl groups, which in the presence of transition metal ions assemble into [2 + 2] metallomacrocycles.[3–5] While mixtures of helical and non-helical tetrahedral complexes were obtained with copper(I),[3] tridentate coordination and preferential formation of the non-helical complex was observed with zinc(II) and nickel(II).[4,5] On the basis of these results, we have modified our ligand design and now report the design, synthesis and recognition properties of ligand **L**^{1}. In the presence of zinc(II), and a suitable guest molecule, exclusive assembly of the helical metallomacrocycle with a substrate bound in the cavity is observed.

Ligand **L**^{1} was prepared in three steps from 6-bromo-6′-methyl-2,2′-bipyridine **1**.[6] Alkynyl linker groups were incorporated into **L**^{1} to preorganize the aromatic spacers to be 6–7 Å apart when assembled into a metallomacrocycle with four or five-coordinate metal centres. Palladium-catalysed coupling of **1** with prop-2-ynyl amine [$Pd(PPh_3)_2Cl_2$, $NHPr^i_2$, CuI, THF–diethyl ether] afforded bipyridine **2** in 80% yield. The amine **2** (2.2 equiv.) was heated with 1,4,7,8-naphthalene tetracarboxylic anhydride in dimethylacetamide for 6 h to give **L**^{1} in 57% yield.†

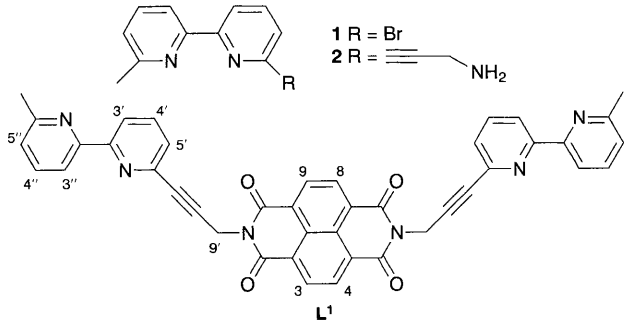
Treatment of **L**^{1} with 2.1 equiv. of zinc(II) triflate afforded complex **3**.‡ In CD_3CN, the diastereotopicity of the methylene protons, expected on formation of a [2 + 2] complex,[3,4] was observed in the ^{1}H NMR spectrum. However, at high concentration (8.3 mmol dm^{-3}), three major AX spin systems and numerous minor AX systems were observed in the region δ 3.8–5.0 [Fig. 1(*a*)], indicating the presence of several complexes. When the sample was diluted, the number and relative intensities of the AX systems changed dramatically, and at low concentrations (< 0.74 mmol dm^{-3}), the methylene protons H$^{9'}$ appeared as one AX spin system [Fig. 1(*b*)] and all signals were assigned to a single [2 + 2] complex **3a**.

Similar equilibration of the complexes present in **3** was observed in titration experiments with substituted benzenes. Addition of *o*-dimethoxybenzene, which is colourless, to a yellow solution of **3** in MeCN gave a faint red solution which suggested formation of a charge-transfer complex. In the presence of 1 equiv. of *o*-dimethoxybenzene, only signals due to **3a** were observed in the ^{1}H NMR spectrum, *i.e.* the presence of 1 equiv. of the substrate shifted the equilibrium so that the formation of the complex **3a** was favoured. More importantly, *o*-dimethoxybenzene formed a complex only with **3a** and not with the other oligomeric complexes present in concentrated solutions of **3** that give rise to the multiple resonances in Fig. 1(*a*).

Clear evidence for the inclusion of *o*-dimethoxybenzene in the cavity of **3a** was obtained from the changes in chemical shifts of the protons near the interior of the metallomacrocycle and changes in the appearance of the aromatic spacer protons on addition of the substrate. At 298 K the naphthalene tetraimide rings are rotating rapidly on the NMR timescale and hence appear as a singlet [Fig. 2(*a*)]. This signal broadened on addition of 1 equiv. of *o*-dimethoxybenzene, and in the presence of 5 equiv. of substrate, appeared as a very broad signal [Fig. 2(*c*)], consistent with slow rotation of the aryl rings on the NMR timescale due to inclusion of *o*-dimethoxybenzene in the cavity of the [2 + 2] metallomacrocycle **3a**.§ A variable-temperature experiment was carried out, and at 240 K, the aryl protons H^{3,4,8,9} appeared as two distinct doublets [Fig. 2(*d*)]. The inequivalence of these protons at low temperature indicates a crossed configuration of the aromatic spacers with respect to each other, and **3a** was assigned to have the helical configuration.¶

Binding constants for methoxybenzene, the three isomers of dimethoxybenzene, and nitrobenzene[7] were measured using NMR titration experiments (Table 1). From these results, both electron-rich and -poor substrates bind weakly in the cavity, presumably by favourable electrostatic interactions with the aromatic spacers. Some discrimination between the isomers of dimethoxybenzene was observed, with *p*-dimethoxybenzene binding more weakly than the *ortho* and *meta* isomers.

In summary, ligand **L**^{1}, in the presence of zinc(II) and *o*-dimethoxybenzene assembles into the chiral, helical metallomacrocycle **3a**. The presence of the substrate stabilizes the supramolecular complex and drives the equilibrium to favour the chiral complex **3a**. This gives a new dimension to metal ion self-assembly processes where a ligand not directly coordinated to the metal ions can control the process. In a recent report,



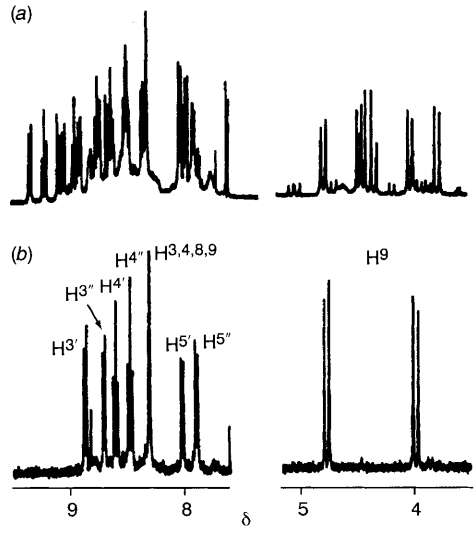


Fig. 1 400 MHz ^{1}H NMR at 300 K of **3** in CD_3CN: (*a*) 8.3 (*b*) 0.74 mmol dm^{-3}

Fujita *et al.* have demonstrated a similar result where an achiral, *metallocage-like* complex was formed with the aid of substrate molecules.[8] In this case, less labile palladium(II) ions were used and the equilibration times were measured in hours compared with this study in which equilibration was effectively instantaneous. The recognition properties of complex **3a** for chiral substrates, which may preferentially stabilize one helical enantiomer are under investigation.

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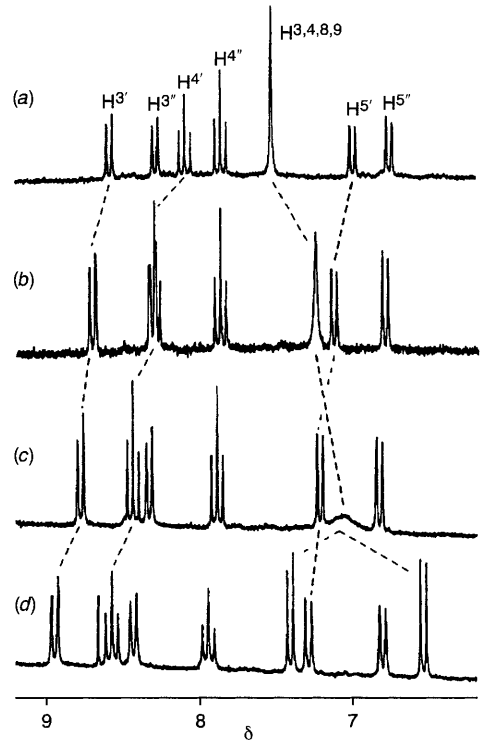

Fig. 2 400 MHz ^{1}H NMR at 300 K in CD_3CN of (*a*) **3a** (370 μmol dm^{-3}); (*b*) **3a** + 1 equiv. of *o*-dimethoxybenzene; (*c*) **3a** + 5 equiv. of *o*-dimethoxybenzene; (*d*) **3a** + 5 equiv. of *o*-dimethoxybenzene at 240 K

Table 1 Stability constants (±10%) for the complexes formed between **3a** and aromatic substrates, determined in CD_3CN at 300 K

Substrate	K/dm^3 mol^{-1}
Methoxybenzene	61
o-Dimethoxybenzene	300
m-Dimethoxybenzene	300
p-Dimethoxybenzene	79
Nitrobenzene	65

Footnotes

† *Selected data* for ligand **L^1**: yellow powder, mp >300 °C; ^{1}H NMR (400 MHz, $CDCl_3/CF_3CO_2D$) δ 2.95 (s, CH_3), 5.34 (s, CH_2), 7.81 (d, *J* 7.9 Hz), 7.87 (d, *J* 7.9 Hz, bipy-H), 8.11–8.15 (m, Ar-H), 8.32 (d, *J* 7.9 Hz, bipy-H), 8.55 (dd, *J* 7.9 Hz, bipy-H), 8.96 (s, H^{3,4,8,9}).

‡ Ligand **L^1** (20 mg, 29.5 μmol) was treated with zinc(II) triflate (2.1 equiv.) in MeCN–$CHCl_3$ (4 : 1) and stirred for 10 min. The solvent was removed, $CHCl_3$ was added and the mixture was refluxed for 2 h. The solution was filtered, the residue washed with hot $CHCl_3$ and water and dried to give complex **3** $Zn_2(L^1)_2(CF_3SO_3)_4{\cdot}5H_2O$ as a light yellow solid (Found: C, 48.5; H, 3.0; N, 7.6%. $C_{88}H_{62}F_{12}N_{12}O_{25}S_4Zn_2$ requires C, 48.6; H, 2.9; N, 7.7%).

§ An independent experiment was carried out in the absence of *o*-dimethoxybenzene. At 240 K, only broad signals were observed indicating that the aromatic rings were still rotating on the NMR time scale. The formation of other complexes, not present at room temperature, was also observed. A blank experiment was also carried out to rule out simple intermolecular association between the ligand strands and the substrate.

¶ In the achiral, non-helical complex, the aromatic protons would appear as two singlets; see ref. 3.

References

1 For leading references see E. C. Constable, *Chem. Ind.*, 1994, 56; J.-M. Lehn and A. Rigault, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1095; U. Koert, M. M. Harding and J.-M. Lehn, *Nature*, 1990, **346**, 339; A. F. Williams, C. Piguet and G. Bernardinelli, *Angew. Chem., Int. Ed. Engl.*, 1991, **11**, 1490; C. Piguet, G. Bernadinelli, B. Bocquet, A. Quattropane and A. F. Williams, *J. Am. Chem. Soc.*, 1992, **114**, 7440.

2 For recent examples of this approach see M. Fujita, J. Yazaki and K. Ogura, *J. Am. Chem. Soc.*, 1990, **112**, 5645; *Chem. Lett.*, 1991, 1031; *Tetrahedron Lett.*, 1991, 5589; A. W. Schwabacher, J. Lee and H. Lei, *J. Am. Chem. Soc.*, 1992, **114**, 7597.

3 A. Bilyk and M. M. Harding, *J. Chem. Soc., Dalton Trans.*, 1994, 77.

4 A. Bilyk, M. M. Harding, P. Turner and T. W. Hambley, *J. Chem. Soc., Dalton Trans.*, 1994, 2783.

5 A. Bilyk, M. M. Harding, P. Turner and T. W. Hambley, *J. Chem. Soc., Dalton Trans.*, in the press.

6 J. Uenishi, T. Tanaka, S. Wakabayashi and S. Oae, *Tetrahedron Lett.*, 1990, 4625.

7 A related macrocycle that binds nitrobenzene has been reported; J. Jazwinski, A. J. Blacker, J.-M. Lehn, M. Cesario, J. Guilhem and J. Pascard, *Tetrahedron Lett.*, 1987, 6057.

8 M. Fujita, S. Nagao and K. Ogura, *J. Am. Chem. Soc.*, 1995, **112**, 1649.