COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Inherent helicity in an extended tris-bipyridyl molecular cage

David F. Perkins,[a] Leonard F. Lindoy,*[a] George V. Meehan*[b] and Peter Turner[a]

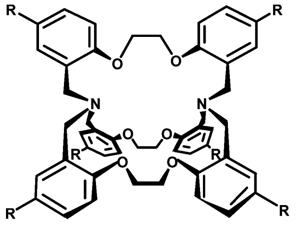
[a] *Centre for Heavy Metals Research, School of Chemistry, University of Sydney, NSW 2006, Australia. E-mail: Lindoy@chem.usyd.edu.au; Fax: +61 2 9351 3329; Tel: +61 2 9351 4400*

[b] *School of Pharmacy and Molecular Sciences, James Cook University, Queensland 4811, Australia. E-mail: george.meehan@jcu.edu.au; Fax: +61 7 4781 6078; Tel: +61 7 4781 4543*

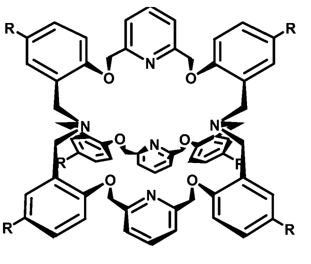
Received (in Cambridge, UK) 13th October 2003, Accepted 4th November 2003

A new molecular cage incorporating three bipyridyl units has been synthesised by a conventional multi-step procedure as well as, much more efficiently, by a Ni(II) template procedure; an X-ray structure of the nickel complex shows that it adopts an *exo* configuration of each of the bridgehead nitrogen lone pairs, the central metal ion acts to promote a triple helical twist that extends ~22 Å along the axial length of the molecule.

The use of cage ligands to generate novel host-guest coordination chemistry has now been well documented.[1] Previously we have reported the synthesis of new cage molecules such as **1**[2] and **2**[3,4] using stepwise synthetic procedures starting from the appropriate dialdehyde precursors and involving functional group interconversion to produce the corresponding diamine and dichloro intermediates. Computational studies and crystal structure evidence for both **1** and **2** indicate that the lone electron pairs of the terminal nitrogens are oriented '*exo*'.[2,3] This in turn causes the adjacent methylene groups to be situated inside the molecule diminishing greatly the potential volume of the cavity. A molecular model of **2** indicates that the cavity is 'slot-like'; indeed, recrystallization of **2** from benzene yields the corresponding product in which a benzene molecule is contained in the cage symmetrically aligned normal to its pseudo C_3-axis.[3] A further feature of both cage structures is that the positioning of the aromatic rings results in each bridgehead cap having a propensity to yield a chiral 'three-bladed propeller' arrangement around the above axis.



1



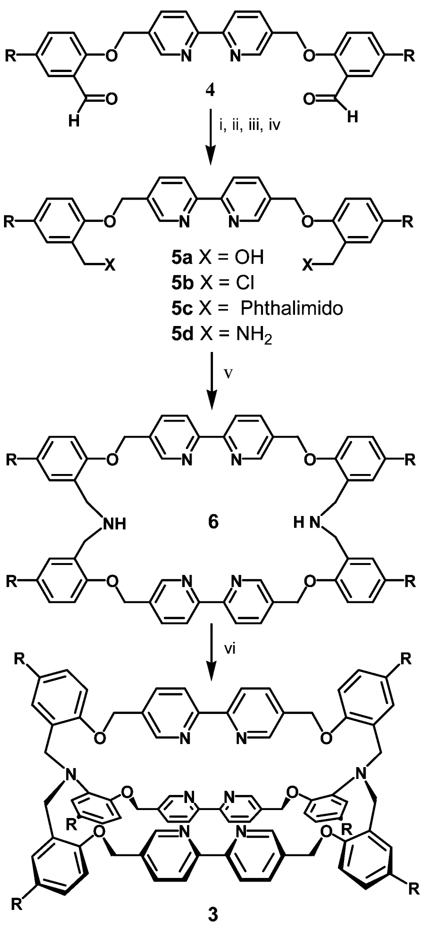
2

In a further development, we now report the expansion of the available cavity in the N_5O_6-cage **2** by replacement of each of the 2,5-pyridyl groups with 5,5′-substituted 2,2′-bipyridyl moieties to yield the extended species **3** (R = H or *t*-Bu). While the product with R = *t*-Bu was initially synthesised in very low yield (overall 1.5% from dialdehyde **4**[†]) by the conventional 'multi-step' procedure (Scheme 1), it was subsequently obtained in improved yield (11% accompanied by 45% of the macrocycle **6**) by means of direct reductive amination of **4** in the presence of an excess of ammonium acetate and sodium cyanoborohydride in refluxing acetonitrile. A more dramatic increase in efficiency was achieved *via* a metal ion template procedure; the Ni(II) complex of **3** was isolated in 75% yield (as its PF_6^- salt) from the same reaction carried out in the presence of 0.33 equivalents of Ni(II) ion.[‡] In these direct reactions the ammonium ion ultimately forms the bridgehead nitrogens of the cage by means of sequential imine condensation and reduction steps.

Inspection of CPK models of **3** (R = H or *t*-Bu) coupled with molecular modelling studies at the semi-empirical [PM3] level in the gas phase indicated that both free cages are conformationally flexible (in accord with their ^{1}H NMR spectra in $CDCl_3$ in which each methylene resonance is a singlet). Modelling also indicated that both will readily bind a metal ion in an octahedral coordination environment to yield a triple helical twist about the cage (long) axis.[§] Indeed, a series of preliminary studies indicated that both derivatives of type **3** readily form 1 : 1 complexes with a number of other transition metal ions besides Ni(II), including Mn(II), Fe(II) and Cu(II).

X-Ray diffraction from single crystals of $[NiL](PF_6)_2$ (L = **3**, R = *t*-Bu)[¶] confirmed the formation of a triple helical twist (Fig. 1(c)) along the axial length (~22 Å — see below) of the complex. This situation is unusual relative to other helical metallo-structures in which multiple metal-ion coordination is required to induce a helical twist along the length of the system.[6]

Despite difficulties with crystal growth, a structure of the free cage was obtained from a microcrystal using synchrotron radiation. Although of poor quality, the structure reveals that the free ligand adopts a 'loose' helical arrangement (Fig. 1(a)).

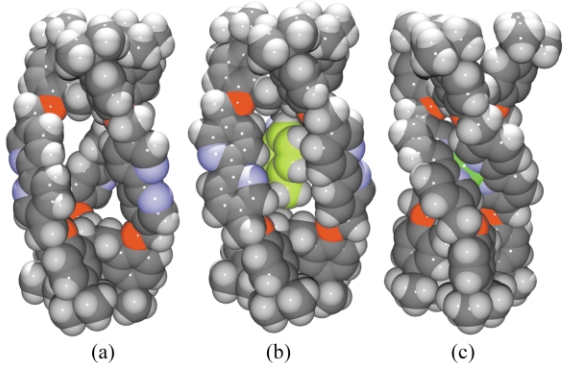


Scheme 1 Synthesis of cage **3**, R = *t*-Bu. *Reagents and conditions*: i, $NaBH_4$, MeOH, reflux 1 h, 88%; ii, $SOCl_2$, CH_2Cl_2 reflux 4 h, 60%; iii, potassium phthalimide, DMF, 120 °C, 4 h, 61%; iv, NH_2NH_2, EtOH–THF, reflux 7 h, then 1 mol dm^{-3} NaOH, 45%; v, **4** 1 equiv., 4 Å molecular sieve, dry MeOH reflux 1.5 h then $NaCNBH_3$ reflux 2 h, 45 %; vi, **5b** 1 equiv., Cs_2CO_3, KI 0.1 equiv., toluene reflux 9 d, 22%.

DOI: 10.1039/b312716h

Both helical enantiomers are present in the respective centrosymmetric crystal structures, and in both cases a bipyridyl strand of one enantiomer slots into the ‘groove’ created by two strands of the complementary enantiomer. In the metal complex structure there are two crystallographically independent complexes, each located on a three fold axis, that effectively form a dimeric unit linked by the groove interaction. In the free ligand structure, 50% of the cage molecules accommodate a toluene guest, and it appears that the nestling of a helical molecule into the grove of neighbour containing a bound toluene molecule precludes solvate binding in the former molecule. The independent angles subtended by the principal cage axis and the bi-pyridyl axis are 38.71(1) and 38.10(1)° in the two metal complexes, and 22.81(6), 30.33(1) and 25.26(1)° for the three strands of the free ligand. The apical nitrogen–nitrogen separation is 13.267(7) Å in the free ligand, and 13.446(6) and 12.571(6) Å in the two independent nickel complexes. The *t*-Bu to *t*-Bu distances along a ligand strand are respectively 21.938(6) and 21.562(10) Å in the two Ni complexes, and 21.578(10), 21.656(11) and 21.573(10) Å in the three strands of the free ligand. One end of the metal complex molecule is more open than its counterpart; the three *t*-Bu residues in the two complexes are respectively 6.17(2) and 6.623(7) Å apart at one end, and 7.004(14) and 8.056(8) Å apart at the opposite end. The nickel ion coordination is pseudo-octahedral, with negligible trigonal twist. The terminal nitrogens are 6.589(4) and 6.857(4) Å from the metal ion in one complex, and 5.943(P4) and 6.629(4) Å in the second complex. The metal complex structure closely matches that predicted by CPK models. Clearly it is the tendency of the capping groups to twist into a propeller-like configuration (left- or right-handed) coupled with the chiral octahedral coordination geometry adopted by the central nickel on coordination to the three bipyridyl residues that promotes and enhances the helical twist along the length of individual complex cations.

We thank the Australian Research Council for support. Use of the ChemMatCARS Sector 15 beamline at the Advanced Photon Source, was supported by the Australian Synchrotron Research Program, which is funded by the Commonwealth of Australia under the Major National Research Facilities Program. ChemMatCARS Sector 15 is also supported by the National Science Foundation/ Department of Energy under grant numbers CHE9522232 and CHE0087817 and by the Illinois board of higher education. The Advanced Photon Source is supported by the U.S. Department of Energy, Basic Energy Sciences, Office of Science, under Contract No. W-31-109-Eng-38.



(a) (b) (c)

Fig. 1 Space-filling depictions highlighting the helical disposition of the ligand in the crystal structures of (a) free ligand **3**, (b) free ligand **3** with toluene guest and (c) the complex cation of [Ni(**3**)](PF_6)$_2$.

Notes and references

† Dialdehyde **4** was prepared in 60% yield by alkylation of 5-*tert*-butylsalicylaldehyde with 5,5′-bis(bromomethyl)-2,2′-bipyridine[5] under phase transfer conditions (toluene–H_2O–NaOH–Bu_4NBr).

‡ Synthesis of [NiL](PF_6)$_2$ (L = **3**, R = *t*-Bu): Dialdehyde **4** (0.25 g, 0.466 mmol) and $Ni(NO_3)_2 \cdot 5H_2O$ (0.042 g, 0.154 mmol) were dissolved in acetonitrile (400 cm^3) and stirred at 50 °C for 20 min. The solution was filtered into a dropping funnel and added dropwise over 3 h to a vigorously stirred solution of ammonium acetate (0.18 g, 2.33 mmol) and sodium cyanoborohydride (0.15 g, 2.33 mmol) in acetonitrile (500 cm^3) warmed at 50°. The reaction was stirred at 50° for a further 1 h and the solvent then removed *in vacuo*. Routine workup yielded a salmon-pink solid which was recrystallised from acetonitrile–ether to give title complex (0.22 g, 0.116 mmol, 75%), mp > 250°. Found: C, 64.33; H, 5.80; N, 5.90; $C_{102}H_{114}F_{12}N_8NiO_6P_2$ requires: C, 64.59; H, 5.80; N, 5.91%; ESMS, found: M^{2+} ($-2PF_6^-$) 802.4, $C_{102}H_{114}N_8NiO_6^{2+}$ requires 802.41.

§ Modelling studies indicate this is not so for the analogous 6,6′-substituted 2,2′-bipyridyl cage in which the cavity is significantly larger than is ideal for transition metal ions; the calculations for metal-free **3** also suggested that there is little difference in the energies of the *exo-exo* and *endo-endo* bridgehead nitrogen arrangements for this cage.

¶ *Free ligand* **3**: data from ChemMatCARS Advanced Photon Source, model formula $C_{112.50}H_{126}N_8O_{6.50}$, M 1694.21, triclinic, space group $P\bar{1}$(#2), a 15.555(4), b 16.622(2), c 23.495(6) Å, α 71.105(11), β 78.998(8), γ70.890(11)°, V 5406(2) Å^3, Z 2, temperature 123(2) Kelvin, λ(synchrotron) 0.56356 Å, μ 0.042 mm^{-1}, $2\theta_{max}$ 36.48, N 101066, N_{ind} 14377(R_{merge} 0.0877), N_{obs} 10853($I > 2\sigma(I)$), $R1(F)$ 0.1613, $wR2(F^2)$ 0.437.[7,8,9] Poor diffraction, rigid bodies for pyridyl and toluene molecules.

Complex [Ni(**3**)](PF_6)$_2$: Data from Bruker SMART 1000, model formula $C_{104.50}H_{117.75}F_{12}N_{9.25}NiO_8P_2$, M 1979.98, trigonal, space group $P\bar{3}$ (#147), a 15.9763(19), b 15.9763(19), c 51.131(9) Å, γ 120.00°, V 11302(3) Å^3, Z 4, temperature 173(2) Kelvin, λ(MoKα) 0.71073 Å, μ(MoKα) 0.273 cm^{-1}, $2\theta_{max}$ 63, N 136109, N_{ind} 24406 (R_{merge} 0.0509), N_{obs} 18113($I > 2\sigma(I)$), $R1(F)$ 0.0750, $wR2(F^2)$ 0.2398.[7,8,9] Two independent complexes each on three fold axis. Twinned with (y,x,$-z$). CCDC 222140 and 222141. See http://www.rsc.org/suppdata/cc/b3/b312716h/ for crystallographic data in .cif or other electronic format.

1 J.-M. Lehn, *Supermolecular Chemistry*, VCH, Weinheim, 1996.

2 I. M. Atkinson, L. F. Lindoy, O. A. Matthews, G. V. Meehan, A. N. Sobolev and A. H. White, *Aust. J. Chem.*, 1994, **47**, 1155; K. R. Adam, I. M. Atkinson, J. Kim, L. F. Lindoy, O. A. Matthews, G. V. Meehan, F. Raciti, B. W. Skelton, N. Svenstrup and A. H. White, *J. Chem. Soc., Dalton Trans.*, 2001, 2388.

3 R. J. A. Janssen, L. F. Lindoy, O. A. Matthews, G. V. Meehan, A. N. Sobolev and A. H. White, *J. Chem. Soc., Chem. Commun.*, 1995, 735.

4 I. M. Atkinson, A. R. Carroll, R. J. A. Janssen, L. F. Lindoy, O. A. Matthews and G. V. Meehan, *J. Chem. Soc., Perkin Trans. 1*, 1997, 295.

5 U. S. Schubert, C. Eschbaumer and G. Hochwimmer, *Synthesis*, 1999, 779.

6 L. F. Lindoy and I. M. Atkinson, *Self-assembly in Supramolecular Chemistry*, Royal Society of Chemistry, Cambridge, UK, 2000, pp. 138–178.

7 Bruker (1995). SMART, SAINT and XPREP. Area detector control and data integration and reduction software. Bruker Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

8 A. Altomare, M. Cascarano, C. Giacovazzo and A. J.Guagliardi, *Appl. Cryst.*, 1993, **26**, 343.

9 G. M. Sheldrick, SHELXL97, Program for crystal structure refinement, University of Göttingen, Germany, 1997.