Diastereoselective preparation of Cu(I) and Ag(I) double helices by the use of chiral bis-bipyridine ligands†

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Received (in Montpellier, France) 21st October 2008, Accepted 10th December 2008
First published as an Advance Article on the web 9th January 2009
DOI: 10.1039/b817610h

Chiral bis-5,6-pinene bipyridine type ligands have been used to form, through self-assembly reaction, dinuclear coordination compounds which show a highly diastereoselective formation of double helices with copper(I) and silver(I) as coordination centers.

Self-assembly due to ligand–metal interactions to form complex supramolecular architectures has been of great interest in recent years.[1] The fundamental role of helicity in nature and its potential role in the field of asymmetric catalysis leads to the design and preparation of different supramolecular structure such as helicates, catenanes, rotaxanes, knots and other interlocked designs.[2–4] The formation of helices occurs when more than one metal ion is present. The crucial point for a successful helical assembly is due to both the arrangement of the binding sites on the ligand and the preferred coordination geometry of the metal ion. Lehn produced a series of polymetallic double helices based on poly-bipyridine ligand strands with ether linkers between each bipyridine subunit.[1] The copper(I) ions enforce a tetrahedral coordination geometry that causes the assembly of the helical structure.

We have already reported the diastereoselective synthesis of a trefoil molecular knot.[5] The strategy developed for the formation of this edifice is the connection of end-groups of the two strands of a double helix. In this publication we describe the latter precursor of the trefoil knot in more detail.

Helical coordination compounds are often prepared using self-assembly methods, where chosen ligands react with appropriate metal ions.[6–16] Helices are chiral objects, which possess a *plus* (*P*) (right handed) or *minus* (*M*) (left handed) configuration (Fig. 1).

Metal directed assembly of achiral ligands used for the preparation of helicoidal compounds yield racemates of the *P* and *M* enantiomers. Some are now available even in enantiomerically pure form.[1,17–19] It is worth noticing that stereoselectivity, *i.e.* diastereoselectivity can be achieved by introducing chiral groups into the molecules forming the strands of the helix.[20–22] This is rendered possible by the use of bis-pinene bipyridine type ligands.[23–26] Indeed, it has been shown that these ligands often react in a stereoselective manner in the presence of transition metal ions.[27]

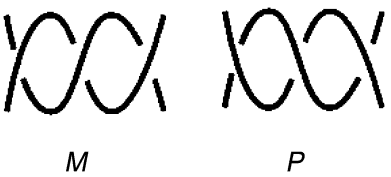

Fig. 1 Left (*M*) and right (*P*) handed double helices.

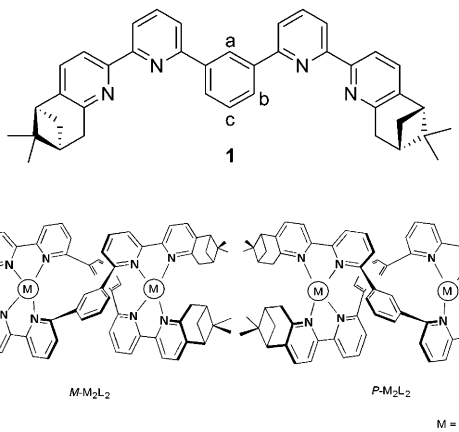

Fig. 2 Diastereoselective formation of *M* and *P* helices during complexation of the ligand bis-5,6-pinene bipyridine [*m*-phenyl] (**1**) with Cu(I) and Ag(I).

A new family of chiral ligands, related to the CHIRAGENS,[24] has been reported earlier. Model considerations show that one of these ligands, bis-5,6-pinene bipyridine [*m*-phenyl] (**1**) (Fig. 2), whose synthesis has previously been published[28] should be ideally suited for the formation of a double helix with tetrahedral coordination centers. Sauvage and coworkers showed the quantitative formation and the high stability of the helical precursor composed of copper(I) bisphenanthroline units with 1,3-phenylene linkers between the two phenanthroline moieties.[29–31] They show that the use of 1,3-phenylene as a spacer group was extremely beneficial as the preparation of the copper(I) double helix turned out to be quantitative.

Complex formation of **1** with Cu(I) or Ag(I), studied by NMR-, CD- and UV/Vis-spectroscopic methods, as well as mass spectrometry and, in one case, by X-ray diffraction, leads, as supposed, to double stranded helices. The details of these investigations will be discussed in the subsequent paragraphs.

† CCDC reference number 279480 (**3**). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b817610h

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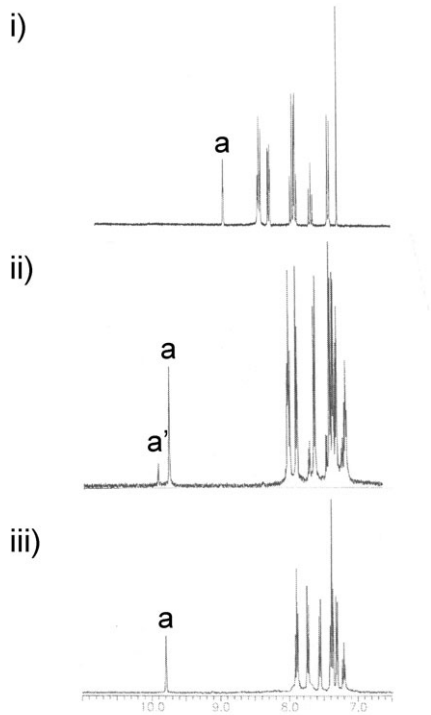


Fig. 3 ^{1}H NMR spectra of ligand **1** (i) and of the Cu(I) **2** (ii) and Ag(I) **3** (iii) complexes.

Fig. 2 represents the possible structures for the double helices *M*-Cu_2L_2, *P*-Cu_2L_2, *M*-Ag_2L_2 and *P*-Ag_2L_2. ^{1}H NMR spectra are well defined and indicate quantitative complex formation for both metal ions, if the latter are reacted in a 1 : 1 molar ratio with the ligand **1**. They have been assigned on the basis of 2D spectra.

Fig. 3 shows the NMR signals of the aromatic protons in the spectra of the free ligand (i) and the two dinuclear complexes with Cu(I) (ii) and Ag(I) (iii), respectively. The signals of the free ligand, corresponding to the bipyridine proton a and the protons b, and c of **1** (Fig. 3) are in the range of 7.25–8.31 ppm, whereas proton a appears at 8.92 ppm. The latter is strongly deshielded in the Ag(I) complex (Fig. 3 iii) appearing at 9.79 ppm. The appearance of one single, strongly shifted signal for proton a and of less strongly shifted signals for the other protons, with no sign of splitting of such signals indicates that: (1) only one species is formed in solution, (2) the symmetry of the complex is such as to leave a C_2-axis bisecting the two bipyridine halves of one ligand molecule. These observations are corroborated by the signals of the protons in the pinene-moiety (0.3–3.2 ppm), not shown in Fig. 3.

The ^{1}H NMR spectra of the $Ag_2L_2^{2+}$ complex thus show unambiguously the stereoselective formation of either *M*-Ag_2L_2 or *P*-Ag_2L_2.

The investigation of the analogous Cu(I) complex (Fig. 3 ii) shows two sets of signals. The well resolved pair of signals of proton a shows the presence of two species (70 : 30), which are with a very high probability the two diastereomeric forms *M*-Cu_2L_2 and *P*-Cu_2L_2, respectively. Again, as in the case of the silver complex, no assignment of absolute configuration

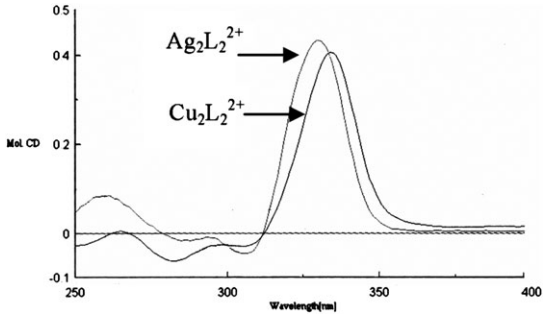


Fig. 4 CD spectra of the Cu(I) and Ag(I) complexes of ligand **1**.

can be given at this point. This can be done through the analysis of the CD spectra of the complexes (Fig. 4).

Whereas ligand **1** itself is CD inactive in the range 250–600 nm, both the Ag(I) and the Cu(I) complex show strong Cotton effects (Fig. 4) with a positive exciton couplet, which provide direct experimental evidence for the formation of the *M* helicate (ΔΔ-configuration at the metal center). As shown by Kuroda and coworkers,[32] the analysis of exciton coupling effects in the CD spectra of polynuclear complexes like our bis-bipyridine ligands is the most common method used to assign the absolute configuration of the metal centers. This analysis is focused on the exciton coupling between chromophores located on the same metal center. The positive sign of the signals indicates a ΔΔ-configuration for $Ag_2L_2^{2+}$ (>95%), and a ratio of 70% (ΔΔ-) to 30% (ΛΛ-) in the case of $Cu_2L_2^{2+}$ was determined by ^{1}H NMR. The Δ- and Λ-configurations describe the chirality at one single metal-centered chromophore. The connection of the two homochiral metal centers to a double stranded helix yields for the Δ-configuration at the metals a *M*-configuration of the helix (Fig. 2). These results are confirmed by the X-ray structure analysis that was carried out with a crystal of $Ag_2L_2(PF_6)_2$.

The crystal structure of the silver(I) complex **3** confirms the formation of the 2^+ charged 2 : 2 complex (Fig. 5). The complex crystallizes in the non-centrosymmetric chiral space group $C222_1$. The absolute structure was determined based on the presence of a heavy atom in the structure [silver atom, Flack parameter x = 0.01(9)]. The crystal structure of this complex is shown in Fig. 5. The structure shows nicely the coiling of the two ligands **1** around the Ag(I) centers. The

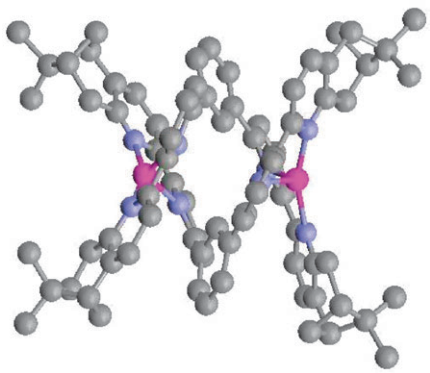
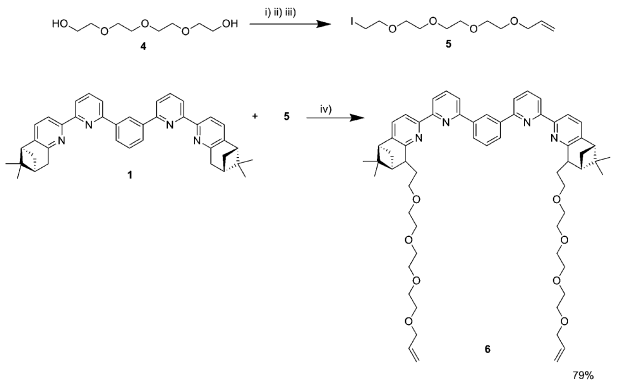


Fig. 5 X-Ray structure of the silver double helix. The figure was drawn with PLATON99.



Scheme 1 Synthesis scheme of ligand **6**. (i) NaOH, THF, allyl bromide; (ii) mesyl chloride, NEt_3, CH_2Cl_2, −5 °C; (iii) NaI, refluxing acetone; (iv) LDA, THF, −40 °C.

metals in this rigid and compact edifice are in a strongly distorted tetrahedral environment geometry. Distances between Ag(I) and N are 2.04–2.42 Å. The Ag···Ag distance is 5.39 Å. As a comparison, the Sauvage copper(I) double helix had a shorter Cu···Cu distance of 4.76 Å.[31]

The configuration of the two individual Ag-chromophores is Δ-, the helicity of the dinuclear species is *M*. The silver structure appears nicely wound and therefore well adapted to the formation of the knot by connecting the appropriate ends of the strands. With the aim of preparing a configurationally predetermined molecular knot,[5] ligand **1** has been alkylated in a stereoselective manner with two polyoxoethylene chains **5**, each possessing a terminal olefin.

The allylic chains **5** were prepared from **4** in 3 steps (Scheme 1).

Deprotonation of the methyl groups adjacent to the pyridine ring of ligand **1**, with LDA, occurs in the opposite direction of the methyl group of the pinene-moiety. The doubly alkylated ligand **6** has been obtained in 75% yield after purification on silica.

As with ligand **1**, complexation of this doubly alkylated ligands occurs with copper(I) and silver(I) metal ions. ^{1}H NMR and ESI-MS spectra confirm also in this case the quantitative formation of double helices. Unlike the results for **1**, also for the Cu(I) complex complete stereoselectivity is observed (Fig. 6). The chains thus enhance the stereoselectivity of the complex formation.

The positive signal of the CD spectrum, almost identical to that of Fig. 4, shows again a Δ-configuration at the metal centers. This induces the *M*-configuration in the double helices as expected from Corey–Pauling–Koltun (CPK) models.

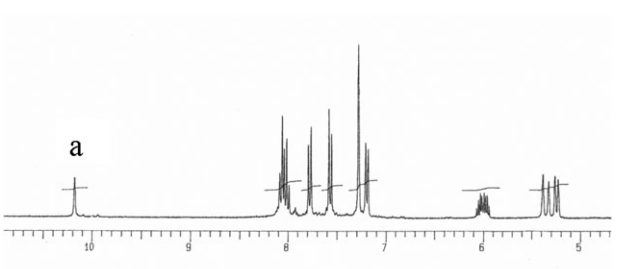


Fig. 6 ^{1}H NMR spectrum of the Cu(I) complex of ligand **6**.

We have presented herein copper(I) and silver(I) double stranded helices as well as the structural characterization by X-ray crystallography of a silver(I) dinuclear complex. We have demonstrated the high diastereoselective formation of these double helices, in the presence of metal ions, which arises from the property of the chiral ligand to induce chirality at the metal centers. We have shown that different diastereoselectivity occurs when different cations are used.

Experimental

General remarks

NMR spectra were recorded on a 'Varian Gemini 300' (300.08 MHz for ^{1}H; 75.4 MHz for ^{13}C) or on a 'Bruker Advance DRX400' (400.13 MHz for ^{1}H; 100.62 MHz for ^{13}C) spectrometer. Mass spectral data were acquired either on a 'VG Instrument 7070E' equipped with a FAB inlet system, on a Hewlett Packard 5988A quadrupole mass spectrometer with an electron ionization (EI) source and/or on a Bruker FTMS 4.7 T BioApex II using a standard electrospray ion source (ESI). UV/Vis spectra were measured on a Perkin Elmer Lambda 40 spectrometer. Wavelengths are given in nm and molar absorption coefficients (ε) in M^{-1} cm^{-1}. Circular dichroism (CD) spectra were recorded on a Jasco J-715 spectropolarimeter.

Synthesis

Cu(I) complex of 1. A degassed solution of $[Cu(CH_3CN)_4]PF_6$(12.67 mg, 0.034 mmol) in acetonitrile (2 mL) was added at room temperature and under argon to a solution of ligand **1** (20 mg, 0.034 mmol) in acetonitrile (1 mL). The resulting dark red mixture was stirred for one hour. A solid product was precipitated with diethyl ether. The solvent was then evaporated, the residue washed with water and dried under vacuum. The compound containing the double helix as cation probably as a mixture of the two diastereomeric forms was obtained in 50% yield as a dark red solid. ^{1}H NMR (CH_2Cl_2, 300 MHz): 9.91 (s, 1H, $H_{(a)\ triplet}$), 9.73 (s, 1H, $H_{(a')\ triplet}$) 7.98–7.78 (m, 4H, $H_{(b)}$, $H_{(3)}$,$H_{(b')}$, $H_{(3')}$), 7.55 (d, 1H, $H_{(3')}$), $^3J_{3'\text{-}4}$ = 7.5 Hz; 7.34 (d, 1H, $H_{(3'')}$), $^3J_{3''\text{-}4}$ = 7.5 Hz; 7.35–7.15 (m, 2H, $H_{(4)}$, $H_{(4')}$), 7.18–7.05 (m, 4H, $H_{(5')}$,$H_{(5'')}$, $H_{(c')}$, $H_{(c'')}$), 3.17–3.02 (m, 2H, $H_{(8)}$, $H_{(8')}$), 2.46 (m, 2H, $H_{(5)}$, $H_{(5')}$), 2.28–2.12 (m, 4H, $H_{(12a,\ 9exo)}$ $H_{(12a',\ 9exo')}$), 1.51–1.42 (m, 2H, $H_{(7)}$,$H_{(7')}$), 1.26 (s, 3H, $H_{(10)}$), 0.94 (s, 3H, $H_{(10')}$), 0.80–0.71 (m, 2H, $H_{(12b)}$,$H_{(12b')}$), 0.61 (d, 1H, $H_{(9endo)}$; $^3J_{9endo\text{-}9exo}$ = 9.3 Hz), 0.35 (d, 1H, $H_{(9endo')}$; $^3J_{9endo'\text{-}9exo'}$ = 9.3 Hz), 0.00 (s, 3H, $H_{(11)}$), −0.18 (s, 3H, $H_{(11')}$). ESI-MS: m/z 637.25 (M^{2+}).

CD: (c = 1.65 × 10^{-5} M, 1 cm cell, CH_3CN): 1(De) = 353 (−0.0095); 299 (+0.0024).

UV/Vis: (c = 1.65 × 10^{-5} M, 1 cm cell, CH_3CN): A = 0.63 (319 nm), A = 0.33 (273 nm), A = 0.44 (254 nm).

Silver complex of 1. The same procedure given for compound **1** has been followed. The diastereomerically pure compound, containing the *M*-double helix, was obtained in 70% yield as a white solid. ^{1}H NMR (CD_3CN, 300 MHz): 9.79 (s, 1H, $H_{(a)\ triplet}$), 7.90 (m, 2H, $H_{(b)}$, $H_{(3)}$), 7.75 (d, 1H, $H_{(3')}$), $^3J_{3'\text{-}4}$ = 7.5 Hz; 7.62 (d, 1H, $H_{(4)}$), $^3J_{4'\text{-}3'}$ = 7.5 Hz, 7.30

(s, 1H, $H_{(5')}$), 7.18 (d, 1H, $H_{(c')}$; $^3J_{c'\text{-}b'}$ = 7.7 Hz), 3.20 (d, 1H, $H_{(8)}$), 2.83 (dd, 1H, $H_{(5)}$); $^3J_{5\text{-}9exo}$ = 5.4 Hz, $^3J_{5\text{-}9endo}$ = 5.7 Hz, 2.78–2.53 (m, 2H, $H_{(12a,\ 9exo)}$), 2.44–2.41 (m-sept., 1H, $H_{(7)}$; ^3J = 3 Hz), 1.90–1.73 (m, 1H, $H_{(12b)}$), 1.36 (s, 3H, $H_{(10)}$), 1.11 (d, 1H, $H_{(9endo)}$; $^3J_{9endo\text{-}9exo}$ = 9.3 Hz), 0.32 (s, 3H, $H_{(11)}$).

ESI-MS: m/z 682.21 (M^{2+}).

CD: ($c = 1.20 \times 10^{-5}$ M, 1 cm cell, CH_3CN): 1(De) = 331 (−0.0012); 308 (+0.0001).

UV/Vis: ($c = 1.20 \times 10^{-5}$ M, 1 cm cell, CH_3CN): A = 0.35 (313 nm), A = 0.15 (282 nm), A = 0.44 (249 nm).

Synthesis of ligand 6. A detailed description has been given in ref. 28.

X-Ray crystallography

A colorless transparent crystal of compound **3** was mounted on a Stoe Imaging Plate Diffractometer System (Stoe and Cie, 1995) equipped with a one-circle φ goniometer and a graphite-monochromator. Data collection was performed at −120 °C using Mo-K_α radiation (λ = 0.71073 Å). The compound crystallizes in the non-centrosymmetric space group $C222_1$; the absolute structure was determined based on the presence of a heavy atom in the structure [silver atom, Flack parameter x = 0.01(9)]. The structure was solved by direct methods using the program SHELXS-97[33] and refined by full matrix least squares on F^2 with SHELXL-97.[34] The hydrogen atoms were included in calculated positions and treated as riding atoms using SHELXL-97 default parameters. An absorption correction was applied using DIFABS in PLATON99[35] (T_{min} = 0.068, T_{max} = 0.510). The compound crystallizes with 2.5 molecules of acetonitrile and one diethyl ether molecule per asymmetric unit resulting in the molecular formula $\{[Ag_2L_2](CH_3CN)_{2.5}(C_4H_{10}O)\}$. $C_{89}H_{93.5}Ag_2F_{12}N_{10.5}OP_2$, M = 1831.92, orthorhombic, a = 16.4766(11), b = 27.872(2), c = 36.378(3) Å, U = 16706(2) Å^3, Z = 8. Final R indices [$I > 2\sigma(I)$]: $R1$ = 0.1196, w$R2$ = 0.3141, R indices (all data): $R1$ = 0.1541, w$R2$ = 0.3372. The crystal was only weakly diffracting (up to 40° in 2θ) due to the solvent loss of the crystal. Nevertheless the crystal structure could be determined and refined without any constraints to the complex cation, the anions and solvent molecules, but only the heavy atoms (Ag, P, F) were refined anisotropically.

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