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Examination of the conformational restraints to a chiral diimine bridged 2,2′-bipyridine

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Abstract—The synthesis of a new bis(2,2′-bipyridine), bridged by a Schiff base cyclohexane moiety is described. Surprisingly, this compound does not appear to form discrete oligonuclear metal complexes on the addition of zinc(II) and iron(II) cations. In order to rationalise this behaviour, the compound's conformation has been explored using a combination of circular dichroism, X-ray crystallography and DFT calculations, indicating that at least two energy barriers need to be overcome to orientate the ligand in a suitable conformation to permit the formation of coordination helicates with control over the metal centred stereochemistry.
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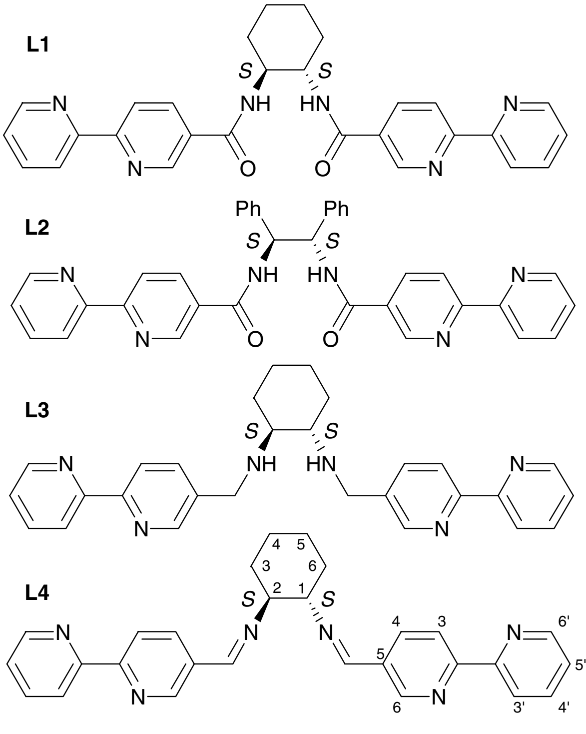
1. Introduction



Scheme 1. Conformationally restricted bis-chelate ligands.

Ligands bearing two or more chelating 2,2′-bipyridine units have attracted considerable attention as building blocks in the preparation of supramolecular architectures in combination with a wide range of transition metals.[1,2] In particular, they have been pivotal in the synthesis of helicates, compounds composed of one or more organic ligand coordinating a series of metal ions to form a discrete oligonuclear assembly.[3,4] Over the last few years we have been attempting to control the stereochemistry in such systems, focussing on triple-stranded helicates. Through the inclusion of chiral units between two chelating 2,2′-bipyridine moieties, we have demonstrated that the metal centred helicity can be tamed to give a single dominant diastereoisomer.[5–7] However, the nature of the linkage between the two chelating groups has a profound influence upon both the stereoselectivity and the final architecture. For example, ligands **L1** and **L2** (Scheme 1) appear to give dinuclear triple-stranded helicates, with the (*S*,*S*)-centres inducing a (Λ,Λ)-M helicity [(*R*,*R*)-centres inducing a (Δ,Δ)-P helicity] in the resulting dinuclear triple helicate with zinc(II).[5,7] Alternatively, ligand **L3** gives rise to ambiguous results, with the ligand showing a range of nuclearities and stoichiometries and is subject to ongoing studies,[8] while a similar enantiopure bridged diether ligand gave rise to a Δ-mononuclear complex.[6] This phenomenon can be rationalised by examining the degree of rigidity in the free ligand strand, and is reflected in the Cotton effect exhibited by each of the ligands, with ligands **L1** and **L2** exhibiting a significant exciton coupling

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in the π–π* absorptions, while **L3** does not. In order to explore the relationship between the rigidity and the resulting behaviour, we report herein on ligand **L4**, which has a much higher degree of rigidity than the species examined in our earlier studies.

2. Results and discussion

The Schiff base derivative **L4** was prepared by reacting 5-formyl-2,2′-bipyridine with (1*S*,2*S*)-(+)-1,2-diaminocyclohexane in reasonable yield and the product characterised by standard techniques. The compound gave a strong specific rotation $\{[\alpha]_D = +105\}$ consistent with ligand **L1**.[5] Following slow solvent evaporation from an aqueous methanolic solution, crystals suitable for X-ray diffraction studies were obtained. The determination confirmed the proposed connectivity and demonstrated that in the solid state, the two-bipyridine groups are positioned above each other in a right-handed (+) orientation (Fig. 1) defined by the torsion angle about N14a–C15a–C15b–N14b (+62.3°). Examination of the packing indicated that the bipyridines align to maximise edge-to-face H–π ring contacts and this result correlates directly with those previously reported for the protonated form of ligand **L1**.[5] The two nitrogen atoms appended to the 1,2-diaminocyclohexyl group adopt an equatorial orientation consistent with previous observations of Kwit and Gawronski[9,10] and Hodacova et al.[11]

The UV studies of the complex indicate a strong absorption at 305 nm ($\varepsilon = 24{,}500\,\mathrm{dm^{-3}\,mol^{-1}\,cm^{-1}}$) attributed to a combination of π–π* and n–π* excitations.[12–14] The observed absorption proved to be broader than that observed for 2,2′-bipyridine, consistent with exciton coupling between the two chromophores. The existence of the restricted orientation of the two organic chromophores was confirmed by the presence of a measurable Cotton effect (Fig. 2) with a positive peak at 310 nm ($\Delta\varepsilon = 12.0\,\mathrm{dm^{-3}\,mol^{-1}\,cm^{-1}}$) and a negative peak at 280 nm ($\Delta\varepsilon = 2.5\,\mathrm{dm^{-3}\,mol^{-1}\,cm^{-1}}$) in dichloromethane. Similar spectra (within 5% of the differential extinction coefficients) were observed in acetonitrile, acetone and DMSO. However in methanolic and aqueous ethanolic mixtures, the observed Cotton effect was dramatically reduced. In a protic environment it would appear that the ligand can adopt a wider range of conformations than in less polar media, presumably due to the formation of hydrogen bonds. Examination of the sign of the Cotton effect and the application of exciton theory indicates that the (*S*,*S*)-configured 1,2-diaminocyclohexane gives a positive (+) orientation of the two chromophores in keeping with previous studies.[5,9,14,15] To confirm that the solution orientation is consistent with the solid state, the CD spectrum of the solid crystalline product was also recorded as a KBr disc. While the Δε scale is meaningless in this case, the sign remains the same (albeit slightly red shifted) indicating a similar orientation of the two chromophores in solution to those in the solid state. More importantly, the complex does not appear to have the two potentially chelating ligands in axial positions, where the anticipated Cotton effect would be negligible.

The solution conformation was further confirmed by ^{1}H NMR studies. The predicted C_2-symmetry was evident, while the two dimensional ^{1}H NOESY spectrum showed a close contact between the bipyridine H^6 proton and the imine proton, indicating that these two protons are in a *syn*-conformation. Similarly, an NOE cross peak was detected between the imine proton and the cyclohexane proton H^1, again indicating a *syn*-conformation, in keeping with the X-ray structure and similar to previously reported compounds.[10,14]

Upon the introduction of zinc(II), cadmium(II), cobalt(II) or iron(II) cations to ligands **L1**, **L2** and **L3**, it was found that, as the ligand strands are brought together to allow inter-ligand exciton coupling, the observed Cotton effect showed a significant increase. In contrast, the addition of metal ions to **L4** did not give

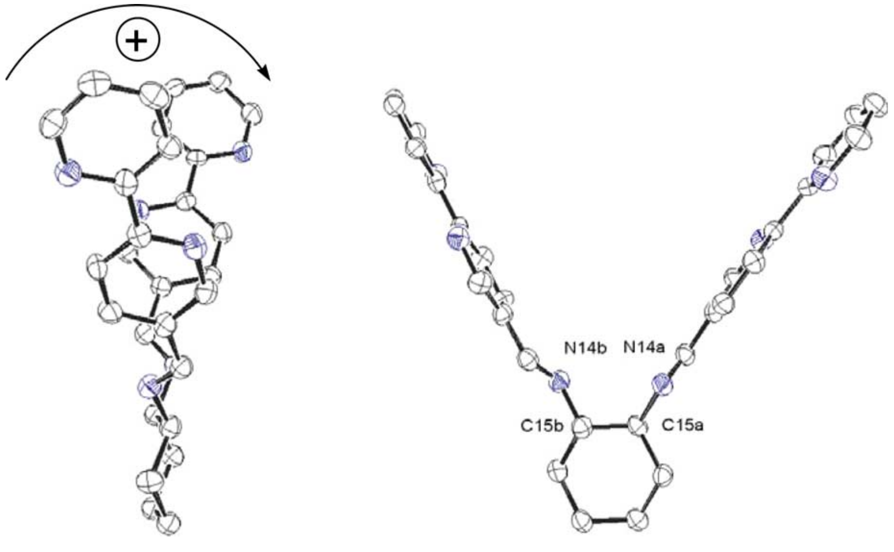

Figure 1. The structure of **L4** with ellipsoids at 50% probability. Hydrogen atoms have been deleted for clarity.

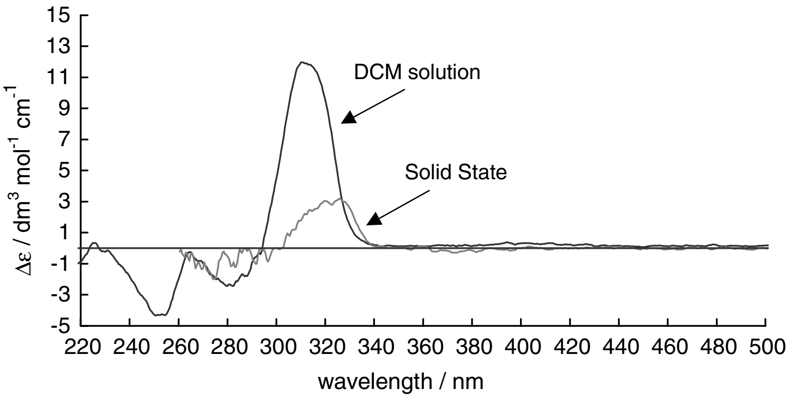

Figure 2. CD spectrum of **L4** (dichloromethane) and in the solid state (KBr disc).

rise to an observed increase in Cotton effect, although the characteristic red/purple colour of an iron(II) bipyridine complex was observed upon the addition of an aqueous iron(II) sulfate solution. Although metal complexes could be precipitated upon addition of ammonium hexafluorophosphate, the resulting intractable materials proved to be impossible to characterise. In particular, there was no observed iron(II) or zinc(II) containing clusters with either electrospray or FAB mass spectroscopy, unlike the preceding studies. It is assumed that the insoluble products from the reactions are predominantly composed of polymeric materials.

To gain an understanding of this apparent inconsistency in behaviour as the ligand series illustrated in Scheme 1 is descended, a series of molecular modelling studies were carried out to explore the imposed rigidity of the two diimine bonds to the orientation of the two 2,2′-bipyridine groups in **L4**. Density functional theory (DFT) calculations were used to optimise the geometry of **L4** in the gas-phase. In these calculations it was assumed that an equatorial orientation of the bipyridine groups is adopted, as appears to be the case in the solid state. A subsequent vibrational frequency calculation on the optimised structure (Fig. 3a) showed that all vibrational frequencies were real and positive, indicating that an energy minimum structure (rather than a transition-state structure) had been located. The calculated structure showed a remarkable similarity to that of the experimentally determined solid state structure (Fig. 3b) with the small discrepancies presumably arising from the intramolecular packing interactions in the solid state. In particular, the bipyridine units adopt the anticipated co-planar conformation, with the N^{py2}–C^{py1}–$C^{py1'}$–$N^{py2'}$ torsion angle at 180.0° [X-ray structural determination being 175.0(8)° and 175.7(8)°, respectively]. Similarly, the imine–pyridine N^{im}–C^{im}–C^{py5}–C^{py6} torsion angle is 179.4° [X-ray structural determination being 160.4(8)° and 174.2(8)°, respectively]. The only nonconjugated bond between the rigid cyclohexane and the imine group adopts a conformation consistent with previous studies by Kwit and Gawronski whereby the axial cyclohexane H^1 and the hydrogen on the imine carbon are in a *syn*-conformation[10] defined by the torsion angles labelled T_1 and T_2 (C^{cy6}–C^{cy1}–N^{im}–C^{im}) calculated to be 119.5° (X-ray structural determination being 114.6(8)° and 103.2(8)°, respectively).

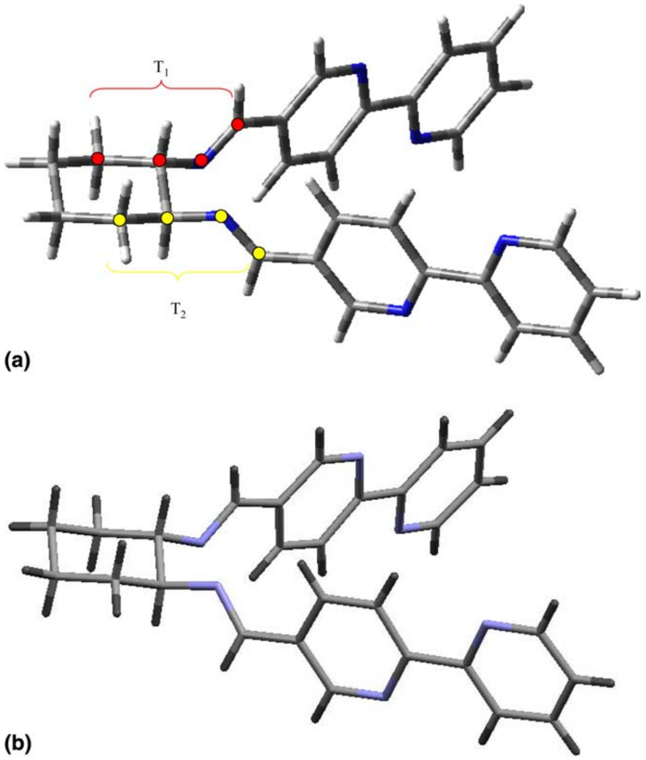

Figure 3. (a) The DFT calculated structure of **L4** and (b) the X-ray structural determination of **L4**.

For **L4** to form discrete oligonuclear triple helicates, the two chelating moieties must reorientate themselves, by changing the torsion angles T_1 and T_2, these being the only nonconjugated bonds capable of a relatively low energy rotation. While this appears to be feasible in **L1** and **L2**, the energy required for this reorientation appears to be prohibitive for **L4**, thereby preventing the formation of discrete oligonuclear species with a well-defined metal centred stereochemistry. To understand this problem, the DFT optimised structure of **L4** was further explored by carrying out a normal scan using semi-empirical AM1 parameters. In this calculation the

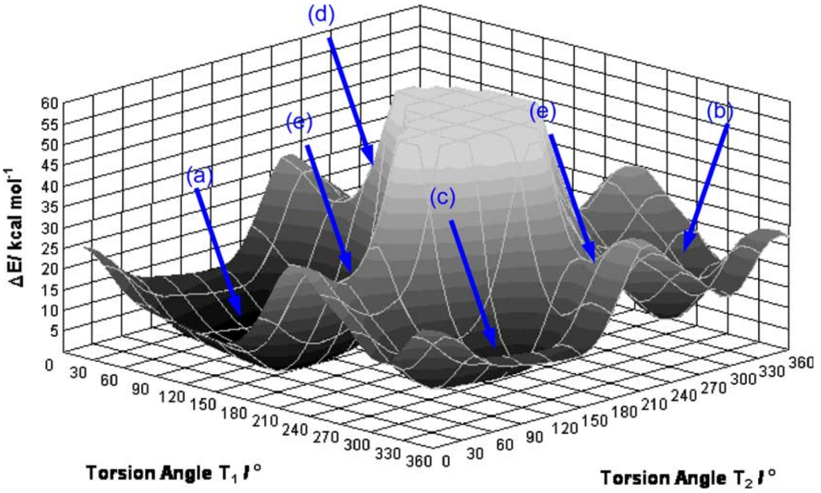

Figure 4. AM1 potential energy surface for the rotation of the DFT optimised structure of **L4** by the rotation around the two C–N cyclohexane imine bonds in 10° steps (signals over 60 kcal mol^{-1} have been omitted to indicate the finer detail).

two torsion angles, T_1 and T_2, were incrementally rotated in 10° steps and the relative energies for each new geometry calculated, giving a potential energy surface (Fig. 4). As expected, the plot was symmetrical reflecting the C_2-symmetry of the system, with a large peak in the centre (T_1 and $T_2 = 190°$) is almost 1800 kcal mol^{-1} higher in energy than the minimum conformation corresponding to the two bipyridine functions occupying the same space. In addition to the optimised energy minimum at approximately T_1 and $T_2 = 120°$ [arrow (a)], three other minima are identified. Again, along the diagonal axis a minimum, 7.5 kcal mol^{-1} higher in energy than the lowest point, occurs as T_1 and $T_2 = 300°$ [arrow (b)]. This conformation corresponds to an *anti*-conformation for both the protons on the cyclohexane group and the hydrogen on the imine carbon.[10] Similarly, two minima were observed with $T_1 = 300°$, $T_2 = 120°$ [arrow (c)] and $T_1 = 120°$, $T_2 = 300°$ [arrow (d)], 5 kcal mol^{-1} higher in energy than the most stable conformation, corresponding to one cyclohexane proton being *syn* to the hydrogen on the imine carbon, and the other *anti*.

For the formation of a triple helicate, both of the two chelating groups must be reorientated into the *anti*-conformation, requiring two energy barriers to be overcome, corresponding to the saddle points [Fig. 4, arrow (e)] at 26.5 kcal mol^{-1} for each of the ligands involved. Alternatively, it is conceivable that an *E*- to *Z*-isomerism of an imine C=N bond could occur, although without protonation this would appear to be energetically extremely unfavourable. Interestingly, Gargiulo et al. demonstrated an inversion of the Cotton effect upon protonation of one imine group, and demonstrated *E*- to *Z*-isomerism in a similar compound.[14] In order to explore the effect of rotation of the two torsion angles T_1 and T_2 on the sign of the Cotton effect, as would be predicted by exciton theory, AM1 optimised conformations were analysed by rotating both T_1 and T_2 in 30° steps and examining the dihedral angle between the long axis of the two chromophores ($C^{1\text{-py5}}$–$C^{1\text{-py5}'}$ and $C^{2\text{-py5}}$–$C^{2\text{-py5}'}$) obtained (Fig. 5). Again the surface confirmed the C_2-symmetry of the structure. The majority of the results indicated a positive dihedral angle, as predicted between the two chromophores, giv-

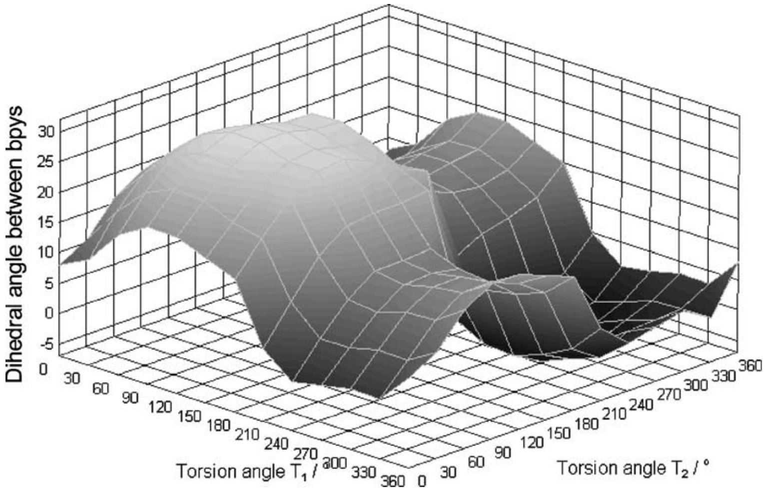

Figure 5. Calculated dihedral angles between the two chromophores using AM1 optimised structures of **L4** by the rotation around the two C–N cyclohexane imine bonds in 30° steps.

ing rise to the anticipated CD spectrum assuming it arises from the coupling of the long axis electronic transitions of the 2,2′-bipyridine chromophore.[16] Interestingly, the sign of the dihedral angle between the two chromophores inverts in the region between $T_{1 \text{ and } 2} = 210–330°$. This conformation corresponds to an *anti*-conformation for both the protons on the cyclohexane group and the hydrogen on the imine carbon and so complexation would be accompanied by an inversion of the Cotton effect, were only a single ligand strand involved in the process.

3. Conclusion

In conclusion, it would appear that **L4** can be prepared, however the increased rigidity in the system prevents the formation of discrete helicates contrary to the studies on ligands **L1** and **L2**. Complexation of **L4** is probably further complicated by the ability of the central diimine section to form coordinate bonds leading to greater opportunities to form cross-linked polymeric coordination networks. Examination of the solution CD and ^{1}H NMR spectra of **L4** indicate that the same conformation is adopted in solution as in the solid state, further confirmed by DFT studies. In order to form a triple-stranded helicate, both the chelating groups must twist around into a less favourable *anti*-conformation, then coordinate to a metal centre, while two other ligands are doing likewise at the same time. This appears to be possible for **L1** and **L2**, but under reversible metal chelation conditions, the energy barriers involved in reorientating the chelating bipyridine groups appear to be prohibitive with **L4**. From the strong Cotton effect observed for **L4**, we would have predicted that this would give rise to a high diastereoselectivity upon complexation to labile metal ions. Unlike ligands **L1** and **L2**, this does not appear to be the case, while ligand **L3**, which has no measurable circular dichroism spectrum gives a strong Cotton effect upon the introduction of zinc(II) ions. This would therefore imply that a reasonably high degree of ligand flexibility is required to induce metal centred helicity upon complexation. It would also appear that by the rotation along a couple of the bonds, the apparent ligand centred helicity can be inverted, despite retaining the same (*S*)-configured stereogenic centres. As a consequence, the (*S*,*S*)-configuration can potentially give rise to both positive and negative helicity depending on the substituent orientation.

4. Experimental

All instrumentation was the same as used in previous publications.[5–7] (1*S*,2*S*)-(+)-1,2-diaminocyclohexane (Aldrich 99%), were used as received. 5-Formyl-2,2′-bipyridine was prepared via a literature procedure.[17]

4.1. *N*,*N*′-Bis(2,2′-dipyridyl-5-methylene)-(1*S*,2*S*)-1,2-diiminocyclohexane L4

(1*S*,2*S*)-(+)-1,2-Diaminocyclohexane (0.438 mmol, 50 mg) was mixed with dry THF (60 mL) with 5-formyl-2,2′-bipyridine (1.31 mmol, 242 mg) and the reaction mixture stirred for 24 h. The volume of solvent was reduced to 20 mL and the resulting solid removed by filtration. The solid was washed with a methanol–water mixture and dried in vacuo. Yield 0.120 g, 61.4%. Mp 170 °C, found C, 70.94; H, 5.90; N, 17.11; analysis calculated for $C_{28}H_{26}N_6 \cdot 1.5H_2O$; C, 71.01; H, 6.17; N, 17.75; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56 (2H, m, H^{C4}), 1.96 (2H, m, H^{C2}), 3.50 (2H, br, C*H*–N), 7.30 (2H, d/d, $J = 4.5$ and 7.2 Hz, bipy$H^{5'}$), 7.80 (2H, d/d, $J = 2.0$ and 7.6 Hz, bipy$H^{4'}$), 8.10 (2H, d, $J = 8.3$ Hz, bipyH^4), 8.26 (2H, S, –CH=N), 8.39 (2H, d, $J = 8.1$ Hz, bipy$H^{3'}$), 8.40 (2H, d, $J = 7.9$ Hz, bipyH^3), 8.66 (2H, d, $J = 4.8$ Hz, bipy$H^{6'}$), 8.80 (2H, S, bipyH^6), ^{13}C NMR (300 MHz, $CDCl_3$) δ 23.57, 31.43, 72.85, 120.00, 121.43, 123.57, 130.00, 134.28, 135.71, 147.86, 148.57, 154.29, 156.43, 157.86, IR (KBr disc) 1641 (–C=N–imine), 1593 (–C=N–bipy), ES-MS: *m*/*z* 447.2 (MH^+, 45%).

4.2. X-ray structural analysis

Crystals of **L4** were grown by slow evaporation from a methanolic/water solution. Data were collected on a Brüker-AXS SMART diffractometer using the SAINT-NT[18] software with graphite monochromated Mo K_α radiation. A crystal was mounted onto the diffractometer under N_2 at ca. 150 K. Crystal stability was monitored with no significant variations ($< \pm 2\%$). ω/phi scans were employed for data collection and Lorentz, polarisation and empirical absorption corrections were applied. The structure was solved using direct methods and refined with the SHELXTL version 5.0 and SHELXL-97 program packages[19] while the non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atom positions were added at idealised positions and a riding model with fixed thermal parameters ($U_{ij} = 1.2U_{eq}$ for the atom to which they are bonded), was used for subsequent refinements. The absolute configuration was assigned based on the fact that pure (*S*,*S*)-1,2-diaminocyclohexane was used in the ligand synthesis. The function minimised was $\Sigma[w(|F_o|^2 - |F_c|^2)]$ with reflection weights $w^{-1} = [\sigma^2|F_o|^2 + (g_1P)^2 + (g_2P)]$ where $P = [\max|F_o|^2 + 2|F_c|^2]/3$. CCDC number 186699 contains the supplementary crystallographic data for the paper. *Crystal data for* $C_{28}H_{26}N_6$: $M = 446.55$, monoclinic, space group $P2_1$, $a = 14.7238(15)$ Å, $b = 5.3857(5)$ Å, $c = 15.2345(15)$ Å, $B = 103.328(2)°$, $U = 1175.5(2)$ Å^{-3}, $Z = 2$, $\mu = 0.078$ mm^{-1}, $R_{int} = 0.0620$. A total of 13,685 reflections were measured for the angle range $2.8 < 2\theta < 57$ and 5207 independent reflections were used in the refinement. The final parameters were $wR2 = 0.1766$ and $R1 = 0.0594$ [$I > 2\sigma I$].

4.3. Calculations

The density functional calculations were carried out using *Gaussian 98*[20] with the hybrid B3-LYP functional and the 6-31G(d) basis set.[21] The modified GDIIS algorithm was used instead of the default rational function optimisation (RFO) because the latter did not reach a stationary point under the 'tight convergence' conditions used throughout this work. Following geometry optimisation using the DFT method, a normal scan was carried out using AM1 model chemistry with each of the two dihedrals T_1 and T_2 were rotated in increments of 10° to obtain the potential energy surface. Dihedral angles between the two bipyridine functions were calculated by AM1 optimisation of each structure restrained to the desired T_1 and T_2 dihedral angles. Several other bonds were restrained to mimic the DFT optimised structure, with the cyclohexane moiety fixed into the chair conformation, by fixing the dihedral angles C^{cy1}–C^{cy2}–C^{cy3}–C^{cy4} and C^{cy2}–C^{cy1}–C^{cy6}–C^{cy5} to 56°, and the imine and bipyridine groups held in a planar conformation, by setting the dihedral angles C^{py5}–C^{py4}–C^{im}–N^{im} and C^{py3}–C^{py2}–$C^{py2'}$–$N^{py1'}$ to 0° for both bipyridine groups.

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