Diastereospecific synthesis of amino-acid substituted 2,2′-bipyridyl complexes

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The L-valine substituted 2,2′-bipyridyl ligand 1 forms Δ-M(1)$_3$ (M = Fe^{II}, Co^{II}, Co^{III}) complexes diastereospecifically, with the L-valinate arms forming a chiral anion-binding pocket in the solid state.

Tris(2,2′-bipyridyl) metal complexes are among the most studied in coordination chemistry. Although the complexes are inherently chiral, simple bipyridines invariably lead to mixtures of enantiomers. To achieve stereoselectivity at the metal centre, the ligands must be modified to introduce an element of chirality as discussed recently by Knof and von Zelewsky.[1] For some years we have been interested in the synthesis of triple helicates using octahedral metal ions binding to multibidentate ligands, and the stereoselective synthesis of such complexes is an obvious challenge. With a view to combining stereo-selectivity and the synthesis of heteronuclear helicates we conceived the ligand valabipy, **1**, comprising three bidentate
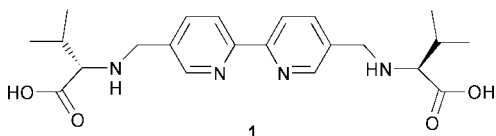
sites, one bipyridyl and two amino acids. The amino acid moiety could induce stereoselectivity in the coordination of metal ions, as demonstrated by Bernauer's group for mononuclear complexes of pyridine-amino acid ligands,[2] and the different ligating powers of bipyridyl and amino acids should allow the binding of different metal ions in the two sites. Ligand **1** is a rare example of a chiral 5,5′-substituted bipyridyl ligand and here we report the surprising observation of diastereospecificity when *only* the achiral bipyridyl chelating unit is occupied, and the observation of anion binding at the amino acid site in the solid state.

Valabipy **1** is prepared in three steps from diethyl-2,2′-dipyridyl-5,5′-dicarboxylate[3] by reduction of this ester to the corresponding alcohol, formation of the chloro derivative, and substitution of the chloride by L-valine in basic methanol.† The neutral ligand is sparingly soluble in water, but dissolves readily in slightly acid solution. If a solution of three equivalents of **1** in dilute HCl is treated with one equivalent of iron(II) perchlorate, a red–violet solution is obtained, indicating complexation of low spin iron(II) in the bipyridyl site. The composition [Fe(**1**)$_3$]$^{2+}$ was confirmed by electrospray mass spectrometry. The ^{1}H NMR spectrum of the diamagnetic complex showed it to be a mixture of diastereomers, most clearly revealed by the signals due to the α proton of the amino acid and the 6,6′-protons of the bipyridyl moiety. The initial ratio of diastereomers was 2:1, but on warming to 60 °C or on standing overnight, the weaker set of signals completely disappeared, indicating a thermodynamically controlled diastereospecificity. On the basis of the sign of the CD bands arising from the exciton coupling of the π–π* transitions, we can assign the Δ

configuration to the thermodynamically stable diastereomer (Fig. 1).[4,5]

If the labile cobalt(II) ion was used instead of iron(II), the complex was less stable in acid solution than [Fe(**1**)$_3$]$^{2+}$ but in the pH range 4–5 the paramagnetic ^{1}H NMR spectrum showed a set of 9 peaks corresponding to [Co(**1**)$_3$]$^{2+}$. The sign of the exciton couplet in the CD spectrum again indicated a Δ-configuration at the metal centre (Fig. 1). [Co(**1**)$_3$]$^{2+}$ could be oxidised by hydrogen peroxide to give the corresponding cobalt(III) complex. The ^{1}H NMR spectrum of the crude product showed predominantly one diastereomer, with traces of some minor products easily removed by crystallisation. The CD spectrum indicated that the oxidation reaction was stereo-retentive, yielding Δ-[Co(**1**)$_3$]$^{3+}$ (Fig. 1).[4,6]

If valabipy is synthesised using D-valine, instead of natural L-valine, the enantiomeric ligand **2** is obtained. As expected, the CD spectrum of [Co(**2**)$_3$]$^{2+}$ was the mirror image of that seen for [Co(**1**)$_3$]$^{2+}$, indicating that the Λ configuration is favoured for [Co(**2**)$_3$]$^{2+}$. Interestingly, when three equivalents of **1**, three equivalents of **2** and two equivalents of cobalt(II) were mixed, the ^{1}H NMR spectrum was identical to that of [Co(**1**)$_3$]$^{2+}$. This demonstrates that the ligands undergo a homochiral self-recognition process, preferentially forming Δ-[Co(**1**)$_3$]$^{2+}$ and Λ-[Co(**2**)$_3$]$^{2+}$ over any mixed ligand species.

Crystals suitable for an X-ray structure determination were obtained from a solution of [Fe(**1**)$_3$]$^{2+}$ in 1 M HCl with added sodium perchlorate.‡ The crystal structure of [Fe(**1**H$_2$)$_2$(**1**H)-Cl$_2$](ClO$_4$)$_4$Cl·14H$_2$O confirmed the Δ-configuration for the [Fe(bipy)$_3$] unit, and revealed, to our surprise, the binding of two chloride ions by the complex. The cation may be regarded as a helicate in which the helical axis is defined by the Cl–Fe–Cl direction [angle Cl–Fe–Cl 179.50(6)] and the **1** ligands twist around the axis (Fig. 2 and 3).

The structure is held together by coordinate bonds between the iron and the bipyridyls, and hydrogen bonds and electro-
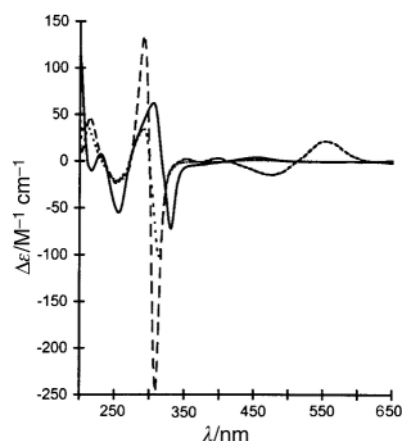

Fig. 1 CD spectra of [Fe(**1**)$_3$]$^{2+}$ (- - - -), [Co(**1**)$_3$]$^{2+}$ (pH 4.2) (·····), and [Co(**1**)$_3$]$^{3+}$ (——) in aqueous solution.
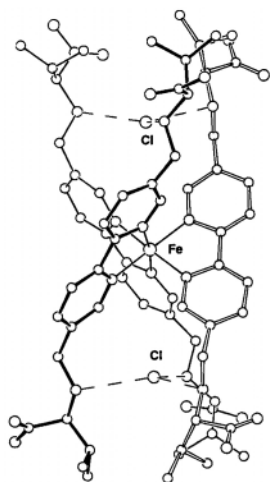
Fig. 2 View of the solid state structure of the [Fe(**1**H)(**1**H₂)₂Cl₂]⁵⁺ cation showing the threefold hydrogen bonding of the chloride ions.
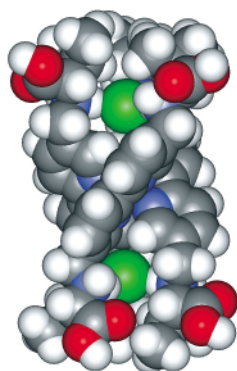
Fig. 3 Space filling view of the structure of the [Fe(**1**H)(**1**H₂)₂Cl₂]⁵⁺ cation perpendicular to the pseudo-threefold axis. The iron atom is hidden by the bipyridyl unit; the chloride ions are shown in green and the carboxylate oxygens in red.

static interactions between the chlorides and the protonated amino residues of the ligand. The geometry of the Fe(bipy)₃ unit is normal[7] with an average Fe–N distance of 1.968 Å, interplane torsional angles for the bipyridyl units between 4 and 8°, and approximate D_3 symmetry. The isopropyl side chains of **1** are oriented so that they are clustered together around the helical axis, while the carboxylates are directed away from the axis to form a hydrophilic surface. The crystal packing of the cations shows an ABCABC packing of layers with the pseudo-threefold axis of the cation perpendicular to the layers and parallel to the [1 1 1] direction. The amino acid moieties are protonated on all the amino groups, and on five of the carboxylates, although the deprotonated carboxylate is delocalised between two sites. One of the N–H protons of each amino group is directed towards the helical axis and is available to hydrogen bond the chloride ions, with average N⋯Cl distances of 3.16 Å, typical of N–H⋯Cl hydrogen bonding. Each chloride forms three hydrogen bonds in an approximately trigonal arrangement, but is displaced slightly out of the N₃ plane towards the iron atom which is 4.98 Å away.

Whilst this manuscript was in preparation, a ruthenium(II) complex with amide-substituted 2,2′-bipyridyl ligands was shown by Beer and coworkers to encapsulate chloride ions in both the solid state and in solution (MeOH–CH₂Cl₂).[8] The anion binding site is very similar, though in the case of **1** the

cationic ammonium units form significantly shorter N–H⋯Cl bonds, and both the chloride ions form three hydrogen bonds in the solid state, whereas in ref. 8 one chloride ion formed two hydrogen bonds and the other three hydrogen bonds.

It is interesting that for [M(**1**)₃]ⁿ⁺, the stereoselective organisation of **1** around the metal ion leads to the generation of a chiral receptor site at each end of the complex. The nature of this site may be modified by changes in the chelating side arms used to construct the ligand and thus these complexes have promise as tunable selective chiral anion sensors—an area of much current interest.[9]

The diastereospecific formation of Δ-[Fe(**1**)₃]²⁺ is initially surprising when the distance of the chiral centres of the ligand from the iron atom is considered. The fact that the complex may be crystallised from strongly acid (1 M HCl) solution implies that an additional stabilising element is present since α-diimine complexes such as [Fe(phen)₃]²⁺ or [Fe(diethyl-2,2′-dipyridyl-5,5′-dicarboxylate)₃]²⁺ are rapidly decomposed under these conditions. The observation that the labile Co^II ion shows immediate diastereoselectivity, whereas the kinetically more inert Fe^II ion takes longer for the ¹H NMR and CD spectra to stabilise indicates that the selectivity is thermodynamic rather than kinetic. Current investigations in this laboratory are focussing on the precise origins of the observed diastereo-selectivity and the behaviour of the anion receptor site in solution.

Notes and references

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