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Iron and cobalt complexes of 5,5′-di(methylene-*N*-aminoacidyl)-2,2′-bipyridyl ligands: ligand design for diastereoselectivity and anion binding †

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Received 13th September 2002, Accepted 28th November 2002
First published as an Advance Article on the web 10th January 2003

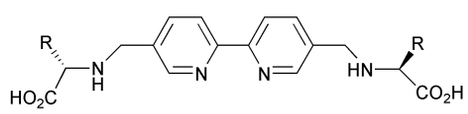
The syntheses and coordination chemistry of 5,5′-di(methylene-*N*-aminoacidyl)-2,2′-bipyridyl ligands, where the amino acid is valine (**1**) or alanine (**2**), are presented. Complexes $[M(\mathbf{1})_3]^{n+}$, where M = Co(II), Co(III) and Fe(II), form diastereoselectively when the amine group of the amino acid arm is protonated. At higher pH the diastereoselectivity drops significantly. The solid state structure of $[Co^{III}(\mathbf{1}H_2)_3]Cl_2(ClO_4)_7$ was determined by X-ray crystallography. Two chloride ions were found to be encapsulated by the amino acid arms of the complex *via* electrostatic attractions and hydrogen bonding to the protonated amine groups, as seen previously for the Fe(II) complex. No anion binding was detected in aqueous solution, but complexes $[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)]^{7+}$ and $[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ bind chloride ions in CD_3OD with binding constants of 60(4) and 24(2) M^{-1} respectively, as determined by ^1H NMR spectroscopy. ^1H NMR spectroscopy suggests considerable conformational change of the ligand sidearms upon chloride binding. Complexes $[Fe^{II}(\mathbf{2})_3]^{2+}$ and $[Co^{II}(\mathbf{2})_3]^{2+}$ are formed with d.e.'s of 33 and 56% respectively.

Introduction

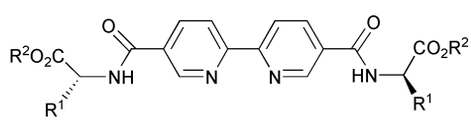
There is considerable current interest in the stereoselective synthesis of transition metal complexes as coordination chemists strive to acquire a deeper understanding of the factors which can exert control over the configuration of the metal centre. One method is to 'predetermine' the metal chirality by introducing chiral information into the ligands, as discussed recently by Knof and von Zelewsky.[1] Examples of this approach can be found in the work of von Zelewsky's group[2] which has shown that the attachment of chiral α-pinene units to bipyridyl ligands can dictate the conformation at the metal centre. Bernauer's group has demonstrated that multidentate pyridine-amino acid ligands can bind to metal ions with high stereoselectivity.[3]

With a view to the stereoselective construction of heteronuclear helicates, we designed the multicompartmental ligand **1** and recently we reported[4] that it forms complexes $[M(\mathbf{1})_3]$ (M = Fe(II), Co(II), Co(III)), where the bipyridyl binding sites are occupied. Given the distance of the chiral centres of the ligand from the metal centre, it was rather surprising to find that these complexes form diastereoselectively, only one of the two possible diastereomers being observed. Around the same time, a report appeared from Hong's group concerning a very similar family of ligands **3** (in which the amino acid is attached *via* an amide linkage) which were shown to complex Fe(II) with moderate diastereoselectivity.[5]

Ligand **1** was also able to encapsulate chloride ions in the chiral pockets formed by the amino acid arms in the solid state to form the complex $[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]^{5+}$.[4] Beer's group recently reported that ruthenium complexes of 5,5′-diamido-substituted bipyridyl ligands were also able to bind chloride ions both in the solid state and in solution.[6] Herein we present the full experimental details of the synthesis of ligands **1** and **2**, the crystal structure of the analogous cobalt(III) complex, together with further observations regarding both the diastereoselectivity of complexation and the behaviour of the anion binding site in solution.



R = i-Pr **1**
R = CH_3 **2**



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Results

Synthesis

The ligands **1** and **2** were prepared according to Scheme 1. Diethyl-2,2′-dipyridyl-5,5′-dicarboxylate (**4**) was prepared *via* a published procedure[7] and subsequent reduction by $NaBH_4$ and chlorination by $SOCl_2$ gave 5,5′-dichloromethyl-2,2′-bipyridine (**6**). Nucleophilic substitution of the chloride by the appropriate L-amino acid in basic methanol afforded **1** and **2** in satisfactory yield (*ca.* 60%). The insolubility of these ligands in cold neutral aqueous solution greatly facilitates their isolation and purification.

The complexes $[Fe^{II}(\mathbf{1})_3]^{2+}$ and $[Co^{II}(\mathbf{1})_3]^{2+}$ can be prepared simply by mixing three equivalents of the ligand and one equivalent of M^{2+} in dilute HCl solution. We were able to show (by ^1H NMR and CD spectroscopy)[8] that these complexes form diastereoselectively the thermodynamically preferred product with the Δ configuration at the metal centre.

Oxidation of Δ-$[Co^{II}(\mathbf{1})_3]^{2+}$ in dilute hydrochloric acid solution with hydrogen peroxide proceeds with retention of configuration to give Δ-$[Co^{III}(\mathbf{1})_3]^{3+}$ which could be precipitated as its perchlorate salt by the addition of dilute $HClO_4$. Recrystallisation from H_2O–$NaClO_4$ yielded a yellow crystal-

† Electronic supplementary information (ESI) available: ^1H NMR spectrum of $[Co(\mathbf{1})_3]^{3+}$ as a function of pH; 2D NOESY ^1H NMR spectrum of $[Co(\mathbf{1})_3Cl_2]^+$; 2D ROESY ^1H NMR spectrum of $[Co(\mathbf{1})_3]^{3+}$. See http://www.rsc.org/suppdata/dt/b2/b208934c/

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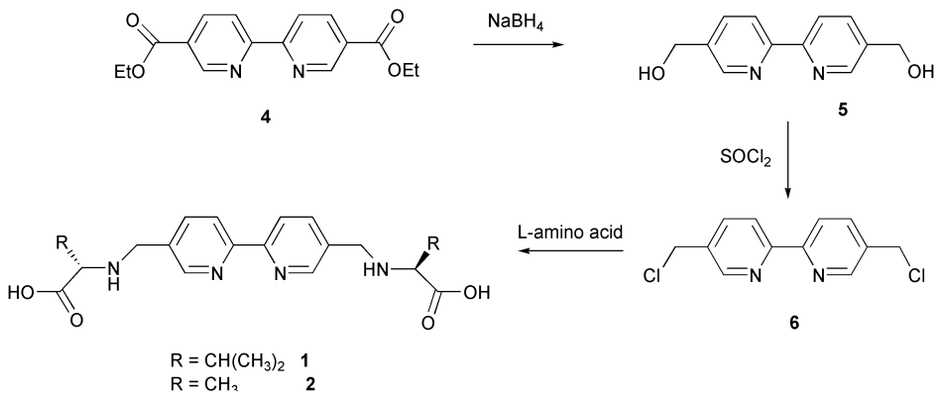


Scheme 1 Ligand synthesis.

line solid which gave an elemental analysis corresponding to $[Co(\mathbf{1}H_2)_3Cl_2](ClO_4)_7$ implying that all six carboxylate groups are protonated and two chloride ions are encapsulated by the complex. This formulation is consistent with the X-ray crystal structure analysis (see below) and is similar to the corresponding Fe(II) complex, $[Fe(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]Cl(ClO_4)_4$.

The pK_a range for the amine groups of the complex Δ-$[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ was established by potentiometric titration which showed that the six pK_as fell in the range 5.2–8.8. This is consistent with the changes observed in the ^1H NMR spectrum as a function of pH where large changes were noted for the chemical shifts of the 6,6′-bpy and α-amino acid protons ($\Delta\delta$ = 0.6 and 1.1 ppm respectively) in the pH range 6.0–8.0.

The X-ray crystal structure of $[Co^{III}(\mathbf{1}H_2)_3(Cl)_2](ClO_4)_7\cdot 12H_2O\cdot 2EtOH$

X-Ray quality single crystals of the complex could be obtained by recrystallising the crude perchlorate salt from a mixture of dilute HCl, dilute $HClO_4$, and ethanol. The X-ray crystal structure determination showed seven perchlorate groups confirming that the carboxylate functions are all protonated, as supported by the C–O bond distances. The crystal structure is very similar to that of $[Fe(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]Cl(ClO_4)_4$ with two chloride ions complexed by three hydrogen bonds to protonated amine functions (N ··· Cl distances 3.234(8), 3.163(8), 3.185(9) Å) (Fig. 1). The complex lies on a crystallographic twofold axis perpendicular to the pseudo-threefold axis of the tris-chelate complex. The coordination sphere of the cobalt is that expected for a tris-bpy unit with Co–N bond lengths between 1.930 and 1.949 Å. The twist angles between the two pyridine planes of the bipyridyl ligand are 3.31(3) and 5.45(3)° for the two crystallographically distinct ligands.

The conformation of the ligand is shown in Fig. 2. The substituents are arranged with the CH_2–NH_2 bond almost perpendicular to the plane of the pyridines, and the torsion angle of the pyridine-CH_2–NH_2–CH bonds close to 180° giving the expected *trans* conformation. This conformation brings the isopropyl groups and the protonated amine functions close to the threefold axis, while the carboxylic acid functions are directed to the exterior. The Cl–Cl distance is 9.63 Å, slightly shorter than in the iron complex (9.67 Å).

Do $[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)]^{7+}$ and $[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ bind chloride in aqueous solution?

The crystallised samples of Δ-$[Fe(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]Cl(ClO_4)_4$ and Δ-$[Co(\mathbf{1}H_2)_3Cl_2](ClO_4)_7$ have both amine and carboxylate functions protonated, and, in view of the measured pK values, their dissolution in water should not lead to dissociation of the protons from the amine groups of the ligand arms. Hence, in solution the complexes could adopt a structure identical to that seen in the solid state where a chloride ion is bound to all three protonated amine groups at each end of the complex. This possibility was probed by ^1H NMR spectroscopy which allows

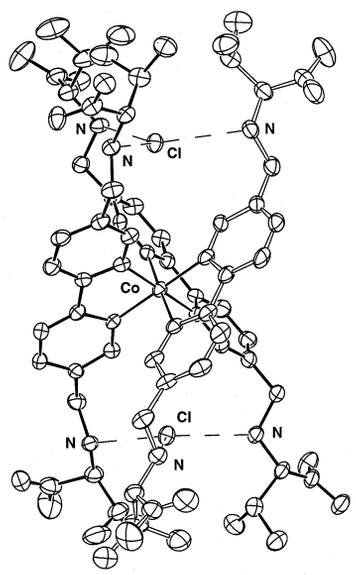


Fig. 1 Structure of the complex $[Co(\mathbf{1}H_2)_3Cl_2]^{7+}$. The ligand with open bonds is bisected by a twofold symmetry axis, the other two are related by this axis.

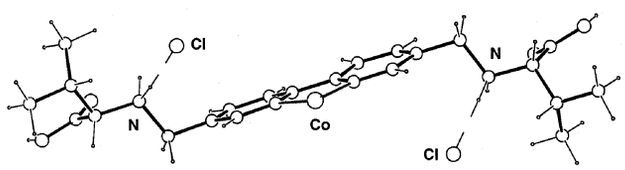


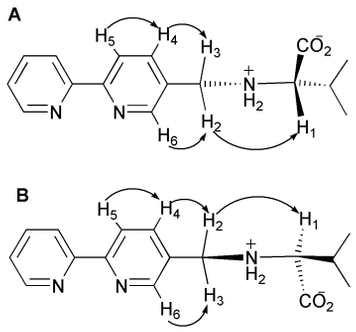
Fig. 2 Conformation of the ligand in the complex $[Co(\mathbf{1}H_2)_3Cl_2]^{7+}$.

a direct and informative characterisation of any binding processes.

A solution of Bu_4NCl was titrated into solutions of both Δ-$[Co^{III}(\mathbf{1}H_2)_3Cl_2](ClO_4)_7$ and Δ-$[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]Cl(ClO_4)_4$ in D_2O and the ^1H NMR spectrum was monitored. Only very minor changes in the ^1H chemical shifts ($\Delta\delta$ < 0.01 ppm) were noted up to the addition of 30 equivalents of chloride ion. Although this result almost totally eliminates the possibility that the complexes bind chloride ions in aqueous solution it might be argued that the binding constant is sufficiently high that the chloride ions shown to be bound by these complexes solid state remain *completely* bound when the complex is dissolved in H_2O. This possibility was excluded by recording the ^1H NMR spectrum of a solution of Δ-$[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]Cl(ClO_4)_4$ before and after the addition of three equivalents of $AgPF_6$ (which precipitated the chloride ions as AgCl). No significant change was observed ($\Delta\delta$ < 0.02 ppm).

A NOESY spectrum of the complex Δ-$[Co(\mathbf{1}H_2)_3Cl_2](ClO_4)_7$ in D_2O (in which it may be assumed that the amines are fully and the carboxylates at least partially protonated) shows strong

cross peaks between protons 3 and 6, 1 and 2, and 2 and 4, and weaker cross peaks between 1 and 3, 3 and 4, and 2 and 6 (Scheme 2). This is consistent with the conformation **B** in



Scheme 2 The strong intraligand NOE signals in complexes of Δ-$[Co(\mathbf{1}H_2)_3]^{9+}$. **A**: when chloride is bound, **B**: in the absence of chloride binding.

Scheme 2 in which the CH_2–NH_2^+–$CH(CO_2)$(–iPr) plane is perpendicular to the plane of the pyridyl group, but, if the Δ configuration implied by the CD spectrum is assumed for the cobalt, this requires the amino acid substituent to be bent away from the pseudo-threefold axis. This arrangement may serve to minimise the electrostatic repulsions between the positively charged nitrogen centres on adjacent ligands. In contrast, the complex adopts conformation **A** in the solid state (where the pyridine–CH_2 bond has been rotated by 180°) which allows the protonated amine groups to bind to the encapsulated chloride ion.

The binding of chloride ions in *non-aqueous* solution

The ^{1}H NMR spectrum of Δ-$[Co^{III}(\mathbf{1}H_2)_3Cl_2](ClO_4)_7$ in a variety of non-aqueous solvents (CD_3CN, DMSO-d_6, acetone-d_6, and CD_3OD) was found to change markedly upon the addition of Bu_4NCl (Fig. 3). The observed chemical shift

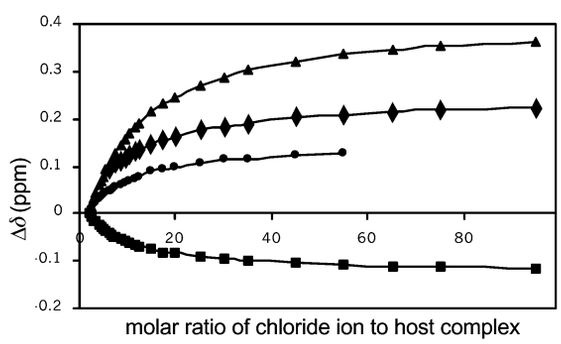


Fig. 3 The dependence of the chemical shift of H^6 (▲), H^2/H^3 (■ and ◆), and H^1 (●) protons of $[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ in CD_3OD on added Bu_4NCl. See Scheme 2 for the proton numbering scheme.

changes suggest that the complex is able to bind chloride ions *via* its protonated amine groups in a manner similar to that seen in the solid state: the protons close to the binding site, notably the alpha protons, the 6,6′-bipyridyl protons and the amine protons, were perturbed significantly ($\Delta\delta$ = 0.09–0.40 ppm after the addition of 50 equivalents of Bu_4NCl), whilst the chemical shifts of the 3,3′- and 4,4′-bipyridyl protons and those of the isopropyl group did not change significantly. Furthermore, the behaviour of the diastereotopic pyridylmethyl group is also indicative of certain structural changes. For example, in CD_3OD the two protons have very similar chemical shifts ($\Delta\delta$ = 0.04 ppm) but upon the addition of Bu_4NCl their anisotropy becomes more pronounced, leading to a chemical shift difference of 0.45 ppm at a $[Co^{III}(\mathbf{1}H_2)_3]^{9+}$: Cl^- ratio of 1 : 50. This increased non-equivalence is consistent with a more rigid arrangement of the amino acid arms which would be expected upon anion binding.

^{1}H NMR titration experiments were performed on the complexes Δ-$[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ and Δ-$[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)]^{7+}$ in order to determine equilibrium constants for the chloride binding process. CD_3OD was chosen as the solvent for reasons of complex stability and solubility at high chloride loadings. The titration results were analysed by the EQNMR program.[9]

The $[M(\mathbf{1}H_x)_3]^{n+}$ complexes have two anion receptor sites and thus two equilibrium models are possible. First, one overall equilibrium constant can be fitted: the receptor sites considered independent from each other with binding at the first site having no influence on binding at the second. Second, a two-step process can be imagined whereby two equilibrium constants can be fitted: the first to give an intermediate complex $[M(\mathbf{1}H_x)_3Cl]^{n+}$, with the second step yielding $[M(\mathbf{1}H_x)_3Cl_2]^{n+}$. We tested both models with the NMR data but we prefer the first model as (i) it gave significantly lower errors for the calculated equilibrium constants, (ii) no systematic deviations between observed and calculated chemical shift values were noted with this model, and (iii) one would not expect chloride binding at the first site to affect binding at the second: any conformational changes at the second site will be severely restricted by the rigidity of the metal centre, and furthermore the overall charge on the complex will remain high. A similar approach was employed by Hamilton and co-workers.[10]

The chemical shift changes of the 6,6′-bipyridyl protons were used to calculate the equilibrium constants as these protons underwent large chemical shift changes, were well separated from the HOD and Et_4N^+ peaks, and appear as a simple singlet. The values of the binding constants for Δ-$[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ and Δ-$[Fe^{II}(\mathbf{1}H_2)_2(\mathbf{1}H)]^{7+}$ were 24(2) and 60(4) M^{-1} respectively. This lower binding constant for the more highly charged Co^{III} complex may be attributed to the higher desolvation energy of this complex.

The ROESY spectrum was recorded for Δ-$[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ in the presence of an excess of chloride where the 1D NMR spectrum showed that the chloride bound species was predominant. The spectrum showed significant differences from that recorded for Δ-$[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ in water: the strong cross relaxation peaks were now observed between protons 1 and 2, 2 and 6, and 3 and 4. This implies that the sidearm with the amino acid has rotated about the pyridyl–carbon bond towards the threefold axis (conformation **A** in Scheme 2), to give a conformation similar to that observed in the crystal structure.

The influence of pH and chloride ions on the diastereoselectivity of $[Fe^{II}(\mathbf{1})_3]^{2+}$ and $[Co^{II}(\mathbf{1})_3]^{2+}$

The effect of omitting chloride ions on the diastereoselectivity of complex formation was investigated by preparing $[Fe^{II}(\mathbf{1})_3]^{2+}$ in (a) dilute aqueous HOTf (*ca.* 0.1%) solution, (b) neutral aqueous solution, and (c) ethanolic solution. The products were characterised by ^{1}H NMR spectroscopy and the results paralleled synthesis in dilute aqueous HCl: a mixture of diastereomers formed initially which, over time, gave Δ-$[Fe^{II}(\mathbf{1})_3]^{2+}$. The preparation of $[Co^{II}(\mathbf{1})_3]^{2+}$ in dilute aqueous HOTf displayed immediate high diastereoselectivity.

$[Co^{II}(\mathbf{1} - 2H)_3]^{4-}$ and $[Fe^{II}(\mathbf{1} - 2H)_3]^{4-}$ were prepared by dissolving ligand **1** in aqueous base before the addition of the metal. The spectral changes were similar to those observed in acidic solution, which indicated that the metal ion was bound in the bipyridyl sites. For $[Fe^{II}(\mathbf{1} - 2H)_3]^{4-}$, both diastereomers of this complex were evident in the ^{1}H NMR spectrum though only the peaks of the 6,6′-bipyridyl protons and the α protons were clearly distinguishable. Unfortunately, the peaks were rather broad which hindered the accurate measurement of integrals though a ratio of 2 : 1 (d.e. = 33%) was able to be estimated. This ratio was unchanged after warming overnight at 50 °C. CD spectroscopy implied a similar composition of

diastereomers — intensity of the signals being around 47% weaker than the complex Δ-$[Fe^{II}(\mathbf{1})_3]^{2+}$.

Synthesis of $[Co^{II}(\mathbf{1} - 2H)_3]^{4-}$ with $(\mathbf{1} - 2H)^{2-}$ led to a complicated paramagnetic ^{1}H NMR spectrum. An identical spectrum resulted when a solution of $[Co^{II}(\mathbf{1}H)_3]^{7+}$ was titrated with NaOD solution from pH 4.0 to 11.3. In the range pH 6–10 the signals were extremely broad though they became well-resolved again at pH 11.3. COSY NMR spectroscopy showed that two paramagnetic complexes were present though the concentration of the minor component was too low to allow full characterisation of the mixture by this method. However, the similarity in their chemical shifts suggested that the two diastereomers of $[Co^{II}(\mathbf{1} - 2H)_3]^{4-}$ were present, and integration of the respective signals gave a ratio of 9 : 2 (d.e. = 64 %). The results from CD spectroscopy were in excellent agreement: the maximum intensity of the spectrum was observed at pH 4.15 (d.e. = 100%), with the intensity diminishing progressively at higher pH values (Fig. 4).

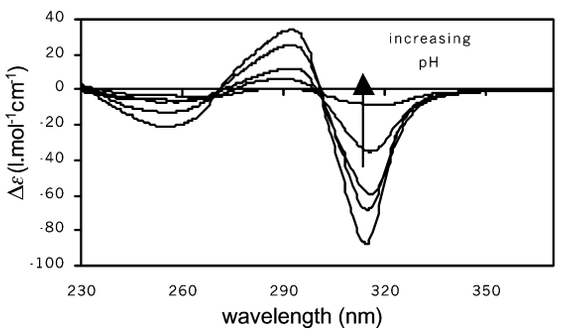


Fig. 4 The CD spectrum of $[Co^{II}(\mathbf{1} - nH)_3]^{(2-n)+}$ as a function of pH. Spectra were recorded at pH 5.4, 6.8, 8.7, 11.8, and 12.5.

The ROESY spectrum of Δ-$[Co^{III}(\mathbf{1}H_2)_3]^{9+}$ at high pH showed cross peaks of equal intensity between protons (2, 3) and (4, 6), and between proton 1 and (2, 3), suggesting a much less rigid conformation when the amine functionalities are deprotonated.

Complexes of 2

Complexes of the alanine-substituted ligand, $[Fe^{II}(\mathbf{2})_3]^{2+}$ and $[Co^{II}(\mathbf{2})_3]^{2+}$, were prepared directly in neutral aqueous solution, with the colours of both solutions (red–violet and golden yellow respectively) indicative of the metal ion occupying the bipyridyl binding sites, as anticipated. The ^{1}H NMR spectrum of the diamagnetic complex $[Fe^{II}(\mathbf{2})_3]^{2+}$ in D_2O (pH 4) clearly showed the presence of two diastereomers, even after prolonged heating at 70 °C. Integration of their respective signals showed that they were in a ratio of 2 : 1 (d.e. = 33%). The ^{1}H NMR spectrum of a 3 : 1 mixture of **2** and Co(II) at pH 5 shows a mixture of Δ- and Λ-$[Co(\mathbf{2})_3]^{2+}$ (7 : 2 ratio, d.e. = 56%), traces of a third paramagnetic complex, and free **2**. Around 80% of the ligand was present as $[Co^{II}(\mathbf{2})_3]^{2+}$, with the remainder uncoordinated. The third, very minor complex was not characterised with certainty though upon the addition of further Co(II) the intensity of its signals increased, leading finally to a very simple spectrum consistent with $[Co^{II}(\mathbf{2})_2]^{2+}$.

The significant drop in d.e. on going from the valine- to the alanine-substituted ligand was reflected by the relatively weak exciton coupling bands seen in the CD spectra of $[Fe^{II}(\mathbf{2})_3]^{2+}$ and $[Co^{II}(\mathbf{2})_3]^{2+}$. The sign of the CD bands indicated that the major diastereomer has the Δ configuration at the metal centre, as for the complexes with **1**.

Discussion

The structure of the cobalt(III) complex of $[\mathbf{1}H_2]^{2+}$ is essentially identical to that of the iron(II) complex reported previously.[4] The encapsulation of chloride ions by these complexes appears to be a consequence of the crystallisation since there is no evidence of anion binding in aqueous solution. NMR spectroscopy suggests that in aqueous solution the substituent arm of the bipyridyl is twisted away from the threefold axis. If the polarity of the solvent is lowered by moving to methanol, anion binding is clearly observed, and is accompanied by a considerable conformational change of the ligand, the side arms folding in a way reminiscent of the tentacles of an octopus (or at least a three legged one) to trap the chloride. The solvent dependence can be ascribed to competition for the binding sites from the water molecules and the higher desolvation energy of chloride ions in aqueous solution. It is also possible that some of the protons of the carboxylate groups dissociate in water, lowering the overall charge on the complex and creating a repulsive negative charge at the termini of the ligand arms. Anion binding, recognition, and sensing are research areas which are currently generating considerable interest[11] and transition metal-based receptors have featured prominently in these fields. Furthermore, chloride-selective receptors are relatively rare. It is hoped that the enantiopure chiral pockets of these complexes may enable them to discriminate between the enantiomers of chiral anions.

The origins of the diastereoselectivity remain somewhat uncertain. Hong *et al*. attributed the varying diastereoselectivity they observe with iron complexes of ligands **3** to intramolecular hydrogen bonding, notably involving the amide functions. Such interactions are not possible in ligands **1** and **2** and there is no evidence for amine–carboxylate interactions in our complexes. Furthermore, in the crystal structure of a similar amide-substituted bipyridyl ligand reported by Beer *et al*.,[6] the conformation of the side arm is quite different from **1**, since the amide function is essentially coplanar with the bipyridyl, and not perpendicular to it as is the case for **1**.

The crystal structures of complexes of **1** suggest that the close contacts between the substituent arms induced by the binding of the chloride ion might act to transfer the chirality of the substituent arm to the bipyridyl centre. However, given the absence of significant chloride ion–complex interactions in aqueous solution, it seems rather unlikely that the chloride ion plays a role in the diastereoselectivity of these complexes. More conclusively, the syntheses of Δ-$[M^{II}(\mathbf{1})_3]^{2+}$ in the absence of chloride ions were 100% diastereoselective. It might be argued that the chloride could be replaced by a hydrogen bonded water molecule(s) or that the protonated amine nitrogens form an intraligand hydrogen bond with the carboxylate groups. However, these hypotheses are weakened by the NMR data which suggest that in aqueous solution the conformation of the ligand arms is different from that in the solid state.

There is a clear increase in diastereoselectivity both upon protonation of the amine groups and upon increasing the steric bulk of the amino acid side chain. Protonation of the amine nitrogen locks it into a tetrahedral, sp^3 hybridized conformation which does not invert rapidly as does a free protonated amine. This would thus rigidify the substituent arms, and provide the appropriate mechanical linkage between the chiral centre of the amino acid and the metal centre. The ROESY spectrum recorded at high pH, where the amines are not protonated, suggests that there is much greater flexibility in these conditions, in agreement with rapid inversion. Further studies to investigate this hypothesis are in progress.

Experimental

General

Starting materials for synthesis were purchased from Fluka AG Buchs, Switzerland unless otherwise stated. Routine NMR spectra were recorded on a Varian Gemini-300 instrument at 300 MHz at 20 °C. The residual solvent signal was used as a

reference (D_2O 4.90 ppm; CD_3CN 1.95 ppm; CD_3OD 3.31 ppm). ^{13}C NMR spectra in D_2O were referenced to dioxane (δ 67.4 ppm). ROESY spectra were recorded on a Bruker 500 spectrometer. UV/Visible spectra were recorded on a Cary 1E spectrometer and CD spectra were recorded on a JASCO J-715 spectropolarimeter. Extinction coefficients and $\Delta\varepsilon$ values are given in units of l mol^{-1} cm^{-1}. A Perkin-Elmer Spectrum One instrument was used for the IR spectra which were recorded as KBr discs. Electrospray mass spectra (ES-MS) were recorded on the Finnigan Mat SSQ 7000 instrument of the Mass Spectrometry Laboratory, University of Geneva. Elemental analyses were performed by Dr H. Eder, University of Geneva.

^{1}H NMR anion binding titrations

Bu_4NCl solutions of approximately 0.15 M were added in aliquots to solutions of $[M(\mathbf{1}H_2)_x]^{n+}$ of approximately 5 mM concentration. In general, up to 90 equivalents of Bu_4NCl were added in 20–25 separate steps. Titrations were repeated at least twice. All spectra were recorded at 295.0 K. The EQNMR program was used to calculate binding constants.[9] The presence of chloride in the solid state samples of $[Co(\mathbf{1}H_2)_3Cl_2](ClO_4)_7$ and $[Fe(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2]Cl(ClO_4)_4$ was allowed for in the analysis.

Synthesis

5,5′-Dihydroxymethyl-2,2′-bipyridine (5). Diethyl 2,2′-bipyridine-5,5′-dicarboxylate (**4**)[7] (9.3 g, 0.031 mol) was added to ethanol (200 ml) and the suspension stirred in a flask equipped with a $CaCl_2$ drying tube. The mixture was cooled in an ice-water bath and $NaBH_4$ (5.2 g) was added in portions over a 20 min period before being allowed to warm slowly to room temperature. The mixture was then refluxed for 15 h, cooled and the solvent removed from the pale orange suspension. Acetone was added (200 ml) and the mixture refluxed for 2 h. The solvent was removed before H_2O (100 ml) was added and the mixture refluxed once again. The solution was concentrated to *ca*. 25 ml on a rotary evaporator and refrigerated for several hours before the product was filtered off as a white solid. Extraction of the filtrate with ethyl acetate yielded a second crop of product. The combined products were dried under vacuum. Yield (5.0 g, 71%). ^{1}H NMR (300 MHz, DMSO-d6): δ 4.59 (d, 2H), 5.39 (t, 1H), 7.86 (d, ^3J = 8.3 Hz), 8.35 (d, 1H), 8.61 (s, 1H). ^{13}C NMR (75.44 MHz, DMSO-d6): δ 60.5, 119.8, 135.5, 137.9, 147.7, 154.0. EI-MS: 216 ([M^+], 100%).

5,5′-Dichloromethyl-2,2′-bipyridine (6). 5,5′-Dihydroxymethyl-2,2′-bipyridine (5.0 g, 0.023 mol) was suspended in freshly distilled dichloromethane (80 ml) in a flask fitted with a $CaCl_2$ drying tube. $SOCl_2$ (9.0 ml) was added slowly with stirring before the reaction mixture was allowed to warm slowly to room temperature. After several hours at room temperature, the suspension was refluxed overnight. After cooling in an ice-water bath, excess $SOCl_2$ was carefully hydrolysed with H_2O (30 ml) and the resulting two layers were separated. The organic layer was washed with H_2O and the combined aqueous solutions neutralised with NH_3 solution. The desired product formed as a white precipitate which was filtered off, washed with H_2O and dried under vacuum. The organic layer was taken to dryness on a rotary evaporator to give a second crop of product. Combined yield (5.5 g, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.62 (s, 2H), 7.82 (d, ^3J = 8.3 Hz, 1H), 8.40 (d, 1H), 8.65 (s, 1H). ^{13}C NMR (75.44 MHz, $CDCl_3$): δ 43.2, 121.3, 133.6, 137.4, 149.3, 155.8. EI-MS: 252 ([M^+], 41%), 217 ([$M - Cl^+$], 100%), 182 ([$M - 2Cl^+$], 26%).

Preparation of 5,5′-di(methylene-*N*-L-valinyl)-2,2′-bipyridine (1). 5,5′-Dichloromethyl-2,2′-bipyridine (4.0g, 0.016 mol) was suspended in MeOH (50 ml) and a solution of L-valine (7.40 g, 0.063 mol) and KOH (3.52 g, 0.063 mol) in MeOH–H_2O (10 : 1, 15 ml) was added. The suspension was refluxed for 48 h and the resulting pale orange solution was cooled to rt and acidified to pH 7 with HCl. A white precipitate formed which was filtered off and washed with H_2O (2 × 5ml). The crude product was dissolved in 0.5 M HCl to give a pale yellow suspension, filtered through Celite to remove a fine precipitate and neutralised to pH 7 with NH_3 solution to re-precipitate the product. After refrigeration for several hours, the white solid was filtered off, washed with H_2O (2 × 5ml) and air-dried. Yield 60%. ^{1}H NMR (300 MHz, D_2O–DCl): δ 1.05–1.15 (dd, 6H), 2.42–2.48 (m, 1H), 4.08 (d, 1H), 4.59 and 4.65 (AB, ^2J = 13.4 Hz, 2H), 8.62 (s, 2H), 9.05 (s, 1H). ^{13}C NMR (75.44 MHz, D_2O–DCl): δ 17.3, 19.1, 30.1, 48.4, 66.8, 125.3 (2C), 131.3, 146.2, 148.6, 171.0. UV-Vis (0.1 M HCl): 307 (24000), 245 nm (13600). CD (0.1 M HCl): 310 (0.70), 208 (4.75). IR: 3407 (w, br), 2969 (m), 1557 (s), 1468 (m), 1322 (m), 843 cm^{-1} (m). Anal. C, 62.22; H, 7.20; N, 13.13. $C_{22}H_{30}N_4O_4 \cdot 0.5H_2O$ requires: C, 62.39; H, 7.39; N, 13.22%.

Preparation of 5,5′-di(methylene-*N*-L-alanyl)-2,2′-bipyridine (2). The ligand was prepared in an analogous fashion to **1**. ^{1}H NMR (300 MHz, D_2O–DCl): δ 1.66 (d, 3H, J = 7.1 Hz), 4.22 (q, 1H), 4.58 (s, 2H), 8.57 (s, 2H), 9.00 (s, 1H). ^{13}C NMR (75.44 MHz, D_2O–DCl): δ 15.37, 46.93, 57.10, 125.22, 131.61, 145.36, 148.34, 149.10, 172.93. UV-Vis (H_2O): 286 (31800), 239 nm (24000). IR: 3448 (br, s), 2982 (m), 2348 (m), 1610 (s), 1467 (m), 1399 (m), 1363 (m), 827 cm^{-1} (m).

Preparation of $[M(\mathbf{1})_3]^{n+}$ complexes in acidic solution

Dichloro-tris(5,5′-di(methylene-*N*-L-valinyl)-2,2′-bipyridyl)-iron(II) tetraperchlorate chloride hexahydrate, $[Fe(\mathbf{1}H)(\mathbf{1}H_2)_2Cl_2](ClO_4)_4Cl \cdot 10H_2O$. Ligand **1** (11.2 mg, 27.0 μmol) was dissolved in a solution of D_2O (0.7 ml) and 10% DCl (60 μl) and $Fe(ClO_4)_2 \cdot 7H_2O$ (3.4 mg, 9.0 μmol) was added. ^{1}H NMR (300 MHz, D_2O): Major (Δ) isomer; δ 0.73 and 0.83 (both d, J = 6.9 Hz, 6H), 2.05–2.09 (m, 1H), 3.49 (d, J = 3.8 Hz, 1H), 4.09 and 4.22 (AB, ^2J = 13.4 Hz, 2H), 7.55 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.54 (d, 1H). Minor (Λ) isomer; (most peaks obscured by major isomer) δ 0.75–0.85 (obscured), 2.05 (obscured), 3.27 (d, J = 3.9 Hz, 1H), 7.30 (s, 1H), 8.15 (obscured), 8.55 (obscured). After standing at room temperature overnight Δ-$[Fe(\mathbf{4})_3]^{2+}$ had formed exclusively. ^{13}C NMR (75.44 MHz, D_2O): δ 17.7, 18.2, 30.3, 48.0, 66.9, 124.9, 131.2, 141.8, 157.5, 159.5, 172.5. UV-Vis (H_2O): 534 (7800), 305 (74100), 255 nm (32100). CD (H_2O): 553 (21.8), 477 (−15.0), 398 (2.9), 352 (1.9), 309 (−247), 292 (133), 253 (23.9), 216 nm (45.2). IR: 3525 (m, br), 29698 (m), 1735 (m), 1614 (w), 1559 (w), 1475 (m), 1265 (m), 1087 (s), 625 cm^{-1} (m). ES-MS (10^{-4} M, H_2O): *m*/*z* 1398.0 ([$Fe(\mathbf{1})_3ClO_4]^+$, 2), 1333.5 ([$Fe(\mathbf{1})_3Cl]^+$, 1), 1298.0 ([$Fe((\mathbf{1})_3 - H)]^+$, 9), 983.3 ([$Fe(\mathbf{1})_2ClO_4]^+$, 10), 1228.9 ([$Fe(\mathbf{1})_2Cl]^+$, 4), 883.3 ([$Fe((\mathbf{1})_2 - H)]^+$, 36), 684.9 ([$Fe((\mathbf{1})_3 + 2H)Cl_2]^{2+}$, 5), 667.0 ([$Fe((\mathbf{1})_3 + H)Cl]^{2+}$, 3), 649.2 ([$Fe(\mathbf{1})_3]^{2+}$, 17), 415.2 ([$\mathbf{1}H^+$], 100%). Solid $NaClO_4$ (15 mg) was then added and the solution was refrigerated overnight. A violet precipitate formed which was filtered off. The solid was recrystallised from a solution of $NaClO_4$ (15 mg) in 1 M HCl (1.5 ml) at around 40 °C. Anal. C, 39.70; H, 5.52; N, 8.36. $[Fe(\mathbf{1}H_2)_2(\mathbf{1}H)Cl_2](ClO_4)_4Cl \cdot 10H_2O$ [$C_{66}H_{115}Cl_7FeN_{12}O_{38}$] requires: C, 39.86; H, 5.83; N, 8.45%.

$[Co^{II}(\mathbf{1})_3]^{2+}$. $Co(NO_3)_2 \cdot 6H_2O$ (9.0 mg, 31.0 μmol) was combined with **1** (38.4 mg, 9.26 μmol) in D_2O (4.2 ml) and DCl (10% in D_2O, 0.50 ml). The yellow solution was stirred at room temperature for 1 h. The pH was then raised to 4–5 by the addition of NaOD solution. ^{1}H NMR (300 MHz, D_2O): δ −1.64 (br s, 3H), −1.41 (br s, 3H), −0.50 (br s, 1H), 1.74 (br s, 1H), 4.17 (br s, 1H), 7.32 (br s, 1H), 14.24 (br s, 1H), 85.74 (br s, 1H), 97.0–98.0 (v br, 1H). UV-Vis (D_2O): 253 (35800), 301 (48300), 310 (sh, 43500). CD (D_2O): 256 (−21.6), 292 (33.6), 314 (−101.8), 457 nm (1.01). ES-MS (H_2O, 10^{-4} M): *m*/*z* 1301.1 ([$Co((\mathbf{1})_3 - H)ClO_4]^+$, 3), 886.2 ([$Co((\mathbf{1})_2 - H)]^+$, 60), 650.9 ([$Co(\mathbf{1})_3]^{2+}$, 90), 415.2 ([$\mathbf{1}H]^+$, 100%).

Dichloro-tris(5,5′-di(methylene-*N*-L-valinyl)-2,2′-bipyridyl)-cobalt(III) heptaperchlorate nonahydrate, $[Co(1H_2)_3Cl_2](ClO_4)_7\cdot 9H_2O$. The solution of $[Co^{II}(\mathbf{1})_3]^{2+}$ from above was oxidised by the addition of H_2O_2 (30%, 25 μl) solution. Removal of the solvent on a rotary evaporator gave a light brown solid. The complex was dissolved in a minimum of water and precipitated by the addition of $HClO_4$ (0.5 ml in H_2O (2 ml)). The resulting yellow powder was recrystallised by warming in H_2O, cooling to room temperature, and adding $NaClO_4$ to give a yellow crystalline solid. ^{1}H NMR (300 MHz, D_2O): δ 0.90 and 0.97 (dd, J = 6.8 Hz, 6H), 2.18–2.25 (m, 1H), 3.63 (d, J = 3.9 Hz, 1H), 4.29 and 4.62 (AB, ^2J = 13.2 Hz, 2H), 7.89 (s, 1H), 8.65 (d, J = 7.7 Hz, 1H), 8.86 (d, 1H). ^{13}C NMR (75.44 MHz, D_2O): δ 18.1, 18.7, 30.7, 48.5, 67.6, 128.8, 136.0, 147.0, 154.8, 156.3, 173.2. UV-Vis (H_2O): 222 (77400), 314 (44550), 327 nm (sh, 37000). CD (H_2O): 230 (6.3), 257 (−55.7), 306 (62.1), 331 (−73.8), 455 nm (4.0). ES-MS (H_2O, 10^{-4} M): m/z 1302.0 ($[Co((\mathbf{1})_3 - 2H)]^+$, 13), 886.2 ($[Co((\mathbf{1})_2 - 2H)]^+$, 21), 651.1 ($[Co((\mathbf{1})_3 - H)]^{2+}$, 69), 570.4 ($[Co(\mathbf{1} - H)ClO_4]^+$, 100), 434.3 ($[Co(\mathbf{1})_3]^{3+}$, 75), 415.3 ($[\mathbf{1}H]^+$, 37%). IR: 3407 (m, br), 2968 (m), 1731 (m), 1615 (w), 1546 (w), 1524 (w), 1265 (m), 1143 (s), 1088 (s), 627 cm^{-1} (m). Anal. C, 35.52; H, 5.08; N, 7.48. $[Co(\mathbf{1}H_2)_3Cl_2](ClO_4)_7\cdot 9H_2O$ $[CoC_{66}H_{114}Cl_9N_{12}O_{49}]$ requires: C, 35.42; H, 5.14; N, 7.51%.

Preparation of $[M(1 - 2H)_3]^{n-}$ complexes

$[Fe^{II}(1 - 2H)_3]^{4-}$. Valbpy (11.2 mg, 27 μmol) was dissolved in a solution of NaOH (2.16 mg, 54 μmol) in D_2O (1.5 ml). $Fe(ClO_4)_2\cdot 6H_2O$ (3.26 mg. 9.0 μmol) was added to give a red–violet solution. ^{1}H NMR (300 MHz, D_2O): δ 0.64–0.70 (br s, 6H, CH_3), 1.55–1.60 (br m, 1H, CH), 2.43 (major) and 2.56 (minor) (both α-Hs visible, br s, total 1H), 3.38 and 3.75 (br AB, 2H), 7.40 (minor) and 7.49 (major) (both 6,6′-bpy Hs visible, 1H total), 7.97 (br s, 1H), 8.51 (br s, 1H). UV-Vis (H_2O): 520 (6100), 300 (60800), 255 nm (38000). CD (H_2O): 310 (−123.4), 290 nm (55.3).

$[Co^{II}(1 - 2H)_3]^{4-}$. This complex could be prepared in the manner described above for the Fe(II) analogue, or by titrating a solution of $[Co^{II}(\mathbf{1})_3]^{2+}$ with NaOH to pH 11.3. ^{1}H NMR (300 MHz, D_2O) major (Δ) isomer: δ 0.12 (br s, 1H, pyr-CH_2), 0.96 (partly obscured by CH_3 peak, methine CH), 1.02 (br s, 3H), 1.78 (br s, 3H), 3.75 (br s, 1H, α-H), 8.17 (br s, 1H, pyr-CH_2), 14.00 (br s, 1H, bpy H), 85.35 (br s, 1H, bpy H), 90.5–91.5 (v br, 1H, bpy H). Peaks of the minor (Λ) isomer which were distinguishable: −1.63 and −1.56 (s, CH_3), 14.20 (s), 84.5 (br s). UV-Vis (H_2O): 301 (53200), 247 nm (36500). CD (H_2O): 315 (−77.0), 293 (13.7), 258 nm (−9.1).

Preparation of $[M(2)_3]^{n+}$ complexes

$[Co^{II}(2)_3]^{2+}$. $Co(NO_3)_2\cdot 6H_2O$ was added to a solution of **2** in D_2O (700 μl). Δ- and Λ-$[Co(\mathbf{2})_3]^{2+}$ (7 : 2 ratio, 80% **2** as $[Co(\mathbf{2})_3]^{2+}$), free **2** (20% of total ligand), and traces of a third paramagnetic complex, and were visible in the ^{1}H NMR spectrum. The acquisition of a COSY spectrum aided ^{1}H NMR peak assignments. ^{1}H NMR (300 MHz, D_2O) Δ isomer: δ −2.45 (s, 3H, CH_3), −1.21 (s, 1H, α-H), 3.10 (s, 1H, py-CH_2), 7.04 (s, 1H, py-CH_2), 14.42 (s, 1H, bpy), 86.1 (br s, 1H, bpy), 96.5 (v br, 1H, bpy). Λ isomer: δ−2.22 (s, 3H, CH_3), −2.12 (s, 1H, α-H), 3.25 (s, 1H, py-CH_2), 5.80 (s, 1H, py-CH_2), 14.68 (s, 1H, bpy), 86.6 (br s, 1H, bpy), 96.5 (v br, 1H, bpy). Very small peaks from a third complex were observed at δ −2.75 and 15.5. UV-Vis (H_2O) (ε and $\Delta\varepsilon$ calculated using a concentration of $[Co(\mathbf{2})_3]^{2+}$ estimated from the product distribution seen in the ^{1}H NMR spectrum): 295 (62300), 244 nm (53100). CD (H_2O): 313 (−21.3), 286 nm (2.1). ES-MS: m/z 1135.5 ($[Co(\mathbf{2} - H)_3]^+$, 84), 776.4 ($[Co(\mathbf{2} - H)_2]^+$, 86), 568.4 ($[Co(\mathbf{2})_3]^{2+}$, 42), 388.9 ($[Co(\mathbf{2})_2]^{2+}$, 35), 360.4 ($[\mathbf{2}H]^+$, 100%).

The addition of further Co(II) eventually led a simple ^{1}H NMR spectrum: δ −3.15 (s, 1H), −2.84 (s), −2.66 (s, 3H), −1.60 (s, 1H), −1.03 (s, 1H), 15.5 (br s, H), 17.2 (s), 86.5 (s).

$[Fe^{II}(2)_3]^{2+}$. Ligand **2** (15.0 mg, 39.0 μmol) was dissolved in 0.1 M HCl (1.5 ml) and $Fe(ClO_4)_2\cdot 6H_2O$ (4.7 mg, 13.0 μmol) was added with stirring. A red–violet colour developed instantaneously. The solution was warmed to 50 °C with stirring for 20 min. The solvent was removed on a rotary evaporator to give a red–violet residue. ^{1}H NMR (300 MHz, D_2O): δ 1.41 (d, CH_3), 3.60–3.65 (m, α-H), 4.05–4.26 (m, py-CH_2), 7.50 and 7.61 (both s, 1H), 8.27 (m, bpy, 2H), 8.66 (m, bpy). ^{13}C NMR (75.44 MHz, D_2O): δ 15.45, 15.64, 47.04 (2C), 56.90, 57.20, 125.71, 125.78, 131.77, 132.01, 141.82 (2C), 156.29, 156.62, 160.13, 160.19, 173.03, 173.22. ES-MS (H_2O, 10^{-4} M): m/z 1229.8 ($[Fe(\mathbf{2}_3 - H)ClO_4]^+$, 1), 871.1 ($[Fe(\mathbf{2}_2 - H)ClO_4]^+$, 8), 771.3 ($[Fe(\mathbf{2}_2 - H)]^+$, 28), 565.5 ($[Fe\mathbf{2}_3]^{2+}$, 100), 529.5 ($[Fe\mathbf{2}_3 - CH_3CHCO_2]^{2+}$, 63), 522.7 ($[Fe\mathbf{2}_3 - (CO_2)_2]^{2+}$, 82), 413.0 ($[Fe(\mathbf{2} - H)]^+$, 16), 359.3 ($[\mathbf{2}H]^+$, 90%). UV-Vis ($H_2O$): 524 (6280), 304 (68600), 254 nm (28400). CD (H_2O): 555 (3.5), 476 (−2.2), 311 (−44.2), 293 nm (26.8).

X-Ray crystallography: Δ-$[Co(1H_2)_3Cl_2](ClO_4)_7$

Crystal data $Co(C_{22}H_{32}N_4O_4)_3Cl_2(ClO_4)_7\cdot(H_2O)_{12}(C_2H_6O)_2$, M = 2384.1, monoclinic, a = 14.4363(9), b = 20.2358(8), c = 20.0112(14) Å, β = 110.184(8)°, U = 5486.9 Å^3, T = 200 K, space group $C2$, Z = 2, μ(Mo-Kα) = 0.47 mm^{-1}, 34570 reflections measured, 10617 unique (R_{int} = 0.058) of which 7000 were used in all calculations. The final $wR(F)$ was 0.057 (observed data, $|F_o| > 4\sigma(F_o)$), and the absolute structure parameter[12] was 0.00(3). Data were recorded with a STOE IPDS system, and the structure was solved by direct methods.[13] Other calculations used the XTAL system.[14]

CCDC reference number 193595.

See http://www.rsc.org/suppdata/dt/b2/b208934c/ for crystallographic data in CIF or other electronic format.

Acknowledgements

The authors thank André Pinto and Xavier Melich for technical assistance and acknowledge the Swiss National Science Foundation for financial assistance. Professor Kenneth Raymond is also thanked for illuminating discussions.

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