Stability Enhancement of Heavy-metal–Macrocycle Complexes *via* Pendant Amide Coordination

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Formation of the pendant-arm macrocyclic ligand 1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane L and subsequent generation of its cadmium(II) complex indicates very significant stabilisation of the complex, compared to that observed for related macrocyclic cadmium(II) complexes, which either lack pendant donors altogether, or have other types of neutral oxygen donors attached to the macrocycle, and compared to complexes of L with lighter metal ions.

Successful sequestration of toxic heavy metals in the presence of higher concentrations of lighter, more beneficial ones, is currently a major scientific objective, with profound implications for the maintenance or re-establishment of environmental and physiological well-being.[1] The thermodynamic approach to this problem rests on the ability of a ligand to bind to the undesired metal ion with a high, and much greater affinity, than that which it has for the other metal ions in the mixture, but usually founders due to the fact that the binding constants for the toxic heavy metals are similar to, if not less than, those for the lighter metals. Indeed, Williams[2] has suggested that in light of the chemical similarity between the toxic Cd^{II} and essential Zn^{II} ion, 'any ligand capable of removing cadmium is also likely to deplete the body of zinc'.

Previously we have noted the effect that the presence of neutral oxygen donors, either as alcohols or ethers, has in enhancing the stability of heavy-metal complexes relative to those of lighter metals. However, we have been equally conscious of the low absolute stability of these complexes, which diminishes their usefulness.[3] In an attempt to enhance the absolute stability whilst still retaining the desired selectivity for heavy metals we have now investigated the situation with pendant amides. The ligand L has been synthesised in high yield through the reaction of 1,4,7,10-tetraazacyclododecane (cyclen) with chloroacetamide in ethanol in the presence of triethylamine. Combination of L with hydrated cadmium perchlorate in aqueous methanol precipitates [Cd(L)]-$(ClO_4)_2 \cdot MeOH$ as a fine white powder.

The ^{13}C NMR spectra of [Cd(L)]$(ClO_4)_2 \cdot MeOH$ recorded in D_2O at various temperatures are shown in Fig. 1 and provide a means both for deducing the structure of the complex in aqueous solution and observing its dynamics: Observation of a single resonance corresponding to the presence of the amide carbonyl carbon (δ 175.6), displaying $^{111/113}Cd$ satellites ($^2J_{C,Cd}$ 9.4 Hz) indicates that all carbonyl groups are equivalent and that they are bound to the Cd^{II} ion. Furthermore, the behaviour of the spectrum with respect to temperature is analogous to that observed previously for 1,4,7,10-tetrakis(2-hydroxyethyl)cyclen complexes[4] and indicates that the complex has approximately square-antiprismatic (C_4) geometry and that it undergoes intramolecular interconversion between its two enantiomeric forms. From the coalescence behaviour of the resonance corresponding to the carbon atoms in the macrocyclic ring (δ 49.3) the mean site lifetime (τ) for the complex in either enantiomeric form is calculated to be 2.5 ms at 295 K, corresponding to a rate constant of 390 s^{-1} and a free energy of activation of 57.5 kJ mol^{-1}, for the interconversion at this temperature. The preservation of the coupling between the amide carbon atoms
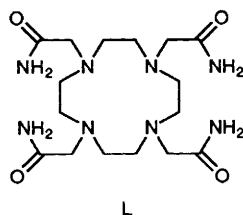
and the ^{111}Cd or ^{113}Cd, as the case may be, in the fast-exchange spectra, strongly suggests a non-dissociative mechanism for the inversion process with the transition state having a cubic structure.

In comparison with the Cd^{II} complex of 1,4,7,10-tetrakis(2-hydroxyethyl)cyclen, [Cd(L)]$^{2+}$ undergoes the intramolecular inversion approximately one order of magnitude more slowly. This points to an enhanced bond strength for the pendant amide–metal interaction, compared to the pendant alcohol–metal interaction, which obstructs the bond lengthening necessary for the molecule to move through the cubic
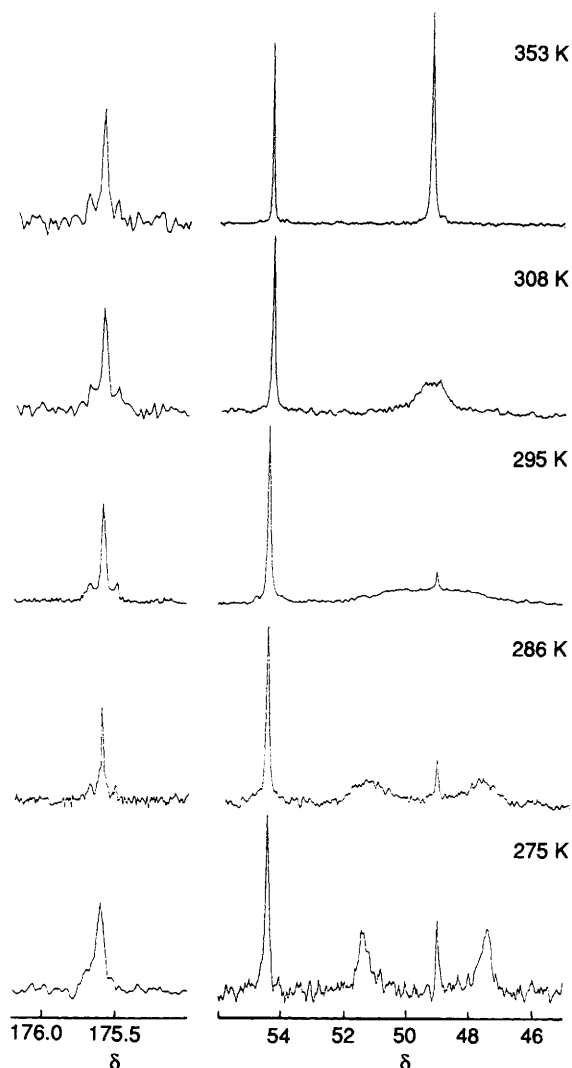

Fig. 1 A selection of $^{13}C\{^1H\}$ 50.32 MHz NMR spectra of [Cd(L)]$(ClO_4)_2 \cdot MeOH$ (0.04 mol dm^{-3}) in D_2O at different temperature. The singlet resonance appearing between the coalescing doublet is due to the methanol of solvation and was assigned a chemical shift of 49.0. Other resonances are referenced with respect to it.

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transition state. The greater steric bulk of the amide moiety, compared to the alcohol, may also be a contributing factor towards the diminished rate of inversion.

Strong bonding between the pendant amide and the metal is also indicated by attempts to measure the stability constant for [Cd(L)]$^{2+}$. The fact that the complex is fully formed even in 1 mol dm^{-3} HNO$_3$ indicates unusually high complex stability, with a log K value in excess of 21, which it has not yet been possible to measure accurately. This is supported by the remarkable observation that addition of Cd^{2+} to an aqueous solution of [Cu(L)]$^{2+}$, for which log K has been determined as 16.4, instantly brings about total decolouration of the solution. By way of comparison, the log K values for the Cd^{2+} and Cu^{2+} complexes of the parent macrocycle, cyclen, are 14.3 and 23.3, respectively,[5] and for the pendant-arm alcohol 1,4,7,10-tetrakis(2-hydroxyethyl)cyclen, are 14.6 and 15.2.[6] Similar observations have been made with Pb^{II}, which is of particular interest in connection with the sequestration of Pb^{II} in the presence of Zn^{II}. We have determined the log K for [Zn(L)]$^{2+}$ and find that it has the considerably lower value of

10.5, which gives an unprecedented selectivity (difference in log K) for Cd^{II} over Zn^{II} of about ten orders of magnitude.

References

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