

Metal ion recognition: The story of an oxa–aza macrocycle

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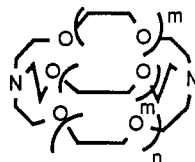
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Abstract - The interaction of a pyridine-derived dioxo-triaza-macrocycle with divalent first row transition metal cations is discussed. Selected crystal structures and speciation studies are presented together with information on application to metal extraction and transport.

The recovery of metals from sulfide-rich ores by pyrometallurgical processes is regarded as environmentally unsatisfactory due to the accompanying production of sulfur dioxide which leads to an enhanced acidity in rainfall. Particulate matter from smoke effluents can also be dispersed and dispensed onto nearby land and, if toxic, give rise to further problems. Therefore it is important to establish processes by which metals of interest can be extracted from what are often low-grade ores by an alternative technology. Consequently there has been much interest in the application of hydrometallurgical techniques which involve a leaching process to dissolve the metals followed by solvent extraction processes to separate and recover the metal ions of interest. Solvent extraction has been used as one of the major techniques in the industrial hydrometallurgy of non-ferrous metals, particularly in the recovery of copper, in cobalt-nickel separation and in the concentration of uranium.^{1,2}

Macrocycles, and macrobicyclic, ligands have been shown to be effective in alkali, and alkaline earth, selectivity.³ This may be related to a cation radius:macrocyclic cavity radius control in which the cation having the 'best fit' for the cavity will be the cation strongest complexed by that macrocycle. As there is a clear and steady increase in ionic radius between the alkali metals as the group is progressed then it becomes possible to discriminate between by careful ligand cavity control. In the example given (Table) evidence can

TABLE Log stability constants, $\log K_1$, for some cryptate complexes in water (from J.M.Lehn and J.P.Sauvage, *J.Chem.Soc., Chem.Comm.*, 1971, 440.)

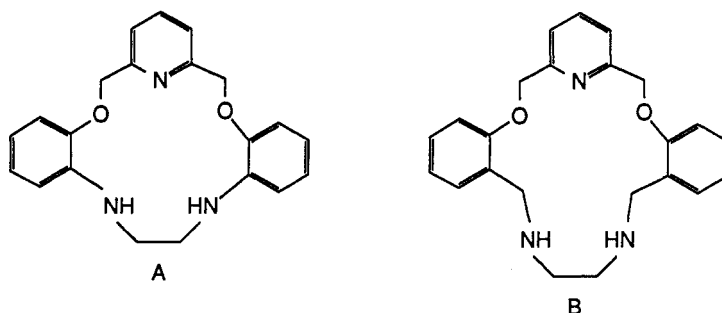


Cation (ionic radius Å)	Li ⁺ 0.86	Na ⁺ 1.12	K ⁺ 1.44	Rb ⁺ 1.58	Cs ⁺ 1.84
Ligand (cavity size in Å)					
[2,1,1], m=0, n=1 (0.8)	4.30	2.80	2.0	2.0	2.0
[2,2,1], m=1, n=0 (1.15)	2.50	5.40	3.95	2.55	2.0
[2,2,2], m=n=1 (1.4)	2.0	3.90	5.40	4.35	2.0
[3,2,2], m=1, n=2 (1.8)	2.0	2.0	2.2	2.05	2.20
[3,3,2], m=2, n=1 (2.1)	2.0	2.0	2.0	0.7	2.0
[3,3,3], m=n=1 (2.4)	2.0	2.0	2.0	0.5	2.0

be seen for both peak selectivity in which one metal is selected at the expense of the others and for plateau selectivity in which one group of metals is more strongly selected. There is also a metal ion:macrocyclic donor atom compatibility requirement based on the Hard and Soft Acid and Base character of the interacting species. If the ligands are oxygen-rich then the stronger complexes are with the alkali metals but as sulfur donors are introduced then the affinity for softer metals such as Ag^{I} and Pb^{II} increases.

For the first row transition metal ions the situation is less clear. The 'best fit' criterion is less evident due to the much smaller change in ionic radius between the metal ions as the row is crossed. Changes in radius for a given metal can also occur with changes in oxidation state and spin state. Furthermore as the periodic table is crossed so the metal ion:macrocyclic donor atom compatibility changes; from O and N for Mn^{II} and Fe^{II} , to N and S for Cu^{II} and Zn^{II} . There is also a preferential site geometry induced by the orthogonal d orbitals, which is not present in the spherically symmetrical s-block metals, and the influence of crystal field stabilisation energies. This is demonstrated in the Irving-Williams order of stability constants for the divalent cations of the first row transition metals in which the sequence follows the order $\text{Mn} < \text{Fe} < \text{Co} < \text{Ni} < \text{Cu} > \text{Zn}$, with the second row metals having a further diminution in value e.g. $\text{Zn} > \text{Cd}$, and in the site geometries found in enzymes such as Cu-Zn bovine erythrocyte superoxide dismutase in which the zinc atom is tetrahedral and the copper is at a distorted tetragonal site.⁴

In order to determine whether macrocycle ligands can be applied to the selectivity of transition metals a series of oxa-azamacrocycles were prepared and investigated. Early work on Schiff base macrocycles had established the value of alkaline earth and main group cations as metal templating devices, and had shown also that the size of the templating cation could influence the nature of the macrocyclic product formed.⁵ Therefore a series of Schiff base macrocycles were synthesised by metal templated cyclocondensation reactions using Pb^{II} and Mn^{II} templates;⁶ the latter being a d^5 ion and so somewhat symmetric has been found to act as a useful probe for calcium in biological systems,⁷ it was therefore considered as an honorary alkaline earth metal for metal-template purposes.



It was not possible to remove the metal templates from the product complexes without causing breakdown of the ligands and so the complexes were reductively demetallated in the presence of NaBH_4 to yield the metal-free oxa-azamacrocycles.⁶ By judicious use of reagents a wide range of macrocycles could be synthesised in which the ring sizes could be increased by sequential addition of single methylene groups, and in which the donor atom sequences could be varied, and to which extra donors could be added.

The pentadentate macrocycle (L^1) was shown to react readily with the first row transition metal nitrates, but only the Cu^{II} and Ni^{II} complexes were isolable as crystals and so accessible for X-ray study.⁶ Stability

constant data revealed that the Cu^{II} was much more strongly bound than the Ni^{II} [Log K, methanol, 6.84(Cu); <3.0 Ni]. The crystal structures showed that a structural 'dislocation' had occurred between the two complexes - structural 'dislocations' arise when the balance between metal co-ordination requirements and ligand flexibility lead to an abrupt change in co-ordination geometry between the complexes of interest - and that whilst the Cu^{II} was bound by all five donor atoms and one monodentate nitrate in a very distorted octahedral environment, the Ni^{II} was octahedrally coordinated by four ligand donors, one oxygen being non-bonded, and two *cis*-monodentate nitrates. The chirality at the ethylenediamine-like nitrogens changed from *RR* (*SS*) in the former to *RS* (*SR*) in the latter.

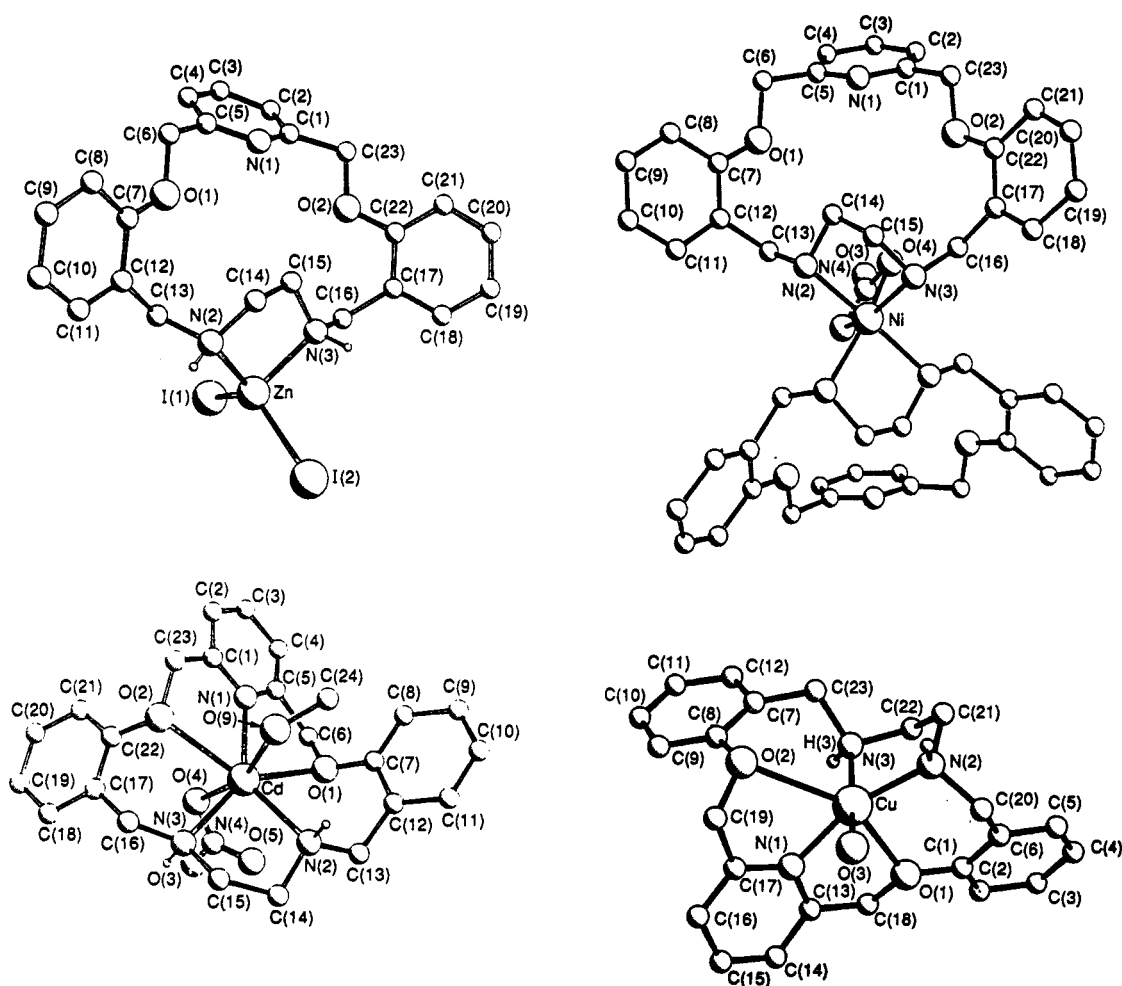


FIGURE: The crystal structures of complexes [1] - [4] depicted in clockwise sequence.

The construction of a model complex in which two extra CH_2 groups were added to the macrocycle in order to expand the cavity size (17-membered ring) indicated that all of the donors should now bind to Ni^{II} . Macrocycle (L^2) was synthesised by application of the previously described route⁶ and it was possible to isolate crystalline complexes of Mn^{II} , Co^{II} , Ni^{II} , Cu^{II} , Zn^{II} , Cd^{II} , and Hg^{II} . The X-ray crystal structures of the complexes disclosed several structural types involving both endo- and exo-macrocyclic ligation.⁸⁻¹⁰

A series of solution studies were undertaken to investigate the speciation of the system.⁸⁻¹⁰ Conductometric titrations of $\text{M}(\text{L}^2)(\text{ClO}_4)_2$ with NH_4Cl were performed in dimethyl sulfoxide (dms). For Mn^{II} an inflection

at 1:2 mole ratio $[\text{NH}_4\text{Cl}]/[\text{complex}]$ indicated that dimerisation had occurred presumably via bridging chloride ions and for Co^{II} , Zn^{II} and Cd^{II} inflections were observed at 1:1 and 2:1 mole ratios indicating the sequential formation of a 1:1 complex of the type $[\text{M}(\text{L}^2)\text{Cl}]^+$ and of a 2:1 complex of the type $\text{M}(\text{L}^2)\text{Cl}_2$ in each case. An inflection at a 1:1 ratio was also observed for Cu^{II} but in contrast an inflection was noted at a 1:2 ratio for Ni^{II} suggesting the formation of a bridged dimer. Spectrophotometric titrations of the nitrates or perchlorates of Cu^{II} or Ni^{II} with (L^2) in dmsO indicated the initial formation of 1:1 species followed by the formation of 1:2 species.

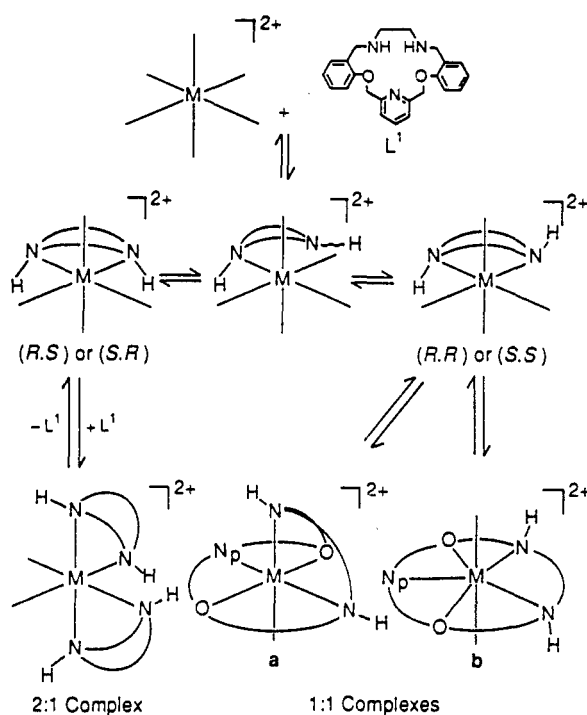
^1H N.m.r. titrations of (L^2) with $\text{M}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ ($\text{M} = \text{Zn}^{\text{II}}, \text{Cd}^{\text{II}}$) were performed in CD_3OD . The aliphatic protons in each complex generally showed significantly large shifts whereas the aromatic proton signals shifted only slightly; all of the spectra broadened as the metal was added and all indicated the formation of 1:1 (metal:ligand) complexes.

Thermodynamic stability constants ($\log K$) were determined in 95% MeOH (25°C , $I = 0.1 \text{ Et}_4\text{NClO}_4$) using the potentiometric (pH) titration method. The values of the stability constants were found to be $\text{Mn}^{\text{II}} < 4.0$, $\text{Co}^{\text{II}} 4.51$, $\text{Ni}^{\text{II}} 6.66$, $\text{Cu}^{\text{II}} 13.92$, $\text{Zn}^{\text{II}} 5.91$, and $\text{Cd}^{\text{II}} 8.73$. The sequence follows the "natural" or Irving-Williams stability order with the exception of the pronounced stability of Cd^{II} relative to Zn^{II} where the "natural" polyamine thermodynamic stability $\text{Zn}^{\text{II}} > \text{Cd}^{\text{II}}$ has been reversed. This has been observed previously for the $-\text{N}_2\text{O}_3$ -donor set; the nature of the 'dislocation' in this latter case was based on a mismatch occurring in the hole size/ionic radii best-fit on moving from an 18- to a 19-membered ring system.¹¹ [Extension of the alkane spacer in (L^1) to a trimethylene unit led to a reversion to the normal sequence of $\text{Zn}^{\text{II}} > \text{Cd}^{\text{II}}$]. The stability of the Cu^{II} complex of (L^2) is much enhanced over that of the corresponding Ni^{II} complex. Flow microcalorimetry studies of the $\text{M}-(\text{L}^2)$ system enabled the determination of the enthalpy (ΔH°) and entropy (ΔS°) of complexation to be calculated for the Cu^{II} , Ni^{II} , and Mn^{II} complexes. For Mn^{II} the enthalpy was endothermic ($\Delta H^\circ = 10.75 \text{ kJ mol}^{-1}$). In contrast ΔH° for Ni^{II} and Cu^{II} was exothermic (-5.04 and $-30.61 \text{ kJ mol}^{-1}$); 1:2 metal: ligand species were also observed ($\Delta H^\circ = -21.59$ and 8.94 kJ mol^{-1}). Calculation of the entropy indicated that this was the driving force for 1:1 complexation in each case [$\Delta S^\circ = 73.6$ (Mn), 110 (Ni), 160 (Cu) $\text{J mol}^{-1} \text{ K}^{-1}$].

On linking the solution data with the structural data a reaction scheme can be proposed (Scheme). Initial chelation of (L^2) via the aliphatic nitrogen atoms leads to exo-macrocyclic complexation involving either $(SR ; RS)$ or $(RR ; SS)$ configurations at the nitrogen atoms; these forms could interconvert via a monodentate intermediate. In the exo-macrocyclic complexes isolated and characterised by X-ray crystallography⁹ ($[\text{Zn}(\text{L}^2)\text{I}_2] \cdot \text{H}_2\text{O}$, [1], and $[\text{Hg}(\text{L}^2)\text{I}_2]$) only the $(SR ; RS)$ configurations have been found. Addition of a second molecule of (L^2) - in this bidentate mode - leads to 2(ligand) : 1(metal) complexes of which $[\text{Ni}(\text{L}^2)_2(\text{NO}_3)]\text{NO}_3 \cdot \text{MeOH}$, [2], has been characterised.⁸

The 1 : 1 complexes of types (a) and (b) in which all of the ligand donor atoms are attached to the metal are formed from the $(RR ; SS)$ isomer. The conformational differences between type (a) and type (b) are evidenced by analysis of the torsion angles in the complexes. Type (a) has been crystallographically identified for $[\text{Cu}(\text{L}^2)(\text{H}_2\text{O})_2](\text{ClO}_4)_2$, [3],⁸ $[\text{Ni}(\text{L}^2)\text{I}]\text{I} \cdot \text{MeOH}$,⁸ $[\text{Co}(\text{L}^2)(\text{NO}_3)]\text{NO}_3$,¹⁰ and $[\text{Zn}(\text{L}^2)(\text{NO}_3)]\text{NO}_3$ ⁹ and type (b) has been identified for $[\text{Mn}(\text{L}^2)\text{Br}(\text{EtOH})]\text{ClO}_4$ ¹⁰ and $[\text{Cd}(\text{L}^2)(\text{NO}_3)(\text{MeOH})]\text{NO}_3$, [4],⁹; the different structural types found for Zn^{II} reflect the relative affinities of the macrocycle and anion for the metal.

Scheme



The equilibria involved will tend to be dynamic and so it is likely that various proportions of a number of forms of a given species will be present in solution at any given time. For example, although one form may predominate contributions from both endo- and exo-macrocylic co-ordination may also be present under a given set of conditions. The nature of the predominating species will depend on a number of factors such as the hole and chelate ring sizes presented by the ligands; the donor atom type and location within the ligands; the ionic radius, donor atom and geometric preferences of the cation; the donor type and denticity of the accompanying anion and solvent molecules; and the conditions under which the reaction is run.

Extraction experiments (from H_2O into $CHCl_3$) and related transport experiments (from H_2O into $CHCl_3$ into H_2O) with Cu^{II} and Ni^{II} were successfully carried out using (L^2) in the organic phase, which also contained hexadecanoic acid to inhibit any bleeding into the aqueous phase of the protonated macrocycle or metal complex.⁸ Under the conditions employed Cu^{II} was favoured over Ni^{II} in all single metal extraction and transport studies, and was exclusively extracted in a competitive metal experiment.

TABLE Extraction and Transport data

Metal	Extraction Ratio, D_m^a	Relative transport rates, $mol\ h^{-1}$
Ni^{II}	0 ^b	2.1×10^{-9}
Cu^{II}	0.04	4.0×10^{-7}
Ni^{II}/Cu^{II}	0 ^b /0.04	0 ^b / 4.9×10^{-7}

Initial metal concentrations in the aqueous source phase were $(1.3 \pm 0.1) \times 10^{-2} mol\ dm^{-3}$ in each case; error for extractions $\pm 20\%$ and for transport $\pm 15\%$. ^a $D_m = [M^{2+}]_{org}/[M^{2+}]_{total}$ ^b [Ni] below normal detection limit.

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