

## Metal-ion recognition: An assault on natural order

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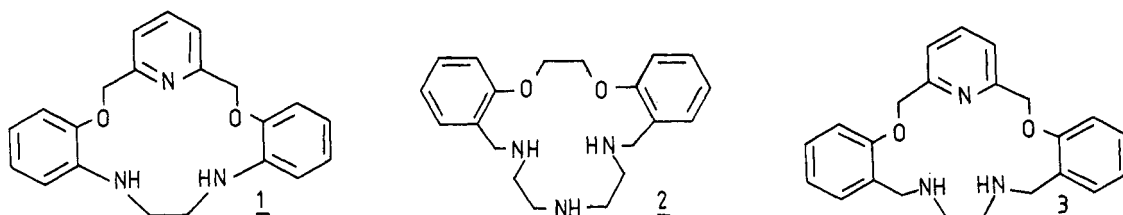
**Abstract** - Four aspects of macrocyclic complexation of metals are discussed: exocyclic complexation, exocyclic aggregation, dinucleating pendants and incorporation of organometallic fragments.

### INTRODUCTION

Discrimination between alkali and alkaline earth metal cations can be made using macro-cyclic and -bicyclic polyether-based ligands as a consequence of a 'best-fit' between the cation and the cavity offered by the ligand (ref. 1) For the first-row transition metal cations the consecutive increments in radius are not large and so it becomes difficult to effect discrimination solely on a cation-cavity 'best-fit'. Other factors become involved; the natural order of stability constants ( the Irving-Williams series ) with its origins in ionic potential and size, the metal ion - ligand donor compatibility derived from Hard and Soft Acid and Base ( or class 'a' and class 'b' ) character and the preferential site geometry required by the cation. We have been investigating the design and synthesis of oxazamacrocyclic ligands with varying ring sizes and flexibilities and including both weak and strong donor atoms in varied donor sets and sequences in order to define the principles underlying transition metal selectivity by macrocyclic ligands (refs. 2,3). Such discrimination is often structurally based; for example a break in a stability constant sequence for a specific ligand can sometimes be related to a 'structural dislocation', a given structural type existing for a series of complexes but a sudden change - one, or more, donor atoms being nonbonded and/or a different conformation of the ligand occurring - causes an energy difference between the complexes such that one metal is stabilised thermodynamically with respect to the next in the sequence. This behavioural trend is now well-documented through the work of Lindoy, Tasker *et al.* ( refs. 4,5). Distinct stability constant differences between zinc and cadmium complexes of the same macrocyclic ligand ( 1st row versus 2nd row transition metal cations ) might be regarded as showing 'best-fit' behaviour because of the greater difference in ionic radius.

### COMPLEXES OF OXAAZAMACROCYCLES

The metal template cyclocondensation of a series of dialdehydes with a series of 1,n-diamines has given a range of Schiff base macrocyclic complexes of manganese(II) and lead(II) which can be reductively demetallated to yield a group of oxazamacrocycles having various ring sizes, donor composition and donor array. These metal-free macrocycles may then be used in metal complexation studies ( refs. 2,3). One long term objective of the project might be described as revolution - the overthrow of the natural order of stability. Some metal ion discrimination has been observed using macrocycle (1); the nickel(II) complex (  $\log K < 3.0$  ) is destabilised relative to the copper(II) complex (  $\log K = 6.84$  ). This is attributed to the non-coordination of one of the ethereal oxygens in the nickel(II) complex whereas all of the ligand donors are bound to the metal in the copper(II) complex ( ref. 3). During the course of our investigation the wider application of oxazamacrocycles has been under review and in this lecture four aspects of metal complexation by macrocycles which have manifested themselves will be presented.



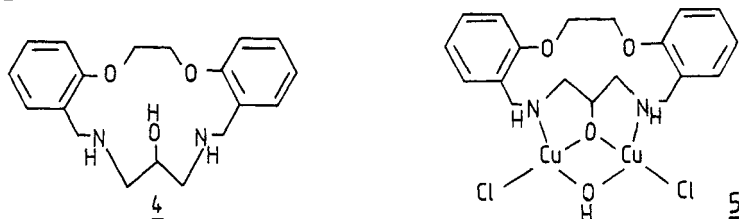
### Exocyclic complexation

Effective discrimination by macrocyclic ligands depends on the incorporation of the metal ion into the donor cavity of the ligand to form a complex. When metal ions are discriminated against by a 'poor-fit' for the cavity the probability exists that the most favourable interaction mode will involve exocyclic complexation using only part of the macrocyclic donor set. This is exemplified in the discrimination between zinc(II) and cadmium(II) by the macrocycle (2); although the cadmium resides in the cavity provided by the five equatorial ligand donor atoms the zinc binds only to the three nitrogen donor atoms in a facial exocyclic arrangement (ref. 4).

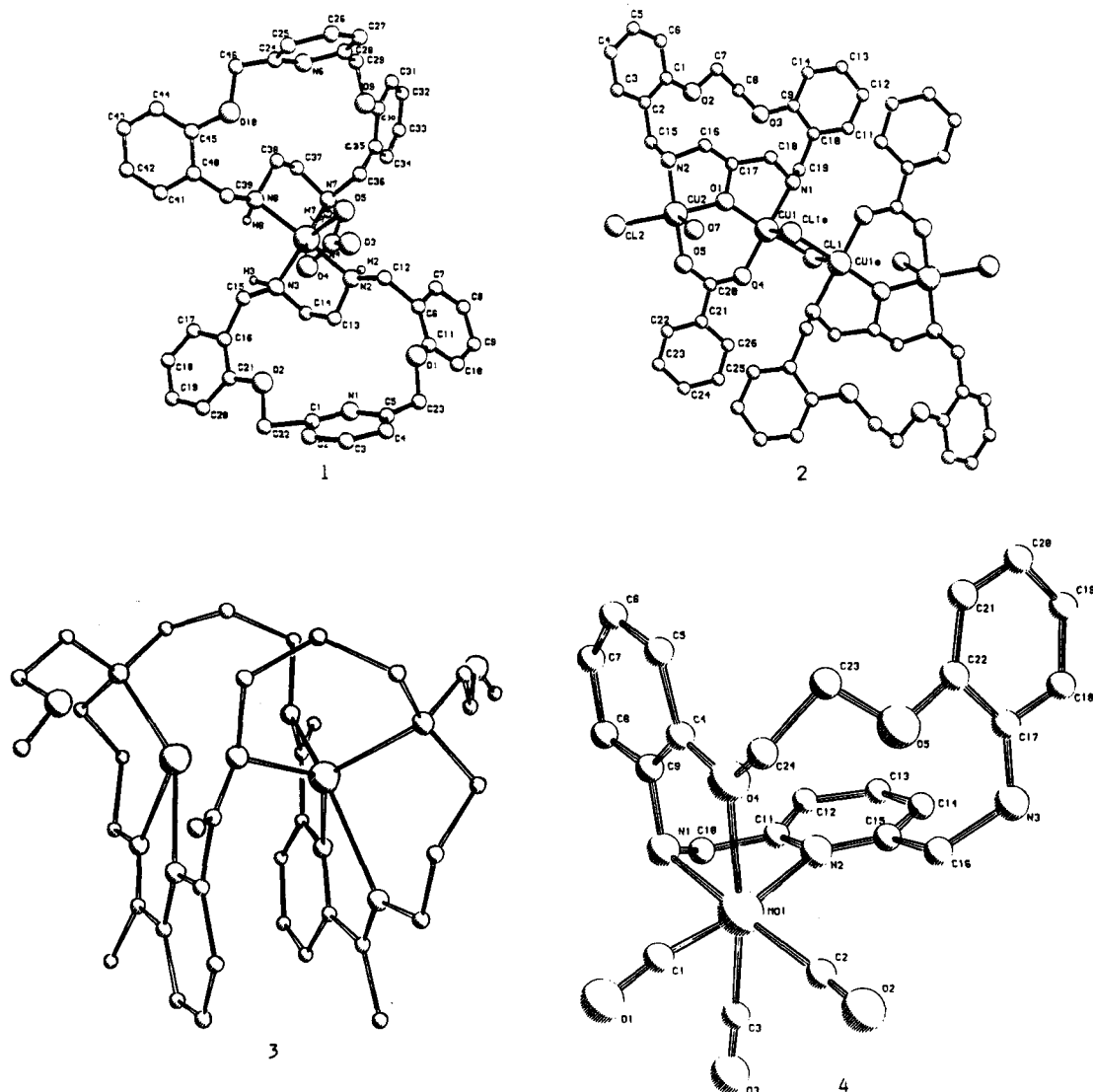
By enlarging the cavity of macrocycle (1) a greater flexibility can be achieved; consequently macrocycle (3) was synthesised by application of the template-reduction route using manganese(II) as the template. Spectrophotometric titrations of (3) with copper(II) and nickel(II) perchlorates in dimethylsulphoxide solutions showed an initial formation of a 1:1 complex followed by the formation of a 2 (ligand) : 1 (metal) species. Crystals were obtained for complexes of both stoichiometries. The crystal structure of  $\text{Cu}(3)(\text{ClO}_4)_2 \cdot 2\text{H}_2\text{O}$  showed the metal to be held in the cavity provided by the five macrocyclic donor atoms. The complex  $\text{Ni}(3)_2(\text{NO}_3)_2 \cdot 2\text{CH}_3\text{OH}$  provided the first structural information on such a species (Fig. 1). The nickel is six-coordinated by chelating nitrogen atoms from each macrocycle and a bidentate nitrate anion; the metal is therefore exocyclically complexed with the macrocycles simply acting as bidentate ligands. There is a distortion from octahedral geometry which is probably caused by the difference in ligand bite sizes (ref. 6). On dissolution it is likely that the anion is replaced by two solvent molecules. The precise speciation involved is difficult to define; the equilibria involved will tend to be dynamic with varying proportions of the species concerned being present. Contributions from exo- and endo-cyclic forms may simultaneously be present although one form might actually dominate. Irrespective of this the copper(II) system was found to give a higher log K (13.9) than the nickel(II) system (6.7).

### Exocyclic aggregation

Exocyclic complexation is not restricted to mononuclear species, the functionalised macrocycle (4), prepared by a nontemplate cyclocondensation of the dialdehyde and diamine precursors followed by an in situ reduction of the Schiff base macrocycle first formed, reacts with  $\text{Cu}(\text{ClO}_4)_2$ , or  $\text{Cu}(\text{NO}_3)_2$ , to give the mononuclear complexes  $\text{Cu}(4')\text{X}$  ( $\text{X} = \text{ClO}_4, \text{NO}_3$ ; 4' = deprotonated macrocycle 4). On reaction with  $\text{CuCl}_2$  the homodinuclear complex  $\text{Cu}_2(4')(\text{OH})\text{Cl}_2$  is formed.



Molecular models indicated that the ligand cavity would be too small to hold a dinuclear fragment and so the structure (5) was proposed for the complex, by analogy with acyclic complexes bearing the diaminopropanolic unit (ref. 7). The complex (5) was recrystallised from benzyl alcohol and the structure is depicted in Fig. 2. It comprises a centrosymmetric tetranuclear complex in which each of the pairs of copper atoms is coordinated exocyclically by the macrocyclic ligand via two amine nitrogen atoms (one to each copper) and by an oxygen atom of the deprotonated hydroxyl group which bridges the two copper atoms. The pair of copper atoms is also bridged by a benzoate anion. At first this was thought to arise from oxidation of the benzyl alcohol by the dinuclear copper complex but it has subsequently been found that the dinuclear unit scavenges residual benzoic acid impurity (0.27%) from the



FIGURES. The crystal structures of macrocyclic complexes.

1. Ni(3)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>·2CH<sub>3</sub>OH.
2. [Cu<sub>2</sub>(4')(C<sub>6</sub>H<sub>5</sub>COO)Cl<sub>2</sub>·H<sub>2</sub>O]<sub>2</sub>.
3. Ag<sub>2</sub>(6)(ClO<sub>4</sub>)<sub>2</sub>·0.5H<sub>2</sub>O.
4. (7)Mo(CO)<sub>3</sub>·CH<sub>2</sub>Cl<sub>2</sub>.

solvent. The ligand is sufficiently flexible to allow incorporation of a 1,3-bridging benzoate anion in place of the singly bridging hydroxide. The coordination sphere of the 'outer' copper of each pair is completed by a terminal chloride and a water molecule; the 'inner' copper atoms are asymmetrically bridged by a pair of chloride ligands. The Cu...Cu distances are 349 and 339pm.

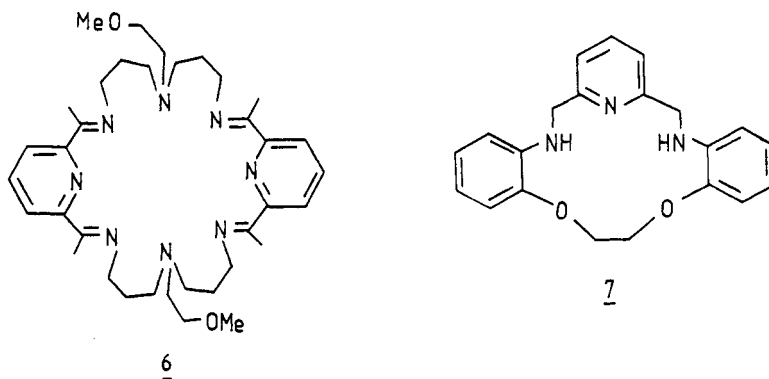
Double bridging involving endogenous alkoxide or phenoxide groups and exogenous groups is a well-established mode of complexation in dinuclear copper(II) compounds derived from a range of acyclic ligands (refs. 8,9). Many of these systems have been used to gather information pertinent to the modelling of the dinuclear copper(II) sites found in tyrosinase and haemocyanin. The closest acyclic analogue to the above exocyclic compound is [μ-benzoato-O:O']-[2,2,2'-(2-hydroxy-1,3-propanediyl)bis(nitrilomethylidene)]bis[phenolato](3-)-N',O',O<sub>1</sub>:N'',O'',O<sub>1</sub>']dicopper(II) in which the copper atoms are separated by a distance of 349pm (ref. 8).

### Dinucleation pendants

We have earlier reported the barium-assisted template synthesis of tetraimine Schiff base macrocycles bearing two flexible side-arms and with additional ligating atoms ( ref.10). These macrocycles were trivially termed 'opened' cryptands; no structural information was available to show the nature of the metal incorporation.

The use of silver(I) salts as the templates has provided a facile route to pendant-armed macrocycles as their dinuclear silver(I) complexes ( ref.13). It has previously been demonstrated that in several silver(I) complexes in which the  $d^{10}$  atoms are held together in pairs by 1,3-bifunctional bidentate ligands the intermetallic contact is similar to, and often shorter than, that in silver metal (ref.11). The crystal structure of  $Ag_2(6)(ClO_4)_2 \cdot 0.5H_2O$  unexpectedly revealed such a short intermetallic contact ( 291pm cf. 288pm for silver metal) (Fig. 3). This may be contrasted with the structure of the silver(I) complex of the corresponding tetraimine Schiff base macrocycle in which there is no pendant arm on the central aliphatic nitrogen atom; in this complex the two silver atoms are separated by 600pm ( ref. 12). It is possible that the presence of the pendant arms restricts the conformational mobility of the ligand and forces the silver atoms into mutual proximity. The silver atoms are in different coordination environments with Ag(1) 'strongly' linked to a pyridinyl nitrogen, a tertiary amino nitrogen and three imino nitrogen atoms whereas Ag(2) is 'strongly' linked to three nitrogen atoms, one each of pyridinyl, tertiary amine and an imine ( 'strongly' indicates a bond distance of < 255pm). The latter silver atom additionally forms a 'weaker' interaction ( 272pm) to the oxygen atom of a pendant alkoxy group the second of which is directed away from the macrocycle. Two diametrically opposed imino-nitrogen atoms form asymmetric bridges between the silver atoms ( 242 and 274pm ; 255 and 283pm). There is no obvious residual electron density at the imino-nitrogen atoms to facilitate such an interaction and it is not likely that there is a pi-involvement of the imines. It is probable that the nitrogen atoms serve as an electrostatic bridge between the proximal silver cations, this proximity being conformationally induced( ref.13).

The silver complexes are sufficiently labile that transmetalation with copper(II) salts leads to the isolation of homodinuclear copper(II) complexes of the pendant armed macrocycles and reductive demetallation affords the metal-free tetraimine macrocycles. These may then be used for further studies on metal-ion selectivity.



### Incorporation of organometallic fragments

Although there is an expanding literature concerning the interface between macrocyclic coordination chemistry and organometallic chemistry ( ref.14) much of the work concerns homo-donor sets such as polyaza-, polyoxa- and polythia-macrocycles. The reaction of the oxazamacrocycle (7) with  $fac-(CH_3CN)_3Mo(CO)_3$  gave crystals of  $(7)Mo(CO)_3 \cdot CH_2Cl_2$ , the structure of which revealed that the  $Mo(CO)_3$  fragment binds to the macrocycle via the pyridinyl nitrogen atom, one amino nitrogen atom and one oxygen atom (Fig. 4); the macrocycle is found to adopt a 'boat' conformation ( ref.15). Bonding of the 'N<sub>3</sub>'-donor set from the macrocycle appears to be sterically disallowed. The conformations of the complexed and noncomplexed ends of the macrocycle appear to be little different from each other suggesting that a 'slippage' between donor sets might be possible. The compound is insoluble in most common organic solvents and dissolution in reasonable donor solvents such as acetonitrile, pyridine and acetone results in decomposition. This phenomenon precludes the acquisition of variable temperature n.m.r. spectra to test this.

### Concluding remarks

The statement " Today, and for the future, if one is an organic chemist every metal in the periodic table is of potential interest; and, if one is an inorganic chemist, so is every type of organic structure" was made by C.K. Ingold. It can be seen here that oxazamacrocycles are capable of acting as versatile hosts for metals and the metals may readily be used to help in the synthesis of a range of macrocyclic ligands. Endo- and exocyclic modes of metal incorporation have been demonstrated and the nature of complexation could have an influence on the selectivity of transition metal cations by the ligand. Exocyclic complexation has also afforded the opportunity to have an aggregation leading to arrays of metal ions and the conformational freedom of the macrocycles has provided the opportunity to include ' a small piece of silver' within the donor cavity enabling intermetallic interaction to occur. The interface between organometallic chemistry and macrocyclic coordination chemistry can also be explored and might reveal some novel and interesting hybrid compounds.

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