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Heavy metal ion chemistry of linked macrocyclic systems incorporating oxygen and/or sulfur in their donor sets

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Contents

Abstract

The heavy metal chemistry of linked macrocyclic ligand systems incorporating all oxygen, all sulfur, oxygen and nitrogen, oxygen and sulfur; nitrogen and sulfur as well as oxygen, nitrogen and sulfur in their donor sets is reviewed. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: Macrocycle; Linked-macrocycles; Heavy-metal; Dendrimer; Transition metal

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1. Introduction

In his pioneering work on the metal ion chemistry of macrocyclic ligands, Busch [1–3] has made a major contribution to what has now grown to be a large and diverse area of chemistry. Since the early studies, there has been an increasing tendency to produce larger, structurally elaborated systems, a path also followed by the Busch group [4,5]. Largely because of their often unique nature, macrocyclic

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rings have been seen as desirable moieties for incorporation in multicomponent molecular systems. Perhaps the most studied examples of this type are the linked macrocyclic systems; a range of examples of linked rings that form di- or, much less commonly, polyfunctional-metal binding systems has now been reported.

There have been a number of motivations for investigating the metal ion chemistry of linked macrocyclic rings. Linked rings that bind simultaneously to two or more metal ions may give rise to complexes exhibiting unusual electronic, catalytic and/or redox properties. Species such as these may, for example, be of interest as models for the charge transfer and electron transport behaviour found in a range of metal-containing biochemical systems.

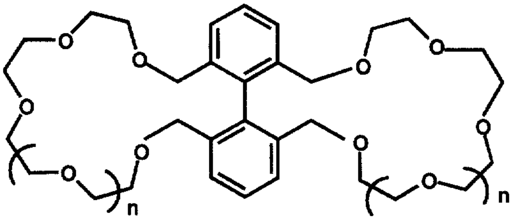
A large number of linked systems of the above type have incorporated polyaza macrocyclic rings and the heavy metal ion chemistry of this category has been reviewed recently by the present author [6]. Interest in the linked tetraaza category has been heightened by the finding that individual compounds of this type have been demonstrated to act as anti-HIV agents, while showing low levels of cytotoxicity [7–10].

This review will focus on the heavy metal chemistry of linked systems containing all oxygen, all sulfur, oxygen and nitrogen, oxygen and sulfur; nitrogen and sulfur as well as oxygen, nitrogen and sulfur in their donor sets.

2. Systems incorporating single donor and mixed donor sets

2.1. All oxygen donors

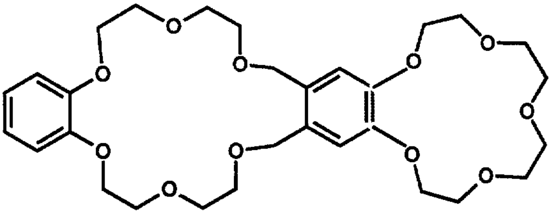
Allosteric interactions occur in enzymes when the binding at one site causes a change which affects the receptivity towards binding of a second site. The possible allosteric effects of binding two metal species to bis(crown ethers) of type (**1**) have been studied [11–14]. In order to avoid the influence of repulsive electrostatic effects, the uncharged mercuric reagent, $Hg(CF_3)_2$, was employed for binding the studies. Two molecules of $Hg(CF_3)_2$ complex with the bis-crown derivative (**1**; $n = 2$), but the statistically corrected (intrinsic) stepwise binding constants are approximately equal, there is no evidence for allosteric behaviour in this case [11]. That is, the binding behaviour of both sites act independently.



(1)

In contrast, the binding of two $Hg(CN)_2$ moieties to (**1**; $n = 1$) exhibited positive cooperativity; the mercury(II) species was found to bind more strongly to the *second* site than to the *first* site [12]. The binding enthalpies are the same for both steps while the entropy for the second step is more favourable [13]. It was proposed that the binding of the first mercury atom may fix the dihedral angle between the rings at an optimum value for complexation and thus promote the binding of the second mercury atom to the second ring.

X-ray studies of the $Hg(CN)_2$ complex of (**1**; $n=1$) and the $Hg(CF_3)_2$ complex of the single ring analogue corresponding to (**1**; $n=2$) appear to provide further insight into the respective behaviour mentioned above [14]. In the first of these X-ray structures, all oxygens of each ring of (**1**; $n=1$) coordinate to mercury, while in the second (single ring) complex, only five of the six ether oxygens of the ring so bind. In the latter species it is one of the benzyl oxygens that remains unbound. If a similar situation occurs in the $Hg(CN)_2$ complex of (**1**; $n=2$), then little restriction will be imposed on the dihedral angle adopted by the biphenyl fragment on binding the first mercury atom and this may have implications for the lack of co-operativity observed in the formation of the dinuclear species.



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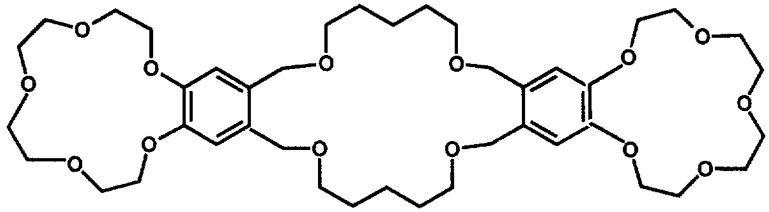

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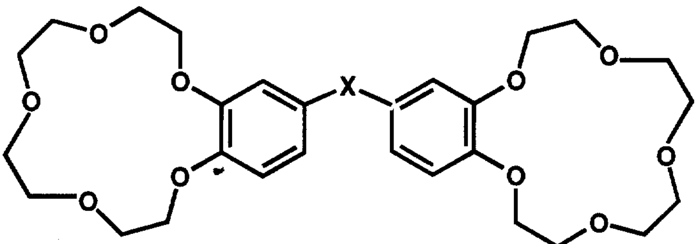

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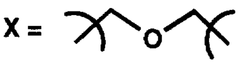
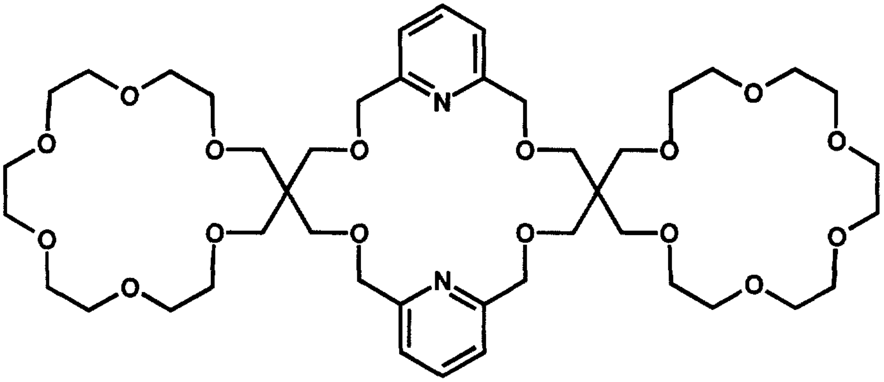


(5)

(6)

Solvent extraction experiments (water/dichloromethane) have been employed to estimate the relative complexing abilities of the linked crowns (**2**)–(**6**) towards a range of metal picrate salts [15] that included Ag(I) picrate. Besides the alkali and alkaline earth ions, the latter included Ag(I). Under the conditions employed, these all-oxygen donor systems were found to be rather poor extractors of the soft Ag(I) ion.

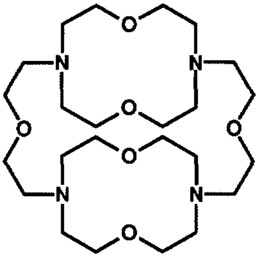
2.2. *Mixed oxygen–nitrogen donor sets*



(7)

Weber et al. [16,17] have prepared the mixed spiro-linked, trifunctional ligand (**7**) and demonstrated that it forms a mixed K^+/Co(II) metal complex in which a potassium ion was proposed to occupy each of the "outside" crown rings while Co(II) filled the central (di-pyridyl-containing) ring, reflecting the enhanced affinity of the relatively softer Co(II) for the ring incorporating nitrogen donors.

The di-linked bis-O_2N_2 macrocyclic system (**8**) has been demonstrated to interact with Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Pb(II) and Ag(I) in aqueous media [18]. This ligand forms dinuclear complexes of type M_2L^{n+} with Cu(II), Zn(II) and Ag(I), accompanied in the latter case by a mononuclear MLH^{2+} species. For Cu(II) and Zn(II) at higher pH-values, dinuclear hydroxo complexes were also observed. The other cations only yielded mononuclear complexes over the pH range investigated, with the respective ML species being accompanied by either protonated and/or hydroxo (mononuclear) species. With this ligand, Cu(II) and Ag(I) were shown to yield the most stable complexes. The X-ray structure of the solid Ag(I) complex confirms that (**8**) acts as a dinucleating ligand, enclosing two silver cations; each metal ion is bound to a macrocyclic O_2N_2-set, an oxygen from a linking group, and an oxygen from a bridging nitrato group [19].



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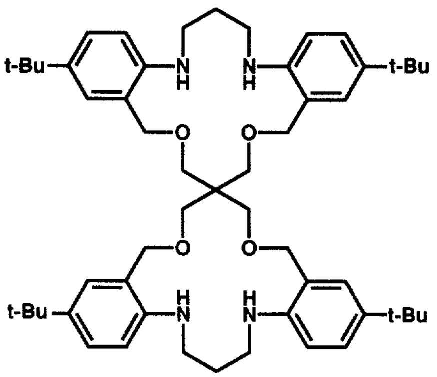

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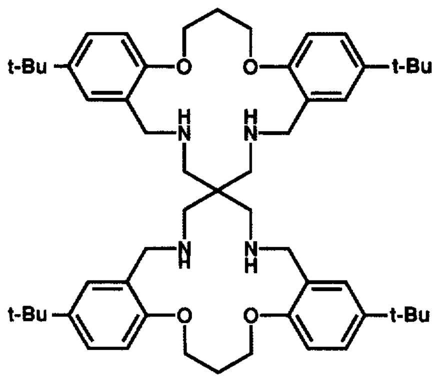

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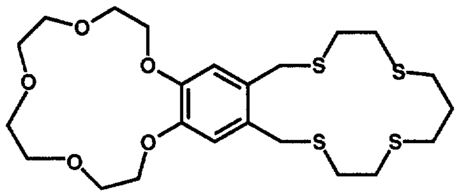
A series of mixed oxygen–nitrogen donor, spiro-linked macrocycles, of which (**9**) and (**10**) are representative, have been synthesized in the author's laboratory [20]. Initial studies give evidence for the formation of 2:1 (metal:ligand) Ni(II) and Cu(II) complexes in solution for both (**9**) and (**10**) [21].

2.3. *Mixed oxygen–sulfur donor sets*

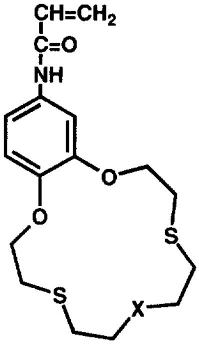


(11)

As expected, enhanced extraction of Ag(I) occurred in the case of the sulfur-containing system (**11**) [15] relative to the related all oxygen systems (**2**)–(**6**) discussed previously. However, this behaviour was reversed for the (hard) thallium] ion: extraction of this ion by (**11**) was significantly lower than observed for the above all-oxygen donor linked systems.

It is possible to use the hetero-ring system (**11**) to obtain mixed metal complexes

[15]. Addition of a stoichiometric mixture of NaNCS and $Co(NCS)_2$ to (**11**) yielded a dark-green product of composition (**11**).NaNCS.$Co(NCS)_2$ in which the Co(II) was postulated to bind to the S_4-ring while the Na^+ ion is bound to the O_6-ring.



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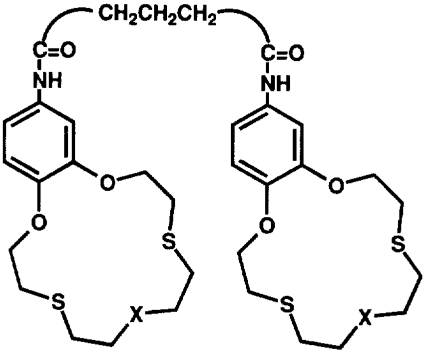
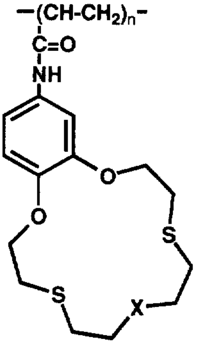


X = -S-
X = $-S(CH_2)_3S-$

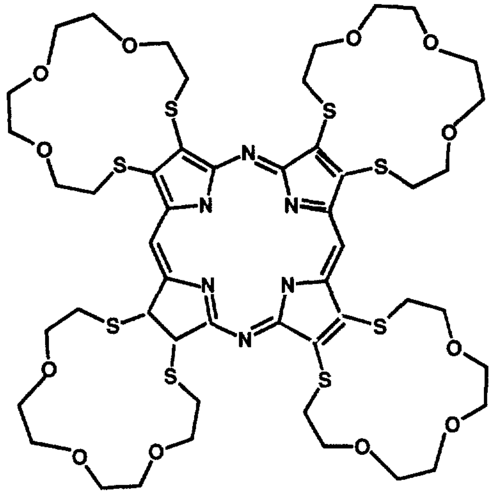
(13)



(14)

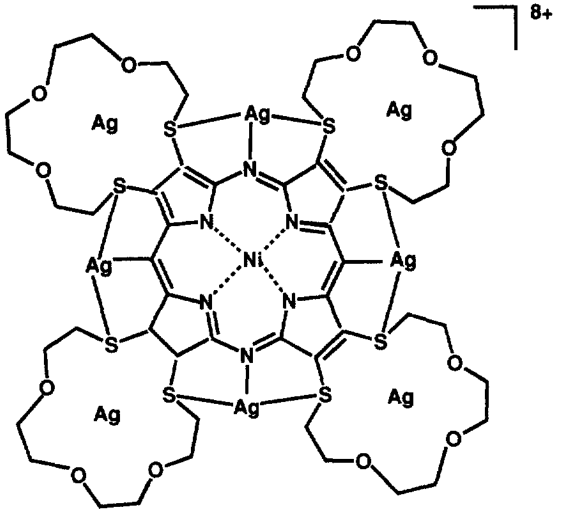
Mono-, bis- and poly-benzothiacrown macrocycles of types (**12**), (**13**) and (**14**) have been employed as extraction reagents for a range of metal ion types in the presence of picrate ion [22,23]. In general, high selectivity for Ag(I) ion was observed when the aqueous phase contained a mixture of this ion with a number of heavy metal ions [including Fe(III), Cu(II), Zn(II), Pb(II) and Bi(III)]. However, when

Hg(II) was present then only this ion was extracted and the selectivity for Ag(I) was lost.



(15)

Reaction of the Ni(II) complex of the crown-modified tetraazaporphyrin (**15**) with Ag(I) ions yielded the corresponding tetra-Ag(I) species in which the four silver ions occupy the four peripheral O_3S_2-macrocyclic sites [24]. Slow evaporation of a chloroform/methanol solution of the parent nickel complex in the presence of excess silver tetrafluoroborate produced a crystalline product containing eight Ag(I) ions. The X-ray structure of this product shows that four Ag(I) ions were contained in the four peripheral macrocyclic rings but that four additional Ag(I) ions occupied the "meso" pockets as shown in (**16**). Each on these latter silver ions has tridentate S–N–S co-ordination involving two bridging thioether S atoms and the meso N atom, the coordination sphere of each of these Ag(I) ions is completed by an oxygen atom from a solvent molecule (not shown).



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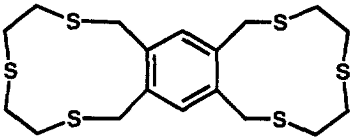
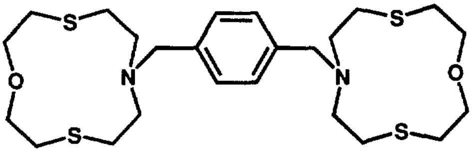
2.4. *All sulfur donor sets*



(17)

The bis(thiacrown ether) (**17**), incorporating two cyclic S_3-donor sites that are separated by a rigid *o*-xylyl spacer group, has been synthesised using a template procedure [25]. This system has been shown to form mixed ligand, binuclear complexes of Cu(I); these may adopt either *anti* or *syn* arrangements. An example of each type, *anti*-$[Cu_2L(PPh_2Me)_2][ClO_4]_2$ and *syn*-$[Cu_2L(\mu\text{-}PPh_2CH_2CH_2PPh_2)][PF_6]_2$, has been characterized by X-ray diffraction (Figs. 1 and 2). In the latter of these complexes, the bridging $PPh_2CH_2CH_2PPh_2$ ligand spans both Cu(I) sites. Undoubtedly, the presence of soft phosphorus and thioether sulfur donors in each of these compounds aids stabilization of the (soft) Cu(I) state.

2.5. *Mixed oxygen–nitrogen–sulfur donor sets*



(18)

The *p*-xylyl linked bis-macrocyclic ligand (**18**) yields both dinuclear Cu(I) and dinuclear Cu(II) complexes (as their tetrafluoroborate salts). The former species in

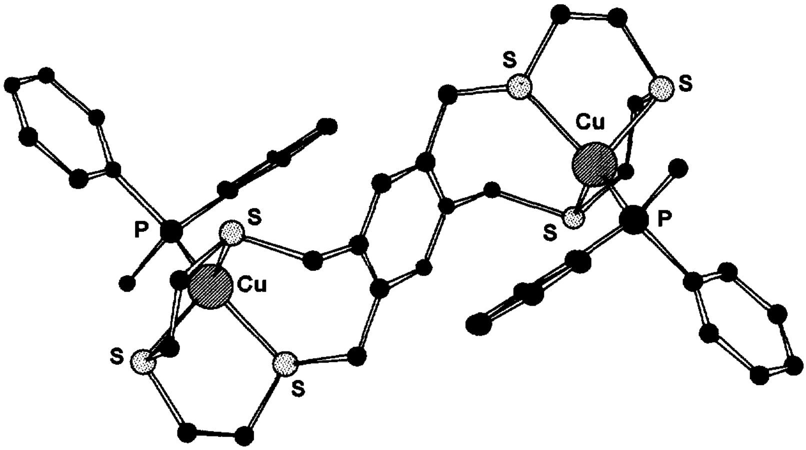


Fig. 1. The X-ray structure of the cation *anti*-$[Cu_2L(PPh_2Me)_2]^{2+}$ [L = (**17**)] [18].

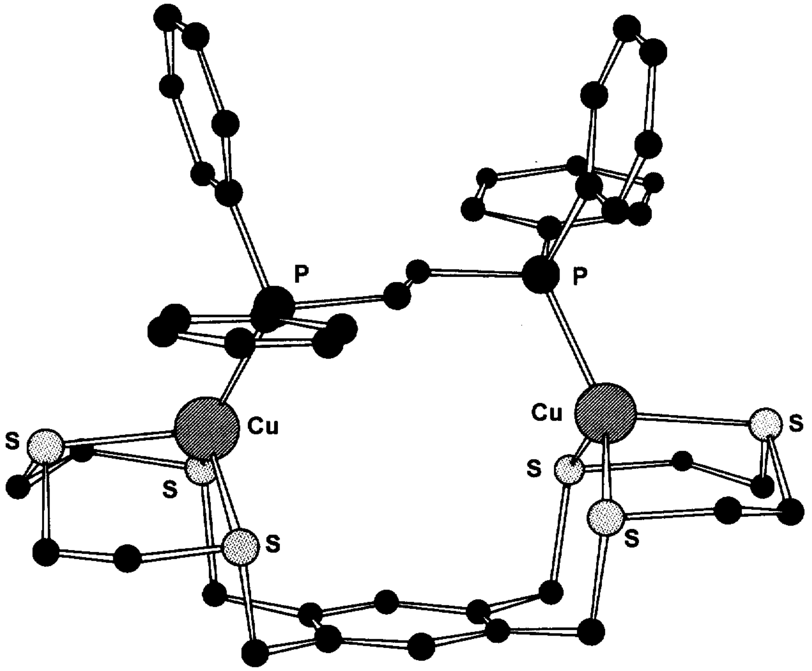
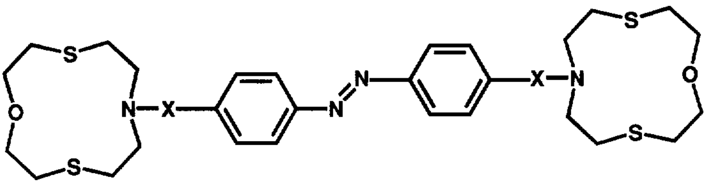


Fig. 2. The X-ray structure of the cation *syn*-$[Cu_2L(\mu\text{-}PPh_2CH_2CH_2PPh_2)]^{2+}$ [L=(**17**)] [28].

propylene carbonate absorbs CO (reversibly), as well as O_2 (partially reversibly) [26]. Treatment of the parent di-Cu(I) complex in nitromethane with NO rather surprisingly results in crystallization of a dark-green tetrafluoroborate salt of the dinuclear Cu(II) cation $[(NO_2)CuLCu(NO_2)]^{2+}$; the latter incorporates two bidentate nitrite ligands [27]. Each Cu(II) has a distorted octahedral geometry, with the coordination shell in each case being completed by the ONS_2-donor set of one of the linked macrocyclic rings.

A related green dinuclear Cu(II) complex is obtained on reaction of Cu(II) tetrafluoroborate with the free ligand (**18**) in propylene carbonate. This product has a normal magnetic moment at room temperature for each copper, indicating the lack of coupling between the Cu(II) ions. A similar conclusion was drawn from an epr study. However, on dissolution of this species in water at pH 6 yields a new species. After isolation, the X-ray structure of this latter complex shows that the two copper ions now have 5-coordinate geometries, being bridged by a single hydroxo group. In this arrangement the ligand has adopted an "ear-muff" configuration with the bridging hydroxo group holding the two Cu(II) ions at a separation of 3.384 Å. The Cu–O–Cu angle is 132.2 Å. The epr spectrum of a powered sample of this complex exhibits triplet state features, with the magnetic properties being typical of two strongly antiferromagnetic coupled ($S = 1/2$) Cu(II) ions.



(19) (X = CH 2 or CO)

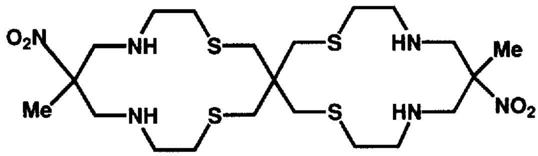
The photo-responsive bis-ONS$_2$-donor macrocycles of type (**19**, X=CH$_2$ or CO) have been investigated and were also expected to yield dinuclear metal complexes with heavy metal ion in view of the behaviour of (**18**) discussed above [28].

The *cis* forms of (**19**; X=CH$_2$) and (**19**; X=CO) are both isomerized thermally to the respective *trans* forms. This isomerization is also promoted by irradiation with visible light, with the photo-induced *cis-trans* interconversion occurring reversibly. Both the *trans* and *cis* forms of (**19**; X=CH$_2$) yield 2:1 Cu(II) complexes; the composition does not change on photoisomerization.

Rate experiments showed that the addition of Cu(II) chloride resulted in an enhancement of the above interconversion when the metal to ligand ratio was greater than 2; below this ratio no rate increase was observed. This observation suggests that Cu(II) is initially bound to the two macrocyclic sites followed by subsequent interaction of this ion with the azo linkage. It appears to be this latter process which is associated with the observed rate enhancement.

The influence of photo-irradiation of (**19**, X=CH$_2$) on the extraction of Co(II), Ni(II), Cu(II), Pb(II) and Hg(II) picrates from water into dichloromethane has been examined [28]. The results confirmed that both the *trans*- and *cis*-forms of this ligand form 2:1 complexes with the above metal ions. In nearly all cases [the exception is for Pb(II), for which the percent extraction slightly decreased] extraction was enhanced on irradiation, but only marginally so. From this, it was inferred that the respective ONS$_2$-rings act nearly independently in their extraction behaviour towards the above metal picrates.

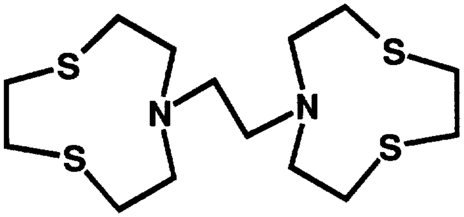
It was anticipated that the di-Cu(I) complex of (**19**, X=CH$_2$) might also show affinity for dioxygen and carbonyl groups in light of the behaviour of the corresponding complex of (**18**) discussed above [26]. In particular, the complex of (**19**, X=CH$_2$) in its "ear muff" configuration was considered to be a likely candidate for such binding based on the expected proximity of the Cu(I) sites in this configuration. This prediction was born out in practice. Initial photoisomerization of (**19**, X=CH$_2$) to the *cis*-form, followed by complexation with Cu(I) and reaction with dioxygen in propylene carbonate led to uptake of O$_2$. The data from three uptake/evacuation cycles showed that the process was partially reversible. In contrast, for the di-Cu(I) complex of the *trans* form of (**19**, X=CH$_2$), dioxygen uptake was irreversible. The study thus demonstrated that, at least in principle, light can be used to control the reversible binding of dioxygen in systems such as the present one.



(20)

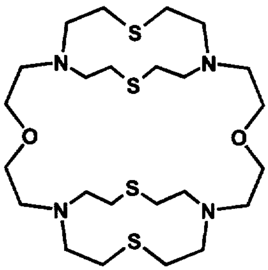
The spiro-linked, bis-macrocyclic species (**20**), incorporating two N_2S_2-donor rings, has been synthesized as its dinuclear Cu(II) complex via a template procedure [29]. The procedure involved condensation of nitromethane and formaldehyde with the di-Cu(II) complex of the corresponding open-chain species, 5,5-bis(4-amino-2-thiabutyl)-3,7-dithianonane-1,9-diamine [29]. The electrochemistry of this binuclear complex shows a Cu(II)/Cu(I) quasi-reversible couple with $E_{1/2} = -0.01$ V. The epr spectrum of the di-Cu(II) species indicates coupling between the two metal centres. Analysis of the spectrum indicated a metal separation of 7.1 ± 0.2 Å in this complex.

2.6. Mixed nitrogen–sulfur donor sets



(21)

Parker et al. [30] have prepared the Ag(I) complex of the bis(NS_2-macrocycle) (**21**). This complex has a metal:ligand stoichiometry of 1:1 (metal:ligand) and an X-ray diffraction study (Fig. 3) showed that all six donor atoms of (**21**) coordinate to the same Ag(I) ion, with the latter having a very distorted octahedral geometry. The "short" dimethylene link in this system causes the two macrocyclic subunit planes to be inclined at 17° to each other in the complex, rather than adopting a configuration in which they were parallel. Potentiometric titration in aqueous solution [$I = 0.1$, $Me_4N(NO_3)$] yielded a stability constant of log 7.00 for AgL [L = (**21**)].



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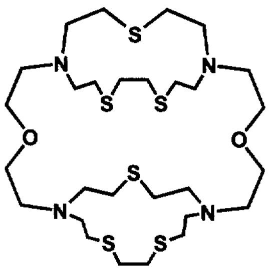

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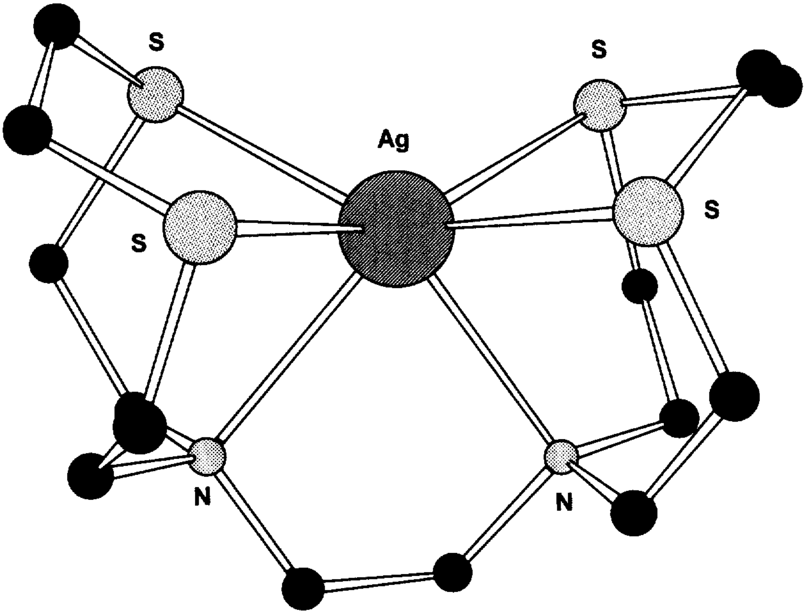
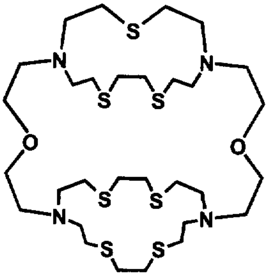


Fig. 3. The X-ray structure of the cation $[AgL]^+$ [L = (**21**)] [23].



(24)

Lehn et al. [31,32] have synthesized a series of "face to face" di-linked ligands of which (**22**)–(**24**) are representative members. Reaction of Cu(I) and Cu(II) perchlorate with (**22**) yielded complexes showing the expected to 2:1 (metal:ligand) ratio, with evidence that a 1:1 species is an intermediate in the complexation process. With (**24**), it proved also possible to form a mixed Cu(I)/Cu(II) species; electronic spectral evidence suggested that the Cu(I) and Cu(II) cations are probably located in the 18- and 12-membered rings, respectively. Cu(II) complexes of the above type were proposed as potential binuclear models for Cu(II) proteins. Thus the di-Cu(II) complex of (**22**) undergoes reversible electrochemical reduction at +0.445 V in aqueous solution [33]. Both copper sites act independently so that only a single reduction potential is observed, with the potential falling in the region observed for type 3 Cu(II) sites in proteins. Epr studies of the above complex indicated the

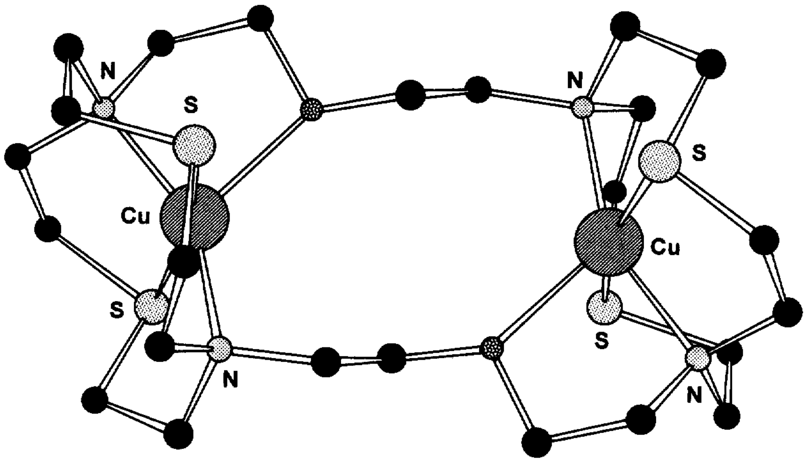


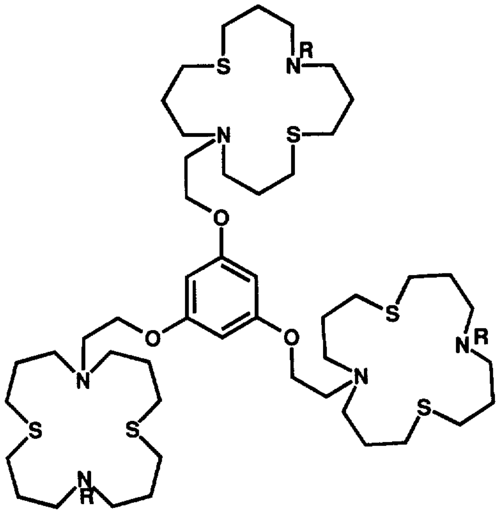
Fig. 4. The X-ray structure of the cation $[Cu_2L]^{4+}$ [L=(**22**)] [27].

presence of exchange coupling [32,34,35] and magnetic studies confirmed the presence of a strong antiferromagnetic interaction [36]. The X-ray structure (Fig. 4) shows that two copper ions are bound inside the cavity with a separation distance of 5.62 Å [34,35]. Each copper in the structure has a tetragonal pyramidal coordination geometry with the metal lying 0.034 Å out of the N_2S_2-plane towards an axial oxygen donor.

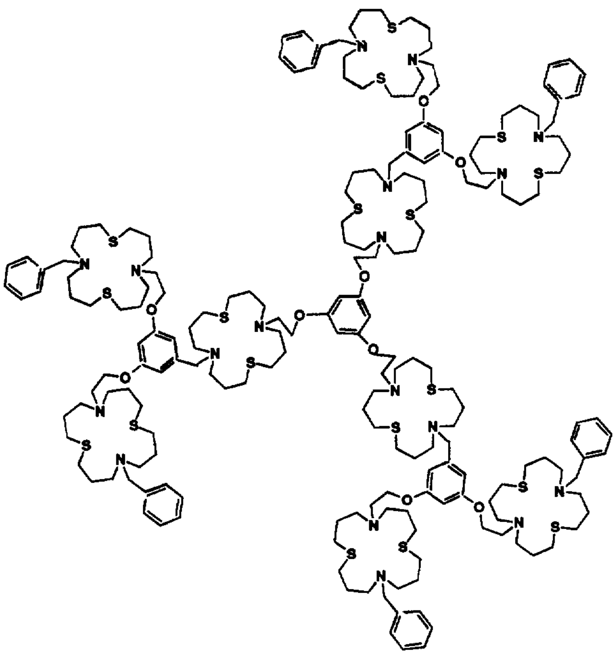
Macrocycle (**22**) also acts as a dinucleating ligand towards Ni(II) and Ag(I) [32]. Like the Cu(II) complex, the Ni(II) centres behave independently during cyclic voltametry with the, $E_{1/2}$ value being -0.54 V for the double 1-electron reduction to Ni(I). Such behaviour is consistent with a large separation of the metal ions as found in the above dinuclear Cu(II) complex. The corresponding di-Ni(II) complex of (**23**), incorporating two N_2S_3-donor macrocyclic rings, behaves as a (2+2) four-electron receptor; two two-electron reduction waves are observed in propylene carbonate corresponding to the formation of di-Ni(I) and di-Ni(0) complexes, respectively.

The di-Ag(I) complex of (**22**) in solution yields a symmetrical ^{13}C nmr spectrum, in agreement with the silver ions being bound in equivalent positions within the macrotricyclic cavity.

Beginning with the parent 16-membered rings containing differentially protected nitrogen donors, it has proved possible to synthesise a number of tri-linked S_2N_2-donor macrocyclic systems in which three such rings are connected symmetrically to a 1,3,5-tribenzyl or a phloroglucinol core (see **25**) [37]. These systems react with the soft metal ions Ag(I), Pd(II), and Pt(II) to yield products in which the metal:ligand ratio is 3:1 [38]. Related complexes of the corresponding single ring derivatives have also been synthesised. Solvent extraction experiments (water/chloroform) using the above single ring and tri-linked ligands as the ionophore in the chloroform phase, and equimolar (10^{-3} mol dm^{-3}) concentrations of Co(II)



(25) **R = H or Bz**



(26)

Ni(II) Cu(II), Zn(II), Cd(II), Ag(I) and Pb(II) nitrates in the aqueous phase, resulted in high extraction selectivity towards Ag(I) in each case.

In an extension of the above studies, the related dendritic system (**26**), incorporating nine linked rings, has been synthetised. In preliminary studies, this species has also been demonstrated to complex with Pd(II) and Pt(II) [38].

Acknowledgements

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