Pure & Appl. Chem., Vol. 56, No. 11, pp 1603-1619, 1984.
Printed in Great Britain.

0033-4545/84 $3.00 + 0.00
Pergamon Press Ltd.

ENCAPSULATED METAL IONS

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Abstract - This paper reviews some of the more interesting and recent phenomena associated with the metal ion cage chemistry involving hexaazamacropolycycles. Synthetic aspects are addressed in relation to making cages with smaller and larger hole sizes in order to modulate redox potentials and electron transfer rates. The introduction of substituents is also examined in relation to these factors along with the effect of ligand geometry and strain. Relevant redox potentials, spectroscopic and photochemical properties of the different metal ion cages are displayed. Aspects of the synthesis of dimer complexes and some properties of the dimer complexes are outlined. The route whereby the metal is extruded from the cage in acid conditions is examined in some detail for the Cusar^{2+} ion. The properties of an extraordinarily stable zinc alkyl cage are examined and finally various prospects for the use of the metal ion cages are reviewed.

Multidentate ligand chemistry has given us a plethora of interesting phenomena over the years, limited only by our ability to make these fascinating molecules. The results are manifest in very stable complexes, static and dynamic selectivity phenomena, stabilization of oxidation states and spin states, solubilization of ions in organic solvents, transport of ions through biological membranes, oxidation of the ligand through a high oxidation state at the metal centre, coupling of chelates through radicals generated on the ligand periphery and antifungal and antibacterial activity to mention some of the more interesting facets.

The ligands themselves are now too numerous to review but in the last 10-15 years large molecules which have a capacity to encapsulate other molecules or ions have become a prominent subclass in this interesting research area (Ref. 1). This lecture addresses that subclass and especially the synthesis and properties of sexidentate ligands of the macropolycyclic type shown in Fig. 1 involving N atom donors. These cage molecules have been constructed about the metal ion by using it as a template to hold the reacting organic fragments and the means whereby that chemistry is carried out has been described previously (Ref. 2 & 3). It is merely outlined again briefly here (Fig. 2) to remind you of itssimplicity and efficiency. Basically the reaction is a way of controlling iminium ion chemistry using a metal ion instead of a proton to activate an imine to nucleophilic

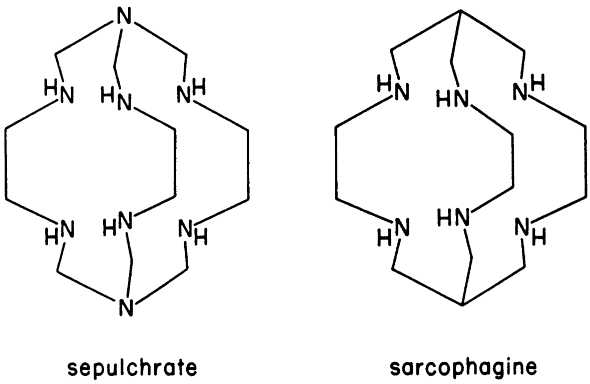


Fig. 1. Stable hexaazamacrobicyclic cage ligands.

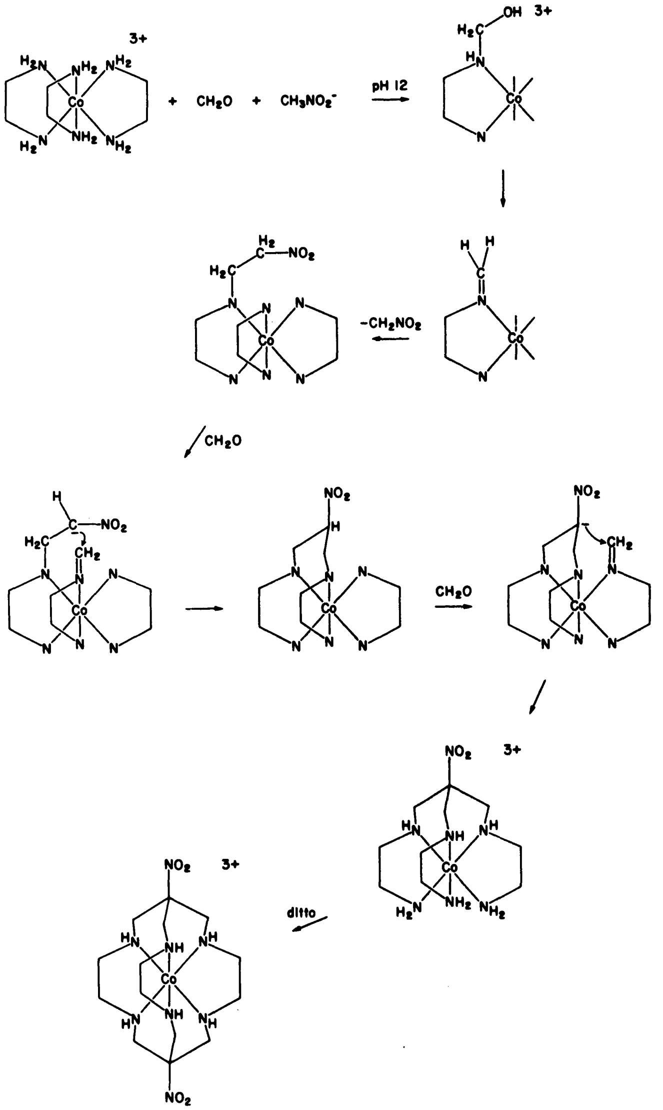


Fig. 2. Mechanistic scheme for the synthesis of $Co(di(NO_2)sar)^{3+}$.

attack. Simple amine complexes such as $M(en)_3^{3+}$ and formaldehyde are reacted to give coordinated imine complexes some of which have been isolated (Ref. 4 & 5) and characterised, Fig. 3. The imine carbon atom can then be treated with a nucleophile such

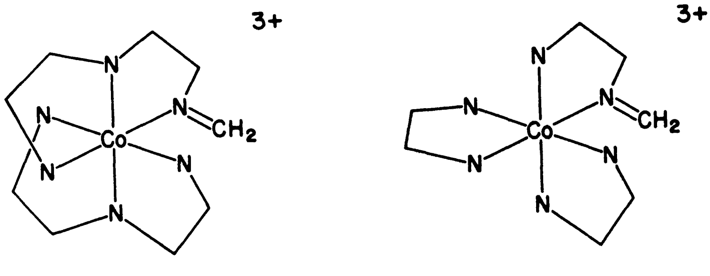


Fig. 3. Isolated exocyclic imine complexes.

as the nitromethane carbanion or ammonia to initiate the encapsulation process. Once another imine is generated adjacent to the now coordinated nitro-ethyl moiety an intramolecular cyclization ensues to make the first ring of the cap. The following condensations and cyclizations lead to one cap and then another to give the fully encapsulated complex in yields ≈ 80% of the Men_3^{3+} ion. Despite the complexity of events and the one pot synthesis, several intermediate species have been detected and some characterized crystallographically (Ref. 5), Fig. 4, including substantial amounts of the monocapped ion if the reaction is quenched at appropriate times. These results imply that the process occurs very much as outlined in Fig. 2. One cap forms faster than the other. However, some deviation from this pattern cannot be discounted. Further support can be adduced for this claim from the fact that $[CoN\text{-methyl}(NO_2)sen]^{3+}$ can be a significant by-product but not $[Co(en)_2N\text{-methylethanediamine}]^{3+}$. The methyl substituents arise from crossed-Cannizzaro reactions of $Co\text{-}N\text{=}CH_2$ groups with CH_2O and clearly a shorter lifetime for the $[Coen_2en\text{-imine}]^{3+}$ complex relative to the $[Co(NO_2)sen\ imine]^{3+}$ complex is implied by the results. The overall synthesis is efficient based on the $Coen_3^{3+}$ concentration but less so relative to the organic reagents. Even so, it is competitive with the straight organic reactions, presumably because of the efficient intramolecular reactions.

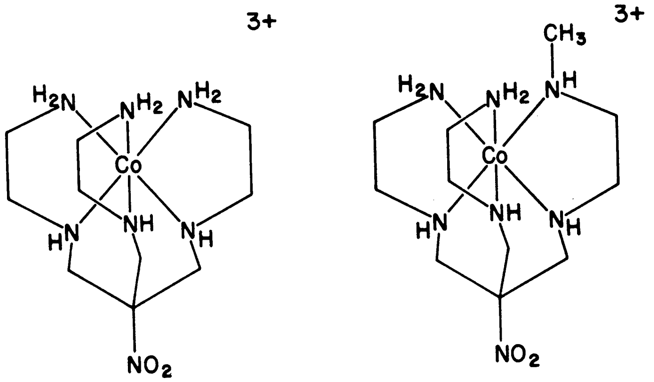


Fig. 4. Products arising during the cage synthesis.

Many obvious extensions flow from these results. Any octahedral face containing three primary amine groups should be susceptible to the capping process provided the amine protons exchange relatively rapidly in the basic conditions used and the appropriate functional group can be orientated properly for the cyclizations. In this way $Coen_3^{3+}$, $Rhen_3^{3+}$, $Iren_3^{3+}$ and $Pten_3^{4+}$ have been encapsulated. We have had little success with $Cren_3^{3+}$ and the divalent ethylenediamine complexes and $[Ni(sepulchrate)]^{2+}$ has only been synthesized in < 1% yield but its structure has been established by X-ray crystallographic analysis (Ref. 6). A claim has also been made for the synthesis of $[Cr(sepulchrate)]^{3+}$ but the product was only characterised by one infrared frequency and no analytical data were provided (Ref. 7). The problem with the $Cren_3^{3+}$ capping process is that as soon as the imine is formed it enhances the rupture of the Cr-N bond (Ref. 8). Once the bond is broken in the aqueous conditions it does not readily reform. Clearly, this strategy for encapsulation is limited to low yields of the desired complex given these circumstances unless the capping process can be made competitive with the Cr-N bond rupture rate.

The labile Men_3^{3+} complexes display similar problems. There are indications that one end of the C_3 axis can be capped fairly readily but the process is also easily diverted to synthesize square planar macrocyclic complexes of various types, especially with Ni(II) and Cu(II), a conclusion also reached by the Korean group (Ref. 6), Fig. 5. $Ruen_3^{3+}$ and $Osen_3^{3+}$ were obvious candidates for the capping process but once the imines are formed these complexes disproportionate spontaneously in the basic conditions to the (II) and (IV) oxidation states. The imines of the former state resist the addition of the nucleophile and the methylene groups in the (IV) oxidation state complexes are spontaneously oxidised to imines (Ref. 10). The capping process is therefore hampered by these effects unless it can be made to occur more rapidly than the disproportionation reactions.

Some of these problems have been circumvented by synthesizing the desired cage complexes from the free ligands sar or $di(NH_2)sar$ obtained by extracting the Co^{2+} ion from the cages using either concentrated HCl or HBr at high temperatures (130-150°C) (Ref. 11). In this way a variety of metal complexes have been made and many have been structurally characterized (Ref. 12). They include $di(NH_2)sar$ and/or sar complexes of Mg^{2+}, Ti(IV), V(IV), (III), Cr(III), Mn(III)(II), Fe(III),(II), Ni(III)(II), Cu(II), Zn(II), Cd(II),

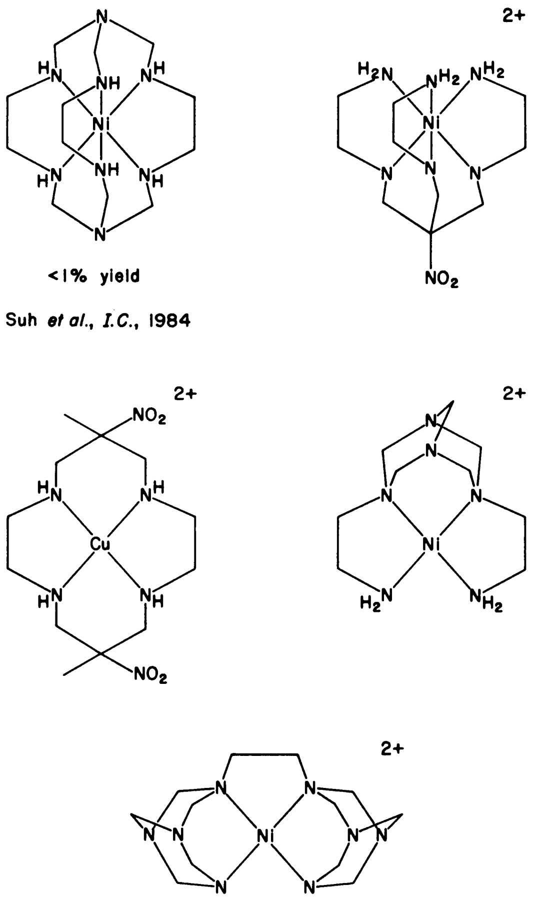


Fig. 5. Labile metal ion complexes arising from the cage synthesis conditions.

Hg(II), Ag(II), Ga(III), In(III), Mg(II). Other oxidation states have also been detected by electrochemical and spectroscopic methods.

Numerous variations are available for substituents in the apical position and these have been documented earlier (Ref. 3 & 13). They include $-NO_2$, $-NHOH$, $-NO$, $-NH_2$, $-\overset{+}{N}H_3$, $\overset{+}{N}(CH_3)_3$, $-OH$, $-Cl$, $-Br$, $-I$, $-COOH$, $-COOR$, $-NHCOCH_3$, $-CN$, $-CONH_2$, $-CH_2OH$. The cage substituents arise from the capping reagent substituents and the subsequent reactions of the cage substituents and of the cage ligand in general. These substituents give a wide range of redox potentials and other properties to the molecules. They span at least 0.6 V in redox range i.e. ten orders of magnitude in equilibrium constant or five orders of magnitude in redox reaction rate for the Co(II)(III) systems (Ref. 13). If the other metal ion couples are included the total redox span is ~ 2 V (~ + 1 V → -1 V) at intervals of ~ 0.1 V using the various substituents (Table 1). This gives an impressive array of redox reagents, although they are not all equally accessible. The magnitude of the variation is somewhat surprising in view of the distance of the substituent from the metal ion and it implies relatively close communication between the apical substituents and the metal centers. That communication is also reflected in the NMR chemical shifts of the apical C atoms and the large coupling constants with the metal in the cage but it is not reflected much in the ligand field spectra (Ref. 10). It has been argued therefore that these effects are due to repulsion of electronic states of the same symmetry transmitted through the bonds.

The substituents also allow a variety of ways other molecules can be coupled to the cage. They include, for example, other metal ions or complexes, other cages, large alkyl groups and polymer surfaces. Several dimer cages have been synthesized with 1,4-diaminomethylphenyl, azo, azoxy, urea and amide linkages and the cages have also been

TABLE 1. Redox potentials at 25°C, μ = 0.2 versus NHE

		E(V)	$[Msar]^{2+/3+}$	
				E(V)
O_2N-	Co -NO_2Å$^{2+/3+}$	+0.06		
H_3N-	-$NH_3^{4+/5+}$	+0.04	Cr	-1.0
CH_3-	-$NH_3^{3+/5+}$	-0.33	Mn	+0.56
			Fe	+0.10
NH_2-	-$NH_2^{2+/3+}$	-0.32	Co	-0.40
H-	-$H^{2+/3+}$	-0.40	Ni	+0.90
Cl-	-$Cl^{2+/3+}$	-0.13	Cu	+1.2
HO-	-$OH^{2+/3+}$	-0.20		
$Co(Me,ClCH_2)absar^{2+/3+}$		-0.50		
$Cosep^{2+/3+}$		-0.30		

attached to polymer beads to make chiral ion exchange columns (Ref. 10), for example. Some of the properties of the transition metal cages bear discussion. The Mn(II), Fe(II), Co(II), Ni(II) sar complexes are all high spin systems at 300 K but Fe(III) and Ni(III) are low spin complexes and Mn(III) may also be in that condition with a large orbital groundstate contribution (Ref. 14). The last yet to be confirmed and the bond length should be a fairly critical piece of information in that regard (Ref. 15).

With di(NH_2)sar, V(IV) forms a six coordinated complex in which two protons are lost from coordinated N atoms and this ion is close to a trigonal prism (~ 17(a)). Clearly, this is as close as it can get to the vanadyl condition (Ref. 16). The V(III) state is accessible but it has not yet been isolated in crystalline form. However magnetic studies and epr measurements show that it is a high spin d^2 ion (Ref. 14).

The Cr(III)(di(NH_2)sar)$^{3+}$ and Cr(III)(sar)$^{3+}$ ions (E ~ -1 V versus NHE) are both photoactive in the solid state at low temperatures (Ref. 17) but the lifetime of the doublet state falls off dramatically as the temperature rises and at room temperature in aqueous solution the lifetime of Cr(III)di(NH_2)sar^{3+} is less than 10 ns, Fig. 6. In dimethylformamide these results are in sharp contrast with those of $Cr(NH_3)_6^{3+}$ (17 μs) and $Cren_3^{3+}$ (6 μs) and the recently reported $Crsep^{3+}$ (10 μs) ions (Ref. 7), Table 2. Photodecomposition for the Cr(III)sar and di(NH_2)sar ions is much reduced as anticipated for the cage molecules but the reason is more doubtful. The ligand has difficulty coming off certainly and there is no sign yet in any of the metal ion chemistry that the coordination number can be increased beyond six. However the lifetime of the excited doublet state is now so short that there is little time for photodissociation to take place. It should be stated, however, that the structural relationship between the $Cren_3^{3+}$ ion and the Crdi(NH_2)sar^{3+} ion is very close. The twist angles ϕ are 51 (± 2)° and the bond lengths are the same (± 0.01 Å). Moreover, the [Crsepulchrate]$^{3+}$ ion would be expected to have the same structure and the differences between the sets of cage complexes is therefore mystifying. The reason for the rapid non-radiative decay of the sar based ions needs further study and in fact the spectroscopy and photochemistry of these ions are being examined in detail at present.

The redox properties were one of the early captivating features of the cage chemistry. For the Co(III)(II)sepulchrate$^{3+/2+}$ ions, despite the "insulating organic coat" the electron self exchange rate was ~ 10^5 fold greater than that for the parent $Coen_3^{2+/3+}$ ions (Ref. 2 & 3). In both sets of ions the ligand field spectroscopy, magnetism and Co-N bond lengths (± 0.01 Å) match closely (Ref. 2, 3 & 18), i.e. the electronic conditions of the pairs match. The only explanation we have for the increased self exchange rate (5 $M^{-1}s^{-1}$) is the strain generated in the ligand by the encapsulation of the ion. This shows up in observed distortions of bond angles and torsion angles (Ref. 2 & 3) and in the molecular mechanics calculations (Ref. 19 & 20). The cage "hole" appears a little too large for Co(III) and a little too small for Co(II). The strain generated in the ligand in both oxidation states aids the stretching of the Co(III)-N bonds and compression of the Co(II)-N bonds. In this

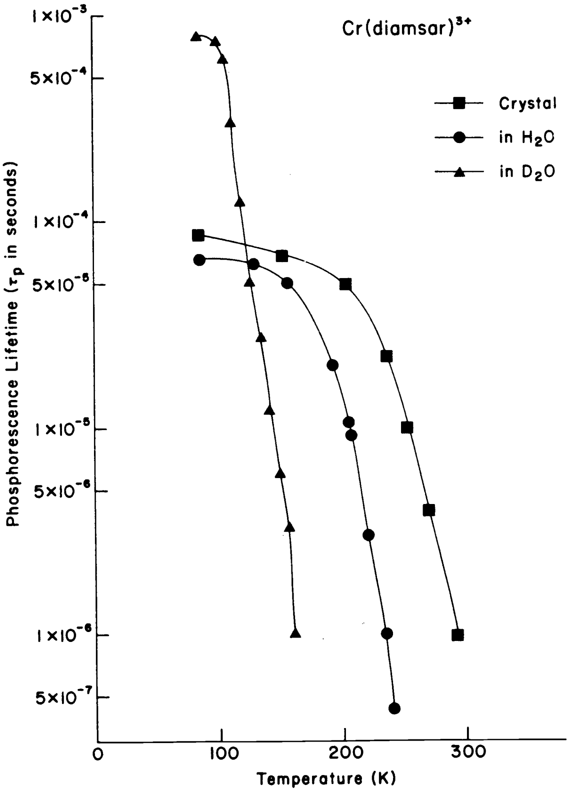


Fig. 6. $Cr(di(NH_2)sar)^{3+}$ doublet state lifetime as a function of temperature.

TABLE 2. Photophysical data for Cr(III) hexaamines

	$Cr(III)di(NH_2)sar^{3+}$	$Cr(III)sar^{3+}$	$Cr(III)sep^{3+}$	$Cren_3{}^{3+b}$	$Cr(NH_3)_6{}^{3+b}$
^2E	14500 ν cm^{-1}	14630	15000	15000	15200
$^4T_2$	21950 22350 (ε 208)	21860 22250 (ε 156)	21740 (ε 100)	21930 (ε 72)	21790
$^4T_1$	28940 (ε 109)	28820 (ε 91)	28990 (ε 102)	28330 (ε 63)	28490
τ_{297K}	< 10 ns	< 10 ns	10 μs	6 μs	17 μs
τ_{77K}	65 μs	60 μs		22 μs	
ϕ_{CR}	< 2.10^{-5}	< 2.10^{-5}	< 3.10^{-2}	0.37	0.45
φPhotoemission 77K	0.02	0.02			
$E_{Cr^{3+}/^{2+}}$ (V)	-1.1		-1.1	-1.1	
Cr-N Bond length (Å)	2.07			2.07	2.06
Twist angle[a]	49°	~ 50° expectation value	~ 50° expectation value	51°	60°

a The twist angle is the dihedral angle between the two faces of the octahedron related by the C_3 axis.
b Data collected in Ref. 7.

way the Cosep^{3+}.Cosep^{2+} assembly is helped towards the transition state even though the strain effect does not appear in the groundstate metal-ligand bond lengths (Ref. 2 & 3).

One of the most interesting aspects of this strain effect is the stereochemistry it engenders about the metal for the different ions. Looking at the cage complex ions along the C_3 axis and at the angle which the trigonal faces related by the C_3 axis bear to each other, interesting facts emerge from the data, Fig. 7 (Ref. 21).

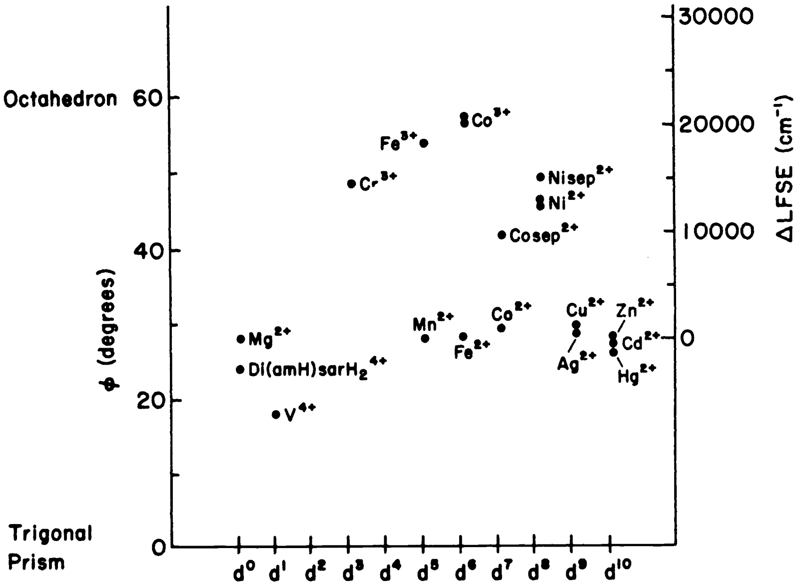


Fig. 7. The proximity of the metal ion cages to an octahedral or trigonal prismatic structure.

It is evident that for all those ions where the ligand field stabilisation energies are small their structures are not much different from that of the metal free diprotonated ligand. Also the trend is more towards the trigonal prism than towards the octahedron. In those ions where the ligand field effect is larger the structures progressively approach that of an octahedron Ni(II) < Cr(III) < Fe(III) < Co(III). Clearly, the ligand dominates the former cases and the metal the latter (Ref. 21). An apparent exception is the [Co(II)sep]$^{2+}$ structure (Ref. 3). Here, however, there are substantial distortions at the angles around the N cap of the ligand (Ref. 2 & 3) and in this manner the distortion about the metal center is relieved. By comparison, the [Co(II)di(NH$_3$)sar]$^{4+}$ structure shows relatively regular geometry in the vicinity of the C-cap and the expected trigonal distortion at the metal center. These distortions, of course, are also reflected in the spectroscopy (visible and epr) of the complexes in solution and in the solid state. Another set of data of note in this study is that comprising the triad Zn(II), Cd(II), Hg(II). They do not differ greatly in structure despite the range of M-N bond lengths (2.19, 2.30, 2.35) and they are all clearly sexidentate merely tending more towards the trigonal prism as the central ion becomes larger. The set does imply access to encapsulated ions of a size we had previously thought not feasible and therefore to a much larger range of complexes in general.

Not only does the Co-N bond length change substantially during the electron transfer process (0.17 Å) but the stereochemistry of the cage also alters sharply (twist angle φ 56° Co(III) to φ 28° Co(II) for Cosar$^{2+/3+}$) and there is a regularity in the sar and di(NH$_2$)sar chemistry. It might be expected therefore with all the Co(II)(III) substituted sar and di(NH$_2$)sar type cages that their electron self exchange rates would be fairly similar, apart from the effect of work terms in bringing the ions together and that seems to be the case as Table 3 indicates.

One interesting example in this electron transfer context is the couple [Cochloro, chloromethyl absar]$^{2+/3+}$. The absar molecule (Fig. 8) arises from a rearrangement of a

TABLE 3. Electron self-exchange rates

	k_{ex} $M^{1}s^{1}$
Co $sep^{2+/3+}$	5.1
Co $sar^{2+/3+}$	2.1
Co di(NH_2) $sar^{2+/3+}$	0.50
Co di(NH_3) sar $H_2{}^{4+/5+}$	0.02
Co di(Cl) $sar^{2+/3+}$	3.0
Co ClMe $sar^{2+/3+}$	2.4
Co Cl_2ClCH_2 $absar^{2+/3+}$	7.3
Co diaza $char^{2+/3+}$	23
Co di(NH_2) $char^{2+/3+}$	1.0
Co di(NH_3) char $H_2{}^{4+/5+}$	0.04
Co (NH_2) $sartacn^{2+/3+}$	0.086
Co (NH_3) $sartacn^{3+/4+}$	0.040

25°C, $\mu = 0.2$

di(NH_2) complexes buffered pH 7.5 HEPES

di(NH_3) " in 0.1 M H^+

char = cage based on tris(1,2-trans-cyclohexanediamine)

sartacn = cage based on NN'N" tris 2-ethylamino-1,3,9-triazacyclononane

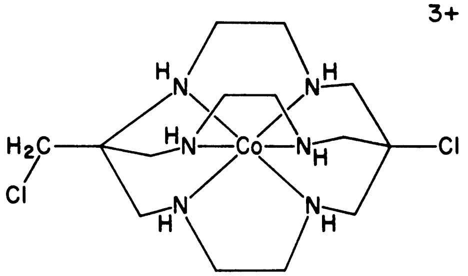


Fig. 8. Rearranged cage arising from the nitrosation of Co(III)(di(NH_2)sar)$^{3+}$ in HCl.

carbocation intermediate during the diazotisation of [Codi(NH_2)sar]$^{3+}$ with NO^+ in aqueous solution (Ref. 5), Fig. 9.

The rearrangement is an interesting aspect in itself but the primary point here is that one cap is now much tighter and the cage is less able to tolerate the larger Co(II) ion. The overall result is an increase in the ligand field strength of the ligand as shown in the visible spectroscopy of the Co(III) ion (λ_{max} 458 nm) and a change in redox potential of -0.23 V compared with the analogous dichlorsar complex (λ_{max} 474 nm). Clearly, the Co(II)

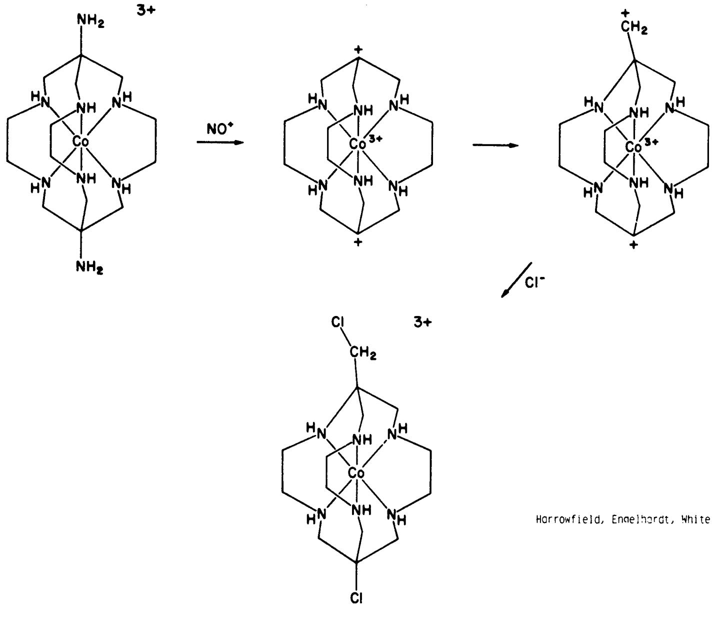


Fig. 9. Reaction scheme for the rearrangement to the absar cage.

was generated less readily in this cage and given the increase in ligand field strength of the ligand a low spin Co(II) complex was a possibility. However, this was not realised nor was there a dramatic change in the electron self exchange rate (7 $M^{-1}s^{-1}$ at 25°C, $\mu = 0.2$ M) (Ref. 22). It can be argued that the push-pull mechanism still applies except that in this instance the Co(III) ion is more readily and the Co(II) ion less readily accommodated in the cage. What is gained in one way is lost in the other so there is no net change in the energy required to reach the transition state. If these explanations are correct it carries a connotation with respect to other systems and especially in regard to metallo-enzyme redox processes. Namely, if the ligand framework is such that either it or the stereochemistry about the metal is strained in a way that helps the system towards the transition state then a more rapid electron self exchange rate can be expected relative to the unstrained system. This expectation is incorporated in the "entatic state " hypothesis of Vallee and Williams (23). Cu(II)(I) systems, for example, could be constrained to largely the same stereochemistry in the two oxidation states by the rigidity of the enzyme donor system. Such an arrangement could lead to rapid reversible electron transfer reactions and plastocyanine (Ref. 24) might be such an example.

We have attempted to prove this strain theory by using the *lel*$_3$ and *ob*$_3$ capped tris (*trans*-1,2-cyclohexanediamine)cobalt(III) complexes (Ref. 25). If the strain calculations are correct they predict substantial differences between the electron self exchange rates for the two sets of redox couples of the capped tris(cyclohexanediamine) complexes.

$$\Lambda\ \underline{lel}_3\ Co(di(NH_2)char)^{3+} + \Delta\ \underline{lel}_3\ Co(di(NH_2)char)^{2+}$$

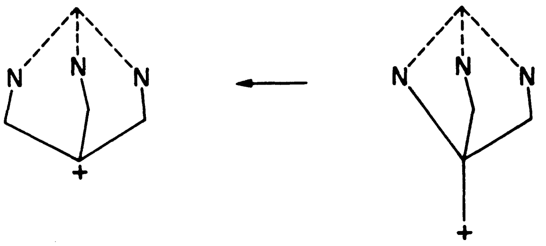
and

$$\Delta\ \underline{ob}_3\ Co(di(NH_2)char)^{3+} + \Lambda\ \underline{ob}_3\ Co(di(NH_2)char)^{2+}$$

So far, we have capped the *lel*$_3$ complexes and measured their self exchange rates. They are somewhat larger than for the analogous di(NH_2)sar ions despite their larger size but not significantly so. The cage based on the tris(cyclohexanediamine) backbone is necessarily more rigid than sar and it cannot undergo the *lel*$_3$ to *ob*$_3$ conformational transformation which the sep, sar and diamsar systems can undergo. The cyclohexane ring fused to the chelate ring prevents that interconversion. Unfortunately, the *ob*$_3$ cyclohexanediamine complexes have resisted the capping process so far. Molecular models indicate that the activated complexes for the intramolecular cyclizations are not as well orientated in these isomers as they are in the *lel*$_3$ systems. We have not succeeded in getting the metal ion out of these cyclohexanediamine based cages yet, nor have we succeeded in trapping any of the *ob*$_3$ form by rearrangements at high temperature in base via the presumed more labile Co(II) form.

Another system which is stereochemically less rigid and less demanding than the cyclohexanediamine based system is that based on 1,2-(*S*)-propanediamine. Here again the *facial* and *meridional* *lel*$_3$ tris(1,2-propanediamine)cobalt(III) ions have been capped but not the ob$_3$ forms (Ref. 26). We are now trying various conditions to get some rearrangement of the lel$_3$ to ob$_3$ forms in the Co(II) state by trapping the products after rapid conversion to the Co(III) complexes. The metal ion, however, has been extracted from these cages and the chiral ligands so obtained should be useful to look at the chiral properties of their various metal ion complexes. In addition, these ligands should be useful to gauge the electron self exchange rates of different metal ion complexes by the polarimetric method.

The absar rearrangement (Fig. 9) is surprising since it occurs counter to expectation in relation to the bridgehead organic chemistry. If anything, the rearrangement would be expected to take place in the reverse direction, i.e.



as observed in analogous adamantyl derivatives (Ref. 27). One reason for the observed phenomenon could be the repulsion between the charges when the cation is generated at the bridgehead close to the Co^{3+} ion. Clearly, the rearrangement would reduce that repulsion. Another explanation could be some relief of strain in the ligand while it is bound to the cobalt(III) ion. There is also a possibility that the rearrangement occurs via a reactive aziridine intermediate although this is somewhat less likely since aziridines bound to Co(III) ions appear to be extraordinarily stable (Ref. 28).

A similar rearrangement has been observed following the treatment of the CoMeNO$_2$sar^{3+} ion with base, Fig. 10. Firstly, a retro-aldol type reaction occurs to break the cage.

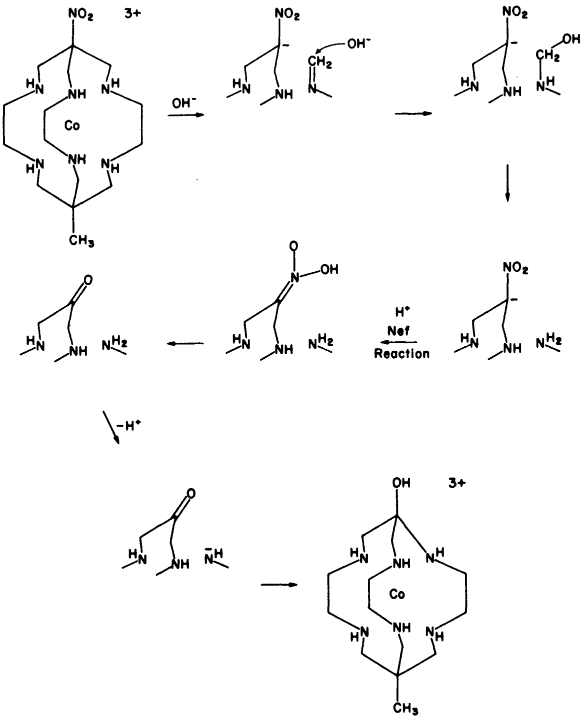


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Fig. 10. Reaction scheme for the formation of Co(MeOHabsar)$^{3+}$ from Co(di(NO$_2$)sar)$^{3+}$.

Then, after loss of the imine in basic conditions, at ~ pH 4, a Nef reaction gives the ketone. Finally, under basic conditions again the ketone condenses with the deprotonated primary amine coordinated to the Co(III) center to give the methylhydroxy absar complex shown (Ref. 29). The properties of this molecule are akin to those of the chloromethyl derivative described earlier in relation to its ligand field spectrum (λ_{max} 458 nm) and redox potential (E = −0.55 v. NHE compared with Co(HOMesar)$^{3+/2+}$ E = −0.30 V, λ_{max} 472). So here at least are two examples of how the cage can be tightened.

An implication in the data observed to date is that an increase in the hole size of the cage will stabilize larger ions and consequently lower oxidation states. This aspect we have attempted to investigate in some detail. An obvious route to pursue would be to cap the [Co(III) tris(1,3-propanediamine)]$^{3+}$ ion (Co(tn)$_3$$^{3+}$), Fig. 11. Our attempts to do that have not yet resulted in a reasonable yield of the encapsulated product (Ref. 30) mainly because in the basic conditions used the Co(tn)$_3$$^{3+}$ ion loses its ligands faster than the more inert Co(en)$_3$$^{3+}$ ion in water. However, the problem can be approached from a variety of other routes. One of these involves the use of the [Co(III) bis(1,1,1-tris(aminomethyl)ethane)]$^{3+}$ ion, (Co(tame)$_2$$^{3+}$), Fig. 12.

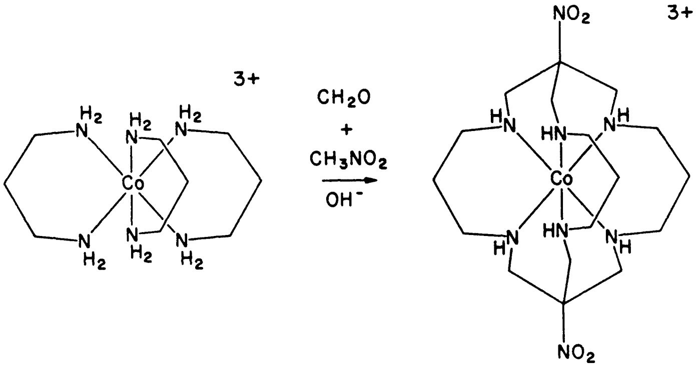
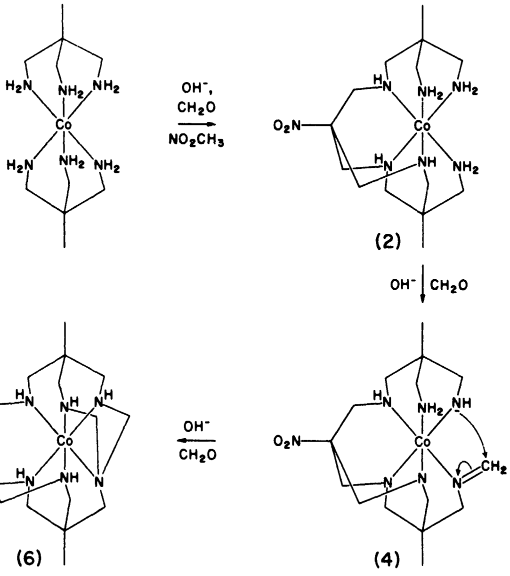


Fig. 11. Possible route to 6-ring cages.



Geue, Gainsford, McCarthy

Fig. 12. Reactions arising from capping Co(tame)$_2$$^{3+}$.

Two faces of this cation have the potential to be capped to yield a cage with solely six-membered chelate rings. However, the reaction does not occur quite as planned: one of the faces is capped readily and the second begins on the right path but after the generation of an imino-methylene moiety an adjacent deprotonated amine attacks the imine carbon to give a very strained four-membered ring (Ref. 30). This is followed by another condensation and cyclization of the same type. So while we have expanded the hole size on one side of the ligand we have tightened it on the other and the molecule is very distorted indeed. These factors in general show up in a marked way in the variation of the electronic spectra within the series of hexaamine cobalt(III) complexes (Ref. 30 & 31) given in Fig. 13.

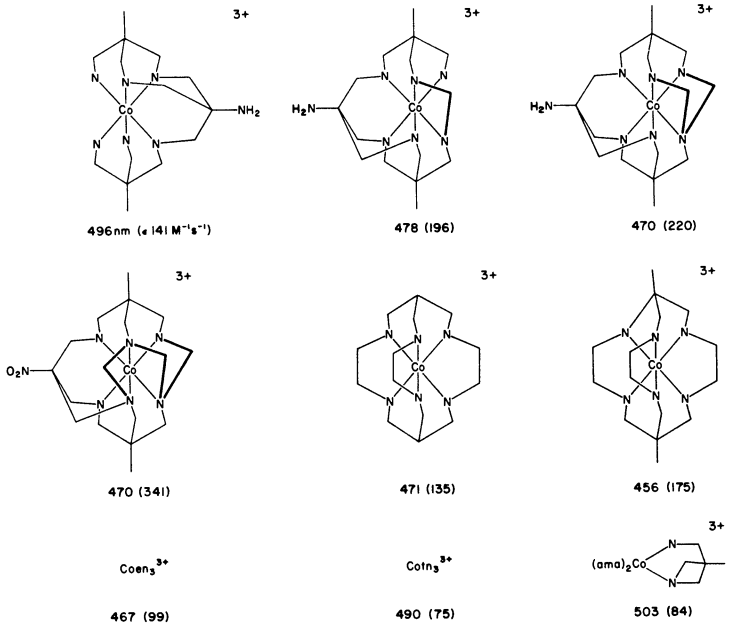
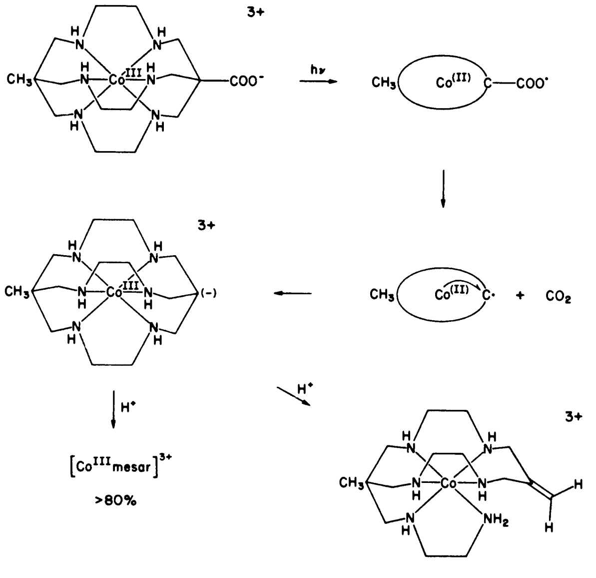


Fig. 13. Cobalt(III) hexaamine complexes and their absorption maxima for the band derived from the $^1A_{1g} \rightarrow {}^1T_{1g}$ transition (O_h).

The molar absorptivities vary by a factor of three and the absorption maxima vary over a range of ~ 50 nm. Much of this variation must come from the distortions of the ligating atoms from regular octahedral positions and distortion of bonding orbitals from ideal overlap. It appears to be the latter which is the more significant in our experience because there are examples where the ligating atoms are close to octahedral but the intrachelate constraints give inferior geometry for the orbital overlap (Ref. 31), e.g. $Co(2\text{-aminomethyl, 2-methylazetidine})_3{}^{3+}$. There are other experiments by which we are trying to achieve the larger hole size and there is not space to outline them here. It suffices to say that we are very close to reasonable yields of an all six-membered cage analogous to the sar and diamsar based on intraligand condensations using the $[Co(tame)_2]^{3+}$ ion.

In general then, the Co(II)(III) cages to this point all show surprisingly rapid electron transfer reactions governed rather precisely by the Hush-Marcus correlations (Ref. 18). The interesting aspects which we are beginning to explore now are the electron self exchange rates and cross reactions for the new metal ion systems (Ref. 32). The series gives us an opportunity to examine these outer sphere electron transfer processes for cases involving different orbital symmetry, exchanges such as those between the pairs of ions Mn(II)($t_{2g}{}^3$, $e_g{}^2$), Mn(III)($t_{2g}{}^3$, $e_g{}^1$) (E = +0.56 V), Fe(II)($t_{2g}{}^4$, $e_g{}^2$), Fe(III)($t_{2g}{}^5$, $e_g{}^0$) (E = +0.1 V), Ni(II)($t_{2g}{}^6$, $e_g{}^2$), Ni(III)($t_{2g}{}^6$, $e_g{}^1$) (E = +0.9 V) (versus NHE). The Ni and Mn systems might be expected to be rapid ($>10^4\ M^{-1}s^{-1}$), for example, whereas the Fe(II)(III) exchange which involves a high and a low spin complex and a substantial change in bond length (0.19 Å) (Ref. 33) could be at least as slow as the Co(III)/Co(II) systems.

The fact that substituents in the apical positions communicate well with the metal ion led us to consider the prospect of communication between two metal ions in cages coupled head to head through these apical positions. It has turned out that the synthesis of the coupled cages is an intriguing matter by itself. One obvious route to take is to couple two radicals and the means whereby they might be generated comes from some old Co(III) amine photochemistry which is usually avoided like the plague. I refer to the ultra-violet ligand to metal charge transfer process that leads to reduction of Co(III) to Co(II) and the generation of a ligand radical. The Co(II) complex then usually decomposes rapidly. The last situation does not occur with the cages and therefore this route becomes a viable proposition to generate a cage radical. An obvious way to start is to take the $[Co(III)MeCOOHsar]^{3+}$ complex shown in Fig. 14 and irradiate it in the UV (Ref. 34).

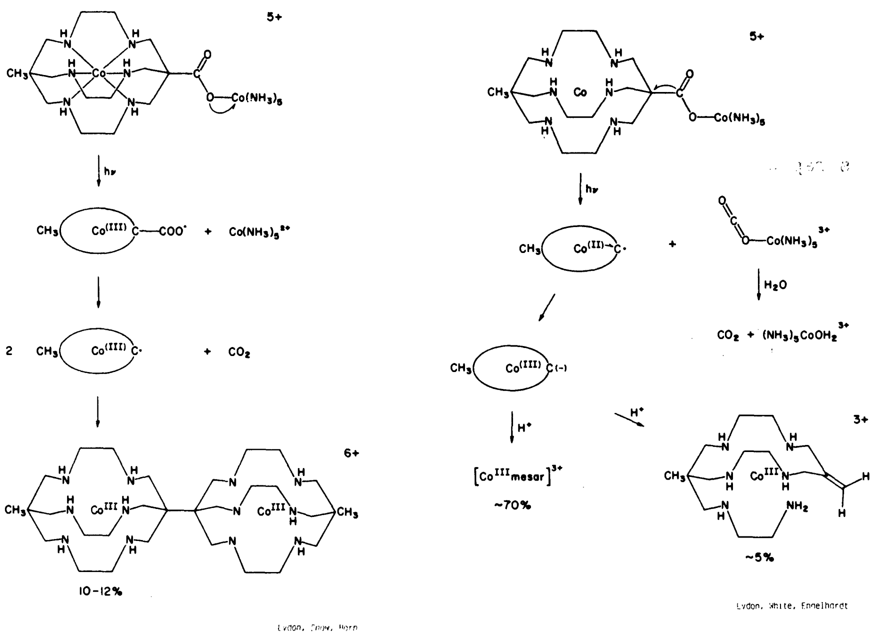


Lydon, Engelhardt, White

Fig. 14. Products from the UV-photolysis of $Co(MeCOOHsar)^{3+}$.

This process gave the carboxy ligand radical as expected which eliminated CO_2 as expected. At this point the Co(II) center then donated an electron back to the ligand and the resulting carbanion captured H^+ to give the $[Co(III)Mesar]^{3+}$ ion largely plus some ring opening of the cage to give an olefin complex as shown in Fig. 14. The reduction by Co(II) was not an expected result but the olefin complex could have been anticipated once the carbanion was formed and it is fairly routine organic chemistry. A new route was then devised to circumvent this decay path. The notion was to add a readily reducible Co(III) center to the carboxyl group such as $Co(NH_3)_5{}^{3+}$, Fig. 15. We anticipated that this Co(III) moiety would reduce (~ 0 V) before the cage Co(III) ion (~ -0.4 V). That turned out not to be the case but the strategy was partly successful. About 75% of the photolysis occurred by initial reduction of the cage Co(III) but 10-12% went by reduction of the $Co(NH_3)_5{}^{3+}$ moiety to give the Co(III) cage carboxy radical which then eliminated CO_2 and dimerised to give the head to head dimer shown in Fig. 15 whose structure has been determined by Horn and Snow (34). So far, there has been little sign of intervalence behavior from the dimer. Both Co(III) centers appear to reduce at the same potential and the visible spectrum of the intermediate appears to be the mean of those of the Co(III)(III) and Co(II)(II) dimers. The electron transfer rates between the dimers is not much different than for the monomers. The rotatory dispersion curves however are not additive but this technique is a much more sensitive probe for communication between the ions and we have yet to unravel the detail.

One aspect which is especially relevant to our understanding of such molecules is how does the metal ion get in and out. There has been some speculation about this problem for encapsulation of metal ions generally and usually only an "on" and "off" rate are observed (Ref. 1). In most instances, we are still pretty much in the dark but in the case of the $Cu(II)sar^{2+}$ ion in the presence of acid we have been fortunate to find two intermediates along with other data which do tell us quite a lot about how the metal ion is extracted from the cage in these conditions (Ref. 35). The facts are as follows in the range pH 1-2. The blue $Cusar^{2+}$ hexaamine cage undergoes a rapid color change ($7\ s^{-1}$ at 25°C, $\mu = 1.0$) to a purple species characteristic of a macrocyclic quadridentate tetraamine complex. In this range the initial process is independent of the acid concentration. However, it is followed by a much slower process ~ 10^3 fold which involves a change from one purple complex to another and the rate law for this process is inverse in acid concentration and



Lydon, Snow, Horn

Lydon, White, Engelhardt

Fig. 15. Products from the UV-photolysis of the $[Co(MesarCOO)Co(NH_3)_5]^{5+}$ ion.

dependent on the anions in solution. The final product is very stable and is not affected by 5 M HCl over a long period. However, both the initial reactant and the first intermediate decompose in 5 M HCl over a few hours ($t_{\frac{1}{2}}$ ~ 4 hrs) to yield the $CuCl_4^{2-}$ ion and protonated ligand and little or no "stable" purple product.

The structures of the initial reactant $Cusar^{2+}$ and the stable purple product have been determined (Ref. 36). The hexaamine has the characteristic sexidentate configuration of the ligand about the metal ion with the same configuration about all six N atoms. The stable purple ion has a planar quadridentate configuration of the ligand about the metal ion with two N atoms no longer coordinated but protonated and a nitrate ion bound monodentate (Cu-O 2.33 Å). The configurations about the coordinated N centers, however, have an RSRS relationship instead of all being either R or S. This implies obviously that two of the centers have inverted during the reactions.

The kinetic data coupled with these structural and stoichiometric observations allow a preliminary analysis of aspects of the mechanism whereby the metal is extruded, Fig. 16. Firstly, the rate law's independence of H^+ for the first step implies that spontaneous Cu-N bond rupture is the rate determining step. Once the N comes off it is captured by a proton and the purple supposed square planar product is stabilised. As the Cu-N bond is broken it can be perceived that the metal could move forward into a square planar condition and possibly one of the remaining N centers could be bound in an axial position, although the stereochemistry for such an arrangement is not very favorable from the ligands' point of view. By implication the configurations about all four coordinated N atoms should be the same as the reactant, i.e. either all R or all S. The rearrangement then from one purple form to the other requires that two of these N centers invert their configuration. Two possibilities present themselves. One is that OH^- removes a proton and the deprotonated N center then inverts and that process occurs twice. This can be eliminated on the grounds that the inversion is taking place in acid conditions, pH 0-2. The concentration of OH^- is therefore miniscule and the pK_a of the N center must exceed 14, since the NH sites cannot be deprotonated fully by OH^-. These two factors together therefore could not accommodate the rate observed. The second possibility is that two more Cu-N bonds are broken and both H_2O molecules and anions, in this instance Cl^-, compete for the vacant coordination positions. In the acid conditions, the N centers which have dissociated become protonated and it follows that to recoordinate them the protons need to be removed along with the halide ions or water molecules. These processes could readily accommodate the paths inverse in H^+ and anion. They would also allow the N centers to invert. Clearly, the deprotonated N centers could recoordinate as either R or S. The proposal also allows for formation of the "stable" purple product and the extrusion of the metal ion as competitive paths. This bifurcation of the products would be governed by the H^+ concentration and also by the anion. If H^+ was large enough few if any N atoms would recoordinate and additional

Cu-N bond ruptures would lead inevitably to $CuCl_4^{2-}$ and protonated cage. Similarly stable Cu-X bonds would inhibit recoordination of the N atoms. Presumably, on a very long timescale the "stable" purple quadridentate would also go over to the same products but this clearly is in months or years, not hours.

The scheme carries an inference but not a requirement for the way the Cu^{2+} and other metal ions enter such ligands which is very reasonable given our general understanding of the coordination of ligands. Namely, the metal ion binds at one -NH- center then at two, etc. to make a quadridentate complex initially which rearranges fractionally to a less stable form that is rapidly captured by the remaining ligand strand to give the stable sexidentate chelate. The stability of the sexidentate appears to reside in the rapid recombination rate for a ruptured M-N bond. Obviously the overall stereochemistry of the cage dictates that each N does not escape far from the metal ion unless it is captured by a proton.

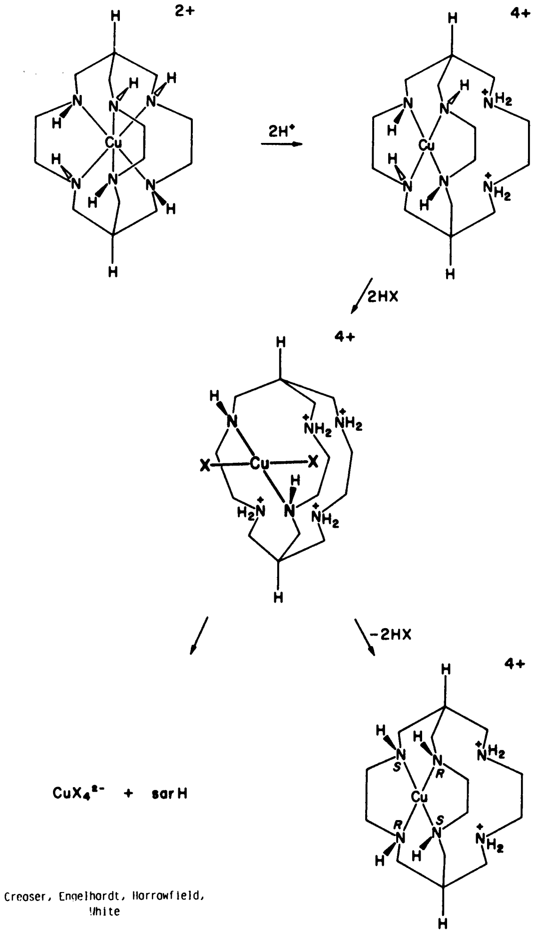
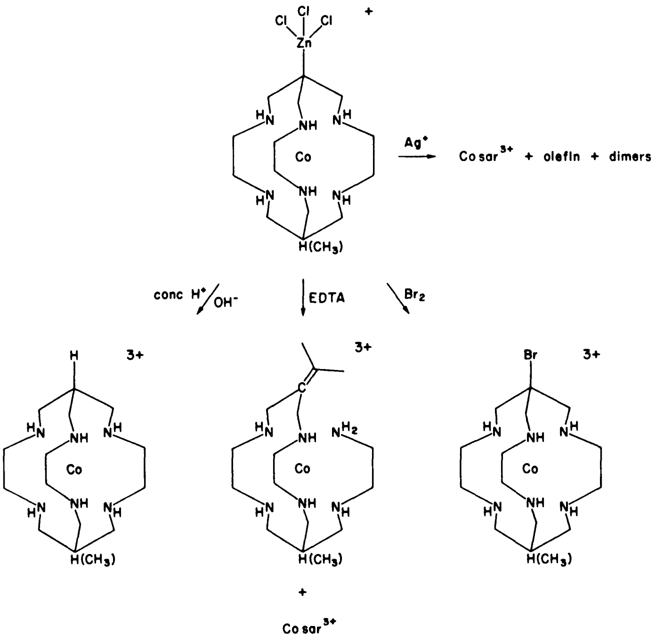


Fig. 16. Route for the extraction of Cu^{2+} from $Cu(sar)^{2+}$ in acid.

Finally, I wish to mention one very unusual result which exemplifies the surprises we have had with the chemistry of these molecules. In the course of reducing $[Co(diClsar)]^{3+}$ or $[Co(MeClsar)]^{3+}$ with Zn dust to remove the halogen we observe by-products (intermediates?) which arise by oxidative addition at Zn^0. Namely, complexes with Zn-alkyl bonds of extraordinary stability. A structure of one of these molecules has been carried out and is shown in Fig. 17. Zinc-alkyl complexes, normally, are known for their reactivity. Many are pyrophoric and decompose rapidly in water or acid solution. These cage zinc-alkyl complexes were isolated from 6 M HCl and clearly demonstrate a stability beyond the ordinary. The additional Cl^- ions attached to the Zn atom may help to stabilize the Zn-C bond but the Zn itself is not especially hindered towards attack by a proton. The Co(III) cage, however, can be considered an electron withdrawing group and this would help to stabilize the Zn-C bond towards protonation and thence rupture. Clearly, we have some way to go in understanding the reactivity of these systems. It suffices to say at this stage that the chemistry the molecules do undergo albeit slowly is largely carbanion-like. The Zn-C bond is attacked by electrophiles like Br_2 and I_2 which yield the appropriate halo substituted cage. Heating the zinc-alkyl cages in acid or base for some time finally does eliminate the zinc and allows protonation of the apical carbon atom to give the sar or methyl sar complex. Ethylenediamine tetraacetic acid removes the zinc also to give a mixture of $Cosar^{3+}$ and the ring opened olefin complex described earlier which is characteristically bridgehead carbanion chemistry (Ref. 37).

These results carry some implications for unusual stability of other metal-alkyl cage



Snow, Horn, Creaser, Lydon

Fig. 17. A zinc-alkyl cage complex and aspects of its reactivity.

complexes. Ni(II)-C, Cu(II)-C, Cr(III)-C, Co(II)-C, even Mg-C bonds might all be relatively stable in aqueous conditions. Such stability would allow systematic studies of their reactivity patterns in the aqueous phase and perhaps new and exciting chemistry.

Hopefully the work described demonstrates the interesting properties of and potential for such caged metal ions. Their stability implies prospects for use in redox cycles and we have used them as efficient electron transfer agents to generate H_2 from the excited state of the $[Ru(2,2'\text{-bipyridine})_3]^{2+}$ ion in the presence of a sacrificial donor and a Pt catalyst (Ref. 38). The cage complexes themselves have so far been disappointing as sensitizers in this role, although there are possibilities we are working on such as addition of an organic sensitizer to the periphery of the cage to make the energy transfer intramolecular and hopefully even more efficient. There are many other avenues which need exploration. The W, Mo and Re cages are very desirable goals as well as the Ru and Os systems. Cage polymers could be interesting electrode materials. Polymerisation of a vinyl cage, for example, at an electrode surface could lead to interesting results. A "nylon" made from the isolated $di(NH_2)sar$ cage and adipic acid might sequester metal ions by kinetic selectivity and such polymers might also be interesting electrode and ion exchange materials. A cage complex alkylated with a long chain paraffin could have interesting properties if it inserted in a membrane either as a spin label or as a redox reagent to interface, for example, with the photosytem of ATPase. Clearly, there are many possibilities for such molecules given the stability of the saturated cages and the stability and inertness of their complexes.

Acknowledgement - I would like to pay tribute to my collaborator and former colleague, Jack Harrowfield, who began this work, and to many colleagues who have worked so hard and thought deeply on the chemistry described in this lecture. I am also greatly in debt to my crystallographic collaborators, Alan White, Michael Snow, Graeme Gainsford and Ward Robinson. Without their monumental results this chemistry would have foundered. Finally, I am in debt to Alan Bond and Keith Murray for their specialist assistance, to ANU for generous support to carry out the work, and to Megan Fauvet and Carol Jacob for their tolerance, expertise and hard work in producing the publications.

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