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Developments in the synthesis and reactivity of encapsulated metal ions

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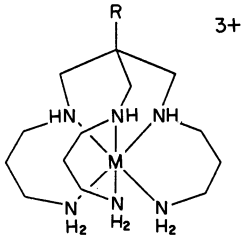
Abstract - The use of the template strategy to make larger and smaller cavity sizes of encapsulating ligands is explored and the effect of cavity size and stereochemistry on redox potentials and electron transfer reactions is examined. The cages have also been modified in a variety of ways by oxidation of the ligand to hydroxylamines, imines, amides and aromatic systems. The mechanisms of extrusion of metal ions from the cages are also discussed.

Much of the interesting chemistry associated with the hexaamine metal ion cages has been related to the rapid redox changes they undergo and their unusual stability, both in a kinetic and thermodynamic sense. These factors make them useful as redox reagents of an innocent kind and the stability allows experiments which mostly are not feasible with their tris(bidentate) analogues. The elaboration of the cages has been carried on with respect to these properties but there are basic issues still to be answered. For example, what happens if the cavity size is increased; is the complex destabilized? Are the redox rates altered dramatically? Is the coordinated ligand reactive and how does the metal ion influence that issue? How does the metal ion come out of the cage? These are all questions which need to be answered in order to understand and use the encapsulation chemistry effectively and this lecture addresses some of those matters.

One obvious problem has been to increase the natural cavity size in the ligand in order to accommodate larger low oxidation state ions and also modulate the redox potentials of couples by this strategy. An obvious route to take was to use the broad capping strategy successful for the tris(1,2-ethanediamine) complexes (ref. 1) and apply it to either tris(1,3-propanediamine) complexes or to sexidentate complexes of type 1:



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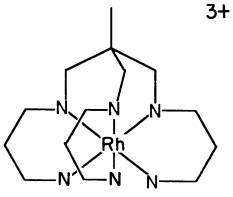

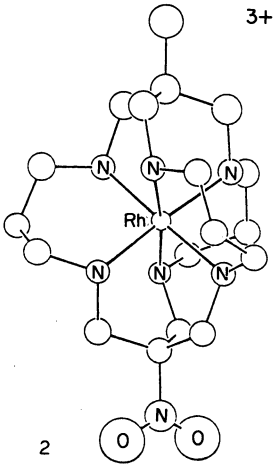

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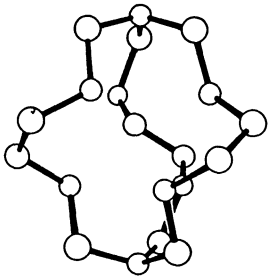
To date using Co(III) and Cr(III) complexes of this type, the strategy has been conspicuously unsuccessful and we believe the problem is largely due to the orientation of the imine intermediates in relation to the adjacent nucleophile for the intramolecular condensations especially for the final reaction to complete the cap (ref. 2). The difficulty appeared to be connected with the metal-nitrogen bond length and the implication from studies of models was that if the bond length was longer than that found for Co(III)-N (1.98 A) the condensation might succeed. That conclusion has turned out to be true and recently a Rh(III) complex of type I (R = CH_3) has been capped in good yield (ref. 2) and its structure is depicted in 2 (ref. 3). The complex has essentially D_3 symmetry and the

three trimethylenediamine chelate rings adopt somewhat distorted "boat" conformations in order to minimise the intrachelate non-bonded interactions. Not only was the expectation that the longer M-N bond length would assist the capping process realised, but the (III)/(II) redox potential was substantially altered (~ +0.4 V) relative to the equivalent capped 1,2-ethanediamine based ligand (sen) (ref. 2). The Rh(II) ion presumably is more readily tolerated in the larger cavity size of the sexidentate where all the rings are 6-chelate. The Rh(II) complex therefore becomes more accessible and presumably more stable although we have not yet measured the relative lifetimes of the Rh(II) ions in aqueous solution. Preliminary pulse radiolysis experiments, however, indicate they are of the order of a second or longer (ref. 2).

The less successful experiments with the shorter M-N bond length Co(III) complexes and the less effective condensation geometry they appear to generate, do not necessarily mean that these Co(III) complexes will not be capped by this method. The intramolecular condensations are very effective and some extraordinarily strained molecules have been made by such routes (ref. 4). So it is still possible they will yield to appropriate conditions. Also, part of the problem with capping these larger ring systems is dissociation of one end of the diamine ligand which aborts the encapsulation process usually. Conditions therefore which minimise this side reaction will also assist the encapsulation process.

The hole size can also be modulated by a more subtle route which involves stabilising one or other of the conformations (ob$_3$ or lel$_3$, 3 and 4) of the sarcophagine type cages.



ob

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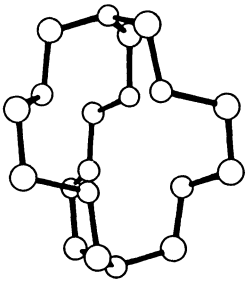
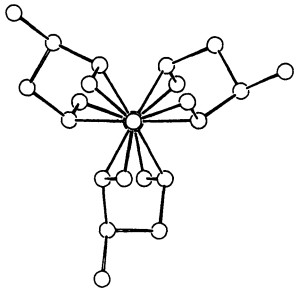
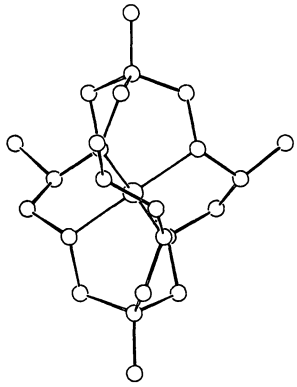


lel

4

3,6,10,13,16,19-hexaaza-bicyclo[6.6.6]eicosane (sarcophagine ≡ sar)





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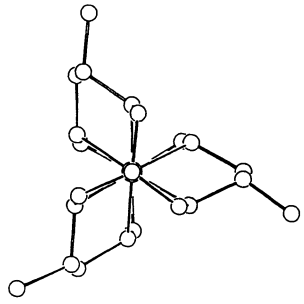
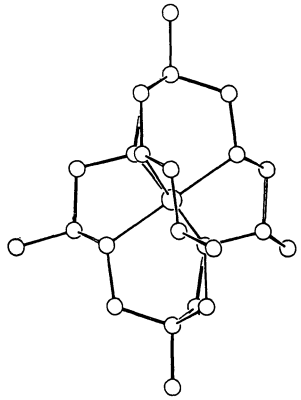
ob-fac-Λ-$[Co(NH_2)_2(R)(Me)_3sar]^{5+}$





6

lel$_3$-fac-Λ-$[Co(NH_3)_2(S)(Me)_3sar]^{5+}$

This could be achieved by capping conformationally rigid systems like ob$_3$ and lel$_3$ [Co tris(R- or S-trans-1,2-cyclohexanediamine)]$^{3+}$ ions. So far we have achieved the capping of the lel ion but have not been able to cap the ob system (ref. 5). Models indicate that the imine orientations for the intramolecular condensations are less favourable than for the lel form. Nor have we been able, yet, to get the cobalt ion out of the lel cyclohexanediamine cage.

However, ob and lel forms of such complexes have been synthesised recently by capping the meridional and facial isomers of the lel-[Co tris(1,2-propanediamine)]$^{3+}$ ions in the first instance (ref. 6). The cobalt was then removed from the chiral cage and reinserted. Under these conditions small quantities of the ob isomers were obtained which were readily separated from the lel forms by ion exchange chromatography (ref. 6).

The structures of the two facial complexes are depicted in 5 and 6 and the ions have very different properties which reflect the conformational differences and the way they impinge

TABLE 1. Self-exchange electron transfer rates for the $[Co(NH_3)_2\text{-pnsar}]^{4+/5+}$ system (25°C, μ = 0.2, 0.1 M CF_3SO_3H) (ref. 6)

Chiral Reactants	E^o (mV vs NHE)	k_{12} ($M^{-1}s^{-1}$)
Facial-Δ-lel_3 + Λ lel_3	+8	0.031(2)
Meridional-Δ-lel_3 + Λ lel_3	+17	0.033(2)
Facial-Δ-ob_3 + Λ ob_3	-324	0.96 (4)
Meridional-Δ-ob_3 + Λ ob_3	-313	1.00 (5)

TABLE 3. Calculated strain energies of the Co(II)/(III) 1,2-propanediamine cage ions (ref. 6)

				kJ/mole
fac	C_3	ob_3	Co(III)	0
fac	C_3	lel_3	Co(III)	12.4
mer	C_3	ob_3	Co(III)	0
mer	C_3	lel_3	Co(III)	17.7
mer	C_3	lel_3	Co(II)	5.0
fac	C_3	lel_3	Co(II)	0
fac + mer	C_3	ob_3	Co(II)	9.8
		"		9.8

TABLE 2. Cross-reaction electron-transfer rates for the $[Co(NH_3)_2\text{-pnsar}]^{4+/5+}$ system (25°C, μ = 0.2, 0.1 M CF_3SO_3H) (ref. 6)

	k_{12}(obs) ($M^{-1}s^{-1}$)	log K_{12}	f_{12}	k_{12}(calc)* ($M^{-1}s^{-1}$)
Mer-Λ-lel_3 + Fac-Δ-ob_3	54	5.77	0.443	90
Δ-lel_3 + "	45			
Fac-Δ-lel_3 + Fac-Δ-ob_3	40	5.62	0.461	77
Λ-lel_3 + "	32			
Mer-Δ-lel_3 + Mer-Δ-ob_3	17	5.58	0.467	75
Mer-Λ-lel_3 + "	14			
Fac-Λ-lel_3 + Mer-Δ-ob_3	13	5.43	0.486	64
Fac-Δ-lel_3 + "	10			

*Calc. from Marcus relationship $k_{12} = (k_{11}.k_{22}.K_{12}f_{12})^{\frac{1}{2}}$ using average values of fac and mer isomers.

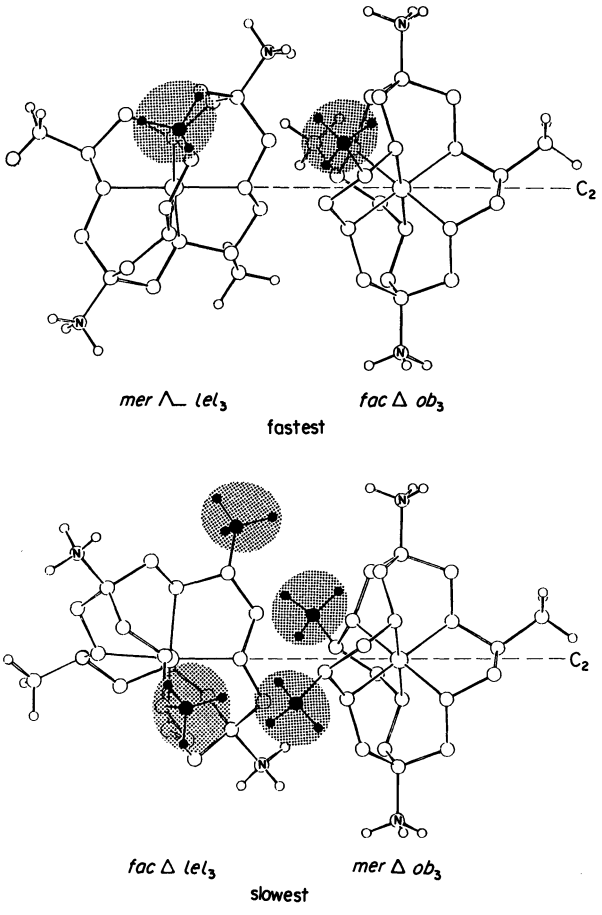
$$\log f_{12} = (\log K_{12})^2/(4 \log k_{11}.k_{22}/Z^2)$$

on the metal ion, Tables 1 and 2. For example, their visible spectra indicate that the ligand field of the Co(III) ob isomer (λ_{max} 450 nm) is appreciably greater than that of the lel form (λ_{max} 480 nm) (ref. 6). The spectra for the meridional and facial isomers in each set are only marginally different and that is not a surprising result since they only differ by the arrangement of the methyl groups about the periphery of the ligand.

The smaller cavity and therefore larger ligand field of the ob conformation also manifests itself in the redox potentials of the ob isomers relative to their lel counterparts. They differ by ~ 0.3 V with the ob forms being more negative. Clearly, the ob forms make it more difficult to generate the larger Co(II) ion in the tighter cage conformation. These observations are supported by the results of strain energy calculations given in Table 3 which clearly show the ob Co(II) cages are more strained than the lel Co(II) cages (ref. 6).

The electron transfer self-exchange rates also differ by a factor of thirty-fold and the rate constants for the ob isomers are not only significantly larger than those of the lel forms but they are also significantly larger than that for the $[Co(NH_3)_2sar]^{4+/5+}$ system (2 $M^{-1}s^{-1}$ at 25°C, μ = 0.2 M). These differences should be influenced by the strain energies of the ground states and transition states of the pairs of ions and these assessments are currently being carried out.

One of the most interesting facets of the electron transfer reactions arises from the cross-reactions between the isomers. The results are displayed in Table 2 where it can be seen that the observed rate constant extremes differ by five-fold whereas the calculated difference based on the Marcus relationship is only 1.4. The difference displays the effect of subtleties of stereochemistry on the electron transfer rate and presumably through the orientation of the reactant ions towards one another. To our knowledge, this is by far the largest effect that has been observed for different stereoisomers in such reactions. It also implies that such orientation effects could be significant in electron transfer reactions.



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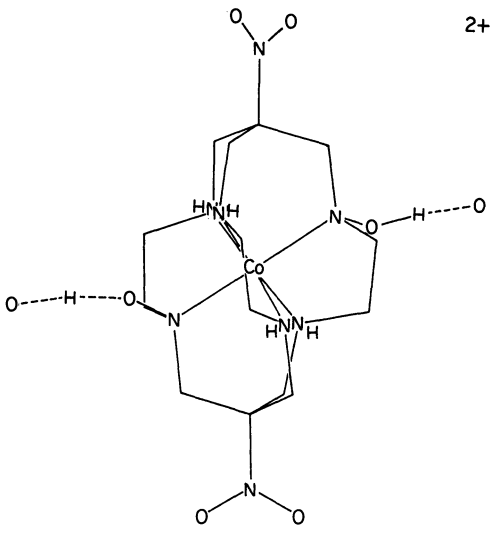

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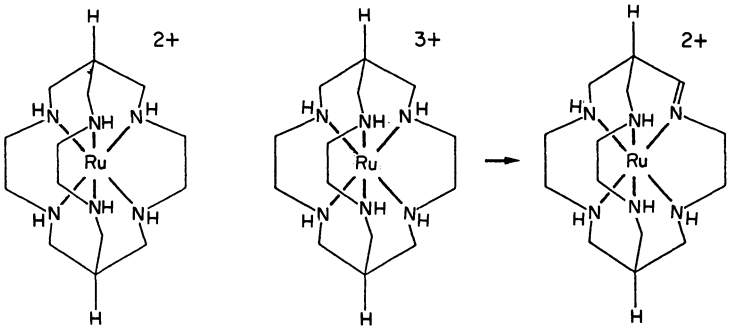
It is to be noted that the differences do not arise either from the ΔΛ and ΔΔ combinations nor from the lel-ob interactions. The latter were kept constant through the set of reactions. It appears that the methyl group interactions are the most significant and that they govern the specific orientation of the reacting partners. An examination of molecular models of the reacting pairs indicates that feasible orientations consistent with the ordering of the rates are those shown (7), for the two extreme cases of Table 2 (ref. 6). The lel-ob interactions do show up, however, in another way through their effect on the redox potentials and self-exchange rate constants. That can be seen in the differences between the self-exchange rate constants for the different conformational forms and between those rate constants and the rate constants for the cross-reactions in Tables 1 and 2. The differences are largely accommodated by the Marcus-Hush relationship except for the orientation effect.

The reactivity of the saturated organic cage itself is rather interesting. It has been possible to oxidise them by a variety of methods to imines, amides, hydroxylamines and even aromatic systems, with and without the participation of the metal ion. Hydrogen peroxide, for example, in basic conditions readily oxidises the coordinated amine sites in $[Co(NO_2)_2sar)]^{3+}$ to hydroxylamines (ref. 7). Up to three such oxidations in the one molecule have been observed and one of the products has been characterised by an X-ray crystallographic analysis (ref. 8). The molecule in question, 8, was isolated in a partly deprotonated condition where one of the protons from the two hydroxylamine sites was removed. The ions then hydrogen bond to each other in the lattice by sharing the remaining proton.

The $[Co(Cl_2sar)]^{3+}$ ion reacted with H_2O_2 in basic solution to give primarily the monohydroxylamine complex even with a large excess of OH^- and H_2O_2. In acidic conditions, this hydroxylamine complex $[Co(Cl_2sar\text{-}NOH)]^{3+}$ shows only a one-electron quasi-reversible wave (cyclic voltammetry 100 mV/s, 81 mV peak to peak vs SCE) with $E_{\frac{1}{2}}$ = -0.31 V in the range 0 to -1.2 V. This makes the Co(II) product less reducing than the parent Co(II) ion by ~ 0.15 V but the effect is even more pronounced for the deprotonated hydroxylamine complex where $E_{\frac{1}{2}}$ ~ -0.85 (vs SCE). The hydroxylamine groups appear to inert towards powerful oxidants such as $Cr_2O_7^{2-}$ and Ce(IV) in acidic solution. However, prolonged treatment with Zn powder under N_2 in these conditions reduces them back to the parent

secondary amine. A most striking result in this context was the rapid reaction of $[Co(Cl_2sarNOH)]^{3+}$ with V^{2+} in 1 M $HClO_4$ to give the $[Co(Cl_2sar)]^{3+}$ ion on mixing the reagents. Clearly, the driving force in this process is the formation of the strong vanadium IV-oxo bond via oxygen atom transfer (ref. 9).

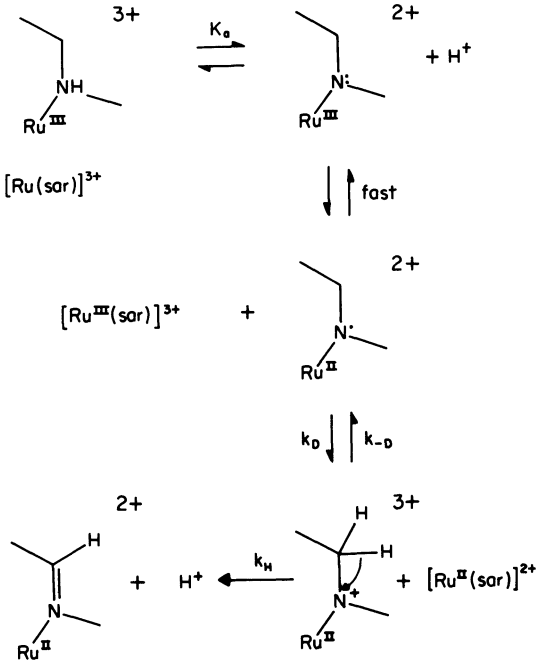
These hydroxylamine complexes are one of the few ways we have so far to derivatise the cage at the N sites in a multiple manner. The derivatisation also leads via deprotonation to 0, +1, +2 and +3 charged cages depending on the degree of deprotonation. These charge changes have a substantial effect on the redox potential of the complexes as indicated earlier. The $[Ru(II)sar]^{2+}$ ion has been synthesised finally using the $[Ru^{II}(O{=}CHNMe_2)_6]^{2+}$ ion and the free ligand (ref. 10). It has a reversible oxidation potential +0.29 V (vs NHE at 25°C) but despite this relatively low oxidant capacity for the $[Ru(III)sar]^{3+}$ (8) ion it oxidises rapidly and spontaneously to the monoimine Ru(II) complex, 11, even in acidic solution in an argon atmosphere. This was a surprising result compared with the same chemistry for the



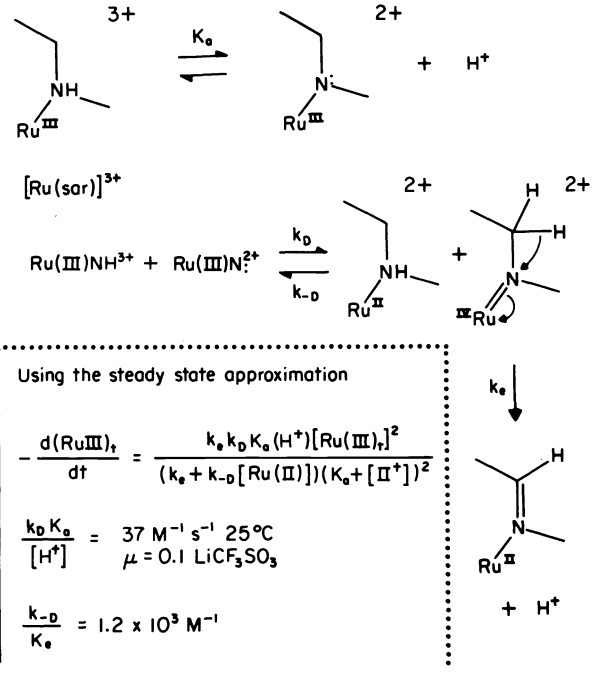
9 10 11

analogous tris(1,2-ethanediamine) complex (ref. 11) $[Ru(en)_3]^{3+}$. It was so surprising that it prompted a closer investigation of the rapid oxidation. The implication in the result is a surprisingly low pKa for the Ru(III) complex coupled with a rapid intramolecular oxidation by Ru(III) of the ligand to produce a ligand radical. The latter would then need to be oxidised by another Ru(III) ion to produce the monoimine, 11, Scheme 1. An alternative proposal involves disproportionation of the deprotonated Ru(III) cage to Ru(II) and Ru(IV) ions. Rapid oxidation of the ligand could then ensue via the Ru(IV) product to generate the Ru(II) imine, 11, intramolecularly, Scheme 2. The NMR evidence clearly puts the imine in the capped portion of the molecule and not in a 1,2-ethanediamine segment.

Scheme 1



Scheme 2



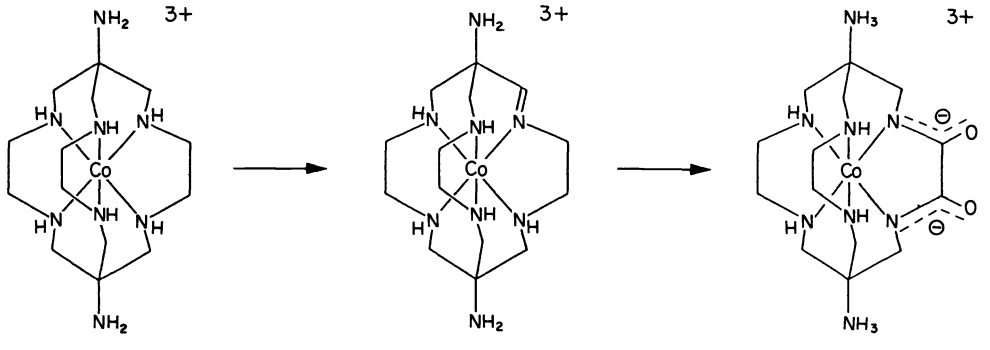
The rate laws deduced for both schemes are the same. Both are pH dependent and second order in Ru(III) and both could show an inverse dependence on the $[Ru(II)sar]^{2+}$ concentration reaching a limiting condition as the Ru(II) concentration falls. The observed rate law does display an inverse dependence on H^+, pH (0 to 5), a second-order dependence on the $[Ru(III)sar]^{3+}$ concentration and an inverse dependence on the $[Ru(II)sar]^{2+}$ ion concentration up to 10^{-2} - 10^{-3} M. Thereafter, the rate becomes independent of the $[Ru(II)sar]^{2+}$ concentration. At present we have no way of distinguishing between these two mechanisms other than by referring to the general chemistry involved (refs 12-15). The related $[Os(IV)(en)_2(en\text{-}H)_2]^{2+}$ ion undergoes spontaneous oxidation to the Os(II) diimine complex, for example (ref. 15).

The rapid oxidation process for the Ru(III) complex obviates the direct measurement of the electron-transfer self-exchange rate by the existing methods available. However, an estimate of this rate constant (ca. 2 x 10^5 $M^{-1}s^{-1}$ at 25°C in 1 M CF_3SO_3H) was obtained through the application of the Marcus-Hush relationship to reactions of $[Ru(II)sar]^{2+}$ with $[(NH_3)_5RuL]^{3+}$ (where L = pyridine, nicotinamide, isonicotinamide) (ref. 16). The rate constant is appreciably larger than those for $[Ru(NH_3)_6]^{2+/3+}$ (3.2 x 10^3 $M^{-1}s^{-1}$) and $[Ru(en)_3]^{2+/3+}$ (2.8 x 10^4 $M^{-1}s^{-1}$) which is consistent with the observed increases for the cage complexes relative to their non-encapsulated analogues. Albeit in this instance, the effect is not as pronounced as for the Co(II)(III) systems, probably because the bond length changes are not as great as the Ru oxidation states are switched. Further oxidation of the Ru(II) monoimine to the diimine and beyond was observed but as the oxidation progressed the control of it diminished. We had hoped to isolate a stable hexaimine complex analogous to the Ru(II) tris(bipyridine) and tris(o-phenanthroline) complexes but so far this has not been achieved.

The speed of the oxidation typifies how effective such Ru and Os ions can be as oxidants in the higher oxidation states. An essential factor seems to be donation of the electron pair of the deprotonated N centre to the d^4 Ru(IV) centre in this instance. This increases the bond order between Ru and N which in turn labilises the protons on the adjacent methylene group by a concerted $2e^-$ transfer to the Ru(IV) ion and the shift of the double bond order from Ru = N to N = C. The other important factor in the process is the stabilisation of the coordinated imine by Ru(II). This is a profound effect arising from the donation of non-bonding electrons on the d^6 Ru(II) ion to the π^* imine orbitals. It is an effect which has been well-documented elsewhere (ref. 17) and there is no need to dwell on it further here.

One unusual facet of this chemistry is the hydration of the imine at low pH to the carbinolamine. The pH at which there are equal amounts of imine and carbinolamine is ~ 2.5 and the rates of hydration can be followed. A similar observation has been made with one of the Co(III) cage imine complexes (ref. 18) but usually, in this type of chemistry, only one form, either imine or carbinolamine, is observed.

Even the Co(III) cages can be oxidised on the ligand by relatively mild methods. In the presence of charcoal, O_2 and Co(II) at pH 8.5, $[Co(diamsar)]^{3+}$ oxidise to both the imine, 11, and the diamide (ref. 18). The former can be produced in substantial amounts. The implication in the results is that the oxidation proceeds in stages through the imine and carbinolamine to the amide and thence the diamide, albeit with rearrangement of the imine into the ethanediamine segment. The Co centre may play an intermediary role in the process but we have not discerned a Co(IV) intermediate yet. The same type of oxidation can also be



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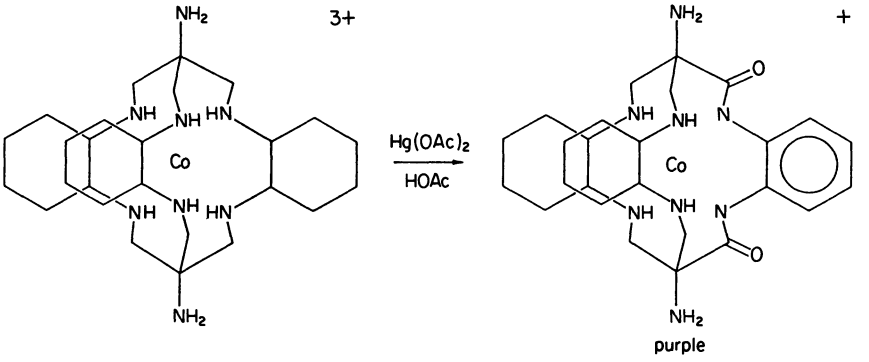
effected by mercuric acetate in acetic acid and substantial yields (~ 60%) of the diamide isomers have been obtained by this route (ref. 18). One of the most interesting results (ref. 18), however, in this context is the oxidation of the Co(III) cage complex derived from tris(trans-1,2-cyclohexanediamine cobalt(III))$^{3+}$ ion (14). This oxidation is effected also by mercuric acetate and it not only generates the amide moieties but it aromatises one



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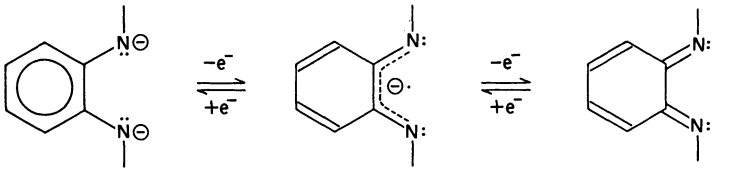
of the cyclohexane rings (15). The structure of this product was assigned initially from ^{1}H and ^{13}C NMR spectra but it has since been established by an X-ray crystallographic analysis (ref. 19).

The product undergoes interesting redox reactions. The ligand, for example, can be oxidised in a two-electron step to the o-benzoquinone diimine equivalent (ref. 16). Reduction of this entity by a three-electron step carries the cage complex back to an aromatic Co(II) derivative. The Co(III) → Co(II) reduction occurs at $E_{\frac{1}{2}}$ -0.41 V (vs NHE). The redox processes are not reversible on the cyclic voltammetry timescale but they can be cycled back and forth relatively rapidly with chemical reagents Ce(IV) and Sn(II), for example. Sn^{2+} ion rapidly reduces the quinone diimine equivalent to the aromatic cage.

This organic chemistry points to a way of doing multiple electron transfers relatively rapidly, mediated by metal ions. The tris(quinone diimine) equivalent, for example, could undergo a seven-electron redox change. Of course, it is not possible to tell, a priori, the voltage span of such a change. Not all the oxidation states might be accessible. Even so, the multiplicity of the changes is there. Moreover, tying such organic redox centres into a cage about the metal ion does give a stability not witnessed generally in the more common tris(chelate) analogues. In this respect, there is an advantage in encapsulation where the prime stability comes from the cage itself. Also, it inherently makes the ligand-metal ion



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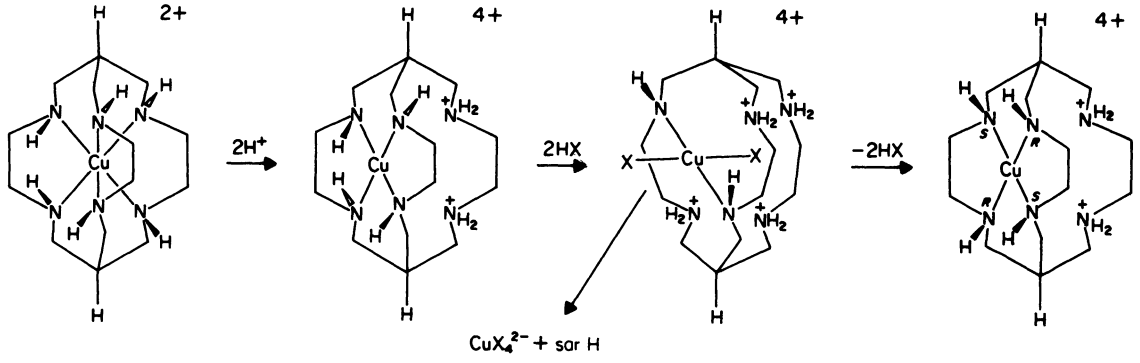
16

combination more kinetically inert and thereby the integrity of the combination can be retained over a number of electron changes. The combination of redox change on ligand and metal ion also avoids difficulties which arise from changes in the metal radius as the metal ion is reduced. The organic moiety alters, of course, as reduction occurs but not so dramatically as the radius change for Co(III) → Co(II) → Co(I), for example.

Finally, one of the important problems of the sarcophagine metal ion cage chemistry has been the extrusion of the metal ion from the cage and the mechanism of such processes. With the oxygen binding cryptates, essentially only one rate is observed and yet often six or more metal-oxygen bonds are broken in the process (ref. 20). Clearly, it cannot be a simple process where all the bonds to the metal ion are broken simultaneously and we need to know more about the details of the process. In some of the metal ion aza-cage chemistry we have been fortunate to see intermediates, complex rate laws involving pH dependent and anion dependent steps and proton exchange phenomena which give us definite indications of the routes whereby the metal ion is extruded.

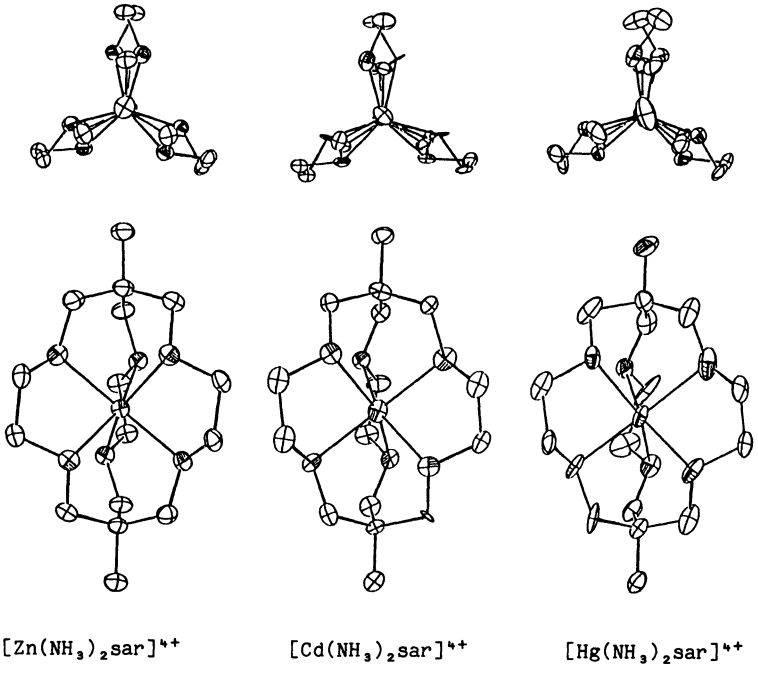
One such study has been described briefly in a previous lecture. It involves the treatment of $Cu(sar)^{2+}$ with HCl where two intermediates are observed in which the ligand is bound as a macrocyclic quadridentate (ref. 21). The pathway for decomposition of the six coordinate $Cu(sar)^{2+}$ ion is shown in Scheme 3. The essential feature is, following rupture of one or

Scheme 3



two Cu-N bonds, that the Cu^{2+} ion moves from the centre of the cage to the planar quadridentate condition while the uncoordinated strand is trapped by protonation. Once in this condition a bond to an entering group such as an anion can be made at the Cu^{2+} ion and this process can then help pull the remaining N atoms from the metal ion. The extrusion of the Cu^{2+} ion is dependent on both H^+ and Cl^- concentration but the concentrations needed are in the range 2 - 5 M and the rate law is therefore difficult to access.

It is instructive then to look at other $[M(sar)]^{2+}$ and $[M(NH_3)_2sar)]^{4+}$ ions which are more labile in this context, namely the Zn, Cd and Hg complexes. Some interesting facts emerge



$[Zn(NH_3)_2sar]^{4+}$ $[Cd(NH_3)_2sar]^{4+}$ $[Hg(NH_3)_2sar]^{4+}$

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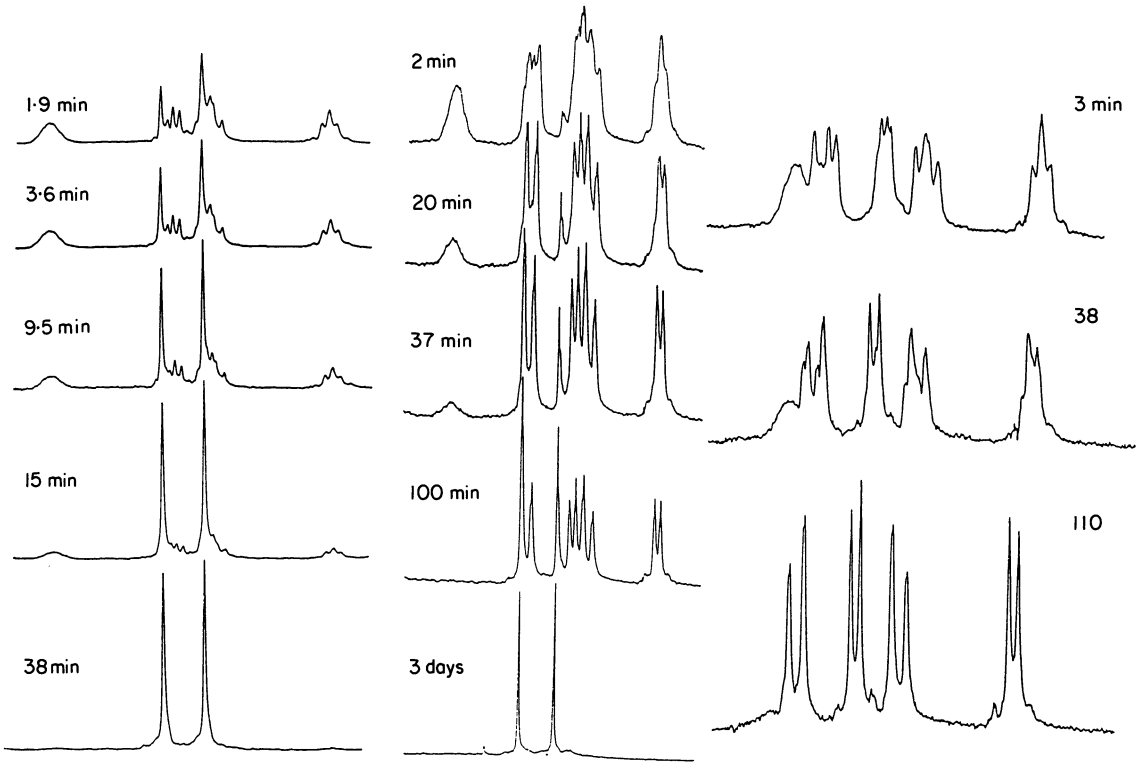
from studies of elimination of the metal ions in acid conditions (ref. 22). Firstly, proton exchange can be followed at the N sites by ^1H NMR spectroscopy in 2 M $DClO_4$ for the $[Zn(NH_3)_2sar]^{4+}$ ion but no metal ion is extruded. Addition of HCl, however, leads directly to extrusion of the Zn^{2+} ion albeit more slowly than proton exchange. For $[Cd(NH_3)_2sar]^{2+}$ in 2 M DCl at 25°C, proton exchange and Cd^{2+} extrusion appear to be synchronous. For $[Zn(NH_3)_2sar]^{4+}$ in 2 M DCl at 60°C, proton exchange is somewhat faster than metal ion loss and in 2 M $DClO_4$, there is an even larger difference (Fig. 1).



$[Cd(diamsarH_2)]^{4+}$ in 1 M DCl, 25°C

$[Zn(diamsarH_2)]^{4+}$ in 2 M DCl, 60°C

$[Zn(diamsarH_2]^{4+}$ in 2 M $DClO_4$, 60°C

$[Hg\ sar(NH_3)_2]^{4+} + H^+ + Cl^-$

$$k_{obs} = \frac{K_T K_{Cl}[Cl^-](k_1 + k_2 K_H[H^+])}{1 + K_{Cl}[Cl^-](1 + K_T + K_H K_T[H^+])}$$

$K_{Cl} = 1.3\ M^{-1}$

$K_T = 0.015$

$k_2 K_{H+} = 2.4\ M^{-1}s^{-1}$

$k_1 = 3.7\ s^{-1}$

$[Hg\ sar]^{2+} + H^+ + Cl^-$

$$k_{obs} = \frac{k_1 K_1 K_2 [H^+]^2 [Cl^-]}{1 + K_1[H^+][Cl^-] + K_1 K_2 [H^+]^2 [Cl^-]}$$

$K_1 = 77\ M^{-1}$

$k_1 K_2 = 88\ M^{-1}s^{-1}$

Fig. 1. ^1H NMR spectra

It is evident that in this acid concentration, OH^- cannot be the reagent to deprotonate the N sites to allow addition of D^+. What must happen is the M-N bond ruptures and there is competition between the metal ion and D^+ for the vacant filled orbital on the secondary N atom. Loss of H^+ from the $>NHD^+$ species and recoordination of the N atom leads to the deuterated complex. It follows from these studies that extrusion of the metal ion is either faster than or equal to proton exchange and that the extrusion takes place as a result of spontaneous M-N bond rupture as the first step.

The extrusion of Hg^{2+} ion from both types of cages has been followed in some detail. The results are shown in Fig. 2 where it can be seen that there is a dependence on both H^+ and Cl^- concentration. The rate laws for the two cases are shown below.

These rate laws are consistent with the proposed mechanisms for the extrusion of the metal ion from the two systems in Schemes 4 and 5. Both display preassociation with Cl^- in different forms coupled with protonation of the amine sites as they peel from the metal ion by spontaneous ligand-metal ion bond rupture. For the $[Hg(NH_3)_2sar]^{4+}$ ion the dependence on Cl^- is much less than for $[Hg(sar)]^{2+}$. In the first instance an ion pair between the 4+ ion and Cl^- is formed. This ion pairing can be observed with the $[Cd(NH_3)_2sar)]^{4+}$ ion by ^1H NMR spectroscopy as a chemical shift in the signals without loss of the D_3 symmetry of ion. So clearly, Cl^- is not binding to the metal centre to give an intermediate of appreciable concentration and lifetime even in 1 M HCl. Unfortunately, the same experiments are not feasible with the Hg(II) systems because the extrusion reaction is too rapid.

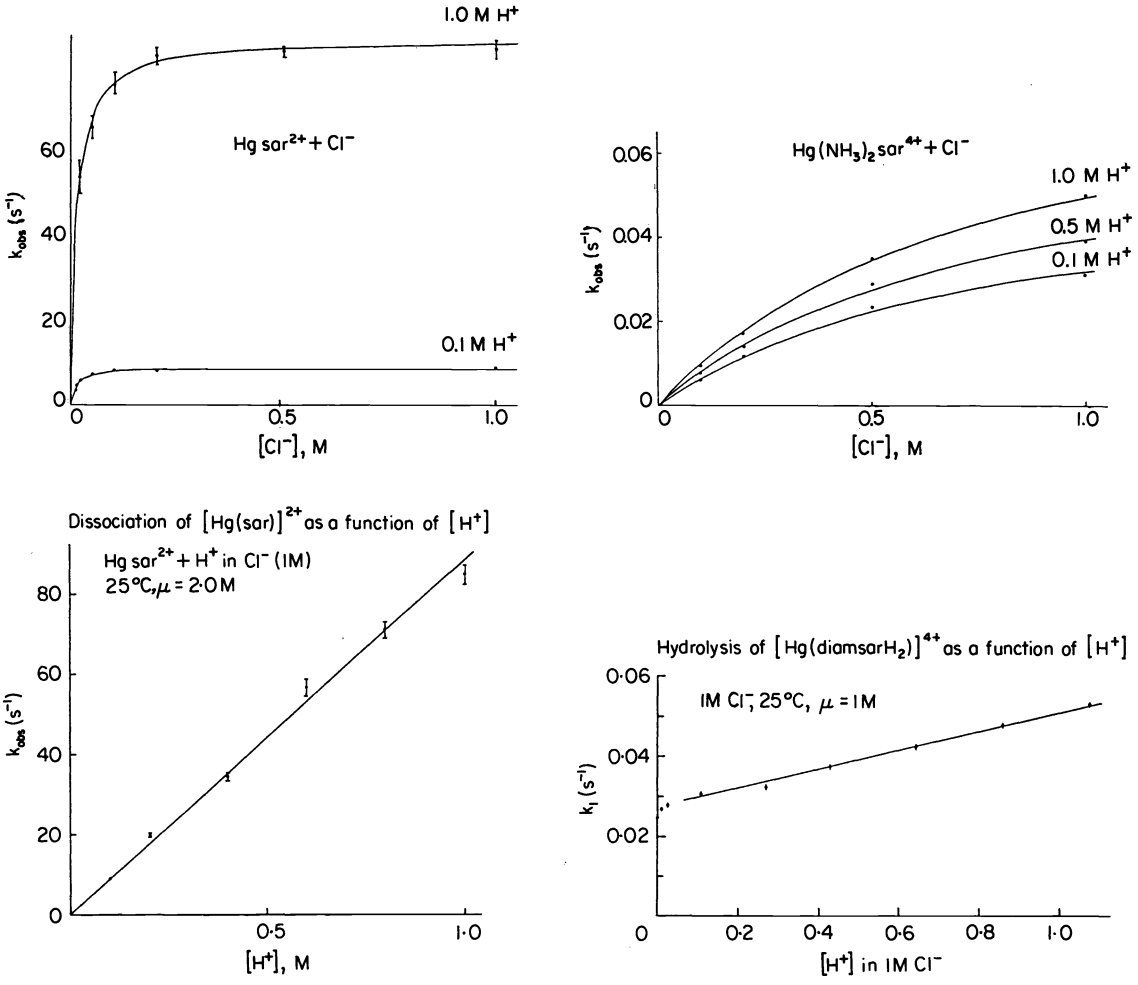
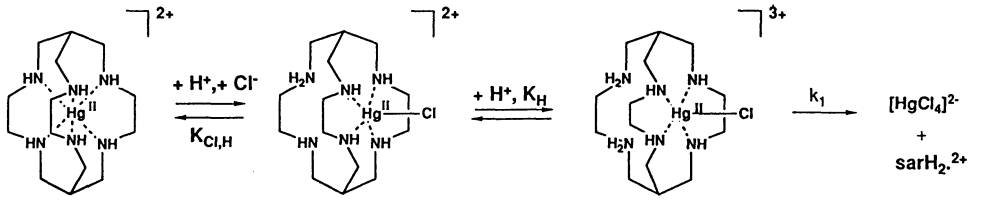


Fig. 2. Kinetics of extrusion of Hg^{2+} ion from $[Hgsar]^{2+}$ and $[Hg(NH_3)_2sar]^{4+}$ ions. (μ = 1.0, 25°C unless otherwise stated)

By comparison, the apparent association constant of Cl^- with $[Hg(sar)]^{2+}$ ion is 88 M^{-1}. This clearly cannot be an ion pair interaction and it requires H^+ to be present in order to observe the result of the association, in the kinetics of the extrusion of Hg^{2+}. Simply, it must be a synergistic effect between H^+ addition to an amine lost from the metal ion and Cl^- binding at the now coordinatively unsaturated metal centre. These are the first steps in the extrusion of the metal. Successive removal of an amine followed by protonation and addition of more Cl^- ion leads to total removal of Hg^{2+} as $HgCl_4^{2-}$.

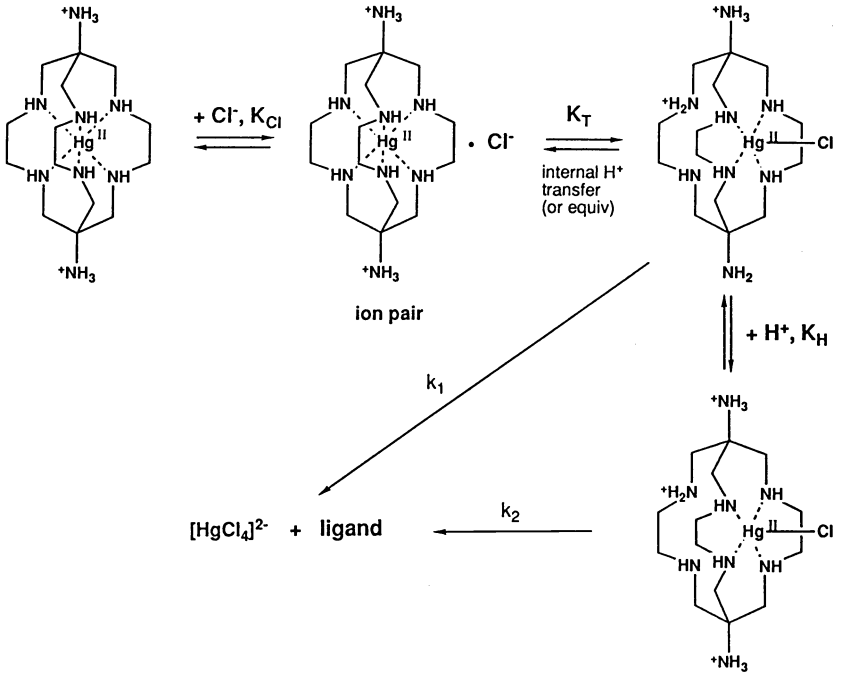
Scheme 4



The difference between the $[Hg(sar)]^{2+}$ and $[Hg((NH_3)_2sar)]^{4+}$ ions in respect to the rate and rate laws is primarily due to the difficulty of protonating an amine which is dissociated from the metal centre when the two exo-amine groups are already protonated. Also, it would seem that the steps leading to loss of the metal ion are not rate determining after the loss of the first two or three N atoms from the metal centre. Such a result is not surprising given the rapid simple ligand exchange rates for these ions in general. Once a substantial part of the cage is peeled off the metal, the remainder can be readily removed. Otherwise, the return rate of the dissociated atoms is fast and reconstitutes the metal ion cage. In

short, none of this chemistry is really surprising; it can all be fitted with aspects of substitution and dissociation at metal centres that we have learned over the past two decades. It is merely the intramolecularity of the processes which appears to make the systems inert and unusually stable.

Scheme 5



The stability constants of the complexes have proved difficult to measure because of the slow rates of attainment of equilibrium from both sides of the equation. However, the stability constant of the $[Hg(sar)]^{2+}$ ion has been measured relative to that of HgI_4^{2-} and the stability constant of an ion with the constitution $[Hg(sarI]^{+}$ has also been obtained. These are given in Table 4. They affirm the unusual stability of the caged metal ion

TABLE 4. Stability constants

Determined by competition with iodide.
$[HgI_4]^{2-}$ measured spectrophotometrically.
T = 25°C, μ = 0.5 M, $[OH^-]$ = 0.1 M
All constants measured relative to HgI_4^{2-}, log β_4 = 29.80.

		log K
Hg^{2+} + sar	$[Hg(sar)]^{2+}$	28.08 ± 0.02
Hg^{2+} + sar + I^-	$[Hg(sar)I]^{+}$	29.14 ± 0.05
$[Hg(sar)]^{2+}$ + I^-	$[Hg(sar)I]^{+}$	1.06 ± 0.07
Hg^{2+} + diamsar + I^-	$[Hg(diamsar)I]^{+}$	28.50 ± 0.01
Hg^{2+} + cyclam	$[Hg(cyclam)]^{2+}$	23.0[1]
Hg^{2+} + cyclam + I^-	$[Hg(cyclam)I]^{+}$	30.83 ± 0.01
$[Hg(cyclam)]^{2+}$ + I^-	$[Hg(cyclam)I]^{+}$	7.83 ± 0.1

[1] M. Kodama and E. Kimura, J. Chem. Soc., Dalton Trans., 1976, 2335.

complexes and indicate the prospect of the [Hg amine.halide] complex claimed in the kinetic analysis. In these experiments, there is no H^+ present to give the synergistic stability observed for HCl. We can presume, however, that HI would yield an even more stable intermediate.

Clearly, there are still interesting facets of the cage chemistry to explore and utilise. Some which we have in train are: coupling the cages to give dimers for electron transfer studies; coupling photosensitizers to the cages for energy capture studies; derivatisation of the cages to site them at different biological surfaces for X-ray, NMR and ESR imaging studies, and the development of the basic chemistry described here and previously.

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