ORIGINAL ARTICLE

Synthesis and characterisation of trinuclear metal complexes derived from carboxymethyl-substituted sarcophagine macrobicyclic cage amines

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Abstract The synthesis and single-crystal x-ray structure determination of two new trinuclear metal complexes is detailed. In these we utilise the appended iminodiacetate substituents, in $[Co(CH_3)NH(CH_2CO_2H)_2sar]^{3+}$, to act as a focus for coordination of other metal ions. Thus, we have made complexes of Cu and Ni utilising the basic carbonates of these metals and $[Co(CH_3)\{N(CH_2CO_2H)_2\}sar]^{3+}$ (**CoL2**) which gave rise to ((**CoL2**–$2H^+$)$_2$M), M = Cu and Ni. The electrochemical study of the latter was inconclusive and provides the impetus for further study.

Keywords Sarcopahgine · Cage · Cobalt · Crystal structures

Introduction

The physical limitations of metal wire as connectors in electronic devices will soon be reached and thus we require alternatives that will be effective in molecular devices suited to the new era of computing. The approach has been to devise so-called "molecular wires" that comprise delocalizable bridges which are capable of carrying charge [1–4].

Our approach is to combine coordination and, its subset, organometallic, chemistry to produce organometallic coordination polymers. This has the advantage of combining a well developed chemistry defining the sites of coordination and stabilization of metal centers with the malleability of organometallic conjugated ligands. Our first efforts utilized organometallic transition metal allenylidenes [5] and most recently we have investigated neutral bipyridyl appended alkynyls [6].

A subject that has continuously elicited interest among inorganic chemists is electronic coupling mediated by two or more metal centers through a ligand, as a consequence of its relevance to important research areas such as intramolecular electron transfer and molecular electronics. We have recently been investigating the chemistry of the electroactive centre afforded by complexes of cage sarcophagine ligands [7–10].

Sarcophagine cages are interesting candidates for the preparation of a wide variety of stable metal complexes [11] which have been utilised in biology [12], and work on cobalt sarcophagine surfactants has demonstrated their utility in killing parasitic worms in vitro, and in vivo in mice [13–15]. These works indicated that the cage complex remained intact during its passage through the animal, with no detectable release of the cobalt metal from the cage. The reversible redox chemistry of sarcophagine complexes containing metals such as V, Mn, Fe, Co and Ni, with reduction potentials ranging over 2 V for readily accessible species [16] provides the possibility of generating redox-switchable functional materials [17].

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Results and discussion

The primary amino group on a cage complex such as $[Co(NH_2)_2sar]^{3+}$ is a relatively poor nucleophile [18], the proximity of the cationic metal centre diminishing this property, and, in cases where it is not convenient to use either the amine or an attacking electrophile in large excess, the cage complex is not an appropriate reagent for efficient synthesis, despite the fact that reactions of this type can be conducted [19, 20]. Logically, it is more appropriate to use an electrophilic centre attached to the cage, since this property should be enhanced by the adjacent charge and indeed it is known that the carboxymethyl derivatives of $[Co(NH_2)_2sar]^{3+}$ can be used efficiently in amide and peptide formation reactions [21]. Acceptably efficient carboxymethylation of $[Co(CH_3)(NH_2)sar]^{3+}$ can be achieved under conditions involving reaction with a large excess of (inexpensive) chloroacetate similar to those used to obtain carboxymethyl derivatives of $[Co(NH_2)_2sar]^{3+}$ [18]. Thus, the complexes $[Co(CH_3)(NHCH_2CO_2H)sar]^{3+}$ (**CoL1**) and $[Co(CH_3)\{N(CH_2CO_2H)_2\}sar]^{3+}$ (**CoL2**) were obtained as outlined in Scheme 1. These complexes, along with $[Co(NH_2)(NHCH_2CO_2H)sar]^{3+}$ [18], provided reactants to which standard peptide coupling methodologies could be applied to obtain derivatives incorporating cystamine residues as disulfide units linking two cages, in work we have already reported [7].

In order to gain some insight into the coordination properties of the iminodiacetate functionalised cage, $CuCO_3\cdot Cu(OH)_2$ and $NiCO_3\cdot 2Ni(OH)_2\cdot 4H_2O$ were added to aqueous solutions of complex **CoL2** and the mixture heated on the steam bath for ca. 1 hour before the mixture was filtered. Dull green crystals of $((\mathbf{CoL2}-2H^+)_2Cu)$ and the analogous yellow Ni complex were then grown by slow vapour diffusion of ethanol into the solution over a period of several days and characterised crystallographically, indicating a composition of $[(\mathbf{CoL2}-2H^+)_2Cu]\cdot Cl_4\cdot 18H_2O$ (Fig. 1). The cation in both complexes is essentially the same, although the solid state structures are not ismorphous. The cation, and atom numbering scheme, for both complexes is depicted in Fig. 1, modelled by the structure of $((\mathbf{CoL2}-2H^+)_2Cu)$, and consists of a centrosymmetric dimer with the additional metal atom situated on a crystallographic inversion centre. Relevant crystal data are given in Table 1, and geometries for both complexes are given in Table 2.

The copper ion in $((\mathbf{CoL2}-2H^+)_2Cu)$ is effectively sandwiched between two cobalt cages via coordination with their iminodiacetate moieties which act as tridentate ligands by coordinating to the metal ion in a facial arrangement through both carboxylates and the tertiary nitrogen atom. The coordination geometry about the copper can be described as distorted octahedral, with a Jahn–Teller distortion of the octahedron reflected in the Cu–N distances (Cu···N 2.35 Å) and the Cu–O distances (Cu···O 2.08 and 1.91 Å). The N atoms do not sit normal to the plane defined by the four coordinated oxygen atoms, displaying two acute N···Cu···O angles of 75° and 82° which might be a result of the large steric bulk of the cage unit directly bound to the coordinated N atom. A similar tilt of the axial ligands has been observed for a Cu bis(iminodiacetate) complex with two bulky Ge(diethylenetriaminepentaacetate) complexes appended to the ligands [22]. In the structure of $((\mathbf{CoL2}-2H^+)_2Cu)$, the two cages coordinated to the copper ion are of opposite chirality (centrosymmetric about the copper ion) and, interestingly, are in the ob_3 conformation. In this case one chloride ion, though crystallographically disordered, is in close contact with only one coordinated NH of the cage
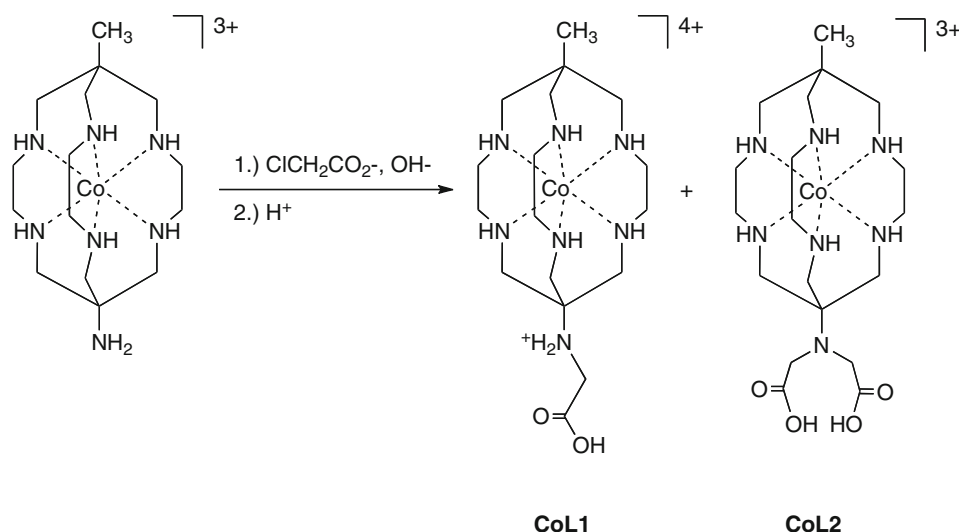
Scheme. 1 Synthesis of the starting materials $[Co(CH_3)(NH_2CH_2CO_2H)sar]^{4+}$ (**CoL1**) and $[Co(CH_3)\{N(CH_2CO_2H)_2\}sar]^{3+}$ (**CoL2**)
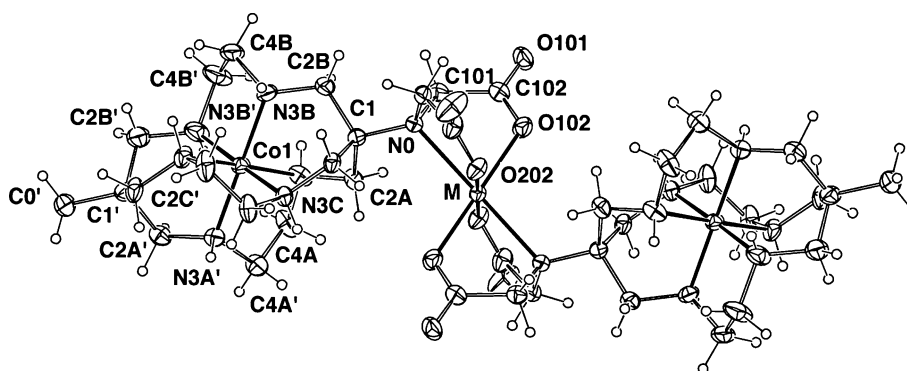
Fig. 1 Molecular projection of the structures of the cation present in $[\{Co(N(CH_2CO_2)_2)(CH_3)sar\}_2M]\cdot Cl_4\cdot nH_2O$ $[(CoL2–2H^+)_2M]$ M = Cu, Ni

Complex	$(CoL2–2H^+)_2Cu)$	$(CoL2–2H^+)_2Ni)$
Empirical formula	$C_{38}H_{86}Cl_4Co_2CuN_{14}O_{14}$	$C_{42}H_{122}Cl_4Co_2N_{14}NiO_{28}$
Formula weight	1286.41	1589.91
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
a (Å)	10.785(2)	11.9822(8)
b (Å)	14.192(3)	12.1079(9)
c (Å)	14.643(3)	13.1186(8)
α (°)	112.384(3)	103.823(6)
β (°)	105.805(3)	102.945(5)
γ (°)	101.902(3)	98.604(6)
V (Å^3)	1869.1(7)	1759.2(2)
Z	1	1
D_c(g cm^{-3})	1.143	1.501
μ (mm^{-1})	0.917	0.969
$T_{max/min}$	0.66	0.93
Crystal dimensions (mm)	$0.32 \times 0.20 \times 0.12$	$0.23 \times 0.22 \times 0.15$
θ_{max} (°)	26.37	32.7
N_{total}	14960	23806
N	7488	11657
R_{int}	0.047	0.036
N_o	4713	7727
Data/restraints/parameters	7488/0/363	11657/22/458
Goodness-of-fit	1.013	0.969
$R1$, $wR2$ [$I > 2\sigma(I)$]	0.0732, 0.1929	0.0546, 0.1548
$R1$, $wR2$ [all data]	0.1058, 0.2096	0.0861, 0.168
Largest peak, hole (e·Å^{-3})	1.372, −0.572	2.588, −1.085

Table 1 Crystal and refinement data for the complexes

(Cl···NH *ca*. 3.04–3.38 Å), consistent with previous ob_3 structures [23]. There are no significant changes to the Co–N bond lengths in this complex compared to the starting material.

All cage amine hydrogen atoms are involved in hydrogen bonding; H(3A) and H(3A′) form H-bonds to Cl(1) and Cl(2) respectively, with H(3B′) and H(3C′) H-bonded to the centrosymmetrically related Cl(1) and Cl(2). While H(3C) forms a H-bond to O(1) of a solvent water molecule. H(3A′) is hydrogen bonded to an uncoordinated carboxylate O of the molecule related by a unit cell translation along the cell *a* direction forming a 3D H-bonded polymeric structure.

The cation of $((CoL2–2H^+)_2Ni)$ also consists of a centrosymmetric dimer with the Ni atom situated on a crystallographic inversion centre. Relevant geometries are given in

**Table 2** Selected bond lengths [Å] and angles [°] for the complexes

	(CoL2–2H$^+$)$_2$Cu)	(CoL2–2H$^+$)$_2$Ni)
Co(1)–N(3C')	1.946(4)	1.957(2)
Co(1)–N(3B')	1.959(4)	1.955(2)
Co(1)–N(3B)	1.961(4)	1.956(2)
Co(1)–N(3C)	1.968(4)	1.966(2)
Co(1)–N(3A)	1.971(4)	1.961(2)
Co(1)–N(3A')	1.973(4)	1.951(2)
M(1)–O(102)	2.077(3)	2.0308(19)
M(1)–O(202)	1.915(3)	2.0417(18)
M(1)–N(0)	2.356(3)	2.148(2)
N(3C')–Co(1)–N(3B')	91.5(2)	91.82(9)
N(3C')–Co(1)–N(3B)	89.81(19)	88.91(9)
N(3B')–Co(1)–N(3B)	87.49(18)	87.23(9)
N(3C')–Co(1)–N(3C)	87.28(16)	87.52(9)
N(3B')–Co(1)–N(3C)	177.78(19)	178.87(9)
N(3B)–Co(1)–N(3C)	90.68(17)	91.84(9)
N(3C')–Co(1)–N(3A)	177.70(18)	178.23(9)
N(3B')–Co(1)–N(3A)	90.8(2)	89.87(9)
N(3B)–Co(1)–N(3A)	90.92(18)	91.70(9)
N(3C)–Co(1)–N(3A)	90.53(16)	90.80(9)
N(3C')–Co(1)–N(3A')	91.47(16)	91.88(9)
N(3B')–Co(1)–N(3A')	90.94(17)	91.50(9)
N(3B)–Co(1)–N(3A')	177.99(18)	178.53(9)
N(3C)–Co(1)–N(3A')	90.92(16)	89.44(9)
N(3A)–Co(1)–N(3A')	87.85(15)	87.55(9)
O(202)–M(1)–O(102)	91.75(15)	92.05(8)
O(202)–M(1)–N(0$^#$)	98.05(13)	97.36(8)
O(102)–M(1)–N(0$^#$)	104.49(12)	100.28(8)
O(202)–M(1)–N(0)	81.95(13)	82.64(8)
O(102)–M(1)–N(0)	75.51(12)	79.72(8)

$^#$ Atom generated by the symmetry operation: $1 - x, 1 - y, 1 - z$

Table 2, in comparison to the Cu analogue. The coordination around the Ni atom is octahedral with the metal atom bonding to the four O atoms of the two carboxylate groups (Ni–O(102,202) 2.0308(19)(3), 2.0417(18) Å) and to the N(0) atoms (Ni–N(0) 2.148(2) Å). All six cage amine hydrogen atoms are involved in H-bonding, either to a water molecule or to one of the Cl$^-$ counter ions. The carboxylate O atoms are also involved in H-bonds to water molecules with one water molecule, O(4), forming H-bonds between both an uncoordinated carboxylate O atom, O(101), and an amine H atom, H(3C). The cationic dimer and associated H-bonded water molecules and Cl$^-$ ions are shown in Fig. 2.

We probed the electrochemical properties of ((CoL2–2H$^+$)$_2$Ni) but, perhaps unsurprisingly, found no additional features other than those associated with the Co(II)/(III) cage couple. Recently, the reaction of Cu^{2+} acetate monohydrate with 2-[N,N-bis(carboxymethyl)aminomethyl]-4-carboxyphenol, 2-[N,N-bis(carboxymethyl)aminomethyl]hydroquinone and the dinucleating 2,5-bis[N,N-bis(carboxymethyl)aminomethyl]hydroquinone in water results in the formation of several Cu^{2+} species, which are in dynamic equilibrium in aqueous solution and their stability is pH dependent [24]. The conclusions reached suggest that the Cu(II) ion is coordinated variously to the iminodiacetate group and/or the phenolic oxygens, dependent on the pH. However, the cyclic voltammograms of the complexes exhibit wave attributable to Cu(II)/Cu reduction and redox waves centered at the ligands.

Perhaps in the case of ((CoL12–2H$^+$)$_2$Ni) at neutral pH the complex does not persist in solution. In this case, we would have expected to see redox features associated with aquated Ni^{2+}, thus we conclude that the redox couple for the NiN$_2$O$_4$ coordination sphere falls outside of the measurable window associated with water.
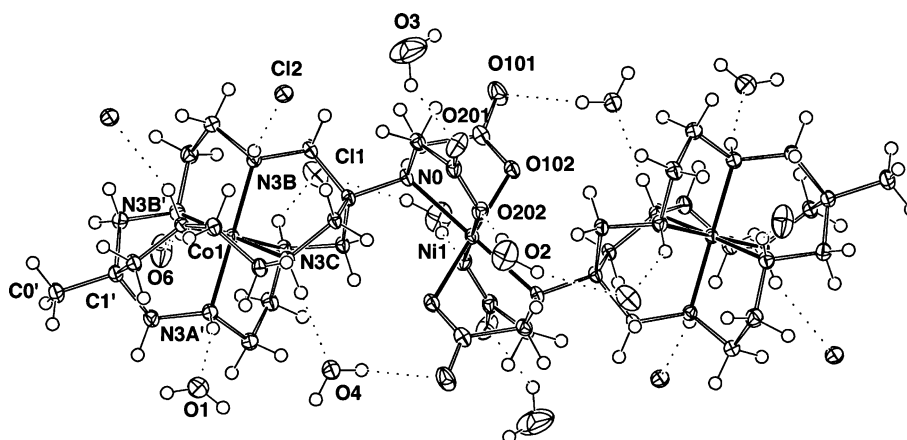
Fig. 2 Molecular projection of the structure of the cation present in [{Co(N(CH$_2$CO$_2$)$_2$)(CH$_3$)sar}$_2$Ni]·Cl$_4$·18H$_2$O·EtOH showing the H-bonding to adjacent water molecules and chloride ions

Conclusion

We have shown that the iminodiacetate substituted sarcophagines are capable of acting as ligands in spite of their adjacent cationic charge associated with the Co(III) cage. These appear to be stable complexes that will form the basis for a much more detailed study in the future. It will be here that some of our more ambitious aims mentioned in the introduction will be realised.

Experimental

Mass spectra were recorded using the electrospray (positive ion trap) or fast-atom bombardment technique on a VG Autospec instrument or QSTAR XL-MS/MS.

Microanalyses for C, N, and H were carried out by The Australian National University Microanalytical Service. All samples were thoroughly dried under vacuum at 50 °C for at least 4 h prior to their analysis.

$[Co(CH_3)(NH_3)sar]Cl_4 \cdot 0.5H_2O$ [25] and $(NH_2)_2sar \cdot 2H_2O$ [26] were synthesised according to literature methods. $NaBH_3CN$, $NaBH_4$ (Aldrich), 10% Pd/C (Fluka), $Co(CH_3CO_2)_2 \cdot 4H_2O$, $Cu(CH_3CO_2)_2 \cdot H_2O$, $CuCO_3 \cdot Cu(OH)_2$, $NiCO_3 \cdot 2Ni(OH)_2 \cdot 4H_2O$ (Ajax), $CoCO_3 \cdot xH_2O$, ZnO, MgO (BDH) were all used as received. "Absolute" EtOH and MeOH was stored over 3 Å molecular sieves prior to use in the following syntheses.

Deionised water was used in all preparations. DMF was predried over 4 Å molecular sieves prior to use. DCM was dried by distillation from CaH_2 and stored over 3 Å molecular sieves. Tri-sodium citrate (Na₃Cit) (Ajax), chloroaceticacid (Ajax), diisopropylethylamine (DIPEA) (Lancaster) was used as received. $[Co(CH_3)(NH_3)sar]Cl_4 \cdot 0.5H_2O$ was prepared are reported [25].

Solution electrochemistry

Solution electrochemical experiments were carried out at room temperature (23 ± 1 °C) on a MacLab Potentiostat or CH Instruments potentiostat model 660B or 440 in 0.1 M $NaClO_{4(aq)}$ adjusted to pH 7.3 with tris(hydroxymethyl)aminomethane/$HClO_4$ buffer, and an analyte concentration of 1 mM. A three-electrode cell system consisting of glassy carbon (3.0 mm diameter) as working electrode, Pt wire as counter electrode and Ag/AgCl (3.0 M KCl) as the reference electrode was employed. The carbon electrodes were cleaned by polishing on a micro-cloth pad with Al_2O_3 slurry (0.05 μm) and washed thoroughly with water before use. For the cyclic voltammetric (CV) studies the scan rate was 100 mV s^{-1} and for the DPV experiments a scan rate of 20 mV s^{-1} and pulse amplitude of 50 mV was used. Cyclic voltammograms (CVs) were scanned in the potential range of 0.2 to −1.1 V versus Ag/AgCl.

Crystallography

The crystal data for the complexes are summarized in Table 1, in the figure, ellipsoids have been drawn at the 30%, for (**CoL2**–2H⁺)₂Cu), and 50%, for ((**CoL2**–2H⁺)₂Ni), probability level. Selected coordination geometries are shown in Table 2. Crystallographic data for the (**CoL2**–2H⁺)₂Cu) were collected at 150(2) K on a Bruker SMART CCD diffractometer, while those for ((**CoL2**–2H⁺)₂Ni), were collected at 100(2) K on an Oxford Diffraction Gemini diffractometer, both fitted with graphite-monochromated Mo Kα radiation yielding N_{total} reflections, these merging to N unique after multiscan absorption correction (R_{int} cited), with N_o reflections having $I > 2\sigma(I)$. The structures were refined against F^2 with full-matrix least-squares using the program SHELXL-97 [27]. For (**CoL2**–2H⁺)₂Cu), all H-atoms were added at calculated positions and refined by use of a riding model with isotropic displacement parameters based on the isotropic displacement parameter of the parent atom. Anisotropic displacement parameters were employed throughout for the non-hydrogen atoms. Although the atoms of the cation are ordered, it was found that both Cl atoms were disordered with components separated by less than 1 Å, this model resulting in a significant improvement. Several residual peaks in the difference map were modelled as water molecules and assigned site occupancies of 1 or 0.5 after initial trial refinement. Since remaining electron density could not be reasonably modelled as water molecules, the program PLATON/SQUEEZE [28] was used to effectively remove these peaks.

For ((**CoL2**–2H⁺)₂Ni) ten solvent peaks were assigned as water molecules, with site occupancies set at 1 or 0.5 after trial refinement. H atoms for O(1)–O(5) were located and refined with geometrical restraints with those on the remaining water molecules not being located with sufficient degree of confidence. The remaining H-atoms were added at calculated positions and refined by use of a riding model with isotropic displacement parameters based on the isotropic displacement parameter of the parent atom. A cluster of atoms with separations too small to be assigned to water molecules, were modelled as an EtOH solvent molecule disordered over two sites with equal site occupancies. These atoms were refined with isotropic displacement parameters. Anisotropic displacement parameters were employed for the remaining non-H atoms.

Synthesis of ((**CoL2**–2H⁺)₂Ni)

$[Co(CH_3)\{N(CH_2CO_2H)_2\}sar]Cl_3 \cdot 2H_2O$ (0.021 g, 3.7×10^{-5} mol) was dissolved in water (ca. 1 mL) and

$NiCO_3 \cdot 2Ni(OH)_2 \cdot 4H_2O$ (0.030 g, 7.9×10^{-5} mol) was added. The mixture was heated on the steam bath until CO_2 stopped evolving, which took 2.5 h. The excess $NiCO_3 \cdot 2Ni(OH)_2 \cdot 4H_2O$ was removed by filtration. Slow diffusion of EtOH into the solution gave $[\{Co(CH_3)(N(CH_2CO_2)_2)$-sar$\}_2Ni] \cdot Cl_4 \cdot 18H_2O \cdot 2EtOH$ (0.05 g, 0.031 mmol, 85%) as yellow crystals.

The Cu complex was prepared from an essentially identical reaction and both complexes gave satisfactory microanalyses.

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