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FULL PAPER

Template synthesis of amidine- and amide-functionalised cobalt(III) hexaaza cage complexes

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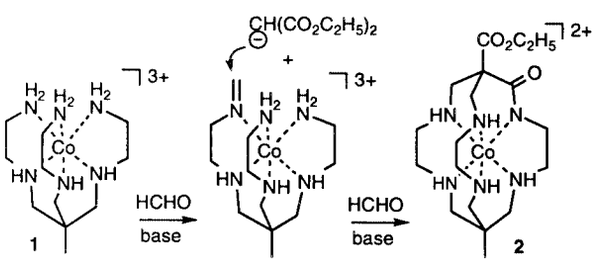
The reaction of $[Co(sen)]Cl_3 \cdot H_2O$ {sen = 4,4′,4″-ethylidynetris(3-azabutan-1-amine)} with methanal and ethyl cyanoacetate in aqueous base led to the synthesis of three functionalised cobalt(III) cage complexes: (1-cyano-8-methyl-2-oxo-3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosanato)cobalt(III) chloride–water(1/3) $[Co(CN,Me\text{-}2\text{-}oxosar - H)]Cl_2 \cdot 3H_2O$; (2-amino-1-carboxy-8-methyl-3,6,10,13,16,19-hexaazabicyclo[6.6.6]icos-2-ene)cobalt(III)]trichloride–ethanol–water(1/0.5/3.5), $[Co(Me,CO_2H\text{-}2\text{-}aminosar\text{-}2\text{-}ene)]Cl_3 \cdot 0.5C_2H_5OH \cdot 3.5H_2O$; and (2-amino-8-methyl-3,6,10,13,16,19-hexaazabicyclo[6.6.6]icos-2-ene)cobalt(III) trichloride–water(1/3), $[Co(Me\text{-}2\text{-}aminosar\text{-}2\text{-}ene)]Cl_3 \cdot 3H_2O$. The amidine-functionalised cages are the first hexaaza cages of that type. The structure of $[Co(CN,Me\text{-}2\text{-}oxosar - H)][ClO_4]_{3/2}Cl_{1/2} \cdot H_2O$ has been established by X-ray crystallographic analysis. The syntheses, chemical reactions and spectroscopic and electrochemical properties of the cage complexes are described.

Introduction

The first synthesis of a functionalised hexaaza cobalt(III) cage complex was achieved by treating $[Co(sen)]^{3+}$ {Scheme 1, **1**;



Scheme 1

sen = 4,4′,4″-ethylidynetris(3-azabutan-1-amine)} with methanal and a carbon acid bearing ester groups.[1] In that template synthesis an amide functional group was incorporated into the framework of a cage ligand by condensing a co-ordinated amine with an ester as part of the capping of a cobalt(III) tripodal complex {Scheme 1}. More recently, similar reactions using carbon acids containing an aldehyde or ketone functional group have been used to prepare imine-functionalised cage complexes.[2,3] In this study the carbon acid was ethyl cyanoacetate, a bifunctional molecule whose nitrile and ester groups are both capable of condensing with co-ordinated amines. Consequently three types of functionalised cage complex could form in this synthesis: amide[1] and amidine cage complexes and one containing both functional groups. The synthesis of a co-ordinated amidine by condensation of a co-ordinated deprotonated amine and a nitrile group is a known reaction in cobalt(III) chemistry[4–6] but has only recently been applied to cage synthesis.[7]

The synthesis of functionalised cage complexes is of interest because the presence of a co-ordinated functional group has been shown to modulate the physical properties of the complex.[8] In addition, amide-bearing ligands have stabilised higher oxidation states in peptide and macrocyclic square-planar complexes of copper, nickel and cobalt metal ions[9–11] hence the synthesis of amide cage ligands is of importance not only to stabilise the oxidation state but also to stabilise the whole co-ordination entity within the cage framework. In this case there was also the possibility of preparing cage complexes containing the related neutral amidine functional group and studying their properties.

Results

Syntheses

Three cage complexes were isolated by ion exchange chromatography from the reaction of ethyl cyanoacetate, methanal and $[Co(sen)]^{3+}$ in aqueous base. The first species, as reported briefly in an earlier paper,[1] was an amide-functionalised cage complex with an apical nitrile substituent, $[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$ {Scheme 2, **3**}. (For an explanation of the trivial cage nomenclature see reference 8.) The ^{13}C NMR spectrum of the complex contained 16 signals, consistent with an asymmetric cage complex with apical methyl and nitrile substituents, and the peaks at δ 116.8 and 171.3 were assigned to the nitrile and amide groups respectively. The structure of this cage complex has now been established by X-ray crystallography (Fig. 1) and the analysis is presented in this report.

A proposed mechanism for the formation of $[Co(CN,Me\text{-}2\text{-}oxosar - H]^{2+}$ is shown in Scheme 2; it is consistent with experimental data and results obtained from similar systems. The initial reaction involves the addition of methanal to a co-ordinated amine on the tripodal complex, $[Co(sen)]^{3+}$, forming a co-ordinated *exo* imine which then condenses with the anion of ethyl cyanoacetate (pK_a 9)[12] at the site of deprotonation. Subsequently, an adjacent deprotonated co-ordinated amine condenses in the same way, and the ester group condenses with the remaining cap amine to form a deprotonated, N-co-ordinated amide group as part of the cage ligand. Condensation with methanal must be the first step in this synthesis, since no reaction with the tripodal complex occurred in its

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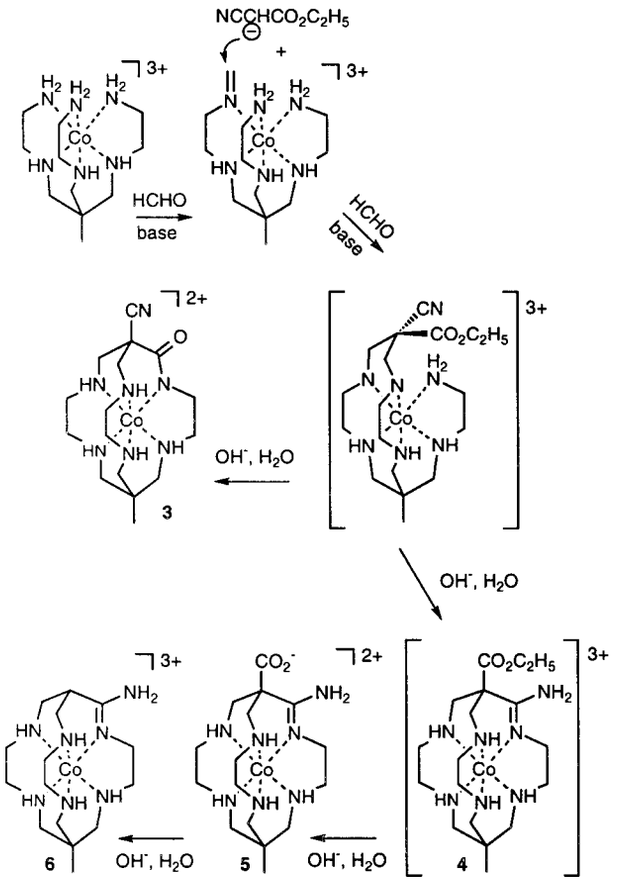


Scheme 2

absence. The order of the second and third condensations however cannot be determined with certainty, but the mechanism is consistent with all available data on these types of syntheses.

The nitrile group in this pathway did not participate directly in amide cage formation but remained intact as an apical substituent. As an electron-withdrawing substituent, however, it did have a substantial effect on the rate of the reaction. In this instance $[Co(sen)]^{3+}$ was completely consumed within one hour's reaction time, compared with a reaction time of several days when the carbon acid was diethyl malonate (pK_a 15.3)[13] as used in the synthesis of $[Co(Me,CO_2H\text{-}2\text{-}oxosar - H)]^{2+}$.[1] Attempts to isolate the cage ligand from $[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$ were unsuccessful. NMR spectroscopy of the products of the demetallation reaction showed a number of organic species were present and they remained unresolved.

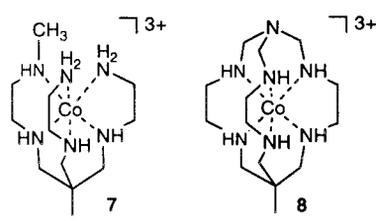
The other cage complexes were identified spectroscopically and by microanalysis and electrospray mass spectrometry. One was assigned the structure of an amidine-functionalised cobalt(III) cage complex which contained apical carboxylic acid and methyl substituents {$[Co(Me,CO_2H,2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$; Scheme 2, **5**}. It chromatographed as a dipositive ion at pH 7 and a tripositive ion at pH < 1. The ^{13}C NMR spectrum contained 16 peaks, consistent with an asymmetric functionalised cage, and two of these, δ 173.6 and 169.4, were assigned to carboxylic acid and amidine functional groups respectively. The ^1H NMR spectrum in $Me_2SO\text{-}d_6$ showed a single broad peak for the amidine *exo* NH_2 group at δ 8.5, separate from the secondary amine signals. The C=N stretching vibration was identified in the IR spectrum at 1671 cm^{-1} and the C=O stretch for the carboxylic acid group at 1723 cm^{-1}. The microanalysis and mass spectrum were also consistent with this structure.

The final cage complex was similar to the amidine-functionalised cage complex described above, except that it lacked the apical carboxylic acid substituent. It was therefore assigned as $[Co(Me\text{-}2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$ {Scheme 2, **6**}. The ^{13}C NMR spectrum consisted of 15 peaks and the peak at δ 169.4 was assigned to the amidine group. The ^1H NMR spectrum in $Me_2SO\text{-}d_6$ showed two peaks for the amidine *exo* NH_2 group at δ 8.35 and 8.58; in this case the diastereotopic amidine protons were resolved. The C=N stretching vibration in the IR spectrum occurred at 1654 cm^{-1} and was within the range expected for simple amidines,[14] as is the analogous vibration for the carboxylate-substituted amidine cage.

The mechanism for the formation of amidine cages is similar to that for $[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$, except that in this case the nitrile group in ethyl cyanoacetate has condensed with a co-ordinated amine. The initial cage product must have been an amidine-functionalised cage complex with an apical ester substituent {Scheme 2, **4**}. This complex was not observed so the ester group has hydrolysed reasonably rapidly to form the carboxylate-substituted amidine cage {Scheme 2, **5**}. Further reaction in aqueous base at 50 °C led to decarboxylation and the final product of this series of reactions was the unsubstituted amidine cage complex {Scheme 2, **6**}.

The co-ordinated amidine functional group was characteristically inert. The amidine cage complexes were stable indefinitely in aqueous acid and base at ambient temperature. They were unreactive towards nitrosation, tetrahydroborate reduction, methylation with iodomethane, and heating in concentrated nitric acid. Prolonged hydrogenation in the presence of palladium on charcoal resulted in a small amount of decomposition of the complex and ligand and recovery of most of the reactant. Demetallation reactions were not attempted since free amidines hydrolyse easily.[15]

Two by-products were isolated from this synthesis and both species have been reported and characterised previously. The major one was $[Co(N\text{-}Me\text{-}sen)]^{3+}$ **7** which arose from reaction of methanal and $[Co(sen)]^{3+}$.[16] The second (minor) species was a cage complex, $[Co(azaMesar)]^{3+}$ **8**, which was formed from



$[Co(sen)]^{3+}$, methanal and ammonia.[16] In this case ammonia was an adventitious reagent which must have arisen from hydrolysis of the nitrile group in ethyl cyanoacetate and subsequent amide hydrolysis during the cage synthesis.

X-Ray crystallography

The structure of $[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$ (as the chloride perchlorate salt) was determined by X-ray analysis and is shown in Fig. 1 and selected bond lengths and angles are listed in Table 1. The structure demonstrates the encapsulation of the metal ion in a pseudo-octahedral environment and that a deprotonated N-bonded amide group is incorporated into the framework of a cage ligand bearing an apical nitrile substituent. Two of the five-membered chelate rings display the *lel* conformation while the third such ring, which is on the same strand as the amide group, has the *ob* conformation.[17] The first amide and amidine cages to be structurally characterised also had this conformation.[1,7] In $[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$ the Co–N_{amido} bond {1.898(3) Å} is shorter (≈0.1 Å) than the Co–N_{amine} bonds and this pattern was also observed in the structure of $[Co(Me,CO_2H\text{-}2\text{-}oxosar - H)][ClO_4]_2$.[1] It is slightly shorter than the analogous bond {1.911(8) Å} in the acyclic primary amide complex $[Co(NH_3)_5(NHCOCH_3)]^{2+}$,[18] and somewhat longer than that in the chelated peptide, $[Co(glyglyO)_2]^-$.[19]

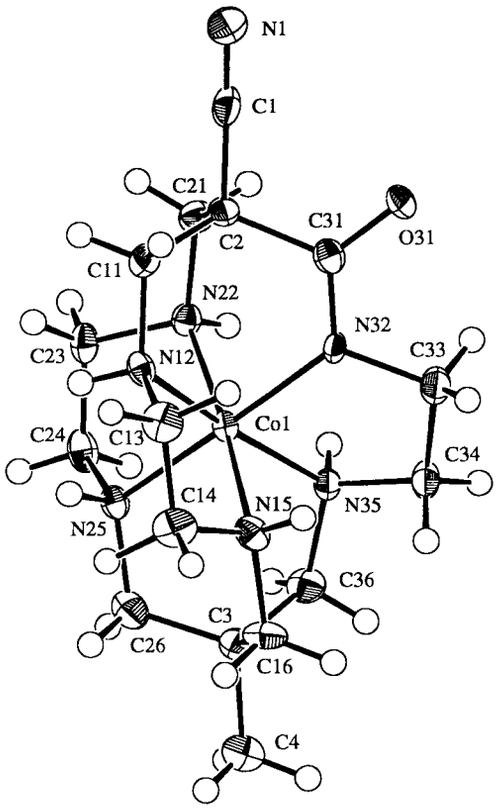


Fig. 1 Thermal ellipsoid diagram of the $[Co^{III}(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$ cation with labelling of selected atoms. Ellipsoids show 50% probability levels, except for hydrogen atoms which are drawn as spheres of arbitrary radius.

Electrochemistry

The cyclic voltammograms for the three cage complexes in aqueous solution showed quasi-reversible Co^{III}–Co^{II} couples whose potentials varied according to the pH of the medium (Table 2). The potential for $[Co(CN,Me\text{-}oxosar - H)]^{2+}$ was −0.76 V at pH 12.04 (*vs.* SCE), comparable with the value of −0.68 V obtained previously by dc polarography and with those published for other hexaaza, amide-functionalised cobalt(III) cage complexes;[1] small differences can be attributed to variation in the nature of the apical substituent.[8] The potential changed in acid solution (pH 1.68) because the cobalt(II) forms of amide-functionalised cages are protonated under those conditions and undergo slow dissociation of the cobalt(II) ion and hydrolysis of the amide linkage.[1] The potentials of the amidine-functionalised cage complexes were approximately −0.7 V in acid solution, and there was a small variation according to the nature of the apical substituent. At pH 12.04 the potential of $[Co(Me,2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$ was slightly reduced and this was attributed to partial deprotonation of the amidine group, the *exo*-NH_2 group in co-ordinated amidines being weakly acidic.[4,6] The cobalt(II) forms of the amidine cage complexes were stable at room temperature under the conditions described.

Electronic absorption spectroscopy

The d–d absorption bands for $[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$ in 0.1 M HCl occur at 342 and 492 nm ($\varepsilon = 216$ and 233 $dm^3\ mol^{-1}\ cm^{-1}$ respectively). The spectrum is similar to that for $[Co(Me,CO_2C_2H_5\text{-}2\text{-}oxosar - H)]^{2+}$ and this was not unexpected since apical substituents have little influence on UV-visible spectra for molecules of this type.[20] For both amidine cage complexes, the d–d absorption bands occur at 343 and 488 nm. The band intensities vary little, for $\{[Co(Me,CO_2H,2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$ $\varepsilon_{342} = 277$ and $\varepsilon_{488} = 233$, for $[Co(Me\text{-}2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$ $\varepsilon_{342} = 208$ and $\varepsilon_{488} = 228\ dm^3\ mol^{-1}\ cm^{-1}$.

Table 1 Selected bond distances (Å) and angles (°) for $[Co^{III}(Me,CN\text{-}2\text{-}oxosar - H)]^{2+}$

Co–N(12)	1.980(3)	Co–N(15)	1.971(4)
Co–N(22)	1.983(3)	Co–N(25)	1.976(3)
Co–N(32)	1.898(3)	Co–N(35)	1.971(3)
O(31)–C(31)	1.259(4)	N(1)–C(1)	1.129(5)
N(12)–C(11)	1.495(5)	N(12)–C(13)	1.482(5)
N(15)–C(14)	1.493(5)	N(15)–C(16)	1.503(5)
N(22)–C(21)	1.491(5)	N(22)–C(23)	1.497(5)
N(25)–C(24)	1.495(5)	N(25)–C(26)	1.494(5)
N(32)–C(31)	1.298(5)	N(32)–C(33)	1.467(5)
N(35)–C(34)	1.499(5)	N(35)–C(36)	1.492(5)
C(1)–C(2)	1.497(5)	C(2)–C(11)	1.534(5)
C(2)–C(21)	1.548(6)	C(2)–C(31)	1.548(5)
C(3)–C(4)	1.525(6)	C(3)–C(16)	1.527(6)
C(3)–C(26)	1.523(6)	C(3)–C(36)	1.527(6)
C(13)–C(14)	1.492(6)	C(23)–C(24)	1.497(6)
C(33)–C(34)	1.512(6)		
N(12)–Co–N(15)	86.5(1)	N(12)–Co–N(22)	90.2(1)
N(12)–Co–N(25)	92.5(1)	N(12)–Co–N(32)	90.5(1)
N(12)–Co–N(35)	170.9(1)	N(15)–Co–N(22)	175.1(1)
N(15)–Co–N(25)	89.9(1)	N(15)–Co–N(32)	94.6(1)
N(15)–Co–N(35)	87.9(1)	N(22)–Co–N(25)	86.7(1)
N(22)–Co–N(32)	89.0(1)	N(22)–Co–N(35)	95.9(1)
N(25)–Co–N(32)	174.8(1)	N(25)–Co–N(35)	94.6(1)
N(32)–Co–N(35)	82.9(1)	Co–N(12)–C(11)	117.8(3)
Co–N(12)–C(13)	107.3(3)	C(11)–N(12)–C(13)	111.6(3)
Co–N(15)–C(14)	107.1(3)	Co–N(15)–C(16)	117.9(3)
C(14)–N(15)–C(16)	112.8(3)	Co–N(22)–C(21)	117.7(3)
Co–N(22)–C(23)	106.7(3)	C(21)–N(22)–C(23)	112.9(3)
Co–N(25)–C(24)	107.2(3)	Co–N(25)–C(26)	117.3(3)
C(24)–N(25)–C(26)	113.7(3)	Co–N(32)–C(31)	125.1(3)
Co–N(32)–C(33)	117.1(3)	C(31)–N(32)–C(33)	116.2(3)
Co–N(35)–C(34)	107.9(2)	Co–N(35)–C(36)	115.9(2)
C(34)–N(35)–C(36)	110.9(3)	N(1)–C(1)–C(2)	178.4(5)
C(1)–C(2)–C(11)	107.1(3)	C(1)–C(2)–C(21)	107.2(4)
C(1)–C(2)–C(31)	109.3(3)	C(11)–C(2)–C(21)	111.3(3)
C(11)–C(2)–C(31)	113.8(3)	C(21)–C(2)–C(31)	107.9(3)
C(4)–C(3)–C(16)	108.5(4)	C(4)–C(3)–C(26)	108.1(4)
C(4)–C(3)–C(36)	107.6(4)	C(16)–C(3)–C(26)	109.5(4)
C(16)–C(3)–C(36)	112.5(4)	C(26)–C(3)–C(36)	110.4(4)
N(12)–C(11)–C(2)	112.2(3)	N(12)–C(13)–C(14)	107.6(4)
N(15)–C(14)–C(13)	106.7(4)	N(15)–C(16)–C(3)	113.3(4)
N(22)–C(21)–C(2)	112.1(3)	N(22)–C(23)–C(24)	106.6(3)
N(25)–C(24)–C(23)	107.0(3)	N(25)–C(26)–C(3)	114.3(4)
O(31)–C(31)–N(32)	126.1(4)	O(31)–C(31)–N(2)	119.7(4)
N(32)–C(31)–C(2)	113.9(3)	N(31)–C(33)–C(34)	108.3(3)
N(35)–C(34)–C(33)	110.9(3)	N(35)–C(36)–C(3)	113.7(4)

Discussion

This paper describes a template synthesis of two types of functionalised cage complex involving the use of a bifunctional carbon acid, ethyl cyanoacetate, as elaborated in Scheme 2. The products of the reaction consisted of approximately equal amounts of amidine- and amide-functionalised cage complexes. The variation in functionality of the cage complexes arose through competition of a co-ordinated nucleophile (a deprotonated amine) for a pendant ester or a nitrile group derived from the carbon acid. That these two functional groups have near equivalent reactivity in this kind of chemical environment has been demonstrated previously in simpler systems where the rates of condensation have been measured. The rate constants for the attack of a co-ordinated aminato ligand on the pendant ester in $[Co(NH_3)_5(NH_2CH_2CO_2C_2H_5)]^{3+}$ and for the attack of a co-ordinated, deprotonated amine on the pendant nitrile in $[Co(en)_2(NH_2CH_2CN)Br]^{3+}$ (en = ethane-1,2-diamine) have been found to be $\approx 10^6\ s^{-1}$.[4,21]

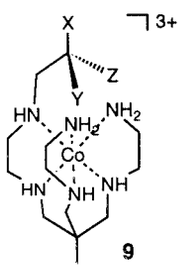
Template syntheses which produced two cage complexes simultaneously have been reported previously, however those reactions involved competition between the direct condensation of a deprotonated co-ordinated amine and a functional group (aldehyde or ketone) and the linking of a co-ordinated amine and a carbon acid with methanal. The results were an imine-

Table 2 Reduction potentials for the Co^{III}–Co^{II} couple of amide- and amidine-functionalised hexaaza cobalt(III) cage complexes and relevant hexaamine analogues[a]

Complex	pH	$E_{1/2}$/V	i_{pc}/i_{pa}	ΔE_p/mV
$[Co(CN,Me\text{-}2\text{-}oxosar - H)]^{2+}$	1.68[b]	−0.71	0.90	130
	12.04[c]	−0.76	0.74	68
$[Co(Me,CO_2H\text{-}2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$	1.68[b]	−0.68	0.92	101
$[Co(Me,2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$	1.68[b]	−0.72	0.95	92
	12.04[c]	−0.74	0.87	68
$[Co(Mesar)]^{3+}$[d]	≈6	−0.65		
$[Co(Me,CO_2^-\text{-}sar)]^{2+}$[d]	≈6	−0.60		
$[Co(Me,CO_2H\text{-}sar)]^{3+}$[d]	≈6	−0.55		

[a] *vs.* SCE, [cage complex] = 1 mM, T = 20 °C, scan rate = 20 mV s^{-1}. [b] Supporting electrolyte 0.05 M $KH_3(C_2O_4)_2$. [c] Supporting electrolyte 0.05 M Na_3PO_4. [d] Ref. 8. Supporting electrolyte 0.1 M $NaClO_4$ or 0.1 M $NaCF_3SO_3$.

functionalised cage and a saturated cage with a functionalised apical substituent (formyl or aroyl group).[2,3] We also note that in this synthesis no cage species containing two co-ordinated functional groups was detected. It may be that the second condensation of a co-ordinated amine with methanal was rapid when compared with its rate of condensation with the remaining functional group. Another aspect to consider is the orientation of the functional groups once ethyl cyanoacetate has been connected to the tripodal $[Co(sen)]^{3+}$. There are six possible orientations (**9**) and these may well interconvert on



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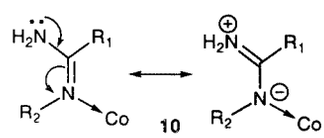
X, Y, Z = H, CN, $CO_2C_2H_5$

deprotonation at the central carbon. It is possible that the conformers with the hydrogen atom in the apical position are energetically disfavoured so that condensation of two functional groups is sterically precluded.

The amidine cage complexes reported here are the first hexaaza cages of that type. Like all known cobalt(III) amidine complexes, the functional group in the cage ligand has been formed by a rapid reaction between nitrile and amine at the metal centre and is remarkable for its chemical stability. In this instance it is even stable in the cobalt(II) state at ambient temperature. The cobalt(III) ion stabilises the amidine to at least the level that it stabilises co-ordinated amides to hydrolysis. In basic solution deprotonation of the *exo*-NH_2 group inhibits attack of hydroxide ion. In acidic solution the cobalt(III) ion inhibits protonation of both nitrogen sites which impedes nucleophilic additions. Binding these groups to metal ions is therefore an important method for stabilising them.

The apical substituents on the amidine-functionalised cage complexes are more reactive than their counterparts on amide cages. The ester group on the first-formed amidine cage {Scheme 2, **4**} was hydrolysed within one hour's reaction time at 50 °C, whereas the analogous reaction for $[Co(Me,CO_2C_2H_5\text{-}2\text{-}oxosar - H)]^{2+}$ required refluxing in K_2CO_3–aqueous ethanol for three hours. Similarly, decarboxylation of $[Co(Me,CO_2H,2\text{-}aminosar\text{-}2\text{-}ene)]^{3+}$ {Scheme 2, **5**} was quite facile but the reaction was not detected for the corresponding amide cage, even after long reactions at elevated temperature in acidic and in basic solutions.[1] This difference in reactivity is attributed to the charge difference between the amidine and amide cage complexes; in the former case there was greater activation of the neutral cage ligand by the metal ion.

The potentials of all the amidine and amide cage complexes were more negative than those found for analogous hexaamine cobalt(III) cage complexes,[8] presumably because of an increased charge density at Co^{III}. For the amide cage complex this can be attributed to the negative charge on the deprotonated amide nitrogen donor atom.[1] For the amidine cage complexes, however, the cage ligand is neutral and the effect must arise from the delocalised electronic structure of the amidine group (**10**). The



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lone pair of electrons on the *exo* amidine nitrogen is delocalised across the whole functional group,[14] consequently the ligating nitrogen atom acts as a better σ donor. The Co^{IV}–Co^{III} couple was not observed in these cage complexes. The major effects of incorporating the amide and amidine functional groups into the cage structure were to stabilise the cobalt(III) state in each case. These complexes were less easy to reduce to their cobalt(II) forms than analogous hexaamine complexes but the cobalt(IV) state was still not accessible under these more favourable conditions.

Experimental

NMR spectra were acquired on a Varian 300 MHz spectrometer and referenced externally using 1,4-dioxane (δ 3.70 $\{^1H\}$ and 67.4 $\{^{13}C\}$ *vs.* TMS), IR spectra with a Perkin-Elmer 1800 FTIR spectrometer using KBr disks, electronic spectra with a Hewlett Packard 8450A UV/Visible spectrophotometer in 1 cm quartz cells using water as solvent and electrospray mass spectra of aqueous solutions using a Fisons/VG Biotech Quatro II mass spectrometer at 80 V (the solvent stream was water). Cyclic voltammograms were recorded on a BAS 100 electrochemical analyser under nitrogen with an EPG working electrode, platinum wire auxiliary and saturated calomel reference electrodes at 25 °C; the scan rate was 20 mV s^{-1}. Ion exchange chromatography was performed with analytical grade Dowex 50 WX2 (200–400 mesh) and SP Sephadex C-25 cation exchange resins.

Synthesis

$[Co(sen)]Cl_3\cdot H_2O$[23] (10 g, 0.023 mol), aqueous methanal (36%, 20 mL), ethyl cyanoacetate (4 mL, 0.035 mol) and Na_2CO_3 (7.2 g, 0.07 mol) were stirred in water (40 mL) at 60 °C for two hours. The reaction was quenched with acetic acid, diluted to five litres with water and adsorbed onto a large column of Sephadex. The column was washed with water and eluted with 0.1 M K_2SO_4; the mixture separated into four bands (**F1**–**F4**) which were collected separately. The first band (**F1**) was chromatographed on Dowex. The column was washed well with

water then eluted with 2 M HCl to remove most of the salt. It was then eluted with 3 M HCl whereupon two orange bands (**F1a** and **F1b**) separated easily.

(1-Cyano-8-methyl-2-oxo-3,6,10,13,16,19-hexaazabicyclo-[6.6.6]icosanato)cobalt(III) dichloride–water(1/3) [Co(CN,Me-2-oxosar − H)]Cl_2·3H_2O. The first orange band (**F1a**) was taken to dryness by rotary evaporation to yield the crude chloride salt. The residue was dissolved in ethanol and the solvent removed by rotary evaporation (2.7 g, 23%). The acid-free product was recrystallised from water (Found: C, 37.5; H, 7.0; Cl, 13.4; N, 19.1. $C_{16}H_{36}Cl_2CoN_7O_4$ requires C, 36.9; H, 7.0; Cl, 13.6; N, 18.8%). $\delta_H(D_2O)$ 0.86 (CH_3) and 2.30–3.82 (complex methylene envelope). $\delta_C(D_2O)$ 20.8 (CH_3), 41.4 (C_qCH_3), 47.1, 50.5, 52.6, 53.3, 55.1, 55.3, 55.6 and 55.7 (CH_2), 58.0 (C_qC=O), 116.8 (C≡N) and 171.3 (C=O). λ_{max}/nm (H_2O) 342 (ε/dm^3 mol^{-1} cm^{-1} 216) 492 (233). $\tilde{\nu}_{max}$/cm^{-1} (C≡N stretch) 2250, (C=O stretch) 1621 and 1605. Low resolution ESMS {*m*/*z*, obs. (calc.), %, (cage) = [$^{12}C_{16}{}^{1}H_{30}{}^{14}N_7$-$^{59}Co^{16}O$]$^{3+}$}: 393.8 (394), 100 [Co(cage)$^{2+}$ − H^+]$^+$; 411.9 (412), 35 [Co(cage)$^{2+}$ − H^+ + H_2O]$^+$; and 429.8 (430), 20 [Co(cage)$^{2+}$ + $^{35}Cl^-$]$^+$.

(2-Amino-1-carboxy-8-methyl-3,6,10,13,16,19-hexaaza-bicyclo[6.6.6]icos-2-ene)cobalt(III) trichloride–ethanol–water (1/0.5/3.5), [Co(Me,CO_2H-2-aminosar-2-ene)]Cl_3·0.5C_2H_5OH·3.5H_2O. The solvent from the orange band (**F1b**) was removed by rotary evaporation and the residue dissolved in ethanol and taken to dryness once more (1.9 g, 14%). The crude product was recrystallised from water (Found: C, 33.3; H, 6.5; Cl, 17.2; N, 16.2. $C_{16}H_{33}Cl_3CoN_7O_2$·0.5C_2H_5OH·3.5H_2O requires C, 33.6; H, 6.6; Cl, 17.5; N, 16.2%). $\delta_H(D_2O)$ 0.86 (CH_3) and 2.30–3.72 (methylene envelope). $\delta_C(D_2O)$ 20.7 (CH_3), 42.0 (C_qCH_3), 49.2, 52.5, 53.6, 54.3, 54.7, 54.8 (2C), 55.0, 55.3, 55.9 and 56.3 (CH_2), 62.1 (C_qCO_2H), 169.4 (C=N) and 173.6 (CO_2H). $\delta_H(Me_2SO$-$d_6)$ 1.02 (CH_3), 2.40–4.10 (complex methylene envelope), 7.0–8.1 (overlapping amine NH) and 8.5 broad (amidine NH_2). λ_{max}/nm (water) 343 (ε/dm^3 mol^{-1} cm^{-1} 277) and 488 (339). $\tilde{\nu}_{max}$/cm^{-1} (carboxylic acid C=O stretch) 1723, (C=N stretch) 1671 and (NH_2 in-plane bending) 1599. Low resolution ESMS {*m*/*z*, obs. (calc.), %, Co(cage) = [$^{12}C_{16}{}^{1}H_{33}{}^{14}N_7{}^{59}Co^{16}O_2$]$^{3+}$}: 367.8 (368), 100 [Co(cage)$^{3+}$ − 2H^+ − CO_2]$^+$; and 411.8 (412), 20 [Co(cage)$^{3+}$ − 2H^+]$^+$.

The bands **F2**–**F4** obtained by chromatography on Sephadex were separately desalted on Dowex (procedure as described for **F1**). **F2** and **F3** were identified by ^{13}C NMR spectroscopy and microanalysis as [Co(azaMesar)]Cl_3 (0.29 g, 3%) and [Co(N-Me-sen)]Cl_3 (1.8 g, 18%) respectively.[16]

(2-Amino-8-methyl-3,6,10,13,16,19-hexaazabicyclo[6.6.6]-icos-2-ene)cobalt(III) trichloride–water(1/3), [Co(Me,2-aminosar-2-ene)]Cl_3·3H_2O. The solvent from band **F4** was removed by rotary evaporation and the crude product dissolved in ethanol and taken to dryness once more. The orange complex was recrystallised from water (1.2 g, 10%) (Found: C, 33.9; H, 7.4; Cl, 20.0; N, 18.4. $C_{15}H_{39}Cl_3CoN_7O_3$ requires C, 33.9; H, 7.4; Cl, 20.0; N, 18.5%). $\delta_H(D_2O)$ 0.87 (CH_3) and 2.30–3.55 (complex methylene envelope). $\delta_H(Me_2SO$-$d_6)$ 0.93 (CH_3), 2.30–3.75 (complex methylene envelope), 6.3–6.8 (overlapping amine NH signals), 8.35 and 8.58 (C–NH_2). $\delta_C(D_2O)$ 20.8 (CH_3), 42.5, 46.9, 47.8, 48.5, 50.1, 54.2, 54.7, 54.8, 55.2, 55.3, 55.6, 55.7 and 56.1 (C_qCH_3, CH_2 and CH) and 169.4 (C=N). λ_{max}/nm (water) 343 (ε/dm^3 mol^{-1} cm^{-1} 208) and 488 (228). $\tilde{\nu}_{max}$/cm^{-1} (C=N stretch) 1654 and (NH_2 in-plane bending) 1618. Low resolution ESMS {*m*/*z*, obs. (calc.), %, Co(cage) = [$^{12}C_{15}{}^{1}H_{33}{}^{14}N_7{}^{59}Co$]$^{3+}$}: 367.8 (368), 100 [Co(cage)$^{3+}$ − 2H^+]$^+$; 403.8 (404), 28 [Co(cage)$^{3+}$ − H^+ + $^{35}Cl^-$]$^+$; and 439.8 (440), 12 [Co(cage)$^{3+}$ − H^+ + $^{35}Cl^-$ + 2H_2O]$^+$.

Attempted demetallation of [Co(CN,Me-2-oxosar − H)]$^{2+}$. A deoxygenated aqueous solution of KCN (74.6 g in 150 mL) was added gradually to a deoxygenated solution of [Co(CN, Me-2-oxosar − H)]Cl_2·3H_2O (28.8 g) and $CoCl_2$·6H_2O (14.28 g) in water (100 mL). The mixture was stirred at 40 °C for one week under a nitrogen atmosphere and a pale yellow solution resulted. The remaining KCN was precipitated from the solution with ethanol (2 L) and removed by filtration. The filtrate was taken to dryness by rotary evaporation and this residue treated with ethanol to extract any organic material present. The organic product(s) of this reaction were isolated by rotary evaporation of solvent ethanol and studied by ^1H and ^{13}C NMR spectroscopy.

Crystal structure analysis of [Co(CN, Me-2-oxosar − H)]-[ClO_4]$_{3/2}$$Cl_{1/2}$·$H_2O$

[Co(CN,Me-2-oxosar − H)]Cl_2·3.5H_2O (0.1 g) was dissolved in the minimum of water and $NaClO_4$ added. The solution was allowed to evaporate slowly in air and orange crystals were formed. **CAUTION**: perchlorate salts are potentially explosive and should only be prepared in small quantities.

Crystal data. $C_{16}H_{32}Cl_2CoN_7O_8$, M = 580.31, monoclinic, space group $C2/c$ (no. 15), a 26.143(1), b 10.794(2), c 17.061(2) Å, β = 108.522(6)°, U = 4565.9(9) Å^3, T = −60 °C, Z = 8, μ(Cu-Kα) 85.88 cm^{-1}, λ(CuKα) 1.5478 Å, 3734 reflections measured (Rigaku AFC6R diffractometer), 3598 unique (R_{int} = 0.028) and 2284 > 3σ which were used in all calculations. The final R was 0.033.

CCDC reference number 186/2103.

See http://www.rsc.org/suppdata/dt/b0/b002531n/ for crystallographic files in .cif format.

Investigation of the reactions of [Co(Me-2-aminosar-2-ene)]$^{3+}$

The reactions of [Co(Me,2-aminosar-2-ene)]Cl_3·3H_2O were investigated in the following ways.

(a) The amidine cage complex (3.6 g) and LiCl (8 g) were dissolved in water (40 mL) and cooled to <5 °C. $NaNO_2$ (1.74 g) was dissolved in the solution which was left on ice for 30 min and conc. HCl (1.3 mL) was added gradually so the solution temperature did not rise above 5 °C. After 30 min more conc. HCl (5 mL) was added, producing an orange precipitate. The reaction mixture was dissolved in water and chromatographed on Dowex. The column was washed with water, eluted with 1 M HCl, and then with 3 M HCl to remove any cage complexes. The solvent was removed by rotary evaporation and the products identified by NMR spectroscopy.

(b) The amidine cage complex (1 g) was dissolved in conc. HNO_3 (50 mL) at 100 °C. After 1 h the solution was diluted with water (1 L) and chromatographed on Dowex. The reaction products were isolated and identified as described in (a).

(c) $NaBH_4$ (1 g) was added to a solution of the amidine cage (1 g) in carbonate buffer solution (50 ml, pH 10), stirred for 1 h then diluted with water and chromatographed on Dowex. The reaction products were isolated and identified as described in (a).

(d) 10% Pd/C (0.5 g) was added to a partial solution of amidine cage (1 g) in dry methanol (50 ml) and the mixture was treated in a hydrogenator for 1 week. During this time the vessel was evacuated and refilled with hydrogen five times. Charcoal was then filtered off, the filtrate added to water (500 mL) and the solution chromatographed on Sephadex. The column was washed with water and eluted with 0.05 M trisodium citrate. The cobalt(III) species isolated by this procedure were then individually chromatographed on Dowex and isolated and identified as described in (a).

(e) [Co(Me,2-amino-sar-2-ene]Cl_3 (0.5 g) and CH_3I (2 mL) were dissolved in dimethyl sulfoxide (10 mL) and triethylamine (1 mL) was added. The solution was stirred in a stoppered flask

for three days then added to diethyl ether (200 mL) and the resulting organic phase then extracted with water (100 mL). The extract was chromatographed on Dowex and cobalt(III) complex(es) isolated as described in (a).

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