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Sterechemistry of cage amine complexes –probing the ligand conformational flexibility with hydrogen bonds

Irene Ling, Alexandre N. Sobolev, Rauzah Hashim, and Jack M. Harrowfield

Structure determinations for some Co(III) complexes of simple derivatives of the cage hexamine 3,6,10,13,16,19-hexa-azabicyclo[6.6.6]icosane (“sarcophagine”) show that there is no evidence that the H-bonding involving the NH centres of the complex cations is influenced by electronic effects due to the substituents. “H-bond chelation” of chloride anions or water molecules results in retention of the symmetrical lel3 conformation.

In earlier investigations of inclusion of cationic Co(III) cage amine complexes by (Scheme 1) p-sulfonatocalix[4]arene, the ligand conformations were not the focus of the analysis of the crystal structures of the isolated inclusates. In fact, the structures described for the 1:1 and 1:2 (Co:calix[4]arene) inclusates of the complex of 1,8-dichlorosarcophagine (Cl2sar) (Scheme 1), and sulfonatocalix[4]arene are interesting in that the first contains the complexed ligand in the very familiar lel3 conformation, while the second contains inequivalent species with the ob-k3 and ob3 conformations. An obvious difference between the two structures is that in the 1:1 species the cation is only partially enveloped by the anionic calixarene, whereas in the 1:2 species it is effectively contained within a capsule formed by two facing calixarene units. Thus, in the former it is possible for three water molecules to approach the cation in a way which results in NH···O···HN bridging in a manner analogous to that observed in all other known structures of the lel3 Co(III) complexes. The conformation therefore appears to be determined by interactions other than those with the calixarene.

The difference in symmetry between the chiral D3 cation and the C2v sulfonated calixarene anion of course means that there is an inherent incompatibility in regard to maintaining either symmetry within their associate, which is in fact a chiral species of C3 symmetry. An ob,lel species, however, has C2 symmetry and in this sense might be considered better fitted for interactions with the calixarene. If this is so, then for the capsule containing this conformer in the 1:2 species the interactions involving H-bond donor NH units and sulfonate-O atoms (water being absent from the vicinity of the cation) are still quite limited, since only two contacts (N13B···O112 3.21(1) Å) lie below 3.50 Å and are indicated to be significant by CrystalExplorer. For the capsule involving the ob3 cation, there are no N···O contacts below 3.50 Å and cation···anion interactions appear to be of the CH···O type instead.

Introduction

Complexes of polycyclic, encapsulating (“cage”) ligands have frequently proven to have exceptional properties leading to their applications in various domains. Derivatives of the cage hexamine 3,6,10,13,16,19-hexa-azabicyclo[6.6.6]icosane, known as “sarcophagine”, are particularly effective complexants of heavy metal ions and applications of this property have been widely investigated, for example, in thernostatic use of the radioisotopes ⁶⁵Cu and ⁶⁸Ga. Since the complexes are chiral, their interactions with biological systems may be influenced by this factor and thus it is important to have a detailed understanding of their stereochemistry.

Structural investigations involving complexes of the cage hexamine sarcophagine and its derivatives are extensive and have involved a variety of metal ions but have provided only a few examples of species where the ligand conformation is not one of the extreme forms designated lel3 and ob3. This nomenclature derives from the consideration of the central C-C bonds of the ligand arms forming five-membered chelate rings as lying either parallel or oblique to the threefold rotation axis of the complex. At least in complexes where the ligand framework as in the parent sarcophagine is retained, these conformational preferences for lel3 or ob3 may reflect their control by H-bonding interactions involving the secondary, coordinated NH centres, interactions of an energy which considerably exceeds that estimated to be the difference between the conformers. The only recognised case of such a complex showing a “mixed” conformation (that is, either lel3ob or ob3lel) is that of lel3ob-[Ni(NH3)2sar]Cl2H2O, where the relatively low charge on the metal ion may have rendered the NH entities less effective as H-bond donors, although an unpublished study of the Co(III) cage complex [Co(NO3)2sar][Gd(dipic)3]·12H2O has shown the crystal lattice to contain some ob3lel species.

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that the structure of a simple salt of [Co(Cl₂sar)]⁺ is unknown and the possibility that the chloro substituent might induce different properties to those seen in the numerous cases where the substituent is an H-bond donor/acceptor species, characterisation of a simple species appeared desirable to better understand the cation properties. Some suitable crystals were in fact available as the unintended products of other efforts to obtain calixarene inclusions where the cation crystallised with anions present other than the sulfonated calixarene, and so were used in the present work. In addition to two structures involving [Co(Cl₂sar)]⁺, a similar structure of a simple salt involving [Co(NO₂)(HO)sar)]³⁻ (Scheme 1), a cation also characterized previously but in an extensively disordered form as an include,¹⁷ is given for comparison.

[Diagram of [Co(Cl₂sar)]⁺ and [Co(NO₂)(HO)sar)]³⁻ cations.]

Scheme 1. Structures of the [Co(Cl₂sar)]⁺ and [Co(NO₂)(HO)sar)]³⁻ cations.

Results and discussion

The X-ray structure determinations on single crystals of [CoCl₃sar]Cl·3.67H₂O, (complex 1), [Co(Cl₂sar)]Cl·Br·5H₂O (complex 2) and [Co(NO₂)(HO)sar)]Cl·2H₂O (complex 3), have shown that the cation in all three cases adopts the intrinsically favored lel₁ conformation. Relatively large trigonal twist angles for all three complexes were observed (ϕ = 54.3° to 56.4°), close to the ideal octahedral arrangement regardless of the variation of functional groups at the terminal trigonal cap. The Co-N bond lengths and angles are in the ranges found for Co(III) cage complexes (Table 1).

Complex 1

Complex 1 crystallizes in the triclinic space group, P ̅ 1, Z = 4, with the asymmetric unit comprising two lel₁ (but inequivalent) [CoCl₃sar]⁺ cations, six chloride anions and 3 2/3 water molecules. The cations, defined in detail in Table 1, can be considered to lie in sheets parallel to the ab plane, the closer pairs of sheets (separation of the mean Co planes 7.2 Å) sandwiching the partially occupied water molecule sites involving O(2), while the chloride ions and other water molecules (one of which, involving O(1) and O(1'), is disordered over two sites) lie partly within the sheets and partly between the more distant sheet units (Co mean plane separation 9.5 Å; Figure 1). In any given sheet, both inequivalent cations are present in a 1:1 ratio but all are of the same absolute configuration, opposite to that in the closer adjacent sheet, so that the sheet chirality alternates along the c direction.

Figure 1 A partial view, down b, of the lattice of I. Co(1) atoms are shown in green, Co(2) in light green, H atoms are omitted.

The partial occupancy and partial disorder of the oxygen atom sites prohibit the application of CrystalExplorer to analysis of the lattice interactions but atom–atom separations are consistent with H-bonding being pervasive. Thus, both the inequivalent but closely similar cations are involved in NH-bond chelation of three chloride ions each, as long known for complexes of this type (Figure 2).¹⁰ Each open octahedral edge of the cations is spanned by a nearly symmetrically bound chloride ion {Cl(1)–H(13B, 16A) 2.223(2), 2.325(3); Cl(2)–H(13C, 16B) 2.228(3), 2.162(3); Cl(3)–H(13A, 16C) 2.285(2), 2.203(2); Cl(4)–H(23B, 26A) 2.329(2), 2.207(2); Cl(5)–H(23C, 26B) 2.221(2), 2.326(3), and Cl(6)–H(23A, 26C) 2.244(2), 2.260(2) Å}. Within a given cation sheet, the inequivalent cations (containing Co1 and Co2) lie in parallel rows along a, each second pair of rows being linked through the infinite chain (along a) of water molecules involving ‘–O(1)(O(1'))–O(6)–O(5)–O(8)–O(3)–O(4)–O(7)–’ (mean OH–O 1.89(8) Å), specifically involving Cl(1)–H(1A), Cl(1)–H(8A), Cl(3)–H(3A), Cl(4)–H(4A), Cl(5)–H(5A) and Cl(5)–H(7A) contacts averaging 2.39(5) Å. Were the site of O(2) to be fully occupied, each cation containing Co(1) would form a centrosymmetric unit with its enantiomer in the closer cation sheet (Co(1)–Co(1') 9.307(2) Å) as a result of NH–Cl–HOH–Cl–HN links (Cl(2)–H(2A) 2.11, Cl(3)–H(2B) 2.20 Å) but seemingly this must only occur for two thirds of these cations.

Other contacts observed are possibly consistent with some contribution from CH–O and CH–Cl interactions, and perhaps even halogen bonding, to the lattice interactions but there is no real evidence to suggest that they would exceed dispersion force effects. While Coulombic forces may be largely responsible for the form of the lattices, they gain directionality through specific contacts such as H-bonding.²⁰
Table 1: Selected Bond Lengths and Angles

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<thead>
<tr>
<th></th>
<th>[Co(Cl$<em>{3}$sar)]$^{1+}$H$</em>{2}$O</th>
<th>[Co(Cl$<em>{3}$sar)]$^{1+}$Br$^{+}$H$</em>{2}$O</th>
<th>[Co(NO$<em>{2}$)(HO)sar]$^{1+}$H$</em>{2}$O</th>
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<td>&lt;Co–N&gt;</td>
<td>1.981(8) [1.974(8)-1.988(8)]</td>
<td>1.978(28) [1.971(29)-1.983(28)]</td>
<td>1.979(17) [1.975(17)-1.987(17)]</td>
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<td>N–(H)...Cl</td>
<td>2.162(3) - 2.329(2)</td>
<td>2.116(23) - 2.429(18)</td>
<td>2.226(5)-2.392(5)</td>
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<td>angles (deg)</td>
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<tr>
<td>&lt;N–Co–N&gt; (intracap)</td>
<td>86.39(3) [85.88(3)-86.99(3)]</td>
<td>86.70(14) [86.29(14)-86.91(14)]</td>
<td>86.51(7) [86.35(7)-86.73(7)]</td>
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<tr>
<td>&lt;N–Co–N&gt; (intercap)</td>
<td>90.58(3) [89.88(3)-91.07(3)]</td>
<td>90.49(13) [89.96(12)-91.10(15)]</td>
<td>90.54(7) [89.81(7)-91.51(7)]</td>
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<tr>
<td>&lt;N–C–C–N&gt;</td>
<td>55.24 (54.85-55.85)</td>
<td>55.97 (55.34-57.35)</td>
<td>55.03 (54.76-55.38)</td>
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<tr>
<td>&lt;twist angle&gt; (ϕ)</td>
<td>54.5, 56.4</td>
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Complex 2

Complex 2 crystallizes in the monoclinic space group $P2_1/c$, $Z = 2$, the crystal unit comprising two [Co(Cl$_3$sar)]$^{1+}$ components in their $lel_3$ conformation, accompanied by five chloride and one bromide anions and five water molecules. Viewed down $a$ (Figure 3) the lattice can be seen to contain homochiral sheets of cations lying parallel to the ac plane, with the chirality alternating from one plane to the next. Water molecules lie between these sheets, chloride ions both within and between, while bromide ions lie between every second pair of sheets. Fractional occupancies and partial disorder once again limit the application of CrystalExplorer to analysis of the lattice interactions but, for 1, H-atom contacts provide evidence for extensive H-bonding. Here, there is but one cation site and, interestingly, the chloride “deficiency” in terms of the ratio Co:Cl of 1:3 which would be required for each $lel_3$ cation to have its own separate sheath of H-bonded chloride ions is not compensated for by bromide, so that one chloride (Cl(2)) forms a bridge as a result of its chelation by pairs of NH units on separate cations. There is, as in 1, a threefold chelation of chloride by the NH units of the $lel$ rings (Figure 2; Cl(1)$^-$H(3A, 6C) 2.242(7), 2.235(9); Cl(2)$^-$H(3B, 6A) 2.31(1), 2.218(1), Cl(3)$^-$H(3C, 6B) 2.116(23), 2.429(18) and Cl(4)$^-$H(3C, 6B) 2.116(23), 2.278(1) Å) and the lattice water molecules do not compete for this role. The apparent coordination geometry of the bridging chloride is close to square planar, not tetrahedral, possibly indicating a dynamic situation involving equivalent forms of three-coordination, consistent with the extruded probability displacement ellipsoid on Cl(2). The cations linked by this bridge are enantiomeric. H-bonding of chloride to water (mean Cl$^-$HO 2.56(17) Å) and water to water (mean O=O 2.09(27) Å) results in a three-dimensional network linking all the cations together. The bromide ions are presumably involved in this network also but there are some anomalously short Br$^-$H and Br$^-$O contacts which indicate that there may be some unresolved disorder associated with these anions and their adjacent water molecules. As for 1, there are some relatively short CH$^-$O and CH$^-$Cl contacts, which may indicate that forces other than conventional H-bonding contribute to the lattice construction.

Figure 2 Equatorial chelation of a triad of chloride anions by the cobalt(III) sarcophagine cations in the complexes 1, 2 and 3. Each cation is arbitrarily shown in its $\Delta$ configuration and, for 1, only one (involving Co(1)) of the two very similar cations is shown while for 2, chloride disorder (Cl(3)/Cl(4)) is not shown.
Complex 3

Complex 3 crystallizes in the orthorhombic space group P2_12_1_2, Z = 4, with the asymmetric unit comprising one [Co(NO_2)(HO)osar]^3^- cation, three chloride anions and two water molecules. Despite its unsymmetrical substitution and the presence of one substituent capable of hydrogen-bond donation, the simplest situation of all arises in that there is but one cation site, all cations necessarily being of the same chirality under the given space group, and there is no disorder or partial site occupancy. Examination of the Hirshfeld surface of the complex obtained by using CrystalExplorer (Figure 4) confirms the occurrence once more of the strong H-bonding chelation of three chloride ions by the led_3 cation (Figure 2; Cl(1)^-H(3A, 6C) 2.338(5), 2.276(5); Cl(2)^-H(3B, 6A) 2.392(5), 2.226(5); Cl(3)^-H(3C, 6B) 2.267(5), 2.240(5) Å) but shows also that there are significant (beyond dispersion effects) CH^-O (mean 2.48(7) Å) and CH^-Cl interactions, only in part associated with the two polar substituents (Figure 5).

While the oxygen atoms of the hydroxyl and nitro substituents appear to act exclusively as CH bond acceptors, the water molecules of the lattice also act as conventional H-bond donors to chloride (Cl(2)^-H(2wA) 2.352(5) Å, H(2wB)^-Cl(1) 2.827(5) Å, Cl(1)^-H(1wA) 2.390(5) Å, H(1wB)^-Cl(2) 2.404(5) Å), providing a network which, in association with the NH^-Cl interactions, leads to a three-dimensional linking of all the cations (Figure 6). The detailed analysis of the lattice of 3 which is possible, coupled to the close general similarities of the three lattices presently discussed, indicates that while conventional H-bonding interactions may be the dominant lattice forces for all three, CH^-O interactions, in particular, are also of general significance.
Conclusions

Taken together, the present structures do not indicate that the different substituents, particularly Cl, here have a significant influence on the observed tendency of Co(III) sarcophagine complexes of 3+ overall charge to adopt a lel3 conformation when a small bridging hydrogen-bond acceptor species such as chloride or water is available. Since molecular mechanics calculations\textsuperscript{15,16} indicate that energy differences between all the possible conformers are very small, it is unsurprising that relatively strong and multiple hydrogen-bonds can lead to a single conformer being favoured but that different conformers may be observed nonetheless when the pattern of hydrogen bonds is altered by changes in the composition of the crystalline solid containing the cage cation.\textsuperscript{7}

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Experimental

Synthesis of complexes 1, 2 and 3

Simple chloride salts of [Co(Cl$_2$sar)]$^{3+}$ and [Co(NO$_2$(HO)sar)]$^{3+}$ were available from earlier work.\textsuperscript{5} Crystals of complex 1 were grown by slow evaporation of a hot aqueous solution of [Co(Cl$_2$sar)]Cl$_3$.

Slow evaporation of an equimolar combination of [Co(Cl$_2$sar)]$^{3+}$ or [Co(NO$_2$(HO)sar)]$^{3+}$, sulfonated calix[8]arene or calix[6]arene, and tetraphenylphosphonium bromide, in a mixture of water and THF (1:1, 2 mL) in the presence of a three-fold excess of gadolinium(III) chloride, afforded crystals of complexes 2 and 3 respectively, which were suitable for X-ray diffraction studies.

Crystallography

All data were measured using an Oxford Diffraction Xcalibur-S, Sapphire CCD diffractometer at T = 100(2) K with monochromatic Mo-Kα radiation ($\lambda = 0.71073$ Å). The images were interpreted and integrated with the program CrystAlisPRO, Oxford Diffraction Ltd. The data were corrected for Lorentz and polarization effects, with absorption corrections applied using multiple symmetry equivalent reflections. The structures were solved by direct methods and refined using full matrix least-squares on F$^2$ with the SHELX-97\textsuperscript{19} crystallographic package, and X-seed\textsuperscript{20} interfaces. Non-hydrogen non-disordered atoms were refined with anisotropic displacement parameters. The positions of hydrogen atoms were partly localized from difference Fourier synthesis, partly calculated and their atomic parameters constrained to the bonded atoms during the refinement with C$_{\text{Me}}$-H = 0.95 Å, C$_{\text{Me}}$-H = 0.98 Å, and 0.99 Å for CH$_2$ groups. CCDC deposition numbers are 1025431-1025433.

Crystal/refinement details for complex 1

C$_{14}$H$_{35}$Cl$_3$CoNs$_{3}$Cl$_3$(Cl)$_3$, 3.67(H$_2$O), C$_{14}$H$_{37}$Cl$_3$CoNs$_{3}$O$_3$Cl$_3$, M = 584.69, orange prism, 0.32 0.29 0.26 mm$^3$, triclinic, space group $P1$(No. 2), $\alpha = 9.4847(2)$, $\beta = 16.2433(3)$, $\gamma = 16.9687(3)$ Å, $\alpha = 97.456(1)$, $\beta = 101.802(2)$, $\gamma = 102.069(2)$, $V = 2464.05(8)$ Å$^3$, $Z = 4$, $D_c = 1.576$ g/cm$^3$, $\mu = 1.270$ mm$^{-1}$, $F_{\text{obs}} = 1219$, $2\theta_{\text{max}} = 74.8^\circ$, 93752 reflections collected, 24665 unique ($R_{\text{int}} = 0.0239$). Final Goof $= 1.004$, $|\Delta F_{\text{max}}| = 0.70(7)$ e Å$^{-3}$, $R_1 = 0.0286$, $wR_2 = 0.0727$, R indices based on 22189 reflections with I >2$\sigma$(I) (refinement on $F^2$), 541 parameters, 0 restraints.

Crystal/refinement details for complex 2

2(C$_{14}$H$_{35}$Cl$_3$CoNs$_{3}$Cl$_3$), 5Cl$^-$, Br$^-$, 5(H$_2$O), C$_{28}$H$_{70}$BrCl$_6$Co$_2$N$_{12}$O$_{5}$, M = 1171.78, yellow needle, 0.34 0.21 0.04 mm$^3$, monoclinic, space group $P2_1/c$ (No. 14), $a = 9.7649(4)$, $b = 27.6067(8)$, $c = 9.5645(4)$ Å, $\beta = 117.183(5)^\circ$, $V = 2293.59(15)$ Å$^3$, $Z = 2$, $D_c = 1.697$ g/cm$^3$, $\mu = 2.170$ mm$^{-1}$, $F_{\text{obs}} = 1208$, $2\theta_{\text{max}} = 61.5^\circ$, 40659 reflections collected, 6677 unique ($R_{\text{int}} = 0.0543$). Final Goof $= 1.019$, $|\Delta F_{\text{max}}| = 1.5(1)$ e Å$^{-3}$, $R_1 = 0.0453$, $wR_2 = 0.1532$, R indices based on 4501 reflections with I >2$\sigma$(I) (refinement on $F^2$), 272 parameters, 0 restraints.

Crystal/refinement details for complex 3

C$_{14}$H$_{35}$CoNS$_{3}$O$_3$Cl$_3$, 3Cl$^-$, 2(H$_2$O), C$_{14}$H$_{35}$Cl$_3$CoN$_{12}$S$_{4}$O$_{5}$, M = 546.77, orange prism, 0.37 0.23 0.11 mm$^3$, orthorhombic, space group $P2_12_12_1$ (No. 19), $a = 8.9691(1)$, $b = 15.3232(3)$, $c = 16.3516(2)$ Å, $V = 2247.30(5)$ Å$^3$, $Z = 4$, $D_c = 1.616$ g/cm$^3$, $\mu = 1.162$ mm$^{-1}$, $F_{\text{obs}} = 1144$, $2\theta_{\text{max}} = 64.6^\circ$, 48711 reflections collected, 7579 unique ($R_{\text{int}} = 0.0341$). Final Goof $= 1.005$, $|\Delta F_{\text{max}}| = 1.10(9)$ e Å$^{-3}$, $R_1 = 0.0326$, $wR_2 = 0.0872$, R indices based on 7323 reflections with I >2$\sigma$(I) (refinement on $F^2$), 272 parameters, 0 restraints. Absolute structure parameter = 0.077(10) (Flack, H. D. Acta Crystallogr. 1983, A39, 876-881).

Notes and references

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* Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

17. (a) I. Ling, Y. Alias, A. N. Sobolev, B. W. Skelton and C. L. Ratson *Dalton Trans.* 2011, **40**, 10337-10344; (b) A similar study involving [Co((HO)2sar)]3+ and where the cation is probably in its let, conformation is C. B. Smith, L. J. Barbour, M. Makha, C. L. Raston and A. N. Sobolev *Chem. Commun.* 2006, 950-952.