The Crystal Structure of the Stable Isomer Λ-*mer,cis-RR* of (1,4,7,11,14,17-Hexaazacycloeicosane)cobalt(III) Ion as the Bromide Trihydrate Salt

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Abstract

The complex $[Co(hace)]^{3+}$ with the macrocyclic hexamine ligand 1,4,7,11,14,17-hexaazacycloeicosane has been obtained (from equilibrium preparations) in only one of the six possible geometric forms. The present crystal structure of $[Co(hace)]Br_3 \cdot 3H_2O$ shows this to be the Λ-*mer,cis-RR* isomer (this enantiomer for the particular crystal selected) with chelate ring conformations δ, chair, λ, δ, chair, λ (in order around the macrocycle). This confirms the detailed structure as predicted by energy minimization. The crystals are orthorhombic, space group $P2_12_12_1$ with unit cell dimensions $a = 8.738(6)$, $b = 9.566(3)$, $c = 28.45(1)$ Å and $Z = 4$. The structure was refined by a full-matrix least-squares procedure to final $R = 0.059$ and $R_w = 0.059$ for 2046 reflections with $I \geqslant 2.5\sigma(I)$. The acentric space group implies that the enantiomers crystallize separately.

Introduction

The modes of coordination of macrocyclic ligands have been of interest recently [1–3], and this paper reports the crystal structure of the cobalt(III) complex formed by the macrocyclic hexamine 1,4,7,11,14,17-hexaazacycloeicosane (hace). This ligand coordinates to form five-membered (en) and six-membered (tn) rings in the order 5,6,5,5,6,5 around the macrocycle.

Syntheses of cyclic compounds with hetero atoms by the Richman–Atkins cyclization procedure yield co-products also. Richman and Atkins noted cyclic 2:2 condensation products, but these were implied as minor by-products which would be readily removable [4].

In our synthesis of the cyclic triamine 1,4,7-triazacyclodecane (tacd) for a study of its cobalt(III) complexes [5], we found two higher polyamine by-products: hace, resulting from 2:2 condensation and cyclization, and 1,16-diamino-3,7,10,13-tetraazahexadecane (dtah), a linear hexamine formed presumably by 2:2 condensation followed by elimination [6]. These by-products showed as weak signals in the ^{13}C NMR spectra of our crude tacd as the tritosyl or trihydrobromide derivatives, and they were not removed by recrystallization [6]. However, on synthesis of the cobalt(III) complexes using the crude tacd·3HBr, these by-products translated into significant proportions of the complexes $[Co(hace)]^{3+}$ (9% of the total Co(III) products isolated) and $[Co(dtah)]^{3+}$ (3%). These complexes were separated using SP-Sephadex chromatography, and isolated (enantiomers were not separated by this procedure). They were each characterized as single geometric species by ^{13}C NMR spectroscopy, and since several geometrically distinct isomers are possible for each complex, the coordination of each hexamine to cobalt(III) is evidently highly stereospecific [5].

The hexamines hace and dtah were subsequently found to be separable, as their mixture, from the tacd by differential elution from cation-exchange resin and the same single isomers of $[Co(hace)]^{3+}$ and $[Co(dtah)]^{3+}$ as those characterized above then resulted from a synthesis of the complexes under equilibrium conditions (charcoal) [6].

For $[Co(hace)]^{3+}$ the six geometric isomers or diastereoisomers which are possible are listed in Table I. The separated single isomer was indicated previously to be the Λ-*mer,cis-RR* (as racemate) from three sets of evidence: (1) the ^{13}C NMR spectrum showed the isomer to have C_2 symmetry; (2) the ^{13}C NMR and visible spectra each indicated a *cis* disposition of the six-membered (tn) rings [5]; (3) an energy minimization analysis of all six diastereoisomeric structures indicated that the above structure should be the most stable [7]*.

The energy minimization was abbreviated however because of the magnitude of the complete task: within each geometry some conformations for

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*The calculations gave the total strain energy of Λ-*mer,cis-RR* as 14 kJ mol^{-1} lower than the next stable isomer Λ-*mer,cis-RS*, accounting for the observed stereospecificity.

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TABLE I. Geometric Isomers and Diastereoisomers of $[Co(hace)]^{3+}$ and their Symmetries

Geometric isomer	Diastereoisomer[a]	Point group
facial		C_{2h}
Λ-*mer,trans*	δ-NH	C_2
	λ-NH	C_2
Λ-*mer,cis*	-*RR*[λ-NH][b, c]	C_2
	-*SS*[λ-NH][b]	C_2
	-*RS*[δ-NH][b]	C_1

[a] Only one optical isomer, corresponding to absolute configuration Λ of the topology, is listed for each diastereoisomer. [b] Specification of the chirality of the NH hydrogens coupling *mer* rings, as given in the parentheses, is unnecessary to define the isomer in the *mer,cis* geometry. [c] The stable isomer.

which Dreiding models indicated severe strains or interactions were eliminated, and for three of the six structures we imposed a C_2 symmetry constraint for the coordinate and energy calculations. The crystal structure analysis of the isolated thermodynamically stable $[Co(hace)]^{3+}$ isomer was necessary to confirm the minimization results.

Experimental

Preparation of Crystals

$[Co(hace)]^{3+}$ was obtained as the bromide salt by elution from a column of Biorex-70 weak-acid cation-exchange resin [5] with 0.1 M HBr. The effluent was evaporated almost to dryness, and the solid was then washed with ethanol which was removed. The product was dissolved in water and left to recrystallize slowly on ethanol vapour diffusion. The mother liquor was removed, and the crystals were washed with 90% ethanol, then with ethanol, and dried under vacuum.

Crystallography

Intensity data for 3007 reflections were measured at room-temperature on an Enraf-Nonius CAD4-F diffractometer with the use of MoK$\bar{\alpha}$ (graphite monochromator) radiation. No significant decomposition of the crystal occurred during the data collection. Corrections were applied for Lorentz and polarization effects and for absorption [8a] using an analytical procedure [9]. Of the reflections measured, 2346 were unique and 2046 satisfied the $I \geqslant 2.5\sigma(I)$ criterion of observability.

Crystal data

$C_{14}H_{40}Br_3CoN_6O_3$, $M_r = 639.2$, orthorhombic, space group $P2_12_12_1$ (D_2^4, No. 19), $a = 8.738(6)$, $b = 9.566(3)$, $c = 28.45(1)$ Å, $U = 2377.9$ Å^3, $D_m = 1.79$, $Z = 4$, $D_x = 1.786$ g cm^{-3}, $F(000) = 1276$, μ(Mo K$\bar{\alpha}$) = 56.71 cm^{-1}, $1 \leqslant \theta \leqslant 22.5°$.

TABLE II. Fractional Atomic Coordinates for Λ-*mer,cis*-*RR*-$[Co(hace)]Br_3 \cdot 3H_2O$

Atom	*x/a*	*y/b*	*z/c*
Co	−0.2538(1)	−0.0360(1)	0.6235(1)
Br(1)	0.2783(1)	0.0249(1)	0.7904(1)
Br(2)	0.7506(1)	0.6017(1)	0.4530(1)
Br(3)	0.7303(2)	0.0521(1)	0.3978(1)
N(1)	−0.1067(9)	0.0114(9)	0.5725(3)
N(2)	−0.3778(10)	−0.1208(9)	0.5728(3)
N(3)	−0.1674(9)	−0.2280(8)	0.6322(3)
N(4)	−0.1246(9)	0.0427(9)	0.6755(3)
N(5)	−0.4072(10)	−0.0774(9)	0.6723(3)
N(6)	−0.3694(9)	0.1423(9)	0.6152(3)
C(1)	−0.1604(11)	−0.0410(13)	0.5251(4)
C(2)	−0.3322(11)	−0.0625(12)	0.5275(4)
C(3)	−0.3656(14)	−0.2799(13)	0.5752(5)
C(4)	−0.2092(14)	−0.3147(11)	0.5911(4)
C(5)	−0.0004(12)	−0.2471(12)	0.6457(5)
C(6)	0.0433(14)	−0.1684(13)	0.6881(5)
C(7)	0.0350(12)	−0.0106(13)	0.6781(5)
C(8)	−0.2073(11)	0.0364(12)	0.7206(4)
C(9)	−0.3265(12)	−0.0764(12)	0.7199(4)
C(10)	−0.5380(11)	0.0210(14)	0.6690(4)
C(11)	−0.4761(13)	0.1648(12)	0.6565(5)
C(12)	−0.2859(12)	0.2773(11)	0.6049(5)
C(13)	−0.1890(11)	0.2641(11)	0.5625(4)
C(14)	−0.0549(13)	0.1626(11)	0.5680(5)
O(1)	0.0989(10)	0.3314(10)	0.1765(4)
O(2)	0.9068(10)	0.2956(9)	0.4541(3)
O(3)	0.5202(11)	0.1794(10)	0.3114(3)

The structure was solved by direct methods using the program MITHRIL [10] and refined by a full-matrix least-squares method [9]. Anisotropic thermal parameters were introduced for non-hydrogen atoms, and hydrogen atoms on C and N were included in the model at their calculated positions. A weighting scheme, $w = k/[\sigma^2(F) + g|F|^2]$, was introduced and the refinement continued until convergence; $R = 0.059$, $R_w = 0.059$, $k = 0.96$, and $g = 0.0087$. The absolute configuration of the compound was determined on the basis of differences in Friedel pairs included in the data set. The analysis of variance showed no special features and the maximum residual electron density peak in the final difference map was approximately 1.0 e Å^{-3} in the vicinity of Br(2). The scattering factors for Co(III) were from ref. 8b and those of the remaining atoms were as incorporated in SHELX-76 [9].

Results and Discussion

Fractional atomic coordinates are listed in Table II. The structure shows discrete molecules of $[Co(hace)]^{3+}$, and the close intermolecular contacts of *ca.* 2.03 Å between the hydrogen atoms on N(5) and N(6) and two of the water molecules indicate significant hydrogen-bonding in the crystal lattice.

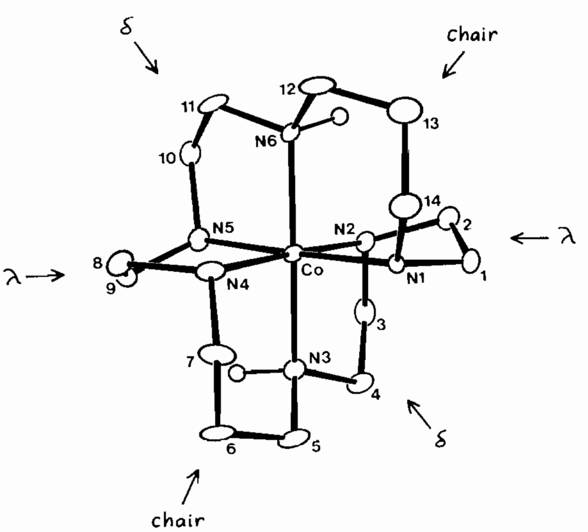

Fig. 1. The structure of the Λ-*mer,cis-RR*-[Co(hace)]$^{3+}$ ion showing the numbering scheme and the ring conformations. Atoms otherwise not indicated are carbons. The hydrogen atoms on the asymmetric donor nitrogens N3 and N6 coupling the *mer* rings are shown, but remaining hydrogen atoms are omitted for clarity.

The crystal selected for the X-ray analysis was solved in the acentric space group $P2_12_12_1$ with $Z = 4$, so that the molecular units in the crystal must be of one chirality, or must be non-dissymmetric. An ORTEP plot [11] of the complex cation with the atom-numbering scheme used is shown in Fig. 1, and selected bond distances and angles relating to the cation geometry are listed in Tables III and IV respectively. The octahedral environment of the six nitrogens of the macrocycle coordinated to the cobalt is distorted, this distortion from ideal geometry showing clearly in deviations of the angles subtended at the cobalt from 90° (or 180°), for example N(1)–Co–N(2) 85.1° and N(5)–Co–N(6) 84.9°. The molecule has a pseudo-C_2 axis, which passes through the cobalt atom and the centre points of N(1), N(4) and N(2), N(5), but this C_2 axis is not crystallographically imposed. The bond lengths and angles are arranged in Tables III and IV in their pseudo C_2-related pairs and there is generally good agreement in the values for the pairs (greatest differences are with N(2)–C(2), C(3)–C(4)–N(3) and C(5)–C(6)–C(7) and their pseudo-C_2 counterparts).

The structure analysis confirms the complex ion to be the diastereoisomer Λ-*mer,cis-RR*. The absolute configuration of the topology is Λ and the configurations about the asymmetric donor nitrogens N(3) and N(6) are both *R*. The space group $P2_12_12_1$ requires that the crystal contains only one enantiomer Λ-*RR* or Δ-*SS*, and this implies that the enantiomers crystallize separately. This is an instance of the less usual situation of 'spontaneous resolution by crystallization' [12, 13].

In the crystal the conformations of the chelate rings follow the sequence δ, chair, λ, δ, chair, λ around the macrocycle, where the labelling of the rings is commenced (arbitrarily) at the ring defined by N(2) and N(3). These conformations are related by the pseudo-C_2 axis, and are as predicted by the minimization calculations.

Tables III and IV include the structural parameters of the Λ-*mer,cis-RR* molecule resulting from the energy minimization calculation. There is good general agreement between the parameters for the crystal and those calculated for an isolated complex molecule, which is shown particularly in the parameters defining the cobalt atom environment. Such agreements add confidence for the usefulness of this energy minimization procedure for predicting detailed geometry and hence in calculating strain energies on relatively complicated molecules [3, 14–17].

Concurrent with our first work on [Co(hace)]$^{3+}$, Margulis and Zompa carried out the synthesis for

TABLE III. Comparison of Bond Distances (Å) Found in the Crystal with those Calculated by Energy Minimization

Crystal (pseudo-C_2 related)				Minimized^a	
Co–N(1)	1.991(9)	Co–N(4)	2.006(8)	Co–N(1)	1.986
Co–N(2)	1.979(8)	Co–N(5)	1.971(8)	Co–N(2)	1.968
Co–N(3)	2.001(8)	Co–N(6)	1.996(8)	Co–N(3)	1.989
N(1)–C(1)	1.512(14)	N(4)–C(8)	1.476(14)	N(1)–C(1)	1.504
N(1)–C(14)	1.520(13)	N(4)–C(7)	1.487(13)	N(1)–C(7′)	1.507
N(2)–C(2)	1.459(14)	N(5)–C(9)	1.526(14)	N(2)–C(2)	1.501
N(2)–C(3)	1.528(16)	N(5)–C(10)	1.483(14)	N(2)–C(3)	1.503
N(3)–C(4)	1.479(14)	N(6)–C(11)	1.515(14)	N(3)–C(4)	1.496
N(3)–C(5)	1.520(13)	N(6)–C(12)	1.513(14)	N(3)–C(5)	1.500
C(1)–C(2)	1.517(14)	C(8)–C(9)	1.500(15)	C(1)–C(2)	1.506
C(3)–C(4)	1.477(17)	C(10)–C(11)	1.520(17)	C(3)–C(4)	1.507
C(5)–C(6)	1.472(17)	C(12)–C(13)	1.478(16)	C(5)–C(6)	1.507
C(6)–C(7)	1.537(17)	C(13)–C(14)	1.530(15)	C(6)–C(7)	1.509

^{a}The primed atoms are related by the imposed C_2 axis.

TABLE IV. Comparison of Bond Angles (deg) Found in the Crystal with those Calculated by Energy Minimization

Crystal (pseudo-C_2 related)				Minimized[a]	
N(1)–Co–N(2)	85.1(4)	N(4)–Co–N(5)	86.5(4)	N(1)–Co–N(2)	87.6
N(1)–Co–N(3)	93.2(3)	N(4)–Co–N(6)	93.0(3)	N(1)–Co–N(3)	91.3
N(1)–Co–N(4)	95.1(4)	identical		N(1)–Co–N(1′)	94.9
N(1)–Co–N(6)	92.6(4)	N(4)–Co–N(3)	92.4(3)	N(1)–Co–N(3′)	94.4
N(2)–Co–N(3)	85.4(3)	N(5)–Co–N(6)	84.9(4)	N(2)–Co–N(3)	88.3
N(2)–Co–N(4)	177.8(4)	N(5)–Co–N(1)	177.1(4)	N(2)–Co–N(1′)	
N(2)–Co–N(5)	93.4(4)	identical		N(2)–Co–N(2′)	90.0
N(2)–Co–N(6)	89.2(4)	N(5)–Co–N(3)	89.2(3)	N(2)–Co–N(3′)	85.8
N(3)–Co–N(6)	171.7(3)	identical		N(3)–Co–N(3′)	
Co–N(1)–C(1)	112.0(6)	Co–N(4)–C(8)	110.5(6)	Co–N(1)–C(1)	109.9
Co–N(1)–C(14)	118.0(7)	Co–N(4)–C(7)	115.9(7)	Co–N(1)–C(7′)	114.7
C(1)–N(1)–C(14)	109.5(9)	C(8)–N(4)–C(7)	113.7(8)	C(1)–N(1)–C(7′)	110.6
Co–N(2)–C(2)	109.8(6)	Co–N(5)–C(9)	108.1(6)	Co–N(2)–C(2)	108.3
Co–N(2)–C(3)	109.7(7)	Co–N(5)–C(10)	110.6(7)	Co–N(2)–C(3)	107.3
C(2)–N(2)–C(3)	113.7(9)	C(9)–N(5)–C(10)	114.2(8)	C(2)–N(2)–C(3)	111.3
Co–N(3)–C(5)	120.2(7)	Co–N(6)–C(12)	120.5(6)	Co–N(3)–C(5)	119.7
Co–N(3)–C(4)	108.9(6)	Co–N(6)–C(11)	109.9(7)	Co–N(3)–C(4)	107.7
C(4)–N(3)–C(5)	111.7(9)	C(11)–N(6)–C(12)	109.0(8)	C(4)–N(3)–C(5)	111.6
N(1)–C(1)–C(2)	108.2(9)	N(4)–C(8)–C(9)	111.0(8)	N(1)–C(1)–C(2)	111.4
C(1)–C(2)–N(2)	111.2(9)	C(8)–C(9)–N(5)	109.7(8)	C(1)–C(2)–N(2)	111.0
N(2)–C(3)–C(4)	107.6(10)	N(5)–C(10)–C(11)	108.4(8)	N(2)–C(3)–C(4)	111.2
C(3)–C(4)–N(3)	110.1(9)	C(10)–C(11)–N(6)	105.7(9)	C(3)–C(4)–N(3)	108.6
N(3)–C(5)–C(6)	113.2(10)	N(6)–C(12)–C(13)	111.2(9)	N(3)–C(5)–C(6)	112.1
C(5)–C(6)–C(7)	109.8(11)	C(12)–C(13)–C(14)	114.2(10)	C(5)–C(6)–C(7)	113.2
C(6)–C(7)–N(4)	112.9(10)	C(13)–C(14)–N(1)	112.6(8)	C(6)–C(7)–N(1′)	115.0

[a] The primed atoms are related by the imposed C_2 axis.

tacd and subsequently prepared the nickel(II) complex from the ligand product. A crystal structure analysis then showed that this product was Λ-*mer*,*cis*-*RR*-[Ni(hace)]$(ClO_4)_2 \cdot (Me_2NCHO)$ (as racemate) rather than one of the anticipated isomers of [Ni(tacd)$_2$]$(ClO_4)_2$ [2]. This result substantiates our findings that higher condensation products such as hace are significant from Richman–Atkins cyclizations. The diastereoisomer formed and the ring conformations were identical to those now found for the [Co(hace)]$^{3+}$ ion, but for the labile [Ni(hace)]$^{2+}$ complex the isomer which crystallized could have been determined by solubility factors rather than thermodynamic stability. In contrast to the cobalt complex, the [Ni(hace)]$(ClO_4)_2 \cdot (Me_2NCHO)$ is reported to form racemic crystals in which the cations lie on crystallographic C_2 axes.

Supplementary Material

Anisotropic thermal parameters, hydrogen-atom parameters, and structure factor tables have been deposited with the Editor-in-Chief.

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