COORDINATION CHEMISTRY OF *N*-(2-HYDROXYBENZYL)-(*S*)-AMINO ACIDS. ABSOLUTE CONFIGURATION OF Λ-*mer-R,R*-[Co(ohb-(*S*)-Ala)$_2$]$^-$ ANION

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Dedicated to Dr Jaromir Plesek on the occasion of his 70th birthday.

The crystal and molecular structure of the Ag[Co(ohb-(*S*)-Ala)$_2$] . 5 H$_2$O have been determined by X-ray diffraction method. The crystals are hexagonal with $a = b = 9.039(0.002)$ Å, $c = 24.896(0.006)$ Å, space group $P3_221$, and $Z = 3$. Each Ag$^+$ counterion coordinated by one water molecule which is a part of hydrogen bond network, is bonded to aromatic rings. The anion adopts Λ-*mer* absolute configuration. *Mer* geometry is in accord with the molecular mechanics calculations. Since CD spectroscopy does not reflect configurational chirality, the absolute configuration has been determined by the X-ray structure analysis and assigned using chirality descriptors. The arrangements at the chiral centers are *R* for both N atoms. The two five-membered rings each assume envelope conformation with C1 and C2 atoms exceptionally deviated (0.378(7) and 1.210(7) Å) from the N–Co–O plane. Both six-membered rings have δ twist boat conformations. The complex described has been also characterized by the electronic and ^{13}C NMR spectroscopies.
Key words: *N*-Terminal tyrosine-like metal complex; *N*-(2-Hydroxybenzyl)-(*S*)-alaninato(2–) ligand; Λ-*mer-R,R*-(λ,λ-δ,δ)-Ag[Co(ohb-(*S*)-Ala)$_2$] absolute configuration.

Metal complexes of the [Co(ohb-(*S*)-aa)$_2$]$^-$ type (ohb-aa means *N*-(2-hydroxybenzyl)-amino acid anion) serve as simple models for the assessment of ligand proximity effects on the metal coordination phenolate site[1] which are evolved in metal–protein coordination (*cf.* transferrin[2]). Ligand flexibility provided by the –CH$_2$–NH– linkage in the 2-hydroxybenzyl ligand moiety, its unsymmetrical nature and interplay between various stereogenic centers allow ohb-aa ligands to coordinate in [Co(ohb-(*S*)-aa)$_2$]$^-$ anion in fifteen

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stereoisomeric forms. However, so far only *fac-all-trans* isomers (aa is glycine, (*S*)-α-alanine, α-aminoisobutyric acid, (*S*)-valine and (*S*)-leucine) have been prepared and characterized[1,3]. Their circular dichroism spectra bear the same pattern as those of Λ- and Δ-*mer* isomers[4] and do not reflect metal atom chirality. Since the stereochemistry of these complexes cannot be deduced from their chiroptical properties, we report here absolute configuration of Λ-*mer-R,R*-[Co(ohb-(*S*)-Ala)$_2$]$^-$ isomer (Ala means α-alanine) determined by single-crystal X-ray diffraction.

EXPERIMENTAL

[Co(ohb-(*S*)-Ala)$_2$]$^-$ anion was prepared by the procedure described previously[1] starting from [Co(NH$_3$)$_6$](NO$_3$)$_3$ and ohb-(*S*)-Ala (reaction time 60 min) and isolated by the addition of AgNO$_3$ to the diluted reaction mixture from which Ag[Co(ohb-(*S*)-Ala)$_2$] . 5 H$_2$O salt deposited in the crystalline form, suitable for X-ray diffraction. For C$_{20}$H$_{32}$N$_2$O$_{11}$AgCo (643.2) calculated: 37.34% C, 5.02% H, 4.36% N; found: 37.54% C, 4.98% H, 4.43% N.

The absorption spectrum was measured on a Specord M 40 spectrophotometer using spectral grade DMSO. The ^{13}C NMR spectrum was recorded with a Bruker AM-400 instrument in (CD$_3$)$_2$SO with DMSO as internal standard. The NMR measurement was carried out on the same sample that was analyzed structurally. Circular dichroism spectrum was obtained using a Jobin Mark V Dichrograph and spectral grade DMSO.

Crystal Structure Determination

The structure of Ag[Co(ohb-(*S*)-Ala)$_2$] . 5 H$_2$O was solved by direct methods and refined by full-matrix least-squares. Hydrogen atoms were found from difference synthesis and from expected geometry and were not refined. Absorption was neglected. The silver atom showed a disorder between two positions with the same occupation factors of 0.25. Crystallographic data and structure refinement parameters are summarized in Table I.

RESULTS AND DISCUSSION

N-(2-Hydroxybenzyl)-(*S*)-aa anion (aa is amino acid) acts as a tridentate ligand coordinating cobalt(III) center *via* phenolate, carboxylate oxygens and secondary nitrogen atom, the chirality of the latter being fixed by coordination in either *R* or *S* configuration. Unsymmetrical nature of this ligand and secondary nitrogen atom chirality give rise to nine facial isomers (four of them are chiral at the cobalt atom) and six meridional isomers (all display chirality at the cobalt center). As follows from the electronic absorption ($\lambda_{max} = 714$ nm, $\varepsilon = 220$ l mol^{-1} cm^{-1}; 525 sh; $\lambda_{max} = 372$ nm, $\varepsilon = 3\,986$ l mol^{-1} cm^{-1}, characteristic splitting of the band under the T_{lg} manifold), ^{13}C NMR spectrum which show double the number of lines than expected (Table II) and X-ray structure determination (*vide infra*), the Ag[Co(ohb-(*S*)-Ala)$_2$] . 5 H$_2$O isolated is Λ-*mer-R,R*-isomer. Preliminary molecular mechanics calculations[5] for the [Co(ohb)-(*S*)-Ala)$_2$]$^-$ anion *in vacuo* show that the formation of meridional isomers is slightly favored over the facial ones and that the potential energy depends both on the secondary nitrogen and cobalt

atom chiralities. For the Λ-*mer* absolute configuration, the order of potential energy is as follows: *R,S* = *S,S* < *R,R*. It should be noted, however, that Λ-*mer-R,R* isomer differs from the other two isomers by having the lowest valence bond deformation and torsion strain energy components.

As follows from the existence of the *fac-all-trans-R,S*-[Co(ohb-(*S*)-Leu)$_2$]$^-$ isomer[3] (Leu is leucine) with sterically bulky nonpolar side chains, specific formation of *mer* isomers (including *mer*-[Co(ohb-aa)$_2$]$^{3-}$ anions[4], where aa is aminodicarboxylic acid anion) cannot be a result of a strain in facially coordinated ligands imposed by steric crowding. According to our opinion this specificity arises from the stereochemical la-

TABLE I
Crystallographic data and structure refinement parameters

Space group	*P3$_2$21*
a, *b*, *c*, Å	9.039(0.002), 9.039(0.002), 24.896(0.006)
Z	3
Crystal size, mm	0.21 × 0.35 × 0.30
Diffractometer and radiation used	Enraf–Nonius CAD4
Scan technique	ω/2θ
Absorption coefficient μ, mm^{-1}	1.60
No. and θ range for lattice parameter refinement	20; 22.97–23.75°
Range of *h*, *k*, *l*	–4→1, 0→12, 0→34
Standard reflections monitored in interval; intesity fluctuation	120 min; –12.5%
θ range, °	2.45–29.95
Value of R_{int}	0.034
No. of unique observed reflections	1 560
Criterion for observed reflections	$I \geq 1.96\sigma(I)$
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0773P)^2 + 2.3971P]$, where $P = (F_o^2 + 2F_c^2)/3$
Parameters refined	171
Values of *R*, *wR*(*F^2*), *S*	0.053, 0.129, 1.058
Flack *x* parameter	–0.02(5)
Ratio of max. least-squares shift to e.s.d. in the last cycle	<0.001
Largest diff. peak and hole, e Å^{-3}	0.28, –0.49
Source of atomic scattering factors	SHELXL93 (ref.[6])
Programs used	SHELXL93 (ref.[6]), SDP (ref.[7]), SHELXS86 (ref.[8]), PARST (ref.[9])

bility produced by the low-ligand field effect of phenolate oxygens, so that [Co(ohb-(S)-aa)$_2$]$^{n-}$ complexes can be considered as spin-bare. From the simple LFSE calculations it follows that energetic accessiblity of cobalt(III) high-spin state approximately corresponds to 57 kJ mol^{-1}. Since LFSE (based on LFSE of [Co(H$_2$O)$_6$]$^{3+}$ and [Co(NH$_3$)$_6$]$^{3+}$) would correspond to Co(III) high-spin ligand exchange activation energy, *fac-all-trans-R,S* (initial product in the isomers synthesis) to Δ-*mer-R,S* and Λ-*mer-S,R* isomerization may occur through high-spin intermediates. Λ-*mer-R,R* structure of the complex described here (*vide infra*) suggests that *fac-all-trans-R,S* isomer initially formed isomerizes with stereochange at the ligand nitrogen atom (note that the synthesis proceeded in alkaline solution which facilitates mutarotation or inversion at an asymmetric nitrogen center).

The structure of [Co(ohb-(S)-Ala)$_2$]$^-$ anion is shown together with the atom numbering scheme in Fig. 1. The *mer*-Ag[Co(ohb-(S)-Ala)$_2$] isomer was isolated from the reaction mixture as pentahydrate and water of hydration provides crystalline stability by forming hydrogen bonds. Hydrogen bonds parameters are given in Table III. View of the unit cell content is presented in Fig. 2. It can be seen from Fig. 2 and Table III

TABLE II
^{13}C NMR spectrum (δ, ppm) of Λ-*mer-R,R*-Ag[Co(ohb-(S)-Ala)$_2$] . 5 H$_2$O

α-C	β-C	CH$_2$N	C$_{ipso}$-CH$_2$	C$_{ipso}$-O$^-$	COO$^-$
59.6	15.1	49.3	125.2	165.1	180.6
60.4	15.9	50.9	125.6	166.3	–
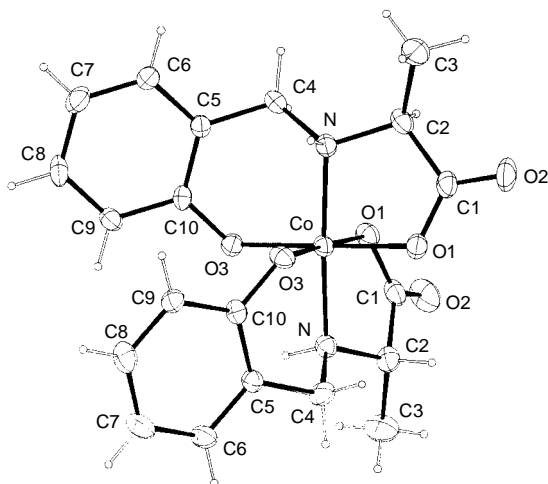
FIG. 1
Crystal structure of Λ-*mer-R,R*-Ag[Co(ohb-(S)-Ala)$_2$] . 5 H$_2$O showing atomic numbering

that interactions occur between the carbonyl oxygen O2, phenolate oxygen O3 and water molecules. Additional hydrogen bonds are found between NH and O3. The anions are linked by silver counterions. Finally, it is interesting to note that each silver ion coordinating one molecule of water is in an intermolecular π contact with carbon atoms of aromatic rings. These interactions contribute together with the aforementioned hy-

TABLE III

Hydrogen bonding distances (Å) and angles (°) for Λ-*mer*-*R*,*R*-Ag[Co(ohb-(*S*)-Ala)$_2$] . 5 H$_2$O

Hydrogen bonds	Donor…Acceptor	H…Acceptor	Donor–H…Acceptor
OW1–H1W1…O3	2.789(11)	1.878(6)	136.4(5)
OW2–H1W2…OW3	2.40(2)	1.82(2)	125.6(5)
OW3–H2W3…OW2	2.40(2)	1.72(2)	159.3(15)
OW2–H1W2…O2[i]	3.051(6)	2.392(5)	137.2(1)
OW3–H1W3…OW1[i]	3.03(3)	2.57(1)	103.6(9)
N–H1N…O3[ii]	2.615(8)	2.304(9)	99.6(5)
OW1–H2W1…O1	3.429(11)	2.680(6)	141.2(5)
OW1–H2W1…OW3[iii]	3.03(2)	2.55(1)	114.4(6)

For atom-labelling scheme, see Fig. 1. Symmetry code: (i) –x + 1, –x + y, –z + 5/3; (ii) y, x, –z + 2; (iii) –x + 1, –x + y + 1, –z + 5/3.
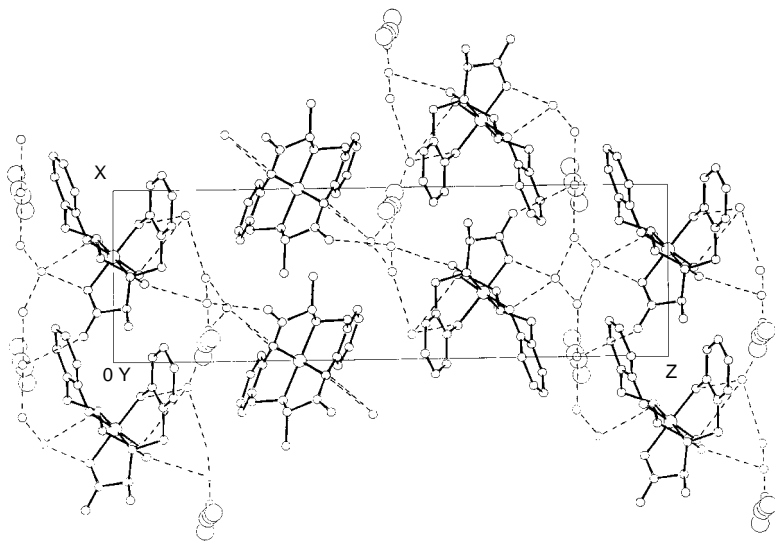

FIG. 2

View of the unit cell of Λ-*mer*-*R*,*R*-Ag[Co(ohb-(*S*)-Ala)$_2$] . 5 H$_2$O

drogen bonds to the stabilization of crystal structure. Intermolecular distances between non-hydrogen atoms shorter than 3.5 Å involving Ag–C interactions are listed in Table IV.

Bond lengths and angles are given in Table V. Comparison of bond lengths associated with the Co(III) coordination sphere reveals that there are no substantial differences in Co–O (carboxylate) and Co–O(phenolate) distances. This is in a marked contrast with the structural data obtained for the *fac-all-trans-R,S*-[Co(ohb-(S)-Leu)$_2$]$^-$ anion where Co–donor atom distances show some asymmetry[3].

The angles subtended by the five- (84.0(2)°) and six-membered (95.7(2)°) chelate rings deviate substantially from the regular octahedron. The angle at the secondary nitrogen atom, C4–N–C2, 115.2(5)° is more opened than that of a strain free tetrahedron. This significant bending can be interpreted either as due to the meridional coordination of ligands or as due to the presence of a "planar" carbon atoms which are parts of both chelate rings. Furthermore, the bond angles at nitrogen within the six-membered rings are larger (113.6(4)°) than the angles within the five-membered rings (108.2(4) °). Further distortion is found at N–C2–C3 angles (113.3(6)°) which may help to reduce NH…CH$_3$ nonbonded interactions. Consistent with this alleviation of strain is the H–N–C2–C3 dihedral angle –44.9(10)°. Comparison of C4–C5–C10–O3 1.6(10)° and O1–C1–C2–N 23.6(9)° dihedral angles, similarly to bond angles, reveals that six-membered rings are more strained than five-membered. Meridional geometry places six-membered rings to the *cis* position.

The five-membered chelate rings adopt the gauche conformation with λ envelope configuration. Both six-membered rings assume twist boat δ conformation. The degree

TABLE IV
Important intermolecular contacts (up to 3.5 Å) between non-hydrogen atoms in Λ-*mer-R,R*-Ag[Co(ohb-(S)-Ala)$_2$] . 5 H$_2$O

Atoms	Distance, Å	Atoms	Distance, Å
Ag…C7[i]	3.19(3)	Ag′…C7[i]	3.39(1)
Ag…C7[ii]	3.12(2)	Ag′…C7[ii]	2.72(1)
Ag…C8[i]	2.55(2)	Ag′…C8[i]	2.82(1)
Ag…C8[ii]	2.52(1)	Ag′…C8[ii]	2.31(1)
Ag…C9[i]	2.49(1)	Ag′…C9[i]	2.44(1)
Ag…C9[ii]	2.63(1)	Ag′…C9[ii]	2.81(1)
Ag…C10[i]	3.09(1)	Ag′…C10[i]	2.73(1)
Ag…C10[ii]	3.29(2)	Ag′…C10[ii]	3.54(1)
		Ag′…C5[i]	3.30(1)
		Ag′…C6[ii]	3.47(1)

Symmetry code: (i) *x*, *y* – 1, *z*; (ii) –*x* + 2, –*x* + *y*, –*z* + 5/3.

TABLE V

Bond distances (Å) and angles (°) for Λ-*mer-R,R*-Ag[Co)ohb-(*S*)-Ala)$_2$] . 5 H$_2$O

Atoms	Distances	Atoms	Distances
Ag–OW2	2.05(2)	OW2–Ag^{iii}	2.05(2)
Co–N^i	1.932(5)	Co–N	1.932(5)
Co–O1	1.910(5)	Co–O1^i	1.910(4)
Co–O3	1.890(5)	Co–O3^i	1.890(5)
N–C2	1.469(9)	N–C4	1.490(8)
O–C1	1.291(9)	O2–C1	1.223(8)
O3–C10	1.349(8)	C1–C2^i	1.547(10)
C2–C1^i	1.547(10)	C2–C3	1.524(10)
C4–C5	1.487(9)	C5–C10	1.400(9)
C5–C6	1.390(8)	C6–C7	1.386(8)
C7–C8	1.383(9)	C8–C9	1.388(10)
C9–C10	1.385(9)		

Atoms	Angles	Atoms	Angles
O3^i–Co–O3	92.4(3)	O3^i–Co–O1	178.6(2)
O3–Co–O1	88.9(2)	O3^i–Co–O1^i	88.9(2)
O3–Co–O1^i	178.6(2)	O1–Co–O1^i	89.8(3)
O3^i–Co–N^i	95.7(2)	O3–Co–N^i	86.4(2)
O1–Co–N^i	84.0(3)	O1^i–Co–N^i	93.8(2)
O3^i–Co–N	86.4(2)	O3–Co–N	95.7(2)
O1–Co–N	93.8(2)	O1^i–Co–N	84.0(2)
N^i–Co–N	176.9(4)	C1–O1–Co	115.3(4)
C10–O3–Co	119.3(4)	C2–N–C4	115.4(5)
C2–N–Co	108.2(4)	C4–N–Co	113.6(4)
O2–C1–O1	124.2(7)	O2–C1–C2^i	121.3(7)
O1–C1–C2^i	114.5(6)	N–C2–C3	113.3(6)
N–C2–C1^i	106.7(6)	C3–C2–C1^i	112.1(6)
C5–C4–N	109.4(5)	C6–C5–C10	119.9(6)
C6–C5–C4	121.1(6)	C10–C5–C4	119.0(6)
C7–C6–C5	120.6(4)	C8–C7–C6	119.4(4)
C7–C8–C9	120.4(7)	C10–C9–C8	120.7(6)
O3–C10–C9	120.0(6)	O3–C10–C5	121.0(6)
C9–C10–C5	119.0(6)		

Symmetry code: (i) *y, x, –z* + 2; (ii) –*x* + 2, –*x* + *y* + 1, –*z* + 5/3.

of puckering in the chelate rings is evidenced by the deviations of carbon atoms from the N–Co–O plane. Degree of these deviations, especially as far as five-membered rings are concerned, is exceptional: C1 0.378(7) Å and C2 1.210(7) Å. This puckering is in response to the small ring angle at cobalt atom 84.0(2)°. The deviations of the C4, C5 and C10 carbon atoms from the plane formed by the N, Co and O3 atoms are –0.465(8), 0.445(7) and 0.618(7) Å. The chelate ring conformation coincidence described here is in contrast with the λ, δ conformations assumed by the chelate rings in the *fac-all-trans*-[Co(ohb-(*S*)-Leu)₂]⁻ isomer where nitrogen atoms adopt *R* and *S* absolute configuration.

The CD spectrum pattern (λ_{max} = 685 nm, $\Delta\varepsilon$ = –12.0; λ_{max} = 506 nm, $\Delta\varepsilon$ = –7.0; λ_{max} = 370 nm, $\Delta\varepsilon$ = +18.0) of the Λ-*mer-R,R* isomer bears common features with that of *fac-all-trans*-Na[Co(ohb-(*S*)-Ala)₂] (*cf.* ref.[1]) confirming that the CD spectra of this type complexes do not reflect different spatial distribution of chelate rings about cobalt(III) center and cannot be used for the absolute configuration assignment from the Cotton effect sign. Hence, the assignment of the absolute configuration was achieved by combination of the X-ray diffraction structural analysis and application of chirality descriptors using the oriented-lines chiral reference system[10]. Based on the application of these methods, the Λ-*mer-R,R*-(λ,λ-δ,δ) configuration was ascribed to the isomer obtained. Furthermore, it is necessary to note that some minor differences in the CD spectra pattern can be observed. These involve enhanced intensity of the band located at 690 nm and apparent splitting of a positive CD peak at 395 nm. The enhanced intensity, which is typical for this type of cobalt(III) complexes containing rigid five-membered and angle expanding six-membered chelate rings, results from reinforcement of individual contributions from chiral C, N atoms, conformation of chelate rings and donor atom deviations from ideal planes. It is likely that the last factor is the major contribution. Theories of optical activity[11] of six-coordinated metal complexes predict significant rotatory strength as a result of ligating atoms displacement from octahedral geometry. Although conformations of chelate rings formed by the *N*-(2-hydroxybenzyl)-(*S*)-amino acid ligands would be, as expected, relatively rigid, the dihedral angles, which are the second way of ring degree puckering evidence, show substantial displacement of atoms supporting the conformational effect importance: N–C4–C5–C10 –58.3(9)°, N–C2–C1–O1 23.6(9)°. Consistent with these angles are dihedral angles involving the nitrogen atom surrounding, O3–Co–N–C2 –149.5(5)° and O1–Co–N–C4 158.7(5)°, which further document anticlinal conformation of meridionally coordinated ligands.

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