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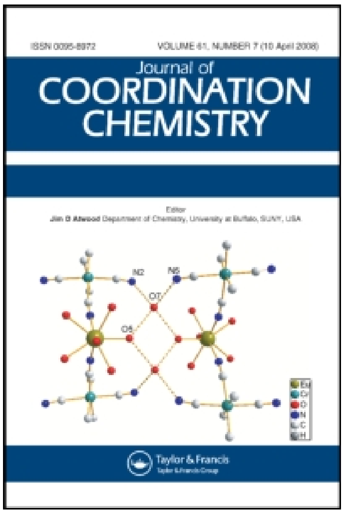

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

Synthesis and Absolute Configuration of Novel Mono- and Dinuclear Cobalt(III) Complexes Containing *S*-Phenylalanine

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Online publication date: 15 September 2010

To cite this Article Miodragović, DJ.U. , Malinar, M. J. , Milosavljević, S. M. , Zarić, S. D. , Vučelić, D. and Ćelap, M. B.(2002) 'Synthesis and Absolute Configuration of Novel Mono- and Dinuclear Cobalt(III) Complexes Containing *S*-Phenylalanine', Journal of Coordination Chemistry, 55: 5, 517 — 526

To link to this Article: DOI: 10.1080/00958970290020829

URL: http://dx.doi.org/10.1080/00958970290020829

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J. Coord. Chem., 2002, Vol. 55(5), pp. 517–526

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SYNTHESIS AND ABSOLUTE CONFIGURATION OF NOVEL MONO- AND DINUCLEAR COBALT(III) COMPLEXES CONTAINING *S*-PHENYLALANINE

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(Received 5 February 2001)

Two diastereomers of *bis*(1,3-diaminopropane)(*S*-phenylalaninato)cobalt(III) were prepared by reaction of *S*-phenylalanine with carbonato*bis*(1,3-diaminopropane)cobalt(III). The diastereomers were separated on an optically active Sephadex QAE column and their absolute configurations assigned by means of circular dichroism. In addition, ^{1}H NMR spectra of the diastereomers were analyzed in terms of the population of the three predominant rotamers of the coordinated *S*-phenylalaninato ligand. One out of 24 theoretically possible diastereomers of the dinuclear species di-μ-hydroxo-*tetrakis*(*S*-phenylalaninato)dicobalt(III) was obtained by direct synthesis and its absolute configuration deduced from CD spectra.

Keywords: Absolute configuration; Circular dichroism; Cobalt(III) complexes; ^{1}H NMR; *S*-phenylalanine; Synthesis

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INTRODUCTION

In the course of our investigation of cobalt(III) complexes with aromatic amino acids four out of six theoretically possible diastereomers of (1,3-diaminopropane)*bis*(*S*-tyrosinato)cobalt(III) [1] and one out of 24 theoretically possible diastereomers of di-μ-hydroxo-*tetrakis*(*S*-tyrosinato)-

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ISSN 0095-8972 © 2002 Taylor & Francis Ltd
DOI: 10.1080/00958970290020829

dicobalt(III) [2] were prepared. Continuing this investigation, we assumed that some of the diastereomers of the two types of complexes which we were not able to prepare could be synthesized if *S*-phenylalanine would be used in the synthesis instead of the formerly used *S*-tyrosine. The reason for this is that the two related ligands differ in their bulk and inductive effects, because, unlike *S*-phenylalanine, *S*-tyrosine contains an influential hydroxyl group.

EXPERIMENTAL

Reagents

All chemicals used in this paper were of reagent grade.

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Preparation of the Complexes of the *bis*(1,3-Diaminopropane)-(aminocarboxylato)cobalt(III) Type with *S*-phenylalaninato and *S*-alaninato Ligands

Synthesis of the diastereomers of *bis*(1,3-diaminopropane)(*S*-phenylalaninato)cobalt(III) was carried out in the same way as the *Bis*(*S*-tyrosinato) cobalt(III) complex [1]. The only difference was that, instead of lithium hydroxide, sodium hydroxide was used for neutralization. The precipitate formed was filtered off and the filtrate was placed on a Dowex 1×4 (200–400 mesh) column in the chloride form (30 × 3 cm). Three bands formed on the column on elution with water. The second, most intensive red band contained a mixture of $[Co(S\text{-phe})(tn)_2]^{2+}$ isomers (about 35% yield). The eluate was evaporated to dryness at 30°C, mixture obtained dissolved in a minimum amount of water (3–4 cm^3) and transferred onto an optically active Sephadex QAE column, in the L-$(+)_{589}$-hydrogentartrate form (65×2 cm). Two bands with opposite sign of rotation (at 589 nm) developed on the column during water elution. However, only the initial part of the first and the end of the second were collected in order to obtain optically pure diastereomers. These eluates were evaporated using a vacuum evaporator at 30°C to small volume (about 5 cm^3), separately transferred onto an anion Merck II column in the chloride form (18 × 2 cm) and eluted with water. The eluates were evaporated to dryness at 30°C and the two red diastereomers kept for one hour in a drying oven at 110°C. *Anal.* Calcd. for $\Lambda\text{-}(+)_{589}\text{-}[Co(S\text{-phe})(tn)_2]Cl_2 \cdot 3H_2O$ (%): C, 36.29; H, 7.32; N, 14.11. Found: C, 36.32; H, 7.23; N, 14.12. Yield

2.8%. Calcd. for Δ-(−)$_{589}$-[Co(*S*-phe)(tn)$_2$]Cl$_2\cdot$1.5H$_2$O (%): C, 38.38; H, 7.10; N, 14.92. Found: C, 38.11; H, 6.98; N, 15.15. Yield 2.2%. The complex with *S*-alanine ligand was obtained in an analogous way but only the optically pure Λ diastereomer was isolated. *Anal.* Calcd. for Λ-(+)$_{589}$-[Co(*S*-ala)-(tn)$_2$]Cl$_2\cdot$2H$_2$O (%): C, 26.87; H, 7.53; N, 17.42. Found: C, 26.54; H, 7.40; N, 17.70. Yield 4.5%. The complex with glycine ligand was obtained by a previously described procedure [3].

Preparation of (−)$_{589}$-*anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*),*cis*(*O*)-di-μ-hydroxo-*tetrakis*(*S*-phenylalaninato)dicobalt(III)

Into a 500 cm^3 flask 1.10 g (6.65 mmol) of *S*-phenylalanine, 0.13 g (3.25 mmol) of NaOH and 100 cm^3 of ethanol–water mixture (1 : 1) was added. When the *S*-phenylalanine had dissolved, 2 cm^3 of 30% H$_2$O$_2$ and a solution of 0.58 g (2 mmol) of Co(NO$_3$)$_2\cdot$6H$_2$O in 20 cm^3 of the same solvent was added dropwise. The reaction mixture was adjusted to pH = 8 using NaOH solution and heated for 2 h on a water bath at 45°C. The suspension obtained was cooled to room temperature and the precipitate filtered off. The violet crystals were washed with water and ethanol and dried in air. *Anal.* Calcd. for [Co$_2$(OH)$_2$(*S*-phe)$_4$]$\cdot$2H$_2$O (%): C, 51.18; H, 5.50; N, 6.34. Found: C, 51.39; H, 5.67; N, 6.74. Yield 4.1%.

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Spectroscopic Measurements

Electronic spectra were recorded on a Varian GBC UV/VIS 911 A spectrophotometer in aqueous solutions in the case of [Co(*S*-phe)(tn)$_2$]Cl$_2$ diastereomers, and in DMSO solution in the case of the dinuclear complex. Circular dichroism spectra were recorded with a Jasco 500 automatic spectropolarimeter. ^{1}H and ^{13}C NMR spectra of [Co(aa)(tn)$_2$]$^{2+}$ (*aa* = aminocarboxylato) were recorded with a Varian Gemini 2000 spectrometer at 200 MHz and 50 MHz, respectively, in D$_2$O. The ^{1}H NMR spectrum of *S*-phenylalanine was recorded in D$_2$O. ^{1}H NMR spectra of dinuclear complexes with *S*-phenylalaninato and *S*-arginine ligands were recorded with the same instrument in DMSO-*d*$_6$. In all cases the internal standard was DSS.

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RESULTS AND DISCUSSION

Syntheses

Our expectations of obtaining new diastereomers of the type (1,3-diaminopropane)*bis*(*S*-aminocarboxylato)cobalt(III) and di-μ-hydroxo-*tetrakis*(*S*-aminocarboxylato)dicobalt(III) by replacing *S*-tyrosinato with *S*-phenylalaninato ligand were not fulfilled. In the first case two diastereomers of *bis*(1,3-diaminopropane)(*S*-phenylalaninato)cobalt(III) were obtained although the synthesis with *S*-phenylalanine was carried out in the same manner as in our previous work with *S*-tyrosine [1].

In the second case, the same type of diastereomer was obtained when *S*-phenylalanine was used, although the synthesis was carried out with a different oxidizing agent (using air the system foamed and hence we used hydrogen peroxide instead). Although *S*-tyrosine is in terms of its bulk and inductive effects different from *S*-phenylalanine, due to the hydroxyl group in the aromatic ring, it is obvious from the syntheses of mono- and dinuclear complexes that this group has an influence only in the synthesis of the mononuclear complex. At this moment we do not have an appropriate explanation for this phenomenon. In the reaction to form the dimer, major reaction product was dihydroxo*bis*(*S*-phenylalaninato)cobalt(III), two diastereomers of *tris*(*S*-phenylalaninato)cobalt(III), already described in the literature [4], and several other unidentified products obtained in relatively low yield.

Mononuclear Complexes

$[Co(S\text{-phe})(tn)_2]^{2+}$ can occur in two diastereomeric forms. Their electronic absorption spectra show two symmetrical absorption bands with maxima at 500 ($^1T_{1g} \leftarrow {}^1A_{1g}$) and 354 nm ($^1T_{2g} \leftarrow {}^1A_{1g}$) (Table I). Complexes

TABLE I Spectroscopic data for diastereomers of $[Co(S\text{-phe})(tn)_2]^{2+}$ and $[Co(S\text{-phe})(en)_2]^{2+}$

Diastereomer	*Electronic spectra*				*Ref.*
	λ_1^*	ε	λ_2	ε	
Λ-$(+)_{589}$-$[Co(S\text{-phe})(tn)_2]^{2+}$	500	8.8	354	13.1	this work
Λ-$(+)_{589}$-$[Co(S\text{-phe})(en)_2]^{2+}$	488	10.4	347	11.8	6
Δ-$(-)_{589}$-$[Co(S\text{-phe})(tn)_2]^{2+}$	501	9.0	354	13.3	this work
Δ-$(-)_{589}$-$[Co(S\text{-phe})(en)_2]^{2+}$	488	10.4	347	11.8	6

*λ in nm; ε in $m^2 mol^{-1}$.

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containing 1,3-diaminopropane exhibit electronic absorption maxima at longer wavelengths relative to analogous complexes containing 1,2-diaminoethane [5], what is in accordance with a weaker ligand field in complexes with six-membered chelating diamine rings [3,6].

^{13}C NMR spectroscopy established that the negative inductive effect of the phenyl group lowers the coordination ability of S-phenylalanine relative to aminocarboxylate ligands lacking the phenyl group or possessing a group that exhibits a positive inductive effect. As a result the carboxylic C-atom of S-phenylalanine ligand is more shielded relative to carboxylic C-atoms in complexes with glycine and S-alanine ligands and resonates at lower chemical shifts: Λ-[Co(S-phe)(tn)$_2$]$^{2+}$ $C_{coo} = 186.7$ ppm; Λ,Δ-[Co(gly)(tn)$_2$]$^{2+}$ $C_{coo} = 187.4$ ppm; Λ-[Co(S-ala)(tn)$_2$]$^{2+}$ $C_{coo} = 188.2$ ppm.

^{1}H NMR spectra of the diastereomers obtained were also investigated (Fig. 1). As far as rotation around the C(α)–C(β) of the phenylalanine

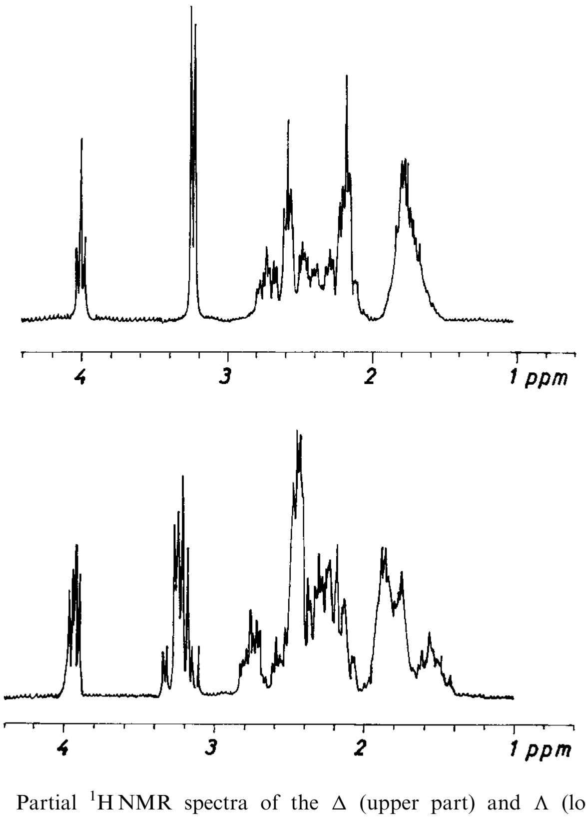

FIGURE 1 Partial ^{1}H NMR spectra of the Δ (upper part) and Λ (lower part) [Co(S-phe)(tn)$_2$]$^{2+}$ diastereomers.

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moiety is concerned, the ^{1}H NMR spectra of the diastereomers revealed different populations of the rotamers. These spectra are averaged over three predominant staggered rotamers, designated for the purpose of labelling and expressing mol fractions as ***t***, ***g*** and ***h***, as illustrated in Fig. 2. The bulky carboxylate and R groups are *anti* (*trans*) in rotamer ***t***, *gauche* in ***g*** and also *gauche* in the most hindered ***h*** rotamer. Rotamer populations may be estimated from the observed vicinal coupling constants J_{AX} and J_{BX}, if sufficiently reliable values of the J_G (*gauche* coupling) and J_T (*anti* coupling) parameters are known. Of the two β hydrogens, the signal of proton H_B is usually found at higher field than that of H_A [7–11]. In Table II the calculated results for rotamer mol fractions for free *S*-phenylalanine and for Λ and Δ diastereomers of *bis*(1,3-diaminopropane)(*S*-phenylalaninato)cobalt(III) are given. From Table II it can be seen that for free *S*-phenylalanine the most populated is rotamer ***t***, over 50%. This is the rotamer in which the bulky carboxylate and benzyl groups are in an *anti* position.

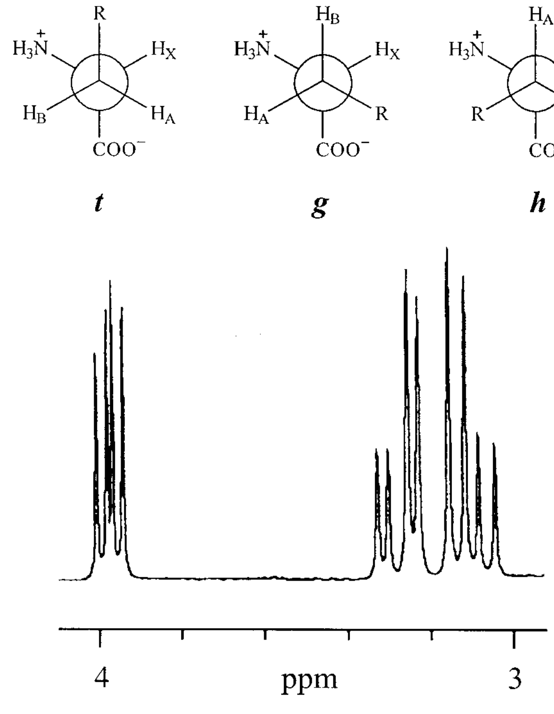

FIGURE 2 Three staggered rotamers for the free amino acid and the ^{1}H NMR spectrum of α and β protons of *S*-phenylalanine.

TABLE II Coupling constants (Hz) and rotamer mol fractions

	J_{AX}	J_{BX}	***t***	***g***	***h***
S-pheH	5.3	7.9	50.46	26.60	22.94
Λ diastereomer	4.7	7.7	48.62	21.10	30.28
Δ diastereomer	5.6	5.6*	58.72		41.28

*$J_{AX} = J_{BX}$.

It was established earlier [7] that in some peptide complexes of Pd^{2+} there is a pronounced increase in the population of rotamer ***h*** of *S*-tyrosinato and *S*-phenylalaninato side chains compared to the free amino acids. This is a conformation which disposes the side chain of aromatic amino acid to take up a position over the metal ion. Our results indicate an increase of rotamer ***h*** at the expense of rotamers ***t*** and ***g*** by 7.34% in Λ the diastereomer in comparison with rotamer population for the free amino acid. The similarity in rotamer mol fractions for free and coordinated *S*-phenylalanine ligand in the Λ diastereomer give rise to similar ABX spectra for α and β protons of the amino acid (Figs. 1 and 2).

On the other hand, the protons of β-methylene in Δ diastereomer were isochronous and equally coupled to the α-methine group giving rise to an A_2X type spectrum (Fig. 1). In this diastereomer we find a pronounced increase in the population of the ***h*** rotamer at the expense of rotamer ***t*** (18.34%) in comparison with rotamer populations for uncoordinated *S*-phenylalanine. In the Λ diastereomer there is a steric interaction between the *S*-phenylalanine side chain in rotamer ***h*** and one of the 1,3-diaminopropane chelate rings. This explains greater population of rotamer ***h*** in the Δ diastereomer.

The absolute configuration of $(+)_{589}$-$[Co(S\text{-glu})(en)_2]^+$ (*S*-*glu* = *S*-glutamato ligand; *en* = 1,2-diamoethane) was determined by X-ray analysis [12]. CD spectrum of this complex exhibits one dominant CD band in the region of the first electronic transition with a positive Cotton effect (Fig. 3). Based on this, the absolute configurations of our $[Co(S\text{-phe})(tn)_2]^{2+}$ complex diastereomers were ascribed by comparing their CD spectra with CD spectrum of the *S*-glutamine complex, taking into account the fact that in the case of *bis*(diamine)cobalt(III) complexes the *tn* and *en* ligands have little influence upon the shape of the corresponding CD spectra [13]. In such a way we assigned to the diastereomer which exhibits a positive Cotton effect of the dominant band in the region of the first electronic transition the Λ absolute configuration, and Δ absolute configuration to the diastereomer with opposite sign (Fig. 3).

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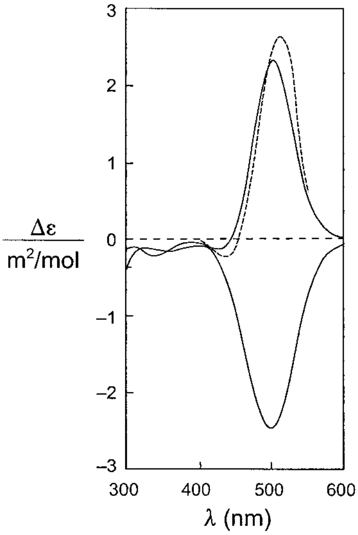

FIGURE 3 CD spectra of Λ (upper), Δ-$[Co(S\text{-phe})(tn)_2]^{2+}$ (—) and Λ-$[Co(S\text{-glu})(en)_2]^{+}$ (- - -).

Dinuclear Complex

As mentioned, we synthesized by direct method one of 24 theoretically possible diastereomers of dinuclear $[Co_2(OH)_2(S\text{-phe})_4]$. This can be concluded on the base of the results of the elemental analysis and ^{1}H NMR data. In the ^{1}H NMR spectrum, signals for the two hydroxyl groups appear in the negative chemical shift region at −0.97 and −1.74 ppm, and in the case of the *anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*),*cis*(*O*)-$[Co_2(OH)_2(S\text{-argH})_4]^{3+}$ complex, the structure of which was determined by X-ray analysis [14], at −1.31 and −1.93; this confirms the bridged character of our complex.

Molecular models for diastereomers of this type show that in 4 diastereomers hydrogens of both NH_2 groups are directed towards the carboxylate oxygen atom, but in three of them could form two N–H···O hydrogen bonds; in the fourth diastereomer a non-bonded steric effect is noted. It is probable that the above three diastereomers would be more stable than the others and we have isolated one of them. In order to check this assumption, we compared electronic and CD spectra of our complex with those of the *S*-arginine complex (Fig. 4). Since both spectra are very similar, we ascribe to the *S*-phenylalanine diastereomer the *anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*),*cis*(*O*) configuration (Fig. 5). Finally, comparison of CD spectra of the dinuclear complexes with *S*-phenylalaninato and *S*-tyrosinato ligands

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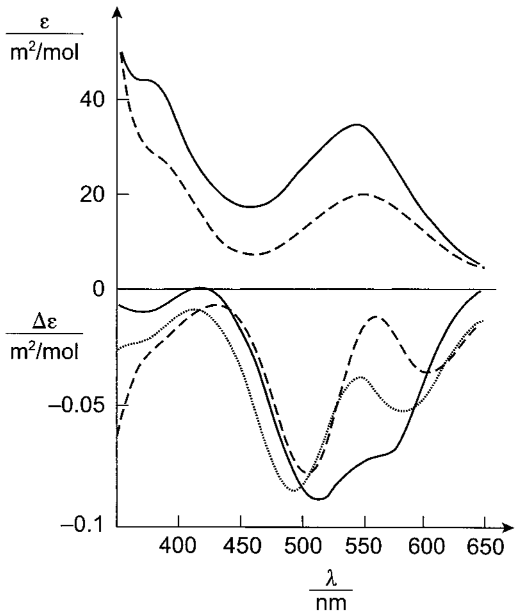

FIGURE 4 Electronic absorption and CD spectra of *anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*), *cis*(*O*)-[$Co_2(OH)_2$(*S*-phe)$_4$] (- - -) and *anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*),*cis*(*O*)-[$Co_2(OH)_2$ (*S*-argH)$_4$]$^{3+}$ (—) complexes and the CD spectrum of *anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*),*cis*(*O*)-[$Co_2(OH)_2$(*S*-tyr)$_4$] (· · ·).

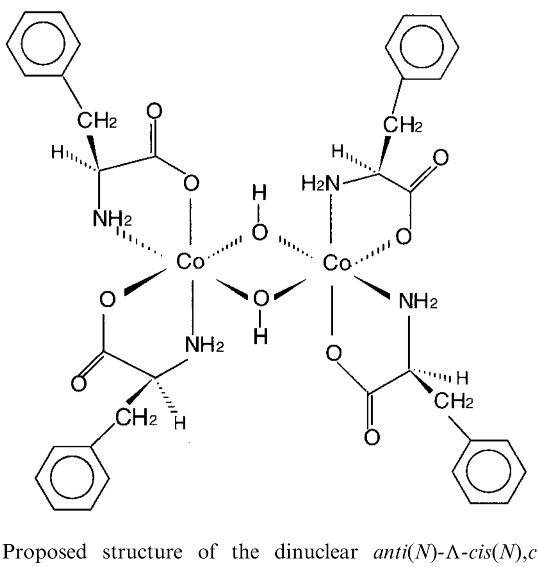

FIGURE 5 Proposed structure of the dinuclear *anti*(*N*)-Λ-*cis*(*N*),*cis*(*O*)-Δ-*cis*(*N*),*cis*(*O*)-[$Co_2(OH)_2$(*S*-phe)$_4$] complex.

shows that the same diastereomer is isolated, although the synthesis was carried out under different conditions.

Acknowledgements

The authors are grateful to the Ministry for Science and Technology of the SR Serbia and the Federal Ministry for Development, Science and Environment of Yugoslavia for their financial support. We appreciate the NMR spectra recorded by Miss Nina Todorović and elemental analyses provided by Miss Marina Blagojević, both from the Chemical Faculty, University of Belgrade, Yugoslavia.

References

[1] M.J. Malinar, Dj.U. Miodragović, S. Milosavljević, M.B. Ćelap and D. Vučelić, *Enantiomer*, **3**, 349 (1998).
[2] M.J. Malinar, Dj.U. Miodragović, M.B. Ćelap, D. Vuković, J.S. Zakrzewska and D. Vučelić, *J. Coord. Chem.*, **42**, 343 (1997).
[3] M.J. Malinar, P.N. Radivojša, M.B. Ćelap, *Rev. Chim. Min.*, **23**, 1 (1986).
[4] P. Vie'les, A. Bonniol, *C.R. Acad. Sc. Paris*, **269 C**, 577 (1969).
[5] C.T. Liu and B.E. Douglas, *Inorg. Chem.*, **3**, 1356 (1964).
[6] F. Woldbye, *Proc. Roy. Soc.*, **297 A**, 79 (1967).
[7] P.I. Vestues and R.B. Martin, *J. Am. Chem. Soc.*, **102**, 7906 (1980).
[8] R.B. Martin, *J. Phys. Chem.*, **83**, 2404 (1979).
[9] R.B. Martin and R. Mathur, *J. Am. Chem. Soc.*, **87**, 1065 (1965).
[10] W.G. Espersen and R.B. Martin, *J. Phys. Chem.*, **80**, 741 (1976).
[11] J.P. Casey and R.B. Martin, *J. Am. Chem. Soc.*, **94**, 6141 (1972).
[12] J.H. Dunlop, R.D. Gillard, N.C. Payne and G.H. Robertson, *Chem. Commun.*, 874 (1966).
[13] Y. Kojima, *Bull. Chem. Soc. Jpn.*, **48**, 2033 (1975).
[14] P.N. Radivojša, N. Juranić, M.B. Ćelap, K. Toriumi, K. Saito, *Polyhedron*, **10**, 2717 (1991).

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