

SYNTHESIS AND CHARACTERIZATION OF
 Δ -*cis*(N)-*trans*(O₅)-RR SODIUM BIS-
 ((S)- α -ALANINATO-N-MONOPROPIONATO)COBALTATE(III) ISOMER

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Of the 12 possible diastereoisomers only Δ -*cis*(N)-*trans*(O₅)-(RR)-Na[Co(alamp)₂] isomer was isolated. Possible reasons explaining stereospecific coordination of ligand are discussed in terms of steric intra- and interligand interactions arising from the mutual position of —CH₃ and N—CH₂—CH₂— groups. These exclude all isomers with *SS* or *RS* configuration of secondary nitrogen atoms. For the determination of the absolute configuration visible absorption, ¹H, ¹³C NMR, circular dichroism and molecular models were employed.

(S)- α -Alaninato-N-monoacetate (alama) coordinates to cobalt(III) giving rise to nine possible isomers. Six of them were prepared by Okamoto and coworkers¹ suggesting the presence of some prohibitive effects in the synthesis. A notable observation is the structural discrimination exerted by the orientation of secondary NH bonds of coordinated terdentate N-(ω -carboxyalkyl)aminoalcanoic acid ligand. In (S)- α -alaninato-N-monopropionate (alamp) ligand system related, but with lengthened chain a new problem arises due to the fact that the ligand may adopt various arrangements around the cobalt(III) atom. In an attempt to determine the effect of six-membered chelate ring on overall stereochemistry of cobalt(III) complexes of linear terdentate N-(ω -carboxyalkyl)aminoalcanoic acids ligands this paper reports the preparation and characterization of Na[Co(alamp)₂] isomers.

EXPERIMENTAL

Ligand and Na[Co(alamp)₂] complex were prepared by the method used by Okamoto and coworkers^{1,2} to synthesise the related Na[Co(alama)₂] (scale 0.035 mol of Co^{II}). The reaction mixture obtained was separated into two fractions on the Dowex 1X2 column (Cl⁻ cycle, 100 to 200 mesh) by elution with 0.04M-NaClO₄. Co content in both fractions obtained was determined by atomic absorption giving isomer ratio 98 : 2. The first band eluted was evaporated *in vacuo*. The residue was extracted with ethanol and dried in air. For C₁₂H₁₈CoN₂NaO₈ (404.2) calculated: 34.66% C, 5.48% H, 6.93% N; found: 34.25% C, 5.52% H, 6.59% N.

The second synthetic procedure consisted in the dissolution of freshly prepared Co(OH)₃ (0.15 mol) in the solution (50 ml) containing 0.2 mol of (S)- α -alaninato-N-monopropionic acid and 0.1 mol of NaOH at 55°C. The mixture was filtered and the filtrate was poured onto a Dowex

1X2 anion exchange column (Cl^- cycle, 100–200 mesh). The adsorbed product was eluted with 0.04M- NaClO_4 . The chromatography gave only one band which was eluted, evaporated, and extracted with ethanol. Elemental analysis of the solid obtained corresponded to the above mentioned formula.

Charcoal catalyzed isomerization. 0.1 g of $\text{Na}[\text{Co}(\text{alamp})_2]$ was dissolved in 50 ml H_2O . To this solution 0.5 g of activated charcoal (Norrit A) was added and the mixture was stirred at 50°C for 4 h. Then the charcoal was filtered off and filtrate was transferred onto Dowex 1X2 column. Elution of the band adsorbed with 0.04M- NaClO_4 gave again only one band.

Base catalyzed isomerization. 0.1 g of $\text{Na}[\text{Co}(\text{alamp})_2]$ was dissolved in 50 ml of 0.05M- NaOH . The solution was heated and stirred for 3 h at 55°C. After chromatographic separation on Dowex 1X2 column, only one band was eluted with 0.04M- NaClO_4 .

Measurements. Electronic absorption spectra were recorded on Specord UV VIS spectrophotometer. Optical rotations were obtained on a Perkin-Elmer 241 polarimeter. Circular dichroism spectra were measured on automatic Jobin-Yvon Mark V dichrograph. ^1H (200.0 MHz) and ^{13}C (50.3 MHz) NMR spectra were taken using Varian XL-200 spectrometer with DSS as internal standard.

RESULTS AND DISCUSSION

It is possible to conceive theoretically 12 isomers of $[\text{Co}(\text{alamp})_2]^-$ anion due to the presence of chiral secondary nitrogen atoms, α -carbon atoms and different chelate ring size. To compare the interplay of these and other effects with $[\text{Co}(\text{alampa})_2]^-$ system, the synthesis of $[\text{Co}(\text{alamp})_2]^-$ was accomplished by the method described by Okamoto¹. This method consists in the oxidation of reaction mixture containing neutralized (*S*)- α -alaninato-*N*-monopropionic acid with PbO_2 and separation of product isolated on anion exchange column. Two isomers were obtained in the ratio 98 : 2. From these two, only the first eluted isomer was obtained in the amount sufficient for full characterization. In addition to the synthesis outlined above the reaction of $\text{Co}(\text{OH})_3$ with aqueous solution of partly neutralized ligand was used. This preparation yielded only one isomer, chiroptical properties of which were the same as those of the first eluted isomer obtained by the oxidative method.

The visible absorption spectrum of the isomer isolated (Fig. 1 and Table I) consists of two symmetrical bands corresponding to T_{1g} and T_{2g} octahedral states. The symmetry of the first absorption band either indicates that the axial and equatorial fields are roughly the same and either excludes both *trans*(*N*) isomers and *cis*(*N*) isomer with rhombic ligand field, *i.e.* *cis*(*N*)-*trans*(O_5O_6) one. Applying arguments concerning effective ligand field, the isomer obtained should have C_2 symmetry (chelate rings conformation is ignored) which is satisfied, however, for both *cis*(*N*)-*trans*(O_5) and *cis*(*N*)-*trans*(O_6) geometry. Considering the presence and distribution of two five- and two six-membered chelate rings and CoN_2O_4 chromophore, it is possible (taking the difference between axial and equatorial ligand field into account) to compare spectral data with those of $[\text{Co}((\text{S})\text{-Asp})_2]^-$ isomers. Comparison of the energies of the first and second absorption bands maxima of *cis*(*N*)- $[\text{Co}(\text{alamp})_2]^-$ with

$[\text{Co}((S)\text{-Asp})_2]^-$ isomers^{3*} allows to assign tentatively the *cis*(N)-*trans*(O₅) geometry to the isomer described in this paper. It should be emphasized that there are steric arguments supporting this geometry (*vide infra*).

Further evidence for the assignment of *cis*(N)-*trans*(O₅) geometry was provided by the ¹H and ¹³C NMR spectra which are presented in Table II. One sharp doublet centered at 1.72 ppm ($J = 7.2$ Hz) and one quartet which is observed at 4.07 ppm

TABLE I
Absorption (nm) and circular dichroism data of Na[Co(alamp)₂]

Absorption, λ_{max} (ϵ)		CD, λ_{max} ($\Delta\epsilon$)	
I band	II band	I band	II band
512 (188.5)	384 (107.7)	632 (-6.36)	383 (+4.36)
		543 (+2.91)	
		493 (-9.18)	

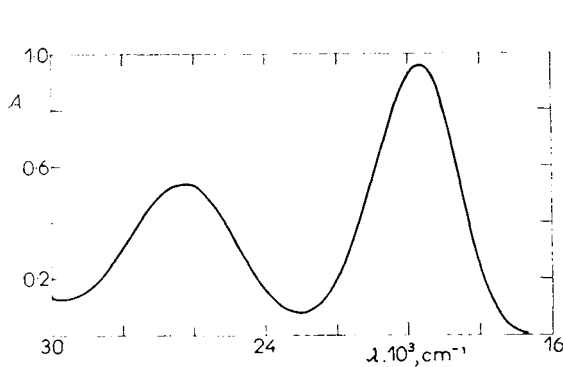


FIG. 1
Electronic absorption spectrum of the Δ -*cis*(N)-*trans*(O₅)-RR-Na[Co(alamp)₂] isomer

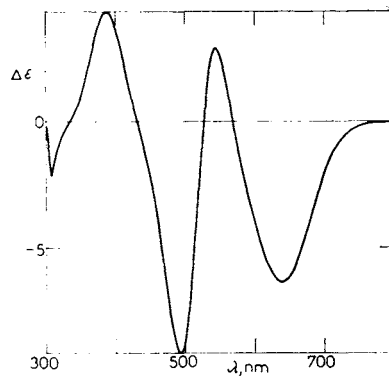


FIG. 2
Circular dichroism spectrum of the Δ -*cis*(N)-*trans*(O₅)-RR-Na[Co(alamp)₂] isomer

* Legg and Neal⁴ compared CD and absorption spectra of closely related cobalt(III) complexes and concluded that opposite assignments of *cis*(N)-[Co((S)-Asp)₂]⁻ isomers should be done than was originally assigned by Douglas and coworkers³. Opposite geometry of *cis*(N)-[Co((S)-Asp)₂]⁻ isomers is considered in the present paper.

correspond to two environmentally equivalent CH_3 and $\alpha\text{-CH}$ protons, respectively. In addition, the resonance observed at 7 ppm assignable to N-H protons gives evidence about the equal configurations of nitrogen centers. Similarly ^1H noisy decoupled ^{13}C NMR spectrum which shows single pattern containing six resonance peaks is also consistent with a C_2 symmetry.

The asymmetric feature of $\text{cis}(\text{N})\text{-trans}(\text{O}_5)\text{-}[\text{Co}(\text{alamp})_2]^-$ anion is attributed to chiral carbon atoms, chiral secondary nitrogen atoms, conformation and chirality about the cobalt(III) ion. The CD spectrum of this anion (Fig. 2, Table I) exhibits in the T_{1g} spectral region three electronic components with a sign sequence $- + -$. The presence of three components indicates rather rhombic than tetragonal field. This, together with larger $\Delta\epsilon$ values obtained for $[\text{Co}(\text{alamp})_2]^+$ isomer are the most notable differences between the CD spectra of $\text{cis}(\text{N})\text{-}[\text{Co}(\text{alamp})_2]^-$ and $\text{cis}(\text{N})\text{-trans}(\text{O}_5)\text{-}[\text{Co}(\text{alamp})_2]^-$ ions. Since the lowest energy band of $\text{cis}(\text{N})\text{-trans}(\text{O}_5)\text{-}[\text{Co}(\text{alamp})_2]^-$ has a negative rotation strength which was ascribed in a series of complexes structurally related to the $[\text{Co}(\text{edta})]^-$ to $\text{A} \rightarrow \text{A}$ transition^{5,6}, it is possible to assign to the complex described here $\Delta\Delta\Delta$ or Δ net absolute configuration. This assignment is consistent both with octant sign method⁷ (negative contribution) and empirical observation of Mason and coworkers⁸ according to which the lowest energy dominant CD band usually corresponds to A transition derived from E_a component of $[\text{Co}(\text{en})_3]^{3+}$. Conclusions concerning the Δ absolute configuration accords well with the inspection of molecular models which exclude on steric ground Λ structure (*vide infra*). As can be seen from Fig. 2, the highest energy component of the first absorption band dominates to CD spectrum, although the transition centered around 630 nm was taken for the assignment of absolute configuration. It must be mentioned, however, that some exceptions⁶ exist as far as the use of dominant CD band for the

TABLE II

^1H and ^{13}C chemical shift data (ppm) for $\text{Na}[\text{Co}(\text{alamp})_2]$ and $\text{OOC}-\overset{\alpha}{\text{C}}(\text{CH}_3)-\overset{\beta}{\text{N}}\text{H}-\text{CH}_2-\overset{\alpha}{\text{C}}-\text{COO}$ ligand

$\alpha\text{-CH}_3$	$\alpha\text{-CH}$	$\beta\text{-CH}_2$	$\alpha\text{-CH}_2$	$\alpha\text{-COO}$	$\beta\text{-COO}$	NH
1.71 d	4.07 t	3.48 m	^1H NMR 2.86 m	—	—	7.0
17.70 ^a	60.50 ^a	44.63 ^a	^{13}C NMR 33.50 ^a	177.05 ^a	177.06 ^a	—
17.42	64.45	48.09	36.67	183.88	187.36	—

^a Ligand.

determination of the absolute configuration is concerned. Van Saun and Douglas⁶ showed that the rotational strength in the series of structurally related complexes, to which the $[\text{Co}(\text{alamp})_2]^-$ anion belongs, the low energy T_{1g} CD band decreases (on the expense of high frequency band) with increasing number of more flexible six-membered chelate rings. Since the *cis*(N)-*trans*(O₅)- $[\text{Co}(\text{alamp})_2]^-$ isomer has the same CD pattern as Λ - $[\text{Co}(\text{en})(\text{mal})_2]^+$ ion (taking the enantiomeric character and signs reversal into account), absolute configuration of which was derived on the basis of the comparison of both CD peaks signs and structural relationship with structurally related Λ - $[\text{Co}(\text{edta})]^-$, the use of above mentioned arguments is substantiated.

Secondary nitrogen atoms of (S)- α -alaninato-N-monopropionate ligands are intrinsically chiral and on coordination can assume *RR*, *RS* or *SS* configurations. However, examination of the structures showed significant nonbonded repulsions when nitrogen atoms have *SS* or *RS* configurations. As follows² from the CD spectra of $[\text{Co}(\text{NH}_3)_3(\text{alamp})]^+$, both N- and C-vicinal effects contribute to the CD spectrum additively giving rise to two peaks of alternating sign both for N(*R*) and C(*S*) chiral atoms: + - (from lower energy side). The lowest positive energy transition of $[\text{Co}(\text{NH}_3)_3(\text{alamp})]^+$ which occurs approximately at 19 000 cm^{-1} (C-vicinal contribution) or at 18 000 cm^{-1} (N(*R*)-vicinal contribution) diminishes apparently the rotatory strength of the lowest energy component of the first absorption band of $[\text{Co}(\text{alamp})_2]^-$ which was used as "dominant" band for the assignment of the general molecular dissymmetry. On the other hand negative components observable in the CD spectra of $[\text{Co}(\text{NH}_3)_3(\text{alamp})]^+$ are undoubtedly responsible for greater intensity of transition occurring approximately at 20 000 cm^{-1} . The ¹H NMR spectrum (Table II) is in accord with the stereospecific coordination of nitrogen atoms inferred from CD spectra, since the NMR spectrum exhibits only a single NH peak.

$[\text{Co}(\text{alamp})_2]^-$ anion can be written due to the stereoheterotopic character of ligands and the presence of three centers of chirality in 12 isomeric forms. These include *trans*(N)-meridional, *trans*(N)-facial and *cis*(N) structures. Inspection of models suggests that there are several sites in the $[\text{Co}(\text{alamp})]^-$ complex, the mutual interplay of which makes the conclusion concerning the stereochemical preference possible: CH₃ groups, secondary nitrogen atoms, —CH₂—CH₂— backbone of six-membered chelate rings and octahedral chirality centers. The most important stereochemical variable is the alternative absolute configuration *R* or *S* at two coordinated nitrogen atoms of both ligands which eliminates, due to the nonbonded interactions arising from the *cis* position of C—CH₃ group with respect to the N—CH₂—CH₂— framework, all diastereoisomers with *SS* or *RS* nitrogen atoms configuration (Fig. 3). Furthermore, analysis of interchelate interactions shows that second stereochemical variable which influences the overall stability of diastereoisomers is conformation of six-membered chelate rings. The detailed evaluation of steric interactions is complicated by the number of conformations which can adopt six-membered chelate ring.

From all these the chair and δ -skew conformations seem to be most plausible ones which experiences for *RR* nitrogen atoms the minimum of interchelate interactions between CH_3 and $\beta\text{-CH}_2$ groups of adjacent chelate rings. We have some evidence according to which six-membered rings in $\Delta\text{-cis(N)-trans(O}_5\text{)-RR}$ isomer assume undistorted gauche conformations. Two vicinal coupling constants $J_{(\text{NH}-\text{CH}_2)}$ are equal (10 Hz) and this is satisfied only when six-membered chelate rings adopt chair or δ -skew conformation.

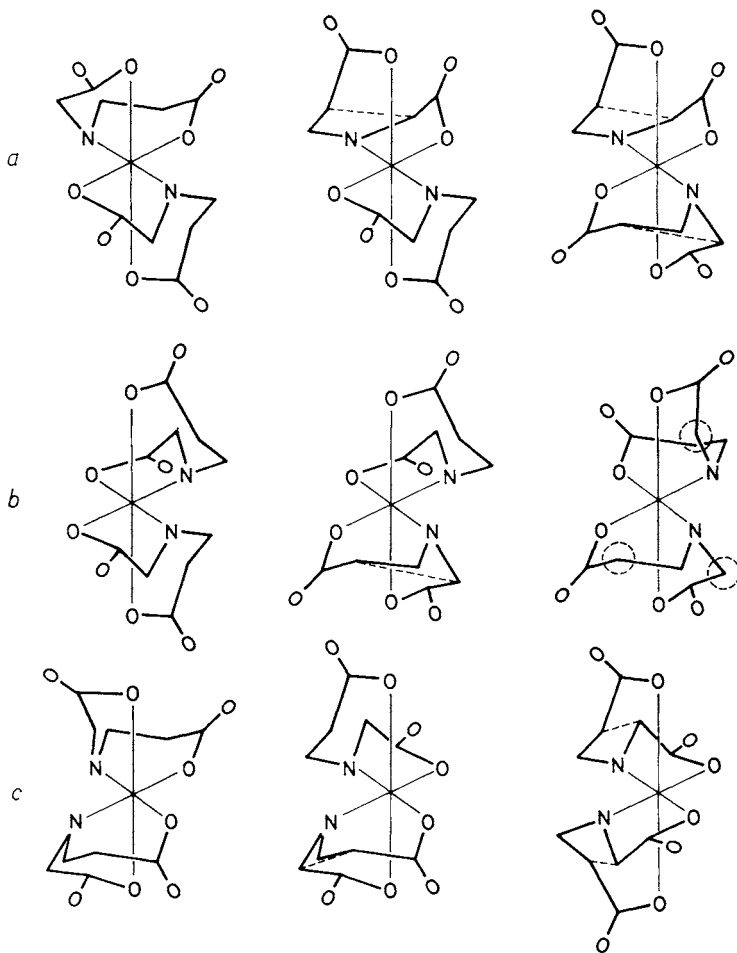


FIG. 3

Selected geometrical and optical isomers of $[\text{Co}(\text{alamp})_2]^-$. *a* *trans(N)*-facial: *RR*, *RS*, *SS*; *b* $\Delta\text{-cis(N)}$: *RR*, *RS*, *SS*; *c* $\Lambda\text{-cis(N)}$: *RR*, *RS*, *SS*. Dashed lines show intraligand non-bonding interactions

Although at least three facial and one meridional form have stable geometry with CH_3 and $\text{N}-\text{CH}_2$ groups *trans* to each other and *RR* nitrogen atoms, only Δ -*cis*(*N*)-*trans*(O_5)-*RR* isomer was isolated. This result shows that the prohibitive effect associated with stereospecific coordination of secondary nitrogen atoms can not be the sole factor responsible for the exclusive isomer formation. The observed stereospecificity is believed to be thermodynamically controlled and must result from different interchelate steric interactions involving six-membered chelate rings. Recent theoretical studies of Herak and Simon⁹ show that amino-acid six-membered chelate ring is more puckered when it forms a part of fused ring system in comparison with isolated β -alaninate ring. This fact supports our assumption concerning the substantial role of six-membered chelate ring in isomer discrimination. Despite to this there is no reason why an above described particular geometry and octahedral chirality would be necessarily favoured. Obviously models do not convincingly revealed appreciable differences in interactions among individual diastereoisomers having *RR* absolute configuration of nitrogen atoms.

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