INVESTIGATION OF THE EFFECT OF THE AMINOCARBOXYLATO CHELATE CONFORMATION ON THE OPTICAL ACTIVITY OF THE *CIS*(NO₂),*TRANS*(NH₂)-BIS(AMINOCARBOXYLATO)DINITROCOBALT/ATE(III) ISOMERS

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Abstract—In the *cis*(NO₂),*trans*(NH₂)-bis(aminocarboxylato)dinitrocobalt/ate(III) isomers, containing glycinato, S-alaninato, S-*n*-valinato, S-valinato, S-*n*-leucinato, S-leucinato, S-*i*-leucinato and S-arginine ligands, respectively, it was found that in the Λ-isomers circular dichroic spectra are determined by the configurational contribution to the optical activity. This is connected in the case of optically active ligands with the chair conformation of the chelate rings and the equatorial position of the ring side group. In the Δ-isomers, λ-conformation of the aminocarboxylato chelate rings and the axial position of the ring side groups induce a considerable contribution to the optical activity, which varies from complex to complex. NMR spectroscopy showed that these variations are related to small changes in the chelate ring conformation in such a way that a more axial position of a ring side group induces a larger contribution. The λ-conformation of a S-aminocarboxylato chelate ring induces a large negative contribution to the circular dichroism of the investigated complexes.

In aminocarboxylatocobalt(III) complexes, the optical activity may arise[1] from the configurational dissymetry of the chelate rings (assymmetry of donor atoms[2]) arrangement, the conformational assymmetry of a chelate ring and from the vicinal effect of an assymmetric centre in an optically active aminocarboxylato ligand. The vicinal contribution to the optical activity in aminocarboxylatocobalt(III) complexes has been considered as an important contribution, while the conformational contribution of an α-aminocarboxylato ring was considered to be of small importance, due to the almost planar arrangement of ring atoms.[3–10] However, in order to extract the vicinal contribution from the total optical activity of a complex, i.e. to separate it from the configurational contribution, an additive and equal vicinal contribution to the optical activity of a diastereomeric pair of a complex has been assumed.[3,4,8] Such an approach has not allowed the investigation of the effect of unequal steric constraints, imposed on the aminocarboxylato ligand in a diastereomeric pair of a complex, on its contribution to the optical activity. It seems that this effect was usually small, which inhibited investigations in this direction. But in the *cis*(NO₂),*trans*(NH₂)-bis(aminocarboxylato)dinitrocobaltate(III) complexes, which contain sterically demanding nitro groups as ligands, a large difference in the effect of aminocarboxylato ligand conformation on the optical activity of their diastereomers has been suggested.[9] Because of that, this series of complexes seems to allow investigation of the effect of the aminocarboxylato chelate ring conformation on the optical activity. However, in earlier work,[9] the optical isomers of *cis*-(NO₂),*trans*(NH₂) - bis(aminocarboxylato)dinitrocobaltate(III) complexes have been separated by fractional crystallization,† which preclude the isolation of optically pure substances and

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†Their absolute configuration was assumed from circular dichroic spectra[9] and later confirmed by crystal structure analysis.[11,12]

the corresponding CD data, which are essential for the above mentioned investigation. We have decided to devise a new procedure for the preparation of some of the optically pure isomers and to use them for such an investigation.

RESULTS AND DISCUSSION

Circular dichroic spectra of the investigated isomers are presented in Figs 1 and 2, and in Table 1 the wavelength and dichroism of their dichroic maximum in the region of the first d–d electronic transition are tabulated. The results differ considerably from those previously reported,[9] mainly due to the higher optical purity of the optical isomers produced in the present work.

As is seen, the diastereomers having a positive sign Cotton effect in the region of the first d–d transition and having the Λ-absolute configuration, exhibit approximately the same CD spectra, irrespective of the type of optically active aminocarboxylato ligand used. There is also only a small difference between the corresponding spectrum of the analogous glycinato complex, which does not possess the vicinal contribution, and the spectra of the complexes with S-aminocarboxylato ligands. The situation is quite different with those diastereomers having a dominant negative Cotton effect and Δ-absolute configuration. In these cases maximal dichroism is more than doubled in the transition from the glycinato to S-valinato or S-isoleucinato complexes.

To understand the observed data it is necessary to consider the structures of the investigated diastereomers,[11-12] general features of which are presented in Fig. 3. In the Λ-isomers the chelate ring side group is strongly repulsed by the bulk nitro group and occupies the equatorial position; because of this the chelate ring adopts the strained chair conformation. In the isomers of Δ-absolute configuration the chelate ring side group is not in the vicinity of a nitro group but it is orientated towards a relatively small coordinated oxygen atom, and therefore the chelate ring adopts a slightly puckered λ-conformation, with the side group in an axial position. This arrangement is not strained, since the same ring conformation is found in a structurally closely related glycinato complex.[13]
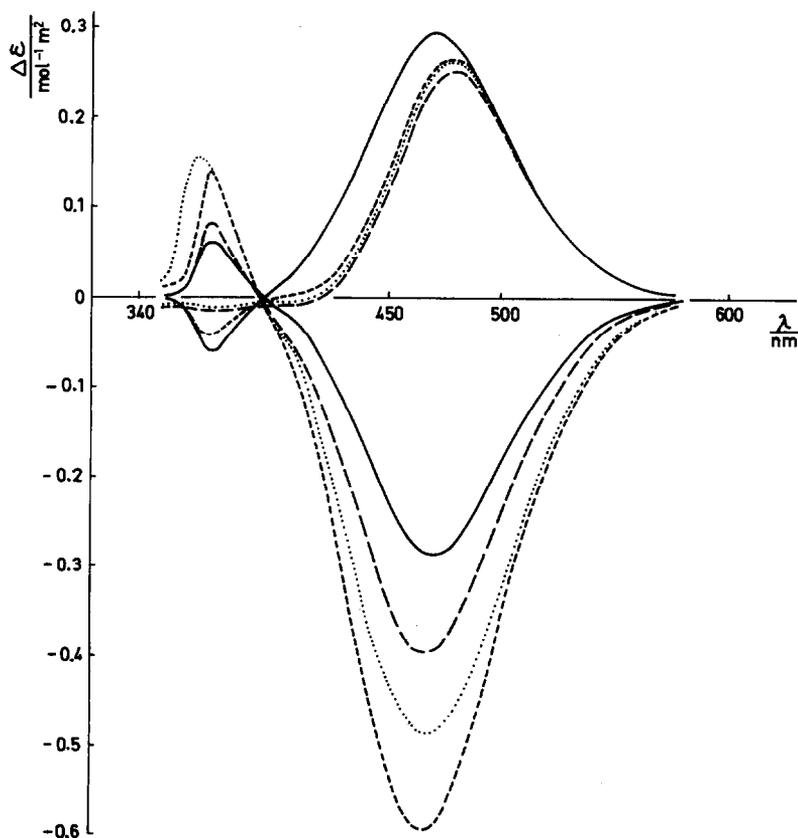

Fig. 1. Circular dichroic spectra of the *cis*(NO₂),*trans*(NH₂) - bis(aminocarboxylato)dinitrocobalt/ate(III) complexes containing glycinato ——, S-alaninato ———, S-*n*-valinato ····, or S-valinato ———— ligands. The positive dominant Cotton effect corresponds to Λ-diastereomers.
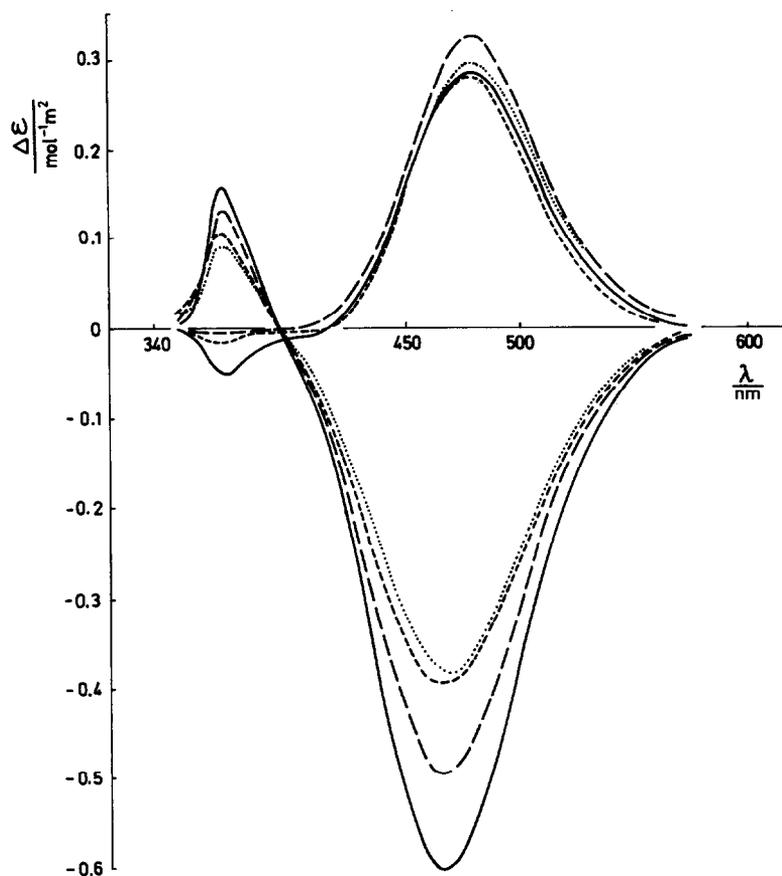
Fig. 2. Circular dichroic spectra of the $cis(NO_2),trans(NH_2)$ - bis(aminocarboxylato)dinitro-cobalt/ate(III) complexes containing S-leucinato ····, S-n-leucinato ————, S-arginine ————, or S-i-leucinato —— ligands. The positive dominant Cotton effect corresponds to Λ-diastereomers.

By applying the concept of the Quadrant rule for conformational and vicinal contributions to the optical activity of octahedral complexes, suggested by Bosnich and Harrowfield,[14] the effect of the ligand conformation on the activity of the con-

sidered isomers could be explained as shown in Fig. 4. In the Λ-isomer the chelate ring chair conformation and equatorial position of the side group would produce small or no net optical activity. Contrary to this, in the Δ-isomer a strong negative cir-

Table 1. Wavelength (λ, nm) of the circular dichroic maximum in the region of the first electronic d–d transition and the corresponding dichroism ($\Delta\varepsilon$, $mol^{-1}m^2$), and the proton chemical shift of the aminocarboxylato ligand α-hydrogen (δ, ppm) for the Λ- and Δ-isomers of the investigated bis (aminocarboxylato)dinitrocobalt/at(III) complexes

	Λ-isomer			Δ-isomer		
Complex[a]	λ	$\Delta\varepsilon$	δ	λ	$\Delta\varepsilon$	δ
$cis(NO_2),trans(NH_2)$						
-Ag[Co(NO$_2$)$_2$(gly)$_2$]	475	+0.298	3.66(equat.)	475	−0.298	3.77(axial)
-Ag[Co(NO$_2$)$_2$(S-ala)$_2$]	475	+0.25	3.76	467	−0.38	3.93
-K[Co(NO$_2$)$_2$(S-nva)$_2$]	480	+0.261	3.66	468	−0.478	3.87
-K[Co(NO$_2$)$_2$(S-val)$_2$]	477	+0.263	3.65	467	−0.596	3.90
-K[Co(NO$_2$)$_2$(S-nle)$_2$]	478	+0.290	3.67	467	−0.393	3.84
-Na[Co(NO$_2$)$_2$(S-leu)$_2$]	477	+0.294	3.67	468	−0.383	3.85
-Na[Co(NO$_2$)$_2$(S-ile)$_2$]	477	+0.292	3.66	466	−0.603	3.90
-[Co(NO$_2$)$_2$(S-argH)$_2$]Cl	478	+0.326	3.70	467	−0.496	3.89

[a] The content of crystallization water in some of the diastereomers is given in Table 2.
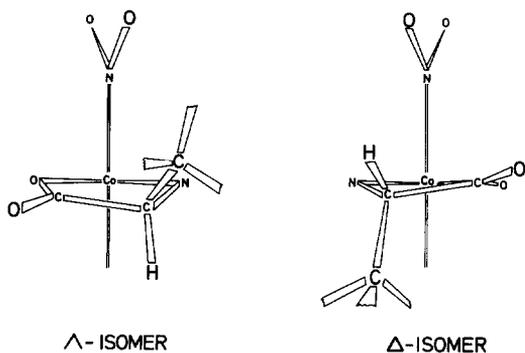
Fig. 3. Main structural feature of the investigated bis(S-aminocarboxylato)dinitrocobalt/ate(III) diastereomers.
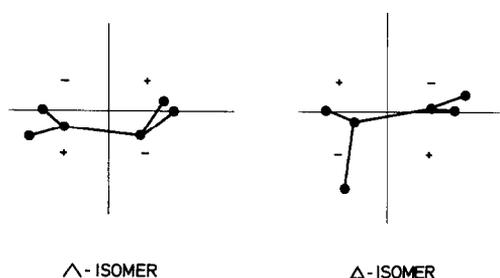

Fig. 4. Aminocarboxylato ligands skeletal atom projection according to the Quadrant rule for their conformational and vicinal contribution to the optical activity of the investigated isomers.

cular dichroism would be predicted on the assumption that the aminocarboxylato chelate ring having the λ-conformation generates negative circular dichroism in the region of the first *d–d* electronic transition. It may be further concluded that Λ-isomers, containing S-aminocarboxylato ligands, possess almost solely a configurational contribution to the optical activity and therefore exhibit circular dichroism similar to that of the corresponding complex with the glycinato ligand. In this isomer the circular dichroism does not depend significantly on the kind of the aminocarboxylato ligand, because the chelate ring side group protrudes into the equatorial region where no constraints for larger group accomodation exists. In the Δ-isomer, the aminocarboxylato ligand is flexible. The dominant steric constraint on a chelate ring side group in this case would be the intraligand interaction with the carboxylato oxygen atom,[15] which may cause a certain change in the orientation of a bulk side group. According to the same rule one can conclude that a more axially oriented side group would enhance the negative contribution to the circular dichroism in the region of the first absorption band. Therefore, we suggest that the large variation in the circular

dichroism of the Δ-isomers, containing S-aminocarboxylato ligands, is due to the conformational and vicinal contribution to the optical activity, which would be the largest for the most axially oriented aminocarboxylato chelate ring side group.

To substantiate the proposed correlation between the chelate ring side group's spatial position and its contribution to the optical activity of the investigated diastereomers we examined their proton NMR spectra. In particular, the chemical shift of the hydrogen atom on the α-carbon atom of the aminocarboxylato ligand was considered, because the spatial positioning of this hydrogen atom is directly related to the positioning of the side group, i.e. when a side group is in an equatorial position the hydrogen atom is in an axial position and *vice versa*. The chemical shifts of the considered hydrogen atom are influenced by the neighbouring magnetic anisotropy of cobalt(III)[16] and carboxylato group.[17] Both influences predict that the chemical shift of this hydrogen atom becomes progressively smaller when the hydrogen atom is moving from an equatorial to an axial position. In accordance with this prediction, the experimental data (Table 1) show that in the diastereomers of Λ-absolute configuration the chemical shift is always smaller than in the diastereomers of Δ-absolute configuration. Besides, the small variations in the chemical shifts among the diastereomers of Λ–absolute configuration could be well explained as a consequence of the different substituents on the α-carbon atom. This effect becomes unimportant when the difference in the hydrogen chemical shift between the members of a diastereomeric pair is considered. This difference varies notably with the kind of aminocarboxylato ligand and it is related to the difference in circular dichroism between diastereomers, as is shown in Fig. 5. Since in the Λ-isomers the circular dichroism has almost the same value for all the investigated aminocarboxylato ligands (the side group orientation cannot vary appreciably), the correlation presented in the figure is proof that in the Δ-isomer the more axially oriented side group induces a larger conformational contribution to the circular dichroism. From the figure it can also be concluded that the bulkiest chelate ring side groups on the first side carbon atom (encountered in the valinato and isoleucinato ligands) are positioned the furthest away in the axial direction (in accordance with the predicted repulsion from the carboxylato oxygen atom).

In conclusion, we point out that our results suggest that the strong negative circular dichroism is associated with the λ-conformation of the aminocarboxylato chelate ring of the S-amino acids. These results may be valuable in the analyses of the
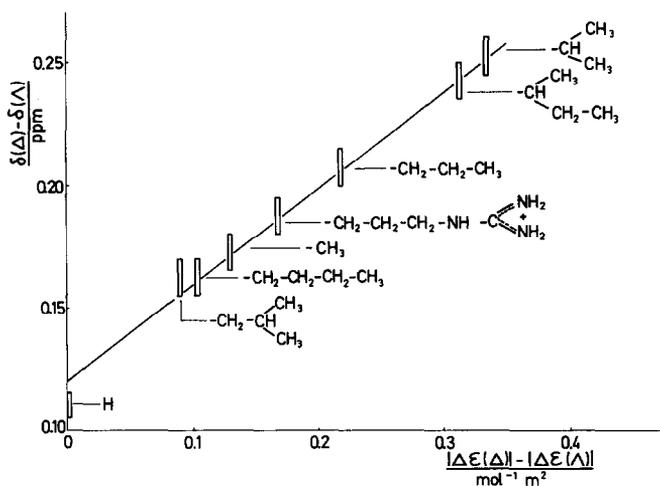
Fig. 5. Correlation between the dichroism and the α-proton chemical shift differences in a diastereomeric pair of the investigated complexes. The formulas represent the α-carbon side groups.

CD spectra of octahedral aminocarboxylato complexes.

EXPERIMENTAL

Preparations

Enantiomers of silver cis(NO_2), trans(NH_2)-*diglycinatodinitrocobaltate*(III). These were obtained by a previously described procedure.[18,19]

Diastereomers of the cis(NO_2),trans(NH_2)-*bis* (*aminocarboxylato*)*dinitrocobaltate*(III) *complex.* These were synthesized according to the procedure described by Ćelap *et al.*[9] The procedure was modified by prolonging the heating of the reaction mixture to 2 h and the mixture of diastereomer obtained was resolved by column chromatography. After the reaction was over, the hot solution was filtered off and the filtrate evaporated to dryness on a rotatory evaporator; the dry residue was extracted with 95% ethanol and evaporated to dryness. The mixture obtained was dissolved in a small amount of water and poured on a Dowex 1-X4 (200–400 mesh, 24 cm length and 4 cm o.d.) column in the chloride form. The column was first washed with water and then elution was carried out with a 0.2 M potassium chloride solution until the first zone was completely eluted, and then with a 0.5 M solution. In the cases of the leucine and isoleucine complexes, instead of potassium chloride, sodium chloride was used. From the eluate of the first zone, the Δ-diastereomer was obtained, whereas the eluate of the third zone yielded the corresponding Λ-diastereomer (the second and the fourth zones were found to contain the corresponding *cis,cis,cis*-diastereomers). When the eluates of the individual zones started to elute

from the column, they were collected in portions of about 50–100 cm^3 and each portion was immediately evaporated on a rotatory evaporator (30°C). Each dry residue was extracted with absolute ethanol and the filtered extracts kept in a refrigerator. The united extracts of one zone were then evaporated to dryness on a rotatory evaporator, and the dry residue was extracted again with absolute ethanol. The filtered extract was concentrated to a small volume on a rotatory evaporator until the crystals began to separate, and then left to stand overnight in a refrigerator. The separated crystals were filtered off and washed with ethanol and ether. The filtrate was again concentrated and cooled in a refrigerator yielding an additional amount of the corresponding substance. The substances thus obtained were almost optically pure and their yields are given in Table 2. The diastereomers obtained, except those of the S-alanine complex, were purified as follows. The Δ-diastereomers were purified by pouring their solutions again onto a Dowex 1-X4 column (200–400 mesh, 4 cm length and 2.5 cm o.d.). The elution (with a 0.2 M solution) and the isolation of substances was carried out as already described. The Λ-diastereomers were purified by extracting them with absolute ethanol and evaporating the extracts obtained on a rotatory evaporator until the crystals started to separate. The optically pure diastereomers of the S-alanine complex were obtained by dissolving about 0.5 g of the corresponding potassium salt, obtained as described above, in 10 cm^3 of water and by adding a 1 M silver nitrate solution (20% more than the equivalent amount). The solution was then filtered off to remove the white precipitate of silver chloride formed as impurity and the filtrate was kept overnight in a refrigerator.

Table 2. The yields and specific optical rotations $[\alpha]_D^{20°}$ of the cis(NO_2),trans(NH_2)-bis(aminocarboxylato)cobaltate(III) diastereomers separated by ion exchange chromatography

No.	Diastereomer	Yield (%)	$[\alpha]_D^{20°}$
1	Δ-Ag[Co(NO_2)$_2$(S-ala)$_2$]	9	−573
2	Λ-Ag[Co(NO_2)$_2$(S-ala)$_2$]	23	+343
3	Δ-K[Co(NO_2)$_2$(S-nva)$_2$]·H_2O	9	−790
4	Λ-K[Co(NO_2)$_2$(S-nva)$_2$]·H_2O	30	+232
5	Δ-K[Co(NO_2)$_2$(S-val)$_2$]·$2H_2O$	4	−795
6	Λ-K[Co(NO_2)$_2$(S-val)$_2$]	32	+165
7	Δ-K[Co(NO_2)$_2$(S-nle)$_2$]·$2H_2O$	15	−666
8	Λ-K[Co(NO_2)$_2$(S-nle)$_2$]	22	+267
9	Δ-Na[Co(NO_2)$_2$(S-leu)$_2$]·H_2O	11	−607
10	Λ-Na[Co(NO_2)$_2$(S-leu)$_2$]·H_2O	29	+294
11	Δ-Na[Co(NO_2)$_2$(S-ile)$_2$]	8	−690
12	Λ-Na[Co(NO_2)$_2$(S-ile)$_2$]	40	+189

The Δ-diastereomer crystallized out in dark brown, cube-like crystals, whereas the Λ-diastereomer separated out in the form of needle-like crystals. The optical rotations of the isomers obtained are given in Table 2.

Diastereomers of cis(NO_2),trans(NH_2)-*bis(S-arginine)dinitrocobalt*(III) *chloride.* These were prepared by an earlier described procedure.[20]

Measurements

Optical rotation. This was measured with a Perkin–Elmer 141 MC polarimeter, using 2×10^{-3} M aqueous solutions.

CD spectra. These were recorded on a JASCO Dichrograph model 500A, using the same solutions.

NMR spectra. These were recorded on a Varian FT-80A spectrometer, using D_2O solutions and DTS as an internal standard.

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