OPTICAL STEREOSPECIFICITY IN COORDINATION OF (S)-(+)-ASPARAGINE AND (S)-(+)-GLUTAMINE IN COBALT(III) COMPLEXES OF THE $Co(N)_3(O)_3$ TYPE

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The reaction of $[Co(NH_3)_6](NO_3)_3$ with (*S*)-(+)-asparagine (Asn) or (*S*)-(+)-glutamine (Gln) in the presence of activated charcoal leads to the synthesis of Λ-*mer*-$[Co(Asn)_3]$ and Λ-*fac*-$[Co(Gln)_3]$. In the synthesis of geometrical isomers the effect of the side chain plays its role (the number of carbon atoms), while the $—CONH_2$ group has a role in the preferred formation of the Λ-isomer. The isolated complexes were characterised by electronic absorption spectra and optical rotatory dispersion. Both isomers display a positive Cotton effect in the region of $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{1g}$ absorption of the $Co(N_3)(O)_3$ chromophore.

The principles of stereospecificity were formulated by Corey and Bailar[1]. According to these authors the corresponding chirality on the central metal atom depends partly on the puckering of the five-membered chelate ring. This leads in the case of cobalt(III) complexes of 1,2-diamines to the preference of one of the possible isomers. The requirement of the non-planar arrangement may be demonstrated by the example of the amino acids complexes the chelate rings of which display only a low degree of puckering[2] and in which the stereospecificity is possible only when the amino acid contains either a sterically bulky non-polar alkyl chain, or, on the contrary, a polar group capable of coordination. The first case was observed in cobalt(III) complexes of (*S*)-(−)-tyrosine[3] and (2*S*,3*S*)-isoleucine[4]. The second example is $[Co(en)_2(Glu)]^{2+}$ (where en means ethylenediamine, Glu glutamic acid) in the case of which the stabilisation of one of the possible isomers takes place in consequence of hydrogen bonding between the γ-carboxyl and the NH_2 group of the ethylenediamine[5].

The aim of this work is the study of factors affecting the stereospecific coordination of the ligands forming with cobalt(III) only weakly puckered chelate rings. For this reason (*S*)-(+)-asparagine (Asn) and (*S*)-(+)-glutamine (Gln) were studied which represent ligands with the possibility of coordination with the primary amino group, carboxyl group, or with the amide group. In addition to this the $—CONH_2$ group may take part in the formation of a hydrogen bond similarly to the $—COO^{(-)}$ group

in $[Co(en)_2(Glu)]^{2+}$; thus these ligands may function as special three-donor reagents. The complexes derived from (*S*)-(+)-asparagine and (*S*)-(+)-glutamine were prepared by substitution reaction starting from $[Co(NH_3)_6](NO_3)_3$, without pH adjustment, in the presence of charcoal. Substitution carried out in basic medium leads to a complex mixture containing complexes of bidentate and tridentate ligands[6].

In tris-bidentate complexes of (*S*)-(+)-asparagine and (*S*)-(+)-glutamine the non-equivalence of donor atoms leads to geometrical isomerism. Each of the geometrical isomers can exist in Λ or Δ configuration (symbols according to[7]). For the differentiation of the symmetry of the $Co(N)_3(O)_3$ chromophore electronic absorption spectra in the *d*–*d* transitions region were employed. The splitting of the $\mathbf{T}_{1g}(O_h)$ band in the case of $[Co(Asn)_3]$ indicates a rhombic symmetry with a meridional arrangement of the donor atoms, while in the case of $[Co(Gln)_3]$ the symmetry of both absorption bands corresponding to the transitions $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{1g}$ and $\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{2g}$ indicates a cubic symmetry with a facial arrangement of the donor atoms. As may be expected the position of the absorption maxima is equal in both complexes. *mer*-$[Co(Asn)_3]$ and *fac*-$[Co(Gln)_3]$ display in the $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{1g}$ region a strong positive Cotton effect (Fig. 1) which indicates that the prepared complexes are chiral at the octahedral center. In addition to the configurational effect which is the result of the separation of the chelate rings, their optical activity is also caused

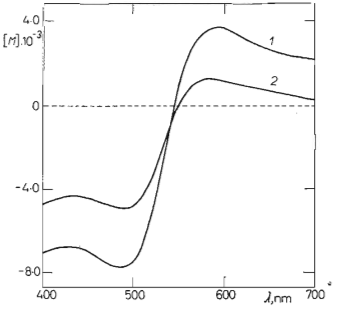

FIG. 1

Optical Rotatory Dispersion

1 Λ-*mer*-$[Co(Asn)_3]$ in conc. hydrochloric acid, *2* Λ-*fac*-$[Co(Gln)_3]$ in dilute hydrochloric acid (1 : 1).

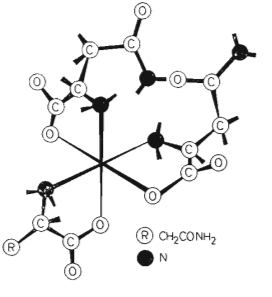

FIG. 2

Possible Arrangement of the $-CONH_2$ Groups and Absolute Configuration of Λ-*mer*-$[Co(Asn)_3]$

by a vicinal effect. This effect comprises any contribution from the chirality centre of the ligand, conformation of the chelate ring, and eventually the differences in interligand interactions. Both mentioned contributions are according to Liu and Douglas[8] additive. Tris-bidentate cobalt(III) complexes when observed in the direction of the C_3 axis (or pseudoaxis C_3) display an opposite helicity from which it follows that the Cotton effect may also have opposite signs. For the determination of absolute configuration of complexes from the Cotton effect sign methods exist utilising a theoretical solution[9]. In addition to this an empirical rule may be utilised according to which the complex with a dominant positive Cotton effect in the region of the band of low energy has a Λ-configuration[10]. From the positive value of the Cotton effect observed in the spectral region of $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{1g}$ absorption of the $Co(N)_3(O)_3$ chromophore of *mer*-$[Co(Asn)_3]$ and *fac*-$[Co(Gln)_3]$ it may be concluded that both complexes have an Λ absolute configuration with the chelate rings forming a left-handed helix around the axis (pseudoaxis) C_3 (Fig. 2).

From the above it follows that (*S*)-(+)-asparagine affords an isomer with a meridional arrangement of the donor atoms, while (*S*)-(+)-glutamine gives a facial arrangement. At the same time both ligands differ only by a $—CH_2$ group. As the present results show this difference has an effect on the distribution of geometrical isomers, which, as was confirmed in a series of other cases[4] depend both on the number of carbon atoms in the amino-acid molecule and on whether the non-polar side alkyl chain is branched or straight. When the diastereoisomers of the cobalt(III) complexes of amino acids are formed, non-bonding interactions evidently exert their influence which usually increases the yield of the Λ-isomer[4,11]. In the absence of any stereoselective contributions the reaction between (*S*)-(+)-asparagine, (*S*)-(+)-glutamine and $[Co(NH_3)_6]^{3+}$ would lead to a 1 : 1 mixture of isomers. However, the synthesis of Λ-isomers shows that the described substitution reaction is stereospecific. In order to demonstrate that this stereospecificity mainly concerns optical isomers we prepared complexes of neutral amino acids of (*S*)-configuration under the reaction conditions with the same number of carbon atoms as in (*S*)-(+)-asparagine and (*S*)-(+)-glutamine. In both cases we obtained a similar result as in the case of $[Co(Asn)_3]$ and $[Co(Gln)_3]$, *i.e.* *mer*-tris[(*S*)-α-amino-n-butyrato(1-)-O,N]-cobalt(III) and *fac*-tris-[(*S*)-norvalinato(1-)-O,N]cobalt(III). However, these complexes are racemic on the octahedral centre. From this it follows that the $—CONH_2$ group situated in the side-chain of the amide plays a role in the stabilisation of the thermodynamically more stable Λ-isomer with the pseudoequatorial disposition of the side chains. The thermodynamic character of the stereospecificity observed follows from the synthesis carried out under catalysis with activated charcoal (the use of activated charcoal as a catalyst was discussed by Dwyer[12]) when a formation of a labile cobalt(II) complex as an intermediate takes place.

As there is an appreciable difference between the behaviour of (*S*)-(+)-asparagine and (*S*)-α-amino-n-butyric acid and (*S*)-(+)-glutamine and (*S*)-norvaline, the ob-

served stereospecific coordination of amides may be ascribed to the effect of the —$CONH_2$ group. This effect manifests in the stabilisation of the given chirality by a hydrogen bond mediated by the —$CONH_2$ group. The study of Dreiding models shows that in the Λ-isomer the conditions for the formation of a hydrogen bond between the oxygen atom of the —$CONH_2$ group of one chelate ring and the hydrogen atom of the same group of the vicinal chelate ring are more favoured (Fig. 2). Study of models also reveals that this bond is possible in the case of (*S*)-(+)-asparagine only in the Λ-*mer* isomer. The extension of the side chain by a —CH_2 group leads in the case of (*S*)-(+)-glutamine to a situation where the hydrogen bond may take place both in the case of Λ-*fac* and the Λ-*mer* isomers. A definite answer to the question concerning the origin of the stereospecificity described will be given by a complete X-ray analysis.

EXPERIMENTAL

(*S*)-(+)-Asparagine ($[\alpha]_D$ +31° in 5M-HCl), (S-(+)-glutamine ($[\alpha]_D$ +44° in 1M-HCl). Electronic absorption spectra in the visible region were measured on an Optica-Milano CF-4 apparatus and optical rotatory dispersion on the Jasco-UV-5 apparatus.

Preparation of complexes: 0·03 mol of the corresponding amide were added to a solution of 0·01 mol of $[Co(NH_3)_6](NO_3)_3$ in 50 ml of water followed after its dissolution by 1 g of activated charcoal. The mixture was heated at 60°C under stirring for 5 hours, then cooled and the separated substance was filtered off on a fritted glass funnel, washed with hot water, and dissolved in concentrated hydrochloric acid. On dilution of the solution a violet substance separated in the case of asparagine, while in the case of glutamine it was a red one. The substances were filtered off, washed with water to neutrality, then with alcohol, and dried in air. Λ-*mer*-$[Co(Asn)_3].H_2O$, yield 67%. Electronic absorption spectrum (in conc. hydrochloric acid): $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{1g}$ 535 nm (ε 110), $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{2g}$ 375 nm (ε 180). For $C_{12}H_{23}CoN_6O_{10}$ (470·3) calculated: 30·64% C, 4·93% H, 17·87% N; found: 30·69% C, 5·05% H, 17·54% N.

Λ-*fac*-$[Co(Gln)_3] . 3\ H_2O$, yield 57%. Electronic absorption spectrum in hydrochloric acid (1 : 1) $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{1g}$ 525 nm (ε 214), $^1\mathbf{A}_{1g} \rightarrow {}^1\mathbf{T}_{2g}$ 380 nm (ε 207). For $CoC_{15}H_{33}N_6O_{12}$ (548·4) calculated: 32·85% C, 6·06% H, 15·33% N; found: 33·00% C, 6·16% H, 15·60% N.

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REFERENCES

1. Corey E. C., Bailar J. C. jr: J. Am. Chem. Soc. *81*, 2620 (1959).
2. Sargeson A. M. in the book: *Transition Metal Chemistry* (R. L. Carlin, Ed.), Part 3, p. 314. Dekker, New York 1966.
3. Hájek B., Wollmanová D., Jursík F.: This Journal *38*, 438 (1973).
4. Jursík F., Hájek B.: This Journal *38*, 907 (1973).

5. Dunlop J. H., Gillard R. D., Payne N. C., Robertson G. B.: Chem. Commun. *1966*, 874.
6. Jursík F.: Unpublished results.
7. IUPAC: Nomeclature of Inorganic Chemistry. Inorg. Chem. *9*, 1 (1970).
8. Liu C. T., Douglas B. E.: Inorg. Chem. *3*, 1356 (1964).
9. Gillard R. D. in the book: *Physical Methods in Advanced Inorganic Chemistry* (H. A. O. Hill, P. Day, Eds). Russian translation, p. 147. Mir, Moscow 1970.
10. Gillard R. D.: Chem. Britain *1967*, 205.
11. Jursík F., Petrů F., Hájek B.: Proc. 3rd Conf. on Coordn. Chem., Debrecen 1970, Vol. 2, p. 251.
12. Dwyer F. P.: Proc. 6th Int. Conf. on Coordn. Chem. Detroit 1961, p. 21.

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