SELECTIVITY IN THE EQUILIBRIUM SYNTHESIS OF TRIS[(S)-SERINATO-N,O(-1-]- OR TRIS[(2S,3S)-THREONINATO-N,O(-1)]COBALT(III) ISOMERS

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Reaction of $[Co(NH_3)_6](NO_3)_3$ with (*S*)-serine or (2*S*,3*S*)-threonine in the molar ratio 1 : 3 in an aqueous solution and in the presence of activated charcoal afforded the Λ-*mer*, Δ-*mer*, and Δ-*fac* isomers of tris[(*S*)-serinato-N,O(-1)]cobalt(III) and tris[(2*S*,3*S*)-threoninato-N,O(-1)]-cobalt(III) complexes. The isomers were identified by electronic absorption spectra and their absolute configuration was inferred from circular dichroism spectra. In the synthesis which affords three of the four possible isomers, the Λ-*mer* isomers predominate. Both the statistical factor and intramolecular interchelate hydrogen bonds between the OH groups of ligands assert themselves in the reaction. Both these factors support the formation of the Λ-*mer* isomer.

The stereoselectivity in cobalt(III) complexes is in principle connected with two effects, namely, conformation of chelate rings[1] and intramolecular (interchelate) bond interactions. The latter effect resembles a three-point attachment of the substrate as known from enzymatic reactions[2]. A specific bonding interaction is possible only in the case of amino acids bearing a polar group in the side chain. Thus for example[3] (*S*)-asparagine and (*S*)-glutamine are specifically coordinated in tris-bidentate cobalt(III) complexes with the formation of Λ-*mer* and Λ-*fac* isomers, resp. The specific coordination was ascribed to the formation of hydrogen bonds between the $—CONH_2$ groups, the most advantageous conditions for this formation being with the Λ-isomers. In view of the importance of polar groups in side chains of amino acids for the structure of metalloproteins (metalloenzymes) and stabilisation of the particular complex chirality, the selective coordination of β-hydroxy-α-amino acids is examined in the present paper.

(*S*)-Serine (Ser) and (2*S*,3*S*)-threonine (Thr) represent bidentate ligands characterised by the specific role of their side chains bearing the OH group. This role is demonstrated (*vide infra*) by the substitution reaction of the appropriate amino acid with $[Co(NH_3)_6]^{3+}$ ion in the presence of activated charcoal. Substitution afforded the following isomers: Λ-*mer*-$[Co((S)\text{-Ser})_3]$, Δ-*mer*-$[Co((S)\text{-Ser})_3]$, Δ-*fac*-$[Co((S)\text{-Ser})_3]$; Λ-*mer*-$[Co((2S,3S)\text{-Thr})_3]$, Δ-*mer*-$[Co((2S,3S)\text{-Thr})_3]$ and Δ-*fac*-$[Co((2S,3S)\text{-Thr})_3]$. The same isomers were obtained by oxidation of Co^{2+} ions

in the presence of (*S*)-serine or (2*S*,3*S*)-threonine, or, by reaction of $Co(OH)_3$ with these ligands under catalysis of activated charcoal[4]. As shown by these results, activated charcoal catalyses the attainment of a thermodynamic equilibrium distribution of isomers.

The facial and meridional arrangement of donor atoms was determined from electronic absorption spectra of isolated isomers on the basis of differences in splitting of the absorption band corresponding to the ${}^1T_{1g} \leftarrow {}^1A_{1g}$ transition[5]. The absolute configuration of isomers was determined with the use of circular dichroism spectra (Fig. 1), the signs of the dominant band observed in the spectral region of the ${}^1T_{1g} \leftarrow {}^1A_{1g}$ transition being compared[6,7] with the sign of the dominant band of the same transition in Λ-$[Co(en)_3]^{3+}$ (en designates ethylenediamine).

As indicated by isolation of three from the four possible stereoisomers (the Λ-*mer* isomers predominated), stereoselective effects assert themselves in the synthesis. The chemical evidence of these effects was examined with the use of the analogous substitution reaction between $[Co(NH_3)_6]^{3+}$ and amino acids with a nonpolar side chain of a bulkiness similar to that of serine and threonine, namely, (*S*)-alanine (Ala) and (*S*)-α-aminobutanoic acid (Abu). The substitution afforded Λ-*fac*-$[Co((S)\text{-Ala})_3]$ and Λ,Δ-*mer*-$[Co((S)\text{-Abu})_3]$. As suggested by these results, the above

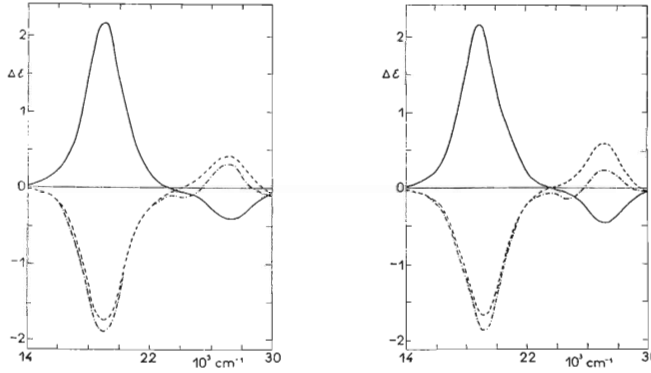

FIG. 1

Circular Dichroism Spectra

a) Λ-*mer* (full line), Δ-*mer* (dashed line), and Δ-*fac* (dot-and-dashed line) isomers of tris-[(*S*)-serinato-N,O(−1)]cobalt(III); *b*) Λ-*mer* (full line), Δ-*mer* (dashed line), and Δ-*fac* (dot-and-dashed line) isomers of tris[(2*S*,3*S*)-threoninato-N,O(−1)]cobalt(III).

mentioned stereoselective coordination is apparently due to the presence of OH groups in coordinated ligands. The comparative reactions also support the idea that the predomination of *mer* isomers (except for (*S*)-Ala, the stereoselective coordination of which is of another origin[8]) can be ascribed to the statistical distribution of *mer* and *fac* isomers. Similarly to the specific coordination[3] of (*S*)-asparagine and (*S*)-glutamine, the above stereoselectivity suggests a chiral recognition at the octahedral centre in the course of the synthesis. The ligands thus behave as special three-dentate ones that are coordinated at two sites in the inner Co(III) coordination sphere, the third bonding point being formed by interaction of OH groups in the outer coordination sphere.

As it may be inferred by inspection of Dreiding models, the present isomers may form interchelate hydrogen bonds. In the case of Λ-*mer* isomers (δ conformation[9]), a multiple hydrogen bond may be constructed between the two *cis*-OH groups and the equatorial hydrogen atom of the $-NH_2$ groups (Fig. 2). On the other hand, only a single hydrogen bond can exist in the case of Δ-*mer* and Δ-*fac* isomers (between the two *cis*-OH groups). No hydrogen bond can be constructed for steric reasons in the case of Λ-*fac* isomers, as it also may be inferred from Dreiding models. When the (*S*) ligand is coordinated in the λ conformation, the formation of a hydrogen bond is not excluded by the model. Consequently, the conformation of the chelate ring does not play any important role, as it also may be expected from the low values of dihedral angles[10].

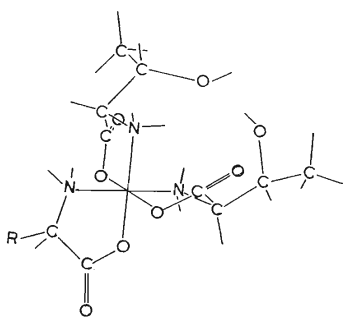

FIG. 2

Arrangement of OH Groups in Λ-*mer*-[Co((2*S*,3*S*)-(Thr)$_3$] from the Standpoint of Hydrogen Bond Formation (R = —CH.(CH_3)OH)

EXPERIMENTAL

Materials. (*S*)-Serine ($[\alpha]_D$ −7·8°, in water) and (2*S*,3*S*)-threonine ($[\alpha]_D$ −29°, in water) were products of Fluka, Switzerland. Norrit A was used as the activated charcoal.

Apparatus. The electronic absorption spectra were measured on a Specord UV VIS apparatus (Carl Zeiss, Jena). The circular dichroism spectra were recorded on a Roussel Jouan 185 Model II apparatus.

Preparation of Complexes

$[Co(NH_3)_6](NO_3)_3$ (0·01 mol) was dissolved in water (60 ml). The appropriate amino acid (0·03 mol) and activated charcoal (0·7 g) were then added to the solution. The whole mixture was heated with constant stirring at 80—90°C for 8 h under a reflux condenser, cooled down, and filtered at room temperature through a sintered-glass funnel. The solid on the filter was washed with water and then dissolved in concentrated hydrochloric acid. The solution was diluted with water to deposit the Λ-*mer* isomer which was collected with suction, washed with water and ethanol, and air-dried:

Λ-*mer*-$[Co((S)\text{-Ser})_3]$. For $C_9H_{18}CoN_3O_9$ (371·2) calculated: 29·12% C, 4·89% H, 11·33% N; found: 28·98% C, 4·98% H, 11·46% N. Electronic absorption spectrum (concentrated hydrochloric acid): 530 nm (ε 101), 375 nm (ε 170).

Λ-*mer*-$[Co((2S,3S)\text{-Thr})_3]$. For $C_{12}H_{24}CoN_3O_9$ (413·3) calculated: 34·04% C, 5·85% H, 10·18% N; found: 34·85% C, 5·98% H, 10·09% N. Electronic absorption spectrum (concentrated hydrochloric acid): 530 nm (ε 100), 375 nm (ε 136).

The filtrate after removal of the Λ-*mer* isomer was passed through a column of Dowex 50 WX8 (H^+) ion exchange resin (100—200 mesh) and the effluent evaporated with a small amount of alumina. A suspension of the residue in the appropriate solvent mixture (6 : 4 acetone–water in the case of serine complexes; 6 : 4 1-propanol–water in the case of threonine complexes) was applied to a dry column (2 × 30 cm) of alumina and the column eluted with the above mentioned solvent mixtures. The *mer* isomers were eluted prior to the *fac* isomers. Evaporation of the eluate fractions afforded the following substances:

Δ-*mer*-$[Co((S)\text{-Ser})_3]$. For $C_9H_{18}CoN_3O_9 \cdot 2\,H_2O$ (408·3) calculated: 26·72% C, 5·43% H, 10·30% N; found: 27·00% C, 5·23% H, 10·39% N. Electronic absorption spectrum (water): 530 nm (ε 105), 375 nm (ε 145).

Δ-*fac*-$[Co((S)\text{-Ser})_3]$. For $C_9H_{18}CoN_3O_9 \cdot 2\,H_2O$ (408·3) calculated: 26·72% C, 5·43% H, 10·30% N; found: 26·69% C, 5·50% H, 10·19% N. Electronic absorption spectrum (water): 525 nm (ε 210), 370 nm (ε 210).

Δ-*mer*-$[Co((2S,3S)\text{-(Thr)}_3]$. For $C_{12}H_{24}CoN_3O_9 \cdot 3\,H_2O$ (467·4) calculated: 30·89% C, 6·46% H, 8·99% N; found: 31·02% C, 6·06% H, 9·01% N. Electronic absorption spectrum (water): 530 nm (ε 100), 375 nm (ε 142).

Δ-*fac*-$[Co((2S,3S)\text{-(Thr)}_3]$. For $C_{12}H_{24}CoN_3O_9 \cdot 2\,H_2O$ (449·3) calculated: 32·07% C, 6·28% H, 9·36% N; found: 32·19% C, 6·09% H, 9·53% N. Electronic absorption spectrum (water): 525 nm (ε 208), 375 nm (ε 209).

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REFERENCES

1. Corey E. J., Bailar J. C. jr: J. Amer. Chem. Soc. *81*, 2620 (1959).
2. Ogston A. G.: Nature *162*, 963 (1948).
3. Jursík F.: This Journal *38*, 3811 (1973).
4. Jursík F.: Unpublished results.
5. Yamatera H.: Bull. Chem. Soc. Jap. *31*, 95 (1958).
6. McCaffery A. J., Mason S. F., Ballard R. E.: J. Chem. Soc. *1965*, 2883.
7. McCaffery A. J., Mason S. F., Norman B. J.: J. Chem. Soc. *1965*, 5094.
8. Dunlop J. H., Gillard R. D.: J. Chem. Soc. *1965*, 6531.
9. International Union of Pure and Applied Chemistry (IUPAC): Nomenclature of Inorganic Chemistry; Inorg. Chem. *9*, 1 (1970).
10. Sargeson A. M. in the book: *Transition Metal Chemistry* (R. L. Carlin, Ed.), Part 3, p. 314. Dekker, New York 1966.

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