SYNTHESIS AND PROPERTIES OF $[Co(NH_3)_2(AB)_2]Cl$ COMPLEXES AND THEIR POSSIBLE ROLE IN THE FORMATION OF TRIS(AMINO-ACIDATO)COBALT(III) ISOMERS STUDIED THROUGH REACTION STEREOCHEMISTRY

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The preparation is described and the electronic absorption, ^1H NMR, and CD spectral patterns are reported for $[Co(NH_3)_2(AB)_2]Cl$ complexes, where AB is glycine (4 isomers of the complex), (*S*)-alanine (5 isomers), or (*S*)-valine (2 isomers). The isomers are intermediate products in the substitution reaction $[Co(NH_3)_6]^{3+} \xrightarrow{AB} [Co(NH_3)_2(AB)_2]^+ \xrightarrow{AB} [Co(AB)_3]$ and undergo activated charcoal-catalyzed disproportionation $[Co(NH_3)_2(AB)_2]^+ \rightarrow [Co(NH_3)_4(AB)]^{2+} +$ $+ [Co(AB)_3]$, and in the presence of amino acid, also substitution resulting in a preferential formation of *mer*-$[Co(AB)_3]$ isomers. The Δ isomers yield predominantly Δ-$[Co(AB)_3]$. Due to the disproportionations, and also isomerizations, of the $[Co(NH_3)_2(AB)_2]^+$ complexes, no straightforward relation exists between the geometry of these complexes and the *mer*-to-*fac* ratio of the final $[Co(AB)_3]$ compounds.

A number of method are available for the synthesis of cobalt(III) amino acids complexes. One of them, in which $[Co(NH_3)_6]^{3+}$ and the amino acid concerned (AB) are used as the starting material, relies on the substitution reaction proceeding by the route

$$[Co(NH_3)_6]^{3+} \xrightarrow{AB} [Co(NH_3)_4(AB)]^{2+} \xrightarrow{AB} [Co(NH_3)_2(AB)_2]^+ \rightarrow \xrightarrow{AB} [Co(AB)_3] .$$

It has been found previously[1] that rather than being purely statistical, the ratio of the $[Co(AB)_3]$ isomers so obtained is to an extent dependent on the nature of the side chain in the α-amino acid. In view of the fact that the intermediate $[Co(NH_3)_2.(AB)_2]^+$ complexes can occur in five geometrical forms, investigation of the substitution reactions in question can add to our understanding of the factors controlling the formation of the individual isomers of $[Co(AB)_3]$.

In the present work, the preparation and the structure of the intermediate products are reported, and the stereochemistry of the final step of the above substitution reac-

tion is studied for amino acids differing by the steric nature of the alkyl groups at the α-carbon atom.

EXPERIMENTAL

Apparatus. The electronic absorption spectra were measured on a Specord UV VIS spectrophotometer (Carl Zeiss, Jena), the CD spectra, on a Roussel–Jouan Dichrograph. The ^{1}H NMR spectra were scanned on a Varian XL 100 A instrument using tetramethylsilane as external standard. The electrophoresis, in 0·05M-$NaClO_4$, was performed on an apparatus of Carl Zeiss, Jena, at 300 V and 20 mA using a paper Whatman No 1.

Isomers of $[Co(NH_3)_2(AB)_2]Cl$ (AB = glycine, (*S*)-alanine, or (*S*)-valine) were prepared and separated on a cation exchanger column (Dowex 50WX8, 100–200 mesh, Na^+ cycle, elution with 0·3M-NaCl) according to Kobayashi and Shibata[2].

The substitution reactions were performed so that 4 mmol of the amino acid with 0·1 g of activated charcoal (Norit A), or the same amount of its sodium salt, was added to the equimolar quantity of the proper $[Co(NH_3)_2(AB)_2]$ isomer in 25 ml of water, the constantly stirred mixture was heated at 60°C under reflux, and after a time cooled, filtered over a glass filter, and transferred onto a column of cation exchanger (Dowex 50WX8, 100–200 mesh, Na^+ cycle). The *mer* and *fac*-$[Co(AB)_3]$ isomer mixture was separated by elution with water. Either band was collected separately, concentrated, and poured onto a column of anion exchanger (Dowex 2X8, 100–200 mesh, Cl^- cycle). By eluting with water, concentrating the eluate in vacuum, and diluting to a known volume, solutions were obtained containing the *mer* and *fac* isomers of $[Co(AB)_3]$. The substances were characterized by their absorption spectra and, for (*S*)-alanine and (*S*)-valine, by their molar optical rotation. The λ_{max} positions (nm) together with the absorptivities (in parentheses) were as follows: $[Co(Gly)_3]$: *mer* 374 (145), 545 (98); *fac* 370 (165), 540 (180); $[Co((S)\text{-}Ala)_3]$: Λ-*mer* 375 (155), 545 (108), $[M]_D = +3\,845°$; Δ-*mer* 375 (96), 545 (62), $[M]_D = -3\,419°$; Δ-*fac* 375 (145), 535 (190), $[M]_D = -2\,356°$; $[Co((S)\text{-}Val)_3]$: Δ-*mer* 375 (157), 548 (100), $[M]_D = -3\,676°$; Δ-*fac* 376 (148), 535 (153), $[M]_D = -2\,056°$. The data are consistent with published values[3,4].

The band adsorbed on the cation exchanger was washed out (separated) by elution with 0·3M-NaCl, and the isomer obtained was characterized by its absorption spectrum (and, where appropriate, its molar optical rotation). The concentration of the $[Co(Gly)_3]$ isomers in eluate was determined photometrically. The filter cake arising from the filtration of the activated charcoal was extracted with hot water. For (*S*)-alanine, the Λ-*mer* isomer was obtained. By extracting the residue on the glass filter with H_2SO_4 (2 : 1) and diluting the solution with water, Λ-*fac* isomers of $[Co((S)\text{-}Ala)_3]$ and $[Co((S)\text{-}Val)_3]$ were isolated.

Disproportionation of $[Co(NH_3)_2(Gly)_2]Cl$ was carried out with the isomers by the above procedure with an addition of activated charcoal in the absence of glycine. The reaction mixture was separated and further proceeded as above.

Disproportionation of $[Co(NH_3)_4Gly]Cl_2$: approximately 0·1 g of the starting complex[5] was dissolved in 25 ml of water, activated charcoal was added, and the constantly stirred mixture was heated under reflux at 60°C for 20 min and filtered. Electrophoresis of filtrate, using detection with Na_2S, revealed the presence of substances with charges of 0, +1, and +2. The filtrate was transferred onto a cation exchanger and the neutral complexes were washed out with water. The eluates were worked up as above.

RESULTS AND DISCUSSION

A $[Co(NH_3)_2(AB)_2]^+$ complex cation (AB is amino acid anion) can exist theoretically in five geometrical isomers: *cis*(N)-*cis*(O)-*cis*$(NH)_3$, *cis*(N)-*trans*(O)-*cis*(NH_3), *trans*(N)-*cis*(O)-*cis*(NH_3), *cis*(N)-*cis*(O)-*trans*(NH_3), and *trans*(N)-*trans*(O)-*trans*.(NH_3); of these, the *cis*(NH_3) isomers occur as enantiomer (diastereoisomer) pairs with respect to the chelate ring distribution. They can be prepared by a direct oxidation of cobalt(II) salt in the presence of ammonia and amino acid. For glycine, Kobayashi and Shibata[2] isolated the *trans*(N)-*cis*(O)-*cis*(NH_3), *cis*(N)-*cis*(O)--*cis*(NH_3), and *cis*(N)-*cis*(O)-*trans*(NH_3) isomers; we were able to isolate an additional isomer, *viz.* *cis*(N)-*trans*(O)-*cis*(NH_3). Other complexes synthesized by us and as yet unreported in the literature were four isomers with (*S*)-alanine and two with (*S*)-valine. The survey of the complexes prepared (the elemental analysis, the yields, and the spectral data) are given in Tables I and II. For none of the amino acids used was synthesized the *trans*(N)-*trans*(O)-*trans*(NH_3) isomer. The preparation also failed of the $(+)_{589}$-*cis*(N)-*trans*(O)-*cis*(NH_3) isomers with alanine and valine and of the $(+)_{589}$ and $(-)_{589}$-*cis*(N)-*trans*(O)-*cis*(NH_3), $(+)_{589}$-*trans*(N)--*cis*(O)-*cis*(NH_3), and $(+)_{589}$-*cis*(N)-*cis*(O)-*cis*(NH_3) and *trans*(NH_3) isomers of $[Co(NH_3)_2((S)\text{-Val})_2]^+$. We ascribed the absence of these isomers to their lability

TABLE I

Results of elemental analysis of the $[Co(NH_3)_2(AB)_2]Cl.x\ H_2O$ complexes prepared

Label	AB	x	M_r	% C		% H		% N	
				calc.	found	calc.	found	calc.	found
G_1	Gly	2	312·6	15·38	16·11	5·78	5·46	17·92	18·00
G_2	Gly	2	312·6	15·38	15·43	5·78	5·27	17·92	18·20
G_3	Gly	0·5	285·6	16·87	16·51	5·30	5·18	19·67	19·67
G_4	Gly	1·5	303·6	15·86	15·92	5·64	5·20	18·49	18·21
A_1	Ala	0	304·6	23·55	23·56	5·93	6·06	18·42	17·53
A_2	Ala	1	322·6	22·38	22·30	6·22	5·93	16·78	16·99
A_3	Ala	0·5	313·6	23·00	22·96	6·08	6·19	17·90	18·18
A_4	Ala	1·5	331·6	21·75	21·37	6·34	5·92	16·93	16·99
A_5	Ala	2	340·6	21·20	21·29	6·48	6·04	16·47	16·54
V_1	Val	2[a]	410·9	29·21	29·26	7·30	7·33	13·63	13·55
V_2	Val	2	396·7	30·18	30·23	7·56	7·58	14·13	14·02

[a] $[Co(NH_3)_2(Val)_2]Cl.2\ H_2O.0{\cdot}25\ NaCl$.

and reactivity (*vide infra*) rather than to a different instability of the isomers of which no rationale exists based on intramolecular nonbonding interactions between the side chains of the amino acids.

The order in which the geometrical isomers eluted from the cation exchanger column was not governed by the nature of the AB ligand; rather, this order seems to be given by their polarity. Similarly as in other instances[6], the *trans*(O) isomers are eluted before the *cis*(O) isomers (the position of the NH_3 group apparently has no effect on the elution order): *trans*(O) > *cis*(O)-*trans*(N) > *cis*(O)-*cis*(N) > > *cis*(O)-*cis*(N)-*trans*(NH_3). In case that the stereoisomers also separated, the $(-)_{589}$ isomers were eluted before the $(+)_{589}$ isomers; in the former, the methyl or isopropyl groups at the α-carbon atoms of alanine or valine are in the axial position, which, in comparison with the $(+)_{589}$ isomers, leads to more pronounced steric interactions with the ion exchanger matrix and, consequently, to a less strong retention.

Identification of Isomers

The geometry of the isomers was elucidated based primarily on their electronic

TABLE II

Yields, absorption band positions $\tilde{\nu}$ and intensities ε (1 mol^{-1} cm^{-1}) for $[Co(NH_3)_2(AB)_2]^+$ complexes

Complex		Yield	$\tilde{\nu}_1$	ε_1	$\tilde{\nu}_2$	ε_2	$\varepsilon_2/\varepsilon_1$
label	isomer (N)—(O)—(NH_3)	%	cm^{-1}		cm^{-1}		
G_1	*cis-trans-cis*	3	18 400 sh	68·6	27 520	95·6	1·39
G_2	*trans-cis-cis-*	45	20 080	77·6	27 960	116·2	1·50
G_3	*cis-cis-cis*	47	19 480	90·6	27 660	107·4	1·19
G_4	*cis-cis-trans*	5	19 700	87·0	28 220	47·3	0·54
A_1	*cis-trans-cis*[a]	2	18 500 sh	87·1	27 400	114·9	1·32
A_2	*trans-cis-cis*[a]	15	20 270	92·7	28 030	128·2	1·38
A_3	*trans-cis-cis*[b]	17	20 210	95·0	27 920	136·0	1·43
A_4	*cis-cis-cis*	61	19 520	114·6	27 840	126·0	1·10
A_5	*cis-cis-trans*	5	19 800	117·4	28 220	57·1	0·49
V_1	*trans-cis-cis*[a]	—	20 260	88·3	28 020	129·9	1·47
V_2	*cis-cis-cis*[a]	—	19 480	114·6	27 560	128·4	1·11

Sign of rotation: [a] $(-)_{589}$; [b] $(+)_{589}$.

absorption and ^1H NMR spectra, which are consistent with the C_1 and C_2 symmetry of the isomers. The electronic spectra (Fig. 2, Table II) exhibit the characteristic excited state splitting corresponding to the $T_{1g}(O_h)$ state, by which the *trans*(O) and *cis*(O) isomers differ[7]. The absorption bands of the *cis* isomers are symmetrical, and the band shape does not point to any effective symmetry lower than O_h. The different symmetry of the *cis*(O) isomers is manifested by higher absorptivities for the C_1-*cis*(O) isomers, shift to higher energies of the bands corresponding to the T_{1g} transition for the C_2-*cis*(O) isomers, and different ratios of the absorptivities of the first and the second absorption bands (Table II). In comparison with the analogous isomers[8] of $[Co(en)(Gly)_2]^+$ and $[Co(en)((S)\text{-}Ala)_2]^+$ (CoN_4O_2 chromophor), the maxima of the first absorption bands (T_{1g}) of the $[Co(NH_3)_2(AB)_2]^+$ complexes are shifted to lower energies owing to the lower NH_3 ligand field strength as compared with ethylenediamine. As to the absorption band intensity, the absorptivities of the $[Co(NH_3)_2(AB)_2]^+$ isomers are lower than those of the $[Co(en)_2(AB)_2]^+$ complexes, obviously because the former complexes, with two monodentate ligands, are less rigid than the latter complexes involving the single ethylenediamine ring.

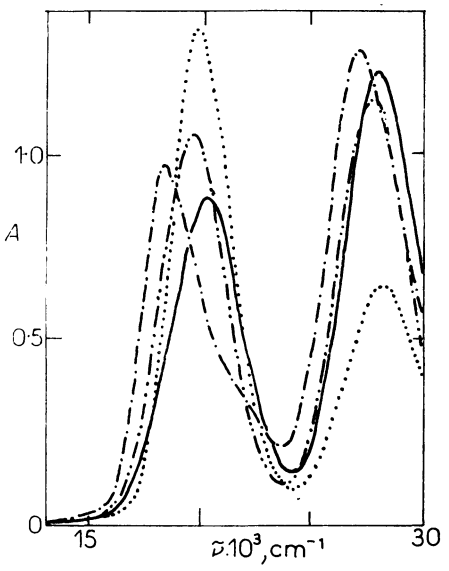


FIG. 1

Electronic absorption spectra of $[Co(NH_3)_2((S)\text{-}Ala)_2]ClO_4$ isomers. -·-·-·- $(-)_{589}$-*trans*(O), ——— $(-)_{589}$-C_2-*cis*(O), ····· *trans*(NH_3), -··-··- $(\pm)_{589}$-C_1-*cis*(O)

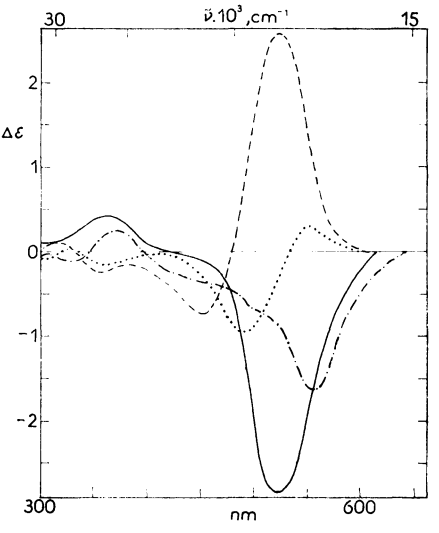


FIG. 2

CD spectra of $[Co(NH_3)_2((S)\text{-}Ala)_2]ClO_4$ isomers. -·-·-·- Δ-*trans*(O), ——— Δ-C_2-*cis*(O) – – – – – Λ-C_2-*cis*(O), ····· *trans*(NH_3)

The identification of the isomers is confirmed by their ^{1}H NMR spectra (Table III), where the difference between the C_1-*cis*(O) and C_2-*cis*(O) isomers is particularly apparent. The nonequivalence of the chelate rings in the C_1 isomers is characterized, for the glycine complexes, by the occurrence of two singlets corresponding to the hydrogen atoms of the CH_2 group[2]; the singlet at 3·56 ppm of C_1-*cis*(O)-$[Co(en).(Gly)_2]^+$ has been attributed[9] to H_a atoms (*I*), the singlet at 3·44 ppm, to H_b atoms. The same should apply to the complexes of alanine and valine, where the quadruplet (α-CH in alanine) and doublet (β-CH in valine) at higher fields can be attributed to ring B, the signals at lower fields, to ring A. Taking into account the C—N bond anisotropy effect on the signal position (ref.[10]), the CH_3 group in alanine, which in the Λ isomer is directed along the C—N bond due to its equatorial orientation, is shielded and its protons resonate at higher fields as compared with the Δ isomer (1·51 ppm for the C_2-*cis*(O) isomer, 1·41 – 1·44 ppm doublet pair for the mixture

TABLE III

Signal positions (ppm) in the ^{1}H NMR spectra of $[Co(NH_3)_2(AB)_2]^+$ complexes; multiplicity: s singlet, d doublet, q quadruplet, m multiplet

Isomer (N)—(O)—(NH_3)	Symmetry	Protons		
AB = Gly		CH_2		
cis-trans-cis	C_2	3·58 s		
trans-cis-cis	C_2	3·66 s (3·71 s)[a]		
cis-cis-cis	C_1	3·44 s 3·56 d (3·49 s 3·62 s)[a]		
cis-cis-trans	C_2	3·39 s (3·44 s)[a]		
AB = (*S*)-Ala		α-CH	CH_3	
cis-trans-cis (Δ)	C_2	3·94 q	1·47 d	
trans-cis-cis (Δ)	C_2	3·87 q	1·55 d	
trans-cis-cis (Λ)	C_2	3·90 q	1·51 d	
cis-cis-cis[b]	C_1, C_1	3·50—4·00	1·41 d 1·44 d 1·49 d 1·47 d	
cis-cis-trans	C_2	3·80 q	1·40 d	
AB = (*S*)-Val		α-CH	β-CH	$CH(CH_3)_2$
trans-cis-cis (Δ)	C_2	3·77 d	2·34 m	0·92 d 1·19 d
cis-cis-cis (Δ)	C_1	3·37 d 3·64 d	2·23 m 2·90 m	0·92 d 1·02 d 0·99 d 1·12 d

[a] Ref.[2]; [b] mixture of diastereoisomers.

of the C_1-*cis*(O) isomers). Clearly, then, NMR can serve also for determining the absolute configuration of the C_2-*cis*(O)-$[Co(NH_3)_2((S)\text{-Ala})_2]^+$ isomers separated into their diasteroisomers, and also the C_1-*cis*(O) isomers. The NMR spectra were also used for establishing the Λ-to-Δ ratio fo the C_1-*cis*(O)-$[Co(NH_3)_2((S)\text{-Ala})_2]^+$ isomers, which, as mentioned above, could not be separated chromatographically; based on the areas corresponding to the doublets due to the CH_3 groups, the Λ-to-Δ ratio was found to be 53 : 47.

The circular dichroism spectra (Fig. 2, Table IV) are split to a greater extent than the electronic absorption spectra; while the latter spectra of the *cis*(O) isomers fail to reveal the presence of two components (the first absorption band is nearly sym-

TABLE IV

Circular dichroism data for cobalt(III) complexes containing (*S*)-alanine or (*S*)-valine

Isomer	Band I region		Band II region	
	$\tilde{\nu}_{max}$ / cm^{-1}	Δε	$\tilde{\nu}_{max}$ / cm^{-1}	Δε
	$[Co(NH_3)_2((S)\text{-Ala})_2]Cl$			
Δ-*trans*(O)	18 300	−1·51	27 400	+0·25
Λ-C_2-*cis*(O)	19 000	+2·54	27 900	−0·23
	21 900	−0·73	31 700	+0·10
Δ-C_2-*cis*(O)	19 200	−2·86	27 800	+0·39
cis(N)-*cis*(O)-*trans*(NH_3)	18 400	+0·28	27 800	−0·14
	20 500	−0·77		
	$[Co(en)((S)\text{-Ala})_2]ClO_4$[a]			
Δ-*trans*(O)	18 300	−2·63	27 800	+0·36
Λ-C_2-*cis*(O)	19 500	+4·26	29 500	+0·25
	22 100	−1·07		
Δ-C_2-*cis*(O)	19 700	−3·67	27 800	+0·33
	$[Co(NH_3)_2((S)\text{-Val})_2]Cl$			
Δ-C_2-*cis*(O)	19 200	−2·94	27 900	+0·41
Δ-C_1-*cis*(O)	19 100	−2·79	25 400	−0·09
			27 900	+0·18
			31 400	−0·10

[a] Ref.[8].

metrical), the circular dichroism spectrum of the Λ-C_2-*cis*(O) isomer exhibit two bands of opposite sign in the T_{1g} transition region.

Except for the *trans*(NH_3) isomers, the CD spectra are dominated by the configurational chirality, which enables Mason's model[11-13] to be employed based on the relative intensities of the low-energy CD bands for *cis*(NH_3) and (+)-$[Co(en)_3]^{3+}$ as the standard, extrapolating from the D_3 symmetry to the approximate C_2 symmetry for isomers with the CoN_4O_2 chromophor. The dominant low-energy band of $[Co(en)_3]^{3+}$ with ^1E_a parity corresponds to the $^1A_2(C_2)$ state. This state, derived from a component of the $^1E_a(D_{4h})$ state, has a wave function invariant in the series $[Co(en)_3]^{3+}$, *cis*-$[Co(NH_3)_4L_2]^{n+}$, *cis*-$[Co(en)_2L_2]^{n+}$, and thus can be employed for the determination of the absolute configuration. If the ^1E_a, and thus the $^1A_1 \rightarrow {}^1A_2(C_2)$, transition has the positive sign, then the $[Co(NH_3)_2(AB)_2]^+$ complex (AB = Ala or Val) possesses the absolute Λ configuration. The absolute configurations so elucidated are consistent with those determined by the ring pairing method[14] and by the octant rule[15].

The configurational CD curves, reflecting the different geometry of the complexes, have the same shape as those of the $[Co(en)((S)\text{-}Ala)_2]^+$ isomers[8]. A principal difference between the CD spectra of the two series is in the (T_{1g}, O_h) rotatory strength. The $[Co(en)((S)\text{-}Ala)_2]^+$ isomers exhibit a higher relative intensity (Table IV) due to the fact that in this compound, three pairs of chelate rings of the same chirality, $\Lambda\Lambda\Lambda$, contribute to the configuration, as against the single contribution in the $[Co(NH_3)_2((S)\text{-}Ala)_2]^+$ complexes. The same conclusion should be valid for the valine complexes, although the comparison cannot be made experimentally.

The *cis*(N)-*cis*(O)-*trans*(NH_3)-$[Co(NH_3)_2((S)\text{-}Ala)_2]^+$ isomer, free of configurational chirality, displays vicinal circular dichroism only. The CD spectrum consists of two bands, the sign of which (proceeding from lower to higher energies) is + and −, respectively. The course and the intensity of the vicinal effect correspond to the calculated CD curve[8] for C_2-*cis*(O)-$[Co(en)((S)\text{-}Ala)_2]^+$.

Substitution and Disproportionation Reactions

Substitution of NH_3 groups in $[Co(NH_3)_6]^{3+}$ by amino acid is a consecutive reaction, the penultimate stage of which is the formation of $[Co(NH_3)_2(AB)_2]^+$ intermediates. With glycine, these isomers – similarly as $[Co(Gly)_3]$ – are enantiomers by nature, and so in the ultimate stage of the substitution reaction only the properties following from the different geometry of the coordination sphere can play a role. By contrast, the $[Co(AB)_3]$ complexes with (*S*)-alanine and (*S*)-valine are diastereoisomers, and this manifests itself in the different stability of the Λ and Δ isomers.

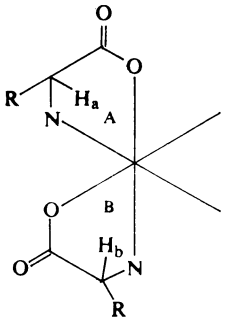
The NH_3 groups in the *cis*(NH_3) isomers of $[Co(NH_3)_2(AB)_2]^+$ are subject to substitution resulting in $[Co(AB)_3]$ isomers in a theoretical ratio of *mer* : *fac* = = 3 : 1:

$$trans(N)\text{-}cis(O)\text{-}cis(NH_3) \xrightarrow{AB} mer\text{-}[Co(AB)_3] \qquad (A)$$

$$cis(N)\text{-}trans(O)\text{-}cis(NH_3) \xrightarrow{AB} mer\text{-}[Co(AB)_3] \qquad (B)$$

$$cis(N)\text{-}cis(O)\text{-}cis(NH_3) \xrightarrow{AB} mer\text{- and } fac\text{-}[Co(AB)_3] \qquad (C)$$

However, the experimental results obtained for the glycine complexes (Table V) show that the substitution leads to a higher *mer*-to-*fac* ratio than as corresponds to the theory, the facial isomer being formed also where the formation of the meridional isomer is only allowed by the initial isomer's structure (reactions (*A*) and (*B*)).



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This suggests that the substitution is accompanied by disproportionation (in the ligand sense) of the starting complexes, and possibly also by their isomerization. This is borne out by the fact that isomers with the NH_3 groups in the *trans* position (G_4) also undergo substitution. To prove this concept, the reactions of the isomers with activated charcoal were studied in the absence of amino acid. As documented by the data of Table V, the formation of the *mer* isomer, which can only be a result of a mere disproportionation of the complex, prevails in all cases. Thus it can be claimed that the synthesis of $[Co(Gly)_3]$ complexes comprises, in addition to the substitution of the NH_3 groups in $[Co(NH_3)_2(Gly)_2]^+$ by a glycine molecule, also disproportionation of the starting complex,

$$2\,[Co(NH_3)_2(Gly)_2]^+ \rightarrow [Co(NH_3)_4(Gly)]^{2+} + [Co(Gly)_3]$$

which leads to a mixture of the *mer* and *fac* isomers with a prevalence of the former. The substitution reaction is additionally complicated by $[Co(NH_3)_4(Gly)]^{2+}$ undergoing nonstoichiometric decomposition in the presence of activated charcoal; in the formed mixture of $[Co(Gly)_3]$ and $[Co(NH_3)_2(Gly)_2]^+$, the latter, in the presence

of glycine and activated charcoal, can undergo substitution, disproportionation, or isomerization. The above processes are likely to occur also with the complexes of (*S*)-alanine and (*S*)-valine, where, however, they could not be studied because of lack of the individual complexes in sufficient amounts. This concept is supported by the presence of Λ-*mer*-[Co((*S*)-Ala)$_3$] in the reaction mixture, although the starting complex was in the Δ configuration (the reactions conducted in the absence of activated charcoal resulted in racemic mixtures).

The substitution and disproportionation lability of the various isomers is not the same, the *trans*(NH_3) isomers with glycine and alanine being undetectable even

TABLE V

Products of substitution and disproportionation reactions of $[Co(NH_3)_2(AB)_2]Cl$ isomers

Starting complex	Ligand	Reaction period min	$[Co(AB)_3]$ *mer*-to-*fac* ratio	Side products
G_1	Gly[a]	7	20 : 1	$G_1 + G_3$
G_1	Gly[a]	20	1 : 1·5	—
G_1	—[a]	30	20 : 1	$G_1 + G_3$
G_2	Gly[a]	20	1 : 2·3	$G_2 + G_3$
G_2	Gly[a]	90	1 : 7·7	—
G_2	—[a]	20	10 : 1	G_2
G_2	—[a]	90	10 : 1	G_2
G_2	Gly[b]	45	2·3 : 1	G_2
G_2	Gly[b]	240	1 : 30	G_2
G_2	—[b]	90	1 : 41	G_2
G_3	Gly[a]	20	2 : 1	$G_1 + G_3$
G_3	Gly[a]	90	1 : 4·7	—
G_3	—[a]	40	9 : 1	$G_1 + G_3$
G_3	Gly[b]	20	25 : 1	$G_1 + G_3$
G_3	Gly[b]	60	82 : 1	G_3
G_3	—[b]	30	11 : 1	$G_1 + G_3$
G_4	Gly[a]	15	7 : 1	G_3
G_4	Gly[a]	30	5 : 1	—
G_4	—[a]	40	9 : 1	G_3
A_1	(*S*)-Ala[a]	40	Δ-*fac*	—
A_2	(*S*)-Ala[a]	40	Δ-*mer* > > Λ-*mer*	—
V_1	(*S*)-val[a]	40	Δ-*mer*	—

[a] In the presence of activated charcoal; [b] sodium salt of glycine.

in 10 min of reaction. Moreover, the *cis*(N)-*cis*(O)-*cis*(NH_3) and *trans*(N)-*cis*(O)-*cis*(NH_3) isomers occur as by-products in virtually each substitution and disproportionation (Table V), thus appearing to be the most stable of the isomers studied. Their resistance to substitution and disproportionation is documented also by the two isomers being present in the reaction mixture for the preparation of $[Co(NH_3)_2.(AB)_2]^+$ in the highest proportions (Table II). Conversely, the *cis*(N)-*trans*(O)-*cis*(NH)$_3$ and *trans*(NH_3) isomers, whose yields are lowest, undergo substitution and disproportionation most readily.

In the activated charcoal-catalyzed substitutions, isomerization of both the starting complexes and the final reaction products is conceivable; in fact, however, isomerization of the former is not very likely, $[Co(Gly)_3]$ being present in the mixture in addition to the "isomerization product" and thus indicating that the "isomeric" $[Co(NH_3)_2(Gly)_2]^+$ product arises by disproportionation rather than isomerization. The final isomer ratio for $[Co(AB)_3]$, on the other hand, will be affected by their isomerization taking place in the presence of activated charcoal. The isomerization is specific, to an extent, for each AB ligand; for instance, the activated charcoal-catalyzed isomerization of *fac*-$[Co(Gly)_3]$ gives, in 90 min, a *mer*-to-*fac* ratio of 1·5 : 1, whereas that of Λ-*mer*-, Δ-*fac*-, and Δ-*mer*-$[Co((S)\text{-Ala})_3]$ gives the Λ-*fac* isomer solely[3]. The Λ-*mer*, Δ-*mer*, and Δ-*fac* isomers of $[Co((S)\text{-Val})_3]$ yield mixtures of Δ-*mer* with Δ-*fac*, in which the former isomer predominates. As visualized by models, for the valine complexes it is the Δ-*mer* isomer in which the isopropyl groups of the side chains exert the least steric interaction.

In conclusion, activated charcoal-catalyzed substitution reactions of $[Co(NH_3)_6]^{3+}$ with amino acids involve, owing to the lability of the coordinated NH_3 groups, also disproportionations and formation of nonspecific intermediate products, $[Co(NH_3)_4.(AB)]^{2+}$, which can affect significantly the $[Co(AB)_3]$ *mer*-to-*fac* ratio as well as their own isomerizations. As a consequence, no straightforward relation exists between the formation of isomers of $[Co(AB)_3]$ and the structure of the intermediate products.

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