SYNTHESIS AND KINETICS OF ISOMERIZATION OF *mer*- AND *fac*-[$CoCO_3$(en)(AMINO ACIDATO)] ISOMERS

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Received March 31, 1995
Accepted May 8, 1995

Dedicated to Professor Otakar Cervinka on the occasion of his 70th birthday.

Reaction of $[CoXY(en)(AB)]^{n+}$ (AB = glycinato or (*S*)-α-alaninato anion, X = H_2O, Y = Cl; AB = (*S*)-valinato anion, X = Y = Cl) with HCO_3^- or Ag_2CO_3 gives mixture of *mer*- and *fac*-[$CoCO_3$(en)(AB)] isomers, ratio of which is temperature dependent. Both isomers undergo in aqueous solution to spontaneous isomerization which does not occur when carbonato group is replaced by oxalato or malonato one. This suggests that the source of stereolability in these complexes is a strain imposed by the four-membered carbonato chelate ring. The equilibrium constants (K = *fac*/*mer*) increase in the order $K_{Gly} < K_{Val} < K_{Ala}$. The total rate constants obtained at 45 °C and 55 °C increase in the order $k_{Ala} < k_{Val} < k_{Gly}$. Λ-*mer*-[$CoCO_3$(en)(*S*)-Val)] isomer undergoes at 22 °C racemization at the octahedral centre yielding the mixture of 59% Δ and 41% Λ isomers.

Several years ago the inversion at the octahedral centre of the Λ-C_1-*cis*(*N*)-[$CoCO_3$((*S*)-Val)$_2$]$^-$ isomer* during the acid hydrolysis of the carbonate group was described[1]. In order to obtain more details on the stereochemistry of octahedral complexes which readily undergo to stereochemical changes during substitution reactions and are thus just spin-paired in their ground state (see for example ref.[2]), we studied[3,4] [$CoCO_3$((*S*)-Val)$_2$]$^-$ and [$CoCO_3$(eddval)]$^-$ isomers. The results obtained show that both synthesis and decarboxylation of the isomers is accompanied in the dependence on the geometry of the appropriate isomer with isomerization. To elucidate factors which may influence the stereochemistry of the carbonato complexes we started to study *mer*- and *fac*-[$CoCO_3$(en)(AB)] isomers. However, our attempt to obtain pure isomers failed due to the isomerization. Since the kinetic and mechanistic data available for the isomerization

* Abbreviations used: AB = amino acid anion. Ala, α-alanine; Gly, glycine; Val, valine; en, ethylenediamine; eddval, (2*S*,2′*S*)-2,2′-ethylenebis(2-amino-3-methylbutanoate). All amino acids (except for glycine) were of (*S*)-configuration.

of cobalt(III) complexes with the CoN_3O_3 chromophore are rather scanty, we report here the preparation of pure geometrical and optical $[CoCO_3(en)(AB)]$ isomers together with the kinetics of their isomerization (racemization).

RESULTS AND DISCUSSION

Preparation and Identification of Isomers

The synthesis of the carbonato complexes in question involves[5] the use of $[Co(NO_2)_2(en)(AB)]$ as starting material which undergoes in a further step to a reaction with excess of concentrated hydrochloric acid yielding in dependence of AB $[CoCl(H_2O)(en)(AB)]Cl$ (AB is Ala or Gly) and $[CoCl_2(en)(Val)]$. Fact, that the replacement of Gly or Ala chelate rings for Val leads to the formation of dichloro product instead of chloroaqua complex suggests that the steric hindrance plays important role in the substitution. In both chloro and chloroaqua complexes obtained, monodentate ligands are subjected to substitution by the carbonato group with the formation of $[CoCO_3(en)(AB)]$ which can exist as a pair of meridional and facial diastereomers (enantiomers in the case of Gly). When AB is Ala or Val, the appropriate dinitro complexes were isolated as insoluble or sparingly soluble Λ isomers. Absolute configuration of the Val complex was deduced from the positive dominant band (474 nm) observed in the circular dichroism spectrum (Fig. 1) corresponding to $^1A_{1g} \rightarrow {}^1T_{1g}$ octahedral transition.

Synthesis of carbonato complexes can be achieved by two synthetic routes. First one, already described in the literature[5] for Gly and (*R*,*S*)-Ala is based on the substitution reaction (*A*)

$$[CoXY(en)(AB)^{n+} \xrightarrow{HCO_3^-} [CoCO_3(en)(AB)] \qquad (A)$$

(X = H_2O, Y = Cl or X = Y = Cl) which leads generally to a mixture of *mer* and *fac* isomers, ratio of which strongly depends on experimental conditions. The second, more convenient synthesis, is described in this paper (Eq. (*B*)).

$$[CoXY(en)(AB)]^{n+} \xrightarrow{Ag_2CO_3} [CoCO_3(en)(AB)] \qquad (B)$$

In this reaction mixture 95 : 5 *mer* to *fac* isomers regardless of amino acid ligand was obtained. As far as the content of *fac* isomer in the reaction mixture is concerned, it depends on the isomeric purity of the starting complexes and/or on the isomerization of *mer* to *fac* form during the spontaneous aquation steps. Since the aqua products dis-

tribution largely reflects the stereochemistry of the reactant[6] and the ratio of [$CoCO_3$(en)(AB)] isomers is independent of AB, we assume that the presence of 5% of *fac* isomer in the reaction mixture corresponds to the original isomer distribution of chloroaqua and/or dichloro complexes.

Aquation is especially fast in the case of [$CoCl_2$(en)(Val)], dissolution of which, as can be inferred from the color change accompanying this process, proceeds only on account of simultaneous acid hydrolysis (reflectance and absorption spectra confirm this assumption). Furthermore, examination of the final products in the case of alanine and valine showed that substitution of XY in [CoXY(en)(AB)] represents stereoretentive step, so that chloroaqua and diaqua product have the same Λ configuration. This is supported by the inspection of the CD spectrum of *mer*-[$CoCO_3$(en)(Val)] which shows all three components of the first energy level (Fig. 1) suggesting that the inversion (i.e.

TABLE I
Electronic absorption spectra of *mer*- and *fac*-[$CoCO_3$(en)(AB)] isomers

Isomer	λ_1 nm	ε_1 mol^{-1} dm^3 cm^{-1}	λ_2 nm	ε_2 mol^{-1} dm^3 cm^{-1}
mer-[$CoCO_3$(en)(Gly)]	546.0	105.5	377.7	128.0
fac-[$CoCO_3$(en)(Gly)]	537.0	129.5	387.5	119.0
mer-[$CoCO_3$(en)((*S*)-Ala)]	545.5	100.0	377.5	117.0
fac-[$CoCO_3$(en)((*S*)-Ala)]	538.0	109.4	372.0	113.0
mer-[$CoCO_3$(en)((*S*)-Val)]	545.5	104.3	379.0	128.0
fac-[$CoCO_3$(en)((*S*)-Val)]	539.0	105.6	374.0	105.0

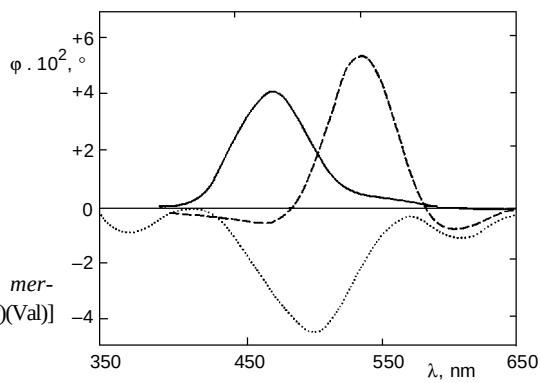

FIG. 1
The circular dichroism spectra of *mer*-[$CoCO_3$(en)(Val)] (– – –), *mer*-[$Co(NO_2)_2$(en)(Val)] (——), *mer*-[$CoCl_2$(en)(Val)] (· · ·)

negative sign band observed in the CD spectrum of aqueous solution of chloroaqua or diaqua complexes) may be purely difference in the intensity or a shift of levels from the dichloro to the carbonato species; that is, two negative and one positive peak apparently make up the first band.

Both *mer*- and *fac*-[$CoCO_3$(en)(AB)] isomers were obtained pure by chromatography of reaction mixture on cation exchange resin with water as an eluent and evaporation of eluates below 40 °C when spontaneous isomerization does not proceed. Meridional isomer due to its symmetry was eluted first[7].

Electronic absorption spectra of both geometrical isomers show the same pattern without apparent splitting of the first band of the *mer* isomer and differ one from each other only slightly in their ratio of absorption coefficients (Table I).

Kinetics of Isomerization

Both *mer*- and *fac*-[$CoCO_3$(en)(AB)] isomers in aqueous solution below 45 °C are quite stable and below this temperature can be isolated as pure isomers. At elevated temperature isomerization occurs with appreciable dependence on temperature i.e. amount of facial isomers increase with temperature up to 85 °C. Higher temperature causes decomposition.

Each of geometrical isomers undergoes at elevated temperature to isomerization and the composition of equilibrium mixture of *mer* and *fac* isomers (cf. Table II) does not depend on whether *mer* or *fac* isomer was equilibrated demonstrating thermodynamic character of isomers' distribution. Results given in Table II further show that facial alaninato isomer predominates in the equilibrium mixture in comparison with valinato one, suggesting that steric hindrance plays a role in the course of isomerization. Indeed, inspection of Dreiding stereomodels reveals that increased steric volume of valine side chain makes facial isomer less stable due to the closer contact of isopropyl side chain with hydrogen atoms of ethylenediamine amino group.

The rate constants of isomerization

$$mer\text{-}[CoCO_3(en)(AB)] \underset{k_2}{\overset{k_1}{\rightleftharpoons}} fac\text{-}[CoCO_3(en)(AB)] \qquad (C)$$

which is of the first order reaction, found after the separation of equilibrium mixture by spectrophotometric method, are together with equilibrium constants, ΔG and $\overline{E}_A$ values given in Table III. In all cases, triplicate runs gave straight-line plots of isomer concentrations vs time. From the comparison of the data obtained for diastereomers it follows that the complex of valine isomerizes faster than that of alanine. Such isomerization rate acceleration can be ascribed again to a greater extent of interference imposed by the valine isopropyl side chain. Furthermore, all [$CoCO_3$(en)(AB)] geometrical isomers

undergo at the elevated temperature, besides isomerization, the carbonato ring opening with the formation of aqua or diaqua complexes. Amount of these products increases logically in the series Gly < Ala < Val. Although results obtained do not allow to imply the mechanism of isomerization, fact that the complexes in which the carbonato group is replaced by the oxalato or malonato bidentate ligands do not isomerize under the same conditions suggests that the carbonato group is a source of stereolability in these complexes.

Successful preparation of a pure Λ- and Δ-[$CoCO_3$(en)(Val)] diastereomers made the study of racemization kinetics possible. At 22 °C racemization of Λ-*mer* isomer proceeds under the formation of an equilibrium mixture consisting of 59% Δ an 41% Λ isomers (K = 1.45, $k_{\Lambda\to\Delta} = 2.07 \cdot 10^{-5}\ s^{-1}$, $k_{\Delta\to\Lambda} = 0.85 \cdot 10^{-5}\ s^{-1}$). Racemization as can be expected proceeded without isomerization.

TABLE II
Equilibrium mixture and equilibrium constants of [$CoCO_3$(en)(AB)] isomers

AB	%*mer*	%*fac*	K
Gly	83.3	16.7	0.2048
Ala	66.9	33.1	0.4948
Val	74.1	25.9	0.3495

TABLE III
Kinetic and thermodynamic parameters of [$CoCO_3$(en)(AB)] *mer* $\underset{k_2}{\overset{k_1}{\rightleftharpoons}}$ *fac* isomerization

AB	t, °C	ΔG, J mol^{-1}	k^a, s^{-1}	k_1, s^{-1}	k_2, s^{-1}	$\bar{E}_A$, J mol^{-1}
Gly	45	4 194	$6.10 \cdot 10^{-5}$	$1.04 \cdot 10^{-5}$	$5.06 \cdot 10^{-5}$	5 908
	55	4 326	$1.08 \cdot 10^{-4}$	$1.84 \cdot 10^{-5}$	$8.96 \cdot 10^{-5}$	
	65	4 458	$1.83 \cdot 10^{-4}$	$3.11 \cdot 10^{-5}$	$15.19 \cdot 10^{-5}$	
Ala	45	1 861	$9.69 \cdot 10^{-6}$	$3.21 \cdot 10^{-6}$	$6.48 \cdot 10^{-6}$	14 835
	55	1 920	$4.02 \cdot 10^{-5}$	$1.33 \cdot 10^{-5}$	$2.69 \cdot 10^{-5}$	
	65	1 978	$1.53 \cdot 10^{-4}$	$5.06 \cdot 10^{-5}$	$10.24 \cdot 10^{-5}$	
Val	45	2 780	$2.21 \cdot 10^{-5}$	$5.72 \cdot 10^{-6}$	$1.64 \cdot 10^{-5}$	14 028
	55	2 868	$8.45 \cdot 10^{-5}$	$2.19 \cdot 10^{-5}$	$6.26 \cdot 10^{-5}$	
	65	2 955	$2.99 \cdot 10^{-4}$	$7.76 \cdot 10^{-5}$	$22.14 \cdot 10^{-5}$	

[a] Total rate constant.

EXPERIMENTAL

All reagents were obtained commercially and used without further purification. The electronic absorption spectra were measured on a Specord M 40 spectrophotometer (Zeiss, Jena) and CD curves were recorded with Roussel–Jouan dichrograph. Optical activity data were obtained with Perkin–Elmer 241 spectropolarimeter.

Preparation of Complexes

The synthesis of $(+)_{589}$-$[Co(NO_2)_2(en)(AB)]$ (AB = Ala or Val) was identical with the preparation of the corresponding glycine complex[5], except 8.9 g (0.1 mol) of Ala or 11.7 g (0.1 mol) Val were used.

The original method[5] was improved by the shortening of air oxidation period from 10 to 0.5 h with the addition of 30% H_2O_2 (5 ml) to the reaction mixture when the complexes desired precipitated immediately. The yield of $[Co(NO_2)_2(en)(Ala)]$ was 13.5 g (45%), ($[\alpha]_{589}$ +295.1°, DMSO). For $C_5H_{14}CoN_5O_6$ (299.1) calculated: 20.08% C, 4.72% H, 23.42% N; found: 20.12% C, 4.79% H, 23.33% N. The yield of $[Co(NO_2)_2(en)(Val)]$ was 15.0 g (46%), ($[\alpha]_{589}$ +204.7°, DMSO). For $C_7H_{18}CoN_5O_6$ (327.1) calculated: 25.70% C, 5.54% H, 21.41% N; found: 25.63% C, 5.61% H, 21.40% N.

The isomers forming the more soluble diastereoisomers were not isolated from the filtrate owing to their small quantity.

$(+)_{589}$-$[CoCl(H_2O)(en)(Ala)]Cl$

$(+)_{589}$-$[Co(NO_2)_2(en)(Ala)]$ (20 g, 0.07 mol) was suspended at room temperature in concentrated HCl (50 ml), stirred until N_2O_4 evolution ceased. Reaction mixture was then evaporated to 1/4 of its original volume in vacuo (< 40 °C). Addition of ethanol (300 ml) and acetone (100 ml) and standing reaction mixture overnight led to violet crystals deposition. These were filtered, washed with 1 : 1 HCl, ethanol and air dried. Yield 9 g (46%). For $C_5H_{16}Cl_2CoN_3O_3$ (296.0) calculated: 20.29% C, 5.45% H, 14.19% N; found: 20.54% C, 5.49% H, 14.48% N.

$(+)_{589}$-$[CoCl_2(en)(Val)]$

$[Co(NO_2)_2(en)(Val)$ (20 g, 0.06 mol) was treated as described above. Synthesis afforded 10 g (53%) of light green crystals. For $C_7H_{18}Cl_2CoN_3O_2$ (306.1) calculated: 27.47% C, 5.93% H, 13.73% N; found: 27.54% C, 5.81% H, 13.78% N.

mer- and *fac*-$[CoCO_3(en)(Gly)]$ Isomers

$[CoCl(H_2O)(en)(Gly)]Cl$ (5 g, 0.02 mol) prepared according to ref.[5], was suspended in water (100 ml) at 0 °C and excess of freshly precipitated Ag_2CO_3 (7 g) was added. After 5 min of stirring AgCl deposited was filtered off and filtrate was concentrated approximately to 10 ml in vacuo (< 40 °C)* and loaded on the top of the column containing Dowex 50WX8 cation exchange resin (Na^+ cycle, 100–200 mesh, 30 × 4.5 cm). Elution with water produced two bands. Eluates containing individual isomers were evaporated to dryness at the temperature below 40 °C. For $C_5H_{12}CoN_3O_5$ (253.1) calculated: 23.72% C,

* Independent experiments revealed that under these conditions no isomerization proceeds.

4.78% H, 16.60% N; found for *mer* isomer: 23.48% C, 4.98% H, 16.66% N; found for *fac* isomer: 23.50% C, 4.79% H, 16.61% N.

mer- and *fac*-[$CoCO_3$(en)(Ala)]

Mixture of both isomers was prepared as described for [$CoCO_3$(en)(Gly)] starting from [$CoCl(H_2O)$(en)(Ala)]Cl (5 g, 0.017 mol) and Ag_2CO_3 (7 g). Isomers obtained were separated as described above. For $C_6H_{14}CoN_3O_5$ (267.1) calculated: 26.98% C, 5.28% H, 15.73% N; found for *mer* isomer: 26.78% C, 5.47% H, 15.67% N; found for *fac* isomer: 26.90% C, 5.32% H, 15.70% N.

mer- and *fac*-[$CoCO_3$(en)(Val)]

For the preparation and separation of isomers above described procedures were used, starting from [$CoCl_2$(en)(Val)] (5 g, 0.016 mol). For $C_8H_{18}CoN_3O_5$ (295.2) calculated: 32.56% C, 6.15% H, 14.24% N; found for *mer* isomer: 32.49% C, 6.20% H, 14.20% N; found for *fac* isomer: 32.33% C, 6.37% H, 14.04% N.

Yields of individual isomers in eluates were determined using atomic absorption spectroscopy (Spectr AA 300-Varian). In all cases *mer* : *fac* ratio was 95 : 5. Purity of isomers was checked by TLC (Alufol precoated plates, water–ethanol 5 : 6).

Kinetic Measurement

Individual isomers (50 mg) were weighted into the ampoules, dissolved in water (1 ml) and the ampoule was sealed and immersed in the thermostat (t ±0.05 °C). The ampoules were removed at given time intervals, cracked and solutions containing mixture of isomers were poured on the top of cation exchange resin (vide supra). Elution with water afforded two well separated bands. Eluates containing individual isomers were collected, their volume was adjusted in a volumetric flask and the isomer content was determined spectrophotometrically at fixed wavelengths (see Table I) on a Specol 21 apparatus. The validity of this procedure was confirmed by the fact that the rate constants obey Arrhenius equation.

The authors wish to thank to Dr J. Dolezal of this Institute for cobalt determination by atomic absorption and to Dr P. Malon, Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, for measurements of the CD spectra.

REFERENCES

1. Gillard R. D., Price M. G.: J. Chem. Soc. *1971*, 2271.
2. Kwak W., Archer R. D.: J. Serb. Chem. Soc. *55*, 753 (1990).
3. Jursik F., Ondrackova J., Hajek B.: Collect. Czech. Chem. Commun. *50*, 1582 (1985).
4. Jursik F., Abdel-Moez S.: Collect. Czech. Chem. Commun. *52*, 1488 (1987).
5. Matsuoka N., Hidaka J., Shimura Y.: Bull. Chem. Soc. Jpn. *39*, 1257 (1966).
6. Basolo F., Pearson R. G.: *Mechanism of Inorganic Reactions*, p. 232. Wiley, New York 1965.
7. Jursik F. in: *Liquid Column Chromatography* (Z. Deyl, K. Macek and J. Janák, Eds), p. 1100. Elsevier, Amsterdam 1975.