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Synthesis of the Mixed Cobalt(III) Glycylglycine Complexes and the Condensation Reaction of the Coordinated Ligands with Acetaldehyde. Crystal Structure of *mer*-(Ethylenediamine)(glycylglycinato)(isothiocyanato)cobalt(III) Hydrate

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The preparation of *mer*-[Co(glygly)L(en)]^n complexes (L = H_2O, CN^-, NCS^-; H_2glygly = glycylglycine; en = ethylenediamine; n = 0, 1+) is described. The structure of the *mer*-[Co(glygly)NCS(en)]·H_2O complex was determined by X-ray analysis. It crystallizes in the orthorhombic system, space group *Pbca*, with cell parameters a = 14.736 (7) Å, b = 22.867 (7) Å, c = 7.550 (3) Å, V = 2544 Å^3, and Z = 8. Condensation reactions of neutral complexes with acetaldehyde were also examined. On the basis of electronic and ^{1}H and ^{13}C NMR spectral data and the results of elemental analysis and paper chromatography, it was established that the following reaction products were obtained: (a) a mixture of *mer*-[Co(threogly)L(en)] (H_2threogly = threonylglycine) and *mer*-[Co(allothreogly)L(en)] (H_2allothreogly = allothreonylglycine), (b) *mer*-[Co(CH_3CH=glygly)L(en)] (CH_3CH=glyglyH$_2$ = *N*-ethylideneglycylglycine), and (c) *mer*-[Co(glygly)NCS(CH_3CH=en)] (CH_3CH=en = *N*-ethylideneethylenediamine). These results prove correct the reaction mechanism assumed in our previous paper[2] where an analogous complex containing NO_2^-, as a unidentate ligand, was examined.

Introduction

In the previous paper[2] it was shown that the base-catalyzed condensation of the dipeptide ligand of the *mer*-[Co(glygly)-NO_2(en)] complex with acetaldehyde takes place at the N-terminal CH_2 group of the coordinated glycylglycine and not at the C-terminal CH_2 group, as reported for the reaction of acetaldehyde with [Co(glygly)$(NH_3)_3$]$^+$ and [Co(glygly)(dien)]$^+$ ions,[3] as well as with [Co(glygly)$_2$]$^-$ ion;[4] it was also established that the reaction proceeds with intermediate formation of the complex of the Schiff base of the glycylglycinato ligand. In this work we have prepared the corresponding complexes containing cyano and isothiocyanato ligands, respectively, instead of the nitro group. Namely, it is expected that the change in the distribution of the electron density in the molecule, caused by the replacement of the nitro group by a ligand of stronger or weaker ligand field, is associated with the change of the reactivity of the coordinated glycylglycine and ethylenediamine in the reaction with acetaldehyde.

Experimental Section

Preparations. *mer*-[Co(glygly)(en)H_2O]Cl·H_2O. To a solution of *mer*-[Co(glygly)NO_2(en)][5] (0.72 g, 2.4 mmol) and urea (0.072 g, 1.2 mmol) in 45 cm^3 of water was added hydrochloric acid (3 cm^3, c_{HCl} 2 mol dm^{-3}). The reaction mixture was heated (80 °C) on a water bath for 1 h and then neutralized with sodium hydroxide solution (c_{NaOH} 2 mol dm^{-3}). The solution obtained was concentrated on a rotatory evaporator to a volume of 2 cm^3 and after addition of 0.5 cm^3 of ethanol allowed to stand at room temperature for 12 h. By this time, *mer*-[Co(glygly)-(en)H_2O]Cl·H_2O (0.5 g, 64%) crystallized out in the form of red crystals. The substance for analysis was recrystallized from warm 50% ethanol and dried at 105 °C for 2 h, whereby it lost 6.30% of its mass, which corresponds to the loss of one water molecule (5.62%). Anal. Calcd for $CoC_6H_{16}N_4O_4Cl$: C, 23.82; H, 5.33; N, 18.52. Found: C, 23.78; H, 5.54; N, 18.65.

***mer*-[CoCN(glygly)(en)].** A suspension of *mer*-[Co(glygly)-(en)H_2O]Cl·H_2O (0.96 g, 0.003 mol) and potassium cyanide (0.29 g, 4.5 mmol) in dimethyl sulfoxide (100 cm^3) was heated (70 °C) on a water bath for 1 h. To the solution obtained was added warm water (about 50 cm^3), and after cooling, the solution was poured onto a cationic Dowex 50W-X8 (200–400 mesh) column (5-cm length and 2.8-cm o.d.), in hydrogen form. The elution was carried out with distilled water (at a rate of 10 cm^3/min), whereby the adsorbed orange zone came off the column 45 min after the beginning of the elution. It was eluted within 90 min. The eluate obtained was concentrated on a rotatory evaporator to a volume of 2 cm^3 and was left to stand at room temperature for 12 h. By this time, there crystallized out from the solution *mer*-[CoCN-(glygly)(en)] (0.75 g, 97%) as orange crystals. Anal. Calcd for $CoC_7H_{14}N_5O_3$: C, 30.56; H, 5.13; N, 25.45. Found: C, 30.42; H, 5.07; N, 25.64.

***mer*-[Co(glygly)NCS(en)]·H_2O.** To a solution of *mer*-[Co(glygly)-(en)H_2O]Cl·H_2O (0.51 g, 1.6 mmol) in 10 cm^3 of water was added potassium thiocyanate (0.15 g, 1.6 mmol). The reaction mixture was heated on a water bath (30 °C) for 30 min. The separated red crystals (0.45 g, 92%) of *mer*-[Co(glygly)NCS(en)]·H_2O were filtered off under reduced pressure. The substance for the analysis was dried at 105 °C for 2 h whereby it lost 5.53% of its mass, which corresponds to the loss of one water molecule (5.54%). Anal. Calcd for $CoC_7H_{14}N_5O_3S$: C, 27.37; H, 4.59; N, 22.79. Found: C, 27.12; H, 4.86; N, 22.54.

Reactions. *mer*-[CoCN(glygly)(en)] with Acetaldehyde. To a solution of *mer*-[CoCN(glygly)(en)] (1.0 g, 3.61 mmol) in 100 cm^3 of water were added acetaldehyde (1.64 cm^3, 0.029 mol) and a volume of sodium hydroxide solution (c_{NaOH} 0.1 mol dm^{-3}), required to adjust the reaction mixture to pH 11.

The solution obtained was allowed to stand at room temperature for 4 h (keeping the pH constant by addition of NaOH solution). Then, it was neutralized with hydrochloric acid (c_{HCl} 0.1 mol dm^{-3}) and evaporated on a rotatory evaporator (30 °C) to a volume of 10 cm^3. The cooled solution was poured onto a cationic Dowex 50W-X8 (200–400 mesh) column (9-cm length and 3-cm o.d.), in hydrogen form. The elution was carried out with distilled water (at a rate of 6 cm^3/min) whereby four zones were formed on the column.

The first zone of pale orange color came off the column about 20 min after the beginning of the elution and was eluted out within 30 min. The eluate obtained was concentrated on a rotatory evaporator (30 °C) to dryness. The ^{1}H NMR spectrum of the dry residue indicated the presence of *mer*-[CoCN(CH_3CH=threogly)(en)] and *mer*-[CoCN-(CH_3CH=allothreogly)(en)].

The second zone came off the column 20 min after the first zone was completely eluted. It was eluted out within 40 min and found to contain *mer*-[CoCN(threogly)(en)] and *mer*-[CoCN(allothreogly)(en)]. The eluate obtained was concentrated on a rotatory evaporator (40 °C) to a volume of 2 cm^3 and left at room temperature for 24 h. By this time there crystallized out a mixture of the diastereomers (0.18 g, 16%) in the form of orange crystals. Anal. Calcd for $CoC_9H_{18}N_5O_4$: C, 33.86; H, 5.68; N, 21.94. Found: C, 34.14; H, 5.64; N, 22.60.

The third zone appeared off the column 30 min after the completion of the elution of the second zone; it contained *mer*-[CoCN(CH_3CH=glygly)(en)] and was eluted out within 100 min. The eluate obtained was evaporated on a rotatory evaporator (40 °C) to a volume of about 3 cm^3 and was allowed to stand at room temperature for 24 h. By this time there crystallized out from the soolution the above mentioned substance

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(0.25 g, 23%) in the form of orange crystals. Anal. Calcd for $CoC_9H_{16}N_5O_3$: C, 35.89; H, 5.35; N, 23.25. Found: C, 35.68; H, 5.23; N, 23.50.

The fourth zone appeared off the column about 85 min after the elution of the third zone was completed; it contained the starting substance.

***mer*-[Co(glygly)NCS(en)]·H_2O with Acetaldehyde.** To a suspension of *mer*-[Co(glygly)NCS(en)]·H_2O (0.98 g, 3 mmol) in 500 cm^3 of water was added acetaldehyde (1.36 cm^3, 0.024 mol) and a volume of sodium hydroxide solution (c_{NaOH} 0.1 mol dm^{-3}) required to adjust the reaction mixture to pH 11. The reaction mixture was then allowed to stand at room temperature for 4 h (keeping the pH constant by addition of NaOH solution) and then neutralized with hydrochloric acid (c_{HCl} 0.1 mol dm^{-3}). The solution obtained was concentrated on a rotatory evaporator (40 °C) to a volume of 15 cm^3 and left at room temeprature for 12 h. By then there crystallized out the greatest part of the starting complex, which was filtered off under reduced pressure. The filtrate obtained was poured onto a cationic Dowex 50W-X8 (200–400 mesh) column (14-cm length and 3-cm o.d.) in hydrogen form. The elution was carried out with distilled water (at a rate of 3 cm^3 per minute) whereby five zones were formed on the column.

The first pale red zone came off the column about 3.5 h after the beginning of the elution and was eluted within 90 min. The eluate obtained was concentrated on a rotatory evaporator (40 °C) to a volume of 1 cm^3 and poured onto a silica gel column (25-cm length and 2-cm o.d.). The adsorbed zone of dark red color containing *mer*-[Co(threogly)NCS(en)] and *mer*-[Co(allothreogly)NCS(en)] was eluted out with water, and the eluate obtained was evaporated to dryness.

After the elution of the first zone was completed, i.e. after about 3 h, the second zone containing *mer*-[Co(glygly)NCS(CH_3CH=en)]·H_2O appeared off the column and was eluted out within 90 min. The solution obtained was concentrated on a rotatory evaporator (40 °C) to a volume of 1 cm^3 and left to stand at room temperature for 24 h. By this time there crystallized out from the solution the aforementioned complex (0.005 g, 0.5%) in the form of small pink crystals that were recrystallized from warm water. Anal. Calcd for $CoC_9H_{18}N_5O_4S$: C, 30.77; H, 5.16; N, 19.94. Found: C, 31.10; H, 5.27; N, 20.02.

The third zone containing *mer*-[Co(CH_3CH=glygly)NCS(en)] appeared off the column about 3 h after the completion of the elution of the second zone and was eluted out within 3 h. The eluate obtained was concentrated on a rotatory evaporator (40 °C) to a volume of about 2 cm^3 and allowed to stand at room temperature for 24 h. By this time, the above complex crystallized out (0.05 g, 5%) in the form of red crystals. The substance for analysis was recrystallized from warm water (40 °C). Anal. Calcd for $CoC_9H_{16}N_5O_3S$: C, 32.44; H, 4.84; N, 21.02. Found: C, 32.32; H, 4.56; N, 20.70.

The fourth zone came off the column about 5 h after the elution of the third zone was completed; it was found to contain the starting substance.

Finally the last zone containing the decomposition products of the starting substance remained fixed on the column.

Decomposition: *mer*-[CoCN(threogly)(en)] and *mer*-[CoCN(allothreogly)(en)]; *mer*-[Co(threogly)NCS(en)] and *mer*-[Co(allothreogly)NCS(en)]. Hydrolysis of Liberated Dipeptides and Identification of Amino Acids Obtained. The decomposition of diastereomeric complexes by means of hydrogen sulfide, and the hydrolysis of the liberated peptides, was carried out by the procedure described in the literature.[3] The identification of the amino acids obtained was performed by ascending paper chromatography.[6]

Electronic Absorption Spectra. Electronic spectra in the visible and ultraviolet regions were recorded on a Varian Ultraviolet Super Scan 3 spectrophotometer. Visible spectra were taken with aqueous solutions having concentrations of 2×10^{-3} mol dm^{-3}, whereas solutions having concentrations of 2×10^{-4} mol dm^{-3} were used for the recording of ultraviolet spectra. The length of the cell used was 0.5 cm.

Proton Magnetic Resonance Spectra. These spectra were taken on a Varian FT-80A spectrophotometer, in D_2O, using DSS as the internal standard.

^{13}C Nuclear Magnetic Resonance Spectra. ^{13}C NMR spectra were run on a Varian FT-80A spectrophotometer, in D_2O. Chemical shifts are given with reference to Me_4Si.

Crystal Data. The dark red crystals of *mer*-[Co(glygly)NCS(en)]·H_2O crystallize as elongated plates. Crystal data: $CoC_7H_{14}N_5O_3S·H_2O$, M_r = 325.2, orthorhombic, *Pbca*, a = 14.736 (7) Å, b = 22.867 (7) Å, c = 7.550 (3) Å, V = 2544 Å^3, Z = 8, ρ_{calcd} = 1.698, ρ_{obsd} = 1.706 g cm^{-3}, Mo Kα radiation, λ = 0.7107 Å, μ(Mo Kα) = 15.66 cm^{-1}.

X-ray Data Collection. The unit cell dimensions were initially obtained from rotation and Weissenberg photographs and later adjusted by least-squares refinement of 25 accurately centered reflections. The space group was deduced from the systematic absences ($h0l$ for l odd, $hk0$ for h odd, $0kl$ for k odd). The intensity data were collected on a PW 11000 four-circle diffractometer, from a crystal of dimensions 0.05 × 0.16 × 0.56 mm. The graphite-monochromatized Mo Kα radiation and the θ–2θ scan technique were used to record the intensities for all nonequivalent reflections for which $3 \le \theta \le 30°$, with a scan speed of 0.04°/s and a scan width of 1.2°. The intensities of three standard reflections monitored every 120 s, showed no significant variations during data collection. The raw intensity data were corrected for Lorentz–polarization effects, but not for absorption nor extinction. A total of 1991 reflections were collected.

Solution and Refinement of the Structure. The structure was solved by routine application of the heavy-atom method; the atomic parameters were refined by full-matrix least-squares calculations. The function minimized was $\sum w\Delta^2$, where $w = 1/\sigma^2(|F|)$ and $\Delta = |F_o| - |F_c|$. All atoms were assumed to be uncharged. Values for the atomic scattering factors and anomalous terms for cobalt and sulfur were taken from the literature.[7]

The cobalt and sulfur atoms were located from Patterson synthesis, and the remaining non-hydrogen atoms were readily found from Fourier difference functions. After anisotropic refinement, all the hydrogen atoms, including those of water molecules, were located from the difference maps and were refined with isotropic temperature factors. Final refinement for 1777 reflections with $F_o \ge 3.5\sigma(F_o)$ and 227 variables converged at R_1 = 0.046 and R_2 = 0.046, where $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$ and $R_2 = \sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$. (The goodness-of-fit parameter $[\sum w(|F_o| - |F_c|)^2/(NO - NP)]^{1/2}$, where NO is number of observations and NP number of parameters was 1.19). The absence of absorption correction caused a number of hydrogen atoms to exhibit low-temperature factors, four of them having negative values. As the geometry of the hydrogen atoms and of the whole complex molecule was in accordance with literature data, the refinement was considered satisfactory. A final difference Fourier map was featureless, showing no significant residual peaks.

Atomic positions, along with their standard deviations as derived from the inverse matrix of the final cycle least-squares refinement, are given in Table I. Tables of thermal parameters and observed and calculated structure factor amplitudes are provided as supplementary material.

The main computer programs used on the CDC-3600 computer were FORDAP, Zalkin's Fourier program,[8] NUCLS, a modification by J. A. Ibers and R. J. Doedens of the full-matrix least-squares program ORFLS,[9] GEOM, K. W. Muir and P. Mallinson's program for molecular geometry and standard deviations, and RING, written by L. K. Parkanyi for calculation of conformational parameters.

Results and Discussion

Synthesis and Structure of New Complexes. Synthesis and Isomerism. As seen from the Experimental Section, in this paper three new mixed (glycylglycinato)cobalt(III) complexes of the type *mer*-[Co(glygly)L(en)]^n (L = H_2O, CN^-, NCS^-) were obtained in high yields (64–97%). By the action of hydrochloric acid on the previously prepared *mer*-[Co(glygly)NO_2(en)] complex[5] in the presence of urea, *mer*-[Co(glygly)(en)H_2O]Cl·H_2O was obtained. The latter in the reaction with potassium thiocyanate gave the *mer*-[Co(glygly)NCS(en)]·H_2O complex, and with potassium cyanide in dimethyl sulfoxide, the *mer*-[CoCN(glygly)(en)] complex.

The trigonal-planar configuration of the deprotonated amide nitrogen of the dipeptidato ligand implies a meridional configuration of all the complexes prepared.

It is known that the SCN group may coordinate to a metal through a nitrogen or sulfur atom.[10,11] In order to determine the

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Table I. Positional Parameters and Their Estimated Standard Deviations for *mer*-[Co(glygly)NCS(en)]·H_2O

atom	*x*	*y*	*z*
Co	0.34915 (4)	0.38337 (2)	0.37487 (8)
S	0.14979 (10)	0.37298 (7)	−0.10802 (19)
O(1)	0.4506 (2)	0.4126 (1)	0.2404 (4)
O(2)	0.5641 (2)	0.3838 (1)	0.0657 (5)
O(3)	0.3562 (2)	0.2127 (1)	0.2846 (5)
O(W)	0.3710 (3)	0.5125 (2)	0.0696 (7)
N(1)	0.3923 (2)	0.3099 (1)	0.3081 (5)
N(2)	0.2534 (3)	0.3394 (2)	0.4962 (6)
N(3)	0.4239 (3)	0.3815 (2)	0.5844 (5)
N(4)	0.3142 (3)	0.4625 (2)	0.4553 (6)
N(5)	0.2713 (3)	0.3877 (2)	0.1712 (5)
C(1)	0.5002 (4)	0.3730 (2)	0.1644 (6)
C(2)	0.4745 (3)	0.3099 (2)	0.2052 (8)
C(3)	0.3392 (3)	0.2638 (2)	0.3325 (6)
C(4)	0.2509 (3)	0.2792 (2)	0.4211 (7)
C(5)	0.3976 (4)	0.4285 (2)	0.7077 (7)
C(6)	0.3744 (4)	0.4813 (2)	0.6025 (9)
C(7)	0.2203 (3)	0.3810 (2)	0.0566 (6)
H(1)	0.205 (3)	0.352 (2)	0.481 (6)
H(2)	0.262 (4)	0.334 (2)	0.618 (8)
H(3)	0.484 (4)	0.386 (2)	0.551 (7)
H(4)	0.422 (4)	0.351 (2)	0.636 (7)
H(5)	0.446 (3)	0.063 (2)	0.290 (6)
H(6)	0.333 (5)	0.419 (3)	0.774 (9)
H(7)	0.435 (4)	0.497 (3)	0.557 (8)
H(8)	0.335 (3)	0.514 (2)	0.676 (6)
H(9)	0.313 (4)	0.484 (3)	0.360 (8)
H(10)	0.253 (4)	0.465 (2)	0.487 (7)
H(11)	0.527 (4)	0.292 (2)	0.260 (7)
H(12)	0.467 (4)	0.288 (3)	0.088 (9)
H(13)	0.204 (3)	0.276 (2)	0.332 (6)
H(14)	0.232 (3)	0.252 (2)	0.523 (7)
WH(1)	0.404 (4)	0.535 (2)	0.039 (4)
WH(2)	0.398 (4)	0.487 (3)	0.103 (9)

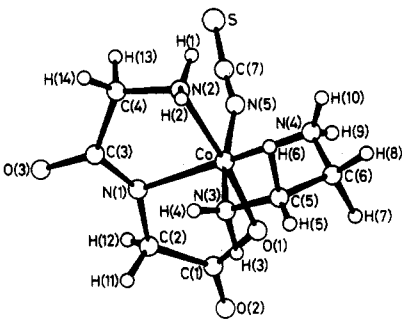

Figure 1. Perspective view of the *mer*-[Co(glygly)NCS(en)] molecule showing the atom-numbering scheme.

bonding type in the reaction product of the *mer*-[Co(glygly)(en)H_2O]$^+$ complex with thiocyanate ion, its X-ray crystal structure analysis has been undertaken.

Crystal Structure of *mer*-[Co(glygly)NCS(en)]·H_2O. The structure of this complex consists of enantiomeric pairs of the complex molecules and molecules of water, joined together by O–H···O, N–H···O, and N–H···S hydrogen bonds. A perspective drawing of the molecule with the numbering scheme of the atoms is given in Figure 1. The bond lengths and angles are listed in Tables II and III, respectively.

The geometry of the cobalt(III) coordination sphere is distorted octahedral. The glycylglycinato ligand is coordinated through carboxylato oxygen, amino nitrogen, and peptide nitrogen atoms as tridentate, forming two fused equatorially disposed five-membered chelate rings. The ethylenediamine ligand is bidentate and forms a five-membered ring. The sixth coordination position is occupied by an N-bonded thiocyanato ligand.

Table II. Bond Distances (Å) in *mer*-[Co(glygly)NCS(en)]·H_2O

Co–O(1)	1.927 (3)	N(4)–H(9)	0.87 (6)
Co–N(1)	1.866 (3)	N(4)–H(10)	0.94 (6)
Co–N(2)	1.960 (5)	N(5)–C(7)	1.156 (6)
Co–N(3)	1.928 (4)	S–C(7)	1.630 (5)
Co–N(4)	1.977 (5)	C(1)–C(2)	1.523 (7)
Co–N(5)	1.921 (4)	C(2)–H(11)	0.97 (6)
O(1)–C(1)	1.297 (6)	C(2)–H(12)	1.02 (7)
O(2)–C(1)	1.226 (6)	C(3)–C(4)	1.505 (6)
O(3)–C(3)	1.249 (5)	C(4)–H(13)	0.97 (4)
N(1)–C(2)	1.439 (6)	C(4)–H(14)	1.03 (5)
N(1)–C(3)	1.326 (5)	C(5)–C(6)	1.485 (7)
N(2)–C(4)	1.489 (7)	C(5)–H(5)	0.96 (5)
N(2)–H(1)	0.78 (4)	C(5)–H(6)	1.09 (7)
N(2)–H(2)	0.94 (6)	C(6)–H(7)	1.02 (6)
N(3)–C(5)	1.474 (7)	C(6)–H(8)	1.09 (5)
N(3)–H(3)	0.93 (6)	O(W)–WH(1)	0.74 (6)
N(3)–H(4)	0.80 (5)	O(W)–WH(2)	0.75 (6)
N(4)–C(6)	1.486 (8)		

Table III. Bond Angles (deg) in *mer*-[Co(glygly)NCS(en)]·H_2O

N(1)–Co–O(1)	84.6 (1)	H(1)–N(2)–C(4)	105 (3)
N(2)–Co–O(1)	169.4 (2)	H(1)–N(2)–H(2)	109 (5)
N(3)–Co–O(1)	89.8 (2)	H(2)–N(2)–Co	115 (3)
N(4)–Co–O(1)	92.7 (2)	H(2)–N(2)–C(4)	105 (3)
N(5)–Co–O(1)	91.4 (2)	H(3)–N(3)–Co	109 (3)
N(2)–Co–N(1)	84.8 (2)	H(3)–N(3)–C(5)	110 (3)
N(3)–Co–N(1)	90.4 (2)	H(3)–N(3)–H(4)	105 (5)
N(4)–Co–N(1)	174.9 (2)	H(4)–N(3)–Co	113 (4)
N(5)–Co–N(1)	91.9 (2)	H(4)–N(3)–C(5)	109 (4)
N(3)–Co–N(2)	90.9 (2)	H(5)–C(5)–N(3)	108 (4)
N(4)–Co–N(2)	98.0 (2)	H(5)–C(5)–C(6)	111 (4)
N(5)–Co–N(2)	88.3 (2)	H(5)–C(5)–H(6)	113 (5)
N(4)–Co–N(3)	85.2 (2)	H(6)–C(5)–N(3)	112 (4)
N(5)–Co–N(3)	177.5 (2)	H(6)–C(5)–C(6)	102 (4)
N(5)–Co–N(4)	92.5 (2)	H(7)–C(6)–N(4)	112 (3)
Co–O(1)–C(1)	115.3 (3)	H(7)–C(6)–C(5)	105 (4)
Co–N(1)–C(2)	115.6 (2)	H(7)–C(6)–H(8)	113 (4)
Co–N(1)–C(3)	118.5 (3)	H(8)–C(6)–N(4)	105 (2)
Co–N(2)–C(4)	108.3 (3)	H(8)–C(6)–C(5)	114 (2)
Co–N(3)–C(5)	110.6 (3)	H(9)–N(4)–Co	105 (4)
Co–N(4)–C(6)	109.8 (3)	H(9)–N(4)–C(6)	118 (4)
Co–N(5)–C(7)	168.6 (4)	H(9)–N(4)–H(10)	99 (5)
S–C(7)–N(5)	178.4 (4)	H(10)–N(4)–Co	113 (3)
O(1)–C(1)–C(2)	115.6 (4)	H(10)–N(4)–C(6)	111 (3)
O(1)–C(1)–O(2)	124.1 (4)	H(11)–C(2)–N(1)	116 (3)
O(2)–C(1)–C(2)	120.3 (4)	H(11)–C(2)–C(1)	106 (3)
O(3)–C(3)–N(1)	125.8 (4)	H(11)–C(2)–H(12)	104 (5)
O(3)–C(3)–C(4)	121.4 (4)	H(12)–C(2)–N(1)	112 (3)
N(1)–C(2)–C(1)	108.6 (4)	H(12)–C(2)–C(1)	108 (4)
N(1)–C(3)–C(4)	112.7 (4)	H(13)–C(4)–N(2)	111 (3)
N(2)–C(4)–C(3)	111.3 (4)	H(13)–C(4)–C(3)	107 (3)
N(3)–C(5)–C(6)	108.4 (4)	H(13)–C(4)–H(14)	106 (4)
N(4)–C(5)–C(6)	107.6 (4)	H(14)–C(4)–N(2)	106 (3)
C(2)–N(1)–C(3)	124.9 (3)	H(14)–C(4)–C(3)	115 (3)
H(1)–N(2)–Co	114 (3)	WH(1)–O(W)–WH(2)	107 (3)

The geometry of the complex molecule is in agreement with previously reported data for (glycylglycinato)cobalt(III) complexes.[12,13] The bond lengths and angles in the coordination polyhedron of cobalt are in the range of the values found in other complexes of Co(III) with amino acids.[14] The bond distances and angles in ethylenediamine and isothiocyanate ligands are also unexceptional.

The conformation of chelate rings, expressed by puckering parameters,[15] relevant torsion angles and root-mean-square torsion

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Table IV. Conformational Parameters of Chelate Rings in *mer*-[Co(glygly)NCS(en)]·H_2O

(a) Puckering Parameters

ring	atoms	puckering amp (q_n), Å	phase angle (Φ), deg	τ
1	Co,O(1),C(1),C(2),N(1)	0.049	279.4	4.2
2	Co,N(1),C(3),C(4),N(2)	0.230	151.2	14.9
3	Co,N(3),C(5),C(6),N(4)	0.393	266.5	32.0

(b) Selected Torsion Angles (deg)

O(1)–C(1)–C(2)–N(1)	6.0 (6)	N(3)–C(5)–C(6)–N(4)	46.6
N(1)–C(3)–C(4)–N(2)	−12.9 (5)		

(c) Distances (Å) of Atoms from Their Least-Squares Mean Planes

ring 1	Co	0.0001 (6)	O(1)	0.003 (3)	C(1)	−0.030 (5)
	C(2)	0.041 (6)	N(1)	−0.012 (4)		
ring 2	Co	0.0025 (6)	N(1)	−0.072 (4)	C(3)	0.042 (4)
	C(4)	0.157 (5)	N(2)	−0.193 (4)		
glygly	Co	0.0010 (6)	O(1)	−0.044 (3)	C(1)	0.015 (5)
residue	C(2)	0.216 (5)	N(1)	0.152 (4)	C(3)	−0.024 (4)
	C(4)	−0.268 (5)	N(2)	0.053 (4)	O(2)	−0.079 (4)
	O(3)	−0.038 (4)				

[a] The conformational parameters are calculated for the molecule in position x, y, z (Table I), which has Λ absolute configuration.

Table V. Hydrogen-Bond Distances (Å) and Angles (deg) in *mer*-[Co(glygly)NCS(en)]·H_2O[a]

	A···B	H···B	A–H···B
N(2)–H(1)···O(2)[1]	3.005 (5)	2.23 (4)	177 (4)
N(2)–H(2)···O(3)[2]	2.908 (6)	2.16 (6)	136 (5)
N(3)–H(3)···S[1]	3.338 (5)	2.50 (6)	151 (5)
N(3)–H(4)···O(3)[2]	2.814 (5)	2.08 (5)	153 (6)
N(4)–H(9)···O(W)	3.239 (7)	2.44 (6)	152 (6)
N(4)–H(10)···O(W)[3]	2.919 (6)	2.00 (6)	168 (6)
O(w)–WH(1)···O(2)[4]	2.753 (5)	2.07 (4)	152 (6)
O(W)–WH(2)···O(1)	2.874 (5)	2.14 (7)	167 (7)

[a] Symmetry code: (1) $^1/_2 + x, y, ^1/_2 - z$; (2) $x, ^1/_2 - y, ^1/_2 + z$; (3) $^1/_2 - x, 1 - y, ^1/_2 + z$; (4) $1 - x, 1 - y, -z$.

angle τ, and deviations of the atoms from their least-squares mean planes, are presented in Table IV.

Analysis of the data shows that, due to the presence of two planar groups, carboxylate and peptide, the C-terminal ring of the dipeptidato ligand is remarkably planar. According to the puckering parameters, the N-terminal ring has an envelope conformation. The angle between the mean planes of the two rings is 6.9°, and the maximum displacement from the plane containing all atoms of the two fused rings is 0.268 Å. The ethylenediamine ring is, as usual, considerably puckered and has a twist conformation. In the enantiomer that has a Λ absolute configuration (taking the rings of the ethylenediamine ligand and C-terminal amino carboxylato residue of glycylglycine as reference rings), the chirality of the N-terminal ring is λ and that of the diamine chelate is δ.[16]

Table V lists the parameters of hydrogen bonds in the crystal structure of *mer*-[Co(glygly)NCS(en)]·H_2O. Every complex molecule is connected by N–H···O and N–H···S hydrogen bonds with three adjacent complexes and two molecules of water. Water molecules, as acceptors for two and donors for two hydrogen bonds, join the three neighboring complex molecules.

Condensation Reactions and Their Mechanism. (a) *mer*-[CoCN(glygly)(en)] with Acetaldehyde. In the reaction of *mer*-[CoCN(glygly)(en)] with acetaldehyde three products were obtained (Table VI, IIa–IVa), two of them being isolated as a mixture (IIa and IIIa). As seen from Table VI, the first absorption maximum in the electronic spectrum of product IVa is shifted 5 nm toward shorter wavelengths with respect to that of the starting substance (Ia). In contrast, the absorption maxima of the starting

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Table VI. First Absorption Maxima and log ε of the Synthesized Compounds[a]

no.	compd	λ, nm	log ε
I	*mer*-[Co(glygly)(en)H_2O]Cl	481	2.26
Ia	*mer*-[CoCN(glygly)(en)]	468	2.41
IIa	*mer*-[CoCN(threogly)(en)]	468	
IIIa	*mer*-[CoCN(allothreogly)(en)]		
IVa	*mer*-[CoCN(CH_3CH=glygly)(en)]	463	2.46
Ib	*mer*-[Co(glygly)NCS(en)]	487	2.32
IIb	*mer*-[Co(threogly)NCS(en)]	487	
IIIb	*mer*-[Co(allothreogly)NCS(en)]		
IVb	*mer*-[Co(CH_3CH=glygly)NCS(en)]	482	2.35
Vb	*mer*-[Co(glygly)NCS(CH_3CH=en)]	485	2.33

[a] Complexes IIa and IIIa, as well as IIb and IIIb, were obtained as a mixture.

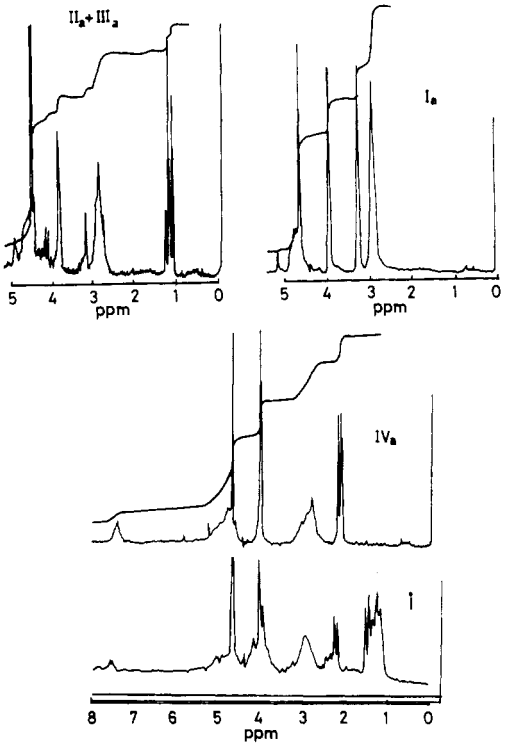

Figure 2. ^{1}H NMR spectra of *mer*-[CoCN(glygly)(en)] complex Ia and its reaction products with acetaldehyde (IIa + IIIa, IVa, I).

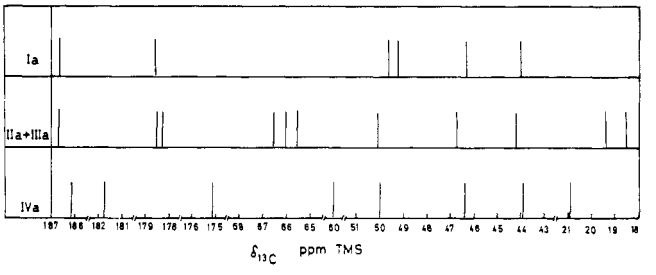

Figure 3. ^{13}C NMR chemical shifts of *mer*-[CoCN(glygly)(en)] complexes Ia and its reaction products with acetaldehyde (IIa + IIIa, IVa).

substance and of the mixture of products IIa and IIIa are found at the same wavelength. On this basis it might be assumed that substance IVa is the reaction product of the amino group, whereas substances IIa and IIIa are the reaction products of some methylene groups of the dipeptidato ligand with acetaldehyde. This assumption is consistent with ^{1}H and ^{13}C NMR spectra of compounds obtained.

Namely, in the ^{1}H NMR spectrum (Figure 2) and ^{13}C NMR spectrum (Figure 3), product IVa gives signals at 2.13 and 7.43 ppm and at 181.75 and 20.88 ppm, respectively, which arise from the *N*-ethylidene group. Since the chemical shift of the N-terminal

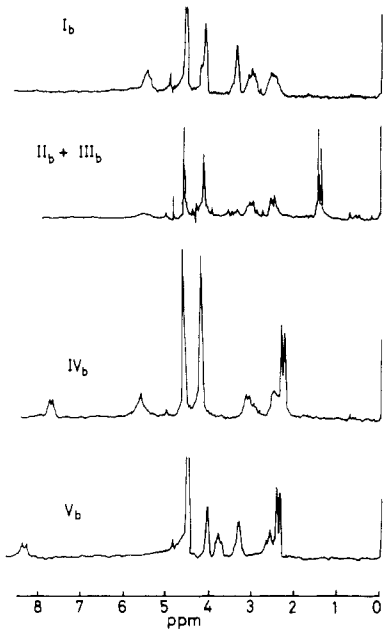

Figure 4. ^{1}H NMR spectra of *mer*-[Co(glygly)NCS(en)] complex Ib and its reaction products with acetaldehyde (IIb + IIIb, IVb, Vb).

CH_2 group protons of the dipeptidato ligand is by 0.8 ppm greater than that of the corresponding protons of the starting substance, it was concluded that this product is the complex containing the Schiff base of the glycylglycinato ligand. As expected, the introduced imino group shifts the signal of the C atom of the N-terminal CH_2 group 10 ppm toward lower magnetic field with respect to the signal of this atom in the spectrum of the starting complex; however, it has no effect on the position of the C atom of the C-terminal CH_2 group.

In the ^{1}H NMR spectrum of the mixture of products IIa and IIIa methyl resonances appearing at 1.28 and 1.18 ppm, as well as the position and the ratio of integrals of signals at 3.25 and 3.95 ppm, show that this mixture consists of complexes that contain threonyl- and/or allothreonylglycine. Since dipeptides liberated from this mixture on hydrolysis gave glycine, threonine, and allothreonine as amino acids, it was concluded that products IIa and IIIa are diasteromeric threonyl- and allothreonylglycinato complexes.

Figure 2 also shows the ^{1}H NMR spectrum of dry residue (İ) obtained by the evaporation of the eluate of the first zone eluted in the course of chromatographic separation of reaction products formed in the reaction of the *mer*-[CoCN(glygly)(en)] complex with acetaldehyde. As seen from the figure, this spectrum has *N*-ethylidene group signals at 2.23 and 2.40 ppm, as well as at 7.60 and 7.80 ppm. Since the signals of threonyl and/or allothreonyl protons (1.50, 3.93, 4.20 ppm) appear at lower magnetic field than the corresponding ones in the spectrum of the mixture of products IIa and IIIa, it could be concluded that the isolated dry residue (İ) contains *N*-ethylidenethreonyl- and *N*-ethylideneallothreonylglycinato complexes. In attempts to purify and isolate these complexes from the solution, a mixture of crystalline products was obtained, whose ^{1}H NMR spectrum was identical with that of the mixture of the products IIa and IIIa. These results are in agreement with our earlier assumption[2] that Schiff bases of threonyl- and allothreonylglycinato ligands are more readily hydrolyzed than the Schiff base of the glycylglycinato ligand.

In contrast to the diamine ligand of nitro[2] and isothiocyanato complexes (part b, below), the ethylenediamine ligand of this complex does not react with acetaldehyde or, if it does, the amounts of the corresponding condensation products are negligible.

(b) *mer*-[Co(glygly)NCS(en)] with Acetaldehyde. From the mixture obtained in the reaction of the *mer*-[Co(glygly)NCS(en)] complex with acetaldehyde, two substances (Table VI, IVb and Vb) were isolated, whereas traces of a mixture of the products IIb and IIIb in the eluate obtained were detected by ^{1}H NMR spectroscopy and by chromatographic analysis of amino acids obtained by their hydrolysis.

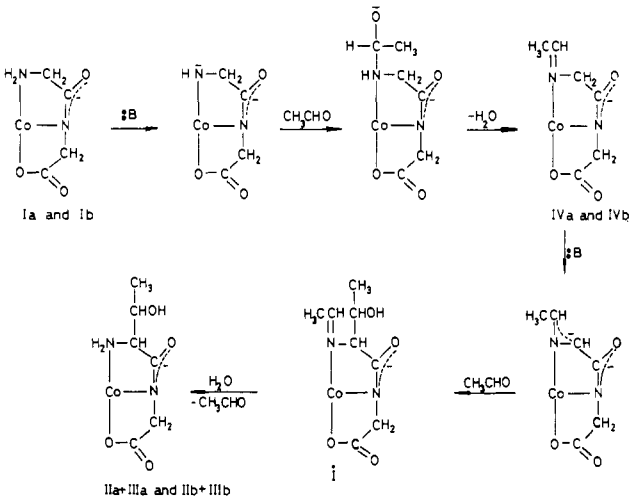

Figure 5. Proposed mechanism for the formation of *mer*-[Co(threogly)L(en)] and *mer*-[Co(allothreogly)L(en)] by condensation of *mer*-[Co(glygly)L(en)] with acetaldehyde.

The ^{1}H NMR spectrum of the products IVb and Vb (Figure 4) gives methyl resonances at 2.29 and 2.50 ppm, as well as signals at 7.75 and 8.40 ppm, arising from one proton. Since the positions of these resonances correspond to those of *N*-ethylidene group protons, it was concluded that these complexes derive from the condensation of the aldehyde with the amino group. One of them (IVb) is the complex of the *N*-ethylideneglycylglycinato ligand, since the spectrum shows that the introduced imino group shifts the signal of the N-terminal CH_2 group by 0.8 ppm toward lower magnetic field with respect to the position of the signal of this group in the spectrum of the starting complex (Ib). The shift of the C-terminal CH_2 group is negligible. An analogous shift of the signal of methylene groups of coordinated ethylenediamine ligand appears in the spectrum of product Vb, which contains the Schiff base of this ligand. On the basis of general features of its ^{1}H NMR spectrum, product Vb was assumed to be a single substance and not a mixture of two possible monocondensation products (in the case of the formation of a mixture of products, the spectrum is expected to be more complex, since one product would contain *N*-ethylidene in the cis and the other in the trans position with respect to the NCS group). This assumption is supported by the fact that paper and thin-layer chromatography on silica gel of this product, using three different solvent systems, afforded only one zone.

On the basis of methyl resonance at about 1.45 ppm in the ^{1}H NMR spectrum of the products IIb and IIIb, as well as on the basis of integrals of the signals at 3.60 and 4.15 ppm, it was concluded that they derive from condensation of acetaldehyde with the N-terminal CH_2 group of the dipeptidato ligand of the starting substance. Chromatographic analysis of amino acids, obtained by hydrolysis of dipeptides liberated from the mixture, has shown that the latter consists of two complexes, one containing coordinated threonylglycine and the other allothreonylglycine.

Hence, the reaction of acetaldehyde with the glycylglycinato ligand of *mer*-[CoCN(glygly)(en)] and of *mer*-[Co(glygly)-NCS(en)] complexes proceeds by the mechanism assumed for the reaction of acetaldehyde with the glycylglycinato ligand of the corresponding nitro complex.[2] Namely, the first phase of the base-catalyzed condensation of coordinated glycylglycine with acetaldehyde involves the formation of *N*-ethylideneglycylglycinato complexes (IVa and IVb) (Figure 5). Diastereoisomeric threonyl- and allothreonylglycinato complexes (IIa and IIIa; IIb and IIIb,

respectively) are obtained by the hydrolysis of *N*-ethylidene-threonyl- and *N*-ethylideneallothreonylglycinato complexes (İ), formed in the second phase of the process, by the reaction of acetaldehyde with the N-terminal CH_2 group of the Schiff base of glycylglycinato ligand. The presence of complexes of type İ was proved in the reaction mixture obtained in the reaction of *mer*-[CoCN(glygly)(en)] with acetaldehyde.

When the results obtained in this and in our previous paper are taken into account,[2] the following can be concluded:

(a) The glycylglycinato ligand of all the investigated *mer*-[Co(glygly)L(en)] complexes (L = CN^-, NCS^-, NO_2^-) in the reaction with acetaldehyde gives rise to the corresponding complexes of Schiff bases, as well as a mixture of diastereomeric threonyl- and allothreonylglycinato complexes. The latter are obtained in a much higher yield when the reaction involves the dipeptidato ligand of cyano (~40%) rather than that of the nitro and isothiocyanato (~6%) complexes, respectively; it seems likely that the greater reactivity of the dipeptidato ligand of *mer*-[CoCN(glygly)(en)] is at least partly due to a decreased electron density at the amino nitrogen, which is caused by the trans effect of the cyano ligand. Thus, the first step of the reaction, i.e. deprotonation of the amino group of the dipeptidato ligand, is facilitated.

(b) When the ligand L is changed, the ratio of complexes present in the mixture obtained is altered.

(c) Only one amino group of the ethylenediamine ligand in nitro and isothiocyanato complexes reacts with acetaldehyde, whereby the *N*-ethylidene group in the *mer*-[Co(glygly)NO_2(CH_3CH=en)] complex was found to be in the trans position with respect to the nitro group.[13]

In view of the fact that the position of the *N*-ethylidene group in *mer*-[Co(glygly)NCS(CH_3CH=en)] is not so far determined and that in the reaction of *mer*-[CoCN(glygly)(en)] with acetaldehyde the corresponding condensation product was not obtained, at present, nothing can be said on the effect of the unidentate ligand on the reaction of coordinated ethylenediamine with aldehyde; this will be the subject of our further investigations.

Registry No. I, 18746-17-3; Ia, 93564-67-1; Ib, 93564-68-2; IIa, 93564-70-6; IIb, 93564-72-8; IIIa, 93711-44-5; IIIb, 93711-45-6; IVa, 93564-71-7; IVb, 93564-74-0; Vb, 93564-73-9; *mer*-[CoCN(CH_3CH=threogly)(en)], 93564-69-3; *mer*-[CoCN(CH_3CH=allothreogly)(en)], 93711-43-4; *mer*-[Co(glygly)NO_2(en)], 70738-74-8; acetaldehyde, 75-07-0; glycylglycine, 556-50-3; ethylenediamine, 107-15-3.

Supplementary Material Available: Listings of thermal parameters and observed and calculated structure factor amplitudes (9 pages). Ordering information is given on any current masthead page.

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Nucleoside Complexing. Evidence for Three Metastable Species in the Reaction of Nucleosides with *cis*-Dichlorobis(dimethyl sulfoxide)platinum(II). Use of Restricted Rotation about Pt-N Bonds for Structural Assignments

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The reactions in Me_2SO of *cis*-Pt(Me_2SO)$_2Cl_2$ with 7-methylinosine (7-MeIno), 7-methyl-9-propylhypoxanthine (7-Me-9-PrHX), cytidine (Cyd), and 5-methylcytidine (5-MeCyd) were examined with high-field 360-MHz ^1H NMR spectroscopy as well as limited studies with ^{13}C NMR spectroscopy. In a typical reaction with 7-MeIno at a ratio of one nucleoside per Pt, the products formed in greater abundance at short time periods were found to be *trans*-Pt(7-MeIno)(Me_2SO)Cl_2 and *cis*-[Pt(7-MeIno)$_2$(Me_2SO)Cl]$^+$. With time, these species slowly converted to the stable product, *cis*-Pt(7-MeIno)(Me_2SO)Cl_2. The conversion from a *cis*-dichloro to a *trans*-dichloro species probably proceeds via the complex *cis*-[Pt(7-MeIno)(Me_2SO)$_2$Cl]$^+$, which could be generated by addition of $AgNO_3$ at the initiation of the reaction. When Cyd was employed, direct evidence for the intermediacy of *cis*-[Pt(Cyd)(Me_2SO)$_2$Cl]$^+$ was obtained in the 360-MHz NMR spectrum of the reaction mixture. This species could be made to be the predominant species by addition of $AgNO_3$ as above. The structures were assigned on the basis of the NMR spectrum of complexes since, in certain geometries, the presence of the chiral D-ribose sugars allowed identification of rotamers that are rendered diastereomeric by the chiral sugars. The barrier to rotation about the Pt-N3 bond in Cyd complexes is so large that no evidence for appreciable rotation was observed even at 80 °C, above which temperatures decomposition set in. For the N1-bound 7-MeIno complexes, rotation is somewhat more facile and estimates of rotation barriers were obtained from the partial collapse of the 7-Me ^1H NMR resonances. From $J_{1'2'}$ coupling constants of the complexes, some evidence was found that the N sugar conformer is favored somewhat over the S conformer relative to the distribution of these conformers in the free ligand. This tendency was greater for Cyd and 5-MeCyd complexes than 7-MeIno complexes. This difference was attributed to the sugar and metal being on the same nitrogen heterocyclic ring in the former complexes but on different rings in the latter complexes.

A Pt(II) drug, *cis*-Pt(NH_3)$_2Cl_2$, is currently the most widely sold antitumor agent in the United States.[1] The mechanism of action of this drug probably involves attack on DNA.[2] Reaction of Pt(II) complexes with DNA and DNA constituents has been studied for two additional reasons. First, Pt is a useful heavy-metal label for EM or X-ray studies of nucleic acids.[3] Second, Pt(II) forms inert complexes, and the effects of metal binding on nucleic acid components and the sites of metal binding can be more readily recognized than when labile metal centers are employed.[4]

The Pt antitumor drugs are bifunctional reagents, and the stepwise process that leads to the attachment of Pt to two nucleic

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