Cobalt(III) complexes of stereospecific linear NSNN tetradentate ligands. Synthesis and characterization of ternary amino acid complexes containing tetradentate ligands with terminal amine donors

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Abstract

The preparation and characterization of *cis*-β-[Co(gee)(gly)]$^+$ (geeH = *N*-{2-[(2-aminoethyl)thio]ethyl}-2-aminoacetamide) and *cis*-β-[Co(ege)(AA)]$^+$ (egeH = *N*-(2-aminoethyl)-2-[(2-aminoethyl)thio]acetamide; AA = gly, L-ala, L-leu, L-ile) complexes as PF_6^- or mixed Cl^-/PF_6^- salts are described. ^1H and ^{13}C NMR spectra of the new cobalt complexes demonstrate that only one geometrical isomer (with respect to the bidentate chelate) is obtained with very high stereoselectivity. X-ray structural studies revealed that orientation of the amino acidato chelate is the β_1 configuration; that is, the isomer with the carboxylate donor of the amino acid coordinated *trans* to the amido function to the tetradentate backbone ligand. β_1-[Co(gee)(gly)]$PF_6 \cdot H_2O$ (**I**) crystallized in the monoclinic space group $P2_1/a$ with $a = 11.748(2)$, $b = 11.810(2)$, $c = 12.341(3)$ Å, $\beta = 101.43(2)°$ and $Z = 4$ and was refined to $R = 0.042$. β_1-[Co(ege)(gly)]PF_6 (**II**) crystallized in the monoclinic space group $P2_1/n$ with $a = 11.467(2)$, $b = 8.173(1)$, $c = 17.421(3)$ Å, $\beta = 106.69(2)°$ and $Z = 4$ and was refined to $R = 0.052$. The complexes, β-[Co(L)Cl_2] (L = gee or ege), were found to be convenient precursors for the hydrolysis of the peptide bond of gly–gly to give β_1-[Co(L)(gly)]$^+$ under mild conditions.

Introduction

In a series of recent studies [1–5], we have reported on the stereospecific enforcement of the *cis*-β or unsymmetrical *cis* coordination geometry by linear NSNN tetradentate ligands. These ligands, exemplified by the monoanions of *N*-[(2-pyridyl)methyl]-2-[(2-aminoethyl)thio]acetamide (pygeH), *N*-{2-[(2-aminoethyl)thio]ethyl}-2-aminoacetamide (geeH) and *N*-(2-aminoethyl)-2-[(2-aminoethyl)thio]acetamide (egeH) (Fig. 1), contain internal thioether and deprotonated amido nitrogen donor atoms. The stereospecificity for the *cis*-β configuration apparently arises from the individual stereochemical preferences of the thioether and amido donors for pyramidal and planar coordination geometries, respectively.

Previously [1], we had demonstrated that ternary complexes of the type β-[Co(pyge(AA)]$^+$ (where AA is the anion of an amino acid) formed *only* geometrical isomers of the β_1 configuration (Fig. 2). Thus, for amino acids such as gly that contain no asymmetric centers,

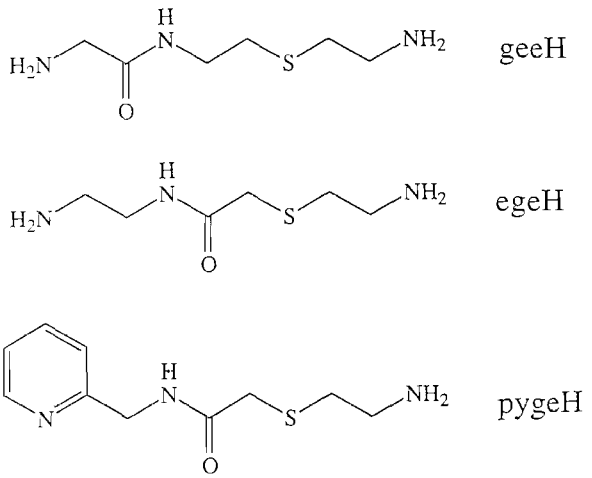

Fig. 1. Structural representations of linear NSNN tetradentate ligands.

a pair of Δ,Λ-β_1 enantiomers was isolated, where the Δ,Λ designation refers to the sense in which the tetradentate ligand is wrapped about the metal center (Fig. 2). If the amino acid ligand was optically active as for L-ala, then the Δ- and Λ-β_1 complexes that formed were diastereomerically related to one another. Herein,

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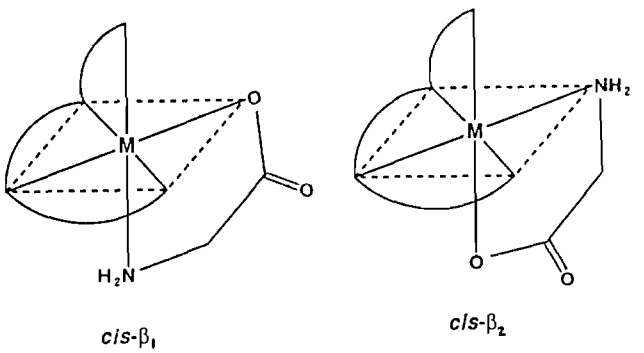

Fig. 2. The two possible geometrical configurations for a chelating gly ligand in a *cis*-β octahedral complex. Only one enantiomer (Δ) is depicted for each configuration. The mirror images would then have the Λ designation.

we report on further investigations involving the preparation and characterization of the complexes β-$[Co(L)(AA)]^+$, where L = gee, AA = gly or L = ege, AA = gly, L-ala, L-leu and L-ile. The configuration of the amino acid ligands have been established via X-ray structural determinations for the complexes β-$[Co(gee)(gly)]PF_6 \cdot H_2O$ (**I**) and β-$[Co(ege)(gly)]PF_6$ (**II**). In addition, we have briefly examined the use of $[Co(L)Cl_2]$ (L = gee or ege) as starting materials for the promotion of the hydrolysis of the peptide bond of glycylglycine.

Experimental

Materials and methods

^1H and ^{13}C NMR spectra were obtained on a Varian XL-300 spectrometer at 299.943 and 75.429 MHz, respectively. Spectra obtained in D_2O solution were referenced to (3-trimethylsilyl)propionic acid, sodium salt (^1H) or dioxane (^{13}C). Visible absorption spectra of dilute aqueous solutions were obtained on either Varian DMS-80 or Shimadzu UV-160 spectrophotometers at ambient temperature. Elemental analyses were determined by Atlantic Microlab, Inc. (Norcross, GA).

Preparation of complexes

A general synthesis for the cationic complexes, *cis*-β_1-$[Co(L)(AA)]^+$, (L = gee, AA = gly; L = ege, AA = gly, L-ala, L-leu, L-ile) will be given. The appropriate free amino acid (2.2 mmol) was added to a solution of β-$[Co(L)Cl_2]$ (2.0 mmol; L = gee or ege [5]) in water (10 ml) and the pH was adjusted to 7.6–7.8 by dropwise addition of NaOH solution (2.5 M). The purple reaction mixture was heated at 50–60 °C until a deep red–orange color was attained (2.5–5.0 h) and filtered while hot. NH_4PF_6 (0.49 g, 3.0 mmol) was added to the filtrate. If a small amount of purplish material precipitated at this point, the mixture was refiltered. Slow evaporation provided red or reddish orange, microcrystalline product. Yields ranged between 40 and 60%.

The new complexes had similar electronic spectra in aqueous solution with one broad absorption in the visible region having λ_{max} 507 ± 2 nm with log ϵ 2.55 ± 0.05. Analytical and NMR spectroscopic data for specific complexes follow. The NMR spectra for the new compounds are rather complicated. This is especially so in cases where the complex cations, that have amino acidato ligands with asymmetric centers, are isolated as equal mixtures of two diastereomers. If resonances for the same group in the ^1H or ^{13}C NMR spectrum of the diastereomers are sufficiently well separated, then the chemical shift values are presented as pairs of values next to the assignment. ^{13}C NMR spectra were not obtained for the less soluble L-leu and L-ile complexes.

For L = gee, AA = gly, the complex was a monohydrate. *Anal.* Calc. for $C_8H_{20}F_6N_4O_4PSCo$: C, 20.35; H, 4.27; N, 11.86. Found: C, 20.11; H, 4.44; N, 11.75%. ^1H NMR (D_2O): δ 2.7–4.1 (complex spectrum of overlapping multiplets). ^{13}C NMR (D_2O): δ 186.09, 179.91, 49.06, 47.03, 46.33, 44.04, 38.28, 35.90.

For L = ege, AA = gly, the complex was anhydrous. *Anal.* Calc. for $C_8H_{18}F_6N_4O_3PSCo$: C, 21.16; H, 3.99; N, 12.34. Found: C, 20.94; H, 4.13; N, 12.22%. ^1H NMR (D_2O): δ 4.03 (d, 1H, SCH_2CO), 3.51 (d, 1H, SCH_2CO), 3.47 (AB q, 2H, gly-CH_2), 2.6–2.8 (complex m, 8H, ege ligand). ^{13}C NMR (D_2O): δ 185.93, 178.06, 47.24, 47.01, 46.00, 44.22, 40.67, 38.71.

For L = ege, AA = L-ala, the complex was anhydrous. *Anal.* Calc. for $C_9H_{20}F_6N_4O_3PSCo$: C, 23.09; H, 4.31; N, 11.97. Found: C, 23.78; H, 4.68; N, 11.65%. ^1H NMR (D_2O): δ (4.04, 4.02) (d, 1H, SCH_2CO), (3.72, 3.63) (q, 1H, ala-CH), 3.51 (slightly broadened d, 1H, SCH_2CO), 2.6–2.8 (complex m, 8H, ege ligand), (1.43, 1.39) (d, 3H, ala-CH_3). ^{13}C NMR (D_2O): δ (187.90, 186.46), 178.24 (broadened), (55.81, 53.83), (47.10, 46.96), (46.11, 46.00), (44.13, 43.97), (40.75, 40.56), 38.76 (broadened), (18.66, 18.60).

For L = ege, AA = L-leu, the complex was considerably less soluble and replacement of Cl by PF_6 was only 20% complete. The material analyzed as a monohydrate. *Anal.* Calc. for $C_{12}H_{28}Cl_{0.8}F_{1.2}N_4O_4P_{0.2}SCo$: C, 32.70; H, 6.40; N, 12.71; Cl, 6.44. Found: C, 33.01; H, 6.49; N, 12.69; Cl, 6.72%. ^1H NMR (D_2O): δ 4.07 (d, 1H, SCH_2CO), 3.59 (complex m, 1H, leu-NCH), 3.50 (d, 1H, SCH_2CO), 2.6–2.8 (complex m, 8H, ege ligand), 1.60–1.90 (complex m, 1H, leu-^{i}PrCH), 0.88–0.94 (four overlapping d, 6H, leu-CH_3).

For L = ege, AA = L-ile, the complex was again considerably less soluble and replacement of Cl by PF_6 was only 65% complete. The material analyzed as a monohydrate. *Anal.* Calc. for $C_{12}H_{28}Cl_{0.35}F_{3.9}N_4O_4P_{0.65}SCo$: C, 29.41; H, 5.76; N, 11.43; Cl, 2.53. Found: C, 28.96; H, 5.72; N, 11.40; Cl, 2.84%. ^1H NMR (D_2O): δ (4.08, 4.06) (d, 1H, SCH_2CO),

3.5–3.8 (complex, 2H, ile-CH and SCH_2CO), 2.6–2.8 (complex m, 8H, ege ligand), 1.95 (m, 1H, ile-^{s}BuCH), 1.23 (m, 2H ile-^{s}BuCH_2), 1.09 (d, 3H, ile-CH_3), 1.03 (d of d, 3H, ile-CH_3), 0.85–0.93 (overlapping d and t, 6H, ile-CH_3).

Hydrolysis of amide bonds by β-[Co(L)Cl$_2$] (L = gee or ege)

The promotion of the hydrolysis of the amide bond of glycylglycine by β-[Co(L)Cl$_2$] (L = gee or ege) was performed analogously to the preparation of the amino acid complexes given above. In each case, the isolated metal complex had visible, ^{1}H NMR and ^{13}C NMR spectra that were essentially identical to those of independently prepared *cis*-β$_1$-[Co(L)(gly)]PF$_6$ (L = gee or ege).

Crystal structure analysis and refinement

Well-formed single crystals of β$_1$-[Co(gee)(gly)]PF$_6$·H$_2$O (**I**) and β$_1$-[Co(ege)(gly)]PF$_6$ (**II**) were obtained by slow evaporation of concentrated aqueous solutions. A Nicolet R3m diffractometer in the θ/2θ mode with variable scan speed and graphite monochromated Mo Kα radiation was used to measure 2204 and 2037 unique reflections with $2 \leqslant 2\theta \leqslant 45°$ for **I** and **II**, respectively. Of these, there were 1710 (for **I**) and 1492 (for **II**) reflections with $|F_o| > 6|F_o|$. Data were corrected for background, attenuators, Lorentz and polarization effects in the usual fashion, but not for absorption [6]. Heavy atoms were located via Patterson maps and full-matrix least-squares refinement was accomplished with the SHELTXL Plus package of programs. Hydrogen atom positions were calculated geometrically, fixed at a C–H distance of 0.96 Å, and not refined. The structures were refined to $R = 0.042$, $R_w = 0.047$ for **I** and $R = 0.052$, $R_w = 0.059$ for **II**. Crystal data are summarized in Table 1 and final atomic positional parameters are provided in Tables 2 and 3 for **I** and **II**, respectively.

TABLE 1. Crystallographic data for β$_1$-[Co(gee)(gly)]PF$_6$·H$_2$O (**I**) and β$_1$-[Co(ege)(gly)]PF$_6$ (**II**)

	I	**II**
Formula	$C_8H_{20}F_6N_4O_4PSCo$	$C_8H_{18}F_6N_4O_3PSCo$
Molecular weight	472.23	454.21
Crystal system	monoclinic	monoclinic
Space group	$P2_1/a$	$P2_1/n$
a (Å)	11.748(2)	11.467(2)
b (Å)	11.810(2)	8.173(1)
c (Å)	12.341(3)	17.421(3)
β (°)	101.43(2)	106.69(2)
V (Å^3)	1678.2(9)	1563.9(9)
$F(000)$	960	920
Z	4	4
λ (Mo Kα) (Å)	0.71069	0.71069
D_{calc} (g cm^{-3})	1.87	1.93
μ (Mo Kα) (cm^{-1})	13.2	14.0

TABLE 2. Atomic coordinates (×10^4) and thermal parameters (Å^2×10^3) for β$_1$-[Co(gee)(gly)]PF$_6$·H$_2$O (**I**)

Atom	x	y	z	U_{iso}
Co(1)	−1513(1)	−1167(1)	1827(1)	19(1)[a]
S(1)	−859(1)	−993(1)	3647(1)	31(1)[a]
O(1)	−4945(3)	−823(3)	1280(3)	31(1)[a]
O(2)	−21(3)	−1447(3)	1467(3)	24(1)[a]
O(3)	1463(3)	−613(3)	911(3)	29(1)[a]
N(1)	−1687(3)	−2796(3)	2071(3)	26(1)[a]
N(2)	−3010(3)	−866(3)	2086(3)	22(1)[a]
N(3)	−2285(3)	−1336(3)	281(3)	22(1)[a]
N(4)	−1168(3)	439(3)	1594(3)	23(1)[a]
C(1)	−1868(4)	−3086(5)	3192(4)	34(2)[a]
C(2)	−989(5)	−2454(5)	4037(4)	43(2)[a]
C(3)	−2131(4)	−288(5)	3962(4)	35(2)[a]
C(4)	−3245(4)	−594(5)	3173(4)	32(2)[a]
C(5)	−3888(4)	−987(4)	1243(4)	22(2)[a]
C(6)	−3562(4)	−1375(4)	185(4)	25(2)[a]
C(7)	553(4)	−575(4)	1283(4)	24(2)[a]
C(8)	73(4)	557(4)	1560(4)	29(2)[a]
P(1)	3365(1)	1835(1)	3398(1)	41(1)[a]
F(1)	3173(4)	2352(4)	4541(3)	70(2)[a]
F(2)	2456(4)	2731(4)	2744(4)	81(2)[a]
F(3)	4266(4)	983(3)	4069(4)	80(2)[a]
F(4)	4348(3)	2766(4)	3414(4)	83(2)[a]
F(5)	2335(4)	967(4)	3439(4)	84(2)[a]
F(6)	3531(6)	1348(6)	2280(4)	141(3)[a]
Ow	1559(3)	3501(3)	463(3)	38(1)

[a] U_{iso} is the equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor.

Results and discussion

The synthesis of *cis*-β-[Co(L)(AA)]$^+$, where L = gee, AA = gly or L = ege, AA = gly, L-ala, L-leu and L-ile, was accomplished by reacting *cis*-β-[Co(L)Cl$_2$] [5] with the corresponding amino acid in slightly basic aqueous solution under mild conditions. This method has been previously utilized by us to prepare *cis*-β-[Co(pyge)(AA)]$^+$ [1]. The amino acidato complexes of gee and ege are somewhat less soluble in water than their pyge analogs. As a consequence, the exchange of chloride counteranion by hexafluorophosphate was not complete for AA = L-leu or L-ile, as indicated by analytical results. The visible electronic spectra of the new complexes were unremarkable, having one broad, relatively symmetrical absorption (see 'Experimental').

Since we have here ternary *cis*-β octahedral complexes containing an unsymmetrical bidentate ligand, two geometrical isomers are possible with respect to the tetradentate ligand. These configurations have been designated as *cis*-β$_1$ and *cis*-β$_2$ (Fig. 2) by literature convention [7]. Due to the handedness imparted by

TABLE 3. Atomic coordinates ($\times 10^4$) and thermal parameters ($Å^2 \times 10^3$) for β_1-[Co(ege)(gly)]PF_6 (**II**)

Atom	*x*	*y*	*z*	U_{iso}[a]
Co(1)	852(1)	−1428(1)	−1188(1)	24(1)
S(1)	−52(1)	−1325(1)	−2506(1)	36(1)
O(1)	2396(4)	−4844(6)	−2260(3)	41(2)
O(2)	−87(4)	351(5)	−942(3)	32(2)
O(3)	−119(5)	3065(6)	−821(3)	42(2)
N(1)	−400(5)	−3000(7)	−1092(3)	31(2)
N(2)	1802(5)	−3148(6)	−1398(3)	26(2)
N(3)	1760(5)	−1760(6)	−58(3)	31(2)
N(4)	1976(5)	276(6)	−1301(3)	31(2)
C(1)	−1065(7)	−3798(9)	−1866(4)	42(3)
C(2)	−1392(7)	−2512(10)	−2501(4)	45(3)
C(3)	903(6)	−2794(8)	−2808(4)	33(3)
C(4)	1793(6)	−3673(8)	−2108(4)	30(2)
C(5)	2594(7)	−3929(9)	−674(4)	39(3)
C(6)	2868(7)	−2722(10)	−32(4)	50(3)
C(7)	290(7)	1801(8)	−1019(4)	32(3)
C(8)	1334(7)	1864(8)	−1401(4)	39(3)
P(1)	1064(2)	7082(3)	4047(1)	43(1)
F(1)	2487(5)	7019(10)	4522(4)	104(3)
F(2)	−319(6)	7009(11)	3594(4)	133(4)
F(3)	909(7)	6696(15)	4896(4)	128(5)
F(4)	846(15)	8894(11)	4177(7)	121(7)
F(5)	966(12)	5237(13)	4094(10)	149(7)
F(6)	1258(8)	7238(17)	3223(4)	140(5)

[a] U_{iso} is the equivalent isotropic *U* defined as one-third of the trace of the orthogonalized U_{ij} tensor.

the manner in which the tetradentate ligand wraps about the metal, each of these geometrical isomers exists as a pair of enantiomers or diastereomers depending upon whether the amino acidato ligand contains an asymmetric center [1]. The ^1H (though complicated) and ^{13}C NMR spectra for β-[Co(L)(AA)]$^+$ strongly suggest that only one of the two geometrical configurations, β_1 or β_2, is formed. This conclusion, which is entirely analogous to that derived for the β-[Co(pyge)(AA)]$^+$ case [1], is based upon the observation of only one set of NMR resonances for the complex containing the achiral gly ligand and two sets of closely-spaced resonances for the complexes containing the chiral L-ala, L-leu or L-ile.

In order to establish unequivocally the orientation of the amino acidato ligands with respect to the tetradentate ligand, we resorted to single crystal X-ray diffraction methods. The structures of the cations of [Co(gee)(gly)]$PF_6 \cdot H_2O$ (**I**) and [Co(ege)(gly)]PF_6 (**II**) are depicted in Figs. 3 and 4, respectively. Selected bond distances and angles for both complexes are provided in Table 4.

The gee and ege ligands of **I** and **II**, respectively, adopt the expected *cis*-β geometry [1–5]. Significant steric strain is evident about the pyramidally coordinated sulfur atom in both complexes; the Co(1)–S(1)–C(2), C(3) angles are 98.6(2), 97.1(2)° for **I** and 96.8(2),

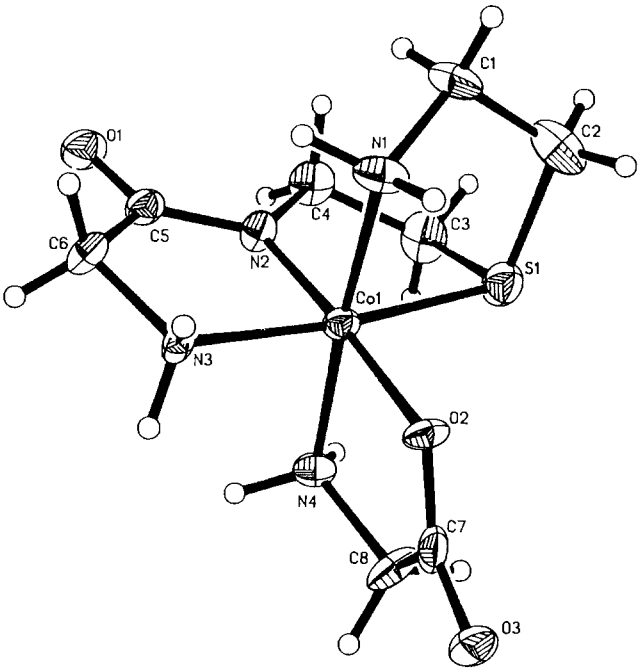

Fig. 3. Molecular structure and atom numbering scheme for **I**.

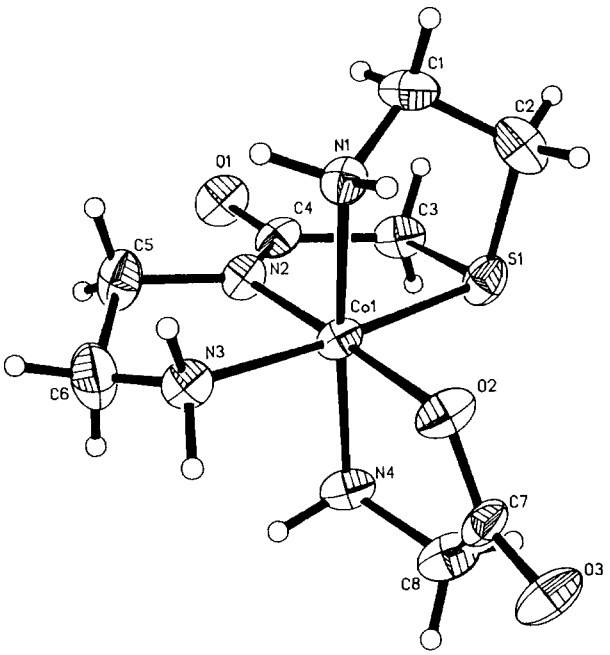

Fig. 4. Molecular structure and atom numbering scheme for **II**.

97.7(2)° for **II**. The Co(1)–N(2) distance in each complex is significantly shorter than those for the Co–N(sp^3) bonds. Approximately trigonally geometry is found about N(2), with the following values for relevant angles for **I** and **II**, respectively: Co(1)–N(2)–C(4) 123.4(3), 125.6(4); Co(1)–N(2)–C(5) 117.1(3), 114.1(4); C(4)–N(2)–C(5) 119.3(4), 120.3(6). Bond lengths and angles within the gee and ege ligands are very similar

TABLE 4. Selected bond lengths (Å) and angles (°) for β_1-[Co(gee)(gly)]$PF_6 \cdot H_2O$ (I) and β_1-[Co(ege)(gly)]PF_6 (II)

	I	II
Co(1)–S(1)	2.235(1)	2.233(2)
Co(1)–N(1)	1.964(4)	1.969(6)
Co(1)–N(2)	1.883(4)	1.878(6)
Co(1)–N(3)	1.953(4)	1.963(5)
Co(1)–N(4)	1.973(4)	1.946(6)
Co(1)–O(2)	1.920(3)	1.929(5)
S(1)–Co(1)–O(2)	95.8(1)	94.4(1)
S(1)–Co(1)–N(1)	87.8(1)	88.7(2)
O(2)–Co(1)–N(1)	89.7(2)	90.3(2)
S(1)–Co(1)–N(2)	87.6(1)	87.2(2)
O(2)–Co(1)–N(2)	176.4(1)	178.3(2)
N(1)–Co(1)–N(2)	91.7(2)	90.4(2)
S(1)–Co(1)–N(3)	172.5(1)	172.7(2)
O(2)–Co(1)–N(3)	91.4(1)	92.9(2)
N(1)–Co(1)–N(3)	90.4(2)	90.8(2)
N(2)–Co(1)–N(3)	85.2(2)	85.5(2)
S(1)–Co(1)–N(4)	91.1(1)	89.7(2)
O(2)–Co(1)–N(4)	84.8(1)	84.9(2)
N(1)–Co(1)–N(4)	174.2(2)	174.8(2)
N(2)–Co(1)–N(4)	93.9(2)	94.5(2)
N(3)–Co(1)–N(4)	91.4(2)	91.4(2)

to those previously reported for β-[Co(gee)$NO_2)_2$]$\cdot H_2O$ [5] and β-[Co(ege)$(NO_2)_2$]$\cdot 4H_2O$ [3].

The structural parameters for the cobalt–glycinato moieties of I and II are also within expected values [1, 8–10]. The orientation of the gly ligand in both complexes is β_1 (see Figs. 3 and 4), with the amino and carboxylato groups of the gly ligand *trans* to the amino and amido groups of the tetradentate ligand, respectively. The solution visible, ^1H NMR and ^{13}C NMR spectra of the crystals used in this study are identical to those of starting materials, which suggests that the β_1 geometry persists in the solution and solid states and that no rearrangements have occurred during the crystallization process.

By extrapolation, we can assign the β_1 configuration to the other $[Co(ege)(AA)]^+$ complexes in this study. This assertion is based upon the fact that the corresponding chemical shifts of the ege ligand in these compounds are very similar to those in the gly complex and that only one set of diastereomers (i.e. two compounds) is isolated. In addition, visible spectra of these other complexes contain one absorption that has virtually the same shape and energy across the series.

An entirely analogous situation was obtained for the series of complexes, β_1-$[Co(pyge)(AA)]^+$ [1]. In that case, we argued that substitution of the coordination position *trans* to the amino group of the pyge ligand is labilized relative to the substitution of the position *trans* to the amido donor. This reasoning was based upon observations of substitution patterns of the two different chloride ligands of β-[Co(pyge)Cl_2] by monodentate nitrite at room temperature. The incoming nitrite ligand was found to substitute first the position *trans* to the amine donor. We feel that similar considerations hold forth in the present investigation involving gee and ege complexes; that is, the β_1 geometry of the amino acidato chelate results from kinetically-controlled substitution, coupled with the preference of Co(III) ions for nitrogen donors [11]. Little or no spectroscopic evidence was found in the filtrates of the preparations of the complexes for formation of the β_2 isomer. These results are in accord with previous observations for the pyge complexes [1] and contrast with studies involving $[Co(trien)(gly)]^{2+}$ (trien = 1,10-diamino-3,7-diazaoctane), where *cis*-α, *cis*-β_1 and *cis*-β_2 isomers could be readily obtained [8–10].

It is also possible that the observed β_1 coordination geometry of the amino acidato ligand is the result of thermodynamic considerations. However, in all cases involving the preparation of $[Co(L)(AA)]^+$ (L = pyge [1], gee or ege; AA = L-ala, L-val, L-leu, L-ile), 50:50 mixtures of the two β_1 diastereomers are isolated. Further, this 50:50 mixture of diastereomers is also found at earlier stages of the preparation when starting material is still present, at least for L = pyge, AA = L-ala.

The isolated 50:50 mixture of β_1 diastereomers for L = pyge, AA = L-ala, can be equilibrated to the thermodynamic equilibrium 63:37 ratio of isomers in dilute base as judged by ^1H NMR spectroscopy [1]. In these equilibration experiments, we argued that rearrangements of ligands about the coordination sphere of the cobalt ion were responsible for the interconversion of the isomers. From these observations one might be tempted to infer that ligand rearrangement about the cobalt center is facile and may be occurring during the preparation of the complexes. However, this isomerization process takes two days to complete at the same temperature and pH at which the preparations of the 50:50 mixture of β_1 isomers are accomplished. We note that in all of these experiments, absolutely no resonances attributable to β_2 diastereomers were detected. Thus, one would be forced to argue that the β_1 isomers are much more stable than the β_2 isomers which, though possible, seems unlikely based upon prior observations involving the trien system [8–10].

Regarding the preferential substitution of the coordination position *trans* to the amine donor rather than the position *trans* to the amide group, we feel that kinetic rather than thermodynamic factors again are likely in operation. Co–NO_2 bond distances *trans* to the amide ligand are either equivalent to or somewhat shorter than the analogous bond distances *trans* to the terminal amino ligand for $Co(L)(NO_2)_2$ (L = pyge [4], gee [3], ege [3]). (We note that one exception to this observation involves the $Co(pyge)(NO_2)_2$ moiety that

is part of the cocrystallized $[Co(pyge)(NO_2)_2]\cdot[Co(pyge)(Cl)(NO_2)]$ [1].) If the transition state for the substitution process resembles the starting material, then the $Co-NO_2$ bond lengths suggest that substitution at the site *trans* to the amino group may occur first. However, arguing kinetic effects based upon ground state effects can be perilous, and the differences in $Co-NO_2$ bond distances are not sufficiently great to warrant confidence in their application in the present case. In conclusion, we feel that kinetic control of the stereochemistry is the better interpretation for the formation of the geometrical isomers in the present instances, but thermodynamic arguments cannot be excluded.

The dichloro complexes, β-$[Co(L)Cl_2]$ (L = gee or ege), were also found to be convenient starting materials for the promotion of the hydrolysis of the peptide bond of glycylglycine (gly–gly) under mild conditions (50–60 °C, pH 7.6–7.8, 2–3 h). This activity is similar to that described for a number of Co(III) complexes [12–15]. Thus, the reaction of the dichloro cobalt complexes with gly–gly gives β_1-$[Co(L)(gly)]^+$, with no detectable intermediate. The spectroscopic (visible, ^1H NMR, ^{13}C NMR) analysis of the cobalt complexes, isolated as their hexafluorophosphate salts, indicates that they have the same β_1 configuration as the complexes prepared directly from gly. If the same kinetic control of coordination is operative as for coordination of the free amino acids (*vide supra*), then the stereoselective formation of the β_1 isomer implies that the dipeptide coordinates at the N-terminal end first. Subsequent coordination of the carbonyl oxygen of the activated carbonyl group, followed by rapid hydrolysis of the peptide bond would account for the formation of β_1-$[Co(L)(gly)]^+$ [1].

Supplementary material

Complete tables of crystallographic data, bond lengths, bond angles, temperature factors, hydrogen atom positions and structure factors for **I** and **II** are available from the authors.

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