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The Stereochemistry of Some Cobalt(III) Triethylenetetramine Complexes of Glycine and Sarcosine[1a]

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Under controlled conditions reaction of glycine and glycine ethyl ester with β-$[Co(trien)OH(H_2O)]^{2+}$ results in the formation of the β_2-$[Co(trien)(gly)]^{2+}$ and β_1-$[Co(trien)(gly)]^{2+}$ ions, respectively. Similar reactions using β-$[Co(trien)Cl(H_2O)]^{2+}$ give the β_1- and β_2-$[Co(trien)(gly)]^{2+}$ complexes, respectively. Sarcosine and sarcosine ethyl ester give one product, β_2-$[Co(trien)(sar)]^{2+}$, on reaction with $[Co(trien)OH(H_2O)]^{2+}$. The β_1- and β_2-$[Co(trien)(gly)]^{2+}$ and β_2-$[Co(trien)(sar)]^{2+}$ ions have been resolved into their optical forms. Both the synthetic methods used and the rotatory dispersion, circular dichroism, and infrared spectra suggest that these complexes contain the β-triethylenetetramine configuration and visible and pmr spectra are consistent with this assignment. A conformational analysis study suggests the stereospecific coordination of sarcosine in the β_2-$[Co(trien)(sar)]^{2+}$ ion. From the known absolute configuration of D(+)$[Co(en)_2(sar)]^{2+}$ the absolute configurations of the D(+)β_2-*SS*-$[Co(trien)(gly)]^{2+}$ and L(−)β_2-*RRS*-$[Co(trien)(sar)]^{2+}$ ions are deduced.

Introduction

In an attempt to establish and understand those factors which are significant in the aqueous metal ion catalyzed hydrolysis of amino acid esters, amides, and peptide molecules several recent investigators have utilized inert complex ions of the type *cis*-$[CoN_4OH(H_2O)]^{2+}$ (N_4 represents the donor N atoms of a coordinated amine) as the active metal site.[2-4] The reasons advanced for this choice of metal ion are (1) that the stereochemistry of both the starting complex and the product $[CoN_4AA]^{2+}$ ion (AA = amino acid anion) are usually well understood and (2) that the inability of such systems to undergo rapid ligand-exchange reactions permits the possibility of studying, and in some instances isolating, the intermediates involved.[5,6] The most successful reagent of this class to be reported is the $[Co(trien)OH(H_2O)]^{2+}$ ion which reacts rapidly with amino acid esters and amides under relatively mild conditions to form the complex ions $[Co(trien)AA]^{2+}$.[3] In the case of the peptide hydrolysis reactions this was shown to involve the N-terminal removal of an amino acid residue, and in favorable cases the amino acids of small peptide molecules were removed in a sequential manner.

Before a detailed study of the mechanism of these reactions is profitable, it is important to establish the stereochemistry of the final product since several configurations and conformations of triethylenetetramine and configurations of the amino acid in the $[Co(trien)AA]^{2+}$ ion are possible. This paper reports the results of such a study where AA = glycine and sarcosine (N-methylglycine).

To put the results in their correct perspective some discussion of the isomeric possibilities is desirable. Triethylenetetramine may adopt three geometrical configurations about cobalt(III) (α, β, and *trans*), but only two of these (α, β) allow *cis* coordination of the glycine chelate. Also, owing to the unsymmetrical nature of glycine, two β isomers are possible, one, β_2, with the amino group of glycine in a *trans* position to a secondary N atom of triethylenetetramine and the other, β_1, with the amino group *trans* to a terminal NH_2 group of the quadridentate. The three possible geometrical isomers are shown in Figure 1, and each will occur in optically active forms. Further, a close examination of Dreiding stereo models reveals two conformations of the triethylenetetramine ligand for each β isomer, controlled by the asymmetry about the planar N atom ("planar" designates that secondary N atom connecting the two coplanar ethylenediamine rings). These conformations are shown in Figure 2. Both might be expected to be stable in acidic solution since their interconversion requires removal of the planar NH proton and inversion of configuration at this N center. Both conformations have been detected in the β-$[Co(trien)(H_2O)_2]^{3+}$ ion with that given by Figure 2B mutarotating to the thermodynamically more stable (~3 kcal mole^{-1}) conformer, Figure 2A, with a term in the rate expression proportional to $[OH^-]$.[7] It was reasoned that this term corresponds more closely to the base-catalyzed ionization of the planar NH proton than to a process whereby mutarotation is governed by water exchange. A similar situation is likely for the conformation of triethylenetetramine in the β-$[Co(trien)(gly)]^{2+}$ structures so that at the pH values used in this study the thermodynamically favored conformation, Figure 2A, is most probably realized. The NH proton attached to the trigonal secondary nitrogen atom of the β structure is stereospecifically orientated owing to the ligand configuration about it. Furthermore, it is likely that this results in a decided preference for one

(1) (a) Taken in part from B.S. Honors Thesis of L. G. M., Brown University, 1965; (b) Biological Inorganic Chemistry Unit, John Curtin School of Medical Research, Australian National University, Canberra, Australia.

(2) D. A. Buckingham and J. P. Collman, *Inorg. Chem.*, in press.

(3) D. A. Buckingham and J. P. Collman, *J. Am. Chem. Soc.*, **85**, 3039 (1963); D. A. Buckingham, J. P. Collman, D. A. R. Happer, and L. G. Marzilli, *ibid.*, **88**, 1082 (1967).

(4) J. P. Collman and S. A. Young, private communication.

(5) M. D. Alexander and D. A. Busch, *J. Am. Chem. Soc.*, **88**, 1130 (1966).

(6) D. A. Buckingham, J. P. Collman, E. Kimura, and L. G. Marzilli unpublished work.

(7) D. A. Buckingham, P. A. Marzilli, and A. M. Sargeson *Inorg. Chem.*, **6**, 1032 (1967).

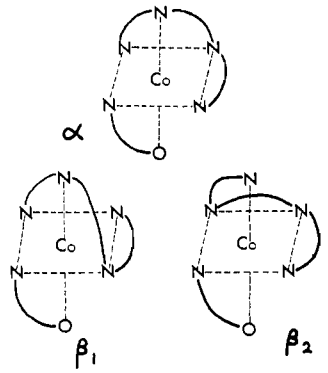

Figure 1.—The α, β_1, and β_2 configurations of the $[Co(trien)(gly)]^{2+}$ ion.

specific for each glycine complex since crystalline diastereoisomers were not obtained on treating the β_1 and β_2 complexes with Ag(SbO(+)tar) and Na(+)$[Co(C_2O_4)_2(en)]\cdot H_2O$, respectively.

During the course of this study two complexes containing monodentate glycine (O bonded) and one containing monodentate glycine ethyl ester (N bonded) were prepared. These reactions are summarized in Table II, together with some of the physical properties of the products. The pmr spectra of these compounds are consistent with the assigned structures. Deuterated β-$[Co(trien)(glyH)_2](ClO_4)_3$ shows two absorptions for the CH_2 protons of glycine split by 1.5 cps (δ 3.7) while deuterated α-$[Co(trien)(glyH)_2](ClO_4)_3$ has

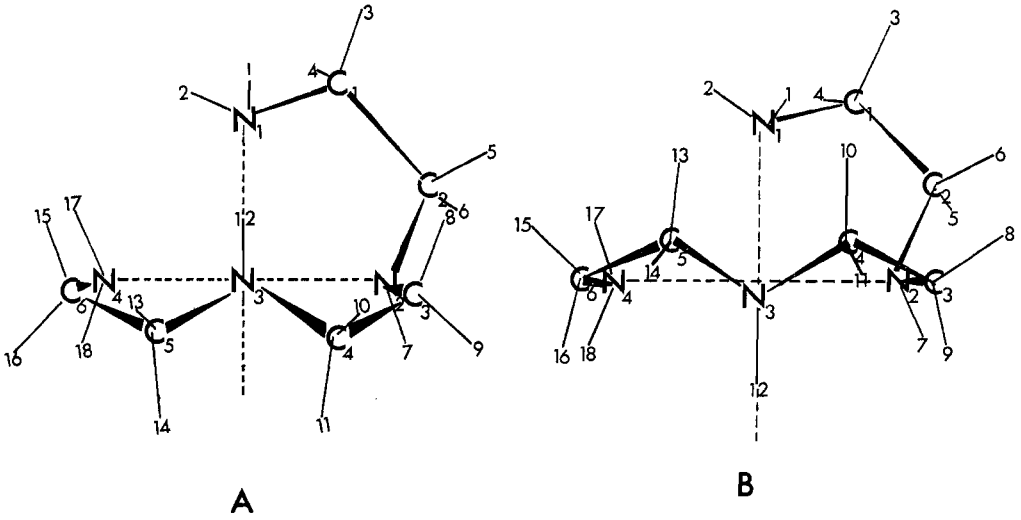

Figure 2.—The two possible conformations of triethylenetetramine viewed down the "planar" N–Co axis: (A) Dβ-*SS*; (B) Dβ-*SR*.

conformational structure of ligand about this nitrogen atom. A similar situation occurs in the α-$[Co(trien)(gly)]^{2+}$ structure where both secondary NH protons are stereospecifically directed and only one ligand conformation is likely for each of the D and L forms.

Results

Reactions with Glycine and Glycine Ethyl Ester. —Starting complexes, reaction conditions, and major products formed using glycine and glycine ethyl ester are given in Table I. The most convenient routes to the β_1 and β_2 isomers are given by reactions 1 and 4, respectively. Spectrophotometric estimation of the final solutions showed that these reactions give >95% isomer purity.

The β_1 and β_2 isomers were resolved into their optical isomers using Na(+)$[Co(C_2O_4)_2(en)]\cdot H_2O$ and Ag(SbO(+)tar), respectively, giving Lβ_1-*RR*-$[Co(trien)(gly)]I_2\cdot 2H_2O$ ($[\alpha]_D$ −330°) and Dβ_2-*SS*-$[Co(trien)(gly)]I_2\cdot 2H_2O$ ($[\alpha]_D$ +205°).[8] These resolving agents are

(8) In this paper the following sequence will be followed in designating optical and geometric structures: D and L describe the over-all chiralty of the ion referred to that of D-$[Co(en)_3]^{3+}$; α and β describe the gross geometrical configuration of triethylenetetramine about the cobalt atom; (+) or (−) refer to the sign of rotation at the Na D line; *R* and *S* designate the asymmetry about the trigonal and planar asymmetric N atoms of triethylenetetramine and the secondary N atom of sarcosine in that order and follow the rules suggested by C. K. Ingold, V. Prelog, and R. S. Cahn, *Angew. Chem. Intern. Ed. Engl.*, **5**, 385 (1966).

TABLE I
SUMMARY OF METHODS USED FOR PREPARING THE β_1- AND β_2-$[Co(trien)(gly)]^{2+}$ IONS

	Reacting complex ion	Glycine deriv	pH	Temp, °C	Major $[Co(trien)(gly)]^{2+}$ product
1.	β-$[Co(trien)OH(H_2O)]^{2+}$	Ester	8	25	β_1
2.	β-$[Co(trien)Cl(H_2O)]^{2+}$ [a]	Ester	6–7	40	β_2
3.	α-$[Co(trien)OH(H_2O)]^{2+}$	Ester	7	30	β_1
4.	β-$[Co(trien)OH(H_2O)]^{2+}$	Acid	5.5, 8–10	25–40	β_2
5.	β-$[Co(trien)Cl(H_2O)]^{2+}$ [a]	Acid	6	40	β_1
6.	α-$[Co(trien)OH(H_2O)]^{2+}$	Acid	7–8	10–50	$\beta_2 + \beta_1$
7.	α-$[Co(trien)OH(H_2O)]^{2+}$	Acid	4.5, 10	50, 20	β_2
8.	β-$[Co(trien)Cl(gly\text{-}OC_2H_5)]^{2+}$	...	8	20	β_2
9.	β-$[Co(trien)(glyH)_2]^{3+}$	...	10	35	β_1
10.	β_2-$[Co(trien)\text{-}(glyglyOC_2H_5)]^{2+}$	...	10	25	β_2

[a] Obtained by aquation of β-$[Co(trien)Cl_2]Cl$.

only one absorption at 3.8 ppm consistent with the C_2 symmetry of the α isomer.

Reactions with Sarcosine and Sarcosine Ethyl Ester. —The various reactions attempted are summarized in Table III. It can be seen that under all conditions only one isomer was isolated. This has been assigned the β_2 configuration. Spectrophotometric estimations of the final solutions indicated that the isolated products were representative of the product isomers formed. β_2-$[Co(trien)(sar)]I_2\cdot 2H_2O$ was resolved into its optical

TABLE II

SUMMARY OF METHODS USED FOR PREPARING MONODENTATE GLYCINE AND GLYCINE ESTER COMPLEXES

Reacting ion	Glycine deriv	Isolated product	Visible absorption spectra[a]	pK_a[b]
β-[Co(trien)OH(H_2O)]$^{2+}$ + gly (excess)	pH 5, 35°	β-[Co(trien)(glyH)$_2$](ClO_4)$_3$	ϵ_{360} 114	8.10
			ϵ_{493} 173	9.18
α-[Co(trien)OH(H_2O)]$^{2+}$ + gly (excess)	pH 5, 35°	α-[Co(trien)(glyH)$_2$](ClO_4)$_3$	ϵ_{512} 221	8.02
				9.05
β-[Co(trien)Cl(H_2O)]$^{2+}$ + $glyOC_2H_5$ (excess)	pH <7, 20°	β_2-[Co(trien)Cl($glyOC_2H_5$)]Cl_2	ϵ_{372} 103	
			ϵ_{487} 99	

[a] Measured in 0.01 M $HClO_4$. [b] Calculated for overlapping pK_a values as given by H. T. S. Britton in "Hydrogen Ions," 4th ed, Chapman and Hall, London, 1955.

TABLE III

SUMMARY OF METHODS USED FOR PREPARING THE [Co(trien)(sar)]$^{2+}$ ION

Reacting ion	Sarcosine deriv	pH	Temp, °C	[Co(trien)-(sar)]$^{2+}$ product
β-[Co(trien)OH(H_2O)]$^{2+}$	Ester	9	20	β_2
β-[Co(trien)Cl(H_2O)]$^{2+}$	Ester	<5.5	60	β_2
β-[Co(trien)OH(H_2O)]$^{2+}$	Acid	5, 8	30	β_2

forms using silver (+)-α-bromo-π-camphorsulfonate (AgBCS) with the least soluble diastereoisomer resulting in Lβ_2-*RRS*-[Co(trien)(sar)]I_2 ([α]D −233°).

Rotatory Dispersion, Circular Dichroism, and Visible Absorption Curves.—For Lβ_1-*RR*-[Co(trien)(gly)]$I_2\cdot 2H_2O$, Dβ_2-*SS*-[Co(trien)(gly)]$I_2\cdot 2H_2O$, and Lβ_2-*RRS*-[Co(trien)(sar)]I_2, these are given in Figures 3–5. The optical activity is the same whether measured in 0.01 M H^+ or 0.01 M OH^-.

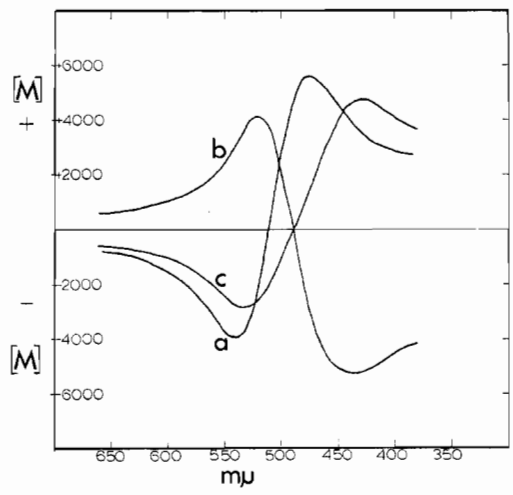

Figure 3.—RD curves for (a) Lβ_1-*RR*-[Co(trien)(gly)]$I_2\cdot 2H_2O$, (b) Dβ_2-*SS*-[Co(trien)(gly)]$I_2\cdot 2H_2O$, and (c) Lβ_2-*RRS*-[Co(trien)(sar)]I_2.

Pmr Spectra.—Proton magnetic resonance spectra for the β_1-[Co(trien)(gly)]$^{2+}$, β_2-[Co(trien)(gly)]$^{2+}$, and β_2-[Co(trien)(sar)]$^{2+}$ ions in D_3O^+ are given in Figure 6. The absorptions are assigned as indicated in Table IV. The N protons are rapidly deuterated in D_2O and OD^- solutions causing a sharpening in the CH_2 absorptions of triethylenetetramine and a reduction from a triplet

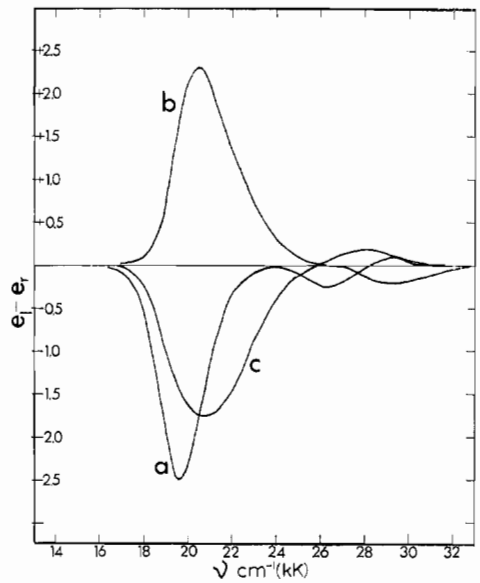

Figure 4.—CD curves for (a) Lβ_1-*RR*-[Co(trien)(gly)]$I_2\cdot 2H_2O$, (b) Dβ_2-*SS*-[Co(trien)(gly)]$I_2\cdot 2H_2O$, and (c) Lβ_2-*RRS*-[Co(trien)(sar)]I_2.

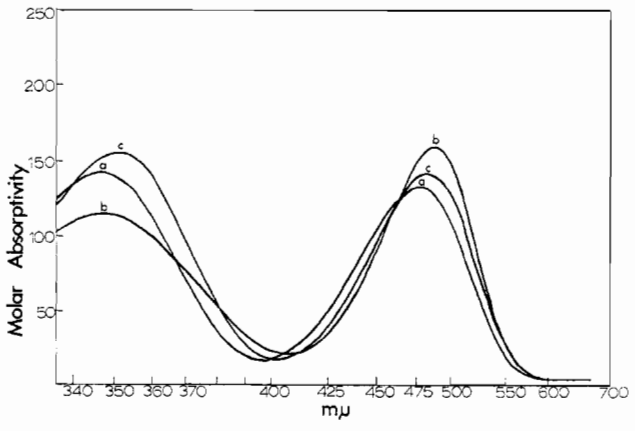

Figure 5.—Visible and near-ultraviolet absorption curves for (a) β_1-[Co(trien)(gly)]$I_2\cdot 2H_2O$ (ϵ_{346} 145, ϵ_{478} 134), (b) β_2-[Co(trien)(gly)]$I_2\cdot 2H_2O$ (ϵ_{346} 125, ϵ_{490} 161), and (c) β_2-[Co(trien)(sar)]I_2 (ϵ_{350} 156, ϵ_{484} 144).

to a single sharp resonance for the CH_2 protons of glycine. Both changes are due to the elimination of coupling of the CH_2 protons with the adjacent NH protons. It is significant to note that in D_3O^+ solutions

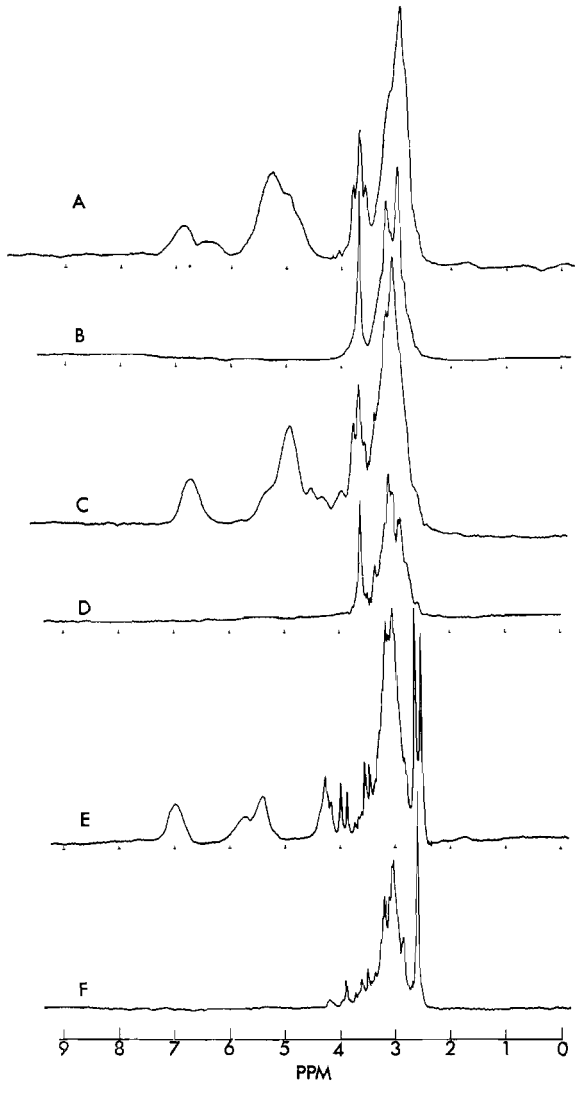

Figure 6.—Pmr spectra for (A) β_1-[Co(trien)(gly)]Cl_2 in 0.1 *M* DCl, (B) β_1-[Co(trien)(gly)]Cl_2 in 0.01 *M* NaOD, (C) β_2-[Co(trien)(gly)]Cl_2 in 1 *M* D_2SO_4, (D) β_2-[Co(trien)(gly)]Cl_2 in 0.01 *M* NaOD, (E) β_2-[Co(trien)(sar)]Cl_2 in 0.1 *M* DCl, and (F) β_2-[Co(trien)(sar)]Cl_2 in 0.01 *M* NaOD.

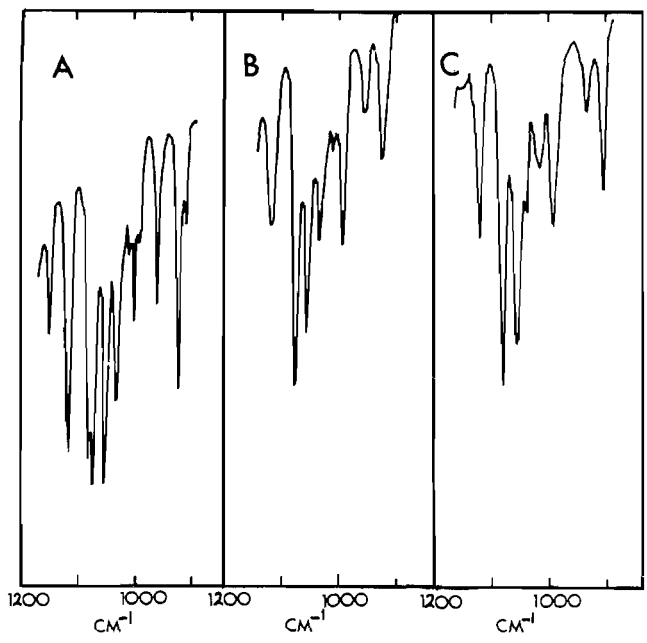

Figure 7.—Infrared spectra of (A) β_1-[Co(trien)(gly)]$I_2 \cdot 2H_2O$, (B) β_2-[Co(trien)(gly)]$I_2 \cdot 2H_2O$, and (C) β_2-[Co(trien)(sar)]$I_2 \cdot 2H_2O$ in the 850–1200-cm^{-1} region.

the pmr spectrum for the β_2-$[Co(trien)(sar)]^{2+}$ ion shows only one sharp doublet for the methyl group and that this reduces to one singlet on deuteration.

Infrared Spectra.—Infrared spectra for β_1-[Co(trien)(gly)]$I_2 \cdot 2H_2O$, β_2-[Co(trien)(gly)]$I_2 \cdot 2H_2O$, and β_2-[Co(trien)(sar)]$I_2 \cdot 2H_2O$, in the 850–1200-cm^{-1} region, are given in Figure 7A, B, and C, respectively. This region has previously been found useful in distinguishing between the α and β configurations of triethylenetetramine complexes.[9] Significant differences in the spectra of the β_1 and β_2 isomers occur throughout the infrared region, but those for β_2-[Co(trien)(gly)]$I_2 \cdot 2H_2O$ and β_2-[Co(trien)(sar)]$I_2 \cdot 2H_2O$ show only minor dissimilarities.

Discussion

Spectra.—The infrared spectra of all three chelated amino acid complexes show bands characteristic of coordinated amino acids.[10] Furthermore, all show at least four strong absorptions in the 990–1100-cm^{-1} region attributable to the β-triethylenetetramine configuration (Figure 7).[9] Only two major absorptions might be expected for the α structure. The infrared spectra of the β_2-glycine and sarcosine isomers in the 990–1100-cm^{-1} region are practically identical, Figure 7B and C, and differ only slightly from that of the β_1-glycine isomer, Figure 7A. More substantial differences between the β_1- and β_2-glycine isomers occur in other regions of the spectrum, although the sarcosine and β_2-glycine spectra are approximately similar throughout. This comparison is possible only in the similarly hydrated iodides since significant changes occur between the dihydrate and anhydrous salts. These differences are not restricted to the O–H stretching (3500–4000-cm^{-1}) and O–H deformation (~1650-cm^{-1}) regions. Other significant differences are found in a comparison of the spectra of the racemic and active β_1-[Co(trien)(gly)]$I_2 \cdot 2H_2O$ salts.

TABLE IV

ASSIGNMENTS OF NH AND CH PROTON RESONANCES IN THE β_1-$[Co(trien)(gly)]^{2+}$, β_2-$[Co(trien)(gly)]^{2+}$, AND β_2-$[Co(trien)(sar)]^{2+}$ IONS[a]

Complex	NH, ppm	Assignment	CH, ppm	Assignment
β_1-$[Co(trien)(gly)]^{2+}$	7.0 (1), 6.4 (1), 5.3 + 5.1 (6)	trien, trien, trien + gly	3.7 (2), 3.4–2.5 (12)	gly, trien
β_2-$[Co(trien)(gly)]^{2+}$	6.9 (2), 5.7–4.9 (4), 4.9–4.3 (~2)	trien, trien + gly, trien	3.7 (2), 3.4–2.6 (12)	gly, trien
β_2-$[Co(trien)(sar)]^{2+}$	6.9 (2), 5.8 (1), 5.5 (2), 4.3 (2)	trien, sar, trien, trien	4.1–3.4 (2), 3.6–2.7 (12), 2.6 (3)	sar, trien, sar

[a] Relative intensities are given in parentheses.

(9) D. A. Buckingham and D. Jones, *Inorg. Chem.*, **4**, 1387 (1965).

(10) A. J. Saraceno, I. Nakagawa, S. Mizushima, C. Curran, and J. V. Quagliano, *J. Am. Chem. Soc.*, **80**, 5018 (1958).

The visible spectra, Figure 3, qualitatively support a correlation between the β_2-glycine and sarcosine complexes since both have a similar ratio of peak heights for bands I and II. That for the β_1 isomer is substantially different. Also, both bands are shifted $\sim$5 mμ to higher wavelengths in the sarcosine complex compared to β_2-[Co(trien)(gly)]$^{2+}$ indicating a slightly reduced ligand field for sarcosine compared to glycine. A similar situation is found in the [Co(en)$_2$(gly)]$^{2+}$ and [Co(en)$_2$(sar)]$^{2+}$ ions.

All three configurations of [Co(trien)(gly)]$^{2+}$ have their donor atoms arranged in C_{4v} symmetry (although the actual molecular symmetry is C_1) so that the first spin-allowed excited state $^1T_{2g}$ (in O_h) will be split into singlet $^1A_2$ and doubly degenerate ^1E states. It has been suggested theoretically[11] and substantiated experimentally[12] that the energy of the $^1A_2$ level is relatively insensitive to X in the [CoN$_5$X]$^{n+}$ ions and is similar in energy to the $^1T_1$ level in [Co(NH$_3$)$_6$]$^{3+}$ (478 mμ). The ^1E level is displaced to higher or lower energies depending on whether the average ligand field of those atoms in the tetragonal positions is greater or less than those in the horizontal plane, respectively. Although the absence of any splitting of band I in the β-[Co(trien)(gly)]$^{2+}$ spectra prevents the assignment of configuration on the basis of visible spectra alone, the position of the combined $^1A_1 \rightarrow {}^1E$ and $^1A_1 \rightarrow {}^1A_2$ transitions[13] does suggest that a distinction may be made between the β_1 and β_2 isomers, Figure 1. The ligand field strengths of the donor groups might be expected to follow the order $NH_2 > NH > O$ so that the isomer with λ_{max} 490 mμ is consistent with the structure given by Figure 1 (β_1) since the average tetragonal field for this structure is less than that for the isomer given by Figure 1 (β_2). Further, λ_{max} for the β_2 isomer (478 mμ) is the same as that found for Co(NH$_3$)$_6^{3+}$ and the close similarity of the averaged apical and planar field for these two ions is in agreement with such a correspondence. No distinction can be made between the β_1 and α structures on this basis.

The specific rotations of the Lβ_1-*RR*-[Co(trien)(gly)]$^{2+}$, Dβ_2-*SS*-[Co(trien)(gly)]$^{2+}$, and Lβ_2-*RRS*-[Co(trien)(sar)]$^{2+}$ ions over the range 650–400 mμ are the same whether measured in 0.01 *M* H$^+$ or 0.01 *M* OH$^-$ and do not change with time indicating the absence of mutarotation at the planar nitrogen atom of triethylenetetramine or secondary nitrogen of sarcosine. The N protons are instantly deuterated in 0.01 *M* base, Figure 6. This result means that these NH protons are stereospecifically oriented in these ions since it has previously been shown that racemization at coordinated asymmetric nitrogen atoms is fast in basic media.[14,15] It also substantiates the view expressed in the Introduction that the conformation adopted by triethylenetetramine in these complex ions will be the thermodynamically favored one, Figure 2A.

The RD and CD curves of all three complexes are very similar, Figures 4 and 5, as might be anticipated from the C_{4v} symmetry of the donor atoms. More exactly, the molecular symmetry is C_1, so the degenerate ^1E (positive) and $^1A_2$ (negative) levels will be further split into two ^1A levels of positive rotatory strength and an $^1A_2$ level of negative rotatory strength. The energy of separation between the parent ^1E and $^1A_2$ components in [Co(en)$_3$]$^{3+}$ is small[16] and it is very likely that a similar situation exists in the [Co(trien)AA]$^{2+}$ isomers so that all three A components might be expected to overlap rather extensively with the major CD band in the visible region taking its sign from the ^1A levels derived from ^1E. Thus the (+)β_1-[Co(trien)(gly)]$^{2+}$, (+)β_2-[Co(trien)(gly)]$^{2+}$, and (+)β_2-[Co(trien)(sar)]$^{2+}$ configurations are related. Furthermore, a comparison of the CD and RD curves of these (+)β-amino acid complexes with that of D(+)[Co(en)$_2$(sar)]$^{2+}$ indicates that these ions have the same absolute configuration.[17] Also it has been shown that the intensities of the CD bands in the visible region for [Co(trien)X$_2$]$^{n+}$ complexes with the β-triethylenetetramine structure are usually less (by a factor of about 2) than those with the α structure.[18] A similar situation might be expected to apply here so that the close correspondence in intensity of the CD (and RD curves) for the two glycine isomers strongly suggests the same triethylenetetramine configuration.

Although no firm rules have yet been established for assigning the structure of Co(III) complexes on the basis of the chemical shift values of hydrogen atoms attached to coordinated nitrogen atoms, certain trends are evident. These trends indicate that, in general, the order of chemical shifts in ppm is $NHR_1R_2 < NH_2R < NH_3$.[19] Thus the secondary NH protons of coordinated triethylenetetramine absorb at lower fields than the terminal NH_2 protons. A similar relationship holds between the secondary NH proton of sarcosine and NH_2 protons of glycine. Also in the [Co(NH$_3$)$_5$X]$^{n+}$ ions it has been found that the NH_3 protons in a position *trans* to an electronegative atom (X = O, F, Cl, Br, I) absorb at higher fields than those *cis* to the electronegative atom.[20,21] Symmetry conditions alone would require that they have a different chemical shift value. Therefore, we might expect those N protons *trans* to the coordinated carboxyl oxygen of glycine to absorb at higher fields than the same protons in a position *cis* to the oxygen atom. On the basis of these general observations it is possible to assign configurations to the two β-[Co(trien)(gly)]$^{2+}$ isomers from their pmr spectra. β_1-[Co(trien)(gly)]$^{2+}$ shows two broad

(11) H. Yamatera, *Bull. Chem. Soc. Japan*, **31**, 95 (1958).
(12) M. Linhard and M. Weigel, *Z. Anorg. Allgem. Chem.*, **266**, 49 (1951).
(13) A separation of the ^1E and $^1A_2$ excited states is observed in the spectra of the β-[Co(trien)(glyOC$_2$H$_5$)Cl]$^{2+}$ ion.
(14) B. Halpern, A. M. Sargeson, and K. R. Turnbull, *J. Am. Chem. Soc.*, **88**, 4630 (1966).
(15) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *ibid.*, **89**, 825 (1967).
(16) A. J. McCaffery and S. F. Mason, *Mol. Phys.*, **6**, 359 (1963).
(17) The absolute configuration of D(+)[Co(en)$_2$(sar)]I$_2$·1.5H$_2$O has recently been determined by X-ray analysis: J. Blount, H. Freeman, K. Turnbull, and A. M. Sargeson, *Chem. Commun.*, in press.
(18) A. M. Sargeson and G. H. Searle, *Inorg. Chem.*, **4**, 45 (1965).
(19) D. A. Buckingham, L. J. Durham, and A. M. Sargeson, *Australian J. Chem.*, **20**, 257 (1967).
(20) P. Clifton and L. Pratt, *Proc. Chem. Soc.*, 339 (1963).
(21) R. C. Heaney, H. F. Holtzclaw, and R. C. Larson, *Inorg. Chem.*, **5**, 940 (1966).

NH absorptions at 7.0 and 6.4 ppm each with an intensity corresponding to one proton, Figure 6A. These may be assigned to the secondary NH protons of triethylenetetramine with the 6.4 ppm absorptions resulting from that proton *trans* to a carboxyl oxygen. In the β_2-[Co(trien)(gly)]$^{2+}$ ion both NH protons occur at 6.9 ppm, Figure 6C, indicating similar environments *trans* to a nitrogen atom. One NH_2 group has been moved to higher field, 4.9–4.3 ppm, and this may be assigned to a terminal NH_2 group of triethylenetetramine *trans* to oxygen. This latter absorption is more clearly evident in the β_2-[Co(trien)(sar)]$^{2+}$ ion at 4.3 ppm, Figure 6e. The NH_2 of glycine occurs together with the NH_2 of triethylenetetramine at 4.9–5.7 ppm, while the secondary NH of sarcosine occurs at a lower field, 5.8 ppm. These assignments establish the β_2 isomer as that configuration given by Figure 1C and are in agreement with the β_1 isomer being that given by Figure 1B. The pmr result does not allow a clear distinction to be made between the β_1 and α structures.

Reaction with Glycine and Glycine Ethyl Ester.—The isolation of α- and β-[Co(trien)(glyH)$_2$](ClO$_4$)$_3$ at pH 4–6 establishes that both the α- and β-[Co(trien)OH(H$_2$O)]$^{2+}$ ions, respectively, react with glycine by initial coordination of the carboxyl oxygen rather than the amino nitrogen atom. A similar result has been found in the reaction of glycine with [Co(NH$_3$)$_5$OH$_2$]$^{3+}$.[22] It is therefore likely that the formation of the β-[Co(trien)(gly)]$^{2+}$ ion using glycine involves initial displacement of a water molecule by the carboxyl oxygen to form the O-bonded monodentate complex β-[Co(trien)(OH$_2$)(glyH)]$^{3+}$ followed by proton loss and rapid chelation by the NH_2 group. Thus β_2-[Co(trien)(gly)]$^{2+}$ is most conveniently formed by the two reactions (Table I, reaction 4)

$$\beta\text{-[Co(trien)OH(H}_2\text{O)]}^{2+} + \text{glyH} + \text{H}^+ \xrightarrow{\text{pH 5.5}} \beta\text{-[Co(trien)(OH}_2\text{)(glyH)]}^{3+} + \text{H}_2\text{O} \quad (1)$$

$$\beta\text{-[Co(trien)(OH}_2\text{)(glyH)]}^{3+} + \text{OH}^- \xrightarrow{\text{pH 8}} \beta\text{-[Co(trien)(OH}_2\text{)(gly)]}^{2+} + \text{H}_2\text{O} \quad (2)$$

$$\beta\text{-[Co(trien)(OH}_2\text{)(gly)]}^{2+} \longrightarrow \beta_2\text{-[Co(trien)(gly)]}^{2+} + \text{H}_2\text{O}$$

Similarly, the isolation of β-[Co(trien)Cl(glyOC$_2$H$_5$)]Cl$_2$ establishes that glycine ethyl ester coordinates as a monodentate through the nitrogen atom. Thus the reaction of glycine ethyl ester with β-[Co(trien)OH(H$_2$O)]$^{2+}$ may be written

$$\beta\text{-[Co(trien)OH(H}_2\text{O)]}^{2+} + \text{glyOC}_2\text{H}_5 \xrightarrow{\text{pH}\sim 8\text{–}10} \beta\text{-[Co(trien)OH(glyOC}_2\text{H}_5\text{)]}^{2+} + \text{H}_2\text{O} \quad (3)$$

$$\beta\text{-[Co(trien)OH(glyOC}_2\text{H}_5\text{)]}^{2+} \longrightarrow \beta_1\text{-[Co(trien)(gly)]}^{2+} + \text{HOC}_2\text{H}_5 \quad (4)$$

The detailed mechanisms for these reactions are at present being studied.

The most significant observation resulting from these experiments is that under controlled conditions glycine and glycine ethyl ester react to form the β_2 and β_1 isomers, respectively, in >95% yields. This requires that of the two sites in β-[Co(trien)OH(H$_2$O)]$^{2+}$ available for initial coordination of the substrate as a monodentate, one site reacts preferentially. Some preference might have been anticipated since the two positions are not equivalent. Furthermore, the proposed configurations of the β_1 and β_2 products requires the most easily replaced water molecule to be that one *trans* to the terminal NH_2 group. The mechanism of formation of the two isomers is then given by Figure 8. Rates of water exchange in the β-[Co(trien)(H$_2$O)$_2$]$^{3+}$ ion are currently being measured to establish this difference as well as to investigate whether the rates of the above reactions are contolled by the water-exchange process. These results will be reported shortly.

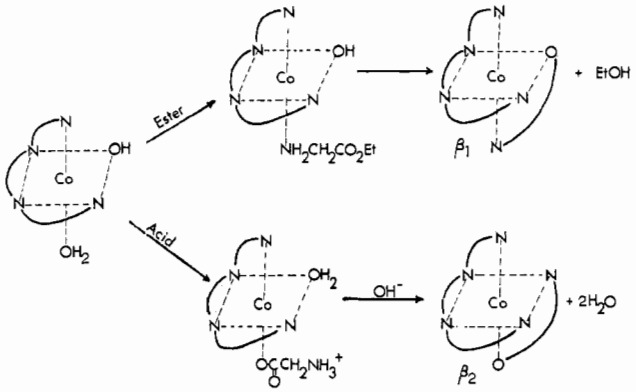

Figure 8.—Mechanism for the formation of β_1-[Co(trien)(gly)]$^{2+}$ and β_2-[Co(trien)(gly)]$^{2+}$ from the β-[Co(trien)OH(H$_2$O)]$^{2+}$ ion.

Treatment of β-[Co(trien)Cl(H$_2$O)]$^{2+}$ with glycine and glycine ethyl ester results in the formation of the β_1- and β_2-[Co(trien)(gly)]$^{2+}$ isomers, respectively, *i.e.*, of opposite structure to those formed in the same reactions with β-[Co(trien)OH(H$_2$O)]$^{2+}$. It has previously been established that β-[Co(trien)Cl(H$_2$O)]$^{2+}$ obtained by aquation of β-[Co(trien)Cl$_2$]$^+$ is largely (>90%) that isomer given in Figure 9.[23] Displacement of the water molecule by a carboxyl oxygen of glycine or NH_2 group of the ester requires the formation of the β products given in Figure 9. The configuration of these products is governed by the configuration of β-[Co(trien)Cl(H$_2$O)]$^{2+}$ which has been derived independently,[23] and the result obtained (Figure 9) is in agreement with that deduced from the spectral data discussed above and from conformational calculations described below.

The inability to obtain a third, presumably α-[Co(trien)(gly)]$^{2+}$, isomer is somewhat disturbing since there is no reason to suggest it is thermodynamically unstable. Attempts to obtain it using α-[Co(trien)Cl$_2$]Cl, α-[Co(trien)Cl(H$_2$O)]$^{2+}$, or α-[Co(trien)(H$_2$O)$_2$]$^{3+}$ invariably resulted in the isolation of mixtures of β_1 and β_2 forms. The isomerization of α-[Co(trien)OH(H$_2$O)]$^{2+}$ to β-[Co(trien)OH(H$_2$O)]$^{2+}$ at pH 7.2 ± 0.1 and 30° is both rapid and essentially com-

(22) J. Fujita, T. Yasui, and Y. Shimura, *Bull. Chem. Soc. Japan*, **38**, 654 (1965).

(23) A. M. Sargeson and G. H. Searle, *Nature*, **200**, 356 (1963).

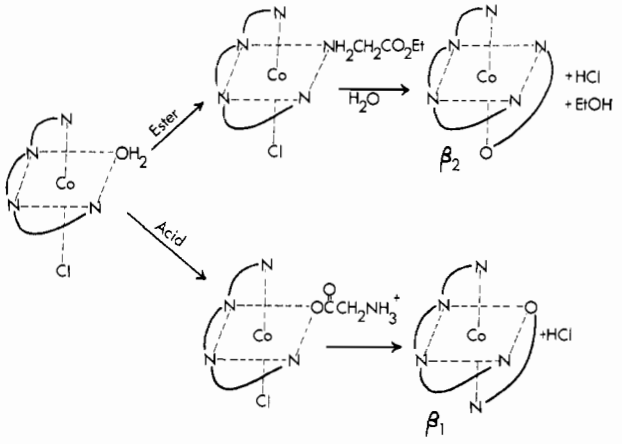

Figure 9.—Mechanism for the formation of β_2-[Co(trien)(gly)]$^{2+}$ and β_1-[Co(trien)(gly)]$^{2+}$ from the β-[Co(trien)Cl(H$_2$O)]$^{2+}$ ion.

plete.[24] Also, glycine ethyl ester reacts with α-[Co(trien)OH(H$_2$O)]$^{2+}$ at pH 7.2 ± 0.1 and 30° at a similar rate to this isomerization reaction and gives rise to β_1-[Co(trien)(gly)]$^{2+}$. β-[Co(trien)OH(H$_2$O)]$^{2+}$ reacts with the ester much more rapidly under these conditions.[24] These results imply that isomerization of α-[Co(trien)OH(H$_2$O)]$^{2+}$ to β-[Co(trien)OH(H$_2$O)]$^{2+}$ precedes the coordination of the ester. It is perhaps of interest to note that the isolation of β-[Co(trien)(gly)]$^{2+}$ products from α reactants requires the inversion of configuration about the cobalt atom at some stage during the reaction, that is, Dα → Lβ. The experimental demonstration of this inversion would constitute strong evidence for structure. Experiments are at present being carried out toward this aim.

Stereospecificity and the β_2-[Co(trien)(sar)]$^{2+}$ Ion.—A possible method of distinguishing between the two β-[Co(trien)AA]$^{2+}$ configurations occurs when AA = sarcosine. This arises from the discovery that sarcosine in the (+)[Co(en)$_2$(sar)]$^{2+}$ ion can exist in only one configuration and this has been attributed to nonbonded repulsions between the ethylenediamine rings and the methyl group of sarcosine.[25] Thus the D(+)[Co(en)$_2$(sar)]$^{2+}$ ion contains R(−)sarcosine, and the energy difference between the D(+)R(−) and D(+)S(+) conformers has been estimated at ∽10 kcal mole^{-1}. The success of conformational analysis in predicting the most stable conformation of sarcosine in [Co(en)$_2$(sar)]$^{2+}$ prompted us to make similar calculations for the β_1- and β_2-[Co(trien)(sar)]$^{2+}$ isomers. The relationship established between β_2-[Co(trien)(sar)]$^{2+}$ and β_2-[Co(trien)(gly)]$^{2+}$ would then give an independent check on the configuration of the glycine complexes.

Using the expression of Hill,[26] the repulsive energies for the three structures given in Figure 10 were calculated. Those for the D(+)β_1R(−) and D(+)β_1S(+) isomers, Figure 10A, were established as in excess of 30 kcal mole^{-1}. In both forms nonbonded interactions between the methyl group and ethylenediamine-type rings are severe. However repulsion energies for the β_2 isomers are much less, with that for the D(+)β_2R(−) structure (Figure 10B) being <0.5 kcal mole^{-1} and that for the D(+)β_2S(+) structure (Figure 10C) being ∽8 kcal mole^{-1}. The order of stability might therefore be expected to be D(+)β_2R(−) > D(+)β_2S(+) >> D(+)-β_1R(−) ∽ D(+)β_1S(+), and if the isomer distribution were governed thermodynamically, the D(+)β_2R(−) + L(−)β_2S(+) forms would be expected to be formed with the virtual exclusion of the other isomers.

Reaction of β-[Co(trien)OH(H$_2$O)]$^{2+}$ with sarcosine and sarcosine ethyl ester under all conditions gave a single homogeneous product (Table III). Although these reactions must be at least in part kinetically controlled, the β-[Co(trien)(sar)]$^{2+}$ formed has pmr, infrared, and visible spectra very similar to β_2-[Co(trien)(gly)]$^{2+}$, and the configuration deduced from these results is in agreement with that predicted to be most stable by the conformational energy calculations.

Further, the D(+)β_2-[Co(trien)((−)sar)]$^{2+}$ ion showed no loss of activity over several hours in 0.01 M NaOH even though the sarcosine nitrogen is instantly deuterated under these conditions, Figure 6C. Mutarotation at the asymmetric N atom of sarcosine might be expected to be observed if the D(+)β_2S(+) isomer were within 2 kcal mole^{-1} of the stability of the D(+)β_2R(−) isomer. The failure to observe any mutarotation is in agreement with the calculated energy difference between the isomers of ∽8 kcal mole^{-1}.

Finally, if L(−)β_2-[Co(trien)(sar)]$^{2+}$ contains S(+)-sarcosine, as has been established for L(−)[Co(en)$_2$(sar)]$^{2+}$, the following relationship between the molecular rotations might be expected to be followed

$$[M]\{(+)\beta_2\text{-[Co(trien)(gly)]}^{2+}\} + [M]\{(-)\beta_2\text{-[Co(trien)((+)sar)]}^{2+}\} = [M]\{(+)\text{[Co(en)}_2\text{(gly)]}^{2+}\} + [M]\{(-)\text{[Co(en)}_2\text{((+)sar)]}^{2+}\}$$

Both sides of this expression have been plotted in Figure 11, and their close similarity demonstrates that the same optical form of sarcosine is present in both L(−)β_2-[Co(trien)(sar)]$^{2+}$ and L(−)[Co(en)$_2$(sar)]$^{2+}$. It also establishes the absolute configuration of D(+)β_2-[Co(trien)(sar)]$^{2+}$ from the known structure of D(+)[Co(en)$_2$(sar)]I$_2$.[17] A similar result, independent of the configuration of the D(+)[Co(en)$_2$(gly)]$^{2+}$ and L(−)-[Co(en)$_2$((+)sar)]$^{2+}$ ions, was found to hold between the rotatory strengths R under the first ligand field band[27]

$$R\{(-)\beta_2\text{-[Co(trien)((+)sar)]}^{2-}\} = \{R(+)\beta_2\text{-[Co(trien)(gly)]}^{2+}\} + R\{(+)\text{[Co(NH}_3\text{)}_4\text{((+)sar)]}^{2+}\}$$

This identity establishes that the configuration about the asymmetric sarcosine N atom in S(+)[Co(NH$_3$)$_4$-

(24) For the isomerization reaction α-[Co(trien)OH(H$_2$O)]$^{2+}$ → β-[Co(trien)OH(H$_2$O)]$^{2+}$, $t_{1/2}$ = 70 min at pH 7.16 and 30° in 0.05 M 2,4,6-collidine–perchloric acid buffer, and for the reactions of α- and β-[Co(trien)OH(H$_2$O)]$^{2+}$ with glycine ethyl ester (0.05 M), $t_{1/2}$ = 88 and 18 min, respectively, at pH 7.29 and 30°.

(25) D. A. Buckingham, S. F. Mason, A. M. Sargeson, and K. R. Turnbull, *Inorg. Chem.*, **5**, 1649 (1966).

(26) J. T. Hill, *J. Chem. Phys.*, **16**, 399 (1948). Atoms found to be significant in the calculation are as numbered in Figure 10. The more significant interactions, with distances in Ångstroms, were as follows: Figure 10B (most stable): H$_1$H$_{22}$, 1.9; H$_1$H$_4$, 1.9. Figure 10C: H$_1$H$_{10}$, 1.6; H$_1$H$_8$, 1.7; H$_2$H$_8$, 1.7; H$_1$N$_2$, 2.1; H$_8$C$_1$, 2.1. Figure 10A: H$_1$H$_{14}$, 1.6; H$_1$H$_{12}$, 1.6; H$_2$H$_{14}$, 1.6; H$_1$C$_4$, 1.6; H$_1$C$_5$, 1.6; H$_1$N$_2$, 1.8.

(27) $R\{(-)\beta_2$-[Co(trien)((+)sar)]$^{2+}\}$ = 2922 mm^2; $R\{(+)\beta_2$-[Co(trien)(gly)]$^{2+}\}$ = 3038 mm^2; $R\{(+)$[Co(NH$_3$)$_4$(sar)]$^{2+}\}$ = +56 − 168 = −112 mm^2.

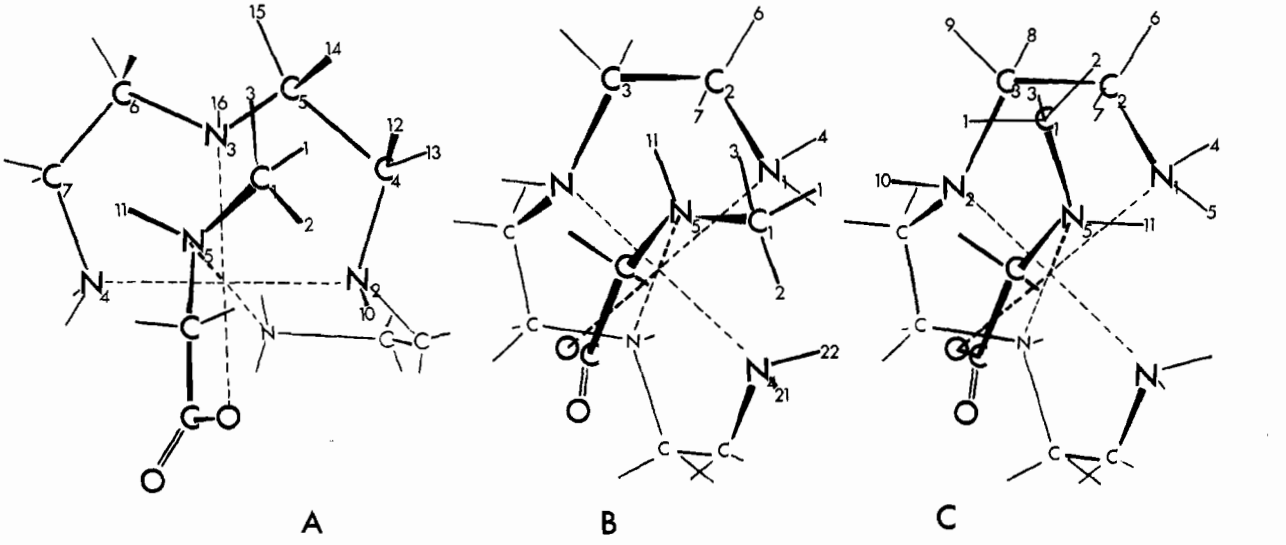

Figure 10.—Ligand conformations used in the conformational analysis study: (A) D(+)β_1-*SSR*; (B) D(+)β_2-*SSR*; and (C) D(+)β_2-*SSS* conformations.

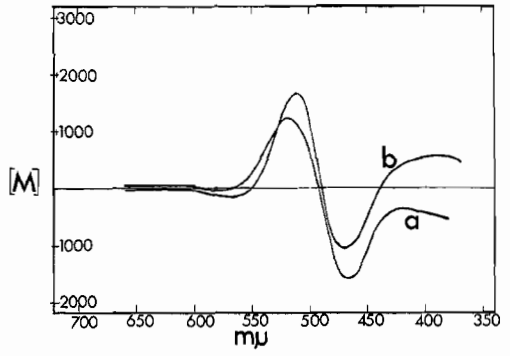

Figure 11.—Molecular rotations for the (a) Dβ_2-*SS*-[Co(trien)(gly)]$^{2+}$ + Lβ_2-*RRS*-[Co(trien)(sar)]$^{2+}$ ions and (b) D-[Co(en)$_2$(gly)]$^{2+}$ + L-*S*-[Co(en)$_2$(sar)]$^{2+}$ ions.

(sar)]$^{2+}$ and L(−)β_2-*RRS*-[Co(trien)(sar)]$^{2+}$ ions is the same.[27a]

Experimental Section

Materials.—Glycine and glycine ethyl ester hydrochloride were purchased from Mann Research Corp., sarcosine (N-methylglycine) was from BDH Ltd., and sarcosine ethyl ester hydrochloride was prepared according to the method of Boissonnas.[28] The free esters were obtained just prior to use by passing ammonia through an ether suspension of the finely powdered ester hydrochloride and removing NH_4Cl and ether.

β-[Co(trien)CO_3]Cl·1.5H_2O, β-[Co(trien)CO_3]ClO_4·H_2O, β-[Co(trien)Cl_2]Cl, α-[Co(trien)CO_3]ClO_4·H_2O, and α-[Co(trien)Cl_2]Cl were prepared according to the methods of Sargeson and Searle.[29]

Instrumentation.—Pmr spectra were obtained using a Perkin-Elmer R-10 60-Mc or Varian HA-60 spectrometer. Visible spectra were measured using either a Cary 14 or Shimadzu RS-27 recording spectrophotometer. Optical rotations were measured in a 1-dm cell using a Perkin-Elmer 141 spectropolarimeter (±0.002°) fitted with a Zeiss monochromator and a quartz-halogen lamp. A Cambridge portable pH meter was employed for pH-controlled reactions. The CD curves were measured on a Jouan Dicographe. Infrared spectra were obtained using either a Perkin-Elmer 337 Infracord or a Unicam SP200 spectrometer.

Preparations and Resolutions.—The following directions are those best found to result in high yields of one isomer. If not followed carefully, mixtures of β_1 and β_2 isomer result.

β_1-Glycinatotriethylenetetraminecobalt(III) Iodide Hydrate.—β-[Co(trien)(H_2O)$_2$](ClO_4)$_3$ was prepared *in situ* by adding to β-[Co(trien)CO_3]ClO_4 (11.4 g) 12 ml of 5 *M* $HClO_4$. After the reaction was complete, the solution was made basic, pH 8, by dropwise addition of 5 *M* NaOH and freshly prepared glycine ethyl ester (3.5 g) added at room temperature. The solution quickly turned red-orange. After 2 hr, excess NaI was added, and the solution stood overnight in the refrigerator. The product was removed and washed with ice-cold NaI solution, methanol, and acetone and was then recrystallized from hot water. All fractions were spectrophotometrically identical; yield, 14.8 g. For analysis, see Table V.

Resolution of β_1-Glycinatotriethylenetetraminecobalt(III) Iodide Hydrate. (−)[**Co(trien)(gly)**](+)[**Co**(C_2O_4)$_2$**(en)**]**I·2H$_2$O.**—Na(+)[Co(C_2O_4)$_2$(en)]·H_2O (2.5 g, [α]D +500°)[30] was added to a warm solution (35 ml) of β_1-[Co(trien)(gly)]I_2·1.5H_2O (5.5 g) and on cooling and scratching the diastereoisomer (−)[Co(trien)(gly)](+)[Co(C_2O_4)$_2$(en)]I·2H_2O (2.25 g) crystallized and was removed after 1 hr. Evaporation of the solution to 20 ml and cooling at 5° overnight resulted in a further 0.83 g; total yield 3.08 g, 84%. A 0.05% solution gave α_{546} −0.68°, whence [α]$_{546}$ −1360°. For analysis, see Table V.

(−)β_1-[**Co(trien)(gly)**]I_2**·2H$_2$O.**—(−)[Co(C_2O_4)(en)$_2$](OAc)[30] (1.6 g, [α]D −920°) was added to (−)[Co(trien)(gly)](+)[Co(C_2O_4)$_2$(en)]I·2H_2O dissolved in the minimum volume of water at 60°, and the solution was cooled and reduced in volume on a rotatory evaporator to 20 ml. The insoluble (−)[Co(C_2O_4)(en)$_2$](+)[Co(C_2O_4)$_2$(en)] was removed, and the volume was further reduced to 8 ml. On addition of NaI and standing, three fractions of (−)β_1-[Co(trien)(gly)]I_2·2H_2O (1.8 g) of equal activity were obtained. Further fractionating of the product resulted in no increase in activity. A 0.1% solution gave α_{380} −0.33° and α_{546} −0.700°, whence [α]D −330° and [α]$_{546}$ −700°. For analysis, see Table V.

(27a) NOTE ADDED IN PROOF.—A recent X-ray study of β_2-[Co(trien)(glyglyOC_2H_5)](ClO_4)$_2$·H_2O has established that the coordinated dipeptide is bound to Co through the terminal NH_2 group and the amide carbonyl oxygen atom [M. Fehlmann, H. Freeman, D. A. Buckingham, and A. M. Sargeson, to be published]. The geometry of the donor atoms is given by Figure 1 (β_2). Furthermore, it has been shown that this complex ion undergoes base hydrolysis to β_2-[Co(trien)(gly)]$^{2+}$ + glyOC_2H_5 without exchange of the N-terminal glycine residue [D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Am. Chem. Soc.*, in press], and this is most easily rationalized in terms of nucleophilic attack by OH^- at the carbonyl carbon atom without rupture of the chelate ring. These results establish the β_2-[Co(trien)(gly)]I_2·2H_2O structure proposed here.

(28) R. A. Boissonnas, S. T. Guttmann, P. A. Jaquenoud, and J. P. Waller, *Helv. Chim. Acta*, **38**, 1491 (1955).

(29) A. M. Sargeson and G. H. Searle, *Inorg. Chem.*, **6**, 787 (1967).

(30) F. P. Dwyer, I. K. Reid, and F. L. Garvan, *J. Am. Chem. Soc.*, **83**, 1285 (1961).

TABLE V
ANALYTICAL DATA FOR COMPLEXES PREPARED

Compound	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
β_1-[Co(trien)(gly)]$I_2 \cdot 1.5H_2O$	17.16	4.50	12.51	17.10	4.36	12.73
(−)β_1-[Co(trien)(gly)](+)[Co$(C_2O_4)_2$(en)]$I \cdot H_2O$	22.81	4.65	13.31	22.58	4.31	13.42
(−)β_1-[Co(trien)(gly)]$I_2 \cdot 2H_2O$	16.89	4.61	12.31	16.77	4.68	12.25
(+)β_1-[Co(trien)(gly)]$I_2 \cdot H_2O$	17.89	4.39	12.71	17.76	4.50	12.58
β_2-[Co(trien)(gly)]$I_2 \cdot 2H_2O$	16.89	4.61	12.31	16.88	4.62	12.18
β_2-[Co(trien)(gly)]$(ClO_4)_2 \cdot 1.5H_2O$	19.05	5.00	13.87	19.20	4.68	13.65
(+)β_2-[Co(trien)(gly)](SbO(+)tar)$_2 \cdot H_2O$	22.53	3.78	8.21	22.64	3.63	8.00
(+)β_2-[Co(trien)(gly)]$I_2 \cdot 2H_2O$	16.89	4.61	12.31	16.72	4.50	12.31
(−)β_2-[Co(trien)(gly)]$I_2 \cdot H_2O$	17.89	4.39	12.71	18.24	4.70	12.70
β_2-[Co(trien)(sar)]I_2	19.76	4.42	12.80	19.52	4.37	12.83
β_2-[Co(trien)(sar)]$I_2 \cdot 2H_2O$	18.54	4.84	12.01	18.58	4.84	12.02
β_2-[Co(trien)(sar)]$Cl_2 \cdot 0.5H_2O$	28.96	6.75	18.77	28.87	6.70	18.70
β_2-[Co(trien)(sar)]$(ClO_4)_2 \cdot H_2O$	21.19	5.12	13.73	21.43	5.15	13.62
(−)β_2-[Co(trien)(sar)]((+)BCS)$_2$	38.12	5.73	7.67	38.23	5.75	7.56
(+)β_2-[Co(trien)(sar)]I_2	19.76	4.42	12.80	19.82	4.20	13.07
(−)β_2-[Co(trien)(sar)]I_2	19.76	4.42	12.80	19.50	4.51	12.82
β-[Co(trien)(glyH)$_2$]$(ClO_4)_3$	18.03	4.30	12.81	18.14	4.37	12.80
α-[Co(trien)(glyH)$_2$]$(ClO_4)_3$	18.03	4.36	12.81	18.07	4.63	13.06
α-[Co(trien)OH(H_2O)]$(ClO_4)_2 \cdot 0.5H_2O$	16.08	4.95	12.51	16.28	4.96	12.50
β-[Co(trien)Cl(glyOC_2H_5)]Cl_2	28.96	6.56	16.89	29.01	6.68	17.00
[Co_2(trien)$_2$($OH)_2$]$(ClO_4)_4 \cdot 4H_2O$	15.75	5.03	12.25	15.44	4.89	11.93

(+)β_1-[**Co(trien)(gly)**]$\mathbf{I_2 \cdot H_2O}$.—Addition of NaI to the filtrate (remaining after separation of the diastereoisomer) gave two fractions (0.55, 0.7 g) of impure (+)β_1-[Co(trien)(gly)]I_2 with the most active form being the more soluble. Two recrystallizations from warm water gave impure (+)β_1-[Co(trien)(gly)]$I_2 \cdot H_2O$, $[\alpha]_D$ +278°. For analysis, see Table V.

β_2-Glycinatotriethylenetetraminecobalt(III) Iodide Dihydrate.—Perchloric acid (8 ml, 5 *M*) was slowly added to β-[Co(trien)CO_3]$ClO_4 \cdot H_2O$ (7.6 g), and when effervescence had ceased, 1 equiv of glycine was added (1.5 g) and the solution was adjusted to pH 5.8 with 5 *M* NaOH solution. This solution was heated to 40° for 1 hr with frequent checks to ensure the pH remained at 5.2–5.8. To the red-orange solution of β-[Co(trien)(H_2O)(*gly*OH)]$^{3+}$ was added 1 equiv of base (4 ml of 5 *M* NaOH) and the mixture stood at room temperature for 1.5 hr. Excess NaI was added and the solution was allowed to stand at room temperature overnight. The orange crystals of β_2-[Co(trien)(gly)]$(ClO_4)_2$ were removed and washed with ice-cold aqueous NaI and a little methanol and air dried; yield, 7.0 g. One recrystallization from hot water gave β_2-[Co(trien)(gly)]$I_2 \cdot 2H_2O$. For analysis, see Table V.

β_2-Glycinatotriethylenetetraminecobalt(III) Perchlorate Hydrate.—This compound was prepared as above except that the final solution was allowed to stand at 35° overnight. On cooling in an ice bath and scratching, orange crystals of β_2-[Co(trien)(gly)]$(ClO_4)_2$ separated (5.1 g). On adding $NaClO_4$ a further 1.1 g was recovered. These products were washed with a little ice-cold $NaClO_4$ solution, ethanol, and ether, and were air dried. For analysis, see Table V.

Resolution of β_2-Glycinatotriethylenetetraminecobalt(III) Iodide Dihydrate. (+)β_2-[**Co(trien)(gly)**](**SbO(+)$C_4H_4O_3$)$_2 \cdot$H$_2$O**.—To a continuously stirred solution of β_2-[Co(trien)(gly)]$I_2 \cdot H_2O$ (5.5 g) in hot water (100 ml, 60°) was added silver antimonyl-*d*-tartrate (7.9 g) in small portions over 10 min. AgI was removed and the filtrate reduced to 20 ml on a rotatory evaporator. On standing overnight orange-yellow crystals of (+)β_2-[Co(trien)(gly)](SbO(+)tar)$_2$ separated. Initially these crystals were obtained only with difficulty, and in subsequent resolutions the solution was seeded at this stage. The diastereoisomer was removed and washed with a little iced water and acetone (3.65 g). No further diastereoisomer could be induced to separate on reducing the solution volume. A 0.1% solution gave α_D +0.234° and α_{546} +0.423°, whence $[\alpha]_D$ 234° and $[\alpha]_{546}$ 423°. Fractionation of the diastereoisomer gave no change in optical activity. For analysis, see Table V.

D(+)β_2-*RR*-[**Co(trien)(gly)**]$\mathbf{I_2 \cdot 2H_2O}$.—The diastereoisomer was ground with $AgNO_3$ (1.5 g) dissolved in water (10 ml); AgSbO-*d*-tar was removed, and the solution was tested with a little NaI for any remaining Ag ions. The filtrate and washings were reduced to 6 ml on a rotatory evaporator and cooled in an ice bath, and NaI was added. On scratching, (+)β_2-[Co(trien)(gly)]$I_2 \cdot H_2O$ formed and was removed on a glass filter; it was washed with a little iced water and acetone and air dried (1.75 g). A 0.1% solution gave α_D +0.205° and α_{546} +0.474°, whence $[\alpha]_D$ +205° and $[\alpha]_{546}$ +474°. Fractionation of this product gave no increase in activity. For analysis, see Table V.

L(−)β_2-*SS*-[**Co(trien)(gly)**]$\mathbf{I_2 \cdot H_2O}$.—To the filtrate left after removal of the diastereoisomer was added $AgNO_3$ (1.7 g) dissolved in water (5 ml), and precipitated AgSbO-*d*-tar was removed; the filtrate was tested for any remaining Ag ions, and the filtrate and washings were reduced to 6 ml on a rotatory evaporator. On cooling in an ice bath and adding NaI, (−)β_2-[Co(trien)(gly)]I_2 separated and was collected in two fractions with the more active product being the more soluble. Two recrystallizations from hot water gave the optically pure *l* isomer. A 0.1% solution gave α_D −0.198° and α_{546} −0.470°, whence $[\alpha]_D$ −198° and $[\alpha]_{546}$ −470°. For analysis, see Table V.

β_2-Glycinatotriethylenetetramine Cobalt(III) Iodide Dihydrate.—Concentrated HCl (26 ml of 10 *N*) was added to β-[Co(trien)CO_3]$Cl \cdot 1.5H_2O$ (33 g) in water (50 ml). After effervescence had ceased, the solution was warmed on the steam bath until β-[Co(trien)Cl_2]Cl first began to crystallize, and then glycine ethyl ester hydrochloride (14.8 g) was added. The pH was adjusted to 5–6 with 5 *M* NaOH and heating at 80° continued with frequent addition of base to maintain the pH. After 10 min a further 3 g of ester hydrochloride was added. The solution quickly turned a deep orange color. After 3 hr excess NaI was added to the cooled solution, NaCl removed on a glass filter, and then a large excess of methanol was rapidly added to the filtrate with stirring. The lumps of precipitate which formed were broken up and the crude product was collected on a glass filter and washed with methanol and acetone; yield, 42.5 g. A further 3 g was obtained on adding excess ethanol. On dissolving in water, cooling in an ice bath, and scratching β_2-[Co(trien)(gly)]I_2 crystallized (17.5 g). This was recrystallized fom hot water, washed with ethanol, and air dried. For analysis, see Table V.

β-Diglycinetriethylenetetraminecobalt(III) Perchlorate.—Perchloric acid (8 ml of 5 *M*) was slowly added to β-[Co(trien)CO_3]$ClO_4 \cdot H_2O$ (7.6 g). After 15 min glycine (5 g) was added to the resulting solution of β-[Co(trien)(H_2O)$_2$](ClO_4); and the pH was

adjusted to 5.9 with 1 *N* NaOH. After standing for 18 hr at 35°, methanol (10 ml) and excess ethanol were added until all excess glycine had crystallized. This was removed (1.5 g). Addition of further ethanol to the solution in an ice bath and scratching resulted in the crystallization of β-[Co(trien)(glyH)$_2$]-(ClO$_4$)$_3$ which was collected, washed with ethanol, and air dried. This product was recrystallized by dissolving it in the minimum volume of water, adding methanol (70 ml) and LiClO$_4$, cooling in an ice bath, and scratching. The brick-red crystals were washed with ethanol and then ether; yield, 8.5 g (dried at 90° at 15 mm for 18 hr). For analysis, see Table V.

α-Diglycinetriethylenetetraminecobalt(III) Perchlorate.—This compound was prepared in a similar manner to that described above for the β isomer. The lavender complex perchlorate was recrystallized from warm water by cooling in an ice bath; yield, 3.5 g. For analysis, see Table V.

The Reaction β-[Co(trien)(glyH)$_2$](ClO$_4$)$_3$ → β$_1$-[Co(trien)(gly)]-(ClO$_4$)$_2$ + glyH + HClO$_4$.—To β-[Co(trien)(glyH)$_2$](ClO$_4$)$_3$ (1.6 g) in water (10 ml) was added 1 equiv of 1 *M* NaOH (2.5 ml), and the solution stood at 35° for 36 hr. To the resulting orange solution was added 1 drop of 5 *M* HClO$_4$ and the volume was reduced to 5 ml on a rotatory evaporator. On addition of NaI and standing overnight at 5° orange-red crystals of β$_1$-[Co(trien)-(gly)]I$_2$ separated (0.9 g). These were recrystallized from hot water and were shown to be spectrophotometrically identical with those obtained previously.

β-Chloro(glycine ethyl ester)triethylenetetraminecobalt(III) Chloride.—β-[Co(trien)Cl$_2$]Cl (6.25 g) was ground to a fine powder in a mortar with glycine ethyl ester hydrochloride (5.6 g). Water (2 ml) was added and then diethylamine (2.4 g) was added dropwise over 10 min with continuous mixing. After about 15 min the mixture began to thicken and after 1 hr it was diluted with ethanol and filtered, and the residue was washed with ethanol and acetone. The crude, brick-red product was dissolved in the minimum volume of water at 80° and filtered; 1 ml of 10 *N* HCl was added and the solution was cooled in an ice bath. The red crystals which separated were removed and washed with dilute, ice-cold HCl, methanol, and finally acetone; yield, 3.4 g. One further recrystallization as above gave a pure product. For analysis, see Table V.

Preparation of β$_1$-[Co(trien)(gly)]I$_2$ from β-[Co(trien)Cl$_2$]Cl and Glycine.—Glycine (1 g) was added to a solution of β-[Co(trien)-Cl$_2$]Cl (0.4 g) in water (5 ml) at 50°. After 1 hr the orange solution was cooled in an ice bath and excess NaI was added. The orange-red crystals which separated were found to be spectrophotometrically identical with β$_1$-[Co(trien)(gly)]I$_2$·H$_2$O.

Preparation of β$_2$-[Co(trien)(gly)]I$_2$·H$_2$O from β-[Co(trien)Cl$_2$]-ClO$_4$ and Glycine Ethyl Ester.—Powdered β-[Co(trien)Cl$_2$]-ClO$_4$ (7.5 g) was dissolved in 10^{-3} *M* HClO$_4$ (300 ml) at room temperature with magnetic stirring and allowed to aquate for 1 hr. To the resulting solution of β-[Co(trien)Cl(H$_2$O)]$^{2+}$ [31] was added 1 equiv of AgClO$_4$ (4.1 g) dissolved in water (10 ml), and the solution volume was reduced to 25 ml on the rotatory evaporator at room temperature. Precipitated AgCl was removed, and freshly prepared glycine ethyl ester was added dropwise over 10 min at 40°. The solution rapidly turned orange, and, on cooling, adding excess NaI, and standing overnight β$_2$-[Co(trien)gly]I$_2$ (7.1 g) separated. This was removed, washed with ice-cold aqueous NaI and acetone, and air dried. One recrystallization from hot water gave spectrophotometrically pure β$_2$-[Co(trien)-(gly)]I$_2$·2H$_2$O.

Preparations of the β$_2$-Sarcosinatotriethylenetetraminecobalt-(III) Ion. (A) β$_2$-[Co(trien)(sar)](ClO$_4$)$_2$·H$_2$O from Sarcosine Ethyl Ester.—To β-[Co(trien)CO$_3$]ClO$_4$·H$_2$O (11 g) was added HClO$_4$ (12 ml of 5 *M*), and after reaction was complete, 5 *M* NaOH was added dropwise to pH 8. Freshly prepared sarcosine ethyl ester (3.5 g) was then added, and after 15 min at room temperature the complex perchlorate began to separate. After 1.5 hr the product was collected and washed with ice-cold water and methanol; yield, 10.3 g. A further 1.7 g was recovered from the filtrate on addition of excess NaClO$_4$ and cooling. One recrystallization from hot water gave analytically pure β$_2$-[Co(trien)(sar)]-(ClO$_4$)$_2$·H$_2$O. For analysis, see Table V.

(B) β$_2$-Sarcosinatotriethylenetetraminecobalt(III) Iodide Dihydrate.—To β-[Co(trien)CO$_3$]Cl·H$_2$O (16.5 g) in water (25 ml) was added hydrochloric acid (13 ml of 10 *N*), and after reaction was complete the solution was heated on a steam bath until β-[Co(trien)Cl$_2$]Cl first appeared. Sarcosine ethyl ester hydrochloride (8 g) was then added, followed by dropwise addition of 5 *N* NaOH until a color change to orange first appeared. A further 4 g of sarcosine ethyl ester hydrochloride was then added and the solution was heated for 4 hr at 80°. To the filtered aqueous solution (150 ml) was added excess NaI when, on scratching and cooling, the complex iodide separated; yield, 12 g. This was washed with ice-cold NaI solution, methanol, and acetone and then recrystallized from hot water by cooling in an ice bath and scratching; yield, 9.6 g. For analysis, see Table V.

The *anhydrous* iodide salt could be obtained by recrystallization of the dihydrate from hot water and adding NaI. It was also obtained by adding NaI (20 g) to a solution of β$_2$-[Co(trien)-(sar)](ClO$_4$)$_2$·H$_2$O (6.5 g) in 40 ml of hot water and scratching. For analysis, see Table V.

β$_2$-Sarcosinatotriethylenetetraminecobalt(III) Chloride.—β$_2$-[Co(trien)(sar)]I$_2$·2H$_2$O (1 g) in water (10 ml) was shaken with excess AgCl for 15 min and filtered, and the filtrate volume was reduced on a rotatory evaporator until crystals first appeared. On cooling in an ice bath and adding ethanol, β$_2$-[Co(trien)(sar)]-Cl$_2$·0.5H$_2$O crystallized. The product was removed on a glass filter and washed with ethanol and acetone. For analysis, see Table V.

β$_2$-[Co(trien)(sar)]ClO$_4$)$_2$·H$_2$O from Sarcosine.—To β-[Co(trien)-CO$_3$]ClO$_4$·H$_2$O (7.4 g) was added HClO$_4$ (8 ml of 5 *N*), and after 30 min sarcosine (1.8 g) was added. The pH was adjusted to 5.6, and the solution was heated at 60° for 5 min and 40° for 4 hr. The pH was then adjusted to the range 7.5–8.0 with 5 *N* NaOH, and the solution was allowed to stand at 40° for 12 hr. On cooling, the yellow-orange crystals were collected and washed with ice-cold water and methanol; yield, 9.5 g. One recrystallization from hot water gave analytically pure material.

Resolution of β$_2$-Sarcosinatotriethylenetetraminecobalt(III) Iodide. (−)β$_2$-[Co(trien)(sar)]((+)BCS)$_2$.—Silver (+)bromocamphor-π-sulfonate monohydrate (26.2 g) was added with rapid stirring to a solution of β$_2$-[Co(trien)(sar)]I$_2$·2H$_2$O (17 g) in water (200 ml) at 80°. After digesting for 15 min at 80°, the solution was filtered and evaporated to dryness on a rotatory evaporator. The residue was dissolved in warm methanol (40 ml) and ethanol was added to incipient precipitation. On standing in an uncovered beaker for 2 days, the orange crystals which formed were removed and washed with ethanol and acetone; yield, 25 g. This was dissolved in hot water (60 ml) and cooled, when on scratching the diastereoisomer crystallized. After the first fraction was removed (4.2 g, $[\alpha]_{546}$ −180°) three further fractions of similar activity ($[\alpha]_{546}$ −140 to −180°) were obtained by reducing the solution volume, 5.3 g. The filtrate was reserved for isolation of the *d* isomer. The diastereoisomer (9.5 g) was fractionally recrystallized to constant rotation with the least soluble fractions being most active. A 0.1% solution gave α_D −0.076° and α_{546} −0.210°, whence $[\alpha]_D$ −76° and $[\alpha]_{546}$ −210°. For analysis, see Table V.

L-β$_2$-*RRS*-[Co(trien)(sar)]I$_2$.—The optically pure diastereoisomer (6.7 g) was converted to the iodide salt by grinding with excess NaI and water (2 ml) containing 1 drop of glacial acetic acid. The active iodide was collected, washed with ice-cold aqueous NaI and ethanol, and air dried. This was recrystallized from hot water and NaI at pH 4. No improvement in optical purity was achieved on fractionation; yield, 2.5 g. A 0.1% solution in 10^{-3} *M* HClO$_4$ gave α_D −0.233° and α_{546} −0.481°, whence $[\alpha]_D$ −233° and $[\alpha]_{546}$ −481°. For analysis, see Table V.

D-β$_2$-*SSR*-[Co(trien)(sar)]I$_2$.—To the filtrate left after separation of the diastereoisomer was added NaI and the *d* iodide obtained fractionally. The first three fractions (2.8 g) were opti-

(31) A. M. Sargeson and G. H. Searle, unpublished work.

cally pure, followed by racemate (2 g). A 0.1% solution in 10^{-3} M $HClO_4$ gave α_D +0.237° and α_{546} +0.487°. For analysis, see Table V.

α-Hydroxoaquotriethylenetetraminecobalt(III) Perchlorate.—Perchloric acid (8 ml of 5 M) was added to α-$[Co(trien)CO_3]ClO_4 \cdot H_2O$ (7.6 g). After 15 min 5 M NaOH was added dropwise when long dark needles separated from the neutral solution. These were removed and washed with water and ethanol and air dried. For analysis, see Table V. Solution in $HClO_4$ yields the α-$[Co(trien)(H_2O)_2]^{3+}$ ion.

Di-μ-hydroxo-bis(triethylenetetramine)dicobalt(III) Perchlorate Tetrahydrate.—On similar treatment of β-$[Co(trien)CO_3]ClO_4 \cdot H_2O$ and standing for several days in a stoppered flask, purple crystals separated. These were removed, washed with water and ethanol, and air dried. The product was recrystallized from hot $HClO_4$ solution. For analysis, see Table V. Treatment with strong acid does not result in either the α- or β-$[Co(trien)(H_2O)_2]^{3+}$ ion being formed.

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Notes

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The Aquation of the Nitropentaamminecobalt(III) Ion in Sulfuric Acid Solutions

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We have previously observed that, in concentrated sulfuric acid, the nitropentaamminecobalt(III) ion is converted to the bisulfatopentaamminecobalt(III) ion *via* the aquopentaamminecobalt(III) ion.[1] This result was rather surprising in view of the low activity of water in concentrated sulfuric acid and in view of the fact that the original nitro complex possesses no cobalt–oxygen bond. Therefore, in order to obtain information about the mechanism of the reaction, we have studied the kinetics of the reaction as a function of the sulfuric acid concentration and have used oxygen-18 as a tracer to determine the source of the oxygen atom in the aquopentaamminecobalt(III) ion.

Experimental Section

Syntheses.—The kinetic measurements were made using $[Co(NH_3)_5NO_2]SO_4$ which had been prepared by the method described by Schlessinger.[2] The solutions in sulfuric acid were undoubtedly highly ion paired, but for simplicity we shall write $Co(NH_3)_5NO_2^{2+}$ for the reactant. A sample of $[Co(NH_3)_5ONO]Cl_2$ was prepared by the method of Jorgensen.[3]

Nmr Procedure.—In sulfuric acid solutions more concentrated than 57%, the kinetics was studied using an A-60 proton magnetic resonance spectrometer[1] to follow the concentration of $Co(NH_3)_5NO_2^{2+}$. (In more dilute solutions of sulfuric acid, the solvent proton peak interferes seriously with the $Co(NH_3)_5NO_2^{2+}$ peak and makes quantitative nmr analysis impossible.) The solutions were initially about 0.15 M in $Co(NH_3)_5NO_2^{2+}$. Generally the nmr tubes were kept in the probe throughout the run. For reactions with half-lives greater than 15 min, the samples were kept in an external bath at the temperature of the probe (31 ± 0.5°) when the spectra were not being run.

Spectroscopic Procedure.—In sulfuric acid solutions less concentrated than 57%, the kinetics was studied by following the concentration of $Co(NH_3)_5NO_2^{2+}$ spectrophotometrically, using a Cary 14 spectrophotometer. The spectra were determined with a 1-cm quartz cell, using the absorbance at 325 mμ (corrected for the solvent blank) as a measure of the $Co(NH_3)_5NO_2^{2+}$ concentration. Inasmuch as the extinction coefficients at 325 mμ for the species $Co(NH_3)_5NO_2^{2+}$, $Co(NH_3)_5OH_2^{3+}$, and $Co(NH_3)_5SO_4^{+}$ are 1650, 28, and 21 l. cm $mole^{-1}$, respectively, a negligible error was made by neglecting the absorbance due to the products. The solutions were initially about 10^{-3} M in $Co(NH_3)_5NO_2^{2+}$, and throughout the runs they were maintained at 25.0 ± 0.2°. Nitrogen (preequilibrated with sulfuric acid of the same concentration as that used in the run) was bubbled through the solutions in an effort to remove any volatile nitrogen compounds formed in the reaction. At acid concentrations greater than 57%, log A *vs.* time plots showed upward curvature rather than straight-line behavior because of formation of the NO^+ ion.[4] The strong absorption of the NO^+ ion, relative to that of the $Co(NH_3)_5NO_2^{2+}$ ion, made quantitative spectrophotometric studies impossible in the more concentrated sulfuric acid solutions.

Sulfuric Acid Preparation.—The sulfuric acid solutions used in the nmr study were prepared by dilution of reagent grade 96% acid. The concentrations were determined by titration of weighed samples with standard base. The sulfuric acid solutions used in the spectrophotometric study were prepared by mixing weighed amounts of water and constant-boiling[5] sulfuric acid (98.48%).

Isotopic Studies.—The solvent samples used for the isotopic studies were prepared by mixing 0.8 ml of 30% O^{18}-enriched water[6] with 4.2 ml of 100% sulfuric acid. The solution was allowed to reach isotopic equilibrium by storing at 50° for at least 48 hr. About 0.3 g of $[Co(NH_3)_5NO_2]SO_4$ was dissolved in 5 ml of the solvent at about 27°. After 15 min (corresponding approximately to a maximum in the yield of the aquo complex), the solution was poured into 10 ml of ice-cold concentrated HBr solution. The cooled mixture was stirred for 5 min, and the resulting mixed precipitate of $[Co(NH_3)_5H_2O]Br_3$, $[Co(NH_3)_5NO_2]Br_2$, and $[Co(NH_3)_5HSO_4]Br_2$ was collected by suction filtration and washed with 5 ml of ice-cold concentrated HBr, 5 ml of ice water, and two 5-ml portions of ice-cold anhydrous methanol. The mixture consisted of approximately 60% $[Co(NH_3)_5H_2O]Br_3$, 20% [Co-

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