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Intramolecular Hydrolysis of Glycinamide and Glycine Dipeptides Coordinated to Cobalt(III). 1. Hg^{2+}, HOCl, and Base Hydrolysis of *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ (R = H, $CH_2CO_2C_3H_7$, $CH_2CO_2^-$) and Properties of *cis*- and *trans*-$[Co(en)_2(OH_2/OH)(glyNHR)]^{3+/2+}$ Ions

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The Hg^{2+}-catalyzed removal of Br^- from *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ results in the immediate formation of $[Co(en)_2(glyNHR)]^{3+}$ containing the chelated amide or dipeptide residue; full retention of configuration about the Co(III) center obtains and no intermediate aqua complex is formed. HOCl-catalyzed oxidation of *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]^{2+}$ results in the formation of some *cis*-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$ as well as $[Co(en)_2(glyglyOC_3H_7)]^{3+}$, both with full retention of the configuration about the metal. Base hydrolysis (pH 9–14) results in the formation of some *trans*-$[Co(en)_2(OH)(glyNHR)]^{2+}$ (~6.2%) as well as *cis*-$[Co(en)_2(OH)(glyNHR)]^{2+}$ (R = H, 34% D, 20% DL; R = $CH_2CO_2C_3H_7$, 44% D, 19% DL; R = $CH_2CO_2^-$, 70% D + DL + trans) and $[Co(en)_2(glyNHR)]^{3+}$ (R = H, 20% D, 20% DL; R = $CH_2CO_2C_3H_7$, 20% D, 10% DL; R = $CH_2CO_2^-$, 30% D + DL). The *trans*-$[CO(en)_2(OH_2/OH)(glyNHR)]^{3+/2+}$ ions cyclize to $[Co(en)_2(glyNHR)]^{3+}$ according to the rate expression $R = k_{H_2O}[[Co(en)_2(OH_2)(glyNHR)]^{3+}] + (k_{OH} + k'_{OH}[OH^-])\cdot[[Co(en)_2(OH)(glyNHR)]^{2+}]$ where $k_{H_2O} = 4\ (\pm 2) \times 10^{-6}\ s^{-1}$, $k_{OH} = 2.8\ (\pm 0.1) \times 10^{-4}\ s^{-1}$, and $k'_{OH} = 5.6 \times 10^{-2}\ M^{-1}\ s^{-1}$ for R = H at 25 °C and $\mu = 1.0$ ($NaClO_4$); this process occurs directly and not via the monodentate cis-aqua or -hydroxo ions. The *cis*-$[Co(en)_2(OH)(glyNHR)]^{2+}$ ions cyclize to $[Co(en)_2(glyO)]^{2+}$ and $[Co(en)_2(glyNHR)]^{3+}$ via a mechanism involving retention of the coordinated hydroxo oxygen atom. In acid solution the *cis*-$[Co(en)_2(OH_2)(glyNHR)]^{3+}$ ion also forms $[Co(en)_2(glyO)]^{2+}$ and $[Co(en)_2(glyNHR)]^{3+}$, but only the former retains the oxygen atom of the coordinated water molecule.

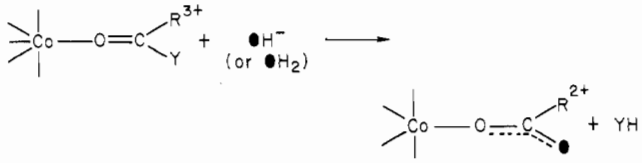
Metal ions and metal complexes have been found to accelerate the hydrolysis of esters, amides, and peptides[1] and the hydration of CO_2 and similar substrates[2] and nitriles,[3-5] and to various degrees these studies have been said to mimic the role played by metal ions in metallo enzymes. In these studies kinetically robust metal ion systems, principally those of cobalt(III), have been used to differentiate between the direct polarization mechanism represented by Scheme I and the alternate "metal–hydroxide" mechanism, Scheme II[6] (the solid oxygen atoms indicate the fate of the hydroxyl function in the product). These experiments showed that whereas Scheme I provides rate enhancements of 10^4–10^6 for all substrates independent of the leaving group,[7-12] Scheme II is effective only with the more reactive species (CO_2, anhydrides, aldehydes, and esters with good leaving groups).[6] Thus the hydrolysis of amino acid esters, amides, and simple peptides has not been observed in a bimolecular "metal–hydroxide" process. Furthermore, in the direct polarization mechanism, the rate enhancement is due entirely to entropy factors, whereas both $\Delta H^\ddagger$ and $\Delta S^\ddagger$ contribute to the latter. Also, whereas Scheme I promotes nucleophilic attack by species other than OH^- (NH_2R, ROH, H_2O),[13,14] only hydrolysis is observed with metal hydroxides,[2] and in particular general acid or general base catalysis has not been observed.

The intramolecular counterpart of Scheme II, as given by Scheme III for the hydration of aminoacetonitrile, has been observed for amino acid esters,[15,16] amides,[17] and nitriles[5,18] where five- and six-membered chelate rings result. For aminoacetonitrile, a rate enhancement of $\sim 10^{11}$ occurs at pH 7,[5,18] and this is to be compared with an acceleration of 10^6 for the Scheme I counterpart.[4] $\Delta H^\ddagger$ factors now become of great significance, and it seems that the large positive $\Delta S^\ddagger$ change found in Scheme I, and presumably arising from desolvation of solvent OH^- in the transition state, is now apparent in the metal–hydroxo reactant.[5,18]

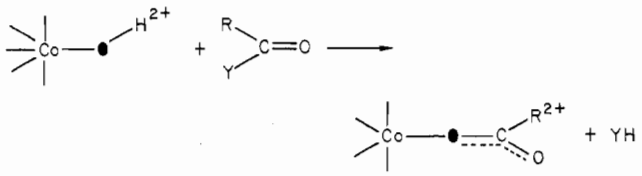
For the amino acid ester[15,16] and amide[17] species, however, the intramolecular hydrolysis reaction has not been observed directly; it was required to occur from results of ^{18}O-tracer studies.[15-17] It has now been possible to isolate the cis-hydroxo and cis-aqua complexes containing glycinamide, glycylglycine, and isopropyl glycylglycinate and to study their subsequent cyclization over the pH range 0–14. This is the first time that metal-facilitated intramolecular hydrolysis of simple amides has been observed in the absence of other equilibrium processes, and the rate profiles as a function of pH, catalysis by buffers, and other mechanistic aspects are of some general significance.

In this paper we give the methods used to obtain the *cis*- and *trans*-$[Co(en)_2(OH_2|OH)(glyNHR)]^{3+/2+}$ ions (R = H, $CH_2CO_2C_3H_7$, $CH_2CO_2^-$), describe in detail the stereochemistry of these reactions, and look at the rates and products of the subsequent reactions of the trans species. A subsequent paper will consider in detail the kinetic and mechanistic aspects

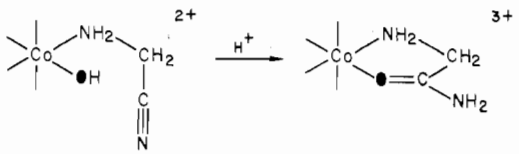
Scheme I



Scheme II



Scheme III



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of the reactions of the cis ions.[23]

Experimental Section

AnalaR reagents were used throughout without further purification. Glycylglycine (Sigma), silver perchlorate and thionyl chloride (BDH), methanol, and 2-propanol (AR) were used following recrystallization and distillation, respectively. $NaClO_4 \cdot H_2O$ (Fluka) was used as supporting electrolyte in the kinetic studies.

Electronic spectra were recorded using Cary 14 or Cary 118C spectrophotometers. ^1H NMR spectra were obtained on Varian HA-100 or JEOLCO Minimar MH-100 spectrometers using 0.1–0.3 M solutions in deuterated solvents (D_2O, Me_2SO-d_6) with NaTPS or Me_4Si as reference.

Cobalt determinations were carried out using Varian-Techtron AA-4 and AA-1000 spectrometers. Optical rotations (α_λ) were measured at 25 °C using a Perkin-Elmer P22 spectropolarimeter and in a 1-dm cell. Determinations of pH were made using a Radiometer PHM26C pH meter fitted with a G202B glass electrode and a calomel electrode protected with a NH_4NO_3 (1.6 M)/$NaNO_3$ (0.2 M) salt bridge. The meter was calibrated with 0.05 M potassium hydrogen phthalate (pH 4.01 (25 °C), 4.03 (37 °C)) or 0.01 M borax (pH 9.18 (25 °C), 9.09 (37 °C)). pH stat titrations were carried out using the above pH equipment in conjunction with a TAA_3 electrode assembly, ABU 12 and ABU 1c autoburets (2.5-mL capacity), a TT.11b titrator, and a SBR_2 titragraph. Rates of reaction were determined spectrophotometrically using a Cary 16K spectrophotometer fitted with a locally constructed thermostated cell (3.2-cm path length, 30 mL of solution) into which was inserted the electrode assembly. The titrant (1.0 or 0.1 M NaOH or $HClO_4$) was added under a nitrogen atmosphere to the magnetically stirred solution. Product separations were carried out using either BioRad Analytical Dowex 50W-X2 (200–400 mesh) or SP-Sephadex C-25 cation-exchange resins following dilution of the neutralized (pH ~4) solutions; eluents were 1–2 M HCl or 0.1–0.5 M $NaClO_4$, respectively.

Preparation of Ligands and Complexes. Methyl glycylglycinate hydrochloride was prepared by adding $SOCl_2$ (30.8 mL) dropwise to ice-cold MeOH (AR, 1.25 L) followed by glycylglycine (52.8 g). After 2-h reflux the solution volume was reduced to ca. 200 mL, and the product was crystallized by adding ether and cooling in ice. The filtered product was washed with ether and air-dried (yield 70 g (96%)). Recrystallization was effected from MeOH/ether. Anal. Calcd for $C_5H_{10}N_2O_3 \cdot HCl$: C, 32.9; H, 6.07; N, 15.3; Cl, 19.4. Found: C, 32.7; H, 6.1; N, 15.2; Cl, 19.2.

Isopropyl glycylglycinate hydrochloride was similarly prepared using $SOCl_2$ (30.8 mL), glycylglycine (52.8 g), and 2-propanol (AR, 2 L). The hot solution was filtered, cooled in ice, and the product washed with ether and air-dried (yield, 70 g (83%)). It was recrystallized from refluxing 2-propanol (90% recovery). Anal. Calcd for $C_7H_{14}N_2O_3 \cdot HCl$: C, 39.9; H, 7.18; N, 13.3; Cl, 16.8. Found: C, 40.2; H, 7.3; N, 13.6; Cl, 17.0.

$[Co(en)_2CO_3]Cl$ and *trans*-$[Co(en)_2Br_2]Br$ were prepared by the published procedures.[20,21] It was shown to be essential to convert the former to the bromide salt before making the latter complex. This was most simply done by dissolution in warm water, adding solid NaBr slowly with scratching, and finally cooling in ice. The $[Co(en)_2CO_3]Br$ was washed with MeOH and air-dried.

cis-$[Co(en)_2Br(glyNH_2)]Br_2 \cdot H_2O$ was prepared by a modification of the published method.[22] *trans*-$[Co(en)_2Br_2]Br$ (83.8 g), glycinamide hydrobromide (32 g), and $CoBr_2 \cdot 6H_2O$ (1 g) were ground to a fine paste with water (30 mL), and a solution of triethylamine (20.4 g) in MeOH (40 mL) added dropwise over 30 min with continuous mixing. Additional H_2O (60 mL in all) was added when required to keep the paste workable, and grinding was continued for a further 30 min. This mixture was dissolved in hot water (600 mL) containing glacial HOAc (5 mL) and filtered, and NaBr was added to the filtrate as it cooled until crystallization began. Following cooling in ice and filtering, the product was washed with MeOH and air-dried (yield 90 g (88%)). It was found necessary to remove a small amount of a highly charged species from the product by ion-exchange chromatography on Dowex 50W-X2 cation-exchange resin (H^+ form). The major purple 2+ band was eluted with 2 M HBr and the eluate volume reduced on a rotary evaporator until crystallization commenced. After the mixture was cooled in ice, recovered $[Co(en)_2Br(glyNH_2)]Br_2$ was recrystallized from hot water (pH ≃5) by addition of NaBr and cooling. The final product was washed on a glass filter with ice-cold MeOH and acetone and air-dried. Anal. Calcd for $[Co(en)_2Br(glyNH_2)]Br_2 \cdot H_2O$: C, 14.6; H, 4.5; N, 17.1. Found: C, 15.1; H, 4.7; N, 17.3. The product was chromatographically pure.

cis-$[Co(en)_2Br(glyglyOCH_3)]Br_2 \cdot 2H_2O$ and *cis*-$[Co(en)_2Br(glyglyC_3H_7)]Br_2 \cdot H_2O$ were prepared in a similar fashion, and it was found unnecessary to purify the products by ion-exchange chromatography.

To prepare *cis*-$[Co(en)_2Br(glyglyOCH_3)]Br_2 \cdot 2H_2O$, $glyglyOCH_3 \cdot HCl$ (36.6 g) dissolved in MeOH (AR, 400 mL) containing triethylamine (20.2 g) was added to *trans*-$[Co(en)_2Br_2]Br$ (83.4 g, 4 mL H_2O). After 4 h of standing, the product was washed with ethanol on a glass filter and recrystallized from hot 0.2 M HBr (130 mL): yield 92 g (75%); ϵ_{542} 82; ^1H NMR (CH_3) 3.66 ppm. Anal. Calcd for $[Co(en)_2Br(glyglyOCH_3)]Br_2 \cdot 2H_2O$: C, 18.0; H, 5.0; N, 14.0. Found: C, 18.1; H, 5.4; N, 14.0.

To prepare *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2 \cdot H_2O$, *trans*-$[Co(en)_2Br_2]Br$ (83.8 g) and $glyglyOC_3H_7 \cdot HCl$ (42.2 g) were intimately mixed to a fine paste with H_2O (6 mL) and MeOH (AR, 60 mL), and triethylamine (20.4 g) was added dropwise over 1 h. The crude product was recovered after a further 1 h (93 g, 76%) and recrystallized twice from warm 0.2 M HBr: yield 33 g (27%); ϵ_{541} 82; ^1H NMR (C_3H_7) 1.14 (doublet) ppm. Anal. Calcd for $[Co(en)_2Br(glyglyOC_3H_7)]Br_2 \cdot H_2O$: C, 21.6; H, 5.28; N, 13.7; Br, 39.2. Found: C, 21.6; H, 5.5; N, 13.6; Br, 39.2.

cis-$[Co(en)_2Br(glyglyOH)]Br_2 \cdot 2H_2O$ was prepared from the methyl ester complex (24 g) by dissolution in water (250 mL) and addition of 48% aqueous HBr (250 mL). After overnight hydrolysis, the solution was cooled in ice and the crystalline product removed. Ethanol and acetone washing gave 16 g (68%) of the crude dipeptide acid complex. This was recrystallized from hot 0.1 M HBr (120 mL), and ^1H NMR spectra confirmed the absence of the methyl signal. Anal. Calcd for $[Co(en)_2Br(glyglyOH)]Br_2 \cdot 2H_2O$: C, 16.4; H, 4.8; N, 14.3; Br, 40.8. Found: C, 16.6; H, 5.1; N, 14.0; Br, 40.8.

Resolution of *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2 \cdot H_2O$ and *cis*-$[Co(en)_2Br(glyNH_2)]Br_2$. Silver $(+)_{589}$-camphor-10-sulfonate (Ag-$(+)_{589}$-CS) was prepared by mixing equimolar quantities of $AgClO_4$ and $(+)_{589}$-camphor-10-sulfonic acid in acetone from which the product crystallized. It was washed with a little ether, air-dried, and stored in a brown bottle in the dark. To *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2 \cdot H_2O$ (12.2 g) in MeOH (100 mL) was added Ag-$(+)_{589}$-CS (13.6 g) and the mixture stirred at ambient temperature for 1 h. The fine precipitate of AgBr was removed by centrifugation and the solution reduced to dryness. To the residue dissolved in MeOH (20 mL) was added acetone (500 mL), and from this solution $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]((+)_{589}\text{-}CS)_2$ crystallized on scratching and cooling in an ice bath. The diastereoisomer was recovered, washed with acetone and ether, and air-dried (5.9 g). It was then recrystallized three times from MeOH/acetone to constant rotation: yield 4.6 g; $[\alpha]_{589} = +81°$, $[\alpha]_{440} = -116°$. Anal. Calcd for $CoC_{31}H_{62}N_6O_{11}S_2$: C, 41.6; H, 7.0; N, 9.4. Found: C, 41.5; H, 6.9; N, 9.7. This slightly hygroscopic diastereoisomer was stored in an evacuated desiccator. To recover the optically active cation the $(+)_{589}$-CS^- anion was removed by passing an aqueous solution down DEAE-Sephadex A-25 anion-exchange resin (NO_3^- or Br^- form). The resulting solution had $[M]_{589} = +820°$, $[M]_{440} = -1870°$ whence $[\alpha]_{589} = +134°$, $[\alpha]_{440} = -306°$ for the bromide salt monohydrate. Further impure diastereoisomer fractions were obtained from the original filtrate giving finally $(-)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]((+)_{589}\text{-}CS)_2$. However, these products were found to be contaminated with the optically active dipeptide chelate complex and were not used further.

cis-$[Co(en)_2Br(glyNH_2)]^{2+}$ was resolved as previously described[17] using ammonium $(+)_{589}$-bromocamphorsulfonate giving $(+)_{589}$- and $(-)_{589}$-$[Co(en)_2Br(glyNH_2)]Br_2$, $[\alpha]_{589} = +118, -116°$, respectively.

HOCl-Induced Hydrolysis of *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2$. A ~1 M HOCl solution was prepared by saturating an ice-cold 1 M $AgClO_4$ solution with Cl_2, filtering, adding 1 M $AgClO_4$ dropwise until in slight excess, and refiltering. *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2$ (ca. 0.5 g) was dissolved in the minimum volume of H_2O (~1 mL) and converted to the nitrate using DEAE-Sephadex A-25 resin (NO_3^- form). The resulting solution was concentrated to near dryness on a rotary evaporator and cooled to ca. 0 °C, the 1 M HOCl solution added (20 mL, 0 °C), and the mixture shaken periodically over 10 min at 0 °C. The pH was then adjusted to 8 (1 M NaOH), the solution was diluted with ice-water (ca. 1 L), and the complexes were sorbed onto and then eluted from SP-Sephadex C-25 resin (0.5 M, $NaClO_4$, pH 8) at ~2 °C. The resulting three bands were (in order of elution) *cis*-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$ (red-violet, ϵ_{498} 103),

$[Co(en)_2(glyO)]^{2+}$ (orange, ϵ_{487} 97), and $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ (orange-yellow, ϵ_{487} 98). The same procedure was used to prepare solutions of *cis*-$[Co(en)_2(OH)(glyglyO)]^+$ although $\simeq$0.2 M $NaClO_4$ was used as eluent.

Base Hydrolysis of $[Co(en)_2Br(glyNHR)]^{2+}$ Complexes. After rapid dissolution of a weighed amount of the complex in 0.10 M glycine buffer (μ = 1.0, $NaClO_4$) at 25 °C, base hydrolysis was followed by spectrophotometry or by base consumption (pH stat titration) against 0.10 M NaOH (ca. 80 mg of complex, 30 mL of 1 M $NaClO_4$, 3.2-cm thermostated cell, Cary 16K). The two major products, $[Co(en)_2OH(glyNHR)]^{2+}$ and $[Co(en)_2(glyNHR)]^{3+}$ (R = $CH_2CO_2^-$, $CH_2CO_2C_3H_7$), were separated by cation-exchange chromatography as described above. For R = H the hydroxo amide could not be obtained in a pure form, even at 2 °C, since some $[Co(en)_2(glyO)]^{2+}$ was formed on the ion-exchange resin; the $[Co(en)_2(glyNH_2)]^{3+}$ ion could, however, be isolated. Also sufficient $[Co(en)_2(OH)(glyNH_2)]^{2+}$ was obtained by this method to identify the products and stereochemistry of its subsequent reactions.[23] Normally the hydroxo products (R = $CH_2CO_2C_3H_7$, $CH_2CO_2^-$) were determined by spectrophotometry and by atomic absorption for Co. For R = H the base-hydrolyzed solution ($5t_{1/2}$) was immediately quenched with HOAc (pH 4) and the $[Co(en)_2(glyNH_2)]^{3+}$ and $[Co(en)_2(glyO)]^{2+}$ ions separated on the ion-exchange column (Dowex 50W-X2).

Isolation and Properties of the *trans*-$[Co(en)_2(OH/H_2O)(glyNHR)]^{2+/3+}$ Ions. *rac*- or $(+)_{589}$-$[Co(en)_2Br(glyNHR)]Br_2$ (R = H, $CH_2CO_2C_3H_7$) was hydrolyzed at pH 10 (6 min, pH stat). For R = H the solution was immediately quenched to pH 2 (1 M $HClO_4$) and left for 15 min after which time all the cis-aqua amide had converted to $[Co(en)_2(glyO)]^{2+}$. For R = $CH_2CO_2C_3H_7$ the hydroxo amide product was separated from the $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ ion by ion-exchange chromatography at ~2 °C (pH ~8) as described earlier. This solution (0.5 M $NaClO_4$) was then treated with phosphate buffer (pH 6.64, 0.15 M, or pH 8.77, 0.07 M, 25.0 °C) for $\sim 6t_{1/2}$ for reaction of the cis ion[23] or was converted to the aqua ion (pH ~2) and allowed to stand for 4 h. For all these experiments the final solutions (R = H, $CH_2CO_2C_3H_7$) were adjusted to pH ~2 and sorbed onto Sephadex C-25 resin, and the $[Co(en)_2(glyO)]^{2+}$ product was eluted with 0.2 M $NaClO_4$ (pH ~2). The trans-aqua product remaining in the 3+ band was then removed (as the trans-hydroxo species) by first cooling the column to ~2 °C, washing the column with 0.2 M "Tris" buffer (pH ~8.1, 2 °C) until basic, and eluting with 0.2 M $NaClO_4$ at pH 8 (10^{-3} M Tris, 2 °C). The visible and ORD spectra of the trans-aqua and trans-hydroxo ions were then immediately recorded at pH ~2 and 8, respectively, and Co concentrations were measured. For R = H, ϵ_{497} is 60 ± 2 (aqua) and ϵ is 72 ± 2 (hydroxo); for R = $CH_2CO_2C_3H_7$, ϵ_{497} is 58 ± 4 (aqua) and ϵ is 78 ± 1 (hydroxo) in 1 M $NaClO_4$ at ~20 °C. The aqua and hydroxo ions (R = H, $CH_2CO_2C_3H_7$) produced from the $(+)_{589}$ bromo complexes showed no optical activity from 600 to 350 nm (~5 × 10^{-4} M solutions).

Reactions of *trans*-$[Co(en)_2(OH/OH_2)(glyNHR)]^{2+/3+}$. Rate data were obtained at 560 nm (hydroxo) or 487 nm (aqua) by continuous monitoring of the absorbance (3.2-cm cell, 25.0 °C, μ = 1.0 ($NaClO_4$), pH stat control). For pH ≥8 the solution was initially degassed and kept under a N_2 atmosphere. At the conclusion of the reaction the products were determined as follows. The solutions were quenched to pH ~2 ($HClO_4$), sorbed onto Sephadex C-25 resin, and eluted at pH ~2 with a $NaClO_4$ gradient (0.4–1.0 M). For the reactions in acid only one 3+ band was obtained, but for R = $CH_2CO_2C_3H_7$ this separated into two when eluted with 0.2 M $NaClO_4$ (pH ~8); the latter ions were identified as $[Co(en)_2(glyglyOC_3H_7)]^{2+}$ and $[Co(en)_2(glyglyO)]^{2+}$ by their rates of hydrolysis at pH 11.0; for R = H only $[Co(en)_2(glyNH_2)]^{3+}$ was found and it was similarly identified. For the products from the trans-hydroxo ions (pH ≥8.0) both 2+ and 3+ products were found and these were identified as $[Co(en)_2(glyO)]^{2+}$ and $[Co(en)_2(glyglyOC_3H_7)]^{3+}$, respectively. However, it was shown that the former derived from the latter under the conditions of the experiment.

^{18}O-Tracer Experiments. $H_2{}^{18}O$ (not normalized, 1.5 and 2.0 atom %) was obtained from Miles Laboratories Inc. (Yeda). The ^{18}O content of the CO_2 recovered from equilibration with the solvent, and from the complexes, was analyzed using an Atlas GD-150 or M-86 mass spectrometer.[24,25] In all experiments the complexes were finally obtained as $[Co(en)_2(glyO)]HgI_4$, and the glycine was recovered by pyrolysis and sublimation under vacuum as described previously.[8] The HgI_4^{2-} salt was precipitated by adding a concentrated solution of HgI_2 dissolved in aqueous NaI to the ion-exchanged product. The following experiments were carried out.

(a) $[Co(en)_2Br(glyglyOC_3H_7)]Br_2{\cdot}H_2O$ (5 g) was dissolved in 50 mL of $H_2{}^{18}O$ (1.6 and 2.0 atom %) and hydrolyzed at pH 9.02 for 25 min by pH stat titration against 5 M NaOH (not enriched). A ~1-mL sample was removed for solvent determination, and the remainder was diluted to 200 mL with iced water and absorbed onto and eluted from SP-Sephadex C-25 cation-exchange resin at 2 °C using 0.5 M $NaClO_4$ at pH 8. Three major products separated: (1) a red-pink band containing $[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$ (~60%); (2) an orange band containing $[Co(en)_2(glyO)]^{2+}$ (~25%); (3) a slow-moving brown band (~10%) which was discarded. Band (1) was flushed with N_2 and divided into two approximately equal parts which were treated as follows. The first part was diluted to 200 mL with degassed water (N_2) and pH-stated at pH 3.77 for 3 h ($\simeq 5t_{1/2}$). The second fraction in 200 mL of 0.07 M phosphate buffer was pH-stated at pH 8.77 for 31 min ($\simeq 10t_{1/2}$).[23] In a separate experiment the ^{18}O-labeled hydroxo complex was kept at pH 8.77 (pH stat control) and 25.0 °C for 15 h. The three solutions were quenched to pH 3.0 ($HClO_4$), diluted three times with H_2O, and sorbed onto CM-Sephadex C-25 exchange resin. The two reaction products $[Co(en)_2(glyO)]^{2+}$ and $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ were separated with 0.2 M $NaClO_4$ and then eluted with a 0.5–1.0 M pyridinium acetate gradient. They were recovered as solids following rotary evaporation and addition of HOAc to remove pyridine. The $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ products were then separately hydrolyzed at pH 11 for 53 min (pH stat, $\simeq 10t_{1/2}$), rechromatographed on CM-Sephadex C-25 (py/HOAc), and recovered as above. The various $[Co(en)_2(glyO)]^{2+}$ ions were isolated as their HgI_4^{2-} salts.

(b) $H^{18}OCl$ was prepared by adding $AgClO_4$ (20.07 g) to ice-cold $H_2{}^{18}O$ (50 ml, 1.6 atom %) and bubbling Cl_2 through the cold (~0 °C) solution for ca. 20 min. AgCl was quickly removed (Hyflo filter) and the solution rapidly back-titrated at ~0 °C to the AgCl end point. The refiltered solution was used as described below. The nitrate salt of *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]^{2+}$ was prepared by ion exchange of the bromide salt (10 g in 40 mL of H_2O at 40 °C; Sephadex A-25, NO_3^-) and reducing to dryness on a rotary evaporator. This complex in 10 mL of $H_2{}^{18}O$ (1.6 atom %) at 0 °C was added over 5 min to the $H^{18}OCl$ solution, and after a further 10 min the red solution was filtered and a sample (1 mL) taken for solvent analysis. The remainder was diluted (~500 mL) and sorbed onto SP-Sephadex C-25 resin at ~2 °C. The two major products, $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ and $[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$, were then separated and collected (0.5 M $NaClO_4$, pH 8, 2 °C) and the latter was kept at pH 3.77 for 4 h (pH stat, 200 mL, 25 °C). The various $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ and $[Co(en)_2(glyO)]^{2+}$ products were isolated and dealt with as described in part (a) above.

Optical Retention Experiments. (a) Hg^{2+}-Catalyzed Reaction of $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]^{2+}$. $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](CS)_2$ (0.282 g, $[\alpha]_{589}$ = +81°, CS = $(+)_{589}$-camphor-10-sulfonate) was converted to its bromide salt (Sephadex A-25) and made up to 20 mL. A 2-mL sample was removed for visible and ORD spectral analysis. $HClO_4$ (1 mL) was added to the remainder followed by a 0.2 M Hg $(ClO_4)_2$ solution (10 mL, 0.09 M $HClO_4$), and the solution stood for 30 min at ca. 25 °C. ORD and visible spectra were then recorded. The solution was then divided into two equal parts and the first was sorbed onto, and then eluted from, SP-Sephadex C-25 resin (0.2–1.0 M $NaClO_4$ gradient), and ORD and visible spectra were taken of the recovered $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ product (1 M $NaClO_4$, pH ~6). The complex was then hydrolyzed by pH stat titration (pH 11, 50 min), the pH was adjusted to ~4 (HOAc), and the visible and ORD spectra of the $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ product were recorded both before and following ion-exchange purification on C-25 resin (0.5 M $NaClO_4$, pH ~6). The second fraction of $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ was immediately hydrolyzed at pH 11 (50 min), precipitated HgO removed, and the pH adjusted to ~4 (HOAc). The $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ was then chromatographed as before, and the visible and ORD spectra of the recovered product were recorded (1.0 M $NaClO_4$, pH ~6).

(b) HOCl-Induced Reaction. The procedure was identical with that described in detail for the ^{18}O-tracer experiment: 1.39 g of $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](CS)_2$ and 40 mL of ≃1 M HOCl were used in a reaction at 0 °C. The ion-exchange-separated solution of $(+)_{589}$-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$ was divided into two parts, the first being treated with 0.07 M phosphate buffer at pH 8.77 (30

Table I. Rate Data for Hg^{2+}-Promoted Removal of Bromide from the *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ Ions[a]

R	$[Hg^{2+}]$, M	$[HClO_4]$, M	$10k_{obsd}$, s^{-1}	k_{Hg},[b] M^{-1} s^{-1}
H	0.02	0.1	7.80	39
	0.01	0.1	4.00	40
	0.01	0.67	4.50	45
	0.005	0.1	2.18	41
$CH_2CO_2C_3H_7$	0.02	0.1	4.78	24
	0.01	0.1	2.31	23
	0.01	0.67	2.54	25
	0.005	0.1	1.16	23
$CH_2CO_2C_2H_5$	0.02	0.1	4.80	24
	0.01	0.1	2.36	24
	0.01	0.67	2.52	25
	0.005	0.1	1.23	25
$CH_2CO_2CH_3$	0.02	0.1	1.24	6.2
	0.01	0.1	0.63	6.3
	0.01	0.67	0.60	6.0
	0.005	0.1	0.33	6.6

[a] 25.0 °C; μ = 1.0 ($NaClO_4$). Spectrophotometric data at 560 nm; [Co] ≈ 5×10^{-4} M; complexes converted from Br^- salts to ClO_4^- salts using Dowex 1-X8 (50–100 mesh) anion-exchange resin. [b] $k_{Hg} = k_{obsd}/[Hg^{2+}]$.

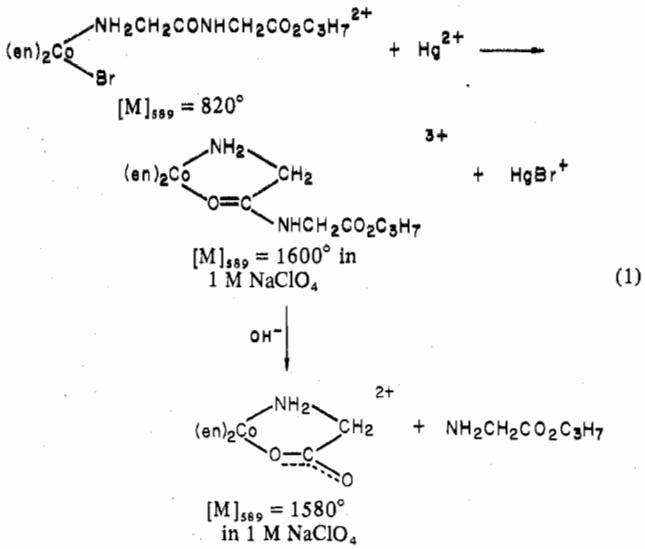
min, 25.0 °C) and the second being held at pH 3.77 (4 h, pH stat). After being quenched to pH ~4 (HOAc) the solutions were sorbed onto, and eluted from, C-25 resin using a $NaClO_4$ gradient (0.5–1.0 M). The visible and ORD spectra of the $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ and $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ products were recorded in 0.5 and 1.0 M $NaClO_4$ at pH ~6, respectively.

(c) Base-Catalyzed Reaction. $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](CS)_2$ (1.39 and 1.25 g, two experiments) in water (50 mL) was hydrolyzed at pH 9.0 (21 min) and 9.5 (8 min) (pH stat control, 1 M NaOH) before adjusting the solutions to pH 8, cooling to ~0 °C, and sorbing the products onto C-25 resin packed and held at ~2 °C. The red 2+ and orange 3+ products were rapidly separated using 0.5 M $NaClO_4$ (pH 8, ~2 °C) and eluted with 0.5 M $NaClO_4$ (pH 8, 2 °C) and 1 M $NaClO_4$ (pH 5), respectively. The visible and ORD spectra were immediately recorded at pH ~2 and ~8 for the 2+ ion and at pH 5 for the 3+ ion. The solution of the former (pH 8) was then divided into two equal parts and treated at pH 8.77 (0.07 M phosphate buffer) and 3.77, respectively, as described previously. The $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ and $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ products were again separated, their visible and ORD spectra recorded, and the latter ion was then hydrolyzed to $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ (pH 11, 53 min, 1.0 M $NaClO_4$, rate recorded). Visible and ORD spectra on the ion-exchange-purified product (50W-X2 resin, 1 M $NaClO_4$) were recorded.

Results and Discussion

1. Hg^{2+}-Induced Removal of Bromide. Table I gives spectrophotometric data for the reaction of Hg^{2+} with *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ (R = H, $CH_2CO_2C_3H_7$, $CH_2CO_2C_2H_5$, $CH_2CO_2CH_3$). Only one rate was observed (560 nm, maximum OD change), and plots of log k_{obsd} vs. time were linear for at least $3t_{1/2}$. The reaction is independent of $[H^+]$ and follows the rate law $R = k_{Hg}[Co(en)_2Br(glyNHR)^{2+}][Hg^{2+}]$. With the exception of the case of the dipeptide methyl ester complex, values of k_{Hg} are greater than those found for other $[Co(en)_2Br(amine)]^{2+}$ complexes, viz. (amine, k_{Hg} in M^{-1} s^{-1}): NH_3, 2.7; NH_2CH_3, 7.9; $NH_2CH_2CO_2CH_3$, 5.1; $NH_2CH_2CO_2C_2H_5$, 4.4; $NH_2CH_2CO_2C_3H_7$, 5.1; $NH_2CH_2CH_2CO_2C_3H_7$, 2.4; NH_2CH_2CN, 0.12. The reasons for this are not clear at the present time. It may arise from changes in the association constant k_{Hg} rather than from variations in the rate of loss of $HgBr^+$, but a detailed investigation of this aspect is outside the scope of the present study. Product analysis results showed that only chelated amide species, $[Co(en)_2(glyNHR)]^{3+}$, were formed and that these were produced directly and not via the intermediate aqua complex. Also, the results require the absence (<2%) of hydrolysis in the monodentate amide function prior to, or following, chelation. The former result was demonstrated by ion-exchange analysis. The *cis*- and *trans*-$[Co(en)_2(OH)glyglyOC_3H_7)]^{2+}$ ions readily separate from $[Co(en)_2(glyNHR)]^{3+}$ at pH ~8 and 2 °C, but neither was detected in the present experiments. Also *cis*-$[Co(en)_2(H_2O)(glyNHR)]^{3+}$ gives rise to appreciable amounts of $[Co(en)_2(glyO)]^{2+}$ in acidic solution and again none was found. The Hg^{2+}-promoted reaction is therefore an excellent method for preparing large amounts of the chelated amide species in a pure form.

Full retention of configuration about the metal center obtains in this reaction. Thus $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]^{3+}$ ($[M]_{589}$ = +820°) gave exclusively the chelated dipeptide ion (3+; $[M]_{589}$ = +1600°) (see eq 1).



(1)

Subsequent hydrolysis at pH 11 resulted in $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ ($[M]_{589}$ = +1580° in 0.5 M $NaClO_4$), and when this compound was compared with optically pure $(+)_{589}$-$[Co(en)_2(glyO)]I_2$ ($[M]_{589}$ = 1546° in H_2O) prepared from glycine and resolved separately,[26] it is clear that both the Hg^{2+}-catalyzed removal of Br^- and base hydrolysis of the chelated dipeptide occur with full retention. Optical rotary dispersion (ORD) and visible spectra for the two products are given in Figure 4 (supplementary material).

Similar results have been found for other *cis*-$[Co(en)_2X(NH_2R)]^{2+}$ complexes where X = Cl or Br and NH_2R = glycinamide,[17] glycine esters,[7-9] or glycinate.[27] The carbonyl or carboxylic acid function appears to be an exceedingly fine competitor for the five-coordinate intermediate generally considered to be formed in such reactions with Hg^{2+},[25,28] especially when five- and six-membered chelate rings are involved (see Scheme IV). This inability of water to compete is supported by the lack of competition by other added anions (NO_3^-, HSO_4^-),[8,9] and although a concerted process involving the simultaneous entry of the carbonyl function during loss of HgX^+ cannot be entirely eliminated, its involvement in the rate-determining transition state is unlikely since no systematic synergic increase in rate is found when the k_{Hg} values are compared with those for complexes which do not contain the >C=O grouping and which involve water (or anion) entry. The full retention of optical configuration obtained with the present complexes is entirely consistent with that found previously with *cis*-$[Co(en)_2X(NH_3)]^{2+}$ ions (X = Cl, Br).[29,30]

2. Base Hydrolysis. Table II contains rate data for the base hydrolysis of the *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ ions (R = H, $CH_2CO_2^-$, $CH_2CO_2C_3H_7$) and the product analysis results are given in Table III.

Large optical density changes were observed at 490 and 360 nm, and at these wavelengths acceptable infinity readings were

Scheme IV

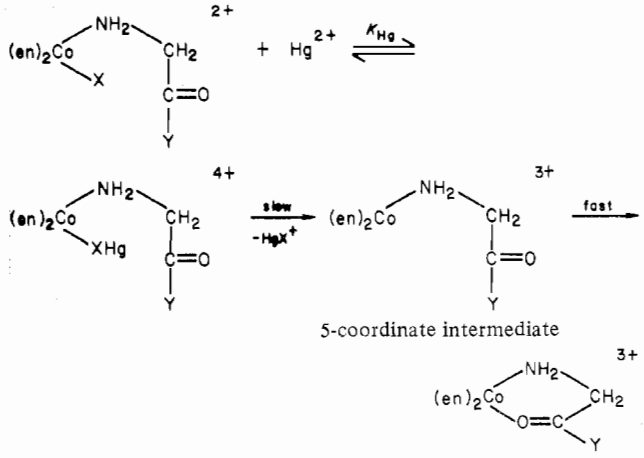


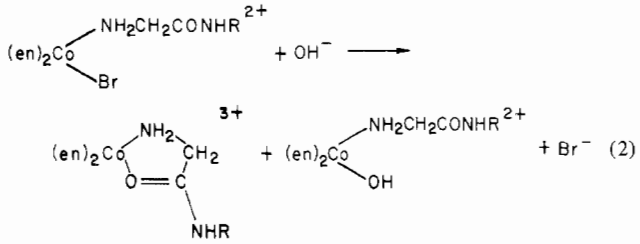
Table II. Rate Data for Base Hydrolysis of the *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ Ions[a]

R	pH	$10k_{obsd}$, s^{-1}	k_{OH},[b] M^{-1} s^{-1}
H[c]	7.84	1.80	153
	8.16	3.73	152
	9.00	25.7	151
	9.5[f]	86	160
$CH_2CO_2^-$ [d]	8.40	6.89	162
	9.09	37.3	179
	9.44	82.7	177
	9.97	275	174
$CH_2CO_2C_3H_7$[e]	8.43	8.47	191
	9.11	43.8	200
	9.57	127	201
	10.11	434	198
	9.0[f]	32.8	193
	1.5[f]	105	195
	10.0[f]	336	198

[a] 25.0 °C; μ = 1.0 ($NaClO_4$); [Co] = (1–2) × 10^{-3} M. [b] $k_{OH} = k_{obsd}/[OH^-]$, where $[OH^-]$ is calculated from pH using pK_w = 13.77. [c] 490 nm; 0.2 M Tris–$HClO_4$ buffer. [d] 360 nm; 0.1 M glycine–$HClO_4$ buffer. [e] 355 nm; 0.1 M glycine–$HClO_4$ buffer. [f] pH stat data (OH^- consumption).

obtained for the process involving removal of bromide; at other wavelengths small subsequent OD changes were observed and were shown to result from events following the removal of bromide (see below). Plots of log $(D_t - D_\infty)$ vs. time were linear for $3t_{1/2}$ in most cases, but occasionally Guggenheim plots were used to evaluate the k_{obsd} values. The pH stat data also gave linear plots of log $(V_\infty - V_t)$ vs. time for the two dipeptide complexes, but a subsequent slow uptake of acid or base (pH <9 or >9, respectively) complicated the analysis for the glycinamide complex. This again was shown to result from the subsequent reaction of the hydroxo glycinamide complex. Both methods gave data consistent with the rate expression $k_{obsd} = k_{OH}[OH^-]$ over a $10–10^2$ variation in $[OH^-]$, Table II, and the second-order rate constants are similar to those obtained with other *cis*-$[Co(en)_2Br(amine)]^{2+}$ ions. Such data are consistent with the generally accepted conjugate base mechanism (S_N1cB) for hydrolysis of cobalt(III)–acido complexes of this type.[30,31]

The product analyses results, Table III, show that in addition to the chelated amide $[Co(en)_2(glyNHR)]^{3+}$ considerable amounts of the hydroxo amide are also formed, eq 2. This



result clearly differs from that found with Hg^{2+}, and a different five-coordinate intermediate is required which competes favorably for both water and >C=O entry.[30] The product ratio is pH independent and is the same in 1 M $NaClO_4$ and 0.1 M KCl.

The occurrence of stable hydroxo amide species differs significantly from that in our previous report on the hydrolysis of the *cis*-$[Co(en)_2Br(glyNH_2)]^{2+}$ ion.[17] In the previous study it was concluded that the hydroxo glycinamide ion reacted rapidly under the conditions of base hydrolysis and that the subsequent process observed spectrophotometrically was hydrolysis of the chelated amide. Unfortunately these measurements[17] were made at wavelengths where only very small OD changes are involved for the hydroxo species and at pHs where the rate is similar to that for the chelated glycinamide ion. The earlier observation of a stable hydroxo species by Chan and Chan[32] is therefore correct, although its subsequent chemistry as reported by them is not.

For R = $CH_2CO_2C_3H_7$ and $CH_2CO_2^-$ the amount of hydroxo dipeptide is given directly by the base consumption data

Table III. Product Distributions on Base Hydrolysis of *cis*-$[Co(en)_2Br(glyNHR)]^{2+}$ Ions[a]

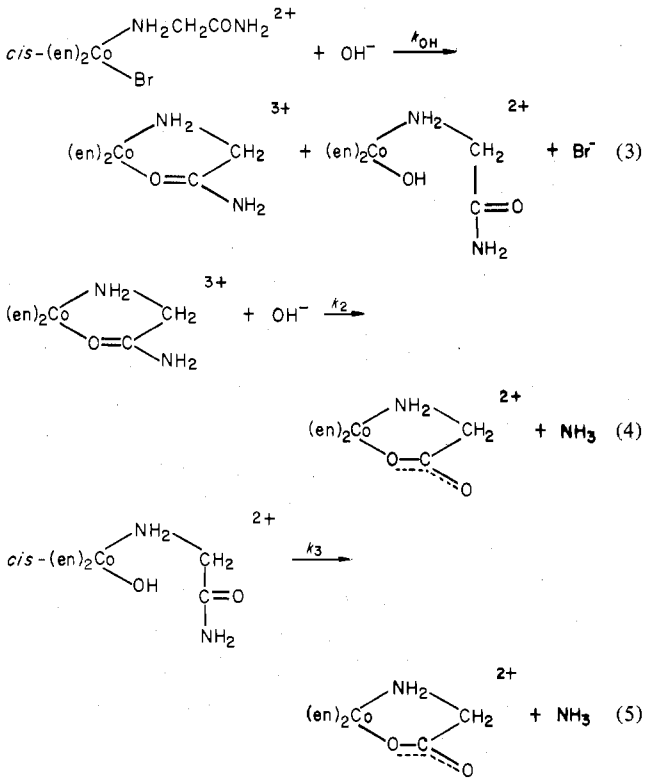
				% obsd prod		% cor prod[e]	
R	pH	reacn time, min	10^3k_1,[b] s^{-1}	$[Co(en)_2(glyNHR)]^{3+}$ [g]	$[Co(en)_2OH(glyNHR)]^{2+}$ or $[Co(en)_2(glyO)]^{2+}$ [g]	$[Co(en)_2(glyNHR)]^{3+}$	$[Co(en)_2(OH)(glyNHR)]^{2+}$
$CH_2CO_2^-$	9.0	30	3	33[c]	67[c]	31[f]	69[f]
	9.5	9	10	27[c]	73[c]	28[f]	72[f]
$CH_2CO_2C_3H_7$	8.06	90	0.76	32[c]	68[c]	32[f]	68[f]
	9.00	25	3.28	29[h,c]	71[h,c]	29[f]	71[f]
H	9.0	22.5	2.6	36.5	67 (53)[c]	42	58 (58)[f]
	9.0[d]	15	5.1	34	66 (55)[c]	39	61 (59)[f]
	9.5	8	8.2	34	70 (63)[c]	40	60 (60)[f]
	9.5[d]	5	16.1	32	68 (63)[c]	40	60 (60)[f]
	10.0	2.3	26	34	70 (65)[c]	39	61 (58)[f]
	10.0[d]	1.5	51	32	68 (69)[c]	38	62 (65)[f]

[a] All runs at 25.0 °C and μ = 1.0 ($NaClO_4$) unless otherwise stated, most experiments were run in duplicate on ≃0.15 g of complex. [b] k_{obsd} for Br^- removal (Table II). [c] From uncorrected base consumption data. [d] 0.1 M KCl supporting electrolyte. [e] Corrected for subsequent hydrolysis of $[Co(en)_2(glyNH_2)]^{3+}$ (k_2 = 25 M^{-1} s^{-1} (1.0 M $NaClO_4$, 0.1 M KCl)) and of $[Co(en)_2OH(glyNH_2)]^{2+}$ (k_3 (pH) = 2.2 (9.0), 3.2 (9.5), 5.4 (10.0) × 10^{-4} s^{-1} in 1.0 M $NaClO_4$; 2.6 (9.0), 4.4 (9.5), 6.5 (10.0) × 10^{-4} s^{-1} in 0.1 M KCl)[23] and for $pK_a(NH_3)$ = 9.38 (1.0 M $NaClO_4$) and 9.27 (0.1 M KCl). [f] Estimated from corrected base consumption data. [g] For R = H the observed 3+ ion (chromatographic separation) contains *trans*-$[Co(en)_2(OH_2)(glyNH_2)]^{3+}$ (5–6%) as well as $[Co(en)_2(glyNH_2)]^{3+}$. [h] Average of 10 experiments.

(pH stat). Reactions subsequent to the removal of bromide are slow so that only minor corrections to the observed base uptake were necessary. Also fair agreement was found between these data and the amount of hydroxo dipeptide separated by ion-exchange chromatography at pH 8 and 2 °C. Some small conversion (<5%) to the chelated dipeptide did appear to have occurred during absorption on or elution from the resin, but this method did provide a reliable procedure for obtaining the pure hydroxo dipeptide ions.

For *cis*-$[Co(en)_2Br(glyNH_2)]^{2+}$ the immediate products were more difficult to determine since appreciable correction is necessary for the subsequent reactions of both the chelated amide and hydroxo amide. The former consumes OH^- on hydrolysis while the latter releases it, and the amounts involved are pH dependent. Direct analysis by ion exchange proved unreliable, even at 0 °C, since the reaction of the hydroxo amide at pH ~8 appeared to be accelerated on the resin. However, this procedure did allow the recovery of sufficient $[Co(en)_2(OH)(glyNH_2)]^{2+}$ free of $[Co(en)_2(glyNH_2)]^{2+}$ (but still containing some $[Co(en)_2(glyO)]^{2+}$) to determine its products under the conditions of base hydrolysis (pH 8–10) and the subsequent analysis procedure (pH ~4). In part these results are dealt with in a subsequent paper,[23] but it is important to note here that the cis-aqua and -hydroxo glycinamide ions form only $[Co(en)_2(glyO)]^{2+}$ (pH ~4 and 8–10, respectively). The small amount of trans-hydroxo amide also formed in the base hydrolysis reaction reacts very slowly under alkaline conditions (to form $[Co(en)_2(glyNH_2)]^{2+}$, see below), and it can also be recovered unchanged from acidic solutions as the 3+ aqua ion. Alkaline hydrolysis of $[Co(en)_2(glyNH_2)]^{3+}$ (pH 8.5–12) forms only $[Co(en)_2(glyO)]^{2+}$; no $[Co(en)_2(OH)(glyNH_2)]^{2+}$ has been detected in this reaction (i.e., the chelate ring does not open up).[23] At pH ~4 the chelated amide shows no hydrolysis (<2%) over 14 days.

Using these results the immediate products of base hydrolysis of $[Co(en)_2Br(glyNH_2)]^{2+}$ were determined (see eq 3–5). Following quenching to pH ~4 after $5t_{1/2}$ for bromide

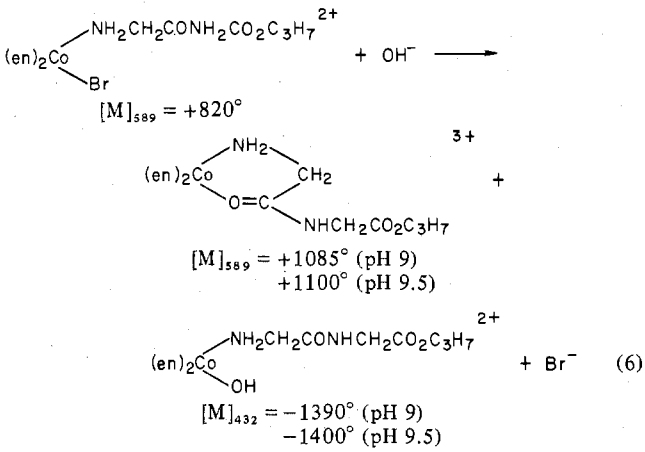


removal, the $[Co(en)_2(glyNH_2)]^{3+}$ and $[Co(en)_2(glyO)]^{2+}$ ions were separated by ion-exchange chromatography and estimated by spectrophotometry and by atomic absorption for Co. These data were then corrected for subsequent hydrolysis of the chelated amide (eq 4), and hydroxo amide (eq 5), using rate data given in the caption to Table III. The corrected product distributions are given in the last two columns of Table III. Alternatively the immediate products were determined from the base consumption data (pH stat) using the observation that reactions 3 and 4 consume OH^- while reaction 5 releases it; corrections were applied for protonation of released ammonia (pK_a = 9.38, 1.0 M $NaClO_4$, 25 °C). Acceptable agreement was found between the two methods, Table III.

It is clear from the results that entry of the >C=O function is greatest with the less bulky glycinamide complex and that ionic strength effects (1.0 M $NaClO_4$ vs. 0.1 M KCl) are unimportant.

The presence of the small amounts of the trans-hydroxo ions in the base hydrolysis products was not apparent until the detailed kinetic study of the cis-hydroxo species was well advanced.[23] For the hydroxo glycinamide ion, but not for the similar dipeptide species, this made its appearance in spectrophotometric runs at pH <11 as a small OD decrease.[23] This resulted from the presence of ~6% *trans*-$[Co(en)_2(OH)(glyNH_2)]^{2+}$ in the products of base hydrolysis and ultimately led to the isolation and characterization of all three (R = H, $CH_2CO_2C_3H_7$, $CH_2CO_2^-$) trans ions.

3. Stereochemistry of Base Hydrolysis. The stereochemistry of the base hydrolysis reaction was investigated using optically pure *cis*-$(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2$ and cis-$(+)_{589}$-$[Co(en)_2Br(glyNH_2)]Br_2$. Base hydrolysis of the former (pH 9, 9.5) followed by ion-exchange separation (pH 8, 2 °C) gave the products and rotations shown in eq 6; ORD results



for these species are given in Figure 5 (supplementary material). The 3+ product is 66 ± 2% optically pure when compared with the same product formed in the Hg^{2+}-induced reaction, while the hydroxo dipeptide is 63 ± 2% optically pure when compared with that obtained following treatment with HOCl (see below). However, when allowance is made for 8.5% trans-hydroxo dipeptide as the 2+ ion, the retention in the cis-hydroxo species is 69 ± 2%. A similar set of results was obtained using *cis*-$(+)_{589}$-$[Co(en)_2Br(glyNH_2)]^{2+}$. In this case the 3+ ion gave $[M]_{589}$ = +842° (51% active) which is in close agreement with that obtained previously (49%).[17] However, the hydroxo glycinamide species contains 10–12% of the trans ion (Table III) which was removed (chromatographically) as a 3+ ion after allowing the cis-aqua complex to cyclize to $[Co(en)_2(glyO)]^{2+}$ at pH ~1. The latter product gave $[M)_{589}$ values of +981 and +998° (two experiments) representing at least 63% retention in the cis-hydroxo reactant. It will be shown below that the cyclization reaction in acid solution occurs with full retention of configuration so that the above value represents the retention in the cis-hydroxo ion

Table IV. Stereochemistry of Products from the Base Hydrolysis of *cis*-$(+)_{589}$-$[Co(en)_2Br(amine)]^{2+}$ Ions[a]

	products				
	$[Co(en)_2(OH)(amine)]^{2+}$			$[Co(en)_2(amine)]^{3+}$ (chelated amide)	
amine	trans	DL-cis	D-cis	DL-cis	D-cis
$NH_2CH_2CONH_2$	6.2	20	34	20	20
$NH_2CH_2CONHCH_2CO_2C_3H_7$	6.2	19	44	10	20
$NH_2CH_2CONHCH_2CO_2^-$	——70——			——30——	
NH_3[b]	23	31	46		

[a] 1 M $NaClO_4$; 25 °C. [b] Average value for bromo, chloro, and nitrato complexes.[30]

formed in the base hydrolysis of Br^-.

The overall stereochemical result for both sets of products is collected in Table IV. For the glycinamide complex the retention in the cis-hydroxo product is similar to that obtained with *cis*-$(+)_{589}$-$[Co(en)_2Br(NH_3)]^{2+}$,[30] but far less trans product is formed even when the path leading to water entry only is considered. Apparently the adjacent >C=O group competes very favorably for the part leading to trans product as well.

4. Isolation and Properties of the *trans*-$[Co(en)_2(H_2O/OH)(amide)]^{3+/2+}$ Ions. Two methods were used to obtain the trans species. Initially the hydroxo glycinamide product obtained by ion-exchange separation (pH ~8, 0.5 M $NaClO_4$, 2 °C) of the products of base hydrolysis of *cis*-$[Co(en)_2Br(glyNH_2)]^{2+}$ was immediately quenched to pH ~1 and left to stand for ~15 min to completely convert the cis-aqua ion to $[Co(en)_2(glyO)]^{2+}$. This 2+ ion was then removed from the trans-aqua 3+ ion by ion-exchange elution at pH ~2 (0.2 M $NaClO_4$, 2 °C) and the trans product recovered as a red-mauve 2+ band by elution at pH ~8 (0.4 M $NaClO_4$, 2 °C). Subsequently it was found possible to obtain the trans-glycinamide species directly from the base hydrolysis products by quenching the base-hydrolyzed (pH stat) solution to pH 1, allowing the cis-aqua ion to cyclize, and chromatographic isolation as before. Both methods were also successful in obtaining *trans*-$[Co(en)_2(H_2O/OH)(glyglyOC_3H_7)]^{3+/2+}$. When carried out with the optically pure bromo reactants, the trans ions (~5×10^{-4} M) showed no optical activity from 600 to 300 nm. Their visible spectra are compared with the cis species in Figure 1. Clearly the ϵ_{max} values for the trans-aqua and trans-hydroxo ions in the visible region are appreciably less than the corresponding cis species; a similar result obtains for the *trans*-$[Co(en)_2(H_2O)(NH_3)]^{2+}$ ion.[33] The visible and ORD spectra for *cis*-$[Co(en)_2(OH)(glyNH_2)]^{2+}$ are very similar to those for *cis*-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$, but the hydroxo species of the former always contained some $[Co(en)_2(glyO)]^{2+}$ (even at 2 °C) presumably resulting from the subsequent cyclization reaction,[23] and the spectra are not recorded here.[34]

Product analysis results gave 6.0 ± 0.2% and 5.8 ± 0.2% trans-hydroxo glycinamide and dipeptide ester among the products of the base hydrolysis reactions, Table III. For the trans-dipeptide ester these results were obtained from experiments where cyclization of the cis species was accelerated by phosphate buffer. When the above values are corrected for the small loss (~8%) due to the subsequent reaction of the trans-hydroxo ions under the conditions of base hydrolysis (see below), some 6.2 ± 0.3% trans ions result from both substrates (Table IV).

It has already been noted that the trans ions were initially observed spectrophotometrically (560 nm) by their reactions at pH >11. Isolation of the trans ions allowed these processes

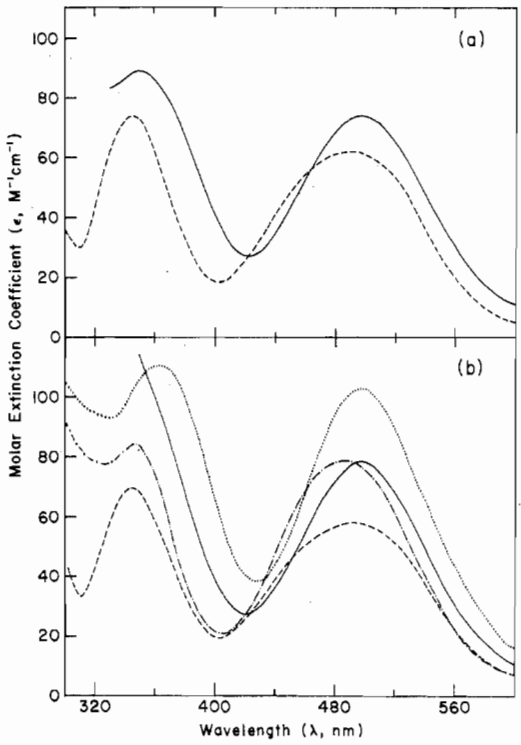


Figure 1. Visible absorption spectra for (a) *trans*-$[Co(en)_2(OH_2/OH)(glyNH_2)]^{3+/2+}$ ions [trans OH (—), trans OH_2 (---)] and (b) *cis*- and *trans*-$[Co(en)_2(OH_2/OH)(glyglyOC_3H_7)]^{3+/2+}$ ions [trans OH (—), trans OH_2 (---), cis OH (····), cis OH_2 (·-··)] in 1.0 M $NaClO_4$, at 25.0 °C.

to be studied in detail, and Figure 2 gives a plot of k_{obsd} for *trans*-$[Co(en)_2(OH_2/OH)(glyNH_2)]^{3+/2+}$ as a function of pH. Data for the other dipeptide complexes are given in Table VI (supplementary material). Clearly three regions of reactivity occur corresponding to the acid-independent reactions of the trans-aqua and trans-hydroxo ions and to the base-dependent reaction of the trans-hydroxo ion.

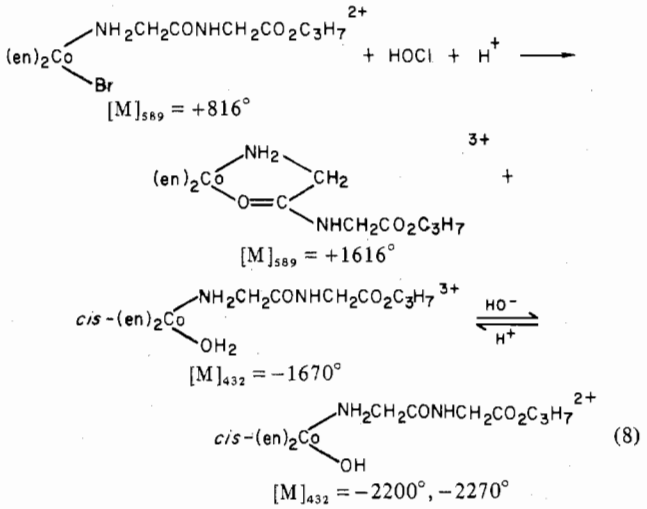
$$k_{obsd} = k_{H_2O} + k_{OH} + k'_{OH}[OH^-] \quad (7)$$

The latter process involves a substantial OD change at pH >11. Values of k_{H_2O}, k_{OH}, and k'_{OH} are 4 (±2) × 10^{-6} s^{-1}, 2.8 (±0.1) × 10^{-4} s^{-1}, and 5.6 × 10^{-2} M^{-1} s^{-1} in 1 M $NaClO_4$ at 25 °C. From the limited data available (Table VI) similar rate constants are suggested for the two trans-dipeptide ions. Unlike the reaction of the cis-hydroxo ions[23] those for the trans species are unaffected by phosphate buffers. The final products at pH 2 and 8 are the racemic chelated amide complexes $[Co(en)_2(glyNHR)]^{3+}$ (R = H, $CH_2CO_2C_3H_7$). At pH 2 (14 days) only $[Co(en)_2(glyNHR)]^{3+}$ was found by ion-exchange chromatography, and this was verified by its subsequent hydrolysis to $[Co(en)_2(glyO)]^{2+}$ in basic solution (k_{obsd} = 2.3 × 10^{-2} s^{-1}, pH 12 (R = H); k_{obsd} = 6.52 × 10^{-3} s^{-1}, pH 12 (R = $CH_2CO_2C_3H_7$)). At pH 8 in the absence of buffers (pH stat) k_{obsd} approaches that for the cis-hydroxo ions,[23] and although some $[Co(en)_2(glyO)]^{2+}$ was found among the products, its presence is due entirely to subsequent hydrolysis of $[Co(en)_2(glyNHR)]^{3+}$. Thus from *trans*-$[Co(en)_2(OH)(glyNH_2)]^{2+}$, 33% $[Co(en)_2(glyO)]^{2+}$ was recovered (37% calculated) after a reaction time of 320 min (pH 8.07, 1 M $NaClO_4$) and 16.2% after 19 h in a similar experiment (pH 8) with *trans*-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$ (15.7% calculated). Thus the acid-independent terms for the trans-aqua (k_{H_2O}) and trans-hydroxo (k_{OH}) ions produce only chelated amide. The immediate product of the base-dependent path of the hydroxo ion (k'_{OH}) is largely the $[Co(en)_2(glyO)]^{2+}$

ion (some decomposition occurred), and this probably results from subsequent hydrolysis of the chelated amide since hydrolysis is fast under these conditions.[23]

Since the *cis*-$[Co(en)_2(H_2O/OH)(glyglyOC_3H_7)]^{3+/2+}$ ions give rise to appreciable amounts of $[Co(en)_2(glyO)]^{2+}$ in their reactions at pH <4 and 8–9,[23] the cis species cannot be intermediates in the reactions of the trans ions. This suggests a concerted process (Scheme V) with the trans-aqua or -hydroxo ligand being synergically displaced by the >C=O group. A comparison of the rates for these reactions with those for *trans*-$[Co(en)_2(H_2O/OH)(NH_3)]^{3+/2+}$ supports this view. The latter species isomerize much more slowly than found here ($k_{H_2O} \simeq 10^{-8}$ s^{-1}, extrapolated data; $k_{OH} \simeq 1 \times 10^{-5}$ s^{-1}),[35] and in the hydroxo form at least this occurs without loss of coordinated hydroxide[35] (i.e., a different mechanism occurs).

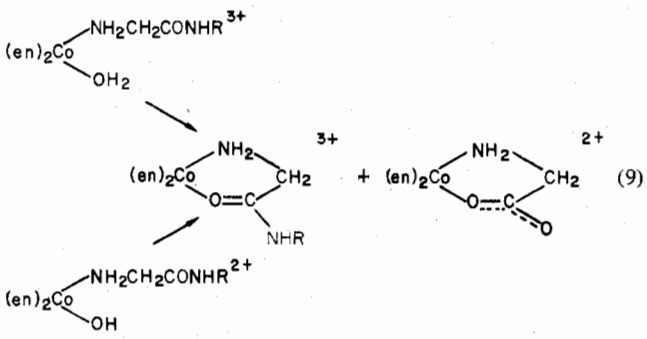
5. Stereochemistry of the HOCl Reaction and of the Reactions of the Cis-Aqua and -Hydroxo Ions. Optical retentions were evaluated using reactants generated by base hydrolysis of *cis*-$(+)_{589}$-$[Co(en)_2Br(glyNH_2)]Br$ and *cis*-$(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](NO_3)_2$ and by the HOCl-catalyzed oxidation of bromide in *cis*-$(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](NO_3)_2$. The HOCl reaction is a useful method of introducing water directly into the coordination sphere[8,29] and almost certainly occurs via an oxidative interchange mechanism.[36] Treatment of *cis*-$(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]^{2+}$ at ~0 °C results in a rapid violet to red-orange color change with both chelated dipeptide and aqua dipeptide ions being formed.



(8)

These ions were separated chromatographically on ion-exchange resin at pH ~8.5 and 2 °C, and ORD and visible spectra for the reactants and separated products are given in Figure 3. The aqua dipeptide ion exists as the hydroxo ion at pH >7.[23]

Subsequent treatment of the aqua ion at pH 3.77 and the hydroxo ion at pH 8.05 (pH stat, 21 h) and 8.77 (0.07 M phosphate buffer, 30 min) gave the two products indicated by eq 9 which, after chromatographic separation, gave the following $[M]_{589}$ values (1 M $NaClO_4$): +1680° (2+ ion), +1530° (3+ ion) at pH 3.77; +1027° (2+ ion), 1010° (3+ ion) at pH 8.05; +1630° (2+ ion), +1480° (3+ ion) at pH 8.77. ORD curves for some of the products are given in Figure 3. These data correspond to complete retention of optical configuration for the products generated from the aqua ion (by comparison with the similar optically pure species formed by treatment with Hg^{2+} (see above)), and 97% and 96% retention, respectively, in $[Co(en)_2(glyO)]^{2+}$ and $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ generated from the hydroxo dipeptide in 0.07 M phosphate buffer. Corresponding retentions of 65 ± 5% and 63 ± 5% were found for the products formed in the absence of buffer at pH 8.05 (pH stat). It is clear that HOCl-induced removal of bromide occurs with full retention of configuration about the metal center, and that a similar result obtains in the hydrolyzed and chelated amide products produced in the subsequent reactions at pH 3.77 (aqua complex) and pH 8.77 in the presence of phosphate buffer (hydroxo complex). Some 35% racemization occurs at pH 8.05 in the absence of the buffer, and since this occurs with only a small amount of exchange of the bound hydroxo group with the solvent (~6%, see below), this process must occur largely via an intramolecular mechanism. A similar result has been observed by Martin and Tobe for isomerization in *trans*-$[Co(en)_2(OH)(NH_3)]^{2+}$.[35]



(9)

Identical treatment of the aqua and hydroxo dipeptide ester ions ($[M]_{432}$ = −1160 and −1390°, respectively) isolated from base hydrolysis of *cis*-$(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](NO_3)_2$ ($[M]_{589}$ = +820°) gave $[Co(en)_2(glyO)]^{2+}$ and $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ products with the following $[M]_{589}$ values (three separate experiments): for the reaction at pH 3.77, +1040, +1050, +1050° (2+ ion) and +1010, +1030, +1090° (3+ ion; the first two entries contain ~13% trans-aqua ion; the third entry has had the trans ion removed); for the reaction at pH 8.77 in 0.07 M HPO_4^{2-} buffer, +1100, +1050, +1060° (2+ ion) and +925, +1000, +990° (3+ ion). ORD curves for the reactants and products are given in Figure

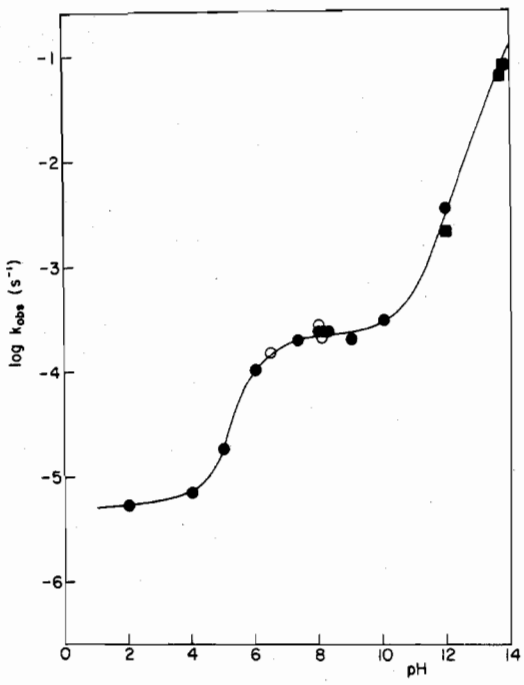


Figure 2. Plot of log k_{obsd} vs. pH for the reaction of *trans*-$[Co(en)_2(OH_2/OH)(glyNH_2)]^{3+/2+}$ to give $[Co(en)_2(glyNH_2)]^{3+}$ at 25.0 °C, μ = 1.0 ($NaClO_4$) (—). The data given by ■ are for the "slower" second reaction observed following base hydrolysis of *cis*-$[Co(en)_2Br(glyNH_2)]^{2+}$ (Figures 1 and 4 of a following paper[23]), and the O data are for the *trans*-$[Co(en)_2(OH_2/OH)(glyglyOC_3H_7)]^{3+/2+}$ under the same conditions.

Scheme V

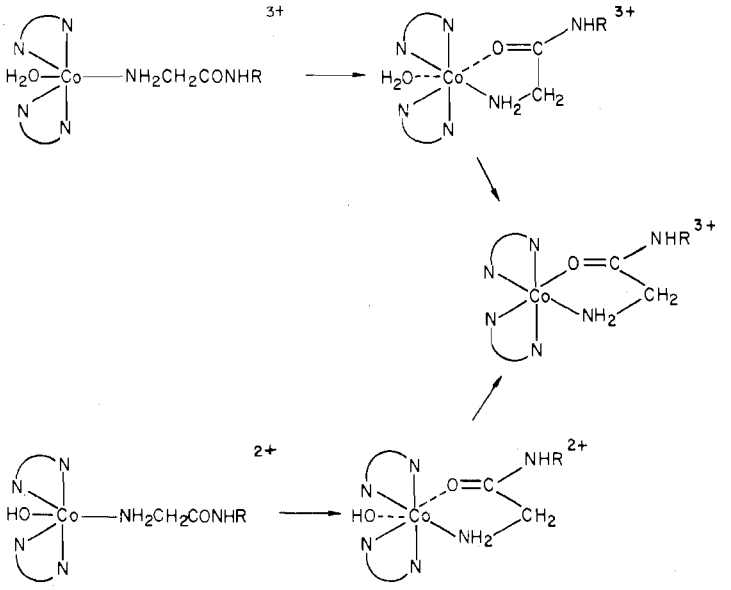


Table V. ^{18}O-Tracer Results for the Base- and HOCl-Catalyzed Hydrolyses of $[Co(en)_2Br(glyglyOC_3H_7)]^{2+}$ and for the Intramolecular Hydrolysis of $[Co(en)_2(H_2O/OH)(glyglyOC_3H_7)]^{3+/2+}$

	3+ product				2+ product	
	R values[a]					
expt	complex	solvent	blank	atom % enrichment[b]	*R* value[a] complex	atom % enrichment[b]
1[c]	0.005 596	0.025 824	0.003 434	9.8 (0.2)[f]		
2[c,g]	0.004 142	0.025 824	0.003 434	3.2	0.013 342	44.5
3[c,g]	22[e]	595[e]		3.7	274[e]	46.1
4[c,g]	0.005 100	0.033 350	0.004 840	0.9	0.017 150	43.5
5[c,h]	0.011 827	0.025 824	0.003 434	37.7	0.013 557	45.5
6[c,h]	0.011 932	0.025 820	0.003 560	37.5	0.013 415	44.1
7[c,i]	0.011 761	0.026 010	0.004 141	35.1	0.013 004	40.8
8[d]	0.005 320	0.033 24	0.004 840	1.7		
9[d,g]	0.005 070	0.033 24	0.004 840	0.8	0.016 750	42.3

[a] Observed *R* values ($R = [46]/([44] + [46])$) for CO_2. [b] Atom % enrichment = $100R/(2 + R) - 100R'/(2 + R')$ where *R* is that for CO_2 recovered from the complex and *R'* that of the normal CO_2 used as the blank. [c] Produced by base hydrolysis of $[Co(en)_2Br(glyglyOC_3H_7)]Br_2$. [d] Produced by HOCl treatment of $[Co(en)_2Br(glyglyOC_3H_7)]Br_2$. [e] Given as % enrichment above background (GD-150 mass spectrometer). [f] The value in parentheses was estimated by substracting the enrichment due to $[Co(en)_2glyglyOC_3H_7]^{3+}$ formed in the subsequent reaction of the hydroxo dipeptide in the time of the experiment (1500 s), 5.3%, and that due to reactions on the column during absorption and separation, 4.3%. [g] Products of reaction at pH 3.77 (pH stat control). [h] Products of reaction in 0.07 M phosphate buffer, pH 8.77. [i] Products of reaction at pH 8.77 (pH stat control).

5 (supplementary material). When compared with those of the optically pure species produced in the Hg^{2+}-catalyzed reaction, the rotations correspond to 68 ± 2% retention in the $[Co(en)_2(glyO)]^{2+}$ ion under the two sets of conditions (pH 3.77, 8.77 [0.07 M HPO_4^{2-}]) and a similar value (71 ± 2%) for the $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ product when allowance is made for the presence of 13% *trans*-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$ (pH 3.77) or a similar amount of racemic chelated dipeptide from the trans-hydroxo ion at pH 8.77. Since it has been shown that cyclization under these conditions occurs with full retention of configuration, it is concluded that the cis-hydroxo ion produced in the base hydrolysis reaction is 70% optically pure. This is in agreement with the value of 69 ± 2% obtained above for the isolated cis-hydroxo species (cf. section 3).

6. ^{18}O-Tracer Results. Table V contains results of reacting $[Co(en)_2Br(glyglyOC_3H_7)]^{2+}$ with OH^- (experiments 1–7) and HOCl (experiments 8 and 9) in ^{18}O-enriched water (1.6 or 2.0 atom %). Experiments 1 and 8 show that the chelated dipeptide complex $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ produced directly by the two sets of conditions contains essentially no solvent label (0.2 and 1.7 atom %, respectively). The remaining data refer to the products obtained from the subsequent reactions of the ^{18}O-enriched aqua and hydroxo dipeptide ions following their separation from $[Co(en)_2(glyglyOC_3H_7)]^{3+}$. These reactions were carried out in normal unenriched water at pH 3.77 (experiments 2–4) and pH 8.77 in the presence (0.07 M, experiments 5 and 6) and absence (experiment 7) of phosphate buffer. The 3+ and 2+ products correspond to those given by eq 9 ($R = CH_2CO_2C_3H_7$), and they were separated by the normal ion-exchange procedure. The $[Co(en)_2(glyO)]^{2+}$ product was isolated and analyzed directly for its ^{18}O content. For $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ it was necessary to further treat the solution at pH ~11 and recover the chelated glycine fragment as $[Co(en)_2(glyO)]HgI_4$; attempts to recover the dipeptide chelate directly proved difficult and wasteful. It has previously been shown that such a procedure involves no scrambling of glycine residues,[37] and the results given below show that little or no oxygen exchange occurs in the coordinated amide function during hydrolysis.

For the reaction at pH 3.77 the $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ product contains little enrichment (3.2, 3.7 atom %), and this probably arises from a small amount of reaction during separation and isolation at pH ~8 and before quenching. The

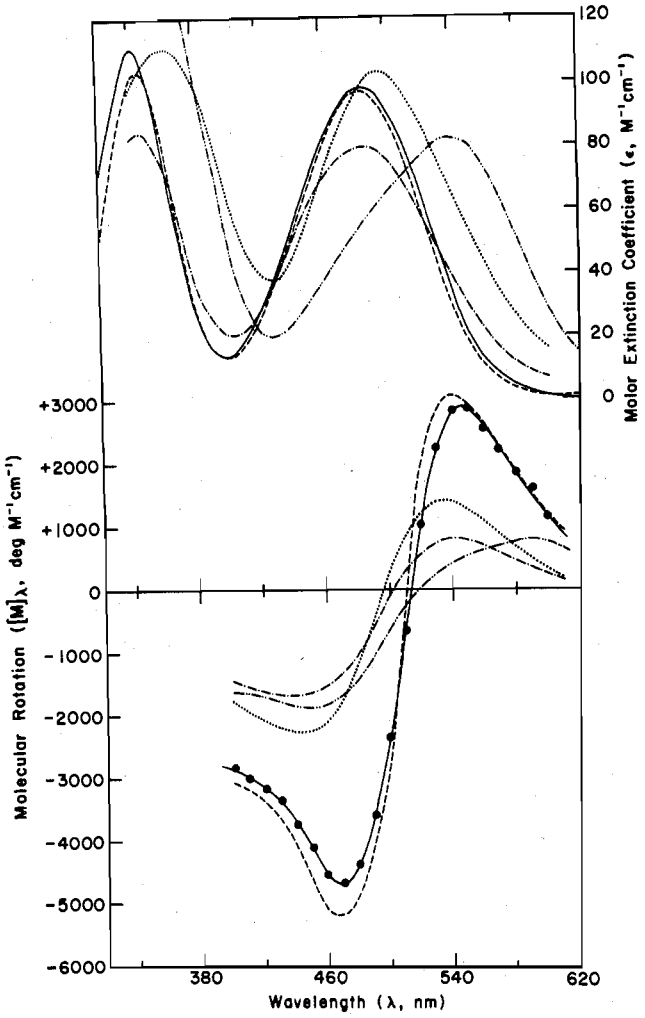


Figure 3. Visible and ORD absorption spectra for *cis*-$(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](NO_3)_2$ (----), HOCl-generated *cis*-$(+)_{589}$-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$ (pH 2) (----) and *cis*-$(+)_{589}$-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{3+}$ (pH 8.5) (····), in 0.5 M $NaClO_4$, and the products of the subsequent cyclization reaction at pH 8.77 (0.07 M phosphate buffer), $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ (---) and $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ (—), both in 1.0 M $NaClO_4$. Data for $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ produced in the initial HOCl reaction of the bromo complex are given by ● and clearly fall on the — curve.

3+ product produced at pH 3.77 therefore results from a process involving displacement of the coordinated aqua group. By contrast, the hydrolyzed product contains close to half of the original solvent enrichment, and one oxygen of the glycinate moiety must therefore derive from the coordinated water molecule. Similar results were obtained from aqua dipeptide produced by the HOCl and base hydrolysis reactions.

Both the 3+ and 2+ products from $[Co(en)_2(^{18}OH)(glyglyOC_3H_7)]^{2+}$ at pH 8.77 contain appreciable amounts of oxygen derived from the coordinated hydroxo group, and this is so in both the presence (experiments 5, 6) and the absence (experiment 7) of phosphate buffer. For $[Co(en)_2(glyO)]^{2+}$ produced in phosphate buffer 90% of the oxygen label is retained whereas the $[Co(en)_2(glyglyOC_3H_7)]_{3+}$ ion retains ~75% of the maximum enrichment (which is half of the solvent enrichment). The former result is similar to that found at pH 3.77, and the discrepancy from 100% probably results from some loss of the label during isolation and/or dilution during analysis. Similar lower than expected retentions have been found in other studies involving these complexes.[9,15] The extra analytical step necessary for the 3+ product may result in the larger discrepancy in this ion, but if it is remembered that ~10% of the hydroxo reactant is the trans species, then the reaction conditions and analytical procedures will result in this appearing in the 3+ product. Since this part occurs by displacement of coordinated water (or hydroxide), correction of the experimental result leads to ~90% retention of ^{18}O label in $[Co(en)_2(glyglyOC_3H_7)]^{3+}$ produced from the cis reactant in phosphate buffer. A similar correction is necessary for the 3+ ion obtained in the absence of phosphate (experiment 7), but the lower result for both the 3+ and 2+ ions in this case suggests some (~6%) water exchange in the cis-hydroxo reactant in 15 h at pH 8.77.

These results dictate the origin of the two products given by eq 9 under the different pH conditions and are of importance when the mechanistic implications are discussed. These are considered in detail in a following publication.[23]

Registry No. *cis*-$[Co(en)_2Br(glyNH_2)]Br_2$, 67784-67-2; *cis*-$[Co(en)_2Br(glyglyOCH_3)]Br_2$, 67784-68-3; *cis*-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2$, 67784-69-4; *cis*-$[Co(en)_2Br(glyglyOH)]Br_2$, 67842-94-8; $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]((+)_{589}\text{-}CS)_2$, 67843-78-1; $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)]Br_2$, 67842-95-9; $(+)_{589}$-$[Co(en)_2Br(glyNH_2)]Br_2$, 30931-80-7; $(-)_{589}$-$[Co(en)_2Br(glyNH_2)]Br_2$, 30931-81-8; $(+)_{589}$-$[Co(en)_2Br(glyglyOC_3H_7)](NO_3)_2$, 67844-45-5; *cis*-$[Co(en)_2Br(glyNHCH_2CO_2C_2H_5)]^{2+}$, 67784-70-7; *cis*-$[Co(en)_2Br(glyNHCH_2CO_2)]^+$, 67842-89-1; $[Co(en)_2(glyO)]^{2+}$, 16070-98-7; *cis*-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$, 67842-90-4; $[Co(en)_2(glyglyOC_3H_7)]^{3+}$, 67844-22-8; $[Co(en)_2(glyNHCH_2CO_2)]^{2+}$, 20528-43-2; $[Co(en)_2(OH)(glyNHCH_2CO_2)]^+$, 67842-91-5; $[Co(en)_2(glyNH_2)]^{3+}$, 30931-79-4; *cis*-$[Co(en)_2(OH)(glyNH_2)]^{2+}$, 53402-85-0; *trans*-$[Co(en)_2(OH)(glyNH_2)]^{2+}$, 67842-92-6; *trans*-$[Co(en)_2(OH_2)(glyNH_2)]^{3+}$, 67842-93-7; *trans*-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$, 67784-61-6; *trans*-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$, 67784-62-7; *cis*-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$, 67842-86-8; *cis*-$(+)_{589}$-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$, 67842-87-9; *cis*-$(+)_{589}$-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$, 67842-88-0; $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$, 19657-80-8; $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$, 67784-63-8; *cis*-$(+)_{589}$-$[Co(en)_2Br(glyNHCH_2CO_2)]^+$, 67784-64-9; D-*cis*-$[Co(en)_2(OH)(glyNH_2)]^{2+}$, 53346-40-0; D-*cis*-$[Co(en)_2(glyNH_2)]^{3+}$, 62357-85-1; *trans*-$[Co(en)_2Br_2]Br$, 15005-14-8; Hg^{2+}, 14302-87-5; $glyglyOCH_3$·HCl, 2776-60-5; $glyglyOC_3H_7$·HCl, 67784-60-5; HOCl, 7790-92-3.

Supplementary Material Available: Table VI containing spectrophotometric rate data for reactions of the isolated *trans*-$[Co(en)_2(OH)(glyNHR)]^{2+}$ ions; Figure 4 containing visible absorption and ORD spectra for optically pure $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$ and $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$; Figure 5 containing ORD curves for $(+)_{589}$-$[Co(en)_2(OH_2)(glyglyOC_3H_7)]^{3+}$, $(+)_{589}$-$[Co(en)_2(OH)(glyglyOC_3H_7)]^{2+}$, $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$, $(+)_{589}$-$[Co(en)_2(glyglyOC_3H_7)]^{3+}$, and $(+)_{589}$-$[Co(en)_2(glyO)]^{2+}$ (3 pages). Ordering information is given on any current masthead page.

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Kinetics and Mechanism of Oxidation of Cobalt(II) Macrocycles by Iodine, Bromine, and Hydrogen Peroxide[1]

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A series of cobalt(II) complexes of tetradentate, 14-membered macrocyclic ligands with nitrogen donor atoms is oxidized by bromine and iodine in acidic aqueous solution to the corresponding monohalocobalt(III) product. The rate law shows a first-order dependence on each reactant; rate constants and reduction potentials were determined for each substance. Only one of the cobalt(II) complexes, $Co^{II}([14]aneN_4)^{2+}$, reacts with hydrogen peroxide in the same manner, and in that reaction positive results were obtained in scavenging for a hydroxyl radical intermediate. The other peroxide reactions apparently do not produce HO·. The mechanisms of all of the reactions are considered and discussed.

Introduction

Complexes of cobalt(II) and macrocyclic ligands are known to act as mild reducing agents. A series consisting of 14-membered tetradentate macrocycles or pseudo-macrocycles having nitrogen donor atoms is shown in Figure 1. They constitute a series which makes possible systematic variations in ligand structure, steric effects, electrode potential, and ionic charge. Furthermore, they are stable in aqueous and semi-aqueous media. Despite these advantages, relatively little is known about the kinetics and mechanisms of their oxidation–reduction reactions.

The emphasis of the present work centers on their reactions with iodine, bromine, and hydrogen peroxide. All of the halogen reactions (but only one of the hydrogen peroxide reactions) conform to the stoichiometry of the net reaction shown in eq 1.

$$2(H_2O)_2(Co^{II}) + X_2 = 2X(Co^{III})H_2O + H_2O \quad (1)$$

(For purposes of generalized notation, the macrocyclic ligand is symbolized by parentheses, and the ionic charge, which varies among the compounds, is omitted. The cobalt(II) reactant is written as a six-coordinate complex, a structure which is known from crystallographic determinations for some of the complexes but only surmised for others.)

Reactions such as this are termed noncomplementary, in that the oxidation state changes do not match. Many such reactions, not only for symmetrical reagents such as I_2, Br_2, and H_2O_2 but also for unsymmetric reagents such as HOBr, ROOH, $PhCH_2Br$, and ICN, are thought to proceed by a sequence of two steps in which a radical or atomic species occurs as an intermediate. (Evidence, however, is not always definitive.) For the symmetrical reagents, the first step of this mechanism, invariably the rate-limiting reaction, is

$$M^{II} + X_2 \rightarrow X\text{-}M^{III} + X\cdot \qquad k_2 \quad (2)$$

This step is then followed by a much more rapid reaction, often presumed to be a further step of oxidation by X· (eq 3) but which could equally well be atom recombination (eq 4) or, for the halogen reagents in the presence of a trace of halide ion, disproportionation (eq 5).

$$M^{II} + X\cdot \rightarrow X\text{-}M^{III} \quad (3)$$

$$2X\cdot \rightarrow X_2 \quad (4)$$

$$2X_2^{-} \rightarrow X_2 + 2X^{-} \quad (5)$$

Previous examples of M(II) complexes whose reactions with various reagents X–Y have been studied mechanistically include $Co(CN)_5^{3-}$,[2] Cr^{2+},[3] edta complexes of Mn(II), Fe(II), and Co(II),[4] V^{2+},[5] V^{3+},[5] U^{3+},[6] Fe_{aq}^{2+},[7] $Fe^{II}(CN)_5$ complexes,[8] and, to a much smaller extent, cobalt(II) complexes of tetradentate macrocyclic ligands with organic halides[9] and peroxides.[10]

The studies reported here consist of determinations of the stoichiometry, products, and kinetics of the reactions of the cobalt(II) complexes shown in Figure 1 with the symmetrical reagents I_2, Br_2, and H_2O_2. Our objective is an understanding of these observations in terms of reaction mechanisms and of the factors affecting the rates of the individual reactions.

Experimental Section

Chemicals. The ligands $[14]aneN_4$, *ms*-$Me_6[14]aneN_4$, and $Me_6[14]$-4,11-$dieneN_4$[11] were purchased (Strem Chemical Co), and various cobalt complexes[12] were prepared by standard methods:

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