The Stereospecificity of CN^- Ion Addition to a Coordinated Imine Centre with [Bis(1,2-ethanediamine) 2-iminopropionatocobalt(III)] Ion

Rodney J. Geue,[a] Johan Springborg,[b,*] and Alan M. Sargeson[a]

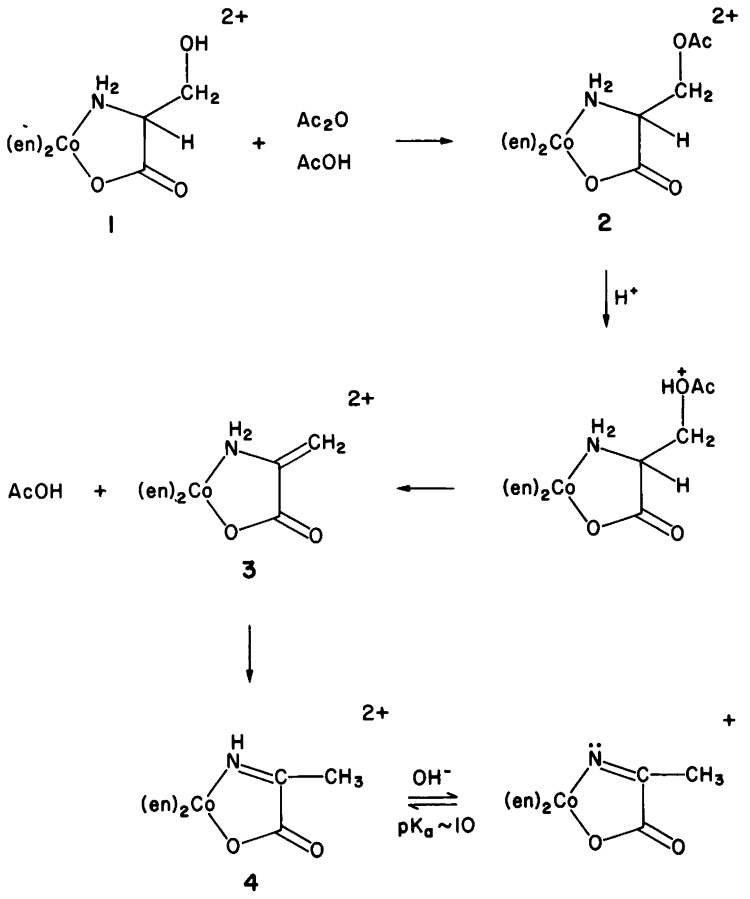
[a]Research School of Chemistry, Australian National University, G.P.O. Box 4, Canberra, A.C.T. 2601, Australia and [b]Chemistry Department, Royal Veterinary and Agricultural University, 40, Thorvaldsensvej, DK-1871 Frederiksberg C, Denmark

Geue, R. J., Springborg, J. and Sargeson, A. M., 1987. The Stereospecificity of CN^- Ion Addition to a Coordinated Imine Centre with [Bis(1,2-ethanediamine)2-iminopropionatocobalt(III)] Ion. – Acta Chem. Scand., Ser. A 41: 158–172.

Addition of CN^- appears to occur rapidly and nearly reversibly at the imine carbon atom of the chelated 2-iminopropionate ion in Δ- or Λ-$[Co(en)_2\{NH{=}C(CH_3)COO\}]^{2+}$ to form a 2-cyanoalanine chelate. The addition is followed by an intramolecular cyclisation of an apical coordinated ethanediamino ion with the nitrile carbon atom to generate a quadridentate amidine chelate, $[Co(NH_2CH_2CH_2NH_2)\{NH_2CH_2CH_2N{=}C(NH_2)C(NH_2)(CH_3)(COO)\}]^{2+}$. There is considerable specificity in this cyclisation to the extent that the (Δ*R*) isomer is preferred (90 %) over the (Λ*S*) form (10 %). The origin of the specificity is ascribed to preferential orbital steering by one of the apical chelated ethanediamino ions towards the nitrile carbon atom. The resulting amidine quadridentate complexes themselves undergo interesting hydrolysis reactions in acid and base, rearrangements, and anation reactions with Cl^- ion. These processes are described and analysed in relation to current views about the mechanisms of such reactions at the metal centre.

The reactions of coordinated imine complexes with nucleophiles have been explored over a considerable period and there is synthetic potential in this strategy both for organic synthesis and coordination complex synthesis.[1-8] The imine bound to the metal ion has some iminium ion character in that it becomes more susceptible to attack by nucleophiles than the parent imine but is less reactive than the protonated molecule. At the same time, it is much more stable than either the parent imine or the iminium ion, especially in aqueous solution. Cobalt(III) complexes of this kind are stable in 12 M HCl for extended periods (> days), even for *exo*- and *endo*-alkyl imines.[6,9] In such instances the metal ion simply protects the imine from protonation and therefore from rapid decay. The Co(III)–N bond is kinetically inert, that is, the ligand-metal bond is not readily broken, and the proton therefore cannot displace the metal ion. This enhanced stability and iminium ion character then leads to new ways to do iminium type chemistry; this paper explores the reactivity of one such coordinated imine towards addition of HCN and also the reactivity of the products of such reactions. Syntheses of 2-iminopropionate complexes have been described previously.[6,10] The chelated imine may be made simply by the condensation of coordinated pyruvic acid with coordinated ammonia under basic conditions. The intervening carbinolamine undergoes base-catalysed elimination of water[6,11] to give the stable 2-iminopropionato complex.[6] However, an equally interesting and more direct route to the chiral complexes required for this study was to use the approach summarized in Scheme 1. The Δ- and Λ-bis(1,2-ethanediamine){(*S*)-serinato}cobalt(III) ions (**1**) are well known and are readily separated and isolated.[10] However, the elimination chemistry outlined in Scheme 1 is of comparatively recent origin.[6,10]

*To whom correspondence should be addressed.



Scheme 1.

The driving force for this chemistry arises from the generation of a species containing a reasonable leaving group ($^-OOCCH_3$) (**2**), which allows access to the very stable imine product **4**.[10] The rearrangement of the enamine is so fast, and the imine so stable, that it has not been possible to intercept the aminoacrylate intermediate (**3**).[10] The route does, however, provide ready access to the stable and pure Δ- and Λ-$[Co(en)_2$(2-iminopropionato)$]^{2+}$ ions, and allows the addition of CN^- to the imine functionality to be explored. Some of this work has been described in a preliminary account,[3] along with structures of one of the quadridentate diastereoisomers and one of the reaction products arising from treatment with HCl.

Experimental

Analytical grade reagents were used for all purposes without further purification. Salts of the imine complex **1** were synthesized using previously published procedures.[10] NMR spectra were recorded using a Jeol 60 MHz instrument with sodium 2-dimethyl-2-silapentane-1-sulfonate (DSS) as internal reference and with tetramethylsilane (TMS) as external reference. Chemical shifts are reported as positive downfield from the references and negative upfield. A Cary 118 spectrophotometer and a Zeiss DMR 21 spectrophotometer were used for recording the absorption spectra and for monitoring kinetic runs. Optical rotations of 0.1 % aqueous solutions were measured with a Perkin-Elmer Model 141 polarimeter. All evaporations were carried out with

Büchi rotary evaporators at ~15 mm Hg pressure so that the temperature of the solutions did not exceed 30 °C (external heating bath 40–50 °C).

(ΔR)(ΛS)-[Co(en)(am)]ZnCl$_4$ · H$_2$O. An ice-cold solution of NaCN (0.74 g) in 1.5 M HCl (8 ml) was added to racemic [Co(en)$_2${NH=C(CH$_3$)COO}]Cl$_2$ · H$_2$O (2.00 g, 5.65 mmol) (*CAUTION:* HCN is evolved in the process. Use of a fume-hood is essential). The suspension was kept at ~20 °C for ~15 min, during which time the imine salt dissolved giving a reddish solution which then turned orange. Ice-cold 12 M HCl (3 ml) was added to the cold solution (~0 °C) and the tetrachlorozincate was precipitated by slow addition of Li$_2$ZnCl$_4$ (4 M, 5 ml). The product was washed thoroughly with 96 % ethanol, with ether and dried in the air. Yield 2.30 g, 79 %. Recrystallization was effected by dissolution (1 g) in HCl (0.005 M, 10 ml) at ~20 °C and slow addition of Li$_2$ZnCl$_4$ (4 M, 2.5 ml). After 1 h at 20 °C the product was collected, washed with 96 % ethanol, ether and dried in the air. Yield 0.82 g, 65 % based on imine. Anal. [Co(C$_2$N$_2$H$_8$)(C$_6$N$_4$H$_{13}$O$_2$)]ZnCl$_4$ · H$_2$O: Co, C, N, H, Cl, Zn. Spectral data are given in Table 1.

(ΔR)(ΛS)-[Co(en)(am)](CF$_3$SO$_3$)$_2$. CF$_3$SO$_3$Na (5.7 g) was added to a filtered solution of (Δ*R*)(Λ*S*)-[Co(en)(am)]ZnCl$_4$ · H$_2$O (1.00 g, 1.93 mmol) in water (12 ml) at room temperature. After stirring at room temperature for 15 min, the product was collected and washed with 50 % (*v*/*v*) acetone in ether (3×20 ml) and then with ether. Yield 0.82 g, 72 %. Found: Co, 10.3 C, 20.2; N, 14.3; H, 4.3; S, 10.9. Calc. for [Co(C$_2$N$_2$H$_8$)(C$_6$N$_4$H$_{13}$O$_2$)](CF$_3$SO$_3$)$_2$: Co, 9.98; C, 20.34; N, 14.24; H, 3.59; S, 10.86. Spectral data are given in Table 1.

(ΔR)(ΛS)-[Co(en)(am)](ClO$_4$)$_2$. (Δ*R*)(Λ*S*)-[Co(en)(am)]ZnCl$_4$ · H$_2$O (5 g, 9.7 mmol) was added to a solution of silver perchlorate (8.8 g) in water (20 ml). The suspension was stirred thoroughly for a few minutes and then filtered. Crystals of the complex perchlorate separated in the filtrate. The residue, containing a mixture of AgCl and some of the complex perchlorate, was washed with water (3×5 ml), which dissolved all the complex perchlorate. NaClO$_4$ (25 g) was added to the combined filtrates and the mixture was cooled in ice for 1 h. The crystals were washed with 96 % ethanol and with ether. Yield 3.5 g, 75 %. The crude product (3.3 g) was dissolved in hot water (90–95 °C) and the solution was filtered while hot through a fine-porosity (G4) sintered-glass filter to remove traces of silver chloride. A saturated solution of sodium perchlorate (8 ml) was added to the filtrate and the mixture was cooled in ice (1 h). Yield 2.8 g, 85 %. Anal. [Co(C$_2$N$_2$H$_8$)(C$_6$N$_4$H$_{13}$O$_2$)](ClO$_4$)$_2$: Co. Spectral data are given in Table 1.

(ΔR)(ΛS)-[Co(en)(am)]Cl$_2$. An aqueous solution of the tetrachlorozincate (8 g, 15.5 mmol) in water (1 l) was adsorbed on a column of Dowex 50W–X2 cation exchange resin (dimensions 5×5 cm, Li$^+$ form). After washing the column with water the complex cation was eluted with 3 M lithium chloride. Since the eluate was supersaturated with respect to complex chloride, the elution was carried out as rapidly as possible. The eluate (120 ml) was then treated with 96 % ethanol (120 ml) and acetone (3.5 l). The resulting mixture of oil and crystals was treated further with 96 % ethanol (100 ml) and the suspension was stirred at room temperature for 1 h. This treatment gave a pure, crystalline product which was collected and dried in the air. Yield ~5 g, 88 %. Anal. [Co(C$_2$N$_2$H$_8$)(C$_6$N$_4$H$_{13}$O$_2$)]Cl$_2$: Co, C, N, H, Cl. Spectral data are given in Table 1.

(+)$_D$-(ΛS)-[Co(en)(am)]S$_2$O$_6$ · H$_2$O. (+)$_D$-Λ-[Co(en)$_2${NH=C(CH$_3$)COO}]Cl$_2$ · H$_2$O (2 g, 5.65 mmol) was treated with a solution of NaCN (0.74 g) in 1.5 M HCl (8 ml) as described above (see *CAUTION*). To the product solution was added an aqueous solution of Na$_2$S$_2$O$_6$ · 2H$_2$O (10 ml, 1.5 g, at 20 °C) and the mixture was then cooled in ice. After 0.5 h, the orange crystals were collected, washed twice with water (5 ml), 50 % ethanol (10 ml), 96 % ethanol (3×10 ml), and then with ether. Yield 1.8 g, 62 %. Recrystallization from aqueous solution (0.5 g in 20 ml of hot water) by addition of a saturated solution of Na$_2$S$_2$O$_6$ · 2H$_2$O (5 ml) and cooling in ice (yield 80 %) gave unchanged optical rotations. Anal. [Co(C$_2$N$_2$H$_8$)(C$_6$N$_4$H$_{13}$O$_2$)]S$_2$O$_6$ · H$_2$O: Co, C, N, H. Spectral data are given in Table 1.

(+)$_D$-(ΛS)-[Co(en)(am)]Cl$_2$ · H$_2$O. (+)$_D$-(Λ*S*)-[Co(en)(am)]S$_2$O$_6$ · H$_2$O (9.5 g, 20.2 mmol) was dissolved in water (3 l) and adsorbed on Dowex 50W–X2 cation exchange resin (Li$^+$ form). After

washing with water, the complex cation was eluted with 3 M LiCl and the eluate (140 ml) was treated with acetone (1400 ml). The resulting two-phase system was separated and more acetone (1400 ml) was added to the aqueous phase. The two-phase system was again separated and 96 % ethanol (400 ml) was added to the aqueous phase. Addition of acetone (1000 ml) to this solution resulted in nearly quantitative precipitation of the chloride salt. After washing with 96 % ethanol and ether the product was dried in the air. Yield 7.0 g, 91 %. Recrystallization from aqueous solution (0.45 g in 1.0 ml) by addition of abs. ethanol (12 ml) gave the complex (75 %), with unchanged optical rotations. Anal. $[Co(C_2N_2H_8)(C_6N_4H_{13}O_2)]Cl_2 \cdot H_2O$: Co. Spectral data are given in Table 1.

mer-*(ΔR)(ΛS)-[Co(en)(amCOOH)Cl]ZnCl₄*.
This complex was prepared from $(\Delta R)(\Lambda S)$-$[Co(en)(am)]^{2+}$, either by direct reaction with 12 M HCl or via base hydrolysis.

Base hydrolysis: $(\Delta R)(\Lambda S)$-$[Co(en)(am)]ZnCl_4 \cdot H_2O$ (5.0 g, 9.7 mmol) was dissolved in 2 M NaOH (30 ml) at ~20 °C to give a reddish-orange solution and a precipitate of $Zn(OH)_2$. After 1 h the solution was cooled in ice and ice-cold 12 M HCl (80 ml) and Li_2ZnCl_4 (4 M, 30 ml) were added. After 5 min with cooling a precipitate of NaCl was filtered off and the solution was then left for 3 h at room temperature. The glass vessel was scratched with a glass rod to induce crystallization, and large reddish-purple crystals separated. These were washed with 96 % ethanol, with ether and then dried in the air. Yield 4.50 g, 87 %. Anal. $[Co(C_2N_2H_8)(C_6N_4H_{14}O_2)Cl]ZnCl_4$: Co, C, N, H, Cl, Zn. Spectral data are given in Table 1.

Acid hydrolysis: A solution of $(\Delta R)(\Lambda S)$-$[Co(en)(am)]Cl_2$ (0.50 g, 1.38 mmol) in 12 M HCl (5 ml) was kept at 25 °C for 18 h. The colour of the solution changed from orange to reddish-purple and a few crystals of the chloride of the chloro complex precipitated. Li_2ZnCl_4 (4 M, 2 ml) was added and crystallization of the tetrachlorizincate was induced by scratching the sides of the vessel. The suspension was stirred for 1 h to redissolve the initially formed chloride salt and the final product was filtered off, washed with 96 % ethanol, then with ether and dried in the air. Yield 0.41 g, 55 %. The product was shown to be identical with the product described above by comparing the ^1H NMR spectra, infrared spectra and visible spectra of the two samples.

(ΛR)(ΔS)-[Co(en)(am)](ClO₄)₂. $(\Delta R)(\Lambda S)$-$[Co(en)_2(am)]ZnCl_4 \cdot H_2O$ (5 g, 9.66 mmol) was dissolved in 2 M NaOH (30 ml) and the solution was kept at 20 °C in a closed bottle for 1.5 h. After neutralization (to pH = 5–7) with 12 M $HClO_4$ (5 ml) the mixture was heated at 100 °C for 45 min. The colour changed from red to orange and the pH remained at 5–7. The solution was cooled and acidified with a few drops of 12 M $HClO_4$ [to prevent precipitation of $Zn(OH)_2$] and $NaClO_4 \cdot H_2O$ (35 g) was added. The solution was kept overnight at 0–5 °C and the product was collected, washed with 96 % ethanol and then with ether. Yield 4.45 g, 94 %. The crude perchlorate (4 g) was dissolved in water (40 ml) at room temperature and a saturated solution of $NaClO_4$ (20 ml) was added to the filtered solution. The precipitate was filtered off, washed with 96 % ethanol and dried in the air. Yield 3.2 g, 80 %. Anal. $[Co(C_2N_2H_8)(C_6N_4H_{13}O_2)](ClO_4)_2$: Co, C, N, H, Cl. Spectral data are given in Table 1.

(ΛR)(ΔS)-[Co(en)(am)]ZnCl₄. A suspension of *mer*-$(\Delta R)(\Lambda S)$-$[Co(en)(amCOOH)Cl]ZnCl_4$ (2 g, 3.73 mmol) in water (4 ml) was heated at 100 °C for a few minutes. This gave a red-orange solution and the pH changed from 5 to 0, indicating that the carboxyl group had recoordinated. Pyridine (0.32 g, 4.10 mmol) was added and the solution (pH 5) was heated for a further 15 min to complete the reaction, Cooling to room temperature and addition of Li_2ZnCl_4 (4 M, 1 ml) led to precipitation of the tetrachlorozincate. Yield 1.65 g, 89 %. The visible absorption spectrum and ^1H NMR spectrum of this product were identical to those of the perchlorate described above (Table 1).

$(-)_D$-*(ΔS)-[Co(en)(am)]S₂O₆*. This complex was prepared from $(+)_D$-(ΛS)-$[Co(en)(am)]^{2+}$ via base or acid hydrolysis as described below.

Base hydrolysis. A solution of $(+)_D$-(ΛS)-$[Co(en)(am)]S_2O_6 \cdot H_2O$ (0.5 g, 1.06 mmol) in 2 M NaOH (3 ml) was kept in a closed bottle at 25 °C for 1 h. During this time quantitative formation

of (ΛS)-[Co(en)(amCOO)(OH)]$^+$ took place. 12 M $HClO_4$ (0.5 ml) was then added and the solution was heated at 100 °C (water-bath) under reflux conditions for 45 min. The colour changed gradually from reddish-purple to orange and crystals of $(-)_D$-(ΔS)-[Co(en)(am)]S_2O_6 separated during the heating. The mixture was cooled in ice (0.5 h) and the crystals were collected. After washing with 96 % ethanol the product was dried in air (0.24 g, 50 %). The product (0.18 g) was fractionally crystallized by dissolving it in boiling water (36 ml) and cooling the filtered solution in ice. Yield 0.07 g. Addition of a saturated solution of $Na_2S_2O_6 \cdot 2H_2O$ (9 ml) led to precipitation of a further 0.03 g, which was isolated as before. The optical rotations of the two fractions were $[M]^{25}_{589}$ = 3160 and 3180 deg M^{-1} m^{-1}, respectively. Anal. $[Co(C_2N_2H_8)(C_6N_4H_{13}O_2)]S_2O_6$: Co, C, N, H, S. Spectral data are given in Table 1.

Acid hydrolysis: A solution of $(+)_D$-(ΛS)-[Co(en)(am)]$Cl_2 \cdot H_2O$ (0.5 g, 1.31 mmol) in 12 M HCl (0.5 ml) was heated at 55 °C for 45 min. The reddish-purple solution, containing essentially pure $(+)_D$-*mer*-(ΛS)-[Co(en)(amCOOH)Cl]$^{2+}$, was cooled in ice and then neutralized (to pH ~6–7) by addition of LiOH (4 M, ~1.5 ml). Solid $Na_2S_2O_6 \cdot 2H_2O$ (0.9 g) was added and the mixture was heated at 100 °C (water-bath under reflux conditions) for 45 min. The colour changed gradually to orange-red, and orange crystals of $(-)_D$-(ΔS)-[Co(en)(am)]S_2O_6 separated. The crystals were collected while the mixture was still hot, washed with water (5×3 ml) and then with 96 % ethanol. Yield 0.25 g, 42 %. The spectral data were identical to those given in Table 1, e.g. $[M]^{25}_{589}$ = 3170 deg M^{-1} m^{-1}. Anal. $[Co(C_2N_2H_8)(C_6N_4H_{13}O_2)]S_2O_6$: Co, C, N, H, S.

mer-(ΛR)(ΔS)-[Co(en)(amCOOH)Cl]$ZnCl_4$. A solution of (ΛR)(ΔS)-[Co(en)(am)]$(ClO_4)_2$ (3 g, 6.11 mmol) in 12 M HCl (20 ml) was kept at 20 °C for 6 min. During this time the colour of the solution changed from orange to reddish-purple. A solution of Li_2ZnCl_4 (4 M, 6 ml) was then added and crystallization commenced within minutes. The crystals were collected, washed with 96 % ethanol, with ether and dried in the air. Yield 3.0 g, 92 %. Found: Co, 11.1; C, 17.3; N, 15.0; H, 4.1; Cl, 32.9; Zn, 12.5. Calc. for [Co$(C_2N_2H_8)(C_6N_4H_{14}O_2)$Cl]$ZnCl_4$: Co, 11.00; C, 17.93; N, 15.69; H, 4.14; Cl, 33.08; Zn, 12.20. Spectral data are given in Table 1.

Enantiomers of [Co(en)(amCOOH)Cl]$^{2+}$. Solutions of the pure enantiomers $(+)_D$-*mer*-(ΛS)- and $(+)_D$-*mer*-(ΔS)-[Co(en)(amCOOH)Cl]$^{2+}$ were prepared as follows and their characterizing data are collected in Table 1.

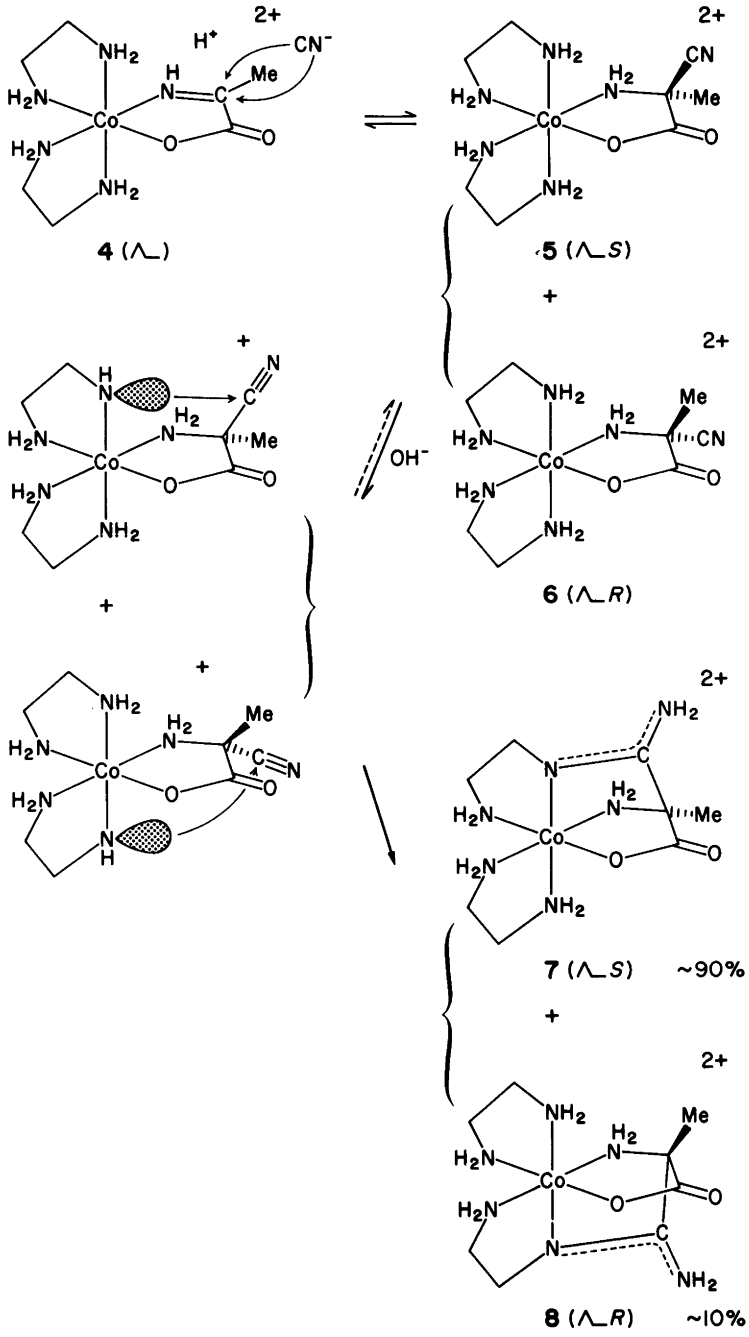
$(+)_D$-mer-(ΛS)-[Co(en)(amCOOH)Cl]$^{2+}$. A solution of $(+)_D$-(ΛS)-[Co(en)(am)]$Cl_2 \cdot H_2O$ in 0.05 M NaOH was kept at 25 °C for 60 min and then 12 M HCl was added to give a final solution 9 M in HCl. The optical rotations and the visible absorption spectrum were followed with time and after 50 min, constant readings were obtained for at least the following 20 min. The final visible absorption spectrum was identical to that of *mer*-(ΔR)(ΛS)-[Co(en)(amCOOH)Cl] $ZnCl_4$.

$(+)_D$-mer-(ΔS)-[Co(en)(amCOOH)Cl]$^{2+}$. The optical rotations and the visible absorption spectrum of a solution of $(-)_D$-(ΔS)-[Co(en)(am)]S_2O_6 were followed with time. After 50 min, constant readings were obtained for at least the following 30 min. The final visible absorption spectrum was identical to that of *mer*-(ΛR)(ΔS)-[Co(en)(amCOOH)Cl]$ZnCl_4$.

The acid-dissociation constant, K_a, for (ΔR)(ΛS)[Co(en)(am)]$^{2+}$ was determined spectrophotometrically at unit ionic strength (maintained with $NaClO_4$) and at 25 °C. Solutions of (ΔR)(ΛS)-[Co(en)(am)]$(CF_3SO_3)_2$ (5×10^{-4} M) were mixed with equal volumes of 0.02–0.7 M NaOH using a stopped-flow apparatus, and the absorbance was measured at the wavelengths 390 nm and 490 nm. Reliable readings were obtained less than 2 sec after mixing, and errors due to the subsequent slower hydrolysis could therefore be ignored. The change in the molar absorptivity ε as a function of [OH^-] followed the expression

$$\varepsilon = \varepsilon_A - K_b(\varepsilon - \varepsilon_{HA})/[OH^-]$$

where $K_a \cdot K_b = K_w = [H^+][OH^-]$ and ε_{HA} and ε_A are the ε-values for the acidic and basic forms of the amidine cation, respectively. Values of ε_{HA} were obtained from the spectrum of the amidine complex in 1 M $NaClO_4$. Plots of ε versus $(\varepsilon-\varepsilon_{HA})/[OH^-]$ were linear and gave, independently of the wavelength, the value K_b =



Scheme 2.

0.23(1) M, which (using the value $-\log K_w$ = 13.77) yields pK_a = 12.13.

Kinetic measurements of the base hydrolysis of $(\Delta R)(\Lambda S)$-$[Co(en)(am)]^{2+}$ were made spectrophotometrically at 370, 390, 490 and 510 nm. For measurements with $[OH^-] \geqq 0.1$ M, solutions of the Co(III) complex (2×10^{-3} M) were made using the tetrachlorozincate salt. In the $[OH^-]$ region $0.0125 < [OH^-] < 0.1$ M less concentrated solutions of complex (5×10^{-4} M) were used, and in order to avoid base consumption by Zn^{2+} the trifluoromethanesulfonate salt was used. All the kinetics were carried out under pseudo first-order conditions. The reaction was followed by repeated scans in the region 550 nm to 350 nm and no further change was detected after one-half to two hours or after a further two hours. Plots of ln $(A-A_\infty)$ versus time were linear for at least four half-lives, and the slopes gave the values for k_{obs} quoted in Table 2.

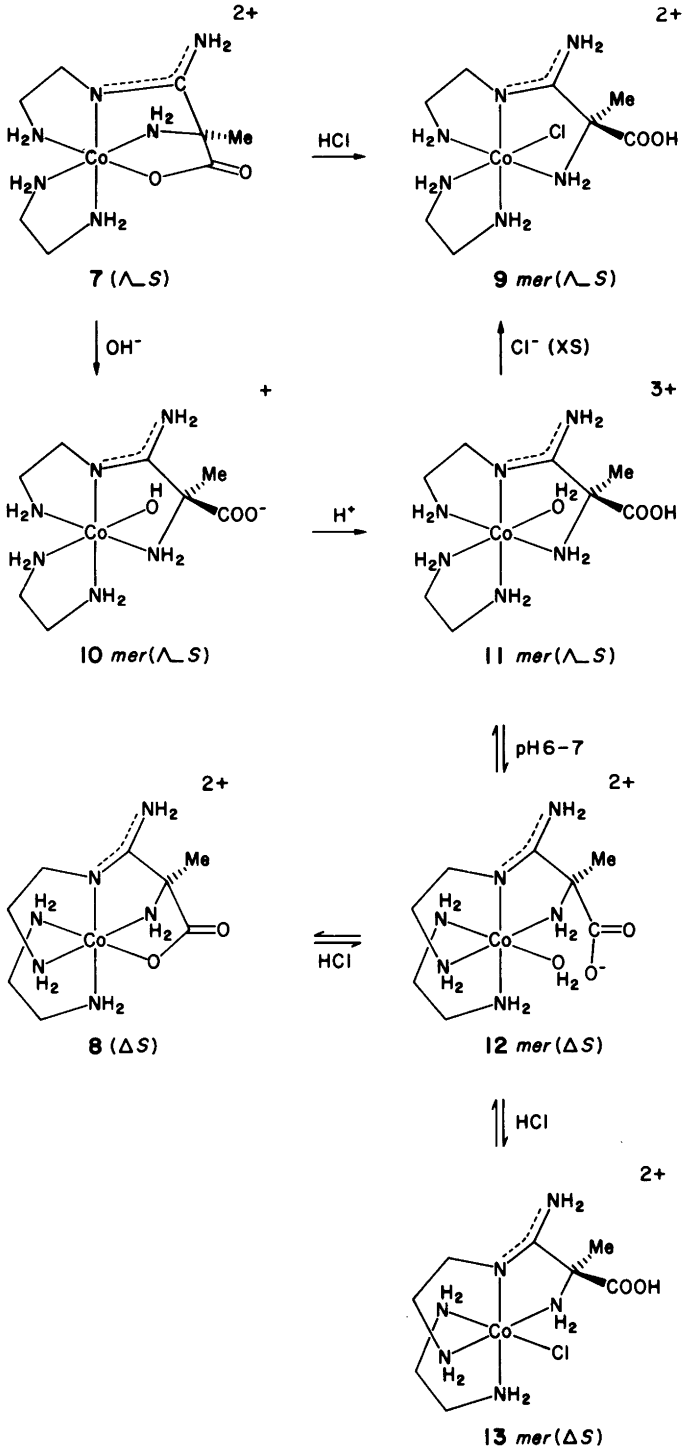
Results

Synthetic procedures. Reaction of the bis(1,2-ethanediamine)(2-iminopropionato)cobalt(III) ion (**4**) with CN^- at pH = 8–10 (Scheme 2) yielded the quadridentate amidine complexes $[Co(en)(am)]^{2+}$ (**7**, **8**). Cyanide ion adds at the imine C atom on either side of the Co iminopropionato chelate plane to give the diastereoisomeric 2-cyanoalaninato complexes **5** and **6**. These then undergo an intramolecular reaction between the $-CN$ group and an adjacent deprotonated amine group to give the amidine chelates (**7**), (**8**). The reaction appears to be quantitative and shows substantial stereoselectivity. Starting with a racemic imine complex it gave the racemic diastereoisomeric $(\Delta R)(\Lambda S)$, (**7**), and $(\Lambda R)(\Delta S)$, (**8**), products in yields of ~90 % and ~10 %, respectively. This product distribution has been assessed by comparing the ^1H NMR spectrum of the product solution with the spectra of the pure isomers (Table 1). It was also evident that this product distribution reflected the growth of the

Table 1. Spectral data for the various salts of the racemic and optically active isomers.[a]

Complex ion	Medium[b]	$(\varepsilon,\lambda)_{max}$[c]			$[M]^{25}_{589}$	$[M]^{25}_{578}$	$[M]^{25}_{546}$	$[M]^{25}_{436}$	$\delta(-CH_3)$
$(+)_D$-(ΛS)-$[Co(en)(am)]^{2+}$	H_2O	(144,484)	(199,322)[d]		+4420[e]	+5510	+5959	−5950	1.65
$(-)_D$-(ΔS)-$[Co(en)(am)]^{2+}$	H_2O	$(84,500)_{sh}$	(103,463)	$(123,340)_{sh}$[f]	−3150[g]	−3670	−4300	+2490	1.68
$(+)_D$-*mer*-$[(\Lambda S)$-Co(en)(amCOOH)Cl$]^{2+}$	3–9 M HCl	(126,547)	(97,463)	$(129,370)_{sh}$[h]	+ 659[i]	+ 465	− 693	0	1.98
$(+)_D$-*mer*-(ΔS)[Co(en)(amCOOH)$]^{2+}$	3–9 M HCl	(129,549)	(98,465)	$(131,370)_{sh}$[j]	+1100[k]	+ 964	0	−1910	2.04
mer-$(\Delta R)(\Lambda S)$[Co(en)(amCOO)(OH)$]^+$	1 M NaOH	(126,478)[l]							1.81
mer-$(\Lambda R)(\Delta S)$[Co(en)(amCOO)(OH)$]^+$	1 M NaOH	(120,476)[m]							1.80
mer-$(\Delta R)(\Lambda S)$-$[Co(en)(amCOOH)(H_2O)]^+$	6 M DCl								2.05
mer-$(\Lambda R)(\Delta S)$-$[Co(en)(amCOOH)(H_2O)]^+$	6 M DCl								2.13

[a]The extremum values for the absorption spectra are given with ε in M^{-1} cm^{-1} and λ in nm. The molar rotation, $[M]^{25}_\lambda$, is given in deg. M^{-1} m^{-1}. $\delta(-CH_3)$ is the position (in ppm) of the methyl singlet in the ^1H NMR spectrum. [b]The quoted media refer to the measurements of the visible absorption spectra and the optical rotations. The ^1H NMR spectra were recorded in the corresponding deuterated media. [c]The ε-values for different salts of the same cation deviate in each case by less than 0.5 % from the quoted average values. [d]Average values for the four racemic and the two optically active salts described in the experimental section. $(\varepsilon,\lambda)_{min}$ = (42,405). [e]This value is for the $(+)_D$-(ΛS) chloride salt. The $(+)_D$-(ΛS) dithionate salt gave $[M]^{25}_{589}$ = 4460 deg. M^{-1} m^{-1}. [f]Average values for the two racemic and the optically active salts described in experimental section. $(\varepsilon,\lambda)_{min}$ = (40,402). [g]Dithionate salt. $(+)_D$-(ΛR)-$[Co(en)(am)]S_2O_6$ gave $[M]^{25}_D$ = +3150 deg. M^{-1} m^{-1}. [h](ε,λ)-values are average values obtained for *mer*-$(\Delta R)(\Lambda S)$-$[Co(en)(amCOOH)Cl]ZnCl_4$ in 3 M HCl and 6 M HCl. The same values were obtained when this cation was made optically active *in situ,* as described under *i.* $(\varepsilon,\lambda)_{min}$ = (91,493), (73,423). [i]Measured for a 0.1 % solution of $(+)_D$-*mer*-(ΛS)-$[Co(en)(amCOOH)Cl]^{2+}$ in 9 M HCl made via base hydrolysis of $(+)_D$-(ΛS)-$[Co(en)(am)]^{2+}$ (see text). [j]The (ε,λ)-values have been obtained for *mer*-$(\Lambda R)(\Delta S)$-[Co(en)(amCOOH)(Cl)]$ZnCl_4$ in 6 M HCl. Almost the same values were obtained in 3 M HCl. Identical values were obtained when this cation was made optically active *in situ,* as described under *k.* $(\varepsilon,\lambda)_{min}$ = (91,495), (74,424). [k]Measured for a 0.1 % solution of $(-)_D$-*mer*-(ΔS)-Co(en)(amCOOH)$(Cl)^{2+}$ made by dissolving $(-)_D$-(ΔS)-$[Co(en)(am)]S_2O_6$ in 9 M HCl (see text). [l]The quoted spectral data are for solutions of *mer*-$(\Delta R)(\Lambda S)$-[Co(en)(COOH)Cl]]$ZnCl_4$ in 1 M NaOH. Almost the same values were obtained in 0.1 M NaOH. Identical values were obtained when $(\Delta R)(\Lambda S)$-$[Co(en)(am)](ClO_4)_2$ was hydrolyzed in 1 M NaOH. $(\varepsilon,\lambda)_{min}$ = (69,404). [m]*mer*-$(\Lambda R)(\Delta S)$-[Co(en)(amCOOH)(Cl)]$ZnCl_4$ in 1 M NaOH. Almost the same values were obtained in 0.1 M NaOH. $(\varepsilon,\lambda)_{min}$ = (70,409).


HCl
OH⁻
Cl⁻ (XS)
H⁺
pH6-7
HCl
HCl
7 (Λ-S)
9 mer(Λ-S)
10 mer(Λ-S)
11 mer(Λ-S)
8 (Δ-S)
12 mer(Δ-S)
13 mer(Δ-S)

Scheme 3.

NMR signals due to the isomers throughout the reaction.

The most abundant isomer was isolated directly from the acidified product mixture by precipitation with tetrachlorozincate ion, giving pure $(\Delta R)(\Lambda S)$-[Co(en)(am)]$ZnCl_4 \cdot H_2O$ (79%). Its structure was established by X-ray crystallographic analysis.[3] The tetrachlorozincate was readily converted into other salts with appropriate anions, e.g. ClO_4^-, Cl^- and $CF_3SO_3^-$. Attempts to isolate the $(\Lambda R)(\Delta S)$ isomers directly from the above reaction mixture failed, and separation of the diastereoisomeric amidine cations using cation exchange resins was not achieved.

The reaction of $(\Delta R)(\Lambda S)$-$[Co(en)(am)]^{2+}$, (**7**), with 12 M HCl was quantitative and stereospecific, giving a chloro complex in which a cobalt-carboxylate bond had been cleaved (Scheme 3). The chloro complex was isolated as a pure salt, *mer*-$(\Delta R)(\Lambda S)$-[Co(en)(amCOOH)Cl]$ZnCl_4 \cdot H_2O$, (**9**), and its structure determined.[3] Alternatively, this compound was obtained via base hydrolysis of the $(\Delta R)(\Lambda S)$ amidine complex (in 1 M NaOH). The cobalt-carboxylate-O-bond was cleaved, giving the cation *mer*-(ΔR) (ΛS)-$[Co(en)(amCOO)(OH)]^+$ (**10**). Subsequent treatment with a large excess of 12 M HCl gave the chloro complex (**9**), which was isolated as its tetrachlorozincate salt as before.

The other diastereoisomer (**8**), $(\Lambda R)(\Delta S)$-[Co (en)(am)]$^{2+}$, was prepared from $(\Delta R)(\Lambda S)$-[Co (en)(am)]$ZnCl_4 \cdot H_2O$ (**7**). Base hydrolysis of the latter complex followed by addition of acid to pH 6–7 gave quantitatively and stereospecifically the deprotonated aqua complex (**11**), *mer*-$(\Delta R)(\Lambda S)$-$[Co(en)(amCOO)(H_2O)]^{2+}$. Upon heating in solution, this cation rearranged and reformed the cobalt-carboxylate bond, and $(\Lambda R)(\Delta S)$-[Co(en) (am)]$(ClO_4)_2$ (**8**) was isolated. Alternatively, the $(\Lambda R)(\Delta S)$ amidine isomers were prepared by heating an aqueous solution of *mer*-$(\Delta R)(\Lambda S)$-[Co(en)(amCOOH)Cl]$ZnCl_4$ (**9**). This treatment gave initially the aqua complex, which slowly rearranged and produced $(\Lambda R)(\Delta S)$-[Co(en)(am)] $ZnCl_4$ as described. Treatment of $(\Lambda R)(\Delta S)$-[Co (en)(am)]$(ClO_4)_2$ with 12 M HCl yielded a new chloro complex (**13**) with the cobalt-carboxylate bond cleaved. This complex was crystallized as *mer*-$(\Lambda R)(\Delta S)$-[Co(en)(amCOOH)Cl]$ZnCl_4$.

The reaction sequences described above were repeated starting with the chiral 2-iminopropionato complex, $(+)_D$-Λ-$[Co(en)_2\{NH{=}C(CH_3)COO\}]Cl_2 \cdot H_2O$. The reaction with CN^- yielded a mixture of the isomers (ΛS) (90%) and (ΛR) (10%), and addition of $Na_2S_2O_6$ to the basic solution yielded a pure salt, $(+)_D$-(ΛS)-[Co(en) (am)] $(S_2O_6) \cdot H_2O$ (**4**) (Yield 62%). Crystallization of this isomer either as a dithionate or as a chloride gave products having the same molar rotation, indicating that the salts were optically pure. Furthermore, ^1H NMR studies showed that contamination with the (ΔR) [or (ΔS)] isomer was less than 1%.

As described above for the racemic isomers, the (ΛS) isomer was then rearranged via base hydrolysis and via acid hydrolysis, respectively, to the (ΔS) isomer, which in both cases was isolated as a pure dithionate salt, $(-)_D$-(ΔS)-[Co(en) (am)]S_2O_6 (Yield 40–50%). From ^1H NMR measurements it was shown that contamination of this product with the (ΛS) [or (ΔR)] isomer was also less than 1%.

The optically active chloro complexes were not characterized as isolated salts, but the *mer*-(ΛS) and *mer*-(ΔS) isomers of $[Co(en)(am\ COOH)Cl]^{2+}$ were both characterized in solution by their ^1H NMR spectra. The addition of Cl^- to the quadridentate amidine complex and its removal to regenerate the quadridentate amidine complex both occur with retention of the chirality of the original reactants.

Cyanide ion addition. The reaction between the 2-iminopropionato complex and CN^- was followed by ^1H NMR spectroscopy by monitoring the disappearance of the methyl singlet of the 2-iminopropionato complex (δ 2.45) and the appearance of the methyl singlets of the amidine complexes (δ 1.65 and δ 1.68). The presence of an intermediate complex was not established with certainty, but in some experiments a very small singlet at δ 2 ppm, which could have been due to the 2-cyanoalaninato intermediate, was observed in the early stages of reaction. The reaction was relatively fast at 22°C ($t_{\frac{1}{2}}$ ~1 min at pH = 7.8 with [HCN] = 2.0 M and $[CN^-]$ = 0.1 M), and at constant [HCN] = 0.25 M the half-life varied with the conditions as follows: ~20 sec for $[CN^-]$ = 0.65 M (pH 9.5); ~3 min for $[CN^-]$ = 0.06 M (pH 8.5); ~7 min for $[CN^-]$ = 0.02 M (pH 8.0). Also, at pH 4 no reaction was observed within 4 d in 0.5 M HCN. These experiments demonstrated that the reaction rate increases with increasing concentration of CN^- and OH^-.

Acid hydrolysis of the $[Co(en)(am)]^{2+}$ isomers. The synthetic chemistry described above is supported by ^1H NMR studies. As noted already, both diastereoisomers of $[Co(en)(am)]^{2+}$ react quantitatively and stereospecifically with 12 M HCl. The reactions were also followed in DCl solutions, using the methyl singlet signal as the primary probe. The (ΔR)(ΛS) isomer reacted much more slowly than the (ΛR)(ΔS) isomer, and in 12 M DCl (25 °C) the half-lives were approximately 2 h and 1 min, respectively. For the reaction of the (ΔR)(ΛS) isomer in 12 M DCl, only methyl singlets for the reactant (**7**) and for the product chloro complex (**9**) were observed. However, in the reaction of the (ΛR)(ΔS) isomer (**8**) in 6 M DCl, one methyl peak for the formation of the intermediate aqua isomer, *mer*-(ΛR)(ΔS)-$[Co(en)(amCOOH)(H_2O)]^{3+}$ (protonated **12**), was seen. The final spectrum was identified as that of pure *mer*-(ΛR)(ΔS)-$[Co(en)(amCOOH)Cl]^{2+}$ (**13**). The overall half-life for the reaction was approximately 5–10 min (6 M DCl, 25 °C). The rates of aquation and anation are therefore of the same order of magnitude in this medium.

Base hydrolysis of the $[Co(en)(am)]^{2+}$ isomers. Both amidine complexes showed acid-base properties, giving red deprotonated products in strong base. The acid-dissociation constant for the (ΔR)(ΛS) racemate was determined spectrophotometrically as $pK_a = 12.13$ (1 M $NaClO_4$, 25 °C).

Hydrolysis of the diastereoisomers of $[Co(en)(am)]^{2+}$ in 1 M NaOD was also studied at 25 °C by ^1H NMR measurements. The total spectra implied that hydrolysis of the (ΔR)(ΛS) isomer yielded *mer*-(ΔR)(ΛS)-$[Co(en)(amCOO)(OH)]^+$ near quantitatively, while hydrolysis of the (ΛR)(ΔS) isomer yielded a mixture of both diastereoisomers, viz. *mer*-(ΔR)(ΛS) and *mer*-(ΛR)(ΔS). However, since the methyl singlet signals for the diastereoisomeric $[Co(en)(amCOO)(OH)]^+$ cations coincide, quantitative conclusions could not be reached on that basis alone. A quantitative analysis was obtained, however, by the following experiments which take advantage of the facts that the anation of the aqua products occurs quantitatively and with retention of configuration in 9 M DCl, and that the product chloro complexes show separated methyl singlet signals.

Concentrated DCl was added to the basic product solutions to give 9 M DCl solutions, which were left at 20 °C for ~10 min in order to complete the anation reaction. In the final chloro product solution, the diastereoisomeric distribution therefore should be identical to that of the parent basic product solution. A prerequisite for this argument is that isomerization of the diastereoisomers of $[Co(en)(am)(OH)]^+$ is slow relative to the time scale for the base hydrolysis, and as shown below, this was found to be the case. The ^1H NMR spectrum of the chloro product solution obtained via base hydrolysis of (ΔR)(ΛS)-$[Co(en)(am)]^{2+}$ showed one methyl signal identical to that of the isomer *mer*-(ΔR)(ΛS). The spectrum of the chloro product solution obtained via base hydrolysis of (ΛR)(ΔS)-$[Co(en)(am)]^{2+}$ showed two methyl singlets corresponding to the diastereoisomers *mer*-(ΔR)(ΛS) and *mer*-(ΛR)(ΔS) in the ratio 2:3. The results therefore establish the following reaction paths:

$$(\Delta R)(\Lambda S)\text{-}[Co(cn)(am)]^{2+} \xrightarrow{1\text{ M NaOD}} mer\text{-}(\Delta R)(\Lambda S)\text{-}[Co(en)(amCOO)(OH)]^+ \quad (\geqq 95\,\%)$$

$$(\Lambda R)(\Delta S)\text{-}[Co(en)(am)]^{2+} \xrightarrow{1\text{ M NaOD}} mer\text{-}(\Delta R)(\Lambda S)\text{-} \quad (40\pm4\,\%)$$

$$+\ mer\text{-}(\Lambda R)(\Delta S)\text{-}[Co(en)(amCOO)(OH)]^+ \quad (60\pm4\,\%)$$

The base hydrolysis of the (ΔR)(ΛS) isomer was studied further by spectrophotometry for $[OH^-] = 10^{-2}$–1.0 M, using pseudo first-order conditions. The change in absorbance obeyed first-order kinetics and plots of $\ln(A_t - A_\infty)$ versus time were linear for >95 % of the reaction. Values of k_{obs} are given in Table 2. The variation of k_{obs} with $[OH^-]$ is consistent with a base-catalyzed hydrolysis of two reactive species, the amidine complex and its deprotonated form, as shown in Scheme 4. This mechanism gives the rate expression

$$k_{calc} = \frac{k_{OH}^{(1)}[OH^-] + k_{OH}^{(2)}[OH^-]^2/K_b}{1 + [OH^-]/K_b}$$

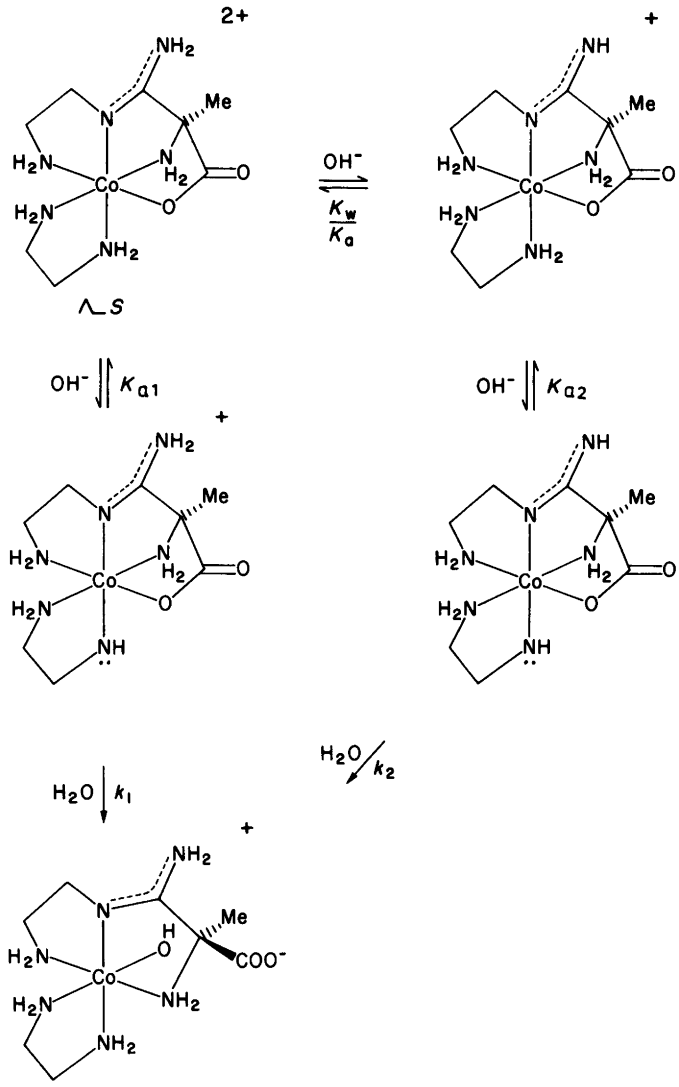
where $k_{OH}^{(1)} = k_1 K_{a1}/K_w$ and $k_{OH}^{(2)} = k_2 K_{a2}/K_w$,

Table 2. Kinetic data[a] for the base hydrolysis of (Δ*R*)(Λ*S*)-[Co(en)(am)]$^{2+}$.

$[OH^-]$/ mol l^{-1}	$10^3 \times k_{obs}$/ s^{-1}	$10^3 \times k_{calc}$/ s^{-1}
1.00[b]	2.32	2.32
0.750[b]	2.27	2.19
0.500[b]	2.00	2.04
0.350[b]	1.92	1.93
0.200[b]	1.68	1.78
0.100[b]	1.60	1.57
0.0375[c]	1.19	1.18
0.0250[c]	0.98	0.99
0.0125[c]	0.70	0.66

[a]At 25 °C, $\mu = 1.0$ M ($NaClO_4$) in H_2O.
[b]$[Co] = 2\times10^{-3}$ M. [c]$[Co] = 5\times10^{-4}$ M.

K_{a1} and K_{a2} are the acid dissociation constants for the two reactive species, and k_1 and k_2 are pseudo first-order rate constants for the aquation of the conjugate bases. The rate expression has been obtained assuming that K_{a1} and K_{a2} are both much less than 10^{-14} M. $K_b = K_w/K_a$, and K_a is the acid dissociation constant for the amidine moiety and has been determined independently of the kinetic data, as described above. Values of k_{calc} and k_{obs} are given in Table 2, and k_{calc} values have been calculated using the derived composite parameter values $k_{OH}^{(1)} = 8.2(2)\times10^{-2}$ M^{-1} s^{-1} and $k_{OH}^{(2)} = 4.7(10)\times10^{-4}$ M^{-1} s^{-1} obtained by least-square analysis. It is noted that use of the simpler expression



Scheme 4.

$$k_{calc} = k_{OH}[OH^-]/(1 + [OH^-]/K_b)$$

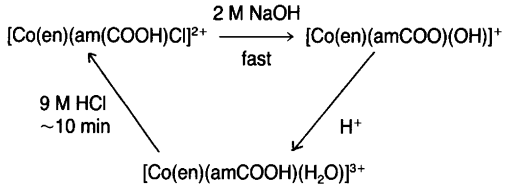
gave significant deviations between k_{calc} and k_{obs}.

Reactions of the aqua and chloro amidine isomers. The reactions of the meridional diastereoisomers of the cation $[Co(en)(amCOOH)Cl]^{2+}$ were also studied in acidic, basic and neutral solutions by ^1H NMR spectroscopy. The methyl signals showed that the diastereoisomers of the chloro complexes equilibrated slowly (~24 h at 55 °C) in 12 M DCl and that net aquation of the chloro complexes did not occur under these conditions. Small amounts of the chloro complexes decomposed during the time required for equilibration, but the products were not identified. These processes may involve hydrolysis of the amidine to amide. However, the decomposition was very slow relative to the equilibration reaction and could therefore be ignored. The stoichiometry for the equilibration is therefore simply expressed by

$$mer\text{-}(\Delta R)(\Lambda S)\text{-}[Co(en)(amCOOH)Cl]^{2+} \overset{K}{\rightleftharpoons} mer\text{-}(\Lambda R)(\Delta S)\text{-}[Co(en)(amCOOH)Cl]^{2+}$$

where $K = [(\Delta R)]/[(\Lambda S)] = 1.0(\pm 0.2)$ and $t_{\frac{1}{2}} = 2.3$ h (12 M DCl, 55 °C).

Base hydrolysis of both diastereoisomers of $[Co(en)(amCOOH)Cl]^{2+}$ gave the respective diastereoisomeric cations $[Co(en)(amCOO)(OH)]^+$ nearly instantaneously and quantitatively. The product solutions obtained by base hydrolysis in 1 M NaOD of the two diastereoisomers *mer*-$(\Delta R)(\Lambda S)$ and *mer*-$(\Lambda R)(\Delta S)$, respectively, gave different ^1H NMR spectra, but with coinciding methyl singlets. The results, therefore, are not definitive with respect to the stereochemistry of the reactions. However, subsequent addition of a large excess of DCl resulted in a quantitative and rapid anation reaction to re-form the chloro complexes. The ^1H NMR spectra of these chloro product solutions each showed one methyl peak (at different positions) and for each diastereoisomer were identical with the ^1H NMR spectrum of the parent chloro complex. The anation reactions of both diastereoisomers of the cation $[Co(en)(amCOOH)(H_2O)]^{3+}$ were fast and complete within minutes in 9 M CDl at 25 °C. These results therefore show that for both diastereoisomers,



Scheme 5.

the reaction sequences shown in Scheme 5 occur with retention of configuration (>95 %).

These results also have the implication that the isomerization reaction between aqua complexes must be substantially slower than the anation reaction in 6–9 M HCl. Isomerization between the hydroxo complexes must also be slow. This follows from the experiments above and the observation of stereospecific re-formation of the chloro complexes observed for basic solutions kept for 1 h at 25 °C before acidification with DCl. This means that the isomerization reaction between the *mer*-$(\Delta R)(\Lambda S)$ and *mer*-$(\Lambda R)(\Delta S)$ isomers of $[Co(en)(amCOO)(OH)]^+$ has a half-life greater than 10 h under these conditions. It also indicates that the products arising from the base hydrolysis of the quadridentate amidine complexes are not equilibrium mixtures.

In aqueous solution at pH ~ 5, both diastereoisomers of $[Co(en)(amCOOH)Cl]^{2+}$ yielded quantitatively, but with quite different rates, the complex $(\Lambda R)(\Delta S)$-$[Co(en)(am)]^{2+}$, and the reactions were followed by ^1H NMR measurements in pyridine-pyridinium buffered D_2O solutions. Hydrolysis of the *mer*-$(\Delta R)(\Lambda S)$ isomer gave initially ($t_{\frac{1}{2}} \sim 10$ min at 25 °C and $[Cl^-] = 1$ M) an equilibrium mixture of the chloro complex and the aquated complex, both with the *mer*-$(\Delta R)(\Lambda S)$ configuration. The equilibration reaction was followed by a much slower rearrangement and cyclisation, giving $(\Lambda R)(\Delta S)$-$[Co(en)(am)]^{2+}$ nearly quantitatively. The half-life of the latter reaction was greater than 5 d at 20 °C and the reaction was therefore completed at an elevated temperature ($t_{\frac{1}{2}} \sim 5$ min at 100 °C). The rearrangement reaction probably involves isomerization of the aqua *mer*-$(\Delta R)(\Lambda S)$ complex to give the *mer*-$(\Lambda R)(\Delta S)$ configuration. The latter isomer then reacts rapidly (see below) to give $(\Lambda R)(\Delta S)$-$[Co(en)(am)]^{2+}$ and was therefore never observed.

The diastereoisomer *mer*-$(\Lambda R)(\Delta S)$-[Co(en)

(amCOOH)Cl]$^{2+}$ released Cl^- similarly, to yield (ΛR)(ΔS)-[Co(en)(am)]$^{2+}$ quantitatively. The reaction had a half-life of ~20 min (25 °C, pH ~ 5), and no intermediate aqua complex was observed. This last observation also implies that the intermediate aqua complex (**12**) cyclises rapidly and quantitatively to the amidine (**8**, Scheme 3).

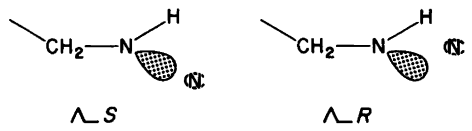
Purity of the [Co(en)(am)]$^{2+}$ diastereoisomers. The diastereoisomers of the [Co(en)(am)]$^{2+}$ cation have different ^{1}H NMR spectra with methyl singlets at slightly different chemical shifts. An estimate of the relative isomer ratio in a mixture of the diastereoisomers could therefore be made by measuring the relative peak areas of the methyl singlets. However, since the peak separation is small, the method is not very accurate and fails to register a small contamination of one isomer by the other. Nevertheless, taking advantage of the fact that the diastereoisomers react at different rates in 6–12 M HCl, it was possible to measure even small amounts of the (ΛR)(ΔS) isomer in a mixture of the isomers (and vice versa). In 6 M HCl, the (ΔR)(ΛS) isomer reacted slowly ($t_{\frac{1}{2}}$ ~ 12 h), yielding *mer*-(ΔR)(ΛS)-[Co(en)(amCOOH)Cl]$^{2+}$, whereas the (ΛR)(ΔS) isomer reacted rapidly ($t_{\frac{1}{2}}$ = 5–10 min) and yielded *mer*-(ΛR)(ΔS)-[Co(en)(amCOOH)Cl]$^{2+}$. This procedure was tested by examining samples of (ΔR)(ΛS)-[Co(en)(am)]Cl_2 artificially contaminated with (ΛR)(ΔS)-[Co(en)(am)]$(ClO_4)_2$ in 6 M DCl. Integration of the methyl singlets for the amidine complex and for the chloro complex, which were well separated, gave a relatively accurate measure of the ratio of the diastereoisomers. Thus, for samples of the pure (ΔR)(ΛS) isomer artificially contaminated with 3.7, 7.5 and 19.9 % of the (ΛR)(ΔS) isomer, respectively, such an analysis gave the values 4.6, 7.9 and 19.7 %. Similarly, using 12 M DCl for samples of pure (ΛR)(ΔS) isomer artificially contaminated with 2.7 and 6.6 % of the (ΔR)(ΛS) isomer, respectively, ^{1}H NMR analysis gave values of 3.4 and 5.8 %. The method described was then used to check the purity of the optically active amidine salt.

Discussion

Cyanide ion addition and intramolecular cyclisation. The results show that CN^- adds to the imine carbon atom on each side of the iminopropionate chelate as in Scheme 2. This is not a surprising result since such coordinated imines have been shown previously to be relatively reactive towards nucleophiles.[3–8] Quite clearly, the coordinated metal ion imposes some iminium ion character on the bound imine. Such studies have also indicated a degree of reversibility for the addition of nucleophiles and notably for the carbanion of nitromethane.[6] Hydroxide ion, for example, in this situation is a good leaving group.[6,11] Also, previously studies on the stabilities of analogous diastereoisomers indicate that they should not differ greatly,[12] certainly not by as much as 9:1. The implication in this analysis is therefore that the preliminary addition of CN^- which occurs on both sides of the planar imine is reversible or nearly reversible. In the early stages of the reaction, a very small singlet at 2 ppm which might be ascribed to the cyanoalanine intermediate was observed in some reaction mixtures, but clearly the concentration of this intermediate is small and the addition of CN^- can be considered as a pre-equilibrium, given the relatively crude kinetic data available. The final product distribution is therefore decided by the relative rates of cyclization to form the amidine products. This last step is clearly established as irreversible.

The overall results indicate CN^- addition to be the preliminary step. No reaction to give the amidine occurred with HCN alone and neither were the cyanoalanine intermediates observed under these conditions. The rate-determining step in the process is therefore probably a coupled deprotonation of one of the apical amine sites with attack of the N-nucleophile at the cyanide carbon centre (Scheme 2). Rapid protonation of the amidine anion follows to yield the quadridentate amidine complex. These steps are consistent with the crude kinetic results which indicate that both CN^- and OH^- are required to effect the reaction. Addition of CN^- can be viewed as a pre-equilibrium when K is small. The region in which saturation arises and the rate law becomes independent of CN^- is not reached under the conditions of the experiments. Studies on the proton exchange for amino acidato complexes[13] of this kind also imply that the exchange rates would be in the region of those we observe for amidine formation.

The stereospecificity in the reaction is an important component [(ΛS)/[(ΛR] = 9). As indicated previously,[12] other types of chemistry



Scheme 6.

would not support the origin of this specificity in the CN^- addition at the imine C center. The implication is, therefore, that the stereochemistry in relation to the entry of the intramolecular N-nucleophile in one activated complex is much preferred to that in the other, and support for such a notion is provided by scale models (Drieding) of the implied activated complexes. The situation is depicted in Scheme 6, in which the orientations of nucleophile and nitrile in the precursor complex are shown for the ΛS and ΛR complexes. In the first instance, one site for deprotonation is clearly ideal for the reaction to occur. In the other, neither site for deprotonation is ideal for attack at the nitrile C atom. The effect need only be quite small: an energy difference of 5.5 kJ mol^{-1} for the two reaction paths accommodates the results. A rather subtle orbital steering of the kind proposed would therefore be adequate to explain the differences.

Finally, it is evident that reduction of the appropriate Co(III) complex and hydrolysis of the amidine would lead readily to a chiral form of the amino methyl melonic acid monoamide, and that the type of chemistry described provides stereospecific routes to such chiral products for substituents other than methyl.

Reactivity of the amidine complexes. We can presume that the reactions of the quadridentate diastereoisomers in base involve carboxylate oxygen-Co bond rupture, and the reaction of the (ΛS) isomer has been studied in some detail. Arguably, the hydrolysis proceeds by the usual conjugate base dissociative path (S_N1CB)[14] as depicted in Scheme 4, leading to Co–O bond rupture. The rate law is consistent with two reactant species arising from the deprotonated and protonated forms of the amidine complex. The dissociation of the carboxylate ion allows rearrangement of the five-coordinate intermediate, before capture of a water molecule, to give the hydroxo tridentate isomer (**10** [*mer*-(ΛS)]) stereospecifically (>95 %). In the process, the amino group of the amino acid has migrated along one edge of the octahedron but the configuration of the Co $(en)_2$ moiety remains unaltered. Such a process would not occur if C–O rupture was the result of base hydrolysis. Both reactants clearly give the same product. The (ΛS)-$[Co(en)(amCOO)Cl]^+$ ion also hydrolyses rapidly in base and generates the same product, so it presumably generates the same five-coordinate intermediate.

The (ΔS) isomer of the quadridentate amidine complex was not studied in the same detail. It hydrolyses in base at approximately the same rate as the (ΛS) isomer, but it generates both the meridional (ΛS) (40 %) and (ΔS) (60 %) isomers throughout the reaction. Also, the (ΔS)-$[Co(en)(amCOO)Cl]^+$ ion hydrolyses rapidly in base to give very largely the (ΔS)-$[Co(en)(amCOO)OH]^+$ ion. It can be inferred from these results that a common five-coordinate intermediate is not generated in these two instances.

The kinetics of the quadridentate amidine reactions in the presence of relatively concentrated HCl were not followed, but there is enough detail in the synthetic results to draw some mechanistic conclusions. Presumably, the rupture of the Co–O(carboxylate) bond is acid-catalysed, as are other simple Co(III)-carboxylate fissions.[15] Water is then largely captured in the process and possibly some Cl^-. However, the bulk of the respective chloro complex which is the final product clearly arises from anation of the *mer*-(ΔS) or (ΛS)-$[Co(en)(amCOOH)(OH_2)]^{3+}$ ions, and that process occurs largely with retention of configuration. It is also evident that these two aqua products slowly cyclise to a common product, the (ΔS)-$[Co(en)(am)]^{2+}$ ion. This implies that the latter is the thermodynamically stable form and that the (ΛS) form is trapped only in the initial condensation reaction; it thereafter rearranges, through dissociation of a monodentate ligand, to the apparently more stable (ΔS) isomer. It is also likely that the rapid cyclisation of the (ΔS) ion occurs by attack of coordinated H_2O on the carboxyl carbon atom.[16] The same route cannot obtain, however, for the (ΛS) isomer, for steric reasons. There, it is required that the (ΛS)-$[Co(en)(amCOOH)(OH_2)]^{3+}$ ion rearranges to the (ΔS) form before cyclisation ensues. This also implies that the (ΛS) isomer should cyclise more slowly than the (ΔS) isomer, which is indeed the case. In fact, the (ΔS) isomer cyclises too rapidly to be observed.

Acknowledgements. This work was supported by a grant from the Danish Natural Science Research Council. We thank Bodil Øby and Bente Nielsen for technical assistance.

References

1. Curtis, N. F. *Coord. Chem. Rev. 3* (1968) 3.
2. Busch, D. H., Farmery, K., Goedken, V., Katovic, V., Melnyk, A. C., Sperati, C. R. and Tokel, N. *Adv. Chem. Ser. 100* (1971) 44.
3. Springborg, J., Geue, R. J., Sargeson, A. M., Taylor, D. and Snow, M. R. *J. Chem. Soc., Chem. Commun.* (1978) 647.
4. Geue, R. J., Snow, M. R., Springborg, J., Herlt, A. J., Sargeson, A. M. and Taylor, D. *J. Chem. Soc., Chem. Commun.* (1976) 285.
5. Golding, B. T., Harrowfield, J. MacB., Robertson, G. B., Sargeson, A. M. and Whimp, P. O. *J. Am. Chem. Soc. 96* (1974) 3697.
6. Harrowfield, J. MacB. and Sargeson, A. M. *J. Am. Chem. Soc. 101* (1979) 1514.
7. Creaser, I. I., Geu, R. J., Harrowfield, J. MacB., Herlt, A. J., Sargeson, A. M. and Springborg, J. *J. Am. Chem. Soc. 104* (1982) 6016; Geue, R. J., Hambley, T. W., Harrowfield, J. MacB., Sargeson, A. M. and Snow, M. R. *J. Am. Chem. Soc. 106* (1984) 5478.
8. Harrowfield, J. MacB., Sargeson, A. M., Springborg, J., Snow, M. R. and Taylor, D. *Inorg. Chem. 22* (1983) 186.
9. Gainsford, A. R. and Sargeson, A. M. *Unpublished work.*
10. Chong, E. K., Harrowfield, J. MacB., Jackson, W. G., Sargeson, A. M. and Springborg, J. *J. Am. Chem. Soc. 107* (1985) 2015 and references therein.
11. Gainsford, A. R., Pizer, R. D., Sargeson, A. M. and Whimp, P. O. *J. Am. Chem. Soc. 103* (1981) 792.
12. Sargeson, A. M. In: Douglas, B. E. and Saito, Y., Eds., *Stereochemistry of Optically Active Transition Metal Compounds, ACS Symp. Ser. 119* (1980) 115 and references therein.
13. Halpern, B., Sargeson, A. M. and Turnbull, K. R. *J. Am. Chem. Soc. 88* (1966) 4630.
14. Tobe, M. L. *Adv. Inorg. Bioinorg. Chem. 2* (1983) 1 and references therein.
15. Dasgupta, T. P. and Tobe, M. L. *Inorg. Chem. 11* (1972) 1011.
16. Boreham, C. J., Buckingham, D. A., Francis, D. J., Sargeson, A. M. and Warner, L. G. *J. Am. Chem. Soc. 103* (1981) 1975.

Received November 7, 1986.