

# Thionyl Chloride Oxidation of Chelated Glycinate in Bis(1,2-ethanediamine)glycinatocobalt(III): Syntheses of *N,O*-bound *N*-Formyl Oxamate and Thiooxamate

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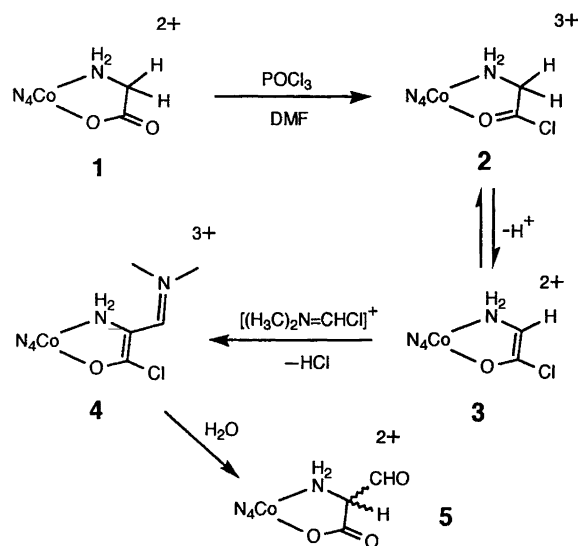
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Addition of  $\Lambda(+)$ <sub>589</sub>-bis(1,2-ethanediamine)glycinatocobalt(III) bis(trifluoromethanesulfonate)trifluoromethanesulfonic acid,  $\Lambda(+)$ <sub>589</sub>-[(en)<sub>2</sub>Co(GlyO)](O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub>·HO<sub>3</sub>SCF<sub>3</sub>, to a solution of SOCl<sub>2</sub> in *N,N*-dimethylformamide (DMF) followed by hydrolysis resulted in oxidation and formylation of the glycinate ligand affording the derivative *N*-formyloxamato complex and elemental sulfur. The crystal structure and absolute configuration of the *N*-formyloxamato complex,  $\Lambda(+)$ <sub>578</sub>-[(en)<sub>2</sub>Co(OOCCONCHO)]ClO<sub>4</sub>, was established by X-ray diffraction [orthorhombic, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>; *a* = 7.871(2), *b* = 8.311(2), *c* = 21.307(4) Å; *V* = 1394 Å<sup>3</sup> and *Z* = 4]. Addition of SOCl<sub>2</sub> to a solution of [(en)<sub>2</sub>Co(GlyO)](O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub>·HO<sub>3</sub>SCF<sub>3</sub> in DMF followed by hydrolysis afforded the thiooxamato complex, [(en)<sub>2</sub>Co(OOCCSNH)]Cl and sulfate. Hydrolysis of the *N*-formyloxamato complex at ca. pH 11.5 gave the oxamato complex, [(en)<sub>2</sub>Co(OOCCONH)]<sup>+</sup>. This complex and the thiooxamato complex each generated the *N*-formyloxamato complex when added to a SOCl<sub>2</sub>/DMF solution. Proposals for the mechanisms of formation of the isolated products are discussed.

Coordination of an  $\alpha$ -amino acid to a metal centre significantly alters the reactivity of the amino acid. The positive charge and Lewis acid character of the metal ion contribute to the activation or deactivation of different functionalities of the amino acid ligand. In general, bidentate *N,O*-coordination of an  $\alpha$ -amino acid to a metal ion activates the proton(s) at the  $\alpha$ -carbon atom, and carbanionic reactivity of this atom towards simple aldehydes was observed at an early stage.<sup>1</sup> Thus, initial metal-promoted carbanion formation was inferred for the reactions of glycinatecopper(II) complexes with acetaldehyde yielding the corresponding threoninato and allo-threoninato complexes in aqueous base.<sup>2</sup>

More recently, even greater activation of the  $\alpha$ -proton(s) was achieved in non-aqueous conditions through *in situ* acid halide formation of amino acidate ligands at the substitutionally inert cobalt(III) centre. For example, the introduction of a formyl group at the  $\alpha$ -carbon atom of chelated glycinate in **1** to form the 2-formylglycinato complex (**5**) was achieved by a Vilsmeier–Haack-type reaction using POCl<sub>3</sub> in *N,N*-dimethylformamide (DMF) as reagents followed by hydrolysis<sup>3–5</sup> (Scheme 1).

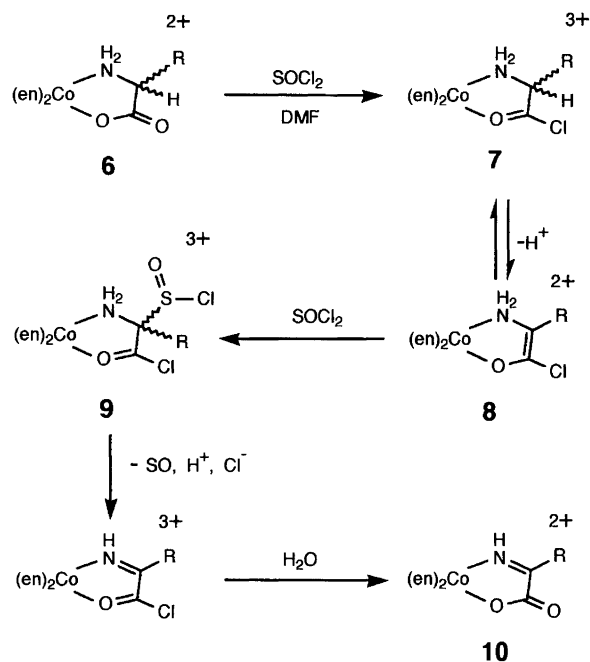


Scheme 1.

In these conditions  $\text{POCl}_3$  and DMF form the *N,N*-dimethylchloromethaniminium ion,  $[(\text{H}_3\text{C})_2\text{N}=\text{CHCl}]^+$ , which is the active formylating agent.<sup>3</sup> From the reaction of the  $[(\text{en})_2\text{Co}(\text{GlyO})]^{2+}$  complex [tren = tris(2-aminoethyl)amine] a stable dimethyliminium acid chloride intermediate, **4** ( $\text{N}_4 = \text{tren}$ ), was isolated and crystallographically characterized.<sup>3</sup> All the evidence supports the reaction mechanism presented in Scheme 1. In the Scheme ' $\text{N}_4$ ' denotes a ligand 'backbone' ('tren' or '(en)<sub>2</sub>', en = 1,2-ethanediamine) providing ligating amine groups at the four remaining coordination sites in the six-coordinate complexes. These backbone ligands remain invariant throughout. Initial formation of the acid chloride **2** would favour reversible loss of an  $\alpha$ -proton leading to the proposed enolate (**3**), which would be resonance stabilized. In a nucleophilic reaction **3** then adds to the formylating agent followed by elimination of HCl to form **4**, which gives the 2-formylglycinato complex (**5**) on hydrolysis. The amine and carboxylate groups of this complex are protected by coordination to the metal while the aldehyde group is available for further synthesis.<sup>4,5</sup> After the completion of such syntheses the amino acid may be readily liberated by reduction of the metal to the cobalt(II) level, which is substitutionally labile.

Substantial prospects for ligand modification along these lines now exist, not least with a view to applications for organic synthesis. In this context, the alternative prospect of creating an electrophilic functionality at the  $\alpha$ -carbon by selective oxidation at this site to the imine level appears particularly attractive. On cobalt(III), *N*-coordinated imines are generally deactivated towards hydrolysis but remain susceptible to attack by carbanionic nucleophiles providing facile routes to a variety of compounds.<sup>6</sup> The oxidation of simple chelated amino acids, excluding glycine, to form imines and other products with  $\text{SOCl}_2$  as the oxidant in DMF have been reported.<sup>7-11</sup> In the reactions elemental sulfur is typically formed as a byproduct, and Scheme 2 gives a general mechanism for the  $\text{SOCl}_2$  oxidation of the  $\alpha$ -amino acidates (**6**) to form the imines (**10**).<sup>9</sup> Again, initial acid chloride formation (**7**) is invoked to facilitate reversible deprotonation of the amino acid ligand generating a resonance-stabilized enolate complex (**8**). Once this has formed,  $\text{SOCl}_2$  may add to afford a transient  $\alpha$ -sulfinyl chloride (**9**). Elimination of HCl and SO ( $\rightarrow \text{S} + \text{SO}_2$ ) followed by hydrolysis of the acid chloride would give the imine (**10**).

This paper describes the reaction of the bis-(1,2-ethanediamine)glycinatocobalt(III) complex,  $[(\text{en})_2\text{Co}(\text{GlyO})]^{2+}$ , with  $\text{SOCl}_2$  in DMF. In this instance, the oxidation goes beyond the imine and additional reactions take place. A preliminary communication has appeared,<sup>12</sup> but considerably more information is now known about the reaction. In a later communication we will report on the synthesis of the glyoxylateimine complex,  $[(\text{en})_2\text{Co}(\text{OOCCH}=\text{NH})]^{2+}$ , derived from  $[(\text{en})_2\text{Co}(\text{GlyO})]^{2+}$  by selective oxidation.



Scheme 2.

## Experimental

Absorption spectra and optical rotations were monitored in water with Cary 118 or Hewlett-Packard 8450A spectrophotometers and a Perkin-Elmer P22 polarimeter ( $\pm 0.002^\circ$ ), respectively; for the latter in 1 dm quartz cells at ca.  $20^\circ\text{C}$ . Within experimental error all listed values for specific rotations (in units of  $^\circ\text{ml g}^{-1}\text{dm}^{-1}$ ) of chiral products did not change on further recrystallization of the product. This was taken as evidence of optical purity. NMR spectra were recorded on a modified (250 MHz) Bruker HX-270 spectrometer and a Jeol JNM-FX 200 instrument using 1,4-dioxane ( $^{13}\text{C}$ ) or sodium 3-(trimethylsilyl)propanesulfonate ( $^1\text{H}$ ) as internal standards. Chemical shifts  $\delta$  (positive downfield) are given in ppm relative to these standards. X-Ray powder diffraction patterns were obtained using a Hagg-Guinier camera XDC 700 with quartz-crystal-monochromated  $\text{Cu K}\alpha$  radiation.

Dimensions of cation exchange columns are given as diameter  $\times$  length, and the Bio-Rad AG 50W-X2 resin was 200–400 mesh. Routine evaporation of solvents was carried out at reduced pressure (ca. 20 Torr) on a Buchi rotary evaporator using a water aspirator and water bath ( $45^\circ\text{C}$ ). All commercial chemicals were analytical grade.  $\text{KO}_3\text{SCF}_3$  was obtained from aqueous  $\text{HO}_3\text{SCF}_3$  and KOH followed by evaporation and recrystallization from ethanol. Chiral  $[(\text{en})_2\text{Co}(\text{OOCCH}_2\text{O})]\text{Br}\cdot\text{H}_2\text{O}$  was obtained by resolution<sup>13</sup> of the racemic chloride salt<sup>14</sup> as described. For quantitative assessment of sulfur(VI) production in selected syntheses excess  $\text{BaCl}_2$  was dissolved in the effluent that resulted during quantitative application on the cation exchange column of the diluted ( $\text{H}_2\text{O}$ )

reaction mixture. The amount of precipitated BaSO<sub>4</sub> was determined gravimetrically by standard procedures.

[(en)<sub>2</sub>Co(OOCCONCHO)]Cl·1.5H<sub>2</sub>O. Thionyl chloride (20 ml, 0.3 mol) was added dropwise with stirring to dry (3 Å molecular sieves) *N,N*-dimethylformamide (100 ml) that had been cooled to <5°C (NaCl/crushed ice mixture). Stirring was continued for 10 min before solid [(en)<sub>2</sub>Co(GlyO)](O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub>·HO<sub>3</sub>SCF<sub>3</sub><sup>15</sup> (21.0 g, 30.0 mmol) was added and dissolved. Soon a massive orange-coloured precipitate formed and the slurry was stirred mechanically for 30 min without cooling at ca. 20°C before it was mixed with crushed ice (0.5 kg). The resulting suspension was subjected to a vacuum (water aspirator) for partial removal of gaseous components (SO<sub>2</sub>). Water-insoluble products (including liberated sulfur) were removed by filtration through Celite. Occasionally, orange crystals (max. 2 g) of poorly soluble [(en)<sub>2</sub>Co(OOCCONCHO)](O<sub>3</sub>SCF<sub>3</sub>)·H<sub>2</sub>O were identified among these products. The diluted filtrate (2 l) was adsorbed on a column of AG 50W-X2 resin (6.5 × 15 cm) in the H<sup>+</sup> form. After washing with water (1 l) the column was eluted with 0.5 M HCl, whereby three orange bands developed. The eluate of the leading (major) band was collected and subsequently evaporated to near dryness. Treatment of the residue with water (20 ml) induced crystallization which was completed by addition of excess ethanol (ca. 30 ml). The solid product (8.7 g) was collected, washed with ethanol and recrystallized by dissolution in boiling water (40 ml) followed by addition of ethanol (20 ml) and slow cooling to 0°C. The racemic product (7.1 g, 66%) of orange crystals was collected, washed with 50% aqueous ethanol, abs. ethanol and diethyl ether and dried in air. Found: Co 16.5; C 23.5; H 5.6; Cl 9.8; N 19.6. Calcd. for CoC<sub>7</sub>H<sub>17</sub>ClN<sub>5</sub>O<sub>4</sub>·1.5H<sub>2</sub>O: Co 16.52; C 23.57; H 5.65; Cl 9.94; N 19.64. <sup>13</sup>C NMR (ca. 8 M DCl): δ 113.6 (CHO); 103.7, 102.6 (C=O); -20.8, -21.6, -22.1, -22.8 (en CH<sub>2</sub>); (D<sub>2</sub>O, ca. pD 7): δ 113.7 (CHO); 102.9 (C=O, superimposed); -21.3, -21.9, -22.6, -23.2 (en CH<sub>2</sub>). <sup>1</sup>H NMR (D<sub>2</sub>O): δ 9.58 (s, CHO); 7.0–6.8, 5.5–4.6, 5.2–5.0 (br, en NH<sub>2</sub>); 3.0–2.6 (br, en CH<sub>2</sub>). UV-visible λ<sub>max</sub>/nm (ε<sub>max</sub>/M<sup>-1</sup> cm<sup>-1</sup>): 488 (135), 217 (22300). The remaining two minor orange to red bands on the column were eluted with 1–2 M and 2–3 M HCl and identified from spectral evidence as the chlorides of [(en)<sub>2</sub>Co(OOCCSNH)]<sup>+</sup> (see below) and [(en)<sub>2</sub>Co(GlyO)]<sup>2+</sup>, respectively.

[(en)<sub>2</sub>Co(OOCCONCHO)](O<sub>3</sub>SCF<sub>3</sub>)·H<sub>2</sub>O. The above chloride salt (0.25 g) was dissolved in water (15 ml) at 50°C followed by addition of KO<sub>3</sub>SCF<sub>3</sub> (0.28 g) dissolved in water (10 ml). From the resulting solution large orange crystals of the poorly soluble trifluoromethanesulfonate (triflate) salt separated. Found: Co 12.9; C 20.6; H 4.1; N 15.3; S 6.6. Calcd. for CoC<sub>8</sub>H<sub>17</sub>F<sub>3</sub>N<sub>5</sub>O<sub>7</sub>S·H<sub>2</sub>O: Co 12.78; C 20.83; H 4.15; N 15.18; S 6.95.

Λ(+)<sub>578</sub>-[(en)<sub>2</sub>Co(OOCCONCHO)]Cl·2/3H<sub>2</sub>O. This chiral complex was synthesized from Λ(+)<sub>589</sub>-[(en)<sub>2</sub>Co(GlyO)](O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub>·HO<sub>3</sub>SCF<sub>3</sub><sup>15</sup> analogously to the racemic chloride. Found: Co 17.3; C 24.4; H 5.4; N 20.5; Cl 11.2. Calcd. for CoC<sub>7</sub>H<sub>17</sub>ClN<sub>5</sub>O<sub>4</sub>·2/3H<sub>2</sub>O: Co 17.25; C 24.61; H 5.41; N 20.50; Cl 10.38. Specific rotations (0.02%, in H<sub>2</sub>O): [α]<sub>578</sub> 560, [α]<sub>546</sub> 890, [α]<sub>436</sub> -1200, [α]<sub>365</sub> -1190.

Λ(+)<sub>578</sub>-[(en)<sub>2</sub>Co(OOCCONCHO)]ClO<sub>4</sub>. Crystals were grown from a solution of the chiral chloride (0.2 g) in water (50 ml) by slow (several hours) addition of saturated NaClO<sub>4</sub> solution (ca. 10 ml). The isolated crystals were suitable for an X-ray study. Found: Co 15.0; C 21.4; H 4.3; N 17.8. Calcd. for CoC<sub>7</sub>H<sub>17</sub>ClN<sub>5</sub>O<sub>8</sub>: Co 14.97; C 21.36; H 4.35; N 17.79. Specific rotations (0.03%, in H<sub>2</sub>O): [α]<sub>578</sub> 475; [α]<sub>546</sub> 760; [α]<sub>463</sub> -1040; [α]<sub>365</sub> -1040.

Products from the reaction of SOCl<sub>2</sub> with [(en)<sub>2</sub>Co(GlyO)](O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub> in DMF. Thionyl chloride (10.7 ml, 150 mmol) was added dropwise (over 15 min) to a stirred solution of [(en)<sub>2</sub>Co(GlyO)](O<sub>3</sub>SCF<sub>3</sub>)<sub>2</sub>·0.33HO<sub>3</sub>SCF<sub>3</sub> (18.5 g, 30 mmol) in DMF (100 ml) cooled to ca. 5°C. During this addition, an orange precipitate formed in the reaction mixture. After stirring and continued cooling for 50 min the mixture was poured onto crushed ice (0.5 kg) and the resulting solution subjected to vacuum (water aspirator) for partial removal of gaseous components prior to filtration through Celite. The filtrate was diluted with water to 4 l and was passed through an AG 50W-X2 column (7 × 27 cm) in the H<sup>+</sup> form. The orange effluent from this passage which contained neutral or negatively charged species, was collected as band 1. The positively charged complexes appeared as a narrow band at the top of the column and on elution, initially with 0.5 M HCl, this band separated into four orange bands, each of which were eluted and collected in the following way: band 2 (1 M HCl), band 3 (2 M HCl), band 4 (2–3 M HCl) and band 5 (3–4 M HCl). *Band 1* (20%): On standing at ca. 20°C (days) fine crystals separated from the eluate. These were collected, washed with water, ethanol and diethyl ether and dried in air. Found: Co 14.3; C 17.5; H 4.5; N 16.6; S 14.0. Calcd. for CoC<sub>6</sub>H<sub>22</sub>N<sub>5</sub>O<sub>8</sub>S<sub>2</sub>: Co 14.19; C 17.35; H 5.34; N 16.86; S 15.44. *Band 2* (<2%) was not always observed but proved to be [(en)<sub>2</sub>Co(OOCCONCHO)]Cl. *Band 3* (20%): On standing at ca. 20°C for several days, large red conglomerate crystals of [(en)<sub>2</sub>Co(OOCCSNH)]Cl separated which were collected, washed with EtOH, diethyl ether and dried. Found: Co 18.6; C 22.3; H 5.4; Cl 11.3; N 21.9; S 9.9. Calcd. for CoC<sub>6</sub>H<sub>17</sub>ClN<sub>5</sub>O<sub>2</sub>S: Co 18.55; C 22.69; H 5.39; Cl 11.16; N 22.05; S 10.09. <sup>13</sup>C NMR (ca. 0.1 M HO<sub>3</sub>SCF<sub>3</sub> in ca. 90% D<sub>2</sub>O): δ -21.2, -21.9, -22.1, -22.9 (en CH<sub>2</sub>). UV-visible λ<sub>max</sub>/nm (ε<sub>max</sub>/M<sup>-1</sup> cm<sup>-1</sup>): 480 (206), 309 (11400). *Band 4* (50%): The eluate was

concentrated to dryness and the residue identified as  $[(en)_2Co(GlyO)]Cl_2$  on the basis of spectral evidence. *Band 5* (<2%): The eluate was concentrated to dryness and the residue redissolved in water. Some elemental sulfur separated from this solution, but no further attempts were made to identify the compound(s).

$[(en)_2Co(OOCCSNH)]O_3SCF_3 \cdot H_2O$ . This compound was obtained by dropwise addition (over days) of saturated  $KO_3SCF_3$  to a solution of the chloride,  $[(en)_2Co(OOCCSNH)]Cl$ , (0.11 g) in 1 mM HCl (30 ml). The crystals (0.14 g) thus produced were used for a crystallographic study.<sup>15</sup> Found: C 18.9; H 4.4; F 11.8; N 15.4; S 12.2. Calcd. for  $CoC_7H_{17}F_3N_5O_5S_2 \cdot H_2O$ : C 18.71; H 4.26; F 12.69; N 15.59; S 14.27.

$[(en)_2Co(OOCCONH)]Cl \cdot H_2O$ .  $[(en)_2Co(OOCCONCHO)]Cl \cdot 1.5H_2O$  (4.8 g, 13 mmol) in 0.25 l 0.20 M  $Et_3N/Et_3NHCl$  buffer, pH 11.5, was left with vigorous stirring for 1/2 h. After acidification with 12 M HCl (7.0 ml) the solution was diluted with 1 l water and adsorbed on a column of AG 50W-X2 resin (6.5 × 14 cm) in the  $H^+$  form. After washing with ca. 1 l 0.5 M HCl to remove  $[Et_3NH]^+$  ions and a minor red to orange band, the main orange band was eluted with 2.0 M HCl and the eluate concentrated to dryness. Treatment of the glassy residue with water (10 ml) induced crystal formation which was completed by subsequent gradual addition of ethanol (ca. 20 ml). The crude product (4.2 g) was washed with ethanol and diethyl ether and crystallized from 50% ethanol (30 ml) yielding orange crystals (3.60 g, 82%). These were washed with ethanol and diethyl ether before drying in air. Found: Co 19.0; C 22.2; H 6.1; N 21.9. Calcd. for  $CoC_6H_{17}ClN_5O_3 \cdot H_2O$ : Co 18.44; C 22.55; H 5.99; N 21.91.  $^{13}C$  NMR ( $D_2O$ ):  $\delta$  105.7, 101.1 (CO); -21.1, -21.8, -22.1, -23.0 (en  $CH_2$ ). UV-visible  $\lambda_{max}/nm(\epsilon_{max}/M^{-1} cm^{-1})$ : 486 (137), 344 (84), 206 (18100).

$\Lambda(+)_578^-[(en)_2Co(OOCCONH)]Cl \cdot H_2O$ . This complex was obtained from  $\Lambda(+)_578^-[(en)_2Co(OOCCONCHO)]Cl \cdot 2/3H_2O$  as described above for the racemate. Found: Co 18.9; C 22.3; H 6.1; N 21.7. Specific rotations (0.02%, in water):  $[\alpha]_{578}$  1030;  $[\alpha]_{546}$  1660;  $[\alpha]_{436}$  -2140;  $[\alpha]_{364}$  -1950;  $[\alpha]_{313}$  -2250. Crystalline samples of the racemic and chiral chloride monohydrates gave rise to identical X-ray powder diffraction patterns implying that both salts crystallize in the same acentric space group ('spontaneous resolution').

*Formylation of the  $[(en)_2Co(OOCCONH)]^+$  (oxamato) and  $[(en)_2Co(OOCCSNH)]^+$  (thiooxamato) complexes.* In small-scale experiments the oxamato and thiooxamato complexes were each formylated to form the *N*-formyl-oxamato complex under essentially the same conditions as used above. Racemic  $[(en)_2Co(OOCCONH)]Cl \cdot H_2O$

(0.34 g, 1.0 mmol) was added to an ice-cold solution of  $SOCl_2$  (0.7 ml) and DMF (5 ml) and the mixture was stirred for 30 min. Workup and isolation procedures were carried out as described for the *N*-formyl-oxamato complex. The major product was identified as  $[(en)_2Co(OOCCONCHO)]Cl \cdot 1.5H_2O$  from the powder diffraction pattern and the absorption spectrum. Likewise,  $[(en)_2Co(OOCCSNH)][(O_3SCF_3) \cdot H_2O]$  (0.15 g, 0.3 mmol) was added to an ice-cold  $SOCl_2/DMF$  (2 ml/20 ml) mixture, and the resulting clear orange solution was stirred at ca. 20 °C for 30 min. When mixing with ice (0.2 kg) some elemental sulfur precipitated. The aqueous solution was partly degassed (by vacuum), filtered (Celite) and adsorbed on an AG 50W-X2 column (4 × 11 cm) in the  $H^+$  form. Elution with 0.5–1.0 M HCl revealed two major orange bands which were identified spectrophotometrically as containing  $[(en)_2Co(OOCCONCHO)]^+$  (leading) and  $[(en)_2Co(OOCCSNH)]^+$ , respectively. The former was also identified by elemental analysis after crystallization.

*Reaction of  $[(en)_2Co(OOCCSNH)]Cl$  with  $H_2O_2$ .* To a solution of  $[(en)_2Co(OOCCSNH)]Cl$  (25 mg, 80  $\mu$ mol) in 5 ml  $H_2O$  was added 2 ml 30%  $H_2O_2$ . After standing at ca. 20 °C for 20 h the solution was diluted and adsorbed on an AG 50W-X2 column (2 × 7 cm). Elution with 2 M HCl revealed one band due to  $[(en)_2Co(OOCCONH)]Cl$  identified by its UV-vis absorption and  $^{13}C$ -NMR spectra.

*Hydrolysis of  $\Lambda(+)_578^-[(en)_2Co(OOCCONCHO)]Cl \cdot 2/3H_2O$  in 1 M NaOH.* Under continuous stirring with a magnetic bar the salt (0.34 g, 1.0 mmol) was rapidly added to 1.0 M NaOH (5.0 ml). After 60 s, 0.5 ml 12 M HCl was added followed by dilution to 0.5 l with water. The resulting solution was sorbed on a column (5 × 21 cm) of  $Na^+$ -form SP Sephadex C-25 resin which was washed with water and left overnight before elution with 0.20 M HCl. The elution pattern displayed four separate bands, a leading red (1) followed by an orange (2) and two minor red bands. The eluates of bands 1 ( $\Lambda(+)_589^-[(en)_2Co(OOCCOO)]Cl$ ) and 2 ( $\Lambda(+)_578^-[(en)_2Co(OOCCONH)]Cl$ ), which together accounted for at least 95% of the products, were each collected for quantitative assessment. Optical rotations and absorption spectra of these solutions indicated at least 97% retention of chirality.

*Crystal structure determination of  $\Lambda(+)_578^-[(en)_2Co(OOCCONCHO)]ClO_4$ .* Relevant crystal data are summarized in Table 1. A tabular, orange crystal of dimensions 0.41 × 0.16 × 0.07 mm with tabular faces 01(-1) and 0(-1)1 was mounted with the rotational axis parallel to the longest edge and the *a*-axis. Precession and

Table 1. Crystal data for  $\Lambda(+)$ <sub>589</sub> - [Co(en)<sub>2</sub>(*N*-formyloxamato)]ClO<sub>4</sub>.

Formula	CoC <sub>7</sub> H <sub>17</sub> ClN <sub>5</sub> O <sub>8</sub>
Formula weight/g mol <sup>-1</sup>	393.63
Space group	Orthorhombic <i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub> (No. 19)
<i>a</i> /Å	7.871(2)
<i>b</i> /Å	8.311(2)
<i>c</i> /Å	21.307(4)
<i>V</i> /Å <sup>3</sup>	1394
<i>d</i> <sub>obsd</sub> /g cm <sup>-3</sup> (295 ± 2 K)	1.79(1)
<i>d</i> <sub>calcd</sub> /g cm <sup>-3</sup> (105 ± 5 K)	1.874
<i>Z</i>	4
$\mu$ /cm <sup>-1</sup>	14.68
<i>F</i> (000)/electrons	808

Weissenberg photographs uniquely determined the space group. Intensity data were collected on an Enraf-Nonius CAD4 diffractometer at 105 ± 5 K with graphite-crystal-monochromated Mo *K*α radiation ( $\lambda = 0.71073$  Å) using the  $\omega$ -scan technique with  $\Theta$  varied between 1 and 32° (0 ≤ *h* ≤ 11, 0 ≤ *k* ≤ 12, 0 ≤ *l* ≤ 31). Determination of lattice constants, scanning [scan range (1.2 + 0.34 tan  $\Theta$ )°; max. scan speed 5.5° min<sup>-1</sup>; max. scan time 180 s], and checking of centering and the intensities of three reference reflections (400, 040 and 004) were performed essentially as described before.<sup>16</sup> The reference reflections displayed a gradual intensity loss averaging to 2.6% over the entire period of exposure and the data were corrected assuming this loss to have increased linearly with exposure time. All computations were performed with the Enraf-Nonius Structure Determination Package (1982 version) on a PDP11/23 computer. A total of 2752 reflections, all unique, were measured and reduced, including corrections for Lorentz and polarization effects and for absorption (transmission coefficients between 0.72 and 0.88). 2190 reflections for which  $I \geq 2\sigma(I)$  were retained in the final structure analysis.

The Co and Cl atoms were located using the MULTAN 11/82 package and further structure solution and refinement was carried out as described<sup>16</sup> keeping H-atom isotropic thermal parameters fixed at  $B = 1.5$ . After the final refinement cycle the *R* values were  $R = 0.030$  and  $R_w = 0.033$ . No parameter was shifted more than 0.11σ and a final Fourier synthesis had the 10 largest residuals between 0.3 and 0.4 e Å<sup>-3</sup>. The  $\Lambda$  absolute configuration of the complex cation was confirmed applying the Rogers test<sup>17</sup> as outlined before.<sup>16</sup> The calculations gave  $R = 0.031$ ,  $R_w = 0.034$ , assuming the  $\Lambda$  absolute configuration, and  $R = 0.043$ ,  $R_w = 0.051$  for the  $\Delta$  absolute configuration, which clearly reflect the former to represent the better model.

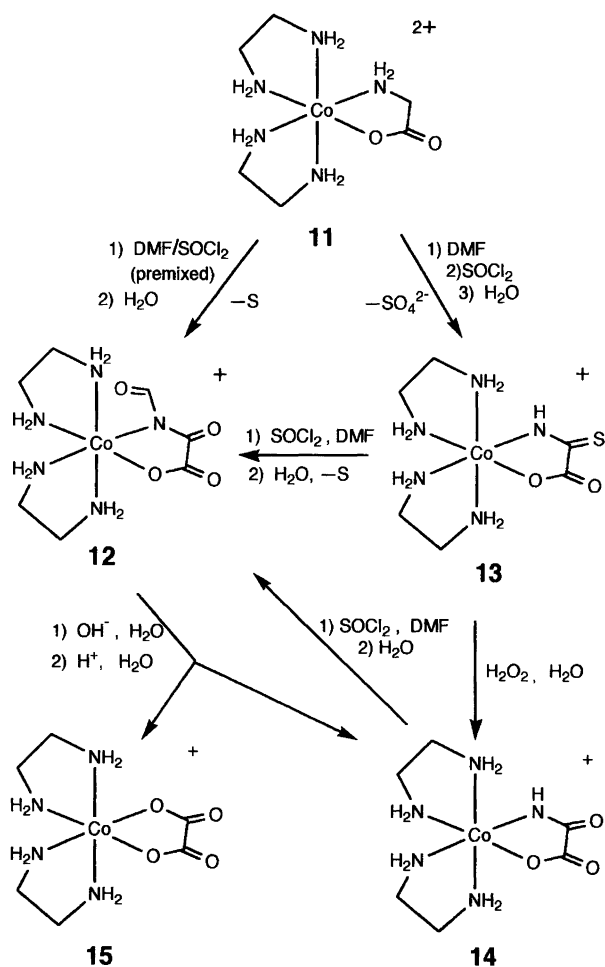
Table 2 lists atomic fractional coordinates for all atoms. Tables of anisotropic thermal parameters and structure factor amplitudes are available from one of the authors (A. H.).

Table 2. Atomic fractional coordinates.

Atom	<i>x</i>	<i>y</i>	<i>z</i>
Co	0.51500(4)	0.39150(5)	0.38324(2)
N1	0.3054(3)	0.3665(3)	0.3346(1)
N2	0.6722(3)	0.3725(3)	0.3125(1)
N3	0.5439(3)	0.1608(3)	0.3924(1)
N4	0.7022(3)	0.4288(3)	0.4431(1)
N5	0.5021(3)	0.6264(3)	0.3784(1)
O1	0.3633(2)	0.3980(3)	0.45402(8)
O2	0.0861(3)	0.4042(3)	0.47861(9)
O3	0.0157(3)	0.3949(3)	0.35223(9)
O4	0.3880(3)	0.2998(3)	0.23487(9)
C1	0.2040(3)	0.3979(4)	0.4408(1)
C2	0.1617(3)	0.3869(4)	0.3705(1)
C3	0.2764(4)	0.3192(4)	0.2741(1)
C4	0.7153(4)	0.1995(4)	0.3002(1)
C5	0.7036(3)	0.1099(4)	0.3617(1)
C6	0.7462(4)	0.6036(4)	0.4451(1)
C7	0.5825(4)	0.6945(4)	0.4359(1)
C11	0.35316(8)	0.08907(9)	0.86688(3)
O11	0.3694(3)	-0.0420(3)	0.9108(1)
O12	0.3456(3)	0.2382(3)	0.9012(1)
O13	0.4924(3)	0.0909(4)	0.8246(1)
O14	0.1960(3)	0.0708(3)	0.8320(1)
H201	0.762(5)	0.423(5)	0.319(2)
H202	0.630(4)	0.412(5)	0.277(2)
H301	0.542(5)	0.139(5)	0.431(2)
H302	0.453(4)	0.114(5)	0.377(1)
H401	0.662(4)	0.398(5)	0.483(2)
H402	0.795(4)	0.375(5)	0.441(2)
H501	0.393(5)	0.654(5)	0.377(2)
H502	0.561(5)	0.673(4)	0.348(2)
H31	0.159(5)	0.299(5)	0.260(2)
H41	0.830(5)	0.195(5)	0.282(2)
H42	0.625(4)	0.157(5)	0.271(2)
H51	0.796(5)	0.139(5)	0.388(2)
H52	0.694(5)	0.002(4)	0.354(2)
H61	0.825(4)	0.628(5)	0.413(2)
H62	0.805(5)	0.633(5)	0.486(2)
H71	0.505(5)	0.671(4)	0.468(2)
H72	0.600(5)	0.810(5)	0.434(2)

## Results

Reagent-product relationships are summarized in Scheme 3. Addition of [(en)<sub>2</sub>Co(GlyO)]<sup>2+</sup> (**11**) to a SOCl<sub>2</sub>/DMF mixture at ≤ 5°C (initially) and stirring for 30 min as the mixture slowly warmed to ca. 20°C followed by addition of crushed ice yielded the *N*-formyloxamato complex, [(en)<sub>2</sub>Co(OOCCONCHO)]<sup>+</sup> (**12**), as the major product (66%). The identity of this complex cation was established by an X-ray crystallographic study of its perchlorate salt. The *N,O*-bound ligand formally constitutes doubly deprotonated *N*-formyloxamic acid, here referred to as '*N*-formyloxamate'. Elemental sulfur separated upon addition of water to the reaction mixture. The ionic sulfate produced during the reaction amounted to less than 2 mol %. Ion-exchange chromatography of the soluble products revealed a major (leading) band of *N*-formyloxamato complex (**12**) in addition to two minor bands of the thiooxamato complex, [(en)<sub>2</sub>Co(OOCCSNH)]<sup>+</sup> (**13**) (see below), and unreacted



Scheme 3.

starting material (**11**), respectively. Occasionally, crystals of the poorly soluble triflate monohydrate salt, [(en)<sub>2</sub>Co(OOCCONCHO)]O<sub>3</sub>SCF<sub>3</sub>·H<sub>2</sub>O, formed in the reaction mixture.

Changing the reaction conditions [ $T \leq 5^\circ\text{C}$  throughout, prolonged reaction time, lower SOCl<sub>2</sub>/complex ratio (ca. 5) and with reversed order of reagent addition] led to, at most, 20% of the thiooxamato complex (**13**). Under these conditions the *N*-formyloxamato complex (**12**) was almost absent ( $\leq 2\%$ ) among the products after ca. 1 h of reaction time, but a significant amount of unreacted starting material, **11** (ca. 50%), remained after quenching with water. Overall, no significant amount of sulfur was liberated, but the amount of SO<sub>4</sub><sup>2-</sup> produced in one experiment corresponded to ca. 17 mol %. With increased reaction times (ca. 3 h) an increase in the yield of *N*-formyloxamato complex (**12**) and elemental sulfur upon water quenching was observed. In addition to these complexes (**11**–**13**) chromatography of the products revealed two additional orange species, one (ca. 20%) presumed to be neutral and the other ( $\leq 2\%$ ) of higher charge ( $> 3+$ ). When their eluates were concentrated and re-

dissolved in water, separation of sulfur was observed in each case. However, the eluate of the neutral species slowly deposited solid material and the elemental analysis of this product implied a Co:S ratio of 1:2. Neither product was further characterised.

Attempts to concentrate the eluate containing the thiooxamato complex (**13**) led only to decomposition and liberation of sulfur. However, if the eluate was left some days crystals of the chloride, [(en)<sub>2</sub>Co(OOCCSNH)]Cl, slowly precipitated. This product was converted into the less soluble triflate, [(en)<sub>2</sub>Co(OOCCSNH)]O<sub>3</sub>SCF<sub>3</sub>·H<sub>2</sub>O, and crystals of this were used for an X-ray crystallographic study which confirmed the identity of the complex cation. The detailed crystallographic results are published separately.<sup>15</sup>

The oxamato complex, [(en)<sub>2</sub>Co(OOCCONH)]<sup>+</sup> (**14**), was readily obtained by H<sub>2</sub>O<sub>2</sub> oxidation of the thiooxamato complex (**13**) in water or by base hydrolysis (Et<sub>3</sub>N/Et<sub>3</sub>NH<sup>+</sup> buffer, ca. pH 11.5) of the *N*-formyloxamato complex (**12**). In 1 M NaOH the *N*-formyloxamato complex (**12**) also gave significant amounts of oxalato complex, [(en)<sub>2</sub>Co(OOCCOO)]<sup>+</sup> (**15**), when the base treatment was rapidly followed by acid quenching and incubation for 12 h. Thus, chiral *N*-formyloxamato complex (**12**) in 1 M NaOH produced both **14** and **15** in comparable amounts optically pure ( $\geq 97\%$ ). The formation of the oxalato complex (**15**) from the *N*-formyloxamato complex (**12**) requires Co–N bond rupture at some point along the reaction path. Quantitative experiments indicated that the oxalato complex (**15**) was favoured with increasing initial base concentration. However, if acid quenching was omitted and the reaction was quenched by dilution with water followed by chromatography, no oxalato complex (**15**) was observed. Instead, after 12 h in base the end products were [(en)<sub>2</sub>Co(OOCCONH)]<sup>+</sup> (**14**) and [(en)<sub>2</sub>Co(OH)<sub>2</sub>]<sup>+</sup>. The mechanistic aspects of this base-induced reaction are being pursued.

The oxamato complex (**14**) was never detected in the reaction mixtures prepared from the glycinate complex (**11**), SOCl<sub>2</sub> and DMF. On elution of products with HCl it would have appeared as a separate band eluting after the thiooxamato (**13**) band and prior to the glycinate (**11**) band on AG 50W-X2 resin.

The *N*-formyloxamato complex (**12**) was also obtained from the oxamato (**14**) and thiooxamato (**13**) complexes when each of these were subjected to Vilsmeier–Haack-type reaction conditions (SOCl<sub>2</sub>/DMF mixture) followed by aqueous hydrolysis. In the case of the thiooxamato complex (**13**) elemental sulfur was observed after the hydrolysis. The transformation of the oxamato complex (**14**→**12**) formally corresponds to *N*-formylation of the oxamate ligand. However, for the thiooxamato complex (**13**) the results imply that, in addition, the reaction (**13**→**12**) also involves replacement of the thiocarbonyl sulfur atom by oxygen. This is consistent with the observation that elemental sulfur separated.

Above ca. pH 3 the *N*-formyloxamato complex (**12**), the thiooxamato complex (**13**) and the oxamato complex (**14**) are all singly charged, their *N*-bound amide ligands each having lost a proton. In high acid (HCl) concentrations, spectral changes with varying [H<sup>+</sup>] are consistent with reprotonation. Presumably such protonation takes place at the amide *exo*-oxygen or sulfur atoms.<sup>20</sup> Analyses of the spectral changes gave approximate p*K*<sub>a</sub> values of -0.5 for [(en)<sub>2</sub>Co(OOCCONCHO(H))]<sup>2+</sup>, -0.3 for [(en)<sub>2</sub>Co(OOCCSNH(H))]<sup>2+</sup> and 0.7 for [(en)<sub>2</sub>Co(OOCCONH(H))]<sup>2+</sup>. These p*K*<sub>a</sub> values are consistent with the observed elution order of the complexes on AG 50W-X2 resin (HCl eluent) where the *N*-formyloxamato complex elutes first.

*Structure of Λ(+)<sub>578</sub>-[(en)<sub>2</sub>Co(OOCCONCHO)]ClO<sub>4</sub>.* A perspective view of the cation is given in Fig. 1; selected interatomic distances and angles are listed in Table 3. The tris(bidentate) complex displays Λ absolute configuration and the ethylenediamine rings adopt the δ conformation. The third ligand, doubly deprotonated *N*-formyloxamic acid (*N*-formyloxamate<sup>-</sup>), is coordinated to the metal center by the nitrogen atom and one carboxylate oxygen atom and thus constitutes an *N,O*-bound imidate. However, the Co-N1 distance of 1.960(2) Å is significantly longer than known Co-N distances (1.87–1.91 Å) of amido<sup>18,19</sup> and thioamido<sup>15</sup> analogues. In the latter systems a decreased N-C(carbonyl) distance compared with free amide or thioamide is also observed. Here, the N1-C2 and N1-C3 bond lengths of 1.376(3) and 1.367(4) Å, respectively, are longer than the average N-C(carbonyl) distance (1.33 Å) in free peptides.<sup>20</sup> The formyl group is oriented in such a way that it allows some degree of intramolecular hydrogen bonding with H2O2 of the *cis*-amine group (N2), Table 4, thus representing the

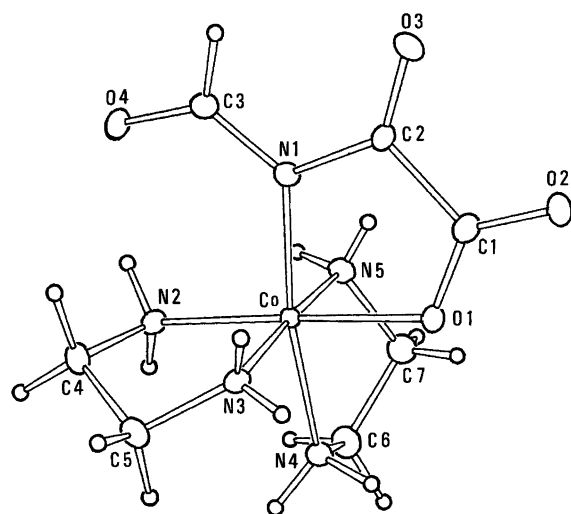


Fig. 1. Structure of the cation in  $\Lambda(+)$ <sub>578</sub>-[(en)<sub>2</sub>Co(OOCCONCHO)]ClO<sub>4</sub> showing the atomic numbering.

Table 3. Selected interatomic distances (in Å) and bond angles (°).

Co-N1	1.960(2)	O3-C2	1.215(3)
Co-N2	1.957(2)	O4-C3	1.224(4)
Co-N3	1.941(3)	C1-C2	1.538(4)
Co-N4	1.973(2)	N2-C4	1.501(4)
Co-N5	1.957(2)	N3-C5	1.480(4)
Co-O1	1.925(2)	C4-C5	1.509(4)
N1-C2	1.376(3)	N4-C6	1.495(4)
N1-C3	1.367(4)	N5-C7	1.491(4)
O1-C1	1.285(3)	C6-C7	1.507(4)
O2-C1	1.230(3)		
N1-Co-N2	96.7(1)	N4-Co-O1	87.27(9)
N1-Co-N3	92.7(1)	N5-Co-O1	88.9(1)
N1-Co-N3	170.9(1)	Co-N1-C2	112.6(2)
N1-Co-N5	92.0(1)	Co-N1-C3	132.1(2)
N1-Co-O1	83.98(9)	C2-N1-C3	115.0(2)
N2-Co-N3	85.6(1)	Co-N1-C3	115.7(2)
N2-Co-N4	92.2(1)	O1-C1-O2	126.3(3)
N2-Co-N5	94.2(1)	O1-C1-C2	115.1(2)
N2-Co-O1	176.8(1)	O2-C1-C2	118.5(2)
N3-Co-N4	90.1(1)	N1-C2-O3	127.3(2)
N3-Co-N5	175.3(1)	N1-C2-C1	111.8(2)
N3-Co-O1	91.2(1)	O3-C2-C1	120.9(2)
N4-Co-N5	85.2(1)	N1-C3-O4	124.2(3)

Table 4. Hydrogen-bonding contact distances.

Atoms			<i>d</i> (N-H...O) /Å	<i>d</i> (H...O) /Å	Angle/°
N2	H201	O3 <sup>a</sup>	2.840(3)	2.13(4)	143(4)
N2	H202	O4	2.848(3)	2.30(4)	119(3)
N2	H202	O14 <sup>b</sup>	3.121(3)	2.38(4)	141(3)
N3	H301	O2 <sup>b</sup>	2.821(3)	1.99(3)	169(4)
N3	H302	O14 <sup>c</sup>	2.990(4)	2.16(4)	158(4)
N4	H401	O11 <sup>d</sup>	3.175(3)	2.33(4)	149(4)
N4	H402	O2 <sup>a</sup>	3.123(3)	2.44(4)	137(4)
N5	H501	O12 <sup>e</sup>	2.999(4)	2.15(4)	161(3)
N5	H502	O4 <sup>f</sup>	2.942(3)	2.09(4)	160(4)

<sup>a</sup>(*x*+1, *y*, *z*). <sup>b</sup>(0.5+*x*, 0.5-*y*, 1-*z*). <sup>c</sup>(0.5-*x*, -*y*, *z*-0.5). <sup>d</sup>(1-*x*, 0.5+*y*, 1.5-*z*). <sup>e</sup>(0.5-*x*, 1-*y*, *z*-0.5). <sup>f</sup>(1-*x*, 0.5+*y*, 0.5-*z*).

*Z* isomer with respect to the N-C(formyl)-bond. The ligand is somewhat twisted away from planarity. The Dunitz amide deformation parameters<sup>21</sup> for the N1-C2 amide linkage are  $\chi_C = 0.6^\circ$ ,  $\chi_N = -5.5^\circ$  and  $\tau = -168.8^\circ$  as calculated from the torsion angles with respect to this bond. The crystal structure is characterised by extensive hydrogen bonding and all amine hydrogen atoms are involved in such contacts, Table 4.

## Discussion

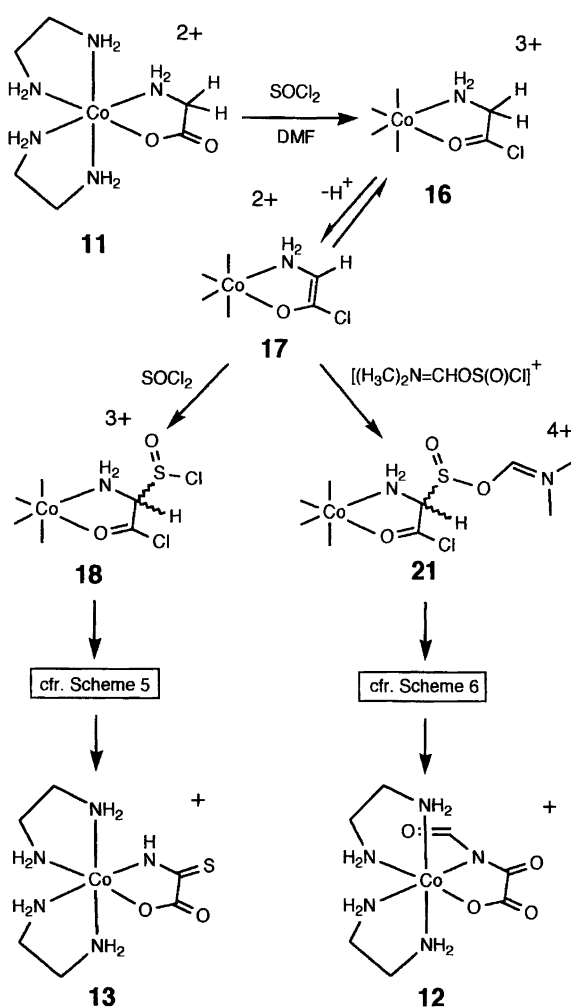
Oxidations by thionyl chloride in DMF of other  $\alpha$ -amino acidato complexes, all carrying tertiary  $\alpha$ -carbon centres, have been described.<sup>7-10</sup> These reactions and the surprising oxidation and formylation reactions of the glycinate complex (**11**) proceed under similar conditions but give different products. The  $\alpha$ -amino acidato complexes with

tertiary  $\alpha$ -carbon centres generally produced the corresponding  $\alpha$ -imino acidato complexes (Scheme 2) whereas the glycinate complex (**11**) was carried to a higher oxidation level to give mainly the *N*-formyloxamato (**12**) or thiooxamato (**13**) complexes (Scheme 3).

For the glycinate system the product distribution appears to depend largely on the order of addition of reactants. Thus, with premixed  $\text{SOCl}_2$ -DMF solution, the *N*-formyloxamato complex (**12**) was the dominant product (66% isolated yield) accompanied by elemental sulfur and negligible amounts of ionic sulfate and thiooxamato complex (**13**). Qualitatively, the amount of elemental sulfur formed seemed to parallel the amount of *N*-formyloxamato complex (**12**). Conversely, with  $\text{SOCl}_2$  added after dissolution of the glycinate complex (**11**) in DMF very little *N*-formyloxamato complex (**12**) (ca. 2%) but more thiooxamato complex (**13**) (ca. 20%) featured among the products. Overall, the amount of ionic sulfate produced crudely matched the amount of thiooxamato complex (**13**) formed. This pattern was also seen for the similar and somewhat cleaner reaction of the related sarcosinato complex,  $[(\text{en})_2\text{Co}(\overline{\text{OOCCH}_2\text{NHCH}_3})]^{2+}$ , to form the *N*-methylthiooxamato complex,  $[(\text{en})_2\text{Co}(\overline{\text{OCCSNCH}_3})]^+$  (77%) and sulfate (70%).<sup>11</sup>

The dependence of the product ratios on the addition order may be rationalized in terms of different reacting species. Solutions of thionyl chloride in DMF are reported<sup>22-26</sup> to generate almost exclusively the *N,N*-dimethylchlorosulfonyloxymethaniminium chloride,  $[(\text{H}_3\text{C})_2\text{N}=\text{CHOS}(\text{O})\text{Cl}]\text{Cl}$ , at a measurable rate.<sup>27</sup> On heating, the iminium ion reversibly forms the *N,N*-dimethylchloromethaniminium ion,  $[(\text{H}_3\text{C})_2\text{N}=\text{CHCl}]^+$ , with liberation of  $\text{SO}_2$ .<sup>23</sup> Thus, in the premixed  $\text{SOCl}_2$ /DMF solution the  $[(\text{H}_3\text{C})_2\text{N}=\text{CHOS}(\text{O})\text{Cl}]^+$  ion would be the dominant reagent at the time of complex addition. Conversely, with complex added before  $\text{SOCl}_2$ , complex and solvent (DMF) should compete for added  $\text{SOCl}_2$ . The implication is that the complex (**11**) competes so efficiently that in this latter case  $\text{SOCl}_2$  becomes the reagent.

Below, mechanisms for the two paths leading to the thiooxamato complex (**13**) and the *N*-formyloxamato complex (**12**), respectively, are proposed (Scheme 4). In both instances, the first step is attributed to the formation of an acid chloride (**16**). Thionyl chloride is a standard chlorinating agent and crystallographic evidence for the formation of such chelated amino acid chlorides (**16**) is provided by the reaction of  $[(\text{tren})\text{Co}(\text{GlyO})]^{2+}$  with  $\text{POCl}_3$  in DMF (Scheme 1).<sup>3</sup> Such  $\alpha$ -amino acid chlorides (**16**) are activated towards deprotonation at the  $\alpha$ -carbon resulting in formation of an enolate species (**17**). Similar enolate formation is generally inferred for Hell-Volhard-Zelinskii-type reactions at the  $\alpha$ -carbon of simple carboxylic halides,<sup>28,29</sup> but in **17** the enolate would be further stabilized by the metal. Compelling evidence for the proton loss is also offered by related complex systems under similar conditions. Thus, for the reaction of



Scheme 4.

$[(\text{tren})\text{Co}(\text{GlyO})]^{2+}$  with  $\text{POCl}_3$  in DMF (Scheme 1) further reaction of **3** involved electrophilic attack at the  $\alpha$ -carbon rather than at the N atom of the acid chloride.<sup>3</sup> Furthermore, treatment of an equimolar mixture of  $\Delta$ - and  $\Lambda$ - $[(\text{en})_2\text{Co}(\text{S-ValO})]^{2+}$  with one equivalent of  $\text{SOCl}_2$  in DMF gives a quantitative recovery of complex but with a different diastereomeric ratio ( $(\Delta\text{S},\Delta\text{R}):(\Delta\text{S},\Delta\text{R}) \approx 2$ ).<sup>8</sup> This implies that epimerization at the  $\alpha$ -carbon centre has taken place. Such inversion is consistent with initial deprotonation at the  $\alpha$ -centre as a result of the acid halide formation. For parallels in organic chemistry an added base catalyst is sometimes required<sup>28,29</sup> but for the present system the base does not appear necessary. Presumably the solvent fulfils the role of acting as a proton acceptor.

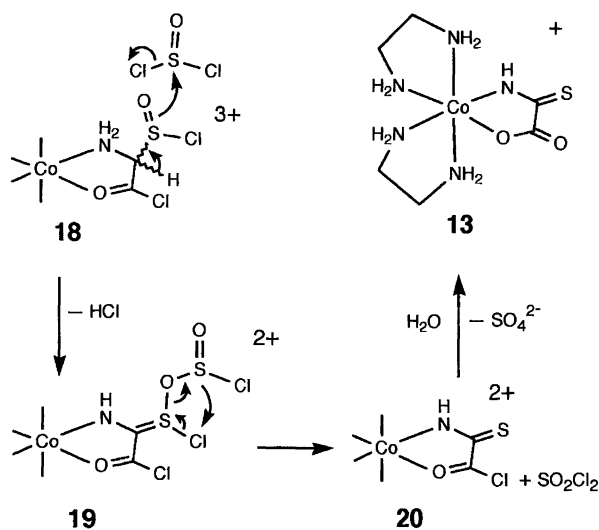
Depending on whether DMF and  $\text{SOCl}_2$  are premixed or  $\text{SOCl}_2$  is added after the complex (**11**), the enolate complex (**17**) may react predominantly with the  $[(\text{H}_3\text{C})_2\text{N}=\text{CHOS}(\text{O})\text{Cl}]^+$  ion or  $\text{SOCl}_2$  to produce **21** or **18**, respectively.

The formation of the thioamide (**13**) from the enolate (**17**) is now addressed. Electrophilic reaction of  $\text{SOCl}_2$



with the enolate would lead to a transient  $\alpha$ -sulfinyl chloride (**18**) based on organic precedent.<sup>28-30</sup> The equivalent species (**9**, Scheme 2) derived from an  $\alpha$ -amino acid with a tertiary  $\alpha$ -carbon atom were argued<sup>9</sup> to extrude sulfur monoxide (in equilibrium with SO<sub>2</sub> and elemental sulfur)<sup>31</sup> to form the observed imine products (**10**) after hydrolysis. By contrast, the  $\alpha$ -sulfinyl chloride derivative (**18**) of the glycinate complex carries another proton at the  $\alpha$ -carbon centre and an alternative reaction path for **18** is therefore available. The electron-withdrawing capacity of the sulfinyl chloride group would make the  $\alpha$ -proton of **18** even more acidic than the  $\alpha$ -protons of the parent  $\alpha$ -amino acid chloride (**16**). Thus, loss of the proton from the  $\alpha$ -sulfinyl chloride (**18**) combined with nucleophilic attack by the sulfinyl oxygen atom at another molecule of thionyl chloride is proposed to afford **19** (Scheme 5). Decomposition of **19** in the manner illustrated leads to **20** and SO<sub>2</sub>Cl<sub>2</sub> which hydrolyse to the observed thiooxamato complex (**13**) and sulfate ion. The closely related sarcosinato (*N*-methylglycinato) complex, [(en)<sub>2</sub>Co(SarO)]<sup>2+</sup>, was also oxidized by the SOCl<sub>2</sub>/DMF reagent to give predominantly the *N*-methylthiooxamato complex (*N*-methyl equivalent of **13**) and ionic sulfate.<sup>11</sup>

The course of the reactions of SOCl<sub>2</sub> with compounds containing active methylene groups is generally stated<sup>29</sup> as being variable. However, activated methylene compounds with an adjacent carbon atom forming part of a  $\pi$ -electron accepting group (e.g. carbonyl, carboxyl) typically leads to the  $\alpha$ -chlorosulfonyl chloride derivative (R<sub>2</sub>C(Cl)SOCl) when treated with excess SOCl<sub>2</sub> (3–15 molar equiv.) in the presence of a base catalyst.<sup>29</sup> This conversion is generally accepted<sup>29</sup> to proceed by a Pummerer-type rearrangement mechanism in which the initial steps correspond to steps **16**–**19** of Schemes 4 and 5. The standard mechanism and that proposed here deviate with respect to the fate of **19**. The standard mechanism leads to an  $\alpha$ -chlorosulfonyl chloride due to collapse of **19** with



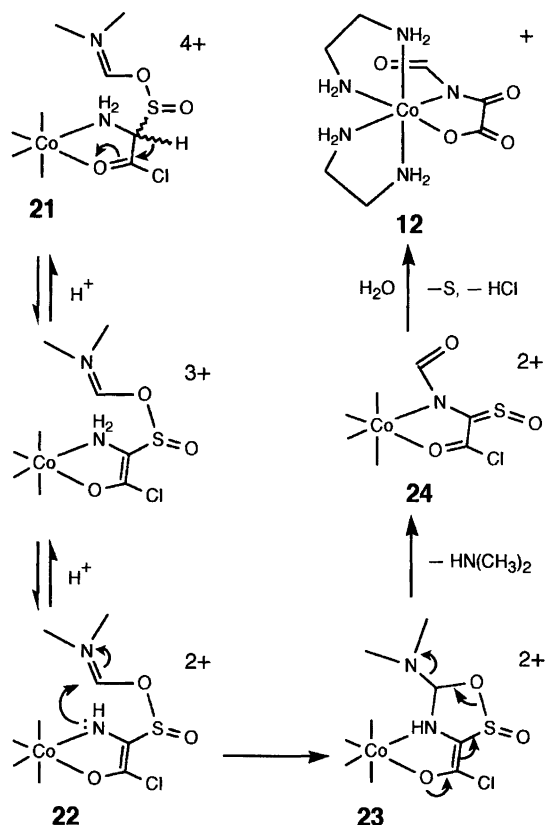
Scheme 5.

loss of SO<sub>2</sub>, whereas here the end product is the observed thioamide (**13**) accompanied by sulfur(VI) production. Thioamides may result from an  $\alpha$ -chlorosulfonyl chloride, for example by dechlorination with triphenylphosphine.<sup>32</sup> Therefore, an  $\alpha$ -chlorosulfonyl chloride cannot be dismissed as an intermediate in the reaction giving **20**. However, such an event would require dechlorination by SO<sub>2</sub> [(in order to give the observed sulfur(VI)] which would seem less obvious than the argued direct conversion of **19** into **20**.

In an earlier paper<sup>11</sup> the possibility of a sulfine intermediate<sup>33,34</sup> (R<sub>2</sub>C=S=O) arising from HCl elimination from **18** in the reaction leading to the thioamide (**13**) was raised. Further reaction to the thioamide level would then have required subsequent reduction of the sulfine. However, sulfines, if formed, are generally observed to be stable in the presence of SOCl<sub>2</sub>.<sup>29</sup> In particular, sulfines derived from primary or secondary thioamides are usually further stabilized.<sup>33</sup> Furthermore, no precedent appears to exist for the reduction of a sulfine with SOCl<sub>2</sub> to the thiocarbonyl level, although such reductions may be accomplished<sup>33</sup> with other reagents. Finally, organic lore only predicts a methinesulfinyl chloride to transform into a sulfine when a stoichiometric amount of SOCl<sub>2</sub> is used.<sup>29</sup> In contrast, the Pummerer-type rearrangement is the preferred path with excess SOCl<sub>2</sub> as employed here.

In Scheme 5 the complexes **13**, **19** and **20** are depicted as deprotonated at the coordinated N atom. For **13** this is based on the structural results and the pK<sub>a</sub> value (ca. -0.3) for the acid form. The carboxylate group of **13** appears as the acid chloride derivative in **19** and **20**. Hence the amide protons of these complexes would be expected to be even more acidic.

The *N*-formyloxamato complex (**12**) clearly dominates as a product in the reaction mixture when SOCl<sub>2</sub> and DMF are mixed prior to addition of the glycinate complex (**11**). Under these conditions the dominant reactive species, [(H<sub>3</sub>C)<sub>2</sub>N=CHOS(O)Cl]<sup>+</sup>,<sup>22-27</sup> is an even better chlorinating agent than is thionyl chloride,<sup>22</sup> and the chloroenolate complex (**17**) may be readily formed. In Scheme 4 nucleophilic substitution by **17** with another molecule of the reagent is proposed to form **21** in a similar manner to the formation of **18** with SOCl<sub>2</sub>. The initial loss of the  $\alpha$ -proton and one amine proton of the highly charged (4+) complex (**21**) will together generate a coordinated amidate nucleophile (**22**) (Scheme 6). This species would be ideally poised to effect the formylation reaction intramolecularly. It could lead to the *N*-formylated sulfine of coordinated oxamic acid chloride (**24**) via the cyclic ligand system of **23** with loss of dimethylamine. Hydrolytic decomposition of the sulfine (**24**) to the carbonyl derivative of **12** with sulfur production has a precedent in organic chemistry.<sup>33</sup> The driving force for the reaction **23**→**24** is proposed to originate from the gain in resonance stabilization represented by **24**. Such conjugated structures appear to be remarkably stabilized by the metal ion.<sup>3,4</sup>



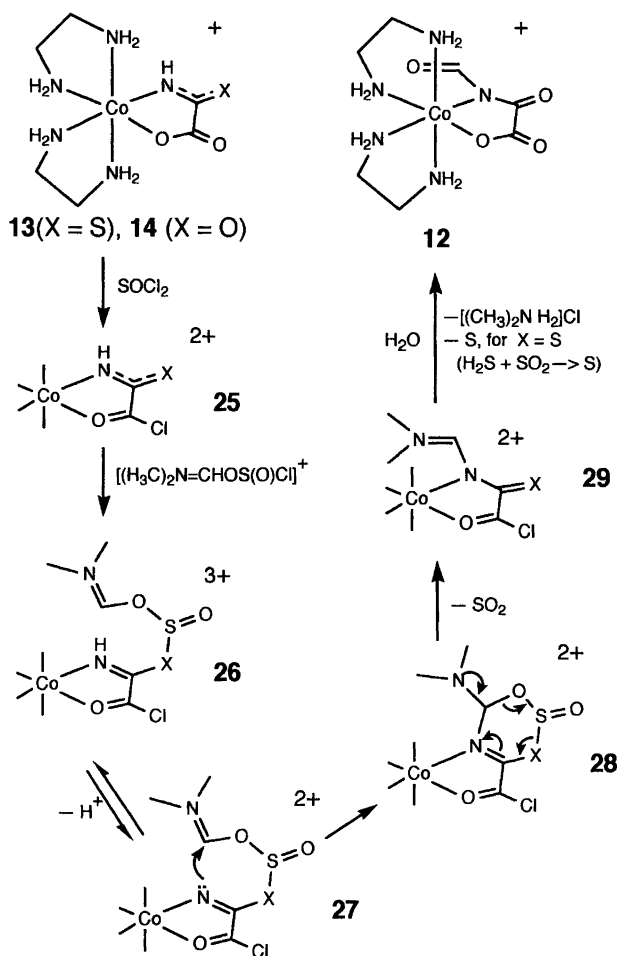
Scheme 6.

In Scheme 6 the formation of the *N*-formyloxamato complex (12) takes place via an intramolecular mechanism. However, the present evidence does not exclude the possibility of a sulfine being formed initially from 21 by elimination of H<sup>+</sup> and DMF followed by formylation of the nitrogen by another molecule of the formylating agent. If this were the case, the sulfine formed might be expected to have the sulfine oxygen engaged in hydrogen bonding to the nitrogen proton of the same ligand. Such an interaction is invoked as the explanation for the special stability of sulfines derived from primary and secondary thioamides.<sup>33</sup> On steric grounds such an interaction would be expected to lower the probability for a subsequent formylation reaction at the nitrogen. Consequently, some non-formylated complexes such as, for example, the oxamato complex (14) and its putative sulfine precursor, would be expected among the products. Such products were not observed and, on balance, this path is less likely.

The intermediate 24, derived from 23, is presented in Scheme 6 with the *E* configuration of the formyl carbonyl group with respect to the N–C(formyl) bond. This configuration differs from the *Z* configuration found in the crystal structure of 12 where the formyl oxygen atom is hydrogen bonded to a neighbouring amine. However, in the structure the N–C(formyl) bond distance of 1.367(4) Å is somewhat longer than is typical for amides, and consequently the barrier to rotation may also be lower. Most certainly, the observed *Z* configuration is dictated by the

stabilisation provided by the hydrogen-bonding interaction and a rotation is therefore implied in reaction 24 → 12.

The thiooxamato complex (13) and the oxamato complex (14) each resulted in the *N*-formyloxamato complex (12) when treated with the SOCl<sub>2</sub>–DMF mixture followed by water addition (Scheme 3). In both instances, the overall chemical change corresponds to an *N*-formylation reaction apart from the replacement of the thioamidate sulfur by oxygen in the case of the thiooxamato complex (13). Similar mechanisms for the two reactions are therefore proposed and are summarised in Scheme 7. By analogy with the reaction path proposed above (Schemes 4 and 6) for the production of 12 from the glycinate complex (11) the mechanisms outlined in Scheme 7 also assume that the key formylation step at the coordinated thioamidate or amidate N atoms takes place by an intramolecular route. After presumed acid chloride formation, the *exo*-sulfur or oxygen atoms of the thioamidate [25(X = S)] and amidate [25(X = O)] moieties will be the most reactive centres for attack by the sulfur atom of the electrophile, [(H<sub>3</sub>C)<sub>2</sub>N=CHOS(O)Cl]<sup>+</sup>, leading to the complex 26.



Scheme 7.

After deprotonation to generate a coordinated iminate nucleophile (**27**), the cyclic intermediate **28** may be formed intramolecularly. This essentially represents the key formylation step since subsequent loss of SO<sub>2</sub> would give the *exo*-iminyl species **29** which upon hydrolysis would lead to the observed *N*-formyloxamato product (**12**). After the hydrolysis step liberated H<sub>2</sub>S would appear as elemental sulfur (2H<sub>2</sub>S + SO<sub>2</sub> → 3S + 2H<sub>2</sub>O).

In Scheme 4, acid chloride formation at the carboxylate site is included as a critical initial step in the reactions of the coordinated  $\alpha$ -amino carboxylates with thionyl chloride and DMF. Initial acid chloride formation is also assumed for the formylation reactions depicted in Scheme 7. However, this is not necessarily warranted on the present evidence and, in any case, would seem less likely to be a prerequisite, in terms of activation, for the subsequent reaction steps. Furthermore, the formylation reactions of **13** and **14** could also proceed by direct attack by the amidate nitrogen atom on the iminium carbon atom of the [(H<sub>3</sub>C)<sub>2</sub>N=CHOS(O)Cl]<sup>+</sup> reagent. However, as argued above, this is considered less likely.

While the examined reactions in this study have gone further in terms of oxidation than originally was expected, they have been revealing mechanistically. The study implies the role of various intermediates and in so doing reveals how the various possible reaction paths might be controlled by substituents and the electrophilic species in solution.

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