Synthesis, Structure, and Stereochemistry of Some Cysteine- and Penicillaminecobalt(III) Complexes

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Received July 27, 1977

The synthesis, characterization, and properties of salts of Λ- and Δ-N,S-Co(en)$_2$[(R)-cysteinato]$^{n+}$ and Co(en)$_2$[(S)-penicillaminato]$^{n+}$ are described. The less stable Λ-cysteine isomer can be prepared in $\geq$95% yield by a second-order asymmetric transformation. Both OH$^-$ and Co(II) effect mutarotation about cobalt, and the homogeneous equilibria have been measured: (R)cysS, 70 $\pm$ 2% Δ, 30 $\pm$ 2% Λ; (S)penS, 70 $\pm$ 2%, 30 $\pm$ 2%. The configurations of the Δ and Λ N,S bound (R)-cysteine isomers, as established by single-crystal X-ray crystallographic analysis, are consistent with those deduced from equilibrium data and spectroscopic and rotatory dispersion measurements. Crystals of Δ-[Co(en)$_2$$(R)$cysS]ClO$_4$·H$_2$O and Λ-[Co(en)$_2$$(R)$cysS]ClO$_4$ are orthorhombic, space group $P2_12_12_1$ with cell dimensions 15.000 (4), 12.411 (3), 8.492 (2) Å and 13.870 (1), 11.7415 (8), 8.9907 (7) Å, respectively. The structures consist of discrete Co(en)$_2$$(R)$cysS$^+$ cations, in which the cysteine residues are bound by N and S and perchlorate anions and water molecules of hydration. The Co–S bond lengths are 2.252 (2) and 2.234 (1) Å for the Δ and Λ complexes, respectively. The Co–N bonds trans to sulfur are lengthened relative to the average cis Co–N(en) bond lengths by 0.04 Å (Δ) and 0.05 Å (Λ).

Introduction

(R)-Cysteine and its C-dimethyl derivative (S)-penicillamine (Figure 1) are potential tridentate ligands which bind stereospecifically to metal ions. However, when these ligands function as bidentate chelates the choice of two of the three potential O, N, and S donor atoms raises a linkage isomer problem. Moreover, the presence of the chiral carbon center gives rise to additional diastereoisomerism when the metal center is also chiral. Our interest in these problems stemmed from a need to synthesize Co(en)$_2$$(R)$cysSH^{2+} and Co-(en)$_2$$(S)$penSH^{2+} (Figure 2) resolved about cobalt and having the amino acid N,O bonded to the metal ion.[2]

This paper describes the synthesis, some chemistry, and an X-ray crystallographic study of two diastereoisomers of Co(en)$_2$$(R)$cysS$^+$ and analogous work on Co(en)$_2$$(S)$penS^{n+}. Busch et al.[3a] and Krueger et al.[3b] have previously reported different syntheses of Co(en)$_2$$(R)$cysS$^+$, in poor yield. Also the diastereoisomerism was ignored and, moreover, the chemistry described herein was largely unexplored.

Experimental Section

Visible, ultraviolet, and rotatory dispersion spectra were recorded on Cary 16 and Perkin-Elmer P22 digital and self-recording instruments respectively. ^{1}H and ^{13}C NMR spectra were measured with JEOL Minimar (100 MHz) and JEOL FX60 spectrometers. Dowex 50W-X2, 200–400 mesh (Na$^+$ or H$^+$ form) resin was used for all ion-exchange chromatography. Chloride salts for NMR measurements were prepared in situ by anion exchange of perchlorates on Dowex AG 1X8 (Cl$^-$ form, 200–400 mesh) resin.

Λ-N,S-[Co(en)$_2$$(R)$cysS]ClO$_4$ and Λ-N,S-[Co(en)$_2$$(R)$cysS]-(ClO$_4$)$_2$·H$_2$O. Separate solutions of Co(ClO$_4$)$_2$·6H$_2$O (73.2 g, 0.2 mol) in water (150 mL) and (R,R)-cystine (24.0 g, 0.1 mol) in aqueous (250 mL) ethylenediamine (36.0 g, 0.6 mol) were deoxygenated by the vigorous passage of N$_2$ for 10 min, and then the amine mixture was added quickly to the Co(II) under N$_2$. The clear solution rapidly turned brown and crystals deposited. After standing 6 h, it was cooled on ice for 1 h and filtered. The product was washed with ethanol and ether and air-dried; yield 76 g, 96%. The pale brown filtrate sorbed on Dowex and eluted with 0.5 M Na$^+$ (pH 7 phosphate buffer) gave two bands, Δ isomer (70%) and Λ isomer (30%). The crystallized product eluted under the same conditions as a single band, corresponding to the second band. The product was recrystallized from the minimum volume of hot water, by addition of NaClO$_4$ and cooling, or HClO$_4$ solution by adjusting the pH to ~7 with Na$_3$PO$_4$. Anal. Calcd for [Co(en)$_2$SCH$_2$CH(CO$_2$H)NH$_2$]ClO$_4$: C, 21.2; H, 5.3; N, 17.6; S, 8.1; Cl, 8.9. Found: C, 21.0; H, 5.5; N, 17.4; S, 8.1; Cl, 8.9.

The product was converted to the first protonated form as follows. Concentrated HClO$_4$ (70%, 11.6 M, 20 mL, 0.23 mol) was added to N,S-[Co(en)$_2$$(R)$cysS]ClO$_4$ (39.8 g, 0.1 mol) partly dissolved in hot water (200 mL) and the resultant deep brown solution filtered without delay and treated with more HClO$_4$ (70%, 50 mL). On

cooling, deep chocolate brown needles deposited. After 1 h at 0 °C, these were collected, washed with 2-propanol or cold ethanol, followed by ether, and then air-dried; yield 46.5 g (90%). Anal. Calcd for [Co(en)$_2$SCH$_2$CH(CO$_2$H)NH$_2$](ClO$_4$)$_2$·H$_2$O: C, 16.3; H, 4.7; N, 13.6; S, 6.2; Cl, 13.7. Found: C, 16.2; H, 4.7; N, 13.5; S, 6.2; Cl, 13.8. The dichloride salt was prepared from the diperchlorate by anion (Cl$^-$) exchange on Dowex, and the product crystallized from water/ethanol. Diiodide and dithionate salts crystallized from saturated aqueous solutions of the diperchlorate in 10^{-3} M HCl on addition of NaI and Li$_2$S$_2$O$_6$, respectively. Iodide and hemidithionate salts were obtained by trituration of the respective 2+ ion salts with aqueous Na$_2$CO$_3$ whence they initially dissolved and then quickly crystallized. Analytical results for all the salts obtained, after the products were washed with ethanol and ether and dried in air, were satisfactory.

Δ-N,S-[Co(en)$_2$$(R)$cysS](ClO$_4$)$_2$·H$_2$O and Λ-N,S-[Co(en)$_2$$(R)$-cysS]ClO$_4$·H$_2$O. A mixture of Δ (70%) and Λ (30%) isomers was prepared as described for the Λ-isomer preparation above but using CoCl$_2$·6H$_2$O (47.6 g, 0.2 mol) in place of Co(ClO$_4$)$_2$·6H$_2$O. The resultant deep brown solution was chromatographed (A) or fractionally crystallized (B) as described below.

Method A. The mixture was greatly diluted with water, acidified (pH 1, HCl), and then sorbed on a large Dowex H$^+$ form column (3 × 15 in.). The column was washed with water (2 × 500 mL), 0.2 M HCl (500 mL) which quickly eluted residual pink Co^{2+}, and then finally water (2 × 500 mL) and 0.5 M Na$^+$ (pH 7, phosphate buffer; 0.167 M Na$_2$HPO$_4$, 0.167 M NaH$_2$PO$_4$) which eluted and separated the faster running Δ from the Λ isomer. Δ was collected and then the eluent changed to HCl (0.01 M, 2 × 500 mL; 0.5 M, 500 mL; finally 1–3 M). Δ was freed of sodium phosphate by dilution, resorption, and elution (HCl) from Dowex H$^+$ resin. Each isomer in HCl was taken to near dryness (~200 mL) by rotary evaporation and crystallized by careful addition of 70% HClO$_4$ (~50 mL; 0 °C, 2 h). The products were collected and recrystallized from 10^{-3} M HCl/HClO$_4$ as described for the Λ isomers. Yields: Δ, 67 g, 65%; Λ, 25.8 g, 25%. Anal. Calcd for [Co(en)$_2$SCH$_2$CH(CO$_2$H)-NH$_2$](ClO$_4$)$_2$·H$_2$O: C, 16.3; H, 4.7; N, 13.6; S, 6.2; Cl, 13.7. Found (Δ): C, 16.3; H, 5.0; N, 13.4; S, 5.9; Cl, 14.0.

Method B. NaClO$_4$ (100 g) was added to the crude reaction mixture following the redox reaction (~6 h). Λ-N,S-[Co(en)$_2$-(R)cysS]ClO$_4$ (41 g) quickly crystallized on scratching or seeding. After ~1 h at 0 °C, the solution was quickly filtered and Λ-[Co-(en)$_2$$(R)$cysS](ClO$_4$)$_2$ (34 g) obtained from the filtrate on addition of 70% HClO$_4$ (60 mL) and further cooling (0 °C, 2 h). Both fractions were recrystallized as the diperchlorates from dilute HCl/HClO$_4$. Some $\Delta \rightleftharpoons \Lambda$ interconversion occurs under the conditions of the initial crystallization, reflected in the final yields: Λ, 49 g, 47.5%; Δ, 30.5 g, 29.6%. Each isomer eluted as a single band from Dowex Na$^+$ resin (0.5 M Na$^+$ phosphate buffer, pH 7). Δ-N,S-[Co(en)$_2$$(R)$cysS]Cl$_2$ was prepared from the diperchlorate in water by anion exchange on Dowex and recrystallized as deep brown-black needles from 10^{-3} M HCl/acetone. Anal. Calcd for [Co(en)$_2$SCH$_2$CH(CO$_2$H)NH$_2$]-Cl$_2$·H$_2$O: C, 21.7; H, 6.2; N, 18.1; S, 8.3; Cl, 18.3. Found: C, 21.9;

(R)Cysteine (cysSH)   (S)Penicillamine (penSH)

Figure 1.

Figure 2. Λ-N,O-Co(en)$_2(S)$penSH^{2+}.

H, 6.1; N, 18.0; S, 8.2; Cl, 18.2. Δ-N,S-[Co(en)$_2(R)$cysS]ClO$_4$·H$_2$O was prepared from the diperchlorate by trituration with aqueous Na$_2$CO$_3$. The product redeposited from hot water (pH 8, HCO$_3^-$) by addition of aqueous NaClO$_4$ as shiny brown-olive crystals. Anal. Calcd for [Co(en)$_2$SCH$_2$CH(CO$_2$)NH$_2$]ClO$_4$·H$_2$O: C, 20.2; H, 5.6; N, 16.9; S, 7.7; Cl, 8.5. Found: C, 20.1; H, 5.4; N, 16.7; S, 7.9; Cl, 8.6.

Λ-N,S-[Co(en)$_2(R)$cysSH](ClO$_4$)$_3$. Λ-N,S-[Co(en)$_2(R)$cysS]ClO$_4$ (5.0 g) was covered with hot water (5 mL) and 70% HClO$_4$ (50 mL) added in one lot while stirring. The solid dissolved to a deep brown solution which quickly lightened to an orange solution on the further addition of HClO$_4$. The orange crystals which deposited were collected after 12 h at 0 °C and pumped dry. The product proved difficult to store or analyze; washing with alcohol or dissolution in water quantitatively regenerated Δ-N,S-[Co(en)$_2(R)$cysS](ClO$_4$)$_2$·H$_2$O.

Λ-N,S-[Co(en)$_2(S)$penS]S$_2$O$_6$·2H$_2$O and Δ-N,S-[Co(en)$_2(S)$-penS](ClO$_4$)$_2$. (S)-Penicillamine (Sigma; 29.8 g, 0.2 mol) in aqueous sodium hydroxide (100 mL; ~12.0 g, 0.3 mol; pH adjusted to ~10) was oxidized quantitatively to (S,S)-penicillamine disulfide by sucking air through the solution (~24 h, 20 °C) in the presence of Fe^{3+} catalysts (FeCl$_3$, ~0.1 g). When the blue-violet Fe^{3+}-free thiol color had disappeared, the solution was neutralized to pH ~2 (0.15 mol, 11.6 M HClO$_4$, ~26.0 mL, 70%) and ethylenediamine (36.0 g, 0.6 mol) was added. The mixture was deoxygenated (N$_2$, 10 min) and then finally added to Co(ClO$_4$)$_2$·6H$_2$O (73.2 g, 0.2 mol) in O$_2$-free water (150 mL). After ~18 h, the deep brown product mixture (70% Λ, Δ 30%) was chromatographed on Dowex Na$^+$ resin, as described for (R)-cysteine. The Λ and Δ isomers were recovered as chloride salts from Dowex H$^+$ resin (HCl eluent) and were taken to dryness and then crystallized readily from water using Li$_2$S$_2$O$_6$ and 70% HClO$_4$, respectively. For further characterization, the Λ-(ClO$_4$)$_2$ and Δ-ZnCl$_4$·2H$_2$O, Δ-S$_2$O$_6$·2H$_2$O salts were also obtained. Anal. Calcd for [Co(en)$_2$SC(CH$_3$)$_2$CH(CO$_2$H)NH$_2$]S$_2$O$_6$·2H$_2$O: C, 20.7; H, 5.8; N, 13.4; S, 18.4. Found (Λ): C, 21.0; H, 5.6; N, 13.4; S, 18.5. Found (Δ): C, 21.1; H, 5.8; N, 13.2; S, 18.7. Calcd for [Co(en)$_2$SC-(CH$_3$)$_2$CH(CO$_2$H)NH$_2$](ClO$_4$)$_2$: C, 20.5; H, 5.0; N, 13.3; S, 6.1; Cl, 13.5. Found (Δ): C, 20.3; H, 4.8; N, 13.0; S, 6.1; Cl, 13.7. Found (Λ): C, 20.6; H, 5.0; N, 13.2; S, 6.3; Cl, 13.3. Yields: Λ-S$_2$O$_6$, 45.0 g (43%); Δ-(ClO$_4$)$_2$, 26.3 g (25%).

An effective isomer separation was also achieved by fractional crystallization of the Λ,Δ mixture (70:30) from water utilizing the convenient relative solubilities $\Lambda \ll \Delta$ (S$_2$O$_6$), $\Lambda \gg \Delta$ ((ClO$_4$)$_2$).

Equilibration Experiments. Λ-N,S-[Co(en)$_2(R)$cysS]Cl$_2$ (2.0 g, 5.4 × 10^{-3} mol) in deoxygenated water was mixed with CoCl$_2$·6H$_2$O (0.24 g, 1.0 × 10^{-3} mol), and (R,R)-cystine (0.12 g, 5 × 10^{-4} mol) in aqueous (50 mL) ethylenediamine (0.6 g, 1.0 × 10^{-2} mol) under N$_2$. After ~18 h, the mixture was acidified (HCl) and chromatographed on Dowex Na$^+$ resin (0.5 M Na$^+$ phosphate buffer, pH 7 eluent). The [Co] in the two well-separated brown bands was determined from both the visible and ORD spectra (Δ, ϵ_{483} 127, [M]$^{20}_{478}$ +10 940; Λ, ϵ_{484} 129, [M]$^{20}_{398}$ -9500; 0.5 M Na$^+$ phosphate, pH 7) and the isomer ratio from this and the measured volumes of eluate. Identical results were obtained using the Λ or Δ form and

Table I. ^{13}C and ^{1}H NMR Data for N,S-Co(en)$_2(R)$cysS^{2+} and Co(en)$_2(S)$penS^{2+} [a]

Iso-mer	^{1}H NMR, $\tau^{c,e}$	Assignment	^{13}C NMR,[b] ppm	Assignment
		N,S-[Co(en)$_2(R)$cysS]Cl$_2$		
Λ	6.43, t, 1 H	CH	-106.7	COOH
	J = 5.5 Hz[d]		4.2	N-CH
			20.5	
			21.3	} N-CH$_2$
			21.8	
			22.9	
			34.8	S-CH$_2$
Δ	6.45, t, 1 H	CH	-106.7	COOH
	J = 5.5 Hz[d]		3.4	N-CH
			21.0	
			21.6	} N-CH$_2$
			22.1	
			22.9	
			35.8	S-CH$_2$
		N,S-[Co(en)$_2(S)$penS]Cl$_2$		
Δ	6.94, s, 1 H	CH	-104.9	COOH
			-3.4	N-CH
	8.56, s, 3 H	} C(CH$_3$)$_2$	19.2	
	8.90, s, 3 H		20.8	} N-CH$_2$(en)
			21.6, 21.6	
			23.1	S-C
			36.4	} C(CH$_3$)
			38.7	
Λ	7.04, s, 1 H	CH	-104.9	COOH
			-4.2	N-CH
			19.0	
	8.54, s, 3 H	} C(CH$_3$)$_2$	20.3	} N-CH$_2$(en)
	8.90, s, 3 H		21.8, 21.8	
			22.6	S-C
			35.8	} C(CH$_3$)$_2$
			37.9	

[a] 10^{-2} M DCl solvent. [b] Relative to dioxane (0 ppm). Upfield is defined as positive. [c] Key: t = triplet, s = singlet. [d] Individual proton couplings to the diastereotopic α-S-methylene protons were not resolved (100 MHz). [e] Amine protons exchanged; added CO$_3^{2-}$. Data refer to the 1+ deprotonated ions.

using varying amounts of Co(II)–cystine–en provided the pH was $\geq$10. No equilibration was demonstrated using en, Co(II), or en–Co(II) without added (R,R)-cystine.

Λ- or Δ-[Co(en)$_2(R)$cysS]Cl$_2$ was dissolved in 1 M NaOH such that [Co] $\simeq$ 0.1 M, pH ~13. After 12 h, the solutions were diluted, acidified (HCl, pH 1) and chromatographed on Na$^+$ Dowex to separate the Δ and Λ forms, the proportions of which were determined as above. Similar experiments at [Co] $\leq$ 10^{-3}M showed no evidence of mutarotation. The same reactions were monitored in the ^{1}H NMR using the methine triplet which for each isomer is distinct (Table I) These experiments showed unequivocally the absence of both methine and S-methylene proton exchange during mutarotation, as seen in the maintenance of the proton coupling, and proton integration, and mere appearance of the product methine signal.

Attempted equilibration on activated charcoal (Norit A) led to significant disproportionation and decomposition.

The equilibrium isomer distribution for the (S)-pencillamine complexes was determined as described for the (R)-cysteine derivatives. Again, the major isomer (70 ± 2% Λ) eluted more readily on Na$^+$ form Dowex using the phosphate eluent, and Co concentrations were determined as before using the following data: Λ, ϵ_{478} 164, [M]$^{20}_{491}$ = -7787; Δ, ϵ_{479} 163, [M]$^{20}_{464}$ + 11 500; 0.5 M Na$^+$ phosphate, pH 7.

The hydroxide ion induced isomer equilibration involved some decomposition and it could not be satisfactorily monitored by NMR. However, this and the Co(II)-induced equilibration of each of the pure isomers gave the same isomer proportions as the direct (homogeneous) preparation, as established chromatographically.

X-Ray Diffraction Studies of the Two (R)-Cysteine Complexes. Δ-N,S-[Co(en)$_2(R)$cysS]ClO$_4$·H$_2$O. Preliminary precession and Weissenberg photographs displayed *mmm* Laue symmetry and systematic absences 0h0 for h = 2n + 1, 0k0 for k = 2n + 1, and 00l for l = 2n + 1 which uniquely correspond to the noncentro-

Table II. Unit Cell Data

	Δ-N,S-[Co(en)$_2$-(R)cysS]ClO$_4$·H$_2$O	Λ-N,S-[Co(en)$_2$-(R)cysS]ClO$_4$
Formula	CoClSO$_7$N$_5$C$_7$H$_{23}$	CoClSO$_6$N$_5$C$_7$H$_{21}$
Molecular wt	415.7	397.7
Unit cell symmetry	Orthorhombic	Orthorhombic
a, Å	15.000 (4)	13.870 (1)
b, Å	12.411 (3)	11.7415 (8)
c, Å	8.469 (2)	8.9907 (7)
V, Å^3	1576.7 (5)	1464.1 (1)
Z	4	4
d_m,^{a} g cm^{-3}	1.74	1.77
d_c, g cm^{-3}	1.75	1.80
Space group	$P2_12_12_1$	$P2_12_12_1$

^{a} Measured by flotation.

Table III. Absorption Parameters

	Δ-N,S-[Co(en)$_2$-(R)cysS]ClO$_4$·H$_2$O				Λ-N,S-[Co(en)$_2$-(R)cysS]ClO$_4$			
	h	k	l	d^a	h	k	l	d^a
Crystal faces	2	-2	-1	0.0100	1	0	1	0.0196
	1	-1	2	0.0057	0	1	1	0.0145
	2	2	1	0.0095	2	1	0	0.0148
	1	1	-2	0.0057	1	-1	0	0.0127
	0	1	-2	0.0018	-1	-1	1	0.0080
	0	2	1	0.0037	0	-1	0	0.0127
	0	-1	2	0.0018	-2	-1	0	0.0080
	0	-2	-1	0.0037	-1	1	0	0.0157
	-1	-1	2	0.0057	0	-1	-1	0.0133
	-2	2	1	0.0100	-1	0	-1	0.0177
	-1	1	-2	0.0057	0	1	0	0.0176
	-2	-2	-1	0.0095	1	1	-1	0.0090
Grid size	6 × 6 × 6				6 × 6 × 6			
μ, cm^{-1}	14.2				15.2			
A_{max}^{b}	1.119				1.399			
A_{min}	1.047				1.255			
Mean A	1.073				1.299			

^{a} Distance in cm from an arbitrary point within the crystal. ^{b} A is the absorption coefficient.

symmetric orthorhombic space group $P2_12_12_1$.[4]

Accurate cell dimensions were obtained with an Enraf-Nonius CAD-4F diffractometer using monochromated Mo Kα radiation ($\lambda_{K\alpha_1}$ 0.709 30 Å)[4] at 21 ± 1 °C. Subroutine SEARCH was used to find 18 reflections at low values of θ. Subroutine INDEX was then used to calculate a preliminary unit cell which was found to correspond to that determined by photography. Seventeen reflections between 28 and 40° in 2θ were accurately centered using subroutine SETANG in order to calculate an orientation matrix suitable for data collection.

Intensity data were collected in two sections: $2 \leq 2\theta \leq 50°$ and $50 < 2\theta \leq 56°$. The crystal-to-counter distance was 208 mm and the crystal-to-detector distance 173 mm. Reflections were scanned using an ω–(2/3)2θ scan at a variable scan rate ranging from about 6°/min for the strongest ones to 0.6°/min for the weakest ones, the maximum time allowed for the scan being 150 s. The scan width in ω was given by (1.0 + 0.35 tan θ)° and the width of the horizontally variable aperture at the detector was given by (1.6 + 0.35 tan θ) mm. The takeoff angle of the X-ray tube was 2.8°. Of the 96 steps in the scan, the first and last 16 steps were considered as first and second backgrounds, respectively. During data collection three standard reflections were measured after every 10 000 s of X-ray exposure time. These showed a consistent drop in intensity with time; at the end of data collection their intensities had dropped to about 90% of their original values. In addition, after every 50 reflections, the position of the next strong reflection was measured precisely and if its rotation vector differed by more than 0.13° from its calculated vector, a new orientation matrix was calculated using a list of 17 reference reflections. A total of 2275 reflections (including standards) were scanned and assigned intensities according to the equation

$$I = P - 2(B_1 + B_2)$$

with

$$\sigma_{stat}(I) = [P + 4(B_1 + B_2)]^{1/2}$$

Reflections with $I < \sigma_{stat}(I)$ in the prescan were not remeasured. Otherwise, each reflection was scanned twice in opposite directions. Only those reflections with positive Miller indices were measured (i.e., one complete octant) and any reflection with a net negative peak count was assigned a structure factor of zero.

Accurate cell dimensions were calculated using 2θ values of 17 reflections between 28 and 40° in 2θ measured by subroutine DETTH. These data are given in Table II, together with other crystal information.

The data were corrected for Lorentz and double-polarization effects (assuming the graphite monochromator to be ideally imperfect[6] and its 2θ angle to be 12.18°) and for decomposition. Absorption corrections were not applied at this stage.

The structure was solved using the direct-methods program MULTAN.[7] Eight sets of phases were calculated using the 371 $|E|$'s greater than 1.4. The set of phases with the highest combined figure of merit was used to calculate an E map which yielded the positions of the atoms in the complex ion and the chlorine atom. A Fourier map based on this model revealed the perchlorate oxygens and a water molecule. Absorption corrections were applied using the Gaussian integration method and a 6 × 6 × 6 grid. The absorption parameters are given in Table III. The structure was refined using full-matrix least squares. The function minimized was $\sum w(|F_o| - s|F_c|)^2$. The

weights $w = \sigma^{-2}(F)$ were derived from a polynomial obtained by analyzing $\langle \Delta F - \sigma_{stat}(F) \rangle$ over ranges of F, where $\Delta F = ||F_o| - s|F_c||$ and $\sigma_{stat}(F)$ is the standard deviation of the observed structure factor based on counting statistics. The weighting scheme was checked after each cycle and recomputed if necessary. The refinement proceeded smoothly to an R factor of 0.054 where R is defined as $\sum||F_o| - s|F_c||/\sum|F_o|$. All atoms had anisotropic temperature factors. An $(F_o - F_c)$ synthesis revealed significant electron density at positions expected for hydrogen atoms. Each hydrogen atom was included at its calculated position with an isotropic temperature factor equal to that of the atom to which it was bound. The water hydrogens (H22 and H23) were included at their observed positions. None of the hydrogen atom parameters was refined in subsequent cycles. The final residuals were $R = 0.0418$ and the weighted residual $R_w = (\sum w(|F_o| - s|F_c|)^2/\sum w|F_o|^2)^{1/2} = 0.0538$ for 1155 reflections with $I > 3\sigma_{stat}(I)$. Weights for the final cycles were given by $1/\sigma^2(F)$ where $\sigma^2(F) = \sigma_{stat}^2(F) - 1.613 + 0.2533F - 0.00022F^2$. In the final cycle no parameter changed by more than 0.1σ. A final $(F_o - F_c)$ synthesis revealed no peak greater than 0.5 e Å^{-3}. The final positional and thermal parameters are given in Table IV.

Λ-N,S-[Co(en)$_2$(R)cysS]ClO$_4$. Preliminary precession and Weissenberg photographs showed mmm Laue symmetry and systematic absences $h00$ for $h = 2n + 1$, $0k0$ for $k = 2n + 1$, and $00l$ for $l = 2n + 1$, consistent with space group $P2_12_12_1$.

The parameters for data collection were similar to those for the Δ isomer. The maximum 2θ value was 62° and an ω–2θ scan was used. The maximum time for the final scan was 90 s. The scan range was (1.0 + 0.35 tan θ)° and the aperture at the detector was (1.2 + 0.35 tan θ) mm. There was no noticeable drop in intensity of the standard reflections during data collection. A total of 2853 reflections were scanned. Accurate cell dimensions were obtained using 2θ values between 40 and 50° of 25 reflections. These data are given in Table II, together with other crystal information. The data were corrected for Lorentz and double-polarization effects but not for absorption at this stage.

The structure was solved by a combination of direct and Fourier methods. Using the 201 reflections with $|E| > 1.6$, the program MULTAN[7] gave 64 sets of phases. The set with the highest combined figure of merit was used to calculate an E map which revealed the positions of the cobalt atom and of the cysteine residue. A Fourier map phased on this fragment revealed the rest of the structure. Positional and isotropic vibrational parameters were refined using unit weights to $R = 0.070$. Absorption corrections were applied using a 6 × 6 × 6 grid. The absorption parameters are given in Table III. Weighted refinement was continued to $R = 0.042$ with anisotropic temperature factors for all atoms. The hydrogen atoms were located in an $(F_o - F_c)$ synthesis. Each of them was included at its calculated position with an isotropic temperature factor equal to that of the atom to which it was bound. In subsequent refinement cycles the positional parameters of the hydrogen atoms were allowed to vary but their temperature factors were held constant. Refinement converged at

Table IV. Final Positional and Thermal Parameters for Δ-N,S-[Co(en)$_2$(R)cysS]ClO$_4$·H$_2$O[a,b]

Atom	$10^4 x$	$10^4 y$	$10^4 z$	$10^3 U_{11}$	$10^3 U_{22}$	$10^3 U_{33}$	$10^3 U_{12}$	$10^3 U_{13}$	$10^3 U_{23}$
Co	244 (1)	3409 (1)	9371 (2)	16.7 (5)	19.8 (5)	22.9 (5)	−1.5 (5)	2.4 (6)	−0.1 (6)
Cl	2477 (2)	1234 (2)	6944 (4)	31 (1)	41 (1)	46 (2)	2 (1)	2 (1)	−3 (1)
S	320 (2)	5216 (2)	9570 (3)	21 (1)	22 (1)	43 (2)	2 (1)	−4 (1)	−3 (1)
O(1)	3230 (5)	3566 (7)	10849 (12)	32 (4)	45 (5)	85 (7)	8 (4)	−18 (5)	11 (5)
O(2)	3416 (5)	5228 (6)	10016 (10)	29 (4)	43 (4)	76 (6)	−13 (4)	−17 (4)	1 (4)
O(3)	3251 (7)	651 (10)	6910 (18)	61 (7)	110 (9)	134 (11)	42 (7)	12 (8)	−5 (9)
O(4)	2103 (12)	1139 (12)	8449 (17)	221 (17)	125 (11)	105 (10)	90 (12)	102 (12)	29 (9)
O(5)	2634 (10)	2326 (8)	6646 (20)	139 (12)	46 (6)	145 (12)	−23 (7)	−45 (10)	35 (7)
O(6)	1880 (9)	867 (11)	5818 (20)	123 (11)	113 (10)	156 (15)	−48 (9)	−84 (11)	17 (10)
O(7)	3424 (7)	7082 (8)	8452 (11)	67 (6)	70 (6)	49 (5)	4 (5)	27 (5)	8 (5)
N(1)	1538 (5)	3381 (6)	9797 (8)	25 (4)	17 (3)	26 (4)	−5 (3)	2 (3)	−8 (4)
N(2)	186 (5)	1789 (5)	9362 (11)	25 (4)	21 (4)	41 (4)	−1 (4)	11 (5)	2 (4)
N(3)	−32 (5)	3282 (7)	11621 (10)	20 (4)	35 (5)	25 (4)	1 (3)	1 (3)	3 (4)
N(4)	−1035 (5)	3535 (7)	8852 (10)	18 (4)	33 (4)	33 (4)	4 (4)	−5 (3)	7 (4)
N(5)	445 (5)	3432 (7)	7081 (10)	30 (5)	32 (4)	30 (4)	−3 (4)	8 (4)	4 (5)
C(1)	2006 (6)	4408 (7)	9546 (13)	19 (4)	27 (5)	32 (5)	−6 (4)	−4 (4)	−4 (5)
C(2)	2973 (6)	4379 (9)	10185 (12)	21 (4)	36 (5)	33 (6)	5 (5)	0 (4)	−15 (5)
C(3)	1453 (7)	5297 (8)	10323 (12)	25 (5)	31 (5)	35 (7)	1 (4)	−1 (5)	−8 (5)
C(4)	251 (7)	1388 (7)	11020 (11)	35 (5)	26 (5)	41 (6)	−2 (5)	3 (6)	13 (4)
C(5)	−297 (8)	2156 (8)	12022 (12)	45 (6)	42 (6)	28 (5)	−13 (6)	2 (6)	13 (5)
C(6)	−1141 (8)	3500 (16)	7104 (15)	37 (6)	131 (13)	36 (7)	5 (9)	−20 (6)	−7 (10)
C(7)	−389 (8)	3599 (19)	6278 (15)	35 (7)	219 (21)	28 (6)	−33 (11)	−10 (6)	9 (10)

Atom	$10^4 x$	$10^4 y$	$10^4 z$	U, Å^2	Atom	$10^4 x$	$10^4 y$	$10^4 z$	U, Å^2
H(1)	2013	4523	8433	23	H(13)	441	3447	12173	22
H(2)	1450	5204	11439	27	H(14)	−1249	4135	9215	29
H(3)	1701	5983	10077	27	H(15)	−1330	2995	9260	29
H(4)	1777	2894	9189	19	H(16)	−1392	2838	6825	63
H(5)	1613	3191	10783	19	H(17)	−1525	4078	6814	63
H(6)	630	1533	8805	23	H(18)	−377	4343	5893	69
H(7)	−313	1579	8949	23	H(19)	−422	3138	5411	69
H(8)	32	683	11096	34	H(20)	666	2808	6787	26
H(9)	861	1409	11358	34	H(21)	827	3935	6852	26
H(10)	−912	2053	11802	36	H(22)	3302	6549	8883	55
H(11)	−189	2017	13111	36	H(23)	3276	7725	8922	55
H(12)	−464	3710	11862	22					

[a] Anisotropic temperature factors are of the form $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$. [b] Isotropic temperature factors are of the form $\exp[-8\pi^2U((\sin\theta)/\lambda)^2]$.

$R = 0.0275$ ($R_w = 0.0369$) for 2375 reflections with $I > 3\sigma_{stat}(I)$. The final weighting scheme was $w = \sigma^{-2}(F)$ where $\sigma^2(F) = \sigma_{stat}^2(F) + 1.638 + 0.063F + 0.0015F^2$. In the final cycle no parameter changed by more than 0.1σ and a final $(F_o - F_c)$ synthesis revealed no peaks greater than 0.4 e Å^{-3}. The final positional and thermal parameters are given in Table V.

Absolute configurations of the complexes were initially assigned using the known R configuration of L-cysteine. Refinement of both complexes reversing the signs of the imaginary component of the anomalous dispersion of Co, Cl, and S revealed that the initially assigned absolute configurations were correct at the 0.995 significance level.[8]

Scattering factors for all atoms together with anomalous dispersion terms for Co, Cl, and S were taken from ref 9.

Results and Discussion

Chemistry. A. (R)-Cysteine Complexes. Reactions between free thiols and cobalt(III) complexes typically result in reduction, disproportionation, and polymerization. Co(en)$_2$-(R)cysS$^+$ was first prepared by such a route, using free (R)-cysteine and *trans*-Co(en)$_2$Cl$_2$$^+$ in aqueous OH$^-$. We have not been able to reproduce the yield claimed (50%) but have observed irreproducible amounts of Co(en)$_2$(R)cysS$^+$ not exceeding 5%, mixed with cobalt(II) and a multitude of brown products including polymers.

However, reaction between Co(ClO$_4$)$_2$ (1 equiv) and (R,R)-cysteine[10] (0.5 equiv) dissolved in aqueous ethylenediamine (3 equiv), and in the absence of air, gave an almost quantitative yield of brown crystalline [Co(en)$_2$(R)cystS]ClO$_4$ ($\sim$95%). This cobalt(II)–disulfide route to cobalt(III) mercaptides, which is a fairly general reaction,[11] obviates the problems mentioned above. The internal redox between Co(II) and the disulfide presumably occurs in an intermediate of the
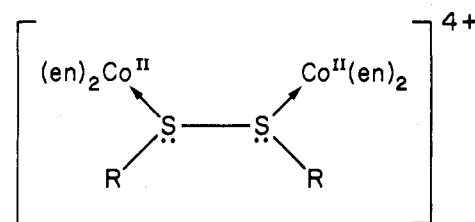

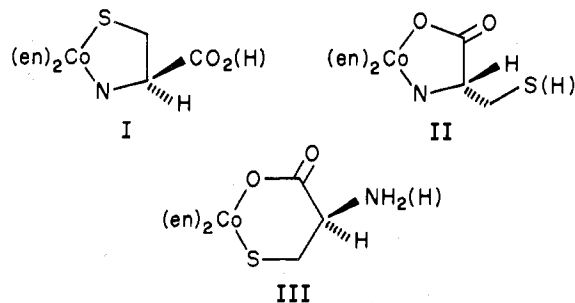**Figure 3.** Disulfide–cobalt(II) redox intermediate.

Figure 4. The three possible Co(en)$_2$(R)cysS(H)$^{n+}$ linkage isomers.

form shown (Figure 3) and yields monomeric Co^{III}–$\overset{..}{S}$R^{2+} after electron transfer. This point is important for cysteine since Co–S bonding in the product excludes the N,O linkage isomer possibility (II, Figure 4).

The identification of the N,S bonded isomer was confirmed as follows (I, Figure 4). The similar brown [Co(en)$_2$-(NH$_2$(CH$_2$)$_2$S)](ClO$_4$)$_2$ was prepared[12] from Co(II), en, and cystamine ((NH$_2$(CH$_2$)$_2$S)$_2$). Here N,S bonding of the chelate

Table V. Final Positional and Thermal Parameters for Λ-N,S-[Co(en)$_2$(R)cysS]ClO$_4$

Atom	10^4x	10^4y	10^4z	10^3U_{11}	10^3U_{22}	10^3U_{33}	10^3U_{12}	10^3U_{13}	10^3U_{23}
Co	5748.8 (3)	1610.5 (3)	5360.5 (4)	14.0 (1)	13.2 (1)	15.2 (1)	0.6 (1)	0.1 (1)	0.3 (1)
Cl	7315.7 (6)	5610.7 (8)	3787 (1)	25.0 (3)	31.3 (4)	58.5 (6)	1.5 (3)	9.5 (4)	−0.8 (4)
S	5947.8 (5)	−101.9 (6)	4322.0 (8)	21.8 (3)	17.8 (3)	20.2 (3)	−1.0 (2)	−0.1 (2)	−4.3 (2)
O(1)	8381 (2)	1557 (2)	4368 (3)	28 (1)	34 (1)	33 (1)	−12 (1)	8.8 (9)	−1 (1)
O(2)	8680 (2)	−311 (3)	4241 (3)	30 (1)	43 (1)	29 (1)	13 (1)	7 (1)	−7 (1)
O(3)	6385 (3)	5091 (3)	3892 (7)	39 (2)	53 (2)	138 (4)	−16 (2)	26 (2)	−10 (3)
O(4)	7421 (3)	6142 (4)	2350 (5)	60 (2)	84 (3)	75 (3)	−15 (2)	−8 (2)	34 (3)
O(5)	7412 (3)	6470 (4)	4889 (6)	72 (3)	82 (3)	111 (4)	−20 (3)	21 (3)	−53 (3)
O(6)	8041 (3)	4767 (5)	3949 (6)	62 (2)	92 (3)	96 (3)	50 (2)	22 (2)	27 (3)
N(1)	6982 (2)	1346 (2)	6433 (3)	14.4 (9)	20 (1)	17 (1)	2.1 (8)	−0.1 (8)	−2.9 (8)
N(2)	5538 (2)	3085 (2)	6481 (3)	23 (1)	16 (1)	27 (1)	1.1 (9)	−0.1 (9)	−1.9 (9)
N(3)	5008 (2)	926 (2)	7003 (3)	18 (1)	19 (1)	20 (1)	1.2 (9)	1.4 (9)	2.5 (9)
N(4)	4578 (2)	1814 (2)	4160 (3)	20 (1)	24 (1)	24 (1)	2.7 (9)	−2.6 (9)	3.6 (9)
N(5)	6414 (2)	2384 (2)	3701 (3)	24 (1)	23 (1)	24 (1)	−1 (1)	3 (1)	7 (1)
C(1)	7531 (2)	299 (2)	6012 (3)	15 (1)	22 (1)	18 (1)	3 (1)	0.1 (9)	−1 (1)
C(2)	8251 (2)	537 (3)	4757 (3)	14 (1)	31 (1)	18 (1)	−1 (1)	−0 (1)	−4 (1)
C(3)	6825 (2)	−640 (3)	5650 (4)	20 (1)	16 (1)	30 (1)	1.4 (9)	2 (1)	3 (1)
C(4)	5316 (2)	2787 (3)	8049 (4)	28 (1)	24 (1)	23 (1)	7 (1)	0 (1)	−6 (1)
C(5)	4602 (2)	1813 (3)	8004 (4)	22 (1)	29 (2)	25 (1)	7 (1)	8 (1)	−2 (1)
C(6)	4773 (3)	2593 (4)	2896 (4)	37 (2)	40 (2)	29 (2)	3 (2)	−7 (1)	13 (2)
C(7)	5786 (3)	2375 (4)	2375 (4)	45 (2)	49 (2)	21 (1)	−1 (2)	−1 (2)	11 (1)

Atom	10^4x	10^4y	10^4z	U, Å^2	Atom	10^4x	10^4y	10^4z	U, Å^2
H(1)	7920 (27)	113 (33)	6820 (44)	17	H(11)	4498 (28)	1468 (35)	8916 (46)	22
H(2)	7155 (28)	−1290 (34)	5289 (47)	21	H(12)	4564 (29)	349 (35)	6585 (46)	20
H(3)	6530 (29)	−875 (33)	6589 (49)	21	H(13)	5412 (29)	422 (34)	7431 (45)	20
H(4)	7361 (28)	1987 (33)	6246 (45)	15	H(14)	4363 (28)	1055 (33)	3877 (43)	21
H(5)	6869 (26)	1389 (33)	7434 (43)	15	H(15)	4119 (30)	2121 (34)	4659 (47)	21
H(6)	6043 (28)	3573 (34)	6408 (43)	17	H(16)	4333 (34)	2478 (38)	2111 (52)	33
H(7)	4988 (28)	3431 (37)	6069 (42)	17	H(17)	4818 (31)	3515 (41)	3240 (51)	33
H(8)	5094 (29)	3429 (38)	8570 (47)	23	H(18)	6044 (34)	2875 (40)	1793 (55)	33
H(9)	5941 (31)	2562 (34)	8576 (48)	23	H(19)	5803 (32)	1503 (38)	1833 (50)	33
H(10)	4008 (30)	2122 (35)	7684 (47)	22	H(20)	6583 (28)	3217 (35)	3935 (47)	22
					H(21)	7040 (31)	2100 (34)	3641 (49)	22
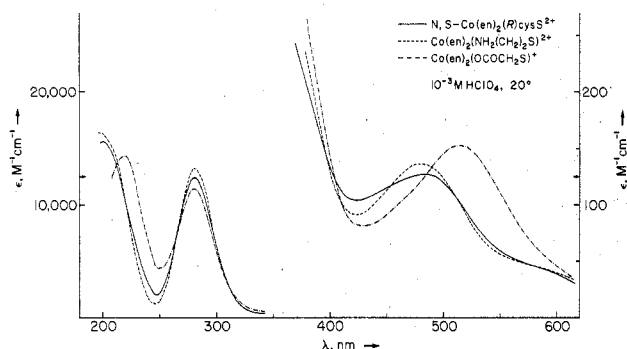
Figure 5. Visible and near-ultraviolet spectra of Co(en)$_2$(R)cysS^{2+} (—), Co(en)$_2$(NH$_2$(CH$_2$)$_2$S)$^{2+}$ (···), and Co(en)$_2$(SCH$_2$OCO)$^+$ (- - -) in 10^{-3} M HClO$_4$ at 20 °C.

is the only prospect and has been confirmed by a single-crystal X-ray structure analysis.[13] Red-violet [Co(en)$_2$SCH$_2$OCO]ClO$_4$, from Co(II), en, and mercaptoacetic acid disulfide,[14] has S,O bonding[13] as the only possibility. Comparison of the visible spectra (Figure 5) of the three mercaptides clearly identifies the CoN$_5$S chromophore in Co(en)$_2$(R)cysS^{2+} and excludes the S,O case III (Figure 4). Orange Co(en)$_2$(R)cysSH^{2+} has subsequently been synthesized where the cysteine is N,O bound (II, Figure 4), and two ligand field bands at 485 and 345 nm distinguish this linkage isomer.[15] The strong ligand-to-metal charge-transfer transitions in the S-bound mercaptides obscure the second ligand field band, and this appears to be characteristic of sulfur coordination (Figure 5).

Co(en)$_2$(R)cysS^{n+} was crystallized as both protonated (pH <3) and deprotonated (pH >4) forms. The effect of the ionizable proton (p$K_a \sim 3.5$) is also reflected in the chromatography (+ ion, pH 7; 2+ ion, pH 0). The pK_a's of −CO$_2$H, −NH$_3^+$, and −SH are expected[16] to be $\sim$3, 9, and 10, respectively (I, II, and III, Figure 4). The brown complex

showed increased solubility in HClO$_4$ above $\sim$4 M. The solution became orange and deposited an orange crystalline triperchlorate on standing in $\sim$8 M HClO$_4$. These properties are consistent with the N,S bonding of the cysteine moiety with a free COOH group and a feebly basic coordinated mercaptide. The marked change in visible spectrum in strong HClO$_4$ indicates protonation at S without Co–S rupture, since the reaction is completely reversible (dilution) and the Co–S charge transfer is retained throughout. Kinetic evidence exists for protonation at sulfur in thiolatochromium(III) analogues,[11,12] but such acid forms do not seem to have been isolated previously.

Given that (R)-cysteine and its Co(III) complexes do not mutarotate at carbon under preparative conditions, there are two possible N,S-Co(en)$_2$(R)cysS^{n+} diastereoisomers ($\Lambda(R)$ and $\Delta(R)$), differing in configuration about cobalt. Fractional crystallization of N,S-Co(en)$_2$(R)cysS^{n+} as several salts of both the + and 2+ ion forms gave homogeneous crystals having constant properties (visible, rotatory dispersion, ^{1}H and ^{13}C NMR spectra). Moreover, extensive chromatography failed to split the single band observed. Marked stereospecificity was not expected and, since the yield exceeded 90% and the product was apparently a single isomer, it was suspected, and subsequently confirmed, that the isomer obtained was simply the less soluble form and that a labile equilibrium existed in solution between the two N,S diastereoisomers.

Chromatography of the acidified filtrate ($\sim$5% of the total cobalt) from the original preparation revealed the second isomer; two brown bands readily separated on Dowex 50W-X2 resin when sodium phosphate eluent (0.5 M Na$^+$, pH $\sim$7) was used. The minor (30%), slower running component was identified as the N,S-Co(en)$_2$(R)cysS^{n+} isomer already obtained. This same 70:30 isomer distribution was obtained in large-scale preparations using CoCl$_2$ in place of Co(ClO$_4$)$_2$. Under these conditions the products do not crystallize as soon as they are formed. It therefore seemed that the 70:30 ratio
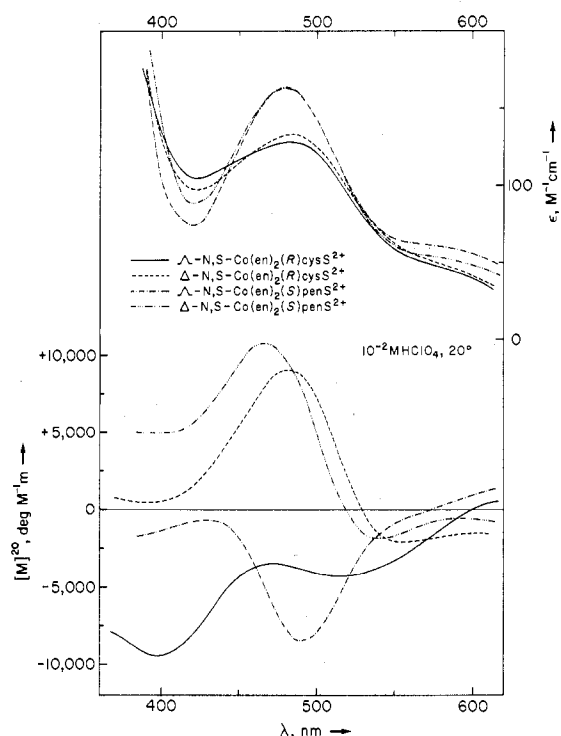
Figure 6. Rotatory dispersion spectra of N,S-Co(en)$_2$(R)cysS^{2+} (Λ, —; Δ, - - -) and Co(en)$_2$(S)penS (Δ, - ⋯ -; Λ, ⋯⋯) in 10^{-2} M HClO$_4$ at 20 °C.

represented the true equilibrium figure. This was confirmed by separately equilibrating each of the pure isomers as described below.

The major material obtained from CoCl$_2$ had spectra (^{1}H and ^{13}C NMR, visible and UV) very similar to those of the other isomer and its properties confirmed the N,S bonding. The measured solubilities of the two N,S-[Co(en)$_2$(R)-cysS]ClO$_4$ salts were significantly different, the minor form being less soluble. This in part accounted for the asymmetric synthesis of one pure isomer from Co(ClO$_4$)$_2$, and it remained to establish the nature of the interconversion between the two isomers in solution.[17]

The assignment of the two isomers as Λ(R) and Δ(R) (rather than, say, Λ(R) and Λ(S)) followed from their rotatory dispersion spectra (Figure 6) and was confirmed by separating the pure species from mixtures equilibrated with both cobalt(II) and OH$^-$ and showing they had identical properties. Mutarotation in strong OH$^-$ does not involve proton exchange (^{1}H NMR) and hence inversion at the methine carbon.

^{1}H and ^{13}C NMR data for the two N,S-Co(en)$_2$(R)cystS^{n+} isomers are given in Table I. The assignments follow from the coupled and ^{1}H-decoupled NMR spectra and from comparison with other (R)-cysteine derivatives. In acid or dilute base the isomers were stable indefinitely but mutarotation occurred in strong OH$^-$ (0.1–1 M), provided [Co] was high ($\geq$0.1 M). This observation, together with the irreproducible rates, suggested base induced formation of cobalt(II) which catalytically brought about mutarotation via electron transfer on the labile Co(II) state. In the ^{1}H NMR, the reaction was monitored in the methine proton region. Independently of the direction from which the equilibrium between the two isomers was approached, the methine triplets of both isomers were clearly evident. If the reaction was allowed to proceed in strong base for >24 h, the NMR resolution was lost due to paramagnetic Co(II) accumulation, but up to this point neither significant methine proton nor S-methylene proton exchange occurred.[18] Complex recovered from the NMR tubes was chromatographed and the 70:30

isomer ratio found (visible and rotatory dispersion spectra) commencing with either pure isomer.

The failure of strong base to exchange the methine proton or invert the (R)-cysteine contrasts sharply with other Co(en)$_2$(amino acidato)$^{n+}$ systems.[19] However, the necessary carbanion formation is inhibited by the reduced electron-withdrawing effect of CoSCH$_2$– (cf. CoOC(O)–) since the amino acid has N,S rather than the usual N,O bonding. Also, the presence of the anionic –CO$_2$$^-$ methine substituent restricts dianion formation, blocking methine H exchange and hence the path to inversion.

In separate experiments direct Co(II) equilibration was established as follows. To each of the pure Co(en)$_2$(R)cysS$^+$ isomers was added a catalytic amount ($\sim$0.1 equiv) of CoCl$_2$/en/(R,R)-cysteine (1:3:0.5) in the absence of O$_2$. After 18 h, chromatography revealed the common 70:30 isomer distribution. No equilibration occurred if any of the Co(II), en, or (R,R)-cystine were omitted. These conditions, which simulate those of the Co(en)$_2$(R)cysS^{n+} preparations, were used to directly and quantitatively convert one isomer into the other having the less soluble perchlorate, confirming the earlier account. The high efficiency ($\sim$95%) of this asymmetric transformation provides a convenient source of one pure diastereoisomer in the Co(en)$_2$(R)cystS^{n+} system, namely, the less stable form.

Absolute configurations about cobalt in N,O-Co(en)$_2$(amino acid)$^{2+}$ diastereoisomers are normally ascertained from their rotatory dispersion or circular dichroism spectra which are approximately catoptric; the absolute configurations of several reference compounds are known from single-crystal X-ray structural studies. No such reference complexes are known for sulfur-bonded (amino acid)cobalt(III) complexes and the rotatory dispersion curves of Λ- and Δ-Co(en)$_2$(R)cysS^{2+} (Figure 6) are far from catoptric. The strong Co ← S charge-transfer transitions in the near-ultraviolet carry large rotations which tail well into the visible region and preclude any reliable determination of the absolute configuration using this method. Therefore the isomers were initially assigned on the basis of steric arguments as follows.

The Λ,Δ-Co(en)$_2$(R)pn^{3+} resembles the present system in that both pn and cysS form puckered five-membered rings having configurations with the preferred equatorial disposition of the CH$_3$ and CO$_2$$^-$ substituents, respectively. As expounded elsewhere,[20] the Λ(R) and Δ(R) Co(en)$_2$ (R)pn^{3+} diastereoisomers are (lel)$_2$ob and (lel)$_3$, respectively, and the latter is observed to be preferred over the former to the extent of 2.5:1. This corresponds to an isomer ratio of 68:32 which is very close to that found here. Accordingly the major (70%) (R)cysS isomer is assigned Δ; the minor, Λ. Although the arguments are strictly valid only in the gas phase, they are supported by experimental data on several condensed-phase systems involving closely related isomeric ions.[20]

B. (S)-Penicillamine Complexes. Both Λ- and Δ-Co(en)$_2$(S)penS^{n+} have been synthesized by a route analogous to that described for (R)-cysteine. The equilibrium proportions of isomers are identical and the physical and chemical properties of the two forms are analogous. The isomer assignments follow directly, and since (S)-penicillamine has the opposite absolute configuration to (R)-cysteine, the major isomer ((lel)$_3$; 70%) is Λ. The visible and ORD spectra (Figure 6) of the two diastereoisomers confirm the approximate mirror image relationship with the (R)-cysteine system and hence the N,S bonding and absolute configurations. The higher solubilities made asymmetric transformations difficult. Preparations starting from CoCl$_2$ or Co(ClO$_4$)$_2$ were in each case homogeneous and gave the same isomer proportions. The ^{1}H and ^{13}C data for Λ- and Δ-[Co(en)$_2$(S)penS]Cl$_2$ are given in Table I.
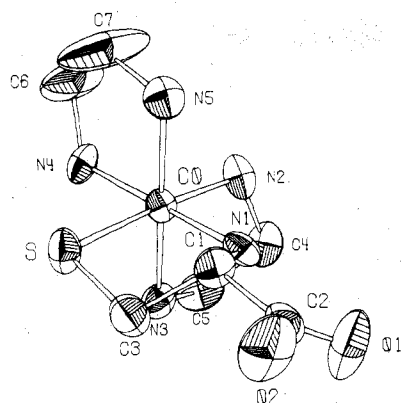
Figure 7. Stereoscopic view of the Δ-*N,S*-[Co(en)₂(*R*)cysS]⁺ ion.
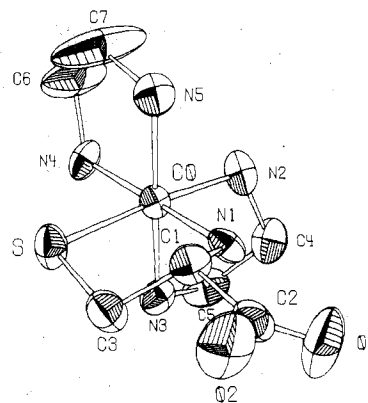
Figure 8. Stereoscopic view of the Λ-*N,S*-[Co(en)₂(*R*)cysS]⁺ ion.

We undertook the X-ray crystal structure analyses of both Co(en)₂(*R*)cysS⁺ isomers to substantiate the above conclusions. In particular, there was a need to be certain of the absolute configurations in view of the facility with which mutarotation about cobalt can occur and because of the fact that several derivatives have since been prepared and appear to be inverted about cobalt.[21]

Description of the Structures. Both cysteine complexes exist as discrete cations and anions, and the structures of the complex cations are given in Figures 7 and 8. The cysteine residues are bound to cobalt by sulfhydryl and amino groups. The carboxyl groups are free and deprotonated. The absolute configurations are consistent with the known configuration of (*R*)-cysteine.

Bond lengths and angles are listed in Tables VI and VII for the Δ and Λ complexes, respectively. The results for the Λ complex are the more precise. The anomalous dimensions of the trans(N) en ring in the Δ complex are ascribed to either motion of the ring or disorder.

The coordination polyhedra of the metal atoms show no abnormal characteristics. As in the case of [Co(en)₂(NH₂-(CH₂)₂S)](NCS)₂[13] the cobalt–nitrogen bond opposite to sulfhydryl group is significantly lengthened. In the present two structures the average lengthening of the trans(S) Co–N bond is 0.046 Å, equivalent to the 0.046 Å found in [Co-(en)₂(NH₂(CH₂)₂S)](NCS)₂.

The five-membered chelate rings formed by the cysteine residues have identical dimensions within experimental error. However, both show differences from the N–S ring in [Co-(en)₂(NH₂(CH₂)₂S)](NCS)₂. The average Co–S–C$_\beta$ angle

Table VI. Bond Lengths (Å) and Angles (deg) for Δ-*N,S*-[Co(en)₂(*R*)cysS]ClO₄·H₂O[a]

Co–S	2.252 (3)	C(2)–O(2)	1.25 (1)
Co–N(1)	1.974 (8)	N(2)–C(4)	1.50 (1)
Co–N(2)	2.011 (7)	C(4)–C(5)	1.52 (1)
Co–N(3)	1.961 (8)	C(5)–N(3)	1.49 (1)
Co–N(4)	1.975 (8)	N(4)–C(6)	1.49 (2)
Co–N(5)	1.968 (8)	C(6)–C(7)	1.33 (2)
S–C(3)	1.82 (1)	C(7)–N(5)	1.44 (2)
C(3)–C(1)	1.53 (1)	Cl–O(3)	1.37 (1)
C(1)–N(1)	1.47 (1)	Cl–O(4)	1.40 (1)
C(1)–C(2)	1.55 (1)	Cl–O(5)	1.40 (1)
C(2)–O(1)	1.22 (1)	Cl–O(6)	1.37 (1)
S–Co–N(1)	87.3 (2)	N(1)–C(1)–C(2)	112.1 (8)
S–Co–N(2)	175.9 (3)	C(1)–C(2)–O(1)	118.5 (9)
S–Co–N(3)	91.0 (3)	C(1)–C(2)–O(2)	115.9 (9)
S–Co–N(4)	89.3 (3)	O(1)–C(2)–O(2)	125.5 (9)
S–Co–N(5)	92.9 (3)	C(1)–N(1)–Co	115.3 (6)
N(1)–Co–N(2)	91.5 (3)	Co–N(2)–C(4)	109.0 (6)
N(1)–Co–N(3)	91.6 (3)	N(2)–C(4)–C(5)	106.4 (8)
N(1)–Co–N(4)	175.7 (4)	C(4)–C(5)–N(3)	108.4 (8)
N(1)–Co–N(5)	91.8 (3)	C(5)–N(3)–Co	110.7 (6)
N(2)–Co–N(3)	85.1 (4)	Co–N(4)–C(6)	108.8 (7)
N(2)–Co–N(4)	92.1 (3)	N(4)–C(6)–C(7)	116 (1)
N(2)–Co–N(5)	91.0 (4)	C(6)–C(7)–N(5)	118 (1)
N(3)–Co–N(4)	91.1 (3)	C(7)–N(5)–Co	109.7 (7)
N(3)–Co–N(5)	174.9 (4)	O(3)–Cl–O(4)	108.3 (9)
N(4)–Co–N(5)	85.8 (3)	O(3)–Cl–O(5)	111.4 (9)
Co–S–C(3)	97.4 (3)	O(3)–Cl–O(6)	111.9 (9)
S–C(3)–C(1)	108.3 (7)	O(4)–Cl–O(5)	108 (1)
C(3)–C(1)–N(1)	107.7 (7)	O(4)–Cl–O(6)	110 (1)
C(3)–C(1)–C(2)	111.9 (8)	O(5)–Cl–O(6)	107.6 (9)

[a] The figures in parentheses are the esd's in the least significant figures shown.

Table VII. Bond Lengths (Å) and Angles (deg) for Λ-N,S-[Co(en)$_2$(R)cysS]ClO$_4$[a]

Co–S	2.234 (1)	C(1)–H(1)	0.93 (4)
Co–N(1)	1.988 (2)	C(3)–H(2)	0.95 (4)
Co–N(2)	2.024 (3)	C(3)–H(3)	0.98 (4)
Co–N(3)	1.971 (3)	N(1)–H(4)	0.93 (4)
Co–N(4)	1.965 (3)	N(1)–H(5)	0.91 (4)
Co–N(5)	1.975 (3)	N(2)–H(6)	0.91 (4)
S–C(3)	1.818 (3)	N(2)–H(7)	0.94 (4)
C(3)–C(1)	1.509 (4)	C(4)–H(8)	0.94 (4)
C(1)–N(1)	1.495 (4)	C(4)–H(9)	1.02 (4)
C(1)–C(2)	1.532 (4)	C(5)–H(10)	0.95 (4)
C(2)–O(1)	1.261 (4)	C(5)–H(11)	0.93 (4)
C(2)–O(2)	1.249 (4)	N(3)–H(12)	0.99 (4)
N(2)–C(4)	1.484 (4)	N(3)–H(13)	0.90 (4)
C(4)–C(5)	1.513 (5)	N(4)–H(14)	0.97 (4)
C(5)–N(3)	1.488 (4)	N(4)–H(15)	0.86 (4)
N(4)–C(6)	1.484 (4)	C(6)–H(16)	0.94 (5)
C(6)–C(7)	1.502 (6)	C(6)–H(17)	1.13 (5)
C(7)–N(5)	1.477 (5)	C(7)–H(18)	0.87 (5)
Cl–O(3)	1.431 (4)	C(7)–H(19)	1.13 (5)
Cl–O(4)	1.442 (4)	N(5)–H(20)	1.03 (4)
Cl–O(5)	1.420 (5)	N(5)–H(21)	0.93 (4)
Cl–O(6)	1.419 (4)		

S–Co–N(1)	87.48 (7)	N(1)–C(1)–C(2)	116.6 (2)
S–Co–N(2)	174.62 (8)	C(1)–C(2)–O(1)	118.1 (3)
S–Co–N(3)	90.59 (8)	C(1)–C(2)–O(2)	116.0 (3)
S–Co–N(4)	88.96 (8)	O(1)–C(2)–O(2)	125.8 (3)
S–Co–N(5)	92.33 (9)	C(1)–N(1)–Co	116.3 (2)
N(1)–Co–N(2)	90.9 (1)	Co–N(2)–C(4)	107.5 (2)
N(1)–Co–N(3)	91.2 (1)	N(2)–C(4)–C(5)	106.8 (3)
N(1)–Co–N(4)	175.4 (1)	C(4)–C(5)–N(3)	107.4 (2)
N(1)–Co–N(5)	92.1 (1)	C(5)–N(3)–Co	111.4 (2)
N(2)–Co–N(3)	84.3 (1)	Co–N(4)–C(6)	110.1 (2)
N(2)–Co–N(4)	92.9 (1)	N(4)–C(6)–C(7)	107.7 (3)
N(2)–Co–N(5)	92.9 (1)	C(6)–C(7)–N(5)	107.4 (3)
N(3)–Co–N(4)	91.7 (1)	C(7)–N(5)–Co	109.3 (2)
N(3)–Co–N(5)	175.7 (1)	O(3)–Cl–O(4)	109.6 (3)
N(4)–Co–N(5)	85.2 (1)	O(3)–Cl–O(5)	110.0 (3)
Co–S–C(3)	96.9 (1)	O(3)–Cl–O(6)	109.6 (3)
S–C(3)–C(1)	108.8 (2)	O(4)–Cl–O(5)	107.9 (3)
C(3)–C(1)–N(1)	109.0 (2)	O(4)–Cl–O(6)	108.9 (3)
C(3)–C(1)–C(2)	113.4 (2)	O(5)–Cl–O(6)	110.9 (4)

[a] The figures in parentheses are the esd's in the least significant figures shown.

for the cysteine complexes is 97.2 (3)° compared with 94.2 (3)° for the cysteamine complex while the comparable N–Co–S angles are 87.4 (2) and 88.2 (2)°, respectively. As a result the bites of the three ligands are identical (2.919 Å for the cysteine complexes and 2.921 Å for the NH$_2$(CH$_2$)$_2$S complex). The carboxyl groups are both planar within experimental error and the dimensions do not differ significantly from other values.

The ethylenediamine rings have identical dimensions within experimental error. The average C–C (1.52 (1) Å) and C–N (1.48 (1) Å) bond lengths are normal. The shorter C–C distance reported for the NH$_2$(CH$_2$)$_2$S complex, 1.47 (1) Å, is ascribable to disorder.

In Δ-[Co(en)$_2$(R)cysS]ClO$_4$·H$_2$O, the cysteine residue adopts the λ conformation and the en rings are λ (trans(S)) and δ, respectively. The high thermal parameters observed for the latter five-membered ring are consistent with the expected small energy barrier between the δ and λ conformations.

The corresponding ring conformations in Λ-[Co(en)$_2$(R)cysS]ClO$_4$ are δ, δ(trans(S)), and λ. The carboxyl group is thus unexpectedly axial but a clear intramolecular hydrogen bond is formed between N(5) and O(1) (d(N···O) = 2.957 (4) Å, d(H···O) = 2.07 (4) Å). Also it is the formation of this hydrogen bond that requires the trans(N) en ring to be λ.

Thus the conformations of both Λ and Δ forms in the crystal are (lel)$_2$ob. In one instance, the Δ isomer, the en chelates have catoptric conformations, although the cysteine moiety

Table VIII

Atoms	Δ-N,S-[Co-(en)$_2$(R)cysS]-ClO$_4$·H$_2$O	Λ-N,S-[Co-(en)$_2$(R)cysS]-ClO$_4$
Torsion Angles (deg)		
S–C(3)–C(1)–N(1)	−53	50.9
N(2)–C(4)–C(5)–N(3)	−49	51.1
N(4)–C(6)–C(7)–N(5)	17[b]	−49.0
Sum of Torsion Angles (deg)		
CysS ring	164	152.0
Trans(S) en ring	152	157.7
Trans(N) en ring	49[b]	151.7
Dihedral Angles[a] (deg)		
CysS ring	(36, −44)	(−40.9, 33.8)
Trans(S) en ring	(40, −35)	(−43.8, 33.5)
Trans(N) en ring	(−11, 11)[b]	(35.2, −39.2)

[a] Defined as the angle between the normal of adjacent planes containing the metal atom and two consecutive atoms in the ring. [b] Ring affected by disorder.

Table IX. Intermolecular Contacts in Δ-N,S-[Co(en)$_2$(R)cysS]ClO$_4$·H$_2$O

A···B	d(A···B), Å	Symmetry operation[a]
O(1)···N(4)	2.84 (1)	$1/2 + x$, $1/2 − y$, $2 + z$
O(1)···N(2)	2.97	$1/2 + x$, $1/2 − y$, $2 + z$
O(2)···O(7)	2.66	x, y, z
O(2)···N(5)	2.96	$1/2 − x$, $1 − y$, $1/2 + z$
O(3)···N(3)	3.15	$1/2 + x$, $1/2 − y$, $2 + z$
O(4)···N(2)	3.09	x, y, z
O(4)···N(1)	3.13	x, y, z
O(6)···N(4)	3.17	$−x$, $y − 1/2$, $3/2 − z$
O(7)···N(3)	2.91	$1/2 − x$, $1 − y$, $z − 1/2$

[a] To move atom B into contact with atom A.

Table X. Hydrogen Contacts in Λ-N,S-[Co(en)$_2$(R)cysS]ClO$_4$

A–H···B	d-(A···B), Å	d-(H···B), Å	Angle at H, deg	Symmetry operation[a]
N(1)···O(1)	2.70	2.27[b]	112	x, y, z
N(1)···O(2)	2.95	2.20	139	$3/2 − x$, $−y$, $1/2 + z$
N(2)···O(1)	3.12	2.26[b]	150	$x − 1/2$, $1/2 − y$, $1 − z$
N(3)···O(6)	2.97	2.17	137	$x − 1/2$, $1/2 − y$, $1 − z$
N(3)···O(2)	2.81	2.06	139	$3/2 − x$, $−y$, $1/2 − z$
N(4)···O(1)	2.86	2.06	155	$x − 1/2$, $1/2 − y$, $1 − z$
N(5)···O(3)	3.18	2.22	156	x, y, z
N(5)···O(1)	2.96	2.07	158	x, y, z

[a] To move atom B into contact with atom A. [b] Best considered as short contacts and not as hydrogen bonds.

has the carboxylate equatorially disposed as predicted earlier. In the Λ isomer not only are the en chelates δ and λ but also the cysteine moiety has the carboxylate disposed axially, again antithetical to the prediction. The variation can be ascribed to lattice forces and does not negate the stability argument described previously. For example, in the case of M(en)$_3^{3+}$, the five-membered metal en chelate rings have been found[23] in the crystal as (lel)$_3$, (lel)$_2$ob, (lel)(ob)$_2$, or (ob)$_3$, depending upon the counterion and metal ion. Therefore the only surprising conformational feature observed in the present complexes was the δ cysteine ring with an axial –CO$_2^-$ in the Λ complex. Here the energetically unfavorable arrangement is compensated by the intramolecular H bond to an en NH proton.

Conformational angles for the chelate rings are given in Table VIII. It should be noted that all five-membered rings appear to be equally puckered judging by the sum of the dihedral angles and the sum of the torsion angles.

Details of the hydrogen bonding are given in Tables IX and X. The strongest hydrogen bonds in both complexes are formed by the carboxyl groups. In the Δ isomer one carboxyl

oxygen atom is hydrogen bonded to two amino groups in an adjacent complex, and the other carboxyl oxygen is hydrogen bonded to an amino group in a different complex as well as to the water molecule. This is the only contact made by the water molecule which can be unequivocably assigned as a hydrogen bond.

The perchlorate oxygens have characteristically high thermal parameters but are not disordered. The bond lengths and angles are normal, and the hydrogen bonding involving the perchlorate groups is very weak.

Registry No. Λ-*N,S*-[Co(en)₂(*R*)cysS]ClO₄, 66417-03-6; Λ-*N,-S*-[Co(en)₂(*R*)cysS](ClO₄)₂, 66417-02-5; Δ-*N,S*-[Co(en)₂(*R*)-cysS](ClO₄)₂, 66417-01-4; Δ-*N,S*-[Co(en)₂(*R*)cysS]ClO₄·H₂O, 66417-00-3; Λ-*N,S*-[Co(en)₂(*R*)cysSH](ClO₄)₃, 66513-17-5; Λ-*N,S*-[Co(en)₂(*S*)penS]S₂O₆, 66416-98-6; Δ-*N,S*-[Co(en)₂(*S*)-penS](ClO₄)₂, 66416-97-5; Λ-*N,S*-[Co(en)₂(*R*)cysS]Cl₂, 66416-96-4; Δ-*N,S*-[Co(en)₂(*R*)cysS]Cl₂, 66416-95-3; Λ-*N,S*-[Co(en)₂(*S*)penS]Cl₂, 66416-94-2; Δ-*N,S*-[Co(en)₂(*S*)penS]Cl₂, 66416-93-1; Co(en)₂-(NH₂(CH₂)₂S)²⁺, 42901-32-6; Co(en)₂SCH₂OCO⁺, 42901-31-5.

Supplementary Material Available: Listings of structure factor amplitudes (30 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) University of Sydney. (b) Australian National University.
(2) Abbreviations used: cysS = cysteine deprotonated at sulfur; similarly, penS = penicillamine. To avoid confusion, no formal distinction is made between the ions with or without the carboxylate proton since this should be evident from the bonding mode, indicated as a prefix (e.g., N,S or N,O), and the formal charge carried by the ion.
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(10) (*R,R*)-Cystine ≡ (NH₂CH(CO₂H)CH₂S)₂, the oxidized form of (*R*)-cysteine ≡ L-(–)-cystine.
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(17) Since this work was completed, Krueger et al.[3] prepared [Co(en)₂-(*R*)cysS]ClO₄ by this route. The diastereoisomerism was ignored, and although the yield was not stated, our indicate that, under their conditions, the Λ isomer was obtained in ≲30% yield.
(18) Reference 3a states that both the –CH– and –CH₂ protons of the cysteine moiety in Co(en)₂(*R*)cysS⁺ exchange in 0.1 M NaOD, although no direct indication of time scale is given. Decomposition was evident, and it seems likely that the ¹H NMR changes observed were at least partly attributable to mutarotation.
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Structure, Bonding, and Chemistry of *closo*-Tetraphosphorus Hexakis(methylimide), P₄(NCH₃)₆, and Its Derivatives. 2. Polymorphs of the Monothio Derivative

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The title compound can be obtained in two crystalline polymorphs. By sublimation one obtains an orthorhombic form: space group *Pbc*2₁, *a* = 12.658 (4) Å, *b* = 14.940 (3) Å, *c* = 16.448 (4) Å, *V* = 3110 (1) Å³, *Z* = 8, *d*ₓ = 1.41 g cm⁻³. By recrystallization one obtains a monoclinic form: space group *P*2₁/*n*, *a* = 14.182 (3) Å, *b* = 13.681 (3) Å, *c* = 7.934 (2) Å, *β* = 101.09 (2)°, *V* = 1510 (1) Å³, *Z* = 4, *d*ₓ = 1.45 g cm⁻³. In both cases the X-ray data are of only mediocre quality; the molecular dimensions are therefore determined with relatively low accuracy but are consistent over the three crystallographically independent molecules that comprise the two crystal forms. The molecule has virtual *C₃ᵥ* symmetry. Only two of the three types of P–N distances have significantly different lengths (Å): SP–NP, 1.63 (2); SPN–P, 1.73 (2); P–NP, 1.70 (1). The P–S bond length is 1.92 (1) Å. Other dimensions are normal.

Introduction

A program of study of the structural and spectroscopic properties of the closo *N*-methylphosphoramide P₄(NMe)₆ and its derivatives, with the objective of elucidating the bonding in these systems, has been under way for several years.²⁻⁶ Structures of many of the sulfur and oxygen derivatives have been determined and a variety of spectroscopic studies made. This is the second of a series of detailed reports on these studies.

In the case of SP₄(NMe)₆, we first determined the structure using a crystal grown by sublimation. This was found to have a large orthorhombic unit cell with two molecules in the asymmetric unit, and, unfortunately, the amount of data which could be collected was disappointingly small, namely, only 1466 observed reflections for 246 parameters (for a ratio of 6.0). Moreover, there were sizable variations in the values obtained for what should have been equivalent bond lengths and angles.

Therefore, an effort was made to obtain a crystal of better quality by slow crystallization from hexane solution. It was found that the crystals so obtained were of a different polymorph, belonging to a monoclinic space group. Although the data to parameter ratio (6.2) is only marginally better than for the orthorhombic form, the structural features are somewhat more precisely defined. In any event, the second structure affords independent confirmation of the pattern of variation of P–N bond lengths, a feature of key importance in attempting to understand the molecular electronic structure. We report here both crystal structure determinations and present and discuss the best values of molecular dimensions thus obtained.

Experimental Section

The preparation of SP₄(NCH₃)₆ has been described previously.⁶ The material was sublimed in an evacuated (10⁻³ mmHg), sealed tube placed horizontally in a temperature gradient (25–65 °C) for ca. 4