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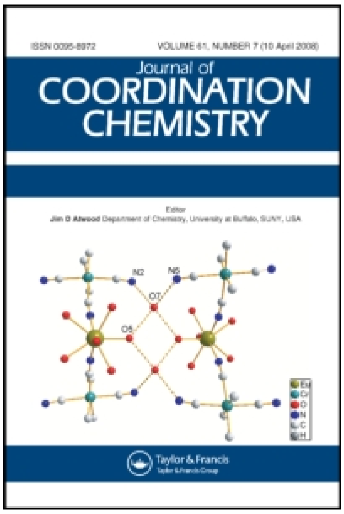

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
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Synthesis and Characterization of Chiral Isomers of Tris(1-Oxo-22(1H)-Pyridinethionate)Iron(III), Chromium(III), and Cobalt(III) Complexes

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To cite this Article Abu-Dari, Kamal and Raymond, Kenneth N.(1992) 'Synthesis and Characterization of Chiral Isomers of Tris(1-Oxo-22(1H)-Pyridinethionate)Iron(III), Chromium(III), and Cobalt(III) Complexes', Journal of Coordination Chemistry, 26: 1, 1 — 14

To link to this Article: DOI: 10.1080/00958979209407907

URL: http://dx.doi.org/10.1080/00958979209407907

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J. Coord. Chem. 1992 Vol. 26, pp. 1-14
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SYNTHESIS AND CHARACTERIZATION OF CHIRAL ISOMERS OF TRIS(1-OXO-22(1H)-PYRIDINETHIONATE)IRON(III), CHROMIUM(III), AND COBALT(III) COMPLEXES[1]

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(*Received 13 August 1991*)

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Among the chelating functional groups found in the microbial iron-transport agents called siderophores are hydroxamate, catecholate, and thiohydroxamate. The synthesis and properties of several chiral ligands containing 1-hydroxy-22(1H)-pyridinethione are reported. The synthesis and properties of ferric, chromic and cobaltic complexes of these ligands are reported as well. The Cr(III) and Co(III) complexes give electronic absorption spectra which show the two expected *d-d* transition for d^3 and low-spin d^6 octahedral complexes superimposed on very broad ligand transitions. Two absorption maxima are also seen in the electronic spectra of the ferric complexes, and which appear to be charge transfer transitions. These spectra resemble those of corresponding thiobenzohydroxamate complexes. Since the ligands are chiral, four diastereomers are possible, but only one isomer has been observed for each complex. All complexes seem to have the *cis* (or *facial*) geometry, with C_3 point symmetry, and both configurations, Λ and Δ, have been observed. The chirality of the complexes is assigned based on the signs of the CD bands of the low-energy transition in Cr(III) and Co(III) d^3 low-spin d^6 systems, respectively, and by comparing the shape and signs of CD bands of these complexes with those of the resolved optical isomers of tris(thiobenzohydroxamato)iron(III), chromium(III) and cobalt(III).

Keywords: Chelates, siderophores, 1-hydroxy-22(1H)-pyridinethione, chirality, complexes

INTRODUCTION

The problem posed by the insolubility of ferric hydroxide at physiological pH and yet the requirement of iron for microbial growth is overcome by the production of a wide range of powerful sequestering agents known as siderophores. These are low-molecular-weight compounds whose manufacture by microbes, in order to facilitate the uptake of ferric iron, have been described in previous papers in this series[1] and in recent reviews.[2–4] The most common functional groups in the siderophores are the hydroxamate and catecholate moieties (Figure 1), which act as strong, bidentate chelating agents. Another type of chelating group assignable to the siderophore class of compounds came with the discovery that cupric and ferric complexes of *N*-methylthioformohydroxamic acid could be isolated from culture broths of *Pseudomonas fluorescens* grown on *n*-paraffin or sucrose as the only source of carbon.[5,6]

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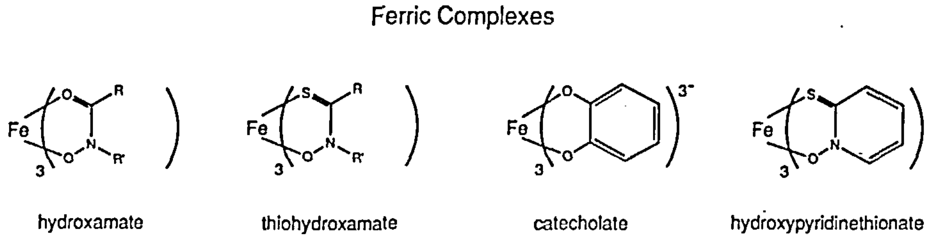

FIGURE 1 Examples of simple hydroxamates, thiohydroxamates, catecholates and 1-oxo-22(1H)-pyridinethiones as ferric ion complexes.

Previously we reported the synthesis and resolution of tris(thiobenzohydroxamato) chromium(III), cobalt(III), and (high-spin)-iron(III) complexes,[7] and the resolution of similar tris(benzohydroxamato) complexes[8] using the same technique. The circular dichroism (CD) spectra of the optical isomers of tris(benzohydroxamato)iron(III) compare well with those of chiral ferric complexes with naturally-occurring chiral siderophores.[8,9] However such comparison was not made for the thiohydroxamato complexes due to the lack of chiral ligands.

We report here the synthesis of several chiral 1-hydroxy-22(1H)-pyridinethione derivatives, the synthesis of the chromic, cobaltic and ferric complexes of these ligands, and their CD spectra and assigned chirality.

EXPERIMENTAL

Analytical grade ferric nitrate nonahydrate (Mallinckrodt) was used for the synthesis of ferric complexes. The tetrahydrofuran adduct of chromic chloride, $CrCl_3 \cdot 3THF$, was prepared by literature methods and protected from moisture.[10] Sodium cobaltinitrite (Matheson Coleman and Bell), reagent grade, was used without further purification for the synthesis of cobaltic complexes. Dimethylformamide was dried over alumina and distilled over molecular sieves. Triethylamine was dried over potassium hydroxide and distilled prior to use; 2,6-dibromopyridine (Aldrich), *R*-(+)-1-methylbenzylamine (Aldrich), *S*-(−)-1-methylbenzylamine (Aldrich), 1*R*,2*S*-(−)-ephedrine (Aldrich), *S*-alanine ethylester hydrochloride (Sigma), *S*-lysine methylester dihydrochloride (Sigma), and 1,1′-carbonyldiimidazole (Aldrich) were used without further purification. Laboratory grade solvents and reagents were used throughout the syntheses without further purification. NMR spectra were collected on a custom-built 200 MHz FT spectrometer. Infrared spectra were obtained in KBr pellets using a Nicolet 5/DX FT spectrometer. Electronic spectra were recorded on a Hewlett-Packard 8450A spectrometer. CD spectra were measured in $CHCl_3$ solutions using a Jasco J500-C automatic spectrophotometer. Melting points were measured in open capillaries with a Buchi apparatus and are uncorrected. Elemental analyses were performed by the Analytical Laboratory, University of California, Berkeley.

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Ligand Syntheses

The species 2-mercaptopyridine-1-oxide-6-carboxylic acid (**1**) was prepared from 2,6-dibromopyridine as described elsewhere.[11] The following general procedure was used for the synthesis of 1-methylbenzylamides and the ephedrine amide of compound **1**.

A solution of 1,1′-carbonyldiimidazole (1.62 g, 10.0 mmol) in DMF (20 cm^3) was added to a solution of compound **1** (1.71 g, 10.0 mmol) in 20 cm^3 DMF under N_2. The solution colour of compound **1** changed immediately from yellow to wine red with the evolution of gas (CO_2). The solution was stirred under N_2 for 15 min. and the solution of the amine (10.0 mmol) in DMF (20 cm^3) was added. The colour changed to yellowish green within 20 min.

The solution was stirred overnight under N_2. Most of the DMF was removed under pressure and 100 cm^3 of water was added, resulting in a clear solution. The pH was adjusted to *ca* 4.5 with 3M HCl while the solution was well stirred. The resulting precipitate was removed by filtration, washed with cold water, and dried under vacuum over P_2O_5. Additional small amounts of product could be obtained by extracting the filtrate with a large volume of chloroform. The combined product was dissolved in *ca* 5 cm^3 DMF and 50 cm^3 of cold water was added with vigorous stirring; the yellowish-green precipitate was filtered, washed with water and dried under vacuum over P_2O_5. Yield was 90%.

N-(1-hydroxy-22(1H)-pyridinethione-6-carbonyl)-*R*-(+)-1-methylbenzylamine (**2**), m.p. 96–98°C (dec). Anal.; calc. (found) for $C_{14}H_{14}N_2O_2S$: C, 61.3 (61.6); H, 5.14 (5.02); N, 10.2 (10.4); S, 11.7 (11.8)%.

N-(1-hydroxy-22((1H)-pyridinethione-6-carbonyl)-*S*-(−)-1-methylbenzylamine (**3**), m.p. 96–98°C (dec). Anal.; calc. (found) for $C_{14}H_{14}N_2O_2S$: C, 61.3 (61.7); H, 5.14 (5.07); N, 10.2 (10.3); S, 11.7 (11.7)%.

N-(1-hydroxy-22(1H)-pyridinethione-6-carbonyl)-1*R*,2*S*-(−)-ephedrine (hygroscopic) (**4**), m.p. 110–114°C (dec). Anal.; calc. (found) for $C_{16}H_{18}N_2O_3S \cdot 1/2H_2O$: C, 58.7 (58.8); H, 5.85 (5.49); N, 8.56) (8.98); S, 9.79 (10.3)%. *S*-alanine ethylester and *S*-lysine methylester amide derivatives of compound **1** were prepared using the same procedure as above, except that a slight excess of dry triethylamine was added to the DMF solution of amino acid hydrochloride salt to neutralize the HCl.

N-(1-hydroxy-22(1H)-pyridinethione-6-carbonyl)-*S*-alanine ethylester (**5**), m.p. 123–126°C (dec). Anal.; calc. (found) for $C_{11}H_{14}N_2O_4S$: C, 48.9 (49.8); H, 5.22 (5.00); N, 10.4 (11.9); S, 11.9 (12.2)%.

N,*N*′-bis(1-hydroxy-22(1H)-pyridinethione-6-carbonyl)-*S*-lysine methylester (**6**), m.p. 167–170°C (dec). Anal.; calc. (found) for $C_{19}H_{22}N_4O_6S_2$: C, 48.9 (48.9); H, 4.75 (4.62); N, 12.0 (11.9); S, 13.7 (13.6)%.

SYNTHESIS OF METAL COMPLEXES

Ferric complexes

All ferric complexes were prepared using the same general procedure described below for the synthesis of the ferric complex **7**. Yields were 85–95%.

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Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-*R*-(+)-1-methylbenzylamine) iron(III) (**7**). Solutions of compound **2** (0.825 g, 3.0 mmol) in DMF (5 cm^3) and ferric nitrate nonahydrate (0.404 g, 1.0 mmol) in DMF (5 cm^3) were combined and stirred for a few minutes, after which time water (100 cm^3) was added while stirring. The resulting dark violet precipitate was removed by filtration, washed with water and dried under vacuum over P_2O_5, m.p. 131–134°C (dec). Anal.; calc. (found) for $Fe(C_{14}H_{13}N_2O_2S)_3$: C, 57.6); H, 4.49 (4.49); N, 9.60 (9.27); S, 11.0 (10.6)%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-*S*-(−)-1-methylbenzylamine) iron(III) (**8**), m.p. 132–134°C (dec). Anal.; calc. (found) for $Fe(C_{14}H_{13}N_2O_2S)_3$: C, 57.6 (56.9); H, 4.49 (4.50); N, 9.60 (9.39); S, 11.0 (10.8)%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-1*R*,2*S*-(−)-ephedrine)iron(III) (**9**), (hygroscopic) decomposes at temp. >138°C. Anal.; calc. (found) for $Fe(C_{16}H_{17}N_2O_3S)_3 \cdot 2H_2O$: C, 55.2 (55.1); H, 5.31 (4.88); N, 8.05 (8.21); S, 9.21 (9.85)%.

Ferric complexes of compounds **5** and **6** were isolated but are not reported here.[11]

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Chromic complexes

All chromic complexes were prepared using the same procedure described below for the synthesis of the chromic complex **10**. Overall yield was 40–70%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-*R*-(+)-1-methylbenzylamine) chromium(III) (**10**). The tetrahydrofuran adduct of $CrCl_3$ (0.374 g, 1.0 mmol) was added to a degassed solution of compound **2** (0.825 g, 3.0 mmol) and sodium methoxide (3.0 mmol) in methanol (150 cm^3) under N_2. The mixture was degassed again and boiled at reflux for three hours in the dark. The volume of the solution was reduced to 5 cm^3 under vacuum after which water (100 cm^3) was added. The resulting green precipitate was removed by filtration, washed with water and dried under vacuum over P_2O_5, m.p. 133–135°C (dec). Anal.; calc. (found) for $Cr(C_{14}H_{13}N_2O_2S)_3 \cdot 2H_2O$ (hygroscopic): C, 55.5 (55.3); H, 4.77 (4.60); N, 9.26 (8.96); S, 10.6 (11.1)%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl-*S*-(−)-1-methylbenzamine)chromium(III) (**11**), m.p. 134–136°C (dec). Anal.; calc. (found) for $Cr(C_{14}H_{13}N_2O_2S)_3 \cdot 2H_2O$ (hygroscopic): C, 55.5 (55.1); H, 4.77 (4.72); N, 9.26 (8.84); S, 10.6 (10.1)%.

Tric(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-1*R*,2*S*-(-1-ephedrine)chromium(III) (**12**), decomposes at temp. >160°C. Anal.; calc. (found) for $Cr(C_{16}H_{17}N_2O_3S)_3 \cdot 3H_2O$: C, 54.5 (54.6); H, 5.42 (4.70); N, 7.98); S, 9.09 (9.89)%.

Cobaltic complexes

All cobaltic complexes were prepared using the same procedure described below for the synthesis of the cobaltic complex **13**. Overall yield was 50–80%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-*R*-(+)-1-methylbenzylamime) cobalt(III) (**13**). Sodium cobaltinitrite (0.404 g, 1.0 mmol) was added to a degassed solution of compound **2** (0.825 g, 3.0 mmol) and sodium methoxide (3.0 mmol) in methanol (100 cm^3) under N_2. The mixture was degassed again and then boiled at reflux in the dark for 10 hours. The volume was reduced to 5 cm^3 under vacuum, then water (100 cm^3) was added while stirring. The yellowish-green precipitate was removed by filtration, washed with water and dried under vacuum over P_2O_5, m.p. 136–138°C (dec). Anal.; calc. (found) for $Co(C_{14}H_{13}N_2O_2S)_3$: C, 57.4 (57.1); H, 4.47 (4.35); N, 9.56(9.44); S, 10.9 (10.5)%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-*S*-(−)-1-methylbenzylamine) cobalt(III) (**14**), m.p. 138–140°C (dec). Anal.; calc. (found) for $Co(C_{14}H_{13}N_2O_2S)_3$: C, 57.4 (57.4); H, 4.47 (4.43); N, 9.56 (9.51); S, 10.9 (10.4)%.

Tris(*N*-(1-oxo-22(1H)-pyridinethione-6-carbonyl)-1*R*,2*S*-(−)-ephedrine)cobalt(III) (**15**) (hygroscopic), decomposes at temp. >150°C. Anal.; calc. (found) for $Co(C_{16}H_{17}N_2O_3S)_3 \cdot 1.5H_2O$: C, 55.5 (55.4); H, 5.24 (5.13); N, 8.10 (8.40); S, 9.26 (9.23)%.

RESULTS AND DISCUSSION

The preparation of several chiral hydroxypyridinethionate ligands, including two enantiomers, provides structural analogues for similar chiral siderophore complexes. The chiral bidentate ligands are amides of 2-mercaptopyridine-6-carboxylic acid with chiral amines or amino acid esters and have been prepared using the procedures outlined in Scheme I and reported in detail elsewhere.[12] The corresponding tris (bidentate) complexes FeL_3, CrL_3 and CoL_3 have been prepared and their electronic

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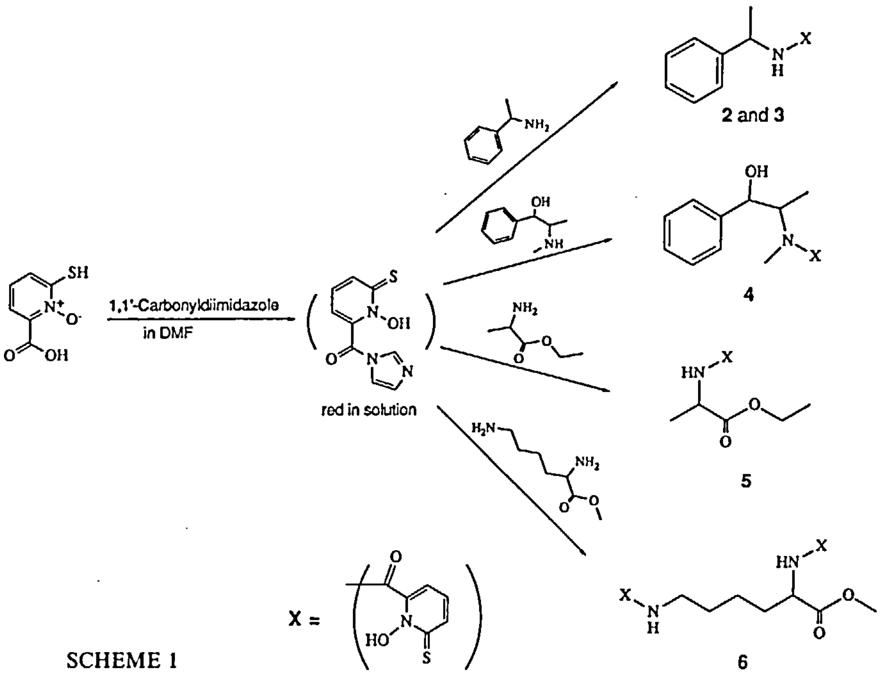

SCHEME 1

and CD spectra analyzed. The IR spectra of these amides show no band in the region 1700–2900 cm^{-1}, indicating the absence of S–H stretching and that these compounds are the thione tautomer. The C═S stretching frequencies of the ligands appear in the region 1100–1120 cm^{-1} and are shifted to lower wave numbers in the metal complexes, indicating coordination *via* the sulfur donor atom. The IR spectra of compounds **10**, **11**, **12** and **15** show broad bands in the region 3200–3600 cm^{-1} due to water H–O stretching. The most distinctive feature in the NMR spectra of the amides is the presence of two doublets at $\delta 6.9$ and $\delta 7.6$ and a triplet at $\delta 7.3$ corresponding to the three protons of the 1-hydroxy-22(1H)-pyridinethione ring. These are further split into doublets in the NMR spectrum of compound **6**.

The chromic and cobaltic tris chelate complexes are slightly air and light sensitive; hence all preparations were carried out using degassed solvents under nitrogen in Schlenk apparatus. All ferric, chromic and cobaltic complexes when examined by thin layer chromatography (tlc) showed the existence of only one isomer [earlier studies, which included the resolution of the usually labile ferric complexes of similar thiohydroxamate[7] and hydroxamate[8] ligands, show that in $CHCl_3$ these complexes do not undergo racemization or ligand exchange over periods of weeks at room temperature]. Since the ligands are chiral, four diastereomers are possible for these tris chelate metal complexes, Λ-*cis*, Δ-*cis*, Λ-*trans* and Δ-*trans* (Figure 2); the tlc results show that only one diastereomer is present in measurable amount for each metal complex. All similar tris(thiohydroxamato) metal complexes have been found to exist in the *cis* (or *facial*) geometry.[7,13,14] There is also a marked similarity in the CD and electronic spectra of the metal complexes reported here with those of tris(thiohydroxamato) metal complexes. Corresponding complexes of these two types of ligands are therefore assigned the same geometry.

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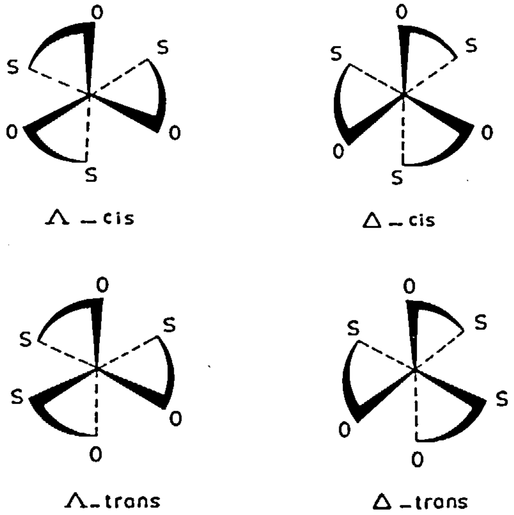

Λ – cis

Δ – cis

Λ – trans

Δ – trans

FIGURE 2 Geometrical and optical isomers of simple tris(thiohydroxamate) metal complex.

The electronic and CD spectra of the metal complexes are shown in Figures 3–10 (and are summarized in Table I). The tris(chelate)iron(III) complexes show two absorption maxima in the region 450–650 nm, a property shared by the spectra of tris(thiohydroxamato)iron(III) complexes[7] and by *N*,*N*′,*N*″-tris(1-oxo-22(1H)-pyridinethione-6-carbonyl)-2,2′,2″-triaminotriethylamine iron(III)[12] which crystallizes with *cis* (or *facial*) geometry. These absorptions are assigned to charge transfer transitions, since for ferric high-spin d^5 systems there are no spin-allowed *d-d* transitions. The tris(chelate)chromium(III) and -cobalt(III) complexes exhibit two absorption maxima in the visible region; the high-energy absorption in each case is unresolved and appears as a shoulder, due to the presence of strong ligand absorption in the near-UV region. These spectra are similar to those of other d^3 and spin-paired d^6 systems in pseudo-octahedral ligand fields. The ground states and spin-allowed excited states are $^4A_{2g} < {}^4T_{2g} < {}^4T_{1g}$ for Cr(III) and $^1A_{1g} < {}^1T_{1g} < {}^1T_{2g}$ for Co(III). This leads to the same symmetries for the spin-allowed transitions: T_1 (low energy) and T_2 (high energy).

The CD spectra of ferric complexes **7** and **8** (Figure 3) are very similar to those of the resolved optical isomers of tris(thiobenzohydroxamato)iron(III), showing one

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TABLE I

Band maxima and extinction coefficients for the electronic and circular dichroism spectra of the tris(chelate) complexes of Fe(III), Cr(III) and Co(III).

Compound	*Metal*	*Ligand*	*Configuration*	*Abs max, nm* (ε^a)	*CD bands, nm* ($\Delta\varepsilon^a$)
7	Fe	2	Λ	616 (2.92 × 10³) 525 (2.48 × 10³)	605 (−7.78), 510 (+5.37) 403 (−8.14)
8	Fe	3	Δ	616 (2.92 × 10³) 525 (2.48 × 10³)	605 (+7.78), 510 (−5.37) 403 (+8.14)
9	Fe	4	Λ	566 (4.04 × 10³) 522 (3.65 × 10³) sh.	580 (−17.1) 490 (+8.10) sh, 440 (+16.0)
(ref. 11)	Fe	5	Δ	612 (3 × 10³) 520 (3 × 10³)	600 (+11) 505 (−9), 440 (−5), 388 (+8)
10	Cr	2	Δ	660 (171) 450 (435) sh.	730 (−0.020), 625 (+0.14) 450 (−0.16)
11	Cr	3	Λ	660 (171) 450 (435) sh.	730 (+0.020), 625 (−0.14) 450 (+0.16)
12	Cr	4	Δ	640 (178) 474 (208) sh.	740 (+0.261), 635 (−2.64) 485 (+0.717), 420 (−0.35), 396 (+3.15)
ref. 11)	Cr	5	Λ	654 (180) 468 (350)	750 (−0.8), 628 (+4) 477 (−1.5), 420 (−5)
13	Co	2	Λ	649 (495) 500 (679)	644 (−18.9) 506 (−4.0), 444 (+13.1)
14	Co	3	Δ	649 (495) 500 (495)	644 (+18.9) 506 (+4.0), 444 (−13.1)
15	Co	4	Λ	644 (262) 492 (346)	642 (−9.68) 502 (−2.07), 422 (+6.82)

[a] Units are $M^{-1}\,cm^{-1}$.

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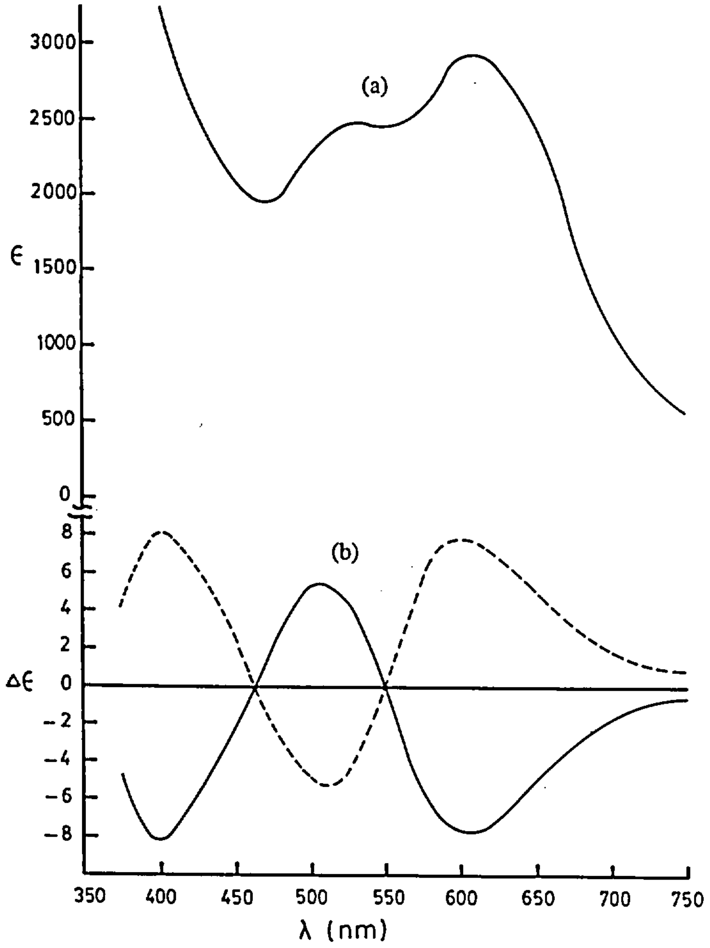

FIGURE 3 (Upper) Visible absorption spectrum of compounds 7 and 8 (Scheme I). (Lower) Circular dichroism spectra of compounds 7 (——, Λ) and 8 (– – –, Δ) in $CHCl_3$.

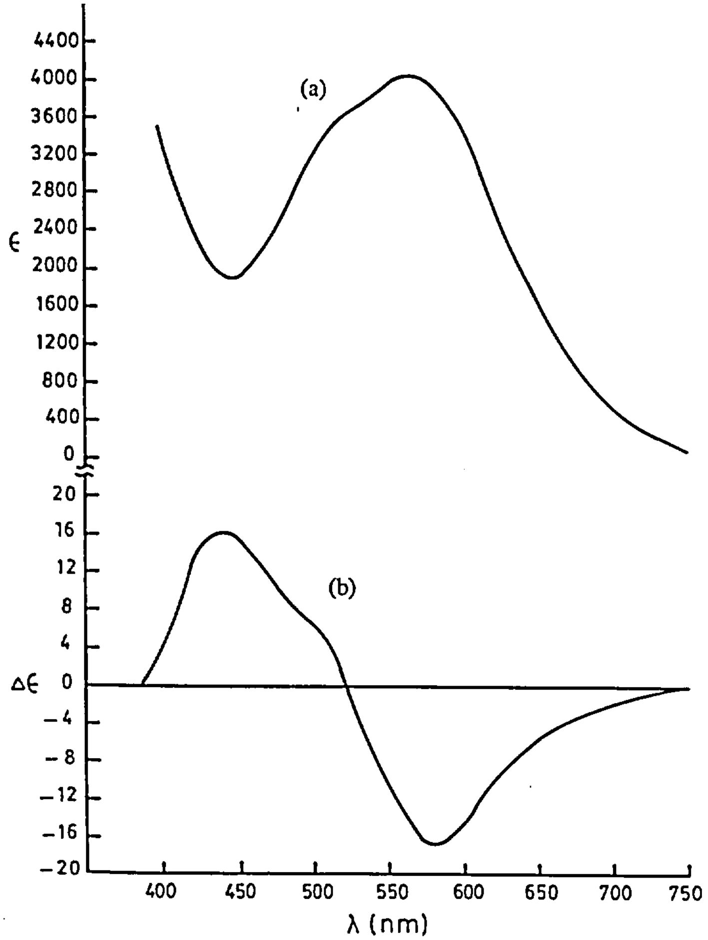

FIGURE 4 Visible absorption spectrum (upper) and circular dichroism spectrum (lower) of compound 9 (Scheme I) (Λ).

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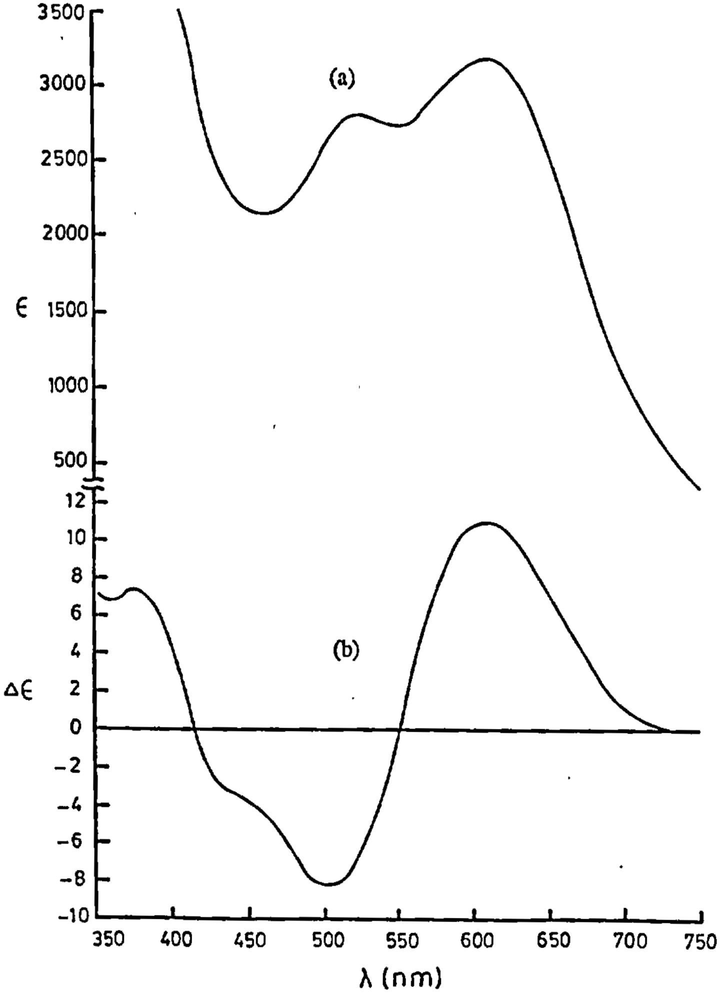

FIGURE 5 Visible absorption spectrum (upper) and circular dichroism spectrum (lower) of tris(*N*-(1-oxo-22(1H)-pyridine-thione-6-carbonyl)-*S*-alanine ethylester)iron(III) (Scheme I) (Δ) in $CHCl_3$ (see ref. 11).

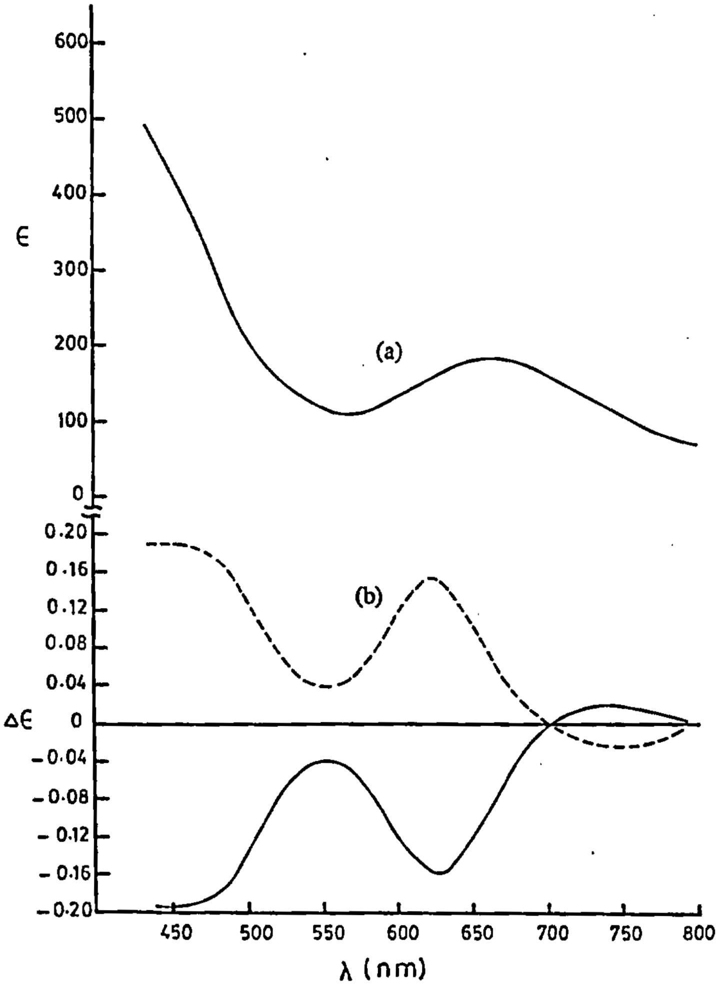

FIGURE 6 (Upper) Visible absorption spectra of compounds **10** and **11** (Scheme I). (Lower) Circular dichroism spectra of compounds **10** (—, Δ) and **11** (– – –, Λ) in $CHCl_3$.

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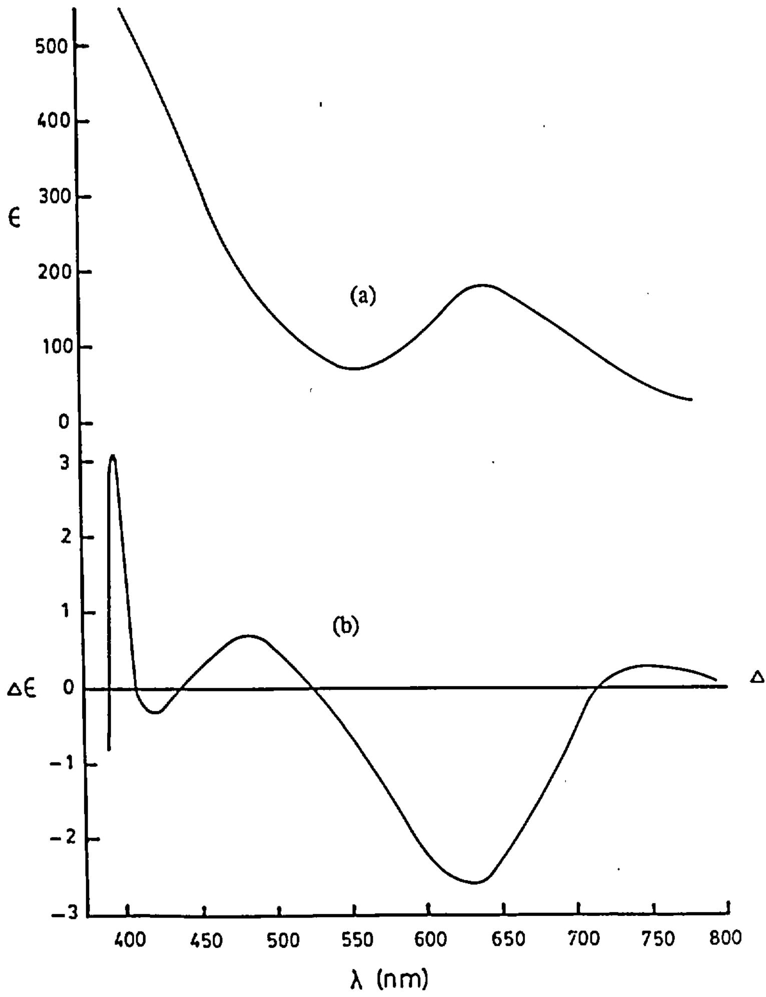

FIGURE 7 Visible absorption spectrum (upper) and circular dichroism spectrum (lower) of compound 12 (Scheme I) (Δ) in $CHCl_3$.

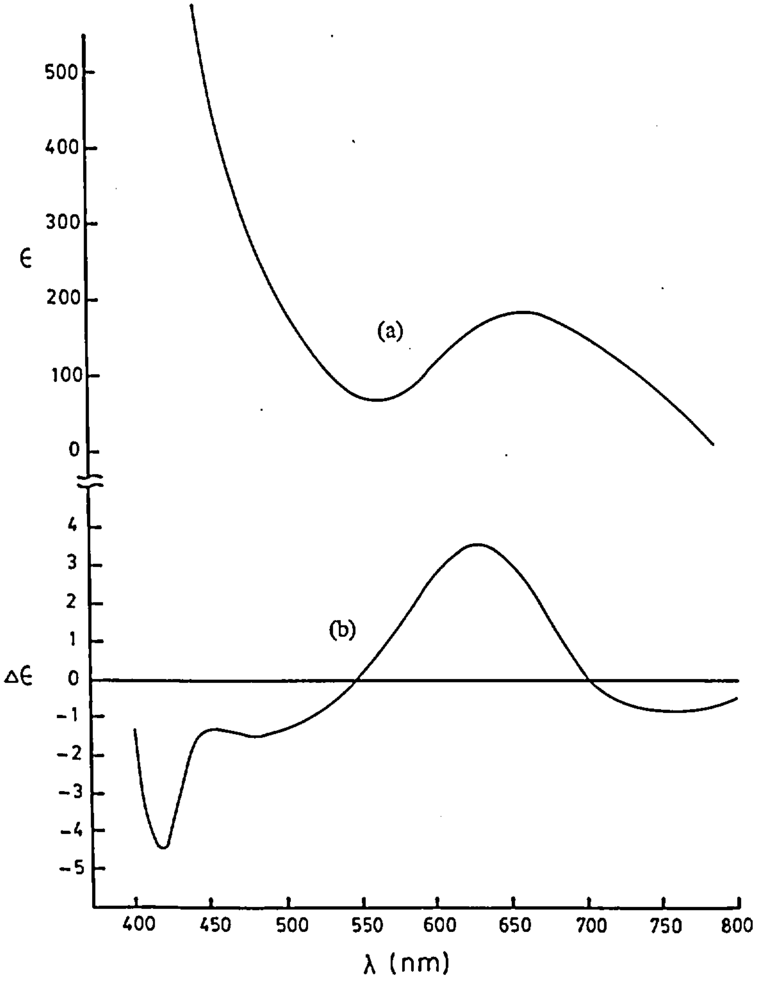

FIGURE 8 Visible absorption spectrum (upper) and circular dichroism spectrum (lower) of tris(*N*-(-oxo-22(1H)-pyridinethione-6-carbonyl)-*S*-alanine ethylester)chromium(III) (Scheme I) (Λ) in $CHCl_3$ (see ref. 11).

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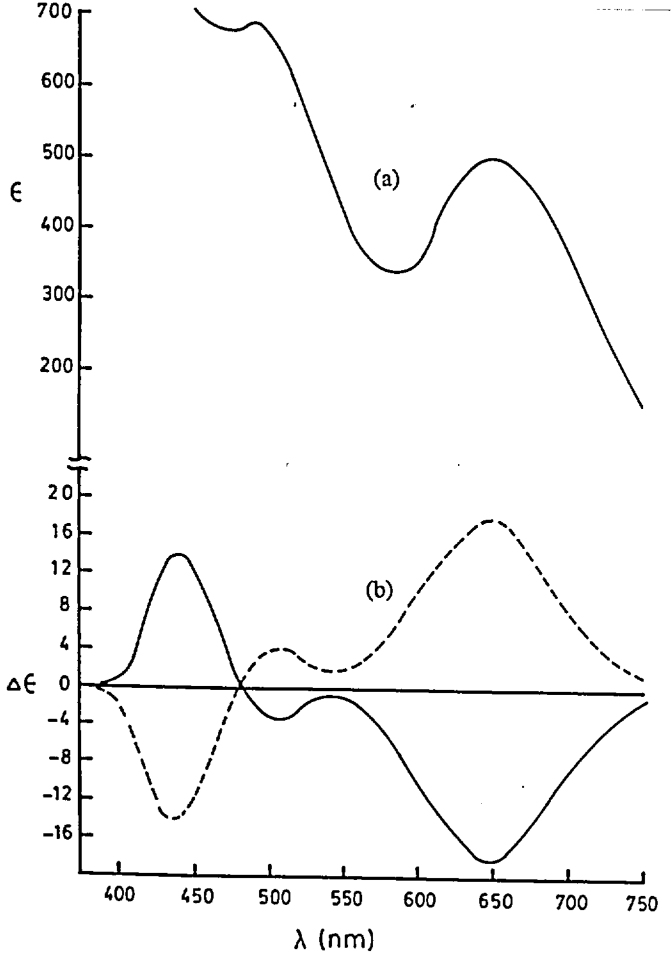

FIGURE 9 (Upper) Visible absorption spectra of compounds 13 and 14 (Scheme I). (Lower) Circular dichroism spectra of compounds 13 (—, Λ) and 14 (---, Δ) in $CHCl_3$.

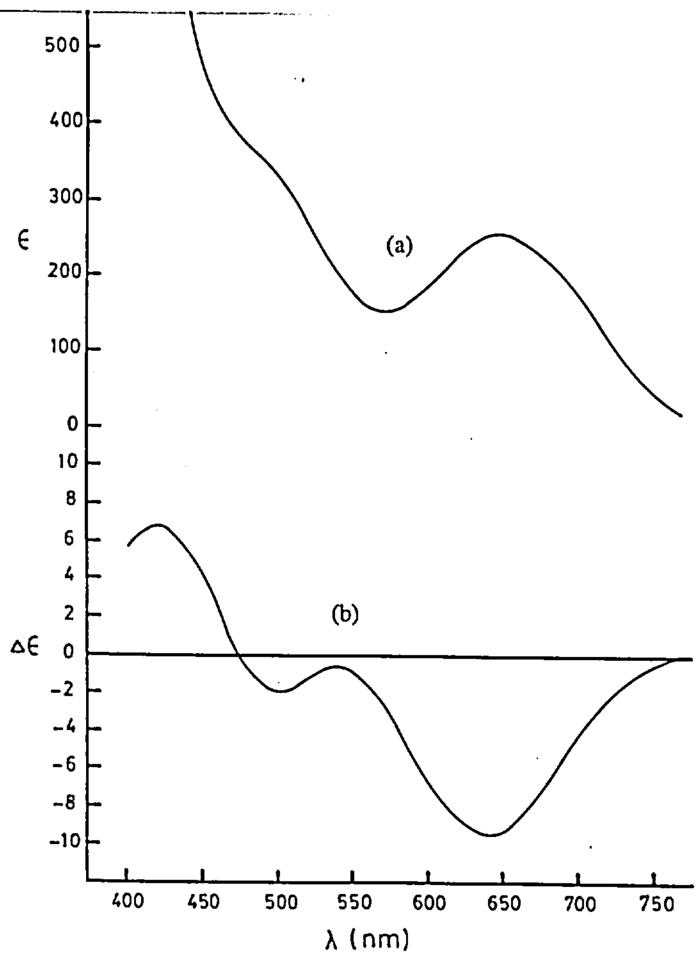

FIGURE 10 Visible absorption spectrum (upper) and circular dichroism (lower) of compound 15 (Λ) in $CHCl_3$.

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CD band in the region of the low energy transition and two CD bands with opposite signs in the region of the high energy transition. The assignment of the configuration can be based on the sign of the CD band at the low energy transition, similar to the assignment for the tris(thiobenzohydroxamato)iron(III) isomers.[7] Thus the isomer with a positive CD band at 600 nm can be assigned as having the Δ configuration (8), and the isomer with a negative CD band at 600 nm, (7). The CD spectrum of the ferric complex of the ephedrine derivative (9) is shown in Figure 4; following the same argument, this complex is assigned a Λ configuration [in this complex the second visible absorption is not resolved, and which results in the overlap of the CD bands, to give two CD bands and a shoulder]. The CD spectrum of the ferric complex of the *S*-alanine derivative[11] is shown in Figure 5 and displays three CD bands and an additional shoulder. This complex is assigned a Δ configuration. The CD spectrum (not shown) of the ferric complex of the *S*-lysine derivative[11] shows the complex also has the Δ configuration.

CD spectra of the chromic and cobaltic complexes are shown in Figures 6–10. In passing from O_h to the C_1 symmetry of the *trans* complex, each of the two *d-d* manifolds (T_1 and T_2) is expected to split into 3 transitions. For the C_3 symmetry *cis* isomer these manifolds each split into 2 (A and E) transitions. A similar pattern was reported for several cobalt(III)-amino acid complexes,[15–19] although fewer bands were found in the spectra of other complexes.[20]

Two weak CD bands, with opposite signs, are found in the CD spectra of the chromium(III) complexes (Figures 6, 7 and 8) in the low-energy absorption region. This is interpreted as implying that these are all *cis* isomers. Two or more weak CD bands are found in the spectra of the chromic complexes in the high-energy absorption region (some of these are probably due to ligand transitions).

Although most complexes with *cis* (or *facial*) geometry show fewer CD bands in the high-energy absorption region, three CD bands were found in this region in the spectra of *cis* isomers of some amino acid metal complexes,[15,21] in the spectrum of $(-)\text{-}[Co(ox)_3]^3\text{-}(D_3$ symmetry),[22] and the spectra of Δ- and Λ-tris(thiobenzohydroxamato)chromium(III) complexes.[7]

In the spectra of *cis* isomers of chromic complexes (d^3 system), with C_3 symmetry, the $^4A \rightarrow ^4E$ transition should have positive chiral signs for the Λ configuration and negative signs for the Δ configuration. The transition $^4A \rightarrow ^4A$ should have the opposite sign to the above transition.[20] A main difficulty arises in deciding which of the two bands from the low-energy T manifold is the E band. The relative energies of the E and A states depend upon the trigonal distortion and vary from one complex to another. Although it is generally accepted that the energy order is $A > E$ for five-membered rings formed by diamines and amino acid complexes,[15–19] the opposite order was found for several other complexes[19,23–25] including the chromium tris(hydroxamate)[26,27] tris(catecholate)[28] and tris(thiohydroxamate)[7] complexes.

In general, the CD bands of the low-energy transition for the chromium complexes reported here are similar to those bands of the chromic hydroxamate and thiohydroxamate complexes. Thus the energy order $E > A$ is also expected for the chromic complexes reported here, with the $^4A \rightarrow ^4E$ band the dominant band in each case. We thus tentatively assign the Δ configuration to the chromic complex with positive dominant CD band at 625 nm ($^4A \rightarrow {}^4E$ band) and negative CD band at ~750 nm ($^4A \rightarrow {}^4A$ band). These assignments of configuration and CD spectra for the chromic complexes are similar to those of tris(thiobenzohydroxamato)chromium(III) isomers.[7] Chromic complexes **10** and **11** showed weak CD activities, while complex **12** and the chromic complex of ligand **5**[11] showed much stronger activities (Table I).

The much more intense CD spectra of cobalt complexes are shown in Figures 9 and 10. These spectra are very similar to those of the resolved tris(thiobenzohydroxamato) cobalt(III) isomers,[7] with dominant $^1A \rightarrow {}^1A$ CD bands (as observed for several cobalt(III) complexes of amino acids).[16] We thus assign the Λ configuration to the cobaltic complex with negative CD band at 650 nm ($^1A \rightarrow {}^1A$ band).

In summary, several chiral derivatives of 1-hydroxy-22(1H)-pyridinethione have been prepared by coupling 2-mercaptopyridine-1-oxide-6-carboxylic acid to chiral amines and amino acids. The ferric, chromic and cobaltic tris chelate complexes of these chiral ligands are prepared and each is found to exist in only one stereomeric form. In each case examined, the ferric and cobaltic complexes derived from the same ligand were found to have the same configuration, which appears to be opposite to that of the corresponding chromic complex. However the weak CD spectra of the chromic complexes, presumably due to the larger bite angle, may lower the certainty of this assignment. The CD spectra and the signs of the CD bands of these complexes are similar to those of the previously reported tris(thiobenzohydroxamato)ferric, chromic, and cobaltic optical isomers.

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ACKNOWLEDGEMENTS

We thank Mr Tim Karpishin for assistance with recording the CD spectra and Ms Linda Uhlir for assistance with the NMR spectra.

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