Optically Active Co-ordination Compounds. Part XXXV.[1a] Configurations, Preparations, and Reactivities of Some Complexes of Amino-acids

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A comparison of c.d. spectra in solution and solid phases has been made for various complexes of α-amino-acidates. Such comparisons are found to be unreliable as guides to the configurations of [Cu(L-aa)]₂ complexes.§ Some unexpected effects are observed for the chiroptical *d–d* spectra of the insoluble isomers ‖ Λ-(+)-β-[Co(L-aa)₃] (where aa = the anion of L-ala, L-val, L-leu, L-pro, and L-thr), of their isomorphous chromium(III) and rhodium(III) analogues, and of Δ-(−)-β-[Co(L-leu)₃]. Reasons are advanced for the observed c.d. spectra. Full details of preparation and separation are given for isomers of [Co(L-thr)₃], [Co(L-lys)₃], [Cr(aa)₃] (where aa = the anions of gly and L-ala), and of some novel dimeric complexes of cobalt(III). Geometric and optical configurations are assigned to many of the new isomers. A number of isomerisations, carried out in water above 100°, are reported and discussed, and experimental details are given for some reactions of [M(aa)ₙ] and related compounds. Useful lines of further work are indicated.

METHODS which comment on the relationship between molecular configurations in the solid state and in solution are of obvious value. We recently concluded,[1b] with certain caveats, that, in general, kinetically inert species (which are not expected to undergo changes of configuration upon dissolution) should show the same c.d. in both phases. Likewise, if a kinetically labile species shows the same c.d. in both phases then the predominant configuration in solution must be that of the solid. We can now report exceptions to these simple conclusions both for the kinetically inert complexes of amino-acids with cobalt(III), chromium(III), and rhodium(III), and for the kinetically labile complexes with copper(II).

Bis(amino-acidato)copper(II).—For [Cu(L-aa)₂], (aa = ileu, val, tyr, or ser), the c.d. consists of a broad negative Cotton effect in the region of the *d–d* electronic transitions for both the solid state and aqueous solutions. Since the configuration of the tyrosine complex has been established[2] as *trans* from an *X*-ray crystallographic analysis, we inferred from the close similarity in c.d. that all the above complexes were also *trans* in both phases.

Such conclusions are now obviated by the findings[3,4] that the compounds containing L-serine and L-isoleucine have the *cis*-configuration in the solid state. Since our preparations of these two complexes were carried out in the same manner and the samples were of the same crystalline form as those used for the *X*-ray crystallographic analysis, it appears that the c.d. is unaffected to any detectable extent by the geometrical configuration about the copper ion. From the c.d. spectrum of

[Cu(L-ala)₂] the broad envelope encompasses at least two *d–d* transitions and both therefore appear, rather surprisingly, to be insensitive to the configuration about the metal ion. It is hence necessary to treat correlations of configurations for these copper(II) complexes between the solid and solution phases with caution.

Tris(amino-acidato)complexes of Cobalt(III), Chromium-(III), and Rhodium(III).—The tris(amino-acidato) complexes of cobalt(III), [Co(L-aa)₃], have been studied extensively.[5-12] For one enantiomer of the ligand, there are two possible geometrical isomers of the complex, *cis-cis*, facial, *abc* (or β), and *cis-trans*, meridional, *abd* (or α); both of these may exist with Λ (formerly [9,12] D) or Δ (formerly [9,12] L) configurations about the cobalt. Although there is no doubt about the correct assignment of the local microsymmetry at the cobalt(III) chromophore,[10,13,14] the evidence for the generally accepted tris-chelate monomeric structure is not so strong, except in a few cases, *e.g.* the crystal structure of Λ-(+)-α-[Co(L-ala)₃] is known.[15] No structural information has been available for the β-isomers of cobalt(III), though the crystal and molecular structures of racemic β-[Cr(gly)₃] have recently been established.[16]

Of particular interest are those Λ-β-isomers which are extremely insoluble in water. The high heats of sublimation of [Cr(gly)₃] and [Cr(L-ala)₃] (which from the given preparation method seem likely to be the β- and Λβ-isomers respectively) have been attributed either to the presence of polynuclear complexes or to strong intermolecular forces.[17] This latter explanation, specifically

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§ Abbreviations used throughout are: aa, amino-acid anion; gly, glycinate; ala, alaninate; leu, leucinate; ileu, isoleucinate; val, valinate; pro, prolinate; thr, threoninate; ser, serinate; tyr, tyrosinate; glu, glutamate; γ-Me-L-glu, γ-methyl-L-glutamate; asp, aspartate; pic, picolinate; en, ethylenediamine.

‖ We refer throughout this paper to the ' Λ-β-isomers ' without prejudice to the species actually present.

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[15] M. G. B. Drew, J. H. Dunlop, R. D. Gillard, and D. Rogers, *Chem. Comm.,* 1966, 42.

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in terms of intermolecular hydrogen bonding, was advanced by Douglas and Yamada [8] to account for the extreme insolubility * of Λ-$(+)$-β-[Co(L-ala)$_3$]. Since we find that Λ-$(+)$-β-[Co(L-ala)$_3$] is isomorphous with its chromium(III) and rhodium(III) analogues (which are also extremely insoluble in water) and racemic β-[Co(gly)$_3$] is isomorphous with the chromium(III) analogue [Supplementary Publication No. SUP 20990 (26 pp.)],† comments on structure in the solid state must apply to all

TABLE 1

Circular dichroism spectra of isomers of tris(L-amino-acidato)cobalt(III) complexes where agreement between solid and solution phases is good

| Complex | C.d. maxima/nm | |
	Solution	Solid [a]
Λ-α-[Co(L-ala)$_3$]	534 $(+)$ [b]	590 $(-0\cdot8)$, 530 $(+1\cdot0)$ [c]
Λ-α-[Co(L-leu)$_3$]	530 $(+)$ [d]	525 $(+1\cdot0)$, 465 $(-0\cdot38)$
Δ-α-[Co(L-leu)$_3$]	530 $(-$broad$)$ [d]	560 $(-1\cdot0)$, 495 $(-0\cdot88)$
Δ-α-[Co(L-val)$_3$]	520 $(-$broad$)$ [d]	560 $(-1\cdot0)$, ca. 500 $(-0\cdot85)$
Lα:Dα-[Co(L-val)$_3$] [e]	560 $(-0\cdot86)$, 480 $(-1\cdot0)$	570 $(-1\cdot0)$, 480 $(-0\cdot91)$
Λ-α-[Co(γ-Me-L-glu)$_3$]	520 $(+1\cdot0)$ ca. 450 $(-0\cdot67)$	580 $(-0\cdot19)$, 520 $(+1\cdot0)$, 460 $(-0\cdot22)$
Δ-β-[Co(L-thr)$_3$]	524 $(-)$	530 $(-$broad$)$

[a] KBr Discs and Nujol mulls. [b] In H$_2$O. [c] Sign and relative intensity in parentheses. [d] In ethanol. [e] Quasi-racemate, ref. 46.

three cases. One exception to this extreme insolubility of the Λ-β-isomers is that of the L-threonine complex of

Tables 1 and 2 present a comparison of the solid-state and solution c.d. spectra for some α- and β-tris(amino-acidato)complexes of cobalt(III) and chromium(III). Some of these c.d. spectra together with the electronic spectra are recorded in the Supplementary Publication.† For all the α complexes studied, regardless of the optical configuration at the cobalt centre, the sign of the dominant component of the lower energy d–d band is the same for the solid and solution phases. This is in line both with our experience [1b] and that of others [18] with several other optically active, kinetically inert, monomeric complexes. Furthermore, we find, in agreement with others,[10] that the magnitude of the Cotton effect of these α-isomers shows only a minor dependence on the solvent.

In the case of the Λ-β-isomers (where aa = L-ala, L-leu, L-val, and L-thr) the magnitude of the c.d. was found to be markedly dependent on the solvent so that the sign of the predominant Cotton effect in the d–d lower energy absorption band depends on the solvent employed. Similar observations have been made by others [8] on Λ-$(+)$-β-[Co(D-ala)$_3$] and Δ-$(-)$-β-[Co(L-leu)$_3$]. This latter complex is particularly interesting because it, like the Λ-β-isomers, is extremely insoluble in water.

The predominant (positive) Cotton effect in the lower energy d–d envelope for the Λ-β-isomers in H$_2$O–H$_2$SO$_4$ mixtures has been used as the criterion for establishing their optical configuration as Λ.[19] In the solid state, however, the predominant Cotton effect is negative for all the Λ-β-isomers of Co^{III} studied. Furthermore, although c.d. spectra in our solid state experiments are

TABLE 2

Circular dichroism spectra of isomers of tris(L-amino-acidato)metal complexes where the dominant Cotton effect is dependent on the phase

| Complex | | C.d. maxima/nm | |
		Solution	Solid [a]
Λ-$(+)$-β-[Co(L-ala)$_3$]	50% H$_2$SO$_4$ CF$_3$COOH DMF	535 $(+1\cdot0)$, 470 $(-0\cdot25)$ [b] 550 $(+0\cdot5)$, 490 $(-1\cdot0)$ 495 $(-$broad$)$	495 $(-1\cdot0)$, 410 $(+0\cdot14)$
Δ-$(-)$-β-[Co(L-leu)$_3$]	50% H$_2$SO$_4$	525 $(-)$	560 $(-0\cdot07)$, 500 $(+1\cdot0)$
Λ-$(+)$-β-[Co(L-leu)$_3$]	50% H$_2$SO$_4$	540 $(+1\cdot0)$, 490 $(-0\cdot2)$	500 $(-$broad$)$
Λ-$(+)$-β-[Co(L-val)$_3$]	50% H$_2$SO$_4$	540 $(+1\cdot0)$, 475 $(-0\cdot3)$	545 $(-1\cdot0)$, 490 $(-0\cdot8)$
Λ-$(+)$-β-[Co(L-thr)$_3$]	H$_2$O, 50% H$_2$SO$_4$	528 $(+)$ 545 $(+)$	515 $(-)$
Λ-$(+)$-β-[Co(L-pro)$_3$]	50% H$_2$SO$_4$	560 $(+1\cdot0)$, 495 $(-0\cdot1)$	575 $(+0\cdot2)$, 520 $(-1\cdot0)$
Λ-$(+)$-β-[Cr(L-ala)$_3$]	50% HClO$_4$ [c]	522 $(+0\cdot1)$, 400 $(+0\cdot13)$	546 $(-0\cdot8)$, 478 $(+1\cdot0)$

[a] KBr Discs and Nujol mulls. [b] Sign and relative intensity in parentheses. [c] Chromium(III) complexes decompose in 50% H$_2$SO$_4$.

cobalt(III); presumably the hydroxylic groups of the ligand confer the limited water solubility observed in this case.

* Really pure β-[Co(gly)$_3$] (which has often been studied in ' aqueous solution ') is actually insoluble in cold water and dissolves (slowly) only on boiling.

† X-Ray powder data, thermal isomerisation and decomposition data, and figures displaying electronic absorption, optical rotatory dispersion, and circular dichroism spectra of several of the complexes of this study have been deposited in Supplementary Publication No. SUP 20990 (26 pp., 1 microfiche). For details of the Supplementary Publication Scheme see Notice to Authors No. 7 in J.C.S. Dalton, 1973, index issue.

only semi-quantitative, it is clear that, compared with the corresponding α-isomers, and with the soluble Δ-β-isomers, the insoluble β-isomers have low intensities in the solid state. A similar observation has been made with Λ-β-[Cr(L-ala)$_3$] (Supplementary Publication).

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[19] R. D. Gillard in ' Physical Methods in Advanced Inorganic Chemistry,' eds. H. A. O. Hill and P. Day, Interscience, 1968, and references therein; C. J. Hawkins, ' Absolute Configurations of Metal Complexes,' Wiley–Interscience, New York, 1971, p. 210ff, and references therein.

Conversely, the water insoluble Δ-(—)-β-[Co(L-leu)₃] gave a predominantly negative Cotton effect in H₂O–H₂SO₄ mixtures but a predominantly positive one in the solid state. Similarly, for the highly water insoluble Λ-β-[Rh(L-ala)₃], c.d. spectra for a potassium bromide disc, a fresh solution in 50% sulphuric acid, and a fresh solution in trifluoroacetic acid were different; also the c.d. of the latter solution changed with time, indicating the presence of more than one species.[20]

The ¹H n.m.r. spectra of the β-[Co(L-ala)₃] isomers have been previously recorded.[10,21] In all cases the methyl groups were shown to be magnetically equivalent, consistent with the C_3 symmetry of the β structure. We have recorded the ¹H n.m.r. spectra of the Λ-(+)-β-[Co(L-ala)₃] isomer in D₂SO₄ and CF₃CO₂D solvents (Table 3); again the methyl groups are shown to be

TABLE 3

Chemical shifts and couplings of the methyl protons of
Λ-(+)-β-[Co(L-ala)₃]

Solvent	τ (p.p.m.)	J/Hz	Ref.
50% H₂SO₄	−2·07 (1), −2·18 (1) [a,b]	6	c
95% D₂SO₄	−1·6 (1), −1·7 (1) [d]	6·5	21
CF₃CO₂D	−1·44 (1), −1·54 (1) [a]	6	c
e	−1·79 (1), −1·91 (1) [a]	7	10

[a] At 60 MHz. [b] Relative intensities in parentheses. [c] This work; τ relative to tetramethylsilane as an external standard; resonance positions are concentration independent. [d] At 100 MHz. [e] Δ-(—)-β-[Co(L-ala)₃] in D₂O.

magnetically equivalent. Our results would also suggest that, like the Cotton effects, the resonances of the methyl groups are solvent dependent.

However, such a conclusion must be treated with caution since the use of tetramethylsilane as an external standard in the resonance measurements does not reveal the effect of the solvent susceptibility on the quoted resonance positions.

DISCUSSION

The β-isomers of [Co(L-aa)₃] are of formal C_3 symmetry and hence two magnetic dipole allowed transitions ¹E ⟵ ¹A and ¹A ⟵ ¹A are expected under the low energy band of ¹T₁ₘ ⟵ ¹A₁ₘ (O_h parentage). The transition perpendicular to the C_3 axis (¹E ⟵ ¹A) should have a positive chiroptical sign for the Λ configuration about the cobalt centre, while the ¹A ⟵ ¹A transition parallel to the C_3 axis should show a negative rotatory power for this optical configuration. Assuming that the ordering of the energy levels is the same as that in the tris(ethylenediamine)cobalt(III) ion, i.e. A > E, then the (+)-β-isomers should have the Λ configuration. The

* The recently reported crystal structure of [Co(en)₃]₂(HPO₄)₃,- 9H₂O strongly supports this suggestion, since exactly this feature is found (ref. 23).

application of such symmetry rules to the deduction of absolute configuration has been shown to be reliable for a number of tris-chelated compounds of cobalt(III).[19] From the results now presented, the application of symmetry rules to the insoluble tris-complexes studied here is unreliable, since the Cotton effects are markedly dependent on the phase and on the solvent employed.

This breakdown of the simple rule may be attributed to any one of several causes. Specific interactions, arising either (i) from the acidic solvents employed, or (ii) in the solid state, could result in changes in relative rotational strengths of the A and E transitions within the monomeric tris-chelated β-isomer. (iii) Complexes with lowered symmetries may be present in solution, in which case the selection rules for C_3 symmetry are inapplicable and the absolute configuration cannot be deduced from chiroptical signs. (iv) Finally the solid may be made up of units other than monomeric [M(aa)₃]. We consider these possibilities in turn.

(i) Specific interactions in solution are well known both for bis(amino-acidato)cobalt(III) complexes[22a] (where conformational change in the ring gives large changes in d–d c.d. spectra) and for cationic complexes,[22b] where changes in rotatory strengths occur on the addition of such anions as PO₄³⁻. These changes are attributed to the formation of specific contact ion-pairs in which the tetrahedral anion is sited on the C_3 axis of a complex such as [Co(en)₃]³⁺, so that its own C_3 axis is collinear and three hydrogen-bonding contacts between N–H of the cation and O–P of the anion result.* In the acidic solvents required to dissolve the Λ-β-isomer, it is not necessary to invoke similar specific solvent effects (e.g. hydrogen bonding dictating[22a] the presence of one particular conformer), since Λ-(+)-β-[Co(L-thr)₃] exhibits the same changes in Cotton effects (solid ⟶ solution phases) on dissolution in water alone.

Because the solvents required are so strongly acidic, we have looked into the possibility that protonation may underly the chiroptical changes in solution. Such acid–base equilibria in complexes have occasionally [as for the cations salicylatobis(ethylenediamine)cobalt(III)[24] and cis-di-isothiocyanatobis(ethylenediamine)cobalt(III)[25]] given rise to fairly substantial variations in c.d. In testing this notion we have examined solutions of α-[Co(gly)₃] in hydrochloric acid; such solutions were reported[26] to give solids of composition Co(gly)₃,3HCl, Co(gly)₃,2HCl, and Co(gly)₃,HCl. (We have, in passing, re-examined these solids.) The electronic spectrum of a solution of α-[Co(gly)₃] in 11M-hydrochloric acid is still consistent with the co-ordination sphere of the cobalt comprising three N and three O donor atoms, i.e. chloride is not involved as a ligand. The ¹H n.m.r. spectrum shows a shift of the methylene protons relative to water: based on our experience with the protonation of chelated

²⁰ R. D. Gillard and P. R. Mitchell, unpublished observations.
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²³ E. N. Duesler and K. N. Raymond, Inorg. Chem., 1971, 10, 1486.
²⁴ K. Garbett and R. D. Gillard, J. Chem. Soc. (A), 1968, 979.
²⁵ R. D. Gillard and R. Maskill, J. Chem. Soc. (A), 1971, 2813.
²⁶ V. P. Ogoleva, Trudy Dagestan, Sel'skokhoz. Inst., 1955, 7, 130.

α-amino-acidate ligands in other complexes,[20] we attribute this to protonation without ring opening. However, judging from the great similarity of the c.d. of α-[Co(aa)₃] complexes in water and in acids, such protonation, *per se*, causes little change in Cotton effects: it is unlikely to account for the dramatic changes found in the chiroptical properties of β-isomers in acid solutions.

(ii) Specific solid state effects, *e.g.* interaction with the halide ions in potassium halide discs, can be ruled out, since: (*a*) c.d. spectra recorded in KBr or KCl discs or in Nujol mulls were identical; (*b*) the c.d. spectrum of a KBr disc of Λ-β-[Co(L-ala)₃] dissolved in H_2O–H_2SO_4 was identical with that of pure Λ-β-[Co(L-ala)₃] dissolved in the same solvent; and (*c*) for all the α-isomers and water soluble β-isomers studied the solid state and solution spectra were virtually identical. However, in line with the change in the relative intensities of the A and E components of band (I) of [M(LL)₃]³⁺ (where M = Co or Cr and LL is an aliphatic 1,2-diamine) on addition of polarisable anions, it is possible that the structure of these insoluble β-isomers is such that enhancement, by intensity borrowing, of the higher energy band relative to that of the lower energy occurs in the solid state. That is, the observed c.d. spectrum is that of the crystal rather than that of the molecule. For this to be true in this particular case, but in no other that we yet know of, the coupling would have to be comparable with the molecular effects.

(iii) The presence in solution (for the Λ-β-isomers) of species other than tris-chelate is suggested by the magnitude of the Cotton effect ($\Delta\varepsilon < 1$) which is smaller than that of other known tris-chelates of cobalt(III) and chromium(III) ($\Delta\varepsilon$ 2—3). The magnitude of $\Delta\varepsilon$ is more consistent with the presence of at least some bischelated species. Two apparent exceptions to this are Λ-(+)-β-[Co(L-pro)₃] ($\Delta\varepsilon$ *ca.* 4), which may be treated as a special case because of the extra asymmetry arising from the co-ordinated nitrogen atom, and Λ-(+)-β-[Co(L-thr)₃] ($\Delta\varepsilon$ +2·6) for which the contributions to the optical activity from the configuration and vicinal effects are found to be additive, as is often the case with similar genuine tris-chelated species.[8] The values found for the absorption maxima of β-[Cr(gly)₃] in the solid state (503 nm)[16] and in solution in acid (539 nm in 70% $HClO_4$) are different, again suggesting some chemical reactions on dissolution.

(iv) We know, from the crystallographic work of Bryan *et al.*,[16] that the insoluble form of [Cr(gly)₃] has the β-monomeric structure, and we know from our own demonstration of isomorphism, that β-[Co(gly)₃] is isostructural. However, because we have little information on the Λ-β-isomers of tris-L-amino-acidates, we must consider the possibility * that the solid Λ-β-isomers may be polymeric. Despite some apparent differences in solubilities of the samples of Λ-(+)-β-[Co(L-ala)₃], all

were isomorphous and exhibited a well defined X-ray powder pattern. Our attempts to measure molecular weights in sulphuric acid solutions gave only ambiguous results because of the uncertainty as to the nature of the protonated species present.

Any polymeric species which may be suggested must be made up according to the stoicheiometry [Co(L-aa)₃], which has been repeatedly established. The local microsymmetry at the cobalt ion is also known to be β. A variety of polymers can be envisaged, ranging from dimers to polymers, in which two or all three aminoacidate ligands are shared.

In summary, then, the highly insoluble A-(+)-β-[Co(L-aa)₃] complexes give rise to anomalous chiroptical properties. These properties may be the result of molecular association (*e.g.* through hydrogen bonding or through bridging ligands) in the solid state or of the existence of species other than monomeric tris-chelates in solution. The variable nature of the Cotton effects with change of phase and of solvent means that the relationship between optical activity and the absolute configuration based on simple selection rules is inapplicable and their Λ-β nature is thus not rigorously proven. The currently available results, in fact, can equally well be explained with either *cis*- or *trans*-bis-bidentate structures and even the possibility of the Δ-optical configuration existing in the solid state cannot be dismissed. These comments, which also apply to the water soluble Λ-(+)-β-[Co(L-thr)₃], to the corresponding isomorphous isomers of the chromium(III) and rhodium(III) complexes, and to the water insoluble Δ-(−)-β-[Co(L-leu)₃], indicate lines of useful future work required to lend rigour to this area of configurational deduction.

Some New Complexes of α-Amino-acid with Cobalt(III) and Chromium(III).—Tris(L-threoninato)cobalt(III). The insoluble pink product of composition [Co(L-thr)₃], obtained by the decomposition of [Co(en)₂(L-thr)]²⁺, has been assigned[27] the Λ-β-configuration. This dismutation has been repeated and followed by extensive chromatography which shows the formation of the Λ-β-isomer (isolated as a dihydrate) to be completely stereoselective. That is, the reaction

$$3[Co(en)_2(L\text{-thr})]I_2 \longrightarrow$$
$$2[Co(en)_3]I_3 + \text{Λ-}(+)\text{-β-}[Co(L\text{-thr})_3]$$
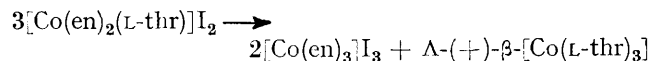
represents a novel asymmetric synthesis.

The remaining three isomers of [Co(L-thr)₃] have also been prepared and separated by means of column chromatography (see Experimental section). Their electronic, o.r.d., and c.d. spectra have been deposited in the Supplementary Publication. Assignment of the Λ and Δ configurations to the purple α isomers was by comparison of the dominant Cotton effect of the longest wavelength d–d band with that of (+)-α-[Co(L-ala)₃] which is known[15] to have the Λ configuration.

The spectroscopic properties of all the isomers of [Co(L-thr)₃] differ to a marked extent from those of the

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* That is, although we know that racemic β-[Co-gly)₃] contains tris-chelated monomeric complexes as formulated, this does not constitute direct evidence on the complex species present in either Λ-β-[Co(gly)₃] or Λ-β-[Co(aa)₃] where aa is an L-aminoacidate.

²⁷ P. M. Harrison and R. D. Gillard, *J. Chem. Soc. (A)*, 1967, 1657.

corresponding isomers of other amino-acid complexes. For the β-isomers of [Co(L-thr)₃] ε of the longest wavelength d–d band is approximately half that normally

doubt, however, that the β-isomers are optically pure since no further change in optical rotation was observed on further recrystallisation or chromatography.

TABLE 4

Spectroscopic properties of tris(amino-acidato)cobalt(III) complexes [a]

Complex aa		Λ-α Band I	Λ-α Band II	Δ-α Band I	Δ-α Band II	Λ-β Band I	Λ-β Band II	Δ-β Band I	Δ-β Band II	L-α:D-αAdduct Band I	L-α:D-αAdduct Band II	Refs.[b]
Glycine	λmax	542	374	542	374	520	377	520	377			
	ε	96	141	94	141	144	120	144	120			c
	λCD	535										
	Δε	+2·75										
L-Alanine	λmax	542	370	544	375	518	373	515	375			8, 10, 12
	ε	93	150	106	165	188	166	212	174			
	Solvent	H₂O		H₂O		50% H₂SO₄		H₂O				
	[A]	12 600		10 000				11 400				
	λCD	526		532				530				
	Δε	+3·3		−2·6				+2·9				
L-Phenylalanine	λmax			530	380			525	380			d
L-Valine	λmax	532	572	533	372	522	373	532	373	530	381	12, 46
	ε	100	168	117	167	151	126	153	142	150	173	
	Solvent	EtOH		EtOH		50% H₂SO₄		H₂O		60% HClO₄		
	[A]	8600		15 000		5500		3400				
	λCD	527		523		540		576 & 478		520		
	Δε	+2·1		−3·25		+1·1		−0·72	−0·97	−1·43		
L-Leucine	λmax	535	375	537	375	520	375	516	372			10, 12
	ε	104	169	109	165	205	203	207	179			
	Solvent	EtOH		EtOH		50% H₂SO₄		50% H₂SO₄				
	[A]	8750		11 800		6000		9500				
	λCD	528		529		548		528				
	Δε	+3·2		−2·8		+1·1		−2·6				
L-Proline	λmax			546	382	541	383	529	385			10
	ε			103	160	156	202	111	138			
	Solvent			EtOH		95% H₂SO₄		H₂O				
	λCD			571		565		562				
	Δε			−1·9		+4·1		−2·6				
L-Aspartic acid	λmax	522	364	522	364	520	380	520	380			11
	ε	126	178	126	178	219	182	219	182			
	Solvent	60% HClO₄		60% HClO₄		60% HClO₄		60% HClO₄				
	[A]	13 700		13 700		7500		6880				
	λCD	517		509		536		526				
	Δε	+2·75		−2·3		+1·5		−1·5				
L-Glutamic acid	λmax			541	373	521	376					e
	ε			197	210	224	221					
	λCD			571		550						
	Δε			low		+1·1						
δ-Methyl-L-glutamic acid	λmax	541	375	545	373							12
	ε	121	184	112	173							
	[A]	14 700		10 600								
	λCD	525		521								
	Δε	+3·9		−2·6								
L-Threonine	λmax	538	370	536	370	524	362	520	374			f
	ε	100	160	100	150	87	160	154	150			
	λCD	532		536		528		524				
	Δε	+1·5		−0·66		+2·6		−1·57				
L-Lysine	λmax	525	369	525	369							f
	ε	109	178	121	180							
	[A]	10 300		13 600								
	λCD	532		526								
	Δε	+1·64		−1·82								
L-Cysteine	λmax			570	440							g
	ε			892	681							
	λCD			590								
	Δε			−6·4								
[Co(gly)₂(L-val)]	Solvent	H₂O				50% H₂SO₄		H₂O				43
	[A]					6400						
	λCD	530				541		532				
	Δε	+2·6				+1·3		−2·0				
[Co(L-val)₂(gly)]	Solvent					50% H₂SO₄						43
	[A]					5950						
	λCD					540						
	Δε					+1·1						
[Co(L-val)₂(L-ala)]	Solvent					50% H₂SO₄						43
	[A]					5560						
	λCD					541						
	Δε					+0·92						
[Co(L-val)₂(D-ala)]	Solvent							50% H₂SO₄				43
	λCD							530				
	Δε							−2·0				
[Co(gly)₂(L-ala)]	Solvent					50% H₂SO₄						43
	[A]					5210						
	λCD					540						
	Δε					+1·4						
[Co(L-ala)₂(D-ala)]	Solvent					50% H₂SO₄						43
	[A]					4800						
	λCD					541						
	Δε					+1·3						

[a] Unless given otherwise the solvent is water. [b] In most cases average values are listed where more than one reference is cited. In a few instances, where values given in references were in disagreement, the values listed in the reference giving the largest Δε value for the particular isomer were chosen. Uncertainty limits are λmax. ± 1%, ε ± 3%, [A] ± 2%. [c] Ref. 45 and R. D. Gillard, J. R. Lyons, and C. Thorpe, *J.C.S. Dalton*, 1972, 1584. [d] P. Vieles and A. Bonniol, *Compt. rend. D.*, 1969, **269**, 577. [e] E. Larsen and S. F. Mason, *J. Chem. Soc.* (*A*), 1966, 313 and I. Lifschitz, *Proc. Acad. Sci.* (*Amsterdam*), 1936, **39**, 1192. [f] This work. [g] R. D. Gillard and R. Maskill, *Chem. Comm.*, 1968, 160.

observed, while Δε for the Λ-β- is larger than that of the Δ-β-isomer (for easy reference the results are summarised for all [Co(aa)₃] species in Table 4). There seems little

Furthermore, the optical activity from the configurational contribution was found to be enantiomeric for the two β-isomers; an observation which has previously

been found [28] to be consistent with optical purity. The $\Delta\varepsilon$ values of the α-isomers are considerably smaller than normally found for such isomers and, since solids were not isolated in these cases, their optical purity must be regarded as questionable. The presence of other species in the aqueous solutions of the two α-isomers can be ruled out since they were chromatographically homogeneous and displayed electronic spectra typical of other authentic α-isomers.

Tris(L-*lysinato*)*cobalt*(III). Air-oxidation of aqueous cobalt(II)–L-lysine solutions was found to produce the α-isomers (mainly Δ-α-) of [Co(L-lys)₃]; only traces of the β-isomers were observed. Surprisingly, the same stereoselective formation of the α-isomers was also obtained by heating hexa-amminecobalt(III) in the presence of the amino-acid and charcoal, a route which frequently favours the formation of the β-isomers. It seems reasonable, by comparison with the other tris(amino-acidato) complexes, to assume that the unusual side-chain of L-lysine (–[CH₂]₄NH₂) is, by some unknown mechanism, controlling the stereoselective formation of the α- isomers.

The electronic absorption, o.r.d., and c.d. spectra of the purple isomers obtained (see Supplementary Publication) are typical of the α-isomers of other tris(amino-acidato)cobalt(III) complexes. Assignment of the Δ and Λ configurations again is made by comparison of the dominant Cotton effects of the longest wavelength *d–d* band with that of α-(+)-[Co(L-ala)₃].

Tris(L-*amino-acidato*)*chromium*(III). Tris-complexes of chromium(III) with the anions of glycine and L-alanine have previously been reported,[17,29–31] but no attention has been given to the isomerism of these complexes. The red compounds of formulae [Cr(gly)₃] and [Cr(L-ala)₃], formed on neutralisation of a solution containing a chromium(III) : amino-acid ratio between 1 : 5 and 1 : 10, were found to be isomorphous (for *d*-spacings see Supplementary Publication) with their β-[Co(aa)₃] analogues (β- for aa⁻ = gly, and Λ-β- for aa⁻ = L-ala). Hence the red chromium(III) compounds are also assigned a β configuration. Their electronic absorption, o.r.d., and c.d. spectra are contained in the Supplementary Publication.

The preparation of purple α-[Cr(gly)₃] has been claimed.[32] In our numerous attempts to repeat this preparation, we did indeed obtain a dark purple material; however, our results consistently indicate that this purple fraction is a hydrated form of the dihydroxo-bridged dimer, *i.e.* [Cr₂(gly)₄(OH)₂],6H₂O. Under vacuum at 100° this reverts to the known anhydrous dimer. We have also made the analogous L-alanine complex [Cr₂(L-ala)₄(OH)₂],7H₂O which also forms the anhydrous dimer *in vacuo*.

L,L′-*Tetrakis*(*amino-acidato*)*di*-μ-*hydroxo-dicobalt*-(III,III). The binuclear complexes of chromium(III) with glycine and alanine are well known,[29,31,33] but to

our knowledge there has been no report on the cobalt(III) analogues. We now wish to report such compounds of cobalt(III) with the amino-acids glycine, L-alanine, and L-valine; their *d*-spacings given in Table 5 show them to be isomorphous.

For a compound of formulae [(aa)₂M-(μ-OH)₂M(aa)₂] there are three possible geometrical isomeric configurations around each metal ion: *trans* N-*cis* O, *cis* N-*trans* O, and *cis* N-*cis* O. In addition each metal ion is a dissymmetric centre, bringing the total number of geometrical and optical isomers to 21. One of the methods employed in the synthesis of the cobalt(III) dimers involves the conversion of a carbonato-ligand into an aquo-ligand by acidification. This is commonly considered to be a ' configuration retaining reaction '. However, the recent demonstration [34] that the same reaction in one instance results in an inversion eliminates any attempt here to correlate the configuration of the dimeric products and the initial reactants.

The large optical activity associated with the dimeric L-alanine and L-valine products indicates that a high degree of stereoselectivity occurs among the 21 possible isomers. From the nature of the Cotton effects of the long-wavelength *d–d* band we tentatively conclude that the Δ configuration predominates at both cobalt centres in the dinuclear complexes.

Two points make these complexes worthy of study from a stereochemical viewpoint. First, the large stereoselectivity observed, although this may well result from the insolubility of the products obtained. Second, the differences in electronic absorption, o.r.d., and c.d. spectra between the L-alanine and L-valine complexes are greater than normally observed with amino-acid complexes of cobalt(III); these differences may indicate that stereoselectivity favours different geometric isomers for the two amino-acids. Finally, pertinent results for these complexes are summarised in Table 5 together with the relevant data for the dimeric L-alanine complex of chromium(III).

Reactions of Chelated Amino-acids.—(a) *Exchange with* D₂O. Due to the low solubility of [Co(gly)₃] in water, we were unable to follow exchange of the methylene protons with D₂O using ¹H n.m.r. A slow rate of exchange, however, was established in 0·5M-NaOD; this is in contrast to [Co(en)₂(gly)]²⁺ which readily undergoes D–H exchange under similar conditions.[35] After 24 h (in 0·5M-NaOD) a quantitative conversion into perdeuterioglycine was achieved, as confirmed by the ¹H n.m.r. spectrum of the product in 6M-HCl which showed only a single resonance from the protons of the amino-group and none from the methylene group.

Treatment of [Co(L-ala)₃] (as a mixture of the soluble isomers) with 0·5M-NaOD resulted in racemisation. This was shown by isolating and purifying the ligand,

[28] C. T. Liu and B. E. Douglas, *Inorg. Chem.*, 1964, **3**, 1356.
[29] M. Husain, R. Hague, and W. U. Malik, *J. Indian Chem. Soc.*, 1964, **41**, 394.
[30] H. Matsukawa, M. Ota, S. Takata, and R. Tsuchiya, *Bull. Chem. Soc. Japan*, 1965, **38**, 1235.

[31] H. Ley and K. Ficken, *Berichte*, 1912, **45**, 377.
[32] N. Israily, *Compt. rend. (C)*, 1966, **262**, 1426.
[33] A. Earnshaw and J. Lewis, *J. Chem. Soc.*, 1961, 396.
[34] R. D. Gillard and M. G. Price, *J. Chem. Soc. (A)*, 1971, 2271.
[35] W. H. Williams and D. H. Busch, *J. Amer. Chem. Soc.*, 1965, **87**, 4644.

then utilising it as a substrate for D-amino-acid oxidase. In heavy water, under the same conditions, the ^{1}H n.m.r. spectrum of the ligand shows that no deuterium is incorporated into the methyl group.

The amino-acids were treated in a similar way in the presence of copper(II), and the products isolated. The results show that, (a) glycine becomes fully deuteriated in the methylene group: this constitutes an efficient,

TABLE 5

Spectroscopic properties of tetrakis(amino-acidato) dihydroxo-bridged binuclear complexes of cobalt(III) and chromium(III)

Amino-acidate (aa)		L,L'-[Co$_2$(aa)$_4$(OH)$_2$]		L,L'-[Cr(aa)$_4$(OH)$_2$]	
		Band I	Band II	Band I	Band II
gly	λ_{max}	532	379	521	392
	ε	240	252	59	70
	Solvent	60% HClO$_4$		70% HClO$_4$	
L-ala	λ_{max}	526	378	524	392
	ε	227	225	50	65
	Solvent	60% HClO$_4$		70% HClO$_4$	
	[A]	3650		3600	
	λCD	495		575	
	$\Delta\varepsilon$	−0·99		−1·23	
L-val	λ_{max}	530			
	ε	150			
	Solvent	60% HClO$_4$			
	[A]	3130			
	λCD	520			
	$\Delta\varepsilon$	−1·43			

almost quantitative, synthesis of $H_2NCD_2CO_2H$. (b) L-Alanine similarly gives (within 12 h) $H_2NCD(CH_3)CO_2H$; however, in this case, racemisation also occurs, more slowly, so that after 48 h we obtained DL-$H_2NCD(CH_3)$-CO_2H. No deuterium is incorporated in the methyl group. (c) L-Proline shows no exchange at carbon or racemisation during several weeks under these conditions. (d) No deuteriation occurs at carbon with β-alanine in this experiment.

It is well known that the methylene groups in glycinate type ions become activated upon chelation and the present results support this. The observation that the D–H exchange is stereoselective for L-alanine in the presence of copper(II), but not with cobalt(III), has been previously reported.[36] The non-exchange found with L-proline and β-alanine probably arises from different causes. Steric crowding at the imino-nitrogen of the co-ordinated L-proline may well preclude attack by hydroxide ion; similar reasoning has been advanced[37] for the slow D–H exchange observed for the L-phenyl-alaninato-complex of palladium(II). In the case of β-alanine, it seems fairly certain that the presence of an extra methylene group in the chelate ring will reduce the electron-withdrawing effect of the metal ion via the co-ordinated carbonyl group, and hence activation of the α-methylene group will also be reduced.

(b) *Synthesis of α-Carbon Substituted Amino-acids*

[36] R. D. Gillard and D. A. Phipps, *Chem. Comm.*, 1970, 800.
[37] T. P. Pitner and R. B. Martin, *J. Amer. Chem. Soc.*, 1971, 93, 4400.

from Co-ordinated Glycine. The activation of the methylene group of co-ordinated glycine has been used to form new amino-acids by the condensation of aldehydes with glycinate [in the form of cobalt(III)[27,38] and copper-(II)[39] complexes]. We have attempted, using [Co(en)$_2$-(gly)]$^{2+}$, to establish conditions for the synthesis of α-carbon substituted amino-acids from co-ordinated glycine. The reactions studied were:

(i) [Co(en)$_2$(gly)]$^{2+}$ + RCHO

$\downarrow$ OH$^-$

R·CH·OH
|
[Co(en)$_2$(NH$_2$·CH·CO$_2^-$)]$^{2+}$ + H$_2$O

(ii) [Co(en)$_2$(gly)]$^{2+}$ + RX

$\downarrow$ OH$^-$

R
|
[Co(en)$_2$(NH$_2$·CH·CO$_2^-$)]$^{2+}$ + HX (X = Br$^-$, I$^-$)

In general the starting complex was treated with a ten-fold excess of aldehyde or alkyl halide in the presence of base for 12 h. The conditions used and the product yields are summarised in Table 6. The yields are comparable to those obtained by Nakahara *et al.*[39] by similar

TABLE 6

Reactions of [Co(en)$_2$(gly)]$^{2+}$

Reactant[a]	Solvent	Base	Yield[b]
HCHO	H$_2$O	Na$_2$CO$_3$	50%
CH$_3$CHO	H$_2$O	Na$_2$CO$_3$	50%
PhCHO	H$_2$O–EtOH (1 : 5)	Na$_2$CO$_3$	50%
PhCH$_2$Br	H$_2$O	Na$_2$CO$_3$	10%[c]
	H$_2$O–DMF (1 : 10)	Na$_2$CO$_3$	10%
EtBr	H$_2$O–DMF (1 : 10)	KOH	Trace
MeI	H$_2$O–DMF (1 : 10)	KOH	20%[d]
MeI	H$_2$O–DMF (1 : 10)	Pyridine	Decomposed[e]
MeI	H$_2$O–DMF (1 : 10)	Na$_2$CO$_3$	
MeI	H$_2$O–EtOH (1 : 5)	KOH	Trace
MeI	H$_2$O–DMSO (1 : 10)	KOH	Decomposed

[a] In 10-fold molar excess, at room temperature. [b] Yield after 12 h, of total product amino-acid, based on original glycine. [c] Dr. A. Pasini of Milan informs us that while his results using paper chromatography as an analytical method agree with ours, when g.l.c. of the N-trifluoroacetyl butyl esters of the amino-acids was done, phenylalanine was not detected. It may be that in this case N-condensation occurs, giving a product with R$_F$ very close to that of phenylalanine. [d] Using resolved [Co(en)$_2$(gly)]$^{2+}$ considerable racemisation occurred during the reaction. [e] Usually disproportionation, to [Co(en)$_3$]$^{3+}$ and [Co(gly)$_3$], and formation of brown ' cobaltic hydroxide.'

reactions using N-salicylideneglycinatoaquocopper(II) as the form of co-ordinated glycine. Attempts to prepare optically active amino-acids via a stereospecific reaction

[38] M. Muakami and K. Takahashi, *Bull. Chem. Soc. Japan*, 1959, 32, 308.
[39] A. Nakahara, S. Nishikawa, and J. Mitani, *Bull. Chem. Soc. Japan*, 1967, 40, 2212.

involving the resolved forms of [Co(en)₂(gly)]²⁺ were unsuccessful; as noted in section (a) above, basic conditions lead to racemisation of co-ordinated amino-acids.

β-Phenylserine (as identified by ¹H n.m.r. and paper chromatography) was also obtained by the reaction of benzaldehyde with [Co(gly)₃] under similar conditions to the reactions above. A number of attempts, using various solvents, to cause formation of alanine (from methyl iodide) and aspartic acid (from iodoacetic acid) were made using [Co(gly)₃]. In general, however, conditions in which the complex remained intact were too mild to induce ready reaction and only a little alanine (2—3%) was usually formed.

(c) *Reactivity of* [Co(gly)₃] *with Hydrochloric Acid.* Ogoleva [26] evaporated solutions containing one, two, and three moles of hydrochloric acid per mole of α-[Co(gly)₃] to dryness and constant weight. The blue-violet products so obtained were characterised as [Co(gly)ₙ-(glyn)₃ ₋ ₙCl₃ ₋ ₙ] (*n* = 0, 1, or 2), where glyn represents the nitrogen bonded unidentate ligand NH₂·CH₂·COOH. We have repeated these syntheses with the intention of further characterising these complexes by means of electronic and *X*-ray powder spectroscopy.

Efforts to obtain clear *X*-ray powder patterns were, in general, not successful. In the one case where a reasonably good powder pattern was obtained only lines associated with the original α-[Co(gly)₃] were present. Examination of the blue products under a polarising microscope revealed that they were mixtures of red-violet crystals (presumably unreacted α-[Co(gly)₃]) and a blue non-crystalline solid. Magnetic measurements further revealed that all three salts were paramagnetic suggesting the presence of cobalt(II) in the mixture.

The electronic spectra of aqueous solutions of these blue products, both before and after passage through an anion exchange resin (in the OH⁻ form) followed by passage through a cation exchange resin (in the H⁺ form), displayed absorbance maxima between 524 and 537 nm, suggesting the solutions to be a mixture of the α ($\lambda_{max.}$ 546 nm) and β ($\lambda_{max.}$ 520 nm) isomers of [Co(gly)₃]. On standing, these solutions slowly precipitated a pink solid, which was subsequently identified as the β-isomer. Final proof of the presence of α- and β-isomers in the blue solutions was obtained by column chromatography using Sephadex C-25 as support and water as eluant: two bands were obtained, a purple (α) fraction and a pink (β) fraction.

Thermal Isomerisations and Decompositions.—A consequence of the general insolubility of the Λ-β-[Co(aa)₃] isomers is that equilibration of the other isomers in aqueous solution invariably leads to the formation of the Λ-β isomer, as the equilibration is displaced by its precipitation. Equilibration is generally catalysed by the use of charcoal, which is thought to act by the formation of catalytic amounts of labile cobalt(II) species. An early observation of Ley and Ficken,[40] that the β-isomer of a related complex, trispicolinatocobalt(III), trans-

formed into the α-isomer on heating in water above 100°, was therefore of particular interest.

We have successfully repeated Ley and Ficken's preparation of the two isomers of [Co(pic)₃], although we found that their method did not give a pure β-fraction. We can also confirm that β- ⟶ α-isomerisation occurs, as found by earlier workers, and have extended the isomerisation measurements over a wider range of conditions (in sealed Pyrex tubes). The results obtained are summarised in the Supplementary Publication. In some cases small amounts of cobalt(II) were found after heating above 130°, so that labile cobalt(II) species may be the reactive intermediates in the isomerisations. Interestingly, no isomerisation occurred on heating the solid β-isomer or its dilute aqueous solution; isomerisation only proceeded when saturated solutions were formed at the required temperatures.

At 380° small amounts of 2,2'-bipyridyl were formed from the decomposition of the complex and the (metal-ion-catalysed) decarboxylation of the picolinate ions. We have also found [41] that 2,2'-bipyridyl (up to a 13% yield) could be obtained by heating bis(picolinato)-copper(II) hydrate to 400° for 17 h. Similarly, Morgan and Burstall [42] found that heating iron(III) or cobalt(II) chlorides with pyridine, under pressure, yielded 2,2'-bipyridyl and other products. These reactions could provide the bases of relatively cheap routes to the synthesis of the important 2,2'-bipyridyl.

The results on the analogous reactions of the tris-(amino-acidato)cobalt(III) complexes, given in the Supplementary Publication, are limited because of the more ready decomposition of these complexes. The results do, however, show some particularly interesting aspects. For example, the α-isomers of [Co(gly)₃] and [Co(L-ala)₃] appear to be thermodynamically more stable than their β-isomers. On the other hand, the β-isomers, particularly the Δ-β-, are the more stable for [Co(L-leu)₃]. In this latter case both geometric isomerisation and optical inversion were observed to occur in the same molecule, *i.e.* Λ-α- ⟶ Δ-β-. Addition of simple cobalt(II) salts was not found to catalyse isomerisation; this observation, however, does not rule out the presence of catalytic amounts of cobalt(II) species which are more likely to be of the form [Coᴵᴵ(aa)₃]⁻.

EXPERIMENTAL

L-*Threoninatobis(ethylenediamine)cobalt*(III) *Iodide.*—The method used by Liu and Douglas [28] to prepare the corresponding complex of glycine was followed in detail, with the exception that the temperature was never allowed to rise above 10°. The solution was allowed to stand overnight at 4°, and then filtered {the solid residue was set aside for the isolation of Λ-β-(+)-[Co(L-thr)₃]} and the filtrate subjected to chromatography on Sephadex G10. Those fractions with $\lambda_{max.}$ 485 nm were collected and concentrated *in vacuo*. A two-fold excess of potassium iodide was added and the resultant solution evaporated slowly. Red crystals of the required product ($\lambda_{max.}$ 483 nm, ε 115; 348 nm, ε 135)

[40] H. Ley and K. Ficken, *Berichte*, 1917, **50**, 1123.
[41] R. D. Gillard and S. H. Laurie, unpublished observations.
[42] G. T. Morgan and F. H. Burstall, *J. Chem. Soc.*, 1932, 20; 1933, 1.

could be collected after several days (Found: C, 17·4; H, 4·5; N, 12·5. $C_8H_{24}CoI_3N_5O_3$ requires C, 17·4; H, 4·4; N, 12·7%).

Separation of the [Co(en)₂(L-thr)]²⁺ *Diastereoisomers.*—The complex was separated into diastereoisomers by the method of Liu and Douglas,[28] using freshly prepared silver antimony tartrate. The diastereoisomers were then reconverted to the iodide salts and the c.d. measured. Λ-(+)₅₈₉-Isomer: $\varepsilon_L - \varepsilon_R$ = +2·30 (505 nm), −0·10 (368 nm), +0·10 (344 nm): Δ-(−)₅₈₉-isomer: $\varepsilon_L - \varepsilon_R$ = −2·20 (505 nm), +0·10 (410 nm).

The Iodide Catalysed Disproportionation.—An aqueous solution of ' racemic ' [Co(en)₂(L-thr)]I₂ was heated to 50° for 10 min and chromatographed on Sephadex G10. Three components were identified by their electronic spectra. The first was the Λ-β-(+)-tris(amino-acid) complex, the second was unchanged starting material, and the third contained racemic tris(ethylenediamine)cobalt(III) ion. Despite careful chromatography, the tris(amino-acid) complex showed no sign of contamination by any other isomer.

Λ-(+)-β-*Tris*(L-*threoninato*)*cobalt*(III)   *Dihydrate.*—The preparation of the [Co(L-thr)₃] complex has not been reported in detail although the Λ-β-isomer has been isolated previously [27] from the decomposition of the L-threoninato-bis(ethylenediamine)cobalt(III) iodide. In this work the Λ-β-isomer was obtained by extracting the solid residue from the [Co(en)₂(L-thr)] preparation, outlined above, with several volumes of cold water, leaving the required product (Found: C, 31·9; H, 6·8; N, 9·3. $C_{12}H_{28}CoN_3O_{11}$ requires C, 32·0; H, 6·2; N, 9·3%). The presence of two molecules of water of crystallisation was supported by the i.r. spectrum which showed strong bands in the region 3600—3200 cm⁻¹; the rest of the spectrum was uninformative, consisting of very broad bands. Sufficiently strong aqueous solutions were obtained to measure the conductivity (Λ = 15 Ω⁻¹).

Δ-(−)-β-*Tris*(L-*threoninato*)*cobalt*(III).—A mixture of the remaining three isomers was prepared by treating an aqueous slurry of freshly prepared cobaltic hydroxide with half the stoicheiometric amount of L-threonine. After two days at room temperature the resulting mixture was filtered (to remove the excess of unreacted cobaltic hydroxide) and the filtrate was passed through a column of cation-exchange resin in the acid form (to remove any unreacted amino-acid).

The emergent solution was then chromatographed on Sephadex G10. A separation into two components was immediately apparent, one purple, one red. The purple fractions from a number of preparations were set aside and the red ones pooled and then rechromatographed. The red solution obtained in this fashion was allowed to evaporate, yielding irregular crystals of the required product, as the heptahydrate (Found: C, 25·1; H, 5·5; N, 7·3. $C_{12}H_{38}CoN_3O_{16}$ requires C, 25·5; H, 6·6; N, 7·8%). The i.r. spectrum was uninformative, appearing almost as a continuum. The conductivity was measured (Λ = 15 Ω⁻¹).

The α-*Isomers of* Tris(L-*threoninato*)*cobalt*(III).—The pooled purple fractions described above were rechromatographed; the leading and trailing fractions were collected. This process was repeated until no further changes in spectroscopic properties of these fractions occurred on further chromatography. No solids were isolated from these solutions.

Tris(*picolinato*)*cobalt*(III).—The α- and β-forms of this compound were prepared by the original method.[40] However, the β-isomer so obtained is contaminated by some α-product,

which we removed using several extractions with warm dimethylformamide, leaving pure solid β-isomer.

Tris(L-*lysinato*)*cobalt*(III).—Whether it was obtained from air oxidation of aqueous cobalt(II) nitrate in the presence of L-lysine, or by heating a mixture of hexa-amminecobalt(III) chloride and L-lysine with activated charcoal as catalyst, the reaction product contained mostly α-isomers (with an excess of Δ-α). The purple solution was taken to dryness, extracted with 95% ethanol, and the extract chromatographed on acid-washed Alumina (CAMAG, MFC, pH 6, 100—240 mesh), with 95% methanol as eluant. Two bands were formed, a small pink-violet one, strongly absorbed, and a larger violet band.

Δ-α-[Co(L-*lysinate*)₃],3H₂O.—Elution of the alumina column with ethanol–water (4 : 1) gave a sample which was purified by further chromatography with ethanol–water (9 : 1) and finally by crystallisation (Found: C, 39·2; H, 8·2; N, 15·1. $C_{18}H_{45}CoN_6O_9$ requires C, 39·4; H, 8·2; N, 15·3%).

Λ-α-[Co(L-*lysinate*)₃],3H₂O.—After the removal of the Δ-α-isomer, this Λ-α-compound could be eluted using alcohol–water (65 : 35). The fraction was slightly impure (contaminants were Δ-α- and a little Δ-β-) so further chromatography, with ethanol–water (7 : 3) was followed by crystallisation at room temperature (Found: C, 39·3; H, 8·1; N, 15·2. $C_{18}H_{45}CoN_6O_9$ requires C, 39·4; H, 8·2; N, 15·3%).

Tetrakis(*glycinato*)-*di-μ-hydroxo-dicobalt*(III,III)   *Mono-hydrate.*—(*a*) Cobaltous carbonate (2·27 g, 0·01 mol) and glycine (0·02 mol) were mixed with distilled water (10 cm³) and boiled for 10 min. After the mixture had cooled to room temperature, 30% hydrogen peroxide (10 cm³) was added dropwise with stirring. A few cm³ of 95% ethanol were included to prevent excessive foaming. The resulting slurry was heated on a water-bath for 1 h. When cool, the slurry was centrifuged and the excess liquid removed by decanting. The solid residue was treated with 2M-hydrochloric acid to dissolve out the excess of cobalt(II) carbonate and the small amount of mauve solid remaining was collected and washed exhaustively with 2M-hydrochloric acid, boiling water, and ethanol, and dried with acetone (yield *ca.* 3%). (*b*) A solution containing unresolved potassium bis(glycinato)carbonatocobaltate(III) [43] was treated with the minimum amount of 70% perchloric acid to liberate all the carbonate as carbon dioxide. Potassium hydroxide was added dropwise to the solution until the pH was between 7 and 8, the precipitated potassium perchlorate removed by filtration, and the resulting purple solution allowed to concentrate on a steam-bath. After a short interval a mauve precipitate appeared and was removed from solution by filtration. The precipitate was exhaustively washed with 4M-hydrochloric acid, water, 95% ethanol, and acetone, and dried at 100 °C. The product was the same dihydroxo-bridged dimer as was obtained above, this fact being verified by X-ray powder photographs, analyses, and electronic spectra (yield *ca.* 10%) (Found: C, 20·3; H, 4·2; Co, 24·9; N, 12·3. $C_8H_{20}Co_2N_4O_{11}$ requires C, 20·6; H, 4·3; Co, 25·3; N, 12·0%).

Δ,Δ-*Tetrakis*(L-*alaninato*)*di-μ-hydroxo-dicobalt*(III,III).—This compound was prepared by the methods used for the glycine analogue. Yields of *ca.* 3% [method (*a*)] and 10% [method (*b*)] were obtained. X-Ray powder photographs, electronic spectra, and analysis confirmed that both methods produced the same product (Found: Co, 23·0;

[43] M. Shibata, H. Nishikawa, and Y. Nishida, *Inorg. Chem.* 1968, **7**, 9.

C, 28·4; H, 5·3; N, 11·0. $C_{12}H_{26}Co_2N_4O_{10}$ requires Co, 23·4; C, 28·6; H, 5·2; N, 11·1%).

Δ,Δ'-*Tetrakis*(L-*valinato*)*di*-μ-*hydroxo-dicobalt*(III,III).—
This compound was prepared by the methods used for the glycine analogue. Yields were *ca.* 2% [method (*a*)] and 10% [method (*b*)], identity of products was confirmed as for the alanine analogue (Found: C, 38·8; H, 7·0; Co, 18·8; N, 9·2. $C_{20}H_{42}Co_2N_4O_{10}$ requires C, 37·9; H, 6·9; Co, 18·6; N, 8·8%).

β-*Trisglycinatochromium*(III).—(*a*) Hexa-aquochromium-(III) chloride (26·7 g, 0·1 mol) and glycine (30 g, 0·4 mol) were dissolved in water (120 cm³) and the solution heated under reflux for *ca.* half an hour. Sodium hydroxide (12·0 g, 0·3 mol) dissolved in water (30 cm³) was then added drop-wise to the hot solution with stirring. A red crystalline precipitate of β-[Cr(gly)₃] appeared almost immediately and was removed from the hot solution by filtration. Further precipitates were contaminated with [Cr₂(gly)₄(OH)₂]. These two components were very efficiently separated by flotation in ethanol, the red crystals of the monomer being more dense than those of the mauve dimer. The red crystalline precipitate of β-[Cr(gly)₃] was washed with hot water, ethanol, and acetone, and dried at 90 °C. The yield was 60%.

(*b*) Chloropenta-amminechromium(III) chloride (24·4 g, 0·1 mol) and glycine (30 g, 0·4 mol) were added to water (350 cm³) and the mixture heated under reflux until no more ammonia was evolved. The hot solution was filtered and the solid washed with hot water, ethanol, and acetone. Flotation of this crystalline mixture in ethanol produced β-[Cr(gly)₃], in 18% yield, the remainder consisting of the dimeric dihydroxo-bridged compound.

(*c*) Ammonium dichromate (25·2 g, 0·1 mol) and glycine (60·0 g, 0·8 mol) were dissolved in water (250 cm³) and heated on a steam-bath for two days. The purple solution was filtered while hot to remove a small quantity of dark purple crystals. These crystals were subsequently found to be [Cr₂(gly)₄(OH)₂],6H₂O (X). When the solution had cooled, red crystals of β-[Cr(gly)₃] were precipitated together with [Cr₂(gly)₄(OH)₂]. The compounds were separated by flotation in ethanol and the crystals of β-[Cr(gly)₃] were washed with ethanol and acetone before drying at 90°. A yield of 40% was obtained (Found: C, 26·3; H, 4·3; Cr, 18·8; N, 15·2. $C_6H_{12}CrN_3O_6$ requires C, 26·3; H, 4·4; Cr, 19·0; N, 15·3%).

Λ-β-Cr(L-*alaninate*)₃.—(*a*) Hexa-aquochromium(III) chloride (26·7 g, 0·1 mol) and L-alanine (53·4 g, 0·6 mol) were dissolved in water (120 cm³) and the solution was heated under reflux for 30 min. Sodium hydroxide (12·0 g, 0·3 mol) in water (30 cm³) was added dropwise to the solution with stirring. A precipitate of impure Λ-β-[Cr(L-ala)₃] appeared almost immediately and was removed from the hot solution. Upon cooling, the filtrate deposited pure Λ-β-[Cr(L-ala)₃]. Reduction in the volume of this filtrate produced more Λ-β-[Cr(L-ala)₃] together with a little [Cr₂(L-ala)₄(OH)₂]. The two insoluble complexes were separated by flotation in ethanol, the crystals of [Cr₂(L-ala)₄(OH)₂] being more dense than those of [Cr(L-ala)₃]. The crystals were washed well with hot water, ethanol, and acetone and dried at 90 °C, to give Λ-β-[Cr(L-ala)₃] (yield 90%).

(*b*) The method of preparation of Λ-β-[Cr(L-ala)₃] from chloropenta-amminechromium(III) chloride was the same as that described for β-[Cr(gly)₃] [method (*b*)]. Only the monomeric Λ-β-[Cr(L-ala)₃] was isolated (yield 92%).

(*c*) Λ-β-[Cr(L-ala)₃] was also obtained alone from ammon-

ium dichromate as described for β-[Cr(gly)₃] [method (*c*)], yield 85% (Found: C, 33·8; H, 5·6; Cr, 16·4; 13·3. $C_9H_{18}CrN_3O_6$ requires C, 33·9; H, 5·6; Cr, 16·5; N, 13·2%).

Tetrakis(*glycinato*)*di*-μ-*hydroxo-dichromium*(III).— (*a*) Hexa-aquochromium(III) chloride (26·7 g, 0·1 mol) and glycine (22·5 g, 0·3 mol) were dissolved in water (200 cm³) and the solution heated under reflux for half an hour. Sodium hydroxide (12·0 g, 0·3 mol) was dissolved in water (50 cm³) and added dropwise to the solution. Any precipitated β-[Cr(gly)₃] was removed by filtration, and the filtrate heated under reflux for a further half hour. When the solution had cooled, the mauve precipitate of [Cr₂(gly)₄-(OH)₂] (U) was filtered off. The remaining solution was reduced in volume at room temperature and the remainder of the dimeric complex was precipitated. The mauve crystals were thoroughly washed with 2M-hydrochloric acid, hot water, ethanol, and acetone, and dried at 90 °C. The yield of [Cr(gly)₄(OH)₂] was 75%.

(*b*) This dimer (U) was also prepared from chloropenta-amminechromium(III) chloride by the method (*b*) described for β-[Cr(gly)₃], with an 85% yield.

(*c*) Ammonium dichromate (25·2 g, 0·1 mol) and glycine (45·0 g, 0·6 mol) were dissolved in water (250 cm³) and heated on a steam-bath for two days. The solution was filtered while still hot to remove a small quantity of dark purple crystals (V). These dark purple crystals were washed well with hot water, ethanol, and acetone, and dried over silica gel, yield 3·25 g, 6%. Fractional crystallisation of the filtrate yielded a small amount of red β-[Cr(gly)₃], and then gave mauve anhydrous [Cr₂(gly)₄(OH)₂] (U) alone. Any β-[Cr(gly)₃] was removed by flotation in ethanol. The mauve crystals (U) were washed with 2M-hydrochloric acid, water, ethanol, and acetone, and dried at 90 °C. The yield of anhydrous [Cr₂(gly)₄(OH)₂ (U) was 72%.

When (V) was heated at 110° under vacuum for two days, the purple crystals lost six molecules of water of crystallisation and formed the mauve complex [Cr₂(gly)₄(OH)₂] (U). The electronic spectrum of (V) was very similar to that of (U), allowing for the molecules of water of crystallisation in (V) [(U) Found: C, 22·1; H, 4·3; Cr, 23·7; N, 12·8. $C_8H_{10}Cr_2N_4O_{10}$ requires C, 22·1; H, 4·2; Cr, 24·0; N, 12·9%]. [(V) Found: C, 17·7; H, 5·4; Cr, 19·0; N, 10·4. $C_8H_{30}Cr_2N_4O_{10}$ requires C, 17·7; H, 5·5; Cr, 19·2; N, 10·3%.]

Δ,Δ'-*Tetrakis*(L-*alaninato*)*di*-μ-*hydroxo-dichromium*(III).— (*a*) Hexa-aquochromium(III) chloride (26·7 g, 0·1 mol) and L-alanine (26·7 g, 0·3 mol) were dissolved in water (300 cm³), and the solution heated under reflux for half an hour. Sodium hydroxide (12·0 g, 0·3 mol) in water (80 cm³) was added dropwise to the rapidly stirred solution. The hot solution was sufficiently dilute to preclude precipitation of pink Λ-β-[Cr(L-ala)₃]. A small quantity (3·1 g, 5%) of purple crystals (Y) were filtered off, washed with cold water, ethanol, acetone, and dried over silica gel. The filtrate was again heated under reflux for 30 min, slightly reduced in volume, and allowed to cool very slowly. A mixed precipitate of pink [Cr(L-ala)₃] and mauve [Cr₂(L-ala)₄(OH)₂] (X) resulted, being denser than the monomer. (X) was washed with 2M-hydrochloric acid, water, ethanol, and acetone and dried at 90°. Further fractions, obtained by reducing the volume of the solution, contained mostly pink [Cr(L-ala)₃]. The yield of [Cr₂(L-ala)₄(OH)₂] (X) was 35%.

When [Cr₂(L-ala)₄(OH)₂],7H₂O (Y) was heated at 110° under vacuum for two days, the purple crystals lost seven molecules of water of crystallisation to form the mauve complex [Cr₂(L-ala)₄(OH)₂] (X). The u.v.–visible, o.r.d.,

and c.d. spectra of (Y) were identical to those of (X) allowing for the molecules of water of crystallisation in (Y) [(X) Found: C, 29·4; H, 5·5; Cr, 21·1; N, 11·6. $C_{12}H_{26}$-$Cr_2N_4O_{10}$ requires C, 29·4; H, 5·3; Cr, 21·2; N, 11·4%]. [(Y) Found: C, 23·4; H, 6·5; Cr, 16·3; N, 9·0. $C_{12}H_{40}$-$Cr_2N_4O_{17}$ requires C, 23·4; H, 6·4; Cr, 16·9; N, 9·1%.]

For the chromium(III) complexes synthesised in this work the effective magnetic moments were measured at 293 K, and found to be (Bohr magnetons): β-[Cr(gly)$_3$], 3·82; Λ-β-[Cr(L-ala)$_3$], 3·83; [Cr$_2$(gly)$_4$(OH)$_2$], 3·79; L,L'-[Cr$_2$(L-ala)$_4$-(OH)$_2$], 3·83. Morishita et al.[44] obtained values of 3·89 and 3·37 for [Cr(gly)$_3$] and [Cr$_2$(gly)$_4$(OH)$_2$] respectively, at 289·2 K. Our results differ from these but are in good agreement with those of Earnshaw and Lewis[33] who reported values of 3·80 and 3·84 B.M., at 293 K, for the glycinate and L-phenylalaninate dimers respectively.

Other complexes used in this study were prepared and resolved by published methods as follows; α,β-[Co(gly)$_3$],[6,45] α,β-[Co(L-ala)$_3$],[45] Λ-β-[Rh(L-ala)$_3$],[9] Λ-β-[Co(L-pro)$_3$],[10] Δα:Λα-[Co(L-val)$_3$],[46] Λ-α-[Co(L-glu)$_3$],[12] [Co(en)$_2$(gly)]I$_2$,[28] K[Co(gly)$_2$CO$_3$],[43] K[Co(L-ala)$_2$CO$_3$],[43] K[Co(L-val)$_2$CO$_3$].[43]

Analyses.—D-Amino-acid oxidase from a crude extract from hog kidney (Sigma) was used to assay D-alanine following the method of Kunitz.[47]

Cobalt was estimated as follows. Between 5 and 15 mg of complex was weighed directly into a 25 cm³ flask. Concentrated nitric acid (1 cm³) and concentrated sulphuric acid (0·25 cm³) were added. The solution was heated until evolution of oxides of nitrogen ceased. Additional concentrated nitric acid (1 cm³) was then added and the heating repeated. After cooling, water (3—4 cm³), acetone (12 cm³), hydrochloric acid (1 cm³), and freshly prepared ammonium thiocyanate (50% w/v, 2 cm³) were added and, after standing for 10 min, the absorbance measured at 625 nm. The concentration was then determined by reference to a previously prepared calibration curve.

Chromium was determined by oxidation to chromium(VI) in alkaline solution using sodium peroxide, followed by slow acidification. An excess of potassium iodide was then added and the liberated iodine titrated with sodium thiosulphate.

Carbon, hydrogen, nitrogen, and chlorine analyses were performed by the microanalytical service of this laboratory.

Methods of Separation.—Chromatography on Sephadex G10 was frequently useful for separating complexes of differing charge and/or geometry. For example, the column gave well defined and separate bands of [Co(en)$_3$]$^{3+}$, [Co(en)$_2$(aa)]$^{2+}$, and [Co(aa)$_3$], and also separated the geometrical isomers of the latter complex. For this latter separation the cation exchange material Sephadex C25 proved to be even more efficient than Sephadex G10.

Deuteriation Procedures.—(a) *Bis(amino-acidato)copper*(II) *complexes.* CuSO$_4$,5H$_2$O (0·001 mol) with the amino-acid (0·004 mol) were dissolved in a 1M-solution (10 cm³) of NaOD in D$_2$O, and the solution shaken at room temperature. In the case of optically active amino-acids, samples were withdrawn periodically for c.d. measurements. After 12 h the solution was acidified, concentrated *in vacuo*, then adsorbed onto a cation exchange column (Dowex 225, 50

mesh, H$^+$ form, 20 × 2 cm) which was washed with water until the washings were neutral. The amino-acid was then eluted with 2M-aqueous ammonia, and the effluent concentrated *in vacuo* to crystallisation. The amino-acid was collected and identified by analysis and paper chromatography, and the ^{1}H n.m.r. spectrum then recorded.

(b) *Trisglycinatocobalt*(III). A solution of 2·0 g of α-[Co(gly)$_3$] in 20 cm³ of 0·5M-NaOD was kept for 24 h, then acidified to pH 4 and evaporated to dryness. The solid was redissolved in water, and the solution treated with sodium sulphide. After filtration and concentration, the solution was chromatographed on Sephadex G10. Fractions containing simple amino-acids were collected and identified by paper chromatography. Chromatography (on Whatman No. 1 paper) was used for separating mixtures of amino-acids. The preferred solvent was n-butanol : acetic acid : water (4 : 1 : 5); ninhydrin in acetone (0·25% w/v) was the developer. Authentic specimens were always run under the same conditions to define R_F values.

Synthesis of α-Carbon-substituted Amino-acids from Co-ordinated Glycine.—One gram of the complex [Co(en)$_2$-(gly)]I$_2$ was treated with a ten-fold molar excess of the appropriate aldehyde or halide, under the conditions outlined in Table 7. After having been shaken for 12 h at room temperature, the solutions were acidified and evaporated to dryness. The resultant solid was extracted with water, and the solution obtained submitted to chromatography on Sephadex G10. Fractions with maximal absorbance at 485 nm {corresponding to $\lambda_{max.}$ for [Co(en)$_2$-(DL-aa)]$^{n+}$} were treated with sodium sulphide, filtered to remove cobalt(II) sulphide, and the filtrate taken to dryness. The solid obtained was extracted with isopropyl alcohol (5 × 1 cm³) and the alcoholic solution used directly for paper chromatography. Samples for ^{1}H n.m.r. spectra were obtained by removing the solvent and dissolving the solid in water, filtering, evaporating, redissolving in water, evaporating, and finally redissolving in heavy water. Synthesis involving [Co(gly)$_3$] and the subsequent analysis were carried out in exactly the same manner.

Instrumental Techniques.—Electronic spectra were recorded on Unicam SP 800 or Hitachi–Perkin-Elmer 124 spectrophotometers. For absorbance measurements at specific wavelengths a Unicam SP 600 spectrophotometer was used. O.r.d. spectra were measured using a Bendix NPL Polarmatic 62 spectropolarimeter, calibrated with an aqueous sucrose solution. C.d. spectra were recorded with a Roussel Jouan dichrographe B instrument, calibrated either with isoandrosterone or, more cheaply, using a solution of (+)-camphor in absolute alcohol.* Experimental c.d. curves were analysed into their components by means of a Dupont 310 Curve Resolver. I.r. spectra were measured with Perkin-Elmer 337 or 457 spectrometers. A Philips Conductivity Bridge PR 9500 was used to measure conductivities of aqueous solutions. Magnetic moments were obtained with a Newport Instruments Gouy Balance at room temperature. A Guinier camera using Cu-K_α radiation was employed to obtain the X-ray powder photographs; the quoted d-spacings are uncorrected for film shrinkage. ^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R10

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* Investigation of this latter method showed that the calibration was reproducible to better than 1% and that the presence of water in the alcohol had no significant effect, whereas satisfactory results using the relatively expensive isoandrosterone, as recommended by the manufacturers, are only obtained if the dioxan, used as solvent, is rigorously purified.

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[45] M. Mori, M. Shibata, E. Kyono, and M. Kanaya, *Bull. Chem. Soc. Japan*, 1961, **34**, 1837.
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[47] M. Kunitz, *J. Gen. Physiol.*, 1947, **30**, 291.

spectrometer at 60 MHz with a probe temperature of 33·5 °C. Either t-butyl alcohol or sodium 3-trimethylsilyl-propanesulphonate were used as internal reference standards in aqueous or deuterium oxide solutions. Electrophoresis experiments were carried out using an apparatus constructed in these laboratories which used a current of *ca.* 10 mA at 250 V.