Co-ordination Complexes of Amino-acids: Separation and Spectroscopic Properties of The Diastereoisomers of Some Amino-acidatobis(acetylacetonato)cobalt(III) Complexes

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Fractional crystallisation and column chromatography on D-lactose, have been successfully used to separate the diastereoisomers of L-phenylalaninatobis(acetylacetonato) cobalt(III) and L-valinatobis(acetylacetonato)cobalt(III) but were unsuccessful in fully separating the isomers of the corresponding complex of L-alanine. The o.r.d., c.d., and n.m.r. spectra of the diastereoisomers obtained have been recorded and related to their possible configurations.

AMINO-ACID complexes of the type [Co(amine)$_n$(aa)], where aa = amino-acidato † and n = 1, 2, or 4 depending on the denticity of the amine, have been extensively studied and a rule formulated[1,2] relating the absolute configurations of the optical isomers of such complexes with the sign of the Cotton effects exhibited in their low-energy *d*–*d* electronic transitions. Little work has been done on relating absolute configurations and optical activity of complexes containing ligands other than the alkylamine type. Other useful ligands would be the unsaturated ones, such as 2,2′-bipyridyl (bipy), 1,10-phenanthroline (phen), and acetylacetone (acac), whose charge-transfer transitions may also be of diagnostic use; some work in this area has already been reported.[3,4]

The resolution of tris(acetylacetonato)cobalt(III) into its optical isomers has attracted a great deal of attention.[5] More recently the resolution of some *cis*-diaminebis(acetylacetonato)cobalt(III) complexes have also been reported.[6] Here we report the separation of the diastereoisomers of the complexes [Co(acac)$_2$(L-val)] and [Co(acac)$_2$(L-phe)], the attempted separation of the isomers of [Co(acac)$_2$(L-ala)], and the spectroscopic properties of the diastereoisomers obtained.

EXPERIMENTAL

Preparations of the complexes [Co(acac)$_2$(aa)] have been reported elsewhere.[7] Separation of the diastereoisomers of [Co(acac)$_2$(L-val)] and [Co(acac)$_2$(L-phe)] complexes were achieved by repeated fractional crystallisation, followed by passing the more optically active fractions, so obtained, down a 120 × 1·5 cm column of D-lactose monohydrate (Koch–Light ' Puriss ' grade).

A 1 : 1 mixture of AnalaR grades chloroform and light petroleum (b.p. 60—80°) was used as solvent and developer, except in the case of the, less soluble, (+)$_{546}$-[Co(acac)$_2$(L-phe)] isomer where only chloroform was used. The ratio (optical rotation at 546 nm)/(optical density at 560 nm) was used as a measure of the optical purity. For the (+)$_{546}$ isomers, no further improvement in optical purity was obtained after passing through D-lactose; for the more soluble (−)$_{546}$ isomers a slight improvement ($\leqslant$4%) was achieved. Fractional crystallisation of [Co(acac)$_2$(L-ala)] lead to a partial separation (*ca.* 75%) beyond which no improvement could be obtained even after D-lactose chromatography.

Electronic absorption spectra were recorded with a Unicam SP 800 spectrophotometer, optical rotary dispersion spectra with a Bendix NPL ' Polarmatic 62 ' spectropolarimeter, circular dichroism spectra with a Roussel Jouan dichrographe Model B; all measurements were made at room temperature, 20—22 °C. Some of the spectra were also measured with a Jasco UV/ORD/CD-5 spectrophometer. N.m.r. spectra were recorded at 60 MHz and 33 °C with a Perkin-Elmer R10 instrument.

RESULTS AND DISCUSSION

Fractional crystallisation alone may not always lead to complete separation of optical isomers. In the case of [Co(L-val)$_3$] for example, the least soluble form was found[8] to be a 1 : 1 adduct of the D- and L-forms.‡ In the present work this may well explain the inability to fully separate the diastereoisomers of [Co(acac)$_2$(L-ala)], on the other hand, it could merely be that the D- and L-isomers are insufficiently different in their chemical properties for a full separation to be affected. For the L-phenylalanine and L-valine complexes column chromatography, after fractional crystallisation, gave little or no improvement in optical activity, so it may be assumed that the isomers obtained are optically pure. Quite obviously, the optical activities reported earlier for these complexes[7] were a result of partial separation during the purification of the racemic complexes.

The diastereoisomers are observed to retain their optical activity indefinitely in the solid state and no loss of optical activity is found after refluxing in chloroform or in benzene for several days. Because diastereoisomers are obtained, with different solubilities, no attempt has been made to look for any stereoselectivity in their formation.

Optical Rotatory Dispersion and Circular Dichroism.—The electronic absorption spectra of these complexes have already been discussed.[7] Formally, for the trivial C_1 symmetry of the amino-acid complexes, three magnetic-dipole-allowed transitions of ${}^1A$ mode would

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† Abbreviations used throughout: ala, alaninato; val, valinato; phe, phenylalaninato; en, ethylenediamine; hmc, (+)-hydroxymethylenecamphorate.

‡ D and L here are used to define the configuration of the metal centre, by relation to that of D(+)-[Co(en)$_3$]$^{3+}$.

[1] R. D. Gillard, *Proc. Roy. Soc.*, 1967, A, **297**, 134.

[2] S. F. Mason, *Quart. Rev.*, 1963, **17**, 20.

[3] B. Bosnich, *Inorg. Chem.*, 1968, **7**, 178; B. Bosnich, *Accounts Chem. Res.*, 1969, **2**, 266.

[4] A. J. McCaffery, S. F. Mason, and B. J. Norman, *J. Chem. Soc.* (*A*), 1969, 1428.

[5] R. C. Fay, A. Y. Girgis, and V. Klabunde, *J. Amer. Chem. Soc.*, 1970, **92**, 7056, and references therein.

[6] L. J. Boucher, *Inorg. Chem.*, 1970, **9**, 1202.

[7] S. H. Laurie, *Austral. J. Chem.*, 1968, **21**, 679.

[8] R. D. Gillard, N. C. Payne, and D. C. Phillips, *J. Chem. Soc.* (*A*), 1968, 973.

be expected under the lower-energy band. Strictly, spectroscopic correlations are of little use in establishing configurations of low-symmetry species, since exact assignment is not always possible and a Gaussian analysis of the observed Cotton effects is not without ambiguity.[9]

Fortunately, it has been found that by relating the transitions to the higher symmetry of the metal chromophore, with care, the absolute configurations of such complexes may be obtained *via* a simple rule. This rule [1] states, that for monomeric complexes of cobalt(III), containing two or three five-membered (or smaller) chelate rings, the enantiomer having a dominantly positive Cotton effect for the longest-wavelength, spin-allowed, *d–d* absorption band has the D-configuration at the metal centre. To be more strict the dominant Cotton effect must be associated [2] with the ${}^1E \longleftarrow {}^1A_{1g}$ transition. That the rule can be correctly applied even to low-symmetry species has been shown by its success in the correct prediction [10] of the absolute configuration of α-(+)-[Co(L-ala)$_3$].

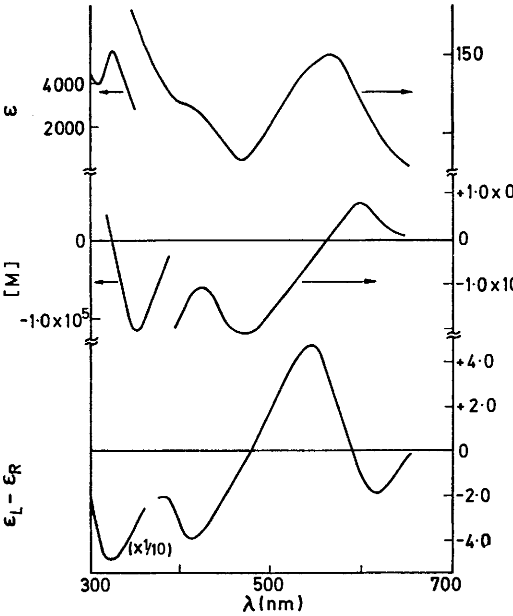
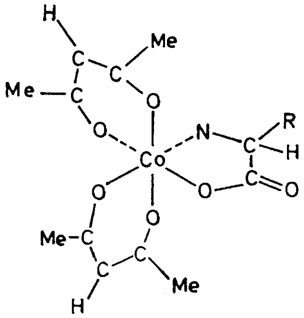


FIGURE 1 Electronic absorption (upper curve), o.r.d. (middle curve), and c.d. (lower curve) spectra of $(-)_{546}$-[Co(acac)$_2$-L-val)] in CHCl$_3$

If we relate the [Co(acac)$_2$(aa)] complexes to the C_{4v} symmetry of the CoO$_5$N chromophore, then two transitions, E and A_2, would be expected under the T_{1g} band, the E transition occurring at higher energy, and with a greater amplitude, than the A_2 mode.[11] (Under the lower molecular symmetry the E transition would be expected to split into two ${}^1A$ modes but this is frequently not observed, *viz* the c.d. spectra [12] of [Co(en)$_2$(aa)]$^{2+}$ ions). Typical o.r.d. and c.d. spectra are given in Figure 1 and, in more detail, in Table 1. The o.r.d. curves, because of their nature, are of less diagnostic use than the c.d. spectra. Two Cotton effects are observed under the ${}^1T_{1g} \longleftarrow {}^1A_{2g}$ envelope with the more dominant component (E) at higher energy.

Table 2, which lists the electronic absorption and c.d. spectra of other cobalt(III) acetylacetonate complexes, shows that the complexes $(-)_{546}$-[Co(acac)$_2$-(L-val)], $(-)_{546}$-[Co(acac)$_2$(L-phe)], $(+)_{546}$-[Co(acac)$_2$-(en)]$^+$, $(+)_{546}$-[Co(acac)$_2$(NH$_3$)$_2$]$^+$, $(-)_{546}$-[Co(acac)$_2$-(C$_2$O$_4$)]$^-$, and the related $(-)_{546}$-[Co(hmc)$_3$], are similar in the number, signs, and relative intensities of the Cotton effects under the ${}^1T_{1g} \longleftarrow {}^1A_{2g}$ band. Since these complexes are chemically similar it is a safe assumption that they must have the same configuration at the cobalt(III) centre (ligand conformational and vicinal contributions to the optical activity are negligible). The $(-)_{546}$-[Co(hmc)$_3$] isomers (of the 1,2,3 and 1,2,6 geometric isomers) have been shown to form stereoselectively and on the bases of molecular models and the c.d. spectra were assigned the D-configuration.[13] The $(+)_{546}$-[Co(en)$_2$(acac)] isomer, from the similarity of its c.d. spectrum to that of $(+)_{546}$-[Co(en)$_3$]$^{3+}$, has also been assigned the D-configuration.[14] It therefore follows that the $(-)_{546}$ isomers of [Co(acac)$_2$(L-aa)] must have the D-configuration (1) and the $(+)_{546}$ isomers the L-configuration. All the above complexes assigned the D-configuration possess a predominantly positive Cotton effect for the E mode under the low-energy *d–d* band, in keeping with the empirical rule.



D-$(-)_{546}$-[Co(acac)$_2$(L-aa)]

(1)

The Cotton effect observed at *ca.* 416 nm for the [Co(acac)$_2$(L-aa)] complexes can be assigned to the ${}^1T_{2g} \longleftarrow {}^1A_{1g}$ *d–d* transition. Only weak optical activity is expected for this transition since formally it is not magnetic-dipole-allowed; the relatively large activity found in the present cases arises from overlap with the intense charge-transfer band at *ca.* 326 nm. This latter band is of no diagnostic use at present

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[9] R. D. Gillard in ' Physical Methods in Advanced Inorganic Chemistry,' eds. H. A. O. Hill and P. Day, Interscience, New York, 1968.

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[11] T. S. Piper, *J. Chem. Phys.*, 1961, **35**, 1246.

[12] C. T. Liu and B. E. Douglas, *Inorg. Chem.*, 1964, **3**, 1356.

[13] J. H. Dunlop, R. D. Gillard, and R. Ugo, *J. Chem. Soc.* (*A*), 1966, 1540.

[14] A. J. McCaffery, S. F. Mason, and B. J. Norman, *J. Chem. Soc.*, 1965, 5094.

TABLE 1

Electronic absorption, o.r.d., and c.d. spectral data for the optical isomers of [Co(acac)$_2$(L-aa)] (peak positions in nm)

Complex	λ(ε) [a]	o.r.d. ([M]) [b]	c.d. ($\varepsilon_L - \varepsilon_R$)
$(-)_{546}$-[Co(acac)$_2$(L-val)]	565 (150)	595 (+7·87 × 10^3)	618 (−1·6), 545 (+4·7)
	327 (5500)	470 (−2·0 × 10^4)	414 (−4·0)
		355 (−1·2 × 10^5)	324 (−48·5)
$(+)_{546}$-[Co(acac)$_2$(L-val)]	566 (159)	595 (−8·43 × 10^3)	618 (+1·3), 546 (−5·5)
	327 (4988)	470 (+2·2 × 10^4)	416 (+3·8)
		347 (+1·1 × 10^5)	330 (+50·5)
$(-)_{546}$-[Co(acac)$_2$(L-phe)]	565 (150)	592 (+7·11 × 10^3)	620 (−1·1), 546 (+4·7)
	327 (5200)	463 (−2 × 10^4)	416 (−3·5)
		357 (−9·4 × 10^4)	326 (−49·2)
$(+)_{546}$-[Co(acac)$_2$(L-phe)]	566 (130)	598 (−6·75 × 10^3)	616 (+0·97), 542 (−4·5)
	327 (4500)	465 (+2·6 × 10^4)	417 (+3·2)
		350 (+9·7 × 10^4)	325 (+43·5)

[a] In all cases a shoulder is observed at 410 nm. [b] Molar rotation in degrees.

TABLE 2

Electronic absorption and c.d. spectral data of some cobalt(III) complexes

Complex	λ (log ε)	c.d. ($\varepsilon_L - \varepsilon_R$)	Assignment [a]	Ref.
$(+)_{546}$-[(Co(acac)$_2$en]$^+$	538 (2·17)	578 (−0·8)	$A_1 \longrightarrow B_1$	b
		513 (+3·1)	$A_1 \longrightarrow A_2 + B_2$	
	417	397 (−1·8)	$A_1 \longrightarrow A_1 + B_1 + B_2$	
	325 (3·84)	329 (−47)	$d\pi \longrightarrow \pi^*$	
$(+)_{546}$-[Co(acac)$_2$(NH$_3$)$_2$]$^+$	546 (2·07)	588 (−1·6)	$A_1 \longrightarrow B_1$	b
		521 (+2·5)	$A_1 \longrightarrow A_2 + B_2$	
	417	400 (−2·0)	$A_1 \longrightarrow A_1 + B_1 + B_2$	
	325 (3·85)	331 (−54)	$d\pi \longrightarrow \pi^*$	
$(-)_{546}$-[Co(acac)$_2$(C$_2$O$_4$)]$^-$	600 (2·2) [c]	d		e
		580 (+5·5)		
	420	450 (−4)		
	360 (3·75)	333 (−60)		
$(+)_{546}$-[Co(en)$_2$(acac)]$^{2+}$	505 (2·20)	510 (+2·6)	$A_1 \longrightarrow A_2 + B_1 + B_2$	f
	385 (2·33)	380 (−1·2)		
	330 (2·52)	325 (−9·5)		
$(-)_{546}$-[Co(hmc)$_3$] [g]	610 (2·24)	700 (−0·4)	A_2	h
		610 (+5·2)	E_a	
	440 (2·72)	460 (−5·5)	E_b	

[a] Assignments are those of the authors. [b] L. J. Boucher, *Inorg. Chem.*, 1970, **9**, 1202. [c] Data interpolated from spectra given in *e*. [d] Spectra not recorded above 600 nm. [e] F. P. Dwyer, I. K. Reid, and A. M. Sargeson, *Austral. J. Chem.*, 1965, **18**, 1919. [f] A. J. McCaffery, S. F. Mason, and B. J. Norman, *J. Chem. Soc.*, 1965, 5094. [g] This isomer is a mixture of two geometric isomers of closely similar c.d. spectra, see ref. 13 of text. [h] A. J. McCaffery, S. F. Mason, and R. E. Ballard, *J. Chem. Soc.*, 1965, 2883.

because of the uncertainty of its assignment[15] and of other difficulties[3,4] which make assignment of transitions in the u.v. region hazardous.

Nuclear Magnetic Resonance.—For complexes of the type [Co(acac)$_2$(LL')], where LL' is an unsymmetrical bidentate ligand, the low molecular symmetry means that the four methyl groups and the two methine protons of the acac ligands are non-equivalent, so that the separate resonances are expected for each group. This is observed in the present cases (Figures 2

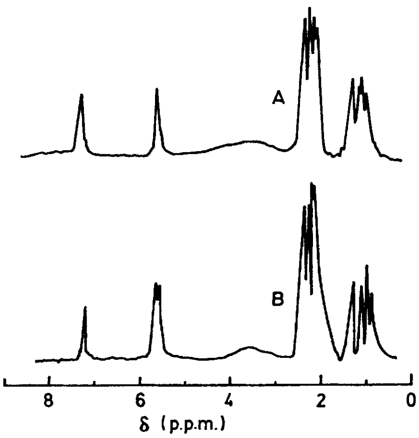

FIGURE 2 60 MHz N.m.r. spectra of (A) $(+)_{546}$-[Co(acac)$_2$(L-val)], and (B) $(-)_{546}$-[Co(acac)$_2$(L-val)]

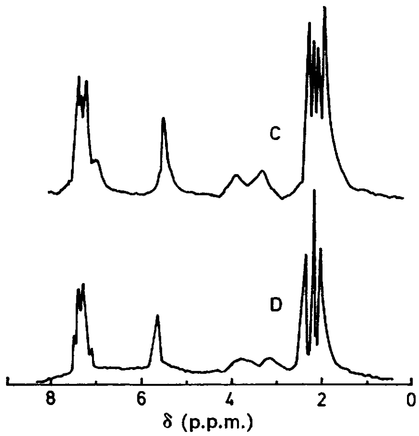

FIGURE 3 60 MHz N.m.r. spectra of (C) $(+)_{546}$-[Co(acac)$_2$(L-phe)], and (D) $(-)_{546}$-[Co(acac)$_2$(L-phe)]

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[15] D. E. Barnum, *J. Inorg. Nuclear Chem.*, 1961, **22**, 183; T. S. Piper, *J. Chem. Phys.*, 1962, **36**, 3330; I. Hanazaki, F Hanazaki, and S. Nogakura, *ibid.*, 1969, **50**, 265.

and 3, Table 3), where LL′ = amino-acidato; four methyl proton resonances of equal intensity are observed at *ca.* 2 p.p.m., except for the $(-)_{546}$ isomer of the L-phenylalanine complex where three resonances are observed with an intensity ratio 1 : 2 : 1. For only one isomer, that of the more soluble $(-)_{546}$-[Co(acac)$_2$(L-val)], is the methine doublet observed, for the remaining isomers only a singlet is found. These assignments are supported by the integrated intensities and are in accord with those of other workers.[16,17] The resonances of the α-CH, β-CH$_{(2)}$, and NH$_2$ protons of the amino-acid ligands are not easily observed because of the broadness of the CH resonances (multiplets), their small intensity, and the broadening effect of the nuclear quadrupole moment of the nitrogen nucleus.

TABLE 3

^{1}H N.m.r. data (p.p.m. from tetramethylsilane as internal reference) for [Co(acac)$_2$(L-aa)] in CDCl$_3$ [a]

	acac		L-aa	
Complex	CH$_3$	CH	CH$_3$	C$_6$H$_5$
$(+)_{546}$-[Co(acac)$_2$(L-val)]	2·08	5·59	0·94	
	2·12		1·06	
	2·20		1·10	
	2·29		1·23	
$(-)_{546}$-[Co(acac)$_2$(L-val)]	2·13	5·67	0·84	
	2·16		0·95	
	2·27		1·11	
	2·34		1·22	
$(+)_{546}$-[Co(acac)$_2$(L-phe)]	1·97	5·51		7·35 (multiplet)
	2·08			
	2·16			
	2·24			
$(-)_{546}$-[Co(acac)$_2$(L-phe)]	2·02	5·55		7·40 (multiplet)
	2·13 (doublet)	5·62		
	2·29			

[a] A resonance observed at *ca.* 7·3—7·4 p.p.m. arises from the *ca.* 1% CHCl$_3$ present in the solvent.

The ^{1}H n.m.r. spectrum of free L-valine displays a quadruplet methyl resonance, which may be assigned[18] as a pair of doublets from the magnetically non-equivalent methyl groups of the isopropyl moiety. For $(+)_{546}$-[Co(acac)$_2$(L-val)] these doublets occur at 1·01 and 1·16 p.p.m., and for the $(-)_{546}$ isomer at 0·90 and 1·16 p.p.m. In both cases for the CH$_3$–CH–CH$_3$ system, the coupling constant, J_{AX_3}, is 7 Hz as found for free valine. The greater separation of the doublets for the $(+)_{546}$ isomer over that of the $(-)_{546}$ isomer (*viz.*: 15·6 and 9·6 Hz respectively) is of particular interest. An examination of Dreiding molecular models suggests that in the D-configuration, the methyl groups of the valine approach much closer to one of the acac methyl groups than in the L-configuration. Thus the average field of the methyl groups is different in the two configurations.

Buckingham, Durham, and Sargeson[16] have made a similar observation for the two diastereoisomers of [Co(en)$_2$(L-val)]. The $(+)_{546}$ isomer which was assigned the D-configuration from the similarity in o.r.d. spectrum with that of D(+)-[Co(en)$_3$]$^{3+}$, exhibited a bigger difference between the methyl doublets than did the $(-)_{546}$ isomer. Their explanation of the difference in resonances is, however, in error since they assigned the wrong configurations to the isomers (ref. 17, Figure 22).

Correlations have also been made[19] between chemical shifts and absolute configurations for cobalt(III) complexes of L-alanine, however, any such attempt with the acetylacetonate complexes would be meaningless at the present time because of the limited data and unproved configurations.

Finally, it is evident[16] that the ^{1}H n.m.r. spectra of the diastereoisomeric mixtures results from an additive contribution from the resonances of the two optical isomers. Common resonances in the spectra of the two complexes would therefore indicate incomplete separation; the absence of such resonances for the complexes reported here is a further indication of complete separation of the diastereoisomers.

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[19] E. A. Berends and J. G. Brushmiller, *Inorg. Nuclear Chem. Letters*, 1970, **6**, 847.