Amino-acid Complexation to a Cobalt(III) Complex of Optically-active (2*R*,5*R*,8*R*,11*R*)-2,5,8,11-Tetraethyl-1,4,7,10-tetra-azacyclododecane (L). Preparation, Characterization, and Structure Determinations of $[Co^{III}\{(R)$- or $(S)\text{-alaO}\}L]Br[ClO_4]\cdot H_2O$†

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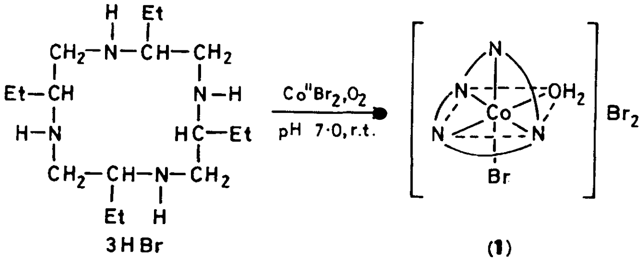
The complex $[Co^{III}Br(H_2O)L]Br_2$ [L = optically-active (2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethyl-1,4,7,10-tetra-azacyclododecane] reacts with amino acids under mild reaction conditions, at room temperature and at pH 8.0, to give the corresponding amino acidato complexes. The crystal structures of two such complexes, $[Co\{(R)alaO\}L]Br[ClO_4]\cdot H_2O$ (**2**) and $[Co\{(S)\text{-}alaO\}L]Br[ClO_4]\cdot H_2O$ (**3**), were determined by *X*-ray analyses. Crystal data for (**2**): tetragonal, space group $P4_3$, a = 14.320(6), c = 13.377(2) Å, and Z = 4; for (**3**): tetragonal, space group $P4_3$, a = 14.319(3), c = 13.325(7) Å, and Z = 4. Least-squares refinement converged at R = 0.044 and 0.042 for 2 618 and 2 413 unique reflections respectively. Both complexes show a *cis*-octahedral geometry, with the macrocycle co-ordinated in a folded manner, and the chiralities of the four nitrogen atoms of the macrocycle are *SSSR* as found in the starting complex. In both alaninato complexes, each amino acid co-ordinates in the β form with ε and δ conformations, respectively. The release of alanine from complex (**3**) is also discussed.

Recently we have prepared a cobalt(III) complex with the optically-active ligand L by the usual oxidation procedure and characterized it on the basis of various spectral measurements and *X*-ray analysis.[1–3] The sole product was *cis*-*SSSR*-aquabromo[(2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethyl-1,4,7,10-tetra-azacyclododecane]cobalt(III) bromide, $[Co^{III}Br(H_2O)L]Br_2$ (**1**) (see Scheme), although at least eight realizable isomers are possible. The ^1H and ^{13}C n.m.r., and the circular dichroism (c.d.) spectra of the complex showed time and solvent dependencies. Temperature dependence was also observed in the ^{81}Br n.m.r. spectrum. Further, the field desorption mass spectrum of the complex cation indicated that the parent ion from MeOH appeared at m/z 501, $[CoBr_2L]^+$, and that from aqueous solution at m/z 422, $[CoBrL]^+$. Thus the complex behaves essentially as a 1:1 electrolyte in MeOH, and as a 2:1 electrolyte in aqueous solution, suggesting the occurrence of $[CoBr_2L]^+$ and $[CoBr(H_2O)L]^{2+}$ cations respectively. These behaviours can be explained by a slow exchange and/or substitution at the fifth and sixth positions by the bromide anions or the solvent molecule used.

The tetra-azamacrocycle L is unique in the geometry of complex (**1**) in forming a *cis*-distorted octahedral chromophore. Because of the small ring size, the ligand does not co-ordinate to the metal in a planar manner but is folded in a *cis* position as found in all known octahedral transition-metal complexes of 1,4,7,10-tetra-azacyclododecanes.[4] Several unusual bond parameters and angle deformations from the octahedral values are observed in complex (**1**).[3] In particular, the Co–O bond distance of 1.948(7) Å is significantly longer than those (1.91—1.92 Å) found in other complexes.[3] The weaker binding may relate to the lability of the complex.



L•3HBr

(**1**)

Scheme. r.t. = Room temperature

The shape of the *cis* geometry leaves space available for the co-ordination of two other monodentate ligands or a bidentate one. Therefore, many different ligands can co-ordinate to form a six-co-ordinate complex. The lability described above is useful for this co-ordination reaction to (**1**). We have undertaken a program of studies on the syntheses and structural characterization of Co^{III} complexes of the optically-active ligand L involving amino acids and other functional bidentate compounds. We report here on the reaction of complex (**1**) with several neutral amino acids (Haa) and characterization of the complexes obtained on the basis of various spectral data, together with the *X*-ray structure determinations of the (*R*)- and (*S*)-alaninato(1–) complexes $[Co^{III}\{(R)alaO\}L]Br[ClO_4]\cdot H_2O$ (**2**) and $[Co^{III}\{(S)alaO\}L]Br[ClO_4]\cdot H_2O$ (**3**).

Ajioka *et al.*[5] recently showed that the release of alanine from an alaninato complex containing an optically-active tetradentate open-chain system, (6*R*,8*R*)-6,8-dimethyl-2,5,9,12-tetra-azatridecane, was carried out with retention of the chiral carbon centre, while also preserving the complex. This reaction is very useful for the asymmetric synthesis of an amino acid and allows the starting complex (**1**) to be reused. Since the specific goal of this study was an asymmetric induction using complex (**1**) as the

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† *cis*-β-*SSSR*-[(*R*)- or (*S*)-alaninato][(2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethyl-1,4,7,10-tetra-azacyclodecane]cobalt(III) bromide perchlorate monohydrate.

Supplementary data available: see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1987, Issue 1, pp. xvii—xx.

Table 1. Analytical and spectral data

		Analysis[b] (%)			Spectra	
Complex[a]	Yield (%)	C	H	N	Visible absorption $10^{-3}\ \tilde{\nu}_{max.}/cm^{-1}$ ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$)	C.d. $10^{-3}\ \tilde{\nu}_{ext.}/cm^{-1}$ ($\Delta\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$)
(**2**) $[Co\{(R)alaO\}L]Br[ClO_4]\cdot H_2O$	56	36.30 (36.30)	7.15 (7.05)	11.10 (11.15)	20.4 (305), 28.6 (244)	19.2 (0.72), 22.3 (0.72), 28.2 (0.27)
(**3**) $[Co\{(S)alaO\}L]Br[ClO_4]\cdot H_2O$	67	36.30 (36.30)	7.00 (7.05)	11.25 (11.15)	20.4 (306), 28.6 (240)	19.6 (1.05), 22.1 (−0.64), 28.4 (0.81)
(**4**) $[Co\{(R)valO\}L]Br[ClO_4]\cdot H_2O$	46	38.25 (38.40)	7.40 (7.35)	10.55 (10.65)	20.4 (220), 28.6 (180)	18.9 (0.73), 22.2 (0.66), 27.9 (0.39)
(**5**) $[Co\{(S)valO\}L]Br[ClO_4]\cdot H_2O$	31	38.15 (38.40)	7.35 (7.35)	10.95 (10.65)	20.4 (217), 28.2 (174)	19.3 (0.82), 21.7 (−0.56), 28.2 (0.50)
(**6**) $[Co\{(R)proO\}L]Br[ClO_4]\cdot H_2O$	61	38.55 (38.50)	7.00 (7.10)	10.70 (10.70)	20.0 (236), 28.6 (204)	18.9 (1.37), 20.7 (−0.75), 27.9 (0.83)
(**7**) $[Co\{(S)proO\}L][ClO_4]_2\cdot 1.5H_2O$	43	36.80 (36.90)	6.85 (6.95)	10.20 (10.25)	20.0 (214), 28.2 (178)	20.3 (1.02), 26.3 (0.25)
(**8**) $[Co\{(S)serO\}L]Br[ClO_4]\cdot H_2O$	54	35.55 (35.35)	6.80 (6.85)	10.90 (10.85)	20.4 (230), 28.6 (181)	19.3 (0.85), 21.3 (−0.25), 23.2 (0.16), 28.6 (0.54)
(**9**) $[Co\{(S)thrO\}L][ClO_4]_2\cdot 1.5H_2O$	45	34.10 (34.50)	6.50 (6.90)	9.90 (10.05)	20.4 (224), 28.6 (179)	19.3 (0.71), 22.6 (0.43), 28.6 (0.31)
(**10**) $[Co\{(S)trpO\}L]Br[ClO_4]\cdot H_2O$	40	43.55 (43.55)	6.75 (6.65)	11.10 (11.30)	20.4 (200), 28.6 (305)	19.5 (0.61), 22.5 (−0.48), 28.2 (0.32), 32.2 (−0.09)
(**11**) $[Co(glyO)L]Br[ClO_4]\cdot H_2O$	49	35.10 (35.15)	6.80 (6.90)	11.45 (11.40)	20.4 (196), 28.6 (162)	19.5 (0.95), 22.7 (0.16), 28.2 (0.51)

[a] alaO = alaninate(1−), valO = valinate(1−), proO = prolinate(1−), serO = serinate(1−), thrO = threoninate(1−), trpO = tryptophanate(1−), and glyO = glycinate(1−). [b] Calculated values are given in parentheses.

starting reagent, we also examined the possibility of releasing the amino acid from complex (**3**) and to regenerate (**1**).

Experimental

Preparation of Compounds.—The ligand L and the starting complex (**1**) were prepared according to the literature.[1,2] The amino acidato cobalt(III) complexes, $[Co^{III}(aa)L]^{2+}$, were obtained by a modification of the method of Job and Bruice.[6] The pH of an aqueous red-violet solution of the parent complex (**1**) (300 mg, 0.5 mmol) and the appropriate amino acid (0.5 mmol) was adjusted to pH 8.0 with 0.1 N NaOH. The colour of the solution turned orange-red at pH 7. After *ca.* 5 min, the solvent was evaporated to near dryness, and $NaClO_4$ (150 mg) added to the residue. The resulting orange-red precipitate was usually recrystallized from water. The yields, analytical data, and spectral data are listed in Table 1.

$[Co^{III}\{(S)alaO\}L]Br[ClO_4]\cdot H_2O$ (**3**). The reaction product obtained by the method described above using alanine was also purified on a column of SP Sephadex C-25 cation-exchange resin (30 × 400 mm) in the Na form. Four bands were developed by 0.1 mol dm^{-3} $NaClO_4$ on the column. The minor first pink and the fourth orange bands moved at rates consistent with 1+ and 3+ ions, respectively. They did not contain an alaninato moiety. The cations were thus assumed to be $[CoBr_2L]^+$ and $[Co(H_2O)_2L]^{3+}$ respectively, based on ^1H n.m.r. data. The second pink 2+ fraction was assigned to the unreacted starting complex cation $[CoBr(H_2O)L]^{2+}$. Only the third orange-red 2+ band contained an alaninato moiety, and this was assigned to the β complex (**3**).

The selectivity of co-ordination for (*S*)-ala was examined by ^1H n.m.r. spectroscopy. An equimolar mixture of (**1**) and (*S*)-ala in D_2O in an n.m.r. tube was made basic by 0.1 N NaOD and the spectrum recorded. We could observe only one set of signals for the corresponding co-ordinated ala, a doublet (1.52 p.p.m., CH_3) and a quartet (3.95 p.p.m., CH). When unreacted ala remained in the tube, the corresponding signals at 1.47 (d) and 3.78 (q) p.p.m. (immediately after adjusting pH), which were assigned by addition of new free ala in the same tube, were observed together with those of the co-ordinated ala.

Measurements.—Visible absorption spectra were recorded with a Hitachi 330 spectrophotometer, and c.d. spectra with a JASCO J-20 spectropolarimeter. ^1H N.m.r. (400 MHz) spectra were obtained on a JEOL JNM-GX400 spectrometer using sodium $[^2H_4]$-3-trimethylsilylpropionate as an internal reference in D_2O.

X-*Ray Data Collection.*—Prismatic, orange-red crystals of the alaninato complexes (**2**) and (**3**) were used for the analyses. Intensity data were obtained on a Rigaku AFC-5 four-circle diffractometer using graphite-monochromatized Mo-K_α radiation (λ = 0.710 73 Å), and ω ($2\theta < 30°$) and ω–2θ ($2\theta > 30°$) scan methods at a scan rate of 4.0° min^{-1} for $2\theta \leqslant 55°$. Four standard reflections were measured after every 150 reflections. The data were corrected for Lorentz polarization factors, but not for absorption. The crystal data and experimental details are given in Table 2.

Solution and refinement of the structures. Both structures were solved by the direct method, initially assuming space group $P4_1$. However, both absolute configurations of chiral centres in the ligand which were used as internal reference of asymmetric centres were found to be opposite. For each complex, therefore, space group $P4_3$ was chosen, and refinement was by block-diagonal least squares. Unit weights were used for all reflections. All non-hydrogen atoms were anisotropic and H atoms isotropic. Hydrogen atomic co-ordinates were generated assuming standard bond lengths and angles. Both final difference maps showed no peaks higher than 0.7 e $Å^{-3}$. Atomic scattering factors were taken from International Tables.[7] Calculations were performed on a FACOM M-380 computer of this Institute using the UNICS III[8] and MULTAN 78 program systems.[9] Positional parameters for the non-hydrogen atoms are given in Table 3.

Release of Alanine from the Alaninato Complex (**3**) *to*

Table 2. Crystallographic parameters and experimental conditions for [Co{(*R*)alaO}L]Br[ClO$_4$]·H$_2$O (**2**) and [Co{(*S*)alaO}L]Br[ClO$_4$]·H$_2$O (**3**)

Complex	(**2**)	(**3**)
Formula	$C_{19}H_{44}BrClCoN_5O_7$	$C_{19}H_{44}BrClCoN_5O_7$
M	628.87	628.87
Crystal system	Tetragonal	Tetragonal
Space group	$P4_3$	$P4_3$
a/Å	14.320(6)	14.319(3)
c/Å	13.377(2)	13.325(7)
U/Å^3	2 743(1)	2 732(2)
Z	4	4
D_m/Mg m^{-3} [a] (temp./K)	1.53 (293)	1.53 (293)
D_c/Mg m^{-3}	1.523	1.529
F(000)	1 312	1 312
μ(Mo-K_α)/mm^{-1}	2.21	2.22
Crystal dimensions/mm	0.25 × 0.40 × 0.55	0.40 × 0.45 × 0.38
No. of observed reflections [b]	2 934	3 656
No. of unique reflections used	2 618	2 413
No. of unobserved reflections	931	1 122
No. of variables	476	476
R [c]	0.044	0.042
R' [d]	0.046	0.045
Largest shift/error value on final cycle	0.29 (Br)	0.16 (Br)

[a] Flotation method in CCl$_4$–CBr$_4$. [b] Criterion: $|F_o| > 3\sigma(|F_o|)$. [c] $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|)$. [d] $R' = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{\frac{1}{2}}$.

Table 3. Atomic co-ordinates (× 10^4) for complexes (**2**) and (**3**)

	(*a*) Complex (**2**)			(*b*) Complex (**3**)		
Atom	*x*	*y*	*z*	*x*	*y*	*z*
Co	2 967(1)	1 457(1)	0	2 917(1)	1 446(1)	0
N(1)	3 813(5)	1 414(4)	1 130(5)	3 763(4)	1 423(5)	1 146(5)
C(2)	4 405(6)	2 302(6)	1 173(6)	4 338(5)	2 299(6)	1 188(7)
C(3)	4 411(5)	2 746(6)	143(7)	4 361(5)	2 740(6)	161(7)
N(4)	3 464(4)	2 691(4)	−303(5)	3 426(4)	2 669(4)	−296(5)
C(5)	3 374(5)	2 893(5)	−1 385(6)	3 343(5)	2 870(5)	−1 390(6)
C(6)	2 428(5)	2 506(5)	−1 687(6)	2 396(5)	2 483(5)	−1 695(6)
N(7)	2 362(4)	1 518(4)	−1 323(5)	2 330(4)	1 501(4)	−1 328(5)
C(8)	2 817(5)	837(5)	−2 030(6)	2 786(5)	821(5)	−2 038(7)
C(9)	3 470(5)	205(5)	−1 450(6)	3 451(5)	189(6)	−1 435(7)
N(10)	3 967(4)	810(4)	−728(5)	3 926(4)	786(4)	−694(5)
C(11)	4 687(5)	401(5)	−43(6)	4 642(5)	374(5)	−4(7)
C(12)	4 366(6)	532(6)	1 040(6)	4 308(6)	535(6)	1 078(6)
C(21)	3 998(7)	2 934(7)	1 983(7)	3 945(7)	2 943(7)	2 001(7)
C(22)	4 625(8)	3 762(7)	2 220(9)	4 560(9)	3 770(8)	2 215(9)
C(51)	3 507(6)	3 928(6)	−1 629(7)	3 464(7)	3 913(6)	−1 647(8)
C(52)	3 531(8)	4 127(7)	−2 737(9)	3 520(9)	4 113(7)	−2 749(9)
C(81)	2 098(6)	278(6)	−2 630(7)	2 076(6)	244(6)	−2 624(7)
C(82)	1 518(7)	861(7)	−3 359(7)	1 445(8)	827(8)	−3 298(7)
C(111)	4 941(6)	−611(7)	−248(7)	4 876(6)	−654(6)	−185(7)
C(112)	5 727(8)	−953(8)	423(10)	5 674(8)	−984(8)	474(10)
N(13)	1 930(5)	1 967(4)	786(6)	1 819(4)	1 951(4)	691(5)
C(14)	1 220(5)	1 233(5)	1 006(6)	1 515(5)	1 280(5)	1 491(6)
C(15)	1 714(5)	294(5)	902(6)	1 804(5)	289(5)	1 139(6)
O(16)	2 440(4)	280(3)	369(5)	2 369(4)	272(3)	399(5)
C(141)	701(7)	1 371(6)	1 959(8)	498(6)	1 359(6)	1 775(8)
O(151)	1 344(5)	−399(4)	1 291(5)	1 478(5)	−383(4)	1 563(5)
Br	1 599(1)	4 230(1)	400(1)	1 643(1)	4 244(1)	468(1)
Cl	2 286(2)	2 861(2)	4 287(3)	2 277(2)	2 847(2)	4 350(3)
O(1)	2 116(6)	1 885(5)	4 281(7)	2 161(7)	1 898(6)	4 225(9)
O(2)	3 245(5)	3 073(6)	4 292(9)	3 224(6)	3 097(7)	4 305(8)
O(3)	1 823(7)	3 327(8)	4 963(14)	1 838(8)	3 265(10)	5 139(13)
O(4)	1 998(9)	3 149(8)	3 232(11)	1 819(9)	3 252(9)	3 426(14)
O_W	3 035(6)	661(6)	2 924(6)	3 252(5)	648(5)	3 064(6)

regenerate the Starting Complex (**1**).—The procedure was carried out by a method similar to that described by Ajioka *et al.*[5] Complex (**3**) (63 mg) was dissolved in 0.1 mol dm^{-3} Na$_2$CO$_3$ aqueous solution and allowed to stand at room temperature for 3 h. After the solution was neutralized with an equimolar amount of H$_2$SO$_4$, separation of ala and the complex from the reaction product was carried out on a column of SP-Sephadex C-25 cation-exchange resin. The alanine was found to pass through the column without adsorption, and was detected by high pressure liquid chromatography (h.p.l.c.) (JASCO TWINKLE) using an ERC-ODS 1171 column (6 mm inside diameter, 200 mm length, Hypersil ODS, 3 μm particle diameter,

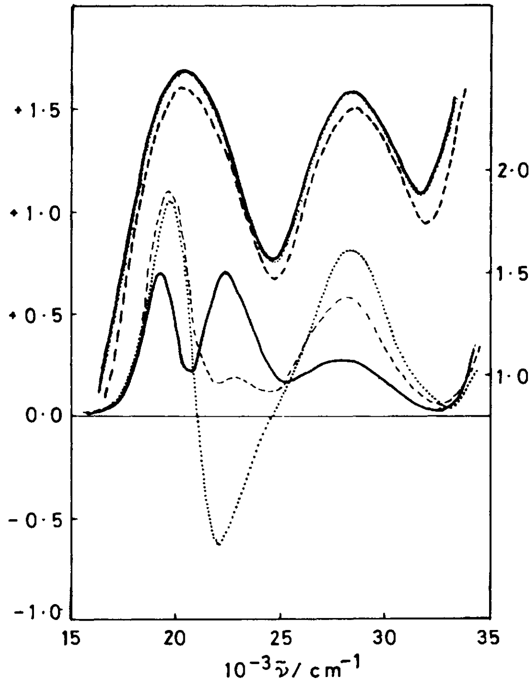

Figure 1. Visible absorption (upper traces) and c.d. spectra (lower traces) of (**2**) (——), (**3**) (· · · ·), and (**11**) (– – – –)

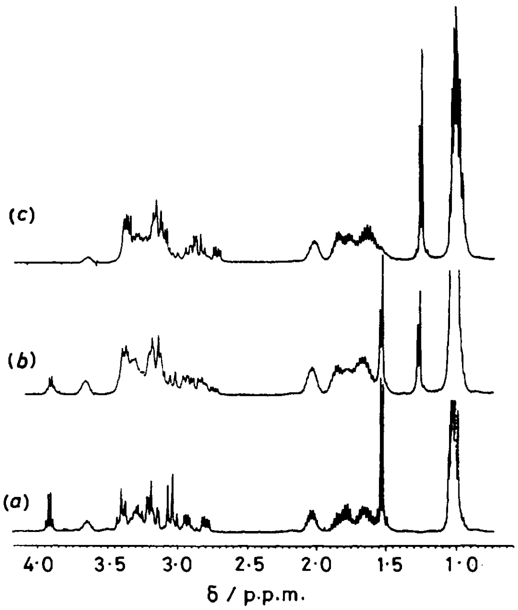

Figure 2. ^1H N.m.r. spectra of (**3**) in 0.1 mol dm^{-3} Na_2CO_3–D_2O solution; (*a*) almost immediately after dissolution, (*b*) after 0.5 h, and (*c*) after 3 h

ERMA Optical Works Ltd.) with a copper complex of *N*,*N*-dipropyl-(*S*)-alanine as mobile phase for optical resolution of the amino acid.[10]

The complex on the Sephadex column was recovered as crystals by elution with 0.1 mol dm^{-3} Na_2SO_4 followed by treatment with concentrated HBr. The crystals regenerated (22 mg, 37%) were found to be identical with (**1**) from analytical and spectral data (Found: C, 31.90; H, 6.30; N, 9.25. Calc. for $C_{16}H_{38}Br_3CoN_4O$: C, 31.95, H, 6.35, N, 9.30%). The sample could be reused as usual.

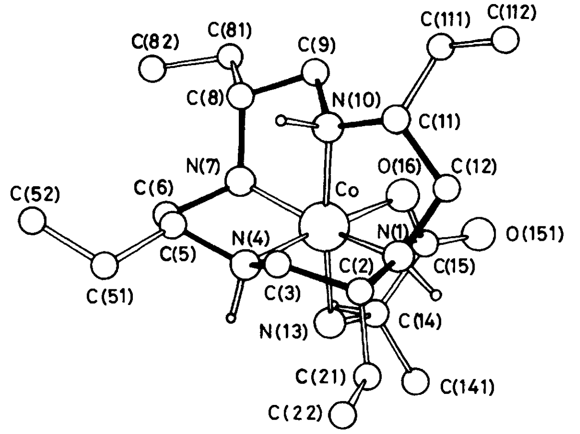

Figure 3. Molecular structure of (**2**). Only the hydrogen atoms at the asymmetric nitrogens, and at the chiral centre in alaninate are attached for clarity

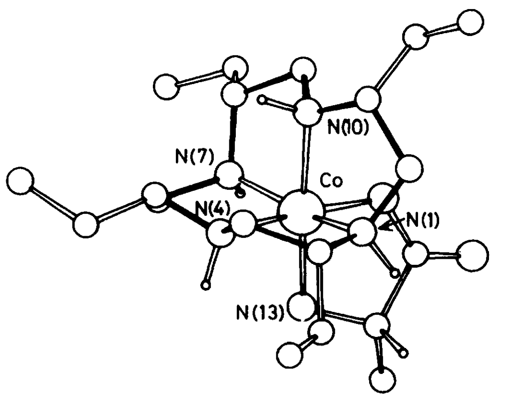

Figure 4. Molecular structure of (**3**)

Results and Discussion

Synthesis and Characterization of Amino Acidato Complexes.—The reaction of complex (**1**) with an equivalent of an amino acid at ambient temperature and at pH 8.0 gave the corresponding amino acidato complexes $[Co^{III}(aa)L]^{2+}$. Thus there is rapid production of a six-co-ordinate complex during the first few minutes under mild reaction conditions. The results of chromatography and an experiment carried out in an n.m.r. tube (see Experimental section) showed that only one product was obtained, and that no other structural isomers were present in the product. Therefore, the reaction of complex (**1**) with a neutral amino acid is considered to be exactly regioselective. This may be due to the presence of two different reactive sites at *cis* positions in (**1**); at low pH the carboxylate group of the amino acid first attacks the neutral site rather than the bromide, and subsequently the bromide ion is replaced by the amino group in basic solution.

The visible absorption and c.d. spectra of the amino acidato complexes are summarized in Table 1, and those of (**2**), (**3**), and $[Co(glyO)L]Br[ClO_4]\cdot H_2O$ (**11**) are shown in Figure 1. The pattern of visible absorption spectra in all the compounds is typical for a N_5O chromophore.[11] For the (*R*)- and (*S*)-alaninato complexes (**2**) and (**3**), the visible absorption spectra show very similar curves. In the c.d. spectra however, the first absorption splits in different ways: two positive peaks for (**2**), a positive and a negative curve for (**3**). The second Cotton effect is

Table 4. Bond lengths (Å) and angles (°) around the cobalt ion

	(2)	**(3)**
Co–N(1)	1.938(7)	1.950(7)
Co–N(4)	1.948(6)	1.938(6)
Co–N(7)	1.972(6)	1.962(6)
Co–N(10)	1.972(6)	1.959(7)
Co–N(13)	1.961(7)	1.961(6)
Co–O(16)	1.911(5)	1.929(5)
N(1)–Co–N(4)	87.9(3)	86.6(3)
N(1)–Co–N(7)	167.4(3)	167.0(3)
N(1)–Co–N(10)	85.2(3)	84.5(3)
N(1)–Co–N(13)	93.8(3)	97.8(3)
N(1)–Co–O(16)	91.0(3)	91.3(3)
N(4)–Co–N(7)	86.2(3)	86.6(3)
N(4)–Co–N(10)	92.9(3)	93.6(3)
N(4)–Co–N(13)	92.9(3)	93.6(3)
N(4)–Co–O(16)	176.4(3)	175.1(3)
N(7)–Co–N(10)	84.1(2)	84.8(3)
N(7)–Co–N(13)	97.6(3)	93.7(3)
N(7)–Co–O(16)	95.6(2)	96.3(3)
N(10)–Co–N(13)	173.7(3)	172.5(3)
N(10)–Co–O(16)	90.0(2)	90.6(3)
N(13)–Co–O(16)	83.7(2)	82.3(2)

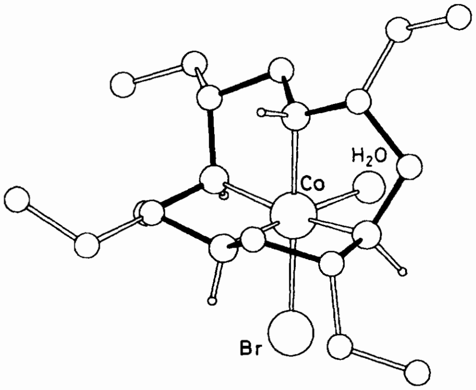

Figure 5. Molecular structure of (**1**)

assigned to the vicinal effect of the amino acid co-ordinated without racemization. From the spectral data, however, it is difficult to confirm the way in which the amino acid co-ordinates to the Co^{III} ion as either β_1 or β_2 forms with respect to the unsymmetrical topology of the N_4 ligand.[12,*] This is because the signs of c.d. spectra of the first absorption band in a N_5O cobalt(III) complex are not always consistent with the absolute configuration, even though the complexes have similar stereochemistry.[13] The close analogy between the c.d. patterns of the (*R*)-alaninato and (*R*)-valinato complexes [(**2**) and (**4**)] suggests the similarity of their structures. The same may be said of (**3**) and (**5**). On the other hand, the pattern of c.d. curves for the prolinato- and threoninato-complexes (**6**), (**7**), and (**9**) differ from those of the other amino acidato complexes listed in Table 1. This may be caused by the additional vicinal effect due to the asymmetric pyrrolidine N atom newly formed by co-ordination of proline (**6**) and (**7**), and due to another chiral centre in the threonine of (**9**). Therefore, all the complexes obtained here may have similar geometries.

Table 5. Bond angles (°) of 12-membered ring

	(2)	**(3)**
Co–N(1)–C(2)	110.5(5)	110.8(5)
Co–N(1)–C(12)	107.2(5)	106.9(5)
C(2)–N(1)–C(12)	114.3(6)	115.3(6)
N(1)–C(2)–C(3)	108.5(6)	109.2(7)
N(1)–C(2)–C(21)	107.9(7)	109.2(7)
C(3)–C(2)–C(21)	113.5(7)	113.4(7)
C(2)–C(3)–N(4)	109.7(6)	109.0(6)
Co–N(4)–C(3)	107.4(5)	108.6(5)
Co–N(4)–C(5)	110.4(4)	110.1(5)
C(3)–N(4)–C(5)	117.5(6)	117.6(6)
N(4)–C(5)–C(6)	105.4(6)	105.2(6)
N(4)–C(5)–C(51)	112.8(6)	113.2(7)
C(6)–C(5)–C(51)	114.0(6)	113.3(7)
C(5)–C(6)–N(7)	108.3(6)	108.2(6)
Co–N(7)–C(6)	107.8(4)	107.9(5)
Co–N(7)–C(8)	110.1(4)	110.7(5)
C(6)–N(7)–C(8)	112.3(6)	112.1(6)
N(7)–C(8)–C(9)	109.4(7)	108.7(7)
N(7)–C(8)–C(81)	112.1(6)	112.5(6)
C(9)–C(8)–C(81)	111.8(6)	111.2(6)
C(8)–C(9)–N(10)	106.3(6)	107.1(6)
Co–N(10)–C(9)	104.4(4)	104.8(5)
Co–N(10)–C(11)	112.5(5)	113.9(5)
C(9)–N(10)–C(11)	120.1(6)	120.0(6)
N(10)–C(11)–C(12)	108.9(6)	107.7(6)
N(10)–C(11)–C(111)	115.3(7)	115.6(7)
C(12)–C(11)–C(111)	111.1(7)	111.1(7)
N(1)–C(12)–C(11)	109.8(6)	110.3(6)
C(2)–C(21)–C(22)	112.6(8)	113.2(8)
C(5)–C(51)–C(52)	113.3(7)	114.2(8)
C(8)–C(81)–C(82)	114.5(7)	113.6(7)
C(11)–C(111)–C(112)	112.2(8)	111.9(8)

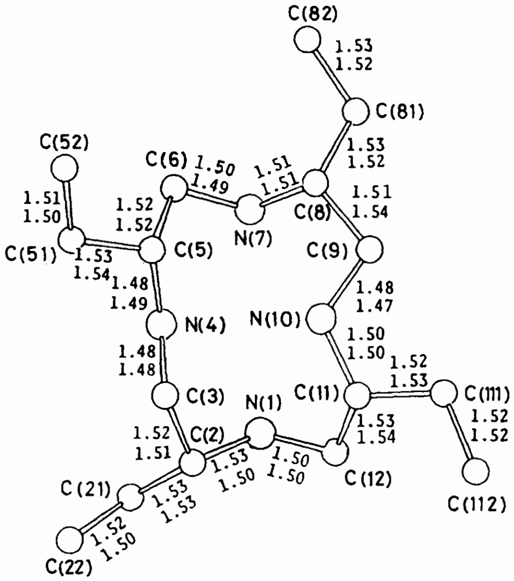

Figure 6. Bond lengths in the 12-membered ring (Å): upper, (**2**); lower, (**3**). The standard deviations are 0.01 Å for the ring and 0.02 Å for the ethyl groups

The ^1H n.m.r. pattern for the alaninato complexes consists of four different sets of signals for the ligand and a single set of resonances for the co-ordinated ala (*cf.* Figure 2). This is also the case for the other amino acidato complexes obtained here, which means that each ligand L has C_1 symmetry as well as the

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[*] For amino acidates, β_1 and β_2 refer to the unsymmetrical topology of the N_4 ligand with the amino acidato N atoms *trans* to the apical N for β_1, and that of the O atom for β_2 respectively.

Table 6. Bond parameters for the alaninato five-membered ring

	(2)	**(3)**
(*a*) Bond distances (Å)		
N(13)–C(14)	1.49(1)	1.50(1)
C(14)–C(15)	1.53(1)	1.55(1)
C(15)–O(16)	1.26(1)	1.28(1)
C(14)–C(141)	1.49(1)	1.51(1)
C(15)–O(151)	1.24(1)	1.21(1)
(*b*) Bond angles (°)		
Co–N(13)–C(14)	111.1(5)	109.3(4)
N(13)–C(14)–C(15)	106.7(6)	107.1(6)
C(14)–C(15)–O(16)	116.6(6)	114.8(6)
C(15)–O(16)–Co	117.3(4)	117.1(5)
N(13)–C(14)–C(141)	114.6(7)	114.2(6)
C(14)–C(15)–O(151)	118.1(7)	119.0(7)
O(16)–C(15)–O(151)	125.2(6)	126.2(7)
C(15)–C(14)–C(141)	115.2(7)	113.7(6)
(*c*) Torsion angles (°)		
O(16)–Co–N(13)–C(14)	−13.4(5)	27.8(5)
Co–N(13)–C(14)–C(15)	21.5(7)	−28.8(6)
N(13)–C(14)–C(15)–O(16)	−22.5(9)	13.1(9)
C(14)–C(15)–O(16)–Co	12.7(9)	9.9(8)
C(15)–O(16)–Co–N(13)	0.6(5)	−22.1(5)
(*d*) Displacements (Å) of atoms from the plane CoN(13)O(16)		
C(14)	−0.32(1)	0.66(1)
C(15)	−0.01(1)	0.43(1)
C(141)	0.29(2)	0.24(2)

Table 7. Hydrogen-bond distances and intermolecular contacts (Å)

	(2)	**(3)**	
(*a*) Hydrogen bonds			
Atom 1 ··· Atom 2			Symmetry*
N(1) ··· O_W	2.86(1)	2.88(1)	I
N(7) ··· O(15)	2.826(8)	2.836(8)	II
N(10) ··· Br	3.364(6)	3.398(7)	III
N(13) ··· Br	3.315(6)	3.307(6)	I
N(13) ··· O(15)		3.064(9)	IV
O(1) ··· O_W	2.85(1)	2.84(1)	I
(*b*) Intermolecular contacts ($\leqslant$ 3.5 Å)			
C(6) ··· O(15)	3.41(1)	3.38(1)	II
C(9) ··· O(3)	3.25(1)	3.16(2)	V
C(2) ··· O(2)	3.43(1)	3.49(2)	VI
C(81) ··· O(15)	3.44(1)		II
C(81) ··· O(3)	3.49(1)	3.45(1)	III
C(82) ··· O(151)	3.36(1)		II
C(14) ··· O(151)	3.19(1)		IV

* Symmetry of atom 2: I x, y, z; II $-y, x, z + \frac{3}{4}$; III $1 - y, x, z + \frac{3}{4}$; IV $-y, x, z - \frac{1}{4}$; V $x, -y, z + \frac{1}{4}$; VI $1 - y, x, z - \frac{1}{4}$.

starting complex (**1**), and that the original conformation of the macrocycle is maintained even after co-ordination of the amino acid. Although the quartets for the proton of the chiral centre of alaninate in the two diastereomeric complexes can be distinguished; 3.905 for (**2**) and 3.899 p.p.m. for (**3**), there is no difference in the chemical shift for the methyl doublet (1.506 p.p.m.) in D_2O. This indicates that the overall conformations of the two diastereomers are quite similar.

X-Ray Crystal Structures of Alaninato Complexes.—Figures 3 and 4 show the molecular structures of (**2**) and (**3**) respectively.

Table 8. Torsion angles (°) of 12-membered ring

	(2)	**(3)**
C(12)–N(1)–C(2)–C(3)	99.8(8)	100.1(8)
N(1)–C(2)–C(3)–N(4)	41.0(8)	40.6(9)
C(2)–C(3)–N(4)–C(5)	−166.7(6)	−166.8(6)
C(3)–N(4)–C(5)–C(6)	163.4(6)	164.5(6)
N(4)–C(5)–C(6)–N(7)	−50.7(7)	−50.8(7)
C(5)–C(6)–N(7)–C(8)	−83.3(7)	−83.4(7)
C(6)–N(7)–C(8)–C(9)	130.4(6)	130.1(6)
N(7)–C(8)–C(9)–N(10)	−41.9(6)	−40.3(8)
C(8)–C(9)–N(10)–C(11)	−178.8(6)	−178.5(6)
C(9)–N(10)–C(11)–C(12)	−117.9(7)	−120.6(7)
N(10)–C(11)–C(12)–N(1)	−32.0(8)	−31.7(8)
C(11)–C(12)–N(1)–C(2)	−78.7(8)	−79.2(8)

Table 9. Mean planes and deviations (Å) through Co ion

	(2)	**(3)**
Plane 1:		
Co	0.0016(3)	0.0005(3)
N(4)	−0.024(5)	−0.044(5)
N(10)	−0.014(4)	0.036(4)
N(13)	−0.021(6)	0.035(4)
O(16)	−0.021(4)	−0.041(5)
Plane 2:		
Co	−0.0006(2)	−0.0001(3)
N(1)	0.111(5)	0.118(5)
N(7)	0.096(4)	0.109(4)
N(10)	−0.092(4)	−0.144(5)
N(13)	−0.122(6)	−0.104(4)
Plane 3:		
Co	0.0049(3)	0.0043(3)
N(1)	−0.193(5)	−0.191(5)
N(4)	0.073(5)	0.092(5)
N(7)	−0.169(4)	−0.169(4)
O(16)	0.049(4)	0.058(4)
Dihedral angles between planes (°)		
1—2	91.9(2)	91.5(2)
1—3	88.5(2)	90.9(2)
2—3	88.7(2)	86.8(2)

For comparison, a perspective view of the parent complex (**1**) is also given in Figure 5. Bond parameters are listed in Tables 4—8 and Figure 6. The result confirms co-ordination of the amino acid without altering the stereochemistry of the co-ordination sphere and the ligand except for the direction of the flexible terminal ethyl groups. Thus both complex cations have distorted-octahedral and six-co-ordinate geometries, where four N atoms of the macrocycle, and the N and O atoms of alaninate are co-ordinated to the cobalt ion in a *cis* β form with retention of the respective configurations. Further, the result indicates that the molecular conformations and dimensions of (**2**) are quite similar to those of (**3**) except for the alaninate moieties as expected. The 12-membered ring in both compounds bends about the line connecting N(1) and N(7), and the configurations of the asymmetric nitrogens formed are *SSSR* (C_1 symmetry). Therefore the type of *cis* co-ordination of the alaninate is specified as β_1 regarding N(10) which has *R* configuration. The absolute configurations of the complex cations were assigned from the known absolute configuration of the ligand as an internal reference.[1]

Bond distances and angles about Co are listed in Table 4. The mean value of the Co–N bond distances for the macrocyclic ligands in both complexes, 1.955(7) Å, is comparable to those found in other cobalt complexes of 1,4,7,10-tetra-azacyclododecanes (1.95—1.97 Å).[4] On the other hand, the mean Co–N [1.961(7) Å] and Co–O [1.920(5) Å] distances for the alaninato moieties are not necessarily comparable. In particular, the latter are significantly longer than those reported in several Co^{III} alaninato chelates: Co–N (av.) and Co–O (av.) are 1.93(10) and 1.90(1) Å for (*R*)alaO in Ag[Co(NO$_2$)$_2${(*R*)-alaO}$_2$],[14] 1.969(14) and 1.893(9) Å in Λ-β$_2$-[Co{(*R*)-alaO}L′]Br$_2$·3H$_2$O [L′ = (6*R*,8*R*)-6,8-dimethyl-2,5,9,12-tetra-azatridecane],[15] and 1.954(10) and 1.885(9) Å in *mer*-[Co{(*S*)alaO}$_3$].[16] Similarly, distortion from a regular octahedron is found for (**2**) and (**3**) [av. 167.2(3)° for N(1)–Co–N(7) and 84.5(3)° for N(7)–Co–N(10)], as is found for (**1**) and other 1,4,7,10-tetra-azacyclododecane complexes.[3,4] On the other hand, three mean planes CoN(4)N(10)N(13)O(16), CoN(1)N(7)N(10)N(13), and CoN(1)N(4)N(7)O(16) are essentially orthogonal to each other, as listed in Table 8. The Co ion is always located near the mean plane in a similar manner as in (**1**). Analogy with the conformation of the N$_4$ moiety in the parent complex (**1**) is also observed. As shown in Figure 5, the [2424] ring conformation[17,*] for the 12-membered ring is maintained even after alanine is co-ordinated. The bond parameters are almost normal except for the bond angle of 120.1(6)° for C(9)–N(10)–C(11), whose value is slightly smaller than that found in (**1**), 121.3°. The conformations of the five-membered chelate rings for the tetra-azamacrocycles in (**2**) and (**3**) are the same as those in (**1**) (ε, λ, δ, and δ).

Each alaninato ligand forms a five-membered chelate ring. The conformations can be designated as ε and δ, respectively, in agreement with those found in Ag[Co(NO$_2$)$_2${(*R*)alaO}$_2$], [Co{(*R*)alaO}L′]Br$_2$·3H$_2$O, and [Co{(*S*)alaO}$_3$].[14–16] The carbon atoms C(14) and C(15) lie 0.32(1) and 0.01(1) Å below the plane formed by N(13), Co, and O(16) in (**2**) as shown in Table 6. The corresponding deviations in (**3**) are 0.66(1) and 0.43(1) Å respectively. The position of the methyl group with respect to the chelate ring is equatorial in both cases. The angles N(13)–Co–O(16) in the alaninato chelate rings are 83.7(2) and 82.3(2)° for (**2**) and (**3**) respectively, which are slightly smaller than those found in the cobalt(III) alaninato complexes above: 86.1(5) (av.), 84.6(5), and 85.6(4)° (av.) respectively.[14–16]

The hydrogen bonds and intermolecular contacts are listed in Table 7. There is one more hydrogen bond in (**3**) than in (**2**). This may be related to a larger density. Both space groups are the same, and the lattice constants and their crystal habits bear a remarkable resemblance. However, one can distinguish them by differences in $|F_o|$ and their densities. In particular, the resolution of an ether mixture of equal amounts of (**2**) and (**3**) was carried out by flotation in CCl$_4$–benzene. Ten specimens of crystals selected from the heavier ones were found to be (**3**) only.

Release of Alanine from Complex (**3**).—The reaction in a 0.1 mol dm^{-3} Na$_2$CO$_3$–D$_2$O solution was followed by ^{1}H n.m.r. spectroscopy at room temperature as shown in Figure 2. The signals of the methyl and the methine protons of the co-ordinated alaninate at δ 1.51 and 3.90 respectively gradually decrease to zero, while a new doublet assigned to CH$_3$ of free alanine appears at δ 1.34. The methine resonance for the latter is superimposed on the lower-field multiplets arising from the ring protons of L. The signals at δ 1.51 and 3.90 have disappeared completely after 3 h. The alanine released was detected by h.p.l.c. as (*S*)ala together with a small amount of the *R* isomer ($<$ 5%). This means that either a slight epimerization of (**3**) or racemization of the ala released occurred during the reaction. In addition, the starting complex (**1**) could also be recovered and reused as described for the asymmetric synthesis of ala.[5]

Ajioka *et al.*[5] suggested that the lability of an alaninato complex relates closely to the strength of the ligand field.[5] The absorption maxima in the visible spectra for the present complexes show higher energy compared with several alaninato complexes consisting of open-chain tetradentate ligands. The release of ala from (**3**), however, was recognized under milder reaction conditions. Although it is said that macrocyclic ligands normally produce stronger ligand fields than comparable non-macrocyclic ones owing to a constraining effect,[18] there are little comparable data for related compounds. At present, therefore, the lability may be accounted for by the delicate balance between the stability of the macrocyclic ligand and the co-ordinated alanine.

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[*] The conformation type is expressed by a series of numbers within brackets, each giving the number of bonds in one side of the 12-membered ring.