Studies on Metal Complexes of Chiral Cyclen. Part 14.[1] Configurational Isomerism in a Complex of Cobalt(III)†

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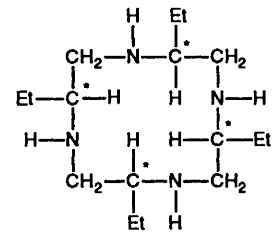
The chiral 12-membered cyclic tetramine (2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethyl-1,4,7,10-tetraazacyclododecane (L) reacts with $CoBr_2$ to give mainly *cis-SSSR*-$[Co^{III}Br(H_2O)L]Br_2$ **1**. Another isomeric complex **2** has recently been isolated from the reaction mixture obtained under mild alkaline conditions. In order to clarify the geometry, the structures of *cis*-(*RSRS*)-[Co{(*S*)-alaO}L]$[ClO_4]_2$ **4** (alaO = alaninate) and *cis*-(*RSRS*)-[Co{(*S*)-thrO}L]$[ClO_4]_2 \cdot 3H_2O$ **6** (thrO = threoninate) derived from **2** have been determined by X-ray analysis. All complexes prepared are *cis*-octahedral, each Co^{III} is surrounded by four N from L and by N and O of the amino acid, and the configurations of the four asymmetric nitrogen atoms are *RSRS*. This means that the cobalt ion in **2** co-ordinates to the crowded face of the N_4 plane of L, and the ligations of the metal to L in **1** and **2** occur from opposite directions. The absorption band maxima of the respective visible spectra of all the *RSRS* complexes shift approximately 400 cm^{-1} to higher energy than those of the corresponding *SSSR* ones. A slow exchange reaction between the fifth and sixth ligands is observed for **1**, and release of the amino acid from a *SSSR*-amino acidato complex takes place in Na_2CO_3 solution. No such reactions occur in **2** and in *RSRS*-amino acidato complexes. These results are probably related to the ligand-field strength.

The chiral 12-membered cyclic tetramine (chiral cyclen) (2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethyl-1,4,7,10-tetraazacyclododecane (L)[2] reacts with $CoBr_2$ to give *cis*-(*SSSR*)-$[Co^{III}Br(H_2O)L]Br_2$ **1**.[3,4] Recently another configurational isomer of the cobalt(III) complex, **2**, has been isolated from the reaction mixture obtained under mild alkaline conditions. It gave only poor crystals. In order to clarify the molecular structure, therefore, we have prepared several good crystalline derivatives of **2** containing amino acid anions.

Our main interest lies in the stereochemistry of such optically active complexes, and on the possibility of using them as asymmetric agents or models for biological systems. The present paper is concerned with the structures, various spectra, and comparison of the stereochemistries of two isomeric complexes.

Owing to its small size, the chiral cyclen L co-ordinates to metals not in a planar manner but in a folded form at *cis* positions.[4] The same situation is also observed in all known octahedral cobalt(III) complexes of 1,4,7,10-tetraazacyclododecane[5–8] (cyclen) or of its 1,7-dimethyl derivative.[9] For such *cis* type cobalt(III) complexes of achiral cyclen, three isomers are possible as shown in Scheme 1(*a*). For steric reasons, both hydrogen atoms or substituents attached to the N(1) and N(7) corners must be directed not inside (*endo*) but outside (*exo*) of the folding macrocycle. The cobalt(III) complexes of achiral cyclen all have the *exo-exo-exo-endo* arrangement [**II** in Scheme 1(*a*)]. Exceptionally, **I** (all-*exo*) is found in the octahedral low-spin nickel(II) complex of the 1,7-dimethyl derivative of cyclen.[10]

The C_4 symmetry molecule L consists of four repeating head-to-tail units, and the configurations of the four chiral carbon centres are all *R*. For an octahedral *cis* cobalt(III) complex of L, 16 possible isomers[3] are to be considered. Steric requirements, however, reduce this number to the six isomers shown in Scheme 1(*b*). Provided that the fifth and sixth ligands are the same, these can be divided into three symmetry groups: C_4 (isomers, **A**, **D**), C_1 (**B**, **E**) and C_2 (**C**, **F**). Isomer *SSSR* (**E**) is only one obtained so far.[3]



L

The *SSSR* complex **1** is sterically stable, but undergoes relatively slow exchange between the fifth (Br) and sixth (H_2O) ligands.[3] The system requires over 2 weeks to attain the equilibrium state in solution. Complex **1** co-ordinates stereoselectively with amino acids to give the corresponding amino acidato complexes[11,12] which dissociate completely into the amino acids and the parent complex **1** in Na_2CO_3 solution. The two components are separately recovered in good yield, although a slightly racemized amino acid is obtained in certain cases. By using **1** as a resolving agent, optical resolution of functionalized amino acids such as α-methylserine, which is capable of three-point binding, is effectively achieved under mild conditions in aqueous solution.[12] Thus, **1** is unique in this regard.

The NMR and CD spectra of complex **2** suggest that the molecule has C_2 symmetry, and has *RSRS* rather than *SRSR* configurations. This has been confirmed by X-ray analysis of two amino acidato complexes derived from **2**: *cis*-(*RSRS*)-[Co{(*S*)-alaO}L]$[ClO_4]_2$ **4** (alaO = alaninate) and *cis*-(*RSRS*)-[Co{(*S*)-thrO}L]$[ClO_4]_2 \cdot 3H_2O$ **6** (thrO = threoninate). The structure of the *SSSR*-(*S*)-thrO complex **5** derived from **1** was also determined for comparison.

Experimental

Preparation of Compounds.—The chiral cyclen L and *SSSR* complexes **1**, **3** [with (*S*)-alaO], and **5** were prepared according

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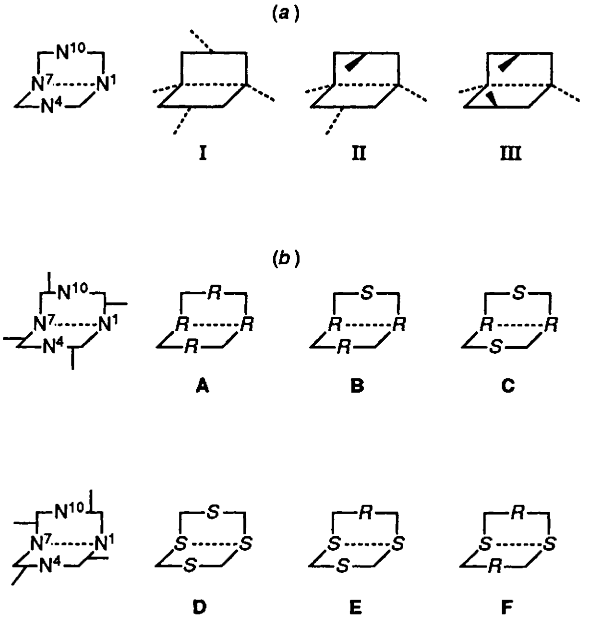
† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1992, Issue 1, pp. xx–xxv.



Scheme 1 (*a*) The possible isomers for an achiral cyclen by *endo-exo* description. (*b*) Possible configurational isomers for a chiral cyclen: *R* or *S* designates the configuration of the chiral nitrogen atom; – – –, bending line of L.

to refs. 2, 3 and 11. Complex **2**, and the corresponding amino acidato complexes derived from it, **4** and **6**, were synthesised by a modification of the above methods.

cis-(*RSRS*)-[CoBr$_2$L]Br **2**. A solution of the HBr salt of L (6.66 g, 12.7 mmol) and CoBr$_2$·6H$_2$O (8.30 g, 25 mmol) in water (100 cm^3) was stirred at pH 7.0–8.5 at room temperature for 1 d in the open air. The dark greenish reaction mixture was acidified with concentrated HBr and the resulting red solution was allowed to stand for several days until red-violet crystals of complex **1** separated (5.67 g, 74.3%). From the dark brown residue the isomeric complex **2** was obtained as a brown-red precipitate in 8.8% (0.67 g) yield, m.p. 205.5 °C (Found: C, 32.80; H, 6.15; Br, 41.55; N, 9.55. Calc. for C$_{16}$H$_{36}$Br$_3$CoN$_4$: C, 32.95; H, 6.20; Br, 41.10; N, 9.60%). NMR (D$_2$O): ^{1}H, δ 0.90–1.03 (12 H, two t, CH$_3$), 1.61–1.80 (4 H, m, $\mathrm{CH_3C}H_2$), 1.85–1.97 (4 H, m, $\mathrm{CH_3C}H'_2$), 2.74 (2 H, dd, CH$_2$), 2.83 (2 H, dd, CH$'_2$), 3.14–3.20 (4 H, m, CH$''_2$ and 2 CH), 3.62 (2 H, dd, CH$'''_2$) and 3.92 (2 H, dt, 2CH$'$); ^{13}C, δ 6.07, 6.50 (CH$_3$), 18.66, 19.58 ($\mathrm{CH_3}C\mathrm{H_2}$), 44.75, 48.03 (CH$_2$) and 60.85, 62.93 (CH). When the reaction mixture was kept neutral during the oxidation process the only product was **1** and no other isomeric complex was found.

cis-(*RSRS*)-[Co{(*S*)-alaO}L][ClO$_4$]$_2$ **4**. The pH of an aqueous solution of complex **2** (120 mg, 0.2 mmol) and (*S*)-ala (18 mg, 0.2 mmol) was adjusted to pH 8.0 with 0.1 mol dm^{-3} NaOH. After 1 h the solvent was evaporated to near dryness. Addition of a slight excess of 1 mol dm^{-3} NaClO$_4$ gave crystals of the diperchlorate **4** in 63% yield (Found: C, 36.05; H, 6.60; N, 10.95. Calc. for C$_{19}$H$_{42}$Cl$_2$CoN$_5$O$_{10}$: C, 36.20; H, 6.60; N, 11.10%). NMR (D$_2$O): ^{1}H, δ 0.90–1.03 (12 H, four t, $\mathrm{C}H_3\mathrm{CH_2}$), 1.53 (3 H, d, CH$_3$ of ala), 1.54–2.06 (8 H, m, $\mathrm{CH_3C}H_2$), 2.66–3.52 (12 H, m, $\mathrm{C}H_2\mathrm{CH}$) and 3.86 (1 H, q, CH of ala); ^{13}C, δ 12.85, 13.14, 13.26, 13.29 ($C\mathrm{H_3CH_2}$), 20.75 (CH$_3$ of ala), 25.67, 25.73, 26.61, 26.80 ($\mathrm{CH_3}C\mathrm{H_2}$), 50.88, 52.18, 55.03, 55.59 (CH$_2$), 55.60, 66.99, 68.01, 68.57 (CH), 69.79 (CH of ala) and 187.99 (C=O).

cis-(*RSRS*)-[Co{(*S*)-thrO}L][ClO$_4$]$_2$·3H$_2$O **6**. Complex **2** (360 mg, 0.6 mmol) and (*S*)-thr (85 mg, 0.7 mmol) were treated by the procedure described above. Prismatic orange-red crystals of the diperchlorate **6** were obtained in 30% (135 mg) yield (Found: C, 34.10; H, 6.85; N, 9.85. Calc. for C$_{20}$H$_{44}$Cl$_2$CoN$_5$O$_{11}$·2H$_2$O: C, 34.50; H, 6.85; N, 10.05%). NMR (D$_2$O): ^{1}H, δ 0.91–1.02 (12 H, four t, $\mathrm{C}H_3\mathrm{CH_2}$), 1.44 (3 H, d, CH$_3$ of thr), 1.51–2.05 (8 H, m, $\mathrm{CH_3C}H_2$), 2.69–3.59 (11 H, m, $\mathrm{C}H_2\mathrm{C}H$), 3.69 (1 H, d, $\mathrm{C}H\mathrm{NH_2}$), 3.94 (1 H, q, CH$'$) and 4.47 (1 H, dq, $\mathrm{C}H\mathrm{OH}$); ^{13}C, δ 12.78, 13.14 ($C\mathrm{H_3CH_2}$), 22.01 (CH$_3$ of thr), 25.57, 25.81, 26.23, 26.35 ($\mathrm{CH_3}C\mathrm{H_2}$), 50.89, 51.34, 54.75, 55.30 (CH$_2$), 64.22, 67.06, 67.83, 68.45 (CH), 69.47 (CHNH$_2$ of thr), 69.55 (CHOH) and 186.86 (C=O).

X-Ray Data Collection and Processing.—The crystal data and the experimental conditions are listed in Table 1. Complex **5**[11] was analysed as its ZnCl$_4$ salt. All have the same space group (orthorhombic, $P2_12_12_1$) and the same number of molecules in the unit cell ($Z = 4$). The densities of these orange-red crystals were obtained by the flotation method in CCl$_4$–benzene. A Rigaku AFC-4 four-circle automated diffractometer with graphite-monochromatized Mo-Kα radiation (λ = 0.710 73) was employed; ω (2θ < 30°) and ω–2θ (2θ > 30°) scan modes, at scan rate 4.0° min^{-1}. Three standard reflections were monitored every 150 for each sample and showed no systematic decrease in intensity.

Structure analysis and refinement. The same procedure was used in each case. Direct method, block-diagonal least-squares refinement with all non-hydrogen atoms anisotropic, isotropic for all H atoms. The H atoms were located in calculated positions. Unit weights were used for all reflections. The absolute configurations of the complexes were assigned from the known absolute configurations of the ligand as an internal reference. The final difference maps showed no peaks higher than 0.9 e Å^{-3} except for complex **5** where a few residual peaks, *ca*. 2.0 e Å^{-3}, remain near the Cl positions of the ZnCl$_4$ group. These are due to the rotational disorder of the group, and further refinement was not possible. Programs used and sources of scattering factor data are given in refs. 11 and 12. Calculations were performed on a FACOM M-780 computer of this Institute. The atomic parameters for the structures are given in Tables 2–4, and molecular structures are shown in Figs. 4–6.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

Other Measurements.—Electronic absorption spectra were obtained on a Hitachi 330 spectrophotometer, CD spectra on a JASCO J-20A spectropolarimeter. These measurements were made on aqueous solutions *ca*. 1 × 10^{-3} mol dm^{-3} at the equilibrium state. Proton spectra were recorded on a JEOL GX-500 (500.0 MHz) spectrometer with sodium 3-trimethylsilylpropionate as an internal reference, ^{13}C NMR spectra on a JEOL GX-400 (100.4 MHz) spectrometer with dioxane as an internal reference. Melting points were measured on a Metller FP52 apparatus.

Results and Discussion

Preparation and Characterization of the Complexes.—Complex **2** was obtained as the by-product of **1** from the reaction mixture of L and CoBr$_2$ under mild alkaline conditions. The main product is always the *SSSR* complex **1**, and the ratio of **1** to **2** is approximately 10:1 (w/w). The brownish red precipitate of **2** was recrystallized from water.

The largest difference between complexes **1** and **2** is their behaviour in solution. The CD and NMR spectra of **1** showed a slow but significant time dependence.[3] The ^{13}C NMR spectrum in D$_2$O or in [^{2}H$_4$]methanol shows 32 lines at equilibrium. This result and other solution properties[3] suggest that an exchange reaction occurs between the fifth and sixth ligands, and there is an equilibrium between the respective two species in water or in methanol [equations (1) and (2)]. On the other hand, no such lability is observed in **2**. Only eight signals were found in its ^{13}C NMR spectrum in D$_2$O. This number is equal

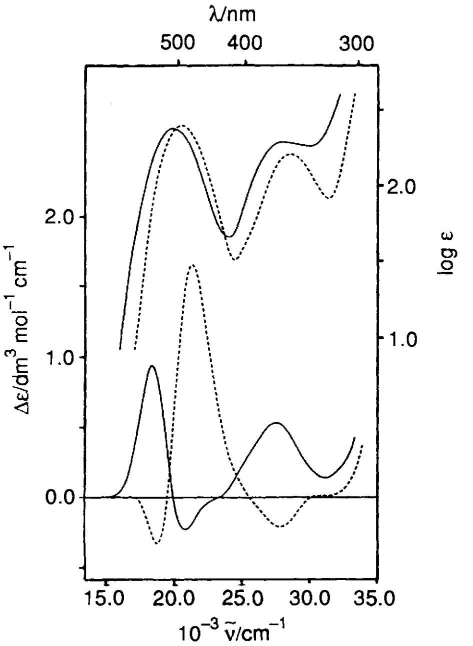


Fig. 1 Visible absorption (upper traces) and CD spectra (lower traces) of complexes **1** (———) and **2** (– – –)

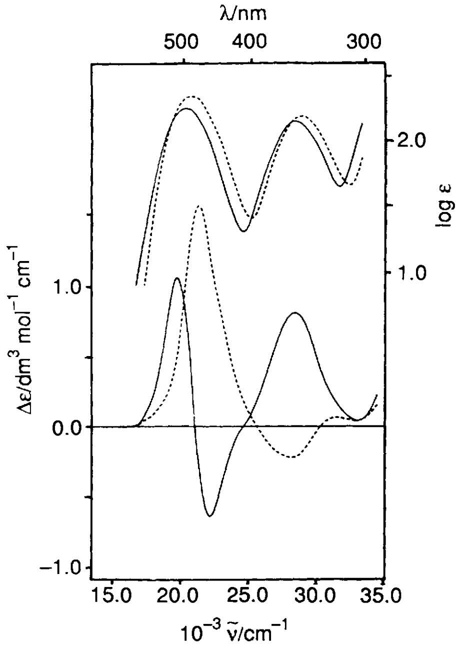
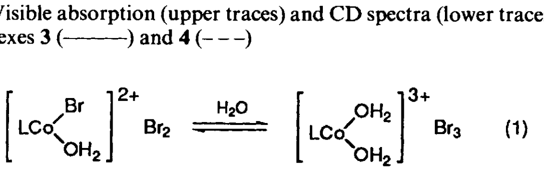
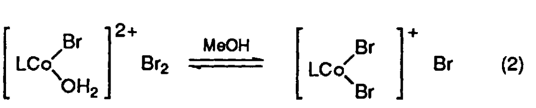


Fig. 2 Visible absorption (upper traces) and CD spectra (lower traces) of complexes **3** (———) and **4** (– – –)



$$\left[\mathrm{LCo}\begin{smallmatrix}\mathrm{Br}\\ \mathrm{OH_2}\end{smallmatrix}\right]^{2+}\mathrm{Br_2} \overset{\mathrm{H_2O}}{\rightleftharpoons} \left[\mathrm{LCo}\begin{smallmatrix}\mathrm{OH_2}\\ \mathrm{OH_2}\end{smallmatrix}\right]^{3+}\mathrm{Br_3} \qquad (1)$$



$$\left[\mathrm{LCo}\begin{smallmatrix}\mathrm{Br}\\ \mathrm{OH_2}\end{smallmatrix}\right]^{2+}\mathrm{Br_2} \overset{\mathrm{MeOH}}{\rightleftharpoons} \left[\mathrm{LCo}\begin{smallmatrix}\mathrm{Br}\\ \mathrm{Br}\end{smallmatrix}\right]^{+}\mathrm{Br} \qquad (2)$$

to half the carbon composition of **2**, and the complex is assumed to be a C_2 molecule (**C** or **F**). Thus **1** is a rather labile cobalt(III) complex, and **2** seems to be a common inert one.

Fig. 1 shows the absorption and CD spectra of complexes **1** and **2**. Two absorption maxima of **2** appear at higher energy than those of **1**, and the signs of the respective CD peaks are opposite to those of **1**. These results suggest that **2** has a

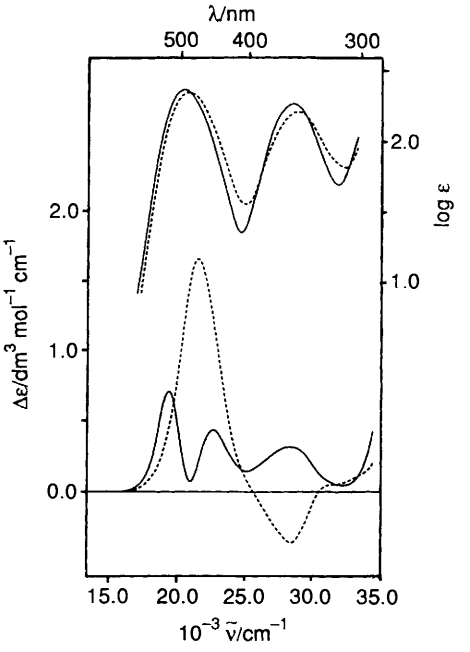


Fig. 3 Visible absorption (upper traces) and CD spectra (lower traces) of complexes **5** (———) and **6** (– – –)

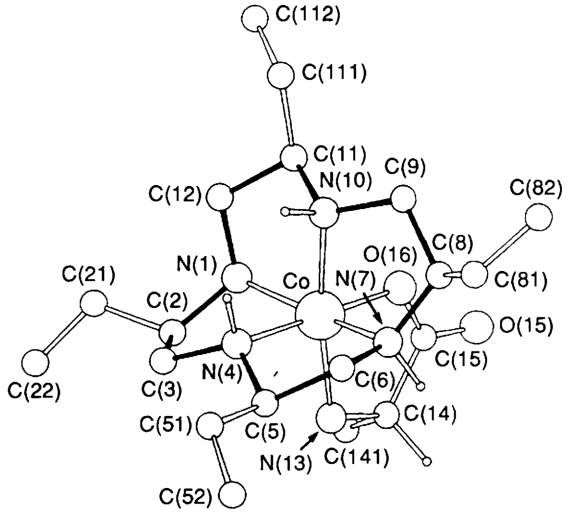


Fig. 4 Molecular structure of complex **4**. Only the hydrogen atoms at the asymmetric nitrogens and the chiral centre in the amino acidate are shown for clarity

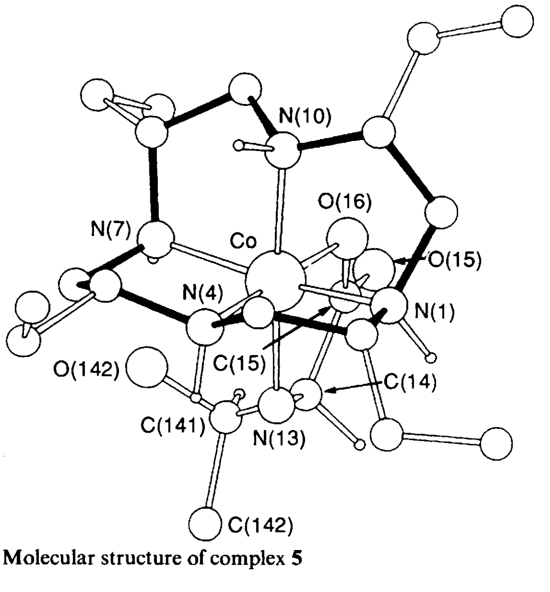


Fig. 5 Molecular structure of complex **5**

Table 1 Crystal data (space group $P2_12_12_1$, $Z = 4$) and experimental conditions

Complex	**4**	**5**	**6**
Formula	$C_{19}H_{42}Cl_2CoN_5O_{10}$	$C_{20}H_{46}Cl_4CoN_5O_4Zn$	$C_{20}H_{50}Cl_2CoN_5O_{14}$
M	630.41	686.73	714.48
a/Å	14.962(3)	19.152(7)	14.998(9)
b/Å	14.729(3)	16.222(5)	14.757(5)
c/Å	13.675(2)	9.684(3)	14.323(4)
U/Å^3	3013(1)	3009(2)	3170(2)
D_m/Mg m^{-3}	1.456	1.520	1.502
D_c/Mg m^{-3}	1.469	1.516	1.497
F(000)	1408	1432	1512
μ(Mo-Kα)/mm^{-1}	0.8	1.8	0.8
Crystal dimensions/mm	0.44 × 0.38 × 0.42	0.35 × 0.42 × 0.35	0.40 × 0.43 × 0.46
No. of observed reflections[a]	2965	2804	3113
No. of unique reflections	2868	2717	3030
No. of unobserved reflections	997	1160	1022
No. of variables	521	493	556
R[b]	0.082	0.103	0.067
R'[c]	0.085	0.119	0.066
Δ/σ on final cycle	0.17	0.44	0.41

[a] Criterion: $|F_o| > 3\sigma(|F_o|)$. [b] $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|$). [c] $R' = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2)]^{\frac{1}{2}}$.

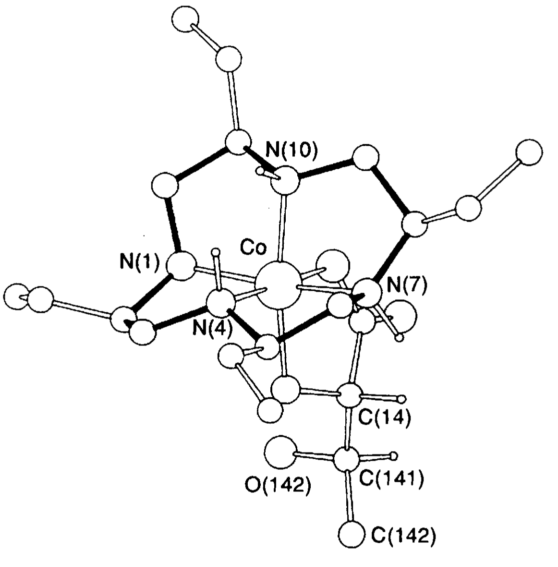


Fig. 6 Molecular structure of complex **6**

stronger ligand field than that of **1** and is the *RSRS* isomer **C** rather than the *SRSR* one **F**.

The visible absorption and CD spectra of the (*S*)-alaninato complexes **3**[11] and **4** and of the (*S*)-threoninato ones, **5**[11] and **6** are shown in Figs. 2 and 3. The structure of **3** has already been determined by X-ray analysis. Each absorption spectrum shows a typical pattern for an N_5O-type cobalt(III) complex. The respective absorption maxima of **4** and **6** are shifted approximately 400 cm^{-1} toward higher energy than those of the corresponding *SSSR* ones, similar to the case of **1** and **2**. The CD curves for **4** and **6** resemble each other, regardless of the different co-ordinated amino acid. In contrast, the spectral patterns for **3** and **5** are markedly different. This may be due to a large additional vicinal effect of the (*S*)-amino acid co-ordinating to the parent *SSSR* complex which has higher dissymmetry.

Geometries of the Complexes.—Figs. 4–6 show the molecular structures **4**–**6** analysed in this work. All are slightly distorted octahedral with six-co-ordinate geometry, where four N of the macrocycle and N and O atoms of the amino acid are co-ordinated to the cobalt ion in a *cis* form. Each amino acid ligand forms a five-membered pseudo ε chelate ring. In **5**, (*S*)-thrO binds in *cis*-β_1 form similar to the other *SSSR*-amino acidato complexes analysed previously.[11–15]

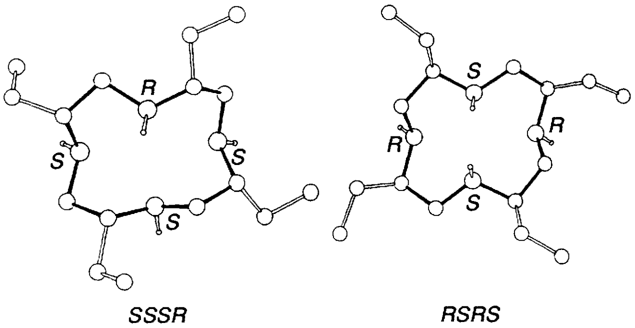


Fig. 7 Structure of the 12-membered rings of complexes **5** and **6**

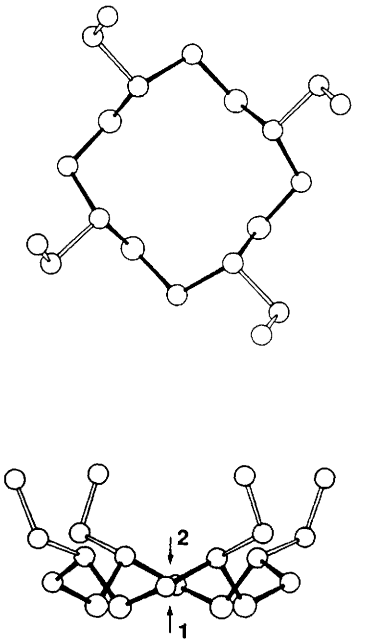


Fig. 8 Molecular structure of (2*R*,5*R*,8*R*,11*R*)-2,5,8,11-tetraethyl-1,4,7,10-tetraazacyclododecane L. The direction of co-ordination of the cobalt in complexes **1** and **2** is arrowed.

The geometries of the respective cyclen rings in complexes **5** and **6** are shown in Fig. 7. On forming the complex the cyclen ligand bends about the line connecting N(1) and N(7). The

Table 2 Atomic coordinates (× 10^4)

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
(*a*) Complex **4**							
Co	459(1)	800(1)	3031(1)	C(112)	−2999(9)	970(10)	3780(12)
N(1)	−64(6)	733(6)	4348(7)	N(13)	1614(6)	192(6)	3360(8)
C(2)	555(8)	1170(8)	5033(9)	C(14)	1553(8)	−795(8)	3220(10)
C(3)	949(8)	2030(8)	4541(10)	C(15)	665(8)	−1032(7)	2761(8)
N(4)	813(6)	1997(5)	3432(7)	O(16)	115(5)	−392(5)	2641(6)
C(5)	1553(7)	2273(7)	2813(9)	C(141)	1634(15)	−1280(11)	4236(18)
C(6)	1209(8)	2081(8)	1756(7)	O(151)	528(6)	−1831(4)	2532(7)
N(7)	868(6)	1121(6)	1726(7)	Cl(1)	−1411(3)	−1192(2)	5578(3)
C(8)	114(7)	928(6)	1017(8)	O(1)	−873(9)	−1070(7)	4752(10)
C(9)	−783(8)	1000(7)	1510(9)	O(2)	−1816(10)	−423(8)	5874(11)
N(10)	−683(6)	1238(5)	2599(7)	O(3)	−2117(9)	−1786(10)	5213(12)
C(11)	−1361(7)	923(6)	3277(8)	O(4)	−982(10)	−1643(10)	6317(10)
C(12)	−964(8)	1137(8)	4272(9)	Cl(2)	−1455(3)	3833(3)	5142(3)
C(21)	165(11)	1412(10)	6044(10)	O(5)	−561(8)	3744(8)	4880(10)
C(22)	835(11)	1660(11)	6775(11)	O(6)	−1771(10)	3059(11)	5460(14)
C(51)	1841(8)	3255(7)	2935(12)	O(7)	−1509(11)	4370(13)	5957(14)
C(52)	2678(11)	3532(10)	2419(14)	O(8)	−1900(14)	4025(22)	4364(20)
C(81)	181(10)	1438(12)	90(13)	O(W1)	2779(8)	493(7)	1669(9)
C(82)	−442(12)	1123(14)	−682(11)	O(W2)	4300(10)	1051(11)	2096(13)
C(111)	−2279(7)	1332(8)	3136(11)				
(*b*) Complex **5**							
Co	2127(2)	2896(2)	159(3)	C(82)	1124(21)	4546(20)	3118(38)
N(1)	3035(10)	2488(13)	−524(21)	C(111)	3586(14)	2625(19)	3283(30)
C(2)	2976(13)	1562(14)	−975(24)	C(112)	4349(16)	2418(25)	3268(32)
C(3)	2293(13)	1200(13)	−422(25)	N(13)	1862(10)	3492(10)	−1590(19)
N(4)	1744(9)	1851(10)	−432(19)	C(14)	1915(12)	4412(12)	−1416(24)
C(5)	1082(13)	1653(12)	409(18)	C(15)	2305(10)	4563(11)	−67(26)
C(6)	690(12)	2510(14)	587(24)	O(151)	2408(10)	5295(9)	316(21)
N(7)	1232(10)	3102(10)	1092(19)	O(16)	2512(9)	3952(9)	690(14)
C(8)	1342(14)	3037(15)	2653(23)	C(141)	1198(12)	4834(13)	−1498(23)
C(9)	2101(16)	3021(16)	3045(22)	C(142)	921(16)	4807(25)	−2981(26)
N(10)	2427(10)	2444(11)	1982(19)	O(142)	750(11)	4411(12)	−605(20)
C(11)	3204(12)	2286(16)	1982(22)	Zn	1039(1)	976(2)	−5045(3)
C(12)	3514(12)	2607(16)	689(25)	Cl(1)	2052(2)	791(2)	−6368(5)
C(21)	3055(13)	1499(18)	−2517(27)	Cl(2)	43(2)	1226(3)	−6431(5)
C(22)	3838(21)	1652(18)	−2924(35)	Cl(3)	1209(3)	2140(3)	−3695(5)
C(51)	537(17)	1040(19)	−254(24)	Cl(4)	882(3)	−201(3)	−3713(6)
C(52)	821(15)	131(14)	121(36)	O(W1)	3310(12)	3602(12)	−3057(22)
C(81)	851(23)	3675(19)	3408(26)				
(*c*) Complex **6**							
Co	475(1)	4149(1)	1953(1)	N(13)	1611(5)	4800(4)	1663(5)
N(1)	−11(4)	4209(5)	685(5)	C(14)	1628(5)	5652(5)	2193(6)
C(2)	617(6)	3736(6)	38(7)	C(15)	666(5)	5957(5)	2370(6)
C(3)	1019(7)	2914(7)	539(7)	O(151)	508(5)	6733(4)	2601(5)
N(4)	814(4)	2955(4)	1570(5)	O(16)	82(4)	5336(4)	2287(4)
C(5)	1565(6)	2661(5)	2223(7)	C(141)	2229(7)	6379(7)	1804(9)
C(6)	1186(6)	2859(5)	3177(7)	C(142)	3205(8)	6139(8)	1837(11)
N(7)	865(4)	3826(4)	3204(5)	O(142)	1941(7)	6543(8)	900(8)
C(8)	95(6)	4031(6)	3859(6)	Cl(1)	1597(2)	1227(2)	5481(2)
C(9)	−807(5)	3906(6)	3365(6)	O(1)	1092(7)	1565(7)	6185(8)
N(10)	−668(4)	3698(4)	2357(5)	O(2)	1053(7)	999(6)	4705(6)
C(11)	−1337(5)	4046(5)	1667(6)	O(3)	2216(6)	1884(6)	5187(7)
C(12)	−929(6)	3822(6)	733(6)	O(4)	2037(6)	452(6)	5807(7)
C(21)	247(7)	3465(8)	−921(7)	Cl(2)	3487(2)	3840(2)	46(2)
C(22)	−38(9)	4237(12)	−1491(9)	O(5)	4389(7)	3753(9)	−69(10)
C(51)	1830(6)	1668(6)	2062(9)	O(6)	3208(8)	4689(7)	−264(8)
C(52)	2668(8)	1431(9)	2579(11)	O(7)	3006(9)	3202(8)	−499(9)
C(81)	154(8)	3514(8)	4766(8)	O(8)	3280(7)	3791(8)	938(8)
C(82)	−482(9)	3891(10)	5508(8)	O(W1)	2901(6)	4171(7)	3309(8)
C(111)	−2269(5)	3652(6)	1804(7)	O(W2)	4135(8)	4062(8)	4775(11)
C(112)	−2955(7)	4053(9)	1164(9)	O(W3)	4441(11)	3314(11)	2572(13)

chiralities of the N atoms in **5** are assigned as 1*S*, 4*S*, 7*S* and 10*R*, as is observed in **3** and **1**. On the other hand, the configurations in **6** are *RSRS* as anticipated for the structure of **2**, **4** also has a *RSRS* ring. These *SSSR* and *RSRS* configurations of the asymmetric nitrogen atoms mean that the co-ordination of the metal to L in **1** and **2** occurs from opposite directions as shown in Fig. 8. Since the four ethyl groups are vertical to the N_4 plane of the cyclen, it had been thought that these three (**A**–**C**) arrangements were not preferred geometries.

Bond parameters of all new compounds are listed in Tables 5 and 6. There are no particularly abnormal values compared with complex **1** and other related complexes. The hydroxyl group of (*S*)-thrO in the *SSSR* complex **5** forms an internal hydrogen bond between N(7) and O(142) in the ligand. This is a

Table 3 Bond lengths (Å) and angles (°) around the cobalt ion in complexes **4**–**6**

	4	**5**	**6**
Co–N(1)	1.965(9)	1.975(20)	1.958(7)
Co–N(4)	1.921(8)	1.935(17)	1.926(7)
Co–N(7)	1.946(9)	1.968(19)	1.944(7)
Co–N(10)	1.920(8)	1.996(18)	1.928(6)
Co–N(13)	1.998(10)	2.015(19)	1.999(7)
Co–O(16)	1.905(7)	1.935(15)	1.909(5)
N(1)–Co–N(4)	84.0(4)	86.6(8)	83.3(3)
N(1)–Co–N(7)	167.9(4)	168.1(8)	167.8(3)
N(1)–Co–N(10)	86.8(4)	85.4(8)	87.9(3)
N(1)–Co–N(13)	96.7(4)	95.8(8)	95.9(3)
N(1)–Co–O(16)	95.9(4)	92.9(8)	94.4(3)
N(4)–Co–N(7)	87.2(4)	87.3(7)	87.2(3)
N(4)–Co–N(10)	91.4(4)	92.8(8)	91.3(3)
N(4)–Co–N(13)	96.2(4)	94.4(7)	97.9(3)
N(4)–Co–O(16)	179.5(4)	178.2(7)	177.6(3)
N(7)–Co–N(10)	85.1(4)	84.7(8)	84.6(3)
N(7)–Co–N(13)	92.5(4)	94.9(8)	93.0(3)
N(7)–Co–O(16)	93.0(4)	93.4(7)	95.0(3)
N(10)–Co–N(13)	171.9(4)	172.8(7)	170.4(3)
N(10)–Co–O(16)	89.0(3)	88.9(7)	88.1(3)
N(13)–Co–O(16)	83.3(4)	84.0(7)	82.8(3)

Table 4 Selected bond parameters (lengths in Å, angles in °) of the 12-membered rings in complexes **4**–**6**

	4	**5**	**6**
N(1)–C(2)	1.47(2)	1.57(3)	1.50(1)
N(1)–C(12)	1.48(1)	1.50(3)	1.49(1)
C(2)–C(3)	1.55(2)	1.53(3)	1.53(1)
C(3)–N(4)	1.53(2)	1.49(3)	1.50(1)
N(4)–C(5)	1.45(1)	1.54(3)	1.50(1)
C(5)–C(6)	1.56(2)	1.59(3)	1.51(1)
C(6)–N(7)	1.50(1)	1.50(3)	1.51(1)
N(7)–C(8)	1.52(1)	1.53(3)	1.52(1)
C(8)–C(9)	1.51(2)	1.50(3)	1.54(1)
C(9)–N(10)	1.54(1)	1.53(3)	1.49(1)
N(10)–C(11)	1.45(1)	1.51(3)	1.50(1)
C(11)–C(12)	1.52(2)	1.48(3)	1.51(1)
C(2)–N(1)–C(12)	116.3(9)	112.6(18)	115.5(7)
N(1)–C(2)–C(3)	108.8(10)	109.4(18)	109.1(8)
C(2)–C(3)–N(4)	110.7(9)	109.2(17)	111.0(8)
C(3)–N(4)–C(5)	117.9(9)	115.4(16)	118.2(7)
N(4)–C(5)–C(6)	103.8(9)	105.3(16)	103.6(7)
C(5)–C(6)–N(7)	107.9(9)	105.6(18)	109.1(7)
C(6)–N(7)–C(8)	116.6(8)	112.0(17)	116.6(7)
N(7)–C(8)–C(9)	111.3(9)	112.6(19)	111.1(7)
C(8)–C(9)–N(10)	111.3(9)	103.7(18)	110.4(7)
C(9)–N(10)–C(11)	118.5(8)	120.5(18)	118.4(6)
N(10)–C(11)–C(12)	103.5(8)	109.6(18)	103.8(6)
N(1)–C(12)–C(11)	109.6(9)	111.9(19)	109.4(7)
Torsion angles			
C(12)–N(1)–C(2)–C(3)	−79.4(12)	101.2(22)	−83.1(9)
C(2)–N(1)–C(12)–C(11)	154.5(9)	−71.4(24)	154.1(7)
N(1)–C(2)–C(3)–N(4)	−17.5(13)	34.5(24)	−13.4(10)
C(2)–C(3)–N(4)–C(5)	−137.2(10)	−165.9(17)	−140.8(8)
C(3)–N(4)–C(5)–C(6)	175.7(9)	164.4(17)	175.8(7)
N(4)–C(5)–C(6)–N(7)	−51.2(11)	−49.5(20)	−51.8(8)
C(5)–C(6)–N(7)–C(8)	149.8(9)	−82.3(20)	151.0(7)
C(6)–N(7)–C(8)–C(9)	−94.2(11)	134.4(20)	−89.6(8)
N(7)–C(8)–C(9)–N(10)	−0.7(12)	−42.7(24)	−5.1(9)
C(8)–C(9)–N(10)–C(11)	−150.6(9)	177.6(19)	−146.2(7)
C(9)–N(10)–C(11)–C(12)	170.6(9)	−115.5(22)	172.8(7)
N(10)–C(11)–C(12)–N(1)	−53.8(10)	−36.3(25)	−54.3(8)

Table 5 Selected bond parameters (lengths in Å, angles in °) of the amino acidato five-membered ring of complexes **4**–**6**

	4	**5**	**6**
N(13)–C(14)	1.47(1)	1.51(3)	1.47(1)
C(14)–C(15)	1.51(2)	1.52(3)	1.53(1)
C(14)–C(141)	1.57(3)	1.54(3)	1.51(1)
C(15)–O(151)	1.24(1)	1.26(2)	1.215(9)
C(15)–O(16)	1.26(1)	1.29(3)	1.274(9)
C(141)–O(142)		1.53(3)	1.51(2)
C(141)–O(142)		1.40(3)	1.39(2)
Co–N(13)–C(14)	111.1(7)	111.4(14)	108.6(5)
N(13)–C(14)–C(15)	109.7(9)	106.7(17)	108.7(6)
N(13)–C(14)–C(141)	109.3(11)	112.1(18)	115.6(8)
C(15)–C(14)–C(141)	109.3(12)	114.3(18)	114.6(7)
C(14)–C(15)–O(151)	118.1(10)	118.7(19)	120.6(7)
C(14)–C(15)–O(16)	117.1(9)	120.9(17)	114.9(6)
O(151)–C(15)–O(16)	124.8(11)	120.4(22)	124.7(8)
Co–O(16)–C(15)	118.8(7)	114.2(13)	118.1(5)
C(14)–C(141)–C(142)		110.2(20)	113.7(9)
C(14)–C(141)–O(142)		107.3(18)	106.5(9)
C(142)–C(141)–O(142)		110.6(21)	111.9(11)
Torsion angles			
O(16)–Co–N(13)–C(14)	−5.0(7)	−14.9(13)	22.4(5)
N(13)–Co–O(16)–C(15)	2.5(8)	14.7(14)	−12.8(6)
Co–N(13)–C(14)–C(15)	6.3(11)	12.3(20)	−27.3(7)
N(13)–C(14)–C(14)–O(16)	−4.8(14)	−0.9(26)	19.2(9)
C(13)–C(15)–O(16)–Co	0.7(13)	−11.6(24)	−0.4(9)

Table 6 Hydrogen-bond distances (Å)*

Atom 1 Atom 2	**4**	**5**	**6**
N(7) ··· O(142)		2.84(3)$^{\mathrm{I}}$	
N(1) ··· O(1)	2.97(1)$^{\mathrm{II}}$		
N(4) ··· O(151)	2.96(1)$^{\mathrm{III}}$		2.959(9)$^{\mathrm{X}}$
N(7) ··· O(W1)	3.00(1)$^{\mathrm{I}}$		3.10(1)$^{\mathrm{I}}$
N(10) ··· O(151)	2.90(1)$^{\mathrm{IV}}$		2.911(8)$^{\mathrm{XI}}$
N(13) ··· O(W1)	2.93(2)$^{\mathrm{I}}$	3.12(3)$^{\mathrm{VII}}$	3.19(1)$^{\mathrm{I}}$
N(13) ··· O(7)	3.03(2)$^{\mathrm{V}}$		
O(4) ··· O(W2)	2.87(2)$^{\mathrm{VI}}$		
O(7) ··· O(W2)	3.00(3)$^{\mathrm{V}}$		
O(8) ··· O(W1)	2.89(3)$^{\mathrm{IV}}$		
O(W1) ··· O(W2)	2.47(2)$^{\mathrm{I}}$		
N(1) ··· O(W1)		3.09(3)$^{\mathrm{VII}}$	
N(10) ··· Cl(1)		3.20(2)$^{\mathrm{VII}}$	
N(13) ··· Cl(3)		3.24(2)$^{\mathrm{VII}}$	
O(151) ··· O(W1)		2.75(3)$^{\mathrm{VIII}}$	
O(142) ··· Cl(4)		3.26(2)$^{\mathrm{III}}$	
O(142) ··· O(3)			2.83(1)$^{\mathrm{XII}}$
N(1) ··· O(W2)			3.15(2)$^{\mathrm{IX}}$
N(1) ··· O(2)			3.12(1)$^{\mathrm{IV}}$
N(13) ··· O(8)			3.09(1)$^{\mathrm{I}}$
O(142) ··· O(W2)			2.45(2)$^{\mathrm{XII}}$
O(1) ··· O(W3)			3.06(2)$^{\mathrm{XIII}}$
O(2) ··· O(W2)			2.97(2)$^{\mathrm{XIII}}$
O(6) ··· O(W1)			3.13(2)$^{\mathrm{VIII}}$
O(8) ··· O(W3)			3.00(2)$^{\mathrm{I}}$
O(W1) ··· O(W2)			2.80(2)$^{\mathrm{I}}$
O(W1) ··· O(W3)			2.84(2)$^{\mathrm{I}}$

* Roman numeral superscripts denote symmetry of atom 2: I x, y, z; II $1 + x, y, z$; III $-x, \frac{1}{2} + y, \frac{1}{2} - z$; IV $1 - x, \frac{1}{2} + y, \frac{1}{2} - z$; V $\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$; VI $\frac{3}{2} - x, 1 - y, \frac{1}{2} + z$; VII $x, y, 1 + z$; VIII $\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$; IX $\frac{3}{2} - x, 1 - y, z - \frac{1}{2}$; X $-x, y - \frac{1}{2}, \frac{1}{2} - z$; XI $1 - x, y - \frac{1}{2}, \frac{1}{2} - z$; XII $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$; XIII $x - \frac{1}{2}, \frac{1}{2} - y, 1 - z$.

three-point attachment as stated previously.[12] Such hydrogen bonds are usually found in *SSSR*-functionalized (*R*)-amino acid complexes. The new *SSSR*-(*R*)-thrO complex also reveals such internal hydrogen bonding.[16] The presence of a similar interaction in a pair of diastereomeric crystals produced is undesirable because it results in a smaller solubility difference between them.[16]

The *RSRS*-(*S*)-thrO complex **6** does not have such an internal hydrogen bond, but N(1), N(7) and the hydroxyl group of the amino acid interact with water molecules and an oxygen atom of one cocrystallized perchlorate anion.

Exchange Reaction.—The release of amino acid from the *SSSR* complex was easily achieved in Na_2CO_3 solution.[11,12] The reaction of **4** was also followed by the measurement of ^1H NMR spectra at regular time intervals in Na_2CO_3–D_2O solution. A new methyl doublet in the spectrum appeared after 30 min near δ 1.0 and the height of the original methyl and methine signals of the amino acid was gradually reduced. The new signal was identified as not that of the free amino acid but that a doublet of a methyl group originating perhaps from a partially dissociated amino acid. No other methyl doublet was found.

It seems likely that the different behaviour between the two diastereomeric complexes in solution arises from their different geometries. The *SSSR* complexes have an appropriate ligand field so that the amino acid and the parent complex can be separately recovered in good yield. In conclusion, complex **1** is a good resolving agent for an amino acid or perhaps a chiral bidentate compound, but **2** is a poor one for such systems. This information would be helpful in designing a molecule with a high efficiency as an asymmetric agent.

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