Chiral metal complexes
31*. Enhanced enantioselectivity in a Co(III)-mediated synthesis of alanine, including the crystal structure of the intermediate Λ-β_1-[(3*R*,4*R*-diphenyl-1,6-di(2-pyridyl)-2,5-diazahexane)(2-amino-2-methylpropandioicacidato)cobalt(III)] perchlorate dihydrate

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Abstract

Reaction of the 2-amino-2-methylpropandioicacidato anion ($AMMA^{2-}$) with the Λ-β-[Co(*R*,*R*-picstien)Cl_2]$^+$ complex cation (*R*,*R*-picstien is 3*R*,4*R*-diphenyl-1,6-di(2-pyridyl)-2,5-diazahexane) results in displacement of the chloride ions with retention of absolute configuration of the metal atom and the bidentate $AMMA^{2-}$ stereospecifically adopting the β_1 and stereoselectively the *pro-S* configurations. Decarboxylation of this complex in warm acidic solution produces a mixture comprising 93 ± 3% Λ-β_1-[Co(*R*,*R*-picstien)(*R*-ala)]$^{2+}$ and 7 ± 3% Λ-β_1-[Co(*R*,*R*-picstien)(*S*-ala)]$^{2+}$, as shown by NMR experiments. The chiral environment imposed on the prochiral $AMMA^{2-}$ fragment by the coordinated *R*,*R*-picstien ligand thus results in a stereoselective asymmetric synthesis of *R*-alanine in high enantiomeric excess. The crystal structure of the intermediate Λ-β_1-[Co(*R*,*R*-picstien)(AMMA)]$ClO_4 \cdot 2H_2O$ complex has been determined at −135 °C. Crystal data: $C_{30}H_{35}N_5O_{10}Cl_1Co_1$ is orthorhombic, space group $P2_12_12_1$, with $a = 9.598(2)$, $b = 11.964(2)$, $c = 26.477(3)$ Å and $Z = 4$. The structure was refined by block-matrix least-squares methods to $R = 0.039$ for 2622 diffractometer data. In the complex cation the bidentate $AMMA^{2-}$ fragment coordinates such that an internal hydrogen bond exists between the uncoordinated carboxyl group and one of the amine hydrogens of the central link, (NH···O 2.770(5) Å). This forces the coordinated amino acid intermediate to adopt the *R* (*pro-S*) configuration.

Introduction

We have reported recently on a number of metal-mediated stereoselective syntheses of α-aminoacidates [1–3]. In this system, involving the decarboxylation of a coordinated aminomalonate precursor under warm acidic conditions using a chiral template to induce asymmetry, chiral α-aminoacidates have been produced in high enantiomeric excess. The predominant hand of the aminoacidate product is determined by the topology of the metal complex and varies from species to species, although the Λ-β complexes studied stereoselectively produce the *R* (i.e. *pro-S*) diastereoisomers as the reaction intermediates.

The tetradentate ligand picstien† stereospecifically adopts the rigid unsymmetrical β topology on coordination to cobalt(III) and retains this topology during substitution of the two remaining *cis* positions of the coordination sphere with a variety of ligands [4]. This system therefore provides an ideal chiral steric environment for the asymmetric synthesis of α-amino acids. The previously reported synthesis of the *cis*-β-dichlorocobalt(III) complex involved the isolation of several intermediates with the inherent reduction of overall yield. Here we report an improved facile method which is essentially a one-pot synthesis starting with the optically pure stilbenediamine-tar-

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†Picstien is 3,4-diphenyl-1,6-di(2-pyridyl)-2,5-diazahexane, picchxn is *N*,*N'*-di(2-picolyl)diaminocyclohexane, $AMMAH_2$ is 2-amino-2-2-methylpropandioic acid (α-amino-α-methylmalonic acid), ala is the α-alaninate anion, stien is 1,2-diphenyl-1,2-diaminoethane.

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trate salt and producing the cobalt(III) *cis*-β-dichloro complex in high overall yield (>50%). It is demonstrated that this cobalt(III) tetradentate system may be used to synthesise alanine in significant enantiomeric excess.

Experimental

Microanalyses were carried out by AMDEL Laboratories, Melbourne. NMR spectra were recorded on a Varian XL-200 spectrometer and are reported in ppm relative to DSS, TMS or known solvent resonances used as internal calibrants. Circular dichroism (CD) spectra were recorded on a JASCO SP-500C spectropolarimeter at ambient temperatures. Optical rotations were measured at 589 nm on an Optical Activity AA-10 automatic polarimeter. Electronic spectra were recorded using a Shimadzu UV-160 recording spectrophotometer.

Λ-β-[Co(R,R-picstien)Cl$_2$]ClO$_4$·H$_2$O

A sample of [*R*,*R*-stienH$_2$][*S*,*S*(−)tart] salt [4] ($[\alpha]_D = +11.0°$, $c = 1$, H_2O), (5.0 g, 13.8 mmol) was suspended in cold water (50 cm^3) and 2 M NaOH (150 cm^3) was added slowly. The diamine was extracted with dichloromethane (2×50 cm^3 portions) and the organic extract dried with anhydrous Na_2SO_4; removal of the solvent on a rotary evaporator left the free diamine as a white solid. Benzene (150 cm^3) was added and the mixture vigorously stirred while pyridine-2-carboxaldehyde (Aldrich) (2.96 g, 27.6 mmol) was added slowly. Stirring was continued for *c.* 0.5 h, then the solvent was removed under reduced pressure at 50 °C to leave a pale yellow solid. Glacial acetic acid (60 cm^3) was added to the solution at 20 °C followed by slow addition of a solution of dimethylaminoborane (Fluka) (3.5 g) in glacial acetic acid (15 cm^3) with stirring being continued for a further hour. Removal of the acetic acid on a rotary evaporator left a yellow oil to which was added water (50 cm^3) to decompose any remaining borane complex. After the water was removed at reduced pressure the residue was dissolved in absolute ethanol (150 cm^3), 10 M HCl (10 cm^3) was added and again the solvent removed on the rotary evaporator. The resulting orange oil was dissolved in absolute ethanol (300 cm^3) and 10 M HCl (1 cm^3) was added followed by the slow addition of a solution $CoCl_2 \cdot 6H_2O$ (3.28 g, 13.8 mmol) in absolute ethanol (50 cm^3), the addition being at such a rate as to allow any cloudiness to disperse before further addition. When the addition was complete, 30% (wt./vol.) hydrogen peroxide (3 cm^3) was added, the solution was stirred for *c.* 0.5 h, saturated $NaClO_4$ solution (5 cm^3) was added and the mixture cooled in an ice bath.

The resulting fine, purple, sparingly-soluble crystals were collected at the pump, washed with cold water (2×20 cm^3), ethanol (2×20 cm^3), acetone (2×20 cm^3) and air dried. The authenticity of the product was verified by its chiroptical properties and NMR spectrum [4]. Yield: 4.96 g (56% based on the diamine-tartrate salt).

Λ-β$_1$-[Co(R,R-picstien)(AMMAH)](ClO$_4$)$_2$·0.5H$_2$O

To a suspension of Λ-β-[Co(*R*,*R*-picstien)Cl_2]-$ClO_4 \cdot H_2O$ (0.20 g, 0.312 mmol) in water (20 cm^3) was added dipotassium-aminomethylmalonate (AMMAK$_2$) [5] (0.32 g, 1.53 mmol). The mixture was stirred at room temperature for 24 h, filtered and saturated $NaClO_4$ solution (2 cm^3) was added. The resulting fine, orange crystals were collected at the pump, washed with a minimum amount of ice-cold water and air dried. Yield: 0.034 g (13.7%). *Anal.* Calc. for $C_{30}H_{33}N_5O_{12.5}Cl_2Co$: C, 45.4; H, 4.2; N, 8.8. Found: C, 45.3; H, 4.2; N, 8.8%.

Λ-β$_1$-[Co(R,R-picstien)(AMMA)]ClO$_4$·2H$_2$O

The mother liquor and washings from the above synthesis were diluted to *c.* 500 cm^3 and applied to a column of CM Sephadex®-C25 (2.5 cm×40 cm) in the Na^+ form. The complex species was washed with water and then eluted with 0.1 M sodium chloride solution. A fast moving, optically inactive, pale purple minor band eluted first. The remaining adsorbed dark orange compound eluted as one band, with the leading and tailing edges having identical chiroptical properties. To the orange eluate was added saturated sodium perchlorate solution (1 cm^3). This was then left to evaporate *in vacuo* over silica gel for *c.* 6 weeks. The resulting dark orange crystals were collected at the pump, washed with a few drops of ice-cold water, and air dried. The composition was confirmed by the single crystal X-ray analysis reported below.

Λ-β$_1$-[Co(R,R-picstien)(R-ala)](ClO$_4$)$_2$·H$_2$O

A suspension of Λ-β-[Co(*R*,*R*-picstien)Cl_2]-$ClO_4 \cdot H_2O$ (0.322 g, 0.5 mmol) and *R*-alanine (0.18 g, 2.0 mmol) in water (50 cm^3) containing a few drops of methanol was heated gently until a clear orange solution resulted. Solid hydrated $LiClO_4$ (0.2 g) was then added and the solution filtered. The solution was evaporated slowly on a steam bath to *c.* 20 cm^3, 5 M HCl (1 cm^3) was added, and the solution further reduced, whereupon small rosettes of orange crystals appeared. The mixture was cooled slowly to room temperature and then to 0 °C. The resulting fine orange crystals were collected at the pump, washed with a few drops of ice-cold water and air dried. Yield: 0.27 g (71%). *Anal.* Calc. for

$C_{29}H_{34}N_5O_{11}Cl_2Co$: C, 45.9; H, 4.5; N, 9.2. Found: C, 45.7; H, 4.5; N, 9.0%.

Λ-β₂-[Co(R,R-picstien)(S-ala)](ClO₄)₂·3.5H₂O

A suspension of Λ-β-[Co(*R*,*R*-picstien)Cl_2]$ClO_4\cdot H_2O$ (0.25 g, 0.39 mmol) and *S*-alanine (0.10 g, 1.1 mmol) in water (45 cm^3) was heated on a steam-bath to produce a clear orange solution. This was diluted to 250 cm^3 and applied to a column of CM Sephadex®-C25 cation exchange resin in the Na^+ cycle (2.5×40 cm). The adsorbed material was washed with water followed by 0.1 M NaCl, which eluted a minor fast-moving purple band and separated the adsorbed material into two well-defined orange bands. A small amount of an immobile purple species remained. The two orange bands were eluted using 0.25 M NaCl solution and collected separately.

The faster moving band, which proved to contain the β_2 isomer, was reduced over silica gel to a volume of *c.* 5 cm^3. This resulted in the formation of fine, dark orange crystals, which were collected at the pump, washed with a few drops of ice-cold water and air dried. Yield: 0.04 g. *Anal.* Calc. for $C_{29}H_{39}N_5O_{13.5}Cl_2Co$: C, 43.4. H, 4.9; N, 8.7. Found: C, 43.1; H, 4.8; N, 8.7%.

Λ-β₁-[Co(R,R-picstien)(S-ala)](ClO₄)₂·2.5H₂O

The second orange band from the above preparation was collected (*c.* 200 cm^3) and its volume reduced to about 100 cm^3 at 0.5 atm. and ambient temperature, then reduced over silica gel as above. The fine, orange plates which formed were collected at the pump, washed with a few drops of ice-cold water and air dried. Yield: 0.07 g. *Anal.* Calc. for $C_{29}H_{37}N_5O_{12.5}Cl_2Co$: C, 44.3; H, 4.8; N, 8.9. Found: C, 44.2; H, 5.0; N, 9.2%.

Determination of the isomeric ratio of coordinated alanine

The reaction of Λ-β-[Co(*R*,*R*-picstien)Cl_2]ClO_4 with alanine was repeated again without separation of the isomeric products.

Initially the same reactants as above were used, with the eluted orange bands being combined and acidified to pH 1 with concentrated HCl. A 10 cm^3 aliquot was removed and taken to dryness at reduced pressure (50 °C). Under these conditions there was no evidence of unwanted decomposition of the products. The entire orange residue was dissolved in DMSO-d_6, and its NMR spectrum recorded. The β_1:β_2 ratio was determined by careful integration of the methyl doublet resonances.

In a second experiment substitution of *rac*-alanine for *S*-alanine provided the selected isomeric ratio of coordinated (β_1)-*R*-alanine:(β_1)-*S*-alanine:(β_2)-*S*-alanine.

Decarboxylation experiments

Method 1

A sample of Λ-β-[Co(*R*,*R*-picstien)(AMMAH)](ClO_4)$_2\cdot 0.5H_2O$ was dissolved in 1 M DCl in an NMR tube, the solution heated at 70 °C for 2 h, and the spectrum recorded. The ratio of *R*:*S*-alanine produced was determined by careful integration of the respective methyl CH_3 singlets. This ratio was re-confirmed by the same method after longer reaction times.

Method 2

Λ-β-[Co(*R*,*R*-picstien)(AMMAH)](ClO_4)$_2\cdot 0.5H_2O$ (150 mg) was dissolved in 1 M HCl (45 cm^3) and three samples (50 mg in 15 cm^3) were decarboxylated by heating for 1, 2 and 3 h, respectively. At these times each sample was evaporated to dryness at 70 °C under reduced pressure. Under these conditions decarboxylation was found to be complete, and there was no evidence of decomposition of any of the alaninate products. In each case the entire sample was dissolved in DMSO-d_6 and its NMR spectrum recorded. Again the *R*:*S*-alanine ratio was determined by the careful integration of the methyl doublet resonances.

Crystal and molecular structure of Λ-β₁-[Co(R,R-picstien)(R-AMMA)]ClO₄·2H₂O

Crystal data

$C_{30}H_{35}N_5O_{10}ClCo$, $M_r = 720.0$, orthorhombic, $a = 9.598(2)$, $b = 11.964(2)$, $c = 26.477(3)$ Å, $U = 3040.4$ Å^3, $Z = 4$, $D_c = 1.573$ Mg m^{-3}, $F(000) = 1496$, μ(Mo Kα) = 7.47 cm^{-1}, space group $P2_12_12_1$ (No. 19).

Unit cell parameters were initially determined from precession photographs using Mo Kα radiation. Accurate cell parameters were obtained from a least-squares fit to diffractometer data. The crystal used for data collection had dimensions 0.32×0.24×0.26 mm with pinacoids {100}, {011}, {0$\bar{1}$1}. Intensities were collected at −135 °C on a Nicolet XRD-P3 four-circle diffractometer [6] in the range $4 < 2\theta < 52°$ using Mo Kα radiation. Reflections were corrected for Lorentz, polarisation and absorption effects [6]. With respect to the latter, the maximum and minimum transmission factors were 0.951 and 0.915, respectively. Of the 3512 reflections measured 2622 gave counts for which $I > 3\sigma(I)$, and these were used for the structure determination.

Structure determination

The structure was solved by the heavy atom method and was refined by least-squares calculations in which the function minimised was $\Sigma w\Delta^2$, the weights applied being based on counting statistics. Difference maps were used to locate the positions of the hydrogen atoms, whose positional parameters only were refined. Due to the large number of variable parameters, block matrices were used during anisotropic refinement, which was terminated when the change in the minimisation function was $<0.1\%$. Final values for R and R' $[=(\Sigma w\Delta^2/\Sigma w|F_o|^2)^{1/2}]$ were 0.039 and 0.026, respectively. A final difference map showed no density $>|0.4|$ e Å^{-3}. All calculations were carried out on a FACOM 340S computer using programs written by F.S.S. Neutral atom scattering factors, with corrections being applied for anomalous dispersion, were taken from ref. 7.

The final atomic positional parameters are given in Tables 1 and 2, respectively.

Results and discussion

Synthesis of complexes

When the *cis*-β-dichloro complex is reacted with a molar excess of the dipotassium salt of $AMMAH_2$, any attempt to adjust the low pH of the reaction mixture to neutrality results in a mixture of products, the main one being an as yet unidentified yellow–green species. However, under the original reaction conditions the replacement of the two chloride ions by $AMMA^{2-}$ is essentially complete after 24 h and any sparingly soluble unreacted starting complex can be removed by filtration. Addition of aqueous $NaClO_4$ precipitates the protonated species, which is shown to be the Λ-β_1 complex with the $AMMAH^-$ coordinated predominately R (*pro-S*) with a small amount of S (*pro-R*) diastereomer, as confirmed by NMR measurements. Treatment of the mother liquor and washings on CM Sephadex®-C25 cation exchange resin in the Na^+ cycle effects the deprotonation of the complex, thus producing the corresponding monovalent species on which the crystal structure analysis was carried out. This compound is isolated as the isomerically pure R (*pro-S*) species.

Coordination of unsymmetrical bidentates such as α-aminoacidates in these types of complexes leads to two possible stereoisomers, designated as β_1 or β_2 [2]. Previous ^{1}H NMR [8, 9] and X-ray crystallographic determinations [10] on related species have shown how these coordination modes may be distinguished spectroscopically. Deshielding effects of the coordinated secondary amine group result in a downfield shift of *c*. 1 ppm for the resonance attributed to the H(11) doublet of the β_2 as compared with the β_1 isomer. Correspondingly, the electronic environment of the methyl group of each isomer is not equivalent, resulting in unique chemical shifts for each methyl doublet (ppm: $R=\beta_1$ 1.211; S-β_1 0.944; S-β_2 1.171, for the Λ complex) as shown in Fig. 1. The CD and visible spectral data for the complexes, given in Table 3 and Fig. 2, are very similar to those for the analogous picchxn complexes [8]. These also demonstrate similar characteristic differences between the spectra for the β_1 and β_2 complexes, with the latter having a negative peak at higher wavelength (≈ 530 nm) and a positive peak

TABLE 1. Final atomic coordinates (fractional × 10^4) for non-hydrogen atoms of Λ-β_1-[Co(R,R-picstien)(AMMA)]$ClO_4 \cdot 2H_2O$ with e.s.d.s in parentheses

	x	*y*	*z*
Co	390.2(8)	1854.3(6)	1685.0(3)
N(1)	1309(5)	816(4)	1238(2)
N(2)	−1359(4)	1287(3)	1425(2)
N(11)	2280(4)	2218(3)	1881(1)
N(21)	156(5)	2984(4)	1168(1)
N(3)	335(5)	839(3)	2275(2)
O(31)	−452(4)	2918(3)	2126(1)
O(32)	−634(4)	3322(3)	2938(1)
O(33)	−2414(4)	478(3)	2328(1)
O(34)	−2633(4)	1160(3)	3115(1)
C(31)	−496(6)	2638(4)	2599(2)
C(32)	−448(7)	1373(4)	2706(2)
C(33)	−1975(6)	970(4)	2726(2)
C(3m)	315(8)	1127(5)	3210(2)
C(11)	2696(6)	3119(5)	2150(2)
C(12)	4028(6)	3220(5)	2334(2)
C(13)	4993(6)	2366(5)	2233(2)
C(14)	4558(7)	1444(4)	1947(2)
C(15)	3193(6)	1407(4)	1772(2)
C(16)	2631(6)	437(5)	1482(2)
C(1)	307(6)	−109(4)	1114(2)
C(2)	−1104(6)	421(4)	1012(2)
C(21)	1130(6)	3699(5)	1001(2)
C(22)	770(7)	4578(5)	680(2)
C(23)	−605(7)	4689(5)	536(2)
C(24)	−1607(6)	3949(5)	699(2)
C(25)	−1200(5)	3091(5)	1016(2)
C(26)	−2179(6)	2254(5)	1239(2)
C(111)	866(5)	−854(4)	695(2)
C(112)	1592(5)	−1817(5)	816(2)
C(113)	2208(6)	−2464(4)	442(2)
C(114)	2065(6)	−2161(4)	−63(2)
C(115)	1331(6)	−1204(5)	−191(2)
C(116)	724(6)	−536(4)	184(2)
C(211)	−2327(5)	−367(4)	1007(2)
C(212)	−3472(6)	−163(4)	700(2)
C(213)	−4639(6)	−831(5)	736(2)
C(214)	−4689(6)	−1745(5)	1077(2)
C(215)	−3536(6)	−1958(5)	1373(2)
C(216)	−2358(6)	−1295(5)	1341(2)
Cl	4287.7(14)	2770.7(11)	457.8(5)
O(a)	5554(4)	2491(3)	197(1)
O(b)	3508(4)	1769(3)	580(1)
O(c)	4638(4)	3349(3)	925(1)
O(d)	3437(4)	3487(3)	150(1)
O(w1)	4790(5)	327(4)	3412(2)
O(w2)	2845(5)	−293(4)	2681(2)

TABLE 2. Final atomic coordinates (fractional $\times 10^3$) for hydrogen atoms[a] of Λ-β_1-[Co(R,R-picstien)(AMMA)]$ClO_4 \cdot 2H_2O$ with e.s.d.s in parentheses

	x	y	z
H(11)	191(6)	367(5)	220(2)
H(12)	436(6)	386(4)	251(2)
H(13)	618(6)	240(5)	239(2)
H(14)	521(6)	88(5)	187(2)
H(21)	215(6)	364(5)	111(2)
H(22)	137(7)	497(5)	59(2)
H(23)	−93(6)	530(5)	39(2)
H(24)	−260(6)	408(5)	62(2)
H(112)	178(5)	−207(4)	116(2)
H(113)	281(5)	−319(4)	55(2)
H(114)	246(6)	−251(5)	−30(2)
H(115)	130(6)	−94(5)	−54(2)
H(116)	23(6)	14(4)	9(2)
H(212)	−338(5)	57(4)	43(2)
H(213)	−544(6)	−64(4)	54(2)
H(214)	−565(6)	−223(4)	112(2)
H(215)	−360(6)	−266(4)	160(2)
H(216)	−165(5)	−147(4)	159(2)
H(1)	28(6)	−61(4)	146(2)
H(2)	−107(6)	94(5)	65(2)
H(N1)	158(6)	120(5)	94(2)
H(N2)	−182(6)	91(5)	174(2)
H(16a)	247(6)	−30(4)	175(2)
H(16b)	325(6)	13(5)	124(2)
H(26a)	−302(5)	214(5)	97(2)
H(26b)	−274(6)	269(5)	151(2)
H(Cma)	45(7)	38(4)	330(2)
H(Cmb)	141(6)	140(5)	319(2)
H(Cmc)	−31(7)	145(4)	352(2)
H(N3a)	129(6)	63(5)	240(2)
H(N3b)	−19(7)	17(5)	221(2)
H(w1a)	501(7)	0(5)	365(2)
H(w1b)	553(6)	47(6)	333(2)
H(w2a)	335(6)	4(5)	295(2)
H(w2b)	251(8)	−67(5)	279(3)

[a] For hydrogen atoms $B = 1.5$ Å^2.

($\approx$475 nm) with a much larger $\Delta\epsilon$ value than for the corresponding β_1 complexes.

When S-alanine was reacted with the dichloro complex and the product applied to a small column of CM Sephadex®-C25, the entire product eluted was shown by NMR measurements to be a mixture of the β_1 and β_2 isomers in a 80:20 ± 3 ratio. Similarly, when *rac*-alanine was used and in a repeat experiment the ratio R-β_1:S-β_1:S-β_2 was found to be 38:38:24, which demonstrates both the stereo- and the enantioselectivity of this system. This result complements related experiments using Λ-β-[Co(R,R-picchxn)Cl_2]$^+$, in which these three isomeric forms were obtained as well [8].

Decarboxylation experiments

The protonated complex Λ-β_1-[Co(R,R-picstien)(AMMAH)]$(ClO_4)_2 \cdot 0.5H_2O$ was decarboxylated in 1 mol dm^{-3} HCl(aq) at 70 °C [1] to give diastereomeric products containing coordinated alanine. Their subsequent isolation could be effected by taking the acidic reaction solution to dryness at 70 °C on a rotary evaporator. No starting material could be detected in any of the experiments (decarboxylation at 70 °C over 1, 2 or 3 h), nor was there any evidence of undesired decomposition of the complex under these strongly acidic conditions. However, neutralisation of the reaction mixture prior to solvent removal results in decomposition of the complex to give the characteristic purple colour of the dichloro species. This instability allows the reaction to become cyclic, with the relatively insoluble *cis*-β-dichloro complex being easily recoverable by filtration.

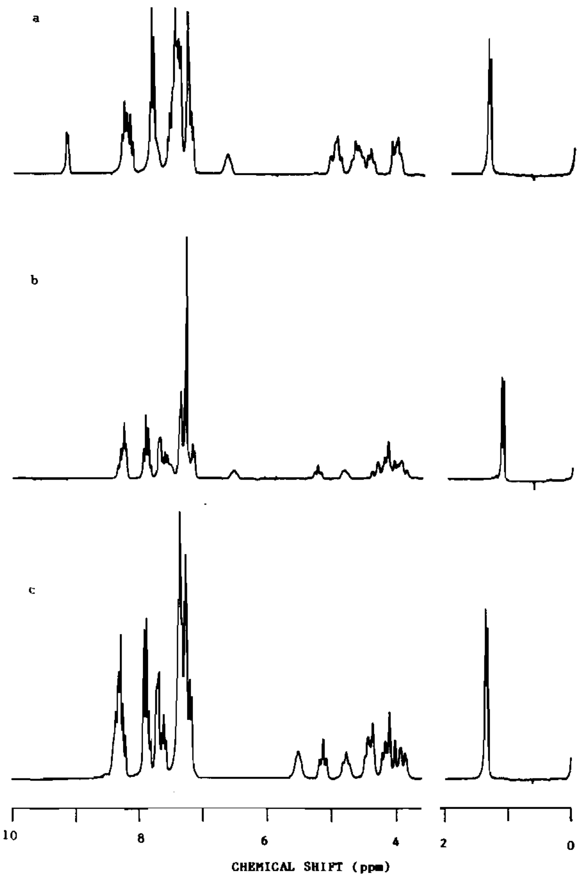

Fig. 1. 200 MHz proton NMR spectra of the picstien–aminoacid–cobalt(III) complexes (solvent DMSO-d_6): a, Λ-β_2-[Co(R,R-picstien)(S-ala)]$^{2+}$; b, Λ-β_1-[Co(R,R-picstien)(S-ala)]$^{2+}$; c, Λ-β_1-[Co(R,R-picstien)(R-ala)]$^{2+}$.

The entire decarboxylation product was dissolved in DMSO-d_6 and the optical yields determined from NMR spectra by careful integration of the methyl resonances attributable to the isomeric forms of the coordinated aminoacidates. These spectral assignments were confirmed by comparison with those of

TABLE 3. Electronic spectral data for picstien metal complexes

Complex[a]	λ (nm)	$\epsilon \times 10^{-3}$ (dm^2 mol^{-1})	$\Delta\epsilon$ (dm^2 mol^{-1})
Λ-β_1-[Co(*R*,*R*-L)(*R*-ala)]$^{2+}$			
	505		+17.46
	455		+11.75
	448	2.17	
	357		−5.87
Λ-β_1-[Co(*R*,*R*-L)(*S*-ala)]$^{2+}$			
	486	2.09	
	485		+14.04
	353		−6.79
Λ-β_2-[Co(*R*,*R*-L)(*S*-ala)]$^{2+}$			
	530		−13.81
	490	1.74	
	475		+25.85
	347		−11.69
Λ-β_1-[Co(*R*,*R*-L)(AMMAH)]$^{2+}$			
	490		+20.42
	486	2.48	
	414	0.53	
	353		−8.20

[a] L = picstien.

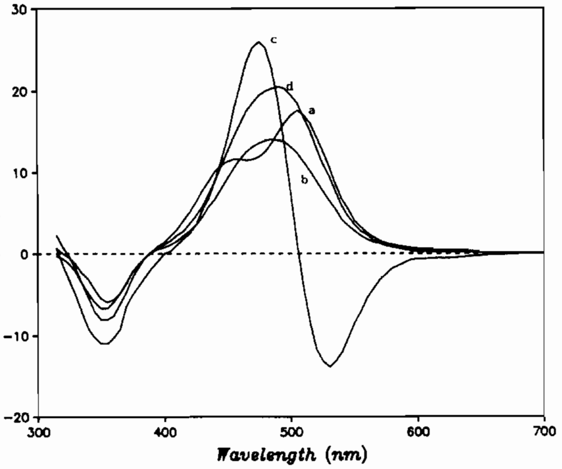

Fig. 2. Visible circular dichroism spectra of the complexes (solvent H_2O): a, Λ-β_1-[Co(*R*,*R*-picstien)(*R*-ala)]$^{2+}$; b, Λ-β_1-[Co(*R*,*R*-picstien)(*S*-ala)]$^{2+}$; c, Λ-β_2-[Co(*R*,*R*-picstien)(*S*-ala)]$^{2+}$; d, Λ-β_1-[Co(*R*,*R*-picstien)(AMMA)]$^+$.

the individual complexes prepared from the optically pure amino acids. Unlike the NMR spectra of the analogous picchxn complexes [1], where the methyl signals are partially obscured by the cyclohexane resonances and isomeric ratios have to be determined from the broad NH resonances or those due to pyridyl H atoms, these picstien species have unobstructed alanine–methyl resonances which are easily integrated.

The separate *in situ* decarboxylation NMR experiments (1.0 M D_2O/DCl at 70 °C) demonstrate that, without concentration of the solution, the reaction is incomplete after 3 h, although with a diminishing proportion of starting material remaining with increasing time. However, the ratio of *R*:*S*-alanine produced remains constant throughout, demonstrating that the isomeric ratio observed is not determined by kinetic effects. The ratio of *R*:*S*-alanine produced in this reaction is 93:7 ± 3. It thus represents the largest enantiomeric excess (86%) so far obtained in experimental systems of this kind [2, 3].

During reaction of the coordinated aminomalonic acid in HCl solutions, the relative configuration of the asymmetric carbon atom of the amino acid is inverted, since *R*-alanine is produced predominantly from the Λ-β-(*pro-S*) complex. This is in accord with several other related observations [1, 3], but contrasts with analogous aromatic amino acid syntheses [2, 3] where retention of the configuration of the asymmetric carbon atom is observed. The reasons for this latter result are discussed elsewhere [2].

It should be noted that removal of free analine from the complex reported here is facile, as compared with related complexes of *R*,*R*-picchxn. Thus the system could be used to synthesise alanine in a cyclic system.

Crystal and molecular structure of Λ-β_1-[Co(R,R-picstien)(AMMA)]$ClO_4 \cdot 2H_2O$

The crystal structure of the complex confirms the absolute configuration of the metal complex to be Λ-β_1 and the bidentate methylaminomalonic acid ligand to be coordinated with *R* (*pro-S*) absolute configuration. The pendant carboxyl group forms an intramolecular hydrogen bond to H(N2) (Fig. 3 [11] and Table 4) which would not be possible in an *S* (*pro-R*) configuration, as is observed in the structure of the related complex Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-APMA)]$^+$ [3]. An analogous three-point mode of attachment of AMMA has been reported for three related complexes [2, 12, 13], and it would appear that this serves to stabilise the *R*-aminomalonate coordination in the Λ-β_1 diastereoisomer over its alternative *S* form.

In the crystal lattice there is an extensive hydrogen bonding network which involves the complex cation, the perchlorate anion and both water molecules of the asymmetric unit, the details of which are presented in Table 4, together with other short intermolecular contacts. The bond lengths and angles in the molecular cation (Table 5) show the dimensions of the octahedral coordination sphere to be in accord

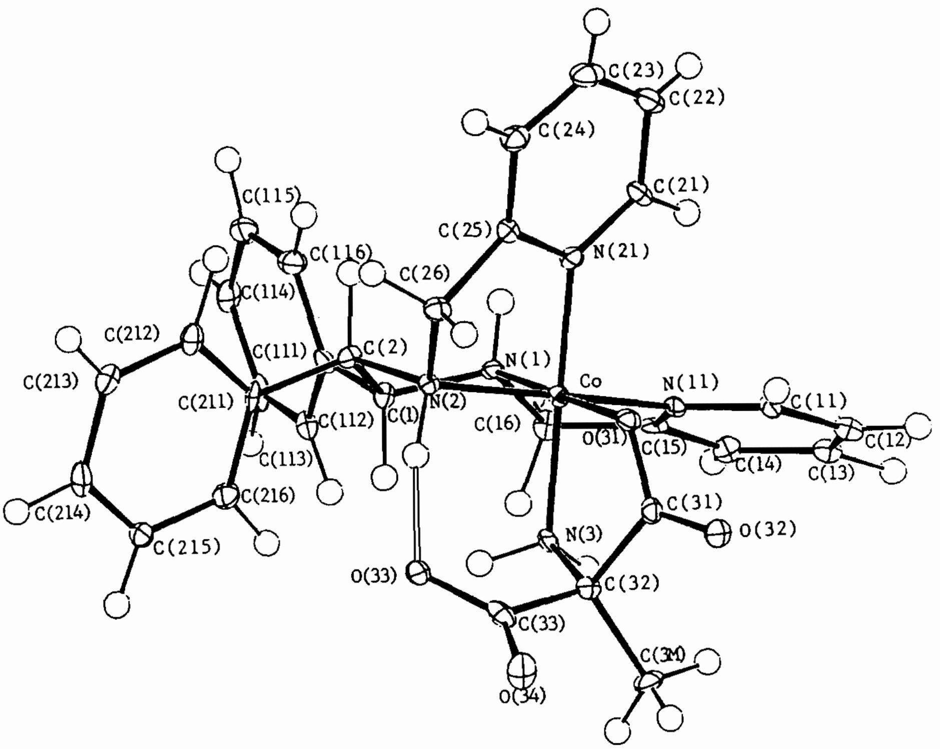

Fig. 3. Perspective drawing of the Λ-β_1-[Co(*R*,*R*-picstien)(AMMA)]$^+$ cation showing the atom labelling scheme. Thermal ellipsoids are scaled to include 35% probability.

TABLE 4. Contact distances (Å) for Λ-β_1-[Co(*R*,*R*-picstien)(AMMA)]ClO$_4$·2H$_2$O with e.s.d.s in parentheses

Proposed hydrogen bonding[a]

Donor···Acceptor	D···A	H···A	D–H···A (°)
N(2)–H(N2)··O(33)	2.770(5)	1.73(6)	169(5)
N(1)–H(N1)···O(b)	2.966(5)	2.19(6)	138(5)
N(3)–H(N3a)···O(w2)	2.966(7)	2.00(6)	160(5)
N(3)–H(N3b)···$O(32^{I})$	3.076(5)	2.38(6)	129(5)
O(w1)–H(w1a)···$O(c^{II})$	2.977(6)	2.30(6)	151(6)
O(w1)–H(w1b)···$O(34^{III})$	2.780(6)	2.02(6)	169(7)
O(w2)–H(w2a)···O(w1)	2.789(7)	1.88(5)	160(5)
O(w2)–H(w2b)···$O(31^{I})$	3.182(6)	2.61(7)	153(8)

Intermolecular contacts <3.30 Å[a]

O(b)···C(16)	2.933(7)	O(32)···$C(1^{V})$	3.151(6)
O(a)···$O(d^{IV})$	3.142(5)	O(33)···$C(11^{I})$	3.154(6)
O(d)···C(21)	3.171(6)	O(33)···$C(12^{I})$	3.240(7)
O(d)···C(22)	3.198(7)	O(33)···$C(14^{III})$	3.286(7)
O(w2)···C(15)	3.169(6)	O(w2)···C(14)	3.286(7)
O(w2)···C(3m)	3.277(8)	O(w2)···C(16)	3.299(7)

[a] Roman numeral superscripts refer to the following equivalent positions relative to x, y, z: I: $-x, y-1/2, 1/2-z$; II: $1-x, 1/2+y, 1/2-z$; III: $x-1, y, z$; IV: $1/2+x, 1/2-y, -z$; V: $-x, 1/2+y, 1/2-z$.

with previously reported *R*,*R*-picchxn analogues [2, 3, 14, 15]. The central chelate ring adopts the λ conformation, consistent with the two phenyl substituents being in quasi equatorial positions (Fig. 3). Hence the tetradentate mimics the *R*,*R*-picchxn ligand, in which restraints on the chelate ring derived from the *trans*-cyclohexanediamine fragment enforces the adoption of a λ conformation. One advantage of picstien, however, is its NMR window in the 0–4 ppm region, allowing easier assessment of isomeric

TABLE 5. Selected molecular dimensions for the Λ-β_1-[Co(*R*,*R*-picstien)(AMMA)]$^+$ cation with e.s.d.s in parentheses

Distances (Å)			
Co–N(11)	1.937(4)	Co–N(1)	1.929(4)
Co–N(21)	1.937(4)	Co–N(2)	1.937(4)
Co–O(31)	1.907(3)	Co–N(3)	1.979(4)
C(31)–O(31)	1.296(5)	C(32)–N(3)	1.510(6)
C(31)–O(32)	1.221(5)	C(32)–C(31)	1.540(6)
C(33)–O(33)	1.278(6)	C(32)–C(33)	1.545(8)
C(33)–O(34)	1.229(6)	C(32)–C(3m)	1.549(7)
Angles (°)			
N(11)–Co–N(1)	83.2(2)	N(11)–Co–N(21)	98.1(2)
N(21)–Co–N(2)	83.8(2)	N(11)–Co–O(31)	94.7(2)
N(1)–Co–N(2)	87.3(2)	N(11)–Co–N(3)	87.2(2)
O(31)–Co–N(3)	85.1(2)	N(1)–Co–N(21)	94.0(2)
N(11)–Co–N(2)	170.4(2)	N(1)–Co–N(3)	95.8(2)
N(21)–Co–N(3)	169.4(2)	N(2)–Co–O(31)	94.8(2)
N(1)–Co–O(31)	177.7(2)	N(2)–Co–N(3)	92.4(2)
Co–O(31)–C(31)	115.7(3)	N(21)–Co–O(31)	85.3(2)
Co–N(3)–C(32)	110.5(3)	C(31)–C(32)–N(3)	106.9(4)
O(31)–C(31)–O(32)	122.6(5)	C(31)–C(32)–C(33)	106.5(5)
O(31)–C(31)–C(32)	115.5(4)	C(31)–C(32)–C(3m)	111.1(4)
O(32)–C(31)–C(32)	121.7(4)	N(3)–C(32)–C(33)	111.4(4)
O(33)–C(33)–O(34)	127.3(5)	N(3)–C(32)–C(3m)	111.1(5)
O(33)–C(33)–C(32)	115.4(5)	C(33)–C(32)–C(3m)	109.6(5)
O(34)–C(33)–C(32)	117.2(5)		
	$n=1$	$n=2$	
Co–N(*n*1)–C(*n*1)	126.7(4)	126.6(4)	
Co–N(*n*1)–C(*n*5)	113.1(3)	112.5(4)	
C(*n*1)–N(*n*1)–C(*n*5)	119.9(5)	120.5(5)	
Co–N(*n*)–C(*n*6)	108.6(3)	107.7(3)	
Co–N(*n*)–C(*n*)	108.4(3)	110.7(3)	
C(*n*6)–N(*n*)–C(*n*)	114.5(4)	112.1(4)	

ratios for species containing methyl or methylene groups.

Supplementary material

Lists of anisotropic thermal parameters, complete Tables of bond lengths and angles, and observed and calculated structure factors are available from F.S.S. on request.

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