Chiral Metal Complexes. 27*. Stereoselectivity in the Synthesis and Reactions of Coordinated Aminomalonic Acid Derivatives

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(Received November 23, 1987)

Abstract

The synthesis is reported of a series of ternary cationic complexes of general form $[Co(R,R\text{-picchxn})(ARMA)]^+$ (where picchxn is the N_4 tetradentate *N,N'*-di(2-picolyl)-1,2-diaminocyclohexane and ARMA is a bidentate α-substituted-α-aminomalonate dianion). The aminomalonic acid ($NH_2 \cdot C(COOH)_2 \cdot R$) derivatives investigated have R = $-CH_3$ ($AMMAH_2$), $-CH_2 \cdot CH_3$ ($AEMAH_2$), $-CH_2 \cdot CH_2 \cdot CH_3$ ($APMAH_2$), $-CH_2 \cdot (CH_2)_2 \cdot CH_3$ ($ABuTMAH_2$), $-CH_2 \cdot C_6H_5$ ($ABMAH_2$), $-CH_2 \cdot (p\text{-}C_6H_4) \cdot C(CH_3)_3$ ($ABuBMAH_2$) and $-CH_2 \cdot C_{10}H_7$ ($ANMAH_2$). The isomeric species in the complex products have been separated using cation exchange chromatography and each isomer has been characterised using NMR and circular dichroism techniques. In each synthesis the major isomeric product obtained has a Λ-β_1 topology. However, where $ARMAH_2$ possesses a lengthy alkyl sidechain trace amounts of Δ-α-$[Co(R,R\text{-picchxn})(ARMA)]^+$ isomers have been observed during the synthetic reactions. This unusual isomeric form readily undergoes inversion of its absolute configuration in DMSO solution to yield the more thermodynamically stable Λ-β_1-$[Co(R,R\text{-picchxn})(R\text{-ARMA})]^+$ species stereospecifically.

In the case of Λ-β_1-$[Co(R,R\text{-picchxn})(S\text{-APMA})]ClO_4 \cdot 2NaClO_4 \cdot 5H_2O$ the crystal structure has been determined. The compound crystallises in the orthorhombic space group $P2_12_12_1$, with $a = 10.056(3)$, $b = 16.475(7)$, $c = 23.370(7)$ Å and $Z = 4$. The structure was refined to $R = 0.079$ for 4460 non-zero reflexions, and confirms the absolute configuration of each chiral centre to be consistent with the NMR and circular dichroism interpretations.

The decarboxylation of these chelate $ARMAH_2$ derivatives under acid conditions leads to corresponding complexes containing mixtures of coordinated *R*- and *S*-α-aminoacids in various ratios. This ratio has been determined in each case, and factors which may influence the degree of chiral induction observed are discussed.

Introduction

Recently we reported the use of chiral ternary complexes of Co(III) containing *N,N'*-di(2-picolyl)-1*R*,2*R*-diaminocyclohexane (*R,R*-picchxn) and substituted aminopropandioic acids to produce α-amino acids in high optical yields [1, 2]. This system induces greater chirality in the reaction of the substrate than has been generally observed in related complexes. A high degree of stereoselectivity is found in these and closely related Co(III) species. Invariably, Λ-β coordination has been observed for the Co(*R,R*-picchxn) fragment. Although both β_1 and β_2 geometries are possible in ternary complexes containing amino acids, a marked preference for the β_1 form is observed in products obtained from aqueous solutions. This β_1 preference is even more pronounced for complexes of aminopropandioic (α-aminomalonic) acids with the absolute configuration of the α-carbon atom being dependent on which carboxylic acid group coordinates. However, when either of these α-alkyl-aminomalonate derivatives is decarboxylated in aqueous acid, the same degree of chiral induction is obtained in the product.

Hydrophobic stacking interactions apparent in the crystal structure of Λ-β_1-$[Co(R,R\text{-picchxn})(R\text{-ABMA})]^{+}$ † have been identified as a possible source

*Part 26 is: R. R. Fenton, R. S. Vagg and P. A. Williams, preceding paper.

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†$ABMAH_2$ = 2-amino-2-benzylpropandioic acid (**Ia**); abuH = α-aminobutyric acid; $AMMAH_2$ = 2-amino-2-methylpropandioic acid; picstien = 3,4-diphenyl-1,6-di(2-pyridyl)-2,5-diazahexane; alaH = alanine; pheH = phenylalanine; $AEMAH_2$ = 2-amino-2-ethylpropandioic acid; norvalH = norvaline; norleuH = norleucine.

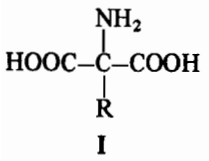
0020-1693/88/$3.50

of chiral discrimination both in the complex itself and as a determinant in its decarboxylation to phenylalanine diastereoisomers [2]. In order to investigate this possibility we have studied the system further using related α-aminomalonic acid substrates, and the results of this work are presented below.

Experimental

Elemental analyses were carried out by Mrs A. Dams in the Department of Chemistry, Cardiff. Electronic and CD spectra were recorded using a Perkin-Elmer Lambda-5 spectrophotometer and a Jobin-Yvon Dichrographe III, respectively. Atomic absorption (AA) measurements were made with a Varian AA-275 spectrometer using aqueous solutions of Λ-β-[Co(*R*,*R*-picchxn)Cl_2]ClO_4·0.5H_2O as standards. NMR spectra were recorded on a Bruker WM-360 instrument, for solutions in D_2O or DMSO-d_6 with TSS or TMS as internal standards, respectively. All spectra were recorded at 278 K.

Starting materials Λ-β-[Co(*R*,*R*-picchxn)Cl_2]ClO_4·0.5H_2O and α-amino-malonic acid derivatives were synthesized using published procedures [3, 4]. Of the latter, the following salts were isolated with respect to the free acids (I). $APMAH_2$·1.25H_2O: Calc. for $C_6H_{13.5}N_1O_{5.25}$: C, 39.2; H, 7.4; N, 7.6. Found: C, 39.3; H, 6.0; N, 7.5%. $ABuTMAH_2$·H_2O: Calc. for $C_7H_{15}N_1O_5$: C, 43.5; H, 7.8; N, 7.3. Found: C, 43.0; H, 6.0; N, 7.0%. $K_2ABuBMA$·0.5H_2O: Calc. for $C_{14}H_{18}N_1O_{4.5}K_2$: C, 48.0; H, 5.2; N, 4.0. Found: C, 48.1; H, 5.2; N, 4.6%. Low hydrogen analyses for the former two derivatives are accounted for by loss of water of crystallisation in the gas stream prior to combustion. The purity of these aminomalonates was confirmed by NMR measurements.



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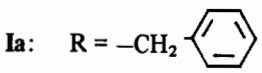
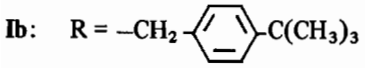


Ia: R = $-CH_2-C_6H_5$ $ABMAH_2$



Ib: R = $-CH_2-C_6H_4-C(CH_3)_3$ $ABuBMAH_2$

Ic: R = $-CH_2CH_2CH_2CH_3$ $ABuTMAH_2$
Id: R = $-CH_2CH_2CH_3$ $APMAH_2$
Ie: R = $-CH_2CH_3$ $AEMAH_2$

Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-norleu)](ClO$_4$)$_2$·1.5H_2O

The synthesis of this complex is similar to that previously reported for related compounds [1, 2]. To a solution of Λ-β-[Co(*R*,*R*-picchxn)Cl_2]ClO_4·0.5H_2O (0.50 g, 0.94 mmol) in water (30 cm^3) was added *S*-norleucine (0.40 g, 3.1 mmol) dissolved in water (20 cm^3) containing 1.0 cm^3 of 1 mol dm^{-3} aqueous NaOH. The solution was stirred for 18 h at 40 °C, was diluted two-fold with water, and then was applied to a column of CM-Sephadex® C-25 cation exchange resin in the Na^+ cycle (40 × 2 cm). After it had been flushed with water the column was eluted with 0.1 mol dm^{-3} aqueous $NaClO_4$. Two orange bands separated clearly, and these were collected in fractions using an LKB Ultraroc® II fraction collector. CD and electronic spectral measurements confirmed that each band contained only one isomer. The combined fractions of the slower-moving band containing the bulk of the product were reduced in volume *in vacuo* to about 30 cm^3 and then evaporated further at room temperature over silica gel to yield the desired complex as a microcrystalline powder. Yield: 0.232 g. *Anal.* Calc. for $C_{24}H_{39}N_5O_{11.5}Cl_2Co$: C, 40.5; H, 5.5; N, 9.8. Found: C, 40.3; H, 5.9; N, 10.1%. Spectral data (H_2O): ϵ_{482} = 1976, ϵ_{352} = 2207 dm^2 mol^{-1} (maxima), $\Delta\epsilon_{489}$ = +16.9, $\Delta\epsilon_{355}$ = −4.7 dm^2 mol^{-1} (extrema). The yields reported here and elsewhere in this paper refer to the actual amounts of the solid substances isolated. These necessarily are low due to losses associated with the considerable solubilities of the perchlorate salts, and therefore do not represent the total amount of each cationic species synthesised.

Λ-β_2-[Co(*R*,*R*-picchxn)(*S*-norleu)](ClO$_4$)$_2$·5H_2O

This salt was obtained from the faster-moving band described above using a similar isolation procedure. Yield: 0.069 g. *Anal.* Calc. for $C_{24}H_{46}N_5O_{15}Cl_2Co$: C, 37.2; H, 6.0; N, 9.0. Found: C, 37.3; H, 4.7; N, 9.5%. H_2O is lost during analysis prior to combustion. Calc. for the anhydrate: H, 4.7%. Spectral data (H_2O): ϵ_{478} = 1595, ϵ_{349} = 2146 dm^2 mol^{-1} (maxima), $\Delta\epsilon_{533}$ = −6.5, $\Delta\epsilon_{483}$ = +22.5 dm^2 mol^{-1} (extrema).

Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-norval)](ClO$_4$)$_2$·2H_2O

A synthetic procedure similar to that outlined above was followed with *S*-norvaline substituted for *S*-norleucine. Development of the column gave a faster-moving orange minor band which contained too little material to isolate. CD spectral measurements on this band indicated that it consisted solely of the Λ-β_2 isomer. The large slower-moving band was shown to consist of only one isomer from which the β_1 complex was isolated. Yield: 0.265 g. *Anal.* Calc. for $C_{23}H_{38}N_5O_{12}Cl_2Co$: C, 39.1; H, 5.4 (4.9 as anhydrate); N, 9.9. Found: C, 38.9; H, 4.8; N, 10.0%. Spectral data (H_2O): ϵ_{486} = 1815, ϵ_{350} = 1555 dm^2 mol^{-1} (maxima), $\Delta\epsilon_{487}$ = +16.1, $\Delta\epsilon_{352}$ = −4.1 dm^2 mol^{-1} (extrema).

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

The synthesis of this complex is analogous to those described above. Upon elution of the Sephadex® column, two orange bands developed. The minor faster-moving one was collected in fractions and CD and electronic spectral measurements indicated that two isomers were present. It has proved impossible to separate or crystallise either of these species in a pure state. However, combined fractions from the band were evaporated to dryness and the ^{1}H NMR measurements of the residue in DMSO-d$_6$ showed, by analogy with related species, that one of the isomers was the Λ-β$_2$ isomer. The other species corresponds to the Δ-α isomer (*vide infra*).

Only one isomer is present in the slower-moving band and evaporation of combined fractions gave the title complex as fine orange crystals. Yield: 0.023 g, after recrystallisation from hot water (the complex is very water soluble). *Anal.* Calc. for $C_{24}H_{38}N_5O_{11}Cl_2Co$: C, 41.0; H, 5.4; N, 10.0. Found: C, 40.8; H, 6.1; N, 9.3%. Spectral data (H_2O): $\epsilon_{487} = 1841$, $\epsilon_{349} = 1637$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{501} = +22.9$, $\Delta\epsilon_{353} = -1.2$ dm^2 mol^{-1} (extrema).

Λ-β$_1$-[Co(R,R-picchxn)(R-norval)](ClO$_4$)$_2$·1.5H$_2$O

The title complex was obtained in a similar manner to like compounds described above. Again, the faster-moving orange band was demonstrated to contain both Λ-β$_1$ and Δ-α isomers by ^{1}H NMR measurements of fractions taken to dryness. As with the corresponding *R*-norleucine compound, too little material was present in these fractions to separate or fractionally crystallise as pure diastereoisomeric salts.

The Λ-β$_1$ complex crystallised upon concentrating fractions from the slower-moving band. Yield: 0.339 g. *Anal.* Calc. for $C_{23}H_{37}N_5O_{11.5}Cl_2Co$: C, 39.6; H, 5.3; N, 10.0. Found: C, 39.5; H, 5.0; N, 10.2%. Spectral data (H_2O): $\epsilon_{482} = 1949$, $\epsilon_{348} = 1709$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{503} = +23.9$, $\Delta\epsilon_{351} = -1.4$ dm^2 mol^{-1} (extrema).

Λ-β$_1$-[Co(R,R-picchxn)(R-APMAH)](ClO$_4$)$_2$

Λ-β-[Co(*R*,*R*-picchxn)Cl$_2$]ClO$_4$·0.5H$_2$O (0.50 g, 0.94 mmol) and APMAH$_2$·1.25H$_2$O (0.77 g, 4.2 mmol) were dissolved in water (50 cm^3) at room temperature, the pH of the solution was adjusted to 8.0 with dilute aqueous NaOH, and the mixture allowed to stand overnight. The resulting deep orange solution was diluted four-fold with water and applied to a CM-Sephadex® C-25 cation exchange column (35 × 1.5 cm) in the H$^+$ cycle. The column was flushed with water and then was eluted with 0.1 mol dm^{-3} aqueous NaClO$_4$ whereupon two orange bands separated clearly. These were shown by the usual spectral measurements to each contain only one isomer. Fractions from the faster-moving band were combined, reduced to about 20 cm^3 *in vacuo* at 30 °C, and were slowly evaporated over silica gel at room temperature. No crystalline material formed, hence an aliquot was taken to dryness. The whole residue, containing considerable NaClO$_4$, was dissolved in DMSO-d$_6$, and the ^{1}H NMR spectrum of this solution was recorded. Chemical shift patterns [1, 2] confirmed the nature of the isomer. Spectral data (0.1 mol dm^{-3} NaClO$_4$, Co concentrations obtained by AA): $\epsilon_{484} = 2303$, $\epsilon_{346} = 2430$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{488} = +19.4$, $\Delta\epsilon_{353} = -4.5$ dm^2 mol^{-1} (extrema).

Λ-β$_1$-[Co(R,R-picchxn)(S-APMAH)]ClO$_4$·2NaClO$_4$·5H$_2$O

Fractions from the minor, slower-eluting orange band from the above reaction were combined and slowly evaporated over silica gel at room temperature. Deep orange prisms of the complex slowly crystallised from the very concentrated solution. The product was filtered off and any excess moisture was removed by absorption on dry filter paper. Yield: 0.174 g. *Anal.* Calc. for $C_{24}H_{43}N_5O_{21}Cl_3Co_1Na_2$: C, 30.4; H, 4.6; N, 7.4. Found: C, 30.3; H, 4.5; N, 7.3%. Spectral data (H_2O): $\epsilon_{483} = 1806$, $\epsilon_{348} = 1628$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{483} = +23.4$, $\Delta\epsilon_{350} = -3.7$ dm^2 mol^{-1} (extrema).

Δ-α-[Co(R,R-picchxn)(ABuTMAH)](ClO$_4$)$_2$

ABuTMAH$_2$·H$_2$O was reacted with Λ-β-[Co(*R*,*R*-picchxn)Cl$_2$]ClO$_4$·0.5H$_2$O using the same general method as was employed to synthesise the complexes described above. Upon elution of the reaction mixture on CM-Sephadex® C-25 with 0.1 mol dm^{-3} aqueous NaClO$_4$ two orange bands separated, the former containing the larger amount of Co(III). A comparison of $\Delta A/A$ values for fractions of this band showed small variations. The fractions were combined and evaporated *in vacuo* at 30 °C to a volume of *ca.* 10 cm^3. An orange crystalline product was obtained initially upon storage of the concentrate over silica gel at room temperature. This proved to be the anhydrous Δ-α diastereoisomer. Yield: 0.043 g (obtained from reaction of 0.5 g of dichloro starting material). *Anal.* Calc. for $C_{25}H_{36}N_5O_{10}Cl_2Co$: C, 41.2; H, 5.0; N, 9.6. Found: C, 41.2; H, 4.8; N, 9.7%. Spectral data (H_2O): $\epsilon_{484} = 1147$, $\epsilon_{346} = 1758$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{496} = -30.3$, $\Delta\epsilon_{372} = -2.3$ dm^2 mol^{-1} (extrema).

Λ-β$_1$-[Co(R,R-picchxn)(R-ABuTMAH)](ClO$_4$)$_2$

The filtrate remaining after isolation of the Δ-α isomer was concentrated to yield a further crop of orange crystals. This proved to be a mixture of the Δ-α isomer and the title complex. Subsequent evaporation of the filtrate remaining failed to yield any further crystalline isomer due to the presence of large amounts of solid NaClO$_4$. An aliquot of the

supernatant was taken to dryness and the resulting solid dissolved in DMSO-d_6 for NMR analysis. This showed the title complex to be the only coordination species present. Spectral data (0.1 mol dm^{-3} $NaClO_4$, Co(III) determined by AA): $\epsilon_{484} = 1944$, $\epsilon_{346} = 2042$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{482} = +17.1$, $\Delta\epsilon_{349} = -4.5$ dm^2 mol^{-1} (extrema).

Λ-β$_1$-[Co(R,R-picchxn)(S-ABuTMAH)](ClO$_4$)$_2$

The slower-moving band from the above synthetic reaction was shown, using the usual spectral measurements, to consist of only one isomer. However, crystallisation did not occur after evaporation of the combined fractions. ^{1}H NMR measurements of an aliquot of the eluate after solvent removal showed, by comparison with previously characterised analogues [1, 2], that it contained the title isomer. Spectral data (obtained as for the *R*-ABuTMAH species): $\epsilon_{486} = 2273$, $\epsilon_{344} = 2234$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{481} = +26.4$, $\Delta\epsilon_{352} = -6.0$ dm^2 mol^{-1} (extrema).

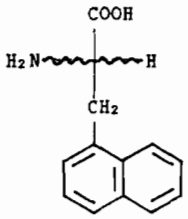
Λ-β$_1$-[Co(R,R-picchxn)(R-ABuBMA)]ClO$_4$·2.5H$_2$O

This complex was synthesised by the reaction of the parent dichloro species with K_2ABuBMA·H_2O. Elution of this reaction solution on the cation exchange column with an aqueous 2% *w/v* NaCl solution caused the development of a single orange band which was shown to consist of one isomer. Fractions were combined, reduced in volume by one half and then saturated aqueous $NaClO_4$ (10 cm^3) was added. Upon standing overnight, a light orange crystalline product formed. The crystals were filtered off, washed sparingly with ice-cold water, and air dried. Yield: 0.198 g. *Anal.* Calc. for $C_{32}H_{46}N_5O_{10.5}Cl_1Co$: C, 50.4; H, 4.6; N, 9.2. Found: C, 50.2; H, 6.0; N, 8.6%. Spectral data (H_2O): $\epsilon_{483} = 2004$ dm^2 mol^{-1} (maximum), $\Delta\epsilon_{489} = +21.1$ dm^2 mol^{-1} (extremum).

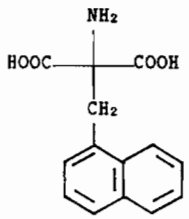
Complexes of (1-naphthyl)alanine (IIa and IIb) and its α-aminomalonic acid precursor (IIc)

Using the synthetic procedure previously described for the production of α-substituted-α-aminomalonic acids [4] the desired product, in this case, proved to be particularly susceptible to decarboxylation during the alkaline hydrolysis of its diethylester precursor. Hence isolation of the aminomalonic acid in a pure form proved impossible. Rather a mixture of the three compounds (**IIa–IIc**) was obtained, as revealed by the NMR spectrum of the isolated product. This mixture was reacted directly with Λ-β-[Co(*R,R*-picchxn)Cl_2]$^+$, and the diastereoisomeric products then were separated chromatographically.

In a typical synthesis diethylformamidomalonic acid (9.16 g, 45 mmol) and sodium metal (1.04 g, 45 mmol) were reacted in benzene (Na-dried, 100 cm^3) under reflux. After reaction was complete a further 100 cm^3 of benzene was added followed by the dropwise addition of a hot solution of 1-(bromoethyl)naphthalene (8.18 g, 37 mmol) in dry benzene (40 cm^3). The mixture was refluxed for a further 24 h, cooled to room temperature, and the solvent removed under reduced pressure to yield a pale yellow oil. This was dissolved in chloroform (100 cm^3), was washed with water (50 cm^3), and the solvent removed. The oily product was dissolved in ethanol (50 cm^3) then water (30 cm^3) was added, and the resulting mixture was reduced in volume. A white crystalline solid (the formamide diethylester of **IIc**) separated out. This was filtered off, washed with diethyl ether, and air dried. Yield: 9.1 g.



IIa R-NA
IIb S-NA



IIc $ANMAH_2$

2-Formamido-2-(2-methylnaphthyl)propandioc acid diethylester (18.9 g, 55 mmol) was refluxed with 5.0 mol dm^{-3} aqueous KOH (100 cm^3) for four days. The mixture then was cooled to 0 °C and the pH adjusted to 5.9 using 30% aqueous acetic acid with the temperature being maintained below 4 °C. A solution of lead(II) acetate (30 g) in water (100 cm^3) was added to the reaction solution causing the precipitation of the lead(II) salt of the aminoacid products. The mixture was cooled at −4 °C overnight and the solid was collected and washed with ice-cold water. Hydrogen sulphide gas was bubbled through a suspension of the salt in cold water until the formation of PbS was complete. The mixture was filtered and the filtrate evaporated under reduced pressure at 30 °C to yield a white solid (4.2 g). This was filtered off, washed with water and air-dried. ^{1}H NMR measurements showed the product to consist of a mixture of the compounds (**IIa–IIc**) in approximately equal proportions.

A portion (0.55 g) of the above product mixture was added to a solution of Λ-β-[Co(*R,R*-picchxn)Cl_2]ClO_4·0.5H_2O (1.00 g, 1.9 mmol) in water (30 cm^3), followed by 1 mol dm^{-3} aqueous NaOH (2.2 cm^3). The reaction mixture was stirred for 72 h at room temperature, filtered, and the filtrate added to a column of CM-Sephadex® C-25 resin (40 × 1.5 cm) in the H^+ cycle. This was washed with water and then eluted with 0.05 mol dm^{-3} aqueous NaCl. A faint pale purple band appeared first, which was discarded. Then followed three orange bands, which were eluted with 0.2 mol dm^{-3} aqueous NaCl after they had

separated. Fractions of the fastest-moving orange band gave constant values for $\Delta A/A$, and they showed identical CD spectra. These fractions were recombined, saturated aqueous $NaClO_4$ was added, and the solution allowed to evaporate slowly at room temperature. During two weeks, peach-coloured leaflets of Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ANMAH)]-$(ClO_4)_2 \cdot 3H_2O$ crystallised. These were filtered off, washed with ice-cold water, then diethyl ether, and were air-dried. Yield: 0.350 g. *Anal.* Calc. for $C_{32}H_{42}N_5O_{15}Cl_2Co$: C, 44.4; H, 4.9; N, 8.1. Found: C, 44.2; H, 5.0; N, 7.5%. Spectral data (H_2O): $\epsilon_{482} = 2098$, $\epsilon_{345} = 5584$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{483} = +22.9$, $\Delta\epsilon_{348} = -15.8$ dm^2 mol^{-1} (extrema).

CD and electronic spectral measurements of fractions collected from the second orange band indicated that a small amount of a Λ-β_2 isomer was present in its trailing edge. The bulk of the band, however, had a CD spectrum characteristic of a Λ-β_1 complex of an *S*-aminoacidate. Fractions containing this isomeric form were treated as above to yield orange leaflets of Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-NA)]-$(ClO_4)_2 \cdot 2.5H_2O$. Yield: 0.055 g. *Anal.* Calc. for $C_{31}H_{41}N_5O_{12.5}Cl_2Co$: C, 45.8; N, 8.6. Found: C, 45.8; N, 8.2%. Spectral data (H_2O): $\epsilon_{480} = 2000$, $\epsilon_{346} = 5319$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{482} = +19.1$, $\Delta\epsilon_{351} = -15.0$ dm^2 mol^{-1} (extrema).

The slowest-moving orange band was collected in fractions which showed consistent $\Delta A/A$ values, and each had a constant CD spectrum analogous with related complexes containing an *R*-aminoacidate. From this band the complex Λ-β_1-[Co(*R*,*R*-picchxn)-(*R*-NA)]$(ClO_4)_2 \cdot 3.5H_2O$ was isolated as deep orange leaflets. Yield: 0.088 g. *Anal.* Calc. for $C_{31}H_{38}N_5O_{11.5}Cl_2Co$: C, 44.8; H, 5.2; N, 8.4. Found: C, 44.8; H, 5.2; N, 8.0%. Spectral data (H_2O): $\epsilon_{484} = 2091$, $\epsilon_{340} = 4646$ dm^2 mol^{-1} (maxima), $\Delta\epsilon_{500} = +26.8$, $\Delta\epsilon_{351} = -3.2$ dm^2 mol^{-1} (extrema).

Decarboxylation Experiments

For the pure α-aminomalonic acid derivatives that were isolated their decarboxylation to the corresponding aminoacid complexes was carried out as described elsewhere [1, 2]. However, when a mixture of a precursor complex with $NaClO_4$ only could be obtained analogous reaction conditions were employed after the Co concentration had been determined using AA. When these reactions had ceased, the product mixtures were diluted ten-fold with water and then were chromatographed as previously outlined [1, 2]. Decarboxylation of the Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ANMAH)]$^{2+}$ complex was carried out in a DCl/D_2O solution, and estimation of the diastereoisomer distribution in the product mixture in this case was made by integration of the signals in its NMR spectrum.

The Crystal and Molecular Structure of Λ-β_1-[Co(R,R-picchxn)(S-APMA)]$ClO_4 \cdot 2NaClO_4 \cdot 5H_2O$

Crystal data

$C_{24}H_{43}N_5O_{21}Cl_3Co_1Na_2$, $M_r = 948.9$, orthorhombic, $a = 10.056(3)$, $b = 16.475(7)$, $c = 23.370(7)$ Å, $U = 3871.8$ Å^3, $Z = 4$, $D_c = 1.628$ Mg m^{-3}, $F(000) = 2536$, μ(Mo Kα) = 7.33 cm^{-1}, space group $P2_12_12_1$ (no. 19).

The crystal used for data collection was 0.25 × 0.33 × 0.58 mm in size, with prominent faces (011), $(0\bar{1}\bar{1})$, $(0\bar{1}1)$, $(01\bar{1})$, (212) and $(\bar{4}\bar{1}3)$. Unit cell parameters initially were determined from precession photographs using Mo Kα radiation. Accurate cell parameters were obtained from a least-squares fit to diffractometer data. Intensities were collected at −135 °C on a Nicolet XRD P3 four-circle diffractometer [5] in the range $5° < 2\theta < 55°$ using Mo Kα radiation. Reflexions were corrected for Lorentz, polarisation and absorption effects. With respect to the latter, the maximum and minimum transmission factors were 0.744 and 0.640, respectively. Of the 4940 reflexions measured, 4460 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. Difference maps, used to locate the perchlorate and lattice water oxygen atoms, revealed that some disorder was present. Accordingly, for the disordered species, occupancies were assigned on the basis of peak heights in the difference maps. The positions of the hydrogen atoms in the complex cation were calculated assuming appropriate geometries for the atoms to which they are bonded. In the case of the pendant methyl group approximate H positions were obtained from the difference maps, and these then were optimised. The structure was refined by least-squares calculations in which the function minimised was $\Sigma w\Delta^2$, the weights being based on counting statistics. Hydrogen atom parameters were not refined. Due to the large number of variable parameters, block matrices were used during anisotropic refinement, which was terminated when the maximum 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 0.079 and 0.063, respectively. All calculations were carried out on a FACOM 340S computer using programs written by F.S.S. Neutral atom scattering factors were taken from ref. 6, with corrections being applied for anomalous dispersion.

The final non-hydrogen atomic parameters are given in Table I. See also 'Supplementary Material'.

TABLE I. Final Atomic Coordinates (fractional × 10^4) for Non-hydrogen Atoms[a]

	x	y	z	Occupancy[b]
Co	1830(1)	880(1)	1280(1)	
N(1)	3229(8)	1430(4)	1682(3)	
N(2)	1062(8)	1945(4)	1095(3)	
N(11)	2753(8)	−76(5)	1552(3)	
N(21)	604(8)	971(4)	1916(3)	
N(3)	2760(8)	766(4)	539(3)	
O(31)	458(7)	297(4)	908(3)	
O(32)	126(7)	−617(4)	224(3)	
C(31)	856(10)	−111(5)	436(4)	
C(32)	2186(9)	102(5)	197(4)	
C(33)	1981(11)	351(5)	−443(4)	
C(34)	3281(11)	574(5)	−767(4)	
C(35)	2930(10)	823(6)	−1379(4)	
C(41)	3163(12)	−624(5)	222(4)	
O(41)	2748(7)	−1293(4)	−11(3)	
O(42)	4293(7)	−506(4)	433(3)	
C(11)	2216(10)	−828(6)	1602(4)	
C(12)	2985(13)	−1456(6)	1776(4)	
C(13)	4359(15)	−1325(6)	1935(5)	
C(14)	4863(11)	−551(6)	1912(4)	
C(15)	4029(11)	70(6)	1714(4)	
C(16)	4467(10)	953(5)	1648(4)	
C(1)	3317(11)	2273(5)	1431(4)	
C(2)	1880(13)	2565(5)	1446(4)	
C(3)	1811(13)	3429(5)	1154(4)	
C(4)	2695(11)	3996(5)	1500(5)	
C(5)	4113(12)	3695(6)	1530(5)	
C(6)	4215(11)	2847(5)	1793(4)	
C(21)	628(11)	523(6)	2413(4)	
C(22)	−430(13)	609(7)	2799(5)	
C(23)	−1469(12)	1097(7)	2697(5)	
C(24)	−1462(11)	1557(7)	2199(5)	
C(25)	−413(10)	1495(6)	1828(4)	
C(26)	−340(10)	1950(5)	1259(4)	
Cl(1)	4524(3)	1236(1)	3262(1)	
Cl(2)	3452(3)	7043(2)	4590(1)	
Cl(3)	1127(4)	3164(2)	3042(1)	
O(1a)	3890(9)	1651(4)	3727(3)	
O(1b)	3497(8)	891(4)	2911(3)	
O(1c)	5310(9)	1765(4)	2926(3)	
O(1d)	5363(9)	615(4)	3487(3)	
O(2a)	4638(10)	6637(6)	4725(4)	
O(2b)	3417(8)	7221(4)	3979(3)	
O(2c)	2343(11)	6456(6)	4740(4)	0.80
O(2d)	3451(23)	7756(7)	4898(6)	0.80
O(2e)	2349(47)	7494(21)	4838(13)	0.40
O(3a)	260(10)	3494(5)	2623(4)	
O(3b)	2523(15)	3484(13)	3007(6)	0.65
O(3c)	1624(16)	2392(6)	2867(4)	0.85
O(3d)	−25(20)	2620(12)	3335(9)	0.50
O(3e)	697(15)	3320(10)	3577(6)	0.75
O(3f)	1912(83)	3859(35)	3392(16)	0.25
Na(1)	1927(5)	3819(3)	4474(2)	
Na(2)	4294(5)	1875(2)	4743(2)	
O(w1)	3992(7)	3202(4)	4298(3)	
O(w2)	2323(17)	5000(8)	3855(6)	0.55
O(w3)	499(16)	2491(8)	4531(6)	0.50
O(w4)	2341(24)	6163(12)	907(8)	0.40
O(w5)	1685(27)	5211(20)	56(11)	0.50
O(w6)	3266(23)	6529(10)	562(6)	0.50
O(w7)	956(21)	7304(12)	678(8)	0.40
O(w8)	3494(16)	7129(8)	174(6)	0.55
O(w9)	837(25)	1348(12)	3949(8)	0.35
O(w10)	1970(67)	5118(41)	−206(35)	0.25

[a]e.s.d.s given in parentheses. [b]Occupancy is unity unless otherwise stated.

Results and Discussion

The Crystal and Molecular Structure of Λ-β$_1$-[Co(R,R-picchxn)(S-APMA)]ClO$_4$·2NaClO$_4$·5H$_2$O

Previous reports in this series of papers have dealt with the use of CD and NMR methods to characterise the diastereoisomers formed when an optically active aminoacidate or a prochiral α-aminomalonic acid derivative is coordinated to Co(III) together with *R,R*-picchxn [1–3]. Crystal structure determinations of the Λ-β$_1$-[Co(*R,R*-picchxn)(*R*-ABMA)]$^+$ and Λ-β$_1$-[Co(*R,R*-picstien)(*R*-AMMA)]$^+$ cations [2, 7] have confirmed these characterisations. Information on the *S*-APMAH$_2$ analogue, reported here, furnishes an unequivocal correlation between the structural and spectroscopic characteristics of diastereoisomers of this type.

A perspective view [8] of the complex cation is shown in Fig. 1. Significant bond lengths and angles in the coordination sphere, and for the coordinated aminomalonate, are listed in Table II. There is nothing unusual about the general coordination geometry of the cation. The stereochemistry of the APMA group is as predicted [1–3], with the β$_1$ complex geometry being adopted in conjunction with an *S* (*pro-R*) absolute configuration of the asymmetric acidate carbon atom. The propyl group has an extended staggered conformation.

In this arrangement the pendant carboxylic acid group is unable to complete an internal hydrogen bond to *H*(N2), as is the case with corresponding *R* (*pro-S*) diastereoisomers [2, 3, 7]. Hence the complex cation is zwitterionic, although in the crystal interatomic contacts to the water molecules are evident [O(41) 2.74(1) to O(W8) at $x, y-1, z$, 2.82(2) and 2.85(1) to O(W9) and O(W3) both at $\frac{1}{2}-x, -y, z-\frac{1}{2}$ respectively; O(W42) 2.81(1) to O(W1) at $1-x, y-\frac{1}{2}, \frac{1}{2}-z$, 2.71(3) and 2.82(7) Å to O(W5) and O(W10) both at $\frac{1}{2}+x, \frac{1}{2}-y, -z$ respectively]. Significant contacts however are observed for the interaction between the pendant carboxylic group and the adjacent pyridyl ring. This situation is akin to that observed in the structure of Λ-β$_1$-[Co(*R,R*-

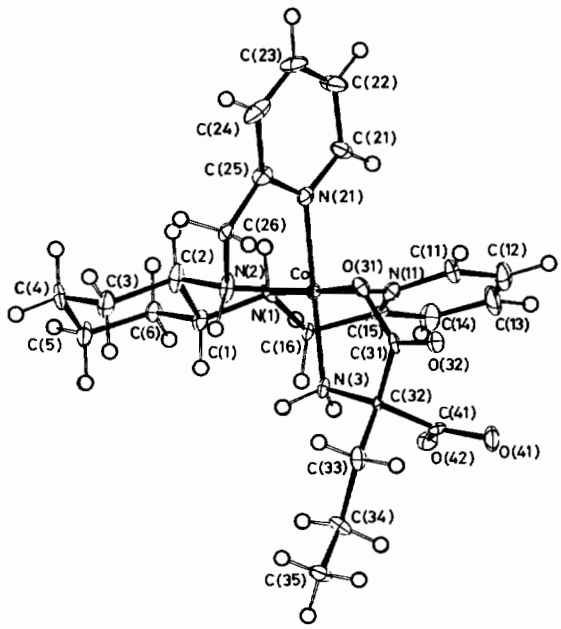


Fig. 1. Perspective view of the Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-APMA)]$^+$ cation. Thermal ellipsoids are drawn to include 35% probability.

picchxn)(*R*-ABMA)]$^+$ [3], in which the cation geometry appears to be stabilised not only by an internal hydrogen bond but also by hydrophobic stacking interactions involving the pendant phenyl ring and an adjacent coordinated pyridyl group. Although the planes of the pyridyl ring (1) and the pendant carboxylic group are not parallel (dihedral angle of 153°) a significant contact between this ring and the carbonyl–oxygen atom O(42) is apparent. This atom lies 3.06 Å from the plane of the pyridyl ring, and its projected position onto that plane is 0.29 Å, towards the centroid of the ring, from the centre of the N(11)–C(15) bond. The contact distances to N(11) and C(15) are 3.12(1) and 3.15(1) Å, respectively.

In the crystal lattice the complex cations form spiral chains of ions parallel to the *a* axis and utilising the screw axes at $x, \frac{1}{4}, 0$ and $x, \frac{3}{4}, \frac{1}{2}$. Contained within each of these chains, and hydrogen bonded via the N–H groups, are the perchlorate counter ions. This arrangement creates channels, again parallel to the *a* axis but centred about the alternate screw-axis positions of $x, \frac{1}{4}, \frac{1}{2}$ and $x, \frac{3}{4}, 0$, that contain the two sodium perchlorate ion pairs and the lattice water molecules held by a complex hydrogen bond net-

TABLE II. Significant Bonding Parameters in the Crystal Structure of Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-APMA)]$ClO_4 \cdot 2NaClO_4 \cdot 5H_2O$ [a]

Bond lengths (Å)			
Co–N(1)	1.919(7)	Co–N(11)	1.935(8)
Co–N(2)	1.964(7)	Co–N(21)	1.936(8)
Co–N(3)	1.976(7)	Co–O(31)	1.893(6)
N(3)–C(32)	1.473(10)	C(31)–O(31)	1.352(10)
C(31)–C(32)	1.492(13)	C(31)–O(32)	1.216(10)
C(32)–C(41)	1.548(13)	C(41)–O(41)	1.299(10)
C(32)–C(33)	1.565(12)	C(41)–O(42)	1.255(12)
C(33)–C(34)	1.555(14)	C(34)–C(35)	1.528(12)
Bond angles (°)			
N(11)–Co–N(1)	82.6(3)	N(11)–Co–N(2)	170.8(3)
N(21)–Co–N(2)	81.3(3)	N(21)–Co–N(3)	168.7(3)
N(1)–Co–N(2)	88.5(3)	N(1)–Co–O(31)	177.3(3)
N(3)–Co–O(31)	83.9(3)		
Co–N(11)–C(11)	125.5(7)	Co–N(21)–C(21)	126.5(7)
Co–N(11)–C(15)	113.6(7)	Co–N(21)–C(25)	114.5(7)
C(15)–N(11)–C(12)	120.9(9)	C(25)–N(21)–C(21)	118.9(9)
Co–N(1)–C(16)	110.0(5)	Co–N(2)–C(26)	109.1(6)
Co–N(1)–C(1)	106.6(6)	Co–N(2)–C(2)	105.3(6)
C(1)–N(1)–C(16)	114.8(8)	C(2)–N(2)–C(26)	111.7(8)
Co–N(3)–C(32)	111.1(5)	Co–O(31)–C(31)	114.3(6)
O(41)–C(41)–O(42)	125.5(7)	O(31)–C(31)–O(32)	119.7(9)
O(32)–C(41)–O(42)	113.6(7)	C(32)–C(31)–O(31)	117.0(8)
C(32)–C(41)–O(42)	120.9(9)	C(32)–C(31)–O(32)	123.3(9)
C(31)–C(32)–C(41)	111.9(7)	N(3)–C(32)–C(31)	108.8(5)
C(31)–C(32)–C(33)	107.5(8)	N(3)–C(32)–C(33)	112.0(6)
C(33)–C(32)–C(41)	108.8(7)	N(3)–C(32)–C(41)	107.8(5)
C(32)–C(33)–C(34)	114.7(8)	C(33)–C(34)–C(35)	109.0(9)

[a]e.s.d.s given in parentheses.

work. Each sodium ion is surrounded, in an irregular fashion, by a number of oxygen atoms from carboxylic groups, perchlorate ions and water molecules with Na···O contacts ranging from 2.20 to 2.62 Å.

Isomer Distributions in the Ternary Species

In the new complexes reported here, the pattern of isomer distribution mirrors that of analogous systems [1–3]. The Λ-β_1 diastereoisomers of both the *R*- and *S*-aminoacid complexes are observed to form in preference to Λ-β_2 species. In the α-aminomalonic acid derivatives these acids coordinate preferentially with *R* absolute configuration. In the $ABuBMAH_2$ and $ANMAH_2$ compounds this choice of coordination mode is observed exclusively for Λ-β complexes of *R,R*-picchxn. Characteristic high-resolution ^1H NMR data for the various diastereoisomers are given in Tables III, IV and V. Proton numbering schemes are shown in III and IV.

Hitherto it had been found that *R,R*-picchxn coordinates to Co(III) to yield complexes of Λ-β topology only, with this topology being maintained in a large number of substitution reactions. It was somewhat surprising to observe the formation of small amounts of Δ-α diastereoisomer intermediates

TABLE III. Characteristic ^1H NMR Data for the Norvaline and Norleucine Complexes

Measured δ or J	Complex[a]				
	A	B	C	D	E
H(14)	7.92	7.92	7.93	7.93	7.85
H(13)	8.35	8.36	8.36	8.36	8.31
H(12)	7.88	7.87	7.88	7.88	7.86
H(11)	8.21	8.24	8.22	8.24	9.01
H(24)	7.76	7.75	7.76	7.75	7.68
H(23)	8.17	8.17	8.17	8.17	8.12
H(22)	7.55	7.55	7.55	7.55	7.53
H(21)	7.02	7.00	7.02	7.00	7.17
$J_{13,14}$	8.7	7.9	7.8	7.9	8.4
$J_{12,13}$	7.1	7.5	7.2	7.7	7.7
$J_{11,12}$	5.3	5.6	5.4	5.4	5.5
$J_{23,24}$	7.7	7.8	7.7	7.6	7.8
$J_{22,23}$	7.7	7.6	7.7	7.4	7.4
$J_{21,22}$	5.6	5.6	5.7	5.9	5.9
H(N1)	6.90	7.38	6.86	7.40	7.78
H(N2)	6.90	6.88	6.86	6.88	7.44
Hα[b]	3.46	[c]	[c]	3.25	3.24
N*H*[b]	6.03	5.19	5.98	5.17	6.72
N*H*'[b]	3.71	4.83	3.67	4.84	4.40
C*H*$_3$[b]	0.82	0.84	0.82	0.87	0.90

[a]In DMSO-d_6; A = Λ-β_1-[CoL(*S*-norval)]$^{2+}$, B = Λ-β_1-[CoL(*R*-norval)]$^{2+}$, C = Λ-β_1-[CoL(*S*-norleu)]$^{2+}$, D = Λ-β_1-[CoL(*R*-norleu)]$^{2+}$, E = Λ-β_2-[CoL(*S*-norleu)]$^{2+}$, L = *R,R*-picchxn; chemical shifts are in ppm relative to TMS as internal standard; coupling constants are in Hz. [b]Aminoacidate signals. [c]Obscured by H_2O resonance.

TABLE IV. Characteristic ^1H NMR Data for the [Co(*R,R*-picchxn)(α-aminomalonate)]$^{2+}$ Complexes

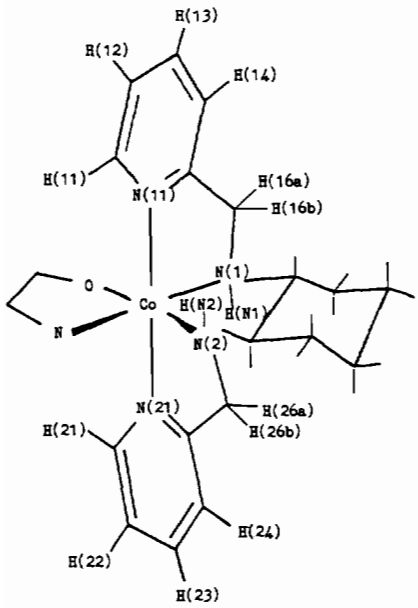
Measured δ or J	Complex[a]						
	A	B	C	D	E	F	G
H(14)	7.73	7.92	7.75	7.74	7.84	7.73	7.74
H(13)	8.31	8.32	8.22	8.21	8.32	8.10	8.14
H(12)	7.44	7.85	7.58	7.64	7.86	7.52	7.62
H(11)	7.70	8.21	8.02	7.99	8.20	9.17	8.98
H(24)	7.75	7.74	7.78	7.77	7.75	7.77	7.88
H(23)	8.11	8.14	8.15	8.15	8.13	8.19	8.26
H(22)	7.40	7.53	7.54	7.53	7.73	7.68	7.81
H(21)	6.86	7.06	7.00	6.96	7.04	8.34	8.53
$J_{13,14}$	7.3	7.9	7.7	7.5	7.8	6.4	7.6
$J_{12,13}$	8.1	7.7	8.8	8.0	8.1	8.1	7.9
$J_{11,12}$	5.9	5.6	5.3	5.4	5.4	5.2	5.7
$J_{23,24}$	6.8	8.0	8.3	7.4	7.7	7.9	8.2
$J_{22,23}$	7.4	7.5	8.0	7.7	7.8	8.1	7.5
$J_{21,22}$	7.0	5.6	5.3	5.5	5.6	5.3	5.7
*H*N1)	6.86	6.84	6.87	6.78	6.90	7.43[d]	[e]
H(N2)	10.74	10.76	7.02	6.98	9.65	7.73[d]	[e]
C*H*$_3$[b]	1.19	0.76	0.86	0.83	0.73	0.55	0.58
N*H*[b]	6.24	5.74	6.01	6.20	5.80	6.91[d]	[e]
N*H*'[b]	4.20	4.58	4.85	4.76	4.73	3.92[d]	[e]
H-phenyl	6.88–6.99						

[a]Spectra A–F were recorded in DMSO-d_6, G in D_2O; chemical shifts are reported in ppm relative to TMS or TSS as internal standards; coupling constants are in Hz; A = Λ-β_1-[CoL(*R*-ABuBMA)]$^+$, B = Λ-β_1-[CoL(*R*-ABuTMA)]$^+$, C = Λ-β_1-[CoL(*S*-ABuTMA)]$^+$, D = Λ-β_1-[CoL(*S*-APMA)]$^+$, E = Λ-β_1-[CoL(*R*-APMA)]$^+$, F, G = Δ-α-[CoL(ABuTMA)]$^+$, L = *R,R*-picchxn; no conjugate acid species are distinguished for these complexes; solutions used for the spectra of B, C and E were saturated in $NaClO_4$. [b]Aminoacid resonances. [c]Exchanged. [d]We do not distinguish between these pairs of resonances.

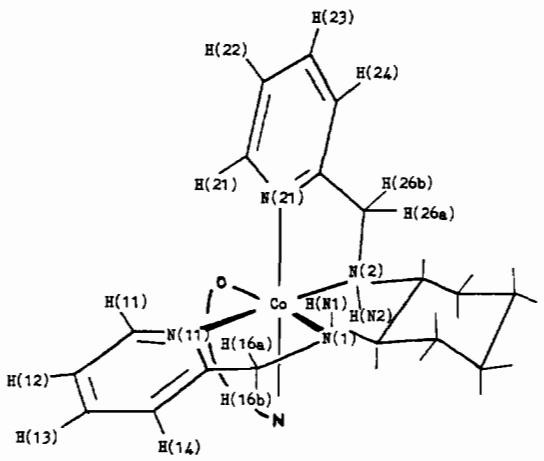
TABLE V. Characteristic ^1H NMR Data for the Ternary Complexes of α-(1-Naphthyl)alanine and its α-Aminomalonic Acid Precursor

Measured δ or J	Complex[a]		
	A	B	C
H(11)	7.45	8.32	8.26
H(13)	8.08	8.32	8.26
H(21)	6.80	6.99	6.98
H(23)	7.83	8.18	8.18
$J_{11,12}$	5.4	5.4	5.4
$J_{21,22}$	5.6	5.5	5.7
H(N1)	8.03	7.06	8.20
H(N2)	11.20	6.98	7.04
N*H*[b]	7.05	6.21	5.64
N*H*'[b]	6.62	4.14	5.46

[a]Recorded in DMSO-d_6 with TMS as internal standard; δ in ppm; J in Hz; A = Λ-β_1-[CoL(*R*-ANMA)]$^+$, B = Λ-β_1-[CoL(*S*-NA)]$^{2+}$, C = Λ-β_1-[CoL(*R*-NA)]$^{2+}$, L = *R,R*-picchxn. [b]Aminoacidate protons.



III



IV

during the reactions of certain of the *R*-aminoacids with Λ-β-[Co(*R*,*R*-picchxn)Cl_2]$^+$ under the conditions described here. No such species are observed in corresponding reactions with *S*-aminoacids. Their formation appears to be confined to *R*-aminoacidate complexes in which the aminoacid possesses a normal alkyl side chain; in the present case, *R*-norvaline and *R*-norleucine. A large scale (5 mmol based on Co) preparation of corresponding complexes of *R*-α-aminobutyric acid also showed that traces of the Δ-α intermediate form. In each case the low concentrations of these isomers precluded their separate crystallisation, and they have proved impossible to separate from the minor amounts of Λ-β_2 isomers also formed during these reactions (using ion exchange chromatographic techniques). Their nature was established, using NMR measurements of the mixtures, by comparison with Δ-α-[Co(*R*,*R*-picchxn)(ABuTMAH$_2$)](ClO$_4$)$_2$, the one Δ-α complex which was able to be isolated. It should be noted that the Δ-α isomer which is observed in the reaction of this α-aminomalonic acid derivative is the sole example among all those which have been investigated thus far.

In the reaction of ABuTMAH$_2$ with Λ-β-[Co(*R*,*R*-picchxn)Cl_2]$^+$ no Λ-β_2 diastereoisomer was detected. Fractional crystallisation of the larger orange band separated chromatographically from the reaction mixture yielded the pure Δ-α isomer as a minor product. This was due to its perchlorate salt being much less water soluble than that of Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ABuTMAH)]$^{2+}$ or its conjugate base. The CD spectrum of Δ-α-[Co(*R*,*R*-picchxn)(ABuTMA)]$^+$ confirms the absolute configuration of the complex with respect to the metal centre. ^{1}H NMR measurements in D_2O and DMSO-d_6 (if carried out quickly), Table II, prove the tetradentate to be coordinated in the α mode. The aromatic regions of the spectra of the Δ-α isomer in these solvents are shown in Fig. 2. In D_2O all eight pyridyl proton resonances are separately observed and no overlapping of N–*H* proton resonances is evident.

Inspection of the pattern of aromatic resonances immediately indicates that the compound is not a β complex. An upfield resonance at *ca.* 7 ppm, that of the ring-shielded proton *H*(21) in β diastereoisomers of this class of tetradentate, is not observed (the usual numbering scheme is shown in **III**). Rather, in D_2O, both the *H*(11) and *H*(21) signals are observed at lower field (8.98 and 8.53 ppm respectively). In DMSO-d_6 a similar pattern of chemical shifts is encountered. This result is consistent with observed chemical shift patterns for *H*(11) in other β_1 and β_2 diastereoisomers, depending upon whether this proton is in proximity to the amine or carboxyl group of the coordinated aminoacid, and also with related complexes of general form Δ,Λ-[Ru(diimine)$_2$(amino-acidate)]$^{n+}$, [9]. The absolute configuration of the coordinated α-aminomalonic acid in this complex is indefinite, although since the presence of α isomers has been detected only with *R*-aminoacidates we may infer that the bidentate is coordinated in the *pro-R* (*S*) mode.

To date it has been assumed that the observed preference for Λ-β topologies displayed by *R*,*R*-picchxn in its Co(III) complexes is based on thermodynamic factors. The results reported here confirm that this indeed is so. Δ-α-[Co(*R*,*R*-picchxn)-

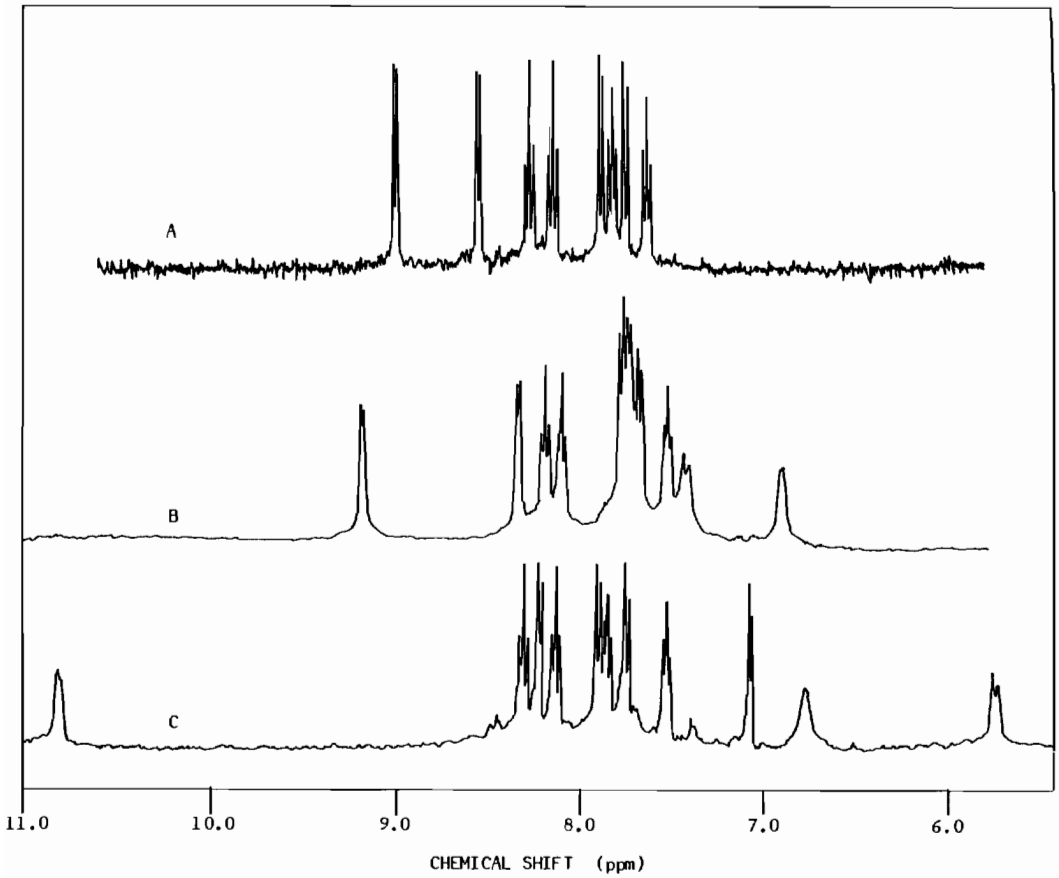


Fig. 2. The aromatic region of the 360 MHz ^{1}H NMR spectrum for A: Δ-α-[Co(*R*,*R*-picchxn)(ABuTMAH)]$^{2+}$ dissolved in D_2O; B, the same complex in DMSO-d_6 solution; C: the same solution as in B after 4 h showing the almost complete inversion of the octahedron to yield Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ABuTMAH)]$^{2+}$.

(ABuTMAH)]$^{2+}$ is kinetically stable in aqueous solution, permitting the assignment of its NMR signals by the usual spin-decoupling experiments. However this is not so for solutions of the complex in DMSO. In this solvent, Δ-α-[Co(*R*,*R*-picchxn)-(ABuTMAH)]$^{2+}$ isomerises ($t_{1/2}$ *ca.* 1.5 h at 25 °C) to yield the Λ-β_1 diastereoisomer (Fig. 2). Although the mechanism of this octahedral inversion is unknown, only the β_1 isomeric product is indicated by the NMR spectrum in DMSO-d_6 after about 24 h. This isomerisation process must reflect the magnitude of the chiral discrimination energy between the α and β_1 diastereoisomers, and must be thermodynamic in origin. Considering the detection limits of the technique we conclude that this discrimination must be greater than 10 kJ mol^{-1} in favour of the β_1 form. It should be noted that no signal is detectable in the final solution to indicate the presence either of a β_2 species or of the Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-ABuTMAH)]$^{2+}$ isomer. Therefore, our previous conclusions of the various isomers which are possible in these systems [1–3] are vindicated.

Decarboxylation Experiments

Complexes containing the coordinated α-aminomalonic acid derivatives were decarboxylated in 1 mol dm^{-3} HCl(aq) at 70 °C to give the diastereoisomeric products with coordinated aminoacids. Optical yields for these reactions were estimated by comparison of the products' ^{1}H NMR spectra with those of the pure isolated salts of chiral aminoacid species synthesised independently. In the case of the *R*- and *S*-NA complexes, the nature of the two diastereoisomers was established by reference to the characteristic CD spectra of Λ-β_1-[Co(*R*,*R*-picchxn)-(*R*- or *S*-aminoacidate)]$^{2+}$ cations and their elution characteristics on CM-Sephadex® C-25 cation exchange columns.

These procedures were not possible in the case of the reaction of the *R*-BuBMAH$_2$ complex, since complexes of the chiral aminoacids could not be synthesised independently. The assignment of the nature of the species present was made on the basis of the very close correlation between most of their NMR signals and those of the analogous pheH diastereoisomers.

TABLE VI. Ratios of Coordinated *R*- and *S*-Aminoacids Produced in the Decarboxylation Experiments[a]

Starting Complex	Aminoacid product	*R*- :*S*-Aminoacid ratio in the product
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-AMMAH)]$^{2+}$	alaH	89.0:11.0 ± 0.5[b]
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-AEMAH)]$^{2+}$	abuH	83.2:16.8 ± 2.7[c]
Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-AEMAH)]$^{2+}$	abuH	84.2:15.8 ± 1.3[c]
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-APMAH)]$^{2+}$	norvalH	69.8:30.2 ± 0.1
Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-APMAH)]$^{2+}$	norvalH	68.2:31.8 ± 1.2
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ABuTMAH)]$^{2+}$	norleuH	67.6:32.4 ± 1.0
Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-ABuTMAH)]$^{2+}$	norleuH	64.4:35.6 ± 1.0
Δ-α-[Co(*R*,*R*-picchxn)(ABuTMAH)]$^{2+}$	norleuH	50.0:50.0 ± 0.7
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ABMAH)]$^{2+}$	pheH	24.2:75.8 ± 3.1[c]
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ABuBMAH)]$^{2+}$	(4-bu^t)pheH	34.7:65.3 ± 0.1
Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ANMAH)]$^{2+}$	NAH, IIa, b	21.9:78.1 ± 1.4

[a]Reaction conditions: 1.0 M $HCl_{(aq)}$, 70 °C. [b]Data from ref. 1. [d]Data from ref. 2.

Further, the CD spectrum of the product mixture closely resembles that of a Λ-β_1 complex of an *S*-aminoacid [1–3]. Several decarboxylations were carried out in each case, and the results are presented in Table VI.

Complexes containing aminomalonates with linear alkyl side groups demonstrate a considerable degree of chiral induction during decarboxylation, resulting in products with the *R*-aminoacidate in excess. This result is independent of the choice of *R*- or *S*-aminomalonate as reactant. In either case the same ratio of *R*-aa:*S*-aa is obtained. This is consistent with analogous systems [1, 2] and suggests that the chiral inductions observed are determined by thermodynamic rather than kinetic influences.

Although coordinated *R*-ABuTMAH$_2$ and *R*-APMAH$_2$ demonstrate a preference for inversion during reaction to produce *R*-norleucine and *R*-norvaline, respectively, this is not the case in the corresponding reactions of coordinated α-aminomalonic acids with aromatic side chains. Of those that we have examined thus far, only Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-α-aminomalonate)]$^{n+}$ complexes result from reaction of the α-aminomalonic acid with Λ-β-[Co(*R*,*R*-picchxn)Cl$_2$]$^+$. Subsequent decarboxylation of these *R* (*pro-S*) ternary species results in product mixtures containing mainly coordinated *S*-aminoacids, *viz.* the relative configuration at the carbon is retained in the reactions.

This finding would be consistent with the stabilisation of an intermediate with *pro-S* configuration through hydrophobic stacking interactions, as was suggested for the analogous Λ-β_1-[Co(*R*,*R*-picchxn)-(*R*-ABMA)]$^+$ cation [2]. In order to further investigate this possibility we prepared the ABuBMAH$_2$ analogue, in which such a stacking interaction should be hindered by the tertiary butyl group. As is shown in Table VI, the degree of chiral induction upon decarboxylation in this latter case is somewhat less than that observed with the phenylalanine precursor. Hence it would appear that intramolecular aromatic interactions in these kinds of species are important determinants of chiral induction. Furthermore, a higher degree of stereoselectivity is observed when the complex Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ANMAH)]$^{2+}$ is decarboxylated in aqueous acid to produce *S*-NA species. In the diastereoisomeric product, the ratio *S*-Na:*R*-NA is 78.1:21.9 ± 1.4. An inspection of molecular models reveals that in the *S*-NA and *R*-ANMA complexes, somewhat greater aromatic interactions are permitted by the introduction of the larger naphthyl group.

An additional factor affecting selectivity is evidenced by the decrease observed in the preference for *R*-aminoacids containing linear alkyl side chains as these chains are increased in length. This may reflect greater hydrophobic interactions in the coordinated *R*-α-amino-α-alkyl-malonate precursors. The variation of the *R*-aa:*S*-aa ratio for these species ranges from 90:10 to 70:30 with respect to alanine and norvaline, respectively.

In conclusion, we have been able to show here, and in conjunction with previous work [1, 2], that systems based on, and analogous to, Co(III) complexes of chiral picchxn may be used to stereoselectively synthesise aminoacids in high optical yield. The synthetic utility of the system appears to extend to aminoacids with quite disparate types of side chains. This might be used to effect in the synthesis of isotopically-labelled aminoacids, given the choice of suitably labelled precursors and of decarboxylation solvent (e.g. D_2O *versus* H_2O). Furthermore it has been shown here that α-aminoacids which are not naturally occurring also may be produced stereoselectively, depending on the aminomalonic acid precursor chosen. The free aminoacids may be generated from the products with negligible epimerisation at the α-carbon atom simply by reaction of the complexes with aqueous sodium bicarbonate. As a consequence, the carbonato

complex also is generated, and this may be used to recycle the overall reaction. However, the sense of chiral induction in the products is obviously dependent on a number of chiral discriminatory factors. The appropriate choice of starting complex, Λ-β-[Co(*R,R*-picchxn)Cl_2]$^+$ or Δ-β-[Co(*S,S*-picchxn)Cl_2]$^+$ or its congeners, may be made keeping in mind the desired hand of aminoacid product.

It is noteworthy that the β topology of these complexes is a significant determinant of chiral induction in these reactions. In contrast, the decarboxylation of Δ-α-[Co(*R,R*-picchxn)(ABuTMAH)]$^{2+}$ under the same reaction conditions shows no selectivity, giving a mixture of diastereoisomers of *R*- and *S*-norleucine in equal proportions.

Supplementary Material

Lists of hydrogen atom parameters, anisotropic thermal parameters, complete Tables of bond lengths and angles, and observed and calculated structure factors are available from the authors.

Acknowledgements

We wish to thank the S.E.R.C. for financial support for this project, and the Royal Society/ Australian Science Academies for travel grants to P.A.W. and R.S.V., and Dr W. Robinson of the University of Canterbury, N.Z., for the collection of X-ray intensity data.

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