CHIRAL METAL COMPLEXES. 24. DIASTEREOISOMERISM IN TERNARY COMPLEXES OF THE TYPE [(AMINOACIDATE) (3*R*-METHYL-1,6-DI(2-PYRIDYL)-2,5-DIAZAHEXANE)COBALT(III)]

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CHIRAL METAL COMPLEXES. 24*. DIASTEREOISOMERISM IN TERNARY COMPLEXES OF THE TYPE [(AMINOACIDATE) (3R-METHYL-1,6-DI(2-PYRIDYL)-2,5-DIAZAHEXANE)COBALT(III)]

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A series of complexes of the type β-[Co(R-picpn)(R- or S-aa)]$^{n+}$, where R-picpn is 3R-methyl-1, 6-di(2-pyridyl)-2,5-diazahexane and aa is an α-aminoacidate, have been synthesised by reaction of Λ-α-[Co(R-picpn)Cl$_2$]$^+$ with the appropriate aminoacid in aqueous solution. The aminoacids used were valine, phenylalanine, tryptophane and proline, all of which have relatively bulky side-chains. The number of diastereoisomers produced with each chiral aminoacid, with the exception of proline, shows that variation of the size of the aminoacid side-chain has little effect in enforcing any particular geometry on the tetradentate in these ternary complexes. It is evident that more extensive substitution on the central chelate ring of the tetradentate is necessary to enforce its stereoselective coordination to Co(III).

The crystal and molecular structure of Δ-β_1-*exo*-[Co(R-picpn) (S-pro)](ClO$_4$)$_2$, where S-pro is the S-prolinate anion, has been determined. The crystals are orthorhombic, space group $P2_12_12_1$, with $a = 10.305(1)$, $b = 10.857(1)$ and $c = 22.650(2)$ Å, and $Z = 4$. The structure was refined by full-matrix least-squares methods to $R = 0.051$ for 2161 non-zero reflexions. This structural analysis proves the geometry of the complex, as had been deduced previously by nmr methods, to be correct in every detail, with both R-picpn amine nitrogen atoms having an S absolute configuration. The correlation of the spectroscopic characteristics of other related species, especially those derived from CD and nmr measurements, is made possible by the determination of the molecular structure of this S-pro complex.

Keywords: Chiral, complexes, cobalt, structure, tetradentates.

INTRODUCTION

Over the last few years we have been evaluating the extent and effects of the elements of chiral discrimination in coordination complexes.[1] Particular attention has been focussed on complexes containing facultative tetradentate ligands together with aminoacidates. These kinds of complexes embody a wealth of stereochemical information and particular species which probe both steric and electronic effects on stability can be devised. In earlier studies we examined some ternary Co(III) complexes containing an aminoacid and the chiral ligand§ R-picpn.[2]

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§R-picpn = 3R-methyl-1,6-di(2-pyridyl)-2,5-diazahexane, alaH = alanine, picen = 1,6-di(2-pyridyl)-2,5-diazahexane, valH = valine, pheH = *phenylalanine*, trpH = tryptophane, proH = proline, glyH = glycine.

The tetradentate was first incorporated into complexes of Co(III) and Cr(III) by Bosnich[3] who proposed that the most stable or least soluble diastereoisomer, which could be isolated from the appropriate reaction mixture, adopted the Λ-α configuration. This conclusion was brought into doubt by other workers,[4] but was subsequently shown to be in fact true by the careful work of Michelsen[5] and confirmed in related studies of octahedral inversions which could be observed during the reaction of Λ-α-[Co(R-picpn)Cl$_2$]$^+$ with various other ligands.[2] The nature of the Λ-α complex was proven crystallographically,[6,7] although it has now become apparent that other diastereoisomers may also be isolated under certain conditions.[2,5]

One of our particular interests has been the elucidation of the causes of chiral discriminations observed in complexes of the kind mentioned above. With this in mind, we have synthesised complexes, generally formulated as [Co(R-picpn) (ala)]$^{2+}$, and analogues, and have shown that of many possible diastereoisomeric possibilities, but few geometries are obtained.[8,9] With S-alaH and R-alaH three and two, respectively, species are formed in their reactions with Λ-α-[Co(R-picpn)Cl$_2$]$^+$ in aqueous solution at steam bath temperatures. All species contain the tetradentate with β-coordination geometry; both Δ and Λ absolute configurations are permitted by the tetradentate.

Nevertheless, alanine is the least discriminating optically active aminoacid by virtue of the relatively small size of its side chain. In view of our efforts[10] to use such complexes in reactions leading to stereospecifically produced products, we thought it worthwhile to pursue the study of Co(III) complexes of R-picpn and chiral aminoacidates which contained rather bulkier side groups than alanine. Here we report the results of this study, which shows in fact that the single methyl substitution in the picen backbone is not sufficient to induce stereospecific coordination, irrespective of the nature of the aminoacidate chosen. These results are reviewed in the light of molecular mechanics calculations carried out on some related complexes.[11]

EXPERIMENTAL

Physical Methods

Electronic and circular dichroism (CD) spectra were recorded using a Pye Unicam SP8000 spectrophotometer and a Jobin-Yvon CNRS Dichrographe III, respectively. The 360 MHz ^{1}H nmr spectra were obtained using a Bruker WM360 instrument with solutions prepared in D$_2$O or dmso-d_6 and results are reported relative to TMS or TSS as internal standards. Saturated solutions were used. All measurements were carried out at 298 K.

CHN analyses were performed by Mrs A. Dams of the Department of Chemistry, University College, Cardiff and water of hydration was determined separately using a Stanton Redcroft TG 750 thermogravimetric balance.

Chromatographic separations were carried out using CM Sephadex® C–25 cation exchange resin in the Na$^+$ cycle, and fractions were collected upon elution using an LKB 2070 Ultrorac® II collector. *Exo: endo* isomer ratios in solids isolated from the various fractions were obtained by integration of appropriate signals in nmr spectra.

Syntheses

Λ-α-[Co(R-picpn)Cl$_2$]ClO$_4$.

This complex was synthesised as reported previously.[2]

Λ-β_2-exo, endo-$[Co(R$-$picpn)(S$-$val)](ClO_4)_2$

An aqueous solution (40 cm^3) containing 0.506g (0.104 mmol) of Δ-α-$[Co(R$-picpn)-Cl$_2]$ClO$_4$ was warmed to 40°C. To this was added an aqueous solution (20 cm^3) containing 0.597g (0.510 mmol) of S-valine and 1.0 cm^3 of 1.0M NaOH(aq) and the resulting solution was stirred at 40°C overnight during which time its colour changed from cherry-red to orange. The solution was then diluted five-fold with distilled water and applied to a 30 × 1.5cm CM Sephadex® C-25 column in the Na$^+$ cycle. The column was flushed thoroughly with water, and elution carried out with an aqueous 0.1M NaClO$_4$ solution. Three orange bands developed, the first two being considerably overlapped. The slowest moving band separated cleanly.

Fractions of the three bands were collected, their electronic and CD spectra measured, and values of $\Delta Abs_\lambda/Abs_\lambda$ for each fraction calculated.* The fractions eluting fastest had consistent $\Delta Abs_\lambda/Abs_\lambda$ values and the several solutions were combined and evaporated to dryness at 40°C *in vacuo*. The solid residue was redissolved in the minimum volume of cold water and allowed to slowly evaporate over silica gel at room temperature. Over several days, an orange crystalline precipitate formed. This was collected at the pump, washed with a few drops of ice-cold water and sucked dry. Analysis showed it to contain the title compounds with an *exo:endo* ratio of 1:7.0. This means that both isomers were eluted from the column with negligible separation under the conditions employed.

Λ-β_1-exo,endo-$[Co(R$-$picpn)(S$-$val)](ClO_4)_2 \cdot 2H_2O$

Fractions from the trailing edge of the second eluted band above were also shown, within experimental error, to have consistent $\Delta Abs_\lambda/Abs_\lambda$ values. These fractions were combined and subjected to the above work up to yield the title compounds with an *exo:endo* ratio of 1:0.6. The *endo* isomer was a pale orange microcrystalline powder, mixed with small crystals of the *exo* isomer, but the bulk of the latter crystallized as stout dark orange crystals which could be separated by hand picking.

The fractions intermediate between those containing the Δ-β_2 and Λ-β_1 isomers had CD spectra characteristic of a Λ-β_2 isomer, but insufficient complex was present to allow isolation.

Δ-β_1-exo,endo-$[Co(R$-$picpn)(S$-$val)](ClO_4)_2 \cdot 2H_2O$

The slowest eluting and cleanly separated band mentioned above was fractionated and analysed as described. All fractions had constant $\Delta Abs_\lambda/Abs_\lambda$ values and so were combined and worked up to yield the title compounds as a red-orange microcrystalline precipitate with an *exo: endo* ratio of 6.4:1. The presence of both *exo* and *endo* isomers indicates that these isomers also eluted with negligible separation under the conditions employed.

Spectral (electronic and CD) and analytical data for the $[Co(R$-picpn)(S-val)]$(ClO_4)_2$ complexes and congeners are given in Tables I, II and III.

Δ-β_2-endo-$[Co(R$-$picpn)(R$-$val)](ClO_4)_2$

Λ-α-$[Co(R$-picpn)Cl$_2]$ClO$_4$ and R-valine were reacted as described above for the S-valine case. Elution of the reaction mixture yielded three orange bands, the slowest of

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*The wavelength was that of the visible absorbance maximum and that of the extremum in the visible CD in each case.

TABLE I

Isomeric ratios and yields for the isolated complexes [Co(R-picpn)(aa)](ClO₄)₂·nH₂O.

Isomer description	exo:endo ratio	Amino acidate	% yield*
Δ-β_2-	1:7.0	S-val	3.7
Λ-β_1-	1:0.6	S-val	32.3
Δ-β_1	6.4:1	S-val	17.8
Δ-β_2-	0:1	R-val	16.4
Λ-β_1-	1:1.1	R-val	23.4
Δ-β_1-	5.4:1	R-val	28.6
Δ-β_2-	3.3:1	S-phe	9.2
Δ-β_2-	1:0	S-phe	} 3.0
Λ-β_2-	1:1	S-phe	
Λ-β_2-	1:1	S-phe	} 42.4
Λ-β_1-	1:1	S-phe	
Δ-β_1-	1:1	S-phe	29.9
Δ-β_2-	0.4:1	R-phe	14.6
Λ-β_1-	1:0.9	R-phe	20.3
Δ-β_1-	6.3:1	R-phe	21.0
Δ-β_1-	0:1	S-trp	5.7
Λ-β_1-	1:1.3	S-trp	3.0
Λ-β_2-	1:0.9	S-trp	27.2
Δ-β_1-	1:0	S-trp	3.5
Λ-β_1-	1:0.6	R-trp	2.7
Δ-β_2-	1:1	R-trp	34.8
Δ-β_1-	1:0	R-trp	7.2
Δ-β_1-	1:0	S-pro	5.7

*Based on Co.

TABLE II

Microanalytical data for the complexes [Co(R-picpn)(aa)](ClO₄)₂·nH₂O.

Isomer description[a]	Amino Acidate	n	% Found (% Calculated)			
			C	H	N	H₂O
Δ-β_2-exo, endo-	S-val	0	37.9(38.1)	4.8(4.8)	10.9(11.1)	
Λ-β_1-exo, endo-	S-val	2	35.8(36.0)	4.5(5.1)	10.1(10.5)	5.2(5.4)
Δ-β_1-exo, endo-	S-val	2	35.5(36.0)	5.0(5.1)	10.2(10.5)	6.0(5.4)
Δ-β_2-endo-	R-val	0	38.1(38.1)	4.8(4.8)	10.9(11.1)	
Λ-β_1-exo, endo-	R-val	0	38.0(38.1)	4.8(4.8)	11.1(11.1)	
Δ-β_1-exo, endo-	R-val	0	38.0(38.1)	4.2(4.8)	10.3(11.1)	
Δ-β_2-exo, endo-	S-phe	0	42.1(42.5)	4.0(4.4)	9.8(10.3)	
Λ-β_1, β_2-exo, endo-	S-phe	1	41.4(41.4)	4.4(4.6)	8.9(10.1)	2.0(2.8)
Δ-β_1-exo-	S-phe	0	42.4(42.5)	4.4(4.4)	9.4(10.3)	
Δ-β_2-exo, endo-	R-phe	3	39.4(39.4)	5.1(5.0)	9.1(9.6)	8.0(7.9)
Λ-β_1-exo, endo-	R-phe	2	40.3(40.4)	4.8(4.8)	9.3(9.8)	5.0(5.4)
Δ-β_1-exo, endo-	R-phe	2	40.8(40.4)	4.6(4.8)	9.8(9.8)	6.0(5.4)
Δ-β_1-endo-	S-trp	0	43.2(43.5)	4.7(4.4)	11.5(11.7)	
Λ-β_1-exo, endo-	S-trp	2	40.4(41.4)	4.6(4.7)	11.2(11.2)	5.0(4.8)
Λ-β_1-exo, endo-	S-trp	2	41.4(41.4)	4.5(4.7)	10.4(11.2)	5.2(4.8)
Δ-β_1-exo-	S-trp	0	43.9(43.5)	4.8(4.4)	11.5(11.7)	
Λ-β_1-exo, endo-	R-trp	0	43.0(43.5)	4.4(4.4)	11.5(11.7)	
Δ-β_2-exo, endo-	R-trp	0	43.1(43.5)	4.3(4.4)	11.5(11.7)	
Δ-β_1-exo-	R-trp	0	43.2(43.5)	4.4(4.4)	11.6(11.7)	
Δ-β_1-exo-	S-pro	0	38.3(38.2)	4.4(4.5)	11.0(11.1)	

[a] exo:endo ratios are given in Table I.

TABLE III
Electronic and CD spectral data for the complexes $[Co-(R\text{-picpn})(aa)]^{2+}$.

Isomer description	exo:endo ratio	Amino acidate	λ (nm)	$10^{-3}\varepsilon$ (dm²mol⁻¹)	λ (nm)	$\Delta\varepsilon$ (dm²mol⁻¹)
$\Delta\text{-}\beta_2\text{-}$	1:7.0	S-val	480	1.15	462	−9.48
			349	1.32	359	+4.71
					298	−0.88
$\Lambda\text{-}\beta_1\text{-}$	1:0[a]	S-val	480	1.54	478	+13.00
			347	1.33	352	−4.78
$\Lambda\text{-}\beta_1\text{-}$	1:0.6	S-val	480	1.29	478	+11.47
			347	1.10	352	−4.03
$\Lambda\text{-}\beta_1\text{-}$	0:1[b]	S-val	480	1.34	478	+8.92
			347	1.15	352	−2.80
$\Delta\text{-}\beta_1\text{-}$	6.4:1	S-val	490	2.01	476	−14.33
			355	1.86	353	+7.24
$\Delta\text{-}\beta_2\text{-}$	1:0	R-val	480	1.82	538	+9.19
			354	1.75	480	−20.09
					350	+8.87
$\Lambda\text{-}\beta_1\text{-}$	1:1.1	R-val	486	1.79	504	+26.03
			352	1.53	354	−0.92
$\Delta\text{-}\beta_1\text{-}$	5.4:1	R-val	490	2.08	482	−15.19
			354	1.74	352	+10.13
$\Delta\text{-}\beta_2\text{-}$	3.3:1	S-phe	478	2.11	530	+2.96
			348	2.40	460	−27.46
					352	+11.71
$\Lambda\text{-}\beta_1\text{-}, \beta_2\text{-}$	1:1[c]	S-phe	482	1.69	484	+18.60
			340	1.80	346	−3.32
$\Delta\text{-}\beta_1$	1:0	S-phe	492	2.04	478	−14.86
			350	1.98	354	+8.07
$\Delta\text{-}\beta_2\text{-}$	0.4:1	R-phe	482	1.89	533	+4.70
			345	2.22	478	−13.80
					348	+8.31
$\Lambda\text{-}\beta_1\text{-}$	1:0.9	R-phe	482	1.86	500	+21.16
			345	2.14	354	−2.28
$\Delta\text{-}\beta_1\text{-}$	6.3:1	R-phe	488	2.06	480	−16.38
			345	2.14	346	+10.32
$\Delta\text{-}\beta_1\text{-}$	0:1	S-trp	470	2.06	536	+6.12
			354	3.72	465	−29.75
					353	+2.45
$\Lambda\text{-}\beta_1\text{-}$	1:1.3	S-trp	465	2.35	485	+20.48
			342	3.76	397	−7.27
					355	−10.64
					308	+2.84
$\Lambda\text{-}\beta_2\text{-}$	1:0.9	S-trp	450	1.75	495	+22.91
			335	3.50	430	−5.81
					390	−8.11
					338	−2.30
					311	+1.53
$\Delta\text{-}\beta_1\text{-}$	1:0	S-trp	480	2.42	479	−20.09
			347	3.90	398	−3.41
					352	+4.48
					310	−2.33
$\Lambda\text{-}\beta_1$	1:0.6	R-trp	460	1.76	469	+23.90
			345	4.41	351	−3.93
$\Delta\text{-}\beta_2$	1:1[b]	R-trp	450	1.67	483	−14.02
			349	3.45	388	+5.86
					348	+4.60
$\Delta\text{-}\beta_1$	1:0	R-trp	472	2.53	483	−17.93
			352	3.82	403	+10.12
					359	+16.09
					299	−13.76
$\Delta\text{-}\beta_1\text{-}$	1:0	S-pro	492	2.11	522	−9.41
			352	1.80	478	−6.20
					356	+5.94
					308	−1.84

[a]Hand-picked crystals (see Experimental section). [b]Calculated from. $\Lambda\text{-}\beta_1\text{-}exo\text{-}$ and $\Lambda\text{-}\beta_1\text{-}exo,\ endo\text{-}$ data. [c]Each of the four diastereoisomers is of approximately equal abundance.

which separated cleanly. Fractions from the fastest moving band had consistent $\Delta Abs_\lambda/Abs_\lambda$ values and were combined and worked up as described above, yielding the title compound as an orange microcrystalline powder. The fractions immediately following this band, up to, but not including the ensuing band, were worked up yielding an orange microcrystalline powder which was shown to be a mixture of six isomers. Two were demonstrated to be the Δ-β_1-*exo, endo* isomers described below, and a third the present title compound. By analogy to other reactions described later it is likely that the other isomers are the Δ-β_2-*exo* and Λ-β_2- *exo, endo* complexes. It has not yet been possible to separate these isomers by fractional crystallisation or chromatographic techniques.

Λ-β_1-exo, endo-*[Co(R-picpn)(R-val)](ClO₄)₂*

Fractions from the trailing edge of the second eluted band were shown to have consistent $\Delta Abs_\lambda/Abs_\lambda$ values and were combined and worked up to yield the title compounds as a red-orange microcrystalline powder with an *exo:endo* ratio of 1:1.1. The isolation of both *exo* and *endo* isomers indicates that negligible separation of these isomers was achieved under the conditions employed.

Δ-β_1-exo, endo-*[Co(R-picpn)(R-val)](ClO₄)₂*

All fractions from the third and cleanly separated band were shown to have consistent $\Delta Abs_\lambda/Abs_\lambda$ values. They were combined and worked up as described above to yield the title compounds as small red-orange featherlike crystals with an *exo:endo* ratio of 5.5:1. The presence of *exo* and *endo* isomers indicates in this case also that both isomers eluted from the column with negligible separation under the conditions employed.

Δ-β_2-exo, endo-*[Co(R-picpn)(S-phe)](ClO₄)₂*

S-Phenylalanine was reacted with Λ-α-[Co(R-picpn)Cl₂]ClO₄ as described above. Elution of the reaction mixture yielded two overlapping orange bands followed by a third and cleanly separated band. Fractions from the leading edge of the fastest moving band had constant $\Delta Abs_\lambda/Abs_\lambda$ values and these were combined and worked up to yield the title compounds as an orange microcrystalline powder with an *exo:endo* ratio of 3.3:1.

Fractions immediately following those taken above were worked up and shown to contain a further amount of the Δ-β_2-*exo* and *endo* isomers, the *exo* isomer eluting from the column at a slower rate.

Λ-β_1, β_2-exo, endo-*[Co(R-picpn)(S-phe)](ClO₄)₂·H₂O*

The second band to elute was fractioned and electronic and CD spectra of the fractions were measured. The overall band was shown to consist of fractions of very similar CD, but a slight shift in wavelength of the maximum absorbance in the visible region could be discerned and this was accompanied by a change in the values of $\Delta Abs_\lambda/Abs_\lambda$ throughout. Therefore this band was split into two halves; fractions up to that of maximum CD value were separated from those following. Work up of each yielded orange microcrystalline solids, both of which were shown to contain four isomers. Δ-β_2-*exo, endo* isomers were present in both samples, and the forerunning fractions

were enriched in the Δ-β_2-endo isomer while the following fractions were enriched in the Λ-β_1-exo isomer. The presence of Δ-β_1 and Λ-β_2 isomers in both parts of this band indicates that these isomers eluted from the column with very little separation. However, some degree of separation of the Λ-β_1-exo, endo isomers was achieved under the conditions employed, the endo isomer eluting fastest.

Δ-β_1-exo-$[Co(R$-picpn$)(S$-phe$)](ClO_4)_2$

$\Delta Abs_\lambda/Abs_\lambda$ values were constant for all fractions collected from the slowest moving and cleanly separated band. The fractions were combined and worked up to yield the title compound as a dark orange crystalline powder.

Δ-β_2-exo, endo-$[Co(R$-picpn$)(R$-phe$)](ClO_4)_2 \cdot 3H_2O$

R-Phenylalanine was reacted with Δ-α-$[Co(R$-picpn$)Cl_2]ClO_4$ as described above. Elution of the reaction mixture yielded four bands. Fractions collected from the fastest moving band were combined and worked up to yield the title compounds as an orange micro-crystalline powder. The exo:endo ratio was 0.4:1. Optically active species in the second band were found to be too dilute to permit isolation of any solids.

Δ-β_2-exo,endo-$[Co(R$-picpn$)(R$-phe$)](ClO_4)_2 \cdot 2H_2O$

Fractions from the third eluted band had constant $\Delta Abs_\lambda/Abs_\lambda$ values and were combined and worked up to yield the title compounds as a pale orange microcrystalline powder. The exo:endo ratio was 1:0.9.

Δ-β_1-exo,endo-$[Co(R$-picpn$)(R$-phe$)](ClO_4)_2 \cdot 2H_2O$

Upon complete elution, the slowest moving band was essentially separate from the preceeding bands. CD and electronic spectra were measured and used to eliminate fractions of likely overlap. The remaining fractions had constant $\Delta Abs_\lambda/Abs_\lambda$ values, and were combined and worked up to yield the title compound as an orange microcrystalline powder.

Λ-β_1-exo, endo-$[Co(R$-picpn$)(S$-trp$)](ClO_4)_2 \cdot 2H_2O$

A reaction mixture was chromatographed as described above. Fractions from the tail of the fastest moving band were shown to have a CD maxima at 484nm for the greater part of the band, and at 494nm for fractions from the trailing edge. The change in wavelength of the major visible absorbance was accompanied by a change in the value of $\Delta Abs_\lambda/Abs_\lambda$. The former fractions were combined and worked up to yield the tile compounds as an orange microcrystalline powder with an exo:endo ratio of 1:1.3.

Λ-β_2-exo, endo-$[Co(R$-picpn$)(S$-trp$)](ClO_4)_2 \cdot 2H_2O$

Fractions from the trailing edge of the faster moving band were combined and worked up to yield the title compounds as an orange microcrystalline powder with exo:endo ratio of 1:0.9.

Δ-β_1-exo-*[Co(R-picpn)(S-trp)](ClO$_4$)$_2$*

Fractions from the slower moving and cleanly separated band were shown to have constant $\Delta Abs_\lambda/Abs_\lambda$ values and so were combined and worked up to yield the title compound as an orange microcrystalline powder.

Λ-β_1-exo, endo-*[Co(R-picpn)(R-trp)](ClO$_4$)$_2$*

R-tryptophan was reacted with Λ-α-[Co(*R*-picpn)Cl$_2$]ClO$_4$ as described above. Elution of the reaction mixture gave rise to two orange bands, the faster of which was also shown by spectral measurements to contain numerous isomers. Fractions from the leading edge of the faster moving band had constant $\Delta Abs_\lambda/Abs_\lambda$ values and these were combined and worked up to yield the title compounds as an orange microcrystalline powder with an *exo:endo* ratio of 1:0.6.

Δ-β_2-exo, endo-*[Co(R-picpn)(R-trp)](ClO$_4$)$_2$*

Fractions collected from the trailing edge of the faster moving band were worked up in several portions as described above to yield the title compounds as dark orange microcrystalline powders. The isomeric ratio varied in the different portions, but was approximately 1:1 overall. The faster eluting fractions were enriched in the *exo* isomer while the slower eluting fractions were enriched in the *endo* isomer. This indicates that some degree of separation of the isomers was achieved under the conditions employed.

Δ-β_1-exo-*[Co(R-picpn)(R-trp)](ClO$_4$)$_2$*

All fractions collected from the slower moving and cleanly separated band were shown to have constant $\Delta Abs_\lambda/Abs_\lambda$ values and were combined and worked up to yield the title compound as small orange hair-like needles.

Δ-β_1-exo-*[Co(R-picpn)(S-pro)](ClO$_4$)$_2$*

S-proline was reacted with Λ-α-[Co(*R*-picpn)Cl$_2$]ClO$_4$ as described above. Elution of the reaction mixture gave rise to only one small orange band accompanied by several yellow-brown bands. The orange band was shown by spectral measurements to contain several isomers.

Fractions which, within experimental error, gave constant $\Delta Abs_\lambda/Abs_\lambda$ values were combined and worked up as previously described. Fractions from the trailing edge of this band yielded the title compound as squat equant crystals which were the colour of red wine. No other complex could be isolated from this reaction mixture. The corresponding reaction with *R*-proline failed to yield any aminoacid complex in sufficient quantity to be isolated, although faint orange bands were discerned on chromatographic columns during elution with aqueous NaClO$_4$.

The Crystal and Molecular Structure of Δ-β_1-exo-*[Co(R-picpn) (S-pro)](ClO$_4$)$_2$*

Crystal Data: C$_{20}$H$_{28}$N$_5$O$_{10}$Cl$_2$Co,M_r = 628.3, orthorhombic,a = 10.305(1),b = 10.857(1), c = 22.650(2) Å,U = 2534.1 Å^3,Z = 4,D_c = 1.647 Mg m^{-3},$F(000)$ = 1296,μ(Mo-$K\alpha$) = 0.98 mm^{-1}. Systematic absences: $h00$ when h = $2n+l$, $0k0$ when k = $2n+1$, $00l$ when

$l = 2n+1$, space group $P2_12_12_1$ (No. 19).

Cell parameters were determined initially from single crystal oscillation and Weissenberg photographs using Cu-$K\alpha$ radiation. Accurate cell parameters were obtained from a least-squares fit to diffractometer data. Intensities were collected on an Enraf-Nonius CAD4 diffractometer using Mo-$K\alpha$ radiation by Dr M.B. Hursthouse at Queen Mary College, London. Of the 2542 reflexions recorded 2161 had $I>3\sigma(I)$ and these were used for the structure analysis. The intensities were corrected for Lorentz, polarisation and absorption effects, the latter using an empirical method. Minimum, maximum and average transmission constants were 95.41, 99.95 and 97.24%, respectively.

The structure was solved by the heavy atom method and refined by full-matrix least-squares calculations in which the function minimised was $\Sigma w\Delta^2$. The weight used for each reflexion was that obtained from counting statistics. After several cycles of anisotropic refinement a difference synthesis was used to locate all of the hydrogen atoms. These were optimised assuming C-H and N-H to be 1.0 Å, and refinement was continued with the H atoms held in these positions and with $B = 2.5$ Å^2.

TABLE IV

Final atomic coordinates (fractional x10^4) for non-hydrogen atoms with estimated standard deviations in parentheses.

	x/a	y/b	z/c
Co	3874.1(10)	6469.5(9)	1745.2(5)
N(11)	5491(7)	7235(6)	1488(3)
N(12)	3051(7)	7746(6)	1268(3)
N(13)	2100(6)	5847(6)	1874(3)
N(14)	3895(7)	5253(6)	1095(3)
N	3944(7)	7506(5)	2467(3)
O(1)	4614(5)	5219(5)	2219(2)
O(2)	5462(5)	4802(5)	3090(2)
C(1)	5017(7)	5528(8)	2745(4)
C(2)	4867(8)	6891(7)	2902(4)
C(3)	4286(11)	7069(9)	3511(4)
C(4)	2925(13)	7148(13)	3383(5)
C(5)	2765(9)	7876(9)	2824(4)
C(111)	5324(9)	8091(8)	1057(4)
C(112)	6376(8)	8813(8)	868(4)
C(113)	7539(10)	8715(10)	1138(4)
C(114)	7708(10)	7845(10)	1573(5)
C(115)	6672(7)	7104(8)	1730(4)
C(11)	4016(8)	8202(7)	816(4)
C(12)	1841(8)	7242(8)	1022(4)
C(m12)	972(8)	8206(8)	707(4)
C(13)	1166(8)	6672(7)	1549(4)
C(14)	2061(8)	4535(8)	1666(4)
C(141)	2885(8)	4431(8)	1139(4)
C(142)	2723(9)	3532(8)	715(4)
C(143)	3603(12)	3486(10)	246(5)
C(144)	4622(10)	4309(10)	214(4)
C(145)	4725(8)	5178(8)	650(4)
Cl(1)	5713(2)	4148(2)	8106(1)
O(11)	5448(10)	3859(9)	8701(4)
O(12)	5911(18)	3150(10)	7772(5)
O(13)	4643(11)	4753(14)	7879(5)
O(14)	6661(11)	5051(13)	8081(5)
Cl(2)	6316(4)	5083(3)	5544(2)
O(21)	7096(11)	5710(10)	5160(6)
O(22)	6329(13)	5397(14)	6124(6)
O(23)	5090(10)	4961(17)	5345(4)
O(24)	6828(13)	3866(10)	5521(4)

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The refinement process was terminated when the change in the minimisation function was <1%, at which stage the maximum shift in any parameter was <0.1σ. A final difference map showed no unusual features, with the maximum electron density <|0.7| e Å^{-3}. The final R, based on all 2161 reflexions, was 0.051, and R_w $[=(\Sigma w \Delta^2 / \Sigma w |F_o|^2)^{1/2}]$ was 0.056.

All calculations were carried out on a FACOM M3405 computer using programmes written by F.S.S. Scattering factors used were taken from *International Tables for X-Ray Crystallography*,[12] with corrections being applied for anomalous dispersion. Final atomic parameters are given in Tables IV and V. Hydrogen atom positions are included because of their relevance to the nmr measurements reported here. Tables of anisotropic thermal parameters and observed and calculated structure factors have been deposited with the Editor and are available upon request.

RESULTS AND DISCUSSION

The Crystal and Molecular Structure of Δ-β_1-exo-[Co(R-picpn) (S-pro)](ClO$_4$)$_2$

The molecular structure of the cation, together with the non-hydrogen atomic labelling scheme,[13] is shown in Figure 1. Because of the internal chiral labels, R-picpn and S-proH, no ambiguity exists as to the Δ absolute configuration of the complex ion. On the basis of ^{1}H nmr spectral studies we had previously assigned[9] a quite analogous complex to be the Δ-β_1-exo-[Co(R-picpn)(S-ala)]$^{2+}$ diastereoisomer. It was not possible

TABLE V

Atomic parameters (coordinates: fractional × 10^3) for hydrogen atoms

|	x/a	y/b	z/c
H(m12a)	76	890	100
H(m12b)	142	859	36
H(m12c)	14	783	58
H(112)	624	942	54
H(113)	828	924	102
H(114)	856	776	177
H(115)	680	642	203
H(142)	196	295	74
H(143)	350	283	−5
H(144)	526	424	−12
H(145)	547	581	63
H(N12)	281	845	154
H(N13)	189	586	230
H(N)	428	834	237
H(2)	574	729	288
H(3a)	465	780	372
H(3b)	447	631	377
H(4a)	249	763	372
H(4b)	252	635	334
H(5a)	280	880	290
H(5b)	196	767	262
H(11a)	383	907	72
H(11b)	393	768	45
H(12)	209	662	72
H(13a)	84	732	181
H(13b)	42	616	140
H(14a)	240	399	199
H(14b)	114	429	158

For hydrogen atoms B = 2.5 Å^2.
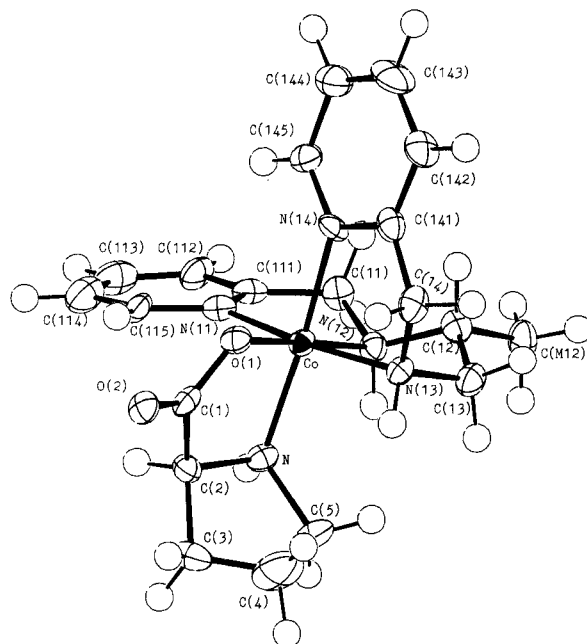
FIGURE 1 Perspective drawing of the complex cation Δ-β_1-exo- $[Co(R$-picpn$)(S$-pro$)]^{2+}$

to grow crystals of this S-ala complex of sufficient quality as to enable an X-ray structural determination to be carried out. However, it is clear that the present S-pro analogue has exactly the same stereochemical characteristics, as demonstrated by CD and ^{1}H nmr spectral studies (*vide infra*). The present structure shows that our earlier deductions[9] were correct in every detail. The aminoacidate is coordinated in the β_1 fashion, the R-picpn ligand is disposed in the Δ-β-exo mode, and the absolute configuration of $N(12)$ is opposite to that enforced in the Λ-α-$[Co(R$-picpn$)Cl_2]^+$ complex (or indeed in any Λ-α diastereoisomer of this tetradentate).

No unusual structural features attend the molecular cation. A list of bond lengths and angles is given in Table VI, which includes data for the perchlorate anions. Figure 2 shows a view of the packing in the unit cell. Hydrogen bonds involving perchlorate oxygen atoms, the carboxylic oxygen atom and the three amine groups link the ions in the structure (Table VII).

Sources of Isomerism in the Complexes

When Λ-α-$[Co(R$-picpn$)Cl_2]^+$ reacts with aminoacidates in aqueous solution, only ternary complexes with β topology are formed. For species of general form β-$[Co(R$- or S-picpn$)$ $(R$- or S-aa$)]^{n+}$ sixty-four diastereoisomeric forms are theoretically possible, although sixteen only could have been expected from the synthetic experiments reported above since only R-picpn was used and each synthesis was carried out using an optically pure aminoacid. This number of diastereoisomers arises from possible combinations of overall absolute configuration at the metal centre (*i.e.* Δ or Λ, 1 or2), β_1 or β_2 coordination of the aminoacidate (3 or4), the *exo* or *endo* disposition of the picpn methyl group with respect to the fold of the tetradentate ligand (5 or6), and the absolute configuration of the in-plane secondary amine group (R or S, 7-10). The configuration

TABLE VI
Bond lengths and angles with estimated standard deviations in parentheses.

a) Distances (Å)

Co–N(11)	1.951(7)	Co–N(14)	1.978(6)
Co–N(12)	1.952(7)	Co–N(13)	1.970(6)
Co–N	1.986(6)	Co–O(1)	1.891(5)
C(1)–O(1)	1.306(9)	C(1)–O(2)	1.201(9)
C(1)–C(2)	1.530(11)	C(2)–C(3)	1.517(12)
N–C(2)	1.524(10)	C(3)–C(4)	1.434(15)
N–C(5)	1.513(10)	C(4)–C(5)	1.501(15)
N(11)–C(115)	1.342(10)	N(14)–C(141)	1.324(10)
C(115)–C(114)	1.384(12)	C(145)–C(144)	1.371(12)
C(114)–C(113)	1.376(14)	C(144)–C(143)	1.380(14)
C(113)–C(112)	1.349(13)	C(143)–C(142)	1.398(13)
C(112)–C(111)	1.404(11)	C(142)–C(141)	1.379(11)
C(111)–N(11)	1.359(10)	C(141)–N(14)	1.374(10)
C(111)–C(11)	1.460(12)	C(141)–C(14)	1.469(12)
N(12)–C(11)	1.510(10)	N(13)–C(14)	1.502(10)
N(12)–C(12)	1.471(10)	N(13)–C(13)	1.508(10)
C(12)–C(m12)	1.552(11)	C(13)–C(12)	1.513(11)
Cl(1)–O(11)	1.411(8)	Cl(2)–O(21)	1.366(9)
Cl(1)–O(12)	1.336(10)	Cl(2)–O(22)	1.357(10)
Cl(1)–O(13)	1.382(11)	Cl(2)–O(23)	1.349(11)
Cl(1)–O(14)	1.385(10)	Cl(2)–O(24)	1.424(11)

b) Angles (°)

|			
N(11)–Co–N(12)	84.3(3)	N(14)–Co–N(13)	83.8(3)
N(12)–Co–N(13)	85.6(3)	N–Co–O(1)	85.7(2)
N(11)–Co–N(13)	169.3(3)	N(12)–Co–N(14)	93.8(3)
N(12)–Co–O(1)	178.0(3)	N(12)–Co–N	94.0(3)
N(14)–Co–N	172.2(3)	N(13)–Co–O(1)	92.5(2)
N(11)–Co–N(14)	93.0(3)	N(13)–Co–N	96.1(3)
N(11)–Co–O(1)	97.5(3)	N(14)–Co–O(1)	86.5(2)
N(11)–Co–N	88.5(3)		
Co–N(11)–C(111)	113.5(6)	Co–N(14)–C(141)	111.8(5)
Co–N(11)–C(115)	127.4(6)	Co–N(14)–C(145)	127.8(6)
C(111)–N(11)–C(115)	118.7(8)	C(141)–N(14)–C(145)	120.3(7)
Co–N(12)–C(11)	108.8(5)	Co–N(13)–C(13)	108.4(5)
Co–N(12)–C(12)	108.2(4)	Co–N(13)–C(14)	107.7(5)
C(11)–N(12)–C(12)	115.1(7)	C(13)–N(13)–C(14)	113.1(6)
Co–N–C(2)	107.9(4)	Co–O(1)–C(1)	117.5(5)
Co–N–C(5)	124.2(6)	O(1)–C(1)–O(2)	123.1(8)
C(2)–N–C(5)	105.7(6)	O(1)–C(1)–C(2)	115.4(7)
C(1)–C(2)–N	109.7(6)	O(2)–C(1)–C(2)	121.5(8)
C(1)–C(2)–C(3)	112.0(7)	C(111)–C(11)–N(12)	109.1(7)
N–C(2)–C(3)	106.6(7)	N(12)–C(12)–C(13)	104.1(7)
C(2)–C(3)–C(4)	102.1(8)	N(12)–C(12)–C(m12)	114.3(7)
C(3)–C(4)–C(5)	108.0(10)	C(13)–C(12)–C(m12)	111.9(7)
C(4)–C(5)–N	102.9(6)	C(12)–C(13)–N(13)	109.5(7)
		N(13)–C(14)–C(141)	108.2(6)
C(11)–C(111)–N(11)	116.2(7)	C(14)–C(141)–N(14)	116.5(7)
C(11)–C(111)–C(112)	123.6(8)	C(14)–C(141)–C(142)	123.3(8)
N(11)–C(111)–C(112)	120.2(8)	N(14)–C(141)–C(142)	120.1(8)
C(111)–C(112)–C(113)	120.2(9)	C(141)–C(142)–C(143)	118.4(9)
C(112)–C(113)–C(114)	119.4(9)	C(142)–C(143)–C(144)	120.7(8)
C(113)–C(114)–C(115)	119.0(10)	C(143)–C(144)–C(145)	117.8(9)
C(114)–C(115)–N(11)	122.2(9)	C(144)–C(145)–N(14)	122.6(8)
O(11)–Cl(1)–O(12)	112.9(7)	O(21)–Cl(2)–O(22)	119.0(8)
O(11)–Cl(1)–O(13)	107.8(7)	O(21)–Cl(2)–O(23)	112.8(9)
O(11)–Cl(1)–O(14)	109.4(6)	O(21)–Cl(2)–O(24)	102.7(7)
O(12)–Cl(1)–O(13)	107.3(9)	O(22)–Cl(2)–O(23)	111.0(7)
O(12)–Cl(1)–O(14)	116.3(9)	O(22)–Cl(2)–O(24)	105.4(9)
O(13)–Cl(1)–O(14)	102.2(8)	O(23)–Cl(2)–O(24)	104.0(10)
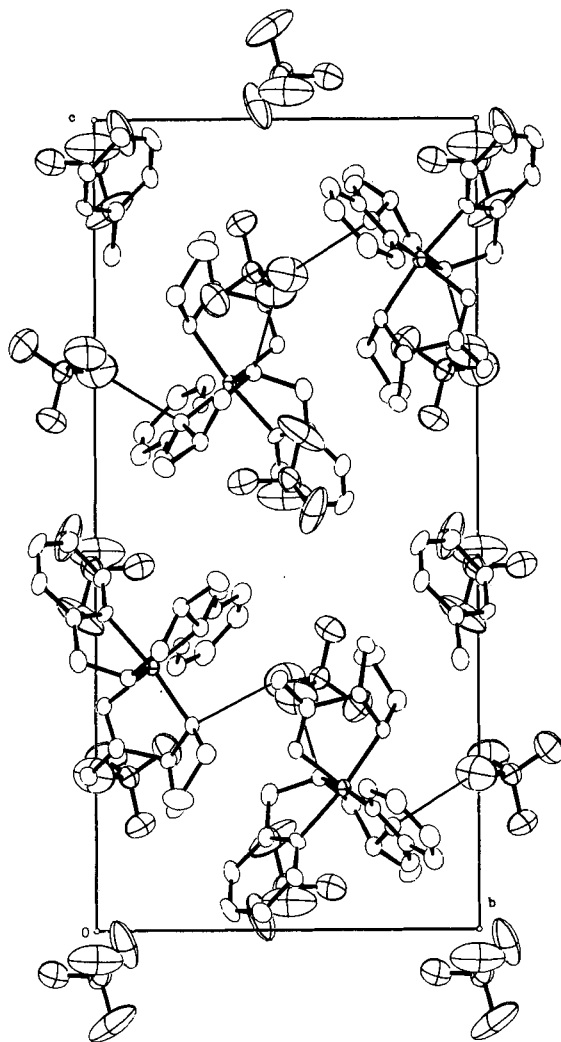
FIGURE 2   Packing of Δ-β_1-exo-[Co(R-picpn)(S-pro)](ClO$_4$)$_2$ in the unit cell, viewed down a

TABLE VII

Proposed hydrogen bonding scheme for Δ-β_1-exo-[Co(R-picpn)-(S-pro)](ClO$_4$)$_2$.

Bond	Acceptor at	Distance ($\mathring{A}$)
N(12)–H(N12) . . . O(14)	x–1/2, 3/2–y, 1–z	3.15(2)
N(13)–H(N13) . . . O(13)	1/2–x, 1–y, z–1/2	2.97(1)
N–H(N) . . . O(2)	1–x, 1/2+y, 1/2–z	2.86(1)
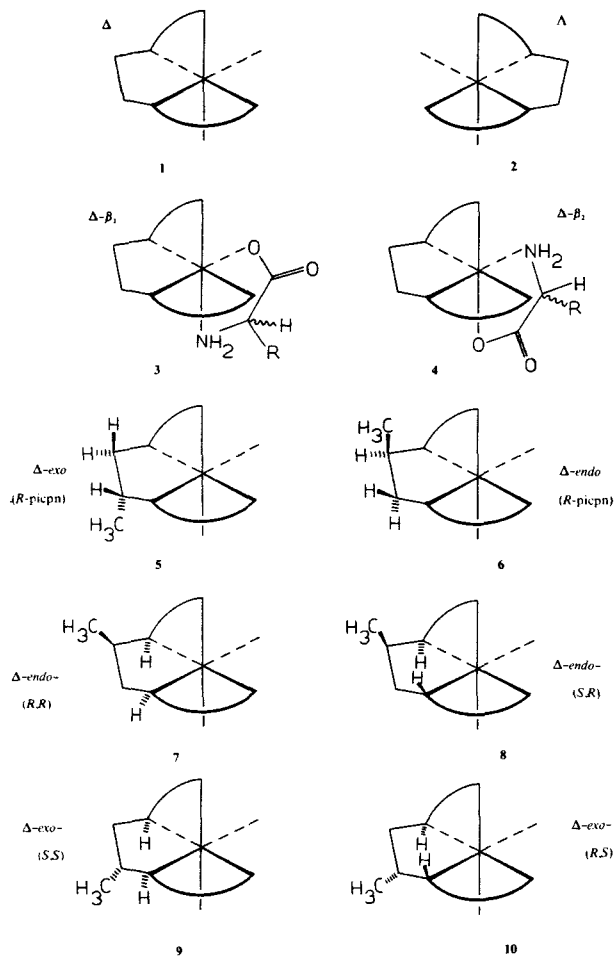
of the amine at the fold of the tetradentate is fixed by the overall absolute configuration of the diastereoisomer. It should be noted, as is demonstrated in **7–10**, that the *exo, endo* disposition of the picpn methyl group changes the *absolute* but *not* the *relative* configurations of the amine nitrogen atoms. However, in these β-isomers containing *R*-picpn the absolute configuration of the in-plane nitrogen atom is fixed. This is dependent on whether an *exo* or *endo* isomer is formed, which, in turn, is determined by the requirement that the methyl group should lie as close as possible to an equatorial position with respect to the central chelate ring, as discussed below. Assignments of absolute configuration and β_1 or β_2 topologies can be made on the basis of CD and nmr measurements (*vide infra*), and this is verified by the crystallographic results reported here and elsewhere.[8]

It is evident from nmr studies that the only other variation in isomerism arises from the possibility of either *exo* or *endo* forms. Pairs of *exo/endo* diastereoisomers, with differing *exo:endo* ratios, may be isolated by crystallising perchlorate salts of different fractions taken from the chromatographic columns. These different ratios are still evident in the ^{1}H nmr spectra of these solids when dissolved in D_2O, and after the amine hydrogen atoms have completely exchanged for deuterons. If the isomer populations

observed were to reflect different absolute configurations at N(12) (see 11 for the numbering scheme) then the *same* formation ratio for the pairs of diastereoisomers would *always* be observed. A similar "locking in" of the absolute configuration of N(12) by R-picpn has been found previously in other closely related β complexes of Co(III).[14] Thus the number of β-Co(III) diastereoisomers containing both R-picpn and a *chiral* aminoacid which could feasibly be formed reduces to eight. In previous studies[8,9] it was found that only three isomers of β-[Co(R-picpn)(S-ala)]$^{2+}$ and only two of β-[Co(R-picpn) (R-ala)]$^{2+}$ formed in aqueous solutions under experimental conditions similar to those employed for the syntheses reported here. We were somewhat surprised therefore to discover that all eight possible diastereoisomers were present in synthetic mixtures resulting from the reaction of Λ-α-[Co(R-picpn)Cl₂]$^+$ with chiral aminoacids containing much bulkier side groups than the methyl group of alaH.

Distribution of Isomers in β-[Co(R-picpn)(R- or S-aa)]$^{2+}$ Mixtures, and Their Characterisation

As was mentioned above, the CD and nmr measurements adequately serve to characterise the isomers produced. Absolute configurations are based on the sign of the CD spectrum in the visible range,[15] and β₁ and β₂ diastereoisomers may be distinguished by the relative positions of the H(145) proton resonances in the ^{1}H nmr spectra. This latter signal occurs up to 1 ppm further downfield in β₂ diastereoisomers compared with the corresponding β₁ forms in the same solvent. This is ascribed to the partial shielding of H(145) by the coordinated carboxylic group of the aminoacidate in the β₁ forms.[9,16] Characteristic ^{1}H nmr data for the isomers isolated in this study are listed in Tables VIII and IX. *Exo* and *endo* dispositions of the picpn methyl group also may be deduced on the basis of the nmr spectrum by reference to known structures in most cases. For Λ-β₁ isomers the R-picpn methyl group experiences greater shielding effects from the apical aromatic ring when it occupies an *endo* rather than an *exo* position. Shielding in Δ-β₁ diastereoisomers is more subtle. The exclusive formation of the Δ-β₁-*exo*-[Co(R-picpn) (S-ala)]$^{2+}$ isomer as the only Δ species from the reaction of Λ-α-[Co(R-picpn)Cl₂]$^{2+}$ with S-alaH was suggested to be due to unfavourable steric interactions between the R-picpn methyl group and the adjacent bridging methylene group in the corresponding *endo* form. This assignment is completely vindicated by the structure of the analogous S-pro complex species reported here, although in some

TABLE VIII

^{1}H Nmr R-picpn methyl resonances[a] in the complexes β-[Co(R-picpn) (R- or S-aminoacidate)]$^{2+}$.

Amino-acidate	Isomer							
	Δ-β₂-exo	Δ-β₂-endo	Λ-β₂-exo	Λ-β₂-endo	Λ-β₁-exo	Λ-β₁-endo	Δ-β₁-exo	Δ-β₁-endo
S-ala[b]					1.57	1.30	1.24	
R-ala[b]					1.57	1.28		
S-val	1.26	1.46	*	*	1.58	1.31	1.26	1.48
R-val		1.47	*	*	1.59	1.30	1.27	1.49
S-phe	1.42	1.52	1.25	1.19	1.46[c]	1.18[c]	1.14[c]	
R-phe	1.26	1.40	*	*	1.53	1.26	1.25	1.51
S-trp			1.14[c]	1.09[c]	1.45[c]	1.16[c]	1.11[c]	1.28[c]
R-trp	1.12[c]	1.17[c]			1.40[c]	1.28[c]	1.11[c]	
S-pro							1.19[c]	

[a]Coupling constants for this doublet varied from 6.1 to 6.4 Hz. [b]Data from ref. 9. [c]Recorded in dmso-d₆ solution, and all others in D₂O. Chemical shifts are in ppm relative to internal standard. *Present in small amounts as implied by CD measurements of appropriate fractions from chromatographic columns, but not in sufficient quantity to permit isolation.

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TABLE IX

Other characteristic ^{1}H Nmr data[a] for the major complexes of general form β-[Co(R-picpn) (R-or S-aminoacidate)]$^{2+}$.

δ or J	Complex[b]										
	A[c]	B[c]	C	D	E	F	G	H	I[c]	J[c]	K
H(115)	8.40	8.40	8.40	8.35	8.04	8.37	7.80	8.21	8.40	8.40	8.40
H(145)	7.27	7.29	7.28	7.19	7.00	7.22	6.94	6.84	7.25	7.31	7.25
$J_{114,115}$	5.7	5.7	5.2	5.3	6.7	6.5	5.2	5.8	5.7	5.7	5.2
$J_{144,145}$	5.4	6.5	5.6	5.4	5.3	5.9	5.8	5.7	5.7	6.6	5.8
CH_3^d	1.18	1.41	0.88	1.02					1.20	1.41	0.92
$CH_3'^d$			0.51	1.04							0.51

δ or J	Complex[b]									
	L	M	N	O	P	Q[c]	R	S	T	U	V
H(115)	8.35	8.11	8.37	7.79	8.21	8.31	8.26	8.27	8.28	7.82	7.84
H(145)	7.21	6.98	7.17	6.98	6.86	7.00	6.92	6.95	6.92	6.75	6.68
$J_{114,115}$	5.2	5.4	6.5	5.1	5.8	5.7	5.6	5.4	5.5	5.5	7.9
$J_{144,145}$	5.6	6.6	5.9	6.6	6.5	5.1	5.8	5.8	5.7	6.1	5.8
CH_3^d	1.02					1.51	1.11	0.85			
$CH_3'^d$	1.04						1.05	1.07			

δ or J	Complex[b]									
	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG
H(115)	7.80	8.36	7.79	8.55	8.55	8.48	8.86	8.39	8.53	8.48	8.88
H(145)	6.69	6.64	6.77	7.24	7.24	6.76	7.03	6.94	6.81	6.76	7.00
$J_{114,115}$	7.6	6.6	7.5	5.9	5.9	5.7	5.5	5.7	5.7	5.7	5.8
$J_{144,145}$	5.8	5.9	5.8	5.5	5.5	5.8	6.5	5.8	5.8	5.8	6.6
CH_3^d								1.22	1.22		
$CH_3'^d$								1.22	1.07		

[a]Chemical shifts (δ) in ppm relative to internal standard, coupling constants (J) in Hz. [b]Complexes and solvents for spectra are A: Λ-β_1-exo-[Co(L) (S-ala)]$^{2+}$ in D_2O; B: Λ-β_1-exo-[Co(L) (R-ala)]$^{2+}$ in D_2O; C: Λ-β_1-exo-[Co(L) (S-val)]$^{2+}$ in D_2O; D: Λ-β_1-exo-[Co(L) (R-val)]$^{2+}$ in D_2O; E: Λ-β_1-exo-[Co(L) (S-phe)]$^{2+}$ in dmso-d_6; F: Λ-β_1-exo-[Co(L) (R-phe)]$^{2+}$ in D_2O; G: Λ-β_1-exo-[Co(L) (S-trp)]$^{2+}$ in dmso-d_6; H: Λ-β_1-exo-[Co(L) (R-trp)]$^{2+}$ in dmso-d_6 ($L = R$-picpn); I-P: the endo analogues of A-H in the same solvents; Q-X: Δ-β_1-exo- isomers containing S-ala, S-val, R-val, S-phe, R-phe, S-trp, R-trp and S-pro, respectively. The S-phe and latter three spectra measured in dmso-d_6, otherwise in D_2O; Y: Δ-β_1-endo-[Co(L) (S-trp)]$^{2+}$ in dmso-d_6; Z,AA: Λ-β_2-exo- and Λ-β_2-endo-[Co(L) (S-trp)]$^{2+}$, respectively in dmso-d_6; AB,AC: Δ-β_2-exo-[Co(L) (R-phe)]$^{2+}$ and its R-trp analogue in D_2O and dmso-d_6, respectively. AD-AG: Δ-β_2-endo- isomers containing S-val, R-val, R-phe and R-trp, respectively. The last was measured in dmso-d_6, the others in D_2O. [c]Data from ref. 9. [d]Aminoacidate resonances.

II*
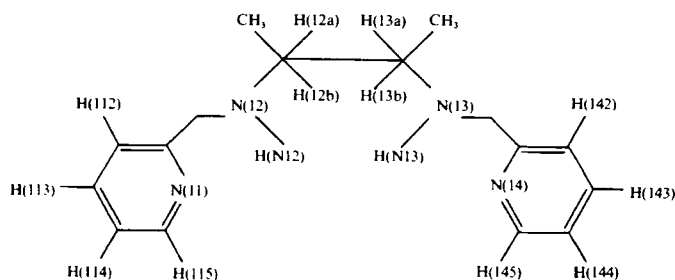
*The proton numbering scheme is given with N(11), N(12) and N(13) being disposed meridionally in the coordination sphere. Of course, not all methyl group protons indicated in the backbone of the ligand are present in any one isomer.[9]

systems minor amounts of the *endo* isomers are also formed. In these cases some contact deshielding of the R-picpn methyl group causes its resonance to appear at lower fields than in corresponding *exo* diastereoisomers. No crystallographic information is yet available concerning the β_2 isomers. However, for these isomers the same shielding/deshielding arguments as were forwarded for the β_1 species are applied to the ^{1}H nmr data, and assignments of *endo:exo* ratios are made accordingly.

An example of the complex distribution of diastereoisomers obtained in some of the synthetic experiments is shown by reference to Figure 3, which illustrates the course of elution from the cation exchange column of the species β-[Co(R-picpn) (R-phe)]$^{2+}$. Four bands develop, the first two partially overlapping, but the latter two are quite well-resolved. The Figure also illustrates how plots of $\Delta A/A$ may be used to select fractions containing only one diastereoisomer. Both absorbance and differential absorbance (CD in arbitrary units) were measured in this case at 470 nm, near to λ_{max} for all of the R-pheH isomers. The sign of the plot allows the assignment of absolute configuration to individual species or to *exo/endo* pairs. The order of elution of the R-pheH isomers was Δ-β_2-*exo,endo*, Λ-β_2-*exo,endo*, Λ-β_1-*exo,endo* and Δ-β_1-*exo,endo*. Six of these species have been crystallised as *exo/endo* pairs. The concentrations of the Λ-β_2-*exo,endo* fractions were low, and, in conjunction with the solubilities of their perchlorate salts, could not be obtained in solid form. The CD spectra of the fractions from the second band, however, were quite analogous to other isolated Λ-β_2 complexes.

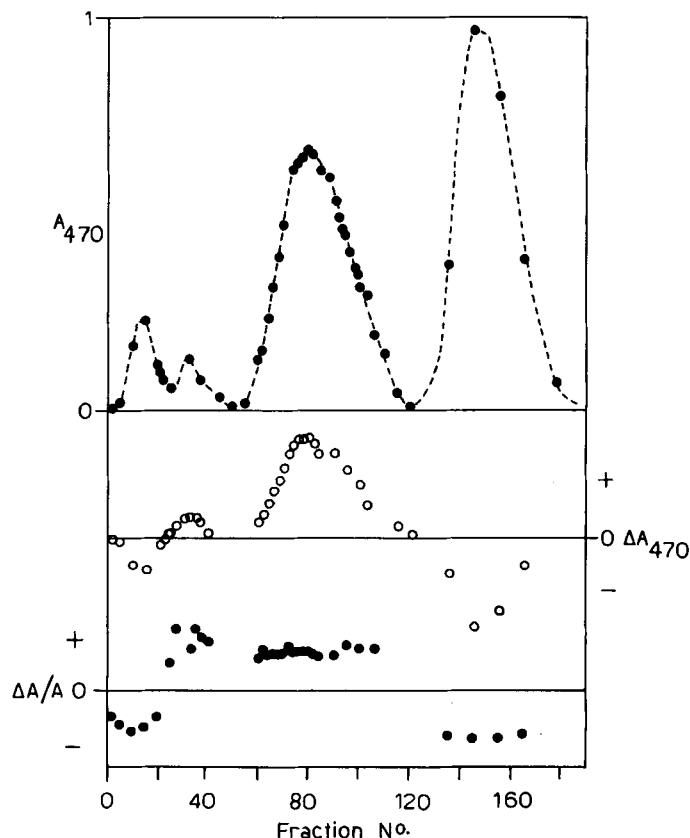FIGURE 3   Elution pattern from a CM-Sephadex® C-25 column of the reaction mixture of Λ-α-[Co(R-picpn)Cl$_2$]$^+$ with R-pheH. Absorbance and differential absorbance are in arbitrary units

In this particular case all eight possible diastereoisomers were formed, although in unequal amounts. The observed pattern of isomer distribution is set out in Table I. Generally, the main isomers formed were the Λ-β_1-*exo,endo* and Δ-β_1-*exo,endo* species.

With R-trpH and S-proH, only the *exo* isomer of the latter pair could be detected, and with R-alaH the only species formed were the Λ-β_1-*exo,endo* ones. It is possible that this pattern of isomer distribution may reflect different solubilities as well as various discriminatory interactions, as discussed below, but this is not certain. Complexes containing R-proH and S-proH, except for Δ-β_1-*exo*-[Co(R-picpn) (S-pro)]$^{2+}$, are apparently much less stable than analogues containing other aminoacidate ligands. The abovementioned order of elution from the chromatographic column is the same for all complexes save those containing S- or R-trpH. With the former, the Δ-β_1-*endo* isomer elutes first, followed by Λ-β_1-*exo,endo*, then Λ-β_2-*exo,endo* complex cations. The Δ-β_1-*exo* diastereoisomer elutes last. A somewhat different pattern of isomer distribution is found for R-trpH analogues, but the Λ-β_1-*exo,endo* species are observed to elute first followed then by the Δ-β_2-*exo,endo* forms. Both Δ-β_1-*exo* and Δ-β_1-*endo* diastereoisomers were eluted in the slowest moving band, similar to the other aminoacidate complexes.

In most cases, little if any chromatographic separation of *exo* and *endo* pairs was achieved. A notable exception concerned the Δ-β_1-*exo* and Δ-β_1-*endo* forms of [Co(R-picpn) (S-trp)]$^{2+}$, which were eluted first and last, respectively, from the Sephadex® column. We can discern no obvious reason for this fact. The mutual presence of *exo* and *endo* isomers in the solid state for the majority of other cases may be a reflection of cocrystallisation phenomena, and has been observed for Λ-β_1-*exo,endo*-[Co(R-picpn) (S-ala)]$^{2+}$ and their R-alaH congeners.[8]

Alternatively, the isolated solids may be mixtures of the two solid diastereoisomeric perchlorates, as is the case with Λ-β_1-*exo,endo*-[Co(R-picpn) (S-val)] (ClO$_4$)$_2$. Both of these isomers had about the same retention time on the column, but the *exo* form could be separated by hand-picking its dark-orange prismatic crystals from the fine needles of the *endo* complex. It is possible that increasing the bulkiness of the aminoacid side-chain prevents the packing of both diastereoisomers in the same crystal unit cell. Nevertheless, this has not been established for the other complexes. Crystals formed generally were of the same habit (needles) and were too small to enable nmr spectra to be recorded for solutions containing only single dissolved crystals.

Brubaker and co-workers[11,17] have carried out strain energy minimisation calculations on some of the complexes discussed here and on the {Co(picpn)} fragment in more general terms. We have made use of the usual mirror relationships (they performed calculations on the S-picpn molecule) to compare their results with our work. Calculations concerning four of the possible eight Δ,Λ-β-[Co(R-picpn)X$_2$]$^+$ diastereoisomers were carried out. These concerned the species **8** and **10** and the corresponding Λ-β-*endo*-(R or S) and Λ-β-*exo*-(S or R) forms. It should be noted particularly that these four species have the *same* amine nitrogen absolute configurations as those forced upon them in the α-diastereoisomers from which they are derived *via* a single edge displacement involving one of the pyridyl rings. The calculations indicated that the Λ-β-*endo*-[Co(R-picpn)X$_2$]$^+$ diastereoisomer was slightly more stable than its Λ-β-*exo* counterpart, but that the difference was small. This conclusion is in accord with *exo/endo* distributions in Λ-β pairs synthesised in this work. However, it was concluded[17] also that the corresponding Δ-β-*exo,endo* species were considerably less stable.

Torsional and angular deformation strains in the chiral amine bridge of the tetradentate were thought to be important discriminatory factors. Unfortunately, no calculations were carried out for the isomers shown in **7** and **9**, which have the absolute configurations of the in-plane amine atom reversed from those in the related α

complexes. On the basis of spectroscopic and molecular model studies we previously deduced[8] that Δ-β_1-exo-[Co(R-picpn) (S-ala)]$^{2+}$ did indeed have its structure based on 9. This conclusion is confirmed by the solution of the X-ray structure of the S-proline salt discussed above. It is evident that this alteration of stereochemistry serves to make certain Δ diastereoisomers containing R-picpn approximately as stable as those with the Λ absolute configuration, as judged by the isomer distributions found here and elsewhere.[8] Furthermore, since the energy differences are small in any case, other discriminatory effects, particularly those involving solvation effects, are perhaps just as significant as steric ones. The type of calculations carried out, therefore, are possibly not sufficiently discriminating to be applied to these ternary complexes in solution.

Brubaker and Massura[11] also performed similar calculations on Λ-β_1 and Λ-β_2-endo-[Co(R-picpn)(gly)]$^{2+}$ complexes and their R- and S- alaH analogues. Species with the β_1 topology were found to be slightly more stable. This would be in accord with our synthetic results in that β_1 complexes were always found in far larger amounts than their β_2 counterparts. It may be that this finding has its origin in steric effects. However, since so many isomers have been shown to be present in certain of the systems studied, it is clear that discriminatory forces may well be subtle in these ternary species. This could involve many different contributions, granted that the isomer distributions observed do reflect thermodynamic preferences and not kinetic factors associated with the synthetic conditions.

In any case, it is clear that in Co(III) complexes of this type more extensive substitution of the central chelate ring of the tetradentate is necessary to force a stereospecific coordination. This is true even when aminoacids with bulky α-substituents, and which might be expected to influence the choice of complex geometry, are employed to complete the coordination sphere.

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