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Chiral Metal Complexes. 14.* High Resolution ^{1}H NMR Studies of β-[Co(2,5-diaza-3-methyl-1,6-di(2-pyridyl)hexane)(alaninate)]$^{2+}$ and Related 1,2-Diaminoethane Complexes

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*Several isomers of the complex [Co(*R*-picpn)(ala)]$^{2+}$ have been synthesised, where* R*-picpn is 2,5-diaza-3*R*-methyl-1,6,-di(2-pyridyl)hexane, and ala is the anion of* R- *or* S*-alanine. The isomers have been studied using circular dichroism and high resolution ^{1}H nmr techniques. Of the 40 possible isomers accessible in this system only 5 are observed to form in aqueous solution from* Λ*-α-[Co(*R*-picpn)Cl$_2$]$^+$. Two contain* R*-ala, and three contain* S*-ala. Four of the isomers (or their mirror images) correspond to those which have been previously characterized using X-ray crystallographic methods. Several diastereomers are found to cocrystallize.* Λ*-α-[Co(*R*-picpn)Cl$_2$]$^+$ reacts with 1,2-diaminoethane to form one main isomer which has also been characterized spectroscopically. Extensive rearrangement of the Co(III) coordination sphere is found to take place in all reactions.*

Introduction

Four diastereoisomers† of β-[Co(picpn)(*S*-ala)]$^{2+}$ cocrystallize as a perchlorate salt, and each has been structurally characterised [1]. Another isomer also may be synthesised. Co(III) complexes of picpn have been shown to adopt a wide variety of geometries [2] and high resolution nmr studies have been useful in the assignment of their structures [2, 3]. Here we present the results of such an investigation involving the β-[Co(picpn)(ala)]$^{2+}$ system as well as that of the related complexes β-[Co(picpn)(en)]$^{3+}$. The study was undertaken as part of a broader effort aimed at an understanding of chiral discriminations between various diastereoisomers in these kinds of coordination complexes.

*Part 13 is ref. [1].

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†Picpn = 2,5-diaza-3-methyl-1,6-di(2-pyridyl)hexane, proH = proline, alaH = alanine, en = 1,2-diaminoethane.

Experimental

Analyses were carried out by Mrs. A. Dams in the Department of Chemistry, Cardiff. Electronic and circular dichroism (CD) spectra were recorded in aqueous solution using a Beckman DK2A ratio recording spectrophotometer and a CNRS-Jobin-Yvon Dichrographe III, respectively. The 360 MHz ^{1}H nmr spectra were measured using a Bruker WM 360 instrument at 298 K. Saturated solutions of the complexes were prepared and spectra measured in D_2O or DMSO-d_6 solutions are reported relative to DSS or TMS as internal standards, respectively. For the 200 MHz spectrum, a Varian XL-200 spectrometer was used.

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

This was prepared as reported previously [1].

Δ-β_1-exo-*[Co(*R*-picpn)(*S*-ala)](ClO$_4$)$_2$·H$_2$O*

As mentioned in the previous paper [1], a second orange band could be eluted from the cation exchange column after that which yielded the Δ,Λ-β_1-*exo,endo*-isomers. This band was collected, reduced in volume at 30 °C using a rotary evaporator, and the concentrated solution left to stand over silica gel. Over a period of several days, the complex crystallized as well-formed orange needles up to 5 mm in length. These were collected at the pump, washed with ice-cold water and air dried. *Anal.*: Found C, 34.7; H, 4.6; N, 11.3%. Calc. for $C_{18}H_{28}N_5O_{11}Cl_2Co$: C, 34.9; H, 4.6; N, 11.3%. Spectral details: ϵ_{490} = 2088, ϵ_{347} = 1740 dm^2 mol^{-1}; $\Delta\epsilon_{490}$ = −15.8, $\Delta\epsilon_{357}$ = +8.6, $\Delta\epsilon_{301}$ = −1.4 dm^2 mol^{-1}. Wavelengths (nm) refer to maxima in the electronic spectrum and extrema in the CD spectrum.

Λ-β_1-exo,endo-*[Co(*R*-picpn)(*S*-ala)](ClO$_4$)$_2$·H$_2$O*

This complex was synthesised as was the Δ,Λ,β_1-*exo,endo*-isomeric mixture with *R,S*-picpn, but

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using Λ-α-[Co(*R*-picpn)Cl_2]ClO_4 [2] as starting material. The reaction mixture was admitted to a column of CM Sephadex® C-25 cation exchange resin in the Na^+ form, and upon elution with 0.1 mol dm^{-3} aqueous $NaClO_4$, two orange bands developed. The latter consisted of the Δ-β_1-*exo* isomer (above). The former was collected and slowly reduced in volume over silica gel at room temperature. Well-formed plates of the complex perchlorate crystallized slowly. Both *exo-* and *endo-* isomers cocrystallized, and attempts to separate them using ion-exchange chromatography have so far proved unsuccessful. The crystals were collected at the pump, washed with ice-cold water and air dried. *Anal.*: Found C, 35.0; H, 4.8; N, 11.2%. Calc. for $C_{18}H_{28}N_5O_{11}Cl_2Co$: C, 34.9; H, 4.6; N, 11.3%. Spectral details: ϵ_{482} = 2103–2131 dm^2 mol^{-1}, ϵ_{338} = 1691–1714 dm^2 mol^{-1} (depending on fraction collected from Sephadex® column, and thus on the isomer distributions therein); $\Delta\epsilon_{487}$ = +21.8 – +22.0 dm^2 mol^{-1}, $\Delta\epsilon_{350}$ = –4.9––5.0 dm^2 mol^{-1}.

Λ-β_1-exo,endo-*[Co(*R*-picpn)(*R*-ala)]*$(ClO_4)_2 \cdot 0.5H_2O$

This was prepared as outlined above but using *R*-alanine as well as Λ-α-[Co(*R*-picpn)Cl_2]ClO_4. Elution of the Sephadex® column under the same conditions gave rise to only one band which contained both isomers and which also cocrystallized as stout needles. Attempts to separate these diastereomers have as well been so far unsuccessful. *Anal.*: Found C, 35.5; H, 4.5%. Calc. for $C_{18}H_{27}N_5O_{10.5}Cl_2Co$: C, 35.4; H, 4.5%. Spectral details: ϵ_{474} = 1780–1810 dm^2 mol^{-1}, ϵ_{346} = 1670–1683 dm^2 mol^{-1}; $\Delta\epsilon_{495}$ = +19.5–+20.0 dm^2 mol^{-1}, $\Delta\epsilon_{351}$ = –2.6––2.8 dm^2 mol^{-1} (depending on fraction number from cation exchange column and thus the isomer distribution therein).

Λ-β-exo-*[Co(*R*-picpn)(en)]*I_3

This complex was prepared in the same fashion as the *S*-alanine species, except that 1,2-diaminoethane was substituted for the amino acidate. The reaction mixture was added to the Sephadex® column and eluted as a yellow orange band with 0.5 mol dm^{-3} aqueous $NaClO_4$. The elute was taken to dryness and dissolved in the minimum volume of warm 1 mol dm^{-3} aqueous NaI. Upon cooling and evaporation in a dessicator over silica gel, crystals slowly formed. These were collected at the pump, washed with a minimum of ice-cold water and air-dried. *Anal.*: Found C, 27.0; H, 4.0; N, 10.9%. Calc. for $C_{17}H_{28}N_6I_3Co$: C, 27.0; H, 3.7; N, 11.1%. Spectral details: ϵ_{460} = 2128, ϵ_{333} = 1848 dm^2 mol^{-1}; $\Delta\epsilon_{469}$ = +30.2, $\Delta\epsilon_{335}$ = –6.7 dm^2 mol^{-1}.

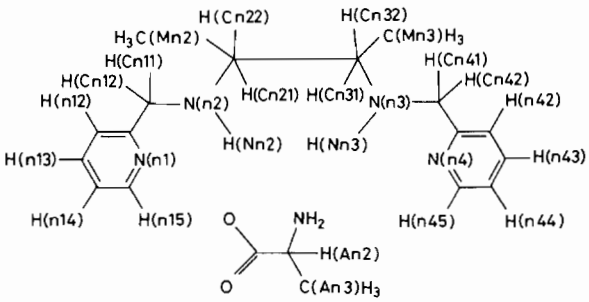

Fig. 1. Proton numbering scheme for the various diastereoisomers. In the case of Λ-isomers, n = 1 and for Δ-isomers, n = 2.

Results and Discussion

We have previously outlined [1] the nomenclature adopted to describe the various possible β-isomers in the $[Co(picpn)(ala)]^{2+}$ system. In total, 64 β-isomers are accessible as a result of choices between the absolute configurations of the metal centre, the amino acidate and the picpn ligand, β_1 or β_2 coordination of the aminoacidate, *exo-* or *endo-* disposition of the methyl group of the tetradentate, a variation not possible when such a ligand derived from a diamine with two-fold symmetry such as optically active 2,3-diaminobutane is employed, and the chirality of the secondary nitrogen atoms of the tetradentate. These both are asymmetrically substituted when coordinated to the metal centre. Similar considerations reveal that 16 diastereomers of α-$[Co(picpn)(ala)]^{2+}$ are also accessible. In the α-topology the absolute configurations of the picpn secondary nitrogens are dictated by that of the metal centre and the *exo,endo-* choice is no longer applicable. However the amine nitrogen atom of the aminoacidate may coordinate in a *cis* or *trans* position with respect to the methyl group of the unsymmetrical picpn ligand. Again, if a tetradentate with two-fold symmetry is employed, this latter complication is eliminated.

The numbering scheme used to identify individual protons is that shown in Fig. 1, and is the same as that employed for the crystallographic structure determinations [1] of the four diastereomers Δ,Λ-β_1-*exo,endo-*$[Co(R,S\text{-picpn})(S\text{-ala})]^{2+}$. For all isomers described in this work, the tetradentate is taken to be coordinated such that the three nitrogen atoms *N*(n1), *N*(n2) and *N*(n3) are disposed meridionally in the Co(III) coordination sphere.

When *S*-alanine is reacted with Δ,Λ-α-$[Co(R,S\text{-picpn})Cl_2]^+$ in aqueous solution column ion-exchange chromatography of the reaction products gives rise to two orange coloured bands containing isomers of $[Co(picpn)(S\text{-ala})]^{2+}$. The faster moving band

*Please see footnote on facing page.

proved to contain four diastereomers*, Λ-β_1-*exo*-*R,R*- and Λ-β_1-*endo*-*R,R*-[Co(*R*-picpn)(*S*-ala)]$^{2+}$, and Δ-β_1-*exo*-*S,S*- and Δ-β_1-*endo*-*S,S*-[Co(*S*-picpn)(*S*-ala)]$^{2+}$. All four diastereoisomers cocrystallize and have been structurally characterized [1]. In separate experiments the corresponding band was collected from a column, evaporated to dryness and nmr measurements of solutions of the mixture of products showed that no other isomers were present. These diastereoisomers arise as the result of a complex rearrangement of the coordination spheres of the two Co(III) starting dichloroenantiomers. The Λ-β and Δ-β isomers are derived from Λ-α- and Δ-α[Co(picpn)Cl_2]$^+$ cations respectively.

The second orange band eluted from the column in the above-mentioned experiment proved to contain only one diastereoisomer. Its electronic and CD spectral properties (previous section) show that it is a Δ-diastereoisomer [5], and nmr studies, reported below, indicate that it too is a β_1-species. Synthetic studies have also established that the absolute configuration of the picpn ligand in this isomer is *R*. This latter work, involving the syntheses of limited numbers of the isomers found in the above reaction, and in which a number of other cocrystallization phenomena are evident, has made possible an unambiguous assignment of practically all resonances in the ^{1}H nmr spectra of the various diastereoisomers.

When a slurry of Λ-α-[Co(*R*-picpn)Cl_2]ClO_4 is allowed to react in aqueous solution at steambath temperatures with *S*-alanine, only species containing *R*-picpn can be formed. Elution of the reaction products on a cation exchange column again separated two orange compounds, the slower moving one being identical in all properties to the Δ-β-[Co(picpn)(*S*-ala)]$^{2+}$ isomer mentioned above. This complex is easily precipitated as the perchlorate salt, forming fine needles up to 5 mm in length. Nmr spectroscopy has been used to show the first band to contain the two isomers Λ-β_1-*exo,endo*-*R,R*-[Co(*R*-picpn)(*S*-ala)]$^{2+}$ by reference to the spectrum of the mixture Δ,Λ-β_1-*exo,endo*-[Co(*R,S*-picpn)(*S*-ala)]$^{2+}$. The two Λ-isomers also cocrystallized as the perchlorate salt in beautiful plates up to 5 × 5 × 1 mm in size. This phenomenon was verified by nmr measurements of solutions made up of single crystals. Indeed, the separation of the three diastereomers into Δ-β_1-[Co(*R*-picpn)(*S*-ala)]$^{2+}$ and Λ-β_1-*exo,endo*-[Co(*R*-picpn)(*S*-ala)]$^{2+}$ by using cation exchange techniques was subsequently found to be unnecessary.

*Absolute configurations of the nitrogen atoms are given outside the brackets not accounting for the methyl substitution in the picpn ligands, as has been generally adopted in the past [4].

TABLE I. 360 MHz ^{1}H Nmr Spectral Data[a] for the Δ,Λ-β_1-*exo,endo*-[Co(*R,S*,-picpn)(*S*-ala)]$^{2+}$ Complexes in D_2O Solution at 298 K.

	Λ; *R*-picpn (n = 1)		Δ; *S*-picpn (n = 2)	
	endo	*exo*	*endo*	*exo*
H(n12)	7.868	7.868	7.859	7.859
H(n13)	8.343	8.346	8.343	8.346
H(n14)	7.904	7.904	7.889	7.889
H(n15)	8.395	8.395	8.395	8.395
H(n42)	7.832	7.832	7.833	7.824
H(n43)	8.169	8.169	8.169	8.169
H(n44)	7.497	7.497	7.497	7.497
H(n45)	7.251	7.267	7.309	7.291
H(Cn11)[b]	4.663	4.600	4.592	4.690
H(Cn12)[b]	4.286	4.352	4.250	4.356
H(Cn41)[b]	4.459	4.459	4.500	4.503
H(Cn42)[b]	4.415	4.415	4.500	4.503
H(Cn21)	3.761	3.227	3.603	3.112
H(Cn22)		3.054		3.092
H(Cn31)	2.400	3.165	2.691	3.169
H(Cn32)	3.778		3.795	
C(Mn2)H_3	1.303		1.280	
C(Mn3)H_3		1.572		1.572
C(An3)H_3	1.204	1.182	1.406	1.406
H(An2)	3.903	3.925	3.000	3.027
$J_{An2,An3}$	7.4	8.5	7.1	7.1
$J_{Cn21,Cn22}$		−11.0		−11.9
$J_{Cn21,Cn31}$	13.4	13.2	12.6	13.0
$J_{Cn21,Cn32}$	4.3		4.3	
$J_{Cn21,Mn2}$	4.8		6.2	
$J_{Cn22,Cn31}$		2.9		4.5
$J_{Cn31,Cn32}$	−12.6		−13.3	
$J_{Cn31,Mn3}$		5.9		5.0
$J_{Cn11,Cn12}$	−16.8	−17.1	−16.9	−17.4
$J_{Cn41,Cn42}$	−20.3	−20.3	−18.5	−18.5
$J_{n12,n13}$	7.9	7.9	9.0	9.0
$J_{n13,n14}$	7.9	7.9	7.0	7.0
$J_{n14,n15}$	5.7	5.7	5.7	5.7
$J_{n42,n43}$	7.7	7.7	7.8	7.8
$J_{n43,n44}$	7.8	7.8	7.0	7.0
$J_{n44,n45}$	5.7	5.4	6.6	6.5

[a]Chemical shifts in ppm. [b]We do not distinguish between the pairs of protons *H*(Cn11), *H*(Cn12) and *H*(Cn41), *H*(Cn42). Errors in chemical shifts are ±0.002 ppm and in coupling constants ±0.05 Hz.

When mixtures of the three isomers are crystallized as their perchlorates, the former and the latter two, together, adopt their distinctive habits and may be conveniently separated mechanically. Such is also the case with the Δ-β isomer and Δ,Λ-β_1-*exo,endo*-

TABLE II. Selected 360 ^{1}H Nmr Data[a] for the Δ,Λ-β_1-*exo, endo*-[Co(*R,S*-picpn)(*S*-ala)]$^{2+}$ Complexes in DMSO-d_6 Solution at 298 K.

	Λ; *R*-picpn (n = 1)		Δ; *S*-picpn (n = 2)	
	endo	*exo*	*endo*	*exo*
H(n12)	7.890	7.897	7.944	7.904
H(n13)	8.349	8.361	8.353	8.365
H(n14)	7.885	7.886	7.884	7.866
H(n15)	8.231	8.227	8.250	8.267
H(n42)	7.818	7.818	7.830	7.782
H(n43)	8.186	8.186	8.186	8.186
H(n44)	7.579	7.579	7.579	7.558
H(n45)	7.062	7.076	7.192	7.110
C(Mn2)H_3	1.201		1.186	
C(Mn3)H_3		1.457		1.472
C(An3)H_3	1.090	1.072	1.277	1.294
$J_{Cn21,Mn2}$	6.0		5.6	
$J_{Cn31,Mn3}$		5.9		5.3
$J_{An2,An3}$	6.5	6.9	6.7	5.9
$J_{n12,n13}$	7.7	7.7	7.6	7.6
$J_{n13,n14}$	7.0	7.4	8.5	8.4
$J_{n14,n15}$	4.6	4.2	4.1	4.2
$J_{n42,n43}$	5.9	5.6	7.6	7.9
$J_{n43,n44}$	8.5	8.8	6.8	6.5
$J_{n44,n45}$	4.9	4.6	6.6	6.5

[a]Chemical shifts in ppm relative to TMS as internal reference. Errors are estimated to be ±0.002 ppm in shifts and ±0.05 Hz in coupling constants.

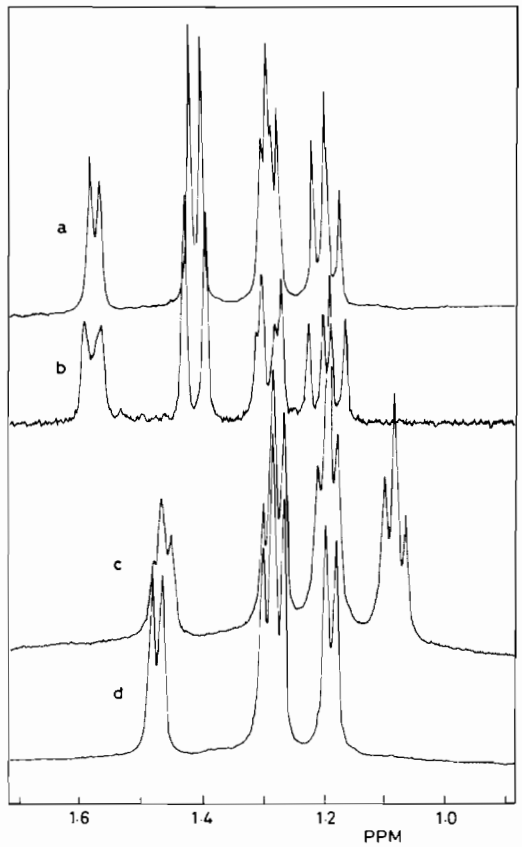

Fig. 2. ^{1}H nmr spectra of the methyl region; a, b: Δ,Λ-β_1-*exo, endo*-[Co(*R,S*-picpn)(*S*-ala)]$^{2+}$ in D_2O. Spectrum b is recorded at 200 MHz; c: as for a, but in DMSO-d_6; d: Λ-β_1-*exo, endo*-[Co(*R*-picpn)(*R*-ala)]$^{2+}$ in DMSO-d_6.

[Co(*R,S*-picpn)(*S*-ala)](ClO$_4$)$_2$, which crystallizes in stout prisms.

In a separate experiment, Λ-α-[Co(*R*-picpn)Cl$_2$]$^+$ was reacted with *R*-alanine. Chromatography of the products gave rise to only one orange band which yielded orange needle-like crystals up to 9 mm in length and 1 mm thick. ^{1}H nmr spectra of solutions of single crystals showed that two diastereomers were again cocrystallized and that these corresponded to the Δ-β_1-*exo,endo*-[Co(*S*-picpn)(*S*-ala)]$^{2+}$ species in the Δ,Λ-β_1-*exo,endo* mixture of isomers containing both *R*- and *S*-picpn. This result is, naturally, only to be expected since from the enantiomorphic relationship of the various appropriate experiments, we would anticipate the presence of Λ-β_1-*exo,endo*-[Co(*R*-picpn)(*R*-ala)]$^{2+}$, as obtained.

Tables I and II contain ^{1}H nmr data for the Δ,Λ-β_1-*exo,endo* [Co(*R,S*-picpn)(*S*-ala)]$^{2+}$ complexes (and of course their enantiomers). Isomer counting in this system is facilitated by the fact that each diastereomer gives rise to two doublets at high field corresponding to the methyl groups of picpn and alanine. Spin decoupling allowed the assignment of all protons unambiguously, except for those of the bridging methylene groups of the picpn ligand. In D_2O solution, all amine hydrogen atoms quickly exchange and this also simplified the interpretation of the spectra. in DMSO-d_6, such protons do not quickly exchange and many of the signals arising from the protons of the picpn 'backbone' and the alanine α-proton are considerably broadened, thus rendering a complete assignment in this solvent impossible.

The four isomers present in single crystals of Δ,Λ-β_1-*exo,endo*-[Co(*R,S*-picpn)(*S*-ala)](ClO$_4$)$_2$ are clearly distinguished by ^{1}H nmr measurements. In Fig. 2 is shown the region of the spectrum in which all the methyl resonances lie. Some overlapping of signals is evident in both D_2O and DMSO–d_6 solution, although in the former, the two upfield sets of overlapping doublets are clearly resolved at 200 MHz. Enhanced resolution of the downfield groups of signals is evident in DMSO-d_6 solution, and the multiplicity of signals is easily rationalized by comparison to those found for Λ-β_1-*exo,endo*-[Co(*R*-picpn)(*R*-ala)]$^{2+}$, as shown in Fig. 2.

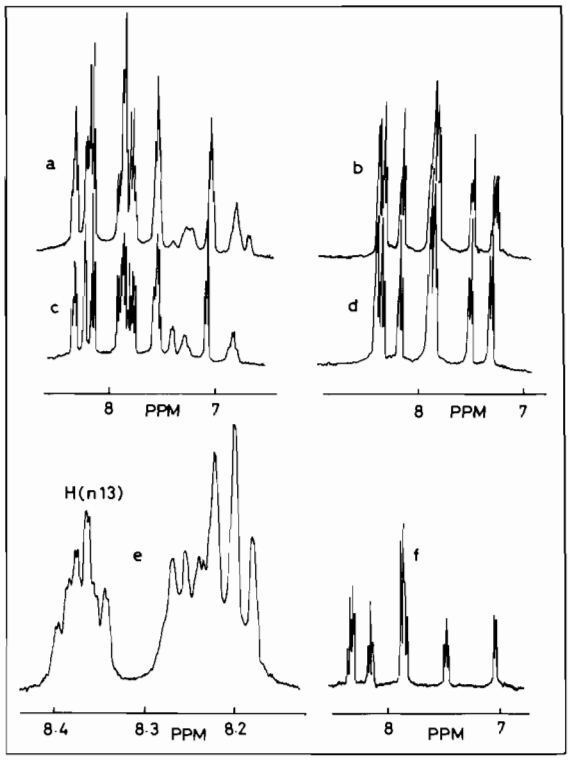

Fig. 3. 360 MHz ^{1}H nmr spectra of a: Δ,Λ-β_1-*exo,endo*-[Co(*R,S*-picpn)(*S*-ala)]$^{2+}$ in DMSO-d_6 in the aromatic region; b: as for a, but in D_2O; c: Λ-β_1-*exo,endo*-[Co(*R*-picpn)(*R*-ala)]$^{2+}$ aromatic region in DMSO-d_6; d: as for c, but in D_2O; e: as for a. The signals from the *H*(n13) protons are marked; f: Aromatic region of Δ-β_1-*exo*-[Co(*R*-picpn)(*S*-ala)]$^{2+}$ in D_2O solution.

Distinctions between signals due to the *exo-* and *endo* isomers were made in several ways. The *exo-* species were present in a minor amount in crystals containing the four diastereomers, as determined crystallographically, and nmr measurements of the complex always gave solutions which had equal amounts of *exo-* and *endo-* isomers, or were enriched in the two isomers assigned the *endo-* geometry. Correspondingly, a similar pattern of isomer distinction was found in the syntheses of Λ-β_1-*exo, endo*-[Co(*R*-picpn)(*R*-ala)]$^{2+}$ and [Co(*R*-picpn)(*S*-ala)]$^{2+}$. We do not claim that the ratios of diastereoisomers present in the crystals necessarily reflect equilibrium concentrations of the various species, although it is possible that they do depend on slight energetic differences as revealed by strain energy minimization calculations carried out on isomers of [Co(picpn)Cl_2]$^+$ by Brubaker and Euler [6].

Other evidence for the assignment comes from the chemical shift data for the various methyl resonances. Those species in which the methyl group of the picpn ligand lies *exo-*, with respect to the tetradentate fold, should be deshielded with respect to those in *endo-* environments because of the positioning of the pyridyl residue *trans* to the amine group of the aminoacidate. This assignment is consistent with our spectral observations and the observed isomer distributions. A related effect concerning the chemical shifts arising from the alanine methyl groups can also be discerned. In Λ-β_1 isomers, the methyl group lies beneath a pyridyl ring of *R*-picpn when the alanine has the *S*-configuration. Thus the chemical shifts of these resonances in the Λ-β_1-*exo,endo*-[Co(*R*-picpn)(*S*-ala)]$^{2+}$ isomers lie at higher field than those of the *quasi*-enantiomeric Δ-β_1-*exo, endo*-[Co(*S*-picpn)(*S*-ala)]$^{2+}$ diastereomers. Subtle differences are evident for the resonances corresponding to protons in the central bridge of the picpn ligand in the various isomers. However, these signals are generally well resolved in D_2O solution and observed coupling constants are in good agreement with values expected on the basis of the X-ray crystallographic investigations [1].

Considerable overlapping of pyridyl proton signals is evident, especially in D_2O solution. In Fig. 3 is shown the aromatic region of the spectrum of the four Δ,Λ-β_1-*exo,endo*-[Co(*R,S*-picpn)(*S*-ala)]$^{2+}$ diastereomers. Even at 360 MHz, the only significant differences correspond to the *H*(n45) signals, these protons being shielded by the other pyridyl ring. A typical pattern of resonances for β-complexes containing this type of tetradentate [2, 3] is observ-

TABLE III. 360 MHz ^{1}H Nmr Data[a] for the Complex Δ-β_1-*exo-R,S*-[Co(*R*-picpn)(*S*-ala)]$^{2+}$ in D_2O at 298 K.

H(212)	7.865	$J_{212,213}$	7.7
H(213)	8.339	$J_{213,214}$	7.0
H(214)	7.845	$J_{214,215}$	5.7
H(215)	8.314	$J_{242,243}$	7.7
H(242)	7.865	$J_{243,244}$	7.7
H(243)	8.152	$J_{244,245}$	5.1
H(244)	7.454		
H(245)	7.004		
H(C211)[b]	4.084	$J_{C211,C212}$	−17.1
H(C212)[b]	4.428		
H(C241)[b]	4.374	$J_{C241,C242}$	−18.1
H(C242)[b]	4.868[c]		
H(C222)	2.786	$J_{222,231}$	3.3
H(C231)	3.672	$J_{222,232}$	12.4
H(C232)	3.651	$J_{222,M22}$	6.2
H(A12)	3.647	$J_{231,232}$	−14.5
C(Al3)H_3	1.509		
C(M22)H_3	1.243		

[a]Chemical shifts in ppm relative to DSS as internal standard. [b]We do not distinguish between the pairs of protons *H*(C211), *H*(C212) and *H*(C241), *H*(C242). [c]Partially obscured by HDO peak. Errors in chemical shifts ±0.002 ppm and in coupling constants ±0.05 Hz.

ed. As expected, the *H*(n15) resonances are widely separated from those due to *H*(n45) protons. However, for these isomers with β_1 geometry, the *H*(n15) protons experience some shielding, compared with related dichloro- and dinitro complexes [2, 3] because they are directed towards the coordinated carbonyl group of the aminoacidate*. This fact is of some importance to the understanding of the nature of the fifth isomer isolated during the reaction of *S*-alaH with Δ,Λ-α-$[Co(R,S\text{-picpn})Cl_2]^+$, as mentioned below. Some other resonances in the aromatic region are better separated in DMSO-d_6 solution as also shown in Fig. 3. We draw particular attention to the pattern of signals centred at 8.47 ppm, which corresponds to the four *H*(n13) triplets. These may be uniquely assigned by reference to the spectra of the Δ-β_1-*exo,endo*-$[Co(S\text{-picpn})(S\text{-ala})]^{2+}$ species.

As mentioned above, the only other isomer detected in this system is Δ-β-$[Co(R\text{-picpn})(S\text{-ala})]^{2+}$, whose ^1H nmr spectral data is collected in Table III. The close relationship of the resonances in the aromatic region of the spectrum (Fig. 3) and particularly the chemical shift of the *H*(215) proton, indicates that it too has the β_1 topology.

The questions then remain of the Δ-β_1-$[Co(R\text{-picpn})(S\text{-ala})]^{2+}$ isomer as to whether it is an *exo*- or an *endo*- species, and whether *N*(22) has *R* or *S* absolute configuration. We cannot look to the chemical shift of the picpn methyl resonance in this connection because in a Δ-β complex of *R*-picpn, the methyl is not shielded by a pyridyl ring whether it lies *exo*- or *endo*- to the fold in the tetradentate. However, the chemical shift of the alanine methyl resonance at 1.509 ppm indicates that it is not shielded by a pyridyl ring, and this supports the assignment of the β_1 geometry. Molecular models suggest that the Δ-β_2 isomer with *S*-alanine cannot form because of considerable non-bonded interactions between the alanine methyl group and *H*(215).

Since the Δ-β_1 isomer is formed during the reaction of *S*-alaH with Λ-α-$[Co(R\text{-picpn})Cl_2]^+$, it is the product of an octahedral inversion. Owing to the fact that the picpn ligand has no two-fold symmetry, the inversion, *via* an edge displacement [8] of a pyridyl group may occur in two ways and this choice in turn dictates the *exo*- or *endo*- disposition of the *R*-picpn methyl group in the final product. With an *endo*- diastereomer, models suggest significant steric interactions between the methyl group and a bridging picolyl methylene group. This interaction has been commented upon by other workers [6] and on this basis it seems reasonable to suggest that the species isolated here is an *exo*-isomer. Given this probability, it must be pointed out that if the *N*(22) atom retains the *S*-configuration of the Λ-α-starting material the picpn methyl group cannot lie in an equatorial position with respect to the central five-membered chelate ring of the tetradentate. If, however, this nitrogen atom inverts *via* proton exchange in aqueous solution, a process known to occur by the ^1H nmr spectral results in D_2O, the coordination sphere geometry is unstrained and an equatorial disposition of the methyl group of the *R*-picpn ligand is ensured. Thus, in the absence of a structural determination, we propose that the fifth isomer is Δ-β_1-*exo*-*R,S*-$[Co(R\text{-picpn})(S\text{-ala})]^{2+}$.

There is no obvious reason from model studies why the corresponding Λ-β_1-$[Co(S\text{-picpn})(S\text{-ala})]^{2+}$ isomer should not form. The chiral discriminations in this system responsible for the formation of but five diastereomers with *S*-alanine of some forty possible are somewhat difficult to discern. Since Co(III) complexes of *R*-picpn can be isolated with both Δ and Λ absolute configurations, and with α and β coordination geometries [2, 3], depending upon the other ligands attached to the metal ion, it is evident that the optically active tetradentate is not particularly stereoselective, as was originally suggested [9]. It is possible that kinetic factors may play a role in determining isomer distributions in any particular experiment and solubility phenomena may cause the isolation of particular species from complex reaction mixtures. This last point is highlighted in the reaction of Λ-$\alpha[Co(R\text{-picpn})Cl_2]^+$ with 1,2-diaminoethane, in which a somewhat different set of isomers is obtained.

Two isomers are found in the reaction products, but one is only present in trace amounts. It remained in the filtrate after collection of the main isomer whose iodide salt is much less soluble, but the

TABLE IV. 360 MHz ^1H Nmr Spectral Data[a] for Λ-β-*exo*-$[Co(R\text{-picpn})(en)]^{3+}$ in D_2O solution at 298 K.

H(112)	7.893	$J_{112,113}$	8.03
H(113)	8.340	$J_{113,114}$	7.51
H(114)	7.924	$J_{114,115}$	5.71
H(115)	8.576	$J_{142,143}$	7.86
H(142)	7.844	$J_{143,144}$	7.72
H(143)	8.192	$J_{144,145}$	5.93
H(144)	7.546		
H(145)	7.324		
C(M13)H_3	1.566	$J_{C131,M13}$	6.22

[a]Chemical shifts ±0.002 ppm relative to DSS as internal standard and coupling constants ±0.02 Hz. The signals for the en protons and those of *H*(C121), *H*(C122) and *H*(C131) occur in a complex overlapping group between 2.7 and 3.3 ppm.

*The *H*(n15) resonances in β_2 isomers of related complexes of *S*-alaH and *S*-proH with *N,N'*-di(2-picolyl)*trans*-1,2-diaminocyclohexane occur some 0.8 ppm downfield from those in corresponding β_1 isomers [7].

concentration of the second species was too low to isolate and characterise it. The electronic and CD spectra of the isolated $[Co(R\text{-picpn})(en)]I_3$ complex (previous section) shows it to have the Λ configuration and comparison of its ^1H nmr spectrum (Table IV) with those of the alanine complexes indicates that the picpn ligand adopts the *exo*-configuration. The only significant difference in the aromatic portion of the ^1H nmr spectrum compared to that of the corresponding Λ-β_1-*exo*-$[Co(R\text{-picpn})(S\text{-ala})]^{2+}$ isomer is that the position of the *H*(115) resonance is shifted somewhat downfield in the en isomer. This is expected to be the case due to the absence of shielding by the carbonyl group of the aminoacidate, as described earlier.

It is again evident that the main product of this raction arises as a result of a major rearrangement of the coordination sphere of the Co(III) starting complex. Apparently β-isomers of *R*-picpn prefer to adopt the Λ-configuration, but one Δ-isomer has been isolated in the alanine series of complexes and a Δ-β-$[Co(R\text{-picpn})Cl_2]^+$ complex is known [3]. The energy differences between pairs of *exo*- and *endo*- isomers appear to be slight. Given that the picpn complex can accommodate several geometries, it might be expected that slight variations in reaction conditions could lead to different isomers being isolated, as has been found for a series of oxalate diastereomers [2]. In this latter case, solubility differences between isomers was an important factor in determining the course of the reaction.

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