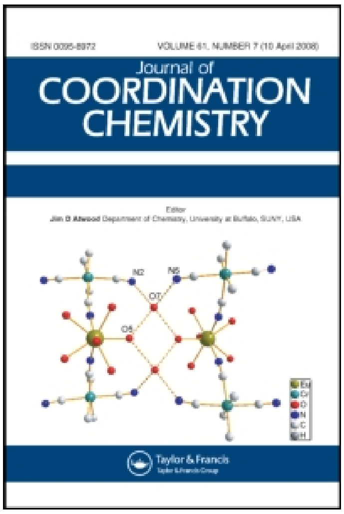

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CHIRAL METAL COMPLEXES. 50. X-RAY STRUCTURE OF THE DNA PROBE Δ-α-[*N,N'*-DIMETHYL-*N,N'*-DI(2-PICOLYL)-1*R*,2*R*-DIAMINOCYCLOHEXANE]-[*S*-PHENYLALANINATO(1-)]COBALT(III) PERCHLORATE HYDRATE

Peter Leverett[a]; Janice Petherick[a]; Peter A. Williams[a]; Robert S. Vagg[b]
[a] School of Science. University of Western Sydney Nepean, Kingswood, New South Wales, Australia [b] School of Chemistry, Macquarie University, New South Wales, Australia

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CHIRAL METAL COMPLEXES. 50.* X-RAY STRUCTURE OF THE DNA PROBE Δ-α-[*N*,*N*′-DIMETHYL-*N*,*N*′-DI(2-PICOLYL)-1*R*,2*R*-DIAMINOCYCLOHEXANE]-[*S*-PHENYLALANINATO(1-)]COBALT(III) PERCHLORATE HYDRATE

PETER LEVERETT[a], JANICE PETHERICK[a],
PETER A. WILLIAMS[a,†] and ROBERT S. VAGG[b,†]

[a] *School of Science, University of Western Sydney Nepean, P.O. Box 10, Kingswood, New South Wales 2747, Australia;* [b] *School of Chemistry, Macquarie University, New South Wales 2103, Australia*

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The complex salt Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)](ClO$_4$)$_2 \cdot$ H$_2$O, where *R*,*R*-picchxnMe$_2$ = *N*,*N*′-dimethyl-*N*,*N*′-di(2-picolyl)-1*R*,2*R*-diaminocyclohexane and *S*-phe is the monovalent anion of *S*-phenylalanine, has been prepared and its structure determined by single-crystal X-ray methods. Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)](ClO$_4$)$_2 \cdot$ H$_2$O is orthorhombic, space group $P2_12_12_1$, with $a = 10.208(1)$, $b = 16.804(1)$, $c = 19.194(3)$ Å, $V = 3292.5$ Å^3, $Z = 4$, $D_c = 1.542$ and $D_m = 1.49$ Mg m^{-3}. The structure was refined to $R = 0.046$ for 3554 independent reflections with $I > 2\sigma(I)$. As is the case with the *R*-phe analogue, the phenyl ring of the coordinated aminoacidate is not in the extended conformation, but lies adjacent to one of the pyridyl rings of the coordinated tetradentate. The attractive intramolecular π–π interaction which stabilises this conformation is analogous to that which serves to stabilise the stacking of parallel base pairs in DNA.

Keywords: Cobalt(III); tetradentate; phenylalanine; van der Waals bond;
X-ray structure; DNA

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[*] Part 49 is Ref. [1].

[†] Authors for correspondence.

INTRODUCTION

For some time, we have been exploring various structural and electronic effects which serve to discriminate between several classes of chiral metal complexes (see Ref. [1] and the literature cited therein). More recently, we have explored the nature of complexes designed to be employed as structural probes of DNA and related biomolecules.[2] A characteristic of one of the classes of complex examined is that they contain a chiral tetradentate which is used to discriminate between the chiralities of the octahedral metal centre and the possible geometric dispositions of a linear tetradentate, and which can be chosen to be complementary to the helicity of double-stranded DNA (the Δ-α diastereoisomer gives the best complementary fit to the right handed helix of B-DNA).

It has been known for quite some time that free aromatic amino acids such as *S*-phenylalanine (*S*-pheH) and *S*-tryptophane (*S*-trpH) will bind to DNA via intercalation with the aromatic base pairs of DNA.[3-5] This is akin to related studies of complexes containing coordinated aromatic bidentates.[2,6] With this in mind, we have developed the complexes Δ,Λ-α-$[Co(R^*,R^*\text{-picchxnMe}_2)(R^*\text{-aa})]^{2+}$, in which the tetradentate picchxnMe$_2$ is *N*,*N*′-dimethyl-*N*,*N*′-di(2-picolyl)-1,2-diaminocyclohexane and *R**-aa is the monovalent anion of an α aminoacidate with an aromatic side chain such as *R**-phe, as probes of the structure of DNA. Since the complex is positively charged, electrostatic interactions would be favoured, and binding would be enhanced if the phenyl group of the amino acid were to intercalate between the base pairs of DNA. The single-crystal X-ray structure of Δ-α-$[Co(R,R\text{-picchxnMe}_2)(R\text{-phe})](ClO_4)_2$ has been reported[7] and shows the phenyl group of the amino acid to be bonded by π–π interactions to one of the pyridyl rings of the tetradentate. Remarkably, this weak bond was shown to persist in solution, using a variety of solvents.

Here we report the crystal and molecular structure of the related diastereoisomeric salt Δ-α-$[Co(R,R\text{-picchxnMe}_2)(S\text{-phe})](ClO_4)_2 \cdot H_2O$, which shows the same kind of π–π interaction in the solid state and which suggests that these complexes are excellent models for face-to-face π–π interactions of aromatic molecules including intercalated DNA adducts.

EXPERIMENTAL

Electronic and CD spectra were recorded on a Shimadzu UV-2100 recording spectrophotometer and a Jasco J-500C spectropolarimeter, respectively.

All materials used were of reagent grade. Δ-α-[Co(*R*,*R*-picchxnMe$_2$)Cl$_2$]-(ClO$_4$)$_2$ was synthesised as described previously.[8]

Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)](ClO$_4$)$_2$ · H$_2$O

This complex was synthesised and purified in a manner analogous that reported for the *R*-phenylalanine diastereoisomer,[7] but by substituting *S*-pheH in the first step. Characteristic spectroscopic data: $\lambda_{max} = 498$ nm, $\varepsilon = 95.6\,M^{-1}cm^{-1}$, $\Delta\varepsilon_{525} = -3.8$, $\Delta\varepsilon_{337} = +0.9\,M^{-1}cm^{-1}$, in water. The analytical composition of the complex salt was confirmed by a single-crystal X-ray structure determination (*vide infra*).

X-ray Structure of Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)](ClO$_4$)$_2$ · H$_2$O

Crystal data $C_{29}H_{40}N_5O_{11}Cl_2Co$, $M_r = 764.5$, $a = 10.208(1)$, $b = 16.804(1)$, $c = 19.194(3)$ Å, $V = 3292.5$ Å^3, $Z = 4$, $D_c = 1.542$, $D_m = 1.49\,Mg\,m^{-3}$, $F(000) = 1592.0$, μ(MoKα) = 0.75 mm^{-1}, orthorhombic, space group $P2_12_12_1$ (No. 19).

Unit cell parameters were initially determined from single-crystal precession photographs using MoKα radiation and refined via a least-squares fit to the diffractometer data. A crystal that was 0.32 × 0.24 × 0.20 mm in size was used. Data for the complex were collected at 278 K on an Enraf-Nonius FAST area detector diffractometer using documented procedures.[9] Intensity data were determined for reflections in the range $4.24 < 2\theta < 50.34$. The intensities were corrected for Lorentz and polarisation effects but absorption corrections were not applied. A total of 8222 measured reflections was merged to give 5167 unique reflections of which 3554 had $I > 2\sigma(I)$, and these were used for the structure determination. The structure was solved by the heavy atom method using the programs SHELXS-86[10] and SHELXL-93[11] and refined by full-matrix least-squares techniques in which the function $\sum w(F_o^2 - F_c^2)^2$ was minimised. The weight for each reflection in the final cycles of refinement is given by $w = 1/[\sigma^2(F_o)^2 + (0.0452P)^2]$ where $P = (\max(F_o^2, 0) + F_c^2)/3$, as defined by SHELXL-93. This weighting scheme gives a uniform analysis of variance in terms of F_c^2. After anisotropic refinement of the structure excluding hydrogen atoms, all hydrogen atoms, except the two in the water molecule, were positioned using the appropriate geometry and relevant C–H and N–H bond lengths; the accuracy of these positions was confirmed by a subsequent difference Fourier synthesis. The hydrogen atoms on the water molecule were located from electron density maps and then held in these positions, with thermal parameters derived from the oxygen atom. Refinement was continued with hydrogen atoms riding on the atoms to which they are bonded, with fixed isotropic thermal parameters, and with anisotropic temperature factors for all other atoms. The refinement process was terminated when the minimisation factor changed by $<0.1\%$ and a final difference map showed no residual electron density greater than $|0.5|$ e Å^{-3}. The final R value was 0.046 for 3554 reflections with $I > 2\sigma(I)$. The final weighted R_w $[= \{\sum w(F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2\}^{1/2}]$ was 0.102 for all 5167 data.

RESULTS AND DISCUSSION

A perspective view of the complex cation Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)]$^{2+}$ showing the atom labelling scheme, is shown in Figure 1. Table I lists final atomic coordinates of non-hydrogen atoms and Table II gives selected bonding parameters and interatomic distances for the complex. Examination of bond lengths and angles does not reveal any anomaly. In the crystal lattice, the perchlorate groups are generally constrained and a hydrogen bonding network links a perchlorate ion and the water of crystallization to the complex cation; the water molecule has hydrogen bonds to O32 (1.785 Å) of the aminoacidate and O12 (2.261 Å) of a perchlorate ion. Another hydrogen bond links N31 and O22a (2.143 Å).

In the complex cation, a similar intramolecular hydrophobic bond to that observed[7] in the solid state in Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*R*-phe)]$^{2+}$, is also

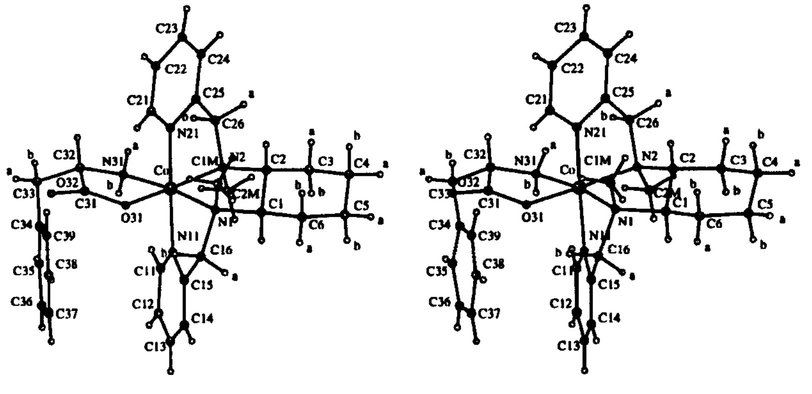

FIGURE 1 A drawing of the Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)]$^{2+}$ cation showing the atom labelling scheme.

TABLE I Final atomic coordinates for the non-hydrogen atoms with estimated standard deviations in parentheses for the complex Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)](ClO$_4$)$_2$ · H$_2$O

	x/a	*y/b*	*z/c*
Co	0.9854(1)	0.0330(1)	0.0690(1)
O31	1.0185(3)	−0.0036(2)	0.1603(2)
N1	0.8403(4)	−0.0458(2)	0.0609(2)
N31	1.1214(4)	0.1119(2)	0.0913(2)
N11	0.8449(4)	0.0994(3)	0.1084(2)
N2	0.9549(2)	0.0601(2)	−0.0312(2)
N21	1.1211(4)	−0.0353(2)	0.0293(2)
O32	1.1649(4)	−0.0031(2)	0.2459(2)
Cl1	0.0079(2)	−0.2408(1)	−0.1429(1)
O11	0.0269(7)	−0.1627(4)	−0.1670(3)
O12	−0.1122(7)	−0.2696(5)	−0.1648(4)
O13	0.0158(8)	−0.2416(4)	−0.0716(3)
O14	0.0957(11)	−0.2823(6)	−0.1704(7)
Cl2	0.4437(1)	0.1324(1)	−0.0070(1)
O21	0.4600(5)	0.0605(3)	0.0314(2)
O22	0.3486(5)	0.1801(2)	0.0224(3)
O23	0.3953(5)	0.1108(3)	−0.0746(3)
O24	0.5598(4)	0.1730(3)	−0.0163(3)
C1	0.7644(5)	−0.0240(3)	−0.0038(3)
C11	0.8401(6)	0.1792(4)	0.1148(3)
C12	0.7399(6)	0.2179(4)	0.1497(3)
C13	0.6423(7)	0.1718(5)	0.1778(3)
C14	0.6434(6)	0.0924(5)	0.1711(3)
C15	0.7446(5)	0.0564(3)	0.1363(3)
C16	0.7574(5)	−0.0301(4)	0.1241(3)
C1M	0.8816(6)	−0.1313(3)	0.0632(4)
C2	0.8633(5)	−0.0021(3)	−0.0606(3)
C21	1.1797(5)	−0.0959(3)	0.0599(4)
C22	1.2668(6)	−0.1428(4)	0.0255(4)
C23	1.2948(6)	−0.1280(4)	−0.0440(4)
C24	1.2390(5)	−0.0641(3)	−0.0756(4)
C25	1.1511(5)	−0.0182(3)	−0.0378(3)
C26	1.0832(4)	0.0519(3)	−0.0663(3)
C2M	0.9091(5)	0.1433(3)	−0.0435(3)
C3	0.7965(5)	0.0203(3)	−0.1282(3)
C31	1.1251(5)	0.0216(3)	0.1905(3)
C32	1.2031(5)	0.0829(3)	0.1495(3)
C33	1.2549(5)	0.1507(3)	0.1955(3)
C34	1.1491(5)	0.2064(3)	0.2202(3)
C35	1.0558(6)	0.1835(4)	0.2682(3)
C36	0.9576(6)	0.2339(4)	0.2892(3)
C37	0.9493(7)	0.3108(3)	0.2622(3)
C38	1.0411(8)	0.3330(4)	0.2151(4)
C39	1.1379(7)	0.2820(4)	0.1939(3)
C4	0.7066(5)	−0.0453(3)	−0.1529(3)
C5	0.6069(6)	−0.0632(4)	−0.0982(3)
C6	0.6722(6)	−0.0884(3)	−0.0302(3)
OW	1.4333(5)	−0.0646(4)	0.2514(3)

TABLE II Selected bond lengths (Å) and angles (°) for the complex Δ-α-[Co(*R*,*R*-picchxnMe$_2$)(*S*-phe)](ClO$_4$)$_2$ · H$_2$O

(a) *Bond lengths*			
Co–N1	1.993(4)	N31–C32	1.480(6)
Co–N2	2.001(4)	C32–C31	1.520(7)
Co–N11	1.966(4)	C31–O31	1.306(6)
Co–N21	1.953(4)	C31–O32	1.212(6)
Co–N31	1.970(4)	C32–C33	1.536(7)
Co–O31	1.888(3)	C33–C34	1.507(7)
		C34–C35	1.379(7)
		C35–C36	1.374(7)
		C36–C37	1.397(8)
		C37–C38	1.356(8)
		C38–C39	1.368(8)
		C39–C34	1.378(7)
(b) *Angles*			
N11–Co–N21	178.3(2)	N31–Co–O31	83.8(1)
N1–Co–N31	171.8(2)	Co–O31–C31	117.2(3)
N2–Co–O31	173.9(4)	O31–C31–C32	115.2(4)
		C31–C32–N31	108.9(4)
		C32–N31–Co	109.7(3)
(c) *Non-bonded contacts between the two weakly bonded aromatic rings* (Å; *see text*)			
N11···C34	4.185(6)		
C11···C35	3.676(8)		
C12···C36	3.493(9)		
C13···C37	4.239(9)		
C14···C38	5.799(9)		
C15···C39	5.633(8)		
(d) *Proposed hydrogen bonds*[a]			
O32···HW1	1.758(4)		
O12···HW2	2.261(5)		
H31a···O22a^{I}	2.143(6)		

[a] The superscript refers to an atom at relative position. *I*: 1+*x*, *y*, *z*.

found between one of the pyridyl rings of the tetradentate and the phenyl ring of the coordinated aminoacidate (Figure 2). The dihedral angle between the two planes is 24.9°. Figure 2 illustrates the fact that the two weakly bonded rings do not overlap each other to any significant extent and it is evident that the van der Waals interaction, at least in the solid state, is weaker than in the *R*-phe analogue. The closest interatomic distances are on one side of the phenyl ring, where C11–C35 and C12–C36 are 3.676 and 3.493 Å, respectively. On the opposite side of the ring, C14–C38 and C15–C39 are 5.799 and 5.633 Å, respectively. However, NMR experiments indicate that the weak interaction for the present complex also persists in solution. A detailed study of the solution thermodynamics of these species will appear elsewhere.[12]

The weak interaction between the aromatic rings described here appears to be quite general for this class of complexes. Thus analogous

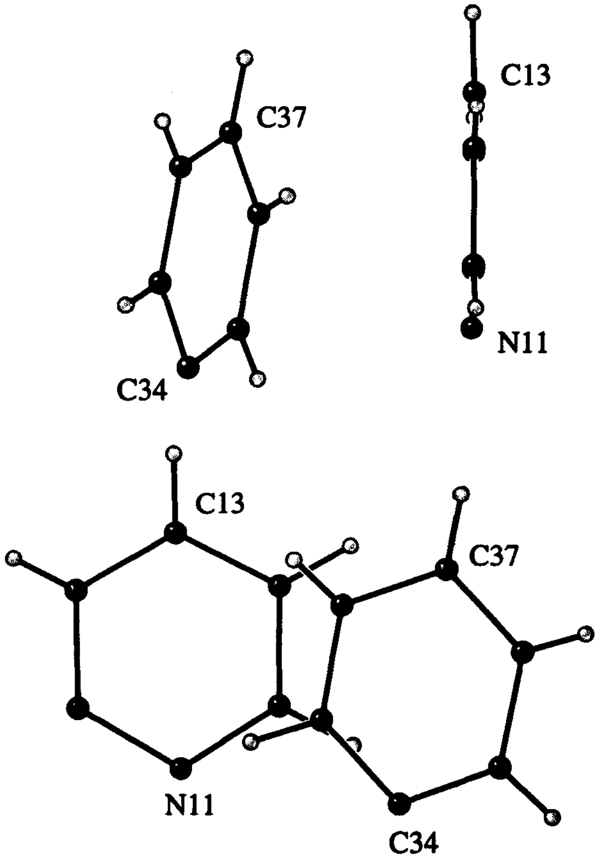

FIGURE 2 Orthogonal views of the relative orientations of the two weakly bonded rings illustrating the inclination of the planes ($\phi = 24.9°$), and the small extent of ring overlap. The rotation axis used to generate the two projections passes through N11 and C13.

bonding is seen to exert a significant influence on the course of reaction of Λ-β_1-[Co(*R*,*R*-picchxn)(*R*-ABMA)]$^+$ (picchxn = *N*,*N*′-di(2-picolyl)-1,2-diaminocyclohexane; ABMAH$_2$ = 2-amino-2-benzylmalonic acid) to form a complex containing an enantiomeric excess of *S*-phe.[13] In similar fashion in the solid state structure[14] of Λ-β_1-[Co(*R*,*R*-picchxn)(*S*-α-Me-trp)]$^{2+}$, there is π-stacking between one of the pyridyl rings of the *R*,*R*-picchxn ligand and the indole substituent of the coordinated tryptophan derivative.

The nature of π–π or van der Waals interactions of the kind described here has been the subject of much experimentation. However, for systems of various degrees of complexity, ranging from the benzene dimer to elaborate model compounds, edge-to-face rather than face-to-face bonding is frequently preferred.[15–19] It should be noted that the former mode is also important in various host–guest interactions[20] and in biological systems is responsible for stabilising certain protein[21] conformations. The class of complexes that we have developed appears to be ideal for a systematic exploration of model face-to-face interactions that are responsible for the structure of DNA and the interaction of certain drugs with nucleic acids.[22]

Acknowledgements

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Supplementary Material

Full lists of crystallographic data are available from the authors upon request.

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