metal-organic compounds

Retroracemization using new forms of Belokon's original ligand: intermediate Ni^{II} complexes of N-({2-[N-(S)-alkylprolylamino]-phenyl}phenylmethylene)-(S)-phenyl-alanine (alkyl is 2-picolyl, 3-picolyl or ethyl)

Alexander J. Blake,* Binod B. De, Wan-Sheung Li and Neil R. Thomas

School of Chemistry, The University of Nottingham, University Park, Nottingham NG7 2RD, England
Correspondence e-mail: a.j.blake@nottingham.ac.uk

In the title compounds, [N-(phenyl{2-[N-(S)-(2-picolyl)prolyl-amino]phenyl}methylene)-(S)-phenylalaninato]nickel(II), [Ni-($C_{33}H_{30}N_4O_3$)], (I), [N-(phenyl{2-[N-(S)-(3-picolyl)prolylamino]-phenyl}methylene)-(S)-phenylalaninato]nickel(II) hemihy-drate, [Ni($C_{33}H_{30}N_4O_3$)]·0.5H$_2$O, (II), and [N-({2-[N-(S)-ethylprolylamino]phenyl}phenylmethylene)-(S)-phenylala-ninato]nickel(II), [Ni($C_{29}H_{29}N_3O_3$)], (III), the Ni^{II} centres have approximate square-planar coordination geometries from N$_3$O donor sets. The picolyl N atoms in (I) and (II) are too remote from the metal centres to interact significantly, but the metal coordination geometries experience tetrahedral distortion and/or displacement of the metal centre from the N$_3$O plane. These are linked to conformational differences between the ligands of the symmetry-independent complexes (Z' = 2), which in turn are related to molecular packing. In (III), where a less sterically demanding ethyl group replaces the picolyl substituents, there are none of the distortions or displacements seen in (I) and (II).
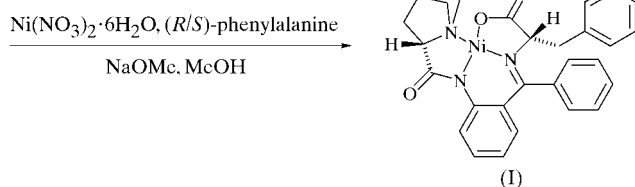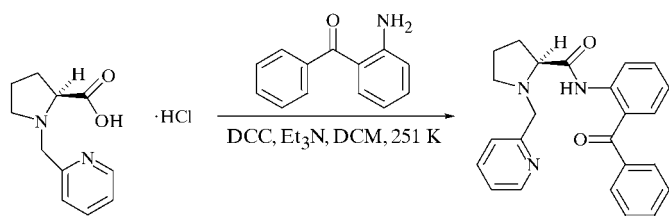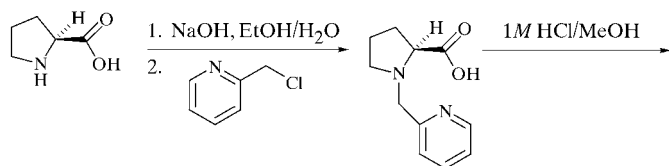
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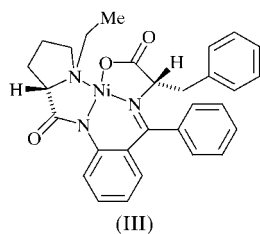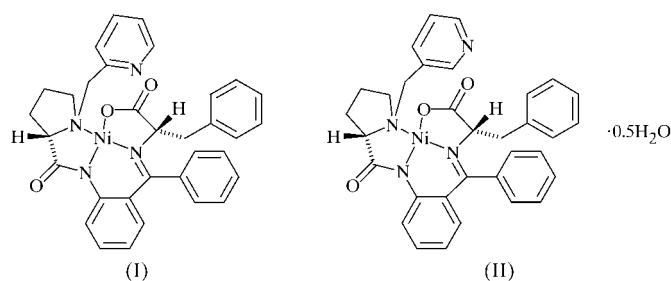
The asymmetric synthesis of α-amino acids has been an area of intense interest over the past few decades and a number of elegant approaches have established themselves for use in research or industrial scale syntheses. However, many indus-trial processes still involve classical resolutions in which large quantities of chemical waste in the form of amino acids of the wrong stereochemistry are produced. Belokon et al. (1983) reported the first example of a process they termed retro-racemization, in which a racemic α-amino acid mixture could be enriched in one of its enantiomeric forms by selective protonation of a prochiral amino acid enolate generated in an asymmetric environment formed from the amino acid, Cu^{II} or Ni^{II}, and (S)-2-[(N-benzylprolyl)amino]benzaldehyde, aceto-phenone or benzophenone. The combination of Ni^{II} and (S)-2-[(N-benzylprolyl)amino]benzophenone [(S)-BPB] proved the most successful in the retroracemizations, and in the stereo-selective alkylation of complexes containing the glycine enolate. More recently, a number of modified forms of the original Belokon' ligands have been investigated. These include a variety of ligands in which the N-benzyl group has been replaced by the bulkier naphthalen-1-ylmethyl group, the smaller ethyl derivative, and 2-picolyl or 3-picolyl groups, which may offer a further coordination site for binding to the metal in the complex (De & Thomas, 1997). N-(2-Benzoyl-phenyl)pyridine-2-carbamide (PBP) was studied by Belokon et al. (2001), who have investigated glycine enolate alkylation reactions under phase-transfer catalysis (PTC) conditions, and Popkov et al. (2000), who have reported the use of (S)-2-[(N-2,4,6-trimethylbenzylprolyl)amino]benzophenone [(S)-TMB-PB] to give improved diastereoselectivity and enantio-selectivity in the synthesis of (S)-alanine when compared with (S)-BPB.
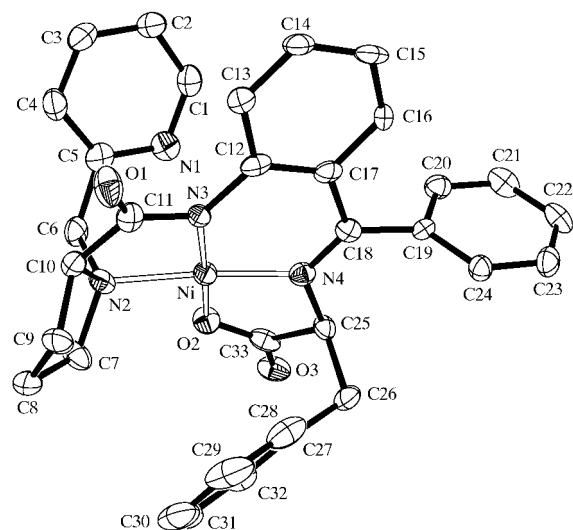
In our investigation, two approaches to improving the diastereoselectivity of the retroracemization process were investigated. Initially, we examined the possibility of increasing the steric bulk of the prolyl substituent by replacing the N-benzyl group of (S)-BPB with diphenylmethyl, trityl or naphthalen-1-ylmethyl groups. It proved to be impossible to form the Schiff base complexes with either (S)-2-[(N-1-di-phenylmethylprolyl)amino]- or (S)-[(N-1-tritylprolyl)amino]-benzophenone and either racemic phenylalanine or glycine. In the case of (S)-{[N-1-(naphthalen-1′-ylmethyl)prolyl]amino}-benzophenone, a small increase in the enantiomeric excess of the product α-amino acid was observed after conducting the retroracemization procedure and decomposing the complex, when compared with the use of (S)-BPB. However, the yield of the amino acid product was generally 10–15% lower. As an alternative strategy, we investigated the introduction of prolyl substituents, which should be capable of providing a further coordination site for the metal in the Schiff base complex, such that one face of the prochiral α-amino acid enolate generated during the retroracemization process would be rendered totally inaccessible to protonation or alkylation. This was inspired by the fact that the square-planar Cu^{II} complex of pyruvyl Gly-D-Phe reacts with imidazole-4-carboxaldehyde to give a square-pyramidal intermediate (Owa et al., 1988). It was anticipated that inclusion of a 2-picolyl or 3-picolyl substituent in the (S)-2-[(N-alkylprolyl)amino]benzophenone would cause the Schiff base formed with Ni^{II} or Cu^{II} and an α-amino acid to adopt a square-pyramidal or octahedral geometry, the latter involving a solvent ligand. Thus, the three title compounds, viz. (I), (II) and (III), were prepared and their crystal structures are presented here.

Both picolyl complexes, (I) and (II), crystallize with two independent molecules in the asymmetric unit. Each Ni^{II} centre adopts an approximately square-planar geometry (Figs. 1 and 2, and Tables 1 and 2), with the distance from the

Ni centre to the sp^3-hybridized N2 atom being longer than the other three distances. However, there are significant differences in the detailed geometry of the independent molecules. In the first molecule of (I), the tetrahedral distortion is much less than in the second (the r.m.s. deviation of the constituent atoms from the N_3O donor-atom plane is 0.064 Å in the first molecule *versus* 0.148 Å in the second), as is the displacement of the Ni^{II} centre from this plane [0.008 (3) *versus* 0.038 (3) Å, the latter in the direction of atom N1*A*].

Figure 1
A view of one of the two independent molecules of (I), showing the atom-numbering scheme. H atoms have been omitted for clarity and displacement ellipsoids are drawn at the 50% probability level.

the greater displacement, but this is not the case in (II). We believe that the origin of these differences in the coordination geometries lies in the different conformations of the ligands (see below).

The N atoms of both the 2-picolyl and 3-picolyl substituents are too remote from the metal centres to form Ni—N bonds. In both of these complexes with picolyl substituents, (I) and (II), there are two independent molecules with similar, but slightly different, conformations (Figs. 3 and 4). In the 2-picolyl complex, (I), the pyridyl N—Ni distances are

Figure 2
A view of one of the two independent molecules of (II), showing the atom-numbering scheme. H atoms have been omitted for clarity and displacement ellipsoids are drawn at the 50% probability level.

In (II), the two molecules also have different degrees of tetrahedral distortion, indicated by r.m.s. deviations of 0.139 and 0.074 Å, as well as different displacements of 0.001 (5) and 0.044 (4) Å (away from N1*A*) of the metal centre from the N_3O plane. Interestingly, there is no correlation between the degree of tetrahedral distortion and the displacement of the metal centre. In (I), the greater distortion is associated with
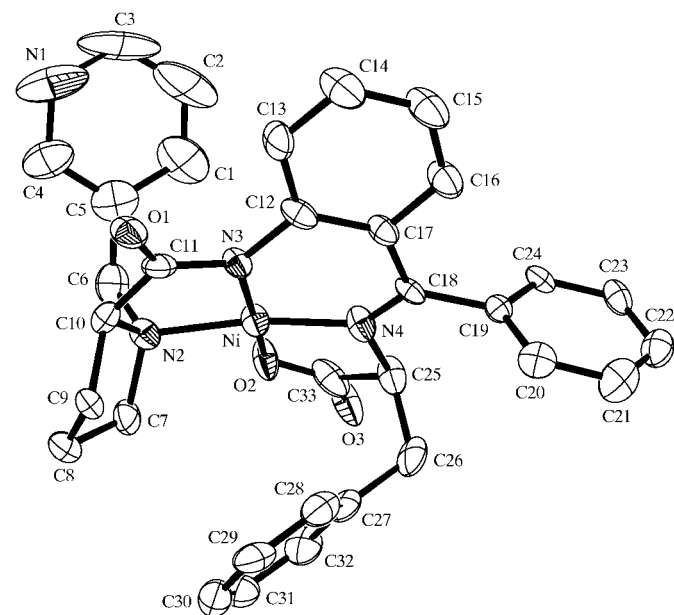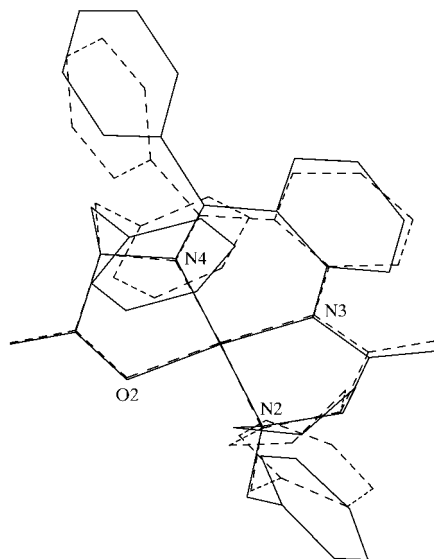
metal-organic compounds

Figure 3
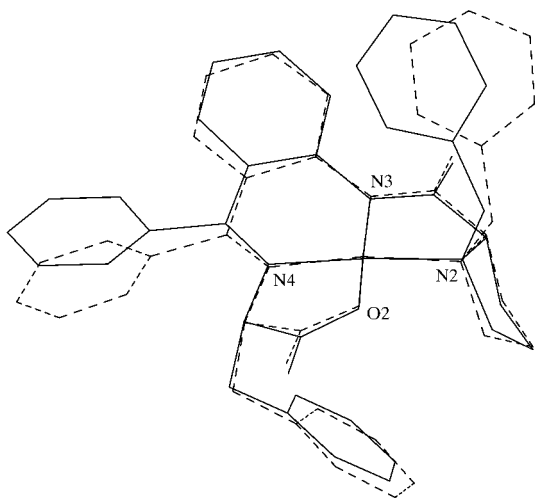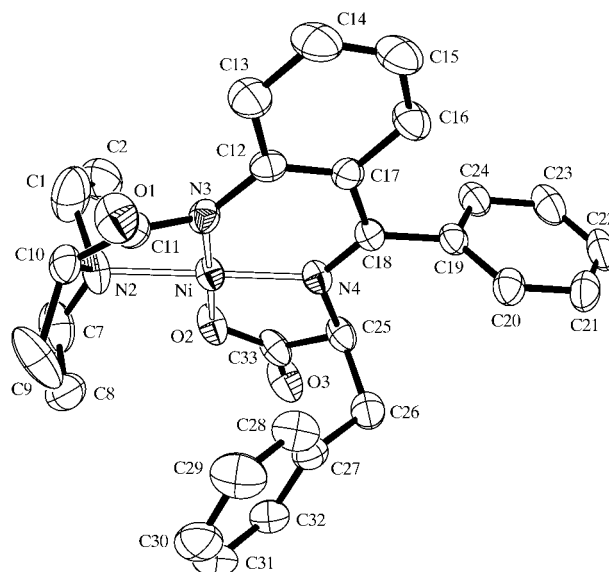The results of a least-squares fit to the labelled donor atoms of the two molecules in (I). The molecules are distinguished by solid and dotted bonds.

Figure 5
A view of the molecule of (III), showing the atom-numbering scheme. H atoms have been omitted for clarity and displacement ellipsoids are drawn at the 30% probability level.

2.861 (7) and 2.954 (8) Å, while in the 3-picolyl complex, (II), these are even longer, at 5.339 (15) and 5.024 (12) Å. Despite these differences, and the presence in (II) of a poorly defined water molecule which is hydrogen bonded to the complex *via* atom N1 [N1···O1W = 2.88 (2) Å], the space groups are the same, the unit-cell dimensions are similar and the unit-cell volumes differ by only 0.7%. We believe that the differences in the coordination geometry at the Ni centre in (I) and (II) can be traced to the different ligand conformations (Figs. 3 and 4), which induce differing types and degrees of distortion. In turn, the adoption of these ligand conformations allows efficient packing between adjacent symmetry-independent molecules.

Figure 4
The results of a least-squares fit to the labelled donor atoms of the two molecules in (II). The molecules are distinguished by solid and dotted bonds.

This packing involves a number of interactions between aromatic rings, including some face-to-edge interactions.

These two crystal structures show a significant similarity with those of (S)-BPB/Ni^{II} and a wide variety of α-amino acids that have been reported previously [(S)-BPB with Ni^{II} and (2S,3S)-2-(trifluoromethyl)threonine (Soloshonok *et al.*, 1993); (S)-BPB with Ni^{II} and ω-ethyl (2S,3S)-3-trifluoro-methylglutamate (Soloshonok *et al.*, 1997); (S)-BPB with Ni^{II} and (2S,3S,4R)-3-trifluoromethyl-4-methylpyroglutamic acid (Soloshonok *et al.*, 1999); (S)-BPB with Ni^{II} and dehydro-aminobutanoic acid (Belokon' *et al.*, 1990); (S)-2-[N-(N'-benzylprolyl)amino]acetophenone with Cu^{II} and glycine (Belokon *et al.*, 1983); and (S)-2-[N-(N'-benzylprolyl)amino]-acetophenone with Ni^{II} and (R)-valine (Lindeman *et al.*, 1985)].

A square-planar geometry around Ni^{II} is also observed in the third complex, (III), where the picolyl substituents have been replaced by a less sterically demanding ethyl group (Fig. 5 and Table 3). Here, there is only one molecule per asymmetric unit, and the distance from the Ni centre to the sp^3-hybridized N2 atom is again longer than the other three Ni—N/O distances, in this case by approximately 0.1 Å. There is no significant tetrahedral distortion (the r.m.s. deviation of the constituent atoms from the N$_3$O donor-atom plane is only 0.016 Å) and the metal centre lies in this plane [calculated deviation 0.003 (4) Å].

Experimental

Complexes (I)–(III) were prepared using the standard literature methods of Belokon' (1992*a,b*). The ligand (S)-2-{[N-(2-picolyl)pro-lyl]amino}- [for (I)], (S)-2-{[N-(3-picolyl)prolyl]amino}- [for (II)] or (S)-2-[(N-ethylprolyl)amino]benzophenone [for (III)], racemic phenyl-

alanine (5 equivalents) and nickel(II) nitrate hexahydrate (2 equivalents) were dissolved in anhydrous methanol, and a 1.3 M solution of sodium methoxide (22 equivalents) in methanol was added. The resulting orange-coloured solution was heated for 2 h at 323 K, cooled in ice and then quenched with water. The resulting suspension was extracted with dichloromethane and the combined organic phases were dried over sodium sulfate, before being concentrated *in vacuo* to give a red–brown residue. The required complex was obtained after purification of this residue on silica gel (8:1 chloroform–acetone). All three complexes were dark red–brown and the crystals used for analysis were grown in acetone with the addition of pentane and under cooling. Further optimization of the method for producing the complexes has appeared since we conducted our research (Nadvornik & Popkov, 2002; Belokon' *et al.*, 1998).

Compound (I)

Crystal data

[Ni(C$_{33}$H$_{30}$N$_4$O$_3$)]
$M_r = 589.32$
Orthorhombic, $P2_12_12_1$
$a = 11.722$ (2) Å
$b = 18.391$ (14) Å
$c = 25.528$ (6) Å
$V = 5503$ (4) Å^3
$Z = 8$
$D_x = 1.423$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 35 reflections
$\theta = 13–15°$
$\mu = 0.75$ mm^{-1}
$T = 150$ (2) K
Block, red
$0.42 \times 0.33 \times 0.29$ mm

Data collection

Stoe Stadi-4 four-circle diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (*X-RED*; Stoe & Cie, 1995)
$T_{min} = 0.730$, $T_{max} = 0.825$
6352 measured reflections
5359 independent reflections
4490 reflections with $I > 2\sigma(I)$

$R_{int} = 0.136$
$\theta_{max} = 25.1°$
$h = 0 \rightarrow 13$
$k = 0 \rightarrow 21$
$l = 0 \rightarrow 30$
3 standard reflections frequency: 60 min intensity variation: ±15.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.115$
$S = 1.18$
5355 reflections
740 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0088P)^2 + 15.94P]$
    where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.48$ e Å^{-3}
$\Delta\rho_{min} = -0.46$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.00049 (11)
Flack parameter = −0.03 (2)

Table 1
Selected geometric parameters (Å, °) for (I).

Ni—N2	1.932 (6)	NiA—N2A	1.932 (6)
Ni—N3	1.862 (5)	NiA—N3A	1.846 (6)
Ni—N4	1.833 (6)	NiA—N4A	1.855 (6)
Ni—O2	1.872 (5)	NiA—O2A	1.863 (5)
Ni···N1	2.861 (7)	NiA···N1A	2.954 (8)
N2—Ni—N3	88.2 (3)	N2A—NiA—N3A	88.8 (2)
N2—Ni—N4	175.1 (3)	N2A—NiA—N4A	168.2 (2)
N2—Ni—O2	89.5 (2)	N2A—NiA—O2A	90.2 (2)
N3—Ni—N4	95.4 (2)	N3A—NiA—N4A	95.3 (3)
N3—Ni—O2	175.0 (3)	N3A—NiA—O2A	173.0 (3)
N4—Ni—O2	87.0 (2)	N4A—NiA—O2A	87.1 (2)

Compound (II)

Crystal data

[Ni(C$_{33}$H$_{30}$N$_4$O$_3$)]·0.5H$_2$O
$M_r = 598.33$
Orthorhombic, $P2_12_12_1$
$a = 11.522$ (4) Å
$b = 18.623$ (6) Å
$c = 25.828$ (7) Å
$V = 5542$ (3) Å^3
$Z = 8$
$D_x = 1.434$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 32 reflections
$\theta = 12.4–13.7°$
$\mu = 0.75$ mm^{-1}
$T = 150$ (2) K
Tablet, dark red
$0.35 \times 0.27 \times 0.16$ mm

Data collection

Stoe Stadi-4 four-circle diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (*X-RED*; Stoe & Cie, 1995)
$T_{min} = 0.789$, $T_{max} = 0.864$
5291 measured reflections
4765 independent reflections
3785 reflections with $I > 2\sigma(I)$

$R_{int} = 0.044$
$\theta_{max} = 23.5°$
$h = 0 \rightarrow 12$
$k = -20 \rightarrow 20$
$l = 0 \rightarrow 29$
3 standard reflections frequency: 60 min intensity variation: ±5.2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.066$
$wR(F^2) = 0.126$
$S = 1.29$
4765 reflections
748 parameters

H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + 16.36P]$
    where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.004$
$\Delta\rho_{max} = 0.48$ e Å^{-3}
$\Delta\rho_{min} = -0.42$ e Å^{-3}

Table 2
Selected geometric parameters (Å, °) for (II).

Ni—N2	1.914 (9)	NiA—N2A	1.934 (9)
Ni—N3	1.853 (6)	NiA—N3A	1.851 (8)
Ni—N4	1.828 (8)	NiA—N4A	1.856 (8)
Ni—O2	1.865 (6)	NiA—O2A	1.874 (6)
Ni···N1	5.339 (15)	NiA···N1A	5.024 (12)
N2—Ni—N3	87.6 (3)	N2A—NiA—N3A	88.3 (4)
N2—Ni—N4	171.0 (3)	N2A—NiA—N4A	175.6 (3)
N2—Ni—O2	89.9 (3)	N2A—NiA—O2A	89.8 (3)
N3—Ni—N4	96.7 (3)	N3A—NiA—N4A	95.6 (4)
N3—Ni—O2	170.7 (3)	N3A—NiA—O2A	173.3 (4)
N4—Ni—O2	87.1 (3)	N4A—NiA—O2A	86.5 (3)

Compound (III)

Crystal data

[Ni(C$_{29}$H$_{29}$N$_3$O$_3$)]
$M_r = 526.26$
Orthorhombic, $P2_12_12_1$
$a = 9.692$ (3) Å
$b = 10.047$ (2) Å
$c = 26.060$ (6) Å
$V = 2537.6$ (11) Å^3
$Z = 4$
$D_x = 1.377$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 35 reflections
$\theta = 12.5–14.5°$
$\mu = 0.80$ mm^{-1}
$T = 220$ (2) K
Block, dark red
$0.78 \times 0.47 \times 0.39$ mm

Data collection

Stoe Stadi-4 four-circle diffractometer
ω/θ learnt-profile scans
Absorption correction: numerical (*X-RED*; Stoe & Cie, 1995)
$T_{min} = 0.568$, $T_{max} = 0.765$
2570 measured reflections
2560 independent reflections
2358 reflections with $I > 2\sigma(I)$

$R_{int} = 0.011$
$\theta_{max} = 25°$
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 31$
3 standard reflections frequency: 60 min intensity variation: ±3.6%

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Table 3
Selected geometric parameters (Å, °) for (III).

Ni—N2	1.944 (5)	Ni—N4	1.847 (5)
Ni—N3	1.832 (5)	Ni—O2	1.851 (4)
N2—Ni—N3	85.7 (2)	N3—Ni—N4	95.1 (2)
N2—Ni—N4	179.2 (2)	N3—Ni—O2	178.1 (2)
N2—Ni—O2	92.7 (2)	N4—Ni—O2	86.5 (2)

The known absolute configurations of the amino acid moieties were confirmed by the values found for the Flack (1983) parameters, *viz.* −0.03 (2), 0.01 (3) and −0.03 (3) for (I), (II) and (III), with 0, 194 and 0 Friedel pairs recorded. The C—H atoms in (I) and (II) were placed geometrically and refined riding on their parent atoms, at distances of 0.95–1.00 Å and with U_{iso}(H) values of 1.2U_{eq}(C). The corresponding C—H range in (III) was 0.94–0.99 Å and methyl H atoms had U_{iso}(H) values of 1.5U_{eq}(C). The water H atoms in (II) were not located.

For all compounds, data collection: *STADI*4 (Stoe & Cie, 1995); cell refinement: *STADI*4; data reduction: *X-RED* (Stoe & Cie, 1995); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL/PC* (Bruker, 1997); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2002).

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