ASYMMETRIC SYNTHESIS OF (*S*)-2-AMINO-3-(1-NAPHTHYL)PROPANOIC ACID VIA CHIRAL NICKEL COMPLEX. CRYSTAL STRUCTURE, CIRCULAR DICHROISM, ^{1}H AND ^{13}C NMR SPECTRA OF THE COMPLEX

Alexander POPKOV[a,*], Ivana CÍSAŘOVÁ[b], Jana SOPKOVÁ[c], Josef JIRMAN[d], Antonín LYČKA[e] and Konstantin A. KOCHETKOV[f,*]

[a] *Faculty of Health and Social Studies, University of South Bohemia, 370 01 České Budějovice, Czech Republic; e-mail: sasha@jcu.cz*

[b] *Department of Inorganic Chemistry, Faculty of Natural Sciences, Charles University, Hlavova 2030, 128 40 Prague 2, Czech Republic; e-mail: cisarova@natur.cuni.cz*

[c] *UFR des Sciences Pharmaceutiques, 5 rue Vaubénard, 14032 Caen, France*

[d] *Research Institute for Pharmacy and Biochemistry, U Kabelovny 130, 102 37 Prague 10, Czech Republic; e-mail: jirman@vufb.cz*

[e] *Research Institute for Organic Syntheses, Rybitví 296, 532 18 Pardubice 20, Czech Republic; e-mail: antonin.lycka@vuosas.cz*

[f] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Vavilov Street 28, 117813 Moscow, Russia; e-mail: const@ineos.ac.ru*

Received March 2, 2005
Accepted June 6, 2005

The recently published environmentally friendly preparation of a glycine synthon **2** from regeneratable chiral auxiliary **BPB** ((*S*)-*N*-(2-benzoylphenyl)-*N*′-benzylprolinamide) was used for preparative asymmetric synthesis of the non-coded amino acid 3-(1-naphthyl)alanine (**1**). Full assignment of ^{1}H and ^{13}C NMR of both intermediate complex **3** and **1** and X-ray structure determination of complex **3** were made. Cotton effects observed in circular dichroism spectrum of complex **3** are consistent with published empirical rules.

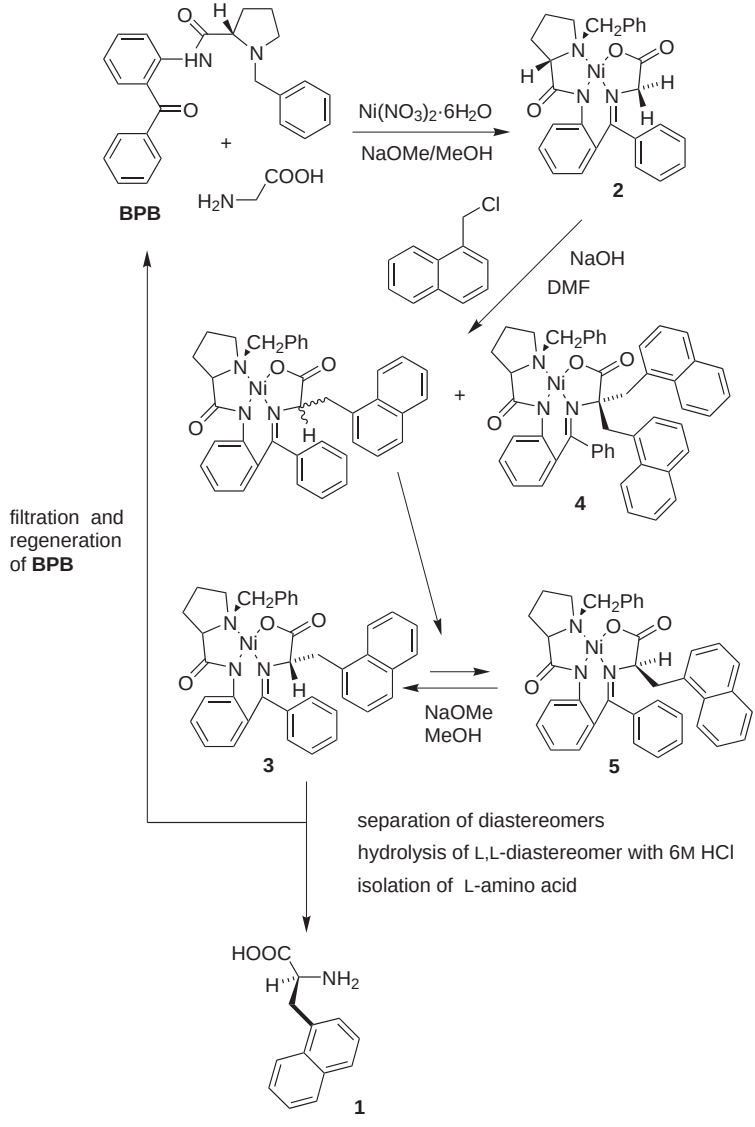
Keywords: Amino acids; Biomimetic synthesis; BPB; Circular dichroism; Chiral auxiliaries; Crystal structure determination; Naphthylalanine; Nickel; NMR spectroscopy; Schiff bases.

Heavy environmental impact of waste-water and by-products released by chemical and pharmaceutical industry requires development of new "green" synthetic procedures for manufacture of active pharmaceutical intermediates. Efficient catalytic approaches have been suggested for a big number of α-amino acids[1]. Development of such catalytic syntheses often requires time-consuming screening for an optimal catalyst, precursor and reaction conditions. Chiral stoichiometric α-amino acids synthons are often the optimal choice for preparation of small batches of new α-amino acids and for special application like preparation of radiolabeled α-amino ac-

ids[2]. Many stoichiometric approaches lead to destruction of a chiral auxiliary used. A synthetic pathway employing chiral nickel complexes prepared from α-amino acids and chiral auxiliary **BPB** ((*S*)-*N*-(2-benzoylphenyl)-*N*′-benzylprolinamide) is an exception. After preparation of desired α-amino acid, enantiomerically pure **BPB**·HCl is regenerated in high yield (>90%)[3]. The complexes provide easy generation of intermediate carbanion due to high acidity of α-hydrogen of an amino acid fragment ($pK_a \geq 19$)[4]. Unlike many other chiral synthons, they enable asymmetric synthesis of substituted prolines from α,β-unsaturated aldehydes and ketons via 1,4-addition followed by hydrolysis of a complex and reduction of C=N bond[5]. Another unique feature of the complexes is a bis-alkylation of the glycine synthon with CH_2Cl_2 followed by hydrolysis which lead to enantiomerically pure (*S*,*S*)-2,4-diaminoglutaric acid. This diamino dicarboxylic acid has been prepared by a number of multistep syntheses[6]. Based on known alkylation of the glycine synthon with CH_2Br_2 [7], we developed a very simple approach for bis-alkylation of a glycine synthon where CH_2Cl_2 was used both as an alkylating agent and as a solvent[8]. Recently, a preparative modification of this synthesis was published[9]. Complex of enantiomerically pure (*S*,*S*)-2,4-diaminoglutaric acid could be also prepared by one-pot reaction of **BPB** with nickel nitrate and *S*-(2-aminoethyl)cysteine in MeONa/MeOH [10]. In this article we describe a preparative asymmetric synthesis of non-coded amino acid 3-(1-naphthyl)alanine ((*S*)-2-amino-3-(1-naphthyl)propanoic acid; **1**) (Scheme 1), full assignment of ^1H and ^{13}C NMR spectra of both the intermediate complex **3** and amino acid **1**, a comparison of X-ray structures of single crystals of glycine synthon **2** and complex **3** and circular dichroism spectra of their methanolic solutions. The synthesis applies a recently published environmentally friendly preparation of the starting metallocomplex glycine synthon **2** (Scheme 2)[11–13].

Preparative applications of the synthon were developed by several groups[14]. Most of the syntheses described in the literature deal with amino acids soluble in water in a wide pH range. This specific property requires sorption–desorption on a cation-exchange resin for separation of amino acid and nickel cations present in aqueous solution after hydrolysis of a single diastereomer of an alkylated complex. Amino acid **1** is not water-soluble at pH 7. The isolation procedure used in this work thus could be considered a model approach for isolation of highly lipophilic amino acids (for another example, see ref.[15]). Earlier we fully assigned NMR spectra of several similar complexes bearing H, NMe_2 or Br substituents on the α-carbon atom on amino acid fragment (C-19)[16]. The spectra of compound **3** (presented here) are more complex due to overlap of a number of aromatic hydrogen

and carbon signals. X-ray structure determination of complex **3** followed by its comparison with the published structure of the starting synthon **2** [17] aimed at deeper understanding of intra- molecular interactions affected

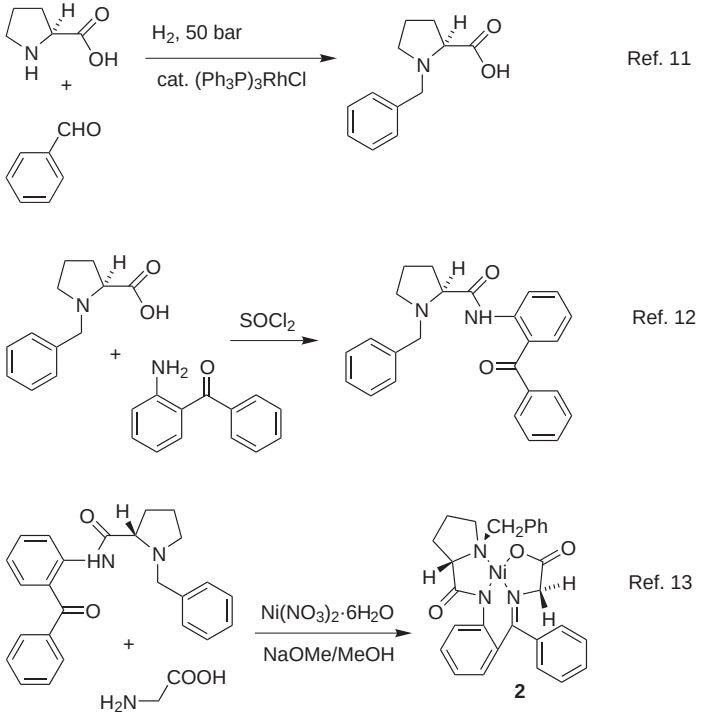


SCHEME 1
Synthesis of **1**

stereochemical outcome of alkylation of complex **2**. Although naphthylalanine **1** is a steric analogue of L-tryptophan, it is a poor substrate for tryptophan decarboxylases, deaminases and hydroxylases. When tryptophan is replaced by naphthylalanine in a peptide, amide bonds formed by naphthylalanine are much more stable to enzymatic transformations. This non-coded amino acid is manufactured by a number of vendors for design of peptidomimetic drug candidates[18].

RESULTS AND DISCUSSION

The most common application of nickel complexes as chiral amino acids synthons consists of several standard steps (Scheme 1): (i) Template preparation of the starting complex **2** from glycine, nickel salt and re-usable chiral auxiliary **BPB**. (ii) Alkylation of complex **2** with an electrophile (1-(chloromethyl)naphthalene in our case) in an aprotic solvent. (iii) Retro-



SCHEME 2
Preparation of complex **2**

racemisation of the reaction mixture in MeONa/MeOH [19]. (iv) Separation of diastereomers of the alkylated complex **3** and **5**, starting complex **2** and a minor amount of a product of bis-alkylation **4**. (v) Optional retroracemisation of the undesired diastereomer **5** in MeONa/MeOH. (vi) Acid hydrolysis of diastereomerically pure complex **3**, isolation of the amino acid and regeneration of **BPB**.

Preparation of the starting complex was optimised in order to reduce the amount of nickel in aqueous-organic waste[13]. The alkylation reaction was performed under heterogeneous conditions employing minimum amount of (toxic) aprotic solvent DMF. High concentrations of reagents increase the speed of the reaction. Stereochemistry of alkylation of such complexes in aprotic solvents is usually kinetically controlled. In order to increase the diastereomeric purity of the alkylated complex, the thermodynamically controlled retroracemisation in MeONa/MeOH should be used for the crude alkylation product[19]. In thermodynamically controlled conditions diastereomeric excess of the desired L,L-diastereomer is favored by repulsion between *ortho*-protons of the benzyl group and equatorial substituents of C-19 [16a]. For separation of predominant diastereomer, flash chromatography of retroracemised crude product was applied. L,L-Configuration of the main product was confirmed by X-ray structure determination taking into account L-configuration of **BPB** [17]. Circular dichroism (CD) spectra were employed for routine determination of configuration at C-19. The difference between CD spectrum of complex **2** and those of alkylated complexes (e.g. complexes **3**–**5**) is due to chromophore distortion introduced by C-19 substituents. In the case of bulky naphthalen-1-ylmethyl substituent the difference is very significant (Fig. 1, solid line corresponds to **3**, dashed line corresponds to **2**). In good agreement with the previously published empirical rules[19,20], methanolic solution of complex **3** demonstrates a positive Cotton effect in the range 610–480 nm and a negative Cotton effect in the range 370–480 nm. Retroracemisation decreased the amount of L,D-diastereomer **5** (nickel complex of a Schiff base of (*R*)-2-amino-3-(1-naphthyl)-propanoic acid and **BPB**) to far less than 1% in crude reaction mixture. Attempts to isolate **5** by preparative TLC on silica gal failed. High-melting complex **4**, the only by-product resulting from bis-alkylation of C-19 (nickel complex of the Schiff base of bis(1-naphthylmethyl)glycine and **BPB**), was isolated in 1% yield only. After hydrolysis of **3**, filtration of **BPB**·HCl, and adjusting pH to 9–10, amino acid **1** was filtered off (Scheme 1). The amino acid could be used for preparation of protected derivatives for peptide synthesis[18] without additional purification. Analytical sample was recrystallised from water–ethanol.

Recrystallised recovered **BPB** was re-used for preparation of **2** thus justifying biomimetic, enzyme-like character of this synthetic approach. We assume that chromatographic purification of **3** is not necessary for high-scale preparation of **1**. After retroracemisation the mixture of complexes (**3** and negligible amounts of **4** and **5**) could be hydrolysed followed by one or two crystallisations of amino acid **1** in order to remove traces of D-enantiomer and bis(1-naphthylmethyl)glycine.

NMR Spectroscopy

The ^{1}H and ^{13}C chemical shifts were assigned using gs (gradient selected)-H,H-COSY, 1D-gs-NOESY, gs-HSQC (optimised for $^{1}J(^{13}C,^{1}H) \approx 160$ Hz) and gs-HMBC (optimised for $^{3}J(^{13}C,^{1}H) = 7$ Hz). H,H-COSY provided us with proton-proton connectivity and 1D-gs-NOESY showed the through-space interaction of amino acid protons H-32 and H-34. The ^{13}C chemical shifts assignment was straightforward using HSQC and HMBC spectra[21,22].

Main arguments for assignment of some crucial signals and space direction of some atoms of complex **3** (for NMR numbering, see Fig. 2) are:

Protons H-4, H-19 and ortho protons of benzyl group (H-23 and H-27) have NOESY cross-peaks. It means they have to be on upper site of the com-

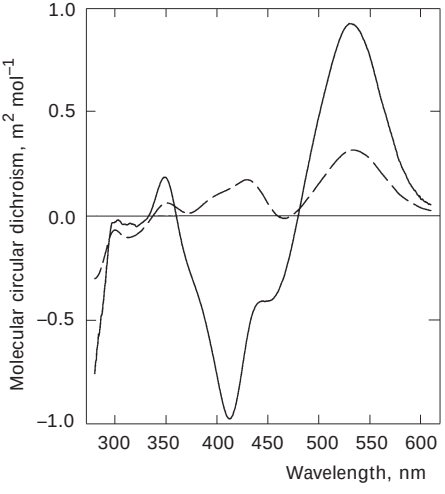


FIG. 1
Circular dichroism spectra of methanolic solutions of complexes **2** (dashed line) and **3** (solid line)

plex plane and benzyl group is rotated towards H-19. Proton H-37 of naphthalene ring has a NOESY cross-peak with H-18 proton. Proton H-37 of naphthalene ring has a NOESY cross-peak with proton H-19 and both methylene protons H-28. Proton H-19 has a NOESY cross-peak with naphthalene ring protons H-36 and H-37. There are positive cross-peaks in NOESY TPPI spectrum between pairs of protons H-14 and H-18 and H-15 and H-17. It means slow rotation of phenyl ring around the bond C-12/C-13. Such rotation has been observed in similar complexes[16a]. H-19 and H-28a should be closer through space then H-19 and H-28b because there exists bigger cross-peak in first pair in NOESY spectrum. It corresponds with its coupling constants that in case of pair H-19/H-28b shows higher dihedral angle of bonds C-19/H-19 and C-28/H-28b.

Previously, ^{13}C and ^{1}H NMR spectra were fully assigned for nickel complex of the Schiff base of L-2-dimethylaminoglycine and **BPB** (L,L-DMGK)[16a]. While having the same stereochemistry of all chiral centres as complex **3**, this complex bears a dimethylamino substituent at C-19. Unlike the dimethylamino group in L,L-DMGK, 1-naphthylmethyl group in complex **3** strongly affects several signals of the nucleus belonging to the core of the complex by its electron-rich aromatic rings, both H_a-3 and H_b-3 signals were shifted 0.99 and 0.73 ppm downfield in ^{1}H NMR spectrum of **3**, respectively. C-12 signal is shifted 3.9 ppm upfield, C-19 signal – 13.81 ppm upfield and C-20 signal – 2.29 ppm downfield. These carbon atoms are proximate to those of 1-naphthylmethyl group; the proximity of H-37 to H-19 was also confirmed by both NOE and X-ray data. *N*-Benzyl group in $CDCl_3$ solution is rotated towards C-19 and the nickel atom. This arrangement is confirmed by NOE cross-peaks between pairs of protons H-4 H-23 (H-27) and H-23 (H-27) H-19. In the single crystal the benzyl group is ro-

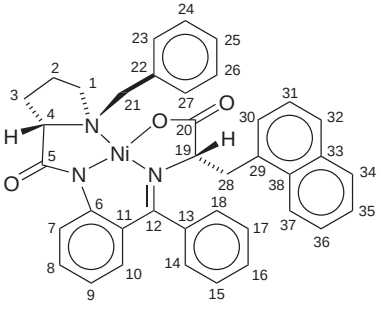


FIG. 2
NMR numbering scheme for **3**

tated outside the nickel atom. Proximity of H-37 to H-18 observed in $CDCl_3$ solution does not occur in the single crystal. Differences between ^{13}C and ^{1}H NMR spectra of 1-naphthylmethyl group in complex **3** and in amino acid **1** are much lower and could be mostly attributed to recording the spectra in different solvents and at different pH.

*X-ray Crystallography of Complex **3***

Structure description. The molecular structures of the Ni complex of Schiff base of **BPB** and two amino acids (glycine or 3-(1-naphthyl)alanine) were compared (Scheme 1). Molecular structure of **3** with the atom numbering scheme is shown in Fig. 3. The structure of **2** has been published elsewhere[17]. The core of the title compounds, i.e. atoms in the neighbourhood of Ni, has in all structures an approximately planar arrangement. Root-mean-square deviation from the least-square plane fitted through the five central atoms – O2, N1, N2, N3 (atoms that co-ordinate Ni1) and Ni1 ca. 0.065 Å for **3**. The Ni1 atom lies in the centre of a planar core of the two compounds, and is co-ordinated by four atoms, three nitrogens (N1, N2 and N3) and one oxygen (O2). The arrangement of Ni1 co-ordination is

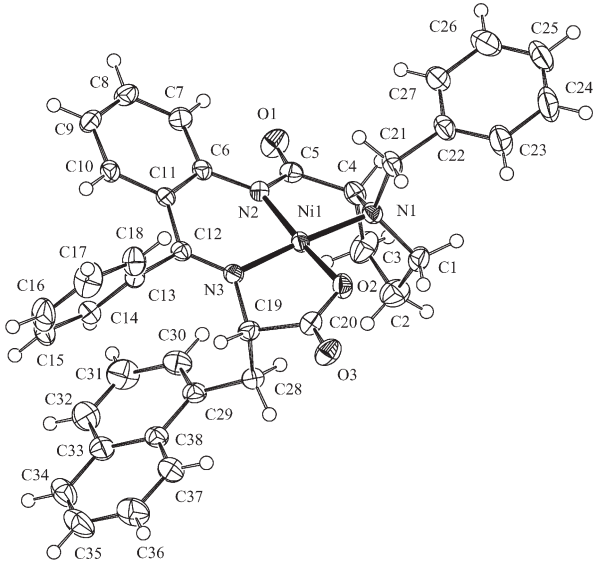


FIG. 3

A perspective view of complex **3** with the atom labelling scheme for non-hydrogen atoms. Displacement ellipsoids are shown at the 50% probability level

square planar. The N–Ni1 and O–Ni1 bond lengths are very close in the two complexes (see Table I), but they are slightly shorter than the published average values – 2.07 Å for the N–Ni1 and 2.06 Å for O–Ni1 [23]. Furthermore, the N1–Ni1 bond lengths are longer by ca. 0.1–0.07 Å than the other three Ni co-ordinated bonds in both structures, whose bond lengths are very close (1.84–1.87 Å).

The phenyl group bonded to the C13 atom is oriented approximately perpendicularly the core plane, taking up a position perpendicular to the phenylene group which is situated with the Ni1 core (C6, C7, C8, C9, C10 and C11). These two aromatic rings form an acute angle of 89.5° in the complex **2**, and an acute angle of 85.57(7)° in the complex **3**. Benzyl group is oriented in both complexes above the Ni(II) plane approximately parallel to this centre plane (see Fig. 3). However, its relative position with respect to the Ni1 atom changes as a function of the complex. In complex **2** it lies towards the Ni1 atom, and in complex **3** it is oriented away from the Ni1 atom (see Fig. 3). The naphthalene ring in this complex lies on the other side of the Ni1 core plane from the N1 benzyl group and away from the Ni1 (see Fig. 3). The benzyl and the naphthalene rings are both positioned parallel to the Ni1 plane. In both **2** and **3** the pyrrolidine ring (C1, C2, C3, C4 and N1) is perpendicular to the Ni1 core plane in the direction below the core plane with respect to the N1 benzyl group. It takes a half-chair conformation.

π-Charge delocalization. We observed a charge delocalization in the proximity of the N2 atom due to the free π-orbital of this nitrogen atom. The bonds between the N2 and C6 and C5 (N2–C6 1.406(2) Å; N2–C5 1.366(3) Å) are shorter than the published average value for N–C(sp^2) bond ($d_{C-N} \approx$ 1.47(1) Å [23], and we find also a small deviation of the bond length of C5–O1

TABLE I
Selected distances (in Å) and angles (in °) of atoms co-ordinating the Ni atom

Distance	**2**	**3**	Angle	**2**	**3**
Ni1–O2	1.8357(12)	1.868(2)	N1–Ni1–N2	88.72(5)	87.60(7)
Ni1–N1	1.9229(12)	1.936(2)	N1–Ni1–N3	168.84(5)	176.78(8)
Ni1–N2	1.8384(12)	1 857(2)	N1–Ni1–O2	89.04(5)	91.88(7)
Ni1–N3	1.8357(12)	1.845(2)	N2–Ni1–N3	95.33(5)	94.53(7)
			N2–Ni1–O2	175.88(6)	173.69(7)
			N3–Ni1–O2	87.50(5)	86.27(7)

(1.225(3) Å) from the published value $d_{C=O} \approx 1.19(1)$ Å [23]. The situation in the proximity of N3 is more complicated and we observed only small deviations which are not significant, with the exception of the N3=C12 bond (1.296(3) Å) which is shorter than the reference value $d_{N=C} \approx 1.34$ Å.

Crystal packing. In both the complexes the usual hydrogen bond donors N–H, O–H are absent, the hydrogen is involved only in one "hydrogen bond", C(18)–H18···O1 (C···O 3.288(3) Å, H···O 2.51 Å, C–H···O 142°), which is significantly shorter than the sum of van der Walls radii. Neither strong intermolecular interaction of π system of aromatic rings nor any electron donation to Ni1 atom was found in complex **3**, therefore, its crystal packing is probably controlled by weak van der Walls interactions. Detailed description of inter- and intramolecular interactions in crystals of **2** was published elsewhere[17b,17c].

CONCLUSIONS

The described procedure for asymmetric syntheses of α-amino acids is an optimal approach for preparation of small batches of new α-amino acids for research and industrial purposes. Stereochemistry of intermediate chiral complexes could be disclosed by circular dichroism, X-ray crystallography or by NOE interactions in ^{1}H NMR spectra. For extremely demanding applications like preparation of enantiomerically pure [^{11}C]amino acids for positron emission tomography, next generation chiral auxiliaries could be used instead of **BPB** [24].

EXPERIMENTAL

Optical rotation was measured with a Perkin–Elmer M241 polarimeter. Circular dichroism spectra were recorded on Jasco J-715 instrument. The ^{13}C (125.76 MHz) and ^{1}H (500.13 MHz) NMR spectra of compounds **3** and **1** were measured at ambient temperature on a Bruker Avance 500 spectrometer equipped with a 5-mm broadband probe with z-shielding and a SGI O_2 computer. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. Amino acid **1** (4 mg) was dissolved in a mixture of D_2O (0.6 ml) and two drops of CF_3COOD. The ^{13}C and ^{1}H NMR chemical shifts were referred to DSS ($\delta(^{13}C)$ 0.00, $\delta(^1H)$ 0.00 in D_2O). Complex **3** (30 mg) was dissolved in $CDCl_3$ (0.5 ml). The ^{13}C and ^{1}H NMR chemical shifts were referred to TMS ($\delta(^{13}C)$ 0.00, $\delta(^1H)$ 0.00 in $CDCl_3$). Two-dimensional gs-H,H-COSY, 1D-gs-NOESY, gs-HSQC, and gs-HMBC spectra were measured using standard microprograms provided by Bruker.

Structure Determination

Crystal data for **3**: $C_{38}H_{33}N_3NiO_3$, M = 638.38, monoclinic, $P2_1$ (No. 4), a = 10.3270(2) Å, b = 8.8190(2) Å, c = 17.4540(3) Å, β = 102.748(1)°, V = 1550.42(3) Å^3, Z = 2, D_x = 1.367 Mg m^{-3}.

A red crystal 0.4 × 0.2 × 0.01 mm was mounted on a glass capillary with epoxy glue and measured on a Nonius KappaCCD diffractometer using monochromatised MoKα radiation (λ = 0.71073 Å) at 150(2) K. Absorption was neglected (μ = 0.669 mm^{-1}). A total of 21 891 measured reflections in the range h = –13 to 13, k = –11 to 11, l = –22 to 2 (θ_{max} = 27.5°), of which 7099 were unique (R_{int} = 0.044), 6553 were observed according to the $I > 2\sigma(I)$ criterion. Cell parameters were obtained from 3745 reflections (θ = 1–27.5°). The structure was solved by direct methods (SIR92)[25] and refined by full-matrix least squares based on F^2 (SHELXL97)[26]. The hydrogen atoms on carbons were fixed in idealised positions (riding model) and assigned temperature factors H_{iso}(H) = 1.2 U_{eq}(pivot atom). The refinement converged (Δ/σ_{max} = 0.002) to R = 0.032 for observed reflections and wR = 0.071, GOF = 1.040 for 406 parameters and all 7099 reflections. The final difference map displayed no peaks of chemical significance ($\Delta\rho_{max}$ = 0.324, $\Delta\rho_{min}$ = –0.324 e $Å^{-3}$). CCDC 261140 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

The mass spectra of compound **4** were measured on a ZAB-SEQ double-focusing mass spectrometer (VG Analytical). The fast atom beam used was generated from xenon ions, which were accelerated to 8 kV. The liquid matrix of bis(2-hydroxyethyl)disulfide (DS) was used for measurement. The samples were dissolved in chloroform and added to the matrix. For high-resolution measurements the instrument was tuned to a resolution of 5000 (10% valley definition).

Note: High-purity argon atmosphere should be used in the alkylation reaction. Argon-vacuum line is strongly recommended. The use of technical nitrogen instead of high-purity argon leads to oxidation of carbanions.

Nickel(II) Complex of the Schiff Base of (*S*)-*N*-(2-Benzoylphenyl)-*N′*-benzylprolinamide and (*S*)-2-Amino-3-(1-naphthyl)propanoic Acid **3**

To a stirred mixture of **2** [11–13] (10 g, 20 mmol) and powdered NaOH (3.6 g, 90 mmol) in DMF (30 ml) was added 1-(chloromethyl)naphthalene (3.9 g, 22 mmol) in two portions under Ar. After 1 h the reaction mixture was poured into a 5% solution of citric acid (400 ml). The red precipitate was filtered, washed with water and air-dried for 15 h. The precipitate was dissolved in MeONa/MeOH (0.5 mol/l, 200 ml) under Ar. After 2 h the reaction mixture was poured into 5% solution of citric acid (400 ml). Methanol and a part of water were evaporated in vacuum. The red precipitate was filtered off, washed with water and air dried for 15 h. The precipitate was purified by column chromatography on silica gel (80 × 5 cm, $CHCl_3$). The first red fraction contains the bis-alkylation product **4**, the second (main) fraction contains complex **3**. Analytical samples were additionally purified by preparative TLC on silica gel followed by gel chromatography on Sephadex LH-20 (toluene/methanol 2:1).

Compound **4**: Red crystals. Yield 0.15 g (1% based on **2**), m.p. 303–305 °C. EI-MS: 777.9 (2.7%), 733.9 (18%), 636.8 (8.2%), 495.6 (10%), 439.5 (10%), 217.3 (13%), 160.3 (100%), 91.17 (73.6%). High resolution FAB-MS: 778.2496; for ($C_{49}H_{41}N_3NiO_3$ + H^+) calculated: 778.2579.

Compound **3**: Red crystals. Yield 11 g (86% based on **2**), m.p. 259–261 °C. ^{1}H NMR (500 MHz, $CDCl_3$): $H1_a$ 1.94 $H1_b$ 3.17, $H2_a$ 1.94 $H2_b$ 3.00, $H3_a$ 2.44 $H3_b$ 2.46, H4 1.94 ^3J_a = 10.1 ^3J_b = 7.1, H7 8.16, H8 7.09, H9 6.60, H10 6.48, H14 7.12, H15 7.30, H16 7.20, H17

6.79, H18 5.91, H19 4.42 ^3J_a = 7.7 ^3J_b = 5.0, H21$_a$ 3.45 H21$_b$ 4.31 ^2J_a = 12.7, H23 8.00, H24 7.28, H25 7.12, H26 7.28, H27 8.00, H28$_a$ 3.82 ^3J_a = 14.1 ^3J_b = 5.0, H28$_b$ 4.05 ^3J_a = 14.1 ^3J_b = 7.7, H30 7.38, H31 7.76, H32 7.35, H34 7.76, H35 7.35, H36 7.19, H37 7.55. ^{13}C NMR (125 MHz, $CDCl_3$): C1 57.02, C2 23.63, C3 30.77, C4 70.44, C5 180.06, C7 123.18, C8 132.24, C9 120.47, C10 133.57, C11 126.11, C12 170.78, C13 134.50, C14 127.25, C15 128.40, C16 129.06[a], C17 128.35, C18 127.49, C19 71.33, C20 178.58, C21 63.01, C22 133.16, C23 131.39, C24 128.76, C25 128.74[a], C26 128.76, C27 131.39, C28 39.87, C29 132.55, C30 126.20, C31 128.26[b], C32 125.45[c], C33 131.85, C34 128.15[b], C35 128.74[c], C36 125.75, C37 123.40, C38 133.11 ([a, b, c] – assignment can be interchanged).

Note: Some assignments of naphthalene ring carbons in ^{13}C NMR spectrum of **3** have a smaller confidence, because experiments were made in inversion mode and resolution in F1 axis was not so good from point of view of very crowded spectrum area belonging to the naphthalene carbons and protons (even in 125 and 500 MHz spectra, respectively). For $C_{38}H_{33}N_3NiO_3$ (637.2) calculated: 71.49% C, 5.21% H, 6.58% N; found: 71.68% C, 5.22% H, 6.52% N.

(*S*)-2-Amino-3-(1-naphthyl)propanoic Acid **1**

A mixture of **3** (9.5 g, 15 mmol), 50 ml MeOH and 6 M HCl was refluxed for 1 h and then evaporated to dryness. Water (50 ml) was added to the residue and the insoluble material (corresponding to **BPB**·HCl) was filtered off, washed with water (4 × 50 ml), dried and stored (similar to ref.[15]). Under stirring, pH of the water solution was adjusted to 9–10 with aqueous NH_3, the precipitate of **1** was filtered off, washed with chloroform (40 ml), water (100 ml), cold MeOH (40 ml), and dried.

Amino acid **1**: Yield (73% based on **3**), m.p. 229–231 °C. $[\alpha]_D^{21}$ –15.0 (*c* 1, 0.3 M HCl), ref.[27] $[\alpha]_D^{20}$ –15.0 (*c* 0.97, 0.3 M HCl). ^{1}H NMR (500 MHz, $CDCl_3$): H19 4.56 ^3J_a = 9.2 ^3J_b = 5.9, H28$_a$ 3.64 ^3J_a = 14.8 ^3J_b = 5.9, H28$_b$ 4.05 ^3J_a = 14.8 ^3J_b = 9.2, H30 7.58, H31 7.63, H32 8.06, H34 8.12, H35 7.73, H36 7.78, H37 8.22. ^{13}C NMR (125 MHz, $CDCl_3$): C19 56.05, C20 174.11, C28 35.89, C29 136.53, C30 131.19, C31 128.52, C32 131.57, C33 132.82, C34 131.87, C35 129.15, C36 129.77, C37 125.63, C38 133.88. For $C_{13}H_{13}NO_2$ (215.3) calculated: 72.54% C, 6.09% H, 6.51% N; found: 72.67% C, 6.15% H, 6.40% N.

The authors thank Dr M. Durchan for assistance in circular dichroism spectra measurement and Dr K. Ubik for recording the mass spectra. Access to Jasco J-715 (grant MSMT 123100002) is acknowledged.

REFERENCES AND NOTES

1. a) Ma J. A.: *Angew. Chem., Int. Ed.* **2003**, *42*, 4290; b) Maruoka K., Takashi O.: *Chem. Rev.* **2003**, *103*, 3013.
2. a) Schöllkopf U.: *Tetrahedron* **1983**, *39*, 2085; b) Bull S. D., Davies S. G., Epstein S. W., Leech M. A., Ouzman J. V. A.: *J. Chem. Soc., Perkin Trans. 1* **1998**, 2321; c) Evans D. A., Bartroli H., Shih T. L.: *J. Am. Chem. Soc.* **1981**, *103*, 2127; d) Evans D. A., Weber A. E.: *J. Am. Chem. Soc.* **1986**, *108*, 6757; e) Seebach D., Sting A. R., Hoffmann M.: *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2708; f) Hintermann T., Seebach D.: *Helv. Chim. Acta* **1998**, *81*, 2093; g) Seebach D., Hoffmann M.: *Eur. J. Org. Chem.* **1998**, 1137; h) Oppolzer W.,

Moretti R., Zhou C.: *Helv. Chim. Acta* **1994**, *77*, 2363; i) Bourne G. T., Crich D., Davies J. W., Horwell. D. C.: *J. Chem. Soc., Perkin Trans. 1* **1991**, 1693. For review, see: j) Duthaler R. O.: *Tetrahedron* **1994**, *50*, 1539; k) Bailey P. D., Clayson J., Boa A. N.: *Contemp. Org. Synth.* **1995**, *2*, 173.

3. Belokon Yu. N., Bulychev A. G., Vitt S. V., Struchkov Yu. T., Batsanov A. S., Timofeeva T. V., Tsyryapkin V. A., Ryzhov M. G., Lysova L. A., Bakhmutov V. I., Belikov V. I.: *J. Am. Chem. Soc.* **1985**, *107*, 4252.
4. Terekhova M. I., Belokon Yu. N., Maleev V. I., Chernoglazova N. I., Kochetkov K. A., Belikov V. M., Petrov E. S.: *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985**, 905.
5. a) Belokon Yu. N., Bulychev A. G., Pavlov V. A., Fedorova E. B., Tsyryapkin V. A., Bakhmutov V. I., Belikov V. M.: *J. Chem. Soc., Perkin Trans. 1* **1988**, 2075; b) Chung H.-H., Benson D., Schultz P. G.: *Science* **1993**, *259*, 806.
6. a) Avenoza A., Cativiela C., Peregrina J. M., Zurbano M. M.: *Tetrahedron: Asymmetry* **1996**, *7*, 1555; b) Krasnov V. P., Zhdanova E. A., Korolyova M. A., Bukrina I. M., Kodess M. I., Kravtsov V. K., Biyushkin V. N.: *Russ. Chem. Bull.* **1997**, *46*, 319; c) Avenoza A., Cativiela C., Peregrina J. M., Zurbano M. M.: *Tetrahedron: Asymmetry* **1997**, *8*, 863; d) Tanaka K., Sawanishi H.: *Tetrahedron: Asymmetry* **1998**, *9*, 71, e) Tanaka K., Sawanishi H.: *Tetrahedron: Asymmetry* **2000**, *11*, 3837.
7. Belokon Yu. N., Chernoglazova N. I., Batsanov A. S., Garbalinskaya N. S., Bakhmutov V. I., Struchkov Yu. T., Belikov V. M.: *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987**, 852.
8. Popkov A., Votavová H.: *Chem. Listy* **1999**, *93*, 757.
9. Taylor S. M., Yamada T., Ueki H., Soloshonok V. A.: *Tetrahedron Lett.* **2004**, *45*, 9159.
10. Popkov A.: *XXVth Conference of Organic Chemists, Kutná Hora, Czech Republic, May 14–17, 2001*, Abstract No. KS 16. Pardubice University, Pardubice 2001.
11. Tararov V. I., Kadyrov R., Fischer C., Börner A.: *Synlett* **2004**, 1961.
12. Belokon Yu. N., Tararov V. I., Maleev V. I., Saveleva T. F., Ryzhov M. G.: *Tetrahedron: Asymmetry* **1998**, *9*, 4249.
13. Nádvorník M., Popkov A.: *Green Chem.* **2002**, *4*, 71.
14. a) Belokon Yu. N.: *Izv. Acad. Nauk, Ser. Khim.* **1992**, 1106; *Bull. Russ. Acad. Sci., Div. Chem. Sci.* **1992**, *41*, 868 (Engl. Trans.); and references therein; b) Belokon Yu. N.: *Pure Appl. Chem.* **1992**, *64*, 191; c) Soloshonok V. A., Avilov D. V., Kukhar V. P., Tararov V. I., Saveleva T. F., Churkina T. D., Ikonnikov N. S., Kochetkov K. A., Orlova S. A., Pisarevsky A. P., Struchkov Y. T., Raevsky N. I., Belokon Yu. N.: *Tetrahedron: Asymmetry* **1995**, *6*, 1741; d) De B. B., Thomas N. R.: *Tetrahedron: Asymmetry* **1997**, *8*, 2687; e) Belokon Yu. N., Tararov V. I., Maleev V. I., Saveleva T. F., Ryzhov M. G.: *Tetrahedron: Asymmetry* **1998**, *9*, 4249; f) Collet S., Bauchat P., Danion-Bougot D., Danion R.: *Tetrahedron: Asymmetry* **1998**, *9*, 2121; g) Soloshonok V. A., Cai C. Z., Hruby V. J.: *Tetrahedron* **1999**, *55*, 12045; h) Tang X., Soloshonok V. A., Hruby V. J.: *Tetrahedron: Asymmetry* **2000**, *11*, 2917; i) Cai C., Soloshonok V. A., Hruby V. J.: *J. Org. Chem.* **2001**, *66*, 1339; j) Belokon Yu. N., Kochetkov K. A., Ikonnikov N. S., Strelkova T. V., Harutyunyan S. R., Saghiyan A. S.: *Tetrahedron: Asymmetry* **2001**, *12*, 481; k) Debache A., Collet S., Bauchat P., Danion D., Euzenat L., Hercouet A., Carboni B.: *Tetrahedron: Asymmetry* **2001**, *12*, 761; l) Larionov O. V., Saveleva T. F., Kochetkov K. A., Ikonnokov N. S., Kozhushkov S. I., Yufit D. S., Howard J. A. K., Khrustalev V. N., Belokon Yu. N., de Meijere A.: *Eur. J. Org. Chem.* **2003**, 869; m) Belokon Yu. N., Kochetkov K. A., Borkin D. A.: *Mendeleev Commun.* **2003**, 132; n) Ueki H., Ellis T. K., Martin C. H., Boettiger T. U., Bolene S. B., Soloshonok V. A.: *J. Org. Chem.* **2003**, *68*, 7104; o) Saghiyan A. S., Geolchanyan A. V., Petrosyan

S. G., Ghochikyan T. V., Haroutunyan V. S., Avetisyan A. A., Belokon Yu. N., Fischer K.: *Tetrahedron: Asymmetry* **2004**, *15*, 705; p) Gu X. Y., Ndungu J. A., Qiu W., Ying J. F., Carducci M. D., Wooden H., Hruby V. J.: *Tetrahedron* **2004**, *60*, 8233.

15. Tararov V. I., Saveleva T. F., Kuznetsov N. Y., Ikonnikov N. S., Orlova S. A., Belokon Yu. N., North M.: *Tetrahedron: Asymmetry* **1997**, *8*, 79.
16. a) Jirman J., Popkov A: *Collect. Czech. Chem. Commun.* **1995**, *60*, 990; b) Jirman J., Nádvorník M., Sopková J., Popkov A.: *Magn. Reson. Chem.* **1998**, *36*, 351; c) Popkov A., Jirman J., Nádvorník M., Manorik P. A.: *Collect. Czech. Chem. Commun.* **1998**, *63*, 990.
17. a) Popkov A. N., Nádvorník M., Jirman J., Sopková J., Manorik P. A., Fedorenko M. A.: *Zh. Obshch. Khim.* **1998**, *68*, 1305; *Russ. J. Gen. Chem.* **1998**, *68*, 1242 (Engl. Trans.); b) Popkov A., Langer V., Manorik P. A., Weidlich T.: *Transition Met. Chem.* **2003**, *28*, 475; c) Kožíšek J., Fronc M., Skubák P., Popkov A., Breza M., Fuess H., Paulmann C.: *Acta Crystallogr. A* **2004**, *60*, 510.
18. a) For the preparation of *N*-Boc derivative, see: Medina E., Vidal-Ferran A., Moyano A., Pericas M. A., Riera A.: *Tetrahedron: Asymmetry* **1997**, *8*, 1581; b) General procedure for the preparation of *N*-Boc derivatives of α-amino acids via chiral nickel complexes without separation of nickel salts, BPB and α-amino acids after hydrolysis: Ouchi H., Kumagai M., Sakurada S., Takahata H.: *Heterocycles* **2004**, *64*, 505.
19. Belokon Yu. N., Bakhmutov V. I., Chernoglazova N. I., Kochetkov K. A., Vitt S. V., Garbalinskaya N. S., Belikov V. M.: *J. Chem. Soc., Perkin Trans. 1* **1988**, 305.
20. Belokon Yu. N., Maleev V. I., Vitt S. V., Ryzhov M. G., Kondrashov Y. D., Golubev S. N., Vauchskii Y. P., Kazika A. I., Novikova M. I., Krasutskii P. A., Yurchenko A. G., Dubchak L., Shklover V. E., Struchkov Y. T., Bakhmutov V. I., Belikov V. M.: *J. Chem. Soc., Dalton Trans.* **1985**, 17.
21. Hull W. in: *Two-Dimensional NMR Spectroscopy. Application for Chemists and Biochemists* (W. R. Croasmun and R. M. K. Carlson, Eds), 2nd ed., Chap. 2. VCH Publishers, New York 1994.
22. Braun S., Kalinowski H.-O., Berger S.: *150 and More Basic NMR Experiments*, 2nd ed. Wiley–VCH, Weinheim 1998.
23. Glusker J. P., Lewis M., Rossi M.: *Crystal Structure Analysis For Chemists and Biologists*. VHC, New York 1994.
24. a) Popkov A., Gee A., Nádvorník M., Lyčka A.: *Transition Met. Chem.* **2002**, *27*, 884; b) Saghiyan A. S., Hambardzumyan H. H., Manasyan L. L., Petrosyan A. A., Maleev V. I., Peregudov A. S.: *Synth. Commun.* **2005**, *35*, 449.
25. *SIR92* in: Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., Burla M. C., Polidori G., Camalli M.: *J. Appl. Crystallogr.* **1994**, *27*, 435.
26. Sheldrick G. M.: *SHELXL97*. University of Göttingen, Göttingen 1997.
27. Yabe Y., Miura C., Horikoshi H., Baba Y.: *Chem. Pharm. Bull.* **1976**, *24*, 3149.