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Synthesis of novel chiral Ni^{II} complexes of dehydroalanine Schiff bases and their reactivity in asymmetric nucleophilic addition reactions. Novel synthesis of (*S*)-2-carboxypiperazine

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ABSTRACT

New chiral Ni^{II} complexes of Schiff bases of dehydroalanine with modified chiral auxiliaries (*S*)-2-*N*-[*N*′-(3,4-dichlorobenzyl)prolyl]aminobenzophenone (3,4-DCBPB), (*S*)-2-*N*-[*N*′-(3,4-dimethylbenzyl)prolyl]-aminobenzophenone (3,4-DMBPB), (*S*)-2-*N*-[*N*′-(2-chlorobenzyl)prolyl]aminobenzophenone (2-CBPB), and (*S*)-2-*N*-[*N*′-(2-fluorobenzyl)prolyl]-aminobenzophenone (2-FBPB) have been synthesized. Asymmetric Michael addition reactions of primary and secondary amines and thiols to the dehydroalanine moieties of the complexes were studied. (*S*)-2-FBPB was found to be the best chiral auxiliary in terms of both selectivity of the reactions (*de* ~92–96%) and reactivity of the complexes. A novel synthetic route toward (*S*)-2-carboxypiperazine was developed based on the auxiliary.

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1. Introduction

Non-proteinogenic α-amino acids can serve as building blocks or surrogates of proteinogenic amino acids in known physiologically active peptides, some of which possess biological activity. In recent years, a great deal of effort has been focused on the synthesis of enantiomerically pure non-proteinogenic as well as rare proteinogenic α-amino acids.[1] A special branch of the non-proteinogenic family includes β-*N*-amino-substituted derivatives of L-α-amino acids, α,β-diamino acids.[2] This structural motif is widespread among a number of molecules with therapeutic applications. Some of the compounds are neurotoxic to animals,[3a] and some represent important constituents of natural peptidic antibiotics such as viomycin, bleomycin, Sch37137, napsamycin, lavendomycin, and others.[2] An important anti-HIV drug, indinavir is a derivative of 2-carboxypiperazine.[2] Some of the amino acids have been used in the synthesis of drugs,[3b,4] in microbiology for selection of highly active strain-producers of proteinogenic amino acids,[5] etc.

A method which was previously described by us for the asymmetric synthesis of β-substituted L-α-amino acids with aliphatic, aromatic, and heterocyclic substituents in the side chain consisted of the addition of nucleophiles (amines, thiols and alcoholate ions) to the C=C bond of the dehydroalanine moiety in the Ni^{II} complexes of a Schiff base of dehydroalanine with a chiral auxiliary (*S*)-2-*N*-[*N*′-benzylprolyl)aminobenzophenone (BPB)—Ni^{II}-(*S*)-BPB-Δ-Ala. Usually, the stereoselectivities (de) of the addition reactions were in the range of 84–90% while the reaction took from 3 to 120 h to go to completion at ambient temperature.[6–8]

Later we reported on the synthesis of modified chiral auxiliaries (*S*)-2-*N*-[*N*′-(3,4-dichlorobenzyl)prolyl]aminobenzophenone (3,4-DCBPB), (*S*)-2-[*N*-(*N*′-3,4-dimethylbenzyl) prolyl]aminobenzophenone (*S*)-3,4-DMBPB), and (*S*)-2-[*N*-(*N*′-2-chlorobenzyl)prolyl] aminobenzophenone (*S*)-2-CBPB) and Ni^{II} complexes of their Schiff bases with glycine, alanine, and dehydroaminobutanoic acid. The study of the complexes in the alkylation and nucleophilic addition reactions clearly indicated their superior performance than the original complexes derived from BPB in terms of both better reactivity and stereoselectivity of the reactions.[9,10] The best results were found for the complexes with chiral auxiliary (*S*)-2-CBPB). Even better performances were found for another auxiliary (*S*)-2-*N*-[*N*′-(2-fluorobenzyl)prolyl]aminobenzophenone (2-FBPB).[11] The auxiliary derived glycine Ni^{II} complex was even more active and its alkylation reaction with $C_6H_5CH_2Br$ was complete within 3 min at room temperature under standard conditions.[11]

It could be assumed that the dehydroalanine complexes derived from these modified chiral auxiliaries would also provide the initial material for better selectivity and efficiency of β-substituted L-α-amino acid synthesis.

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Herein we report the asymmetric synthesis of β-substituted L-α-amino acids using new modified Ni^{II} complexes of Schiff bases of dehydroalanine with auxiliaries (*S*)-3,4-DCBPB, (*S*)-3,4-DMBPB, (*S*)-2-CBPB, and (*S*)-2-FBPB. In addition, a novel synthetic route toward (*S*)-2-carboxypiperazine has been developed.

2. Results and discussion

The dehydroalanine complexes were prepared from the initial (*R*)-serine complexes **1**–**4**, according to the earlier developed procedure for the synthesis of Ni^{II}-(*S*)-BPB-Δ-Ala (see Scheme 1).[9] The synthesis of **1**–**3** was described earlier[9] and **4** was prepared for the first time. Compounds Ni^{II}-(*S*)-3,4-DCBPB-Δ-Ala **5**, Ni^{II}-(*S*)-3,4-DMBPB-Δ-Ala **6**, Ni^{II}-(*S*)-2-CBPB-Δ-Ala **7,** and Ni^{II}-(*S*)-2-FBPB-Δ-Ala **8** were prepared and isolated by crystallization from a mixture of acetone/heptane (1:1).

The structures of the complexes were confirmed by physical and chemical analytical methods (see Section 4). The ORTEP drawing of the X-ray determined structure of complex Ni^{II}-(*S*)-2-CBPB-Δ-Ala **7** is presented in Figure 1.

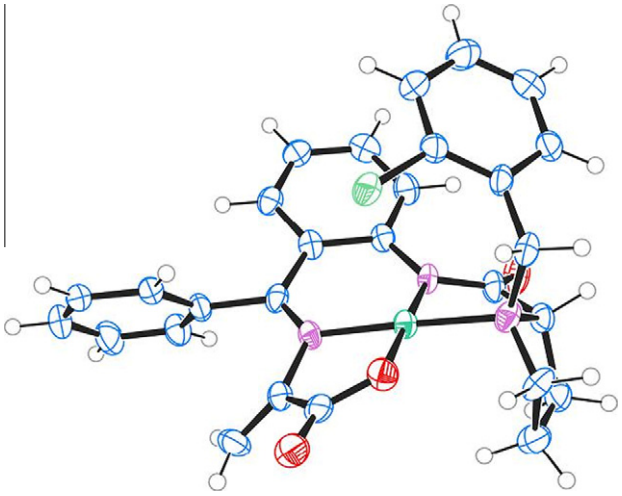


Figure 1. The ORTEP drawing of the X-ray determined structure of Ni^{II}-(*S*)-2-CBPB-Δ-Ala **7**.

An important feature of the complex Ni^{II}-(*S*)-2-CBPB-Δ-Ala is the significant puckering of the chelate rings and a short Cl–Ni distance.3.086 Å. The latter may hint at a kind of electrostatic interaction of the partially positively charged Ni-atom and negatively charged end of the C–Cl bond dipole.

The Michael additions of imidazole, methylamine, benzylamine, ethanolamine, diethanolamine, isopropylamine, and 2-mercaptoethanol to the C=C bond of dehydroalanine moieties of complexes **5**–**8** were conducted in acetonitrile at 22 and 50 °C (Scheme 2). The reactions were monitored by TLC [SiO_2, $CH_3COCH_3/CHCl_3$ (1:3) or $CH_3COOC_2H_5/CHCl_3$ (1:3)], following the disappearance of traces of the initial complexes **5**–**8** and establishment of the thermodynamic equilibrium between the diastereoisomeric complexes of the addition products **9**–**12a**–**g**. The addition could also be monitored by ^1H NMR spectroscopy following the disappearance of the vinyl hydrogen atom resonances of dehydroalanine moieties of the initial complexes **5**–**8**.

The major diastereomeric complexes **9a**–**g**, **11a**–**g**, and **12a**–**g** were separated by preparative chromatography [SiO_2, 20 × 30 cm, $CHCl_3/CH_3COCH_3$ (3:1)]. Compounds **10c**–**f** could not be isolated in the analytically pure form due to some decomposition on SiO_2 during chromatography with partial regeneration of the initial complex **6**.

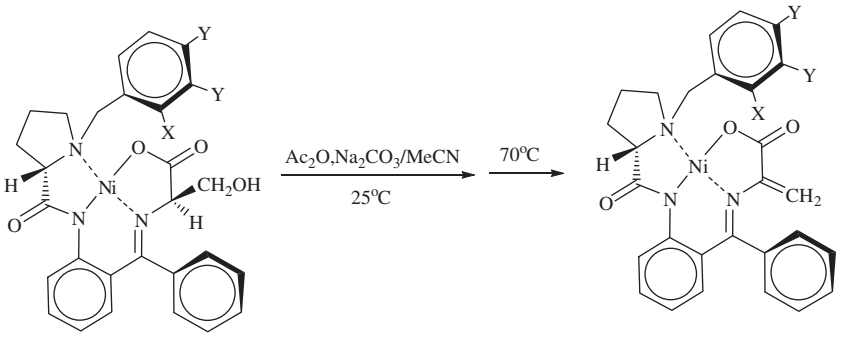
The absolute configurations of the amino acid moieties in the diastereomeric complexes **9a**–**g**–**12a**–**g** were determined by measuring the sign of the specific rotation of the complexes at 589 nm, as was previously done for similar complexes of the same amino acids based on the unmodified auxiliary (*S*)-BPB.[6,7]

The diastereomeric compositions of the products of the nucleophilic additions were determined by chiral GLC or HPLC enantiomeric analyses of the amino acids recovered from the reaction mixture of diastereomeric complexes before their separation by chromatography. ^1H NMR spectroscopy was also employed for the same purpose. In this case, the ratio of the integral intensities of the resonances of methylene protons of *N*-benzyl groups reflects the ratio of the diastereoisomers in the mixture. The results are shown in Table 1.

For the sake of comparison, Table 1 also presents similar data obtained earlier with the unmodified complex Ni^{II}-(*S*)-BPB-Δ-Ala (runs 28–33).[6,7]

The data summarized in Table 1 (runs 14–20 and 21–27) clearly indicated that the dehydroalanine complexes **7** and **8** were the best starting material for the β-substituted amino acid synthesis in terms of both diastereoselectivity (*de* 94–96%) and reactivity (shorter reaction times), when compared to **5** and **6** (runs1–13) and the unmodified complex Ni^{II}-(*S*)-BPB-Δ-Ala (runs 28–33).

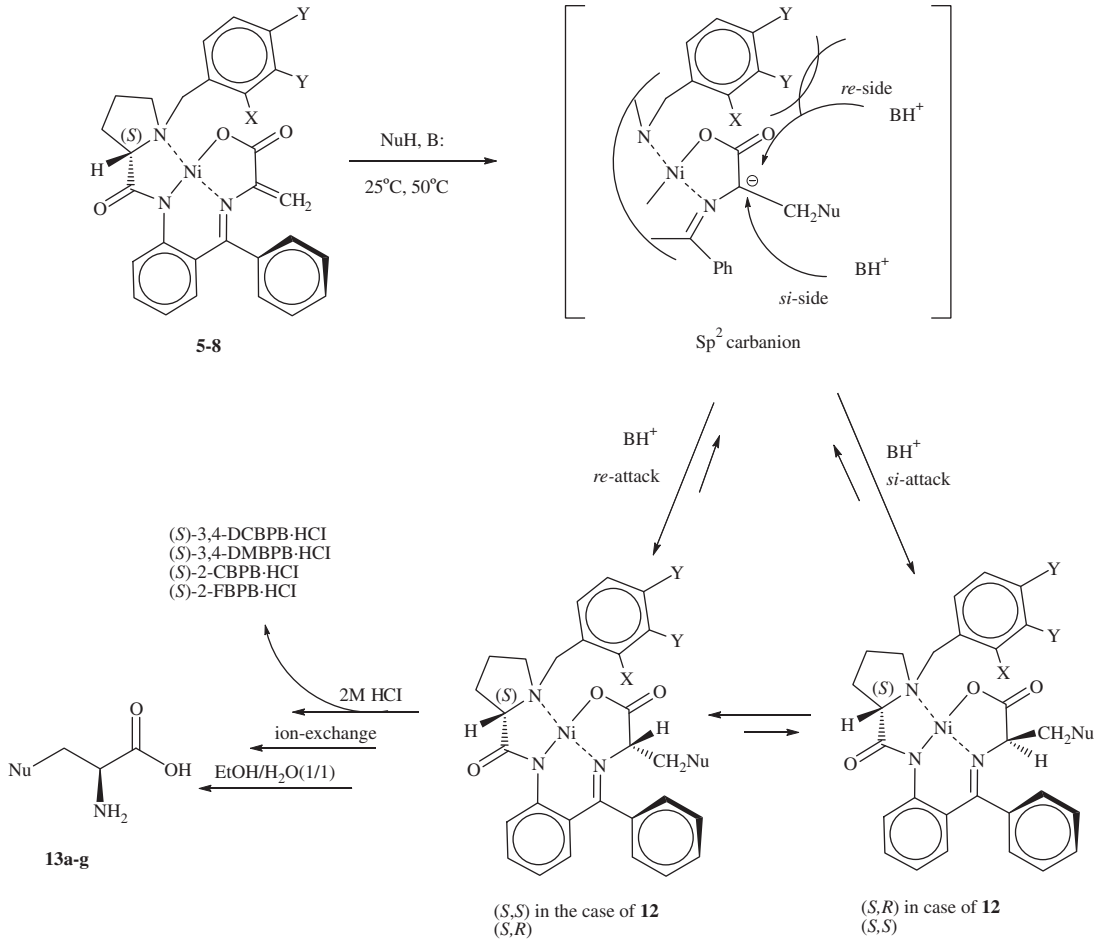
The results obtained on the asymmetric addition of the nucleophiles to the C=C bond of dehydroalanine in the modified complex



1-4 **5-8**

X = H, Y = Cl, Ni^{II}-(*S*)-3,4-DCBPB-(*R*)-Ser **1**, Ni^{II}-(*S*)-3,4-DCBPB-Δ-Ala **5**;
X = H, Y = CH_3, Ni^{II}-(*S*)-3,4-DMBPB-(*R*)-Ser **2**, Ni^{II}-(*S*)-3,4-DMBPB-Δ-Ala **6**;
X = Cl, Y = H, Ni^{II}-(*S*)-2-CBPB-(*R*)-Ser **3**, Ni^{II}-(*S*)-2-CBPB-Δ-Ala **7**;
X = F, Y = H, Ni^{II}-(*S*)-2-FBPB-(*R*)-Ser **4**, Ni^{II}-(*S*)-2-FBPB-Δ-Ala **8**

Scheme 1.



X=H, Y=C l**9**; X=H, Y=Me **10**, X=Cl, Y=H **11**, X=F, Y=H **12**

Nu = $C_6H_5CH_2NH$ (**a**); Imidazol-1-yl (**b**); CH_3NH (**c**); $HOCH_2CH_2NH$ (**d**); $(HOCH_2CH_2)_2N$ (**e**); $(CH_3)_2CHNH$ (**f**); $HOCH_2CH_2S$ (**g**).

Scheme 2.

7 clearly correlated with the previously obtained data on the asymmetric C-alkylation of glycine and alanine moieties in the complexes derived from the chiral auxiliary 2-CBPB.[9]

The recovery of the amino acids and the chiral auxiliaries (*S*)-3,4-DCBPB, (*S*)-3,4-DMBPB, (*S*)-2-CBPB and (*S*)-2-FBPB was carried out similar to the previously reported procedure.[6,11] The decomposing of the diastereoisomerically pure complexes **9a**,**g**–**12a**–**g** was brought about with aqueous HCl, followed by the recovery the insoluble hydrochlorides of the auxiliaries (95%) and purification of the amino acids by an ion-exchange protocol.[6,11] The target amino acids, β-substituted L-α,β-diamino acids **13a**–**e** and (*S*)-(2-hydroxyethyl)-L-cysteine **13g** were isolated with high enantiomeric purity (ee >99%) after crystallization from an aqueous/ethanol (1:1) solution. It should be noted that an alternative asymmetric synthesis by a known Zeebach procedure in the case of amino acid **13c** only gives the racemic product.[12] Some synthesized β-substituted L-α,β-diamino acids, in particular β-(*N*-methylamino)-α-alanine **13c**, β-(*N*-ethanolamino)-α-alanine **13d,** and β-(*N*,*N*-diethanolamino)-α-alanine **13e** were isolated in the form of hydrochlorides, since in the free form these amino acids are unstable and on storage gradually darkened and acquired an unpleasant smell.

The adduct of **8** and ethanolamine (see Table 1, run 24) served as the initial material for the preparation of (*S*)-2-carboxypiperazine, according to Scheme 3.

3. Conclusion

Herein, a universal method for the highly selective and relatively rapid asymmetric synthesis of optically active β-substituted L-α-amino acids has been elaborated through a Michael nucleophilic addition to the C=C bond of the modified chiral dehydroalanine complexes. As a result, the amino acid L- or (*S*)-β-(*N*-isopropylamino)-α-alanine has been synthesized for the first time. A novel synthetic route toward (*S*)-2-carboxypiperazine was also elaborated.

4. Experimental

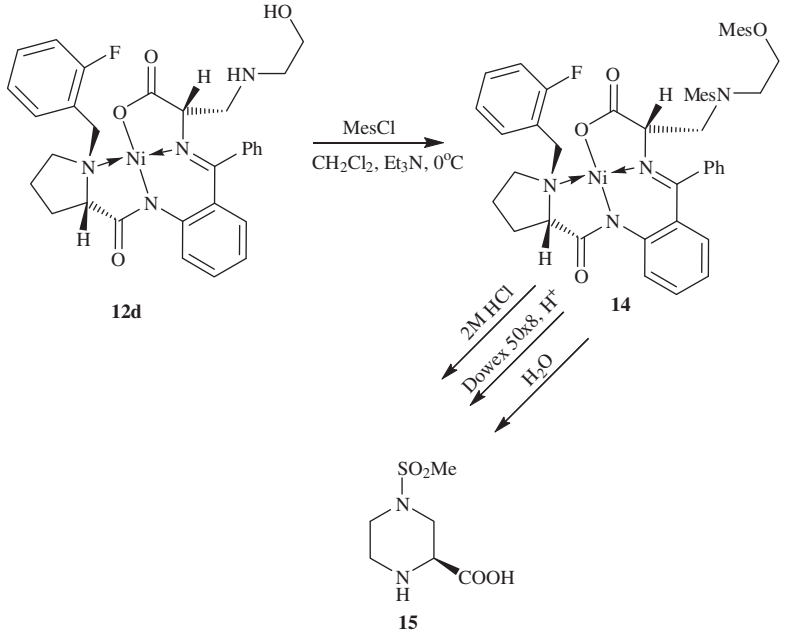
The amino acids were produced by the CJSC 'SRI of Biotechnology' (Armenia); silica gel L-40/100 from 'Merk' (Germany), $(CH_2O)n$, $CHCl_3$, $(CH_3CO)_2O$, CH_3COOH, $(CH_3)_2CO$, $CH_3COOC_2H_5$, CH_3CN, DMF, *i*-PrOH, Na_2CO_3, NH_4OH, HCl and KOH from 'Reakhim' (Russia); imidazole, $CH_3NH_2{\cdot}HCl$, $HOCH_2CH_2NH_2$, $(HOCH_2CH_2)_2NH$, $C_6H_5CH_2NH_2$, $HOCH_2CH_2SH$, and 2-aminobenzophenone from Aldrich (USA). All solvents used were freshly distilled.

The enantiomeric GLC analysis of the amino acids as their *N*-trifluoroacetyl derivatives of their isopropyl esters was performed using a '*Chiral Val*' type with 0.12 μm film thickness at column temperature 125 °C, using helium as the carrier gas. The enantiomeric

Table 1
Results of the asymmetric addition of nucleophiles to chiral complexes **5**–**8** in CH_3CN at 50 °C[a]

Run	Initial dehydroalanine complex	NuH	Duration (min)	(*S*,*S*)/(*S*,*R*)[b] (%)	Yield[c] (%)
1[a]	Ni^{II}-(*S*)-3,4-DCBPB-Δ-Ala **5**	$C_6H_5CH_2NH_2$	180	88.5/11.5 (92/8)	65
2	'—'	Imidazole	480	(95/5)	20
3[e]	'—'	$CH_3NH_2 \times HCl$	360	89.4/10.6	45
4	'—'	$HOCH_2CH_2NH_2$	120	85/15	60
5	'—'	$(HOCH_2CH_2)_2NH$	180	96.5/3.5	60
6[e]	'—'	$HOCH_2CH_2SH$	10	3.8/96.2	90
7[a]	Ni^{II}-(*S*)-3,4-DMBPB-Δ-Ala **6**	$C_6H_5CH_2NH_2$	150	92/8	30
8	'—'	Imidazole	480	94/6	20
9[e]	'—'	$CH_3NH_2 \cdot HCl$	360	89/11	15
10	'—'	$HOCH_2CH_2NH_2$	780	92/8	40
11	'—'	$(HOCH_2CH_2)_2NH$	510	88/12	40
12	'—'	$(CH_3)_2CHNH_2$	720	86/14	20
13[e]	'—'	$HOCH_2CH_2SH$	900	8/92	10
14[a]	Ni^{II}-(*S*)-2-CBPB-Δ-Ala **7**	$C_6H_5CH_2NH_2$	15	97/3	75
15	'—'	Imidazole	110	94.6/5.4	60
16[e]	'—'	$CH_3NH_2 \cdot HCl$	90	96.81/3.19 (97.5/3.5)	65
17	'—'	$HOCH_2CH_2NH_2$	180	97.5/2.5 (94/6)	50
18	'—'	$(HOCH_2CH_2)_2NH$	240	96/4	40
19	'—'	$(CH_3)_2CHNH_2$	220	94.5/5.5	40
20[e]	'—'	$HOCH_2CH_2SH$	180	3.8/96.2 (1/99)	50
21[a]	Ni^{II}-(*S*)-2-FBPB-Δ-Ala **8**	$C_6H_5CH_2NH_2$	100	97/3	55
22	'—'	Imidazole	90	98/2	60
23[e]	'—'	$CH_3NH_2 \cdot HCl$	210	97/3	50
24	'—'	$HOCH_2CH_2NH_2$	20	98/2	80
25	'—'	$(HOCH_2CH_2)_2NH$	60	98/2	75
26	'—'	$(CH_3)_2CHNH_2$	200	99/1	60
27[e]	'—'	$HOCH_2CH_2SH$	25	99/1	60
28[b,d]	Ni^{II}-(*S*)-BPB-Δ-Ala	$C_6H_5CH_2NH_2$	240	93/7	20
29[d]	'—'	Imidazole	300	94/6	20
30[d,e]	'—'	$CH_3NH_2 \times HCl$	~50 hr	93/7	>5
31[d]	'—'	$HOCH_2CH_2NH_2$	~50 hr	90/10	>5
32[d]	'—'	$(HOCH_2CH_2)_2NH$	~50 hr	94/6	>5
33[d,e]	'—'	$HOCH_2CH_2SH$	300	7/93	91

[a] The addition of benzylamine (runs 1, 7, 14, 21 and 28) was carried out in the presence of NaOH (complex/benzylamine/NaOH = 1:1:1).
[b] Determined by chiral GLC or HPLC and ^1H NMR (in brackets).
[c] Chemical yield at the stage of nucleophile addition after 10 min at the beginning of the reaction.
[d] Literature data.[6,11]
[e] The addition of 2-mercaptoethanol and the hydrochlorides of the amines (runs 3, 6, 9, 13, 16, 20, 23, 27, 30, 33) was carried out in CH_3CN/K_2CO_3 (complex/NuH/K_2CO_3 = 1:2:3).



Scheme 3.

purity of the amino acids was determined by HPLC on the chiral phase Diaspher-110-Chirasel-E-PA 6.0 mkm 4.0 × 250 mm with 20%-MeOH—80%-0.1 M $NaH_2PO_4 \times 2H_2O$ was used as an eluent. ^1H NMR spectra were recorded on a 'Mercury-300 Varian'

(300 MHz) in DMSO-d_6/CCl_4: 1:3 (unless otherwise indicated). Optical rotations were measured on a 'Perkin Elmer-341' polarimeter.

The modified complexes of (*R*)-serine **1**–**4** were synthesized in accordance with the previously developed procedure.[9] Modified complexes of dehydroalanine Ni^{II}-(*S*)-3,4-DCBPB-Δ-Ala **5**, Ni^{II}-(*S*)-3,4-DMBPB-Δ-Ala **6**, Ni^{II}-(*S*)-2-CBPB-Δ-Ala **7,** and Ni^{II}-(*S*)-2-FBPB-Δ-Ala **8** were synthesized in accordance with the procedure.[11]

4.1. The synthesis of complex 8 was carried out according to the previously described method[11]

Complex **8**. Calcd for $C_{28}H_{24}N_3O_3NiF$ (528.2): C, 63.67; H, 4.58; N, 7.96. Found: C, 63.69; H, 4.60; N, 7.94. Mp 158–160 °C. $[\alpha]_D^{20} = +2337.5$ (*c* 0.08, $CH_3OH/CHCl_3$ (3:1)). ^1H NMR ($CDCl_3/CCl_4$ ~1:1): 2.09 (1H, ddd, Pro, $^2J = 10.8$, $^3J = 9.8$, $^3J = 6.5$), 2.20 (1H, m, Pro), 2.55 (1H, m, Pro), 2.79 (1H, m, Pro), 3.47 (1H, dd, Pro, $^3J = 10.7$, $^3J = 5.7$), 3.57 (1H, m, Pro), 3.66 (1H, m, Pro), 3.75 (1H, dd, N$CH_2C_6H_5F$, $^2J = 12.9$, $^4J_{H,F} = 1.1$), 4.13 (1H, d, C=CH_2, $^2J = 1.2$), 4.32 (1H, dd, N$CH_2C_6H_5F$, $^2J = 12.9$, $^4J_{H,F} = 1.5$), 5.60 (1H, d, C=CH_2, $^2J = 1.2$), 6.70 (1H, ddd, Ar, $^3J = 8.3$, $^3J = 6.9$, $^4J = 1.4$), 6.86 (1H, dd, Ar, $^3J = 8.3$, $^4J = 1.8$), 7.04 (1H, ddd, Ar, $^3J_{H,F} = 10.2$, $^3J = 7.9$, $^4J = 1.8$), 7.14–7.23 (5H, m, Ar), 7.42–7.50 (3H, m, Ar), 8.20 (1H, dd, Ar, $^3J = 8.7$, $^4J = 1.2$), 8.41 (1H, ddd, Ar, $^4J_{H,F} = 7.3$, $^3J = 7.3$, $^4J = 2.0$). ^{13}C NMR: ($CDCl_3/CCl_4$ ~1:1): 24.15 (γ-Pro), 30.86 (β-Pro), 55.73 (N$CH_2C_6H_5F$), 57.50 (δ-Pro), 70.69 (α-Pro, d, $^5J_{C,F} = 2.7$), 114.94 (C=CH_2), 116.31 (Ar, d, $^2J_{C,F} = 22.3$), 120.81 (Ar), 120.84 (Ar, d, $^2J_{C,F} = 14.4$), 123.87 (Ar), 124.74 (Ar, d, $^4J_{C,F} = 3.7$), 127.26 (Ar), 128.5 (Ar, br), 130.18 (Ar, br), 131.29 (Ar, d, $^3J_{C,F} = 8.5$), 134.23 (Ar), 134.30 (Ar, d, $^3J_{C,F} = 3.3$), 135.66 (Ar), 143.98 (Ar), 161.77 (Ar, d, $^1J_{C,F} = 247.5$), 169.09 (Ar), 170.20 (Ar), 179.98 (Ar).

4.2. The synthesis of complexes 9–12a–f

The addition of $C_6H_5CH_2NH_2$ (0.38 mmol) to complexes **5**–**8** (0.38 mmol) was carried out in CH_3CN (5 ml) in the presence of NaOH (0.38 mmol), while the addition of imidazole, methylamine, ethanolamine, diethanolamine, isopropylamine, and 2-mercaptoethanol to complexes **5**–**8** was carried out in CH_3CN in the presence of K_2CO_3 (1.7 mol) at 50 °C according to the previously described methods.[6,11] The individually pure major diastereomeric complexes **9**–**12g** were isolated from the reaction mixture by TLC [SiO_2, 20 × 30 cm, $CHCl_3/CH_3COOC_2H_5$ (1:2)] and characterized by spectroscopic methods of analysis.

Complex **9a**. Mp 100–102 °C, $[\alpha]_D^{25} = +1956$ (*c* 0.046, $CHCl_3$).

Complex **9b**. Mp 199–201 °C, $[\alpha]_D^{25} = +2094.1$ (*c* 0.051, $CHCl_3$).

Complex **9c**. Yield: 65% (0.15 g, 0.24 mmol). Calcd for $C_{29}H_{28}N_4O_3NiCl_2$ (610.16): C, 57.09; H, 4.63; N, 9.18. Found: C, 57.12; H, 4.66; N, 9.14. Mp 132–134 °C. $[\alpha]_D^{20} = +1998.5$ (*c* 0.05, $CHCl_3$). ^1H NMR ($CDCl_3/CCl_4$ ~1:1): 1.62 (3H, s, CH_3NH–), 2.00 (2H, m, Pro), 2.51 (1H, m, Pro), 2.56 (1H, m, Pro), 2.68 (1H, m, Pro), 2.92 (1H, dd, CHCH_2NH, $^2J = 12.3$, $^3J = 6.9$), 3.12 (2H, m, Pro), 3.22 (1H, dd, N$CH_2C_6H_3Cl_2$, $^2J = 12.5$), 3.32 (1H, dd, CHCH_2NH, $^2J = 12.3$, $^3J = 3.6$); 4.20 (1H, dd, N$CH_2C_6H_3Cl_2$, $^2J = 12.5$), 4.45 (1H, dd, CHCH$_2$N, $^3J = 6.9$, $^3J = 3.6$), 6.65–8.69 (12H, m, Ar).

Complex **9d**. Mp 135–137 °C, $[\alpha]_D^{25} = +1969.2$ (*c* 0.052, $CHCl_3$).

Complex **9e**. Yield: 90% (0.23 g, 0.342 mmol). Calcd for $C_{32}H_{34}N_4O_5NiCl_2$ (684.24): C, 56.17; H, 5.01; N, 8.19. Found: C, 56.21; H, 5.05; N, 8.28. Mp 138–140 °C. $[\alpha]_D^{20} = +1856.3$ (*c* 0.05, $CHCl_3$). ^1H NMR ($CDCl_3$): 2.00–2.15 (3H, m, Pro), 2.31 (1H, m, Pro), 2.53 (2H, m, N$(CH_2CH_2OH)_2$), 2.60–2.78 (2H, m, N$(CH_2CH_2OH)_2$), 2.66 (1H, dd, CH–CH_2–N, $^3J = 11.3$, $^3J = 5.1$), 3.18–3.26 (2H, m, N$(CH_2CH_2OH)_2$), 3.30 (1H, d, $^2J = 12.5$, $CH_2C_6H_3Cl_2$), 3.41 (1H, dd, Pro, $^3J = 11.1$, $^3J = 5.6$), 3.48 (2H, ddd, N$(CH_2CH_2OH)_2$, $^2J = 11.8$, $^3J = 9.3$, $^3J = 2.4$), 3.56–3.75 (2H, m, Pro), 3.63 (1H, dd, CH–CH_2–N, $^2J = 12.7$, $^3J = 11.3$), 3.77 (2H, m, OH), 4.00 (1H, dd, CH–CH$_2$–N, $^3J = 11.3$, $^3J = 5.1$), 4.37 (1H, d, $CH_2C_6H_3Cl_2$, $^2J = 12.5$), 6.65–6.74 (2H, m, Ar), 6.97 (1H, dt, Ar, $^3J = 7.6$, $^4J = 1.5$), 7.21 (1H, ddd, Ar, $^3J = 8.7$, $^3J = 6.5$, $^4J = 2.2$), 7.38 (1H, dt, Ar, $^3J = 7.5$, $^4J = 1.5$), 7.40 (1H, d, Ar, $^3J = 8.1$), 7.48 (1H, td, Ar, $^3J = 7.5$, $^4J = 1.5$) 7.56 (1H, tt, Ar, $^3J = 7.5$, $^4J = 1.4$), 7.65 (1H, td, Ar, $^3J = 7.5$, $^4J = 1.5$), 7.82 (1H, dd, Ar, $^3J = 8.1$, $^4J = 2.1$), 8.06 (1H, dd, Ar, $^3J = 8.7$, $^4J = 1.1$) 8.76 (1H, d, Ar, $^4J = 2.1$).

Complex **9f**. Yield: 90% (0.21 g, 0.342 mmol). Calcd for $C_{31}H_{32}N_4O_3NiCl_2$ (638.21): C, 58.34; H, 5.05; N, 8.78. Found: C, 58.51; H, 5.08; N, 8.85. Mp 155–157 °C. $[\alpha]_D^{20} = +2104.8$ (*c* 0.05, $CHCl_3$). ^1H NMR: ($CDCl_3$) 0.95 (3H, d, CH_3, $^3J = 6.2$), 1.06 (3H, d, CH_3, $^3J = 6.2$), 1.50 (1H, m, NH), 2.06 (1H, m, Pro), 2.21 (1H, m, Pro), 2.53–2.67 (2H, m, Pro), 2.79 (1H, m, $CH(CH_3)_2$), 2.88 (1H, dd, CH–CH_2–NH, $^2J = 12.8$, $^3J = 4.2$), 3.28 (1H, d, $CH_2C_6H_3Cl_2$, $^2J = 12.6$), 3.31–3.41 (2H, m, CH–CH_2–NH, Pro), 3.58 (1H, m, Pro), 3.85 (1H, m, Pro), 4.02 (1H, dd, CH–CH$_2$–NH, $^3J = 7.2$, $^3J = 4.2$), 4.33 (1H, d, $CH_2C_6H_3Cl_2$, $^2J = 12.6$), 6.60–6.71 (2H, m, Ar), 6.96 (1H, m, Ar), 7.20 (1H, m, Ar), 7.33 (1H, m, Ar), 7.38 (1H, d, Ar, $^3J = 8.2$), 7.46–7.58 (3H, m, Ar), 7.76 (dd, 1H, Ar, $^3J = 8.2$, $^4J = 1.7$), 8.13 (1H, d, Ar, $^3J = 8.6$), 8.85 (1H, d, Ar, $^4J = 1.7$).

Complex **9g**. Yield: 90% (0.22 g, 0.34 mmol). Calcd for $C_{30}H_{29}Cl_2N_3$ Ni O_4S (657.23): C, 54.52; H, 4.45; N, 6.39. Found: C, 54.47; H, 4.57; N, 6.45. Mp 167–169 °C. $[\alpha]_D^{20} = +2892.8$ (*c* 0.05, $CHCl_3$). ^1H NMR ($CDCl_3$) 2.04–2.20 (2H, m, Pro), 2.47–2.66 (2H, m, Pro), 2.77 (1H, dd, CH–CH_2–S, $^2J = 13.8$, $^3J = 5.8$), 2.80 (1H, m, SCH_2CH_2OH)2.86 (dd, 1H, CH–CH_2–S, $^2J = 13.8$, $^3J = 3.3$), 2.88 (1H, m, SCH_2CH_2OH), 3.30 (1H, d, $CH_2C_6H_3Cl_2$, $^2J = 12.5$), 3.37 (1H, dd, Pro, $^3J = 10.8$, $^3J = 6.2$), 3.65 (1H, m, Pro), 3.69 (2H, dd, OCH_2, $^3J = 5.9$, $^3J = 5.3$), 3.79 (1H, m, Pro), 4.24 (1H, dd, CH–CH$_2$–S, $^3J = 5.8$, $^3J = 3.3$), 4.35 (1H, d, $CH_2C_6H_3Cl_2$, $^2J = 12.5$), 6.62–6.71 (2H, m, Ar), 6.97 (1H, m, Ar), 7.20 (1H, ddd, Ar, $^3J = 8.6$, $^3J = 6.5$, $^4J = 2.2$), 7.32 (1H, dt, Ar, $^3J = 6.7$, $^4J = 1.8$), 7.38 (1H, d, Ar, $^3J = 8.2$), 7.46–7.61 (3H, m, Ar), 7.75 (1H, dd, Ar, $^3J = 8.2$, $^4J = 2.1$), 8.17 (1H, dd, Ar, $^3J = 8.6$, $^4J = 1.0$), 8.90 (1H, d, Ar, $^3J = 2.1$).

Complex **10a**. Yield: 69% (0.16 g, 0.26 mmol). Calcd for $C_{37}H_{38}N_4O_3Ni$ (645.42): C, 68.85; H, 5.93; N, 8.68. Found: C, 68.83; H, 5.98; N, 8.70. Mp 183–185 °C. $[\alpha]_D^{20} = +3002.8$ (*c* 0.05, $CHCl_3$). ^1H NMR ($CDCl_3$) 1.78 (3H, s, Me), 1.98 (3H, s, Me), 2.02 (2H, m, Pro), 2.08 (1H, m, CH_2NHCH$_2$Ph), 2.55 (1H, m, Pro), 2.63 (1H, m, Pro), 2.88 (1H, dd, CHCH_2NH, $^2J = 12.5$, $^3J = 5.6$), 2.91 (1H, dd, CHCH_2NH, $^2J = 12.5$, $^3J = 3.4$), 3.50–3.52 (2H, m, Pro), 3.85 (1H, d, HNCH_2Ph, $^2J = 13.1$), 3.65 (1H, m, Pro), 3.77 (1H, dd, NCH_2Ar, $^2J = 12.4$), 3.92 (1H, d, HNCH_2Ph, $^2J = 13.1$), 3.99 (1H, dd, CHCH$_2$NH, $^3J = 5.6$, $^3J = 3.4$), 4.8 (1H, dd, NCH$_2$Ar, $^2J = 12.4$), 6.6–8.6 (17H, m, Ar).

Complex **10b**. Calcd for $C_{33}H_{33}N_5O_3Ni$ (606.34): C, 65.37; H, 5.49; N, 11.55. Found: C, 65.42; H, 5.58; N, 11.50. Mp 155–157 °C, $[\alpha]_D^{20} = +2566.6$ (*c* 0.05, $CHCl_3$). ^1H NMR: ($CDCl_3$): 1.95 (3H, s, Me), 1.98 (2H, m, H Pro), 2.07 (3H, s, Me), 2.49 (1H, m, Pro), 2.55 (1H, m, Pro), 2.58 (1H, m, Pro), 3.22 (2H, m, H Pro), 3.24 (2H, dd, NCH_2Ar, $^2J = 12.5$), 3.66 (1H, m, CHCH_2imidazole), 4.21 (2H, dd, NCH_2Ar, $^2J = 12.5$), 4.24 (1H, m, CHCH_2imidazole), 4.40 (1H, m, CHCH$_2$N), 6.66–8.98 (12H, m, Ar).

Complex **11a**. Calcd for $C_{31}H_{33}N_4O_3ClNi$: C, 61.67; H, 5.51; N, 9.28. Found: C, 61.69; H, 5.52; N, 9.30. Mp 108–110 °C. $[\alpha]_D^{20} = +1985.3$ (*c* 0.05, $CHCl_3$). ^1H NMR: ($CDCl_3$): 2.00 (2H, m, Pro), 2.02 (1H, m, CH_2NHCH$_2$Ph), 2.51 (1H, m, Pro), 2.73 (1H, m, Pro), 2.90 (1H, dd, CH_2NH, $^2J = 12.6$, $^3J = 5.6$), 2.91 (1H, dd, CH_2NH, $^2J = 12.6$, $^3J = 3.6$), 3.49–3.51 (2H, m, Pro), 3.85 (1H, d, HNCH_2Ph, $^2J = 13.2$), 3.65 (1H, m, Pro), 3.73 (1H, dd, NCH_2PhCl, $^2J = 12.4$), 3.95 (1H, d, HNCH_2Ph, $^2J = 13.2$), 3.98 (1H, dd, NCHCH$_2$NH, $^3J = 5.6$, $^3J = 3.6$), 4.5 (1H, dd, NCH_2PhCl, $^2J = 12.4$) 6.4–8.3 (18H, m, Ar).

Complex **11b**. Calcd for $C_{31}H_{28}ClN_5NiO_3$: C, 60.77; H, 4.61; N, 11.43. Found: C, 61.69; H, 4.65; N, 11.40. Mp 123–125 °C. $[\alpha]_D^{20} = +2333.4$ (*c* 0.05, $CHCl_3$). ^1H NMR: ($CDCl_3$): 1.97 (2H, m, H

Pro), 2.50 (1H, m, Pro), 2.54 (1H, m, Pro), 2.58 (1H, m, Pro), 3.20 (2H, m, H Pro), 3.21 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.5), 3.65 (1H, m, CHC*H*$_2$imidazole), 4.19 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.5), 4.20 (1H, m, CHC*H*$_2$imidazole), 4.35 (1H, m, *CH*CH$_2$N), 6.67–8.92 (16H, м, Ar).

Complex **11c**. Calcd for $C_{29}H_{29}ClN_4NiO_3$ (575.71): C, 60.50; H, 5.08; N, 9.73. Found: C, 60.53; H, 5.14; N, 9.65. Mp 156–158 °C. $[\alpha]_D^{20} = +2876.2$ (*c* 0.05, $CHCl_3$). ^{1}H NMR: ($CDCl_3$): 1.68 (3H, s, *CH*$_3$NH), 1.88 (2H, m, Pro), 2.47 (1H, m, Pro), 2.57 (1H, m, Pro), 2.68 (1H, m, Pro), 2.89 (1H, dd, CHC*H*$_2$N, ^2J = 12.28, ^3J = 6.9), 3.10 (2H, m, Pro), 3.19 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.5), 3.27 (1H, dd, CHC*H*$_2$N, ^2J = 12.28, ^3J = 3.6), 4.22 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.5), 4.41 (dd, 1H, *CH*CH$_2$N, ^3J = 6.9, ^3J = 3.6), 6.69–8.94 (13H, m, Ar).

Complex **11d**. Calcd for $C_{30}H_{31}ClN_4NiO_4$ (605.74): C, 59.48; H, 5.16; N, 9.73. Found: C, 59.51; H, 5.21; N, 9.75. Mp 143–145 °C. $[\alpha]_D^{20} = +1896.4$ (*c* 0.05, $CHCl_3$). ^{1}H NMR: ($CDCl_3$): 2.12 (2H, m, Pro), 2.39 (1H, m, Pro), 2.46 (1H, m, Pro), 2.27 (1H, m, CHC*H*$_2$N), 2.35 (2H, m, NHC*H*$_2$CH$_2$OH), 2.56 (1H, m, Pro), 2.71 (1H, m, Pro), 4.11 (1H, m, CHC*H*$_2$N), 3.28 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.76), 3.40 (2H, m, NHCH$_2$C*H*$_2$OH), 3.50 (1H, m, Pro), 3.73 (1H, dd, *CH*CH$_2$N, ^3J = 8.0, ^3J = 3.9), 4.32 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.76), 6.67–8.03 (13H, m, Ar).

Complex **11e**. Calcd for $C_{32}H_{35}ClN_4NiO_5$ (649.79): C, 59.15; H, 5.43; N, 8.62. Found: C, 59.19; H, 5.51; N, 8.65. Mp 123–125 °C. $[\alpha]_D^{20} = +1653.3$ (*c* 0.05, $CHCl_3$). ^{1}H NMR: ($CDCl_3$): 1.98 (2H, m, Pro), 2.32 (2H, ddd, *CH*$_2$N, ^2J = 12.8, ^3J = 9.6, ^3J = 4.1), 2.38 (1H, m, Pro), 2.43 (2H, ddd, *CH*$_2$N, ^2J = 13.8, ^3J = 3.0, ^3J = 2.1), 2.56 (1H, m, Pro), 2.60 (1H, m, Pro), 2.65 (1H, dd, CHC*H*$_2$N, ^2J = 12.7, ^3J = 5.0), 2.81 (1H, m, Pro), 3.20 (2H, dt, OCH$_2$, ^2J = 11.8, ^3J = 3.5), 3.22 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.78), 3.45 (2H, m, CH$_2$O), 3.56 (1H, dd, CHC*H*$_2$N, ^2J = 12.7, ^2J = 11.2), 3.69 (1H, m, Pro), 4.09 (1H, dd, *CH*CH$_2$N, ^2J = 11.3, ^3J = 5.0,), 4.18 (1H, dd, NC*H*$_2$PhCl, ^2J = 12.78), 6.63–8.21 (13H, m, Ar).

Complex **11f**. Calcd for $C_{31}H_{33}ClN_4NiO_3$ (03.77): C, 61.67; H, 5.51; N, 9.28. Found: C, 61.71; H, 5.66; N, 9.55. Mp 137–139 °C. $[\alpha]_D^{20} = +2186.3$ (*c* 0.05, $CHCl_3$). ^{1}H NMR: ($CDCl_3$): 0.92 (3H, d, CH_3, ^3J = 6.2), 1.04 (3H, d, CH_3, ^3J = 6.2), 1.53 (1H, m, NH), 2.06 (1H, m, Pro), 2.18 (1H, m, Pro), 2.54–2.69 (2H, m, Pro), 2.86 (1H, dd, CHC*H*$_2$N), 2.98 (1H, m, CH(CH$_3$)$_2$), 3.11 (1H, m, Pro), 3.47–3.54 (2H, m, CHC*H*$_2$N, Pro), 3.83 (1H, m, Pro), 3.88 (1H, d, CH$_2$C$_6$H$_4$Cl, ^2J = 12.9), 4.00 (1H, dd, ^3J = 7.1, ^3J = 4.0, *CH*CH$_2$N), 4.50 (1H, d, ^2J = 12.9, CH$_2$C$_6$H$_4$Cl), 6.60–6.71 (2H, m, Ar), 6.98 (1H, m, Ar), 7.12–7.22 (2H, m, Ar), 7.27–7.37 (3H, m, Ar), 7.46–7.57 (3H, m, Ar), 8.08 (1H, dd, ^3J = 8.6, ^3J = 0.9, Ar), 8.21 (1H, d, ^3J = 7.5, Ar).

Complex **11g**. Calcd for $C_{30}H_{30}N_3O_4SNiCl$: C, 57.86; H, 4.86; N, 6.75. Found: C, 57.83; H, 4.90; N, 6.71. Mp 165–167 °C. $[\alpha]_D^{25} = +1940$ (*c* 0.05, $CHCl_3$). ^{1}H NMR: ($CDCl_3$): 2.0–2.20 (2H, m, Pro), 2.40–2.71 (2H, m, Pro), 2.78 (1H, dd, ^2J = 13.6, ^3J = 5.8, CH–*CH*$_2$–S), 2.86 (1H, dd, ^2J = 13.6, ^3J = 3.2, CH–*CH*$_2$–S), 3.0–3.12 (2H, m, CH–CH$_2$–S*CH*$_2$), 3.41–3.56 (2H, m, Pro), 3.69 (2H, dd, ^3J = 5.8, ^3J = 5.2, OCH$_2$), 3.80 (1H, m, Pro), 3.89 (1H, d, ^2J = 12.6, *CH*$_2$–C$_6$H$_4$Cl), 4.20 (1H, dd, ^3J = 5.8, ^3J = 3.3, *CH*–CH$_2$–S), 4.55 (1H, d, ^2J = 12.6, *CH*$_2$–C$_6$H$_4$Cl), 6.62–8.20 (13H, m, Ar).

Complex **12a**. Calcd for $C_{35}H_{33}N_4NiO_3F$: C, 66.17; H, 5.24; N, 8.82. Found: C, 66.21; H, 5.26; N, 8.80. Mp 158–160 °C, $[\alpha]_D^{25} = +1678.0$ (*c* 0.05, CH_3OH): ^{1}H NMR: ($CDCl_3$/CCl_4 ~1:1): 2.02 (1H, m, Pro), 2.02 (1H, m, Pro), 2.02 (1H, br, NH$_{bz}$), 2.46 (1H, m, Pro), 2.75 (1H, m, Pro), 2.86 (1H, dd, CHC*H*$_2$NH, ^2J = 12.6, ^3J = 5.6), 2.90 (dd, 1H, CHC*H*$_2$NH, ^2J = 12.6, ^3J = 3.7), 3.43 (1H, dd, α-Pro, ^3J = 10.8, ^3J = 6.0), 3.48 (1H, m, Pro), 3.55 (1H, d, NHC*H*$_2$C$_6$H$_5$, ^2J = 13.3), 3.63 (1H, m, Pro), 3.85 (1H, dd, ^2J = 13.0, $^4J_{H,F}$ = 1.1, *CH*$_2$C$_6$H$_4$F), 3.95 (1H, d, NHC*H*$_2$C$_6$H$_5$, ^2J = 13.3), 3.96 (1H, dd, *CH*CH$_2$, ^3J = 5.6, ^3J = 3.7), 4.41 (1H, dd, ^2J = 13.0, $^4J_{H,F}$ = 1.4, *CH*$_2$C$_6$H$_4$F), 6.34 (1H, dt, Ar, ^3J = 7.6, ^4J = 1.6), 6.56 (1H, dd, Ar, ^3J = 8.2, ^4J = 1.9), 6.65 (1H, ddd, Ar, ^3J = 8.2, ^3J = 6.8, ^4J = 1.0), 7.06 (1H, ddd, Ar, $^3J_{H,F}$ = 10.1, ^3J = 8.0, ^4J = 1.5), 7.17 (1H, m, Ar), 7.18 (3H, m, Ar), 7.18 (1H, m, Ar), 7.20 (1H, m, Ar), 7.24 (1H, m, Ar), 7.26 (1H, m, Ar), 7.37 (2H, m, Ar), 7.43 (1H, m, Ar), 7.48 (1H, m, Ar), 8.26 (1H, dd, Ar, ^3J = 8.7, ^4J = 1.3), 8.37 (1H, td, ^3J = 7.4, ^4J = 2.0).

^{13}C NMR ($CDCl_3$/CCl_4 ~1:1): 23.62 (Pro), 30.87 (Pro), 52.16 (CH*CH*$_2$NH), 53.33 (*CH*$_2$C$_6$H$_5$), 55.78 (*CH*$_2$C$_6$H$_4$F), 57.12 (Pro), 70.54 (α-CH, Pro, d, $^5J_{C,F}$ = 2.1) 70.65 (*CH*CH$_2$NH), 116.26 (C$_6$H$_4$F, d, $^2J_{C,F}$ = 22.4), 120.65 (C$_6$H$_4$F, d, $^2J_{C,F}$ = 14.3), 120.71 (C$_6$H$_4$), 124.00 (C$_6$H$_4$), 124.60 (C$_6$H$_4$F, d, $^4J_{C,F}$ = 3.5) 126.68 (C), 127.19 (C), 127.26 (C), 127.93 (C$_6$H$_5$), 128.41 (CH$_2$C$_6$H$_5$), 128.56 (CH$_2$C$_6$H$_5$), 128.98 (C), 129.03 (C), 129.72 (C), 129.72 (C), 131.28 (C$_6$H$_4$F, d, $^3J_{C,F}$ = 8.4), 132.31 (C), 133.31 (C), 134.03 (C), 134.48 (C$_6$H$_4$F, d, $^3J_{C,F}$ = 3.3), 139.96 (C), 142.88 (C), 161.89 (C$_6$H$_4$F, d), 170.64 (C), 178.57 (C), 180.13 (C).

Complex **12b**. Calcd for $C_{31}H_{28}N_5O_3NiF$: C, 62.48; H, 4.80; N, 3.22. Found: C, 62.44; H, 4.73; N, 3.19. Mp 165–167 °C. $[\alpha]_D^{25} = +1940$ (*c* 0.05, $CHCl_3$). ^{1}H NMR: ($CDCl_3$): 1.81 (1H, m, Pro), 1.95 (1H, ddd, Pro, ^2J = 10.8, ^3J = 9.6, ^3J = 7.0), 2.38 (1H, m, Pro), 2.52 (1H, m, Pro), 2.62 (1H, m, Pro), 3.26 (1H, dd, Pro, ^3J = 9.8, ^3J = 7.0), 3.47 (1H, ddd, Pro, ^2J = 10.8, ^3J = 6.6, ^3J = 3.3), 3.70 (1H, dd, *CH*$_2$C$_6$H$_4$F, ^2J = 12.9, $^4J_{H,F}$ = 1.0), 3.77 (1H, m, CHC*H*$_2$imidazol), 3.98 (1H, dd, *CH*$_2$C$_6$H$_4$F, ^2J = 12.9, $^4J_{H,F}$ = 1.0), 4.20 (2H, m, *CHCH*$_2$imidazol), 6.65 (1H, m, Ar), 6.66 (1H, m, Ar), 6.95 (1H, m, CHimidazol), 6.96 (1H, s, CHimidazol), 6.98 (1H, ddd, Ar, ^3J = 10.1, ^3J = 8.2, ^4J = 1.5), 7.10 (1H, m, Ar), 7.14 (1H, m, Ar), 7.17 (1H, m, Ar), 7.23 (1H, s, CHimidazol), 7.31 (1H, m, Ar), 7.53 (1H, m, Ar), 7.47–7.61 (3H, m, Ar), 8.16 (1H, m, Ar), 8.31 (1H, m, Ar).

Complex **12c**. Calcd for $C_{29}H_{29}N_4NiO_3F$: C, 62.28; H, 5.22; N, 10.02. Found: C, 62.32; H, 5.18; N, 10.04. Mp 166–168 °C. $[\alpha]_D^{20} = +3969.9$ (*c* 0.18, $CHCl_3$). ^{1}H NMR ($CDCl_3$/CCl_4 ~1:1): 1.90 (1H, br, NH), 2.02 (1H, m, Pro), 2.15 (1H, m, Pro), 2.17 (3H, s, CH_3), 2.52 (1H, m, CH_2, Pro), 2.77 (1H, dd, CH_2NH, ^2J = 12.9, ^3J = 3.7), 2.82 (1H, m, Pro), 3.15 (1H, dd, CH_2NH, ^2J = 12.9, ^3J = 7.2), 3.42 (1H, dd, Pro, ^3J = 10.8, ^3J = 6.0), 3.47 (1H, dd, Pro, ^2J = 10.0, ^3J = 6.0), 3.73 (1H, m, Pro), 3.82 (1H, dd, CH_2, ^2J = 13.0, $^4J_{H,F}$ = 1.0), 3.98 (1H, dd, CH, ^3J = 7.2, ^3J = 3.7), 4.38 (1H, dd, CH_2, ^2J = 13.0, $^4J_{H,F}$ = 1.5), 6.62 (1H, dd, Ar, ^3J = 8.2, ^4J = 2.2), 6.65 (1H, ddd, Ar, ^3J = 8.2, ^3J = 6.6, ^4J = 1.2), 6.97 (1H, m, Ar), 7.04 (1H, ddd,Ar, $^3J_{H,F}$ = 9.9, ^3J = 8.0, ^4J = 1.5), 7.13 (1H, m, Ar), 7.17 (1H, m, Ar), 7.20 (1H, m, Ar), 7.28 (1H, m, Ar), 7.43–7.55 (3H, m, Ar), 8.18 (1H, dd, Ar, ^3J = 8.6, ^4J = 1.2), 8.33 (1H, ddd, Ar, $^4J_{H,F}$ = 7.4, ^3J = 7.4, ^4J = 2.1). ^{13}C NMR ($CDCl_3$/CCl_4 ~1:1): 23.72 (Pro), 30.84 (Pro), 35.92 (CH_3), 55.72 (CH_2), 55.89 (CH_2NH), 57.13 (Pro), 69.47 (*CH*CH$_2$NH), 70.51 (Pro, d, $^5J_{C,F}$ = 2.5), 116.21 (C, d, $^2J_{C,F}$ = 22.0), 120.60 (C, d, $^2J_{C,F}$ = 14.7), 120.76 (C), 124.01 (C), 124.59 (CH, d, $^4J_{C,F}$ = 3.7), 126.67 (C), 127.55 (CH), 128.02 (CH), 129.07 (C), 129.07(C), 129.86 (C), 131.24 (C, d, $^3J_{C,F}$ = 8.5), 132.27 (CH), 133.29 (CH), 133.99 (C), 134.37 (CH, d, $^3J_{C,F}$ = 3.6), 142.69 (C), 161.77 (C, d, $^1J_{C,F}$ = 247.8), 170.48 (C), 178.51 (C), 180.09 (C).

Complex **12d**. Calcd for $C_{30}H_{31}N_4NiO_4F$: C, 61.16; H, 5.30; N, 9.51. Found: C, 61.21; H, 5.28; N, 9.52. Mp 159–161 °C. $[\alpha]_D^{20} = +2384.8$ (*c* 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$/CCl_4 ~1:1): 2.06 (1H, ddd, Pro, ^2J = 11.6, ^3J = 10.2, ^3J = 6.3), 2.15 (2H, m, Pro), 2.33 (1H, m, NHC*H*$_2$CH$_2$O), 2.43 (1H, m, NHC*H*$_2$CH$_2$O), 2.53 (1H, m, Pro), 2.80 (1H, m, Pro), 3.30 (1H, dd, CHC*H*$_2$N, ^2J = 12.9, ^3J = 8.0), 3.38 (2H, m, OCH$_2$), 3.41 (1H, m, Pro), 3.47 (1H, dd, Pro, ^3J = 10.2, ^3J = 6.3), 3.67 (1H, m, CHC*H*$_2$N), 3.80 (1H, dd, CH_2, ^2J = 13.0, $^4J_{H,F}$ = 0.9), 3.96 (1H, dd, *CH*CH$_2$N, ^3J = 8.0, ^3J = 3.9), 4.37 (1H, dd, CH_2, ^2J = 13.0, $^4J_{H,F}$ = 1.4), 6.62 (1H, dd, Ar, ^3J = 8.2, ^4J = 2.3), 6.65 (1H, ddd, Ar, ^3J = 8.2, ^3J = 6.3, ^4J = 1.2), 6.97 (1H, ddd, Ar, ^3J = 6.1, ^4J = 2.2, ^4J = 1.6), 7.03 (1H, ddd, Ar, $^3J_{H,F}$ = 10.1, ^3J = 8.0, ^4J = 1.5), 7.11–7.30 (4H, m, Ar), 7.43–7.56 (3H, m, Ar), 8.16 (1H, dd, Ar, ^3J = 8.6, ^4J = 0.9), 8.29 (1H, ddd, Ar, $^4J_{H,F}$ = 7.3, ^3J = 7.3, ^4J = 2.0). ^{13}C NMR ($CDCl_3$/CCl_4 ~1:1): 23.85 (Pro), 30.83 (Pro), 50.61 (NCH$_2$CH$_2$O), 53.56 (NCH$_2$CH), 55.81 (CH_2), 57.22 (Pro), 60.91 (OCH$_2$), 69.85 (*C*HCH$_2$N), 70.45 (Pro, d, $^5J_{C,F}$ = 2.1), 116.20 (CH, d, $^2J_{C,F}$ = 22.3), 120.61 (C, d, $^2J_{C,F}$ = 14.4), 120.82 (CH), 124.01 (CH), 124.60 (CH, d, $^4J_{C,F}$ = 3.6), 126.52 (C), 127.45 (C), 127.88 (C),

129.14 (C), 129.14 (C), 129.92 (C), 131.27 (C, d, $^3J_{C,F}$ = 8.5), 132.37 (C), 133.31 (C), 133.88 (C), 134.29 (C, d, $^3J_{C,F}$ = 3.3), 142.66 (C), 161.76 (C, d, $^1J_{C,F}$ = 248.2), 170.77 (C), 178.76 (C), 180.10 (C).

Complex **12e**. Calcd for $C_{32}H_{35}N_5O_4NiF$: C, 60.69; H, 5.57; N, 8.86. Found: C, 60.72; H, 5.54; N, 8.85. Mp 173 °C. $[\alpha]_D^{20} = +2941.7$ (*c* 0.42, $CHCl_3$). ^{1}H NMR ($CDCl_3/CCl_4$ ~1:1): 2.00 (1H, ddd, NCH_2, J_1 = 12.5, J_2 = 9.3, J_3 = 3.4), 2.07 (1H, ddd, Pro, ^2J = 11.8, ^3J = 9.9, ^3J = 5.8), 2.22 (1H, m, Pro), 2.47 (1H, ddd, NCH_2, J_1 = 13.5, J_2 = 3.8, J_3 = 2.2), 2.55 (1H, m, Pro), 2.63 (1H, dd, $CHCH_2N$, ^2J = 12.7, ^3J = 5.1), 2.74 (1H, m, Pro), 3.16 (2H, dt, OCH_2, J_1 = 11.8, J_2 = 3.5), 3.43 (1H, m, Pro), 3.44 (2H, m, OCH_2), 3.45 (1H, dd, Pro, ^3J = 10.8, ^3J = 6.0), 3.57 (1H, m, Pro), 3.59 (1H, dd, $CHCH_2N$, ^2J = 12.7, ^3J = 11.3), 3.77 (1H, dd, CH_2, ^2J = 12.9), 3.87 (2H, br, OH), 3.93 (1H, dd, $CHCH_2N$, ^3J = 11.3, ^3J = 5.1), 4.31 (1H, dd, $CH_2C_6H_5F$, ^2J = 12.9, $^4J_{H,F}$ = 1.2), 4.41 (1H, dd, $CH_2C_6H_5F$, ^2J = 12.9, $^4J_{H,F}$ = 1.4), 6.62 (1H, dd, Ar, ^3J = 8.1, ^4J = 2.1), 6.64 (1H, ddd, Ar, ^3J = 8.1, ^3J = 6.2, ^4J = 1.2), 6.95 (1H, dt, Ar, ^3J = 7.4, ^4J = 1.6), 7.01 (1H, ddd, Ar, $^3J_{H,F}$ = 10.1, ^3J = 8.0, ^4J = 1.5), 7.13 (1H, m, Ar), 7.16 (1H, m, Ar), 7.21 (1H, m, Ar), 7.31 (1H, dt, Ar, ^3J = 7.5, ^4J 1.6), 7.44 (1H, td, Ar, ^3J = 7.4, ^4J = 1.6), 7.50 (1H, m, Ar), 7.58 (1H, m, Ar), 8.08 (1H, dd, Ar, ^3J = 8.6, ^4J = 1.1), 8.29 (1H, ddd, Ar, $^4J_{H,F}$ = 7.3, ^3J = 7.3, ^4J = 2.0). ^{13}C NMR ($CDCl_3/CCl_4$ ~1:1): 24.29 (Pro), 30.72 (Pro), 55.97 (CH_2), 57.36 (Pro), 58.04 ($N(CH_2)_2$), 59.73 ($O(CH_2)_2$), 60.08 ($CHCH_2N$), 68.87 ($CHCH_2N$), 70.45 (Pro, d, $^5J_{C,F}$ = 2.5), 116.11 (CH, d, $^2J_{C,F}$ = 22.2), 120.64 (C, d, $^2J_{C,F}$ = 14.5), 120.85 (CH), 124.02 (CH), 124.62 (CH, d, $^4J_{C,F}$ = 3.6), 126.24 (C), 127.72 (C), 127.84 (CH), 128.82 (C), 129.39(C), 129.99 (CH), 131.26 (CH, d, $^3J_{C,F}$ = 8.4), 132.37 (CH), 133.28 (CH), 133.31 (C), 134.17 (CH, d, $^3J_{C,F}$ = 3.3), 142.41 (C), 161.64 (C, d, $^1J_{C,F}$ = 247.8), 170.77 (C), 179.90 (C), 180.07 (C).

Complex **12f**. Calcd for $C_{31}H_{33}N_4NiO_3F$: C, 63.40; H, 5.66; N, 9.54. Found: C, 63.42; H, 5.63; N, 9.57. Mp 175–177 °C. $[\alpha]_D^{20} = +3585.3$ (*c* 0.19, CH_3OH). ^{1}H NMR ($CDCl_3/CCl_4$ ~1:1): 0.88 (3H, d, CH_3, *i*-Pr, ^3J = 6.2), 1.00 (3H, d, CH_3, *i*-Pr, ^3J = 6.2), 1.93 (1H, br, NH), 2.02 (1H, m, Pro), 2.11 (1H, m, Pro), 2.53 (1H, sp, CH, *i*-Pr, ^3J = 6.2), 2.53 (1H, m, Pro), 2.83 (1H, dd, CH_2NH, ^2J = 12.7, ^3J = 3.8), 2.85 (1H, m, Pro), 3.06 (1H, dd, CH_2NH, ^2J = 12.7, ^3J = 6.8), 3.41 (1H, dd, Pro, ^3J = 10.8, ^3J = 6.2), 3.49 (1H, dd, Pro, ^2J = 9.6, ^3J = 6.0), 3.77 (1H, m, Pro), 3.84 (1H, dd, CH_2, ^2J = 12.9, $^4J_{H,F}$ = 1.2), 3.97 (1H, dd, CH, ^3J = 6.8, ^3J = 3.8), 4.39 (1H, dd, CH_2, ^2J = 12.9, $^4J_{H,F}$ = 1.5), 6.60 (1H, dd, Ar, ^3J = 8.2, ^4J = 2.2), 6.65 (1H, ddd, Ar, ^3J = 8.2, ^3J = 6.6, ^4J = 1.2, 6.95 (1H, m, Ar), 7.03 (1H, ddd, Ar, $^3J_{H,F}$ = 10.0, ^3J = 8.0, ^4J = 1.5), 7.13 (1H, m, Ar), 7.16 (1H, m, Ar), 7.21 (1H, m, Ar), 7.27 (1H, m, Ar), 7.42–7.54 (3H, m, Ar), 8.18 (1H, dd, Ar, ^3J = 8.6, ^4J = 1.0), 8.30 (1H, ddd, Ar, $^4J_{H,F}$ = 7.3, ^3J = 7.3, ^4J = 2.0). ^{13}C NMR ($CDCl_3/CCl_4$ ~1:1): 22.77 (CH_3), 23.32 (CH_3), 23.83 (Pro), 30.83 (Pro), 48.14 (CH, *i*-Pr), 50.93 (CH_2NH), 55.62 (CH_2), 56.99 (Pro), 70.27 ($CHCH_2NH$), 70.49 (Pro, d, $^5J_{C,F}$ = 2.4), 116.17 (CH, d, $^2J_{C,F}$ = 22.3), 120.52 (C, d, $^2J_{C,F}$ = 14.6), 120.71 (CH), 123.93 (CH), 124.55 (CH, d, $^4J_{C,F}$ = 3.6), 126.73 (C), 127.42 (CH), 127.88 (CH), 129.07(C), 129.07 (C), 129.82 (CH), 131.21 (CH, d, $^3J_{C,F}$ = 8.4), 132.24 (CH), 133.27 (CH), 134.08 (C), 134.34 (CH, d, $^3J_{C,F}$ = 3.3), 142.72 (C), 161.74 (C, d, $^1J_{C,F}$ = 248.0), 170.44 (C), 178.48 (C), 179.96 (C).

Complex **12g**. Calcd for $C_{30}H_{30}N_3NiO_3SF$: C, 59.43; H, 4.98; N, 10.55. Found: C, 59.46; H, 4.94; N, 10.52; Mp 240–242 °C $[\alpha]_D^{20} = +3192.8$ (*c* 0.32, CH_3OH). ^{1}H NMR ($CDCl_3/CCl_4$ ~1:1): 2.07 (1H, m, Pro), 2.10 (1H, m, Pro), 2.48 (1H, dt, SCH_2CH_2O, ^2J = 14.1, ^3J = 6.1), 2.55 (1H, m, Pro), 2.75 (1H, dd, CH_2S, ^2J = 13.7, ^3J = 5.9), 2.80 (1H, dt, SCH_2CH_2O, ^2J = 14.1, ^3J = 5.3), 2.84 (1H, dd, CH_2S, ^2J = 13.7, ^3J = 3.4), 2.94 (1H, m, Pro), 3.45 (1H, dd, Pro, ^3J = 10.6, ^3J = 6.5), 3.55 (1H, dd, Pro, ^2J = 9.5, ^3J = 6.3), 3.65 (2H, dd, OCH_2, ^3J = 6.1, ^3J = 5.3), 3.72 (1H, m, Pro), 3.86 (1H, dd, CH_2, ^2J = 12.9, $^4J_{H,F}$ = 1), 4.21 (1H, dd, CH, ^3J = 5.9, ^3J = 3.4), 4.41 (1H, dd, CH_2, ^2J = 12.9, $^4J_{H,F}$ = 1.4), 6.63 (1H, dd, Ar, ^3J = 8.2, ^4J = 2.2), 6.67 (1H, ddd, Ar, ^3J = 8.2, ^3J = 6.2, ^4J = 1.1), 7.00 (1H, dt, Ar, ^3J = 6.5, ^4J = 1.8), 7.05 (1H, ddd, Ar, $^3J_{H,F}$ = 10.2, ^3J = 8.0, ^4J = 1.5), 7.13 (1H, m, Ar), 7.16 (1H, m, Ar), 7.21 (1H, m, Ar), 7.27 (1H, m, Ar), 7.45–7.58 (3H, m, Ar), 8.23 (1H, dd, Ar, ^3J = 8.6, ^4J = 1.0), 8.32 (1H, ddd, Ar, $^4J_{H,F}$ = 7.3, ^4J 2.0). ^{13}C NMR ($CDCl_3/CCl_4$ ~1:1): 23.56 (Pro), 30.95 (Pro), 35.52 (SCH_2CH), 36.86 (SCH_2CH_2O), 56.16 (CH_2), 57.24 (Pro), 61.23 (OCH_2), 69.89 ($CHCH_2S$), 70.87 (Pro, d, $^5J_{C,F}$ = 2.4), 116.29 (CH, d, $^2J_{C,F}$ = 22.2), 120.73 (C, d, $^2J_{C,F}$ = 13.4), 120.83 (CH), 124.04 (CH), 124.65 (CH, d, $^4J_{C,F}$ = 3.8), 126.49 (C), 127.28 (CH), 127.89 (CH), 129.25 (C), 129.35(C), 130.10 (C), 131.34 (C, d, $^3J_{C,F}$ = 8.5), 132.72 (CH), 133.55 (CH), 134.23 (C), 134.41 (CH, d, $^3J_{C,F}$ = 3.5), 143.16 (C), 161.88 (C, d, $^1J_{C,F}$ = 247.5), 171.62 (C), 178.23 (C), 180.19 (C).

4.2.1. Isolation of the target amino acids 13a–g

Decomposition of the diastereomeric complexes **9**–**12a**–**g** and isolation of the target β-substituted α-amino acids **13a**–**g** were carried out according to the earlier procedure.[6] Amino acids **13c**–**e** were isolated in the form of their hydrochlorides.

4.2.2. L-β-(*N*-Methylamino)-α-alanine·HCl [or (*S*)-2-amino-3-(methylamino)propionic acid] 13c

Obtained 1.43 g (0.0121 mol) (79.2%). $[\alpha]_D^{25} = +23.2$ (*c* 1, 6 M HCl), Lit. $[\alpha]_D^{25} = +23.2$ (*c* 1, 6 M HCl).

4.2.3. L-β-(*N*-Benzylamino)-α-alanine [or (*S*)-2-amino-3-(benzylamino)propionic acid] 13a

Obtained 0.24 g (0.0012 mol) (83%). $[\alpha]_D^{25} = +26.8$ (*c* 10, 6 M HCl), Lit. $[\alpha]_D^{25} = +26.8$ (*c* 10, 6 M HCl).

4.2.4. L-β-(*N*-Imidazolyl)-α-alanine [or (*S*)-2-amino-3-imidazol-1-yl)propionic acid] 13b

Obtained 0.177 g (0.00114 mol) (70%). $[\alpha]_D^{20} = -2.2$ (*c* 10, 6 M HCl), Lit. $[\alpha]_D^{20} = -2.2$ (*c* 10, 6 M HCl).

4.2.5. L-β-(*N*-Ethanolamino)-α-alanine·HCl [or (*S*)-2-amino-3-(2-hydroxyethylamino)propionic acid] 13d

Obtained 0.186 g (0.00126 mol) (76%). $[\alpha]_D^{25} = +15.1$ (*c* 0.053, 6 M HCl), Lit. $[\alpha]_D^{25} = +15.1$ (*c* 0.053, 6 M HCl).

4.2.6. L-β-(*N*,*N*-Diethanolamino)-α-alanine·HCl [or (*S*)-2-amino-3-[bis(2-hydroxyethyl)amino]-propionic acid] 13e

Obtained 0.474 g (0.00247 mol) (80%). $[\alpha]_D^{25} = +27.2$ (*c* 0.9, 6 M HCl), Lit. $[\alpha]_D^{25} = +27.2$ (*c* 0.9, 6 M HCl).

4.2.7. L-β-(*N*-Isopropylamino)-α-alanine [or (*S*)-2-amino-3-(isopropylamino)-propionic acid] 13f

Obtained 0.58 g (0.00397 mol) (75.3%). Mp = 126–128 °C. Calcd for $C_6H_{14}N_2O_2$: C, 49.30; H, 9.65; N, 19.16. Found: C, 49.28; H, 9.60; N, 19.18. ^{1}H NMR (DMSO, δ, m, d, *J*, Hz): 1.31 (6H, d, $(CH_3)_2CH$–), 3.40 (2H, m, –$NHCH_2CH$–), 3.51 (1H, m, –CH_2CHNH_2), 4.35 (1H, m, $(CH_3)_2CHNH$–). $[\alpha]_D^{20} = -32.5$ (*c* 0.16, 6 M HCl).

4.2.8. L-S-(2-Hydroxyethyl)cysteine [or (*R*)-2-amino-3-(2-hydroxyethylthio)propionic acid] 13g

Obtained 0.231 g (0.0014 mol) (71%). $[\alpha]_D^{25} = +12.8$ (*c* 0.952, 6 M HCl), Lit. $[\alpha]_D^{25} = +12.8$ (*c* 0.952, 6 M HCl).

4.2.9. (*S*)-2-Carboxy-4-*N*-mesyl-pyperazine 15

To a solution of the initial complex **12d** (2.5 g, 0.004 mol) in 45 ml of CH_2Cl_2 at 0 °C was added 1.5 ml of Et_3N followed by 0.5 ml of MesCl under stirring. The solution was additionally stirred for an additional 5 min at 0 °C and then the cooling was stopped and the mixture was stirred for another 30 min. The reaction was monitored by TLC (SiO_2, $CHCl_3$/MeOH = 95:5). Additional amounts of MesCl and Et_3N were added with stirring if the reaction was not complete. After the initial material had disappeared, the reaction mixture was poured into water (100 ml). The organic layer was separated and the water layer was extracted with $CHCl_3$

(3 × 10 ml). The organic solutions were combined, washed with water, dried over $MgSO_4$, and evaporated. The final product was purified by chromatography (SiO_2 column, $CHCl_3$/MeOH (95:5)) to give 0.66 g (0.9 mmol) of doubly mesylated complex (see Scheme 3).

Complex **14**. Mp 123–126 °C (decomp.). Calcd for $C_{32}H_{36}N_4NiO_8FS_2 \times 0.2$ EtOH × $0.2C_6H_6 \times 0.20.4$ $CHCl_3$: C, 51.04; H, 4.89; N, 7.00. Found: C, 51.29; H, 4.81; N, 6.87. $[\alpha]_D^{20} = +1813$ (*c* 0.058, MeOH). ^{1}H NMR ($CDCl_3/CCl_4$ ~1:1): 2.12 (m, 1H, γ-Pro), 2.25 (m, 1H, β-Pro), 2.54 (m, 1H, γ-Pro), 2.81 (m, 1H, δ-Pro), 2.95 (s, 3H, Me), 3.10 (s, 3H, Me), 3.29 (m, 2H, β-Pro, δ-Pro), 3.45 (m, 3H, NCH_2-*CH*$_2$-OMs, *CH*CH_2N), 3.56 (d, *J* = 12.3 Hz, 1H, NCH_2Ph), 3.71 (m, 1H, α-Pro), 4.01 (dd, *J* = 9.6, 5.1 Hz, 1H, CH–*CH*$_2$–N), 4.06 (m, 2H, N–*CH*$_2$–CH_2OMs), 4.38 (d, *J* = 12.3, 1H, NCH_2Ph), 4.67 (dd, *J* = 15.0, 9.6 Hz, 1H, CH–*CH*$_2$–N), 6.65 (m, 2H, Ar), 7.06 (m, 1H, Ar), 7.15 (m, 1H, Ar), 7.21 (m, 1H, Ar), 7.27 (m, 1H, Ar), 7.36 (m, 2H, Ar), 7.56 (m, 3H, Ar), 8.07 (d, *J* = 7.0 Hz, 2H, Ar), 8.13 (d, *J* = 9.0 Hz, 1H, Ar).

4.2.10. Isolation of (*S*)-2-carboxy-4-*N*-mesyl-pyperazine 15

Complex **14** was decomposed as usual; the exception was that the final neutralization before the column had to be carried out with a concentrated solution of Na_2CO_3. The amino acid was then recovered by the usual ion exchange protocol. The initial 0.66 g of the complex gave 0.18 г (0.86 mmol) of (methylsulfonyl)piperazine-2-carboxylic acid), which was recrystallized from hot water to give (0.066 g, 0.31 mmol) of the pure amino acid. Another 0.028 g (0.13 mmol) of the amino acid was additionally recovered from the mother liquor.

4.2.11. (*S*)-2-Carboxy-4-*N*-mesyl-pyperazine 15

Mp 268–270 °C (decomp.). Calcd for $C_6H_{12}N_2O_4S$: C, 34.60; N, 13.46; H, 5.81. Found: C, 34.28; N, 13.32; H, 5.72. $[\alpha]_D^{25} = +23.5$ (*c* 1, 6 M HCl). ^{1}H NMR (DMSO): 3.01 (s, 3H, CH_3), 3.09 (ddd, *J* = 13.0, 9.5, 3.4 Hz, 1H $NHCH_2$–*CH*$_2$N-Ms), 3.27 (ddd, *J* = 12.5, 9.5, 3.0 Hz, 1H, NH–*CH*$_2$–CH_2N–Ms), 3.34 (ddd, *J* = 12.5, 3.9, 3.0 Hz, 1H, $NHCH_2$–*CH*$_2$–N-Ms), 3.52 (ddd, *J* = 13.0, 3.9, 3.4 Hz, 1H, NH–*CH*$_2$–CH_2N-Ms), 3.40 (dd, *J* = 12.9, 8.9 Hz, 1H, NHCH–*CH*$_2$-NMs), 3.74 (dd, *J* = 12.9, 3.2 Hz, 1H, NHCH–*CH*$_2$-NMs), 4.31 (dd, *J* = 8.9, 3.2 Hz, 1H, NH–*CH*–CH_2NMs), 9.90 and 10.2 (br s, 1H both, NH and COOH). ^{13}C NMR: 35.73 (CH_3), 42.22 ($NHCH_2$–CH_2N-Ms), 42.29 ($NHCH_2$–CH_2N-Ms), 44.61 (NHCH–CH_2N-Ms), 56.47 (NHCH–CH_2N-Ms), 167.9 (COOH).

4.2.12. X-ray crystal structure determination

The crystal of **7** ($C_{28}H_{24}N_3O_3ClNi{\cdot}0.5CCl_4$, *M* = 621.57) is monoclinic, space group *C*2, at *T* = 120 K: *a* = 22.469(2), *b* = 8.6483(8), *c* = 16.0975(14) Å, *β* = 120.377(2)°, *V* = 2698.6(4) Å^3, *Z* = 4, d_{calc} = 1.530 g/cm^3, *F*(0 0 0) = 1276, *μ* = 1.053 mm^{-1}. 13,897 total reflections (6437 unique reflections, R_{int} = 0.041) were measured on a Bruker SMART 1000 CCD diffractometer (*λ*(MoKα)-radiation, graphite monochromator, *ω* and *φ* scan mode, $2\theta_{max} = 56^o$) and corrected for absorption. The structure was determined by direct methods and refined by full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The independent part of the unit cell of **7** contains one tetrachloromethane solvate molecule occupying a special position on the twofold axis. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters ($U_{iso}(H) = 1.2U_{eq}(C)$). The absolute structure of **7** was determined objectively by the refinement of Flack parameter which has become equal to 0.001(18). The final divergence factors were $R_1 = 0.052$ for 5016 independent reflections with $I > 2\sigma(I)$ and $wR_2 = 0.136$ for all independent reflections, *S* = 1.013. All calculations were carried out using the SHELXTL program. Crystallographic data for **7** have been deposited with the Cambridge Crystallographic Data Center, CCDC 746863. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).

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