Nucleophilic addition to an achiral dehydroalanine Schiff base Ni(II) complex as a route to amino acids. A case of stereodetermining asymmetric protonation in the presence of TADDOL

Yuri N. Belokon,*[a] Syuzanna Harutyunyan,[a] Evgeni V. Vorontsov,[a] Alexander S. Peregudov,[a] Viktor N. Chrustalev,[a] Konstantin A. Kochetkov,[a] Dmitriy Pripadchev,[a] Ashot S. Sagyan,[b] Albert K. Beck,[c] and Dieter Seebach*[c]

[a] A.N. Nesmeyanov Institute of Organo-Element Compounds, Russian Academy of Sciences, 119991, Moscow, Vavilov 28, Russian Federation, Department of Chemistry. [b] Department of Chemistry, Yerevan State University, Manukyan 1, Yerevan, Armenia
E-mail: yubel@ineos.ac.ru
[c] Laboratorium für Organishe Chemie der Eidgenössischen Technishen Hochschule, ETH-Hönggerberg, Wolfgang-Pauli-Strasse 10, CH-80903, Zürich, Switzerland
E-mail: seebach@org.chem.ethz.ch

Dedicated to Professor Mieczyslaw Makosza on his 70th birthday

(received 31 Jul 03; accepted 13 Jan 04; published on the web 30 Jan 04)

Abstract

We describe herein the elaboration of a new type of a substrate based on the Ni(II) complex of a Schiff base of dehydroalanine, **1**, and Michael addition of nucleophiles to it, leading to the synthesis of racemic α-amino acids. We have also developed a catalytic method for the asymmetric 1,4 conjugate addition of achiral CH-acids to **1** promoted by TADDOLs with enantioselective catalytic protonation of the intermediate enolate in the stereodetermining stage of the reaction. A sizable 80% *ee* of the product was observed.

Keywords: Michael addition, amino acid, asymmetric protonation, TADDOL

Introduction

Enantioselective conjugate addition is a fundamentally important transformation in asymmetric synthesis.[1] The asymmetric catalytic version of the reaction was used for amino acid synthesis with remarkable success, applying condensation of O'Donnel's glycine imine derivatives and acrylic acid esters catalyzed by Cinchona alkaloid ammonium salts and synthetic quaternary ammonium salts as efficient chiral phase-transfer catalysts.[2] It is generally assumed that the stereoselective formation of the C-C bonds and consequently of the amino acid occur at the stage of the addition of the intermediate enolate of the glycine derivative to the activated C=C bond of acrylic derivatives

within the ion pair formed by Cinchona alkaloid ammonium salt and the enolate.[3] Another possibility of introducing asymmetry into the adduct by enantioselective catalytic protonation of the intermediate enolate was generally neglected. To the best of our knowledge only a few papers have been published on the subject of asymmetric catalytic C-H bond formation without a preceding enantioselective C-C-bond-forming step in the Michael addition.[4]

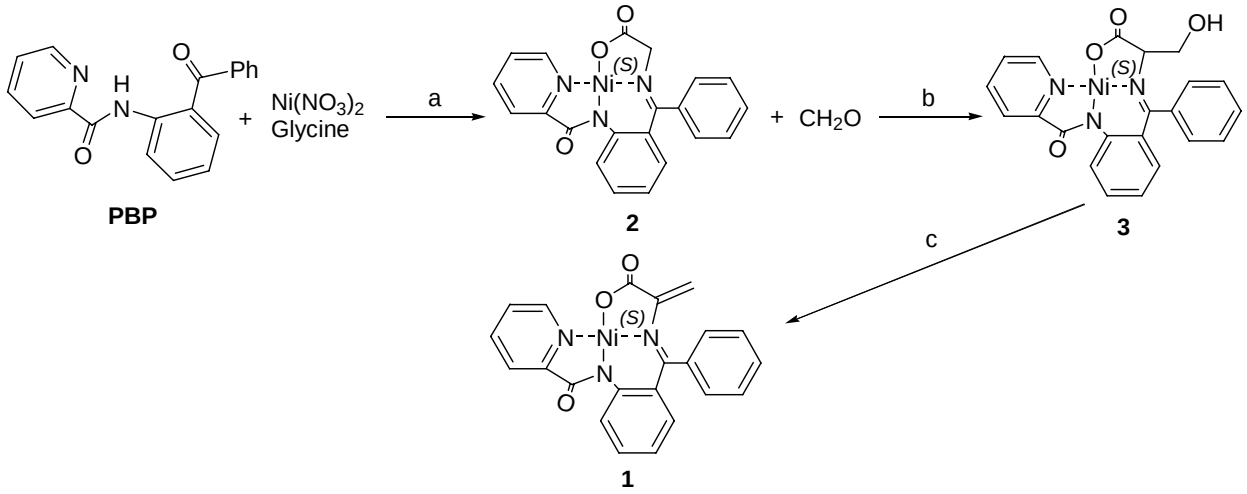
In recent years intense research efforts have been directed towards studying enantioselective protonation of enolates by chiral acids.[5] One of the possibilities is the protonation of a complex formed between an enolate and a chiral ligand with an achiral proton source.[6] Recently, Guenca et al. have found that TADDOL (α,α,α',α'-tetraaryl-1,3-dioxalan-4,5-dimethanol) can serve as an efficient chiral proton source and affected highly enantioselective stoichiometric protonation of some Li-enolates.[7] On the other hand Belokon et al. have found that alkali metal TADDOLates functioned as efficient catalytic hydrophobic bases in asymmetric C-alkylation of CH- acids with alkyl halides.[8]

We describe herein the elaboration of a new type of a substrate based on the Ni(II) complex of a Schiff's base of dehydroalanine, **1**, and Michael-type addition of nucleophiles occur leading to racemic α-amino acids. We have also attempted to develop a catalytic variation for the asymmetric 1,4 conjugate addition of achiral CH-acids to **1** promoted by TADDOLs with asymmetric catalytic protonation of the intermediate enolate in the sterodetermining stage of the reaction.

Results and Discussion

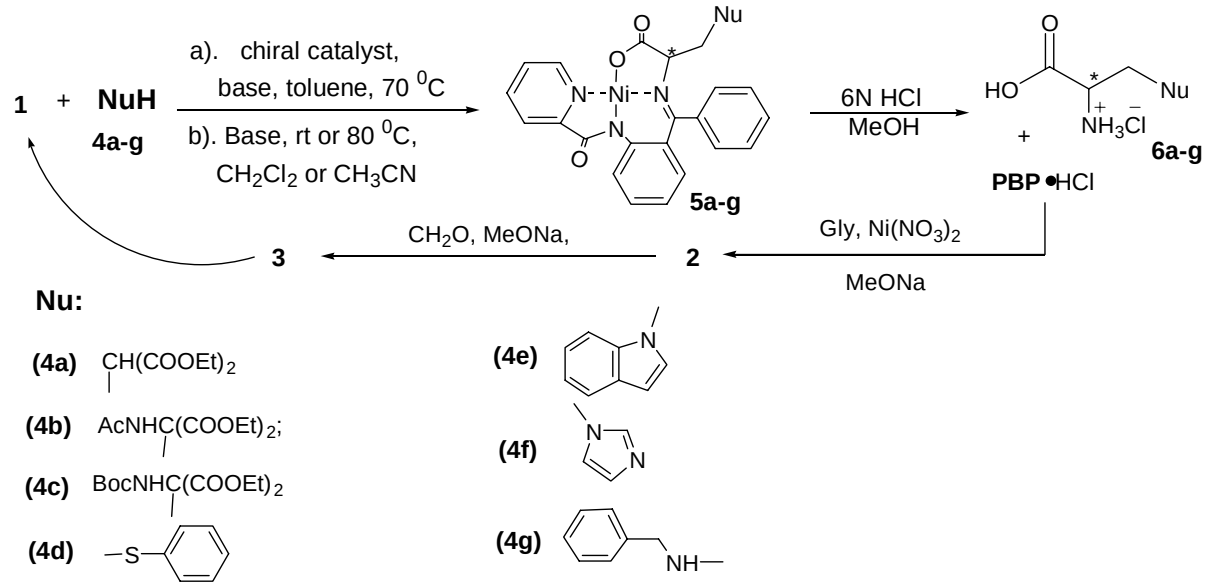
The achiral complex **1** was derived from the Ni(II) complex of the Schiff's base of glycine and PBP (pyridine-2-carboxylic acid (2-benzoyl-phenyl)-amide)[9] **2**, which was converted into the serine derivative **3,** followed by dehydration in acetic anhydride/Na_2CO_3 system (Scheme 1, overall yield 84%). A great advantage of **1** is its high crystallinity and stability, as compared to known analogs of dehydroalanine,[10a-d] as well as its red color, making TLC monitoring of the reactions easy.

The substrate **1** proved to be very convenient for the synthesis of racemic α-amino acids by Michael addition of nucleophiles in analogy with an earlier described procedure for the synthesis of non-racemic amino acids, using chiral Ni(II) dehydroalanine Schiff base complexes with BPB.[10e,f] The reaction of **1** with nucleophiles was carried out according to Scheme 2, and the course of the reaction was monitored by TLC (SiO_2, $CHCl_3$/acetone). After completion, the reaction mixture was neutralized and the red solid residue purified either by chromatography or by crystallization. The crystal structure of the product of malonic ester addition to **1** is shown in Figure 1. The decomposition of the final complexes was effected by dilute aqueous MeOH/HCl within 5-60 minutes, with heating under reflux. The process was easily followed by the change of the solution color from red to blue. Insoluble hydrochloride of **PBP** is removed by filtration in almost quantitative yield, and $NiCl_2$ and the amino acid are easily separated by ion exchange chromatography or by using EDTA (see experimental part).



(a) MeONa, MeOH, reflux, 20min. (b) MeONa, MeOH, reflux, 1h. (c) Ac_2O, Na_2CO_3, CH_3CN, reflux, 5h.

Scheme 1. Synthesis of substrate **1**.



Scheme 2. Michael addition of various nucleophiles **4** to substrate **1**.

All results of Michael additions of nucleophiles **4a-g** are presented in Table 1. The addition of **4a** proceeded without any catalyst in the presence of bases in CH_2Cl_2 and gave complex **5a** in high yield (Table1, run 1). Racemic glutamic acid could be recovered from the complex after hydrolysis.

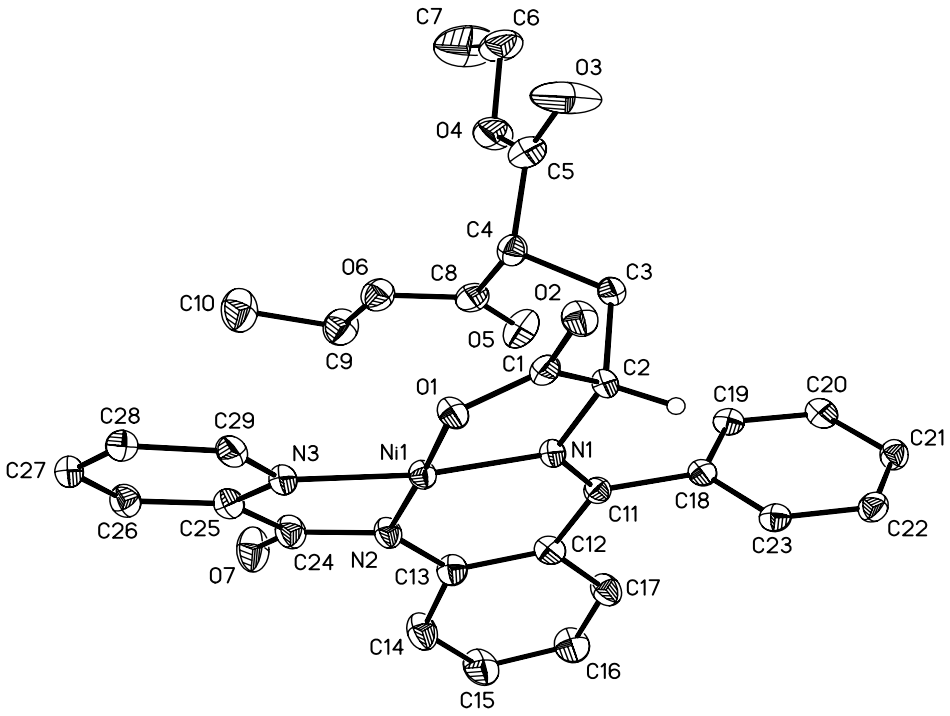
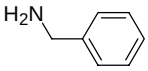
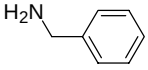
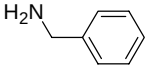


Figure 1. Structure of the complex **5a**.

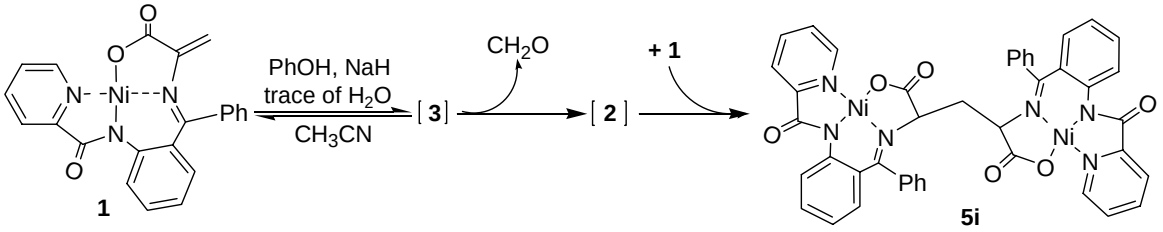
Table 1. Reaction of the complex **1** with different types of nucleophiles in the presence of NaH under conditions *b* of Scheme 2

Run[a]	NuH[b], 4	(±)-**5**	Solvent/ Temp [^{0}C]	Time [min]	Yield [%]
1	$CH_2(COOEt)_2$	**a**	CH_2Cl_2 / [20]	10	85[c]
2	PhSH	**d**	CH_2Cl_2 / [20]	25	75[c]
3		**e**	CH_3CN / [80]	180	80[d]
4		**f**	CH_3CN /[80]	90	88[e]
5		**g**	CH_2Cl_2 / [20]	60	58
6		**g**	iPrOH/[80]	15	56[e,f]
7		**g**	*t*BuOH/[80]	15	70[e,f]

[a] Concentration of the substrate 0.23M. [b] 10-50 mol % of NaH was employed (see experiment). [c] Ratio **4/1** was 3. [d] Ratio of **4/1** was 1.2. [e] Ratio of **4/1** was 2. [f] The reaction was carried out without NaH.

The reactions with thiophenol and benzylamine occurred readily to give the corresponding complexes **5d** and **5g** in good chemical yields (Table 1, run 2, 5). The absence of any absorption in the region of 2500-2650 cm^{-1} for **5d** proved that the addition for thiophenol occurred via its sulfur atom, as usual, and shown earlier for a similar addition to a chiral analogue of 1.[10e] Less active nucleophiles such as indole and imidazole required harsher reaction conditions (CH_3CN at reflux temperature for several hours, Table 1 run 3, 4) leading to the corresponding racemic complexes **5e,f**. Analyses of the structures of complexes **5e,f** by IR and NMR spectroscopy showed that the addition of imidazol and indol both occurred via formation of N-C bonds. Comparison of the chromatographic behavior of samples of the amino acids with samples of histidine and tryptophane is compatible with this conclusion.

An attempt with phenol failed: no product of addition to **1** was detected. Still a new product was formed in 25% yield: meso-compound **5i** as proved by NMR spectroscopy (see experiment) and X-ray single-crystal analysis (Figure 2). Apparently, the reaction proceeded as described in Scheme 3.



Scheme 3. A possible synthetic route leading to **5i**.

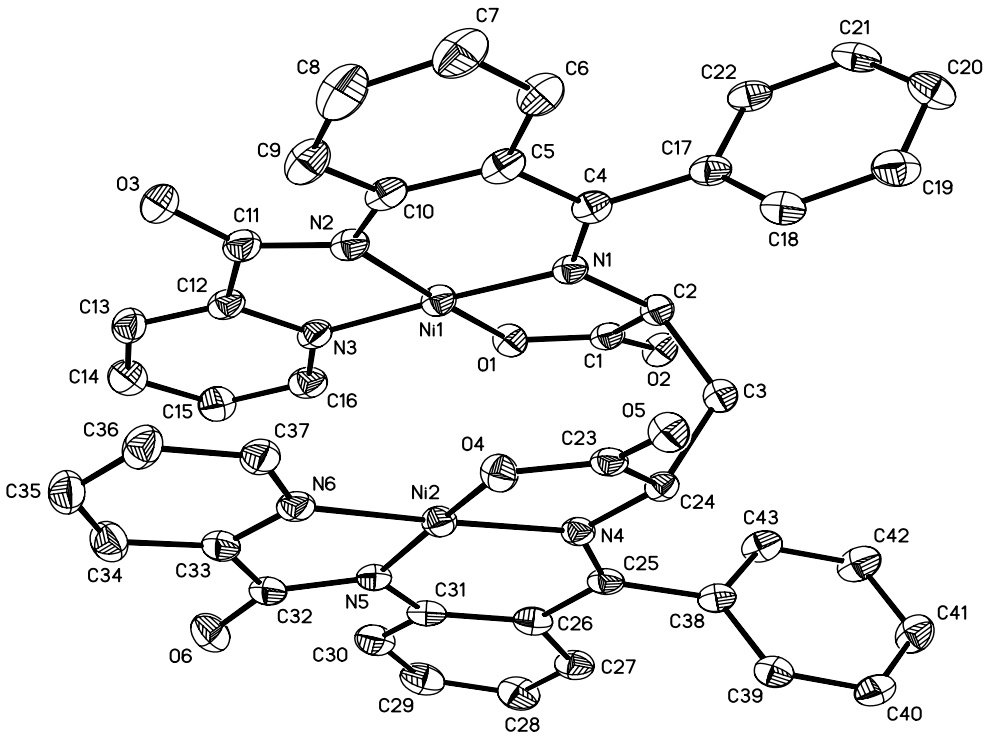
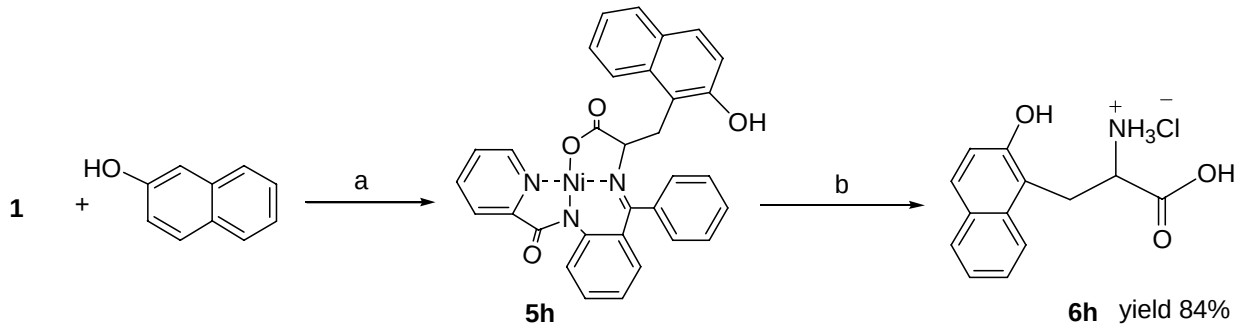


Figure 2. X-ray structure of complex **5i**.

The addition of 2-naphtol to 1 was conducted in MeCN at a ratio **4**/**1** equal to 1.2 at 80°C. The addition proceeded via C(1) of 2-naphtol, according to Scheme 4. It was proved by the presence of OH band in the IR spectrum of the adduct and its COESY NMR spectra. The ^{1}H N MR spectrum of **5h** displays two doublets of an AB system at 7.04 and 7.29 ppm that we attribute to the C(3)- and C(4)-H atoms of the naphtyl moiety. In addition, there was a broad resonance at 9.9 ppm assigned to the proton of the hydroxy group of the naphtyl moiety. Comparison of the ^{13}C spectra of **5i**, **5h** and free 2-naphtol and, in addition, ^{1}H-^{13}C COSY spectra of **5h** show resonances at 113.76 and 117.44, corresponding to the C(3) and C(1) atoms of the naphtyl moiety with C(1) bearing no hydrogen. Finally, interactions in ^{1}H-^{13}C HMBC spectra of **5h** testified that the CH_2 group of the amino acid moiety is bonded to C(1).



(a) NaH, CH_3CN, 80 ^{0}C, 2h. (b) 6N HCl/MeOH.

Scheme 4. Addition of 2-naphthol to complex **1**.

Thus, complex **1** constitutes a useful starting material that can be successfully employed for the synthesis of a variety of racemic α-amino acids.

Next, we have attempted to use the substrate **1** in a catalytic asymmetric version of the Michael addition.

Recently we have shown that the asymmetric alkylation reaction of the complex **2** with alkyl halides could be performed catalytically with TADDOL or NOBIN (2'-Amino-[1,1']binaphthalenyl-2-ol) as catalysts[8,9] (Chart 1). We applied the same chiral catalysts in the addition of malonic ester to substrate **1** with the significant difference that the formation of a C-H and not of a C-C bond was the step introducing the chirality center.

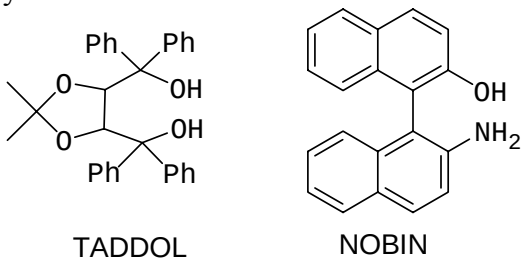


Chart 1

NOBIN, although a good catalyst for the reaction, gave a disappointingly low enantiomeric excess of only 10%, whereas TADDOL **7a** led to a sizable enantiopurity of the product (Table 2).

The variation of bases and solvents lead to toluene and *t*BuOK or KOH as solvent and bases of choice (Table 2, run 9, 10).

A range of TADDOL derivatives were also tested as catalysts. Any substitution of OH groups in TADDOL **7a** by Cl-, SH-, $NHCOCF_3$ or NH_2- groups invariably decreased the enantioselectivity of the process (Table 3, run 1-6).

Table 2. Reaction of the dehydroalanine derivative **1**[a] with $CH_2(CO_2Et)_2$[b], catalyzed by 10 % mol of (*R,R*)-TADDOL **7a**

Run	Solvent	Base [0.2eq]	Temp [^{0}C]	Time [min]	Yield[c] of **5a** [%]	*ee* of *(S)*-**6a** [%][d]
1	CH_2Cl_2	NaH	20	4	79	12
2	CH_2Cl_2	NaH	40	4	88	15
3	CH_2Cl_2	NaH	-20	5	35	12
4	CH_2Cl_2	*t*BuLi	20	4	82	9
5	CH_2Cl_2	*t*BuOK	20	4	82	36
6	Hexane	*t*BuOK	20	30	8	0
7	Toluene	NaH	20	30	30	21
9	Toluene	*t*BuOK	20	5	15	54
10	Toluene	KOH	20	5	17	54
11	Toluene	NaOH	20	5	20	29

[a] The substrate was 0.115M. [b] 4 Equivalents $CH_2(CO_2Et)_2$. [c] The yield of product was calculated from **1** and determined by weighing the isolated complex **5a**. [d] GLC Analysis of isolated amino acids were performed on chiral Chirasil-Val columns.

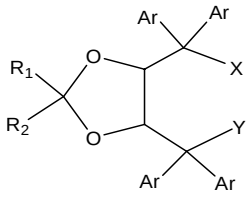
Changing the substitutes on TADDOL from ketal (R_1, $R_2 \neq H$) to acetal ($R_2 = H$) also influenced the outcome of the reaction. For example, the TADDOLs **7j-o** gave very moderate enantioselectivities in the range of 18-37 % (Table 3, run 10-15). Changing the aryl group of the catalysts led to striking effect on the enantioselctivities: the original TADDOL **7a** and the $(CF_3)_2$-substituted TADDOL **7t** gave rise to *ee* values of 54% and < 1 % respectively (Table 3, runs 1 and 19). Another type of electron-withdrawing aryl group, C_6F_5, resulted in reversal of the product sense of chirality (Table 3, runs 1 and 20).

The derivative **7e** containing two TADDOL moieties did not lead to any significant change of stereoselectivity or yield (Table 3, run 5). Substitution of the 2-napthyl moieties for Ph resulted in some decrease of the stereoselectivity (Table 3, run 1 and 8). The TADDOL with 1-napthyl groups (**7s** and **7g**) invariably led to increased enantioselectivities (Table 3, run 1 and 7, 17 and 18) and gave a maximum of 75% *ee* of **5a** at ambient temperature, although in poor yield.

An attempt to increase the yields of the reaction by changing either the nature of the base or its amount at 20^{o}C were unsuccessful (Table 4, runs 1-5) with partial racemization of **5a**, accompanying the increase in the amount of the base (Table 4, runs 3 and 5). The yield of the reaction (up to 80%) and its *ee* (up to 80%) could be increased by switching to higher temperature

of 70°C with *t*BuOK serving as a base (Table 4, run 6). Increase of the size of the cation (Rb and Cs instead of K) had little influence on yield and *ee* (Table 4, runs 7 and 8). The optimal ratio of base/catalyst/Ni-substrate at room temperature was 0.1/0.05/1.

Table 3. Reaction of substrate **1** with $CH_2(CO_2Et)_2$, catalyzed by **7a-u** in toluene in the presence of 0.2eq. *t*BuOK



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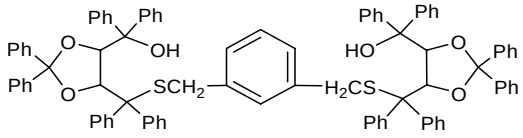


7e

Run [a]	**7**	R_1	R_2	Ar	X	Y	Yield of **5a** [%][b]	*ee* of *(S)*-**6a** [%]
1	**A**	Me	Me	Ph	OH	OH	18	54
2	**B**	Me	Me	Ph	OH	SH	28	19
3	**C**	Me	Me	Ph	OH	NH_2	25	13
4	**D**	Me	Me	Ph	OH	$NHCOCF_3$	25	19
5	**E**	Me	Me	Ph	OH	see formula	31	22
6	**f**∗OEt_2	Me	Me	Ph	OH	$NH\text{-}SO_2CF_3$	11	15
7	**g**∗MeOH	Me	Me	Naphtyl-1	OH	OH	30	75
8	**H**	Me	Me	Naphtyl-2	OH	OH	32	35
9	**I**	Ph	Ph	Ph	OH	OH	30	44
10	**J**	Ph	H	Ph	OH	OH	34	34
11[c]	**K**	*p*-BrPh	H	Ph	OH	OH	28	18
12[c]	**L**	*p*-BrPh	H	Ph	OH	OTMS	28	9
13[c]	**M**	*p*-BrPh	H	Ph	OTMS	OTMS	16	18
14	**N**	Naphtyl-1	H	Ph	OH	OH	31	30
15	**O**	*t*Bu	H	Ph	OH	OH	33	37
16	**P**	tBu	H	Naphtyl-1	OH	OH	30	56-62
17	**R**	$-(CH_2)_5-$		Ph	OH	OH	30	50
18	**S**	$-(CH_2)_5-$		Naphtyl-1	OH	OH	29	62
19[d]	**T**	Me	Me	$3,5(CF_3)_2Ph$	OH	OH	90	0
20[e]	**U**	Me	Me	C_6F_5	OH	OH	54	(*R*)-41

[a] Reaction conditions: the reactions were run in toluene, concentration of **1** is 0.115 M, ratio of the $CH_2(CO_2Et)_2$: substrate = 4:1, **7**:substrate = 1:10, tBuOK:(*R,R*)-**7** = 2:1, room temperature, 15 minute, under Ar. [b] Yield of the product determined after separation from unreacted **1**. [c] Compounds 7k,l,m were prepared by O.Larionov in Zürich and will be described elsewhere. [d] The reaction was run at 70 ^{0}C for 4 min. [e] The reaction was run at 70 ^{0}C for 15 min with ratio of $CH_2(CO_2Et)_2$:substrate:**7**:*t*BuOK = 4:1:0.05:1.2.

Table 4. Reaction of complex **1** with $CH_2(CO_2Et)_2$, catalyzed by **7g** in toluene

Run[a]	Catalyst **7g** [eq]	Base [eq]	Temp [^{0}C]	Time [min]	Yield[b] of **5a** [%]	*ee* of **6a** [%]
1	0.1	NaOH (0.2)	20	15	31	32
2	0.1	KOH (0.2)	20	15	31	67
3	0.1	*t*BuOK (0.2)	20	15	30	75
4	0.1	*t*BuOK(0.1)	20	15	18	65
5	0.4	*t*BuOK (0.8)	20	15	44	55
6	0.05	*t*BuOK (0.1)	70	4	80	80
7	0.05	50% RbOH (0.1)	70	4	76	52
8	0.05	$CsOH{\cdot}H_2O$ (0.1)	70	4	70	77
9	0.05	*t*BuOK (0.1)	70	20	91	55
10	0.05	*t*BuOK (0.1)	20	360	48	76

[a] Reaction conditions: the concentration is 0.115 M, ratio of the $CH_2(CO_2Et)_2$: **1** = 4:1. [b] Yield of the product **5a** determined after separation from unreacted **1**.

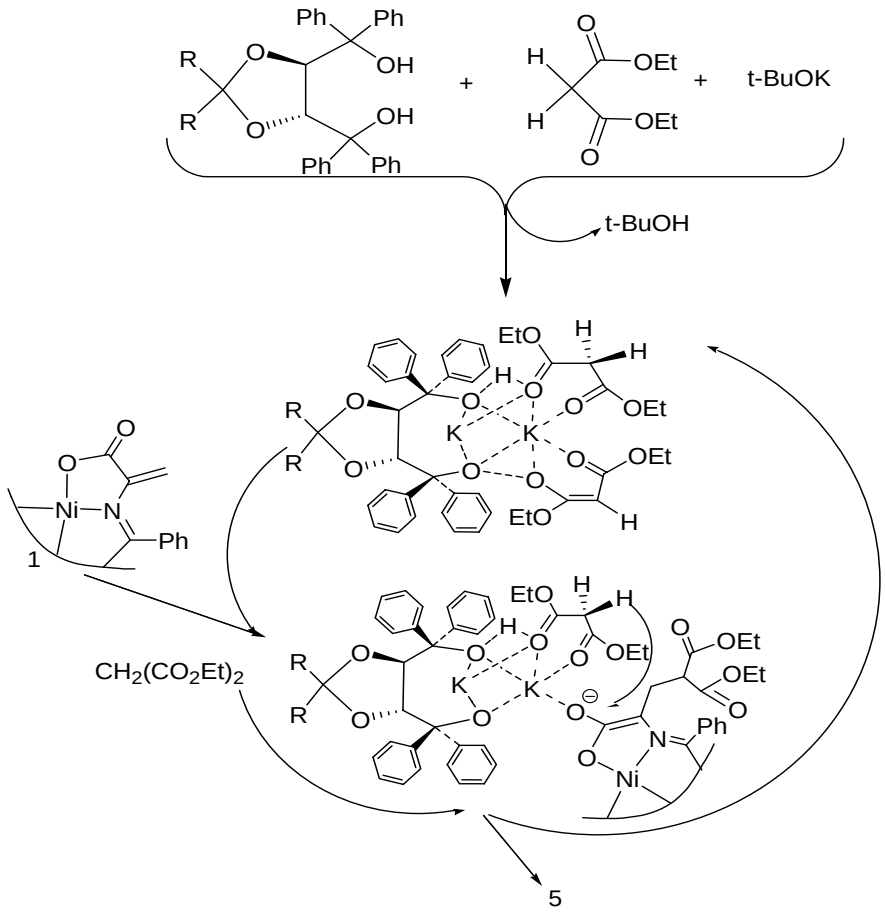
Some racemization of **5a** was observed if the reaction was run longer than 4 minutes (Table 4, run 9). The enantiomeric purity of **5a** could be improved up to *ee* 88% by a single recrystallyzation (Table 4, run 6)

Experiments with other nucleophiles in asymmetric version of the reaction showed that the most efficient nucleophiles were other derivatives of malonic ester, which gave moderate enantioselectivities and yields (Table 5, runs 1-3), whereas thiophenol added to **1** totally non-selectively (Table 5, run 4). Also amines as nucleophiles reacted with **1** without any detectable enantioselectivity.

Table 5. Reaction of the complex **1** with different type of nucleophils catalyzed by (*R*)-**7g** in toluene at 70^{o}C

Run[a]	NuH	(*S*)-**5**	*t*BuOK [eq]	Time [min]	Yield of **5** [%][b]	*ee* of (*S*)-**5** [%]
1	$CH_2(COOEt)_2$	**a**	0.1	4	80	80[c] (88%)[d]
2	$AcNHCH(COOEt)_2$	**b**	0.1	4	65	78[e] (80)[d]
3	$BocNHCH(COOEt)_2$	**c**	0.1	4	56	64[e] (83)[d]
4	PhSH	**d**	0.1	4	64	<1

[a] Reaction conditions: the reactions were run in toluene, concentration of **1** 0.115M, ratio of the **1**:NuH:**7g**:tBuOK=1:4:0.05:0.1, 70^{0}C, under Ar. [b] Yield of the product **5** determined after separation from unreacted **1**. [c] Enantiomeric excess was determined by GLC analysis on chiral column. [d] The *ee* was determined after crystallization. [e] The *ee* was determined by comparison of optical rotations.



Scheme 5. A hypothetical mechanism for the overall Michael addition of malonic ester to **1** catalyzed by TADDOL.

As the enantioselectivity of the reaction is determined in the protonation step of the intermediate enolate, the observed results are not likely to be due to protonation by TADDOL: the pKa of TADDOLs in DMSO would most likely lie in the range 28-30 whereas **2** and derivatives such as **5** have a pKa in the range of 17-19.[11] On the other hand, malonic esters and acetylacetate do have their pKa close to that of **5** and, in addition, are capable of chelating alkali ions. An admittedly speculative mechanism of the process (Scheme 5) might include the formation of a mixed chelate of TADDOL and malonic ester, with the latter functioning to deliver a proton to quench the intermediate enolate of **5**. The function of TADDOL might be the increase of malonic ester acidity by hydrogen bonding and forming a chiral environment for recognition of the enantiotopic enolate of **5** in the cause of proton transfer.

Conclusions

A new type of substrate based on an achiral Ni(II) complex of a Schiff base of dehydroalanine was elaborated for the synthesis of amino acids. We have developed an efficient catalytic method of asymmetric 1,4 conjugate addition of CH-acids to Michael acceptors catalyzed by TADDOLs.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 400 and Avance-300 spectrometers with 400.13MHz and 300.13MHz accordingly. The resonances in ^{1}H and ^{13}C spectra of **5f**, **5h**, and **5i** were attributed to the corresponding ^{1}H and ^{13}C nucleus according to a series of 1D and 2D homo- and heteronuclear experiments such as ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY and also ^{1}H-^{13}C HMBC experiments with *J*-filtration to suppress 1,3 spin-spin interactions. Very significant overlap of resonances in ^{1}H spectra made difficult to attribution of the resonances to the protons of pyridine and phenyl moieties.

The numbering of atoms in the **PBP** moiety of every Ni-complex in experiment section corresponds to the numeration in X-ray structure of **5a** (Fig.1).

IR spectra were made on a "Magna-IR 750" spectrometer (Nicolet). The optical rotations angles were measured on a Perkin-Elmer 241 polarimeter. Chiral GLC analyses of the amino acids were performed on a Chirasil-L-Val type phase, by using n-propyl esters of N-trifluoroacetyl derivatives of amino acids. All manipulations were performed under dried and deoxygenated argon. Reactions were carried out in a flame-dried round-bottomed flasks equipped with a magnetic stir bar and water- cooled reflux condenser. All the reagents were acquired from Aldrich. TADDOLs were available from previous work.[12]

Crystal structure determination. Data were collected on a Bruker SMART 1000 CCD diffractometer (λ(MoKα)-radiation, graphite monochromator, φ and θ scan mode) and corrected for Lorentz and polarization effects and for absorption[13]; details are given in Table 6. The structures were determined by direct methods and by full-matrix least squares refinement with anisotropic thermal parameters for non-hydrogen atoms. The crystal of **5i** contains seven solvate chloroform molecules one of which is disordered over two sites with occupancies 0.6 and 0.4, respectively. The hydrogen atoms of both compounds were placed in calculated positions and refined in riding model with fixed thermal parameters (Uiso(H) = 1.5Ueq(C) for the CH_3-groups and Uiso(H) = 1.2Ueq(C) for the other groups). All calculations were carried out by use of the SHELXTL (PC Version 5.10) program package.[14]

1.1. Pyridine-2-carboxylic acid(2-benzoyl-phenyl)-amide (PBP) and Ni(II) complex 2 derived from the Schiff base of PBP and 2-aminoacetic acid were synthesized by a procedure described previously.[9]

1.2. Synthesis of Ni(II) complex 3 derived from the Schiff base of PBP and (±)-serine. To the suspension of **2** (10g, 0.024mol) in CH_3OH (90 ml) under Ar were added CH_3ONa (22ml, 4N) and $(CH_2O)n$ (2g, 0.067mol). The mixture was stirred under reflux for 1h until disappearance of the initial complex. The course of the reaction was monitored by TLC ($CHCl_3$: CH_3COCH_3 = 5: 1). Then the reaction mixture was cooled down to r.t. and quenched with aq AcOH. The precipitate was filtered by dense filter, washed with water several times and dried at air to afford **3**. The dry product (10.1g, 0.023mol, 94%) was put in 60ml of $CHCl_3$. The mixture was stirred at rt for 1h. The precipitate was filtered and dried at air to afford 9.45g (0.021mol, 88 %) pure **3** with very low solubility in any organic solvents: mp 249-253 ^oC. Anal. Calcd for $C_{22}H_{17}N_3NiO_4$: C, 59.23; H, 3.84; N, 9.42; Found: C, 59.21; H, 3.78; N, 9.36; ^1H NMR (400.13 MHz, $CDCl_3$): δ: 2.83 (m, 1H, OH); 3.78 (m, 1H, CH_2); 3.96 (m, 1H, CH_2); 4.10 (m, 1H, CH); 6.8 (m, 2H, ArH); 7.12 (d, 1H, ArH(CH-17), *J* = 7.4 Hz); 7.29 (m, 1H, ArH); 7.37 (m, 1H, ArH); 7.45 (m, 1H, ArH); 7.55 (m, 3H, ArH); 7.92 (d, 1H, ArH, *J* = 7.8 Hz); 8.02 (м, 1H, ArH); 8.22 (d, 1H, ArH(CH-29), *J* = 4.0 Hz); 8.95 (d, 1H, ArH(CH-14), *J* = 8.8 Hz); IR, (ν/cm^{-1}; KBr): 1654 (COO), 1638 (amide); 1606 (C=N), 1586 (amide); 3270 (OH).

1.3. Synthesis of Ni(II) complex 1 derived from the Schiff base of PBP and 2-amino-acrylic acid. The mixture of **3** (9g, 0.02 mol) in 68ml CH_3CN and Ac_2O (15ml) was stirred for 1 h under reflux. Na_2CO_3 (6.36g, 0.06 mol) was then added. The reaction mixture was stirred under Ar at reflux for 5-6 h until disappearance of the initial complex. The course of the reaction was monitored by TLC ($CHCl_3$: CH_3COCH_3 = 5:1).The reaction mixture was quenched by adding 500ml water. After 1h the precipitate was filtered, washed with water and dried over P_2O_5 giving **1** (8.2 g, 0.019mol, 96%). The isolated product was then refluxed in 80ml MeOH during 1h. Then the mixture was cooled down to r.t. and precipitate was filtered and dried at air to afford pure product **1** (7.6g, 0.018mol, 89%): mp 259-262 ^oC. Anal. Calcd for $C_{22}H_{15}N_3NiO_3$: C, 61.73; H, 3.53; N, 9.82; Found C, 61.77; H, 3.44; N, 9.91; ^1H NMR (400.13 MHz, $CDCl_3$): δ:.4.22 (d, 1H, $=CH_2$, *J* = 1.3 Hz) 5.68 (d, 1H, $=CH_2$, *J* = 1.3 Hz); 6.82 (t, 1H, ArH(CH-16), *J* = 7.6 Hz); 7.02 (dd, 1H, ArH(CH-17), *J* = 8.4 Hz, *J* = 1.6 Hz); 7.20 (m, 2H, ArH); 7.38 (m, 1H, ArH); 7.45-7.55 (m, 4H, ArH); 7.92 (m, 1H, ArH); 8.02 (t, 1H, *J* = 7.8 Hz, ArH); 8.25 (d, 1H, ArH(CH-29), *J* = 5.0 Hz); 8.9 (d, 1H, ArH(CH-14), *J* = 8.7 Hz); ^{13}C NMR (400.13MHz, $CDCl_3$): δ 116.34 ($=CH_2$); 121.47 (C-16); 123.27 (C-17); 124.18 (C-14); 127.03 (C-15); 127.42 (C-11); 128.18; 129.26; 130.22; 134.30; 135.52; 135.64 (C-18); 140.61; 144.17 (C-13); 146.89 (C-29); 147.16 (=C); 153.15 (C-25); 169.68; 170.63. IR (ν/cm^{-1}; KBr): 1667 (COO), 1646 (amide); 1606 (C=N), 1586 (amide).

1.4. Typical procedure for the asymmetric Michael addition as illustrated by synthesis of 5a

1.4.1. Ni(II) Complex 5a of a Schiff base of PBP and (S)-2-amino-4-ethoxycarbonyl-pentanedioic acid 5-ethyl ester. (*R*)**-7g** (0.082g, 0.117mmol) was dissolved in toluene (20 ml) and the solution was carefully purged with Ar, then (0.026g, 0.23mmol) C_4H_9OK were added into the solution with stirring under Ar at room temperature. After 9 min, the initial **1** (1g, 2.3mmol) was added to the mixture under Ar with stirring at 70^0C, followed 6 min later by malonic ethyl ester

(1.49g, 9.3mmol) and the reaction mixture was agitated for additional 4 min at 70^{0}C [the course of the reaction was monitored by TLC ($CHCl_3$/Me_2CO, 5/1)]. Then the reaction mixture was quenched with aq AcOH and some CH_2Cl_2 was added to the solution. The organic layer was separated and an aliquot was used to check *ee* of the glutamic acid (80%). The remainder of the organic layer was evaporated and the residue (1.17g, 2mmol, 87%) purified by chromatography on SiO_2 column ($CHCl_3$/Me_2CO, 5/1). The main fraction was evaporated giving the final Michael adduct with (*S*)-configuration and yield 80% (1g, 1.84mmol): $[\alpha]^{25}_D$ +2127° (c 0.02, $CHC1_3$, for complex with *ee* 80%.). After crystallization from mixture of MeOH/H_2O enantiomeric purity was increased up to 88% ($[\alpha]^{25}_D$ +2340); mp 178-182°C. Anal. Calcd. for $C_{29}H_{27}N_3NiO_7$: C, 59.21; H, 4.63; N, 7.14; Found (after cryst.) C, 59.29; H, 4.68; N, 7.11; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.15 (t, 3H, Me, *J* = 7.1 Hz); 1.18 (t, 3H, Me, *J* = 7.1 Hz); 2.21, 2.67 (m, 2H, CH_2); 3.96-4.19 (m, 5H, CH, $2CH_2$); 4.27 (m, 1H, CH); 6.77 (m, 2H, ArH); 7.23 (d, 1H, ArH, *J* = 5.0 Hz); 7.35 (m, 2H, ArH); 7.46 (m, 1H, ArH); 7.54(m, 3H, ArH); 7.91 (d, 1H, ArH, *J* = 7.8 Hz); 8.01 (t, 1H, ArH, *J* = 7.8 Hz); 8.24 (d, 1H, ArH(CH-29), *J* = 4.6 Hz); 8.97 (d, 1H, ArH(CH-14), *J* = 8.0 Hz); ^{13}C NMR (400.13MHz, $CDCl_3$): δ 13.77 (CH_3); 13.83 (CH_3); 32.07 (CH_2); 48.18 (CH); 61.62 (*CH*$_2$CH$_3$); 62.02 (*CH*$_2$CH$_3$); 69.39 (*CH*CH$_2$); 121.35 (C-16); 123.25 (C-17); 123.80 (C-14); 126.44 (C-11); 126.66; 126.92 (C-15); 128.17; 128.91; 129.74; 133.56; 134.76; 140.50; 142.98 (C-13); 146.82 (C-29); 153.03 (C-25); 168.19; 169.37; 169.90; 173.62; 178.24; IR, (ν/cm^{-1}; KBr): 1678; 1648; 1606; 1590; 1746; 1728.

1.4.2. Synthesis of Ni(II) complex 5b of a Schiff base of PBP and (*S*)-2-acetylamino-4-amino-2-ethoxycarbonyl-pentanedioic acid 1-ethyl ester. The experiment was conducted similar to the one described in section **1.4.1.** starting from **1** (0.5g, 1.17mmol) in toluene (10ml), using C_4H_9OK (0.0131g 0.117mmol) as a base, **7g** (0.04g, 0.0584mmol) and 2-acetylamino-malonic acid diethyl ester (0.75g, 3.45 mmol). The reaction was over within 4min. Yield of **5b** was 93% (0.7g, 1.1mmol): $[\alpha]^{25}_D$ +2090° (c 0.02, $CHC1_3$, for complex with *ee* 78 % assuming similar specific rotations of **5a** and **5b**.). The product was crystallized from $CHCl_3$/Hexane: mp 260^{0}C (decomp). Anal. Calcd. for $C_{31}H_{30}N_4NiO_8 \cdot 0.5CHCl_3$: C, 53.67; H, 4.36; N, 7.95; Found: C, 53.27; H, 4.19; N, 7.64; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.17 (t, 6H, Me, *J* = 7.0 Hz); 1.75 (s, 3H, Ac); 2.78, 3.54 (AB part of ABX system, 2H, CH_2, J_{AB} = 14.56 Hz); 3.97 (X part ABX of system, 1H, CH, J_{AX} = 4.2 Hz, J_{BX} = 9.6 Hz); 4.0-4.24 (m, 4H, $2CH_2$); 6.72-6.79 (m, 2H, ArH); 7.14 (bs, 1H, ArH); 7.2 (d, 1H, ArH, *J* = 4.0 Hz); 7.34 (m, 1H, ArH); 7.44-7.59 (m, 4H, ArH); 7.95 (d, 1H, ArH, *J* = 7.0 Hz); 8.03 (m, 1H, ArH); 8.16 (d, 1H, ArH(CH-29), *J* = 5.3 Hz); 8.96 (d, 1H, ArH(CH-14), *J* = 9.0 Hz); ^{13}C NMR (400.13 MHz, $CDCl_3$): δ 14.46 ($2CH_3$); 23.33 (Ac); 37.05 (CH_2); 63.33 (*CH*$_2$CH$_3$); 63.59 (*CH*$_2$CH$_3$); 64.90 (C); 68.65 (*CH*CH$_2$); 122.15 (C-16); 124.09 (C-17); 124.92 (C-14); 127.13 (C-11); 127.34; 127.53 (C-15); 129.31; 128.39; 130.22; 130.32; 133.92 (C-18); 134.36; 135.38; 141.29; 143.76 (C-13); 147.10 (C-29); 154.12 (C-25); 167.59; 169.76; 170.53; 173.45; 179.11; δ ; (IR, (ν/cm-1; KBr): 1667; 1640; 1605; 1591; 1684; 1744; 3414 (NH).

1.4.3. Synthesis of Ni(II) complex 5c of a Schiff base of PBP and (*S*) 4-amino-2-tert-butoxycarbonylamino-2-ethoxycarbonyl-pentanedioic acid 1-ethyl ester. The experiment was conducted similar to the one described in section **1.4.1.**, starting from **1** (0.5g, 1.17mmol) in toluene (10ml), using C_4H_9OK (0.0131g 0.117 mmol) as a base, **7g** (0.04g, 0.0584mmol) and 2-Boc-amino-malonic acid diethyl ester (0.96g, 3.5mmol). The reaction was over within 4min. Yield of **5c** was

91% (0.74g, 1.06mmol): $[\alpha]^{25}_D$ +1700° (c 0.02, $CHC1_3$, for complex with *ee* 64 %.). The product was crystallized from $CHCl_3$/Hexane. Enantiomeric purity for precipitate was <1 % (35 % yield) and of the filtrate 80 % (56 % yield): mp 238-240 °C. Anal. Calcd. for $C_{34}H_{36}N_4NiO_9$: C, 58.06; H, 5.16; N, 7.97; Found: C, 58.01; H, 4.91; N, 7.91; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.169 (t, 3H, Me, *J* = 7.1 Hz); 1.170 (bs, 9H, *t*Bu); 1.20 (t, 3H, Me, *J* = 7.1 Hz); 2.7 and 3.12 (AB part of ABX system, 2H, CH_2, J_{AB} = 15.2 Hz, J_{AX} = 3.9 Hz, J_{BX} = 6.3 Hz); 4.07-4.29 (m, 5H, CH, $2CH_2$); 6.72 (m, 2H, ArH); 7.17 (d, 1H, ArH, *J* = 6.4 Hz); 7.3 (m, 2H, ArH); 7.49 (m, 3H, ArH); 7.91 (d, 1H, ArH, *J* = 7.8 Hz); 8.01 (t, 1H, ArH, *J* = 7.8 Hz); 8.17 (d, 1H, ArH (CH-29), *J* = 5.3 Hz); 9.06 (d, 1H, ArH (CH-14), *J* = 8.9 Hz); ^{13}C NMR (400.13MHz, $CDCl_3$): δ 13.67 (CH_3); 13.89 (CH_3); 27.75 ($3CH_3$); 35.13 (CH_2);; 62.52 (CH_2CH_3); 63.13 (CH_2CH_3); 64.75 (C); 68.38 ($CHCH_2$); 80.62 (C(tBu)); 121.28 (C-16); 123.52 (C-17); 124.03 (C-14); 126.60 (C-11); 126.65; 126.72 (C-15); 128.68; 128.89; 129.33; 129.76; 133.40; 133.66 (C-18); 134.68; 140.41; 143.51 (C-13); 146.85 (C-29); 153.60 (C-25); 154.62; 167.50; 167.67; 169.79; 172.51; 177.87; IR, (ν/cm^{-1}; KBr): 1668; 1634; 1604; 1592; 1714, 1739,1762; 1744; 3406 (NH).

1.4.4. Synthesis of Ni(II) complex 5d of a Schiff base of PBP and (±)2-amino-3-phenylsulfanyl-propionic acid. The experiment was conducted similar to the one described in section **1.4.1.**, starting from **1** (1.5g, 3.5mmol) in CH_2Cl_2 (15ml), using NaH (0.014g 0.35mmol) as a base and thiophenol (1g, 9mmol). The reaction was over within 25min at rt. The product was purified by chromatography on SiO_2 column ($CHCl_3$/Me_2CO, 5/1). Yield of **5d** was 75 % (1.43g, 2.65mmol): mp 230-235°C. Anal. Calcd. for $C_{28}H_{21}N_3NiO_3S{\cdot}0.5H_2O$: C, 61.45; H, 4.05; N, 7.68; Found: C, 61.81; H, 3.70; N, 7.48; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.95 and 3.40 (AB part of ABX system, 2H, CH_2, J_{AB} = 14.2 Hz); 4.37 (X part of ABX system, 1H, J_{AX} = 6.4 Hz, J_{BX} = 2.2 Hz); 6.72 (m, 2H, ArH); 6.80 (d, 1H, ArH(CH-16), *J* = 7.4 Hz); 7.07 (m, 3H, ArH); 7.25 (m, 1H, ArH); 7.34-7.45 (m, 3H, ArH); 7.52 (m, 4H, ArH); 7.9 (d, 1H, ArH, *J* = 7.48 Hz); 8.0 (t, 1H, ArH, *J* = 14.6 Hz); 8.09 (d, 1H, ArH (CH-29), *J* = 6.4 Hz); 8.96 (d, 1H, ArH(CH-14), *J* = 8.5 Hz); ^{13}C NMR (300.13 MHz, $CDCl_3$): δ 37.91 (CH_2); 70.55 (CH); 121.31 (C-16); 123.61 (C-17); 124.05 (C-14); 126.86 (C-15); 126.91; 126.97; 127.72; 128.86; 129.27; 130.05; 131.22; 133.65; 133.98; 134.56; 140.36; 143.60; 147.14; 165.27; 170.02; 172.86; 176.39; IR, (ν/cm^{-1}; KBr): 1672; 1642; 1606; 1592.

1.4.5. Synthesis of Ni(II) complex 5e of a Schiff's base of PBP and (±)2-amino-3-indol-1-yl-propionic acid. The reaction was conducted in 15ml CH_3CN starting from complex **1** (1.5g, 3.5mmol), indole (0.63g, 4.2mmol) and NaH (0.035g, 0.875mmol). The reaction time was 2.5-3h at 80 °C. To the reaction mixture was added 10% aq.AcOH, then it was quenched by adding 200ml water. After 1h the precipitate was filtered and washed with water and dried at air After purification by column chromatography ($CHCl_3$:MeCOMe = 8:1) the yield of pure **5e** was 80 % (1.5g, 2.8 mmol): mp 290-292°C. Anal. Calcd. for $C_{30}H_{22}N_4NiO_3{\cdot}0.25{\cdot}CHCl_3$: C, 63.18; H, 3.90; N, 9.74; Found: 63.46; H, 3.77; N, 9.70; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 4.35-4.41 (m, 2H, CH_2); 4.76 (m, 1H, CH); 6.4 (d, 1H, *Ind*-3, *J* = 3.2 Hz); 6.77-6.87 (m, 3H, ArH); 7.01-7.1 (m, 2H, ArH); 7.13-7-17 (m, 2H, ArH); 7.24 (d, 1H, *Ind*-2, *J* = 3.2 Hz); 7.29 (m, 1H, ArH); 7.36 (m, 2H, ArH); 7.41-7.5 (m, 2H, ArH);7.57 (m, 2H, ArH); 7.68 (d, 1H, ArH, *J* = 7.4 Hz); 7.86 (t, 1H, ArH, *J* = 7.4 Hz); 8.8 (d, 1H, ArH(CH-14), *J* = 8.9 Hz); ^{13}C NMR (400.13MHz, $CDCl_3$): δ 50.27 (CH_2); 72.27 (CH); 102.62 (C-3, *Ind*); 110.64 (C-7, *Ind*); 120.12; 120.45; 121.39; 121.93; 123.59; 123.87; 126.51 (C-2,

Ind); 126.68 (C-11); 127.26; 127.37; 129.09 (C-9, *Ind*); 129.39; 129.59; 130.27; 133.44; 133.86; 134.59; 137.23 (C-8, *Ind*); 139.76; 143.64 (C-13); 146.33 (C-29); 152.79 (C-25); 169.40; 172.37; 177.25; IR, (ν/cm^{-1}; KBr): 1668; 1639; 1609, 1589.

1.4.6. Synthesis of Ni(II) complex 5f of a Schiff base of PBP and (±)2-amino-3-imidazol-1-yl-propionic acid. The reaction was conducted in 15ml CH_3CN starting from complex **1** (1.5g, 3.5 mmol) imidazole (0.47g, 7mmol) and NaH (0.03g, 0.75mmol). The reaction time was 1.5h at 80^{0}C. To the reaction mixture was added 10% aq.AcOH, then it was quenched by adding 200ml water. After 1h the precipitate was filtered and washed with water and dried at air After purification by column chromatography ($CHCl_3$:MeCOMe:MeOH= 5/1/3) the yield of pure **5f** was 83.5% (1.45g, 2.92mmol): mp 236-238 ^{o}C (decomp). Anal. Calcd. for $C_{25}H_{19}N_5NiO_3$: C, 60.52; H, 3.86; N, 14.12; Found: C, 60.88; H, 3.52; N, 14.47; ^{1}H NMR (300.13MHz, $CDCl_3$, T = 330K): δ 4.01 and 4.06 (AB part of ABX system, 2H, CH_2, J_{AB} = 14.4 Hz, J_{AX} = 4.0 Hz, J_{BX} = 2.8 Hz); 4.73 (bs, 1H, CH); 6.72 (t, 1H, ArH(CH-16), *J* = 7.3 Hz); 6.87 (dd, 1H, ArH(CH-17), *J* = 8.2 Hz, *J* = 1.6 Hz); 7.07 (bs, 1H, ArH); 7.15 (bs, 1H, *imidazol*-5); 7.33 (bs, 1H, *imidazol*-4); 7.40-7.51 (m, 3H, ArH); 7.58 (m, 3H, ArH); 7.82 (bs, 1H, *imidazol*-2); 7.92 (t, 1H, ArH, *J* = 7.5 Hz); 8.02 (d, 1H, ArH (CH-29), *J* = 7.3 Hz); 8.4 (bs, 1H, ArH); 8.8 (d, 1H, ArH(CH-14), *J* = 8.7 Hz); ^{13}C NMR (300.13MHz, $CDCl_3$, T = 330K): δ 50.45 (CH_2); 71.16 (CH); 121.67; 122.55 (*imidazol*-4); 124.42; 125.97; 126.71; 127.33; 128.41; 129.33; 129.81; 130.16 (*imidazol* 5); 130.44; 134.00; 134.20; 136.52; 139.91 (*imidazol*-2); 140.54; 143.73 (C-13); 146.93 (C-29); 152.03 (C-25); 168.60; 173.39; 175.28; IR, (ν/cm^{-1}; KBr): 1676; 1628; 1605, 1587.

1.4.7. Synthesis of Ni(II) complex 5g of a Schiff base of PBP and (±)-2-amino-3-benzylamino-propionic acid. To the complex **1** (1.5g, 3.51mmol) in CH_2Cl_2 (10ml) under Ar were added $C_6H_5CH_2NH_2$ (1.2 ml, 10.54mmol) and NaH (0.014g, 0.351mmol). The mixture was stirred at r.t. for 1h until disappearance of the initial complex. The course of the reaction was monitored by TLC ($CHCl_3$: CH_3COCH_3 = 5: 1). Then the reaction mixture was quenched with 10% aq AcOH. The precipitate was filtered by dense filter, washed with water several times, dried at air and giving **5g** with yield 1,1g (2.06mmol, 58 %). For getting pure sample for analyses the product was crystallized from CH_3Cl / Hexane: mp 176-178 ^{o}C. Anal. Calcd. for $C_{29}H_{24}N_4NiO_3$ 0.125$CHCl_3$ C, 63.59; H, 4.42; N, 10.18; Found: C, 63.73; H, 4.25; N, 9.8; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 2.04 (bs, 1H, NH); 2.92-3.02 (m, 2H, CH_2); 3.72 (AB system 2H, CH_2, J_{AB} =13.5 Hz); 4.06 (m, 1H, CH); 6.42 (d, 1H, ArH, *J* = 7.4 Hz); 6.74 (m, 2H, ArH); 7.09 (m, 3H); 7.23-7.48 (m, 8H, ArH); 7.90 (m, 1H, ArH); 7.97 (m, 1H, ArH); 8.2 (d, 1H, ArH (CH-29), *J* = 5,2 Hz); 8.96 (d, 1H, ArH(CH-14), *J* = 8.7 Hz); ^{13}C NMR (400.13MHz, $CDCl_3$): δ 52.15 (CH_2); 52.86 (CH_2); 71.09 (CH); 121.29; 123.51; 124.05; 127.78; 126.86; 127.01; 127.99; 128.07; 128.18; 128.75; 129.00; 129.68; 133.29; 133.79 (C-18); 134.41; 140.08; 140.37; 143.25 (C-13); 147.00 (C-29); 153.49 (C-25); 169.95; 171.81; 178.84; IR, (ν/cm-1; KBr): 1668; 1644; 1606; 1591; 1587; 3321 (NH).

1.4.8. Synthesis of Ni(II) complex 5h of a Schiff base of PBP and (±)2-amino-3-(naphthalen-2-yloxy)-propionic acid. The reaction was conducted in 15ml CH_3CN starting from complex **1** (1.5g, 3.5mmol) 2-naphtol (0.6g, 4.2mmol) and NaH (0.07g, 1.75mmol). The reaction time was 2h at 80^{0}C. To the reaction mixture was added 10% aq. AcOH, then it was quenched by adding 200ml water. After 1h the precipitate was filtered and washed with water and dried at air After purification

by column chromatography ($CHCl_3$:MeCOMe = 5:1) the yield of pure product was 84 % (1.68g, 2.94mmol): mp 289-292 ^oC. Anal. Calcd. for $C_{32}H_{23}N_3NiO_4$: C, 67.17; H, 4.05; N, 7.34; Found: C, 66.91; H, 3.84; N, 7.19; ^1H NMR (300.13 MHz, $CDCl_3$): δ 3.40 (m, 1H, CH_2); 3.72 (m, 1H, CH_2); 4.02 (m, 1H, CH); 6.68 (d, 1H, *J* = 8.3 Hz); 6.84 (m, 2H, ArH); 7.04 and 7.29 (AB system, 2H, *Naph*-3, *Naph*-4, *J* = 8.8 Hz); 7.07-7.26 (m, 3H, ArH); 7.32-7.38 (m, 3H, ArH); 7.49-7.65 (m, 5H, ArH); 7.69 (d, 1H, ArH, *J* = 7.6 Hz); 8.07 (t, 1H, ArH, J = 7.3Hz); 8.75 (d, 1H, ArH, *J* = 8.52 Hz); 9.89 (s, 1H, OH); ^{13}C NMR (300.13MHz, DMSO-D_6): δ 28.80 (CH_2); 71.68 (CH); 113.76 (*Naph*-1); 117.44 (*Naph*-3); 121.02; 121.83; 123.00; 123.08; 123.40; 125.72; 127.31; 127.59; 127.91; 127.94; 128.04; 128.36; 128.56; 128.92; 129.07; 129.76; 132.45; 133.50; 133.84; 134.63; 140.82; 143.15; 145.43; 152.08 (C-25); 154.96 (*Naph*-2); 168.73; 170.64; 177.05; IR, (ν/cm^{-1}; KBr): 1680; 1624; 1603; 1592; 3325 (OH).

1.4.9. Synthesis of Ni(II) complex 5i of a Schiff base of PBP and (±)-2,4 diamino-pentanedioic acid 5i. To the suspension of **1** (4g, 9.37mmol) in CH_3CN (40ml) under Ar were added C_6H_5OH (1.04g, 11.05mmol) and NaH (0.372g, 9.3mmol). The reaction time was 2h at 80 ^0C. The course of the reaction was monitored by TLC ($CHCl_3$: CH_3COCH_3 = 5:1). In accordance to TLC besides the main product there were many byproducts in the reaction mixture. To the reaction mixture was added 10% aq.AcOH, then it was quenched by adding 700ml water. In 1h the precipitate was filtered washed with water and dried at air After purification by column chromatography ($CHCl_3$:MeCOMe = 5:1) the main product was washed with acetone, filtered by dense filter and dried giving 25% pure **5i** (1.0g, 1.18mmol). For analyses the product was crystallized from MeOH/$CHCl_3$: mp 298-300 ^oC (decomp). Anal. Calcd. for $C_{43}H_{30}N_6Ni_2O_6$ $0.33H_2O$: C, 60.75; H, 3.64; N, 9.89; Found: C, 60.48; H, 3.29; N, 9.62; ^1H NMR (300.13 MHz, $CDCl_3$): δ 2.01 (t, *J* = 4.4 Hz, 2H, CH_2); 4.15 (t, 2H, 2CH, *J* = 4.4 Hz,); 6.86 (t, 2H, ArH(CH-16), *J* = 7.5 Hz); 7.05 (dd, 2H, ArH(CH-17), *J* = 8.3 Hz, *J* = 1.4 Hz); 7.25 (m, 2H, ArH); 7.30-7.45 (m, 12H, ArH); 7.81 (t, 4H, ArH, *J* = 7.4 Hz); 8.2 (d, 2H, ArH(CH-29), *J* = 5,2 Hz); 8.91 (d, 2H, ArH(CH-14), *J* = 8.56 Hz); ^{13}C NMR (300.13MHz, $CDCl_3$): δ 35.25 (CH_2); 68.28 (CH); 122.07 (C-16); 123.28 (C-17); 123.84 (C-14); 126.02; 126.98 (C-15); 127.02 (C-11); 128.38; 128.86; 129.67; 130.19; 133.73; 134.49 (C-18); 135.44; 140.02 ; 142.76 (C-13); 147.46 (C-29); 152.55 (C-25); 170.09 (C-24); 177.47 (C-12); 179.61 (COO); IR, (ν/cm^{-1}; KBr):): 1668; 1644; 1606; 1591; 1587; 1327.

1.5. Methods of recovery and analytical data of chiral and achiral amino acids

1.5.1. (S)-2-Amino-pentanedioic acid (6a). The complex (*S*)-**5a** 1.08g (1.84mmol) was decomposed by refluxing its suspension in a mixture of aq. 6N HCl (5 ml) and MeOH (6 ml) for 2h, then the solution was evaporated to dryness. Water was added to the residue and the insoluble material was filtered off, washed with water and dried to afford hydrochloride of **PBP**. The pH of the aqueous layer was adjusted to 7 using aqueous ammonia solution and the mixture was extracted with $CHCl_3$ (3 x 10 ml) to remove small amounts of remaining **PBP**. The amino acid was recovered from the aq. solution by the ion-exchange technique (DOWEX-50, H^+ form). The amino acid was crystallized from EtOH/water with yielding 0.17g (1.156mmol, 63 %) **6a** (ee 92%).

1.5.2. 2-Amino-3-phenylsulfanyl-propionic acid (6d).[15] A mixture of **5d** (1.4g, 2.6mmol), 10ml MeOH and 6N HCl was refluxed 20 min, and then evaporated to dryness. Water (10ml) was added to the residue and the insoluble material filtered, washed with water and dried to afford ligand. To

the water solution conc. aqueous ammonia solution is added to bring the pH of the solution to 9-10, followed by ETDA (0.87g, 2.6mmol) and 10ml of benzene. The mixture was stirred for 1h and then the water layer was separated and concentrated. The precipitate was filtered and washed with aq ETDA solution and water and finally recrystallized from 1N HCl giving **6d** with 61% yield: mp 200^0C. Anal. Calcd. for . $C_9H_{11}NO_2S \cdot 0.05HCl$: C, 54.30; H, 5.59; N, 7.04; Found: C, 54.1; H, 5.57, N, 7.2.

1.5.3. 2-Amino-3-indol-1-yl-propionic acid (6e). The complex **5e** 1.5g, (2.8 mmol) was decomposed by refluxing its suspension in a mixture of aq. 6N HCl (10 ml) and MeOH (7 ml) for 40min, then the solution was evaporated to dryness. Water was added to the residue and the insoluble material was filtered off, washed with water and dried to afford hydrochloride **PBP**. The pH of the aqueous layer was adjusted to 7 using aqueous ammonia solution and the mixture was extracted with $CHCl_3$ (3 x 10 ml) to remove small amounts of remaining **PBP**. The amino acid was recovered from the aq. solution by ion-exchange technique (DOWEX-50, H^+ form). The amino acid was crystallized from EtOH/water yielding 0.3g (1.47mmol, 52%) **6e**: mp 218-220 ^{0}C. Anal. Calcd. for $C_{11}H_{12}N_2O_2$ 0.57HCl: C, 58,70; H, 5,63; N, 12,45; Found: C, 58.54; H, 5.32; N, 12.31. ^{1}H NMR: (400.13 MHz, DMSO-D_6): δ 3.62 (m, 1H, CH); 4.35 (m, 1H, CH_2); 4.62 (m, 1H, CH_2); 6.43 (d, 1H, *Ind*-3, *J* = 3.1 Hz); 7.02 (t, 1H, *Ind*, *J* = 7.2 Hz); 7.14 (t, 1H, *Ind*, *J* = 7.4 Hz); 7.37 (d, 1H, *Ind*-2, *J* = 3.0 Hz); 7.53 (m, 2H, *Ind*); ^{13}C NMR (400.13 MHz, DMSO-D_6): δ 48.53 (CH_2); 55.89 (CH); 102.31 (*Ind*-3); 111.07 (*Ind*-7); 120.32 (*Ind*-6); 121.53 (*Ind*-4); 122.33 (*Ind*-5); 129.57 (*Ind*-9); 130.40 (*Ind*-2); 137.23 (*Ind*-8); 169.20 (COO)

1.5.4. 2-Amino-3-(naphthalen-2-yloxy)-propionic acid (6h). To a solution of **5h** (1.68g, 2.94mmol) in 10ml of MeOH was added 6N HCl (10ml) with stirring at reflux for 40 minutes. Then the solvent was evaporated and water was added to the solution. The pH of the aqueous solution was adjusted to 8 by aqueous ammonia and the ligand was extracted with CH_2Cl_2. The insoluble amino acid was filtered off to give 0.4g **6h** (1.73mmol, 58%). The amino acid was crystallized from 3N HCl yielding 0.3g (1.47mmol, 52 %) **6h**: mp 249^0C (decomp). Anal. Calcd. for $C_{13}H_{14}ClNO_3.0.66H_2O$: C, 55.70; H, 5.53; N, 4.93;. Found: C, 55.41; H, 5.84; N, 5.01. ^{1}H NMR: (400.13 MHz, DMSO-D_6): δ 3.40 and 3.55 (AB part of ABX system, 2H, CH_2, J_{AB} = 14.0Hz); 3.85 (X part ABX of system, 1H, CH, J_{AX} = 6.2 Hz, J_{BX} = 8.6 Hz); 7.44 (AB system, 2H, *Naph*-3, *Naph*-4), *J* = 9.0 Hz); 7.29 (t, 1H, *Naph*-6, *J* = 7.2 Hz); 7.46 (t, 1H, *Naph*-7, *J* = 7.2 Hz); 7.79 (d, 1H, naph-5, *J* = 8.1 Hz); 7.98 (d, 1H, *Naph*-8, *J* = 8.4 Hz); ^{13}C NMR (400.13MHz, DMSO-D_6): δ 27.70 (CH_2); 59.97 (CH); 114.72 (*Naph*-1); 119.71 (N*aph*-3); 123.42 (*Naph*); 123.48 (*Naph*); 127.60 (*Naph*); 129.36 (*Naph*-10); 129.69(*Naph*); 129.74 (*Naph*); 134.44 (*Naph*-9); 155.14 (*Naph*-2); 171.85 (COO).

Supporting information is available

http://www.arkat-usa.org/ark/journal/2004/I03_Makosza/MM-853G/853Gsupportinginfo.pdf

Acknowledgments

The work was supported by Swiss grant SCOPES (Project № 7SUPJ62125) and also by Russian Foundation for Basic Research (Project № 02-03-32050). Authors thank Dr Ikonnikov N.S. for conducting GLC asymmetric analyses.

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