Alkylations of Chiral Nickel(II) Complexes of Glycine under Phase-Transfer Conditions

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Dedicated to Professor *Dieter Seebach* on the occasion of his 75th birthday

Alkylation reactions of nickel(II) complex **6** derived from glycine and 2-[(1-benzyl-L-prolyl)amino]benzophenone (BPBP) were studied under phase-transfer-catalysis (PTC) conditions. The goal of this work was to find an alternative suitable solvent for these reactions to replace the commonly used CH_2Cl_2 which leads to the formation of several by-products, thus lowering the yield of target compounds. We demonstrate that 1,2-dichloroethane is a markedly better solvent providing higher yields (75–99%) of the desired products **10** with 36–88% diastereoisomer purity (*Scheme 3* and *Table*). Furthermore, we show that the stereochemical outcome of these PTC reactions (kinetic control) can be easily improved to >95% de by treatment of the PTC products with MeONa/MeOH. The scope of these reactions includes alkylations with methyl iodide as well as activated halides such as benzyl, allyl or propargyl, bromides and most notably ethyl 2-bromoacetate (*Table*).

Introduction. – Among numerous methods for the asymmetric synthesis of α-amino acids [1], the most versatile strategy involves the diastereoselective homologation of nucleophilic chiral glycine equivalents. To realize this approach, many research groups have developed the corresponding reagents, which were derived from glycine and contain a chiral auxiliary, designed to protect one of the enolate faces from the incoming electrophile. Several such chiral nucleophilic glycine equivalents have shown remarkable synthetic applications and have been commercialized. Most notably, bis-lactim ethers **1** (*Fig.*) and 5,6-diphenylmorpholin-2-one **2** were introduced by the

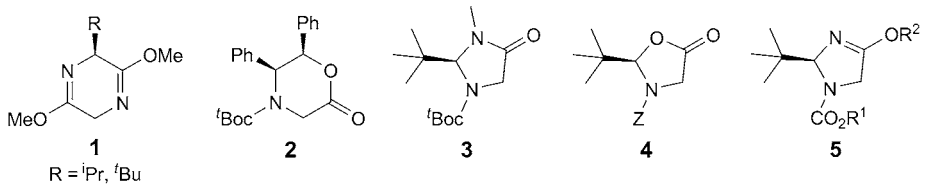

Figure. *Chiral nucleophilic glycine equivalents*

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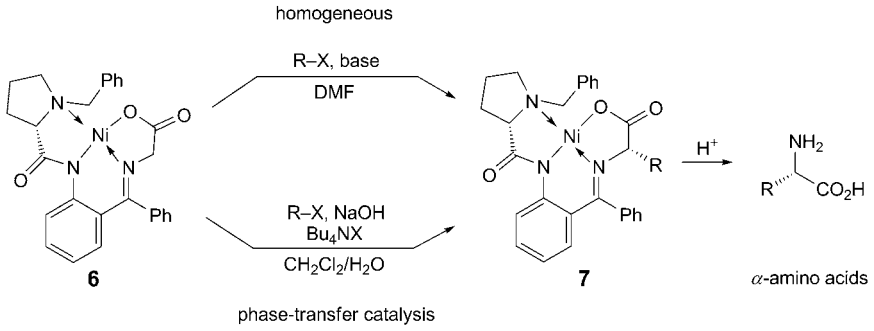
Schöllkopf [2] and *Williams* [3] group, respectively. The most commonly used chiral glycine equivalent reagents are the cyclic 'acetal' (=aminal) **3** [4], oxazolidinone **4** [5], and dihydro-1*H*-imidazole-1-carboxylate **5** [6], introduced by *Seebach* and co-workers. Reagents **3**–**5** can be easily prepared on large scale and are relatively inexpensive. The major advantage of **3**–**5** is that their homologation to the target amino acids proceeds with virtually complete diastereoselectivity. Furthermore, isolation of the desired amino acid can be conducted under mild acidic conditions, and the only by-product, pivalaldehyde, can be removed simply by solvent-evaporation workup.

In this context, the Ni^{II} complex **6**, introduced by *Belokon* and co-workers [7] (*Scheme 1*), derived from glycine and 2-[(1-benzyl-L-prolyl)amino]benzophenone (BPBP) cannot rival the synthetic efficiency of the reagents **1**–**5** in terms of the diastereoselectivity (for the high-scale preparation of **6**, see [7f][7g]). In most cases, the homologation of Ni^{II} complex **6** results in the formation of diastereoisomeric products with up to 90–95% de. However, in contrast to other methods, the homologation of chiral glycine equivalent **6** can be conducted at room temperature and in not specially dried solvents, allowing for a large-scale preparation of target amino acids [8]. We believe that this unique feature of reagent **6** has a great synthetic potential. Consequently, our group has a long-standing interest in the chemistry of reagent **6**, particularly in the development of its reactions with sterically constrained electrophiles [9] and the design of new generations of Ni^{II}-templated glycine equivalents [10]. The highly acidic methylene moiety in reagent **6** allows for its straightforward homologation *via* alkylation [11], *Michael* [12], *Mannich* [13], or aldol [14] reactions under operationally convenient conditions and in high chemical yields. Furthermore, we demonstrated that *Michael*-addition reactions of **6** [12][15] and its analogues [16] can be performed with virtually complete stereoselectivities, offering the method of choice for the preparation of *trans*-β-substituted (pyro)glutamic acids and prolines [17].

Scheme 1. *Strategies for the Homologation on Ni^{II} Complex* **6**

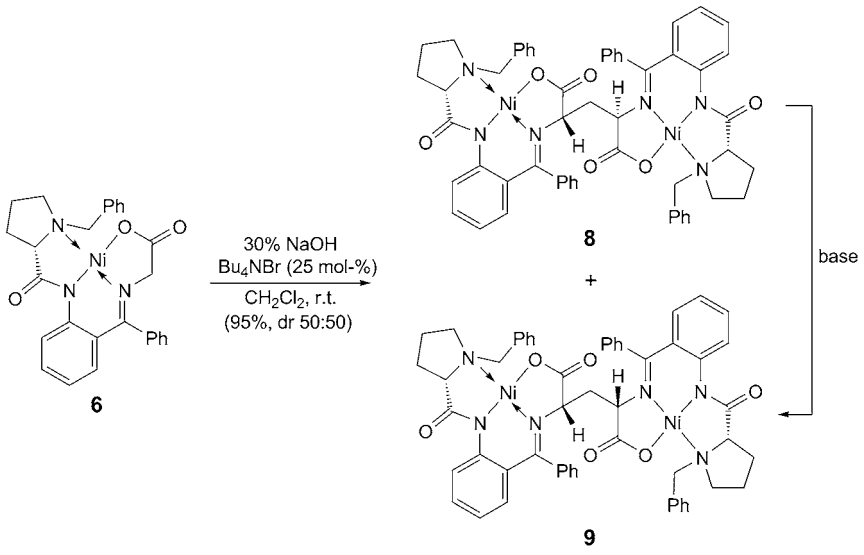


Alkylations of complex **6** are typically carried out under homogeneous conditions to achieve the best stereoselectivity in the corresponding homologated products **7** (de > 90%). However, the chemical yields of these transformations are often compromised because of double-alkylation side reactions [18]. In fact, the presence of an excess of alkylating reagent is a convenient way to access symmetrically α,α-

disubstituted α-amino acids starting from achiral analogues of **6** [19]. An additional drawback is the somewhat harsh conditions required which sometimes are not compatible with the alkylating reagents employed.

In contrast, heterogeneous phase-transfer catalysis (PTC) conditions are usually milder and never lead to double alkylation products. Nevertheless, limitations of PTC include its incompatibility with some electronically disadvantageous or sterically hindered electrophiles. More importantly, those reactions under PTC occur with lower kinetic diastereoselectivity. It should also be mentioned that quite low solubility of complex **6** in usual PTC solvents such as benzene or toluene limits the generality and the synthetic potential of these reactions. As a result, all examples reported so far dealing with phase-transfer alkylations of **6** employed CH_2Cl_2 as organic solvent [7d][20]. However, we previously demonstrated that CH_2Cl_2 is also a practical reagent for the 'methylene dimerization' of nickel complex **6** under PTC, producing diastereoisomeric 'dimers' **8** and **9** as an equimolecular mixture which subsequently equilibrated to the (*S*,*S*,*S*′,*S*′)-isomer **9** by treatment with base [21] (*Scheme 2*). Therefore, 'methylene dimerization' might compete with the PTC alkylations of **6** when CH_2Cl_2 is the solvent which may significantly decrease the yield of the desired alkylated products **7**.

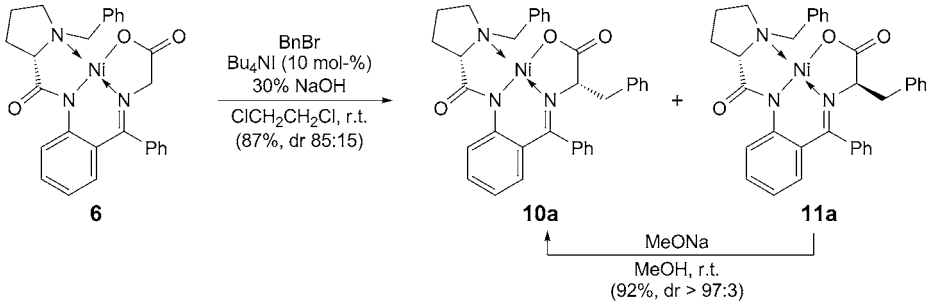
Scheme 2. '*Methylene Dimerization*' *of* **6**



Considering these literature results, one may agree that there is a room for improvement in the development of suitable PTC conditions for the alkylation of Ni^{II} complex **6** with a variety of alkyl halides. For this purpose, we first needed to find a different solvent to avoid the problems associated with the use of CH_2Cl_2. Our second challenge was to search for a convenient procedure to equilibrate the resulting mixture of diastereoisomers to the thermodynamically most stable one.

Results and Discussion. – We first experimented with several halogenated solvents (CCl_4, $CHCl_3$, $ClCH_2CH_2Cl$) and eventually found that 1,2-dichloroethane gave the best outcome in terms of solubility, with no trace of possible 'dimerization' products. For instance, benzylation of **6** in the presence of tetrabutylammonium iodide (Bu_4NI; 10 mol-%) in a 1:1 mixture of $ClCH_2CH_2Cl$ and 30% aqueous NaOH solution afforded diastereoisomeric phenylalanine-derived complexes **10a** and **11a** in a 85:15 ratio, in good overall yield (*Scheme 3*). After purification, the minor isomer **11a** could be epimerized to the most stable (*S*,*S*) isomer **10a** by treatment with MeONa.

Scheme 3. *Benzylation of* **6** *under PTC*

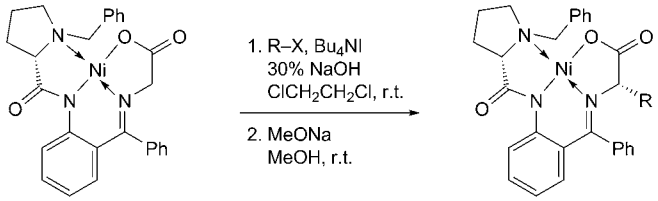


For practical purposes, we were able to carry out the two-step procedure without purification of the initial mixture of diastereoisomers **10a** and **11a**. In this manner, essentially the single isomer **10a** was obtained in excellent overall yield (*Table*, *Entry 1*). For comparison, the literature results showed that benzylation of **6** under PTC with CH_2Cl_2 as organic solvent afforded a 79:21 mixture of **10a**/**11a**, whereas under homogeneous conditions (NaOH, DMF), a 96:4 ratio was achieved [7d].

Next, alkylation of **6** with different alkyl halides by this two-step protocol was pursued. Reactions with substituted benzyl bromides (*Table*, *Entries 2–5*), allyl bromides (*Entries 6* and *7*) or propargyl bromide (*Entry 8*) proceeded in good overall yields and diastereoselectivities after MeONa-mediated equilibration. It is worth mentioning that most previously reported protocols based on homogeneous conditions afforded lower yields of alkylated compounds **10** compared to PTC. Ethyl bromoacetate was also successfully employed although the subsequent equilibration with MeONa produced a transesterification to result in product **10i** (*Entry 9*). It should be noted that this reaction can hardly be conducted under the homogeneous conditions.

On the other hand, PTC alkylations of **6** with nonactivated alkyl halides were less successful compared to the activated electrophiles. For instance, reaction with MeI needed the addition of 5.0 equiv. to work well in terms of yield but produced alanine-derived complex **10j** as the major product of a 90:10 mixture of diastereoisomers after equilibration, most likely due to the small size of the Me substituent (*Table*, *Entries 10* and *11*). In the case of BuI, a moderate yield of the corresponding alkylated product **10k** was obtained (*Entry 12*), and the reaction did not proceed with sterically demanding alkyl iodides (*Entry 13*).

Table. *Alkylation of Complex* **6** *under PTC*



6 **10**

Entry	R	X	Product	de [%] after step 1[a])	de [%] after step 2[a])	Yield [%][b])
1	Bn	Br	**10a**	70	>95	93
2	4-F–$C_6H_4CH_2$	Br	**10b**	68	>95	77
3	3,5-F_2–$C_6H_3CH_2$	Br	**10c**	80	>95	87
4	4-CF_3–$C_6H_4CH_2$	Br	**10d**	82	>95	85
5	4-NO_2–$C_6H_4CH_2$	Br	**10e**	78	>95	96
6	Allyl CH_2=$CHCH_2$	Br	**10f**	80	>95	87
7	(*E*)-PhCH=$CHCH_2$	Br	**10g**	56	>95	97
8	CH≡CCH_2	Br	**10h**	88	>95	75
9	MeO_2CCH_2[c])	Br	**10i**	76	>95	84
10	Me	I	**10j**	38	–	70[d])
11[e])	Me	I	**10j**	36	80	99
12[e])	Bu	I	**10k**	n.d.	–	55[d])
13[e])	i-Pr	I	**10l**	–	–	0

[a]) Measured by integration in the ^{1}H-NMR spectra. [b]) Yield of isolated product. [c]) Methyl ester after transesterification; step 1 with R–X = EtO_2CCH_2Br. [d]) Conversion estimated by NMR. [e]) 5.0 equiv. of alkyl halide were employed.

Conclusions. – We found that despite the fact that 1,2-dichloroethane is an alkyl halide itself, it can be used as efficient solvent for PTC alkylation reactions of the chiral Ni^{II} complex **6** of glycine with various activated alkyl halides. The reactions result in medium-level diastereoselectivity which can be improved to >95% de of the thermodynamically more stable diastereoisomer after a treatment of the resulting products with MeONa/MeOH.

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Experimental Part

General. All reagents and solvents were used as received. The reactions were monitored by TLC. TLC: precoated silica gel (SiO_2) plates: visualization by UV light. Flash column chromatography (FC): silica gel (SiO_2; 0.040–0.063 mm). Optical rotations: *Jasco-P-2000* polarimeter. ^{1}H-, ^{13}C-, and ^{19}F-NMR Spectra: *Bruker Advance 300*; at 300, 75, and 376.4 MHz, resp.; δ in ppm rel. to Me_4Si (referenced to the resonances of the solvents), *J* in Hz. HR-MS: ESI-ion trap mass spectrometer *Agilent Synapt G2* and a TOF (time-of-flight) detector; in *m*/*z*.

Phase-Transfer-Catalyzed Alkylations of **6**: *General Procedure.* To a soln. of Ni^{II} complex **6** (1 equiv.) in $ClCH_2CH_2Cl$ (0.25M), 30% aq. NaOH soln. (40 equiv.) was added followed by Bu_4NI (10 mol-%) and the corresponding alkyl halide (1.5 equiv.). After stirring at r.t. for 2 h, the mixture was diluted with H_2O

and extracted with CH_2Cl_2 and the org. phase dried (Na_2SO_4) and concentrated. The resulting product was dissolved in MeOH (0.1M), and MeONa (1.5 equiv.) was added. Sat. aq. NH_4Cl soln. was added after stirring at r.t. for 1.5 h. The mixture was extracted with CH_2Cl_2, the org. phase dried (Na_2SO_4) and concentrated, and the residue purified by CC (SiO_2, CH_2Cl_2/acetone 5:1): **10**.

*{*N*-{Phenyl{2-{{[(1*R*,2*S*)-1-(phenylmethyl)pyrrolidin-2-yl-κ*N*]carbonyl}amino-κ*N*}phenyl}methylene}-*L*-phenylalaninato(2−)-κ*N*,κ*O*}nickel* (='(*S*)-Phenylalanine-Ni-(*S*)-BPBP'; **10a**): From **6** (76 mg, 0.153 mmol) and BnBr (27 µl, 0.229 mmol): 84 mg (93%) of **10a**. Spectral features: matching those previously described [7d].

{4-Fluoro-N*-{phenyl{2-{{[(1*R*,2*S*)-1-(phenylmethyl)pyrrolidin-2-yl-κ*N*]carbonyl}amino-κ*N*}phenyl}methylene}-*L*-phenylalaninato(2−)-κ*N*,κ*O*}nickel* (='(*S*)-(4-Fluorobenzyl)glycine-Ni-(*S*)-BPBP'; **10b**): From **6** (114 mg; 0.229 mmol) and 4-fluorobenzyl bromide (43 µl, 0.343 mmol): 107 mg (77%) of **10b**. Spectral features: matching those previously described [18].

{3,5-Difluoro-N*-{phenyl{2-{{[(1*R*,2*S*)-1-(phenylmethyl)pyrrolidin-2-yl-κ*N*]carbonyl}amino-κ*N*}phenyl}methylene}-*L*-phenylalaninato(2−)-κ*N*,κ*O*}nickel* (='(*S*)-(3,5-Difluorobenzyl)glycine-Ni-(*S*)-BPBP'; **10c**): From **6** (105 mg, 0.211 mmol) and 3,5-difluorobenzyl bromide (41 µl, (0.316 mmol): 115 mg (87%) of **10c**. $[\alpha]_D^{25} = +1679.7$ ($c = 0.039$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.86–2.10 (*m*, 2 H); 2.40–2.56 (*m*, 2 H); 2.65–2.84 (*m*, 1 H); 2.93 (*dd*, *J* = 13.6, 6.3, 1 H); 3.03 (*dd*, *J* = 13.7, 4.0, 1 H); 3.27 (*dd*, *J* = 7.7, 7.1, 1 H); 3.39 (*dd*, *J* = 9.5, 7.3, 1 H); 3.54 (*d*, *J* = 12.6, 1 H); 4.26 (*t*, *J* = 5.1, 1 H); 4.35 (*d*, *J* = 12.6, 1 H); 6.64 (*d*, *J* = 6.1, 2 H); 6.70 (*d*, *J* = 3.9, 2 H); 6.82 (*t*, *J* = 8.8, 1 H); 6.96 (*d*, *J* = 7.3, 1 H); 7.15–7.23 (*m*, 2 H); 7.29–7.38 (*m*, 3 H); 7.46–7.65 (*m*, 3 H); 8.05 (*d*, *J* = 7.3, 2 H); 8.27 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 23.2; 30.6; 39.7; 57.1; 63.2; 70.3; 70.7; 102.8 (*t*, ^2J(C,F) = 25.1); 113.0 (*dd*, ^2J(C,F) = 24.4, ^4J(C,F) = 7.6); 120.6; 123.5; 125.9; 127.1; 127.6; 128.8; 129.0; 129.2; 129.9; 131.4; 132.6; 133.1; 133.4; 133.9; 139.5 (*t*, ^3J(C,F) = 9.2); 142.8; 163.0 (*dd*, ^1J(C,F) = 249.4, ^3J(C,F) = 12.7); 171.4; 171.9; 180.3. ^{19}F-NMR (376.4 MHz, $CDCl_3$): −109.3 (*s*, 2 F). HR-ESI-MS (TOF): 624.1617 ($[M+H]^+$, $C_{34}H_{30}F_2N_3NiO_3^+$; calc. 624.1609).

*{*N*-{Phenyl{2-{{[(1*R*,2*S*)-1-(phenylmethyl)pyrrolidin-2-yl-κ*N*]carbonyl}amino-κ*N*}phenyl}methylene}-4-(trifluoromethyl)-*L*-phenylalaninato(2−)-κ*N*,κ*O*}nickel* (='(*S*)-((4-Trifluoromethyl)benzyl)glycine-Ni-(*S*)-BPBP'; **10d**): From **6** (107 mg, 0.215 mmol) and 4-(trifluoromethyl)benzyl bromide (77 mg, 0.322 mmol): 120 mg (85%) of **10d**. $[\alpha]_D^{25} = +1407.5$ ($c = 0.077$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.82–1.98 (*m*, 2 H); 2.20–2.40 (*m*, 3 H); 2.90 (*dd*, *J* = 13.7, 5.8, 1 H); 3.05–3.15 (*m*, 2 H); 3.33 (*dd*, *J* = 10.1, 6.7, 1 H); 3.49 (*d*, *J* = 12.6, 1 H); 4.30 (*d*, *J* = 12.7, 1 H); 4.34 (*dd*, *J* = 5.7, 4.4, 1 H); 6.86 (*d*, *J* = 4.3, 2 H); 6.95 (*d*, *J* = 7.6, 1 H); 7.14–7.22 (*m*, 2 H); 7.29–7.37 (*m*, 5 H); 7.40–7.54 (*m*, 1 H); 7.55–7.65 (*m*, 2 H); 7.67 (*d*, *J* = 8.1, 2 H); 8.03 (*d*, *J* = 7.0, 2 H); 8.27 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 22.9; 30.6; 39.2; 57.0; 63.3; 70.2; 70.9; 120.6; 122.4; 124.2 (*q*, ^1J(C,F) = 271.4); 125.7 (*q*, ^3J(C,F) = 3.4); 125.9; 127.1; 127.7; 128.8; 129.0; 129.2; 129.8 (*q*, ^2J(C,F) = 32.3); 129.9; 130.8; 131.4; 132.6; 133.2; 133.5; 134.1; 140.0; 142.9; 171.5; 178.1; 180.3. ^{19}F-NMR (376.4 MHz, $CDCl_3$): −62.4 (*s*, 3 F). HR-ESI-MS (TOF): 656.1669 ($[M+H]^+$, $C_{35}H_{31}F_3N_3NiO_3^+$; calc. 656.1671).

{4-Nitro-N*-{phenyl{2-{{[(1*R*,2*S*)-1-(phenylmethyl)pyrrolidin-2-yl-κ*N*]carbonyl}amino-κ*N*}phenyl}methylene}-*L*-phenylalaninato(2−)-κ*N*,κ*O*}nickel* (='(*S*)-(4-Nitrobenzyl)glycine-Ni-(*S*)-BPBP'; **10e**): From **6** (102 mg; 0.205 mmol) and 4-nitrobenzyl bromide (66 mg, 0.307 mmol): 124 mg (96%) of **10e**. $[\alpha]_D^{25} = +1474.8$ ($c = 0.044$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.76–1.90 (*m*, 1 H); 1.94–2.05 (*m*, 1 H); 2.32–2.42 (*m*, 2 H); 2.44–2.60 (*m*, 1 H); 3.04–3.23 (*m*, 3 H); 3.38 (*dd*, *J* = 9.0, 7.6, 1 H); 3.50 (*d*, *J* = 12.6, 1 H); 4.30 (*t*, *J* = 5.3, 1 H); 4.32 (*d*, *J* = 12.6, 1 H); 6.70–6.73 (*m*, 2 H); 6.98 (*d*, *J* = 7.5, 1 H); 7.16–7.27 (*m*, 4 H); 7.29–7.38 (*m*, 3 H); 7.49–7.55 (*m*, 1 H); 7.59–7.64 (*m*, 2 H); 8.05 (*d*, *J* = 7.1, 2 H); 8.24 (*d*, *J* = 8.6, 1 H); 8.24 (*d*, *J* = 8.6, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 23.2; 30.6; 39.9; 57.2; 63.4; 70.1; 70.8; 120.7; 123.5; 123.7; 125.8; 127.2; 127.5; 128.8; 128.8; 129.0; 129.3; 130.0; 131.1; 131.4; 132.7; 133.1; 133.5; 133.9; 142.8; 143.5; 147.5; 171.6; 177.8; 180.3. HR-ESI-MS (TOF): 633.1661 ($[M+H]^+$, $C_{34}H_{31}N_4NiO_5^+$; calc. 633.1648).

*{(2*S*)-2-{{Phenyl{2-{{[(1*R*,2*S*)-1-(phenylmethyl)pyrrolidin-2-yl-κ*N*]carbonyl}amino-κ*N*}phenyl}methylene}amino-κ*N*}pent-4-enoato(2−)-κ*O*}nickel* (='(*S*)-Allylglycine-Ni-(*S*)-BPBP'; **10f**): From **6** (107 mg, 0.215 mmol) and allyl bromide (28 µl, 0.322 mmol): 101 mg (87%) of **10f**. Spectral features: matching those previously described [22].

{(2S,4E)-5-Phenyl-2-{{phenyl{2-{{[(1R,2S)-1-(phenylmethyl)pyrrolidin-2-yl-κN]carbonyl}amino-κN}phenyl}methylene}amino-κN}pent-4-enoato(2−)-κO}nickel (= '(*S*)-*trans*-Cinnamylglycine-Ni-(*S*)-BPBP'; **10g**): From **6** (85 mg, 0.172 mmol) and *trans*-cinnamyl bromide (38 µl, 0.257 mmol): 103 mg (97%) of **10g**. Spectral features: matching those previously described [8a].

{(2S)-2-{Phenyl-2-{{[(1R,2S)-1-(phenylmethyl)pyrrolidin-2-yl-κN]carbonyl}amino-κN}phenyl}methylene}amino-κN}pent-4-ynoato(2−)-κO}nickel (= '(*S*)-Propargylglycine-Ni-(*S*)-BPBP'; **10h**). From **6** (105 mg, 0.212 mmol) and propargyl bromide (35 µl, 80% (wt.), 0.318 mmol): 85 mg (75%) of **10h**. Spectral features: matching those previously described [23].

{4-Methyl N-*{Phenyl{2-{{[(1R,2S)-1-(phenylmethyl)pyrrolidin-2-yl-κN]carbonyl}amino-κN}phenyl}methylene}*-L-*aspartato(2−)-κN,κO}nickel* (= 'Methyl (*S*)-aspartate-Ni-(*S*)-BPBP'; **10i**): From **6** (105 mg, 0.211 mmol) and ethyl bromoacetate (35 µl, 0.316 mmol): 101 mg (84%) of **10i**. $[\alpha]_D^{25} = +1381.5$ ($c = 0.048$, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.05–2.20 (*m*, 2 H); 2.46–2.56 (*m*, 1 H); 2.52 (*dd*, *J* = 16.1, 7.3, 1 H); 2.76 (*dd*, *J* = 16.1, 3.0, 1 H); 2.86–3.00 (*m*, 1 H); 3.48 (*dd*, *J* = 10.3, 6.6, 1 H); 3.60–3.72 (*m*, 2 H); 3.64 (*d*, *J* = 12.7, 1 H); 3.76 (*s*, 3 H); 4.22 (*dd*, *J* = 7.0, 3.0, 1 H); 4.44 (*d*, *J* = 12.7, 1 H); 6.64–6.71 (*m*, 2 H); 6.97 (*d*, *J* = 7.2, 1 H); 7.14–7.20 (*m*, 1 H); 7.22 (*t*, *J* = 7.5, 1 H); 7.28–7.32 (*m*, 1 H); 7.31 (*t*, *J* = 7.6, 2 H); 7.48–7.60 (*m*, 3 H); 8.10 (*d*, *J* = 7.3, 2 H); 8.23 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 23.0; 30.6; 37.8; 51.9; 57.2; 63.3; 66.4; 70.5; 120.4; 123.5; 126.1; 126.6; 127.5; 128.6; 128.9; 129.8; 131.4; 132.2; 133.2; 133.3; 133.8; 142.7; 169.5; 171.6; 178.7; 180.5. HR-ESI-MS (TOF): 570.1551 ($[M+H]^+$, $C_{30}H_{30}N_3NiO_5^+$; calc. 570.1539).

*{*N-*{Phenyl-{2-{{[(1R,2S)-1-(phenylmethyl)pyrrolidin-2-yl-κN]carbonyl}amino-κN}phenyl}methylene}*-L-*alaninato(2−)-κN,κO}nickel* (= '(*S*)-Alanine-Ni-(*S*)-BPBP; **10j**): From **6** (97 mg, 0.195 mmol) and MeI (61 µl, 0.974 mmol): 95 mg of **10j** and and 5 mg of its (D)-diastereoisomer; total yield 99%. Spectral features; matching those previously described [7d].

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