Catalytic asymmetric Michael addition of α,β-unsaturated aldehydes to Ni(II) complexes of the Schiff base of glycine†

Xiaoyan Luo, Zhichao Jin, Pengfei Li, Jiabin Gao, Weimin Yue, Xinmiao Liang and Jinxing Ye*

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The conjugate addition of Ni(II) complexes of glycine Schiff base to α,β-unsaturated aldehydes catalyzed by (*S*)-2-(diphenyl(trimethylsilyloxy)methyl)pyrrolidine afforded adducts in excellent yields with up to 49 : 1 dr and 95% ee. This method enables the construction of two adjacent chiral centers in one step, and offers an alternative route to chiral α-amino acid derivatives.

Introduction

α-Amino acids and their derivatives are important compounds,[1,2] and their synthesis has attracted a great deal of attention. Although countless approaches for the preparation of α-amino acids and their derivatives have been developed,[3] most have serious drawbacks from the standpoint of practicality.[4] As one of the most promising approaches, glycine derivatives and their equivalents have received considerable attention, and many impressive results have been achieved.[5–7] Among these nucleophilic glycine equivalents, nickel(II) complexes of the Schiff base of glycine have been successfully used for the synthesis of structurally varied tailor-made α-amino acids.[5d,6j] However, these reports focused on the reactions of nickel(II) complexes of chiral glycine Schiff base and achiral reagents. To the best of our knowledge, there is no report on the catalytic asymmetric Michael addition of nickel(II) complexes of achiral glycine Schiff base to α,β-unsaturated aldehydes, which would be an alternative methodology for the preparation of α-amino acids or their derivatives. A chiral catalyst, an *N*-acyl derivative of iso-NOBIN, has been used to catalyze the reaction of nickel(II) complexes of achiral glycine Schiff base and propenal, but this reaction proceeded in 50% yield and with 0% ee.[6g]

Recently, our group has successfully applied a Lewis base–Brønsted base two-component catalytic system in the asymmetric Michael addition of nitroalkanes[8] and malonates[9] to various α,β-unsaturated aldehydes.[10,11] We here describe the first organocatalytic asymmetric Michael addition of achiral nickel(II)-complexed glycine derivatives to α,β-unsaturated aldehydes, affording adducts with good to excellent yields and asymmetric inductions.

Results and discussion

We started our investigation with the asymmetric conjugate addition between cinnamaldehyde (**6a**) and achiral nickel(II)-complexed glycine derivative **5a** under various conditions. Representative results are shown in Table 1.

The screening of organocatalysts was initially carried out in a CH_2Cl_2/MeOH mixed solvent system. The conjugate addition of **5a** and **6a** catalyzed by L-proline (**1a**) gave poor results (entry 1). When lithium (*S*)-pyrrolidine-2-carboxylate (**1b**) was used as the catalyst, the conversion improved to more than 99% (entry 2). However, the enantioselectivities still remained poor, the Michael addition with the catalyst **2** affording no more than 40% ee (entry 3). A remarkable enhancement was achieved when **3** was used as catalyst. Using lithium benzoate as an additive base and **3a** as the catalyst, the conjugate addition proceeded with up to 86% asymmetric induction (entry 4). In the presence of **3b**, excellent conversion and enantioselectivities were obtained, although the diastereoselectivity remained low (entry 5). When LiOAc was introduced into the catalytic system, more than 99% conversion and 91% ee (94% ee for the minor isomer) was obtained, and the diastereoselectivity was also improved slightly from 1.6 : 1 dr to 1.9 : 1 dr (entry 6).

As a result of these investigations, different additives were screened (entries 7–9). Using **4** as an additive clearly did not change the diastereo- or enantioselectivities, showing that the chirality of the *N*-protected amino acid did not have an effect on the stereoselectivity of the reaction (entry 7). However, it was found that the reaction catalyzed by **3b** and lithium benzoate gave better results – more than 99% conversion, 1.9 : 1 dr and 90% (98%) ee (entry 8). This prompted us to use these catalytic conditions in subsequent experiments. As the choice of solvent could be very important, we then optimized the reaction conditions with this in mind. Reaction in methanol afforded high conversion and diastereoselectivity with low enantioselectivities, in contrast to that obtained in CH_2Cl_2 (entries 10 and 11). The results in other solvents, such as $CHCl_3$, EtOAc, THF and MeCN, were similar to those in CH_2Cl_2 (entries 12–15).

After full screening of solvents and additives, we found that the best results (>99% conversion and 2.8 : 1 dr with 95% (96%) ee) were obtained using the MeOH/CH_2Cl_2 mixed solvent system (entry 17). Additionally, it should be noted that 1,4-adducts with >99% asymmetric induction were formed smoothly in the mixed solvent when lithium 4-methoxybenzoate or lithium 4-nitrobenzoate were employed as additives (entries 18 and 19). These encouraging results indicated that this two-component catalytic system could also be applied successfully in the asymmetric

Engineering Research Center of Pharmaceutical Process Chemistry, Ministry of Education, School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai, 200237, China. E-mail: yejx@ecust.edu.cn

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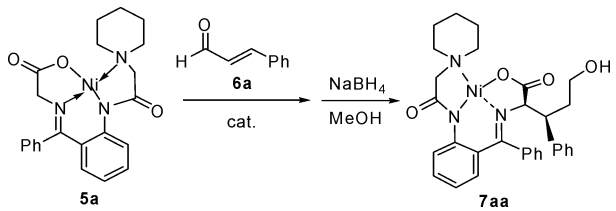
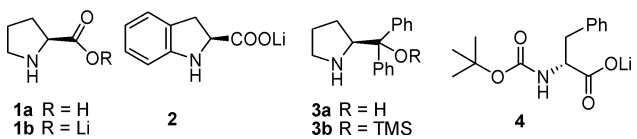
Table 1 Catalyst and solvent screening for the conjugate addition[a]



Entry	Cat.	Additive	Solvent	Conv. (%)	dr [b]	ee[c] (%)
1	**1a**	None	CH_2Cl_2/MeOH = 7/5	49	3.0 : 1	nd (16)
2	**1b**	None	CH_2Cl_2/MeOH = 7/5	>99	7.3 : 1	18 (9)
3	**2**	None	CH_2Cl_2/MeOH = 7/5	78	2.1 : 1	32 (−32)
4	**3a**	$PhCO_2Li$	CH_2Cl_2/MeOH = 7/5	48	1.3 : 1	70 (86)
5	**3b**	None	CH_2Cl_2/MeOH = 7/5	95	1.6 : 1	82 (93)
6	**3b**	LiOAc	CH_2Cl_2/MeOH = 7/5	>99	1.9 : 1	91 (94)
7	**3b**	**4**	CH_2Cl_2/MeOH = 7/5	99	1.6 : 1	87 (95)
8	**3b**	$PhCO_2Li$	CH_2Cl_2/MeOH = 7/5	>99	1.9 : 1	90 (98)
9	**3b**	$PhCO_2H$	CH_2Cl_2/MeOH = 7/5	63	1.5 : 1	92 (89)
10	**3b**	$PhCO_2Li$	MeOH	>99	8.1 : 1	86 (49)
11	**3b**	$PhCO_2Li$	CH_2Cl_2	36	2.2 : 1	87 (91)
12	**3b**	$PhCO_2Li$	$CHCl_3$	14	2.4 : 1	86 (85)
13	**3b**	$PhCO_2Li$	EtOAc	33	2.1 : 1	91 (88)
14	**3b**	$PhCO_2Li$	THF	11	1.9 : 1	86 (93)
15	**3b**	$PhCO_2Li$	MeCN	76	2.0 : 1	92 (84)
16	**3b**	$PhCO_2Li$	EtOAc/MeOH = 7/5	70	1.6 : 1	89 (91)
17	**3b**	$PhCO_2Li$	DCM/MeOH = 1/5	>99	2.8 : 1	95 (96)
18	**3b**	4-$MeOC_6H_4CO_2Li$	DCM/MeOH = 1/5	>99	2.1 : 1	93 (>99)
19	**3b**	4-$NO_2C_6H_4CO_2Li$	DCM/MeOH = 1/5	>99	2.0 : 1	95 (>99)

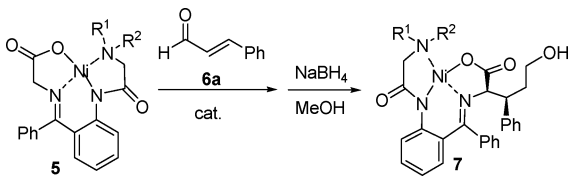
[a] Unless otherwise noted, all reactions were performed with 0.5 mmol of **5a**, 0.6 mmol of **6a**, 0.05 mmol of catalyst and 0.1 mmol of additive in 1.2 mL solvent at room temperature for 24 h. nd = not determined. [b] Determined by HPLC. [c] Determined by HPLC on chiral stationary phase (the data in parenthesis relates to the minor isomer).

Michael addition of achiral nickel(II) complexes of glycine Schiff bases to α,β-unsaturated aldehydes.



Under the optimized conditions, the asymmetric Michael additions between a series of achiral nickel(II) complexes of glycine Schiff bases and cinnamaldehyde were studied, and the results are presented in Table 2. As Soloshonok[5d] stated, different substituents (R^1, R^2) on the nitrogen atom lead to a different performance of compound **5** in the reaction system – a result that is truly remarkable, and underscores the synthetic power of this type of nucleophilic glycine equivalent. The piperidine-substituted achiral nickel(II) complex **5a** reacted with enal **6a** quite successfully to afford 1,4-adducts in 98% isolated yield and 2.8 : 1 dr with 95% ee for major adduct and 95% ee for minor adduct (entry 1). The dimethyl-substituted **5b** also afforded 1,4-adducts in 92% isolated yield and 1.6 : 1 dr with 81% (99%) ee (entry 2). Even using the more sterically hindered diisopropyl-substituted **5c**, the adducts were formed in 83% yield with up to 96% (97%) ee, although with low diastereoselectivity (1.3 : 1 dr, entry 3). The more lipophilic **5d** and **5e** were found to react slowly, with lower isolated yields and diastereoselectivities, but the enantioselectivities from **5d** were still up to 89% (99%) (entries 4–5). Although all the diastereoselectivities of the conjugate additions are not ideal, the diastereoisomers could be separated easily by silica gel chromatography.

Table 2 Asymmetric Michael addition of **5** to **6a**[a]

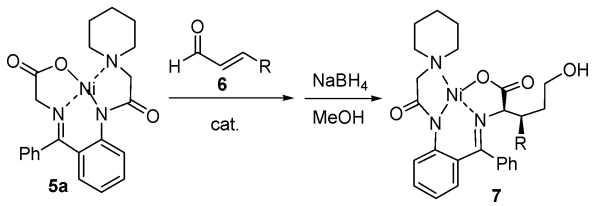


Entry	5	R^1	R^2	Yield[b] (%)	dr[c]	ee[d] (%)
1	**5a**	$-C_5H_{10}-$		**7aa**, 98	2.8 : 1	95 (95)
2	**5b**	Me	Me	**7ba**, 92	1.6 : 1	81 (99)
3	**5c**	*i*-Pr	*i*-Pr	**7ca**, 83	1.3 : 1	96 (97)
4	**5d**	Me	Bn	**7da**, 44	1.3 : 1	89 (99)
5	**5e**	Bn	Bn	**7ea**, 25[e]	1.6 : 1	75 (78)

[a] Reaction conditions: A mixture of **5** (0.5 mmol), **6a** (0.6 mmol), and **3b** (10 mol%) and $PhCO_2Li$ (20 mol%) in CH_2Cl_2 (0.2 mL)/MeOH (1.0 mL) was stirred at room temperature for 24 h. [b] Isolated yield (the data relates to the combined isolated yield of the diastereomers). [c] Determined by ^1H NMR of the crude product. [d] Determined by chiral HPLC (the data in parenthesis relates to the minor isomer). [e] Conversion.

To further extend the scope of this type of Michael addition, a series of α,β-unsaturated aldehydes **6b–n** were reacted with **5a**, and the results are displayed in Table 3. It turned out that the electronic nature of the substituent group and its position on the aromatic

Table 3 Asymmetric Michael addition of **5a** to enal **6**[a]



Entry	R	*t* (h)	Yield[b] (%)	dr[c]	ee[d] (%)
1	2-ClC_6H_4, **6b**	72	**7ab**, 52	1.9 : 1	95 (92)
2	4-ClC_6H_4, **6c**	48	**7ac**, 88	2.3 : 1	91 (99)
3	4-FC_6H_4, **6d**	72	**7ad**, 59	1.5 : 1	92 (96)
4	4-BrC_6H_4, **6e**	48	**7ae**, 94	2.2 : 1	89 (89)
5	2-MeC_6H_4, **6f**	24	**7af**, 99	10 : 1	91 (91)
6	3-MeC_6H_4, **6g**	48	**7ag**, 93	2.4 : 1	92 (95)
7	4-MeC_6H_4, **6h**	24	**7ah**, 94	5.7 : 1	89 (82)
8	2-$MeOC_6H_4$, **6i**	24	**7ai**, 96[e]	49 : 1	91 (nd)
9	3-$MeOC_6H_4$, **6j**	24	**7aj**, 99	2.6 : 1	90 (>99)
10	4-$MeOC_6H_4$, **6k**	24	**7ak**, 85[e]	6.7 : 1	90 (nd)
11	Naphthalen-2-yl, **6l**	24	**7al**, 98	3.8 : 1	87 (71)
12	2,3-$(MeO)_2C_6H_3$, **6m**	24	**7am**, 93[e]	19 : 1	95 (nd)
13	2,4-$(MeO)_2C_6H_3$, **6n**	24	**7an**, 95[e]	24 : 1	88 (nd)

[a] Reaction conditions: A mixture of **5a** (0.5 mmol), **6** (0.6 mmol), and **3b** (10 mol%) and $PhCO_2Li$ (20 mol%) in CH_2Cl_2 (0.2 mL)/MeOH (1.0 mL) was stirred at room temperature for the time given. [b] Isolated yield (the data relates to the combined isolated yield of the diastereomers). [c] Determined by ^1H NMR of crude product. [d] Determined by HPLC on chiral stationary phase (the data in parenthesis relates to the minor isomer). [e] The yield of major product (2*R*,3*S*).

ring had a clear influence on the yield and diastereoselectivity, while the enantioselectivities were less affected. For example, using 2-chlorocinnamaldehyde **6b**, 52% yield and 1.9 : 1 dr with 95% (92%) ee were obtained (entry 1). 4-Chlorocinnamaldehyde **6c** afforded 88% yield and 2.3 : 1 dr with up to 91% (99%) ee (entry 2). When 4-fluorocinnamaldehyde **6d** was used, lower yield and diastereoselectivity were obtained. However, the enantioselectivities were still up to 92% (96%) (entry 3). It was found that 4-bromocinnamaldehyde **6e** reacted very well, giving 94% yield and 2.2 : 1 dr with ee values for both isomers near 90% (entry 4). In addition to weakly electron-withdrawing substituents, electron-donating substituents could also be introduced onto the aromatic ring (entries 5–13). In the presence of electron-donating substituents on the aromatic ring, all the α,β-unsaturated aldehydes gave excellent yields with good to excellent enantioselectivities (88–95%). The reaction of 2-methylcinnamaldehyde **6f** proceeded with 10 : 1 dr and 91% ee for both isomers (entry 5). The moderate to good diastereoselectivities (2.4 : 1, 5.7 : 1 dr) with 82–95% of enantioselectivities were also obtained from 3-methylcinnamaldehyde **6g** and 4-methylcinnamaldehyde **6h** respectively (entries 6 and 7). It should be noted that 96% isolated yield with up to 49 : 1 dr and 91% ee for major adduct were obtained from 2-methoxycinnamaldehyde **6i** (entry 8), while >99% (90%) ee was obtained when 3-methoxycinnamaldehyde **6j** was used (entry 9). The major adduct was smoothly formed in 85% yield with 6.7 : 1 dr and 90% ee from 4-methoxycinnamaldehyde **6k** and **5a** (entry 10). The large 3-(naphthalen-2-yl)acrylaldehyde **6l** was also tested, and gave the Michael adduct in 98% yield and 3.8 : 1 dr with 87% (71%) ee (entry 11). The dimethoxy-substituted enals **6m** and **6n** were found to react with the nucleophile quite successfully, and afford the 1,4-adducts in 93% and 95% yield and high diastereoselectivity, with 95% and 88% ee, respectively (entries 12 and 13).

The reactions of 3-chlorocinnamaldehyde and 3-fluorocinnamaldehyde with **5a** under the same conditions proceeded slowly, giving less than 20% conversion of **5a**. Unexpectedly, the reactions of **5a** with aliphatic enals, such as *trans*-2-pentanal and *trans*-2-hexenal, did not take place under the same conditions, no desired products being found in the reaction mixtures by NMR analysis. This may be attributable to the formation of the dienamine, which decreased the electrophilicity of the β-carbon of the enal.[12]

The absolute configurations of the two adjacent stereocenters in the major adduct **7ai** were unambiguously determined to be (2*R*,3*S*) by X-ray crystallographic analysis (Fig. 1).

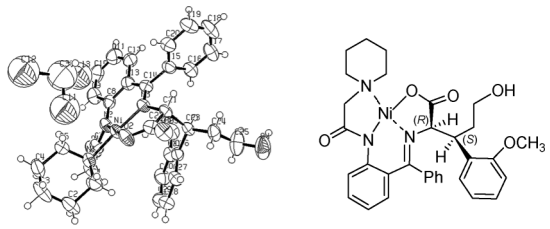
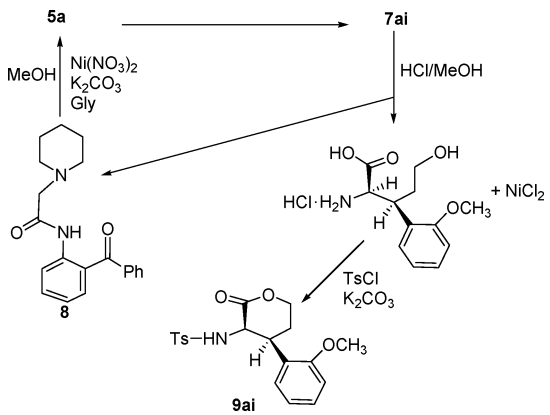


Fig. 1 X-ray crystal structure of **7ai**.

The compound **7ai** was easily hydrolyzed by hydrochloride in methanol. Notably, the compound **8** could be easily recovered quantitatively and reused to give **5a** (Scheme 1), and the corresponding amino acid could be further treated with TsCl to give compound **9ai**.



Scheme 1

Conclusions

In conclusion, we have extended the Lewis base–Brønsted base two-component catalytic system to the asymmetric Michael addition between α,β-unsaturated aldehydes and achiral nickel(II) complexes of the Schiff base of glycine. Using this method, we can construct two adjacent stereocenters in one step with excellent yield and asymmetric induction, offering a new approach for the preparation of chiral α-amino acid derivatives.

Experimental

General methods

All solvents and inorganic reagents were from commercial sources and used without purification unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz) or a Bruker AM 500 spectrometer (500 MHz and 125 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to the residual solvent peak ($CDCl_3$: 7.26 ppm). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the residual solvent peak ($CDCl_3$: 77.16 ppm). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). High-resolution mass spectrometry (ESI) was carried out using an ACQUITYTM Ultra Performance Liquid Chromatography system (Waters, Milford, MA) coupled with a Q-TOF premier instrument (Waters MS Technologies, Manchester, UK). High-resolution mass spectra (EI) were measured on a Waters Micromass GCT spectrometer. High-performance liquid chromatography (HPLC) was performed on an Agilent 1200 Series chromatograph using a Chiralpak IA-H or IC-H and Regis (*R*,*R*)-Whelk O1 column (0.46 cm × 25 cm) as noted. X-ray analysis of **7ai**-major was performed at the X-ray crystallography facility of Bruker–Nonius SMART APEX II CCD. Optical rotations were measured on an Autopol III automatic polarimeter.

General Procedure for asymmetric Michael addition and reduction

(*S*)-2-(Diphenyl(trimethylsilyloxy)methyl)pyrrolidine (16.2 mg, 0.05 mmol), lithium benzoate (12.8 mg, 0.1 mmol) and enal (0.6 mmol) were added to a solution of the Ni(II) complex of glycine Schiff base (0.5 mmol) in CH_2Cl_2/MeOH = 1/5 (v/v, 1.2 mL). The reaction mixture was stirred at room temperature for the time indicated in the tables and then MeOH (1.5 mL) and $NaBH_4$ (37.8 mg, 1 mmol) were added. The reaction mixture was stirred at room temperature for 2.5 h. The solvent was removed under vacuum, and the residue purified by silica gel chromatography to afford the product as a red solid. Yields of the products are given in the tables.

7aa-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 8.8 Hz, 1H), 7.66–7.53 (m, 6H), 7.51–7.49 (m, 2H), 7.34–7.28 (m, 2H), 7.15–7.14 (m, 1H), 6.80–6.75 (m, 2H), 4.42 (d, *J* = 4.0 Hz, 1H), 3.28 (m, 2H), 3.27 (d, *J* = 16.4 Hz, 1H), 3.03 (d, *J* = 16.4 Hz, 1H), 2.95–2.90 (m, 1H), 2.88–2.82 (m, 2H), 2.39–2.31 (m, 1H), 2.21–2.12 (m, 1H), 1.97–1.86 (m, 2H), 1.67–1.58 (m, 1H), 1.51–1.41 (m, 2H), 1.33–1.26 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 175.3, 170.5, 142.8, 140.1, 133.8, 133.7, 132.7, 130.5, 130.0, 129.3, 129.0, 128.9, 128.0, 127.9, 127.4, 126.8, 123.5, 121.1, 73.5, 60.4, 60.2, 55.4, 54.6, 47.4, 33.8, 22.7, 19.7, 19.4. HRMS (EI) calculated for $C_{31}H_{33}N_3O_4Ni$ $[M]^+$: 569.1825, Found: 569.1826. mp >178 °C (decomp.). $[\alpha]_D^{22}$ −1446 (*c* 0.175 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, hexane/EtOH = 6 : 1, 0.8 mL/min]: 25.496 min (major), 34.427 min (minor), ee = 95%.

7aa-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 8.8 Hz, 1H), 7.51–7.45 (m, 2H),7.42–7.36 (m, 4H), 7.29–7.22 (m, 4H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 4.0 Hz, 2H), 4.27 (d, *J* = 2.8 Hz, 1H), 3.66–3.63 (m, 1H), 3.45 (s, 2H), 3.28–3.17 (m, 2H), 3.00 (d, *J* = 13.2 Hz, 1H), 2.61–2.52 (m, 1H), 2.42 (m, 1H), 2.39 (d, *J* = 13.2 Hz, 1H), 2.30 (brs, 1H), 2.05–1.94 (m, 2H), 1.70–1.23 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 175.7, 171.5, 143.1, 139.3, 134.3, 133.6, 132.9, 130.0, 129.9, 129.8, 129.0, 128.7, 128.6, 128.0, 127.6, 127.0, 123.0, 120.9, 75.1, 60.6,59.9, 55.9, 54.3, 47.8, 35.0, 22.8, 19.8, 19.2. HRMS (EI) calculated for $C_{31}H_{33}N_3O_4Ni$ $[M]^+$: 569.1825, Found: 569.1837. mp >130 °C (decomp.). $[\alpha]_D^{22}$ +1418 (*c* 0.205 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, hexane/^{i}PrOH = 5 : 1, 0.8 mL/min]: 30.850 min (major), 39.428 min (minor), ee = 95%.

7ba-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (d, *J* = 8.5 Hz, 1H), 7.65–7.50 (m, 8H), 7.31–7.28 (m, 2H), 7.14 (d, *J* = 7.0 Hz, 1H), 6.80–6.76 (m, 2H), 4.39 (d, *J* = 4.0 Hz, 1H), 3.21 (m, 1H), 3.20 (d, *J* = 15.5 Hz, 1H), 2.90–2.83 (m, 2H), 2.61 (d, *J* = 16.0 Hz, 1H), 2.44 (s, 3H), 2.26 (brs, 1H), 2.15–2.08 (m, 1H), 1.93–1.87 (m, 1H), 1.60 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 174.8, 170.6, 142.8, 140.1, 133.8, 133.7, 132.8, 130.5, 130.1, 129.3, 129.0, 128.9, 128.1, 128.0, 127.4, 126.7, 123.4, 121.2, 73.6, 67.1, 60.3, 49.7, 47.5, 47.3, 33.8. HRMS (ESI) calculated for $C_{28}H_{30}N_3O_4Ni$ $[M + H]^+$: 530.1590, found: 530.1567. mp >265 °C (decomp.). $[\alpha]_D^{22}$ −1383 (*c* 0.240 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 92.5 : 7.5, 0.4 mL/min]: 7.423 min (major), 8.112 min (minor), ee = 81%.

7ba-minor. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (d, *J* = 8.5 Hz, 1H), 7.50–7.39 (m, 6H), 7.29–7.27 (m, 2H), 7.22 (d, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 6.78–6.73 (m, 2H), 4.29 (d, *J* = 3.0 Hz, 1H), 3.62 (d, *J* = 16.0 Hz, 1H), 3.59–3.57 (m, 1H), 3.17–3.12 (m, 2H), 2.74 (d, *J* = 16.0 Hz, 1H), 2.65 (brs, 1H), 2.46 (s, 3H), 2.25–2.18 (m, 1H), 1.97–1.90 (m, 1H), 1.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.1, 177.8, 171.7, 143.1, 139.3, 134.5, 133.6, 133.1, 130.2, 130.1, 129.9, 129.1, 128.8, 128.7, 128.1, 127.8, 126.9, 122.9, 121.0, 75.1, 67.6, 59.9, 49.5, 47.9, 47.8, 35.2. HRMS (ESI) calculated for $C_{28}H_{30}N_3O_4Ni$ $[M + H]^+$: 530.1590, Found: 530.1576. mp >259 °C (decomp.). $[\alpha]_D^{22}$ +1790 (*c* 0.245 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 92.5 : 7.5, 0.4 mL/min]: 8.556 min (major), 7.782 min (minor), ee>99%.

7ca-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (d, *J* = 8.5 Hz, 1H), 7.63–7.52 (m, 3H), 7.47–7.44 (m, 2H), 7.42–7.39 (m, 2H), 7.30–7.28 (m, 3H), 7.22 (d, *J* = 7.5 Hz, 1H), 6.83–6.81 (m, 1H), 6.77–6.74 (m, 1H), 4.41 (d, *J* = 3.5 Hz, 1H), 3.35 (d, *J* = 17.5 Hz, 1H), 3.19–3.14 (m, 1H), 2.95–2.91 (m, 1H), 2.72 (m, 2H), 2.68 (d, *J* = 17.5 Hz, 1H), 2.45–2.40 (m, 1H), 2.05 (brs, 1H), 1.91–1.87 (m, 2H), 1.63 (d, *J* = 6.0 Hz, 3H), 1.60 (d, *J* = 6.5 Hz, 3H), 1.17 (d, *J* = 6.5 Hz, 3H), 0.83 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.9, 177.8, 171.8, 142.9, 138.8, 134.6, 133.8, 132.9, 129.9, 129.4, 129.1, 128.9, 128.8, 128.0, 127.3, 126.3, 123.0, 120.8, 72.8, 60.3, 59.4, 55.4, 53.0, 46.6, 34.4, 22.1, 21.9, 20.7, 14.6. HRMS (ESI) calculated for $C_{32}H_{38}N_3O_4Ni$ $[M + H]^+$: 586.2216, Found: 586.2199. mp >260 °C (decomp.). $[\alpha]_D^{22}$ −1936 (*c* 0.110 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 99.5 : 0.5, 0.65 mL/min]: 7.762 min (major), 10.949 min (minor), ee = 96%.

7ca-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 8.4 Hz, 1H), 7.36–7.34 (m, 2H), 7.27–7.21 (m, 1H), 7.15–7.11 (m, 2H), 7.08–7.04 (m, 3H), 6.85 (d, *J* = 7.2 Hz,2H), 6.68–6.64 (m, 1H), 6.54 (d, *J* = 8.0 Hz,1H), 5.77 (d, *J* = 7.2 Hz, 1H), 4.49–4.43 (m,1H), 4.08 (d, *J* = 8.0 Hz, 1H), 3.98 (d, *J* = 17.6 Hz, 1H), 3.59–3.54 (m,1H), 3.34–3.28 (m,1H), 3.26–3.19 (m, 1H), 2.87 (d, *J* = 17.2 Hz, 1H), 2.61 (d, *J* = 6.0 Hz, 3H), 2.59–2.56 (m, 1H), 2.54–2.49 (m, 1H), 2.12–2.03 (m, 1H), 1.89 (brs, 1H), 1.78 (d, *J* = 6.4 Hz, 3H), 1.64 (d, *J* = 6.4 Hz, 3H), 1.08 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6, 177.3, 170.9, 142.7, 138.4, 134.2, 133.4, 132.9, 129.2, 129.0, 128.7, 128.5, 128.4, 127.5, 127.1, 126.6, 122.5, 120.7, 75.3, 60.5, 59.9, 56.2, 52.6, 48.8, 34.1, 23.6, 22.8, 20.4, 14.4. HRMS (ESI) calculated for $C_{32}H_{38}N_3O_4Ni$ [M + H]$^+$: 586.2216, Found: 586.2210. mp >215 °C (decomp.). $[\alpha]_D^{22}$ +1560 (*c* 0.135 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [01 column, 240 nm, DCM/EtOH = 94 : 6, 0.8 mL/min]: 6.627 min (major), 5.102 min (minor), ee = 97%.

7da-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.5 Hz, 1H), 7.66–7.53 (m, 8H), 7.50 (d, *J* = 7.0 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.31–7.28 (m, 2H), 7.25–7.21 (m, 2H), 7.12 (d, *J* = 7.0 Hz, 1H), 6.78–6.74 (m, 2H), 4.43 (d, *J* = 4.0 Hz, 1H), 3.88 (d, *J* = 13.0 Hz, 1H), 3.64 (d, *J* = 13.0 Hz, 1H), 3.25–3.22 (m, 1H),3.08 (d, *J* = 16.0 Hz, 1H), 2.91 (d, *J* = 16.0 Hz, 1H), 2.87–2.82 (m, 2H), 2.21 (brs, 1H), 2.18–2.11 (m, 1H), 1.92–1.88 (m, 1H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 174.9, 170.4, 142.7, 140.1, 133.8, 133.6, 132.6, 131.8, 130.6, 130.5, 130. 1, 129.3, 129.1, 129.0, 128.9, 128. 7, 128.0, 128. 1, 127.5, 126.7, 123.5, 121.0, 73.5, 64.8, 63.4, 60.5, 47.3, 45.4, 33.9. HRMS (ESI) calculated for $C_{34}H_{34}N_3O_4Ni$ [M + H]$^+$: 606.1903, Found: 606.1882. mp >170 °C (decomp.). $[\alpha]_D^{22}$ −1444 (*c* 0.240 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, hexane/DCM/EtOH = 31 : 62 : 7, 0.7 mL/min]: 5.016 min (major), 6.400 min (minor), ee = 89%.

7da-minor. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (d, *J* = 9.0 Hz, 1H), 7.74 (d, *J* = 7.0 Hz, 2H), 7.52–7.47 (m, 2H), 7.45–7.39 (m, 4H), 7.30–7.28 (m, 5H), 7.21–7.16 (m, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 4.0 Hz, 2H), 4.31 (d, *J* = 3.5 Hz, 1H), 3.96 (d, *J* = 13.0 Hz, 1H), 3.71–3.67 (m, 1H), 3.54 (d, *J* = 13.0 Hz, 1H), 3.48 (d, *J* = 16.5 Hz, 1H), 3.23 (m, 1H), 3.15 (m, 1H), 3.08 (d, *J* = 16.5 Hz, 1H), 2.19–2.13 (m, 1H), 2.04 (brs, 1H), 1.97–1.92 (m, 1H), 1.88 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8, 175.2, 171.5, 142.9, 139.4, 134.2, 133.6, 132.8, 131.7, 131.0, 130.2, 130.0, 129.9, 129.0, 128.9, 128.8, 128.7, 128.1, 127.7, 126.8, 122.8, 120.8, 75.0, 64.9, 63.9, 59.8, 47.9, 46.3, 35.2. HRMS (ESI) calculated for $C_{34}H_{34}N_3O_4Ni$ [M + H]$^+$: 606.1903,Found: 606.1887. mp >129 °C (decomp.). $[\alpha]_D^{22}$ +1709 (*c* 0.135 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [O1 column, 240 nm, DCM/EtOH = 97 : 3, 0.8 mL/min]: 12.976 min (major), 9.669 min (minor), ee = 99%.

7ea-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, *J* = 7.5 Hz, 2H), 7.76–7.73 (m, 2H), 7.70–7.67 (m, 2H), 7.64–7.51 (m, 5H), 7.41–7.37 (m, 4H), 7.24–7.21 (m, 2H), 7.19–7.18 (m, 2H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.04–7.00 (m, 2H), 6.66–6.63 (m, 2H), 4.45 (d, *J* = 4.0 Hz, 1H), 3.76 (d, *J* = 12.5 Hz, 1H), 3.58 (d, *J* = 16.0 Hz, 1H), 3.44 (d, *J* = 14.0 Hz, 1H), 3.24–3.19 (m, 1H), 3.14 (d, *J* = 14.0 Hz, 1H), 2.97 (d, *J* = 12.5 Hz, 1H), 2.90–2.86 (m, 2H), 2.59 (d, *J* = 16.0 Hz, 1H), 2.19–2.12 (m, 1H), 1.95–1.89 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 175.6, 170.3, 142.2, 140.3, 134.3, 133.8, 133.1, 132.1, 131.8, 131.3, 130.8, 130.3, 130.0, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.1, 128.0, 127.6, 126.4, 123.6, 120.7, 73.4, 62.8, 62.6, 62.6, 60.4, 47.2, 33.9. HRMS (ESI) calculated for $C_{40}H_{38}N_3O_4Ni$ [M + H]$^+$: 682.2216, Found: 682.2217. mp >274 °C (decomp.). $[\alpha]_D^{22}$ −862 (*c* 0.170 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [O1 column, 240 nm, hexane/DCM/EtOH = 60 : 30 : 10, 0.8 mL/min]: 12.514 min (major), 17.158 min (minor), ee = 75%.

7ea-minor. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (d, *J* = 7.0 Hz, 2H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.54–7.45 (m, 5H), 7.39–7.33 (m, 7H), 7.28 (d, *J* = 7.0 Hz, 2H), 7.19–7.16 (m, 2H), 7.00–6.94 (m, 2H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.64–6.60 (m, 2H), 4.32 (d, *J* = 4.0 Hz, 1H), 3.95 (d, *J* = 16.5 Hz, 1H), 3.89 (d, *J* = 12.5 Hz, 1H), 3.82–3.78 (m, 1H), 3.63 (d, *J* = 13.5 Hz, 1H), 3.58 (d, *J* = 13.5 Hz, 1H), 3.23–3.19 (m, 1H), 3.14–3.09 (m, 1H), 2.97 (d, *J* = 12.5 Hz, 1H), 2.74 (d, *J* = 16.5 Hz, 1H), 2.17–2.12 (m, 1H), 1.94–1.88 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8, 176.0, 171.5, 142.5, 139.6, 134.3, 133.8, 133.7, 132.4, 131.8, 131.2, 130.5, 130.0, 129.9, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.0, 127.8, 126.5, 122.8, 120.5, 75.0, 63.2, 63.2, 62.7, 59.8, 47.9, 35.5. HRMS (ESI) calculated for $C_{40}H_{38}N_3O_4Ni$ [M + H]$^+$: 682.2216, Found: 682.2185. mp >255 °C (decomp.). $[\alpha]_D^{22}$ +438 (*c* 0.165 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [O1 column, 240 nm, hexane/DCM/EtOH = 60 : 30 : 10, 0.8 mL/min]: 16.190 min (major), 10.708 min (minor), ee = 78%.

7ab-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, *J* = 9.0 Hz, 1H), 7.80–7.78 (m, 1H),7.69 (m, 1H), 7.58–7.52 (m, 5H), 7.36–7.29 (m, 3H), 6.77–6.74 (m, 2H), 4.37 (d, *J* = 3.0 Hz, 1H), 3.62 (m, 1H), 3.32 (d, *J* = 16.0 Hz, 1H), 3.28–3.23 (m, 1H), 3.20–3.16 (m, 1H), 3.09 (d, *J* = 15.5 Hz, 1H), 2.91 (d, *J* = 9.5 Hz, 2H), 2.37–2.31 (m, 1H), 2.10–2.03 (m, 1H), 1.91–1.86 (m, 2H), 1.48–1.25 (m,6H). ^{13}C NMR(100 MHz, $CDCl_3$): δ 177.3, 174.9, 171.5, 143.0, 138.4, 137.0, 133.8, 133.7, 132.8, 131.1, 130.1, 130.0, 129.2, 128.8, 127.8, 127.6, 127.0, 123.3, 120.9, 73.9, 60.5, 60.2, 55.6, 54.8, 42.1, 34.8, 22.8, 19.8, 19.5. HRMS (ESI) calculated for $C_{31}H_{33}N_3O_4ClNi$ [M + H]$^+$: 604.1513, Found: 604.1509. mp >270 °C (decomp.). $[\alpha]_D^{22}$ −1295 (*c* 0.210 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.9 mL/min]: 11.523 min (major), 21.614 min (minor), ee = 95%.

7ab-minor. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (d, *J* = 8.5 Hz, 1H), 7.40–7.33 (m, 4H), 7.18–7.06 (m, 5H), 6.72–6.60 (m, 2H), 6.40–6.30 (m, 1H), 5.07–4.98 (m, 1H), 4.29 (d, *J* = 1.5 Hz, 1H), 3.66 (dd, *J* = 15.5, 53.0 Hz, 2H), 3.50–3.46 (m, 1H), 3.37–3.33 (m, 2H), 3.12 (d, *J* = 12.0 Hz, 1H), 3.00 (d, *J* = 13.0 Hz, 1H), 2.92–2.87 (m, 1H), 2.68 (brs, 1H), 1.75–1.38 (m, 8H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 175.7, 170.7, 142.9, 137.1, 135.3, 134.2, 133.2, 132.8, 129.7, 129.2, 128.7, 128.6, 128.3, 127.9, 127.2, 127.0, 123.2, 121.0, 74.5, 60.9, 60.0, 56.5, 54.2, 35.7, 29.2, 22.9, 20.0, 19.3. HRMS (ESI) calculated for $C_{31}H_{33}N_3O_4ClNi$ [M + H]$^+$: 604.1513, Found: 604.1511. mp >154 °C (decomp.). $[\alpha]_D^{22}$ +1260 (*c* 0.230 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.9 mL/min]: 19.506 min (major), 16.329 min (minor), ee = 92%.

7ca-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.4 Hz, 1H), 7.60–7.51 (m, 5H), 7.44–7.42 (m, 2H), 7.31–7.26 (m, 2H), 7.16–7.10 (m, 1H), 6.78–6.76 (m, 2H),4.32 (d, *J* = 4.0 Hz, 1H), 3.38

(d, J = 16.0 Hz, 1H), 3.27–3.21 (m, 1H), 3.19–3.16 (m, 1H), 3.08 (d, J = 16.4 Hz, 1H), 2.99–2.95 (m, 1H), 2.90–2.88 (m, 1H), 2.87–2.82 (m, 1H), 2.37–2.28 (m, 1H), 2.13 (brs, 1H), 2.10–2.01 (m, 1H),1.94–1.83 (m, 2H), 1.65–1.23 (m, 6H). ^{13}C NMR(100 MHz, $CDCl_3$): δ 177.1,175.5, 170.8, 142.8, 138.5, 134.0, 133.8, 133.7, 132.9, 131.8, 130.1, 129.4, 129.1, 128.9,128.0, 127.4, 126.7, 123.5, 121.2, 73.4, 60.1, 60.0, 55.6, 54.6, 46.8, 33.6, 22.7, 19.7, 19.3.HRMS (EI) calculated for $C_{31}H_{32}N_3O_4ClNi$ $[M]^+$: 603.1435, Found: 603.1436. mp >268 °C (decomp.). $[\alpha]_D^{22}$ −2101 (*c* 0.275 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM, 0.5 mL/min]: 12.132 min (major), 15.678 min (minor), ee = 91%.

7ca-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 8.8 Hz, 1H), 7.54–7.41 (m, 3H), 7.33–7.29 (m, 3H), 7.24 (d, J = 7.6 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 7.6 Hz, 1H), 6.79–6.73 (m, 2H), 4.24 (d, J = 4.0 Hz, 1H), 3.58 (s, 2H), 3.51–3.46 (m, 1H), 3.38–3.26 (m, 2H), 3.12 (d, J = 13.2 Hz, 1H), 2.98–2.90 (m, 1H), 2.76–2.69 (m, 1H), 2.63–2.58 (m, 1H), 2.17–2.06 (m, 1H), 1.77–1.59 (m, 4H), 1.50–1.41 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 175.9, 171.6, 143.0, 137.4, 134.2, 133.7, 133.4, 133.0, 130.9, 130.0, 129.4, 129.1, 128.8, 128.6, 127.9, 127.0, 123.2, 121.1, 74.9, 60.6, 60.0, 56.4, 54.4, 46.9, 34.1, 22.8, 19.9, 19.3. HRMS (EI) calculated for $C_{31}H_{32}N_3O_4ClNi$ $[M]^+$:603.1435, Found: 603.1437. mp >260 °C (decomp.). $[\alpha]_D^{22}$ +1421(*c* 0.200 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 9.491 min (major), 7.124 min (minor), ee = 99%.

7ad-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.5 Hz, 1H), 7.63–7.54 (m, 3H),7.49–7.46 (m, 2H), 7.35–7.29 (m, 4H), 7.12 (d, J = 7.0 Hz, 1H), 6.78 (d, J = 4.0 Hz, 2H), 4.39 (d, J = 3.5 Hz, 1H), 3.37 (d, J = 16.5 Hz, 1H), 3.30 (d, J = 12.5 Hz, 1H), 3.26–3.22 (m, 1H), 3.08 (d, J = 16.0 Hz, 1H), 2.98 (d, J = 13.0 Hz, 1H), 2.90–2.84 (m, 2H), 2.43–2.37 (m, 1H), 2.14–2.07 (m, 1H), 1.99 (m, 1H), 1.90–1.84 (m, 1H), 1.76 (brs, 1H), 1.67–1.62 (m, 2H), 1.53–1.34 (m,4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 175.3, 170.7, 142.9, 135.8, 135.7, 133.8, 133.7,132.9, 131.9, 131.8, 130.1, 129.4, 129.0, 128.0, 127.5, 126.7, 123.5, 121.1, 115.7, 115.5, 73.4, 60.4, 60.3, 55.8, 54.7, 46.7, 34.0, 22.8, 19.8, 19.4. HRMS (ESI) calculated for $C_{31}H_{33}N_3O_4FNi$ $[M + H]^+$: 588.1809, Found: 588.1795. mp >262 °C (decomp.). $[\alpha]_D^{22}$ −1684 (*c* 0.280 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.9 mL/min]: 11.936 min (major), 19.113 min (minor), ee = 92%.

7ad-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 8.8 Hz, 1H), 7.54–7.44 (m, 3H),7.33–7.29 (m, 1H), 7.23 (d, J = 7.6 Hz, 1H), 7.00 (d, J = 6.8 Hz, 4H), 6.85 (d, J = 7.2 Hz, 1H), 6.79–6.73 (m, 2H), 4.22 (d, J = 3.6 Hz, 1H), 3.59 (s, 2H), 3.52–3.46 (m, 1H), 3.39–3.27 (m, 2H), 3.14–3.05 (m, 2H), 2.81–2.65 (m, 2H), 2.16–2.10 (m, 1H), 1.96 (brs, 1H), 1.75–1.68 (m, 1H), 1.62–1.53 (m, 2H), 1.50–1.29 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 175.9, 171.5,142.9, 134.7, 134.2, 133.6, 132.9, 131.0, 130.9, 130.0, 129.3, 129.1, 128.8, 127.8, 127.0, 123.2, 121.1, 115.4, 115.2, 74.9, 60.7, 59.9, 56.5, 54.4, 46.7, 34.3, 22.8, 19.9, 19.3. HRMS (ESI) calculated for $C_{31}H_{33}N_3O_4FNi$ $[M + H]^+$: 588.1809, Found: 588.1791. mp >271 °C (decomp.). $[\alpha]_D^{22}$ +1309 (*c* 0.250 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 98 : 2, 0.5 mL/min]: 13.147 min (major), 9.448 min (minor), ee = 96%.

7ae-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.0 Hz,2H), 7.57–7.49 (m, 3H), 7.36 (d, J = 8.0 Hz, 2H), 7.24–7.22 (m, 2H), 7.09 (d, J = 6.8 Hz, 1H), 6.76–6.71 (m, 2H), 4.26 (d, J = 3.6 Hz, 1H), 3.36 (d, J = 16.4 Hz, 1H), 3.24–3.18 (m, 1H), 3.14 (m, 1H), 3.08 (d, J = 16.4 Hz, 1H),2.96 (d, J = 13.2 Hz, 1H), 2.87 (m, 1H), 2.84–2.79 (m, 1H), 2.33–2.26 (m, 2H), 2.05–1.96 (m, 1H), 1.92–1.89 (m, 1H), 1.88–1.82 (m, 1H), 1.64–1.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 175.5, 170.8, 142.8, 139.0, 133.7, 133.6, 132.8, 132.2, 131.8, 130.1, 129.3, 129.1, 127.9, 127.3, 126.6, 123.5, 122.0, 121.1, 73.5, 60.0, 59.9, 55.6, 54.5, 46.9, 33.6, 22.7, 19.6, 19.3. HRMS (EI) calculated for $C_{31}H_{32}N_3O_4NiBr$ $[M]^+$: 649.0909, Found: 649.0908. mp >260 °C (decomp.). $[\alpha]_D^{22}$ −950 (*c* 0.205 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 99.5 : 0.5, 0.8 mL/min]: 8.095 min (major), 9.249 min (minor), ee = 89%.

7ae-minor. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.60 (d, J = 8.5 Hz, 1H), 7.54–7.46 (m, 5H),7.32–7.30 (m, 1H), 7.24 (d, J = 7.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 7.0 Hz, 1H), 6.79–6.76 (m, 2H), 4.24 (d, J = 2.5 Hz, 1H), 3.58 (s, 2H), 3.46 (m, 1H), 3.34 (d, J = 12.5 Hz,1H), 3.30 (m, 1H), 3.12 (d, J = 12.5 Hz, 1H), 2.87–2.89 (m, 1H), 2.70 (t, J = 12.5 Hz, 1H), 2.57 (d, J = 12.5 Hz, 1H), 2.09 (brs, 1H), 1.70 (m, 2H), 1.61–1.31 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 175.9, 171.7, 143.0, 138.0, 134.3, 133.7, 133.0, 131.6, 131.3, 130.0,129.4, 129.1, 128.8, 127.9, 126.9, 123.2, 121.6, 121.1, 74.8, 60.6, 59.9, 56.4, 54.4, 46.9, 34.2, 22.8, 19.9, 19.3. HRMS (EI) calculated for $C_{31}H_{32}N_3O_4NiBr$ $[M]^+$: 649.0909, Found: 649.0905. mp >249 °C (decomp.). $[\alpha]_D^{22}$ +937 (*c* 0.205 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 95 : 5, 0.8 mL/min]: 6.007 min (major), 5.196 min (minor), ee = 89%.

7af-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, J = 8.4 Hz, 1H), 7.58–7.55 (m, 5H),7.47–7.40 (m, 2H), 7.31–7.28 (m, 2H), 7.15 (d, J = 6.8 Hz, 1H), 6.79–6.75 (m, 2H), 4.31 (d, J = 2.4 Hz, 1H), 3.26 (d, J = 16.0 Hz, 2H), 3.20 (d, J = 13.6 Hz, 1H), 3.12 (d, J = 16.0 Hz, 2H), 2.94–2.92 (m, 1H), 2.85 (d, J = 13.2 Hz, 1H), 2.29 (brs, 1H), 2.24 (s, 3H), 1.95 (m, 2H), 1.89 (m, 2H), 1.64–1.29 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 175.2, 170.6, 142.8, 139.1, 138.6, 133.7, 133.5, 132.8, 130.1, 129.3, 129.2, 127.6, 127.4, 127.1, 126.8, 123.4, 121.0, 75.0, 60.4, 60.0, 55.4, 54.7, 42.1, 35.6, 22.7, 20.5, 19.7, 19.5. HRMS (ESI) calculated for $C_{32}H_{36}N_3O_4Ni$ $[M + H]^+$: 584.2059, Found: 584.2031. mp >280 °C (decomp.). $[\alpha]_D^{22}$ −2178 (*c* 0.245 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.8 mL/min]: 14.010 min (major), 27.034 min (minor), ee = 91%.

7af-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 8.8 Hz, 1H), 7.47–7.45 (m, 2H),7.30–7.28 (m, 5H), 7.24–7.19 (m, 2H), 6.89–6.61 (m, 3H), 4.48 (m, 1H), 4.34 (d, J = 4.4 Hz, 1H), 3.42 (dd, J = 16.0, 28.0 Hz, 2H), 3.26–3.20 (m, 2H), 3.08–3.00 (m, 2H), 2.62–2.54 (m, 1H), 2.49 (s, 3H), 2.40–2.36 (m, 1H), 1.82–1.56 (m, 5H), 1.42–1.32 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 175.6, 171.0, 143.1, 138.9, 138.0, 134.4, 133.5, 132.9, 131.1, 130.0, 129.8, 128.7, 128.6, 128.1, 127.2, 127.0, 126.3, 123.0, 120.9, 75.0, 60.6, 59.8, 55.7, 54.1, 37.2, 29.7, 22.8, 20.0, 19.8, 19.2. HRMS

(ESI) calculated for $C_{32}H_{36}N_3O_4Ni$ [M + H]$^+$: 584.2059, Found 584.2058. mp >247 °C (decomp.). $[\alpha]_D^{22}$ +825 (*c* 0.250 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 6.463 min (major), 5.702 min (minor), ee = 91%.

7ag-major. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.5 Hz, 1H), 7.62–7.52 (m, 4H),7.43 (d, *J* = 7.5 Hz, 1H), 7.33–7.30 (m, 4H), 7.16 (d, *J* = 7.0 Hz, 1H), 6.81–6.76 (m, 2H), 4.38 (d, *J* = 4.0 Hz, 1H), 3.30 (d, *J* = 16.0 Hz, 1H), 3.27–3.22 (m, 2H), 3.04 (d, *J* = 16.0 Hz, 1H), 2.95 (d, *J* = 13.0 Hz, 1H), 2.89 (m, 1H),2.79–2.83 (m, 1H), 2.43 (s, 3H), 2.39–2.34 (m, 1H), 2.28 (brs, 1H), 2.18–2.10 (m, 1H), 1.99–1.88 (m, 2H), 1.67–1.60 (m, 1H), 1.52–1.42 (m, 2H), 1.35–1.26 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 175.4, 170.3, 142.8, 140.0, 138.8, 133.8, 133.7, 132.7, 130.0, 129.3, 129.0, 128.8, 128.7, 128.0, 127.5, 126.8, 123.5, 121.1, 73.5, 60.5, 60.1, 55.4, 54.5, 47.3, 33.8, 22.8, 21.6, 19.7, 19.3. HRMS (EI) calculated for $C_{32}H_{35}N_3O_4Ni$ [M]$^+$: 583.1981, Found: 583.1981. mp >246 °C (decomp.). $[\alpha]_D^{22}$ −1719 (*c* 0.260 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, DCM/EtOH = 99 : 1, 0.65 mL/min]: 5.848 min (major), 6.921 min (minor), ee = 92%.

7ag-minor. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.60 (d, *J* = 8.5 Hz, 1H), 7.52–7.45 (m, 2H),7.43–7.40 (m, 1H), 7.32–7.27 (m, 2H), 7.23–7.18 (m, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 6.0 Hz, 1H), 6.80 (d, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 4.0 Hz, 2H), 4.25 (d, *J* = 3.5 Hz, 1H), 3.64–3.61 (m, 1H), 3.47 (s, 2H), 3.30–3.26 (m, 1H), 3.23–3.17 (m, 1H), 3.03 (d, *J* = 13.0 Hz, 1H), 2.62–2.56 (m, 1H), 2.42 (d, *J* = 15.0 Hz, 1H), 2.39–2.35 (m, 1H), 2.28 (s, 3H), 2.07 (brs, 1H), 2.01–1.97 (m, 2H),1.70–1.53 (m, 2H), 1.43–1.26 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 175.8, 171.4, 143.0, 139.1, 138.4, 134.3, 133.6, 132.9, 130.8, 130.0, 129.8, 129.0, 128.7, 128.5, 128.4, 128.1, 127.1, 127.0, 123.0, 121.0, 75.1, 60.5, 60.0, 55.9, 54.2, 47.7, 34.8, 22.8, 21.5, 19.8, 19.2. HRMS (EI) calculated for $C_{32}H_{35}N_3O_4Ni$ [M]$^+$: 583.1981, Found: 583.1978. mp >147 °C (decomp.). $[\alpha]_D^{22}$ +1548 (*c* 0.230 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 8.635 min (major), 6.425 min (minor),ee = 95%.

7ah-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.4 Hz, 1H), 7.55–7.47 (m, 3H), 7.39–7.34 (m, 4H), 7.25–7.20 (m, 2H), 7.08 (d, *J* = 6.0 Hz, 1H), 6.74–6.69 (m, 2H), 4.27 (d, *J* = 4.0 Hz, 1H), 3.26 (d, *J* = 15.6 Hz, 1H), 3.21–3.11 (m, 2H), 2.96 (d, *J* = 16.0 Hz, 1H), 2.89–2.81 (m, 2H), 2.80–2.75 (m, 1H), 2.47 (brs, 1H), 2.45 (s, 3H), 2.30–2.23 (m, 1H), 2.07–1.98 (m, 1H), 1.88–1.81 (m, 2H), 1.63–1.20 (m, 6H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 175.2, 170.3, 142.7, 137.3, 136.9, 133.6, 132.5, 130.3, 130.0, 129.4, 129.2, 129.0, 127.9, 127.2, 126.8, 123.4, 121.0, 73.9, 60.1, 55.3, 54.5, 47.0, 33.9, 22.7, 21.2, 19.6, 19.3. HRMS (EI) calculated for $C_{32}H_{35}N_3O_4Ni$ [M]$^+$: 583.1981, Found: 583.1983. mp >266 °C (decomp.). $[\alpha]_D^{22}$ −1952 (*c* 0.215 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 5.463 min (major), 6.423 min (minor), ee = 89%.

7ah-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, *J* = 8.8 Hz, 1H), 7.53–7.40 (m, 4H), 7.31–7.28 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 4.0 Hz, 2H), 4.26 (d, *J* = 2.8 Hz, 1H), 3.61–3.58 (m, 1H), 3.47 (dd, *J* = 16.4, 24.0 Hz, 2H), 3.38–3.33 (m, 1H), 3.28 (d, *J* = 13.2 Hz, 1H), 3.24–3.20 (m, 1H), 3.04 (d, *J* = 13.2 Hz, 1H), 2.62–2.54 (m, 1H), 2.37 (m, 1H), 2.39 (s, 3H), 2.05–1.97 (m, 1H), 1.73–1.57 (m, 4H), 1.44–1.38 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 175.7, 171.4, 143.0, 137.3, 136.0, 134.3, 133.7, 132.9, 130.0, 129.9, 129.8, 129.4, 129.0, 128.7, 128.1, 127.1, 123.0, 121.0, 75.3, 60.4, 60.2, 55.9, 54.2, 47.4, 34.9, 22.8, 21.2, 19.8, 19.2. HRMS (EI) calculated for $C_{32}H_{35}N_3O_4Ni$ [M]$^+$: 583.1981, Found: 583.1964. mp >278 °C (decomp.). $[\alpha]_D^{22}$ +1424 (*c* 0.225 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 8.796 min (major), 6.701 min (minor), ee = 82%.

7ai-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.4 Hz, 1H), 7.55–7.48 (m, 5H), 7.25–7.16 (m, 4H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.75–6.68 (m, 2H), 4.25 (d, *J* = 4.4 Hz, 1H), 3.62–3.57 (m, 1H), 3.27 (s, 3H), 3.22 (m, 1H), 3.21 (d, *J* = 16.0 Hz, 1H), 3.14 (t, *J* = 5.2 Hz, 1H), 2.96 (d, *J* = 16.0 Hz, 1H), 2.85 (d, *J* = 13.2 Hz, 2H), 2.54 (brs, 1H), 2.35–2.28 (m, 1H), 2.17–2.08 (m, 1H), 1.97–1.94 (m, 1H), 1.76–1.68 (m, 1 H), 1.59–1.52 (m, 1H), 1.41–1.38 (m, 2H), 1.26–1.17 (m, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 175.3, 170.9, 158.4, 142.4, 133.9, 133.4, 132.2,130.0, 129.9, 129.1, 129.0, 128.9, 128.7, 128.1, 127.4, 126.8, 123.3, 121.2, 120.8, 110.1,73.5, 60.6, 60.3, 55.4, 54.8, 54.7, 37.6, 33.7, 22.8, 19.7, 19.4. HRMS (ESI) calculated for $C_{32}H_{35}N_3O_5Ni$ [M]$^+$: 599.1930, Found: 599.1935. mp >259 °C (decomp.). $[\alpha]_D^{22}$ −1554 (*c* 0.150 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 254 nm, DCM/EtOH = 99 : 1, 0.65 mL/min]: 6.053 min (major), 7.379 min (minor), ee = 91%.

Note: Recrystallization by slow evaporation of $CHCl_3$ and ether gave red crystalsof the major stereoisomer of adduct **7ai** suitable for single-crystal X-ray diffraction.

7aj-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.8 Hz, 1H), 7.56–7.48 (m, 4H),7.28–7.24 (m, 2H), 7.13–7.11 (m, 2H), 7.05–7.00 (m, 2H), 6.75–6.72 (m, 2H), 4.33 (d, *J* = 4.0 Hz, 1H), 3.76 (s, 3H), 3.29 (d, *J* = 16.0 Hz, 1H), 3.23–3.19 (m, 2H), 3.08 (d, *J* = 16.0 Hz, 1H), 2.94 (d, *J* = 12.8 Hz, 1H), 2.87 (m,1H), 2.82–2.77 (m, 1H), 2.39 (brs, 1H), 2.36–2.33 (m, 1H), 2.14–2.00 (m, 2H), 1.91–1.86 (m, 1H), 1.66–1.56 (m, 1H), 1.28–1.22 (m, 5H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 175.4, 170.4, 160.1, 142.9, 141.6, 133.7, 133.6, 132.7, 130.0, 129.8, 129.3, 129.0, 128.0, 127.4, 126.7, 123.5, 122.9, 121.0, 115.1, 113.9, 73.5, 60.4, 60.1, 55.4, 55.2, 54.5, 47.4, 33.8, 22.8, 19.7, 19.3. HRMS (ESI) calculated for $C_{32}H_{36}N_3O_5Ni$ [M + H]$^+$: 600.2008, Found: 600.1998. mp >258 °C (decomp.). $[\alpha]_D^{22}$ −1641 (*c* 0.165 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm,DCM/EtOH = 98 : 2, 0.65 mL/min]: 5.298 min (major), 5.703 min (minor), ee = 90%.

7aj-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 8.4 Hz, 1H), 7.51–7.44 (m, 2H),7.41–7.38 (m, 1H), 7.32–7.23 (m, 3H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.77–6.72 (m, 4H), 4.26 (d, *J* = 3.2 Hz, 1H), 3.79–3.76 (m, 1H), 3.70 (s, 3H), 3.54 (dd, *J* = 16.4 Hz, 30.8 Hz, 2H), 3.39–3.33 (m, 1H), 3.29–3.23 (m, 2H), 3.06 (d, *J* = 13.2 Hz, 1H), 2.69–2.63 (m, 1H), 2.55 (d, *J* = 13.2 Hz, 1H), 2.46–2.38 (m, 1H), 2.04–1.98 (m, 1H), 1.91 (brs, 1H), 1.74–1.56 (m, 2H), 1.46–1.29 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 175.9, 171.3, 159.9, 143.1, 140.7,134.3, 133.6, 132.9, 129.9, 129.7, 129.5, 128.9, 128.6, 128.0, 126.9, 123.0, 122.3, 120.9, 114.8, 113.7, 75.2, 60.5, 60.0, 56.0, 55.2, 54.2, 48.2, 34.9, 22.8, 19.8, 19.2.

HRMS (ESI) calculated for $C_{32}H_{36}N_3O_5Ni$ [M + H]$^+$: 600.2008, Found: 600.1988. mp >252 °C (decomp.). $[\alpha]_D^{22}$ +1147 (*c* 0.275 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.9 mL/min]: 19.210 min (major), 13.171 min (minor), ee = 100%.

7ak-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 8.4 Hz, 1H), 7.61–7.52 (m, 3H),7.40 (d, *J* = 8.0 Hz, 2H), 7.32–7.29 (m, 2H), 7.17–7.11 (m, 3H), 6.78–6.75 (m, 2H), 4.37 (d, *J* = 4.0 Hz, 1H), 3.89 (s, 3H), 3.31 (d, *J* = 16.0 Hz, 1H), 3.26 (d, *J* = 10.8 Hz, 1H), 3.05 (d, *J* = 16.0 Hz, 1H), 2.92 (t, *J* = 13.6 Hz, 2H),2.80 (t, *J* = 9.2 Hz, 1H), 2.43–2.36 (m, 1H), 2.23 (brs, 1H), 2.16–2.05 (m, 2H), 1.90–1.78 (m, 2H), 1.65–1.24 (m, 6H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 175.3, 170.3, 159.6, 142.8, 133.8, 133.7, 132.7, 131.8, 131.4, 130.0, 129.3, 129.0, 128.1, 127.5, 126.8, 123.4, 121.0, 114.2, 73.5, 60.6, 60.2, 55.5, 54.7, 46.7, 33.9, 22.8, 19.7, 19.4. HRMS (ESI) calculated for $C_{32}H_{36}N_3O_5Ni$ [M + H]$^+$: 600.2008, Found: 600.1982. mp >272 °C (decomp.). $[\alpha]_D^{22}$ −1362 (*c* 0.230 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.9 mL/min]: 13.245 min (major), 25.841 min (minor), ee = 90%.

7al-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.99–7.93 (m, 2H), 7.59–7.52 (m, 6H), 7.31–7.29 (m, 2H), 7.24 (d, *J* = 6.4 Hz, 1H), 6.82–6.76 (m, 2H), 4.42 (d, *J* = 2.8 Hz, 1H), 3.27 (m, 1H), 3.09 (d, *J* = 14.4 Hz, 1H), 3.04 (m, 1H), 2.96 (m, 1H), 2.89 (d, *J* = 16.0 Hz,1H), 2.82 (d, *J* = 12.8 Hz, 1H), 2.25–2.20 (m, 1H), 2.10–1.94 (m, 2H), 1.87 (m, 1H), 1.48–1.41 (m, 1H), 1.34–1.28 (m, 2H), 1.12–1.00 (m, 2H), 0.89–0.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 175.6, 170.5, 142.9, 137.3, 133.8, 133.7, 133.4, 132.8, 130.8, 129.3, 129.1, 128.3, 128.0, 127.5, 126.8, 126.7, 126.6, 123.5, 121.0, 73.8, 60.4, 59.2, 54.9, 54.2, 47.5, 33.7, 22.5, 19.2, 19.0. HRMS (ESI) calculated for $C_{35}H_{36}N_3O_4Ni$ [M + H]$^+$:620.2059, Found: 620.2028. mp >277 °C (decomp.). $[\alpha]_D^{22}$ −1767 (*c* 0.230 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IC column, 240 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 16.318 min (major), 31.464 min (minor), ee = 87%.

7al-minor. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (d, *J* = 8.8 Hz, 1H), 7.88 (t, *J* = 8.8 Hz, 2H), 7.80–7.76 (m, 2H), 7.48–7.34 (m, 6H), 7.22 (d, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.75–6.71 (m, 2H), 4.38 (d, *J* = 2.4 Hz, 1H), 3.78 (t, *J* = 4.4 Hz, 1H), 3.28–3.22 (m, 1H), 3.18 (d, *J* = 16.0 Hz, 2H), 3.11 (d, *J* = 12.0 Hz, 1H), 2.91 (d, *J* = 13.2 Hz, 1H), 2.69 (d, *J* = 16.4 Hz, 1H), 2.57 (brs, 1H), 2.31–2.26 (m, 2H), 2.11–2.02 (m, 1H), 1.70 (m, 1H), 1.56–1.39 (m, 2H), 1.31–1.04 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 175.9, 171.7, 143.2, 136.7, 134.4, 133.7, 133.6, 133.1, 133.0, 130.0, 129.9, 129.1, 129.0, 128.7, 128.1, 128.0, 127.9, 127.5, 127.0, 126.4, 126.3, 122.9, 120.9, 75.2, 59.9, 59.8, 55.5, 54.0, 47.8, 35.0, 22.7, 19.4, 19.0. HRMS (ESI) calculated for $C_{35}H_{36}N_3O_4Ni$ [M + H]$^+$: 620.2059, Found: 620.2029. mp >266 °C (decomp.). $[\alpha]_D^{22}$ +1561 (*c* 0.255 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 8.000 min (major), 6.221 min (minor), ee = 71%.

7am-major. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.4 Hz, 1H), 7.51 (m, 3H), 7.24–7.17 (m, 5H), 7.12 (d, *J* = 8.0 Hz, 1H), 6.71–6.66 (m, 2H), 4.25 (d, *J* = 4.4 Hz, 1H), 3.86 (s, 3H), 3.60 (s, 3H), 3.51 (m, 1H), 3.23 (d, *J* = 15.6 Hz, 2H), 3.19 (m, 1H), 3.04 (d, *J* = 16.0 Hz, 1H), 2.86 (m, 2H), 2.46–2.40 (m, 2H), 2.00–1.94 (m, 1H), 1.82–1.77 (m, 1H), 1.60–1.25 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.9, 174.8, 171.0, 153.1, 149.0, 142.8, 133.9, 133.8, 133.5, 132.4, 129.8, 129.0, 128.8, 128.2, 127.4, 127.0, 124.1, 123.3, 121.7, 120.7, 111.9, 73.4, 60.6, 60.5, 60.3, 56.1, 55.6, 54.6, 38.0, 34.6, 22.8, 19.8, 19.5. HRMS (ESI) calculated for $C_{33}H_{38}N_3O_6Ni$ [M + H]$^+$: 630.2114, Found: 630.2093. mp >257 °C (decomp.). $[\alpha]_D^{22}$ −1546 (*c* 0.240 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 98 : 2, 0.65 mL/min]: 5.234 min (major), 6.179 min (minor), ee = 95%.

7an-major. 1H NMR (400 MHz, CDCl3): δ 8.33 (d, J = 8.8 Hz, 1H), 7.50–7.42 (m, 4H),7.20 (m, 3H), 6.74–6.67 (m, 4H), 4.20 (d, J = 3.6 Hz, 1H), 3.84 (s, 3H), 3.51 (m, 1H), 3.26 (s, 3H), 3.24 (m, 2H), 3.16–3.14 (m, 1H), 3.00 (d, J = 16.0 Hz, 1H), 2.87 (d, J = 14.0 Hz, 1H), 2.81 (m, 1H), 2.52 (brs, 1H), 2.39–2.32 (m, 1H), 2.10–2.05 (m, 2H), 1.73–1.68 (m, 1H), 1.60–1.55 (m, 1H), 1.42–1.19 (m, 5H).13 C NMR (100 MHz, CDCl3): δ 177.8, 175.3, 170.8, 160.3, 159.4, 142.5, 133.9, 133.4,132.2, 130.4, 129.8, 129.0, 128.9, 128.1, 127.4, 126.8, 123.3, 120.9, 120.8, 105.4,97.6, 73.7,60.7, 60.2, 55.5, 55.4, 54.8, 54.7, 37.4, 33.7, 22.8, 19.6, 19.4. HRMS (ESI) calculated for $C_{33}H_{38}N_3O_6Ni$ [M + H]$^+$: 630.2114, Found: 630.2090. mp >272 °C (decomp.). $[\alpha]_D^{22}$ −2156 (*c* 0.265 g/100 mL, CH_2Cl_2). The enantiomeric excess was determined by HPLC. [IA column, 240 nm, DCM/EtOH = 98 : 2, 0.5 mL/min]: 6.972 min (major), 8.193 min (minor), ee = 88%.

General Procedure for the preparation of the corresponding derivative of the related amino acid

To a solution of **7ai** (0.2 mmol) in methanol (2 mL) was added an aqueous solution of hydrochloride (6 N, 0.2 mL), and the mixture was refluxed in a sealed tube for 20 min. Then the reaction mixture was evaporated *in vacuo* to dryness. The residue was dissolved in MeCN (1 mL), then K_2CO_3 (0.8 mmol) and TsCl (4.4 mmol) were added successively. The reaction mixture was then stirred vigorously for 6 h, followed by quenching with 1 N HCl (to pH 2) and extraction of the product with CH_2Cl_2. The organic phase was evaporated *in vacuo*. After removal of the solvent, the crude product was purified by column chromatography to give pure **9ai** as a white solid.

***N*-((3*R*,4*S*)-4-(2-Methoxyphenyl)-2-oxotetrahydro-2*H*-pyran-3-yl)-4-methylbenzenesulfonamide (9ai).** The product was obtained in 79% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66–7.64 (m, 2H), 7.29–7.24 (m, 3H), 6.98–6.96 (dd, *J* = 7.2, 1.6 Hz, 1H), 6.91–6.85 (m, 2H), 5.23–5.21 (d, *J* = 6.4 Hz, 1H), 4.35–4.27 (m, 3H), 3.92–3.85 (q, *J* = 26.4 Hz, 1H), 3.73 (s, 3H), 2.42 (s, 3H), 2.32–2.25 (m, 1H), 2.17–2.07 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ (ppm) 170.7, 156.7, 143.5, 136.8, 131.1, 129.6, 128.9, 127.1, 121.0, 110.7, 66.3, 54.1, 53.2, 29.7, 29.3, 21.5. HRMS (EI): exact mass calculated for [M]$^+$ ($C_{19}H_{21}NO_5S$) requires *m/z* 375.1140, found m/z 375.1143. mp 55 °C. $[\alpha]_D^{20}$ = −161.9 (*c* 1.0 g/100 mL, CH_2Cl_2).

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