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JOC The Journal of Organic Chemistry

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Chemical Dynamic Thermodynamic Resolution and *S*/*R* Interconversion of Unprotected Unnatural Tailor-made α-Amino Acids

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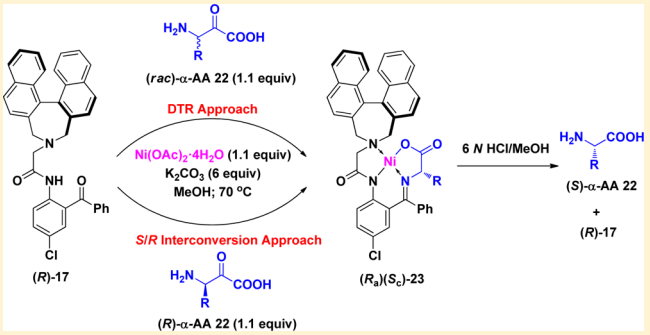
Supporting Information

ABSTRACT: Described here is an advanced, general method for purely chemical dynamic thermodynamic resolution and *S*/*R* interconversion of unprotected tailor-made α-amino acids (α-AAs) through intermediate formation of the corresponding nickel(II)-chelated Schiff bases. The method features virtually complete stereochemical outcome, broad substrate generality (35 examples), and operationally convenient conditions allowing for large-scale preparation of the target α-AAs in enantiomerically pure form. Furthermore, the new type of nonracemizable axially chiral ligands can be quantitatively recycled and reused, rendering the whole process economically and synthetically attractive.



INTRODUCTION

Interest in the development of new methods for preparation of tailor-made α-amino acids (α-AAs) in enantiomerically pure form is at an all-time high, because of their ever-increasing applications in pharmaceutical and healthcare industries.[1,2] In particular, the area of peptide-based drugs is the most promising and fast-growing sector in the new pharmaceuticals design. Currently, substitution of a natural α-AA by an unnatural, tailor-made analogue in polypeptide drugs is a widely used approach to overcome the disadvantages related to poor chemical and pharmacokinetic profiles of natural polypeptides. High pharmaceutical potential of unnatural, tailor-made α-AAs can be best illustrated using examples of the most recently developed very successful drugs. For instance, telaprevir (**1**) (Figure 1) is an all-tailor-made α-AAs tetrapeptide possessing remarkably strong anti-HCV activity.[3] Degarelix (**2**), a polypeptide containing six key tailor-made α-AA residues, is an exceptionally selective gonadotrophin releasing hormone (GnRH) receptor antagonist, prescribed for the treatment of advanced prostate cancer.[4] Both drugs were developed starting from all-natural AAs peptides using tailor-made α-AA scan approach. Another notable example of a powerful peptide-based drug is carfilzomib (**3**), which was developed from the natural product epoxomicin.[5] Substitution of phenylalanine for tailor-made homophenylalanine resulted in a remarkable activity of **3** as a chymotrypsin-like protease inhibitor. Furthermore, besides peptide-based drugs, there are a number of important low molecular weight drugs containing fragments of tailor-made α-AAs, for example, DPP-IV inhibitor saxagliptin (**4**) and antiepileptic agent lacosamide (**5**) (Figure 1).[6,7]

Considering the pharmaceutical potential of unnatural, tailor-made α-AAs, the development of new approaches for preparation of structurally varied AAs in enantiomerically pure form has been one of the most actively studied areas of organic synthesis.[8,9] The current wealth of synthetic methodology allows for preparation of virtually any structurally or stereochemically complex α-AAs. On the other hand, the aspects of practicality and cost of target α-AAs have often been neglected rendering the known chemical methods prohibitively expensive even for gram-scale preparations.[10] Consequently, the cost-per-structure issue is currently the major key factor in the quality assessment of a new synthetic method. Particularly, high yields and degree of stereocontrol accessible under operationally convenient conditions, such as an easily maintainable temperature and the use of air- and moisture-stable reagents, are unarguably essential requirements of a truly practical synthetic method.[11]

Received: June 9, 2015
Published: September 9, 2015

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DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

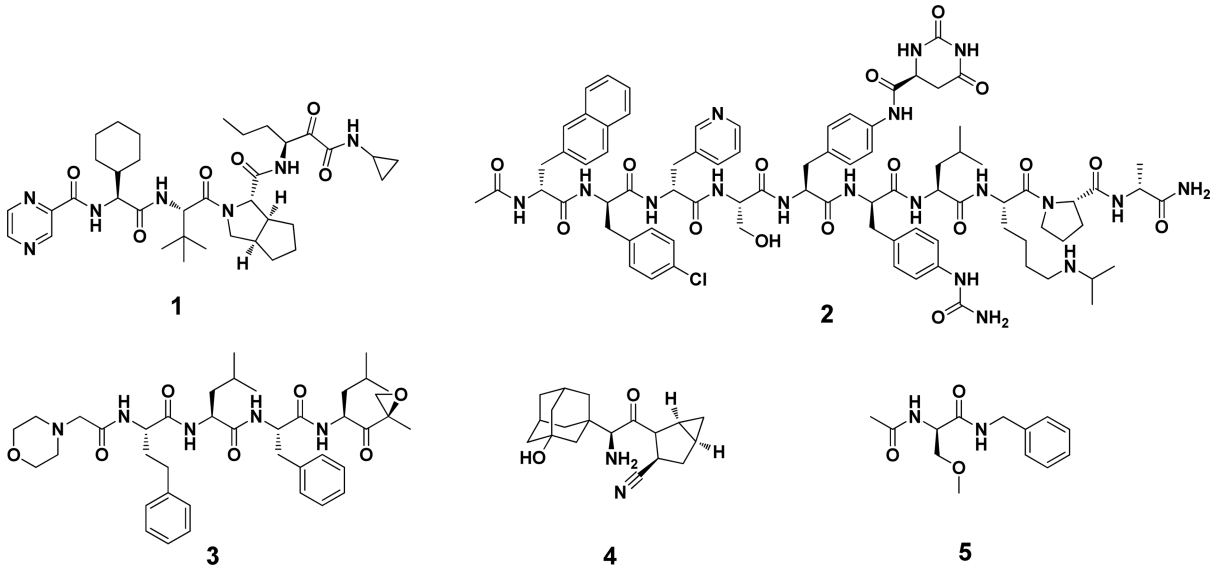
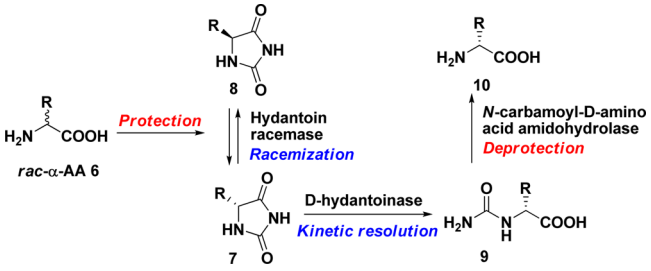


Figure 1. Structures of current representative pharmaceuticals containing tailor-made α-AAs.

Considering the subject of preparation of enantiomerically pure α-AAs from the stand point of practicality, it might be a general consensus that resolution of racemic α-AAs (*rac*-α-AAs); in particular, dynamic resolution is the most economically feasible approach, including dynamic kinetic resolution (DKR) and dynamic thermodynamic resolution (DTR). DKR of *rac*-α-AAs is mainly dominated by the enzymatic approaches, while chemical methods, despite the intellectual brilliance and reaction ingenuity, play a rather ornamental role. For example, state-of-the-art enzymatic approach (Scheme 1) can involve up to three

Scheme 1. General Biocatalytic Approach for DKR of Protected *rac*-α-AA Derivatives

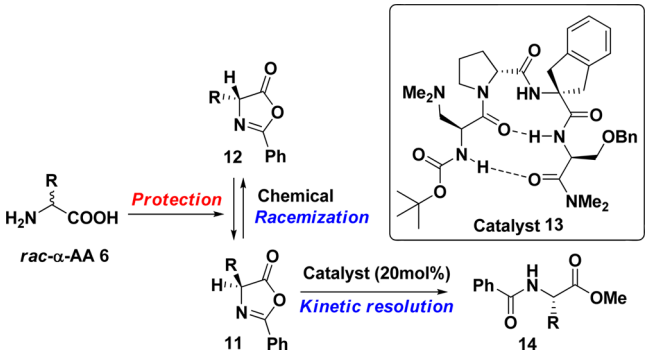


biocatalytic reactions including racemization, kinetic resolution, and deprotection stages.[12] However, the whole process requires a purely chemical step for proper protection of the starting *rac*-α-AAs **6**.

In the field of nonenzymatic, chemical DKR of *rac*-α-AAs,[13,14] one of the outstanding methods is a catalytic alcoholytic opening of oxazol-5(4*H*)-ones (Scheme 2).[15] This approach makes use of very high C−H acidity and reactivity of oxazolones **11**, **12** allowing for quite efficient racemization and catalytic ring opening under very mild conditions. This process also necessitates special preparation of oxazolones **11**, **12**, and deprotection of the intermediate derivatives **14**.

Nevertheless, the direct dynamic resolution of unprotected α-AAs is difficult to realize, and there are only two literature precedents based on the application of chiral ligands **15** and **16** that could achieve this (Figure 2).[16] Both methods are purely chemical and make use of in situ formation of the corresponding

Scheme 2. Example of Chemical Approach for DKR of Protected *rac*-α-AA Derivatives



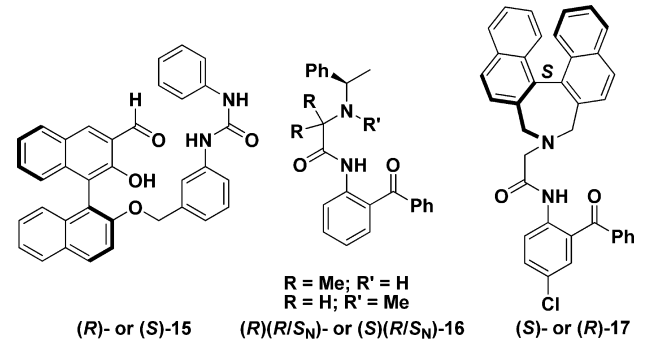


Figure 2. Structural types of the known ligands **15** and **16** and the new ligand **17** for direct dynamic resolution of unprotected α-AAs.

Schiff bases starting from unprotected α-AAs. While these reports have made a significant methodological breakthrough, the synthetic value of ligands **15** and **16** is rather limited due to the lack of substrate generality and incomplete stereochemical outcome.

Consistent with our longstanding interest in the development of synthetic methods for preparation of tailor-made amino acids,[17] we have developed a modular approach for the design of new ligands and the corresponding Ni(II) complexes for general asymmetric synthesis of α- and β-AAs.[18] One of the major

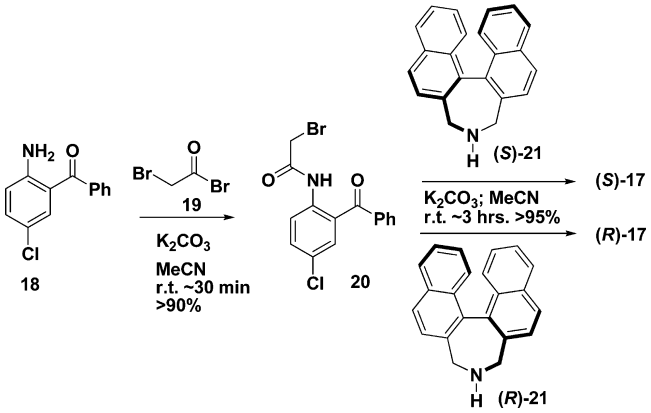
DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

breakthroughs in this research is the development of specially designed, axially chiral ligands (*S*)- and (*R*)-**17** (Figure 2) and their use for DTR of several natural proteinogenic α-AAs based on thermodynamic equilibration of diastereomeric products.[19−21] Here, we report a detailed account of our research on the application of (*S*)- and (*R*)-**17** for general DTR of unprotected *rac*-α-AAs. Furthermore, we demonstrate that ligands (*S*)- and (*R*)-**17** can also be used for *S*/*R* interconversion of unprotected α-AAs, underscoring synthetic range and flexibility of this approach. In the present work, we focus entirely on unnatural, tailor-made α-AAs of high pharmaceutical potential. We demonstrate a remarkable generality of this method using 35 examples of polyfunctional, structurally varied α-AAs and provide detailed mechanistic rationale for the observed thermodynamically controlled stereochemical outcome. The chemical process presented in this paper features virtually complete yields and diastereoselectivity, fully recyclable chiral ligands (*S*)- and (*R*)-**17**, and operationally simple reaction conditions.

RESULTS AND DISCUSSION

Synthesis of Axially Chiral Ligands. Synthesis of ligands (*S*)- and (*R*)-**17** (Scheme 3) is a very straightforward two-step

Scheme 3. Synthesis of Axially Chiral Ligands (*S*)- and (*R*)-17



process involving high-yielding reactions. The first step, the acylation of 2-amino-5-chlorobenzophenone **18** with bromoacetyl bromide **19**, is conducted at ambient temperature affording the intermediate amide **20** in a high yield. The second step is *N*-alkylation of enantiomerically pure axially chiral secondary amine **21** with amide **20**, which proceeds at room temperature with a quantitative yield. Enantiomerically pure amines (*S*)- and (*R*)-**21** can be reliably prepared on a large scale by resolution of inexpensive racemic **21** with L-(−)-tartaric acid.[22] The whole procedure is noticeably very simple and operationally convenient and can be reproduced on > 300 g scale. For the large-scale synthesis, this route can be conducted as a one-pot process without purification of amide **20** affording ligands (*S*)- and (*R*)-**17** of at least, 85% chemical purity, which can be directly used for the DTR or *S*/*R* interconversion of tailor-made α-AAs.

Application of Ligands (*S*)- and (*R*)-17 for DTR of Tailor-made *rac*-α-AAs. With the aim of optimizing the reaction conditions and understanding the mode of stereochemical preferences, we conducted a series of experiments carefully monitoring the reaction composition over time using HPLC analysis. As a representative example, we selected multifunctional *rac*-6-Cl-tryptophan **22a** (Figure 3). The reaction between ligand

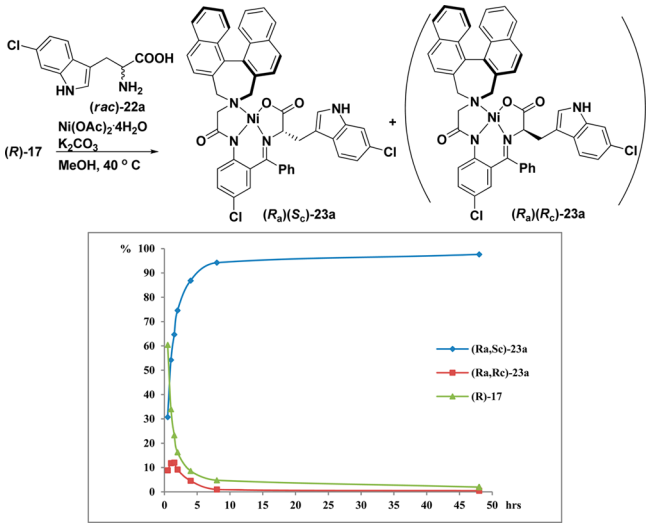


Figure 3. Reaction of ligand (*R*)-**17** with *rac*-6-Cl-tryptophan **22a**.

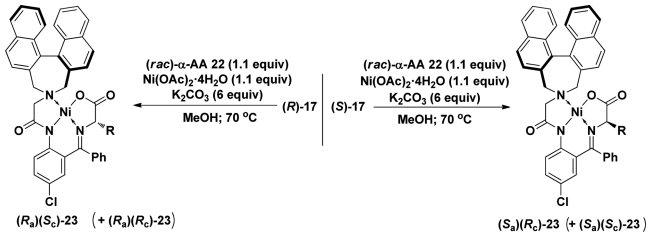
(*R*)-**17** and unprotected *rac*-**22a** was conducted in methanol at 40 °C, using $Ni(OAc)_2{\cdot}4H_2O$ and K_2CO_3 as a base. As one can see from Figure 3, on the early reaction stage the ratio between diastereomers $(R_a)(S_c)$-**23a** and $(R_a)(R_c)$-**23a** was about 3:1, indicating rather low kinetic stereoselectivity. However, with the reaction progress over time, the amount of major diastereomer $(R_a)(S_c)$-**23a** was rapidly increasing while the quantity of minor stereoisomer $(R_a)(R_c)$-**23a** was correspondingly decreasing. Thus, at nearly 90% conversion of starting ligand (*R*)-**17**, the ratio $(R_a)(S_c)$-**23a**/$(R_a)(R_c)$-**23a** was about 9:1, clearly suggesting that the former diastereomer is the thermodynamically preferred product. Final thermodynamic control was achieved after almost 48 h, furnishing diastereomers $(R_a)(S_c)$-**23a** and $(R_a)(R_c)$-**23a** in a ratio of 99.54:0.46 (see Table S1, Supporting Information). Major product $(R_a)(S_c)$-**23a** was isolated in diastereomerically pure form (> 99% de) with an excellent 97% yield. It can be reasonably assumed that under the reaction conditions minor diastereomer $(R_a)(R_c)$-**23a** undergoes base-catalyzed α-epimerization, via the corresponding intermediate enolate to form the thermodynamic product $(R_a)(S_c)$-**23a** (see Figure S1, Supporting Information).

Additional optimization of the reaction conditions revealed that the thermodynamic control can be considerably accelerated at elevated temperatures; in particular, 70 °C was found to be most optimal, as virtually no byproducts were detected in the crude reaction mixture. Furthermore, we found that only 10% excess of both the *rac*-α-AA and $Ni(OAc)_2{\cdot}4H_2O$ is needed for optimal reaction rates and complete consumption of the starting ligand (*R*)-**17**. Using these standard conditions, we advanced to the substrate generality study, and the most representative results are collected in Table 1.

Phenylalanine (Phe) derivatives represent one of the most frequently used types of tailor-made α-AAs for modification of natural peptides.[4,5] Therefore, we decided to study relatively large series of various phenylalanine derivatives *rac*-**22b−m**. The reactions of ligand (*S*)-**17** with unprotected *ortho*-substituted phenylalanines *rac*-**22b−e** gave rise to products $(S_a)(R_c)$-**23** with very good stereochemical outcomes (entries 2−5). The level of diastereoselectivity, ranging from 92 to 99% de, was rather in line with the optimized reaction (entry 1). On the other hand, the variable yields may be attributed to generally lower reaction rates due to the steric effect of the *ortho* substituents. In agreement

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

Table 1. DTR of Unprotected Tailor-made *rac*-α-AAs 22a−dd with Axially Chiral Ligand (*S*)- or (*R*)-17[a]



Entry	17	22	23 yield (%)[b]	23 dr[c]	t (h)
1	(*R*)	 (**a**)	97	99:1	2
2	(*S*)	2-Br-benzyl (**b**)	95	98:2	12
3	(*S*)	2-MeO-benzyl (**c**)	70	96:4	6
4	(*S*)	2-OH-benzyl (**d**)	98	97:3	3
5[d]	(*S*)	2-CN-benzyl (**e**)	77	>99:1	5
6	(*S*)	3-Br-benzyl (**f**)	97	94:6	12
7	(*S*)	3-OH-benzyl (**g**)	98	94:6	3
8	(*S*)	3-MeO-benzyl (**h**)	99	91:9	6
9	(*S*)	4-Br-benzyl (**i**)	99	>99:1	12
10	(*S*)	4-Cl-benzyl (**j**)[e]	99	99:1	12
11	(*S*)	4-F-benzyl (**k**)	99	99:1	12
12[d]	(*S*)	4-CF_3-benzyl (**l**)	92	94:6	6
13[d]	(*S*)	4-acetyl-benzyl (**m**)	78	93:7	6
14	(*S*)	 (**n**)	98	>99:1	24
15	(*S*)	1,1'-biphenyl (**o**)	98	97:3	24
16	(*S*)	 (**p**)	92	>99:1	15
17	(*R*)	 (**q**)	97	>99:1	9
18	(*R*)	 (**r**)	97	>99:1	7
19	(*R*)	 (**s**)	62	99:1	5
20	(*R*)	allyl (**t**)	98	97:3	2
21	(*R*)	 (**u**)	98	93:7	2
22	(*S*)	 (**v**)	99	98:2	36
23	(*S*)	 (**w**)[f]	97	>99:1	24
24	(*S*)	*n*-propyl (**x**)	99	94:6	2
25	(*S*)	*n*-butyl (**y**)[e]	99	93:7	2
26	(*R*)	*n*-hexyl (**z**)	97	92:8	2
27	(*R*)	 (**aa**)	99	96:4	2
28	(*S*)	*c*-butyl (**bb**)[e]	96	96:4	2
29	(*R*)	*t*-butyl (**cc**)	88	70:30	2
30	(*S*)	phenyl (**dd**)	98	86:14	5

[a]Reaction conditions: (*S*)-**17** or (*R*)-**17** (0.176 mmol), *rac*-α-AAs **22** (0.194 mmol), $Ni(OAc)_2{\cdot}4H_2O$ (0.194 mmol), and K_2CO_3 (1.06 mmol) were refluxed in methanol (6 mL) at 70 °C for 2−36 h. [b]Combined yield of isolated product **23**. [c]Determined by LC/MS analysis of the crude reaction mixtures. [d]Reactions rate was relatively high; therefore, the reactions were conducted at 40 °C. [e]The reaction was performed with 500 mg of ligand (*S*)-**17** for the following disassembly process. [f]The reaction was reproduced on a largescale starting with 10 g of ligand (*S*)-**17** (97% yield, > 99:1 dr).

with assumption, the yields obtained in the reactions of ligand (*S*)-**17** with *meta*-substituted derivatives *rac*-**22f−h** were truly excellent, although the diastereoselectivity was a bit lower (entries 6−8). Virtually quantitative yields were also obtained in the reactions of *para*-substituted phenylalanines *rac*-**22i−m** with ligand (*S*)-**17** (entries 9−13), with the exception of the *p*-acetyl group containing *rac*-**22m** (78%, entry 13). In this case, the lower yield might be explained by rather special physicochemical properties of the products due to the very polar nature of acetyl moiety. Importantly, in this series of tailor-made phenylalanine derivatives neither electronic nor steric properties of the substituents did not show any apparent effects on the stereochemical outcome of the reactions. In particular, we would like to mention excellent stereochemical outcomes observed in the reactions of ligand (*S*)-**17** with *rac*-**22d,g** (entries 4 and 7), bearing free hydroxyl group, which usually require proper protection in the corresponding enzymatic methods. Another example worth mentioning is the DTR of *p*-Cl-phenylalanine *rac*-**22j**, used in the design of degarelix (**2**) (Figure 1).[4] Using our method, this α-AA can be prepared quite efficiently (yield 99% with 98% de; entry 10) in both enantiomeric forms.

Another structural group of α-AAs used in this study are polyaromatic derivatives represented by β-naphthylalanine *rac*-**22n**, used in the design of degarelix (**2**) (Figure 1)[4] and *p*-phenyl-phenylalanine *rac*-**22o** (entries 14 and 15). The corresponding reactions with ligand (*S*)-**17** proceeded with excellent stereochemical outcomes allowing preparation of target products $(S_a)(R_c)$-**23n,o** in diastereomerically pure form with 98% yield. Tailor-made α-AAs containing aromatic heterocyclic moieties are usually quite formidable targets, but they are in great demand as key structural features in the design of peptide-based drugs.[4] To explore this special structural type, we selected four α-AAs *rac*-**22p−s** and performed their reactions with both (*S*)- and (*R*)-**17**. The results obtained were exceptionally good in terms of both diastereoselectivity and chemical yields (entries 16−19). One more unusual and synthetically challenging structural type of tailor-made α-AAs is represented by allyl group containing *rac*-**22t,u** (entries 20 and 21). Gratifyingly, we found that the reactions of unprotected *rac*-**22t,u** with ligand (*R*)-**17** proceeded quite smoothly, affording products $(R_a)(S_c)$-**23t,u** with excellent stereochemical outcomes. Another relatively large group of tailor-made α-AAs studied in this work represents aliphatic derivatives containing various linear as well as sterically constrained cyclic fragments. For example, unprotected *rac*-**22v,w** (entries 22, 23), bearing cyclopropyl and -hexyl rings, reacted with (*S*)-configured ligand **17** exceptionally well, furnishing major diastereomers $(S_a)(R_c)$-**23v,w** with excellent yields and stereoselectivity. On the other hand, the reactions of α-AAs *rac*-**22x−z**, bearing linear alkyl groups (entries 24−26), and *rac*-**22aa**, possessing a phenethyl moiety (entry 27), also gave satisfactory yields and stereoselectivity. Of particular interest was the reaction of α-AA *rac*-**22bb** containing a sterically constrained cyclobutyl ring (entry 28). The outcome was quite satisfactory, affording diastereomer $(S_a)(R_c)$-**23bb** in a very good yield and diastereomeric excess. Finally, we believe it is very important to

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

mention a few less successful results pointing to some limitations of this method. For example, the reaction of sterically bulky *rac-tert*-leucine **22cc** with ligand (*R*)-**17** proceeded at slow rate and with far from incomplete thermodynamic control (entry 29). On the other hand, *rac*-phenylglycine **22dd** (entry 30) reacted with ligand (*S*)-**17** at a rather good rate but with noticeably lower diastereoselectivity. Taking advantage of the nearly perfect stereochemical outcome in the case of *cyclo*-hexane containing AA *rac*-**22w** (entry 23), we performed large-scale experiments using 10 g of the starting ligand (*S*)-**17**. The reaction proceeded without any complications to furnish diastereomerically pure (S_a)(R_c)-**23w** with 94% isolated yield.

To conclude this part of the study, we emphasize that axially chiral ligands (*S*)- and (*R*)-**17** were evidently proven to be very efficient reagents for direct DTR of various unprotected tailor-made *rac*-*α*-AAs. In most of the cases reported in Table 1, the reactions took place under operationally convenient conditions to afford the major products with synthetically valuable diastereoselectivity and chemical yields. It should be mentioned that due to the significant differences in physicochemical properties between major (S_a)(R_c)-**23** and minor (S_a)(S_c)-**23** diastereomers, the purification of the former can be readily achieved by recrystallization or regular gravity-driven column chromatography.

Application of Ligands (*S*)- and (*R*)-17 for *S*/*R* Interconversion of Tailor-made *α*-AAs. Inspired by the exciting results obtained for the DTR of tailor-made *rac*-*α*-AAs, we decided to explore an additional methodological opportunity such as *S*/*R* interconversion of *α*-AAs. Compared to the DTR of *rac*-*α*-AAs, conversion of (*S*)-*α*-AAs to (*R*) enantiomers and vice versa is obviously of much lesser general use for production of enantiomerically pure *α*-AAs. However, in some cases, such as utilization of undesired enantiomers, availability of the *S*/*R*-interconversion method can be of critical practical importance. Furthermore, a synthetic concept allowing the use of the same chiral ligands, reagents, and even conditions to pursue simply by choice of either DTR or *S*/*R* interconversion has never been realized to date. Thus, the obvious novelty of this idea was an additional motivation to conduct the present study.

As we did in the research on DTR, we decided to investigate first the reaction progress and the chemical composition over time. As a model reaction, we chose (*R*)-6-Cl-tryptophan **22a** as the expected products (R_a)(S_c)-**23a** and (R_a)(R_c)-**23a** were already characterized and monitored by HPLC (Table S2). The reaction of (*R*)-**22a** with ligand (*R*)-**17** was conducted under the standard conditions: heating reagents in methanol at 40 °C. Composition of starting ligand (*R*)-**17** and products (R_a)(S_c)-**23a** and (R_a)(R_c)-**23a** were carefully monitored by HPLC analysis; the results are presented in Figure 4.

As expected, diastereomer (R_a)(R_c)-**23a** was a kinetic product on the early reaction stage. From the data obtained, it was apparently clear that the rate of (R_a)(R_c)-**23a** formation was a bit faster than the rate of its based-catalyzed *α*-epimerization (via intermediate enolate) to form the thermodynamic product (R_a)(S_c)-**23a**, rendering (R_a)(R_c)-**23a** as a major product until about 50% consumption of the starting ligand (*R*)-**17**. However, quite rapidly the relative amounts of (R_a)(R_c)-**23a** were gradually decreasing, while diastereomer (R_a)(S_c)-**23a** became a major product after about 1.5 h of reaction time. Ultimately, after 33 h under full thermodynamic control, kinetic (R_a)(R_c)-**23a** was virtually completely transformed to (R_a)(S_c)-**23a** with a final ratio of 99.63:0.37 (see Table S2, Supporting Information).

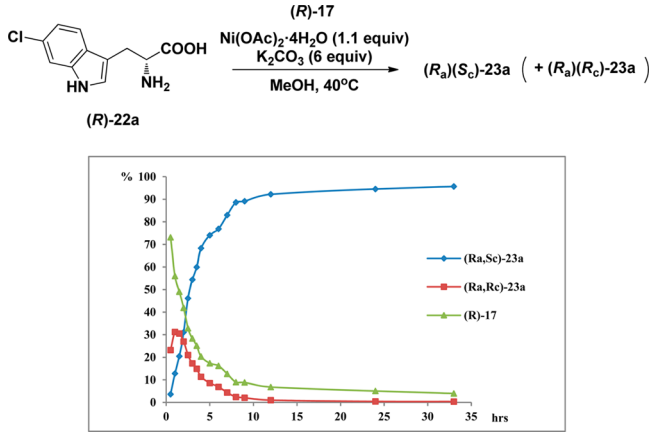
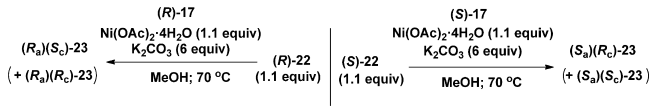


Figure 4. Reaction of ligand (*R*)-**17** with (*R*)-**22a**: progress and stereochemical outcome over time.

With these data in hand, we next proceeded to study the substrate generality of the *S*/*R*-interconversion method; some selected results are presented in Table 2.

Table 2. *S*/*R* Interconversion of Unprotected Tailor-made *α*-AAs Using Ligand (*S*)- or (*R*)-17[a]



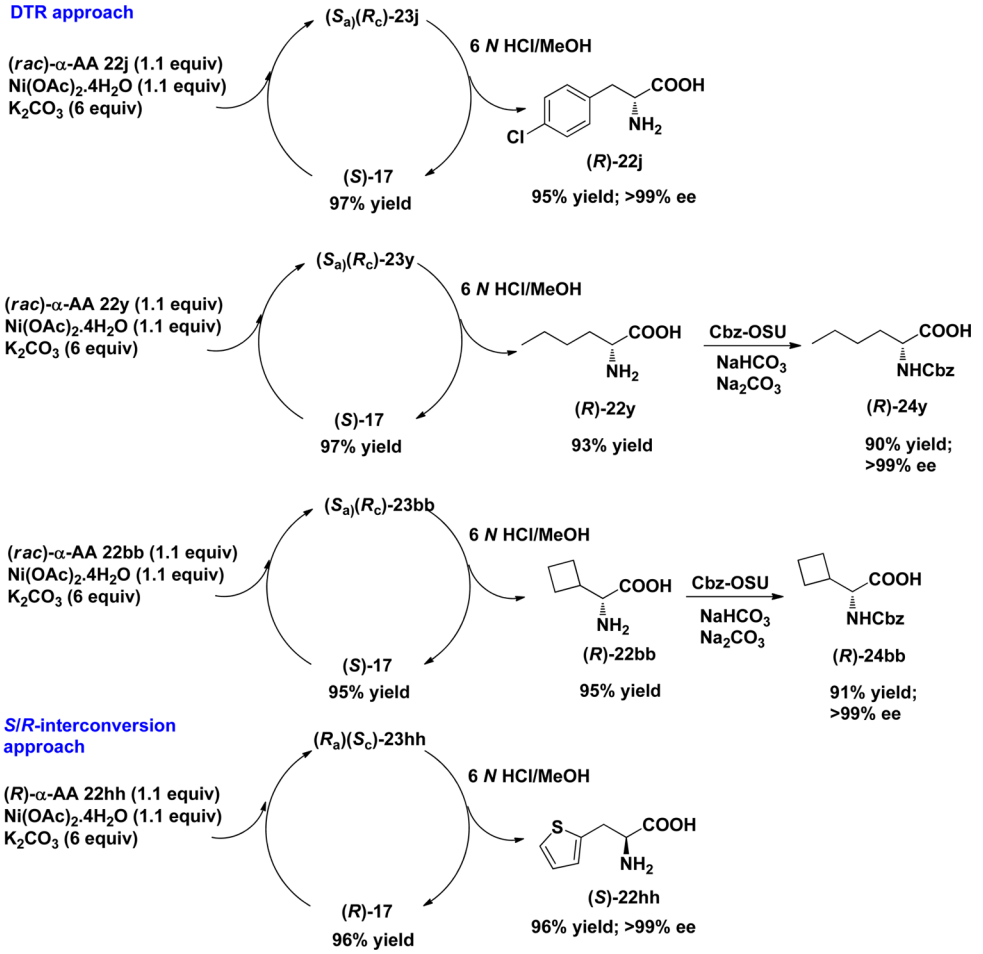
Entry	17	22	23 yield (%)[b]	23 dr[c]	t (h)
1	(*R*)	(*R*)	 (**a**)	97	99:1	2
2	(*S*)	(*S*)	 (**a**)	98	>99:1	2
3	(*S*)	(*S*)	4-Cl-benzyl (**j**)	99	>99:1	2
4	(*S*)	(*S*)	4-CH_3-benzyl (**ee**)	98	>99:1	4
5	(*R*)	(*R*)	3,4-di-F-benzyl (**ff**)	97	97:3	7
6	(*S*)	(*S*)	 (**gg**)	99	90:10	28
7	(*R*)	(*R*)	 (**hh**)[e]	88	97:3	7
8[d]	(*R*)	(*R*)	propargyl (**ii**)	97	93:7	8
9	(*S*)	(*S*)	*n*-butyl (**y**)	99	94:6	4

[a]Reaction conditions: (*S*)-**17** or (*R*)-**17** (0.176 mmol), (*S*)- or (*R*)-*α*-AAs **22** (0.194 mmol), $Ni(OAc)_2·4H_2O$ (0.194 mmol), and K_2CO_3 (1.06 mmol) were refluxed in methanol (6 mL) for 2−28 h. [b]Combined yield of isolated product **23**. [c]Determined by LC/MS analysis of the crude reaction mixtures. [d]Reactions conducted at 40 °C. [e]The reaction was performed with 500 mg of ligand (*R*)-**17** for the following disassembly process.

First, we reproduced the above-described procedure using optically pure AA **22a** and ligand **17** of both opposite absolute configurations. The reaction of ligand (*S*)-**17** with (*S*)-configured **22a** gave a virtually identical stereochemical outcome allowing preparation of product (S_a)(R_c)-**23a** with virtually complete chemical yield and diastereoselectivity (entry 1 vs 2). Similarly excellent results were obtained in the reactions of 4-Cl-Phe (*S*)-**22j** (entry 3) and 4-Me-Phe (*S*)-**22ee** (entry 4) with ligand (*S*)-**17** furnishing diastereomerically pure products (S_a)(R_c)-**23j,ee**. An interesting example of disubstituted

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

Scheme 4. Disassembly of $(S_a)(R_c)$-23j,y,bb, and $(R_a)(S_c)$-hh: Isolation of the Target AAs (R)-22j,y,bb and (S)-22hh, Recycling, and Reuse of the Chiral Ligands (S)-17 and (R)-17



derivative 3,4-difluoro-Phe **22ff** is presented in entry 5. In this case, the reaction of (R)-**22ff** with (R)-**17** resulted in a complete inversion of the α-configuration giving rise to complex $(R_a)(S_c)$-**23ff** with an excellent yield and stereoselectivity. Sterically bulky β-Ph-Phe (S)-**22gg** reacted with ligand (S)-**17** at relatively high rate; however, the diastereoselectivity was less than expected (entry 6). Three more examples featuring (R)-to-(S) conversion of thienylalanine (R)-**22hh** (entry 7), propargylglycine (R)-**22ii** (entry 8), and (S)-to-(R) transformation of *n*-butylglycine (S)-**22y** (entry 9) provide some additional evidence of the wide range of structural generality of this method.

Disassembly of Products 23, Isolation of Free Amino Acids 22, and Recovery/Reuse of Chiral Ligands 17. To demonstrate the isolation of free α-AAs from products **23**, we selected *para*-Cl-Phe (R)-**22j** (Scheme 4) of known pharmaceutical importance,[4] quite interesting long-chain *n*-butyl (R)-**24y**, and sterically constrained cyclobutyl (R)-**24bb** containing AAs, as well as an example of heterocyclic thienylalanine (S)-**22hh**, representing both the DTR and *S*/*R*-interconversion approaches. Disassembly of Ni(II) complexes of amino acid Schiff bases is usually conducted under acidic conditions with an option to isolate the target free amino acid or conduct its *N*-derivatization in situ.[8] Taking advantage of the truly exceptional stereochemical outcome (DTR approach; Table 1, entry 10) obtained in the preparation of $(S_a)(R_c)$-**23j**, we performed its disassembly without any additional purification. Due to a relatively high solubility of Ni(II) complex $(S_a)(R_c)$-**23j** in methanol (Scheme 4), its disassembly under the action of 6 N HCl occurred at very high rate to afford enantiomerically pure (> 99% ee) free (R)-4-Cl-phenylalanine **22j** in an excellent isolated yield (95%). Similarly, diastereomerically pure Ni(II) complexes $(S_a)(R_c)$-**23y**, $(S_a)(R_c)$-**23bb**, obtained using DTR and $(R_a)(S_c)$-**23hh**, using the *S*/*R*-interconversion approach, were disassembled to furnish free amino acids (R)-**22y**, (R)-**22bb**, and (S)-**22hh** in > 90% yields.

It should be emphasized that along with the target AAs (R)-**22j,y,bb** and (S)-**22hh**, ligands (S)-**17** and (R)-**17** were virtually quantitatively (>95% yield) recovered. Without any additional purification, ligands (S)-**17** and (R)-**17** can be successfully reused for DTR or *S*/*R* interconversion of any target α-AA. One may agree that convenient recycling and reuse of the chiral ligands **17** render the present approach economically very attractive, surpassing efficiency and practicality of biocatalytic approaches.

Assignment of the Absolute Configurations and Rationale for the Observed Stereochemical Outcome. The absolute configuration of α-AA residues in products $(S_a)(R_c)$-**23j,y,bb** and $(R_a)(S_c)$-**23hh** was made by comparison of the optical properties of isolated AAs (R)-**22j,y,bb** and (S)-**22hh** with the literature data. Furthermore, we performed a crystallographic analysis of Ni(II) complex **23j**, confirming its $(S_a)(R_c)$ configuration (see CIF and Figure S2 in the Supporting Information). Stereochemistry of other products **23a−i,k−x,z−aa,cc−gg**, was assigned on the basis of their matching

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

spectroscopic and optical properties with complexes $(S_a)(R_c)$-**23j,y,bb** and $(R_a)(S_c)$-**23hh**.

The crystallographic structure of Ni(II) complex $(S_a)(R_c)$-**23j**, containing a (*R*)-4-Cl-Phe moiety, has several unexpected, rather unique features.[23] First, strikingly, there are no stereochemical contacts between the chiral auxiliary's bisnaphthyl frame and the amino acid residue. What is evident from the structure is that the observed preference for the (*R*) absolute configuration of the (*R*)-4-Cl-Phe moiety is not directly controlled by the chiral auxiliary. Another prominent peculiarity of the crystallographic structure of $(S_a)(R_c)$-**23j** is a notably severe twisting of the chelate rings around the Ni(II). Thus, while the coordination to Ni(II) by the three nitrogen and one oxygen atoms is nearly perfectly coplanar, the chelate rings **A**, **B**, and **C** (Figure 5) are

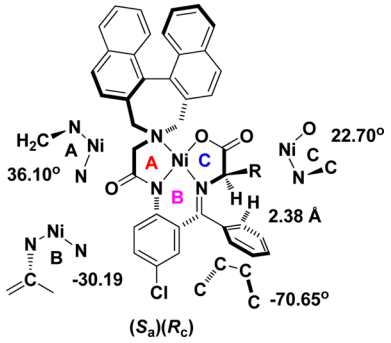


Figure 5. Mechanistic rationale for the observed stereochemical outcome in the DTR and *S*/*R*-interconversion methods.

noticeably puckered out of this plane. In particular, the ring **A** is puckered up above the plane, showing a torsion angle (N−Ni−N−CH_2) of 36.10°. By contrast, the ring **B** is puckered down out of this plane with a torsion angle (N−Ni−N−-C) of −30.19°. Subsequently, the ring **C** is puckered up above the plane. As a result of this sterically congested arrangement, the benzophenone phenyl ring is skewed by −70.65° and located right below the chelate ring **C**. The distance between the phenyl *ortho*-hydrogen and the hydrogen of the amino acid C−H group is only 2.38 Å, strongly indicating that the position of the 4-Cl-benzyl group up and away from the phenyl is the only stereochemically feasible option. On the basis of these structural features, one can assume the following mode of the observed stereocontrol. First, the helical chirality of the bisnaphthyl moiety induces the chiral puckering of the three chelate rings **A**, **B**, and **C** up and down the Ni(II) coordination plane. Second, the phenyl group of the ring **B** is positioned underneath the amino acid bearing ring **C**, forcing the R substituent to be pointed in the opposite direction, avoiding any repulsive stereochemical interactions. One might agree that this type of indirect asymmetric induction is rather distinctive to these Ni(II) complexes.

CONCLUSIONS

In summary, we have developed an advanced purely chemical DTR and *S*/*R*-interconversion methods for preparation of tailor-made, unnatural α-AAs using novel axially chiral ligands (*S*)- and (*R*)-**17**. These approaches can be used starting directly from unprotected α-AAs. All reactions can be conducted under operationally convenient conditions with good-to-excellent chemical yields and stereoselectivity (up to > 99:1). These methods show broad structural generality as demonstrated on 35 examples including various α-benzyl-, α-alkyl-, α-alkenyl, and α-heteroaryl-containing tailor-made α-AAs. The source of chirality in the presented methods, specially designed chiral and nonracemizable ligands (*S*)-**17** and (*R*)-**17**, can be virtually completely recycled and reused for continuous production of the target enantiomerically pure α-AAs. Overall, the operational ease of the presented methods coupled with structural generality and attractive stereochemical outcome bode well for their widespread practical applications.

EXPERIMENTAL SECTION

General Information. The chemicals were purchased from commercial sources and used without further purification. Analytical thin-layer chromatography (TLC) was performed on HSGF 254 (0.15−0.2 mm thickness). All products were characterized by NMR and MS spectra. ^{1}H and ^{13}C NMR spectra were recorded in deuterochloroform ($CDCl_3$), dimethyl sulfoxide-d_6 (DMSO-d_6), or deuterium oxide (D_2O) on a 400 or 500 MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (p), doublet of triplets (dt), and multiplet (m). High-resolution mass spectra (HRMS) were measured on a Q-TOF spectrometer. The determination of dr was performed via LC/MS analysis. The determination of ee was performed via HPLC analysis or UFLC analysis. Optical rotations were measured using a 1 mL cell with a 10 mm path length on an automatic polarimeter and were reported as follows: $[\alpha]^{25}_D$ (*c*: g/100 mL, in solvent). Melting points were measured on a melting point apparatus. All physicochemical data reported for the Ni(II) complexes are due to the single diastereomer after purification by chromatography or crystallization.

General Procedure. *General Procedure for the Synthesis of* $(R_a)(S_c)$-***23a***. A suspension of (*R*)-**17** (100 mg, 0.176 mmol, 1 equiv), *rac*-6-Cl-tryptophan **22a** or (*R*)-6-Cl-tryptophan **22a** (46 mg, 0.194 mmol, 1.1 equiv), $Ni(OAc)_2{\cdot}4H_2O$ (48 mg, 0.194 mmol, 1.1 equiv), and K_2CO_3 (146 mg, 1.06 mmol, 6 equiv) was refluxed in methanol (6 mL) at 70 °C for 2 h. After cooling, the mixture was diluted with icy 2.5% aqueous acetic acid (25 mL) and then extracted three times with dichloromethane. The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. The crude reaction mixture was subjected to column chromatography on silica gel. Eluent PE/EA = 4:1 was used to remove the residual ligand (*R*)-**17** followed by using eluent DCM/MeOH = 20:1 to obtain the mixture of the two diastereomers $(R_a)(S_c)$-**23a** and $(R_a)(R_c)$-**23a** (144 mg, yield 97%) for analysis (dr = 99:1). The mixture was purified again by column chromatography on silica gel (DCM/MeOH = 80:1) to give the major pure diastereomer $(R_a)(S_c)$-**23a** as a red solid.

Large-Scale Preparation of $(S_a)(R_c)$-***23w***. A suspension of (*R*)-**17** (10.0 g, 17.6 mmol, 1 equiv), *rac*-cyclohexylalanine **22w** (3.3 g, 19.4 mmol, 1.1 equiv), $Ni(OAc)_2{\cdot}4H_2O$ (4.8 g, 19.4 mmol, 1.1 equiv), and K_2CO_3 (14.6 g, 106 mmol, 6 equiv) was refluxed in methanol (100 mL) at 70 °C for 12 h. After cooling, the mixture was concentrated in vacuo, and then the residue was dissolved in dichloromethane, diluted with icy 2.5% aqueous acetic acid (500 mL), and extracted three times with dichloromethane. The combined organic layers were dried with Na_2SO_4, concentrated in vacuo, and then purified by column chromatography on silica gel to give the crude products $(R_a)(S_c)$-**23w** and $(R_a)(R_c)$-**23w** (13.3 g, yield 97%) for analysis (dr >99:1). The crude products were purified again by recrystallization in ethanol to give the major pure diastereomer $(R_a)(S_c)$-**23w** as a red solid (12.9 g, yield 94%).

*General Procedure for the Synthesis of (R)-**22j***. A suspension of $(S_a)(R_c)$-**23j** (500 mg, 0.621 mmol, 1 equiv) in methanol (15 mL) was added 6 N HCl, and the whole was heated at 40 °C for 6 h. The reaction mixture was concentrated to dryness upon disappearance of the red color of the starting complex. The residue was added ethyl acetate (20 mL) and water (5 mL), stirred, and separated. The organic phase was extracted sequentially with 1 N HCl (4 mL) and water (4 mL). The resulting organic phase was washed with saturated sodium hydrogen carbonate solution (5 mL), water (5 mL), and brine (5 mL), dried with Na_2SO_4, and concentrated to afford the recovered (*S*)-**17** (341 mg, yield 97%). The combined aqueous phase was evaporated in vacuo to the residue, which was dissolved in methanol (4 mL) and separated by

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

preparative performance liquid chromatography using an Agilent 1200 Series spectrometer with Eclipse XDB-C18 column (9.4 × 250 mm, 5 μm) (MeOH/H_2O = 5/95, λ= 214 nm, 5.0 mL/min) to afford pure (*R*)-**22j** as a white solid (118 mg, yield 95%).

*General Procedure for the Synthesis of (R)-**22y**.* A suspension of (S_a)(R_c)-**23y** (500 mg, 0.621 mmol, 1 equiv) in methanol (15 mL) was added 6 N HCl, and the whole was heated at 40 °C for 8 h. The reaction mixture was concentrated to dryness upon disappearance of the red color of the starting complex. To the residue were added ethyl acetate (20 mL) and water (5 mL), and the mixture was stirred and separated. The organic phase was extracted sequentially with 1 N HCl (4 mL) and water (4 mL). The resulting organic phase was washed with saturated sodium hydrogen carbonate solution (5 mL), water (5 mL), and brine (5 mL), dried with Na_2SO_4, and concentrated to afford the recovered (*S*)-**17** (373 mg, yield 97%). The combined aqueous phase was evaporated in vacuo to the residue, which was redissolved in a minimum amount deionized water and loaded on a Dowex 50 × 2 100 ion-exchange column. The column was washed with deionized water until neutral and then washed with 10% aq NH_4OH. The first fraction (400 mL) was collected and evaporated under vacuum to afford (*R*)-**22y** as a white solid (82 mg, yield 93%).

*General Procedure for the Synthesis of (R)-**24y**.* *N*-[(Benzyloxy)-carbonyl]oxysuccinimide (114 mg, 0.457 mmol, 1 equiv) was dissolved in 1 mL of acetone at 0 °C, which was added a solution of (*R*)-**22y** (60 mg, 0.457 mmol, 1 equiv), sodium hydrogen carbonate (77 mg, 0.914 mmol, 2 equiv), and sodium carbonate (49 mg, 0.457 mmol, 1 equiv) in water (3 mL) and acetone (1 mL). The whole was stirred at room temperature for 12 h and then concentrated to remove the acetone. The residual aqueous phase was acidified with 1 N HCl to pH 4, and then the white solid was precipitated out. The solid was collected by filtration to afford (*R*)-**24y** (109 mg, yield 90%, ee >99%).

Analytical Characterization Data of Products. *Nickel(II)−(R)-17/(S)-6-chlorotryptophan Schiff base complex **23a**:* red solid (144 mg, yield 97%); mp 277.8−279.6 °C; $[\alpha]^{25}_D$ = +2134 (*c* 0.058, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 9.3 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 1.0 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.57 (m, 3H), 7.51−7.41 (m, 2H), 7.38 (d, *J* = 8.8 Hz, 1H), 7.34−7.27 (m, 2H), 7.25−7.17 (m, 3H), 7.11 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 1.5 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 4.46 (d, *J* = 12.1 Hz, 1H), 4.16 (dd, *J* = 5.5, 1.5 Hz, 1H), 3.47 (s, 1H), 3.32 (d, *J* = 14.3 Hz, 1H), 3.26 (d, *J* = 15.8 Hz, 1H), 2.83 (d, *J* = 14.0 Hz, 1H), 2.68 (dd, *J* = 14.5, 6.2 Hz, 1H), 2.50 (d, *J* = 15.3 Hz, 1H), 2.40 (d, *J* = 12.3 Hz, 1H), 1.49 (d, *J* = 14.4 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.8, 173.5, 168.4, 141.5, 137.3, 135.3, 134.0, 133.4, 133.4, 132.4, 131.5, 131.5, 131.3, 130.6, 130.4, 130.3, 129.4, 129.1, 128.7, 128.6, 128.6, 128.5, 128.5, 128.1, 128.1, 127.9, 127.4, 126.9, 126.7, 126.7, 126.5, 126.3, 126.3, 125.4, 124.0, 121.4, 119.4, 111.4, 108.9, 79.2, 71.0, 64.8, 60.3, 59.8, 55.7, 29.1, 20.8, 14.1; HRMS (ESI) *m*/*z* calcd for $C_{48}H_{34}Cl_2N_4NiO_3Na^+$ [M + Na]$^+$ 865.1254, found 865.1248. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 15.530 min, t_R (minor diastereomer) = 21.123 min, dr = 99:1.

*Nickel(II)−(S)-17/(R)-2-bromophenylalanine Schiff base complex **23b**:* red solid (142 mg, yield 95%); mp 233.5−235.1 °C; $[\alpha]^{25}_D$ = −2230 (*c* 0.044, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.1 Hz, 1H), 8.45 (d, *J* = 9.1 Hz, 1H), 8.22−8.03 (m, 2H), 8.01−7.87 (m, 3H), 7.68−7.40 (m, 10H), 7.40−7.16 (m, 6H), 6.75 (d, *J* = 2.2 Hz, 1H), 4.57 (d, *J* = 12.4 Hz, 1H), 4.24 (t, *J* = 2.7 Hz, 1H), 3.85 (d, *J* = 15.4 Hz, 1H), 3.19 (dd, *J* = 14.0, 4.8 Hz, 2H), 3.07 (dd, *J* = 13.8, 3.5 Hz, 1H), 2.76 (d, *J* = 15.3 Hz, 1H), 2.69 (d, *J* = 13.9 Hz, 1H), 2.53 (d, *J* = 12.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 173.4, 170.2, 141.1, 136.5, 135.5, 134.8, 133.7, 133.6, 133.2, 133.1, 132.3, 132.2, 132.1, 131.0, 130.7, 130.6, 129.9, 129.1, 128.9, 128.8, 128.8, 128.6, 128.2, 128.2, 128.1, 128.0, 128.0, 127.4, 127.0, 126.9, 126.5, 126.0, 126.0, 125.4, 124.7, 72.0, 65.6, 61.0, 57.2, 38.0; HRMS (ESI) *m*/*z* calcd for $C_{46}H_{34}BrClN_3NiO_3^+$ [M + H]$^+$ 848.0820, found 848.0811. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 33.869 min, t_R (minor diastereomer) = 54.419 min, dr = 98:2.

*Nickel(II)−(S)-17/(R)-2-methoxyphenylalanine Schiff base complex **23c**:* red solid (99 mg, yield 70%); mp 211.1−212.0 °C; $[\alpha]^{25}_D$ = −1223 (*c* 0.056, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.2 Hz, 1H), 8.32 (d, *J* = 9.0 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.99−7.89 (m, 3H), 7.79 (t, *J* = 7.4 Hz, 1H), 7.59−7.44 (m, 6H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.36−7.29 (m, 3H), 7.29−7.18 (m, 5H), 7.09 (d, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 1.8 Hz, 1H), 4.52 (d, *J* = 12.2 Hz, 1H), 4.14−4.07 (m, 1H), 3.63 (d, *J* = 15.3 Hz, 1H), 3.37 (s, 3H), 3.21 (dd, *J* = 13.7, 6.1 Hz, 2H), 2.85 (d, *J* = 14.0 Hz, 1H), 2.66 (dd, *J* = 13.3, 1.9 Hz, 1H), 2.60 (d, *J* = 15.3 Hz, 1H), 2.38 (d, *J* = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.8, 174.3, 170.3, 159.0, 141.1, 136.0, 135.2, 134.0, 133.7, 133.7, 133.1, 132.2, 132.2, 131.5, 131.2, 131.1, 130.2, 129.4, 129.4, 129.2, 129.1, 129.0, 128.9, 128.6, 128.5, 128.4, 127.9, 127.7, 127.4, 127.4, 127.1, 126.5, 126.4, 126.3, 125.8, 125.4, 125.1, 121.3, 110.3, 72.6, 65.9, 61.5, 57.6, 54.8, 33.2; HRMS (ESI) *m*/*z* calcd for $C_{47}H_{36}ClN_3NiO_4Na^+$ [M + Na]$^+$: 822.1640, found 822.1630. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 37.472 min, t_R (minor diastereomer) = 65.897 min, dr = 96:4.

*Nickel(II)−(S)-17/(R)-2-hydroxyphenylalanine Schiff base complex **23d**:* red solid (136 mg, yield 98%); mp 246.2−247.9 °C; $[\alpha]^{25}_D$ = −2186 (*c* 0.050, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 9.0 Hz, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 2H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.66 (t, *J* = 8.1 Hz, 1H), 7.59−7.41 (m, 8H), 7.38−7.27 (m, 4H), 7.25−7.18 (m, 4H), 6.74 (d, *J* = 2.5 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.19 (dd, *J* = 5.0, 2.7 Hz, 1H), 3.74 (d, *J* = 15.7 Hz, 1H), 3.17 (d, *J* = 14.0 Hz, 1H), 3.10 (dd, *J* = 13.5, 5.2 Hz, 1H), 2.87 (d, *J* = 14.1 Hz, 1H), 2.75−2.63 (m, 2H), 2.53 (d, *J* = 12.2 Hz, 1H), 1.99 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.1, 173.6, 169.0, 157.3, 141.6, 135.6, 135.5, 134.1, 134.1, 133.5, 132.7, 132.6, 132.5, 131.7, 131.6, 131.2, 131.1, 130.7, 130.5, 130.4, 130.1, 129.4, 129.1, 128.9, 128.8, 128.8, 128.6, 128.5, 128.4, 128.3, 127.9, 127.4, 126.7, 126.5, 126.3, 126.2, 125.4, 123.8, 122.7, 119.5, 115.3, 71.5, 65.3, 60.5, 56.4, 32.4; HRMS (ESI) *m*/*z* calcd for $C_{46}H_{35}ClN_3NiO_4^+$ [M + H]$^+$ 786.1664, found 786.1667. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 29.411 min, t_R (minor diastereomer) = 51.382 min, dr = 97:3.

*Nickel(II)−(S)-17/(R)-2-cyanophenylalanine Schiff base complex **23e**:* red solid (108 mg, yield 77%); mp 240.8−242.0 °C; $[\alpha]^{25}_D$ = −1743 (*c* 0.044, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.3 Hz, 1H), 8.50 (d, *J* = 9.1 Hz, 1H), 8.13−8.07 (m, 2H), 7.94 (t, *J* = 8.2 Hz, 3H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.80 (t, *J* = 7.1 Hz, 1H), 7.61−7.39 (m, 9H), 7.34−7.19 (m, 5H), 6.75 (d, *J* = 2.3 Hz, 1H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.29 (t, *J* = 4.1 Hz, 1H), 3.68 (d, *J* = 15.2 Hz, 1H), 3.19 (d, *J* = 14.0 Hz, 1H), 3.16−3.05 (m, 2H), 2.76 (d, *J* = 15.3 Hz, 1H), 2.65 (d, *J* = 13.9 Hz, 1H), 2.50 (d, *J* = 12.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 173.3, 171.6, 141.1, 140.2, 135.5, 134.9, 133.6, 133.3, 133.2, 132.6, 132.3, 132.2, 131.0, 130.7, 130.5, 130.0, 129.2, 128.9, 128.7, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.4, 127.0, 126.9, 126.7, 126.5, 126.1, 126.0, 126.0, 125.5, 124.4, 117.8, 114.9, 71.4, 65.5, 61.0, 57.5, 37.4; HRMS (ESI) *m*/*z* calcd for $C_{47}H_{34}ClN_4NiO_3^+$ [M + H]$^+$ 795.1667, found 795.1686. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 19.638 min, t_R (minor diastereomer) = not found, dr >99:1.

*Nickel(II)−(S)-17/(R)-3-bromophenylalanine Schiff base complex **23f**:* red solid (145 mg, yield 97%); mp 236.5−238.4 °C; $[\alpha]^{25}_D$ = −2000 (*c* 0.048, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.2 Hz, 1H), 8.36 (d, *J* = 9.1 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 8.02−7.88 (m, 4H), 7.79 (s, 1H), 7.64−7.44 (m, 7H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.30−7.20 (m, 4H), 7.18 (d, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.1 Hz, 1H), 6.69 (d, *J* = 1.7 Hz, 1H), 4.56 (d, *J* = 12.2 Hz, 1H), 4.22 (dd, *J* = 5.2, 2.7 Hz, 1H), 3.74 (d, *J* = 15.3 Hz, 1H), 3.31 (d, *J* = 14.0 Hz, 1H), 3.03 (d, *J* = 14.2 Hz, 1H), 2.99 (dd, *J* = 13.8, 2.2 Hz, 1H), 2.69 (d, *J* = 15.4 Hz, 1H), 2.53 (dd, *J* = 13.6, 5.7 Hz, 1H), 2.49 (d, *J* = 12.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 173.7, 169.7, 141.0, 138.5, 135.7, 134.8, 133.7, 133.6, 133.2, 132.5, 132.3, 132.0, 131.1, 130.7, 130.7, 130.5,

DOI: 10.1021/acs.joc.5b01292
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130.1, 130.1, 129.9, 129.0, 129.0, 128.8, 128.7, 128.4, 128.1, 128.0, 127.6, 127.4, 127.1, 127.0, 126.9, 126.8, 126.6, 126.1, 126.0, 125.9, 125.9, 125.7, 124.7, 123.0, 71.1, 65.5, 61.2, 57.5, 38.0; HRMS (ESI) m/z calcd for $C_{46}H_{34}BrClN_3NiO_3^+$ $[M + H]^+$: 848.0820, found 848.0819. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 32.911 min, t_R (minor diastereomer) = 58.600 min, dr = 94:6.

Nickel(II)−(S)-17/(R)-3-hydroxyphenylalanine Schiff base complex ***23g:*** red solid (136 mg, yield 98%); mp 242.1−243.0 °C; $[\alpha]^{25}_D$ = −2352 (c 0.048, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 9.23 (s, 1H), 8.37 (d, J = 9.1 Hz, 1H), 8.18 (d, J = 7.5 Hz, 2H), 8.11 (t, J = 9.7 Hz, 2H), 7.70−7.49 (m, 5H), 7.45−7.12 (m, 9H), 6.91 (s, 1H), 6.74 (d, J = 6.5 Hz, 2H), 6.23 (s, 1H), 4.55 (d, J = 12.0 Hz, 1H), 3.89 (d, J = 15.0 Hz, 1H), 3.83 (s, 1H), 3.17 (d, J = 13.3 Hz, 1H), 3.03 (d, J = 13.9 Hz, 1H), 2.71 (d, J = 13.3 Hz, 1H), 2.46−2.31 (m, 2H), 2.08 (d, J = 10.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.1, 174.2, 169.1, 158.4, 142.1, 137.8, 136.0, 134.5, 134.0, 133.9, 132.8, 132.0, 131.7, 131.2, 130.9, 130.8, 130.2, 129.9, 129.6, 129.3, 129.2, 129.1, 129.1, 128.8, 128.4, 128.3, 127.8, 127.2, 127.1, 126.9, 126.9, 126.8, 126.7, 125.9, 124.5, 122.5, 118.4, 115.3, 71.7, 65.9, 61.0, 56.8, 38.7; HRMS (ESI) m/z calcd for $C_{46}H_{35}ClN_3NiO_4^+$ $[M + H]^+$: 786.1664, found 786.1666. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 23.764 min, t_R (minor diastereomer) = 32.856 min, dr = 94:6.

Nickel(II)−(S)-17/(R)-3-methoxyphenylalanine Schiff base complex ***23h:*** red solid (140 mg, yield 99%); mp 234.2−235.7 °C; $[\alpha]^{25}_D$ = −2142 (c 0.048, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 8.3 Hz, 1H), 8.37 (d, J = 9.1 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 7.99−7.92 (m, 3H), 7.62−7.44 (m, 6H), 7.43−7.30 (m, 4H), 7.28−7.21 (m, 3H), 7.18 (d, J = 7.4 Hz, 1H), 7.10−7.05 (m, 2H), 6.96 (d, J = 7.5 Hz, 1H), 6.67 (d, J = 2.5 Hz, 1H), 4.56 (d, J = 12.2 Hz, 1H), 4.21 (dd, J = 5.3, 3.0 Hz, 1H), 3.84 (s, 3H), 3.78 (d, J = 15.3 Hz, 1H), 3.25 (d, J = 13.9 Hz, 1H), 3.00 (dd, J = 13.4, 2.7 Hz, 1H), 2.90 (d, J = 13.8 Hz, 1H), 2.63 (d, J = 15.2 Hz, 1H), 2.56 (dd, J = 13.5, 5.4 Hz, 1H), 2.45 (d, J = 12.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 173.8, 169.3, 159.9, 140.9, 137.5, 135.6, 134.8, 133.6, 133.2, 132.4, 132.3, 131.9, 131.0, 130.7, 130.6, 130.0, 129.5, 129.0, 128.9, 128.8, 128.6, 128.4, 128.2, 128.0, 127.8, 127.5, 127.1, 127.0, 126.9, 126.6, 126.1, 125.9, 125.9, 125.6, 124.8, 123.5, 115.6, 113.9, 71.5, 65.5, 61.1, 57.1, 55.0, 38.6; HRMS (ESI) m/z calcd for $C_{47}H_{37}ClN_3NiO_4^+$ $[M + H]^+$ 800.1821, found 800.1827. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 30.174 min, t_R (minor diastereomer) = 48.851 min, dr = 91:9.

Nickel(II)−(S)-17/(R)-4-bromophenylalanine Schiff base complex ***23i:*** red solid (148 mg, yield 99%); mp 250.0−250.9 °C; $[\alpha]^{25}_D$ = −1896 (c 0.056, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 8.3 Hz, 1H), 8.40 (d, J = 9.1 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.94 (t, J = 9.4 Hz, 2H), 7.83 (d, J = 8.1 Hz, 2H), 7.66−7.27 (m, 11H), 7.26−7.12 (m, 3H), 7.05 (d, J = 7.2 Hz, 1H), 6.68 (d, J = 2.6 Hz, 1H), 4.62 (d, J = 12.2 Hz, 1H), 4.20 (t, J = 4.0 Hz, 1H), 3.76 (d, J = 15.6 Hz, 1H), 3.19 (d, J = 13.8 Hz, 1H), 2.92 (dd, J = 13.5, 3.3 Hz, 1H), 2.73 (dd, J = 14.7, 9.0 Hz, 2H), 2.55 (dd, J = 13.6, 4.8 Hz, 1H), 2.47 (d, J = 12.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6, 173.9, 169.8, 140.9, 135.6, 134.8, 134.7, 133.5, 133.2, 132.9, 132.3, 131.9, 131.5, 130.9, 130.6, 130.4, 130.0, 129.0, 128.7, 128.1, 128.0, 127.7, 127.3, 127.0, 127.0, 126.9, 126.5, 126.0, 125.9, 125.8, 125.7, 124.8, 121.5, 71.3, 65.5, 61.2, 57.5, 38.1; HRMS (ESI) m/z calcd for $C_{46}H_{33}BrClN_3NiO_3Na^+$ $[M + Na]^+$ 870.0640, found 870.0635. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 46.207 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(S)-17/(R)-4-chlorophenylalanine Schiff base complex ***23j:*** red solid (702 mg, yield 99%); mp 256.5−257.9 °C; $[\alpha]^{25}_D$ = −2067 (c 0.052, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 8.2 Hz, 1H), 8.39 (d, J = 9.2 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.95 (t, J = 8.7 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.63−7.30 (m, 11H), 7.25−7.19 (m, 2H), 7.14 (d, J = 7.7 Hz, 1H), 7.05 (d, J = 7.2 Hz, 1H), 6.66 (d, J = 2.4 Hz, 1H), 4.61 (d, J = 12.0 Hz, 1H), 4.20 (t, J = 3.2 Hz, 1H), 3.75 (d, J = 15.6 Hz, 1H), 3.19 (d, J = 13.7 Hz, 1H), 2.95 (dd, J = 13.4, 2.7 Hz, 1H), 2.71 (dd, J = 14.6, 4.6 Hz, 2H), 2.57 (dd, J = 13.2, 4.7 Hz, 1H), 2.45 (d, J = 12.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 174.4, 170.2, 141.4, 136.1, 135.2, 134.9, 134.0, 133.9, 133.7, 133.0, 132.8, 132.4, 131.5, 131.1, 130.9, 130.5, 129.5, 129.5, 129.3, 129.1, 128.6, 128.5, 128.5, 128.2, 127.8, 127.5, 127.4, 127.0, 126.5, 126.4, 126.3, 126.2, 125.3, 71.9, 66.0, 61.7, 58.0, 38.5; HRMS (ESI) m/z calcd for $C_{46}H_{34}Cl_2N_3NiO_3^+$ $[M + H]^+$ 804.1325, found 804.1303. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 17.230 min, t_R (minor diastereomer) = 20.807 min, dr = 99:1.

Nickel(II)−(S)-17/(R)-4-fluorophenylalanine Schiff base complex ***23k:*** red solid (138 mg, yield 99%); mp 210.5−212.0 °C; $[\alpha]^{25}_D$ = −2385 (c 0.052, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 8.3 Hz, 1H), 8.38 (d, J = 9.2 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.03−7.87 (m, 3H), 7.66−7.26 (m, 14H), 7.24−7.15 (m, 2H), 7.05 (d, J = 7.1 Hz, 1H), 6.68 (s, 1H), 4.60 (d, J = 12.2 Hz, 1H), 4.20 (t, J = 3.9 Hz, 1H), 3.75 (d, J = 15.5 Hz, 1H), 3.22 (d, J = 13.9 Hz, 1H), 2.96 (d, J = 13.0 Hz, 1H), 2.73 (t, J = 14.5 Hz, 2H), 2.58 (dd, J = 14.0, 4.6 Hz, 1H), 2.48 (d, J = 12.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 173.8, 169.7, 162.4 (d, J = 246.0 Hz), 140.8, 135.6, 134.7, 133.5, 133.2, 132.6 (d, J = 7.0 Hz), 132.3, 131.9, 131.6, 131.0, 130.6, 130.4, 130.0, 129.0, 128.8, 128.8, 128.1, 128.0, 127.8, 127.3, 126.9, 126.9, 126.7, 126.6, 126.0, 125.9, 125.7, 124.7, 115.3 (d, J = 21.2 Hz), 71.5, 65.6, 61.2, 57.5, 37.9; HRMS (ESI) m/z calcd for $C_{46}H_{33}ClFN_3NiO_3Na^+$ $[M + Na]^+$ 810.1440, found 810.1429. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 23.932 min, t_R (minor diastereomer) = 40.639 min, dr = 99:1.

Nickel(II)−(S)-17/(R)-4-trifluoromethylphenylalanine Schiff base complex ***23l:*** red solid (136 mg, yield 92%); mp 242.0−243.9 °C; $[\alpha]^{25}_D$ = −2121 (c 0.072, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 8.3 Hz, 1H), 8.41 (d, J = 9.2 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 8.00−7.91 (m, 5H), 7.65−7.53 (m, 5H), 7.52−7.44 (m, 2H), 7.39 (d, J = 8.4 Hz, 1H), 7.35−7.19 (m, 6H), 7.08 (d, J = 7.4 Hz, 1H), 6.71 (d, J = 2.5 Hz, 1H), 4.59 (d, J = 12.2 Hz, 1H), 4.27−4.24 (m, 1H), 3.56 (d, J = 15.6 Hz, 1H), 3.20 (d, J = 14.3 Hz, 1H), 3.02 (dd, J = 13.4, 3.4 Hz, 1H), 2.72 (d, J = 15.5 Hz, 1H), 2.65 (dd, J = 13.5, 5.0 Hz, 1H), 2.58 (d, J = 14.0 Hz, 1H), 2.48 (d, J = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 174.2, 170.5, 141.5, 140.6, 136.1, 135.2, 134.0, 133.7, 133.0, 132.8, 132.5, 131.9, 131.4, 131.1, 130.8, 130.6, 130.3 (q, J = 32.4 Hz), 129.5, 129.3, 129.3, 128.6, 128.5, 128.4, 128.1, 127.8, 127.5, 127.4, 127.3, 127.1, 126.9, 126.5, 126.4, 126.4, 126.3, 126.2, 125.7 (q, J = 3.3 Hz), 125.2, 124.5 (q, J = 272.1 Hz), 71.6, 65.7, 61.5, 58.0, 38.8; HRMS (ESI) m/z calcd for $C_{47}H_{34}ClF_3N_3NiO_3^+$ $[M + H]^+$: 838.1589, found 838.1569. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 37.403 min, t_R (minor diastereomer) = 63.798 min, dr = 94:6.

Nickel(II)−(S)-17/(R)-4-acetylphenylalanine Schiff base complex ***23m:*** red solid (112 mg, yield 78%); mp 236.8−238.7 °C; $[\alpha]^{25}_D$ = −2145 (c 0.040, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.3 Hz, 1H), 8.34 (d, J = 9.0 Hz, 1H), 8.26 (d, J = 7.8 Hz, 2H), 8.08 (d, J = 8.6 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.94 (dd, J = 11.1, 8.4 Hz, 2H), 7.65−7.53 (m, 5H), 7.48 (q, J = 8.3 Hz, 2H), 7.40 (d, J = 8.5 Hz, 1H), 7.35−7.18 (m, 6H), 7.10 (d, J = 6.7 Hz, 1H), 6.73 (d, J = 2.2 Hz, 1H), 4.57 (d, J = 12.1 Hz, 1H), 4.27−4.23 (m, 1H), 3.47 (d, J = 15.7 Hz, 1H), 3.18 (d, J = 13.8 Hz, 1H), 3.06 (dd, J = 13.2, 3.1 Hz, 1H), 2.79 (s, 3H), 2.73−2.60 (m, 3H), 2.48 (d, J = 12.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 176.7, 173.8, 169.9, 141.5, 140.9, 136.9, 135.7, 134.6, 133.5, 133.2, 132.4, 132.3, 132.0, 131.3, 131.0, 130.6, 130.4, 130.1, 129.1, 129.0, 128.8, 128.3, 128.1, 128.1, 128.0, 127.7, 127.4, 127.0, 127.0, 126.8, 126.7, 126.6, 126.1, 126.0, 125.9, 125.9, 125.8, 124.8, 71.2, 65.2, 61.2, 57.5, 38.5, 26.6; HRMS (ESI) m/z calcd for $C_{48}H_{37}ClN_3NiO_4^+$ $[M + H]^+$: 812.1821, found 812.1821. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min). t_R (major diastereomer) = 23.559 min, t_R (minor diastereomer) = 37.073 min, dr = 93:7.

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

Nickel(II)−(S)-17/(R)-3-(2-Naphthyl)alanine Schiff Base Complex ***23n.*** red solid (142 mg, yield 98%). mp 242.4−243.8 °C. $[\alpha]^{25}_{D}$ = −2443 (*c* 0.044, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.1 Hz, 1H), 8.32 (d, *J* = 9.2 Hz, 1H), 8.25 (dd, *J* = 7.6, 4.4 Hz, 2H), 8.10 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.69−7.32 (m, 11H), 7.29−7.17 (m, 5H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.74 (d, *J* = 2.1 Hz, 1H), 4.38 (d, *J* = 12.1 Hz, 1H), 4.36−4.32 (m, 1H), 3.74−3.65 (m, 1H), 3.06 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.99 (d, *J* = 15.4 Hz, 1H), 2.70 (d, *J* = 14.0 Hz, 1H), 2.29 (t, *J* = 13.5 Hz, 2H), 1.53 (d, *J* = 14.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 174.0, 169.4, 141.4, 135.8, 135.1, 134.4, 134.0, 134.0, 133.5, 133.1, 132.7, 132.7, 132.4, 131.4, 131.1, 130.8, 130.5, 130.5, 129.5, 129.4, 129.2, 128.9, 128.7, 128.6, 128.4, 128.0, 127.8, 127.4, 127.4, 127.2, 127.0, 126.9, 126.9, 126.4, 126.3, 126.2, 126.0, 125.2, 72.0, 65.5, 61.3, 56.7, 35.6; HRMS (ESI) *m*/*z* calcd for $C_{50}H_{37}ClN_3NiO_3^+$ $[M + H]^+$: 820.1871, found 820.1872. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 38.932 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(S)-17/(R)-1,1′-biphenylglycine Schiff base complex ***23o:*** red solid (144 mg, yield 98%); mp 258.0−258.8 °C; $[\alpha]^{25}_{D}$ = −1479 (*c* 0.048, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 8.2 Hz, 1H), 8.49 (d, *J* = 9.1 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 8.04−7.92 (m, 3H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.61−7.19 (m, 18H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.71 (s, 1H), 6.13 (d, *J* = 7.8 Hz, 1H), 4.92 (d, *J* = 12.2 Hz, 1H), 4.79 (s, 1H), 4.67 (d, *J* = 15.6 Hz, 1H), 3.81 (d, *J* = 14.0 Hz, 1H), 3.71 (d, *J* = 14.1 Hz, 1H), 3.18 (d, *J* = 15.6 Hz, 1H), 2.79 (d, *J* = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 174.4, 171.7, 140.8, 140.6, 139.9, 136.3, 135.7, 135.1, 133.7, 133.3, 132.7, 132.5, 132.1, 131.1, 130.8, 130.6, 129.5, 129.1, 128.8, 128.4, 128.3, 128.3, 128.0, 127.6, 127.5, 127.1, 127.1, 127.1, 127.0, 126.9, 126.7, 126.6, 126.2, 126.0, 125.9, 125.7, 124.8, 74.3, 65.9, 61.6, 58.5; HRMS (ESI) *m*/*z* calcd for $C_{51}H_{37}ClN_3NiO_3^+$ $[M + H]^+$ 832.1871, found 832.1881. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 24.023 min, t_R (minor diastereomer) = 40.287 min, dr = 97:3.

Nickel(II)−(S)-17/(R)-3-(2-quinolyl)alanine Schiff base complex ***23p:*** red solid (133 mg, yield 92%); mp 247.8−249.2 °C; $[\alpha]^{25}_{D}$ = −1425 (*c* 0.072, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.3 Hz, 1H), 8.37 (d, *J* = 9.1 Hz, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.98−7.75 (m, 5H), 7.65−7.27 (m, 9H), 7.26−7.07 (m, 4H), 6.84 (d, *J* = 6.3 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 4.51 (d, *J* = 12.3 Hz, 1H), 4.30 (dd, *J* = 5.4, 3.6 Hz, 1H), 3.26 (dd, *J* = 12.9, 3.6 Hz, 1H), 3.02 (d, *J* = 13.7 Hz, 2H), 2.47−2.14 (m, 3H), 2.09 (d, *J* = 14.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 174.1, 170.5, 157.7, 141.3, 136.5, 135.8, 135.2, 133.9, 133.5, 133.2, 132.5, 132.4, 131.3, 131.0, 130.9, 130.4, 130.3, 130.2, 129.4, 129.2, 128.9, 128.5, 128.3, 128.3, 128.0, 127.9, 127.5, 127.4, 127.4, 127.2, 126.9, 126.4, 126.3, 126.2, 125.9, 125.1, 123.9, 71.2, 65.2, 61.5, 57.4, 41.6; HRMS (ESI) *m*/*z* calcd for $C_{49}H_{36}ClN_4NiO_3^+$ $[M + H]^+$ 821.1824, found 821.1829. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 110.603 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(R)-17/(S)-3-(3-benzothienyl)alanine Schiff base complex ***23q:*** red solid (141 mg, yield 97%); mp 238.5−241.0 °C; $[\alpha]^{25}_{D}$ = +2015 (*c* 0.046, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.3 Hz, 1H), 8.36 (d, *J* = 9.1 Hz, 1H), 8.30 (d, *J* = 8.1 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.94−7.89 (m, 3H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.65−7.26 (m, 10H), 7.24−7.05 (m, 6H), 6.70 (d, *J* = 2.6 Hz, 1H), 4.46 (d, *J* = 12.3 Hz, 1H), 4.23 (dd, *J* = 5.5, 2.9 Hz, 1H), 3.38 (dd, *J* = 14.1, 1.9 Hz, 1H), 3.23 (d, *J* = 15.3 Hz, 1H), 2.87 (dd, *J* = 14.2, 6.0 Hz, 2H), 2.39 (d, *J* = 15.2 Hz, 1H), 2.31 (d, *J* = 12.3 Hz, 1H), 1.76 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 173.8, 169.2, 141.0, 140.1, 139.8, 135.4, 134.6, 133.5, 133.0, 132.3, 132.3, 131.9, 130.9, 130.6, 130.4, 130.0, 129.0, 128.7, 128.4, 128.2, 128.1, 127.9, 127.5, 127.3, 126.9, 126.8, 126.6, 126.4, 125.9, 125.8, 125.5, 124.9, 124.8, 124.7, 123.1, 122.2, 70.8, 65.1, 61.0, 56.4, 31.8; HRMS (ESI) *m*/*z* calcd for $C_{48}H_{35}ClN_3NiO_3S^+$ $[M + H]^+$ 826.1436, found 826.1443. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 36.297 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(R)-17/(S)-3-(3-thienyl)alanine Schiff base complex ***23r:*** red solid (133 mg, yield 97%); mp 255.6−255.9 °C; $[\alpha]^{25}_{D}$ = +2125 (*c* 0.052, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 9.1 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.96 (q, *J* = 7.4, 6.8 Hz, 3H), 7.75−7.70 (m, 1H), 7.62−7.39 (m, 9H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.26−7.16 (m, 4H), 7.03 (d, *J* = 6.9 Hz, 1H), 6.68 (d, *J* = 2.0 Hz, 1H), 4.61 (d, *J* = 12.2 Hz, 1H), 4.25−4.13 (m, 1H), 4.05 (d, *J* = 15.2 Hz, 1H), 3.32 (d, *J* = 13.9 Hz, 1H), 3.21−2.93 (m, 2H), 2.74 (d, *J* = 15.3 Hz, 1H), 2.63 (dd, *J* = 13.9, 5.0 Hz, 1H), 2.50 (d, *J* = 12.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 174.4, 170.1, 141.3, 136.5, 136.1, 135.3, 134.0, 133.7, 132.9, 132.7, 132.4, 131.5, 131.2, 131.2, 131.0, 130.5, 129.4, 129.4, 129.3, 129.0, 128.8, 128.6, 128.4, 128.3, 127.8, 127.5, 127.4, 127.3, 127.0, 126.5, 126.4, 126.1, 125.4, 125.2, 125.1, 71.7, 66.0, 61.6, 57.8, 33.6; HRMS (ESI) *m*/*z* calcd for $C_{44}H_{33}ClN_3NiO_3S^+$ $[M + H]^+$ 776.1279, found 776.1284. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 28.499 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(R)-17/(S)-3-(2-pyridyl)alanine Schiff base complex ***23s:*** red solid (84 mg, yield 62%); mp 239.7−242.3 °C; $[\alpha]^{25}_{D}$ = +1846 (*c* 0.048, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.1 Hz, 1H), 8.75 (d, *J* = 8.3 Hz, 1H), 8.32 (d, *J* = 9.1 Hz, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 8.00−7.92 (m, 4H), 7.64−7.46 (m, 7H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.34−7.31 (m, 2H), 7.28−7.20 (m, 3H), 7.10 (d, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 4.61 (d, *J* = 12.2 Hz, 1H), 4.26−4.22 (m, 1H), 3.74 (d, *J* = 15.3 Hz, 1H), 3.37 (d, *J* = 13.9 Hz, 1H), 3.11 (dd, *J* = 13.3, 2.6 Hz, 1H), 2.91 (d, *J* = 14.1 Hz, 1H), 2.87 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.72 (d, *J* = 15.3 Hz, 1H), 2.45 (d, *J* = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 173.4, 170.0, 157.0, 149.6, 140.6, 136.2, 135.6, 134.8, 133.6, 133.3, 132.7, 132.0, 132.0, 131.1, 130.7, 130.6, 129.8, 128.9, 128.8, 128.6, 128.5, 128.2, 128.0, 128.0, 127.8, 127.6, 127.0, 126.9, 126.7, 126.3, 126.1, 126.0, 125.6, 125.1, 124.7, 122.0, 70.6, 65.5, 61.1, 57.8, 40.2; HRMS (ESI) *m*/*z* calcd for $C_{45}H_{34}ClN_4NiO_3^+$ $[M + H]^+$ 771.1667, found 771.1662. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 20.853 min, t_R (minor diastereomer) = 38.453 min, dr = 99:1.

Nickel(II)−(R)-17/(S)-allylglycine Schiff base complex ***23t:*** red solid (125 mg, yield 98%); mp 234.9−235.2 °C; $[\alpha]^{25}_{D}$ = +2579 (*c* 0.056, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.3 Hz, 1H), 8.41 (d, *J* = 9.1 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.99 (dd, *J* = 14.1, 8.2 Hz, 3H), 7.63−7.45 (m, 7H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.29 (d, *J* = 6.7 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 6.9 Hz, 1H), 6.78 (dt, *J* = 17.3, 8.6 Hz, 1H), 6.68 (d, *J* = 2.3 Hz, 1H), 5.76 (d, *J* = 10.0 Hz, 1H), 5.37 (d, *J* = 17.1 Hz, 1H), 5.30 (s, 1H), 4.78 (d, *J* = 12.2 Hz, 1H), 4.52 (d, *J* = 15.2 Hz, 1H), 3.96 (dd, *J* = 5.5, 3.5 Hz, 1H), 3.70 (d, *J* = 13.8 Hz, 1H), 3.61 (d, *J* = 13.9 Hz, 1H), 3.06 (d, *J* = 15.4 Hz, 1H), 2.71 (d, *J* = 12.1 Hz, 1H), 2.48 (d, *J* = 14.6 Hz, 1H), 2.25 (dt, *J* = 13.8, 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 174.4, 170.0, 141.1, 136.0, 135.5, 134.1, 133.7, 132.8, 132.6, 132.6, 132.4, 131.5, 131.3, 131.0, 130.3, 129.5, 129.3, 129.3, 129.2, 128.7, 128.5, 128.4, 127.9, 127.5, 127.5, 127.4, 127.3, 127.0, 126.5, 126.5, 126.5, 126.4, 126.2, 125.1, 120.5, 70.8, 66.6, 61.6, 59.2, 38.2; HRMS (ESI) *m*/*z* calcd for $C_{42}H_{33}ClN_3NiO_3^+$ $[M + H]^+$ 720.1558, found 720.1570. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) ($MeOH/H_2O$ = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 22.352 min, t_R (minor diastereomer) = 31.724 min, dr = 97:3.

Nickel(II)−(R)-17/(S)-3-methyl-2-butenylglycine Schiff base complex ***23u:*** red solid (134 mg, yield 98%); mp 224.0−225.5 °C; $[\alpha]^{25}_{D}$ = +1943 (*c* 0.054, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.3 Hz, 1H), 8.43 (d, *J* = 9.3 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.02−7.93 (m, 3H), 7.57−7.44 (m, 7H), 7.36 (d, *J* = 8.6 Hz, 1H), 7.31−7.23 (m, 2H), 7.20 (d, *J* = 6.9 Hz, 1H), 6.96 (d, *J* = 7.0 Hz, 1H), 6.68 (d, *J* = 1.3 Hz, 1H), 6.29 (t, *J* = 7.1 Hz, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 15.4 Hz, 1H), 3.98 (t, *J* = 4.1 Hz, 1H), 3.72 (d, *J* = 13.5 Hz, 1H), 3.58 (d, *J* = 13.8 Hz, 1H), 3.04 (d, *J* = 15.5 Hz, 1H), 2.70 (d, *J* = 12.0 Hz, 1H), 2.51−2.39 (m, 1H), 2.26 (s, 3H), 2.24−2.19 (m, 1H), 1.65 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 173.9, 169.1, 140.7, 137.0, 135.6,

DOI: 10.1021/acs.joc.5b01292
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135.0, 133.6, 133.3, 132.1, 132.0, 131.1, 130.8, 130.6, 129.8, 129.0, 128.8, 128.8, 128.7, 128.2, 128.2, 128.1, 128.0, 127.6, 127.1, 127.0, 127.0, 126.8, 126.7, 126.1, 126.0, 125.7, 124.6, 118.1, 70.8, 66.1, 61.3, 58.7, 32.3, 26.8, 17.8; HRMS (ESI) m/z calcd for $C_{44}H_{37}ClN_3NiO_3^+$ $[M + H]^+$ 748.1871, found 748.1884. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 32.454 min, t_R (minor diastereomer) = 51.081 min, dr = 93:7.

Nickel(II)−(S)-17/(R)-3-cyclopropylalanine Schiff base complex ***23v:*** red solid (128 mg, yield 99%); mp 240.1−242.0 °C; $[\alpha]^{25}_D$ = −1993 (c 0.056, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, J = 8.3 Hz, 1H), 8.43 (d, J = 9.1 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.03−7.93 (m, 3H), 7.59−7.35 (m, 9H), 7.31−7.21 (m, 2H), 7.06 (d, J = 7.6 Hz, 1H), 6.92 (d, J = 7.1 Hz, 1H), 6.60 (d, J = 2.3 Hz, 1H), 4.76 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 15.4 Hz, 1H), 3.79−3.63 (m, 3H), 3.04 (d, J = 15.5 Hz, 1H), 2.98−2.82 (m, 1H), 2.76−2.58 (m, 3H), 2.37 (p, J = 9.8 Hz, 1H), 1.96−1.71 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 174.0, 168.7, 140.4, 135.6, 135.0, 133.7, 133.3, 132.1, 131.1, 130.8, 130.5, 129.8, 129.1, 128.7, 128.7, 128.6, 128.3, 128.2, 128.2, 128.0, 127.6, 127.6, 127.0, 126.9, 126.8, 126.1, 126.0, 126.0, 125.7, 124.6, 73.6, 66.3, 61.1, 58.8, 40.0, 25.2, 17.6; HRMS (ESI) m/z calcd for $C_{43}H_{35}ClN_3NiO_3^+$ $[M + H]^+$ 734.1715, found 734.1718. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 27.758 min, t_R (minor diastereomer) = 40.486 min, dr = 98:2.

Nickel(II)−(S)-17/(R)-3-cyclohexylalanine Schiff base complex ***23w:*** red solid (13.3 g, yield 97%); mp 238.1−240.0 °C; $[\alpha]^{25}_D$ = −1893 (c 0.056, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.2 Hz, 1H), 8.42 (d, J = 9.2 Hz, 1H), 8.15 (d, J = 8.3 Hz, 1H), 7.99 (t, J = 9.2 Hz, 3H), 7.59−7.43 (m, 8H), 7.43−7.27 (m, 3H), 7.20 (d, J = 7.3 Hz, 1H), 6.92 (d, J = 6.9 Hz, 1H), 6.66 (s, 1H), 4.82 (d, J = 11.9 Hz, 1H), 4.54 (d, J = 15.5 Hz, 1H), 3.86 (d, J = 7.5 Hz, 1H), 3.79−3.58 (m, 2H), 3.07 (d, J = 15.5 Hz, 1H), 2.73 (d, J = 12.2 Hz, 1H), 2.09 (t, J = 11.3 Hz, 1H), 1.98−1.62 (m, 4H), 1.49−0.74 (m, 7H), 0.37 (q, J = 12.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 174.5, 169.3, 140.9, 136.0, 135.5, 134.1, 133.7, 132.7, 132.5, 132.4, 131.5, 131.2, 131.0, 130.2, 129.4, 129.2, 129.1, 129.1, 128.7, 128.7, 128.5, 128.4, 128.0, 127.9, 127.7, 127.5, 127.4, 127.4, 127.3, 127.2, 126.4, 126.1, 125.1, 69.1, 66.5, 61.7, 58.9, 43.5, 34.6, 33.7, 32.1, 26.3, 26.3, 26.0; HRMS (ESI) m/z calcd for $C_{46}H_{41}ClN_3NiO_3^+$ $[M + H]^+$ 776.2184, found 776.2190. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 55.558 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(S)-17/(R)-n-propylglycine Schiff base complex ***23x:*** red solid (126 mg, yield 99%); mp 236.3−237.8 °C; $[\alpha]^{25}_D$ = −2111 (c 0.044, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J = 8.3 Hz, 1H), 8.43 (d, J = 9.1 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H), 8.02−7.94 (m, 3H), 7.56 (d, J = 8.2 Hz, 1H), 7.53−7.35 (m, 7H), 7.30−7.20 (m, 3H), 7.04 (d, J = 7.6 Hz, 1H), 6.90 (d, J = 7.2 Hz, 1H), 6.59 (d, J = 2.3 Hz, 1H), 4.78 (d, J = 12.2 Hz, 1H), 4.55 (d, J = 15.6 Hz, 1H), 3.89−3.83 (m, 1H), 3.75 (d, J = 13.9 Hz, 1H), 3.65 (d, J = 14.1 Hz, 1H), 3.05 (d, J = 15.5 Hz, 1H), 2.62 (d, J = 12.2 Hz, 1H), 2.52−2.41 (m, 1H), 1.92−1.74 (m, 1H), 1.62−1.53 (m, 1H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 174.1, 169.2, 140.5, 135.6, 135.0, 133.7, 133.3, 132.3, 132.1, 132.0, 131.1, 130.8, 130.6, 129.8, 129.0, 128.8, 128.7, 128.7, 128.3, 128.2, 128.0, 127.6, 127.1, 127.0, 126.9, 126.6, 126.1, 126.0, 126.0, 125.8, 124.7, 70.3, 66.1, 61.3, 58.6, 36.5, 18.1, 13.6; HRMS (ESI) m/z calcd for $C_{42}H_{35}ClN_3NiO_3^+$ $[M + H]^+$ 722.1715, found 722.1719. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 26.690 min, t_R (minor diastereomer) = 40.220 min, dr = 94:6.

Nickel(II)−(S)-17/(R)-n-butylglycine Schiff base complex ***23y:*** red solid (642 mg, yield 99%); mp 246.9−248.8 °C; $[\alpha]^{25}_D$ = −2157 (c 0.054, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.3 Hz, 1H), 8.42 (d, J = 9.1 Hz, 1H), 8.16 (d, J = 8.2 Hz, 1H), 8.00 (d, J = 8.7 Hz, 1H), 7.98 (d, J = 8.5 Hz, 2H), 7.57−7.45 (m, 7H), 7.37 (d, J = 8.3 Hz, 1H), 7.30−7.24 (m, 3H), 7.22−7.18 (m, 1H), 6.92 (dt, J = 7.5, 1.4 Hz, 1H), 6.67 (d, J = 2.5 Hz, 1H), 4.81 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 15.5 Hz, 1H), 3.89−3.84 (m, 1H), 3.75 (d, J = 13.9 Hz, 1H), 3.64 (d, J = 13.9 Hz, 1H), 3.09 (d, J = 15.4 Hz, 1H), 2.73 (d, J = 12.2 Hz, 1H), 2.57−2.45 (m, 1H), 1.87−1.75 (m, 2H), 1.32 (dt, J = 14.8, 7.5 Hz, 2H), 1.28−1.22 (m, 1H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 174.0, 169.3, 140.4, 135.6, 135.0, 133.7, 133.3, 132.3, 132.1, 132.0, 131.1, 130.8, 130.6, 129.8, 129.0, 128.8, 128.7, 128.7, 128.3, 128.2, 128.1, 128.0, 127.6, 127.1, 127.0, 126.9, 126.5, 126.1, 126.0, 126.0, 125.8, 124.7, 70.5, 66.2, 61.3, 58.7, 34.1, 27.0, 22.1, 13.6; HRMS (ESI) m/z calcd for $C_{43}H_{36}ClN_3NiO_3Na^+$ $[M + Na]^+$ 758.1691, found 758.1685. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 33.298 min, t_R (minor diastereomer) = 53.250 min, dr = 93:7.

Nickel(II)−(R)-17/(S)-n-hexylglycine Schiff base complex ***23z:*** red solid (130 mg, yield 97%); mp 208.8−210.9 °C; $[\alpha]^{25}_D$ = +2056 (c 0.042, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 8.3 Hz, 1H), 8.42 (d, J = 9.1 Hz, 1H), 8.16 (d, J = 8.3 Hz, 1H), 8.05−7.93 (m, 3H), 7.56−7.44 (m, 7H), 7.37 (d, J = 8.4 Hz, 1H), 7.30−7.24 (m, 3H), 7.18−7.13 (m, 1H), 6.91 (d, J = 7.2 Hz, 1H), 6.65 (d, J = 2.5 Hz, 1H), 4.80 (d, J = 12.2 Hz, 1H), 4.53 (d, J = 15.5 Hz, 1H), 3.86 (dd, J = 6.5, 3.5 Hz, 1H), 3.75 (d, J = 13.9 Hz, 1H), 3.64 (d, J = 13.9 Hz, 1H), 3.08 (d, J = 15.4 Hz, 1H), 2.70 (d, J = 12.3 Hz, 1H), 2.58−2.49 (m, 1H), 1.90−1.75 (m, 2H), 1.65−1.58 (m, 2H), 1.34−1.29 (m, 5H), 0.90 (t, J = 5.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 174.5, 169.6, 140.9, 136.1, 135.4, 134.1, 133.8, 132.8, 132.6, 132.4, 131.6, 131.2, 131.0, 130.2, 129.5, 129.2, 129.2, 129.1, 128.8, 128.6, 128.5, 128.5, 128.1, 127.5, 127.4, 127.3, 127.0, 126.6, 126.5, 126.4, 126.2, 125.1, 70.9, 66.6, 61.7, 59.2, 34.9, 31.8, 29.1, 25.4, 22.6, 14.1; HRMS (ESI) m/z calcd for $C_{45}H_{41}ClN_3NiO_3^+$ $[M + H]^+$ 764.2184, found 764.2180. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 61.085 min, t_R (minor diastereomer) = 111.063 min, dr = 92:8.

Nickel(II)−(R)-17/(S)-4-chlorohomophenylalanine Schiff base complex ***23aa:*** red solid (143 mg, yield 99%); mp 230.1−241.0 °C; $[\alpha]^{25}_D$ = +2394 (c 0.032, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 8.2 Hz, 1H), 8.44 (d, J = 9.1 Hz, 1H), 8.16 (d, J = 8.3 Hz, 1H), 8.02−7.98 (m, 2H), 7.97 (d, J = 3.0 Hz, 1H), 7.55−7.45 (m, 5H), 7.44−7.34 (m, 3H), 7.32−7.23 (m, 3H), 7.19−7.09 (m, 3H), 6.97 (d, J = 8.2 Hz, 2H), 6.86 (d, J = 7.6 Hz, 1H), 6.64 (d, J = 2.3 Hz, 1H), 4.85 (d, J = 12.2 Hz, 1H), 4.51 (d, J = 15.6 Hz, 1H), 3.79 (dd, J = 9.1, 3.1 Hz, 1H), 3.74 (d, J = 13.7 Hz, 1H), 3.62 (d, J = 13.9 Hz, 1H), 3.20 (ddd, J = 13.6, 9.1, 4.2 Hz, 1H), 3.07 (d, J = 15.5 Hz, 1H), 2.86−2.78 (m, 1H), 2.75 (d, J = 12.3 Hz, 1H), 2.37 (dtd, J = 13.7, 9.2, 4.7 Hz, 1H), 1.81−1.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 174.3, 169.7, 140.6, 138.3, 135.6, 135.1, 133.6, 133.3, 132.3, 132.1, 132.0, 131.4, 131.1, 130.8, 130.6, 129.8, 129.5, 129.0, 128.8, 128.7, 128.3, 128.2, 128.1, 128.0, 127.8, 127.5, 127.0, 127.0, 126.8, 126.7, 126.4, 126.1, 126.0, 126.0, 125.8, 124.7, 69.1, 65.9, 61.5, 58.4, 36.4, 30.3; HRMS (ESI) m/z calcd for $C_{47}H_{36}Cl_2N_3NiO_3^+$ $[M + H]^+$ 818.1482, found 818.1480. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 65.602 min, t_R (minor diastereomer) = 104.797 min, dr = 96:4.

Nickel(II)−(S)-17/(R)-c-butylglycine Schiff base complex ***23bb:*** red solid (625 mg, yield 96%); mp 242.4−244.2 °C; $[\alpha]^{25}_D$ = −2298 (c 0.046, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 9.2 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H), 8.08−7.92 (m, 3H), 7.57 (d, J = 8.3 Hz, 1H), 7.54−7.44 (m, 6H), 7.36 (d, J = 8.7 Hz, 1H), 7.31−7.23 (m, 3H), 7.19 (d, J = 7.4 Hz, 1H), 6.94 (d, J = 7.0 Hz, 1H), 6.66 (d, J = 2.2 Hz, 1H), 4.77 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 15.5 Hz, 1H), 3.77 (d, J = 4.4 Hz, 1H), 3.76−3.64 (m, 2H), 3.07 (d, J = 15.3 Hz, 1H), 2.90 (p, J = 8.9 Hz, 1H), 2.77−2.57 (m, 3H), 2.36 (p, J = 9.9 Hz, 1H), 1.96−1.69 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 174.0, 168.7, 140.5, 135.6, 135.0, 133.7, 133.3, 132.1, 131.1, 130.8, 130.6, 129.8, 129.1, 128.7, 128.7, 128.6, 128.4, 128.2, 128.2, 128.0, 127.7, 127.6, 127.0, 126.8, 126.1, 126.0, 126.0, 125.8, 124.6, 73.6, 66.3, 61.1, 58.8, 40.1, 25.2, 25.2, 17.6; HRMS (ESI) m/z calcd for $C_{43}H_{35}ClN_3NiO_3^+$ $[M + H]^+$ 734.1715, found 734.1725. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 80/20, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 107.052 min, t_R (minor diastereomer) = 168.542 min, dr = 96:4.

DOI: 10.1021/acs.joc.5b01292
J. Org. Chem. 2015, 80, 9817−9830

Nickel(II)−(R)-17/(S)-tert-butylglycine Schiff base complex ***23cc:*** red solid (114 mg, yield 88%); mp 246.6−248.0 °C; $[\alpha]^{25}_{D}$ = +757 (*c* 0.060, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, *J* = 8.4 Hz, 1H), 8.57 (d, *J* = 9.0 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.00 (dd, *J* = 8.2, 3.5 Hz, 2H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.54−7.47 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.38−7.27 (m, 4H), 7.25−7.16 (m, 2H), 7.07 (d, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.63 (s, 1H), 4.62 (d, *J* = 15.7 Hz, 1H), 4.57 (d, *J* = 12.1 Hz, 1H), 3.78 (s, 1H), 3.69 (d, *J* = 13.9 Hz, 1H), 3.60 (d, *J* = 13.5 Hz, 1H), 3.02 (d, *J* = 15.1 Hz, 1H), 2.54 (d, *J* = 12.1 Hz, 1H), 1.50 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 174.0, 170.3, 141.5, 139.9, 136.0, 135.4, 134.2, 133.8, 133.4, 133.0, 132.8, 131.5, 131.2, 130.9, 130.6, 130.4, 129.7, 129.1, 128.9, 128.8, 128.6, 128.4, 128.2, 127.3, 127.3, 127.2, 126.6, 126.5, 126.4, 126.4, 126.0, 124.2, 80.1, 67.2, 61.0, 59.1, 37.4, 28.4; HRMS (ESI) *m*/*z* calcd for $C_{43}H_{37}ClN_3NiO_3^+$ $[M + H]^+$ 736.1871, found 736.1869. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 29.882 min, t_R (minor diastereomer) = 41.896 min, dr = 70:30.

Nickel(II)−(S)-17/(R)-phenylglycine Schiff base complex ***23dd:*** red solid (131 mg, yield 98%); mp 242.0−243.9 °C; $[\alpha]^{25}_{D}$ = −1752 (*c* 0.050, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 8.3 Hz, 1H), 8.47 (d, *J* = 8.6 Hz, 1H), 8.17 (d, *J* = 8.6 Hz, 1H), 8.04−7.93 (m, 3H), 7.68 (dd, *J* = 7.1, 2.0 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.54−7.47 (m, 4H), 7.45−7.40 (m, 2H), 7.33−7.22 (m, 7H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 2.5 Hz, 1H), 6.06 (d, *J* = 7.7 Hz, 1H), 4.92 (d, *J* = 12.2 Hz, 1H), 4.74 (s, 1H), 4.66 (d, *J* = 15.6 Hz, 1H), 3.79 (d, *J* = 14.6 Hz, 1H), 3.68 (d, *J* = 14.0 Hz, 1H), 3.18 (d, *J* = 15.6 Hz, 1H), 2.81 (d, *J* = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 174.4, 171.7, 140.7, 137.4, 135.7, 135.1, 133.7, 133.3, 132.7, 132.4, 132.1, 131.1, 130.8, 130.6, 129.5, 129.1, 128.8, 128.3, 128.3, 128.2, 128.0, 127.8, 127.6, 127.4, 127.1, 127.0, 126.9, 126.9, 126.3, 126.1, 126.0, 126.0, 126.0, 125.9, 125.7, 124.8, 74.5, 65.9, 61.6, 58.5; HRMS (ESI) *m*/*z* calcd for $C_{45}H_{32}ClN_3NiO_3Na^+$ $[M + Na]^+$ 778.1378, found 778.1375. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 26.473 min, t_R (minor diastereomer) = 41.177 min, dr = 86:14.

Nickel(II)−(S)-17/(R)-4-methylphenylalanine Schiff base complex ***23ee:*** red solid (136 mg, yield 98%); mp 230.7−233.0 °C; $[\alpha]^{25}_{D}$ = −1978 (*c* 0.046, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 7.9 Hz, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 7.5 Hz, 1H), 8.05−7.83 (m, 3H), 7.69−7.28 (m, 13H), 7.25−7.18 (m, 2H), 7.10 (dd, *J* = 23.5, 6.3 Hz, 2H), 6.65 (s, 1H), 4.55 (d, *J* = 13.7 Hz, 1H), 4.19 (s, 1H), 3.63 (d, *J* = 14.9 Hz, 1H), 3.18 (d, *J* = 13.6 Hz, 1H), 2.96 (d, *J* = 13.2 Hz, 1H), 2.73 (s, 3H), 2.69−2.49 (m, 3H), 2.40 (d, *J* = 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 173.8, 169.3, 140.9, 136.8, 135.5, 134.9, 133.5, 133.2, 132.9, 132.4, 132.2, 131.9, 131.2, 131.0, 130.7, 130.6, 129.9, 129.2, 129.0, 128.9, 128.9, 128.6, 128.2, 128.2, 128.0, 127.9, 127.5, 127.1, 127.0, 127.0, 126.6, 126.6, 126.0, 125.9, 125.6, 124.8, 71.8, 65.3, 61.0, 57.3, 38.3, 21.2; HRMS (ESI) *m*/*z* calcd for $C_{47}H_{37}ClN_3NiO_3^+$ $[M + H]^+$ 784.1871, found 784.1882. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 37.976 min, t_R (minor diastereomer) = not found, dr >99:1.

Nickel(II)−(R)-17/(S)-3,4-difluorophenylalanine Schiff base complex ***23ff:*** red solid (138 mg, yield 97%); mp 238.8−234.0 °C; $[\alpha]^{25}_{D}$ = +2044 (*c* 0.052, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 8.4 Hz, 1H), 8.40 (d, *J* = 9.1 Hz, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.66−7.26 (m, 13H), 7.26−7.20 (m, 1H), 7.12−6.99 (m, 2H), 6.72 (d, *J* = 2.5 Hz, 1H), 4.64 (d, *J* = 12.2 Hz, 1H), 4.20 (dd, *J* = 5.0, 3.5 Hz, 1H), 3.79 (d, *J* = 15.5 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 2.95 (dd, *J* = 13.6, 3.2 Hz, 1H), 2.86 (d, *J* = 13.9 Hz, 1H), 2.80 (d, *J* = 15.6 Hz, 1H), 2.58 (dd, *J* = 13.0, 3.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 174.1, 170.4, 141.4, 136.1, 135.2, 134.0, 133.7, 133.0, 132.8, 132.5, 131.5, 131.1, 130.8, 130.6, 129.5, 129.5, 129.3, 129.3, 128.6, 128.5, 128.4, 128.1, 127.8, 127.5, 127.4, 127.2, 127.0, 126.6, 126.4, 126.4, 126.4, 126.2, 125.2, 120.2 (d, *J* = 16.6 Hz), 117.5 (d, *J* = 16.5 Hz), 71.5, 66.0, 61.8, 58.4, 38.3; HRMS (ESI) *m*/*z* calcd for $C_{46}H_{33}ClF_2N_3NiO_3^+$ $[M + H]^+$ 806.1527, found 806.1538. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 30.903 min, t_R (minor diastereomer) = 53.744 min, dr = 97:3.

Nickel(II)−(S)-17/(R)-3,3-diphenylalanine Schiff base complex ***23gg:*** red solid (148 mg, yield 99%); mp 237.0−247.8 °C; $[\alpha]^{25}_{D}$ = −1460 (*c* 0.052, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.3 Hz, 1H), 8.42 (d, *J* = 9.1 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 8.00−7.89 (m, 3H), 7.77−7.64 (m, 5H), 7.53−7.37 (m, 6H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.27 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.25−7.21 (m, 3H), 7.15−7.06 (m, 3H), 7.06−6.99 (m, 2H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 2.5 Hz, 1H), 4.67 (d, *J* = 2.5 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.05 (d, *J* = 2.6 Hz, 1H), 3.93 (d, *J* = 15.4 Hz, 1H), 3.11 (d, *J* = 14.0 Hz, 1H), 2.73 (d, *J* = 4.8 Hz, 1H), 2.69 (d, *J* = 6.1 Hz, 1H), 2.48 (d, *J* = 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 173.9, 169.5, 141.1, 139.3, 139.0, 135.5, 134.9, 133.6, 133.2, 132.4, 132.1, 131.1, 130.8, 130.6, 129.8, 129.2, 128.9, 128.9, 128.7, 128.6, 128.4, 128.2, 128.0, 128.0, 127.8, 127.6, 127.5, 127.5, 127.2, 127.0, 126.9, 126.7, 126.7, 126.2, 126.0, 125.9, 125.9, 125.6, 124.5, 74.9, 65.5, 61.1, 57.5, 56.8; HRMS (ESI) *m*/*z* calcd for $C_{52}H_{39}ClN_3NiO_3^+$ $[M + H]^+$: 846.2028, found 846.2026. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 44.666 min, t_R (minor diastereomer) = 80.637 min, dr = 90:10.

Nickel(II)−(R)-17/(S)-3-(2-thienyl)alanine Schiff base complex ***23hh:*** red solid (121 mg, yield 88%); mp 248.2−250.1 °C; $[\alpha]^{25}_{D}$ = +2300 (*c* 0.048, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.2 Hz, 1H), 8.37 (d, *J* = 9.2 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 8.03−7.92 (m, 3H), 7.74 (d, *J* = 4.8 Hz, 1H), 7.67−7.39 (m, 9H), 7.36 (d, *J* = 8.7 Hz, 1H), 7.32−7.21 (m, 4H), 7.10 (d, *J* = 6.8 Hz, 1H), 6.72 (d, *J* = 2.0 Hz, 1H), 4.65 (d, *J* = 12.1 Hz, 1H), 4.20 (dd, *J* = 4.9, 2.3 Hz, 1H), 4.04 (d, *J* = 15.3 Hz, 1H), 3.39 (d, *J* = 13.9 Hz, 1H), 3.28 (dd, *J* = 14.6, 2.0 Hz, 1H), 3.12 (d, *J* = 13.9 Hz, 1H), 2.78 (dd, *J* = 14.9, 5.5 Hz, 2H), 2.56 (d, *J* = 12.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 174.3, 170.3, 141.3, 137.7, 136.0, 135.3, 134.0, 133.7, 132.9, 132.7, 132.4, 131.5, 131.2, 131.0, 130.5, 129.5, 129.4, 129.3, 129.0, 128.8, 128.7, 128.6, 128.4, 128.3, 128.0, 127.9, 127.6, 127.5, 127.4, 127.2, 126.9, 126.5, 126.4, 126.1, 125.8, 125.3, 71.7, 66.0, 61.5, 58.0, 33.0; HRMS (ESI) *m*/*z* calcd for $C_{44}H_{33}ClN_3NiO_3S^+$ $[M + H]^+$ 776.1279, found 776.1281. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 27.524 min, t_R (minor diastereomer) = 42.329 min, dr = 97:3.

Nickel(II)−(R)-17/(S)-propargylglycine Schiff base complex ***23ii:*** red solid (126 mg, yield 97%); mp 242.0−243.9 °C; $[\alpha]^{25}_{D}$ = +2700 (*c* 0.060, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.3 Hz, 1H), 8.41 (d, *J* = 9.1 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.97 (dd, *J* = 8.2, 4.3 Hz, 3H), 7.59−7.44 (m, 7H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.33−7.25 (m, 2H), 7.28−7.21 (m, 1H), 7.19 (d, *J* = 7.1 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 2.5 Hz, 1H), 4.82 (d, *J* = 12.2 Hz, 1H), 4.51 (d, *J* = 15.4 Hz, 1H), 3.92 (dd, *J* = 5.8, 2.7 Hz, 1H), 3.77−3.62 (m, 2H), 3.07 (d, *J* = 15.3 Hz, 1H), 3.01 (t, *J* = 2.6 Hz, 1H), 2.72 (d, *J* = 12.2 Hz, 1H), 2.63 (dt, *J* = 17.0, 2.6 Hz, 1H), 2.24 (ddd, *J* = 17.0, 5.8, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6, 174.0, 170.3, 141.0, 135.7, 135.0, 133.6, 133.3, 132.4, 132.1, 132.0, 131.1, 130.8, 130.6, 130.0, 129.1, 129.0, 128.9, 128.6, 128.4, 128.2, 128.0, 128.0, 127.5, 127.0, 127.0, 126.9, 126.9, 126.3, 126.1, 126.0, 126.0, 125.7, 124.9, 79.5, 74.2, 67.9, 66.3, 61.2, 58.7, 23.5; HRMS (ESI) *m*/*z* calcd for $C_{42}H_{31}ClN_3NiO_3^+$ $[M + H]^+$ 718.1402, found 718.1397. The dr was determined by LC/MS with an Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm) (MeOH/H_2O = 85/15, λ = 254 nm, 1.0 mL/min) t_R (major diastereomer) = 19.027 min, t_R (minor diastereomer) = 24.946 min, dr = 93:7.

(R)-4-Chlorophenylalanine ***22j:*** white solid (118 mg, yield 95%); mp 238.2−238.9 °C; $[\alpha]^{25}_{D}$ = +29.0 (*c* 0.048, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.28 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 3.85 (t, *J* = 6.4 Hz, 1H), 3.12 (dd, *J* = 14.5, 5.1 Hz, 1H), 2.98 (dd, *J* = 14.6, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, D_2O) δ 170.7, 132.9, 132.2, 130.7, 128.8, 53.5, 34.6; HRMS (ESI) *m*/*z* calcd for $C_9H_{10}ClNO_2Na^+$ $[M + Na]^+$ 222.0292, found 222 0.0292. The ee was determined by HPLC with an Astec CHIROBIOTIC T chiral HPLC column (4.6 mm × 25 cm, 5 μm) (MeOH/H_2O = 90/10, λ = 214 nm, 0.5 mL/min) t_R (major

DOI: 10.1021/acs.joc.5b01292
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enantiomer) = 21.173 min, t_R (minor enantiomer) = not found, ee >99%.

(R)-n-Butylglycine ***22y:*** white solid (82 mg, yield 93%); mp >300 °C; $[\alpha]^{25}_D = -29.0$ (c 0.056, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 3.80 (t, J = 6.2 Hz, 1H), 1.88−1.71 (m, 3H), 1.32−1.19 (m, 4H), 0.78 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, D_2O) δ 173.6, 53.8, 29.7, 26.2, 21.6, 12.9; HRMS (ESI) m/z calcd for $C_6H_{14}NO_2^+$ $[M + H]^+$ 132.1019, found 132.1018.

(R)-c-Butylglycine ***22bb:*** white solid (86 mg, yield 96%); mp >300 °C; $[\alpha]^{25}_D = -39.6$ (c 0.048, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 3.87 (d, J = 9.1 Hz, 1H), 2.67 (h, J = 9.3 Hz, 1H), 2.06−1.63 (m, 6H).; ^{13}C NMR (125 MHz, D_2O) δ171.5, 56.7, 35.2, 25.0, 24.8, 17.3; HRMS (ESI) m/z calcd for $C_6H_{12}NO_2^+$ $[M + H]^+$ 130.0863, found 130.0862.

(S)-3-(2-Thienyl)alanine ***22hh:*** white solid (106 mg, yield 96%); mp 222.4−224.0 °C; $[\alpha]^{25}_D = -8.3$ (c 0.048, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.28 (d, J = 4.8 Hz, 1H), 6.96−6.89 (m, 2H), 4.19 (t, J = 5.7 Hz, 1H), 3.54−3.20 (m, 2H); ^{13}C NMR (125 MHz, D_2O) δ 171.5, 135.2, 128.2, 127.7, 126.3, 54.3, 29.7; HRMS (ESI) m/z calcd for $C_7H_{10}NO_2S^+$ $[M + H]^+$ 172.0427, found 172.0427. The ee was determined by HPLC with an Astec CHIROBIOTIC T chiral HPLC column (4.6 mm × 25 cm, 5 μm) (MeOH/H_2O = 80/20, λ = 214 nm, 1.0 mL/min) t_R (major enantiomer) = 6.174 min, t_R (minor enantiomer) = not found, ee >99%.

(R)-N-Cbz-n-Butylglycine ***24y:*** white solid (109 mg, yield 90%); mp 54.2−54.8 °C; $[\alpha]^{25}_D = +7.1$ (c 0.056, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.54 (s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.42−7.20 (m, 5H), 5.03 (s, 2H), 3.91 (td, J = 9.1, 4.8 Hz, 1H), 1.74−1.49 (m, 2H), 1.33−1.22 (m, 4H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.5, 156.6, 137.5, 128.8, 128.2, 128.2, 65.8, 54.2, 30.9, 28.2, 22.1, 14.2; HRMS (ESI) m/z calcd for $C_{14}H_{20}NO_4^+$ $[M + H]^+$ 266.1392, found 266.1381. The ee was determined by UFLC with a Chiralpak AD-H column (4.6 mm × 25 cm) (n-hexane +0.1% TFA/i-PrOH = 90/10, λ = 214 nm, 1.0 mL/min) t_R (major enantiomer) = 31.147 min, t_R (minor enantiomer) = not found, ee >99%.

(R)-N-Cbz-c-Butylglycine ***24bb:*** white solid (111 mg, yield 91%); mp 106.4−107.2 °C; $[\alpha]^{25}_D = -6.5$ (c 0.062, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.41−7.24 (m, 5H), 5.03 (s, 2H), 3.91 (t, J = 8.5 Hz, 1H), 2.67−2.50 (m, 1H), 2.03−1.59 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.4, 156.7, 137.5, 128.8, 128.3, 128.2, 65.9, 58.7, 36.6, 25.5, 25.3, 17.9; HRMS (ESI) m/z calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 264.1236, found 264.1225. The ee was determined by UFLC with a Chiralpak AD-H column (4.6 mm × 25 cm) (n-hexane +0.1% TFA/i-PrOH = 85/15, λ = 214 nm, 1.0 mL/min) t_R (major enantiomer) = 21.294 min, t_R (minor enantiomer) = 14.294, ee >99%.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01292.

X-ray crystal structure of compound (S_a)(R_c)-**23j** (CIF)
^{1}H and ^{13}C NMR spectra; LC/MS and HPLC experimental data (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

S.W., S.Z., J.W., Y.N., and H.L. received funding from the National Natural Science Foundation of China (81302633, 21472209 and 91229204), the National High Technology Research and Development Program of China (2012AA020302), and Major Project of Chinese National Programs for Fundamental Research and Development (2015CB910304).

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