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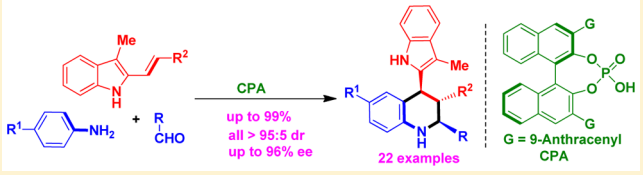
Application of 3-Methyl-2-vinylindoles in Catalytic Asymmetric Povarov Reaction: Diastereo- and Enantioselective Synthesis of Indole-Derived Tetrahydroquinolines

Wei Dai, Xiao-Li Jiang, Ji-Yu Tao, and Feng Shi*

School of Chemistry and Chemical Engineering and Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou 221116, China

Supporting Information

ABSTRACT: The first application of 3-methyl-2-vinylindoles in catalytic asymmetric Povarov reactions has been established via the three-component reactions of 3-methyl-2-vinylindoles, aldehydes, and anilines in the presence of chiral phosphoric acid, providing easy access to chiral indole-derived tetrahydroquinolines with three contiguous stereogenic centers at high yields (up to 99%) and with excellent diastereo- and enantioselectivities (all >95:5 dr, up to 96% ee). This mode of catalytic asymmetric three-component reaction offers a step-economic and atom-economic strategy for accessing enantioenriched indole-derived tetrahydroquinolines with structural diversity and complexity.



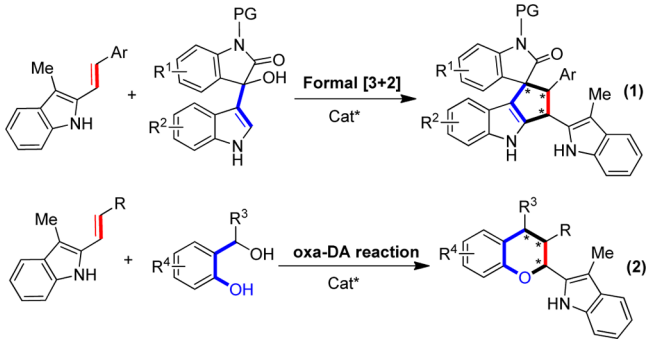
INTRODUCTION

An indole framework constitutes the core structure of numerous natural products and man-made compounds, many of which are chiral molecules.[1] Therefore, the synthesis of chiral indole derivatives has been the focus of substantial interest from the synthetic community.[2] Many indole-derived reactants have been developed and utilized in catalytic asymmetric reactions for the enantioselective preparation of indole derivatives. Among these numerous reactants, vinylindoles have been recognized as versatile building blocks for the enantioselective construction of cyclic scaffolds bearing an indole moiety.[3−5] However, despite this previous work, exploiting new types of vinylindole and utilizing them for catalytic asymmetric synthesis remains a longstanding goal in organic synthesis.

In this context, we have recently developed 3-methyl-2-vinylindoles as a new class of vinylindoles, which have a strong tendency to act as mono-olefins rather than dienes, due to the existence of a C3-methyl group (Scheme 1).[6] This type of vinylindole has been successfully used for catalytic asymmetric formal [3 + 2] cycloadditions[6a] (Scheme 1, eq 1) and inverse-electron-demand oxa-Diels−Alder (DA) reactions[6b] (eq 2) to construct five-membered carbocyclic and six-membered oxygenous heterocyclic frameworks in a highly diastereo- and enantioselective fashion. The application of 3-methyl-2-vinylindoles to other catalytic asymmetric reactions has yet to be achieved, but is desirable.

The catalytic asymmetric Povarov reaction[7,3d] has been shown to have great potential in synthesizing chiral tetrahydroquinoline derivatives, which possess a wide range of important bioactivities (e.g., antitumoral, antibacterial, and antioxidant activities).[8] Following the establishment of inverse-electron-demand oxa-DA reactions of 3-methyl-2-vinylindoles, we consider whether or not this class of vinylindoles can be applied to the catalytic asymmetric Povarov reaction, associated with the construction of an indole-derived tetrahydroquinoline framework with three adjacent stereogenic centers. In addition, the integration of two biologically important indole and tetrahydroquinoline scaffolds should provide a good opportunity to discover new bioactivities after bioassays.

Scheme 1. Profile of 3-Methyl-2-vinylindole Associated Reactions



Against this background and our continuous work on chiral phosphoric acid[9] (CPA)-catalyzed reactions for the synthesis of enantioenriched indole derivatives,[6,10] we designed a catalytic asymmetric three-component Povarov reaction of 3-methyl-2-vinylindoles with anilines and aldehydes in the presence of CPA, wherein 3-methyl-2-vinylindoles and in situ-generated aldimines would be simultaneously activated by CPA via dual hydrogen-bonding interaction, thus facilitating the formation of indole-

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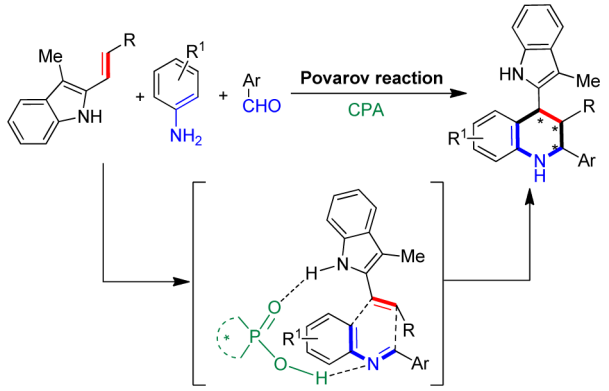
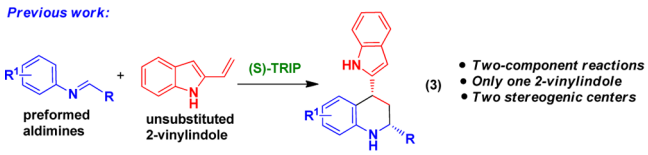
derived tetrahydroquinolines in a stereoselective fashion (Scheme 2).

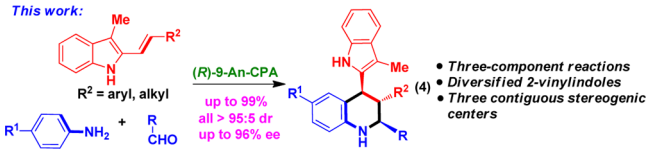
Scheme 2. Design of 3-Methyl-2-vinylindole Associated Catalytic Asymmetric Povarov Reaction



It should be mentioned that Ricci, Bernardi, and co-workers previously reported an asymmetric two-component Povarov reaction of aldimines with 2-vinylindole, in the presence of (*S*)-2,4,6-triisopropylphenyl-substituted CPA (TRIP), resulting in the creation of tetrahydroquinoline derivatives bearing two stereogenic centers (eq 3).[3d] Despite this elegant work, the



aldimines utilized in this reaction must be prepared in advance, and only one unsubstituted 2-vinylindole is used in the reaction. Therefore, the multicomponent reaction mode of our designed reaction (eq 4) and the diversified structure of 3-methyl-2-



vinylindoles should provide a simple, efficient, stereoselective method for constructing structurally diversified tetrahydroquinoline scaffolds with three contiguous stereogenic centers.

Herein, we report the first application of 3-methyl-2-vinylindoles in catalytic asymmetric Povarov reactions; the proposed approach provides easy access to chiral indole-derived tetrahydroquinolines bearing three contiguous stereogenic centers at high yields (up to 99%) and excellent diastereo- and enantioselectivities (all >95:5 dr, up to 96% ee).

RESULTS AND DISCUSSION

Initially, the three-component reaction of 4-nitrobenzaldehyde **1a**, 4-methoxyaniline **2a**, and 3-methyl-2-vinylindole **3a** was used to verify our hypothesis in the presence of CPA (*R*)-**5a**, which underwent the anticipated Povarov reaction and afforded the indole-derived tetrahydroquinoline **4aaa** with good diastereo- and enantioselectivity but at a low yield (Table 1, entry 1). After screening a series of (*R*)-BINOL-derived CPAs **5a**–**5g** (entries 1–7), it was found that CPA **5e** bearing bulky 9-anthracenyl substituents delivered the reaction with the highest enantioselectivity of 94% ee, albeit at a moderate yield of 56% (entry 5). Subsequent evaluation of different types of solvents (entries 5 and 8–11) revealed that only arene and chloralkane, as exemplified by toluene and chloroform, could facilitate the reaction (entries 5 and 8); the reaction failed to occur in other solvents such as ester, nitrile, and ether (entries 9–11). Then, in a solvent of toluene, different additives including molecular sieves (MS) and anhydrous sulfates as water absorbers were examined (entries 5 and 12–15); the addition of magnesium sulfate to the reaction system enhanced the yield to 72% with retained enantioselectivity of 94% ee (entry 15). Finally, increasing the stoichiometry of 3-methyl-2-vinylindole **3a** led to a significant improvement in the yield (entries 16–17); the product **4aaa** was generated at a quantitative yield of 99% and maintained a high ee value of 94% (entry 17).

After establishing the optimal reaction conditions, we performed an investigation on the substrate scope of this three-component Povarov reaction. First, the applicability of aromatic aldehydes **1** was examined by a reaction with 4-methoxyaniline **2a** and 3-methyl-2-vinylindole **3a** under optimal reaction conditions. As shown in Table 2, a variety of benzaldehydes bearing electron-poor, -neutral, or -rich substituents could be used in the reaction that offered the indole-derived tetrahydroquinolines **4** containing three contiguous stereogenic centers at generally high yields and with good stereoselectivities. However, the electronic nature of the substituents appeared to have an impact on the reactivity and the enantioselectivity. In most cases, electronically poor benzaldehydes displayed much higher reactivity and enantioselective control than electronically neutral and rich ones (entries 1–4 and 6–7 vs 8–9), delivering the products at high yields of 72–99% with excellent enantioselectivities of 90–94% ee (entries 1–4 and 6–7). In contrast, electronically neutral and rich benzaldehydes **1h**–**1i** showed relatively low reactivity in the Povarov reaction, which hardly proceeds under optimal conditions. Nevertheless, by increasing the stoichiometry of 3-methyl-2-vinylindole **3a** and extending the reaction time, these aldehydes finally afforded the corresponding products at moderate yields, excellent diastereoselectivities, and considerable enantioselectivities (entries 8–9). Moreover, the position of the substituents also had some effect on the enantioselectivity; *para*- or *meta*-nitro-substituted benzaldehydes **1a** and **1d**, for example, delivered products with much higher enantioselectivities than their *ortho*-substituted analogue **1e** (entries 1 and 4 vs 5), although all of the three aldehydes smoothly participated in the reaction at quantitative yields.

Second, we investigated the generality of anilines by reactions with reactants **1a** and **3a** (Table 3). To avoid the regioselective issue, we utilized *para*-substituted anilines **2** in the reactions. A series of electronically different anilines were clearly amenable to the three-component Povarov reaction, generating the desired products **4** at uniformly excellent yields (90–99%) and with high stereoselectivities (all >95:5 dr, 88–96% ee). It seemed that the electronic nature of the substituents did not have a clear effect on the reaction, because electronically rich (entries 1–3), neutral (entry 4) and poor (entries 5–6) anilines could take part in the catalytic asymmetric Povarov reaction at similar yields and with similar stereoselectivities, except for **2a** (entry 2). Notably, electron-poor anilines **2f**–**2g** proved to be competent reaction components with regard to both reactivity and stereoselectivity, thus, expanding the application of this reaction given that such

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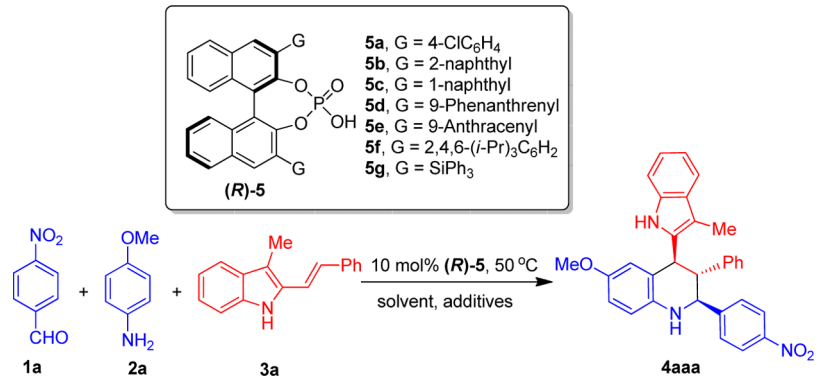
Table 1. Screening of Catalysts and Optimization of Reaction Conditions[a]



entry	cat.	solvent	additives	yield (%)[b]	dr[c]	ee (%)[d]
1	(*R*)-**5a**	toluene	3 Å	33	>95:5	80
2	(*R*)-**5b**	toluene	3 Å	33	>95:5	71
3	(*R*)-**5c**	toluene	3 Å	21	>95:5	84
4	(*R*)-**5d**	toluene	3 Å	33	>95:5	77
5	(*R*)-**5e**	toluene	3 Å	56	>95:5	94
6	(*R*)-**5f**	toluene	3 Å	65	>95:5	92
7	(*R*)-**5g**	toluene	3 Å	trace	–	–
8	(*R*)-**5e**	$CHCl_3$	3 Å	45	>95:5	90
9	(*R*)-**5e**	EtOAc	3 Å	trace	–	–
10	(*R*)-**5e**	CH_3CN	3 Å	trace	–	–
11	(*R*)-**5e**	1,4-dioxane	3 Å	trace	–	–
12	(*R*)-**5e**	toluene	4 Å	60	>95:5	93
13	(*R*)-**5e**	toluene	5 Å	61	>95:5	93
14	(*R*)-**5e**	toluene	Na_2SO_4	67	>95:5	93
15	(*R*)-**5e**	toluene	$MgSO_4$	72	>95:5	94
16[e]	(*R*)-**5e**	toluene	$MgSO_4$	86	>95:5	93
17[f]	(*R*)-**5e**	toluene	$MgSO_4$	99	>95:5	94

[a]Unless otherwise indicated, the reaction was carried out at 0.1 mmol scale and catalyzed by 10 mol % (*R*)-**5** in a solvent (1 mL) with additives (100 mg) for 24 h. The molar ratio of **1a**:**2a**:**3a** was 1.2:1:1.5. [b]Isolated yield. [c]The dr value was determined by high-performance liquid chromatography (HPLC) and proton nuclear magnetic resonance (^{1}H NMR). [d]The ee value was determined by HPLC. [e]The molar ratio of **1a**:**2a**:**3a** was 1.2:1:2.0. [f]The molar ratio of **1a**:**2a**:**3a** was 1.2:1:2.5.

anilines have often been reported to be inferior to electron-rich ones in terms of enantioselective control.[10d,11b]

Finally, the substrate scope of 3-methyl-2-vinylindoles **3** was studied by the reactions with 4-nitrobenzaldehyde **1a** and 4-methoxyaniline **2a**. As listed in Table 4, a range of 3-methyl-2-vinylindoles **3** bearing different terminal groups were applicable to the catalytic asymmetric three-component Povarov reaction, which gave the cycloaddition products **4** with multiple chiral centers at high yields (80−99%) and with perfect diastereoselectivities (all >95:5 dr) and excellent enantioselectivities (90−96% ee). Basically, the position and the electronic nature of the substituents on the terminal phenyl groups had no marked influence on the stereoselectivity, due to the fact that 3-methyl-2-vinylindoles **3** bearing either electron-donating or -withdrawing terminal substituents could deliver the products with equivalent enantioselectivities (entries 1−3 vs 4−6). It is worth noting that alkyl groups such as methyl could also serve as suitable terminal substituents of 3-methyl-2-vinylindoles, which readily underwent the desired reaction at a quantitative yield of 99% and with the highest enantioselectivity of 96% ee (entry 7). This result greatly extends the application of this type of vinylindole for synthesizing enantioenriched indole-derived tetrahydroquinolines with structural diversity.

In previous work by Ricci,[3d] the absolute configurations of the tetrahydroquinoline products were assigned by theoretical calculations. In our case, the absolute configuration of product **4aaa** (>99% ee after recrystallization) was unambiguously determined to be (2*S*,3*R*,4*S*) by single-crystal X-ray diffraction analysis (in Scheme 3).[12] The absolute configurations of other products **4** were assigned by analogy. On the basis of the experimental results and previous calculations on the transition states,[11] a possible reaction pathway was suggested to explain the stereochemistry of the reaction. Normally, the Povarov reaction is regarded as involving stepwise cycloaddition that mainly includes the vinylogous Mannich reaction and the intramolecular Friedel−Crafts reaction. As shown in Scheme 3, CPA (*R*)-**5e** simultaneously activated both 3-methyl-2-vinylindoles **3** and aldimines **A** via hydrogen bonds, which were generated in situ from aldehydes **1** and anilines **2**. This dual activation mode facilitated the enantioselective vinylogous Mannich reaction to form a transient intermediate **B**, which further underwent the intramolecular Friedel−Crafts reaction to give the final product **4** with a (2*S*,3*R*,4*S*)-configuration.

Finally, to demonstrate the role of the free N−H group in the moiety of 3-methyl-2-vinylindoles **3**, *N*-methyl-protected substrate **3i** was used in the three-component reaction under the standard conditions (Scheme 4). As expected, no cycloaddition product **4aai** was detected, and only aldimine was observed in the reaction mixture, which was generated from the condensation of substrates **1a** and **2a**. This control experiment

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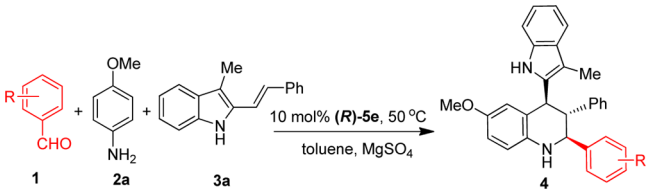
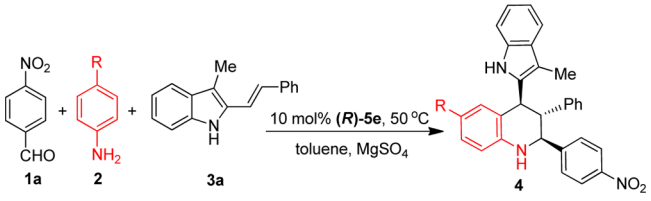
Table 2. Substrate Scope of Aromatic Aldehydes 1[a]



entry	4	R (1)	yield (%)[b]	dr[c]	ee (%)[d]
1	**4aaa**	4-NO_2 (**1a**)	99	>95:5	94
2	**4baa**	4-CN (**1b**)	99	>95:5	94
3	**4caa**	4-CF_3 (**1c**)	79	>95:5	90
4	**4daa**	3-NO_2 (**1d**)	99	>95:5	92
5	**4eaa**	2-NO_2 (**1e**)	99	>95:5	68
6	**4faa**	3,4-Cl_2 (**1f**)	82	>95:5	92
7	**4gaa**	3-Cl,4-F (**1g**)	72	>95:5	92
8[e]	**4haa**	H (**1h**)	48	>95:5	76
9[f]	**4iaa**	3-Me (**1i**)	41	>95:5	68

[a]Unless otherwise indicated, the reaction was carried out at 0.1 mmol scale and catalyzed by 10 mol % (*R*)-**5e** in toluene (1 mL) with $MgSO_4$ (100 mg) at 50 °C for 24 h. The molar ratio of **1**:**2a**:**3a** was 1.2:1:2.5. [b]Isolated yield. [c]The dr value was determined by ^{1}H NMR. [d]The ee value was determined by HPLC. [e]The reaction time was 48 h, and the molar ratio of **1h**:**2a**:**3a** was 1.2:1:5. [f]The reaction was performed at 70 °C for 48 h, and the molar ratio of **1i**:**2a**:**3a** was 1.2:1:5.

Table 3. Substrate Scope of Anilines 2[a]



entry	4	R (2)	yield (%)[b]	dr[c]	ee (%)[d]
1	**4aba**	Me (**2b**)	99	>95:5	90
2	**4aca**	EtO (**2c**)	99	>95:5	88
3	**4ada**	PhO (**2d**)	99	>95:5	96
4	**4aea**	H (**2e**)	99	>95:5	94
5	**4afa**	F (**2f**)	90	>95:5	94
6	**4aga**	Cl (**2g**)	97	>95:5	94

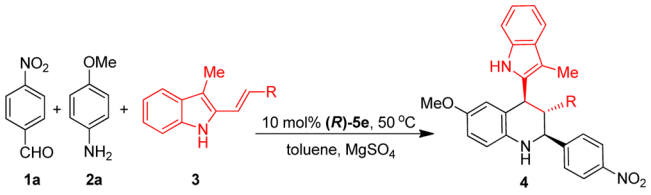
[a]Unless otherwise indicated, the reaction was carried out at 0.1 mmol scale and catalyzed by 10 mol % (*R*)-**5e** in toluene (1 mL) with $MgSO_4$ (100 mg) at 50 °C for 24 h. The molar ratio of **1a**:**2**:**3a** was 1.2:1:2.5. [b]Isolated yield. [c]The dr value was determined by ^{1}H NMR. [d]The ee value was determined by HPLC.

implied that the free N−H group of 3-methyl-2-vinylindoles **3** is crucial for the desired Povarov reaction, by forming hydrogen bonds with the catalyst.

CONCLUSIONS

In summary, we demonstrated the first application of 3-methyl-2-vinylindoles in catalytic asymmetric Povarov reactions that takes advantage of the three-component reactions of 3-methyl-2-vinylindoles, aldehydes, and anilines in the presence of chiral phosphoric acid. This approach provides easy access to chiral indole-derived tetrahydroquinolines bearing three contiguous stereogenic centers at high yields (up to 99%), with excellent diastereo- and enantioselectivities (all >95:5 dr, up to 96% ee). Moreover, this transformation will not only expand the

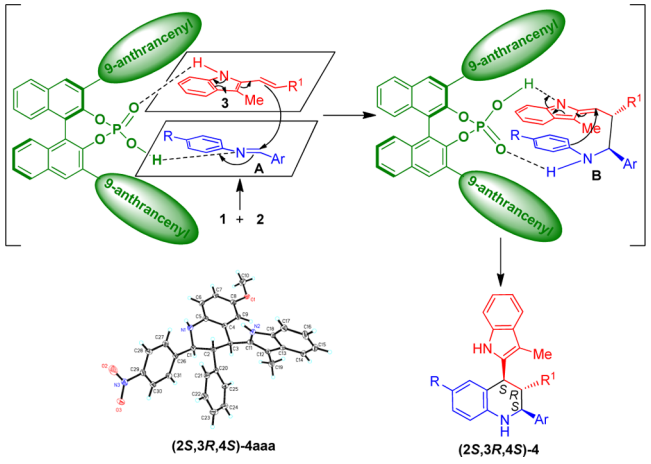
Table 4. Substrate Scope of 3-Methyl-2-vinylindoles 3[a]



entry	4	R (3)	yield (%)[b]	dr[c]	ee (%)[d]
1	**4aab**	4-MeC_6H_4 (**3b**)	92	>95:5	92
2	**4aac**	4-*t*-BuC_6H_4 (**3c**)	80	>95:5	90
3	**4aad**	3-MeC_6H_4 (**3d**)	84	>95:5	94
4	**4aae**	4-ClC_6H_4 (**3e**)	98	>95:5	94
5	**4aaf**	3-BrC_6H_4 (**3f**)	90	>95:5	96
6	**4aag**	3-FC_6H_4 (**3g**)	92	>95:5	94
7	**4aah**	Me (**3h**)	99	>95:5	96

[a]Unless otherwise indicated, the reaction was carried out at 0.1 mmol scale and catalyzed by 10 mol % (*R*)-**5e** in toluene (1 mL) with $MgSO_4$ (100 mg) at 50 °C for 24 h. The molar ratio of **1a**:**2a**:**3** was 1.2:1:2.5. [b]Isolated yield. [c]The dr value was determined by ^{1}H NMR. [d]The ee value was determined by HPLC.

Scheme 3. Possible Reaction Pathway



application of vinylindoles in catalytic asymmetric synthesis of chiral indole derivatives but also enrich the chemistry of the catalytic asymmetric Povarov reaction and multicomponent reaction. The mode of the catalytic asymmetric three-component reaction should offer a good opportunity to access enantioenriched indole-derived tetrahydroquinolines with structural diversity and complexity, which is promising for diversity-oriented synthesis and related bioassays.

EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS (ESI) was determined by a HRMS/MS instrument. Enantiomeric excesses (ee) were determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral column used for the determination of enantiomeric excesses by chiral HPLC was Chiralpak OD-H, AD-H, IA, and IC columns. Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at the temperatures indicated. The X-ray source used for the single crystal X-ray diffraction analysis of compound **4aaa** was CuKα (λ = 1.54178), and the thermal ellipsoid was drawn at the 30% probability level. Analytical grade solvents for the column chromatography and commercially available reagents were

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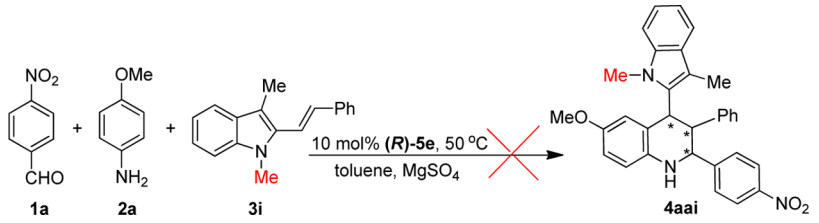
Scheme 4. Control Experiment To Demonstrate the Role of the N−H Group



used as received. All starting materials commercially available were used directly. Substrates **3** were synthesized according to the literature methods.[6a]

Typical Procedure for the Catalytic Asymmetric Povarov Reaction. After a solution of aldehydes **1** (0.12 mmol), anilines **2** (0.1 mmol), the catalyst (***R***)-**5e** (0.01 mmol), and magnesium sulfate (100 mg) in toluene (0.5 mL) was stirred at 50 °C for 30 min, the solution of 3-methyl-2-vinylindoles **3** (0.25 mmol) in toluene (0.5 mL) was added. After being stirred at 50 °C for 24 h, the reaction mixture was filtered to remove the magnesium sulfate, and the solid powder was washed with ethyl acetate. The resultant solution was concentrated under the reduced pressure to give the residue, which was purified through flash column chromatography on silica gel to afford pure products **4**.

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-3-phenyl-1,2,3,4-tetrahydroquinoline (**4aaa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (48.5 mg); yellow solid; mp 242−243 °C; $[\alpha]_D^{20}$ = −95.0 (*c* 0.63, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.99 (d, *J* = 8.8 Hz, 2H), 7.59 (s, 1H), 7.37 (t, *J* = 7.8 Hz, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.13−7.06 (m, 1H), 7.05−6.98 (m, 4H), 6.83−6.78 (m, 2H), 6.77−6.72 (m, 1H), 6.67 (d, *J* = 8.7 Hz, 1H), 6.37 (d, *J* = 2.2 Hz, 1H), 4.83 (d, *J* = 11.0 Hz, 1H), 4.77 (d, *J* = 10.3 Hz, 1H), 4.11 (s, 1H), 3.58 (s, 3H), 3.32 (t, *J* = 10.7 Hz, 1H), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 149.1, 147.2, 139.5, 138.8, 135.8, 134.3, 128.9, 128.6, 128.3, 128.1, 126.9, 124.2, 123.3, 121.3, 118.7, 118.3, 115.8, 114.9, 114.2, 110.4, 62.3, 55.8, 54.2, 43.1, 8.1; IR (KBr): 3348, 3031, 2913, 1598, 1504, 1456, 1347, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{27}N_3O_3-H)^-$ requires *m*/*z* 488.1974, found *m*/*z* 488.1974; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 10.64 min (major), t_R = 24.39 min (minor).

*(2S,3R,4S)-4-[6-Methoxy-4-(3-methyl-1H-indol-2-yl)-3-phenyl-1,2,3,4-tetrahydro-quinolin-2-yl]-benzonitrile (**4baa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (46.5 mg); pale-yellow solid; mp 133−134 °C; $[\alpha]_D^{20}$ = −92.1 (*c* 0.91, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.61 (s, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.13−7.06 (m, 1H), 7.06−7.00 (m, 4H), 6.83−6.77 (m, 1H), 6.76−6.71 (m, 1H), 6.65 (d, *J* = 8.7 Hz, 1H), 6.37 (d, *J* = 2.3 Hz, 1H), 4.83 (d, *J* = 11.0 Hz, 1H), 4.71 (d, *J* = 10.3 Hz, 1H), 4.09 (s, 1H), 3.58 (s, 3H), 3.30 (t, *J* = 10.7 Hz, 1H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 147.1, 139.7, 138.9, 135.8, 134.4, 131.9, 128.9, 128.5, 128.2, 128.1, 126.8, 124.2, 121.3, 118.8, 118.7, 118.3, 115.7, 114.9, 114.2, 111.3, 110.5, 110.4, 62.6, 55.8, 54.2, 43.1, 8.1; IR (KBr): 3356, 3027, 2912, 1510, 1503, 1461, 1411, 737 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{27}N_3O-H)^-$ requires *m*/*z* 468.2076, found *m*/*z* 468.2075; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 8.28 min (major), t_R = 20.74 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-3-phenyl-2-(4-trifluoromethyl-phenyl)-1,2,3,4-tetrahydro-quinoline (**4caa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 79% (40.5 mg); pale-yellow solid; mp 126−127 °C; $[\alpha]_D^{20}$ = −95.4 (*c* 0.78, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.60 (s, 1H), 7.47−7.32 (m, 5H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.13−7.07 (m, 1H), 7.06−7.00 (m, 4H), 6.86−6.79 (m, 1H), 6.77−6.72 (m, 1H), 6.64 (d, *J* = 8.7 Hz, 1H), 6.38 (d, *J* = 2.2 Hz, 1H), 4.82 (d, *J* = 11.0 Hz, 1H), 4.73 (d, *J* = 10.4 Hz, 1H), 4.06 (s, 1H), 3.58 (s, 3H), 3.35 (t, *J* = 10.7 Hz, 1H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.7, 145.6, 140.0, 139.2, 135.8, 134.6, 129.7 (*J* = 32.1 Hz), 128.9, 128.3, 128.2, 128.1, 126.7, 125.1 (*J* = 3.7 Hz), 124.3, 124.0 (*J* = 270.4 Hz), 121.3, 118.7, 118.3, 115.6, 115.0, 114.2, 110.5, 110.4, 62.4, 55.8, 54.1, 43.3, 8.1; IR (KBr): 3394, 3027, 2915, 1502, 1461, 1419, 1324, 747 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{27}F_3N_2O-H)^-$ requires *m*/*z* 511.1997, found *m*/*z* 511.2018; Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 4.73 min (major), t_R = 14.10 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-2-(3-nitro-phenyl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4daa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (48.5 mg); yellow solid; mp 205−206 °C; $[\alpha]_D^{20}$ = −133.7 (*c* 0.93, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.21 (s, 1H), 8.01−7.94 (m, 1H), 7.64 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.13−7.06 (m, 1H), 7.06−6.98 (m, 4H), 6.87−6.79 (m, 2H), 6.77−6.72 (m, 1H), 6.67 (d, *J* = 8.7 Hz, 1H), 6.38 (d, *J* = 2.3 Hz, 1H), 4.85 (d, *J* = 11.1 Hz, 1H), 4.79 (d, *J* = 10.3 Hz, 1H), 4.14 (s, 1H), 3.58 (s, 3H), 3.35 (t, *J* = 10.7 Hz, 1H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 148.1, 143.9, 139.6, 138.8, 135.9, 134.4, 134.1, 129.0, 128.9, 128.3, 128.2, 126.8, 124.2, 122.7, 122.6, 121.3, 118.7, 118.3, 115.8, 114.9, 114.2, 110.5, 110.4, 62.1, 55.8, 54.2, 43.1, 8.1; IR (KBr): 3398, 2917, 1656, 1528, 1501, 1460, 1451, 738 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{27}N_3O_3-H)^-$ requires *m*/*z* 488.1974, found *m*/*z* 488.1954; Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 8.61 min (major), t_R = 28.76 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-2-(2-nitro-phenyl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4eaa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (48.5 mg); yellow solid; mp 128−129 °C; $[\alpha]_D^{20}$ = −219.4 (*c* 0.78, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.81−7.76 (m, 1H), 7.60 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.25−7.14 (m, 2H), 7.12−7.06 (m, 1H), 7.06−7.00 (m, 1H), 7.00−6.95 (m, 3H), 6.79−6.67 (m, 4H), 6.36 (d, *J* = 2.2 Hz, 1H), 5.36 (d, *J* = 10.5 Hz, 1H), 4.76 (d, *J* = 10.9 Hz, 1H), 4.27 (s, 1H), 3.58 (s, 3H), 3.45 (t, *J* = 10.7 Hz, 1H), 1.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 153.0, 152.9, 150.4, 139.4, 139.1, 135.8, 135.4, 134.3, 132.5, 129.6, 128.9, 128.3, 128.2, 127.8, 126.8, 124.3, 123.6, 121.3, 118.7, 118.3, 116.2, 114.9, 114.3, 110.7, 110.4, 56.1, 55.8, 53.2, 53.1, 43.6, 8.0; IR (KBr): 3352, 3027, 2914, 1657, 1530, 1504, 1486, 1462, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{27}N_3O_3-H)^-$ requires *m*/*z* 488.1974, found *m*/*z* 488.1952; Enantiomeric excess: 68%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 9.32 min (major), t_R = 12.99 min (minor).

*(2S,3R,4S)-2-(3,4-Dichloro-phenyl)-6-methoxy-4-(3-methyl-1H-indol-2-yl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4faa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; > 95:5 dr; yield: 82% (42.0 mg); pale-yellow solid; mp 105−106 °C; $[\alpha]_D^{20}$ = −87.2 (*c* 0.84, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.57 (s, 1H), 7.41 (d, *J* = 1.8 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.13−7.00 (m, 5H), 6.99−6.93 (m, 1H), 6.85−6.79 (m, 2H), 6.77−6.71 (m, 1H), 6.65 (d, *J* = 8.7 Hz, 1H), 6.36 (d, *J* = 2.6 Hz, 1H), 4.79 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 10.4 Hz, 1H), 4.03 (s, 1H), 3.58 (s, 3H), 3.27 (t, *J* = 10.7 Hz, 1H), 1.77 (s, 3H);

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^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.7, 142.0, 139.8, 139.0, 135.8, 134.5, 132.2, 131.3, 129.9, 129.5, 128.9, 128.3, 128.2, 127.2, 126.8, 124.2, 121.3, 118.7, 118.3, 115.6, 114.9, 114.1, 110.5, 110.4, 61.8, 55.8, 54.1, 43.2, 8.1; IR (KBr): 3390, 2913, 1504, 1462, 1455, 1416, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{26}Cl_2N_2O-H)^-$ requires m/z 511.1344, found m/z 511.1340; Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.05 min (major), t_R = 25.10 min (minor).

*(2S,3R,4S)-2-(3-Chloro-4-fluoro-phenyl)-6-methoxy-4-(3-methyl-1H-indol-2-yl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4gaa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 72% (35.7 mg); pale-yellow solid; mp 115−116 °C; $[\alpha]_D^{20}$ = −86.5 (*c* 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.57 (s, 1H), 7.40−7.33 (m, 2H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.12−6.96 (m, 6H), 6.88 (t, *J* = 8.7 Hz, 1H), 6.84−6.78 (m, 2H), 6.76−6.71 (m, 1H), 6.65 (d, *J* = 8.7 Hz, 1H), 6.36 (d, *J* = 2.2 Hz, 1H), 4.79 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 10.4 Hz, 1H), 4.04 (s, 1H), 3.58 (s, 3H), 3.26 (t, *J* = 10.7 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 157.2 (*J* = 247.2 Hz), 152.7, 140.0, 139.1, 138.8 (*J* = 3.8 Hz), 135.8, 134.6, 129.6, 128.9, 128.2, 127.6 (*J* = 7.1 Hz), 126.7, 124.2, 121.3, 120.7 (*J* = 17.6 Hz), 118.7, 118.3, 116.1 (*J* = 20.9 Hz), 115.6, 115.0, 114.1, 110.5, 110.4, 61.8, 55.8, 54.3, 43.2, 8.1; IR (KBr): 3352, 3055, 2912, 1504, 1462, 1455, 1415, 1249, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{26}ClFN_2O-H)^-$ requires m/z 495.1640, found m/z 495.1662; Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.44 min (major), t_R = 19.06 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-2,3-diphenyl-1,2,3,4-tetrahydro-quinoline (**4haa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 48 h; >95:5 dr; yield: 48% (21.4 mg); pale-yellow solid; mp 132−133 °C; $[\alpha]_D^{20}$ = −109.4 (*c* 0.28, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.61 (s, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.24−7.11 (m, 6H), 7.11−7.06 (m, 1H), 7.04−6.94 (m, 4H), 6.85−6.79 (m, 2H), 6.74−6.70 (m, 1H), 6.63 (d, *J* = 8.7 Hz, 1H), 6.36 (d, *J* = 2.2 Hz, 1H), 4.79 (d, *J* = 10.9 Hz, 1H), 4.65 (d, *J* = 10.4 Hz, 1H), 4.06 (s, 1H), 3.58 (s, 3H), 3.35 (t, *J* = 10.7 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.4, 141.5, 140.6, 139.6, 135.8, 135.0, 128.9, 128.3, 128.1, 127.9, 127.7, 127.6, 126.3, 124.3, 121.1, 118.6, 118.2, 115.4, 115.0, 114.0, 110.3, 110.2, 62.8, 55.8, 54.1, 43.4, 8.1; IR (KBr): 3396, 3027, 2915, 1503, 1461, 1455, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{28}N_2O-H)^-$ requires m/z 443.2124, found m/z 443.2144; Enantiomeric excess: 76%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 7.46 min (major), t_R = 11.42 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-3-phenyl-2-m-tolyl-1,2,3,4-tetrahydro-quinoline (**4iaa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 48 h; >95:5 dr; yield: 41% (18.8 mg); yellow solid; mp 101−102 °C; $[\alpha]_D^{20}$ = −78.9 (*c* 0.28, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.63 (s, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.16−6.92 (m, 9H), 6.88−6.82 (m, 2H), 6.77−6.72 (m, 1H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.38 (d, *J* = 2.1 Hz, 1H), 4.80 (d, *J* = 10.9 Hz, 1H), 4.64 (d, *J* = 10.4 Hz, 1H), 4.07 (s, 1H), 3.61 (s, 3H), 3.37 (t, *J* = 10.6 Hz, 1H), 2.25 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.4, 141.4, 140.7, 139.6, 137.7, 135.8, 135.1, 128.9, 128.4, 128.3, 128.0, 127.9, 126.3, 124.9, 124.3, 121.1, 118.5, 118.2, 115.4, 115.0, 114.0, 110.3, 110.2, 62.7, 55.8, 54.0, 43.5, 21.3, 8.1; IR (KBr): 3417, 2962, 1606, 1504, 1462, 1454, 738 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{30}N_2O-H)^-$ requires m/z 457.2280, found m/z 457.2278; Enantiomeric excess: 68%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.99 min (major), t_R = 10.21 min (minor).

*(2S,3R,4S)-6-Methyl-4-(3-methyl-1H-indol-2-yl)-2-(4-nitro-phenyl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4aba**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (46.9 mg); yellow solid; mp 135−136 °C; $[\alpha]_D^{20}$ = −81.6 (*c* 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, *J* = 8.8 Hz, 1H), 7.59 (s, 1H), 7.39 (d, *J* = 8.8 Hz, 3H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.14−7.09 (m, 1H), 7.07−7.00 (m, 4H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.84−6.78 (m, 2H), 6.66 (d, *J* = 8.1 Hz, 1H), 6.61 (s, 1H), 4.83 (t, *J* = 10.1 Hz, 2H), 4.21 (s, 1H), 3.32 (t, *J* = 10.7 Hz, 1H), 2.13 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.2, 147.2, 142.3, 139.6, 135.8, 134.6, 130.1, 128.9, 128.6, 128.3, 128.2, 128.1, 126.9, 123.3, 122.9, 121.3, 118.7, 118.3, 114.8, 110.6, 110.5, 62.1, 54.3, 42.8, 20.5, 8.1; IR (KBr): 3418, 2915, 2853, 1614, 1515, 1505, 1487, 742 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{27}N_3O_2-H)^-$ requires m/z 472.2025, found m/z 472.2023; Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 4.61 min (major), t_R = 5.02 min (minor).

*(2S,3R,4S)-6-Ethoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitro-phenyl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4aca**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (49.8 mg); yellow solid; mp 235−236 °C; $[\alpha]_D^{20}$ = −79.8 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-d_6) δ (ppm): 9.78 (s, 1H), 8.01 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.07−6.85 (m, 7H), 6.76 (d, *J* = 8.7 Hz, 1H), 6.70−6.64 (m, 1H), 6.20 (d, *J* = 2.3 Hz, 1H), 5.39 (s, 1H), 5.00−4.86 (m, 2H), 3.78−3.59 (m, 3H), 2.03 (s, 3H), 1.15 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, Acetone-d_6) δ (ppm): 151.3, 150.6, 147.0, 140.6, 139.3, 139.2, 136.3, 135.2, 129.1, 128.7, 128.3, 127.8, 126.3, 124.4, 122.8, 120.6, 118.0, 117.7, 115.4, 115.2, 113.7, 110.4, 110.3, 108.8, 63.4, 62.0, 52.2, 42.5, 14.2; IR (KBr): 3367, 2912, 1597, 1520, 1504, 1455, 739 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{29}N_3O_3-H)^-$ requires m/z 502.2131, found m/z 502.2121; Enantiomeric excess: 88%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.27 min (major), t_R = 11.30 min (minor).

*(2S,3R,4S)-4-(3-Methyl-1H-indol-2-yl)-2-(4-nitro-phenyl)-6-phenoxy-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4ada**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (54.6 mg); yellow solid; mp 128−129 °C; $[\alpha]_D^{20}$ = −21.5 (*c* 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.01 (d, *J* = 8.8 Hz, 2H), 7.60 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.26−7.16 (m, 3H), 7.13−7.07 (m, 1H), 7.05−6.93 (m, 5H), 6.89−6.79 (m, 5H), 6.70 (d, *J* = 8.6 Hz, 1H), 6.59 (d, *J* = 1.9 Hz, 1H), 4.85 (d, *J* = 10.5 Hz, 2H), 4.28 (s, 1H), 3.35 (t, *J* = 10.8 Hz, 1H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 158.6, 149.0, 148.3, 147.3, 141.1, 139.3, 135.8, 133.8, 129.5, 128.8, 128.6, 128.3, 128.1, 127.0, 124.4, 123.4, 122.1, 121.7, 121.4, 120.1, 118.8, 118.4, 116.9, 115.6, 110.7, 110.4, 62.1, 53.8, 43.0, 8.2; IR (KBr): 3390, 3055, 3028, 1593, 1538, 1516, 1504, 739 cm^{-1}; ESI FTMS exact mass calcd for $(C_{36}H_{29}N_3O_3-H)^-$ requires m/z 550.2131, found m/z 550.2147; Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.53 min (major), t_R = 11.79 min (minor).

*(2S,3R,4S)-4-(3-Methyl-1H-indol-2-yl)-2-(4-nitro-phenyl)-3-phenyl-1,2,3,4-tetrahydro-quinoline(**4aea**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (45.5 mg); yellow solid; mp 133−134 °C; $[\alpha]_D^{20}$ = −118.5 (*c* 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.01 (d, *J* = 8.8 Hz, 2H), 7.58 (s, 1H), 7.43−7.35 (m, 3H), 7.19 (d, *J* = 7.9 Hz, 1H), 7.16−7.07 (m, 2H), 7.07−6.99 (m, 4H), 6.86−6.80 (m, 2H), 6.78−6.70 (m, 2H), 6.70−6.63 (m, 1H), 4.95−4.80 (m, 2H), 4.34 (s, 1H), 3.35 (t, *J* = 10.8 Hz, 1H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.1, 147.3, 144.5, 139.4, 135.8, 134.3, 130.0, 128.9, 128.6, 128.3, 128.1, 127.9, 126.9, 123.4, 122.9, 121.3, 118.8, 118.7, 118.3, 114.6, 110.7, 110.4, 62.0, 53.8, 42.7, 8.2; IR (KBr): 3412, 3054, 2913, 1604, 1587, 1515, 1485, 743 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{25}N_3O_2-H)^-$ requires m/z 458.1869, found m/z 458.1864; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 17.28 min (major), t_R = 22.80 min (minor).

*(2S,3R,4S)-6-Fluoro-4-(3-methyl-1H-indol-2-yl)-2-(4-nitro-phenyl)-3-phenyl-1,2,3,4-tetrahydro-quinoline (**4afa**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 90% (42.9 mg); yellow solid; mp 147−148

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°C; $[\alpha]_D^{20}$ = −144.8 (*c* 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, *J* = 8.8 Hz, 2H), 7.56 (s, 1H), 7.38 (d, *J* = 8.7 Hz, 3H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.14−7.07 (m, 1H), 7.07−6.99 (m, 4H), 6.87−6.78 (m, 3H), 6.68−6.61 (m, 1H), 6.54−6.45 (m, 1H), 4.91−4.74 (m, 2H), 4.23 (s, 1H), 3.32 (t, *J* = 10.8 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 156.3 (*J* = 235.7 Hz), 148.8, 147.3, 140.8, 140.7, 139.1, 135.8, 133.6, 128.8, 128.5, 128.4, 128.0, 127.0, 124.3 (*J* = 6.2 Hz), 123.4, 121.6, 118.9, 118.4, 116.0 (*J* = 22.6 Hz), 115.5 (*J* = 7.5 Hz), 114.9 (*J* = 22.8 Hz), 110.8, 110.4, 62.2, 53.5, 42.9, 8.1; IR (KBr): 3395, 3055, 2913, 1599, 1517, 1502, 1461, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{24}FN_3O_2-H)^-$ requires *m*/*z* 476.1775, found *m*/*z* 476.1779; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 7.92 min (major), t_R = 23.01 min (minor).

*(2S,3R,4S)-6-Chloro-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-3-phenyl-1,2,3,4-tetrahydroquinoline (**4aga**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 97% (47.8 mg); yellow solid; mp 147−148 °C; $[\alpha]_D^{20}$ = −52.9 (*c* 0.90, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.99 (d, *J* = 8.8 Hz, 2H), 7.56 (s, 1H), 7.38 (t, *J* = 7.6 Hz, 3H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.16−7.09 (m, 1H), 7.08−6.99 (m, 5H), 6.83−6.77 (m, 2H), 6.74 (d, *J* = 1.4 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 1H), 4.87−4.77 (m, 2H), 4.33 (s, 1H), 3.30 (t, *J* = 10.8 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 148.7, 147.3, 143.1, 139.0, 135.9, 133.3, 129.3, 128.8, 128.5, 128.4, 128.0, 127.9, 127.1, 124.4, 123.4, 123.3, 121.6, 118.9, 118.4, 115.8, 111.0, 110.5, 61.9, 53.4, 42.6, 29.7, 8.2; IR (KBr): 3399, 3027, 2916, 1600, 1518, 1489, 1460, 741 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{24}ClN_3O_2-H)^-$ requires *m*/*z* 492.1479, found *m*/*z* 492.1487; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 10.42 min (major), t_R = 34.70 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-3-(p-tolyl)-1,2,3,4-tetrahydroquinoline (**4aab**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 92% (46.3 mg); yellow solid; mp 137−138 °C; $[\alpha]_D^{20}$ = −94.7 (*c* 0.90, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, *J* = 8.8 Hz, 2H), 7.61 (s, 1H), 7.42−7.33 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.12−6.99 (m, 2H), 6.82 (d, *J* = 7.8 Hz, 2H), 6.76−6.71 (m, 1H), 6.70−6.62 (m, 3H), 6.36 (d, *J* = 2.3 Hz, 1H), 4.80 (d, *J* = 11.0 Hz, 1H), 4.75 (d, *J* = 10.3 Hz, 1H), 4.10 (s, 1H), 3.57 (s, 3H), 3.29 (t, *J* = 10.7 Hz, 1H), 2.17 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 149.4, 147.2, 138.8, 136.4, 136.3, 135.8, 134.5, 129.0, 128.9, 128.6, 127.9, 124.3, 123.3, 121.3, 118.7, 118.3, 115.7, 114.9, 114.1, 110.5, 110.4, 62.4, 55.8, 53.7, 43.1, 20.9, 8.2; IR (KBr): 3418, 3027, 2943, 1547, 1517, 1503, 1448, 743 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{29}N_3O_3-H)^-$ requires *m*/*z* 502.2131, found *m*/*z* 502.2136; Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 8.94 min (major), t_R = 21.87 min (minor).

*(2S,3R,4S)-3-(4-(tert-Butyl)phenyl)-6-methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-1,2,3,4-tetrahydroquinoline (**4aac**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 80% (43.6 mg); yellow solid; mp 130−131 °C; $[\alpha]_D^{20}$ = −83.4 (*c* 0.84, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.98 (d, *J* = 8.8 Hz, 2H), 7.58 (s, 1H), 7.38 (d, *J* = 8.7 Hz, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.12−7.06 (m, 1H), 7.06−7.00 (m, 3H), 6.77−6.63 (m, 4H), 6.37 (d, *J* = 2.3 Hz, 1H), 4.77 (t, *J* = 10.9 Hz, 1H), 4.08 (s, 1H), 3.58 (s, 3H), 3.28 (t, *J* = 10.6 Hz, 1H), 1.74 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 149.8, 149.4, 147.2, 138.9, 136.4, 135.8, 134.6, 128.9, 128.6, 127.7, 125.1, 124.3, 123.2, 121.3, 118.7, 118.3, 115.7, 114.9, 114.2, 110.6, 110.4, 62.2, 55.8, 53.7, 43.2, 34.3, 31.2, 8.0; IR (KBr): 3391, 3027, 2959, 1518, 1504, 1462, 1415, 738 cm^{-1}; ESI FTMS exact mass calcd for $(C_{35}H_{35}N_3O_3-H)^-$ requires *m*/*z* 544.2600, found *m*/*z* 544.2611; Enantiomeric excess: 90%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 7.46 min (major), t_R = 19.08 min (minor).

*(2S,3R,4S)-6-Methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-3-(m-tolyl)-1,2,3,4-tetrahydroquinoline (**4aad**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 84% (42.3 mg); yellow solid; mp 154−155 °C; $[\alpha]_D^{20}$ = −85.1 (*c* 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, *J* = 8.8 Hz, 2H), 7.60 (s, 1H), 7.42−7.33 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.12−7.06 (m, 1H), 7.05−7.00 (m, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.76−6.72 (m, 1H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.60 (d, *J* = 8.9 Hz, 2H), 6.37 (d, *J* = 2.4 Hz, 1H), 4.83 (d, *J* = 11.0 Hz, 1H), 4.75 (d, *J* = 10.3 Hz, 1H), 4.08 (s, 1H), 3.58 (s, 3H), 3.28 (t, *J* = 10.7 Hz, 1H), 2.11 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 149.3, 147.2, 139.4, 138.8, 137.7, 135.8, 134.5, 128.9, 128.8, 128.6, 128.1, 127.6, 125.2, 124.3, 123.3, 121.3, 118.7, 118.3, 115.7, 114.9, 114.2, 110.4, 62.4, 55.8, 54.1, 43.0, 21.3, 8.1; IR (KBr): 3390, 3017, 2937, 1606, 1558, 1530, 1516, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{29}N_3O_3-H)^-$ requires *m*/*z* 502.2131, found *m*/*z* 502.2151; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 8.77 min (major), t_R = 18.86 min (minor).

*(2S,3R,4S)-3-(4-Chlorophenyl)-6-methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-1,2,3,4-tetrahydroquinoline (**4aae**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 98% (51.3 mg); yellow solid; mp 151−152 °C; $[\alpha]_D^{20}$ = −99.9 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.02 (d, *J* = 8.8 Hz, 2H), 7.62 (s, 1H), 7.44−7.34 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.14−7.08 (m, 1H), 7.07−6.97 (m, 3H), 6.79−6.70 (m, 3H), 6.65 (d, *J* = 8.7 Hz, 1H), 6.35 (d, *J* = 2.3 Hz, 1H), 4.76 (t, *J* = 11.1 Hz, 2H), 4.11 (s, 1H), 3.57 (s, 3H), 3.34 (t, *J* = 10.7 Hz, 1H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.8, 148.8, 147.3, 138.7, 138.2, 135.9, 133.9, 132.6, 129.4, 128.8, 128.6, 128.5, 123.8, 123.5, 121.5, 118.9, 118.4, 115.8, 114.8, 114.3, 110.6, 110.4, 62.2, 55.8, 53.6, 43.1, 8.3; IR (KBr): 3396, 3014, 2918, 1599, 1518, 1504, 1461, 1345, 739 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{26}ClN_3O_3-H)^-$ requires *m*/*z* 522.1585, found *m*/*z* 522.1592; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak AD-H, hexane/isopropanol = 90/10, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 21.15 min (minor), t_R = 24.80 min (major).

*(2S,3R,4S)-3-(3-Bromophenyl)-6-methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-1,2,3,4-tetrahydroquinoline (**4aaf**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 90% (51.0 mg); yellow solid; mp 139−140 °C; $[\alpha]_D^{20}$ = −90.4 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.03 (d, *J* = 8.8 Hz, 2H), 7.60 (s, 1H), 7.43−7.34 (m, 3H), 7.20−7.00 (m, 5H), 6.82 (t, *J* = 7.8 Hz, 1H), 6.77−6.71 (m, 1H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 1H), 6.35 (d, *J* = 2.5 Hz, 1H), 4.80 (d, *J* = 11.0 Hz, 1H), 4.73 (d, *J* = 10.3 Hz, 1H), 4.12 (s, 1H), 3.57 (s, 3H), 3.31 (t, *J* = 10.7 Hz, 1H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.9, 148.7, 147.3, 142.0, 138.6, 135.9, 133.7, 130.6, 130.1, 129.8, 128.8, 128.6, 127.4, 123.8, 123.5, 122.3, 121.5, 118.9, 118.4, 115.8, 114.8, 114.3, 110.7, 110.5, 62.3, 55.8, 54.0, 42.9, 8.2; IR (KBr): 3397, 3055, 2915, 1518, 1503, 1460, 1427, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{26}BrN_3O_3-H)^-$ requires *m*/*z* 568.1058, found *m*/*z* 568.1051; Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 10.34 min (major), t_R = 24.62 min (minor).

*(2S,3R,4S)-3-(3-Fluorophenyl)-6-methoxy-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-1,2,3,4-tetrahydroquinoline (**4aag**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 92% (46.7 mg); yellow solid; mp 217−218 °C; $[\alpha]_D^{20}$ = −93.4 (*c* 0.86, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.02 (d, *J* = 8.8 Hz, 2H), 7.61 (s, 1H), 7.44−7.34 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.14−7.08 (m, 1H), 7.07−7.01 (m, 1H), 6.70−6.92 (m, 1H), 6.77−6.68 (m, 2H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.62 (d, *J* = 9.8 Hz, 1H), 6.54 (d, *J* = 7.7 Hz, 1H), 6.36 (d, *J* = 2.3 Hz, 1H), 4.80 (d, *J* = 11.1 Hz, 1H), 4.74 (d, *J* = 10.3 Hz, 1H), 4.11 (s, 1H), 3.58 (s, 3H), 3.35 (t, *J* = 10.7 Hz, 1H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 162.6 (*J* = 244.6 Hz), 152.9, 148.7, 147.3, 142.3 (*J* = 7.0 Hz), 138.6, 135.9, 133.9, 129.9 (*J* = 8.3 Hz), 128.8, 128.6, 124.2,

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124.1, 123.8, 123.4, 121.5, 118.9, 118.4, 115.8, 114.9, 114.7 (J = 21.3 Hz), 114.3, 114.0 (J = 20.9 Hz), 110.6, 110.4, 62.2, 55.8, 54.0, 43.0, 8.2; IR (KBr): 3391, 2938, 1613, 1591, 1543, 1527, 1463, 1327, 748 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{26}FN_3O_3-H)^-$ requires m/z 506.1880, found m/z 506.1891; Enantiomeric excess: 94%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 10.95 min (major), t_R = 25.78 min (minor).

*(2S,3R,4S)-6-Methoxy-3-methyl-4-(3-methyl-1H-indol-2-yl)-2-(4-nitrophenyl)-1,2,3,4-tetrahydroquinoline (**4aah**).* Flash column chromatography eluent, petroleum ether/ethyl acetate = 5/1; reaction time = 24 h; >95:5 dr; yield: 99% (42.3 mg); yellow solid; mp 124−125 °C; $[\alpha]_D^{20}$ = −70.6 (c 0.81, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.24 (d, J = 8.8 Hz, 2H), 7.67−7.61 (m, 3H), 7.59−7.53 (m, 1H), 7.22−7.18 (m, 1H), 7.17−7.09 (m, 2H), 6.71−6.65 (m, 1H), 6.57 (d, J = 8.6 Hz, 1H), 6.34−6.25 (m, 1H), 4.30−4.20 (m, 2H), 3.94 (s, 1H), 3.57 (s, 3H), 2.37 (s, 3H), 2.34−2.24 (m, 1H), 0.65 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.7, 149.9, 147.7, 138.8, 135.8, 134.8, 128.9, 128.8, 123.8, 123.7, 121.6, 119.0, 118.3, 115.4, 115.1, 113.7, 110.8, 110.5, 63.6, 55.7, 43.1, 41.0, 16.3, 8.9; IR (KBr): 3390, 2959, 2920, 1518, 1504, 1462, 1455, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{26}H_{25}N_3O_3-H)^-$ requires m/z 426.1818, found m/z 426.1830; Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.98 min (major), t_R = 12.69 min (minor).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02476.

Characterization data (including ^1H, ^{13}C NMR and HPLC spectra) for all products **4** (PDF)

Single crystal data of product **4aaa**(CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: fshi@jsnu.edu.cn.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For some reviews: (a) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875. (b) Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608. (c) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489.

(2) For some reviews: (a) You, S.-L.; Cai, Q.; Zeng, M. *Chem. Soc. Rev.* **2009**, *38*, 2190. (b) Zeng, M.; You, S.-L. *Synlett* **2010**, *2010*, 1289. (c) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Chem. Soc. Rev.* **2010**, *39*, 4449. (d) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023. (e) Cheng, D.-J.; Ishihara, Y.; Tan, B.; Barbas, C. F., III *ACS Catal.* **2014**, *4*, 743. (f) Dalpozzo, R. *Chem. Soc. Rev.* **2015**, *44*, 742.

(3) For some 2-vinylindole involved catalytic asymmetric reactions: (a) Jones, S. B.; Simmons, B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 13606. (b) Zheng, C.; Lu, Y.; Zhang, J.; Chen, X.; Chai, Z.; Ma, W.; Zhao, G. *Chem. - Eur. J.* **2010**, *16*, 5853. (c) Wang, X.-F.; Chen, J.-R.; Cao, Y.-J.; Cheng, H.-G.; Xiao, W.-J. *Org. Lett.* **2010**, *12*, 1140. (d) Bergonzini, G.-L.; Gramigna, L.-C.; Mazzanti, A.; Fochi, M.; Bernardi, L.; Ricci, A. *Chem. Commun.* **2010**, *46*, 327. (e) Cao, Y.-J.; Cheng, H.-G.; Lu, L.-Q.; Zhang, J.-J.; Cheng, Y.; Chen, J.-R.; Xiao, W.-J. *Adv. Synth. Catal.* **2011**, *353*, 617. (f) Tian, X.; Hofmann, N.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2014**, *53*, 2997. (g) Wang, Y.; Tu, M.-S.; Yin, L.; Sun, M.; Shi, F. *J. Org. Chem.* **2015**, *80*, 3223.

(4) For some 3-vinylindole involved catalytic asymmetric reactions: (a) Gioia, C.; Hauville, A.; Bernardi, L.; Fini, F.; Ricci, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 9236. (b) Tan, B.; Hernández-Torres, G.; Barbas, C. F., III *J. Am. Chem. Soc.* **2011**, *133*, 12354. (c) Liu, Y.-K.; Nappi, M.; Arceo, E.; Vera, S.; Melchiorre, P. *J. Am. Chem. Soc.* **2011**, *133*, 15212. (d) Enders, D.; Joie, C.; Deckers, K. *Chem. - Eur. J.* **2013**, *19*, 10818. (e) Chen, J.; Geng, Z.-C.; Li, N.; Huang, X.-F.; Pan, F.-F.; Wang, X.-W. *J. Org. Chem.* **2013**, *78*, 2362. (f) Terada, M.; Moriya, K.; Kanomata, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 12586. (g) Wang, Y.; Zhang, P.; Liu, Y.; Xia, F.; Zhang, J. *Chem. Sci.* **2015**, *6*, 5564. (h) Zheng, H.-F.; Liu, X.-H.; Xu, C.-R.; Xia, Y.; Lin, L.-L.; Feng, X.-M. *Angew. Chem., Int. Ed.* **2015**, *54*, 10958.

(5) For some other vinylindole involved catalytic asymmetric reactions: (a) Tønder, J. E.; Tanner, D. *Tetrahedron* **2003**, *59*, 6937. (b) Enders, D.; Jeanty, M.; Bats, J. W. *Synlett* **2009**, *2009*, 3175. (c) Caruana, L.; Fochi, M.; Franchini, M. C.; Ranieri, S.; Mazzanti, A.; Bernardi, L. *Chem. Commun.* **2014**, *50*, 445. (d) Shi, F.; Zhang, H.-H.; Sun, X.-X.; Liang, J.; Fan, T.; Tu, S.-J. *Chem. - Eur. J.* **2015**, *21*, 3465.

(6) (a) Tan, W.; Li, X.; Gong, Y.-X.; Ge, M.-D.; Shi, F. *Chem. Commun.* **2014**, *50*, 15901. (b) Zhao, J.-J.; Sun, S.-B.; He, S.-H.; Wu, Q.; Shi, F. *Angew. Chem., Int. Ed.* **2015**, *54*, 5460.

(7) For early reports on metal-catalyzed transformations: (a) Ishitani, H.; Kobayashi, S. *Tetrahedron Lett.* **1996**, *37*, 7357. (b) Sundararajan, G.; Prabagaran, N.; Varghese, B. *Org. Lett.* **2001**, *3*, 1973. (c) Xie, M.-S.; Chen, X.-H.; Zhu, Y.; Gao, B.; Lin, L.-L.; Liu, X.-H.; Feng, X.-M. *Angew. Chem., Int. Ed.* **2010**, *49*, 3799. For early reports on organo-catalyzed transformations: (d) Akiyama, T.; Morita, H.; Fuchibe, K. *J. Am. Chem. Soc.* **2006**, *128*, 13070. (e) Liu, H.; Dagousset, G.; Masson, G.; Retailleau, P.; Zhu, J. *J. Am. Chem. Soc.* **2009**, *131*, 4598. (f) Wang, C.; Han, Z.-Y.; Luo, H.-W.; Gong, L.-Z. *Org. Lett.* **2010**, *12*, 2266. (g) Xu, H.; Zuend, S. J.; Woll, M. G.; Tao, Y.; Jacobsen, E. N. *Science* **2010**, *327*, 986. For reviews: (h) Masson, G.; Lalli, C.; Benohoud, M.; Dagousset, G. *Chem. Soc. Rev.* **2013**, *42*, 902. (i) Jiang, X.-X.; Wang, R. *Chem. Rev.* **2013**, *113*, 5515.

(8) (a) Dorey, G.; Lockhart, B.; Lestage, P.; Casara, P. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 935. (b) Ramesh, E.; Manian, R. D. R. S.; Raghunathan, R.; Sainath, S.; Raghunathan, M. *Bioorg. Med. Chem.* **2009**, *17*, 660. (c) Kouznetsov, V. V.; Arenas, D. R. M.; Arvelo, F.; Forero, J. S. B.; Sojo, F.; Muñoz, A. *Lett. Drug Des. Discovery* **2010**, *7*, 632. (d) Kouznetsov, V. V.; Leonor, Y.; Acevedo, A. M. *Lett. Drug Des. Discovery* **2010**, *7*, 710.

(9) For some reviews: (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (b) Terada, M. *Chem. Commun.* **2008**, *35*, 4097. (c) Terada, M. *Synthesis* **2010**, *2010*, 1929. (d) Yu, J.; Shi, F.; Gong, L.-Z. *Acc. Chem. Res.* **2011**, *44*, 1156. (e) Parmar, D.; Sugiono, E.; Raja, S.; Rueping, M. *Chem. Rev.* **2014**, *114*, 9047. (f) Wu, H.; He, Y.-P.; Shi, F. *Synthesis* **2015**, *47*, 1990.

(10) (a) Zhang, Y.-C.; Zhao, J.-J.; Jiang, F.; Sun, S.-B.; Shi, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 13912. (b) Liu, Y.; Zhang, H.-H.; Zhang, Y.-C.; Jiang, Y.; Shi, F.; Tu, S.-J. *Chem. Commun.* **2014**, *50*, 12054. (c) Wang, Y.; Shi, F.; Yao, X.-X.; Sun, M.; Dong, L.; Tu, S.-J. *Chem. - Eur. J.* **2014**, *20*, 15047. (d) Shi, F.; Xing, G.-J.; Zhu, R.-Y.; Tan, W.; Tu, S.-J. *Org. Lett.* **2013**, *15*, 128.

(11) For a review: (a) Cheong, P. H.-Y.; Legault, C. Y.; Um, J. M.; Çelebi-Ölçüm, N.; Houk, K. N. *Chem. Rev.* **2011**, *111*, 5042. For a recent example: (b) Shi, F.; Xing, G.-J.; Tao, Z.-L.; Luo, S.-W.; Tu, S.-J.; Gong, L.-Z. *J. Org. Chem.* **2012**, *77*, 6970.

(12) CCDC 1414995 for **4aaa**. See the Supporting Information for details.

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