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Access to Chiral 2,5-Pyrrolidinyl Dispirooxindoles via Dinuclear Zinc Catalyzed Asymmetric Cascade Reactions

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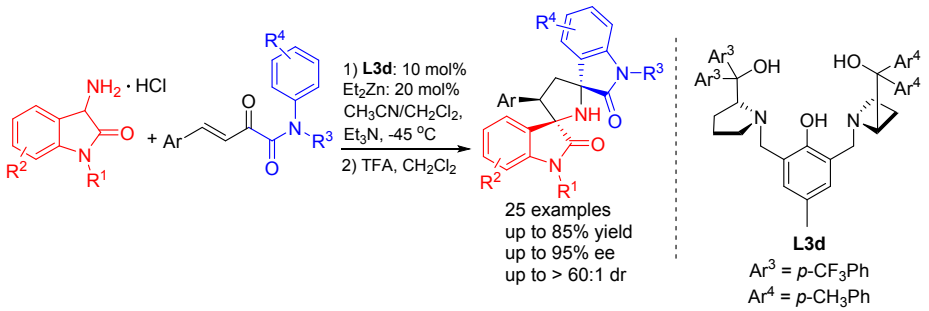


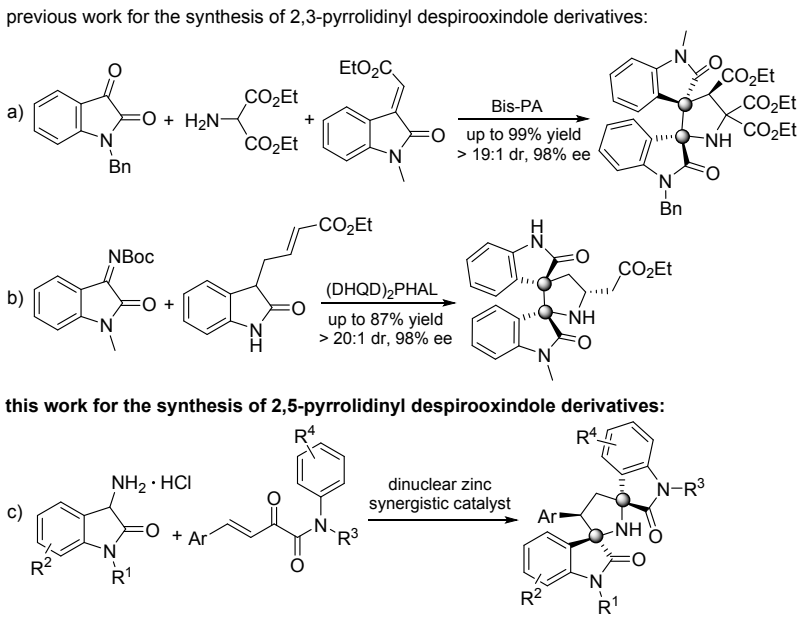
Abstract: A series of new nonsymmetric semi-azacrown ether ligands were developed and applied to the asymmetric Michael/cyclic keto-imine formation/Friedel-Crafts alkylation reactions of 3-amino oxindole hydrochlorides and *β,γ*-unsaturated *α*-keto amides. A diversity of 2,5-pyrrolidinyl dispirooxindoles containing two nonadjacent spiro-quaternary stereocenters were obtained in excellent diastereoselectivities and moderate to excellent enantioselectivities (up to 95% ee). A possible catalytic cycle was proposed to explain the origin of the asymmetric induction.

INTRODUCTION

The 3,2'-pyrrolidinyl spirooxindole frameworks are privileged structural motifs that widely exist in a large variety of natural and synthetic compounds.[1] Among them, the enantiomerically pure 3,2'-pyrrolidinyl spirooxindoles exhibit a broad spectrum of important biological and pharmaceutical activities[2] including antimycobacterial[2a] and cytotoxic to MCF-7 cells[2b]. Given the significance of this promising structural core in

both organic and medicinal chemistry,[3] some effective synthetic methods have been developed to asymmetrically construct this prevalent structural skeletons in recent years.[4] Among these elegant methods, most of which are limited to the construction of 3,2'-pyrrolidinyl spirooxindoles bearing only one spiro-quaternary stereocenter.

Scheme 1. Strategies for the Synthesis of Pyrrolidinyl Dispirooxindoles



Owing to the more complex structures of pyrrolidinyl dispirooxindoles, which contain two spiro-quaternary stereocenters and more chiral carbon atoms, only a few catalytic asymmetric examples have been reported for the synthesis of pyrrolidinyl dispirooxindoles up to now.[5] In 2015, the Tu group reported the synthesis of 2,3-pyrrolidinyl dispirooxindoles by a chiral bis-phosphoric acid (Bis-PA) catalyzed asymmetric 1,3-dipolar cycloadditions of isatin-derived azomethine ylides and methyleneindolinones (Scheme 1a).[5a] In 2016, Enders and co-workers described a novel one-pot $(DHQD)_2PHAL$ catalyzed Mannich/deprotection/aza-Michael sequence, leading to a series of 2,3-pyrrolidinyl dispirooxindole derivatives (Scheme 1b).[5b] Notably, all the catalysts used in above approaches were confined to organocatalysts, but the metal-catalysed asymmetric synthesis of pyrrolidinyl dispirooxindoles has not been reported to date. In addition, the two spiro-quaternary stereocenters of the corresponding products are all vicinal (2-, 3-position of pyrrolidine, Scheme 1). Therefore,

it is highly desirable to develop new catalytic system and new methodology for the construction of pyrrolidinyl dispirooxindoles.

α-Hydroxy carbonyl compounds as nucleophiles have been widely applied in catalytic asymmetric reactions promoted by organocatalysts[6c-d] and metallic catalysts.[6e-l] *α*-Amino carbonyl compounds, as the analogues of *α*-hydroxy carbonyl compounds, are also used in organocatalytic asymmetric reactions.[7] However, to our best knowledge, there have been no reports on the use of *α*-amino carbonyl compounds as donator in metal-catalytic asymmetric reactions. The possible reasons are: 1) the reactivity of *α*-amino carbonyl compounds is relatively lower than *α*-hydroxy carbonyl compounds; 2) the amino group has a strong ability to chelate metal, and this may lead to the destruction of the catalytic cycle. Therefore, it would be a formidable challenge to conquer these problems.

During the past few years, we have concentrated on the applications of dinuclear zinc synergistic catalysts in a number of efficient catalytic enantioselective transformations.[8] As part of our ongoing efforts towards this study, we recently find that it is effective to improve the reactivity of *α*-amino carbonyl compounds as nucleophiles through a bimetallic cooperative catalyst.

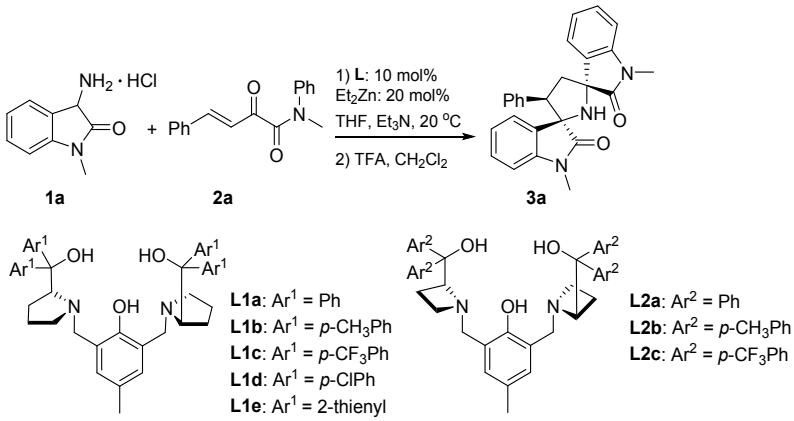
Herein, we report a Michael/cyclic keto-imine formation/Friedel-Crafts alkylation cascade reactions of 3-amino oxindole hydrochloride **1** and *β,γ*-unsaturated *α*-keto amides **2** catalyzed by a dinuclear zinc catalyst. A diversity of novel pyrrolidinyl dispirooxindoles containing two nonadjacent spiro-quaternary stereocenters (2-, 5-position of pyrrolidine, Scheme 1c) were obtained in excellent diastereoselectivities and moderate to excellent enantioselectivities (up to 60:1 dr, 95% ee).

RESULTS AND DISCUSSION

The research work began with the evaluation of the ability of dinuclear zinc synergistic catalysts in the Michael/cyclic keto-imine formation/Friedel-Crafts alkylation cascade reactions of 3-amino oxindole

hydrochloride **1a** and *β,γ*-unsaturated *α*-keto amides **2a**. Gratifyingly, in the presence of catalyst, generated from 10 mol% ligand **L1a**, 20 mol% $ZnEt_2$, the reaction proceeded smoothly at 20 °C for 3 h, and gave the desired product 2,5-pyrrolidinyl dispirooxindole **3a** in 62% yield with only 24% ee (Table 1, entry 1). Encouraged by this result, we examined a series of *C2*-symmetric ligands **L1**[9] and **L2** with various substitutions. The results were summarized in Table 1 (entries 2-8). Unfortunately, it was found that all of these ligands gave the inferior results in terms of enantioselectivities (up to 33% ee).

Table 1. Screening of Ligands[a]

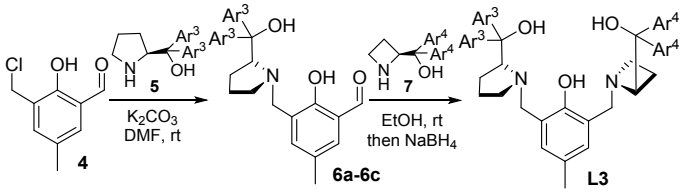


entry	ligand	yield[b] (%)	ee[c] (%)
1	**L1a**	62	24
2	**L1b**	**58**	**33**
3	**L1c**	62	25
4	**L1d**	68	21
5	**L1e**	56	9
6	**L2a**	61	10
7	**L2b**	53	8
8	**L2c**	60	4

[a]Reaction conditions: Unless otherwise noted, all reactions were conducted with **1a** (0.25 mmol), **2a** (0.275 mmol), Et_3N (0.325 mol), 10 mol% of **L**, 20 mol% of $ZnEt_2$ (1 M in hexanes) in THF (2.5 mL) under nitrogen for 3 h. After evaporation of the solvent, CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) were added. [b]Yield of isolated product **3a**. [c]Determined by chiral HPLC analysis. All dr value were up to >20:1 detected by ^1H NMR.

Based on previous work, we found that chiral space of the catalysts greatly affected the catalytic performances in the asymmetric reactions. The fine adjustment of catalysts' structure, which could lead to the change of their chiral microenvironment, made them suitable for different reaction systems and substrates.[8,9] In addition, there was no fundamental reason why *C2*-symmetric ligands must be superior to their nonsymmetrical counterparts, and in some reactions, the *C1*-symmertric ligands with electronically and sterically divergent units performed more effective stereocontrol than *C2*-symmetric ligands.[10] Therefore, this propelled us to design and synthesize more *C1*-symmertric ligands with different chiral nitrogen heterocycles and electronically different aromatic rings (Scheme 2). By changing the symmetrical characteristic of the ligands, we sought to improve the enantioselectivities of this Michael/cyclic keto-imine formation/Friedel-Crafts alkylation cascade reactions of 3-amino oxindole hydrochloride **1a** and *β,γ*-unsaturated *α*-keto amides **2a**.

Scheme 2. Synthesis of a New Family of Nonsymmetric Semi-azacrown Ether Ligands L3

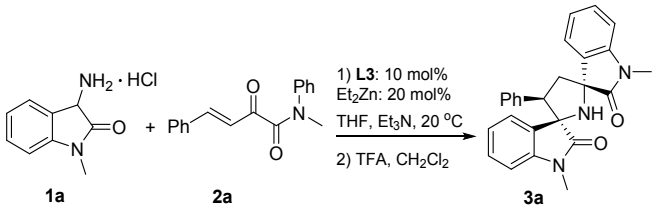


L3a: Ar^3 = Ph, Ar^4 = Ph,
L3b: Ar^3 = *p*-CH_3Ph, Ar^4 = Ph,
L3c: Ar^3 = Ar^4 = *p*-CH_3Ph,
L3d: Ar^3 = *p*-CF_3Ph, Ar^4 = *p*-CH_3Ph,
L3e: Ar^3 = Ar^4 = *p*-CF_3Ph,
L3f: Ar^3 = Ph, Ar^4 = *p*-CH_3Ph,
L3g: Ar^3 = Ph, Ar^4 = *p*-CF_3Ph.

The synthesis of designed ligands **L3** with *C1*-symmetry was shown in Scheme 2. Starting from the source of 3-(chloromethyl)-2-hydroxy-5-methyl-benzaldehyde **4**,[11] which could be prepared from commercially available *p*-cresol, the synthetic route consisted of two steps. The intermolecular nucleophilic substitution reaction of the benzyl chloride **4** and the prolinol **5** afforded the aldehyde **6** under basic conditions. A series of desired nonsymmetric ligands **L3a-3g** were achieved through a reductive amination of **6** and the azetidino alcohol **7**[8a] that was prepared by our previously developed procedures.

With these new ligands **L3a**-**L3g** in hand, we re-examined the Michael/cyclic keto-imine formation/Friedel-Crafts alkylation cascade reactions. The results were shown in Table 2. It was found that changing the ligand's symmetric nitrogen heterocyclic backbones to nonsymmetric frameworks led to an increase of the reaction's enantioselectivity (Table 2, entries 1, 3, and 5 *vs* Table 1, entries 1-3 and 6-8 respectively). Meanwhile, the electronic nature of aromatic rings in the ligands also had an obvious influence on enantioselectivity of the reaction.[10b,12] Through the screening of these ligands **L3a-3g** (Table 2), ligand **L3d** was relatively effective, and the corresponding product **3a** was obtained in 67% yield with an increased ee value from 33% to 49% (Table 2, entry 4). This result encouraged us to screen other conditions in detail.

Table 2. Evaluation of the New Ligands L3[a]



1a **2a** **3a**

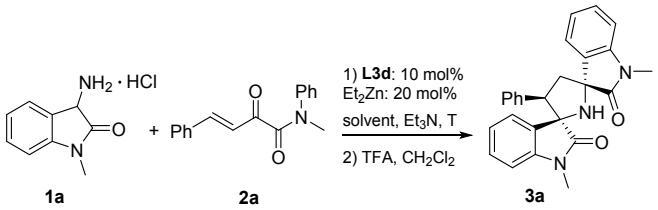
entry	ligand	yield[b] (%)	ee[c] (%)
1	**L3a**	66	37
2	**L3b**	45	45
3	**L3c**	55	38
4	**L3d**	**67**	**49**
5	**L3e**	56	35
6	**L3f**	62	39
7	**L3g**	61	18

[a]Reaction conditions: Unless otherwise noted, all reactions were conducted with **1a** (0.25 mmol), **2a** (0.275 mmol), Et_3N (0.325 mol), 10 mol% of **L3**, 20 mol% of $ZnEt_2$ (1 M in hexanes) in THF (2.5 mL) under nitrogen for 3 h. After evaporation of the solvent, CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) were added. [b]Yield of isolated product **3a**. [c]Determined by chiral HPLC analysis. All dr value were up to >20:1 detected by ^1H NMR.

As known to all, solvents usually played a crucial role in catalytic asymmetric reactions. The effect of solvents was investigated deeply. In THF (Table 3, entry 1), halogenated solvents (Table 3, entries 2 and 3) or toluene

(Table 3, entry 4), the reaction yield were higher, but the enantioselectivities were lower than in 1,4-dioxane (Table 3, entry 5). Fortunately, CH_3CN afforded the much better results, and the product **3a** was obtained in a much-improved 76% ee (Table 3, entry 6). Then, mixed solvents were also examined (Table 3, entries 7-9). It was found that CH_3CN/CH_2Cl_2 (1:1) was the more suitable combination, and afforded the product **3a** in 76% yield with 80% ee (Table 3, entry 7).

Table 3. Optimization of Solvents, Temperature, Additives and Catalysts Loadings[a]



1a **2a** **3a**

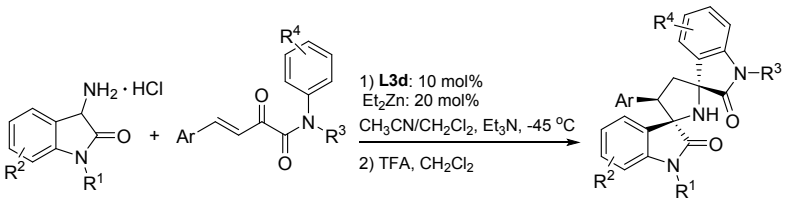
entry	solvent	T (°C)	yield[b] (%)	ee[c] (%)
1	THF	20	67	49
2	CH_2Cl_2	20	75	42
3	$CHCl_3$	20	77	15
4	toluene	20	80	37
5	1,4-dioxane	20	66	59
6	CH_3CN	20	76	76
7	CH_3CN/CH_2Cl_2(1:1)	20	76	80
8	CH_3CN/CH_2Cl_2(1:3)	20	79	79
9	CH_3CN/CH_2Cl_2(3:1)	20	76	79
10	CH_3CN/CH_2Cl_2(1:1)	0	80	83
11	CH_3CN/CH_2Cl_2(1:1)	-20	80	83
12	CH_3CN/CH_2Cl_2(1:1)	-40	84	87
13[d]	**CH_3CN/CH_2Cl_2(1:1)**	**-45**	**85**	**89**
14[e]	CH_3CN/CH_2Cl_2(1:1)	-50	81	87
15[e]	CH_3CN/CH_2Cl_2(1:1)	-60	70	84
16[f]	CH_3CN/CH_2Cl_2(1:1)	-45	78	79
17[g]	CH_3CN/CH_2Cl_2(1:1)	-45	68	54
18[h]	CH_3CN/CH_2Cl_2(1:1)	-45	83	86
19[i]	CH_3CN/CH_2Cl_2(1:1)	-45	76	73

[a]Reaction conditions: Unless otherwise noted, all reactions were conducted with **1a** (0.25 mmol), **2a** (0.275 mmol), Et_3N (0.325 mol), 10 mol% of **L3d**, 20 mol% of $ZnEt_2$ (1 M in hexanes) in solvent (2.5 mL) under nitrogen for 3-24 h. After evaporation of the solvent, CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) were added. [b]Yield of isolated product **3a**. [c]Determined by chiral HPLC analysis. All dr value were up to

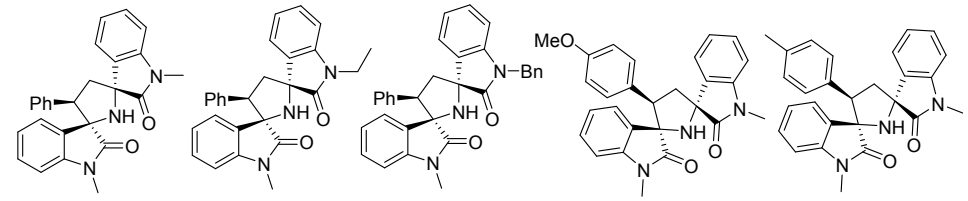
>20:1 detected by ^{1}H NMR. [d]The reaction time was 18 h. [e]The reaction time is 24 h. [f]4Å molecular sieve (50 mg) was used. [g]5 mol% of **L3d** was used. [h]15 mol% of **L3d** was used. [i]Mg(*n*-Bu)$_2$ was used.

Next, temperature, additives and catalysts loading were also explored. When the reaction temperature was lowered from 20 to 0, -20, -40, -45 ^{o}C, the ee of product **3a** increased to 89% progressively (Table 3, entries 10-13). Further lowering the temperature to -50, -60 ^{o}C led to a small decrease ee of product **3a** (Table 3, entries 14 and 15). The addition of 4Å MS showed a negative effect on enantioselectivity (Table 3, entry 16). Finally, the catalyst loadings were explored without additives at -45 ^{o}C. Disappointingly, a larger loss in yield and enantioselectivity was obtained once the catalyst loading is reduced to 5 mol% (Table 3, entry 17). Increasing the catalyst loading to 15 mol% resulted in a slight reduction of the product's ee value (Table 3, entry 13 vs entry 18). In addition, the use of Mg(*n*-Bu)$_2$ led to an obvious decrease of the product's ee value (entry 19).

Table 4. Generality of the Cascade Reaction Catalyzed by New Dinuclear Zinc Catalysts[a-d]



1a: R^1 = Me, R^2 = H; **1b**: R^1 = Bn, R^2 = H
1c: R^1 = Me, R^2 = 5-Me; **1d**: R^1 = Me, R^2 = 5-F



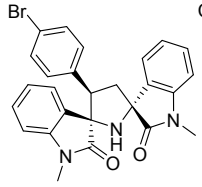
3a, 85%
> 20:1 dr, 89% ee

3b, 82%
> 20:1 dr, 54% ee

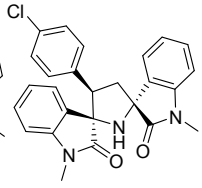
3c, 82%
> 25:1 dr, 70% ee

3d, 74%
> 20:1 dr, 89% ee

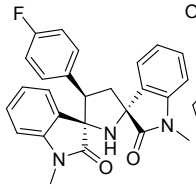
3e, 81%
17:1 dr, 79% ee



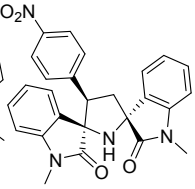
3f, 74%
> 20:1 dr, 68% ee



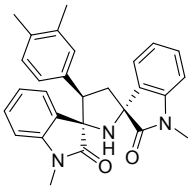
3g, 84%
> 20:1 dr, 65% ee



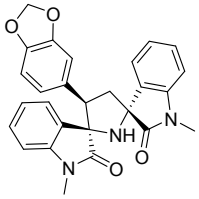
3h, 82%
> 20:1 dr, 70% ee



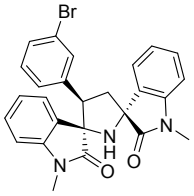
3i, 66%
22:1 dr, 43% ee



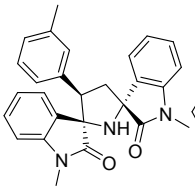
3j, 72%
> 60:1 dr, 84% ee



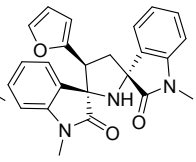
3k, 79%
> 20:1 dr, 90% ee



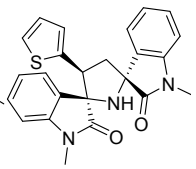
3l, 68%
25:1 dr, 84% ee



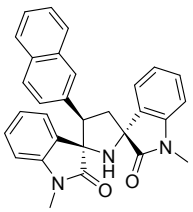
3m, 82%
> 20:1 dr, 68% ee



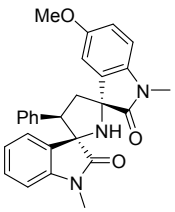
3n, 70%
> 20:1 dr, 68% ee



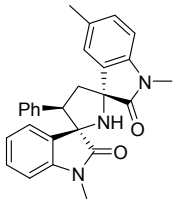
3o, 82%
> 20:1 dr, 83% ee



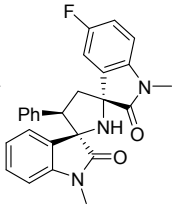
3p, 83%
29:1 dr, 78% ee



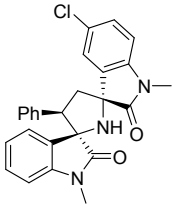
3q, 82%
29:1 dr, 72% ee



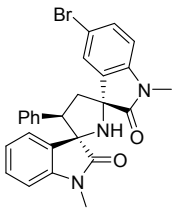
3r, 84%
> 20:1 dr, 73% ee



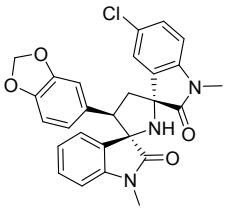
3s, 79%
> 20:1 dr, 70% ee



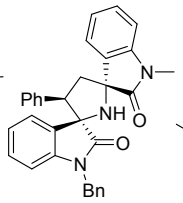
3t, 80%
> 20:1 dr, 95% ee



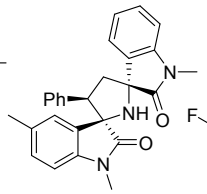
3u, 85%
> 20:1 dr, 70% ee



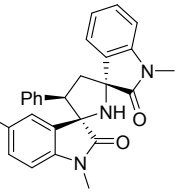
3v, 73 %
> 20:1 dr, 60% ee



3w, 73%
> 20:1 dr, 90% ee



3x, 82%
> 20:1 dr, 91% ee



3y, 75%
> 20:1 dr, 74% ee

[a]Reaction conditions: Unless otherwise noted, all reactions were conducted with **1** (0.25 mmol), **2** (0.275 mmol), Et_3N (0.325 mol), 10 mol% of **L3d**, 20 mol% of $ZnEt_2$ (1 M in hexanes) in CH_3CN/CH_2Cl_2 (1/1, 2.5 mL) under nitrogen for 18 h. After evaporation of the solvent, CH_2Cl_2 (2.0 mL) and TFA (2.0 mL) were added. [b]Yield of isolated product **3**. [c]Determined by ^1H NMR. [d]Determined by chiral HPLC analysis.

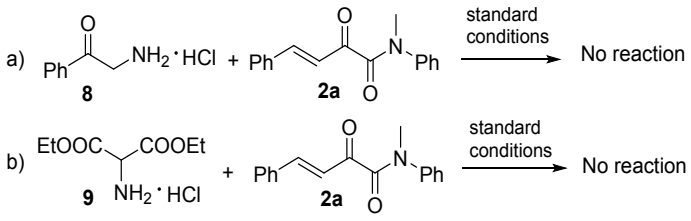
With the optimal reaction conditions established, we subsequently explored the substrate scope, and the results were compiled in Table 4. First, the substrates **2b** and **2c** with different bulky protecting group R^3 (ethyl and benzyl) on nitrogen atom were examined under the standard conditions. The corresponding products **3b**-**3c** were obtained in good yield with excellent dr and 54%, 70% ee, respectively. A series of *β,γ*-unsaturated *α*-keto amides **2** with various substituents at the aromatic ring were tested. Substrates **2d**-**2i** with different electronic nature groups at the *para* position of the aromatic ring (Ar) gave the corresponding products in 66-84% yields with 43-89% ee. It was found that the electron-donating groups (MeO-, Me-) at the *para* position on the aromatic ring (Ar) led to higher enantioselectivities than electron-withdrawing groups (Br-, Cl-, F-, O_2N-). These results enlightened us to test substrates **2j**-**2k** bearing more electron-rich groups (3,4-dimethylphenyl and *γ*-pipernoyl). Treatment of **2j** and **2k** with 3-amino oxindole **1a**, respectively, gave good results in terms of 84% and 90% ee. The substrates **2l**-**2m** with the substituents at the *meta* position of the aromatic ring (Ar) were tolerated. This protocol was also suitable for *γ*-heteroaromatic ring substrates **2n-2o** and *γ*-naphthyl ring substrate **2p**, providing the corresponding products in good yields, with excellent diastereoselectivities and moderate to good enantioselectivities (up to 83% ee). The influences of substituents R^4 on the other aromatic ring (at the side of N atom) were also explored. Both electron-donating and electron-withdrawing R^4 (MeO-, CH_3-, F-, Cl-, Br-) at the *para* position of the aromatic ring were tolerated in this reaction, furnishing the desired products **3q-3u** in good yields and moderate to good enantioselectivities. In addition, there was a dramatically improvment of the reaction enantioselectivity (95% ee of products **3t**) when substrate **2t** with Cl group was treated with 3-amino oxindole under the standard condition. And the reaction of substrate **2v** and 3-amino oxindole **1a** was also carried out, affording the corresponding product **3v** in 73% yield with 60% ee.

To further investigate the scope of the asymmetric cascade reaction, we examined the different nucleophiles **1b**-**1d** (Table 4). It was found that changing the substituent R^1 on the nitrogen atom of the substrate **1** from Me

to benzyl had a slight influence on the reaction. The corresponding product **3w** was obtained in 73 yield with > 20:1 dr and 90% ee. Furthermore, 3-amino oxindoles **1c**-**d** with electron-donating or electron-withdrawing substituents (Me- or F-) on the aromatic ring were explored, and the corresponding products **3x**-**y** were achieved in good yields with excellent dr and 91%, 74% ee, respectively.

We also examined some *α*-amino carbonyl compounds, such as *α*-aminoacetophenone hydrochloride **8** and *α*-aminomalonic acid diethyl ester hydrochloride **9**, but no reaction occurred under the standard conditions (Scheme 3). The possible reason is owing to lower reactivity of these two α-amino carbonyl compounds.

Scheme 3. Reaction of 2a and Other *α*-Amino Carbonyl Compounds 8 and 9

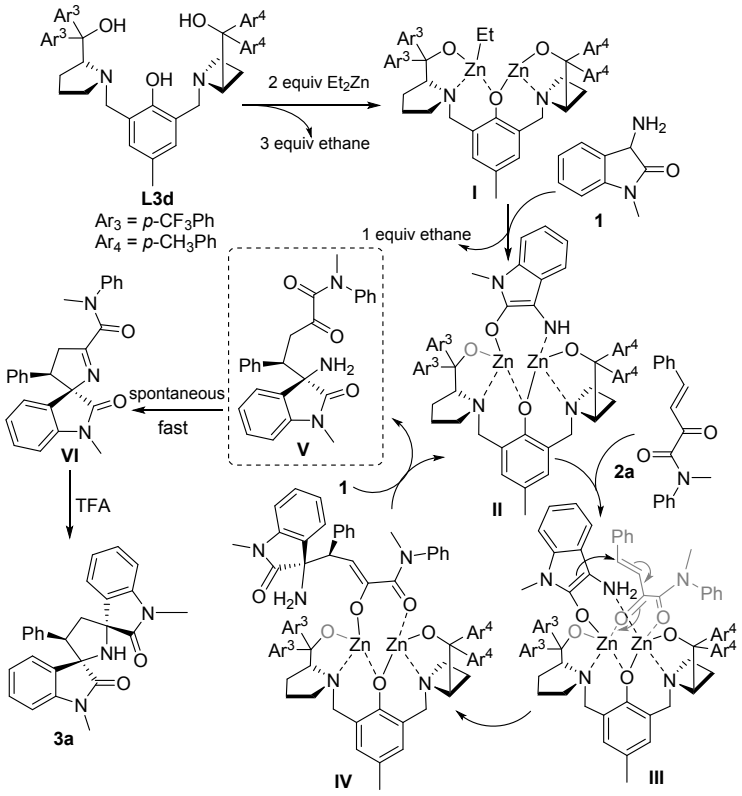


Moreover, a single crystal of product **3l** was obtained, and its absolute configuration was determined to be (***3R,3'R,5'R***) by the X-ray crystallographic analysis (See SI, section 1).

On basis of the absolute structure of product **3l** and previous reports on the mechanism of dinuclear zinc catalysis,[8,9] a possible catalytic cycle was proposed to explain the chirality transfer in the catalytic asymmetric reaction (Scheme 4). Treatment of ligand **L3d** with 2 equivalents of $ZnEt_2$ afforded the dinuclear zinc complex Ⅰ. Next, the reaction of 3-amino oxindole **1a** with complex Ⅰ generated intermediate Ⅱ accompanied by the formation of 1 equivalent of ethane. Then, *β,γ*-unsaturated α-keto amide **2a** coordinated to both zinc atoms from the other less hindered face to form Ⅲ, which underwent a Michael reaction to afford the complex Ⅳ. Next, intermediate Ⅴ and the species Ⅱ were released by a proton exchange with another 3-amino oxindole, and the catalytic cycle was restarted. Intermediate Ⅴ immediately transformed into its condensation product

Ⅵ that was isolated, and characterized. Finally, the product **3a** was obtained via an intramolecular Fridel-Crafts alkylation under acidic conditions.

Scheme 4. Proposed Chirality Transformation in the Catalitic Asymmetric Reaction



CONCLUSION

In conclusion, a series of new unsymmetric semi-azacrown ether ligands have been designed and synthesized. These *C1*-symmetric ligands show better asymmetric catalytic performance than the *C2*-symmetric Azephenol ligands and Prophenol ligands in the new asymmetric Michael/cyclic keto-imine formation/Friedel-Crafts alkylation reactions of 3-amino oxindoles and *β,γ*-unsaturated *α*-keto amides. It is remarkable that changing the ligand's skeletons and the electronic nature of aromatic rings in the ligands can enhance the enantioselectivities of the reaction. An array of chiral 2,5-pyrrolidinyl dispirooxindole containing two nonadjacent spiro-quaternary chiral centers are achieved in moderate to good yields with good diastereoselectivities and moderate to excellent enantioselectivities (up to 95% ee). According to the

experiment results and the absolute structure of product **3l**, a possible catalytic cycle is proposed to explain the origin of the asymmetric induction. The application of these new *C1*-symmetric ligands to other reactions is ongoing in our laboratory.

Experimental Section

General Information. Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at 20 °C. ^{1}H and $^{13}C\{^{1}H\}$ NMRspectra were recorded on Bruker AVANCE 400 MHz spectrometer and the chemical shifts are reported in ppm downfield from tetramethylsilane (δ = 0.00 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) for $^{13}C\{^{1}H\}$ NMRspectroscopy. High−resolution mass spectra (HRMS) were performed on a Q-TOF Micro LC/MS System ESI spectrometer. The enantiomeric excesses (ee) were determined by HPLC (chiral column; mobile phase hexane/*i*-PrOH). Compounds **1a-d**,[13] **4**,[11] **5a** (Ar^3 = Ph),[14a] **5b** (Ar^3 = *p*-CF_3Ph),[14b] and 7[8a] were synthesized according to the literature. Compound **5c** (Ar^3 = *p*-CH_3Ph) were used as purchased.

General Procedure for the Preparation of 6a-c. To a suspension of (*S*)-**5** (3.54 mmol, 1.0 equiv) and potassium carbonate (1.470 g, 10.62 mmol, 3.0 equiv) in DMF (14 mL) at 0 °C, was added benzylchloride **4** (0.718 g, 3.72 mmol, 1.05 equiv). The reaction mixture was stirred at rt for 16h before phosphate buffer (50 mL) (pH = 7) and EtOAc (50 mL) were added. The layers were separated and the aqueous phase was extracted with EtOAc (3 X 150 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to yield an orange residue. The crude product was purified by flash column chromatography on silica gel (Petroleum ether:EtOAc = 90:10 to 80:20) to yield **6**.

*(S)-2-hydroxy-3-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)-5-methylbenzaldehyde (**6a**)*. White solid, 1.12 g, 79% yield, mp 108.7-109.4 °C, $[\alpha]_D$ = +35.2 (*c* =0.65, $CHCl_3$); IR 3349, 2879, 2825, 1644, 1620, 1602, 1491, 1448, 1381, 1318, 1248, 1212, 1099, 1067, 1033, 970, 874, 800, 767, 745, 709, 699, 648, 590, 526 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.81 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 7.7 Hz, 2H), 7.31-7.24 (m, 4H), 7.20-7.12 (m, 3H), 7.07 (s, 1H), 4.47-4.43 (m, 1H), 3.37 (d, *J* = 13.6 Hz, 1H), 3.25-3.22 (m, 1H), 3.05 (d, *J* = 13.6 Hz, 1H), 2.96-2.89 (m, 1H), 2.29 (s, 3H), 2.17-2.08 (m, 1H), 2.04-1.95 (m, 1H), 1.25 (s, 2H). ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$) δ ppm 197.7, 159.1, 148.3, 145.6, 139.4, 133.5, 130.0, 129.6, 129.5, 128.1, 128.0, 127.6, 127.3, 127.1, 121.6, 77.3, 73.7, 55.8, 52.1, 31.1, 21.7, 21.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{28}NO_3^+$ 402.2064; Found 402.2065.

*(S)-2-hydroxy-3-((2-(hydroxybis(4-(trifluoromethyl)phenyl)methyl)pyrrolidin-1-yl)methyl)-5-methylbenzaldehyde (**6b**)*.[11b] White foam, 1.37 g, 72% yield. $[\alpha]_D$ = +31.3 (*c* =0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.80 (s, 1H), 7.88 (*J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.56-7.52 (m, 4H), 7.20 (d, *J* = 1.3 Hz, 1H), 7.05 (d, *J* = 1.7 Hz, 1H), 4.04-4.00 (m, 1H), 3.33 (d, *J* = 12.8 Hz, 1H), 3.24 (d, *J* = 12.9 Hz, 1H), 2.94-2.89 (m, 1H), 2.50-2.44 (m, 1H), 2.28 (s, 3H), 1.95-1.84 (m, 1H), 1.66-1.52 (m, 3H).

*(S)-2-hydroxy-3-((2-(hydroxydi-p-tolylmethyl)pyrrolidin-1-yl)methyl)-5-methylbenzaldehyde (**6c**)*. White foam, 1.14 g, 75% yield, mp 54.3-55 ^{o}C, $[\alpha]_D$ = +43.2 (*c* =0.74, $CHCl_3$); IR 2920, 2864, 1648, 1617, 1604, 1508, 1458, 1377, 1263, 1213, 1164, 1098, 1020, 867, 807, 715, 599, 568, 511 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.78 (s, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 1.5 Hz, 1H), 7.08-7.02 (m, 5H), 3.98-3.92 (m, 1H), 3.35-3.24 (m, 1H), 2.91-2.85 (m, 1H), 2.45-2.38 (m, 1H), 2.27 (s, 3H), 2.25 (s, 3H), 2.20 (s, 3H), 1.96-1.86 (m, 1H), 1.76-1.67 (m, 1H), 1.62-1.51 (m, 2H). ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$) δ ppm 196.4, 157.6, 145.3, 144.2, 138.6, 135.7, 135.6, 132.0, 128.9, 128.7, 128.6, 128.0, 125.6, 125.4, 120.2, 70.8, 55.4, 53.8, 29.7, 23.8, 21.0, 20.9, 20.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{32}NO_3^+$ 430.2377; Found 430.2381.

General Procedure for the Preparation of Ligands 3. To a suspension of aldehyde **6** (1.57 mmol, 1.0 equiv) in EtOH (8.0 mL) was added (*S*)-pyrrolidin-2-ylbisphenylmethanol **7**[8a] (1.73 mmol, 1.1 equiv). The reaction was stirred at rt for 2 h. $NaBH_4$ (66 mg, 1.73 mmol, 1.1 equiv) was added in one portion and the

mixture was stirred at rt for additional 3 h before phosphate buffer (50 mL) (pH = 7) and EtOAc (50 mL) were added. The layers were separated and the aqueous phase was extracted with EtOAc (3 X 100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo to yield a white residue. The crude product was purified by flash column chromatography on silica gel (Petroleum ether:EtOAc = 20:100) to yield **L3** as a white foam.

*2-(((S)-2-(hydroxydiphenylmethyl)azetidin-1-yl)methyl)-6-(((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)-4-methylphenol (**L3a**).* 0.92 g, 94% yield, mp 78.3-79.1 °C; $[\alpha]_D$ = +50.6 (*c* = 0.66, $CHCl_3$); IR 2953, 1599, 1475, 1447, 1032, 988, 866, 745, 697, 637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* ppm 7.66 (d, *J* = 7.8 Hz, 2H), 7.58-7.53 (m, 4H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.33-7.25 (m, 8H), 7.23-7.09 (m, 4H), 6.58 (s, 1H), 6.52 (s, 1H), 4.37 (s, 1H), 3.94 (s, 1H), 3.33-3.17 (m, 5H), 2.87-2.83 (m, 2H), 2.39-2.35 (m, 1H), 2.28-2.20 (m, 1H), 2.13 (s, 3H), 2.08-1.95 (m, 2H), 1.78-1.51 (m, 4H), 1.21 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) *δ* ppm 152.6, 146.5, 129.0, 128.6, 128.3, 128.2, 128.0, 127.4, 127.0, 126.8, 126.7, 126.4, 126.0, 125.95, 124.2, 78.8, 72.7, 71.5, 65.8, 58.0, 57.5, 55.1, 50.1, 29.6, 24.1, 20.4, 19.5, 15.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{42}H_{45}N_2O_3^+$ 625.3425; Found 625.3427.

*2-(((S)-2-(hydroxydi-p-tolylmethyl)pyrrolidin-1-yl)methyl)-6-(((S)-2-(hydroxydiphenylmethyl)azetidin-1-yl)methyl)-4-methylphenol (**L3b**)*. 0.97 g, 95% yield, mp 83.4-84.1 °C; $[\alpha]_D$ = +51.3 (*c* = 0.67, $CHCl_3$); IR 2970, 1601, 1476, 1447, 1380, 1249, 1159, 1066, 990, 866, 808, 783, 699, 743, 635, 569 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* ppm 7.57 (d, *J* = 7.4 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.45-7.39 (m, 5H), 7.32-7.24 (m, 5H), 7.22-7.18 (m, 1H), 7.17-7.14 (m, 1H), 7.10-7.05 (m, 5H), 6.59 (s, 1H), 6.54 (s, 1H), 4.43-4.38 (t, *J* = 7.9 Hz, 1H), 3.95-3.91 (m, 1H), 3.41 (d, *J* = 12.8 Hz, 1H), 3.28-3.18 (m, 3H), 3.13-3.09 (d, *J* = 13.2 Hz, 1H), 2.93-2.80 (m, 2H),2.43-2.35 (m, 1H), 2.28 (s, 3H), 2.26 (s, 1H), 2.24-2.21 (m, 5H), 2.13 (s, 3H), 1.99-1.95 (m, 1H), 1.82-1.74 (m, 1H), 1.65-1.58 (m, 1H), 1.57-1.48 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) *δ* ppm 152.7, 146.1, 144.2, 144.1, 143.7, 136.1,

135.9, 129.0, 128.9, 128.8, 128.6, 128.3, 128.2, 128.1, 127.4, 127.0, 126.8, 126.0, 125.9, 125.72, 125.70, 125.3, 123.9, 122.0, 78.8, 76.6, 75.6, 71.6, 57.9, 57.3, 55.1, 50.0, 29.5, 24.0, 21.0, 20.96, 20.45, 19.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{44}H_{49}N_2O_3^+$ 653.3738; Found 653.3738.

*2-(((S)-2-(hydroxydi-p-tolylmethyl)azetidin-1-yl)methyl)-6-(((S)-2-(hydroxydi-p-tolylmethyl)pyrrolidin-1-yl)methyl)-4-methylphenol (**L3c**).* 0.99 g, 93% yield, mp 81.0-81.6 °C; $[\alpha]_D$ = +52.0 (*c* = 0.67, $CHCl_3$); IR 2965, 2920, 1610, 1509, 1475, 1168, 1098, 1038, 1020, 990, 864, 809, 782, 597, 571 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* ppm 7.52 (d, *J* = 8.1 Hz, 2H), 7.43-7.39 (m, 5H), 7.31-7.29 (m, 2H), 7.11-7.04 (m, 9H), 6.60 (s, 1H), 6.53 (s, 1H), 4.36-4.32 (t, *J* = 8.0 Hz, 1H), 3.95-3.91 (dd, *J* = 5.0, 9.1 Hz, 1H), 3.38-3.26 (m, 2H), 3.24- 3.13 (m, 3H), 2.88-2.80 (m, 2H), 2.43-2.36 (m, 1H), 2.28-2.22(m, 14H), 2.13 (s, 3H), 1.98-1.94 (m, 1H), 1.81-1.73 (m, 1H), 1.65-1.55 (m, 1H), 1.53-1.46 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) *δ* ppm 152.7, 144.3, 143.8, 143.1, 141.5, 136.5, 136.2, 136.0, 135.8, 129.1, 128.99, 128.97, 128.92, 128.7, 127.4, 125.85, 128.81, 125.7, 124.2, 121.8, 78.6, 76.5, 72.8, 71.4, 58.0, 57.2, 55.1, 50.0, 29.6, 24.0, 21.06, 21.01, 20.98, 20.95, 20.4, 19.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{46}H_{53}N_2O_3^+$ 681.4051; Found 681.4051.

*2-(((S)-2-(hydroxybis(4-(trifluoromethyl)phenyl)methyl)pyrrolidin-1-yl)methyl)-6-(((S)-2-(hydroxydi-p-tolylmethyl)azetidin-1-yl)methyl)-4-methylphenol (**L3d**).* 1.19 g, 96% yield, mp 81.8-82.3 °C; $[\alpha]_D$ = +41.2 (*c* = 0.67, $CHCl_3$); IR 2969, 2867, 1615, 1510, 1477, 1414, 1322, 1161, 1119, 1067, 1016, 815, 770, 596, 572 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* ppm 7.88 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 4H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.61 (s, 1H), 6.51 (s, 1H), 4.33-4.29 (t, *J* = 8.0 Hz, 1H), 4.00-3.97 (m, 1H), 3.34 (d, *J* = 12.5 Hz, 1H), 3.27-3.21 (m, 2H), 3.17-3.11 (m, 2H), 2.86-2.75 (m, 2H), 2.49-2.42 (m, 1H), 2.33-2.24 (m, 8H), 2.13-2.08 (m, 4H), 1.98-1.88 (m, 1H), 1.67-1.57 (m, 2H), 1.47-1.35 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) *δ* ppm 152.8, 151.3, 150.2, 142.3, 141.2, 136.9, 136.6, 129.6, 129.1, 129.0, 128.8 (q, *J* = 32.6 Hz), 128.6 (q, *J* = 31.1 Hz), 127.5, 126.5, 126.2, 126.0,

125.9, 125.2 (q, *J* = 3.8 Hz), 125.0 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 271.9 Hz), 124.15 (q, *J* = 271.9 Hz), 121.1, 78.0, 77.1, 73.2, 70.5, 60.6, 55.6, 54.9, 50.3, 29.8, 23.7, 21.0, 20.9, 20.4, 19.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{46}H_{47}F_6N_2O_3^+$ 789.3485; Found 789.3488.

*2-(((S)-2-(hydroxybis(4-(trifluoromethyl)phenyl)methyl)azetidin-1-yl)methyl)-6-(((S)-2-(hydroxybis(4-(trifluoromethyl)phenyl)methyl)pyrrolidin-1-yl)methyl)-4-methylphenol (**L3e**).* 1.27 g, 90% yield, mp 81.3-82.1 °C; $[\alpha]_D$ = +37.2 (*c* = 0.68, $CHCl_3$); IR 2970, 1731, 1616, 1478, 1413, 1320, 1252, 1161, 1117, 1066, 1016, 830, 770, 733, 667, 602, 512, 471 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.84 (d, *J* = 8.3 Hz, 2H), 7.67 (t, *J* = 8.5 Hz, 4H), 7.59-7.54 (m, 8H), 7.48 (d, *J* = 8.3 Hz, 2H), 6.54 (s, 1H), 6.48 (s, 1H), 4.45-4.41 (t, *J* = 8.0 Hz, 1H), 4.03-3.99 (m, 1H), 3.38 (d, *J* = 12.8 Hz, 1H), 3.29 (s, 2H), 3.25-3.19 (m, 2H), 2.96-2.90 (m, 1H), 2.87-2.82 (m, 1H), 2.47-2.40 (m, 1H), 2.16-2.11 (m, 4H), 2.02-1.93 (m, 2H), 1.73-1.62 (m, 2H), 1.59-1.50 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) δ ppm 152.4, 150.5, 149.6, 149.3, 147.3, 129.5 (q, *J* = 32.4 Hz), 129.34 (q, *J* = 31.5 Hz),129.3, 129.2 (q, *J* = 32.3 Hz), 129.0 (q, *J* = 32.4 Hz), 128.8, 126.3, 126.2, 126.13, 126.11, 125.5, 125.4, 125.38, 125.34, 125.27, 125.2, 124.6 (q, *J* = 271.6 Hz), 124.02 (q, *J* = 271.6 Hz), 123.98 (q, *J* = 271.1 Hz), 123.8, 122.73, 122.67, 121.6, 78.5, 76.4, 72.5, 71.0, 58.5, 57.5, 55.1, 29.6, 23.8, 20.3, 19.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{46}H_{41}F_{12}N_2O_3^+$ 897.2920; Found 897.2923.

*2-(((S)-2-(hydroxydi-p-tolylmethyl)azetidin-1-yl)methyl)-6-(((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)-4-methylphenol (**L3f**).* 0.94 g, 92% yield, mp 76.4-77.1 °C; $[\alpha]_D$ = +50.5 (*c* = 0.82, $CHCl_3$); IR 3677, 2972, 2895, 1475, 1450, 1403, 1393, 1250, 1224, 1066, 879, 810, 744, 702, 638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.67 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.31-7.24 (m, 7H), 7.18-7.00 (m, 7H), 6.60 (s, 1H), 6.52 (s, 1H), 4.32 (t, *J* = 8.0 Hz, 1H), 3.98-3.94 (m, 1H), 3.28 (s, 2H), 3.21-3.12 (m, 3H), 2.87-2.81 (m, 2H), 2.44-2.37 (m, 1H), 2.29-2.21 (m, 8H), 2.13 (s, 3H), 1.99-1.93 (m, 1H), 1.80-1.72 (m, 1H), 1.65-1.56 (m, 1H), 1.54-1.42 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) δ ppm 152.6, 147.2, 146.6, 143.0, 141.4,

136.6, 136.3, 129.2, 129.0, 128.9, 128.6, 128.2, 127.4, 126.6, 126.4, 125.9, 125.8, 124.4, 121.7, 78.7, 76.6, 72.9, 71.4, 58.6, 56.8, 55.1, 50.1, 29.7, 24.0, 21.1, 20.99, 20.4, 19.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{44}H_{49}N_2O_3^+$ 653.3738; Found 653.3740.

*2-(((S)-2-(hydroxybis(4-(trifluoromethyl)phenyl)methyl)azetidin-1-yl)methyl)-6-(((S)-2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)-4-methylphenol (**L3g**).* 1.12 g, 94% yield, mp 77.3-77.9 °C; $[\alpha]_D$ = +39.5 (*c* = 0.68, $CHCl_3$); IR 2967, 1615, 1477, 1448, 1413, 1322, 1162, 1067, 1016, 833, 767, 747, 702, 637, 602, 514 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.71 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 7.4 Hz, 2H), 7.57-7.49 (m, 10H), 7.33-7.27 (m, 4H), 7.19 (t, J = 7.4 Hz, 1H), 6.51 (s, 2H), 4.44 (t, J = 7.8 Hz, 1H), 3.97-3.94 (m, 1H), 3.41 (d, J = 13 Hz, 1H), 3.31-3.18 (m, 4H), 3.01-2.95 (m, 1H), 2.84-2.79 (m, 1H), 2.38-2.31 (m, 1H), 2.10 (s, 3H), 2.07-2.06 (m, 1H), 2.03-1.93 (m, 2H), 1.87-1.79 (m, 1H), 1.71-1.62 (m, 1H), 1.60-1.51 (m, 1H); $^{13}C\{^1H\}$ NMR(100 MHz; $CDCl_3$) δ ppm 152.6, 150.1, 147.7, 146.3, 146.1, 129.2 (q, *J* = 32.5 Hz), 129.1 (q, *J* = 32.3 Hz), 129.0, 128.6, 128.4, 128.2, 127.4, 126.9, 126.7, 126.3, 126.1, 125.9, 125.3 (q, *J* = 3.7 Hz), 125.2 (q, *J* = 3.6 Hz), 124.14 (q, *J* = 272.0 Hz), 124.13 (q, *J* = 271.9 Hz), 123.2, 122.4, 79.4, 75.9, 71.9, 71.7, 59.4, 56.2, 55.2, 50.0, 29.5, 24.1, 20.4, 19.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{44}H_{43}F_6N_2O_3^+$ 761.3172; Found 761.3176.

General Procedure for the Synthesis of *β,γ*-Unsaturated *α*-Keto Amides 2. To a solution of potassium salt[6j] (0.1 mol) in H_2O (150 mL) at room temperature was added a solution of concentrated HCl. Then a great deal of precipitation appeared and the reaction stirred at rt for 4 h. The precipitate was collected by filtration, washed thrice with distilled water and dried under vacuum to furnish the keto-acid which was used as an intermediate, without further purification.To a solution of keto-acid (20 mmol) in 30 mL dry CH_2Cl_2 was added 5 drops DMF followed by the corresponding oxalyl chloride (25 mmol, 1.25 equiv) drop by drop at 0 °C. Then the reaction was stirred at rt for 4 h. Concentration in vacuo gave the keto acyl chloride which was used as an intermediate without further purification. To a solution of keto acyl chloride in 30 mL dry DCM at 0 °C was

added a solution of *N*-methylbenzeneamine (15 mmol) and Et_3N (25 mmol) in 20 mL dry CH_2Cl_2 by dropping. The reaction mixture was stirred at room temperature overnight. Then saturated aqueous $NaHCO_3$ (100 mL) was added and resulting mixture was extracted with dichloromethane (3 × 50 mL). The combined organic layer was washed with brine (40 mL), dried over Mg_2SO_4, filtered, evaporated, and purified via column chromatography on silica gel (eluent: n-pentane/ethyl acetate = 5:1).

*(E)-N-methyl-2-oxo-N,4-diphenylbut-3-enamide (**2a**).* Yellow solid; 3.87 g, 73% yield in three steps; mp 90-92 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.60 (d, J = 16.3 Hz, 1H), 7.52 (dd, J = 7.0, 2.0 Hz, 2H), 7.40 (td, J = 7.1, 6.2, 3.3 Hz, 3H), 7.32 (dd, J = 8.2, 6.3 Hz, 2H), 7.27 (dd, J = 7.8, 1.5 Hz, 1H), 7.23-7.16 (m, 2H), 6.76 (d, J = 16.3 Hz, 1H), 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 190.1, 167.1, 147.5, 141.7, 134.0, 131.31, 129.6, 129.3, 129.1, 129.0, 128.9, 128.7, 128.1, 126.6, 125.4, 123.5, 36.5. IR: 1639, 1678, 1179, 729, 689, cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO_2^+$ 266.1176; Found 266.1179.

*(E)-N-methyl-2-oxo-N,4-diphenylbut-3-enamide (**2b**).* Yellow solid; 3.52 g, 63% yield in three steps; mp 127-129^oC. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.60 (d, J = 16.3 Hz, 1H), 7.52 (dd, J = 7.0, 2.0 Hz, 2H), 7.40 (td, J = 7.1, 6.2, 3.3 Hz, 3H), 7.32 (dd, J = 8.2, 6.3 Hz, 2H), 7.27 (dd, J = 7.8, 1.5 Hz, 1H), 7.23-7.16 (m, 2H), 6.76 (d, J = 16.3 Hz, 1H), 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 190.6, 167.0, 148.5, 147.7, 140.3, 134.4, 131.9, 131.6, 129.9, 129.5, 129.4, 129.2, 129.1, 128.7, 128.4, 128.2, 127.6, 123.9, 44.2, 13.2. IR: 1679, 1646, 1101, 769, 755, 700, 685 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO_2^+$ 280.1332; Found 280.1332.

*(E)-N-benzyl-2-oxo-N,4-diphenylbut-3-enamide (**2c**).* Yellow solid; 4.84 g, 71% yield in three steps; mp 117-119 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62– 7.24 (m,14H), 7.05-7.02 (m, 2H), 6.72 (d, J = 16.36 Hz, 1H), 5.05 (s, 2H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 190.1, 167.0, 147.6, 140.1, 136.5, 134.0, 131.3,

129.5, 129.4, 129.1, 128.8, 128.7, 128.7, 128.4, 128.0, 127.9, 123.6, 52.7. IR: 1681, 1640, 1179, 729, 689 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}NO_2^+$ 342.1489; Found 342.1488.

*(E)-4-(4-methoxyphenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2d**).* Yellow solid; 3.72 g, 63% yield in three steps; mp 90-92 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.56 (d, J = 16.24 Hz, 1H), 7.50-7.47 (m, 2H), 7.34-7.25 (m, 3H), 7.21-7.18 (m, 2H), 6.91 (d, J = 8.68 Hz, 2H), 6.66-6.61 (m, 1H), 3.83 (s, 3H), 3.43 (d, J = 1.4 Hz, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 190.1, 167.3, 162.3, 147.4, 141.9, 130.6, 129.5, 128.0, 126.7, 126.5, 121.3, 114.6, 55.5, 36.5. IR: 1680, 1639, 1171, 837, 760, 733, 681 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO_3^+$ 296.1281; Found 296.1282.

*(E)-N-methyl-2-oxo-N-phenyl-4-(p-tolyl)but-3-enamide (**2e**).* Yellow solid; 3.46 g, 62% yield three steps; mp 93-95 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.56 (d, J = 16.24 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.35-7.18 (m, 7H), 6.72 (d, J = 16.32 Hz, 1H), 3.44 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 190.3, 167.2, 147.7, 142.1, 141.8, 131.4, 129.8, 129.6, 128.8, 128.1, 126.6, 122.6, 36.6, 21.6. IR: 1644, 1594, 1114, 791, 774, 739, 698 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO_2^+$ 280.1332; Found 280.1334.

*(E)-4-(4-bromophenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2f**).* Yellow solid; 4.34 g, 63% yield in three steps; mp 103-105 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.55- 7.50 (m, 3H), 7.40-7.26 (m, 5H), 7.20-7.17 (m, 2H), 6.77 (d, J = 16.36 Hz, 1H); 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ 189.6, 166.8, 145.8, 141.7, 132.9, 132.3, 130.0, 129.6, 128.1, 126.5, 125.7, 123.9, 36.6. IR: 1663, 1644,1111, 814, 771 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}BrNO_2^+$ 344.0281; Found 344.0282.

*(E)-4-(4-chlorophenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2g**).* Yellow solid; 3.18 g, 53% yield in three steps; mp 83-86 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54 (d, J = 16.32 Hz, 1H), 7.46 (d, J = 8.48 Hz, 2H), 7.38-7.26 (m, 5H), 7.20-7.17 (m, 2H), 6.75 (d, J = 16.32 Hz, 1H), 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$):

δ (ppm) 189.6, 166.8, 145.7, 141.7, 137.3, 132.5, 129.8, 129.6, 129.4, 128.1, 126.5, 123.8, 36.6. IR: 1661, 1644, 1087, 772, 696 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}ClNO_2^+$ 300.0786; Found 300.0786.

*(E)-4-(4-fluorophenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2h**).* Yellow solid; 3.57 g, 63% yield in three steps; mp 80-82 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59-7.50 (m, 3H), 7.36-7.26 (m, 3H), 7.19 (d, *J* = 7.44Hz, 2H), 7.11-7.06 (m, 2H), 6.71 (d, *J* = 16.32 Hz, 1H), 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 189. 8, 167.0, 164.5 (d, *J* = 253.4 Hz), 146.1, 141.8, 130.8 (d, *J* = 8.8 Hz), 129.6, 128.1, 126.5, 123.2 (d, *J* = 2.2 Hz), 116.3 (d, *J* = 22.0 Hz), 36.6. IR: 1680, 1639, 1163, 839, 814, 769, 704, 692 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}FNO_2^+$ 284.1081; Found 284.1082.

*(E)-N-methyl-4-(4-nitrophenyl)-2-oxo-N-phenylbut-3-enamide (**2i**).* Yellow solid; 3.41 g, 55% yield in three steps; mp 139-141 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.26 (d, *J* = 8.44 Hz, 2H), 7.70-7.59 (m, 3H) 7.38-7.18 (m, 5H), 6.93 (d, *J* = 16.32 Hz, 1H), 3.45 (s, 3H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 189.2, 166.7, 149.3, 144.0, 142.0, 140.4, 130.1, 129.6, 128.7, 127.1, 126.9, 124.6, 37.1. IR: 1688,1641, 1091, 848, 766, 741, 681 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}N_2O_4^+$ 311.1026; Found 311.1023.

*(E)-4-(3,4-dimethylphenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2j**).* Yellow solid; 4.34 g, 74% yield in three steps; mp 99.4-100.1 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55 (d, *J* = 16.3 Hz, 1H), 7.34-7.24 (m, 5H), 7.20-7.14 (m, 3H), 6.70 (d, *J* = 16.3 Hz, 1H), 3.44 (s, 3H), 2.28 (d, *J* = 5.6 Hz, 6H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): δ (ppm) 190.4, 167.3, 148.0, 141.8, 140.9, 137.4, 131.7, 130.3, 129.9, 129.6, 128.0, 126.6, 126.5, 122.4, 36.5, 20.0, 19.8. IR: 2921, 1643, 1620, 1594, 1494, 1449, 1423, 1388, 1303, 1254, 1237, 1214, 1198, 1178, 1157, 1073, 1033, 1019, 998, 981, 956, 917, 890, 874, 822, 799, 774, 699, 629, 542, 471 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{20}NO_2^+$ 294.1489; Found 294.1492.

*(E)-4-(benzo[d][1,3]dioxol-5-yl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2k**).* Yellow solid; 4.52 g, 73% yield in three steps; mp 89-91°C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.50 (d, *J* = 10.76 Hz, 1H), 7.34-7.27 (m, 3H),

7.19 (d, *J* = 5.00 Hz, 2H), 7.03-7.01 (m, 2H), 6.81 (d, *J* = 5.28 Hz, 1H), 6.59 (d, *J* = 10.80 Hz, 1H), 6.01 (s,2H), 3.43 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): *δ* (ppm) 189.9, 167.2, 150.6, 148.5, 147.3, 141.8, 129.6, 129.3, 128.5, 126.5, 125.8, 125.4, 121.6, 108.7, 106.7, 101.8, 36.5. IR: 1639, 1678, 1179, 729, 689, cm^{-1} . HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_4^+$ 310.1074; Found 310.1078.

*(E)-4-(3-bromophenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2l**).* Yellow solid; 3.86 g, 56% yield in three steps; mp 79-81 °C. ^1H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.95 (d, *J* = 16.32 Hz, 1H), 7.62 (d, *J* = 7.88 Hz, 1H), 7.56 (d, *J* = 7.76, 1H), 7.37-7.22 (m, 7H), 6.65 (d, *J* = 16.32 Hz, 1H), 3.46 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): *δ* (ppm) 190.6, 167.2, 146.2, 141.9, 134.4, 134.0, 132.5, 130.0, 129.8, 128.6, 128.4, 128.3, 127.2, 126.4, 37.0. IR: 1641,1591,1174, 831, 771, 760, 697 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}BrNO_2^+$ 344.0281; Found 344.0281.

*(E)-4-(3-bromophenyl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2m**).* Yellow solid; 2.90 g, 52% yield in three steps; mp 75-78 °C. ^1H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.58 (d, *J* = 16.32 Hz, 1H), 7.35-7.26 (m, 6H), 7.25-7.22 (m, 1H), 7.21-7.18 (m, 2H), 6.74 (d, *J* = 16.32 Hz, 1H), 3.44 (s, 3H), 3.36 (s, 3H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): *δ* (ppm) 190.2, 167.1, 147.7, 141.8, 138.8, 134.0, 132.2, 129.6, 129.3, 128.9, 128.0, 126.6, 126.0, 123.3, 36.5, 21.3. IR: 1644,1592,1176, 829, 775, 763, 695 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO_2^+$ 280.1332; Found 280.1333.

*(E)-4-(furan-2-yl)-N-methyl-2-oxo-N-phenylbut-3-enamide (**2n**).* Yellow solid; 2.71 g, 53% yield in three steps; mp 137-139 °C. ^1H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.52 (s, 1H), 7.38-7.28 (m, 4H), 7.19 (d, *J* = 7.72 Hz, 2H), 6.72 (d, *J* = 3.08 Hz, 1H), 6.67-6.62 (m, 1H), 6.51-6.49 (m, 1H), 3.42 (d, *J* = 0.72 Hz, 3H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$): *δ* (ppm) 189.6, 167.0, 150.7, 146.0, 141.8, 132.9, 129.6, 129.3, 128.0, 126.4, 126.4, 120.8, 117.5, 117.5, 113.0, 36.5. IR: 1640, 1618, 1110, 801, 773, 740, 697 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}NO_3^+$ 256.0968; Found 256.0965.

*(E)-N-methyl-2-oxo-N-phenyl-4-(thiophen-2-yl)but-3-enethioamide (**2o**).* Yellow solid; 2.22 g, 41% yield in three steps; mp 135-137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.72 (d, J = 15.96 Hz, 1H), 7.48-7.06 (m, 8H), 6.59 (d, J = 15.92 Hz, 1H), 3.41 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (pp m) 189.4, 167.0, 141.8, 139.6, 132.9, 130.4, 129.6, 128.6, 128.1, 126.5, 122.1, 36.6. IR: 1639, 1678, 1179, 729, 689, cm^{-1} . HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{14}NO_2S^+$ 272.0740; Found 272.0743.

*(E)-N-methyl-4-(naphthalen-2-yl)-2-oxo-N-phenylbut-3-enamide (**2p**).* Yellow solid; 3.22 g, 51% yield in three steps; mp 137-139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.95 (s, 1H), 7.87-7.73 (m, 4H), 7.65-7.61 (m, 1H), 7.56-7.49 (m, 2H), 7.35-7.20 (m, 4H), 6.88 (d, J = 16.24 Hz, 1H), 3.46 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 190.0, 167.1, 147.5, 141.8, 134.7, 133.2, 131.6, 131.2, 129.6, 128.9, 128.8, 128.1, 127.8, 127.8, 129.9, 126.6, 123.6, 123.5, 36.6. IR: 1641, 1612, 1109, 855, 814, 752, 697 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{18}NO_2^+$ 316.1332; Found 316.1332.

*(E)-N-(4-methoxyphenyl)-N-methyl-2-oxo-4-phenylbut-3-enamide (**2q**).* Yellow solid; 3.60 g, 61% yield in three steps; mp 99-101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59-7.55 (m, 1H), 7.53-7.51 (m, 2H), 7.42-7.38 (m, 3H), 7.11 (d, J = 8.84 Hz, 2H), 6.82 (d, J = 8.84 Hz, 2H), 6.72 (d, J = 16.36 Hz, 1H), 3.76 (s, 3H), 3.39 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 190.7, 167.3, 159.2, 147.4, 134.3, 134.1, 131.3, 129.1, 127.7, 128.2, 123.6, 114.7, 55.4, 36.8. IR: 1641, 1591, 1174, 830, 771, 762, 700 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{18}NO_3^+$ 296.1281; Found 296.1284.

*(E)-N-methyl-2-oxo-4-phenyl-N-(p-tolyl)but-3-enamide (**2r**).* Yellow solid; 3.41 g, 61% yield in three steps; mp 108-110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61-7.50 (m, 3H), 7.43-7.36 (m, 3H), 7.09 (dd, J = 8.24 Hz, 4H), 6.77-6.72 (m, 1H), 3.41 (s, 3H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 190.4, 167.2, 147.4, 139.1, 138.1, 134.1, 131.3, 130.2, 129.1, 128.7, 126.5, 123.6, 36.6, 21.1. IR: 1677, 1639, 1089, 825, 762 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{18}NO_2^+$ 280.1332; Found 280.1333.

*(E)-N-(4-fluorophenyl)-N-methyl-2-oxo-4-phenylbut-3-enamide (**2s**)*. Yellow solid; 2.44 g, 43% yield in three steps; mp 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55-7.50 (m, 3H), 7.39-7.35 (m, 2H), 7.34-7.26 (m, 3H), 7.20-7.17 (m, 2H), 6.76 (d, J = 16.36 Hz, 1H), 3.43 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 190.0, 166.9, 161.8 (d, J = 247.3 Hz), 147.8, 137.7 (d, J = 3.1 Hz), 133.9, 131.4, 129.1, 128.8, 128.6 (d, J = 8.7 Hz), 123.4, 116.5 (d, J = 22.7 Hz), 36.8. IR: 1660, 1643, 1112, 840, 814, 765, 684 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{15}FNO_2^+$ 284.1081; Found 284.1085.

*(E)-N-(4-chlorophenyl)-N-methyl-2-oxo-4-phenylbut-3-enamide (**2t**)*. Yellow solid; 3.36 g, 56% yield in three steps; mp 92-94 °C. ^{1}H NM R (400 MHz, $CDCl_3$): δ (ppm) 7.54 (d, J = 10.84 Hz, 1H), 7.46 (d, J = 5.60 Hz, 1H), 7.38-7.28 (m, 5H), 7.18 (d, J = 4.96 Hz, 2H), 6.74 (d, J = 10.88 Hz, 1H), 3.44 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 189.6, 166.8, 145.8, 141.7, 137.3, 132.5, 129.9, 129.6, 128.4, 128.1, 126.5, 123.8, 36.6. IR: 1647,1618,1115,875,766 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{15}ClNO_2^+$ 300.0786; Found 300.0783.

*(E)-N-(4-bromophenyl)-N-methyl-2-oxo-4-phenylbut-3-enamide (**2u**)*. Yellow solid; 2.89 g, 42% yield in three steps; mp 107-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63-7.58 (m, 1H), 7.55-7.53 (m, 2H), 7.46-7.39 (m, 5H), 7.07 (d, J = 8.28 Hz, 1H), 6.81 (d, J = 16.28 Hz, 1H), 3.41 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 189.7, 166.8, 147.9, 141.0, 133.9, 132.8, 131.5, 129.1, 128.8, 128.2, 123.3, 121.9, 36.6. IR: 1678, 1641, 835, 827, 762, 710 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{15}BrNO_2^+$ 344.0281; Found 344.0286.

(E)-4-(benzo[d][1,3]dioxol-5-yl)-N-(4-chlorophenyl)-N-methyl-2-oxobut-3-enamide (***2v***). Yellow solid; 2.74 g, 40% yield in three steps; mp 107.2-107.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51 (d, J = 16.2 Hz, 1H), 7.31-7.26 (m, 2H), 7.13-7.03 (m, 4H), 6.83 (d, J = 8.2 Hz, 1H), 6.63 (d, J = 16.2 Hz, 1H), 6.03 (s, 2H), 3.40 (s, 3H); ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$): δ (ppm) 189.5, 167.0, 150.8, 148.5, 147.6, 140.5, 133.8, 129.8, 128.4, 127.8, 126.0, 121.3, 108.8, 106.8, 101.8, 36.6. IR: 1655, 1639, 1618, 1596, 1489, 1450, 1360, 1259, 1216,

1092, 1033, 974, 927, 854, 809, 805, 771, 732, 548 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{14}ClNNaO_4^+$ 366.0504; Found 366.0506.

General procedure for the Preparation of products 3. In a flame-dried Schlenk tube, a solution of diethylzinc (50 μL, 1.0 M in hexane) was added to a solution of the chiral ligand **L3d** (9.2 mg, 10 mol%) in dry CH_3CN/CH_2Cl_2 (1/1, 2.5 mL) under nitrogen. The mixture was stirred at room temperature for 30 min. Then Et_3N (0.325mmol), 3-amino oxindole hydrochloride **1** (0.25 mmol), and *β,γ*-unsaturated *α*-keto amide **2** (0.275 mmol) were added to the mixture successively. The mixture was stirred at -45 °C until the starting material was completely consumed (monitored by TLC). The solvent is evaporated to give the residue. Then the trifluoroacetic acid (1 mL) and CH_2Cl_2 (1mL) was added to the residue, and the mixture was stirred at room temperature for 0.5 h. Then the mixture was quenched with sat. aq $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (CH_2Cl_2/acetone = 35/1) to give the pure product 3.

(3R,3'R,5'R)-1,1''-dimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3a***). White solid. mp 220.5-221 °C. 87 mg, 85% yield, >20:1 dr (determined by ^1H NMR), 89% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 15.56 min, t (major) = 11.52 min. $[\alpha]_D^{20}$ = +128.5 (*c* = 0.56, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.16–8.14 (m, 1H), 8.08 (d, *J* = 7.0 Hz, 1H), 7.37-7.33 (m, 1H), 7.23-7.20 (m, 1H), 7.12-7.07 (m, 2H), 7.05-6.96 (m, 5H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.50-6.48 (m, 1H), 4.40-4.35 (dd, *J* = 5.8, 14.5 Hz, 1H), 3.32-3.25 (m, 4H), 3.10 (s, 3H), 2.85 (brs, 1H), 2.35-2.30 (dd, *J* = 5.9, 12.3 Hz, 1H). 13C{^1H} NMR(100 MHz, $CDCl_3$) *δ* 179.4, 178.7, 142.5, 142.2, 135.1, 134.7, 131.0, 129.0, 128.6, 127.7, 127.5, 127.2, 125.6, 124.0, 123.6, 123.0, 108.2, 107.6, 73.4, 69.5, 56.0, 42.2, 26.6, 26.3. IR:

3359, 2921, 1705, 1610, 1492, 1470, 1371,1346, 1120, 1089, 1078, 1025, 748,708 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{24}N_3O_2^+$ 410.1863; Found 410.1865.

(3R,3'R,5'R)-1''-ethyl-1-methyl-3'-phenyldispiro[indol-ine-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3b***).

White solid. mp 152.7-153.2 °C. 87 mg, 82% yield, >20:1 dr (determined by ^1H NMR), 54% ee, HPLC (Chiral IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 36.55 min, t (major) = 22.90 min. $[\alpha]_D^{20}$ = +144.8 (*c* = 0.84, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.16-8.14 (m, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 7.35-7.31 (m, 1H), 7.22-7.18 (m, 1H), 7.10-7.06 (m, 2H), 7.04-6.96 (m, 5H), 6.89 (d, *J* = 7.2 Hz, 1H), 6.49-6.47 (m, 1H), 4.41-4.36 (dd, *J* = 5.8, 14.4 Hz, 1H), 3.84-3.80 (m, 2H), 3.32-3.26 (m, 1H), 3.10 (s, 3H), 2.34-2.29 (dd, *J* = 5.8, 12.3 Hz, 1H), 1.32-1.29 (m, 3H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.0, 178.7, 142.2, 141.6, 135.1, 134.9, 131.0, 129.0, 128.6, 127.7, 127.5, 127.2, 125.6, 124.2, 123.4, 122.9, 108.4, 107.6, 73.4, 67.5, 55.9, 42.3, 35.2, 26.3, 12.7. IR: 3357, 2913, 1703, 1610, 1487, 1465, 1369, 1349, 1119, 1080, 1024, 751, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}N_3O_2^+$ 424.2020; Found 424.2024.

(3R,3'R,5'R)-1''-benzyl-1-methyl-3'-phenyldispiro[indo-line-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3c***).

White solid. mp 198.3-198.8 °C. 99.5 mg, 82% yield, >25:1 dr (determined by ^1H NMR), 70% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 14.25 min, t (major) = 11.36 min. $[\alpha]_D^{20}$ = +137.6 (*c* = 1.06, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.18-8.16 (m, 1H), 8.12-8.09 (m, 1H), 7.31-7.23 (m, 5H), 7.21-7.15 (m, 2H), 7.11-6.97 (m, 7H), 6.77-6.75 (m, 1H), 6.49-6.47 (m, 1H), 5.02-4.92 (m, 2H), 4.43-4.38 (dd, *J* = 5.8, 14.4 Hz, 1H), 3.39-3.33 (m, 1H), 3.09 (s, 3H), 2.53 (brs, 1H), 2.39-2.35 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.6, 178.7, 142.3, 141.6, 135.6, 135.1, 134.7, 131.0, 128.94, 128.87, 128.7, 127.75, 127.72, 127.6, 127.2, 125.6, 124.1, 123.7, 123.0, 109.3, 107.7, 73.5, 67.6, 55.9, 44.2, 42.5, 26.3. IR: 3359, 2920, 1705, 1612, 1486, 1466, 1454, 1349, 1256, 1189, 1157, 1080, 1026, 754, 739, 697 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{28}N_3O_2^+$ 486.2176; Found 486.2183.

(3R,3'R,5'R)-3'-(4-methoxyphenyl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3d***). White solid. mp 167.3-168.2 °C. 81 mg, 74% yield, >20:1 dr (determined by ^{1}H NMR), 89% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 22.44 min, t (major) = 14.96 min. $[\alpha]_D^{20}$ = +163.6 (*c* = 1.05, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.17 (d, *J* = 6.4 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.36-7.31 (m, 1H), 7.22-7.18 (m, 1H), 7.13-7.06 (m, 2H), 6.89-6.86 (m, 3H), 6.57-6.49 (m, 3H), 4.34-4.29 (dd, *J* = 5.7, 14.5 Hz, 1H), 3.65 (s, 3H), 3.27-3.18 (m, 4H), 3.09 (s, 3H), 2.84 (brs, 1H), 2.31-2.26 (dd, *J* = 5.8, 12.2 Hz, 1H). ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$) *δ* 179.5, 178.8, 158.6, 142.5, 142.3, 134.8, 131.2, 129.0, 128.6, 127.1, 125.6, 124.0, 123.6, 122.9, 113.1, 108.2, 107.7, 73.4, 67.4, 55.5, 55.1, 42.6, 26.6, 26.3. IR: 3348, 2921, 2851, 1715, 1699, 1611, 1514, 1490, 1467, 1371, 1346, 1245, 1121, 1080, 1020, 840, 744, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}N_3O_3^+$ 440.1969; Found 440.1972.

(3R,3'R,5'R)-1,1''-dimethyl-3'-(p-tolyl)dispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3e***). White solid. mp 163.4-164.7 °C. 86 mg, 81% yield, 17:1 dr (determined by ^{1}H NMR), 79% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 15.79 min, t (major) = 11.19 min. $[\alpha]_D^{20}$ = +179.6 (*c* = 0.90, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.15 (m, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.36-7.32 (m, 1H), 7.23-7.19 (m, 1H), 7.13-7.06 (m, 2H), 6.88-6.81 (m, 5H), 6.51 (d, *J* = 6.8 Hz, 1H), 4.37-4.32 (dd, *J* = 5.8, 14.4 Hz, 1H), 3.29-3.22 (m, 4H), 3.10 (s, 3H), 2.84 (brs, 1H), 2.32-2.28 (dd, *J* = 5.8, 12.2 Hz, 1H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$) *δ* 179.5, 178.8, 142.5, 142.3, 136.7, 134.8, 132.0, 131.2, 129.0, 128.6, 128.4, 127.4, 125.6, 124.0, 123.6, 122.9, 108.2, 107.6, 73.4, 67.4, 55.7, 42.5, 26.6, 26.3, 21.0. IR: 3348, 2923, 1708, 1611, 1491, 1468, 1372, 1346, 1118, 1083, 818, 749, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}N_3O_2^+$ 424.2020; Found 424.2024.

(3R,3'R,5'R)-3'-(4-bromophenyl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3f***). White solid. mp 167.7-168.3 °C. 90 mg, 74% yield, > 20:1 dr (determined by ^{1}H NMR), 68% ee, HPLC (Chiral

IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 17.86 min, t (major) = 15.25 min. $[\alpha]_D^{20}$ = +116.2 (*c* = 1.32, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.14 (d, *J* = 6.9 Hz, 1H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.36-7.32 (m, 1H), 7.22-7.07 (m, 5H), 6.88-6.83 (m, 3H), 6.53 (d, *J* = 7.4 Hz, 1H), 4.33-4.28 (dd, *J* = 5.7, 14.4 Hz, 1H), 3.26-3.18 (m, 4H), 3.11 (s, 3H), 2.83 (brs, 1H), 2.32-2.28 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.2, 178.5, 142.5, 142.2, 134.5, 134.2, 130.8, 130.7, 129.2, 129.1, 128.9, 125.6, 123.9, 123.6, 123.1, 121.2, 108.3, 107.9, 73.2, 67.4, 55.4, 42.4, 26.6, 26.3. IR: 3348, 2923, 1707, 1612, 1490, 1468, 1372, 1346, 1119, 1078, 1010, 837, 749, 693 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}BrN_3O_2^+$ 488.0968; Found 488.0973.

(3R,3'R,5'R)-3'-(4-chlorophenyl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3g***).

White solid. mp 185.7-186.3 °C. 93 mg, 84% yield, > 20:1 dr (determined by ^1H NMR), 65% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 16.87 min, t (major) = 14.21 min. $[\alpha]_D^{20}$ = +123.2 (*c* = 1.21, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.15 (d, *J* = 6.9 Hz, 1H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.37-7.32 (m, 1H), 7.23-7.19 (m, 1H), 7.15-7.10 (m, 2H), 7.01-6.99 (m, 2H), 6.91-6.86 (m, 3H), 6.53 (d, *J* = 7.4 Hz, 1H), 4.35-4.30 (dd, *J* = 5.8, 14.4 Hz, 1H), 3.28-3.18 (m, 4H), 3.11 (s, 3H), 2.82 (brs, 1H), 2.33-2.28 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.3, 178.5, 142.5, 142.2, 134.5, 133.7, 133.0, 130.7, 129.1, 128.91, 128.89, 127.9, 125.6, 123.9, 123.6, 123.1, 108.3, 107.9, 73.3, 67.4, 55.3, 42.4, 26.6, 26.3. IR: 3348, 2921, 2851, 1706, 1611, 1468, 1491, 1372, 1346, 1120, 1083, 834, 750, 693 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}ClN_3O_2^+$ 444.1473; Found 444.1477.

(3R,3'R,5'R)-3'-(4-fluorophenyl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3h***).

White solid. mp 159.7-160.2 °C. 88 mg, 82% yield, > 20:1 dr (determined by ^1H NMR), 70% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 15.81 min, t (major) = 12.67 min. $[\alpha]_D^{20}$ = +169.1 (*c* = 0.98, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.15 (d, *J* = 6.2 Hz, 1H), 8.05 (d, *J*

= 7.2 Hz, 1H), 7.36-7.32 (m, 1H), 7.22-7.19 (m, 1H), 7.14-7.06 (m, 2H), 6.95-6.86 (m, 3H), 6.74-6.69 (m, 2H), 6.51 (d, *J* = 7.1 Hz, 1H), 4.36-4.31 (dd, *J* = 5.7, 14.4 Hz, 1H), 3.27-3.18 (m, 4H), 3.10 (s, 3H), 2.83 (brs, 1H), 2.33-2.28 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.3, 178.6, 161.8 (d, *J* = 245.9 Hz), 142.5, 142.2, 134.6, 130.9, 129.1 (d, *J* = 2.7 Hz), 129.0 (d, *J* = 7.9 Hz), 128.8, 125.5, 124.0, 123.6, 123.0, 114.6 (d, *J* = 21.3 Hz), 108.3, 107.7, 73.4, 67.4, 55.3, 42.4, 26.6, 26.3. IR: 3348, 2930, 1708, 1611, 1509, 1491, 1468, 1347, 1372, 1224, 1119, 1083, 835, 746, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}FN_3O_2^+$ 428.1769; Found 428.1773.

(3R,3'R,5'R)-1,1''-dimethyl-3'-(4-nitrophenyl)dispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione ***(3i)***. White solid. mp 199.2-201.1 °C. 75 mg, 66% yield, 22:1 dr (determined by ^{1}H NMR), 43% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 33.72 min, t (major) = 25.53 min. $[\alpha]_D^{20}$ = +85.4 (*c* = 0.79, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.14 (d, *J* = 6.7 Hz, 1H), 8.05 (d, *J* = 7.3 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.38-7.35 (m, 1H), 7.24-7.20 (m, 1H), 7.16-7.08 (m, 4H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.2 Hz, 1H), 4.47-4.42 (dd, *J* = 5.7, 14.3 Hz, 1H), 3.33-3.26 (m, 4H), 3.13 (s, 3H), 2.87 (brs, 1H), 2.41-2.36 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR(100 MHz, $CDCl_3$) *δ* 180.0, 178.1, 147.0, 143.0, 142.5, 142.0, 134.2, 130.2, 129.3, 128.4, 125.5, 123.9, 123.7, 123.3, 122.9, 108.4, 108.0, 73.4, 67.6, 55.4, 42.2, 26.6, 26.4. IR: 3348, 2924, 1715, 1614, 1511, 1491, 1469, 1373, 1343, 1119, 1082, 858, 746, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}N_4O_4^+$ 455.1714; Found 455.1718.

(3R,3'R,5'R)-3'-(3,4-dimethylphenyl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione ***(3j)***. White solid. mp 159.3-160.5 °C. 78 mg, 72% yield, >60:1 dr (determined by ^{1}H NMR), 84% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 10.75 min, t (major) = 9.49 min. $[\alpha]_D^{20}$ = +210.0 (*c* = 1.33, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.17 (m, 1H), 8.08-8.06 (m, 1H), 7.35-7.31 (m, 1H), 7.22-7.18 (m, 1H), 7.09-7.07 (m, 2H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.77-6.75 (m, 2H),

6.69-6.66 (m, 1H), 6.50-6.48 (m, 1H), 4.34-4.29 (dd, *J* = 5.8, 14.5 Hz, 1H), 3.28-3.21 (m, 4H), 3.10 (s, 3H), 2.83 (brs, 1H), 2.31-2.26 (dd, *J* = 5.8, 12.3 Hz, 1H), 2.05-2.03 (m, 6H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.5, 178.9, 142.5, 142.3, 135.8, 135.3, 134.8, 132.4, 131.3, 129.0, 128.94, 128.93, 128.5, 125.7, 124.9, 124.0, 123.6, 122.8, 108.2, 107.6, 73.4, 67.4, 55.7, 42.7, 26.6, 26.3, 19.5,19.3. IR: 3343, 2921, 1709, 1611, 1491, 1468, 1372, 1346, 1119, 1083, 1047, 819, 750, 693 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{28}N_3O_2^+$ 438.2176; Found 438.2182.

*(3R,3'R,5'R)-3'-(benzo[d][1,3]dioxol-5-yl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (**3k**)*. White solid. mp 163.8-164.3 °C. 90 mg, 79% yield, >20:1 dr (determined by ^1H NMR), 90% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 21.29 min, t (major) = 17.76 min. $[\alpha]_D^{20}$ = +115.2 (*c* = 1.00, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.13 (d, *J* = 6.9 Hz, 1H), 8.05 (d, *J* = 7.3 Hz, 1H), 7.35-7.31 (m, 1H), 7.22-7.07 (m, 3H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 8.9 Hz, 1H), 5.76 (d, *J* = 4.9 Hz, 2H), 4.32-4.27 (dd, *J* = 5.7 Hz, 1H), 3.26 (s, 3H), 3.20-3.11 (m, 4H), 2.30-2.25 (dd, *J* = 5.8, 12.3 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.4, 178.7, 147.1, 146.5, 142.5, 142.3, 134.6, 131.1, 129.0, 128.9, 128.7, 125.6, 124.0, 123.6, 123.0, 121.0, 108.2, 107.85, 107.76, 100.8, 73.2, 67.3, 55.6, 42.7, 29.7, 26.6, 26.3. IR: 3343, 2922, 1705, 1610, 1504, 1490, 1469, 1443, 1372, 1255, 1118, 1082, 1036, 927, 818, 745, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{24}N_3O_4^+$ 454.1761; Found 454.1762.

*(3R,3'R,5'R)-3'-(3-bromophenyl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (**3l**)*. White solid. mp 219.8-220.3 °C. 83 mg, 68% yield, 25:1 dr (determined by ^1H NMR), 84% ee, HPLC (Chiral IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 39.07 min, t (major) = 28.02 min. $[\alpha]_D^{20}$ = +140.6 (*c* = 0.72, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.13 (m, 1H), 8.04 (m, 1H), 7.37-7.32 (m, 1H), 7.23-7.19 (m, 1H), 7.16-7.07 (m, 4H), 6.89-6.87 (m, 3H), 6.53 (m, 1H), 4.33-4.28 (dd, *J* = 5.8, 14.4 Hz, 1H),

3.27 (s, 3H), 3.25-3.18 (m, 1H), 3.13 (s, 3H), 2.33-2.28 (dd, *J* = 5.9, 12.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.2, 178.4, 142.5, 142.1, 137.6, 134.4, 130.8, 130.6, 130.3, 129.2, 129.1, 128.9, 126.0, 125.5, 124.0, 123.7, 123.1, 121.8, 108.3, 107.8, 73.4, 67.5, 55.5, 42.0, 26.6, 26.3. IR: 3354, 2922, 1703, 1609, 1490, 1466, 1371, 1345, 1120, 1083, 1053, 798, 747, 696 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}BrN_3O_2^+$ 488.0968; Found 488.0975.

*(3R,3'R,5'R)-1,1''-dimethyl-3'-(m-tolyl)dispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (**3m**).* White solid. mp 186.8-187.6 °C. 87 mg, 82% yield, >20:1 dr (determined by ^{1}H NMR), 68% ee, HPLC (Chiral IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 51.10 min, t (major) = 32.74 min. $[\alpha]_D^{20}$ = +154.0 (*c* = 0.89, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.16-8.14 (m, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.36-7.32 (m, 1H), 7.11-7.05 (m, 2H), 6.92-6.74 (m, 5H), 6.50-6.48 (m, 1H), 4.36-4.31 (dd, *J* = 5.7, 14.4 Hz, 1H), 3.30-3.23 (m, 4H), 3.10 (s, 3H), 2.84 (brs, 1H), 2.32-2.28 (dd, *J* = 5.8, 12.2 Hz, 1H), 2.13 (s, 3H). $^{13}C\{^{1}H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.5, 178.8, 142.5, 142.2, 137.2, 135.0, 134.7, 131.1, 129.0, 128.6, 128.5, 127.8, 127.5, 125.6, 124.5, 124.0, 123.6, 122.8, 108.2, 107.6, 73.5, 67.5, 56.0, 42.3, 26.6, 26.2, 21.2. IR: 3358, 2923, 1703, 1610, 1492, 1469, 1371, 1345, 1246, 1121, 1084, 795, 772, 745, 694 cm^{-1}. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{27}H_{26}N_3O_2^+$ 424.2020; Found 424.2019.

*(3R,3'S,5'R)-3'-(furan-2-yl)-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (**3n**).* White solid. mp 107.3-108.0 °C. 70 mg, 70% yield, >20:1 dr (determined by ^{1}H NMR), 68% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/40, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 27.65 min, t (major) = 13.47 min. $[\alpha]_D^{20}$ = +112.4 (*c* = 0.60, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.04-7.98 (m, 2H), 7.35-7.31 (m, 1H), 7.21-7.16 (m, 2H), 7.08-7.04 (m, 1H), 7.00-6.99 (m, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 6.01-5.99 (m, 1H), 5.81 (d, *J* = 3 Hz, 1H), 4.45-4.40 (dd, *J* = 6.2, 14.2 Hz, 1H), 3.25 (s, 3H), 3.24-3.20 (m, 4H), 2.43-2.39 (dd, *J* = 6.2, 12.4Hz, 1H). $^{13}C\{^{1}H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.0, 178.4, 150.7, 142.6, 142.5, 141.6,

134.4, 131.0, 129.0, 128.8, 125.6, 124.0, 123.6, 123.0, 109.8, 108.2, 107.6, 106.5, 72.0, 67.7, 49.5, 41.8, 26.6, 26.5. IR: 3330, 2921, 2851, 1708, 1610, 1491, 1467, 1372, 1348, 1119, 1077, 1021, 750, 693 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{22}N_3O_3^+$ 400.1656; Found 400.1656.

(3R,3'S,5'R)-1,1''-dimethyl-3'-(thiophen-2-yl)dispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3o***). White solid. mp 143.6-144.2 °C. 85 mg, 82% yield, >20:1 dr (determined by ^1H NMR), 83% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 20.36 min, t (major) = 12.12 min. $[\alpha]_D^{20}$ = +196.3 (*c* = 0.92, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.13 (d, *J* = 6.8 Hz, 1H), 8.02 (d, *J* = 7.2 Hz, 1H), 7.36-7.31 (m, 1H), 7.22-7.15 (m, 2H), 7.12-7.08 (m, 1H), 6.94-6.92 (m, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.69-6.59 (m, 3H), 4.64-4.58 (dd, *J* = 5.9, 14.2 Hz, 1H), 3.26 (s, 3H), 3.20-3.13 (m, 4H), 2.48-2.44 (dd, *J* = 6, 12.3 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.0, 178.3, 142.7, 142.5, 138.5, 134.4, 130.9, 129.1, 128.9, 126.1, 125.9, 125.2, 124.3, 123.9, 123.6, 123.1, 108.3, 107.8, 73.0, 67.4, 51.6, 44.6, 26.6, 26.4. IR: 3343, 2920, 1709, 1610, 1491, 1468, 1347, 1372, 1243, 1118, 1084, 751, 693 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{22}N_3O_2S^+$ 416.1427; Found 416.1427.

(3R,3'R,5'R)-1,1''-dimethyl-3'-(naphthalen-2-yl)dispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3p***). White solid. mp 218.7-219.5 °C. 95 mg, 83% yield, 29:1 dr (determined by ^1H NMR), 78% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 14.64 min, t (major) = 13.25 min. $[\alpha]_D^{20}$ = +195.5 (*c* = 0.88, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.22 (d, *J* = 7.2 Hz, 1H), 8.13 (d, *J* = 7.3 Hz, 1H), 7.62 (d, *J* = 6.9 Hz, 2H), 7.49-7.46 (m, 2H), 7.37-7.31 (m, 3H), 7.24-7.20 (m, 1H), 7.08-6.97 (m, 3H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.37 (d, *J* = 7.6 Hz, 1H), 4.57-4.51 (dd, *J* = 5.8, 14.4 Hz, 1H), 3.44-3.37 (m, 1H), 3.27 (s, 3H), 3.06 (s, 3H), 2.42-2.37 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.4, 178.8, 142.5, 142.2, 134.7, 132.9, 132.8, 132.5, 131.0, 129.0, 128.7, 127.6, 127.4, 127.2, 126.8, 125.9, 125.70, 125.68, 125.5, 124.0, 123.7, 123.0,108.3, 107.7, 73.5, 67.6, 56.1, 42.7, 26.6, 26.3. IR: 3350, 2938, 1709, 1611, 1491,

1467, 1348, 1086, 825, 747, 694 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{26}N_3O_2^+$ 460.2020; Found 460.2025.

(3R,3'R,5'R)-5''-methoxy-1,1''-dimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3q***). White solid. mp 181.7-182.6 °C. 90 mg, 82% yield, 29:1 dr (determined by ^1H NMR), 72% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 14.95 min, t (major) = 11.55 min. $[\alpha]_D^{20}$ = +158.3 (*c* = 1.17, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.12-8.10 (m, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.11-6.96 (m, 7H), 6.88-6.85 (m, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 6.8 Hz, 1H), 4.40-4.34 (dd, *J* = 5.7, 14.4 Hz, 1H), 3.91 (s, 3H), 3.31-3.25 (m, 4H), 3.10 (s, 3H), 2.34-2.30 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.1, 178.9, 156.8, 142.3, 136.0, 135.8, 135.1, 131.0, 128.7, 127.7, 127.5, 127.2, 125.6, 122.9, 113.9, 111.0, 108.8, 107.6, 73.4, 67.9, 56.0, 55.7, 42.4, 26.7, 26.3. IR: 3361, 2922, 2852, 1705, 1608, 1491, 1469, 1346, 1279, 1258, 1118, 1025, 811, 781, 762, 751, 705, 693 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}N_3O_3^+$ 440.1969; Found 440.1975.

(3R,3'R,5'R)-1,1'',5''-trimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3r***). White solid. mp 175.1-175.8 °C. 89 mg, 84% yield, >20:1 dr (determined by ^1H NMR), 73% ee, HPLC (Chiral IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 46.41 min, t (major) = 21.37 min. $[\alpha]_D^{20}$ = +164.0 (*c* = 0.97, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.17 (d, *J* = 6.1 Hz, 1H), 7.87 (s, 1H), 7.14-6.98 (m, 8H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.48 (d, *J* = 7.7 Hz, 1H), 4.41-4.36 (dd, *J* = 5.7, 14.4 Hz, 1H), 3.31-3.25 (m, 4H), 3.10 (s, 3H), 2.84 (brs, 1H), 2.45 (s, 3H), 2.33-2.29 (dd, *J* = 5.8, 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 179.4, 178.8, 142.2, 140.1, 135.1, 134.8, 133.3, 131.0, 129.2, 128.6, 127.7, 127.5, 127.2, 125.7, 124.7, 122.9, 108.0, 107.6, 73.5, 67.6, 55.9, 42.2, 26.6, 26.2, 21.3. IR: 3362, 2920, 1705, 1609, 1495, 1468, 1346, 1257, 1120, 1074, 1054, 816, 785, 765, 708, 692 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}N_3O_2^+$ 424.2020; Found 424.2024.

(3R,3'R,5'R)-5''-fluoro-1,1''-dimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3s***).

White solid. mp 171.4-172.6 °C. 84 mg, 79% yield, >20:1 dr (determined by ^{1}H NMR), 70% ee, HPLC (Chiral IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 30.89 min, t (major) = 26.29 min. $[\alpha]_D^{20}$ = +180.2 (*c* = 0.97, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.08 (d, *J* = 6.6 Hz, 1H), 7.90-7.88 (m, 1H), 7.11-6.96 (m, 8H), 6.81-6.78 (m, 1H), 6.49 (d, *J* = 7.2 Hz, 1H), 4.35-4.30 (dd, *J* = 5.7, 14.4 Hz, 1H), 3.29-3.22 (m, 4H), 3.1 (s, 3H), 2.33-2.28 (dd, *J* = 5.8, 12.2 Hz, 1H). ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$) *δ* 179.1, 178.8, 159.9 (d, *J* = 242.3 Hz), 142.3, 138.3, 136.4 (d, *J* = 7.5 Hz), 134.9, 130.8, 128.8, 127.7, 127.5, 127.3, 125.5, 122.9, 115.1 (d, *J* = 23.9 Hz), 112.5 (d, *J* = 25.1 Hz), 108.8 (d, *J* = 8.0 Hz), 107.7, 73.4, 67.8, 55.6, 42.4, 26.8, 26.3. IR: 3365, 2922, 1706, 1610, 1493, 1470, 1416, 1347, 1272, 1117, 1088, 1058, 864, 819, 764, 753, 710, 679, 653 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}FN_3O_2^+$ 428.1769; Found 428.1774.

(3R,3'R,5'R)-5''-chloro-1,1''-dimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3t***).

White solid. mp 181.6-182.5 °C. 89 mg, 80% yield, >20:1 dr (determined by ^{1}H NMR), 95% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 15.56 min, t (major) = 9.90 min. $[\alpha]_D^{20}$ = +190.8 (*c* = 0.89, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.12-8.07 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.11-7.06 (m, 6H), 6.95 (d, *J* = 3.0 Hz, 2H), 6.48 (d, *J* = 6.7 Hz, 1H), 4.37-4.32 (dd, *J* = 5.8, 14.4 Hz, 1H), 3.66 (s, 3H), 3.29 (t, 1H), 3.10 (s, 3H), 2.32-2.28 (dd, *J* = 5.9, 12.3 Hz, 1H). ^{13}C{^{1}H} NMR(100 MHz, $CDCl_3$) *δ* 180.1, 178.7, 142.2, 139.7, 138.1, 134.8, 134.6, 130.8, 128.8, 127.7, 127.5, 127.3, 125.6, 124.8, 123.2, 123.0, 107.7, 102.6, 73.5, 67.2, 55.6, 42.9, 30.3, 26.3. IR: 3364, 2922, 1704, 1610, 1488, 1470, 1415, 1345, 1255, 1120, 1085, 1052, 875, 784, 763, 753, 708, 692 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}ClN_3O_2^+$ 444.1473; Found 444.1478.

(3R,3'R,5'R)-5''-bromo-1,1''-dimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3u***).

White solid. mp 182.5-183.3 °C. 104 mg, 85% yield, >20:1 dr (determined by ^{1}H NMR), 70% ee, HPLC (Chiral

IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 28.80 min, t (major) = 23.84 min. $[\alpha]_D^{20}$ = +187.2 (*c* = 1.48, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.20 (d, *J* = 1.8 Hz, 1H), 8.08-8.06 (m, 1H), 7.47-7.44 (m, 1H), 7.11-7.05 (m, 2H), 7.03-7.01 (m, 3H), 6.98-6.95 (m, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.50-6.47 (m, 1H), 4.35-4.30 (dd, *J* = 5.8, 14.5 Hz, 1H), 3.28-3.22 (m, 4H), 3.10 (s, 3H), 2.52 (brs, 1H), 2,33-2.28 (dd, *J* = 5.9, 12.4 Hz, 1H). $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 178.9, 178.6, 142.3, 141.5, 136.7, 134.8, 131.9, 130.8, 128.8, 127.7, 127.5, 127.4, 127.3, 125.5, 122.9, 116.4, 109.7, 107.7, 73.4, 67.6, 55.6, 42.4, 26.7, 26.3. IR: 3365, 2923, 1705, 1608, 1469, 1414, 1343, 1256, 1120, 1079, 1051, 817, 783, 751, 707, 647 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}BrN_3O_2^+$ 488.0968; Found 488.0971.

*(3R,3'R,5'R)-3'-(benzo[d][1,3]dioxol-5-yl)-5''-chloro-1,1''-dimethyldispiro[indoline-3,2'-pyrrolidine-5',3''-indolin e]-2,2''-dione (**3v**).* White solid. mp 117.5-118.1 °C. 89 mg, 73% yield, >20:1 dr (determined by ^1H NMR), 60% ee, HPLC (Chiral IF cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 30.39 min, t (major) = 57.10 min. $[\alpha]_D^{20}$ = +97.2 (*c* = 0.87, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.07-8.05 (m, 2H), 7.31-7.27 (m, 1H), 7.16-7.06 (m, 2H), 6.78 (d, *J* = 8.3 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 6.47-6.44 (m, 3H), 5.78-5.76 (m, 2H), 4.27-4.22 (dd, *J* = 5.8, 14.5 Hz, 1H), 3.25 (s, 3H), 3.17-3.10 (m, 4H), 2.78 (s, 1H), 2.29-2.24 (dd, *J* = 5.8, 12.3 Hz, 1H); $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) *δ* 178.9, 178.7, 147.1, 146.6, 142.4, 141.0, 136.3, 130.8, 129.0, 128.8, 128.86, 128.6, 125.5, 124.6, 123.0, 121.0, 109.2, 107.84, 107.8, 107.6, 100.8, 73.2, 67.4, 55.2, 42.8, 26.7, 26.3. IR: 3355, 2915, 1710, 1610, 1488, 1467, 1346, 1232, 1088, 1037, 927, 809, 728, 694, 542 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{23}ClN_3O_4^+$ 488.1372; Found 488.1373.

*(3R,3'R,5'R)-1-benzyl-1''-methyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (**3w**).* White solid. mp 180.5-181.0 °C. 88 mg, 73% yield, >20:1 dr (determined by ^1H NMR), 90% ee, HPLC (Chiral IF cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 31.65 min, t (major) = 25.85 min. $[\alpha]_D^{20}$ = +195.4 (*c* = 1.14, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) 8.22 (d, *J* = 7.3 Hz, 1H), 8.10 (d, *J* = 7.4 Hz,

1H), 7.35-7.32 (m, 1H), 7.23-7.19 (m, 4H), 7.07-6.98 (m, 9H), 6.87 (d, *J* = 7.7 Hz, 1H), 6.40 (d, *J* = 7.6 Hz, 1H), 4.94 (d, *J* = 15.8 Hz, 1H), 4.68 (d, *J* = 15.8 Hz, 1H), 4.46-4.41 (dd, *J* = 5.8 14.5 Hz, 1H), 3.34-3.26 (m, 4H), 2.92 (s, 1H), 2.38-2.33 (dd, *J* = 5.9, 12.3 Hz, 1H); δ $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) δ 179.4, 179.0, 142.5, 141.7, 135.4, 135.0, 134.7, 131.2, 129.0, 128.7, 128.6, 128.1, 127.9, 127.5, 127.32, 127.28, 126.0, 124.0, 123.7, 123.0, 108.8, 108.3, 73.3, 67.5, 56.1, 44.1, 42.9, 26.6. IR: 3362, 2918, 1712, 1610, 1488, 1467, 1364, 1347, 1303, 1180, 1130, 1076, 1018, 964, 752, 695, 662, 539 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{28}N_3O_2^+$ 486.2176; Found 486.2178.

(3R,3'R,5'R)-1,1'',5-trimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3x***). White solid. mp 147.5-148.1 °C. 87 mg, 82% yield, >20:1 dr (determined by ^1H NMR), 91% ee, HPLC (Chiral IC cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 51.67 min, t (major) = 22.21 min. $[\alpha]_D^{20}$ = +220.5 (*c* = 0.96 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) 8.10 (d, *J* = 7.4 Hz, 1H), 7.94 (s, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.22-7.18 (m, 1H), 7.04-6.95 (m, 5H), 6.88-6.85 (m, 2H), 6.36 (d, *J* = 7.8 Hz, 1H), 4.40-4.34 (dd, *J* = 5.8, 14.5 Hz, 1H), 3.31-3.24 (m, 4H), 3.07 (s, 3H), 2.84 (s, 1H), 2.37 (s, 3H), 2.32-2.27 (dd, *J* = 5.8, 12.2 Hz, 1H); δ $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) δ 179.4, 178.6, 142.5, 139.9, 135.3, 134.7, 132.4, 131.1, 129.0, 128.8, 127.7, 127.6, 127.1, 126.3, 124.1, 123.6, 108.2, 107.3, 73.5, 67.5, 55.8, 42.2, 26.6, 26.3, 21.3. IR: 3327, 2924, 1706, 1611, 1492, 1469, 1349, 1303, 1247, 1119, 1076, 1046, 909, 748, 696, 645, 552, 539 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{26}N_3O_2^+$ 424.2020; Found 424.2022.

(3R,3'R,5'R)-5-fluoro-1,1''-dimethyl-3'-phenyldispiro[indoline-3,2'-pyrrolidine-5',3''-indoline]-2,2''-dione (***3y***). White solid. mp 192.7-193.2 °C. 80 mg, 75% yield, >20:1 dr (determined by ^1H NMR), 74% ee, HPLC (Chiral IF cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 17.36 min, t (major) = 20.91 min. $[\alpha]_D^{20}$ = +117.8 (*c* = 1.43, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) 8.02-7.99 (m, 2H), 7.36-7.32 (m, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.07-6.95 (m, 5H), 6.87 (d, *J* = 7.7 Hz, 1H), 6.79-6.74 (m, 1H), 6.39-6.36 (dd, *J* = 4.0, 8.5 Hz,

1H), 4.36-4.31 (dd, *J* = 5.9, 14.5 Hz, 1H), 3.27-3.20 (m, 4H), 3.08 (s, 3H), 2.82 (s, 1H), 2.35-2.30 (dd, *J* = 6.0, 12.4 Hz, 1H).; δ $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) δ 179.4, 178.3, 159.5 (d, *J* = 239.7 Hz), 142.6, 138.1 (d, *J* = 1.9 Hz), 134.7, 134.3, 132.9 (d, *J* = 8.0 Hz), 129.2, 127.8, 127.44, 127.38, 123.9, 123.6, 114.7 (d, *J* = 23.8 Hz), 113.9 (d, *J* = 25.4 Hz), 108.3, 108.1 (d, *J* = 8.0 Hz), 73.74, 73.73, 67.4, 56.3, 41.8, 26.6, 26.4. IR: 3352, 2928, 1698, 1612, 1490, 1468, 1350, 1258, 1176, 1111, 1077, 857, 813, 751, 696, 632, 558 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}FN_3O_2^+$ 428.1769; Found 428.1768.

(3R,3'R)-N,1-dimethyl-2-oxo-N,3'-diphenyl-3',4'-dihydrospiro[indoline-3,2'-pyrrole]-5'-carboxamide (VI). White solid. mp 154.5-155.1 °C. 89 mg, 87% yield, >20:1 dr (determined by ^1H NMR), 90% ee, HPLC (Chiral IA cloumn), *i*-PrOH/*n*-Hexane = 20/80, Flow rate: 1.0 mL/min, λ = 254 nm, t (minor) = 15.37 min, t (major) = 17.19 min. $[\alpha]_D^{20}$ = +117.6 (*c* = 0.85, in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) 7.43-7.25 (m, 5.18H), 7.16-7.03 (m, 4.69H), 6.86-6.70 (m, 2.10H), 6.62-6.55 (m, 1.52H), 6.33 (d, *J* = 7.0 Hz, 0.19H), 6.07 (d, *J* = 7.4 Hz, 0.70H), 4.07 (m, 0.24H), 3.92 (t, *J* = 8.3 Hz, 0.74H), 3.78-3.70 (m, 0.41H), 3.64-3.28 (m, 4.81H), 3.24 (s, 0.72H), 3.09 (s, 2.28H), 2.70 (s, 0.12H); δ $^{13}C\{^1H\}$ NMR(100 MHz, $CDCl_3$) δ 175.6, 175.1, 165.6, 143.3, 142.4, 137.4, 129.7, 129.0, 128.1, 128.0, 127.6, 127.4, 127.0, 126.4, 125.5, 122.0, 107.8, 85.1, 50.6, 43.2, 37.1, 26.3. IR: 3057, 2934, 1715, 1652, 1611, 1492, 1422, 1372, 1349, 1261, 1090, 1023, 974, 811, 774, 757, 699, 610, 592, 542 cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{24}N_3O_2^+$ 410.1863; Found 410.1865.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: XXX.

Crystal data and structure refinement for **3l**，HPLC traces of **3a-3y** and **VI**, and ^1H and ^{13}C spectra for **6a-6c**, **L3a-L3g**, **2a-2v**, **3a-3u**, **VI** (PDF)

X-ray crystallographic data for **3l** (CIF)

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Notes

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