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Access to 2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-ones via amino acid derived phosphine-catalyzed asymmetric [4+2] annulation with easily available oxindole-derived α , β -unsaturated imines

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ABSTRACT

The phosphine-catalyzed asymmetric [4+2] annulation of vinyl ketones with more easily available oxindole-derived α , β -unsaturated imines has been further developed in the presence of an easily available multifunctional thiourea-phosphine catalyst derived from natural amino acid, providing the enantioselective synthesis of 2',3'-dihydro-1'*H*-spiro[indoline-3,4'-pyridin]-2-ones in good yields and moderate de values with higher enantioselectivities under mild conditions.

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1. Introduction

Spirooxindoles are the structural valuable motifs frequently existing in a variety of pharmacological agents and natural alkaloids.¹ In particular, some spiro heterocyclic oxindoles have drawn considerable interest in the area of synthetic organic chemistry and medicinal chemistry since they have various types of biological activities and the potential clinical significance.² Although many synthetic methods have been disclosed for the synthesis of spirooxindoles,³ their enantioselective preparation with several chiral centers including the stereogenic carbon at C3 is a still challenging and demanding task.⁴ Notably, existing stereoselective catalytic syntheses of substituted six-membered heterocyclic spirooxindoles from simple substrates and catalysts are very few.⁵ Thus, the design and development of new and highly enantioselective methods for direct construction of this skeleton is highly desirable.

The development of nucleophilic phosphine organocatalysis has seen remarkable progress in recent years,⁶ and phosphinemediated reactions have emerged as a powerful tool for the

0040-4020/\$ – see front matter @ 2014 Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.tet.2014.02.052 rapid generation of enantiomerically enriched compounds with complex molecular structures.⁷ More recently, several reports about the enantioselective synthesis of spirocyclopenteneoxindoles via phosphine-catalyzed reactions have been disclosed.⁸ For example, Zhong, Loh and Chi and their co-workers reported several novel [4+2] annulations initiated by a phosphinecatalyzed aza-Rauhut-Currier reaction that provides a practical access to highly functionalized tetrahydropyridines.⁹ On the basis of these studies and our previous work on chiral phosphines as nucleophilic catalysts in asymmetric synthesis,^{10,11} we have just reported a phosphine-catalyzed asymmetric [4+2] annulation of vinyl ketones with oxindole-derived α,β -unsaturated imines, which is the first phosphine-catalyzed enantioselective synthesis of isatin-based spiro-fused six-membered heterocycle derivatives in 47-88% yields with 5.0:1-20:1 de values and 87-98% ee values.¹² Since these spiro-fused six-membered heterocycles are very interesting compounds, herein we wish to report the full detail of another version of this asymmetric [4+2] annulation of vinyl ketones with more easily available oxindole-derived α_{β} unsaturated imines in the presence of a more common chiral phosphine catalyst easily derived from amino acid to provide 2',3'dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-ones in 54-88% and moderate de values with higher enantioselectivities (94-99% ee values in most cases).





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2. Results and discussion

We initiated the study by investigating the reaction between more easily available (3E)-1-methyl-3-((E)-2-phenyl-2а tosyliminoethylidene)indolin-2-one 1a (see Supplementary data) and methyl vinyl ketone (MVK) 2a using various chiral phosphines **CP1–CP9** (20 mol %) in toluene at room temperature (see Table SI-1 in Supplementary data). Gratifyingly, we found that the more easily available chiral phosphine CP9 derived from L-valine could produce the desired product 3a in 74% yield with 6.3:1 dr and 99% ee (Table SI-1). With the identification of the best catalyst in this reaction, we next attempted to further optimize the reaction conditions by screening of several solvents, such as THF, CH₂Cl₂, Et₂O, and CH₃CN. The reaction outcomes revealed that toluene was still the best choice as a solvent, and using 20 mol % CP9 as the catalyst at room temperature for 2 days gave **3a** with the best reaction outcome, which served as the best conditions in this reaction (Table 1, entries 1–5).

Table 1

Optimization of the reaction conditions^a



^a Reactions were performed with **1a** (0.10 mmol) and **2a** (0.30 m mol) in the presence of 20 mol % of **CP9** in solvent (1 mL) at room temperature.

^b Yield of isolated single isomer.

^c Determined by ¹H NMR analysis of the crude reaction mixture.

^d Determined by chiral HPLC analysis.

^e 10 mol % of **CP9** was used.

Having determined the optimal reaction conditions for the highly enantioselective synthesis of **3a**, we turned our attention to the scope and limitations of this multifunctional chiral phosphinecatalyzed asymmetric [4+2] annulation of vinyl ketones with these more easily available oxindole-derived α . β -unsaturated imines, and the results are summarized in Table 2. The synthesis of these more easily available α,β -unsaturated imines has been shown in Supplementary data. Their structures including Z- and E-configuration have been confirmed by X-ray diffraction (Figs. 1 and 2). Under the optimal reaction conditions, using MVK (2a) as substrate, we first examined its reaction with substrates **1b**-**d** to investigate the influence of the protecting group R^1 in substrates **1** on this annulation. It was found that the reactions of **1b**–**d** with **2a** proceeded smoothly to give the corresponding products **3b**-**d** in good yields (67-85%) with 5.3:1-8.3:1 drs and 97-99% ees (Table 2, entries 1–3) and the substrate 1d with 3,5-dimethylbenzyl group as a protecting group gave the best result. Substrates 1e and 1f were then tested to elucidate the effect of the protecting group R^3 on the stereoselective induction, and the tosyl group proved to be a good choice (Table 2, entries 4–5). With the optimal groups R^1 and R^3 established, the scope of (3E)-1-(3,5-dimethylbenzyl)-3-(2tosyliminoethylidene)indolin-2-one **1** was then explored. Regardless of whether R^2 is an electron-rich or -deficient aromatic ring, the reactions proceeded smoothly to give the corresponding annulation products **3g**–**n** in moderate to good yields (47–82%) with good dr values (2.8:1–7.7:1) and excellent ee values (96–99%), respectively (Table 2, entries 6–14). Only in the case of (3*E*)-1-(3,5-dimethylbenzyl)-3-((*Z*)-2-(4-nitrophenyl)-2-tosyliminoethylidene) indolin-2-one **1m**, the corresponding adduct **3m** was obtained in relative lower yield along with relative lower dr value (2.8:1 dr), perhaps due to the electronic effect (Table 2, entry 13). Using (3*E*)-1-(3,5-dimethylbenzyl)-3-((*Z*)-2-(4-bromophenyl)-2-

tosyliminoethylidene)indolin-2-one **1I**['], which is the Z-isomer of (3*E*)-1-(3,5-dimethylbenzyl)-3-((*E*)-2-(4-bromophenyl)-2-

tosyliminoethylidene)indolin-2-one **11** as substrate, similar results were obtained, suggesting that the *E* or *Z*-configuration of substrate **1** did not influence the reaction outcomes (Table 2, entry 12). When R^2 is a sterically more bulky 1-naphthalene moiety (R^2 =naphtha-1-yl) or more substituted aromatic group (R^2 =2,4-Cl₂C₆H₃), the reactions also proceeded efficiently to afford the corresponding products **30** and **3p** in 78 and 87% yields with 6.3:1 and 2.3:1 dr and equally excellent ee values (Table 2, entries 15–16). Gratifyingly, the reaction tolerated an aliphatic moiety (R^2 =isopropyl) in (3*E*)-1-(3,5-dimethylbenzyl)-3-(3-methyl-2-tosyliminobutylidene)indo-

lin-2-one 1q, the corresponding adduct 3q (double bond migrated product) was obtained in 54% yield along with 8.3:1 dr, albeit in only 17% ee, perhaps due to the steric influence (Table 2, entry 17). Using methyl vinyl ketone (2a) as substrate, we next examined its reactions with substrates 1r - v bearing different substituents on their isatin-based benzene rings, and it was found that all of the reactions proceeded smoothly to produce the corresponding products **3r**-v in good yields (75-83%) along with 5.9:1-7.7:1 dr and 99% ee values, respectively (Table 2, entries 18-22). Next, the investigation on the scope of vinyl ketones was continued using 1a as substrate (Table 2, entries 23–24). When R⁵ is ethyl group (**2b**, R^{5} =Et), the reaction also proceeded smoothly to give the corresponding annulation product **3v** in 64% yield with 4.2:1 dr and 98% ee (Table 2, entry 23). However, when \mathbb{R}^5 is phenyl group (2c, R^5 =Ph), the corresponding annulation product could not be obtained, perhaps due to the easy self-polymerization of 1phenylprop-2-en-1-one 2c under the standard reaction conditions (Table 2, entry 24). The absolute configuration of **31** has been assigned as (3S, 3'S)-configuration by X-ray diffraction. The ORTEP drawing has been shown in Fig. 3 and the CIF data are summarized in Supplementary data.

The 3-substituted 3-hydroxyoxindole unit is encountered in a large variety of alkaloids and natural products with a wide spectrum of biological activities.¹³ An aldol reaction of **3a** with 1methylindoline-2,3-dione could proceed smoothly to give the corresponding product **4a** in 67% yield along with 1.7:1 dr value, which contains not only an isatin-based spiro-fused six-membered heterocycle skeleton but also a 3-substituted 3-hydroxyoxindole unit (Scheme 1). Deprotection of the tosyl of the chiral model product **3a** could also be readily carried out under mild reaction conditions to produce the absolute configuration maintained imine **5a** in 66% yield (Scheme 2).

The catalytic annulation is postulated to go through a tandem Rauhut–Currier/S_N2-substitution sequence.^{9,14,15} With the assistance of intermolecular hydrogen bonding, the steric hindrance between the oxindole-derived α , β -unsaturated imine and the sterically bulky diarylmethyl group of the catalyst plays significant role in the stereoselectivity (Fig. 4, TS-1). The high diastereoselectivity likely resulted from a favorable S_N2 reaction of TS-II (Fig. 4).

In conclusion, an interesting and useful asymmetric [4+2] annulation reaction of vinyl ketones with more easily available oxindole-derived α , β -unsaturated imines has been developed by

Table 2

The substrate scope of [4+2] annulation^a



Entry	Substrate 1	\mathbb{R}^1	R ²	R ³	\mathbb{R}^4	Substrate 2 (R ⁵)	Yield ^b (%)	dr ^c	ee ^d (%)
1	1b	Bn	C ₆ H ₅	Ts	Н	2a (Me)	3b , 67 ^e	6.5:1	97
2	1c	Н	C ₆ H ₅	Ts	Н	2a (Me)	3c ^f , 74 ^e	5.3:1	99
3	1d	3,5-DMBn ^g	C ₆ H ₅	Ts	Н	2a (Me)	3d , 85	8.3:1	99
4	1e ^h	3,5-DMBn	C ₆ H ₅	Ns ⁱ	Н	2a (Me)	3e , 44	6.3:1	90
5	1f	3,5-DMBn	C ₆ H ₅	Bs ^j	Н	2a (Me)	3f , 78	7.7:1	99
6	1g	3,5-DMBn	4-MeC ₆ H ₄	Ts	Н	2a (Me)	3g , 79	7.7:1	99
7	1h	3,5-DMBn	$4-FC_6H_4$	Ts	Н	2a (Me)	3h , 82	7.1:1	97
8	1i ^k	3,5-DMBn	2-CIC ₆ H ₄	Ts	Н	2a (Me)	3i , 72	6.3:1	97
9	1j	3,5-DMBn	3-CIC ₆ H ₄	Ts	Н	2a (Me)	3j , 74	7.7:1	96
10	1k	3,5-DMBn	4-CIC ₆ H ₄	Ts	Н	2a (Me)	3k , 80	7.1:1	98
11	11 ¹	3,5-DMBn	4-BrC ₆ H ₄	Ts	Н	2a (Me)	31 , 78	6.7:1	98
12	11 ^{′m}	3,5-DMBn	4-BrC ₆ H ₄	Ts	Н	2a (Me)	31 , 76	6.7:1	97
13	1m ⁿ	3,5-DMBn	$4-NO_2C_6H_4$	Ts	Н	2a (Me)	3m , 47	2.8:1	97
14	1n	3,5-DMBn	$4-CF_3C_6H_4$	Ts	Н	2a (Me)	3n , 64	5.3:1	96
15	10	3,5-DMBn	Naphtha-1-yl	Ts	Н	2a (Me)	30 , 78	6.3:1	96
16	1p	3,5-DMBn	2,4-Cl ₂ C ₆ H ₃	Ts	Н	2a (Me)	3p , 87	2.3:1	94
17	1q	3,5-DMBn	Isopropyl	Ts	Н	2a (Me)	3q °, 54	8.3:1	17
18	1r	3,5-DMBn	C ₆ H ₅	Ts	5-F	2a (Me)	3r , 75	7.7:1	99
19	1s	3,5-DMBn	C ₆ H ₅	Ts	5-Cl	2a (Me)	3s , 76	7.1:1	99
20	1t	3,5-DMBn	C ₆ H ₅	Ts	5-Br	2a (Me)	3t , 78	6.7:1	99
21	1u	3,5-DMBn	C ₆ H ₅	Ts	5-Me	2a (Me)	3u , 75	5.9:1	99
22	1v	3,5-DMBn	C ₆ H ₅	Ts	6-Me	2a (Me)	3v , 83	7.7:1	99
23	1a	3,5-DMBn	C ₆ H ₅	Ts	Н	2b (Et)	3w , 64 ^e	4.2:1	98
24	1a	3,5-DMBn	C ₆ H ₅	Ts	Н	2c (Ph)	Trace	—	_

^a Reactions were performed with 1 (0.10 mmol) and 2 (0.30 mmol) in the presence of 20 mol % of CP9 and toluene (1 mL) at room temperature.

^b Isolated yields.

^c Determined by ¹H NMR of the crude reaction mixture.

^d Determined by HPLC analysis.

e Yield of single isomer.

^f An additional Michael addition of substrate **1c** with methyl vinyl ketone **2a** took place.

^g 3,5-DMBn=3,5-dimethylbenzyl.

^h Substrate **1e** was isolated as only Z-configuration.

i Ns=Nitrophenylsulfonyl.

^j Bs=Benzenesulfonyl.

^k Substrate **1i** was assigned as *Z*-configuration by X-ray diffraction.

¹ The configuration of **11** has been assigned by X-ray diffraction as *E*-configuration.

^m Substrate **1***I*′ is *Z*-configuration, which was isolated as the *Z*-isomer of **1***I*.

ⁿ Substrate **1m** was isolated as only *Z*-configuration.

^o The structure of **3q** is listed in the upper right corner of the table, which is a double bond migrated product.

utilizing a more easily available multifunctional thioureaphosphine catalyst **CP9** derived from a common natural amino acid, which provides the corresponding isatin-based spiro-fused six-membered heterocycle derivatives with higher ee values compared with our previous work.¹² Further efforts are in progress to develop the use of this reaction in the synthesis of biologically active molecular complexes.

3. Experimental section

3.1. General remarks

Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin-Elmer-341 MC digital polarimeter; $[\alpha]_D$ -values are given in unit of 10 deg⁻¹ cm² g⁻¹. ¹H NMR spectra were recorded on a Bruker AM-300 and AM-400 spectrometer for solution in CDCl₃ with tetramethylsilane (TMS) as an internal standard; coupling constants *J* are given in Hertz. ¹³C NMR spectra were recorded on a Bruker AM-

300 and AM-400 spectrophotometers (75 or 100 MHz) with complete proton decoupling spectrophotometers (CDCl₃: 77.0 ppm). Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm⁻¹. Flash column chromatography was performed using 300-400 mesh silica gel. For thin-layer chromatography (TLC), silica gel plates (Huanghai GF254) were used. Chiral HPLC was performed on a Waters 2487 series with chiral columns (Chiralpak AD-H, IC-H columns 4.6×250 mm (Daicel Chemical Ind., Ltd.), Phenomenex Lux 5µ Cellulose-1 column 4.6×250 mm (PC-1, (Phenomenex Ind., Ltd.)) and Phenomenex Lux 5µ Cellulose-2 column 4.6×250 mm (PC-2, (Phenomenex Ind., Ltd.))). Mass spectra were recorded by ESI and HRMS was measured on a HP-5989 instrument. Catalysts CP1–CP8, which are known compounds, were prepared according to the same procedures in the previous literature and CP9 was prepared in the same way (see Supplementary data).

Compound (*S*)-**CP9**. A white solid; mp 67–68 °C; IR (KBr): ν 3275, 3051, 2958, 2922, 1532, 1480, 1354, 1264, 1182, 1021, 813, 738, 696 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 0.54–0.64 (m, 6H, 2CH₃), 1.88–1.96 (m, 1H, CH), 2.17–2.31 (m, 8H, 2CH₃+CH₂), 4.99



Fig. 1. ORTEP drawing of 1i.



Fig. 2. ORTEP drawing of 1l.



Fig. 3. ORTEP drawing of 31.

(br, 1H, NH), 5.09 (br, 1H, CH), 5.36 (br, 1H, NH), 6.32 (br, 1H, CH), 7.03–7.16 (m, 8H, ArH), 7.41–7.49 (m, 10H, ArH); 31 P NMR (CDCl₃, 161.93 MHz, 85% H₃PO₄): δ –24.56; HRMS (ESI) calcd for-C₃₃H₃₈N₂PS⁺¹ (M+OH)⁺ requires 525.2493, found: 525.2487; $[\alpha]_D^{20}$ –23.1 (*c* 1.00, CHCl₂).

3.2. Spectroscopic data of the reaction products

3.2.1. (3S,3'S)-3'-Acetyl-1-methyl-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3a). A colorless solid, 36 mg, 74% yield; mp 94–95 °C; IR (CH₂Cl₂): v 2962, 2360, 1711, 1610, 1492, 1470, 1355, 1259, 1167, 1084, 1018, 799, 710, 698, 658 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.02 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.96 (dd, 1H, J=3.2, 11.6 Hz, CH), 3.18 (s, 3H, CH₃), 4.37 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.70 (dd, 1H, J=3.2, 14.0 Hz, CH₂), 4.92 (s, 1H, =CH), 6.48 (d, 1H, J=7.6 Hz, ArH), 6.82 (d, 1H, J=7.6 Hz, ArH), 6.95 (t, 1H, J=7.6 Hz, ArH), 7.20–7.28 (m, 4H, ArH), 7.32–7.38 (m, 4H, ArH), 7.65 (d, 2H, *J*=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.6, 26.5, 28.7, 46.1, 49.1, 52.6, 108.5, 117.8, 122.0, 122.4, 127.6, 127.7, 127.9, 128.5, 128.7, 129.8, 130.3, 136.3, 137.5, 141.4, 144.1, 144.5, 177.0, 203.5; HRMS (ESI) calcd for $C_{28}H_{27}N_2O_4S^{+1}$ (M+H)⁺ requires 487.1692, found: 487.1682; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; tminor=24.04 min, $t_{\text{maior}} = 26.22 \text{ min; ee\%} > 99\%; [\alpha]_D^{20} + 161.4 (c 1.00, CH_2Cl_2)].$

3.2.2. (3S,3'S)-3'-Acetyl-1-benzyl-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (**3b**). A colorless solid, 38 mg, 67% yield; mp 95–96 °C; IR (CH₂Cl₂): ν 3058, 2922, 1708, 1609, 1488, 1466, 1355, 1267, 1166, 1106, 1090, 986, 955, 815, 753, 734, 709, 697, 658 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.03 (s, 3H, CH₃), 2.48 (s, 3H, CH₃), 3.03 (dd, 1H, *J*=2.8, 11.6 Hz, CH), 4.42 (dd, 1H, *J*=11.6, 14.0 Hz, CH₂), 4.73 (dd, 1H, *J*=2.8, 14.0 Hz, CH₂), 4.85 (d, 1H, *J*=16.0 Hz, CH₂), 4.90 (d, 1H, *J*=16.0 Hz, CH₂), 4.95 (s, 1H, =CH), 6.51 (d, 1H, *J*=7.6 Hz, ArH), 6.67 (d, 1H, *J*=7.6 Hz, ArH), 6.91 (t, 1H, *J*=7.6 Hz, ArH), 7.13 (t, 1H, *J*=7.6 Hz, ArH), 7.21–7.25 (m, 6H, ArH), 7.31–7.36 (m, 6H, ArH), 7.65 (d, 2H, *J*=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.6, 28.8, 44.2, 46.2, 49.2, 52.7, 109.6,



Scheme 1. Aldol reaction of 3a with 1-methylindoline-2,3-dione.



Scheme 2. Deprotection of the tosyl of product 3a.

 t_{minor} =38.92 min, t_{major} =46.64 min; ee%=98%; [α]_D²⁰ +57.9 (*c* 1.00, CH₂Cl₂)].

3.2.4. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (**3d**). A colorless solid, 50 mg, 85% yield; mp 95–96 °C; IR (CH₂Cl₂): ν 2921, 1710, 1609, 1488, 1466, 1355, 1167, 1091, 988, 812, 756, 736, 710, 698, 659 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.00 (s, 3H, CH₃), 2.23 (s, 6H, 2CH₃), 2.48 (s, 3H, CH₃), 3.00 (dd, 1H, *J*=2.8, 12.0 Hz, CH₂), 4.71 (dd, 1H, *J*=2.8, 14.0 Hz, CH₂), 4.79





117.9, 122.1, 122.5, 127.4, 127.6, 127.7, 127.8, 127.9, 128.57, 128.63, 128.7, 129.8, 130.3, 135.8, 136.4, 137.5, 141.5, 143.2, 144.5, 177.0, 203.5; HRMS (ESI) calcd for $C_{34}H_{31}N_2O_4S^{+1}$ (M+H)⁺ requires 563.2005, found: 563.1990; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =43.48 min, t_{maior} =73.92 min; ee%=97%; [α]_D²⁰ +161.3 (*c* 1.00, CH₂Cl₂)].

3.2.3. (3S,3'S)-3'-Acetyl-1-(3-oxobutyl)-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3c). A colorless solid, 40 mg, 74% yield; mp 97-98 °C; IR (CH₂Cl₂): v 2923, 2854, 1710, 1609, 1489, 1466, 1356, 1166, 1091, 992, 812, 754, 711, 698, 658 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.06 (s, 3H, CH₃), 2.16 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.85–2.95 (m, 2H, CH₂), 2.98 (dd, 1H, J=3.2, 11.6 Hz, CH), 3.81–3.88 (m, 1H, CH₂), 3.95–4.02 (m, 1H, CH₂), 4.34 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.70 (dd, 1H, J=3.2, 14.0 Hz, CH₂), 4.89 (s, 1H, =CH), 6.48 (dd, 1H, J=2.0, 7.6 Hz, ArH), 6.92-6.95 (m, 2H, ArH), 7.20-7.32 (m, 6H, ArH), 7.36 (d, 2H, J=8.0 Hz, ArH), 7.64 (d, 2H, *J*=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.6, 28.7, 30.2, 34.8, 39.9, 46.0, 48.8, 52.9, 108.9, 117.6, 122.1, 122.3, 127.6, 127.7, 127.8, 128.5, 128.7, 129.8, 130.3, 136.2, 137.4, 141.4, 143.0, 144.5, 177.2, 203.5, 206.9; HRMS (ESI) calcd for $C_{31}H_{31}N_2O_5S^{+1}$ (M+H)⁺ requires 543.1954, found: 543.1934; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.60 mL/min; (s, 2H, CH₂), 4.96 (s, 1H, ==CH), 6.51 (d, 1H, *J*=7.6 Hz, ArH), 6.71 (d, 1H, *J*=7.6 Hz, ArH), 6.86 (s, 1H, ArH), 6.90–6.95 (m, 3H, ArH), 7.14 (t, 1H, *J*=7.6 Hz, ArH), 7.21–7.29 (m, 3H, ArH), 7.33–7.37 (m, 4H, ArH), 7.66 (d, 2H, *J*=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.6, 28.8, 44.2, 46.1, 49.2, 52.4, 109.6, 117.9, 122.1, 122.4, 125.1, 127.6, 127.7, 127.8, 128.5, 128.6, 129.2, 129.8, 130.3, 135.6, 136.3, 137.5, 138.2, 141.4, 143.3, 144.4, 176.9, 203.4; HRMS (ESI) calcd for C₃₆H₃₅N₂O₄S⁺¹ (M+H)⁺ requires 591.2318, found: 591.2305; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.60 mL/min; *t*_{minor}=38.30 min, *t*_{major}=51.64 min; ee%=99%; [α]²⁰₂+114.7 (*c* 1.00, CH₂Cl₂)].

3.2.5. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-1'-((4-nitrophenyl) sulfonyl)-6'-phenyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (**3e**). A colorless solid, 27 mg, 44% yield; mp 117–118 °C; IR (CH₂Cl₂): ν 2923, 2854, 1711, 1608, 1531, 1488, 1348, 1171, 1090, 855, 740, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.05 (s, 3H, CH₃), 2.25 (s, 6H, 2CH₃), 3.44 (dd, 1H, *J*=2.8, 11.6 Hz, CH), 4.48 (dd, 1H, *J*=11.6, 13.6 Hz, CH₂), 4.76–7.87 (dd, 3H, CH₂), 4.79 (s, 2H, CH₂+CH₂), 5.02 (s, 1H, =CH), 6.77 (d, 1H, *J*=7.6 Hz, ArH), 6.87 (s, 1H, ArH), 6.96 (s, 2H, ArH), 7.02–7.10 (m, 6H, ArH), 7.19–7.26 (m, 2H, ArH), 7.73 (d, 2H, *J*=8.8 Hz, ArH), 8.23 (d, 2H, *J*=8.8 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.3, 29.1, 44.3, 46.4, 49.4, 54.6, 109.8, 118.3, 122.5, 123.0, 124.0, 125.3, 127.9, 128.3, 128.91, 128.95,

129.0, 129.4, 130.1, 135.5, 136.0, 138.4, 140.8, 143.3, 145.6, 150.1, 176.5, 203.3; HRMS (ESI) calcd for $C_{35}H_{32}N_{3}O_{6}S^{+1}$ (M+H)⁺ requires 622.2012, found: 622.2011; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =42.06 min, t_{major} =57.80 min; ee%=90%; [α]_D²⁰ +169.62 (*c* 1.00, CH₂Cl₂)].

3.2.6. (3S.3'S)-3'-Acetvl-1-(3.5-dimethylbenzvl)-6'-phenyl-1'-(phenylsulfonyl)-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3f). A colorless solid, 45 mg, 78% yield; mp 106-107 °C; IR (CH₂Cl₂): v 2922, 2854, 1713, 1610, 1488, 1466, 1447, 1357, 1170, 1091, 757, 728, 693 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 1.99 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.99 (dd, 1H, J=2.8, 12.0 Hz, CH), 4.46 (dd, 1H, J=12.0, 13.6 Hz, CH₂), 4.72 (dd, 1H, J=2.8, 13.6 Hz, CH₂), 4.79 (s, 2H, CH₂), 4.97 (s, 1H, =CH), 6.57 (d, 1H, J=7.2 Hz, ArH), 6.71 (d, 1H, *I*=8.0 Hz, ArH), 6.86 (s, 1H, ArH), 6.89–6.95 (m, 3H, ArH), 7.15 (t, 1H, J=8.0 Hz, ArH), 7.20-7.33 (m, 5H, ArH), 7.54-7.58 (m, 2H, ArH), 7.65–7.69 (m, 1H, ArH), 7.76 (d, 2H, J=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 28.9, 44.2, 46.1, 49.2, 52.6, 109.6, 117.9, 122.1, 122.5, 125.1, 127.70, 127.73, 127.76, 128.6, 128.7, 129.2, 130.2, 133.3, 135.5, 137.3, 138.3, 139.3, 141.4, 143.3, 176.8, 203.4; HRMS (ESI) calcd for $C_{35}H_{33}N_2O_4S^{+1}$ (M+H)⁺ requires 577.2161, found: 577.2155; enantiomeric excess was determined by HPLC with a Chiralcel IC column [λ =230 nm; eluent: hexane/isopropanol=60/40; flow rate: 0.60 mL/min; t_{minor}=86.17 min, t_{major} =123.57 min; ee%=99%; [α]_D²⁰ +139.9 (*c* 1.00, CH₂Cl₂)].

3.2.7. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-6'-(p-tolyl)-1'-tosyl-2'.3'-dihvdro-1'H-spirolindoline-3.4'-pvridinl-2-one (**3g**). A colorless solid, 48 mg, 79% yield; mp 109-110 °C; IR (CH₂Cl₂): v 2921. 1713, 1609, 1488, 1466, 1356, 1167, 1106, 1091, 1021, 988, 818, 762, 745, 708, 693, 661 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.00 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.33 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.97 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.41 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.70 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.79 (s, 2H, CH₂), 4.92 (s, 1H, =CH), 6.46 (d, 1H, J=7.6 Hz, ArH), 6.70 (d, 1H, J=7.6 Hz, ArH), 6.86 (s, 1H, ArH), 6.90 (t, 1H, J=7.6 Hz, ArH), 6.95 (s, 2H, ArH), 7.05 (d, 2H, J=8.0 Hz, ArH), 7.14 (t, 1H, J=7.6 Hz, ArH), 7.24 (d, 2H, J=8.0 Hz, ArH), 7.36 (d, 2H, J=8.4 Hz, ArH), 7.66 (d, 2H, J=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.3, 21.6, 28.9, 44.2, 46.2, 49.3, 52.4, 109.6, 117.2, 122.1, 122.4, 125.2, 127.6, 127.9, 128.5, 128.6, 129.2, 129.8, 130.5, 134.8, 135.6, 136.4, 138.3, 138.5, 141.4, 143.3, 144.4, 177.0, 203.5; HRMS (ESI) calcd for C₃₇H₃₇N₂O₄S⁺¹ (M+H)⁺ requires 605.2474, found: 605.2454; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; tminor=45.23 min, t_{major} =84.98 min; ee%=99%; [α]_D²⁰ +135.4 (*c* 1.00, CH₂Cl₂)].

3.2.8. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-6'-(4-fluorophenyl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3h). A colorless solid, 50 mg, 82% yield; mp 104-105 °C; IR (CH₂Cl₂): v 2922, 1712, 1608, 1508, 1488, 1466, 1356, 1222, 1168, 1106, 1091, 1014, 987, 843, 765, 708, 693 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.00 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.49 (s, 3H, CH₃), 3.00 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.41 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.71 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.79 (t, 2H, J=16.8 Hz, CH₂), 4.92 (s, 1H, =CH), 6.51 (d, 1H, J=7.6 Hz, ArH), 6.72 (d, 1H, J=8.0 Hz, ArH), 6.86 (s, 1H, ArH), 6.89–6.95 (m, 5H, ArH), 7.15 (t, 1H, J=7.6 Hz, ArH), 7.28-7.32 (m, 2H, ArH), 7.37 (d, 2H, J=8.0 Hz, ArH), 7.64 (d, 2H, *J*=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.6, 28.9, 44.3, 46.1, 49.3, 52.5, 109.7, 114.8 (d, J=21.6 Hz), 117.8, 122.1, 122.5, 125.2, 127.8, 128.8, 129.3, 129.5 (d, J=8.5 Hz), 129.9, 130.2, 133.6 (d, J=3.0 Hz), 135.6, 136.3, 138.3, 140.5, 143.4, 144.7, 162.9 (d, J=246.7 Hz), 176.9, 203.4; ¹⁹F NMR (376 MHz, CDCl₃, CFCl₃): δ –112.93; HRMS (ESI) calcd for C₃₆H₃₄FN₂O₄S⁺¹ (M+H)⁺ requires 609.2223, found: 609.2210; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =26.78 min, t_{major} =36.06 min; ee%=97%; [α]_D²⁰ +122.0 (*c* 1.00, CH₂Cl₂)].

3.2.9. (3S.3'S)-3'-Acetvl-6'-(2-chlorophenvl)-1-(3.5-dimethvlbenzvl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3i). A colorless solid, 45 mg, 72% vield; mp 110–111 °C; IR (CH₂Cl₂); v 2921, 1711, 1609, 1488, 1466, 1435, 1355, 1265, 1167, 1109, 1091, 1033, 991, 883, 860, 814, 756, 735, 704, 686, 661 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 1.97 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.44 (s, 3H, CH₃), 3.03 (br, 1H, CH), 4.45 (dd, 1H, *J*=11.6, 14.0 Hz, CH₂), 4.63-4.66 (m, 1H, CH₂), 4.73 (d, 1H, J=15.6 Hz, CH₂), 4.86 (d, 1H, J=15.6 Hz, CH₂), 4.92 (s, 1H, =CH), 6.70 (d, 1H, J=8.0 Hz, ArH), 6.83-6.88 (m, 2H, ArH), 6.92-6.99 (m, 3H, ArH), 7.13-7.37 (m, 7H, ArH), 7.64 (br, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.1, 21.6, 29.0, 44.3, 45.3, 49.2, 109.7, 119.0, 122.3, 122.6, 125.2, 126.1, 127.7, 128.7, 129.2, 129.5, 129.6, 131.6, 135.6, 136.3, 138.3, 143.4, 176.5, 203.5; HRMS (ESI) calcd for $C_{36}H_{34}CIN_2O_4S^{+1}\ (M{+}H)^+$ requires 625.1928, found: 625.1923; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =32.91 min, t_{maior} =62.82 min; ee%=96%; $[\alpha]_{D}^{20}$ +147.8 (c 1.00, $CH_2Cl_2)].$

3.2.10. (3S,3'S)-3'-Acetyl-6'-(3-chlorophenyl)-1-(3,5dimethylbenzyl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3j). A colorless solid, 46 mg, 74% yield; mp 94–95 °C; IR (CH₂Cl₂): v 2920, 1713, 1610, 1487, 1466, 1356, 1168, 1091, 994, 852, 791, 738, 706, 685 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS); δ 2.01 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.48 (s, 3H, CH₃), 3.07 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.40 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.70 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.77 (d, 1H, J=15.6 Hz, CH₂), 4.82 (d, 1H, J=15.6 Hz, CH₂), 5.00 (s, 1H, =CH), 6.63 (d, 1H, J=7.6 Hz, ArH), 6.73 (d, 1H, J=8.0 Hz, ArH), 6.87 (s, 1H, ArH), 6.93-6.96 (m, 3H, ArH), 7.14-7.26 (m, 5H, J=8.0 Hz, ArH), 7.36 (d, 2H, J=7.6 Hz, ArH), 7.63 (d, 2H, J=7.6 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): *δ* 21.3, 21.6, 28.9, 44.3, 46.0, 49.3, 52.7, 109.8, 118.7, 122.2, 122.6, 125.2, 126.0, 127.5, 127.8, 128.5, 128.8, 129.1, 129.3, 129.9, 130.0, 133.7, 135.5, 136.2, 138.3, 139.2, 140.2, 143.4, 144.8, 176.8, 203.3; HRMS (ESI) calcd for $C_{36}H_{34}CIN_2O_4S^{+1}$ (M+H)⁺ requires 625.1928, found: 625.1916; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; $t_{\text{minor}}=24.40 \text{ min}, t_{\text{maior}}=32.84 \text{ min}; ee\%=96\%; [\alpha]_D^{20} +131.8 (c$ 1.00, CH₂Cl₂)].

3.2.11. (35,3'S)-3'-Acetyl-6'-(4-chlorophenyl)-1-(3,5dimethylbenzyl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3k). A colorless solid, 50 mg, 80% yield; mp 96–97 °C; IR (CH₂Cl₂): v 2920, 1712, 1609, 1488, 1466, 1356, 1167, 1090, 1014. 987, 837, 727, 706, 689 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.00 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.50 (s, 3H, CH₃), 2.99 (dd, 1H, J=2.8, 12.0 Hz, CH), 4.40 (dd, 1H, J=12.0, 13.6 Hz, CH₂), 4.69 (dd, 1H, J=2.8, 13.6 Hz, CH₂), 4.79 (s, 2H, CH₂), 4.96 (s, 1H, =CH), 6.50 (d, 1H, J=7.6 Hz, ArH), 6.72 (d, 1H, J=8.0 Hz, ArH), 6.86 (s, 1H, ArH), 6.90-6.95 (m, 3H, ArH), 7.15 (t, 1H, J=8.0 Hz, ArH), 7.20 (d, 2H, J=8.4 Hz, ArH), 7.27 (d, 2H, J=8.4 Hz, ArH), 7.38 (d, 2H, J=8.0 Hz, ArH), 7.65 (d, 2H, J=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.6, 28.8, 44.2, 46.0, 49.2, 52.3, 109.7, 118.2, 122.0, 122.5, 125.1, 127.8, 127.9, 128.7, 128.9, 129.2, 129.9, 130.0, 134.4, 135.5, 136.0, 136.1, 138.3, 140.4, 143.3, 144.7, 176.8, 203.3; HRMS (ESI) calcd for C₃₆H₃₄ClN₂O₄S⁺¹ (M+H)⁺ requires 625.1928, found: 625.1910; enantiomeric excess was determined by HPLC with a Chiralcel PC-2 column [λ =230 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =28.34 min, t_{major} =74.26 min; ee%=98%; $[\alpha]_D^{20}$ +213.7 (*c* 1.00, CH₂Cl₂)].

3.2.12. (35,3'S)-3'-Acetyl-6'-(4-bromophenyl)-1-(3,5*dimethylbenzyl*)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (31). A colorless solid, 52 mg, 78% yield; mp 113-114 °C; IR (CH₂Cl₂): v 2921, 1713, 1677, 1610, 1488, 1466, 1357, 1168, 1106, 1091, 1010, 820, 712, 683, 659 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.01 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.51 (s, 3H, CH₃), 2.99 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.39 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.69 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.79 (s, 2H, CH₂), 4.96 (s, 1H, =CH), 6.50 (d, 1H, J=7.2 Hz, ArH), 6.72 (d, 1H, J=8.0 Hz, ArH), 6.87 (s, 1H, ArH), 6.90–6.95 (m, 3H, ArH), 7.15 (t, 1H, J=7.2 Hz, ArH), 7.20 (d, 2H, *J*=8.4 Hz, ArH), 7.35–7.39 (m, 4H, ArH), 7.64 (d, 2H, *J*=8.4 Hz, ArH); ^{13}C NMR (100 MHz, CDCl₃, TMS): δ 21.3, 21.7, 28.9, 44.3, 46.1, 49.2, 52.4, 109.8, 118.3, 122.1, 122.6, 122.7, 125.2, 127.9, 128.8, 129.2, 129.3, 129.97, 130.04, 131.0, 135.5, 136.1, 136.5, 138.3, 140.5, 143.4, 144.8, 176.8, 203.4; HRMS (ESI) calcd for C₃₆H₃₄BrN₂O₄S⁺¹ (M+H)⁺ requires 669.1423, found: 669.1405; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =230 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =45.30 min, t_{maior} =62.34 min; ee%=98%; $[\alpha]_{D}^{20}$ +114.8 (c 1.00, $CH_2Cl_2)].$

3.2.13. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-6'-(4-nitrophenyl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3m)and (3R,3'R)-3'-acetyl-1-(3,5-dimethylbenzyl)-6'-(4-nitrophenyl)-1'tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3m'). A colorless solid, 30 mg, 47% yield; IR (CH₂Cl₂): v 2922, 2837, 1714, 1598, 1519, 1487, 1343, 1167, 1090, 855, 715, 683, 659 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 1.99 (s, 3H, CH₃), 2.23 (s, 6H, 2CH₃), 2.52 (s, 3H, CH₃), 2.94–2.97 (m, 1H, CH), 4.43 (dd, 1H, *J*=12.0, 14.0 Hz, CH₂), 4.64 (dd, 1H, *J*=2.8, 14.0 Hz, CH₂), 4.75–4.84 (m, 2H, CH₂), 5.11 (s, 1H, =CH), 6.51 (d, 1H, *J*=7.6 Hz, ArH), 6.75 (d, 1H, *J*=8.0 Hz, ArH), 6.87 (s, 1H, ArH), 6.91-6.96 (m, 3H, ArH), 7.16-7.20 (m, 1H, ArH), 7.43 (d, 2H, J=8.0 Hz, ArH), 7.54 (d, 2H, J=8.8 Hz, ArH), 7.69 (d, 2H, J=8.0 Hz, ArH), 8.13 (d, 2H, J=8.8 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS) : δ 21.2, 21.3, 21.66, 21.73, 28.9, 29.0, 44.3, 44.6, 45.5, 45.9, 49.3, 50.4, 50.9, 51.9, 109.88, 109.92, 119.2, 120.7, 122.1, 122.6, 123.19, 123.28, 123.31, 124.7, 125.1, 125.3, 127.87, 127.88, 128.0, 128.1, 128.5, 129.0, 129.3, 129.5, 129.6, 130.14, 130.18, 134.7, 135.0, 135.4, 135.6, 138.3, 138.4, 139.59, 139.63, 142.0, 143.4, 144.1, 144.6, 145.0, 145.2, 147.61, 147.63, 175.6, 176.4, 203.0, 204.4 (a mixture of **3m** and **3m**'); HRMS (ESI) calcd for $C_{36}H_{34}N_3O_6S^{+1}$ (M+H)⁺ requires 636.2168, found: 636.2141; enantiomeric excess of 3m was determined by HPLC with a Chiralcel PC-1 column [λ =230 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =18.86 min, t_{maior} =33.60 min; ee%=97%; [α]_D²⁰+82.76 (c 1.00, $CH_2Cl_2)].$

3.2.14. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-1'-tosyl-6'-(4-(trifluoromethyl)phenyl)-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (**3n**). A colorless solid, 42 mg, 64% yield; mp 100–101 °C; IR (CH₂Cl₂): v 2922, 1711, 1610, 1488, 1466, 1356, 1322, 1166, 1122, 1110, 1066, 1017, 842, 739, 709, 698, 677, 661 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): 2.00 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.49 (s, 3H, CH₃), 3.04 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.42 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.70 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.75-4.84 (m, 2H, CH₂), 5.04 (s, 1H, =CH), 6.58 (d, 1H, *J*=7.6 Hz, ArH), 6.73 (d, 1H, *J*=7.6 Hz, ArH), 6.87 (s, 1H, ArH), 6.93–6.97 (m, 3H, ArH), 7.17 (td, 1H, J=2.4, 7.6 Hz, ArH), 7.36 (d, 2H, J=7.6 Hz, ArH), 7.43 (d, 2H, J=8.4 Hz, ArH), 7.48 (d, 2H, J=8.4 Hz, ArH), 7.63 (d, 2H, J=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.5, 28.9, 44.3, 46.0, 49.3, 52.3, 109.8, 119.6, 122.1, 122.6, 124.7 (q, J=3.5 Hz), 125.2, 127.9, 128.9, 129.3, 129.9, 130.0, 135.5, 135.93, 135.94, 138.3, 140.3, 141.1 (q, J=1.1 Hz), 143.4, 144.9, 176.6, 203.2; ¹⁹F NMR (376 MHz, CDCl₃, CFCl₃): δ -62.47; HRMS (ESI) calcd for $C_{36}H_{34}FN_2O_4S^{+1}$ (M+H)⁺ requires 609.2223, found: 609.2210; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =24.38 min, t_{major} =38.68 min; ee%=96%; [α]_D²⁰ +332.0 (*c* 1.00, CH₂Cl₂)].

3.2.15. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-6'-(naphthalen-1yl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (30). A colorless solid, 50 mg, 78% yield; mp 106-107 °C; IR (CH₂Cl₂): v 3060, 2922, 1713, 1609, 1488, 1466, 1355, 1185, 1168, 1091, 1015, 803, 776, 759, 706, 690 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.09 (s, 3H, CH₃), 2.18 (s, 3H, CH₃), 2.22 (s, 6H, 2CH₃), 3.44 (dd, 1H, J=2.4, 11.2 Hz, CH), 4.65-4.71 (m, 1H, CH₂), 4.77–4.86 (m, 2H, CH₂), 4.94 (dd, 1H, *J*=2.4, 13.6 Hz, CH₂), 5.05 (s, 1H, =CH), 6.71-6.74 (m, 3H, ArH), 6.84 (s, 1H, ArH), 6.95 (s, 2H, ArH), 7.02-7.20 (m, 5H, ArH), 7.26-7.48 (m, 4H, ArH), 7.59 (d, 1H, J=8.0 Hz, ArH), 7.66–7.34 (m, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.19, 21.25, 29.1, 44.3, 44.8, 49.5, 54.4, 109.6, 118.2, 122.5, 122.7, 124.7, 125.1, 125.3, 125.5, 126.3, 127.0, 127.6, 128.5, 128.7, 128.9, 129.2, 129.4, 130.6, 131.5, 132.8, 133.5, 135.60, 135.62, 138.2, 140.2, 143.0, 143.3, 176.8, 203.8; HRMS (ESI) calcd for $C_{40}H_{37}N_2O_4S^{+1}$ (M+H)⁺ requires 641.2474, found: 641.2468; enantiomeric excess was determined by HPLC with a Chiralcel PC-2 column [λ =230 nm; eluent: hexane/isopropanol=70/30; flow rate: 1.00 mL/min; $t_{\text{minor}}=12.51 \text{ min, } t_{\text{maior}}=28.87 \text{ min; ee} = 96\%; \ [\alpha]_D^{20} + 265.8 \ (c$ 1.00, CH₂Cl₂)].

3.2.16. (3S,3'S)-3'-Acetyl-6'-(2,4-dichlorophenyl)-1-(3,5dimethylbenzyl)-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3p). A colorless solid, 58 mg, 87% yield; mp 106-107 °C; IR (CH₂Cl₂): v 2920, 1712, 1608, 1586, 1486, 1466, 1355, 1265, 1167, 1100, 989, 864, 814, 761, 735, 691, 661 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 1.97 (s, 3H, CH₃), 2.25 (s, 6H, 2CH₃), 2.47 (s, 3H, CH₃), 3.01 (br, 1H, CH), 4.43 (dd, 1H, *J*=11.6, 14.0 Hz, CH₂), 4.62-4.65 (m, 1H, CH₂), 4.74 (d, 1H, J=15.6 Hz, CH₂), 4.87 (d, 1H, J=15.6 Hz, CH₂), 4.93 (s, 1H, =CH), 6.72 (d, 1H, J=8.0 Hz, ArH), 6.79-6.83 (m, 1H, ArH), 6.87 (s, 1H, ArH), 6.97 (s, 2H, ArH), 7.14-7.33 (m, 6H, ArH), 7.64 (br, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.6, 28.9, 44.3, 45.2, 49.2, 109.7, 119.4, 122.3, 122.6, 125.2, 126.5, 127.6, 128.8, 129.2, 129.6, 132.2, 134.1, 135.5, 135.9, 138.2, 143.3, 176.3, 203.3; HRMS (ESI) calcd for C₃₆H₃₃Cl₂N₂O₄S⁺¹ (M+H)⁺ requires 659.1538, found: 659.1538; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor}=30.81 min, t_{major}=80.20 min; ee%=94%; $[\alpha]_{D}^{20}$ +149.4 (*c* 1.00, CH₂Cl₂)].

3.2.17. (3S,5'S)-5'-Acetyl-1-(3,5-dimethylbenzyl)-2'-(propan-2ylidene)-1'-tosylspiro[indoline-3,4'-piperidin]-2-one (3q). A colorless solid, 30 mg, 54% yield; mp 91–92 °C; IR (CH₂Cl₂): v 2920, 1701, 1611, 1489, 1467, 1359, 1325, 1155, 1091, 1036, 959, 814, 755, 739, 674 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 1.20 (s, 3H, CH₃), 1.86 (s, 3H, CH₃), 2.18 (s, 3H, CH₃), 2.27 (s, 6H, 2CH₃), 2.44 (s, 3H, CH₃), 3.17 (d, 1H, J=11.6 Hz, CH₂), 3.54 (dd, 1H, J=3.2 Hz, 10.8 Hz, CH), 3.61 (d, 1H, J=11.6 Hz, CH₂), 4.01 (dd, 1H, J=8.4, 10.8 Hz, CH₂), 4.56 (dd, 1H, J=3.2, 8.4 Hz, CH₂), 4.82 (d, 1H, J=15.2 Hz, CH₂), 4.89 (d, 1H, J=15.2 Hz, CH₂), 6.76 (d, 1H, J=7.6 Hz, ArH), 6.90 (m, 3H, ArH), 7.01 (t, 1H, J=7.6 Hz, ArH), 7.18 (t, 1H, J=7.6 Hz, ArH), 7.35 (d, 2H, J=8.4 Hz, ArH), 7.74 (d, 1H, J=7.6 Hz, ArH), 7.90 (d, 2H, J=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): *δ* 21.3, 21.6, 21.8, 21.9, 28.5, 43.5, 44.8, 46.0, 48.1, 50.9, 108.7, 122.7, 124.9, 126.6, 126.8, 127.6, 128.1, 129.3, 129.7, 129.8, 130.6, 135.8, 137.0, 138.4, 142.9, 143.9, 176.9, 206.6; HRMS (ESI) calcd for C₃₃H₃₇N₂O₄S⁺¹ (M+H)⁺ requires 557.2474, found: 557.2467; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; *t*_{minor}=16.97 min, *t*_{maior}=61.33 min; ee%=17%; $[\alpha]_D^{20}$ +2.27 (*c* 1.00, CH₂Cl₂)].

3.2.18. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-5-fluoro-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3r). A colorless solid, 46 mg, 75% yield; mp 114-115 °C; IR (CH₂Cl₂): v 2922, 2854, 1712, 1608, 1492, 1447, 1356, 1337, 1264, 1167, 1089, 990, 851, 814, 781, 736, 710, 699, 659 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.09 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.51 (s, 3H, CH₃), 2.85 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.40 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.77–4.82 (m, 3H, CH₂+CH₂), 4.93 (s, 1H, =CH), 5.93–5.95 (m, 1H, ArH), 6.57–6.60 (m, 1H, ArH), 6.81 (td, 1H, J=8.8, 2.4 Hz, ArH), 6.87 (s, 1H, ArH), 6.93 (s, 2H, ArH), 7.26-7.32 (m, 3H, ArH), 7.38-7.42 (m, 4H, ArH), 7.68 (d, 2H, J=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.5, 28.7, 44.3, 46.4, 49.5, 52.1, 110.0 (d, *J*=22.9 Hz), 110.2 (d, J=6.1 Hz), 114.7 (d, J=23.1 Hz), 117.6, 125.1, 127.7, 127.8, 127.9, 128.8, 129.3, 130.0, 132.0 (d, J=7.7 Hz), 135.3, 136.1, 137.3, 138.3, 139.2 (d, J=1.9 Hz), 141.8, 144.9, 159.0 (d, J=239.8 Hz), 176.8, 203.1; ¹⁹F NMR (376 MHz, CDCl₃, CFCl₃): δ –102.32; HRMS (ESI) calcd for $C_{36}H_{34}FN_2O_4S^{+1}$ (M+H)⁺ requires 609.2223, found: 609.2202; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor}=27.90 min, t_{major} =44.60 min; ee%=99%; $[\alpha]_D^{20}$ +162.3 (c 1.00, CH₂Cl₂)].

3.2.19. (3S,3'S)-3'-Acetyl-5-chloro-1-(3,5-dimethylbenzyl)-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3s). A colorless solid, 48 mg, 76% yield; mp 108-109 °C; IR (CH₂Cl₂): v 2921, 1712, 1677, 1607, 1484, 1446, 1428, 1355, 1265, 1166, 1118, 1090, 989, 848, 813, 775, 710, 698, 658 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.10 (s, 3H, CH₃), 2.23 (s, 6H, 2CH₃), 2.53 (s, 3H, CH₃), 2.74 (dd, 1H, *J*=2.8, 12.0 Hz, CH), 4.40 (dd, 1H, *J*=12.0, 14.0 Hz, CH₂), 4.76 (s, 2H, CH₂), 4.78 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.92 (s, 1H, =CH), 6.16 (d, 1H, J=2.4 Hz, ArH), 6.58 (d, 1H, J=8.4 Hz, ArH), 6.86 (s, 1H, ArH), 6.93 (s, 2H, ArH), 7.07 (dd, 1H, J=2.4, 8.4 Hz, ArH), 7.27-7.32 (m, 3H, ArH), 7.41-7.44 (m, 4H, ArH), 7.70 (d, 2H, J=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.7, 28.6, 44.3, 46.3, 49.2, 51.9, 110.6, 117.5, 122.4, 125.0, 127.6, 127.7, 127.8, 127.9, 128.4, 128.8, 129.3, 130.1, 132.0, 135.1, 135.9, 137.5, 138.4, 141.8, 142.0, 145.0, 176.7, 203.0; HRMS (ESI) calcd for C₃₆H₃₄ClN₂O₄S⁺¹ (M+H)⁺ requires 625.1928, found: 625.1924; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor} =27.30 min, t_{major} =39.95 min; ee% >99%; [α]_D²⁰ +164.2 (c 1.00, $CH_2Cl_2)].$

3.2.20. (3S,3'S)-3'-Acetyl-5-bromo-1-(3,5-dimethylbenzyl)-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3t). A colorless solid, 52 mg, 78% yield; mp 110-111 °C; IR (CH₂Cl₂): v 2921, 1712, 1604, 1481, 1446, 1423, 1355, 1337, 1265, 1166, 1091, 989, 846, 811, 775, 735, 709, 698, 658 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.10 (s, 3H, CH₃), 2.23 (s, 6H, 2CH₃), 2.55 (s, 3H, CH₃), 2.69 (dd, 1H, *J*=2.8, 11.6 Hz, CH), 4.41 (dd, 1H, *J*=11.6, 14.4 Hz, CH₂), 4.76–4.81 (m, 3H, CH₂+CH₂), 4.92 (s, 1H, =CH), 6.33 (d, 1H, *I*=1.6 Hz, ArH), 6.54 (d, 1H, *I*=8.8 Hz, ArH), 6.86 (s, 1H, ArH), 6.92 (s, 2H, ArH), 7.22 (dd, 1H, J=2.0, 8.4 Hz, ArH), 7.29-7.34 (m, 3H, ArH), 7.42–7.45 (m, 4H, ArH), 7.71 (d, 2H, J=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.2, 21.9, 28.6, 44.3, 46.2, 49.1, 51.9, 111.1, 114.8, 117.5, 125.0, 125.1, 127.7, 127.8, 127.9, 128.8, 129.3, 130.2, 131.3, 132.4, 135.1, 135.9, 137.5, 138.4, 141.9, 142.5, 145.0, 176.6, 202.9; HRMS (ESI) calcd for $C_{36}H_{34}BrN_2O_4S^{+1}$ (M+H)⁺ requires 669.1423, found: 669.1404; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor}=32.49 min, t_{major} =46.88 min; ee% >99%; [α]_D²⁰ +147.9 (*c* 1.00, CH₂Cl₂)].

3.2.21. (35,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-5-methyl-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (**3u**). A colorless solid, 45 mg, 75% yield; mp 95–96 °C; IR (CH₂Cl₂): v 2918, 1708, 1599, 1493, 1446, 1355, 1336, 1265, 1184, 1167, 1117, 1090, 1022, 988, 812, 778, 734, 709, 698, 659 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.00 (s, 3H, CH₃), 2.23-2.25 (m, 9H, 3CH₃), 2.49 (s, 3H, CH₃), 2.55 (s, 3H, CH₃), 2.91 (dd, 1H, J=2.4, 11.6 Hz, CH), 4.39–4.45 (m, 1H, CH₂), 4.71–4.76 (m, 3H, CH₂+CH₂), 4.97 (s, 1H, =CH), 6.24 (s, 1H, ArH), 6.58 (d, 1H, J=8.0 Hz, ArH), 6.85 (s, 1H, ArH), 6.92-6.94 (m, 3H, ArH), 7.24-7.29 (m, 3H, ArH), 7.37–7.39 (m, 4H, ArH), 7.68 (d, 2H, *J*=7.2 Hz, ArH); ¹³C NMR (75 MHz, CDCl₃, TMS): δ 21.0, 21.1, 21.6, 28.8, 44.1, 46.2, 49.2, 52.2, 109.3, 118.3, 122.8, 125.0, 125.2, 127.5, 127.7, 127.9, 128.5, 128.9, 129.1, 129.8, 130.2, 131.8, 135.6, 137.6, 138.1, 140.9, 141.1, 144.3, 176.8, 203.4; HRMS (ESI) calcd for $C_{37}H_{37}N_2O_4S^{+1}$ (M+H)⁺ requires 605.2474, found: 605.2482; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=70/30; flow rate: 0.70 mL/min; t_{minor}=25.51 min, t_{major} =46.50 min; ee% >99%; $[\alpha]_D^{20}$ +130.3 (c 1.00, CH₂Cl₂)].

3.2.22. (3S,3'S)-3'-Acetyl-1-(3,5-dimethylbenzyl)-6-methyl-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3v). A colorless solid, 50 mg, 83% yield; mp 105-106 °C; IR (CH₂Cl₂): v 2921, 1713, 1617, 1495, 1447, 1356, 1226, 1167, 1120, 1091, 1027, 987, 846, 814, 778, 710, 699, 659 $\rm cm^{-1}; \ ^1H$ NMR (400 MHz, CDCl₃, TMS): δ 2.00 (s, 3H, CH₃), 2.24 (s, 6H, 2CH₃), 2.27 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.96 (dd, 1H, J=2.8, 11.6 Hz, CH), 4.41 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.69 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.77 (s, 2H, CH₂), 4.95 (s, 1H, =CH), 6.38 (d, 1H, J=7.2 Hz, ArH), 6.54 (s, 1H, ArH), 6.73 (d, 1H, J=7.2 Hz, ArH), 6.86 (s, 1H, ArH), 6.94 (s, 2H, ArH), 7.22-7.29 (m, 3H, ArH), 7.33-7.37 (m, 4H, ArH), 7.66 (d, 2H, I=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS); δ 21.2, 21.6, 21.8, 28.9, 44.1, 46.1, 49.0, 52.3, 110.4, 118.2, 121.8, 123.1, 125.0, 127.3, 127.6, 127.7, 127.8, 128.5, 129.1, 129.8, 135.7, 136.3, 137.5, 138.2, 138.9, 141.2, 143.4, 144.4, 177.2, 203.6; HRMS (ESI) calcd for C₃₇H₃₇N₂O₄S⁺¹ (M+H)⁺ requires 605.2474, found: 605.2471; enantiomeric excess was determined by HPLC with a Chiralcel PC-2 column [λ =230 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.70 mL/min; *t*_{minor}=25.05 min, *t*_{maior}=51.90 min; ee%=99%; $[\alpha]_D^{20}$ +119.8 (*c* 1.00, CH₂Cl₂)].

3.2.23. (3S,3'S)-1-Methyl-6'-phenyl-3'-propionyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (3w). A colorless solid, 32 mg, 64% yield; mp 61–62 °C; IR (CH₂Cl₂): v 3057, 2936, 1712, 1610, 1492, 1470, 1360, 1168, 1085, 967, 816, 754, 710, 698, 655 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 0.90 (t, 3H, *J*=7.2 Hz, CH₃), 2.18–2.28 (m, 1H, CH₂), 2.41–2.50 (m, 4H, CH₃+CH₂), 3.00 (dd, 1H, J=2.8, 11.6 Hz, CH), 3.19 (s, 3H, CH₃), 4.38 (dd, 1H, J=11.6, 14.0 Hz, CH₂), 4.69 (dd, 1H, J=2.8, 14.0 Hz, CH₂), 4.91 (s, 1H, =CH), 6.47 (d, 1H, J=7.6 Hz, ArH), 6.82(d, 1H, J=8.0 Hz, ArH), 6.94 (t, 1H, *J*=7.6 Hz, ArH), 7.19–7.32 (m, 6H, ArH), 7.36 (d, 2H, *J*=8.0 Hz, ArH), 7.64 (d, 2H, J=8.0 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 7.3, 21.6, 26.5, 34.3, 46.3, 49.1, 51.9, 108.5, 117.9, 122.0, 122.4, 127.6, 127.7, 127.9, 128.5, 128.7, 129.8, 130.5, 136.4, 137.5, 141.4, 144.1, 144.4, 177.2, 206.3; HRMS (ESI) calcd for $C_{29}H_{29}N_2O_4S^{+1}$ (M+H)⁺ requires 501.1848, found: 501.1839; enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ =214 nm; eluent: hexane/ isopropanol=80/20; flow rate: 0.70 mL/min; tminor=29.81 min, t_{major} =40.92 min; ee%=98%; $[\alpha]_D^{20}$ +156.9 (c 1.00, CH₂Cl₂)].

3.2.24. (3S,3'S)-3'-(2-(3-Hydroxy-1-methyl-2-oxoindolin-3-yl)acetyl)-1-methyl-6'-phenyl-1'-tosyl-2',3'-dihydro-1'H-spiro[indoline-3,4'-pyridin]-2-one (**4a**). A white solid, 65 mg, 67% yield; IR (CH₂Cl₂): ν 2953, 2923, 2853, 1720, 1613, 1494, 1459, 1376, 1259, 1169, 1090, 1020, 973, 814, 754, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.44 (s, 1.8H, 0.6CH₃), 2.50 (s, 3H, CH₃), 2.54 (d, 0.6H, *J*=16.8 Hz, 0.6CH₂), 2.78 (d, 1H, *J*=16.8 Hz, CH₂), 2.88 (d, 1H, *J*=16.8 Hz, CH₂), 3.00–3.08 (m, 5.2H, CH₃+CH+0.6CH+0.6CH₂), 3.14–3.16 (m, 6.6H, CH₃+0.6CH₃+0.6CH₃), 3.95 (s, 1H, OH), 4.29–4.37 (m, 2.2H, CH₂+0.6CH₂+0.6OH), 4.44–4.54 (m, 1.6H, CH₂+0.6CH₂), 4.89 (s, 1H, ==CH), 4.91 (s, 0.6H, 0.6CH=), 6.49–6.54 (m, 1.6H, ArH+0.6ArH), 6.68 (d, 0.6H, J=7.6 Hz, 0.6ArH), 6.76 (d, 1H, J=7.6 Hz, ArH), 6.80–6.93 (m, 4.8H, 3ArH+1.8ArH), 6.96–7.01 (m, 2.6H, 2ArH+0.6ArH), 7.18–7.36 (m, 14.4H, 9ArH+5.4ArH), 7.53 (d, 1.2H, J=8.4H, 1.2ArH), 7.59 (d, 2H, J=8.4 Hz, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): δ 21.58, 21.62, 26.27, 26.31, 26.4, 26.5, 45.1, 45.3, 46.6, 47.8, 49.0, 49.2, 52.1, 53.2, 73.8, 74.2, 108.58, 108.59, 108.61, 108.64, 117.1, 117.2, 122.36, 122.39, 122.6, 122.8, 123.0, 123.1, 123.6, 123.7, 127.51, 127.56, 127.68, 127.70, 127.76, 127.86, 128.52, 128.54, 128.9, 129.0, 129.3, 129.5, 129.68, 129.75, 129.88, 129.94, 136.1, 137.39, 137.43, 141.65, 141.72, 143.2, 143.4, 143.7, 144.0, 144.5, 144.5, 175.2, 175.6, 176.0, 204.9, 206.2; HRMS (ESI) calcd for C₃₇H₃₄N₃O₆S⁺¹ (M+H)⁺ requires 648.2168, found: 648.2174; [α]₂^D +148.3 (c 1.00, CH₂Cl₂).

3.2.25. (3S,3'S)-3'-Acetyl-1-methyl-6'-phenyl-3',5'-dihydro-2'Hspiro[indoline-3,4'-pyridin]-2-one (5a). A colorless solid, 22 mg, 66% yield; mp 133–134 °C; IR(CH₂Cl₂): v 3057, 2927, 1703, 1611, 1494, 1471, 1421, 1349, 1262, 1172, 1091, 1041, 802, 753, 733, 693 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, TMS): δ 2.01 (s, 3H, CH₃), 2.78–2.83 (m, 1H, CH₂), 2.91 (dd, 1H, J=18.0, 1.6 Hz, CH₂), 3.21 (s, 3H, CH₃), 3.34 (dd, 1H, J=10.8, 7.6 Hz, CH), 4.39 (dd, 1H, J=17.6, 5.2 Hz, CH₂), 4.46–4.54 (m, 1H, CH₂), 6.84 (d, 1H, J=8.0 Hz, ArH), 7.05 (t, 1H, J=7.6 Hz, ArH), 7.10-7.11 (m, 1H, ArH), 7.26–7.39 (m, 4H, ArH), 7.73–7.76 (m, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃, TMS): *b* 26.1, 30.3, 35.1, 44.5, 48.5, 52.3, 108.2, 121.4, 122.4, 126.0, 128.2, 128.6, 129.9, 131.6, 138.8, 143.8, 162.1, 177.6, 206.7; HRMS (ESI) calcd for $C_{21}H_{21}N_2O_2^{+1}$ (M+H)⁺ requires 333.1603, found: 333.1599: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column; λ =214 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.5 mL/min; t_{minor}=27.55 min, t_{major} =36.72 min; ee%=98%; $[\alpha]_{D}^{20}$ +185.8 (*c* 1.00, CH₂Cl₂).

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Supplementary data

Spectroscopic data and chiral HPLC traces of the compounds shown in Tables 1 and 2 and Schemes 1 and 2, the detailed descriptions of experimental procedures for the preparation of imine substrates and the crystal structures of **1i** (929404), **1l** (CCDC 917363) and **3l** (CCDC 918762). This material is available free of charge via the Internet at the website. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/ j.tet.2014.02.052

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