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Organocatalytic Asymmetric Michael/Friedel–Crafts Cascade Reaction of 3-Pyrrolyl-oxindoles and α,β-Unsaturated Aldehydes for the Construction of Chiral Spiro[5,6-dihydropyrido[1,2-*a*]pyrrole-3,3′-oxindoles]

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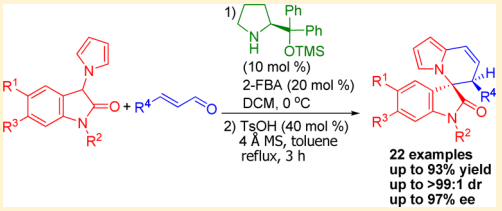
Supporting Information

ABSTRACT: An efficient and unprecedented organocatalytic asymmetric reaction of 3-pyrrolyl-oxindoles with α,β-unsaturated aldehydes to generate spirocyclic oxindole compounds was developed. The reactions were catalyzed by diphenylprolinol silyl ether and 2-fluorobenzoic acid via an asymmetric Michael/Friedel–Crafts cascade process, followed by dehydration with *p*-toluenesulfonic acid to afford a wide variety of structurally diverse spiro[5,6-dihydropyrido[1,2-*a*]pyrrole-3,3′-oxindole] derivatives in high yields (up to 93%) and with high to excellent diastereo- and enantioselectivities (up to >99:1 dr and 97% ee).



Spirooxindole cores are widely distributed in the architecture of a number of natural and unnatural biologically active compounds and have been embedded into many medicinally important agents and drug candidates.[1] The key structural characteristic of spirooxindole frameworks is the oxindole moiety spiro-fused at the C3-position with other diverse cyclic motifs. In general, the assembly of different cycles with oxindoles at the C3-position in a spiro ring fusion pattern will certainly result in a different class of spirocycles that may show promise as biologically active compounds.[2] Accordingly, considerable efforts have been devoted toward the development of various strategies to generate diverse spirocyclic oxindole compounds.[2,3] Despite the substantial achievements made thus far, it is still highly desirable to explore creative methods to allow easy access to novel spirocyclic oxindole molecules in consideration of the fact that the structural complexity and well-defined architecture of molecules are normally correlated with specificity of action and potentially useful biological properties.[4] In this context, we have also extended our general interest in developing new methodologies for the construction of multifarious spirocyclic oxindole compounds.[5]

Organocatalytic cascade reactions were found to be efficient synthetic strategies for the formation of new bonds and the generation of chiral centers as well as for the preparation of optically active cyclic compounds in just one operation.[6] Moreover, they have been proven to be powerful tools for stereoselective construction of complex molecules that are difficult to access through common methods. In the aforementioned research field, diarylprolinol silyl ethers as catalysts for the asymmetric transformations of α,β-unsaturated aldehydes via an iminium-enamine cascade process have been the subject of extensive studies and have become an important element in asymmetric synthetic chemistry.[7] As part of our ongoing research program in the enantioselective synthesis of 3,3′-disubstituted oxindoles,[8] we have recently disclosed that 3-pyrrolyl-oxindoles could serve as efficient nucleophiles for the synthesis of structurally diverse 3,3′-disubstituted oxindole derivatives with organocatalysts.[9] In that study, we noticed that the pyrrole moiety of 3-pyrrolyl-oxindoles was liable to undergo an aza-Friedel–Crafts reaction, thus leading to the formation of an optically active heptacyclic oxindole compound containing three stereocenters.[9]

Inspired by our previous observations and the asymmetric organocatalysis with diarylprolinol silyl ethers as catalysts,[7,9] we reasoned that an asymmetric Michael/Friedel–Crafts cascade reaction[10] of 3-pyrrolyl-oxindoles and α,β-unsaturated aldehydes could be achieved with diphenylprolinol silyl ether as catalyst, leading to the generation of a class of spirocyclic oxindole derivatives. The subsequent dehydration treatment of the obtained spirocyclic products under acidic reaction conditions will result in a novel type of spirocyclic oxindole bearing a 5,6-dihydropyrido[1,2-*a*]pyrrole ring system (Scheme 1), which is a pharmaceutically important motif and widely

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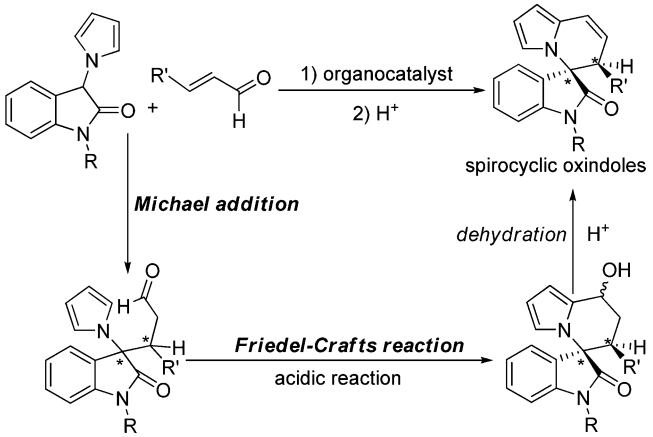
Scheme 1. Design of an Asymmetric Michael/Friedel-Crafts Cascade Reaction of 3-Pyrrolyl-oxindoles and α,β-Unsaturated Aldehydes

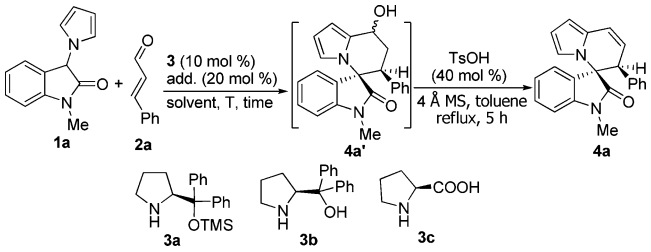


present in naturally occurring and synthetic biologically active molecules.[11] Herein, we report our research results on the subject.

To probe the validity of our envisioned design for the asymmetric Michael/Friedel−Crafts cascade reaction, we probed a model reaction between *N*-methyl-3-pyrrolyl-oxindole **1a** and *trans*-cinnamaldehyde **2a** with organocatalysts **3**. As shown in Table 1, the reaction could occur only in the presence of 10 mol % (*S*)-diphenylprolinol-TMS ether catalyst **3a** in dichloromethane (DCM) at room temperature to give the expected Michael/Friedel−Crafts product **4a**′ (entry 1). To facilitate separation and analysis, we directly treated product **4a**′ with 40 mol % *p*-toluenesulfonic acid (TsOH) in reflux toluene for dehydration, giving spirocyclic oxindole **4a** in only 20% yield (entry 1). To our delight, using benzoic acid (BA) as an additive for accelerating the turnover of the reaction, we could obtain **4a** in 87% isolated yield with 80:20 dr and 76% ee after 12 h (entry 2). (*S*)-Diphenylprolinol **3b** as a catalyst showed relatively lower reactivity and gave 62% yield with 83% ee (entry 3). However, the reaction did not work with 10 mol % L-proline (entry 4). To further improve the results, we surveyed some other acids as additives (TFA, TsOH, 2-FBA, 2-CBA, and 2,4-DNBA) (entries 5−9) and with catalyst **3a**; 2-fluorobenzoic acid (2-FBA) was found to be the best additive for furnishing product **4a** in a set of acceptable results (entry 7). Then, switching from DCM to other solvents (DCE, $CHCl_3$, toluene, and CH_3CN) (entries 10−13), 1,2-dichloroethane gave similar results to that with DCM as the asymmetric reaction medium (entry 10). However, the other solvents gave inferior results compared to using DCM as solvent (entries 11−13 vs entry 7). Finally, upon decreasing the reaction temperature to 0 °C, we found that the asymmetric cascade reaction proceeded to completion in 17 h and afforded desired product **4a** in 82% yield with 85:15 dr and 94% ee (entry 14). Elevating the reaction temperature to 40 °C, **4a** could be obtained in 93% yield but with 80:20 dr and a lower 82% ee value (entry 15). Decreasing the catalyst loading from 10 to 5 and 2 mol %, the cascade reactions could still occur but gave relatively poor reactivity and selectivity (entries 16 and 17, respectively).

With the optimal reaction conditions in hand (Table 1, entry 12), the substrate scope and the limitation of this organocatalytic Michael/Friedel−Crafts cascade reaction was explored, and the results are summarized in Table 2. First, various

Table 1. Conditions Optimization[a]



entry	solvent	additive	3	time (h)	yield (%)[b]	dr[c]	ee (%)[d]
1	DCM		**3a**	24	20	nd	nd
2	DCM	BA	**3a**	12	87	80:20	76
3	DCM	BA	**3b**	55	62	43:57	83
4	DCM	BA	**3c**	72	trace	nd	nd
5	DCM	TFA	**3a**	12	trace	nd	nd
6	DCM	TsOH	**3a**	12	trace	nd	nd
7	DCM	2-FBA	**3a**	12	90	83:17	92
8	DCM	2-CBA	**3a**	12	87	76:24	93
9	DCM	2,4-DNBA	**3a**	18	88	79:21	85
10	DCE	2-FBA	**3a**	12	89	83:17	90
11	$CHCl_3$	2-FBA	**3a**	12	87	87:13	89
12	toluene	2-FBA	**3a**	12	88	81:19	85
13	CH_3CN	2-FBA	**3a**	12	83	81:19	53
14	DCM	2-FBA	**3a**	17	82	85:15	94[e]
15	DCM	2-FBA	**3a**	5	93	80:20	82[f]
16	DCM	2-FBA	**3a**	12	89	78:22	92[g]
17	DCM	2-FBA	**3a**	48	58	49:51	88[h]

[a]Unless otherwise noted, the reactions were carried out with **1a** (0.1 mmol), **2a** (0.15 mmol), catalyst **3** (10 mol %), and additive (20 mol %) in solvent (2 mL) at room temperature for the specified reaction time. After the first reaction step, intermediate **4a**′ was isolated by flash chromatography on silica gel, and then **4a**′ was heated with TsOH (40 mol %) and 4 Å MS (60 mg) in toluene (3 mL) at reflux temperature for 5 h for dehydration. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Determined by chiral HPLC analysis. [e]Ran at 0 °C. [f]Ran at 40 °C. [g]Used 5 mol % catalyst. [h]Used 2 mol % catalyst. BA, benzoic acid; 2-FBA, 2-fluorobenzoic acid; 2-CBA, 2-chlorobenzoic acid; 2,4-DNBA, 2,4-dinitrobenzoic acid.

substituted α,β-unsaturated aldehydes were examined by reacting with 3-pyrrolyl-oxindole **1a** (entries 1−11). Not only electron-donating but also electron-withdrawing groups on the benzene ring of aldehydes were well tolerated, yielding expected products **4b−h** in very good yields (68−86%) and high stereoselectivities (75:25−87:13 dr and 83−94% ee, entries 1−7). Additionally, heterocyclic α,β-unsaturated aldehyde, such as thienyl, was also well tolerated and afforded corresponding product **4i** in 82% yield with 88:12 dr and high 94% ee (entry 8). Meanwhile, fused aromatic α,β-unsaturated aldehyde **2j** also reacted efficiently with **1a**, giving good yield and excellent stereoselectivity (entry 9). Furthermore, α,β-unsaturated aldehydes with alkenyl or alkyl substituents, such as styryl or methyl, also reacted smoothly with **1a** to afford corresponding products **4k** and **4l** in acceptable results (entry 10 and 11).

Conversely, to further investigate the scope of the reaction, we focused on the nucleophiles 3-pyrrolyl-oxindoles **1b−i** (Table 3). Substituents on the *N*-protecting group were varied; it was found that all of the 3-pyrrolyl-oxindoles bearing *N*-H, *N*-Et, *N*-Ph, *N*-Bn, *N*-Ac could react with cinnamaldehyde (**2a**) under the optimized conditions to afford the desired spirocyclic

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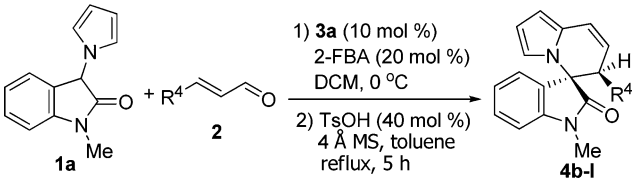
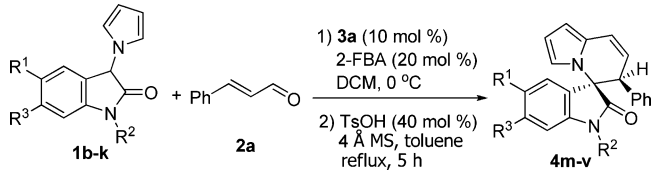
Table 2. Substrate Scope of the Michael/Friedel–Crafts Cascade Reaction for α,β-Unsaturated Aldehydes[a]



entry	1	2	time (h)	4/yield (%)[b]	dr[c]	ee (%)[d]
1	1a	R^4 = 4-MeC_6H_4 (2b)	24	4b/86	87:13	91
2	1a	R^4 = 3-MeC_6H_4 (2c)	13	4c/75	75:25	90
3	1a	R^4 = 3-$MeOC_6H_4$ (2d)	12	4d/68	86:14	93
4	1a	R^4 = 4-ClC_6H_4 (2e)	13	4e/68	82:18	94
5	1a	R^4 = 3-BrC_6H_4 (2f)	15	4f/71	85:15	83
6	1a	R^4 = 4-BrC_6H_4 (2g)	14	4g/86	85:15	92
7	1a	R^4 = 4-FC_6H_4 (2h)	13	4h/77	83:17[e]	94
8	1a	R^4 = 2-thienyl (2i)	12	4i/82	88:12	94
9	1a	R^4 = 1-naphthyl (2j)	18	4j/70	92:8[e]	95
10	1a	R^4 = 2-$ClC_6H_4(CH)_2$ (2k)	13	4k/62	>99:1	80
11	1a	R^4 = Me (2l)	20	4l/64	77:23	97

[a]Unless otherwise noted, the reactions were carried out with **1a** (0.15 mmol), **2** (0.225 mmol), 2-FBA (20 mol %), and catalyst **3a** (10 mol %) in CH_2Cl_2 (3 mL) at 0 °C for the specified reaction time. After the first reaction step, the product was isolated by flash chromatography on silica gel, and then the product was heated with TsOH (40 mol %) and 4 Å MS (90 mg) in toluene (3 mL) at reflux temperature for 5 h for dehydration to give **4**. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Determined by chiral HPLC analysis. [e]^{1}H NMR analysis used to determine dr.

Table 3. Substrate Scope of the Cascade Michael/Friedel–Crafts Reaction for 3-Pyrrolyl-oxindoles[a]



entry	1	time (h)	4/yield (%)[b]	dr[c]	ee (%)[d]
1	R^1 = H, R^2 = H, R^3 = H (1b)	10	4m/72	92:8	92
2	R^1 = H, R^2 = Et, R^3 = H (1c)	14	4n/86	72:28	96
3	R^1 = H, R^2 = Ph, R^3 = H (1d)	11	4o/76	83:17	96
4	R^1 = H, R^2 = Bn, R^3 = H (1e)	14	4p/75	>99:1	96
5	R^1 = H, R^2 = Ac, R^3 = H (1f)	8	4q/81	>99:1[e]	67
6	R^1 = F, R^2 = Me, R^3 = H (1g)	11	4r/80	86:14	89
7	R^1 = Br, R^2 = Me, R^3 = H (1h)	12	4s/75	87:13	91
8	R^1 = Me, R^2 = Me, R^3 = H (1i)	23	4t/78	80:20	94
9	R^1 = Cl, R^2 = Me, R^3 = H (1j)	17	4u/74	98:2	92
10	R^1 = H, R^2 = Me, R^3 = Cl (1k)	17	4v/78	90:10	94

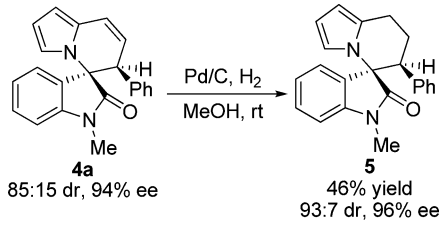
[a]Unless otherwise noted, the reactions were carried out with **1** (0.15 mmol), **2a** (0.225 mmol), 2-FBA (20 mol %), and catalyst **3a** (10 mol %) in CH_2Cl_2 (3 mL) at 0 °C for the specified reaction time. After the first reaction step, the product was isolated by flash chromatography on silica gel, and then the product was heated with TsOH (40 mol %) and 4 Å MS (90 mg) in toluene (3 mL) at reflux temperature for 5 h for dehydration to give **4**. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Determined by chiral HPLC analysis. [e]^{1}H NMR analysis used to determine dr.

oxindole compounds **4m–q** (entries 1–5). In the cases of the formation of **4p** and **4q** in particular, we were pleased to find that high to >99:1 dr values could be obtained (entries 4 and 5). We also evaluated the substituted oxindoles **1g–i** containing electron-withdrawing 5-F and 5-Br substituents and an electron-donating 5-methyl substituent on the phenyl ring. These substrates were tolerated in the reaction with **2a**, furnishing spirocyclic oxindoles **4r–t** in 75–80% yield with 80:20–87:13 dr and 89–94% ee (entries 6–8). The absolute configuration of major isomer **4s** was determined to be (C7*R*,C9*S*) by single-crystal X-ray analysis. The configurations of the other derivatives were assigned by analogy.[12] For oxindole substrates **1j** and **1k** bearing the same substituent but at different positions, it was observed that there is no significant difference in their transformation to products **4u** and **4v** (entries 9 and 10, respectively).

To demonstrate the synthetic utility of this methodology, we developed conditions for reduction of the carbon–carbon double bond in the 5,6-dihydropyrido[1,2-*a*]pyrrole moiety by hydrogenation (Scheme 2). It was observed that Pd-catalyzed hydrogenation in methanol at room temperature could deliver corresponding spirocyclic oxindole **5** in 46% isolated yield without loss of ee and slightly higher diastereoselectivity.

With regard to the mechanism, we assume that the reaction of the (*S*)-diphenylprolinol-TMS ether catalyst **3a** with α,β-unsaturated aldehydes **2** results in intermediary iminimu ion **A** (Scheme 3). Subsequently, the Michael addition of intermediate **A** with 3-pyrrolyl-oxindoles **1** gives rise to another intermediate **B**, which, after hydrolysis, yields adduct **C** and releases catalyst **3a**. The following intramolecular Friedel–Crafts reaction of **C** leads to the expected Michael/Friedel–Crafts product **4′**. Finally, under acidic reaction conditions, intermediate **4′** is dehydrated to generate spirocyclic oxindole **4** bearing a 5,6-dihydropyrido[1,2-*a*]pyrrole ring system (Scheme 3).

Scheme 2. Product Transformation



In conclusion, we have demonstrated the first organocatalytic enantioselective cascade reaction of 3-pyrrolyl-oxindoles and α,β-unsaturated aldehydes. In the developed protocol, with diphenylprolinol silyl ether and 2-fluorobenzoic acid as catalyst, a series of 3-pyrrolyl-oxindoles reacted smoothly with various α,β-unsaturated aldehydes under mild conditions via an asymmetric Michael/Friedel–Crafts cascade process. After dehydration with *p*-toluenesulfonic acid, a wide variety of structurally diverse spiro[5,6-dihydropyrido[1,2-*a*]pyrrole-3,3′-oxindole] derivatives in high yields (up to 93%) and with high to excellent diastereo- and enantioselectivities (up to >99:1 dr

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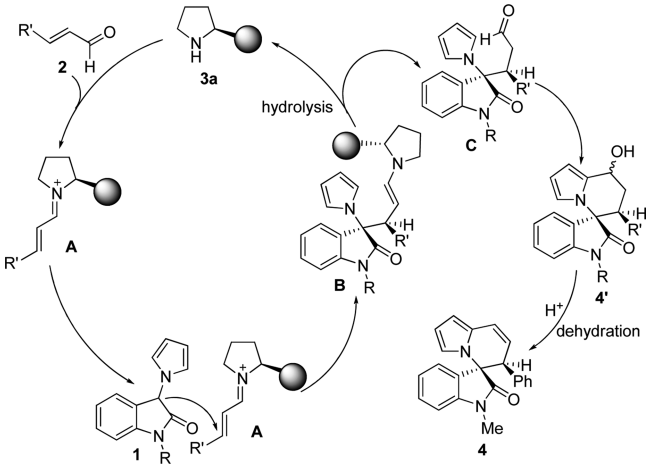
Scheme 3. Proposed Reaction Pathway for the Michael/Friedel−Crafts Cascade Process



and 97% ee) were obtained. Additional transformation of the product into another spirocyclic oxindole was also presented.

EXPERIMENTAL SECTION

General Methods. Reagents were purchased from commercial sources and were used as received unless otherwise mentioned. Reactions were monitored by TLC. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm, DMSO-d_6 at 39.51 ppm). Melting points were recorded on a melting point apparatus.

General Procedure for the Synthesis of Compounds 4. A solution of compounds **1** (0.15 mmol), compounds **2** (0.225 mmol), catalyst **3a** (10 mol %), and 2-fluorobenzoic acid (20 mol %) in DCM (3 mL) was stirred at 0 °C for the indicated time. After completion of the reaction, as indicated by TLC, the intermediate was isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1−2/1). Then, to a solution of the intermediate in toluene (3 mL) were added *p*-toluenesulfonic acid (40 mol %) and 4 Å molecular sieve (90 mg). The reaction mixture was allowed to stir under reflux for 5 h and then cooled to room temperature; the mixture was filtered through a Celite plug, and the filter cake was eluted with dichloromethane. The filtrate was concentrated under vacuum and purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1) to obtain products **4**.

*8′-Hydroxy-1-methyl-6′-phenyl-7′,8′-dihydro-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4a′**).* White solid; 49.6 mg, 96% yield; mp 79.9−81.6; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (brs, 1H), 2.09−2.15 (m, 1H), 2.76 (s, 3H), 3.38−3.49 (m, 1H), 4.13 (dd, J = 2.4, 13.2 Hz, 1H), 5.30 (t, J = 2.7 Hz, 1H), 6.06−6.08 (m, 1H), 6.14−6.17 (m, 1H), 6.30−6.32 (m, 1H), 6.49 (d, J = 7.8 Hz, 1H), 6.86−6.89 (m, 2H), 6.99−7.10 (m, 3H), 7.11−7.17 (m, 1H), 7.23−7.29 (m, 1H), 7.44 (d, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7, 30.1, 44.1, 62.0, 67.9, 107.9, 108.0, 109.7, 118.7, 123.1, 124.1, 127.3, 127.5, 128.7, 129.1, 129.8, 132.7, 136.9, 143.6, 173.7; HRMS (EI) calcd for $C_{22}H_{20}N_2O_2$ $[M]^+$ 344.1525, found 344.1531.

*(3R,6′S)-1-Methyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4a**).* White solid; 40.1 mg, 82% yield; 85:15 dr, 94% ee; $[\alpha]_D^{20}$ +209.4 (c 0.53, $CHCl_3$); mp 119.7−120.9 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 4.5 min, t_{major} = 5.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.66 (s, 3H), 4.31−4.33 (m, 1H), 5.84 (dd, J = 2.4, 9.9 Hz, 1H), 6.16−6.19 (m, 2H), 6.29−6.35 (m, 1H), 6.50 (d, J = 7.8 Hz, 1H), 6.81 (dd, J = 3.0, 9.9 Hz, 1H), 6.87−6.90 (m, 2H), 7.04−7.13 (m, 3H), 7.17−7.23 (m, 1H), 7.29−7.34 (m, 1H), 7.52−7.55 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.4, 51.8, 68.1, 107.8, 109.1, 110.0, 119.7, 120.5, 121.0, 123.0, 124.4, 127.3, 127.5, 128.2, 129.3, 129.4, 130.0, 136.9, 144.1, 172.3; HRMS (ESI-TOF) calcd for $C_{22}H_{18}N_2NaO$ $[M + Na]^+$ 349.1311, found 349.1314.

*(3R,6′S)-1-Methyl-6′-(p-tolyl)-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4b**).* White solid; 43.8 mg, 86% yield; 87:13 dr, 91% ee; $[\alpha]_D^{20}$ +140.1 (c 0.86, $CHCl_3$); mp 76.5−77.8 °C; ee was determined by HPLC (Chiralpak AD-H, i-PrOH/hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 5.1 min, t_{major} = 6.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.22 (s, 3H), 2.69 (s, 3H), 4.27−4.29 (m, 1H), 5.82 (dd, J = 2.4, 9.9 Hz, 1H), 6.13−6.17 (m, 2H), 6.28−6.34 (m, 1H), 6.50−6.53 (m, 1H), 6.75−6.80 (m, 3H), 6.83−6.91 (m, 2H), 7.12−7.22 (m, 1H), 7.29−7.35 (m, 1H), 7.51−7.54 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 21.0, 25.4, 51.4, 68.1, 107.8, 109.0, 110.0, 119.6, 120.4, 121.4, 122.9, 124.4, 128.2, 128.4, 129.3, 129.6, 130.0, 133.9, 136.9, 144.2, 172.5; HRMS (ESI-TOF) calcd for $C_{23}H_{20}N_2NaO$ $[M + Na]^+$ 363.1468, found 363.1475.

*(3R,6′S)-1-Methyl-6′-(m-tolyl)-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4c**).* White solid; 38.2 mg, 75% yield; 75:25 dr, 90% ee; $[\alpha]_D^{20}$ +194.8 (c 0.93, $CHCl_3$); mp 78.4−79.7 °C; ee was determined by HPLC (Chiralpak AD-H, i-PrOH/hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 4.5 min, t_{major} = 6.8 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.13 (s, 3H), 2.66 (s, 3H), 4.26−4.28 (m, 1H), 5.84 (dd, J = 2.1, 9.9 Hz, 1H), 6.14−6.20 (m, 2H), 6.28−6.35 (m, 1H), 6.49 (d, J = 7.8 Hz, 1H), 6.65−6.71 (m, 2H), 6.80 (dd, J = 3.0, 9.9 Hz, 1H), 6.85−6.98 (m, 2H), 7.17−7.22 (m, 1H), 7.28−7.34 (m, 1H), 7.51−7.54 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 21.1, 25.4, 51.9, 68.2, 107.7, 109.1, 110.0, 119.7, 120.5, 121.2, 122.9, 124.4, 126.5, 127.3, 128.0, 128.4, 129.9, 130.1, 130.7, 136.8, 137.0, 144.3, 172.4; HRMS (ESI-TOF) calcd for $C_{23}H_{20}N_2NaO$ $[M + Na]^+$ 363.1468, found 363.1472.

*(3R,6′S)-6′-(3-Methoxyphenyl)-1-methyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4d**).* White solid; 36.3 mg, 68% yield; 86:14 dr, 93% ee; $[\alpha]_D^{20}$ +235.1 (c 1.82, $CHCl_3$); mp 114.5−115.6 °C; ee was determined by HPLC (Chiralpak AD-H, i-PrOH/hexane = 20/80, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 6.9 min, t_{major} = 14.7 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.69 (s, 3H), 3.56 (s, 3H), 4.27−4.30 (m, 1H), 5.84 (dd, J = 2.4, 9.9 Hz, 1H), 6.15−6.19 (m, 2H), 6.30−6.34 (m, 2H), 6.51−6.57 (m, 2H), 6.68 (dd, J = 2.4, 8.1 Hz, 1H), 6.80 (dd, J = 3.0, 9.9 Hz, 1H), 6.97−7.02 (m, 1H), 7.18−7.23 (m, 1H), 7.29−7.35 (m, 1H), 7.51−7.54 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.4, 51.9, 55.0, 68.1, 107.8, 109.2, 110.0, 113.9, 114.1, 119.7, 120.5, 120.9, 121.8, 122.9, 124.3, 128.3, 128.5, 129.3, 130.1, 138.4, 144.3, 158.7, 172.3; HRMS (ESI-TOF) calcd for $C_{23}H_{20}N_2NaO_2$ $[M + Na]^+$ 379.1417, found 379.1418.

*(3R,6′S)-6′-(4-Chlorophenyl)-1-methyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4e**).* White solid; 36.8 mg, 68% yield; 82:18 dr, 94% ee; $[\alpha]_D^{20}$ +256.5 (c 1.84, $CHCl_3$); mp 80.2−81.4 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 9.2 min, t_{major} = 14.7 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.72 (s, 3H), 4.28−4.30 (m, 1H), 5.75 (dd, J = 2.4, 9.9 Hz, 1H), 6.15−6.17 (m, 2H), 6.30−6.34 (m, 1H), 6.52−6.57 (m, 1H), 6.77−6.92 (m, 3H), 7.00−7.06 (m, 2H), 7.14−7.23 (m, 1H), 7.31−7.37 (m, 1H),7.50−7.53 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 51.1, 67.9, 108.1, 109.4, 110.2, 119.8, 120.3, 120.8, 123.1, 124.3, 127.7, 128.0, 129.5, 130.3, 130.8, 133.3, 135.6, 144.1, 172.1; HRMS (ESI-TOF) calcd for $C_{22}H_{17}ClN_2NaO$ $[M + Na]^+$ 383.0922, found 383.0924.

*(3R,6′S)-6′-(3-Bromophenyl)-1-methyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4f**).* White solid; 43.0 mg, 71% yield; 85:15 dr, 83% ee; $[\alpha]_D^{20}$ −137.0 (c 0.83, $CHCl_3$); mp 66.3−67.7 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 10/90, flow rate = 1.0

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mL/min, λ = 254 nm, major diastereomer t_{minor} = 11.6 min, t_{major} = 17.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 3.08 (s, 3H), 3.77−3.82 (m, 1H), 5.69 (dd, J = 2.7, 9.9 Hz, 1H), 5.98 (d, J = 8.4 Hz, 1H), 6.07−6.17 (m, 2H), 6.24−6.37 (m, 1H), 6.71 (dd, J = 2.7, 9.9 Hz, 1H), 6.78−6.84 (m, 1H), 6.97−7.12 (m, 2H), 7.15−7.20 (m, 1H), 7.28−7.31 (m, 1H), 7.35−7.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 26.0, 48.4, 66.5, 108.3, 109.2, 110.0, 119.2, 119.7, 120.1, 122.6, 123.3, 124.2, 124.8, 126.6, 129.1, 129.9, 130.2, 130.5, 132.8, 138.7, 143.9, 172.6; HRMS (ESI-TOF) calcd for $C_{22}H_{18}BrN_2O$ $[M + H]^+$ 405.0597, found 405.0617.

*(3R,6′S)-6′-(4-Bromophenyl)-1-methyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4g**).* White solid; 52.2 mg, 86% yield; 85:15 dr, 92% ee; $[\alpha]_D^{20}$ +120.3 (c 1.41, $CHCl_3$); mp 59.7−61.1 °C; ee was determined by HPLC (Chiralpak AD-H, i-PrOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 10.9 min, t_{major} = 13.8 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.72 (s, 3H), 4.26−4.28 (m, 1H), 5.74 (dd, J = 2.4, 9.9 Hz, 1H), 6.15−6.17 (m, 2H), 6.30−6.32 (m, 1H), 6.54−6.57 (m, 1H), 6.75−6.82 (m, 3H), 7.15−7.23 (m, 3H), 7.31−7.37 (m, 1H), 7.50−7.53 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 51.1, 67.8, 108.1, 109.5, 110.2, 119.8, 120.2, 120.9, 121.5, 123.2, 124.3, 127.9, 129.6, 130.3, 130.7, 131.1, 136.1, 144.0, 172.1; HRMS (ESI-TOF) calcd for $C_{22}H_{17}BrN_2NaO$ $[M + Na]^+$ 427.0416, found 427.0411.

*(3R,6′S)-6′-(4-Fluorophenyl)-1-methyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4h**).* White solid; 39.6 mg, 77% yield; 83:17 dr, 94% ee; $[\alpha]_D^{20}$ +256.3 (c 1.47, $CHCl_3$); mp 177.5−178.6 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 6.6 min, t_{major} = 7.3 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.70 (s, 3H), 4.29−4.31 (m, 1H), 5.77 (dd, J = 2.4, 9.9 Hz, 1H), 6.14−6.17 (m, 2H), 6.29−6.34 (m, 1H), 6.51−6.55 (m, 1H), 6.72−6.89 (m, 5H), 7.17−7.23 (m, 1H), 7.30−7.33 (m, 1H), 7.51−7.54 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 51.0, 68.0, 108.0, 109.4, 110.1, 114.4 (d, J = 21.2 Hz, 1C), 119.8, 120.7 (d, J = 8.0 Hz, 1C), 123.1, 124.3, 128.1, 129.6, 130.2, 131.0, 131.1, 132.8 (d, J = 3.2 Hz, 1C), 144.1, 162.1 (d, J = 244.7 Hz, 1C), 172.3; HRMS (ESI-TOF) calcd for $C_{22}H_{17}FN_2NaO$ $[M + Na]^+$ 367.1217, found 367.1230.

*(3R,6′S)-1-Methyl-6′-(thiophen-2-yl)-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4i**).* White solid; 40.8 mg, 82% yield; 88:12 dr, 94% ee; $[\alpha]_D^{20}$ +197.8 (c 1.58, $CHCl_3$); mp 183.8−184.9 °C; ee was determined by HPLC (Chiralpak OD-H, i-PrOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 28.7 min, t_{major} = 10.3 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.79 (s, 3H), 4.59−4.61 (m, 1H), 5.87 (dd, J = 2.4, 9.9 Hz, 1H), 6.13−6.18 (m, 2H), 6.30−6.31 (m, 1H), 6.61−6.64 (m, 2H), 6.75−6.80 (m, 2H), 7.01−7.03 (m, 1H), 7.19−7.25 (m, 1H), 7.35−7.41 (m, 1H), 7.48−7.51 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.6, 46.6, 67.8, 107.9, 109.5, 110.1, 120.0, 120.6, 120.8, 121.4, 123.2, 124.3, 124.8, 126.2, 127.0, 128.3, 130.4, 139.2, 144.7, 172.1; HRMS (ESI-TOF) calcd for $C_{20}H_{16}N_2NaOS$ $[M + Na]^+$ 355.0876, found 355.0878.

*(3R,6′S)-1-Methyl-6′-(naphthalen-1-yl)-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4j**).* White solid; 39.5 mg, 70% yield; 92:8 dr, 95% ee; $[\alpha]_D^{20}$ +565.8 (c 1.07, $CHCl_3$); mp 182.0−183.1 °C; ee was determined by HPLC (Chiralpak OD-H, i-PrOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 24.2 min, t_{major} = 10.3 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.66 (s, 3H), 5.29−5.32 (m, 1H), 5.82 (dd, J = 2.7, 9.9 Hz, 1H), 6.19−6.21 (m, 2H), 6.23−6.28 (m, 1H), 6.36−6.38 (m, 1H), 6.89 (dd, J = 2.7, 9.9 Hz, 1H), 7.00−7.03 (m, 2H), 7.18−7.24 (m, 1H), 7.26−7.31 (m, 1H), 7.37−7.42 (m, 1H), 7.57−7.60 (m, 1H), 7.63−7.70 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 44.8, 68.5, 107.6, 109.2, 110.1,118.5, 119.5, 120.5, 121.8, 122.5, 122.6, 122.8, 124.8, 124.9, 125.1, 127.9, 128.1, 128.3, 129.8, 130.5, 131.5, 133.0, 133.8, 143.4, 173.0; HRMS (ESI-TOF) calcd for $C_{26}H_{20}N_2NaO$ $[M + Na]^+$ 399.1468, found 399.1462.

*(3R,6′R)-6′-((E)-2-Chlorostyryl)-1-methyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4k**).* White solid; 35.9 mg, 62% yield; >99:1 dr, 80% ee; $[\alpha]_D^{20}$ −47.6 (c 1.01, $CHCl_3$); mp 51.5−52.8 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 10.4 min, t_{major} = 11.7 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 3.10 (s, 3H), 3.84−3.89 (m, 1H), 5.73 (dd, J = 2.7, 9.9 Hz, 1H), 5.95 (dd, J = 9.0 Hz, 15.6 Hz,1H), 6.12−6.18 (m, 2H), 6.26−6.28 (m, 1H), 6.53(d, J = 15.6 Hz, 1H), 6.72 (dd, J = 2.7, 9.9 Hz, 1H), 6.81 (d, J = 7.8 Hz, 1H), 7.11−7.15 (m, 2H), 7.16−7.21 (m, 1H), 7.22−7.28 (m, 2H), 7.35−7.41 (m, 1H), 7.42−7.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 26.0, 48.5, 66.5, 108.3, 109.2, 110.0, 119.4, 119.7, 120.0, 123.4, 124.2, 126.7, 126.9, 128.0, 128.5, 128.6, 129.5, 130.1, 130.2, 130.8, 132.8, 134.9, 143.9, 172.7; HRMS (ESI-TOF) calcd for $C_{24}H_{20}ClN_2O$ $[M + H]^+$ 387.1259, found 387.1261.

*(3R,6′R)-1,6′-Dimethyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4l**).* White solid; 25.2 mg, 64% yield; 77:23 dr, 97% ee; $[\alpha]_D^{20}$ +60.6 (c 0.59, $CHCl_3$); mp 69.2−71.1 °C; ee was determined by HPLC (Chiralpak OD-H, i-PrOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 7.8 min, t_{major} = 8.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 0.76 (d, J = 7.2 Hz, 3H), 3.35 (s, 3H), 3.37−3.42 (m, 1H), 5.52 (dd, J = 2.4, 9.6 Hz, 1H), 6.07−6.09 (m, 1H), 6.17−6.20 (m, 1H), 6.30−6.32 (m, 1H), 6.60 (dd, J = 3.0, 9.6 Hz, 1H), 6.87−6.96 (m, 2H), 7.09−7.20 (m, 1H), 7.26−7.30 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 14.4, 26.6, 38.1, 68.0, 108.2, 108.4, 110.0, 119.3, 119.8, 123.1, 123.4, 124.4, 127.4, 129.3, 129.6, 141.7, 175.5; HRMS (ESI-TOF) calcd for $C_{17}H_{16}N_2NaO$ $[M + Na]^+$ 287.1155, found 287.1163.

*(3R,6′S)-6′-Phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4m**).* White solid; 33.7 mg, 72% yield; 92:8 dr, 92% ee; $[\alpha]_D^{20}$ +156.7 (c 1.18, $CHCl_3$); mp 211.4−212.5 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 10.7 min, t_{major} = 8.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 4.32−4.34 (m, 1H), 5.84 (dd, J = 2.4, 9.9 Hz, 1H), 6.14−6.16 (m, 2H), 6.29−6.31 (m, 1H), 6.58 (d, J = 7.8 Hz, 1H), 6.77 (dd, J = 3.0, 9.9 Hz, 1H), 6.92−6.96 (m, 2H), 7.05−7.10 (m, 2H), 7.13−7.21 (m, 2H), 7.23−7.29 (m, 1H), 7.49−7.52 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 51.4, 68.1, 109.3, 109.9, 110.2, 119.9, 120.4, 121.1, 123.1, 124.8, 127.5, 127.8, 128.8, 129.7, 130.1, 130.3, 136.9, 141.3, 174.6; HRMS (ESI-TOF) calcd for $C_{21}H_{16}N_2NaO$ $[M + Na]^+$ 335.1155, found 335.1166.

*(3R,6′S)-1-Ethyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4n**).* White solid; 43.7 mg, 86% yield; 72:28 dr, 96% ee; $[\alpha]_D^{20}$ +223.3 (c 0.85, $CHCl_3$); mp 130.2−131.5 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 6.2 min, t_{major} = 11.1 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 0.64 (t, J = 7.2 Hz, 3H) 3.07−3.12 (m, 1H), 3.44−3.49 (m, 1H), 4.34−4.36 (m, 1H), 5.86 (dd, J = 2.4, 9.9 Hz,1H), 6.14−6.16 (m, 2H), 6.29−6.35 (m, 1H), 6.51−6.57 (m, 1H), 6.80 (dd, J = 3.0, 9.9 Hz, 1H), 6.89−6.93 (m, 2H), 7.01−7.15 (m, 3H), 7.17−7.23 (m, 1H), 7.30−7.36 (m, 1H), 7.54−7.57 (m,1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 11.6, 34.0, 51.3, 67.8, 107.9, 109.0, 110.0, 119.6, 120.4, 121.1, 122.8, 124.7, 127.3, 127.7, 129.3, 129.6, 129.7, 130.0, 137.0, 143.5, 171.9; HRMS (ESI-TOF) calcd for $C_{23}H_{20}N_2NaO$ $[M + Na]^+$ 363.1468, found 363.1476.

*(3R,6′S)-1,6′-Diphenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4o**).* White solid; 44.2 mg, 76% yield; 83:17 dr, 96% ee; $[\alpha]_D^{20}$ +135.4 (c 1.47, $CHCl_3$); mp 92.3−93.9 °C; ee was determined by HPLC (Chiralpak OD-H, EtOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 19.1 min, t_{major} = 8.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 4.41−4.43 (m, 1H), 5.85−5.89 (m, 1H), 6.20−6.23 (m, 1H), 6.31−6.34 (m, 2H), 6.38−6.54 (m, 1H), 6.71 (d, J = 7.5 Hz, 2H), 6.81 (dd, J = 3.0, 9.9 Hz, 1H), 6.94−6.97 (m, 3H), 7.04−7.16 (m, 2H), 7.19−7.34 (m, 5H), 7.60−7.63 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 52.0, 68.1, 109.2, 109.3, 110.3, 119.8, 120.6, 120.9, 123.5, 124.7, 126.3, 127.5, 127.8, 127.9, 129.2, 129.8, 130.0, 133.5, 137.1, 144.3, 171.4; HRMS (ESI-TOF) calcd for $C_{27}H_{20}N_2NaO$ $[M + Na]^+$ 411.1468, found 411.1463.

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*(3R,6′S)-1-Benzyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4p**).* White solid; 45.2 mg, 75% yield; >99:1 dr, 96% ee; $[\alpha]_D^{20}$ +121.9 (*c* 1.50, $CHCl_3$); mp 120.1−121.4 °C; ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 16.6 min, t_{major} = 6.6 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 4.34 (d, *J* = 15.9 Hz, 1H), 4.46−4.47 (m, 1H), 4.65 (d, *J* = 15.9 Hz, 1H), 5.89 (dd, *J* = 2.4, 9.9 Hz, 1H), 6.13−6.14 (m, 1H), 6.18 (t, *J* = 3.3 Hz, 1H), 6.32−6.36 (m, 2H), 6.56 (d, *J* = 6.6 Hz, 2H), 6.83 (dd, *J* = 3.0, 9.9 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 2H), 7.08−7.25 (m, 8H), 7.57−7.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 43.5, 50.8, 67.9, 109.2, 109.4, 110.2, 119.6, 120.4, 121.4, 123.1, 124.6, 126.6, 127.2, 127.4, 128.0, 128.3, 128.5, 130.0, 130.1, 130.5, 134.9, 137.3, 143.6, 172.6; HRMS (ESI-TOF) calcd for $C_{28}H_{22}N_2NaO$ $[M + Na]^+$ 425.1624, found 425.1620.

*(3R,6′S)-1-Acetyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4q**).* White solid; 37.7 mg, 72% yield; >99:1 dr, 67% ee; $[\alpha]_D^{20}$ +105.1 (*c* 0.84, $CHCl_3$); mp 94.4−95.7 °C; ee was determined by HPLC (Chiralpak OJ-H, EtOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 30.1 min, t_{major} = 19.5 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ (major diastereomer) 2.19 (s, 3H), 4.45−4.47 (m, 1H), 5.77 (dd, *J* = 2.1, 9.9 Hz, 1H), 6.08−6.09 (m, 2H), 6.26−6.28 (m, 1H), 6.73−6.81 (m, 3H), 7.04−7.16 (m, 3H), 7.37−7.44 (m, 2H), 7.69−7.73 (m, 1H), 7.76−7.80 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (major diastereomer) 25.6, 51.5, 67.6, 109.3, 110.3, 115.3, 120.0, 120.4, 120.7, 124.9, 126.0, 126.9, 127.8, 129.0, 129.1, 130.4, 130.5, 136.2, 140.0, 169.2, 172.9; HRMS (ESI-TOF) calcd for $C_{23}H_{18}N_2NaO_2$ $[M + Na]^+$ 377.1260, found 377.1272.

*(3R,6′S)-5-Fluoro-1-methyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4r**).* White solid; 41.3 mg, 80% yield; 86:14 dr, 89% ee; $[\alpha]_D^{20}$ +105.0 (*c* 1.13, $CHCl_3$); mp 190.7−192.1 °C; ee was determined by HPLC (Chiralpak OD-H, EtOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 24.4 min, t_{major} = 8.8 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.66 (s, 3H), 4.25−4.28 (m, 1H), 5.82 (dd, *J* = 2.4, 9.9 Hz, 1H), 6.17−6.18 (m, 2H), 6.31−6.35 (m, 1H), 6.37−6.45 (m, 1H), 6.80 (dd, *J* = 3.0, 9.9 Hz, 1H), 6.92 (d, *J* = 6.9 Hz, 2H), 6.99−7.15 (m, 4H), 7.31 (dd, *J* = 2.4 Hz, 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 52.0, 68.4, 108.5 (d, *J* = 7.9 Hz, 1C), 109.4, 110.4, 112.3, 112.6, 116.4 (d, *J* = 23.3 Hz, 1C), 119.6, 120.6, 120.8, 127.5, 127.6, 129.3, 130.0 (d, *J* = 7.6 Hz, 1C), 130.6, 136.6, 140.1, 159.4 (d, *J* = 240.7 Hz, 1C), 172.1; HRMS (ESI-TOF) calcd for $C_{22}H_{17}FN_2NaO$ $[M + Na]^+$ 367.1217, found 367.1217.

*(3R,6′S)-5-Bromo-1-methyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4s**).* White solid; 45.6 mg, 75% yield; 87:13 dr, 91% ee; $[\alpha]_D^{20}$ +121.9 (*c* 1.53, $CHCl_3$); mp 140.5−142.1 °C; ee was determined by HPLC (Chiralpak AD-H, EtOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 7.5 min, t_{major} = 8.6 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.64 (s, 3H), 4.26−4.28 (m, 1H), 5.82 (dd, *J* = 2.4, 9.9 Hz, 1H), 6.18−6.19 (m, 2H), 6.31−6.34 (m, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.80 (dd, *J* = 3.0, 9.9 Hz, 1H), 6.89−6.92 (m, 2H), 7.07−7.18 (m, 3H), 7.44 (dd, *J* = 1.8, 8.4 Hz, 1H), 7.67−7.68 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 51.9, 68.2, 109.3, 109.5, 110.4, 115.4, 119.6, 120.6, 120.8, 127.5, 127.6, 127.7, 129.4, 130.5, 132.2, 132.9, 136.6, 143.2, 171.8; HRMS (ESI-TOF) calcd for $C_{22}H_{17}BrN_2NaO$ $[M + Na]^+$ 427.0416, found 427.0418.

*(3R,6′S)-1,5-Dimethyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4t**).* White solid; 39.8 mg, 78% yield; 80:20 dr, 94% ee; $[\alpha]_D^{20}$ +173.3 (*c* 1.25, $CHCl_3$); mp 66.9−68.5 °C; ee was determined by HPLC (Chiralpak OD-H, EtOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 14.5 min, t_{major} = 7.7 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.43 (s, 3H), 2.63 (s, 3H), 4.28−4.30 (m, 1H), 5.83 (dd, *J* = 2.4, 9.9 Hz, 1H), 6.15−6.19 (m, 2H), 6.29−6.31 (m, 1H), 6.36−6.40 (m, 1H), 6.77−6.82 (m, 1H), 6.87−6.95 (m, 2H), 7.02−7.15 (m, 4H), 7.36 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 21.2, 25.4, 51.8, 68.2, 107.6, 109.0, 109.9, 119.7, 120.5, 121.1, 125.0, 127.3, 127.5, 128.4, 129.4, 129.6, 130.3, 132.6, 137.1, 141.8, 172.3; HRMS (ESI-TOF) calcd for $C_{23}H_{20}N_2NaO$ $[M + Na]^+$ 363.1468, found 363.1463.

*(3R,6′S)-5-Chloro-1-methyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4u**).* White solid; 40.1 mg, 74% yield; 98:2 dr, 92% ee; $[\alpha]_D^{20}$ +214.1 (*c* 1.46, $CHCl_3$); mp 184.2−185.7 °C; ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 15/85, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 13.6 min, t_{major} = 6.6 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.65 (s, 3H), 4.26−4.28 (m, 1H), 5.82 (dd, *J* = 2.4, 9.9 Hz, 1H), 6.18−6.20 (m, 2H), 6.31−6.33 (m, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 6.80 (dd, *J* = 3.0, 9.9 Hz, 1H), 6.89−6.92 (m, 2H), 7.06−7.15 (m, 3H), 7.30 (dd, *J* = 2.1, 8.4 Hz, 1H), 7.54 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 51.9, 68.3, 108.8, 109.5, 110.4, 119.6, 120.6, 120.8, 124.8, 127.6, 127.7, 128.3, 129.4, 130.0, 130.2, 130.5, 136.6, 142.7, 171.9; HRMS (EI) calcd for $C_{22}H_{17}N_2OCl$ $[M]^+$ 360.1029, found 360.1020.

*(3R,6′S)-6-Chloro-1-methyl-6′-phenyl-6′H-spiro[indoline-3,5′-indolizin]-2-one (**4v**).* White solid; 42.2 mg, 78% yield; 90:10 dr, 94% ee; $[\alpha]_D^{20}$ +209.0 (*c* 1.62, $CHCl_3$); mp 237.5−238.9 °C; ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 35.1 min, t_{major} = 10.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 2.64 (s, 3H), 4.26−4.28 (m, 1H), 5.82 (dd, *J* = 2.1 Hz, 9.9 Hz, 1H), 6.16−6.17 (m, 2H), 6.30−6.32 (m, 1H), 6.49−6.51 (m, 1H), 6.80 (dd, *J* = 3.0, 9.9 Hz, 1H), 6.89−6.92 (m, 2H), 7.07−7.20 (m, 4H), 7.45 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 25.5, 51.8, 67.9, 108.6, 109.4, 110.3, 119.5, 120.6, 120.8, 122.8, 125.4, 126.7, 127.6, 127.7, 129.4, 130.6, 135.9, 136.6, 145.3, 172.3; HRMS (EI) calcd for $C_{22}H_{17}N_2OCl$ $[M]^+$ 360.1029, found 360.1035.

Transformation of Product 4a to 5. A mixture of **4a** (65.2 mg, 0.2 mmol) and 10% Pd/C (13 mg, 20%) in MeOH (15 mL) was stirred vigorously under an atmosphere of hydrogen at room temperature for 12 h. Then, the mixture was filtered through a Celite plug, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to furnish compond **5** as a white solid.

*(3R,6′S)-1-Methyl-6′-phenyl-7′,8′-dihydro-6′H-spiro[indoline-3,5′-indolizin]-2-one (**5**).* 30.2 mg, 46% yield; 93:7dr, 96% ee; $[\alpha]_D^{20}$ +295.6 (*c* 0.63, $CHCl_3$); mp 172.2−173.1 °C; ee was determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, major diastereomer t_{minor} = 6.4 min, t_{major} = 8.8 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ (major diastereomer) 1.91−1.98 (m, 1H), 2.77 (s, 3H), 3.01−3.08 (m, 1H), 3.20−3.34 (m, 2H), 3.48 (d, *J* = 12.9 Hz, 1H), 5.98−6.02 (m, 2H), 6.07−6.12 (m, 1H), 6.48 (d, *J* = 7.8 Hz, 1H), 6.81−6.88 (m, 2H), 7.00−7.19 (m, 4H), 7.22−7.28 (m, 1H), 7.40 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (major diastereomer) 22.3, 23.7, 25.7, 50.9, 67.8, 105.2, 107.8, 109.3, 117.2, 122.9, 124.0, 127.2, 127.4, 128.5, 128.7, 129.3, 129.7, 130.5, 137.6, 143.6, 174.1; HRMS (ESI-TOF) calcd for $C_{22}H_{20}N_2NaO$ $[M + Na]^+$ 351.1468, found 351.1477.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H, ^{13}C NMR, and HPLC spectra for new products and single crystal X-ray crystallography data for product **4s**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00597.

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Notes

The authors declare no competing financial interest.

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