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Organocatalytic Asymmetric Michael/Cyclization Cascade Reactions of 3-Hydroxyoxindoles/3-Aminooxindoles with α,β-Unsaturated Acyl Phosphonates for the Construction of Spirocyclic Oxindole-γ-lactones/lactams

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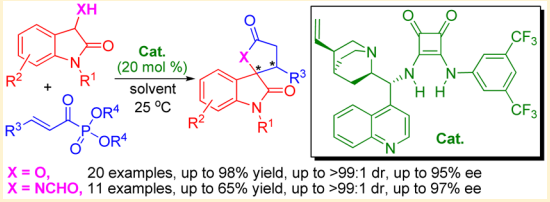
Supporting Information

ABSTRACT: Enantioselective Michael/cyclization cascade reactions of 3-hydroxyoxindoles/3-aminooxindoles with α,β-unsaturated acyl phosphonates by using a cinchonine derived squaramide as the catalyst were developed. A broad range of spirocyclic oxindole-γ-lactones/lactams could be obtained in moderate to excellent yields (up to 98%) with good to excellent diastereo- and enantioselectivities (up to >99:1 dr and 97% ee) under mild conditions. This work represents the first example about the α,β-unsaturated acyl phosphonates for the asymmetric construction of spirocyclic oxindoles.



Optically active spirocyclic oxindoles are common structural motifs in a variety of architecturally complex natural products and pharmaceutical moleculars.[1] A large number of elegant synthetic methods for the construction of the privileged spirocyclic scaffolds have been documented over the past decade.[2] In particular, the catalytic asymmetric synthesis of chiral spirocyclic oxindole-γ-lactones/lactams has attracted great attention from scientists,[3] and various creative strategies have been established, including NHC-catalyzed [3 + 2] annulations of α,β-unsaturated aldehydes with isatins[3a−d] or isatinimines[3g,h] and Michael/cyclization of 3-hydroxyoxindoles with α,β-unsaturated aldehydes[3e] or α,β-unsaturated esters.[3f] However, with a literature survey, we noticed that using α,β-unsaturated acyl phosphonates as Michael acceptors for the synthesis of spirocyclic oxindole compounds has not been exploited. In this context, considering the importance of the spirocyclic oxindoles in pharmaceutical science, it is conceivable that the development of an efficient method to access structurally diverse spirocyclic oxindole-γ-lactones/lactams by using α,β-unsaturated acyl phosphonates will be desirable and meaningful.

α,β-Unsaturated acyl phosphonates were widely employed in catalytic asymmetric synthesis[4] and commonly played a role as activated ester surrogates for generating ester or amide compounds by using the lability of the C−P bond (Scheme 1).[5] Recently, our group developed a chiral squaramide-catalyzed asymmetric Michael addition of 3-monosubstituted oxindoles to α,β-unsaturated acyl phosphonates, giving a series of 3,3′-disubstituted oxindole derivatives in good results.[6] On the other hand, 3-hydroxyoxindoles/3-aminooxindoles containing two reactive sites have been successfully applied in some asymmetric reactions.[7] Nevertheless, we also demonstrated that 3-hydroxyoxindoles/3-aminooxindoles could serve as a type of special nucleophiles for the synthesis of 3,3′-disubstituted oxindoles and spirooxindoles.[8] In this context, as part of our ongoing investigations aimed at developing new strategies for the construction of structurally diverse spirocyclic oxindole compounds,[9] we envisioned that a catalytic asymmetric Michael/cyclization cascade reaction of 3-hydroxyoxindoles/3-aminooxindoles with α,β-unsaturated acyl phosphonates would be realized under certain asymmetric conditions and would allow us to produce a chiral acyl phosphonate intermediate (Scheme 1). Subsequently, this intermediate will preferentially undergo an intramolecular cyclization reaction via acyl-transfer process, thus leading to a class of spirocyclic oxindole-γ-lactones/lactams (Scheme 1). Importantly, this work represents the first example of α,β-unsaturated acyl phosphonates used in catalytic asymmetric reactions for the construction of spirocyclic oxindole compounds. Herein, we wish to report our studies about this subject.

Our investigations began with the screening of various chiral bifunctional cinchona alkaloid derived squaramides **4a−d**, as shown in Table 1. The reaction of *N*-methyl-3-hydroxyoxindole

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Scheme 1. Design Strategy for the Construction of Spirocyclic Oxindole-γ-lactones/lactams

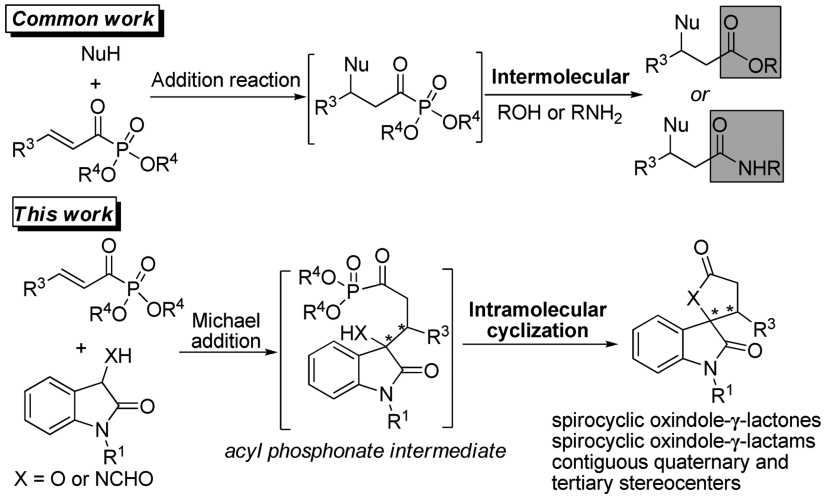
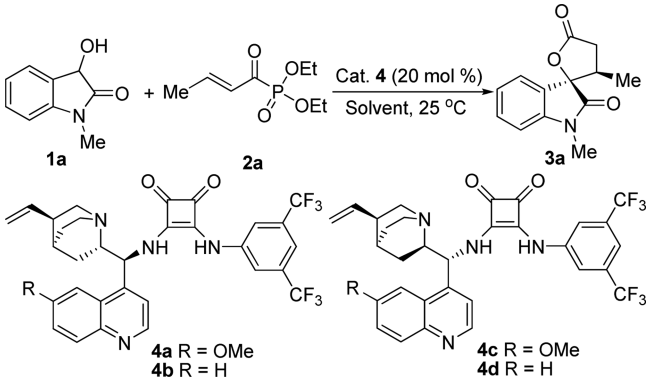


Table 1. Conditions Optimization[a]



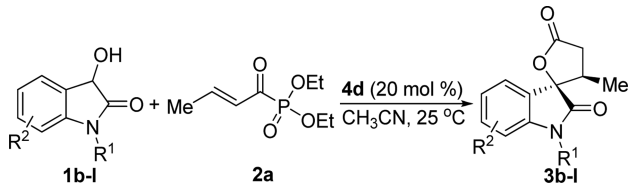
entry	cat.	solvent	time (h)	yield[b] (%)	dr[c]	ee[c] (%)
1	**4a**	DCM	9	53	>99:1	92[d]
2	**4b**	DCM	9	46	99:1	93[d]
3	**4c**	DCM	9	39	>99:1	94
4	**4d**	DCM	9	51	>99:1	94
5	**4d**	$CHCl_3$	9	53	97:3	94
6	**4d**	DCE	9	55	>99:1	93
7	**4d**	toluene	6	38	94:6	85
8	**4d**	C_6H_5Cl	6	43	95:5	87
9	**4d**	THF	3	54	>99:1	94
10	**4d**	Et_2O	3	41	97:3	92
11	**4d**	CH_3CN	3	70	>99:1	94
12[e]	**4d**	CH_3CN	27	81	99:1	94
13[f]	**4d**	CH_3CN	27	96	99:1	94

[a]Unless otherwise noted, all reactions were performed with **1a** (0.1 mmol), **2a** (0.1 mmol), and **4** (20 mol %) in solvent (2.0 mL). [b]Isolated yield. [c]Determined by chiral HPLC. [d]Contrary configuration to **3a**. [e]**1a**:**2a** = 1:1.5. [f]**1a**:**2a** = 1:2. DCE = 1,2-dichloroethane.

1a with diethyl but-2-enoylphosphonate **2a** could proceed to completion within 9 h in dichloromethane (DCM) at 25 °C with 20 mol % catalyst **4a**, affording the desired spirocyclic oxindole-γ-lactone **3a** in 53% yield with >99:1 dr and 92% ee (entry 1). Other squaramides **4b**–**d** gave comparable results (entries 2–4). By comparison, cinchonine derived squaramide **4d** offered the best results (entry 4). Afterward, a series of solvents including halohydrocarbons, arenes, ethers, and acetonitrile were evaluated (entries 5–11). It was found that acetonitrile was the suitable solvent and gave the product **3a** in 70% yield with >99:1 dr and 94% ee (entry 11). To further improve the yield, the molar ratio of **1a** to **2a** was also investigated (entries 12–13). It was observed that when 2.0 equiv of **2a** was used, the yield increased to 96% without erosion in the diastereo- and enantioselectivity (entry 13). Unfortunately, trying to reduce the catalyst loading to 10 and 5 mol %, results worse than that with 20 mol % catalyst were obtained (not shown). Accordingly, in light of the above surveys, the optimal reaction conditions of 0.1 mmol **1a** and 2.0 equiv of **2a** in 2 mL acetonitrile with 20 mol % of **4d** at 25 °C were established.

With the optimal reaction conditions in hand, the substrate scope was explored, and the results are summarized in Table 2. Various substituted 3-hydroxyoxindoles **1b**–**l** were examined by reacting with α,β-unsaturated acyl phosphonate **2a**, and the desired spirocyclic oxindole-γ-lactones **3b**–**l** were obtained in

Table 2. Scope of Asymmetric Michael/Cyclization Cascade Reaction of 3-Hydroxyoxindoles 1 with α,β-Unsaturated Acyl Phosphonate 2a[a]



entry	R^1/R^2	time (h)	3	yield[b] (%)	dr[c]	ee[c] (%)
1	^{i}Pr/H (**1b**)	30	**3b**	94	97:3	87
2	^{n}Bu/H (**1c**)	30	**3c**	96	99:1	94
3	^{i}Bu/H (**1d**)	30	**3d**	98	99:1	95
4	Allyl/H (**1e**)	16	**3e**	90	99:1	93
5	Bn/H (**1f**)	30	**3f**	98	99:1	95
6	Ph/H (**1g**)	28	**3g**	92	99:1	95
7	H/H (**1h**)	28	**3h**	94	98:2	95
8	Me/5-Me (**1i**)	30	**3i**	82	>99:1	93
9	Me/5-F (**1j**)	8	**3j**	89	>99:1	95
10	Me/5-Br (**1k**)	8	**3k**	97	>99:1	95
11	Me/6-Cl (**1l**)	8	**3l**	91	99:1	94

[a]Unless otherwise noted, all reactions were performed with **1** (0.1 mmol), **2a** (0.2 mmol), and **4d** (20 mol %) in CH_3CN (2.0 mL). [b]Isolated yield. [c]Determined by chiral HPLC.

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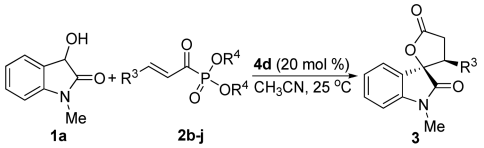
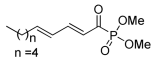
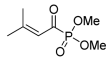
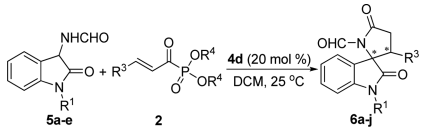
Table 3. Scope of Asymmetric Michael/Cyclization Cascade Reaction *N*-Methyl-3-hydroxyoxindole 1a to *α,β*-Unsaturated Acyl Phosphonates 2[a]

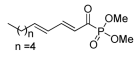
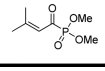


entry	R^3/R^4	Time (h)	3	yield[b] (%)	dr[c]	ee[c] (%)
1	Me/Me (**2b**)	24	**3a**	87	99:1	94
2	Me/^{i}Pr (**2c**)	33	**3a**	92	99:1	94
3	Me/^{n}Bu (**2d**)	33	**3a**	97	99:1	94
4	^{n}Pr/^{n}Bu (**2e**)	35	**3m**	94	98:2[d]	95
5	^{n}Pr/Me (**2f**)	35	**3m**	88	96:4[d]	94
6	Ph/Me (**2g**)	24	**3n**	90	81:19	71
7	2-furyl/Me (**2h**)	24	**3o**	96	92:8	78
8	 (**2i**)	24	**3p**	88	95:5[d]	93
9	 (**2j**)	72	**3q**	33	-	89

[a]Unless otherwise noted, all reactions were performed with **1a** (0.1 mmol), **2** (0.2 mmol) and **4d** (20 mol %) in CH_3CN (2.0 mL). [b]Isolated yield. [c]Determined by chiral HPLC. [d]Dr values were determined by ^{1}H NMR analysis of crude reaction mixture.

Table 4. Scope of the Asymmetric Michael/Cyclization Cascade Reaction of 3-Aminooxindoles 5 to *α,β*-Unsaturated Acyl Phosphonates 2[a]



entry	R^1	R^3/R^4	Time (h)	6	yield[b] (%)	dr[c]	ee (%)[c]
1[d]	Me (**5a**)	Me/Et (**2a**)	20	**6a**	11	94:6	90
2	Me (**5a**)	Me/Et (**2a**)	20	**6a**	51	98:2	96
3	Et (**5b**)	Me/Et (**2a**)	29	**6b**	49	>99:1[e]	97
4	Bn (**5c**)	Me/Et (**2a**)	29	**6c**	60	98:2	97
5	Ph (**5d**)	Me/Et (**2a**)	29	**6d**	31	92:8	96
6	H (**5e**)	Me/Et (**2a**)	29	**6e**	55	98:2	96
7	Bn (**5c**)	Me/Me (**2b**)	29	**6c**	65	98:2	94
8	Bn (**5c**)	^{n}Pr/Me (**2f**)	48	**6f**	41	98:2	93
9	Bn (**5c**)	Ph/Me (**2g**)	48	**6g**	55	94:6	88
10	Bn (**5c**)	2-furyl/Me (**2h**)	48	**6h**	51	99:1	95
11	Bn (**5c**)	 (**2i**)	48	**6i**	31	92:8	94
12	Bn (**5c**)	 (**2j**)	120	**6j**	35	-	85

[a]Unless otherwise noted, all reactions were performed with **5** (0.1 mmol), **2** (0.2 mmol), and **4d** (20 mol %) in DCM (2.0 mL). [b]Isolated yield. [c]Determined by chiral HPLC. [d]Acetonitrile was used as a solvent. [e]Dr value was determined by ^{1}H NMR analysis of crude reaction mixture.

82−98% yields with up to >99:1 dr and 87−95% ee. It was found that the substituents R^1 on N atom of 3-hydroxyoxindoles had slight effects on the reactivities and stereoselectivities. Both aliphatic and aromatic substituents on N atom of 3-hydroxyoxindoles **1b−g** were tolerated, affording the desired spirocyclic oxindole-*γ*-lactones in 90−98% yields, 97:3−99:1 dr, and 87−95% ee (entries 1−6). Gratifyingly, the reaction of 3-hydroxyoxindole **1h** without N-protecting group proceeded well to provide spirocyclic oxindole-*γ*-lactone **3h** in good yield and excellent ee value (entry 7). Furthermore,

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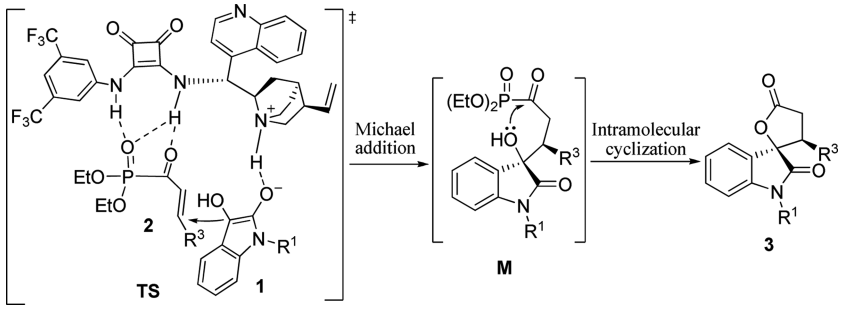
Scheme 2. A Proposed Transition State for This Transformation



electron-donating and electron-withdrawing substituents on the aromatic ring of 3-hydroxyoxindoles with different positions were investigated, and the corresponding products were obtained in high yields (up to 97% yield) with excellent diastereoselectivities (up to >99:1 dr) and enantioselectivities (up to 95% ee) (entries 8−11). The absolute configuration of the major isomer **3k** was assigned as (C7R, C9R) through the single crystal X-ray analysis (see the Supporting Information). The stereochemistry of the other products in Tables 2 and 3 was assigned by analogy.[10]

To further investigate the scope of the asymmetric reaction, we focused on the examinations of α,β-unsaturated acyl phosphonates **2b−j** with **1a** as the donor (Table 3). The substituents R^4 of acyl phosphonates were first tested. It was found that substituents R^4 of esters only slightly affected the yields, providing the desired **3a** in good to excellent yields with excellent stereoselectivities (entries 1−3). The introduction of bulky alkyl substituents to the β-position of α,β-unsaturated acyl phosphonates led to comparable results (entry 4 vs 3 and entry 5 vs 1). However, aromatic groups had obvious effects on the stereoselectivities and furnished the desired products in good yields with acceptable ee values (entries 6 and 7). This protocol was also broadened to conjugated unsaturated acyl phosphonate **2i**, and good result was obtained (entry 8). In addition, hindered β-disubstituted acyl phosphonate **2j** could also react with **1a**, but provided **3q** in only 33% yield with 89% ee (entry 9).

Inspired by the above-achieved results, we next directed our efforts to the task of constructing spirocyclic oxindole-γ-lactams. As shown in Table 4, the reaction of 3-aminooxindole **5a** with α,β-unsaturated acyl phosphate **2a** was conducted in acetonitrile with **4d** as the catalyst, and the desired spirocyclic oxindole-γ-lactam **6a** was obtained in poor yield but with good stereoselectivity (Table 4, entry 1). However, to our delight, replacing acetonitrile with dichloromethane obviously led to a set of improved results (entry 2). Then, we explored the generality of the Michael/cyclization cascade reaction with respect to various 3-aminooxindoles **5** and α,β-unsaturated acyl phosphonates **2**. First, a variety of 3-aminooxindoles **5b−e** bearing different substituent groups on N atom were examined by reacting with diethyl but-2-enoylphosphonate **2a** (entries 3−6). It was found that both aliphatic and aromatic substituents were tolerated, furnishing the desired products **6b−d** in moderate yields (31−60%) with excellent diastereoselectivities (up to >99:1 dr) and enantioselectivities (96−97% ee) (entries 3−5). Additionally, 3-aminooxindole **5e**, without N-protecting group, could also react with **2a** and afforded the corresponding product **6e** in 55% yield with 98:2 dr and 96% ee (entry 6). On the other hand, a survey of α,β-unsaturated acyl phosphonates was also conducted. α,β-Unsaturated acyl phosphonate **2b** reacting with **5c** smoothly afforded 65% yield, albeit with slightly lower enantioselectivity (entry 7). It was observed that the substituents R^3 at the β-position of acyl phosphonates had a slight effect on the yields and enantioselectivities and acceptable results could be obtained regardless of aliphatic and aromatic groups (entries 8−10). Furthermore, the conjugated unsaturated acyl phosphonate **2i** was found to be compatible for giving **6i** with 94% ee (entry 11). Moreover, when β-disubstituted acyl phosphonate **2j** was used as an acceptor, the expected product **6j** was furnished in 35% yield and 85% ee (entry 12).

Based on our experiment results and the absolute configuration of the major isomer **3k**, a possible reaction mechanism has been tentatively proposed. As shown in Scheme 2, with the dual activation of catalyst **4d**, the 3-hydroxyoxindoles **1** as the Michael donors were enolized by the tertiary amine moiety. Synchronously, the α,β-unsaturated acyl phosphonates **2** as acceptors were directed by the squaramide motif through a hydrogen-bonding interaction. And then, the enolized oxindole (from *Si* face) would attack the α,β-unsaturated acyl phosphonate (to *Re* face) to generate the chiral acyl phosphonate intermediate **M**. And then, the intermediate **M** will further undergo an intramolecular cyclization reaction via acyl-transfer process, resulting spirocyclic oxindole-γ-lactones **3** (Scheme 2).

In summary, we have developed a highly enantioselective Michael/cyclization cascade reaction of 3-hydroxyoxindoles/3-aminooxindoles with α,β-unsaturated acyl phosphonates catalyzed by a cinchonine derived quaramide catalyst. With this developed protocol, a broad range of spirocyclic oxindole-γ-lactones/lactams could be obtained in moderate to excellent yields (up to 97%), with good to excellent diastereo- and enantioselectivities (up to >99:1 dr and 97% ee) under mild conditions. Notably, this work represents the first example of α,β-unsaturated acyl phosphonates used in catalytic asymmetric reactions for the generation of spirocyclic γ-lactones/lactams.

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR and ^{13}C NMR (300 and 75 MHz, respectively) spectra were recorded in $CDCl_3$. ^{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). Data are reported as the follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm). Melting points were recorded on a Buchi Melting Point B-545.

3-hydroxyoxindoles[3e] (**1a−l**), 3-aminooxindoles[8a,11] (**5a−e**), and α,β-unsaturated acyl phosphonates[5a,12] (**2a−j**) were prepared according to the reported procedures or similarly. Unless otherwise

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noted, materials were purchased from commercial suppliers and used without further purification. All reactions have been carried out with distilled and degassed solvents in oven-dried glassware.

General Procedure for the Synthesis of Spirocyclic Oxindole-γ-lactones 3. Under the protection of nitrogen, an oven-dried 20 mL reaction tube was charged with 3-hydroxyoxindole **1** (0.1 mmol, 1.0 equiv), catalyst **4d** (0.02 mmol, 20 mol %), and CH_3CN (1.0 mL). After 10 min of stirring at 25 °C, α,β-unsaturated acyl phosphonate **2** (0.2 mmol, 2.0 equiv) in CH_3CN (1.0 mL) was added. The stirring was maintained at the same temperature until the total consumption of 3-hydroxyoxindoles **1** (monitored by TLC). The crude reaction mixture was diluted with CH_2Cl_2 and filtered through a pad of silica gel. The solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to give the desired products **3**.

*(2R,3R)-1′,3-Dimethyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3a**).*[3e,f] White solid; 22.2 mg, 96% yield; 99:1 dr, 94% ee. The ee was determined by HPLC (Chiralpak OD-H column, EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 11.2 min, t_{minor} = 14.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, J = 6.5 Hz, 3H), 2.72 (dd, J = 7.4 Hz, J = 15.6, 1H), 2.85−2.95 (m, 1H), 3.03 (dd, J = 12.5 Hz, J = 15.5 Hz, 1H), 3.20 (s, 3H), 6.86 (d, J = 7.8 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 7.4 Hz, 1H), 7.40 (td, J = 1.1 Hz, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 26.2, 35.0, 40.2, 86.1, 108.6, 123.5, 124.2, 124.8, 131.2, 144.6, 173.0, 175.4; HRMS (ESI-TOF) calcd for $C_{13}H_{13}NNaO_3$ $[M + Na]^+$: 254.0788, found 254.0777.

*(2R,3R)-1′-Isopropyl-3-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3b**).* Colorless oil; 24.4 mg, 94% yield; 97:3 dr, 87% ee; $[\alpha]_D^{20}$ = +54.8 (c = 0.73, $CHCl_3$). The ee was determined by HPLC (Chiralpak OJ-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.9 min, t_{minor} = 7.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, J = 6.5 Hz, 3H), 1.48 (dd, J = 4.6 Hz, J = 7.0 Hz, 6H), 2.70 (dd, J = 7.6 Hz, J = 15.7 Hz, 1H), 2.78−2.89 (m, 1H), 3.01 (d, J = 12.3 Hz, J = 15.7 Hz, 1H), 4.47−4.56 (m, 1H), 6.99 (d, J = 7.9 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.33−7.39 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.4, 19.1, 19.5, 34.9, 40.7, 44.3, 85.8, 110.0, 122.9, 124.4, 125.2, 130.8, 143.2, 172.7, 175.6; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NNaO_3$ $[M + Na]^+$: 282.1101, found 282.1094.

*(2R,3R)-1′-Butyl-3-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3c**).* Colorless oil; 26.2 mg, 96% yield; 99:1 dr, 94% ee; $[\alpha]_D^{20}$ = +64.0 (c = 0.79, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.8 min, t_{minor} = 8.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J = 7.3 Hz, 3H), 1.00 (d, J = 6.5 Hz, 3H), 1.32−1.44 (m, 2H), 1.60−1.70 (m, 2H), 2.72 (dd, J = 7.4 Hz, J = 15.7 Hz, 1H), 2.84−2.93 (m, 1H), 3.02 (dd, J = 15.6 Hz, J = 12.5 Hz, 1H), 3.54−3.63 (m, 1H), 3.71−3.80 (m, 1H), 6.86 (d, J = 7.8 Hz, 1H), 7.12 (td, J = 0.8 Hz, J = 7.6 Hz, 1H), 7.33−7.41 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 13.7, 20.0, 29.4, 35.0, 39.8, 40.3, 86.0, 108.9, 123.2, 124.3, 124.9, 131.1, 144.0, 172.9, 175.6; HRMS (ESI-TOF) calcd for $C_{16}H_{19}NNaO_3$ $[M + Na]^+$: 296.1257, found 296.1254.

*(2R,3R)-1′-Isobutyl-3-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3d**).* Colorless oil; 26.7 mg, 98% yield; 99:1 dr, 95% ee; $[\alpha]_D^{20}$ = +68.3 (c = 0.96, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.9 min, t_{minor} = 11.6 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (dd, J = 1.7 Hz, J = 6.7 Hz, 6H), 1.02 (d, J = 6.5 Hz, 3H), 2.05−2.17 (m, 1H), 2.72 (dd, J = 7.3 Hz, J = 15.6 Hz, 1H), 2.84−2.97 (m, 1H), 3.03 (dd, J = 15.5 Hz, J = 12.5 Hz, 1H), 3.36 (dd, J = 7.3 Hz, J = 13.9 Hz, 1H), 3.59 (dd, J = 7.7 Hz, J = 14.0 Hz, 1H), 6.86 (d, J = 7.9 Hz, 1H), 7.12 (td, J = 0.8 Hz, J = 7.6 Hz, 1H), 7.33−7.40 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.8, 20.2, 20.2, 27.0, 35.0, 40.1, 47.7, 85.9, 109.1, 123.2, 124.3, 124.8, 131.1, 144.5, 173.3, 175.5; HRMS (ESI-TOF) calcd for $C_{16}H_{19}NNaO_3$ $[M + Na]^+$: 296.1257, found 296.1253.

*(2R,3R)-1′-Allyl-3-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3e**).* Colorless oil; 23.2 mg, 90% yield; 99:1 dr, 93% ee; $[\alpha]_D^{20}$ = +57.5 (c = 0.79, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 50/50, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.1 min, t_{minor} = 10.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (d, J = 6.5 Hz, 3H), 2.73 (dd, J = 7.1 Hz, J = 15.5 Hz, 1H); 2.84−2.97 (m, 1H), 3.03 (dd, J = 15.4 Hz, J = 12.5 Hz, 1H); 4.19 (dd, J = 5.3 Hz, J = 16.4 Hz, 1H), 4.43 (dd, J = 5.1 Hz, J = 16.4 Hz, 1H), 5.20−5.26 (m, 2H), 5.75−5.87 (m, 1H), 6.85 (d, J = 7.7 Hz, 1H), 7.13 (t, J = 7.0 Hz, 1H), 7.34−7.39 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 34.9, 40.3, 42.3, 86.0, 109.5, 117.9, 123.5, 124.3, 124.7, 130.7, 131.1, 143.7, 172.8, 175.5; HRMS (ESI-TOF) calcd for $C_{15}H_{15}NNaO_3$ $[M + Na]^+$: 280.0944, found 280.0940.

*(2R,3R)-1′-Benzyl-3-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3f**).* White solid; 30.1 mg, 98% yield; 99:1 dr, 95% ee; $[\alpha]_D^{20}$ = +48.5 (c = 0.78, $CHCl_3$); Mp: 145.1−146.3 °C. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 50/50, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 9.1 min, t_{minor} = 37.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, J = 6.5 Hz, 3H), 2.76 (dd, J = 7.3 Hz, J = 15.6 Hz, 1H), 2.90−2.98 (m, 1H), 3.07 (dd, J = 15.5 Hz, J = 12.5 Hz, 1H), 4.74 (d, J = 15.7 Hz, 1H), 5.02 (d, J = 15.7 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 7.10 (td, J = 0.8 Hz, J = 7.7 Hz, 1H), 7.25−7.37 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.8, 35.0, 40.3, 43.9, 86.0, 109.7, 123.5, 124.3, 124.7,127.2, 127.9, 128.9, 131.1, 135.0, 143.7, 173.2, 175.5; HRMS (ESI-TOF) calcd for $C_{19}H_{17}NNaO_3$ $[M + Na]^+$: 330.1101, found 330.1090.

*(2R,3R)-3-Methyl-1′-phenyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3g**).* White solid; 27.0 mg, 92% yield; 99:1 dr, 95% ee; $[\alpha]_D^{20}$ = +74.9 (c = 0.91, $CHCl_3$); Mp: 183.2−184.1 °C. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 50/50, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.3 min, t_{minor} = 12.3 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (d, J = 6.4 Hz, 3H), 2.76 (dd, J = 6.2 Hz, J = 14.6 Hz, 1H), 2.93−3.10 (m, 2H), 6.84 (d, J = 7.9 Hz, 1H), 7.18 (t, J = 7.9 Hz, 1H), 7.31−7.46 (m, 5H), 7.51−7.56 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 34.8, 40.9, 86.1, 109.9, 124.0, 124.5, 126.3, 128.6, 129.8, 129.8, 131.0, 133.3, 144.4, 172.4, 175.4; HRMS (ESI-TOF) calcd for $C_{18}H_{15}NNaO_3$ $[M + Na]^+$: 316.0944, found 316.0931.

*(2R,3R)-3-Methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3h**).* Colorless oil; 20.5 mg, 94% yield; 98:2 dr, 95% ee; $[\alpha]_D^{20}$ = +53.1 (c = 0.71, $CHCl_3$). The ee was determined by HPLC (Chiralpak OJ-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 9.9 min, t_{minor} = 6.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (d, J = 6.3 Hz, 3H), 2.75 (dd, J = 6.4 Hz, J = 14.6 Hz, 1H), 2.86−3.03 (m, 2H), 6.93 (d, J = 7.9 Hz, 1H), 7.11 (t, J = 7.5 Hz, 1H), 7.31−7.36 (m, 2H), 8.63 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 34.9, 40.4, 86.5, 110.7, 123.5, 124.5, 125.1, 131.2, 141.6, 175.5, 175.7; HRMS (ESI-TOF) calcd for $C_{12}H_{11}NNaO_3$ $[M + Na]^+$: 240.0631, found 240.0627.

*(2R,3R)-1′,3,5′-Trimethyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3i**).* Colorless oil; 20.0 mg, 82% yield; >99:1 dr, 93% ee; $[\alpha]_D^{20}$ = +60.4 (c = 0.87, $CHCl_3$). The ee was determined by HPLC (Chiralpak OD-H column, EtOH/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 7.7 min, t_{minor} = 8.7 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, J = 6.5 Hz, 3H), 2.34 (s, 3H), 2.71 (dd, J = 7.4 Hz, J = 15.7 Hz, 1H), 2.83−2.92 (m, 1H), 3.02 (dd, J = 15.6 Hz, J = 12.5 Hz, 1H), 3.17 (s, 3H), 6.74 (d, J = 7.8 Hz, 1H), 7.16 (s, 1H) 7.18 (d, J = 10.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 21.0, 26.2, 35.0, 40.2, 86.2, 108.4, 124.7, 125.0, 131.3, 133.2, 142.1, 173.0, 175.6; HRMS (ESI-TOF) calcd for $C_{14}H_{15}NNaO_3$ $[M + Na]^+$: 268.0944, found 268.0935.

*(2R,3R)-5′-Fluoro-1′,3-dimethyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3j**).* White solid; 22.1 mg, 89% yield; >99:1 dr, 95% ee; $[\alpha]_D^{20}$ = +77.0 (c = 0.73, $CHCl_3$); Mp: 212.5−213.3 °C. The ee was determined by HPLC (Chiralpak OD-H column, *i*PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 7.3 min, t_{minor} = 8.0 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, J = 6.5 Hz, 3H), 2.72 (dd, J = 7.5 Hz, J = 15.5 Hz, 1H), 2.81−2.90 (m, 1H), 3.01 (dd, J = 15.4 Hz, J = 12.1 Hz, 1H), 3.18 (s, 3H), 6.80 (dd, J = 3.9 Hz, J = 9.2 Hz, 1H), 7.08−7.14 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 26.3, 34.7, 40.4, 85.8, 109.4 (d, J = 7.9 Hz), 112.5 (d, J

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= 25.1 Hz), 117.5 (d, J = 23.4 Hz), 126.3 (d, J = 8.0 Hz), 140.4, 159.5 (d, J = 241.6 Hz), 172.8, 175.1; HRMS (ESI-TOF) calcd for $C_{13}H_{12}FNNaO_3$ $[M + Na]^+$: 272.0693, found 272.0689.

*(2R,3R)-5′-Bromo-1′,3-dimethyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3k**).* White solid; 30.2 mg, 97% yield; >99:1 dr, 95% ee; $[\alpha]_D^{20}$ = +57.2 (c = 0.76, $CHCl_3$); Mp: 206.3−207.2 °C. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 50/50, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.6 min, t_{minor} = 12.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, J = 6.4 Hz, 3H), 2.72 (dd, J = 7.1 Hz, J = 15.3 Hz, 1H), 2.82−2.93 (m, 1H), 2.99 (dd, J = 15.2 Hz, J = 12.3 Hz, 1H), 3.17 (s, 3H), 6.75 (d, J = 8.3, 1H), 7.47 (d, J = 1.7, 1H), 7.52 (dd, J = 1.9 Hz, J = 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 26.3, 34.7, 40.2, 85.6, 110.1, 116.0, 126.7, 127.5, 133.9, 143.5, 172.5, 175.0; HRMS (ESI-TOF) calcd for $C_{13}H_{12}BrNNaO_3$ $[M + Na]^+$: 331.9893, found 331.9879.

*(2R,3R)-6′-Chloro-1′,3-dimethyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3l**).* White solid; 24.1 mg, 91% yield; 99:1 dr, 94% ee; $[\alpha]_D^{20}$ = +37.4 (c = 0.78, $CHCl_3$); Mp: 159.3−159.9 °C. The ee was determined by HPLC (Chiralpak OD-H column, EtOH/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 8.6 min, t_{minor} = 10.1 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, J = 6.5 Hz, 3H), 2.72 (dd, J = 7.3 Hz, J = 15.5 Hz, 1H), 2.82−2.92 (m, 1 H), 3.00 (dd, J = 15.4 Hz, J = 12.3 Hz, 1H), 3.18 (s, 3H), 6.86 (d, J = 1.7 Hz, 1H), 7.11 (dd, J = 1.8 Hz, J = 8.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 26.3, 34.8, 40.2, 85.5, 109.5, 123.1, 123.4, 125.2, 137.1, 145.7, 173.0, 175.1; HRMS (ESI-TOF) calcd for $C_{13}H_{12}ClNNaO_3$ $[M + Na]^+$: 288.0398, found 288.0387.

*(2R,3R)-1′-Methyl-3-propyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3m**).* Colorless oil; 24.4 mg, 94% yield; 98:2 dr, 95% ee; $[\alpha]_D^{20}$ = +36.8 (c = 0.80, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 6.7 min, t_{minor} = 9.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (t, J = 7.1 Hz, 3H), 1.12−1.25 (m, 3H), 1.38−1.45 (m, 1H), 2.70−2.84 (m, 2H), 2.92−2.99 (m, 1H), 3.19 (s, 3H), 6.86 (d, J = 7.8 Hz, 1H), 7.14 (td, J = 0.8 Hz, J = 7.6 Hz, 1H), 7.35 (d, J = 7.4 Hz, 1H), 7.40 (td, J = 1.2 Hz, J = 7.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.3, 26.2, 30.3, 33.7, 45.3, 85.5, 108.6, 123.5, 124.2, 125.2, 131.1, 144.4, 173.2, 175.5; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NNaO_3$ $[M + Na]^+$: 282.1101, found 282.1094.

*(2R,3S)-1′-Methyl-3-phenyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3n**).*[3f] White solid; 26.4 mg, 90% yield; 81:19 dr, 71% ee. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 8.0 min, t_{minor} = 10.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.81 (s, 3H), 2.91 (dd, J = 7.9 Hz, J = 16.7 Hz, 1H), 3.82 (dd, J = 16.7 Hz, J = 13.7 Hz, 1H), 4.07 (dd, J = 7.9 Hz, J = 13.7 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.92 (d, J = 7.7 Hz, 2H), 7.15−7.23 (m, 4H), 7.38 (td, J = 1.2 Hz, J = 7.7 Hz, 1H), 7.54 (dd, J = 0.51 Hz, J = 7.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8, 32.2, 51.0, 86.4, 108.6, 123.5, 124.1, 124.8, 127.5, 128.3, 128.4, 131.3, 132.1, 144.3, 172.6, 174.7; HRMS (ESI-TOF) calcd for $C_{18}H_{15}NNaO_3$ $[M + Na]^+$: 316.0944, found 316.0934.

*(2R,3S)-3-(Furan-2-yl)-1′-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3o**).*[3f] White solid; 27.2 mg, 96% yield; 92:8 dr, 78% ee. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 8.5 min, t_{minor} = 15.2 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.98 (dd, J = 7.5 Hz, J = 17.0 Hz, 1H), 3.00 (s, 3H), 3.70 (dd, J = 17.0 Hz, J = 13.4 Hz, 1H), 4.14 (dd, J = 8.4 Hz, J = 13.3 Hz, 1H), 6.02 (d, J = 3.2 Hz, 1H); 6.22 (dd, J = 1.8 Hz, J = 3.2 Hz, 1H), 6.78 (d, J = 7.8 Hz, 1H), 7.15−7.20 (m, 2H), 7.41 (td, J = 1.1 Hz, J = 7.8 Hz, 1H), 7.46 (d, J = 7.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 32.2, 44.5, 84.6, 107.8, 108.7, 110.5, 123.5, 124.1, 124.6, 131.3, 142.5, 144.3, 147.6, 172.4, 174.1; HRMS (ESI-TOF) calcd for $C_{16}H_{13}NNaO_4$ $[M + Na]^+$: 306.0737, found 306.0726.

*(2R,3S)-3-((E)-Hept-1-en-1-yl)-1′-methyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3p**).* Colorless oil; 27.6 mg, 88% yield; 95:5 dr, 93% ee; $[\alpha]_D^{20}$ = −15.5 (c = 0.71, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 5.1 min, t_{minor} = 7.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, J = 7.1 Hz, 3H), 0.96−1.04 (m, 2H), 1.08−1.25 (m, 4H), 1.77−1.91 (m, 2H), 2.74 (dd, J = 7.9 Hz, J = 16.6 Hz, 1H), 3.15 (s, 3H), 3.23 (dd, J = 16.6 Hz, J = 12.8 Hz, 1H), 3.33−3.42 (m, 1H), 5.18 (dd, J = 7.6 Hz, J = 15.3 Hz, 1H), 5.27−5.34 (m, 1H), 6.81 (d, J = 7.7 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.36−7.41 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.3, 26.1, 28.4, 30.7, 32.0, 33.7, 49.0, 85.5, 108.5, 122.5, 123.4, 124.1, 124.7, 131.0, 137.3, 144.4, 173.0, 175.3; HRMS (ESI-TOF) calcd for $C_{19}H_{23}NNaO_3$ $[M + Na]^+$: 336.1570, found 336.1558.

*(R)-1′,3,3-Trimethyl-3H-spiro[furan-2,3′-indoline]-2′,5(4H)-dione (**3q**).* Colorless oil; 8.1 mg, 33% yield; 89% ee; $[\alpha]_D^{20}$ = +48.4 (c = 0.47, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 25/75, flow rate 1.0 mL/min, λ = 254 nm, t_{major} = 10.0 min, t_{minor} = 9.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 3H), 1.29 (s, 3H), 2.38 (d, J = 16.7 Hz, 1H), 3.19 (s, 3H), 3.41 (d, J = 16.8 Hz, 1H), 6.87 (d, J = 7.8 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.36−7.43(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 26.0, 26.2, 41.6, 43.2, 88.5, 108.7, 122.3, 122.7, 127.0, 131.0, 144.9, 174.8, 175.7; HRMS (ESI-TOF) calcd for $C_{14}H_{15}NNaO_3$ $[M + Na]^+$: 268.0944, found 268.0940.

General Procedure for the Synthesis of Spirocyclic Oxindole-γ-lactams 6. An oven-dried 20 mL reaction tube was charged with 3-aminooxindoles **5** (0.1 mmol, 1.0 equiv), catalyst **4d** (0.02 mmol, 20 mol %), and CH_2Cl_2 (1.0 mL). After 10 min of stirring at 25 °C, α,β-unsaturated acyl phosphonate **2** (0.2 mmol, 2.0 equiv) in CH_2Cl_2 (1.0 mL) was added. The stirring was maintained at the same temperature until the total consumption of 3-aminooxindoles **5** (monitored by TLC). The crude reaction mixture was diluted with CH_2Cl_2 and filtered through a pad of silica gel. The solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel (eluted with petroleum ether/ethyl acetate) to give the desired products **6**.

*1,3′-Dimethyl-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6a**).* Colorless oil; 13.1 mg, 51% yield; 98:2 dr, 96% ee; $[\alpha]_D^{20}$ = +21.0 (c = 0.47, $CHCl_3$). The ee was determined by HPLC (Chiralpak OD-H column, EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 10.0 min, t_{minor} = 10.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (d, J = 6.3 Hz, 3H), 2.62−2.74 (m, 2H), 2.81−2.93 (m, 1H), 3.25 (s, 3H), 6.90 (d, J = 7.8 Hz, 1H), 7.07−7.16 (m, 2H), 7.36 (td, J = 1.4 Hz, J = 7.7 Hz, 1H), 9.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.4, 26.4, 37.4, 38.6, 68.4, 108.7, 122.1, 123.3, 126.8, 129.9, 143.9, 159.4, 172.9, 176.1; HRMS (ESI-TOF) calcd for $C_{14}H_{14}N_2NaO_3$ $[M + Na]^+$: 281.0897, found 281.0891.

*1-Ethyl-3′-methyl-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6b**).* Colorless oil; 13.3 mg, 49% yield; > 99:1 dr, 97% ee; $[\alpha]_D^{20}$ = +15.2 (c = 0.32, $CHCl_3$). The ee was determined by HPLC (Chiralpak OD-H column, EtOH/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm, t_{major} = 12.0 min, t_{minor} = 13.1 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, J = 6.3 Hz, 3H), 1.27 (t, J = 7.2 Hz, 3H), 2.63−2.73 (m, 2H), 2.81−2.92 (m, 1H), 2.70−3.88 (m, 2H), 6.91 (d, J = 7.9 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 7.16 (d, J = 7.4 Hz, 1H), 7.35 (td, J = 1.4 Hz, J = 7.8 Hz, 1H), 9.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.4, 12.5, 35.0, 37.4, 38.6, 68.3, 108.7, 122.3, 123.1, 127.0, 129.8, 143.0, 159.4, 172.5, 176.1; HRMS (ESI-TOF) calcd for $C_{15}H_{16}N_2NaO_3$ $[M + Na]^+$: 295.1053, found 295.1045.

*1-Benzyl-3′-methyl-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6c**).* White solid; 20.0 mg, 60% yield; 98:2 dr, 97% ee; $[\alpha]_D^{20}$ = +23.1 (c = 0.43, $CHCl_3$); Mp: 189.5−190.5 °C. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, t_{major} = 28.9 min, t_{minor} = 67.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (d, J = 6.3 Hz, 3H), 2.69−2.78 (m, 2H), 2.92 (dd, J = 14.8 Hz, J = 18.8 Hz, 1H); 4.97 (s, 2H), 6.74 (d, J = 7.8 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 7.17 (d, J = 6.6 Hz, 1H), 7.22 (dd, J = 1.2 Hz, J = 7.7 Hz, 1H), 7.29−7.35 (m, 5H), 9.06 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.7, 37.5, 38.8, 44.2,, 68.4, 109.8, 122.2, 123.3, 126.8, 127.2, 127.7, 128.8, 129.8, 135.1, 143.1, 159.5, 173.1, 176.1; HRMS (ESI-TOF) calcd for $C_{20}H_{18}N_2NaO_3$ $[M + Na]^+$: 357.1210, found 357.1204.

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*3′-Methyl-2,5′-dioxo-1-phenylspiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6d**).* White solid; 10.0 mg, 31% yield; 92:8 dr, 96% ee; $[\alpha]_D^{20}$ = +8.9 (*c* = 0.63, $CHCl_3$); Mp: 229.9−231.5 °C. The ee was determined by HPLC (Chiralpak AD-H column, *i*PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 10.4 min, t_{minor} = 9.4 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (d, *J* = 6.0 Hz, 3H), 2.71−2.84 (m, 2H), 2.92 (dd, *J* = 15.1 Hz, *J* = 18.5 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 6.8 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.39−7.46 (m, 3H), 7.54 (t, *J* = 7.2 Hz, 2H), 9.07 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 37.5, 38.9, 68.5, 109.9, 122.4, 123.7, 126.6, 126.7, 128.6, 129.7, 129.8, 133.9, 144.2, 159.6, 172.7, 176.0; HRMS (ESI-TOF) calcd for $C_{19}H_{16}N_2NaO_3$ $[M + Na]^+$: 343.1053, found 343.1042.

*3′-Methyl-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6e**).* Colorless oil; 13.4 mg, 55% yield; 98:2 dr, 96% ee; $[\alpha]_D^{20}$ = +24.4 (*c* = 0.46, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, *i*PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 12.7 min, t_{minor} = 15.8 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, *J* = 6.3 Hz, 3H), 2.63−2.76 (m, 2H), 2.84 (dd, *J* = 14.4 Hz, *J* = 18.3 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 6.7 Hz, 1H), 7.29 (td, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H), 7.92 (s, 1H), 9.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6, 37.4, 38.7, 68.7, 110.4, 122.5, 123.3, 127.3, 129.9, 140.9, 159.6, 174.5, 176.0; HRMS (ESI-TOF) calcd for $C_{13}H_{12}N_2NaO_3$ $[M + Na]^+$: 267.0740, found 267.0737.

*1-Benzyl-2,5′-dioxo-3′-propylspiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6f**).* Colorless oil; 14.9 mg, 41% yield; 98:2 dr, 93% ee; $[\alpha]_D^{20}$ = +13.7 (*c* = 0.61, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, *i*PrOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 31.8 min, t_{minor} = 29.9 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (t, *J* = 7.0 Hz, 3H), 1.02−1.12 (m, 2H), 1.33−1.43 (m, 2H), 2.52−2.63 (m, 1H), 2.74 (dd, *J* = 7.8 Hz, *J* = 17.1 Hz, 1H), 2.87 (dd, *J* = 12.8 Hz, *J* = 17.1 Hz, 1H), 4.92 (d, *J* = 15.8 Hz, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 7.06 (td, *J* = 0.6 Hz, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 6.5 Hz, 1H), 7.23 (dd, *J* = 1.2 Hz, *J* = 7.7 Hz, 1H), 7.27−7.34 (m, 5H), 9.05 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.0, 30.3, 36.0, 44.0, 44.2, 68.1, 109.7, 122.2, 123.3, 127.2, 127.3, 127.8, 128.8, 129.8, 135.2, 143.2, 159.5, 173.3, 176.0; HRMS (ESI-TOF) calcd for $C_{22}H_{22}N_2NaO_3$ $[M + Na]^+$: 385.1523, found 385.1519.

*1-Benzyl-2,5′-dioxo-3′-phenylspiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6g**).* White solid; 21.8 mg, 55% yield; 94:6 dr, 88% ee; $[\alpha]_D^{20}$ = −57.9 (*c* = 0.67, $CHCl_3$); Mp: 85.5−86.3 °C. The ee was determined by HPLC (Chiralpak AD-H column, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 15.1 min, t_{minor} = 34.5 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.92 (dd, *J* = 7.5 Hz, *J* = 16.8 Hz, 1H), 3.75 (dd, *J* = 16.8 Hz, *J* = 13.8 Hz, 1H), 3.96 (dd, *J* = 7.5 Hz, *J* = 13.8 Hz, 1H), 4.39 (d, *J* = 16.1 Hz, 1H), 4.86 (d, *J* = 16.1 Hz, 1H), 6.45 (d, *J* = 7.7 Hz, 1H), 6.52 (d, *J* = 7.1 Hz, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 7.06−7.24 (m, 7H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.39 (dd, *J* = 1.0 Hz, *J* = 6.9 Hz, 1H), 9.16 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.8, 43.8, 49.1, 69.5, 110.0, 122.1, 123.2, 126.3, 126.4, 127.2, 128.2, 128.5, 128.6, 128.6, 130.0, 132.0, 134.5, 143.1, 159.4, 172.6, 175.5; HRMS (ESI-TOF) calcd for $C_{25}H_{20}N_2NaO_3$ $[M + Na]^+$: 419.1366, found 419.1360.

*1-Benzyl-3′-(furan-2-yl)-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6h**).* White solid; 19.6 mg, 51% yield; 99:1 dr, 95% ee; $[\alpha]_D^{20}$ = −51.5 (*c* = 0.85, $CHCl_3$); Mp: 73.2−74.1 °C. The ee was determined by HPLC (Chiralpak AD-H column, *i*PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 16.0 min, t_{minor} = 21.8 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.97 (dd, *J* = 8.0 Hz, *J* = 17.2 Hz, 1H), 3.64 (dd, *J* = 17.2 Hz, *J* = 13.3 Hz, 1H), 4.02 (dd, *J* = 7.9 Hz, *J* = 13.3 Hz, 1H), 4.63 (d, *J* = 15.9 Hz, 1H), 4.90 (d, *J* = 15.9 Hz, 1H), 6.05 (d, *J* = 3.3 Hz, 1H), 6.27 (dd, *J* = 1.9 Hz, *J* = 3.3 Hz, 1H), 6.63 (d, *J* = 7.7 Hz, 1H), 6.96−7.00 (m, 2H), 7.13 (t, *J* = 6.6 Hz, 1H), 7.21−7.28 (m, 5H), 7.31 (dd, *J* = 0.8 Hz, *J* = 6.6 Hz, 1H), 9.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.2, 42.9, 44.0, 68.0, 108.7, 109.9, 110.5, 122.1, 123.3, 126.6, 126.9, 127.4, 128.7, 130.0, 134.8, 142.9, 143.2, 147.5, 159.4, 172.3, 174.7; HRMS (ESI-TOF) calcd for $C_{23}H_{18}N_2NaO_4$ $[M + Na]^+$: 409.1159, found 409.1153.

*1-Benzyl-3′-((E)-hept-1-en-1-yl)-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6i**).* Colorless oil; 12.9 mg, 31% yield; 92:8 dr, 94% ee; $[\alpha]_D^{20}$ = −1.0 (*c* = 0.35, $CHCl_3$). The ee was determined by HPLC (Chiralpak IA column, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 12.2 min, t_{minor} = 15.1 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.0 Hz, 3H), 0.97−1.23 (m, 6H), 1.76−1.89 (m, 2H), 2.71−2.78 (m, 1H), 3.10−3.26 (m, 2H), 4.87 (d, *J* = 15.9 Hz, 1H), 4.99 (d, *J* = 15.9 Hz, 1H), 5.19−5.37 (m, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 7.08 (td, *J* = 0.9 Hz, *J* = 7.5 Hz, 1H), 7.19−7.26 (m, 2H), 7.28−7.38 (m, 5 H), 9.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.4, 28.5, 31.0, 32.3, 36.0, 44.1, 47.5, 68.3, 109.7, 122.2, 122.3, 123.2, 126.6, 127.1, 127.6, 128.8, 129.7, 135.1, 137.7, 143.1, 159.5, 173.0, 175.8; HRMS (ESI-TOF) calcd for $C_{26}H_{28}N_2NaO_3$ $[M + Na]^+$: 439.1992, found 439.1972.

*1-Benzyl-3′,3′-dimethyl-2,5′-dioxospiro[indoline-3,2′-pyrrolidine]-1′-carbaldehyde (**6j**).* Colorless oil; 12.1 mg, 35% yield; 85% ee; $[\alpha]_D^{20}$ = +64.6 (*c* = 0.63, $CHCl_3$). The ee was determined by HPLC (Chiralpak AD-H column, *i*PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 12.3 min, t_{minor} = 10.3 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 3H), 1.21 (s, 3H), 2.45 (d, *J* = 16.7 Hz, 1H), 3.23 (d, *J* = 16.8 Hz, 1H), 4.89 (d, *J* = 15.8 Hz, 1H), 5.01 (d, *J* = 15.8 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 7.02 (td, *J* = 0.9 Hz, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.22 (dd, *J* = 1.2 Hz, *J* = 7.7 Hz, 1H), 7.27−7.35 (m, 5H), 9.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 26.7, 40.4, 44.2, 44.6, 71.2, 110.0, 122.3, 123.6, 125.2, 127.2, 127.7, 128.8, 129.7, 135.1, 143.5, 159.8, 174.3, 176.3; HRMS (ESI-TOF) calcd for $C_{21}H_{20}N_2NaO_3$ $[M + Na]^+$: 371.1366, found 371.1359.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02253.

Copies of ^{1}H, ^{13}C NMR and HPLC spectra for the products (PDF)

Single crystal X-ray crystallography data for product **3k** (CIF)

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Notes

The authors declare no competing financial interest.

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