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Synthesis of Optically Pure Spiro[cyclohexane-oxindoline] Derivatives via Catalytic Asymmetric Diels–Alder Reaction of Brassard-Type Diene with Methyleneindolines

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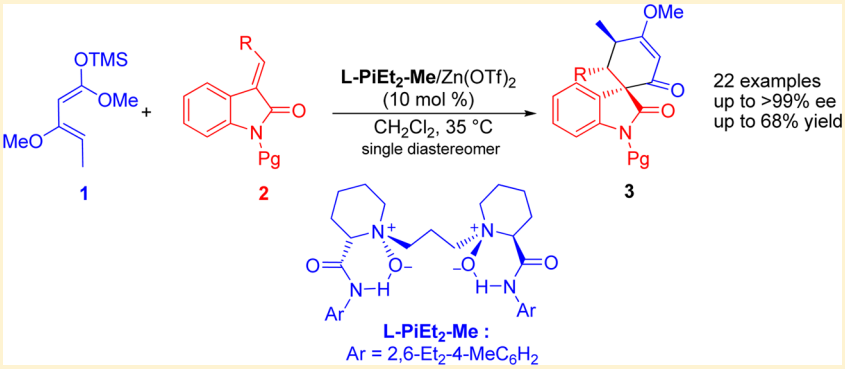
Supporting Information



ABSTRACT: A highly efficient *N*,*N*′-dioxide–Zn(II) complex catalytic system for the asymmetric Diels–Alder reaction of Brassard-type diene with methyleneindolines was developed. The optically pure spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate-2, 2′-dione derivatives containing three stereocenters were obtained in moderate yields with 98% to >99% ee in a stereospecific manner.

Chiral spirocyclic oxindoles have fascinated synthetic chemists over the past years, due to their potential biological activity and as privileged molecular architectures in a variety of natural products and pharmacological compounds.[1] As one family of spirocyclic oxindoles, the spiro[cyclohexane-oxindoline] derivatives have attracted continuous attention, which is exemplified by gelsemine as well as pharmacologically important compounds as shown in Figure 1.[2] Therefore, considerable efforts have been devoted to develop efficient protocols to access these interesting motifs. On the catalytic asymmetric version, to the best of our knowledge, organocatalytic Michael/Michael/Aldol addition reaction,[3] double Michael addition reaction,[4] Michael/Povarov reaction,[5] and Michael/Aldol reaction[6] have been documented to be venerable transformations for achieving this class of molecules.

On the other hand, the asymmetric Diels–Alder (D-A) reactions are among the most powerful and effective transformations to construct chiral six-membered ring structures.[7] Especially, the asymmetric D-A reaction of 3-methyleneindolinone derivatives provides a one-step synthesis of spiro[cyclohexane-oxindoline] derivatives with remarkable step, atom, and redox economy.[8] Recently, Antilla and co-workers reported the synthesis of chiral spiro[cyclohexane-oxindoline] derivatives via the asymmetric D-A reaction of 3-methyleneindolinone derivatives with Danishefsky's diene[9] by using a chiral

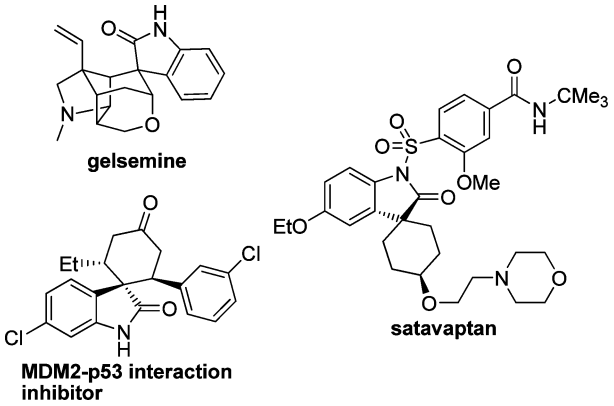


Figure 1. Some biologically active compounds with spirocyclohexaneoxindole core.

magnesium phosphate.[8c] As electron-rich as the Danishefsky's diene, Brassard's dienes[10] are relatively less-developed for the difficulty of controlling the enantioselectivity which caused by the terminal substituents,[11] however, have attracted much

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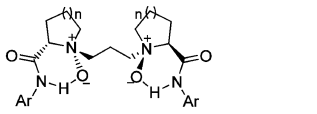
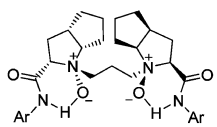
attention, including ours,[12] in recent years for the easily construction of six-membered δ-lactones and δ-lactams.[13] The D-A reaction of Brassard's dienes with 3-methyleneindolinones could provide spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate-2, 2′-dione derivatives and can be used for preparation of new derivatives of this class (Figure 2).



L-PiPh: Ar = C_6H_5, n = 2
L-PiMe$_2$: Ar = 2,6-$Me_2C_6H_3$, n = 2
L-PiEt$_2$: Ar = 2,6-$Et_2C_6H_3$, n = 2
L-PiEt$_2$-Me: Ar = 2,6-Et_2-4-MeC_6H_2, n = 2
L-PrEt$_2$-Me: Ar = 2,6-Et_2-4-MeC_6H_2, n = 1



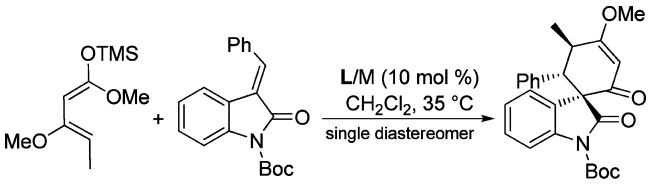
L-RaEt$_2$-Me: Ar = 2,6-Et_2-4-MeC_6H_2

Figure 2. Chiral ligands used in this study.

Herein, we report a highly enantioselective D-A reaction of Brassard-type diene with 3-methyleneindolinones to construct optically pure spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate-2, 2′-dione derivatives containing three stereocenters by using a chiral Zn(OTf)$_2$-*N*,*N*′-dioxide complex[14] under mild reaction conditions.

To begin our investigation, the reaction of 3-methyleneindolinone **2a** with Brassard-type diene **1** was selected as a model reaction to optimize the reaction conditions. Initially, various metal salts coordinated in situ with L-pipecolic acid-derived *N*,*N*′-dioxide **L-PiPh** were examined in CH_2Cl_2 at 35 °C. As shown in Table 1, the complex of **L-PiPh**−Mg(ClO$_4$)$_2$ afforded the desired adduct **3a** only in 31% yield and 39% ee (Table 1, entry 1). When the complex of Cu(OTf)$_2$ or Fe(OTf)$_3$ was applied, no product was detected (Table 1, entries 2 and 3). To our delight, the combination of Zn(OTf)$_2$ and **L-PiPh** afforded the desired adduct **3a** with 53% ee, though the yield was only 28% (Table 1, entry 4). Encouraged by the result, the structure of ligand was then examined. Increasing the steric hindrance of ortho-substituents on the aniline ring benefited the yield and enantioselectivity of the reaction, and the *N*,*N*′-dioxide **L-PiMe$_2$** bearing 2,6-dimethyl-substituted aniline increased the yield to 49% and the ee sharply to 98% (Table 1, entry 5). Meanwhile, **L-PiEt$_2$** with more steric ethyl substituents increased the yield to 55% with maintained ee value (Table 1, entry 6). When ligand **L-PiEt$_2$-Me** containing a more methyl group on the aniline moiety was used, the yield and ee could be further improved to 63% and >99%, respectively (Table 1, entry 7). Subsequently, the structure of the ligand was probed. It was proved that L-pipecolic acid-derived **L-PiEt$_2$-Me** was superior to L-proline-derived **L-PrEt$_2$-Me** and L-ramipril acid-derived **L-RaEt$_2$-Me** in this reaction (Table 1, entries 8 and 9). The relatively low yield of the desired product **3a** was caused by the Vinylogous Michael side reaction that existed in this catalytic system. In the hope of transforming the Vinylogous Michael byproduct to the desired **3a**, base additives such as K_2CO_3 and DMAP were added, but no better results were obtained (Table 1, entries 10 and 11).

Table 1. Optimization of the Reaction Conditions[a]



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

entry	ligand	metal	yield [%][b]	ee [%][c]
1	**L-PiPh**	Mg(ClO$_4$)$_2$	31	39
2	**L-PiPh**	Cu(OTf)$_2$	0	n.d
3	**L-PiPh**	Fe(OTf)$_3$	0	n.d
4	**L-PiPh**	Zn(OTf)$_2$	28	53
5	**L-PiMe$_2$**	Zn(OTf)$_2$	49	98
6	**L-PiEt$_2$**	Zn(OTf)$_2$	55	98
7	**L-PiEt$_2$-Me**	Zn(OTf)$_2$	63	>99
8	**L-PrEt$_2$-Me**	Zn(OTf)$_2$	20	90
9	**L-RaEt$_2$-Me**	Zn(OTf)$_2$	50	98
10[d]	**L-PiEt$_2$-Me**	Zn(OTf)$_2$	23	83
11[e]	**L-PiEt$_2$-Me**	Zn(OTf)$_2$	0	n.d

[a]Unless otherwise noted, the reactions were performed with metal/**L** (10 mol %, 1/1), **1** (0.15 mmol), and **2a** (0.10 mmol) in CH_2Cl_2 (0.5 mL) under nitrogen at 35 °C for 1 h. [b]Isolated yield. [c]Determined by chiral HPLC analysis. [d]K_2CO_3 (1 equiv) was used. [e]DMAP (1 equiv) was used.

Therefore, the optimal reaction conditions were 10 mol % of **L-PiEt$_2$-Me**−Zn(OTf)$_2$ in CH_2Cl_2 at 35 °C for 1 h, which afforded the product with 63% yield and >99% ee in a stereospecific manner.

Under the optimized reaction conditions, a wide range of methyleneindolinones **2** was investigated, and the results were summarized in Table 2. Initially, variation of the R^1 was investigated. For aromatic R^1, it was found that electronic nature of the substituents on the aromatic ring of methyleneindolinones had no obvious influence on the enantioselectivity but a slight influence on the yield (Table 2, entries 1−12). Generally, methyleneindolinones with electron-donating substituted phenyl groups afforded higher yields than those with electron-withdrawing ones. Remarkably, the naphthyl ring and 2-furyl substituted methyleneindolinones **2m**−**2o** were also suitable for the reaction, affording the desired products in 54%−62% yields with excellent enantioselectivities (>99% ee) (Table 2, entries 13−15). When R^1 was an ester group, methyleneindolines **2p**−**2t** were also tolerated in the catalytic system (Table 2, entries 16−20). Next, the nitrogen protecting group was varied. Methyleneindolinones **2u**−**2v** with carbonyl-based Ac or Cbz protecting group proceeded well in the reaction, giving **3u** in 63% yield with >99% ee and **3v** in 68% yield with 98% ee, respectively (Table 2, entries 21 and 22). However, when R^2 was Bn without a carbonyl group, no product could be detected. The results indicated that the coordination of dienophile **2** to the catalyst in a bidentate fashion with two carbonyl groups played a key role in the catalytic process. It is noteworthy that only a single diastereomer was detected in all cases, and the reactions were completed in 1 h. The absolute configuration of product **3a** was determined to be (1*R*, 5*R*, 6*S*) by X-ray crystallographic study.[15] The absolute configurations of **3b**−**3v** were also assigned to be (1*R*, 5*R*, 6*S*) by comparing their circular dichroism spectra with that of **3a**.

To illustrate the origin of the asymmetric induction, the relationship between the enantiomeric excess of **L-PiEt$_2$-Me** and that of the product **3a** was investigated (Figure 3). A clear linear effect was observed, which indicated that monomeric catalyst might be the main active species in the catalytic system. In addition, HRMS analysis of the mixture of **2a** and catalyst suggested that **2a** coordinated to the catalyst in a 1:1 molecular

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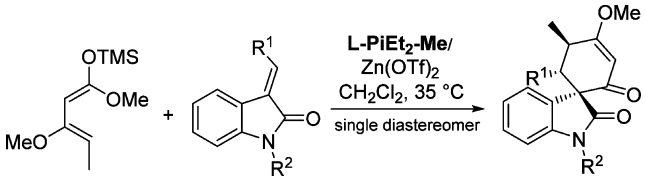
Table 2. Substrate Scope of Methyleneindolinones in the Asymmetric D-A Reaction[a]



1 2a-2v 3a-3v

entry	R^1	R^2	yield [%][b]	ee [%][c]
1	Ph	Boc	63 (**3a**)	>99
2	3-ClC_6H_4	Boc	52 (**3b**)	>99
3	3-BrC_6H_4	Boc	55 (**3c**)	>99
4	3-MeC_6H_4	Boc	64 (**3d**)	98
5	3-$MeOC_6H_4$	Boc	63 (**3e**)	>99
6	3-$PhOC_6H_4$	Boc	63 (**3f**)	98
7	4-FC_6H_4	Boc	62 (**3g**)	98
8	4-ClC_6H_4	Boc	52 (**3h**)	99
9	4-BrC_6H_4	Boc	51 (**3i**)	98
10	4-$F_3CC_6H_4$	Boc	56 (**3j**)	>99
11	4-$O_2NC_6H_4$	Boc	54 (**3k**)	>99
12	4-MeC_6H_4	Boc	55 (**3l**)	>99
13	1-naphthyl	Boc	55 (**3m**)	>99
14	2-naphthyl	Boc	62 (**3n**)	>99
15	2-furyl	Boc	54 (**3o**)	>99
16	CO_2Me	Boc	52 (**3p**)	98
17	CO_2Et	Boc	51 (**3q**)	>99
18	$CO_2{}^iPr$	Boc	60 (**3r**)	>99
19	$CO_2{}^tBu$	Boc	59 (**3s**)	>99
20	CO_2Bn	Boc	63 (**3t**)	98
21	Ph	Ac	63 (**3u**)	>99
22	Ph	Cbz	68 (**3v**)	98
23	Ph	Bn	N.R.	N.D.

[a]Unless otherwise noted, the reactions were preformed with $Zn(OTf)_2$/L-**PiEt$_2$-Me** (10 mol %, 1/1), **1** (0.15 mmol), **2** (0.10 mmol) in CH_2Cl_2 (0.5 mL) under nitrogen at 35 °C for 1 h. [b]Isolated yield. [c]Determined by chiral HPLC analysis.

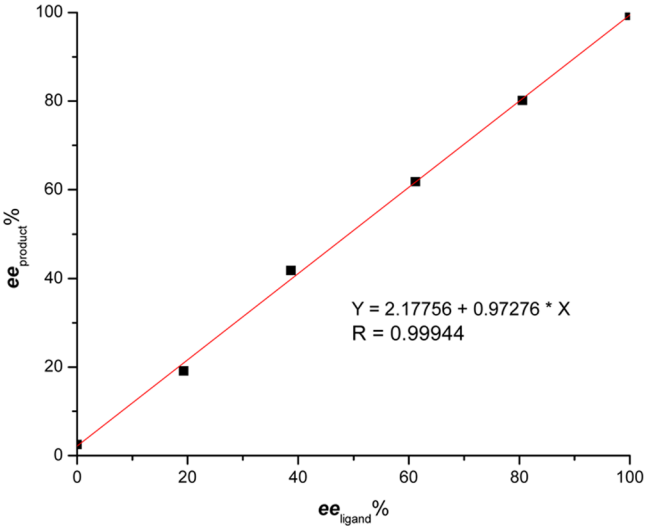


Figure 3. Nonlinear effects observed in the $Zn(OTf)_2$-L-**PiEt$_2$-Me** catalyzed DA reaction of **1** and **2a**.

ratio, because a peak at m/z 1154.4109 was detected which was corresponding to the complex of [Zn^{2+} + **2a** + (L-**PiEt$_2$-Me**) + OTf^-)] (m/z calcd 1154.4478). What's more, the reaction of **1** with **2a** was monitored by operando IR experiments. It can be seen from Figure 4 that the desired product **3a** was formed with the depletion of **2a** at the beginning of the reaction, which can be tracked by the changes of the peaks at 1335 and 1350 cm^{-1}.

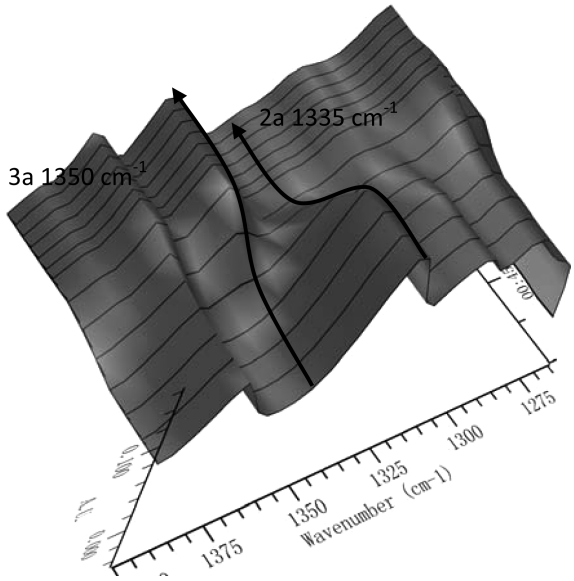


Figure 4. 3D ATR-FTIR profile of the catalytic asymmetric D-A reaction.

Based on the above observations, the absolute configuration of products, and our previous study,[12e] a possible catalytic model was proposed. As shown in Figure 5, oxygen atoms of

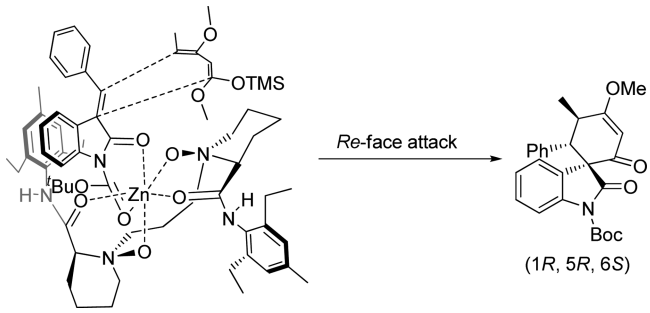


Figure 5. Proposed catalytic model of the catalytic asymmetric D-A reaction.

the amide and *N*-oxide are coordinated with Zn^{II} in a tetradentate manner to form a six-membered chelate ring. Meanwhile, the methyleneindolinone **2a** coordinates to the Zn(II) in a bidentate fashion with its dicarbonyl groups. Then, Brassard-type diene **1** attacks **2a** from the *Re* face of **2a**, since the *Si* face is shielded by the neighboring 2,6-diethyl-4-methylphenyl group of the L-**PiEt$_2$-Me**. Thus, the (1*R*, 5*R*, 6*S*) product **3a** is obtained, which is in good agreement with X-ray study of **3a**.

In summary, we have disclosed a highly enantioselective D-A reaction of Brassard-type diene with 3-methyleneindolines catalyzed by a chiral $Zn(OTf)_2$–*N*,*N*′-dioxide complex. The method enables the construction of functionalized chiral spirooxindoles containing three stereocenters in moderate

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yields with 98% to >99% ee in a stereospecific manner. And a possible transition model was also proposed.

EXPERIMENTAL SECTION

General Remarks. Reactions were carried out using commercially available reagents in a dry apparatus. CH_2Cl_2 was directly distilled before use. 3-methyleneindolinones were prepared. Enantiomeric excesses (ee's) were determined by HPLC analysis using the corresponding commercial chiral column as stated in the experimental procedures at 23 °C with a UV detector at 254 nm. Optical rotations were reported as follows: $[\alpha]_D^T$ (c g/100 mL, solvent). ^{1}H NMR spectra were recorded on commercial instruments (400 MHz). ^{13}C NMR spectra was collected on commercial instruments (100 MHz) with complete proton decoupling. HRMS was recorded on a commercial apparatus. Circular dichroism (CD) spectra were recorded on a CD spectropolarimeter, using a 1 cm quartz cuvette.

General Procedure for the Catalytic Asymmetric Reaction. In a test tube, 3-methyleneindolinone **2a** (0.10 mmol, 32.1 mg), ligand **L-PiEt$_2$-Me** (0.01 mmol, 6.2 mg), $Zn(OTf)_2$ (0.01 mmol, 3.6 mg) were added. The tube was filled with N_2 gas, and 0.5 mL of CH_2Cl_2 was added. The reaction was stirred at 30 °C for 0.5 h. Subsequently, the Brassard-type diene **1** (1.5 equiv, 40 μL) was added at 35 °C, and the reaction mixture was stirred for 1 h. The crude mixture was purified by flash chromatography (petroleum ether:EtOAc = 3:1) to afford the product **3a**. The ee was determined by high-performance liquid chromatography (HPLC), and the diastereoselectivity was determined by ^{1}H NMR.

*tert-Butyl-4-methoxy-5-methyl-2,2′-dioxo-6-phenylspiro-[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3a**).* Purified by flash chromatography (petroleum ether:EtOAc = 3:1) to afford a white solid 27.2 mg, 63% yield, >99% ee, mp 169−171 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 5.50 min, t_{r2} = 6.64 min, ee = >99%. $[\alpha]_D^{21.8}$ = +229.9 (c = 1.10 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.1 Hz, 1H), 7.33−7.23 (m, 2H), 7.19−7.08 (m, 2H), 7.03 (t, J = 7.5 Hz, 2H), 6.76 (d, J = 5.5 Hz, 2H), 5.66 (s, 1H), 3.88 (s, 3H), 3.72 (d, J = 11.4 Hz, 1H), 3.40−3.24 (m, 1H), 1.49 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 180.1, 173.1, 148.3, 140.8, 135.2, 129.2, 128.0, 127.7, 125.4, 123.9, 123.4, 115.7, 101.6, 83.9, 65.6, 56.7, 53.7, 35.4, 27.9, 14.9. HRMS (ESI-TOF) calcd for $C_{26}H_{27}NKO_5$ ([M + K^+]) = 472.1526; found 472.1524.

*tert-Butyl-6-(3-chlorophenyl)-4-methoxy-5-methyl-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3b**).* Purified by flash chromatography (petroleum ether:EtOAc = 3:1) to afford a white solid 24.3 mg, 52% yield, >99% ee, mp 122−124 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 6.86 min, t_{r2} = 10.17 min, ee = >99%. $[\alpha]_D^{13.9}$ = +155.6 (c = 0.49 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.1 Hz, 1H), 7.33−7.27 (m, 2H), 7.16 (td, J = 7.6, 0.9 Hz, 1H), 7.10 (ddd, J = 8.0, 1.9, 0.9 Hz, 1H), 6.96 (t, J = 7.9 Hz, 1H), 6.79 (s, 1H), 6.62 (s, 1H), 5.66 (d, J = 1.0 Hz, 1H), 3.88 (s, 3H), 3.69 (d, J = 11.5 Hz, 1H), 3.35−3.20 (m, 1H), 1.51 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 179.7, 172.8, 148.3, 140.8, 137.4, 133.9, 129.5, 129.2, 127.9, 125.0, 124.1, 123.3, 115.8, 101.6, 84.2, 65.4, 56.7, 53.4, 35.3, 27.9, 15.0. HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{34.9689}ClNNaO_5$ ([M + Na^+]) = 490.1397; found 490.1398, HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{36.9659}ClNNaO_5$ ([M + Na^+]) = 492.1368; found 492.1388.

*tert-Butyl-6-(3-bromophenyl)-4-methoxy-5-methyl-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3c**).* Purified by flash chromatography (petroleum ether:EtOAc = 3:1) to afford a white solid 28.2 mg, 55% yield, >99% ee, mp 98−100 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 6.71 min, t_{r2} = 9.71 min, ee = >99%. $[\alpha]_D^{12.8}$ = +226.0 (c = 0.39 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.1 Hz, 1H), 7.36−7.24 (m, 3H), 7.16 (td, J = 7.5, 0.7 Hz, 1H), 6.90 (t, J = 7.9 Hz, 2H), 6.67 (s, 1H), 5.66 (s, 1H), 3.88 (s, 3H), 3.68 (d, J = 11.5 Hz, 1H), 3.36−3.18 (m, 1H), 1.52 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 179.7, 172.8, 148.3, 140.8, 137.6, 130.9, 129.5, 124.9, 124.1, 123.3, 122.0, 115.8, 101.6, 84.2, 65.4, 56.7, 53.4, 35.3, 27.9, 15.0. HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{78.0183}BrNNaO_5$ ([M + Na^+]) = 534.0892; found 534.0891. HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{80.9163}BrNNaO_5$ ([M + Na^+]) = 536.0872; found 536.0880.

*tert-Butyl-4-methoxy-5-methyl-2,2′-dioxo-6-m-tolylspiro-[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3d**).* Purified by flash chromatography (petroleum ether:EtOAc = 3:1) to afford a white solid 28.6 mg, 64% yield, 98% ee, mp 78−80 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 5.00 min, t_{r2} = 5.89 min, ee = 98%. $[\alpha]_D^{13.1}$ = +175.3 (c = 0.49 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.1 Hz, 1H), 7.31−7.23 (m, 2H), 7.14 (td, J = 7.6, 0.9 Hz, 1H), 6.96−6.83 (m, 2H), 6.57 (s, 1H), 6.51(s, 1H), 5.66 (d, J = 1.0 Hz, 1H), 3.87 (s, 3H), 3.67 (d, J = 11.4 Hz, 1H), 3.30 (ddd, J = 11.4, 6.6, 1.1 Hz, 1H), 2.11 (s, 3H), 1.49 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 180.3, 173.1, 148.4, 140.9, 137.5, 135.1, 129.1, 128.3, 127.7, 125.6, 123.8, 123.4, 115.6, 101.6, 83.8, 65.6, 56.6, 53.7, 35.4, 27.9, 21.2, 15.0. HRMS (ESI-TOF) calcd for $C_{27}H_{29}NNaO_5$ ([M + Na^+]) = 470.1943; found 470.1936.

*tert-Butyl-4-methoxy-6-(3-methoxyphenyl)-5-methyl-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3e**).* Purified by flash chromatography (petroleum ether:EtOAc = 3:1) to afford a white solid, 29.2 mg, 63% yield, >99% ee, mp 143−145 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 6.59 min, t_{r2} = 9.45 min, ee = >99%. $[\alpha]_D^{13.4}$ = +211.7 (c = 0.45 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 7.9 Hz, 2H), 7.21−7.09 (m, 1H), 6.95 (t, J = 7.9 Hz, 1H), 6.72−6.59 (m, 1H), 6.48−6.06 (m, 2H), 5.65 (d, J = 1.0 Hz, 1H), 3.87 (s, 3H), 3.69 (d, J = 11.4 Hz, 1H), 3.50 (s, 3H), 3.35−3.20 (m, 1H), 1.49 (s, 9H), 1.09 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 180.1, 173.0, 159.1, 148.4, 140.9, 136.7, 129.2, 128.9, 125.6, 123.9, 123.3, 115.8, 114.1, 101.6, 83.9, 65.6, 56.6, 55.0, 53.7, 35.5, 27.9, 15.0. HRMS (ESI-TOF) calcd for $C_{27}H_{29}NNaO_6$ ([M + Na^+]) = 486.1893; found 486.1891.

*tert-Butyl-4-methoxy-5-methyl-2,2′-dioxo-6-(3-phenoxyphenyl)-spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3f**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 33.1 mg, 63% yield, 98% ee, mp 75−77 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 7.68 min, t_{r2} = 12.19 min, ee = 98%. $[\alpha]_D^{14.6}$ = +202.7 (c = 0.56 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 1H), 7.29−7.18 (m, 5H), 7.05 (t, J = 7.4 Hz, 3H), 6.77 (dd, J = 8.1, 2.0 Hz, 1H), 6.69 (d, J = 8.0 Hz, 3H), 6.36 (s, 1H), 5.63 (s, 1H), 3.86 (s, 3H), 3.73 (d, J = 11.5 Hz, 1H), 3.32−3.17 (m, 1H), 1.53 (s, 9H), 1.09 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 179.9, 173.0, 157.0, 156.6, 148.5, 140.7, 137.4, 129.7, 129.3, 125.2, 124.10, 123.3, 123.0, 118.7, 118.4, 115.8, 101.5, 84.0, 65.5, 56.6, 53.4, 35.3, 28.0, 14.9. HRMS (ESI-TOF) calcd for $C_{32}H_{31}NNaO_6$ ([M + Na^+]) = 548.2049; found 548.2056.

*tert-Butyl-6-(4-fluorophenyl)-4-methoxy-5-methyl-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3g**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 28.0 mg, 62% yield, 98% ee, mp 97−99 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 8.01 min, t_{r2} = 11.02 min, ee = 98%. $[\alpha]_D^{13.7}$ = +152.2 (c = 0.46 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.57 (m, 1H), 7.32−7.27 (m, 2H), 7.18−7.12 (m, 1H), 6.74 (d, J = 6.7 Hz, 4H), 5.65 (s, 1H), 3.88 (s, 3H), 3.72 (d, J = 11.5 Hz, 1H), 3.32−3.18 (m, 1H), 1.50 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 179.9, 173.1, 163.4, 160.9, 148.2, 140.8, 131.1, 129.4, 125.1, 124.0, 123.4, 115.8, 115.0, 114.8, 101.6, 84.1, 65.6, 56.7, 52.9, 35.6, 27.9, 15.0. HRMS (ESI-TOF) calcd for $C_{26}H_{26}FNNaO_5$ ([M + Na^+]) = 474.1693; found 474.1698.

*tert-Butyl-6-(4-chlorophenyl)-4-methoxy-5-methyl-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3h**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 24.3 mg, 52% yield, 99% ee, mp 108−110 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 8.60 min, t_{r2} = 11.89 min, ee = 99%. $[\alpha]_D^{24.6}$ =

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+151.4 (c = 0.62 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, 1H), 7.30 (d, J = 8.3 Hz, 2H), 7.14 (dd, J = 14.8, 7.1 Hz, 1H), 7.02 (d, J = 8.5 Hz, 2H), 6.70 (d, J = 7.1 Hz, 2H), 5.64 (s, 1H), 3.88 (s, 3H), 3.71 (d, J = 11.5 Hz, 1H), 3.37−3.17 (m, 1H), 1.51 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 179.8, 173.0, 148.2, 140.8, 133.9, 133.6, 130.0, 129.4, 128.2, 125.0, 124.0, 123.4, 115.9, 101.6, 84.2, 65.5, 56.7, 53.0, 35.4, 27.9, 15.0. HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{34.9689}ClNNaO_5$ ([M + Na^+]) = 490.1397; found 490.1404, HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{36.9659}ClNNaO_5$ ([M + Na^+]) = 492.1368; found 492.1368.

*tert-Butyl-6-(4-bromophenyl)-4-methoxy-5-methyl-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3i**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 26.1 mg, 51% yield, 98% ee, mp 114−116 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 8.26 min, t_{r2} = 11.25 min, ee = 98%. $[\alpha]_D{}^{12.3}$ = +152.0 (c = 0.45 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, 1H), 7.34−7.26 (m, 2H), 7.23−7.09 (m, 3H), 6.64 (d, J = 7.2 Hz, 2H), 5.65 (s, 1H), 3.88 (s, 3H), 3.70 (d, J = 11.5 Hz, 1H), 3.26 (ddd, J = 11.5, 6.7, 1.2 Hz, 1H), 1.51 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 179.7, 173.0, 148.1, 140.8, 134.4, 131.2, 129.5, 124.9, 124.0, 123.4, 121.8, 115.9, 101.6, 84.2, 65.4, 56.7, 53.1, 35.3, 27.9, 14.9. HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{78.0183}BrNNaO_5$ ([M + Na^+]) = 534.0892; found 534.0891, HRMS (ESI-TOF) calcd for $C_{26}H_{26}{}^{80.9163}BrNNaO_5$ ([M + Na^+]) = 536.0872; found 536.0876.

*tert-Butyl-4-methoxy-5-methyl-2,2′-dioxo-6-(4-(trifluoromethyl)-phenyl)spiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3j**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 28.1 mg, 56% yield, >99% ee, mp 118−120 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 7.60 min, t_{r2} = 10.29 min, ee = >99%. $[\alpha]_D{}^{13.2}$ = +162.2 (c = 0.47 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.56 (m, 1H), 7.36−7.27 (m, 4H), 7.17 (td, J = 7.7, 0.9 Hz, 1H), 6.90 (d, J = 6.9 Hz, 2H), 5.67 (s, 1H), 3.89 (s, 3H), 3.80 (d, J = 11.5 Hz, 1H), 3.40−3.26 (m, 1H), 1.48 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.1, 179.6, 172.8, 148.0, 140.7, 139.5, 130.2, 129.8, 129.6, 129.0, 125.2, 125.0−124.7, 124.1, 123.4, 115.9, 101.6, 84.3, 65.3, 56.7, 53.5, 35.3, 27.8, 14.9. HRMS (ESI-TOF) calcd for $C_{27}H_{26}F_3NNaO_5$ ([M + Na^+]) = 524.1661; found 524.1664.

*tert-Butyl-4-methoxy-5-methyl-6-(4-nitrophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3k**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 25.8 mg, 54% yield, >99% ee, mp 165−167 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 13.90 min, t_{r2} = 16.50 min, ee = >99%. $[\alpha]_D{}^{18.3}$ = +186.8 (c = 0.51 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.2 Hz, 1H), 7.31 (t, J = 7.3 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 7.6 Hz, 2H), 5.67 (s, 1H), 3.88 (d, J = 12.9 Hz, 4H), 3.42−3.28 (m, 1H), 1.49 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 179.2, 172.7, 148.0, 147.4, 143.0, 140.6, 129.8, 124.5, 124.3, 123.4, 123.2, 115.9, 101.5, 84.6, 65.1, 56.8, 53.2, 35.3, 27.9, 15.0. HRMS (ESI-TOF) calcd for $C_{26}H_{26}N_2NaO_7$ ([M + Na^+]) = 501.1638; found 501.1639.

*tert-Butyl-4-methoxy-5-methyl-2,2′-dioxo-6-p-tolylspiro-[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3l**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 24.6 mg, 55% yield, >99% ee, mp 169−171 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 5.29 min, t_{r2} = 6.19 min, ee = >99%. $[\alpha]_D{}^{12.3}$ = +171.5 (c = 0.53 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.69−7.57 (m, 1H), 7.31−7.26 (m, 2H), 7.13 (dd, J = 11.0, 4.1 Hz, 1H), 6.83 (d, J = 8.0 Hz, 2H), 6.63 (d, J = 6.8 Hz, 2H), 5.64 (s, 1H), 3.87 (s, 3H), 3.68 (d, J = 11.4 Hz, 1H), 3.38−3.20 (m, 1H), 2.19 (s, 3H), 1.49 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 180.3, 173.2, 148.4, 140.8, 137.2, 132.1, 129.1, 128.7, 125.5, 123.9, 123.4, 115.7, 101.6, 83.8, 65.7, 56.6, 53.4, 35.5, 27.9, 20.9, 14.9. HRMS (ESI-TOF) calcd for $C_{27}H_{29}NNaO_5$ ([M + Na^+]) = 470.1943; found 470.1945.

*tert-Butyl-4-methoxy-5-methyl-6-(naphthalen-1-yl)-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3m**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 26.6 mg, 55% yield, >99% ee, mp 155−157 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 10.03 min, t_{r2} = 11.78 min, ee = >99%. $[\alpha]_D{}^{18.0}$ = +356.2 (c = 0.53 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.7 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.63 (dd, J = 14.0, 8.2 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 7.8 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 6.46 (d, J = 7.4 Hz, 1H), 5.76 (s, 1H), 4.80 (d, J = 11.2 Hz, 1H), 3.91 (s, 3H), 3.35 (td, J = 13.5, 6.9 Hz, 1H), 1.11 (s, 9H), 1.02 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 180.5, 172.2, 148.3, 141.3, 133.8, 132.5, 131.6, 129.4, 128.3, 126.1, 125.8, 125.6, 124.3, 123.9, 123.5, 115.8, 101.9, 83.3, 65.0, 56.7, 45.7, 37.5, 27.4, 14.6. HRMS (ESI-TOF) calcd for $C_{30}H_{29}NNaO_5$ ([M + Na^+]) = 506.1943; found 506.1939.

*tert-Butyl-4-methoxy-5-methyl-6-(naphthalen-2-yl)-2,2′-dioxospiro[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3n**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 30.0 mg, 62% yield, >99% ee, mp 153−155 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 5.96 min, t_{r2} = 6.76 min, ee = >99%. $[\alpha]_D{}^{13.5}$ = +218.6 (c = 0.49 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.70−7.65 (m, 1H), 7.61 (d, J = 4.2 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.38 (ddd, J = 8.4, 4.6, 0.9 Hz, 4H), 7.28 (dd, J = 7.7, 1.3 Hz, 1H), 7.19 (td, J = 7.5, 0.9 Hz, 1H), 6.73 (s, 1H), 5.69 (s, 1H), 3.95−3.85 (m, 4H), 3.45 (tt, J = 12.5, 6.4 Hz, 1H), 1.29 (s, 9H), 1.09 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 180.1, 173.1, 148.1, 140.8, 133.1−132.6, 129.3, 127.9, 127.4, 126.0, 125.4, 123.9, 123.4, 115.8, 101.7, 83.8, 65.7, 56.7, 53.9, 35.4, 27.7, 15.0. HRMS (ESI-TOF) calcd for $C_{30}H_{29}NNaO_5$ ([M + Na^+]) = 506.1943; found 506.1945.

*tert-Butyl-6-(furan-2-yl)-4-methoxy-5-methyl-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-1′-carboxylate (**3o**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 22.8 mg, 54% yield, >99% ee, mp 156−158 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 6.44 min, t_{r2} = 9.19 min, ee = >99%. $[\alpha]_D{}^{13.5}$ = +138.3 (c = 0.32 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 1H), 7.26 (dd, J = 15.7, 1.3 Hz, 1H), 7.24−7.19 (m, 1H), 7.10 (td, J = 7.6, 0.9 Hz, 1H), 7.06−6.99 (m, 1H), 6.08 (dd, J = 3.2, 1.9 Hz, 1H), 5.84 (d, J = 3.2 Hz, 1H), 5.59 (s, 1H), 3.92 (d, J = 11.4 Hz, 1H), 3.86 (s, 3H), 3.48−3.34 (m, 1H), 1.58 (s, 9H), 1.17 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 179.6, 173.4, 150.2, 148.7, 141.9, 140.5, 129.1, 125.7, 123.9, 123.4, 115.6, 110.0, 108.2, 101.3, 84.2, 64.7, 56.6, 47.2, 34.4, 28.0, 15.3. HRMS (ESI-TOF) calcd for $C_{24}H_{25}NNaO_6$ ([M + Na^+]) = 446.1580; found 446.1576.

*1′-tert-Butyl-6-methyl-4-methoxy-5-methyl-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-1′,6-dicarboxylate (**3p**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 21.6 mg, 52% yield, 98% ee, mp 99−101 °C; HPLC (Chiralcel IB, hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 7.00 min, t_{r2} = 8.68 min, ee =98%. $[\alpha]_D{}^{18.9}$= +133.9 (c = 0.42 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.2 Hz, 1H), 7.38−7.28 (m, 1H), 7.07 (d, J = 4.3 Hz, 2H), 5.52 (s, 1H), 3.83 (s, 3H), 3.62 (d, J = 10.7 Hz, 1H), 3.49−3.39 (m, 1H), 3.36 (s, 3H), 1.66 (s, 9H), 1.34 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 178.8, 173.7, 169.7, 149.0, 140.5, 129.5, 125.6, 124.3, 123.1, 115.8, 100.7, 84.4, 61.7, 56.7, 52.0, 32.1, 28.1, 17.3. HRMS (ESI-TOF) calcd for $C_{22}H_{25}NNaO_7$ ([M + Na^+]) = 438.1529; found 438.1530.

*1′-tert-Butyl-6-ethyl-4-methoxy-5-methyl-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-1′,6-dicarboxylate (**3q**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 21.9 mg, 51% yield, >99% ee, mp 148−150 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 9.62 min, t_{r2} = 10.79 min, ee = >99%. $[\alpha]_D{}^{20.4}$ = +215.5 (c = 0.48 in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 1H), 7.34−7.27 (m, 1H), 7.13−7.02 (m, 2H), 5.50 (s, 1H), 3.88−3.75 (m, 5H), 3.60 (d, J = 10.6 Hz, 1H), 3.53−3.40 (m, 1H), 1.65 (s,

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9H), 1.35 (d, J = 6.6 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2, 178.9, 173.8, 169.2, 148.9, 140.6, 129.5, 125.8, 124.3, 123.1, 115.6, 100.5, 84.4, 61.6, 61.3, 56.7, 51.4, 32.0, 28.1, 17.6, 13.4. HRMS (ESI-TOF) calcd for $C_{23}H_{27}NKO_7$ ([M + K$^+$]) = 468.1425; found 468.1421.

*1′-tert-Butyl-6-isopropyl-4-methoxy-5-methyl-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-1′,6-dicarboxylate (**3r**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 26.6 mg, 60% yield, >99% ee, mp 124−126 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 8.77 min, t_{r2} = 9.45 min, ee = >99%. $[\alpha]_D^{13.0}$ = +151.4 (c = 0.44 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 1H), 7.33−7.27 (m, 1H), 7.09−7.02 (m, 2H), 5.49 (s, 1H), 4.68 (dt, J = 12.5, 6.3 Hz, 1H), 3.83 (s, 3H), 3.57 (d, J = 10.6 Hz, 1H), 3.51−3.41 (m, 1H), 1.65 (s, 9H), 1.36 (d, J = 6.5 Hz, 3H), 1.06 (d, J = 6.3 Hz, 3H), 0.72 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.4, 179.0, 173.7, 168.7, 149.0, 140.8, 129.4, 125.9, 124.2, 123.1, 115.8, 100.4, 84.3, 69.3, 61.6, 56.6, 51.3, 32.1, 28.1, 21.4, 20.7, 17.8. HRMS (ESI-TOF) calcd for $C_{24}H_{29}NNaO_7$ ([M + K$^+$]) = 466.1842; found 466.1845.

*Di-tert-butyl-4-methoxy-5-methyl-2,2′-dioxospiro[cyclohex[3]-ene-1,3′-indoline]-1′,6-dicarboxylate (**3s**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 27.0 mg, 59% yield, >99% ee, mp 178−180 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 7.29 min, t_{r2} = 7.90 min, ee = >99%. $[\alpha]_D^{20.9}$= +411.8 (c = 0.62 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 1H), 7.31 (dd, J = 8.5, 4.3 Hz, 1H), 7.06 (d, J = 4.3 Hz, 2H), 5.47 (s, 1H), 3.81 (s, 3H), 3.52 (d, J = 10.5 Hz, 1H), 3.46−3.36 (m, 1H), 1.64 (s, 9H), 1.35 (d, J = 6.5 Hz, 3H), 1.07 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.5, 179.1, 173.8, 168.3, 149.1, 140.9, 129.4, 126.4, 124.2, 123.0, 115.7, 100.3, 84.3, 82.5, 61.7, 56.6, 51.7, 32.1, 28.1, 27.2, 17.9. HRMS (ESI-TOF) calcd for $C_{25}H_{31}NNaO_7$ ([M + Na$^+$]) = 480.1998; found 480.1996.

*6-Benzyl-1′-tert-butyl-4-methoxy-5-methyl-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-1′,6-dicarboxylate (**3t**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 30.9 mg, 63% yield, 98% ee, mp 170−172 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 11.55 min, t_{r2} = 12.03 min, ee =98%. $[\alpha]_D^{14.4}$ = +180.9 (c = 0.40 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.2 Hz, 1H), 7.26−7.19 (m, 4H), 7.10−6.97 (m, 4H), 5.47 (s, 1H), 4.80 (s, 2H), 3.82 (s, 3H), 3.68 (d, J = 10.6 Hz, 1H), 3.49 (ddd, J = 10.6, 6.6, 1.2 Hz, 1H), 1.58 (s, 9H), 1.36 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 178.7, 173.5, 169.3, 148.7, 140.5, 134.6, 129.4, 128.6, 128.3, 125.6, 124.1, 122.9, 115.9, 100.4, 84.2, 67.2, 61.6, 56.6, 51.2, 32.2, 28.1, 17.6. HRMS (ESI-TOF) calcd for $C_{28}H_{29}NNaO_7$ ([M + Na$^+$]) = 514.1842; found 514.1844.

*1′-Acetyl-4-methoxy-5-methyl-6-phenylspiro[cyclohex[3]ene-1,3′-indoline]-2,2′-dione (**3u**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 24.6 mg, 63% yield, >99% ee, mp 116−118 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 8.02 min, t_{r2} = 9.05 min, ee = >99%. $[\alpha]_D^{25.7}$ = +212.9 (c = 0.33 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.1 Hz, 1H), 7.33−7.23 (m, 2H), 7.19−7.08 (m, 2H), 7.03 (t, J = 7.5 Hz, 2H), 6.76 (d, J = 5.5 Hz, 2H), 5.66 (s, 1H), 3.88 (s, 3H), 3.72 (d, J = 11.4 Hz, 1H), 3.40−3.24 (m, 1H), 1.49 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 180.1, 173.1, 148.3, 140.8, 135.2, 129.2, 128.0, 127.7, 125.4, 123.9, 123.4, 115.7, 101.6, 83.9, 65.6, 56.7, 53.7, 35.4, 27.9, 14.9. HRMS (ESI-TOF) calcd for $C_{24}H_{23}NNaO_5$ ([M + Na$^+$]) = 428.1474; found 428.1467.

*Benzyl-4-methoxy-5-methyl-2,2′-dioxo-6-phenylspiro[cyclohex-[3]ene-1,3′-indoline]-1′-carboxylate (**3v**).* Purified by flash chromatography (petroleum ether: EtOAc = 3:1) to afford a white solid, 31.8 mg, 68% yield, 98% ee, mp 116−118 °C; HPLC (Chiralcel IA, hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_{r1} = 10.74 min, t_{r2} = 15.94 min, ee =98%. $[\alpha]_D^{25.1}$ = +187.2 (c = 0.84 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 1H), 7.41−7.34 (m, 4H), 7.33−7.25 (m, 3H), 7.17 (t, J = 7.5 Hz, 1H), 7.06 (t, J = 7.3 Hz, 1H), 6.96 (t, J = 7.6 Hz, 2H), 6.75 (d, J = 6.8 Hz, 2H), 5.64 (s, 1H), 5.28 (q, J = 12.6 Hz, 2H), 3.86 (s, 3H), 3.75 (d, J = 11.4 Hz, 1H), 3.41−3.25 (m, 1H), 1.07 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 180.2, 173.0, 150.0, 140.3, 135.1, 129.4, 128.5, 128.2, 127.7, 125.6, 124.4, 123.5, 115.9, 101.4, 68.2, 65.8, 56.7, 53.6, 35.5, 15.0. HRMS (ESI-TOF) calcd for $C_{29}H_{25}NNaO_5$ ([M + Na$^+$]) = 490.1630; found 490.1636.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01318.

Preliminary mechanistic studies, ^{1}H and ^{13}C NMR spectra, CD spectra, HPLC data (PDF)

X-ray crystal data of compound **3a** (CIF)

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Notes

The authors declare no competing financial interest.

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(15) CCDC 1048951 (**3a**) contains the supplementary crystallographic data for this paper. It can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.

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