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N-Heterocyclic Carbene Catalytic [4 + 2] Cyclization of 3-Alkylenyloxindoles with Enals: γ-Carbon Activation for Enantioselective Assembly of Spirocarbocyclic Oxindoles

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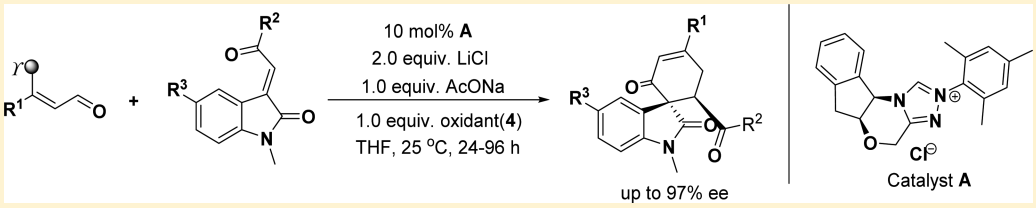
Supporting Information



ABSTRACT: The ubiquitous structure of all-carbospirocyclic oxindoles makes the development of new methods for their enantioselective and stereoselective synthesis a significant ongoing challenge. Herein, we disclose a formal [4 + 2] annulation through *N*-heterocyclic carbene (NHC) catalysis for highly enantioselective synthesis of intriguing spirocarbocyclic oxindoles in the presence of Lewis acids. This protocol features good substrates tolerance, good yields, and excellent diastereoselectivities and enantioselectivities (up to 97% ee) under mild conditions.

INTRODUCTION

Spirocarbocyclic oxindoles bearing a quaternary stereocenter at the C_3 position are a class of unique scaffolds widely present in naturally occurring alkaloid-type products and synthetic molecules of interesting bioactivities (Figure 1).[1] Although considerable progress has been acquired for their syntheses,[2] the construction of a C_3-quaternary stereocenters with a neighboring congested carbon stereocenter in a single assembly step under mild condition still remains a significant challenge.

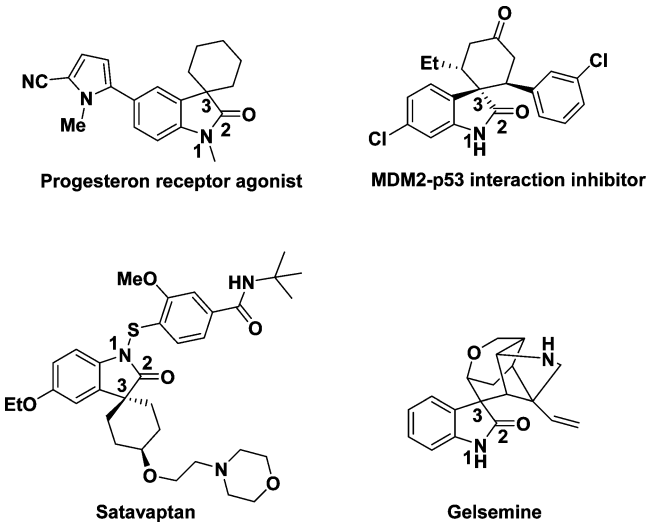


Figure 1. Examples of naturally occurring and biologically active spirocarbocyclic oxindoles.

Over the past decade, the application of *N*-heterocyclic carbenes in chemistry has developed rapidly.[3] Their unique umpolung nature has become an important strategy for synthesizing spiroheterocyclic oxindole compounds.[4] After Nair's pioneering synthesis of spirocyclic latones from 1,2-diketones and enals,[5] numerous spirocyclic lactones and lactams have been realized by Ye,[6] Chi,[7] Glorius,[8] Scheidt,[9] Wang,[10] Yao,[11] Lu,[12] and Zhong[13] et al. However, compared with these diversified NHC-catalyzed synthesis of spiroheterocycles, the all-carbon spirocarbocycles are still under developed. To the best of our knowledge, there are only a few reports concerning NHC-catalyzed synthesis of all-carbon spirocarbocyclic oxindoles. Chi et al.[14] reported a pioneering NHC-catalyzed [3 + 2] annulation of oxindole-derived β,β-disubstituted imines and enals to produce spirocyclopenteneoxindoles with only 53% ee. Recently, Ye et al.[15] (Scheme 1, eq 1) and Yao et al.[16] (Scheme 1, eq 2) independently disclosed a facile [4 + 2] annulation of 3-alkylenyloxindoles with different highly active α,β-unsaturated aldehyde equivalents to give all-carbon spirocarbocyclic oxindoles; however, no high enantioselectivities were obtained (ee <10%). Therefore, it seems that there are significant barriers for the direct activation of common

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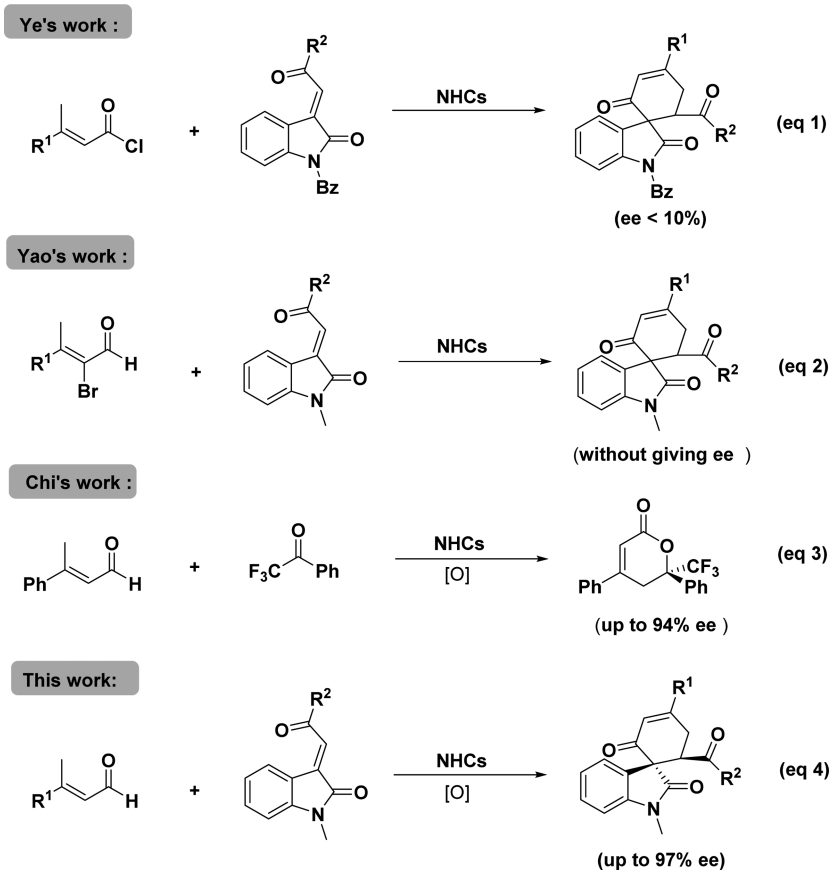
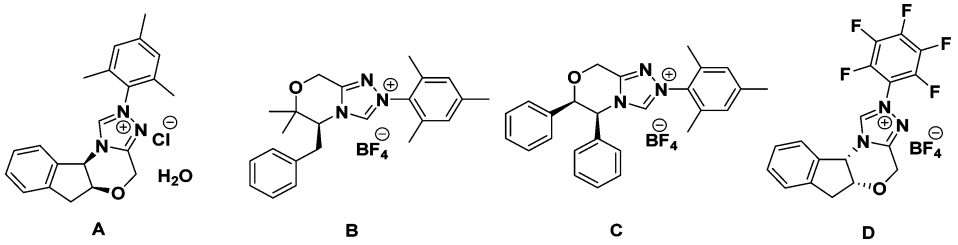
Scheme 1. NHC-Catalyzed [4 + 2] Annulation





α,β-unsaturated aldehydes to fulfill a [4 + 2] annulation to further build all-carbon spirocarbocyclic oxindoles with higher enantioselectivities. In particular, the [4 + 2] annulation of enals involves the activation of the γ-carbon, and the relatively remote distance between the chiral NHCs and the γ-positon of substrates makes the chiral induction difficult.[17] Recently, Chi et al.[17b] developed an elegant γ-carbon activation of enals to generate lactones via a [4 + 2] annulation pathway with high enantioselectivities (Scheme 1, eq 3). On the basis of these inspirations and our interest in NHC-catalyzed γ-carbon activation[18] and the synthesis of spirocyclic oxindoles,[19] we herein report a NHC-catalyzed [4 + 2] annulation for construction of interesting all-carbon spirooxindoles via an oxidative γ-carbon activation of common α,β-unsaturated aldehydes (Scheme 1, eq 4).

RESULTS AND DISCUSSION

Our investigation began with β-methyl-substituted α,β-unsaturated aldehyde **1a** and 3-alkylenyloxindole **2a** as the model substrates. Quinone **4**, previously explored in NHC-catalyzed oxidations,[17b,20] was used as an oxidant. The key experimental results of condition screening and optimization were summarized in Table 1. Interestingly, we found that the reaction could take place under the catalysis of chiral triazolium NHC catalysts generated in situ from their precursor **A** in the presence of K_2CO_3 in THF and furnished the desired [4 + 2] annulation product **3a** in good yield (82%) and excellent diastereoselectivity (99:1) but only in moderate enantioselectivity of 68% ee (Table 1, entry 1). And there was no improvement by further condition screening. Schiedt's group had made great contribution to the cooperative catalysis of NHC and Lewis acid,[9,21] and inspired by their seminal work, we tried to apply this dual catalysis strategy to our catalytic system to improve the reaction's enantioselectivity (Table 1, entries 5−11). Encouraging results emerged when 1 eq of LiBr or LiCl was used as the additive (Table 1, entries 10−11), and LiCl gave a better yield (45%). However, the addition of these additives led to the annulation transformation taking longer. Further exploration indicated that 2 eq of LiCl could slightly improve the ee (89% ee). Subsequent bases screening revealed that AcONa (Table 1, entry 17) was the best choice among the tested bases although other weak organic (TEA) (Table 1,

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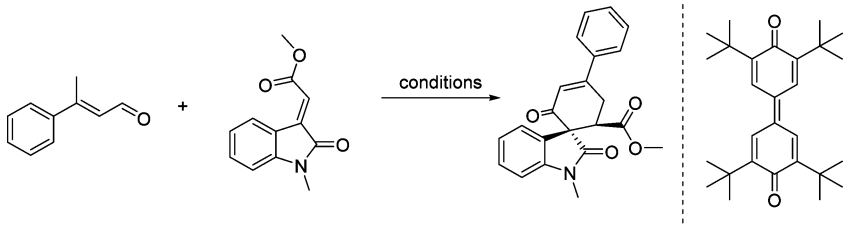
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a 4

entry	cat	additive	base	solvent	time	yield (%)[b]	dr[c]	ee (%)[d]
1	**A**	–	K_2CO_3	THF	12 h	82	99:1	68
2	**B**	–	K_2CO_3	THF	12 h	80	98:2	−7
3	**C**	–	K_2CO_3	THF	12 h	86	99:1	−4
4	**D**	–	K_2CO_3	THF	12 h	trace	–[e]	–[e]
5[f]	**A**	$Mg(OTf)_2$	K_2CO_3	THF	72 h	<10	–[e]	–[e]
6[f]	**A**	$Sc(OTf)_3$	K_2CO_3	THF	72 h	<10	–[e]	–[e]
7[f]	**A**	$Ti(Oi\text{-}Pr)_4$	K_2CO_3	THF	72 h	<10	–[e]	–[e]
8[f]	**A**	*o*FBA	K_2CO_3	THF	72 h	60	97:3	72
9[f]	**A**	*o*ClBA	K_2CO_3	THF	72 h	71	99:1	78
10[e]	**A**	LiBr	K_2CO_3	THF	72 h	30	90:10	86
11[f]	**A**	LiCl	K_2CO_3	THF	72 h	45	95:5	86
12[g]	**A**	LiCl	K_2CO_3	THF	96 h	43	96:4	89
13[g]	**A**	LiCl	Na_2CO_3	THF	96 h	47	95:5	92
14[g]	**A**	LiCl	NaOH	THF	12 h	–[h]	–[e]	–[e]
15[g]	**A**	LiCl	DBU	THF	96 h	–[h]	–[e]	–[e]
16[g]	**A**	LiCl	TEA	THF	96 h	74	98:2	88
17[g]	**A**	LiCl	AcONa	THF	96 h	65	95:5	94
18[g]	**A**	LiCl	AcONa	Toluene	12 h	78	98:2	78
19[g]	**A**	LiCl	AcONa	DCM	12 h	77	99:1	75
20[g]	**A**	LiCl	AcONa	Ether	24 h	62	98:2	85
21[g,i]	**A**	**LiCl**	**AcONa**	**THF**	**24 h**	**70**	**96:4**	**97**

[a]Unless otherwise stated, all reactions were carried out using **1a** (0.30 mmol), **2a** (0.15 mmol), **4** (0.30 mmol), catalyst (0.015 mmol), base (0.15 mmol), and solvent (2−3 mL) at 25 °C under Ar protection. [b]Isolated yields based on **2a**. [c]Determined by LC−MS analysis of the crude product. [d]Enantiomeric excess of **3a** determined via chiral phase HPLC analysis. [e]Not determined. [f]Using 0.15 mmol of additive. [g]Using 0.30 mmol of additive. [h]The reaction did not give desired product. [i]Using 0.15 mmol of oxidant (**4**).

entry 13) or inorganic (Na_2CO_3) (Table 1, entry 16) could also give comparative enantioselecitity. To contrast, strong bases such as NaOH (Table 1, entry 14) and DBU (Table 1, entry 15) were detrimental to the reaction. Then solvent screening revealed that THF was the best choice compared to DCM, toluene, and ether (Table 1, entries 17−20). Surprisingly, reducing the equivalent of the oxidant to 1 eq increased the yield up to 70% with good diastereoselectivity of 96:4 and enantioselectivity of 97% ee (Table 1, entry 21).

With the optimal conditions in hand, we further examined the substrate scope using various enals **1**. The results are summarized in Table 2. Initially we investigated the tolerance of the process by varying the R^1 of aldehyde **1** (Table 2, entries 1−14). Both electron-donating and electron-withdrawing groups on the *β*-phenyl group were tolerated (Table 2, entries 2−10). A substituent at the ortho or meta of the phenyl ring of R^1 showed no negative effect and gave the desired annulation products (**3h**−**3j**) in moderate to good yields (49−73%), diastereoselectivities (90:10−98:2) and enantioselectivities (84−93%), except the 2-F-phenyl substituent (**3g**, 66% ee). Replacing the *β*-phenyl substituent with a 2-naphthyl group (**3k**) had little influence on the reaction yield or enantioselectivity. However, *β*-heteroaryl such as 2-furyl and 2-thienyl as well as cyclohexyl-substituted enals (Table 2, entries 12−14) could also take reactions to give excellent diastereoselectivities (93:7−99:1) and moderate enantioselectivities (75−87% ee) albeit poor to moderate yields which was caught by the uncomplete consumption of the starting materials. The *R*,*R*-configuration of **3f** was determined by the X-ray analysis of its crystal (see Figure S1).[22]

The scope of the oxindole substrates was also examined. As shown in Table 3, electron-withdrawing (Cl) or electron-donating (Me, OMe) could be introduced to the 5-position of oxindole derivatives (Table 3, entries 1−3). We found it maintained good diastereoselectivities (81:19−98:2), enantioselectivities (87−94% ee), and moderate yields (31−51%). Besides the ester group, both the aryl (Ph) and alkyl (Me) groups were also tolerated as the active ketone under the current conditions, which demonstrated the broad applicability of this reaction (Table 3, entries 4−7). Additionally, when a small steric hindrance methyl group was introduced into R^2 position, good enantioselectivities (77:23−97:3) and enantioselectivities (78−90% ee) were maintained, but there was a slight decrease in reaction yields (31−62%). The ***R*,*R***-configuration of **5g** and the ***rac***-configuration of **5i** were determined by the X-ray analysis of their crystals (see Figure S2 and Figure S3).[23]

Some useful transformations were also achieved. For example, the two carbonyl groups could be selectively reduced to primary or secondary alcohol (Scheme 2), which can be

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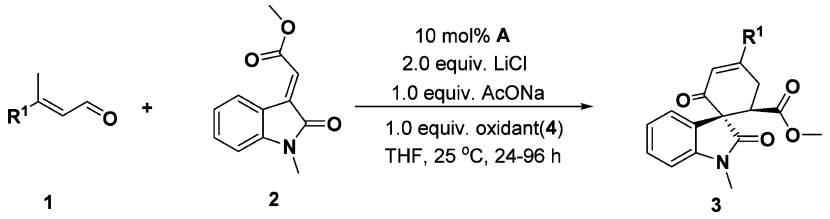
Table 2. Studies on the Variation of Enal 1[a]

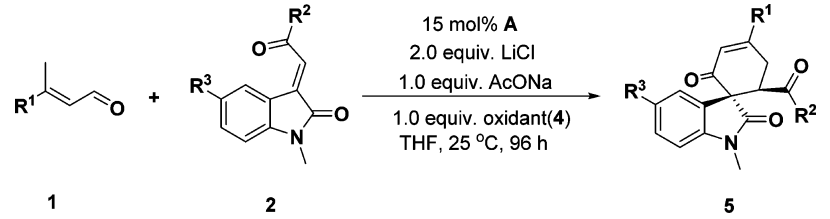


1 2 3

entry	compound	R^1	yield (%)[b]	dr[c]	ee (%)[d]
1	**3a**	Ph	70	96:4	97
2[e]	**3b**	4-$CH_3OC_6H_4$	51	95:5	90
3[e]	**3c**	4-$NO_2C_6H_4$	57	87:13	92
4	**3d**	4-FC_6H_4	68	90:10	90
5	**3e**	4-ClC_6H_4	62	91:9	95
6[e]	**3f**	4-BrC_6H_4	65	89:11	91
7	**3g**	2-FC_6H_4	50	91:9	66
8	**3h**	2-ClC_6H_4	49	98:2	93
9	**3i**	3-FC_6H_4	73	93:7	89
10	**3j**	3-ClC_6H_4	66	90:10	84
11[e]	**3k**	2-naphthalene	46	92:8	92
12[e]	**3l**	2-furyl	33	92:8	81
13[e]	**3m**	2-thienyl	41	93:7	87
14[f]	**3n**	cyclohexyl	20	99:1	75

[a]Unless otherwise stated, all reactions were carried out using **1** (0.30 mmol), **2** (0.15 mmol), **4** (0.15 mmol), catalyst **A** (0.015 mmol), AcONa (0.15 mmol), and THF (2−3 mL) at 25 °C under Ar protection for 24 h. [b]Isolated yields based on **2**. [c]Determined by LC−MS analysis of the crude product. [d]Enantiomeric excess of **3** determined via chiral phase HPLC analysis. [e]Reaction for 48 h. [f]Reaction for 96 h.

Table 3. Studies on the Variation of Oxindole 2[a]



1 2 5

entry	compound	R^1	R^2	R^3	yield (%)[b]	dr[c]	ee (%)[d]
1	**5a**	Ph	OCH_3	OCH_3	41	81:19	87
2	**5b**	4-ClC_6H_4	OCH_3	Cl	37	95:5	90
3	**5c**	4-ClC_6H_4	OCH_3	CH_3	51	98:2	94
4	**5d**	Ph	Ph	H	63	95:5	92
5	**5e**	4-FC_6H_4	Ph	H	68	93:7	91
6	**5f**	3-FC_6H_4	Ph	H	73	93:7	93
7	**5g**	4-BrC_6H_4	Ph	H	50	89:11	79
8	**5h**	Ph	CH_3	H	60	97:3	90
9	**5i**	4-FC_6H_4	CH_3	H	31	87:13	80
10	**5j**	3-FC_6H_4	CH_3	H	62	93:7	84
11	**5k**	2-FC_6H_4	CH_3	H	44	96:4	76
12	**5l**	4-ClC_6H_4	CH_3	H	36	93:7	82
13	**5m**	3-ClC_6H_4	CH_3	H	42	77:23	84
14	**5n**	2-ClC_6H_4	CH_3	H	36	96:4	86
15	**5o**	4-BrC_6H_4	CH_3	H	47	94:6	78

[a]Unless otherwise stated, all reactions were carried out using **1** (0.30 mmol), **2** (0.15 mmol), **4** (0.15 mmol), catalyst **A** (0.022 mmol), AcONa (0.15 mmol), and THF (2−3 mL) at 25 °C under Ar protection for 96 h. [b]Isolated yields based on **2**. [c]Determined by LC−MS analysis of the crude product. [d]Enantiomeric excess of **5** determined via chiral phase HPLC analysis.

easily transformed to its derivatives. For compounds **3a**, **3d**, and **3e**, containing the ketone and ester groups simultaneously, when treated with diisobutyl aluminum hydride (DIBAL-H), their primary alcohol derivatives **6a**, **6d**, and **6e** were obtained in good yields (75%−78%) and enantioselectivities (84−92%) with the ester group were reduced. While cerous chloride heptahydrate and sodium borohydride were employed, only the ketone group reacted and the secondary alcohol derivatives **7a**, **7d**, and **7e** were obtained without influencing the ester group and with good diastereoselectivities (>99:1), maintained

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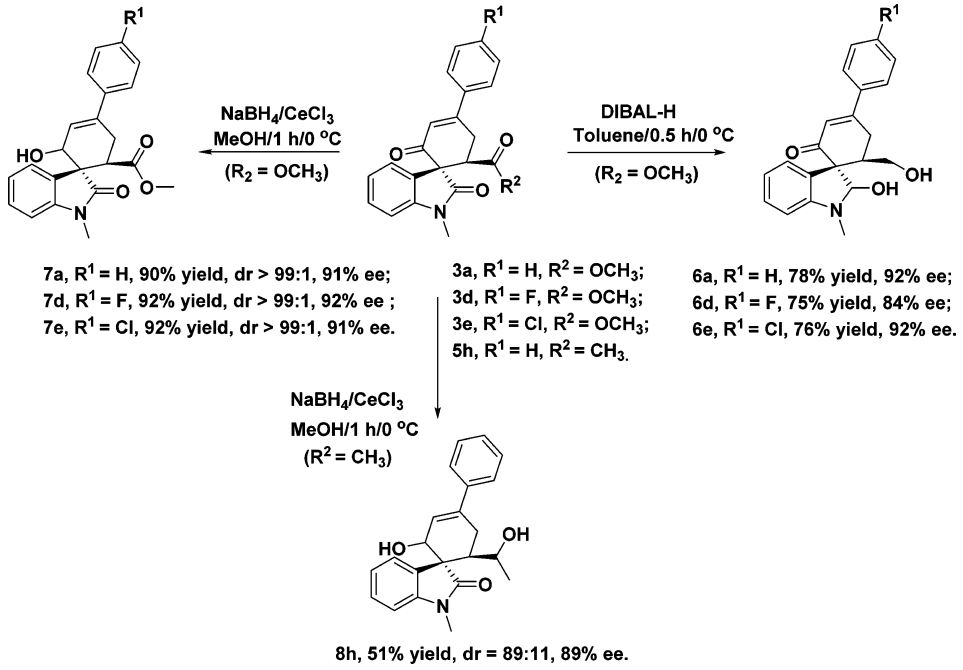
Scheme 2. Synthetic Transformations of 3a, 3f, 3g, and 5h



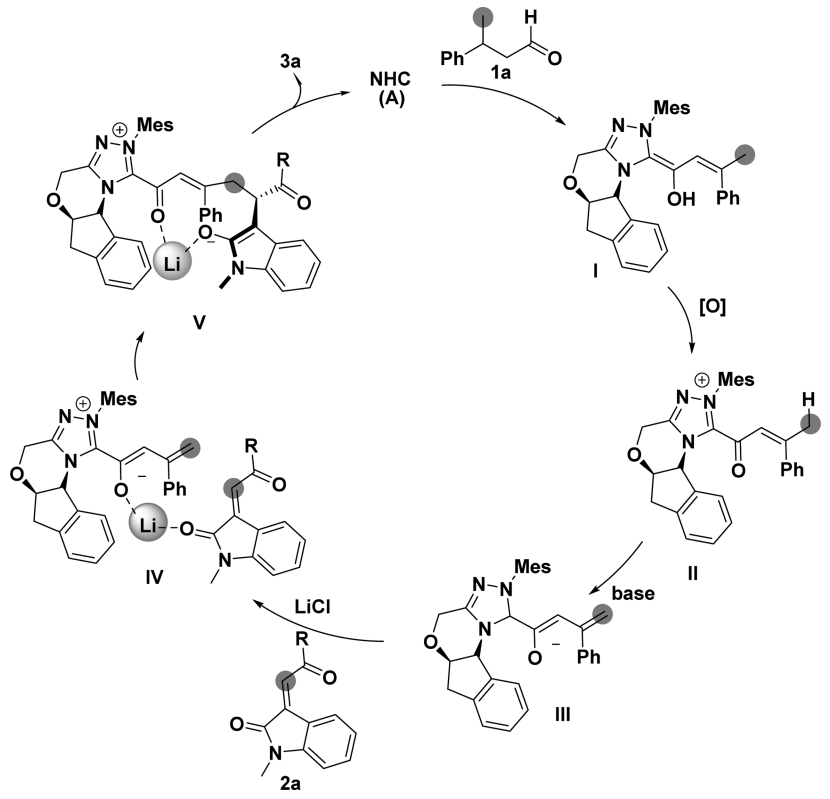


Figure 2. Postulated catalytic cycle.

enantioselectivities (91−92% ee), and good yields. Meanwhile, for compound **5h**, a completely reduced product **8h** was obtained with moderate diastereoselectivity (89:11) and good enantioselectivity (89% ee). The structure of **6d** was established by the X-ray analysis of its crystal (see Figure S4).[24]

A plausible mechanism was proposed in Figure 2. The addition of NHC to the enal carbonyl group gives the extended Breslow intermediate (**I**), γ-deprotonation of the oxidatively generated intermediate (**I**) and γ-deprotonation of the oxidatively generated α,β-unsaturated acyl azolium (**II**) gives to vinyl enolate intermediate (**III**).[17b,25] Lithium chloride, which has good affinity for carbonyl oxygens and carboxylates,[9] brings **2a** into close proximity with intermediate **III** and the chiral NHC catalyst to favor an intermediate **IV**. Then with the activation of lithium chloride, vinyl enolate undergoes intramolecular nucleophilic addition to the unsaturated amide to

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form **V**, which undergoes an intramolecular acylation to give the final annulation product **3a** and regenerated the NHC catalyst.

CONCLUSIONS

In summary, we have presented an enantioselective *N*-heterocyclic carbene catalyzed formal [4 + 2] annulation of α,β-unsaturated aldehydes with 3-alkylenyloxindoles to give the corresponding six-membered all-carbon spirocarbocyclic oxindoles under mild conditions. The challenging remote chiral control was realized through the aid of a Lewis acid. The reaction worked well for a diverse array of derivatives of both aldehydes and alkylenyloxindoles. NHCs have been widely used in the asymmetric construction of various spiroheterocyclic oxindoles; therefore, this enantioselectively NHC-catalyzed all carbon cyclization may inspire more reactions via NHC organocatalysis to access structurally diverse spirocarbocyclic oxindoles with high enantioselectivities.

EXPERIMENTAL SECTION

General Information. The reagents (chemicals) were purchased from commercial sources and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15−0.2 mm thickness). All products were characterized by their NMR and MS spectra. ^{1}H and ^{13}C NMR spectra were recorded in deuterochloroform ($CDCl_3$) on 400, 500, and 600 MHz instruments. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low- and high-resolution mass spectra (LRMS and HRMS) were measured on a spectrometer. Optical rotations were measured using a 1 mL cell with a 10 mm path length on an Auto pol V PLVS matic polarimeter and are reported as follows: $[\alpha]^{20}_{D}$ (c: mg/mL, in solvent). Melting points were measured on melting point apparatus, and PXRD was taken on a powder X-ray diffractometer.

General Procedure for the Preparation of Spirocarbocyclic Oxindoles. A vial equipped with a magnetic stir bar was charged with unsaturated aldehyde **1** (0.3 mmol), oxindole-derived olefins **2** (0.15 mmol), catalyst **A** (0.015−0.022 mmol), LiCl (0.3 mmol), AcONa (0.15 mmol), and freshly distilled dry THF (2−3 mL) was added and was capped with septa. Then the vial was evacuated and backfilled with argon, and water and oxygen are forbidden. After that, the reaction mixture was stirred at 25 °C until the olefins were completely consumed (monitored by TLC). After removal of the solvent, the residue was purified by flash chromatography on silica gel to give the desired product.

Preparation of Alcohol 6a, 6d, and 6e. To a stirred solution of ketones or esters (**3a**, **3d**, **3e**, 0.05 mmol) in dry toluene (1.0 mL) at 0 °C under Ar was slowly added diisobutyl aluminum hydride (DIBAL-H) (1.5 M in toluene, 0.5 mL, 0.75 mmol). The reaction was stirred at 0 °C for 0.5 h. Then the solution was quenched with a 1 M HCl solution. The aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified via column chromatography on silica gel (petroleum ether/AcOEt 1:1) to afford alcohol products (**6a**, **6d**, and **6e**).

Preparation of Alcohol 7a, 7d, 7e, and 8h. To a stirred solution of ketones or esters (**3a**, **3d**, **3e**, **5h**, 0.05 mmol) and $CeCl_3{\cdot}7H_2O$ (0.05 mmol) in MeOH (1.0 mL) at 0 °C was slowly added NaBH4 (0.75 mmol). The reaction was stirred at 0 °C for 1 h. Then the solution was quenched with an 0.1 M HCl solution. The aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified via column chromatography on silica gel (petroleum ether/AcOEt 2:1) to afford alcohol products (**7a**, **7d**, **7e**, and **8h**).

*(1R,6R)-Methyl 1′-Methyl 4-Phenyl-2,2′-dioxospiro[cyclohex[3]-ene-1,3′-indo-line]-6-carboxylate (**3a**).* 37.9 mg, 70% yield, 97% ee, 96:4 dr, $[\alpha]_D^{20}$ = +270.2 (4.6 mg/mL, CHCl3), pale yellow solid. M.P.: 150.7−153.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70−7.64 (m, 2H), 7.54−7.46 (m, 3H), 7.32−7.28 (m, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.97−6.93 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.63−6.58 (m, 1H), 6.63−6.58 (m, 1H), 4.12−4.05 (m, 1H), 3.44 (m, 1H), 3.35−3.26 (m, 4H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.0, 175.0, 170.0, 156.8, 144.6, 136.8, 130.5, 128.9, 128.6, 125.8, 123.3, 122.7, 121.9, 108.4, 59.8, 51.8, 44.2, 26.9, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{19}O_4NNa$ $[M + Na]^+$, 384.1217; found, 384.1206. HPLC conditions for ee determination: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate =1.0 mL/min, λ = 254 nm, and retention time = 30.005 min (major) and 64.340 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 60/40, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 10.946 min, and t_{minor} = 13.143 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Methoxylphenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3b**).* 30.1 mg, 51% yield, 90% ee, 95:5 dr, $[\alpha]_D^{20}$ = +252.7 (4.1 mg/mL, CHCl3), white solid. M.P.: 185.3−189.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 9.4, 2.5 Hz, 2H), 7.33−7.24 (m, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 7.03−6.97 (m, 2H), 6.97−6.85 (m, 2H), 6.57 (d, *J* = 1.8 Hz, 1H), 4.04 (dd, *J* = 11.3, 6.3 Hz, 1H), 3.89 (d, *J* = 7.3 Hz, 3H), 3.50 (s, 3H), 3.45−3.34 (m, 2H), 3.34−3.29 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.5, 175.7, 170.6, 162.1, 156.6, 145.1, 129.3, 129.2, 128.0, 126.6, 123.2, 122.4, 121.8, 114.5, 108.9, 60.3, 55.5, 52.3, 44.7, 27.2, 26.7. HRMS (ESI-TOF): calculated for $C_{23}H_{21}O_5NNa$ $[M + Na]^+$, 414.1323; found, 414.1313. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 41.037 min (major) and 59.329 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 216 nm), t_{major} = 8.331 min, and t_{minor} = 9.534 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Nitrophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-dicarboxylate (**3c**).* 34.7 mg, 57% yield, 92% ee, 87:13 dr, $[\alpha]_D^{20}$ = +257.1 (3.5 mg/mL, CHCl3), yellow solid. M.P.: 234.8−239.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (d, *J* = 9.0 Hz, 2H), 7.86−7.80 (m, 2H), 7.37−7.30 (m, 1H), 7.08 (dd, *J* = 7.5, 0.7 Hz, 1H), 6.97 (m, 2H), 6.65 (s, 1H), 4.07 (dd, *J* = 10.2, 7.0 Hz, 1H), 3.53 (s, 3H), 3.48−3.39 (m, 2H), 3.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.5, 174.5, 169.6, 154.1, 148.5, 144.5, 143.0, 129.2, 126.8, 125.8, 125.4, 123.8, 122.6, 122.1, 108.6, 59.7, 52.0, 44.1, 27.0, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_6N_2Na$ $[M + Na]^+$, 429.1057; found, 429.1057. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 41.088 min (major) and 93.219 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/15, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 10.279 min, and t_{minor} = 12.167 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3d**).* 38.5 cmg, 68% yield, 90% ee, 90:10 dr, $[\alpha]_D^{20}$ = +315.9 (4.6 mg/mL, CHCl3), white solid. M.P.: 205.1−207.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75−7.63 (m, 2H), 7.35−7.28 (m, 1H), 7.19 (t, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 7.5 Hz, 1H), 6.99−6.88 (m, 2H), 6.57 (s, 1H), 4.09−3.98 (m, 1H), 3.51 (s, 3H), 3.43−3.38 (m, 2H), 3.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.3, 175.4, 170.4, 164.4 (d, *J* = 252.7 Hz), 156.0, 145.1, 133.33, 129.4, 128.4(d, *J* = 8.6 Hz), 126.3, 123.6, 123.2, 122.4, 116.28 (d, *J* = 21.8 Hz), 108.97, 60.2, 52.4, 44.65, 27.4, 26.7. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NFNa$ $[M + Na]^+$, 402.1112; found, 402.1100. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 85:15, flow rate =1.0 mL/min, λ = 254 nm, and retention time = 59.878 min (major) and 121.011 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 7.318 min, and t_{minor} = 8.280 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Chlorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3e**).* 36.7 mg, 62% yield, 95% ee, 91:9 dr, $[\alpha]_D^{20}$ = +302.1 (2.4 mg/mL, CHCl3),

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white solid. M.P.: 200.1−201.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 8.7 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.31 (dd, J = 8.3, 7.3 Hz, 1H), 7.06 (d, J = 7.3 Hz, 1H), 6.98−6.88 (m, 2H), 6.58 (s, 1H), 4.05 (t, J = 8.7 Hz, 1H), 3.51 (s, 3H), 3.42−3.37 (m, 2H), 3.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.3, 175.3, 170.3, 155.8, 145.1, 137.2, 135.6, 129.4, 127.6, 126.2, 124.0, 123.2, 122.4, 109.0, 60.3, 52.4, 44.6, 27.3, 26.8. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NClNa$ $[M + Na]^+$, 418.0817; found, 418.0806. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 59.479 min (major) and 93.778 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 16.277 min, and t_{minor} = 18.511 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Bromophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3f**).* 42.9 mg, 65% yield, 91% ee, 89:11 dr, $[\alpha]_D^{20}$ = +331.0 (2.9 mg/mL, CHCl3), white solid. M.P.: 210.4−211.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.59 (m, 2H), 7.59−7.51 (m, 2H), 7.33−7.29 (m, 1H), 7.08−7.03 (m, 1H), 6.95−6.93 (m, 2H), 6.59 (t, J = 1.5 Hz, 1H), 4.05 (t, J = 8.7 Hz, 1H), 3.51 (s, 3H), 3.40 (dd, J = 8.7, 1.5 Hz, 2H), 3.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.3, 175.4, 170.3, 155.9, 145.1, 136.1, 132.4, 129.5, 127.8, 126.2, 125.6, 124.0, 123.2, 122.4, 109.0, 60.3, 52.4, 44.6, 27.3, 26.8. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NBrNa$ $[M + Na]^+$, 462.0322; found, 462.0316. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 52.199 min (minor) and 71.101 min (major). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 19.887 min, and t_{minor} = 22.754 min.

*(1R,6R)-Methyl 1′-Methyl 4-(2-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3g**).* 28.2 mg, 50% yield, 66% ee, 91:9 dr, $[\alpha]_D^{20}$ = +354.2 (2.3 mg/mL, CHCl3), white solid. M.P.: 179.1−181.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.41 (m, 2H), 7.34−7.32 (m, 1H), 7.28−7.23 (m, 1H), 7.22−7.16 (m, 2H), 7.01−6.99 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.45 (d, J = 1.9 Hz, 1H), 4.06 (dd, J = 11.7, 5.8 Hz, 1H), 3.58−3.50 (m, 1H), 3.50 (s, 3H), 3.36 (d, J = 5.8 Hz, 1H), 3.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.7, 174.9, 169.8, 159.5 (d, J = 251.4 Hz), 154.5, 144.7, 131.4 (d, J = 8.7 Hz), 129.0, 128.5 (d, J = 3.0 Hz), 127.1 (d, J = 3.7 Hz), 126.1 (d, J = 12.5 Hz), 125.7, 124.4 (d, J = 3.4 Hz), 122.8, 122.1, 116.2 (d, J = 22.5 Hz), 108.5, 59.9, 51.9, 44.4, 28.4 (d, J = 4.9 Hz), 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NFNa$ $[M + Na]^+$, 402.1112; found, 402.1109. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 10.069 min (major) and 20.164 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 8.907 min, and t_{minor} = 11.546 min.

*(1R,6R)-Methyl 1′-Methyl 4-(2-Chlorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3h**).* 28.7 mg, 49% yield, 93% ee, 98:2 dr, $[\alpha]_D^{20}$ = +312.7 (4.1 mg/mL, CHCl3), white solid. M.P.: 156.1−160.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42−7.39 (m, 1H), 7.30−7.27 (m, 2H), 7.27 (dd, J = 3.7, 1.7 Hz, 1H), 7.26−7.21 (m, 2H), 6.97−6.91 (m, 1H), 6.86−6.81 (m, 1H), 6.14 (d, J = 1.8 Hz, 1H), 4.04−3.98 (m, 1H), 3.45−3.37 (m, 4H), 3.24 (s, 3H), 3.17 (ddd, J = 19.7, 5.7, 0.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.1, 175.4, 170.2, 158.9, 145.1, 138.5, 131.3, 130.4, 130.3, 129.5, 129.0, 128.2, 127.4, 126.1, 123.4, 122.6, 109.0, 60.4, 52.3, 44.9, 29.6, 26.8. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NClNa$ $[M + Na]^+$, 418.0817; found, 418.0814. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 13.538 min (major) and 23.392 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 12.965 min, t_{minor} = 17.913 min, and dr = 98:2.

*(1R,6R)-Methyl 1′-Methyl 4-(3-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3i**).* 41.4 mg, 73% yield, 89% ee, 93:7 dr, $[\alpha]_D^{20}$ = +414.1 (3.9 mg/mL, CHCl3), white solid. M.P.: 204.6−206.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.45 (m, 2H), 7.40−7.34 (m, 1H), 7.33−7.31 (m, 1H), 7.24−7.17 (m, 1H), 7.07 (dd, J = 7.5, 0.6 Hz, 1H), 6.98−6.94 (m, 1H), 6.91 (d, J = 7.7 Hz, 1H), 6.59−6.58 (m, 1H), 4.05 (t, J = 8.7 Hz, 1H), 3.52 (s, 3H), 3.41 (dd, J = 8.7, 1.5 Hz, 2H), 3.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.9, 174.9, 169.8, 162.6 (d, J = 247.6 Hz), 155.4, 144.6, 139.1 (d, J = 7.2 Hz), 130.3 (d, J = 8.3 Hz), 129.1, 125.7, 124.1, 122.7, 122.0, 121.6 (d, J = 2.8 Hz), 117.4 (d, J = 21.2 Hz), 112.9 (d, J = 22.8 Hz), 108.6, 59.9, 51.9, 44.2, 27.0, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NFNa$ $[M + Na]^+$, 402.1112; found, 402.1115. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 10.082 min (major) and 17.941 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 8.952 min, and t_{minor} = 9.762 min.

*(1R,6R)-Methyl 1′-Methyl 4-(3-Chlorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3j**).* 38.9 mg, 66% yield, 84% ee, 90:10 dr, $[\alpha]_D^{20}$ = +325.1 (3.5 mg/mL, CHCl3), white solid. M.P.: 193.2−195.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 1.8 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.41−7.34 (m, 2H), 7.26−7.22 (m, 1H), 7.00 (d, J = 7.3 Hz, 1H), 6.88 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 6.50 (s, 1H), 3.97 (t, J = 8.7 Hz, 1H), 3.44 (s, 3H), 3.32 (d, J = 7.8 Hz, 2H), 3.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.8, 174.8, 169.8, 155.3, 144.6, 138.7, 134.8, 130.4, 129.9, 129.1, 126.0, 125.7, 124.2, 124.0, 122.7, 122.0, 108.6, 59.8, 52.0, 44.2, 26.9, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_4NClNa$ $[M + Na]^+$, 418.0817; found, 418.0804. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 11.246 min (major) and 21.356 min (minor). The dr was determined by LC-MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 17.556 min, and t_{minor} = 21.830 min.

*(1R,6R)-Methyl 1′-Methyl 4-(Naphathalen-2-yl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3k**).* 28.3 mg, 46% yield, 92% ee, 92:8 dr, $[\alpha]_D^{20}$ = +303.1 (5.5 mg/mL, CHCl3), white solid. M.P.: 185.4−188.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 1.1 Hz, 1H), 7.93 (dd, J = 8.7, 5.3 Hz, 2H), 7.89 (dd, J = 5.9, 3.2 Hz, 1H), 7.76 (dd, J = 8.7, 1.8 Hz, 1H), 7.61−7.52 (m, 2H), 7.34−7.28 (m, 1H), 7.13 (d, J = 7.1 Hz, 1H), 6.98−6.87 (m, 2H), 6.76 (d, J = 1.1 Hz, 1H), 4.17−4.02 (m, 1H), 3.64−3.55 (m, 2H), 3.54 (s, 3H), 3.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.1, 175.1, 170.1, 156.5, 144.6, 134.0, 133.9, 132.6, 129.0, 128.5, 127.4, 127.3, 126.6, 126.3, 125.9, 123.6, 122.8, 122.6, 122.0, 108.5, 60.0, 51.9, 44.3, 26.9, 26.3. HRMS (ESI-TOF): calculated for $C_{26}H_{21}O_4NNa$ $[M + Na]^+$, 434.1374; found, 434.1364. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 23.383 min (major) and 35.904 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 23.052 min, and t_{minor} = 24.814 min.

*(1R,6R)-Methyl 1′-Methyl 4-(Furan-2-yl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3l**).* 17.1 mg, 33% yield, 81% ee, 92:8 dr, $[\alpha]_D^{20}$ = +127.1 (2.4 mg/mL, CHCl3), pale yellow solid. M.P.: 192.1.4−193.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (d, J = 1.5 Hz, 1H), 7.31−7.26 (m, 1H), 7.08 (d, J = 7.0 Hz, 1H), 6.97−6.86 (m, 3H), 6.62 (d, J = 1.6 Hz, 1H), 6.59 (dd, J = 3.5, 1.8 Hz, 1H), 4.02 (dd, J = 11.7, 6.1 Hz, 1H), 3.49 (s, 3H), 3.38−3.32 (m, 1H), 3.31 (s, 3H), 3.29−3.24 (m, 1H).^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 175.0, 169.9, 150.7, 145.5, 144.6, 144.3, 128.9, 126.1, 122.8, 121.9, 119.0, 113.6, 112.4, 108.4, 60.1, 51.9, 43.9, 26.3, 24.2. HRMS (ESI-TOF): calculated for $C_{20}H_{17}O_5NNa$ $[M + Na]^+$, 374.0999; found, 374.0989. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 22.155 min (major) and 60.493 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 214 nm), t_{major} = 3.886 min, and t_{minor} = 5.429 min.

*(1R,6R)-Methyl 1′-Methyl 4-(Thiophen-2-yl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3m**).* 22.4 mg, 41%

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yield, 87% ee, 93:7 dr, $[\alpha]_D^{20}$ = +221.0 (2.0 mg/mL, $CHCl_3$), yellow solid. M.P.: 132.8−135.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59−7.53 (m, 2H), 7.33−7.26 (m, 1H), 7.18 (dd, J = 5.1, 3.8 Hz, 1H), 7.09 (dd, J = 7.5, 0.6 Hz, 1H), 6.97−6.91 (m, 1H), 6.89 (d, J = 7.9 Hz, 1H), 6.57 (d, J = 1.4 Hz, 1H), 4.06 (dd, J = 11.5, 6.2 Hz, 1H), 3.56−3.52 (m, 1H), 3.51 (s, 3H), 3.47 (dd, J = 6.2, 0.7 Hz, 1H), 3.43 (dd, J = 11.5, 2.1 Hz, 1H), 3.32 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 175.0, 169.9, 149.7, 144.6, 141.0, 129.7, 129.0, 128.2, 128.1, 126.0, 122.8, 122.0, 120.7, 108.5, 60.0, 51.9, 44.0, 26.8, 26.3. HRMS (ESI-TOF): calculated for $C_{20}H_{17}O_4NNaS$ $[M + Na]^+$, 390.0770; found, 390.0767. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 28.171 min (major) and 70.958 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 214 nm), t_{major} = 5.976 min, and t_{minor} = 6.807 min.

(1R,6R)-Methyl 1′-Methyl 4-(Cyclohexyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**3n**). 11.1 mg, 20% yield, 75% ee, 99:1 dr, $[\alpha]_D^{20}$ = +150.8 (2.0 mg/mL, $CHCl_3$), white solid. M.P.: 162.0−166.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.26 (m, 1H), 6.99−6.95 (m, 2H), 6.88 (d, J = 7.8 Hz, 1H), 6.06−6.01 (m, 1H), 3.88 (dd, J = 11.6, 6.0 Hz, 1H), 3.47 (d, J = 5.9 Hz, 3H), 3.29 (s, 3H), 3.08−2.87 (m, 2H), 1.97−1.82 (m, 4H), 1.77 (d, J = 12.7 Hz, 1H), 1.41−1.33 (m, 4H), 1.28−1.22 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.2, 175.2, 170.1, 168.5 144.6, 128.8, 125.9, 122.7, 122.6, 121.8, 108.42, 60.2, 51.8, 45.8, 44.2, 31.1, 30.5, 27.3, 26.2, 25.8, 25.7. HRMS (ESI-TOF): calculated for $C_{22}H_{25}O_4NNa$ $[M + Na]^+$, 390.1676; found, 390.1675. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 13.501 min (major) and 30.831 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 254 nm), and t_{major} = 18.844 min.

(1R,6R)-Methyl 1′-Methyl-5′-methoxyl-4-phenyl-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**5a**). 23.8 mg, 41% yield, 87% ee, 81:19 dr, $[\alpha]_D^{20}$ = +236.5 (4.6 mg/mL, $CHCl_3$), dark red solid. M.P.: 145.1−148.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72−7.63 (m, 2H), 7.49 (dd, J = 5.5, 1.7 Hz, 3H), 6.81 (d, J = 0.7 Hz, 2H), 6.72 (s, 1H), 6.60 (d, J = 1.0 Hz, 1H), 4.05 (dd, J = 10.9, 6.6 Hz, 1H), 3.71 (s, 3H), 3.53 (s, 3H), 3.50−3.34 (m, 1H), 3.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.4, 175.1, 170.4, 157.4, 155.5, 138.7 137.2, 131.0, 129.1, 127.7, 126.3, 123.8, 112.2, 112.1, 109.0, 60.6, 55.8, 52.3, 44.6, 27.4, 26.8. HRMS (ESI-TOF): calculated for $C_{23}H_{21}O_5NNa$ $[M + Na]^+$, 414.1312; found, 414.1306. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 24.920 min (major) and 47.551 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 8.204 min, and t_{minor} = 14.460 min.

(1R,6R)-Methyl 1′-Methyl-5′-Chloro-4-(4-chlorophenyl)-2,2′-dioxospiro[cyclohex [3]ene-1,3′-indoline]-6-carboxylate (**5b**). 23.6 mg, 37% yield, 90% ee, 95:5 dr, $[\alpha]_D^{20}$ = +292.9 (1.6 mg/mL, $CHCl_3$), brown solid. M.P.: 215.8−219.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69−7.59 (m, 2H), 7.48 (d, J = 8.8 Hz, 2H), 7.29 (dd, J = 8.4, 2.1 Hz, 1H), 7.00 (d, J = 1.9 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 6.59 (d, J = 1.6 Hz, 1H), 4.04 (dd, J = 11.5, 5.9 Hz, 1H), 3.55 (s, 3H), 3.45 (dd, J = 19.1, 5.9 Hz, 1H), 3.38−3.27 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 174.9, 170.1, 156.1, 143.8, 137.4, 135.4, 129.5, 129.4, 127.9, 127.7, 127.6, 123.8, 123.6, 109.8, 60.3, 52.5, 44.6, 27.2, 26.9. HRMS (ESI-TOF): calculated for $C_{23}H_{21}O_5NNa$ $[M + Na]^+$, 414.1312; found, 414.1306. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 12.334 min (major) and 16.588 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 13.608 min, and t_{minor} = 18.181 min.

(1R,6R)-Methyl 1′-Methyl-5′-methyl-4-(4-chlorophenyl)-2,2′-dioxospiro[cyclohex [3]ene-1,3′-indoline]-6-carboxylate (**5c**). 31.3 mg, 51% yield, 94% ee, 98:2 dr, $[\alpha]_D^{20}$ = +279.3 (4.6 mg/mL, $CHCl_3$), pale yellow solid. M.P.: 232.8−236.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.58 (m, 2H), 7.53−7.41 (m, 2H), 7.10 (d, J = 7.4 Hz, 1H), 6.84−6.75 (m, 2H), 6.57 (d, J = 1.7 Hz, 1H), 4.06 (dd, J = 11.4, 5.5 Hz, 1H), 3.45−3.38 (m, 1H), 3.29 (s, 3H), 3.22 (dd, J = 18.9, 5.3 Hz, 1H), 2.24 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.6, 192.3, 175.1, 155.8, 142.1, 137.2, 135.8, 132.2, 129.7, 129.4, 127.6, 126.1, 124.3, 124.0, 108.9, 60.6, 52.2, 29.1, 27.1, 26.8, 21.2. HRMS (ESI-TOF): calculated for $C_{23}H_{21}O_4NCl$ $[M + H]^+$, 410.1154; found, 410.1158. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 33.490 min (major) and 54.497 min (minor). The dr was determined by LC−MS with an Extend-C18 column (250 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 70/30, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 11.579 min, and t_{minor} = 13.416 min.

(1R,6R)-Phenyl 1′-Methyl 4-Phenyl-2,2′-dioxospiro[cyclohex[3]-ene-1,3′-indoline]-2,6-dione (**5d**). 38.3 mg, 63% yield, 92% ee, 95:5 dr, $[\alpha]_D^{20}$ = +346.6 (3.1 mg/mL, $CHCl_3$), white solid. M.P.: 204.3−207.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85−7.75 (m, 2H), 7.68−7.59 (m, 2H), 7.59−7.51 (m, 1H), 7.50−7.37 (m, 5H), 7.36−7.28 (m, 1H), 7.15 (d, J = 7.5 Hz, 1H), 7.02−6.98 (m, 1H), 6.86 (d, J = 7.8 Hz, 1H), 6.68 (d, J = 1.3 Hz, 1H), 4.93 (dd, J = 11.0, 5.4 Hz, 1H), 3.50 (ddd, J = 18.9, 11.0, 2.3 Hz, 1H), 3.33 (dd, J = 19.0, 5.4 Hz, 1H), 3.07 (s, 3H). ^{13}C NMR (126 MHz, $CHCl_3$): δ 198.0, 192.4, 174.5, 157.4, 144.4, 137.3, 135.8, 133.5, 130.9, 129.1, 129.0, 128.7, 128.6, 126.5, 126.2, 124.0, 123.8, 122.5, 108.9, 60.9, 47.2, 28.7, 26.4. HRMS (ESI-TOF): calculated for $C_{27}H_{21}O_3NNa$ $[M + Na]^+$, 430.1425; found, 430.1416. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 38.974 min (minor) and 94.243 min (major). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 5.898 min, and t_{minor} = 6.969 min.

(1R,6R)-Phenyl 1′-Methyl 4-(4-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5e**). 43.2 mg, 68% yield, 91% ee, 93:7 dr, $[\alpha]_D^{20}$ = +267.2 (2.9 mg/mL, $CHCl_3$), white solid. M.P.: 205.1−207.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81−7.73 (m, 2H), 7.66−7.60 (m, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.33−7.29 (m, 1H), 7.18−7.10 (m, 3H), 7.02−6.96 (m, 1H), 6.84 (d, J = 7.8 Hz, 1H), 6.62 (d, J = 1.3 Hz, 1H), 4.91 (dd, J = 10.7, 5.4 Hz, 1H), 3.46 (ddd, J = 18.9, 10.8, 2.2 Hz, 1H), 3.30 (dd, J = 19.0, 5.3 Hz, 1H), 3.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.0, 192.2, 174.4, 164.3 (d, J = 252.5 Hz), 156.1, 144.4, 135.8, 133.6, 129.1, 128.7 (d, J = 14.2 Hz), 128.3 (d, J = 8.6 Hz), 126.5, 123.9, 123.8, 122.6, 116.2 (d, J = 21.8 Hz), 109.0, 60.9, 47.2, 29.7, 28.7, 26.4. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NFNa$ $[M + Na]^+$, 386.1163; found, 386.1161. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 48.044 min (minor) and 154.728 min (major). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) ($MeOH/H_2O$ = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 6.254 min, and t_{minor} = 7.357 min.

(1R,6R)-Phenyl 1′-Methyl 4-(3-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5f**). 46.4 mg, 73% yield, 93% ee, 93:7 dr, $[\alpha]_D^{20}$ = +314.8 (4.4 mg/mL, $CHCl_3$), white solid. M.P.: 204.6−206.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (dd, J = 8.4, 1.2 Hz, 2H), 7.59−7.53 (m, 1H), 7.46−7.40 (m, 4H), 7.35−7.28 (m, 2H), 7.21−7.15 (m, 1H), 7.13 (dd, J = 7.5, 0.7 Hz, 1H), 7.02−6.98 (m, 1H), 6.86 (d, J = 7.6 Hz, 1H), 6.65 (dd, J = 2.1, 0.9 Hz, 1H), 4.91 (dd, J = 10.5, 5.5 Hz, 1H), 3.45 (ddd, J = 18.9, 10.6, 2.3 Hz, 1H), 3.31 (ddd, J = 19.0, 5.5, 0.9 Hz, 1H), 3.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.4, 191.7, 173.8, 162.6 (d, J = 247.6 Hz), 155.4, 144.0, 139.2 (d, J = 7.4 Hz), 135.3, 133.2, 130.3 (d, J = 8.2 Hz), 128.7, 128.2 (d, J = 17.4 Hz), 126.0, 124.4, 123.5, 122.2, 121.5 (d, J = 2.7 Hz), 117.24 (d, J = 21.2 Hz), 112.9, 112.8, 108.5, 60.4, 46.7, 28.2, 26.0. HRMS (ESI-TOF): calculated for $C_{27}H_{20}O_3NFNa$ $[M + Na]^+$, 448.1319; found, 448.1312. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 16.948 min (minor) and 20.880 min (major). The dr was determined by LC−MS with an Extend-C18 column (150

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× 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 6.519 min, and t_{minor} = 8.068 min.

*(1R,6R)-Phenyl 1′-Methyl 4-(4-Bromophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5g**).* 36.3 mg, 50% yield, 79% ee, 89:11 dr, $[\alpha]_D^{20}$ = +220.1 (2.7 mg/mL, CHCl3), pale yellow solid. M.P.: 229.0−232.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.72 (m, 2H), 7.62−7.57 (m, 2H), 7.52−7.47 (m, 2H), 7.42 (dd, J = 10.5, 4.9 Hz, 2H), 7.38−7.33 (m, 1H), 7.31 (dd, J = 7.7, 1.2 Hz, 1H), 7.14−7.09 (m, 1H), 7.02−6.98 (m, 1H), 6.85 (d, J = 7.5 Hz, 1H), 6.67−6.63 (m, 1H), 4.90 (dd, J = 10.6, 5.4 Hz, 1H), 3.50−3.41 (m, 1H), 3.34−3.16 (m, 1H), 3.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 198.0, 192.2, 174.3, 156.0, 144.4, 136.2, 135.8, 133.7, 132.4, 131.8, 129.2, 128.7, 128.6, 128.0, 127.7, 126.4, 125.4, 124.2, 124.0, 122.6, 109.0, 60.9, 47.2, 28.5, 26.4. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NBrNa$ $[M + Na]^+$, 446.0362; found, 446.0364. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 41.500 min (minor) and 84.303 min (major). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 214 nm), t_{major} = 18.721 min, and t_{minor} = 19.452 min.

*(1R,6R)-Methyl 1′-Methyl 4-Phenyl-2,2′-dioxospiro[cyclohex[3]-ene-1,3′- indoline]-2,6-dione (**5h**).* 30.9 mg, 60% yield, 90% ee, 97:3 dr, $[\alpha]_D^{20}$ = +451.4 (3.2 mg/mL, $CHCl_3$), white solid. M.P.: 171.7−174.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71−7.63 (m, 2H), 7.54−7.46 (m, 3H), 7.32−7.26 (m, 1H), 7.06 (d, J = 7.5 Hz, 1H), 6.94 (ddd, J = 12.7, 9.6, 4.4 Hz, 2H), 6.63−6.58 (m, 1H), 4.08 (dd, J = 11.5, 5.7 Hz, 1H), 3.44 (ddd, J = 18.8, 11.5, 2.3 Hz, 1H), 3.36−3.24 (m, 4H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.1, 191.8, 174.8, 156.7, 144.1, 136.8, 130.5, 128.7, 128.7, 125.7, 125.5, 123.4, 122.9, 122.1, 108.6, 60.1, 51.8, 28.5, 26.9, 26.2. HRMS (ESI-TOF): calculated for $C_{22}H_{20}O_3N$ $[M + H]^+$, 346.1438; found, 346.1430. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 1.0 mL/min, λ = 254 nm, and retention time = 12.683 min (major) and 15.824 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 8.374 min, and t_{minor} = 9.479 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5i**).* 16.8 mg, 31% yield, 80% ee, 87:13 dr, $[\alpha]_D^{20}$ = +213.5 (3.4 mg/mL, $CHCl_3$), white solid. M.P.: 193.3−195.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71−7.64 (m, 2H), 7.30 (m, 1H), 7.21−7.17 (m, 2H), 7.04 (d, J = 7.5 Hz, 1H), 6.94 (ddd, J = 13.6, 10.2, 4.3 Hz, 2H), 6.55 (d, J = 1.6 Hz, 1H), 4.07 (dd, J = 11.4, 5.6 Hz, 1H), 3.41 (ddd, J = 18.8, 11.4, 2.3 Hz, 1H), 3.33−3.22 (m, 4H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.5, 192.2, 175.2, 164.4 (d, J = 252.7 Hz), 155.9, 144.6, 133.4 (d, J = 3.3 Hz), 129.3, 128.3 (d, J = 8.6 Hz), 126.0, 123.7, 123.4, 122.6, 116.3 (d, J = 21.8 Hz), 109.2, 60.5, 52.2, 29.0, 27.4, 26.7. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NFNa$ $[M + Na]^+$, 386.1163; found, 386.1158. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 18.937 min (major) and 22.682 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 6.241 min, and t_{minor} = 7.400 min.

*(1R,6R)-Methyl 1′-Methyl 4-(3-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5j**).* 33.6 mg, 62% yield, 94% ee, 93:7 dr, $[\alpha]_D^{20}$ = +283.6 (3.4 mg/mL, $CHCl_3$), white solid. M.P.: 229.1−233.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51−7.43 (m, 2H), 7.35 (ddd, J = 7.1, 4.7, 1.6 Hz, 1H), 7.30 (dd, J = 7.8, 1.2 Hz, 1H), 7.21 (ddd, J = 9.0, 5.1, 2.3 Hz, 1H), 7.04 (d, J = 6.9 Hz, 1H), 6.98−6.94 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.58 (d, J = 1.4 Hz, 1H), 4.07 (dd, J = 11.3, 5.7 Hz, 1H), 3.41 (ddd, J = 18.9, 11.3, 2.3 Hz, 1H), 3.32 (s, 3H), 3.26 (dd, J = 18.9, 5.6 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.0, 191.6, 174.6, 162.6 (d, J = 247.9 Hz), 155.2, 144.1, 139.2 (d, J = 7.3 Hz), 130.3 (d, J = 8.2 Hz), 128.9, 125.4, 124.2, 123.0, 122.2, 121.5 (d, J = 2.8 Hz), 117.4 (d, J = 21.2 Hz), 112.8 (d, J = 22.7 Hz), 108.7, 60.1, 51.7, 28.6, 26.9, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NFNa$ $[M + Na]^+$, 386.1163; found, 386.1154. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 9.966 min (major) and 12.067 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 7.525 min, and t_{minor} = 9.185 min.

*(1R,6R)-Methyl 1′-Methyl 4-(2-Fluorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5k**).* 23.9 mg, 44% yield, 76% ee, 96:4 dr, $[\alpha]_D^{20}$ = +244.0 (2.5 mg/mL, $CHCl_3$), white solid. M.P.: 161.5−162.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.42 (m, 2H), 7.32 (dd, J = 7.7, 1.2 Hz, 1H), 7.29 (dd, J = 3.8, 1.2 Hz, 1H), 7.25−7.19 (m, 1H), 7.19−7.15 (m, 1H), 7.01−6.97 (m, 1H), 6.92 (d, J = 7.7 Hz, 1H), 6.44 (d, J = 1.6 Hz, 1H), 4.06 (dd, J = 11.7, 5.4 Hz, 1H), 3.60−3.45 (m, 1H), 3.32 (s, 3H), 3.29−3.20 (m, 1H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.9, 191.6, 174.7, 159.5 (d, J = 251.2 Hz), 154.3, 144.3, 131.4 (d, J = 8.7 Hz), 128.8, 128.5 (d, J = 3.1 Hz), 127.2 (d, J = 3.1 Hz), 126.1 (d, J = 12.7 Hz), 125.5, 124.4 (d, J = 3.4 Hz), 123.0, 122.2, 116.2 (d, J = 22.4 Hz), 108.7, 60.1, 52.1, 28.4 (d, J = 5.2 Hz), 28.3, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NFNa$ $[M + Na]^+$, 386.1163; found, 386.1158. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 1 mL/min, λ = 254 nm, and retention time = 10.738 min (major) and 12.671 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 7.101 min, and t_{minor} = 8.076 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Chlorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5l**).* 20.4 mg, 36% yield, 82% ee, 93:7 dr, $[\alpha]_D^{20}$ = +204.0 (5.8 mg/mL, $CHCl_3$), white solid. M.P.: 211.3−214.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.57 (m, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.33−7.26 (m, 1H), 7.04 (d, J = 6.9 Hz, 1H), 6.98−6.87 (m, 2H), 6.57 (d, J = 1.5 Hz, 1H), 4.07 (dd, J = 11.3, 5.6 Hz, 1H), 3.45−3.37 (m, 1H), 3.32 (s, 3H), 3.27−3.15 (m, 1H), 2.12 (s, 3H). ^{1}C NMR (126 MHz, $CDCl_3$): δ 204.4, 192.1, 175.1, 155.7, 144.5, 137.2, 135.7, 129.4, 129.3, 127.5, 125.9, 124.0, 123.4, 122.6, 109.2, 60.5, 52.1, 29.7, 27.2, 26.7. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NClNa$ $[M + Na]^+$, 402.0867; found, 402.0866. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 24.246 min (major) and 27.558 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 11.099 min, and t_{minor} = 12.832 min.

*(1R,6R)-Methyl 1′-Methyl 4-(3-Chlorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5m**).* 23.8 mg, 42% yield, 84% ee, 77:23 dr, $[\alpha]_D^{20}$ = +300.0 (4.6 mg/mL, $CHCl_3$), white solid. M.P.: 214.5−217.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (t, J = 1.7 Hz, 1H), 7.59−7.54 (m, 1H), 7.52−7.48 (m, 1H), 7.48−7.42 (m, 1H), 7.34−7.30 (m, 1H), 7.08−7.03 (m, 1H), 7.00−6.98 (m, 1H), 6.93 (d, J = 7.8 Hz, 1H), 6.59 (d, J = 1.4 Hz, 1H), 4.08 (dd, J = 11.3, 5.6 Hz, 1H), 3.48−3.36 (m, 1H), 3.33 (s, 3H), 3.30−3.22 (m, 1H), 2.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.9, 191.6, 174.6, 155.1, 144.1, 138.8, 134.9, 130.4, 130.0, 128.9, 126.0, 125.4, 124.3, 123.9, 123.0, 122.2, 108.7, 60.0, 51.7, 28.6, 26.9, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NClNa$ $[M + Na]^+$, 402.0867; found, 402.0868. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 90:10, flow rate = 0.5 mL/min, λ = 254 nm, and retention time = 62.148 min (major) and 73.497 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 214 nm), t_{major} = 11.536 min, and t_{minor} = 13.686 min.

*(1R,6R)-Methyl 1′-Methyl 4-(2-Chlorophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1,3′-indoline]-2,6-dione (**5n**).* 20.4 mg, 36% yield, 86% ee, 96:4 dr, $[\alpha]_D^{20}$ = +153.3 (5.4 mg/mL, CHCl3), white solid. M.P.: 176.9−180.8 °C. 1H NMR (400 MHz, CDCl3): δ 7.52−7.48 (m, 1H), 7.40−7.37 (m, 2H), 7.35−7.29 (m, 3H), 7.04−7.02 (m, 1H), 6.92 (d, J = 7.7 Hz, 1H), 6.22 (dd, J = 2.5, 1.0 Hz, 1H), 4.10 (dd, J = 11.6, 5.4 Hz, 1H), 3.46−3.42 (m, 1H), 3.32 (s, 3H), 3.21−3.15 (m, 1H), 2.09 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.8, 191.5, 174.7, 158.2, 144.3, 138.1, 130.8, 130.0, 129.9, 128.8, 128.6, 127.9,

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127.0, 125.5, 123.0, 122.2, 108.7, 60.1, 52.2, 29.1, 28.3, 26.3. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NClNa$ $[M + Na]^+$, 402.0867; found, 402.0859. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 90:10, flow rate = 0.5 mL/min, λ = 254 nm, retention time = 64.632 min (major) and 75.134 min (minor). The dr was determined by LC−MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 10.100 min, and t_{minor} = 11.536 min, dr =96:4.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Bromophenyl)-2,2′-dioxospiro-[cyclohex[3]ene-1, 3′-indoline]-2,6-dione (**5o**).* 29.7 mg, 47% yield, 78% ee, 94:6 dr, $[\alpha]_D^{20}$ = +265.8 (3.6 mg/mL, CHCl3), pale yellow solid. M.P.: 215.1−217.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65−7.60 (m, 2H), 7.55−7.51 (m, 2H), 7.32−7.26 (m, 1H), 7.03 (d, J = 6.9 Hz, 1H), 6.97−6.94 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.57 (d, J = 1.5 Hz, 1H), 4.06 (dd, J = 11.4, 5.6 Hz, 1H), 3.44−3.37 (m, 1H), 3.31 (s, 3H), 3.24 (dd, J = 18.9, 5.5 Hz, 1H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.4, 192.1, 175.1, 155.8, 144.5, 136.2, 132.4, 129.3, 127.7, 125.9, 125.5, 124.1, 123.4, 122.6, 109.2, 60.5, 52.1, 29.0, 27.1, 26.8. HRMS (ESI-TOF): calculated for $C_{22}H_{18}O_3NBrNa$ $[M + Na]^+$, 446.0362; found, 446.0364. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 70:30, flow rate = 0.9 mL/min, λ = 254 nm, and retention time = 30.449 min (minor) and 45.697 min (major). The dr was determined by LC-MS with an Extend-C18 column (150 × 4.6 mm, 5 μm) (MeOH/H_2O = 65/35, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 14.286 min, and t_{minor} = 18.041 min, dr =94:6.

*(1R,6R)-1′-Methyl-2′-hydroxy-4-phenyl-6-(hydroxymethyl)spiro-[cyclohex[3]ene-1,3′-indoline]-2-one (**6a**).* 13.1 mg, 78% yield, 92% ee, $[\alpha]_D^{20}$ = +144.2, (1.8 mg/mL, CHCl3), white solid. M.P.: 181.0−183.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51−7.46 (m, 2H), 7.38 (dd, J = 8.1, 6.6 Hz, 2H), 7.35−7.29 (m, 1H), 7.24−7.18 (m, 1H), 7.05 (d, J = 7.8 Hz, 1H), 6.78−6.68 (m, 2H), 6.27 (s, 1H), 4.36 (d, J = 9.4 Hz, 1H), 3.74 (d, J = 4.4 Hz, 1H), 3.67 (d, J = 6.8 Hz, 1H), 3.54 (d, J = 8.8 Hz, 1H), 3.42 (dd, J = 12.2, 3.8 Hz, 1H), 3.15 (dd, J = 12.3, 8.8 Hz, 1H), 2.82 (s, 3H), 2.42−2.31 (m, 2H), 2.17−2.04 (m, 1H), 1.62 (br, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.2, 160.5, 139.8, 137.8, 129.2, 128.6, 127.9, 127.3, 126.9, 125.2, 124.9, 122.0, 109.6, 71.6, 65.4, 64.2, 52.4, 44.1, 28.0. HRMS (ESI-TOF): calculated for $C_{21}H_{21}O_3NNa$ $[M + Na]^+$, 358.1414; found, 358.1409. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, retention time = 8.484 min (major) and 15.269 min (minor).

*(1R,6R)-1′-Methyl-2′-hydroxy-4-(4-fluorophenyl)-6-(hydroxymethyl)spiro[cyclo-hex[3]ene-1,3′-indoline]-2-one (**6d**).* 13.3 mg, 75% yield, 84% ee, $[\alpha]_D^{20}$ = +161.2, (1.7 mg/mL, CHCl3), white solid. M.P.: 107.7−112.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.46 (m, 1H), 7.35−7.28 (m, 1H), 7.08 (dd, J = 12.1, 5.3 Hz, 2H), 7.02−6.95 (m, 1H), 6.90 (d, J = 7.8 Hz, 1H), 6.14 (s, 1H), 4.91 (s, 1H), 3.31−3.18 (m, 3H), 2.85−2.67 (m, 1H), 2.52−2.41 (m, 1H), 1.69 (br, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 180.8, 164.1 (d, J = 247.6 Hz), 146.7, 138.0, 136.9, 130.4, 128.5, 128.4 (d, J = 8.1 Hz), 127.1, 126.5, 124.1, 116.9 (d, J = 21.4 Hz), 110.0, 74.4, 65.4, 56.9, 43.3, 29.7, 28.0. HRMS (ESI-TOF): calculated for $C_{21}H_{20}O_3NFNa$ $[M + Na]^+$, 376.1319; found, 376.1318. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, and retention time = 8.931 min (major) and 12.392 min (minor).

*(1R,6R)-1′-Methyl-2′-hydroxy-4-(4-chlorophenyl)-6-(hydroxymethyl)spiro[cyclo-hex[3]ene-1,3′-indoline]-2-one (**6e**).* 14.1 mg, 76% yield, 92% ee, $[\alpha]_D^{20}$ = +147.1, (2.0 mg/mL, CHCl3), white solid. M.P.: 189.9−193.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J = 8.6 Hz, 1H), 7.40−7.30 (m, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.19 (s, 1H), 4.93 (s, 1H), 3.32−3.21 (m, 1H), 2.84−2.66 (m, 1H), 2.49 (dd, J = 16.9, 10.3 Hz, 1H), 1.56 (br, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.15, 145.33, 137.76, 136.50, 133.95, 129.05, 128.80, 127.66, 126.63, 125.49, 124.99, 122.64, 108.55, 72.96, 63.97, 55.42, 41.87, 28.03, 26.57. HRMS (ESI-TOF): calculated for $C_{21}H_{20}O_3NClNa$ $[M + Na]^+$, 392.1024; found, 392.1012. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, and retention time = 9.849 min (major) and 13.695 min (minor).

*(1R,6R)-Methyl 1′-Methyl 4-Phenyl-2-hydroxyl-2′-oxospiro-[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**7a**).* 16.4 mg, 90% yield, 91% ee, > 99:1 dr, $[\alpha]_D^{20}$ = +132.3, (2.0 mg/mL, CHCl3), white solid. M.P.: 124.3−126.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58−7.51 (m, 2H), 7.45−7.39 (m, 2H), 7.38−7.35 (m, 1H), 7.34−7.29 (m, 1H), 7.13−7.09 (m, 1H), 6.99−6.93 (m, 1H), 6.90 (d, J = 7.7 Hz, 1H), 6.17 (d, J = 1.6 Hz, 1H), 4.90 (s, 1H), 3.59−3.48 (m, 4H), 3.29 (d, J = 4.1 Hz, 3H), 3.13−2.98 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 178.2, 170.8, 145.4, 138.5, 136.5, 128.5, 128.2, 127.8, 126.7, 125.4, 124.9, 124.3, 121.9, 107.8, 72.5, 53.4, 51.6, 44.0, 27.2, 26.1. HRMS (ESI-TOF): calculated for $C_{22}H_{21}O_4NNa$ $[M + Na]^+$, 386.1363; found, 386.1353. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, and retention time = 6.961 min (major) and 11.832 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 254 nm) and t_{major} = 12.952 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Fluorophenyl)-2-hydroxyl-2′-oxospiro[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**7d**).* 17.6 mg, 92% yield, 92% ee, > 99:1 dr, $[\alpha]_D^{20}$ = +146.4, (1.9 mg/mL, CHCl3), white solid. M.P.: 185.5−186.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.47 (m, 2H), 7.35−7.29 (m, 1H), 7.13−7.04 (m, 3H), 7.00−6.93 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.11 (d, J = 1.7 Hz, 1H), 4.89 (s, 1H), 3.59−3.46 (m, 4H), 3.29 (s, 3H), 3.10−2.92 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 178.1, 170.7, 162.2 (d, J = 247.9 Hz), 145.4, 135.6, 134.6 (d, J = 3.3 Hz), 128.6, 126.6, 126.6 (d, J = 7.9 Hz), 125.3, 124.2, 121.9, 115.1 (d, J = 21.5 Hz), 107.85, 72.42, 53.33, 51.62, 43.92, 27.33, 26.15. HRMS (ESI-TOF): calculated for $C_{22}H_{20}O_4NFNa$ $[M + Na]^+$, 404.1269; found, 404.1263. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, and retention time = 8.449 min (major) and 13.400 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 254 nm), and t_{major} = 12.958 min.

*(1R,6R)-Methyl 1′-Methyl 4-(4-Chlorophenyl)-2-hydroxyl-2′-oxospiro[cyclohex[3]ene-1,3′-indoline]-6-carboxylate (**7e**).* 18.3 mg, 92% yield, 91% ee, > 99:1 dr, $[\alpha]_D^{20}$ = +130.6, (2.0 mg/mL, CHCl3), white solid. M.P.: 197.6−199.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.44 (m, 2H), 7.41−7.36 (m, 2H), 7.35−7.29 (m, 1H), 7.08−7.03 (m, 1H), 7.00−6.94 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.16 (d, J = 1.6 Hz, 1H), 4.89 (s, 1H), 3.58−3.49 (m, 4H), 3.29 (s, 3H), 3.05−2.97 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 178.1, 170.6, 145.3, 136.8, 135.4, 133.6, 128.6, 128.4, 127.2, 126.2, 125.2, 124.1, 122.0, 107.9, 72.4, 53.3, 51.6, 43.9, 27.1, 26.2. HRMS (ESI-TOF): calculated for $C_{22}H_{20}O_4NClNa$ $[M + Na]^+$, 420.0973; found, 420.0962. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, and retention time = 8.449 min (major) and 12.557 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 254 nm) and t_{major} = 13.886 min.

*(1R,6R)-1′-Methyl 4-Phenyl-6-(1-hydroxyethyl)-2′-oxospiro-[cyclohex[3]ene-1,3′-indoline]-2-alcohol (**8h**).* 9.9 mg, 51% yield, 89% ee, white solid, 89:11 dr, $[\alpha]_D^{20}$ = +159.3, (2.2 mg/mL, CHCl3). M.P.: 85.2−87.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60−7.54 (m, 2H), 7.45−7.38 (m, 2H), 7.38−7.31 (m, 2H), 7.21 (dd, J = 7.5, 0.6 Hz, 1H), 7.04−6.97 (m, 1H), 6.94 (d, J = 7.8 Hz, 1H), 6.16 (d, J = 1.6 Hz, 1H), 4.92 (s, 1H), 3.86−3.77 (m, 1H), 3.30 (s, 3H), 3.08−2.96 (m, 1H), 2.71 (dd, J = 18.4, 5.7 Hz, 1H), 2.58−2.48 (m, 1H), 1.11 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 178.4, 144.4, 139.2, 137.8, 128.7, 128.2, 127.6, 126.1, 125.9, 125.1, 124.9, 122.4, 108.3, 73.1, 67.5, 56.3, 44.9, 26.0, 22.9, 20.8. HRMS (ESI-TOF): calculated for $C_{22}H_{23}O_3NNa$ $[M + Na]^+$, 372.1570; found, 372.1566. HPLC conditions: chiralpak IA-H, hexane/iso-PrOH = 75:25, flow rate = 1 mL/min, λ = 254 nm, and retention time = 7.343 min (major) and 9.305 min (minor). The dr was determined by LC−MS with an Eclipse-C18 column (250 × 4.6 mm, 5 μm) (MeOH/H_2O = 60/40, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 7.718 min, and t_{minor} = 12.224 min.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01596.

X-ray crystallography, ^{1}H spectra, ^{13}C NMR spectra, and HPLC chromatograms (PDF)
(1*R*, 6*R*)-**3f** (CIF)
(1*R*, 6*R*)-**5g** (CIF)
(1*R*, 6*R*)-**5i** (CIF)
(1*R*, 6*R*)-**6h** (CIF)

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Author Contributions

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Notes

The authors declare no competing financial interest.
Crystallographic data (CCDC 1457039 (**3f**), 1457052 (**5g**), 1457058 (**5i**), and 1457169 (**6h**)) may be accessed free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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