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Enantioselective Construction of Spirooxindole-Fused Cyclopentanes

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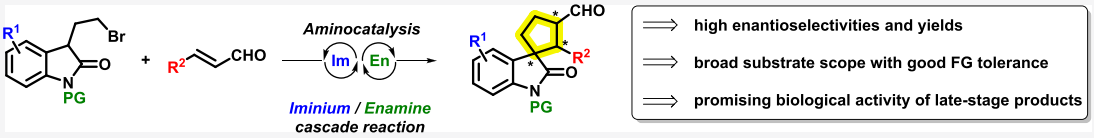

ABSTRACT: The present study reports an asymmetric organocatalytic cascade reaction of oxindole derivates with α,β-unsaturated aldehydes efficiently catalyzed by simple chiral secondary amine. Spirooxindole-fused cyclopentanes were produced in excellent isolated yields (up to 98%) with excellent enantiopurities (up to 99% *ee*) and moderate to high diastereoselectivities. The synthetic utility of the protocol was exemplified on a set of additional transformations of the corresponding spiro compounds. In addition, a study showing the promising biological activity of selected enantioenriched products was accomplished.

INTRODUCTION

Optically active spirooxindoles are naturally occurring compounds with unique structural features. They are present in various natural products such as oxindole-based alkaloids or fungal metabolites (Figure 1A).[1] In particular, the spirooxindole motif is often found in medicinally relevant compounds with antiviral,[2] anticancer,[3] antimicrobial,[4] anti-inflammatory,[5] analgesic, antioxidant, antimalarial, and insecticidal activities (Figure 1B).[6−8]

Consequently, the development of efficient enantioselective synthetic strategies for the preparation of chiral spirooxindoles has attracted considerable research interest in the past decade. Organocatalysis has brought unprecedented progress to this area.[9] To date, impressive advances were made on organocatalytic strategies to prepare spirooxindole-fused three-[10] and six-membered[11] all-carbon rings. On the other hand, the development of the atom-economic catalytic enantioselective construction of cyclopentane-containing spirooxindoles is still highly desirable.[12] Organocatalytic cascade reactions using aminocatalysis or non-covalent catalysis represent one of the most powerful approaches for enantioselective synthesis of highly substituted cyclopentanes.[13,14] Among these approaches, one of the most commonly applied organocatalytic concepts is based on the Michael initiated ring-closing reaction.[15−19] In 2009, Melchiorre and Rios independently reported stereoselective Michael addition of 3-substituted oxindole derivatives to enals using the chiral amine catalyzed Michael reaction (Scheme 1A).[20,21] Three years later, our group described the stereoselective Michael/α-alkylation[22] reaction between nonstabilized alkyl halide malonate derivatives and enals that led to the formation of 1,1,2,3-tetrasubstituted cyclopentanes.[15a] Nearly simultaneously,

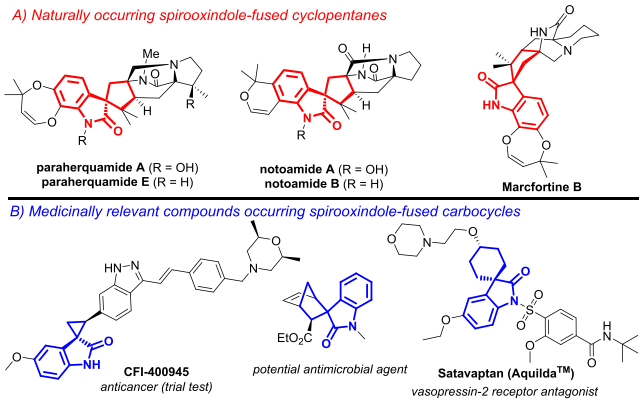

Figure 1. Selected examples of naturally and medicinally relevant compounds.

Wang reported the stereoselective Michael/spirocyclization reaction,[15b] using 3-substituted oxindole and methyleneindolinones, for construction of spirocyclopentane bioxindoles containing three contiguous stereocenters (Scheme 1C). Based on our previous work, we envisioned that alkyl halide tethered oxindoles could associate with secondary amine-activated enals, to accomplish the Michael/spirocyclization cascade reaction (Scheme 1). Herein, we wish to report an atom-

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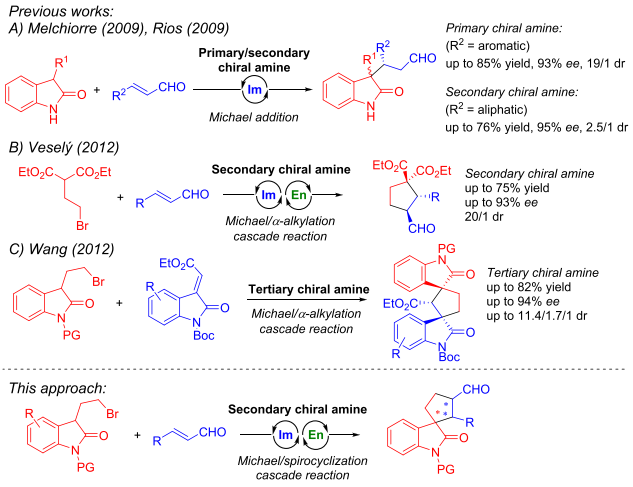
Scheme 1. Previous Approaches toward the Preparation of Substituted Oxindoles and Cyclopentanes



economical strategy for the construction of chiral spirooxindole-fused cyclopentanes using an organocatalytic approach.

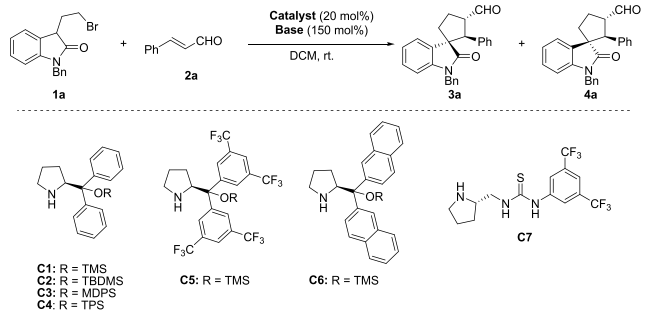
RESULTS AND DISCUSSION

We began our investigation by mixing readily accessible 1-benzyl-3-(2-bromoethyl)indolin-2-one[23] (**1a**) and *trans*-cinnamaldehyde (**2a**) in the presence of a chiral Hayashi/Jørgensen catalyst and $NaHCO_3$ as a base. Complete conversion of starting materials was observed in 5 days, resulting in readily separable **3a** and **4a** in a moderate combined yield with high enantiocontrol (entry 1, Table 1). Interestingly, the reaction rate was increased when using K_2CO_3 (entry 2) and pyridine-like bases, such as 2,6-lutidine or 2,4,6-collidine (entries 3 and 4). The corresponding products were obtained in almost quantitative yield and with higher diastereocontrol. Then, the efficiency and stereochemical effect of various prolinol-based catalysts were evaluated. The use of diphenylprolinol-derived catalysts bearing bulkier silyl groups (**C2**–**C4**, entries 5–7) resulted in slightly increased enantioselectivities. The reaction between **1a** and **2a** mediated by Jørgensen catalysts (**C5**, entry 8) or sterically demanding dinaphthalenylprolinol derivative **C6** (entry 9) provided products after prolonged reaction time and with reduced stereocontrol. Interestingly, enantiocontrol was almost lost in the reaction catalyzed by prolinol-derived thiourea catalyst **C7** (entry 10). Apart from **C1**–**C7**, we tested other secondary amine catalysts (for details, please see the Supporting Information). Unfortunately, none of the amine catalysts tested afforded **4a** in the yield and enantiopurity comparable to the reaction catalyzed by **C2** (entry 5). Additionally, various solvents were tested in the model reaction, and dichloromethane was found to be optimal (entries 11–13, Table 1, and Table S3 in the Supporting Information). Further changes of reaction conditions, including catalyst loading and temperature, did not improve the reaction efficiency and stereocontrol (Tables S1–S5 in the Supporting Information).

After optimizing the reaction conditions, we began exploring the scope of the developed Michael/spirocyclization cascade reaction by varying the *N*-protecting group of oxindole **1** (Scheme 2).

In general, the reaction tolerates various *N*-alkyl groups, such as methyl and allyl, affording the corresponding spirocycles **4b** and **4c** in high isolated yields (55–57%) with

Table 1. Optimization Studies of the Cascade Reaction



entry[a]	cat.	base	time (h)	dr[b]	yield[c] (%)	ee[d] (%)
1[e]	**C1**	$NaHCO_3$	120	1/1.2	57 (30)	93/94
2	**C1**	K_2CO_3	49	1/1.3	96 (57)	92/93
3	**C1**	lutidine	40	1/2.3	98 (68)	95/98
4	**C1**	collidine	16	1/2.3	98 (72)	96/97
5	**C2**	collidine	12	1/2.3	98 (70)	99/98
6	**C3**	collidine	12	1/1.8	97 (62)	98/98
7	**C4**	collidine	12	1/1.7	99 (65)	98/99
8	**C5**	collidine	120	1/1.7	79 (52)	92/96
9	**C6**	collidine	16	1/2.3	97 (71)	94/96
10	**C7**	collidine	120	3.0/1	47 (39)	11/12[f]
11[g]	**C2**	collidine	40	1.5/1	98 (60)	96/93
12[h]	**C2**	collidine	24	1.9/1	91 (56)	94/93
13[i]	**C2**	collidine	24	2.8/1	87 (63)	88/93
14[j,e]	**C2**	collidine	120	1/2.0	88 (58)	97/99

[a]Reactions were conducted with 0.105 mmol of **1a**, 0.1 mmol of **2a**, 0.15 mmol of 2,4,6-collidine, and 20 mol % of catalyst in 0.5 mL of solvent at rt. [b]Determined by ^{1}H NMR of the crude reaction mixture (**3a**/**4a**). [c]Isolated combined yield; the isolated yield of a major diastereomer is shown in brackets. [d]Determined by chiral HPLC analysis (**3a**/**4a**). [e]Conversion of the starting aldehyde was not full. [f]Opposite enantiomers were isolated. [g]Benzene was used. [h]Et_2O was used. [i]MeOH was used. [j]10 mol % of the catalyst was used. TMS - trimethylsilyl, TBDMS - *tert*-butyldimethylsilyl, MDPS - methyldiphenylsilyl, TPS - triphenylsilyl, lutidine - 2,6-lutidine, collidine - 2,4,6-collidine.

excellent enantiopurities (both 99% *ee*). Interestingly, the reaction with unprotected oxindole **1d** proceeded with reverse diastereocontrol, probably due to reduced steric hindrance on lactam and the presence of an acidic amide moiety, providing spirocycle **3d** with high enantioselectivity (90% *ee*). Subsequently, we studied the process using substituted oxindoles **1**. We assessed the effect of the electronic properties of the substituents at the aromatic ring on reactivity and on the stereochemical outcome. Spiro compounds derived from oxindoles **1e** and **1f** containing electron-donating groups at position 5 of the ring were produced in high yields with an excellent degree of enantioselectivities (typically 99% *ee*) producing diastereomer **4** predominantly.

Conversely, oxindoles substituted at position 5 with halogens, representing electron-withdrawing groups, showed opposite diastereocontrol, giving **3g**–**i** in high yields (68–72%) with excellent enantioselectivities (96–98% *ee*). Remarkably, a decreasing trend of enantiopurities of minor diastereomers **4g**–**i** was observed. Unfortunately, we were not successful with the preparation of oxindoles bearing strong electron-withdrawing groups due to failed key oxidation of indole derivatives to oxindoles (see the Supporting Information for details). It is noteworthy that substitution in position 4 on the oxindole ring renders a higher diastereoselectivity of the

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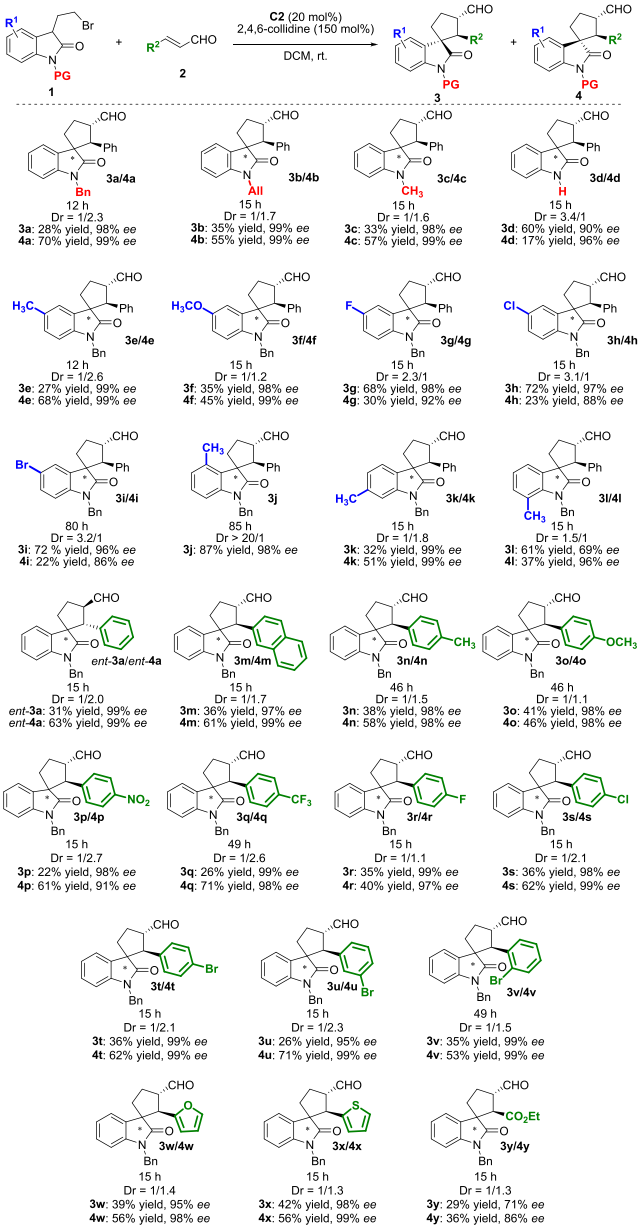
Scheme 2. Substrate Scope of the Michael/Spirocyclization Cascade Reaction



reaction. For example, spiro compound **3j** with methyl at position 4 was formed as a single diastereomer in excellent yield and enantiopurity, in comparison to spiro compounds bearing a methyl substituent at different positions. Next, the scope of the developed Michael/spirocyclization cascade reaction was investigated by varying enal substrates **2**. In general, high to excellent yields of spiro compounds **3** and **4** with excellent enantioselectivities and moderate diastereoselectivities were obtained with aromatic enals bearing electron-donating groups (**4n**, **4o**) and electron-withdrawing groups (**4p**−**t**) in a *para* position on the aromatic ring. Similarly, *meta*- and *ortho*-substituted aromatic enals and heteroaromatic enals afforded the corresponding products **4u**−**x** in high yields with excellent enantioselectivities. Besides aromatic enals, aliphatic enals were also explored. Unfortunately, aliphatic α,β-unsaturated aldehydes bearing γ-protons provided a complex mixture with only traces of the desired products. Nevertheless, the reaction of **1a** with ethyl (*E*)-4-oxobut-2-enoate provided **4y** in acceptable yield with reduced enantioselectivity.

The structure and relative configuration of spirooxindole-fused cyclopentanes **3** and **4** were adopted on the basis of characteristic chemical shifts and *J* values of the aldehyde group of products (for details, please see the Supporting Information). In addition, the absolute configuration of diastereomeric **3v** and **4b** was ascertained using X-ray diffraction analysis. The configuration of **3v** and **4b** was assigned as (1*S*, 2*R*, 3*S*) and (1*R*, 2*S*, 3*S*), respectively (Figure 2; for details, see the Supporting Information).

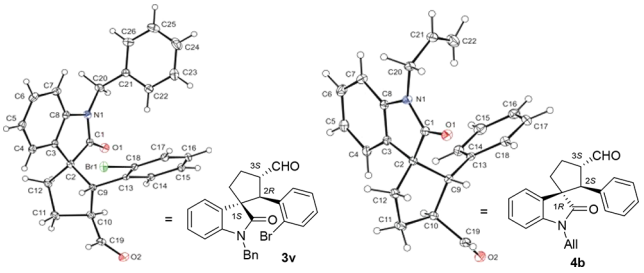
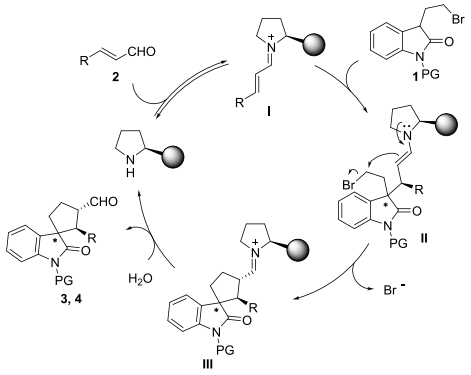


Figure 2. X-ray single-crystal structures of **3v** and **4b**, the displacement ellipsoids at 30% probability level.

Based on the determined absolute configuration and the previous report,[24] a mechanism of the developed Michael/spirocyclization cascade reaction was proposed (Scheme 3). Initially, enal **2** is activated via condensation with the chiral secondary amine, generating iminimum intermediate **I**. Subsequently, the formed iminium ion **I** with a shielded *Si*-face is stereoselectively attacked by nucleophilic oxindole derivative **1**, affording enamine **II**. Next, an intramolecular 5-*exo-tet* cyclization of enamine **II** results in the formation of spirocyclic intermediate **III**, which upon hydrolysis in the final stage furnishes spirocyclic products **3** and **4** and releases a chiral amine back to the catalytic cycle.

Scheme 3. Proposed Reaction Mechanism



To expand the developed organocatalytic process toward the construction of spiro compounds containing 3-, 6-, and 7-membered rings (Scheme 4), oxindoles **1** bearing various lengths of alkyl chain in position 3 of the oxindole ring were subjected to the reaction with a cinnamic aldehyde **2a**. Inspired by the previous report,[25] we performed a cyclopropanation reaction with oxindole bearing chlorine as a leaving group (**1m**) as a one-pot sequence with a Wittig reaction using methyl (triphenylphosphoranylidene)acetate to prevent epi-

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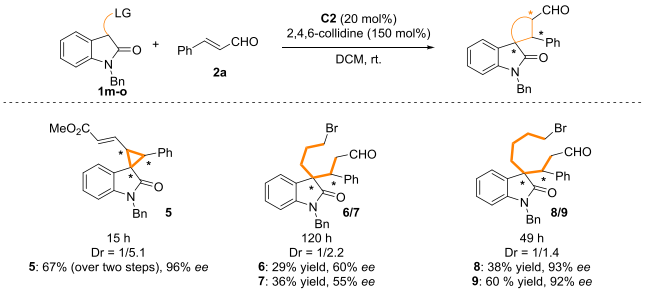
Scheme 4. Substrate Scope with Diverse Oxindoles



merization of cyclopropane product during workup. Cyclopropane **5** was formed in high yield with high diastereo- and enantioselectivity. Unfortunately, the reaction performed with oxindoles bearing three- and four-carbon alkyl chains (**1n**, **1o**) did not undergo 6- and 7-*exo-tet* cyclizations and uncyclized Michael adducts (**6**–**9**) were isolated instead.

Our observation was supported by DFT studies proposed for transition states of 5- and 6-*exo-tet* intramolecular ring-closing alkylation (Figure 3). We found an additional methylene group in the alkyl chain distorting the bonding angle probably due to steric hindrance, which led to an increase in activation energy by 18.7 kJ/mol. For more details, see the Supporting Information.

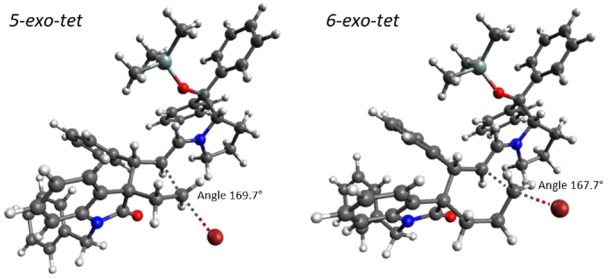
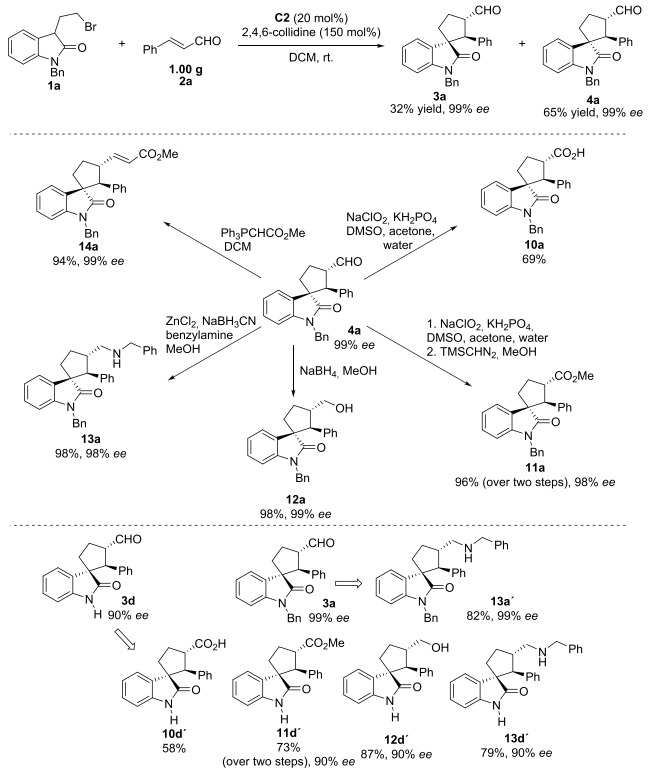


Figure 3. Calculated transition states for intramolecular ring-closing alkylation.

To demonstrate the synthetic utility of the developed cascade reaction, we performed a reaction between **1a** and **2a** in gram scale, giving the products **3a** and **4a** in 32 and 65% yield, respectively, with the same enantioselectivities (99%/99% *ee*) and slightly decreased diastereoselectivity (Scheme 5). As an example of subsequent transformations, spirocyclic compounds **4a** and **3d** were converted to spirocycles **10**–**14**. Spiro compounds **4a** and **3d** were selectively oxidized to carboxylic acids **10** using Pinnick oxidation with acceptable yields. Nevertheless, higher yields of the corresponding methyl esters **11** were reached by subsequent methylation using trimethylsilyl-diazomethane, due to easier separation compared to acids **10**. Other selected examples of the transformation of spiro compounds **3** and **4** included reduction of the aldehyde moiety, reductive amination, and Wittig olefination. Corresponding alcohols **12**, amines **13**, and α,β-unsaturated ester **14a** were prepared in excellent yields without losing enantiomeric purities.

All compounds (**10**–**14**) were subjected to screening for antimicrobial activity on a broad panel of pathogenic fungi, including both yeasts and filamentous fungi, G^+ and G^- bacteria, and mycobacteria (see the Supporting Information for complete details). While no effect against fungal strains was

Scheme 5. Gram-Scale Experiment and Late-Stage Functionalizations



recorded in all compounds except for marginal activity of **13a′** against *C. krusei* and *T. interdigitale* (MIC 62.5 μmol/L), spirooxindole **13a′** and its diastereomer **13a** displayed promising activity against both G^+ bacteria and mycobacteria. The MIC values of **13a′** against *S. aureus*, methicillin resistant *S. aureus*, and *S. epidermidis* were 31.25, 15.62, and 7.81 μmol/L, respectively, after 48 h of incubation, and those of **13a** were just slightly lower. Antimycobacterial activities of **13a′** and **13a** were even more promising, matching the standard antimycobacterial drug isoniazide against *M. smegmatis* and *M. aurum* (7.81 and 3.91 μg/mL, respectively, vs 15.625 and 3.91 μg/mL for isoniazide). Their effect against *M. tuberculosis* (MIC = 1.98 μg/mL) is also noteworthy, being almost comparable to that of isoniazide or ciprofloxacin. Thus, spirooxindoles **13a′** and **13a** can be regarded as possible leads for further development as antimycobacterial or antimicrobial agents. The structure of these intriguing heterocycles offers several sites for tuning of biological activity via structural modifications, namely, both amino groups, the phenyl moiety attached to the cyclopentane ring, and the aromatic ring of oxindole.

CONCLUSION

In summary, we have developed enantioselective organocatalytic cascade spirocyclization of readily available oxindole derivatives with α,β-unsaturated aldehydes. The reaction is efficiently catalyzed by a chiral secondary amine, affording chiral spirooxindole-fused cyclopentanes in excellent yields and enantioselectivities. The developed synthetic protocol is suitable for late-stage functionalization, as shown by a set of additional transformations, affording medicinally relevant compounds.

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EXPERIMENTAL SECTION

Chemicals and solvents were purchased from commercial suppliers and purified using standard techniques. For thin-layer chromatography (TLC), silica gel plates Merck 60 F_{254} were used, and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (AMC) or vanillin followed by heating. Column chromatography was performed using silica gel Fluka (40−63 μm) or SiliCycle-SiliaFlash P60 (particle size, 40−63 μm; pore diameter, 60 Å). ^{1}H, ^{13}C NMR, and ^{19}F spectra were recorded with a Bruker AVANCE III 400 instrument. Chemical shifts for protons are given in δ relative to tetramethylsilane (TMS), and they are referenced to residual protium in the NMR solvent (chloroform-*d*: δ_H = 7.26 ppm). Chemical shifts for carbon are referenced to the carbon of NMR solvent (chloroform-*d*: δ_C = 77.0 ppm). The coupling constants *J* are given in hertz. IR DRIFT spectra were recorded with a Nicolet AVATAR 370 FT-IR instrument in cm^{-1}. Chiral HPLC was carried out using a LC20AD Shimadzu liquid chromatograph with an SPD-M20A diode array detector with columns Daicel Chiralpak IA, Daicel Chiralpak IB, Daicel Chiralpak AD, and Daicel ChiralpakODH. Samples for measurement of chiral HPLC were prepared by dissolving of corresponding sample in heptane/*i*-PrOH (8/2, *v*/*v*) mixture. Optical rotations were measured on an AU-Tomatica polarimeter, Autopol III, and specific optical rotations are given in concentrations *c* [g/100 mL]. Melting points were measured using a Bu-chi melting point B-545 apparatus. All melting points were measured in an open glass capillary, and all values are uncorrected. High-resolution mass spectra were recorded with a LCQ Fleet spectrometer. Samples for measurement of HRMS were prepared by dissolving of the corresponding sample in methanol.

Preparation of Organocatalyst and Starting Material. Chiral secondary amines were purchased from commercial suppliers, or they were prepared according to previously reported procedures.[26] *α,β*-Unsaturated aldehydes (**2**) were purchased from commercial suppliers; if it is not possible, they were prepared by Wittig reaction.[27] 1-Benzyl-3-chloroindolin-2-one (**1m**) was prepared according to a previously reported procedure.[28]

*(R)-2-(((tert-Butyldimethylsilyl)oxy)diphenylmethyl)pyrrolidine (ent-**C2**).* Inspired by the previously reported procedure for the opposite enantiomer.[26c] TBDMSOTf (1.36 mL, 5.92 mmol, 3.0 equiv) was dropwise added to a stirred solution of (*R*)-diphenylprolinol (500 mg, 1.97 mmol, 1.0 equiv) and 2,6-lutidine (1.15 mL, 9.87 mmol, 5.0 equiv) in dry DCM (10.0 mL) at 0 °C (cooled by water/ice mixture). The mixture was stirred for 20 h at room temperature. The reaction was quenched by careful addition of a saturated solution of NH_4Cl (20 mL). The organic layer was separated, and the water phase was extracted with DCM (3 × 30 mL). The collected organic phases were washed with a solution of KOH (1 M, 25 mL) and brine (1 × 25 mL) and dried over $MgSO_4$. After filtration of drying agent, solvents were removed under reduced pressure. The crude product was purified by column chromatography with a mixture of hexane/EtOAc as an eluent (gradient of polarity - from 3:1 to 1:1). The purified product was dried under reduced pressure at 60 °C (to remove the rest of the 2,6-lutidine). Colorless oil. Yield = 85% (615 mg). $[\alpha]_D^{20}$ = +22.2 (*c* = 1.6, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.57−7.50 (m, 2H), 7.42−7.36 (m, 2H), 7.33−7.26 (m, 6H), 4.04 (t, *J* = 7.3 Hz, 1H), 2.84 (ddd, *J* = 10.1, 7.6, 6.3 Hz, 1H), 2.71 (ddd, *J* = 10.1, 7.5, 5.5 Hz, 1H), 1.76 (s, 1H), 1.72−1.48 (m, 3H), 1.35−1.18 (m, 1H), 0.98 (s, 9H), −0.19 (s, 3H), −0.43 (s, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 146.5, 145.2, 129.3 (2C), 128.3 (2C), 127.6 (2C), 127.2 (2C), 127.0, 126.9, 83.0, 65.7, 47.2, 27.9, 26.3 (3C), 26.0, 19.1, −2.7, −3.3 ppm. IR (KBr): ν = 3059 (N—H), 1068 (O—Si) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{23}H_{34}NOSi$ $[M + H]^+$, 368.2405; found, 368.2404.

Preparation of Tryptophols (GP1). Oxalyl chloride (3.0 equiv) was added dropwise at 0 °C (cooled by water/ice mixture) to a stirred solution of substituted indole (1.0 equiv) in anhydrous Et_2O (100 mL per 19.0 mmol of indole). The resulting mixture was heated up to room temperature and stirred for the indicated time. Conversion of starting indole was checked by TLC. The reaction was quenched by careful (slightly exothermic reaction) adding of anhydrous MeOH (5.0 equiv). The resulting suspension was stirred for 2 h at room temperature. The suspension was filtered, and crude product (filtrate cake) was washed with Et_2O. The resulting methyl ester was used in the next step without other purification. A solution of Synhydride (70% in toluene, 4.0 equiv) was dropwise added at 0 °C (cooled by water/ice mixture) to a solution of crude methyl ester (1.0 equiv) in anhydrous THF (35 mL per 15.0 mmol of methyl ester). The reaction was heated up in an oil bath to 80 °C and stirred for 2 h. Conversion of starting material was checked by ^{1}H NMR of the reaction mixture. The reaction was cooled to room temperature and quenched by careful adding of water solution of NaOH (10%, *w*/*w*, 20 mL per 15 mmol of ester). The suspension was stirred vigorously for 20 min, and the suspension was filtered through a short pad of Celite (rinsed with EtOAc). The organic phase was separated, and water phases were extracted with EtOAc (3 × 50 mL, per 15.0 mmol of starting material). The collected organic phases were washed with brine (1 × 50 mL, per 15.0 mmol of the starting material) and dried over $MgSO_4$. After filtration of drying agent, solvents were removed under reduced pressure. Crude product was purified by column chromatography with a mixture of hexane/EtOAc as an eluent (1:1).

5-Methyltryptophol. The title compound was synthesized according to general procedure GP1, starting from 5-methylindole (2.50 g, 19.1 mmol). Light brown amorphous solid. Yield = 84% (2.80 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29a]

5-Methoxytryptophol. The title compound was synthesized according to general procedure GP1, starting from 5-methoxyindole (2.50 g, 17.0 mmol). Brown oil. Yield = 67% (2.38 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29b]

5-Fluorotryptophol. The title compound was synthesized according to general procedure GP1, starting from 5-fluoroindole (2.50 g, 18.5 mmol). Brown amorphous solid. Yield = 78% (2.59 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29c]

5-Chlorotryptophol. The title compound was synthesized according to general procedure GP1, starting from 5-chloroindole (2.50 g, 16.5 mmol). Light brown amorphous solid. Yield = 91% (2.93 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29d]

4-Methyltryptophol. The title compound was synthesized according to general procedure GP1, starting from 4-methylindole (2.50 g, 19.1 mmol). Light brown amorphous solid. Yield = 52% (1.72 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29e]

6-Methyltryptophol. The title compound was synthesized according to general procedure GP1, starting from 6-methylindole (2.50 g, 19.1 mmol). Pink amorphous solid. Yield = 78% (2.12 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29a]

7-Methyltryptophol. The title compound was synthesized according to general procedure GP1, starting from 4-methylindole (2.50 g, 19.1 mmol). White amorphous solid. Yield = 76% (2.55 g, over three steps). Our physical and spectroscopic data matched previously reported data.[29a]

Preparation of Oxindoles 1 (GP2). Inspired by previously reported procedures.[23] TBDMSCl (1.2 equiv) were added portion-wise to a stirred solution of corresponding tryptophol (1.0 equiv) and imidazole (1.2 equiv) in anhydrous THF (0.5 M) at rt. The reaction mixture was stirred typically for 2 h at room temperature. Conversion of starting indole was checked by TLC. After the composition of starting material, water (50 mL) was added. The organic phase was separated, and the water phase was extracted with EtOAc (3 × 50 mL). The collected organic phases were washed with brine (1 × 50 mL) and dried over $MgSO_4$. After filtration of the drying agent, solvents were removed under reduced pressure. Crude *O*-protected product (quantitative yield) was used directly in the next step. NaH (60% oil suspension, 1.2 equiv) was added portion-wise to a stirred solution of *O*-protected indole (1.0 equiv) in anhydrous THF (0.5 M)

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at 0 °C (cooled by water/ice mixture). The reaction mixture was stirred for 15 min at this temperature; then, the reaction mixture was heated to rt and stirred for 30 min. Then, corresponding alkylation agents (1.2 equiv) were added dropwise or portion-wise at room temperature. The reaction mixture was stirred at rt (typically overnight). Conversion of starting material was checked by TLC. After composition of starting material, the reaction was quenched by a solution of NH_4Cl (50 mL per 10 mmol of starting material). The organic phase was separated, and the water phase was extracted with EtOAc (3 × 50 mL, per 10 mmol of starting material). The collected organic phases were washed with brine (1 × 50 mL, per 10 mmol of starting material) and dried over $MgSO_4$. After filtration of drying agent, solvents were removed under reduced pressure. Crude product was purified by filtration via a short pad of silica gel (eluting with hexane/EtOAc mixtures). The corresponding *N*,*O*-protected indole (quantitative yield) was directly used in the next step. Hydrochloric acid (7.0 mL per 10 mmol of indole, conc.) was dropwise added to a stirred solution of *N*,*O*-protected indole (1.0 equiv) in DMSO (5.0 mL per 10 mmol of indole) at rt. At this temperature, the reaction mixture was stirred (typically 1 h). Conversion of starting indole was checked by TLC. After, the composition of the starting material reaction was quenched carefully by a saturated solution of (in some cases also followed by solid) $NaHCO_3$ until pH ∼ 8. The mixture was extracted with EtOAc (3 × 50 mL, per 10 mmol of indole). The collected organic phases were washed with brine (1 × 50 mL) and dried over $MgSO_4$. After filtration of the drying agent, solvents were removed under reduced pressure. Crude *N*-protected oxindole was purified by filtration via a short pad of silica gel (eluting with hexane/EtOAc - 1:1 to 1:2). The corresponding *N*-protected oxindole (yields typically 80−95%) was directly used in the next step. NBS (1.2 equiv) and PPh_3 (1.2 equiv) were added in one portion to a stirred solution of *N*-protected oxindole (1.0 equiv) in dry DCM (150 mL per 10.0 mmol of oxindole) at 0 °C (cooled by water/ice mixture). The reaction mixture was stirred at room temperature typically for 1−2 h. Conversion of starting material was checked by TLC. After the composition of starting oxindole, silica gel was added, and solvents were removed under reduced pressure. The resulting solids were directly loaded on the column and purified (eluting with hexane/EtOAc mixtures).

*1-Benzyl-3-(2-bromoethyl)indolin-2-one (**1a**).* The title compound was synthesized according to general procedure GP2 using commercially available 3-hydroxyethylindole (10.00 g, 62.0 mmol) as a starting material and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 46% (9.42 g, over four steps). Our physical and spectroscopic data matched previously reported data.[23]

*3-(2-Bromoethyl)indolin-2-one (**1b**).* The title compound was synthesized according to the last two steps (oxidation and Appel reaction) from general procedure GP2 using commercially available 3-hydroxyethylindole (500 mg, 3.1 mmol) as a starting material. White amorphous solid. Yield = 31% (231 mg, over two steps). Our physical and spectroscopic data matched previously reported data.[23]

*3-(2-Bromoethyl)-1-methylindolin-2-one (**1c**).* The title compound was synthesized according to general procedure GP2 using commercially available 3-hydroxyethylindole (500 mg, 3.1 mmol) as a starting material and methyl iodide as an alkylating agent. Light yellow amorphous solid. Yield = 41% (324 mg, over four steps). Our physical and spectroscopic data matched previously reported data.[23]

*1-Allyl-3-(2-bromoethyl)indolin-2-one (**1d**).* The title compound was synthesized according to general procedure GP2 using commercially available 3-hydroxyethylindole (500 mg, 3.1 mmol) as a starting material and allyl bromide as an alkylating agent. Light yellow amorphous solid. Yield = 24% (207 mg, over four steps). Our physical and spectroscopic data matched previously reported data.[15b]

*1-Benzyl-3-(2-bromoethyl)-5-methylindolin-2-one (**1e**).* The title compound was synthesized according to general procedure GP2 using 5-methyltryptophol (500 mg, 2.9 mmol) as a starting material and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 40% (382 mg, over four steps). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.35−7.26 (m, 5H), 7.12−7.07 (m, 1H), 7.02−6.96 (m, 1H), 6.63 (d, J = 7.9 Hz, 1H), 4.89 (d, J = 2.0 Hz, 2H), 3.81−3.67 (m, 2H), 3.61 (ddd, J = 10.0, 7.6, 6.4 Hz, 1H), 2.56−2.46 (m, 1H), 2.46−2.37 (m, 1H), 2.32 (s, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 177.0, 141.0, 135.9, 132.2, 128.8 (2C), 128.5, 127.8, 127.6, 127.3 (2C), 124.8, 109.0, 44.0, 43.8, 34.3, 30.0, 21.1 ppm. IR (KBr): ν = 1701 (C═O, amide), 692 (C—Br) cm^{-1}. HRMS (EI+) m/z: calcd for $C_{18}H_{18}NOBr$ [M], 343.0572; found, 343.0573.

*1-Benzyl-3-(2-bromoethyl)-5-methoxyindolin-2-one (**1f**).* The title compound was synthesized according to general procedure GP2 using 5-methoxytryptophol (500 mg, 2.6 mmol) as a starting material and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 39% (365 mg, over four steps). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.37−7.28 (m, 5H), 6.91 (dd, J = 2.5, 1.1 Hz, 1H), 6.73 (ddd, J = 8.5, 2.5, 0.7 Hz, 1H), 6.64 (d, J = 8.5 Hz, 1H), 4.90 (d, J = 1.4 Hz, 2H), 3.78 (s, 3H), 3.78−3.71 (m, 2H), 3.62 (ddd, J = 10.1, 7.6, 6.3 Hz, 1H), 2.58−2.49 (m, 1H), 2.49−2.40 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 176.7, 156.0, 136.8, 135.9, 129.1, 128.8 (2C), 127.7, 127.3 (2C), 112.3, 111.6, 109.5, 55.8, 44.4, 43.8, 34.2, 29.9 ppm. IR (KBr): ν = 1699 (C═O, amide), 701 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{18}H_{19}BrNO_2$ [M + H]$^+$, 360.0590; found, 360.0594.

*1-Benzyl-3-(2-bromoethyl)-5-fluoroindolin-2-one (**1g**).* The title compound was synthesized according to general procedure GP2 using 5-fluorotryptophol (500 mg, 2.8 mmol) as a starting material and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 44% (428 mg, over four steps). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.37−7.28 (m, 5H), 7.05 (ddd, J = 7.9, 2.6, 1.2 Hz, 1H), 6.91 (tdd, J = 8.5, 2.6, 0.8 Hz, 1H), 6.66 (dd, J = 8.6, 4.2 Hz, 1H), 4.91 (s, 2H), 3.83−3.73 (m, 2H), 3.62 (ddd, J = 10.2, 7.2, 6.4 Hz, 1H), 2.61−2.49 (m, 1H), 2.44 (dtd, J = 14.4, 7.1, 6.3 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 176.7, 159.2 (d, J = 241.2 Hz, 1C), 139.2 (d, J = 2.1 Hz, 1C), 135.5, 129.4 (d, J = 8.2 Hz, 1C), 128.9 (2C), 127.8, 127.3 (2C), 114.5 (d, J = 23.3 Hz, 1C), 112.2 (d, J = 24.9 Hz, 1C), 109.7 (d, J = 8.1 Hz, 1C), 44.2 (d, J = 1.9 Hz, 1C), 43.9, 34.0, 29.7 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −120.36 (td, J = 8.7, 4.2 Hz, 1F) ppm. IR (KBr): ν = 1705 (C═O, amide), 694 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{17}H_{16}BrFNO$ [M + H]$^+$, 348.0389; found, 348.0394.

*1-Benzyl-3-(2-bromoethyl)-5-chloroindolin-2-one (**1h**).* The title compound was synthesized according to general procedure GP2 using 5-chlorotryptophol (500 mg, 2.6 mmol) as a starting material and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 18% (167 mg, over four steps). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.38−7.31 (m, 3H), 7.30−7.24 (m, 5H), 7.18 (ddd, J = 8.3, 2.1, 0.8 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 4.91 (s, 2H), 3.83−3.70 (m, 2H), 3.62 (ddd, J = 10.2, 7.2, 6.4 Hz, 1H), 2.48 (dddd, J = 27.7, 14.4, 7.3, 6.4 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 176.5, 141.9, 135.3, 129.5, 128.9 (2C), 128.2, 128.1, 127.9, 127.3 (2C), 124.5, 110.1, 43.9, 43.9, 34.0, 29.7 ppm. IR (KBr): ν = 1705 (C═O, amide), 810 (C—Cl), 698 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{17}H_{16}BrClNO$ [M + H]$^+$, 364.0092; found, 364.0098.

*1-Benzyl-3-(2-bromoethyl)-5-bromoindolin-2-one (**1i**).* The title compound was synthesized according to general procedure GP2 using commercially available 5-bromotryptophol (450 mg, 1.9 mmol) as a starting material and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 27% (209 mg, over four steps). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.39 (dd, J = 2.0, 1.1 Hz, 1H), 7.35−7.27 (m, 4H), 7.24 (t, J = 1.6 Hz, 1H), 6.60 (d, J = 8.3 Hz, 1H), 4.88 (s, 2H), 3.75 (dt, J = 10.3, 7.1 Hz, 2H), 3.60 (ddd, J = 10.2, 7.2, 6.4 Hz, 1H), 2.55−2.46 (m, 1H), 2.46−2.36 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 176.4, 142.4, 135.3, 131.1, 129.9, 128.9 (2C), 127.9, 127.2 (2C + 1C, *overlapped*), 115.3, 110.6, 43.8 (2C, *overlapped*), 34.0, 29.7 ppm. IR (KBr): ν = 1711 (C═O, amide), 696 (C—Br) cm^{-1}. HRMS (APCI+) m/z: calcd for $C_{17}H_{16}ONBr_2$ [M + H]$^+$, 407.9593; found, 407.9594.

*1-Benzyl-3-(2-bromoethyl)-4-methylindolin-2-one (**1j**).* The title compound was synthesized according to general procedure GP2 using 4-methyltryptophol (500 mg, 2.9 mmol) as a starting material, and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 19% (181 mg, over four steps). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.38−7.28 (m, 5H), 7.12 (td, J = 7.8, 0.7 Hz, 1H), 6.86 (dt, J = 7.8,

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0.8 Hz, 1H), 6.61 (d, J = 7.8 Hz, 1H), 5.00−4.82 (m, 2H), 3.76 (dd, J = 8.9, 3.2 Hz, 1H), 3.69 (ddd, J = 10.0, 8.5, 7.7 Hz, 1H), 3.50 (ddd, J = 10.0, 8.2, 4.4 Hz, 1H), 2.75 (dtd, J = 14.5, 8.3, 3.2 Hz, 1H), 2.48−2.39 (m, 1H), 2.38 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 177.1, 143.5, 135.9, 134.4, 128.8 (2C), 128.2, 127.6, 127.3 (2C), 125.4, 124.6, 106.9, 43.8 (2C, *overlapped*), 32.8, 30.0, 18.6 ppm. IR (KBr): ν = 1703 (C═O, amide), 700 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{18}H_{18}BrNNaO$ $[M + Na]^+$, 366.0462; found, 366.0462.

*1-Benzyl-3-(2-bromoethyl)-6-methylindolin-2-one (**1k**).* The title compound was synthesized according to general procedure GP2 using 6-methyltryptophol (500 mg, 2.9 mmol) as a starting material and benzyl bromide as an alkylating agent. Colorless oil. Yield = 17% (166 mg, over four steps). ^1H NMR (400 MHz, chloroform-*d*): δ 7.37−7.28 (m, 5H), 7.17 (dd, J = 7.6, 1.0 Hz, 1H), 6.89−6.83 (m, 1H), 6.59 (d, J = 1.3 Hz, 1H), 4.98−4.85 (m, 2H), 3.81−3.68 (m, 2H), 3.62 (ddd, J = 10.0, 7.5, 6.4 Hz, 1H), 2.58−2.47 (m, 1H), 2.47−2.36 (m, 1H), 2.32 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 177.4, 143.5, 138.4, 135.9, 128.8 (2C), 127.6, 127.2 (2C), 124.7, 123.7, 123.1, 110.0, 43.8, 43.7, 34.3, 30.0, 21.8 ppm. IR (KBr): ν = 1699 (C═O, amide), 707 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{18}H_{19}BrNO$ $[M + H]^+$, 344.0639; found, 344.0645.

*1-Benzyl-3-(2-bromoethyl)-7-methylindolin-2-one (**1l**).* The title compound was synthesized according to general procedure GP2 using 7-methyltryptophol (500 mg, 2.9 mmol) as a starting material, and benzyl bromide as an alkylating agent. White amorphous solid. Yield = 23% (225 mg, over four steps). ^1H NMR (400 MHz, chloroform-*d*): δ 7.44−7.30 (m, 2H), 7.28−7.23 (m, 1H), 7.17 (tdd, J = 7.1, 2.3, 0.9 Hz, 3H), 7.01−6.96 (m, 2H), 5.21 (s, 2H), 3.84−3.73 (m, 2H), 3.65 (ddd, J = 10.0, 7.5, 6.3 Hz, 1H), 2.61−2.43 (m, 2H), 2.30 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 178.0, 141.5, 137.6, 132.2, 128.9 (2C), 128.4, 127.2, 125.6 (2C), 122.7, 121.9, 120.0, 45.0, 43.5, 34.7, 30.0, 18.8 ppm. IR (KBr): ν = 1699 (C═O, amide), 725 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{18}H_{19}BrNO$ $[M + H]^+$, 344.0637; found, 344.0645.

Preparation of Oxindoles 1 (GP3). Inspired by the previously reported procedure for Larock indole synthesis.[30] *N*-Benzyl-2-iodoaniline (1000 mg, 3.24 mmol, 1.0 equiv), *n*-Bu_4NCl (898 mg, 3.24 mmol, 1.0 equiv), Na_2CO_3 (1717 mg, 16.20 mmol, 5.0 equiv), and PPh_3 (43 mg, 0.16 mmol, 0.05 equiv) were evacuated and flushed by argon (three times). Then, dry DMF (60 mL) was added, and the suspension was degassed. Then, the corresponding alkyne (6.48 mmol, 2.0 equiv) and $Pd(OAc)_2$ were added. The reaction mixture was heated to 100 °C in an oil bath, typically for 4 h. Conversion of starting aniline was checked by TLC. After composition of the starting material, the reaction was cooled to room temperature, quenched by a solution of NH_4Cl (50 mL), and diluted by Et_2O (50 mL). The organic phase was separated, and the water phase was extracted with Et_2O (3 × 50 mL). The collected organic phases were washed with brine (2 × 50 mL) and dried over $MgSO_4$. After filtration of the drying agent, solvents were removed under reduced pressure. Crude product was purified by column chromatography using a hexane/EtOAc mixture as an eluent. The last two steps (deprotection/oxidation to oxindole and Appel reaction) were performed according to previously described procedures—GP2.

*1-Benzyl-3-(4-bromopropyl)indolin-2-one (**1n**).* The title compound was synthesized according to general procedure GP3. Colorless oil. Yield = 20% (223 mg, over three steps). ^1H NMR (400 MHz, chloroform-*d*): δ 7.38−7.26 (m, 6H), 7.20 (tt, J = 7.8, 1.0 Hz, 1H), 7.06 (td, J = 7.5, 1.0 Hz, 1H), 6.78−6.73 (m, 1H), 4.98 (d, J = 15.6 Hz, 1H), 4.89 (d, J = 15.6 Hz, 1H), 3.60 (t, J = 6.0 Hz, 1H), 3.43 (t, J = 6.6 Hz, 2H), 2.30−2.11 (m, 2H), 2.11−1.81 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 177.4, 143.4, 135.9, 128.8 (2C), 128.4, 128.0, 127.6, 127.3 (2C), 123.9, 122.5, 109.1, 44.7, 43.7, 33.2, 29.3, 28.8 ppm. IR (KBr): ν = 1715 (C═O, amide), 700 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{18}H_{19}BrNO$ $[M + H]^+$, 344.0650; found, 344.0658.

*1-Benzyl-3-(4-bromobutyl)indolin-2-one (**1o**).* The title compound was synthesized according to general procedure GP3. Colorless oil. Yield = 21% (245 mg, over three steps). ^1H NMR (400 MHz, chloroform-*d*): δ 7.37−7.29 (m, 6H), 7.28−7.23 (m, 1H), 7.05 (td, J = 7.5, 1.0 Hz, 1H), 6.75 (dd, J = 7.9, 0.9 Hz, 1H), 5.01 (d, J = 15.6 Hz, 1H), 4.87 (d, J = 15.6 Hz, 1H), 3.57 (t, J = 5.9 Hz, 1H), 3.40 (t, J = 6.7 Hz, 2H), 2.16−1.99 (m, 2H), 1.91 (dqd, J = 8.0, 6.7, 1.5 Hz, 2H), 1.65−1.43 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 177.7, 143.5, 135.9, 128.8 (3C), 127.9, 127.6, 127.3 (2C), 123.9, 122.4, 109.1, 45.3, 43.7, 33.3, 32.6, 29.9, 24.5 ppm. IR (KBr): ν = 1718 (C═O, amide), 724 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{19}H_{21}BrNO$ $[M + H]^+$, 358.0801; found, 358.0799.

General Procedure for the Michael/Spirocyclization Cascade Reaction (GP4). The catalyst **C2** (7.4 mg, 0.02 mmol, 0.2 equiv) was added to a solution of the corresponding α,β-unsaturated aldehyde **2** (0.1 mmol, 1.0 equiv) in DCM (0.5 mL). The mixture was stirred for 10 min at room temperature. Then, 2,4,6-collidine (20.0 μL, 0.15 mmol, 1.5 equiv) and oxindole **1** (0.105 mmol, 1.05 equiv) were added. The reaction was stirred for the indicated time (TLC control). With complete conversion of aldehyde **2**, the reaction was quenched by hydrochloric acid (1 M, 1 × 1 mL). The organic phase was separated, and the solvents were evaporated. The crude product was purified by column chromatography (eluting with hexane/EtOAc mixtures).

Note: For racemic reactions, catalyst *rac*-**C1** was used.

1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 12 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3a**/**4a** = 1/2.3 and overall yield of **3a**/**4a** = 98%.

Opposite enantiomers of both diastereomers were prepared according to the modified general procedure (GP4)—catalyst *ent*-**C2** was used instead of **C2** (reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of *ent*-**3a**/*ent*-**4a** = 1/2.0 and an overall yield of *ent*-**3a**/*ent*-**4a** = 94%.

*(1S,2S,3S)-1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3a**).* Yellow oil. Yield = 28% (11 mg). 98% *ee*. The enantiomeric excess of product **3a** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 214 nm); t_R = 9.6 min, t_R = 25.7 min. $[\alpha]_D^{20}$ = −97.1 (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.77 (d, J = 2.2 Hz, 1H), 7.47−7.37 (m, 1H), 7.24−7.17 (m, 1H), 7.17−7.05 (m, 7H), 7.05−7.00 (m, 2H), 6.51−6.45 (m, 2H), 6.41−6.35 (m, 1H), 5.08−4.94 (m, 1H), 4.31−4.20 (m, 2H), 3.80 (d, J = 11.7 Hz, 1H), 2.74−2.59 (m, 1H), 2.45−2.35 (m, 1H), 2.35−2.22 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ = 202.3, 178.4, 142.8, 135.5, 135.1, 131.3, 128.5 (2C), 128.4 (2C), 128.2, 128.1 (2C), 127.5, 127.1, 126.4 (2C), 122.7, 122.3, 109.1, 60.1, 56.5, 54.1, 43.3, 35.5, 24.4 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (EI+) m/z: calcd for $C_{26}H_{23}NO_2$ $[M]^+$, 381.1729; found, 381.1730. R_f = 0.18 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4a**).* Yellow oil. Yield = 70% (27 mg). 99% *ee*. The enantiomeric excess of product **4a** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm, t = 25 °C); t_R = 11.2 min, t_R = 14.9 min. $[\alpha]_D^{20}$ = +65.9 (c = 1.6, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.66 (d, J = 3.1 Hz, 1H), 7.32−7.28 (m, 1H), 7.19−6.92 (m, 10H), 6.80−6.75 (m, 2H), 6.45−6.40 (m, 1H), 5.08 (d, J = 15.9 Hz, 1H), 4.53 (d, J = 16.0 Hz, 1H), 4.00 (d, J = 12.1 Hz, 1H), 3.67 (dddd, J = 12.4, 9.6, 7.6, 3.1 Hz, 1H), 2.60 (ddd, J = 12.1, 9.9, 8.3 Hz, 1H), 2.56−2.42 (m, 2H), 2.13 (ddd, J = 12.1, 7.9, 4.3 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.6, 178.5, 142.1, 135.3, 135.1, 131.3, 128.5 (2C), 128.2 (2C), 128.1 (2C + 1C, *overlapped*), 127.5, 127.2, 126.6 (2C), 124.0, 122.3, 109.3, 60.3, 56.6, 55.3, 43.7, 35.4, 24.2 ppm. IR (KBr): ν = 1712 (C═O, aldehyde, amide) cm^{-1}. HRMS (EI+) m/z: calcd for $C_{26}H_{23}NO_2$ $[M]^+$, 381.1729; found, 381.1732. R_f = 0.24 (hexane/EtOAc - 5:1).

*(1R,2R,3R)-1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (ent-**3a**).* Yellow oil. Yield = 31% (12 mg).

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99% *ee*. $[\alpha]_D^{20}$ = +65.0 (*c* = 0.5, $CHCl_3$). The analytical data matched the data for the opposite enantiomer (see **3a**).

*(1S,2R,3R)-1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (ent-**4a**).* White foam. Yield = 63% (24 mg). 99% *ee*. $[\alpha]_D^{20}$ = −64.0 (*c* = 0.9, $CHCl_3$). The analytical data matched the data for the opposite enantiomer (see **4a**).

1′-Allyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 5:1 to 4:1) with a diastereomeric ratio of **3b**/**4b** = 1/1.7 and an overall yield of **3b**/**4b** = 90%. *Note*: Enantiomeric excesses of products were determined after derivatization by Wittig reaction; for more details, see products **14b** and **14b′**.

*(1S,2S,3S)-1′-Allyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3b**).* Yellow oil. Yield = 35% (12 mg). $[\alpha]_D^{20}$ = −45.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.76 (d, *J* = 2.2 Hz, 1H), 7.51−7.39 (m, 1H), 7.21 (td, *J* = 7.7, 1.4 Hz, 1H), 7.18−7.05 (m, 4H), 6.99−6.92 (m, 2H), 6.61−6.52 (m, 1H), 5.26 (dddd, *J* = 17.3, 10.2, 5.5, 4.4 Hz, 1H), 4.85 (dq, *J* = 10.4, 1.5 Hz, 1H), 4.41 (dtd, *J* = 17.2, 1.8, 1.0 Hz, 1H), 4.29 (ddt, *J* = 16.5, 4.2, 2.0 Hz, 1H), 4.21 (dtt, *J* = 11.8, 7.2, 2.2 Hz, 1H), 3.78 (ddt, *J* = 16.5, 5.5, 1.6 Hz, 1H), 3.73 (d, *J* = 11.7 Hz, 1H), 2.74−2.57 (m, 1H), 2.42−2.20 (m, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.4, 178.4, 142.9, 135.3, 131.2, 130.7, 128.1 (3C), 127.9 (2C), 127.5, 122.6, 122.2, 116.7, 108.8, 60.1, 57.1, 53.9, 41.7, 34.7, 24.5 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{22}H_{22}NO_2$ $[M + H]^+$, 332.1645; found, 332.1644. R_f = 0.20 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Allyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4b**).* White solid (crystals suitable for X-ray analysis were grown by the dissolution of **4b** in a minimal amount of boiling heptane/*i*-PrOH mixture, 8/2, *v*/*v*, followed by standing at rt overnight). Yield = 55% (18 mg). mp = 149−150 °C (heptane/*i*-PrOH, 8/2, *v*/v). $[\alpha]_D^{20}$ = +56.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.66 (d, *J* = 3.2 Hz, 1H), 7.26 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.14 (td, *J* = 7.7, 1.3 Hz, 1H), 7.10−6.98 (m, 4H), 6.99−6.91 (m, 2H), 6.59 (dd, *J* = 7.8, 1.0 Hz, 1H), 5.58 (ddt, *J* = 17.3, 10.2, 5.0 Hz, 1H), 4.99 (dq, *J* = 10.4, 1.5 Hz, 1H), 4.71−4.57 (m, 1H), 4.43 (ddt, *J* = 16.6, 4.8, 1.9 Hz, 1H), 4.03 (ddt, *J* = 16.6, 5.2, 1.7 Hz, 1H), 3.96 (d, *J* = 12.0 Hz, 1H), 3.67 (dddd, *J* = 12.4, 7.6, 6.7, 3.2 Hz, 1H), 2.66−2.36 (m, 3H), 2.18−2.01 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.7, 178.2, 142.2, 135.2, 131.3, 130.8, 128.0, (2C + 2C + 1C, *overlapped*), 127.4, 123.9, 122.2, 117.0, 109.0, 60.3, 56.6, 55.0, 42.2, 35.0, 24.4 ppm. IR (KBr): ν = 1724 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{22}H_{22}NO_2$ $[M + H]^+$, 332.1645; found, 332.1648. R_f = 0.14 (hexane/EtOAc - 5:1).

1′-Methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 5:1 to 4:1) with a diastereomeric ratio of **3c**/**4c** = 1/1.6 and an overall yield of **3c**/**4c** = 90%. *Note*: Enantiomeric excesses of products were determined after derivatization by Wittig reaction; for more details, see products **14c** and **14c′**.

*(1S,2S,3S)-1′-Methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3c**).* Yellow oil. Yield = 33% (10 mg). $[\alpha]_D^{20}$ = −35.4 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.73 (d, *J* = 2.2 Hz, 1H), 7.41−7.35 (m, 1H), 7.21 (td, *J* = 7.7, 1.3 Hz, 1H), 7.16−7.01 (m, 4H), 6.96−6.89 (m, 2H), 6.57 (dt, *J* = 7.8, 0.7 Hz, 1H), 4.15 (dddd, *J* = 12.0, 9.7, 7.1, 2.3 Hz, 1H), 3.66 (d, *J* = 11.7 Hz, 1H), 2.82 (s, 3H), 2.69−2.56 (m, 1H), 2.36−2.18 (m, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.4, 178.7, 143.6, 135.3, 131.2, 128.2, 127.9 (2C), 127.7 (2C), 127.4, 122.6, 122.1, 107.7, 60.2, 57.2, 54.0, 34.3, 25.6, 24.4 ppm. IR (KBr): ν = 1716 (C═O, amide), 1693 (C═O, aldehyde) cm^{-1}. HRMS (EI+) *m*/*z*: calcd for $C_{20}H_{19}NO_2$ $[M]^+$, 305.1416; found, 305.1414. R_f = 0.22 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4c**).* White amorphous solid. Yield = 57% (17 mg). $[\alpha]_D^{20}$ = +49.7 (*c* = 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.63 (d, *J* = 3.2 Hz, 1H), 7.20−7.09 (m, 2H), 7.07−6.95 (m, 4H), 6.95−6.87 (m, 2H), 6.57 (dt, *J* = 7.7, 0.8 Hz, 1H), 3.94 (d, *J* = 11.8 Hz, 1H), 3.63 (dddd, *J* = 11.8, 9.4, 7.5, 3.2 Hz, 1H), 3.05 (s, 3H), 2.58−2.36 (m, 3H), 2.13−2.03 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.8, 178.7, 142.9, 135.5, 131.4, 128.0, 127.9 (2C), 127.7 (2C), 127.3, 123.8, 122.2, 107.9, 60.3, 56.3, 54.9, 34.8, 26.2, 24.5 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (EI+) *m*/*z*: calcd for $C_{20}H_{19}NO_2$ $[M]^+$, 305.1416; found, 305.1415. R_f = 0.18 (hexane/EtOAc - 5:1).

2′-Oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 3:1) with a diastereomeric ratio of **3d**/**4d** = 3.4/1 and an overall yield of **3d**/**4d** = 77%.

*(1S,2S,3S)-2′-Oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3d**).* White amorphous solid. Yield = 60% (18 mg). 90% *ee*. The enantiomeric excess of product **3d** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 254 nm); t_R = 12.2 min, t_R = 13.8 min. $[\alpha]_D^{20}$ = −58.3 (*c* = 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.73 (d, *J* = 2.2 Hz, 1H), 7.70 (s, 1H), 7.41−7.34 (m, 1H), 7.21−7.02 (m, 5H), 7.01−6.95 (m, 2H), 6.67−6.60 (m, 1H), 4.13 (dddd, *J* = 11.8, 9.5, 7.2, 2.2 Hz, 1H), 3.70 (d, *J* = 11.7 Hz, 1H), 2.65−2.51 (m, 1H), 2.40−2.31 (m, 1H), 2.31−2.13 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.4, 180.9, 140.7, 135.4, 131.8, 128.2, 128.1 (2C), 127.8 (2C), 127.5, 122.7, 122.6, 109.4, 60.4, 56.8, 54.1, 35.0, 24.4 ppm. IR (KBr): ν = 3226 (N—H), 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (EI+) *m*/*z*: calcd for $C_{19}H_{17}NO_2$ $[M]^+$, 291.1259; found, 291.1256. R_f = 0.31 (hexane/EtOAc - 3:1).

*(1R,2S,3S)-2′-Oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4d**).* Colorless oil. Yield = 17% (5 mg). 96% *ee*. The enantiomeric excess of product **4d** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 254 nm); t_R = 10.6 min, t_R = 11.6 min. $[\alpha]_D^{20}$ = +47.3 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.64 (d, *J* = 3.1 Hz, 1H), 7.99 (s, 1H), 7.16 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.13−7.01 (m, 4H), 6.97 (ddd, *J* = 8.7, 5.8, 1.5 Hz, 3H), 6.67 (dd, *J* = 7.7, 1.4 Hz, 1H), 3.95 (d, *J* = 11.8 Hz, 1H), 3.64 (dddd, *J* = 11.9, 9.6, 7.7, 3.2 Hz, 1H), 2.59−2.36 (m, 3H), 2.16−2.06 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.7, 180.6, 139.8, 135.4, 131.8, 128.1, 128.0 (2C), 127.9, 127.4 (2C), 124.3, 122.3, 109.7, 60.6, 56.2, 55.1, 35.4, 24.5 ppm. IR (KBr): ν = 3217 (N—H), 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (EI+) *m*/*z*: calcd for $C_{19}H_{17}NO_2$ $[M]^+$, 291.1259; found, 291.1261. R_f = 0.24 (hexane/EtOAc - 3:1).

1′-Benzyl-5′-methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3e**/**4e** = 1/2.6 and an overall yield of **3e**/**4e** = 95%.

*(1S,2S,3S)-1′-Benzyl-5′-methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3e**).* Colorless oil. Yield = 27% (11 mg). 99% *ee*. The enantiomeric excess of product **3e** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 217 nm); t_R = 8.2 min, t_R = 18.2 min. $[\alpha]_D^{20}$ = −44.9 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.2 Hz, 1H), 7.27−7.20 (m, 2H), 7.17−7.03 (m, 7H), 6.90 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H), 6.53−6.44 (m, 2H), 6.28 (d, *J* = 7.9 Hz, 1H), 5.05−4.97 (m, 1H), 4.32−4.22 (m, 2H), 3.81 (d, *J* = 11.6 Hz, 1H), 2.75−2.65 (m, 1H), 2.45−2.27 (m, 6H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.4, 178.7, 140.4, 135.6, 135.2, 132.2, 131.4, 128.5 (2C), 128.4 (2C + 1C, *overlapped*), 128.1 (2C), 127.5, 127.0, 126.4 (2C), 123.1, 108.8, 60.1, 56.5, 54.2, 43.3, 35.6, 24.6, 21.2 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{28}H_{30}NO_2$ $[M + MeOH + H]^+$, 428.2219; found, 428.2220. R_f = 0.32 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-5′-methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4e**).* Light yellow

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semisolid. Yield = 68% (27 mg). 99% *ee*. The enantiomeric excess of product **4e** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 9.0 min, t_R = 12.3 min. $[\alpha]_D^{20}$ = +118.8 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.65 (d, *J* = 3.3 Hz, 1H), 7.19−7.08 (m, 5H), 7.08−7.01 (m, 2H), 7.00−6.93 (m, 2H), 6.85 (ddd, *J* = 7.9, 1.7, 0.9 Hz, 1H), 6.80−6.71 (m, 2H), 6.30 (d, *J* = 7.9 Hz, 1H), 5.06 (d, *J* = 15.9 Hz, 1H), 4.50 (d, *J* = 16.0 Hz, 1H), 3.98 (d, *J* = 12.1 Hz, 1H), 3.66 (dddd, *J* = 12.4, 9.4, 7.8, 3.3 Hz, 1H), 2.65−2.54 (m, 1H), 2.54−2.42 (m, 2H), 2.32 (s, 3H), 2.11 (ddd, *J* = 12.1, 7.6, 4.6 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.9, 178.5, 139.8, 135.4, 135.2, 131.8, 131.4, 128.5 (2C), 128.3 (2C + 1C, *overlapped*), 128.2 (2C), 127.5, 127.2, 126.7 (2C), 124.8, 109.0, 60.5, 56.6, 55.4, 43.7, 35.4, 24.3, 21.3 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{26}NO_2$ $[M + H]^+$, 396.1956; found, 396.1958. R_f = 0.26 (hexane/EtOAc - 5:1).

1′-Benzyl-5′-methoxy-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3f**/**4f** = 1/1.2 and an overall yield of **3f**/**4f** = 80%.

*(1S,2S,3S)-1′-Benzyl-5′-methoxy-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3f**).* Colorless oil. Yield = 35% (14 mg). 98% *ee*. The enantiomeric excess of product **3f** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 15.2 min, t_R = 41.6 min. $[\alpha]_D^{20}$ = −170.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.1 Hz, 1H), 7.26−7.21 (m, 1H), 7.19−7.13 (m, 3H), 7.12−6.99 (m, 5H), 6.62 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.52−6.44 (m, 2H), 6.28 (d, *J* = 8.4 Hz, 1H), 5.01 (d, *J* = 16.0 Hz, 1H), 4.33−4.19 (m, 2H), 3.83 (s, 3H), 3.79 (d, *J* = 11.7 Hz, 1H), 2.75−2.63 (m, 1H), 2.48−2.38 (m, 1H), 2.38−2.20 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.4, 178.5, 156.1, 136.3, 135.5, 135.2, 132.7, 128.5 (2C), 128.4 (2C), 128.2 (2C), 127.5, 127.0, 126.5 (2C), 112.4, 109.7, 109.5, 60.5, 56.6, 55.9, 54.1, 43.3, 35.6, 24.5 ppm. IR (KBr): ν = 1704 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{26}NO_3$ $[M + H]^+$, 412.1911; found, 412.1907. R_f = 0.28 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-5′-methoxy-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4f**).* Colorless oil. Yield = 45% (19 mg). 99% *ee*. The enantiomeric excess of product **4f** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 15.2 min, t_R = 19.0 min. $[\alpha]_D^{20}$ = +119.3 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.68 (d, *J* = 3.1 Hz, 1H), 7.22−7.13 (m, 4H), 7.12−7.06 (m, 2H), 7.04−6.99 (m, 2H), 6.89 (d, *J* = 2.5 Hz, 1H), 6.81−6.75 (m, 2H), 6.58 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.33 (d, *J* = 8.5 Hz, 1H), 5.08 (d, *J* = 15.8 Hz, 1H), 4.52 (d, *J* = 15.9 Hz, 1H), 4.02 (d, *J* = 12.0 Hz, 1H), 3.77 (s, 3H), 3.66 (dddd, *J* = 12.5, 9.9, 7.4, 3.1 Hz, 1H), 2.65−2.41 (m, 3H), 2.17−2.09 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.7, 178.2, 155.6, 135.8, 135.4, 135.2, 132.7, 128.6 (2C), 128.3 (2C), 128.2 (2C), 127.5, 127.2, 126.7 (2C), 112.3, 111.6, 109.4, 60.7, 56.4, 55.9, 55.3, 43.8, 35.5, 24.3 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{26}NO_3$ $[M + H]^+$, 412.1911; found, 412.1907. R_f = 0.20 (hexane/EtOAc - 5:1).

1′-Benzyl-5′-fluoro-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3g**/**4g** = 2.3/1 and an overall yield of **3g**/**4g** = 98%.

*(1S,2S,3S)-1′-Benzyl-5′-fluoro-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3g**).* Colorless oil. Yield = 68% (27 mg). 98% *ee*. The enantiomeric excess of product **3g** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 9.1 min, t_R = 21.8 min. $[\alpha]_D^{20}$ = −71.9 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.1 Hz, 1H), 7.27−7.22 (m, 1H), 7.22−7.14 (m, 4H), 7.14−7.02 (m, 4H), 6.79 (ddd, *J* = 9.3, 8.5, 2.6 Hz, 1H), 6.51−6.43 (m, 2H), 6.29 (dd, *J* = 8.5, 4.2 Hz, 1H), 5.07−4.95 (m, 1H), 4.35−4.20 (m, 2H), 3.79 (d, *J* = 11.6 Hz, 1H), 2.77−2.62 (m, 1H), 2.49−2.38 (m, 1H), 2.36−2.20 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.0, 178.5, 159.4 (d, *J* = 241.1 Hz, 1C), 138.6 (d, *J* = 2.0 Hz, 1C), 135.2, 134.8, 133.1 (d, *J* = 7.7 Hz, 1C), 128.6 (2C), 128.5 (2C), 128.1 (2C), 127.7, 127.2, 126.4 (2C), 114.5 (d, *J* = 23.4 Hz, 1C), 110.4 (d, *J* = 24.7 Hz, 1C), 109.7 (d, *J* = 8.1 Hz, 1C), 60.5 (d, *J* = 1.9 Hz, 1C), 56.6, 54.1, 43.4, 35.5, 24.4 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −119.94 (ddd, *J* = 9.3, 7.9, 4.2 Hz, 1F) ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}FNO_2$ $[M + H]^+$, 400.1709; found, 400.1707. R_f = 0.30 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-5′-fluoro-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4g**).* Colorless oil. Yield = 30% (12 mg). 92% *ee*. The enantiomeric excess of product **4g** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 207 nm); t_R = 10.3 min, t_R = 13.8 min. $[\alpha]_D^{20}$ = +52.6 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.68 (d, *J* = 3.0 Hz, 1H), 7.23−7.13 (m, 4H), 7.13−7.06 (m, 2H), 7.06−6.94 (m, 3H), 6.84−6.71 (m, 3H), 6.35 (dd, *J* = 8.6, 4.3 Hz, 1H), 5.08 (d, *J* = 16.0 Hz, 1H), 4.54 (d, *J* = 16.0 Hz, 1H), 4.03 (d, *J* = 12.0 Hz, 1H), 3.73−3.53 (m, 1H), 2.69−2.38 (m, 3H), 2.14 (ddd, *J* = 11.9, 8.4, 3.8 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.3, 178.3, 158.9 (d, *J* = 240.8 Hz, 1C), 138.1 (d, *J* = 2.0 Hz, 1C), 135.1, 134.8, 132.9 (d, *J* = 7.8 Hz, 1C), 128.7 (2C), 128.3 (2C), 128.2 (2C), 127.7, 127.4, 126.7 (2C), 114.3 (d, *J* = 23.2 Hz, 1C), 112.11 (d, *J* = 24.9 Hz, 1C), 109.8 (d, *J* = 8.2 Hz, 1C), 60.79 (d, *J* = 1.7 Hz, 1C), 56.5, 55.1, 43.9, 35.4, 24.2 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −120.51 (td, *J* = 8.7, 4.3 Hz) ppm. IR (KBr): ν = 1711 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}FNO_2$ $[M + H]^+$, 400.1709; found, 400.1707. R_f = 0.26 (hexane/EtOAc - 5:1).

1′-Benzyl-5′-chloro-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 7:1) with a diastereomeric ratio of **3h**/**4h** = 3.1/1 and an overall yield of **3h**/**4h** = 95%.

*(1S,2S,3S)-1′-Benzyl-5′-chloro-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3h**).* Colorless oil. Yield = 72% (30 mg). 97% *ee*. The enantiomeric excess of product **3h** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 207 nm); t_R = 8.6 min, t_R = 17.3 min. $[\alpha]_D^{20}$ = −175.1 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.78 (d, *J* = 2.1 Hz, 1H), 7.43 (d, *J* = 2.1 Hz, 1H), 7.27−7.21 (m, 1H), 7.21−7.13 (m, 3H), 7.13−7.02 (m, 5H), 6.51−6.43 (m, 2H), 6.29 (d, *J* = 8.3 Hz, 1H), 5.08−4.96 (m, 1H), 4.34−4.19 (m, 2H), 3.80 (d, *J* = 11.6 Hz, 1H), 2.75−2.61 (m, 1H), 2.51−2.19 (m, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.9, 178.3, 141.3, 135.1, 134.6, 133.2, 128.6 (2C), 128.5 (2C), 128.2 (2C), 128.1 (2C, *overlapped*), 127.7, 127.2, 126.4 (2C), 122.8, 110.1, 60.2, 56.6, 54.1, 43.4, 35.6, 24.5 ppm. IR (KBr): ν = 1712 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{26}ClNNaO_3$ $[M + MeOH + Na]^+$, 470.1495; found, 470.1493. R_f = 0.28 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-5′-chloro-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4h**).* Yellow oil. Yield = 23% (10 mg). 88% *ee*. The enantiomeric excess of product **4h** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 211 nm); t_R = 9.6 min, t_R = 12.4 min. $[\alpha]_D^{20}$ = +114.3 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.68 (d, *J* = 3.0 Hz, 1H), 7.25 (d, *J* = 2.0 Hz, 1H), 7.23−7.14 (m, 4H), 7.14−7.07 (m, 2H), 7.07−6.96 (m, 3H), 6.77 (ddd, *J* = 6.4, 1.9, 1.1 Hz, 2H), 6.35 (d, *J* = 8.4 Hz, 1H), 5.08 (d, *J* = 15.9 Hz, 1H), 4.53 (d, *J* = 16.0 Hz, 1H), 4.02 (d, *J* = 12.1 Hz, 1H), 3.67 (dddd, *J* = 12.5, 10.0, 7.5, 3.0 Hz, 1H), 2.67−2.42 (m, 3H), 2.22−2.05 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.2, 178.1, 140.7, 135.0, 134.7, 133.1, 128.7 (2C), 128.4 (2C), 128.2 (2C), 128.0, 127.7, 127.7, 127.5, 126.7 (2C), 124.4, 110.2, 60.6,

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56.6, 55.1, 43.8, 35.3, 24.2 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{26}H_{23}ClNO_2$ $[M + H]^+$, 416.1412; found, 416.1412. R_f = 0.22 (hexane/EtOAc - 5:1).

1′-Benzyl-5′-bromo-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3i**/**4i** = 3.2/1 and an overall yield of **3i**/**4i** = 94%.

*(1S,2S,3S)-1′-Benzyl-5′-bromo-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3i**).* Colorless oil. Yield = 72% (33 mg). 96% *ee*. The enantiomeric excess of product **3i** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 212 nm); t_R = 8.7 min, t_R = 17.2 min. $[\alpha]_D^{20}$ = −189.3 (*c* = 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.78 (d, *J* = 2.1 Hz, 1H), 7.57 (d, *J* = 1.9 Hz, 1H), 7.28−7.23 (m, 1H), 7.21 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.17 (ddd, *J* = 8.9, 6.7, 1.6 Hz, 3H), 7.13−7.02 (m, 4H), 6.49−6.40 (m, 2H), 6.25 (d, *J* = 8.3 Hz, 1H), 5.07−4.94 (m, 1H), 4.32−4.19 (m, 2H), 3.80 (d, *J* = 11.6 Hz, 1H), 2.75−2.60 (m, 1H), 2.47−2.38 (m, 1H), 2.38−2.19 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.9, 178.2, 141.8, 135.2, 134.6, 133.6, 131.1, 128.6 (2C), 128.5 (2C), 128.1 (2C), 127.7, 127.3, 126.4 (2C), 125.6, 115.4, 110.6, 60.2, 56.6, 54.1, 43.3, 35.6, 24.5 ppm. IR (KBr): ν = 1712 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{26}BrNNaO_3$ [M + MeOH + Na]$^+$, 514.0999; found, 514.0988. R_f = 0.36 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-5′-bromo-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4i**).* Colorless oil. Yield = 22% (10 mg). 86% *ee*. The enantiomeric excess of product **4i** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 9.9 min, t_R = 13.0 min. $[\alpha]_D^{20}$ = +100.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.68 (d, *J* = 3.0 Hz, 1H), 7.38 (d, *J* = 1.9 Hz, 1H), 7.22−7.09 (m, 7H), 7.02−6.97 (m, 2H), 6.80−6.75 (m, 2H), 6.31 (d, *J* = 8.3 Hz, 1H), 5.07 (d, *J* = 16.0 Hz, 1H), 4.53 (d, *J* = 16.0 Hz, 1H), 4.02 (d, *J* = 12.1 Hz, 1H), 3.73−3.61 (m, 1H), 2.67−2.42 (m, 3H), 2.14 (ddd, *J* = 11.8, 8.2, 3.9 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.3, 178.0, 141.2, 135.0, 134.6, 133.5, 130.9, 128.7 (2C), 128.4 (2C), 128.2 (2C), 127.7, 127.5, 127.1, 126.7 (2C), 115.0, 110.7, 60.6, 56.6, 55.2, 43.8, 35.3, 24.2 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{26}H_{23}BrNO_2$ $[M + H]^+$, 460.0907; found, 460.0907. R_f = 0.28 (hexane/EtOAc - 5:1).

1′-Benzyl-4′-methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compound was synthesized according to the general procedure (GP4, reaction time: 85 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3j**/**4j** > 20/1.

*(1S,2S,3S)-1′-Benzyl-4′-methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3j**).* Colorless oil. Yield = 87% (34 mg). 98% *ee*. The enantiomeric excess of product **3j** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 209 nm); t_R = 9.4 min, t_R = 25.6 min. $[\alpha]_D^{20}$ = −121.2 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.78 (d, *J* = 2.4 Hz, 1H), 7.27−7.20 (m, 1H), 7.12 (dddd, *J* = 23.3, 8.5, 6.5, 1.6 Hz, 5H), 7.06−6.96 (m, 3H), 6.93−6.87 (m, 1H), 6.49−6.42 (m, 2H), 6.26 (d, *J* = 7.7 Hz, 1H), 4.97 (d, *J* = 16.0 Hz, 1H), 4.34 (dddd, *J* = 11.9, 9.4, 8.0, 2.4 Hz, 1H), 4.24 (d, *J* = 16.0 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 2.68−2.50 (m, 5H), 2.49−2.37 (m, 1H), 2.37−2.26 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.5, 179.1, 143.2, 135.5, 135.2, 133.6, 128.5 (2C), 128.4 (2C), 128.2 (3C), 128.0, 127.5, 127.0, 126.4 (2C), 125.5, 107.0, 60.2, 53.7, 52.8, 43.4, 31.9, 25.3, 18.5 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{28}H_{29}NNaO_3$ [M + MeOH + Na]$^+$, 450.2164; found, 450.2151. R_f = 0.26 (hexane/EtOAc - 5:1).

1′-Benzyl-6′-methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3k**/**4k** = 1/1.8 and an overall yield of **3k**/**4k** = 83%.

*(1S,2S,3S)-1′-Benzyl-6′-methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3k**).* Colorless oil. Yield = 32% (13 mg). 99% *ee*. The enantiomeric excess of product **3k** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 210 nm); t_R = 8.6 min, t_R = 15.2 min. $[\alpha]_D^{20}$ = −82.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.78 (d, *J* = 2.2 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.27−7.20 (m, 1H), 7.20−7.04 (m, 7H), 6.93 (ddd, *J* = 7.6, 1.5, 0.8 Hz, 1H), 6.54−6.48 (m, 2H), 6.25−6.21 (m, 1H), 5.10−4.93 (m, 1H), 4.38−4.20 (m, 2H), 3.80 (d, *J* = 11.6 Hz, 1H), 2.75−2.53 (m, 1H), 2.48−2.26 (m, 3H), 2.24 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.4, 179.1, 142.9, 138.3, 135.6, 135.3, 128.5 (2C), 128.4 (2C), 128.3, 128.2 (2C), 127.5, 127.0, 126.3 (2C), 123.3, 122.0, 109.8, 59.9, 56.3, 54.1, 43.2, 35.7, 24.4, 21.8 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{28}H_{29}NNaO_3$ [M + MeOH + Na]$^+$, 450.2045; found, 450.2040. R_f = 0.32 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-6′-methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4k**).* Colorless oil. Yield = 51% (20 mg). 99% *ee*. The enantiomeric excess of product **4k** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 9.8 min, t_R = 12.5 min. $[\alpha]_D^{20}$ = +72.8 (*c* = 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.67 (d, *J* = 3.2 Hz, 1H), 7.23−7.11 (m, 5H), 7.11−7.03 (m, 2H), 7.02−6.96 (m, 2H), 6.83 (ddd, *J* = 7.6, 1.6, 0.8 Hz, 1H), 6.81−6.75 (m, 2H), 6.33−6.23 (m, 1H), 5.09 (d, *J* = 16.0 Hz, 1H), 4.52 (d, *J* = 16.0 Hz, 1H), 3.99 (d, *J* = 12.1 Hz, 1H), 3.75−3.56 (m, 1H), 2.66−2.41 (m, 3H), 2.21 (s, 3H), 2.15−2.05 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.8, 178.8, 142.3, 138.2, 135.5, 135.3, 128.6 (2C), 128.3 (2C), 128.2 (2C), 127.5, 127.2 (2C), 126.6 (2C), 123.7, 122.9, 110.1, 60.2, 56.4, 55.4, 43.6, 35.7, 24.2, 21.7 ppm. IR (KBr): ν = 1711 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{26}NO_2$ $[M + H]^+$, 396.1956; found, 396.1958. R_f = 0.24 (hexane/EtOAc - 5:1).

1′-Benzyl-7′-methyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3l**/**4l** = 1.5/1 and an overall yield of **3l**/**4l** = 98%.

*(1S,2S,3S)-1′-Benzyl-7′-methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3l**).* Colorless oil. Yield = 61% (24 mg). 69% *ee*. The enantiomeric excess of product **3l** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 213 nm); t_R = 10.7 min, t_R = 37.2 min. $[\alpha]_D^{20}$ = −73.8 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.1 Hz, 1H), 7.34 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.28−7.22 (m, 1H), 7.20−7.03 (m, 8H), 6.91 (dt, *J* = 7.7, 1.0 Hz, 1H), 6.46−6.27 (m, 2H), 5.20 (d, *J* = 17.0 Hz, 1H), 4.67 (d, *J* = 17.0 Hz, 1H), 4.28 (dddd, *J* = 11.9, 9.5, 7.0, 2.2 Hz, 1H), 3.83 (d, *J* = 11.7 Hz, 1H), 2.78−2.58 (m, 1H), 2.46−2.37 (m, 1H), 2.37−2.24 (m, 2H), 2.05 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.4, 179.6, 141.0, 137.3, 135.6, 132.1, 132.0, 128.7 (2C), 128.4 (2C), 128.3 (2C), 127.6, 126.6, 125.1 (2C), 122.8, 120.3, 119.6, 59.5, 56.5, 54.2, 44.5, 36.5, 24.3, 18.4 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{28}H_{29}NNaO_3$ [M + MeOH + Na]$^+$, 450.2045; found, 450.2040. R_f = 0.32 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-7′-methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4l**).* Colorless oil. Yield = 37% (15 mg). 96% *ee*. The enantiomeric excess of product **4l** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 209 nm); t_R = 12.2 min, t_R = 22.4 min. $[\alpha]_D^{20}$ = +46.0 (*c* = 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.67 (d, *J* = 3.1 Hz, 1H), 7.22 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.20−7.09 (m, 6H), 7.05−7.00 (m, 2H), 6.97 (t, *J* = 7.6 Hz,

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1H), 6.87 (dt, J = 7.7, 1.1 Hz, 1H), 6.64−6.57 (m, 2H), 5.31 (d, J = 17.0 Hz, 1H), 4.89 (d, J = 17.0 Hz, 1H), 4.02 (d, J = 12.2 Hz, 1H), 3.69 (dddd, J = 12.3, 9.4, 7.9, 3.1 Hz, 1H), 2.68−2.57 (m, 1H), 2.56−2.42 (m, 2H), 2.14 (ddd, J = 12.4, 7.5, 4.9 Hz, 1H), 2.06 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.8, 179.5, 140.4, 137.3, 135.5, 132.2, 132.2, 128.7 (2C), 128.5 (2C), 128.3 (2C), 127.6, 126.82, 125.2 (2C), 122.4, 122.1, 119.9, 59.7, 56.8, 55.8, 45.0, 36.3, 24.3, 18.6 ppm. IR (KBr): ν = 1708 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{26}NO_2$ $[M + H]^+$, 396.1960; found, 396.1958. R_f = 0.28 (hexane/EtOAc - 5:1).

1′-Benzyl-2-(naphthalen-2-yl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 4:1 to 3:1) with a diastereomeric ratio of **3m**/**4m** = 1/1.7 and an overall yield of **3m**/**4m** = 97%.

*(1S,2S,3S)-1′-Benzyl-2-(naphthalen-2-yl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3m**).* Yellow oil. Yield = 36% (16 mg). 97% *ee*. The enantiomeric excess of product **3m** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 228 nm); t_R = 10.4 min, t_R = 13.7 min. $[\alpha]_D^{20}$ = −105.4 (c = 0.9, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.81 (d, J = 2.1 Hz, 1H), 7.75 (dd, J = 8.2, 1.3 Hz, 1H), 7.66 (dd, J = 8.2, 1.3 Hz, 1H), 7.61−7.57 (m, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.52−7.48 (m, 1H), 7.45 (ddd, J = 8.2, 6.8, 1.5 Hz, 1H), 7.40 (ddd, J = 8.2, 6.8, 1.5 Hz, 1H), 7.14 (td, J = 7.5, 1.2 Hz, 1H), 7.11−7.01 (m, 2H), 6.92−6.85 (m, 1H), 6.53−6.46 (m, 2H), 6.34−6.29 (m, 1H), 6.25−6.16 (m, 2H), 5.06−4.94 (m, 1H), 4.47−4.35 (m, 1H), 4.17 (d, J = 16.0 Hz, 1H), 3.98 (d, J = 11.7 Hz, 1H), 2.78−2.67 (m, 1H), 2.50−2.40 (m, 1H), 2.40−2.28 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.3, 173.7, 142.8, 134.8, 133.2 (2C, *overlapped*), 132.9, 131.3, 128.7, 128.3, 128.2, 128.1 (2C), 127.9, 127.5, 126.9 (2C, *overlapped*), 126.4, 126.1 (2C), 126.0, 125.9, 122.8, 122.3, 109.1, 60.2, 56.6, 54.2, 43.3, 35.6, 24.5 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{30}H_{26}NO_2$ $[M + H]^+$, 432.1957; found, 432.1958. R_f = 0.52 (hexane/EtOAc - 3:1).

*(1R,2S,3S)-1′-Benzyl-2-(naphthalen-2-yl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4m**).* Colorless oil. Yield = 61% (26 mg). 99% *ee*. The enantiomeric excess of product **4m** was determined by HPLC using a Chiralpak IB column (heptane/*i*-PrOH - 90:10, flow rate = 1.0 mL/min, λ = 229 nm); t_R = 14.4 min, t_R = 18.6 min. $[\alpha]_D^{20}$ = +127.2 (c = 1.2, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.71 (d, J = 3.1 Hz, 1H), 7.72 (dd, J = 7.5, 1.9 Hz, 1H), 7.69−7.61 (m, 1H), 7.56 (d, J = 1.8 Hz, 1H), 7.49 (d, J = 8.6 Hz, 1H), 7.48−7.38 (m, 3H), 7.10−6.95 (m, 4H), 6.73−6.66 (m, 2H), 6.60−6.50 (m, 2H), 6.40−6.30 (m, 1H), 5.21−5.07 (m, 1H), 4.44 (d, J = 16.0 Hz, 1H), 4.19 (d, J = 12.3 Hz, 1H), 3.82 (dddd, J = 12.5, 9.6, 7.7, 3.1 Hz, 1H), 2.75−2.63 (m, 1H), 2.63−2.51 (m, 2H), 2.19 (ddd, J = 12.1, 7.7, 4.3 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.6, 178.4, 142.2, 134.8, 133.1, 132.9, 132.8, 131.4, 128.3 (2C), 128.2, 128.0, 127.9, 127.7, 127.4, 127.1, 126.3 (2C), 126.0 (2C, *overlapped*), 125.6, 124.0, 122.4, 109.5, 60.6, 57.0, 55.5, 43.7, 35.5, 24.3 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{30}H_{26}NO_2$ $[M + H]^+$, 432.1962; found, 432.1958. R_f = 0.46 (hexane/EtOAc - 3:1).

1′-Benzyl-2′-oxo-2-(p-tolyl)spiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 46 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3n**/**4n** = 1/1.5 and an overall yield of **3n**/**4n** = 96%.

*(1S,2S,3S)-1′-Benzyl-2′-oxo-2-(p-tolyl)spiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3n**).* Colorless oil. Yield = 38% (15 mg). 98% *ee*. The enantiomeric excess of product **3n** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 213 nm); t_R = 8.3 min, t_R = 13.5 min. $[\alpha]_D^{20}$ = −113.5 (c = 0.6, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.77 (d, J = 2.2 Hz, 1H), 7.50−7.40 (m, 1H), 7.23−7.04 (m, 5H), 6.94 (s, 4H), 6.58−6.48 (m, 2H), 6.46−6.32 (m, 1H), 5.12−4.94 (m, 1H), 4.33−4.19 (m, 2H), 3.78 (d, J = 11.7 Hz, 1H), 2.66 (tdd, J = 10.2, 8.0, 5.1 Hz, 1H), 2.47−2.21 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.5, 178.8, 142.8, 137.0, 135.2, 132.4, 131.4, 129.1 (2C), 128.4 (2C), 128.1, 128.0 (2C), 127.1, 126.5 (2C), 122.7, 122.3, 109.1, 60.0, 56.3, 54.2, 43.3, 35.5, 24.4, 21.2 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z calcd for $C_{27}H_{26}NO_2$ $[M + H]^+$, 396.1958; found, 396.1970. R_f = 0.24 (hexane/EtOAc - 6:1).

*(1R,2S,3S)-1′-Benzyl-2′-oxo-2-(p-tolyl)spiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4n**).* Colorless oil. Yield = 58% (23 mg). 98% *ee*. The enantiomeric excess of product **4n** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 9.6 min, t_R = 11.5 min. $[\alpha]_D^{20}$ = +73.9 (c = 1.1, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.64 (d, J = 3.1 Hz, 1H), 7.35−7.28 (m, 1H), 7.22−7.09 (m, 3H), 7.09−6.98 (m, 2H), 6.84 (s, 4H), 6.75 (dq, J = 7.5, 1.0 Hz, 2H), 6.45−6.39 (m, 1H), 5.18−5.04 (m, 1H), 4.50 (d, J = 16.0 Hz, 1H), 3.95 (d, J = 12.2 Hz, 1H), 3.63 (dddd, J = 12.5, 9.7, 7.5, 3.2 Hz, 1H), 2.66−2.54 (m, 1H), 2.54−2.37 (m, 2H), 2.22 (s, 3H), 2.11 (ddd, J = 12.0, 8.0, 4.0 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.5, 178.8, 142.8, 137.0, 135.2, 132.4, 131.4, 129.1 (2C), 128.4 (2C), 128.1, 128.0 (2C), 127.1, 126.5 (2C), 122.7, 122.3, 109.1, 60.0, 56.3, 54.2, 43.3, 35.5, 24.4, 21.2 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{26}NO_2$ $[M + H]^+$, 396.1958; found, 396.1958. R_f = 0.20 (hexane/EtOAc - 6:1).

1′-Benzyl-2-(4-methoxyphenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 46 h). The products were purified by column chromatography (hexane/EtOAc - 7:1) with a adiastereomeric ratio of **3o**/**4o** = 1/1.1 and an overall yield of **3o**/**4o** = 87%.

*(1S,2S,3S)-1′-Benzyl-2-(4-methoxyphenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3o**).* Colorless oil. Yield = 41% (17 mg). 98% *ee*. The enantiomeric excess of product **3o** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 10.3 min, t_R = 12.6 min. $[\alpha]_D^{20}$ = −96.1 (c = 0.8, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.77 (d, J = 2.3 Hz, 1H), 7.45−7.40 (m, 1H), 7.19−7.07 (m, 5H), 6.98−6.92 (m, 2H), 6.69−6.62 (m, 2H), 6.53−6.47 (m, 2H), 6.43−6.36 (m, 1H), 5.14−5.03 (m, 1H), 4.29 (d, J = 16.0 Hz, 1H), 4.22 (dddd, J = 11.8, 9.5, 7.1, 2.2 Hz, 1H), 3.78−3.73 (m. 4H), 2.71−2.56 (m, 1H), 2.46−2.36 (m, 1H), 2.36−2.22 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 202.5, 178.9, 159.1, 142.9, 135.1, 131.5, 129.1 (2C), 128.4 (2C), 128.1, 127.4, 127.1, 126.5 (2C), 122.7, 122.3, 113.7 (2C), 109.1, 60.0, 56.1, 55.0, 54.2, 43.2, 35.3, 24.4 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{26}NO_3$ $[M + H]^+$, 412.1908; found, 412.1906. R_f = 0.46 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-2-(4-methoxyphenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4o**).* Colorless oil. Yield = 46% (19 mg). 98% *ee*. The enantiomeric excess of product **4o** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 205 nm); t_R = 11.7 min, t_R = 13.6 min. $[\alpha]_D^{20}$ = +68.9 (c = 0.8, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.65 (d, J = 3.2 Hz, 1H), 7.37−7.31 (m, 1H), 7.22−7.12 (m, 3H), 7.12−7.00 (m, 2H), 6.90−6.85 (m, 2H), 6.78−6.72 (m, 2H), 6.61−6.56 (m, 2H), 6.48−6.44 (m, 1H), 5.13 (d, J = 16.0 Hz, 1H), 4.52 (d, J = 16.0 Hz, 1H), 3.95 (d, J = 12.4 Hz, 1H), 3.71 (s, 3H), 3.62 (dddd, J = 12.6, 9.7, 7.6, 3.2 Hz, 1H), 2.61 (ddd, J = 12.3, 10.1, 8.4 Hz, 1H), 2.55−2.39 (m, 2H), 2.13 (ddd, J = 12.1, 8.0, 4.1 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.9, 178.5, 159.0, 142.2, 135.1, 131.5, 129.3 (2C), 128.5 (2C), 128.1, 127.3, 127.1, 126.7 (2C), 123.9, 122.3, 113.5 (2C), 109.4, 60.4, 56.3, 55.6, 55.1, 43.7, 35.1, 24.1 ppm. IR (KBr): ν = 1712 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{26}NO_3$ $[M + H]^+$, 412.1908; found, 412.1907. R_f = 0.42 (hexane/EtOAc - 5:1).

1′-Benzyl-2-(4-nitrophenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc -

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3:1 to 2:1) with a diastereomeric ratio of **3p**/**4p** = 1/2.7 and an overall yield of **3p**/**4p** = 83%.

*(1S,2S,3S)-1′-Benzyl-2-(4-nitrophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3p**).* Colorless oil. Yield = 22% (9 mg). 98% *ee*. The enantiomeric excess of product **3p** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 212 nm); t_R = 10.0 min, t_R = 13.1 min. $[\alpha]_D^{20}$ = −122.4 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.83 (d, *J* = 1.8 Hz, 1H), 7.94−7.80 (m, 2H), 7.51−7.41 (m, 1H), 7.22−7.10 (m, 5H), 7.10−7.03 (m, 2H), 6.71−6.62 (m, 2H), 6.60−6.53 (m, 1H), 4.91 (d, *J* = 15.7 Hz, 1H), 4.34 (d, *J* = 15.7 Hz, 1H), 4.31−4.20 (m, 1H), 3.92 (d, *J* = 11.3 Hz, 1H), 2.89−2.75 (m, 1H), 2.52−2.38 (m, 1H), 2.38−2.25 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.2, 178.2, 147.3, 143.4, 142.7, 135.1, 130.4, 128.9 (2C), 128.7, 128.4 (2C), 127.6, 126.8 (2C), 123.3 (2C), 123.1, 122.3, 109.2, 60.0, 55.3, 54.2, 43.4, 35.5, 24.7 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide), 1520 (NO_2), 1348 (NO_2) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}N_2O_4$ $[M + H]^+$, 427.1659; found, 427.1665. R_f = 0.30 (hexane/EtOAc - 2:1).

*(1R,2S,3S)-1′-Benzyl-2-(4-nitrophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4p**).* Yellow solid (crystals suitable for X-ray analysis were grown by the dissolution of **4p** in a minimal amount of boiling heptane/*i*-PrOH mixture, 8/2, *v*/*v*, followed by standing at rt overnight). Yield = 61% (26 mg). mp = 103−105 °C (heptane/*i*-PrOH, 8/2, *v*/*v*). 91% *ee*. The enantiomeric excess of product **4p** was determined by HPLC using a Chiralpak AD column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 210 nm); t_R = 7.3 min, t_R = 9.7 min. $[\alpha]_D^{20}$ = +23.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.68 (d, *J* = 3.0 Hz, 1H), 7.84−7.76 (m, 2H), 7.29 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.25−7.19 (m, 1H), 7.19−6.99 (m, 6H), 6.93−6.85 (m, 2H), 6.60−6.52 (m, 1H), 5.00 (d, *J* = 15.6 Hz, 1H), 4.56 (d, *J* = 15.6 Hz, 1H), 4.08 (d, *J* = 12.1 Hz, 1H), 3.68 (dddd, *J* = 12.4, 9.6, 8.0, 3.0 Hz, 1H), 2.70−2.41 (m, 3H), 2.15 (ddd, *J* = 12.1, 7.9, 4.3 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 200.5, 177.9, 147.1, 143.1, 142.1, 135.1, 130.5, 129.0 (2C), 128.7, 128.6 (2C), 127.8, 127.1 (2C), 123.8, 123.3 (2C), 122.6, 109.5, 60.3, 55.6, 55.2, 43.9, 35.4, 24.6 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide), 1520 (NO_2), 1348 (NO_2) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}N_2O_4$ $[M + H]^+$, 427.1659; found, 427.1663. R_f = 0.26 (hexane/EtOAc - 2:1).

1′-Benzyl-2′-oxo-2-(4-(trifluoromethyl)phenyl)spiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 49 h). The products were purified by column chromatography (hexane/EtOAc - 4:1 to 3:1) with a diastereomeric ratio of **3q**/**4q** = 1/2.6 and an overall yield of **3q**/**4q** = 97%.

*(1S,2S,3S)-1′-Benzyl-2′-oxo-2-(4-(trifluoromethyl)phenyl)spiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3q**).* Yellow oil. Yield = 26% (12 mg). 99% *ee*. The enantiomeric excess of product **3q** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 217 nm); t_R = 9.0 min, t_R = 9.7 min. $[\alpha]_D^{20}$ = −106.3 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.81 (d, *J* = 1.9 Hz, 1H), 7.48−7.43 (m, 1H), 7.41−7.36 (m, 2H), 7.22−7.08 (m, 7H), 6.62−6.56 (m, 2H), 6.50−6.43 (m, 1H), 5.02 (d, *J* = 16.0 Hz, 1H), 4.32 (d, *J* = 15.8 Hz, 1H), 4.30−4.21 (m, 1H), 3.89 (d, *J* = 11.4 Hz, 1H), 2.82−2.70 (m, 1H), 2.47−2.39 (m, 1H), 2.39−2.26 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.6, 178.4, 142.7, 140.0, 135.0, 130.7, 129.7 (q, *J* = 32.6 Hz, 1C) 128.6 (2C), 128.5 (3C, *overlapped*), 127.4, 126.4 (2C), 125.2 (q, *J* = 3.8 Hz, 2C), 124.0 (q, *J* = 272.2 Hz, 1C) 122.9, 122.3, 109.3, 60.0, 55.5, 54.3, 43.4, 35.8, 24.5 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −62.34 (3F) ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide), 1325 (C—CF_3), 1169, 1122 (CF_3), 752 (CF_3) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{28}H_{27}F_3NO_3$ $[M + MeOH + H]^+$, 482.1938; found, 482.1938. R_f = 0.54 (hexane/EtOAc - 2:1).

*(1R,2S,3S)-1′-Benzyl-2′-oxo-2-(4-(trifluoromethyl)phenyl)spiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4q**).* Colorless oil. Yield = 71% (32 mg). 98% *ee*. The enantiomeric excess of product **4q** was determined by HPLC using a Chiralpak IC column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 9.0 min, t_R = 10.0 min. $[\alpha]_D^{20}$ = +45.5 (*c* = 1.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.68 (d, *J* = 3.1 Hz, 1H), 7.36−7.31 (m, 1H), 7.31−7.29 (m, 1H), 7.27 (s, 1H), 7.25−7.02 (m, 7H), 6.84−6.78 (m, 2H), 6.51 (dd, *J* = 8.0, 1.0 Hz, 1H), 5.11 (d, *J* = 15.8 Hz, 1H), 4.53 (d, *J* = 15.8 Hz, 1H), 4.07 (d, *J* = 12.1 Hz, 1H), 3.70 (dtd, *J* = 12.0, 8.9, 3.1 Hz, 1H), 2.70−2.59 (m, 1H), 2.59−2.46 (m, 2H), 2.16 (ddd, *J* = 12.1, 7.1, 4.9 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 200.9, 178.1, 142.1, 139.5, 135.0, 130.8, 129.7 (q, *J* = 32.5 Hz, 1C), 128.6 (4C, *overlapped*), 128.5, 127.5, 126.7 (2C), 125.0 (q, *J* = 3.8 Hz, 2C), 123.9 (q, *J* = 272.1 Hz, 1C), 123.9, 122.5, 109.5, 60.3, 55.9, 55.3, 43.8, 35.5, 24.3 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −62.53 (3F) ppm. IR (KBr): ν = 1722 (C═O, aldehyde, amide), 1327 (C—CF_3), 1275, 1186, 1167 (CF_3), 1117 (CF_3), 752 (CF_3) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{23}F_3NO_2$ $[M + H]^+$, 450.1675; found, 450.1673. R_f = 0.42 (hexane/EtOAc - 2:1).

1′-Benzyl-2-(4-fluorophenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 5:1 to 4:1) with a the diastereomeric ratio of **3r**/**4r** = 1/1.1 and an overall yield of **3r**/**4r** = 75%.

*(1S,2S,3S)-1′-Benzyl-2-(4-fluorophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3r**).* Yellow oil. Yield = 35% (14 mg). 99% *ee*. The enantiomeric excess of product **3r** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 218 nm); t_R = 9.3 min, t_R = 13.9 min. $[\alpha]_D^{20}$ = −70.5 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.2 Hz, 1H), 7.46−7.40 (m, 1H), 7.23−7.10 (m, 5H), 7.03−6.94 (m, 2H), 6.85−6.75 (m, 2H), 6.57−6.51 (m, 2H), 6.50−6.41 (m, 1H), 5.02 (d, *J* = 15.9 Hz, 1H), 4.31 (d, *J* = 15.9 Hz, 1H), 4.21 (dddd, *J* = 11.8, 9.7, 7.2, 2.1 Hz, 1H), 3.80 (d, *J* = 11.6 Hz, 1H), 2.78−2.61 (m, 1H), 2.47−2.38 (m, 1H), 2.37−2.24 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 202.0, 178.6, 162.3 (d, *J* = 245.8 Hz, 1C), 142.8, 135.1, 131.3 (d, *J* = 3.3 Hz, 1C), 131.1, 129.7 (d, *J* = 8.1 Hz, 2C), 128.5, 128.3 (2C), 127.3, 126.5 (2C), 122.8, 122.3, 115.2 (d, *J* = 21.2 Hz, 2C), 109.1, 60.0, 55.6, 54.2, 43.3, 35.3, 24.5 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −114.92 (tt, *J* = 8.6, 5.3 Hz) ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide), 1510 (C—F) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{27}FNO_3$ $[M + MeOH + H]^+$, 432.1970; found, 432.1963. R_f = 0.32 (hexane/EtOAc - 4:1).

*(1R,2S,3S)-1′-Benzyl-2-(4-fluorophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4r**).* Yellow oil. Yield = 40% (16 mg). 97% *ee*. The enantiomeric excess of product **4r** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 10.4 min, t_R = 13.5 min. $[\alpha]_D^{20}$ = +76.0 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.67 (d, *J* = 3.2 Hz, 1H), 7.35−7.30 (m, 1H), 7.25−7.16 (m, 3H), 7.11 (td, *J* = 7.7, 1.4 Hz, 1H), 7.05 (td, *J* = 7.5, 1.2 Hz, 1H), 6.96−6.88 (m, 2H), 6.79 (ddd, *J* = 6.2, 2.0, 1.1 Hz, 2H), 6.77−6.67 (m, 2H), 6.52−6.46 (m, 1H), 5.09 (d, *J* = 15.8 Hz, 1H), 4.54 (d, *J* = 16.0 Hz, 1H), 3.98 (d, *J* = 12.3 Hz, 1H), 3.68−3.52 (m, 1H), 2.68−2.57 (m, 1H), 2.57−2.44 (m, 2H), 2.23−2.05 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.4, 178.3, 162.2 (d, *J* = 246.3 Hz, 1C), 142.2, 135.1, 131.1, 131.0 (d, *J* = 3.2 Hz, 1C), 129.8 (d, *J* = 8.1 Hz, 2C), 128.6 (2C), 128.3, 127.4, 126.7 (2C), 123.9, 122.4, 115.0 (d, *J* = 21.3 Hz, 2C), 109.4, 60.3, 55.9, 55.5, 43.7, 35.1, 24.2 ppm. ^{19}F NMR (376 MHz, chloroform-*d*): δ −114.77 (tt, *J* = 8.6, 5.3 Hz, 1F) ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide), 1510 (C—F) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{27}FNO_3$ $[M + MeOH + Na]^+$, 454.1789; found, 454.1790. R_f = 0.28 (hexane/EtOAc - 4:1).

1′-Benzyl-2-(4-chlorophenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 5:1 to 4:1) with a diastereomeric ratio of **3s**/**4s** = 1/2.1 and an overall yield of **3s**/**4s** = 98%.

*(1S,2S,3S)-1′-Benzyl-2-(4-chlorophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3s**).* Colorless oil.

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Yield = 36% (15 mg). 98% *ee*. The enantiomeric excess of product **3s** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 10.2 min, t_R = 14.3 min. $[\alpha]_D^{20}$ = −131.6 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.1 Hz, 1H), 7.46−7.39 (m, 1H), 7.22−7.16 (m, 3H), 7.16−7.06 (m, 4H), 7.00−6.92 (m, 2H), 6.60−6.50 (m, 2H), 6.50−6.40 (m, 1H), 5.06 (d, *J* = 15.8 Hz, 1H), 4.29 (d, *J* = 15.9 Hz, 1H), 4.22 (dddt, *J* = 11.8, 9.6, 7.3, 2.0 Hz, 1H), 3.80 (d, *J* = 11.6 Hz, 1H), 2.79−2.65 (m, 1H), 2.49−2.38 (m, 1H), 2.38−2.23 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.9, 178.5, 142.8, 135.0, 134.1, 133.5, 130.9, 129.5 (2C), 128.6 (2C), 128.5 (2C), 128.4, 127.3, 126.4 (2C), 122.8, 122.3, 109.2, 60.0, 55.6, 54.1, 43.4, 35.4, 24.5 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{27}ClNO_3$ [M + MeOH + H]$^+$, 448.1674; found, 448.1674. R_f = 0.22 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-2-(4-chlorophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4s**).* Yellow oil. Yield = 62% (26 mg). 99% *ee*. The enantiomeric excess of product **4s** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 11.1 min, t_R = 12.4 min. $[\alpha]_D^{20}$ = +61.5 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.67 (d, *J* = 3.2 Hz, 1H), 7.37−7.30 (m, 1H), 7.26−7.16 (m, 3H), 7.11 (td, *J* = 7.7, 1.4 Hz, 1H), 7.06 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.04−6.99 (m, 2H), 6.95−6.85 (m, 2H), 6.81−6.73 (m, 2H), 6.54−6.47 (m, 1H), 5.12 (dd, *J* = 15.9, 1.0 Hz, 1H), 4.52 (d, *J* = 16.0 Hz, 1H), 3.96 (d, *J* = 12.3 Hz, 1H), 3.62 (dtd, *J* = 12.1, 8.8, 3.1 Hz, 1H), 2.69−2.57 (m, 1H), 2.57−2.42 (m, 2H), 2.14 (ddd, *J* = 12.2, 7.0, 5.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.2, 178.2, 142.2, 135.0, 133.8, 133.4, 131.0, 129.6 (4C, *overlapped*), 128.4 (3C, *overlapped*), 127.4, 126.6 (2C), 123.8, 122.5, 109.5, 60.3, 56.0, 55.4, 43.7, 35.2, 24.2 ppm. IR (KBr): ν = 1712 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}ClNO_2$ [M + H]$^+$, 416.1412; found, 446.1412. R_f = 0.16 (hexane/EtOAc - 5:1).

1′-Benzyl-2-(4-bromophenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 5:1 to 4:1) with a diastereomeric ratio of **3t**/**4t** = 1/2.1 and an overall yield of **3t**/**4t** = 98%.

*(1S,2S,3S)-1′-Benzyl-2-(4-bromophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3t**).* Colorless oil. Yield = 36% (17 mg). 99% *ee*. The enantiomeric excess of product **3t** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 11.0 min, t_R = 14.3 min. $[\alpha]_D^{20}$ = −129.1 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.79 (d, *J* = 2.1 Hz, 1H), 7.46−7.39 (m, 1H), 7.27−7.18 (m, 5H), 7.13 (dd, *J* = 5.6, 3.2 Hz, 2H), 6.95−6.84 (m, 2H), 6.58−6.49 (m, 2H), 6.48−6.42 (m, 1H), 5.07 (d, *J* = 15.7 Hz, 1H), 4.29 (d, *J* = 15.9 Hz, 1H), 4.26−4.12 (m, 1H), 3.78 (d, *J* = 11.5 Hz, 1H), 2.76−2.65 (m, 1H), 2.47−2.38 (m, 1H), 2.38−2.23 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.9, 178.5, 142.8, 135.0, 134.7, 131.5 (2C), 130.9, 129.8, (2C) 128.6 (2C), 128.4, 127.3, 126.4 (2C), 122.8, 122.3, 121.6, 109.2, 59.9, 55.6, 54.1, 43.4, 35.5, 24.5 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{27}BrNO_3$ [M + MeOH + H]$^+$, 492.1169; found, 492.1166. R_f = 0.30 (hexane/EtOAc - 5:1).

*(1R,2S,3S)-1′-Benzyl-2-(4-bromophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4t**).* Yellow oil. Yield = 62% (29 mg). 99% *ee*. The enantiomeric excess of product **4t** was determined by HPLC using a Chiralpak IB column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 207 nm); t_R = 8.3 min, t_R = 9.7 min. $[\alpha]_D^{20}$ = +54.3 (*c* = 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.66 (d, *J* = 3.1 Hz, 1H), 7.33 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.22 (dd, *J* = 5.2, 2.0 Hz, 3H), 7.20−7.14 (m, 2H), 7.12 (td, *J* = 7.7, 1.4 Hz, 1H), 7.05 (td, *J* = 7.5, 1.2 Hz, 1H), 6.88−6.80 (m, 2H), 6.80−6.73 (m, 2H), 6.50 (dd, *J* = 7.5, 1.1 Hz, 1H), 5.22−5.02 (m, 1H), 4.51 (d, *J* = 16.0 Hz, 1H), 3.95 (d, *J* = 12.2 Hz, 1H), 3.62 (dtd, *J* = 12.1, 8.8, 3.1 Hz, 1H), 2.67−2.56 (m, 1H), 2.56−2.43 (m, 2H), 2.14 (ddd, *J* = 12.1, 6.9, 5.4 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.2, 178.1, 142.2, 135.0, 134.3, 131.3 (2C), 131.0, 129.9 (2C), 128.6 (3C, *overlapped*), 128.4, 127.4, 126.6 (2C), 123.9, 122.5, 121.6, 109.5, 60.3, 56.0, 55.3, 43.7, 35.2, 24.2 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}BrNO_2$ [M + H]$^+$, 460.0907; found, 490.0905. R_f = 0.24 (hexane/EtOAc - 5:1).

1′-Benzyl-2-(3-bromophenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 4:1) with a diastereomeric ratio of **3u**/**4u** = 1/2.3 and an overall yield of **3u**/**4u** = 97%.

*(1S,2S,3S)-1′-Benzyl-2-(3-bromophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3u**).* Colorless oil. Yield = 26% (12 mg). 95% *ee*. The enantiomeric excess of product **3u** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 214 nm); t_R = 8.5 min, t_R = 20.7 min. $[\alpha]_D^{20}$ = −91.0 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.81 (d, *J* = 1.9 Hz, 1H), 7.46−7.39 (m, 1H), 7.39−7.30 (m, 1H), 7.21−7.10 (m, 6H), 7.02−6.92 (m, 2H), 6.67−6.58 (m, 2H), 6.51−6.43 (m, 1H), 5.07−4.95 (m, 1H), 4.33 (d, *J* = 15.9 Hz, 1H), 4.22 (dddd, *J* = 10.0, 9.1, 5.8, 2.0 Hz, 1H), 3.78 (d, *J* = 11.5 Hz, 1H), 2.82−2.63 (m, 1H), 2.46−2.37 (m, 1H), 2.37−2.18 (m, 2H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.8, 178.5, 142.8, 138.1, 135.2, 131.0, 130.8, 130.7, 129.8, 128.6 (2C), 128.4, 127.3, 126.8, 126.5 (2C), 122.9, 122.4, 122.2, 109.2, 60.0, 55.6, 54.1, 43.4, 35.5, 24.4 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{27}BrNO_3$ [M + MeOH + H]$^+$, 492.1169; found, 492.1163. R_f = 0.22 (hexane/EtOAc - 4:1).

*(1R,2S,3S)-1′-Benzyl-2-(3-bromophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4u**).* Colorless oil. Yield = 71% (33 mg). 99% *ee*. The enantiomeric excess of product **4u** was determined by HPLC using a Chiralpak IC column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 26.4 min, t_R = 31.7 min. $[\alpha]_D^{20}$ = +71.6 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.69 (d, *J* = 3.0 Hz, 1H), 7.34−7.29 (m, 1H), 7.28−7.24 (m, 1H), 7.24−7.19 (m, 3H), 7.17 (q, *J* = 1.3 Hz, 1H), 7.14−7.00 (m, 2H), 6.94−6.78 (m, 4H), 6.53−6.45 (m, 1H), 5.10 (d, *J* = 15.9 Hz, 1H), 4.57 (d, *J* = 15.9 Hz, 1H), 3.98 (d, *J* = 12.1 Hz, 1H), 3.64 (dtd, *J* = 11.9, 8.7, 3.0 Hz, 1H), 2.67−2.57 (m, 1H), 2.57−2.46 (m, 2H), 2.15 (ddd, *J* = 12.2, 6.9, 5.5 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.1, 178.3, 142.2, 137.9, 135.1, 131.4, 130.9, 130.7, 129.6, 128.7 (2C), 128.4, 127.4, 126.8, 126.7 (2C), 123.9, 122.5, 122.3, 109.5, 60.3, 55.9, 55.4, 43.9, 35.4, 24.4 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}BrNO_2$ [M + H]$^+$, 460.0907; found, 460.0900. R_f = 0.18 (hexane/EtOAc - 4:1).

1′-Benzyl-2-(2-bromophenyl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 49 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3v**/**4v** = 1/1.5 and an overall yield of **3v**/**4v** = 88%.

*(1S,2R,3S)-1′-Benzyl-2-(2-bromophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3v**).* White solid (crystals suitable for X-ray analysis were grown by the dissolution of **3v** in a minimal amount of boiling heptane/*i*-PrOH mixture, 8/2, *v*/*v*, followed by standing at rt overnight). Yield = 35% (16 mg). mp = 151−152 °C (heptane/*i*-PrOH, 8/2, *v*/*v*). 99% *ee*. The enantiomeric excess of product **3v** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 213 nm); t_R = 8.8 min, t_R = 18.0 min. $[\alpha]_D^{20}$ = −22.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 9.74 (d, *J* = 2.2 Hz, 1H), 7.70 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.62−7.49 (m, 1H), 7.38 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.24−6.99 (m, 7H), 6.79−6.73 (m, 2H), 6.49−6.43 (m, 1H), 5.06 (d, *J* = 15.8 Hz, 1H), 4.64 (d, *J* = 11.4 Hz, 1H), 4.46 (d, *J* = 15.9 Hz, 1H), 4.01 (dddd, *J* = 11.9, 9.5, 6.7, 2.2 Hz, 1H), 2.81−2.62 (m, 1H), 2.48−2.25 (m, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 201.7, 178.8, 142.5, 135.9, 135.3, 133.1, 129.0,

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129.8, 128.8, 128.6 (2C), 128.2, 127.7, 127.2, 126.7 (2C), 125.8, 124.3, 122.4, 108.8, 60.0, 57.4, 53.0, 43.4, 36.6, 24.7 ppm. IR (KBr): ν = 1724 (C═O, aldehyde), 1709 (C═O, amide), 746 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{27}H_{27}BrNO_3$ $[M + MeOH + H]^+$, 492.1169; found, 492.1166. R_f = 0.24 (hexane/EtOAc - 5:1).

*(1R,2R,3S)-1′-Benzyl-2-(2-bromophenyl)-2′-oxospiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4v**).* Yellow oil. Yield = 53% (24 mg). 99% *ee*. The enantiomeric excess of product **4v** was determined by HPLC using a Chiralpak IC column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 204 nm); t_R = 36.5 min, t_R = 40.8 min. $[\alpha]_D^{20}$ = +20.3 (c = 0.7, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.80 (d, J = 2.4 Hz, 1H), 7.42 (dd, J = 7.9, 1.3 Hz, 1H), 7.28−7.20 (m, 3H), 7.19−6.99 (m, 7H), 6.83 (td, J = 7.6, 1.0 Hz, 1H), 6.64−6.53 (m, 2H), 5.04 (d, J = 15.7 Hz, 1H), 4.70 (d, J = 15.7 Hz, 1H), 4.65 (d, J = 8.7 Hz, 1H), 3.47 (qd, J = 8.5, 2.4 Hz, 1H), 2.81−2.68 (m, 1H), 2.53−2.41 (m, 2H), 2.28−2.13 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.9, 179.6, 142.8, 137.3, 135.5, 133.0, 130.1, 128.9, 128.7, 128.6 (2C), 128.1, 127.4, 127.1 (2C), 127.0, 126.7, 124.1, 122.0, 109.0, 58.3, 57.9, 52.9, 43.7, 36.5, 25.3 ppm. IR (KBr): ν = 1716 (C═O, aldehyde, amide), 754 (C—Br) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{26}H_{23}BrNO_2$ $[M + H]^+$, 460.0907; found, 460.0904. R_f = 0.20 (hexane/EtOAc - 5:1).

1′-Benzyl-2-(furan-2-yl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 7:1) with a diastereomeric ratio of **3w**/**4w** = 1/1.4 and an overall yield of **3w**/**4w** = 95%.

*(1S,2R,3S)-1′-Benzyl-2-(furan-2-yl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3w**).* Green oil. Yield = 39% (15 mg). 95% *ee*. The enantiomeric excess of product **3w** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 217 nm); t_R = 13.0 min, t_R = 18.4 min. $[\alpha]_D^{20}$ = −50.0 (c = 0.6, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.88 (d, J = 1.8 Hz, 1H), 7.40−7.34 (m, 1H), 7.24 (dd, J = 4.9, 1.9 Hz, 3H), 7.16 (td, J = 7.7, 1.4 Hz, 1H), 7.14−7.07 (m, 2H), 6.97−6.90 (m, 2H), 6.62−6.56 (m, 1H), 6.18 (dd, J = 3.3, 1.8 Hz, 1H), 5.93 (dt, J = 3.3, 0.8 Hz, 1H), 5.07 (dd, J = 15.8, 1.0 Hz, 1H), 4.51 (d, J = 15.8 Hz, 1H), 4.20−4.09 (m, 1H), 3.96 (dd, J = 11.3, 0.7 Hz, 1H), 2.82−2.62 (m, 1H), 2.38−2.17 (m, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.8, 178.5, 151.0, 142.8, 141.8, 135.5, 130.9, 128.6 (2C), 128.2, 127.3, 127.0 (2C), 122.8, 122.2, 110.2, 109.0, 107.1, 58.6, 53.9, 49.0, 43.4, 35.9, 24.0 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{24}H_{22}NO_3$ $[M + H]^+$, 372.1594; found, 372.1590. R_f = 0.28 (hexane/EtOAc - 6:1).

*(1R,2R,3S)-1′-Benzyl-2-(furan-2-yl)-2′-oxospiro[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4w**).* Pink oil. Yield = 56% (21 mg). 98% *ee*. The enantiomeric excess of product **4w** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 14.6 min, t_R = 15.7 min. $[\alpha]_D^{20}$ = +62.5 (c = 1.1, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.78 (d, J = 2.8 Hz, 1H), 7.35−7.29 (m, 2H), 7.28−7.20 (m, 3H), 7.13−7.04 (m, 2H), 7.00 (dd, J = 1.9, 0.8 Hz, 1H), 6.93 (td, J = 7.6, 1.1 Hz, 1H), 6.64 (dt, J = 7.8, 0.8 Hz, 1H), 6.06 (dd, J = 3.3, 1.9 Hz, 1H), 5.86 (dt, J = 3.3, 0.9 Hz, 1H), 5.14 (d, J = 15.7 Hz, 1H), 4.75 (d, J = 15.7 Hz, 1H), 4.15 (dd, J = 10.9, 0.8 Hz, 1H), 3.62−3.52 (m, 1H), 2.57−2.37 (m, 3H), 2.18−2.08 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.2, 178.9, 151.3, 142.2, 141.7, 135.6, 131.2, 128.7 (2C), 128.0, 127.5, 127.3 (2C), 123.8, 122.3, 109.9, 109.0, 107.1, 58.6, 55.2, 48.8, 43.9, 36.5, 24.9 ppm. IR (KBr): ν = 1711 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{24}H_{22}NO_3$ $[M + H]^+$, 372.1594; found, 372.1598. R_f = 0.22 (hexane/EtOAc - 6:1).

1′-Benzyl-2′-oxo-2-(thiophen-2-yl)spiro[cyclopentane-1,3′-indoline]-3-carbaldehyde. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **3x**/**4x** = 1/1.3 and an overall yield of **3x**/**4x** = 98%.

*(1S,2R,3S)-1′-Benzyl-2′-oxo-2-(thiophen-2-yl)spiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**3x**).* White amorphous solid. Yield = 42% (16 mg). 98% *ee*. The enantiomeric excess of product **3x** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 213 nm); t_R = 13.4 min, t_R = 25.4 min. $[\alpha]_D^{20}$ = −72.6 (c = 0.5, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.87 (d, J = 2.1 Hz, 1H), 7.44−7.37 (m, 1H), 7.22−7.11 (m, 5H), 7.04 (dd, J = 5.1, 1.2 Hz, 1H), 6.85 (dd, J = 5.1, 3.5 Hz, 1H), 6.76 (dt, J = 3.6, 1.0 Hz, 1H), 6.69−6.64 (m, 2H), 6.53−6.48 (m, 1H), 5.06 (d, J = 15.9 Hz, 1H), 4.39 (d, J = 15.9 Hz, 1H), 4.30−4.18 (m, 1H), 4.07 (dd, J = 11.5, 0.8 Hz, 1H), 2.78−2.65 (m, 1H), 2.46−2.23 (m, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.8, 178.4, 143.3, 138.5, 135.3, 130.6, 128.6 (2C), 128.5, 127.2, 126.7, 126.6 (2C), 125.2, 124.2, 122.8, 122.3, 109.1, 60.0, 55.5, 51.3, 43.4, 35.2, 24.0 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{24}H_{22}NO_2S$ $[M + H]^+$, 388.1366; found, 388.1368. R_f = 0.42 (hexane/EtOAc - 4:1).

*(1R,2R,3S)-1′-Benzyl-2′-oxo-2-(thiophen-2-yl)spiro-[cyclopentane-1,3′-indoline]-3-carbaldehyde (**4x**).* Colorless oil. Yield = 56% (22 mg). 99% *ee*. The enantiomeric excess of product **4x** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 207 nm); t_R = 14.4 min, t_R = 16.6 min. $[\alpha]_D^{20}$ = +56.7 (c = 0.9, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.73 (d, J = 2.8 Hz, 1H), 7.34 (dd, J = 7.4, 1.2 Hz, 1H), 7.24−7.12 (m, 4H), 7.07 (td, J = 7.6, 1.1 Hz, 1H), 7.00 (dd, J = 5.1, 1.2 Hz, 1H), 6.89−6.82 (m, 2H), 6.77 (dd, J = 5.1, 3.5 Hz, 1H), 6.75−6.71 (m, 1H), 6.59−6.50 (m, 1H), 5.18−5.08 (m, 1H), 4.62 (d, J = 15.9 Hz, 1H), 4.32 (d, J = 11.9 Hz, 1H), 3.53 (dddd, J = 12.2, 10.1, 7.6, 2.9 Hz, 1H), 2.66−2.39 (m, 3H), 2.22−2.08 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.1, 178.0, 142.6, 138.6, 135.1, 131.2, 128.6 (2C), 128.5, 127.3, 126.7 (2C), 126.5, 126.2, 125.0, 124.1, 122.5, 109.4, 60.2, 57.8, 52.2, 43.8, 35.1, 24.1 ppm. IR (KBr): ν = 1712 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{24}H_{22}NO_2S$ $[M + H]^+$, 388.1366; found, 388.1362. R_f = 0.36 (hexane/EtOAc - 4:1).

Ethyl 1′-Benzyl-3-formyl-2′-oxospiro[cyclopentane-1,3′-indoline]-2-carboxylate. The title compounds were synthesized according to the general procedure (GP4, reaction time: 15 h). The products were purified by column chromatography (hexane/EtOAc - 3:1) with a diastereomeric ratio of **3y**/**4y** = 1/1.3 and an overall yield of **3y**/**4y** = 65%.

*Ethyl 1′-Benzyl-3-formyl-2′-oxospiro[cyclopentane-1,3′-indoline]-2-carboxylate (**3y**).* Yellow oil. Yield = 29% (11 mg). 71% *ee*. The enantiomeric excess of product **3y** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 214 nm); t_R = 14.4 min, t_R = 15.5 min. $[\alpha]_D^{20}$ = −24.1 (c = 0.4, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.97 (d, J = 1.1 Hz, 1H), 7.40−7.29 (m, 6H), 7.19 (td, J = 7.7, 1.3 Hz, 1H), 7.07 (td, J = 7.5, 1.0 Hz, 1H), 6.74 (dt, J = 7.8, 0.8 Hz, 1H), 4.98 (d, J = 15.6 Hz, 1H), 4.86 (d, J = 15.7 Hz, 1H), 4.02−3.88 (m, 3H), 3.85 (d, J = 8.5 Hz, 1H), 2.79−2.65 (m, 1H), 2.23−2.09 (m, 2H), 1.99 (ddd, J = 14.3, 10.2, 8.9 Hz, 1H), 0.98 (t, J = 7.1 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.2, 179.2, 170.5, 142.8, 136.0, 131.9, 128.7 (2C), 128.2, 127.6, 127.4 (2C), 122.7, 121.9, 109.0, 61.1, 56.1, 53.2, 52.0, 43.7, 37.7, 24.6, 13.8 ppm. IR (KBr): ν = 1732 (C═O, ester, aldehyde, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{23}H_{23}NNaO_4$ $[M + Na]^+$, 400.1519; found, 400.1516. R_f = 0.20 (hexane/EtOAc - 3:1).

*Ethyl (1R,2R,3S)-1′-Benzyl-3-formyl-2′-oxospiro[cyclopentane-1,3′-indoline]-2-carboxylate (**4y**).* Brown oil. Yield = 36% (14 mg). 86% *ee*. The enantiomeric excess of product **4y** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 207 nm); t_R = 11.4 min, t_R = 13.7 min. $[\alpha]_D^{20}$ = +12.0 (c = 0.4, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.89 (d, J = 1.1 Hz, 1H), 7.41−7.29 (m, 5H), 7.22−7.12 (m, 2H), 6.99 (td, J = 7.5, 1.0 Hz, 1H), 6.77 (dt, J = 7.8, 0.8 Hz, 1H), 5.09 (d, J = 15.5 Hz, 1H), 4.84 (d, J = 15.5 Hz, 1H), 3.92 (d, J = 9.4 Hz, 1H), 3.82−3.71 (m, 2H), 3.63−3.49 (m, 1H), 2.47−2.27 (m, 3H), 1.98 (ddd, J = 12.2, 6.4, 4.6 Hz, 1H), 0.47 (t, J = 7.1 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR

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(101 MHz, chloroform-*d*): δ 200.3, 178.8, 170.2, 142.6, 135.8, 131.4, 128.7 (2C), 128.4, 127.7, 127.6 (2C), 123.1, 122.6, 109.0, 60.8, 56.4, 53.3, 52.5, 44.2, 37.9, 25.2, 13.2 ppm. IR (KBr): ν = 1722 (C═O, ester, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{23}H_{24}NO_4$ $[M + H]^+$, 378.1700; found, 378.1697. R_f = 0.16 (hexane/EtOAc - 3:1).

*Methyl (E)-3-(1′-Benzyl-2′-oxo-2-phenylspiro[cyclopropane-1,3′-indolin]-3-yl)acrylate (**5**).* The catalyst **C2** (7.4 mg, 0.02 mmol, 0.2 equiv) was added to a solution of *trans*-cinnamaldehyde (**2a**) (13.2 mg, 0.1 mmol, 1.0 equiv) in DCM (0.5 mL). The mixture was stirred for 10 min at room temperature. Then, 2,4,6-collidine (20.0 μL, 0.15 mmol, 1.5 equiv) and 1-benzyl-3-chloroindolin-2-one (**1m**) (27.1 mg, 0.105 mmol, 1.05 equiv) were added. The reaction was stirred for 15 h (TLC and ^1H NMR control of conversion and diastereomeric ratio). After complete conversion of aldehyde **2a**, methyl (triphenylphosphoranylidene)acetate (133.6 mg, 0.4 mmol, 4.0 equiv) was added and the reaction was stirred at room temperature overnight (TLC control); the reaction was quenched by hydrochloric acid (1 M, 1 × 1 mL). The organic phase was separated, and the solvents evaporated. The crude product was purified by column chromatography (hexane/EtOAc - 5:1), Dr = 1/5.1 (determined for carbaldehyde). Yellow amorphous solid. Yield = 67% (27 mg, over two steps). 96% *ee*. The enantiomeric excess of product **5** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 10.1 min, t_R = 11.9 min. $[\alpha]_D^{20}$ = −160.0 (*c* = 0.6, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 7.41−7.29 (m, 7H), 7.27−7.15 (m, 6H), 7.10 (td, *J* = 7.6, 1.0 Hz, 1H), 6.88−6.82 (m, 1H), 6.26 (dd, *J* = 15.5, 0.7 Hz, 1H), 4.90 (q, *J* = 15.7 Hz, 2H), 3.77 (s, 3H), 3.53−3.40 (m, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 172.4, 166.2, 143.4, 143.0, 136.0, 133.5, 129.1 (2C), 128.7 (2C), 128.2 (2C), 127.7, 127.6, 127.4 (3C, *overlapped*), 126.7, 124.1, 122.2, 120.9, 109.3, 51.7, 44.1, 43.3, 40.5, 38.3 ppm. IR (KBr): ν = 1716 (C═O, ester, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{24}NO_3$ $[M + H]^+$, 410.1751; found, 410.1753. R_f = 0.50 (hexane/EtOAc - 3:1).

3-(1-Benzyl-3-(3-bromopropyl)-2-oxoindolin-3-yl)-3-phenylpropanal. The title compounds were synthesized according to the general procedure (GP4, reaction time: 120 h). The products were purified by column chromatography (hexane/EtOAc - 6:1) with a diastereomeric ratio of **6**/**7** = 1/2.2 and an overall yield of **6**/**7** = 65%.

*3-(1-Benzyl-3-(3-bromopropyl)-2-oxoindolin-3-yl)-3-phenylpropanal (**6**).* Yellow oil. Yield = 29% (14 mg). 60% *ee*. The enantiomeric excess of product **6** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 206 nm); t_R = 12.9 min, t_R = 18.8 min. $[\alpha]_D^{20}$ = −3.4 (*c* = 0.4, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.54 (dd, *J* = 2.4, 1.3 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 4H), 7.21−7.12 (m, 6H), 7.10−7.01 (m, 4H), 6.63 (d, *J* = 7.8 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 4.74 (d, *J* = 15.6 Hz, 1H), 3.85 (dd, *J* = 9.8, 5.4 Hz, 1H), 3.30−3.15 (m, 2H), 3.01−2.82 (m, 2H), 2.21 (ddd, *J* = 13.0, 11.7, 4.5 Hz, 1H), 1.89 (ddd, *J* = 13.0, 12.1, 4.3 Hz, 1H), 1.58−1.47 (m, 1H), 1.21 (dqd, *J* = 18.5, 7.2, 3.6 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 200.9, 178.6, 143.0, 137.9, 135.5, 129.5 (2C), 129.3, 128.8 (2C), 128.3, 128.0 (2C), 127.7, 127.4 (3C, *overlapped*), 124.4, 122.5, 109.1, 55.2, 46.3, 43.9, 43.5, 34.9, 32.9, 27.9 ppm. IR (KBr): ν = 1705 (C═O, aldehyde, amide), 702 (C—Br) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{28}H_{30}BrNNaO_3$ $[M + Na]^+$, 530.1301; found, 530.1301. R_f = 0.34 (hexane/EtOAc - 5:1).

*3-(1-Benzyl-3-(3-bromopropyl)-2-oxoindolin-3-yl)-3-phenylpropanal (**7**).* White amorphous solid. Yield = 36% (17 mg). 55% *ee*. The enantiomeric excess of product **7** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 204 nm); t_R = 15.3 min, t_R = 31.6 min. $[\alpha]_D^{20}$ = +30.6 (*c* = 0.4, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.54 (dd, *J* = 2.3, 1.6 Hz, 1H), 7.33 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.24−7.05 (m, 8H), 6.90−6.82 (m, 2H), 6.68 (dd, *J* = 7.6, 1.9 Hz, 2H), 6.49 (dd, *J* = 7.6, 1.1 Hz, 1H), 4.74 (d, *J* = 15.8 Hz, 1H), 4.48 (d, *J* = 15.8 Hz, 1H), 3.84 (dd, *J* = 10.1, 5.4 Hz, 1H), 3.34−3.22 (m, 2H), 3.20−3.03 (m, 2H), 2.27−2.07 (m, 2H), 1.71−1.61 (m, 1H), 1.40−1.26 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 200.6, 177.9, 143.5, 137.9, 135.2, 129.1 (3C, *overlapped*), 129.1, 128.7, 128.6, 128.1 (2C), 127.5, 127.3, 126.7 (2C), 123.8, 122.6, 109.5, 55.9, 46.7, 44.3, 43.6, 34.3, 33.2, 27.7 ppm. IR (KBr): ν = 1707 (C═O, aldehyde, amide), 698 (C—Br) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{28}H_{30}BrNNaO_3$ $[M + Na]^+$, 530.1301; found, 530.1300. R_f = 0.26 (hexane/EtOAc - 5:1).

3-(1-Benzyl-3-(4-bromobutyl)-2-oxoindolin-3-yl)-3-phenylpropanal. The title compounds were synthesized according to the general procedure (GP4, reaction time: 49 h). The products were purified by column chromatography (hexane/EtOAc - 7:1) with a diastereomeric ratio of **8**/**9** = 1/1.4 and an overall yield of **8**/**9** = 98%.

*3-(1-Benzyl-3-(4-bromobutyl)-2-oxoindolin-3-yl)-3-phenylpropanal (**8**).* Yellow oil. Yield = 38% (19 mg). 93% *ee*. The enantiomeric excess of product **8** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 209 nm); t_R = 12.8 min, t_R = 20.5 min. $[\alpha]_D^{20}$ = +13.2 (*c* = 0.8, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.54 (dd, *J* = 2.3, 1.4 Hz, 1H), 7.35−7.29 (m, 1H), 7.28−7.24 (m, 1H), 7.23−7.11 (m, 6H), 7.11−7.05 (m, 2H), 7.05−6.99 (m, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.71 (d, *J* = 15.6 Hz, 1H), 3.84 (dd, *J* = 9.2, 5.9 Hz, 1H), 3.31−3.11 (m, 2H), 3.01−2.79 (m, 2H), 2.11 (ddd, *J* = 13.0, 12.0, 4.6 Hz, 1H), 1.89−1.63 (m, 3H), 1.11 (dddd, *J* = 17.7, 9.8, 7.6, 4.5 Hz, 1H), 0.90−0.73 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 201.0, 178.9, 143.1, 138.1, 135.6, 129.6, 129.5 (2C), 128.8 (2C), 128.2, 128.0 (2C), 127.6, 127.4 (2C), 127.3, 124.3, 122.3, 55.6, 46.3, 43.9, 43.6, 35.4, 33.0, 32.6, 23.3 ppm. IR (KBr): ν = 1706 (C═O, aldehyde, amide), 695 (C—Br) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{28}H_{29}BrNO_2$ $[M + H]^+$, 490.1376; found, 490.1370. R_f = 0.42 (hexane/EtOAc - 5:1).

*3-(1-Benzyl-3-(4-bromobutyl)-2-oxoindolin-3-yl)-3-phenylpropanal (**9**).* Colorless oil. Yield = 60% (29 mg). 92% *ee*. The enantiomeric excess of product **9** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 214 nm); t_R = 15.8 min, t_R = 38.0 min. $[\alpha]_D^{20}$ = +28.0 (*c* = 0.8, $CHCl_3$). ^1H NMR (400 MHz, chloroform-*d*): δ 9.53 (t, *J* = 2.0 Hz, 1H), 7.32−7.29 (m, 1H), 7.24−7.14 (m, 5H), 7.11 (ddd, *J* = 8.0, 7.2, 1.4 Hz, 3H), 6.91−6.84 (m, 2H), 6.75−6.68 (m, 2H), 6.50 (dd, *J* = 7.7, 1.0 Hz, 1H), 4.72 (d, *J* = 15.8 Hz, 1H), 4.53 (d, *J* = 15.8 Hz, 1H), 3.82 (dd, *J* = 8.9, 6.6 Hz, 1H), 3.27 (t, *J* = 6.8 Hz, 2H), 3.13−3.01 (m, 2H), 2.04 (qdd, *J* = 12.9, 11.0, 5.0 Hz, 2H), 1.86−1.66 (m, 2H), 1.18 (dddt, *J* = 13.0, 11.0, 9.2, 5.5 Hz, 1H), 1.00−0.82 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*): δ 200.8, 178.0, 143.6, 138.1, 135.3, 129.5, 129.1 (2C), 128.6 (2C), 128.5, 128.1 (2C), 127.5, 127.3, 126.8 (2C), 123.7, 122.4, 109.4, 56.3, 46.8, 44.4, 43.5, 34.9, 33.0, 32.7, 23.3 ppm. IR (KBr): ν = 1709 (C═O, aldehyde, amide), 700 (C—Br) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{28}H_{29}BrNO_2$ $[M + H]^+$, 490.1376; found, 490.1373. R_f = 0.38 (hexane/EtOAc - 5:1).

Gram Scale Cascade Reaction. The catalyst **C2** (556 mg, 1.51 mmol, 0.2 equiv) was added to a solution of the *trans*-cinnamaldehyde (**2a**) (1,0 mg, 7.57 mmol, 1.0 equiv) in DCM (38 mL). The mixture was stirred for 10 min at room temperature. Then, 2,4,6-collidine (1.51 mL, 11.36 mmol, 1.5 equiv) and oxindole (**1a**) (2,62 g, 7.95 mmol, 1.05 equiv) were added. The reaction was stirred for 15 h. The reaction was quenched by careful adding of diluted hydrochloric acid (1 M, 20 mL). The heterogeneous mixture was stirred for 10 min. Then, the organic phase was separated and the water phase was extracted with DCM (3 × 20 mL). The collected organic phases were washed with brine (1 × 30 mL) and dried under $MgSO_4$. After filtration of the drying agent, solvents were removed under reduced pressure. The crude product was purified by column chromatography using hexane/EtOAc (6:1) as an eluent. Diastereomeric ratio of **3a**/**4a** = 1/1.9; yield of **3a**/**4a** = 32% (0.92 g)/65% (1.88 g), overall yield of **3a**/**4a** = 97%.

All analytical data matched the data of identical compounds prepared on a smaller scale.

Pinnick Oxidation—GP5. A solution of $NaClO_2$ (80%, 56.5 mg, 0.5 mmol, 5.0 equiv) and KH_2PO_4 (68.1 mg, 0.5 mmol, 5.0 equiv) in water (3.0 mL) was added dropwise to a stirred solution of spirocycle **3** or **4** (0.1 mmol, 1.0 equiv) in a mixture of acetone (4.0 mL) and

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DMSO (1.6 mL) at room temperature. The reaction mixture was stirred at the same temperature overnight. After the reaction was completed (TLC control), the volatile solvents were evaporated. The resulting mixture was diluted with water (10.0 mL) and extracted with diethyl ether (3 × 10 mL). The collected organic phases were washed with brine (2 × 10 mL) and dried under anhydrous $MgSO_4$. After filtration of solid, the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (eluting with hexane/EtOAc or hexane/acetone mixtures).

*(1R,2S,3S)-1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carboxylic acid (**10a**).* The title compound was synthesized according to the general procedure (GP5) using aldehyde **4a** (38 mg, 0.1 mmol) as a starting material. The product was purified by column chromatography (hexane/EtOAc - 1:1). White amorphous solid. Yield = 69% (27 mg). $[\alpha]_D^{20}$ = +99.3 (*c* = 0.7, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.36−7.32 (m, 1H), 7.23−6.99 (m, 8H), 6.98−6.90 (m, 2H), 6.78−6.69 (m, 2H), 6.45−6.35 (m, 1H), 5.09 (d, *J* = 16.0 Hz, 1H), 4.51 (d, *J* = 16.0 Hz, 1H), 4.10 (d, *J* = 12.3 Hz, 1H), 3.72 (dt, *J* = 12.3, 9.0 Hz, 1H), 2.75−2.59 (m, 2H), 2.59−2.45 (m, 1H), 2.16−2.00 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 178.7 (2C, *overlapped*), 142.1, 135.7, 135.1, 131.8, 128.5 (2C), 128.2 (2C), 128.0, 127.9 (2C), 127.2 (2C, *overlapped*), 126.7 (2C), 124.0, 122.2, 109.2, 60.4, 58.5, 47.8, 43.7, 35.3, 28.1 ppm. IR (KBr): ν = 3087 (O—H), 1709 (C═O, aldehyde, amide, acid) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{23}NNaO_3$ $[M + Na]^+$, 420.1570; found, 420.1569.

*(1S,2S,3S)-2′-Oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carboxylic acid (**10d′**).* The title compound was synthesized according to the general procedure (GP5) using aldehyde **3d** (29 mg, 0.1 mmol) as a starting material. The product was purified by column chromatography (hexane/acetone - 3:1). White amorphous solid. Yield = 58% (18 mg). $[\alpha]_D^{20}$ = −37.3 (*c* = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.90 (s, 1H), 7.43 (d, *J* = 1.5 Hz, 1H), 7.24−6.98 (m, 5H), 6.94 (dt, *J* = 6.8, 1.6 Hz, 2H), 6.70−6.60 (m, 1H), 4.06 (dddd, *J* = 11.7, 7.8, 5.8, 2.1 Hz, 1H), 3.78 (d, *J* = 11.8 Hz, 1H), 2.75−2.61 (m, 1H), 2.41−2.26 (m, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 181.8, 179.7, 140.5, 135.4, 132.3, 128.1, 127.9 (2C), 127.7 (2C), 127.3, 122.8, 122.7, 109.5, 60.3, 59.2, 46.3, 34.9, 28.6 ppm. IR (KBr): ν = 3211 (N—H), 3082 (O—H), 1709 (C═O, aldehyde, amide, acid) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{19}H_{17}NNaO_3$ $[M + Na]^+$, 330.1101; found, 330.1098.

Pinnick Oxidation/Esterification—GP6. A solution of $NaClO_2$ (80%, 56.5 mg, 0.5 mmol, 5.0 equiv) and KH_2PO_4 (68.1 mg, 0.5 mmol, 5.0 equiv) in water (3.0 mL) was added dropwise to a stirred solution of spirocycle **3** or **4** (0.1 mmol, 1.0 equiv) in a mixture of acetone (4.0 mL) and DMSO (1.6 mL) at room temperature. The reaction mixture was stirred at the same temperature overnight. After the reaction was completed (TLC control), the volatile solvents were evaporated. The resulting mixture was diluted with water (10.0 mL) and extracted with diethyl ether (3 × 10 mL). The collected organic phases were washed with brine (2 × 10 mL) and dried under anhydrous $MgSO_4$. After filtration of solid, the filtrate was concentrated under reduced pressure. Crude carboxylic acid was dissolved in a mixture of dry diethyl ether (0.9 mL) and methanol (0.1 mL). A solution of $TMSCHN_2$ (2.0 M in diethyl ether, 0.5 mL, 1.0 mmol, 10.0 equiv) was added dropwise (gas evolution) at 0 °C (cooled by water/ice mixture). The reaction was stirred at the same temperature for 10 min (TLC control). After the reaction was completed, silica gel (1−2 mL) was added to quench the excess of $TMSCHN_2$ (gas evolution). Solvents were evaporated under reduced pressure, and the resulting solid was loaded directly on the column and purified (eluting with hexane/EtOAc mixtures).

*Methyl (1R,2S,3S)-1′-Benzyl-2′-oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carboxylate (**11a**).* The title compound was synthesized according to the general procedure (GP6) using aldehyde **4a** (38 mg, 0.1 mmol) as a starting material. The product was purified by column chromatography (hexane/EtOAc - 5:1). Colorless amorphous solid. Yield = 96% (40 mg, over two steps). 98% *ee*. The enantiomeric excess of product **11a** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 209 nm); t_R = 10.2 min, t_R = 11.3 min. $[\alpha]_D^{20}$ = +89.0 (*c* = 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.39−7.30 (m, 1H), 7.20−7.05 (m, 4H), 7.05−6.97 (m, 4H), 6.97−6.88 (m, 2H), 6.77−6.65 (m, 2H), 6.45−6.33 (m, 1H), 5.08 (dd, *J* = 15.9, 1.0 Hz, 1H), 4.48 (d, *J* = 16.0 Hz, 1H), 4.09 (d, *J* = 12.5 Hz, 1H), 3.80−3.65 (m, 1H), 3.60 (s, 3H), 2.75−2.53 (m, 2H), 2.46 (dddd, *J* = 15.4, 11.1, 8.4, 5.5 Hz, 1H), 2.07 (ddd, *J* = 12.4, 8.3, 4.3 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 178.7, 174.6, 142.2, 135.8, 135.2, 131.9, 128.5 (2C), 128.2 (2C), 128.0, 127.9 (2C), 127.2 (2C), 126.7 (2C), 124.0, 122.2, 109.2, 60.2, 58.8, 52.0, 48.1, 43.7, 35.2, 28.1 ppm. IR (KBr): ν = 1736 (C═O, ester), 1709 (C═O, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{27}H_{26}NO_3$ $[M + H]^+$, 412.1907; found, 412.1910.

*Methyl (1S,2S,3S)-2′-Oxo-2-phenylspiro[cyclopentane-1,3′-indoline]-3-carboxylate (**11d′**).* The title compound was synthesized according to the general procedure (GP6) using aldehyde **3d** (29 mg, 0.1 mmol) as a starting material. The product was purified by column chromatography (hexane/EtOAc - 3:1). Colorless oil. Yield = 73% (24 mg, over two steps). 90% *ee*. The enantiomeric excess of product **11d′** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 209 nm); t_R = 5.0 min, t_R = 6.6 min. $[\alpha]_D^{20}$ = −53.8 (*c* = 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.50−7.39 (m, 1H), 7.23−7.04 (m, 6H), 7.00−6.94 (m, 2H), 6.67−6.60 (m, 1H), 4.15−4.00 (m, 1H), 3.81 (d, *J* = 11.9 Hz, 1H), 3.62 (s, 3H), 2.72−2.58 (m, 1H), 2.44−2.17 (m, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 180.8, 175.6, 140.5, 135.7, 132.4, 128.0, 127.9 (2C), 127.7 (2C), 127.2, 122.8, 122.6, 109.2, 60.0, 59.5, 51.9, 46.4, 35.1, 28.6 ppm. IR (KBr): ν = 3271 (N—H), 1722 (C═O, ester, aldehyde, amide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{20}H_{19}NNaO_3$ $[M + Na]^+$, 344.1257; found, 344.1257.

Borohydride Reduction—GP7. Sodium borohydride (19 mg, 0.5 mmol, 5.0 equiv) was added in one portion to a solution of corresponding aldehyde **3** and **4** (0.1 mmol, 1.0 equiv) in MeOH (2 mL) at 0 °C (cooled by water/ice mixture). The mixture was stirred for 1 h at the same temperature (TLC control). After the reaction was completed, the reaction was quenched with a solution of HCl (1 M, 1 mL), followed by the addition of EtOAc (5 mL). The heterogeneous mixture was stirred for 5 min. Then, the organic phase was separated and the water phase was extracted with EtOAc (3 × 5 mL). The collected organic phases were washed with brine (1 × 5 mL) and dried under $MgSO_4$, the solids were filtered, and the solvent was evaporated. The crude product was purified by column chromatography (eluting with hexane/EtOAc mixtures).

*(1R,2S,3S)-1′-Benzyl-3-(hydroxymethyl)-2-phenylspiro-[cyclopentane-1,3′-indolin]-2′-one (**12a**).* The title compound was synthesized according to the general procedure (GP7) using aldehyde **4a** (38 mg, 0.1 mmol) as a starting material. The product was purified by column chromatography (hexane/EtOAc - 3:1). Colorless oil. Yield = 98% (38 mg). 99% *ee*. The enantiomeric excess of product **12a** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 8.9 min, t_R = 13.2 min. $[\alpha]_D^{20}$ = +60.7 (*c* = 1.6, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.51−7.38 (m, 1H), 7.20−7.06 (m, 4H), 7.06−6.98 (m, 4H), 6.98−6.91 (m, 2H), 6.73−6.64 (m, 2H), 6.43−6.33 (m, 1H), 5.09 (d, *J* = 16.0 Hz, 1H), 4.46 (d, *J* = 16.0 Hz, 1H), 3.74 (dd, *J* = 10.7, 4.7 Hz, 1H), 3.63 (dd, *J* = 10.7, 6.8 Hz, 1H), 3.50 (d, *J* = 12.2 Hz, 1H), 3.07 (ddtd, *J* = 14.3, 9.2, 7.1, 4.6 Hz, 1H), 2.60−2.39 (m, 2H), 2.19−1.96 (m, 2H), 1.76 (br s, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.5, 142.1, 136.9, 135.2, 132.4, 128.5 (2C + 2C, *overlapped*), 128.0 (2C), 127.7, 127.1 (2C), 126.6 (2C), 124.2, 122.1, 109.1, 65.7, 60.8, 58.4, 45.7, 43.6, 35.1, 27.3 ppm. IR (KBr): ν = 3419 (O—H), 1709 (C═O) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{26}NO_2$ $[M + H]^+$, 384.1958; found, 384.1960.

*(1S,2S,3S)-3-(Hydroxymethyl)-2-phenylspiro[cyclopentane-1,3′-indolin]-2′-one (**12d′**).* The title compound was synthesized according to the general procedure (GP7) using aldehyde **3d** (29 mg, 0.1 mmol) as a starting material. The product was purified by column chromatography (hexane/EtOAc - 2:1). White semisolid. Yield = 87% (26 mg). 90% *ee*. The enantiomeric excess of product

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12d′ was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 5.3 min, t_R = 6.1 min. $[\alpha]_D^{20}$ = −57.9 (*c* = 0.7, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.43−7.37 (m, 1H), 7.20−7.06 (m, 5H), 7.06−6.92 (m, 3H), 6.66−6.55 (m, 1H), 3.75 (d, *J* = 10.8 Hz, 1H), 3.58 (dt, *J* = 10.5, 5.1 Hz, 1H), 3.45−3.32 (m, 1H), 3.28 (d, *J* = 11.9 Hz, 1H), 2.48 (dtd, *J* = 12.4, 8.5, 5.5 Hz, 1H), 2.37 (ddd, *J* = 13.6, 8.8, 6.1 Hz, 1H), 2.21 (ddd, *J* = 13.6, 10.5, 5.6 Hz, 1H), 1.99 (dddd, *J* = 12.4, 10.4, 8.4, 6.0 Hz, 1H), 1.28 (br s, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 181.2, 140.4, 136.6, 133.5, 128.2 (2C), 128.0 (2C), 127.7, 127.1, 122.6, 122.5, 109.0, 64.5, 60.4, 59.1, 44.0, 34.7, 27.3 ppm. IR (KBr): ν = 3211 (N—H), 3060 (O—H), 1705 (C═O) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{19}H_{19}NNaO_2$ $[M + Na]^+$, 316.1308; found, 316.1309.

Reductive Amination (GP8). $ZnCl_2$ (16.4 mg, 0.12 mmol, 1.2 equiv) was added in one portion to a solution of corresponding aldehyde **3** and **4** (0.1 mmol, 1.0 equiv) in MeOH (2 mL) at room temperature, followed by the addition of benzylamine (13.1 μL, 0.12 mmol, 1.2 equiv). The reaction mixture was stirred for 5 min at room temperature. Then, $NaBH_3CN$ (8.3 mg, 0.12 mmol, 1.2 equiv) was added in one portion at room temperature. The mixture was stirred for 1 h at the same temperature (TLC control). The reaction was quenched by a solution of NaOH (1 M, 10 mL). The mixture was extracted with EtOAc (3 × 5 mL). The collected organic phases were washed with brine (1 × 5 mL) and dried under $MgSO_4$, the solids were filtered, and the solvents were evaporated. The crude product was purified by column chromatography (eluting with EtOAc).

*(1R,2S,3S)-1′-Benzyl-3-((benzylamino)methyl)-2-phenylspiro-[cyclopentane-1,3′-indolin]-2′-one (**13a**).* The title compound was synthesized according to the general procedure (GP8) using aldehyde **4a** (38 mg, 0.1 mmol) as a starting material. Colorless oil. Yield = 98% (46 mg). 98% *ee*. The enantiomeric excess of product **13a** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 50:50, flow rate = 1.0 mL/min, λ = 256 nm); t_R = 6.6 min, t_R = 7.5 min. $[\alpha]_D^{20}$ = +61.9 (*c* = 1.8, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.46−7.40 (m, 1H), 7.34−7.29 (m, 2H), 7.28−7.21 (m, 3H), 7.21−7.09 (m, 4H), 7.09−6.99 (m, 4H), 6.97−6.92 (m, 2H), 6.79−6.66 (m, 2H), 6.43−6.31 (m, 1H), 5.11 (d, *J* = 16.0 Hz, 1H), 4.47 (d, *J* = 16.1 Hz, 1H), 3.83−3.66 (m, 2H), 3.43 (d, *J* = 12.2 Hz, 1H), 3.09 (ddt, *J* = 12.4, 7.9, 4.4 Hz, 1H), 2.83−2.66 (m, 2H), 2.65−2.40 (m, 2H), 2.11−1.92 (m, 2H), 1.71 (br s, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.6, 142.1, 140.2, 137.0, 135.3, 132.6, 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.9 (2C), 127.7, 127.1, 127.0, 126.93, 126.6 (2C), 124.3, 122.1, 109.0, 60.7, 60.5, 54.2, 54.0, 43.7, 43.6, 34.9, 29.0 ppm. IR (KBr): ν = 3327 (N—H), 1709 (C═O) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{33}H_{33}N_2O$ $[M + H]^+$, 473.2587; found, 473.2585.

*(1S,2S,3S)-1′-Benzyl-3-((benzylamino)methyl)-2-phenylspiro-[cyclopentane-1,3′-indolin]-2′-one (**13a′**).* The title compound was synthesized according to the general procedure (GP8) using aldehyde **3a** (38 mg, 0.1 mmol) as a starting material. Orange oil. Yield = 82% (39 mg). 99% *ee*. The enantiomeric excess of product **13a′** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 50:50, flow rate = 1.0 mL/min, λ = 258 nm); t_R = 8.4 min, t_R = 11.6 min. $[\alpha]_D^{20}$ = −52.4 (c = 1.3, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.44−7.39 (m, 1H), 7.34−7.29 (m, 2H), 7.29−7.19 (m, 4H), 7.19−7.05 (m, 7H), 7.04−6.99 (m, 2H), 6.54−6.44 (m, 2H), 6.35 (d, *J* = 1.7 Hz, 1H), 5.03 (d, *J* = 16.0 Hz, 1H), 4.26 (d, *J* = 16.0 Hz, 1H), 3.84 (d, *J* = 13.4 Hz, 1H), 3.74 (d, *J* = 13.4 Hz, 1H), 3.49 (dqd, *J* = 12.7, 8.4, 4.4 Hz, 1H), 3.24 (d, *J* = 11.9 Hz, 1H), 2.80 (dd, *J* = 11.7, 4.4 Hz, 1H), 2.69−2.54 (m, 2H), 2.42 (ddd, *J* = 13.6, 8.8, 6.8 Hz, 1H), 2.25 (ddd, *J* = 13.6, 10.4, 5.1 Hz, 1H), 1.89 (dddd, *J* = 12.5, 10.3, 8.9, 6.8 Hz, 1H), 1.75 (br s, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.5, 142.7, 140.4, 137.0, 135.4, 133.4, 128.50 (4C, *overlapped*), 128.3 (2C), 128.2 (2C), 128.0 (2C), 127.7, 127.0, 126.9, 126.8, 126.5 (2C), 122.5, 122.2, 108.8, 61.3, 60.1, 53.9, 53.0, 43.3, 42.1, 35.5, 29.7 ppm. IR (KBr): ν = 3256 (N—H), 1705 (C═O) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{33}H_{33}N_2O$ $[M + H]^+$, 473.2587; found, 473.2583.

*(1R,2S,3S)-1′-Benzyl-3-((benzylamino)methyl)-2-phenylspiro-[cyclopentane-1,3′-indolin]-2′-one (**13d′**).* The title compound was synthesized according to the general procedure (GP8) using aldehyde **3d** (29 mg, 0.1 mmol) as a starting material. Colorless oil. Yield = 79% (30 mg). 90% *ee*. The enantiomeric excess of product **13d′** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 50:50, flow rate = 1.0 mL/min, λ = 256 nm); t_R = 5.1 min, t_R = 6.5 min. $[\alpha]_D^{20}$ = −23.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.34−7.27 (m, 3H), 7.25−7.18 (m, 4H), 7.15−7.03 (m, 5H), 6.96−6.86 (m, 2H), 6.64−6.56 (m, 1H), 3.80 (d, *J* = 13.4 Hz, 1H), 3.70 (d, *J* = 13.4 Hz, 1H), 3.34 (dtd, *J* = 12.7, 8.4, 4.3 Hz, 1H), 3.11 (d, *J* = 11.9 Hz, 1H), 2.73 (dd, *J* = 11.8, 4.4 Hz, 1H), 2.61−2.46 (m, 2H), 2.34 (ddd, *J* = 13.6, 8.8, 6.7 Hz, 1H), 2.17 (ddd, *J* = 13.6, 10.4, 5.2 Hz, 1H), 1.82 (dddd, *J* = 12.6, 10.4, 9.0, 6.7 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 181.3, 140.5, 136.7, 133.8, 128.4 (2C), 128.1 (2C + 2C, *overlapped*), 128.0 (2C), 127.7, 127.0 (2C), 122.5, 122.4, 109.0, 61.5, 60.4, 53.6, 52.7, 41.7, 34.8, 29.5 ppm. IR (KBr): ν = 3159 (N—H), 1705 (C═O) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{26}H_{27}N_2O$ $[M + H]^+$, 383.2118; found, 383.2117.

Wittig Reaction (GP9). Methyl (triphenylphosphoranylidene)-acetate (1.5 equiv) was added to a stirred solution of corresponding aldehyde **3** and **4** (1.0 equiv) in DCM (0.1 M) at room temperature. The mixture was stirred (typically for 24 h) at the same temperature (TLC control). After the reaction was completed, the solvent was evaporated. The crude product was purified by column chromatography (eluting with hexane/EtOAc mixtures).

*Methyl (E)-3-((1R,2S,3R)-1′-Benzyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indolin]-3-yl)acrylate (**14a**).* The title compound was synthesized according to the general procedure (GP9) using aldehyde **4a** (38 mg, 0.1 mmol) as a starting material. Colorless oil. The crude product was purified by column chromatography (eluting with hexane/EtOAc - 10:1). Yield = 94% (41 mg). 99% *ee*. The enantiomeric excess of product **14a** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 208 nm); t_R = 11.2 min, t_R = 15.3 min. $[\alpha]_D^{20}$ = +90.7 (*c* = 1.8, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.41−7.34 (m, 1H), 7.21−7.11 (m, 3H), 7.10−7.04 (m, 1H), 7.03 (s, 4H), 6.93 (dd, *J* = 15.7, 7.3 Hz, 1H), 6.90−6.84 (m, 2H), 6.81−6.72 (m, 2H), 6.43−6.32 (m, 1H), 5.81 (dd, *J* = 15.6, 0.8 Hz, 1H), 5.06 (d, *J* = 16.0 Hz, 1H), 4.50 (d, *J* = 16.0 Hz, 1H), 3.64 (d, *J* = 8.5 Hz, 5H), 2.62 (ddd, *J* = 13.0, 10.8, 6.1 Hz, 1H), 2.54−2.41 (m, 1H), 2.18 (ddt, *J* = 10.7, 8.6, 5.2 Hz, 1H), 2.09 (ddd, *J* = 12.9, 8.5, 5.4 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.3, 166.7, 149.9, 142.2, 135.7, 135.2, 132.4, 128.5 (2C), 128.4 (2C), 127.9 (2C), 127.8, 127.2, 127.1, 126.7 (2C), 124.1, 122.2, 121.6, 109.1, 60.9, 60.4, 51.5, 46.2, 43.7, 35.0, 30.1 ppm. IR (KBr): ν = 1712 (C═O, ester, aldehyde, aamide) cm^{-1}. HRMS (ESI+) *m*/*z*: calcd for $C_{29}H_{28}NO_3$ $[M + H]^+$, 438.2064; found, 438.2062.

*Methyl (E)-3-((1R,2S,3R)-1′-Allyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indolin]-3-yl)acrylate (**14b**).* The title compound was synthesized according to the general procedure (GP9) using aldehyde **4b** (17 mg, 0.05 mmol) as a starting material. The crude product was purified by column chromatography (eluting with hexane/EtOAc - 9:1). Colorless oil. Yield = 94% (18 mg). 99% *ee*. The enantiomeric excess of product **14b** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 90:10, flow rate = 1.0 mL/min, λ = 211 nm); t_R = 9.8 min, t_R = 11.6 min. $[\alpha]_D^{20}$ = +86.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.36−7.30 (m, 1H), 7.09 (td, *J* = 7.7, 1.3 Hz, 1H), 7.03−6.95 (m, 4H), 6.95−6.87 (m, 1H), 6.87−6.80 (m, 2H), 6.53 (dt, *J* = 7.9, 0.7 Hz, 1H), 5.87−5.77 (m, 1H), 5.54 (ddt, *J* = 17.2, 10.2, 5.0 Hz, 1H), 4.96 (dq, *J* = 10.4, 1.5 Hz, 1H), 4.64 (dtd, *J* = 17.2, 1.8, 0.9 Hz, 1H), 4.39 (ddt, *J* = 16.6, 4.8, 1.9 Hz, 1H), 3.98 (ddt, *J* = 16.6, 5.3, 1.7 Hz, 1H), 3.65 (s, 3H), 3.61−3.53 (m, 2H), 2.57 (ddd, *J* = 13.0, 10.8, 5.8 Hz, 1H), 2.45 (dddd, *J* = 12.7, 10.0, 8.3, 5.7 Hz, 1H), 2.20−2.10 (m, 1H), 2.06 (ddd, *J* = 13.0, 8.6, 5.7 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.0, 166.7, 149.8, 142.2, 135.5, 132.3, 130.9, 128.1 (2C), 127.7 (2C + 1C, *overlapped*), 127.0, 124.0, 122.0, 121.6, 117.0, 108.8, 60.9, 60.3, 51.5, 45.7, 42.2, 34.5, 30.2 ppm. IR (KBr): ν = 1709

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(C═O, ester, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{25}H_{26}NO_3$ $[M + H]^+$, 388.1907; found, 388.1905.

*Methyl (E)-3-((1S,2S,3R)-1′-Allyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indolin]-3-yl)acrylate (**14b′**).* The title compound was synthesized according to the general procedure (GP9) using aldehyde **3b** (17 mg, 0.05 mmol) as a starting material. The crude product was purified by column chromatography (eluting with hexane/EtOAc - 9:1). Yellow oil. Yield = 96% (19 mg). 99% *ee*. The enantiomeric excess of product **14b′** was determined by HPLC using a Chiralpak IA column (heptane/*i*-PrOH - 90:10, flow rate = 1.0 mL/min, λ = 211 nm); t_R = 7.3 min, t_R = 8.0 min. $[\alpha]_D^{20}$ = −34.0 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.46−7.37 (m, 1H), 7.20 (td, J = 7.6, 1.4 Hz, 1H), 7.14 (td, J = 7.5, 1.2 Hz, 1H), 7.12−7.03 (m, 3H), 6.90 (dd, J = 15.7, 8.0 Hz, 1H), 6.86−6.80 (m, 2H), 6.60−6.52 (m, 1H), 5.87 (dd, J = 15.7, 1.1 Hz, 1H), 5.17 (dddd, J = 17.2, 10.2, 5.7, 4.4 Hz, 1H), 4.83 (dq, J = 10.4, 1.5 Hz, 1H), 4.41 (ddd, J = 17.0, 2.3, 1.3 Hz, 1H), 4.25 (ddt, J = 16.5, 4.2, 2.0 Hz, 1H), 4.03 (dddd, J = 12.1, 9.1, 7.8, 1.1 Hz, 1H), 3.77−3.69 (m, 1H), 3.67 (s, 3H), 3.31 (d, J = 12.0 Hz, 1H), 2.55−2.36 (m, 2H), 2.33−2.22 (m, 1H), 2.15−1.94 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 178.9, 166.9, 150.2, 142.9, 135.3, 132.8, 130.9, 128.1 (2C), 128.0 (2C), 127.9, 127.2, 122.6, 122.2, 121.5, 116.6, 108.6, 62.2, 59.8, 51.4, 44.2, 41.8, 34.0, 30.9 ppm. IR (KBr): ν = 1709 (C═O, ester, amide) cm^{-1}. HRMS (ESI+) m/z: calcd for $C_{25}H_{26}NO_3$ $[M + H]^+$, 388.1907; found, 388.1909.

*Methyl (E)-3-((1R,2S,3R)-1′-Methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indolin]-3-yl)acrylate (**14c**).* The title compound was synthesized according to the general procedure (GP9) using aldehyde **4c** (15 mg, 0.05 mmol) as a starting material. The crude product was purified by column chromatography (eluting with hexane/EtOAc - 7:1). White semisolid. Yield = 97% (18 mg). 99% *ee*. The enantiomeric excess of product **14c** was determined by HPLC using a Chiralpak IC column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 209 nm); t_R = 12.3 min, t_R = 26.5 min. $[\alpha]_D^{20}$ = +92.8 (c = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.28 (d, J = 1.6 Hz, 1H), 7.13 (td, J = 7.7, 1.2 Hz, 1H), 7.05−6.97 (m, 4H), 6.97−6.89 (m, 1H), 6.88−6.81 (m, 2H), 6.54 (dt, J = 7.8, 0.8 Hz, 1H), 5.85 (dd, J = 15.6, 0.7 Hz, 1H), 3.67 (s, 3H), 3.60 (q, J = 2.2 Hz, 2H), 3.05 (s, 3H), 2.57 (ddd, J = 13.1, 10.7, 5.5 Hz, 1H), 2.51−2.40 (m, 1H), 2.22−2.12 (m, 1H), 2.07 (ddd, J = 13.1, 8.5, 6.2 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.5, 166.7, 149.8, 142.8, 135.6, 132.4, 127.8 (2C + 1C, *overlapped*), 127.6 (2C), 126.9, 123.9, 122.0, 121.6, 107.7, 60.7, 60.4, 51.5, 45.4, 34.1, 30.4, 26.2 ppm. IR (KBr): ν = 1716 (C═O, ester, amide) cm^{-1}. HRMS (EI+) m/z: calcd for $C_{23}H_{23}NO_3$ $[M]^+$, 361.1678; found, 361.1680.

*Methyl (E)-3-((1S,2S,3R)-1′-Methyl-2′-oxo-2-phenylspiro-[cyclopentane-1,3′-indolin]-3-yl)acrylate (**14c′**).* The title compound was synthesized according to the general procedure (GP9) using aldehyde **3c** (15 mg, 0.05 mmol) as a starting material. The crude product was purified by column chromatography (eluting with hexane/EtOAc - 7:1). Yellow oil. Yield = 95% (17 mg). 98% *ee*. The enantiomeric excess of product **14c′** was determined by HPLC using a Chiralpak IC column (heptane/*i*-PrOH - 80:20, flow rate = 1.0 mL/min, λ = 258 nm); t_R = 9.4 min, t_R = 11.7 min. $[\alpha]_D^{20}$ = −12.5 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, chloroform-*d*): δ 7.38 (dt, J = 7.3, 0.8 Hz, 1H), 7.23 (td, J = 7.7, 1.3 Hz, 1H), 7.14 (td, J = 7.5, 1.1 Hz, 1H), 7.12−7.02 (m, 3H), 6.89 (dd, J = 15.7, 8.0 Hz, 1H), 6.84−6.78 (m, 2H), 6.58 (dt, J = 7.6, 0.7 Hz, 1H), 5.86 (dd, J = 15.7, 1.1 Hz, 1H), 3.99 (dddd, J = 12.1, 9.1, 7.9, 1.2 Hz, 1H), 3.67 (s, 3H), 3.27 (d, J = 12.0 Hz, 1H), 2.77 (s, 3H), 2.50 (dtd, J = 12.1, 8.2, 7.6, 4.0 Hz, 1H), 2.40 (ddd, J = 13.6, 8.7, 7.3 Hz, 1H), 2.25 (ddd, J = 13.6, 10.6, 4.1 Hz, 1H), 2.10−1.92 (m, 1H) ppm. ^{13}C{^{1}H} NMR (101 MHz, chloroform-*d*): δ 179.1, 166.9, 150.2, 143.6, 135.3, 132.8, 128.0, 127.9 (2C), 127.7 (2C), 127.1, 122.6, 122.1, 121.4, 107.6, 62.4, 60.0, 51.4, 44.2, 33.6, 30.9, 25.6 ppm. IR (KBr): ν = 1709 (C═O, ester, amide) cm^{-1}. HRMS (EI+) m/z: calcd for $C_{23}H_{23}NO_3$ $[M]^+$, 361.1678; found, 361.1675.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01116.

Reaction condition optimization, crystallographic data, description of computational methods, complete biological activity screening copies of ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR, and copies of chiral HPLC (PDF)

FAIR data, including the primary NMR FID files, for all compounds (ZIP)

Accession Codes

CCDC 2053813−2053815 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

V.D. and A.V. performed the synthesis of all compounds. P.M. performed the DFT studies. K.K., O.J., and M.P. performed screening of biological activities. I.C. performed the X-ray analysis. V.D., O.J., M.P., and J.V. wrote the manuscript. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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