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Asymmetric Diastereoselective Synthesis of Spirocyclopropane Derivatives of Oxindole

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A new asymmetric organocatalytic synthesis of spirocyclopropane oxindoles has been developed. The method is based on the Michael addition of *N*-Boc-protected 3-chlorooxindole to unsaturated 1,4-dicarbonyl compounds, affording *trans*-substituted spirocyclopropane oxindole derivatives in high diastereo- and enantioselectivity.

Introduction

The synthesis of spirocyclic oxindole derivatives has recently gained considerable attention.[1] This core structure can be found in many natural and synthetic compounds exhibiting a diverse range of biological activities, including antimalarial,[2] anti-HIV,[3] and anticancer activities.[4] Their medical importance has made them valuable synthetic targets and has spurred research towards the creation of convenient and highly selective methods for their synthesis. The asymmetric construction of a spirocyclopropane motif is especially challenging due to the presence of three consecutive stereogenic centers in the highly strained three-membered ring. From a stereochemical point of view, the synthesis of α,β-identically substituted cyclopropane derivatives of oxindole is even more complex because of the formation of an enantiomeric *trans*-substituted derivative structure with a nonstereogenic C-3 center, together with an achiral diastereoisomeric *cis*-isomer with a pseudo-asymmetric center at C-3 (Figure 1).

Previously, we described the synthesis of spirocyclopropane oxindoles starting from alkylidene oxindoles or 3-chlorooxindoles.[5] The latter are very useful building blocks for the creation of all-carbon quaternary centers by cascade reactions using the dualistic properties of the carbon at the third position of oxindole. Chlorine increases the acidity of the C–H bond, making the carbon atom more nucleophilic, and chloride is also a good leaving group for the nucleophilic substitution. Thus, Michael-initiated ring closure (MIRC)[6] between α,β-unsaturated carbonyl compounds and 3-chlorooxindole is a straightforward method for spirocyclopropanation of oxindoles. Unsaturated 1,4-dicarbonyl compounds have also been used in MIRC for the preparation of substituted cyclopropanes,[7] although there are only few examples of asymmetric reactions.[8] To the best of our knowledge, there are no reports concerning asymmetric organocatalytic cyclopropanation on symmetric unsaturated 1,4-diketones.

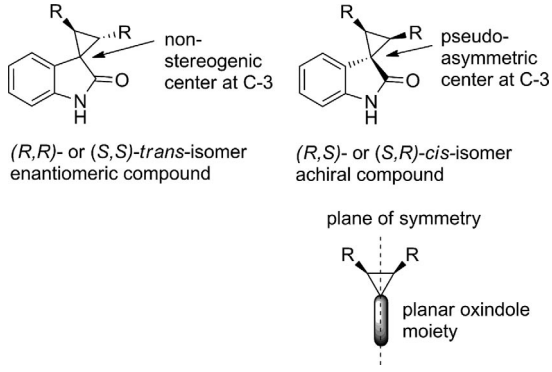
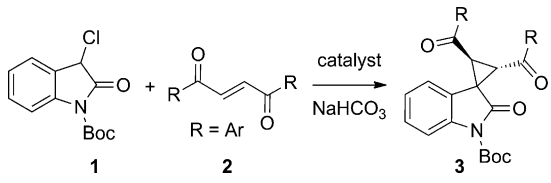


Figure 1. Stereochemistry of *trans*- and *cis*-substituted spirocyclopropane oxindoles.

Results and Discussion

To explore the feasibility of the synthesis of symmetric spirocyclopropane oxindoles, the cascade reaction between *N*-Boc-protected 3-chlorooxindoles **1** and aromatic unsaturated 1,4-diketones **2** was investigated (Scheme 1).



Scheme 1. General scheme for the synthesis of spirocyclopropane oxindoles.

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This reaction cascade is an example of enantioselective MIRC and consists of a Michael addition followed by an intramolecular nucleophilic substitution, leading to the formation of cyclopropane derivatives **3**. Based on our recent results in the asymmetric desymmetrization of unsaturated 1,4-diketones,[9] various enantiomeric thiourea, *Cinchona* alkaloid, or squaramide catalysts **I**–**V** were used to catalyze reactions (Figure 2).

In our first experiments, an unprotected NH oxindole as a synthetically preferable starting material was used.[10] However, due to the insufficient acidity of the hydrogen at C3, no reaction took place.[11]

N-Boc-protected 3-chlorooxindole **1a** reacted smoothly with unsaturated aromatic 1,4-diketone **2a** and provided spirocyclopropane oxindole **3a** in good yield and enantioselectivity (Table 1, entry 1). Protecting the oxindole nitrogen with an electron-withdrawing group increases the acidity of the C–H bond at C3. On the other hand, it provides the opportunity for the formation of additional H-bonds between the catalyst and the substrate. In this model reaction the ratio of spirocyclopropane oxindole **3a**, uncyclized Michael adduct **4a**, and achiral compound **5a**, together with the enantiomeric purity of **3a** were determined. To facilitate the purification of the product **3a**, the crude mixture was treated with trifluoroacetic acid (TFA) and the product was isolated as a free N-H oxindole **3a**-NH as a single diastereoisomer (side-products **4a** and **5a** were identified by ^{1}H NMR spectroscopic analysis of the crude mixture). All thiourea-derived catalysts gave quite similar *ee* values for the product (Table 1, entries 1, 2 and 5). Squaramide catalyst **III** was clearly inappropriate for the cyclopropanation. The highest enantio- and diastereoselectivity was achieved with *Cinchona* alkaloid **IV**, but the poor yield obtained (21% for **3a**) made it unattractive for practical use (Table 1, entry 4). The highest yield (70%) was obtained by sacrificing enantioselectivity in running the reaction with catalyst **II** (Table 1, entry 2).

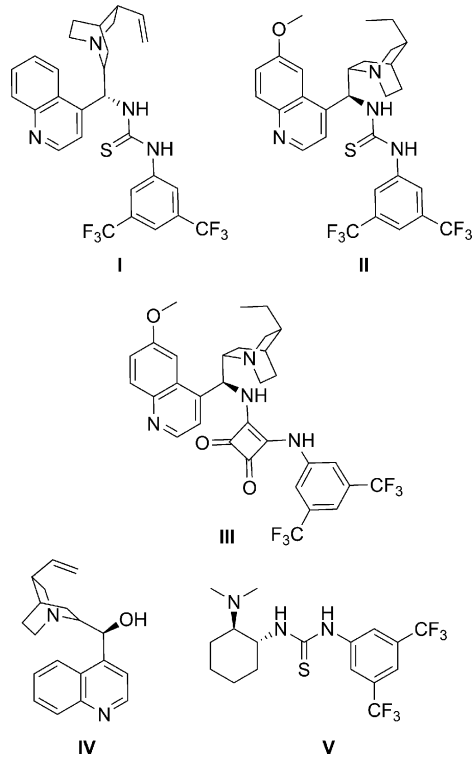
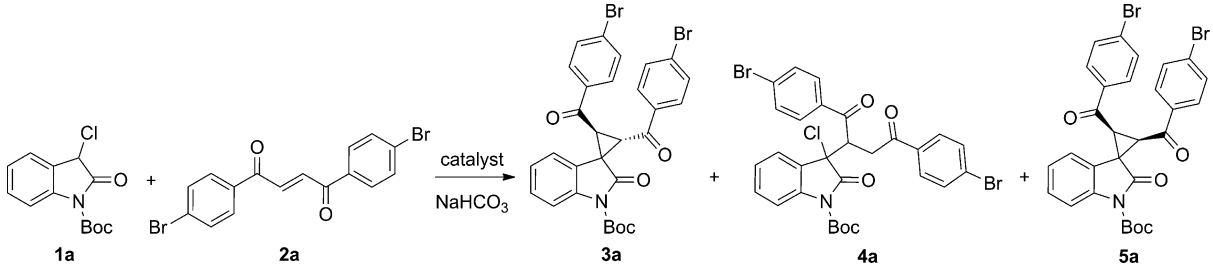


Figure 2. Catalysts used in the study.

Table 1. Screening of the catalyst and optimization.[a]



Entry	Catalyst (mol-%)	Solvent	*t* [°C]	Time [h]	Ratio **3a/4a/5a**[b]	Yield [%][c]		*ee* [%][d]
						N-Boc	N-H	
1	**I** (10)	$CHCl_3$	r.t.	18	n.d.	61		–67
2	**II** (10)	$CHCl_3$	r.t.	48	1:0.1:0.2	70		67
3	**III** (10)	$CHCl_3$	r.t.	48	1:0.9:0.5	n.d.		n.d.
4	**IV** (10)	$CHCl_3$	r.t.	48	1:0.6:0.05	21		80
5	**V** (10)	$CHCl_3$	r.t.	48	1:0.6:0.2		42	–75
6	**II** (20)	$CHCl_3$	60	18	1:0.4:0.3		51	48
7	**II** (10)	toluene	r.t.	48	1:0.1:0.1		57	86
8	**II** (10)	CH_2Cl_2	r.t.	48	1:0.2:0.2		44	63
9	**II** (10)	DCE	r.t.	48	1:0.2:0.2		44	65
10	**II** (10)	toluene	4	96	1:0.2:0.1		59	90

[a] Reaction conditions (0.1 mmol scale, 0.2 M solution): **1** (1 equiv.), **2a** (1.2 equiv.), $NaHCO_3$ (2 equiv.). [b] Determined by ^{1}H NMR spectroscopic analysis of the crude mixture. [c] The main product **3a** or **3a**-NH was isolated as a single diastereoisomer. [d] The *ee* of **3** was determined by chiral HPLC analysis of the isolated product.

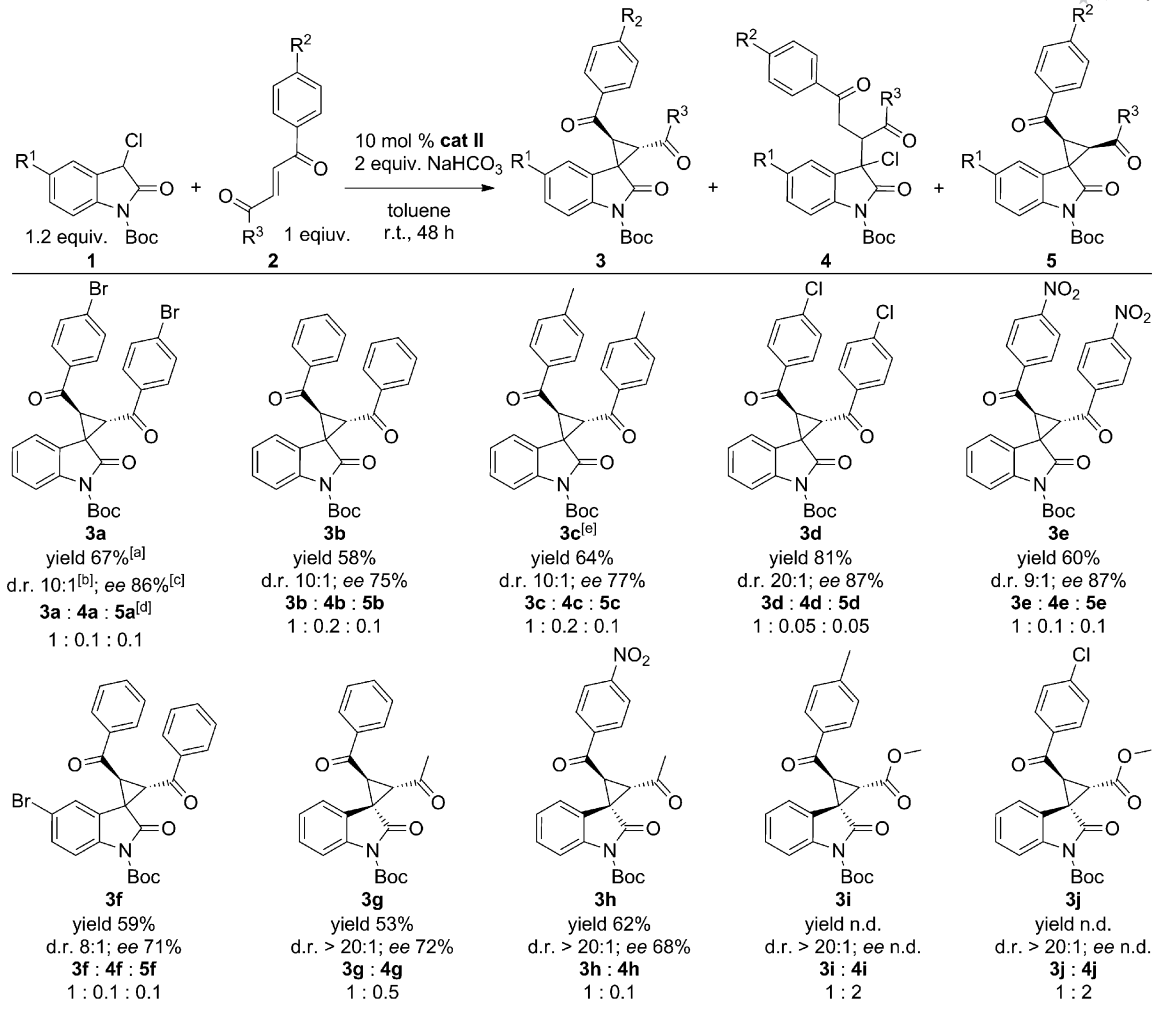


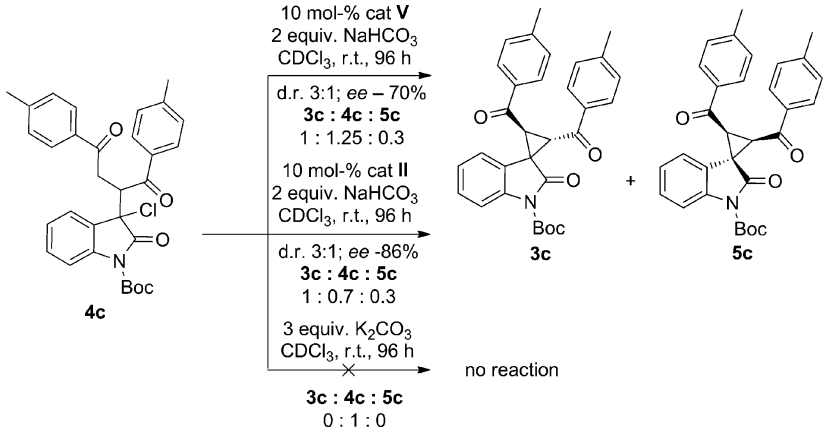
Figure 3. Scope of the reaction. [a] The main product **3** was isolated as a single diastereoisomer. [b] Diastereomeric ratio was determined by ^{1}H NMR spectroscopic analysis of the crude mixture. [c] The *ee* was determined by chiral HPLC analysis of the isolated product. [d] Determined by ^{1}H NMR spectroscopic analysis of the crude mixture. [e] The reaction was stirred for 96 h.

We then turned our attention to further improving the efficiency of the thiourea **II** catalyzed cascade reaction (Table 1, entries 6–9). Increasing temperature and catalyst loading did not improve the yield, instead, the selectivity decreased dramatically (Table 1, entry 6). Solvent screening revealed that the product **3a**-NH could be obtained in moderate yield in 48 h in all cases, but the best enantio- and diastereoselectivity were obtained in toluene (Table 1, entry 7). Decreasing the reaction temperature from room temperature to 4 °C had little influence on stereoselectivity, but an extended reaction time was required to achieve reasonable yield (Table 1, entry 10).

With optimal conditions in hand [**1** (1.2 equiv.), **2** (1 equiv.), $NaHCO_3$ (2 equiv.), and **II** (10 mol-%) in toluene at room temp.], the scope of the reaction was investigated first by using various symmetric diketones **2**. The obtained compounds and the product parameters are presented in Figure 3.

Electron-donating or electron-withdrawing substituents in the aromatic ring of the diketones **2** provided products with two tertiary stereocenters with similar results in terms of yield (from 58 to 81%) and enantioselectivity (*ee* from 75 to 87%) (Figure 3, compounds **3a**–**e**). Diastereoselectivity varied from excellent (Figure 3, compound **3d**) to high (Figure 3, compound **3e**). Bromo-substituted oxindole did not noticeably affect the results of the cascade (Figure 3, compound **3f**). However, the reaction between Boc-protected 3-chlorooxindole **1a** and aliphatic diketone [(*E*)-hex-3-ene-2,5-dione] did not proceed, probably due to the lower electrophilicity of the latter. A similar observation emerged from the work of Liao et al. in the case of the addition of 3-alkyl-substituted oxindoles to unsaturated 1,4-diketones.[12]

The scope of the reaction was then broadened to include nonsymmetric unsaturated 1,4-dicarbonyl compounds, which led to spiro-oxindoles containing two tertiary and one quaternary center (Figure 3, compounds **3g**–**j**). Although nonsymmetric unsaturated 1,4-diketones have two different electrophilic centers for Michael addition, the nucleophilic attack was regioselective. Two regioisomers of the intermediate should give different diastereoisomers after intramolecular cyclization, but only one out of four possible stereoisomers was formed (Figure 3, compound **3g** and **3h**).



Scheme 2. Cyclization of Michael adduct **4c**.

Unsaturated keto esters reacted smoothly with 3-chlorooxindole, but the main product was non-cyclized compound **4**, which could not be separated from **3** (Figure 3, compounds **3i** and **3j**). Even though only a small amount of **3** formed, the diastereoselectivity was very high, indicating that, similar to nonsymmetric 1,4-diketones, Michael addition to unsaturated keto esters was also regioselective.

The relative stereochemistry of symmetric spiro-oxindoles **3a**–**f** was determined by ^{1}H NMR spectroscopic analysis, whereas the absolute stereochemistry of one of the products, **3c**-NH, was determined by vibrational circular dichroism (VCD) (Figure 4).

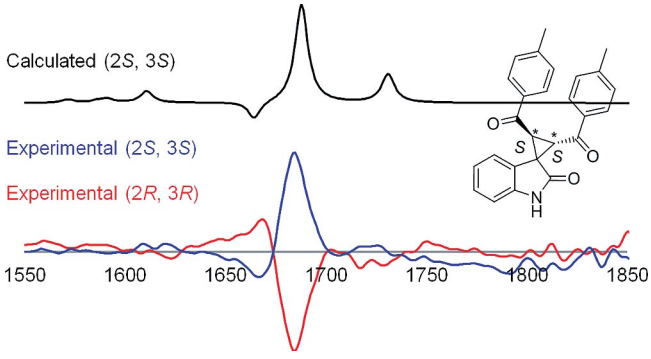


Figure 4. VCD analysis of **3c**-NH.

The assigned absolute stereochemistry was interpolated to other compounds in the series. The relative stereochemistry of spiro-oxindoles **3g**–**j** was determined by NOESY NMR experiments (for details, see the Supporting Information).

In an additional experiment, non-cyclic Michael adduct **4c** (6:1 mixture of diastereoisomers) was cyclized in the presence of organocatalysts **II** or **V** (Scheme 2). The reaction was very slow, indicating the importance of the catalyst/substrate complex throughout the cascade reaction. Diastereoisomers of **4c** cyclized in the presence of catalyst **II** with different rates, and the diastereomeric ratio of recovered **4c** changed to 20:1. In the presence of catalyst **V**, the ratio remained unchanged. It is known that 3-chlorooxindoles afford the *syn*-product in Michael addition to nitrostyrenes,[5a] but the relative stereochemistry of non-cyclized intermediate **4c** was not determined because during the cyclization the stereogenic center at C3 is lost. Although the racemic product **3c** was obtained from the starting materials in the presence of an inorganic base, no reaction with non-cyclic intermediate **4c** was observed under the same conditions using the same base. This study also suggests that the stereochemistry of the final product **3c** is determined in the first step of the cascade (Michael addition) because two different chiral organocatalysts **II** and **V** afforded the same enantiomer in reaction with non-cyclic intermediate **4c**, whereas enantiomers of **3c** were obtained in separate reactions with starting materials **1a** and **2c**.

Conclusions

Herein, we have described the synthesis of spiro-oxindoles through asymmetric organocatalytic reaction of symmetric unsaturated 1,4-diketones and 3-chlorooxindoles. This methodology provides products **3a**–**f** with two identically substituted tertiary stereocenters in moderate yields and with very high diastereo- and enantioselectivities. In the case of unsaturated 1,4-keto esters and non-symmetric diketones, the first conjugated addition is highly regioselective and provides spiro-oxindoles **3g**–**j** containing two tertiary and one quaternary center with excellent diastereoselectivity.

Experimental Section

General Methods and Materials: Full assignment of ^{1}H and ^{13}C chemical shifts was based on the 1D and 2D FT NMR spectra obtained with a Bruker Avance III 400 MHz instrument. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$: δ = 7.26/77.16 ppm; DMSO: δ = 2.50/39.52 ppm). HRMS spectra were recorded with an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS spectrometer by using AJ-ESI ionization. Optical rotations were obtained with an Anton Paar GWB Polarimeter MCP500. Chiral HPLC was performed using a Chiralpak AD-H column. Precoated silica gel 60 F_{254} plates were used for TLC, and Merck silica gel was used for column chromatog-

raphy. Chiral catalysts **IV** and **V** were commercially available from Aldrich or Strem, and **I**, **II** and **III** were prepared according to reported procedures.[13,14] Commercial reagents were generally used as received. CH_2Cl_2 and EtOAc were distilled from P_2O_5.

General Procedure for the Synthesis of *N*-Boc-Oxindoles: *N*-Boc-oxindoles were prepared according to a reported procedure from commercially available oxindoles.[15] To a solution of the corresponding oxindoles (1 equiv.) in anhydrous THF (0.25 M), Na_2CO_3 (9 equiv.) and Boc_2O (2.5 equiv.) were added at room temperature and the resulting mixture was stirred at 70 °C for 12 h. The solid was filtered off and the solvent was evaporated. The crude product was purified by silica gel column chromatography (heptane/ethyl acetate, 10:1).

***tert*-Butyl 2-Oxoindoline-1-carboxylate:** The title compound was obtained as a pink solid in 70% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (ddd, J = 8.2, 1.0, 0.5 Hz, 1 H, ArH), 7.30 (dddt, J = 8.4, 7.5, 1.6, 0.9 Hz, 1 H, ArH), 7.24 (ddd, J = 7.4, 1.4, 0.6 Hz, 1 H, ArH), 7.13 (td, J = 7.5, 1.1 Hz, 1 H, ArH), 3.65 (s, 2 H, CH_2), 1.65 (s, 9 H, Boc) ppm.

***tert*-Butyl 5-Bromo-2-oxoindoline-1-carboxylate:** The title compound was obtained as a pink solid in 53% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, J = 8.7 Hz, 1 H, ArH), 7.42 (ddt, J = 8.7, 1.8, 0.8 Hz, 1 H, ArH), 7.39–7.36 (m, 1 H, ArH), 3.64 (s, 2 H, CH_2), 1.63 (s, 9 H, Boc) ppm.

General Procedure for the Synthesis of *N*-Boc-3-chlorooxindoles 1a and 1b: A solution of corresponding *N*-Boc-oxindoles (1 equiv.) in THF (0.7 M) was added over 10 min at –78 °C to a solution of LiHMDS [generated in situ from *n*BuLi (1.6 M in hexanes, 2.2 equiv.) and hexamethyldisilazane (2.3 equiv.) in THF (0.5 M) at 0 °C]. The mixture was stirred at –78 °C for 40 min, then *N*-chlorosuccinimide (1.05 equiv.) was added in one portion. The mixture was warmed slowly to room temperature and stirred overnight. A mixture of saturated aqueous NH_4Cl and H_2O (1:1) was added, and the mixture was extracted with CH_2Cl_2. The combined organic fractions were dried with $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (heptane/ethyl acetate, 7:1).

***tert*-Butyl 3-Chloro-2-oxoindoline-1-carboxylate (1a):** The title compound was obtained as a red amorphous solid in 49% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.3 Hz, 1 H, ArH), 7.45 (d, J = 7.5 Hz, 1 H, ArH), 7.40 (dddd, J = 8.3, 7.7, 1.4, 0.8 Hz, 1 H, ArH), 7.22 (td, J = 7.6, 1.0 Hz, 1 H, ArH), 5.23 (s, 1 H, CH), 1.64 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.96, 148.84, 140.09, 130.88, 125.71, 125.25, 124.56, 115.58, 85.28, 52.10, 28.17 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{14}ClNO_3Na^+$ $[M + Na]^+$ 290.0554; found 290.0566.

***tert*-Butyl 5-Bromo-3-chloro-2-oxoindoline-1-carboxylate (1b):** The title compound was obtained as a red amorphous solid in 12% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, J = 8.7 Hz, 1 H, ArH), 7.60–7.54 (m, 1 H, ArH), 7.52 (ddd, J = 8.7, 2.1, 0.7 Hz, 1 H, ArH), 5.20 (d, J = 1.0 Hz, 1 H, CH), 1.63 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.07, 148.66, 139.11, 133.86, 128.76, 126.48, 118.13, 117.29, 85.71, 51.36, 28.16 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{13}BrClNO_3Na^+$ $[M + Na]^+$ 367.9660; found 367.9674.

General Procedure for the Synthesis of Symmetric Unsaturated 1,4-Diketones 2a–d: Synthesized by Friedel–Crafts acylation reaction according to a reported procedure from the corresponding substituted benzenes and fumaryl chloride.[16]

(*E*)-1,4-Bis(4-bromophenyl)but-2-ene-1,4-dione (2a): Obtained as a tan brown solid in 46% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 2 H, 2× CH), 7.92 (d, J = 8.7 Hz, 4 H, 4× ArH), 7.68 (d, J = 8.7 Hz, 4 H, ArH, 4× ArH) ppm.

(*E*)-1,4-Diphenylbut-2-ene-1,4-dione (2b): Obtained as a bright-yellow solid in 70% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.03 (m, 4 H, 4× ArH), 8.01 (s, 2 H, 2× CH), 7.66–7.60 (m, 2 H, 2× ArH), 7.56–7.49 (m, 4 H, 4× ArH) ppm.

(*E*)-1,4-Di-*p*-tolylbut-2-ene-1,4-dione (2c): Obtained as a yellow solid in 45% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (s, 2 H, 2× CH), 7.97 (d, J = 8.2 Hz, 4 H, 4× ArH), 7.32 (d, J = 8.0 Hz, 4 H, 4× ArH), 2.45 (s, 6 H, 2× $ArCH_3$) ppm.

(*E*)-1,4-Bis(4-chlorophenyl)but-2-ene-1,4-dione (2d): Obtained as a bright-yellow solid in 46% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.7 Hz, 4 H, 4× ArH), 7.98 (s, 2 H, 2× CH), 7.51 (d, J = 8.7 Hz, 4 H, 4× ArH) ppm.

(*E*)-1,4-Bis(4-nitrophenyl)but-2-ene-1,4-dione (2e): The title compound was prepared by a two-step procedure. In the first step, *p*-nitroacetophenone was transformed into *p*-nitro-α-oxo-benzeneacetaldehyde by using a reported procedure.[17] In the second step, *p*-nitro-α-oxo-benzeneacetaldehyde (375 mg; 2.09 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL), and a solution of 1-*p*-nitrophenyl-2-triphenylphosphoranylidene-ethanone (1.2 g; 2.8 mmol/10 mL) in CH_2Cl_2 was added dropwise. After 10 min, a yellow solid started to precipitate. After completion of the reaction, the mixture was filtered, and the solid was washed with cold chloroform. The solid was recrystallized from the mixture of chloroform and ethyl acetate to give **3e** (450 mg, 66% yield). ^{1}H NMR (400 MHz, DMSO): δ = 8.39 (d, J = 8.9 Hz, 4 H, 4× ArH), 8.31 (d, J = 8.9 Hz, 4 H, 4× ArH), 7.94 (s, 2 H, 2× CH) ppm.

General Procedure for the Synthesis of Nonsymmetric Unsaturated 1,4-Diketones and Keto Esters 2g–j: Prepared by an in situ oxidation-Wittig reaction sequence according to a reported procedure from the corresponding Wittig reagents and either hydroxyacetone or methyl glycolate.[18]

(*E*)-1-Phenylpent-2-ene-1,4-dione (2g): Obtained as a light-yellow solid in 88% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02–7.95 (m, 2 H, 2× ArH), 7.70 (d, J = 15.8 Hz, 1 H, CH), 7.66–7.60 (m, 1 H, ArH), 7.55–7.49 (m, 2 H, 2× ArH), 7.09 (d, J = 15.7 Hz, 1 H, CH), 2.44 (s, 3 H, CH_3) ppm.

(*E*)-1-(4-Nitrophenyl)pent-2-ene-1,4-dione (2h): Obtained as a light-yellow solid in 78% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (d, J = 8.8 Hz, 2 H, 2× ArH), 8.14 (d, J = 8.9 Hz, 2 H, 2× ArH), 7.66 (d, J = 15.7 Hz, 1 H, CH), 7.14 (d, J = 15.7 Hz, 1 H, CH), 2.46 (s, 3 H, CH_3) ppm.

(*E*)-Methyl-4-oxo-4-(*p*-tolyl)but-2-enoate (2i): Obtained as an orange solid in 85% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 15.6 Hz, 1 H, CH), 7.91 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.31 (d, J = 8.0 Hz, 2 H, 2× ArH), 6.88 (d, J = 15.5 Hz, 1 H, CH), 3.84 (s, 3 H, OCH_3), 2.43 (s, 3 H, $ArCH_3$) ppm.

(*E*)-Methyl-4-(4-chlorophenyl)-4-oxobut-2-enoate (2j): The title compound was obtained as a yellow solid in 87% yield according to the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.7 Hz, 2 H, 2× ArH), 7.87 (d, J = 15.5 Hz, 1 H, CH),

7.48 (d, J = 8.7 Hz, 2 H, 2× ArH), 6.89 (d, J = 15.5 Hz, 1 H, CH), 3.85 (s, 3 H, OCH_3) ppm.

General Procedure for the Asymmetric Synthesis of Spirocyclopropane Oxindoles 3a–j: Unsaturated 1,4-dicarbonyl compound **2** (1 equiv., 0.1 mmol), *N*-Boc 3-chlorooxindole **1** (1.2 equiv., 0.12 mmol), $NaHCO_3$ (2 equiv., 16.8 mg, 0.2 mmol) and thiourea **II** (10 mol-%, 6.0 mg) were dissolved in toluene (0.5 mL) and stirred at room temp. for 48 h. The progress of the reaction was monitored by NMR spectroscopy. Upon completion of the reaction, the mixture was directly purified by silica gel column chromatography (heptane/ethyl acetate). The diastereomeric ratio was determined by ^{1}H NMR spectroscopic analysis of the crude mixture and the enantiomeric purity was determined by chiral HPLC analysis.

(2*S*,3*S*)-*tert*-Butyl 2,3-Bis(4-bromobenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3a): The title compound was synthesized according to the general procedure from *N*-Boc 3-chlorooxindole **1a** and (*E*)-1,4-bis(4-bromophenyl)but-2-ene-1,4-dione (**2a**). Product was isolated as a single diastereoisomer in 67% yield (42 mg) as a reddish solid with *dr* 10:1 (^{1}H NMR analysis of crude material) and *ee* 86% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 9:1; 1 mL/min; 25 °C; 230 nm; t_R = 18.5 (major), 24.0 (minor) min]. $[\alpha]_D^{25}$ = +180.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.2 Hz, 1 H, oxindole-H), 7.83 (d, J = 8.6 Hz, 2 H, 2× ArH), 7.67 (d, J = 8.5 Hz, 2 H, 2× ArH), 7.58 (d, J = 8.6 Hz, 2 H, 2× ArH), 7.53 (d, J = 8.5 Hz, 2 H, 2× ArH), 7.34 (td, J = 8.0, 1.3 Hz, 1 H, oxindole-H), 7.30 (dd, J = 7.8, 1.3 Hz, 1 H, oxindole-H), 7.15 (td, J = 7.6, 1.1 Hz, 1 H, oxindole-H), 4.35 (d, J = 8.0 Hz, 1 H, CH), 4.08 (d, J = 8.0 Hz, 1 H, CH), 1.57 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 190.7, 189.0, 169.7, 148.8, 140.4, 135.3, 134.9, 132.4, 132.3, 130.3, 130.1, 129.8, 129.3, 129.3, 124.9, 122.7, 122.0, 115.4, 85.3, 41.3, 40.5, 40.0, 28.2 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{29}H_{23}Br_2NO_5Na^+$ [M + Na]$^+$ 645.9835; found 645.9847.

[(2*S*,3*S*)-2′-Oxospiro(cyclopropane-1,3′-indoline)-2,3-diyl]bis[(4-bromophenyl)methanone] (3a-NH): To a stirred solution of **3a** (30 mg, 0.049 mmol) in chloroform (5 mL) was added trifluoroacetic acid (0.5 mL) at 0 °C. After stirring for 1 h at room temp. the mixture was concentrated to give the pure product (30 mg, quant) as a white solid. ^{1}H NMR (400 MHz, DMSO): δ = 10.78 (s, 1 H, NH), 7.80 (d, J = 8.7 Hz, 2 H, 2× ArH), 7.73 (d, J = 8.7 Hz, 2 H, 2× ArH), 7.70 (d, J = 8.6 Hz, 2 H, 2× ArH), 7.62 (d, J = 8.6 Hz, 2 H, 2× ArH), 7.21 (td, J = 7.7, 1.2 Hz, 1 H, oxindole-H), 7.05 (d, J = 7.4 Hz, 1 H, oxindole-H), 6.94 (td, J = 7.6, 0.9 Hz, 1 H, oxindole-H), 6.89 (d, J = 7.7 Hz, 1 H, oxindole-H), 4.38 (d, J = 7.8 Hz, 1 H, CH), 4.06 (d, J = 7.8 Hz, 1 H, CH) ppm. ^{13}C NMR (101 MHz, DMSO): δ = 191.1, 190.4, 172.1, 142.6, 135.1, 134.9, 132.2, 132.0, 130.0, 129.8, 128.6, 128.4, 127.9, 123.6, 121.9, 121.7, 110.1, 38.3, 38.1 ppm. HRMS (ESI): *m*/*z* $C_{24}H_{15}Br_2NO_3Na^+$ calcd. for [M + Na]$^+$ 545.9311; found 545.9311.

(2*S*,3*S*)-*tert*-Butyl 2,3-Dibenzoyl-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3b): Synthesized according to the general procedure from *N*-Boc 3-chlorooxindole **1a** and (*E*)-1,4-diphenylbut-2-ene-1,4-dione (**2b**). The product was isolated as a single diastereoisomer in 58% yield (27 mg) as a pink solid with *dr* 10:1 (^{1}H NMR analysis of crude material) and *ee* 75% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 9:1; 1 mL/min; 25 °C; 230 nm; t_R = 12.27 (major), 18.8 (minor) min]. $[\alpha]_D^{25}$ = +387.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.96 (m, 2 H, 2× ArH), 7.89 (d, J = 8.1 Hz, 1 H, oxindole-H), 7.86–7.81 (m, 2 H, 2× ArH), 7.59–7.51 (m, 2 H, 2× ArH), 7.48–7.42 (m, 2 H, 2× ArH), 7.42–7.35 (m, 3 H, 2× ArH, oxindole-H), 7.32 (td, J = 8.0, 1.4 Hz, 1 H, oxindole-H), 7.15 (td, J = 7.7, 1.0 Hz, 1 H, oxindole-H), 4.45 (d, J = 8.1 Hz, 1 H, CH), 4.16 (d, J = 8.1 Hz, 1 H, CH), 1.57 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 191.7, 190.0, 169.8, 149.0, 140.4, 136.7, 136.2, 134.2, 133.8, 129.0, 128.9, 128.8, 128.7, 124.8, 123.2, 122.1, 115.2, 85.0, 41.4, 40.8, 40.3, 28.2 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{29}H_{25}NO_5Na^+$ [M + Na]$^+$ 490.1625; found 490.1639.

(2*S*,3*S*)-*tert*-Butyl 2,3-Bis(4-methylbenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3c): (*E*)-1,4-di-*p*-tolylbut-2-ene-1,4-dione (**2c**; 1 equiv., 0.1 mmol), *N*-Boc 3-cholrooxindole **1a** (1.2 equiv., 0.12 mmol), $NaHCO_3$ (2 equiv., 16.8 mg, 0.2 mmol), and thiourea **II** (10 mol-%, 6.0 mg) were dissolved in toluene (0.5 mL) and stirred at room temp. for 96 h. Product was isolated as a single diastereoisomer in 64% yield (32 mg) as a pink solid with *dr* 10:1 (^{1}H NMR analysis of crude material) and *ee* 77% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 9:1; 1 mL/min; 20 °C; 230 nm; t_R = 17.9 (major), 22.1 (minor) min]. $[\alpha]_D^{25}$ = +209.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.87 (ddd, J = 8.2, 1.0, 0.5 Hz, 1 H, oxindole-H), 7.73 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.34 (ddd, J = 7.7, 1.3, 0.5 Hz, 1 H, oxindole-H), 7.30 (ddd, J = 8.2, 7.7, 1.4 Hz, 1 H, oxindole-H), 7.23 (d, J = 7.9 Hz, 2 H, 2× ArH), 7.18 (d, J = 7.9 Hz, 2 H, 2× ArH), 7.13 (td, J = 7.7, 1.1 Hz, 1 H, oxindole-H), 4.42 (d, J = 8.1 Hz, 1 H, CH), 4.13 (d, J = 8.1 Hz, 1 H, CH), 2.37 (s, 3 H, $ArCH_3$), 2.36 (s, 3 H, $ArCH_3$), 1.56 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 191.3, 189.7, 169.9, 149.0, 145.2, 144.7, 140.4, 134.3, 133.9, 129.6, 129.6, 129.0, 128.8, 128.7, 124.8, 123.4, 122.1, 115.2, 84.9, 41.2, 40.9, 40.4, 28.1, 21.9, 21.8 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{29}NO_5Na^+$ [M + Na]$^+$ 518.1938; found 518.1948.

***tert*-Butyl 3-Chloro-3-(1,4-dioxo-1,4-di-*p*-tolylbutan-2-yl)-2-oxoindoline-1-carboxylate (4c):** Obtained as a side product in the synthesis of **3c**. Compound **4c** (8.5 mg, 16%) was isolated as a red solid with *dr* 5:1 (^{1}H NMR analysis of crude material). For the main isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.89–7.84 (m, 3 H, 2× ArH, oxindole-H), 7.45 (dd, J = 7.6, 0.8 Hz, 1 H, oxindole-H), 7.31–7.27 (m, 1 H, oxindole-H), 7.26–7.23 (m, 2 H, 2× ArH), 7.19 (d, J = 7.9 Hz, 2 H, 2× ArH), 7.05 (td, J = 7.6, 1.0 Hz, 1 H, oxindole-H), 5.48 (t, J = 5.3 Hz, 1 H, CH), 4.50 (dd, J = 18.7, 5.0 Hz, 1 H, CH_2), 3.34 (dd, J = 18.7, 5.6 Hz, 1 H, CH_2), 2.40 (s, 3 H, $ArCH_3$), 2.35 (s, 3 H, $ArCH_3$), 1.70 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.3, 196.8, 171.8, 149.2, 144.8, 144.6, 139.3, 133.7, 133.0, 130.7, 129.5, 129.5, 129.2, 128.8, 127.8, 125.0, 123.9, 115.7, 85.0, 64.1, 50.7, 37.3, 28.3, 21.8, 21.8 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_3OClNO_5Na^+$ [M + Na]$^+$ 554.1705; found 554.1709.

(1*s*,2*R*,3*S*)-*tert*-Butyl 2,3-Bis(4-methylbenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (5c): Obtained as a side product in the synthesis of **3c**. Compound **5c** (4.3 mg, 9%) was isolated as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.0 Hz, 1 H, oxindole-H), 7.84 (d, J = 8.2 Hz, 4 H, 4× ArH), 7.39 (td, J = 7.9, 1.3 Hz, 1 H, oxindole-H), 7.23 (td, J = 7.5, 1.0 Hz, 1 H, oxindole-H), 7.21 (d, J = 8.0 Hz, 4 H, 4× ArH), 7.03 (dd, J = 7.5, 0.8 Hz, 1 H, oxindole-H), 3.61 (s, 2 H, 2× CH), 2.38 (s, 6 H, 2× $ArCH_3$), 1.54 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 189.3, 167.6, 149.6, 144.2, 140.3, 134.4, 129.4, 128.9, 128.7, 127.2, 124.4, 118.1, 115.5, 84.4, 42.9, 36.7, 28.2, 21.9 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{29}NO_5Na^+$ [M + Na]$^+$ 518.1938; found 518.1940.

[(2*S*,3*S*)-2′-Oxospiro(cyclopropane-1,3′-indoline)-2,3-diyl]bis(*p*-tolylmethanone) (3c-NH): To a stirred solution of **3c** (30 mg, 0.06 mmol) in chloroform (5 mL) was added trifluoroacetic acid (0.5 mL) at

0 °C. After stirring for 1 h at room temp. the mixture was concentrated to give pure product (23 mg, quant) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (s, 1 H, NH), 7.85 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.72 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.31 (d, J = 7.6 Hz, 1 H, oxindole-H), 7.22 (td, J = 7.8, 1.0 Hz, 1 H, oxindole-H), 7.15 (d, J = 8.2 Hz, 2 H, 2× ArH), 7.14 (d, J = 8.1 Hz, 2 H, 2× ArH), 7.01 (td, J = 7.7, 0.9 Hz, 1 H, oxindole-H), 6.90 (d, J = 7.8 Hz, 1 H, oxindole-H), 4.38 (d, J = 7.9 Hz, 1 H, CH), 4.14 (d, J = 7.9 Hz, 1 H, CH), 2.34 (s, 3 H, $ArCH_3$), 2.33 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 190.5, 189.1, 172.2, 143.9, 143.5, 140.2, 133.2, 132.7, 128.5, 128.4, 127.7, 127.5, 127.4, 123.5, 121.7, 121.6, 109.2, 39.9, 38.6, 37.8, 20.7 (2× C) ppm. HRMS (ESI): m/z calcd. for $C_{26}H_{21}NO_3Na^+$ $[M + Na]^+$ 418.1414; found 418.1425.

(2*S*,3*S*)-*tert*-Butyl 2,3-Bis(4-chlorobenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3d): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1a** and (*E*)-1,4-bis(4-chlorophenyl)but-2-ene-1,4-dione (**2d**). The product was isolated as a single diastereoisomer in 81% yield (43 mg) as a pink solid with *dr* 20:1 (^{1}H NMR analysis of crude material) and *ee* 87% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 9:1; 1 mL/min; 25 °C; 230 nm; t_R = 16.9 (major), 19.7 (minor) min]. $[\alpha]_D^{25}$ = +257.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 8.7 Hz, 2 H, 2× ArH), 7.89 (d, J = 7.9 Hz, 1 H, oxindole-H), 7.75 (d, J = 8.6 Hz, 2 H, 2× ArH), 7.40 (d, J = 8.7 Hz, 2 H, 2× ArH), 7.36 (d, J = 8.6 Hz, 2 H, 2× ArH), 7.34–7.29 (m, 2 H, 2× oxindole-H), 7.15 (td, J = 7.7, 0.9 Hz, 1 H, oxindole-H), 4.36 (d, J = 8.0 Hz, 1 H, CH), 4.09 (d, J = 8.0 Hz, 1 H, CH), 1.57 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 190.4, 188.8, 169.7, 148.8, 140.9, 140.4, 140.4, 134.8, 134.5, 130.2, 130.0, 129.3, 129.3, 129.2, 124.9, 122.7, 122.0, 115.4, 85.2, 41.3, 40.5, 40.0, 28.1 ppm. HRMS (ESI): m/z calcd. for $C_{29}H_{23}Cl_2NO_5Na^+$ $[M + Na]^+$ 558.0845; found 558.0859.

(2*S*,3*S*)-*tert*-Butyl 2,3-Bis(4-nitrobenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3e): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1a** and (*E*)-1,4-bis-(4-nitrophenyl)but-2-ene-1,4-dione (**2e**). The product was isolated as a single diastereoisomer in 60% yield (33 mg) as a light-orange solid with *dr* 9:1 (^{1}H NMR analysis of crude material) and *ee* 87% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 8:2; 1 mL/min; 25 °C; 230 nm; t_R = 53.5 (major), 61.2 (minor) min]. $[\alpha]_D^{25}$ = +222.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, J = 8.9 Hz, 2 H, 2× ArH), 8.25 (d, J = 8.9 Hz, 2 H, 2× ArH), 8.12 (d, J = 8.9 Hz, 2 H, 2× ArH), 7.97 (d, J = 8.9 Hz, 2 H, 2× ArH), 7.90 (d, J = 8.2 Hz, 1 H, oxindole-H), 7.38 (ddd, J = 8.3, 7.6, 1.4 Hz, 1 H, oxindole-H), 7.32 (dd, J = 7.8, 0.8 Hz, 1 H, oxindole-H), 7.18 (td, J = 7.7, 1.1 Hz, 1 H, oxindole-H), 4.41 (d, J = 7.8 Hz, 1 H, CH), 4.17 (d, J = 7.8 Hz, 1 H, CH), 1.56 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 190.3, 188.4, 169.4, 151.0, 150.8, 148.5, 140.6, 140.5, 140.1, 129.9, 129.8, 129.6, 125.1, 124.3, 124.2, 122.0, 121.8, 115.7, 85.6, 41.8, 40.3, 40.2, 28.1 ppm. HRMS (ESI): m/z calcd. for $C_{29}H_{23}N_3O_9Na^+$ $[M + Na]^+$ 580.1327; found 580.1342.

(2*S*,3*S*)-*tert*-Butyl 2,3-Dibenzoyl-5′-bromo-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3f): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1b** and (*E*)-1,4-diphenylbut-2-ene-1,4-dione (**2b**). The product was isolated as a single diastereoisomer in 59% yield (32 mg) as a light-orange solid with *dr* 8:1 (^{1}H NMR analysis of crude material) and *ee* 71% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 9:1; 1 mL/min; 25 °C; 230 nm; t_R = 9.7 (major), 13.1 (minor) min]. $[\alpha]_D^{25}$ = +215.5 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–7.98 (m, 2 H, 2× ArH), 7.86–7.82 (m, 2 H, 2× ArH), 7.80 (d, J = 8.7 Hz, 1 H, oxindole-H), 7.63–7.52 (m, 3 H, 2× ArH, oxindole-H), 7.50–7.38 (m, 5 H, 4× ArH, oxindole-H), 4.46 (d, J = 8.1 Hz, 1 H, CH), 4.13 (d, J = 8.1 Hz, 1 H, CH), 1.55 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 191.4, 189.6, 169.0, 148.8, 139.5, 136.6, 136.0, 134.3, 134.0, 132.0, 129.0, 129.0, 128.9, 128.7, 125.4, 125.3, 117.9, 116.8, 85.4, 41.2, 40.9, 40.4, 28.1 ppm. HRMS (ESI): m/z calcd. for $C_{29}H_{24}Br_1NO_5Na^+$ $[M + Na]^+$ 568.0730; found 568.0748.

(1*S*,2*S*,3*S*)-*tert*-Butyl 2-Acetyl-3-benzoyl-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3g): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1a** and (*E*)-1-phenylpent-2-ene-1,4-dione (**2g**). The product was isolated as a single diastereoisomer in 53% yield (21 mg) as a pink solid with *dr* > 20:1 (^{1}H NMR analysis of crude material) and *ee* 72% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 8:2; 1 mL/min; 25 °C; 230 nm; t_R = 10.1 (major), 7.7 (minor) min]. $[\alpha]_D^{25}$ = +181.9 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.2 Hz, 1 H, oxindole-H), 7.80–7.75 (m, 2 H, 2× ArH), 7.52 (tt, J = 7.0, 1.2 Hz, 1 H, ArH), 7.42–7.32 (m, 4 H, 2× ArH, 2× oxindole-H), 7.20 (td, J = 7.6, 0.9 Hz, 1 H, oxindole-H), 3.91 (d, J = 8.1 Hz, 1 H, CH), 3.77 (d, J = 8.1 Hz, 1 H, CH), 2.29 (s, 3 H, $COCH_3$), 1.55 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.2, 189.8, 169.7, 149.0, 140.5, 136.0, 133.9, 129.1, 128.9, 128.6, 124.8, 122.9, 122.3, 115.3, 85.0, 43.4, 41.1, 40.4, 32.1, 28.1 ppm. HRMS (ESI): m/z calcd. for $C_{24}H_{23}NO_5Na^+$ $[M + Na]^+$ 428.1468; found 428.1476.

(1*S*,2*S*,3*S*)-*tert*-Butyl 2-Acetyl-3-(4-nitrobenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′-carboxylate (3h): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1a** and (*E*)-1-(4-nitrophenyl)pent-2-ene-1,4-dione (**2h**). The product was isolated as a single diastereoisomer in 62% yield (28 mg) as a red solid with *dr* > 20:1 (^{1}H NMR analysis of crude material) and *ee* 68% for the major isomer [Chiralpak AD-H; Hex/*i*PrOH, 8:2; 1 mL/min; 25 °C; 230 nm; t_R = 12.8 (major), 37.6 (minor) min]. $[\alpha]_D^{25}$ = +261.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (d, J = 8.8 Hz, 2 H, 2× Ar), 7.96–7.90 (m, 3 H, 2× Ar, oxindole-H), 7.41 (ddd, J = 8.3, 7.6, 1.4 Hz, 1 H, oxindole-H), 7.32 (dd, J = 7.7, 0.9 Hz, 1 H, oxindole-H), 7.22 (td, J = 7.6, 1.0 Hz, 1 H, oxindole-H), 3.91 (d, J = 8.0 Hz, 1 H, CH), 3.75 (d, J = 8.0 Hz, 1 H, CH), 2.30 (s, 3 H, $COCH_3$), 1.55 (s, 9 H, Boc) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 199.7, 188.8, 169.7, 150.7, 148.7, 140.4, 140.3, 129.5 (2× C), 125.0, 124.2, 122.3, 122.2, 115.5, 85.3, 43.3, 41.0, 39.8, 32.0, 28.1 ppm. HRMS (ESI): m/z calcd. for $C_{24}H_{22}N_2O_7Na^+$ $[M + Na]^+$ 473.1319; found 473.1319.

(1*R*,2*S*,3*S*)-1′-*tert*-Butyl 2-Methyl-3-(4-methylbenzoyl)-2′-oxospiro[cyclopropane-1,3′-indoline]-1′,2-dicarboxylate (3i): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1a** and (*E*)-methyl-4-oxo-4-(*p*-tolyl)but-2-enoate (**2i**). The product was isolated as an inseparable mixture (13 mg) of **3i** (*dr* > 20:1) and one of the diastereoisomers of **4i** with ratio 1.2:1 (^{1}H NMR analysis of crude material). ^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of **3i** and **4i**, normalized to **3i**) = 7.97–7.90 (m, 3.48 H, ArH **4i**, oxindole-H **4i**, oxindole-H **3i**), 7.68 (d, J = 8.2 Hz, 2 H, 2× ArH **3i**), 7.52 (dd, J = 7.8, 0.9 Hz, 1 H, oxindole-H **3i**), 7.44 (dd, J = 7.7, 1.1 Hz, 0.8 H, oxindole-H **4i**), 7.43–7.37 (m, 1.9 H, 2× oxindole-H **4i**), 7.30 (d, J = 8.0 Hz, 1.7 H, 2× ArH **4i**), 7.22 (tdd, J = 7.6, 3.6, 1.0 Hz, 2 H, 2× oxindole-H **3i**), 7.17 (d, J = 8.0 Hz, 2 H, 2× ArH **3i**), 4.26 (dd, J = 10.5, 2.7 Hz, 0.8 H, CH **4i**), 3.94 (dd, J = 17.4, 10.5 Hz, 0.9 H, CH_2 **4i**), 3.82 (d, J = 8.1 Hz, 1 H, CH **3i**), 3.80 (dd, J = 17.4, 2.7 Hz, 0.8 H, CH_2 **4i**), 3.72 (s, 3 H, OCH_3 **3i**), 3.52 (d, J = 8.1 Hz, 1 H, CH **3i**), 3.45 (s, 2.5 H, OCH_3 **4i**), 2.43 (s, 2.4 H, $ArCH_3$ **4i**),

2.36 (s, 3 H, $ArCH_3$ **3i**), 1.67 (s, 8.4 H, Boc **4i**), 1.54 (s, 9 H, Boc **3i**) ppm. HRMS (ESI): *m/z* for **3i**: calcd. for $C_{25}H_{25}NO_6Na^+$ [M + Na]$^+$ 458.1574; found 458.1576. HRMS (ESI): *m/z* for **4i**: calcd. for $C_{25}H_{26}ClNO_6Na^+$ [M + Na]$^+$ 494.1341; found 494.1341.

(1*R*,2*S*,3*S*)-1′-*tert*-Butyl 2-Methyl-3-(4-chlorobenzoyl)-2′-oxospiro-[cyclopropane-1,3′-indoline]-1′,2-dicarboxylate (3j): Synthesized according to the general procedure from *N*-Boc-3-chlorooxindole **1a** and (*E*)-methyl-4-(4-chlorophenyl)-4-oxobut-2-enoate (**2j**). The product was isolated as an inseparable mixture (44 mg) of **3j** (*dr* > 20:1) and two diastereoisomers of **4j** with ratio 2:1.5:1 (^{1}H NMR analysis of crude material). ^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of **3j** and **4j**, normalized to **3j**) = 8.01–7.90 (m, 4.5 H), 7.88 (d, *J* = 8.2 Hz, 0.6 H, oxindole-H **4j**), 7.71 (d, *J* = 8.6 Hz, 2 H, 2× ArH **3j**), 7.55 (dd, *J* = 7.6, 1.3 Hz, 0.6 H, oxindole-H **4j**), 7.50 (dd, *J* = 7.9, 1.3 Hz, 1 H, oxindole-H **3j**), 7.49–7.37 (m, 5.9 H), 7.34 (d, *J* = 8.6 Hz, 2 H, 2× ArH **3j**), 7.25–7.17 (m, 2.2 H), 4.25 (dd, *J* = 10.5, 2.7 Hz, 0.8 H, CH **4j**), 4.20 (dd, *J* = 9.3, 3.5 Hz, 0.6 H, CH **4j**), 3.98–3.86 (m, 1.4 H, CH_2 **4j**), 3.83–3.74 (m, 1.37 H, CH_2 **4j**), 3.79 (d, *J* = 8.0 Hz, 1 H, CH **3j**), 3.72 (s, 3 H, OCH_3 **3j**), 3.49 (d, *J* = 8.0 Hz, 1 H, CH **3j**), 3.44 (s, 2.3 H, OCH_3 **4j**), 3.43 (s, 1.6 H, OCH_3 **4j**), 1.66 (s, 7.2 H, Boc **4j**), 1.66 (s, 5.3 H, Boc **4j**), 1.54 (s, 9 H, Boc **3j**) ppm. HRMS (ESI): *m/z* for **3j**: calcd. for $C_{24}H_{22}ClNO_6Na^+$ [M + Na]$^+$ 478.1028; found 478.1030. HRMS (ESI): *m/z* for **4j**: calcd. for $C_{24}H_{23}Cl_2NO_6Na^+$ [M + Na]$^+$ 514.0795; found 514.0800.

Supporting Information (see footnote on the first page of this article): Experimental data, computational details of the configuration assignment of **5c**, **3h**, and **3c**-NH. ^{1}H and ^{13}C NMR spectra, chiral HPLC chromatograms, and computational details.

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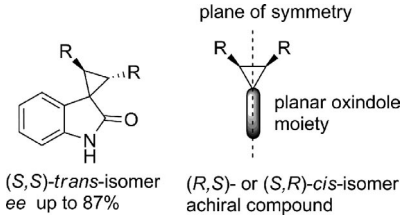
Symmetrically substituted *trans*-isomers of spirocyclopropane oxindole were obtained in high *ee* through asymmetric organocatalysis, whereas the racemic *cis*-isomer was only formed as a minor product.



Keywords: Organocatalysis / Asymmetric synthesis / Cyclization / Michael addition / Small ring systems

