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Highly Enantioselective Synthesis of Spiro[cyclohexanone-oxindoles] and Spiro[cyclohexanone-pyrazolones] by Asymmetric Cascade [5+1] Double Michael Reactions

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The asymmetric catalytic synthesis of naturally occurring and biologically active spiro compounds is a challenge for modern chemical methodology. Here we report the construction of spiro compounds through cascade [5+1] double Michael reactions between divinyl ketones and *N-unprotected* oxindoles or *N*-phenyl-protected pyrazolones catalyzed by a combination of the easily available 9-amino-9-deoxy-*epi*-quinine with *N*-Boc-D-phenylglycine. The desired multistereogenic spiro[cyclohexanone-oxindoles and -pyrazolones] were obtained with high yields (up to 98 %) and stereoselectivities (up to >20:1 *dr*, 99 % *ee*).

Introduction

Oxindoles[1] and pyrazolones[2] are two important types of structural motif, constituting core structural elements common in a large number of biologically active naturally occurring products and a series of pharmaceutically active compounds. Chitosenine (Figure 1), for instance, exhibits short-lived inhibitory activity of ganglionic transmission in vivo in rats and rabbits,[3] whereas NITD609 kills the blood stages of *Plasmodium falciparum* and *Plasmodium vivax*.[4] Strychnofoline inhibits mitosis in a number of cell lines[5] and aspidophylline A can reverse drug resistance in resistant KB cells.[6] Among the natural pyrazoline derivatives, the p38 inhibitor in Figure 1 is very important for treatment of inflammation[7] and the depicted HIV-1 integrase inhibitor[7–8] and hydantoin have been reported to display specific activities against bacteria.[9] Thanks to the broad biological activities and structural complexity of spirocyclic oxindole and pyrazolone compounds, the development of synthetically effective protocols for such compounds is of considerable topical interest.[10]

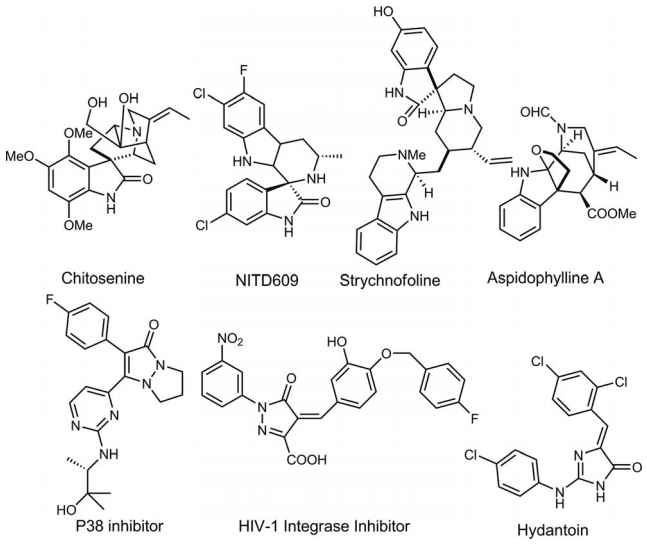

Figure 1. Naturally occurring and biologically active oxindole and pyrazoline derivatives.

Spiro[cyclohexanone-1,3′-indoline] and spiro[cyclohexanone-1,5′-pyrazolone] compounds, which are intriguing combinations of multistereogenic cyclohexanone and oxindole or pyrazolone motifs, are promising subsets with potential bioactivities. The asymmetric synthesis of the two classes of compounds involves the stereocontrolled installation of a spiro quaternary chiral carbon center, which has been a challenging goal for synthetic chemists.[11] In addition, another urgent goal for synthetic chemists is to find effective and sustainable methodologies to construct the multistereogenic centers of these complex structures in one-pot fashion and in a catalytic way.[12] Over the past decade, asymmetric organocatalysis, as a new and powerful methodology, has grown rapidly and become one of the most active and attractive research fields in organic chemistry.[13] Notably, organocatalytic cascade reactions are viewed as powerful tools for the synthesis of such spirocyclic oxindole and pyrazolone compounds.[14]

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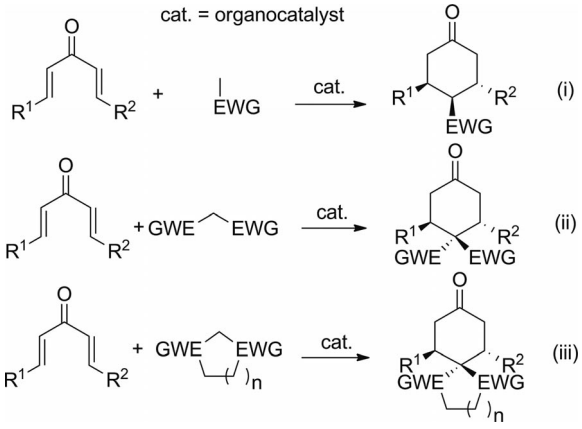
After Melchiorre and co-workers, in 2009, has pioneeringly achieved the organocatalytic synthesis of spiro[cyclohexanone-oxindoles] through a [4+2] tandem iminium and enamine catalytic sequence,[15] Gong's,[16] Wang's,[17] and our group[18] sequentially reported that the multistereogenic structures of spiro[cyclohexanone-oxindoles] can be constructed through asymmetric formal [4+2] cycloadditions or [4+2] domino double Michael additions catalyzed by Brønsted acid/Lewis base bifunctional organocatalysts or primary amine catalysts. Recently, Barbas III's group presented a remarkable organocatalytic methodology for the construction of bispiro-oxidoles containing three quaternary stereocenters in a cascade approach with use of a single multifunctional organocatalyst,[19] followed by an enantioselective synthesis of spiro[cyclopentene-oxindoles] through a phosphane-catalyzed [3+2] cycloaddition reaction.[20] During this period, more asymmetric organocatalytic methodologies for the construction of the intriguing spirocyclic oxindole skeletons in the presence of primary amines, secondary amines, or Brønsted acid/Lewis base bifunctional organocatalysts were successfully developed. They include a cascade Michael/Michael/aldol reaction[21] or a domino Michael/Michael/Michael/aldol reaction for spiro[cyclohexenecarbaldehyde-oxindoles],[22] a Michael/ketone aldol/dehydration domino reaction for spiro[cyclohexenone-oxindoles],[17] a formal [2+2+2] annulation for spiro[cyclohexanol-oxindoles] and spiro[cyclopiperidine-oxindoles],[23] a Knoevenagel/Michael cyclization for spiro[4*H*-pyran-oxindoles],[24] and direct asymmetric intermolecular aldol reaction for spiro[cyclooxazolidinethione-oxindoles].[25] On the other hand, there are only a few literature reports for the organocatalytically asymmetric synthesis of spiropyrazolone derivatives. In 2011, Rios et al. reported that spiro[cyclohexenecarbaldehyde-pyrazolones] bearing three or four contiguous chiral centers could be synthesized in a highly enantioselective manner through domino Michael/Michael/aldol/dehydration sequences between pyrazolones and enals[26] or between unsaturated pyrazolones, enolizable aldehydes, and enals catalyzed by secondary amine catalysts.[27]

To the best of our knowledge, divinyl ketones as latent electrophilic acceptors, aided by asymmetric organocatalysis, have only come to be exploited this year. Our group reported that a thiourea-modified cinchona alkaloid and a base catalyzed stepwise [5+1] cyclizations of divinyl ketones with nitromethane, furnishing optically active 4-nitrocyclohexanones with good yields, excellent diastereoselectivities, and high enantioselectivities (Scheme 1, Eq. i).[28] Yan and co-workers,[29] and later Lattanzi's group,[30] disclosed that 9-amino-9-deoxy-*epi*-quinine and quinine efficiently catalyze double-conjugate additions of malononitrile to dienones. Various 3,4,4,5-tetrasubstituted cyclohexanones were prepared with good yields and diastereoselectivities and excellent enantioselectivities (Scheme 1, Eq. ii). Otherwise, highly enantioselective [5+1] double Michael reactions of *N*-Boc- or *N*-CO_2Et-protected oxindoles as active methylene pronucleophiles with dienones were developed by Wang's group[31] to access spirocyclic oxindole derivatives with excellent enantioselectivities, catalyzed by a combination of a cinchona-based chiral primary amine and a BINOL-phosphoric acid (Scheme 1, Eq. iii).



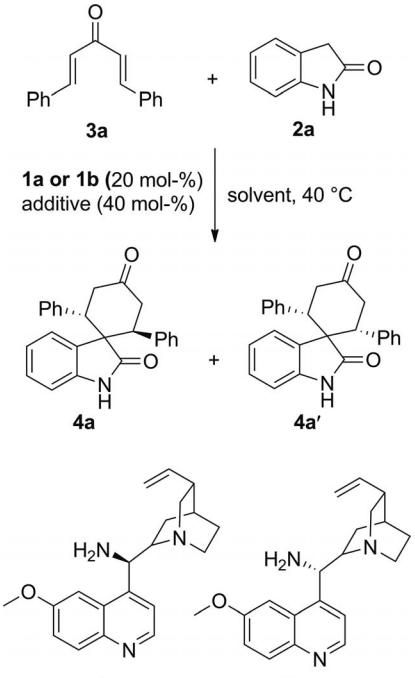
Scheme 1. Reported models for asymmetric cascade [5+1] double Michael additions of divinyl ketones with active methylene pronucleophiles.

Here we disclose that [5+1] double Michael additions between divinyl ketones and *N-unprotected* oxindoles or *N*-phenyl-protected pyrazolones can be efficiently catalyzed by amine-modified cinchona alkaloids and α-amino acid derivatives to afford the desired multistereogenic spiro[cyclohexanone-oxindoles] and spiro[cyclohexanone-pyrazolones] in moderate to high yields and with good to excellent diastereoselectivities and enantioselectivities.

Results and Discussion

Encouraged by previous success in establishing primary amine salts in asymmetric iminium ion catalysis, we began the investigation by testing the model reaction between *N*-unprotected oxindole **2a** (Table 1) and dienone **3a** catalyzed by primary amine **1a** (20 mol-%) and with TFA (40 mol-%) as additive in toluene at 40 °C. To our delight, the enantiomer **4a** was formed in 33% yield, with a good diastereoselectivity and 67% *ee* (Table 1, Entry 1). Use of the pseudoenantiomer **1b** under the same conditions afforded compound **4a** in 46% yield and with 88% *ee* (Table 1, Entry 2). Subsequently, a range of reaction conditions with primary amine **1b** (20 mol-%) were further investigated to improve the catalytic efficacy. When different benzoic acid derivatives were used, no obvious improvements in enantioselectivities were observed (Table 1, Entries 3–5 vs. 2). Increasing the amount of dienone **3a** relative to that of oxindole **2a** was found to improve the yield of **4a** considerably, with the best result (91% yield, 91% *ee*) obtained when two equivalents of **3a** were used in the reaction (Table 1, Entry 8). Asymmetric counterion-directed catalysis (ACDC)[32] has been recognized as an efficient strategy for enantioselective transformations, and so we turned our attention to chiral acids such as Boc-L-proline (Boc = *tert*-butyloxycarbonyl), Boc-L-Phg-OH, and Boc-D-Phg-OH as

Table 1. Screening studies of the asymmetric cascade [5+1] double Michael addition between oxindole **2a** and dienone **3a**.[a]



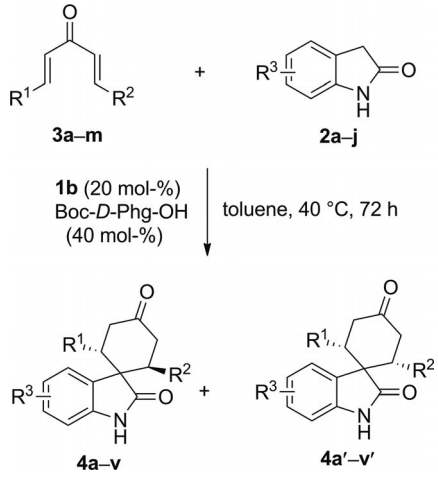
Entry	Additive	Solvent	Time [h]	Yield[b] [%]	*dr*[c]	*ee*[d] [%]
1[e]	TFA	PhMe	60	33	>20:1	67
2	TFA	PhMe	36	46	>20:1	88
3	4-$O_2NC_6H_4COOH$	PhMe	40	61	>20:1	90
4	4-FC_6H_4COOH	DCM	36	48	>20:1	88
5	2-IC_6H_4COOH	DCM	36	56	>20:1	90
6	TFA	PhMe	72	57	>20:1	90
7[f]	TFA	PhMe	72	61	>20:1	90
8[g]	TFA	PhMe	72	91	>20:1	91
9	Boc-L-proline	PhMe	40	50	6:1	86
10	Boc-L-Phg-OH	PhMe	40	52	19:1	93
11	Boc-D-Phg-OH	PhMe	40	56	>20:1	94
12	Boc-D-Phg-OH	PhMe	72	66	>20:1	94
13[g]	Boc-D-Phg-OH	PhMe	72	92	>20:1	94
14[g]	Boc-D-Phg-OH	DCM	72	88	>20:1	89
15[g]	Boc-D-Phg-OH	$CHCl_3$	72	85	>20:1	85
16[g]	Boc-D-Phg-OH	THF	72	67	13:1	87
17[g]	Boc-D-Phg-OH	EtOAc	72	72	>20:1	89

[a] Reactions were performed with **2a** (0.25 mmol), **3a** (0.3 mmol), catalyst **1b** (20 mol-%), and additive (40 mol-%), in solvent (1.0 mL) at 40 °C. [b] Isolated yields. [c] Determined by chiral HPLC or ^{1}H NMR spectroscopy. [d] Determined by chiral HPLC. [e] With catalyst **1a**. [f] With **3a** (0.375 mmol). [g] With **3a** (0.5 mmol).

additives. To our delight, the introduction of *N*-Boc-D-phenylglycine (40 mol-%) and **1b** (20 mol-%), established as an organocatalyst system for Michael additions by Melchiorre and co-workers,[33] resulted in the best enantiomeric excess (94% *ee*) for the reaction (Table 1, Entry 11). Again, when two equivalents of dienone **3a** were used, the reaction led to the desired product in the highest yield (92%) within 72 hours, albeit with the same stereoselectivity (Table 1, Entry 13). Other solvents were also examined, but toluene was still the best choice for this transformation (Table 1, Entries 14–17 vs. 13). Finally, we established optimized reaction conditions for the cascade [5+1] double Michael reaction between divinyl ketone **3a** and N-unprotected oxindole **2a**: a 1:2 molar ratio of **2a** to **3a**, a 20 mol-% catalyst loading of **1b** with 40 mol-% *N*-Boc-D-Phg-OH as additive, and toluene as the reaction solvent at 40 °C for 72 hours.

With the optimized reaction conditions to hand, we next proceed to examine the generality of the reaction, and the results are summarized in Table 2. A variety of substituents on dienones and *N*-unprotected oxindoles were tolerated well in this catalytic system, with the desired products being

Table 2. Asymmetric cascade [5+1] double Michael additions between *N-unprotected* oxindoles **2** and dienones **3**.[a]



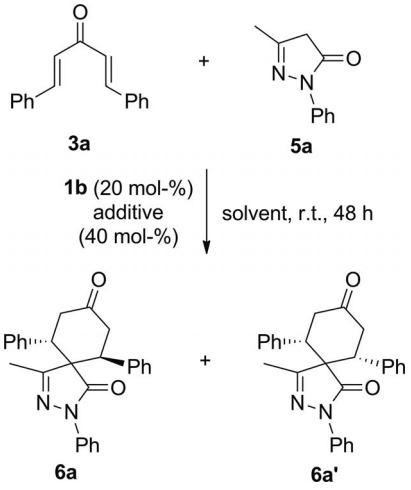
Entry	R^1, R^2	R^3	Yield[b] [%]	*dr*[c]	*ee*[d][e] [%]
1	Ph (**3a**)	H (**2a**)	**4a**/92	>20:1	94
2	4-$MeOC_6H_4$ (**3b**)	H (**2a**)	**4b**/97	>20:1	92
3	4-MeC_6H_4 (**3c**)	H (**2a**)	**4c**/75	>20:1	90
4	4-*i*PrC_6H_4 (**3d**)	H (**2a**)	**4d**/75	>20:1	90
5	4-FC_6H_4 (**3e**)	H (**2a**)	**4e**/83	>20:1	92
6	3-ClC_6H_4 (**3f**)	H (**2a**)	**4f**/84	>20:1	92
7	4-ClC_6H_4 (**3g**)	H (**2a**)	**4g**/70	>20:1	90
8	4-$CF_3C_6H_4$ (**3h**)	H (**2a**)	**4h**/78	>20:1	72
9	2-BrC_6H_4 (**3i**)	H (**2a**)	**4i**/69	>20:1	73
10	2,4-$Cl_2C_6H_3$ (**3j**)	H (**2a**)	**4j**/61	>20:1	90
11	1-naphthyl (**3k**)	H (**2a**)	**4k**/53	>20:1	77
12	2-thienyl (**3l**)	H (**2a**)	**4l**/67	>20:1	96
13	Ph (**3a**)	4-Cl (**2b**)	**4m**/79	13:1	96
14	Ph (**3a**)	4-Br (**2c**)	**4n**/96	10:1	97
15	Ph (**3a**)	5-Br (**2d**)	**4o**/92	>20:1	90
16	Ph (**3a**)	5-Cl-7-Me (**2e**)	**4p**/63	>20:1	96
17	Ph (**3a**)	5-F (**2f**)	**4q**/98	>20:1	96
18	Ph (**3a**)	6-Br (**2g**)	**4r**/91	>20:1	99
19	Ph (**3a**)	5-Cl (**2h**)	**4s**/98	>20:1	92
20	Ph (**3a**)	7-CF_3 (**2i**)	**4t**/86	9:1	97
21	Ph (**3a**)	5,6-$(F)_2$ (**2j**)	**4u**/94	>20:1	91
22	Ph, 4-ClC_6H_4 (**3m**)	H (**2a**)	**4v**/74	1.1:1	94

[a] Unless otherwise noted, the reactions were performed with **2** (0.25 mmol), **3** (0.5 mmol), catalyst **1b** (20 mol-%), and Boc-D-Phg-OH (40 mol-%) in toluene (1 mL) at 40 °C for 72 h. [b] Isolated yields. [c] Determined by chiral HPLC. [d] Determined by chiral HPLC. [e] Absolute configurations were determined by comparing the specific rotations of **4a** and **4s** with those reported in the literature.[15]

obtained in moderate to high yields (53–98%) and with excellent enantioselectivities (72–99% *ee*s). For divinyl ketones with different substituents on the phenyl groups (**3a**–**j**), electronic and steric properties had some effects on the reactivities (61–97% yields) and stereoselectivities (72–94% *ee*s), although the diastereoselectivities (>20:1) could be retained in all cases (Table 2, Entries 1–10). Generally, the presence of electron-donating substituents on the dienones resulted in products with higher yields and enantioselectivities, whereas that of electron-withdrawing substituents on the dienones resulted in products with lower yields and enantioselectivities. The sterically hindered dienone substrates **3i**–**k**, with *ortho*-substituents on their phenyl or naphthyl groups, turned out to be less reactive for this transformation, as evidenced by lower yields (Table 2, Entries 9–11). Pleasingly, the double Michael addition between dienone **3l**, bearing thiophen-2-yl groups, and oxindole **2a** performed very well to afford the desired product **4l** in good yield (67%) and with excellent diastereo- and enantioselectivities (>20:1 *dr*, 96% *ee*, Table 2, Entry 12). On the other hand, double Michael additions between the *N*-unprotected oxindole derivatives **2b**–**j** and **3a** were also investigated and were seen to afford the products in moderate to high yields (63–98%) and with excellent enantioselectivities (90–99% *ee* values, Table 2, Entries 13–21). Notably, the electronic and steric properties of the *N*-unprotected oxindoles with different positional substituents on the indole ring had slight influence on the reactivities and stereoselectivities. Furthermore, the unsymmetrical divinyl ketone **3m** was also examined for this transformation and provided the desired product **4v** in 74% yield with inferior diastereoselectivity (1.1:1 *dr*) but good enantioselectivity (Table 2, Entry 22).

We next further examined the double Michael additions between pyrazolones and dienones assisted by the established catalytic method. The initial screening results are shown in Table 3. When pyrazolone **5a** (Table 3) was treated with dienone **3a** in the presence of catalyst **1b** (20 mol-%) and TFA (40 mol-%) in toluene at room temp. for 48 hours, the desired spirocyclic compound **6a** was obtained in 71% yield, with a moderate diastereoselective ratio and enantioselectivity (6:1 *dr*, 71% *ee*, Table 3, Entry 1). Several chiral or achiral acids, such as benzoic acid, (*R*)- or (*S*)-BINOL-phosphoric acids, and L- or D-Boc-Phg-OHs, were then screened as additives for this reaction. The (*R*)-BINOL-phosphoric acid as additive improved the diastereoselective ratio sharply (19:1 *dr*), albeit with a large loss of enantioselectivity (34% *ee*, Table 3, Entry 4). *N*-Boc-D-phenylglycine as additive proved to be effective in terms of both reactivity and stereoselectivity (73% yield, 7:1 *dr* and 84% *ee*, Table 3, Entry 8). Increasing the amount of **3a** had only a slight influence on the reactivity (Table 3, Entry 9). In $CHCl_3$ as the reaction medium the reaction gave the final product with a higher enantioselectivity, though the diastereoselectivity was somewhat decreased (Table 3, Entries 10 vs. 8). The optimal conditions chosen for the cascade [5+1] double Michael reactions between divinyl ketones and *N*-phenyl-protected pyrazolones were therefore

Table 3. Screening studies of the asymmetric cascade [5+1] double Michael addition between pyrazolone **5a** and dienone **3a**.[a]



Entry	Additive	Solvent	Yield[b] [%]	*dr*[c] **6a/6a′**	*ee*[d] [%]
1	TFA	PhMe	71	6:1	71
2	TFA	DCM	68	1:1	89
3	benzoic acid	PhMe	54	3:1	77
4	(*R*)-BINOL-phosphoric acid	PhMe	44	19:1	34
5	(*S*)-BINOL-phosphoric acid	PhMe	50	>20:1	53
6	Boc-L-Phg-OH	PhMe	79	8:1	69
7	Boc-L-Phg-OH	$CHCl_3$	75	13:1	72
8	Boc-D-Phg-OH	PhMe	73	7:1	84
9[e]	Boc-D-Phg-OH	PhMe	69	6:1	84
10	Boc-D-Phg-OH	$CHCl_3$	65	4:1	89

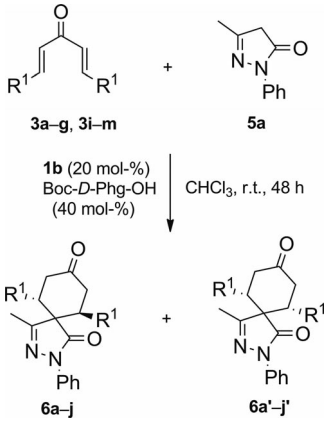
[a] Reactions were performed with **5a** (0.1 mmol), **3a** (0.12 mmol), catalyst **1b** (20 mol-%), and acid (40 mol-%) in solvent (1.0 mL) at room temp. for 48 h. [b] Isolated yields. [c] Determined by chiral HPLC. [d] Determined by chiral HPLC. [e] With **5a** (0.1 mmol) and **3a** (0.2 mmol) for this reaction.

catalyst **1b** (20 mol-%) and *N*-Boc-D-phenylglycine (40 mol-%) in $CHCl_3$ at room temp. for 48 hours.

Having established the optimal reaction conditions, we decided to explore the substrate scope and limitations of this protocol for the double Michael additions of divinyl ketones **3a**–**g** and **3i**–**m** with *N*-phenyl-protected pyrazolone **5a**. The results are shown in Table 4. For the dienone substrates, both electron-donating and electron-withdrawing substituents on phenyl groups were tolerated, with the desired products being obtained in moderate yields (47–70%) and with moderate to good diastereoselectivity ratios (3:1→20:1 *dr*s) and good enantioselectivities (81–97% *ee* values, Table 4, Entries 1–9). Intriguingly, dienones **3e**–**g** and **3m**, bearing *meta*- and *para*-halogen substituents (F, Cl, Br) on their phenyl groups, furnished the desired products with good to excellent enantioselectivities (90–98% *ee*s), but with varying levels of diastereoselectivity (3:1→20:1 *dr*s, Table 4, Entries 5–8). Dienone **3l**, bearing thiophen-2-yl groups, was also suitable for this reaction, giving the desired product **6j** in 52% yield, 1:2 *dr*, and 81% *ee* (Table 4, Entry 10). In contrast, the dienone substrates **3i** and **3j**, with *ortho*-substituents, proved ineffective for these transforma-

tions, probably due to the effects of steric hindrance (Table 4, Entries 11–12).

Table 4. Asymmetric cascade [5+1] double Michael additions between pyrazolone **5a** and dienones **3**.[a]



Entry	R	Yield[b] [%]	*dr*[c] **6/6′**	*ee*[d][e] [%]
1	Ph (**3a**)	**6a**/65	4:1	89
2	4-$MeOC_6H_4$ (**3b**)	**6b**/47	3:1	84
3	4-MeC_6H_4 (**3c**)	**6c**/53	4:1	88
4	4-*i*PrC_6H_4 (**3d**)	**6d**/53	7:1	81
5	4-FC_6H_4 (**3e**)	**6e**/60	7:1	90
6	3-ClC_6H_4 (**3f**)	**6f**/52	>20:1	95
7	4-ClC_6H_4 (**3g**)	**6g**/47	>20:1	97
8	4-BrC_6H_4 (**3m**)	**6h**/70	3:1	92
9	3,5-$(MeO)_2C_6H_3$ (**3k**)	**6i**/56	3:1	84
10	2-thienyl (**3l**)	**6j**/52	1:2	81
11	2-BrC_6H_4 (**3i**)	n.r.[f]	–	–
12	2,4-$Cl_2C_6H_3$ (**3j**)	n.r.[f]	–	–

[a] Unless otherwise noted, the reactions were performed with **5a** (0.1 mmol), **3** (0.12 mol), catalyst **1b** (20 mol-%), and Boc-D-Phg-OH (40 mol-%) in $CHCl_3$ (1 mL) at room temp. for 48 h. [b] Isolated yields. [c] Determined by chiral HPLC. [d] Determined by chiral HPLC. [e] The absolute configurations of the products were not determined. [f] n.r.: no reaction.

Conclusions

In conclusion, we have developed an efficient methodology for the construction of enantiomerically enriched spiro-[cyclohexanone-oxindoles] and spiro[cyclohexanone-pyrazolones] through cascade [5+1] Michael/Michael addition reactions between divinyl ketones and either *N-unprotected* oxindoles or *N*-phenyl-protected pyrazolones, catalyzed by combinations of cinchona-based chiral primary amines and α-amino acid derivatives. The final products were obtained in moderate to high yields and with good to excellent diastereoselectivities and enantioselectivities. Further expansion of the substrate scope of this catalytic system, as well as biological evaluations of the resulting spiro compounds, are in progress in our laboratories.

Experimental Section

General: Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates (0.2 ± 0.03 mm thickness, GF-254, particle size 0.01–0.04 mm). Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed with silica gel (particle size 0.04–0.05 mm). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with Varian Inova-300 or -400 NMR spectrometers. Chemical shifts (δ, ppm) are relative to the resonance of the deuterated solvent as the internal standard ($CDCl_3$, δ = 7.26 ppm for proton NMR, δ = 77.00 ppm for carbon NMR). Coupling constants (J) are given in Hz. Chiral HPLC was performed with an Agilent 1200 Series chromatograph and a Chiralcel OD-H (0.46 cm × 25 cm) or Chiralpak AD-H (0.46 × 25 cm^2) column.

General Procedure for the Asymmetric Double Michael Addition Reactions between Oxindoles and Dienones: An oxindole **2** (0.25 mmol), a dienone **3** (0.5 mmol), catalyst **1b** (20 mol-%), and *N*-Boc-D-Phg-OH (40 mol-%) were stirred in toluene (1.0 mL) under air at 40 °C for 72 h. The reaction mixture was then directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate 5:1 as eluent) to afford the corresponding product **4**.

General Procedure for the Asymmetric Double Michael Addition Reactions between Pyrazolones and Dienones: Pyrazolone **5a** (0.1 mmol), a dienone **3** (0.12 mmol), catalyst **1b** (20 mol-%), and *N*-Boc-D-Phg-OH (40 mol-%) were stirred in $CHCl_3$ (1.0 mL) under air at room temp. for 48 h. The reaction mixture was then directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate 5:1 as eluent) to afford the corresponding product **6**.

2,6-Diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4a): 92% yield, >20:1 *dr*, 94% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 0.75 mL min^{-1}, λ = 210 nm: t_{minor} = 20.547 min, t_{major} = 13.983 min. $[a]_D^{25}$ = –110.8 (c = 0.96 in $CHCl_3$) {ref.:[15] $[a]_D^{rt}$ = –112.9 (c = 0.96 in $CHCl_3$), 2*S*,6*S* enantiomer, 98% *ee*}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.82 (s, 1 H), 7.18–7.15 (m, 3 H), 6.94–6.79 (m, 8 H), 6.64 (t, J = 7.5 Hz, 1 H), 6.45 (d, J = 7.5 Hz, 1 H), 6.10 (d, J = 7.5 Hz, 1 H), 3.88 (t, J = 14.1 Hz, 1 H), 3.72–3.67 (m, 1 H), 3.62–3.51 (m, 2 H), 2.90 (dd, J = 15.0, 4.6 Hz, 1 H), 2.64 (d, J = 14.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.1, 42.9, 45.7, 46.9, 56.1, 109.5, 121.5, 126.1, 127.4, 127.6, 127.8, 128.1, 128.2, 128.3, 128.4, 129.6, 130.2, 138.2, 140.1, 181.0, 211.5 ppm. HRMS (ESI): calcd. for $C_{25}H_{21}NO_2$ $[M + H]^+$ 367.1572; found 367.1683.

2,6-Bis(4-methoxyphenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4b): 97% yield, >20:1 *dr*, 92% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 35.457 min, t_{major} = 25.954 min. $[a]_D^{25}$ = –213.4 (c = 1.10 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.39 (s, 1 H), 6.97 (t, J = 7.5 Hz, 1 H), 6.85–6.71 (m, 7 H), 6.56–6.48 (m, 3 H), 6.22 (d, J = 7.3 Hz, 1 H), 3.89 (t, J = 15.0 Hz, 1 H), 3.75–3.68 (m, 4 H), 3.61–3.59 (m, 5 H), 2.90 (dd, J = 17.4, 7.5 Hz, 1 H), 2.66 (dd, J = 15.0, 1.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.5, 43.3, 44.9, 46.1, 55.2, 55.4, 56.4, 109.5, 113.4, 113.6, 121.5, 126.1, 127.2, 128.0, 129.4, 130.4, 130.6, 132.4, 140.4, 158.6, 158.9, 181.0, 211.9 ppm. HRMS (EI): calcd. for $C_{27}H_{25}NO_4$ $[M]^+$ 427.1784; found 427.1787.

2,6-Bis(4-methylphenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4c): 75% yield, >20:1 *dr*, 90% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 0.75 mL min^{-1}, λ = 210 nm:

t_{minor} = 30.468 min, t_{major} = 13.824 min. $[\alpha]_D^{25}$ = –193.1 (c = 1.14 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.46 (s, 1 H), 7.01–6.94 (m, 3 H), 6.81–6.68 (m, 7 H), 6.53 (d, J = 7.5 Hz, 1 H), 6.18 (d, J = 7.5 Hz, 1 H), 3.92 (t, J = 14.1 Hz, 1 H), 3.75 (dd, J = 13.8, 3.3 Hz, 1 H), 3.66–3.58 (m, 2 H), 2.92 (dd, J = 18.0, 7.5 Hz, 1 H), 2.70 (dd, J = 15.3, 3.0 Hz, 1 H), 2.28 (s, 3 H), 2.11 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 21.3, 42.4, 43.2, 45.3, 46.7, 56.2, 109.5, 121.5, 126.2, 128.1, 128.3, 128.9, 129.6, 130.0, 130.0, 130.4, 135.5, 136.8, 137.2, 140.4, 181.1, 211.9 ppm. HRMS (ESI) calcd. for $C_{27}H_{25}NO_2$ $[M + H]^+$ 395.1885; found 395.1964.

2,6-Bis(4-isopropylphenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4d): 75% yield, >20:1 *dr*, 90% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 8.209 min, t_{major} = 6.819 min. $[\alpha]_D^{25}$ = –148.3 (c = 0.99 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.17 (s, 1 H), 7.04 (d, J = 8.1 Hz, 2 H), 6.92 (t, J = 7.5 Hz, 1 H), 6.82–6.77 (m, 6 H), 6.64 (t, J = 7.5 Hz, 1 H), 6.48 (d, J = 7.5 Hz, 1 H), 6.06 (d, J = 7.5 Hz, 1 H), 3.90 (t, J = 14.1 Hz, 1 H), 3.75–3.55 (m, 3 H), 2.91–2.81 (m, 2 H), 2.71–2.62 (m, 2 H), 1.19 (d, J = 6.9 Hz, 6 H), 1.05 (d, J = 6.9 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.9, 24.1, 33.7, 33.9, 42.3, 43.2, 45.3, 46.7, 56.1, 109.4, 121.4, 126.1, 126.2, 126.4, 128.0, 128.4, 129.6, 130.5, 135.7, 137.7, 140.3, 147.7, 148.3, 180.9, 211.9 ppm. HRMS (ESI): calcd. for $C_{31}H_{33}NO_2$ $[M + H]^+$ 451.2511; found 451.2589.

2,6-Bis(4-fluorophenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4e): 83% yield, >20:1 *dr*, 92% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 26.878 min, t_{major} = 17.434 min. $[\alpha]_D^{25}$ = –115.9 (c = 1.03 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.42 (s, 1 H), 7.03 (t, J = 7.5 Hz, 1 H), 6.89–6.76 (m, 7 H), 6.66 (t, J = 8.4 Hz, 2 H), 6.58 (d, J = 7.5 Hz, 1 H), 6.34 (d, J = 7.5 Hz, 1 H), 3.89 (t, J = 14.7 Hz, 1 H), 3.74–3.69 (m, 2 H), 3.52 (dd, J = 16.2, 5.7 Hz, 1 H), 2.98 (dd, J = 16.2, 6.6 Hz, 1 H), 2.67 (dd, J = 15.6, 1.8 Hz,1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.1, 42.8, 45.0, 45.9, 56.4, 109.7, 114.8, 115.1, 115.2, 115.4, 121.9, 125.7, 128.6, 129.8, 129.9, 130.0, 130.9, 131.0, 133.6, 133.7, 135.6, 135.6, 140.3, 180.8, 211.0 ppm. HRMS (ESI): calcd. for $C_{25}H_{19}F_2NO_2H$ $[M + H]^+$ 403.1384; found 403.1464.

2,6-Bis(3-chlorophenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4f): 83% yield, >20:1 *dr*, 92% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 14.092 min, t_{major} = 9.943 min. $[\alpha]_D^{25}$ = –130.5 (c = 1.23 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.33 (s, 1 H), 7.27–7.14 (m, 2 H), 7.06–7.01 (m, 2 H), 6.95–6.76 (m, 6 H), 6.59 (d, J = 7.5 Hz, 1 H), 6.35 (d, J = 7.5 Hz, 1 H), 3.89 (t, J = 14.4 Hz, 1 H), 3.71–3.67 (m, 2 H), 3.52 (dd, J = 15.9, 5.1 Hz, 1 H), 2.98 (dd, J = 15.9, 6.6 Hz, 1 H), 2.69 (dd, J = 15.3, 1.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.7, 42.4, 45.4, 46.3, 55.9, 109.9, 122.0, 125.7, 126.6, 127.3, 127.7, 127.9, 128.7, 128.8, 129.4, 129.5, 129.6, 129.8, 133.9, 134.1, 140.0, 140.3, 141.7, 180.1, 210.3 ppm. HRMS (EI): calcd. for $C_{25}H_{19}Cl_2NO_2$ $[M]^+$ 435.0793; found 435.0797.

2,6-Bis(4-chlorophenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4g): 70% yield, >20:1 *dr*, 90% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 26.415 min, t_{major} = 19.801 min. $[\alpha]_D^{25}$ = –207.6 (c = 0.98 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.08 (s, 1 H), 7.16 (d, J = 8.4 Hz, 2 H), 7.06–6.97 (m, 3 H), 6.87–6.78 (m, 5 H), 6.57 (d, J = 7.5 Hz, 1 H), 6.39 (d, J = 7.5 Hz, 1 H), 3.87 (t, J = 14.1 Hz, 1 H), 3.71–3.67 (m, 2 H), 3.49 (dd, J = 16.2, 5.4 Hz, 1 H), 2.97 (dd, J = 16.2, 6.9 Hz, 1 H), 2.67 (dd, J = 15.6, 2.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.9, 42.5, 45.3, 45.9, 56.1, 109.9, 122.0, 125.7, 128.4, 128.5, 128.7, 129.8, 130.1, 133.3, 133.6, 136.4, 138.2, 140.2, 140.3, 180.1, 210.5 ppm. HRMS (EI): calcd. for $C_{25}H_{19}Cl_2NO_2$ $[M]^+$ 435.0793; found 435.0797.

2,6-Bis(2,4-dichlorophenyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4j): 61% yield, >20:1 *dr*, 90% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralcel OD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 6.138 min, t_{major} = 8.268 min. $[\alpha]_D^{25}$ = –23.1 (c = 1.09 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.63 (s, 1 H), 7.45–7.31 (m, 3 H), 7.23 (s, 1 H), 7.08–6.95 (m, 3 H), 6.69 (d, J = 7.8 Hz, 1 H), 6.62 (t, J = 7.5 Hz, 1 H), 5.89 (d, J = 7.5 Hz, 1 H), 4.58 (dd, J = 13.5, 6.6 Hz, 1 H), 4.17–4.09 (m, 1 H), 3.96–3.75 (m, 2 H), 2.63 (d, J = 15.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.7, 41.8, 42.3, 43.4, 53.8, 109.5, 119.6, 122.15, 124.9, 127.8, 128.7, 128.8, 129.6, 129.7, 130.2, 133.7, 133.8, 134.4, 135.7, 137.0, 137.4, 138.6, 140.0, 180.6, 209.9 ppm. HRMS (ESI): calcd. for $C_{25}H_{17}Cl_4NO_2$ $[M + H]^+$ 503.0013; found 503.0086.

2,6-Bis(2-thienyl)spiro[cyclohexane-1,3′-indoline]-2′,4-dione (4l): 67% yield, >20:1 *dr*, 96% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (80:20) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 15.901 min, t_{major} = 16.724 min. $[\alpha]_D^{25}$ = –98.6 (c = 1.05 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.76 (s, 1 H), 7.18 (d, J = 4.5 Hz, 1 H), 7.10 (t, J = 7.5 Hz, 1 H), 6.94–6.87 (m, 2 H), 6.80 (t, J = 7.5 Hz, 1 H), 6.72–6.58 (m, 4 H), 6.20 (d, J = 7.5 Hz, 1 H), 4.25 (dd, J = 13.5, 4.2 Hz, 1 H), 3.93–3.79 (m, 3 H), 2.89–2.75 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.5, 42.8, 43.3, 44.4, 55.9, 109.9, 122.1, 124.4, 124.8, 125.6, 125.8, 126.4, 127.0, 127.2, 128.8, 130.0, 140.9, 141.4, 142.8, 180.5, 209.4 ppm. HRMS (ESI): calcd. for $C_{21}H_{17}NO_2S_2$ $[M + H]^+$ 379.0701; found 379.0775.

4′-Chloro-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4m): 79% yield, 13:1 *dr*, 96% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 17.084 min, t_{major} = 19.319 min. $[\alpha]_D^{25}$ = –94.8 (c = 0.98 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.04 (s, 1 H), 7.15–7.13 (m, 2 H), 7.09–7.00 (m, 6 H), 6.89–6.83 (m, 4 H), 6.31 (dd, J = 6.6, 2.1 Hz, 1 H), 4.36 (dd, J = 14.7, 2.1 Hz, 1 H), 4.21 (dd, J = 14.7, 2.7 Hz, 1 H), 4.04–3.89 (m, 2 H), 2.86 (dd, J = 17.1, 2.7 Hz, 1 H), 2.50 (dd, J = 17.1, 2.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.4, 40.5, 42.4, 44.9, 60.3, 108.3, 123.9, 127.1, 127.4, 127.6, 128.1, 128.3, 128.4, 129.8, 130.9, 133.5, 137.4, 138.5, 142.7, 180.4, 211.6 ppm. HRMS (EI): calcd. for $C_{25}H_{20}ClNO_2$ $[M]^+$ 401.1183; found 401.1183.

4′-Bromo-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4n): 96% yield, 10:1 *dr*, 97% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 18.684 min, t_{major} = 21.760 min. $[\alpha]_D^{25}$ = –68.7 (c = 0.92 in $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.95 (s, 1 H), 7.18–7.16 (m, 2 H), 7.09–7.01 (m, 7 H), 6.88–6.78 (m, 3 H), 6.35 (d, J = 7.8 Hz, 1 H), 4.50 (d, J = 14.7 Hz, 1 H), 4.28–4.10 (m, 2 H), 3.98 (t, J = 17.1 Hz, 1 H), 2.90 (d, J = 15.3 Hz, 1 H), 2.60 (dd, J = 17.1, 2.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.9, 40.4, 42.8, 45.0, 60.6, 108.9, 119.8, 127.3, 127.6, 127.8, 128.1, 128.2, 128.4, 128.7, 129.9, 137.4, 138.4, 138.6, 143.1, 180.6, 211.7 ppm. HRMS (EI): calcd. for $C_{25}H_{20}BrNO_2$ $[M]^+$ 445.0677; found 445.0669.

5′-Bromo-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4o): 92% yield, >20:1 *dr*, 90% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 16.478 min, t_{major} = 10.423 min. $[\alpha]_D^{25}$ = –119.9 (*c* = 0.91 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (s, 1 H), 7.28–7.25 (m, 3 H), 7.11–7.02 (m, 4 H), 6.93–6.88 (m, 4 H), 6.43 (d, *J* = 8.2 Hz, 1 H), 6.11 (d, *J* = 1.5 Hz, 1 H), 3.93 (t, *J* = 14.4 Hz, 1 H), 3.74–3.60 (m, 3 H), 2.94 (dd, *J* = 17.4, 6.9 Hz, 1 H), 2.71 (dd, *J* = 15.3, 2.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.9, 42.8, 45.6, 47.0, 56.4, 110.8, 114.3, 127.6, 128.0, 128.3, 128.4, 128.5, 129.4, 129.6, 131.0, 132.3, 137.8, 139.2, 139.7, 180.4, 211.0 ppm. HRMS (EI): calcd. for $C_{25}H_{20}BrNO_2$ $[M]^+$ 445.0677; found 445.0669.

5′-Chloro-7′-methyl-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4p): 63% yield, >20:1 *dr*, 96% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 0.75 mL min^{-1}, λ = 210 nm: t_{minor} = 14.832 min, t_{major} = 11.355 min. $[\alpha]_D^{25}$ = –86.7 (*c* = 0.39 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.27–7.25 (m, 4 H), 7.04–6.79 (m, 7 H), 5.80 (s, 1 H), 3.91 (t, *J* = 14.7 Hz, 1 H), 3.72–3.55 (m, 2 H), 3.10 (dd, *J* = 14.1, 6.6 Hz, 1 H), 2.91 (dd, *J* = 12.0, 1.5 Hz, 1 H), 2.70 (dd, *J* = 15.3, 3.0 Hz, 1 H), 1.98 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.0, 42.9, 45.5, 46.0, 47.1, 56.6, 106.7, 120.0, 123.9, 126.8, 127.5, 128.0, 128.3, 128.3, 128.4, 129.3, 129.6, 137.6, 138.0, 139.8, 183.9, 211.0 ppm. HRMS (EI): calcd. for $C_{25}H_{22}ClNO_2$ $[M]^+$ 415.1339; found 415.1343.

5′-Fluoro-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4q): 98% yield, >20:1 *dr*, 96% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 21.978 min, t_{major} = 10.895 min. $[\alpha]_D^{25}$ = –99.7 (*c* = 0.99 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (s, 1 H), 7.44–7.32 (m, 2 H), 7.26–7.25 (m, 2 H), 7.06–6.99 (m, 3 H), 6.94–6.89 (m, 4 H), 6.67 (td, *J* = 8.8, 2.4 Hz, 1 H), 6.46 (dd, *J* = 8.4, 4.4 Hz, 1 H), 5.78 (dd, *J* = 8.4, 2.0 Hz, 1 H), 3.92 (t, *J* = 14.8 Hz, 1 H), 3.73 (dd, *J* = 14.0, 3.6 Hz, 1 H), 3.68–3.62 (m, 2 H), 2.91 (dd, *J* = 18.4, 7.6 Hz, 1 H), 2.71 (dd, *J* = 15.6, 3.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.7, 42.6, 45.5, 46.6, 56.3, 109.7, 109.8, 113.6, 113.8, 114.3, 114.6, 127.2, 127.3, 127.7, 128.0, 128.1, 128.3, 128.9, 129.3, 131.6, 131.7, 135.9, 137.5, 139.5, 180.8, 210.8 ppm. HRMS (ESI): calcd. for $C_{25}H_{20}FNO_2$ $[M + H]^+$ 385.1478; found 385.1551.

6′-Bromo-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4r): 91% yield, >20:1 *dr*, 99% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 28.473 min, t_{major} = 10.701 min. $[\alpha]_D^{25}$ = –119.4 (*c* = 0.94 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 1 H), 7.26–7.21 (m, 2 H), 7.06–7.00 (m, 4 H), 6.93–6.87 (m, 4 H), 6.83 (dd, *J* = 8.4, 1.2 Hz, 1 H), 6.72 (d, *J* = 1.2 Hz, 1 H), 5.91 (d, *J* = 8.0 Hz, 1 H), 3.93 (t, *J* = 14.0 Hz, 1 H), 3.74 (dd, *J* = 10.0, 3.6 Hz, 1 H), 3.68–3.60 (m, 2 H), 2.91 (dd, *J* = 14.8, 4.0 Hz, 1 H), 2.71 (dd, *J* = 15.6, 3.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.9, 42.8, 45.5, 46.9, 55.8, 112.8, 121.7, 124.4, 127.4, 127.5, 127.8, 128.2, 128.3, 128.4, 129.1, 129.5, 137.8, 139.9, 141.4, 180.5, 211.0 ppm. HRMS (ESI): calcd. for $C_{25}H_{20}BrNO_2$ $[M + H]^+$ 445.0677; found 445.0747.

5′-Chloro-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4s): 98% yield, >20:1 *dr*, 92% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 17.998 min, t_{major} = 10.655 min. $[\alpha]_D^{25}$ = –104.6 (*c* = 1.14 in $CHCl_3$) {ref.:[15] $[\alpha]_D^{rt}$ = –107.1 (*c* = 1.05 in $CHCl_3$), 2*S*,6*S* enantiomer, 94% *ee*}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1 H), 7.41–7.32 (m, 1 H), 7.28–7.27 (m, 2 H), 7.05–6.99 (m, 3 H), 6.95–6.88 (m, 5 H), 6.46 (d, *J* = 8.4 Hz, 1 H), 5.99 (d, *J* = 1.6 Hz, 1 H), 3.92 (t, *J* = 14.4 Hz, 1 H), 3.72 (dd, *J* = 14.0, 4.0 Hz, 1 H), 3.65–3.59 (m, 2 H), 2.93 (dd, *J* = 17.6, 7.2 Hz, 1 H), 2.71 (dd, *J* = 16.0, 3.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.8, 42.7, 45.5, 46.8, 56.4, 110.4, 126.5, 126.9, 127.3, 127.5, 128.0, 128.1, 128.3, 128.4, 129.5, 131.9, 137.7, 138.6, 140.0, 180.7, 210.9 ppm. HRMS (ESI): calcd. for $C_{25}H_{20}ClNO_2$ $[M + H]^+$ 401.1183; found 401.1251.

2,6-Diphenyl-7′-trifluoromethylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4t): 86% yield, 9:1 *dr*, 97% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 17.871 min, t_{major} = 9.827 min. $[\alpha]_D^{25}$ = –74.6 (*c* = 1.01 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1 H), 7.30–7.27 (m, 2 H), 7.18 (d, *J* = 8.0 Hz, 1 H), 7.06–6.98 (m, 4 H), 6.95 (d, *J* = 6.4 Hz, 2 H), 6.86 (d, *J* = 7.2 Hz, 2 H), 6.75 (t, *J* = 7.6 Hz, 1 H), 6.12 (d, *J* = 7.6 Hz, 1 H), 3.97 (t, *J* = 14.4 Hz, 1 H), 3.80–3.71 (m, 2 H), 3.68–3.63 (m, 1 H), 2.92 (dd, *J* = 15.6, 4.0 Hz, 1 H), 2.74 (dd, *J* = 15.2, 3.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.9, 42.7, 42.8, 45.7, 46.9, 55.1, 111.8, 121.2, 124.9, 124.9, 127.6, 127.7, 128.0, 128.1, 128.1, 128.2, 128.4, 128.6, 129.6, 137.4, 137.7, 139.9, 180.1, 210.6 ppm. HRMS (ESI): calcd. for $C_{26}H_{20}F_3NO_2$ $[M + H]^+$ 435.1446; found 435.1519.

5′,6′-Difluoro-2,6-diphenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4u): 94% yield, >20:1 *dr*, 91% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 27.231 min, t_{major} = 10.017 min. $[\alpha]_D^{25}$ = –96.6 (*c* = 1.12 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (s, 1 H), 7.43–7.33 (m, 1 H), 7.30–7.27 (m, 2 H), 7.07–7.02 (m, 3 H), 6.94–6.88 (m, 4 H), 6.39 (dd, *J* = 9.6, 6.4 Hz, 1 H), 5.78 (dd, *J* = 10.0, 7.6 Hz, 1 H), 3.91 (t, *J* = 14.8 Hz, 1 H), 3.72–3.64 (m, 2 H), 3.60–3.56 (m, 1 H), 2.87 (dd, *J* = 16.0, 4.4 Hz, 1 H), 2.71 (dd, *J* = 15.6, 3.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.8, 42.7, 45.7, 46.9, 56.1, 99.3, 99.6, 115.5, 115.7, 125.7, 127.4, 127.7, 128.1, 128.2, 128.5, 128.6, 128.7, 129.1, 129.5, 137.6, 139.6, 139.7, 181.0, 210.7 ppm. HRMS (EI): calcd. for $C_{25}H_{19}F_2NO_2$ $[M]^+$ 403.1384; found 403.1459.

2-(4-Chlorophenyl)-6-phenylspiro[cyclohexane-1,3′-indoline]-2′,4-dione (4v): 74% yield, 1.1:1 *dr*, 94% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 0.75 mL min^{-1}, λ = 210 nm: t_{minor} = 36.349 min, t_{major} = 14.685 min. $[\alpha]_D^{25}$ = –102.8 (*c* = 0.97 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, *trans* and *cis*): δ = 8.18 (s, 1 H), 8.11 (s, 1 H), 7.22–7.16 (m, 5 H), 7.02–6.96 (m, 7 H), 6.93–6.92 (m, 2 H), 6.89–6.87 (m, 4 H), 6.83–6.78 (m, 3 H), 6.72 (t, *J* = 7.6 Hz, 1 H), 6.56 (t, *J* = 8.0 Hz, 2 H), 6.37 (d, *J* = 7.2 Hz, 1 H), 6.16 (d, *J* = 7.2 Hz, 1 H), 4.15–4.05 (m, 1 H), 3.97–3.86 (m, 1 H), 3.78–3.66 (m, 4 H), 3.63–3.50 (m, 2 H), 3.00–2.95 (m, 2 H), 2.73–2.66 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, *trans* and *cis*): δ = 41.7, 41.8, 42.5, 44.8, 45.5, 45.8, 46.6, 55.8, 60.0, 60.5, 109.5, 121.5, 121.6, 125.6, 125.7, 127.3, 127.5, 127.9, 128.1, 128.2, 129.3, 129.6, 129.7, 129.8, 130.5, 132.9, 133.2, 136.5, 137.6, 138.2, 139.7, 140.1, 140.2, 180.5, 210.8, 210.9 ppm. HRMS (ESI): calcd. for $C_{25}H_{20}ClNO_2$ $[M + H]^+$ 401.1183; found 401.1187.

3′-Methyl-1′,2,6-triphenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6a): 65% yield, 4.0:1 *dr*, 89% *ee*. The enantiomeric

excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (80:20) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 12.957 min, t_{major} = 16.371 min. $[\alpha]_D^{25}$ = –36.1 (c = 1.24 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48–7.39 (m, 2 H), 7.34–7.25 (m, 4 H), 7.25–7.13 (m, 9 H), 4.05–3.81 (m, 2 H), 3.66 (d, J = 14.4 Hz, 1 H), 3.38 (dd, J = 16.2, 4.8 Hz, 1 H), 2.99 (dd, J = 16.5, 9.6 Hz, 1 H), 2.69–2.55 (m, 1 H), 1.67 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 40.8, 41.5, 42.6, 44.4, 62.1, 120.0, 125.8, 127.5, 127.8, 127.9, 128.3, 128.8, 128.9, 129.2, 136.8, 137.4, 138.7, 160.8, 175.0, 209.5 ppm. HRMS (ESI): calcd. for $C_{27}H_{24}N_2O_2$ [M + H]$^+$ 408.1838; found 408.1925.

2,6-Bis(4-methoxyphenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6b): 47% yield, 3:1 *dr*, 84% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 13.801 min, t_{major} = 28.255 min. $[\alpha]_D^{25}$ = –42.5 (c = 1.13 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.30 (m, 4 H), 7.14–7.05 (m, 5 H), 6.83–6.71 (m, 4 H), 3.94 (t, J = 14.1 Hz, 1 H), 3.77 (d, J = 6.6 Hz, 1 H), 3.70 (s, 6 H), 3.44 (d, J = 13.8 Hz, 2 H), 2.53 (d, J = 14.1 Hz, 2 H), 2.06 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 29.6, 42.5, 47.5, 55.1, 55.2, 62.0, 113.9, 114.1, 120.0, 120.2, 125.5, 125.7, 128.2, 128.6, 129.5, 137.0, 137.1, 159.1, 160.6, 173.2, 208.1 ppm. HRMS (EI): calcd. for $C_{29}H_{28}N_2O_4$ [M]$^+$ 468.2049; found 468.2049.

3′-Methyl-2,6-bis(4-methylphenyl)-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6c): 53% yield, 4:1 *dr*, 88% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 21.284 min, t_{major} = 14.782 min. $[\alpha]_D^{25}$ = –44.5 (c = 1.04 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.42 (m, 2 H), 7.32 (t, J = 7.5 Hz, 2 H), 7.19–7.01 (m, 9 H), 4.01–3.79 (m, 2 H), 3.63 (d, J = 13.8 Hz, 1 H), 3.47–3.30 (m, 1 H), 2.90 (dd, J = 15.9, 8.4 Hz, 1 H), 2.64–2.50 (m, 1 H), 2.31–2.19 (m, 6 H), 1.62 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 21.1, 41.7, 42.6, 44.2, 48.3, 62.0, 120.0, 125.7, 127.2, 127.7, 127.8, 128.9, 129.4, 129.7, 133.9, 134.7, 135.8, 137.9, 161.1, 175.1, 209.8 ppm. HRMS (EI): calcd. for $C_{29}H_{28}N_2O_2$ [M]$^+$ 436.2151; found 436.2150.

2,6-Bis(4-isopropylphenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6d): 53% yield, 7:1 *dr*, 81% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (80:20) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 19.609 min, t_{major} = 14.179 min. $[\alpha]_D^{25}$ = –62.7 (c = 0.99 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.38 (m, 2 H), 7.32–7.25 (m, 3 H), 7.16–7.08 (m, 3 H), 7.06–7.03 (m, 5 H), 3.90–3.78 (m, 1 H), 3.70–3.58 (m, 1 H), 3.36–3.29 (m, 1 H), 2.99–2.83 (m, 1 H), 2.79–2.73 (m, 1 H), 2.62 (d, J = 15.9 Hz, 1 H), 2.43–2.25 (m, 1 H), 2.11–2.00 (m, 1 H), 1.67 (s, 3 H), 1.21 (d, J = 6.9 Hz, 6 H), 1.09 (d, J = 6.3 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 23.9, 24.1, 30.0, 33.9, 40.8, 41.5, 42.3, 43.7, 62.2, 120.3, 125.9, 126.7, 127.1, 127.8, 127.8, 128.0, 128.9, 134.0, 136.0, 137.4, 148.9, 161.1, 175.2, 210.0 ppm. HRMS (EI): calcd. for $C_{33}H_{36}N_2O_2$ [M]$^+$ 492.2777; found 492.2776.

2,6-Bis(4-fluorophenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6e): 60% yield, 7:1 *dr*, 90% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 29.911 min, t_{major} = 21.142 min. $[\alpha]_D^{25}$ = –41.6 (c = 1.24 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.41 (m, 2 H), 7.35–7.30 (m, 2 H), 7.19–7.09 (m, 5 H), 7.02–6.97 (m, 2 H), 6.92–6.87 (m, 2 H), 3.98–3.77 (m, 2 H), 3.63–3.47 (m, 1 H), 3.27 (dd, J = 13.5, 4.5 Hz, 1 H), 2.97 (dd, J = 16.2, 10.5 Hz, 1 H), 2.62 (d, J = 16.2 Hz, 1 H), 1.76 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 41.2, 42.4, 43.2, 47.6, 61.8, 115.9, 115.9, 116.1, 116.2, 120.0, 120.2, 126.2, 129.0, 129.1, 129.2, 129.2, 129.5, 129.6, 133.4, 136.9, 137.0, 160.2, 163.7, 172.9, 207.3 ppm. HRMS (EI): calcd. for $C_{27}H_{22}F_2N_2O_2$ [M]$^+$ 444.1649; found 444.1651.

2,6-Bis(3-chlorophenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6f): 52% yield, >20:1 *dr*, 95% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 11.498 min, t_{major} = 13.416 min. $[\alpha]_D^{25}$ = –64.0 (c = 0.97 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39 (d, J = 7.8 Hz, 2 H), 7.29–7.19 (m, 5 H), 7.14–7.04 (m, 4 H), 6.97–6.91 (m, 2 H), 3.86–3.69 (m, 2 H), 3.52 (d, J = 14.4 Hz, 1 H), 3.22 (dd, J = 16.2, 4.5 Hz, 1 H), 2.94–2.80 (m, 1 H), 2.57 (d, J = 16.5 Hz, 1 H), 1.68 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 41.9, 42.2, 47.8, 48.0, 61.3, 121.0, 125.6, 125.7, 126.0, 126.1, 126.6, 127.8, 128.9, 129.1, 129.4, 130.5, 135.0, 135.2, 136.8, 137.1, 139.5, 160.1, 172.9, 206.7 ppm. HRMS (EI): calcd. for $C_{27}H_{22}Cl_2N_2O_2$ [M]$^+$ 476.1058; found 476.1052.

2,6-Bis(4-chlorophenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6g): 47% yield, >20:1 *dr*, 97% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 44.419 min, t_{major} = 23.212 min. $[\alpha]_D^{25}$ = –116.7 (c = 0.91 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.44 (m, 2 H), 7.36–7.26 (m, 4 H), 7.19–7.16 (m, 3 H), 7.07–7.03 (m, 4 H), 3.92–3.76 (m, 2 H), 3.60 (d, J = 14.1 Hz, 1 H), 3.27 (dd, J = 16.2, 4.2 Hz, 1 H), 3.00–2.91 (m, 1 H), 2.61 (d, J = 16.2 Hz, 1 H), 1.74 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.7, 40.2, 40.8, 41.7, 43.2, 61.7, 119.6, 122.8, 124.0, 125.9, 128.8, 129.0, 129.1, 134.1, 134.7, 136.6, 136.8, 143.3, 159.9, 174.4, 208.3 ppm. HRMS (EI): calcd. for $C_{27}H_{22}Cl_2N_2O_2$ [M]$^+$ 476.1085; found 476.1068.

2,6-Bis(4-bromophenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6h): 70% yield, 3:1 *dr*, 92% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 59.231 min, t_{major} = 28.282 min. $[\alpha]_D^{25}$ = –49.7 (c = 0.94 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.33 (m, 8 H), 7.25–7.18 (m, 1 H), 7.10–7.07 (m, 4 H), 3.92 (t, J = 14.1 Hz, 2 H), 3.45 (dd, J = 13.8, 3.0 Hz, 2 H), 2.54 (d, J = 14.4 Hz, 2 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 41.9, 47.4, 47.4, 47.7, 61.2, 120.0, 122.3, 122.5, 126.1, 128.8, 132.1, 136.3, 136.7, 138.8, 149.6, 150.7, 157.8, 159.8, 172.6, 206.7 ppm. HRMS (EI): calcd. for $C_{25}H_{22}Br_2N_2O_2$ [M]$^+$ 564.0048; found 564.0020.

2,6-Bis(3,5-dimethoxyphenyl)-3′-methyl-1′-phenyl-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6i): 56% yield, 3:1 *dr*, 84% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 13.551 min, t_{major} = 28.736 min. $[\alpha]_D^{25}$ = –44.9 (c = 1.04 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (d, J = 7.8 Hz, 2 H), 7.36 (t, J = 8.4 Hz, 2 H), 7.16 (t, J = 6.6 Hz, 1 H), 6.36–6.24 (m, 6 H), 3.89–3.79 (m, 2 H), 3.66 (s, 6 H), 3.60 (s, 6 H), 3.37 (dd, J = 16.8, 5.4 Hz, 2 H), 2.87 (dd, J = 16.5, 9.0 Hz, 1 H), 2.61 (dd, J = 16.5, 2.7 Hz, 1 H), 1.70 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.0, 40.8, 41.7, 42.5, 43.3, 45.0, 55.4, 55.5, 55.5, 61.6, 99.8, 100.3, 105.3, 106.0, 106.2, 119.5, 125.7, 129.0, 129.2, 137.6, 139.2, 141.1, 161.3, 175.4, 209.4 ppm. HRMS (EI): calcd. for $C_{31}H_{32}N_2O_6$ [M]$^+$ 528.2260; found 528.2261.

3′-Methyl-1′-phenyl-2,6-bis(2-thienyl)-1*H*-spiro[cyclohexane-1,4′-pyrazole]-4,5′(4*H*)-dione (6j): 52% yield, 1:2 *dr*, 81% *ee*. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H and *n*-hexane/*i*PrOH (85:15) as the eluent. Flow rate: 1 mL min^{-1}, λ = 210 nm: t_{minor} = 16.944 min, t_{major} = 21.412 min. $[\alpha]_D^{25}$ = +107.9 (*c* = 0.81 in $CHCl_3$, dark sample). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.1 Hz, 1 H), 7.36–7.30 (m, 3 H), 7.19–7.09 (m, 3 H), 6.93–6.84 (m, 4 H), 4.17–3.86 (m, 2 H), 3.81–3.57 (m, 2 H), 2.79–2.65 (m, 2 H), 2.17 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 29.6, 42.5, 47.5, 55.1, 62.0, 114.0, 114.1, 120.0, 120.2, 125.7, 128.2, 128.6, 128.8, 129.5, 130.5, 137.0, 159.2, 160.6, 173.2, 208.1 ppm. HRMS (EI): calcd. for $C_{23}H_{20}N_2O_2S_2$ $[M]^+$ 420.0966; found 420.0964.

Supporting Information (see footnote on the first page of this article): ^{1}H NMR and ^{13}C NMR spectra and HPLC traces for the determination of the enantiomeric excess for compounds **4** and compounds **6**.

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