Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c7ob01307h

Chiral squaramide-catalysed enantioselective Michael/cyclization cascade reaction of 3-hydroxyoxindoles with α,β-unsaturated *N*-acylated succinimides†

Sheng Ming, Bo-Liang Zhao and Da-Ming Du *

Received 29th May 2017,
Accepted 1st July 2017

DOI: 10.1039/c7ob01307h

rsc.li/obc

A bifunctional squaramide-catalysed asymmetric Michael/cyclization cascade reaction of 3-hydroxyoxindoles with α,β-unsaturated *N*-acylated succinimides is disclosed. With quinine-derived squaramide as the catalyst, a broad range of the desired spirooxindole lactone derivatives bearing two contiguous stereocenters were obtained in good yields (up to 89%) with high diastereoselectivities (up to >95 : 5 dr) and excellent enantioselectivities (up to 99% ee).

Introduction

In recent years the synthesis of chiral heterocyclic compounds has been studied by many chemists because of the wide distribution of heterocyclic compounds in natural products and their broad applications in pharmaceutical agents.[1] The oxindole skeleton may be the most well-known heterocyclic skeleton and the compounds containing the oxindole skeleton often are provided with antifungal and antibacterial effects.[2] The spirooxindoles containing a spiro center at the 3-position of the oxindole ring often possess multiple stereocenters, and are considered as privileged molecular structures associated with potent pharmaceutical properties. So the development of efficient and highly stereoselective new strategies for the synthesis of such spirooxindoles is one of the most important research directions and attracts the attention of many scientists.[3] Meanwhile the oxaspiro lactone is widely distributed in natural products that are exerted by different organisms, such as fungi, plants, and marine species, what's more, the majority of them perform wonderful biological and pharmaceutical activities.[4a] So it is interesting to combine spirooxindoles with lactones. For example, spironolactone was reported to have the effect of treating heart failure. Trigolutes, a series of complex indole alkaloids were isolated from the plant *Trigonostemon fragilis* in 2013 for the first time, and have been found to be effective for the treatment of renal syndrome, hemorrhagic fever, asthma and so on (Fig. 1).[4] As a result, the spirooxindole lactone scaffolds have broad versatility as intermediates in the synthesis of related natural products.[5]

The promising prospect for clinical application of enantiomerically pure spirooxindole lactone derivatives has resulted in a requirement for the development of efficient asymmetric synthetic methods.[6] As we know, the asymmetric synthesis of spirooxindole lactone derivatives has been implemented by using α,β-unsaturated aldehydes,[7] α,β-unsaturated esters[8] and α,β-unsaturated acyl phosphonates[9] as the Michael acceptors. As readily available and useful compounds, α,β-unsaturated *N*-acylated succinimides[10] can also be used as Michael acceptors for the asymmetric synthesis of spirocyclic oxindoles. Herein, we report an asymmetric Michael/cyclization cascade reaction of 3-hydroxyoxindoles with α,β-unsaturated *N*-acylated succinimides catalysed by a bifunctional squaramide.[11] This enantioselective organocatalysed cascade reaction proceeded smoothly to afford the corresponding spirooxindole lactone derivatives in moderate to high yields (up to 89%) with good to

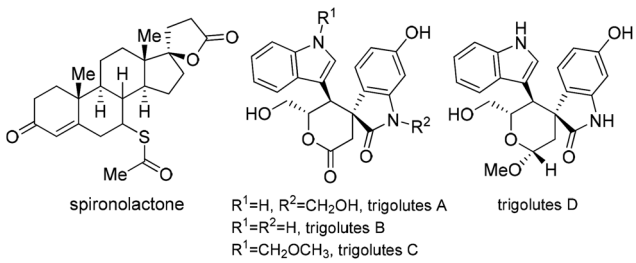


Fig. 1 Examples of bioactive chiral spirooxindole or spirolactone derivatives.

School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, People's Republic of China. E-mail: dudm@bit.edu.cn; Tel: +86 10 68914985

†Electronic supplementary information (ESI) available: Copies of ^{1}H and ^{13}C NMR spectra of products, and HPLC chromatograms. CCDC 1551414. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ob01307h

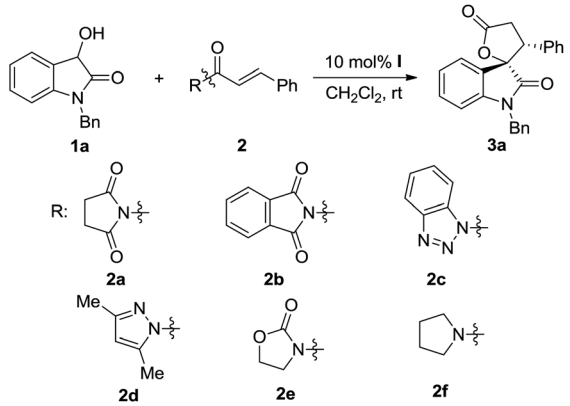
excellent diastereo- and enantioselectivities (up to >95 : 5 dr and 99% ee).

Results and discussion

Initially, we began by studying the reaction of 3-hydroxyoxindole **1a** with α,β-unsaturated *N*-acylated succinimide **2a** using catalyst **I**. This reaction gave the desired product **3a** in 83% isolated yield with high diastereo- and enantioselectivity (92 : 8 dr and 99% ee; Table 1, entry 1). Subsequently we contrasted the reactivity of α,β-unsaturated *N*-acylated succinimide **2a**, α,β-unsaturated *N*-acylated phthalimide **2b**, α,β-unsaturated *N*-acylated benzotriazole **2c**, α,β-unsaturated *N*-acylated dimethylpyrazole **2d**, α,β-unsaturated *N*-acylated oxazolidinone **2e** and α,β-unsaturated *N*-acylated pyrrolidine **2f** in this cascade Michael/cyclization with 3-hydroxyoxindole **1a** using squaramide **I** as a catalyst (Table 1). In terms of yields and stereoselectivities of the target product **3a**, α,β-unsaturated *N*-acylated succinimide **2a** is the optimal Michael acceptor.

According to the above screening results, we select the reaction of α,β-unsaturated *N*-acylated succinimide **2a** with 3-hydroxyoxindole **1a** as the model reaction. Then the catalyst evaluation was performed including some squaramide catalysts and one thiourea catalyst **I–XI** (Fig. 2). From Table 2, we can see that all squaramide catalysts could well promote the reaction in CH_2Cl_2 in the presence of 10 mol% catalyst loading at room temperature for 48 h with good to excellent enantioselectivity except for catalyst **V**, and a mediocre result was obtained by using thiourea organocatalyst **XI**. We ignored cata-

Table 1 Screening of Michael acceptors



Entry[a]	Acceptor	Time (h)	Yield[b] (%)	dr[c]	ee[c] (%)
1	**2a**	48	83	92 : 8	99
2	**2b**	72	22	98 : 2	96
3	**2c**	72	71	99 : 1	0
4	**2d**	72	26	97 : 3	97
5	**2e**	48	72	94 : 6	97
6	**2f**	72	n.r.		

[a] Reaction conditions: **1a** (0.15 mmol), **2** (0.18 mmol), catalyst **I** (10 mol%) in 1.0 mL CH_2Cl_2 at room temperature. [b] Isolated yield. [c] Determined by chiral HPLC analysis. n.r. = no reaction.

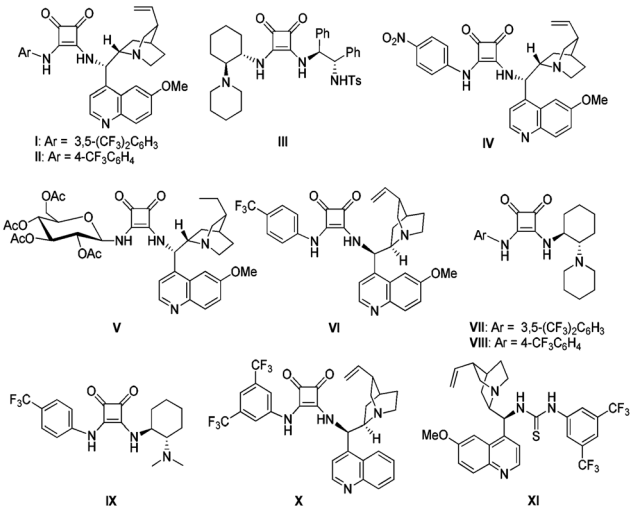
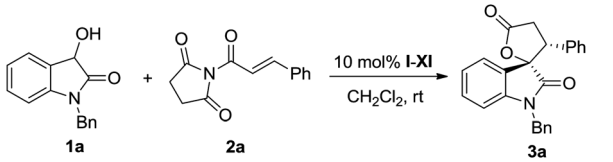


Fig. 2 Squaramide and thiourea organocatalysts.

Table 2 Screening of organocatalysts



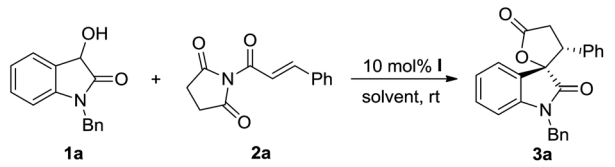
Entry[a]	Catalyst	Yield[b] (%)	dr[c]	ee[c] (%)
1	**I**	83	92 : 8	99
2	**II**	82	77 : 23	98
3	**III**	65	73 : 27	96
4	**IV**	80	82 : 18	98
5	**V**	62	28 : 72	19
6	**VI**	78	77 : 23	95[d]
7	**VII**	55	75 : 25	92
8	**VIII**	60	76 : 24	90
9	**IX**	51	63 : 37	87
10	**X**	70	85 : 15	96[d]
11	**XI**	75	19 : 81	69

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), catalyst (10 mol%) in 1.0 mL CH_2Cl_2 at room temperature for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The opposite enantiomer.

lysts **III** and **VII** because of their unsatisfactory yields. Both catalysts **VI** and **X** gave opposite enantiomers with excellent enantioselectivity, but it is a pity that the yields were not outstanding. To our delight, squaramides **I**, **II** and **IV** all gave the desired product **3a** in good yields with excellent enantioselectivities. In consideration of diastereoselectivities, so we selected squaramide **I** as the best catalyst for this Michael/cyclization cascade reaction.

To further promote the stereoselectivity of the cascade reaction, the optimization of other variables was implemented using squaramide **I** as the catalyst. We firstly carried out the screening of reaction solvents (Table 3, entries 1–8). The results show that the solvent type has little effect on enantioselectivity, but considering the yields, dichloromethane was

Table 3 Optimization of the reaction conditions for the asymmetric cascade reaction



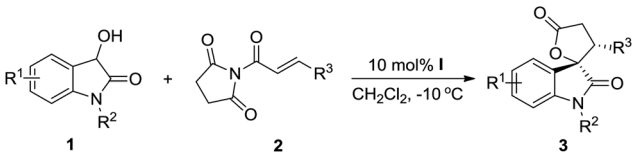
Entry[a]	Solvent	Loading (mol%)	Yield[b] (%)	dr[c]	ee[c] (%)
1	CH_2Cl_2	10	83	92 : 8	99
2	$CHCl_3$	10	81	73 : 27	98
3	$ClCH_2CH_2Cl$	10	80	80 : 20	98
4	PhMe	10	75	78 : 28	98
5	Xylene	10	70	74 : 26	98
6	THF	10	83	84 : 16	97
7	MeCN	10	77	80 : 20	96
8	Et_2O	10	76	81 : 19	97
9[d]	CH_2Cl_2	10	89	92 : 8	99
10	CH_2Cl_2	5	82	79 : 21	97

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), catalyst in 1.0 mL solvent at room temperature for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The reaction was performed at −10 °C for 48 h.

still the best solvent. With the optimal catalyst and solvent in hand, we then investigated other parameters, such as temperature and catalyst loading. When the reaction was carried out at −10 °C, to our delight, it could not only give excellent diastereo- and enantioselectivity, but could also improve the yield slightly (Table 3, entry 9). The side reaction may be suppressed at low temperature, and this reduced the generation of impurities. When the catalyst loading was reduced to 5 mol%, no improved result was obtained (Table 3, entry 10). Lastly, the optimal conditions were determined as the reactions were carried out in dichloromethane at −10 °C with 10 mol% squaramide **I**.

Having identified the optimized conditions for this cascade reaction, the generality of this reaction was then explored. The results are shown in Table 4. We started testing from a range of α,β-unsaturated *N*-acylated succinimides. When the substituents were in the *para* or *meta* position of the aromatic ring, both electron-donating and electron-withdrawing substituents gave the desired products in good yields with good to excellent diastereo- and enantioselectivities (Table 4, entries 2–6). The introduction of a substituent at the *ortho*-position of the aromatic ring leads to a significant drop of the enantioselectivity (Table 4, entry 7). Neither electron-donating nor electron-withdrawing substituents gave satisfactory results. It was proved that the positions of the substituents on the aromatic rings have a great effect on this cascade reaction. Next we replaced aromatic rings with heterocycles, such as furan and thiophene. Although the substrate with a furan substituent performed unsatisfactorily (Table 4, entry 10), the substrates bearing thiophene substituents (Table 4, entries 8 and 9) gave good yields with excellent enantioselectivities. The reaction of 1-naphthyl substituted α,β-unsaturated *N*-acylated succinimide with 3-hydroxyoxindole (Table 4, entry 11) was also evaluated, and the results were satisfactory. Eventually a series of 3-hydroxy-

Table 4 Substrate scope of the Michael/cyclization cascade reaction of 3-hydroxyoxindoles with α,β-unsaturated *N*-acylated succinimides



Entry[a]	R^1	R^2	R^3	Product	Yield[b] (%)	dr[c]	ee[d] (%)
1	H	Bn	Ph	**3a**	89	86 : 14	99
2	H	Bn	4-MeC_6H_4	**3b**	82	84 : 16	99
3	H	Bn	4-BrC_6H_4	**3c**	80	88 : 12	99
4	H	Bn	4-$NO_2C_6H_4$	**3d**	75	94 : 6	98
5	H	Bn	4-ClC_6H_4	**3e**	80	86 : 14	99
6	H	Bn	3-CNC_6H_4	**3f**	86	75 : 25	99
7	H	Bn	2-$MeOC_6H_4$	**3g**	70	> 95 : 5	19
8	H	Bn	2-Thienyl	**3h**	83	84 : 16	99
9	H	Bn	5-Br-2-Thienyl	**3i**	79	80 : 20	98
10	H	Bn	2-Furyl	**3j**	85	80 : 20	39
11	H	Bn	1-Naphthyl	**3k**	82	95 : 5	99
12	4-Br	Bn	Ph	**3l**	82	>95 : 5	98
13	5-F	Bn	Ph	**3m**	85	>95 : 5	98
14	5-Cl	Bn	Ph	**3n**	83	>95 : 5	90
15	5-MeO	Bn	Ph	**3o**	80	91 : 9	99
16	6-Cl	Bn	Ph	**3p**	86	80 : 20	96
17	7-Br	Bn	Ph	**3q**	85	>95 : 5	98
18	H	Allyl	Ph	**3r**	75	85 : 15	99

[a] Reaction conditions: **1** (0.15 mmol), **2** (0.18 mmol), catalyst (10 mol%) in 1.0 mL CH_2Cl_2 at −10 °C for 48 h. [b] Isolated yield. [c] Determined by ^1H NMR analysis. [d] Determined by chiral HPLC analysis.

oxindoles were tested, and these generally gave the desired products in good yields with good to excellent diastereo- and enantioselectivities (Table 4, entries 12–17). This result indicated that the presence of substituents on 3-hydroxyoxindoles has hardly any impact on this reaction. We also tried 3-hydroxyoxindoles with *N*-crotonyl succinimide which has a methyl in R^3, but regrettably the reaction didn't occur.

The configuration of the major diastereomer of compound **3c** was identified as (2*S*,3*R*) (Fig. 3) by single-crystal X-ray diffraction analysis,[12] and the configurations of the other products were inferred to be analogous with **3c**.

To make it clear what the reaction mechanism is, two control experiments are carried out (Scheme 1). First we try to gain 3-cinnamoyl hydroxyoxindole **4** and examine it as a substrate under the reaction conditions, but the reaction doesn't occur and desired **3a** cannot be obtained. Thus we figure out that the first step of the reaction is Michael addition instead of acylation of the hydroxy group of 3-hydroxyoxindoles. Subsequently we want to gain deeper insight into the mechanism, therefore we use deuterated 3-hydroxyoxindole **1aa** to react with α,β-unsaturated *N*-acylated succinimide **2a**. We obtain product **3a** without deuterium, so it is proved that the proton of hydroxyl is abstracted by the carboanion generated by the Michael addition step.

From above experiments, the proposed mechanism to explain the generation of the desired product **3a** is shown in Scheme 2. Quinine-derived squaramide **I** works as a bifunctional catalyst in this reaction. 3-Hydroxyoxindole **1a** is deprotonated by the tertiary amine unit of the quinine, and the resulting nucleophile binds to the squaramide moiety by hydrogen bonding. The electrophile α,β-unsaturated *N*-acylated succinimide **2a** is activated by the catalyst's protonated amine forming transition state **A**.[13] There may be hydrogen bond interactions between the OH group of oxindole with the Michael acceptor (omitted for clarity). The deprotonated 3-hydroxyoxindole **1a** attacks the α,β-unsaturated *N*-acylated succinimide **2a** *via* Michael addition giving intermediate **B**. Subsequently intramolecular cyclization occurred by the attack of an alkoxide anion, meanwhile the removal of a succinimide auxiliary generates spirooxindole lactone **3a**.

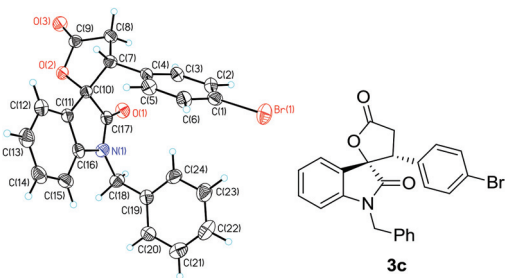
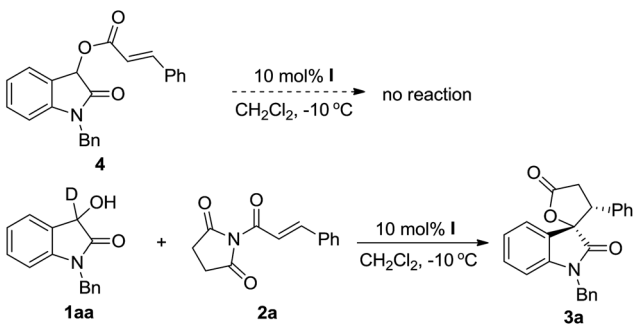
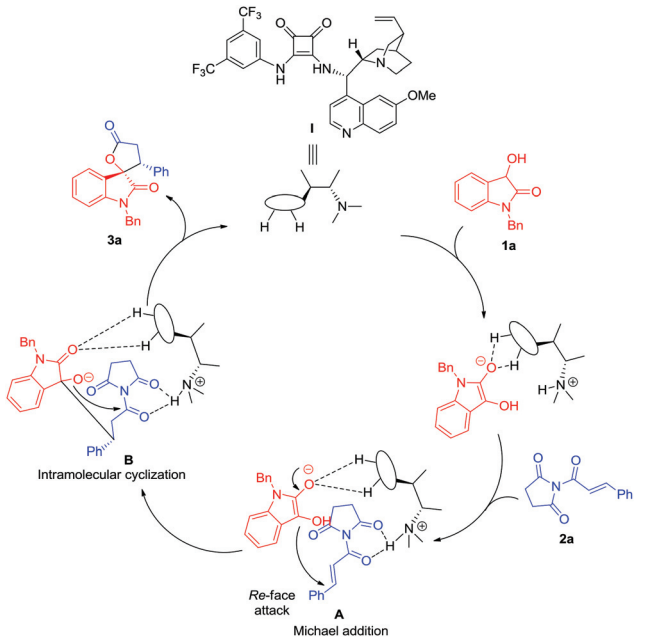


Fig. 3 X-ray structure of **3c** (for clarity, another symmetrical molecule is omitted).



Scheme 1 Mechanistic study.



Scheme 2 Proposed mechanism for the reaction.

Conclusions

In conclusion, we have developed a highly efficient and practical strategy for the asymmetric cascade Michael/cyclization reaction of 3-hydroxyoxindoles with α,β-unsaturated *N*-acylated succinimides using the bifunctional quinine-derived squaramide catalyst. This protocol provides an innovative access to spirooxindole lactone derivatives from α,β-unsaturated *N*-acylated succinimides and the corresponding products were obtained in good yields (up to 89%) with high to excellent stereoselectivities (up to >95 : 5 dr, up to 99% ee). Further studies focusing on the novel access of spirooxindole lactones are currently under way in our laboratory.

Experimental

General methods

Commercially available compounds were used without further purification. Solvents were dried according to standard pro-

cedures. Column chromatography was performed with silica gel (200–300 mesh). Melting points were determined with an XT-4 melting-point apparatus and were uncorrected. ^{1}H NMR spectra were measured with a Bruker Ascend 400 MHz spectrometer. Chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were recorded at 100 MHz; chemical shifts were reported in ppm relative to TMS with the solvent resonance as the internal standard. High resolution mass spectra (electron spray ionization) were recorded with an Agilent 6520 Accurate-Mass Q-TOF LC/MS system. Enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1200 LC instrument with a Daicel Chiralpak IB or AD-H column. α,β-Unsaturated *N*-acylated succinimides[14] and 3-hydroxyoxindoles[15] were synthesized according to literature methods.

General procedure for asymmetric Michael addition/cyclization cascade reactions

To a dried small bottle were added **1** (0.15 mmol), **2** (0.18 mmol) and catalyst **I** (9.45 mg, 0.015 mmol, 10 mol%) in CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at −10 °C for 48 h. Then the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/EtOAc as the eluent, typically 20 : 1 to 5 : 1) to afford the desired product **3**. **3a**,[7b] **3b**,[7b] **3c**,[7b] **3d**,[7b] **3e**,[7b] **3m**,[6d] **3n**,[6d] **3o**,[7b] and **3r**[7c] are known compounds in the literature.

(2*S*,3*R*)-1′-Benzyl-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3a). Employing the general procedure afforded compound **3a** as a white solid (49.3 mg, 89% yield), m.p. 65–66 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 90 : 10, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 32.6 min (minor enantiomer), t_R = 44.0 min (major enantiomer); minor diastereomer: t_R = 39.3, 47.8 min; 99% ee. $[\alpha]_D^{25}$ = +79.2 (c = 2.325, $CHCl_3$), lit.[7b] $[\alpha]_D^{25}$ = +81.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.2 Hz, 1H, ArH), 7.30 (d, J = 7.6 Hz, 1H, ArH), 7.23–7.13 (m, 5H, ArH), 7.08 (t, J = 7.4 Hz, 2H, ArH), 7.01 (d, J = 7.6 Hz, 2H, ArH), 6.45–6.42 (m, 3H, ArH), 4.99 (d, J = 16.0 Hz, 1H, CH_2), 4.20 (d, J = 16.0 Hz, 1H, CH_2), 4.17 (dd, J_1 = 13.6 Hz, J_1 = 8.0 Hz, 1H, CH), 3.91 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.95 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 172.7, 143.6, 134.3, 132.0, 131.3, 128.8, 128.6, 128.4, 128.0, 127.3, 126.3, 124.6, 124.2, 123.5, 109.9, 86.3, 50.7, 43.6, 32.2 ppm.

(2*S*,3*R*)-1′-Benzyl-3-(*p*-tolyl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3b). Employing the general procedure afforded compound **3b** as a white solid (47.2 mg, 82% yield), m.p. 153–154 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 85 : 15, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 18.6 min (minor enantiomer), t_R = 20.3 min (major enantiomer); minor diastereomer: t_R = 25.5, 30.0 min; 99% ee. $[\alpha]_D^{25}$ = +116.6 (c = 1.065, $CHCl_3$), lit.[7b] $[\alpha]_D^{25}$ = +188 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.2 Hz, 1H, AH), 7.22 (d, J = 7.6 Hz, 1H, ArH), 7.16 (t, J = 7.4 Hz, 2H, ArH), 7.07 (t, J = 7.4 Hz, 2H, ArH), 7.01 (d, J = 8.0 Hz, 2H, ArH), 6.89 (d, J = 8.0 Hz, 2H, ArH), 6.47 (d, J = 7.2 Hz, 2H, ArH), 6.44 (d, J = 8.0 Hz, 1H, ArH), 5.02 (d, J = 16.0 Hz, 1H, CH_2), 4.20 (d, J = 16.0 Hz, 1H, CH_2), 4.13 (dd, J_1 = 14.0 Hz, J_2 = 8.0 Hz, 1H, CH), 3.88 (dd, J_1 = 16.8 Hz, J_2 = 14.0 Hz, 1H, CH_2), 2.93 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2), 2.33 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 172.8, 143.6, 138.1, 134.4, 131.2, 129.4, 128.9, 128.5, 127.9, 127.3, 126.4, 124.7, 124.2, 123.4, 109.8, 86.4, 50.5, 43.6, 32.3, 21.2 ppm.

(2*S*,3*R*)-1′-Benzyl-3-(4-bromophenyl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3c). Employing the general procedure afforded compound **3c** as a white solid (53.7 mg, 80% yield), m.p. 157–158 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 90 : 10, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 32.6 min (minor enantiomer), t_R = 42.2 min (major enantiomer); minor diastereomer: t_R = 45.1, 79.7 min; 99% ee. $[\alpha]_D^{25}$ = +126.0 (c = 1.025, $CHCl_3$), lit.[7b] $[\alpha]_D^{25}$ = +140.8 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.2 Hz, 1H, ArH), 7.32 (d, J = 8.4 Hz, 2H, ArH), 7.28–7.24 (m, 1H, ArH), 7.21–7.12 (m, 4H, ArH), 6.87 (d, J = 8.4 Hz, 2H, ArH), 6.50 (d, J = 7.2 Hz, 3H, ArH), 5.04 (d, J = 16.0 Hz, 1H, CH_2), 4.21 (d, J = 16.0 Hz, 1H, CH_2), 4.11 (dd, J_1 = 13.6 Hz, J_2 = 8.0 Hz, 1H, CH), 3.84 (dd, J_1 = 16.8 Hz, J_2 = 14.0 Hz, 1H, CH_2), 2.95 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 172.5, 143.6, 134.2, 131.9, 131.5, 131.1, 129.7, 128.8, 127.6, 127.2, 126.4, 124.2, 123.6, 122.6, 110.0, 85.9, 50.2, 43.8, 32.1 ppm.

(2*S*,3*R*)-1′-Benzyl-3-(4-nitrophenyl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3d). Employing the general procedure afforded compound **3d** as a white solid (46.8 mg, 75% yield), m.p. 72–73 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80 : 20, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 33.3 min (minor enantiomer), t_R = 42.4 min (major enantiomer); minor diastereomer: t_R = 35.6, 81.9 min; 98% ee. $[\alpha]_D^{25}$ = +88.9 (c = 0.79, $CHCl_3$), lit.[7b] $[\alpha]_D^{25}$ = +83.3 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.8 Hz, 2H, ArH), 7.59 (d, J = 7.2 Hz, 1H, ArH), 7.34 (t, J = 7.4 Hz, 1H, ArH), 7.22 (t, J = 7.6 Hz, 1H, ArH), 7.16–7.10 (m, 3H, ArH), 7.04 (t, J = 7.4 Hz, 2H, ArH), 6.63 (t, J = 8.4 Hz, 3H, ArH), 4.88 (d, J = 15.6 Hz, 1H, CH_2), 4.27 (d, J = 15.6 Hz, 1H, CH_2), 4.23 (dd, J_1 = 8.0 Hz, J_2 = 13.6 Hz, 1H, 1H, CH), 3.89 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 3.02 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 172.1, 147.9, 143.5, 139.4, 134.3, 131.8, 128.8, 128.5, 127.9, 126.8, 124.4, 123.9, 123.7, 109.9, 85.6, 50.3, 43.8, 32.0 ppm.

(2*S*,3*R*)-1′-Benzyl-3-(4-chlorophenyl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3e). Employing the general procedure afforded compound **3e** as a white solid (48.5 mg, 80% yield), m.p. 157–158 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80 : 20, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 16.4 min (minor enantiomer), t_R = 20.1 min (major enantiomer); minor diastereomer: t_R = 21.7, 37.8 min; 99% ee. $[\alpha]_D^{25}$ = +128.9 (c = 2.34, $CHCl_3$), lit.[7b] $[\alpha]_D^{25}$ = +127.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 7.2 Hz, 1H, ArH), 7.27–7.23 (m, 1H, ArH), 7.19–7.13 (m, 6H, ArH), 6.92 (d, J = 8.4 Hz, 2H, ArH), 6.51–6.47

(m, 3H, ArH), 5.02 (d, J = 16.0 Hz, 1H, CH_2), 4.20 (d, J = 16.0 Hz, 1H, CH_2), 4.14 (dd, J_1 = 13.8 Hz, J_2 = 8.2 Hz, 1H, CH), 3.84 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.95 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 172.5, 143.5, 134.4, 134.2, 131.4, 130.6, 129.3, 128.9, 128.6, 127.5, 127.1, 126.3, 124.2, 123.6, 109.9, 86.0, 50.0, 43.7, 32.1 ppm.

3-((2*S*,3*R*)-1′-Benzyl-2′,5-dioxo-4,5-dihydro-3*H*-spiro[furan-2,3′-indolin]-3-yl)benzonitrile (3f). Employing the general procedure afforded compound **3f** as a white solid (50.5 mg, 86% yield), m.p. 77–78 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 70 : 30, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 24.7 min (minor enantiomer), t_R = 20.6 min (major enantiomer); minor diastereomer: t_R = 26.6, 34.8 min; 99% ee. $[\alpha]_D^{25}$ = +56.9 (c = 2.35, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.57 (m, 1H, ArH), 7.54–7.51 (m, 1H, ArH), 7.34–7.26 (m, 4H, ArH), 7.22–7.17 (m, 3H, ArH), 7.15–7.11 (m, 2H, ArH), 6.59 (dd, J_1 = 7.4 Hz, J_2 = 1.6 Hz, 2H, ArH), 4.88 (d, J = 15.6 Hz, 1H, CH_2), 4.29 (d, J = 15.6 Hz, 1H, CH_2), 4.18 (dd, J_1 = 13.6 Hz, J_2 = 8.0 Hz, 1H, CH), 3.84 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.99 (dd, J_1 = 16.8 Hz, J_2 = 8.4 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.2, 143.4, 134.2, 133.8, 132.2, 132.0, 131.8, 131.4, 129.5, 128.7, 127.6, 126.5, 124.3, 123.9, 123.7, 117.9, 112.8, 110.0, 85.6, 49.9, 43.7, 31.9 ppm; HRMS (ESI): m/z calcd for $C_{25}H_{22}N_3O_3$ $[M + NH_4]^+$ 412.1656, found 412.1654.

(2*S*,3*R*)-1′-Benzyl-3-(2-methoxyphenyl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3g). Employing the general procedure afforded compound **3g** as a white solid (41.7 mg, 70% yield), m.p. 162–163 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 75 : 25, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 16.6 min (minor enantiomer), t_R = 19.3 min (major enantiomer); minor diastereomer: t_R = 12.4, 24.0 min; 19% ee. $[\alpha]_D^{25}$ = +75.8 (c = 1.565, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.54 (m, 1H, ArH), 7.51 (d, J = 7.2 Hz, 1H, ArH), 7.30–7.26 (m, 1H, ArH), 7.16–7.07 (m, 5H, ArH), 6.95 (t, J = 7.6 Hz, 1H, ArH), 6.67 (d, J = 8.0 Hz, 1H, ArH), 6.46 (d, J = 7.6 Hz, 2H, ArH), 6.40–6.38 (m, 1H, ArH), 5.04 (d, J = 16.0 Hz, 1H, CH_2), 4.82 (dd, J_1 = 13.8 Hz, J_2 = 8.2 Hz, 1H, CH), 4.19 (d, J = 16.0 Hz, 1H, CH_2), 3.84 (dd, J_1 = 16.8 Hz, J_2 = 14.0 Hz, 1H, CH_2), 3.15 (s, 3H, CH_3), 2.88 (dd, J_1 = 16.8 Hz, J_2 = 8.4 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 173.1, 157.8, 143.1, 134.6, 130.4, 129.2, 128.6, 128.3, 127.2, 126.3, 125.4, 125.1, 122.8, 120.9, 120.7, 110.6, 109.3, 86.3, 54.6, 43.6, 42.3, 32.7 ppm; HRMS (ESI): m/z calcd for $C_{25}H_{22}NO_4$ $[M + H]^+$ 400.1543, found 400.1544.

(2*S*,3*S*)-1′-Benzyl-3-(thiophen-2-yl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3h). Employing the general procedure afforded compound **3h** as a pale yellow solid (46.9 mg, 83% yield), m.p. 141–142 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 80.9 min (minor enantiomer), t_R = 140.6 min (major enantiomer); minor diastereomer: t_R = 109.9, 114.9 min; 99% ee. $[\alpha]_D^{25}$ = +61.2 (c = 2.52, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.51 (m, 1H, ArH), 7.27–7.25 (m, 1H, ArH), 7.17–7.12 (m, 5H, ArH), 6.90 (dd, J_1 = 5.2 Hz, J_2 = 3.6 Hz, 1H, ArH), 6.78 (d, J = 3.6 Hz, 1H, ArH), 6.66–6.64 (m, 2H, ArH), 6.55 (d, J = 7.6 Hz, 1H, ArH), 5.00 (d, J = 16.0 Hz, 1H, CH_2), 4.36 (dd, J_1 = 13.6 Hz, J_2 = 8.0 Hz, 1H, CH), 4.30 (d, J = 16.0 Hz, 1H, CH_2), 3.83 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 3.06 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 172.4, 143.9, 134.8, 134.4, 131.4, 128.6, 127.4, 127.1, 126.6, 126.1, 125.3, 124.3, 124.0, 123.5, 109.8, 85.6, 46.2, 43.7, 33.8 ppm; HRMS (ESI): m/z calcd for $C_{22}H_{21}N_2O_3S$ $[M + NH_4]^+$ 393.1267, found 393.1266.

(2*S*,3*S*)-1′-Benzyl-3-(5-bromothiophen-2-yl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3i). Employing the general procedure afforded compound **3i** as a yellow solid (53.6 mg, 79% yield), m.p. 146–147 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 90 : 10, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 40.0 min (minor enantiomer), t_R = 45.0 min (major enantiomer); minor diastereomer: t_R = 47.6, 78.4 min; 98% ee. $[\alpha]_D^{25}$ = +66.4 (c = 2.33, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 7.2 Hz, 1H, ArH), 7.30–7.28 (m, 1H, ArH), 7.25–7.21 (m, 3H, ArH), 7.16 (t, J = 7.6 Hz, 1H, ArH), 6.84 (d, J = 7.6 Hz, 1H, ArH), 6.75–6.73 (m, 2H, ArH), 6.61 (d, J = 8.0 Hz, 1H, ArH), 6.56 (d, J = 8.0 Hz, 1H, ArH), 5.08 (d, J = 15.6 Hz, 1H, CH_2), 4.32 (d, J = 16.0 Hz, 1H, CH_2), 4.25 (dd, J_1 = 13.8 Hz, J_2 = 7.8 Hz, 1H, CH), 3.76 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 3.02 (dd, J_1 = 16.4 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 172.3, 144.0, 136.4, 134.3, 131.7, 130.0, 128.8, 127.6, 126.7, 126.5, 124.3, 123.7, 123.7, 111.9, 110.0, 85.2, 46.4, 43.8, 33.3 ppm; HRMS (ESI): m/z calcd for $C_{22}H_{20}BrN_2O_3S$ $[M + NH_4]^+$ 471.0373, found 471.0374.

(2*S*,3*R*)-1′-Benzyl-3-(furan-2-yl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3j). Employing the general procedure afforded compound **3j** as a white solid (45.5 mg, 85% yield), m.p. 139–140 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 85 : 15, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 28.6 min (minor enantiomer), t_R = 42.1 min (major enantiomer); minor diastereomer: t_R = 32.8, 35.3 min; 39% ee. $[\alpha]_D^{25}$ = +50.2 (c = 0.88, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, 1H, ArH), 7.29–7.26 (m, 2H, ArH), 7.23–7.22 (m, 2H, ArH), 7.18–7.13 (m, 2H, ArH), 6.90 (br s, 2H, ArH), 6.61 (d, J = 8.0 Hz, 1H, ArH), 6.26 (s, 1H, ArH), 6.11 (d, J_1 = 3.2 Hz, 1H, ArH), 5.02 (d, J = 16.0 Hz, 1H, CH_2), 4.41 (d, J = 15.6 Hz, 1H, CH_2), 4.21 (dd, J_1 = 13.2 Hz, J_2 = 8.4 Hz, 1H, CH), 3.78 (dd, J_1 = 16.6 Hz, J_2 = 13.4 Hz, 1H, CH_2), 3.01 (dd, J_1 = 16.8 Hz, J_2 = 8.4 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 172.5, 147.5, 143.7, 142.7, 134.6, 131.3, 128.7, 127.6, 126.9, 124.7, 124.3, 123.5, 110.5, 109.8, 108.5, 84.6, 44.5, 43.8, 32.3 ppm; HRMS (ESI): m/z calcd for $C_{22}H_{17}NO_4$ $[M + NH_4]^+$ 377.1496, found 377.1496.

(2*S*,3*R*)-1′-Benzyl-3-(naphthalen-1-yl)-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3k). Employing the general procedure afforded compound **3k** as a white solid (51.7 mg, 82% yield), m.p. 135–136 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 90 : 10, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 38.5 min (minor enantiomer), t_R = 48.0 min (major enantiomer); minor diastereomer:

t_R = 35.1, 58.7 min; 99% ee. $[\alpha]_D^{25}$ = −78.5 (*c* = 1.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.84–7.79 (m, 3H, ArH), 7.74 (d, *J* = 7.2 Hz, 1H, ArH), 7.48–7.43 (m, 2H, ArH), 7.31 (t, *J* = 7.4 Hz, 1H, ArH), 7.17 (t, *J* = 7.4 Hz, 1H, ArH), 7.12–7.04 (m, 3H, ArH), 6.92 (t, *J* = 7.6 Hz, 2H, ArH), 6.14 (d, *J* = 7.6 Hz, 3H, ArH), 5.10 (dd, J_1 = 13.4 Hz, J_2 = 8.2 Hz, 1H, CH), 4.91 (d, *J* = 16.4 Hz, 1H, CH_2), 4.08 (d, *J* = 16.4 Hz, 1H, CH_2), 4.10–3.98 (dd, J_1 = 13.6 Hz, J_2 = 17.0 Hz, 1H, CH_2), 3.08 (dd, J_1 = 17.0 Hz, J_2 = 8.2 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 173.1, 143.3, 134.0, 133.7, 131.8, 131.1, 129.0, 128.6, 128.4, 128.0, 127.2, 125.9, 125.8, 125.7, 125.6, 125.4, 124.9, 124.4, 123.2, 122.5, 109.9, 86.9, 44.8, 43.5, 34.1 ppm; HRMS (ESI): *m*/*z* calcd for $C_{28}H_{21}NO_3$ $[M + H]^+$ 420.1594, found 420.1590.

(2*S*,3*R*)-1′-Benzyl-4′-bromo-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3l). Employing the general procedure afforded compound **3l** as a white solid (55.0 mg, 82% yield), m.p. 145–146 °C. HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 85 : 15, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 26.5 min (minor enantiomer), t_R = 21.5 min (major enantiomer); minor diastereomer: t_R = 15.0, 18.3 min; 98% ee. $[\alpha]_D^{25}$ = +112.8 (*c* = 1.58, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 7.4 Hz, 1H, ArH), 7.27–7.22 (m, 3H, ArH), 7.16 (t, *J* = 7.4 Hz, 1H, ArH), 7.11–7.04 (m, 5H, ArH), 6.40–6.37 (m, 3H, ArH), 4.96 (d, *J* = 16.0 Hz, 1H, CH_2), 4.90 (dd, J_1 = 13.6 Hz, J_2 = 8.4 Hz, 1H, CH), 4.16 (d, *J* = 16.0 Hz, 1H, CH_2), 3.88 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.97 (dd, J_1 = 16.8 Hz, J_2 = 8.4 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 172.1, 145.5, 133.8, 132.5, 132.2, 128.8, 128.7, 128.4, 128.1, 127.6, 127.5, 126.3, 122.2, 119.8, 108.9, 87.1, 45.6, 43.7, 31.4 ppm; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{22}BrN_2O_3$ $[M + NH_4]^+$ 465.0808, found 465.0803.

(2*S*,3*R*)-1′-Benzyl-5′-fluoro-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3m). Employing the general procedure afforded compound **3m** as a white solid (49.6 mg, 85% yield), m.p. 160–161 °C. HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 85 : 15, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 19.9 min (minor enantiomer), t_R = 21.8 min (major enantiomer); minor diastereomer: t_R = 16.4, 31.9 min; 98% ee. $[\alpha]_D^{25}$ = +120.2 (*c* = 0.835, CH_2Cl_2), lit.[6d] $[\alpha]_D^{20}$ = −96.5 (*c* = 1.0, CH_2Cl_2) for enantiomer. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.31 (m, 2H, ArH), 7.26–7.22 (m, 2H, ArH), 7.16 (t, *J* = 7.2 Hz, 1H, ArH), 7.10–7.03 (m, 4H, ArH), 6.93 (dt, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H, ArH), 6.41 (d, *J* = 7.2 Hz, 2H, ArH), 6.36 (dd, J_1 = 8.4 Hz, J_2 = 4.0 Hz, 1H, ArH), 4.99 (d, *J* = 16.0 Hz, 1H, CH_2), 4.19 (d, *J* = 16.4 Hz, 1H, CH_2), 4.13 (dd, J_1 = 13.8 Hz, J_2 = 8.2 Hz, 1H, CH), 3.90 (dd, J_1 = 16.6 Hz, J_2 = 13.8 Hz, 1H, CH_2), 2.96 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 172.5, 159.4 (d, $^1J_{C-F}$ = −242.0 Hz), 139.5 (d, $^4J_{C-F}$ = 2.1 Hz), 140.0, 131.7, 128.9, 128.7, 128.6, 128.0, 127.5, 126.3, 126.2(d, $^3J_{C-F}$ = 7.9 Hz), 117.7 (d, $^2J_{C-F}$ = 23.3 Hz), 112.3 (d, $^2J_{C-F}$ = 25.0 Hz), 110.8 (d, $^3J_{C-F}$ = 7.8 Hz), 86.1 (d, $^4J_{C-F}$ = 1.6 Hz), 50.9, 43.8, 32.1 ppm.

(2*S*,3*R*)-1′-Benzyl-5′-chloro-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3n). Employing the general procedure afforded compound **3n** as a white solid (50.1 mg, 83% yield), m.p. 201–202 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 90 : 10, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 25.8 min (minor enantiomer), t_R = 44.0 min (major enantiomer); minor diastereomer: t_R = 36.5, 39.2 min; 90% ee. $[\alpha]_D^{25}$ = +164.0 (*c* = 0.99, CH_2Cl_2), lit.[6d] $[\alpha]_D^{20}$ = −140.4 (*c* = 1.0, CH_2Cl_2) for the enantiomer. ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 1.6 Hz, 1H, ArH), 7.34 (t, *J* = 7.2 Hz, 1H, ArH), 7.26–7.14 (m, 4H, ArH), 7.10–7.03 (m, 4H, ArH), 6.40 (d, *J* = 7.6 Hz, 2H, ArH), 6.36 (d, *J* = 7.6 Hz, 1H, ArH), 4.98 (d, *J* = 16.0 Hz, 1H, CH_2), 4.19 (d, *J* = 16.0 Hz, 1H, CH_2), 4.21–4.11 (dd, J_1 = 13.6 Hz, J_2 = 8.0 Hz, 1H, CH), 3.89 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.96 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 172.3, 142.1, 133.8, 131.6, 131.2, 129.0, 128.9, 128.7, 128.6, 128.0, 127.5, 126.4, 126.3, 124.7, 111.0, 86.0, 50.9, 43.8, 32.1 ppm.

(2*S*,3*R*)-1′-Benzyl-5′-methoxy-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3o). Employing the general procedure afforded compound **3o** as a white solid (48.1 mg, 80% yield), m.p. 176–177 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80 : 20, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 21.2 min (minor enantiomer), t_R = 46.5 min (major enantiomer); minor diastereomer: t_R = 26.2, 31.4 min; 99% ee. $[\alpha]_D^{25}$ = +95.9 (*c* = 1.575, $CHCl_3$), lit.[7b] $[\alpha]_D^{25}$ = +135.2 (*c* = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (t, *J* = 7.2 Hz, 1H, ArH), 7.21 (t, *J* = 7.6 Hz, 2H, ArH), 7.17–7.12 (m, 2H, ArH), 7.09–7.03 (m, 4H, ArH), 6.74 (dd, J_1 = 8.6 Hz, J_2 = 2.6 Hz, 1H, ArH), 6.42 (d, *J* = 7.2 Hz, 2H, ArH), 6.33 (d, *J* = 8.8 Hz, 1H, ArH), 4.96 (d, *J* = 16.0 Hz, 1H, CH_2), 4.17 (d, *J* = 16.0 Hz, 1H, CH_2), 4.14 (dd, J_1 = 13.6 Hz, J_2 = 8.0 Hz, 1H, CH), 3.91 (dd, J_1 = 16.8 Hz, J_2 = 14.0 Hz, 1H, CH_2), 3.81 (s, 3H, CH_3), 2.94 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 172.5, 156.5, 136.8, 134.4, 132.0, 128.7, 128.6, 128.3, 128.0, 127.3, 126.3, 125.7, 115.8, 111.1, 110.5, 86.6, 55.8, 50.8, 43.7, 32.2 ppm.

(2*S*,3*R*)-1′-Benzyl-6′-chloro-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3p). Employing the general procedure afforded compound **3p** as a white solid (52.2 mg, 86% yield), m.p. 76–77 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 53.1 min (minor enantiomer), t_R = 61.6 min (major enantiomer); minor diastereomer: t_R = 47.5, 79.0 min; 96% ee. $[\alpha]_D^{25}$ = +89.4 (*c* = 2.565, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.0 Hz, 1H, ArH), 7.35–7.32 (m, 1H, ArH), 7.25–7.21 (m, 3H, ArH), 7.18–7.13 (m, 2H, ArH), 7.11–7.07 (m, 2H, ArH), 7.02 (d, *J* = 7.6 Hz, 2H, ArH), 6.43 (d, *J* = 1.6 Hz, 1H, ArH), 6.41 (d, *J* = 7.2 Hz, 1H, ArH), 4.97 (d, *J* = 16.0 Hz, 1H, CH_2), 4.18–4.12 (m, 2H, CH), 3.88 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.95 (dd, J_1 = 17.2 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 172.6, 144.7, 137.0, 133.7, 131.6, 128.9, 128.7, 128.5, 127.9, 127.5, 126.2, 125.2, 123.5, 123.0, 110.5, 85.7, 50.6, 43.7, 32.0 ppm; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{22}ClN_2O_3$ $[M + NH_4]^+$ 421.1313, found 421.1307.

(2*S*,3*R*)-1′-Benzyl-7′-bromo-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3q). Employing the general procedure afforded compound **3q** as a white solid (57.0 mg, 85% yield),

m.p. 189–190 °C. HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 80 : 20, flow rate 0.5 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 31.1 min (minor enantiomer), t_R = 35.1 min (major enantiomer); minor diastereomer: t_R = 41.9, 44.3 min; 98% ee. $[\alpha]_D^{25}$ = +74.5 (*c* = 2.635, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.2 Hz, 1H, ArH), 7.43 (d, *J* = 8.4 Hz, 1H, ArH), 7.33 (t, *J* = 7.4 Hz, 1H, ArH), 7.22 (t, *J* = 7.6 Hz, 2H, ArH), 7.13–7.00 (m, 6H, ArH), 6.36 (d, *J* = 7.2 Hz, 2H, ArH), 5.09 (*J* = 16.8 Hz, 1H, CH_2), 5.00 (d, *J* = 16.4 Hz, 1H, CH_2), 4.16 (dd, J_1 = 13.6 Hz, J_2 = 8.0 Hz, 1H, CH), 3.86 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 2.95 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 173.4, 141.3, 137.2, 136.2, 131.4, 128.9, 128.6, 128.4, 128.0, 127.8, 126.6, 125.3, 124.7, 123.6, 102.9, 85.2, 50.9, 44.4, 32.2 ppm; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{22}BrN_2O_3$ $[M + NH_4]^+$ 465.0808, found 465.0817.

(2*S*,3*R*)-1′-Allyl-3-phenyl-3*H*-spiro[furan-2,3′-indoline]-2′,5(4*H*)-dione (3r). Employing the general procedure afforded compound **3r** as a white solid (36.1 mg, 75% yield), m.p. 109–110 °C. HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): major diastereomer: t_R = 38.8 min (minor enantiomer), t_R = 40.4 min (major enantiomer); minor diastereomer: t_R = 28.7, 35.9 min; 99% ee. $[\alpha]_D^{25}$ = +43.2 (*c* = 2.015, $CHCl_3$), lit.[7c] $[\alpha]_D^{25}$ = −45.0 (*c* = 0.1, $CHCl_3$) for enantiomer. ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.2 Hz, 1H, ArH), 7.34 (t, *J* = 7.8 Hz, 1H, ArH), 7.21–7.14 (m, 4H, ArH), 6.94 (d, *J* = 7.6 Hz, 2H, ArH), 6.63 (d, *J* = 8.0 Hz, 1H, ArH), 5.25–5.14 (m, 1H, CH), 4.82 (d, *J* = 10.4 Hz, 1H, CH_2), 4.37 (d, *J* = 17.2 Hz, 1H, CH_2), 4.24 (dt, J_1 = 16.8 Hz, J_2 = 2.0 Hz, 1H, CH), 4.10 (dd, J_1 = 13.8 Hz, J_2 = 7.8 Hz, 1H, CH), 3.83 (dd, J_1 = 16.8 Hz, J_2 = 13.6 Hz, 1H, CH_2), 3.71 (dd, J_1 = 16.8 Hz, J_2 = 5.6 Hz, 1H, CH_2), 2.91 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 172.3, 143.5, 131.9, 131.1, 129.9, 128.5, 128.3, 127.7, 124.5, 124.1, 123.4, 116.9, 109.5, 86.4, 51.0, 41.9, 32.0 ppm.

Conflict of interest

There are no conflicts of interest to declare.

Acknowledgements

The authors are grateful for financial support from the National Natural Science Foundation of China (Grant No. 21272024) and the Analysis & Testing Center of the Beijing Institute of Technology.

Notes and references

1 (*a*) N. Hara, S. Nakamura, M. Sano, R. Tamura, Y. Funahashi and N. Shibata, *Chem. – Eur. J.*, 2012, **18**, 9276; (*b*) S. W. Duan, Y. Li, Y. Y. Liu, Y. Q. Zou, D. Q. Shi and W. J. Xiao, *Chem. Commun.*, 2012, **48**, 5160; (*c*) T. J. Greshock, A. W. Grubbs, P. Jiao, D. T. Wicklow, J. B. Gloer and R. M. Williams, *Angew. Chem., Int. Ed.*, 2008, **47**, 3573; (*d*) C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748; (*e*) M. Monari, E. Montroni, A. Nitti, M. Lombardo, C. Trombini and A. Quintavalla, *Chem. – Eur. J.*, 2015, **21**, 11038; (*f*) T. Mugishima, M. Tsuda, Y. Kasai, H. Ishiyama, E. Fukushi, J. Kawabata, M. Watanabe, K. Akao and J. Kobayashi, *J. Org. Chem.*, 2005, **70**, 9430; (*g*) B. M. Trost, D. A. Bringley, T. Zhang and N. Cramer, *J. Am. Chem. Soc.*, 2013, **135**, 16720.

2 (*a*) R. R. Kumar, S. Perumal, P. Senthilkumar, P. Yogeeswari and D. Sriram, *J. Med. Chem.*, 2008, **51**, 5731; (*b*) A. S. Girgis, *Eur. J. Med. Chem.*, 2009, **44**, 91; (*c*) S. Edmondson, S.-J. Danishefsky, L. Sepp-Lorenzino and N. Rosen, *J. Am. Chem. Soc.*, 1999, **121**, 2147; (*d*) M.-N. Cheng, H. Wang and L.-Z. Gong, *Org. Lett.*, 2011, **13**, 2418.

3 For reviews, see: (*a*) W.-Y. Han, J.-Q. Zhao, J. Zuo, X.-Y. Xu, X.-M. Zhang and W.-C. Yuan, *Adv. Synth. Catal.*, 2015, **357**, 3007; (*b*) L. Hong and R. Wang, *Adv. Synth. Catal.*, 2013, **355**, 1023; (*c*) D. Cheng, Y. Ishihara, B. Tan and C. Barbas III, *ACS Catal.*, 2014, **4**, 743.

4 (*a*) Y. Mostinski, D. Lankri and D. Tsvelikhovsky, *Synthesis*, 2017, 2361; (*b*) S.-S. Ma, W.-L. Mei, Z.-K. Guo, S.-B. Liu, Y.-X. Zhao, D.-L. Yang, Y.-B. Zeng, B. Jiang and H.-F. Dai, *Org. Lett.*, 2013, **15**, 1492.

5 (*a*) Y.-G. Chen, J.-C. Wu, G.-Y. Chen, C.-R. Han and X.-P. Song, *Chem. Biodiversity*, 2011, **8**, 1958; (*b*) H. Jayasuriya, D. L. Zink, S. B. Singh, R. P. Borris, W. Nanakorn, H. T. Beck, M. J. Balick, M. A. Goetz, L. Slayton, L. Gregory, M. Zakson-Aiken, W. Shoop and S. B. Singh, *J. Am. Chem. Soc.*, 2000, **122**, 4998; (*c*) S.-G. Liao, H.-D. Chen and J.-M. Yue, *Chem. Rev.*, 2009, **109**, 1092; (*d*) H. Jayasuriya, D. Zink, R. P. Borris, W. Nanankorn, H. T. Beck, M. J. Balick, M. A. Goetz, L. Gregory, W. L. Shoop and S. B. Singh, *J. Nat. Prod.*, 2004, **67**, 228.

6 (*a*) S.-P. Ji, L.-W. Liu, F. Chen, H.-X. Ren, Y. Yang, Z.-B. Zhang, L. Peng and L.-X. Wang, *Eur. J. Org. Chem.*, 2016, 5437; (*b*) E. L. McInturff, J. Mowat, A. R. Waldeck and M. J. Krische, *J. Am. Chem. Soc.*, 2013, **135**, 17230; (*c*) J. Dugal-Tessier, E. A. O'Bryan, T. B. H. Schroeder, D. T. Cohen and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2012, **51**, 4963; (*d*) L.-H. Sun, L.-T. Shen and S. Ye, *Chem. Commun.*, 2011, **47**, 10136; (*e*) Y. Xie, C. Yu, T. Li, S. Tu and C. Yao, *Chem. – Eur. J.*, 2015, **21**, 5355.

7 (*a*) G. Bergonzini and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2012, **51**, 971; (*b*) X.-Y. Chen, K.-Q. Chen, D.-Q. Sun and S. Ye, *Chem. Sci.*, 2017, **8**, 1936; (*c*) S. Mukherjee, S. Joseph, A. Bhunia, R. G. Gonnade, S. R. Yetra and A. T. Biju, *Org. Biomol. Chem.*, 2017, **15**, 2013.

8 B. M. Trost and K. Hirano, *Org. Lett.*, 2012, **14**, 2446.

9 L. Chen, Z.-J. Wu, M.-L. Zhang, D.-F. Yue, X.-M. Zhang, X.-Y. Xu and W.-C. Yuan, *J. Org. Chem.*, 2015, **80**, 12668.

10 B.-L. Zhao and D.-M. Du, *Org. Biomol. Chem.*, 2014, **12**, 1585.

11 (*a*) J. P. Malerich, K. Hagihara and V. H. Rawal, *J. Am. Chem. Soc.*, 2008, **130**, 14416; (*b*) Y. Zhu, J. P. Malerich and V. H. Rawal, *Angew. Chem., Int. Ed.*, 2010, **49**, 153.
12 Crystallographic data for compound **3c** (CCDC 1551414) has been provided as a CIF file in the ESI.†
13 M. N. Grayson, *J. Org. Chem.*, 2017, **82**, 4396.
14 K. Itoh, M. Hasegawa and J. Tanaka, *Org. Lett.*, 2005, **7**, 979.
15 (*a*) B.-L. Zhao and D.-M. Du, *Adv. Synth. Catal.*, 2016, **358**, 3992; (*b*) T.-Y. Chen and M. J. Krische, *Org. Lett.*, 2013, **15**, 2994.