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Chiral Bicyclic Guanidine-Catalyzed Enantioselective Sulfenylation of Oxindoles and Benzofuran-2(3*H*)-ones

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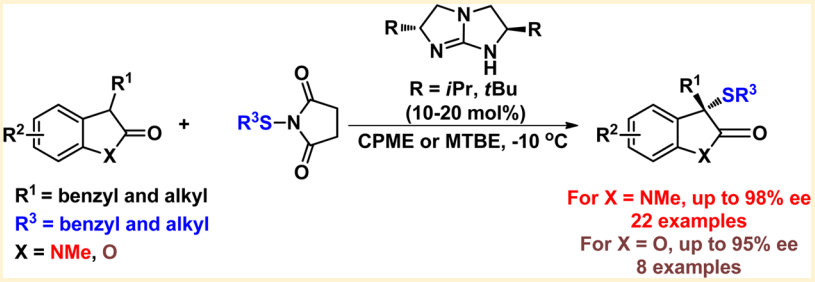
Supporting Information



ABSTRACT: A chiral bicyclic guanidine-catalyzed enantioselective sulfenylation of 3-substituted oxindoles to *N*-(sulfanyl)-succinimides has been developed. A series of unprecedented 3-sulfenylated oxindoles, such as 3-benzyl/alkyl-substituted 3-benzyl/alkyloxindoles, were obtained with high enantioselectivities (up to 98% ee). This methodology is also effective for the first asymmetric sulfenylation of benzofuran-2(3*H*)-ones, providing 3-benzyl-3-benzylthio-substituted benzofuran-2(3*H*)-ones with satisfactory results (up to 95% ee).

3,3-Disubstituted oxindoles, featuring a quaternary or hetero-quaternary stereogenic center on the C3 position, are one of the most common structural scaffolds in bioactive natural and non-natural products.[1] Hence, asymmetric synthesis of 3,3-disubstituted oxindoles has attracted significant attention from chemists during the past few decades.[2] In particular, the direct asymmetric reaction of prochiral 3-substituted oxindoles to electrophiles has been demonstrated as a powerful strategy to access these important chiral molecules.[2] For example, asymmetric sulfenylation of 3-substituted oxindoles has recently been devised to furnish directly stereoselective implantation of sulfur onto the C3 position of oxindoles.[3−5] In 2012, Feng and co-workers presented pioneering work on asymmetric sulfenylation of 3-substituted oxindoles through a cooperative catalysis of achiral a Brønsted base and chiral *N*,*N*′-dioxide-Sc(OTf)$_3$ complex, leading to 3-arylthio-substituted 3-aryl/benzyl/alkyloxindoles with excellent enantioselectivities (Scheme 1a).[5a] Almost simultaneously, the Enders group reported an organocatalytic example with the same substrate scope as the Feng's.[5b] Li, Cheng and co-workers described a highly enantioselective sulfenylation to build 3-arylthio-substituted 3-aryl/alkyloxindoles (Scheme 1b).[5c] Our group developed an asymmetric organocatalytic variant of 3-aryloxindoles to access chiral 3-arylthio-, 3-benzylthio-, and 3-alkylthio-substituted 3-aryloxindoles in satisfactory results (Scheme 1c).[5d] Nevertheless, to date to the best of our knowledge, four kinds of 3-sulfenylated oxindoles, i.e. 3-benzyl/alkyl-substituted 3-benzyl/alkyloxindoles, still remain unexploited (Scheme 1d). In our preliminary work, no reaction was observed between 3-benzyl-substituted oxindole and *N*-(benzylthio)succinimide using our previously reported reaction conditions[5d] (Scheme 1e). Thus, enantioselectivity and the poor reactivity represent the important yet difficult challenges for these unmet asymmetric sulfenylation of 3-substituted oxindoles.

In recent years, we were keen on the development of asymmetric organocatalytic methodologies to synthesize various significant molecules which contain quaternary and heteroquaternay stereogenic centers.[4c,d,5d,6] Among these works, chiral C_2-symmetric bicyclic guanidines exhibited satisfactory ability in stereoselective control toward several reactions using 3-benzyl-substituted oxindoles as nucleophiles, such as 1,4-conjugate addition to *N*-maleimides[6a] and 2-cyclopentenone[6e] as well as alkylation.[6f] Owing to the similarity in structural frameworks between *N*-succinimides and *N*-maleimides, it is plausible that bicyclic guanidine catalysts could lead to similar enantioselective outcomes for these two kinds of electrophiles. More importantly, chiral bicyclic

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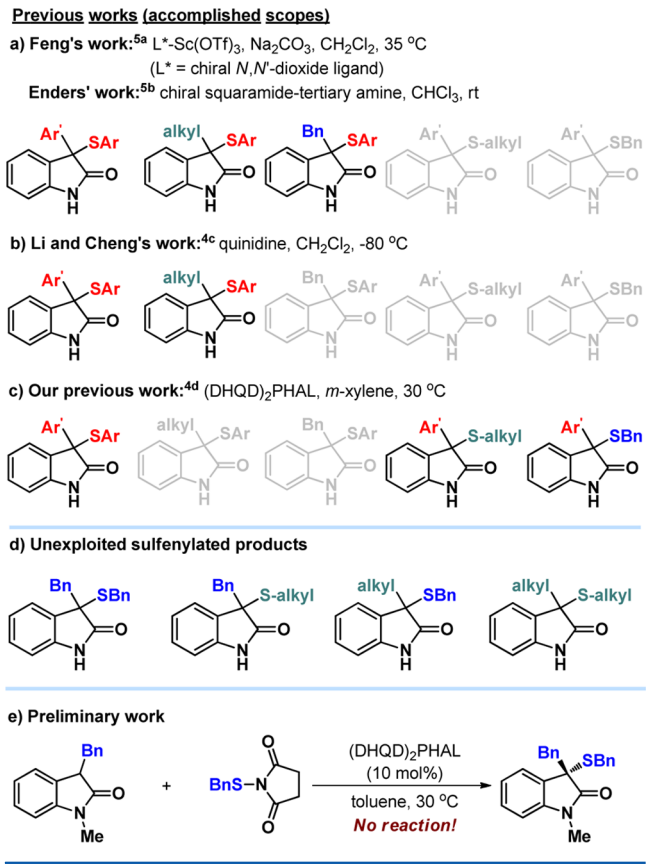
Scheme 1. Established Asymmetric Sulfenylation of 3-Substituted Oxindoles and the Remaining Challenges



guanidines as superbases have been demonstrated as competent catalysts in several sluggish reactions.[7,8] In this regard, we envisioned that chiral bicyclic guanidines should be feasible to accomplish the desired sulfenylation.

To prove the feasibility of the guanidine catalyst, we first attempted an achiral approach of sulfenylation between 3-benzyl-substituted oxindole **1a** and *N*-(benzylthio)succinimide **2a** by employing 10 mol % of 1,1,3,3-tetramethyl guanidine (TMG) as a catalyst in toluene at 30 °C. The reaction completed within 12 h to afford the sulfenylated product **4aa** in 83% yield (Table 1, entry 1). The positive results allowed us to attempt chiral bicyclic guanidines. To our delight, we found that 10 mol % of bicyclic guanidine **I**, which was derived from L-*tert*-leucine, could promote the reaction; the desired adduct **4aa** was obtained in 53% yield with 61% ee after 28 h (entry 2). Afterward, the solvent effect was tested (entries 3−9). It was found that cyclopentyl methyl ether (CPME) was the most suitable solvent for providing the best enantioselectivity (73% ee, entry 8). The lower temperature led to an increase of the enantioselectivity level (entries 10−13), and −10 °C was proven to be the best for producing **4aa** in 56% yield with 82% ee (entry 12).

Since the side chain would probably affect the enantioselectivity, we were engaged to prepare and test a series of other chiral bicyclic guanidines **II**−**V** with distinct side chains (entries 14−17). Bicyclic guanidine **II** with isopropyl as the side chain was discovered to significantly improve the ee value of **4aa** (50% yield, 90% ee, entry 14). The effect of *N*-substituents of 3-oxidoles was then evaluated using 10 mol % of bicyclic guanidine **II** at −10 °C in CPME (entries 18−20). The results described that the oxindole **1b** with methyl as the *N*-substituent group gave the corresponding adduct **4ba** in 45% yield with 92% ee (entry 18). The reactivity was further improved by increasing the amount of catalyst **II** from 0.1 to 0.2 equiv, and **4ba** was obtained in 82% yield with 90% ee after 37 h (entry 21).

With the optimal conditions in hand, the substrate scope, involving various 3-benzyl and alkyl-substituted oxindoles **1** and *N*-(benzyl/alkylthio)succinimides **2**, was investigated (Table 2 and Figure 1). First, we performed the reactions of *N*-(benzylthio)succinimide **2a** with various 3-benzyl-substituted oxindoles (**1e**−**1n**) (entries 1−10). The results showed that the reactions proceeded smoothly and gave the expected adducts (**4ea**−**4na**) in 75−99% yields with 90−98% ee within 37−96 h (entries 1−10). Although the position and electronic properties of the substituents on the aromatic ring of benzyl groups at the C3-position of oxindoles **3** did not affect the ee value, methoxyl as the electron-donating group was found to decrease the reactivity (entries 5−6). Moreover, the substituent groups on the C4, C5, C6, and C7 positions of the aromatic ring of oxindoles **1** made the reaction sluggish (entries 7−10).

Meanwhile, the sulfenylation reactions of 3-benzyl-substituted oxindole **1b** with different *N*-(benzylthio)succinimides **2b**−**g** were conducted, providing the corresponding adducts **4bb**−**bg** in 76−86% yield with 90−95% ee within 63−96 h (entries 11−16). The reaction between oxindole **1b** and *N*-(cyclohexylthio)succinimide **2h** was found to produce 3-alkylthio-substituted 3-benzyloxindole **4bh** in moderate yield and good enantioselectivity (entry 17). Satisfactory results could also be attained for the reactions between 3-alkyl-substituted oxindoles **1o**−**p** and *N*-(benzylthio)succinimides (**2a**−**b** and **2e**) (entries 18−20). Finally, the achieved 3-cyclohexylthio-substituted 3-methyloxindole **4oh** with 65% yield and 92% ee indicated the feasibility of this protocol for the highly enantioselective reaction of 3-alkyl-substituted oxindoles with *N*-(alkylthio)succinimides (entry 21).

In order to illustrate the versatility of this protocol, we were intrigued to examine the sulfenylation of 3-substituted benzofuran-2(3*H*)-ones, mainly due to their analogous structural features to 3-substituted oxindoles as well as the significant potentials of 3,3-disubstituted benzofuran-2(3*H*)-ones in organic and medicinal chemistry.[9−14] Indeed, several asymmetric reactions of 3-substituted benzofuran-2(3*H*)-ones have been disclosed to date, such as Steglich rearrangement,[10] 1,4-conjugate addition,[11] fluorination,[12] amination,[13] and allylic alkylation;[14] however, no example of asymmetric sulfenylation has yet been reported. The reactions of 3-substituted benzofuran-2(3*H*)-ones **3** with *N*-(benzylthio)succinimide **2a** or *N*-(*n*-propylthio)succinimide **2i** were investigated in the presence of 10 mol % of bicyclic guanidine **I** in MTBE as solvent at −10 °C (Scheme 2).[15] The results indicated that 3-substituted benzofuran-2(3*H*)-ones **3** have higher reactivity than 3-substituted oxindoles **2** for the remarkably shortened reaction time (3−5 h). The reaction conditions were suitable to introduce a benzylthio group onto benzofuran-2(3*H*)-ones; the corresponding adducts **5aa**−**5ea** and **5fa** were obtained in 68−93% yield with 71−95% ee. Moderate enantioselectivities (76 and 74% ee) were observed in the creation of 3-*n*-propylthio-substituted benzofuran-2(3*H*)-ones (**5ai** and **5fi**). The absolute configurations of sulfenylated products **4** and **5** were assigned based on X-ray crystallographic analysis of a single crystal of **5aa**.[16]

Next, the synthetic transformation of sulfenylated adducts was attempted to demonstrate the utility of the established

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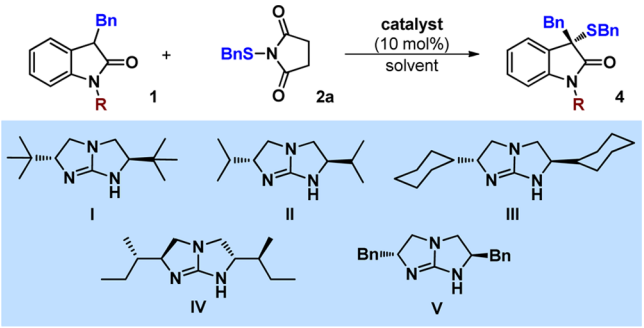
Table 1. Optimization of the Reaction Conditions[a]



entry	1	catalyst	solvent	T (°C)	t (h)	4	yield[b] (%)	ee[c] (%)
1	**1a**	TMG	toluene	30	12	**4aa**	83	N.D.[d]
2	**1a**	**I**	toluene	30	28	**4aa**	53	61
3	**1a**	**I**	CH_2Cl_2	30	14	**4aa**	32	35
4	**1a**	**I**	THF	30	28	**4aa**	N.P.[e]	N.D.[d]
5	**1a**	**I**	Et_2O	30	14	**4aa**	59	63
6	**1a**	**I**	CH_3CN	30	3	**4aa**	40	20
7	**1a**	**I**	hexane	30	14	**4aa**	32	50
8	**1a**	**I**	CPME	30	12	**4aa**	42	73
9	**1a**	**I**	TBME	30	12	**4aa**	28	67
10	**1a**	**I**	CPME	10	12	**4aa**	34	81
11	**1a**	**I**	CPME	0	18	**4aa**	58	81
12	**1a**	**I**	CPME	−10	24	**4aa**	56	82
13	**1a**	**I**	CPME	−20	24	**4aa**	52	81
14	**1a**	**II**	CPME	−10	24	**4aa**	50	90
15	**1a**	**III**	CPME	−10	24	**4aa**	49	87
16	**1a**	**IV**	CPME	−10	24	**4aa**	40	87
17	**1a**	**V**	CPME	−10	24	**4aa**	N.R.[f]	N.D.[d]
18[g]	**1b**	**II**	CPME	−10	24	**4ba**	45	92
19	**1c**	**II**	CPME	−10	24	**4ca**	39	90
20	**1d**	**II**	CPME	−10	24	**4da**	15	79
21[h]	**1b**	**II**	CPME	−10	37	**4ba**	82	90

[a]The reaction was carried out with 0.05 mmol of **1**, 0.06 mmol of **2a**, and 0.05 mmol of catalyst in 0.5 mL of solvent. [b]Isolated yield. [c]Determined by HPLC methods. [d]N.D. = not determined. [e]N.P. = no desired product. [f]N.R. = no reaction. [g]0.1 mmol scale, 94 h, 84% yield, 92% ee. [h]20 mol % of catalyst was used, 0.1 mmol scale.

methodology (Figure 2). It was found that the adduct **3be** could be conveniently oxidized by *m*CPBA in dicholoromethane to provide the sulfone **4** in 95% yield and without compromising the ee value. Subsequently, based on the observed stereochemistry of sulfenylated adducts, a reasonable side-on transition state (TS) was proposed in Figure 2.[6a] The benzyl or alkyl groups of nucleophiles **1** and **3** have longer or bulkier carbon chains than aryl groups, which leads to stronger shielding effects from the side chain of chiral guanidines (*tert*-butyl for catalyst **I** and isopropyl for catalyst **II**), thus presenting higher enantioselective results.

In summary, we have developed two highly enantioselective sulfenylation reactions of oxindoles and benzofuran-2(3*H*)-ones to *N*-(sulfanyl)succinimides, respectively. In the presence of a chiral bicyclic guanidine as the catalyst, the reaction between 3-benzyl/alkyl-substituted oxindoles and *N*-(benzyl/alkylthio)succinimides could work smoothly, affording a series of unprecedented sulfenylated adducts, including 3-benzyl/alkyl-substituted 3-benzyl/alkyloxindoles, in good to excellent yields and enantioselectivities (up to 98% ee). This work successfully replenishes the desired substrate scope in asymmetric sulfenylation of 3-substituted oxindoles. Furthermore, the first asymmetric sulfenylation of benzofuran-2(3*H*)-ones has been accomplished upon this developed methodology, to afford biologically important 3-benzyl-3-benzylthio-substituted benzofuran-2(3*H*)-ones with satisfactory results (up to 95% ee).

EXPERIMENTAL SECTION

General Information. General Procedures and Methods. Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reactions mixtures were stirred in a 4 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in nonvolatile reagents/compounds was removed in high *vacuo* by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in vacuo under ∼30 mmHg and heated with a water bath at 30−35 °C using a rotary evaporator with an aspirator.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on precoated plates, 60 F_{254}. After elution, the plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining $KMnO_4$, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 200−300 mesh. Columns were packed as a slurry of silica gel in petroleum

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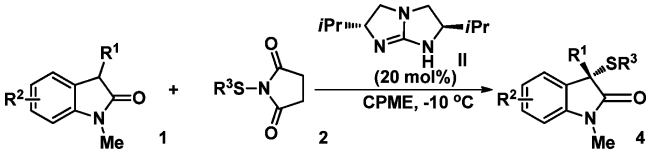
Table 2. Variation of Oxindoles 1 and *N*-(Sulfanyl)succinimides 2[a]



entry	1	2	*t* (h)	4	yield (%)[b]	ee (%)[c]
1	**1e**	**2a**	50	**4ea**	99	92
2	**1f**	**2a**	37	**4fa**	89	93
3[d]	**1g**	**2a**	37	**4ga**	99	93
4[e]	**1h**	**2a**	37	**4ha**	95	92
5	**1i**	**2a**	72	**4ia**	75	95
6	**1j**	**2a**	96	**4ja**	82	90
7	**1k**	**2a**	96	**4ka**	83	92
8	**1l**	**2a**	96	**4la**	75	90
9	**1m**	**2a**	72	**4ma**	97	98
10	**1n**	**2a**	96	**4na**	85	90
11[f]	**1b**	**2b**	72	**4bb**	77	90
12	**1b**	**2c**	96	**4bc**	84	90
13	**1b**	**2d**	96	**4bd**	86	95
14[g]	**1b**	**2e**	63	**4be**	83	90
15	**1b**	**2f**	63	**4bf**	78	92
16	**1b**	**2g**	72	**4bg**	76	92
17	**1b**	**2h**	96	**4bh**	65	86
18	**1o**	**2a**	71	**4oa**	85	90
19	**1p**	**2a**	96	**4pa**	70	92
20	**1o**	**2b**	71	**4ob**	81	92
21	**1o**	**2e**	71	**4oe**	93	92
22	**1o**	**2h**	96	**4oh**	65	92

[a]The reaction was carried out with 0.1 mmol of **1**, 0.12 mmol of **2** and 0.02 mmol of catalyst in 1.0 mL solvent. [b]Isolated yield. [c]Determined by HPLC methods. [d]10 mol % of **II**, 72 h, 99% yield, 93% ee. [e]10 mol % of **II**, 84 h, 80% yield, 92% ee. [f]10 mol % of **II**, 72 h, 70% yield, 90% ee. [g]10 mol % of **II**, 72 h, 75% yield, 90% ee.

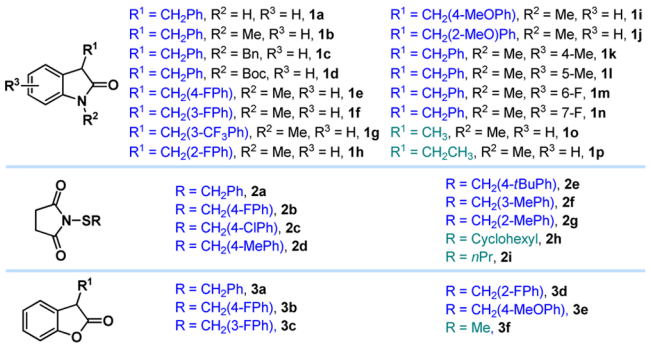
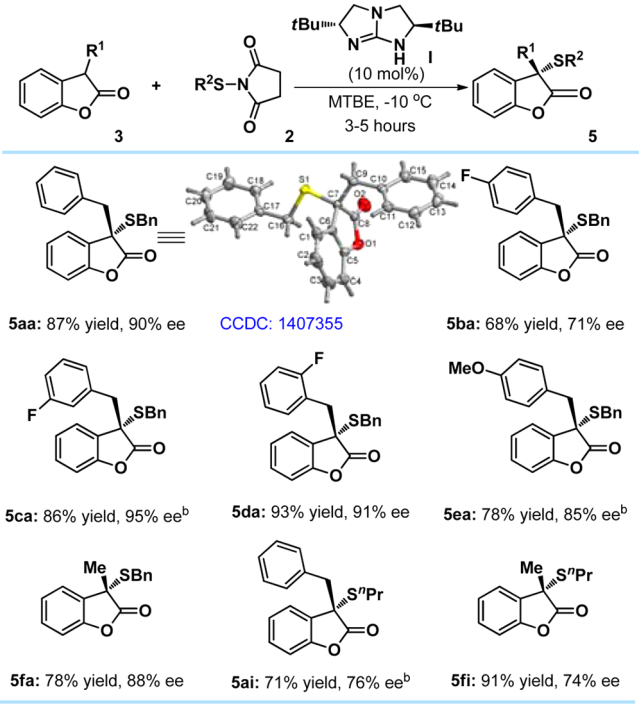


Figure 1. Structures of substrates.

ether and equilibrated solution using the appropriate solvent system. The elution was assisted by applying a pressure of about 2 atm with an air pump.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) and carbon NMR (^{13}C NMR) spectra were recorded in $CDCl_3$ unless otherwise stated. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR were performed on a 300 MHz spectrometer. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *quintet*, *m* (multiplets), *dd* (doublet of doublets), *dt* (doublet of triplets), and *br* (broad). Coupling constants (*J*) were recorded in hertz (Hz). The number of proton atoms (*n*) for a given

Scheme 2. Variation of Benzofuran-2(3*H*)-ones 3 and *N*-(Sulfanyl)succinimides 2[a]



[a]The reaction was carried out with 0.1 mmol of **3**, 0.15 mmol of **2**, and 0.01 mmol of catalyst in 3.0 mL of MTBE at −10 °C (MTBE = methyl *tert*-butyl methyl ether). Yield of isolated product. Ee's were determined by HPLC analysis on a chiral stationary phase. [b]1.0 mL of MTBE was used.

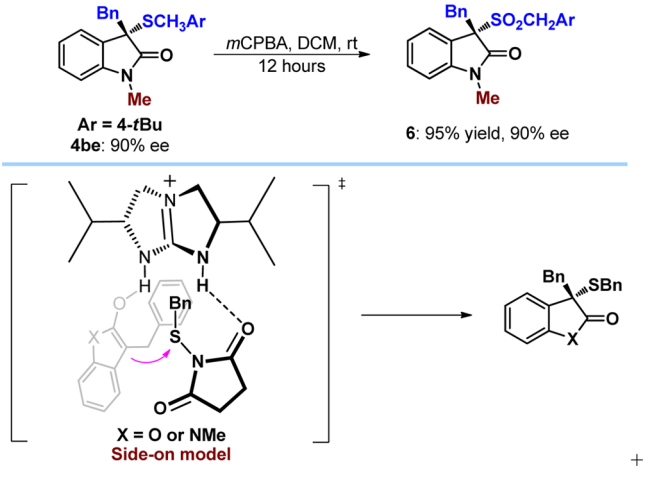


Figure 2. Synthetic transformation of sulfenylated product **4ae** to sulfone **6** and the plausible transition-state model.

resonance was indicated by *n*H. The number of carbon atoms (*n*) for a given resonance was indicated by *n*C. HRMS (Analyzer: TOF) was reported in units of mass of charge ratio (*m*/*z*). Mass samples were dissolved in CH_3CN (HPLC grade) unless otherwise stated. Optical rotations were recorded on a polarimeter with a sodium lamp (wavelength = 589 nm) and reported as follows: $[\alpha]_\lambda^{T\,^\circ C}$ (*c* = g/100 mL, solvent). Melting points were determined on a melting point apparatus.

Enantiomeric excesses were determined by chiral High Performance Liquid Chromatography (HPLC) analysis. UV detection was monitored at 254, 230, and 210 nm at the same time. HPLC samples

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were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Materials. All commercial reagents were purchased with the highest purity grade. They were used without further purification unless specified. All solvents used, mainly petroleum ether (PE) and ethyl acetate (EtOAc), were distilled. Anhydrous CH_2Cl_2 was freshly distilled from CaH_2 and stored under a N_2 atmosphere. Toluene, hexane, diethyl ether, CH_3CN, CPME, TBME, and THF were freshly distilled from sodium/benzophenone before use. All compounds synthesized were stored in a 4 °C freezer, and light-sensitive compounds were protected with aluminum foil.

General Procedure 1. *N*-Methyl-3-benzyl-2-oxindoles **1** (0.1 mmol, 1.0 equiv) and guanidine **II** (0.02 mmol, 0.2 equiv) were dissolved in cyclopentyl methyl ether (1.0 mL) and stirred at −10 °C for 5 min. Then *N*-(sulfanyl)succinimides **2** (0.12 mmol, 1.2 equiv) were added. The reaction mixture was stirred at −10 °C and monitored by TLC. Upon complete consumption of **1**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with petroleum ether/ethyl acetate (10/1−5/1 ratio). Removing the solvent *in vacuo* afforded products **3**.

General Procedure 2. Benzofuran-2(3*H*)-ones **3** (0.1 mmol, 1.0 equiv) and guanidine **I** (0.01 mmol, 0.1 equiv) were dissolved in methyl *tert*-butyl ether (3.0 mL) and stirred at −10 °C for 5 min. Then *N*-(sulfanyl)succinimides **2** (0.15 mmol, 1.5 equiv) were added. The reaction mixture was stirred at −10 °C and monitored by TLC. Upon complete consumption of **3**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with petroleum ether/ethyl acetate (10/1−4/1 ratio). Removing the solvent *in vacuo* afforded products **5**.

4ba, (*S*)-(−)-3-Benzyl-3-(benzylthio)-1-methylindolin-2-one. Colorless oil, 30 mg (0.1 mmol), 82% yield, 90% ee. $[\alpha]_D^{26}$ −37.0 (*c* 0.63, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.24−7.00 (m, 10H), 6.88 (dd, *J* = 7.3, 2.1 Hz, 2H), 6.56 (d, *J* = 7.7 Hz, 1H), 3.70−3.58 (m, 2H), 3.41 (d, *J* = 13.1 Hz, 1H), 3.27 (d, *J* = 13.1 Hz, 1H), 2.84 (s, 3H). ^{13}CNMR (75 MHz, $CDCl_3$) δ 176.0, 143.3, 136.7, 134.7, 130.1, 129.0 (two peaks), 128.3, 127.7, 127.2, 126.9, 124.7, 122.5, 108.0, 56.3, 42.2, 34.0, 26.0 HRMS (ESI) *m*/*z* 360.1421 (M+H$^+$), calcd for $C_{23}H_{21}NOS$ 360.1422. The *ee* was determined by HPLC analysis. CHIRALPAK AD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time: 14.2 min (major) and 11.1 min (minor).

4ea, (*S*)-(−)-3-(Benzylthio)-3-(4-fluorobenzyl)-1-methylindolin-2-one. Colorless oil, 37 mg (0.1 mmol), 99% yield, 92% ee. $[\alpha]_D^{26}$ −29.5 (*c* 0.62, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.4 Hz, 1H), 7.25−7.03 (m, 7H), 6.88−6.79 (m, 2H), 6.72 (t, *J* = 8.4 Hz, 2H), 6.58 (d, *J* = 7.8 Hz, 1H), 3.69−3.58 (m, 2H), 3.38 (d, *J* = 13.1 Hz, 1H), 3.23 (d, *J* = 13.1 Hz, 1H), 2.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 163.49, 160.2, 143.3, 136.6, 131.6 (two peaks), 130.4 (two peaks), 129.0 (two peaks), 128.2 (two peaks), 127.1, 124.5, 122.6, 114.7, 114.4, 108.2, 56.2, 41.4, 34.0, 26.0. HRMS (ESI) *m*/*z* 378.1322 (M+H$^+$), calcd for $C_{23}H_{20}FNOS$ 378.1328. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.7 min (major) and 5.4 min (minor).

4fa, (*S*)-(−)-3-(Benzylthio)-3-(3-fluorobenzyl)-1-methylindolin-2-one. Colorless oil, 34 mg (0.1 mmol), 89% yield, 93% ee. $[\alpha]_D^{26}$ −67.3 (*c* 0.39, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.4, 0.6 Hz, 1H), 7.25−6.97 (m, 8H), 6.76 (td, *J* = 8.4, 2.0 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 6.62−6.55 (m, 2H), 3.70−3.61 (m, 2H), 3.41 (d, *J* = 13.1 Hz, 1H), 3.26 (d, *J* = 13.1 Hz, 1H), 2.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 163.4, 160.9, 143.3, 137.2 (two peaks), 136.6, 129.1 (two peaks), 128.3, 127.9, 127.2, 125.9 (two peaks), 124.5, 122.7, 117.0, 116.8, 113.9, 113.7, 108.2, 56.0, 41.8, 34.0, 26.1. HRMS (ESI) *m*/*z* 378.1324 (M+H$^+$), calcd for $C_{23}H_{20}FNOS$ 378.1328. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.38 min (major) and 5.74 min (minor).

4ga, (*S*)-(−)-3-(Benzylthio)-1-methyl-3-(3-(trifluoromethyl)-benzyl)indolin-2-one. Colorless oil, 42 mg (0.1 mmol), 99% yield, 93% ee. $[\alpha]_D^{26}$ −45.8 (*c* 0.71, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.4 Hz, 2H), 7.26−7.03 (m, 10H), 6.55 (d, *J* = 7.8 Hz, 1H), 3.66 (s, 2H), 3.45 (d, *J* = 13.1 Hz, 1H), 3.29 (d, *J* = 13.1 Hz, 1H), 2.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 143.1, 136.5, 135.6, 133.6, 129.1 (two peaks), 128.2 (two peaks), 127.6, 127.2, 126.7 (two peaks), 124.5, 123.6, 122.7, 108.2, 56.1, 42.1, 34.1, 25.9. HRMS (ESI) *m*/*z* 428.1295 (M+H$^+$), calcd for $C_{24}H_{20}F_3NOS$ 428.1296. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 4.9 min (major) and 4.6 min (minor).

4ha, (*S*)-(−)-3-(Benzylthio)-3-(2-fluorobenzyl)-1-methylindolin-2-one. Colorless oil, 36 mg (0.1 mmol), 95% yield, 92% ee. $[\alpha]_D^{26}$ −35.4 (*c* 0.64, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.4 Hz, 1H), 7.24−7.00 (m, 9H), 6.93−6.84 (m, 1H), 6.77 (t, *J* = 9.0 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 3.73−3.63 (m, 2H), 3.53 (d, *J* = 13.4 Hz, 1H), 3.36 (d, *J* = 13.4 Hz, 1H), 2.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 162.4, 159.2, 143.02, 136.6, 131.7 (two peaks), 128.9 (two peaks), 128.3, 127.8, 127.1, 125.0 (two peaks), 123.5 (two peaks), 122.6, 122.4 (two peaks), 115.2, 114.9, 107.8, 55.7, 33.9, 26.2. HRMS (ESI) *m*/*z* 378.1332 (M+H$^+$), calcd for $C_{23}H_{20}FNOS$ 378.1328. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.7 min (major) and 5.4 min (minor).

4ia, (*S*)-(−)-3-(Benzylthio)-3-(4-methoxybenzyl)-1-methylindolin-2-one. Colorless oil, 29 mg (0.1 mmol), 75% yield, 95% ee. $[\alpha]_D^{26}$ −38.7 (*c* 0.37, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.4 Hz, 1H), 7.29−7.02 (m, 7H), 6.80 (d, *J* = 8.1 Hz, 2H), 6.57 (d, *J* = 7.9 Hz, 3H), 3.68 (s, 3H), 3.63 (s, 2H), 3.34 (d, *J* = 13.2 Hz, 1H), 3.22 (d, *J* = 13.2 Hz, 1H), 2.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 158.3, 143.3, 136.7, 131.2, 128.9 (two peaks), 128.3 (two peaks), 127.1, 126.8, 124.6, 122.5, 113.0, 108.1, 56.4, 55.1, 41.4, 34.0, 26.1. HRMS (ESI) *m*/*z* 390.1524 (M+H$^+$), calcd for $C_{24}H_{23}NO_2S$ 390.1528. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.7 min (major) and 5.4 min (minor).

4ja, (*S*)-(−)-3-(Benzylthio)-3-(2-methoxybenzyl)-1-methylindolin-2-one. Colorless oil, 32 mg (0.1 mmol), 82% yield, 90% ee. $[\alpha]_D^{26}$ −67.7 (*c* 0.54, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.11 (m, 7H), 7.08−7.01 (m, 2H), 6.96 (td, *J* = 7.6, 0.8 Hz, 1H), 6.71 (td, *J* = 7.5, 0.9 Hz, 1H), 6.58−6.55 (m, 2H), 3.67 (d, *J* = 12.5 Hz, 1H), 3.62 (d, *J* = 12.9 Hz, 2H), 3.53 (s, 3H), 3.33 (d, *J* = 13.3 Hz, 1H), 2.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 157.3, 143.1, 136.8, 131.2, 129.1, 128.3 (two peaks), 127.0, 125.5, 123.9, 121.8, 119.8, 109.9, 107.5, 56.2, 54.7, 34.7, 34.0, 26.2. HRMS (ESI) *m*/*z* 390.1521 (M+H$^+$), calcd for $C_{24}H_{23}NO_2S$ 390.1528. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.0 min (major) and 21.1 min (minor).

4ka, (*S*)-(−)-3-Benzyl-3-(benzylthio)-1,4-dimethylindolin-2-one. Colorless oil, 32 mg (0.1 mmol), 83% yield, 92% ee. $[\alpha]_D^{26}$ −14.5 (*c* 0.88, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−6.96 (m, 10H), 6.88 (dd, *J* = 7.0, 2.2 Hz, 2H), 6.46 (d, *J* = 7.9 Hz, 1H), 3.71−3.59 (m, 2H), 3.39 (d, *J* = 13.1 Hz, 1H), 3.25 (d, *J* = 13.1 Hz, 1H), 2.83 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 140.9, 136.8, 134.8, 132.1, 130.2, 129.1 (two peaks), 128.3, 127.7, 127.1, 126.8, 125.3, 107.7, 56.4, 42.2, 34.0, 26.1, 21.2. HRMS (ESI) *m*/*z* 373.1505 (M+H$^+$), calcd for $C_{24}H_{23}NOS$ 373.1500. The *ee* was determined by HPLC analysis. LUX AMYLOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.4 min (major) and 14.8 min (minor).

4la, (*S*)-(−)-3-Benzyl-3-(benzylthio)-1,5-dimethylindolin-2-one. Colorless oil, 28 mg (0.1 mmol), 75% yield, 90% ee. $[\alpha]_D^{26}$ −49.95 (*c* 0.47, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−6.96 (m, 10H), 6.89 (d, *J* = 5.4 Hz, 2H), 6.46 (d, *J* = 7.6 Hz, 1H), 3.72−3.58 (m, 2H), 3.39 (d, *J* = 12.9 Hz, 1H), 3.25 (d, *J* = 13.5 Hz, 1H), 2.83 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 141.0, 136.8, 134.8, 132.1, 130.2, 129.1 (two peaks), 128.3, 127.7, 127.1, 126.8, 125.3, 107.7, 56.4, 42.2, 34.0, 26.1, 21.2. HRMS (ESI) *m*/*z* 373.1505

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J. Org. Chem. 2015, 80, 8933−8941

(M+H$^+$), calcd for $C_{24}H_{23}NOS$ 373.1500. The *ee* was determined by HPLC analysis. CHIRALCEL OD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.7 min (major) and 18.4 min (minor).

4ma, (*S*)-(−)-3-Benzyl-3-(benzylthio)-6-fluoro-1-methylindolin-2-one. Colorless oil, 36 mg (0.1 mmol), 97% yield, 98% ee. $[\alpha]_D^{26}$ −92.2 (*c* 0.24, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29−6.99 (m, 9H), 6.87 (d, *J* = 5.9 Hz, 2H), 6.75 (t, *J* = 8.8 Hz, 1H), 6.29 (d, *J* = 8.8 Hz, 1H), 3.67 (s, 2H), 3.40 (d, *J* = 13.1 Hz, 1H), 3.24 (d, *J* = 13.1 Hz, 1H), 2.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 165.0, 161.7, 144.7 (two peaks), 136.5, 134.5, 130.1, 129.0, 128.3, 127.8, 127.1 (two peaks), 125.8 (two peaks), 123.6 (two peaks), 108.8, 108.5, 97.0, 96.6, 55.8, 42.3, 34.1, 26.2. HRMS (ESI) *m*/*z* 377.1252 (M+H$^+$), calcd for $C_{23}H_{20}FNOS$ 377.1250. The *ee* was determined by HPLC analysis. CHIRALPAK ID-3 (3.0 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.0 min (major) and 11.3 min (minor).

4na, (*S*)-(−)-3-Benzyl-3-(benzylthio)-7-fluoro-1-methylindolin-2-one. Colorless oil, 32 mg (0.1 mmol), 85% yield, 90% ee. $[\alpha]_D^{26}$ −49.98 (*c* 0.14, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (dt, *J* = 6.7, 5.8 Hz, 3H), 7.10 (ddd, *J* = 15.7, 8.0, 4.2 Hz, 6H), 7.04−6.90 (m, 2H), 6.87 (dd, *J* = 7.5, 1.8 Hz, 2H), 3.67 (s, 2H), 3.42 (d, *J* = 13.1 Hz, 1H), 3.24 (d, *J* = 13.1 Hz, 1H), 3.03 (d, *J* = 2.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 136.4, 134.3, 131.3, 130.1, 129.0, 128.3, 127.8, 127.1 (two peaks), 123.0 (two peaks), 120.5, 116.7 (two peaks), 56.4, 42.5, 34.2, 28.5 (two peaks). HRMS (ESI) *m*/*z* 377.1252 (M+H$^+$), calcd for $C_{23}H_{20}FNOS$ 377.1250. The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.7 min (major) and 14.7 min (minor).

4bb, (*S*)-(−)-3-Benzyl-3-((4-fluorobenzyl)thio)-1-methylindolin-2-one. Colorless oil, 29 mg (0.1 mmol), 77% yield, 90% ee. $[\alpha]_D^{26}$ −43.8 (*c* 0.43, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.4 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.07 (dd, *J* = 13.7, 6.2 Hz, 6H), 6.87 (dd, *J* = 10.4, 4.9 Hz, 4H), 6.56 (d, *J* = 7.8 Hz, 1H), 3.68−3.55 (m, 2H), 3.39 (d, *J* = 13.1 Hz, 1H), 3.26 (d, *J* = 13.1 Hz, 1H), 2.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 143.2, 134.5, 132.4 (two peaks), 130.6 (two peaks), 130.1, 129.0, 128.2, 127.7, 126.8, 124.6, 122.6, 115.2, 114.9, 108.0, 56.3, 42.3, 33.3, 26.0. HRMS (ESI) *m*/*z* 378.1326 (M+H$^+$), calcd for $C_{23}H_{20}FNOS$ 378.1328. The *ee* was determined by HPLC analysis. LUX AMYLOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.7 min (major) and 6.3 min (minor).

4bc, (*S*)-(−)-3-Benzyl-3-((4-chlorobenzyl)thio)-1-methylindolin-2-one. Colorless oil, 33 mg (0.1 mmol), 84% yield, 90% ee. $[\alpha]_D^{26}$ −72.0 (*c* 0.30, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.3 Hz, 1H), 7.25−7.13 (m, 3H), 7.12−6.98 (m, 6H), 6.87 (d, *J* = 6.4 Hz, 2H), 6.66−6.42 (m, 1H), 3.74−3.52 (m, 2H), 3.38 (d, *J* = 13.1 Hz, 1H), 3.25 (d, *J* = 13.1 Hz, 1H), 2.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 143.2, 135.3, 134.5, 132.8, 130.4 (two peaks), 129.0, 128.4, 128.1, 127.7, 126.9, 124.7, 122.6, 108.1, 56.3, 42.3, 33.4, 26.0. HRMS (ESI) *m*/*z* 394.1035 (M+H$^+$), calcd for $C_{23}H_{20}ClNOS$ 394.1032. The *ee* was determined by HPLC analysis. LUX AMYLOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.8 min (major) and 19.7 min (minor).

4bd, (*S*)-(−)-3-Benzyl-1-methyl-3-((4-methylbenzyl)thio)-indolin-2-one. Colorless oil, 32 mg (0.1 mmol), 86% yield, 95% ee. $[\alpha]_D^{26}$ −36.9 (*c* 0.26, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.3 Hz, 1H), 7.47 (dd, *J* = 14.9, 7.4 Hz, 2H), 7.32 (dd, *J* = 13.5, 6.6 Hz, 4H), 7.26 (s, 3H), 7.14 (d, *J* = 6.6 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 1H), 3.87 (q, *J* = 12.4 Hz, 2H), 3.66 (d, *J* = 13.1 Hz, 1H), 3.52 (d, *J* = 13.1 Hz, 1H), 3.11 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 143.3, 136.7, 134.7, 133.5, 130.2, 128.9 (two peaks), 128.4, 127.7, 126.8, 124.6, 122.5, 108.0, 56.3, 42.2, 33.6, 26.0, 21.1. HRMS (ESI) *m*/*z* 374.1578 (M+H$^+$), calcd for $C_{24}H_{23}NOS$ 374.1579. The *ee* was determined by HPLC analysis. LUX AMYLOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.6 min (major) and 16.9 min (minor).

4be, (*S*)-(−)-3-Benzyl-3-((4-(*tert*-butyl)benzyl)thio)-1-methylindolin-2-one. Colorless oil, 34 mg (0.1 mmol), 83% yield, 90% ee. $[\alpha]_D^{26}$ −27.6 (*c* 0.70, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.4 Hz, 1H), 7.22 (dd, *J* = 16.6, 8.7 Hz, 3H), 7.05 (t, *J* = 11.0 Hz, 6H), 6.89 (d, *J* = 6.7 Hz, 2H), 6.55 (d, *J* = 7.7 Hz, 1H), 3.71−3.51 (m, 2H), 3.42 (d, *J* = 13.1 Hz, 1H), 3.28 (d, *J* = 13.1 Hz, 1H), 2.83 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 149.9, 143.3, 134.7, 133.5, 130.2, 128.8 (two peaks), 128.3, 127.7, 126.8, 125.2, 124.6, 122.5, 108.0, 56.3, 42.2, 34.5, 33.6, 31.3, 26.0. HRMS (ESI) *m*/*z* 416.2049 (M+H$^+$), calcd for $C_{27}H_{29}NOS$ 416.2048. The *ee* was determined by HPLC analysis. LUX AMYLOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; low rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.5 min (major) and 6.1 min (minor).

4bf, (*S*)-(−)-3-Benzyl-1-methyl-3-((3-methylbenzyl)thio)-indolin-2-one. Colorless oil, 29 mg (0.1 mmol), 78% yield, 92% ee. $[\alpha]_D^{26}$ −27.8 (*c* 0.88, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.3 Hz, 1H), 7.22 (dd, *J* = 15.0, 7.3 Hz, 2H), 7.16−7.00 (m, 5H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 6.9 Hz, 3H), 6.56 (d, *J* = 7.7 Hz, 1H), 3.74−3.50 (m, 2H), 3.42 (d, *J* = 13.0 Hz, 1H), 3.27 (d, *J* = 13.0 Hz, 1H), 2.85 (s, 3H), 2.27 (s, 3H) . ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 143.3, 137.9, 136.4, 134.7, 130.1, 129.8, 128.9, 128.2 (two peaks), 127.8 (two peaks), 126.8, 126.1, 124.6, 122.5, 108.0, 56.3, 42.2, 34.0, 26.0, 21.3. HRMS (ESI) *m*/*z* 374.1581 (M+H$^+$), calcd for $C_{24}H_{23}NOS$ 374.1579. The *ee* was determined by HPLC analysis. CHIRALPAK AD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 14.0 min (major) and 12.3 min (minor).

4bg, (*S*)-(−)-3-Benzyl-1-methyl-3-((2-methylbenzyl)thio)-indolin-2-one. Colorless oil, 28 mg (0.1 mmol), 76% yield, 92% ee. $[\alpha]_D^{26}$ −33.2 (*c* 0.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.3 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.16−7.00 (m, 8H), 6.91 (d, *J* = 5.1 Hz, 2H), 6.60 (d, *J* = 7.8 Hz, 1H), 3.75 (d, *J* = 11.4 Hz, 1H), 3.60 (d, *J* = 11.4 Hz, 1H), 3.47 (d, *J* = 13.1 Hz, 1H), 3.29 (d, *J* = 13.1 Hz, 1H), 2.96 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 143.2, 137.1, 134.8, 134.1, 130.3 (two peaks), 128.9, 128.5, 127.6 (two peaks), 126.8, 125.9, 124.6, 122.6, 108.0, 56.4, 42.0, 31.6, 26.1, 19.0. HRMS (ESI) *m*/*z* 374.1570 (M+H$^+$), calcd for $C_{24}H_{23}NOS$ 374.1579. The ee was determined by HPLC analysis. CHIRALCEL OD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.2 min (major) and 5.4 min (minor).

4bh, (*S*)-(−)-3-Benzyl-3-(cyclohexylthio)-1-methylindolin-2-one. Colorless oil, 23 mg (0.1 mmol), 65% yield, 86% ee. $[\alpha]_D^{26}$ −40.1 (*c* 0.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.4 Hz, 1H), 7.19 (dt, *J* = 7.7, 3.8 Hz, 1H), 7.14−6.99 (m, 4H), 6.86 (dd, *J* = 7.3, 1.9 Hz, 2H), 6.58 (d, *J* = 7.7 Hz, 1H), 3.41 (d, *J* = 12.9 Hz, 1H), 3.24 (d, *J* = 13.0 Hz, 1H), 2.98 (s, 3H), 2.64 (s, 1H), 1.79 (d, *J* = 13.0 Hz, 1H), 1.72−1.52 (m, 4H), 1.48−1.31 (m, 2H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9, 142.9, 134.7, 130.1, 129.4, 128.7, 127.6, 126.7, 124.5, 122.5, 107.9, 56.2, 43.2, 42.3, 35.1, 34.1, 26.2, 25.8 (two peaks), 25.4. HRMS (ESI) *m*/*z* 352.1732 (M+H$^+$), calcd for $C_{22}H_{25}NOS$ 352.1735.The ee was determined by HPLC analysis. CHIRALCEL OZ-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.0 min (major) and 23.3 min (minor).

4oa, (*S*)-(−)-3-(Benzylthio)-1,3-dimethylindolin-2-one. Colorless oil, 24 mg (0.1 mmol), 85% yield; 90% ee. $[\alpha]_D^{26}$ −56.6 (*c* 0.55, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.27 (m, 2H), 7.24−7.05 (m, 6H), 6.79 (d, *J* = 7.8 Hz, 1H), 3.59 (s, 2H), 3.06 (s, 3H), 1.66 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 136.64, 130.9, 128.9 (two peaks), 128.3, 127.1, 123.7, 123.0 108.2, 50.7, 34.2, 26.3, 22.6. HRMS (ESI) *m*/*z* 284.1107 (M+H$^+$), calcd for $C_{17}H_{17}NOS$ 284.1109. The ee was determined by HPLC analysis. LUX CELLULOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 0.5 mL/min; 25 °C; 254 nm; retention time: 11.7 min (major) and 12.6 min (minor).

4pa, (*S*)-(−)-3-(Benzylthio)-3-ethyl-1-methylindolin-2-one. Colorless oil, 21 mg (0.1 mmol), 70% yield, 92% ee. $[\alpha]_D^{26}$ −114.7 (*c* 0.16, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.9 Hz, 2H), 7.22−7.06 (m, 6H), 6.79 (d, *J* = 7.7 Hz, 1H), 3.59 (s, 2H), 3.07

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J. Org. Chem. 2015, 80, 8933−8941

(s, 3H), 2.24−1.98 (m, 2H), 0.69 (t, J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 143.6, 136.8, 128.9 (two peaks), 128.3, 127.0, 124.1, 122.9 9, 108.1, 55.6, 33.7, 29.4, 26.2, 23.5, 9.0. HRMS (ESI) m/z 297.1186 ($M+H^+$), calcd for $C_{18}H_{19}NOS$ 297.1187. The ee was determined by HPLC analysis. CHIRALPAK IB (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.5 min (major) and 13.3 min (minor).

4ob, (*S*)-(−)-3-((4-Fluorobenzyl)hio)-1,3-dimethylindolin-2-one. Colorless oil, 24 mg (0.1 mmol), 81% yield, 92% ee. $[\alpha]_D^{26}$ −78.0 (c 0.39, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.22 (m, 2H), 7.20−7.00 (m, 3H), 6.88 (t, J = 8.2 Hz, 2H), 6.80 (d, J = 7.9 Hz, 1H), 3.57 (s, 2H), 3.08 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 163.5, 160.2, 142.7, 132.4, 130.9−130.3, 129.0, 123.7, 123.0, 115.2, 115.0, 108.3, 50.8, 33.4, 26.3, 22.7. HRMS (ESI) m/z 302.1016 ($M+H^+$), calcd for $C_{17}H_{16}FNOS$ 302.1015. The ee was determined by HPLC analysis. CHIRALCEL OZ-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.0 min (major) and 17.1 (minor).

4oe, (*S*)-(−)-3-((4-(*tert*-Butyl)benzyl)thio)-1,3-dimethylindolin-2-one. Colorless oil, 31 mg (0.1 mmol), 93% yield, 92% ee. $[\alpha]_D^{26}$ −36.5 (c 1.20, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.18 (m, 4H), 7.10 (t, J = 7.3 Hz, 1H), 7.02 (d, J = 7.6 Hz, 2H), 6.78 (d, J = 7.7 Hz, 1H), 3.57 (s, 2H), 3.05 (s, 3H), 1.67 (s, 3H), 1.27 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 149.9, 142.8, 133.5, 131.0, 128.7 (two peaks), 125.2, 123.7, 122.9, 108.2, 50.7, 34.5, 33.8, 31.3, 26.3, 22.7. HRMS (ESI) m/z 340.1732 ($M+H^+$), calcd for $C_{21}H_{25}NOS$ 340.1735. The ee was determined by HPLC analysis. CHIRALCEL OZ-H 4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 11.7 (major) and 13.2 (minor).

4oh, (*S*)-(−)-3-(Cyclohexylthio)-1,3-dimethylindolin-2-one. Colorless oil, 18 mg (0.1 mmol), 65% yield, 92% ee. $[\alpha]_D^{26}$ −94.0 (c 0.10, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.29 (m, 2H), 7.11 (dd, J = 11.2, 3.8 Hz, 1H), 6.91−6.78 (m, 1H), 3.24 (s, 3H), 2.57 (s, 1H), 1.86−1.73 (m, 1H), 1.65 (s, 3H), 1.57 (d, J = 7.9 Hz, 3H), 1.51−1.28 (m, 3H), 1.18 (dd, J = 13.3, 7.0 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3, 142.4, 132.1, 128.7, 123.7, 123.0, 108.2, 50.5, 42.4, 35.2, 34.2, 26.5, 25.9 (two peaks), 25.5, 23.4. HRMS (ESI) m/z 276.1428 ($M+H^+$), calcd for $C_{16}H_{21}NOS$ 276.1422. The ee was determined by HPLC analysis. CHIRALCEL OZ-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.4 (major) and 19.1 (minor).

5aa, (*S*)-(+)-3-Benzyl-3-(benzylthio)benzofuran-2(3*H*)-one. White solid, mp 98.5−100.4 °C, 30 mg (0.1 mmol), 87% yield, 90% ee. $[\alpha]_D^{26}$ +21.31 (c 0.40, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.17 (m, 8H), 7.17−7.09 (m, 3H), 7.01−6.89 (m, 3H), 3.84 (d, J = 12.2 Hz, 1H), 3.70 (d, J = 12.2 Hz, 1H), 3.52 (d, J = 13.4 Hz, 1H), 3.38 (d, J = 13.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8, 152.6, 135.8, 133.9, 130.1, 129.8, 129.2, 128.6, 128.2, 127.4 (two peaks), 126.9, 124.8, 124.4, 110.9, 55.2, 42.3, 34.5. HRMS (EI) m/z 346.1030 (M^+), calcd for $C_{22}H_{18}O_2S$ 346.1028, The ee was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 10.1 min (minor) and 10.8 min (major).

5ba, (*S*)-3-(Benzylthio)-3-(4-fluorobenzyl)benzofuran-2(3*H*)-one. White solid, mp 123.5−124.8 °C, 25 mg (0.1 mmol), 68% yield, 71% ee. $[\alpha]_D^{26}$ +10.34 (c 0.60, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.20 (m, 2H), 7.19−7.06 (m, 6H), 6.87−6.77 (m, 3H), 6.72 (t, J = 8.7 Hz, 2H), 3.72 (d, J = 12.2 Hz, 1H), 3.59 (d, J = 12.2 Hz, 1H), 3.38 (d, J = 13.5 Hz, 1H), 3.24 (d, J = 13.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 163.7, 160.4, 152.6, 135.7, 131.7 (two peaks), 130.0, 129.6, 129.2, 128.6, 127.5, 126.7, 124.6 (two peaks), 115.3, 115.0, 111.0, 55.2, 41.5, 34.5. HRMS (EI) m/z 364.0930 (M^+), calcd for $C_{22}H_{17}FO_2S$ 364.0933. The ee was determined by HPLC analysis. CHIRALPAK IC−IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 19.9 min (major) and 27.0 min (minor).

5ca, (*S*)-(+)-3-(Benzylthio)-3-(3-fluorobenzyl)benzofuran-2(3*H*)-one. White solid, mp 87.7−89.2 °C, 31 mg (0.1 mmol), 86% yield, 95% ee. $[\alpha]_D^{26}$ +22.00 (c 0.30, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.07 (m, 8H), 7.00 (td, J = 7.9, 6.2 Hz, 1H), 6.85 (d, J = 8.0 Hz, 1H), 6.75 (td, J = 8.4, 2.2 Hz, 1H), 6.65 (d, J = 7.7 Hz, 1H), 6.55 (dd, J = 9.7, 1.8 Hz, 1H), 3.73 (d, J = 12.2 Hz, 1H), 3.61 (d, J = 12.2 Hz, 1H), 3.40 (d, J = 13.4 Hz, 1H), 3.26 (d, J = 13.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 164.0, 160.7, 152.6, 136.3 (two peaks), 135.7, 130.1, 129.7 (two peaks), 129.2, 128.6, 127.6, 126.6, 125.9 (two peaks), 124.6 (two peaks), 117.2, 116.9, 114.6, 114.3, 111.0, 54.9, 41.9 (two peaks), 34.5. HRMS (EI) m/z 364.0932 (M^+), calcd for $C_{22}H_{17}FO_2S$ 364.0933. The ee was determined by HPLC analysis. CHIRALPAK IC−IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 18.9 min (major) and 21.2 min (minor).

5da, (*S*)-(+)-3-(Benzylthio)-3-(2-fluorobenzyl)benzofuran-2(3*H*)-one. White solid, mp 95.1−96.8 °C, 34 mg (0.1 mmol), 93% yield, 91% ee. $[\alpha]_D^{26}$ +26.00 (c 0.40, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27−7.19 (m, 1H), 7.20−7.08 (m, 6H), 7.08−6.97 (m, 3H), 6.90−6.80 (m, 2H), 6.74 (t, J = 9.1 Hz, 1H), 3.76 (d, J = 12.1 Hz, 1H), 3.63 (d, J = 12.1 Hz, 1H), 3.51 (d, J = 13.7 Hz, 1H), 3.39 (d, J = 13.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8, 162.4, 159.2, 152.5, 135.7, 131.6 (two peaks), 129.9, 129.5, 129.4 (two peaks), 129.2, 128.6 (two peaks), 127.5, 126.5, 125.2 (two peaks), 124.4, 124.1 (two peaks), 121.6 (two peaks), 115.5, 115.2, 110.6, 54.6, 43.2, 34.5, 34.4 (two peaks). HRMS (EI) m/z 364.0932 (M^+), calcd for $C_{22}H_{17}FO_2S$ 364.0933. The ee was determined by HPLC analysis. CHIRACEL OD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.6 min (minor) and 8.4 min (major).

5ea, (*S*)-(+)-3-(Benzylthio)-3-(4-methoxybenzyl)benzofuran-2(3*H*)-one. yellow oil, 29 mg (0.1 mmol), 78% yield, 85% ee. $[\alpha]_D^{26}$ +44.88 (c 0.40, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (t, J = 5.5 Hz, 1H), 7.20 (ddd, J = 14.2, 6.4, 4.6 Hz, 8H), 6.91 (d, J = 7.9 Hz, 1H), 6.84 (d, J = 8.6 Hz, 2H), 6.63 (d, J = 8.6 Hz, 2H), 3.78 (d, J = 12.2 Hz, 1H), 3.70 (s, 3H), 3.65 (d, J = 12.2 Hz, 1H), 3.42 (d, J = 13.5 Hz, 1H), 3.29 (d, J = 13.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 158.8, 152.7, 135.8, 131.2, 129.8, 129.2, 128.5, 127.4, 127.1, 125.9, 124.8, 124.4, 113.6, 110.9, 55.2 (two peaks), 41.5, 34.5, 29.7. HRMS (EI) m/z 376.1136 (M^+), calcd for $C_{23}H_{20}O_3S$ 376.1133. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 95/5; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 9.8 min (minor) and 11.6 min (major).

5fa, (*S*)-3-(Benzylthio)-3-methylbenzofuran-2(3*H*)-one. Colorless oil, 21 mg (0.1 mmol), 78% yield, 88% ee. $[\alpha]_D^{26}$ +15.06 (c 0.64, $CHCl_3$), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.30 (m, 2H), 7.25−7.07 (m, 7H), 3.73 (d, J = 12.2 Hz, 1H), 3.63 (d, J = 12.2 Hz, 1H), 1.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 152.3, 135.8, 129.8, 129.2 (two peaks), 128.5, 127.4, 124.8, 124.0, 111.0, 49.3, 34.6, 22.9. HRMS (ESI) m/z 271.0801 ($M+H^+$), calcd for $C_{16}H_{15}O_2S$ 271.0793. The ee was determined by HPLC analysis. CHIRALPAK IC−IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.7 min (minor) and 22.9 min (major).

5ai, (*S*)-(+)-3-Benzyl-3-(propylthio)benzofuran-2(3*H*)-one. White solid, mp 48.4−50.1 °C, 21 mg (0.1 mmol), 71% yield, 76% ee. $[\alpha]_D^{26}$ +54.18 (c 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (dt, J = 10.0, 4.9 Hz, 1H), 7.19−6.99 (m, 5H), 6.92−6.78 (m, 3H), 3.42 (d, J = 13.4 Hz, 1H), 3.27 (d, J = 13.4 Hz, 1H), 2.45 (dt, J = 11.7, 7.2 Hz, 1H), 2.30 (dt, J = 11.7, 7.5 Hz, 1H), 1.48−1.33 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 152.5, 134.1, 130.1, 129.6, 128.2, 127.4 (two peaks), 124.8, 124.4, 110.7, 54.6, 42.3, 31.6, 22.1, 13.5. HRMS (EI) m/z 298.1030 (M^+), calcd for $C_{18}H_{18}O_2S$ 298.1028. The ee was determined by HPLC analysis. LUX CELLULOSE-4 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 0.8 mL/min; 25 °C; 254 nm; retention time: 11.0 min (minor) and 12.3 min (major).

5fi, (*S*)-(+)-3-Methyl-3-(propylthio)benzofuran-2(3*H*)-one. Colorless oil, 20 mg (0.1 mmol), 91% yield, 74% ee. $[\alpha]_D^{26}$ +35.01 (c 0.40, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.25−7.01 (m, 3H), 2.49−2.19 (m, 2H), 1.71 (s, 3H), 1.40 (dd, J = 14.1, 7.0 Hz, 2H), 0.83 (t, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 151.2, 128.9, 128.6, 123.7, 122.8, 109.8, 47.6, 30.7, 21.8, 21.0,

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12.4. HRMS (EI) m/z 222.0719 (M^+), calcd for $C_{12}H_{14}O_2S$ 222.0715. The ee was determined by HPLC analysis. LUX CELLULOSE-4 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 0.8 mL/min; 25 °C; 254 nm; retention time: 7.4 min (minor) and 8.0 min (major).

6, (*S*)-(+)-3-Benzyl-3-((4-(*tert*-butyl)benzyl)sulfonyl)-1-methylindolin-2-one. Colorless oil, 95% yield, 90% ee. $[\alpha]_D^{26}$ +33.8 (c 0.31, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J = 7.5 Hz, 1H), 7.32−7.21 (m, 4H), 7.19 (d, J = 6.2 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 7.00−6.89 (m, 3H), 6.80 (dd, J = 7.3, 1.6 Hz, 2H), 6.52 (d, J = 7.8 Hz, 1H), 4.54 (d, J = 13.4 Hz, 1H), 4.42 (d, J = 13.4 Hz, 1H), 3.73 (d, J = 12.8 Hz, 1H), 3.55 (d, J = 12.8 Hz, 1H), 2.90 (s, 3H), 1.22 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 152.0, 144.4, 132.7, 131.2, 130.6, 129.9, 128.0, 127.2, 126.7, 125.7, 123.1 (two peaks), 121.4, 108.5, 75.2, 54.9, 37.3, 34.7, 31.2. HRMS (ESI) m/z 447.1869 ($M+H^+$), calcd for $C_{27}H_{29}O_3NS$ 447.1868. The ee was determined by HPLC analysis. LUX CELLULOSE-1 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.1 (major) and 26.8 (minor).

7, (*S*)-(+)-3-Benzyl-3-(*p*-tolylthio)benzofuran-2(3*H*)-one. White solid, mp 125.4−128.7, 25 mg (0.1 mmol), 72% yield; 75% ee. $[\alpha]_D^{26}$ +12.06 (c 0.70, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.36 (m, 1H), 7.22−7.04 (m, 7H), 6.97 (dd, J = 10.3, 6.1 Hz, 4H), 6.72−6.63 (m, 1H), 3.51 (d, J = 13.4 Hz, 1H), 3.43 (d, J = 13.4 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 152.6, 140.4, 136.6, 134.2, 130.1, 129.6 (two peaks), 128.2, 127.3, 125.1 (two peaks), 124.1, 110.6, 58.9, 41.7, 21.3; HRMS (ESI) m/z 347.1109 ($M+H^+$), calcd for $C_{22}H_{19}O_2S$ 347.1106. The *ee* was determined by HPLC analysis. CHIRALPAK IC-IC (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 25.9 min (major) and 28.3 min (minor).

8, (*S*)-(+)-3-Methyl-3-(*p*-tolylthio)benzofuran-2(3*H*)-one. White solid, mp 73.5−76.0, 20 mg (0.1 mmol), 72% yield, 75% ee. $[\alpha]_D^{26}$ +11.94 (c 0.60, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (dd, J = 7.3, 1.5 Hz, 1H), 7.25−7.07 (m, 4H), 6.98 (d, J = 7.9 Hz, 2H), 6.91−6.82 (m, 1H), 2.28 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 152.2, 140.4, 129.6 (three peaks), 125.7, 124.4, 124.1, 110.6, 53.1, 22.0, 21.3; HRMS (ESI) m/z 271.0791 ($M+H^+$), calcd for $C_{16}H_{15}O_2S$ 271.0793. The *ee* was determined by HPLC analysis. LUX CELLULOSE-4 (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 10.6 min (minor) and 11.9 min (major).

9, (*S*)-3-(Benzylthio)-3-phenylbenzofuran-2(3*H*)-one. Colorless oil, 23 mg (0.1 mmol), 69% yield, 0% ee. ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 7.2 Hz, 2H), 7.30 (dt, J = 11.8, 7.2 Hz, 5H), 7.11 (ddd, J = 8.4, 7.7, 5.0 Hz, 7H), 3.71 (d, J = 11.8 Hz, 1H), 3.55 (d, J = 11.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 152.2, 135.4 (two peaks), 130.0, 129.2 (two peaks), 128.5 (three peaks), 127.5, 125.5, 124.8, 111.2, 57.2, 35.4; HRMS (ESI) m/z 333.0946 ($M+H^+$), calcd for $C_{21}H_{17}O_2S$ 333.0949. The *ee* was determined by HPLC analysis. LUX CELLULOSE-2 (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.9 and 10.6 min.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01606.

Copies of HPLC spectra, compounds **7**−**9**, determination of the absolute configuration by X-ray crystallography and copies of NMR spectra (PDF)

More experimental data (ZIP)

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Notes

The authors declare no competing financial interest.

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(15) Catalyst **II** gave slightly decreased enantioselectivity. Moreover, the results for other kinds of sulfenylated products **7**−**9**, including 3-benzyl/alkyl-3-arylthio-substituted and 3-aryl-3-benzylthio-substituted benzofuran-2(3*H*)-ones, are summarized in the Supporting Information.
(16) CCDC1407355 (**5aa**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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