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Preparation of 3-Sulfonylated 3,3-Disubstituted Oxindoles by the Addition of Sulfinate Salts to 3-Halooxindoles

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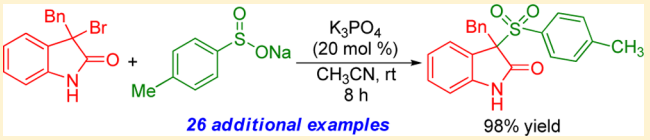
Supporting Information

ABSTRACT: An efficient method for the preparation of 3-sulfonylated 3,3-disubstituted oxindole derivatives has been developed. The protocol involves a base-catalyzed addition of sulfinate salts to 3-halooxindoles, affording a wide range of 3-sulfonylated 3,3-disubstituted oxindoles in good to excellent yields under mild conditions. A preliminary trial of asymmetric catalytic version was conducted and gave promising enantioselectivity. The mechanism for the reaction was tentatively explored with the help of mass spectrometric analysis.



A 3,3-disubstituted oxindole core is present as a characteristic structural motif in numerous alkaloids that exhibit diverse biological and pharmaceutical activities.[1] In particular, 3,3-disubstituted oxindoles bearing a heteroatom at the C-3 position have received considerable attention owing to their potential applications in medicinal chemistry.[1,2] Consequently, a variety of synthetic strategies have been reported to access various 3-heteroatom-containing 3,3-disubstituted oxindoles,[1] including 3-aminooxindoles,[2h] 3-hydroxyoxindoles,[2f,g] 3-chlorooxindoles,[2d] 3-fluorooxindoles,[2e] etc.[2a−c] Notably, it has been found that many 3,3-disubstituted oxindoles bearing a sulfur atom at the C-3 position possess some antitubercular, antifungal, or anticancer activities.[3] In this context, the synthesis of 3-sulfur-containing 3,3-disubstituted oxindoles has been widely explored and many approaches have been developed.[4] Despite all this, we noticed that a method for the direct construction of 3-sulfonylated 3,3-disubstituted oxindoles remained elusive.

Among the remarkable advancements in the construction of 3,3-disubstituted oxindoles,[1] to the best of our knowledge, the corresponding progress in the functionalization of 3-halooxindoles to access 3,3-disubstituted oxindoles is limited. Inspired by pioneering work of Hinman and Bauman[5] as well as Stoltz[6] employing 3-halooxindoles as electrophiles in substitution chemistry, we reported the related enantioselective stereoablative reactions of 3-halooxindoles.[7] In the intervening time, some strategies taking advantage of the electrophilicity of 3-halooxindoles for the synthesis of oxindole derivatives have also been reported.[8] Additionally, sulfinate salts are well-known to serve as a class of nucleophilic reagents in some addition reactions.[9] Based on these concerns, as part of our ongoing efforts in the application of 3-halooxindoles as electrophiles precursor for the synthesis of 3,3-disubstituted oxindoles,[7,10] we envisioned that it would be possible to develop a direct sulfonylation of 3-halooxindoles with sulfinate salts as nucleophiles, giving a new class of 3,3-disubstituted oxindoles containing a sulfonyl group. Herein, we report our progress on this subject. Notably, this represents the first example regarding the synthesis of 3-arylsulfonyl-3,3-disubstituted oxindole compounds.

We began our studies on the sulfonylation of 3-halooxindoles by investigating the reaction of 3-benzyl-3-bromooxindole (**1a**) and sodium *p*-toluenesulfinate (**2a**) (Table 1). First, the background reaction provided the sulfonated product **3a** in less than 10% yield after 36 h in CH_2Cl_2 at room temperature (entry 1). Afterward, a screening for various bases was performed with 200 mol % loading in CH_2Cl_2 (entries 2−7); K_3PO_4 appeared to be the most active catalyst for the reaction, furnishing **3a** in 85% yield (entry 3). To our delight, the subsequent catalyst loading screening (entries 8−10) revealed that **3a** could be obtained in almost quantitative yield with only 20 mol % K_3PO_4 (entry 10). Ultimately, the effect of solvent was examined in the presence of 20 mol % K_3PO_4 (entries 11−15). CH_3CN turned out to be the best choice for the reaction in light of the reactivity and yield (entry 13). In particular, the reaction could proceed to completion at room temperature in CH_3CN within only 8 h with K_3PO_4 (entry 13). Under similar conditions, **3a** could be obtained in 97% yield after 13 h with Na_3PO_4 (entry 16). The structure of **3a** has been confirmed by X-ray crystal structure analysis.[11]

Table 2 summarizes the scope of the reaction conducted under the optimized conditions. First, we employed different 3-

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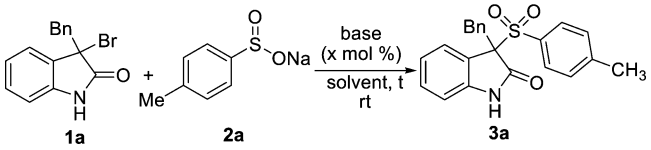
Table 1. Optimization Studies for the Sulfonylation of 3-Halooxindoles[a]

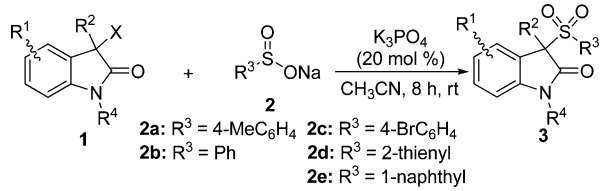


entry	solvent	base	x	t (h)	yield (%)[b]
1	CH_2Cl_2	–	–	36	<10
2	CH_2Cl_2	K_2CO_3	200	16	74
3	CH_2Cl_2	K_3PO_4	200	16	85
4	CH_2Cl_2	NaOH	200	10	38
5	CH_2Cl_2	DBU	200	8	35
6	CH_2Cl_2	NEt_3	200	8	25
7	CH_2Cl_2	Na_2CO_3	200	48	52
8	CH_2Cl_2	K_3PO_4	100	16	86
9	CH_2Cl_2	K_3PO_4	50	16	90
10	CH_2Cl_2	K_3PO_4	20	16	98
11	DCE	K_3PO_4	20	16	82
12	$CHCl_3$	K_3PO_4	20	16	95
13	CH_3CN	K_3PO_4	20	8	98
14	toluene	K_3PO_4	20	16	87
15	THF	K_3PO_4	20	16	94
16	CH_3CN	Na_3PO_4	20	13	97

[a]Reactions were performed with **1a** (0.1 mmol), **2a** (0.12 mmol), and base (x mol %) in solvent (2.0 mL) at room temperature for the specified time. [b]Isolated yield. DCE = 1,2-dichloroethane, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

benzyl-3-bromooxindoles **1b–i**, containing electron-donating or -withdrawing groups at different positions on the aryl moiety, reacting with **2a**. It was observed that the reactions were completed within 8 h at room temperature under the catalysis of 20 mol % K_3PO_4, furnishing 3-sulfonylated 3,3-disubstituted oxindoles **3b–i** in good to excellent yields (entries 1–8). The naphthyl moiety incorporated to 3-bromooxindole was tolerated in the sulfonylation reaction and resulted in **3j** in 66% yield (entry 9). Nevertheless, two heteroaromatic 3-bromooxindoles were successfully employed for generating **3k** and **3l** in good yields, thereby broadening the scope of the reaction (entries 10 and 11). Installing an aliphatic group on the 3-bromooxindole as substrate **1m** could deliver the product in good yield (entry 12). By employing a substrate bearing other functional groups, for example, a carbamate group, the same level of yield was obtained (entry 13). The presence of Cl or Br at the indolinone moiety had no influence on the reactivity, affording the products in excellent yields (entries 14 and 15). Meanwhile, we treated **1a** with several sodium aromatic sulfinates **2b–d** under the standard conditions, and the products **3q–s** could be obtained in moderate to excellent yields (entries 16–18). Disappointingly, when 1-naphthalene substituted sodium sulfinate **2e** was reacted with **1a**, the reaction gave **3t** only at trace levels, which might be caused by the steric hindrance (entry 19). Gratifyingly, the current reaction system was also effective for 3-benzyl-3-chlorooxindole (**1q**) and 3-phenyl-3-chlorooxindole (**1r**), affording the corresponding products in excellent yield (entries 20 and 21). Notably, installing a methyl group to the nitrogen of **1s** or **1t** was significantly detrimental to the reaction (entries 22 and 23). The steric size of the *N*-protecting group did not seem to be important, as methyl (**1u**) and benzyl (**1v**) gave similar results (entries 24 and 25). Our attempt to employ *N*-Boc-

Table 2. Substrate Scope of the Sulfonylation of 3-Halooxindoles[a]



entry	1	2	3	yield (%)[b]
1	R = 2-MeC_6H_4 (**1b**)	**2a**	**3b**	98
2	R = 3-MeC_6H_4 (**1c**)	**2a**	**3c**	96
3	R = 4-MeC_6H_4 (**1d**)	**2a**	**3d**	99
4	R = 2-ClC_6H_4 (**1e**)	**2a**	**3e**	80
5	R = 3-ClC_6H_4 (**1f**)	**2a**	**3f**	92
6	R = 4-ClC_6H_4 (**1g**)	**2a**	**3g**	85
7	R = 2-BrC_6H_4 (**1h**)	**2a**	**3h**	81
8	R = 3-BrC_6H_4 (**1i**)	**2a**	**3i**	97
9	R = 1-napthyl (**1j**)	**2a**	**3j**	66
10	R = 2-thienyl (**1k**)	**2a**	**3k**	89[c,d]
11	R = 2-furyl (**1l**)	**2a**	**3l**	82[c,d]
12	R = -$CHCH_2$ (**1m**)	**2a**	**3m**	75[e]
13	R = -CH_2NHCO_2Me (**1n**)	**2a**	**3n**	75[c,f]
14	R^1 = 4-Cl (**1o**)	**2a**	**3o**	97
15	R^1 = 5-Br (**1p**)	**2a**	**3p**	95
16	**1a**	**2b**	**3q**	95[d]
17	**1a**	**2c**	**3r**	97
18	**1a**	**2d**	**3s**	51[g]
19	**1a**	**2e**	**3t**	trace[g]
20	R^2 = Bn (**1q**)	**2a**	**3a**	94[d]
21	R^2 = Ph (**1r**)	**2a**	**3u**	96[d]
22	R^4 = Me, R^2 = Bn, X = Br (**1s**)	**2a**	**3v**	31[h]
23	R^4 = Me, R^2 = Bn, X = Cl (**1t**)	**2a**	**3v**	<10[h]
24	R^4 = Me, R^2 = Ph, X = Cl (**1u**)	**2a**	**3w**	63[e]
25	R^4 = Bn, R^2 = Ph, X = Cl (**1v**)	**2a**	**3x**	57[e]
26	R^4 = Boc, R^2 = Ph, X = Cl (**1w**)	**2a**	**3y**	messy[e]

[a]Unless noted, reactions were run with **1** (0.1 mmol), **2** (0.12 mmol), and K_3PO_4 (20 mol %) in CH_3CN (2.0 mL) at room temperature for 8 h. [b]Isolated yields. [c]Using 100 mol % K_3PO_4. [d]Run for 12 h. [e]Run for 24 h. [f]Run for 15 h. [g]Run for 36 h. [h]Run for 48 h.

protected 3-chlorooxindole **1w** as a substrate showed that the reaction system became very messy under the developed conditions (entry 26).

An asymmetric version of this methodology was attempted by using cinchonidine-derived squaramide **Cat** as a catalyst for

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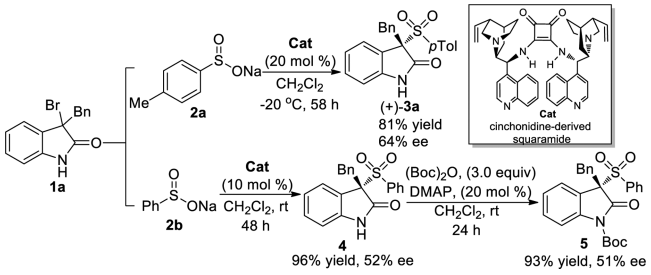
enantioselective synthesis of 3-sulfonylated 3,3-disubstituted oxindoles (Scheme 1).[12] The enantioselective reaction of **1a**

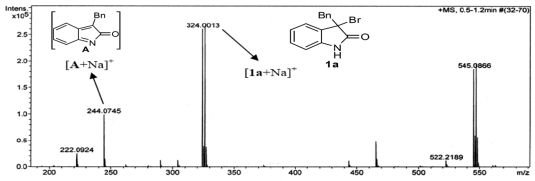
Scheme 1. Asymmetric Sulfonylation of 3-Halooxindoles Catalyzed by Chiral Organocatalyst and the Transformation of 4 into *N*-Boc-Protected Oxindole 5



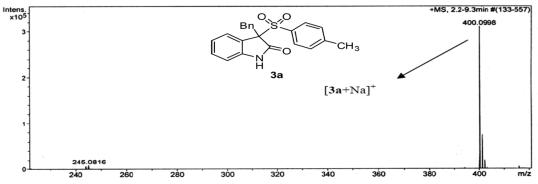
and **2a** proceeded well with 20 mol % of **Cat** in CH_2Cl_2 at −20 °C, furnishing (+)-**3a** in 81% yield with 64% ee. We also conducted the asymmetric sulfonylation reaction of **1a** with **2b** at room temperature with 20 mol % **Cat**; chiral product **4** could be obtained after 48 h in 96% yield with 52% ee. After treatment of **4** with Boc-anhydride and dimethylaminopyridine (DMAP) in CH_2Cl_2, *N*-Boc-protected oxindole **5** was readily obtained in 93% yield without loss in the enantiomeric excess. The absolute configuration of product **5** was determined by comparison of the specific rotation of the compound with literature data.[4e] Chiral products (+)-**3a** and **4** were assumed to have the same configuration as **5**.

On the basis of our experimental results and previous related studies,[6−8] we performed some experiments to obtain insight into the reaction mechanism. First, the examination of the background reaction of **1a** and **2a** (Table 1, entry 1) revealed that the base catalyst was essential for the reactivity of the sulfonylation of 3-halooxindoles. Further studies were carried out with the help of MS spectroscopy. When a 5:1 mixture of **1a** and Na_3PO_4 was analyzed by ESI-MS, a base peak at *m*/*z* 244.0745 was detected and assigned as *o*-azaxylylene intermediate **A**, while a peak at *m*/*z* 324.0013 was assigned as **1a** (Figure 1, (**1**); Table 3, entry 1). This observation led us to propose a base-mediated dehydrohalogenation process for the generation of *o*-azaxylylene intermediate **A** from 3-halooxindoles **1**. Adding sodium *p*-toluenesulfinate **2a** into the mixture, the peaks of **A** and **1a** almost completely disappeared, but the mass of **3a** characterized by a base peak at *m*/*z* 400.0998 was clearly observed (Figure 1, (**2**); Table 3, entry 2). Meanwhile for the *N*-substituted 3-halooxindoles, when **1u** was mixed with K_3PO_4, a new species characterized by a base at *m*/*z* 222.0934 was detected and assigned to be 1-methyl-*o*-azaxylylene-1-ium intermediate **B**, while a peak at *m*/*z* 280.0526 was assigned as **1u** (Figure 1, (**3**); Table 3, entry 3). After the conduct of program 4, only the species was obviously detected by a base peak at *m*/*z* 400.1008 and assigned to be **3w** (Figure 1, (**4**); Table 3, entry 4). Notably, these studies here represent the first spectral evidence for the intermediates **A** and **B** in situ generated from 3-halooxindoles and base.

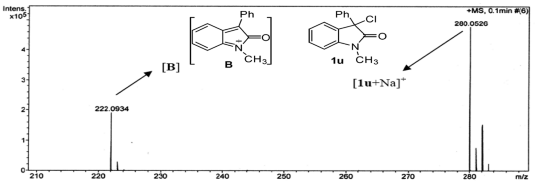
In light of the above-mentioned clues, we propose the following reaction pathways for the reaction of 3-halooxindoles with sulfinate salts (Scheme 2). 3-Halooxindoles **1** are subjected to K_3PO_4 or Na_3PO_4, thus readily generating an *o*-azaxylylene intermediate **A** or 1-alkyl-o-azaxylylene-1-ium **B**. For the *N*-unsubstituted substrates **1**, the *o*-azaxylylene



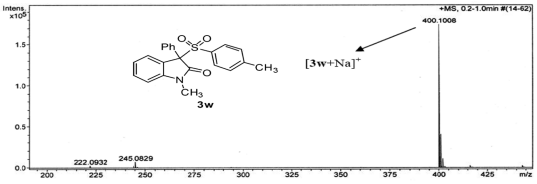
(1) program 1: **1a**+20 mol % Na_3PO_4



(2) program 2: **1a**+20 mol % Na_3PO_4+**2a**



(3) program 3: **1u**+20 mol % K_3PO_4



(4) program 4: **1u**+20 mol % K_3PO_4+**2a**

Figure 1. New species detected by ESI-MS analysis in different experimental program.

intermediate **A** is readily generated under the action of base,[5,6] while for the *N*-substituted substrates **1**, due to the function of the added base, it probably promotes the elimination of the halide of the 3-halooxindoles **1**, thus leading to the generation of intermediate **B**.[12] Afterward, the addition of sulfinate salts to the intermediate **A** or **B** leads to the formation of 3-sulfonylated 3,3-disubstituted oxindoles.

In summary, we have developed an efficient method for the sulfonylation of 3-halooxindoles to produce 3-sulfonylated 3,3-disubstituted oxindoles. The protocol involves the addition of sulfinate salts to 3-halooxindoles with K_3PO_4 as the catalyst under mild conditions, affording a range of 3-sulfonylated 3,3-disubstituted oxindoles in good to excellent yields. This new methodology was also extended to asymmetric catalysis with a chiral organocatalyst, giving the chiral 3-sulfonated oxindoles with promising enantioselectivity. Furthermore, the mechanism for the transformation was tentatively explored with the help of mass spectrometric analysis. The studies provide the first spectral evidence for the two classes of intermediates **A** and **B** in situ generated from 3-halooxindoles and a base.

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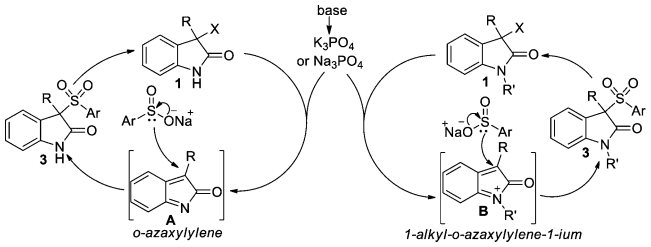
Table 3. ESI-MS Analysis for the Insight into the Reaction Mechanism[a]

program	*m/z*		
1	$C_{15}H_{11}NNaO$ [**A** + Na]$^+$	$C_{15}H_{12}BrNNaO$ [**1a** + Na]$^+$	
	C.:244.0733; F.:244.0745	C.:323.9994; F.:324.0013	
2[b]	dis.	dis.	$C_{22}H_{19}NNaO_3S$ [**3a** + Na]$^+$
			C.:400.0978; F.:400.0998
3	$C_{15}H_{12}NO$ [**B**]	$C_{15}H_{12}ClNNaO$ [**1u** + Na]$^+$	
	C.:222.0913; F.:222.0934	C.:280.0500; F.:280.0526	
4[b]	dis.	dis.	$C_{22}H_{19}NNaO_3S$ [**3w** + Na]$^+$
			C.:400.0978; F.:400.1008

[a]Reactions were run with CH_3CN as solvent. [b]**2a** (1.2 equiv to **1a** or **1u**) was added to the corresponding mixture. dis. = disappeared. C. = calcd. F. = found.

Scheme 2. Proposed Reaction Pathways



EXPERIMENTAL SECTION

General Methods. Reagents were purchased from commercial sources and were used as received unless mentioned otherwise. Reactions were monitored by TLC. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm, DMSO-d_6 at 39.51 ppm). Melting points were recorded on a melting point apparatus.

General Procedure for the Synthesis of Compounds 3. A solution of 3-halooxindole **1** (0.1 mmol), sulfinate salts **2** (0.12 mmol), and K_3PO_4 (0.02 or 0.1 mmol) in CH_3CN (2 mL) was stirred at room temperature for the indicated time. Solvent was removed in vacuo. The products **3** were isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3/1).

*3-Benzyl-3-tosylindolin-2-one (**3a**).* White solid, 37.0 mg, 98% yield; mp 268.4−270.1 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.35 (s, 3H), 3.59 (d, J = 12.9 Hz, 1H), 3.67 (d, J = 12.9 Hz, 1H), 6.47 (d, J = 7.5 Hz, 1H), 6.93−7.10 (m, 6H), 7.17 (t, J = 7.5 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 7.2 Hz, 1H), 10.48 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 34.4, 75.8, 109.5, 121.6, 121.7, 127.0, 127.1, 128.0, 129.3, 130.0, 130.4, 131.9, 133.4, 142.9, 145.3, 170.4. HRMS (ESI-TOF) calcd for $C_{22}H_{19}NNaO_3S$ [M + Na]$^+$: 400.0978; found: 400.0974.

*3-(2-Methylbenzyl)-3-tosylindolin-2-one (**3b**).* White solid, 38.3 mg, 98% yield; mp 255.6−257.4 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.23 (s, 3H), 2.35 (s, 3H), 3.70 (s, 2H), 6.53 (d, J = 7.8 Hz, 1H), 6.65 (d, J = 7.8 Hz, 1H), 6.82−6.99 (m, 3H), 7.07 (t, J = 7.5 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.61 (d, J = 7.5 Hz, 1H), 10.54 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 19.7, 21.1, 30.5, 75.6, 109.6, 121.8, 122.0, 125.4, 127.0, 129.1, 129.2, 130.0, 130.3, 130.6, 131.8, 132.3, 136.9, 143.1, 145.3, 170.7. HRMS (ESI-TOF) calcd for $C_{23}H_{21}NNaO_3S$ [M + Na]$^+$: 414.1134; found: 414.1133.

*3-(3-Methylbenzyl)-3-tosylindolin-2-one (**3c**).* White solid, 37.6 mg, 96% yield; mp 254.1−255.8 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.06 (s, 3H), 2.36 (s, 3H), 3.53 (d, J = 12.9 Hz, 1H), 3.62 (d, J = 12.9 Hz, 1H), 6.48 (d, J = 7.8 Hz, 1H), 6.68 (d, J = 7.2 Hz, 1H), 6.74−6.92 (m, 3H), 7.07−7.18 (m, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 7.2 Hz, 1H), 10.49 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 20.9, 21.1, 34.4, 75.7, 109.6, 121.6, 121.7, 127.0, 127.1, 127.6, 127.8, 129.3, 130.0, 130.4, 130.7, 132.0, 133.3, 136.9, 142.9, 145.3, 170.4. HRMS (ESI-TOF) calcd for $C_{23}H_{21}NNaO_3S$ [M + Na]$^+$: 414.1134; found: 414.1127.

*3-(4-Methylbenzyl)-3-tosylindolin-2-one (**3d**).* White solid, 38.7 mg, 99% yield; mp 267.0−268.4 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.10 (s, 3H), 2.35 (s, 3H), 3.53 (d, J = 12.9 Hz, 1H), 3.61 (d, J = 12.9 Hz, 1H), 6.47 (d, J = 7.5 Hz, 1H), 6.78−6.86 (m, 4H), 7.06 (t, J = 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 7.5 Hz, 1H), 10.47 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 20.5, 21.1, 34.0, 75.8, 109.6, 121.6, 121.7, 127.1, 128.6, 129.3, 129.9, 130.0, 130.3, 130.4, 132.0, 136.0, 142.9, 145.3, 170.4. HRMS (ESI-TOF) calcd for $C_{23}H_{21}NNaO_3S$ [M + Na]$^+$: 414.1134; found: 414.1130.

*3-(2-Chlorobenzyl)-3-tosylindolin-2-one (**3e**).* White solid, 32.9 mg, 80% yield; mp 265.3−266.9 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.35 (s, 3H), 3.66 (d, J = 13.8 Hz, 1H), 4.06 (d, J = 13.8 Hz, 1H), 6.52 (d, J = 7.8 Hz, 1H), 7.00 (d, J = 8.4 Hz, 2H), 7.08−7.27 (m, 4H), 7.32 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 7.5 Hz, 1H), 10.73 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.2, 30.7, 75.3, 109.6, 121.0, 121.6, 127.1, 127.4, 129.0, 129.3, 129.6, 130.1, 130.6, 130.7, 131.6, 131.9, 133.7, 142.9, 145.5, 170.7. HRMS (ESI-TOF) calcd for $C_{22}H_{18}ClNNaO_3S$ [M + Na]$^+$: 434.0588; found: 434.0592.

*3-(3-Chlorobenzyl)-3-tosylindolin-2-one (**3f**).* White solid, 37.9 mg, 92% yield; mp 260.9−262.6 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.35 (s, 3H), 3.57 (d, J = 12.9 Hz, 1H), 3.72 (d, J = 12.9 Hz, 1H), 6.50 (d, J = 7.8 Hz, 1H), 6.88 (d, J = 6.9 Hz, 1H), 6.96−7.14 (m, 4H), 7.20 (t, J = 6.9 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 7.2 Hz, 1H), 10.59 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.5, 34.2, 76.0, 110.1, 121.6, 122.3, 127.5, 127.6, 129.1, 129.7, 130.2, 130.3, 131.0, 132.1, 132.8, 136.4, 143.2, 145.8, 170.7. HRMS (ESI-TOF) calcd for $C_{22}H_{18}ClNNaO_3S$ [M + Na]$^+$: 434.0588; found: 434.0595.

*3-(4-Chlorobenzyl)-3-tosylindolin-2-one (**3g**).* White solid, 35.0 mg, 85% yield; mp 270.2−271.9 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.35 (s, 3H), 3.55 (d, J = 12.9 Hz, 1H), 3.69 (d, J = 12.9 Hz, 1H), 6.49 (d, J = 7.5 Hz, 1H), 6.93 (d, J = 7.8 Hz, 2H), 7.05−7.22 (m, 4H), 7.30−7.40 (m, 4H), 7.67 (d, J = 7.2 Hz, 1H), 10.54 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.5, 34.1, 76.0, 110.0, 121.7, 122.3, 127.5, 128.3, 129.7, 130.3, 131.0, 132.2, 132.9, 143.2, 145.8, 170.7. HRMS (ESI-TOF) calcd for $C_{22}H_{18}ClNNaO_3S$ [M + Na]$^+$: 434.0588; found: 434.0599.

*3-(2-Bromobenzyl)-3-tosylindolin-2-one (**3h**).* White solid, 36.9 mg, 81% yield; mp 267.4−269.1 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.36 (s, 3H), 3.70 (d, J = 13.8 Hz, 1H), 4.08 (d, J = 13.8 Hz, 1H), 6.53 (d, J = 7.8 Hz, 1H), 6.96−7.04 (m, 3H), 7.10−7.18 (m, 2H), 7.31−7.45 (m, 5H), 7.59 (d, J = 7.5 Hz, 1H), 10.75 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 33.3, 75.4, 109.6, 121.0, 121.6, 125.0, 127.5, 127.7, 129.2, 129.3, 130.0, 130.2, 130.7, 131.5, 132.9, 133.7, 142.9, 145.5, 170.7. HRMS (ESI-TOF) calcd for $C_{22}H_{18}BrNNaO_3S$ [M + Na]$^+$: 478.0083; found: 478.0086.

*3-(3-Bromobenzyl)-3-tosylindolin-2-one (**3i**).* White solid, 44.3 mg, 97% yield; mp 256.6−258.3 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.35 (s, 3H), 3.56 (d, J = 12.9 Hz, 1H), 3.71 (d, J = 12.9 Hz, 1H), 6.50 (d, J = 7.8 Hz, 1H), 6.92 (d, J = 7.8 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 7.09 (d, J = 5.4 Hz, 2H), 7.19 (d, J = 7.5 Hz, 1H), 7.25 (d, J = 8.1 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.68

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(d, J = 7.5 Hz, 1H), 10.59 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.5, 34.2, 76.0, 110.1, 121.4, 121.6, 122.3, 127.6, 129.5, 129.7, 130.3, 130.4, 131.0, 132.1, 133.0, 136.6, 143.2, 145.8, 170.7. HRMS (ESI-TOF) calcd for $C_{22}H_{18}BrNNaO_3S$ [M + Na]$^+$: 478.0083; found: 478.0094.

3-(Naphthalen-1-ylmethyl)-3-tosylindolin-2-one (**3j**). White solid, 28.2 mg, 66% yield; mp 267.1−268.8 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.36 (s, 3H), 4.09 (d, J = 13.8 Hz, 1H), 4.23 (d, J = 13.8 Hz, 1H), 6.41 (d, J = 7.8 Hz, 1H), 6.92−7.20 (m, 4H), 7.33 (d, J = 8.1 Hz, 2H), 7.44−7.51 (m, 4H), 7.65 (t, J = 6.9 Hz, 2H), 7.77 (d, J = 7.8 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 10.52 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.2, 29.9, 75.7, 109.5, 121.5, 124.2, 124.9, 125.7, 125.9, 127.5, 127.8, 127.9, 128.4, 129.3, 130.0, 130.1, 130.5, 131.7, 131.9, 133.2, 143.0, 145.4, 170.7. HRMS (ESI-TOF) calcd for $C_{26}H_{21}NNaO_3S$ [M + Na]$^+$: 450.1134; found: 450.1144.

3-(Thiophen-2-ylmethyl)-3-tosylindolin-2-one (**3k**). White solid, 34.1 mg, 89% yield; mp 264.2−265.8 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.34 (s, 3H), 3.77 (d, J = 14.1 Hz, 1H), 3.90 (d, J = 14.1 Hz, 1H), 6.54 (d, J = 7.8 Hz, 1H), 6.64 (d, J = 2.7 Hz, 1H), 6.71−6.73 (m, 1H), 7.07−7.22 (m, 3H), 7.31 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.58 (d, J = 7.2 Hz, 1H), 10.56 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 29.4, 75.2, 109.7, 121.6, 122.0, 125.8, 126.5, 126.8, 128.0, 129.3, 130.0, 130.8, 131.8, 134.5, 143.4, 145.5, 170.3. HRMS (ESI-TOF) calcd for $C_{20}H_{17}NNaO_3S_2$ [M + Na]$^+$: 406.0542; found: 406.0526.

3-(Furan-2-ylmethyl)-3-tosylindolin-2-one (**3l**). White solid, 30.1 mg, 82% yield; mp 239.6−241.4 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.35 (s, 3H), 3.55 (d, J = 14.4 Hz, 1H), 3.77 (d, J = 14.4 Hz, 1H), 5.82 (d, J = 2.7 Hz, 1H), 6.11 (d, J = 0.9 Hz, 1H), 6.58 (d, J = 7.8 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.27−7.32 (m, 3H), 7.38 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 7.5 Hz, 1H), 10.59 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 28.0, 73.6, 108.3, 109.6, 110.4, 121.6, 121.8, 126.8, 129.3, 130.0, 130.6, 131.5, 142.5, 143.1, 145.5, 147.8, 170.4. HRMS (ESI-TOF) calcd for $C_{20}H_{17}NNaO_4S$ [M + Na]$^+$: 390.0770; found: 390.0775.

3-Allyl-3-tosylindolin-2-one (**3m**). White solid, 24.5 mg, 75% yield; mp 201.4−203.2 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.36 (s, 3H), 2.91−2.96 (m, 1H), 3.08−3.15 (m, 1H), 4.91−5.20 (m, 3H), 6.70 (d, J = 7.8 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.26−7.39 (m, 5H), 7.47 (d, J = 7.5 Hz, 1H), 10.69 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 33.6, 74.0, 109.8, 120.7, 121.7, 122.0, 126.6, 129.2, 129.4, 129.8, 129.9, 130.5, 131.8, 143.0, 145.3, 170.4. HRMS (ESI-TOF) calcd for $C_{18}H_{17}NNaO_3S$ [M + Na]$^+$: 350.0821; found: 350.0831.

Methyl (2-(2-Oxo-3-tosylindolin-3-yl)ethyl)carbamate (**3n**). White solid, 29.1 mg, 75% yield; mp 206.7−208.4 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.33 (s, 3H), 2.36−2.50 (m, 2H), 2.56−2.66 (m, 2H), 3.35 (s, 3H), 6.73 (d, J = 7.8 Hz, 1H), 7.04−7.13 (m, 2H), 7.29−7.42 (m, 6H), 10.75 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 29.5, 36.0, 51.3, 73.3, 110.0, 121.4, 122.1, 126.3, 129.2, 130.0, 130.6, 131.6, 143.2, 145.3, 156.3, 170.5. HRMS (ESI-TOF) calcd for $C_{19}H_{20}N_2NaO_5S$ [M + Na]$^+$: 411.0985; found: 411.1000.

3-Benzyl-4-chloro-3-tosylindolin-2-one (**3o**). White solid, 39.9 mg, 97% yield; mp 249.4−251.3 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.37 (s, 3H), 3.61 (d, J = 13.2 Hz, 1H), 4.08 (d, J = 13.2 Hz, 1H), 6.48 (d, J = 7.8 Hz, 1H), 7.04−7.12 (m, 6H), 7.19 (t, J = 7.9 Hz, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 10.83 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.2, 31.6, 78.3, 108.8, 118.5, 124.0, 127.2, 128.3, 129.3, 129.4, 129.8, 132.0, 132.1, 132.2, 133.7, 145.3, 145.6, 169.6. HRMS (ESI-TOF) calcd for $C_{22}H_{18}ClNNaO_3S$ [M + Na]$^+$: 434.0588; found: 434.0601.

3-Benzyl-5-bromo-3-tosylindolin-2-one (**3p**). White solid, 43.3 mg, 95% yield; mp 273.4−275.1 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.37 (s, 3H), 3.53 (d, J = 12.9 Hz, 1H), 3.72 (d, J = 12.9 Hz, 1H), 6.46 (d, J = 8.4 Hz, 1H), 6.95 (t, J = 3.6 Hz, 2H), 7.07−7.08 (m, 3H), 7.37 (d, J = 8.4 Hz, 3H), 7.45 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 1.5 Hz, 1H), 10.67 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.2, 34.4, 76.0, 111.5, 113.3, 124.0, 127.1, 128.1, 129.5, 129.8, 129.9, 130.0, 131.6, 133.2, 142.2, 145.7, 170.2. HRMS (ESI-TOF) calcd for $C_{22}H_{18}BrNNaO_3S$ [M + Na]$^+$: 478.0083; found: 478.0084.

3-Benzyl-3-(phenylsulfonyl)indolin-2-one (**3q**). White solid, 34.5 mg, 95% yield; mp 255.0−256.8 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 3.60 (d, J = 12.9 Hz, 1H), 3.70 (d, J = 12.9 Hz, 1H), 6.45 (d, J = 7.5 Hz, 1H), 6.94−7.10 (m, 6H), 7.17 (t, J = 7.2 Hz, 1H), 7.53−7.70 (m, 6H), 10.50 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 34.3, 75.8, 109.6, 121.4, 121.8, 127.0, 127.2, 128.0, 128.8, 129.9, 130.0, 130.5, 133.4, 134.6, 134.7, 142.9, 170.3. HRMS (ESI-TOF) calcd for $C_{21}H_{17}NNaO_3S$ [M + Na]$^+$: 386.0821; found: 386.0821.

3-Benzyl-3-((4-bromophenyl)sulfonyl)indolin-2-one (**3r**). White solid, 42.9 mg, 97% yield; mp 257.3−259.2 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 3.57 (d, J = 12.9 Hz, 1H), 3.69 (d, J = 12.9 Hz, 1H), 6.50 (d, J = 7.5 Hz, 1H), 6.91−6.94 (m, 2H), 7.04−7.20 (m, 5H), 7.44 (d, J = 8.7 Hz, 2H), 7.68 (d, J = 7.2 Hz, 1H), 7.77 (d, J = 8.7 Hz, 2H), 10.56 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 34.2, 75.9, 109.6, 121.1, 121.9, 127.0, 127.1, 127.9, 129.0, 129.9, 130.6, 131.8, 131.9, 133.1, 133.9, 142.8, 170.1. HRMS (ESI-TOF) calcd for $C_{21}H_{16}BrNNaO_3S$ [M + Na]$^+$: 463.9926; found: 463.9952.

3-Benzyl-3-(thiophen-2-ylsulfonyl)indolin-2-one (**3s**). White solid, 18.8 mg, 51% yield; mp 261.8−263.6 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 3.62 (d, J = 12.9 Hz, 1H), 3.68 (d, J = 12.9 Hz, 1H), 6.52 (d, J = 7.8 Hz, 1H), 6.92−6.95 (m, 2H), 7.05−7.07 (m, 4H), 7.17−7.20 (m, 2H), 7.41−7.63 (m, 2H), 8.11−8.12 (m, 1H), 10.54 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 34.5, 76.3, 109.6, 121.5, 121.8, 127.0, 127.2, 127.9, 128.0, 130.0, 130.6, 133.3, 134.7, 136.9, 137.6, 143.1, 170.1. HRMS (ESI-TOF) calcd for $C_{19}H_{15}NNaO_3S_2$ [M + Na]$^+$: 392.0386; found: 392.0409.

3-Phenyl-3-tosylindolin-2-one (**3u**). White solid, 34.9 mg, 96% yield; mp 220.5−222.4 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.32 (s, 3H), 6.76 (d, J = 7.8 Hz, 1H), 7.19−7.29 (m, 5H), 7.35 (t, J = 6.9 Hz, 1H), 7.43−7.45 (m, 3H), 7.84 (d, J = 7.5 Hz, 1H), 7.92−7.95 (m, 2H), 10.96 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 76.4, 110.3, 122.1, 122.3, 128.4, 128.6, 129.0, 129.1, 129.2, 130.1, 130.8, 132.2, 142.6, 145.2, 169.7. HRMS (ESI-TOF) calcd for $C_{21}H_{17}NNaO_3S$ [M + Na]$^+$: 386.0821; found: 386.0838.

3-Benzyl-1-methyl-3-tosylindolin-2-one (**3v**). White solid, 12.1 mg, 31% yield; mp 202.7−204.4 °C. ^{1}H NMR (DMSO-d_6, 300 MHz), δ (ppm): 2.34 (s, 3H), 2.69 (s, 3H), 3.63 (d, J = 12.9 Hz, 1H), 3.71 (d, J = 12.9 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 6.89−7.04 (m, 5H), 7.13 (t, J = 7.5 Hz, 1H), 7.23−7.34 (m, 5H), 7.71 (d, J = 7.2 Hz, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.1, 26.1, 33.9, 75.6, 108.6, 120.8, 122.5, 126.9, 127.0, 128.0, 129.2, 129.7, 129.8, 130.6, 131.5, 133.3, 144.1, 145.5, 169.0. HRMS (ESI-TOF) calcd for $C_{23}H_{21}NNaO_3S$ [M + Na]$^+$: 414.1134; found: 414.1159.

1-Methyl-3-phenyl-3-tosylindolin-2-one (**3w**). White solid, 23.8 mg, 63% yield; mp 173.5−174.9 °C. ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 2.34 (s, 3H), 3.00 (s, 3H), 6.67 (d, J = 7.8 Hz, 1H), 7.08 (d, J = 8.1 Hz, 2H), 7.21−7.40 (m, 7H), 8.00−8.04 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 21.6, 26.5, 76.9, 108.3, 108.5, 122.3, 122.8, 126.8, 128.3, 128.6, 128.9, 129.2, 129.4, 130.5, 130.6, 132.2, 144.2, 145.0, 169.0. HRMS (ESI-TOF) calcd for $C_{22}H_{19}NNaO_3S$ [M + Na]$^+$: 400.0978; found: 400.1005.

1-Benzyl-3-phenyl-3-tosylindolin-2-one (**3x**). White solid, 25.9 mg, 57% yield; mp 185.7−187.4 °C. ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 2.36 (s, 3H), 4.70 (d, J = 15.9 Hz, 1H), 4.84 (d, J = 15.9 Hz, 1H), 6.61 (d, J = 7.5 Hz, 1H), 7.06 (d, J = 7.8 Hz, 4H), 7.19−7.30 (m, 5H), 7.37−7.40 (m, 5H), 8.02−8.08 (m, 3H); ^{13}C NMR (DMSO-d_6, 75 MHz), δ (ppm): 21.7, 44.2, 76.8, 109.6, 122.4, 122.8, 127.1, 127.6, 128.4, 128.7, 128.8, 128.9, 129.2, 129.3, 129.4, 130.4, 130.8, 132.4, 134.7, 143.4, 145.0, 169.3. HRMS (ESI-TOF) calcd for $C_{28}H_{23}NNaO_3S$ [M + Na]$^+$: 476.1291; found: 476.1313.

General Procedure for the Asymmetric Sulfonylation of 3-Halooxindoles Catalyzed by Chiral Organocatalyst and the Transformation of 4 into *N*-Boc-protected Oxindole 5. A solution of **1a** (0.1 mmol), **2a** (0.12 mmol), and **Cat** (0.02 mmol) in DCM (2 mL) was stirred at −20 °C for 58 h. The residue was purified by column chromatography using EtOAc/petroleum ether (1:3) as the eluent to afford (+)-**3a** as a white solid in 81% yield, 64% ee, $[\alpha]_D^{20}$ = +21.8 (c 1.18, $CHCl_3$). The ^{1}H and ^{13}C data were in agreement with those of the racemic compound (**3a**). Chiral HPLC condition: Daicel

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Chiralpak OD-H, hexanes/*i*-PrOH = 85/15, Flow rate = 1.0 mL/min, UV = 230 nm, t_{major} = 8.67 min, and t_{minor} = 16.54 min.

A solution of **1a** (0.1 mmol), **2b** (0.12 mmol), and **Cat** (0.02 mmol) in DCM (2 mL) was stirred at room temperature for 48 h. The residue was purified by column chromatography using EtOAc/petroleum ether (1:3) as the eluent to afford **4** as a white solid in 96% yield, 52% ee. The mass and ^{1}H, ^{13}C data were in agreement with those for the racemic compound (**3q**). HPLC analysis: Chiralcel OD-H column, hexanes/*i*-PrOH = 90/10, Flow rate = 1 mL/min, λ = 230 nm, t_{major} = 7.9 min, t_{minor} = 17.2 min.

To a solution of **4** (0.09 mmol) and DMAP (0.018 mmol) in CH_2Cl_2 (4 mL) was added $(Boc)_2O$ (0.27 mmol). The resulting mixture was stirred at room temperature for 20 min. The mixture was directly purified by column chromatography using EtOAc/petroleum ether (1:5) as the eluent to afford analytically pure **5** as a white solid in 93% yield (41.3 mg), 51% ee, $[\alpha]_D^{20}$ = +19.9 (*c* 2.00, $CHCl_3$); The mp, mass, and ^{1}H, ^{13}C data were in agreement with the literature.[4e] HPLC analysis: Chiralcel OD-H column, hexanes/*i*-PrOH = 90/10, Flow rate = 0.8 mL/min, λ = 230 nm, t_{major} = 10.4 min, t_{minor} = 12.4 min.

■ ASSOCIATED CONTENT

Supporting Information

Copies of the NMR spectra for products **3**; HPLC spectra for products (+)-**3a**, **4**, and **5**; X-ray structures for product **3a**. This materials is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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