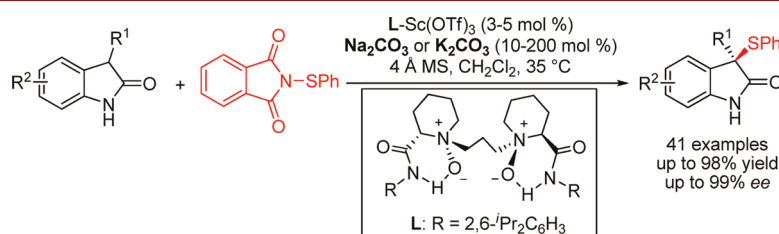


Catalytic Asymmetric Sulfenylation of
Unprotected 3-Substituted OxindolesYunfei Cai, Jun Li, Weiliang Chen, Mingsheng Xie, Xiaohua Liu, Lili Lin, and
Xiaoming Feng*Key Laboratory of Green Chemistry & Technology, Ministry of Education,
College of Chemistry, Sichuan University, Chengdu 610064, P. R. China

xmfeng@scu.edu.cn

Received April 11, 2012

ABSTRACT



Catalytic asymmetric sulfenylation of unprotected 3-substituted oxindoles has been developed via cooperative catalysis of a chiral *N,N*-dioxide–Sc(OTf)₃ complex and a Brønsted base. Utilizing readily available *N*-(phenylthio)phthalimide as the sulfur source, a wide range of optically active 3-phenylthiooxindoles were obtained in excellent yields with excellent enantioselectivities under mild reaction conditions.

Oxindoles bearing a chiral quaternary stereogenic center at the 3-position constitute an important structural motif in the library of natural products and biologically active

drugs.¹ In view of the importance of chiral 3-heteroatom substituted oxindoles in medicinal chemistry,^{2–5} enantioselective syntheses of 3-heteroatom substituted oxindoles, such as 3-fluorooxindoles,² 3-chlorooxindoles,³ 3-amino-oxindoles,⁴ and 3-hydroxyoxindoles,⁵ have been established in recent years.

However, the enantioselective synthesis of 3-thiooxindoles⁶ is unavailable. Catalytic asymmetric sulfenylation

(1) For reviews, see: (a) Williams, R. M.; Cox, R. J. *Acc. Chem. Res.* **2003**, *36*, 127. (b) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945. (c) Lin, H.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 36. (d) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209. (e) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748. (f) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003. (g) Zhou, F.; Liu, Y. L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (h) Shen, K.; Liu, X. H.; Lin, L. L.; Feng, X. M. *Chem. Sci* **2012**, *3*, 327.

(2) For catalytic asymmetric synthesis of 3-fluorooxindoles, see: (a) Hamashima, Y.; Suzuki, T.; Takano, H.; Shimura, Y.; Sodeoka, M. *J. Am. Chem. Soc.* **2005**, *127*, 10164. (b) Shibata, N.; Kohno, J.; Takai, K.; Nakamura, S.; Toru, T.; Kagemasa, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 4204. (c) Ishimaru, T.; Shibata, N.; Horikawa, T.; Yasuda, N.; Nakamura, S.; Toru, T.; Shiro, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4157. (d) Deng, Q.-H.; Wadepohl, H.; Gade, L. H. *Chem.—Eur. J.* **2011**, *17*, 14922. (e) Wu, L.; Falivene, L.; Drinkel, E.; Grant, S.; Linden, A.; Cavallo, L.; Dorta, R. *Angew. Chem., Int. Ed.* **2012**, *51*, 2870.

(3) For catalytic asymmetric synthesis of 3-chlorooxindoles, see: (a) Zheng, W. H.; Zhang, Z. H.; Kaplan, M. J.; Antilla, J. C. *J. Am. Chem. Soc.* **2011**, *133*, 3339. (b) Zhao, M.-X.; Zhang, Z.-W.; Chen, M.-X.; Tang, W.-H.; Shi, M. *Eur. J. Org. Chem.* **2011**, 3001.

(4) For catalytic asymmetric synthesis of 3-aminooxindoles, see: (a) Bui, T.; Borregan, M.; Barbas, C. F., III *J. Org. Chem.* **2009**, *74*, 8935. (b) Cheng, L.; Liu, L.; Wang, D.; Chen, Y. *J. Org. Lett.* **2009**, *11*, 3874. (c) Qian, Z. Q.; Zhou, F.; Du, T. P.; Wang, B. L.; Zhou, J. *Chem. Commun.* **2009**, 6753. (d) Mouri, S.; Chen, Z.; Mitsunuma, H.; Furutachi, M.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 1255. (e) Yang, Z. G.; Wang, Z.; Bai, S.; Shen, K.; Chen, D. H.; Liu, X. H.; Lin, L. L.; Feng, X. M. *Chem.—Eur. J.* **2010**, *16*, 6632. (f) Shen, K.; Liu, X. H.; Wang, G.; Lin, L. L.; Feng, X. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4684.

(5) For catalytic asymmetric synthesis of 3-hydroxyoxindoles, see: (a) Shintani, R.; Inoue, M.; Hayashi, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 3353. (b) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488. (c) Sano, D.; Nagata, K.; Itoh, T. *Org. Lett.* **2008**, *10*, 1593. (d) Itoh, J.; Han, S. B.; Krische, M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6313. (e) Tomita, D.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 6946. (f) Itoh, T.; Ishikawa, H.; Hayashi, Y. *Org. Lett.* **2009**, *11*, 3854. (g) Bui, T.; Candeias, N. R.; Barbas, C. F., III *J. Am. Chem. Soc.* **2010**, *132*, 5574. (h) Liu, Y.-L.; Wang, B.-L.; Cao, J.-J.; Chen, L.; Zhang, C.; Wang, Y.-X.; Zhou, J. *J. Am. Chem. Soc.* **2010**, *132*, 15176. (i) Zhang, Z.; Zheng, W.; Antilla, J. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 1135.

(6) For synthesis of racemic thiooxindoles, see: (a) Li, Y.; Shi, Y.; Huang, Z.; Wu, X.; Xu, P.; Wang, J.; Zhang, Y. *Org. Lett.* **2011**, *13*, 1210. (b) England, D. B.; Merey, G.; Padwa, A. *Heterocycle* **2007**, *74*, 491.

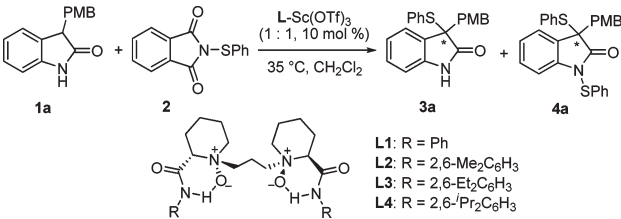
(7) (a) Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 794. (b) Sobhani, S.; Fielenbach, D.; Marigo, M.; Wabnitz, T. C.; Jørgensen, K. A. *Chem.—Eur. J.* **2005**, *11*, 5689. (c) Jereb, M.; Togni, A. *Org. Lett.* **2005**, *7*, 4041. (d) Jereb, M.; Togni, A. *Chem.—Eur. J.* **2007**, *13*, 9384. (e) Sirisailam, S. K.; Togni, A. *Tetrahedron: Asymmetry* **2006**, *17*, 2603–2607. (f) Fang, L.; Lin, A.-J.; Hu, H.-W.; Zhu, C.-J. *Chem.—Eur. J.* **2009**, *15*, 7039. (g) Lin, A.; Fang, L.; Zhu, X.; Zhu, C.; Cheng, Y. *Adv. Synth. Catal.* **2011**, *353*, 545.

of 3-substituted oxindoles is the most straightforward and promising method to this functionality. Although the successful organocatalytic asymmetric sulfenylation of aliphatic aldehydes and β -keto esters has been realized,⁷ the relatively higher pK_a value of α -proton of oxindoles, especially *N*-protecting-group-free oxindoles, makes them sluggish carbon nucleophiles.⁸ In addition, when employing a Lewis acid as a catalyst, the introduction of sulfur-based substituents might cause the problem of the undesired association of sulfur with a central metal. Thus, the development of asymmetric sulfenylation of oxindoles is still desirable and also a challenge. Herein, we realized the asymmetric substitution of oxindoles with *N*-(phenylthio)phthalimide. The cooperative catalysis⁹ of a chiral *N*, *N'*-dioxide–Sc(OTf)₃ complex¹⁰ and a Brønsted base furnished the optically active 3-phenylthiooxindoles with excellent outcomes.

Initially, we probed the optimal reaction conditions using unprotected 3-(4-methoxybenzyl)-2-oxindole (**1a**) as the model substrate¹¹ and stable and commercially available *N*-(phenylthio)phthalimide **2** as the sulfenylating agent. When *N*, *N'*-dioxide–Sc(OTf)₃ was used exclusively as the Lewis acid catalyst, no reaction was observed (Table 1, entry 1). Then, Brønsted bases were investigated to initiate the reaction. Inspiringly, we found that Na₂CO₃ could promote the reaction to afford the desired 3-phenylthiooxindole derivative **3a** in 46% yield (Table 1, entry 2). In the presence of Na₂CO₃, the catalytic and stereoselective ability of the chiral *N*, *N'*-dioxide–Sc(OTf)₃ catalyst was investigated to realize the catalytic asymmetric version of this reaction (Table 1, entries 3–6). Excitingly, (*S*)-pipecolic acid derived *N*, *N'*-dioxide **L4** with sterically hindered diisopropyl substituents on the phenyl ring afforded **3a** in 87% yield with 94% *ee* (Table 1, entry 6). Further survey of other bases (Table 1, entries 7–10) showed that K₂CO₃ could accelerate the generation of the product **3a** in 88% yield with maintained *ee* within 2 h (Table 1, entry 8). Thus, the **L4**–Sc(OTf)₃/K₂CO₃ system was chosen to assess other reaction parameters (see the Supporting Information for details).¹² The use of 4 Å molecular sieves (M.S.) and low reaction concentration improved the enantioselectivity to 98% *ee* (Table 1, entry 11). Reducing the catalyst loading to 3 mol % had little influence on the yield and *ee* value (Table 1, entry 12). Although complete conversion could be achieved, the desired product **3a** suffered somewhat from the *N*-sulfenylation process to generate the byproduct **4a**. This matter

was settled by using 1.05 equiv of **2**. The formation of *N*-adduct **4a** was effectively prevented, and the isolated yield of **3a** increased to 98% with 97% *ee* (Table 1, entry 13). It should be noted that the catalytic amount of base was effective in promoting the reaction with similar results by prolonging the reaction time (Table 1, entry 14).

Table 1. Optimization of the Reaction Conditions^a



entry	ligand	base	time (h)	yield (%) ^b	<i>ee</i> (%) ^c
1	L1–L4	—	20	0	—
2 ^d	—	Na ₂ CO ₃	20	46(20)	—
3	L1	Na ₂ CO ₃	20	45(21)	0
4	L2	Na ₂ CO ₃	20	71(19)	46
5	L3	Na ₂ CO ₃	20	86(12)	76
6	L4	Na ₂ CO ₃	20	87(11)	94
7	L4	Li ₂ CO ₃	20	65(15)	94
8	L4	K ₂ CO ₃	2	88(12)	94
9	L4	Cs ₂ CO ₃	1	89(8)	90
10	L4	Lud	20	86(9)	94
11 ^e	L4	K ₂ CO ₃	6	88(10)	98
12 ^{e,f}	L4	K ₂ CO ₃	10	87(11)	97
13 ^{e,g}	L4	K ₂ CO ₃	10	98(<2)	97
14 ^{e,g,h}	L4	K ₂ CO ₃	36	92(5)	98

^a Unless otherwise noted, all reactions were performed with **L**–Sc(OTf)₃ (1:1, 10 mol %), base (0.1 mmol), **1a** (0.1 mmol), PMB = *p*-methoxybenzyl, *N*-(phenylthio)phthalimide **2** (0.12 mmol) in CH₂Cl₂ (0.5 mL) under N₂ at 35 °C for the indicated time. Lud = 2,6-dimethylpyridine. ^b Yield of isolated product **3a**. Data in parentheses were the isolated yield of **4a**. ^c Determined by HPLC analysis on a chiral stationary phase using a Chiralcel OD-H column. ^d Without Lewis acid **L**–Sc(OTf)₃. ^e 4 Å MS (25.0 mg), K₂CO₃ (200 mol %) were added in CH₂Cl₂ (2.0 mL). ^f Using 3 mol % of **L4**–Sc(OTf)₃. ^g 1.05 equiv of **2** was used. ^h Using 10 mol % of K₂CO₃ instead of 200 mol % of K₂CO₃.

With the optimized reaction conditions in hand (Table 1, entry 13), the substrate scope was investigated as shown in Tables 2 and 3. The reactions performed well with a series of 3-benzyl substituted oxindoles, giving the corresponding thiofunctionalized products in 91–98% yield with 92–97% *ee*, regardless of the electronic nature or the position of the substituents on the phenyl ring (Table 2, entries 1–13). Variation of the C3-substituent to naphthylmethyl or thienylmethyl was also satisfied to deliver the desired products in 85–98% yield with 94–98% *ee* (Table 2, entries 14–16). Notably, with Na₂CO₃ (200 mol %) or K₂CO₃ (15 mol %) employed as a Brønsted base cocatalyst, oxindoles with aliphatic substituents at the C3

(8) The pK_a value of 3-substituted oxindoles can be expected to be substantially higher, considering the pK_a value of oxindole ($pK_a \sim 18$), compared with β -keto esters ($pK_a \sim 13$).

(9) For selected reviews on cooperative catalysis, see: (a) Shibasaki, M.; Yoshikawa, N. *Chem. Rev.* **2002**, *102*, 2187. (b) Yamamoto, H.; Futatsugi, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 1924. (c) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222. (d) Kumagai, N.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4760.

(10) For reviews, see: (a) Liu, X. H.; Lin, L. L.; Feng, X. M. *Acc. Chem. Res.* **2011**, *44*, 574. (b) Malkov, A. V.; Kočovský, P. *Eur. J. Org. Chem.* **2007**, 29.

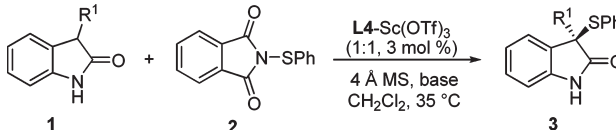
(11) 3-Benzyl-2-oxindole was not used as the model substrate, for it was hard to separate the substrate and the product via TLC or silica gel.

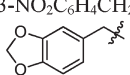
(12) Using other sulfenylating agents like *N*-(benzylthio)phthalimide, BnSSBn or PhSSPh, no desired products were observed.

(13) For these substrates, when using 200 mol % K₂CO₃, the products were obtained with lower *ee* (such as, for **1q**: 75% *ee*; for **5a**: 87% *ee*) due to the excess of K₂CO₃ promoted background reaction.

position were tolerated well for this reaction (88–95% yield, 86–98% *ee*; Table 2, entries 17–24), among which sterically hindered substituted ones gave higher *ee* value.¹³ Oxindoles with a 3-allyl or 3-CH₂CO₂Me substituent underwent the reaction with good results (85–98% yield, 95–96% *ee*; Table 2, entries 25 and 26).

Table 2. Substrate Scope of 3-Alkyl Substituted Oxindoles^a

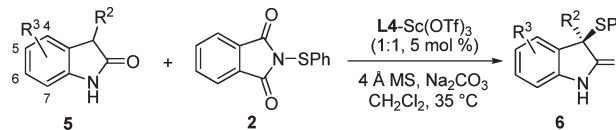


entry	R ¹	time (h)	prod.	yield (%) ^b	ee (%) ^c
1 ^d	4-MeOC ₆ H ₄ CH ₂	12(24)	3a	98(92)	97 (97, <i>R</i>)
2	2-MeC ₆ H ₄ CH ₂	24	3b	91	95 (<i>R</i>)
3	3-MeC ₆ H ₄ CH ₂	20	3c	96	97 (<i>R</i>)
4	4-MeC ₆ H ₄ CH ₂	20	3d	97	97 (<i>R</i>)
5	2-ClC ₆ H ₄ CH ₂	20	3e	95	94 (<i>R</i>)
6	3-ClC ₆ H ₄ CH ₂	20	3f	96	95 (<i>R</i>)
7	4-ClC ₆ H ₄ CH ₂	12	3g	97	96 (<i>R</i>)
8	4-FC ₆ H ₄ CH ₂	20	3h	95	95 (<i>R</i>)
9	4-BrC ₆ H ₄ CH ₂	20	3i	92	97 (<i>R</i>)
10	4-NO ₂ C ₆ H ₄ CH ₂	20	3j	95	92 (<i>R</i>)
11	3-NO ₂ C ₆ H ₄ CH ₂	20	3k	94	94 (<i>R</i>)
12		20	3l	94	96 (<i>R</i>)
13	Bn	12	3m	96	97 (<i>R</i>)
14	1-Naphthylmethyl	12	3n	98	97 (<i>R</i>)
15 ^e	2-Naphthylmethyl	12	3o	95	97 (<i>R</i>)
16	2-Thienylmethyl	20	3p	85	94 (<i>R</i>)
17 ^{d,e}	Me	48(24)	3q	83(78)	87(85, <i>R</i>)
18 ^{d,e}	Et	48(24)	3r	82(80)	95(95, <i>R</i>)
19 ^{d,e}	<i>n</i> Pr	48(24)	3s	85(76)	97(98, <i>R</i>)
20 ^{d,e}	<i>n</i> Bu	48(24)	3t	89(87)	98(98, <i>R</i>)
21 ^{d,e}	<i>i</i> Bu	48(24)	3u	91(85)	98(98, <i>R</i>)
22 ^{d,e}	3-Ethylbutyl	48(24)	3v	90(83)	98(98, <i>R</i>)
23 ^{d,e}	Neopentyl	48(24)	3w	90(88)	91(87, <i>R</i>)
24 ^{d,e}	<i>i</i> Pr	48	3x	92	95(<i>R</i>)
25 ^{d,e}	Allyl	48(24)	3y	85(73)	95(98, <i>R</i>)
26 ^{d,e}	MeCO ₂ CH ₂	20	3z	98	96(<i>R</i>)

^a Unless specified, the reactions were performed with **1** (0.1 mmol), **L4**–Sc(III) complex (1:1, 3 mol %) and 4 Å MS (25.0 mg), K₂CO₃ (0.2 mmol), *N*-(phenylthio)phthalimide **2** (0.105 mmol) in CH₂Cl₂ (2.0 mL) at 35 °C for the indicated time. ^b Isolated yield of the product **3**. ^c Determined by HPLC analysis (see Supporting Information). ^d Using 5.0 mol % of **L4**–Sc(III) complex and 200 mol % of Na₂CO₃. ^e Data in parentheses were the results using 5.0 mol % of **L4**–Sc(III) complex and 15 mol % of K₂CO₃.

3-Aryl oxindoles were also suitable substrates in this catalyst system in the presence of Na₂CO₃ (120 mol %) or K₂CO₃ (15 mol %).¹³ As shown in Table 3, the electronic nature or the position of substituents on the C3-phenyl ring or the benzo moiety of the oxindole core had little influence on the yields and *ee*'s (88–97% yield, 93–99% *ee*; Table 2,

Table 3. Substrate Scope of 3-Aryl Substituted Oxindoles^a



entry	R ²	R ³	time (h)	prod.	yield (%) ^b	ee (%) ^c
1 ^d	Ph	H	48 (24)	6a	95 (93)	99 (97)
2	2-MeC ₆ H ₄	H	72	6b	92	>99
3	3-MeC ₆ H ₄	H	48	6c	93	99
4	4-MeC ₆ H ₄	H	48	6d	94	99
5	4-FC ₆ H ₄	H	48	6e	97	98
6	4-ClC ₆ H ₄	H	48	6f	91	97
7	4-MeOC ₆ H ₄	H	48	6g	90	98
8	1-Naphthyl	H	48	6h	91	99
9	2-Naphthyl	H	48	6i	92	97
10	Ph	5-Me	48	6j	90	99
11	Ph	5-MeO	48	6k	97	98
12	Ph	5-F	48	6l	93	97
13	Ph	5-Cl	48	6m	92	95
14	Ph	6-Br	48	6n	93	94
15	Ph	7-F	72	6o	88	93

^a Unless specified, the reactions were performed with **5** (0.1 mmol), **L4**–Sc(III) complex (1:1, 5 mol %) and 4 Å MS (25.0 mg), Na₂CO₃ (0.12 mmol), *N*-(phenylthio)phthalimide **2** (0.105 mmol) in CH₂Cl₂ (2.0 mL) at 35 °C for the indicated time. ^b Isolated yield of the product **6**. ^c Determined by HPLC analysis (see Supporting Information). ^d Data in parentheses were the results using 15 mol % of K₂CO₃ instead of 120 mol % of Na₂CO₃.

entries 1–7 and 10–15). 3-Naphthyl substituted ones also delivered the desired products in 91–92% yield with 97–99% *ee*.

Additionally, the absolute configuration of the product **3p** was unambiguously determined to be *R* by X-ray crystallography.¹⁴ A comparison with the Cotton effect in the CD spectra of **3p** showed that the absolute configuration of other 3-phenylthiooxindoles **3** was *R* (see Supporting Information for details).

To show the synthetic utility of the catalyst system, sulfenylation of oxindole **1a** was expanded to a gram scale, and the desired 3-phenylthiooxindole **3a** was accomplished in 94% yield with 97% *ee*. After a single recrystallization of the product, an 82% yield with 99% *ee* was obtained (Scheme 1a). In addition, deprotection of byproduct **4a** to **3a** with NaBH₄ also had little influence on *ee* (Scheme 1b).

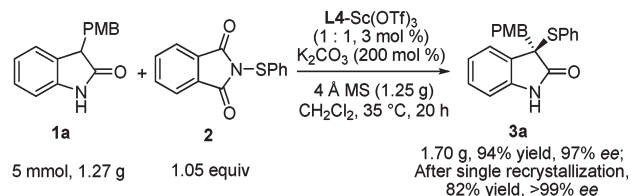
Control experiments were carried out to elucidate the reaction process (see Supporting Information). When the amount of sulfenylating reagent **2** changed from 2.0 to 1.05 equiv, the yield of the C3-product **3a** increased from 12% to 98% with the decreased yield of *N*-adduct **4a**. Meanwhile, upon treatment with K₂CO₃, **3a** could react with

(14) CCDC 869058 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

sulfonylating agent **2** smoothly and convert to **4a** completely after 20 h. This implied that a substituted reaction occurred prior to the C3-position of oxindole, followed by *N*-addition with an excess amount of **2**.

Scheme 1. Synthetic Utility

a) Sulfenylation of oxindole **1a** on a gram scale



b) Deprotection of the by-product **4a** to **3a**

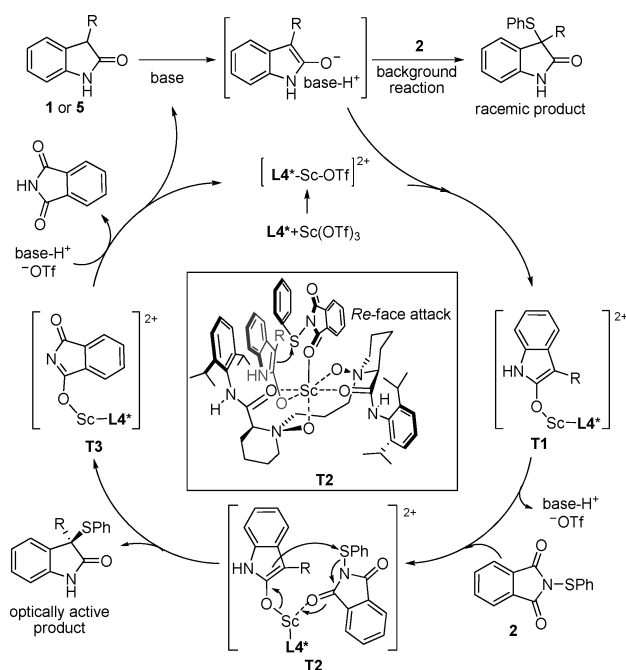
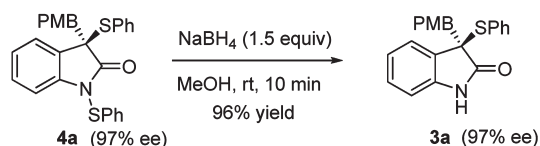


Figure 1. Proposed catalytic cycle.

Knowing that the reaction did not occur in the absence of a base, we assume that the reaction is initiated by the

(15) (a) Wabnitz, T. C.; Yu, J.-Q.; Spencer, J. B. *Chem.—Eur. J.* **2004**, *10*, 484. (b) Mikami, K.; Terada, M.; Matsuzawa, H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3554.

(16) For a review on nonlinear effects, see: Satyanarayana, T.; Abraham, S.; Kagan, H. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 456.

(17) Liu, Y. L.; Shang, D. J.; Zhou, X.; Liu, X. H.; Feng, X. M. *Chem.—Eur. J.* **2009**, *15*, 2055.

formation of an enolate anion via a Brønsted base promoted deprotonation of 3-substituted-2-oxindole. HRMS experiments were performed to shed light on the reaction mechanism. The spectrum of the sample obtained from the mixture of **L4**-Sc(OTf)₃ and oxindole **1a** revealed an ion at m/z 1094.4995, which corresponded to the intermediate $[\text{Sc}^{3+} + \mathbf{1a} + (\mathbf{L4-H})^{-} + \text{TfO}^{-}]^{+}$. Upon addition of K₂CO₃, a new signal appeared at m/z 944.4796 related to $[\text{Sc}^{3+} + (\mathbf{1a-H})^{-} + (\mathbf{L4-H})^{-}]^{+}$. It was conceivable that the base enabled the generation of an enolate ion which was caught by the oxophilic scandium catalyst¹⁵ (see Supporting Information).

A linear effect¹⁶ between the *ee* values of the ligand **L4** and the product **3a** indicated a monomeric catalyst as the main catalytic active species. In light of the X-ray structures of the product **3p**¹⁴ and the *N,N'*-dioxide–Sc(III) complex,¹⁷ a proposed catalytic cycle and the catalytic activation model **T2** were provided to explain the observed sense of asymmetric induction (Figure 1). In the presence of the chiral scandium catalyst, the racemic products generated from the achiral Brønsted base catalyzed background reaction was effectively slowed down and the base-assisted Lewis acid catalyzed asymmetric sulfonylation reaction dominated the reaction process via cooperative catalysis to afford the optically active product. In the catalytic model **T2**, the oxygen atoms of *N*-oxide and the amide moieties of the ligand **L4**, oxindoles, and sulfonylation reagent **2** were coordinated together with the scandium center. The *Si*-face of oxindole was shielded by the neighboring 2,6-diisopropylphenyl group. Therefore, the *Re*-face attacking the sulfur of **2** yielded the corresponding *R*-configured product which was in accordance with the observed experimental result.

In summary, we have developed a highly efficient enantioselective sulfenylation of unprotected oxindoles via cooperative catalysis of a *N,N'*-dioxide–Sc(OTf)₃ complex and a Brønsted base. With readily available *N*-(phenylthio)phthalimide as the sulfur source, this method provides the first access to optically active 3-phenylthio-substituted oxindole derivatives in excellent yields (82–98% yield) with excellent enantioselectivities (up to 99% *ee*) under mild reaction conditions. Further realization of other catalytic asymmetric functionalizations of 3-substituted unprotected oxindoles is underway in our laboratory.

Acknowledgment. We appreciate the National Natural Science Foundation of China (Nos. 21021001 and 21172151), and National Basic Research Program of China (973 Program: No. 2010CB833300) for financial support.

Supporting Information Available. Experimental procedures, spectral and analytical data for the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.