Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 1833–1843

Highly diastereoselective reactions of 2-lithiated indoles with chiral *N*-*tert*-butanesulfinyl aldimines for the synthesis of chiral (2-indolyl) methanamine derivatives

Liang Cheng,[a,b] Li Liu,[a,*] Yong Sui,[a,b] Dong Wang[a] and Yong-Jun Chen[a,*]

[a]*Beijing National Laboratory for Molecular Sciences (BNLMS), Laboratory for Chemical Biology, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, PR China*
[b]*Graduate School of Chinese Academy of Sciences, Beijing 100049, PR China*

Received 25 June 2007; accepted 18 July 2007

Abstract—Nucleophilic addition reactions of 2-lithiated *N*-phenylsulfonylindoles with (*R*)-*N*-*tert*-butanesulfinyl aldimines provided chiral (2-indolyl) methanamine derivatives in moderate to good yields (up to 100%) with excellent diastereoselectivities (>99:1), in which no additional Lewis acids were required.

1. Introduction

Indole moieties occur widely in natural products, functional materials and pharmaceutical compounds.[1] As a matter of fact, the synthesis of indole derivatives has gained much attention in organic chemistry for many decades.[2] Although well-established classical methods have been successfully applied to the construction of the indole ring, the functionalization of existing indole ring systems has not been extensively developed.

Indoles bearing a substitution at the C-2 position are an important structural unit of many alkaloids and bioactive substances.[3] The Friedel–Crafts alkylation of indoles generally provides C-3 substituted products. Among the various synthetic methodologies, *ortho*-metallation of indole followed by trapping with electrophiles has emerged as an important route for generating 2-functionalized indoles.[4]

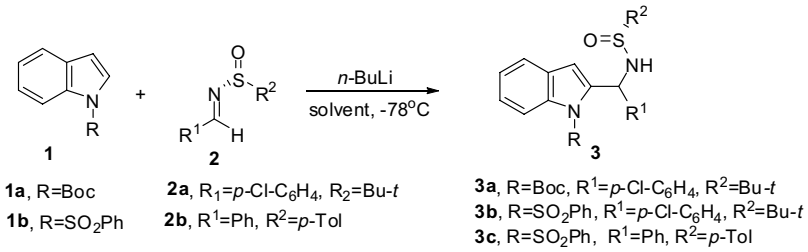
Recently the asymmetric addition of indoles with imines has been successfully developed to provide enantiopure 3-indolyl methanamine derivatives.[5] As important C-3 indole analogues, (2-indolyl)methanamines could be used as inhibitors of HIV protease,[6] $5HT_{2B}$ receptor antagonists,[7] as well as chiral ligands.[8] Although the reaction of 2-metallated indole with imines could provide 2-indolyl methanamines efficiently,[9] the development of such an asymmetric version was limited.[10] Recently, chiral sulfinyl aldimines were widely used in asymmetric synthesis.[11] In the addition of 5-methylfuryllithium with chiral sulfinylimines, high diastereoselectivity was obtained, however stoichiometric Lewis acid was necessary.[12] Herein, we report highly diastereoselective addition reactions of 2-lithiated indole with *N*-*tert*-butanesulfinyl aldimines without any additive in application for the synthesis of chiral (2-indolyl)-methanamine derivatives.

2. Results and discussion

Initially, the *ortho*-metallation reaction of *N*-Boc-indole **1a** with *n*-BuLi was carried out in THF at −78 °C, followed by the addition with (*R*)-*N*-*tert*-butanesulfinyl aldimine **2a** in THF. The reaction provided (2-indolyl)methanamine **3a** in low yield (Scheme 1, Table 1, entry 1). Fortunately, when *N*-SO_2Ph-indole **1b** was used in the reaction with **2a**, [(1-phenylsulfonyl-1*H*-indol-2-yl)phenylmethane]-*tert*-butane-sulfinamide **3b** was obtained in high yield with excellent diastereoselectivity (dr >99:1) (Table 1, entry 2). The choice of solvent had great influence on the reaction yield, but less on the diastereoselectivity (entries 2–4).

* Corresponding authors. Tel.: +86 10 62554614; fax: +86 10 62554449 (L.L.); e-mail addresses: lliu@mail.iccas.ac.cn; yjchen@mail.iccas.ac.cn

0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.07.029



Scheme 1.

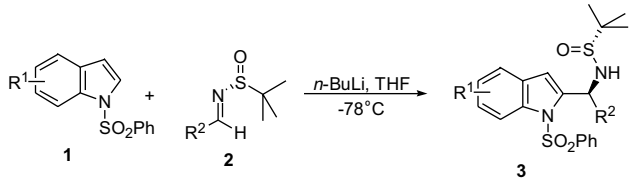
Table 1. Reaction of 2-lithiated indoles **1** with chiral sulfinyl aldimines **2**[a]

Entry	Indole	Imine	Solvent	Time (h)	Product	Yield[b] (%)	dr[c]
1	**1a**	**2a**	THF	2	**3a**	25	nd[d]
2	**1b**	**2a**	THF	2	**3b**	84	>99:1
3	**1b**	**2a**	Et_2O	2	**3b**	68	>99:1
4	**1b**	**2a**	Toluene	2	**3b**	10	>99:1
5[e]	**1b**	**2a**	THF	2	**3b**	70	>99:1
6	**1b**	**2b**	THF	0.5	**3c**	80	86:14

[a] Reactants ratio: indole/imine/base 1.0:0.8:1.2.
[b] Isolated yields.
[c] Determined by ^{1}H NMR and ^{13}C NMR of the crude reaction mixture.
[d] Not determined.
[e] LDA was used as base.

When Et_2O and toluene were used, the yields of **3a** decreased to 68% and 10%, respectively, which implied the lower efficiency of these solvents on disaggregation of the lithium complex in solution. However, the diastereoselectivity remained as high as >99:1. The change of the base from *n*-BuLi to LDA resulted in a slight drop of the yield, without any loss of diastereoselectivity (Table 1, entry 5). When (*R*)-*N*-*p*-toluenesulfinyl imine **2b** was used in the reaction with **1a**, although the reaction was completed in 0.5 h and provided **3c** in 80% yield, the diastereoselectivity decreased to 86:14 (Table 1, entry 6).

Subsequently, various chiral *N*-butanesulfinyl aldimines **2** were reacted with indoles **1** under the optimized reaction conditions (Scheme 2, Table 2). All imines derived from the alkyl (entries 1 and 2), aryl (entries 3–12), heteroaryl (entry 13), as well as α,β-unsaturated (entry 14) aldehydes provided the desired products in excellent diastereoselectivities (>99:1) and moderate to good yields. On the other hand, substituted indoles **1c**,**d** could also afford the respective products **3r**–**s** in excellent diasteroselectivities and good yields (entries 16 and 17).

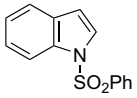
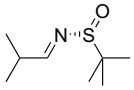
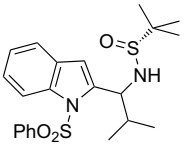
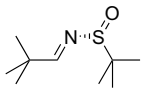
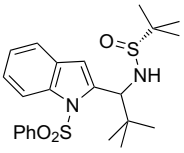
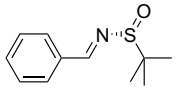
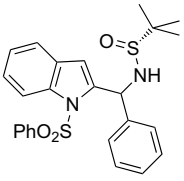
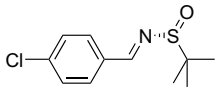
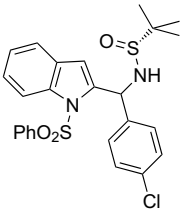
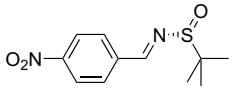
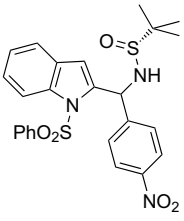
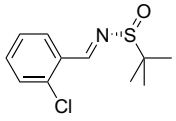
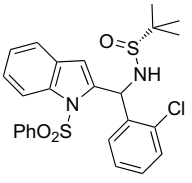
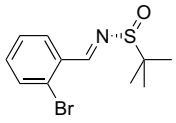
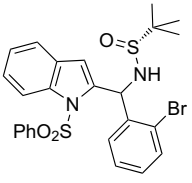
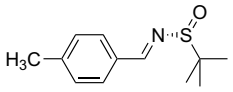
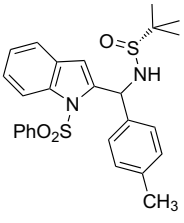


Scheme 2.

The stereochemical assignment for the detectable diastereomer of the addition reaction is based on X-ray single-crystal diffraction. The new stereogenic centre generated, from the analysis of product **3i** (Fig. 1), is (*S*)-configured. The observed stereoselectivity is consistent with the prediction of the Yamamoto model,[13] which 2-lithioindole attacks the C=N bond from *Re* face, other than through the six-membered ring transition state, which is proposed in the case of the addition using Grignard reagent.[11] Unlike the addition of some lithium reagents with chiral *N*-butanesulfinylimines, in which Lewis acids were necessary for the chelation with both the nitrogen and sulfinyl oxygen of imine,[12,14] the present reaction could achieve high diastereoselectivity without any additive, probably due to the coordination of lithium with the sulfonyl oxygen of indole, which might facilitate the steric hindrance effect (Fig. 2).

In order to cleave the chiral auxiliary, products **3** were subjected to facile acidic hydrolysis conditions. It was found that the sulfinyl group was cleaved cleanly under the conditions employed. As to the potential instability of the generated free amine on silica gel, the hydrolysis product was subsequently protected with Tos group. All the chiral *N*-protected amines **5a**–**g** were obtained in good yields with excellent enantioselectivities [Scheme 3 (1), Table 3, entries 3–9]. On the other hand, the *tert*-butyl sulfinyl group could also be oxidized conveniently into a Bus group **4a**,**b**, which is often utilized in organic synthesis as a protecting group [Scheme 3 (2), Table 3, entries 1 and 2]. Finally, the cleavage of the *N*-protecting group ($PhSO_2$–) in the indole ring was performed [Scheme 3 (3)]. The product was also required to be protected by a Tos group to give (*S*)-(2-indolyl) methyl (*p*-chlorophenyl) amine **6** in 45% overall yield with 97% ee.

Table 2. 1,2-Additions of 2-lithioindole **1b–d** to *N*-sulfinyl aldimines **2a,c–q**[a]

Entry	Indole		Aldimine	Time (h)		Product	Yield[b] (%)	dr[c]
1	**1b** 	**2c**		1.5	**3d**		66	>99.1
2	**1b**	**2d**		1	**3e**		66	>99.1
3	**1b**	**2e**		1	**3f**		53	>99.1
4	**1b**	**2a**		2	**3b**		84	>99.1
5	**1b**	**2f**		2	**3g**		68	>99.1
6	**1b**	**2g**		1	**3h**		72	>99.1
7	**1b**	**2h**		1	**3i**		75	>99.1
8	**1b**	**2i**		1.5	**3j**		63	>99.1

(*continued on next page*)

Table 2 (*continued*)

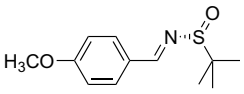
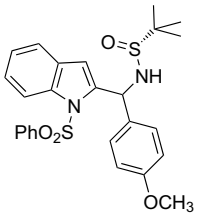
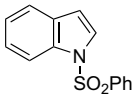
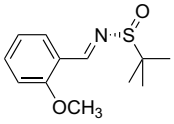
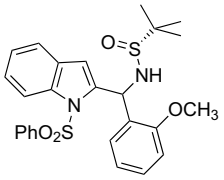
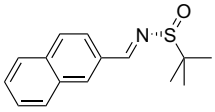
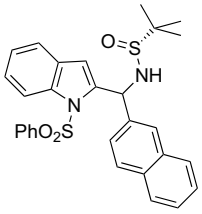
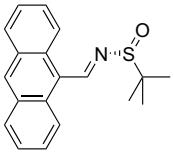
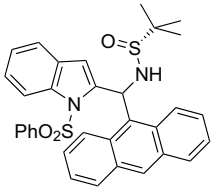
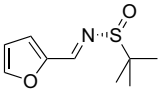
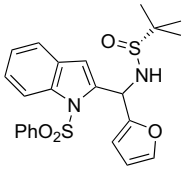
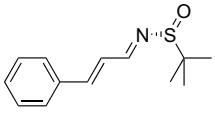
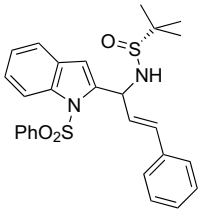
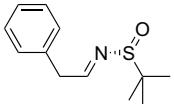
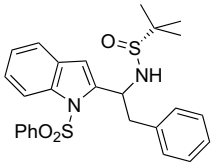
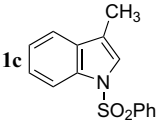
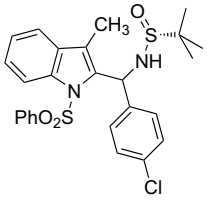
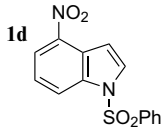
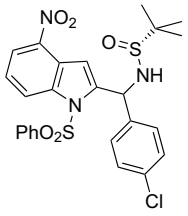
Entry	Indole	Aldimine	Time (h)	Product	Yield[b] (%)	dr[c]
9	**1b**	**2j** 	1	**3k** 	76	>99.1
10	**1b** 	**2k** 	2	**3l** 	79	>99.1
11	**1b**	**2l** 	1.5	**3m** 	100	>99.1
12	**1b**	**2m** 	3	**3n** 	88	>99.1
13	**1b**	**2n** 	1	**3o** 	74	>99.1
14	**1b**	**2o** 	1	**3p** 	91	>99.1
15	**1b**	**2p** 	1	**3q** 	64	>99.1
16	**1c** 	**2b**	1	**3r** 	85	>99.1

Table 2 (*continued*)

Entry	Indole	Aldimine	Time (h)	Product	Yield[b] (%)	dr[c]
17[d]	**1d** 	**2b**	1	**3s** 	77	>99.1

[a] Reactants ratio: indole/aldimine/base 1.0:0.8:1.2.
[b] Isolated yields.
[c] Determined by ^{1}H NMR and ^{13}C NMR of the crude reaction mixture.
[d] LDA was used instead of *n*-BuLi.

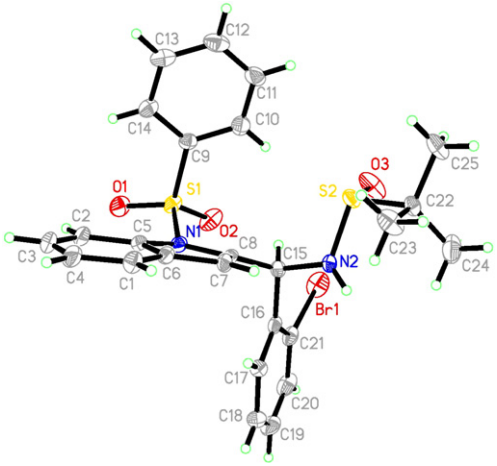


Figure 1. ORTEP presentation of (R_S,*S*)-**3i**.

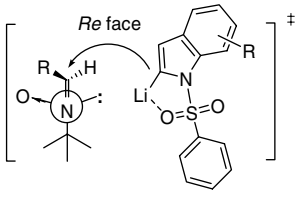


Figure 2. Yamamoto-type non-chelation addition modle.

3. Conclusion

In conclusion, we have demonstrated a highly diastereoselective nucleophilic addition of 2-lithiated *N*-phenylsulfonylindoles with (*R*)-*N*-*tert*-butanesulfinyl aldimines. After the cleavage of the chiral auxiliary, 2-indolyl methanamines were obtained in good yields with excellent enantioselectivities. Further application of this methodology into the synthesis of some bioactive substances is currently under research in our lab.

4. Experimental

4.1. General

IR spectra were recorded on a Perkin–Elmer 782 infrared spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ with Bruker DMX-300 (300 MHz) spectrometer. Chemical shifts are given in ppm relative to tetramethylsilane (TMS). Elemental analyses were performed on a Carlo Flash 1112 Element Analysis instrument. Mass spectra were recorded on a Bruker APEX-2 spectrometer using the FAB technique or a GCT-MS Micromass spectrometer. HPLC analyses were performed on Shimadzu CTO_10ASVP equipped with chiral columns. Melting points were measured using a Beijing-Taike X-4 apparatus and were uncorrected. Optical rotations were measured on Optical AA-10 digital polarimeter. X-ray structure was determined on a Bruker Smart-1000 X-ray diffraction meter. Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. Tetrahedrofuran (THF), toluene and diethyl ether (Et_2O) were distilled from Na/benzophenone. Dry CH_2Cl_2 was distilled from CaH_2. All reactions were carried out under a N_2 atmosphere in oven-dried glassware.

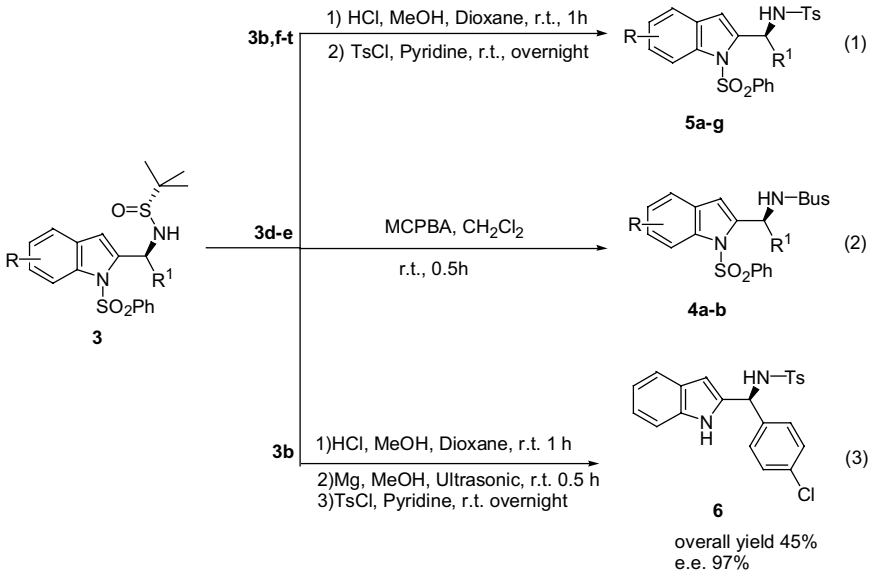
4.2. The synthesis of *N*-phenylsulfonyl indoles

Starting from indoles and $PhSO_2Cl$, *N*-phenylsulfonyl indoles **1a–d** were synthesized.[15]

4.2.1. 4-Nitro-1-(phenylsulfonyl)-1*H*-indole 1d. Yield 91%. Yellow powder, mp 179–180 °C. FTIR (KBr): 595, 679, 741, 856, 913, 1089, 1128, 1176, 1214, 1308, 1340, 1520, 1769 cm^{-1}. ^{1}H NMR (300 MHz) δ 7.40–7.51 (m, 4H), 7.56–7.61 (m, 1H), 7.81–7.83 (d, 1H, $J = 3.9$ Hz), 7.88–7.91 (m, 2H), 8.17–8.20 (d, 1H, $J = 8.1$ Hz), 8.33–8.36 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 108.4, 119.7, 120.2, 124.1, 125.3, 126.8, 129.6, 130.1, 134.5, 136.4, 137.7, 140.8. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{10}N_2O_4S$, 302.0361; found: 302.0363.

4.3. Typical experimental procedure for the synthesis of *N*-*tert*-butanesulfinyl aldimines 2[16]

The *tert*-butanesulfinamide (100 mg, 0.824 mmol) and benzaldehyde (87 mg, 0.8 mmol) were mixed in dry CH_2Cl_2 (5 mL) under N_2, $Ti(OEt)_4$ (1 mL, 4.1 mmol) was added into the solution. The reaction mixture was stirred at room temperature until completion as indicated by TLC, quenched with H_2O and filtered through diatomite. The filter residue was washed with CH_2Cl_2 and the aqueous layer



Scheme 3.

Table 3. Cleavage of the chiral auxiliary

Entry	Sulfinamide		Product		Yield[a] (%)	ee[b] (%)
			R	R^1		
1	**3d**	**4a**	H	*i*-Pr	99	99
2	**3e**	**4b**	H	*t*-Bu	92	>99
3	**3b**	**5a**	H	4-Cl–C_6H_4	90	>99
4	**3g**	**5b**	H	4-NO_2–C_6H_4	96	99
5	**3i**	**5c**	H	2-Br–C_6H_4	67	>99
6	**3k**	**5d**	H	4-OMe–C_6H_4	80	99
7	**3o**	**5e**	H	2-Furyl	92	98
8	**3s**	**5f**	3-Me	4-Cl–C_6H_4	96	98
9	**3t**	**5g**	4-NO_2	4-Cl–C_6H_4	98	98

[a] Isolated yields.
[b] Determined by chiral HPLC.

was extracted with CH_2Cl_2. The organic phase was collected and dried over Na_2SO_4. Most of the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (elute: PE/EtOAc = 4:1) to afford product **2e** (147 mg, yield 85%) as a colourless oil.

4.3.1. (*R*,*E*)-*N*-(4-Nitrobenzylidene)-2-methylpropane-2-sulfinamide 2f. Yield 76%. Yellow solid, mp 142–144 °C. $[\alpha]_D^{20} = -58.0$ (*c* 2.5, $CHCl_3$). FTIR (KBr): 493, 661, 688, 734, 836, 856, 1086, 1175, 1341, 1469, 1518, 1589, 2949, 3108 cm^{-1}. ^1H NMR (300 MHz) δ 1.27 (s, 9H), 7.99–8.02 (d, 2H, $J = 8.7$ Hz), 8.29–8.32 (d, 2H, $J = 8.7$ Hz), 8.65 (s, 1H). ^{13}C NMR (75 MHz) δ 22.2, 58.0, 123.8, 129.6, 138.5, 149.4, 160.3. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{11}H_{14}N_2O_3S$, 254.0725; found, 254.0729.

4.3.2. (*R*,*E*)-*N*-(2-Chlorobenzylidene)-2-methylpropane-2-sulfinamide 2g. Yield 79%. Colourless oil. $[\alpha]_D^{20} = -195.6$ (*c* 4.3, $CHCl_3$). FTIR (KBr): 453, 583, 683, 758, 1087, 1179, 1274, 1362, 1468, 1590, 2963 cm^{-1}. ^1H NMR (300 MHz) δ 1.21 (s, 9H), 7.28–7.37 (m, 3H), 7.98–8.00 (d, 1H, $J = 7.2$ Hz), 8.98 (s, 1H). ^{13}C NMR (75 MHz) δ 22.2, 57.5, 126.7, 128.8, 129.9, 130.9, 132.8, 136.1, 159.3. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{11}H_{14}NOSCl$, 243.0485; found, 243.0488.

4.3.3. (*R*,*E*)-*N*-(2-Bromobenzylidene)-2-methylpropane-2-sulfinamide 2h. Yield 64%. Colourless oil. $[\alpha]_D^{20} = -207.2$ (*c* 3.1, $CHCl_3$). FTIR (KBr): 448, 583, 662, 760, 1026, 1087, 1179, 1273, 1361, 1463, 1588, 2961 cm^{-1}. ^1H NMR (300 MHz) δ 1.26 (s, 9H), 7.32–7.38 (m, 2H), 7.61–7.64 (dd, 1H, J = 1.2, 7.5 Hz), 8.01–8.04 (dd, 1H, $J = 2.1$, 7.5 Hz), 8.96 (s, 1H). ^{13}C NMR (75 MHz) δ 22.2, 57.5, 126.0, 127.3, 129.2, 132.5, 132.9, 133.3, 161.8. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{11}H_{14}NOSBr$, 286.9979; found, 286.9975.

4.3.4. (*R*,*E*)-*N*-(2-Methoxybenzylidene)-2-methylpropane-2-sulfinamide 2k. Yield 84%. White solid, mp 55–56 °C. $[\alpha]_D^{20} = -230.4$ (*c* 1.9, $CHCl_3$). FTIR (KBr): 756, 1083, 1163, 1254, 1358, 1466, 1597, 2963 cm^{-1}. ^1H NMR (300 MHz) δ 1.24 (s, 9H), 3.87 (s, 3H), 6.93–7.01 (m, 2H), 7.42–7.45 (m, 1H), 7.95–7.99 (dd, 1H, $J = 1.8$,

7.8 Hz), 9.05 (s, 1H); ^{13}C NMR (75 MHz) δ 22.2, 55.1, 57.2, 111.0, 120.3, 122.4, 127.8, 133.5, 158.4, 159.3. HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{17}NO_2S$, 239.0980; found, 239.0982.

4.4. Typical experimental procedure for the nucleophilic addition of 2-lithilated indoles 1 to *N*-*tert*-butanesulfinyl aldimines 2

To a solution of *N*-phenylsulfonyl indole **1b** (52 mg, 0.2 mmol) in THF (2 mL) at −78 °C was added *n*-BuLi (0.13 mL, 0.22 mmol, 1.6 M in hexane) dropwise. After the reaction was aged for 1 h at −78 °C, the solution of (*R*)-*N*-(4-chlorobenzylidene)-2-methylpropanesulfinamide **2a** (44 mg, 0.18 mmol) in THF (2 mL) was added in one portion and the mixture stirred at −78 °C for 2 h. The reaction mixture was quenched by a saturated aqueous solution of NH_4Cl (5 mL), followed by extraction with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4. Most of the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (elute: PE/EtOAc = 2:1 to 1:1) to afford product **3b** (67 mg, yield 84%) as a white solid.

4.4.1. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-chlorophenyl)methane]-2-*tert*-butanesulfinamide 3b. White solid, mp 75–76 °C. $[\alpha]_D^{20} = +46.7$ (c 0.6, $CHCl_3$). FTIR (KBr): 588, 647, 685, 730, 832, 910, 1017, 1062, 1147, 1176, 1370, 1450, 1489, 1589, 2961, 3215 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.26 (s, 9H), 3.71 (br s, 1H), 6.50 (s, 1H), 6.90 (s, 1H), 7.20–7.35 (m, 8H), 7.45–7.58 (m, 4H), 8.14–8.16 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (75 MHz) δ 22.2, 55.8, 56.0, 111.8, 114.7, 120.7, 123.6, 124.7, 126.0, 128.5, 128.6, 128.7, 129.3, 133.3, 133.8, 137.4, 138.0, 138.4, 140.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{25}H_{25}N_2O_3S_2Cl$, 500.0995; found, 500.1000.

4.4.2. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*iso*-propanyl)methane]-2-*tert*-butanesulfinamide 3d. White solid, mp 134–136 °C. $[\alpha]_D^{20} = +145.3$ (c 1.8, $CHCl_3$). FTIR (KBr): 570, 590, 629, 685, 749, 836, 1050, 1126, 1175, 1368, 1449, 2962 cm^{-1}. ^{1}H NMR (300 MHz) δ 0.86–0.89 (d, 3H, $J = 6.7$ Hz), 1.12–1.15 (d, 3H, $J = 6.9$ Hz), 1.22 (s, 9H), 2.42–2.44 (m, 1H), 3.51–3.52 (d, 1H, $J = 3.3$ Hz), 5.22 (s, 1H), 6.58 (s, 1H), 7.19–7.31 (m, 2H), 7.36–7.51 (m, 4H), 7.78–7.80 (d, 2H, $J = 7.5$ Hz), 8.19–8.21 (d, 1H, $J = 8.1$ Hz), ^{13}C NMR (75 MHz) δ 15.9, 19.5, 22.1, 33.3, 55.6, 57.5, 111.1, 115.0, 120.3, 123.6, 124.2, 126.1, 128.8, 129.1, 133.4, 137.2, 137.8, 142.2. HRMS (FAB) m/z: $[M+Na]^+$ calcd for $C_{22}H_{28}N_2O_3S_2$, 455.1434; found, 455.1437.

4.4.3. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*tert*-butyl)methane]-2-*tert*-butanesulfinamide 3e. White solid, mp 209–210 °C. $[\alpha]_D^{20} = +211.2$ (c 2.9, $CHCl_3$). FTIR (KBr): 569, 591, 627, 687, 751, 839, 1065, 1142, 1181, 1219, 1368, 1449, 1474, 2963 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.06 (s, 9H), 1.16 (s, 9H), 3.56–3.57 (d, 1H, $J = 2.4$ Hz), 5.44–5.45 (d, 1H, $J = 2.7$ Hz), 6.56 (s, 1H), 7.22–7.46 (m, 6H), 7.88–7.90 (d, 2H, $J = 7.8$ Hz), 8.24–8.26 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 22.1, 26.1, 36.2, 55.4, 58.7, 112.6, 115.4, 120.2, 123.6, 124.1, 126.7, 128.6, 129.1, 133.3, 136.9, 137.8, 141.2. HRMS (FAB) m/z: $[M+Na]^+$ calcd for $C_{23}H_{30}N_2O_3S_2$, 469.1590; found, 469.1586.

4.4.4. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)phenylmethane]-2-*tert*-butanesulfinamide 3f. White solid, mp 188–190 °C. $[\alpha]_D^{20} = +38.0$ (c 2.0, $CHCl_3$). FTIR (KBr): 588, 634, 691, 729, 835, 1061, 1176, 1370, 1450, 2960, 3074 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.26 (s, 9H), 3.73 (br s, 1H), 6.56–6.57 (d, 1H, $J = 2.4$ Hz), 6.93 (s, 1H), 7.22–7.46 (m, 10H), 7.50–7.58 (m, 3H), 8.13–8.15 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (75 MHz) δ 22.2, 55.7, 56.3, 111.7, 114.7, 120.6, 123.5, 124.5, 126.2, 127.9, 128.0, 128.5, 128.7, 128.8, 133.3, 137.2, 137.9, 139.9, 141.4. HRMS (EI) m/z: $[M]^+$ calcd for $C_{25}H_{26}N_2O_3S_2$, 466.1385; found, 466.1390.

4.4.5. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-nitrophenyl)methane]-2-*tert*-butanesulfinamide 3g. White solid, mp 96–98 °C. $[\alpha]_D^{20} = +67.7$ (c 2.7, $CHCl_3$). FTIR (KBr): 445, 741, 1065, 1265, 1348, 3407 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.26 (s, 9H), 4.05 (br s, 1H), 6.57 (s, 1H), 6.95 (s, 1H), 7.21–7.30 (m, 4H), 7.41–7.59 (m, 6H), 7.99–8.04 (m, 2H), 8.09–8.12 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 22.2, 56.1, 56.5, 112.6, 114.7, 120.9, 123.4, 123.9, 125.1, 125.8, 128.6, 128.9, 133.6, 137.4, 137.8, 139.8, 147.1. HRMS (FAB) m/z: $[M+1]^+$ calcd for $C_{25}H_{25}N_5O_3S_2$, 512.1308; found, 512.1294.

4.4.6. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*o*-chlorophenyl)methane]-2-*tert*-butanesulfinamide 3h. White solid, mp 188–189 °C. $[\alpha]_D^{20} = +23.4$ (c 1.0, $CHCl_3$). FTIR (KBr): 587, 771, 1059, 1176, 1219, 1371, 1447, 2960 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.12 (s, 9H), 3.80 (s, 1H), 6.75–6.76 (d, 1H, $J = 4.2$ Hz), 6.83 (s, 1H), 6.95–7.00 (m, 2H), 7.09–7.20 (m, 5H), 7.29–7.31 (m, 2H), 7.38–7.40 (d, 1H, $J = 7.5$ Hz), 7.55–7.58 (d, 2H, $J = 7.7$ Hz), 8.02–8.04 (d, 1H, $J = 8.2$ Hz). ^{13}C NMR (75 MHz) δ 22.2, 54.1, 56.0, 113.1, 114.5, 120.8, 123.5, 124.7, 126.1, 126.6, 128.4, 128.8, 129.3, 129.4, 129.7, 133.4, 133.6, 136.7, 137.4, 138.2, 140.1. HRMS (FAB) m/z: $[M+1]^+$ calcd for $C_{25}H_{25}N_2O_3S_2$, 501.1068; found, 501.1066.

4.4.7. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*o*-bromophenyl)methane]-2-*tert*-butanesulfinamide 3i. White solid, mp 194–195 °C. $[\alpha]_D^{20} = +38.3$ (c 2.2, $CHCl_3$). FTIR (KBr): 586, 649, 686, 750, 832, 916, 1061, 1147, 1176, 1222, 1270, 1370, 1448, 1568, 2959, 3062 cm^{-1}. ^{1}H NMR (300 MHz) δ 1.26 (s, 9H), 3.82–3.83 (d, 1H, $J = 3.3$ Hz), 6.80–6.81 (d, 1H, $J = 3.0$ Hz), 6.95 (s, 1H), 7.10–7.18 (m, 3H), 7.26–7.37 (m, 5H), 7.45–7.54 (m, 2H), 7.63–7.66 (m, 1H), 7.70–7.73 (m, 2H), 8.13–8.16 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 22.7, 56.4, 56.7, 113.7, 114.9, 121.2, 123.8, 124.6, 125.1, 126.6, 127.6, 128.8, 129.2, 129.9, 130.2, 133.6, 133.7, 137.7, 138.57, 138.60, 140.4. HRMS (FAB) m/z: $[M+Na]^+$ calcd for $C_{25}H_{25}BrN_2O_3S_2$, 567.0382; found, 567.0382. The crystal used for the X-ray study had the dimensions $0.24 \times 0.20 \times 0.18$ mm. Crystal data: $C_{25}H_{25}BrN_2O_3S_2$, M 545.50, monoclinic, space group $P2(1)$, $a = 8.587(2)$ Å, $b = 16.232(4)$ Å, $c = 9.929(3)$ Å, $V = 1288.9(6)$ Å^3, $Z = 2$, $D_{calcd} = 1.406$ g cm^{-3}, $F_0 = 560$, reflections collected: 6365, λ=0.71073 Å.

4.4.8. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-methylphenyl)methane]-2-*tert*-butanesulfinamide 3j. White solid. $[\alpha]_D^{20} = +54.9$ (*c* 2.6, $CHCl_3$). Mp 144–145 °C. FTIR (KBr): 589, 751, 1061, 1175, 1369, 1449, 2968 cm^{-1}. ^1H NMR (300 MHz) δ 1.16 (s, 9H), 2.22 (s, 3H), 3.60 (br s, 1H), 6.43 (s, 1H), 6.83 (s, 1H), 6.97–6.99 (d, 2H, $J = 7.8$ Hz), 7.12–7.23 (m, 6H), 7.32–7.49 (m, 4H), 8.04–8.06 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (75 MHz) δ 20.6, 22.2, 55.7, 56.0, 111.6, 114.7, 120.6, 123.4, 124.4, 126.2, 127.9, 128.6, 128.8, 129.1, 133.1, 137.0, 137.3, 137.7, 138.0, 141.6. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{26}H_{28}N_2O_3S_2$, 480.1541; found, 480.1547.

4.4.9. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-methoxyphenyl)methane]-2-*tert*-butanesulfinamide 3k. White solid, mp 168–169 °C. $[\alpha]_D^{20} = +51.9$ (*c* 1.1, $CHCl_3$). FTIR (KBr): 589, 752, 832, 1059, 1175, 1252, 1369, 1450, 1512, 1585, 3381 cm^{-1}. ^1H NMR (300 MHz) δ 1.22 (s, 9H), 3.70 (s + br s, 4H), 6.53 (s, 1H), 6.73–6.76 (d, 2H, $J = 8.6$ Hz), 6.95 (s, 1H), 7.21–7.37 (m, 7H), 7.49–7.57 (m, 3H), 8.11–8.14 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 22.7, 55.3, 56.1, 56.2, 111.9, 114.1, 115.1, 121.1, 123.9, 124.8, 126.5, 129.1, 129.2, 129.7, 132.4, 133.6, 127.6, 138.3, 142.2, 159.5. HRMS (FAB) *m*/*z*: $[M+1]^+$ calcd for $C_{26}H_{28}N_2O_4S_2$, 497.1563; found, 497.1556.

4.4.10. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*o*-methoxyphenyl)methane]-2-*tert*-butanesulfinamide 3l. Sticky oil. $[\alpha]_D^{20} = -20.9$ (*c* 2.8, $CHCl_3$). FTIR (KBr): 589, 752, 1056, 1176, 1246, 1371, 1449, 2958 cm^{-1}. ^1H NMR (300 MHz) δ 1.25 (s, 9H), 3.91 (s, 3H), 3.94–3.96 (d, 1H, $J = 5.7$ Hz), 6.72 (s, 1H), 6.82–6.85 (m, 2H), 6.93–6.96 (d, 1H, $J = 8.1$ Hz), 7.01 (d, 1H, $J = 7.5$ Hz), 7.22–7.36 (m, 5H), 7.44–7.47 (m, 2H), 7.70–7.72 (d, 2H, $J = 7.5$ Hz), 8.10–8.13 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (75 MHz) δ 22.2, 52.0, 55.2, 55.9, 110.8, 112.3, 114.6, 120.2, 120.5, 123.3, 124.3, 126.3, 128.2, 128.4, 128.6, 128.7, 129.1, 133.2, 137.2, 138.2, 141.5, 156.4. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{26}H_{28}N_2O_4S_2$, 496.1491; found, 496.1499.

4.4.11. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)naphthylmethane]-2-*tert*-butanesulfinamide 3m. White solid, mp 103–104 °C. $[\alpha]_D^{20} = +17.1$ (*c* 1.2, $CHCl_3$). FTIR (KBr): 478, 587, 650, 685, 741, 822, 863, 912, 1062, 1147, 1175, 1273, 1306, 1370, 1450, 1508, 1599, 1722, 1807, 1912, 2869, 2961, 3060, 3212 cm^{-1}. ^1H NMR (300 MHz) δ 1.27 (s, 9H), 3.80 (br s, 1H), 6.71 (s, 1H), 7.01–7.08 (m, 3H), 7.24–7.34 (m, 3H), 7.42–7.48 (m, 4H), 7.52–7.58 (m, 2H), 7.64–7.65 (m, 2H), 7.77–7.81 (m, 2H), 8.16–8.19 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (75 MHz) δ 22.2, 55.8, 56.5, 111.7, 114.7, 120.6, 123.4, 124.5, 125.8, 125.9, 126.1, 127.2, 127.9, 128.37, 128.41, 128.7, 132.7, 132.8, 133.0, 137.1, 137.4, 138.0, 141.2. HRMS (EI) *m*/*z*: calcd for $[M+Na]^+$ $C_{29}H_{28}N_2O_3S_2$, 539.1439; found, 539.1445.

4.4.12. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(9-anthryl)methane]-2-*tert*-butanesulfinamide 3n. Pale solid, mp 120–121 °C. $[\alpha]_D^{20} = -69.3$ (*c* 1.0, $CHCl_3$). FTIR (KBr): 424, 583, 649, 684, 741, 789, 837, 911, 1058, 1176, 1220, 1367, 1449, 1717, 2959, 3054 cm^{-1}. ^1H NMR (300 MHz) δ 1.27 (s, 9H), 4.25–4.26 (d, 1H, $J = 3.0$ Hz), 6.77–6.81 (m, 2H), 6.86–6.91 (m, 2H), 7.15–7.21 (m, 1H), 7.24–7.38 (m, 7H), 7.56–7.59 (m, 1H), 7.70–7.71 (m, 1H), 7.89 (br, 2H), 8.01–8.04 (m, 1H), 8.30 (s, 1H), 8.56 (br, 2H). ^{13}C NMR (75 MHz) δ 22.3, 52.2, 56.1, 113.2, 114.7, 120.8, 123.5, 124.0, 124.4, 124.5, 126.0, 128.1, 128.4, 128.85, 128.91, 129.8, 130.4, 131.2, 132.4, 138.0, 138.4, 142.7. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{33}H_{30}N_2O_3S_2$, 566.1698; found, 566.1705.

4.4.13. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(fur-2-yl)methane]-2-*tert*-butanesulfinamide 3o. White solid, mp 168–170 °C. $[\alpha]_D^{20} = -16.0$ (*c* 0.9, $CHCl_3$). FTIR (KBr): 586, 686, 746, 909, 1062, 1176, 1369, 1450, 2959 cm^{-1}. ^1H NMR (300 MHz) δ 1.25 (s, 9H), 3.93 (br s, 1H), 6.30 (d, 1H, $J = 1.2$ Hz), 6.55–6.57 (d, 1H, $J = 5.7$ Hz), 6.80 (s, 1H), 7.23–7.39 (m, 6H), 7.46–7.49 (d, 2H, $J = 7.4$ Hz), 7.68–7.71 (d, 2H, $J = 7.6$ Hz), 8.10–8.13 (d, 1H, $J = 8.3$ Hz). ^{13}C NMR (75 MHz) δ 22.1, 51.0, 56.1, 108.8, 110.3, 112.2, 114.7, 120.8, 123.6, 124.7, 126.1, 128.7, 128.8, 133.4, 137.0, 137.9, 139.3, 142.3, 152.1. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{23}H_{24}N_2O_4S_2$, 456.1178; found, 456.1172.

4.4.14. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)styrylmethane]-2-*tert*-butanesulfinamide 3p. White solid, mp 160–161 °C. $[\alpha]_D^{20} = +6.5$ (*c* 2.2, $CHCl_3$). FTIR (KBr): 416, 446, 587, 750, 764, 1051, 1260, 1276, 1449, 1585, 2922, 3400 cm^{-1}. ^1H NMR (300 MHz) δ 1.23 (s, 9H), 3.90 (s, 1H), 6.08 (s, 1H), 6.42–6.50 (dd, 1H, $J = 6.6$, 15.9 Hz), 6.60–6.65 (d, 1H, $J = 15.9$ Hz), 6.81 (s, 1H), 7.19–7.38 (m, 10H), 7.46–7.48 (d, 1H, $J = 7.5$ Hz), 7.78–7.80 (d, 2H, $J = 7.5$ Hz), 8.14–8.16 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 22.7, 55.0, 56.3, 111.6, 115.2, 121.1, 124.0, 125.0, 126.6, 126.8, 128.2, 128.6, 129.0, 129.26, 129.31, 133.3, 133.8, 136.1, 137.6, 138.5, 141.8. HRMS (FAB) *m*/*z*: calcd for $[M+1]^+$ $C_{27}H_{28}N_2O_3S_2$, 493.1614; found, 493.1621.

4.4.15. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)benzylmethane]-2-*tert*-butanesulfinamide 3q. Colourless oil. $[\alpha]_D^{20} = +4.4$ (*c* 0.2, $CHCl_3$). FTIR (KBr): 423, 590, 751, 1062, 1177, 1368, 1450, 2960 cm^{-1}. ^1H NMR (300 MHz) δ 1.14 (s, 9H), 3.09–3.13 (m, 1H), 3.62–3.68 (dd, 2H, $J = 4.9$, 13.8 Hz), 5.59 (s, 1H), 6.59 (s, 1H), 7.23–7.51 (m, 11H), 7.76–7.79 (d, 2H, $J = 7.6$ Hz), 8.17–8.20 (d, 1H, $J = 8.2$ Hz). ^{13}C NMR (75 MHz) δ 22.1, 43.3, 52.8, 55.5, 110.9, 114.8, 120.5, 123.5, 124.4, 126.1, 126.7, 128.3, 128.9, 129.0, 129.3, 133.4, 136.1, 137.1, 137.7, 141.7. HRMS (FAB) *m*/*z*: $[M+1]^+$ calcd for $C_{26}H_{28}N_2O_3S_2$, 481.1614; found, 481.1616.

4.4.16. (R_S,*S*)-*N*-[(1-Phenylsulfonyl-1*H*-3-methyl-indol-2-yl)(*p*-chlorophenyl)methane]-2-*tert*-butanesulfinamide 3r. White solid, mp 85–87 °C. $[\alpha]_D^{20} = +93.7$ (*c* 0.8, $CHCl_3$). FTIR (KBr): 595, 668, 751, 808, 861, 960, 1018, 1091, 1126, 1173, 1219, 1318, 1363, 1450, 1768, 2928, 3374 cm^{-1}. ^1H NMR (300 MHz) δ 1.20 (s, 9H), 2.34 (s, 3H), 6.33 (br, 1H), 7.09–7.45 (m, 12H), 7.53–7.55 (m, 1H), 8.16–8.19 (d, 1H, $J = 8.0$ Hz). ^{13}C NMR (75 MHz) δ 9.8, 22.6, 56.1, 56.6, 115.1, 119.2, 119.5, 123.8, 125.7, 126.1, 128.3, 128.4, 128.9, 130.2, 133.2, 133.4, 135.9,

136.7, 138.7, 138.9. HRMS (EI) m/z: $[M]^+$ calcd for $C_{26}H_{27}N_2O_3S_2Cl$, 514.1152; found, 514.1161.

4.4.17. (R_S,S)-*N*-[(1-Phenylsulfonyl-1*H*-4-nitro-indol-2-yl)-(*p*-chlorophenyl)methane]-2-*tert*-butanesulfinamide 3s. Yellow powder, mp 204–206 °C. $[\alpha]_D^{20} = +144.6$ (c 2.0, $CHCl_3$). FTIR (KBr): 599, 685, 731, 804, 1065, 1175, 1281, 1337, 1519, 2923 cm^{-1}. ^1H NMR (300 MHz) δ 1.25 (s, 9H), 4.05 (br s, 1H), 6.57 (s, 1H), 6.95 (s, 1H), 7.21–7.30 (m, 4H), 7.41–7.59 (m, 5H), 7.99–8.04 (m, 2H), 8.09–8.12 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 22.6, 56.6, 56.9, 113.0, 115.1, 121.3, 123.8, 124.3, 125.5, 126.2, 129.0, 129.3, 134.0, 137.8, 138.1, 140.2, 147.5, 178.2. HRMS (FAB) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}N_3O_5S_2Cl$, 568.0738; found, 568.0723.

4.5. The synthesis of chiral (2-indolyl)methanamine derivatives through deprotection of chiral *tert*-butylsulfinyl group

According to the reported procedures, cleavage of the chiral *tert*-butylsulfinyl group was carried out either through hydrolysis[17a] or oxidation reaction.[17b]

4.5.1. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-2-yl)(*iso*-propanyl) methane]-*tert*-butanesulfonamide 4a. White powder, mp 143–144 °C. $[\alpha]_D^{20} = +42.9$ (c 0.9, $CHCl_3$). FTIR (KBr): 590, 751, 902, 1126, 1173, 1307, 1448, 1700, 2971 cm^{-1}. ^1H NMR (300 MHz) δ 0.62–0.64 (d, 3H, $J = 7.0$ Hz), 1.15–1.17 (d, 3H, $J = 6.7$ Hz), 1.29 (s, 9H), 2.46–2.47 (m, 1H), 4.49–4.53 (d, 1H, $J = 10.3$ Hz), 5.28–5.31 (d, 1H, $J = 10.0$ Hz), 6.69 (s, 1H), 7.00–7.05 (t, 1H, $J = 7.4$ Hz), 7.10–7.15 (t, 2H, $J = 7.4$ Hz), 7.21–7.34 (m, 4H), 7.75–7.77 (d, 2H, $J = 7.6$ Hz), 7.95–7.98 (d, 1H, $J = 8.2$ Hz). ^{13}C NMR (75 MHz) δ 14.6, 20.1, 23.8, 33.5, 58.2, 60.0, 110.5, 114.7, 120.5, 123.6, 124.1, 126.5, 128.7, 129.0, 133.4, 137.29, 137.34, 143.3. HRMS (FAB) m/z: $[M+Na]^+$ calcd for $C_{22}H_{28}N_2O_4S_2$, 471.1383; found, 471.1379. Ee was determined by HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 10.2$ min, $t_{major} = 8.2$ min.

4.5.2. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indole-2-yl)(*tert*-butyl) methane]-*tert*-butanesulfonamide 4b. White powder, mp 126–128 °C. $[\alpha]_D^{20} = +134.7$ (c 1.5, $CHCl_3$). FTIR (KBr): 591, 751, 909, 1125, 1303, 1366, 1448, 1701, 2976, 3291 cm^{-1}. ^1H NMR (300 MHz) δ 1.10 (s, 9H), 1.43 (s, 9H), 4.60–4.63 (d, 1H, $J = 10.2$ Hz), 5.66–5.69 (d, 1H, $J = 10.2$ Hz), 6.73 (s, 1H), 6.98–7.01 (m, 1H), 7.09–7.19 (m, 2H), 7.34–7.44 (m, 3H), 7.81–7.84 (d, 1H, $J = 8.4$ Hz), 8.02–8.05 (d, 2H, $J = 7.2$ Hz). ^{13}C NMR (75 MHz) δ 23.9, 26.4, 36.6, 59.1, 60.1, 110.0, 114.4, 120.4, 123.1, 123.6, 127.3, 128.5, 128.6, 133.2, 136.1, 138.0, 143.0. HRMS (FAB) m/z: $[M+Na]^+$ calcd for $C_{23}H_{30}N_2O_4S_2$, 485.1539; found, 485.1547. Ee was determined by HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 11.7$ min, $t_{major} = 10.8$ min.

4.5.3. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-chlorophenyl)methane]-*p*-toluenesulfonamide 5a. Viscous oil. $[\alpha]_D^{20} = +122.7$ (c 1.5, $CHCl_3$). FTIR (KBr): 567, 590, 664, 745, 817, 926, 1018, 1090, 1160, 1334, 1370, 1448, 1490, 1596, 3063, 3275 cm^{-1}. ^1H NMR (300 MHz) δ 2.27 (s, 3H), 5.81 (br s, 1H), 6.30–6.33 (d, 1H, $J = 8.2$ Hz), 6.75 (s, 1H), 6.93–6.96 (d, 1H, $J = 8.3$ Hz), 7.07–7.09 (d, 4H, $J = 8.4$ Hz), 7.18–7.30 (m, 4H), 7.35–7.47 (m, 4H), 7.58–7.61 (d, 2H, $J = 8.2$ Hz), 7.99–8.02 (d, 1H, $J = 8.2$ Hz). ^{13}C NMR (75 MHz) δ 20.3, 54.5, 112.3, 113.8, 120.1, 123.0, 124.2, 125.3, 126.0, 127.0, 127.7, 128.0, 128.4, 128.9, 132.7, 132.9, 136.2, 136.3, 136.5, 137.1, 137.8, 142.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{28}H_{23}N_2O_4S_2Cl$, 550.0788; found, 550.0793. Ee was determined by HPLC (Daicel Chiralcel OD-H, hexane/i-PrOH = 7:3, 0.5 mL min^{-1}): $t_{minor} = 13.1$ min, $t_{major} = 15.1$ min.

4.5.4. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-nitrophenyl)methane]-*p*-toluenesulfonamide 5b. White solid, mp 94–95 °C. $[\alpha]_D^{20} = +103.2$ (c 2.8, $CHCl_3$). FTIR (KBr): 566, 590, 665, 751, 816, 928, 1089, 1160, 1347, 1448, 1523, 1600, 3276 cm^{-1}. ^1H NMR (300 MHz) δ 2.27 (s, 3H), 5.85 (br s, 1H), 6.38–6.41 (d, 1H, $J = 8.7$ Hz), 6.73 (s, 1H), 7.07–7.10 (d, 2H, $J = 8.1$ Hz), 7.22–7.49 (m, 10H), 7.58–7.61 (d, 2H, $J = 8.3$ Hz), 7.95–8.00 (m, 3H). ^{13}C NMR (75 MHz) δ 20.9, 55.3, 113.7, 114.5, 120.8, 123.2, 123.9, 125.2, 125.7, 126.6, 127.5, 127.7, 128.1, 128.7, 129.1, 133.6, 136.7, 137.3, 137.7, 143.5, 145.4, 147.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{28}H_{23}N_3O_6S_2$, 561.1028; found, 561.1033. Ee was determined by HPLC (Daicel Chiralcel OD-H, hexane/i-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 23.5$ min, $t_{major} = 39.3$ min.

4.5.5. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*o*-bromophenyl)methyl]-*p*-toluenesulfonamide 5c. Pale yellow solid, mp 95–97 °C. $[\alpha]_D^{20} = +52.6$ (c 2.3, $CHCl_3$). FTIR (KBr): 405, 568, 589, 666, 724, 750, 814, 924, 1089, 1157, 1335, 1372, 1446, 3273 cm^{-1}. ^1H NMR (300 MHz) δ 2.24 (s, 3H), 5.06–5.08 (d, 1H, $J = 6.3$ Hz), 6.49 (s, 1H), 6.65–6.67 (d, 1H, $J = 6.6$ Hz), 6.87–7.03 (m, 5H), 7.13–7.32 (m, 5H), 7.39–7.47 (m, 4H), 7.66–7.69 (d, 2H, $J = 8.1$ Hz), 8.01–8.04 (d, 1H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz) δ 21.0, 55.5, 113.6, 114.5, 120.7, 123.5, 124.0, 124.7, 126.3, 127.09, 127.12, 128.3, 128.8, 128.9, 129.3, 129.5, 133.1, 133.5, 137.2, 137.3, 138.0, 138.4, 143.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{28}H_{23}N_2O_4S_2Br$, 594.0283; found, 594.0286. Ee was determined by HPLC (Daicel Chiralcel OD-H, hexane/i-PrOH = 7:3, 0.5 mL min^{-1}): $t_{minor} = 19.3$ min, $t_{major} = 17.3$ min.

4.5.6. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(*p*-metho-xyphenyl)methane]-*p*-toluenesulfonamide 5d. Pale yellow powder, mp 78–80 °C. $[\alpha]_D^{20} = +78.6$ (c 2.0, $CHCl_3$). FTIR (KBr): 590, 665, 801, 1091, 1170, 1257, 1369, 1448, 1511, 2962, 3285 cm^{-1}. ^1H NMR (300 MHz) δ 2.30 (s, 3H), 3.74 (s, 3H), 5.34 (br s, 1H), 6.29–6.31 (d, 1H, $J = 7.1$ Hz), 6.65–6.67 (d, 2H, $J = 7.8$ Hz), 6.77 (s, 1H), 6.88–6.91 (d, 2H, $J = 8.0$ Hz), 7.12–7.28 (m, 6H), 7.39–7.45 (m, 4H), 7.62–7.64 (d, 2H, $J = 7.6$ Hz), 7.97–8.00 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (75 MHz) δ 21.4, 55.3, 55.7, 112.8, 114.0, 114.8, 121.0, 123.8, 124.8, 126.5, 127.2, 128.6, 128.9, 129.5, 131.0, 133.5, 137.3, 137.5, 138.2, 143.4, 159.4. HRMS (EI) m/z: $[M]^+$ calcd for

$C_{29}H_{26}N_2O_5S_2$, 546.1283; found, 546.1281. Ee was determined by HPLC (Daicel Chiralcel OD-H, 10 °C, hexane/*i*-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 18.2$ min, $t_{major} = 19.7$ min.

4.5.7. (*R*)-*N*-[(1-Phenylsulfonyl-1*H*-indol-2-yl)(2-furyl)-methyane]-*p*-toluenesulfonamide 5e. Viscous oil. $[\alpha]_D^{20} = +64.6$ (*c* 1.3, $CHCl_3$). FTIR (KBr): 589, 680, 745, 815, 911, 1089, 1161, 1222, 1334, 1369, 1448, 1718, 2922, 3271 cm^{-1}. ^1H NMR (300 MHz) δ 2.28 (s, 3H), 5.75 (br s, 1H), 6.09–6.10 (d, 1H, $J = 2.7$ Hz), 6.20 (d, 1H, $J = 2.4$ Hz), 6.51–6.54 (d, 1H, $J = 8.4$ Hz), 6.74 (s, 1H), 7.08–7.48 (m, 9H), 7.62–7.65 (d, 4H, $J = 8.1$ Hz), 7.96–7.99 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (75 MHz) δ 20.9, 49.8, 108.2, 110.2, 112.6, 114.5, 120.8, 123.5, 124.7, 126.2, 126.7, 128.6, 128.7, 129.0, 133.4, 136.9, 137.4, 137.5, 142.0, 143.0, 150.6. HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{26}H_{22}N_2O_5S_2$, 506.0970; found, 506.0966. Ee was determined by HPLC (Daicel Chiralcel AD-H, hexane/*i*-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 24.7$ min, $t_{major} = 27.6$ min.

4.5.8. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-3-methyl-indol-2-yl)(*p*-chlorophenyl)methane]-*p*-toluenesulfonamide 5f. White solid, mp 124–125 °C. $[\alpha]_D^{20} = +117.5$ (*c* 0.6, $CHCl_3$). FTIR (KBr): 553, 594, 673, 752, 811, 960, 1091, 1123, 1163, 1224, 1340, 1450, 1490, 2915, 3326 cm^{-1}. ^1H NMR (300 MHz) δ 1.98 (s, 3H), 2.21 (s, 3H), 6.18–6.22 (d, 1H, $J = 10.8$ Hz), 6.79–6.86 (m, 5H), 7.05–7.10 (m, 6H), 7.25–7.39 (m, 4H), 7.48–7.51 (d, 2H, $J = 8.1$ Hz), 7.99–8.01 (d, 1H, $J = 7.5$ Hz). ^{13}C NMR (75 MHz) δ 9.09, 20.7, 51.8, 114.4, 118.9, 121.4, 123.5, 125.4, 125.6, 125.8, 127.0, 128.0, 128.36, 128.39, 129.4, 131.8, 132.8, 133.1, 136.2, 136.3, 136.7, 137.8, 142.6. HRMS (FAB) *m*/*z*: $[M+Na]^+$ calcd for $C_{29}H_{25}ClN_2O_4S_2$, 587.0836; found, 587.0840. Ee was determined by HPLC (Daicel Chiralcel OD-H, hexane/*i*-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 11.3$ min, $t_{major} = 13.1$ min.

4.5.9. (*S*)-*N*-[(1-Phenylsulfonyl-1*H*-4-nitro-indol-2-yl)(*p*-chlorophenyl) methane]-*p*-toluenesulfonamide 5g. Pale yellow solid, mp 251–253 °C. $[\alpha]_D^{20} = +77.8$ (*c* 0.7, $CHCl_3$). FTIR (KBr): 569, 680, 747, 808, 1090, 1161, 1336, 1519, 3294 cm^{-1}. ^1H NMR (300 MHz) δ 2.25 (s, 3H), 5.49 (br s, 1H), 6.45–6.48 (d, 1H, $J = 7.5$ Hz), 6.99–7.59 (m, 15H), 8.16–8.19 (d, 1H, $J = 8.1$ Hz), 8.39–8.41 (d, 1H, $J = 8.4$ Hz). ^{13}C NMR (75 MHz) δ 21.3, 55.4, 120.6, 120.8, 123.4, 124.4, 126.5, 127.1, 128.9, 129.0, 129.4, 129.5, 134.4, 134.5, 136.5, 137.1, 137.6, 138.8, 140.4, 143.8. HRMS (FAB) *m*/*z*: $[M+Na]^+$ calcd for $C_{28}H_{22}ClN_3O_6S_2$, 618.0531; found, 618.0540. Ee was determined by HPLC (Daicel Chiralcel OD-H, hexane/*i*-PrOH = 7:3, 0.6 mL min^{-1}): $t_{minor} = 31.9$ min, $t_{major} = 25.5$ min.

4.5.10. (*S*)-*N*-[(1*H*-Indol-2-yl)(*p*-chlorophenyl)methyl]-*p*-toluenesulfonamide 6. Overall yield 45%. Yellow solid, mp 199–200 °C. $[\alpha]_D^{20} = -24.3$ (*c* 2.8, CH_2Cl_2). FTIR (KBr): 569, 665, 709, 747, 812, 842, 925, 1014, 1046, 1091, 1159, 1328, 1419, 1455, 1492, 2850, 2920, 3270, 3283 cm^{-1}. ^1H NMR (300 MHz) δ 2.31 (s, 3H), 5.65–5.68 (d, 1H, $J = 8.6$ Hz), 5.73–5.76 (d, 1H, $J = 8.7$ Hz), 5.87–5.88 (t, 1H, $J = 0.9$ Hz), 6.99–7.07 (m, 5H), 7.11–7.15 (m, 3H), 7.22–7.25 (d, 1H, $J = 7.0$ Hz), 7.40–7.42 (d, 1H, $J = 7.8$ Hz), 7.45–7.48 (d, 2H, $J = 8.3$ Hz), 8.56 (br s, 1H). ^{13}C NMR (75 MHz) δ 21.4, 55.6, 102.7, 111.2, 120.0, 120.6, 122.5, 127.0, 127.7, 128.7, 128.8, 129.5, 134.0, 136.47, 136.51, 136.59, 136.64, 143.9. Anal. Calcd for $C_{22}H_{19}N_2O_2SCl$: C, 64.30; H, 4.66; N, 6.82; Found: C, 64.07; H, 4.73; N, 6.86. Ee was determined by HPLC (Daicel Chiralpak OD-H, hexane/*i*-PrOH = 7:3, 0.6 mL min): $t_{minor} = 20.2$ min and $t_{major} = 16.6$ min.

Acknowledgement

We thank the National Natural Science Foundation of China and the Chinese Academy of Sciences for financial support.

References

1. Sundberg, R. J. *Indoles*; Academic Press: San Diego, 1996.
2. (a) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113–1126; (b) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045–1075; (c) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873–2920; (d) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875–2911.
3. (a) Sundberg, R. J. In *The Chemistry of Indoles*; Blomquist, A. T., Ed.; Academic Press: New York, 1970; (b) Modi, S. P.; Zayed, A.-H.; Archer, S. *J. Chem. Soc., Chem. Commun.* **1970**, 1095–1096; (c) Brown, R. K. In *Heterocyclic Compounds*; Houlihan, W. J., Ed.; Wiley-Interscience: New York, 1972; Vol. 25, (d) Kuehne, M. E.; Podhorez, D. E.; Mulamba, T.; Bornmann, W. G. *J. Org. Chem.* **1987**, *52*, 347–353; (e) Leon, P.; Garbay-Jaureguiberry, C.; Barsi, M. C.; Le pecq, J. B.; Roques, B. P. *J. Med. Chem.* **1987**, *30*, 2074–2080; (f) Hashimoto, C.; Husson, H.-P. *Tetrahedron Lett.* **1988**, *29*, 4563–4566; (g) Laronze, M.; Sapi, J. *Tetrahedron Lett.* **2002**, *43*, 7925–7928.
4. For examples on the applications of 2-lithioindoles, see: (a) Hasan, I.; Marinelli, E. R.; Chang, L.-C.; Fowler, F. W.; Levy, A. B. *J. Org. Chem.* **1981**, *46*, 157–164; (b) Gmeiner, P.; Kraxner, J.; Bollinger, B. *Synthesis* **1996**, *10*, 1196–1198; (c) Manabe, S.; Ito, Y. *J. Am. Chem. Soc.* **1999**, *121*, 9754–9755; (d) Kraxner, J.; Gmeiner, P. *Synthesis* **2000**, *8*, 1081–1083; For other 2-metallated indoles, see Palladium: (e) Itahara, T.; Ikeda, M.; Sakakibara, T. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1361–1363; Magnesium: (f) Kondo, Y.; Yoshida, A.; Sakamoto, T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2331–2332; Stannium: (g) Beddoes, R. L.; Cheeseright, T.; Wang, J.; Quayle, P. *Tetrahedron Lett.* **1995**, *36*, 283–286.
5. (a) Jia, Y.-X.; Xie, J.-H.; Duan, H.-F.; Wang, L.-X.; Zhou, Q.-L. *Org. Lett.* **2006**, *8*, 1621–1624; (b) Wang, Y.-Q.; Song, J.; Hong, R.; Li, H.; Deng, L. *J. Am. Chem. Soc.* **2006**, *128*, 8156–8157; (c) Kang, Q.; Zhao, Z.-A.; You, S.-L. *J. Am. Chem. Soc.* **2007**, *129*, 1484–1485.
6. Varney, M. D.; Appelt, K.; Kalish, V.; Reddy, R.; Tatlock, J.; Palmer, C. L.; Romines, W. H.; Wu, B.-W.; Musick, L. *J. Med. Chem.* **1994**, *37*, 2274–2284.
7. Giorgioni, G.; Accorroni, B.; Stefano, A. D.; Marucci, G.; Siniscalchi, A.; Claudi, F. *Med. Chem. Res.* **2005**, *14*, 57–73.
8. Cozzi, P. G.; Prati, G. P.; Umani-Ronchi, A. *Gazz. Chim. Ital.* **1997**, *127*, 403–405.
9. (a) Sundberg, R. J.; Russell, H. F. *J. Org. Chem.* **1973**, *38*, 3324–3330; (b) Love, B. E.; Raje, P. S. *J. Org. Chem.* **1994**, *59*, 3219–3222.

10. Enders, D.; Signore, G. D. *Tetrahedron: Asymmetry* **2004**, *15*, 747–751.
11. (a) Davis, F. A.; Zhou, P.; Chen, B. *Chem. Soc. Rev.* **1998**, *1*, 13–18; (b) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984–995; (c) Zhou, P.; Chen, B.; Davis, F. A. *Tetrahedron* **2004**, *60*, 8003–8030; (d) Davis, F. A.; Yang, B.; Deng, J.; Zhang, J. *ARKIVOC* **2006**, *vii*, 120–128; (e) Senanayaka, C. H.; Krishnamurthy, D.; Lu, Z.-H.; Han, Z.; Gallou, I. *Aldrichim. Acta* **2005**, *38*, 93–104; (f) Morton, D.; Stockman, R. A. *Tetrahedron* **2006**, *62*, 8869–8905; (g) Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 11276–11282; (h) Kochi, T.; Ellman, J. A. *J. Am. Chem. Soc.* **2004**, *126*, 15652–15653; (i) Davis, F. A.; Yang, B. *J. Am. Chem. Soc.* **2005**, *127*, 8398–8407; (j) Beenen, M. A.; Deix, D. J.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 6304–6305.
12. Borg, G.; Chino, M.; Ellman, J. A. *Tetrahedron Lett.* **2001**, *42*, 1433–1435.
13. (a) Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Am. Chem. Soc.* **1984**, *106*, 5031–5033; (b) Yamamoto, Y.; Maruyama, K.; Komatsu, T.; Ito, W. *J. Am. Chem. Soc.* **1986**, *108*, 7778–7786.
14. (a) Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 268–269; (b) Cogan, D. A.; Liu, G.; Ellman, J. A. *Tetrahedron* **1999**, *55*, 8883–8904; (c) Jiang, W.; Chen, C.; Marinkovic, D.; Tran, J. A.; Chen, C. W.; Arellano, L. M.; White, N. S.; Tucci, F. C. *J. Org. Chem.* **2005**, *70*, 8924–8931.
15. Uchiyama, M.; Matsumoto, Y.; Nakamura, S.; Ohwada, T.; Kobayahsi, N.; Yamashita, N.; Matsumiya, A.; Sakamoto, T. *J. Am. Chem. Soc.* **2004**, *126*, 8755–8759.
16. Bolshan, Y.; Batey, R. A. *Org. Lett.* **2005**, *7*, 1481–1484.
17. (a) Beenen, M. A.; Weix, D. J.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 6304–6305; (b) Jiang, W.; Chen, C.; Marinkovic, D.; Tran, J. A.; Chen, C. W.; Arellano, L. M.; White, N. S.; Tucci, F. C. *J. Org. Chem.* **2005**, *70*, 8924–8931.