Synthesis of Chiral Sulfinyl-Substituted 1-Indolyl Enones and Asymmetric Conjugate Addition by an Arylcopper Reagent

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The asymmetric conjugate addition of arylcopper reagents to chiral 1-[2-(*p*-tolylsulfinyl)]indolyl and 1-[3-(*p*-tolylsulfinyl)]indolyl enones was examined. With the 2-sulfinyl-indolyl derivatives, the reaction of the arylcopper reagent gave high diastereoselectivities (81—88% de's) to afford the adducts in excellent yields, although the similar addition reaction of the 3-sulfinyl derivatives afforded poor diastereoselectivities.

Key words chiral indolyl sulfoxide; conjugate addition; aryl copper reagent; diastereoselectivity

We have recently reported that the conjugate addition of α,β-unsaturated enones **1**, derived from a chiral sulfinyl auxiliary **2**, proceeds smoothly to give the adduct **3** with high diastereoselectivity (**3** *vs.* **4**).[1)] It is noted that the major adduct **3** was treated with an alkoxide to afford the ester **5** (or **6**), along with efficient recovery of the sulfoxide **2** without any loss of optical purity (Chart 1).

In connection with asymmetric synthesis using chiral sulfoxides, we were intrigued by the use of chiral 2- and 3-sulfinyl indolyl enones **7** and **8** as for conjugate addition reactions (Chart 2). In contrast to pyrrole sulfoxide **1**, steric interactions between the H-7 of the indole ring and the *N*-substituent (=the enoyl group) of **7** and **8** may influence the conformational flexibility of the transition structure. We here describe the synthesis of **7** and **8** and their conjugate additions with organocuprates.

Chiral auxiliary **9** for the synthesis of **7** commenced from 1-(triisopropylsilyl)indole, which provides selectively the C(3)-lithiated indole[2)] by the action of an alkyllithium reagent. It is known that 3-lithio derivative, generated from 1-(benzenesulfonyl)indole by an alkyllithium, readily undergoes C(3)→C(2) migration of lithium to produce the 2-lithio indole during the reaction.[3)] Selective C-3 lithiation of 1-(triisopropylsilyl)indole was thus attempted by the procedure according to the literature method.[2)] After treatment of 1-(triisopropylsilyl)indole with 1.5 eq of *t*-butyllithium and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (1.8 eq) in hexane at 0 °C for 3 h followed by addition of (S_s)-(−)-*l*-menthyl *p*-toluenesulfinate (−78 °C for 1 h) in THF, a considerable amount of undesired product **10** (30% yield) was produced by migration of the triisopropylsilyl group.[2)] The desired compound **11** was also isolated as the minor product (17% yield) under the conditions. Additionally, exposure of **11** obtained to tetrabutylammonium fluoride afforded **9** with low enantiomeric excess (ee; 34% ee).

Therefore, we sought an alternative route to **9** *via* the 3-iodoindole **12** as shown in Chart 3. Kondo *et al.*[3)] reported that the use of ethylmagnesium bromide effects iodine–metal (*i.e.*, magnesium) exchange reaction of **12** to afford the 3-magnesio indole without extensive rearrangement to the 2-magnesio species.

In fact, treatment of **12** with ethylmagnesium bromide in THF at 0 °C followed by addition of (S_s)-(−)-*l*-menthyl *p*-toluenesulfinate produced the 3-sulfinyl indole **13** in 78%

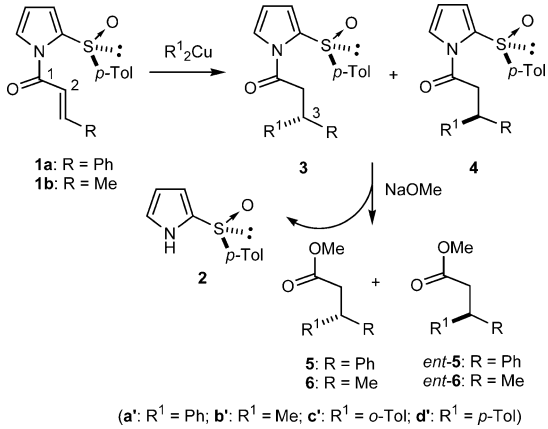

Chart 1

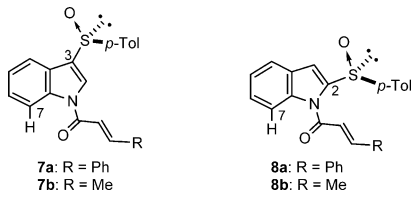

Chart 2

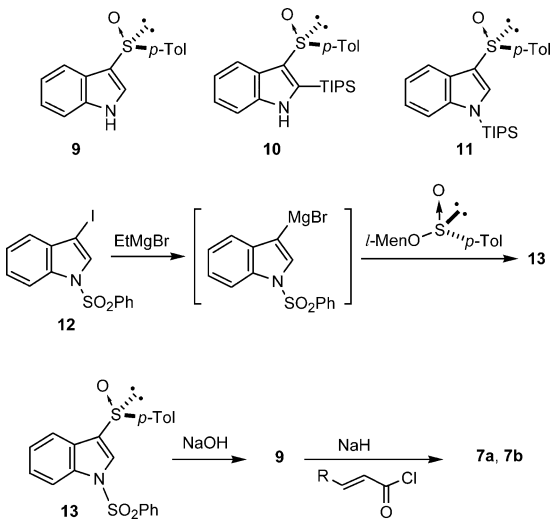

Chart 3

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yield. No 2-sulfinyl product was detected in the reaction mixture. Although chiral HPLC analysis of **13** was unsuccessful due to decomposition of a sample through the column, the sulfoxide **9**, after which was treated with base, showed high enantiomeric excess (99% ee) on chiral HPLC. Incorporation of an enone group into **9** was carried out by the method previously described.[1] Treatment of **9** with (*E*)-cinnamoyl- and crotonyl chloride in the presence of sodium hydride afforded **7a** and **7b**, respectively, in 77% and 58% yields. With crotonyl chloride (contaminated with (*Z*)-1-butenoyl chloride), the minor product, the 1-[(*Z*)-1-butenoyl]indole was readily removed after recrystallization of the crude product.

On the other hand, the synthesis of the key precursor **14** for **8** was achieved starting from 1-(benzenesulfonyl)indole (Chart 4). Treatment of 1-(benzenesulfonyl)indole with 1 eq of lithium diisopropylamide (LDA) resulted in ready formation of the 2-lithio species,[4,5] after which was quenched with (−)-*l*-menthyl *p*-toluenesulfinate to give the sulfoxide **15** in 74% yield. Alkaline hydrolysis of **15** afforded the requisite 2-sulfinyl indole **14** (>99% ee) in quantitative yield.

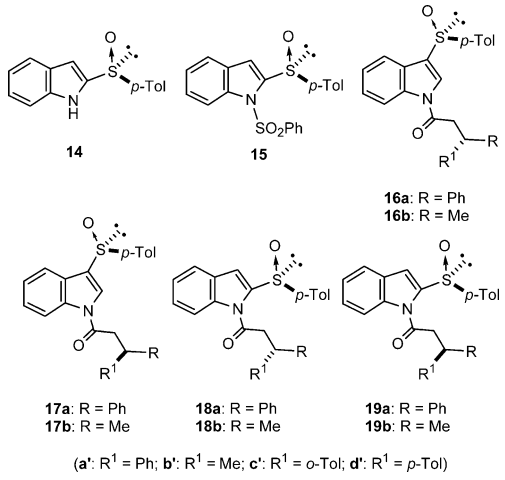

Chart 4

In a similar manner to the reaction (**9**→**7**), the sulfoxides **8a** and **8b** were obtained in good yields. Having obtained the sulfoxides **7** and **8**, we first examined the conjugate addition of **7** with an arylcopper reagent. In the previous results,[1] it had been shown that these reagents for conjugate additions of **1** afford better results in diastereoselectivity and yields than the use of the cuprates derived from organolithiums.[6] Therefore, the reaction was carried out by the diarylcuprate [prepared from an aryl Grignard reagent (6 eq) and Cu(I) (3 eq)] at −30 °C for 1 h. When the reaction was conducted by a smaller amount of the organocuprate, the reaction was often incomplete within several hours. The results are summarized in Table 1.

Disappointingly, the diastereoselectivities were poor, resulted in the production of nearly equal amounts of two diastereoisomers **16** and **17**. In all cases, diastereoisomers **17** were produced in favor to **16**. The diastereoselectivity and absolute stereochemistry were determined by chiral HPLC analysis of the methyl esters **5** and **6**[1] obtained by methanolysis of the crude product mixture.

On the other hand, under the conditions, the reaction of the 2-sulfinyl indoles **8** gave moderate to high diastereoselectivities to afford **18** as the major products (Table 2). Although, with the cinnamoyl derivative **8a**, an alkylcuprate ($Me_2Cu\cdot MgBr\cdot MgBrI$) provided low diastereoselectivity (59% de; entry 1, Table 2), addition reaction of di-*o*-tolyl- and di-*p*-tolylcuprates to **8a** gave high diastereoselectivities (84—86% de's). The reaction of the crotonoyl derivatives **8b** also gave high diastereoselectivities (entries 4—6, Table 2).

The reaction mechanism of the highly diastereoselective

Table 1. Conjugate Addition of an Arylcopper Reagent to 3-Sulfinyl-Substituted Indolyl Enones **7**[a]

Entry	Substrate	Organocopper reagent	Major product	Isolated yield (%)	ee/%[b] of	ester **5** or **6**	de/%[c] of	**16** *vs.* **17**
1	**7a**	$(2\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**17ac′**	99	16	**6c′**<*ent*-**6c′**	16	**16ac′**<**17ac′**
2	**7a**	$(4\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**17ad′**	99	4	**6d′**<*ent*-**6d′**	4	**16ad′**<**17ad′**
3	**7b**	$Ph_2CuMgBr\cdot MgBrI$	**17ba′**	99	19	**5b′**<*ent*-**5b′**	19	**16ba′**<**17ba′**
4	**7b**	$(2\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**17bc′**	94	33	**5c′**<*ent*-**5c′**	33	**16bc′**<**17bc′**
5	**7b**	$(4\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**17bd′**	96	34	**5d′**<*ent*-**5d′**	34	**16bd′**<**17bd′**

a) The reaction was carried out at −30 °C for 1 h in tetrahydrofuran. Sulfoxide **7** with 98—99% ee was employed for the reaction. *b*) Enantiomeric excess of **5** and **6** was determined by chiral HPLC analysis. *c*) Diastereoisomeric excess was determined by chiral HPLC analysis of **5** and **6**, since the C(3) methine protons of two diastereoisomeric products were not well-resolved in the ^{1}H-NMR spectrum. Absolute configuration at the C(3) position of the major product was determined by comparison with the chiral HPLC behavavior (retention times) of the methyl ester (**5** and **6**) obtained by methanolysis.

Table 2. Conjugate Addition of Organocopper Reagent to 2-Sulfinyl-Substituted Indolyl Enones **8**[a]

Entry	Substrate	Organocopper reagent	Major product	Isolated yield (%)	ee/%[b] of	ester **5** or **6**	de/%[c] of	**18** *vs.* **19**
1	**8a**	$Me_2CuMgBr\cdot MgBrI$	**18ab′**	94	58	**5b′**>*ent*-**5b′**	59	**18ab′**>**19ab′**
2	**8a**	$(2\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**18ac′**	96	84	**5c′**>*ent*-**5c′**	84	**18ac′**>**19ac′**
3	**8a**	$(4\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**18ad′**	98	84	**5d′**>*ent*-**5d′**	86	**18ad′**>**19ad′**
4	**8b**	$Ph_2CuMgBr\cdot MgBrI$	**18ba′**	99	85	*ent*-**5b′**>**5b′**	86	**18ba′**>**19ba′**
5	**8b**	$(2\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**18bc′**	96	88	**6c′**>*ent*-**6c′**	88	**18bc′**>**19bc′**
6	**8b**	$(4\text{-}MeC_6H_4)_2CuMgBr\cdot MgBrI$	**18bd′**	98	81	**6d′**>*ent*-**6d′**	81	**18bd′**>**19bd′**

a) The reaction was carried out by 2—3 eq of Cu(I) and 4—6 eq of an aryl Grignard reagent at −30 °C for 2 h in tetrahydrofuran. Sulfoxide **8** with 98—99% ee was employed for the reaction. *b*) Enantiomeric excess was determined by chiral HPLC. *c*) Diastereoisomeric excess was determined by ^{1}H-NMR analysis [the methine protons at C(3)] of the crude products and/or by ee values from chiral HPLC analysis of **5** and **6**. Absolute configuration of the C(3) position of the major product was determined by comparison with the chiral HPLC behavavior (retention times) of **5** and **6**.

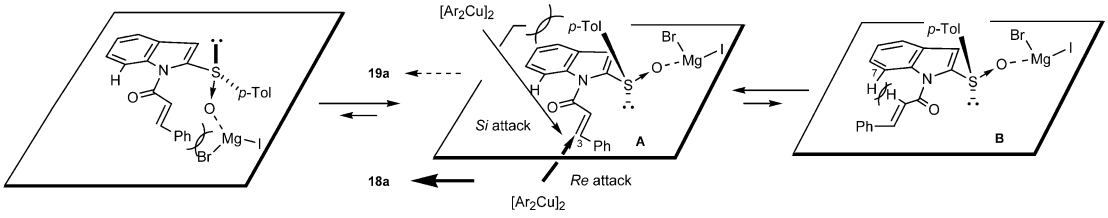

Fig. 1

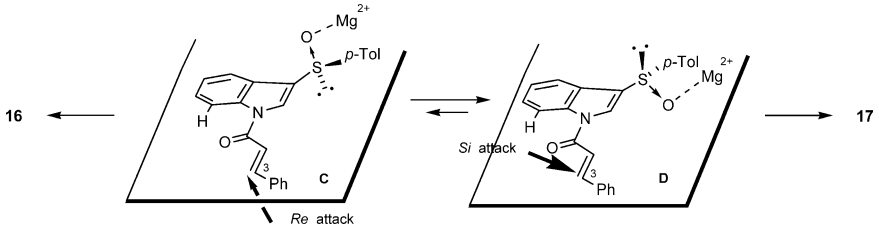

Fig. 2

conjugate addition of **8** induced by the chiral sulfinyl moiety is consistent with previous proposals.[1)] Generally, the preferred orientation of the S→O group of the α,β-unsaturated sulfoxide moiety is coplanar with the carbon–carbon double bond [S(O)–C=C–].[1)] Since it is assumed that the conjugate addition takes place *via* the *s-cis* conformation of the enone group (N–C(O)–C=C–), a diarylcopper reagent, which would be dimeric[7,8)] could attack preferentially from the C(3)-*Re* face of transition state A, affording **18** as shown in Fig. 1. The transition state B would be unstable due to a steric 1,5-interaction[9)] between the C(7) hydrogen and the hydrogen in the α,β-enone substituent.

Instead, the poor diastereoselectivities in the reaction of **7** reflect that the chiral sufinyl group remote from the reaction site would not participate in the addition reaction. The reasons for reversal in the observed selectivity (**17** produced in slightly preference to **16**) should reflect that the syncoplanar orientation (transition structure D) of the S→O group with the C(2)–C(3) double bond in the indole ring is preferred (Fig. 2).[10)]

In summary, we have shown that asymmetric 1,4-addition of arylcopper reagents to the chiral 2-sulfinyl-substituted indolyl enone proceeds smoothly to give the addition product with high diastereoselectivity in high yield. With the indolyl sulfoxide, 1,6-asymmetric induction has been achieved, and the chiral auxiliary was efficiently recovered without any loss of optical purity.

Experimental

The symbol S_s expresses that the absolute configuration of the sulfinyl center is *S*. Melting points were determined with a Yanaco micro melting point apparatus and are uncorrected. Boiling point for bulb-to-bulb distillation indicates bath temperature. IR spectra were recorded as film or KBr disk on a Perkin-Elmer Spectrum One FT-IR spectrometer. NMR spectra were measured in $CDCl_3$ solution with tetramethylsilane as internal standard, on a JEOL JNM-GX270 or EX-400 spectrometer. The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of dq (ddq), multiplet (m), and broad (br). *J*-Values are given in Hz. Mass spectra were taken with a JEOL JMS-D300 or JMS-SX102A spectrometer. Optical rotations were recorded on a JASCO DIP-360 digital polarimeter. Extracts were dried over anhydrous $MgSO_4$ before evaporation of solvents on a rotary evaporator under reduced pressure. Dry THF and diethyl ether were freshly distilled from sodium benzophenone ketyl prior to use. *m*-Chloroperbenzoic acid (*m*-CPBA) was used after purification by washing with phosphate buffer, pH 7.5, according to the literature method.[11)] TLC analyses were performed using Merck precoated silica $60F_{254}$ plates (0.2 mm). Column chromatography was carried out on Merck silica (70—230 mesh) or Merck silica (230—400 mesh). Chiral HPLC analyses were performed using a chiral column (4.6×250 mm). Peak ratios by HPLC were determined with an integrator (Shimadzu Chromatopac C-R6A). Grignard reagents (THF solution) were purchased commercially and diluted with THF to the appropriate concentrations, and titrated[12)] prior to use.

3-[(S_s)-(*p*-Tolylsulfinyl)]-1-(triisopropylsilyl)indole (11) To a cooled solution of 1-(triisopropylsilyl)indole[13)] (175 mg, 0.64 mmol) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (0.17 ml, 1.15 mmol) in dry hexane (10 ml) at 0 °C was added *t*-BuLi (2.6 ml of a 0.37 mol dm^{-3} solution in hexane, 0.96 mmol) and the mixture was stirred for 3 h at the same temperature. After being cooled to −78 °C, a solution of (S_s)-(−)-*l*-menthyl *p*-toluenesulfinate (377 mg, 1.28 mmol) in dry THF (10 ml) was added. The mixture was stirred for 1 h at the same temperature and then quenched with a saturated NH_4Cl solution and the aqueous layer was extracted with Et_2O (30 ml×3). The combined extracts were washed with brine, dried, and concentrated. The crude product was purified by flash chromatography on silica using hexane–AcOEt (5 : 1) as eluent to give **10** (80 mg, 30%) and **11** (46 mg, 17%). Sulfoxide **10**: mp 174—176 °C (from AcOEt); ^{1}H-NMR (270 MHz) δ 1.19 (9H, d, *J*=7.5, Me), 1.25 (9H, d, *J*=7.5, Me), 1.6—1.8 (3H, m, CH), 2.37 (3H, s, Me), 6.9—7.0 (1H, m, ArH), 7.1—7.35 (2H, m, ArH), 7.24 (2H, d, *J*=8.1, *p*-Tol), 7.4—7.5 (1H, m, ArH), 7.53 (2H, d, *J*=8.1, *p*-Tol), 8.71 (1H, s, NH). Sulfoxide **11**: mp 130—132 °C (from Et_2O/hexane); ^{1}H-NMR (270 MHz) δ 1.14 (9H, d, *J*=7.7, Me), 1.15 (9H, d, *J*=7.7, Me), 1.6—1.8 (3H, m, CH), 2.37 (3H, s, Me), 7.0—7.1 (1H, m, ArH), 7.1—7.2 (1H, m, ArH), 7.26 (2H, d, *J*=8.1, *p*-Tol), 7.4—7.5 (2H, m, ArH), 7.49 (2H, d, *J*=8.1, *p*-Tol), 7.68 (1H, s, H-2).

To a solution of **11** (25 mg, 0.06 mmol) obtained in dry THF (4 ml) was added $Bu_4NF\cdot 3H_2O$ (38 mg) in dry THF (1 ml) at 0 °C. The mixture was stirred for 1 h at the same temperature and then diluted with Et_2O (5 ml). After the usual work-up, the product was purified by column chromatography on silica using hexane–AcOEt (1 : 2) as eluent to give **9** (23 mg, 82%). The ee of **9** obtained showed 34% by chiral HPLC (*vide infra*).

1-Benzenesulfonyl-3-[(S_s)-(*p*-tolylsulfinyl)]indole (13) To an ice-cooled solution of 1-benzenesulfonyl-3-iodoindole[5)] **12** (3.88 g, 10.1 mmol) in dry THF (25 ml) at 0 °C was added EtMgBr (26.5 ml of a 0.46 mol dm^{-3} solution in THF, 12.2 mmol) and the mixture was stirred for 0.5 h at the same temperature, and allowed to stand at room temperature for 0.5 h. After being cooled to 0 °C, a solution of (S_s)-(−)-*l*-menthyl *p*-toluenesulfinate (3.59 g, 12.2 mmol) in dry THF (30 ml) was added. The mixture was stirred at 0 °C overnight in the dark. The reaction mixture was then quenched with a diluted $NaHCO_3$ solution and the aqueous layer was extracted with Et_2O (50 ml×3). The combined extracts were washed with brine, dried, and concentrated. The crude product was purified by flash chromatography on silica using hexane–AcOEt (20 : 1→15 : 1→1 : 1) as eluent to give **13** (3.13 g, 78%). mp 153—154 °C (from EtOAc); $[\alpha]_D^{21}$ +97.4° (*c*=1.1, $CHCl_3$) for 99% ee (S_s>R_s). IR cm^{-1} (KBr) 1372 (NSO_2), 1044 (S→O). ^{1}H-NMR

(270 MHz) δ 2.38 (3H, s, Me), 7.16 (1H, dt, J=8.1, 0.9, ArH), 7.25—7.35 (3H, m, ArH), 7.4—7.65 (6H, m, ArH), 7.9—8.0 (3H, m, ArH), 8.01 (1H, s, H-2). ^{13}C-NMR (67.5 MHz) δ 21.1, 113.6, 120.4, 124.0, 124.9 (2C), 125.3, 125.7, 125.8, 126.8 (2C), 127.9, 129.4 (2C), 129.8 (2C), 134.3, 135.4, 137.3, 139.7, 141.5. EI-MS m/z 395 (M^+), 379, 347, 238, 223, 206. *Anal.* Calcd for $C_{21}H_{17}NO_3S_2$: C, 63.79; H, 4.33; N, 3.54. Found: C, 63.69; H, 4.27; N, 3.64.

3-[(S_s)-(*p*-Tolylsulfinyl)]indole (9) To a solution of sulfonamide **13** (2.76 g, 6.98 mmol) in dioxane (70 ml) was added 4% aq. NaOH (50 ml, w/v) and the mixture was stirred at room temperature for 2 h in the dark. The reaction mixture was then extracted with Et_2O (50 ml×3). The combined extracts were washed with saturated brine (30 ml), dried, and concentrated to give **9** (1.73 g, 97%) as a pale yellow solid. mp 131—133 °C (dec.) (from AcOEt); $[\alpha]_D^{23}$ +44.8° (c=1.0, $CHCl_3$) for 99% ee (S_s>R_s). IR cm^{-1} (KBr) 3569 (NH), 1019 (S→O). ^{1}H-NMR (270 MHz) δ 2.38 (3H, s, Me), 6.95—7.05 (1H, m, ArH), 7.05—7.4 (3H, m, ArH), 7.18 (1H, d, J=2.9, H-2), 7.26 (2H, d, J=8.3, *p*-Tol), 7.54 (2H, d, J=8.3, *p*-Tol), 10.36 (1H, br s, NH). ^{13}C-NMR (67.5 MHz) δ 21.2, 112.6, 115.8, 119.0, 121.2, 123.2, 123.6, 125.0 (2C), 129.7 (2C), 130.0, 137.3, 140.0, 140.6. EI-MS m/z 255 (M^+), 239, 207. *Anal.* Calcd for $C_{15}H_{13}NOS$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.57; H, 5.16; N, 5.56.

For determination of the enantiomeric excess of **9**, an analytical sample of **9** and *ent*-**9** (=the enantiomer of **9**) was prepared by the following sequence. Treatment of **9** with Zn–$TiCl_4$ afforded the corresponding sulfide, which was oxidized with *m*-CPBA to produce (±)-**9** (mp 138—140 °C; lit.[14] mp 120.5—121.5 °C). Since a pair of peaks was resolved by chiral HPLC, the ee (99%) of the product was confirmed. Chiral HPLC: Chiralpak AS-H, 254 nm, hexane–2-propanol: 6 : 1; 1.0 ml/min; **9**: 80.9 min, *ent*-**9**: 98.5 min.

1-(*E*)-Cinnamoyl-3-[(S_s)-(*p*-tolylsulfinyl)]indole (7a) Sulfinyl indole **9** (549 mg, 2.15 mmol) in dry THF (15 ml) was added dropwise to an ice-cooled suspension of NaH (129 mg, 60% dispersion in mineral oil, 3.22 mmol) in dry THF (5 ml) and the mixture was then stirred at room temperature for 1 h. The mixture was cooled to 0 °C and (*E*)-cinnamoyl chloride (537 mg, 3.22 mmol) in dry THF (15 ml) was added to the mixture. After being stirred for 1.5 h, the mixture was quenched with diluted $NaHCO_3$ (20 ml) and the aqueous layer was extracted with Et_2O (15 ml×3). The combined extracts were washed with saturated brine (30 ml), dried, and concentrated to give **7a** (641 mg, 77%) as a solid. mp 203—205 °C (from AcOEt); $[\alpha]_D^{24}$ −156° (c=1.0, THF) for 98% ee (S_s>R_s). IR cm^{-1} (KBr) 1701 (C=O), 1035 (S→O). ^{1}H-NMR (270 MHz) δ 2.39 (3H, s, Me), 7.15—7.5 (8H, m, ArH+CH=), 7.65—7.75 (5H, m, ArH), 8.05 (1H, d, J=15.4, CH=), 8.20 (1H, s, ArH), 8.52 (1H, d, J=8.4, ArH). ^{13}C-NMR (100 MHz) δ 21.4, 116.1, 117.3, 119.7, 124.5, 125.6 (3C), 126.3, 126.4, 128.6 (3C), 129.2 (2C), 130.1 (2C), 131.3, 134.0, 137.0, 140.3, 142.0, 148.3, 164.1. EI-MS m/z 385 (M^+), 369, 131, 103. *Anal.* Calcd for $C_{24}H_{19}NO_2S$: C, 74.79; H, 4.97; N, 3.63. Found: C, 74.69; H, 4.91; N, 3.56.

1-[(*E*)-2-Butenoyl]-3-[(S_s)-(*p*-tolylsulfinyl)]indole (7b) Crotonamide **7b** was obtained after recrystallization in 58% yield from **9** (2.87 g) and crotonyl chloride (1.77 ml, contaminated by isocrotonyl chloride) in a manner similar to the procedure for **7a**, except for the reaction time (3.5 h): mp 118—119 °C (from hexane–AcOEt); geometrical purity >99%; $[\alpha]_D^{22}$ +11.4° (c=1.0, $CHCl_3$) for >99% ee (S_s>R_s). IR cm^{-1} (KBr) 1694 (C=O), 1036 (S→O). ^{1}H-NMR (270 MHz) δ 2.08 (3H, dd, J=7.0, 1.7, Me), 2.38 (3H, s, Me), 6.72 (1H, dq, J=14.8, 1.7, CH=), 7.15—7.41 (6H, m, ArH+CH=), 7.64 (2H, d, J=8.2, *p*-Tol), 8.07 (1H, s, ArH), 8.46 (1H, d, J=8.4, ArH). ^{13}C-NMR (100 MHz) δ 18.7, 21.4, 117.2, 119.6, 121.5, 124.4, 125.2, 125.4 (3C), 126.1, 126.6, 130.1 (2C), 136.9, 140.2, 141.9, 148.7, 163.8. EI-MS m/z 323 (M^+), 307, 275, 239, 207, 69. EI-HR-MS Calcd for $C_{19}H_{17}NO_2S$: 323.0980. Found: 323.0989. *Anal.* Calcd for $C_{19}H_{17}NO_2S\cdot 1/4H_2O$: C, 69.62; H, 5.38; N, 4.27. Found: C, 69.60; H, 5.46; N, 4.30. No satisfactory elemental analysis was obtained due to ready absorption of water.

Typical Procedure for Preparation of 16 and 17 from 7 (Table 1, Entry 1) To a sonicated suspension of Cu(I)I (297 mg, 1.6 mmol) in dry THF (10 ml) cooled at −10 °C was added *o*-tolylmagnesium bromide (31 ml of a 0.10 mol dm^{-3} solution in THF, 3.1 mmol) dropwise. After 0.5 h, a cooled solution of **7a** (200 mg, 0.52 mmol, 99% ee) in dry THF (10 ml) was added dropwise at −30 °C, and the yellow solution was stirred for 1 h at the same temperature. The reaction mixture was then quenched with a saturated NH_4Cl solution and the aqueous layer was extracted with Et_2O (30 ml×3). The combined extracts were washed with brine, dried, and concentrated. The crude product was purified by flash chromatography on silica using hexane–AcOEt (20 : 1→2 : 1) as eluent to give a mixture of **16ac′** and **17ac′** (246 mg, 99%). Signals for **16ac′** and **17ac′** were not adequately resolved in the ^{1}H-NMR spectrum of the product mixture; therefore, the product ratio was determined by chiral HPLC analysis of the methyl esters[1] (**5b′** : *ent*-**5c′**=42 : 58, 16% ee) by methanolysis (*vide infra*). After recrystallization of the product mixture, the product ratio changed to 81 : 9 (62% de) by judging from chiral HPLC of the esters (61% ee).

1-[(*S*)-3-Phenyl-3-(*o*-tolyl)propanoyl]-3-[(S_s)-(*p*-tolylsulfinyl)]indole (17ac′) mp 194—197 °C (from AcOEt/hexane) (3*S*+3*R* mixture). $[\alpha]_D^{22}$ +63.2° (c=1.0, $CHCl_3$) for ≥98% ee (S_s>R_s), 62% de (3*S*>3*R* after recrystallization). IR cm^{-1} (KBr) (3*S*+3*R* mixture). 1718 (C=O), 1036 (S→O). ^{1}H-NMR (270 MHz) δ 2.34 (3H, s, Me), 2.37 (3H, s, Me), 3.69 (2H, d, J=7.5, CH_2), 5.02 (1H, t, J=7.5, PhC<u>H</u>), 7.1—7.35 (14H, m, ArH), 7.55—7.65 (2H, m, ArH), 7.97 (1H, s, H-2), 8.35—8.4 (1H, m, ArH). ^{13}C-NMR (67.5 MHz) δ 19.9, 21.4, 42.2, 42.4, 117.2, 119.6 (2C), 124.5, 125.5 (2C), 126.1, 126.2, 126.3 (2C), 126.7, 126.8, 128.0 (2C), 128.7 (2C), 130.1 (2C), 131.0, 136.4, 136.7, 140.2, 140.8, 141.9, 142.0, 142.7, 169.5. EI-MS m/z 477 (M^+), 461, 239, 181. *Anal.* Calcd for $C_{31}H_{27}NO_2S$: C, 77.97; H, 5.70; N, 2.93. Found: C, 77.76; H, 5.54; N, 2.89.

Typical Procedure for Alcoholysis of Adduct To a solution of the crude mixture of **16ac′** and **17ac′** (30 mg, 0.06 mmol), obtained by the reaction of **7a** (≥98% ee), in dry THF (4 ml) cooled in an ice-bath was added NaOMe (1.0 ml of a 0.1 mol dm^{-3} solution in MeOH, 0.1 mmol) dropwise. After being stirred for 1 h at that temperature, the mixture was quenched with a saturated NH_4Cl solution and the aqueous layer was extracted with Et_2O (10 ml×3). The extracts were washed with brine, dried, and concentrated. The crude product was purified by column chromatography on silica using hexane–AcOEt (4 : 1→0 : 1) as eluent to give the esters **5c′** and *ent*-**5c′**[1] (12 mg, 78%, *ent*-**5c′**-enriched) and the sulfinyl indole **9** (12 mg, 75%, ≥98% ee). Chiral HPLC: Chiralcel OD-H, 254 nm, hexane–2-propanol: 100 : 1; 1.0 ml/min; *ent*-**5c′**: 14.1 min, **5c′**: 20.3 min.

1-[(*S*)-3-Phenyl-3-(*p*-tolyl)propanoyl]-3-[(S_s)-(*p*-tolylsulfinyl)]indole (17ad′) In a similar manner, the products **16ad′** and **17ad′** was obtained in 99% yield. Methanolysis of the crude mixture afforded **5d′** and *ent*-**5d′** (48 : 52, 4% ee, 79% yield) and **9** (84% yield, 99% ee). Chiral HPLC: Chiralcel OD-H, 254 nm, hexane–2-propanol: 100 : 1; 0.5 ml/min; **5d′**: 17.1 min, *ent*-**5d′**: 35.1 min.

17ad′: mp 147—148 °C (from Et_2O/hexane) (3*S*+3*R* mixture). $[\alpha]_D^{23}$ +2.7° (c=1.0, $CHCl_3$) for 98% ee (S_s>R_s), 11% de (3*R*>3*S* after recrystallization). IR cm^{-1} (KBr) (3*S*+3*R* mixture) 1723 (C=O), 1038 (S→O). ^{1}H-NMR (270 MHz) δ 2.29 (3H, s, Me), 2.37 (3H, s, Me), 3.70 (2H, d, J=7.3, CH_2), 4.79 (1H, t, J=7.3, PhC<u>H</u>), 7.35—7.5 (14H, m, ArH), 7.60 (2H, d, J=8.1, *p*-Tol), 7.99 (1H, s, ArH), 8.35—8.4 (1H, m, ArH). ^{13}C-NMR (67.5 MHz) δ 20.9, 21.4, 42.0, 46.0, 117.2, 119.5, 119.6, 124.4, 125.3, 125.5 (2C), 125.6, 126.3, 126.7, 127.5 (2C), 127.6 (2C), 128.7 (2C), 129.5 (2C), 130.1 (2C), 136.4, 136.7, 140.0, 140.2, 141.9, 143.3, 169.5. EI-MS m/z 477 (M^+), 461, 239, 181. *Anal.* Calcd for $C_{31}H_{27}NO_2S$: C, 77.97; H, 5.70; N, 2.93. Found: C, 77.76; H, 5.76; N, 2.98.

1-[(*R*)-3-(Phenyl)butanoyl]-3-[(S_s)-(*p*-tolylsulfinyl)]indole (17ba′) The reaction of **7b** with diphenylcuprate afforded the products **16ba′** and **17ba′** which were treated with sodium methoxide to give a mixture of *ent*-**5b′** and **5b′** (40.7 : 59.3, 19% ee, 90% yield) and **9** (91% yield, 99% ee). Chiral HPLC: Chiralcel OD-H, 254 nm, hexane–2-propanol: 100 : 1; 1.0 ml/min; *ent*-**5b′**: 13.3 min; **5b′**: 6.3 min.

17ba′: mp 53—55 °C (from Et_2O/hexane) (3*S*+3*R* mixture), $[\alpha]_D^{20}$ +7.1° (c=1.0, $CHCl_3$) for 99% ee (S_s>R_s), 2% de (3*R*>3*S*, after recrystallization). IR cm^{-1} (KBr) 1733 (C=O), 1037 (S→O). ^{1}H-NMR (270 MHz) δ 1.45 (3H, d, J=7.0, Me), 2.38 (3H, s, Me), 3.17 (1H, dd, J=16.1, 7.5, C(O)C<u>H</u>H), 3.29 (1H, dd, J=16.1, 6.2, C(O)CH<u>H</u>), 3.5—3.65 (1H, m, PhC<u>H</u>), 7.1—7.4 (10H, m, ArH), 7.61 (2H, d, J=8.1, *p*-Tol), 7.91 (1H, s, H-2), 8.43 (1H, s, ArH). ^{13}C-NMR (100 MHz) δ 21.4, 21.8, 36.0, 44.1, 117.1, 119.6, 124.3, 125.2, 125.3 (2C), 125.4, 126.2, 126.3, 126.7 (2C), 128.7 (3C), 130.0 (2C), 136.6, 140.1, 141.9, 145.1, 170.0. EI-MS m/z 401 (M^+), 385, 353, 239, 207, 105. *Anal.* Calcd for $C_{25}H_{23}NO_2S$: C, 74.79; H, 5.78; N, 3.49. Found: C, 74.70; H, 6.05; N, 3.14.

1-[(*R*)-3-(*o*-Tolyl)butanoyl]-3-[(S_s)-(*p*-tolylsulfinyl)]indole (17bc′) mp 139—141 °C (from Et_2O) (3*S*+3*R* mixture), $[\alpha]_D^{20}$ +0.75° (c=2.0, $CHCl_3$) for 99% ee (S_s>R_s), 33% de (3*R*>3*S*, after recrystallization). IR cm^{-1} (KBr) 1725 (C=O), 1035 (S→O). ^{1}H-NMR (270 MHz) δ 1.39 (3H, d, J=7.0, Me), 2.38 (3H, s, Me), 2.41 (3H, s, Me), 3.21 (1H, dd, J=16.5, 8.1, C<u>H</u>H), 3.28 (1H, dd, J=16.5, 5.9, CH<u>H</u>), 3.7—3.9 (1H, m, MeCH), 7.1—7.4 (9H, m, ArH), 7.61 (2H, d, J=8.4, ArH), 7.95 (1H, s, H-2), 8.43 (1H, d, J=8.8, ArH). ^{13}C-NMR (100 MHz) δ 19.5, 21.4, 21.5, 30.8, 43.4, 117.1, 119.6, 124.4, 125.0 (2C), 125.4 (2C), 126.3 (2C), 126.4, 126.5 (2C), 130.1 (2C), 130.7, 135.2, 136.6, 140.0, 141.9, 143.4, 170.1. EI-MS m/z 415 (M^+), 399, 239, 207, 119. *Anal.* Calcd for $C_{26}H_{25}NO_2S$: C, 75.16; H, 6.07; N 3.37. Found: C, 74.98; H, 6.05; N 3.36.

1-[(*R*)-3-(*p*-Tolyl)butanoyl]-3-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (17bd′) mp 124—126 °C (from Et$_2$O/light petroleum) (3*S*+3*R* mixture), $[\alpha]_D^{21}$ −11.5° (*c*=2.0, CHCl$_3$) for 99% ee (*S*$_s$>*R*$_s$), 51% de (3*R*>3*S* after recrystallization). IR cm^{-1} (KBr) 1740 (C=O), 1035 (S→O). ^{1}H-NMR (270 MHz) δ 1.42 (3H, d, *J*=7.0, Me), 2.32 (3H, s, Me), 2.37 (3H, s, Me), 3.14 (1H, dd, *J*=16.1, 7.5, CHH), 3.26 (1H, dd, *J*=17.1, 6.4, CHH), 3.4—3.6 (1H, m, MeCH), 7.10—7.35 (9H, m, ArH), 7.60 (2H, d, *J*=8.1, *p*-Tol), 7.90 (1H, s, H-2), 8.42 (1H, d, *J*=8.2, ArH). ^{13}C-NMR (100 MHz) δ 21.0, 21.4, 21.9, 35.6, 44.3, 117.1, 119.6, 124.4, 125.3 (2C), 125.4 (2C), 126.3, 126.6 (3C), 129.4 (2C), 130.1 (2C), 136.3, 136.7, 140.1, 141.9, 142.1, 170.1. EI-MS *m/z* 415 (M$^+$), 399, 239, 207, 119. EI-HR-MS Calcd for $C_{26}H_{25}NO_2S$: 415.1614. Found: 415.1606. *Anal.* Calcd for $C_{26}H_{25}NO_2S \cdot 1/3H_2O$: C, 74.14; H, 6.06; N, 3.33. Found: C, 74.10; H, 6.00; N 3.31.

1-Benzenesulfonyl-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (15) Butyllithium (2.3 ml of a 1.57 mol dm^{-3} solution in hexane, 3.42 mmol) was added slowly to an ice-cooled solution of diisopropylamine (0.48 ml, 3.42 mmol) in dry THF (15 ml) under an argon atmosphere. After being stirred at the same temperature for 0.5 h, 1-(benzenesulfonyl)indole[5] (800 mg, 3.11 mmol) in dry THF (20 ml) was added to the solution at −78 °C. After being stirred for 1 h, (*S*$_s$)-(−)-*l*-menthyl *p*-toluenesulfinate (1.1 g, 3.73 mmol) in dry THF (10 ml) was added. The reaction mixture was stirred at the same temperature overnight and quenched with saturated NH$_4$Cl (50 ml). The organic phase was separated and the aqueous layer was extracted with Et$_2$O (10 ml×3). The combined extracts were washed with saturated brine (10 ml), dried, and concentrated. The residue was purified by flash chromatography on silica with hexane–EtOAc (6 : 1) to give **15** (906 mg, 74%) as a solid: mp 175—176 °C (from EtOAc); $[\alpha]_D^{23}$ +32.8° (*c*=1.0, CHCl$_3$) for 99% ee (*S*$_s$>*R*$_s$). IR cm^{-1} (KBr) 1374, 1176 (NSO$_2$), 1055 (S→O). ^{1}H-NMR (270 MHz) δ 2.30 (3H, s, Me), 7.25—7.6 (9H, m, ArH), 7.75—7.85 (4H, m, ArH), 8.02 (1H, d, *J*=8.4, ArH). ^{13}C-NMR (100 MHz) δ 21.5, 114.1, 114.4, 122.1, 124.4, 126.4, 126.7 (2C), 127.0 (2C), 128.9, 129.3 (2C), 130.0 (2C), 134.4, 137.1, 138.5, 141.6, 142.5, 143.8. EI-MS *m/z* 395 (M$^+$), 379, 347, 238, 223, 206. *Anal.* Calcd for $C_{21}H_{17}NO_3S_2$: C, 63.79; H, 4.33; N, 3.54. Found: C, 63.70; H, 4.32; N, 3.43.

2-[(*S*$_s$)-(*p*-Tolylsulfinyl)]indole (14) Sulfoxide **14** was obtained in 99% yield from **15** (603 mg) in a manner similar to the procedure for **11**, except for the reaction time (overnight): mp 165—166 °C (from Et$_2$O); $[\alpha]_D^{23}$ +20.3° (*c*=2.1, CHCl$_3$) for 99% ee (*S*$_s$>*R*$_s$). IR cm^{-1} (KBr) 3569 (NH), 1029 (S→O). ^{1}H-NMR (270 MHz) δ 2.39 (3H, s, Me), 6.86 (1H, dd, *J*=2.1, 0.7, H-3), 7.1—7.2 (1H, m, ArH), 7.2—7.4 (2H, m, ArH), 7.29 (2H, d, *J*=8.1, *p*-Tol), 7.58 (2H, d, *J*=8.1, *p*-Tol), 7.55—7.7 (1H, m, ArH), 9.54 (1H, br s, NH). ^{13}C-NMR (100 MHz) δ 21.3, 106.6, 112.4, 120.6, 121.6, 124.5, 124.9 (2C), 126.9, 130.0 (2C), 136.4, 138.1, 140.0, 141.6. EI-MS *m/z* 255 (M$^+$), 239, 207. *Anal.* Calcd for $C_{15}H_{13}NOS$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.31; H, 5.08; N, 5.44. Enantiomeric excess of **14** was determined by chiral HPLC analysis. A racemic sample for analytical chiral HPLC was prepared in a similar manner to the procedure described earlier. Chiral HPLC: Chiralpak AS, 254 nm, hexane–2-propanol: 9 : 1; 1.0 ml/min; **14**: 43.0 min, *ent*-**14**: 48.9 min.

1-(*E*)-Cinnamoyl-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (8a) The cinnamoyl amide **8a** was obtained in 58% yield from **14** (386 mg, 98% ee) and (*E*)-cinnamoyl chloride (378 mg) in a manner similar to the procedure for **7a**, except for the reaction time (overnight): mp 121—123 °C (from Et$_2$O); $[\alpha]_D^{22}$ −145° (*c*=1.0, CHCl$_3$) for 98% ee (*S*$_s$>*R*$_s$). IR cm^{-1} (KBr) 1678 (C=O), 1049 (S→O). ^{1}H-NMR (270 MHz) δ 2.33 (3H, s, Me), 7.21 (2H, d, *J*=8.2, *p*-Tol), 7.25—7.5 (5H, m, ArH), 7.32 (1H, d, *J*=15.8, CH=), 7.55—7.75 (5H, m, ArH), 7.68 (2H, d, *J*=8.2, *p*-Tol), 7.83 (1H, d, *J*=15.8, CH=). ^{13}C-NMR (67.5 MHz) δ 21.7, 113.8, 114.8, 118.8, 122.9, 124.1, 126.2, 127.0 (2C), 128.9 (2C), 129.5 (2C), 129.6, 130.1 (2C), 131.6, 134.4, 137.6, 142.1, 142.4, 144.6, 147.9, 164.8. EI-MS *m/z* 385 (M$^+$), 369, 239, 207, 131, 103. *Anal.* Calcd for $C_{24}H_{19}NO_2S$: C, 74.79; H, 4.97; N, 3.63. Found: C, 74.40; H, 4.90; N, 3.54. The ee of **8a** was estimated as 98% as judged by that of **14**.

1-Crotonoyl-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (8b) Crotonamide **8b** was obtained in 68% yield from **14** (2.40 g, ≥98% ee) and crotonyl chloride (1.35 ml) in a manner similar to the procedure for **8a**, except for the reaction time (6.5 h): mp 132—133 °C (from AcOEt/hexane); geometrical purity 94%; $[\alpha]_D^{24}$ −58.2° (*c*=1.1, CHCl$_3$) for ≥98% ee (*S*$_s$>*R*$_s$). IR cm^{-1} (KBr) 1680 (C=O), 1045 (S→O). ^{1}H-NMR (270 MHz) δ 2.05 (3H, dd, *J*=7.0, 1.7, Me), 2.34 (3H, s, Me), 6.72 (1H, dq, *J*=15.2, 1.7, CH=), 7.1—7.4 (5H, m, ArH+CH=), 7.55—7.75 (5H, m, ArH). ^{13}C-NMR (100 MHz) δ 18.8, 21.4, 112.8, 114.4, 122.5, 123.5, 123.7, 125.6, 126.7 (2C), 129.5, 129.7 (2C), 136.9, 141.7, 142.4, 144.6, 148.3, 164.2. EI-MS *m/z* 323 (M$^+$), 307, 239, 207, 132, 69. *Anal.* Calcd for $C_{19}H_{17}NO_2S$: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.41; H, 5.32; N, 4.21. The ee of **8b** was estimated as ≥98% as judged by that of **14**.

Typical Procedure for Preparation of 18 and 19 from 8 (Table 2, Entry 3) To a sonicated suspension of Cu(I) (295 mg, 1.55 mmol) in dry THF (10 ml) cooled at −10 °C was added *p*-tolylmagnesium bromide (3.1 mmol, 31 ml of a 0.10 mol dm^{-3} solution in THF) dropwise. After 0.5 h, a solution of **8a** (200 mg, 0.52 mmol, 98% ee) in dry THF (10 ml) was added dropwise at −30 °C, and the yellow solution was stirred for 2 h at the same temperature. The reaction mixture was then quenched with a saturated NH$_4$Cl solution and the aqueous layer was extracted with Et$_2$O (30 ml×3). The combined extracts were washed with brine, dried, and concentrated. The crude product was purified by flash chromatography on silica using hexane–AcOEt (20 : 1→1 : 1) as eluent to give a mixture of **18ad′** and **19ad′** (230 mg, 94%). Since the diastereoisomers **18ad′** and **19ad′** were not adequately resolved in the ^{1}H-NMR spectrum, the product ratio (**18ad′**, **19ad′**) was determined by chiral HPLC analysis of the methyl esters (**5d′** and *ent*-**5d′**=92 : 8, 84% ee) by methanolysis. Chiral HPLC of the ester derived after recrystallization of the product mixture showed 89% ee.

1-[(*R*)-3-Phenyl-3-(*p*-tolyl)propanoyl]-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (18ad′) mp 174—177 °C (from AcOEt) (3*S*+3*R* mixture), $[\alpha]_D^{22}$ −25.0° (*c*=1.0, CHCl$_3$) for 98% ee (*S*$_s$>*R*$_s$), 91% de (3*R*>3*S* after recrystallization). IR cm^{-1} (KBr) 1694 (C=O), 1048 (S→O). ^{1}H-NMR (270 MHz) δ 2.31 (3H, s, Me), 2.33 (3H, s, Me), 3.68 (2H, d, *J*=7.1, CH$_2$), 4.71 (1H, t, *J*=7.1, PhCH), 7.0—7.75 (18H, m, ArH). ^{13}C-NMR (100 MHz) δ 21.0, 21.4, 43.6, 45.5, 113.0, 114.2, 122.7, 123.9, 125.9, 126.6, 126.7 (2C), 127.4 (2C), 127.6 (2C), 128.7, 129.3 (2C), 129.4, 129.6 (2C), 129.9, 136.0, 136.5, 140.0, 141.3, 142.5, 143.3, 145.5, 169.4. EI-MS *m/z* 477 (M$^+$), 461, 239, 207, 181. *Anal.* Calcd for $C_{31}H_{27}NO_2S$: C, 77.97; H, 5.70; N, 2.93. Found: C, 77.82; H, 5.64; N, 2.94.

1-[(*R*)-3-(Phenyl)butanoyl]-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (18ab′) The reaction of **8a** with diphenylcuprate afforded the product **18ab′** as the major diastereoisomer. mp 153—156 °C (from hexane/light petroleum) (3*S*+3*R* mixture), $[\alpha]_D^{22}$ +22.9° (*c*=0.6, CHCl$_3$) for 98% ee (*S*$_s$>*R*$_s$), 68% de (3*R*>3*S* after recrystallization). IR cm^{-1} (KBr) 1690 (C=O), 1051 (S→O). ^{1}H-NMR (270 MHz) δ 1.13 (3H, d, *J*=6.8, Me), 2.34 (3H, s, Me), 3.09 (1H, dd, *J*=16.5, 9.0, C(O)CHH), 3.27 (1H, dd, *J*=16.5, 4.7, C(O)CHH), 3.35—3.5 (1H, m, PhCH), 7.1—7.4 (8H, m, ArH), 7.5—7.7 (6H, m, ArH). ^{13}C-NMR (100 MHz) δ 21.2, 21.4, 35.4, 45.6, 113.2, 114.1, 122.7, 123.8, 125.8, 126.6, 126.7 (2C), 127.0 (2C), 128.7 (2C), 129.7 (2C), 129.8, 136.5, 141.7, 142.7, 145.2, 145.3, 170.0. EI-MS *m/z* 401 (M$^+$), 385, 239, 207, 105. *Anal.* Calcd for $C_{25}H_{23}NO_2S$: C, 74.79; H, 5.78; N, 3.49. Found: C, 74.53; H, 5.77; N, 3.38.

1-[(*S*)-3-(Phenyl)butanoyl]-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (19ba′) The reaction of **8b** with dimethylcuprate afforded the product **19ab′** as the major diastereoisomer. mp 163—165 °C (from Et$_2$O) (3*S*+3*R* mixture), $[\alpha]_D^{24}$ −35.7° (*c*=0.8, CHCl$_3$) for ≥99% ee (*S*$_s$>*R*$_s$), 90% de (3*S*>3*R* after recrystallization). IR cm^{-1} (KBr) 1685 (C=O), 1057 (S→O). ^{1}H-NMR (270 MHz) δ 1.26 (3H, d, *J*=6.8, Me), 2.32 (3H, s, Me), 3.21 (1H, dd, *J*=16.5, 8.3, C(O)CHH), 3.28 (1H, dd, *J*=16.5, 5.7, C(O)CHH), 3.43 (1H, ddq, *J*=8.3, 6.6, 5.7, CH), 7.1—7.4 (9H, m, ArH), 7.55—7.75 (5H, m, ArH). ^{13}C-NMR (100 MHz) δ 21.4, 21.7, 35.3, 45.5, 113.1, 114.2, 122.7, 123.8, 125.8, 126.5, 126.6 (2C), 126.8 (2C), 128.6 (2C), 129.6 (2C), 129.9, 136.5, 141.5, 142.6, 145.3, 145.5, 170.0. EI-MS *m/z* 401 (M$^+$), 385, 239, 207. *Anal.* Calcd for $C_{25}H_{23}NO_2S$: C, 74.79; H, 5.78; N, 3.49. Found: C, 74.55; H, 5.84; N, 3.37.

1-[(*S*)-3-(*p*-Tolyl)butanoyl]-2-[(*S*$_s$)-(*p*-tolylsulfinyl)]indole (18bd′) The reaction of **8b** with di-*p*-tolylcuprate afforded the product **18bd′** as the major diastereoisomer. mp 148—150 °C (from hexane/Et$_2$O) (3*S*+3*R* mixture); $[\alpha]_D^{23}$ −41.8° (*c*=0.7, CHCl$_3$) for >99% ee (*S*$_s$>*R*$_s$), 95% de (3*S*>3*R* after recrystallization). IR cm^{-1} (KBr) 1694 (C=O), 1057 (S→O). ^{1}H-NMR (270 MHz) δ 1.23 (3H, d, *J*=6.8, Me), 2.33 (3H×2, s, Me), 3.18 (1H, dd, *J*=16.3, 8.4, CHH), 3.22 (1H, dd, *J*=16.3, 5.5, CHH), 3.37 (1H, ddq, *J*=8.4, 6.8, 5.5, MeCH), 7.0—7.2 (6H, m, ArH), 7.3—7.4 (2H, m, ArH), 7.55—7.75 (5H, m, ArH). ^{13}C-NMR (100 MHz) δ 21.0, 21.4, 21.7, 34.9, 45.7, 113.0, 114.2, 122.6, 123.8, 125.8, 126.5 (2C), 126.8 (2C), 129.3 (2C), 129.6 (2C), 129.9, 136.1, 136.5, 141.4, 142.3, 142.7, 145.5, 170.0. EI-MS *m/z* 415 (M$^+$), 399, 239, 207. *Anal.* Calcd for $C_{26}H_{25}NO_2S$: C, 75.16; H, 6.07; N, 3.37. Found: C, 74.98; H, 6.09; N, 3.36.

Methanolysis of the crude product afforded the esters (**6d′** and *ent*-**6d′**, 92% yield) with recovery of the auxiliary **14** (94% yield, >99% ee). Methyl (*S*)-3-(*p*-Tolyl)butanoate (**6d′**): A colorless oil, bp 130—140 °C/9.3 hPa; $[\alpha]_D^{23}$ +29.5° (*c*=1.5, CHCl$_3$) for 87% ee. Chiral HPLC: Chiralpak AS-H, 254 nm, hexane–2-propanol: 800 : 1; 1.0 ml/min; **6d′**: 7.8 min, *ent*-**6d′**: 10.2 min. Chiral ester *ent*-**6d′** is a known compound; however, the optical rotation was not mentioned.[15]

1-[(*R*)-3-Phenyl-3-(*o*-tolyl)propanoyl]-2-[(S_s)-(*p*-tolylsulfinyl)]indole (18ac′) The reaction of **8a** with di-*o*-tolylcuprate afforded the product **18ac′** as the major diastereoisomer. mp 118—121 °C (from light petroleum/AcOEt) (3*S*+3*R* mixture). $[\alpha]_D^{22}$ −49.9° (*c*=1.0, $CHCl_3$) for 99% ee (S_s>R_s), 91% de (3*R*>3*S* after recrystallization). IR cm^{-1} (KBr) 1709 (C=O), 1041 (S→O). ^{1}H-NMR (270 MHz) δ 2.25 (3H, s, Me), 2.30 (3H, s, Me), 3.61 (1H, dd, *J*=17.1, 6.8, C(O)CHH), 3.71 (1H, dd, *J*=17.1, 6.8, C(O)CHH), 4.91 (1H, dd, *J*=7.8, 6.8, PhCH), 7.00 (2H, d, *J*=7.8, *p*-Tol), 7.0—7.7 (14H, m, ArH), 7.44 (2H, d, *J*=7.8, *p*-Tol). ^{13}C-NMR (100 MHz) δ 19.8, 21.4, 41.9, 43.9, 113.0, 114.1, 122.7, 123.9, 125.5, 125.9, 126.1, 126.4, 126.5 (2C), 126.6, 127.9 (2C), 128.7 (2C), 129.6 (2C), 129.9, 130.8, 136.4, 136.6, 140.5, 141.2, 142.3, 142.6, 145.5, 169.4. EI-MS *m*/*z* 477 (M^+), 461, 239, 207, 181. *Anal.* Calcd for $C_{31}H_{27}NO_2S$: C, 77.97; H, 5.70; N, 2.93. Found: C, 77.66; H, 5.99; N, 2.79.

1-[(*S*)-3-(*o*-Tolyl)butanoyl]-2-[(S_s)-(*p*-tolylsulfinyl)]indole (18bc′) mp 139—140 °C (from hexane/Et_2O); $[\alpha]_D^{24}$ −57.4° (*c*=2.0, $CHCl_3$) for >99% ee (S_s>R_s), >99% de (3*S*>3*R* after recrystallization). IR cm^{-1} (KBr) 1694 (C=O), 1054 (S→O). ^{1}H-NMR (270 MHz) δ 1.23 (3H, d, *J*=6.8, Me), 2.29 (3H, s, Me), 2.30 (3H, s, Me), 3.22 (2H, d, *J*=6.8, CH_2), 3.67 (1H, sextet, *J*=6.8, MeCH), 7.05—7.4 (8H, m, ArH), 7.5—7.75 (5H, m, ArH). ^{13}C-NMR (100 MHz) δ 19.4, 21.4, 21.5, 30.4, 45.0, 113.0, 114.1, 122.7, 123.8, 124.8, 125.8, 126.1, 126.4, 126.7 (2C), 129.6 (2C), 129.9, 130.6, 135.2, 136.5, 141.4, 142.5, 143.5, 145.5, 170.1. EI-MS *m*/*z* 415 (M^+), 399, 239, 207. *Anal.* Calcd for $C_{26}H_{25}NO_2S$: C, 75.16; H, 6.07; N, 3.37. Found: C, 75.00; H, 6.10; N, 3.29.

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