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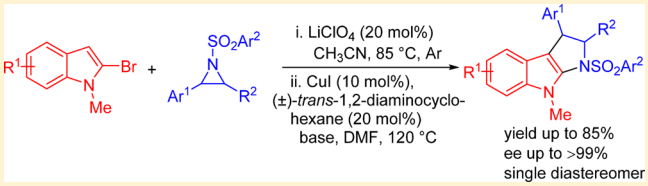
A Synthetic Route to Chiral Tetrahydropyrroloindoles via Ring Opening of Activated Aziridines with 2-Bromoindoles Followed by Copper-Catalyzed C−N Cyclization

Masthanvali Sayyad, Abhijit Mal, Imtiyaz Ahmad Wani, and Manas K. Ghorai*

Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

Supporting Information

ABSTRACT: A new synthetic route to nonracemic tetrahydropyrrolo[2,3-*b*]indoles has been developed via S_N2-type ring opening of enantiopure N-activated aziridines with 2-bromoindoles followed by copper-catalyzed C−N cyclization. A series of N-activated aziridines and 2-bromoindole derivatives with different substitution patterns were studied to afford the corresponding tetrahydropyrrolo[2,3-*b*]indoles in good yields and excellent ee (up to 99%). Highly substituted tetrahydropyrrolo[2,3-*b*]indole was synthesized as a single stereoisomer (de, ee >99%) from enantiopure *trans*-disubstituted aziridine.



INTRODUCTION

Pyrrolo[2,3-*b*]indole alkaloids are an important class of natural products[1] (Figure 1) exhibiting a broad range of biological

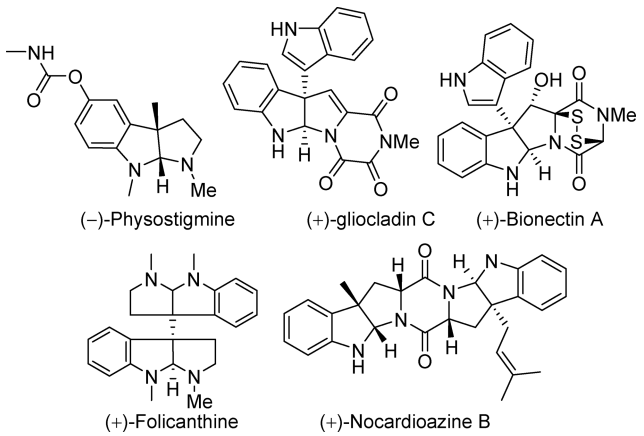


Figure 1. Representative pyrroloindoline natural products.

activities, e.g., anticholinesterase,[2] antibaterial,[3] and anticancer activities, etc.[4] Due to their pharmacological importance and structural complexity, a number of synthetic methodologies have been devoted toward the synthesis of chiral hexahydropyrrolo-[2,3-*b*]indoles.[5,6] Surprisingly, their tetrahydro-analogues, i.e., tetrahydropyrrolo[2,3-*b*]indoles have been less explored in the literature,[7] although they are useful intermediates for assembling various heterocyclic compounds.[8] In this context, Evano and co-workers have reported a new strategy for the synthesis of enantiopure tetrahydropyrroloindoles via copper-catalyzed C−N-cyclization of 2-iodotryptophan[7a] where the substrate scope is limited. Therefore, development of a simple and efficient route for the synthesis of nonracemic tetrahydropyrrolo[2,3-*b*]indoles with broader substrate scope is desired.

We envisioned that nonracemic tetrahydropyrrolo[2,3-*b*]-indoles could easily be synthesized utilizing the promising two step protocols viz. (i) the regio- and stereoselective ring opening of 2-aryl-*N*-sulfonylaziridines with 2-bromoindoles followed by (ii) copper-catalyzed C−N cyclization (Scheme 1). Aziridines

Scheme 1. Synthesis of Tetrahydropyrrolo[2,3-*b*]indole 4a

are useful building blocks for the synthesis of nitrogen-containing heterocyclic structures including natural products.[9,10] Over the years, we have been exploring and exploiting S_N2-type ring opening of enantiopure activated aziridines by a number of nucleophiles to provide nonracemic products with high ee.[11] In recent years copper-catalyzed amination has become a powerful tool in organic synthesis.[12] To date, there are few examples of Lewis acid-catalyzed ring-opening reactions of aziridines with indoles, however, an efficient regio- and enantioselective ring opening of 2-aryl-*N*-tosylaziridines with indoles are still limited.[13]

We have developed a highly efficient approach toward pyrroloindoles via regio- and stereoselective ring opening of 2-aryl-*N*-sulfonylaziridines with 2-bromoindoles in the presence of $LiClO_4$ as a Lewis acid followed by Cu-catalyzed C−N

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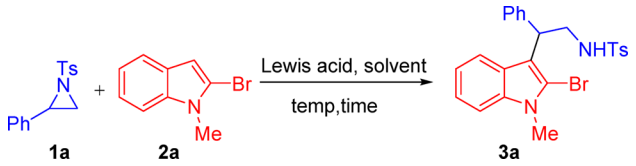
cyclization with high yields and enantiomeric excess. Herein, we discuss our results in detail.

RESULTS AND DISCUSSION

Our study began with the ring opening of 2-pheny-*N*-tosylaziridine **1a** with 2-bromoindole **2a** in the presence of 10 mol % $Cu(OTf)_2$ in CH_2Cl_2 for 30 min to afford the corresponding ring-opening product **3a** with moderate yield (52%). To improve the yield of the reaction, different Lewis acids and different solvents were screened (Table 1), and in all the

Table 1. Regioselective Ring Opening of 1a with 2-Bromoindole 2a under Different Conditions[a]



entry	Lewis acid (mol %)	solvent	temp	time (h)	yield **3a** (%)
1	$Cu(OTf)_2$ (10)	CH_2Cl_2	rt	0.15	42
2	$Sc(OTf)_3$ (10)	CH_2Cl_2	rt	0.15	32
3	$Zn(OTf)_2$ (10)	CH_2Cl_2	rt	1.5	20
4	$BF_3.OEt_2$ (10)	CH_2Cl_2	rt	0.15	45
5	$Yb(OTf)_3$ (10)	CH_2Cl_2	rt	1.5	32
6	$LiClO_4$ (10)	CH_3CN	rt	3.0	nr
7	$LiClO_4$ (10)	CH_3CN	85 °C	6.0	69
8	**$LiClO_4$ (20)**	**CH_3CN**	**85 °C**	**2.5**	**87**

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.1 mmol), solvent (0.2 mL).

cases there was no improvement of the yield of **3a**. For better results in terms of yields, next we explored weak Lewis acids such as $LiClO_4$[12gh,13f]. When the reaction mixture was heated at 85 °C for 6 h, the corresponding ring-opening product **3a** was isolated with 69% yield. Interestingly, with increased catalyst loading to 20 mol %, **3a** was obtained with excellent yield (87%) in shorter reaction time (Table 1).

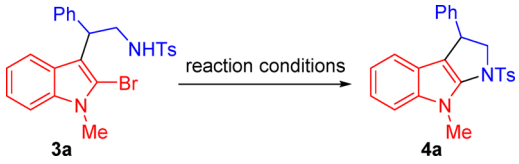
Next, we explored different copper-catalyzed C−N cyclization conditions to obtain the desired tetrahydropyrroloindole product **4a**, and the results are shown in Table 1. Initially, we used 10 mol % of CuI, 20 mol % of L-proline as the ligand and K_2CO_3 as the base in DMF solvent, and the desired product **4a** was obtained with moderate yield. Then, we studied different bases viz. NaH, Cs_2CO_3 and K_3PO_4 and various ligands viz. (±)-*trans*-1,2-diaminocyclohexane, glycine, and ethylene diamine. The best result was obtained with CuI as the catalyst, (±)-*trans*-1,2-diaminocyclohexane as the ligand and K_2CO_3 as the base in DMF solvent at 120 °C to produce **4a** in 85% yield (Table 2, entry 6).

To make our strategy simpler and practical as a synthetic methodology, a one-pot (stepwise) protocol for the synthesis of pyrroloindole **4a** through the ring opening of **1a** with **2a** followed by copper-catalyzed cyclization was explored (Scheme 1), and the expected product **4a** was obtained in 85% overall yield.

Next, to generalize this approach, the ring opening of various aziridines **1b-l** with substituted 2-bromoindoles **2a−c** followed by copper-catalyzed cyclization were studied (Scheme 2), and the results are shown in Table 3. The structure of **4j** was unambiguously confirmed by X-ray crystallographic analysis.[14]

To broaden the scope of our strategy, it was extended further for the synthesis of nonracemic pyrroloindoles. When

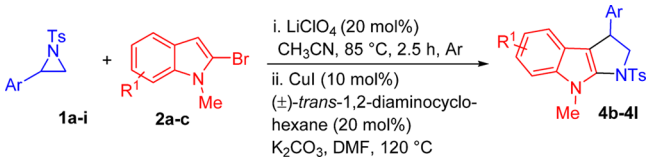
Table 2. Copper-Catalyzed Intramolecular C−N Cyclization of 3a



entry	reaction conditions[a]	yield (%)[a]
1	CuI, L-proline, NaH, DMF, 90, 12	47
2	CuI, L-proline, K_2CO_3, DMF, 90, 15	75
3	CuI, L-proline, Cs_2CO_3, DMF, 90, 15	62
4	CuI, L-proline, K_3PO_4, DMF, 90, 15	65
5	CuI, (±)-*trans*-1,2-diaminocyclohexane, K_2CO_3, DMF, 90, 8	80
6	**CuI, (±)-*trans*-1,2-diaminocyclohexane, K_2CO_3, DMF, 120, 3**	**85**
7	CuI, EDA, K_2CO_3, DMF, 120, 10	55
8	CuI, (±)-*trans*-1,2-diaminocyclohexane, K_2CO_3, PhMe, 120, 15	75
9	Copper powder, DMF, 120, 20	52
10	Copper powder, DMF, 120, 10	75

[a]Reaction conditions: **3a** (0.125 mmol), copper catalyst (10 mol %), ligand (20 mol %), base (1.2 equiv) and solvent (1.0 mL) under Ar. EDA = ethylenediamine.

Scheme 2. Synthesis of Tetrahydropyrrolo[2,3-*b*]indoles 4



enantiopure 2-phenyl-*N*-tosylaziridine (*R*)-**1a**[18a] was reacted with 2-bromoindole **2a** under the optimized condition, to our great pleasure the corresponding product (*R*)-**4a** was obtained with excellent yield (84%) and high ee (95%) (Scheme 3, entry 1, Table 4). Generalization of the protocol was made by studying the reaction with a number of enantiopure aziridines (*R*)-**1a,j−m**[18a] and indoles **2a−b**. In all the cases the corresponding nonracemic pyrroloindoles (*R*)-**4m−r** were obtained with good yields and excellent ee (up to 99%) as shown in Table 4.

Similar reaction of enantiopure (*S*)-2-(2-chlorophenyl)-1-tosylaziridine (*S*)-**1n** with **2a−b** under the same reaction conditions furnished the corresponding nonracemic products (*S*)-**4s−t** with good yield and high ee as shown in Scheme 4.

The synthetic significance of our strategy was further demonstrated by the synthesis of highly substituted pyrroloindole (2*S*,3*S*)-**4u** as a single stereoisomer via the ring-opening/cyclization of enantiopure *trans*-disubstituted aziridine (2*S*,3*S*)-**1o**[18b] with **2a** under optimized reaction conditions (Scheme 5).

Finally, with a view to demonstrating the broader substrate scope so that further synthetic manipulation could be made possible toward important functionalization of the products, the reaction was explored with a different class of aziridines, i.e., vinyl aziridine **1p**. Upon treatment with the nucleophile **2a**, the aziridine **1p** is exclusively attacked through its C-2 position by **2a**, and the corresponding product **4v** was obtained in good yield as the only product (Scheme 6). Next we explored our methodology using alkyl aziridines as the substrates. Under our reaction conditions, 2-alkylaziridines did not react with 2-bromoindoles probably because of (i) lesser reactivity of 2-alkylaziridines

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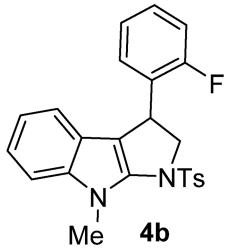
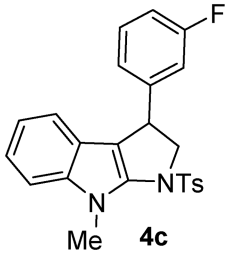
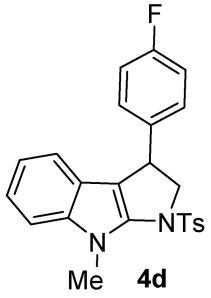
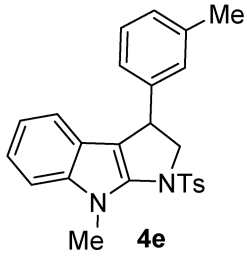
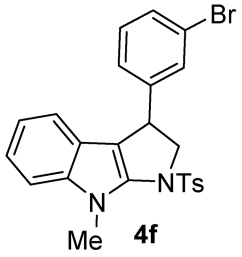
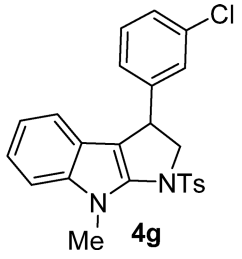
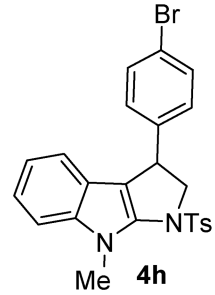
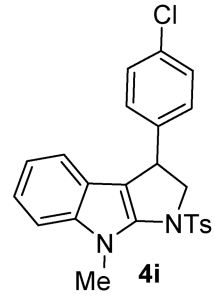
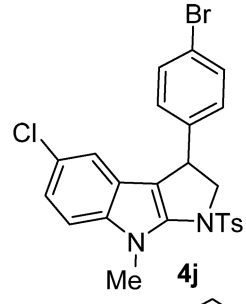
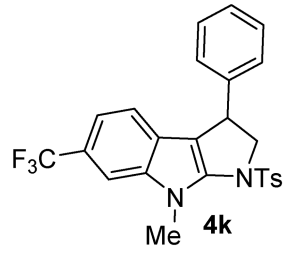
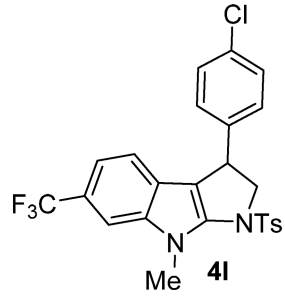
Table 3. Synthesis of Tetrahydropyrrolo[2,3-*b*]indoles[a] 4

entry	1	2	4	Time (h)	yield (%)
1	**1b**	**2a**	 **4b**	3	78
2	**1c**	**2a**	 **4c**	3	82
3	**1d**	**2a**	 **4d**	3	79
4	**1e**	**2a**	 **4e**	3.5	78
5	**1f**	**2a**	 **4f**	3	85
6	**1g**	**2a**	 **4g**	3.5	82
7	**1h**	**2a**	 **4h**	3.5	75
8	**1i**	**2a**	 **4i**	3	78
9	**1h**	**2b**	 **4j**	3.5	81
10	**1a**	**2c**	 **4k**	4	76
11	**1i**	**2c**	 **4l**	4	75

[a]All reactions were carried out with **1a–i** (0.1 mmol), **2a–c** (0.1 mmol), $LiClO_4$ (20 mol %) in acetonitrile (0.2 mL) under argon. CuI (10 mol %), (±)-*trans*-cyclohexane-1,2-diamine (20 mmol %), and K_2CO_3 (1.2 equiv) in DMF (1.0 mL) under argon for 3–4 h at 120 °C.

compared to 2-aryl- and 2-vinylaziridines and (ii) less nucleophilic nature of 2-bromoindoles.

A possible mechanism for the formation of chiral tetrahydropyrroloindoles is described in Figure 2. S_N2-type ring

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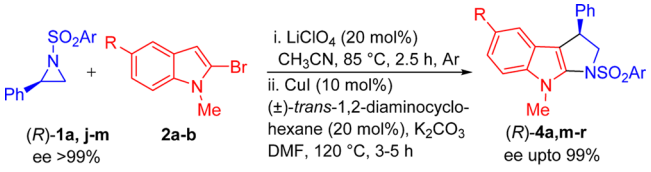
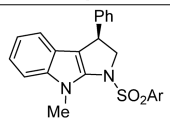
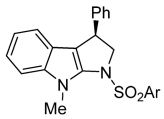
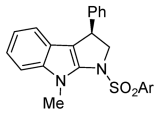
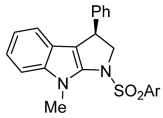
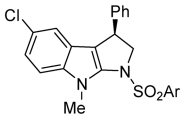
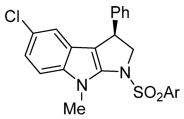
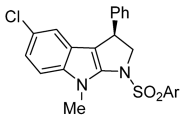
Scheme 3. Synthesis of Chiral Tetrahydropyrrolo[2,3-*b*]indoles 4



(*R*)-**1a, j-m** ee >99% **2a-b** (*R*)-**4a,m-r** ee upto 99%

1a: Ar = 4-MeC$_6$H$_4$; **1j**: Ar = Ph; **1k**: Ar = 2-CF$_3$C$_6$H$_4$; **1l**: Ar =4-OMeC$_6$H$_4$; **1m**: Ar = 4-NO$_2$C$_6$H$_4$; **2a**: R = H; **2b**: R = 5Cl

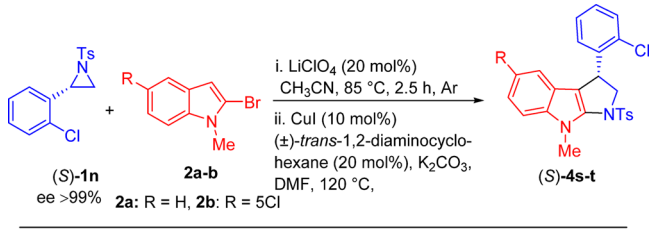
Table 4. Synthesis of Chiral Tetrahydropyrrolo[2,3-*b*]indoles 4

entry	1	2	4	time (h)	yield (%)	ee (%)[b]
1	**1a**	**2a**	 **4a**: Ar = 4-MeC$_6$H$_4$	3	84	95
2	**1j**	**2a**	 **4m**: Ar = C$_6$H$_5$	3.5	82	99
3	**1k**	**2a**	 **4n**: Ar = 2-CF$_3$C$_6$H$_4$	3.5	76	98
4	**1l**	**2a**	 **4o**: Ar = 4-OMeC$_6$H$_4$	3	82	95
5	**1j**	**2b**	 **4p**: Ar = C$_6$H$_5$	3.5	82	96
6	**1a**	**2b**	 **4q**: Ar = 4-MeC$_6$H$_4$	3.5	81	95
7	**1m**	**2b**	 **4r**: Ar = 4-NO$_2$C$_6$H$_4$	4	84	94

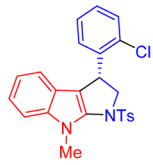
[a]All reactions were carried out with **1a,j–m** (0.1 mmol), **2a–b** (0.1 mmol), LiClO$_4$ (20 mol %) in acetonitrile (0.2 mL) under argon. CuI (10 mol %), (±)-*trans*-cyclohexane-1,2-diamine (20 mmol %), and K$_2$CO$_3$ (1.2 equiv) in DMF (1.0 mL) under argon for 3–4 h at 120 °C. [b]ee determined by chiral HPLC (see the Supporting Information for details).

opening of chiral aziridines **1** with 2-bromoindoles **2** via Friedel–Crafts alkylation at the C3-position of 2-bromoindoles gives ring-opening products **3** which undergo copper catalyzed C–N cyclization to produce the chiral tetrahydropyrroloindoles **4**.

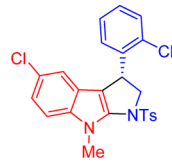
Scheme 4. Synthesis of Chiral Tetrahydropyrrolo[2,3-*b*]indoles from (*S*)-2-(2-Chlorophenyl)-1-tosylaziridine 4



(*S*)-**1n** ee >99% **2a-b** **2a**: R = H, **2b**: R = 5Cl (*S*)-**4s-t**



(*S*)-**4s**, 78%, ee 95%, 3.5 h



(*S*)-**4t**, 76%, ee 94%, 4 h

CONCLUSION

In summary, we have developed a simple route for the synthesis of nonracemic tetrahydropyrroloindoles via S$_N$2-type ring opening of enantiopure *N*-sulfonylaziridines with 2-bromoindoles followed by copper-catalyzed C–N cyclization in good to excellent yields (up to 85%) with excellent ee (up to 99%). Applying our protocol, highly substituted chiral tetrahydropyrroloindole could be synthesized as a single optical isomer (de, ee >99%) from the corresponding *trans*-disubstituted aziridine. The reaction works well with vinyl aziridine paving the way for further functionalization of the products.

EXPERIMENTAL SECTION

General Experimental. Analytical thin-layer chromatography (TLC) was carried out using silica gel 60 F$_{254}$ precoated plates. Visualization was accomplished with UV lamp or I$_2$ stain. Silica gel 230–400 mesh size was used for column chromatography using the combination of ethyl acetate and petroleum ether as an eluent. Unless noted, all reactions were carried out in oven-dried glassware under an atmosphere of nitrogen using anhydrous solvents. Where appropriate, solvents and all reagents were purified prior to use following the guidelines of Perrin and Armarego[15] and Vogel.[16] 2-aryl-1-tosylaziridines were prepared from different styrene derivatives following a reported procedure.[17] Chiral 2-phenyl-1-tosylaziridine,[18a] chiral 2-(2-chlorophenyl)-1-tosylaziridine,[18a] and trans-disubstituted aziridine[18b] were prepared from corresponding amino alcohol following a reported procedure. All 2-bromo indoles were prepared from following reported method.[19] All commercial reagents were used as received without prior purification unless mentioned. IR spectra were recorded in potassium bromide (KBr) pellet. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 400 and 500 MHz. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethyl silane (δ 0.00). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), double doublet (dd), triplet (t), quartet (q), or multiplet (m). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 100 and 125 MHz. Mass spectra (MS) were obtained using FAB and ESI mass spectrometer (TOF). Melting point was determined using a hot stage apparatus and is reported as uncorrected. Enantiomeric ratios (er) were determined by HPLC using chiralpak IA chiralcel OD-H and Cellulose 2 analytical column (detection at 254 nm). Optical rotations were measured using a 6 mL cell with a 1.0 dm path length and are reported as $[\alpha]_D^{25}$ (*c* in gm per 100 mL solvent) at 25 °C.

Experimental Procedure for the Synthesis of Starting Materials 2. 2-bromoindole substrates were prepared from according to the literature.[19]

*2-Bromo-1-methyl-1H-indole (**2a**).* Mp 80–82 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.75 (s, 3H), 6.58 (s, 1H), 7.10 (td, *J* = 8.0, 1.1 Hz, 1H),

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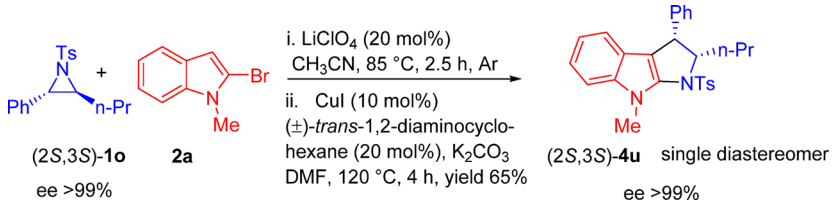
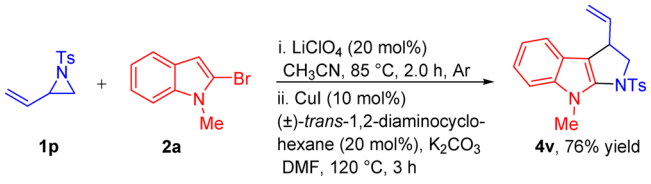
Scheme 5. Synthesis of Highly Substituted Tetrahydropyrrolo[2,3-*b*]indole 4u from Chiral *trans*-Disubstituted Aziridine 1o



Scheme 6. Synthesis of Vinyl-Substituted Tetrahydropyrrolo[2,3-*b*]indole 4v



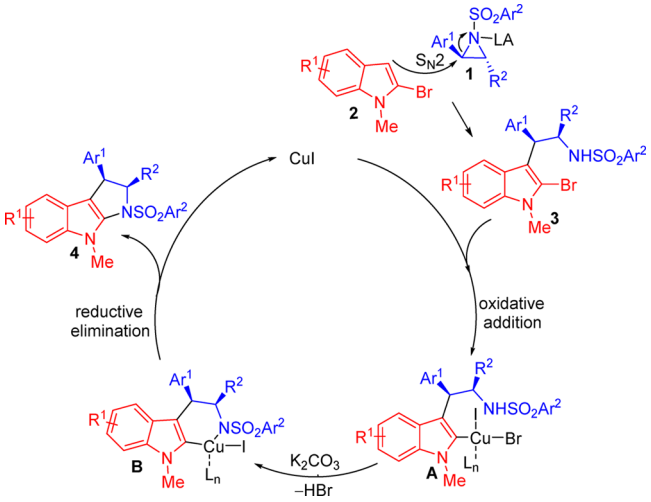


Figure 2. Possible reaction pathway.

7.20 (td, J = 7.1, 1.1 Hz, 1H), 7.26 (t, J = 8.2 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 31.4, 103.8, 109.5, 113.8, 119.8, 120.2, 121.8, 128.0, 137.0; GCMS (EI) calcd for C_9H_8BrN $(M + H)^+$ 208.9840, found 208.9841.

*2-Bromo-5-chloro-1-methyl-1H-indole (**2b**).* Mp 125−127 °C; IR ν_{max} (KBr, cm^{-1}) 2921, 2851, 1644, 1494, 1461, 1439, 1336, 1325, 1266, 1228, 1101, 1066, 981, 914, 873, 783, 738; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 6.51 (s, 1H), 7.14 (dd, J = 8.6, 1.7 Hz, 1H), 7.17 (d, J = 9.2 Hz, 1H), 7.48 (d, J = 1.7 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 31.6, 103.5, 110.5, 115.2, 119.2, 122.1, 126.0, 128.8, 135.5; MS (EI) calcd for C_9H_7BrClN $(M)^+$ 242.9450, found 242.9451.

*2-Bromo-1-methyl-6-(trifluoromethyl)-1H-indole (**2c**).* Mp 110−112 °C; IR ν_{max} (KBr, cm^{-1}) 2928, 2854, 1727, 1624, 1492, 1464, 1421, 1350, 1336, 1313, 1289, 1234, 1164, 1106, 923, 863, 819, 772, 738, 721, 636; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 3H), 6.64 (s, 1H), 7.33 (d, J = 8.6 Hz, 1H), 7.55 (s, 1H), 7.59 (d, J = 8.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 31.6, 104.3, 107.0, 107.1, 116.9, 120.1, 125.0 (q, $1J_{C-F}$ = 271.1 Hz), 130.3, 136.0; GCMS (EI) calcd for $C_{10}H_7BrF_3N$ $(M)^+$ 276.9714, found 276.9716.

Method A: General Procedure for the $LiClO_4$-Catalyzed Ring Opening of Aziridines. In a dry 5.0 mL two-neck round-bottom flask under argon were added aziridine **1a** (54.7 mg, 0.200 mmol), 2-bromoindole **2a** (55.4 mg, 0.200 mmol), anhydrous $LiClO_4$ (4.3 mg, 0.04 mmol), and CH_3CN (0.2 mL). Reaction mixture was stirred at 85 °C for 2.5 h. The reaction mixture was quenched with H_2O. The aqueous layer was extracted with ethyl acetate (3 × 10.0 mL) and dried over anhydrous Na_2SO_4. The crude product was purified by flash column chromatography on silica gel (230−400 mesh) using 15% ethyl acetate in petroleum ether to provide the pure product as thick liquid.

Method B: General Procedure for Cu-Catalyzed C−N Cyclization. A corresponding ring-opening product *N*-(2-(2-bromo-1-methyl-1H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide **3a** (69 mg, 0.125 mmol), CuI (2.4 mg, 10 mol %), and (±)-*trans*-1,2-diaminocyclohexane (2.8 mg, 20 mol %), K_2CO_3 (34.5 mg 1.2 equiv) were dissolved in dry DMF in 1.0 mL. The reaction mixture was heated at 120 °C for the appropriate time, and the reaction was monitored by TLC. It was cooled to room temperature, poured into water, and extracted with ethyl acetate (3 × 10 mL). The combined organic extract was washed with H_2O (3 × 10 mL) and brine (15 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to give crude product, which was purified by flash column chromatography on silica gel (230−400 mesh) using ethyl acetate in petroleum ether to afford the pure product as thick liquid.

Method C: General Procedure for a One-Pot (Stepwise) Protocol for the Synthesis of Tetrahydropyrroloindoles. To solution of aziridine **1a** (54.7 mg, 0.200 mmol), 2-bromoindole **2a** (55.4 mg, 0.200 mmol) and anhydrous $LiClO_4$ (4.3 mg, 0.04 mmol) in CH_3CN (0.2 mL) were added. The reaction mixture was then stirred at 85 °C for the appropriate time for complete consumption of the aziridine **1a**. Subsequently, CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), K_2CO_3 (1.2 equiv), and DMF (2.0 mL) were added to the reaction mixture. Then the reaction mixture was heated for at 120 °C for appropriate time. After complete consumption of the ring-opening product (monitored by TLC), the reaction was quenched by addition of saturated aqueous NH_4Cl (1.0 mL) solution. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (3 × 10.0 mL). The combined extracts were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the crude reaction mixture was purified by flash column chromatography on silica gel (230−400 mesh) using ethyl acetate in petroleum ether as the eluent to afford the pure product as thick liquid.

*N-(2-(2-Bromo-1-methyl-1H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (**3a**).* The general method A described above was followed when **1a** (54.6 mg, 0.200 mmol) reacted with 2-bromoindole **2a** (42.0 mg, 0.200 mmol) at 85 °C for 2.5 h to afford **3a** (84.2 mg, 0.174 mmol) as a thick liquid in 87% yield: R_f 0.23 (40% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3281, 2924, 2853, 1598, 1494, 1465, 1327, 1160, 1093, 813, 699, 663, 550; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.37−3.71 (m, 1H), 3.75 (s, 3H), 3.80−3.86 (m, 1H), 4.34 (bs, 1H), 4.48 (dd, J = 10.3, 6.3 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 7.12−7.23 (m, 7H), 7.27 (t, J = 8.6 Hz, 2H), 7.32 (d, J = 6.3 Hz, 1H), 7.60 (d, J = 6.0 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.6, 31.8, 43.5, 45.9, 109.8, 112.2, 115.4, 118.7, 120.2, 122.2, 125.8, 126.9, 127.2, 127.7, 128.7, 129.7, 136.7, 137.3, 140.5, 143.4 ; HRMS (ESI) calcd for $C_{24}H_{22}BrN_2O_2S$ $(M - H)^-$ 481.0585, found 481.0579.

*8-Methyl-3-phenyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4a**).* The general method B described above was followed when **3a** (48.3 mg, 0.100 mmol) reacted with CuI (1.2 mg, 10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4a** (34.2 mg, 0.085 mmol) as a thick liquid in 85% yield: R_f 0.29 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2925, 1597, 1565, 1482, 1454, 1382, 1354, 1222, 1166, 1088, 991, 877, 808, 741, 701, 671, 588, 575, 549,529; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.86 (t, J = 7.8 Hz, 1H), 3.99 (s, 1H), 4.12 (dd, J = 12.6, 7.6 Hz, 1H), 4.68 (dd, J = 12.6, 8.2 Hz, 1H), 6.85 (dd, J = 7.1, 1.6 Hz, 2H), 7.01−7.04 (m, 4H), 7.09−7.14 (m, 3H), 7.20 (td, J = 6.2, 2.1

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Hz, 1H), 7.33−7.39 (m, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 21.7, 32.1, 42.5, 67.5, 110.4, 110.5, 118.7, 120.4, 121.2, 122.9, 126.6, 127.3, 128.0, 128.5, 129.7, 132.2, 140.6, 141.8, 143.8, 144.6; HRMS (ESI) calcd for $C_{24}H_{23}N_2O_2S$ $(M + H)^+$ 403.1480, found 403.1486.

*8-Methyl-3-phenyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4a**).* The general method C described above was followed when **1a** (27.3 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans* 1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4a** (34.2 mg, 0.085 mmol) as a thick liquid in 85% yield.

*3-(2-Fluorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4b**).* The general method C described above was followed when **1b** (29.1 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans* 1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4b** (32.8 mg, 0.078 mmol) as a white solid in 78% yield: mp 178−180 °C; R_f 0.26 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2925, 1616, 1566, 1485, 1455, 1420, 1384, 1356, 1218, 1185, 1167, 1121, 1034, 994, 877, 812, 759, 741, 721, 680, 650, 589, 545; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.28 (s, 3H), 4.00 (s, 3H), 4.13−4.18 (m, 2H), 4.81 (dd, J = 14.3, 10.3 Hz, 1H), 6.61 (t, J = 7.5 Hz, 1H), 6.72 (t, J = 7.5 Hz, 1H), 6.93−6.97 (m, 3H), 7.06−7.13 (m, 3H), 7.24 (td, J = 8.0, 2.9 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.2, 36.1, 65.9, 108.2, 110.6, 114.8, 115.0, 118.6, 120.6, 121.3, 123.0, 124.1, 127.9, 128.0, 128.6, 128.7, 129.0, 129.1, 129.7, 131.8, 140.7, 144.0, 144.7, 159.5, 160.5 (d, $1J_{C-F}$ = 246.3 Hz); HRMS (ESI) calcd for $C_{24}H_{22}FN_2O_2S$ $(M + H)^+$ 421.1386, found 421.1380.

*3-(3-Fluorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4c**).* The general method C described above was followed when **1c** (29.1 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4c** (34.5 mg, 0.082 mmol) as a thick liquid in 82% yield: R_f 0.21 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2925, 1615, 1591, 1482, 1448, 1355, 1268, 1168, 1088, 805, 743, 717, 680, 585, 548; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.95 (dd, J = 8.6, 6.3 Hz, 1H), 4.00 (s, 3H), 4.15 (dd, J = 12.6, 6.3 Hz, 1H), 4.74 (dd, J = 12.6, 8.6 Hz, 1H), 6.37 (dt J = 10.3, 1.7 Hz, 1H), 6.69 (d, J = 7.5 Hz, 1H), 6.81 (td, J = 8.0, 2.3 Hz, 1H), 7.00 (d, J = 8.0 Hz, 2H), 7.06−7.05 (m, 2H), 7.08−7.12 (m, 1H), 7.21−7.24 (m, 1H), 7.31 (d, J = 8.6 Hz, 2H), 7.39 (d, J = 8.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.1, 41.9, 67.1, 109.3, 110.6, 113.3, 113.5, 114.1, 114.2, 118.5, 120.6, 121.4, 122.9, 122.9, 122.9, 129.0, 129.9, 130.0, 131.8, 140.7, 144.0, 144.9, 145.0, 145.1, 162.9 (d, $1J_{C-F}$ = 245.1 Hz); HRMS (ESI) calcd for $C_{24}H_{22}FN_2O_2S$ $(M + H)^+$ 421.1386, found 421.1381.

*3-(4-Fluorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4d**).* The general method C described above was followed when **1d** (29.1 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4d** (33.2 mg, 0.079 mmol) as a thick liquid in 79% yield: R_f 0.23 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2928, 1704, 1598, 1565, 1508, 1482, 1458, 1381, 1354, 1220, 1166, 1089, 1013, 881, 833, 815, 803, 744, 728, 675, 587, 548; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.88 (t, J = 7.9 Hz, 1H), 3.99 (s, 3H), 4.10 (dd, J = 12.8, 6.7 Hz, 1H), 4.70 (dd, J = 12.8, 7.9 Hz, 1H), 6.79 (d, J = 1.8 Hz, 2H), 6.80 (s, 2H), 7.00−7.06 (m, 4H), 7.25 (td, J = 8.6, 1.2 Hz, 1H), 7.34 (d, J = 8.6 Hz, 2H), 7.39 (d, J = 8.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.1, 41.7, 67.5, 110.0, 110.6, 115.2, 115.4, 118.5, 120.5, 121.3, 122.8, 128.0, 128.7, 129.7, 132.2, 137.7, 140.7, 143.8, 144.8, 161.6 (d, $1J_{C-F}$ = 245.1 Hz); HRMS (ESI) calcd for $C_{24}H_{22}FN_2O_2S$ $(M + H)^+$ 421.1386, found 421.1380.

*8-Methyl-3-m-tolyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4e**).* The general method C described above was followed when **1e** (28.6 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford **4e** (33.2 mg, 0.078 mmol) as a thick liquid in 78% yield: R_f 0.26 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3049, 2924, 2870, 1607, 1597, 1566, 1482, 1458, 1420, 1381, 1355, 1305, 1265, 1222, 1185, 1167, 1130, 1119, 1089, 1013, 990, 805, 781, 743, 728, 717, 703, 672, 549; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.33 (s, 3H), 3.81 (t, J = 8.2 Hz, 1H), 3.99 (s, 3H), 4.12 (dd, J = 12.7, 7.7 Hz, 1H), 4.66 (dd, J = 12.7, 8.2 Hz, 1H), 6.66 (d, J = 7.7 Hz, 1H), 6.71 (s, 1H), 6.95 (d, J = 7.7 Hz, 1H), 6.99−7.06 (m, 5H), 7.19−7.23 (m, 1H), 7.35−7.39 (m, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 21.5, 21.7, 32.0, 42.5, 67.5, 110.5, 110.6, 118.8, 120.4, 121.1, 122.9, 124.4, 127.4, 128.1, 128.5, 129.7, 132.3, 138.1, 140.6, 141.7, 143.8, 144.6; HRMS (ESI) calcd for $C_{25}H_{25}N_2O_2S$ $(M + H)^+$ 417.1637, found 417.1630.

*3-(3-Bromophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4f**).* The general method C described above was followed when **1f** (35.2 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4f** (40.9 mg, 0.085 mmol) as a thick liquid in 85% yield: R_f 0.23 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2921, 2850, 1595, 1564, 1458, 1381, 1355, 1185, 1167, 1120, 996, 810, 777, 743, 719, 682, 584, 549; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.89 (t, J = 8.0 Hz, 1H), 4.00 (s, 3H), 4.14 (dd, J = 12.6, 6.3 Hz, 1H), 4.72 (dd, J = 12.6, 8.0 Hz, 1H), 6.81 (d, J = 7.5 Hz, 1H), 6.98 (t, J = 8.0 Hz, 2H), 7.02−7.08 (m, 4H), 7.21−7.27 (m, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.8, 32.1, 42.0, 67.0, 109.3, 110.6, 118.5, 120.7, 121.4, 122.7, 122.8, 125.9, 128.0, 129.6, 129.7, 130.1, 130.4, 132.0, 140.7, 144.0, 144.5, 144.8; HRMS (ESI) calcd for $C_{24}H_{22}BrN_2O_2S$ $(M + H)^+$ 481.0585, found 481.0580.

*3-(3-Chlorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4g**).* The general method C described above was followed when **1g** (30.8 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford **4g** (35.8 mg, 0.082 mmol) as a thick liquid in 82% yield: R_f 0.24 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 2854, 1731, 1616, 1596, 1565, 1481, 1457, 1381, 1355, 1210, 1185, 1167, 1120, 1088, 997, 864, 811, 781, 743, 719, 690, 672, 650, 585, 549; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.91 (dd, J = 8.6, 6.9 Hz, 1H), 4.00 (s, 3H), 4.15 (dd, J = 12.6, 6.3 Hz, 1H), 4.72 (dd, J = 12.6, 8.6 Hz, 1H), 6.76−6.78 (m, 2H), 7.01−7.03 (m, 3H), 7.06 (d, J = 8.0 Hz, 2H), 7.09 (t, J = 8.0 Hz, 1H), 7.22−7.25 (m, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.8, 32.1, 42.0, 67.0, 109.3, 110.6, 118.5, 120.7, 121.4, 122.8, 125.4, 126.7, 127.5, 128.0, 129.7, 129.8, 131.9, 134.3, 140.7, 140.7, 144.0, 144.3, 144.9; HRMS (ESI) calcd for $C_{24}H_{22}ClN_2O_2S$ $(M + H)^+$ 437.1091, found 437.1094.

*3-(4-Bromophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4h**).* The general method C described above was followed when **1h** (35.2 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford **4h** (36.1 mg, 0.075 mmol) as a thick liquid in 75% yield: R_f 0.23 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 1596, 1564, 1485, 1457, 1421, 1380, 1355, 1211, 1166, 1120, 1089, 1072, 1010, 877, 801, 743, 721, 704, 671, 655, 586, 510; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.89 (dd, J = 8.2, 6.4 Hz, 1H), 3.99 (s, 3H), 4.13 (dd, J = 12.6, 6.2 Hz, 1H), 4.72 (dd, J = 12.6, 8.5 Hz, 1H), 6.69 (d, J = 8.2 Hz, 2H), 6.98−7.07 (m, 4H), 7.18−7.23 (m, 3H), 7.29 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.8, 32.1, 41.7, 67.2, 109.4, 110.7, 118.5, 120.3, 120.6, 121.4, 122.9, 128.0, 129.0, 131.5, 132.0, 140.7, 141.3, 143.9, 145.0; HRMS (ESI) calcd for $C_{24}H_{22}BrN_2O_2S$ $(M + H)^+$ 481.0585, found 481.0586.

*3-(4-Chlorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo-[2,3-b]indole (**4i**).* The general method C described above was followed when **1i** (30.8 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3

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(16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4i** (34.1 mg, 0.078 mmol) as a white solid in 78% yield: mp 198−200 °C; R_f 0.23 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2925, 1616, 1596, 1564, 1491, 1457, 1421, 1381, 1355, 1210, 1166, 1120, 1089, 1014, 994, 878, 802, 772, 743, 722, 704, 687, 672, 658, 586, 548; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.91 (t, J = 8.0 Hz, 1H), 3.99 (s, 3H), 4.13 (dd, J = 12.6, 6.3 Hz, 1H), 4.72 (dd, J = 12.6, 8.0 Hz, 1H), 6.75 (d, J = 8.0 Hz, 2H), 6.99−7.03 (m, 3H), 7.0−7.07 (m, 3H), 7.21−7.25 (m, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.1, 41.7, 67.3, 109.6, 110.6, 118.5, 120.6, 121.4, 122.8, 128.0, 128.6, 129.7, 132.0, 132.3, 140.6, 140.7, 143.9, 144.9; HRMS (ESI) calcd for $C_{24}H_{22}ClN_2O_2S$ $(M + H)^+$ 437.1091, found 437.1099.

*3-(4-Bromophenyl)-5-chloro-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4j**).* The general method C described above was followed when **1h** (35.2 mg, 0.100 mmol) reacted with 2-bromoindole **2b** (24.4 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford **4j** (41.8 mg, 0.081 mmol) as a white solid in 81% yield: mp 160−162 °C; R_f 0.21 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 1730, 1488, 1460, 1356, 1166, 1010, 889, 802, 669, 585, 549; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.84 (dd, J = 8.6, 6.9 Hz, 1H), 3.97 (s, 3H), 4.10 (dd, J = 12.6, 6.3 Hz, 1H), 4.70 (dd, J = 13.2, 8.6 Hz, 1H), 6.66 (d, J = 8.6 Hz, 2H), 6.96 (d, J = 1.7 Hz, 1H), 7.02 (d, J = 8.0 Hz, 2H), 7.15 (dd, J = 9.2, 2.3 Hz, 1H), 7.22−7.23 (m, 2H), 7.27−7.30 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.3, 41.7, 67.2, 109.1, 111.6, 117.8, 120.6, 121.6, 123.7, 126.5, 127.9, 128.8, 129.7, 131.7, 132.0, 139.0, 140.8, 145.0, 145.1; HRMS (ESI) calcd for $C_{24}H_{21}BrClN_2O_2S$ $(M + H)^+$ 515.0196, found 515.0196.

*8-Methyl-3-phenyl-1-tosyl-6-(trifluoromethyl)-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4k**).* The general method C described above was followed when **1a** (27.3 mg, 0.100 mmol) reacted with 2-bromoindole **2c** (27.8 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 4 h to afford **4k** (36.7 mg, 0.076 mmol) as a thick liquid in 76% yield: R_f 0.26 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2925, 2854, 1737, 1627, 1597, 15600, 1455, 1359, 1332, 1223, 1167, 1140, 1113, 1089, 1058, 993, 890, 862, 701; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.90 (t, J = 8.0 Hz, 1H), 4.05 (s, 3H), 4.15 (dd, J = 12.6, 7.5 Hz, 1H), 4.72 (dd, J = 12.6, 8.6 Hz, 1H), 6.82−6.84 (m, 2H), 7.04−7.07 (m, 3H), 7.12−7.16 (m, 3H), 7.25 (s, 1H), 7.36 (d, J = 8.6 Hz, 2H), 7.64 (s, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.3, 42.4, 67.6, 108.0, 110.6, 117.3, 118.7, 124.7 (q, $1J_{C-F}$ = 271.1 Hz), 125.1, 126.8, 127.2, 128.0, 128.7, 129.8, 132.2, 139.5, 141.3, 145.0, 146.1; HRMS (ESI) calcd for $C_{25}H_{22}F_3N_2O_2S$ $(M + H)^+$ 471.1354, found 471.1357.

*3-(4-Chlorophenyl)-8-methyl-1-tosyl-6-(trifluoromethyl)-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4l**).* The general method C described above was followed when **1i** (30.8 mg, 0.100 mmol) reacted with 2-bromoindole **2c** (27.8 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 4 h to afford **4l** (37.9 mg, 0.075 mmol) as a white solid in 75% yield: R_f 0.23 (10% ethyl acetate in petroleum ether); mp 170−172 °C; IR ν_{max} (KBr, cm^{-1}) 2948, 1627, 1596, 1559, 1491, 1460, 1359, 1334, 1283, 1262, 1167, 1140, 1113, 1058, 1014, 891, 863, 811, 758, 731, 689, 659, 586; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.36 (s, 3H), 3.94 (dd, J = 8.0, 6.3 Hz, 1H), 4.05 (s, 3H), 4.15 (dd, J = 12.6, 6.3 Hz, 1H), 4.74 (dd, J = 12.6, 8.6 Hz, 1H), 6.73 (d, J = 8.6 Hz, 2H), 7.03 (d, J = d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.6 Hz, 3H), 7.28 (d, J = 8.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.64 (s, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.4, 41.6, 67.4, 108.1, 109.8, 117.5, 118.5, 124.8 (q, $1J_{C-F}$ = 271.1 Hz), 125.1,, 127.9, 128.5, 128.7, 129.8, 132.1, 132.6, 139.6, 140.2, 145.2, 146.2; HRMS (ESI) calcd for $C_{25}H_{21}ClF_3N_2O_2S$ $(M + H)^+$ 505.0964, found 505.0968.

*(R)-8-Methyl-3-phenyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]-indole (**4a**).* The general method C described above was followed when (*R*)-**1a** (27.3 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford (*R*)-**4a** (34.2 mg, 0.085 mmol) as a thick liquid in 85% yield. $[\alpha]_D^{25}$ = +39.0 (*c* 0.26, CH_2Cl_2) for a 95% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (IA column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 8.55 min (major, *R*), t_R (2) = 9.19 min (minor, *S*).

*(R)-8-Methyl-3-phenyl-1-(phenylsulfonyl)-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4m**).* The general method C described above was followed when (*R*)-**1j** (25.9 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford (*R*)-**4m** (31.9 mg, 0.082 mmol) as a thick liquid in 82% yield: R_f 0.29 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3229, 3060, 2923, 2853, 1691, 1612, 1494, 1469, 1447, 1421, 1266, 1163, 1129, 1093, 1024, 930, 875, 753, 699, 690, 597, 581, 539, 503; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (t, J = 8.0 Hz, 1H), 4.01 (s, 3H), 4.12 (dd, J = 12.6, 8.0 Hz, 1H), 4.67 (dd, J = 12.6, 8.0 Hz, 1H), 6.87 (dd, J = 5.7, 1.7 Hz, 2H), 6.97 (d, J = 8.0 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 7.13−7.14 (m, 3H), 7.21 (td, 8.6, 1.6 Hz, 1H), 7.30 (t, J = 8.6 Hz, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.50−7.53 (m, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 32.0, 42.7, 67.6, 110.5, 110.7, 118.7, 120.4, 121.3, 122.7, 126.8, 127.4, 128.1, 128.6, 129.1, 133.8, 135.2, 140.6, 141.6, 143.7; HRMS (ESI) calcd for $C_{23}H_{21}N_2O_2S$ $(M + H)^+$ 389.1324, found 389.1321. $[\alpha]_D^{25}$ = +86.3 (*c* 0.06, CH_2Cl_2) for a 99% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 15.54 min (major, *R*), t_R (2) = 21.6 min (minor, *S*).

*(R)-8-Methyl-3-phenyl-1-(2-(trifluoromethyl)phenylsulfonyl)-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4n**).* The general method C described above was followed when (*R*)-**1k** (32.7 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford (*R*)-**4n** (34.7 mg, 0.076 mmol) as a thick liquid in 76% yield: R_f 0.22 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 2853, 1720, 1614, 1564, 1493, 1483, 1455, 1372, 1307, 1269, 1223, 1172, 1116, 1094, 878, 810, 768, 745; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (s, 3H), 4.04 (t, J = 7.7 Hz, 1H), 4.22 (dd, J = 12.3, 6.8 Hz, 1H), 4.77 (dd, J = 11.8, 7.7 Hz, 1H), 6.91−6.93 (m, 2H), 7.04−7.07 (m, 2H), 7.11−7.12 (m, 3H), 7.20−7.24 (m, 1H), 7.32−7.38 (m, 2H), 7.53−7.58 (m, 2H), 7.75 (d, J = 7.7 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 32.0, 42.6, 67.0, 110.5, 110.6, 118.7, 120.6, 121.5,122.8, 125.0 (q, $1J_{C-F}$ = 273.2 Hz), 126.8, 127.3, 128.6, 132.0, 132.2, 133.5, 135.6, 140.4, 141.6, 143.2; HRMS (ESI) calcd for $C_{24}H_{20}F_3N_2O_2S$ $(M + H)^+$ 457.1198, found 457.1190. $[\alpha]_D^{25}$ = +56.66 (*c* 0.06, CH_2Cl_2) for a 98% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 12.47 min (minor, *S*), t_R (2) = 14.33 min (major, *R*).

*(R)-1-(4-Methoxyphenylsulfonyl)-8-methyl-3-phenyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4o**).* The general method C described above was followed when (*R*)-**1l** (28.9 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford (*R*)-**4o** (34.3 mg, 0.082 mmol) as a thick liquid in 82% yield: R_f 0.20 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 2852, 1708, 1595, 1576, 1496, 1482, 1456, 1419, 1380, 1353, 1311, 1261, 1223, 1182, 1161, 1130, 1091, 1025, 877, 833, 810, 810, 742, 719, 700, 675, 627, 589, 576, 557; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.89 (t, J = 7.8 Hz, 1H), 3.98 (s, 3H), 4.08−4.14 (m, 1H), 4.68 (dd, J = 12.8, 8.2 Hz, 1H), 6.68 (d, J = 9.1 Hz, 2H), 6.87 (dd, J = 6.0, 2.3 Hz, 2H), 7.01−7.03 (m, 2H), 7.11−7.13 (m, 3H), 7.20 (ddd, J = 8.2, 5.5, 2.8 Hz, 1H), 7.36−7.39 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 31.3, 41.9, 54.9, 66.8, 109.7, 109.8, 113.6, 118.0, 119.7, 120.5, 122.2, 125.9, 125.9, 126.6, 127.8, 129.4, 139.9, 141.2, 143.3, 163.0; HRMS (ESI) calcd for $C_{24}H_{23}N_2O_3S$ $(M + H)^+$ 419.1429, found 419.1429. $[\alpha]_D^{25}$ = +40.4 (*c* 0.06, CH_2Cl_2) for a 95% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 18.67 min (minor, *S*), t_R (2) = 20.89 min (major, *R*).

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*(R)-5-Chloro-8-methyl-3-phenyl-1-(phenylsulfonyl)-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4p**).* The general method C described above was followed when (*R*)-**1j** (25.9 mg, 0.100 mmol) reacted with 2-bromoindole **2b** (24.4 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford (*R*)-**4p** (34.7 mg, 0.082 mmol) as a white solid in 82% yield: R_f 0.17 (10% ethyl acetate in petroleum ether); mp 140−142 °C; IR ν_{max} (KBr, cm^{-1}) 2924, 2853, 1743, 1562, 1493, 1463, 1418, 1358, 1309, 1222, 1170, 990, 884, 793, 748, 729, 688, 587, 566; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (t, *J* = 8.0 Hz, 1H), 3.98 (s, 3H), 4.09 (dd, *J* = 12.6, 8.0 Hz, 1H), 4.65 (dd, *J* = 12.6, 8.0 Hz, 1H), 6.83 (dd, *J* = 5.2, 1.7 Hz, 2H), 6.91 (d, *J* = 2.3 Hz, 1H), 7.13−7.16 (m, 4H), 7.28 (d, *J* = 8.6 Hz, 1H), 7.32 (t, *J* = 8.6 Hz, 2H), 7.49 (dd, *J* = 8.6, 1.2 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 32.2, 42.6, 67.6, 110.3, 111.5, 118.1, 121.5, 123.6, 126.3, 127.1, 127.2, 128.0, 128.8, 129.2, 133.9, 135.2, 138.9, 141.1, 144.8; HRMS (ESI) calcd for $C_{23}H_{20}ClN_2O_2S$ $(M + H)^+$ 423.0934, found 423.0939. $[\alpha]_D^{25}$ = +35.3 (*c* 0.07, CH_2Cl_2) for a 96% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 15.56 min (minor, *S*), t_R (2) = 18.98 min (major, *R*).

*(R)-5-Chloro-8-methyl-3-phenyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4q**).* The general method C described above was followed when (*R*)-**1a** (27.3 mg, 0.100 mmol) reacted with 2-bromoindole **2b** (24.4 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford (*R*)-**4q** (35.4 mg, 0.081 mmol) as a white solid in 81% yield: R_f 0.16 (10% ethyl acetate in petroleum ether); mp 204−206 °C; IR ν_{max} (KBr, cm^{-1}) 2922, 1597, 1561, 1492, 1463, 1351, 1305, 1166, 885, 799, 754, 696, 687, 667, 587, 549; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.80 (t, *J* = 8.2 Hz, 1H), 3.97 (s, 3H), 4.10 (dd, *J* = 12.7, 7.7 Hz, 1H), 4.67 (dd, *J* = 13.6, 8.2 Hz, 1H), 6.81−6.83 (m, 2H), 6.94 (d, *J* = 1.8 Hz, 1H), 7.05 (d, *J* = 8.6 Hz, 2H), 7.11−7.15 (m, 4H), 7.26 (t, *J* = 9.1 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 21.7, 32.2, 42.4, 67.5, 110.1, 111.5, 118.1, 121.4, 123.7, 126.3, 126.8, 127.2, 128.0, 128.7, 129.8, 132.1, 139.0, 141.3, 144.9, 144.9; HRMS (ESI) calcd for $C_{24}H_{22}ClN_2O_2S$ $(M + H)^+$ 437.1091, found 437.1095. $[\alpha]_D^{25}$ = +85.6 (*c* 0.16, CH_2Cl_2) for a 95% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (cellouse 2 column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 36.45 min (minor, *S*), t_R (2) = 40.62 min (major, *R*).

*(R)-5-Chloro-8-methyl-1-(4-nitrophenylsulfonyl)-3-phenyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4r**).* The general method C described above was followed when (*R*)-**1m** (30.4 mg, 0.100 mmol) reacted with 2-bromoindole **2b** (24.4 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 4 h to afford (*R*)-**4r** (39.3 mg, 0.084 mmol) as a white solid in 84% yield: R_f 0.19 (20% ethyl acetate in petroleum ether); mp 170−172 °C; IR ν_{max} (KBr, cm^{-1}) 2924, 1563, 1530, 1493, 1463, 1348, 1311, 1172, 1086, 886, 854, 795, 738, 699, 684, 657, 613, 465; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 (s, 3H), 4.03 (dd, *J* = 8.6, 4.6 Hz, 1H), 4.30 (dd, *J* = 12.6, 4.6 Hz, 1H), 4.84 (dd, *J* = 13.2, 9.2 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 2H), 7.03 (t, *J* = 7.5 Hz, 2H), 7.09 (q, *J* = 7.5 Hz, 2H), 7.20 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.31 (d, *J* = 9.2 Hz, 1H), 7.52 (d, *J* = 9.2 Hz, 2H), 7.91 (d, *J* = 9.2 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 32.4, 41.6, 67.5, 109.8, 111.8, 118.3, 122.2, 124.1, 126.8, 126.9, 128.7, 129.0, 139.2, 140.3, 141.7, 143.7, 150.8; HRMS (EsI) calcd for $C_{23}H_{19}ClN_3O_4S$ $(M + H)^+$ 468.0785, found 468.0781. $[\alpha]_D^{25}$ = +98.2 (*c* 0.25, CH_2Cl_2) for a 94% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (IA column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 18.25 min (major, *R*), t_R (2) = 27.36 min (minor, *S*).

*(S)-3-(2-Chlorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4s**).* The general method C described above was followed when (*S*)-**1n** (30.8 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3.5 h to afford (*S*)-**4s** (34.1 mg, 0.078 mmol) as a thick liquid in 78% yield: R_f 0.26 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 1564, 1456, 1356, 1167, 1088, 1033, 808, 745, 691, 677, 589, 548; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.29 (s, 3H), 4.00 (s, 3H), 4.08 (dd, *J* = 12.2, 6.1 Hz, 1H), 4.18 (t, *J* = 6.7 Hz, 1H), 4.87 (dd, *J* = 12.8, 8.6 Hz, 1H), 6.63 (d, *J* = 7.3 Hz, 1H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 7.06−7.08 (m, 3H), 7.23−7.24 (m, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.40 (d, *J* = 7.9 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.4, 31.7, 40.4, 65.7, 108.2, 110.1, 118.5, 120.6, 121.3, 122.9, 126.8, 127.6, 127.8, 128.6, 129.7, 131.8, 133.1, 139.3, 140.7, 144.1, 144.6; HRMS (ESI) calcd for $C_{24}H_{22}ClN_2O_2S$ $(M + H)^+$ 437.1091, found 437.1096. $[\alpha]_D^{25}$ = +96.0 (*c* 0.20, CH_2Cl_2) for a 95% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (cellouse 2 column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 18.89 min (major, *S*), t_R (2) = 36.25 min (minor, *R*).

*(S)-5-Chloro-3-(2-chlorophenyl)-8-methyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4t**).* The general method C described above was followed when (*S*)-**1n** (30.8 mg, 0.100 mmol) reacted with 2-bromoindole **2b** (24.4 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 4 h to afford (*S*)-**4t** (35.8 mg, 0.076 mmol) as a thick liquid in 76% yield: IR ν_{max} (KBr, cm^{-1}) 2923, 2852, 1741, 1643, 1489, 1466, 1436, 1339, 1224, 1161, 1091, 981, 751, 665, 557; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.98 (s, 3H), 4.05 (dd, *J* = 12.6, 6.3 Hz, 1H), 4.14 (t, *J* = 6.9 Hz, 1H), 4.85 (dd, *J* = 12.6, 8.6 Hz, 1H), 6.58 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.86−6.89 (m, 1H), 6.98−7.00 (m, 3H), 7.09 (td, *J* = 8.0, 1.7 Hz, 1H), 7.17 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.28−7.33 (m, 4H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 32.3, 40.1, 65.6, 108.1, 111.6, 118.0, 121.5, 123.8, 126.4, 127.1, 127.9, 128.0, 128.3, 129.4, 131.9, 133.3, 138.9, 139.0, 144.9, 145.3; HRMS (ESI) calcd for $C_{24}H_{21}Cl_2N_2O_2S$ $(M + H)^+$ 471.0701, found 471.0709. $[\alpha]_D^{25}$ = −93.6 (*c* 0.36, CH_2Cl_2) for a 94% ee sample, the enantiomeric excess was determined by chiral HPLC analysis (cellouse 2 column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, t_R (1) = 20.74 min (major, *S*), t_R (2) = 39.05 min (minor, *R*).

*(2S,3S)-8-Methyl-3-phenyl-2-propyl-1-tosyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4u**).* The general method C described above was followed when (2*S*,3*S*)-**1o** (31.5 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.5 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 4 h to afford (2*S*,3*S*)-**4u** (28.9 mg, 0.065 mmol) as a thick liquid in 65% yield: $[\alpha]_D^{25}$ = −151.22 (*c* 0.06, CH_2Cl_2); IR ν_{max} (KBr, cm^{-1}) 2956, 2923, 2853, 1712, 1641, 1598, 1492, 1463, 1362, 1248, 1210, 1187, 1170, 1082, 1018, 990, 908, 848, 813, 740; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.61−0.68 (m, 1H), 0.75 (t, *J* = 7.5 Hz, 3H), 0.81−0.88 (m, 1H), 1.30−1.38 (m, 1H), 1.58−1.65 (m, 1H), 2.37 (s, 3H), 3.76 (d, *J* = 6.9 Hz, 1H), 3.97 (s, 3H), 4.56−4.61 (m, 1H), 6.97−6.98 (m, 3H), 7.02−7.04 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.19−7.22 (m, 4H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.6 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 13.4, 19.4, 21.8, 31.6, 32.6, 46.9, 109.8, 110.5, 119.2, 120.2, 120.8, 122.7, 126.8, 128.0, 128.2, 129.1, 129.8, 133.6, 137.5, 140.4, 143.3, 144.8; HRMS (ESI) calcd for $C_{27}H_{29}N_2O_2S$ $((M + H)^+$ 445.1950, found 445.1942.

*8-Methyl-1-tosyl-3-vinyl-1,2,3,8-tetrahydropyrrolo[2,3-b]indole (**4v**).* The general method C described above was followed when **1p** (22.3 mg, 0.100 mmol) reacted with 2-bromoindole **2a** (21.0 mg, 0.100 mmol) at 85 °C for 2.0 h followed by treatment with CuI (10 mol %), (±)-*trans*-1,2-diaminocyclohexane (20 mol %), and K_2CO_3 (16.6 mg, 0.12 mmol) at 120 °C for 3 h to afford **4v** (26.8 mg, 0.076 mmol) as a white solid in 76% yield: mp 198−200 °C; R_f 0.23 (10% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2956, 2923, 2853, 1712, 1641, 1598, 1492, 1463, 1362, 1248, 1210, 1187, 1170, 1082, 1018, 990, 908, 848, 813, 740; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.25 (dd, *J* = 14.9, 7.5 Hz, 1H), 3.93 (s, 3H), 3.94−3.96 (m, 1H), 4.43 (dd, *J* = 12.6, 6.3 Hz, 1H), 4.86 (d, *J* = 10.3 Hz, 1H), 4.94 (d, *J* = 16.6 Hz, 1H), 5.29−5.36 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 5.8 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 21.7, 31.9, 41.2, 64.7, 110.4, 110.6, 116.1, 118.2, 120.3, 121.1, 122.9, 128.2, 129.7, 132.4,

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138.1, 140.5, 143.1, 144.7; HRMS (ESI) calcd for $C_{20}H_{21}N_2O_2S$ $(M + H)^+$ 353.1324, found 353.1326.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01049.

NMR spectra of substrates and products, (CIF) and HPLC chromatograms (PDF)

X-ray crystallographic analysis of **4j** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mkghorai@iitk.ac.in. Phone: (+91)-512-2597518. Fax: (+91)-512-2596806.

Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to Professor R. N. Mukherjee on the occasion of his 63rd Birthday.

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