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Domino Ring-Opening Cyclization of Activated Aziridines with Indoles: Synthesis of Chiral Hexahydropyrroloindoles

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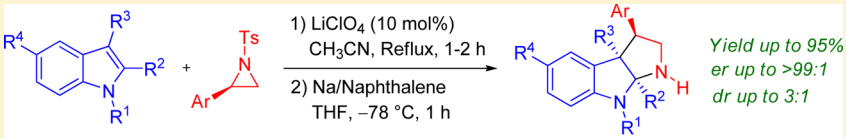
Supporting Information



R^1 = H, Me, Bn, Boc; R^2 = H, Me; R^3= Me; R^2 = R^3 = –$(CH_2)_3$–; R^4 = H, Br; Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 3-FC_6H_4, 3-ClC_6H_4, 3-MeC_6H_4, 2-ClC_6H_4

ABSTRACT: A highly enantioselective synthetic route to hexahydropyrrolo[2,3-*b*]indoles via Lewis acid-catalyzed S_N2-type ring opening of activated aziridines with indoles having substitutions at 3- and other positions followed by cyclization in a domino fashion has been developed. Hexahydropyrrolo[2,3-*b*]indoles have been detosylated in the same pot to afford the corresponding products with free NH group in excellent yields (up to 95%) and enantioselectivity (up to >99%).

INTRODUCTION

Fused indoline skeletons are present as the core structural units in a number of natural products and other biologically active compounds.[1] A wide variety of chiral indole alkaloids containing pyrrolo[2,3-*b*]indole[2] framework are of immense biological relevance and pharmacological utility. Those include the acetylcholinesterase inhibitors physovenine and physostigmine,[3,4] the anticancer agents (−)-Flustramine B,[5] multidrug resistant (MDR) reversal agent (−)-ardeemin[6] and the glycine receptor antagonist corymine, etc. (Figure 1).[7] Hence, the development of novel and innovative synthetic routes to this important class of compounds continues to attract considerable attention.

Many interesting synthetic routes have been developed for this purpose, e.g., [3 + 2] cycloaddition,[8] electrophilic addition/cyclization,[9] cyclopropanation/ring opening/iminium cyclization (CRI reaction),[10] Fischer indolization,[11] copper catalyzed cyclization of iodo-tryptophans[12] and organocatalytic cascade addition-cyclization, etc.[13] Aziridines[14,15] have also been exploited for the synthesis of pyrroloindolines.[16] In 2010, Nakagawa used the annulation protocol to synthesize physostigmine starting from skatole and activated aziridine in the presence of a Lewis acid.[16a] Wang group has developed an interesting strategy for the synthesis of enantioenriched C_3-halogenated pyrroloindolines starting from racemic aziridine in the presence of magnesium catalyst and chiral ligand.[16b] The same group reported asymmetric synthesis of pyrroloindolines by [3 + 2] cycloaddition between *meso*-aziridines and C3-alkylindoles under in situ generated magnesium catalyst and commercial available chiral ligands along with the assistance of an achiral ligand.[16c] Chai and co-workers have synthesized a variety of chiral pyrroloindolines by kinetic resolution of racemic aziridines in the presence of Cu(I) salts and chiral diphosphine ligands. They further demonstrated the synthesis of enantioenriched pyrrolo[2,3-*b*]indole with reduced ee from enantiopure aziridine in the absence of any ligand.[16d] Although the [3 + 2] annulation reactions have made a significant contribution toward catalytic asymmetric synthesis of hexahydropyrrolo[2,3-*b*]indole core structures, the direct application of C3-substituted indole and chiral aziridine in enantioselective formation of this key framework is relatively less explored.

In continuation of our research interest in the area of LA-catalyzed S_N2-type ring opening of activated aziridines/azetidines[17,18] and based on our results related to the synthesis of tetrahydropyrroloindoles (Scheme 1),[17e] we anticipated that another important pyrroloindole skeleton, i.e., hexahydropyrrolo[2,3-*b*]indoles could easily be synthesized via domino ring-opening cyclization (DROC)[18] of activated aziridines with 3-substituted indoles under a single step operation. To the best of our knowledge there is only one report of direct catalytic enantioselective ring-opening followed by cyclization of chiral aziridines with C3-substituted indoles to provide enantioenriched pyrrolo[2,3-*b*]indoles.[16e]

We have developed a simple strategy for the synthesis of chiral hexahydropyrrolo[2,3-*b*]indoles bearing multiple contiguous stereogenic centers with excellent stereoselectivity via LA-catalyzed domino ring-opening cyclization (DROC) of 2-aryl-*N*-tosylaziridines with 3-substituted indoles, followed by deprotection of tosyl group in the same pot. Herein, we report our results in detail as an article.

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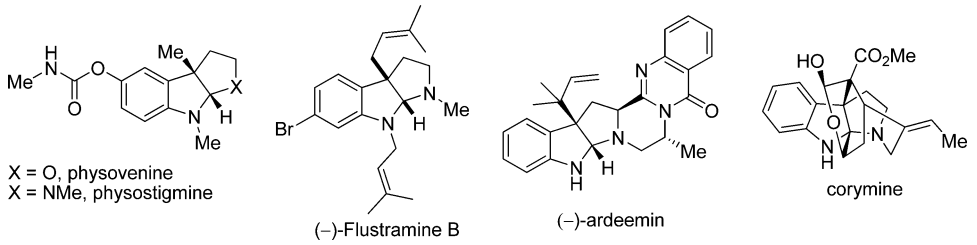
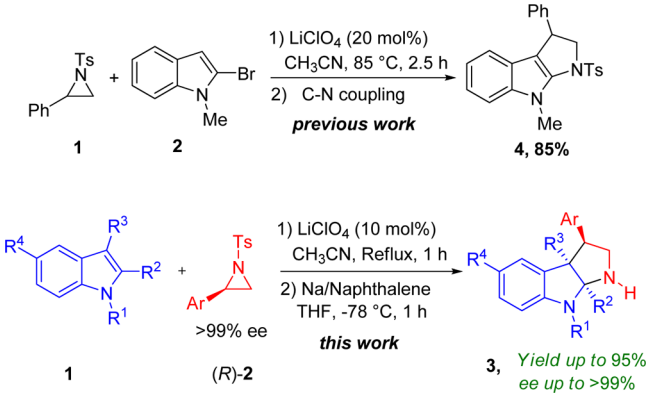


Figure 1. Representatives of the pyrrolo[2,3-*b*]indole containing natural alkaloids.

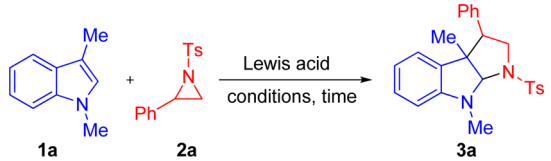
Scheme 1. Construction of Chiral Pyrrolo[2,3-*b*]indole Framework via S_N2-Type Nucleophilic Attack



RESULTS AND DISCUSSION

Our study began with the reaction of 2-phenyl-*N*-tosylaziridine (1.0 equiv) with 1,3-dimethylindole (1.1 equiv) in the presence of catalytic amount of $Sc(OTf)_3$ (5 mol %) and $Zn(OTf)_2$ (5 mol %)[17b] and the corresponding hexahydropyrrolo[2,3-*b*]indole **3a** was obtained in poor yield (46%) (entry 1, Table 1). Although the dual catalysis was highly successful in our previous finding,[17b] but for the present combination of substrates it seems to be not efficient in terms of yield of the desired product. In order to find out the optimum reaction conditions, we screened several Lewis acids and solvents (entries 2−6). When the reaction was carried out in dichloromethane using $Cu(OTf)_2$ (10 mol %) as the LA catalyst, **3a** was obtained in good yield (69%) as an inseparable pair of diastereomers (dr 3:1). At lower temp (0 °C), the reaction was found to be successful but dr remained unchanged (entry 6). Based on our recent study,[17e] when **1a** was treated with **2a** in the presence of catalytic amount of $LiClO_4$ (10 mol %) in acetonitrile at 85 °C for 1 h, to our pleasure **3a** was obtained in excellent yield with dr 3:1 (entry 8). Performing the reaction with half (5 mol %) or double (20 mol %) (entry 10) amount of the catalyst (entry 9), the yield and dr of the product could not be improved further. Thus, the optimal reaction conditions were determined as 10 mol % of $LiClO_4$ in acetonitrile at 85 °C (entry 8).

Table 1. Optimization Study[a,b]

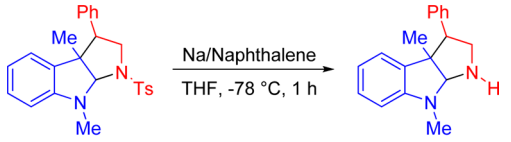


entry	LA catalyst (mol %)	solvent	temp (°C)	time (h)	yield (%)
1	$Sc(OTf)_3$ (5) $Zn(OTf)_2$ (5)	CH_2Cl_2	25	3	46
2	$Sc(OTf)_3$ (10)	CH_2Cl_2	25	2	58
3	$Zn(OTf)_2$ (10)	CH_2Cl_2	25	4	63
4	$Zn(OTf)_2$ (10)	$C_2H_4Cl_2$	65	3	65
5	$Cu(OTf)_2$ (10)	CH_2Cl_2	25	2	69
6	$Cu(OTf)_2$ (10)	CH_2Cl_2	0	4	64
7	$LiClO_4$ (10)	CH_3CN	25	2	Nr
8	$LiClO_4$ (10)	CH_3CN	85	1	84
9	$LiClO_4$ (5)	CH_3CN	85	1.5	79
10	$LiClO_4$ (20)	CH_3CN	85	1	83

[a]All reactions were carried out with **1a** (1.1 mmol) and **2a** (1.0 mmol). [b]All the reactions showed dr 3:1 as estimated by ^1H NMR analysis of the crude mixture.

With a view to separating the diastereomers we attempted desulfonation of -N-Ts group. When the inseparable pair of diastereomers of **3a** were treated with excess sodium naphthalenide in THF at −78 °C, the detosylation took place smoothly and both diastereomers of **3aa** could be isolated in pure forms (by flash column chromatography) with free N−H group which could be further functionalized (Scheme 2).

Scheme 2. Cleavage of *N*-Tosyl Bond of 3a



To make our strategy more applicable as a synthetic methodology, a one-pot (stepwise) protocol for the synthesis **3aa** was explored via DROC and detosylation reaction in the same pot. When the reaction mixture obtained after DROC subjected to detosylation under above-mentioned reaction conditions, gratifyingly detosylated product **3aa** was obtained in excellent yield (Scheme 3).

Generalization of the protocol was made with a number of substituted aziridines and the corresponding substituted hexahydropyrrolo[2,3-*b*]indole products were obtained in excellent yields (Table 2). It is noteworthy that the halo

Scheme 3. DROC Followed by Detosylation in One Pot

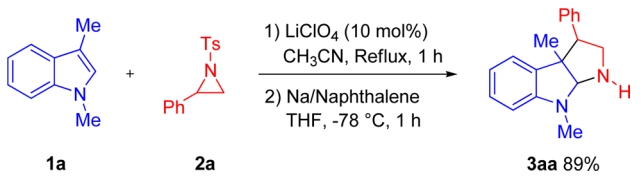


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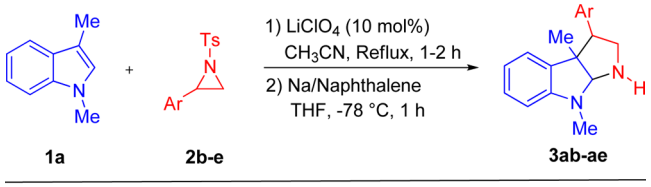
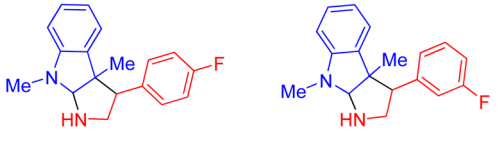
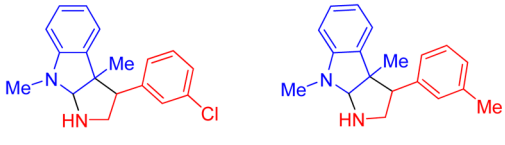
Table 2. Synthesis of Racemic Hexahydropyrrolo[2,3-*b*]indoles[a,b]



1a **2b-e** **3ab-ae**



3ab 84 % **3ac** 92 %



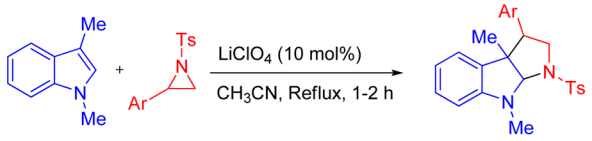
3ad 91 % **3ae** 94 %

[a]All reactions were carried out with **1** (1.1 mmol) and **2** (1.0 mmol). [b]All the reactions showed dr 3:1 as estimated by ^{1}H NMR analysis of the crude reaction mixture.

substituted aziridines were successfully converted directly into target products **3ab**−**3ad** in excellent yields (84−92%), which provided the possibility for further functionalization. 2-*m*-Tolyl-1-tosylaziridine **2e** upon treatment with **1a** produced **3ae** in excellent yield.

Haloaryl-substituted aziridines **2f** and **2g** were reacted with **1a** to generate the corresponding *N*-tosylated hexahydropyrrolo[2,3-*b*]indoles **3af** and **3ag**, respectively, in excellent yields (Scheme 4). Interestingly, diastereomers of **3af** and **3ag** could easily be separated without detosylation by flash column chromatography.

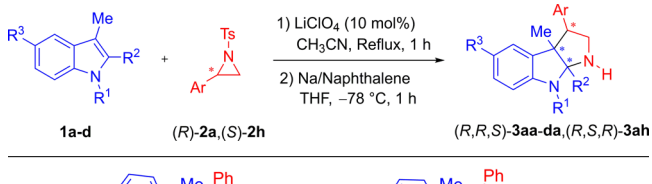
Scheme 4. Substrate Scope of Racemic *N*-Tosylated Hexahydropyrrolo[2,3-*b*]indoles



1a **2f:** Ar = 4-BrC$_6$H$_4$ **2g:** Ar = 4-ClC$_6$H$_4$ **3af:** 93% **3ag:** 95%

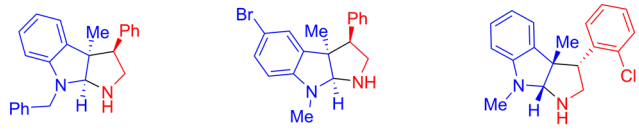
To extend the scope of this strategy for the construction of nonracemic hexahydropyrrolo[2,3-*b*]indoles, enantiopure (*R*)-2-phenyl-*N*-tosylaziridine (*R*)-**2a** was reacted with indole **1a** and the corresponding product (*R*,*R*,*S*)-**3aa** was obtained with excellent yield and stereoselectivity. The approach was generalized with various indoles and nonracemic aziridines (*R*)-**2a** and (*S*)-2-(2-chlorophenyl)-1-tosylaziridine (*S*)-**2h** as shown in Table 3. The reaction of (*R*)-**2a** with indoles **1a-d** bearing electron-neutral (*N*-Me, *N*-Bn, 2-H, 2-Me) and electron-withdrawing (5-Br) groups proceeded smoothly to afford the corresponding products (*R*,*R*,*S*)-**3aa-3da** in high yields (87−90%) and excellent enantiomeric excess (up to >99%). When (*S*)-**2h** (87% ee) was reacted with **1a**, the corresponding product (*R*,*S*,*R*)-**3ah** was obtained without loss of stereochemical integrity (87% ee) in 79% yield.

Table 3. Synthesis of Chiral Hexahydropyrrolo[2,3-*b*]indoles[a−c]



1a-d (*R*)-**2a**,(*S*)-**2h** (*R*,*R*,*S*)-**3aa-da**,(*R*,*S*,*R*)-**3ah**

(*R*,*R*,*S*)-**3aa** 90 % y 95 % ee (*R*,*R*,*S*)-**3ba** 90 % y >99 % ee

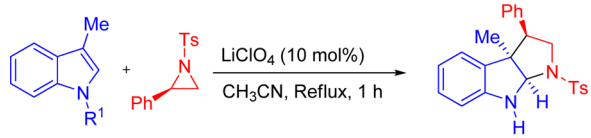


(*R*,*R*,*S*)-**3ca** 87 % y 99 % ee (*R*,*R*,*S*)-**3da** 89 % y 98 % ee (*R*,*S*,*R*)-**3ah** 79 % y 87 % ee

[a]All reactions were carried out with **1** (1.1 mmol) and **2** (1.0 mmol). [b]All the reactions showed dr 3:1 as estimated by ^{1}H NMR analysis of the crude mixture. [c]ee was determined by chiral HPLC analysis.

The reaction of aziridine (*R*)-**2a** with 3-methylindole (**1e**) provided (*R*,*R*,*R*)-**3ea** in moderate yield (73%) and high enantiomeric excess (96%) (Scheme 5). Both the diastereomers

Scheme 5. Reactions of 3-Methyl Indole and *N*-Boc-3-methyl Indole with (*R*)-2-Phenyl-*N*-tosylaziridine



1e: R^1 = H **1f:** R^1 = Boc (*R*)-**2a** (*R*,*R*,*R*)-**3ea:** 73% y 96%ee (*R*,*R*,*R*)-**3ea:** 65% y 96%ee

of (*R*,*R*,*R*)-**3ea** could be separated by flash column chromatography, hence, further one pot detosylation was not performed. The comparatively lower yield of (*R*,*R*,*R*)-**3ea** indicates the possible formation of some *N*-alkylated product from the free N site of indole. Not surprisingly, the indole **1f** bearing electron withdrawing *N*-*tert*-butyloxycarbonyl (Boc) on the N site failed to afford the desired product **3fa** because of reduced reactivity of the indole. Instead, the product (*R*,*R*,*R*)-**3ea** was obtained in moderate yield (65%). Formation of (*R*,*R*,*R*)-**3ea** could be explained, by possible conversion of *tert*-butyl 3-methyl-1*H*-indole-1-carboxylate **1f** to 3-methylindole **1e** after deprotection of the Boc group at 85 °C in the presence of a Lewis acid. The **1e** was further reacted smoothly with aziridine (*R*)-**2a** (Scheme 5) to furnish the product (*R*,*R*,*R*)-**3ea**.

To extend the scope of our strategy further, the reaction of aziridine (*R*)-**2a** with cyclopenta-fused indoles **1g** and **1h** were studied. Under our optimized conditions the reactions proceeded smoothly to afford the corresponding tetracyclic indolines (*R*,*R*,*R*)-**3ga** and (*R*,*R*,*R*)-**3ha** containing quaternary bridging carbons in high yields with excellent enantioselectivity (Scheme 6).

The structure and the relative stereochemistry of **3ea** and **3af** were confirmed by X-ray crystallographic analysis (Figure 2).[19]

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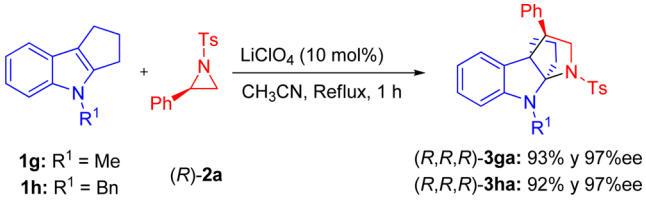
Scheme 6. Synthesis of Tetracyclic Indolines 3ga and 3ha from Cyclopenta-Fused Indoles 1g and 1h

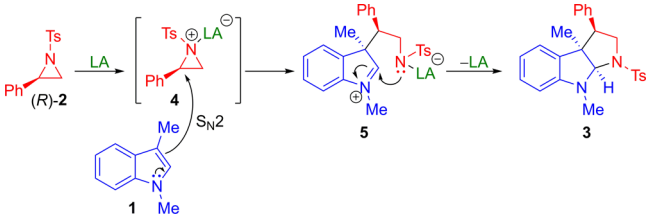


1g: R^1 = Me
1h: R^1 = Bn

(*R*)-**2a**

(*R*,*R*,*R*)-**3ga:** 93% y 97%ee
(*R*,*R*,*R*)-**3ha:** 92% y 97%ee

Scheme 7. Mechanism for the LA-Mediated DROC of Aziridine with Indole



Mechanism. A probable mechanism for the formation of hexahydropyrrolo[2,3-*b*]indoles **3aa**−**3ah**, and **3ba**−**3ha** is described in Scheme 7. We believe that the ring opening of *N*-tosylaziridines **2a**−**h** with indoles **1a**−**h** proceeds via an S_N2-type pathway. The Lewis acid is coordinated to aziridine nitrogen, generating a highly reactive intermediate **4**, which undergoes S_N2-type nucleophilic attack by indole through its C3-position to provide the iminium ion species **5**. Then intramolecular nucleophilic attack of nitrogen to iminium ion in **5** leads to the formation of the final product pyrroloindolines **3**.

CONCLUSION

In conclusion we have developed a simple protocol for the synthesis of racemic and nonracemic hexahydropyrrolo[2,3-*b*]indoles via $LiClO_4$ catalyzed S_N2 type ring-opening followed by intramolecular cyclization in a domino fashion (DROC) followed by sequential detosylation in one pot of *N*-activated aziridines with 3-substituted indoles in excellent yields (up to 95%) and enantioselectivity (up to >99%). The method is environmentally benign as it avoids the use of toxic metallic salts as the Lewis acids.

EXPERIMENTAL SECTION

General Procedures. 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 flash column chromatography using the combination of ethyl acetate and petroleum ether as eluent. Unless noted, all reactions were carried out in oven-dried glassware under an atmosphere of nitrogen/argon using anhydrous solvents. Where appropriate, all reagents were purified prior to use following the guidelines of Perrin, Armerego[20] and Vogel.[21] All monosubstituted aziridines were prepared from the corresponding amino alcohols.[22] All commercial reagents were used as received. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 400 MHz/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), doublet of doublet (dd), triplet (t), quartet (q), multiplet (m). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 100 MHz/125 MHz. HRMS were obtained using an (ESI) mass spectrometer (TOF). IR spectra were recorded in KBr for solids. Melting points were determined using a hot stage apparatus and are uncorrected. Optical rotations were measured using a 6.0 mL cell with a 1.0 dm path length and are reported as $[\alpha]^{25}_D$ (*c* in g per 100 mL solvent) at 25 °C. Enantiomeric excess were determined by HPLC using chiralpak Cellulose 2, IA and OD-H analytical column (detection at 254 nm).

General Procedure for $LiClO_4$-Catalyzed Domino Ring-Opening Cyclization of 2-Phenyl-*N*-tosylaziridines with 3-Methylindoles (A). A solution of the indole **1** (1.1 equiv), aziridine **2** (1.0 equiv) and $LiClO_4$ (10 mol %) in 0.1 mL of dry CH_3CN mixed together under argon at room temperature. The reaction mixture was heated at 85 °C for 1−2 h, and progress of the reaction was monitored by TLC. After completion of the reaction, it was cooled to room temperature and diluted with ethyl acetate (2.0 mL). The suspension was extracted with ethyl acetate (3 × 5.0 mL), washed with a 1:1 mixture of brine. The combined organic extracts were dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on silica gel (230−400 mesh) using 7% ethyl acetate in petroleum ether to afford the pure products.

General Procedure for a One-Pot (Stepwise) Protocol for the Synthesis of Pyrroloindolines (B). A solution of the indole **1** (1.1 equiv), aziridine **2** (1.0 equiv) and $LiClO_4$ (10 mol %) in 0.1 mL of dry CH_3CN mixed together under argon at room temperature. The reaction mixture was heated at 85 °C for 1−2 h, and progress of the reaction was monitored by TLC. After completion of the reaction, it

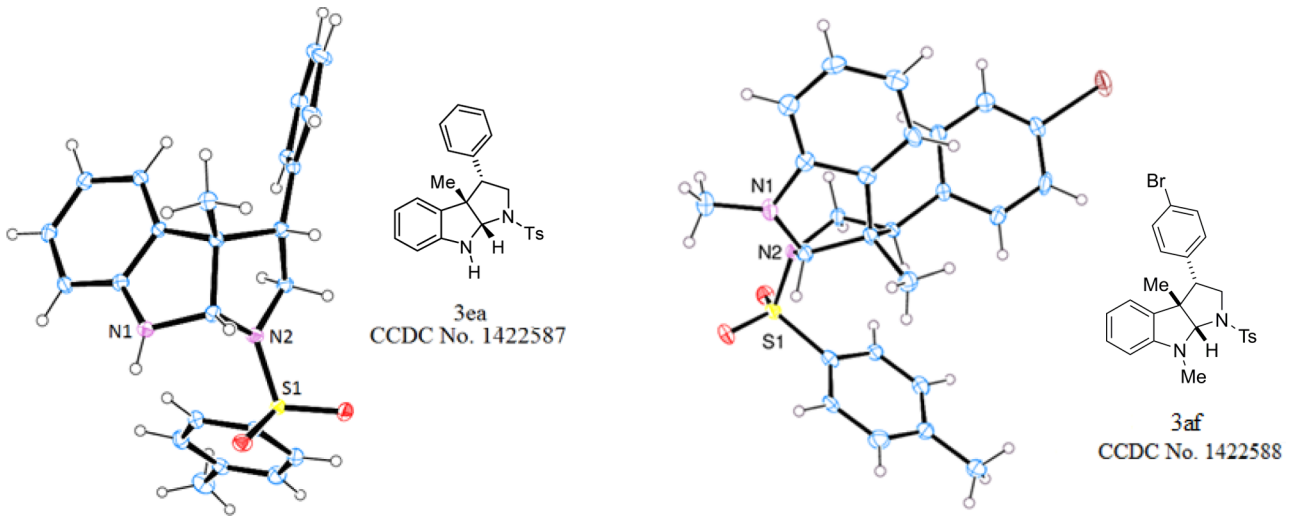


Figure 2. X-ray crystal structure of **3ea** and **3af** (30% thermal ellipsoids).

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was cooled to room temperature. To a solution of reaction mixture **3** in tetrahydrofuran (2.0 mL) cooled in acetone bath at −78 °C, was added sodium naphthalenide (prepared by adding naphthalene (10.0 equiv) in one portion to a vigorously stirred suspension of sodium (7.5 equiv) in tetrahydrofuran (3.0 mL) at 25 °C, the resulting suspension was stirred further for 2 h.) portion wise until the reaction solution formed a persistent, dark-green color. The dark-green solution was stirred at −78 °C for 1 h. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (2.0 mL) and stirred for 2 min at the same temperature. After then it was allowed to warm at RT, the suspension was extracted with ethyl acetate (3 × 5.0 mL), washed with a 1:1 mixture of brine. The combined organic extracts were dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on neutral silica gel (230−400 mesh) using 35% ethyl acetate in petroleum ether to afford the pure products.

*3a,8-Dimethyl-3-phenyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-b]indole (**3a**).*[16e] General procedure **A** was followed when 1,3-dimethyl-1*H*-indole **1a** (59.0 mg, 0.406 mmol) was reacted with 2-phenyl-1-tosylaziridine **2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h to afford **3a** (129.0 mg, 0.308 mmol) as a white solid, mp 128−129 °C in 84% yield; R_f 0.46 (20% ethyl acetate in petroleum ether) as a mixture of two diastereomers major M and minor m in a ∼3:1 ratio; IR ν_{max} (KBr, cm^{-1}) 3031, 2958, 2924, 1605, 1493, 1453, 1429, 1376, 1347, 1303, 1236, 1189, 1163, 1092, 1057, 1023, 1004; ^{1}H NMR for major diastereomer (400 MHz, $CDCl_3$) δ 1.26 (s, 3H), 2.47 (s, 3H), 2.7 (dd, J = 12.6, 6.4 Hz, 1H), 3.03 (s, 3H), 3.39 (t, J = 12.4 Hz, 1H), 3.76 (dd, J = 12.1, 6.4 Hz, 1H), 5.36 (s, 1H), 5.56 (dd, J = 7.3, 0.9 Hz, 1H), 6.27 (dt, J = 7.6, 0.7 Hz, 1H), 6.35 (d, J = 7.8 Hz, 1H), 6.8−6.83 (m, 2H), 7.0 (dt, J = 7.8, 1.14 Hz, 1H), 7.19−7.28 (m, 3H), 7.35 (d, J = 8.0 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H); ^{1}H NMR for minor diastereomer (400 MHz, $CDCl_3$) δ 0.47 (s, 3H), 2.47 (s, 3H), 3.02 (s, 3H), 3.57 (d, J = 11.4, 7.8 Hz, 1H), 3.75 (dd, J = 11.22, 9.6 Hz, 1H), 3.83 (dd, J = 9.6, 7.8 Hz, 1H), 5.05 (s, 1H), 6.51−6.53 (m, 2H), 6.63 (dt, J = 7.3, 0.7 Hz, 1H), 6.91−6.93 (m, 2H), 7.16 (dt, J = 7.8, 1.4 Hz, 1H), 7.19−7.28 (m, 3H), 7.39 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.2 Hz, 2H); ^{13}C NMR for major diastereomer (125 MHz, $CDCl_3$) δ 21.7, 26.0, 31.3, 51.2, 55.0, 56.7, 91.1, 105.0, 116.4, 125.5, 127.3, 128.0, 128.4, 128.6, 128.8, 128.9, 130.0, 135.8, 137.2, 143.8, 150.8; ^{13}C NMR for minor diastereomer (125 MHz, $CDCl_3$) δ 16.5, 21.7, 32.8, 51.9, 52.5, 54.1, 94.4, 107.5, 117.8, 122.4, 127.5, 127.8, 128.2, 128.7, 128.8, 129.9, 132.6, 134.9, 135.3, 144.1, 149.2; HRMS (ESI) calcd for $C_{25}H_{27}N_2O_2S$ $(M + H)^+$ 419.1793, found 419.1796.

*3a,8-Dimethyl-3-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]-indole (**3aa**).* To a solution of mixture of diastereomers **3a** (100.0 mg, 0.239 mmol) in tetrahydrofuran (2.0 mL) cooled in acetone bath at −78 °C, was added sodium naphthalenide (prepared by adding naphthalene (200.0 mg, 1.560 mmol) in one portion to a vigorously stirred suspension of sodium (28.0 mg, 1.217 mmol) in tetrahydrofuran (3.0 mL) at 25 °C, the resulting suspension was stirred further for 2 h.) portion wise until the reaction solution formed a persistent, dark-green color. The dark-green solution was stirred at −78 °C for 1 h. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (2.0 mL) and stirred for 2 min at the same temperature. After then it was allowed to warm at RT, the suspension was extracted with ethyl acetate (3 × 5.0 mL), washed with a 1:1 mixture of brine. The combined organic extracts were dried over anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on neutral silica gel (230−400 mesh) using ethyl acetate in petroleum ether to afford **3aa** (59.0 mg, 0.223 mmol) as a dense liquid in 93% yield; R_f 0.19 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3029, 2924, 2854, 1740, 1601, 1496, 1454, 1377, 1342, 1298, 1216, 1156, 1123, 1077, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5 (s, 3H), 2.91 (s, 3H), 3.09−3.21 (m, 2H), 3.25−3.29 (m, 1H), 4.72 (s, 1H), 5.71 (dd, J = 7.3 Hz, 1 Hz, 1H), 6.25 (dt, J = 7.3, 1 Hz, 1H), 6.34 (d, J = 7.8 Hz, 1H), 6.86−6.89 (m, 2H), 7.0 (dt, J = 7.8, 1.2 Hz, 1H), 7.15−7.2 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 32.6, 50.5, 56.4, 59.2, 93.2, 104.7, 116.3, 125.4, 126.8, 127.8, 127.9, 129.2, 131.0, 138.1, 151.7; HRMS (ESI) calcd for $C_{18}H_{21}N_2$ $(M + H)^+$ 265.1705, found 265.1700.

*3a,8-Dimethyl-3-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]-indole (**3aa**).* General procedure **B** was followed when **1a** (59.0 mg, 0.406 mmol) was reacted with **2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (470.0 mg, 3.667 mmol) stirred with sodium (63.0 mg, 2.739 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford **3aa** (86.0 mg, 0.325 mmol) as a dense liquid in 89% yield; R_f 0.19 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3029, 2924, 2854, 1740, 1601, 1496, 1454, 1377, 1342, 1298, 1216, 1156, 1123, 1077, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5 (s, 3H), 2.91 (s, 3H), 3.09−3.21 (m, 2H), 3.25−3.29 (m, 1H), 4.72 (s, 1H), 5.71 (dd, J = 7.3 Hz, 1 Hz, 1H), 6.25 (dt, J = 7.3, 1 Hz, 1H), 6.34 (d, J = 7.8 Hz, 1H), 6.86−6.89 (m, 2H), 7.0 (dt, J = 7.8, 1.2 Hz, 1H), 7.15−7.2 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 32.6, 50.5, 56.4, 59.2, 93.2, 104.7, 116.3, 125.4, 126.8, 127.8, 127.9, 129.2, 131.0, 138.1, 151.7; HRMS (ESI) calcd for $C_{18}H_{21}N_2$ $(M + H)^+$ 265.1705, found 265.1700.

*3-(4-Fluorophenyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ab**).* General procedure **B** was followed when **1a** (55.0 mg, 0.379 mmol) was reacted with 2-(4-fluorophenyl)-1-tosylaziridine **2b** (100.0 mg, 0.343 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (440.0 mg, 3.433 mmol) stirred with sodium (59.0 mg, 2.565 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford **3ab** (81.0 mg, 0.287 mmol) as a colorless liquid in 84% yield; R_f 0.17 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2924, 2854, 1737, 1605, 1511, 1494, 1455, 1377, 1340, 1297, 1261, 1159, 1100, 1052, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 3H), 2.29 (bs, 1H), 2.89 (s, 3H), 2.99−3.15 (m, 2H), 3.22−3.26 (m, 1H), 4.68 (s, 1H), 5.75 (d, J = 6.7 Hz, 1H), 6.27 (t, J = 7.4 Hz, 1H), 6.32 (d, J = 7.3 Hz, 1H), 6.79−6.88 (m, 4H), 6.99 (dt, J = 7.9, 1.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2, 32.6, 50.8, 56.2, 58.5, 93.2, 104.9, 114.5, 114.6, 116.4, 125.3, 128.1, 130.4, 130.5, 133.8, 151.7, 161.9 (d, $^1J_{C-F}$ = 244.7 Hz); HRMS (ESI) calcd for $C_{18}H_{20}FN_2$ $(M + H)^+$ 283.1611, found 283.1619.

*3-(3-Fluorophenyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ac**).* General procedure **B** was followed when **1a** (55.0 mg, 0.379 mmol) was reacted with 2-(3-fluorophenyl)-1-tosylaziridine **2c** (100.0 mg, 0.343 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (440.0 mg, 3.433 mmol) stirred with sodium (59.0 mg, 2.565 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford **3ac** (89.0 mg, 0.315 mmol) as a colorless liquid in 92% yield; R_f 0.2 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2955, 2924, 2854, 1742, 1606, 1590, 1490, 1455, 1377, 1297, 1271, 1155, 1094, 1050, 1023; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (s, 3H), 2.21 (bs, 1H), 2.89 (s, 3H), 2.99−3.18 (m, 2H), 3.25−3.29 (m, 1H), 4.67 (s, 1H), 5.78 (d, J = 7.3 Hz, 1H), 6.28 (t, J = 7.3 Hz, 1H), 6.33 (d, J = 7.9 Hz, 1H), 6.56 (d, J = 10.4 Hz, 1H), 6.66 (d, J = 7.9 Hz, 1H), 6.87 (dt, J = 7.9, 1.8 Hz, 1H), 6.99 (t, J = 7.9 Hz, 1H); 7.12 (dd, J = 14.0, 7.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.1, 32.6, 50.2, 56.3, 58.5, 93.0, 105.0, 113.5, 113.7, 115.8, 116.0, 116.5, 124.7, 125.0, 128.1, 128.9, 130.4, 151.5, 162.4 (d, $^1J_{C-F}$ = 244.7 Hz); HRMS (ESI) calcd for $C_{18}H_{20}FN_2$ $(M + H)^+$ 283.1611, found 283.1610.

*3-(3-Chlorophenyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ad**).* General procedure **B** was followed when **1a** (52.0 mg, 0.358 mmol) was reacted with 2-(3-chlorophenyl)-1-tosylaziridine **2d** (100.0 mg, 0.325 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (417.0 mg, 3.253 mmol) stirred with sodium (56.0 mg, 2.435 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford **3ad** (88.0 mg, 0.294 mmol) as a colorless liquid in 91% yield; R_f 0.159 (80% ethyl acetate in

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petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3053, 2956, 2924, 2854, 1667, 1605, 1571, 1489, 1464, 1454, 1431, 1376, 1337, 1263, 1216, 1157, 1122, 1083, 1048, 1023; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 3H), 2.04 (bs, 1H), 2.88 (s, 3H), 2.99−3.14 (m, 2H), 3.23−3.26 (m, 1H), 4.68 (s, 1H), 5.78 (dd, J = 7.3, 0.9 Hz, 1H), 6.28 (dt, J = 7.8, 0.9 Hz, 1H), 6.34 (d, J = 8.2 Hz, 1H), 6.7 (d, J = 7.8 Hz, 1H), 6.86 (t, J = 1.8 Hz, 1H), 7.0 (dt, J = 7.8, 1.4 Hz, 1H), 7.07 (t, J = 7.8 Hz, 1H), 7.16−7.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2, 32.6, 50.6, 56.5, 58.9, 93.2, 105.0, 116.5, 125.3, 126.9, 127.5, 128.2, 128.9, 129.3, 130.6, 133.6, 140.4, 151.6; HRMS (ESI) calcd for $C_{18}H_{20}ClN_2$ $(M + H)^+$ 299.1315, found 299.1317.

*3a,8-Dimethyl-3-m-tolyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ae**).* General procedure **B** was followed when **1a** (56.0 mg, 0.386 mmol) was reacted with 2-*m*-tolyl-1-tosylaziridine **2e** (100.0 mg, 0.348 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (446.0 mg, 3.480 mmol) stirred with sodium (60.0 mg, 2.609 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford **3ae** (91.0 mg, 0.327 mmol) as a colorless liquid in 94% yield; R_f 0.186 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3029, 2924, 2855, 1674, 1606, 1491, 1454, 1377, 1340, 1297, 1209, 1156, 1123, 1097, 1051, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 3H), 2.09 (bs, 1H), 2.23 (s, 3H), 2.89 (s, 3H), 3.03−3.12 (m, 2H), 3.22 (dd, J = 8.0, 4.0 Hz, 1H), 4.67 (s, 1H), 5.75 (d, J = 7.4 Hz, 1H), 6.26 (dt, J = 7.4, 1.1 Hz, 1H), 6.33 (d, J = 8.0 Hz, 1H), 6.66 (d, J = 5.7 Hz, 2H), 6.97−7.0 (m, 2H), 7.06 (t, J = 7.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 27.2, 32.7, 50.4, 56.3, 59.0, 93.0, 104.8, 116.3, 125.5, 126.2, 127.5, 127.6, 127.9, 130.1, 130.9, 137.2, 137.7, 151.6; HRMS (ESI) calcd for $C_{19}H_{23}N_2$ $(M + H)^+$ 279.1861, found 279.1869.

*3-(4-Bromophenyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3af**).* General procedure **A** described above was followed **1a** (12.0 mg, 0.083 mmol) was reacted with 2-(4-bromophenyl)-1-tosylaziridine **2f** (25.0 mg, 0.071 mmol) in the presence of $LiClO_4$ (1.0 mg, 0.009 mmol) at 85 °C for 1.5 h to afford **3af** (33.0 mg, 0.066 mmol) as a white solid, mp 164−165 °C in 93% yield; R_f 0.5 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3463, 3029, 2959, 2923, 2852, 1737, 1609, 1489, 1468, 1453, 1428, 1409, 1376, 1349, 1309, 1260, 1235, 1211, 1184, 1167, 1112, 1090, 1057, 1029. 1008; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 3H), 2.46 (s, 3H), 2.68 (dd, J = 12.6, 6.6 Hz, 1H), 3.0 (s, 3H), 3.31 (t, J = 12.6 Hz, 1H), 3.74 (dd, J = 12.4, 6.4 Hz, 1H), 5.35 (s, 1H), 5.64 (dd, J = 7.6 Hz, 1 Hz, 1H), 6.3−6.36 (m, 2H), 6.68 (d, J = 8.5 Hz, 2H), 7.0 (dt, J = 7.8, 1.2 Hz, 1H), 7.34 (dd, J = 7.8, 5.7 Hz, 4H), 7.8 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 26.0, 31.3, 51.3, 54.8, 56.7, 91.1, 105.2, 116.6, 121.5, 125.4, 127.4, 128.3, 128.7, 130.0, 130.6, 131.1, 135.0, 137.1, 144.0, 150.8; HRMS (ESI) calcd for $C_{25}H_{26}BrN_2O_2S$ $(M + H)^+$ 497.0898, found 497.0894.

*3-(4-Chlorophenyl)-3a,8-dimethyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ag**).* General procedure **A** described above was followed **1a** (13.0 mg, 0.089 mmol) was reacted with 2-(4-chlorophenyl)-1-tosylaziridine **2g** (25.0 mg, 0.081 mmol) in the presence of $LiClO_4$ (1.0 mg, 0.009 mmol) at 85 °C for 1 h to afford **3ag** (35.0 mg, 0.077 mmol) as a white solid, mp 146−147 °C in 95% yield; R_f 0.52 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3051, 2924, 1739, 1605, 1493, 1449, 1429, 1413, 1378, 1347, 1302, 1236, 1184, 1090, 1023, 1014; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 3H), 2.46 (s, 3H), 2.69 (d, J = 12.4, 6.4 Hz, 1H), 3.0 (s, 3H), 3.31 (t, J = 12.4 Hz, 1H), 3.75 (dd, J = 12.4, 6.6 Hz, 1H), 5.35 (s, 1H), 5.63 (dd, J = 7.6, 1 Hz, 1H), 6.3 (dt, J = 7.6, 1 Hz, 1H), 6.35 (d, J = 8 Hz, 1H), 6.74 (d, J = 8.5 Hz, 2H), 7.02 (dt, J = 7.6, 1.16 Hz, 1H), 7.18 (d, J = 8.7 Hz, 2H), 7.35 (d, J = 8 Hz, 2H), 7.81 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 26.0, 31.4, 51.3, 54.7, 56.7, 91.1, 105.2, 116.6, 125.4, 127.4, 128.2, 128.3, 128.7, 130.0, 130.2, 133.4, 134.4, 137.1, 144.0, 150.8; HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_2S$ $(M + H)^+$ 453.1404, found 453.1402.

*(3R,3aR,8aS)-3a,8-Dimethyl-3-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3aa**).* General procedure **B** was followed when **1a** (59.0 mg, 0.406 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (470.0 mg, 3.667 mmol) stirred with sodium (63.0 mg, 2.739 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford (*R*,*R*,*S*)-**3aa** (87.0 mg, 0.329 mmol) as a dense liquid in 90% yield; R_f 0.19 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3029, 2924, 2854, 1740, 1601, 1496, 1454, 1377, 1342, 1298, 1216, 1156, 1123, 1077, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5 (s, 3H), 2.91 (s, 3H), 3.09−3.21 (m, 2H), 3.25−3.29 (m, 1H), 4.72 (s, 1H), 5.71 (dd, J = 7.3 Hz, 1 Hz, 1H), 6.25 (dt, J = 7.3, 1 Hz, 1H), 6.34 (d, J = 7.8 Hz, 1H), 6.86−6.89 (m, 2H), 7.0 (dt, J = 7.8, 1.2 Hz, 1H), 7.15−7.2 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 32.6, 50.5, 56.4, 59.2, 93.2, 104.7, 116.3, 125.4, 126.8, 127.8, 127.9, 129.2, 131.0, 138.1, 151.7; HRMS (ESI) calcd for $C_{18}H_{21}N_2$ $(M + H)^+$ 265.1705, found 265.1700. $[\alpha]_D^{25}$ = −142.3 (*c* 0.3, $CHCl_3$) for a 95% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak Cellulose 2 column), *n*-hexane/*i*-propanol = 98:2, flow rate = 0.5 mL/min, $t_R(1)$ = 26.17 min (minor), $t_R(2)$ = 29.87 min (major).

*(3R,3aR,8aS)-3a,8,8a-Trimethyl-3-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ba**).* General procedure **B** was followed when 1,2,3-trimethyl-1*H*-indole **1b** (64.0 mg, 0.402 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (470.0 mg, 3.667 mmol) stirred with sodium (63.0 mg, 2.739 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford (*R*,*R*,*S*)-**3ba** (92.0 mg, 0.330 mmol) as a colorless liquid in 90% yield; R_f 0.24 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3362, 3027, 2967, 2928, 2872, 2808, 1606, 1488, 1450, 1414, 1377, 1309, 1246, 1184, 1154, 1113, 1098, 1057, 1018; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 3H), 1.4 (s, 3H), 2.07 (bs, 1H), 2.8 (s, 3H), 2.96−3.02 (m, 1H), 3.07−3.15 (m, 2H), 5.74 (dd, J = 7.4, 0.7 Hz, 1H), 6.19 (dt, J = 7.3, 0.7 Hz, 1H), 6.25 (d, J = 7.8 Hz, 1H), 6.82−6.85 (m, 2H), 6.96 (dt, J = 7.8, 1.4 Hz, 1H), 7.13−7.2 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.1, 23.4, 27.6, 49.3, 57.7, 60.7, 92.3, 103.5, 115.4, 125.2, 126.7, 127.6, 127.9, 129.2, 130.6, 138.7, 150.7; HRMS (ESI) calcd for $C_{19}H_{23}N_2$ $(M + H)^+$ 279.1861, found 279.1868. $[\alpha]_D^{25}$ = −157.8 (*c* 0.14, $CHCl_3$) for a > 99% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak IA column), *n*-hexane/*i*-propanol = 98:2, flow rate = 0.5 mL/min, $t_R(1)$ = 15.94 min (minor), $t_R(2)$ = 18.47 min (major).

*(3R,3aR,8aS)-8-Benzyl-3a-methyl-3-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ca**).* General procedure **B** was followed when 1-benzyl-3-methyl-1*H*-indole **1c** (89.0 mg, 0.402 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (470.0 mg, 3.667 mmol) stirred with sodium (63.0 mg, 2.739 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford (*R*,*R*,*S*)-**3ca** (108.0 mg, 0.317 mmol) as a colorless liquid in 87% yield; R_f 0.42 (50% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3325, 3029, 2955, 2921, 1948, 1602, 1494, 1452, 1398, 1355, 1301, 1262, 1202, 1159, 1093, 1073, 1047; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5 (s, 3H), 2.18 (bs, 1H), 3.16−3.22 (m, 3H), 4.52 (AB, J = 16.0 Hz, 2H), 4.85 (s, 1H), 5.72 (d, J = 7.6 Hz, 1H), 6.25 (t, J = 7.3 Hz, 1H), 6.3 (d, J = 7.8 Hz, 1H), 6.91−6.95 (m, 3H), 7.18−7.24 (m, 3H), 7.24−7.29 (m, 1H), 7.29−7.36 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4, 49.6, 50.5, 56.4, 59.6, 91.5, 104.6, 116.1, 125.7, 126.8, 127.1, 127.3, 127.8, 127.9, 128.7, 129.2, 130.7, 138.3, 139.1, 151.3; HRMS (ESI) calcd for $C_{24}H_{25}N_2$ $(M + H)^+$ 341.2018, found 341.2013. $[\alpha]_D^{25}$ = −73.3 (*c* 0.06, $CHCl_3$) for a 99% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak OD-H column), *n*-hexane/*i*-propanol = 98:2, flow rate = 0.5 mL/min, $t_R(1)$ = 27.92 min (major), $t_R(2)$ = 40.70 min (minor).

*(3R,3aR,8aS)-5-Bromo-3a,8-dimethyl-3-phenyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3da**).* General procedure **B** was

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followed when 5-bromo-1,3-dimethyl-1*H*-indole **1d** (90.0 mg, 0.402 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.376 mmol) at 85 °C for 1.5 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (470.0 mg, 3.667 mmol) stirred with sodium (63.0 mg, 2.739 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford (*R*,*R*,*S*)-**3da** (112.0 mg, 0.326 mmol) as a colorless liquid in 89% yield; R_f 0.33 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 2955, 2924, 2854, 1743, 1600, 1493, 1463, 1412, 1377, 1271; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 3H), 1.94 (bs, 1H), 2.86 (s, 3H), 3.02−3.14 (m, 2H), 3.23 (dd, J = 10.3, 5.7 Hz, 1H), 4.67 (s, 1H), 5.67 (d, J = 2.3 Hz, 1H), 6.16 (d, J = 8.0 Hz, 1H), 6.86−6.88 (m, 2H), 7.05 (dd, J = 8.6, 2.3 Hz, 1H), 7.23−7.24 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.9, 32.0, 50.5, 56.5, 59.5, 93.1, 105.6, 107.4, 127.2, 127.9, 128.4, 129.0, 130.3, 133.3, 137.7, 150.6; HRMS (ESI) calcd for $C_{18}H_{20}BrN_2$ $(M + H)^+$ 343.0810, found 343.0815. $[\alpha]_D^{25}$ = −22.3 (*c* 0.1, $CHCl_3$) for a 98% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak IA column), *n*-hexane/*i*-propanol = 95:5, flow rate = 0.5 mL/min, $t_R(1)$ = 17.78 min (minor), $t_R(2)$ = 19.24 min (major).

*(3R,3aS,8aR)-3-(2-Chlorophenyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ah**).* General procedure **B** was followed when **1a** (52.0 mg, 0.358 mmol) was reacted with (*S*)-2-(2-chlorophenyl)-1-tosylaziridine (*S*)-**2h** (100.0 mg, 0.325 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h followed by cleavage of N-tosyl bond with excess of sodium naphthalenide (prepared by adding naphthalene (417.0 mg, 3.253 mmol) stirred with sodium (56.0 mg, 2.435 mmol) in tetrahydrofuran (3.0 mL) at 25 °C for 2 h.) in THF at −78 °C for 1 h to afford (*R*,*S*,*R*)-**3ah** (77.0 mg, 0.258 mmol) as a colorless liquid in 79% yield; R_f 0.42 (80% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3323, 3054, 2955, 2924, 2854, 1673, 1605, 1490, 1467, 1452, 1377, 1341, 1298, 1242, 1212, 1156, 1120, 1090, 1052, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (s, 3H), 2.1 (bs, 1H), 2.88 (s, 3H), 3.09 (t, J = 11 Hz, 1H), 3.30 (dd, J = 11, 6.9 Hz, 1H), 3.93 (dd, J = 11.4, 7.3 Hz, 1H), 4.67 (s, 1H), 5.97 (d, J = 6.9 Hz, 1H), 6.27 (t, J = 7.8 Hz, 1H), 6.34 (d, J = 7.8 Hz, 1H), 6.45 (dd, J = 7.8, 1.4 Hz, 1H), 6.86 (t, J = 7.6 Hz, 1H), 6.98 (dt, J = 7.8, 0.9 Hz, 1H), 7.04 (dt, J = 7.3, 1.4 Hz, 1H), 7.34 (dd, J = 8.0, 0.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7, 32.6, 52.1, 53.7, 57.7, 94.5, 105.0, 116.4, 125.1, 125.7, 127.5, 128.0, 129.1, 130.7, 131.5, 134.8, 136.5, 151.6; HRMS (ESI) calcd for $C_{18}H_{20}ClN_2$ $(M + H)^+$ 299.1315, found 299.1313. $[\alpha]_D^{25}$ = +163.6 (*c* 0.22, $CHCl_3$) for a 87% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 0.5 mL/min, $t_R(1)$ = 12.65 min (major), $t_R(2)$ = 14.11 min (minor).

*(3R,3aR,8aR)-3a-Methyl-3-phenyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ea**).* General procedure **A** described above was followed when 3-methyl-1*H*-indole **1e** (53.0 mg, 0.404 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h to afford (*R*,*R*,*R*)-**3ea** (108.0 mg, 0.267 mmol) as a brown solid, mp 166−167 °C in 73% yield; R_f 0.64 (40% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3433, 3036, 2950, 2922, 2854, 1743, 1603, 1495, 1481, 1449, 1407, 1352, 1324, 1307, 1266, 1253, 1155, 1143, 1093, 1074, 1043, 1013; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H), 2.44 (s, 3H), 3.07 (dd, J = 12.2, 7.1 Hz, 1H), 3.52 (dd, J = 11.9, 10.8 Hz, 1H), 3.67 (dd, J = 10.6, 7.1 Hz, 1H), 4.82 (bs, 1H), 5.26 (s, 1H), 5.74 (dd, J = 7.6, 0.7 Hz, 1H), 6.4 (dt, J = 7.3, 0.7 Hz, 1H), 6.58 (d, J = 7.8 Hz, 1H), 6.96−7.0 (m, 3H), 7.24−7.31 (m, 3H), 7.33 (d, J = 8 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 25.4, 50.8, 54.0, 57.8, 85.1, 109.1, 118.3, 125.8, 127.2, 127.7, 128.1, 128.3, 128.7, 129.0, 130.0, 135.7, 136.5, 143.8, 149.3; HRMS (ESI) calcd for $C_{24}H_{25}N_2O_2S$ $(M + H)^+$ 405.1637, found 405.1636. $[\alpha]_D^{25}$ = +43.2 (*c* 0.14, $CHCl_3$) for a 96% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak OD-H column), *n*-hexane/*i*-propanol = 98:2, flow rate = 0.5 mL/min, $t_R(1)$ = 67.62 min (major), $t_R(2)$ = 92.24 min (minor).

*(3R,3aR,8aR)-3a-Methyl-3-phenyl-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole (**3ea**).* General procedure **A** described above was followed when *tert*-butyl 3-methyl-1*H*-indole-1-carboxylate **1f** (94.0 mg, 0.406 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h to afford (*R*,*R*,*R*)-**3ea** (96.0 mg, 0.237 mmol) as a brown solid, mp 166−167 °C in 65% yield; R_f 0.64 (40% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3433, 3036, 2950, 2922, 2854, 1743, 1603, 1495, 1481, 1449, 1407, 1352, 1324, 1307, 1266, 1253, 1155, 1143, 1093, 1074, 1043, 1013; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H), 2.44 (s, 3H), 3.07 (dd, J = 12.2, 7.1 Hz, 1H), 3.52 (dd, J = 11.9, 10.8 Hz, 1H), 3.67 (dd, J = 10.6, 7.1 Hz, 1H), 4.82 (bs, 1H), 5.26 (s, 1H), 5.74 (dd, J = 7.6, 0.7 Hz, 1H), 6.4 (dt, J = 7.3, 0.7 Hz, 1H), 6.58 (d, J = 7.8 Hz, 1H), 6.96−7.0 (m, 3H), 7.24−7.31 (m, 3H), 7.33 (d, J = 8 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 25.4, 50.8, 54.0, 57.8, 85.1, 109.1, 118.3, 125.8, 127.2, 127.7, 128.1, 128.3, 128.7, 129.0, 130.0, 135.7, 136.5, 143.8, 149.3; HRMS (ESI) calcd for $C_{24}H_{25}N_2O_2S$ $(M + H)^+$ 405.1637, found 405.1636. $[\alpha]_D^{25}$ = +43.2 (*c* 0.14, $CHCl_3$) for a 96% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak OD-H column), *n*-hexane/*i*-propanol = 98:2, flow rate = 0.5 mL/min, $t_R(1)$ = 67.62 min (major), $t_R(2)$ = 92.24 min (minor).

*(3aR,8bR,9R)-4-Methyl-9-phenyl-11-tosyl-1,2,3,4-tetrahydro-3a,8b-(epiminoethano)cyclopenta[b]indole (**3ga**).* General procedure **A** described above was followed when 4-methyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole **1g** (70.0 mg, 0.408 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h to afford (*R*,*R*,*R*)-**3ga** (151.0 mg, 0.340 mmol) as a white solid, mp 131−132 °C in 93% yield; R_f 0.5 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3028, 2959, 2869, 1604, 1489, 1427, 1329, 1261, 1151, 1089, 1008; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36−1.49 (m, 2H), 1.59−1.71 (m, 1H), 1.71−1.83 (m, 1H), 2.42 (s, 3H), 2.42−2.56 (m, 2H), 3.12 (s, 3H), 3.36 (t, J = 6.9 Hz, 1H), 3.56 (dd, J = 9.7, 6.3 Hz, 1H), 3.79 (dd, J = 9.7, 6.9 Hz, 1H), 6.39 (d, J = 8.0 Hz, 1H), 6.67 (t, J = 7.4 Hz, 1H), 6.89 (d, J = 6.3 Hz, 1H), 7.07−7.19 (m, 3H), 7.24−7.27 (m, 3H), 7.3 (d, J = 8.6 Hz, 2H), 7.81 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 26.9, 31.8, 34.9, 36.7, 51.6, 54.0, 70.8, 103.8, 106.4, 117.8, 122.6, 127.2, 127.5, 128.4, 128.5, 128.6, 129.6, 134.6, 137.5, 138.8, 143.4, 151.6; HRMS (ESI) calcd for $C_{27}H_{29}N_2O_2S$ $(M + H)^+$ 445.1950, found 445.1944. $[\alpha]_D^{25}$ = −28.8 (*c* 0.29, $CHCl_3$) for a 97% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, $t_R(1)$ = 10.62 min (minor), $t_R(2)$ = 24.26 min (major).

*(3aR,8bR,9R)-4-Benzyl-9-phenyl-11-tosyl-1,2,3,4-tetrahydro-3a,8b-(epiminoethano)cyclopenta[b]indole (**3ha**).*[16e] General procedure **A** described above was followed when 4-benzyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole **1h** (100.0 mg, 0.404 mmol) was reacted with (*R*)-**2a** (100.0 mg, 0.366 mmol) in the presence of $LiClO_4$ (4.0 mg, 0.037 mmol) at 85 °C for 1 h to afford (*R*,*R*,*R*)-**3ha** (175.0 mg, 0.336 mmol) as a white solid, mp 178−179 °C in 92% yield; R_f 0.59 (20% ethyl acetate in petroleum ether); IR ν_{max} (KBr, cm^{-1}) 3029, 2956, 2872, 1603, 1487, 1463, 1452, 1324, 1161, 1088, 1031; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46−1.6 (m, 2H), 1.67−1.79 (m, 1H), 1.86−1.99 (m, 1H), 2.36 (s, 3H), 2.42−2.53 (m, 1H), 2.70−2.81 (m, 1H), 3.42−3.57 (m, 2H), 3.86 (t, J = 9.1 Hz, 1H), 4.44 (d, J = 16.9 Hz, 1H), 5.41 (d, J = 16.4 Hz, 1H), 6.14 (d, J = 7.7 Hz, 1H), 6.64 (t, J = 6.8 Hz, 1H), 6.82 (d, J = 6.4 Hz, 1H), 6.99 (t, J = 7.3 Hz, 1H), 7.08−7.18 (m, 4H), 7.22−7.29 (m, 4H), 7.32 (t, J = 6.8 Hz, 2H), 7.38 (d, J = 7.3 Hz, 2H), 7.51 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 26.7, 34.0, 38.0, 49.4, 51.5, 53.4, 70.4, 77.3, 104.7, 107.0, 117.6, 122.5, 126.5, 126.8, 127.4, 127.7, 128.4, 128.4, 128.7, 129.4, 133.6, 137.0, 137.7, 139.7, 143.5, 150.5; HRMS (ESI) calcd for $C_{33}H_{33}N_2O_2S$ $(M + H)^+$ 521.2263, found 521.2260. $[\alpha]_D^{25}$ = +11.7 (*c* 0.74, $CHCl_3$) for a 97% ee sample. The enantiomeric excess was determined by chiral HPLC analysis (chiralpak OD-H column), *n*-hexane/*i*-propanol = 95:5, flow rate = 1.0 mL/min, $t_R(1)$ = 10.56 min (minor), $t_R(2)$ = 12.0 min (major).

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■ ASSOCIATED CONTENT

Supporting Information

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Copies of ^{1}H and ^{13}C NMR spectra of the compounds, HPLC chromatograms for ee determination and crystal structures (PDF)

Crystal data (CIF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to Prof. Michael Schmittel on the occasion of his 60th birthday.

■ REFERENCES

(1) (a) Hino, T.; Nakagawa, M. Chemistry and Reactions of Cyclic Tautomers of Tryptamines and Tryptophans. *Alkaloids* **1988**, *34*, 1−75. (b) Anthoni, U.; Christophersen, C.; Nielsen, P. H. Naturally Occurring Cyclotryptophans and Cyclotryptamines. *Alkaloids: Chem. Biol. Perspect.* **1999**, *13*, 163−236.

(2) Crich, D.; Banerjee, A. *Acc. Chem. Res.* **2007**, *40*, 151−161.

(3) Takano, S.; Ogasawara, K. Alkaloids of the Calabar Bean. *Alkaloids* **1989**, *36*, 225−251.

(4) (a) Matsuura, T.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 6500−6503. (b) Triggle, D. J.; Mitchell, J. M.; Filler, R. *CNS Drug Rev.* **1998**, *4*, 87−136.

(5) Carle, J. S.; Christophersen, C. *J. Am. Chem. Soc.* **1979**, *101*, 4012−4013.

(6) Chou, T. C.; Depew, K. M.; Zheng, Y. H.; Safer, M. L.; Chan, D.; Helfrich, B.; Zatorska, D.; Zatorski, A.; Bornmann, W.; Danishefsky, S. J. *Proc. Natl. Acad. Sci. U. S. A.* **1998**, *95*, 8369−8374.

(7) Ramirez, A.; Garcia-Rubio, S. *Curr. Med. Chem.* **2003**, *10*, 1891−1915.

(8) (a) Repka, L. M.; Jane, N.; Reisman, S. E. *J. Am. Chem. Soc.* **2010**, *132*, 14418−14420. (b) Wang, H.; Reisman, S. E. *Angew. Chem., Int. Ed.* **2014**, *53*, 6206−6210. (c) Lucarini, S.; Bartoccini, F.; Battistoni, F.; Diamantini, G.; Piersanti, G.; Righi, M.; Spadoni, G. *Org. Lett.* **2010**, *12*, 3844−3847. (d) Spangler, J. E.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 6802−6805. (e) Wang, Y.-N.; Li, T.-R.; Zhang, M.-M.; Cheng, B.-Y.; Lu, L.-Q.; Xiao, W.-J. *J. Org. Chem.* **2016**, DOI: 10.1021/acs.joc.6b00991.

(9) (a) Kawahara, M.; Nishida, A.; Nakagawa, M. *Org. Lett.* **2000**, *2*, 675−678. (b) Kim, J.; Movassaghi, M. *J. Am. Chem. Soc.* **2010**, *132*, 14376−14378. (c) Tu, D.; Ma, L.; Tong, X.; Deng, X.; Xia, C. *Org. Lett.* **2012**, *14*, 4830−4833. (d) Stephens, D. E.; Larionov, O. V. *Eur. J. Org. Chem.* **2014**, *17*, 3662−3670.

(10) (a) Song, H.; Yang, J.; Chen, W.; Qin, Y. *Org. Lett.* **2006**, *8*, 6011−6014. (b) Zhang, D.; Song, H.; Qin, Y. *Acc. Chem. Res.* **2011**, *44*, 447−457. (c) Özüduru, G.; Schubach, T.; Boysen, M. M. K. *Org. Lett.* **2012**, *14*, 4990−4993.

(11) Boal, B. W.; Schammel, A. W.; Garg, N. K. *Org. Lett.* **2009**, *11*, 3458−3461.

(12) (a) Coste, A.; Toumi, M.; Wright, M.; Razafimahaléo, V.; Couty, F.; Marrot, J.; Evano, G. *Org. Lett.* **2008**, *10*, 3841−3844. (b) Bartolucci, S.; Mari, M.; Bedini, A.; Piersanti, G.; Spadoni, G. *J. Org. Chem.* **2015**, *80*, 3217−3222.

(13) Austin, J. F.; Kim, S. G.; Sinz, C. J.; Xiao, W. J.; MacMillan, D. W.C. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5482−5487.

(14) For reviews on aziridines, see: (a) Ghorai, M.; Bhattacharyya, A.; Das, S.; Chauhan, N. Ring Expansions of Activated Aziridines and Azetidines. *Top. Heterocycl. Chem.* **2015**, *41*, 49−142 and references cited therein. (b) Ghorai, M. K.; Shahi, C. K.; Bhattacharyya, A.; Sayyad, M.; Mal, A.; Wani, I. A.; Chauhan, N. *Asian J. Org. Chem.* **2015**, *4*, 1103−1111 and references cited therein. (c) Schneider, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 2082−2084. (d) Takeda, Y.; Ikeda, Y.; Kuroda, A.; Tanaka, S.; Minakata, S. *J. Am. Chem. Soc.* **2014**, *136*, 8544−8547. (e) Callebaut, G.; Meiresonne, T.; De Kimpe, N.; Mangelinckx, S. *Chem. Rev.* **2014**, *114*, 7954−8015 and references cited therein. (f) Takeda, Y.; Kuroda, A.; Sameera, W. M. C.; Morokuma, K.; Minakata, S. *Chem. Sci.* **2016**, *7*, 6141−6152. (g) Dolfen, J.; De Kimpe, N.; D'hooghe, M. *Synlett* **2016**, *27*, 1486−1510.

(15) For some representative examples on aziridine chemistry, see: (a) Craig, R. A., II; O'Connor, N. R.; Goldberg, A. F. G.; Stoltz, B. M. *Chem. - Eur. J.* **2014**, *20*, 4806−4813. (b) Yang, H.-T.; Xing, M.-L.; Lu, X.-W.; Li, J.-X.; Cheng, J.; Sun, X.-Q. *J. Org. Chem.* **2014**, *79*, 11744−11749. (c) Xing, S.; Ren, J.; Wang, K.; Cui, H.; Li, W.; Yan, H. *Tetrahedron* **2015**, *71*, 6290−6299. (d) Samala, S.; Singh, G.; Kumar, R.; Ampapathi, R. S.; Kundu, B. *Angew. Chem., Int. Ed.* **2015**, *54*, 9564−9567. (e) Pathipati, S. R.; Singh, V.; Eriksson, L.; Selander, N. *Org. Lett.* **2015**, *17*, 4506−4509. (f) Sun, H.; Huang, B.; Lin, R.; Yang, C.; Xia, W. *Beilstein J. Org. Chem.* **2015**, *11*, 524−529.

(16) (a) Nakagawa, M.; Kawahara, M. *Org. Lett.* **2000**, *2*, 953−955. (b) Yang, D.; Wang, L.; Han, F.; Li, D.; Zhao, D.; Cao, Y.; Ma, Y.; Kong, W.; Sun, Q.; Wang, R. *Chem. - Eur. J.* **2014**, *20*, 16478−16483. (c) Wang, L.; Yang, D.; Han, F.; Li, D.; Zhao, D.; Wang, R. *Org. Lett.* **2015**, *17*, 176−179. (d) Chai, Z.; Zhu, Y. M.; Yang, P. J.; Wang, S.; Wang, S.; Liu, Z.; Yang, G. *J. Am. Chem. Soc.* **2015**, *137*, 10088−10091. (e) Huang, Y.; Zheng, C.; Pan, L.; Jin, Q.; Zhao, G. *J. Org. Chem.* **2015**, *80*, 10710−10718.

(17) (a) Ghorai, M. K.; Shukla, D.; Bhattacharyya, A. *J. Org. Chem.* **2012**, *77*, 3740−3753. (b) Ghorai, M. K.; Tiwari, D. P.; Jain, N. *J. Org. Chem.* **2013**, *78*, 7121−7130. (c) Samanta, S.; Mal, A.; Halder, S.; Ghorai, M. K. *Synthesis* **2015**, *47*, 3776−3782. (d) Ghorai, M. K.; Sayyad, M.; Nanaji, Y.; Jana, S. *Chem. - Asian J.* **2015**, *10*, 1480−1489. (e) Sayyad, M.; Mal, A.; Wani, I. A.; Ghorai, M. K. *J. Org. Chem.* **2016**, *81*, 6424−6432.

(18) (a) Ghorai, M. K.; Tiwari, D. P. *J. Org. Chem.* **2010**, *75*, 6173−6181. (b) Ghorai, M. K.; Tiwari, D. P. *J. Org. Chem.* **2013**, *78*, 2617−2625. (c) Bhattacharyya, A.; Kavitha, C. V.; Ghorai, M. K. *J. Org. Chem.* **2016**, *81*, 6433−6443.

(19) See Supporting Information for details.

(20) Perrin, D. D.; Armarego, W. L. F. In *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: Oxford, 1988.

(21) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. In *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Longman Group, U.K. Ltd., 1989.

(22) Cernerud, M.; Adolfsson, H.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 2655−2662.

DOI: 10.1021/acs.joc.6b01731
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