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Palladium (II) - Catalyzed C3-Selective Friedel-Crafts Reaction of Indoles with Aziridines

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Abstract

The [$PdCl_2(MeCN)_2$]-catalyzed C3-selective Friedel-Crafts reaction of 2,2-disubstituted and 2-aryl-*N*-tosylaziridines with indoles is reported. For the 2,2-disubstituted substrates, [$PdCl_2(MeCN)_2$] alone, without any ancillary ligands, is an efficient catalyst for the ring-opening reaction. The presence of 1,4-benzoquinone as an additive was found to enhance the ring-opening reaction of the less-reactive 2-arylaziridines. This reaction displayed a broad substrate scope with respect to the indole substrate and is operationally simple. Finally, when 1,3-dimethylindole was employed as a substrate, the de-aromatized pyrroloindoline product was obtained in high yield and good diastereoselectivity.

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Palladium(II)-Catalyzed C3-Selective Friedel--Crafts Reaction of Indoles with Aziridines

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C3 is the magic number: A simple Pd^{II} catalyst that is activated by a 1,4-benzoquinone (BQ) additive has been found to be effective for the ring-opening of arylaziridines, thereby providing a range of functionalized tryptamine derivatives. Importantly, no racemization was observed when a chiral aziridine starting material was used, which opens up a route to enantioenriched β-branched tryptamine derivatives.

Hyland et al. (@UOW) report on #Palladium catalyzed ring-opening of #Arylaziridines

Homogeneous Catalysis

aziridines
homogeneous catalysis
palladium
synthetic methods
tryptamines

The $[PdCl_2(MeCN)_2]$-catalyzed C3-selective Friedel--Crafts reaction of 2,2-disubstituted and 2-aryl-*N*-tosylaziridines with indoles is reported. For the 2,2-disubstituted substrates, $[PdCl_2(MeCN)_2]$ alone, without any ancillary ligands, is an efficient catalyst for the ring-opening reaction. The presence of 1,4-benzoquinone as an additive was found to enhance the ring-opening reaction of the less-reactive 2-arylaziridines. This reaction displayed a broad substrate scope with respect to the indole substrate and is operationally simple. Finally, when 1,3-dimethylindole was employed as a substrate, the de-aromatized pyrroloindoline product was obtained in high yield and good diastereoselectivity.

Introduction

The nucleophilic ring-opening and ring-expansion of aziridines is a powerful method for the synthesis of nitrogen-containing molecules.[1] When indoles are employed as the nucleophile in these reactions, the resultant tryptamine ring-opening products are particularly interesting, because they are found in a broad range of pharmaceutically active compounds and bioactive natural products.[2] Owing to the importance of these indole derivatives, a range of synthetic methods have been reported for their preparation; however, these methods predominantly deal with variation of the substituents around the indole ring, rather than branching at the α and β^^positions.[3] Whilst α-substituted tryptamine derivatives have been shown to have important biological activities,[4] β-branched systems, which do not occur naturally, have yet to be extensively explored. Tryptamines

are also able to undergo direct transformation into pyrroloindolines[5a--c] or tetrahydro-β-carbolines,[5d] as well as other polycyclic nitrogen-containing heterocycles; therefore, β-branched systems are also potential precursors of C3-functionalized analogues of these skeletons.

The C3-selective Lewis-acid-catalyzed ring-opening reaction of 2-arylaziridines with indoles is a potentially powerful synthetic route for the preparation of β-branched tryptamines (Figure^^1<figr1>). Whereas the ring-opening of aziridines with heteroatomic nucleophiles, such as alcohols, amines, thiols, and azides, is widespread,[6a--h] the Friedel--Crafts reaction of electron-rich arenes is less well-developed.[6i--m] In an early report, $LiClO_4$ was shown to efficiently promote this reaction, but with limited substrate scope,[7a] whilst the use of $InCl_3$ as a catalyst gave the products as a mixture of regioisomers.[7b] A dual-catalyst system that consisted of $Sc(OTf)_3/Zn(OTf)_2$ (Tf=trifluoromethanesulfonyl)was used in a single example of a ring-opening reaction between aziridines and indoles, but the product was accompanied by an unidentified by-product.[7c] Notably, in the case of this dual catalyst, a decrease in enantiopurity was observed when using enantiomerically enriched 2-arylaziridines as the starting materials. An enantioselective desymmetrization of *meso*-aziridines with indoles catalyzed by Mg^{II} and a chiral quinone ligand was developed and used to prepare C3-halogenated pyrroloindolines.[5b]

Following our completion of the work reported herein, three reports that detail the synthesis of tryptamine

derivatives were published in the literature. Firstly, an imidazole-based zwitterionic salt that acted as an organocatalyst for the ring-opening reaction of 2-arylaziridines was reported, which included several examples of indoles as the nucleophile.[8a] Furthermore, the ring-opening reactions of aziridines with indoles to afford tryptamines under cationic gold catalysis[8b] and the promotion of a stoichiometric amount of BF_3**<M.>**OEt_2 have also been reported.[8c] To the best of our knowledge, there are no examples of 2,2-disubstituted arylaziridines that undergo ring-opening reactions with indoles, which would lead to the generation of congested quaternary carbons adjacent to an indole.[9a--c] During the course of our recent studies on the Pd^{II}-catalyzed ring-opening reactions of aziridines,[10] we decided to investigate the use of Pd^{II} salts as Lewis acidic catalysts to explore the scope of the ring-opening reaction of aziridines with indoles.

Herein, we report that a simple palladium salt, $[PdCl_2(MeCN)_2]$, can catalyze the ring-opening reaction of 2-aryl-1-tosylaziridines with a range of indoles. We have also found that employing 1,4-benzoquinone as an additive can facilitate this Pd^{II}-catalyzed process with 2-aryl-*N*-tosylaziridines (Figure^^1<xfigr1>). Upon the completion of our investigation, we became aware of an enantiospecific Pd^{II}-catalyzed dearomative [3<M+>2] cycloaddition reaction of 2-arylaziridines with 2-substituted indoles[11a] and a Cu^{I}-catalyzed kinetic resolution of 2-aryl-1-tosylaziridines with indoles.[11b] In contrast, the work presented herein demonstrates the scope of the C3-selective ring-opening

reaction of 2-arylaziridines with indoles to afford tryptamine-derivatives.

Results and Discussion

We initially turned our attention to the ring-opening reaction of 2-aryl-*N*-tosylaziridines, which are readily available from the aziridination of styrene derivatives,[12] with *N*-methylindole. First, we tested a range of Lewis acid catalysts in this reaction and $Cu(OTf)_2$ (Table^^1<tabr1>, entry^^1) and $Sc(OTf)_3$ (Table^^1<xtabr1>, entry^^2) both provided the desired product (**3**) in good-to-moderate yields, but both reactions were accompanied by an inseparable impurity. However, when the catalyst was switched to $[PdCl_2(MeCN)_2]$, the reaction proceeded efficiently and, pleasingly, no by-product was observed (Table^^1<xtabr1>, entry^^3). Interestingly, the yield and conversion could be increased by the addition of a sub-stoichiometric amount of 1,4-benzoquinone, which is believed to increase the π-acidity of the Pd^{II} catalyst (Table^^1<xtabr1>, entry^^4).[13] We found that changing the solvent from DCE to $CHCl_3$ increased the yield further to 77^% (or 68^% without 1,4-benzoquinone; Table^^1<xtabr1>, entries^^6 and 7). However, decreasing the loading of the $[PdCl_2(MeCN)_2]$ catalyst to 5^^mol^% adversely effected the yield, thereby causing it to drop to 56^% without BQ and 58^% with BQ.

Next, we applied our optimized conditions to the synthesis of a range of monosubstituted β-branched tryptamine derivatives (Scheme^^1<schr1>). Pleasingly, the reaction demonstrated excellent functional-group tolerance. Halogen substituents on the aziridine 2-aryl ring were successfully

tolerated to give the corresponding products in moderate-to-good yields (**3^c**--**3^e**). In addition, alkyl and aryl groups, such as methyl and naphthalene, were also well-tolerated, and the corresponding products were afforded in good yields (**3^b** and **3^f**). However, 2-alkyl-*N*-tosylaziridines, such as 7-tosyl-7-azabicyclo[4.1.0]heptane and 2-butyl-1-tosylaziridine, were unreactive in the ring-opening reaction with 1-methylindole. We also examined a series of electron-rich indole derivatives, and *N*-benzylindole and *N*-allylindole reacted with aziridine **1^a** to generate the corresponding β-branched tryptamines (**3^g** and **3^h**), in 60^% and 86^% yields respectively.

Indole derivatives that contained Br, I, and F substituents at the C5^^position afforded the corresponding products (**3^i**, **3^j**, and **3^m**) in good-to-excellent yields (86^%, 72^%, and 60^%, respectively). Curiously, a drop in the yield to 50^% was observed when an indole that contained a methoxy group at the C5^^position was used (product **3^k**). In addition, indoles that contained a substituent at the C7^^position were also tested in the reaction and, gratifyingly, 7-iodo-1-methylindole (**2^i**) gave the target product (**3^l**) in excellent yield. Interestingly, 1*H*-indole has previously been utilized to exclusively synthesize N-alkylated indole derivatives with vinyl aziridines under Pd^0 catalysis;[14] therefore, we were interested in examining the regioselectivity of the substitution reaction of 1*H*-indole with aziridine **1^a** under our conditions. Pleasingly, a good yield and exclusive C3-regioselectivity were observed when 1*H*-indole was subjected to the reaction conditions with aziridine **1^a** (product **3^n**). Furthermore, when 1*H*-pyrrole was used as the nucleophile, the reaction still proceeded, but with much-

lower yield (15^%) of the product (**3^o**) and with the expected C2^^regioselectivity. Notably, C2-substituted indoles were also effective substrates in the reaction; for example, 2-phenyl-1*H*-indole gave the corresponding β-branched tryptamine (**3^p**) in 63^% yield with absolute C3^^regioselectivity.

We also briefly studied the ring-opening reaction of 1-methyl-1-phenyl-*N*-tosylaziridine (**4**) with a range of Lewis acids (Table^^2<tabr2>). This substrate was found to be more reactive than the 2-aryl-*N*-tosylaziridines (**1**), and $[PdCl_2(MeCN)_2]$ alone was an effective catalyst for the preparation of tryptamine derivative **5^a** in 93^% yield (Table^^2<xtabr2>, entry^^1). In contrast to aziridines **1**, an excess of compound **4** was required for this reaction, likely owing to the competing ring-opening and elimination pathways, which afforded compounds **6a** and **6b**, respectively; thus, when only two equivalents of the aziridine were used, the product was formed in lower yield (Table^^2<xtabr2>, entry^^5). $Sc(OTf)_3$ and $AgSbF_6$ (Table^^2<xtabr2>, entries^^2 and 3) were poor catalysts for the reaction, but $Cu(OTf)_2$ was found to be a good Lewis acid for the transformation; however, the increased formation of compound **6b** hindered the purification of the products. Therefore, $[PdCl_2(MeCN)_2]$ was used as the catalyst to evaluate the reaction scope with respect to the indole (Scheme^^2<schr2>).

N-Allylindole was successfully converted into the corresponding product (**5^b**), whilst the presence of halogen substituents at the C5^^position of the indole was also well-tolerated; such products (**5^c**--**5^e**) would be amenable to cross-coupling reactions to further increase their molecular

complexity. Moreover, a C5–methoxy group was found to have a beneficial effect on the reaction yield, by affording compound **5^f** in 85^% yield. Furthermore, we also employed 1*H*–indole as a substrate to examine the chemoselectivity of the reaction and complete selectivity for the C3^^product (**5^g**) was observed in a moderate yield of 56^%, with no N–substitution taking place.

We also demonstrated that 1,3–dimethylindole (**7**) underwent a formal [3<M+>2] cycloaddition reaction with aziridine **1^a** to give pyrroloindoline **8** in high yield and good diastereoselectivity (Scheme^^3<schr3>). In this case, a higher yield was obtained without the 1,4–benzoquinone additive, but the diastereoselectivity remained identical. The diastereomeric mixture of compound **8** could be readily detosylated with Mg/NH_4Cl under ultrasound conditions to give compound **9**, which could be isolated as the pure *trans* diastereoisomer. Upon completion of our investigation, we became aware of two similar syntheses of pyrroloindolines by using this approach: firstly by Chai et^^al., who used a Cu^I/chiral^^diphosphine catalytic system,[11b] and secondly by Zhao and co–workers, who used $[PdCl_2(PhCN)_2]$.[11a]

To investigate the mechanism and stereoselectivity of the reaction, enantiomerically enriched aziridine (*R*)–**1^a'** was subjected to the Pd–catalyzed ring–opening reaction with 1–methylindole **2a** (Scheme^^4<schr4>). No significant erosion of enantiopurity in the ring–opened product ((*R*)–**3^a'**) was observed when $[PdCl_2(MeCN)_2]$ was used alone or with 1,4–benzoquinone as an additive, although, as observed in our optimization studies, the yield of the product was higher in

the presence of 1,4-benzoquinone. We postulated that 1,4-benzoquinone could act as a π-acidic ligand on the Pd^{II} center, thereby increasing the overall Lewis acidity of the catalyst, as π-acidic interactions between palladium(II) and BQ have been shown to be beneficial in allylic C<C->H acetoxylation and amination reactions.[15--16] Another possibility is that the Pd^{II} catalyst undergoes deactivation by reduction into Pd^{0} and aggregation to form Pd black, which was observed in reactions without BQ. Then, BQ may act as a ligand to stabilize the Pd^{0}, so that it could be reoxidized before forming Pd black.[17] The isolation of an enantiomerically enriched product (**3^a**) suggested that the ring-opening reaction proceeded through activation of the aziridine by coordination of the Pd^{II} catalyst, followed by S_N2 attack of the indole on activated aziridine **10** or **11**, rather than a ring-opened intermediate. An S_N2 pathway for the ring-opening reaction of activated aziridines is consistent with the seminal work of Ghorai and co-workers.[7c]

Conclusion

In conclusion, we have reported a detailed study on the $[PdCl_2(MeCN)_2]$-catalyzed C3-selective Friedel--Crafts reaction of indoles with aziridines. A series of tryptamine derivatives that contained a β-substituent have been prepared; furthermore, an all-carbon quaternary center was created in the products of reactions with disubstituted aziridine **4**. A 1,4-benzoquinone additive was found to have a beneficial effect on the yields of reactions with the less-reactive 2-aryl-*N*-tosyl aziridines. We postulated that the 1,4-benzoquinone could act as a π-acid, thereby increasing the Lewis acidity of the Pd^{II} catalyst,

although this theory needs to be investigated in future work. In addition to C3–substitution, a Pd^{II}–catalyzed formal [3<M+>2] annulation reaction with 1,3-dimethylindole (**7**) to give a pyrroloindoline was briefly investigated.

Experimental Section

General Considerations

All of the reactions were performed under a nitrogen atmosphere in oven-dried glassware. Anhydrous solvents were purified by passage through a solvent-purification system (purification over activated alumina, a copper catalyst, and/or molecular sieves). Flash-grade silica gel was used for the column chromatography and thin-layer chromatography was performed on silica gel^^60 F254 aluminum-backed sheets. ^{1}H^^NMR and ^{13}C{1H}^^NMR spectra were recorded in $CDCl_3$; coupling constants (*J*) are reported in Hz; and chemical shifts (δ) are reported in ppm, referenced to residual solvent peaks (^{1}H^^NMR) or to the solvent (^{13}C{1H}^^NMR). The following abbreviations are used in the assignment of ^{1}H^^NMR signals: s=singlet, d=doublet, br=broad, app=apparent, td=doublet of triplets, m=multiplet. Other reagents and starting materials were commercially available and used without further purification. HPLC analysis was performed by using a Waters^^1525 binary pump, a Waters^^486 tunable absorbance detector, and a Chiralpak^^AD (25^^cm×0.46^^cm) column. Optical rotations were measured by using a JASCO P-2000 polarimeter in a 10^^mL cell (path length: 1^^dm) and are reported as [α]<broxl>D<brtr>19</broxl> (*c* in g/100^^mL $CHCl_3$) at 19^°C.

Synthesis and Characterization of the Substrates

All of the aziridines were prepared according to the literature procedure reported by Morgan et. al.:[12] 1-tosyl-2-phenyl aziridine (**1^a**),[18] 2-(*p*-tolyl)-1-tosylaziridine (**1^b**),[18--19] 2-(4-bromophenyl)-1-tosylaziridine (**1^c**),[20] 2-(2-chlorophenyl)-1-tosylaziridine (**1^d**),[21-22] 2-(4-iodophenyl)-1-tosylaziridine (**1^e**), 2-(naphthalen-2-yl)-1-tosylaziridine (**1^f**),[23] and 1-tosyl-2-methyl-2-phenylaziridine (**4**).[24]

*General Procedure for the Synthesis of Indoles **2^a, 2^d--2^i**[25]*

DMSO (0.2^M) was mixed with KOH (4.0^^equiv) under stirring for 30^^min. Then, the corresponding indole (1.0^^equiv) was added and the resulting mixture was stirred at RT for 1^^h. Next, iodomethane (2.0^^equiv) was added dropwise and the mixture was stirred for a further 24^^h. The reaction mixture was diluted with Et_2O (50^^mL) and washed with water (3×50^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. Purification by flash column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the target compounds.

1-Methylindole (2^a): The target compound was synthesized according to the general procedure, with 1*H*-indole (5.00^^g, 38.1^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a brown liquid (4.75^^g, 95^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.60 (d, *J*=7.5^^Hz, 1^H), 7.25 (d, *J*=8.0^^Hz, 1^H), 7.19 (t, *J*=7.0^^Hz, 1^H), 7.08 (t, *J*=7.0^^Hz, 1^H), 6.94 (d, *J*=3.0^^Hz, 1^H), 6.45 (d, *J*=3.0^^Hz, 1^H), 3.64^^ppm (s, 1^H). These data matched the literature data.[26]

5-Bromo-1-methylindole (2^d): The target compound was synthesized according to the general procedure, with 5-bromoindole (300^^mg, 1.53^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a yellow solid (286^^mg, 89^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.74 (s, 1^H), 7.30--7.28 (m, 1^H), 7.19 (d, *J*=8.0^^Hz, 1^H), 7.05 (d, *J*=3.0^^Hz, 1^H), 6.42 (d, *J*=3.0^^Hz, 1^H), 3.77^^ppm (s, 3^H). These data matched the literature data.[26]

5-Iodo-1-methylindole (2^e): The target compound was synthesized according to the general procedure, with 5-iodoindole (500^^mg, 2.06^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a brown solid (508^^mg, 96^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.95 (s, 1^H), 7.46 (d, *J*=9.0^^Hz, 1^H), 7.10 (d, *J*=8.0^^Hz, 1^H), 7.00 (d, *J*=3.5^^Hz, 1^H), 6.40 (d, *J*=2.0^^Hz, 1^H), 3.77^^ppm (s, 3^H). These data matched the literature data.[27]

5-Methoxy-1-methylindole (2^g): The target compound was synthesized according to the general procedure, with 5-methoxyindole (500^^mg, 3.40^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a brown solid (510^^mg, 93^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.21 (d, *J*=9.0^^Hz, 1^H), 7.09 (d, *J*=2.0^^Hz, 1^H), 7.02 (d, *J*=2.5^^Hz, 1^H), 6.89 (dd, *J*=8.5, 2^^Hz, 1^H), 6.40 (d, *J*=3.0^^Hz, 1^H), 3.85 (s, 3^H), 3.77^^ppm (s, 3^H). These data matched the literature data.[28]

7-Iodo-1-methylindole (2^i): The target compound was synthesized according to the general procedure, with 7-

iodoindole (300^^mg, 1.24^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a brown solid (312^^mg, 98^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.66 (d, *J*=7.5^^Hz, 1^H), 7.56 (d, *J*=7.5^^Hz, 1^H), 7.00 (d, *J*=3.0^^Hz, 1^H), 7.76 (t, *J*=8.0^^Hz, 1^H), 6.40 (d, *J*=3.0^^Hz, 1^H), 4.17^^ppm (s, 3^H).[29]

7-Fluoro-1-methylindole (2^f): The target compound was synthesized according to the general procedure, with 5-fluoroindole (300^^mg, 2.22^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a red solid (252^^mg, 76^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.28--7.19 (m, 2^H), 7.07 (d, *J*=3.0^^Hz, 1^H), 6.99--6.93 (m, 1^H), 6.43 (d, *J*=2.4^^Hz, 1^H), 3.78^^ppm (s, 3^H). These data matched the literature data.[30]

1,3-Dimethylindole (7): The target compound was synthesized according to the general procedure, with 3-methylindole (1.00^^g, 7.62^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a yellow liquid in quantitative yield. ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.57 (d, *J*=8.0^^Hz, 1^H), 7.27(t, *J*=8.5^^Hz, 1^H), 7.22 (t, *J*=7.0^^Hz, 1^H), 7.11 (t, *J*=7.0^^Hz, 1^H), 6.82 (s, 1^H), 3.73 (s, 3^H), 2.33^^ppm (s, 3^H). These data matched the literature data.[26]

*Synthesis of N-Benzylindole (**2^b**)*[25]

Benzyl bromide (0.913^^mL, 1.31^^g, 7.68^^mmol, 1.5^^equiv) was added to a solution of 1*H*-indole (600^^mg, 5.12^^mmol, 1.0^^equiv) and KOH (0.431^^mg, 7.68^^mmol, 1.5^^equiv) in DMF (11^^mL). The resulting mixture was stirred overnight, diluted with EtOAc (20^^mL), and washed with

distilled water (3×20^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 30:70 v/v) gave the product as a white solid (871^^g, 82^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.65 (d, *J*=8.0^^Hz, 1^H), 7.31--7.25 (m, 4^H), 7.17 (t, *J*=7.5^^Hz, 1^H), 7.13--7.09 (m, 4^H), 6.55 (s, 1^H), 5.33^^ppm (s, 2^H). These data matched the literature data.[25]

*Synthesis of N-Allylindole (**2^c**)*[31]

Allyl bromide (0.410^^mL, 0.573^^g, 4.70^^mmol, 1.1^^equiv) was added to a solution of 1*H*-indole (500^^mg, 4.27^^mmol, 1.0^^equiv) and NaOH (0.342^^mg, 8.54^^mmol, 2.0^^equiv) in DMSO (11^^mL). The resulting mixture was stirred overnight, diluted with EtOAc (20^^mL), and washed with distilled water (3×20^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 20:80 v/v) gave the product as a white solid (457^^mg, 68^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.64 (t, *J*=7.0^^Hz, 1^H), 7.33 (t, *J*=7.0^^Hz, 1^H), 7.25--7.18 (m, 1^H), 7.13--7.19 (m, 2^H), 6.52 (d, *J*=4.0^^Hz, 1^H), 6.04--5.97 (m, 1^H), 5.21 (dd, *J*=4.5, 6^^Hz, 1^H), 5.10 (d, *J*=17.0^^Hz, 1^H), 4.74^^ppm (d, *J*=1.5^^Hz, 2^H). These data matched the literature data.[32]

*General Procedure for the Synthesis of Compounds **3^a**--**3^p***

Aziridine **1^a**--**1^f** (1.0^^equiv) was added to a solution of indole **2^a**--**2^j** (1.5^^equiv), $[PdCl_2(MeCN)_2]$ (0.1^^equiv), and 1,4-benzoquinone (0.3^^equiv) at RT in air. The resulting

mixture was stirred at RT for 21^^h, diluted with EtOAc (10^^mL), and washed with distilled water (3×10^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) to give the target products.

4-Methyl-*N*-(2-(1-methyl-1^H-indol-3-yl)-2-phenylethyl) benzenesulfonamide (3^a): The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^a**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (57.2^^mg, 77^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.65 (d, *J*=8.1^^Hz, 2^H), 7.28--7.15 (m, 10^H), 6.98 (t, *J*=7.8^^Hz, 1^H), 6.76 (s, 1^H), 4.38 (t, *J*=6.0^^Hz, 1^H), 4.30 (t, *J*=7.5^^Hz, 1^H), 3.71 (s, 3^H), 3.66--3.50 (m, 2^H), 2.42^^ppm (s, 3^H); ^{13}C^^NMR (125^^MHz, $CDCl_3$): δ=143.4, 141.1, 137.2, 136.7, 129.7, 128.8, 127.9, 127.2, 127.0, 126.8, 126.7, 122.0, 119.2, 119.2, 113.9, 109.4, 47.5, 42.5, 32.8, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3743, 3277, 2364, 1741, 1551, 1482, 1424, 1370, 1317, 1213, 1157, 1095, 1050, 915, 868, 809, 763, 703^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{24}N_2O_2SNa$: 427.1456 [*M*<M+>Na]$^{<M+>}$; found: 427.1469.

4-Methyl-*N*-(2-(1-methyl-1^H-indol-3-yl)-2-(p-tolyl)ethyl)benzenesulfonamide (3^b): The target compound was synthesized according to the general procedure, with aziridine **1^b** (100^^mg, 0.348^^mmol) and indole **2^a**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (87.4^^mg, 60^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.65 (d, *J*=7.8^^Hz, 2^H),

7.28--7.19 (m, 5^H), 7.05(s, 4^H), 6.98 (t, *J*=7.2^^Hz, 1^H), 6.75 (s, 1^H), 4.38 (t, *J*=6.0^^Hz, 1^H), 4.26 (t, *J*=7.2^^Hz, 1^H), 3.71 (s, 3^H), 3.63--3.49 (m, 2^H), 2.43 (s, 3^H), 2.29^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=143.4, 142.3, 138.0, 137.2, 136.8, 136.6, 129.7, 129.4, 127.8, 127.2, 126.7, 121.9, 119.2, 119.1, 114.1, 109.3, 47.5, 42.1, 32.8, 21.6, 21.0^^ppm; IR (KBr): <Gn><Ü=>=3323, 2949, 2835, 2367, 1650, 1512, 1449, 1410, 1326, 1157, 1094, 1018, 813, 740, 660^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{25}H_{26}N_2O_2SNa$: 441.1613 [*M*<M+>Na]$^{<M+>}$; found: 441.1635.

***N*-(2-(4-Bromophenyl)-2-(1-methyl-1^H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide (3^c)**: The target compound was synthesized according to the general procedure, with aziridine **1^c** (100^^mg, 0.284^^mmol) and indole **2^a**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless liquid (86.5^^mg, 63^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.63 (d, *J*=8.4^^Hz, 2^H), 7.34 (d, *J*=8.1^^Hz, 2^H), 7.29--7.17(m, 4^H), 7.06--6.96 (m, 4^H), 6.78 (s, 1^H), 4.55 (t, *J*=6.0^^Hz, 1^H), 4.28 (t, *J*=7.8^^Hz, 1^H), 3.72 (s, 3^H), 3.60--3.47 (m, 2^H), 2.43^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=143.5, 140.4, 137.3, 136.6, 131.7, 129.7, 129.7, 127.1, 126.7, 126.7, 122.1, 120.7, 119.3, 119.1, 113.3, 109.5, 47.3, 42.1, 32.8, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3276, 2933, 2360, 1636, 1560, 1486, 1424, 1375, 1327, 1158, 1094, 1072, 1010, 813, 738, 661^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}BrN_2O_2SNa$: 505.0561 [*M*<M+>Na]$^{<M+>}$; found: 505.0591.

***N*-(2-(2-Chlorophenyl)-2-(1-methyl-1^H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide (3^d)**: The target compound was

synthesized according to the general procedure, with aziridine **1^d** (100^^mg, 0.325^^mmol) and indole **2^a**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless liquid (81.3^^mg, 57^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.65 (d, *J*=8.1^^Hz, 2^H), 7.34--7.07 (m, 9^H), 6.99 (t, *J*=7.5^^Hz, 1^H), 6.87 (s, 1^H), 4.84 (t, *J*=6.9^^Hz, 1^H), 4.57 (t, *J*=7.0^^Hz, 1^H), 3.72 (s, 3^H), 3.57 (app^t, *J*=6.6^^Hz, 2^H), 2.42^^ppm (s, 3^H); ^{13}C^^NMR (125^^MHz, $CDCl_3$): δ=143.4, 138.7, 137.2, 136.6, 133.8, 129.8, 129.7, 129.0, 128.1, 127.2, 127.1, 127.0, 127.0, 122.1, 119.2, 119.1, 112.8, 109.4, 46.2, 38.7, 32.8, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3281, 2958, 2356, 1641, 1599, 1565, 1473, 1424, 1375, 1325, 1155, 1094, 1015, 812, 739, 706, 658^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}ClN_2O_2SNa$: 461.1066 [*M*<M+>Na]$^{<M+>}$; found: 461.1073.

***N*-(2-(4-Iodophenyl)-2-(1-methyl-1^H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide (3^e)**: The target compound was synthesized according to the general procedure, with aziridine **1^e** (78.0^^mg, 0.195^^mmol) and indole **2^a**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless liquid (61.0^^mg, 59^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.62 (d, *J*=8.5^^Hz, 2^H), 7.53 (d, *J*=8.5^^Hz, 2^H), 7.26--7.17 (m, 5^H), 6.98 (t, *J*=7.5^^Hz, 1^H), 6.91 (d, *J*=8.5^^Hz, 2^H), 6.77 (s, 1^H), 4.55 (t, *J*=6.0^^Hz, 1^H), 4.26 (t, *J*=7.5^^Hz, 1^H), 3.70 (s. 3^H), 3.60--3.56 (m, 1^H), 3.51--3.47 (m, 1^H), 2.42^^ppm (s, 3^H); ^{13}C^^NMR (125^^MHz, $CDCl_3$): δ=143.5, 141.0, 137.7, 137.3, 136.7, 130.0, 129.7, 127.1, 126.7, 126.7, 122.1, 119.3, 119.1, 113.3, 109.5, 92.3, 47.2, 42.3, 32.8, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3289, 2936, 1701, 1648, 1484, 1328, 1327, 1325, 1159,

1158, 1157, 1090, 1005, 900, 811, 742, 741, 672^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}IN_2O_2SNa$: 553.0423 [*M*<M+>Na]$^{<M+>}$; found: 553.0402.

4-Methyl-*N*-(2-(1-methyl-1^H-indol-3-yl)-2-(naphthalen-2-yl)ethyl)benzenesulfonamide (3^f): The target compound was synthesized according to the general procedure, with aziridine **1^f** (50.0^^mg, 0.155^^mmol) and indole **2^a**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless liquid (55.0^^mg, 78^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): *δ*=7.78--7.85 (m, 1^H), 7.70 (d, *J*=8.4^^Hz, 2^H), 7.63--7.61 (m, 3^H), 7.47--7.40 (m, 3^H), 7.30--7.15 (m, 5^H), 6.96 (t, *J*=7.2^^Hz, 1^H), 6.81 (s, 1^H), 4.52 (t, *J*=5.9^^Hz, 1^H), 4.47 (t, *J*=7.5^^Hz, 1^H), 3.78--3.70 (m, 1^H), 3.70 (s, 3^H), 3.66--3.57 (m, 1^H), 2.41^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=143.3, 138.6, 137.3, 136.8, 133.4, 132.5, 129.7, 128.5, 127.8, 127.6, 127.1, 126.7, 126.8, 126.4, 126.2, 125.8, 122.0, 119.2, 114.0, 109.4, 47.4, 42.7, 32.8, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3290, 3058, 2935, 2319, 1607, 1470, 1420, 1326, 1156, 1093, 1013, 908, 858, 813, 736, 662^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{28}H_{26}N_2O_2SNa$: 477.1613 [*M*<M+>Na]$^{<M+>}$; found: 477.1616.

***N*-(2-(1-Benzyl-1^H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^g)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^b**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a white solid (52.8^^mg, 60^% yield). M.p. 130--135^°C; ^{1}H^^NMR (300^^MHz, $CDCl_3$): *δ*=7.64 (d, *J*=7.8^^Hz, 2^H), 7.34--7.06 (m, 15^H), 6.99 (t, *J*=7.8^^Hz,

1^H), 6.85 (s, 1^H), 5.25 (s, 2^H), 4.38 (t, *J*=5.7^^Hz, 1^H), 4.33 (t, *J*=7.5^^Hz, 1^H), 3.70--3.48 (m, 2^H), 2.42^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=143.4, 141.0, 137.3, 136.9, 136.8, 129.7, 128.8, 128.8, 128.0, 127.7, 127.1, 127.0, 126.6, 126.0, 126.0, 122.2, 119.5, 119.4, 114.7, 109.9, 50.0, 47.5, 42.6, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3290, 3030, 2255, 1599, 1550, 1496, 1453, 1399, 1327, 1157, 1093, 1074, 1017, 908, 814, 730, 699, 662^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{30}H_{28}N_2O_2SNa$: 503.1769 [*M*<M+>Na]$^{<M+>}$; found: 503.1778.

***N*-(2-(1-Allyl-1^H-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (3^h)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^c**. The reaction was performed in CH_2Cl_2. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (67.9^^mg, 86^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): *δ*=7.66 (d, *J*=8.4^^Hz, 2^H), 7.33--7.16 (m, 10^H), 6.99 (t, *J*=7.2^^Hz, 1^H), 6.82 (s, 1^H), 6.01--5.92 (m, 1^H), 5.20 (d, *J*=10.2^^Hz, 1^H), 5.08 (d, *J*=17.1^^Hz, 1^H), 4.66 (d, *J*=5.4^^Hz, 2^H), 4.40 (t, *J*=6.0^^Hz, 1^H), 4.31 (t, *J*=7.8^^Hz, 1^H), 3.70--3.48 (m, 2^H), 2.44^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=143.4, 141.0, 136.8, 136.7, 133.3, 129.9, 129.7, 128.8, 127.9, 127.1, 127.1, 127.0, 125.6, 122.0, 119.3, 117.5, 114.4, 109.8, 48.8, 47.5, 42.6, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3300, 3033, 2926, 1598, 1546, 1494, 1466, 1452, 1405, 1325, 1184, 1156, 1093, 1074, 1016, 990, 909, 813, 735, 731, 699, 663^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{27}H_{28}N_2O_2SNa$: 453.1613 [*M*<M+>Na]$^{<M+>}$; found: 453.1593.

***N*-(2-(5-Bromo-1-methyl-1^H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^i)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^d**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (76.1^^mg, 86^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.66 (d, *J*=8.5^^Hz, 2^H), 7.30--7.22 (m, 7^H), 7.16--7.13 (m, 3^H), 6.83 (s, 1^H), 4.39 (t, *J*=6.0^^Hz, 1^H), 4.19 (t, *J*=7.0^^Hz, 1^H), 3.71 (s, 3^H), 3.55 (app^q, *J*=7.5^^Hz, 2^H), 2.46^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=143.6, 140.7, 136.7 , 135.9, 129.8, 128.9, 128.5, 127.9, 127.8, 127.2, 127.1, 124.9, 121.6, 113.6, 112.6, 110.9, 47.4, 42.2, 33.0, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3296, 2882, 1598, 1477, 1423, 1324, 1213, 1158, 1093, 1073, 908, 814, 793, 730, 701, 662^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{24}BrN_2O_2S$: 483.0742 [*M*<M+>H]$^{<M+>}$; found: 483.0733.

***N*-(2-(5-Iodo-1-methyl-1^H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^j)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^e**. Purification by column chromatography on silica gel (EtOAc/ *n*-hexane, 40:60 v/v) gave the product as a colorless oil (69.9^^mg, 72^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.65 (d, *J*=8.0^^Hz, 2^H), 7.51 (s, 1^H), 7.42 (d, *J*=8.0^^Hz, 1^H), 7.31--7.28 (m, 2^H), 7.26 (d, *J*=8.0^^Hz, 2^H), 7.23--7.20 (m, 1^H), 7.14 (d, *J*=7.0^^Hz, 2^H), 7.03 (d, *J*=8.5^^Hz, 1^H), 6.77 (s, 1^H), 4.42 (t, *J*=6.0^^Hz, 1^H), 4.18 (t, *J*=7.5^^Hz, 1^H), 3.69 (s, 3^H), 3.53 (app^q, *J*=6.5^^Hz, 2^H), 2.46^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=143.6, 140.7, 136.7, 136.3, 130.3, 129.9, 129.4, 128.9, 127.9, 127.8, 127.6, 127.2, 127.1, 113.4, 111.4,

82.8, 47.5, 42.2, 32.9, 21.7^^ppm; IR (KBr): <Gn><Ü=>=3751, 3651, 3275, 2880, 2362, 1650, 1541, 1475, 1422, 1326, 1158, 1093, 909, 813, 792, 732, 665^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}IN_2O_2SNa$: 553.0423 [*M*<M+>Na]$^{<M+>}$; found: 553.0444.

***N*-(2-(5-Methoxy-1-methyl-1^H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^k)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^g**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (39.8^^mg, 50^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.65 (d, *J*=8.0^^Hz, 2^H), 7.26 (d, *J*=7.5^^Hz, 4^H), 7.22--7.15 (m, 4^H), 6.85 (dd, *J*=8.5, 2.5^^Hz, 1^H), 6.72 (s, 1^H), 6.70 (d, *J*=2.0^^Hz, 1^H), 4.40 (t, *J*=6.0^^Hz, 1^H), 4.28 (t, *J*=7.5^^Hz, 1^H), 3.72 (s, 3^H), 3.69 (s, 3^H), 3.64--3.61 (m, 1^H), 3.54--3.50 (m, 1^H), 2.43^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=153.8, 143.4, 141.0, 136.7, 132.1, 132.3, 129.7, 128.8, 127.9, 127.3, 127.1, 127.0, 113.3, 112.1, 110.1, 101.0, 55.8, 47.3, 42.6, 32.9, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3281, 2938, 1623, 1599, 1491, 1452, 1424, 1326, 1266, 1212, 1158, 1093, 1065, 1035, 815, 794, 734, 665^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{25}H_{26}N_2O_3SNa$: 457.1567 [*M*<M+>Na]$^{<M+>}$; found: 457.1562.

***N*-(2-(7-Iodo-1-methyl-1^H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^l)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^i**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (73.8^^mg, 76^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.65 (d, *J*=8.0^^Hz, 2^H),

7.62 (d, *J*=7.0^^Hz, 1^H), 7.27--7.20 (m, 6^H), 7.14 (d, *J*=7.5^^Hz, 2^H), 6.75 (s, 1^H), 6.64 (t, *J*=8.0^^Hz, 1^H), 4.42 (t, *J*=6.0^^Hz, 1^H), 4.27 (t, *J*=7.5^^Hz, 1^H), 4.09 (s, 3^H), 3.63--3.57 (m, 1^H), 3.52--3.46 (m, 1^H), 2.43^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=143.5, 140.6, 136.8, 136.0, 134.4, 129.8, 129.7, 129.3, 128.8, 127.8, 127.2, 127.1, 120.9, 119.3, 113.5, 73.0, 47.4, 42.1, 36.8, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3292, 2919, 1599, 1550, 1482, 1451, 1405, 1324, 1303, 1156, 1089, 1065, 1028, 838, 813, 737, 699, 665^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}IN_2O_2SNa$: 553.0423 [*M*<M+>Na]$^{<M+>}$; found: 553.0433.

***N*-(2-(5-Fluoro-1-methyl-1^H-indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^m)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and indole **2^f**. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (46.4^^mg, 60^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): *δ*=7.65 (d, *J*=8.0^^Hz, 2^H), 7.29--7.14 (m, 8^H), 6.92 (td, *J*=9.0, 2.0^^Hz, 1^H), 6.86 (s, 1^H), 6.79 (dd, *J*=9.5, 2.0^^Hz, 1^H), 4.36 (t, *J*=6.0^^Hz, 1^H), 4.20 (t, *J*=7.5^^Hz, 1^H), 3.72 (s, 3^H), 3.58--3.52 (m, 2^H), 2.44^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=157.5 (d, *J*=234^^Hz), 143.6, 140.8, 136.6, 133.9, 129.8, 128.8, 128.3, 127.8, 127.1, 127.0, 126.9, 113.7 (d, *J*=4.6^^Hz), 110.4 (d, *J*=26.7^^Hz), 110.1 (d, *J*=11.5^^Hz), 104.1 (d, *J*=23^^Hz), 47.3, 42.4, 33.1, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3283, 2933, 1598, 1490, 1452, 1424, 1325, 1158, 1093, 909, 814, 794, 730, 701, 669, 665, 659^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}FN_2O_2SNa$: 423.1543 [*M*<M+>Na]$^{<M+>}$; found: 423.1525.

***N*-(2-(1^H-Indol-3-yl)-2-phenylethyl)-4-methylbenzenesulfonamide (3^n)**: The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and 1*H*-indole. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (54.3^^mg, 76^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=8.06 (br^s, 1^H), 7.66 (d, *J*=8.0^^Hz, 2^H), 7.35 (d, *J*=7.5^^Hz, 1^H), 7.28--7.25 (m, 5^H), 7.22 (d, *J*=7.0^^Hz, 1^H), 7.18--7.15 (m, 3^H), 7.00 (t, *J*=8^^Hz, 1^H), 6.97 (s, 1^H), 4.38 (t, *J*=6.0^^Hz, 1^H), 4.32 (t, *J*=7.5^^Hz, 1^H), 3.69--3.66 (m, 1^H), 3.56--3.53 (m, 1^H), 2.44^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=143.5, 140.9, 136.8, 136.5, 129.7, 128.8, 127.9, 127.1, 127.0, 126.4, 122.5, 121.9, 119.7, 119.2, 115.6, 111.2, 47.4, 42.6, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3438, 3329, 2360, 2157, 1968, 1653, 1491, 1457, 1402, 1317, 1150, 1093, 1012, 867, 808, 755, 699, 657^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{23}H_{22}N_2O_2SNa$: 413.1300 [*M*<M+>Na]$^{<M+>}$; found: 413.1286.

4-Methyl-*N*-(2-phenyl-2-(1^H-pyrrol-3-yl)ethyl)benzenesulfonamide (3^o): The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and 1*H*-pyrrole. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a dark oil (9.35^^mg, 15^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.81 (br^s, 1^H), 7.62 (d, *J*=8.5^^Hz, 2^H), 7.24--7.16 (m, 6^H), 7.02 (d, *J*=7.0^^Hz, 2^H), 6.59 (s, 1^H), 6.07 (d, *J*=2.5^^Hz, 1^H), 5.88 (s, 1^H), 4.39 (t, *J*=6.0^^Hz, 1^H), 4.04 (t, *J*=7.5^^Hz, 1^H), 3.45--3.40 (m, 1^H), 3.37--3.32 (m, 1^H), 2.37^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=142.6, 138.8, 135.7, 129.6, 128.8, 128.0,

127.0, 126.5, 126.1, 116.7, 107.5, 104.7, 46.4, 43.5, 20.5^^ppm; IR (KBr): <Gn><Ü=>=3281, 2935, 1696, 1599, 1550, 1491, 1448, 1395, 1324, 1158, 1093, 1023, 812, 700, 658^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{19}H_{20}N_2O_2SNa$: 363.1143 [*M*<M+>Na]$^{<M+>}$; found: 363.1133.

4-Methyl-*N*-(2-phenyl-2-(2-phenyl-1^H-indol-3-yl)ethyl)benzenesulfonamide (3^p): The target compound was synthesized according to the general procedure, with aziridine **1^a** (50.0^^mg, 0.183^^mmol) and 2-phenyl-1*H*-indole. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (53.8^^mg, 63^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): *δ*=8.31 (br^s, 1^H), 7.44 (d, *J*=8.5^^Hz, 2^H), 7.40 (d, *J*=8.0^^Hz, 1^H), 7.35 (app^s, 6^H), 7.24--7.18 (m, 6^H), 7.09 (d, *J*=7.5^^Hz, 2^H), 6.93 (t, *J*=7.5^^Hz, 1^H), 4.44 (dd, *J*=11.0, 6.0^^Hz, 1^H), 4.22 (app^d, *J*=8.0^^Hz, 1^H), 3.76--3.72 (m, 1^H), 3.64 (t, *J*=11.0^^Hz, 1^H), 2.38^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=143.1, 141.6, 137.7, 136.2, 136.2, 132.1, 129.6, 128.9, 128.7, 128.7, 128.4, 127.7, 127.0, 127.0, 126.7, 122.5, 120.2, 120.0, 111.5, 109.5, 46.7, 42.2, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3346, 2941, 1599, 1491, 1450, 1399, 1319, 1154, 1093, 1019, 922, 845, 813, 743, 700, 661^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{23}H_{22}N_2O_2SNa$: 489.1613 [*M*<M+>Na]$^{<M+>}$; found: 489.1628.

*General Procedure for the Synthesis of Compounds **5^a**--**5^g***

A solution of 2-methyl-2-phenyl-1-tosyl aziridine (**4**; 3.0^^equiv) in anhydrous DCE (30^^mL) was added dropwise over 6^^h to a solution of *N*-methylindole **2^a**--**2^h** (1.0^^equiv) in anhydrous DCE (10^^mL) at 0^°C under a nitrogen atmosphere.

The resulting mixture was stirred at 0^°C overnight, diluted with EtOAc (20^^mL), and washed with distilled water (3×20^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) to give the product as a colorless oil.

4-Methyl-*N*-(2-(1-methyl-1^*H*-indol-3-yl)-2-phenylpropyl)benzenesulfonamide (5^a): The target compound was synthesized according to the general procedure, with aziridine **4** (100^^mg, 0.348^^mmol) and compound **2^a** (15.4^^mg, 0.116^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (45.2^^mg, 93^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.49 (d, *J*=8.5^^Hz, 2^H), 7.28 (d, *J*=8.5^^Hz, 1^H), 7.25--7.14 (m, 8^H), 7.01 (s, 1^H), 6.76--6.72 (m, 2^H), 4.03 (dd, *J*=8.5, 4.5^^Hz, 1^H), 3.79 (s, 3^H), 3.65 (dd. *J*=11.5, 9.0^^Hz, 1^H), 3.53 (dd, *J*=11.5, 4.5^^Hz, 1^H), 2.39 (s, 3^H), 1.73^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=145.7, 143.2, 137.7, 136.1, 129.6, 128.4, 127.8, 126.9, 126.6, 126.5, 125.6, 121.7, 120.7, 118.9, 117.8, 109.4, 51.5, 43.0, 32.9, 27.3, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3337, 2978, 2922, 1647, 1560, 1540, 1473, 1452, 1374, 1317, 1155, 1085, 1045, 879, 663^^cm$^{<M->1}$; HRMS: *m*/*z* calcd for $C_{25}H_{26}N_2O_2SNa$: 441.1613 [*M*<M+>Na]$^{<M+>}$; found: 441.1620.

***N*-(2-(1-Benzyl-1^*H*-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^b)**: The target compound was synthesized according to the general procedure, with aziridine **4** (90.4^^mg, 0.315^^mmol) and compound **2^b** (22.0^^mg, 0.105^^mmol). Purification by column chromatography on silica

gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (73.5^^mg, 81^% yield; 8^% of an inseparable compound was also produced). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.48 (d, *J*=8.5^^Hz, 2^H), 7.35--7.08 (m, 15^H), 6.76 (d, *J*=8.1^^Hz, 1^H), 6.75 (s, 1^H), 5.32 (d, *J*=5^^Hz, 2^H) 4.00 (dd, *J*=7.5, 4.0^^Hz, 1^H), 3.66 (dd, *J*=11.5, 8.5^^Hz, 1^H), 3.54 (dd, *J*=11.0, 4.0^^Hz, 1^H), 2.38 (s, 3^H), 1.73^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=145.5, 143.2, 137.4, 137.3, 136.1, 129.6, 128.9, 128.5, 127.7, 127.1, 127.0, 126.9, 126.6, 126.6, 125.9, 121.9, 120.9, 119.1, 118.8, 110.0, 51.5, 50.1, 43.1, 27.1, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3287, 3061, 2923, 1598, 1543, 1496, 1453, 1402, 1327, 1184, 1160, 1092, 1062, 1029, 965, 909, 814, 729, 699, 665^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{31}H_{30}N_2O_2SNa$: 517.1926 [*M*<M+>Na]$^{<M+>}$; found: 517.1951.

***N*-(2-(1-Allyl-1^*H*-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^c)**: The target compound was synthesized according to the general procedure, with aziridine **4** (130^^mg, 0.452^^mmol) and compound **2^c** (23.7^^mg, 0.151^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (51.0^^mg, 73^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.50 (d, *J*=8.0^^Hz, 2^H), 7.29--7.16 (m, 8^H), 7.12 (t, *J*=7.5^^Hz, 1^H), 7.05 (s, 1^H), 6.78--6.72 (m, 2^H), 6.06--6.00 (m, 1^H), 5.25 (d, *J*=10.0^^Hz, 1^H), 5.14 (d, *J*=17.0^^Hz, 1^H), 4.50 (d, *J*=1.5^^Hz, 2^H), 4.02 (dd, *J*=8.0, 4.0^^Hz, 1^H), 3.66 (dd, *J*=11.0, 8.0^^Hz, 1^H), 3.54 (dd, *J*=11.0, 4.0^^Hz, 1^H), 2.39 (s, 3^H), 1.73^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=145.6, 143.2, 137.2, 136.2, 133.3, 129.6, 128.6, 128.5, 127.0, 126.6, 126.5, 125.9, 121.7, 120.8, 119.0, 118.4, 117.6, 109.8, 51.6, 48.9, 43.1, 27.2, 21.5^^ppm;

IR (KBr): <Gn><Ü=>=3299, 2360, 1635. 1539, 1466, 1399, 1328, 1186, 1161, 1093, 1061, 812, 739, 699, 663^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{27}H_{28}N_2O_2Na$: 467.1769 [*M*<M+>Na]$^{<M+>}$; found: 467.1788.

***N*-(2-(5-Bromo-1-methyl-1^*H*-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^d)**: The target compound was synthesized according to the general procedure, with aziridine **4** (101^^mg, 0.352^^mmol) and compound **2^d** (25.0^^mg, 0.117^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (53.4^^mg, 91^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.47 (d, *J*=8.5^^Hz, 2^H), 7.26--7.12 (m, 9^H), 7.04 (s, 1^H), 6.80 (s, 1^H), 4.01 (dd, *J*=9.0, 4.0^^Hz, 1^H), 3.77 (s, 3^H), 3.65 (dd, *J*=11.0, 8.5^^Hz, 1^H), 3.41 (dd, *J*=11.4, 4.0, 1^H), 2.41 (s, 3^H), 1.71^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=145.2, 143.4, 136.4, 135.8, 129.7, 129.1, 128.6, 127.2, 126.9, 126.8, 126.5, 124.7, 122.9, 117.5, 112.4, 111.0, 51.4, 42.9, 33.1, 27.3, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3289, 2916, 1705, 1653, 1573, 1488, 1420, 1317, 1161, 1093, 1060, 1029, 813, 792, 765, 700, 668^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{25}H_{24}BrN_2O_2S$: 495.0742 [*M*<M->H]$^{<M->}$; found: 495.0720.

***N*-(2-(5-Iodo-1-methyl-1^*H*-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^e)**: The target compound was synthesized according to the general procedure, with aziridine **4** (83.0^^mg, 0.288^^mmol) and compound **2^e** (25.0^^mg, 0.0961^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (23.0^^mg, 44^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=7.47 (d, *J*=8.0^^Hz, 2^H), 7.39 (d, *J*=8.5^^Hz, 1^H), 7.26--7.20 (m, 5^H), 7.12 (d, *J*=7.5^^Hz, 2^H), 7.06 (d,

J=8.5^^Hz, 1^H), 7.02 (m, 1^H), 6.99 (s, 1^H), 4.91--3.99 (m, 1^H), 3.77 (s, 3^H), 3.65 (dd, *J*=11.0, 8.5^^Hz, 1^H), 3.41 (dd, *J*=11.0, 3.5^^Hz, 1^H), 2.42 (s, 3^H), 1.71^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=145.1, 143.4, 136.8, 135.8, 130.1, 129.8, 129.1, 128.7, 128.5, 128.0, 126.8, 126.7, 126.4, 117.2, 111.5, 82.7, 51.4, 42.9, 33.0, 27.3, 21.7^^ppm; IR (KBr): <Gn><Ü=>=3272, 2973, 1701, 1636, 1542, 1471, 1418, 1330, 1160, 1091, 895, 814, 766, 701, 666^^cm$^{<M->1}$; HRMS: *m*/*z* calcd for $C_{25}H_{24}IN_2O_2S$: 543.0603 [*M*<M->H]$^{<M->}$; found: 543.0595.

***N*-(2-(5-Fluoro-1-methyl-1^H-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^f)**: The target compound was synthesized according to the general procedure, with aziridine **4** (143^^mg, 0.496^^mmol) and compound **2^f** (25.0^^mg, 0.165^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (50.4^^mg, 70^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): *δ*=7.47 (d, *J*=8.0^^Hz, 2^H), 7.23--7.13 (m, 8^H), 7.07 (s, 1^H), 6.79 (dd, *J*=8.5, 2.0^^Hz, 1^H), 7.27 (dd, *J*=10.0, 2.0^^Hz, 1^H), 4.07--4.05 (m, 1^H), 3.77 (s, 3^H), 3.65 (dd, *J*=11.0, 8.5^^Hz, 1^H), 3.43 (dd, *J*=11.0, 3.5^^Hz, 1^H), 2.39 (s, 3^H), 1.70^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): *δ*=157.0 (d, *J*=234^^Hz) 145.3, 143.5, 135.8, 134.4, 129.6, 129.5, 128.5, 126.9, 126.7, 126.5, 125.7 (d, *J*=10^^Hz) 117.6 (d, *J*=5^^Hz) 110.2 (d, *J*=9^^Hz) 110.0 (d, *J*=7^^Hz) 105.5 (d, *J*=24^^Hz), 51.3, 42.9, 33.2, 27.2, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3272, 2984, 1700, 1653, 1496, 1490, 1448, 1416, 1325, 1241, 1161, 1083, 1022, 886, 800, 764, 715, 665^^cm$^{<M->1}$; HRMS: *m*/*z* calcd for $C_{25}H_{24}FN_2O_2S$: 435.1543 [*M*<M->H]$^{<M->}$; found: 435.1559.

***N*-(2-(5-Methoxy-1-methyl-1^*H*-indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^g)**: The target compound was synthesized according to the general procedure, with aziridine **4** (131^^mg, 0.457^^mmol) and compound **2^g** (25.0^^mg, 0.152^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (58.8^^mg, 85^% yield). ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.46 (d, *J*=8.0^^Hz, 2^H), 7.25--7.13 (m, 8^H), 6.99 (s, 1^H), 6.80 (dd, *J*=8.7, 2.4^^Hz, 1^H), 6.04 (d, *J*=2.4^^Hz, 1^H), 4.08--4.05 (m, 1^H), 3.75 (s, 3^H), 3.63 (dd, *J*=10.8, 8.4^^Hz, 1^H), 3.49 (dd, *J*=11.0, 3.6^^Hz, 1^H), 3.42 (s, 3^H), 2.38 (s, 3^H), 1.71^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=153.2, 145.7, 143.2, 136.0, 133.1, 129.5, 128.4, 128.3, 126.9, 126.6, 126.5, 125.9, 117.1, 111.7, 110.1, 102.5, 55.3, 51.2, 42.9, 33.0, 27.2, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3263, 2981, 1700, 1653, 1560, 1491, 1424, 1321, 1225, 1162, 1083, 1010, 814, 715, 659^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{26}H_{27}N_2O_3S$: 447.1718 [*M*<M->H]$^{<M->}$; found: 447.1723.

***N*-(2-(1^*H*-Indol-3-yl)-2-phenylpropyl)-4-methylbenzenesulfonamide (5^h)**: The target compound was synthesized according to the general procedure, with aziridine **4** (184^^mg, 0.640^^mmol) and 1*H*-indole (25.0^^mg, 0.213^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (48.3^^mg, 56^% yield). ^{1}H^^NMR (500^^MHz, $CDCl_3$): δ=8.21 (br^s, 1^H), 7.48 (d, *J*=8.0^^Hz, 2^H), 7.34 (d, *J*=8.5^^Hz, 1^H), 7.22--7.16 (m, 9^H), 7.10 (t, *J*=7.5^^Hz, 1^H), 6.76--6.72 (m, 1^H), 4.07--4.05 (m, 1^H), 3.67 (dd, *J*=11.5, 8.5^^Hz, 1^H), 3.53 (dd, *J*=11.0, 4.0^^Hz, 1^H), 2.38 (s, 3^H), 1.73^^ppm (s, 3^H); ^{13}C^^NMR (75^^MHz, $CDCl_3$):

δ=145.5, 143.2, 137.0, 136.1, 129.6, 128.5, 126.9, 126.6, 126.6, 125.2, 123.0, 122.1, 120.6, 119.6, 119.3, 111.4, 51.5, 43.0, 27.1, 21.5^^ppm; IR (KBr): <Gn><Ü=>=3415, 2967, 1705, 1654, 1570, 1458, 1410, 1321, 1157, 1090, 1014, 961, 813, 742, 700, 662^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{24}H_{23}N_2O_2S$: 403.1480 [*M*<M->H]$^{<M->}$; found: 403.1496.

*Synthesis of (3^aR,8^bS)-4,8^b-dimethyl-1-phenyl-3-tosyl-1,2,3,3^a,4,8^b-hexahydrocyclopenta[b]indole (**8**)*

Aziridine **1^a** (125.4^^mg, 0.459^^mmol, 3.0^^equiv) was added to a solution of 1,3-dimethylindole (**7**; 22.5^^mg, 0.153^^mmol, 1.0^^equiv) and [$PdCl_2(MeCN)_2$] (4.00^^mg, 0.0153^^mmol, 10^^mol^%) in $CHCl_3$ (1.5^^mL) at RT in air. The resulting mixture was stirred at RT for 21^^h, diluted with EtOAc (10^^mL), and washed with distilled water (3×10^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 20/80 v/v) gave a mixture of *trans* and *cis* products (7.3:1.0) as a white solid (157^^mg, 82^% yield). M.p. 135--141^°C; ^{1}H^^NMR (300^^MHz, $CDCl_3$): δ=7.87 (d, *J*=8.0^^Hz, 2^H; *cis*), 7.83 (d, *J*=8.0^^Hz, 2^H; *trans*), 7.39 (d, *J*=7.5^^Hz, 2^H; *cis*), 7.36 (d, *J*=7.0^^Hz, 2^H; *trans*), 7.26--7.21(m, 6^H; *trans*<M+>*cis*), 7.16 (t, *J*=8.0^^Hz, 1^H; *cis*), 7.02 (t, *J*=8.0^^Hz; *trans*), 6.94--6.93 (m, 2^H; *cis*), 6.83 (d, *J*=7.5^^Hz, 2^H; *trans*), 6.64 (t, *J*=7.0^^Hz, 1^H; *trans*), 6.53 (t, *J*=5.5^^Hz, 2^H; *trans*), 6.36 (d, *J*=8.0^^Hz, 1^H; *cis*), 6.28 (t, *J*=7.5^^Hz, 1^H; *trans*), 5.57 (d, *J*=7.5^^Hz, 1^H; *trans*), 5.37 (s, 1^H; *trans*), 5.07 (s, 1^H; *cis*), 3.85--3.77 (m, 3^H; *trans*<M+>*cis)*, 3.62--3.58(m, 1^H; *cis*), 3.41(t, *J*=13.0^^Hz, 1^H; *trans*), 3.05 (s,

3^H; *trans*), 3.04 (s, 3^H; *cis*), 2.74--2.70 (m, 1^H; *trans*), 2.49 (s, 3^H; *trans*<M+>*cis*), 1.27 (s, 3^H; *cis*), 0.49^^ppm (s, 3^H; *trans*); ^{13}C^^NMR (75^^MHz, $CDCl_3$): δ=150.8, 143.8, 137.1, 135.7, 132.5, 129.9, 128.8, 128.4, 127.9, 127.5, 127.3, 125.4, 116.4, 104.9, 91.1, 56.7, 54.9, 51.2, 31.2, 25.9, 21.6^^ppm; IR (KBr): <Gn><Ü=>=3329, 2957, 1663, 1599, 1488, 1448, 1346, 1291, 1161, 1091, 1022, 892, 814, 753, 700, 668, 665, 613, 612^^cm$^{<M->1}$; HRMS: *m/z* calcd for $C_{25}H_{26}N_2O_2SNa$: 441.1613 [*M*<M+>Na]$^{<M+>}$; found: 441.1620.

*Synthesis of (3^S,3^aS,8^aR)-3^a,8-dimethyl-3-phenyl-1,2,3,3^a,8,8^a-hexahydropyrrolo[2,3-b]indole (**9**)*[11a]

A mixture of compound **8** (79^^mg, 0.189^^mmol, 1.0^^equiv), Mg (906^^mg, 37.8^^mmol, 200^^equiv), and NH_4Cl (2.02^^g, 37.8^^mmol, 200^^equiv) in anhydrous MeOH (10^^mL) was sonicated for 6^^h at 30^°C. The reaction mixture was passed through a short pad of silica gel (1^^cm), diluted with EtOAc (30^^mL), and washed with distilled water (3×20^^mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (EtOAc) to give the product as a colorless oily liquid (28^^mg, 56^% yield). ^{1}H^^NMR ($CDCl_3$, 500^^MHz): δ=7.19--7.01 (m, 3^H), 6.99 (t, *J*=7.5^^Hz, 1^H), 6.89--6.87 (m, 2^H), 6.34 (d, *J*=8.0^^Hz, 1^H), 6.25 (t, *J*=7.5^^Hz, 1^H), 5.72 (d, *J*=7.0^^Hz, 1^H), 4.70 (s, 1^H), 3.25 (dd, *J*=10.0, 5.5^^Hz, 1^H), 3.18--2.11 (m, 2^H), 2.90 (s, 3^H), 2.76 (br^s, 1^H); 1.50^^ppm (s, 3^H); ^{13}C^^NMR ($CDCl_3$, 125^^MHz): δ=151.7, 138.2, 131.1, 129.1, 127.8, 127.7, 126.7, 125.4, 116.1, 104.6, 93.2, 59.4, 56.3, 50.6, 32.4, 27.3^^ppm; IR (KBr): <Gn><Ü=>=2923, 1738, 1604, 1496, 1452, 1386, 1342,

1297, 1216, 1155, 1123, 1051, 1022, 984, 912, 810, 742, 699^^cm<M->1>; HRMS: *m/z* calcd for $C_{18}H_{21}N_2$: 265.1705 [*M*<M+>H]<M+>; found: 265.1714.

*Synthesis and Characterization of (R)-Phenylaziridine ((R)-**1^a'**)*[33]

Triethylamine (2.54^^mL, 18.2^^mmol, 2.5^^equiv) was added to a solution of (*R*)-2-phenylglycinol (1.00^^g, 7.29^^mmol, 1.0^^eq, 99^% *ee*) in anhydrous CH_2Cl_2 (100^^mL). Aryl sulfonyl chloride (1.53^^g, 8.02^^mmol, 1.1^^equiv) was added as a single portion and the mixture was stirred at RT for 8^^h. The reaction was quenched with water, extracted with CH_2Cl_2, and dried over anhydrous sodium sulfate. The solvent was removed under vacuum to give the crude product (2.22^^g), which was used in the next step without further purification. The crude product was heated at reflux with KOH (1.28^^g, 22.9^^mmol, 3.0^^equiv) and TsCl (1.60^^g, 8.38^^mmol, 1.1^^equiv) in THF (38^^mL) at 65^°C for 3^^h to afford pure (*R*)-2-phenyl-*N*-sulfonylaziridine ((*R*)-**1^a'**; 1.91^^g, 96^% yield). The ^{1}H^^NMR spectrum of compound (*R*)-**1^a'** agreed with that of compound **1^a** and matched the literature data.

*Synthesis and Characterization of (R)-4-Methyl-N-(2-(1-methyl-1^H-indol-3-yl)-2-phenylethyl)benzenesulfonamide ((R)-**3^a'**)*

The target compound was synthesized according to the general procedure for the synthesis of compounds **3**, with aziridine (*R*)-**1^a'** (50.0^^mg, 0.184^^mmol). Purification by column chromatography on silica gel (EtOAc/*n*-hexane, 40:60 v/v) gave the product as a colorless oil (55.9^^mg, 75^%

yield). The spectroscopic data matched the data for compound **3^a**; [α]<broxl>D<brtr>19</broxl>=<M->27.37 (c=0.49 in $CHCl_3$).

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Scheme^^1 Substrate scope for the ring-opening reaction of 2-aryl-*N*-tosylaziridines (**1**) with indoles **2**. The reactions were performed in CH_2Cl_2.

Scheme^^2 Substrate scope for the ring-opening reaction of disubstituted aziridine **4** with *N*-methylindoles (**2**).

Scheme^^3 Cycloaddition of aziridine **1^a** to 1,3-dimethylindole **7**. Ts=4-toluenesulfonyl, BQ=1,4-benzoquinone.

Scheme^^4 Ring-opening studies on enantiomerically enriched aziridine (*R*)-**1^a**.

Figure^^1 Pd^{II}-catalyzed ring-opening reaction of aziridines with indoles and representative bioactive tryptamine derivatives. Ar=aryl.

Table^^1 Selected optimization studies for the ring-opening reaction of *N*-tosylphenylaziridine with *N*-methylindole.[a]<w=1><+><forr1>

Entry	Catalyst (mol^%)	Solvent	*T* [°C]	Yield [%][b]
1	$Cu(OTf)_2$ (10)	DCE	RT	73[c]
2	$Sc(OTf)_3$ (10)	DCE	RT	40[c]
3	$[PdCl_2(MeCN)_2]$ (10)	DCE	RT	62
4	$[PdCl_2(MeCN)_2]$ (10) <M+>BQ (30)	DCE	RT	71
5	$[PdCl_2(MeCN)_2]$ (10)	$CHCl_3$		68
6	$[PdCl_2(MeCN)_2]$ (10) <M+>BQ (30)	$CHCl_3$		77

[a]^^Reaction conditions: aziridine **4^a** (1.0^^equiv), *N*-methylindole (**2^a;** 1.5^^equiv), 21^^h. [b]^^Yield of isolated compound **3^a**. [c]^^The product contained inseparable impurities. DCE=1,2-dichloroethane.

Table^^2 Optimization studies for the ring-opening reaction of aziridine **1** with indole **2^a**.[a]<w=1><+><forr2>

Entry	Catalyst (10^^mol^%)	Solvent	*T* [°C]	Yield [%][c] (**5**/
1	$[PdCl_2(MeCN)_2]$	DCE	0	93<dp> (71:7:
2	$AgSbF_6$	DCE	0	30<dp> (37:4:
3	$Sc(OTf)_3$	DCE	0	63<dp> (49:29

4	$Cu(OTf)_2$	DCE	0	94<dp> (32:5:
5	$[PdCl_2(MeCN)_2]$	DCE[b]	0	66<dp> (86:1:
6	$[PdCl_2(MeCN)_2]$	$CHCl_3$	0	66<dp> (60:40

[a]^^Reaction conditions: aziridine **1** (3^^equiv), *N*–methylindole (**2^a;** 3^^equiv), 21^^h. [b]^^Aziridine **1** (2^^equiv) was used. [c]^^Yield of isolated compound **3.** [d]^^The ratio was determined from the ^{1}H^^NMR spectrum of the crude reaction material.