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Gold-Catalyzed Domino Cycloisomerization/Pictet–Spengler Reaction of 2-(4-Aminobut-1-yn-1-yl)anilines with Aldehydes: Synthesis of Tetrahydropyrido[4,3-*b*]indole Scaffolds

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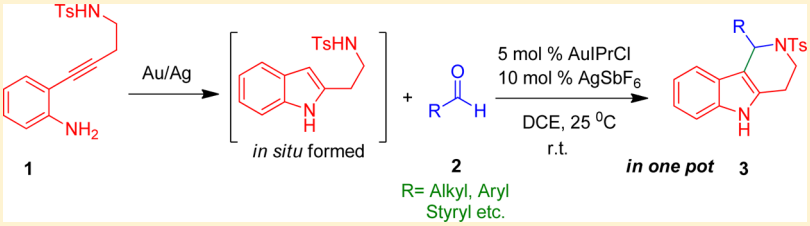
Supporting Information



ABSTRACT: A domino cycloisomerization/Pictet–Spengler reaction of 2-(4-aminobut-1-yn-1-yl)aniline with aldehydes has been achieved using a AuIPrCl (5 mol %)/$AgSbF_6$ (10 mol %) catalytic system to produce the corresponding 1-aryl-*N*-tosyl-2,3,4,5-tetrahydropyrido[4,3-*b*] indole derivatives in good yields. This is the first report on the synthesis of tetrahydro pyrido[4,3-*b*]indole scaffolds through as tandem 5-*endo*-*dig* cyclization and Pictet–Spengler reaction.

Tetrahydropyrido[4,3-*b*]indole core is frequently found in biologically active molecules such as latrepirdine and pyridoindolobenzodiazepine (Figure 1).[1] The latrepirdine, also known as dimebolin, is an orally active, antihistamine drug sold as Dimebon. It has also been shown to inhibit brain cell death in animal models of Alzheimer's disease and Huntington's disease.[2] Generally, tetrahydro-γ-carbolines are prepared by means of Pictet–Spengler reaction. However, a few methods have been reported for the direct synthesis of these tetrahydro-γ-carbolines via tandem processes.[3] On the other hand, the indole ring has been a privileged core structural motif in numerous naturally occurring alkaloids and biologically active molecules.[4] Of various syntheses of indoles, particular attention has been paid to cyclization of 2-alkynylaniline, which is one of the most efficient methods for the preparation of 2-substituted indole derivatives,[5] which can easily be functionalized by electrophilic aromatic substitution at C3 position. A variety of metal complexes have been investigated for the hydroamination of 2-ethynylanilines,[6] but the scope of this reaction has been significantly broadened with gold catalysts. The alkynophilicity of Au(I) and Au(III) complexes provides the new opportunities for the cycloisomerization of a wide range of alkynes tethered with nucleophiles.[7] These catalysts can also act as Lewis acids for the activation of electrophiles[8a−d] to facilitate C–C or C–X bond formation. Inspired by recent advancement in gold catalysis,[9] we herein report a novel strategy for the one-pot synthesis of 1-aryl-*N*-tosyl-2,3,4,5-tetrahydropyrido[4,3-*b*]-indole scaffolds from 2-(4-aminobut-1-yn-1-yl)aniline via an intramolecular hydroamination followed by Pictet–Spengler cyclization.

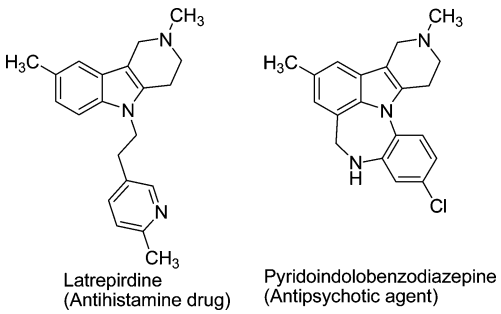


Figure 1. Tetrahydropyrido[4,3-*b*]indole-containing biologically active molecules.

To investigate the feasibility of the reaction, the starting material, 2-(4-aminobut-1-yn-1-yl)aniline (**1**), was prepared by Sonogashira coupling of 2-iodoaniline with 2-(4-aminobut-1-yn-1-yl)aniline[10] and was chosen as a model substrate (Scheme 1).

Initially, we intended to attempt the coupling of 2-(4-aminobut-1-yn-1-yl)aniline (**1**) with 4-bromobenzaldehyde (**2**) in the presence of 10 mol % of $NaAuCl_4{\cdot}2H_2O$ in ethanol. The corresponding tetrahydro-γ-carboline **3a** was isolated only in 44% yield after 12 h. Though $NaAuCl_4{\cdot}2H_2O$ promotes the annulation of 2-alkynylanilines effectively,[12] it did not show much catalytic influence in the present reaction (Table 1, entry f), and moreover, more than 40% of the starting material (**1**) was recovered. Encouraged by these initial findings, we began a

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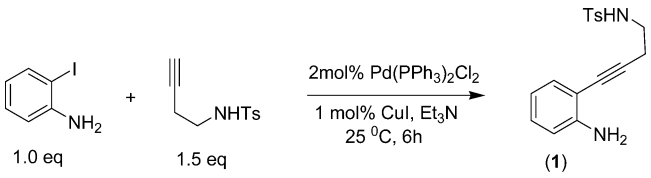
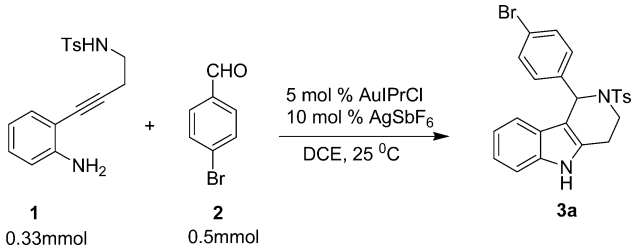
Scheme 1. Preparation of 2-(4-Aminobut-1-yn-1-yl)aniline[11] (1)



systematic screening of various Lewis acids in order to improve the conversion. Preliminary experiments were carried out using $InCl_3$ and $PtCl_2$. Surprisingly, no desired product **3a** was obtained with 10 mol % of $InCl_3$ in toluene at 80 °C (Table 1, entry a). Only a trace amount of **3a** was obtained with 10 mol % $PtCl_2$ (Table 1, entry b). Furthermore, metal triflates such as $Cu(OTf)_2$ and AgOTf also afforded the product **3a** with low yield (Table 1, entries c–e).

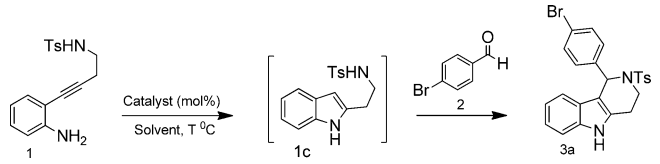
Though $Cu(OTf)_2$ facilitates the intramolecular hydroamination of *N*-protected ethynylaniline,[13] it did not show much catalytic effect in subsequent Pictet–Spengler cyclizations (Table 1, entry c). In order to realize the catalytic efficacy of gold(III) complexes for this reaction, further investigations were carried out using 10 mol % of $AuCl_3$ and $AuCl_3$/AgOTf. No improvement in yields was obtained with Au(III) complexes (Table 1, entries g and h). Therefore, to our disappointment, neither Au(III) salt nor its combination with Ag(I) salt has proved be to an optimal catalyst for this reaction. In several instances of gold catalysis, Au(I) complexes are found to be superior to the Au(III) in the cycloisomerization/C3-functionalization of 2-ethnylanilines with a wide range of aldehydes, nitrostyrenes, and isatin derivatives.[14] Based on this fact, next we investigated the catalytic efficiency of Au(I) complexes such as AuCl, AuIPrCl, Ph_3PAuCl, and their combination with silver salts like AgOTf and $AgSbF_6$. To our surprise, 10 mol % of AuCl in dry DCE at 60 °C afforded the isotryptamine (**1c**) in very low yield (<20%) which upon addition of aldehyde gave the undesired bis-indole derivative (Table 1, entry i) instead of **3a**. After screening several gold(I) catalysts, the best conversions were achieved with NHC–gold complex (AuIPrCl) in combination with $AgSbF_6$ (Table 1, entry m). The results are summarized in Table 1. The role of cocatalyst Ag(I) salt was expected to increase the reaction rate by generating Au(I) cationic species by the liberation of AgCl. As depicted in Table 1, the combination of 5 mol % of AuIPrCl and 10 mol % of $AgSbF_6$ gave the best results (Table 1, entry m, Scheme 2). In the above reaction, we found that more than

Scheme 2. Condensation of *p*-Bromobenzaldehyde with 2-(4-Aminobut-1-yn-1-yl)aniline



70% of 2-(4-aminobut-1-yn-1-yl)aniline (**1**) was converted into isotryptamine **1c** in the presence of 5 mol % of Au(I)/10 mol % of Ag(I) in 1,2-dichloroethane within a short reaction time (2–

Table 1. Screening of the Catalysts for the Cyclization of 2-(4-Aminobut-1-yn-1-yl)aniline (1) with *p*-Bromobenzaldehyde (2)



entry	catalyst (mol %)[a]	solvent	temp (°C)	time (h)	% conversion (**1c**)	yield[b] (%) (**3a**)
a	$InCl_3$ (10)	toluene	reflux	24	NR	NR[c]
b	$PtCl_2$ (10)	toluene	80	12	trace	trace[c]
c	$Cu(OTf)_2$ (10)	toluene	80	24	<10	9
d	AgOTf (10)	DCE	25	12	~30	15
e	AgOTf (10)	DCE	70	20	~35	37
f	$NaAuCl_4{\cdot}2H_2O$ (10)	EtOH	25	12	~50	44
g	$AuCl_3$ (10)	DCE	60	24	<10	15
h	$AuCl_3$ + AgOTf (10)	DCE	60	12	~30	27
i	AuCl (10)	DCE	60	12	<20	<5[d]
j	AuIPrCl + AgOTf (10)	DCE	25	7	>50	55
k	AuIPrCl + $AgSbF_6$ (10)	DCE	25	4	~60	58
l	AuIPrCl + $AgSbF_6$ (10)	CH_3CN	25	4	>50	50
m	**AuIPrCl (5) + $AgSbF_6$ (10)**	**DCE**	**25**	**4**	**>70**	**67**
n	PPh_3AuCl+AgOTf (10)	DCE	25	5	>40	55
o	PPh_3AuCl + $AgSbF_6$ (10)	DCE	25	5	~55	62

[a]Unless specified, the reaction was carried out with **1** (0.33 mmol) and **2** (0.5 mmol) in 2 mL of solvent. [b]Isolated yield after column chromatography. [c]Starting material was recovered. [d]The major product was bisindole (80%).

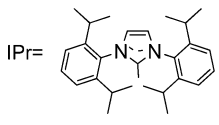


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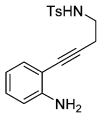
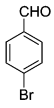
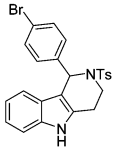
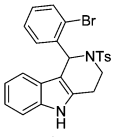
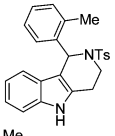
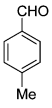
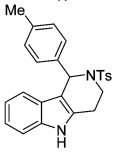
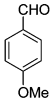
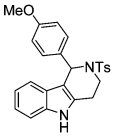
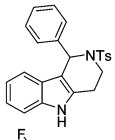
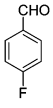
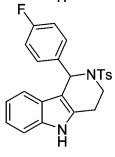
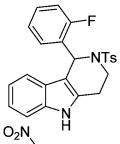
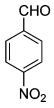
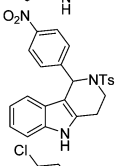
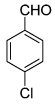
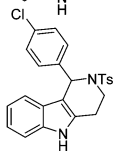
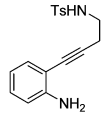
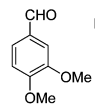
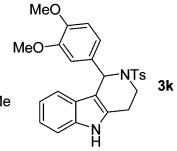
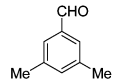
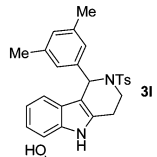
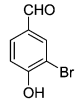
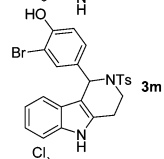
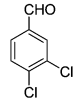
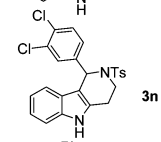
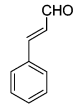
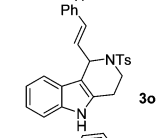
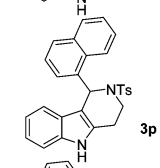
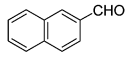
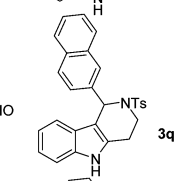
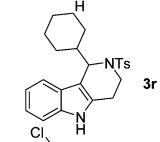
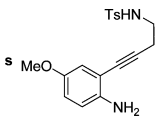
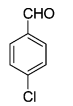
Table 2. Gold(I)-Catalyzed Synthesis of 1-Aryl-/Alkyl-*N*-tosyl-2,3,4,5-tetrahydropyrido[4,3-*b*]indole Scaffolds[a]

Entry	Substrate (**1**)	Aldehyde (**2**)	Product[b] (**3**)	Time (h)	Yield[c](%)
a			 **3a**	4.0	67
b	"		 **3b**	4.0	62
c	"		 **3c**	5.0	64
d	"		 **3d**	3.0	79
e	"		 **3e**	4.0	70
f	"		 **3f**	7.0	52
g	"		 **3g**	5.0	78
h	"		 **3h**	6.0	55
i	"		 **3i**	8.0	51
j	"		 **3j**	4.0	72
k			 **3k**	3.5	71
l	"		 **3l**	6.5	80
m	"		 **3m**	5.0	75
n	"		 **3n**	4.5	59
o	"		 **3o**	7.0	45
p	"		 **3p**	8.0	35
q	"		 **3q**	7.0	48
r	"		 **3r**	5.0	68
s			**3s**	6.0	60

[a]The reaction was carried out with **1a** (0.33 mmol) and **2** (0.5 mmol) in 2 mL of DCE. [b]All of the products were characterized by ^{1}H and ^{13}C NMR, IR, and HRMS spectroscopy . [c]Yield refers to pure products after column chromatography.

3 h). A subsequent cyclization of **1c** with **2** gave the expected product **3a** in 67% yield at 25 °C in 4 h (Table 1, entry m).

This reaction procceds by means of an intramolecular hydroamination followed by Pictet−Spengler reaction. Therefore, an intramolecular hydromination of substrate (**1**) likely generates *N*-tosylisotryptamine **1c**, which simultaneously undergoes cyclization with aldehyde to give the tetrahydro-γ-carboline via a highly reactive *N*-sulfonyliminium intermediate.

Next, we examined the scope of the reaction using various aldehydes. As shown in Table 2, a wide range of aldehydes reacted smoothly with 2-(4-aminobut-1-yn-1-yl)aniline (**1**) under optimized conditions. Both aromatic and aliphatic aldehydes participated smoothly in this reaction. However, the electronic properties of the substituents on the aromatic ring had shown some effect on the outcome of the reaction. Indeed, electron-rich aldehydes afforded the tetrahydro-γ-carbolines in good yields in shorter time compared to electron-withdrawing counterparts. It is noteworthy to mention that several functionalities such as aryl alkyl ethers, phenol, olefin, and halide groups are well-tolerated under the reaction

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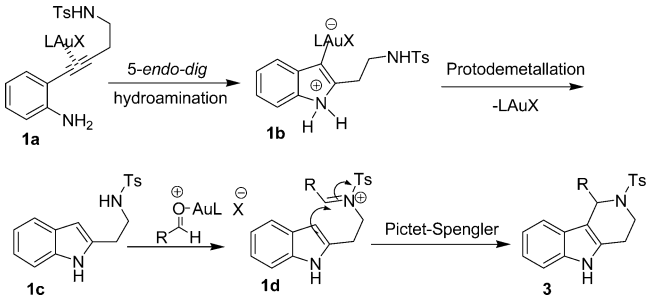
conditions. By using this procedure, a variety of 1-aryl-*N*-tosyl-2,3,4,5-tetrahydropyrido[4,3-*b*]indole derivatives were prepared in fairly good yields (Table 2).

The structure of compound **3g** was confirmed by single-crystal X-ray diffraction analysis.[15] Further experiment was carried out using 2-(4-aminobut-1-yn-1-yl)-5-methoxyaniline to prepare substituted tetrahydrocarboline. Thus, treatment of 2-(4-aminobut-1-yn-1-yl)-5-methoxyaniline with *p*-chlorobenzaldehyde under the optimized reaction conditions for 6 h afforded the methoxy-substituted tetrahydro-γ-carboline **3s** in 60% yield.

Mechanistically, the reaction is expected to proceed via two steps with two intermediates. The first step involves the gold(I)-catalyzed intramolecular hydroamination of 2-(4-aminobut-1-yn-1-yl)aniline to give the isotryptamine **1c** (Scheme 3). It proceeds via an initial π-coordination of Lewis

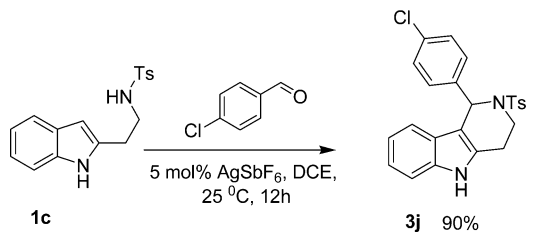
Scheme 3. Plausible Reaction Pathway for Cycloisomerization/Pictet−Spengler Reaction



acidity of cationic Au(I) species with the alkyne moiety of 2-(4-aminobut-1-yn-1-yl)aniline (**1**) to form a π-complex **1a**, and subsequent nucleophilic attack of the tethered amino group leads to ring closure to furnish the cyclic intermediate **1b** which on protodemetalation affords the isotryptamine **1c**. The second step involves the activation of aldehyde with regenerated Au(I) species followed by an intramolecular nucleophilic addition of indole moiety of **1c** to a highly reactive *N*-sulfonyliminium intermediate **1d** (Scheme 3) to provide the tetrahydropyridoindole derivative **3** with regeneration of active cationic gold species (Scheme 3).

To realize the role of excess of $AgSbF_6$, the intermediate isotryptamine **1c** was isolated and then subjected to the Pictet−Spengler cyclization. Interestingly, isotryptamine **1c** underwent smooth cyclization with *p*-chlorobenzaldehyde in the presence of 5 mol % of $AgSbF_6$ in dichloroethane at 25 °C affording the tetrahydro-γ-carboline **3j** in 90% yield. This result clearly reveals that Ag(I) facilitates the second step (Pictet−Spengler reaction) (Scheme 4).

Scheme 4. Ag(I)-Catalyzed Pictet−Spengler Reaction of Isotryptamine 1c



In conclusion, we have successfully demonstrated a novel one-pot strategy for the synthesis of 1-substituted 2-tosyl-2,3,4,5-tetrahydropyrido[4,3-*b*]indole scaffolds through a sequential hydroamination/Pictet−Spengler cyclization. This method allows C−C bond formation with excellent scope and high functional group tolerance under relatively mild and neutral conditions which makes this protocol a valuable alternative to previously described procedures. This reaction further demonstrates the ability of gold complexes to participate in concurrent tandem catalytic processes.

EXPERIMENTAL SECTION

General Methods. All the solvents were dried according to standard procedures. Reactions were performed in oven-dried round-bottom flask. The flasks were fitted with rubber septa and the reactions were conducted under nitrogen atmosphere. Glass syringes were used to transfer the solvent. Crude products were purified by column chromatography on silica gel of 60−120 or 100−200 mesh. TLC plates were visualized by exposure to ultraviolet light and/or by exposure to iodine vapors and/or by exposure to acidic methanolic solution of *p*-anisaldehyde followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated on rotary evaporator at 35−40 °C. IR spectra were recorded on FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR (proton-decoupled) spectra were recorded on 200, 300, 400, or 500 MHz NMR spectrometers in $CDCl_3$ solvent. Chemical shifts (δ) were reported in parts per million (ppm) with respect to TMS as an internal standard. Coupling constants (*J*) are quoted in hertz (Hz). Mass spectra were recorded on a mass spectrometer by electrospray ionization (ESI) or an atmospheric pressure chemical ionization (APCI) technique.

Preparation of Starting Materials. *N-(But-3-yn-1-yl)-4-methylbenzenesulfonamide.* Obtained as a white crystalline solid: yield 75%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 4.98 (brs, 1H), 3.10 (dd, *J* = 6.6, 13.3 Hz, 2H), 2.42 (s, 3H), 2.33 (dt, *J* = 2.2, 6.6, 13.3 Hz, 2H), 2.00−1.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 136.6, 129.5, 126.8, 129.3, 126.9, 117.7, 114.3, 107.7, 91.1, 79.3, 42.0, 21.4, 21.0; IR (KBr) ν 3271, 2923, 2876, 1593, 1416, 1318, 1157, 1066, 926, 677, 581 cm^{-1}; MS (ESI) *m/z* 246 [M + Na]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{11}H_{13}O_2NNaS$ [M + Na]$^+$ 246.05592, found 246.05592.

Typical Procedure for the Synthesis of *N*-(4-(2-Aminophenyl)but-3-yn-1-yl)-4-methylbenzenesulfonamide (1). To a stirred solution of 2-iodoaniline (1 mmol) in Et_3N was added $Pd(PPh_3)_2Cl_2$ (0.02 mmol) and the mixture stirred for 5−10 min. To this mixture were added *N*-(but-3-ynyl)-4-methylbenzenesulfonamide (1.5 mmol) followed by CuI (0.01 mmol), and the resulting mixture was stirred at room temperature until complete consumption of the starting material. Removal of the solvent followed by purification on silica gel using (ethyl acetate/*n*-hexane = 2:1) gradients afforded the pure product **1** as orange solid: yield 70%; mp 92−95 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 2H), 7.19 (d, *J* = 6.6 Hz, 1H), 7.09 (t, *J* = 7.7 Hz, 1H), 6.77−6.63 (m, 2H), 5.19−5.11 (m, 1H), 3.96 (brs, 2H), 3.19 (dd, *J* = 6.6, 13.3 Hz, 2H), 2.65 (t, *J* = 6.6 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.9, 143.4, 136.9, 132.0, 129.7, 129.3, 126.9, 117.7, 114.3, 107.7, 91.1, 79.3, 42.0, 21.4, 21.0; IR (KBr): νν 3473, 3373, 3254, 2925, 1616, 1488, 1449, 1311, 1155, 1072, 745, 549 cm^{-1}; MS (ESI) *m/z* 315 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{17}H_{19}O_2N_2S$ [M + H]$^+$ 315.1167, found 315.1157.

***N*-(4-(2-Amino-5-methoxyphenyl)but-3-yn-1-yl)-4-methylbenzenesulfonamide:** orange solid; yield 65%; mp 82−84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.71 (m, 3H), 7.34−7.25 (m, 2H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.27−6.18 (m, 2H), 3.75 (s, 3H), 3.17 (dd, *J* = 6.0, 12.8 Hz, 2H), 2.62 (t, *J* = 6.0 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 159.8, 149.2, 142.1, 136.9, 132.2, 128.9, 126.1, 102.9, 98.3, 89.5, 78.0, 54.3, 41.5, 20.7, 20.3; IR (KBr) ν 3463, 3353, 3251, 2921, 1620, 1484, 1445, 1311, 1144, 1071, 745, 544 cm^{-1}; MS (ESI) *m/z* 345 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{18}H_{20}O_3N_2S$ [M + H]$^+$ 345.12674, found 345.12650.

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*N-(2-(1H-Indol-2-yl)ethyl)-4-methylbenzenesulfonamide(**1c**).* To a stirred solution of 2-(4-aminobut-1-yn-1-yl)aniline (**1**, 0.33 mmol) in dry DCE (1 mL) under N_2 was added AuIPrCl (5 mol %)/$AgSbF_6$ (10 mol %). The resulting mixture was allowed to stir at room temperature for 2 h. After completion of the reaction as indicated by TLC, the mixture was diluted with ethyl acetate and filtered through a plug of silica gel. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel (60−120 mesh) using (ethyl acetate/hexane = 2:1) to afford the isotrypatamine intermediate (**1c**) as an off-white solid: yield 60%; mp 100−102 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (brs, NH, 1H) 7.70−7.62 (m, 2H), 7.49 (d, J = 7.5 Hz, 1H), 7.32−7.21 (m, 4H), 7.18−7.02 (m, 2H), 6.16 (s, 1H), 4.84 (t, J = 6.0 Hz, 1H), 3.24 (dd, J = 6.4, 12.8 Hz, 2H), 2.91 (t, J = 6.4 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 136.0, 135.3, 129.7, 129.4, 128.1, 127.0, 121.4, 119.8, 110.7, 100.5, 42.8, 28.5, 21.5 ; IR (KBr) ν 3472, 3371, 3252, 2924, 1620, 1488, 1454, 1310, 1155, 1071, 745, 549 cm^{-1}; MS (ESI) m/z 315 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{17}H_{19}O_2N_2S$ [M + H]$^+$ 315.1167, found 315.1162.

General Procedure for Au(I)/Ag(I)-Catalyzed Cyclization. To a stirred solution of 2-(4-aminobut-1-yn-1-yl)aniline (**1**)/*N*-(4-(2-amino-5-methoxy phenyl)but-3-yn-1-yl)-4-methylbenzenesulfonamide (**4**) (0.33 mmol) in dry DCE (1 mL) under N_2 was added AuIPrCl (5 mol %)/$AgSbF_6$ (10 mol %), and the resulting mixture was allowed to stir at room temperature. The progress of the reaction was monitored by TLC. To this mixture was added aldehyde (0.5 mmol), and stirring was continued for the specified time (Table 2). After completion of the reaction as indicated by TLC, the mixture was diluted with ethyl acetate and filtered through a plug of silica gel. The filtrate was concentrated and the residue was purified by column chromatography on silica gel (60−120 mesh) using (ethylacetate/hexane = 4:1−2:1) to afford the pure tetrahydro-γ-carboline.

*1-(4-Bromophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3a**; Table 2, entry a):* yellow solid; yield 67%; mp 191−192 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (brs, 1H, NH), 7.57 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.33−7.20 (m, 1H), 7.19−6.98 (m, 4H), 6.41 (s, 1H), 4.00 (dd, J = 5.1, 14.5 Hz, 1H), 3.30−3.17 (m, 1H), 2.62−2.37 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 139.3, 137.9, 135.7, 132.1, 131.3, 130.3, 129.7, 128.9, 129.4, 127.0, 126.8, 125.8, 121.9, 119.9, 118.3, 110.7, 107.8, 55.1, 38.5, 21.7, 21.4; IR (KBr) ν 3364, 2923, 2854, 1647, 1460, 1287, 1319, 1153, 1084, 747, 658 cm^{-1}; MS-ESI m/z 481 [M + H]$^+$, 483 [(M + 2) + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{22}O_2N_2BrS$ [M + H]$^+$ 483.05364, found 483.05594.

*1-(2-Bromophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3b**; Table 2; entry b):* cream solid; yield 62%; mp 189−191 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (brs, 1H, NH), 7.57 (d, J = 8.3 Hz, 2H), 7.38−7.23 (m, 4H), 7.18−6.99 (m, 4H), 6.94 (dt, J = 2.3, 8.3 Hz, 2H), 6.45 (s, 1H), 4.00 (dd, J = 5.3, 14.4 Hz, 1H), 3.32−3.18 (m, 1H), 2.63−2.37 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 138.1, 136.0, 135.6, 132.0, 131.3, 130.3, 130.2, 129.6, 129.3, 127.0, 126.8, 125.8, 121.9, 119.8, 118.4, 115.2, 114.9 110.7, 108.2, 55.0, 38.4, 21.7, 21.4 ; IR (KBr) ν 3364, 2923, 2854, 1647, 1460, 1287, 1319, 1153, 1084, 747, 658 cm^{-1}; MS-ESI m/z 481 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{22}O_2N_2BrNaS$ 505.05558, found 505.05324.

*1-(o-Tolyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3c**; Table 2, entry c):* off-white solid; yield 64%; mp 145−146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (brs, 1H, NH), 7.46 (d, J = 7.7 Hz, 2H), 7.25 (m, 3H), 7.15−7.05 (m, 2H), 7.01−6.89 (m, 3H), 6.83 (d, J = 8.6 Hz, 2H), 6.68 (s, 1H), 3.89 (dd, J = 5.7, 14.4 Hz, 1H), 3.50−3.39 (m, 1H), 2.78 (s, 3H), 2.62−2.47 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 137.8, 135.6, 131.5, 131.1, 129.5, 129.2, 128.9, 127.9, 127.1, 127.0, 125.6, 125.4, 121.8, 119.7, 118.1, 110.5, 53.5, 38.4, 21.4, 21.1, 20.4; IR (KBr) ν 3341, 2923, 2855, 1649, 1604, 1459, 1318, 1151, 1088, 745 cm^{-1}; MS-ESI: m/z 417 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{25}H_{24}O_2N_2NaS$ [M + Na]$^+$ 439.1456, found 439.1440.

*1-(p-Tolyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3d**; Table 2, entry d):* off-white solid; yield 79%; mp 146−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (brs, 1H, NH), 7.55 (d, J = 8.3 Hz, 2H), 7.27−7.15 (m, 4H), 7.12 (d, J = 7.5 Hz, 2H), 7.08−6.94 (m, 4H), 6.40 (s, 1H), 3.95 (dd, J = 6.0, 14.3 Hz, 1H), 3.32−3.18 (m, 1H), 2.72−2.40 (m, 2H), 2.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 140.5, 138.7, 137.2, 135.6, 129.7, 129.6, 129.3, 129.0, 128.5, 128.0, 127.6, 127.0, 126.9, 121.8, 119.8, 118.6, 115.4 110.6, 55.5, 38.5, 21.8, 21.4, 21.1; IR (KBr) ν 3341, 2923, 2855, 1649, 1604, 1459, 1318, 1151, 1088, 747 cm^{-1}; MS-ESI m/z 417 [M + H]$^+$; HRMS (MS-TOF) exact mass calcd for $C_{25}H_{24}O_2N_2NaS$ [M + Na]$^+$ 439.1456, found 439.1442.

*1-(4-Methoxyphenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3e**; Table 2, entry e):* off-white solid; yield 70%; mp 196−198 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (brs, 1H, NH), 7.56 (d, J = 8.5 Hz, 2H), 7.27−7.21 (m, 3H), 7.14−7.07 (m, 2H), 7.03 (d, J = 8.5 Hz, 2H), 6.99 (dd, J = 6.8, 14.4 Hz, 1H), 6.76 (d, J = 8.5 Hz, 2H), 6.40 (s, 1H), 3.99−3.92 (m, 1H), 3.77 (s, 3H), 3.30−3.22 (m, 1H), 2.64−2.54 (m, 1H), 2.41−2.36 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 142.9, 138.4, 135.7, 132.4, 132.0, 129.8, 129.3, 126.9, 126.1, 121.1, 121.8, 119.8, 118.6, 110.6, 108.9, 55.2, 53.4, 38.4, 21.9, 21.4; IR (KBr) ν 3354, 2920, 2864, 1610, 1509, 1459, 1314, 1151, 1091, 746 cm^{-1}; MS (ESI) m/z 433 [M + H]$^+$; HRMS (MS-TOF) exact mass calcd for $C_{25}H_{24}O_3N_2NaS$ [M + Na]$^+$ 455.1405, found 455.1403.

*1-Phenyl-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3f**; Table 2, entry f):* off-white solid; yield 52%; mp 240−242 °C; ^{1}H NMR (500 MHz, $CDCl_3$+DMSO-d_6) δ 8.57 (brs, 1H, NH), 7.57 (d, J = 9.0 Hz, 2H), 7.38−7.33 (m, 2H), 7.31−7.27 (m, 3H), 7.27−7.23 (m, 3H), 7.15−7.09 (m, 1H), 7.05 (d, J = 8.0 Hz, 2H), 6.96−7.01 (m, 1H), 6.89 (t, J = 7.6 Hz 1H), 6.36 (s, 1H), 3.98−3.92 (m, 1H), 3.33−3.24 (m, 1H), 2.65−2.55 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO) δ 142.8, 140.8, 137.9, 132.4, 135.6, 132.7, 129.5, 128.7, 128.2, 127.6, 127.1, 126.5, 125.3, 120.7, 118.6, 117.7, 114.3, 110.9, 55.3, 38.6, 21.3, 20.8; IR (KBr) ν 3379, 2923, 2853, 1711, 1599, 1464, 1331, 1159, 1090, 756 cm^{-1}; MS-ESI: m/z 403 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{23}O_2N_2S$ [M + H]$^+$ 403.1480, found 403.1463.

*1-(4-Fluorophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3g**; Table 2, entry g):* off-white solid; yield 78%; mp 204−206 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (brs, 1H, NH), 7.58 (d, J = 8.0 Hz, 2H), 7.42−7.26 (m, 4H), 7.20−7.00 (m, 2H), 7.00−6.92 (m, 2H), 6.46 (s, 1H), 3.98 (dd, J = 6.0, 15.0 Hz, 1H), 3.33−3.25 (m, 1H), 2.67−2.57 (m, 1H), 2.52 (dd, J = 5.0, 16.0 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 143.1, 138.1, 136.0, 135.7, 135.6, 132.0, 130.2, 130.3, 129.6, 129.3, 127.0, 126.8, 121.9, 119.8, 118.4, 115.8, 115.2, 114.9 110.6, 55.0, 38.4, 21.7, 21.3; IR (KBr) ν 3365, 3336, 2924, 2858, 1650, 1504, 1464, 1325, 1151, 1087, 746 cm^{-1}; MS-ESI m/z 421 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{22}O_2N_2FS$ [M + H]$^+$ 421.1380, found 421.1381.

*1-(2-Fluorophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3h**; Table 2, entry h):* off-white solid; yield 55%; mp 200−202 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (brs, 1H, NH), 7.48 (d, J = 8.3 Hz, 2H), 7.35−7.13 (m, 6H), 7.12−6.89 (m, 2H), 6.85−6.73 (m, 2H), 6.12 (s, 1H), 4.77−4.62 (m, 1H), 3.14−3.03 (m, 1H), 2.79−2.61 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 143.4, 136.0, 135.3, 132.8, 129.8, 129.6, 128.2, 128.1, 127.7, 126.9, 121.9, 119.2, 118.9, 113.2, 111.0, 114.9 110.6, 42.2, 32.7, 21.4, 21.0; IR (KBr) ν 3374, 2923, 1599, 1487, 1453, 1324, 1156, 1088, 750, 664 cm^{-1}; MS (ESI) m/z 421 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{22}O_2N_2FS$ [M + H]$^+$ 421.13805, found 421.13835.

*1-(4-Nitrophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3i**; Table 2, entry i):* off-white solid; yield 51%; mp 105−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (brs, 1H, NH), 7.48 (d, J = 8.3 Hz, 2H), 7.35−7.13 (m, 6H), 7.12−6.89 (m, 2H), 6.85−6.73 (m, 2H), 6.12 (s, 1H), 4.77−4.62 (m, 1H), 3.14−3.03 (m, 1H), 2.79−2.61 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 147.5, 143.5, 137.8, 135.7, 132.3 129.5, 127.0, 126.8, 125.7, 123.6, 122.3, 120.2, 118.2, 110.9, 107.2, 55.0, 38.8, 21.6, 21.5; IR (KBr) ν 3375, 2921, 2851, 1598, 1485, 1462, 1326, 1150, 1090, 750 cm^{-1}; MS (ESI) m/z 448[M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{21}O_4N_3S$ [M + H]$^+$ 448.13255, found 448.13280.

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*1-(4-Chlorophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3j**; Table 2, entry j):* white solid; yield 72%; mp 182−184 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (brs, 1H, NH), 7.55 (d, J = 8.3 Hz, 2H), 7.31−7.18 (m, 5H), 7.16−6.94 (m, 5H), 6.39 (s, 1H), 3.98 (dd, J = 5.3, 14.4 Hz, 1H), 3.27−3.14 (m, 1H), 2.64−2.37 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 138.7, 133.6, 132.0, 129.9, 129.7, 129.3, 128.3, 126.9, 126.8, 125.8, 122.0, 119.9, 118.4, 114.2 110.7, 108.0, 55.0, 38.5, 21.7, 21.4; IR (KBr) ν 3357, 2924, 2854, 1597, 1461, 1324, 1149, 1088, 806, 652 cm^{-1}; MS (ESI) m/z 437 [M + H]$^+$; HRMS (MS-TOF) exact mass calcd for $C_{24}H_{21}O_2N_2ClNaS$ [M + Na]$^+$ 459.0909, found 459.0892.

*1-(3,4-Dimethoxyphenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido-[4,3-b]indole (**3k**; Table 2, entry k):* orange solid; yield 71%; mp 210−212 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (brs, 1H, NH), 7.59 (d, J = 8.3 Hz, 2H), 7.34−7.21 (m, 2H), 7.18−7.10 (t, J = 7.6 Hz, 2H), 7.09−6.99 (m, 3H), 6,67 (s, 2H), 6.41 (s, 1H), 4.01 (dd, J = 5.3, 14.4 Hz, 1H), 3.86−3.67 (m, 6H), 3.39−3.24 (m, 1H), 2.69−2.35 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.8, 148.6, 142.9, 138.3, 135.6, 132.7, 132.1, 129.7, 129.3, 126.8, 126.1, 121.7, 120.7, 119.7, 118.5, 110.6, 110.2, 108.5, 55.8, 55.5, 38.5, 21.9, 21.4; IR (KBr) ν 3359, 2924, 2852, 1661, 1598, 1512, 1459, 1327, 1259, 1155, 1088, 1022, 747, 548 cm^{-1}; MS-ESI m/z 463 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{26}H_{27}O_4N_2S$ [M + H]$^+$ 463.16860, found 463.16727.

*1-(3,5-Dimethylphenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3l**; Table 2; entry l):* white solid; yield 80%; mp 218−220 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (brs, 1H, NH), 7.55 (d, J = 8.9 Hz, 2H), 7.18−7.10 (m, 2H), 7.05−6.95 (m, 3H), 6.90 (s, 1H), 6,88 (s, 1H), 6.36 (s, 1H), 4.00 (dd, J = 6.7, 14.5 Hz, 1H), 3.37−3.29 (m, 1H), 2.70−2.58 (m, 1H), 2.50 (dd, J = 4.4, 15.5 Hz, 1H), 2.29 (s, 3H), 2.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 140.0, 138.3, 137.6, 135.7, 131.9, 129.6, 129.4, 129.1, 126.9, 126.3, 125.4, 121.7, 119.7, 118.6, 110.5, 108.9, 55.8, 38.6, 22.0, 21.4, 21.3; IR (KBr) ν 3334, 2920, 1604, 1461, 1324, 1151, 1088, 753 cm^{-1}; MS-ESI m/z 431 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{26}H_{27}O_2N_2S$ [M + H]$^+$ 431.17878, found 431.17805.

*2-Bromo-4-(2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indol-1-yl)phenol (**3m**; Table 2; entry m):* light yellowish solid; yield 75%; mp 189−191 °C; ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) δ 10.04 (brs, 1H), 9.48 (1br, 1H), 7.55 (d, J = 8.3 Hz, 2H), 7.35−7.27 (m, 2H), 7.13−7.01 (m, 5H), 6.99−6.89 (m, 1H), 6.84 (d, J = 8.5 Hz, 1H), 6.28 (s, 1H), 4.01−3.91 (m, 1H), 3.35−3.21 (m, 1H), 2.63−2.53 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO) δ 152.9, 142.2, 137.4, 135.3, 132.2, 132.0 (d, J = 4.9 Hz), 128.6, 127.9, 124.9, 120.4, 118.3, 115.2, 110.2, 108.8, 106.2, 54.2, 37.8, 21.2, 20.6; IR (KBr) ν 3379, 2923, 2853, 1606, 1519, 1464, 1325, 1151, 1087, 746 cm^{-1}; MS (ESI) m/z 497[M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{22}O_3N_2BrS$ [M + H]$^+$ 497.05340, found 497.05322.

*1-(2,4-Dichlorophenyl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3n**; Table 2, entry n):* white solid; yield 59%; mp 178−180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (brs, 1H, NH), 7.58 (d, J = 8.3 Hz, 2H), 7.39−7.28 (m, 2H), 7.25−7.01 (m, 6H), 6.38 (s, 1H), 4.10−3.99 (m, 1H), 3.27−3.19 (m, 1H), 2.67−2.41 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 140.5, 138.7, 137.3, 135.7, 129.7, 129.6, 129.3, 129.0, 128.5, 128.0, 127.6, 127.0, 126.9, 121.8, 119.8, 118.7, 115.4 110.6, 55.5, 38.5, 21.8, 21.4; IR (KBr) ν 3355, 2920, 2851, 1600, 1462, 1328, 1159, 1092, 753 cm^{-1}; MS-ESI m/z 437 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{20}O_2N_2NaCl_2S$ [M + Na]$^+$ 493.0520, found 493.0516.

*(E)-1-Styryl-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3o**; Table 2, entry o):* white solid; yield 45%; mp 128−130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (brs, 1H, NH), 7.55 (d, J = 8.3 Hz, 2H), 7.31−7.18 (m, 5H), 7.16−6.94 (m, 5H), 6.39 (s, 1H), 3.98 (dd, J = 5.3, 14.4 Hz, 1H), 3.27−3.14 (m, 1H), 2.64−2.37 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 147.0, 143.2, 137.0, 135.9, 134.2, 130.7, 129.7, 129.3, 129.0, 128.8, 128.3, 127.8, 127.7, 127.0, 126.7, 118.3, 117.2, 115.7, 60.1, 41.4, 26.8, 21.5; IR (KBr) ν 3355, 2920, 2851, 1600, 1462, 1328, 1159, 1092, 754 cm^{-1}; MS-ESI m/z 429 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{26}H_{23}O_2N_2S$ [M − H]$^-$ 427.14748, found 427.14735.

*1-(Naphthalen-1-yl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]-indole (**3p**; Table 2, entry p):* white solid; yield 35%; mp 82−84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (d, J = 7.7 Hz, 1H), 7.96−7.83 (m, 1H), 7.86 (brs, NH, 1H), 7.80−7.67 (m, 2H), 7.64−7.50 (m, 4H), 7.35 (s, 1H), 7.21−7.05 (m, 3H), 7.03−6.90 (m, 4H), 3.75 (dd, J = 6.6, 14.3 Hz, 1H), 3.43−3.33 (m, 1H), 2.86−2.71 (m, 1H), 2.58−2.51 (m, 1H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 137.4, 135.9, 135.1, 134.2, 129.6, 129.1, 128.9, 128.5, 127.9, 127.4, 127.0, 126.8, 125.9, 125.4, 124.6, 121.9, 119.8, 118.3, 115.3, 110.5, 109.6, 52.6, 38.3, 21.4; IR (KBr) ν 3377, 2922, 2852, 1658, 1605, 1459, 1323, 1155, 1087, 739 cm^{-1}; MS-ESI m/z 453 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{28}H_{23}O_2N_2S$ [M − H]$^-$ 451.14748, found 451.14703.

*1-(Naphthalen-2-yl)-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4, 3-b]-indole (**3q**; Table 2, entry q):* white solid; yield 48%; mp 99−101 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (d, J = 9.1 Hz, 1H), 8.15 (brs, 1H), 7.94−7.81 (m, 2H), 7.78−7.65 (m, 2H), 7.63−7.40 (m, 4H), 7.32 (s, 1H), 7.20−7.03 (m, 3H), 7.01−6.87 (m, 3H), 3.71 (dd, J = 6.0, 14.4 Hz, 1H), 3.41−3.28 (m, 1H), 2.89−2.69 (m, 1H), 2.51 (dd, J = 8.3, 16.6 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 136.9, 136.5, 136.1, 135.7, 132.2, 129.7, 129.5, 129.5, 129.1, 128.4, 128.0, 127.9, 127.4, 126.9, 126.6, 124.5, 121.5, 119.7, 118.3, 115.5, 110.7, 50.0, 42.8, 21.5, 21.4; IR (KBr) ν 3355, 2924, 2850, 1718, 1614, 1458, 1324, 1154, 1088, 754 cm^{-1}; MS-ESI m/z 453 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{28}H_{24}O_2N_2NaS$ [M + Na]$^+$ 475.1456, found 475.1454.

*1-Cyclohexyl-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3r**; Table 2, entry r):* pale yellow solid; yield 68%; mp 82−84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (brs, 1H, NH), 7.43 (d, J = 8.1 Hz, 2H), 7.23−7.17 (m, 1H), 7.15−7.06 (m, 2H), 6.86 (d, J = 7.9 Hz, 2H), 4.99 (d, J = 8.3 Hz, 1H), 4.12 (dd, J = 6.8, 15.3 Hz, 1H), 3.67−3.51 (m, 1H), 2.48−2.25 (m, 2H), 2.21 (s, 3H), 2.06−1.55 (m,7H), 1.44−1.04 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6, 138.1, 135.4, 130.4, 128.9, 126.7, 121.5, 119.5, 119.1, 110.8, 110.3, 58.3, 44.1,38.6, 31.2, 30.3, 29.7, 21.3, 21.0 ; IR (KBr) ν 3385, 2928, 2853, 1738, 1619, 1458, 1324, 1153, 1091, 750 cm^{-1}; MS-ESI m/z 409 [M + H]$^+$; HRMS (Orbitrap ESI) exact mass calcd for $C_{24}H_{29}O_2N_2S$ [M + H]$^+$ 409.19443, found 409.19420.

*1-(p-Chlorophenyl)-8-methoxy-2-tosyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (**3s**):* off-white solid; yield 55%; mp 186−188 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (brs, 1H, NH), 7.56 (d, J = 8.5 Hz, 2H), 7.28−7.21 (m, 3H), 7.12−7.08 (m, 2H), 7.03- 6.98 (m, 2H), 6.76 (d, J = 8.4 Hz, 2H), 6.40 (s, 1H), 3.98−3.92 (m, 1H), 3.77 (s, 3H), 3.30−3.22 (m, 1H), 2.46−2.36 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 159.2, 142.9, 138.4, 132.4, 132.0, 129.7, 129.2, 126.9, 126.0, 121.8, 119.8, 118.6, 113.5, 110.5, 55.2, 53.4, 38.3, 21.9, 21.4; IR (KBr) ν 3352, 2921, 2865, 1622, 1504, 1451, 1313, 1159, 1092, 745 cm^{-1}; MS (ESI) m/z 467 [M + H]$^+$; HRMS (Orbitrap-ESI) exact mass calcd for $C_{25}H_{24}O_3N_2ClS$ [M + H]$^+$ 467.11911, found 467.11906.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of products (**3a−r**), preparation of starting materials, and X-ray data of compound **3g** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(15) Supplementary crystallographic data (CIF) and respective ORTEP diagram (Figure 1) for compound **3g** have been provided in the Supporting Information. Also, CCDC-900791 contains the supplementary crystallographic data for the compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.