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Iron-Mediated Selective Sulfonylmethylation of Aniline Derivatives with *p*-Toluenesulfonylmethyl Isocyanide (TosMIC)

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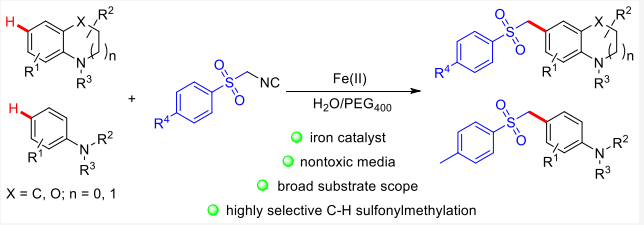
ABSTRACT: An iron-mediated highly selective C−H sulfonylmethylation of aniline derivatives with *p*-toluenesulfonylmethyl isocyanide in a mixture solvent of H_2O and PEG_{400} under an Ar atmosphere has been realized. This transformation proceeds with operational convenience, use of earth-abundant metal catalyst and nontoxic media, broad substrate scope, and good functional group tolerance. The current methodology could be applied to the regioselective C−H sulfonylmethylation of indolines, tetrahydroquinolines, and tertiary anilines.

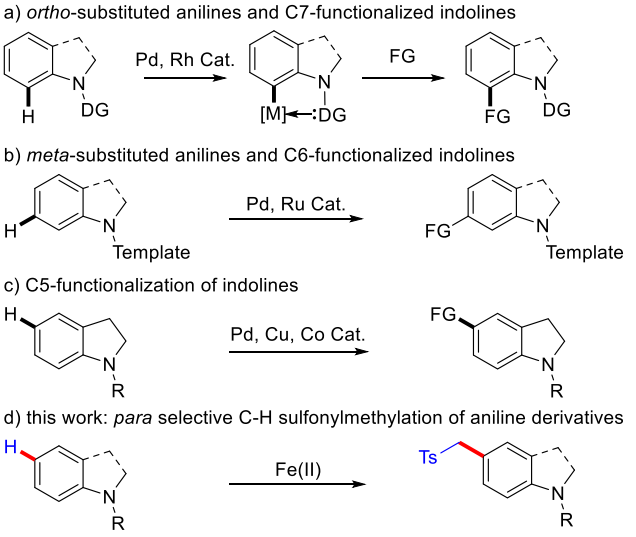


INTRODUCTION

The aniline fragment is recognized as a valuable subunit in bioactive molecules and donor−acceptor compounds with wide application in pharmaceuticals, agrochemicals, and materials chemistry.[1] Meanwhile, indolines are also unique *N*-heterocycles widely existent in many natural products and medicinally important compounds.[2] Consequently, it is highly desirable to develop novel strategies to access functionalized anilines and indolines site-selectively for diversity-oriented synthesis in medicinal chemistry.[3] With development of chelation-assisted C−H functionalization, *ortho*-substituted[4] anilines and C7-functionalized[5] indolines have been well explored (Scheme 1a). Through introduction of directing templates or extended ligand architectures, the past decade has witnessed great advances in remote C−H functionalization,[6] which gave access to *meta*-substituted[7] anilines and C6-functionalized[8] indolines (Scheme 1b). Nevertheless, the general methodology for direct functionalization of anilines at the *para* position remains to be developed.[9] In the case of indolines, only limited C5-functionalization has been reported, including difluoromethylation, nitration, chalcogenation, alkylation, olefination, and amination (Scheme 1c).[10]

Isocyanides are useful organic synthons due to their reactivity toward electrophiles, nucleophiles, and radicals with wide application in multicomponent reactions,[11] insertion reactions,[12] and cycloaddition reactions.[13] Especially, *p*-toluenesulfonylmethyl isocyanide (TosMIC), originally introduced by Van Leusen,[14] has attracted much attention due to its impressive structural features and unique reactivity.[15] Over the past decades, [3 + 2] cycloaddition of TosMIC with polarized functionalities, such as aldehydes, imines, alkenes, and alkynes, have been extensively explored to access five-membered heterocycles.[16] Meanwhile, TosMIC also served as the promising C1,[17] N1,[18] and C1N1[19] building block. Recently, utilization of TosMIC as sulfinyl[20] and sulfonyl[21] sources has

Scheme 1. Site-Selectively Functionalized Anilines and Indolines



also been reported. For example, Bi and co-workers have reported the synthesis of benzoheteroles via heteroaromatization of propargylic alcohols with TosMIC.[21a] Xia et al. have prepared α-sulfonated ketones via coupling between *a*-bromo ketones with TosMIC.[21b] The groups of Bi, Tiwari, Yallapragada, and Shen have independently developed the

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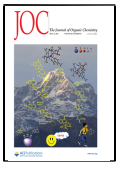

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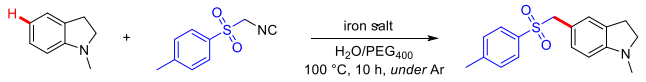
synthesis of vinyl sulfones via functionalization of olefins or alkynes with TosMIC.[21c−f] Despite the above progress, the exploration of TosMIC in other transformations remains to be developed.

Our group has been interested in functionalization of biologically important heterocyclic frameworks. We have developed C7-functionalized indolines via chelation-assisted strategy.[22] Meanwhile, Cu-mediated direct C−H sulfonylation of benzoic acids with TosMIC has also been reported using a PyO-directing group.[23] Recently, we have also realized C−H sulfonylmethylation of imidazopyridines and indoles using TosMIC as the sulfonylmethylating reagent.[24] In continuation of our previous work,[23−25] we herein report iron-induced[26] *para*-selective sulfonylmethylation of aniline derivatives with TosMIC in a solvent mixture of H_2O and PEG_{400} (Scheme 1d). In this protocol, TosMIC serves as a source of the sulfonylmethyl group instead of a typical 1,3 dipole. Meanwhile, the utilization of base-metal and nontoxic reaction medium makes this methodology more practical and convenience to access functionalized anilines. Moreover, C5-sulfonylmethylated indolines were first realized, which could be further oxidized to the corresponding C5-functionalized indoles.

RESULTS AND DISCUSSION

Our investigation commenced with reaction between *N*-methylindoline **1a** and TosMIC **2a** in the presence of $FeSO_4·7H_2O$ in a solvent mixture of H_2O and PEG_{400} (Table 1). To our delight, the desired C5-tosylmethylated

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

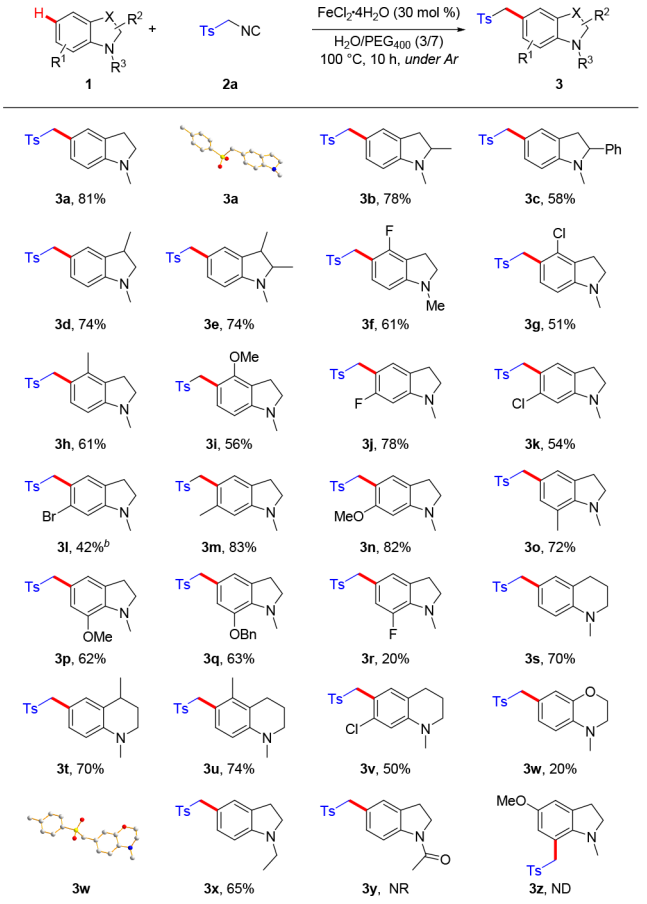
Entry	Iron salt (mol %)	Solvent (ratio)	Yield (%)
1	$FeSO_4·7H_2O$ (100)	H_2O/PEG_{400} (7:3)	61
2	$FeCl_2·4H_2O$ (100)	H_2O/PEG_{400} (7:3)	65
3	$Fe(NO_3)_3·9H_2O$ (100)	H_2O/PEG_{400} (7:3)	16
4	$Fe(acac)_3$ (100)	H_2O/PEG_{400} (7:3)	20
5	$FeCl_3$ (100)	H_2O/PEG_{400} (7:3)	trace
6	$FeCl_2·4H_2O$ (100)	H_2O/PEG_{400} (1:1)	80
7	$FeCl_2·4H_2O$ (100)	H_2O/PEG_{400} (3:7)	83
8	$FeCl_2·4H_2O$ (100)	H_2O/PEG_{400} (1:9)	42
9	**$FeCl_2·4H_2O$ (30)**	**H_2O/PEG_{400} (3:7)**	**81**
10	$FeCl_2·4H_2O$ (20)	H_2O/PEG_{400} (3:7)	64

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), iron salt, H_2O/PEG_{400} (2 mL), 100 °C, 10 h. Isolated yield.

indoline **3a** was obtained in 61% yield at 100 °C for 10 h under Ar (Table 1, entry 1). Subsequently, various earth-abundant metal complexes, including Fe, Ni, Cu, and Al salts, were screened, which indicates Fe salts show better catalytic performance than other metal salts (Table S1). Besides, in the evaluation of iron salts, such as $FeCl_2·4H_2O$, $Fe(NO_3)_3·9H_2O$, $Fe(acac)_3$, and $FeCl_3$ (Table 1, entries 2−5), $FeCl_2·4H_2O$ was the best choice to afford product **3a** in 65% yield (Table 1, entry 2). Next, the effect of solvent on the reactivity was examined. Replacement of solvent mixture H_2O/PEG_{400} with other solvents, such as CH_3OH, EtOH, and DMF, was found to be detrimental (Table S2). The volumetric ratio of H_2O/PEG_{400} was also screened, and H_2O/PEG_{400} (3/7) was employed to afford product **3a** in 83% yield (Table 1, entry 7). Moreover, the amount of Fe salt was optimized and C5-tosylmethylated indoline **3a** could be isolated in 81% yield in the presence of 30 mol % $FeCl_2·4H_2O$ (Table 1, entries 9). Unfortunately, the efficiency was significantly decreased when the dosage of $FeCl_2·4H_2O$ was adjusted from 30 to 20 mol % (Table 1, entry 10). Finally, the molar ratio of **2a**/**1a**, reaction time, and temperature were also evaluated, which all gave inferior results (Table S4). The structure of compound **3a** was further confirmed by NMR, HRMS, and X-ray diffraction (see Supporting Information for details).

With the optimized conditions in hand (Table 1, entry 9), the substrate scope of *N*-alkylindolines and *N*-methyl tetrahydroquinolines was investigated to examine the generality of this reaction (Table 2). Initially, C2- and C3-substituted

Table 2. Substrate Scope of Indolines and Tetrahydroquinolines[a]



[a]Reaction conditions: **1** (0.1 mmol), **2a** (0.3 mmol), $FeCl_2·4H_2O$ (0.03 mmol), H_2O/PEG_{400} (3/7, 2 mL), 100 °C, 10 h, *under* Ar. Isolated yield. [b]50% of starting material was retrieved.

N-methylindolines were examined to provide the corresponding products **3b−e** in 58−78% yields. Subsequently, indolines bearing substitutions on the aryl moiety were also employed. Pleasingly, both electron-donating (Me, OMe, and OBn,) and electron-withdrawing (F, Cl, and Br) groups at the C4, C6, or C7 position were well tolerated to afford C5-tosylmethylated products **3f−q** in 42−83% yields. Nevertheless, C7-fluoro substituted indoline was less reactive to give the corresponding product **3r** in 20% yield. Next, *N*-methyl tetrahydroquinolines

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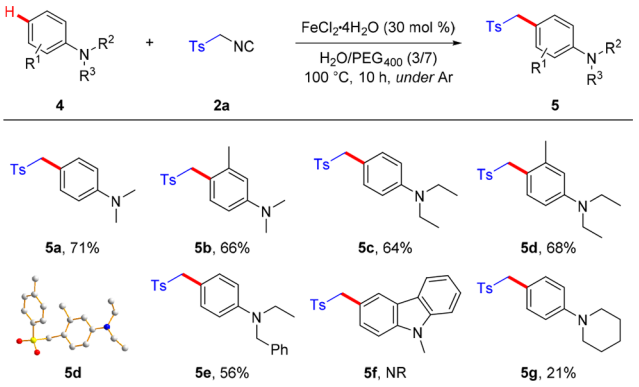
were also employed under the optimized conditions. It was found that both methyl and chloro substituted tetrahydroquinolines proceeded smoothly to provide C6-tosylmethylated products **3s**−**v** in 50−74% yields. Moreover, *N*-methyl benzomorpholine, the scaffold of which is present in some pharmaceuticals,[27] could undergo tosylmethylation to give product **3w** in 20% yield, which is further confirmed by *X*-ray analysis (see the Supporting Information). Finally, *N*-ethyl indoline was also tested to furnish product **3x** in 65% yields. However, *N*-acetyl indoline failed to deliver the corresponding product **3y**. When strongly electron-withdrawing group CF_3 was introduced at the C6 position, no corresponding product could be detected. Meanwhile, when the C5 position was blocked by a methoxy group, no desired C7-substituted product **3z** could be detected. Likewise, NH-free indolines and tetrahydroquinolines were also proven to be unsuccessful for tosylmethylation transformations.

Next, the variation of tertiary aniline derivatives with different substitution patterns was also examined to expand the applicability of the current methodology (Table 3). As

Table 3. Substrate Scope of Anilines[a]

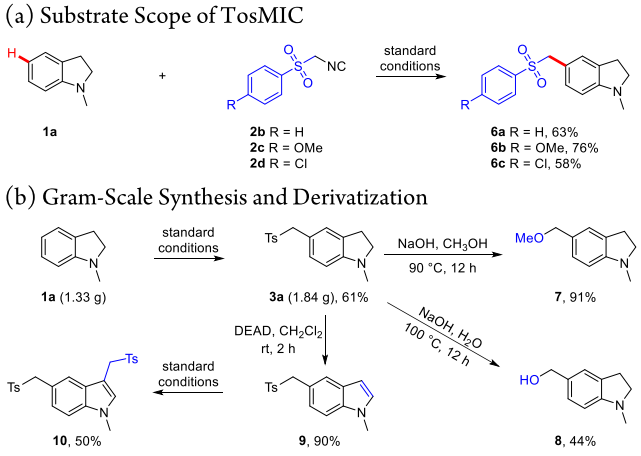


[a]Reaction conditions: **4** (0.1 mmol), **2a** (0.3 mmol), $FeCl_2{\cdot}4H_2O$ (0.03 mmol), H_2O/PEG_{400} (3/7, 2 mL), 100 °C, 10 h, *under* Ar. Isolated yield.

expected, tertiary anilines were tosylmethylated at the *para*-position to afford product **5a**−**e** in 56−71% yields. The structure of **5d** was also determined by X-ray analysis (see the Supporting Information). However, *N*-methylcarbazole exhibits no reactivity. When cyclic amine *N*-phenylpiperidine was employed, the corresponding product **5g** was obtained in 21% yield. Meanwhile, the secondary or primary anilines were also tested, which unfortunately failed to give the corresponding products.

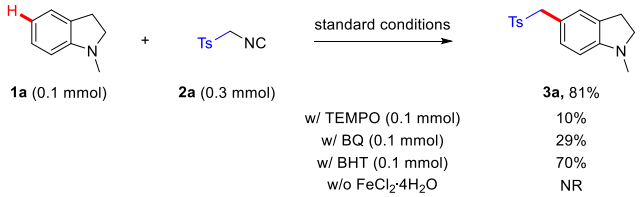
Moreover, substituted TosMIC derivatives **2** were employed to generate products **6a**−**c** in 58−76% yields (Scheme 2a). To demonstrate the synthetic utility of the current methodology, a gram-scale reaction was conducted, and the tosylmethylated product **3a** was isolated in 61% yield. Meanwhile, the obtained **3a** could undergo further derivatizations (Scheme 2b), which delivered methoxymethyl-substituted compound **7** and hydroxy-substituted compound **8** in 91% and 44% yield, respectively. Notably, oxidation of **3a** with diethyl azodicarboxylate (DEAD) as a milder oxidant in dichloromethane at room temperature for 2 h gave indole **9** in 90% yield, which could further be converted into double-tosylmethylated product **10** in 50% yield.

Scheme 2. Substrate Scope of TosMIC, Gram-Scale Synthesis and Derivatization



To explore the reaction mechanism, a set of control experiments were conducted (Scheme 3). In a radical trap

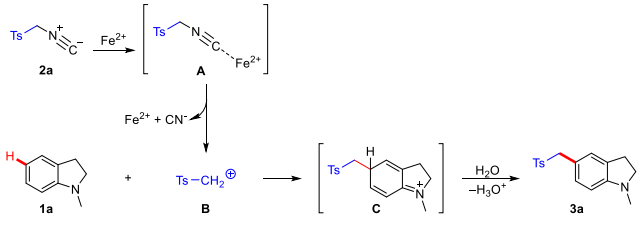
Scheme 3. Control Experiments



experiment, stoichiometric TEMPO, BQ, and BHT were utilized as radical scavengers. The reaction efficiency was suppressed to some extent, which gave product **3a** in 10%, 29%, and 70% yields. This suggested a radical mechanism might not be involved. In the absence of $FeCl_2{\cdot}4H_2O$, no desired product **3a** could be detected, which indicated the necessity of iron salt. Consequently, we speculated that Fe^{2+} could coordinate with isocyanide to facilitate C−N cleavage. Moreover, compared with electron-rich indolines, the ones bearing electron-withdrawing (F, Cl, and Br or *N*-acetyl) groups led to a decreased yield or deactivation of the reaction, indicating tosylmethylation undergoes a Friedel−Crafts-type reaction mechanism.

On the basis of above discussion and previous literature reports,[10,24] a plausible reaction mechanism was proposed (Scheme 4). Initially, Fe^{2+} coordinated with isocyanide to form intermediate **A**. Next, cleavage of the C−N bond gave carbon cation species **B**. Finally, aromatic electrophilic substitution between **B** and **1a** generated intermediate **C**, which underwent a deprotonation process to deliver the desired product **3a**.

Scheme 4. Proposed Reaction Mechanism



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CONCLUSION

In conclusion, we have developed an iron-mediated highly selective C−H sulfonylmethylation of aniline derivatives with TosMIC in a mixture solvent of H_2O and PEG_{400}. A wide range of substrate, including indolines, tetrahydroquinolines, and tertiary anilines, were well tolerated to afford the corresponding products in moderate to high yields. A gram-scale production and multiple derivatizations were investigated to highlight the practical application of this protocol. Notably, the obtained C5-sulfonylmethylated indolines could undergo oxidation and another C3-sulfonylmethylation to give the corresponding disubstituted indole derivatives. Finally, a plausible Friedel−Crafts-type aromatic electrophilic reaction mechanism was proposed.

EXPERIMENTAL SECTION

General Experimental Details. Unless otherwise indicated, all the starting materials (including **4a−d** and **4g**) and reagents were commercially available and used without further purification. Aniline derivatives **1a−1v**,[10g] **1w**,[28a] **1x**,[28e] **1y**,[28c] **1z**,[28d] **4e**,[28g] **4f**,[28f] and TosMIC derivatives **2**[28b] are known compounds and synthesized according to previously reported methods. Melting points were determined on a melting point apparatus. Flash column chromatography was performed using 200−300 mesh silica gel. Analytical and preparative thin-layer chromatography (TLC) plates coated with commercial silica gel GF254 were used to monitor the reactions and purify products. ^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR spectra were recorded on Bruker DPX 400 or Bruker DPX 600 instruments using TMS as an internal standard. Data are reported as follows: chemical shift (δ ppm), multiplicity (s = single, d = doublet, t = triplet, m = multiplet), integration, and coupling constants (J) in hertz (Hz). HRMS were determined on a Q-Tof micro MS/MS system ESI spectrometer. The structures of products **3a** (CCDC file Number 2050319), **3w** (CCDC file Number 2050332), and **5d** (CCDC file Number 2050333) were further confirmed by X-ray diffraction collected on a diffractometer with graphite-monochromated Mo Kα radiation.

General Procedure for the Preparation of Compound of 3, 5 and 6. To a 15 mL sealed tube were added indolines or tetrahydroquinolines **1** or anilines **4** (0.1 mmol), TosMIC derivatives **2** (0.3 mmol), and $FeCl_2{\cdot}4H_2O$ (0.03 mmol, 6.0 mg) in a mixed solvent of PEG_{400} and H_2O (2 mL) under an Ar atmosphere. The reaction mixture was heated at 100 °C for 10 h. After cooling down to room temperature, the reaction mixture was diluted by H_2O (10 mL) and extracted by dichloromethane (3 × 10 mL). The combined organic layers were dried by Na_2SO_4, filtered through Celite, and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel plates using dichloromethane as the eluent to give the corresponding products.

*1-Methyl-5-(tosylmethyl)indoline (**3a**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (24.4 mg, 81%), mp = 147−148 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.86 (s, 1H), 6.69 (d, J = 7.9 Hz, 1H), 6.30 (d, J = 8.0 Hz, 1H), 4.17 (s, 2H), 3.31 (t, J = 8.2 Hz, 2H), 2.89 (t, J = 8.2 Hz, 2H), 2.74 (s, 3H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.8, 144.3, 135.5, 130.7, 130.4, 129.4, 128.7, 126.7, 116.4, 106.5, 62.9, 56.0, 35.8, 28.4, 21.6. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{17}H_{19}NO_2S$, 302.1209; found, 302.1208.

*1,2-Dimethyl-5-(tosylmethyl)indoline (**3b**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (24.6 mg, 78%), mp = 119−120 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.82 (s, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.26 (d, J = 8.0 Hz, 1H), 4.16 (s, 2H), 3.47−3.40 (m, 1H), 3.02 (dd, J = 15.4, 8.3 Hz, 1H), 2.69 (s, 3H), 2.53 (dd, J = 15.4, 10.0 Hz, 1H), 2.42 (s, 3H), 1.30 (d, J = 6.1 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.8, 144.3, 135.5, 130.4, 129.6, 129.4, 128.7, 126.5, 116.4, 106.4, 63.0, 62.7, 37.0, 33.3, 21.6, 18.7. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1369.

*1-Methyl-2-phenyl-5-(tosylmethyl)indoline (**3c**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.6, white solid (21.9 mg, 58%), mp = 153−154 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, J = 8.2 Hz, 2H), 7.35−7.40 (m, 4H), 7.31 (t, J = 7.1 Hz, 1H), 7.27 (d, J = 8.1 Hz, 2H), 6.84 (s, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.34 (d, J = 8.0 Hz, 1H), 4.39 (dd, J = 10.4, 9.2 Hz, 1H), 4.19 (s, 2H), 3.28 (dd, J = 15.7, 8.9 Hz, 1H), 2.86 (dd, J = 15.7, 10.7 Hz, 1H), 2.59 (s, 3H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.7, 144.4, 142.1, 135.6, 130.7, 129.4, 129.0, 128.7, 128.6, 127.7, 127.2, 126.5, 116.7, 106.4, 71.9, 62.9, 39.1, 33.8, 21.6. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{23}H_{23}NO_2S$, 378.1522; found, 378.1524.

*1,3-Dimethyl-5-(tosylmethyl)indoline (**3d**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (23.3 mg, 74%), mp = 105−107 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 6.77 (d, J = 8.0 Hz, 1H), 6.67 (s, 1H), 6.32 (d, J = 8.0 Hz, 1H), 4.18 (q, J = 14.0 Hz, 2H), 3.52 (t, J = 8.5 Hz, 1H), 3.22−3.16 (m, 1H), 2.81 (t, J = 8.4 Hz, 1H), 2.72 (s, 3H), 2.41 (s, 3H), 1.18 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.3, 144.3, 135.6, 135.4, 130.5, 129.4, 128.8, 125.5, 116.6, 106.7, 63.9, 63.0, 35.7, 35.0, 21.6, 18.5. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1369.

*1,2,3-Trimethyl-5-(tosylmethyl)indoline (**3e**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (24.4 mg, 74%), mp = 78−79 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 7.9 Hz, 2H), 6.75 (d, J = 8.0 Hz, 1H), 6.66 (s, 1H), 6.31 (d, J = 8.0 Hz, 1H), 4.18 (q, J = 12.8 Hz, 2H), 2.86−2.81 (m, 1H), 2.71−2.68 (m, 4H), 2.41 (s, 3H), 1.30 (d, J = 6.1 Hz, 3H), 1.18 (d, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.3, 144.3, 135.4, 134.5, 130.5, 129.4, 128.8, 125.0, 116.8, 106.7, 71.0, 63.0, 43.1, 33.7, 21.6, 17.5, 16.7. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{19}H_{23}NO_2S$, 330.1522; found, 330.1523.

*4-Fluoro-1-methyl-5-(tosylmethyl)indoline (**3f**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (19.5 mg, 61%), mp = 140−141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.88 (t, J = 7.7 Hz, 1H), 6.16 (d, J = 8.0 Hz, 1H), 4.25 (s, 2H), 3.38 (t, J = 8.4 Hz, 2H), 2.87 (t, J = 8.4 Hz, 2H), 2.75 (s, 3H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.0 (d, J = 232.3 Hz), 156.6 (d, J = 6.1 Hz), 144.4, 135.6, 132.3 (d, J = 3.6 Hz), 129.4, 128.7, 114.9(d, J = 22.0 Hz), 104.1(d, J = 15.4 Hz), 102.7 (d, J = 2.4 Hz), 56.0 (d, J = 2.0 Hz), 55.9, 35.4, 24.7, 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ −124.33. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{17}H_{18}FNO_2S$, 320.1115; found, 320.1117.

*4-Chloro-1-methyl-5-(tosylmethyl)indoline (**3g**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (17.1 mg, 51%), mp = 143−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 1H), 6.27 (d, J = 8.0 Hz, 1H), 4.41 (s, 2H), 3.39 (t, J = 8.4 Hz, 2H), 2.90 (t, J = 8.4 Hz, 2H), 2.76 (s, 3H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.7, 144.5, 135.8, 132.5, 131.5, 129.4, 128.8, 128.6, 114.0, 104.8, 59.1, 55.1, 35.4, 28.3, 21.7. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{17}H_{18}ClNO_2S$, 336.0820; found, 336.0821.

*1,4-Dimethyl-5-(tosylmethyl)indoline (**3h**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (19.2 mg, 61%), mp = 149−151 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 6.69 (d, J = 8.0 Hz, 1H), 6.20 (d, J = 8.0 Hz, 1H), 4.27 (s, 2H), 3.33 (t, J = 8.3 Hz, 2H), 2.84 (t, J = 8.3 Hz, 2H), 2.73 (s, 3H), 2.43 (s, 3H), 2.01 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 147.6, 144.4, 135.9, 133.7, 132.3, 129.4, 128.8, 121.6, 112.0, 110.4, 59.2, 50.7, 38.8, 27.2, 21.9, 21.7. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1367.

*4-Methoxy-1-methyl-5-(tosylmethyl)indoline (**3i**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (18.6 mg, 56%), mp = 95−96 °C. ^{1}H NMR (600

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MHz, $CDCl_3$) δ 7.60 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 1H), 6.13 (d, J = 8.0 Hz, 1H), 4.32 (s, 2H), 3.59 (s, 3H), 3.32 (t, J = 8.2 Hz, 2H), 3.00 (t, J = 8.2 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 156.5, 155.3, 144.1, 136.4, 131.9, 129.3, 128.8, 118.2, 108.9, 102.2, 59.3, 56.7, 56.1, 35.8, 27.1, 21.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{21}NO_3S$, 332.1315; found, 332.1317.

*6-Fluoro-1-methyl-5-(tosylmethyl)indoline (**3j**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (24.9 mg, 78%), mp = 154−156 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 7.2 Hz, 1H), 5.94 (d, J = 11.0 Hz, 1H), 4.23 (s, 2H), 3.38 (t, J = 8.3 Hz, 2H), 2.90 (t, J = 8.2 Hz, 2H), 2.72 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 161.9 (d, J = 245.5 Hz), 155.4 (d, J = 12.2 Hz), 144.4, 135.6, 129.4, 128.6, 127.0 (d, J = 4.5 Hz), 125.9 (d, J = 2.2 Hz), 102.2 (d, J = 16.5 Hz), 93.9 (d, J = 27.6 Hz), 56.0, 55.9 (d, J = 3.2 Hz), 35.2, 27.7, 21.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ −119.18. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{17}H_{18}FNO_2S$, 320.1115; found, 320.1119.

*6-Chloro-1-methyl-5-(tosylmethyl)indoline (**3k**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (18.1 mg, 54%), mp = 149−150 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.09 (s, 1H), 6.24 (s, 1H), 4.39 (s, 2H), 3.39 (t, J = 8.3 Hz, 2H), 2.93 (t, J = 8.3 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 154.6, 144.5, 135.7, 134.6, 129.6, 129.4, 128.8, 127.8, 113.6, 106.8, 59.4, 55.8, 35.2, 27.9, 21.7. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{17}H_{18}ClNO_2S$, 336.0820; found, 336.0821.

*6-Bromo-1-methyl-5-(tosylmethyl)indoline (**3l**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (16.0 mg, 42%), mp = 142−143 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.13 (s, 1H), 6.42 (s, 1H), 4.42 (s, 2H), 3.39 (t, J = 8.3 Hz, 2H), 2.92 (t, J = 8.3 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 154.7, 144.5, 135.7, 130.3, 129.5, 128.9, 127.9, 125.0, 115.4, 109.9, 61.8, 55.8, 35.1, 28.0, 21.7. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{17}H_{18}BrNO_2S$, 380.0315; found, 380.0314.

*1,6-Dimethyl-5-(tosylmethyl)indoline (**3m**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (26.2 mg, 83%), mp = 141−142 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 7.9 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 6.80 (s, 1H), 6.18 (s, 1H), 4.23 (s, 2H), 3.30 (t, J = 8.1 Hz, 2H), 2.85 (t, J = 8.1 Hz, 2H), 2.73 (s, 3H), 2.42 (s, 3H), 1.97 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 153.9, 144.4, 137.6, 136.0, 129.4, 128.7, 128.2, 127.7, 114.8, 108.8, 60.3, 56.1, 35.8, 28.1, 21.6, 19.7. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1366.

*6-Methoxy-1-methyl-5-(tosylmethyl)indoline (**3n**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.2, white solid (27.2 mg, 82%), mp = 127−128 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 6.97 (s, 1H), 5.80 (s, 1H), 4.30 (s, 2H), 3.33 (t, J = 8.2 Hz, 2H), 3.31 (s, 3H), 2.88 (t, J = 8.2 Hz, 2H), 2.73 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 158.1, 155.2, 143.7, 136.3, 128.9, 128.8, 127.6, 121.9, 104.4, 90.7, 56.9, 56.4, 55.0, 35.7, 27.7, 21.5. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{21}NO_3S$, 332.1315; found, 332.1316.

*1,7-Dimethyl-5-(tosylmethyl)indoline (**3o**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (22.7 mg, 72%), mp = 115−116 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 5.9 Hz, 2H), 6.70 (s, 1H), 6.50 (s, 1H), 4.13 (s, 2H), 3.29 (t, J = 8.5 Hz, 2H), 2.92 (s, 3H), 2.85 (t, J = 8.5 Hz, 2H), 2.42 (s, 3H), 2.26 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 151.8, 144.3, 135.6, 133.6, 131.5, 129.4, 128.7, 124.8, 119.6, 117.9, 62.7, 57.4, 39.8, 28.6, 21.6, 19.3. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1365.

*7-Methoxy-1-methyl-5-(tosylmethyl)indoline (**3p**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.2, white solid (20.5 mg, 62%), mp = 93−94 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 6.50 (s, 1H), 6.29 (s, 1H), 4.17 (s, 2H), 3.62 (s, 3H), 3.26 (t, J = 8.5 Hz, 2H), 2.96 (s, 3H), 2.86 (t, J = 8.5 Hz, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 146.1, 144.4, 141.9, 135.4, 132.5, 129.4, 128.8, 120.3, 118.6, 114.1, 63.0, 57.4, 55.7, 39.3, 29.1, 21.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{21}NO_3S$, 332.1315; found, 332.1316.

*7-(Benzyloxy)-1-methyl-5-(tosylmethyl)indoline (**3q**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (25.7 mg, 63%), mp = 141−142 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.38−7.37 (m, 4H), 7.34−7.30 (m, 1H), 7.25 (d, J = 7.9 Hz, 2H), 6.51 (s, 1H), 6.40 (s, 1H), 4.82 (s, 2H), 4.16 (s, 2H), 3.27 (t, J = 8.5 Hz, 2H), 2.97 (s, 3H), 2.87 (t, J = 8.5 Hz, 2H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 145.2, 144.4, 142.2, 137.0, 135.5, 132.8, 129.4, 128.8, 128.5, 127.9, 127.5, 120.7, 118.5, 115.5, 71.0, 63.0, 57.4, 39.3, 29.1, 21.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{24}H_{25}NO_3S$, 408.1628; found, 408.1631.

*7-Fluoro-1-methyl-5-(tosylmethyl)indoline (**3r**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (6.4 mg, 20%), mp = 124−125 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.67 (s, 1H), 6.47 (d, J = 12.5 Hz, 1H), 4.13 (s, 2H), 3.32 (t, J = 8.4 Hz, 2H), 2.94−2.91 (m, 5H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 148.7 (d, J = 241.2 Hz), 144.6, 140.1 (d, J = 8.6 Hz), 135.3, 134.4 (d, J = 5.7 Hz), 129.5, 128.6, 122.8 (d, J = 2.0 Hz), 118.0 (d, J = 6.3 Hz), 117.8 (d, J = 20.8 Hz), 62.3, 57.0, 38.1 (d, J = 7.0 Hz), 29.3, 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ −137.88. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{17}H_{18}FNO_2S$, 320.1115; found, 320.1115.

*1-Methyl-6-(tosylmethyl)-1,2,3,4-tetrahydroquinoline (**3s**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (22.1 mg, 70%), mp = 101−102 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 6.72 (d, J = 8.3 Hz, 1H), 6.67 (s, 1H), 6.42 (d, J = 8.3 Hz, 1H), 4.14 (s, 2H), 3.22 (t, J = 5.8 Hz, 2H), 2.86 (s, 3H), 2.65 (t, J = 6.4 Hz, 2H), 2.42 (s, 3H), 1.95−1.91 (m, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 146.9, 144.2, 135.6, 131.2, 129.6, 129.4, 128.7, 122.7, 114.5, 110.5, 62.6, 51.1, 38.9, 27.6, 22.2, 21.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1369.

*1,4-Dimethyl-6-(tosylmethyl)-1,2,3,4-tetrahydroquinoline (**3t**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.6, white solid (23.1 mg, 70%), mp = 126−127 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 6.83 (dd, J = 8.3, 1.9 Hz, 1H), 6.59 (d, J = 1.4 Hz, 1H), 6.45 (d, J = 8.4 Hz, 1H), 4.16 (q, J = 14.0 Hz, 2H), 3.26−3.16 (m, 2H), 2.87 (s, 3H), 2.76−2.71 (m, 1H), 2.41 (s, 3H), 1.99−1.94 (m, 1H), 1.65−1.60 (m, 1H), 1.09 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 146.2, 144.2, 135.5, 130.2, 129.6, 129.3, 128.8, 127.7, 114.6, 110.6, 62.8, 48.0, 39.0, 30.6, 29.6, 22.3, 21.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{19}H_{23}NO_2S$, 330.1522; found, 330.1526.

*1,5-Dimethyl-6-(tosylmethyl)-1,2,3,4-tetrahydroquinoline (**3u**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.7, white solid (24.4 mg, 74%), mp = 156−157 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 7.2 Hz, 2H), 6.72 (d, J = 8.5 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 4.30 (s, 2H), 3.17 (t, J = 6.6 Hz, 2H), 2.86 (s, 3H), 2.60 (t, J = 6.6 Hz, 2H), 2.43 (s, 3H), 2.00−1.96 (m, 5H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 147.4, 144.3, 136.5, 136.1, 130.6, 129.4, 128.7, 121.7, 114.0, 109.0, 60.8, 50.7, 39.7, 25.37, 22.5, 21.6, 15.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{19}H_{23}NO_2S$, 330.1522; found, 330.1525.

*7-Chloro-1-methyl-6-(tosylmethyl)-1,2,3,4-tetrahydroquino-line (**3v**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.6, white solid (17.4 mg, 50%), mp = 106−107 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.93 (s, 1H), 6.37 (s, 1H), 4.36 (s, 2H), 3.25 (t, J = 6.3 Hz, 2H), 2.85 (s, 3H), 2.68 (t, J = 6.3 Hz, 2H), 2.42 (s, 3H), 1.96−1.92 (m, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 147.6, 144.4, 135.8, 133.7, 132.3, 129.4, 128.8, 121.6, 112.0, 110.4, 59.2, 50.7, 38.7, 27.2, 21.9, 21.7. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{18}H_{20}ClNO_2S$, 350.0976; found, 350.0979.

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*4-Methyl-7-(tosylmethyl)-3,4-dihydro-2H-benzo[b][1,4]oxaz-ine (**3w**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.6, white solid (6.3 mg, 20%), mp = 106−107 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.3 Hz, 2H), 6.56−6.51 (m, 3H), 4.24 (t, J = 4.3 Hz, 2H), 4.14 (s, 2H), 3.25 (t, J = 4.3 Hz, 2H), 2.86 (s, 3H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 144.4, 144.0, 136.9, 135.6, 129.4, 128.6, 124.1, 118.2, 117.0, 112.0, 64. 7, 62.5, 48.9, 38.6, 21.6. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{17}H_{19}NO_3S$, 318.1159; found, 318.1157.

*1-Ethyl-5-(tosylmethyl)indoline (**3x**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (20.5 mg, 65%), mp = 114−115 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.85 (s, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.29 (d, J = 8.0 Hz, 1H), 4.16 (s, 2H), 3.35 (t, J = 8.3 Hz, 2H), 3.12 (q, J = 7.2 Hz, 2H), 2.89 (t, J = 8.3 Hz, 2H), 2.42 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 152.7, 144.3, 135.5, 130.7, 130.3, 129.4, 128.7, 126.8, 116.1, 106.5, 62.9, 52.1, 42.7, 28.2, 21.6, 11.8. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{18}H_{21}NO_2S$, 316.1366; found, 316.1366.

*N,N-Dimethyl-4-(tosylmethyl)aniline (**5a**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (20.5 mg, 71%), mp = 107−108 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.58 (d, J = 8.7 Hz, 2H), 4.19 (s, 2H), 2.93 (s, 6H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 150.6, 144.3, 135.5, 131.6, 129.4, 128.7, 115.1, 112.2, 62.5, 40.3, 21.6. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{16}H_{19}NO_2S$, 290.1209; found, 290.1211.

*N,N,3-Trimethyl-4-(tosylmethyl)aniline (**5b**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (20.0 mg, 66%), mp = 144−145 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 6.88 (d, J = 8.3 Hz, 1H), 6.47−6.45 (m, 2H), 4.26 (s, 2H), 2.93 (s, 6H), 2.43 (s, 3H), 2.05 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 150.8 144.4, 138.9, 135.9, 132.8, 129.5, 128.7, 114.1, 113.9, 110.1, 59.9, 40.3, 21.6, 19.9. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{17}H_{21}NO_2S$, 304.1366; found, 304.1365.

*N,N-Diethyl-4-(tosylmethyl)aniline (**5c**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (20.3 mg, 64%), mp = 104−105 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.6 Hz, 2H), 6.54 (d, J = 8.6 Hz, 2H), 4.17 (s, 2H), 3.33 (q, J = 7.1 Hz, 4H), 2.42 (s, 3H), 1.14 (t, J = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 148.0, 144.2, 135.6, 131.9, 129.4, 128.7, 113.9, 111.5, 62.6, 44.3, 21.6, 12.5. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{18}H_{23}NO_2S$, 318.1522; found, 318.1520.

*N,N-Diethyl-3-methyl-4-(tosylmethyl)aniline (**5d**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (22.5 mg, 68%), mp = 82−83 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 6.85 (d, J = 8.1 Hz, 1H), 6.42−6.40 (m, 2H), 4.25 (s, 2H), 3.32 (q, J = 7.1 Hz, 4H), 2.43 (s, 3H), 2.06 (s, 3H), 1.14 (t, J = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 148.1, 144.3, 139.1, 136.1, 133.0, 129.4, 128.7, 113.3, 112.7, 109.5, 59.9, 44.2, 21.6, 20.1, 12.5. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{19}H_{25}NO_2S$, 332.1679; found, 332.1678.

*N-Benzyl-N-ethyl-4-(tosylmethyl)aniline (**5e**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (21.3 mg, 56%), mp = 71−72 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, J = 7.9 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.24−7.18 (m, 5H), 6.87 (d, J = 8.4 Hz, 2H), 6.55 (d, J = 8.4 Hz, 2H), 4.49 (s, 2H), 4.15 (s, 2H), 3.45 (q, J = 7.0 Hz, 2H), 2.39 (s, 3H), 1.19 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 148.6, 144.3, 138.8, 135.5, 131.8, 129.4, 128.7, 128.6, 126.9, 126.5, 114.7, 112.0, 62.5, 53.8, 45.3, 21.6, 12.1. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{23}H_{25}NO_2S$, 380.1679; found, 380.1678.

*1-(4-(Tosylmethyl)phenyl)piperidine (**5g**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.4, white solid (6.9 mg, 21%), mp = 155−156 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 7.9 Hz, 2H), 7.23 (d, J = 7.9 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 4.19 (s, 2H), 3.15 (t, J = 5.3 Hz, 4H), 2.42 (s, 3H), 1.70−1.66 (m, 4H), 1.60−1.57 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 152.2, 144.4, 135.4, 131.6, 129.4, 128.7, 117.7, 115.84, 62.4, 50.0, 25.6, 24.3, 21.6. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{19}H_{23}NO_2S$, 330.1522; found, 330.1520.

*1-Methyl-5-((phenylsulfonyl)methyl)indoline (**6a**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (18.1 mg, 63%), mp = 121−122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67−7.66 (m, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 6.84 (s, 1H), 6.69 (d, J = 7.9 Hz, 1H), 6.29 (d, J = 8.0 Hz, 1H), 4.19 (s, 2H), 3.31 (t, J = 8.2 Hz, 2H), 2.88 (t, J = 8.2 Hz, 2H), 2.73 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.8, 138.4, 133.4, 130.7, 130.4, 128.8, 128.7, 126.7, 116.2, 106.5, 62.9, 55.9, 35.8, 28.4. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{16}H_{17}NO_2S$, 288.1053; found, 288.1050.

*5-(((4-Methoxyphenyl)sulfonyl)methyl)-1-methylindoline (**6b**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.3, white solid (24.1 mg, 76%), mp = 118−119 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.86 (s, 1H), 6.68 (d, J = 7.9 Hz, 1H), 6.30 (d, J = 8.0 Hz, 1H), 4.16 (s, 2H), 3.86 (s, 3H), 3.31 (t, J = 8.2 Hz, 2H), 2.89 (t, J = 8.2 Hz, 2H), 2.73 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 163.5, 153.7, 130.9, 130.7, 130.3, 130.0, 126.7, 116.7, 113.9, 106.5, 63.1, 56.0, 55.6, 35.8, 28.4. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{17}H_{19}NO_3S$, 318.1159; found, 318.1165.

*5-(((4-Chlorophenyl)sulfonyl)methyl)-1-methylindoline (**6c**).* Purified by analytical TLC on silica gel with dichloromethane as an eluent with R_f = 0.5, white solid (18.7 mg, 58%), mp = 139−140 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 7.26 (s, 1H), 6.67 (d, J = 7.9 Hz, 1H), 6.29 (d, J = 8.0 Hz, 1H), 4.19 (s, 2H), 3.33 (t, J = 8.3 Hz, 2H), 2.89 (t, J = 8.2 Hz, 2H), 2.74 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.9, 140.2, 136.8, 130.8, 130.4, 130.2, 129.0, 126.6, 115.8, 106.4, 63.0, 55.9, 35.7, 28.3. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{16}H_{16}ClNO_2S$, 322.0663; found, 322.0664.

Gram-Scale Synthesis. To a 500 mL Schlenk bottle were added **1a** (10 mmol, 1.33 g), **2a** (30 mmol, 5.86 g), and $FeCl_2{\cdot}4H_2O$ (3 mmol, 0.60 g) in a mixed solvent of PEG_{400} and H_2O (200 mL) under an Ar atmosphere. The reaction mixture was heated at 100 °C for 10 h. After cooling down to room temperature, the reaction mixture was diluted by H_2O (100 mL) and extracted by dichloromethane (3 × 150 mL). The combined organic layers were dried by Na_2SO_4, filtered through Celite, and concentrated under reduced pressure. The residue was purified through a silica gel column using petroleum ether/dichloromethane = 1/1 as the eluent to give pure products **3a** in 61% isolated yield (1.84 g was isolated).

5-(Methoxymethyl)-1-methylindoline 7. To a 15 mL sealed tube were added **3a** (0.2 mmol, 60.3 mg), NaOH (1.0 mmol, 40 mg), and then CH_3OH (2 mL). The vessel was sealed with a Teflon-lined cap, and the reaction mixture was allowed to stir at 90 °C (oil bath) for 12 h. Then the solvent was directly evaporated, and the residue was purified by preparative TLC on silica gel plates using petroleum/ethyl acetate = 5/1 as the eluent to give the desired product **7** in 91% yield. R_f = 0.6, colorless liquid (32.3 mg, 91%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.06 (s, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.44 (d, J = 7.9 Hz, 1H), 4.32 (s, 2H), 3.33 (s, 3H), 3.28 (t, J = 8.1 Hz, 2H), 2.92 (t, J = 8.1 Hz, 2H), 2.74 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 153.3, 130.7, 127.8, 127.4, 124.6, 106.7, 75.1, 57.6, 56.3, 36.3, 28.6. HRMS (ESI) m/z: (M + H)$^+$ calcd for $C_{11}H_{15}NO$, 178.1227; found, 178.1227.

(1-Methylindolin-5-yl)methanol 8. To a 15 mL sealed tube were added **3a** (0.2 mmol, 60.3 mg), NaOH (1.0 mmol, 40 mg), and then H_2O (2 mL). The vessel was sealed with a Teflon-lined cap, and the reaction mixture was allowed to stir at 100 °C (oil bath) for 12 h. Then the solvent was extracted by dichloromethane (3 × 5 mL). The combined organic layers were dried by Na_2SO_4, filtered through Celite, and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel plates using dichloromethane/ethyl acetate = 1/1 as the eluent to give the desired product **8** in 44% yield. R_f = 0.4, colorless liquid (14.4 mg, 44%). ^{1}H NMR (600 MHz, d_6-DMSO) δ 7.00 (s, 1H), 6.95 (d, J = 7.8 Hz, 1H), 6.44

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(d, J = 7.9 Hz, 1H), 4.85 (t, J = 5.6 Hz, 1H), 4.33 (d, J = 5.5 Hz, 2H), 3.21 (t, J = 8.1 Hz, 2H), 2.84 (t, J = 8.1 Hz, 2H), 2.67 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, d_6-DMSO) δ 152.9, 132.1, 130.3, 126.4, 123.8, 106.9, 63.7, 56.3, 36.6, 28.6. ESI-MS (m/z): $(M + H)^+$ calcd for $C_{10}H_{13}NO$, 164.1070; found, 164.1035.

1-Methyl-5-(tosylmethyl)-1*H*-indole 9. To a solution of **3a** (0.1 mmol, 30.1 mg) in CH_2Cl_2 (10 mL) DEAD (0.11 mmol, 19.2 mg) was added. The mixture was stirred at the room temperature for 2 h and then concentrated and purified by preparative TLC on silica gel plates using dichloromethane as the eluent to give the desired product **9** in 90% yield. R_f = 0.4, white solid (27.0 mg, 90%), mp = 176−177 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, J = 7.5 Hz, 2H), 7.32 (s, 1H), 7.20 (d, J = 8.0 Hz, 3H), 7.04 (s, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.39 (s, 1H), 4.39 (s, 2H), 3.77 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 144.3, 136.7, 135.4, 129.5, 129.4, 128.7, 128.5, 124.1, 123.6, 118.7, 109.2, 101.2, 63.4, 32.9, 21.6. HRMS (ESI) m/z: $(M + H)^+$ calcd for $C_{17}H_{17}NO_2S$, 300.1053; found, 300.1055.

1-Methyl-3,5-bis(tosylmethyl)-1*H*-indole 10. To a 15 mL sealed tube were added **9** (0.1 mmol, 29.9 mg), TosMIC **2a** (0.3 mmol, 58.6 mg), and $FeCl_2{\cdot}4H_2O$ (0.03 mmol, 6.0 mg) in a mixed solvent of PEG_{400} and H_2O (2 mL) under an Ar atmosphere. The reaction mixture was heated at 100 °C for 10 h. After cooling down to room temperature, the reaction mixture was diluted by H_2O (10 mL) and extracted by dichloromethane (3 × 10 mL). The combined organic layers were dried by Na_2SO_4, filtered through Celite, and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel plates using dichloromethane/ethyl acetate = 20/1 as the eluent to give the desired product **10** in 50% yield. R_f = 0.4, white solid (23.5 mg, 50%). mp = 175−176 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 7.9 Hz, 4H), 7.16 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 8.5 Hz, 2H), 6.91 (d, J = 8.4 Hz, 1H), 4.39 (s, 2H), 4.29 (s, 2H), 3.72 (s, 3H), 2.39 (s, 3H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 144.5, 144.4, 136.7, 135.7, 135.4, 131.1, 129.5, 129.4, 128.6, 128.5, 127.7, 124.7, 121.6, 119.4, 109.5, 101.3, 63.2, 54.1, 33.0, 21.6, 21.5. HRMS (ESI) m/z: $(M + Na)^+$ calcd for $C_{25}H_{25}NO_4S_2$, 490.1117; found, 490.1117.

Reaction in the Presence of Radical Scavengers. To a 15 mL sealed tube were added **1a** (0.1 mmol, 13.3 mg), TosMIC derivatives **2** (0.3 mmol, 58.6 mg), and $FeCl_2{\cdot}4H_2O$ (0.03 mmol, 6.0 mg) and radical scavengers (TEMPO, BQ, BHT, 1.0 equiv) in a mixed solvent of PEG_{400} and H_2O (2 mL) under an Ar atmosphere. The reaction mixture was heated at 100 °C for 10 h. After cooling down to room temperature, the reaction mixture was diluted by H_2O (10 mL) and extracted by dichloromethane (3 × 10 mL). The combined organic layers were dried by Na_2SO_4, filtered through Celite, and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel plates using dichloromethane as the eluent to give the corresponding products **3a** in 10%, 29%, and 70% yields, respectively.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00500.

Optimization of reaction conditions; X-ray crystal structure of **3a**, **3w**, and **5d**; NMR spectra of compounds (PDF)

Accession Codes

CCDC 2050319 and 2050332−2050333 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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