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Reactivity of *p*-Toluenesulfonylmethyl Isocyanide: Iron-Involved C−H Tosylmethylation of Imidazopyridines in Nontoxic Media

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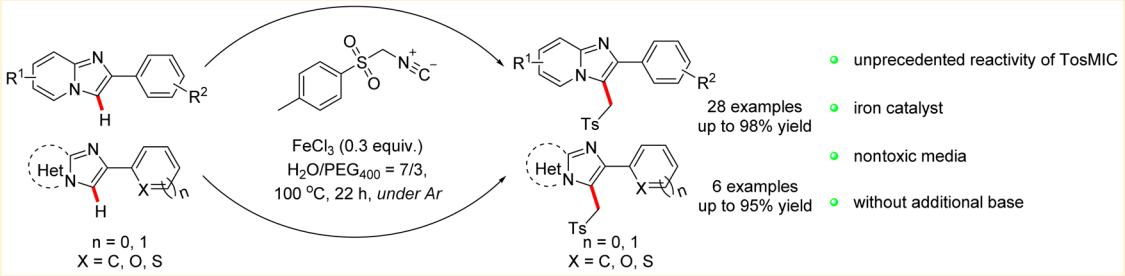
Supporting Information



ABSTRACT: A novel iron-involved tosylmethylation of imidazo[1,2-α]pyridines with *p*-toluenesulfonylmethyl isocyanide in a solvent mixture of H_2O and PEG_{400} under an Ar atmosphere has been developed. This protocol provides a facile synthetic route for the functionalization of the imidazo[1,2-α]pyridine scaffold with broad substrate compatibility, which is less expensive and environmentally friendly. The current methodology could further enable regioselective C−H tosylmethylation of indole at the C3 position. Also, *p*-toluenesulfonylmethyl isocyanide was utilized as the tosylmethylating reagent for the first time.

INTRODUCTION

Nitrogen containing heterocycles have gained much attention due to their utility as valuable intermediates for synthetic transformations as well as their wide applications in pharmaceuticals and agrochemicals. Among the heterocyclic system, imidazo[1,2-α]pyridine have been recognized as a privileged scaffold because of its diverse biological and pharmacological activity such as anti-inflammatory,[1a] antibacterial,[1b] antiviral,[1c,d] anticancer,[1e,f] antiulcer,[1g] anti-HIV,[1h] and antituberculosis properties.[1i] Many drugs bearing an imidazo[1,2-α]pyridine moiety, including zolpidem,[2a] alpidem,[2b] zolimidine,[2c] saripidem,[2d] and olprinone[2e] have been commercialized. Moreover, imidazo[1,2-α]pyridine derivatives exhibit an excited-state intramolecular proton-transfer process, which are widely utilized in optoelectronics.[3]

Consequently, continuous synthetic protocols have been carried out to access the diversity of imidazo[1,2-α]pyridine,[4] such as condensation reaction,[5] tandem reaction,[6] multicomponent reaction,[7] oxidative coupling,[8] intramolecular C−H amination,[9] and dehydrogenative aminooxygenation.[10] Meanwhile, the electron-rich nature of imidazo[1,2-α]pyridine moiety enables direct C−H functionalization on the C-3 position to form a C−C and C−X (heteroatoms) bond.[11] Examples of representative methodologies include alkenylation,[12] arylation,[13] dicarbonylation,[14] thiolation,[15] oxidative cycloaromatization,[16] thiocyanation,[17] and formylation.[18] Although significant work has been undertaken to construct and functionalize the imidazo[1,2-α]pyridine core unit, the development of a cost-effective and environmentally benign system is still limited.

p-Toluenesulfonylmethyl isocyanide (TosMIC) reagents have been widely utilized as a versatile and valuable building block in organic transformations owing to their multiple reactivities and easy removal of the tosyl group.[19] Under basic or metal-catalyzed/promoted conditions, a wide range of bioactive molecules, for example, pyrroles,[20a] oxazoles,[20b] imidazoles,[20c] benzofurans,[20d] imidazo[1,2-α]pyridine (Scheme 1a),[20e] and other *N*-heterocycles[20f−i] have been successfully constructed. TosMIC could also be utilized as a sulfonyl source to afford corresponding benzofurans[20d] and α-sulfonated carbonyl compounds (Scheme 1b).[21] However, the use of TosMIC as a tosylmethylating regent has not yet been reported.

Recently, our group successfully realized C−H functionalization of 2-arylimidazo[1,2-α]pyridines with alkynes, β-nitrostyrenes, ethyl trifluoropyruvate, and 1,1,1-trifluoro-2-iodoethane.[22] In continuation of our ongoing work on C−H functionalization of imidazo[1,2-α]pyridine derivatives, we herein report a novel iron-involved C−H functionalization of imidazo[1,2-α]pyridines with TosMIC to access 3-tosylmethylated imidazo[1,2-α]pyridine (Scheme 1c). Despite the fact that cleavage of the isocyanides has been found in many other isocyanide complexes,[19d] to the best of our knowledge, the

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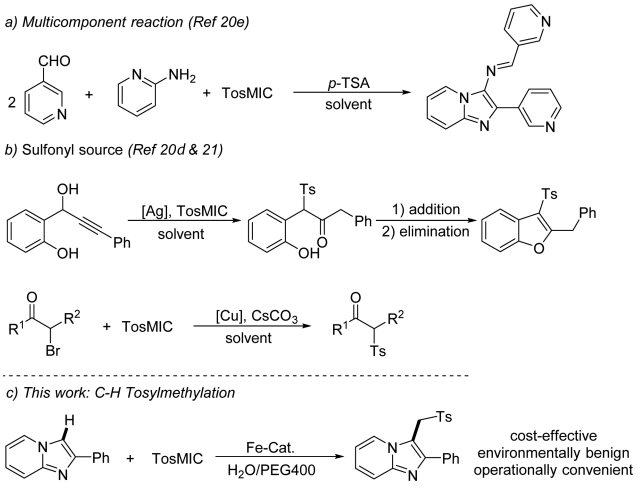
Scheme 1. Versatility of TosMIC in Synthetic Chemistry



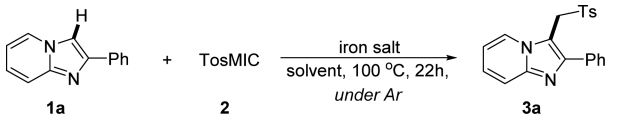
reaction of TosMIC involving isocyanide cleavage to form a $C(sp^2)-C(sp^3)$ bond between substrates and tosylmethylene has not yet been achieved. In accordance with green and sustainable chemistry, we utilized iron salts, the second most earth-abundant metal, as the catalyst and mixture of water and PEG_{400} as the nontoxic media. The obtained tosylmethylene group will be of great interest since it can be further converted into diverse functional groups and commercially available drugs, such as nicopidem, saripidem, *etc.*

RESULTS AND DISCUSSION

Initially, 2-phenylimidazo[1,2-α]pyridine **1a** (0.1 mmol) and TosMIC **2** (0.2 mmol) were employed as the model substrates to test the reactivity. To avoid the usage of expensive catalysts, we commenced our studies by choosing earth-abundant metal complexes including Fe, Co, Ni, Cu, and Zn salts. When $FeCl_3$ (1 equiv) and K_2CO_3 (1 equiv) was employed, unexpectedly, the tosylmethylated product **3a** was obtained in 30% yield in 1,4-dioxane at 100 °C for 22 h under Ar. The structure of compound **3a** was further confirmed by NMR, HRMS and X-ray diffraction (see Supporting Information for details). This reaction represents a new strategy for the C−H functionalization of imidazo[1,2-α]pyridine scaffold.

With this preliminary result in hand, the effects of solvents, iron resources, and base were extensively screened (Table 1). To our delight, the reaction carried out in H_2O gave the best result in 62% yield, despite other solvents, including toluene, THF, and DMSO, were also effective to generate the corresponding product (Table S1). When a mixed solvent of H_2O and PEG_{400} (7:3) was employed, the reaction efficiency was further improved in 90% yield (Table 1, entry 2). Subsequently, various iron salts such as $FeCl_2$, $FeSO_4$, $Fe(OAc)_2$, and FeC_2O_4 were evaluated (Table S1), which provided decreased yields compared with $FeCl_3$. Afterward, the roles of different bases, including ^{t}BuOK, KOAc, $CsCO_3$, and KOH, were investigated (Table S1). Interestingly, it was noticed that the presence of base is not required for the 3-tosylmethylation, which gave **3a** in 83% yield when considering the yield and atom economy (Table 1, entry 3). The amount of $FeCl_3$ was also optimized, which demonstrated that 0.3 equiv was required to obtain the product in 85% yield (Table 1, entry 5). In a control experiment, the desired product could not be detected in the absence of $FeCl_3$, indicating the necessity of iron salts. To further improve the reaction performance, the

Table 1. Optimization of Reaction Conditions[a]



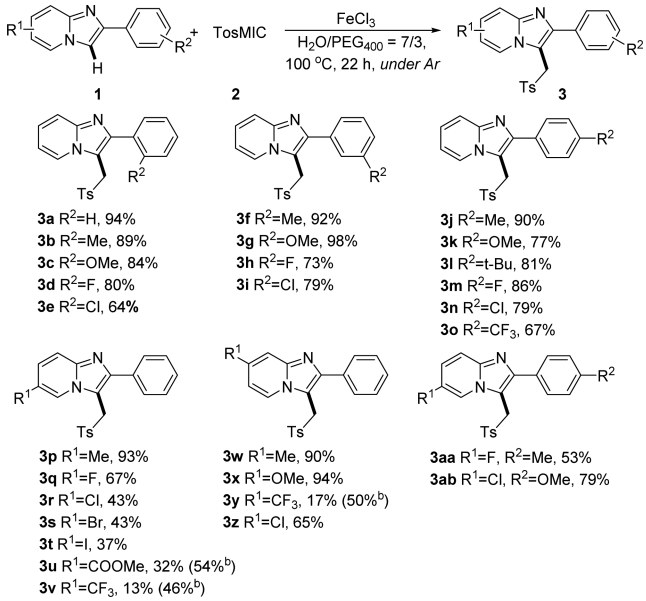
entry	catalyst (equiv)	base (1 equiv)	solvent	yield (%)
1	$FeCl_3$ (1.0)	K_2CO_3	H_2O	62
2	$FeCl_3$ (1.0)	K_2CO_3	H_2O/PEG_{400}[b]	90
3	$FeCl_3$ (1.0)	–	H_2O/PEG_{400}[b]	83
4	$FeCl_3$ (0.5)	–	H_2O/PEG_{400}[b]	82
5	$FeCl_3$ (0.3)	–	H_2O/PEG_{400}[b]	85
6	$FeCl_3$ (0.2)	–	H_2O/PEG_{400}[b]	72
7	–	–	H_2O/PEG_{400}[b]	–
8[c]	$FeCl_3$ (0.3)	–	H_2O/PEG_{400}[b]	33
9[d]	$FeCl_3$ (0.3)	–	H_2O/PEG_{400}[b]	94
10[e]	$FeCl_3$ (0.3)	–	H_2O/PEG_{400}[b]	81
11[f]	$FeCl_3$ (0.3)	–	H_2O/PEG_{400}[b]	46

[a]The reaction was conducted with **1a** (0.1 mmol), **2** (0.2 mmol) in the presence of base in solvent (2 mL) using iron salts for 22 h under Ar. [b]H_2O/PEG_{400} = 7/3. [c]**2** (0.15 mmol) was used. [d]**2** (0.3 mmol) was used. [e]Under air. [f]Under oxygen.

molar ratio of **2**/**1a** was increased from 2/1 to 3/1, which delivered the product **3aa** in 94% yield (Table 1, entry 9). Furthermore, decreased yields were observed when the reaction was carried out under an air or oxygen atmosphere. From the above discussion, conditions listed in entry 9 were therefore utilized as the optimized reaction conditions.

With the optimized conditions in hand (Table 1, entry 9), the substrate scope of 2-arylimidazo[1,2-α]pyridines was extended to examine the generality of our tosylmethylated methodology (Scheme 2). A broad range of substrates bearing various functional groups, including halogen, methyl, methoxy, and ester, were well tolerated under optimized conditions.

Scheme 2. Substrate Scopes of 2-Arylimidazo[1,2-α]pyridine[a]



[a]Reaction conditions: **1** (0.1 mmol), **2** (0.3 mmol), and $FeCl_3$ (0.03 mmol) in H_2O/PEG_{400} (7:3, 2 mL) were stirred at 100 °C for 22 h under Ar. [b]The reaction was carried out for 48 h.

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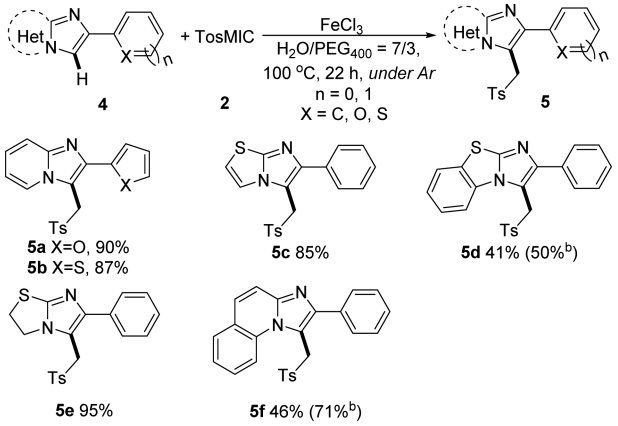
Variation of substituents at the *ortho*, *meta*, and *para* positions of benzenes, including electron-donating (Me, OMe) and electron-withdrawing groups (F, Cl), proceeded smoothly to provide the desired products (**3b**−**3o**) in moderate to excellent yields, with electron-deficient substrates affording slightly lowered yields. Then the electronic effects of various groups on the imidazo[1,2-α]pyridine ring were also evaluated. Despite good yields being achieved for substrates with electron-donating functionalities (Me, OMe), decreased yields were obtained when electron-withdrawing groups (halogen, COOMe, and CF_3) were incorporated. Nevertheless, with a longer reaction time applied, satisfactory yields were achieved for the products **3u**, **3v**, and **3y**. Furthermore, disubstituted imidazo[1,2-α]pyridines **1aa** and **1ab** were also investigated, which furnished the desired product **3aa** and **3ab** in 53% and 79% yield, respectively.

Inspired by the applicability of the current methodology, we next explored the tosylmethylation of imidazo-containing heterocycles (Scheme 3). 2-Heteroaryl-imidazo-[1,2-α]-

Scheme 3. Substrate Scopes of Imidazo-Containing Heterocycles[a]

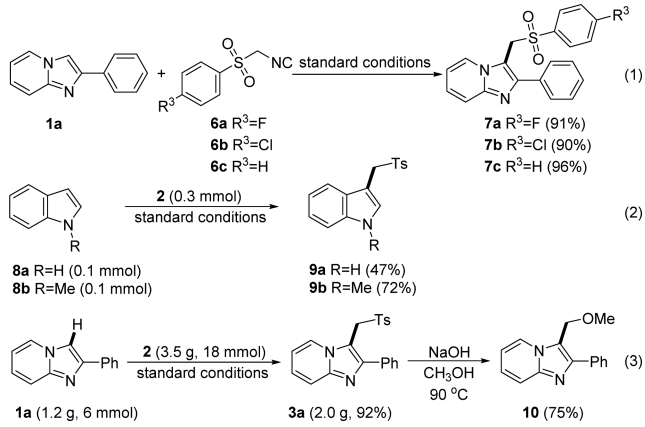


[a]Reaction conditions: **4** (0.1 mmol), **2** (0.3 mmol), and $FeCl_3$ (0.03 mmol) in H_2O/PEG_{400} (7:3, 2 mL) were stirred at 100 °C for 22 h under Ar. [b]The reaction was carried out for 48 h.

pyridines **4a** and **4b** were compatible under standard conditions, which delivered the corresponding product **5a** and **5b** in 90% and 87% yield, respectively. Also, 41−95% yields could be achieved for **5c**−**5f**, respectively. Similarly, when the reaction was conducted for 48 h, increased yields were observed for compounds **5d** and **5f**.

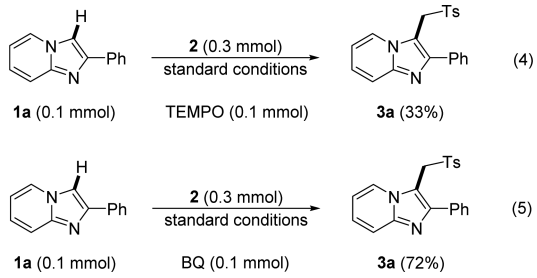
Next, different substituted TosMIC derivatives were examined in reaction with 2-phenylimidazo[1,2-α]pyridine **1a**, which gave the desired product **7a**−**c** in 90−96% yields (Scheme 4, eq 1). Furthermore, other similar hetercyclic moieties were investigated. Delightfully, indoles **8a**−**b** could undergo selective C−H tosylmethylation on C3 position to yield **9a**−**b**[23] in moderate yields (Scheme 4, eq 2). The structure of compound **9a** was further confirmed by X-ray diffraction (see Supporting Information). To highlight the synthetic potential for this protocol, the reaction of 2-phenylimidazo[1,2-α]pyridines **1a** with TosMIC **2** was conducted on a gram scale. Pleasingly, the corresponding tosylmethylated product **3a** was achieved in 92% yield. The obtained **3a** could be converted into methoxymethyl-substituted compound **10** in 75% yield (Scheme 4, eq 3).

Scheme 4. Substrate Scope of Indoles and Gram-Scale Production



Isocyanides can undergo the dealkylation process to form thermodynamically stable metal cyanides,[19d,24] which proceeds via homolysis or heterolysis mechanism.[25] To explore the reaction pathway, control experiments were conducted in the presence of the radical quencher (Scheme 5). Initially, TEMPO

Scheme 5. Control Experiments



(1 equiv) was applied to the reaction, and the efficiency was suppressed from 94% to 33% (Scheme 5, eq 4). When the same reaction was carried out in the presence of BQ (1 equiv), product **3aa** was obtained in 72% yield (Scheme 5, eq 5). Further addition of TEMPO and BQ could not fully suppress the tosylmethylation reaction. These results suggest that both the free radical pathway and direct electrophilic mechanism might be involved at the C3 position.[26] In addition, a decreased yield of 46% was observed under an oxygen atmosphere (Table 1, entry 11), which indicates that the oxygen is not required to fulfill the catalytic cycle.

On the basis of the above discussion and previous literature,[17b] a plausible mechanism of the tosylmethylation is illustrated (Scheme 6). The catalytic cycle initiates with the reaction of TosMIC **2** with $FeCl_3$ to produce radical intermediate **A** *or* carbonium ion **B**, accompanied by the generation of $Fe(CN)_3$ and Cl species. In route a, reaction between radical **A** and **1a** generates intermediate **C**; in route b, electrophilic addition between **1a** and **B** results in the formation of intermediate **D**. Finally, the desired product **3a** was obtained via either $H^{\bullet}$ or H^+ elimination. The detailed mechanism is unclear currently and needed to be clarified through further investigation.

In conclusion, we have developed a novel iron-involved C−H tosylmethylation of imidazo[1,2-α]pyridines with TosMIC in a nontoxic medium under an Ar atmosphere. A broad range of substrates, including aromatic and heteroaromatic, proceeded

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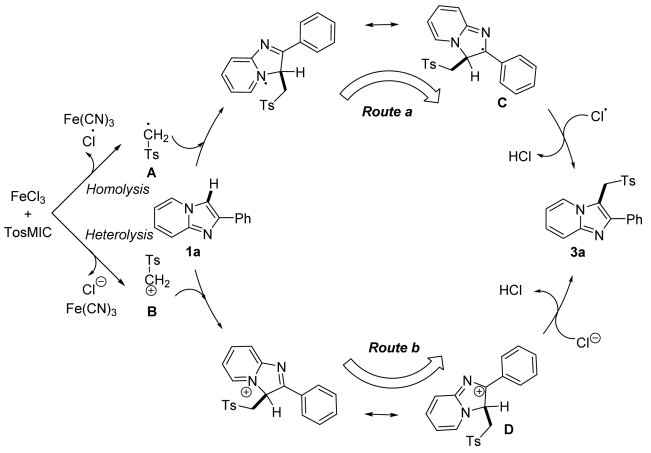
Scheme 6. Proposed Mechanisms



smoothly to afford the corresponding products in moderate to good yields. The strategy could be further applied to the regioselective tosylmethylation of indoles. Unlike a previous known reaction pathway, TosMIC was used as the tosymethylating reagent for the first time. Moreover, the gram-scale preparation of the tosylmethylated products was successfully achieved in high yield. It is worth noting that this protocol is cost-effective, environmentally benign, and operationally convenient.

EXPERIMENTAL SECTION

General Experimental Details. Unless otherwise indicated, all the starting materials and reagents were commercially available and used without further purification. Imidazo[1,2-α]pyridines and TosMIC derivatives **6** were prepared according to previous literature.[27,28] All reactions were carried out using Schlenk techniques. Melting points were measured on a melting point apparatus. ^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard. Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constants (J) in hertz (Hz). HRMS were determined on a Q-Tof Micro MS/MS System ESI spectrometer.

General Procedure for the Preparation of Compound 3, 5, 7, and 9. To a 15 mL sealed tube were added imidazole-containing (hetero)arenes **1** or **4**, or indoles **8** (0.1 mmol), TosMIC derivatives **2** or **6** (0.3 mmol), and $FeCl_3$ (0.03 mmol, 5 mg) in a mixed solvent of H_2O and PEG400 (2 mL) under an Ar atmosphere. The reaction mixture was heated at 100 °C for 22 h. The reaction mixture was directly evaporated, and the residue was purified by preparative thin-layer chromatography (petroleum ether/EtOAc = 1:1) to give the desired product **3**, **5**, **7**, and **9**.

Reaction System under Added TEMPO (or BQ). To a 15 mL sealed tube were added imidazo[1,2-α]pyridines **1a** (0.1 mmol, 19 mg), TosMIC **2** (0.3 mmol, 59 mg), $FeCl_3$ (0.03 mmol, 5 mg), and TEMPO (0.1 mmol, 16 mg) or BQ (0.1 mmol, 11 mg) in a mixed solvent of H_2O and PEG400 (2 mL) under an Ar atmosphere. The reaction mixture was heated at 100 °C for 22 h. The reaction mixture was directly evaporated, and the residue was purified by preparative thin-layer chromatography (petroleum ether/EtOAc = 1:1) to give the desired product **3a** in 33% yield.

Reaction Procedure for the Conversion of 3a to 10. To a stirred solution of **3a** (0.2 mmol, 72 mg) in CH_3OH (2 mL) was added NaOH (1.0 mmol, 40 mg) under an air atmosphere. The reaction mixture was stirred at 90 °C for 36 h. The solvent was directly evaporated, and the residue was purified by preparative thin-layer chromatography (petroleum ether/EtOAc = 3:1) to give the desired product **10** in 75% yield.

*2-Phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3a**).* White solid (34.0 mg, 94%), mp = 68−69 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (d, J = 6.8 Hz, 1H), 7.67 (d, J = 8.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 2H), 7.33−7.27 (m, 6H), 7.09 (d, J = 8.0 Hz, 2H), 6.94 (t, J = 6.7 Hz, 1H), 4.87 (s, 2H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.5, 146.0, 145.3, 134.2, 133.0, 129.8, 128.3, 128.22, 128.16, 128.1, 126.0, 124.9, 117.5, 112.9, 108.3, 52.7, 21.6. HRMS (positive ESI, m/z): [M + H]$^+$ calcd for $C_{21}H_{19}N_2O_2S^+$ 363.1162, found 363.1166. Anal. calcd for $C_{21}H_{18}N_2O_2S{\cdot}H_2O$: C, 66.30; H, 5.30; N, 7.36. Found: C, 66.13; H, 5.32; N, 7.26.

*2-(o-Tolyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3b**).* White solid (33.4 mg, 89%), mp = 133−134 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, J = 7.5 Hz, 1H), 7.63 (d, J = 9 Hz, 1H), 7.33−7.29 (m, 3H), 7.21 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 8.3 Hz, 1H), 7.11 (d, J = 7.9 Hz, 2H), 7.02 (t, J = 7.4 Hz, 1H), 6.95 (td, J = 6.8, 0.8 Hz, 1H), 6.69 (d, J = 7.0 Hz, 1H), 4.72 (s, 2H), 2.40 (s, 3H), 1.99 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.9, 145.7, 145.0, 137.3, 134.5, 132.0, 130.3, 129.8, 128.4, 128.1, 125.6, 125.2, 125.1, 117.6, 112.7, 109.2, 52.4, 21.6, 19.9. HRMS (positive ESI): [M + H]$^+$ calcd for $C_{22}H_{21}N_2O_2S^+$ 377.1318, found 377.1326. Anal. calcd for $C_{22}H_{20}N_2O_2S$: C, 70.19; H, 5.35; N, 7.44. Found: C, 70.17; H, 5.28; N, 7.22.

*2-(2-Methoxyphenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3c**).* White solid (32.8 mg, 84%), mp = 67−68 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, J = 6.9 Hz, 1H), 7.62 (d, J = 9.0 Hz, 1H), 7.29−7.26 (m, 1H), 7.25−7.22 (m, 1H), 7.13 (d, J = 8.2 Hz, 2H), 6.94 (td, J = 6.8, 1.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 2H), 6.87 (dd, J = 7.6, 1.7 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 6.78 (td, J = 7.4, 0.7 Hz, 1H), 4.49 (s, 2H), 3.76 (s, 3H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 155.3, 146.0, 144.7, 143.9, 133.7, 132.1, 129.44, 129.39, 127.8, 125.3, 124.5, 122.0, 120.5, 117.5, 112.6, 110.7, 110.2, 55.7, 52.8, 21.6. HRMS (positive ESI): [M + H]$^+$ calcd for $C_{22}H_{21}N_2O_3S^+$ 393.1267, found 393.1277. Anal. calcd for $C_{22}H_{20}N_2O_3S$: C, 67.33; H, 5.14; N, 7.14. Found: C, 67.12; H, 5.05; N, 6.98.

*2-(2-Fluorophenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3d**).* White solid (30.5 mg, 80%), mp = 80−81 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, J = 6.9 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.33−7.30 (m, 1H), 7.26−7.23 (m, 1H), 7.18 (d, J = 8.1 Hz, 2H), 7.09 (td, J = 7.6, 1.0 Hz, 1H), 7.02−6.93 (m, 5H), 4.89 (d, J = 0.4 Hz, 2H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.8 (d, J = 245.3 Hz), 146.3, 144.9, 141.5, 135.6, 131.9 (d, J = 3.2 Hz), 129.8 (d, J = 8.5 Hz), 129.5, 127.9, 125.9, 124.7, 123.9 (d, J = 3.1 Hz), 120.8 (d, J = 14.1 Hz), 117.7, 115.5 (d, J = 22.7 Hz), 113.0, 110.2, 52.2 (d, J = 9.1 Hz), 21.5. ^{19}F NMR (565 MHz, $CDCl_3$) δ −114.4. HRMS (positive ESI): [M + H]$^+$ calcd for $C_{21}H_{18}FN_2O_2S^+$ 381.1068, found 381.1073. Anal. calcd for $C_{21}H_{17}FN_2O_2S{\cdot}H_2O$: C, 63.30; H, 4.81; N, 7.03. Found: C, 62.94; H, 4.76; N, 6.74.

*2-(2-Chlorophenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3e**).* White solid (25.3 mg, 64%), mp = 48−49 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, J = 6.9 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.35−7.33 (m, 2H), 7.26−7.23 (m, 3H), 7.07−7.05 (m, 3H), 6.99 (t, J = 6.7 Hz, 1H), 6.76 (dd, J = 7.6, 1.3 Hz, 1H), 4.80 (s, 2H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 145.9, 145.0, 144.6, 134.1, 132.4, 132.2, 131.8, 129.8, 129.6, 129.5, 128.0, 126.3, 125.9, 125.0, 117.7, 113.1, 110.1, 52.7, 21.6. HRMS (positive ESI): [M + H]$^+$ calcd for $C_{21}H_{18}ClN_2O_2S^+$ 397.0772, found 397.0779. Anal. calcd for $C_{21}H_{17}ClN_2O_2S$: C, 63.55; H, 4.32; N, 7.06. Found: C, 63.57; H, 4.40; N, 6.85.

*2-(m-Tolyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3f**).* White solid (34.7 mg, 92%), mp = 56−57 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (d, J = 6.9 Hz, 1H), 7.66 (d, J = 9.1 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.32−7.29 (m, 1H), 7.18−7.16 (m, 1H), 7.12−7.10 (m, 5H), 6.93 (td, J = 6.8, 1.0 Hz, 1H), 4.88 (s, 2H), 2.36 (s, 3H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.7, 146.0, 145.2, 138.0, 134.4, 133.0, 129.8, 128.9, 128.9, 128.2, 125.9, 125.2, 125.0, 117.5, 112.8, 108.2, 52.9, 21.6, 21.4. HRMS (positive ESI): [M + H]$^+$ calcd for $C_{22}H_{21}N_2O_2S^+$: 377.1318, found: 377.1326. Anal. calcd for $C_{22}H_{20}N_2O_2S$: C, 70.19; H, 5.35; N, 7.44. Found: C, 69.94; H, 5.43; N, 7.18.

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*2-(3-Methoxyphenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3g**).* White solid (38.8 mg, 98%), mp = 173−174 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, J = 6.8 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.31−7.29 (m, 1H), 7.19 (t, J = 7.9 Hz, 1H), 7.10 (d, J = 8.1 Hz, 2H), 6.96 (s, 1H), 6.93−6.89 (m, 2H), 6.84 (dd, J = 8.2, 2.2 Hz, 1H), 4.88 (s, 2H), 3.82 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.7, 147.5, 146.0, 145.3, 134.5, 134.4, 129.8, 129.3, 128.1, 125.9, 124.9, 120.4, 117.6, 114.2, 113.7, 112.8, 108.3, 55.3, 52.6, 21.5. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_3S^+$: 393.1267, found 393.1270. Anal. calcd for $C_{22}H_{20}N_2O_3S$: C, 67.33; H, 5.14; N, 7.14. Found: C, 67.39; H, 5.09; N, 6.93.

*2-(3-Fluorophenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3h**).* White solid (27.8 mg, 73%), mp = 78−80 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, J = 6.9 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.37 (d, J = 8.2 Hz, 2H), 7.34−7.31 (m, 1H), 7.26−7.23 (m, 1H), 7.14−7.11 (m, 3H), 7.00−6.94 (m, 3H), 4.85 (s, 2H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.8 (d, J = 244.3 Hz), 146.2 (d, J = 2.0 Hz), 146.1, 145.6, 135.4 (d, J = 8.2 Hz), 134.1, 129.9, 129.8 (d, J = 8.2 Hz), 128.2, 126.1, 124.9, 123.6 (d, J = 2.3 Hz), 117.7, 115.3 (d, J = 22.8 Hz), 114.9 (d, J = 20.9 Hz), 113.0, 108.6, 52.5, 21.5. ^{19}F NMR (565 MHz, $CDCl_3$) δ −112.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}FN_2O_2S^+$: 381.1068, found 381.1076. Anal. calcd for $C_{21}H_{17}FN_2O_2S{\cdot}H_2O$: C, 63.30; H, 4.81; N, 7.03. Found: C, 63.72; H, 4.76; N, 6.86.

*2-(3-Chlorophenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3i**).* White solid (31.1 mg, 79%), mp = 178−179 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, J = 6.9 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.37 (d, J = 8.2 Hz, 2H), 7.34−7.31 (m, 1H), 7.27−7.20 (m, 4H), 7.12 (d, J = 8.0 Hz, 2H), 6.95 (td, J = 6.8, 1.0 Hz, 1H), 4.85 (s, 2H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 146.1, 146.0, 145.6, 135.0, 134.4, 134.1, 129.9, 129.5, 128.3, 128.2, 128.1, 126.2, 126.1, 125.0, 117.7, 113.1, 108.7, 52.5, 21.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2S^+$: 397.0772, found 397.0779. Anal. calcd for $C_{21}H_{17}ClN_2O_2S$: C, 63.55; H, 4.32; N, 7.06. Found: C, 63.70; H, 4.24; N, 6.75.

*2-(p-Tolyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3j**).* White solid (33.7 mg, 90%), mp = 58−59 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, J = 6.8 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H), 7.40 (d, J = 8.1 Hz, 2H), 7.30−7.28 (m, 1H), 7.21 (d, J = 7.9 Hz, 2H), 7.09 (t, J = 7.0 Hz, 4H), 6.91 (t, J = 6.8 Hz, 1H), 4.85 (s, 2H), 2.36 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.6, 146.0, 145.2, 137.9, 134.5, 130.2, 129.8, 129.0, 128.2, 128.1, 125.8, 124.9, 117.5, 112.7, 108.0, 52.9, 21.6, 21.2. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_2S^+$: 377.1318, found 377.1324. Anal. calcd for $C_{23}H_{19}F_3N_2O_2S$: C, 70.19; H, 5.35; N, 7.44. Found: C, 70.06; H, 5.22; N, 7.34.

*2-(4-Methoxyphenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3k**).* White solid (30.0 mg, 77%), mp = 49−50 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, J = 6.8 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.42 (d, J = 8.1 Hz, 2H), 7.30−7.27 (m, 3H), 7.12 (d, J = 8.0 Hz, 2H), 6.91 (t, J = 6.7 Hz, 1H), 6.82 (d, J = 8.6 Hz, 2H), 4.84 (s, 2H), 3.83 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.7, 147.4, 145.9, 145.3, 134.5, 129.8, 129.5, 128.2, 125.8, 125.6, 124.8, 117.4, 113.8, 112.7, 107.6, 55.3, 53.0, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_3S^+$: 393.1267, found 393.1273. Anal. calcd for $C_{22}H_{20}N_2O_2S{\cdot}H_2O$: C, 64.37; H, 5.40; N, 6.82. Found: C, 64.58; H, 5.28; N, 6.50.

*2-(4-(tert-Butyl)phenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3l**).* White solid (34.0 mg, 81%), mp = 169−170 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, J = 6.9 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.30−7.23 (m, 5H), 7.05 (d, J = 8.0 Hz, 2H), 6.91 (td, J = 6.8, 0.7 Hz, 1H), 4.89 (s, 2H), 2.35 (s, 3H), 1.34 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 151.1, 147.5, 146.0, 145.1, 134.2, 130.1, 129.7, 128.1, 127.8, 125.7, 125.1, 124.8, 117.5, 112.7, 108.0, 52.7, 34.6, 31.3, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{25}H_{27}N_2O_2S^+$: 419.1788, found 419.1795. Anal. calcd for $C_{25}H_{26}N_2O_2S{\cdot}H_2O$: C, 71.74; H, 6.26; N, 6.69. Found: C, 71.62; H, 6.16; N, 6.48.

*2-(4-Fluorophenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3m**).* White solid (32.5 mg, 86%), mp = 73−74 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, J = 6.8 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.42 (d, J = 8.1 Hz, 2H), 7.35−7.30 (m, 3H), 7.13 (d, J = 8.0 Hz, 2H), 6.98 (t, J = 8.6 Hz, 2H), 6.92 (t, J = 6.8 Hz, 1H), 4.82 (s, 2H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.8 (d, J = 246.8 Hz), 146.6, 146.0, 145.4, 134.5, 130.0 (d, J = 8.1 Hz), 129.9, 129.3 (d, J = 2.7 Hz), 128.2, 126.0, 124.9, 117.5, 115.3 (d, J = 21.1 Hz), 112.9, 108.1, 52.7, 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ −113.5. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}FN_2O_2S^+$: 381.1068, found 381.1070. Anal. calcd for $C_{21}H_{17}FN_2O_2S$: C, 66.30; H, 4.50; N, 7.36. Found: C, 66.40; H, 4.80; N, 7.02.

*2-(4-Chlorophenyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3n**).* White solid (31.2 mg, 79%), mp = 76−77 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, J = 6.9 Hz, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.42 (d, J = 8.2 Hz, 2H), 7.34−7.30 (m, 3H), 7.27−7.25 (m, 2H), 7.13 (d, J = 8.0 Hz, 2H), 6.94 (td, J = 6.8, 1.0 Hz, 1H), 4.83 (s, 2H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 146.3, 146.1, 145.5, 134.4, 134.2, 131.7, 129.9, 129.4, 128.5, 128.2, 126.1, 124.8, 117.6, 113.0, 108.4, 52.7, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2S^+$: 397.0772, found 397.0778. Anal. calcd for $C_{21}H_{17}ClN_2O_2S$: C, 63.55; H, 4.32; N, 7.06. Found: C, 63.38; H, 4.44; N, 6.73.

*2-(4-(Trifluoromethyl)phenyl)-3-(tosylmethyl)imidazo[1,2-a]-pyridine (**3o**).* White solid (28.8 mg, 67%), mp = 168−169 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, J = 6.8 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.55−7.49 (m, 4H), 7.39 (d, J = 8.0 Hz, 2H), 7.34 (t, J = 7.9 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 6.96 (t, J = 6.8 Hz, 1H), 4.87 (s, 2H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 146.2, 145.7, 145.5, 136.8, 134.1, 130.1, 129.8, 129.6, 128.2, 126.3, 125.2 (q, J = 3.5 Hz), 124.9, 124.1 (q, J = 272.0 Hz), 117.8, 113.2, 109.0, 52.4, 21.5. ^{19}F NMR (565 MHz, $CDCl_3$) δ −62.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{18}F_3N_2O_2S^+$: 431.1036, found 431.1044. Anal. calcd for $C_{22}H_{17}F_3N_2O_2S$: C, 61.39; H, 3.98; N, 6.51. Found: C, 61.35; H, 3.97; N, 6.34.

*6-Methyl-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3p**).* White solid (35.0 mg, 93%), mp = 198−199 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.55 (d, J = 9.1 Hz, 1H), 7.37 (d, J = 8.1 Hz, 2H), 7.31−7.26 (m, 5H), 7.14 (d, J = 9.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 4.85 (s, 2H), 2.37 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.3, 145.2, 145.1, 134.3, 133.2, 129.8, 129.0, 128.24, 128.20, 128.1, 127.9, 122.5, 122.4, 116.8, 107.9, 52.8, 21.6, 18.5. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_2S^+$: 377.1318, found 377.1324. Anal. calcd for $C_{22}H_{20}N_2O_2S$: C, 70.19; H, 5.45; N, 7.44. Found: C, 69.96; H, 5.16; N, 7.22.

*6-Fluoro-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3q**).* White solid (25.4 mg, 67%), mp = 179−180 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, J = 1.2 Hz, 1H), 7.63 (q, J = 9.7 Hz, 1H), 7.43 (d, J = 8.1 Hz, 2H), 7.33−7.29 (m, 5H), 7.25−7.21 (m, 1H), 7.12 (d, J = 8.0 Hz, 2H), 4.82 (s, 2H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 153.4 (d, J = 236.5 Hz), 148.8, 145.5, 143.7, 134.3, 132.8, 129.9, 128.4, 128.3, 128.2, 118.02, 117.97 (d, J = 3.8 Hz), 117.8, 111.9 (d, J = 41.5 Hz), 109.8, 52.8, 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ −138.4. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}FN_2O_2S^+$: 381.1068, found 381.1072. Anal. calcd for $C_{21}H_{17}FN_2O_2S$: C, 66.30; H, 4.50; N, 7.36. Found: C, 66.01; H, 4.53; N, 7.41.

*6-Chloro-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3r**).* White solid (17.2 mg, 43%), mp = 184−186 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (d, J = 1.1 Hz, 1H), 7.60 (d, J = 9.5 Hz, 1H), 7.43 (d, J = 8.2 Hz, 2H), 7.38−7.36 (m, 2H), 7.33−7.29 (m, 3H), 7.25 (d, J = 1.9 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 4.83 (s, 2H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.5, 145.6, 144.3, 134.3, 132.7, 130.0, 128.42, 128.36, 128.22, 128.21, 127.3, 122.7, 121.2, 117.9, 109.0, 52.7, 21.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2S^+$: 397.0772, found 397.0778. Anal. calcd for $C_{21}H_{17}ClN_2O_2S{\cdot}H_2O$: C, 63.55; H, 4.32; N, 7.06. Found: C, 63.43; H, 4.37; N, 6.93.

*6-Bromo-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3s**).* White solid (18.8 mg, 43%), mp = 188−189 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.55 (d, J = 9.4 Hz, 1H), 7.44 (d, J = 8.2 Hz, 2H), 7.39−7.30 (m, 6H), 7.13 (d, J = 8.2 Hz, 2H), 4.83 (s, 2H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.3, 145.6, 144.4, 134.4, 132.6, 130.0, 129.3, 128.44, 128.41, 128.25, 128.22, 124.8,

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118.2, 108.9, 107.6, 52.7, 21.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}BrN_2O_2S^+$: 441.0267, found 441.0269. Anal. calcd for $C_{21}H_{17}BrN_2O_2S\cdot$: C, 57.15; H, 3.88 N, 6.35. Found: C, 57.03; H, 4.06; N, 6.29.

6-Iodo-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3t**). White solid (18.0 mg, 37%), mp = 193−195 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.46−7.39 (m, 6H), 7.32−7.30 (m, 3H), 7.13 (d, J = 8.0 Hz, 2H), 4.83 (s, 2H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 147.9, 145.6, 144.5, 134.4, 133.8, 132.6, 130.0, 129.6, 128.42, 128.38, 128.3, 128.2, 118.6, 108.5, 75.7, 52.7, 21.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}IN_2O_2S^+$: 489.0128, found 489.0134. Anal. calcd for $C_{21}H_{17}IN_2O_2S$: C, 51.65; H, 3.51; N, 5.74. Found: C, 51.83; H, 3.80; N, 5.40.

6-Carboxylatemethyl-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]-pyridine (**3u**). White solid (13.4 mg, 32%), mp = 85−86 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.10 (q, J = 0.9 Hz, 1H), 7.85 (dd, J = 9.4, 1.6 Hz, 1H), 7.65 (dd, J = 9.4, 0.8 Hz, 1H), 7.40 (d, J = 8.3 Hz, 2H), 7.38−7.36 (m, 2H), 7.32−7.29 (m, 3H), 7.10 (d, J = 7.9 Hz, 2H), 4.92 (s, 2H), 3.99 (s, 3H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 165.1, 149.1, 146.5, 145.5, 134.2, 132.6, 129.9, 128.8, 128.5, 128.4, 128.2, 125.5, 116.9, 116.8, 109.6, 52.6, 52.4, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{23}H_{21}N_2O_4S^+$: 421.1217, found: 421.1221. Anal. calcd for $C_{23}H_{20}N_2O_4S$: C, 65.70; H, 4.79; N, 6.66. Found: C, 65.63; H, 4.56; N, 6.60.

6-(Trifluoromethyl)-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]-pyridine (**3v**). White solid (5.6 mg, 13%), mp = 128−129 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.75 (d, J = 9.4 Hz, 1H), 7.46−7.42 (m, 5H), 7.36−7.32 (m, 3H), 7.14 (d, J = 8.0 Hz, 2H), 4.88 (s, 2H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 149.4, 145.7, 134.3, 132.4, 130.0, 128.6, 128.5, 128.3, 128.2, 123.9 (q, J = 5.6 Hz), 123.5 (q, J = 271.0 Hz), 121.69, 121.68, 118.3, 117.1 (q, J = 34.3 Hz), 110.0, 52.5, 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ −62.0. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{18}F_3N_2O_2S^+$: 431.1036, found 431.1037. Anal. calcd for $C_{22}H_{17}F_3N_2O_2S\cdot H_2O$: C, 58.92; H, 4.27; N, 6.25. Found: C, 58.90; H, 3.81; N, 5.92.

7-Methyl-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3w**). White solid (33.8 mg, 90%), mp = 86−87 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (d, J = 7.0 Hz, 1H), 7.41 (s, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.26 (s, 5H), 7.07 (d, J = 8.1 Hz, 2H), 6.76 (d, J = 6.9 Hz, 1H), 4.84 (s, 2H), 2.44 (s, 3H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 147.2, 146.4, 145.2, 137.0, 134.2, 133.2, 129.7, 128.22, 128.16, 128.1, 127.9, 124.1, 115.9, 115.4, 107.6, 52.8, 21.6, 21.4. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_2S^+$: 377.1318, found 377.1326. Anal. calcd for $C_{22}H_{20}N_2O_2S\cdot H_2O$: C, 66.98; H, 5.62; N, 7.10. Found: C, 66.70; H, 5.61; N, 6.81.

7-Methoxy-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3x**). White solid (36.7 mg, 94%), mp = 194−196 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, J = 7.5 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.28−7.25 (m, 5H), 7.08 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 2.3 Hz, 1H), 6.62 (dd, J = 7.5, 2.5 Hz, 1H), 4.80 (s, 2H), 3.88 (s, 3H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 158.7, 147.6, 147.2, 145.2, 134.2, 133.2, 129.8, 128.22, 128.16, 128.0, 127.9, 125.4, 107.6, 107.0, 94.8, 55.6, 52.8, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_3S^+$: 393.1267, found 393.1269. Anal. calcd for $C_{22}H_{20}N_2O_3S\cdot 0.5\ H_2O$: C, 65.82; H, 5.27; N, 6.98. Found: C, 65.41; H, 5.06; N, 6.71.

7-(Trifluoromethyl)-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]-pyridine (**3y**). White solid (7.1 mg, 17%), mp = 179−180 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (d, J = 7.2 Hz, 1H), 7.96 (s, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.33−7.31 (m, 5H), 7.11−7.10 (m, 3H), 4.89 (s, 2H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 149.4, 145.6, 144.2, 134.1, 132.4, 129.9, 128.55, 128.45, 128.2, 128.1, 127.7 (q, J = 34.6 Hz), 125.8, 123.2 (q, J = 272.6 Hz), 115.5 (q, J = 4.6 Hz), 110.0, 108.6, 52.5, 21.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ −63.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{18}F_3N_2O_2S^+$: 431.1036, found 431.1042. Anal. calcd for $C_{22}H_{17}F_3N_2O_2S$: C, 61.39; H, 3.98; N, 6.51. Found: C, 61.21; H, 4.02; N, 6.28.

7-Chloro-2-phenyl-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3z**). White solid (25.6 mg, 65%), mp = 193−194 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, J = 7.3 Hz, 1H), 7.64 (d, J = 1.6 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.31−7.27 (m, 5H), 7.10 (d, J = 8.0 Hz, 2H), 6.92 (dd, J = 7.3, 2.0 Hz, 1H), 4.84 (s, 2H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 148.4, 145.9, 145.4, 134.1, 132.7, 132.4, 129.9, 128.4, 128.3, 128.1, 125.4, 116.4, 114.4, 108.6, 52.6, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2S^+$: 397.0772, found 397.0777. Anal. calcd for $C_{21}H_{17}ClN_2O_2S$: C, 63.55; H, 4.32; N, 7.06. Found: C, 63.58; H, 4.69; N, 6.90.

6-Fluoro-2-(p-tolyl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**3aa**). White solid (21.0 mg, 53%), mp = 201−202 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (dd, J = 3.5, 2.2 Hz, 1H), 7.61 (dd, J = 9.7, 5.1 Hz, 1H), 7.45 (d, J = 8.2 Hz, 2H), 7.24−7.19 (m, 3H), 7.12 (dd, J = 18.5, 7.9 Hz, 4H), 4.80 (s, 2H), 2.37 (d, J = 8.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 153.3(d, J = 176.4 Hz), 149.0, 145.4, 138.2, 134.5, 130.0, 129.9, 129.1, 128.2, 128.0, 117.9 (d, J = 8.9 Hz), 117.8, 117.6, 111.8 (d, J = 41.6 Hz), 109.5, 53.0, 21.6, 21.2. ^{19}F NMR (565 MHz, $CDCl_3$): δ −138.8. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{20}FN_2O_2S^+$: 395.1224, found 395.1229. Anal. calcd for $C_{22}H_{19}FN_2O_2S$: C, 66.99; H, 4.86; N, 7.10. Found: C, 67.06; H, 4.76; N, 7.15.

6-Chloro-2-(4-methoxyphenyl)-3-(tosylmethyl)imidazo[1,2-a]-pyridine (**3ab**). White solid (33.6 mg, 79%), mp = 188−189 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, J = 1.2 Hz, 1H), 7.56 (d, J = 9.5 Hz, 1H), 7.48 (d, J = 8.2 Hz, 2H), 7.37−7.35 (m, 2H), 7.23 (dd, J = 9.5, 1.9 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 6.86−6.84 (m, 2H), 4.79 (s, 2H), 3.84 (s, 3H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 159.9, 148.5, 145.6, 144.3, 134.7, 130.0, 129.5, 128.3, 127.0, 125.3, 122.5, 120.9, 117.7, 113.9, 108.4, 55.3, 53.0, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{22}H_{20}ClN_2O_3S^+$: 427.0878, found 427.0881. Anal. calcd for $C_{22}H_{19}ClN_2O_3S$: C, 61.90; H, 4.49; N, 6.56. Found: C, 61.91; H, 4.48; N, 6.35.

2-(Furan-2-yl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**5a**). White solid (31.7 mg, 90%), mp = 163−164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, J = 6.9 Hz, 1H), 7.60 (d, J = 9.1 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.32−7.29 (m, 1H), 7.13 (dd, J = 1.6, 0.5 Hz, 1H), 7.06 (d, J = 7.9 Hz, 2H), 6.94 (td, J = 6.8, 1.0 Hz, 1H), 6.66 (d, J = 1.1 Hz, 1H), 6.31 (dd, J = 3.4, 1.8 Hz, 1H), 5.08 (s, 2H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 149.1, 146.3, 145.1, 142.0, 137.8, 133.9, 129.2, 128.4, 126.3, 124.6, 117.3, 112.9, 111.1, 108.4, 108.0, 52.7, 21.5. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{19}H_{17}N_2O_3S^+$: 353.0954, found 353.0961. Anal. calcd for $C_{19}H_{16}N_2O_3S$: C, 64.76; H, 4.58; N, 7.95. Found: C, 64.72; H, 4.78; N, 7.61.

2-(Thiophen-2-yl)-3-(tosylmethyl)imidazo[1,2-a]pyridine (**5b**). White solid (31.9 mg, 87%), mp = 161−162 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, J = 6.9 Hz, 1H), 7.64 (d, J = 9.1 Hz, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.31−7.26 (m, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.02 (dd, J = 3.6, 1.0 Hz, 1H), 6.95 (dd, J = 5.0, 3.7 Hz, 1H), 6.90 (td, J = 6.8, 1.0 Hz, 1H), 4.90 (s, 2H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 146.0, 145.5, 141.7, 135.9, 134.5, 129.9, 128.3, 127.4, 126.3, 126.1, 125.2, 124.6, 117.4, 113.0, 107.5, 53.1, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{19}H_{17}N_2O_2S_2^+$: 369.0726, found 369.0730. Anal. calcd for $C_{19}H_{16}N_2O_2S_2$: C, 61.93; H, 4.38; N, 7.60. Found: C, 61.75; H, 4.60; N, 7.54.

6-Phenyl-5-(tosylmethyl)imidazo[2,1-b]thiazole (**5c**). White solid (31.3 mg, 85%), mp = 39−40 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, J = 4.5 Hz, 1H), 7.45 (d, J = 8.2 Hz, 2H), 7.24−7.23 (m, 3H), 7.18−7.14 (m, 4H), 6.90 (d, J = 4.5 Hz, 1H), 4.69 (s, 2H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 150.9, 148.7, 145.4, 134.1, 133.2, 129.9, 128.29, 128.27, 127.8, 127.6, 119.1, 112.6, 109.8, 53.6, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{19}H_{17}N_2O_2S_2^+$: 369.0726, found 369.0732. Anal. calcd for $C_{19}H_{16}N_2O_2S_2$: C, 61.93; H, 4.38; N, 7.60. Found: C, 61.73; H, 4.63; N, 7.46.

2-Phenyl-3-(tosylmethyl)benzo[d]imidazo[2,1-b]thiazole (**5d**). White solid (17.1 mg, 41%), mp = 179−180 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, J = 8.3 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.52−7.49 (m, 1H), 7.39 (t, J = 7.8 Hz, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.24−7.22 (m, 5H), 5.08 (s, 2H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 149.7, 148.9, 145.2, 134.0, 133.1, 132.9, 130.2, 129.6, 128.3, 128.2, 127.7, 126.1, 125.0, 124.2, 114.7, 112.1, 52.8, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{23}H_{19}N_2O_2S_2^+$: 419.0882, found 419.0889. Anal. calcd for $C_{23}H_{18}N_2O_2S_2$: C, 66.01; H, 4.34; N, 6.69. Found: C, 65.72; H, 4.39; N, 6.36.

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*6-Phenyl-5-(tosylmethyl)-2,3-dihydroimidazo[2,1-b]thiazole (**5e**).* White solid (35.3 mg, 95%), mp = 48−49 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, J = 8.3 Hz, 2H), 7.18−7.15 (m, 3H), 7.10−7.08 (m, 4H), 4.48 (s, 2H), 4.38 (t, J = 7.3 Hz, 2H), 3.86 (t, J = 7.2 Hz, 2H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 151.3, 147.9, 145.3, 133.9, 133.3, 129.8, 128.2, 128.1, 127.2, 126.8, 114.0, 53.4, 46.3, 34.8, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{19}H_{19}N_2O_2S_2^+$: 371.0882, found 371.0890. Anal. calcd for $C_{19}H_{18}N_2O_2S_2$: C, 61.60; H, 4.90; N, 7.56. Found: C, 61.64; H, 4.85; N, 7.47.

*2-Phenyl-1-(tosylmethyl)imidazo[1,2-a]quinoline (**5f**).* White solid (17.0 mg, 46%), mp = 184−185 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, J = 8.7 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.71 (t, J = 7.9 Hz, 1H), 7.59 (dd, J = 14.5, 9.3 Hz, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7,27 (s, 3H), 7.21−7.19 (m, 2H), 7.16 (d, J = 8.1 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 5.43 (s, 2H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.4, 145.9, 144.9, 134.6, 134.5, 133.1, 129.54, 129.49, 128.7, 128.5, 128.4, 128.3, 128.1, 127.9, 125.1, 124.8, 117.2, 117.1, 112.3, 54.5, 21.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{25}H_{21}N_2O_2S^+$: 413.1318, found 413.1318. Anal. calcd for $C_{25}H_{20}N_2O_2S$: C, 72.79; H, 4.89; N, 6.79. Found: C, 72.50; H, 5.02; N, 6.70.

*3-(((4-Fluorophenyl)sulfonyl)methyl)-2-phenylimidazo[1,2-a]pyridine (**7a**).* Brown solid (33.3 mg, 91%), mp = 37−39 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, J = 6.9 Hz, 1H), 7.67 (d, J = 9 Hz, 1H), 7.44−7.41 (m, 2H), 7.34−7.30 (m, 6H), 6.96 (t, J = 6.6 Hz, 1H), 6.91 (t, J = 8.5 Hz, 2H), 4.93 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.0, 165.2, 147.4, 146.1, 132.9 (d, J = 6.0 Hz), 131.0 (d, J = 9.8 Hz), 128.5, 128.3, 128.1, 126.1, 124.8, 117.6, 116.4 (d, J = 22.8 Hz), 113.0, 107.9, 52.4. ^{19}F NMR (565 MHz, $CDCl_3$): δ −102.6. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{20}H_{16}FN_2O_2S^+$: 367.0911, found 367.0918. Anal. calcd for $C_{20}H_{15}FN_2O_2S$: C, 65.56; H, 4.13; N, 7.65. Found: C, 65.36; H, 4.10; N, 7.65.

*3-(((4-Chlorophenyl)sulfonyl)methyl)-2-phenylimidazo[1,2-a]pyridine (**7b**).* White solid (34.3 mg, 90%), mp = 49−50 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, J = 6.8 Hz, 1H), 7.66 (d, J = 9 Hz, 1H), 7.34−7.25 (m, 8H), 7.17 (d, J = 7.6 Hz, 2H), 6.95 (t, J = 6.8 Hz, 1H), 4.93 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.5, 146.1, 141.1, 135.3, 132.9, 129.5, 129.3, 128.5, 128.2, 128.0, 126.1, 124.8, 117.6, 113.0, 107.8, 52.2. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{20}H_{16}ClN_2O_2S^+$: 383.0616, found 383.0619. Anal. calcd for $C_{20}H_{15}ClN_2O_2S$: C, 62.74; H, 3.95; N, 7.32. Found: C, 62.62; H, 3.95; N, 7.15.

*2-Phenyl-3-((phenylsulfonyl)methyl)imidazo[1,2-a]pyridine (**7c**).* White solid (33.3 mg, 96%), mp = 154−155 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, J = 6.8 Hz, 1H), 7.66 (d, J = 9 Hz, 1H), 7.55−7.51 (m, 3H), 7.35−7.28 (m, 8H), 6.93 (t, J = 6.7 Hz, 1H), 4,89 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 147.7, 146.1, 137.5, 134.2, 133.0, 129.2, 128.5, 128.2, 128.18, 128.15, 126.0, 124.9, 117.6, 112.9, 108.0, 52.7. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{20}H_{17}N_2O_2S^+$: 349.1005, found 349.1014. Anal. calcd for $C_{20}H_{16}N_2O_2S$: C, 68.95; H, 4.63; N, 8.04. Found: C, 68.74; H, 4.66; N, 7.74.

*3-(Tosylmethyl)-1H-indole (**9a**).*[23] Brown solid (13.5 mg, 47%), mp = 160−161 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.55 (d, J = 7.7 Hz, 2H), 7.32−7.25 (m, 2H), 7.02−7.00 (m, 2H), 4.51 (s, 2H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 144.5, 135.8, 135.4, 129.5, 128.6, 127.0, 125.9, 122.4, 120.2, 118.6, 111.3, 102.8, 54.5, 21.6. HRMS (positive ESI): $[M + K]^+$ calcd for $C_{16}H_{15}KNO_2S^+$: 324.0455, found 324.0462. Anal. calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.58; H, 5.33; N, 4.61.

*1-Methyl-3-(tosylmethyl)-1H-indole (**9b**).*[23] Brown solid (21.5 mg, 72%) mp = 106−108 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 3.4 Hz, 1H), 7.20−7.17 (m, 4H), 7.01−6.98 (m, 2H), 4.49 (s, 2H), 3.75 (s, 3H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 144.4, 136.7, 135.6, 130.3, 129.5, 128.6, 127.6, 122.0, 119.8, 118.6, 109.4, 101.1, 54.5, 33.0, 21.6. HRMS (positive ESI): $[M + K]^+$ calcd for $C_{17}H_{17}KNO_2S^+$: 338.0612, found 338.0616. Anal. calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.19; H, 5.65; N, 4.52.

*3-(Methoxymethyl)-2-phenylimidazo[1,2-a]pyridine(**10**).* Colorless oil (17.8 mg, 75%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, J = 6.5 Hz, 1H), 7.78 (d, J = 7.6 Hz, 2H), 7.66 (d, J = 8.9 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H), 6.86 (t, J = 6.2 Hz, 1H), 4.85 (s, 2H), 3.42 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 145.7, 145.3, 134.1, 128.8, 128.6, 128.0, 125.2, 124.3, 117.5, 116.8, 112.5, 63.6, 57.8. HRMS (positive ESI): $[M + H]^+$ calcd for $C_{15}H_{15}N_2O^+$: 239.1179, found 239.1178. Anal. calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.39; H, 6.11; N, 11.53.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01552.

Crystallography of product **3a** and **9a**; spectra copies of **3a**−**10** (PDF)
X-ray data for **3a** (CIF)
X-ray data for **9a** (CIF)

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Notes

The authors declare no competing financial interest.

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