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One-Pot Copper-Catalyzed Three-Component Reaction of Sulfonyl Azides, Alkynes, and Allylamines To Access 2,3-Dihydro-1*H*-imidazo[1,2-*a*]indoles

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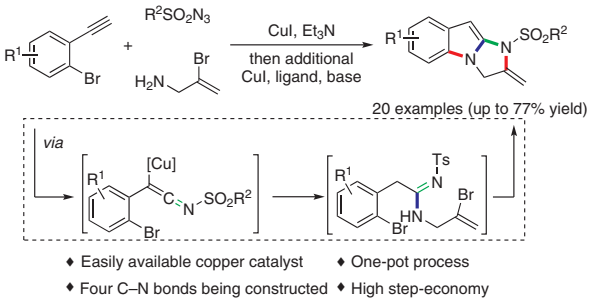

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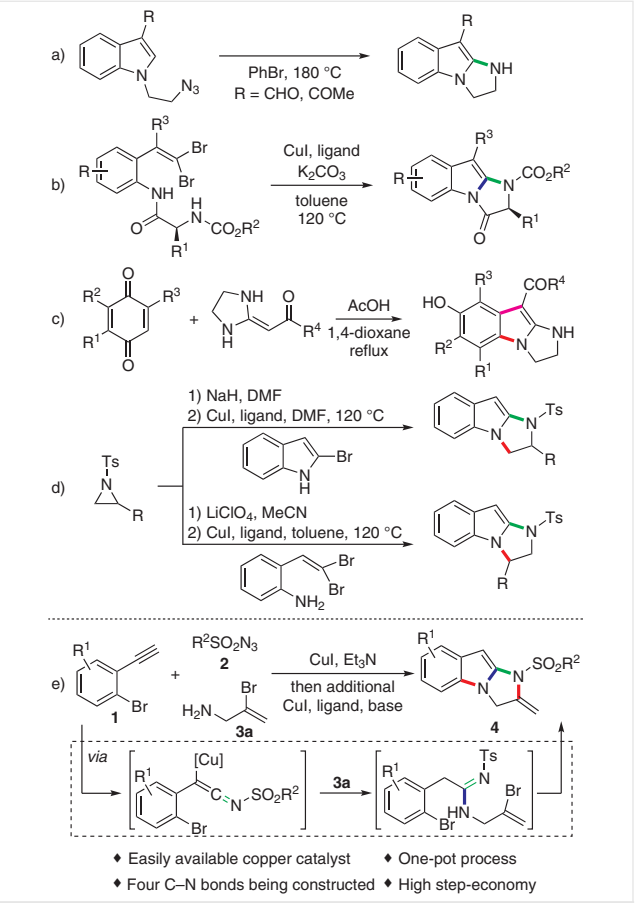
Abstract A copper-catalyzed multicomponent reaction of sulfonyl azides, alkynes, and allylamines affording 2,3-dihydro-1*H*-imidazo-[1,2-a]indoles in moderate yields is reported. Four C–N bonds are constructed by way of azide-alkyne cycloaddition (CuAAC) and double Ullmann-type coupling reactions in a one-pot process.

Key words multicomponent reaction, copper catalysis, azide-alkyne cycloaddition, Ullmann coupling reaction, 2,3-dihydro-1*H*-imidazo[1,2-*a*]indoles

Indole-fused heterocycles are widely found as core structures in many natural products and biologically active molecules.[1] Among them, 2,3-dihydro-1*H*-imidazo[1,2-*a*]-indoles are viewed as promising building blocks to access more complex cyclic compounds such as fumiquinazoline[2] and asperlicin.[3] Over the past several decades, some synthetic methods have been developed to construct the parent 2,3-dihydro-1*H*-imidazo[1,2-*a*]indole. For example, Cruz-Almanza group reported an intramolecular 1,3-dipolar cycloaddition of 1-ω-azidoalkylindoles under high reaction temperatures to give 2,3-dihydro-1*H*-imidazo[1,2-*a*]-indoles (Scheme 1a).[4] Later on, Lautens group disclosed a copper-catalyzed tandem intramolecular amidation of *gem*-dibromovinylanilines affording imidazoindolones in good yields (Scheme 1b).[5] Lin and Yan et al. reported the synthesis of polycyclic indoles from the condensation of heterocyclic ketene aminals (HKAs) and 1,4-benzoquinones (Scheme 1c).[6] More recently, Ghorai et al. described a divergent pathway to access isomeric imidazoindoles from *gem*-dibromovinylanilines and 2-bromoindoles, respectively, via sequential ring-opening of aziridines and C–N coupling reactions (Scheme 1d).[7] Despite a considerable achievement, the existing methods, however, require a tedious design for substrates, and only a narrow scope of 2,3-dihydro-1*H*-imidazo[1,2-*a*]indole derivatives has been presented till now. Consequently, it is still highly desirable to extend the methods for the efficient synthesis of imidazo[1,2-*a*]indoles.



Scheme 1 Synthesis of 2,3-dihydro-1*H*-imidazo[1,2-a]indoles

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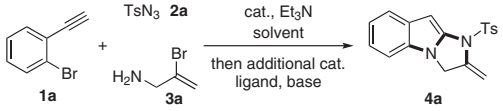
Multicomponent reactions (MCRs) enable the incorporation of three or more simple substrates into a complex molecule via a one-pot cascade procedure, thus exhibiting excellent step-economy, low cost, and high efficiency.[8] In recent years, copper-catalyzed multicomponent reactions involving azide-alkyne cycloaddition (CuAAC)[9] have received much attention since the pioneering work of Chang[10] in 2005. A reactive ketenimine intermediate[11] is formed in situ, which is able to undergo various nucleophilic addition[12–16] and cycloaddition[17–20] reactions leading to the formation of heteroatom-containing acyclic and cyclic compounds, respectively. Of note, the products generating from copper-catalyzed multicomponent reactions may proceed further transformations such as Ullmann-type coupling reaction,[21] which provides a strategy to synthesize heterocyclic compounds in a one-pot manner.[22] As part of our continued interest in copper-catalyzed reactions,[23] we herein report a copper-catalyzed three-component reaction of sulfonyl azides, alkynes, and allylamines involving a CuAAC reaction followed by two consecutive Ullmann-type C–N coupling reactions. This way, 2,3-dihydro-1*H*-imidazo[1,2-*a*]indoles can be accessed in moderate yields with an easy operation.

Initially, we selected the three-component reaction of 2-bromophenylacetylene (**1a**), sulfonyl azide **2a** and 2-bromoprop-2-en-1-amine (**3a**) as the model reaction. The three components were first treated with CuI as a catalyst, triethylamine (Et_3N) as a base in THF at room temperature for 1 hour. Then another portion of CuI, dimethylethylenediamine (**L1**), and K_2CO_3 were sequentially added to the reaction mixture and the reaction temperature was elevated to 80 °C for 6 hours. To our surprise, 2,3-dihydro-1*H*-imidazo[1,2-*a*]indole **4a** was isolated in 35% yield (Table 1, entry 1). Solvents were then screened among which DMSO improved the yield of **4a** to 66% (entries 2–5). Removal of Et_3N in the first step resulted in a sharp decrease in the yield of **4a** (entry 6). Other metal salts were examined and CuI (30 mol%) remained the most efficient one (entries 7–14 vs. 5). A control experiment revealed that copper catalyst played an indispensable role in this reaction (entry 15). Finally, a range of ligands and bases were, respectively, evaluated in the second step of this reaction. It was found that ligand **L1** was the most suitable ligand and K_2CO_3 was the most suitable base (entries 16–23 vs 5).

With the optimal reaction conditions in hand, we first evaluated the substrate scope of sulfonyl azides (Scheme 2). A range of electron-varied functional groups (R) at *para*-position of phenyl ring were compatible in this transformation, providing the corresponding products in moderate yields (→ **4a–e**, Scheme 2). Sterically bulky sulfonyl azides, thiophene-2-sulfonyl azide, and *N*,*N*-dimethylamino-substituted sulfonyl azide were also viable substrates (→ **4f–i**, Scheme 2). In addition, aliphatic sulfonyl azides such as methanesulfonyl azide and butane-1-sulfonyl azide performed efficiently in the reaction affording the desired products in 77% and 55% yield, respectively (→ **4j**, **4k**, Scheme 2). In addition, different 2-halogen-substituted phenylacetylene were subjected to the optimal conditions. It was found that 1-bromo-2-ethnylbenzene exhibited a higher reactivity compared to chloro- and iodo-substituted ones (→ **4a**, Scheme 2). Aromatic alkynes possessing either

Table 1 Screening of the Reaction Parameters[a]



Entry	Solvent	Cat. (mol%)[b]	Ligand	Base	Yield (%)
1	THF	CuI (10/20)	**L1**	K_2CO_3	35
2	MeCN	CuI (10/20)	**L1**	K_2CO_3	40
3	1,4-dioxane	CuI (10/20)	**L1**	K_2CO_3	27
4	DMF	CuI (10/20)	**L1**	K_2CO_3	54
5	**DMSO**	**CuI (10/20)**	**L1**	**K_2CO_3**	**66**
6	DMSO	CuI (10/20)	**L1**	K_2CO_3	16[c]
7	DMSO	CuCl (10/20)	**L1**	K_2CO_3	16
8	DMSO	CuBr (10/20)	**L1**	K_2CO_3	60
9	DMSO	CuSCN (10/20)	**L1**	K_2CO_3	44
10	DMSO	$FeCl_2$ (10/20)	**L1**	K_2CO_3	0
11	DMSO	$NiCl_2$ (10/20)	**L1**	K_2CO_3	0
12	DMSO	CuI (10/0)	**L1**	K_2CO_3	38
13	DMSO	CuI (10/10)	**L1**	K_2CO_3	51
14	DMSO	CuI (10/30)	**L1**	K_2CO_3	65
15	DMSO	–[d]	**L1**	K_2CO_3	0
16	DMSO	CuI (10/20)	**L2**	K_2CO_3	23
17	DMSO	CuI (10/20)	**L3**	K_2CO_3	56
18	DMSO	CuI (10/20)	**L4**	K_2CO_3	18
19	DMSO	CuI (10/20)	**L5**	K_2CO_3	48
20	DMSO	CuI (10/20)	**L1**	–[e]	26
21	DMSO	CuI (10/20)	**L1**	Na_2CO_3	55
22	DMSO	CuI (10/20)	**L1**	K_3PO_4	0
23	DMSO	CuI (10/20)	**L1**	*t*-BuONa	0

[a] Reaction conditions: 1) CuI, Et_3N (1.0 equiv), **1a** (0.5 mmol), **2a** (0.6 mmol), **3a** (0.5 mmol), DMSO (3 mL) at r.t. for 1 h; 2) CuI, ligand (0.3 mmol), K_2CO_3 (2 equiv) at 80 °C for 6 h.
[b] Catalyst loading in the 1st/2nd step is shown in parentheses.
[c] No Et_3N was used.
[d] No catalyst was used.
[e] No base.

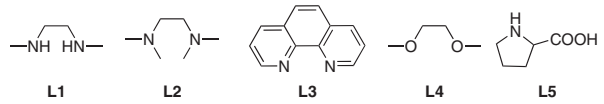
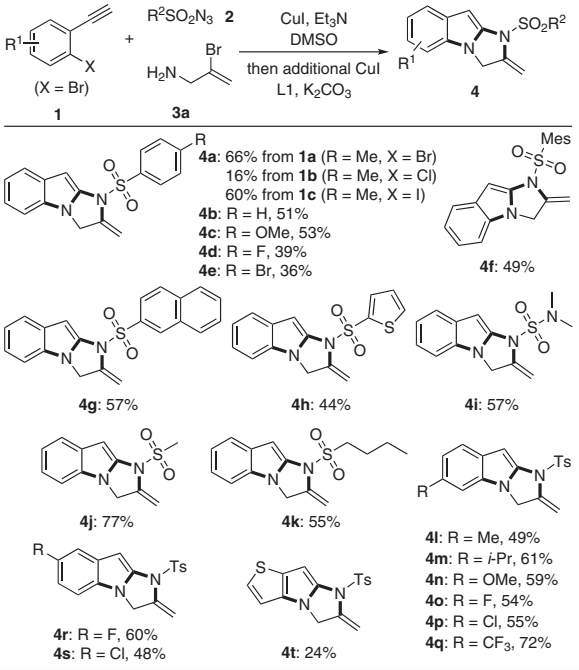


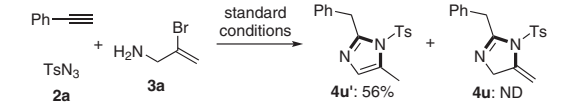
Figure 1 Ligands evaluated in this study: **L1** = *N*,*N*′-dimethylethylenediamine; **L2** = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine; **L3** = 1,10-phenanthroline; **L4** = ethylene glycol dimethyl ether; **L5** = L-proline.

electron-donating or -withdrawing groups reacted smoothly with *p*-toluenesulfonyl azide (→ **4l–s**, Scheme 2). Noteworthy that heteroaromatic alkyne was tolerated under these reaction conditions although it provided the corresponding product in a relatively low yield (→ **4t**, Scheme 2).



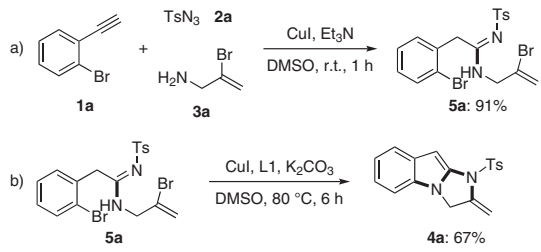
Scheme 2 Substrate scope of azides and alkynes. *Reagents and conditions*: 1) CuI (10 mol%), Et_3N (1.0 equiv), **1** (0.5 mmol), **2** (0.6 mmol), **3a** (0.5 mmol), DMSO (3 mL) at r.t. for 1 h; 2) CuI (20 mol%), **L1** (0.3 mmol), K_2CO_3 (2 equiv) at 80 ° for 6 h. Mes = 2,4,6-Trimethylphenyl.

In addition, we chose phenylacetylene as an alkyne component to react with sulfonyl azides **2a** and 2-bromoprop-2-en-1-amine (**3a**) under the standard conditions (Scheme 3). To our surprise, the imidazole derivative **4u′** was isolated in 56% yield rather than our expected product **4u**. We also tried the reaction of 2-bromophenylacetylene (**1a**) and sulfonyl azide **2a** with allylamine generated in situ from allylamine hydrochloride. However, no desired product was detected under the optimal reaction conditions.



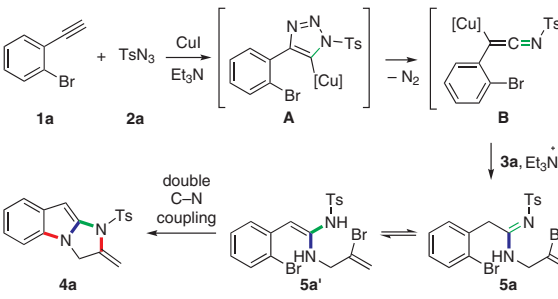
Scheme 3 The reaction of phenylacetylene with **2a** and **3a**. ND: Not detected.

To clarify the possible reaction mechanism, we performed stepwise reactions (Scheme 4). First, the reaction of 2-bromophenylacetylene (**1a**), sulfonyl azide **2a**, and 2-bromoprop-2-en-1-amine **3a** was carried out in the presence of CuI and Et_3N in DMSO at room temperature for 1 hour. As a result, product **5a** was isolated in 91% yield, the structure of which was confirmed by NMR and MS analysis (Scheme 4a). Second, the double C–N coupling reaction of **5a** was examined under indicated reaction conditions affording the desired product **4a** in 67% yield (Scheme 4b). These results suggested that **5a** might be a key intermediate in this three-component reaction.



Scheme 4 Mechanistic experiments

On the basis of previous literature clues[10,21] and mechanistic experiments, a possible reaction mechanism is proposed in Scheme 5. First, a copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC) takes place to generate intermediate **A**, which then transforms to ketenimine **B** by the extrusion of N_2. Nucleophilic addition of 2-bromoprop-2-en-1-amine (**3a**) to intermediate **B** affords carboxamidine **5a** and/or its tautomer **5a′**. Finally, a consecutive copper-catalyzed C–N coupling reactions proceeds to provide 2,3-dihydro-1*H*-imidazo[1,2-*a*]indole **4a**.



Scheme 5 Possible reaction mechanism

In conclusion, a multicomponent reaction of azides, alkynes, and allylamine is successfully developed. This transformation undergoes sequential copper-catalyzed azide-alkyne cycloaddition (CuAAC) followed by double copper-catalyzed C–N coupling reactions, providing 2,3-dihydro-1*H*-imidazo[1,2-*a*]indoles in a one-pot manner. From the synthetic point of view, this protocol thus offers an efficient way to access N-containing heterocycles with an easy operation and high step-economy. Further exploration of copper catalysis in the application of multicomponent reaction is still underway in our laboratory.

Unless otherwise noted, all reactions were conducted in 25 mL flame-dried Schlenk tube under positive N_2 atmosphere. ^1H NMR spectra were recorded on 500 MHz Bruker AVANCE III NMR spectrometer. Chemical shifts (δ) are reported as parts per million (ppm) downfield from TMS. Coupling constants (*J*) are reported in hertz (Hz). High-resolution mass spectra were recorded on a DECAX-60000 LCQ Deca XP spectrometer. Melting points were measured on X4 melting point apparatus and are uncorrected. Flash column chromatography was performed on silica gel (100–200 mesh) with the indicated solvent mixtures. DMSO (extra dry, H_2O content: below 50 ppm) was commercially available and used as received.

2-Methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4a); Typical Procedure

In a 10 mL flame-dried Schlenk tube, anhyd DMSO (3 mL), 2-bromophenylacetylene (**1a**; 90 mg, 0.5 mmol), TsN_3 (**2a**; 118 mg, 0.6 mmol), 2-bromoallylamine (**3a**; 68 mg, 0.5 mmol), and CuI (9.5 mg, 0.05 mmol) were added sequentially under N_2. After stirring for 5 min, Et_3N (50 mg, 0.5 mmol) was added and the mixture was stirred at r.t. for 1 h. CuI (19 mg, 0.1 mmol), K_2CO_3 (138 mg, 1 mmol), and dimethylethylenediamine (26 mg, 0.3 mmol) were added to the reaction mixture. The tube was sealed and stirred at 80 °C for 6 h. After completion, the reaction mixture was diluted with EtOAc (10 mL) and washed with sat. aq NH_4Cl (5 mL). The combined organic phases were concentrated and purified by silica gel column chromatography (PE/EtOAc 15:1 to 7:1) to provide the product **4a**; yield: 107 mg (66%); white solid; mp 140–142 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.5 Hz, 2 H), 7.55–7.52 (m, 1 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.10–7.05 (m, 2 H), 7.03–7.00 (m, 1 H), 6.33 (s, 1 H), 5.66 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.78 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.58 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.35 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.23, 142.43, 141.01, 133.42, 131.64, 130.62, 129.62, 127.42, 120.61 (overlap), 120.17, 108.53, 95.60, 83.52, 46.35, 21.54.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{17}N_2O_2S^+$ [M + H]$^+$: 325.1005; found: 325.1015.

2-Methylene-1-(phenylsulfonyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4b)

Yield: 79 mg (51%); white solid; mp 153–156 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.89 (dd, J_1 = 8.8 Hz, J_2 = 1.3 Hz, 2 H), 7.59–7.54 (m, 2 H), 7.44–7.41 (m, 2 H), 7.10–7.06 (m, 2 H), 7.04–7.02 (m, 1 H), 6.35 (d, *J* = 0.5 Hz, 1 H), 5.69 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.80 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.60 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.45, 140.98, 136.54, 134.12, 131.75, 130.74, 129.07, 127.50, 120.81, 120.78, 120.32, 108.58, 95.84, 83.77, 46.46.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{15}N_2O_2S^+$ [M + H]$^+$: 311.0849; found: 311.0840.

1-[(4-Methoxyphenyl)sulfonyl]-2-methylene-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4c)

Yield: 90 mg (53%); yellow solid; mp 143–146 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.83–7.80 (m, 2 H), 7.56–7.52 (m, 1 H), 7.10–7.05 (m, 2 H), 7.04–7.02 (m, 1 H), 6.87–6.84 (m, 2 H), 6.33 (d, *J* = 0.5 Hz, 1 H), 5.66 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.78 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.60 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 3.79 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.11, 142.63, 141.25, 131.79, 130.73, 129.73, 128.11, 120.72, 120.66, 120.24, 114.23, 108.55, 95.59, 83.69, 55.60, 46.48.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{17}N_2O_3S^+$ [M + H]$^+$: 341.0954; found: 341.0958.

1-[(4-Fluorophenyl)sulfonyl]-2-methylene-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4d)

Yield: 64 mg (39%); yellow solid; mp 147–151 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.5 Hz, 2 H), 7.69 (d, *J* = 8.5 Hz, 2 H), 7.57–7.54 (m, 1 H), 7.12–7.09 (m, 2 H), 7.06–7.03 (m, 1 H), 6.37 (s, 1 H), 5.72 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.85 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.63 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.11 (d, $^1J_{C,F}$ = 255.5 Hz), 142.48, 140.74, 132.51 (d, $^4J_{C,F}$ = 3.3 Hz), 131.66, 130.78, 130.30 (d, $^3J_{C,F}$ = 9.5 Hz), 120.94, 120.84, 120.42, 116.43 (d, $^2J_{C,F}$ = 22.6 Hz), 108.65, 96.06, 83.92, 46.44.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{14}FN_2O_2S^+$ [M + H]$^+$: 329.0755; found: 329.0765.

1-[(4-Bromophenyl)sulfonyl]-2-methylene-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4e)

Yield: 70 mg (36%); yellow brown; mp 168–170 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.75–7.72 (m, 2 H), 7.57–7.54 (m, 3 H), 7.12–7.08 (m, 2 H), 7.06–7.03 (m, 1 H), 6.34 (s, 1 H), 5.68 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.83 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.62 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.40, 140.58, 135.29, 132.41, 131.61, 130.77, 129.55, 128.87, 121.00, 120.87, 120.45, 108.68, 96.21, 83.98, 46.44.

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{14}BrN_2O_2S^+$ [M + H]$^+$: 388.9954, 390.9939; found: 388.9948, 390.9928.

1-(Mesitylsulfonyl)-2-methylene-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4f)

Yield: 86 mg (49%); yellow solid; mp 142–144 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.46 (m, 1 H), 7.09–7.04 (m, 3 H), 6.99 (s, 2 H), 5.89 (s, 1 H), 4.82 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.78 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 4.59 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 2.61 (s, 6 H), 2.31 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.96, 142.40, 141.38, 140.74, 132.53, 132.30, 131.97, 130.56, 120.53, 120.46, 120.17, 108.40, 92.95, 82.21, 46.81, 22.82, 21.06.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{21}N_2O_2S^+$ [M + H]$^+$: 353.1318; found: 353.1335.

2-Methylene-1-(naphthalen-2-ylsulfonyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4g)

Yield: 102 mg (57%); yellow solid; mp 170–172 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.47 (s, 1 H), 7.93 (d, *J* = 7.9 Hz, 1 H), 7.84–7.81 (m, 3 H), 7.63–7.55 (m, 3 H), 7.10–7.04 (m, 2 H), 7.00–6.98 (m, 1 H), 6.42 (d, *J* = 0.5 Hz, 1 H), 5.73 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.78 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.57 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.46, 141.08, 135.50, 133.48, 131.75, 131.72, 130.73, 129.57, 129.50 (overlap), 129.30, 127.88, 127.68, 122.09, 120.77, 120.74, 120.29, 108.57, 95.72, 83.69, 46.44.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{17}N_2O_2S^+$ [M + H]$^+$: 361.1005; found: 361.1020.

2-Methylene-1-(thiophen-2-ylsulfonyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4h)

Yield: 70 mg (44%); yellow solid; mp 125–128 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (dd, J_1 = 3.8 Hz, J_2 = 1.3 Hz, 1 H), 7.58–7.54 (m, 1 H), 7.52 (dd, J_1 = 5 Hz, J_2 = 1.5 Hz 1 H), 7.11–7.08 (m, 2 H), 7.06–7.04 (m, 1 H), 7.01 (dd, J_1 = 4.9 Hz, J_2 = 3.9 Hz, 1 H), 6.34 (s, 1 H), 5.72 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.89 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.63 (dd, J = 2.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.37, 140.35, 135.11, 133.58, 133.42, 131.40, 130.83, 127.35, 120.92, 120.90, 120.34, 108.65, 96.87, 84.51, 46.42.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{13}N_2O_2S_2^+$ [M + H]$^+$: 317.0413; found: 317.0428.

***N*,*N*-Dimethyl-2-methylene-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole-1-sulfonamide (4i)**

Yield: 79 mg (57%); yellow solid; mp 150–152 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.38 (m, 1 H), 7.03–6.98 (m, 3 H), 5.96 (s, 1 H), 5.29 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.76 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 4.63 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 2.88 (s, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.92, 142.50, 131.89, 130.65, 120.47, 120.46, 120.24, 108.40, 93.02, 81.76, 46.80, 39.07.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{16}N_3O_2S^+$ [M + H]$^+$: 278.0958; found: 278.0951.

2-Methylene-1-(methylsulfonyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4j)

Yield: 95 mg (77%); white solid; mp 137–139 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.54 (m, 1 H), 7.16–7.11 (m, 3 H), 6.16 (s, 1 H), 5.58 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.90 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 4.86 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 3.07 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.84, 140.82, 131.65, 130.87, 120.97, 120.78, 120.48, 108.64, 94.58, 82.75, 46.75, 35.42.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{13}N_2O_2S^+$ [M + H]$^+$: 249.0692; found: 249.0700.

1-(Butylsulfonyl)-2-methylene-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4k)

Yield: 80 mg (55%); white solid; mp 107–109 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50–7.48 (m, 1 H), 7.11–7.07 (m, 3 H), 6.08 (s, 1 H), 5.48 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.83 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 4.76 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 3.24 (t, J = 8 Hz, 2 H), 1.84–1.78 (m, 2 H), 1.44–1.37 (m, 2 H), 0.88 (t, J = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.80, 141.25, 131.72, 130.75, 120.71, 120.61, 120.34, 108.56, 93.85, 82.15, 49.38, 46.72, 24.68, 21.41, 13.35.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{19}N_2O_2S^+$ [M + H]$^+$: 291:1162; found: 291.1170.

6-Methyl-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4l)

Yield: 83 mg 49%, pale yellow solid; mp 143–145 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75 (d, J = 8.3 Hz, 2 H), 7.42 (d, J = 8.0 Hz, 1 H), 7.19 (d, J = 8.1 Hz, 2 H), 6.91 (d, J = 8.1 Hz, 1 H), 6.83 (s, 1 H), 6.28 (s, 1 H), 5.66 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.77 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.54 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.40 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.15, 142.64, 140.55, 133.59, 131.08, 130.59, 129.63, 129.41, 127.52, 121.76, 120.40, 108.77, 95.69, 83.54, 46.33, 21.60, 21.59.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{19}N_2O_2S^+$ [M + H]$^+$: 339.1162; found: 339.1167.

6-Isopropyl-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4m)

Yield: 111 mg (61%); brown oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.3 Hz, 2 H), 7.45 (d, J = 8.2 Hz, 1 H), 7.18 (d, J = 8.2 Hz, 2 H), 6.98 (dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz, 1 H), 6.88 (s, 1 H), 6.28 (s, 1 H), 5.65 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.76 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.58 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.95 (m, 1 H), 2.34 (s, 3 H), 1.26 (d, J = 6.9 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.13, 142.62, 142.07, 140.69, 133.57, 130.97, 129.77, 129.62, 127.50, 120.47, 119.39, 105.95, 95.43, 83.40, 46.37, 34.26, 24.48, 21.56.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{23}N_2O_2S^+$ [M + H]$^+$: 367.1475; found: 367.1492.

6-Methoxy-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4n)

Yield: 104 mg (59%); orange solid; mp 138–141 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75 (d, J = 8.4 Hz, 2 H), 7.40 (d, J = 8.6 Hz, 1 H), 7.20 (d, J = 8.1 Hz, 2 H), 6.74 (dd, J_1 = 8.6 Hz, J_2 = 2.3 Hz, 1 H), 6.54 (d, J = 2.2 Hz, 1 H), 6.25 (d, J = 0.7 Hz, 1 H), 5.66 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.77 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.53 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 3.80 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.54, 145.15, 142.56, 140.06, 133.57, 131.37, 129.63, 127.54, 125.67, 121.26, 109.10, 95.73, 93.43, 83.47, 55.79, 46.34, 21.61.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{19}N_2O_3S^+$ [M + H]$^+$: 355.1111; found: 355.1118.

6-Fluoro-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4o)

Yield: 92 mg (54%); yellow solid; mp 149–152 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.74 (d, J = 8.4 Hz, 2 H), 7.40 (dd, J_1 = 8.8 Hz, J_2 = 5.3 Hz, 1 H), 7.19 (d, J = 8.2 Hz, 2 H), 6.83–6.79 (m, 1 H), 6.69 (dd, J_1 = 9.2 Hz, J_2 = 2.2 Hz, 1 H), 6.27 (s, 1 H), 5.65 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.78 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.52 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.34 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.86 (d, $^1J_{C,F}$ =235.8Hz), 145.33, 142.12, 141.22 (d, $^4J_{C,F}$ = 3.2 Hz), 133.43, 130.48 (d, $^3J_{C,F}$ = 12.4 Hz), 129.66, 127.92, 127.44, 121.15 (d, $^3J_{C,F}$ = 9.7 Hz), 108.34 (d, $^2J_{C,F}$ = 23.8 Hz), 95.86, 95.59 (d, $^2J_{C,F}$ = 26.8 Hz), 83.44, 46.34, 21.54.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{16}FN_2O_2S^+$ [M + H]$^+$: 343.0911; found: 343.0923.

6-Chloro-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4p)

Yield: 98 mg (55%); yellow solid; mp 162–164 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.79 (d, J = 8.4 Hz, 2 H), 7.50 (d, J = 8.4 Hz, 1 H), 7.40 (d, J = 8.1 Hz, 2 H), 7.30 (d, J = 1.9 Hz, 1 H), 7.03 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1 H), 6.25 (d, J = 0.7 Hz, 1 H), 5.53 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.95 (dt, J_1 = 2.5 Hz, J_2 = 2.0 Hz, 1 H), 4.80 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H) 2.34 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 145.79, 142.31, 141.14, 132.57, 130.77, 130.08, 129.71, 127.18, 124.94, 121.43, 120.09, 109.54, 95.36, 82.59, 46.41, 21.06.

HRMS (ESI): m/z calcd for $C_{18}H_{16}ClN_2O_2S^+$ [M + H]$^+$: 359.0616; found: 359.0633.

2-Methylene-1-tosyl-6-(trifluoromethyl)-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4q)

Yield: 141 mg (72%); orange solid; mp 156–158 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.4 Hz, 2 H), 7.59 (d, J = 8.3 Hz, 1 H), 7.31 (d, J = 8.5 Hz, 1 H), 7.29 (s, 1 H), 7.22 (d, J = 8.1 Hz, 2 H), 6.38 (d, J = 0.6 Hz, 1 H), 5.70 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.83 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.65 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.36 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 145.57, 143.43, 141.93, 134.39, 133.55, 129.79, 129.71, 127.49, 126.02 (q, $^1J_{C,F}$ = 269.7 Hz), 122.73 (q, $^2J_{C,F}$ = 31.8 Hz), 120.74, 117.08 (q, $^4J_{C,F}$ = 3.6 Hz), 105.97 (q, $^3J_{C,F}$ = 4.3 Hz), 96.12, 83.97, 46.57, 21.58.

HRMS (ESI): m/z calcd for $C_{19}H_{16}F_3N_2O_2S^+$ [M + H]$^+$: 393.0879; found: 393.0891.

7-Fluoro-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4r)

Yield: 103 mg (60%); brown solid; mp 147–149 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.4 Hz, 2 H), 7.22 (d, J = 8.1 Hz, 2 H), 7.19 (dd, J_1 = 9.7 Hz, J_2 = 2.4 Hz, 1 H), 6.91 (dd, J_1 = 8.7 Hz, J_2 = 4.3 Hz, 1 H), 6.81–6.77 (m, 1 H), 6.29 (d, J = 0.5 Hz, 1 H), 5.66 (dt, J_1= 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.79 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.59 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.37 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.33 (d, $^1J_{C,F}$ = 233.4 Hz), 145.39, 142.51, 142.31, 133.54, 132.29 (d, $^3J_{C,F}$ =10.4 Hz), 129.72, 127.52, 127.32, 108.99 (d, $^3J_{C,F}$ = 9.8 Hz), 108.56 (d, $^2J_{C,F}$ = 9.8 Hz), 106.12 (d, $^2J_{C,F}$ = 24.3 Hz), 95.76, 83.87 (d, $^4J_{C,F}$ = 4.3 Hz), 46.67, 21.62.

HRMS (ESI): m/z calcd for $C_{18}H_{16}FN_2O_2S^+$ [M + H]$^+$: 343.0911; found: 343.0925.

7-Chloro-2-methylene-1-tosyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole (4s)

Yield: 86 mg (48%); brown solid; mp 172–174 °C.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.78 (d, J = 8.4 Hz, 2 H), 7.55 (d, J = 2.0 Hz, 1 H), 7.40 (d, J = 8.1 Hz, 2 H), 7.18 (d, J = 8.5 Hz, 1 H), 7.04 (dd, J_1 = 8.5 Hz, J_2 = 2.1 Hz, 1 H), 6.22 (d, J = 0.5 Hz, 1 H), 5.52 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.94 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.82 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.34 (s, 3 H).

^{13}C NMR (150 MHz, acetone-d_6): δ = 146.72, 143.97, 143.44, 134.59, 133.82, 130.75, 130.36, 128.40, 126.26, 121.32, 120.52, 111.21, 96.17, 83.77, 47.41, 21.49.

HRMS (ESI): m/z calcd for $C_{18}H_{16}ClN_2O_2S^+$ [M + H]$^+$: 359.0616; found: 359.0606.

6-Methylene-7-tosyl-6,7-dihydro-5*H*-thieno[2′,3′:4,5]pyrrolo[1,2-*a*]imidazole (4t)

Yield: 40 mg (24%); brown solid; mp 127–130 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, J = 8.0 Hz, 2 H), 7.20 (d, J = 8.1 Hz, 2 H), 6.91 (d, J = 5.2 Hz, 1 H), 6.73 (dd, J_1 = 5.2 Hz, J_2 = 0.4 Hz, 1 H), 6.34 (d, J = 0.5 Hz, 1 H), 5.66 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.78 (dt, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 1 H), 4.53 (dd, J_1 = 2.5 Hz, J_2 = 2.5 Hz, 2 H), 2.36 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.08, 142.66, 139.37, 133.40, 131.43, 129.61, 127.62, 126.58, 121.16, 109.75, 96.65, 85.35, 47.78, 21.61;

HRMS (ESI): m/z calcd for $C_{16}H_{15}N_2O_2S_2^+$ [M + H]$^+$: 331.0569; found: 331.0564.

2-Benzyl-5-methyl-1-tosyl-1*H*-imidazole (4u′)

Yield: 91 mg (56%); white gum.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.23 (m, 7 H), 7.13 (d, J = 8 Hz, 2 H), 6.66 (d, J = 1 Hz, 1 H), 4.43 (s, 2 H), 2.37 (s, 3 H), 2.27 (d, J = 1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.17, 145.46, 137.18, 135.76, 129.93, 129.24, 129.15, 128.46, 127.30, 127.05, 126.58, 35.83, 21.57, 12.00.

MS (ESI): m/z for $C_{18}H_{18}N_2O_2SNa^+$ [M + Na]$^+$ = 349.1.

Procedure for the Stepwise Reactions

N-(2-Bromoallyl)-2-(2-bromophenyl)-*N*′-tosylacetimidamide (5a)

In a 10 mL flame-dried Schlenk tube, anhyd DMSO (3 mL), 2-bromophenylacetylene (**1a**; 90 mg, 0.5 mmol), sulfonyl azide (**2a**; 118 mg, 0.6 mmol), 2-bromoallylamine (**3a**; 68 mg, 0.5 mmol), and CuI (9.5 mg, 0.05 mmol) were added sequentially under N_2. After stirring for 5 min, Et_3N (50 mg, 0.5 mmol) was added and the mixture was stirred at r.t. for 1 h. The reaction mixture was extracted with CH_2Cl_2 and the combined CH_2Cl_2 layers were washed with saturated NH_4Cl solution. The organic phase was evaporated and the residue was purified by silica gel column chromatography (EtOAc/PE 1:5) to provide the product **5a**; yield: 221 mg (91%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.5 Hz, 2 H), 7.63 (d, J = 8.0 Hz, 1 H), 7.38–7.34 (m, 2 H), 7.29 (d, J = 8.0 Hz, 2 H), 7.26–7.22 (m, 1 H), 5.68 (dt, J_1 =2.5 Hz, J_2 = 1.1 Hz, 1 H), 5.48 (d, J = 2.5 Hz, 1 H), 5.43 (s, 1 H), 4.45 (s, 2 H), 4.10 (d, J = 6 Hz, 2 H), 2.42 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.89, 142.47, 140.25, 133.67, 133.10, 132.40, 130.25, 129.21, 128.52, 126.88, 126.61, 125.48, 119.36, 49.44, 40.19, 21.51.

MS (ESI): m/z for $C_{18}H_{18}Br_2N_2O_2SNa^+$ [M + Na]$^+$ = 507.0, 509.0, 511.0.

Under N_2, **5a** (146 mg, 0.3 mmol), CuI (11 mg, 0.06 mmol), K_2CO_3 (83 mg, 0.6 mmol), dimethylethylenediamine (10 mg, 0.12 mmol), and DMSO (2 mL) were added to a dried Schlenk tube. The tube was sealed and stirred at 80 °C for 6 h. After completion of the reaction, the mixture was extracted with EtOAc (10 mL) and the organic layer was washed with sat. aq NH_4Cl (5 mL). The organic phase was concentrated and the residue was purified by silica gel column chromatography to provide the product **4a**; yield: 65 mg (67%).

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Supporting Information

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