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

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Table of Contents

1. Preparation of Substrates S2
   1.1 General procedure for the preparation of alkynes S2
   1.2 General procedure for the preparation of sulfonyl azides S4
   1.3 Preparation of 2-bromoprop-2-en-1-amine S5
2. Optimization of Reaction Conditions S6
3. References S8
4. $^1$H-NMR, $^{13}$C-NMR and MS Spectra S9
1. Preparation of Substrates

1.1 General procedure for the preparation of aromatic alkynes

**General procedure A:**

To a three-necked flask charged with a magnetic stirring bar was added 1-bromo-2-iodobenzene (15 mmol), ethynyltrimethylsilane (15 mmol), Pd(PPh₃)₂Cl₂ (2 mol%), CuI (1 mol%) in triethylamine (50 mL) under nitrogen. The mixture was stirred at 50 °C for 8 hours. The solvent was removed by rotary evaporation. The residue was treated with water and extracted with dichloromethane. The combined organic layer was concentrated under reduced pressure. The crude product was purified flash column chromatography on silica gel using petroleum ether as an eluent.

To a solution of trimethyl(phenylethynyl)silane (10 mmol) in methanol (15 mL) and THF (15 mL) was added K₂CO₃ (4 equiv.) and stirred at rt for 6 hours. The resulting mixture was treated with water and extracted with ethyl ether. The combined organic layer dried over anhydrous Na₂SO₄. The solvent was removed and the residue was purified by silica gel column chromatography to afford the pure product 1a² in 85%
yield. Substrates $1b^2$ and $1c$ were also prepared following the general procedure A.

**General procedure B**: $^{3,4}$

![Chemical structure](image)

To a solution of substituted arylaldehyde (4.0 mmol) in DCM (15 mL) were added CBr₄ (2.65 g, 8.0 mmol) and PPh₃ (2.10 g, 8.0 mmol) at 0 °C and stirred for 60 min. After completion, DCM was evaporated and the residue was purified by column chromatography affording pure 1-bromo-2-(2,2-dibromovinyl)benzene.

A solution of 1-bromo-2-(2,2-dibromovinyl)benzene (3 mmol) in DMSO (40 mL) was added Cs₂CO₃ (2.4 g, 7.5 mmol) and the mixture was stirred at 115 °C for 8 hours. The reaction was poured into water and extracted with DCM. The organic layer was dried over anhydrous Na₂SO₄. DCM was evaporated and the residue was purified by column chromatography. Substrates 1d, 1e, 1f, 1g, 1h$^5$, 1i$^6$, 1j$^7$, and 1l$^8$ were prepared following the general procedure B.

Characterization of new substrates:

**2-bromo-1-ethynyl-4-isopropylbenzene (1c)**

$^1$H NMR (500 MHz, CDCl₃) $\delta$ 7.47-7.44 (m, 1H), 7.45 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.7$ Hz, 1H), 3.33 (s, 1H), 2.89 (m,1H), 1.25 (d, $J = 7.0$ Hz, 6H);

$^{13}$C NMR (125 MHz, CDCl₃) $\delta$ 151.61, 133.99, 130.54, 125.50, 125.39, 121.59, 82.09, 80.90, 33.91, 23.58;

HRMS(EI) Calculated for C$_{11}$H$_{11}$Br: 222.0044, found: 222.0045.

**2-bromo-1-ethynyl-4-methoxybenzene (1d)**

$^1$H NMR (500 MHz, CDCl₃) $\delta$ 7.43 (d, $J = 8.6$ Hz, 1H), 7.11 (d, $J = 2.6$ Hz, 1H), 6.80 (dd, $J = 8.6$, 2.6 Hz, 1H), 3.79 (s, 3H), 3.28 (s, 1H);

$^{13}$C NMR (125 MHz, CDCl₃) $\delta$ 160.21, 134.74, 126.28, 117.83, 116.43, 113.47, 81.90, 80.14, 55.57;

HRMS(EI) Calculated for C$_9$H$_7$BrO: 209.9680, found: 209.9688.

**2-bromo-1-ethynyl-4-fluorobenzene (1e)**
1H NMR (500 MHz, CDCl$_3$) $\delta$ 7.49 (dd, $J = 8.7$, 5.9 Hz, 1H), 7.33 (dd, $J = 8.2$, 2.6 Hz, 1H), 7.01-6.96 (m, 1H), 3.35-3.33 (m, 1H);

13C NMR (125 MHz, CDCl$_3$) $\delta$ 162.13 (d, $^1J_{C,F} = 253.0$ Hz), 135.20 (d, $^3J_{C,F} = 8.9$ Hz), 126.28(d, $^3J_{C,F} = 9.8$ Hz), 120.70 (d, $^4J_{C,F} = 3.8$ Hz), 120.10 (d, $^2J_{C,F} = 24.9$ Hz), 114.72 (d, $^2J_{C,F} = 21.8$ Hz), 81.58 (d, $^1J_{C,F} = 1.5$ Hz), 80.98;

HRMS(EI) Calculated for CsH$_4$FBr: 197.9480, found: 197.9486.

2-bromo-4-chloro-1-ethynylbenzene (1f)

1H NMR (500 MHz, CDCl$_3$) $\delta$ 7.61 (d, $J = 2.1$ Hz, 1H), 7.45 (d, $J = 8.3$ Hz, 1H), 7.27 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.1$ Hz, 1H), 3.41 (s, 1H);

13C NMR (125 MHz, CDCl$_3$) $\delta$ 135.32, 134.62, 132.36, 127.54, 126.09, 122.96, 82.75, 81.01;

HRMS(EI) Calculated for CsH$_4$ClBr: 213.9185, found: 213.9180.

2-bromo-1-ethynyl-4-(trifluoromethyl)benzene (1g)

1g: 1H NMR (500 MHz, CDCl$_3$) $\delta$ 7.85 (s, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 7.52 (dd, $J = 8.1$, 1.0 Hz, 1H), 3.50 (s, 1H);

13C NMR (125 MHz, CDCl$_3$) $\delta$ 134.29, 131.81 (q, $^2J_{C,F} = 33.3$ Hz), 129.46 (q, $^3J_{C,F} = 3.9$ Hz), 128.11, 125.95, 123.87 (q, $^3J_{C,F} = 3.8$ Hz), 122.88 (q, $^1J_{C,F} = 271.1$ Hz), 84.37, 80.79;

HRMS(EI) Calculated for CoH$_4$FsBr: 247.9448, found: 247.9457.

1.2 General procedure for the preparation of sulfonyl azides
General procedure: 9

\[
\text{R-SO-Cl} + \text{NaN}_3 \xrightarrow{\text{Acetone, Water, rt, 12 h}} \text{R-SO}_2\text{N}_3
\]

A 50 mL round bottom flask containing a solution of sodium azide (5.2 mmol) in water (10 mL) and was added with a solution of sulfonyl chloride (5 mmol) in acetone (15 mL). After stirring at room temperature for 12 hours, acetone was evaporated under reduced pressure. The residue was extracted with CH2Cl2, washed with water, dried over anhydrous Na2SO4, and concentrated under reduced pressure to give the sulfonyl azides as a colorless oil. All sulfonyl azides 2a\textsuperscript{10}, 2b\textsuperscript{10}, 2c\textsuperscript{11}, 2d\textsuperscript{11}, 2e\textsuperscript{10}, 2f\textsuperscript{12}, 2g\textsuperscript{10}, 2h\textsuperscript{10}, 2i\textsuperscript{13}, 2j\textsuperscript{10}, and 2k\textsuperscript{14} were prepared according to this procedure and their spectra data were in line with previous reports.

1.3 Preparation of 2-bromoprop-2-en-1-amine\textsuperscript{15}

Potassium phthalimide (5.56 g, 30.0 mmol) was added to a solution of 2,3-dibromoprop-1-ene (5.0 g, 25.0 mmol) in DMF (55 mL) at room temperature. The resulting mixture was stirred for 18 hours. After that the mixture turned to dark brown
and a white precipitate was observed. DCM (50 mL) was added and the mixture poured onto water (50 mL). The aqueous phase was separated and extracted with DCM. The combined organic extract was then washed with NaOH (0.2 M) and dried over anhydrous sodium sulfate. The DCM was removed under vacuo and the residue was purified by column chromatography to afford 2-(2-bromoallyl)isoindoline-1,3-dione in 90% yield as a white solid.

Hydrazine hydrate (0.21 mL, 4.14 mmol) was added to a suspension of 2-(2-bromoallyl)isoindoline-1,3-dione (550 mg, 2.07 mmol) in ethanol (7.0 mL). The resulting mixture was heated under reflux for one hour. Then HCl (6.0 mL, 2.0 M) was added and the mixture was heated for another hour. The reaction mixture was then cooled to 4 °C and the phthalyl hydrazide removed by filtration. The ethanol was removed under vacuo and the solid residue was redissolved in 10 mL NaOH (2.0 M). The solution was extracted with diethyl ether and the organic extract was dried over anhydrous Na₂SO₄, filtered and the solvent was removed to give product in 72% yield.

2. Optimization of Reaction Conditions

**Table S1.** Survey of the reaction parameters

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Base</th>
<th>T/°C</th>
<th>Solvent</th>
<th>Ligand/mmol</th>
<th>1a:2a:3a</th>
<th>Yield/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CuI (10/20)</td>
<td>K₂CO₃</td>
<td>80</td>
<td>THF</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
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<td>CuI (10/20)</td>
<td>K₂CO₃</td>
<td>80</td>
<td>MeCN</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>40</td>
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<td>3</td>
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<td>K₂CO₃</td>
<td>80</td>
<td>Dioxane</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>CuI (10/20)</td>
<td>K₂CO₃</td>
<td>80</td>
<td>DCM</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>6</td>
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<tr>
<td>5</td>
<td>CuI (10/20)</td>
<td>K₂CO₃</td>
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<td>DMF</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
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<tr>
<td>6</td>
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<td>K₂CO₃</td>
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<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
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<td>7</td>
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<td>60</td>
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<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>59</td>
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<td>1:1.2:1</td>
<td>53</td>
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<td>L1/0.3</td>
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<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>60</td>
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<tr>
<td></td>
<td>Reaction conditions unless otherwise noted: 1) 1a (0.5 mmol), 2a (0.6 mmol), 3a (0.5 mmol), catalyst, solvent (3 mL), Et3N (0.5 mmol) at r.t. for 1h; 2) catalyst, ligand, base (1 mmol). b)Catalyst loading in the 1st/2nd step was shown in the parentheses. c)No catalyst. d)No ligand. e)No base. L1 = N,N'-Dimethylethylenediamine, L2 = N,N,N',N'-Tetramethylethylenediamine, L3 = 1,10-Phenanthroline, L4 = Ethylene glycol dimethyl ether, L5 = L-Proline.</td>
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<td>12</td>
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<td>80</td>
<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>0</td>
</tr>
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<td>K2CO3</td>
<td>80</td>
<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
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<td>DMSO</td>
<td>L1/0.3</td>
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<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td>CuI (5/0)</td>
<td>K2CO3</td>
<td>80</td>
<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>22</td>
</tr>
<tr>
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<td>K2CO3</td>
<td>80</td>
<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>38</td>
</tr>
<tr>
<td>18</td>
<td>CuI (10/10)</td>
<td>K2CO3</td>
<td>80</td>
<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>51</td>
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<td>19</td>
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<td>K2CO3</td>
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<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>65</td>
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<td>K2CO3</td>
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<td>DMSO</td>
<td>L1/0.45</td>
<td>1:1.2:1</td>
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<td>DMSO</td>
<td>L1/0.15</td>
<td>1:1.2:1</td>
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<tr>
<td>22</td>
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<td>DMSO</td>
<td>L1/0.45</td>
<td>1:1.2:1</td>
<td>60</td>
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<tr>
<td>23</td>
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<td>DMSO</td>
<td>L2/0.3</td>
<td>1:1.2:1</td>
<td>23</td>
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<td>DMSO</td>
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<td>L4/0.3</td>
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<td>1:1.2:1</td>
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<tr>
<td>32</td>
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<td>DMSO</td>
<td>L1/0.3</td>
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<tr>
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<td>DMSO</td>
<td>L1/0.3</td>
<td>1:1.2:1</td>
<td>64</td>
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</table>

\[\text{L1 = N,N'-Dimethylethylenediamine, L2 = N,N,N',N'-Tetramethylethylenediamine, L3 = 1,10-Phenanthroline, L4 = Ethylene glycol dimethyl ether, L5 = L-Proline.}\]
3. References

4. $^1$H-NMR, $^{13}$C-NMR and MS Spectra

$^1$H NMR for compound 4a

![Chemical structure of 4a](attachment:image)
$^{13}$C NMR for compound 4a
$^1$H NMR for compound 4b

![Chemical Structure](image)
$^{13}$C NMR for compound 4b
$^1$H NMR for compound 4c

4c

δ (ppm)
$^{13}$C NMR for compound 4c

![Chemical Structure](image)

δ (ppm)
$^1$H NMR for compound 4d
$^{13}$C NMR for compound 4d
$^1$H NMR for compound 4e

4e

\[ \ 
\]

\[ \]

\[ \delta \text{ (ppm)} \]

11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0

S17
$^{13}$C NMR for compound 4e
$^1$H NMR for compound 4f

4f
$^{13}$C NMR for compound 4f
$^1$H NMR for compound 4g

\[ \text{Diagram of compound 4g} \]

\[ \text{NMR spectrum with chemical shifts} \]
$^{13}$C NMR for compound 4g

![Chemical Structure of 4g](image)
\(^1\)H NMR for compound 4h

![Chemical Structure](image)

\(\delta\) (ppm)

11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.1
$^{13}$C NMR for compound 4h

![Chemical Structure](image)

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
$^{13}$C NMR for compound 4i
$^1$H NMR for compound 4j
$^{13}$C NMR for compound 4j
$^1$H NMR for compound 4k
$^{13}$C NMR for compound 4k

![NMR Spectrogram](image)
$^{13}$C NMR for compound 4I
$^1$H NMR for compound 4m
$^{13}$C NMR for compound 4m
$^{13}$C NMR for compound 4n
$^1$H NMR for compound 4o
$^1$H NMR for compound 4p
$^{13}$C NMR for compound 4p

δ (ppm)
$^1$H NMR for compound 4q
$^{13}$C NMR for compound 4q
$^1$H NMR for compound 4r

![NMR Spectrum](image)
$^{13}$C NMR for compound 4r
$^1$H NMR for compound 4s
$^{13}$C NMR for compound 4s

![Chemical Structure of 4s](image)
$^1$H NMR for compound 4t

![Chemical Structure of 4t](image)
$^{13}$C NMR for compound 4t
$^1$H NMR for compound 4u'

![NMR spectrum](image)
$^{13}$C NMR for compound 4u'
$^1$H NMR for compound 5a

![NMR spectrum of compound 5a](image)
$^{13}$C NMR for compound 5a
MS Spectrum

**MS (ESI) for compound 5a**

![Chemical Structure of 5a](image)