Halogenation of Indoles with Copper(II) Halides: Selective Synthesis of 2-Halo-, 3-Halo-, and 2,3-Dibromoindoles

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Abstract: A simple and selective protocol for the halogenation of indoles with copper(II) bromide or chloride to synthesize 2-halo-, 3-halo-, and 2,3-dibromoindoles was developed. It was found that both base and water could be used as switches for the selectivity of the halogenation reactions. In the presence of copper(II) halide and sodium hydroxide, 3-haloindoles were obtained as the major products, whereas the selectivity was shifted toward 2,3-dihaloindoles when water was added instead of sodium hydroxide. Moreover, 2-halogenations of 3-substituted indoles were also performed successfully in moderate to good yields under the standard conditions.

Key words: halogenation, indole, copper(II) halide, 2-haloindole, 3-haloindole, 2,3-dibromoindole

Indoles bearing halo substituents on their 2- and/or 3-positions are valuable synthetic intermediates, as well as important units in many biologically active alkaloids and potential candidates for pharmaceuticals.1,2 As a result, considerable efforts have devoted to the halogenation of indoles, and a number of convenient approaches have been developed.1,6 The most commonly used reagents for these approaches include N-halosuccinimides,1b,c,j,3 halogens,4 phosphoryl halides/imidazole,1a,5 and others.6–8 However, the reaction conditions for these methods generally involve highly acidic or basic media. In addition, these methods have several disadvantages including poor selectivity, overhalogenation, sensitivity to air/water, and narrow functional tolerance. Therefore, the development of some mild and selective halogenation protocols for the synthesis of 2-halo- and/or 3-haloindoles is still highly challenging. Copper halides have been reported to be the effective reagents for the halogenation of 3-substituted indoles and azaindoles.8 Balogh-Hergovich and Speier first-studied 2-chlorination of 3-substituted indoles with copper(II) chloride in acetonitrile.8a They found that the chemoselectivity of the products, including 2-chloroindoles, oxygenated products, and dimers, was based on both the amount of copper(II) chloride and the reaction time; chlorinated indoles were obtained as the major products in the presence of excess copper(II) chloride. However, only two 2-chloroindole products were reported. Recently, Gallou and co-workers also employed copper(II) bromide or chloride in the halogenation of azaindoles.8b The results showed that a variety of 6-aza indoles were halogenated regioselectively by copper(II) bromide or chloride at room temperature in acetonitrile to afford the corresponding 3-halo-6-azaindol es in moderate to good yields. Thus, further study extending the scope of the copper(II) halide mediated halogenation of indoles is still significant. After a series of trials, we found that both base and water could be used as switches for the selectivity of the halogenation reactions. In the presence of a copper(II) halide and sodium hydroxide, 3-haloindoles were obtained as the major products, whereas the selectivity was shifted toward 2,3-dihaloindoles when water was added instead of sodium hydroxide.4i,7 Moreover, the 2-halogenation of 3-substituted indoles was successfully performed in moderate to good yields under the standard conditions (Scheme 1).

In the preliminary experiment, treatment of 1-methyl-1H-indole (1a) with copper(II) bromide (2a) was tested to screen the conditions, and the results are summarized in Table 1. Initially, the reaction of 1a with copper(II) bromide (2a) was conducted under Gallou’s reaction conditions (entry 1), unfortunately, a complex mixture of

![Scheme 1](image-url)
products was observed; identical results were obtained using 1,2-dichloroethane as the solvent. According to previous reports, basic conditions may favor the halogenation reaction.2,3 As expected, the presence of base could improve the reaction, and sodium hydroxide gave the best results in term of selectivity and yield (entries 3–5). In the presence of two equivalents of 2a and three equivalents of sodium hydroxide, substrate 1a underwent bromination at room temperature in three hours to afford 3-bromo-1-methyl-1H-indole (3aa) in 60% yield together with 2,3-dibromo-1-methyl-1H-indole (4aa) in 15% yield (entry 5). It was found that further increasing amount of copper(II) bromide (2a) to 4 equivalents gave a complex mixture of products (entry 6). The results also indicated that acetonitrile was not a suitable solvent for the bromination under the same conditions (entry 7). To our delight, both selectivity and rate were enhanced when silica gel (300–400 mesh) was added (entry 8). Substrate 1a was reacted with 2a, sodium hydroxide, silica gel, and 1,2-dichloroethane at room temperature for 15 minutes to afford 3-bromo-1-methyl-1H-indole (3aa) in 68% yield together with 2,3-dibromo-1-methyl-1H-indole (4aa) in 3% yield. Subsequently, we attempted to shift the selectivity toward 2,3-dibromo-1-methyl-1H-indole (4aa). After a series of trials, we found that water could shift the selectivity toward the dibromination reaction (entries 9–12). 2,3-Dibromo-1-methyl-1H-indole (4aa) was isolated exclusively when water was added, and 0.2 mL of water provided the highest yield (entries 9–11). Noteworthy is that the presence of tetrabutylammonium bromide can shorten the reaction time from ten hours to one hour (entry 12). Thus, two optimum reaction conditions were obtained for the selective halogenation reactions: conditions A: 1 (0.5 mmol), CuBr2 (1 mmol), NaOH (1.5 mmol), silica gel (300–400 mesh, 100 mg), DCE (5 mL), r.t. (entry 8); conditions B: 1 (0.5 mmol), CuBr2 (1 mmol), H2O (0.1 mL), TBAB (0.05 mmol), DCE (5 mL) at r.t. (entry 12).

With the optimum reaction conditions in hand, the scope of the selective synthesis of both 3-haloindoles and 2,3-dihaloindoles was examined (Table 2, Scheme 2). As listed in Table 2, a variety of indoles underwent the halogenation successfully under conditions A, and a number of functional groups, such as alkyl, acetyl, alkenyl, and halo groups were well tolerated.

### Table 1
Selective Bromination of 1-Methyl-1H-indole (1a) Mediated by Copper(II) Bromide (2a)*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yieldb (%)</th>
<th>3aa</th>
<th>4aa</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–</td>
<td>MeCN</td>
<td>0.5</td>
<td>trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>DCE</td>
<td>0.5</td>
<td>trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>NaHCO3 (3 equiv)</td>
<td>DCE</td>
<td>2</td>
<td>45</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>K2CO3 (3 equiv)</td>
<td>DCE</td>
<td>2</td>
<td>56</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>NaOH (3 equiv)</td>
<td>DCE</td>
<td>3</td>
<td>60</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>6c</td>
<td>NaOH (3 equiv)</td>
<td>DCE</td>
<td>2</td>
<td>trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>NaOH (3 equiv)</td>
<td>MeCN</td>
<td>0.25</td>
<td>trace</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8d</td>
<td>NaOH (3 equiv), silica gel</td>
<td>DCE</td>
<td>0.25</td>
<td>68</td>
<td>&lt;3</td>
<td></td>
</tr>
<tr>
<td>9c</td>
<td>H2O (0.1 mL)</td>
<td>DCE</td>
<td>10</td>
<td>trace</td>
<td></td>
<td>56</td>
</tr>
<tr>
<td>10c</td>
<td>H2O (0.2 mL)</td>
<td>DCE</td>
<td>10</td>
<td>trace</td>
<td></td>
<td>71</td>
</tr>
<tr>
<td>11c</td>
<td>H2O (0.4 mL)</td>
<td>DCE</td>
<td>10</td>
<td>trace</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>12c</td>
<td>H2O (0.2 mL), TBAB (0.1 equiv)</td>
<td>DCE</td>
<td>1</td>
<td>trace</td>
<td></td>
<td>72</td>
</tr>
</tbody>
</table>

* Reaction conditions: 1a (0.5 mmol), CuBr2 (2a) (1 mmol), solvent (5 mL), r.t.
† Isolated yield. The reaction was monitored by GC-MS and TLC.
‡ CuBr2 (4 equiv).
§ Silica gel (300–400 mesh, 100 mg).
ethyl-1H-indole (1b) also reacted with copper(II) bromide (2a) or copper(II) chloride (2b) smoothly to provide the corresponding 3-haloindoles 3ba and 3bb in 69% and 85% yields, respectively (entries 2, 3). It is interesting to note that other indoles bearing alkyl, nitro, allyl, or bromo groups, all work well with copper(II) bromide (2a) in good yields (entries 4–6). To our delight, 2-substituted indole 1f was a suitable substrate for the reaction after prolonged a reaction time (entry 7).

To our delight, dibrominations of indoles 1a, b, d, e were conducted efficiently in good yields under conditions B (Scheme 2). The reaction of 1a with 2a, water, and tetrabutylammonium bromide, for example, afforded the target product 4aa in 71% yield. Satisfactory yields were achieved for the dibromination of the other indoles bearing allyl, ethyl, and bromo groups in the presence of copper(II) bromide (2a), water, and tetrabutylammonium bromide. Surprisingly, only the monochlorinated product 3ab was isolated from the reaction of 1a with copper(II) chloride (2b), water, and tetrabutylammonium bromide in 1,2-dichloroethane (81% yield).

Interestingly, we found that 3-substituted indoles 1g–m underwent the 2-halogenations smoothly under the standard conditions (Table 3). In the presence of copper(II) halide, water, and tetrabutylammonium bromide (conditions B), both 1,3-dimethyl-1H-indole (1g) and 1-allyl-3-methyl-1H-indole (1h) performed the 2-halogenation reaction efficiently in good yields. Substrate 1g, for exam-

### Table 2 Selective Synthesis of 3-Haloindoles (3) in the Presence of Copper(II) Bromide (2a) or Chloride (2b), Sodium Hydroxide, and Silica Gel

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>CuX₂</th>
<th>Time (h)</th>
<th>Isolated yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>2b</td>
<td>1</td>
<td>89 (3ab) 0 (4ab)</td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>2a</td>
<td>0.25</td>
<td>69 (3ba) &lt;5 (4ba)</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
<td>2b</td>
<td>1</td>
<td>85 (3bb) 0 (4bb)</td>
</tr>
<tr>
<td>4</td>
<td>1c</td>
<td>2a</td>
<td>1</td>
<td>81 (3ca) &lt;3 (4ca)</td>
</tr>
<tr>
<td>5</td>
<td>1d</td>
<td>2a</td>
<td>0.25</td>
<td>67 (3da) 8 (4da)</td>
</tr>
<tr>
<td>6</td>
<td>1e</td>
<td>2a</td>
<td>0.25</td>
<td>82 (3ea) &lt;5 (4ea)</td>
</tr>
<tr>
<td>7</td>
<td>1f</td>
<td>2a</td>
<td>12</td>
<td>90 (3fa) 0</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions A: 1 (0.5 mmol), CuX₂ 2 (1 mmol), NaOH (1.5 mmol), silica gel (100 mg), DCE (5 mL), r.t.

<sup>b</sup> The reaction was monitored by GC-MS and TLC.
ple, was treated with copper(II) bromide (2a) or copper(II) chloride (2b), water, and tetrabutylammonium bromide in 1,2-dichloroethane to give the corresponding 2-haloindoles 5ga and 5gb in 92% and 95% yields, respectively (entries 1 and 2). However, 3-methyl-1H-indole (1i), an N-unprotected indole, afforded a complex mixture of products (entry 5). Gratifyingly, substrate 1i could be halogenated by copper(II) bromide (2a) or copper(II) chloride (2b) smoothly providing good yields when sodium hydroxide (3 equiv) and silica gel (100 mg) were added instead of both water, and tetrabutylammonium bromide (conditions A, entries 6, 7). It was interesting to observe that in the presence of copper(II) bromide (2a), water, and tetrabutylammonium bromide the other 3-substituted indoles 1j and 1k bearing carbonyl or bromo groups, both could also undergo the reaction efficiently to afford the corresponding 2-haloindoles 5ja and 4aa in 80% and 78% yields, respectively (entries 8 and 9). Although a higher reaction temperature was required, a satisfactory yield was still isolated after eight hours in the 2-halogenation of substrate 1l bearing an ester group at the 3-position (entries 10, 11). Unfortunately, substrate 1m was not a suitable substrate in the presence of copper(II) bromide, water, and tetrabutylammonium bromide (entry 12).

In conclusion, we have developed a mild and selective protocol for the synthesis of 2-halo-, 3-halo-, and 2,3-dibromoindoles. Both base and water were found to be used as the switches for the selectivity of the reaction. In the presence of sodium hydroxide, 3-haloindoles were obtained as the major products from the reactions of indoles with copper(II) halides, whereas the selectivity was shifted toward 2,3-dihaloindoles when water was added instead of sodium hydroxide. Compared with earlier reports, several interesting features are obvious for the present reaction: First, the reaction is mild and highly selective. Second, several functional groups, such as carbonyl, alkenyl, nitro, and halo groups, are tolerated well in

Scheme 2 Selective synthesis of 2,3-dihaloindoles 4 in the presence of copper(II) halide, water, and tetrabutylammonium bromide

Table 3 Selective Synthesis of 2-Haloindoles 5 in the Presence of Copper(II) Bromide (2a) or Chloride (2b), Water, and Tetrabutylammonium Bromide

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>CuX₂</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1g</td>
<td>2a</td>
<td>2</td>
<td>92 (5ga)</td>
</tr>
<tr>
<td>2</td>
<td>1g</td>
<td>2b</td>
<td>3</td>
<td>95 (5gb)</td>
</tr>
<tr>
<td>3</td>
<td>1h</td>
<td>2a</td>
<td>1.5</td>
<td>96 (5ha)</td>
</tr>
<tr>
<td>4</td>
<td>1h</td>
<td>2b</td>
<td>2</td>
<td>95 (5hb)</td>
</tr>
<tr>
<td>5*</td>
<td>1i</td>
<td>2a</td>
<td>2</td>
<td>n.d. (5ia)</td>
</tr>
<tr>
<td>6d</td>
<td>1i</td>
<td>2a</td>
<td>2</td>
<td>86 (5ia)</td>
</tr>
<tr>
<td>7d</td>
<td>1i</td>
<td>2b</td>
<td>2.5</td>
<td>61 (5ib)</td>
</tr>
<tr>
<td>8</td>
<td>1j</td>
<td>2a</td>
<td>10</td>
<td>80 (5ja)</td>
</tr>
<tr>
<td>9</td>
<td>1k</td>
<td>2a</td>
<td>1</td>
<td>78 (4aa)</td>
</tr>
<tr>
<td>10</td>
<td>1l</td>
<td>2a</td>
<td>8</td>
<td>trace (5la)</td>
</tr>
<tr>
<td>11e</td>
<td>1l</td>
<td>2a</td>
<td>8</td>
<td>61 (5la)</td>
</tr>
<tr>
<td>12</td>
<td>1m</td>
<td>2a</td>
<td>2</td>
<td>n.d. (5ma)</td>
</tr>
</tbody>
</table>

* Reaction conditions (conditions B): 1 (0.5 mmol), CuX₂ 2 (2 equiv), H₂O (0.2 mL), TBAB (0.1 equiv), DCE (5 mL), r.t.

* Isolated yield.

* Not determined.

* NaOH (3 equiv), silica gel (100 mg) (conditions A) instead of both H₂O and TBAB.

* At 70 °C.
Halogenation of Indoles with Copper(II) Halides

the system. Finally, silica gel was observed to improve the 3-halogenation reaction, and tetrabutylammonium bromide promote the 2,3-dihalogenation reaction. In addition, the standard conditions were also effective for the 2-halogenations of 3-substituted indoles providing moderate to good yields. Further efforts to apply this transformation and these products in organic synthesis, and to study more the roles of sodium hydroxide and water are underway in our laboratory.

NMR spectroscopy was performed on an INOVA-400 (Varian) spectrometer operating at 400 MHz (1H NMR) and 100 MHz (13C NMR). TMS was used as an internal standard and CDCl3 was used as the solvent. All the reagents are used directly from commercial sources and all melting points are uncorrected.

Copper(II) Halide Mediated 3-Halogenation of Indoles (Conditions A): General Procedure
A mixture of indole 1 (0.5 mmol), CuX2 (2 equiv), NaOH (3 equiv), silica gel (100 mg), and DCE (5 mL) was stirred at rt for the indicated time until complete consumption of starting material (monitored by GC-MS and TLC). The mixture was then filtered through a short column and evaporated under vacuum and the residue was purified by flash column chromatography (hexane–EtOAc) to afford the desired product 3.

Copper(II) Halide Mediated 2-Halogenation or 2,3-Halogenation of Indoles (Conditions B): General Procedure
A mixture of indole 1 (0.5 mmol), CuX2 (2 equiv), H2O (0.2 mL), TBAB (0.1 equiv), and DCE (5 mL) was stirred at rt for the indicated time until complete consumption of starting material (monitored by GC-MS and TLC). The mixture was then filtered by through short column and evaporated under vacuum, and the residue was purified by flash column chromatography (hexane–EtOAc) to afford the desired products 4 or 5.

3-Bromo-1-methyl-1H-indole (3ba)
Slightly yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.57 (d, J = 7.6 Hz, 1 H), 7.29–7.16 (m, 3 H), 7.09 (s, 1 H), 5.98–5.88 (m, 1 H), 5.20 (d, J = 10.0 Hz, 1 H), 5.08 (d, J = 17.2 Hz, 1 H), 4.65 (d, J = 5.6 Hz, 2 H).

13C NMR (100 MHz, CDCl3): δ = 135.6, 132.8, 127.4, 126.7, 122.6, 120.2, 119.3, 117.8, 109.8, 89.9, 48.9.

LRMS (EI, 70 eV): m/z (%) = 237 (M+ + 2, 81), 235 (M+, 87), 156 (M+ – Br, 100).


1-Allyl-3-chloro-1H-indole (3ca)
Yellow solid; mp 141.0–143.0 °C.

1H NMR (400 MHz, CDCl3): δ = 7.85 (d, J = 8.4 Hz, 1 H), 7.09 (t, J = 7.2 Hz, 1 H), 7.00 (d, J = 7.6 Hz, 1 H), 6.93 (s, 1 H), 3.95 (s, 3 H), 3.09–3.04 (m, 2 H), 1.32 (t, J = 7.2 Hz, 3 H).

13C NMR (100 MHz, CDCl3): δ = 134.2, 129.4, 128.6, 128.1, 123.5, 120.4, 117.4, 116.9, 36.9, 25.3, 16.5.

LRMS (EI, 70 eV): m/z (%) = 265 (M+ + 2, 15), 254 (M+, 16), 211 (40), 209 (41), 130 (M+ – 45 – Br, 46), 77 (20), 44 (40), 32 (40), 28 (100).

HRMS (EI): m/z [M+] calculated C17H13ClBrN2O: 323.9691; found: 323.9690.

3-Chloro-1H-indole (3da)
White solid; mp 87.4–90.0 °C.

1H NMR (400 MHz, CDCl3): δ = 7.40 (d, J = 8.4 Hz, 1 H), 7.09 (t, J = 7.2 Hz, 1 H), 7.00 (d, J = 7.6 Hz, 1 H), 6.93 (s, 1 H), 3.95 (s, 3 H), 3.09–3.04 (m, 2 H), 1.32 (t, J = 7.2 Hz, 3 H).

13C NMR (100 MHz, CDCl3): δ = 134.2, 129.4, 128.6, 128.1, 123.5, 120.4, 117.4, 116.9, 36.9, 25.3, 16.5.

LRMS (EI, 70 eV): m/z (%) = 265 (M+ + 2, 79), 263 (M+, 84), 185 (14), 184 (M+ – Br, 87), 143 (100).


1-Allyl-3,6-dibromo-1H-indole (3ea)
Slightly yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.45 (s, 1 H), 7.41 (d, J = 8.8 Hz, 1 H), 7.28 (d, J = 8.4 Hz, 1 H), 7.08 (s, 1 H), 5.98–5.88 (m, 1 H), 5.24, 5.09 (dd, J = 10.4, 16.4 Hz, 2 H), 4.63 (d, J = 5.2 Hz, 2 H).

13C NMR (100 MHz, CDCl3): δ = 136.3, 132.3, 127.3, 126.3, 123.6, 123.6, 120.7, 118.2, 116.5, 112.8, 90.2, 49.1.

LRMS (EI, 70 eV): m/z (%) = 317 (M+ + 4, 49), 316 (M+ + 3, 79), 315 (M+ + 2, 100), 313 (M+ + 19), 274 (69), 272 (36), 236 (M+ – Br, 50), 234 (53), 155 (M+ – 2 Br, 53), 154 (46).

HRMS (EI): m/z [M+] calculated C18H12Br2N2O: 312.9102; found: 312.9100.

1-Acetyl-3-bromo-2-octyl-1H-indole (3fa)
Slightly yellow oil.

1H NMR (400 MHz, CDCl3): δ = 7.77 (d, J = 8.8 Hz, 1 H), 7.50 (d, J = 8.8 Hz, 1 H), 7.33–7.21 (m, 2 H), 3.11 (t, J = 7.6 Hz, 2 H), 2.76 (s, 3 H), 1.69–1.58 (m, 2 H), 1.40–1.27 (m, 10 H), 0.87 (t, J = 6.4 Hz, 3 H).

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Slightly yellow oil.  
**1H NMR (400 MHz, CDCl₃):** δ = 7.49 (d, J = 7.6 Hz, 1 H), 7.20–7.18 (m, 2 H), 6.97 (d, J = 8.0 Hz, 1 H), 6.54 (d, J = 7.6 Hz, 2 H), 3.67 (s, 3 H), 2.27 (s, 3 H).  
**13C NMR (100 MHz, CDCl₃):** δ = 136.3, 126.9, 122.8, 120.7, 118.8, 114.8, 109.6, 92.6, 29.7.

2,3-Dibromo-7-ethyl-1-methyl-1H-indole  
Slightly yellow oil.  
**1H NMR (400 MHz, CDCl₃):** δ = 7.74 (d, J = 8.0 Hz, 1 H), 7.24–7.23 (m, 1 H), 7.17 (m, J = 7.6 Hz, 1 H), 3.73 (s, 3 H).  
**13C NMR (100 MHz, CDCl₃):** δ = 136.3, 126.9, 122.8, 120.7, 118.8, 114.8, 109.6, 92.6, 29.7.

2-Chloro-1,3-dimethyl-1H-indole  
Slightly yellow oil.  
**1H NMR (400 MHz, CDCl₃):** δ = 7.51 (d, J = 8.0 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 1 H), 7.19 (t, J = 8.0 Hz, 1 H), 7.10 (d, J = 8.0 Hz, 1 H), 5.90–5.82 (m, 1 H), 5.13, 4.91 (dd, J = 10.4, 17.2 Hz, 2 H), 4.77 (dd, J = 4.8 Hz, 2 H), 2.29 (s, 3 H).

1-Allyl-2-bromo-3-methyl-1H-indole  
Slightly yellow oil.  
**1H NMR (400 MHz, CDCl₃):** δ = 7.51 (d, J = 8.0 Hz, 1 H), 7.18 (t, J = 8.0 Hz, 1 H), 7.06 (t, J = 7.6 Hz, 1 H), 6.97 (d, J = 8.0 Hz, 1 H), 3.99 (s, 3 H), 3.07–3.01 (m, 2 H), 1.30 (t, J = 7.6 Hz, 3 H).

2,3-Dibromo-7-ethyl-1-methyl-1H-indole (4da)  
Slightly yellow solid; mp 81.0–83.5 °C.  
**1H NMR (400 MHz, CDCl₃):** δ = 7.34 (d, J = 8.0 Hz, 1 H), 7.06 (t, J = 7.6 Hz, 1 H), 5.91–5.82 (m, 1 H), 5.15, 4.92 (dd, J = 10.0, 17.2 Hz, 2 H), 4.79 (d, J = 4.8 Hz, 2 H).  
**13C NMR (100 MHz, CDCl₃):** δ = 134.7, 128.0, 127.7, 124.1, 121.0, 117.0, 116.1, 93.7, 35.5, 25.7, 16.4.

1-Allyl-2,3-dibromo-1H-indole  
**1H NMR (400 MHz, CDCl₃):** δ = 7.34 (d, J = 8.0 Hz, 1 H), 7.06 (t, J = 7.6 Hz, 1 H), 5.91–5.82 (m, 1 H), 5.15, 4.92 (dd, J = 10.0, 17.2 Hz, 2 H), 4.79 (d, J = 4.8 Hz, 2 H).  
**13C NMR (100 MHz, CDCl₃):** δ = 134.7, 128.0, 127.7, 124.1, 121.0, 117.0, 116.1, 93.7, 35.5, 25.7, 16.4.

1-Allyl-2,3,6-tribromo-1H-indole  
Slightly yellow solid; mp 75.5–78.0 °C.  
**1H NMR (400 MHz, CDCl₃):** δ = 7.41 (s, 1 H), 7.37 (d, J = 8.8 Hz, 1 H), 7.28 (d, J = 8.4 Hz, 1 H), 5.92–5.83 (m, 1 H), 5.20, 4.94 (dd, J = 10.4, 17.2 Hz, 2 H), 4.76 (d, J = 4.8 Hz, 2 H).  
**13C NMR (100 MHz, CDCl₃):** δ = 136.3, 131.5, 126.0, 124.3, 120.2, 117.7, 116.8, 115.0, 112.9, 93.6, 48.1.

2-Bromo-1,3-dimethyl-1H-indole (5ga)  
Slightly yellow oil.

**1H NMR (400 MHz, CDCl₃):** δ = 7.49 (d, J = 8.0 Hz, 1 H), 7.22 (t, J = 8.4 Hz, 2 H), 7.18 (t, J = 8.0 Hz, 1 H), 3.69 (s, 3 H), 2.28 (s, 3 H).

2-Bromo-1,3-dimethyl-1H-indole (5ja)  
Slightly yellow oil.
\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 8.28 (d, J = 8.0 Hz, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 7.33–7.25 (m, 2 H), 2.84 (s, 3 H), 2.26 (s, 3 H). \]

\[ ^1\text{C NMR (100 MHz, CDCl}_3\text{): } \delta = 169.8, 137.0, 129.4, 125.2, 123.5, 111.8, 111.1, 107.5, 28.2, 10.5. \]

LRMS (EI): m/z (\%) = 253 (M\(^+\) – 22, 32), 251 (M\(^+\), 33), 211 (99), 210 (44), 209 (100), 208 (40), 130 (M\(^+\) – 42 – Br, 88).

1H NMR (400 MHz, CDCl3): \( \delta = 8.28 (s, 1 H), 7.74 (s, 1 H), 7.36 \) (d, \( J = 8.8 \) Hz, 1 H), 7.19 (d, \( J = 8.8 \) Hz, 1 H), 3.91 (s, 3 H), 3.80 (s, 3 H).

\[ ^1\text{C NMR (100 MHz, CDCl}_3\text{): } \delta = 165.0, 136.5, 135.9, 128.0, 125.7, 124.2, 115.6, 111.2, 106.4, 51.1, 33.6. \]

LRMS (EI, 70 eV): m/z (%) = 37 (M\(^+\)), 236 (100), 157 (M\(^+\) – Br, 12).

\[ \text{HRMS (EI): } m/z [M]^+ \text{ calecd } C_{11}H_{10}^{17}BrNO_2: 266.9895; \text{ found: } 266.9893. \]

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References


