

*Electronic Supplementary Information for*

## Regioselective copper-catalyzed chlorination and bromination of arenes with O<sub>2</sub> as the oxidant

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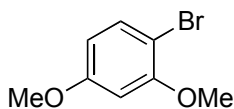
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### General Procedure for Catalytic Halogenation Reactions.

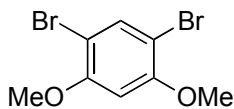
The amounts of CuCl<sub>2</sub> or CuBr<sub>2</sub> and LiCl or LiBr designated in Tables 1 and 2 were combined in disposable culture tubes, and the individual tubes were placed in a 48-well rack mounted on a Glas-Col pulsed shaker. The tubes were sealed, and the atmosphere within the tubes was purged with O<sub>2</sub> (1 atm). Solutions of each substrate (0.3 mmol) in AcOH (1 mL) were dispensed into the tubes, and the reaction mixtures were heated to the appropriate temperature while shaking for the times designated in Tables 1 and 2. When the reaction was complete, the reaction mixture was diluted with 10 mL water and 10 mL CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was washed with saturated Na<sub>2</sub>CO<sub>3</sub> (15 mL) and brine solution (15 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum. The residue was purified by column chromatography (see conditions for each product below).

### Product Characterization Data.



**1b**

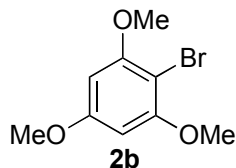
84% yield; oil (elution solvent – hexane:ether = 5:1). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 7.40 (d, J = 8.7 Hz, 1H), 6.48 (d, J = 2.8 Hz, 1H), 6.39 (dd, J = 8.9, 2.5 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 160.5, 156.8, 133.3, 106.1, 102.7, 100.2, 56.3, 55.8; HRMS (EI-EMM): Calcd for C<sub>8</sub>H<sub>9</sub>O<sub>2</sub>Br (<sup>79</sup>Br) *m/z* = 215.9781 found 215.9782.



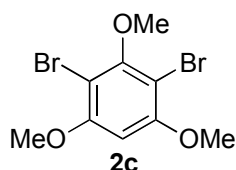
**1c**

100% yield; solid (purified without chromatography). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 7.65 (s, 1H), 6.48 (s, 1H), 3.90 (s, 6H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 156.4, 136.1, 102.6,

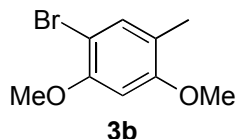
97.6, 56.7; melting point: 138-139°C; HRMS (EI-EMM): Calcd for C<sub>8</sub>H<sub>8</sub>O<sub>2</sub>Br<sub>2</sub> (<sup>79</sup>Br) *m/z* = 293.8886 found 293.8899.



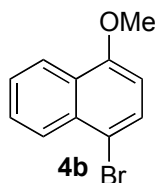
82% yield, solid (elution solvent – gradient, hexane:ethyl acetate = 10:1 →5:1) product obtained as inseparable mixture of **2b:2c** (82:8%). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 6.17 (s, 1H), 3.87 (s, 6H), 3.81 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 160.7, 157.6, 92.2, 91.8, 56.5, 55.7; HRMS (EI-EMM): Calcd for C<sub>9</sub>H<sub>11</sub>O<sub>2</sub>Br (<sup>79</sup>Br) *m/z* = 245.9887 found 245.9892.



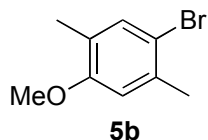
93% yield; solid (purified without chromatography). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 6.35 (s, 1H), 3.91 (s, 6H), 3.87 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 156.8, 155.9, 99.2, 93.4, 60.7, 56.8; melting point: 128-129°C; HRMS (EI-EMM): Calcd for C<sub>9</sub>H<sub>10</sub>O<sub>3</sub>Br<sub>2</sub> (<sup>79</sup>Br) *m/z* = 323.8992 found 323.8996.



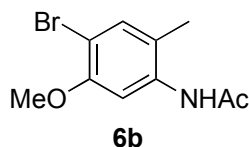
75% yield; solid (elution solvent – hexane:ethyl acetate =10:1). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 7.25 (d, J = 0.7 Hz, 1H), 6.44 (s, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 2.12 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 158.0, 154.9, 134.2, 120.5, 101.4, 96.7, 56.7, 55.8, 15.3; melting point: 89-90°C; HRMS (EI-EMM): Calcd for C<sub>9</sub>H<sub>11</sub>O<sub>2</sub>Br (<sup>79</sup>Br) *m/z* = 229.9937 found 229.9932.



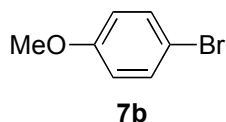
80% yield, oil (elution solvent – hexane:ethyl acetate = 100:1). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 8.27 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.9 (d, J = 8.8 Hz, 1H), 7.62-7.57 (m, 1H), 7.57-7.45 (m, 1H), 6.66 (d, J = 8.1 Hz, 1H), 3.97 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 155.5, 132.6, 129.7, 127.9, 127.0, 126.2, 122.6, 133.5, 104.7, 55.9; HRMS (EI-EMM): Calcd for C<sub>11</sub>H<sub>9</sub>BrO (<sup>79</sup>Br) *m/z* = 235.9832, found 235.9824.



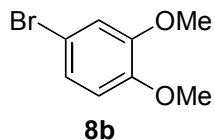
96% yield; oil (purified without chromatography).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.25 (s, 1H), 6.67 (s, 1H), 3.79 (s, 3H), 2.35 (s, 3H), 2.15 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  157.1, 135.9, 133.9, 126.3, 114.8, 112.7, 55.7, 23.1, 15.7; HRMS (EI-EMM): Calcd for  $\text{C}_9\text{H}_{11}\text{BrO}$  ( $^{79}\text{Br}$ )  $m/z = 213.9988$ , found 213.9981.



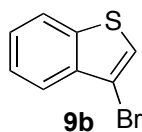
93% yield, solid (Additional purification conditions: The reaction mixture was diluted with 10 mL water and 10 mL  $\text{CH}_2\text{Cl}_2$ , and the phases were separated. Saturated  $\text{Na}_2\text{CO}_3$  (20 mL) was added to the aqueous layer, which was then extracted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with 15 mL of saturated  $\text{Na}_2\text{CO}_3$ , followed by brine solution. column elution solvent – gradient, hexane:ethyl acetate = 1:1  $\rightarrow$  1:2).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.69 (s, 1H), 7.32 (s, 1H), 6.97 (s, 1H), 3.87 (s, 3H), 2.21 (s, 3H), 2.18 (s, 3H);  $^{13}\text{C}$  NMR (500 Hz,  $\text{CDCl}_3$ ):  $\delta$  168.5, 154.6, 136.1, 134.3, 121.0, 106.7, 56.6, 24.9, 16.7; melting point: 194-195°C. HRMS (EI-EMM): Calcd for  $\text{C}_{10}\text{H}_{12}\text{BrNO}_2$  ( $^{79}\text{Br}$ )  $m/z = 257.0046$  found 257.0040.



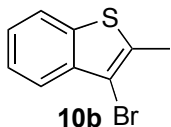
78% yield, oil (elution solvent – hexane: dichloromethane = 5:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.40-7.34 (m, 2H), 6.80-6.74 (m, 2H), 3.78 (s, 3H);  $^{13}\text{C}$  NMR (500 Hz,  $\text{CDCl}_3$ ):  $\delta$  158.9, 132.4, 115.9, 113.0, 55.6; HRMS (EI-EMM): Calcd for  $\text{C}_7\text{H}_7\text{BrO}$  ( $^{79}\text{Br}$ )  $m/z = 185.9675$  found 185.9681.



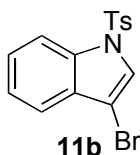
89% yield, oil (elution solvent – hexane:ethyl acetate = 20:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.03 (dd,  $J = 8.6, 2.4$  Hz, 1H), 6.98 (d,  $J = 2.4$  Hz, 1H), 6.73 (d,  $J = 8.6$  Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H);  $^{13}\text{C}$  NMR (500 Hz,  $\text{CDCl}_3$ ):  $\delta$  149.7, 148.3, 123.4, 114.8, 112.7, 112.5, 56.1, 56.0; HRMS (EI-EMM): Calcd for  $\text{C}_8\text{H}_9\text{BrO}_2$  ( $^{79}\text{Br}$ )  $m/z = 215.9781$  found 215.7980.



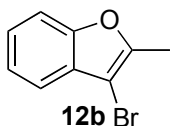
77% yield, oil (elution solvent – pentane).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.87-7.75 (m, 2H), 7.50-7.33 (m, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  138.8, 137.7, 125.5, 125.2, 123.7, 123.4, 122.9, 111.1, 107.9; HRMS (EI-EMM): Calcd for  $\text{C}_8\text{H}_5\text{SBr}$  ( $^{79}\text{Br}$ )  $m/z$  = 211.9290 found 211.9291.



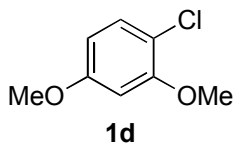
63% yield, solid (elution solvent – hexane).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.73-7.67 (m, 2H), 7.39 (td,  $J$  = 7.6, 1.0 Hz, 1H), 7.31 (td,  $J$  = 7.6, 1.2 Hz, 1H), 2.54 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  138.6, 137.4, 135.4, 125.1, 124.9, 122.8, 122.3, 106.8, 15.7; melting point: 40-42°C; HRMS (EI-EMM): Calcd for  $\text{C}_9\text{H}_7\text{SBr}$  ( $^{79}\text{Br}$ )  $m/z$  = 225.9447 found 225.9444.



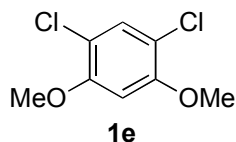
66% yield, solid (elution solvent – hexane:ethyl acetate = 20:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.99 (d,  $J$  = 8.1 Hz, 1H), 7.76 (d,  $J$  = 8.1 Hz, 2H), 7.62 (s, 1H), 7.50-7.42 (m, 1H), 7.41-7.23 (m, 2H), 7.20 (d,  $J$  = 8.7 Hz, 2H), 2.31 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  145.6, 135.1, 134.5, 130.2, 130.0, 127.1, 126.0, 125.0, 124.1, 120.3, 113.8, 99.2, 21.8; melting point: 122-123°C; HRMS (EI-EMM): Calcd for  $\text{C}_{15}\text{H}_{12}\text{NBrO}_2\text{S}$  ( $^{79}\text{Br}$ )  $m/z$  = 348.9767 found 348.9782.



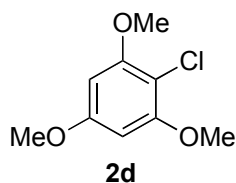
48% yield, oil (elution solvent – hexane:ethyl acetate = 200:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.46-7.31 (m, 2H), 7.30-7.17 (m, 2H), 2.47 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  153.7, 152.3, 128.6, 124.6, 123.3, 119.2, 111.2, 94.7, 12.6; HRMS (EI-EMM): Calcd for  $\text{C}_9\text{H}_7\text{OBr}$  ( $^{79}\text{Br}$ )  $m/z$  = 209.9679 found 209.9675.



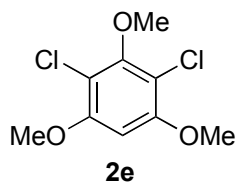
77% yield, oil (condition: hexane:ether = 2:1).  $^1\text{H}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.24 (d,  $J$  = 8.7 Hz, 1H), 6.50 (d,  $J$  = 2.9 Hz, 1H), 6.43 (dd,  $J$  = 8.9, 2.7 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  159.6, 155.8, 130.2, 114.2, 105.3, 100.1, 56.1, 55.7; HRMS (EI-EMM): Calcd for  $\text{C}_8\text{H}_9\text{ClO}_2$  ( $^{35}\text{Cl}$ )  $m/z$  = 172.0286 found 172.0287.



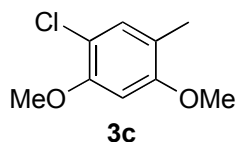
88% yield, solid (elution solvent – hexane:ether = 1:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ),  $\delta$  7.34 (s, 1H), 6.524 (s, 1H), 3.91 (s, 6H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  154.8, 130.8, 114.3, 98.0, 56.8; melting point: 119-121°C; HRMS (EI-EMM): Calcd for  $\text{C}_8\text{H}_8\text{Cl}_2\text{O}$  ( $^{35}\text{Cl}$ )  $m/z = 205.9896$  found 205.9897.



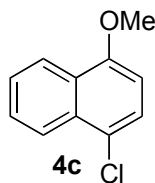
76% yield, solid (elution solvent – hexane:ethyl acetate = 4:1) product obtained as inseparable mixture of **2d:2e** (76:12%).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ),  $\delta$  6.18 (s, 2H), 3.88 (s, 6H), 3.81 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  159.6, 156.8, 91.8, 56.5, 55.7; HRMS (EI-EMM): Calcd for  $\text{C}_9\text{H}_{11}\text{ClO}_3$  ( $^{35}\text{Cl}$ )  $m/z = 202.0392$  found 202.0385.



90% yield, solid (elution solvent – hexane:ethyl acetate = 20:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  6.37 (s, 1H), 3.91 (s, 6H), 3.89 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  155.0, 154.1, 109.9, 93.5, 60.8, 56.7; melting point: 126-127°C; HRMS (EI-EMM): Calcd for  $\text{C}_9\text{H}_{10}\text{Cl}_2\text{O}_3$  ( $^{35}\text{Cl}$ )  $m/z = 236.0002$  found 235.9995.

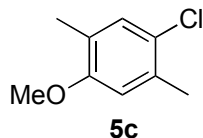


75% yield, oil (elution solvent – hexane:ethyl acetate = 20:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.09 (s, 1H), 6.46 (s, 1H), 3.89 (s, 3H), 3.83 (s, 3H), 2.12 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  157.2, 153.8, 131.4, 119.8, 113.0, 96.8, 56.6, 55.9, 15.3; HRMS (EI-EMM): Calcd for  $\text{C}_9\text{H}_{11}\text{ClO}_2$  ( $^{35}\text{Cl}$ )  $m/z = 186.0443$  found 186.0443

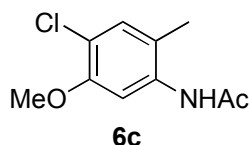


80% yield, oil (elution solvent – hexane:ethyl acetate = 100:1).  $^1\text{H}$  NMR: (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  7.48 (m, 1H), 7.44 (d,  $J = 8.2$  Hz, 1H), 6.69 (d,  $J = 7.9$  Hz, 1H), 3.97 (s, 3H);  $^{13}\text{C}$  NMR (300 Hz,  $\text{CDCl}_3$ ):  $\delta$  154.7, 131.5, 127.7, 126.8, 126.1, 125.9, 124.4, 123.4,

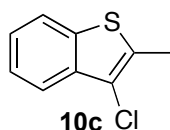
122.6, 104.0, 55.9; HRMS (EI-EMM): Calcd for C<sub>11</sub>H<sub>9</sub>ClO (<sup>35</sup>Cl) *m/z* = 192.03337 found 192.0336.



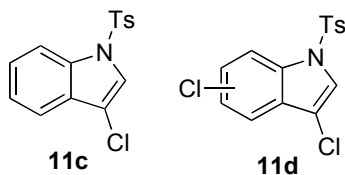
76% yield, oil (elution solvent – hexane: ethyl acetate =3:1), get oil. <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 7.08 (s, 1H), 6.66 (s, 1H), 3.79 (s, 3H), 2.33 (s, 3H), 2.15 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 156.4, 133.9, 130.8, 125.9, 124.9, 112.7, 55.7, 20.2, 15.8; HRMS (EI-EMM): Calcd for C<sub>9</sub>H<sub>11</sub>ClO (<sup>35</sup>Cl) *m/z* = 170.0493, found 170.0494.



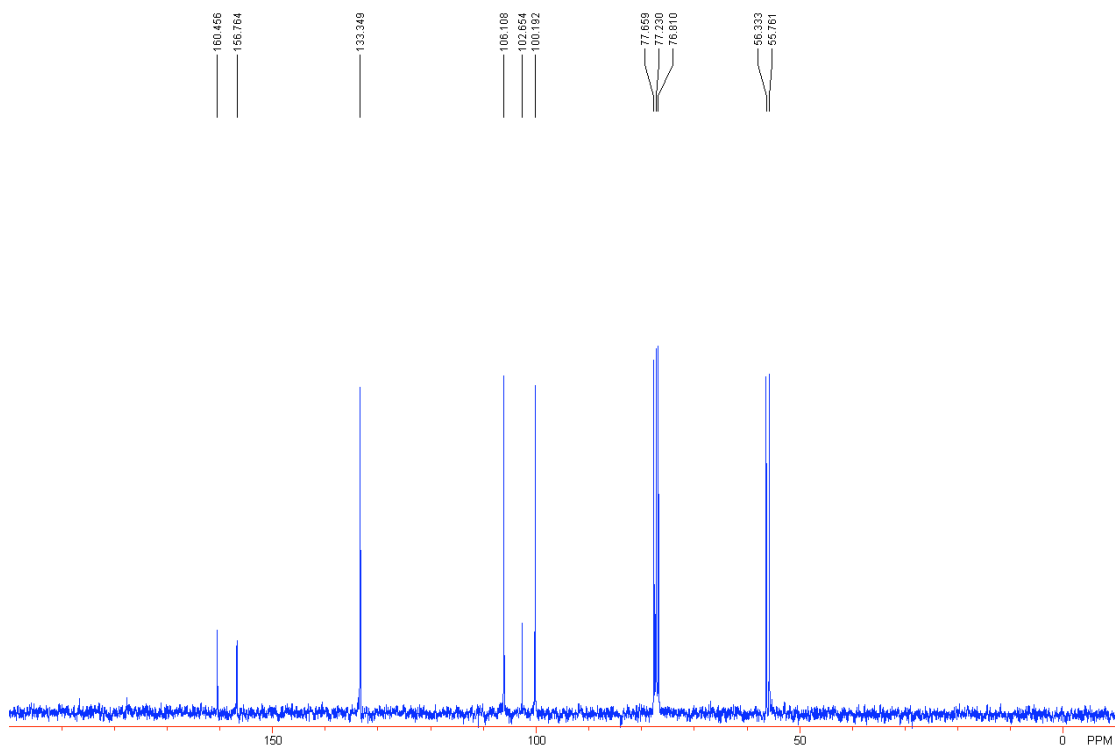
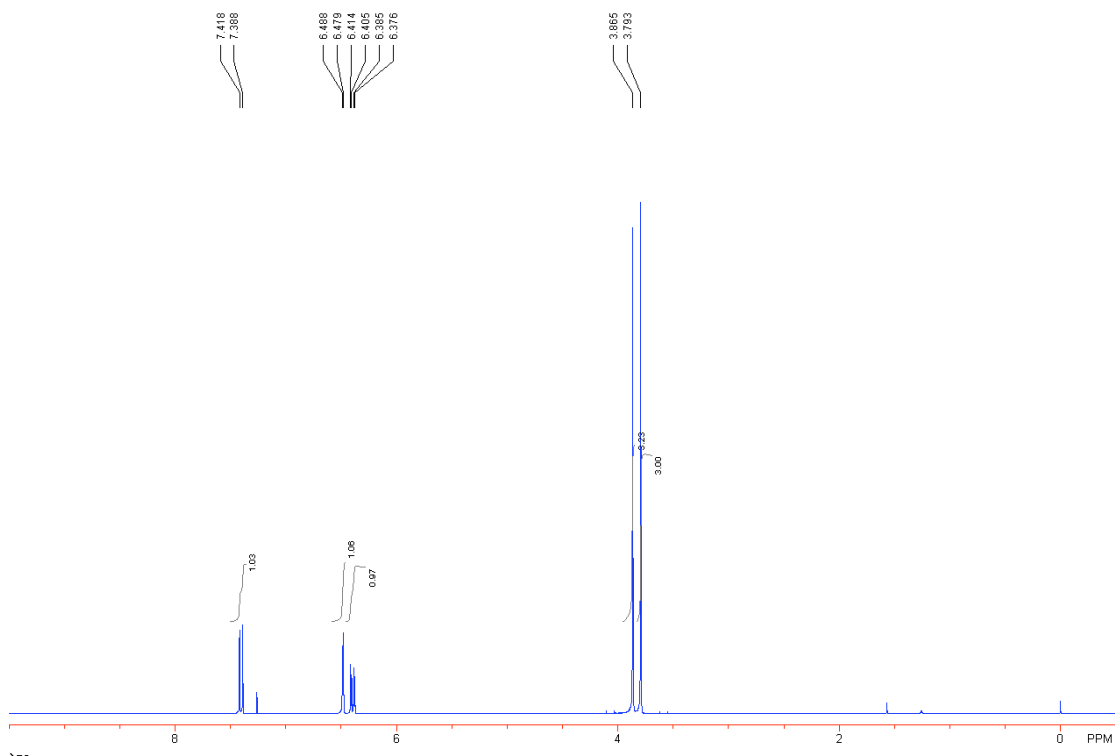
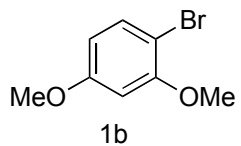
73% yield, solid (Additional purification conditions: The reaction mixture was diluted with 10 mL water and 10 mL CH<sub>2</sub>Cl<sub>2</sub>, and the phases were separated. Saturated Na<sub>2</sub>CO<sub>3</sub> (20 mL) was added to the aqueous layer, which was then extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was washed with 15 mL of saturated Na<sub>2</sub>CO<sub>3</sub>, followed by brine solution. column elution solvent – gradient, hexane:ethyl acetate =1:1 → 1:2) <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>), δ 7.66 (s, 1H), 7.15 (s, 1H), 7.02 (s, 1H), 3.87 (s, 3H), 2.21 (s, 3H), 2.16 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 168.8, 153.7, 135.3, 131.4, 121.1, 118.0, 107.2, 56.5, 24.7, 16.8; HRMS (EI-EMM): Calcd for C<sub>10</sub>H<sub>12</sub>ClNO<sub>2</sub> (<sup>35</sup>Cl) *m/z* = 213.0552 found 213.0558.

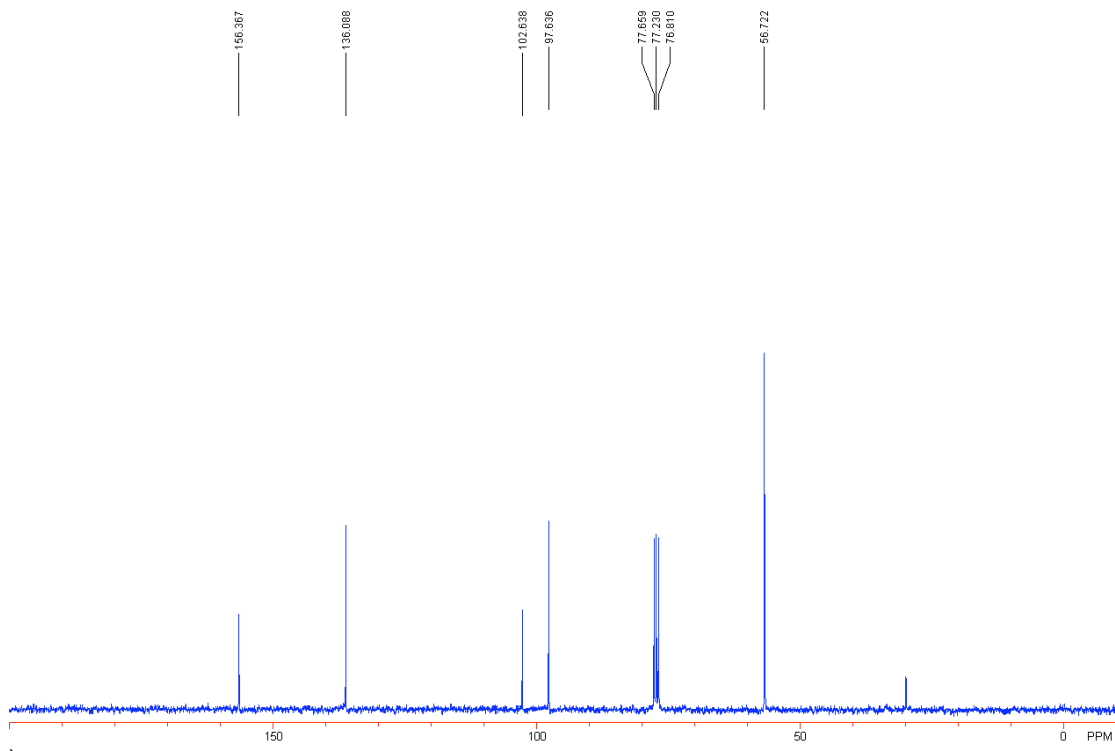
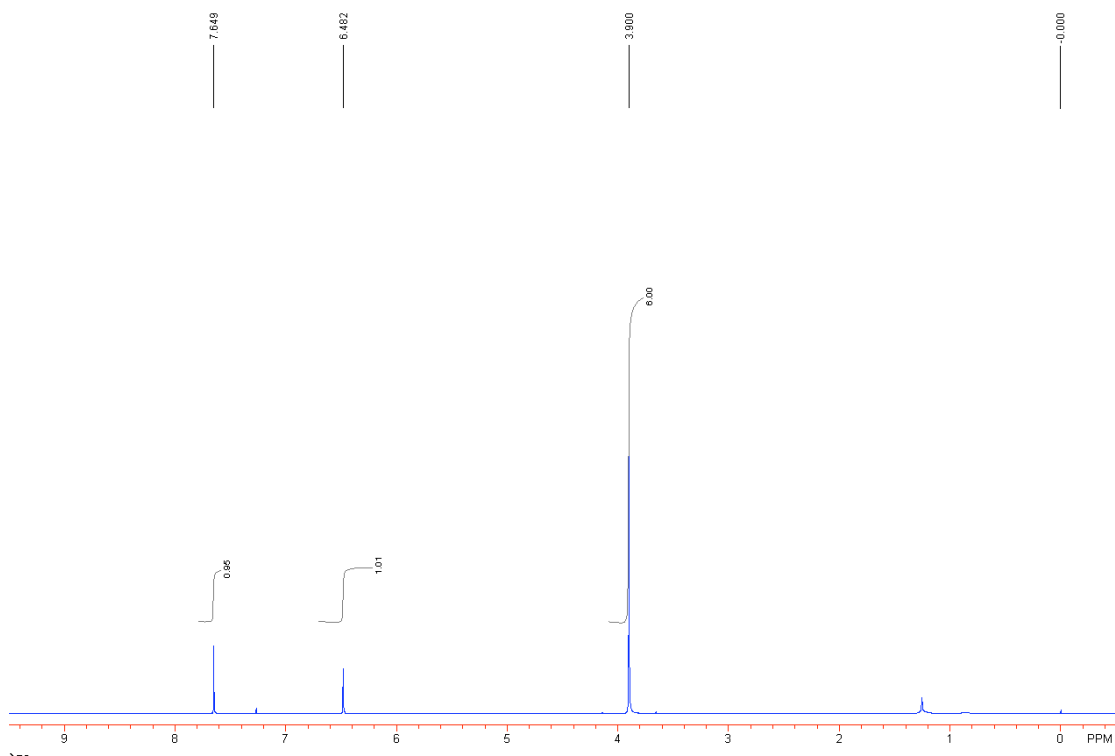
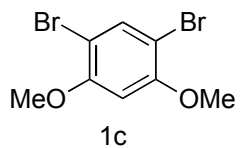


63% yield, oil (elution solvent – hexane). <sup>1</sup>H NMR: (300 Hz, CDCl<sub>3</sub>): δ 7.72 (d, J = 8.5 Hz, 2H), 7.40 (td, J = 7.6, 1.0 Hz, 1H), 7.32 (td, J = 7.6, 1.2 Hz, 1H), 2.54 (s, 3H); <sup>13</sup>C NMR (300 Hz, CDCl<sub>3</sub>): δ 137.2, 136.6, 133.5, 124.9, 124.9, 122.4, 121.4, 111.0, 14.0; HRMS (EI-EMM): Calcd for C<sub>9</sub>H<sub>7</sub>SCl (<sup>35</sup>Cl) *m/z* = 181.9952 found 181.9951.

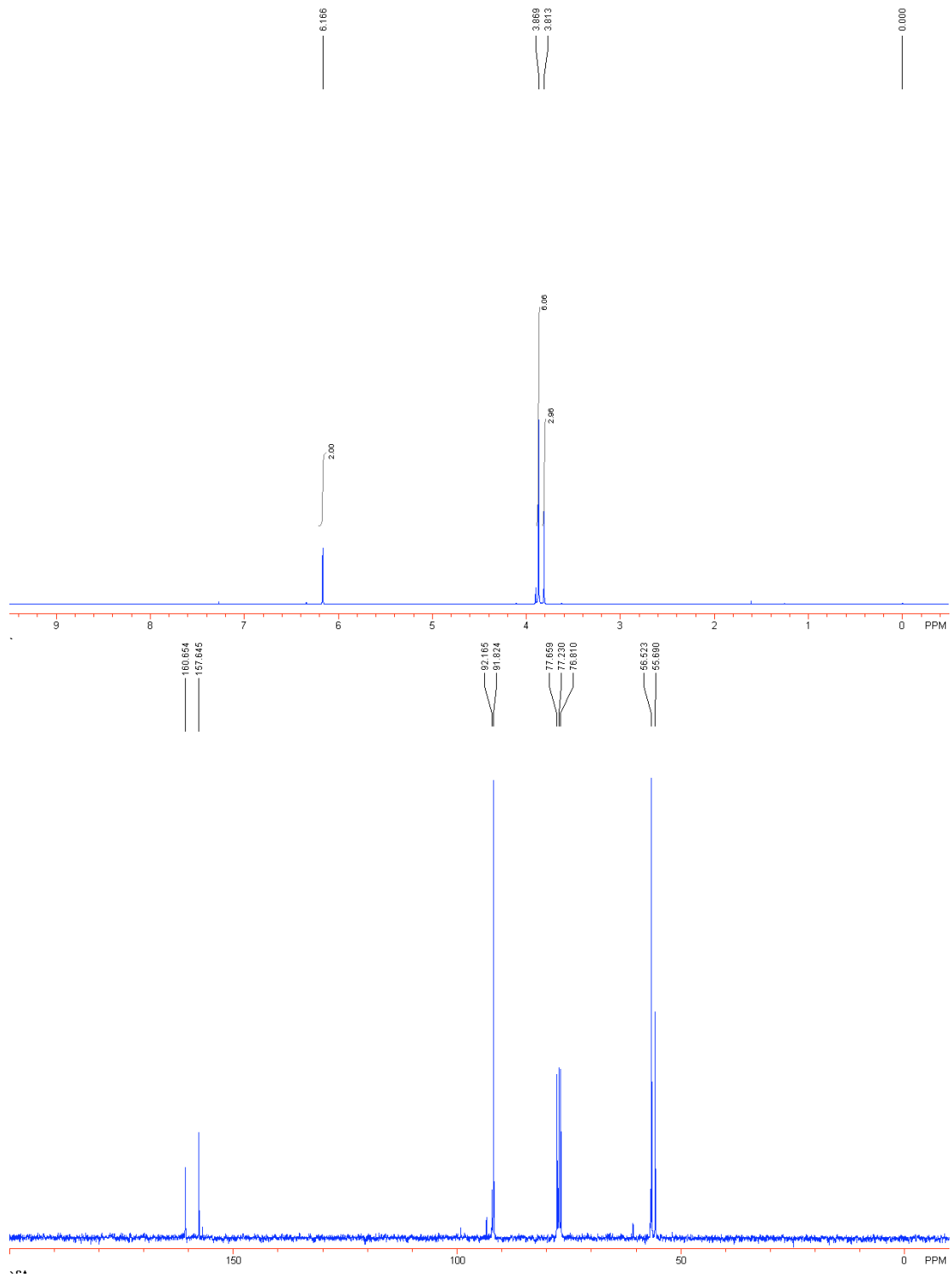
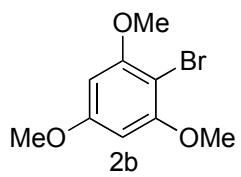


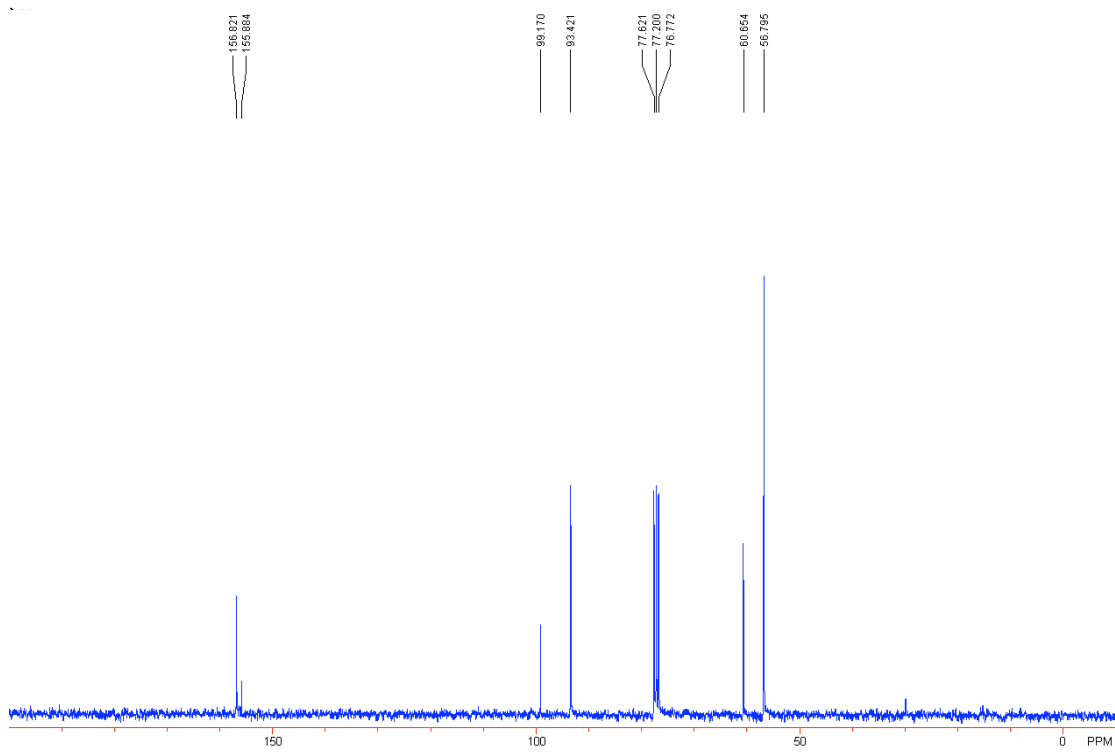
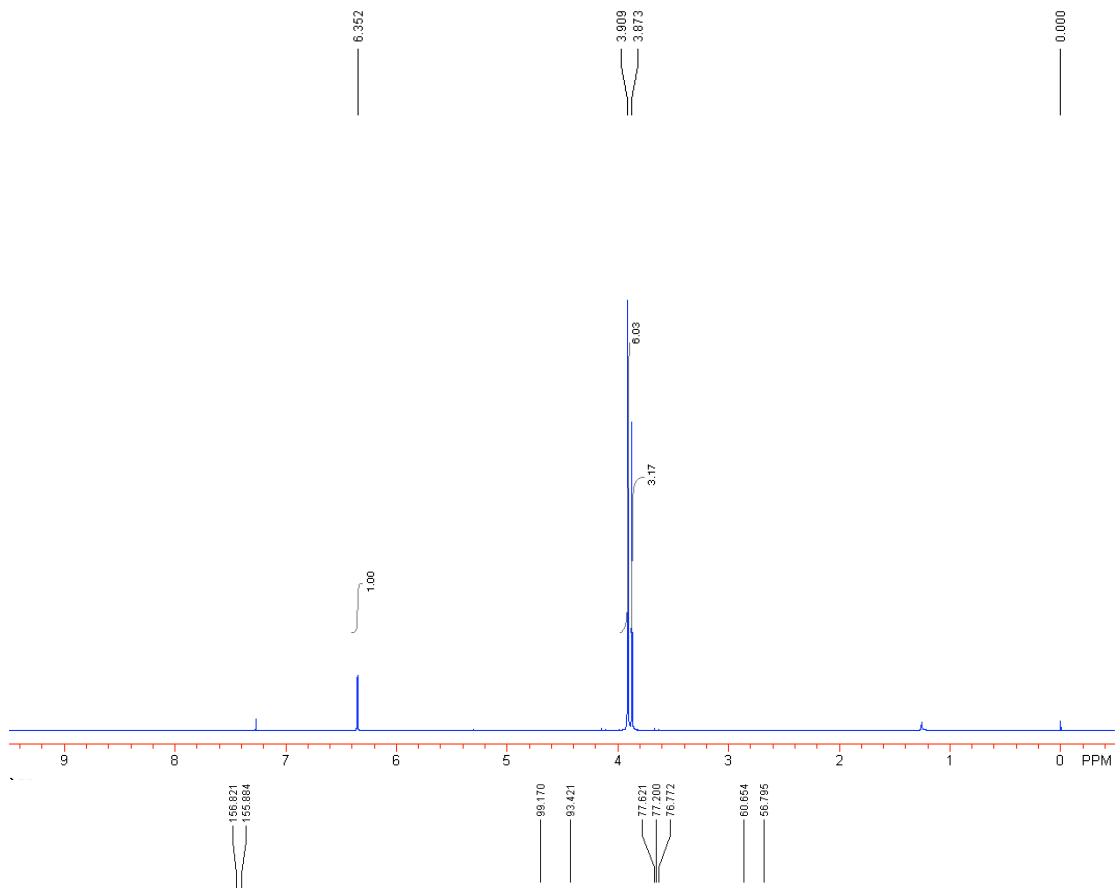
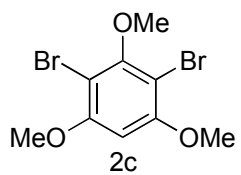
Isolated as a 7/45/15% mixture of **11a**, **11c**, and **11d** (elution solvent – hexane:ethyl acetate = 20:1). **11c**: HRMS (EI-EMM): Calcd for C<sub>15</sub>H<sub>12</sub>ClNO<sub>2</sub>S (<sup>35</sup>Cl) *m/z* = 305.0272 found 305.0276.

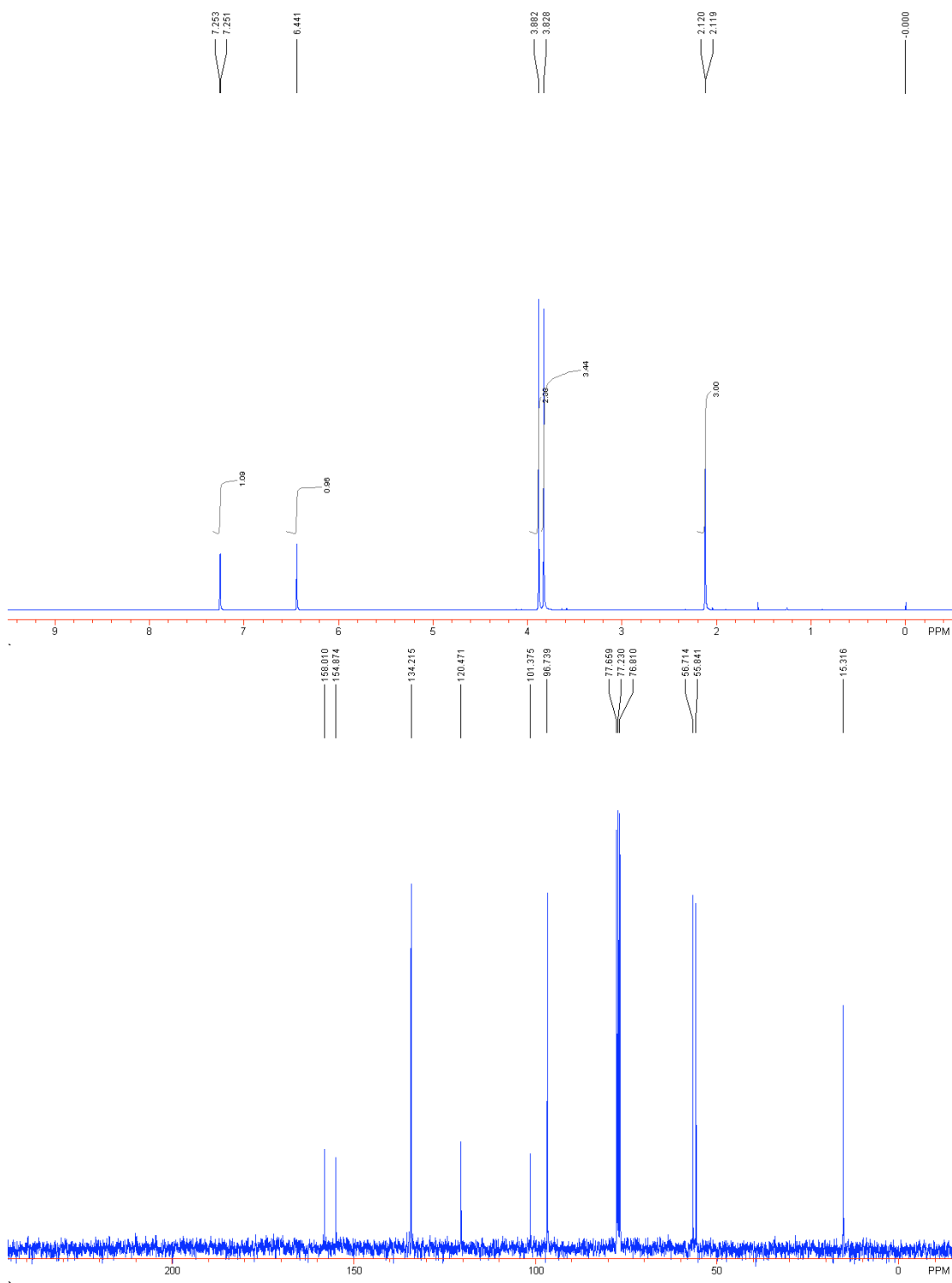
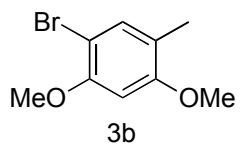


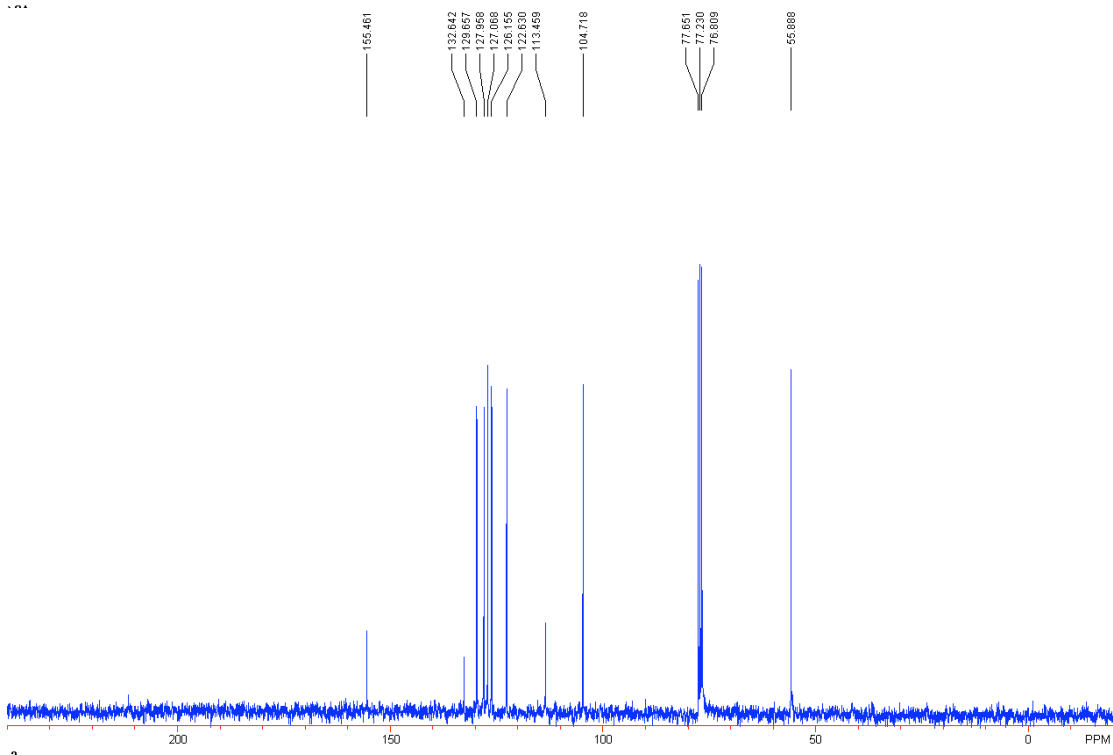
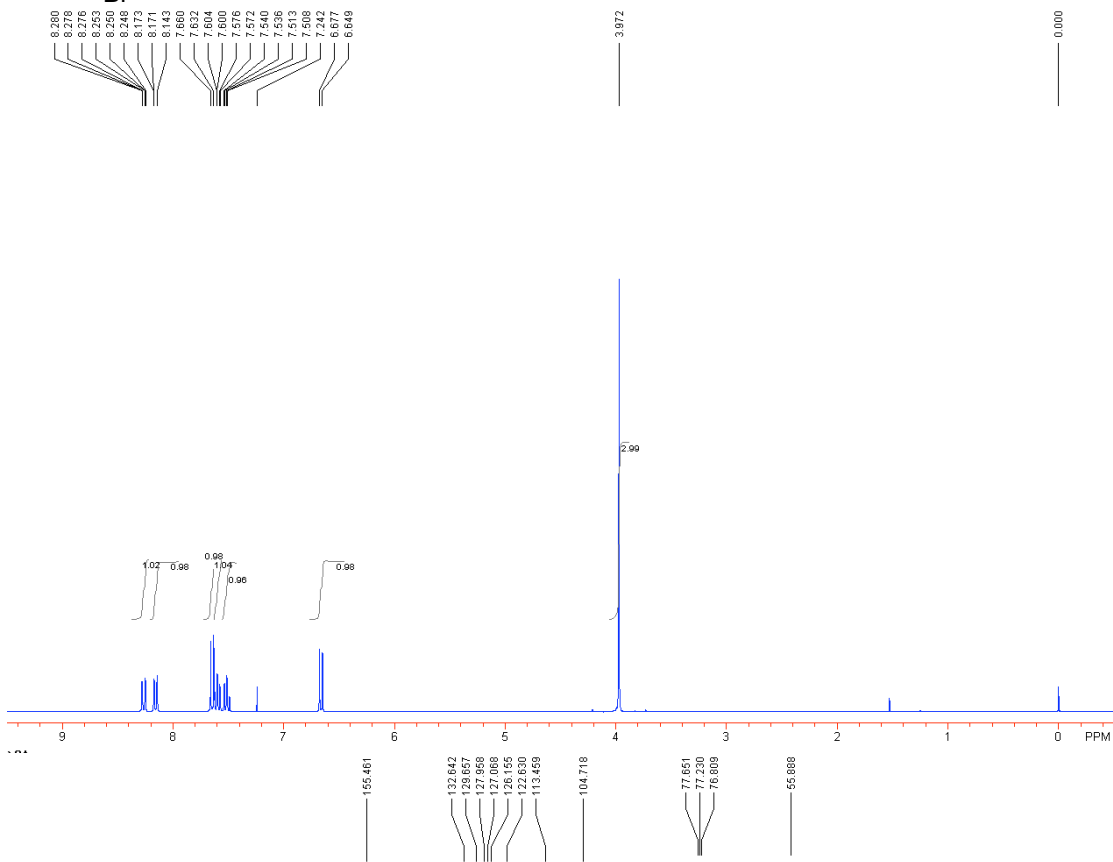
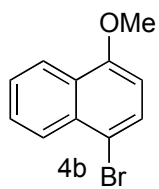


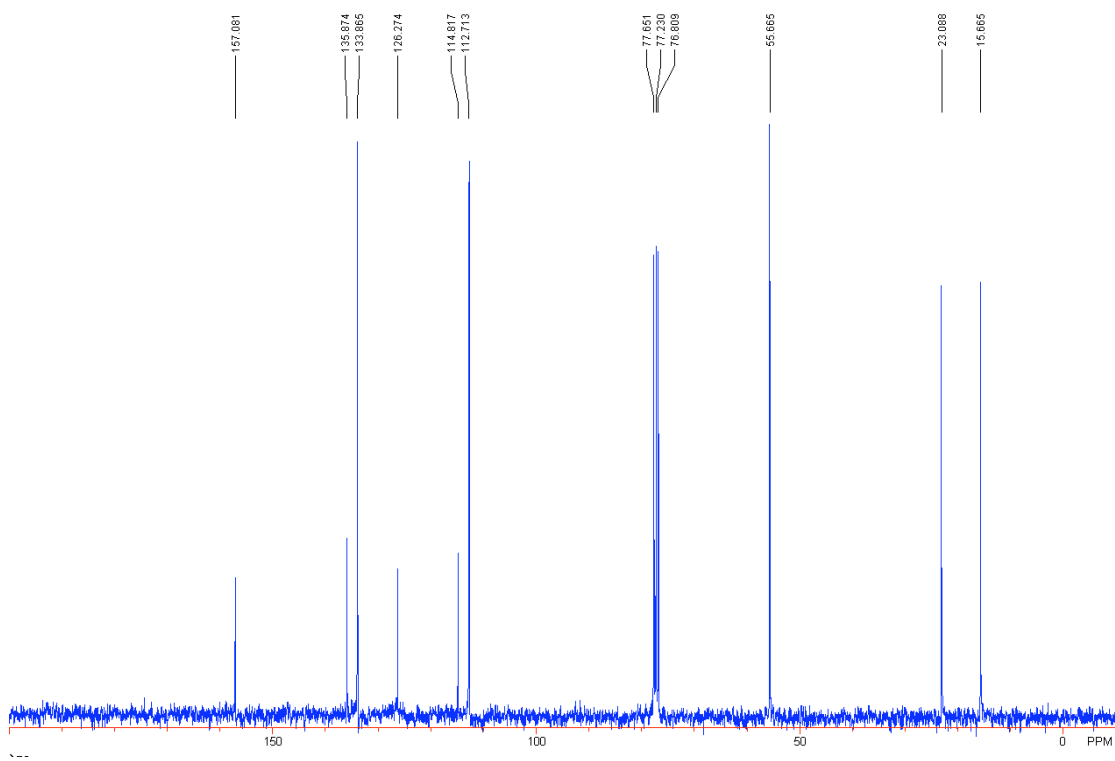
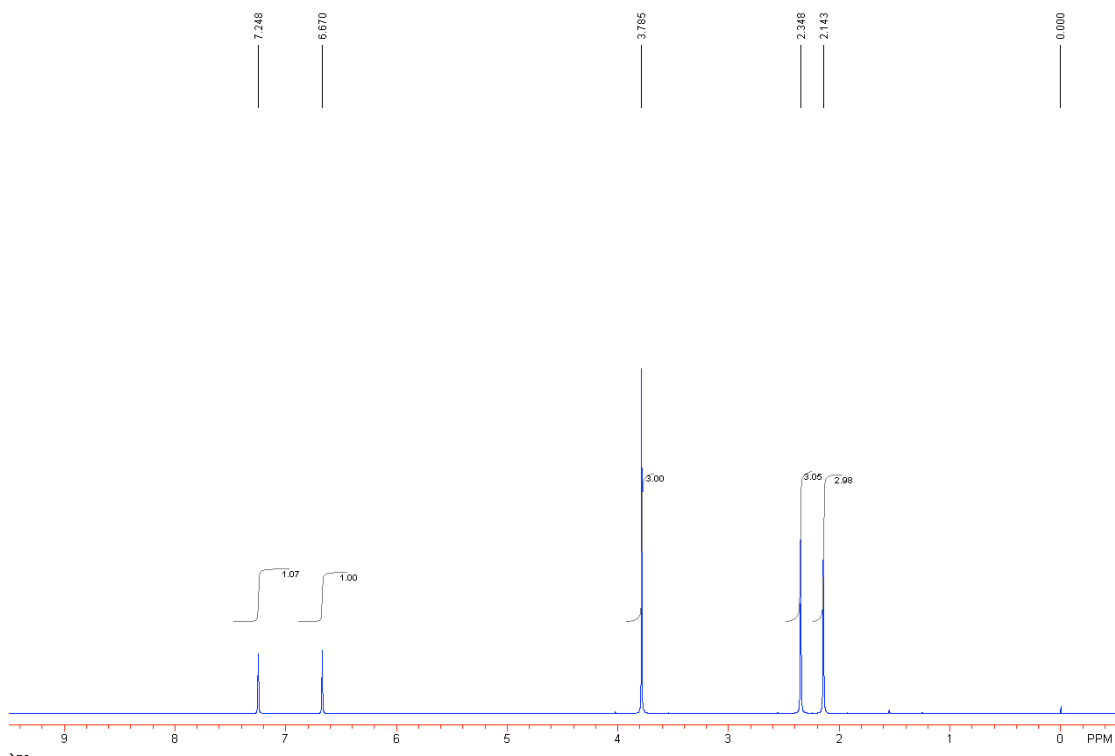
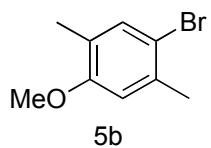


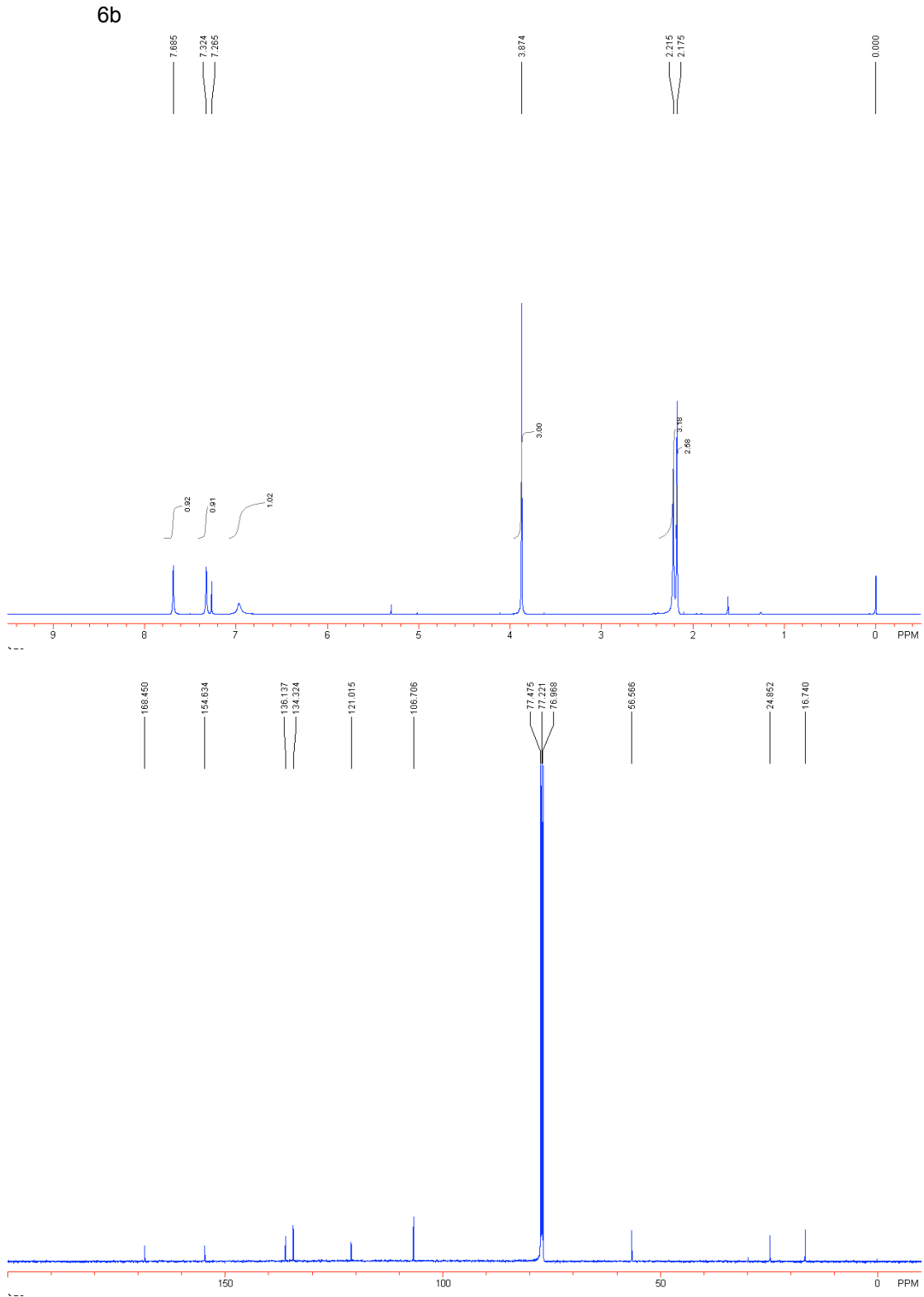
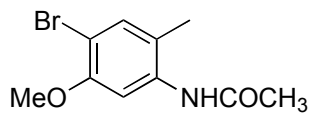


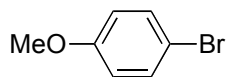












7b

