

Supporting Information

Practical, Mild and Efficient Electrophilic Bromination of Phenols by a New I(III)-based reagent: The PIDA-AlBr₃ System

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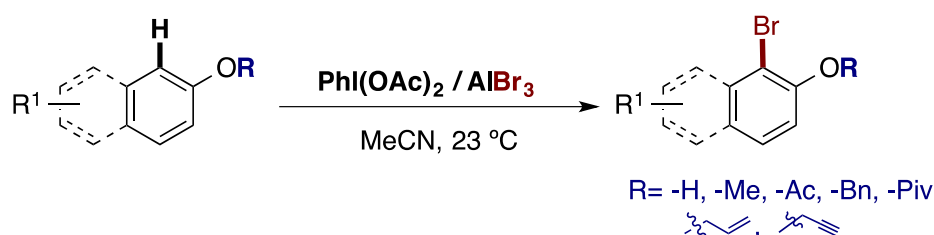
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1. General Information

Unless otherwise specified, all commercial materials were used as received without further purification. Anhydrous solvents were purchased from Sigma Aldrich in SureSeal® bottles. Column chromatography was performed using silica gel of size 100-200 and 230-400 mesh (Sigma aldrich). Thin layer chromatography was performed with TLC Silica gel 60 F256 plates, and visualization was effected with short wavelength UV light (254 nm). Compounds were characterized using ¹H-NMR, ¹³C-NMR. (Copies of ¹H-NMR and ¹³C-NMR spectra are provided for all of the compounds). Data of known compounds were compared with existing literature characterization data and the references are given. ¹H and ¹³C NMR spectra were recorded with 500 MHz and Bruker advance 400 MHz instruments using deuterated solvents purchased from Sigma Aldrich like CDCl₃. ¹H spectra were referenced with tetramethylsilane (TMS, 0.0 ppm) or chloroform (CDCl₃, 7.26 ppm) and are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration. Chemical shifts of the ¹³C NMR spectra were measured relative to CDCl₃ (δ = 77.16 ppm). All the starting materials were synthesized according to reported procedures in the literature.

2. Synthesis of brominated phenols and phenols-ethers

General procedure A



A 25 mL oven-dried round bottom flask equipped with a magnetic stirrer bar was charged with PIDA (diacetoxy)iodobenzene (1.2 equiv) and acetonitrile (0.15 M) at 25 °C. After dissolving and obtaining homogeneous mixture, AlBr_3 (2.4 equiv.) was added and stirred for 10 min. Then naphthol or its corresponding methyl-ether derivative (1 equiv) was added and stirred at 25 °C until fully consumption of the starting material (usually 30 min to 1 h). To quench the reaction, EtOAc (5 mL) was added and concentrated to *vacuo*. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

General procedure B

A 25 mL oven-dried round bottom flask equipped with a magnetic stirrer bar was charged with PIFA [bis(trifluoroacetoxy)iodo]benzene] (1.2 equiv) and acetonitrile (0.15 M) at 25 °C. After dissolving and obtaining homogeneous mixture, AlBr_3 (2.4 equiv) was added and stirred for 10 min. Then naphthol or its corresponding methyl-ether derivative (1 equiv) was added and stirred at 25 °C until fully consumption of the starting material (usually 30 min to 1 h). To quench the reaction, EtOAc (5 mL) was added and concentrated to *vacuo*. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

General procedure C

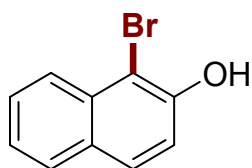
A 25 mL oven-dried round bottom flask equipped with a magnetic stirrer bar was charged with PIDA (1.2 equiv) and acetonitrile (0.15 M) at 25 °C. After dissolving and obtaining homogeneous mixture, AlBr_3 (2.4 equiv) was added and stirred for 10 min. Then the solution was cooled to 0 °C before the corresponding phenol or the methyl-

ether derivative (1 equiv) was added at this temperature. Afterwards the reaction mixture was allowed to reach 25 °C and stirred until fully consumption of the starting material (usually 30 min to 1 h). To quench the reaction, EtOAc (5 mL) was added and concentrated to *vacuo*. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

General procedure D

A 25 mL oven-dried round bottom flask equipped with a magnetic stirrer bar was charged with PIDA (1.2 equiv) and acetonitrile (0.15 M) at 25 °C. After dissolving and obtaining homogeneous mixture, AlBr₃ (2.4 equiv) was added and stirred for 10 min. Then the solution was heated to 80 °C before the corresponding phenol or the methyl-ether derivative (1 equiv) was added at this temperature. The reaction was stirred until fully consumption of the starting material (usually 30 min to 1 h). To quench the reaction, EtOAc (5 mL) was added and concentrated to *vacuo*. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

1-bromonaphthalen-2-ol (1)



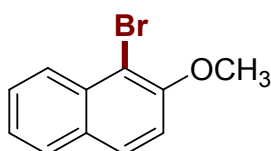
The following compound was obtained according to the general procedure A and B, by using 2-naphthol in 93% (procedure A) or 84% (procedure B) of yield as white solid. The spectroscopic data for this compound match with those previously described.¹

¹H NMR (500 MHz, CDCl₃) δ 7.90 (d, *J* = 8.5 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 1H), 5.83 (s, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 150.6, 132.4, 129.8, 129.4, 128.3, 127.9, 125.4, 124.2, 117.2, 106.2. The spectroscopic data for this compound match with those previously described.¹

Gram scale reaction. A 100 mL dry round bottom flask, was charged with PIDA (diacetoxy)iodobenzene (2.68 g, 1.2 equiv) and acetonitrile (0.15 M) at 25 °C. After dissolving and obtaining homogeneous mixture, AlBr₃ (4.4 g, 2.4 equiv) was added and stirring for 10 min. Then 2-naphthol (1.00 g, 1 equiv) was added and stirred at 25 °C by 30 min. During this time it was observed the fully consumption of the starting material. To quench the reaction, EtOAc (5 mL) was added and concentrated to *vacuo*. Purification was carried out by column chromatography with 5% EtOAc-Hexanes system. 1-bromo-2-naphthol (1.40 g) 91% yield was obtained as white solid.

1-bromo-2-methoxynaphthalene (2)

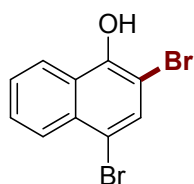


The following compound was obtained according to the general procedure A and B, by using 2-methoxynaphthalene in 88% (procedure A) or 86% (procedure B) of yield as white solid. The spectroscopic data for this compound match with those previously described.²

^1H NMR (500 MHz, CDCl_3) δ 8.23 (d, $J = 8.6$ Hz, 1H), 7.83 (d, $J = 9.0$ Hz, 1H), 7.79 (d, $J = 8.2$ Hz, 1H), 7.57 (t, $J = 7.7$ Hz, 1H), 7.40 (t, $J = 7.5$ Hz, 1H), 7.29 (d, $J = 9.0$ Hz, 1H), 4.04 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.9, 133.2, 129.9, 129.1, 128.1, 127.8, 126.2, 124.4, 113.7, 108.8, 57.2.

2,4-dibromonaphthalen-1-ol (3)

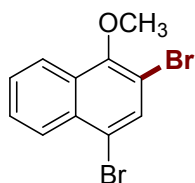


The following compound was obtained according to the general procedure A, by using 4-bromonaphthalen-1-ol in 92% of yield as white solid. The spectroscopic data for this compound match with those previously described.³

^1H NMR (500 MHz, CDCl_3) δ 8.26 (dd, $J = 8.4, 0.6$ Hz, 1H), 8.14 (d, $J = 8.5$ Hz, 1H), 7.80 (s, 1H), 7.63 (ddd, $J = 8.4, 6.9, 1.3$ Hz, 1H), 7.57 (ddd, $J = 8.1, 6.9, 1.2$ Hz, 1H), 5.96 (s, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 148.2, 131.9, 131.1, 128.1, 127.1, 126.9, 125.1, 122.8, 113.3, 103.1.

2,4-dibromo-1-methoxynaphthalene (4)

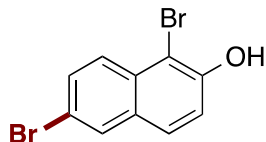


The following compound was obtained according to the general procedure A, by using 4-bromonaphthalen-1-ol in 86% of yield as white solid. The spectroscopic data for this compound match with those previously described.⁴

^1H NMR (500 MHz, CDCl_3) δ 8.18 (d, $J = 7.8$ Hz, 1H), 8.14 (d, $J = 8.5$ Hz, 1H), 7.92 (s, 1H), 7.69-7.52 (m, 2H), 4.00 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.1, 133.0, 132.2, 129.7, 127.8, 127.6, 127.5, 122.5, 118.0, 112.1, 61.6.

1,6-dibromonaphthalen-2-ol (5)

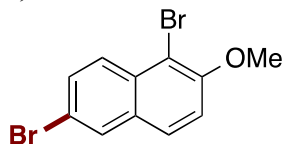


The following compound was obtained according to the general procedure A, by using 6-bromonaphthalen-2-ol in 94% as white solid. The spectroscopic data for this compound match with those previously described.⁵

^1H NMR (500 MHz, CDCl_3) δ 7.85 (s, 1H), 7.81 (d, $J = 9.0$ Hz, 1H), 7.58-7.51 (m, 2H), 7.19 (d, $J = 8.7$ Hz, 1H), 5.85 (s, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 151.0, 131.8, 131.1, 130.7, 130.2, 128.5, 127.3, 118.4, 118.1, 106.2.

1,6-dibromo-2-methoxynaphthalene (6)

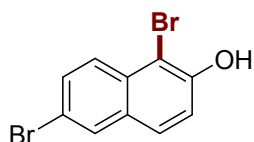


The following compound was obtained according to the general procedure A, by using 6-bromo-2-methoxynaphthalene in 86% as white solid. The spectroscopic data for this compound match with those previously described.⁵

^1H NMR (500 MHz, CDCl_3) δ 8.00 (d, $J = 9.1$ Hz, 1H), 7.85 (s, 1H), 7.62 (d, $J = 9.0$ Hz, 1H), 7.52 (d, $J = 11.0$ Hz, 1H), 7.19 (d, $J = 8.9$ Hz, 1H), 3.94 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.1, 131.8, 131.0, 130.7, 129.9, 128.19, 128.14, 118.3, 114.6, 108.8, 57.1.

1,6-dibromonaphthalen-2-ol (7)

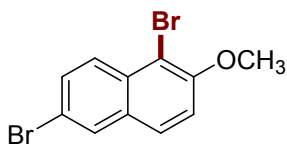


The following compound was obtained according to the general procedure A and B, by using 2-bromonaphthalen-2-ol in 96% (Procedure A) or 92% (procedure B) of yield as white solid. The spectroscopic data for this compound match with those previously described.⁵

¹H NMR (500 MHz, CDCl₃) δ 7.85 (s, 1H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.58-7.51 (m, 2H), 7.19 (d, *J* = 8.7 Hz, 1H), 5.85 (s, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 151.0, 131.8, 131.1, 130.7, 130.2, 128.5, 127.3, 118.4, 118.1, 106.2.

1,6-dibromo-2-methoxynaphthalene (8)

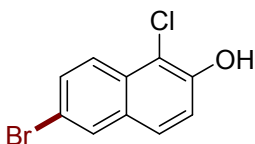


The following compound was obtained according to the general procedure A and B, by using 1-bromo-2-methoxynaphthalene in 88% (Procedure A) or 82% (procedure B) of yield as white solid. The spectroscopic data for this compound match with those previously described.⁵

¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, *J* = 9.1 Hz, 1H), 7.85 (s, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.52 (d, *J* = 11.0 Hz, 1H), 7.19 (d, *J* = 8.9 Hz, 1H), 3.94 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 154.1, 131.8, 131.0, 130.7, 129.9, 128.19, 128.14, 118.3, 114.6, 108.8, 57.1.

6-bromo-1-chloronaphthalen-2-ol (9)

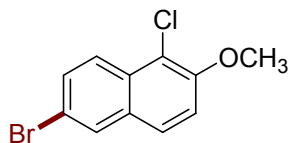


The following compound was obtained according to the general procedure A, by using 1-chloronaphthalen-2-ol in 90% as white solid. The spectroscopic data for this compound match with those previously described.⁶

¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, *J* = 9.9 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 5.84 (s, 1H).

^{13}C NMR (101 MHz, CDCl_3) δ 149.7, 130.9, 130.5, 130.2, 129.7, 127.6, 124.7, 118.5, 118.1, 113.6.

6-bromo-1-chloro-2-methoxynaphthalene (10)

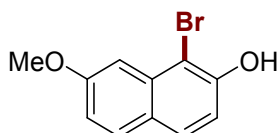


The following compound was obtained according to the general procedure A, by using 1-chloro-2-methoxynaphthalene in 88% as white solid. The spectroscopic data for this compound match with those previously described.⁶

^1H NMR (500 MHz, CDCl_3) δ 8.02 (d, $J = 9.1$ Hz, 1H), 7.88 (d, $J = 1.8$ Hz, 1H), 7.62 (d, $J = 9.0$ Hz, 1H), 7.55 (dd, $J = 9.1, 1.9$ Hz, 1H), 7.25 (d, $J = 9.1$ Hz, 1H), 3.97 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.0, 130.9, 130.6, 130.6, 130.0, 127.1, 125.5, 118.3, 117.3, 114.8, 57.1.

1-Bromo-7-methoxynaphthalen-2-ol (11)

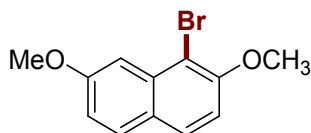


The following compound was obtained according to the general procedure A, by using 7-methoxynaphthalen-2-ol in 54% of yield as white solid.⁷

^1H NMR (500 MHz, CDCl_3) δ 7.60 (dd, $J = 9.2$ Hz, 2H), 7.26 (d, $J = 2.5$ Hz, 1H), 7.06 (d, $J = 8.7$ Hz, 1H), 6.98 (dd, $J = 8.9, 2.5$ Hz, 1H), 5.89 (s, 1H), 3.91 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 159.6, 150.9, 133.8, 129.9, 129.1, 124.9, 116.4, 114.5, 105.3, 104.4, 55.40. The spectroscopic data for this compound match with those previously described.⁶

1-Bromo-2,7-methoxynaphthalen (12)

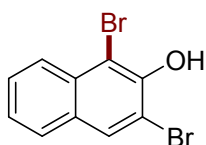


The following compound was obtained according to the general procedure A, by using 2,7-methoxynaphthalen in 84% as white solid. The spectroscopic data for this compound match with those previously described.⁸

¹H NMR (500 MHz, CDCl₃) δ 7.73 (d, *J* = 8.9 Hz, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.50 (s, 1H), 7.12 (d, *J* = 8.9 Hz, 1H), 7.04 (dd, *J* = 8.9, 2.5 Hz, 1H), 4.02 (s, 3H), 3.97 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 159.4, 154.3, 134.6, 129.7, 128.6, 125.2, 117.3, 110.8, 107.5, 104.4, 56.9, 55.3.

1,3-dibromonaphthalen-2-ol (13)

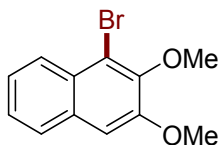


The following compound was obtained according to the general procedure A, by using 3-bromonaphthalen-2-ol and PIDA in 90 % yield as white solid. The spectroscopic data for this compound match with those previously described.⁹

¹H NMR (500 MHz) δ 8.04 (d, *J* = 7.2 Hz, 2H), 7.70 (s, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 8.1 Hz, 1H), 6.21 (s, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 147.3, 131.9, 131.6, 129.9, 128.3, 127.4, 125.9, 125.2, 110.8, 106.5.

1-bromo-2,3-dimethoxynaphthalene (14)

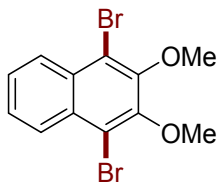


The following compound was obtained according to the general procedure A, by using 2,3-dimethoxynaphthalene and PIDA in 65 % yield as white solid. The spectroscopic data for this compound match with those previously described.¹⁰

¹H NMR (500 MHz, CDCl₃) δ 8.15 (d, *J* = 9.5 Hz, 1H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.46-7.42 (m, 2H), 7.16 (s, 1H), 3.99 (s, 3H), 3.95 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 152.6, 147.3, 131.7, 128.0, 126.88, 127.87, 126.2, 125.2, 116.5, 107.0, 60.8, 56.0.

1,4-dibromo-2,3-dimethoxynaphthalene (15)

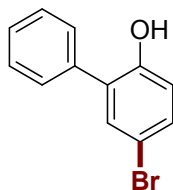


The following compound was obtained according to the general procedure A, by using 2,3-dimethoxynaphthalene and PIDA in 18% yield as white solid. The spectroscopic data for this compound match with those previously described.¹¹

^1H NMR (500 MHz, CDCl_3) δ 8.24 (dd, $J = 6.4$ Hz, 2H), 7.57 (dd, $J = 6.4$ Hz, 1H), 7.56 (d, $J = 6.5$ Hz, 1H), 4.00 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 150.6, 130.3, 127.4, 127.3, 116.2, 61.3.

4-bromo-[1,1'-biphenyl]-2-ol (16)

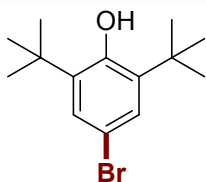


The following compound was obtained according to the general procedure A and B, by using [1,1'-biphenyl]-2-ol in 76% (Procedure A) or 72% (procedure B) of yields as colorless oil. The spectroscopic data for this compound match with those previously described.²

^1H NMR (500 MHz, CDCl_3) δ 7.50 (t, $J = 8.0$ Hz, 2H), 7.43 (d, $J = 8.1$ Hz, 3H), 7.37-7.34 (m, 2H), 6.88 (d, $J = 8.4$ Hz, 1H), 5.22 (s, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 151.7, 135.8, 132.7, 131.9, 130.2, 129.6, 129.0, 128.5, 117.7, 112.9.

4-Bromo-2,6-di-*tert*-butylphenol (17)

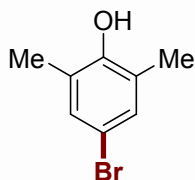


The following compound was obtained according to the general procedure C, by using 2,6-di-*tert*-butylphenol in 62% of yield as yellowish crystals. The spectroscopic data for this compound match with those previously described.¹²

¹H NMR (500 MHz, CDCl₃) δ 7.29 (d, *J* = 3.8 Hz, 2H), 5.19 (s, 1H), 1.45 (s, 18H).

¹³C NMR (126 MHz, CDCl₃) δ 153.0, 138.3, 127.9, 112.7, 34.6, 30.2.

4-Bromo-2,6-dimethylphenol (18)

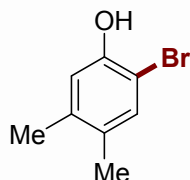


The following compound was obtained according to the general procedure C, by using 2,6-dimethylphenol in 57% of yield as white solid. The spectroscopic data for this compound match with those previously described.¹³

¹H NMR (400 MHz, CDCl₃) δ 7.10 (s, 2H), 4.57 (s, 1H), 2.21 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 151.44, 131.15, 125.31, 112.15, 15.87.

2-Bromo-4,5-dimethylphenol (19)

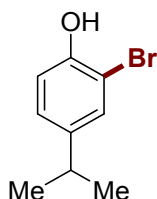


The following compound was obtained according to the general procedure C, by using 4,5-dimethylphenol in 30% of yield is white solid. The spectroscopic data for this compound match with those previously described.¹⁴

^1H NMR (500 MHz, CDCl_3) δ 7.20 (s, 1H), 6.82 (s, 1H), 5.25 (bs, 1H), 2.18 (s, 3H), 2.17 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 150.1, 138.4, 132.3, 130.3, 117.1, 106.9, 19.6, 18.7.

2-Bromo-4-isopropylphenol (20)

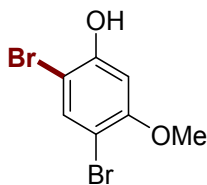


The following compound was obtained according to the general procedure C, by using 4-isopropylphenol in 18% of yield as colorless liquid. The spectroscopic data for this compound match with those previously described.²

^1H NMR (500 MHz, CDCl_3) δ 7.33 (s, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 6.97 (d, $J = 8.3$ Hz, 1H), 5.41 (s, 1H), 2.85 (h, $J = 6.9$ Hz, 1H), 1.24 (d, $J = 7.0$ Hz, 6H).

^{13}C NMR (125MHz, CDCl_3): 150.4, 142.9, 129.9, 127.5, 116.1, 110.3, 33.4, 24.3

2,4-dibromo-5-methoxyphenol (21)

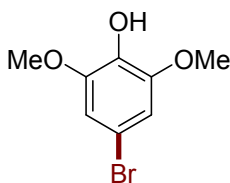


The following compound was obtained according to the general procedure C, by using 4-bromo-5-methoxyphenol in 51% of yield as orange liquid. The spectroscopic data for this compound match with those previously described.¹⁵

^1H NMR (500 MHz, CDCl_3): δ 7.58(s, 1H), 6.62(s, 1H), 5.59(s, 1H), 3.86(s, 3H).

^{13}C NMR (125 MHz, CDCl_3): 156.0, 152.3, 134.6, 102.3, 100.5, 100.1, 56.4.

4-bromo-2,6-dimethoxyphenol (22)

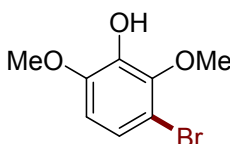


The following compound was obtained according to the general procedure C, by using 4-bromo-5-methoxyphenol in 52% of yield as light yellow solid. The spectroscopic data for this compound match with those previously described.¹⁶

¹H NMR (500 MHz, CDCl₃) δ 6.72 (s, 2H), 5.45 (s, 1H), 3.87 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 147.74, 134.18, 111.73, 108.65, 56.63.

3-bromo-2,6-dimethoxyphenol (23)

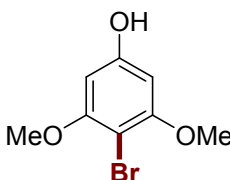


The following compound was obtained according to the general procedure C, by using 4-bromo-5-methoxyphenol in 9% of yield as light yellow solid. The spectroscopic data for this compound match with those previously described.¹⁷

¹H NMR (500 MHz, CDCl₃) δ 7.01 (d, J = 8.8 Hz, 1H), 6.56 (d, J = 8.9 Hz, 1H), 5.64 (s, 1H), 3.92 (s, 3H), 3.88 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 147.4, 144.5, 139.9, 122.5, 108.5, 107.9, 60.8, 56.5.

4-Bromo-3,5-Dimethoxyphenol (24)

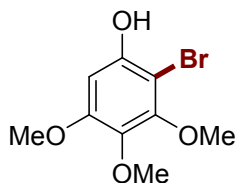


The following compound was obtained according to the general procedure C, by using 3,5-dimethoxyphenol in 43% of yield as white solid. The spectroscopic data for this compound match with those previously described.¹⁸

^1H NMR (500 MHz, CDCl_3) δ 6.17 (s, 2H), 6.04 (s, 1H), 3.90 (s, 6H).

^{13}C NMR (126 MHz, CDCl_3) δ 156.5, 150.8, 91.2, 89.5, 56.7.

2-bromo-3,4,5-trimethoxyphenol (25)

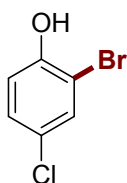


The following compound was obtained according to the general procedure C, by using 3,4,5-trimethoxyphenol in 46% of yield as yellow oil. The spectroscopic data for this compound match with those previously described.¹⁹

^1H NMR (500 MHz, CDCl_3) δ 6.38 (s, 1H), 5.45 (s, 1H), 3.91 (s, 3H), 3.82 (s, 3H), 3.81 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.7, 150.7, 149.2, 136.7, 96.1, 95.6, 61.4, 61.2, 56.1.

2-bromo-4-chlorophenol (26)

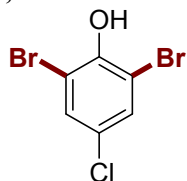


The following compound was obtained according to the general procedure C, by using 4-chlorophenol in 35% of yield as colorless solid. The spectroscopic data for this compound match with those previously described.²⁰

^1H NMR (500 MHz, CDCl_3) δ 7.46 (s, 1H), 7.19 (d, $J = 8.7$, 1H), 6.96 (d, $J = 8.7$ Hz, 1H), 5.47 (s, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 151.2, 131.4, 129.3, 125.9, 117.0, 110.5.

2,6-dibromo-4-chlorophenol (27)

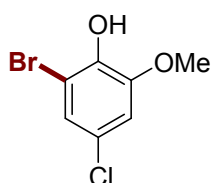


The following compound was obtained according to the general procedure C, by using 4-chlorophenol in 12% of yield as colorless solid. The spectroscopic data for this compound match with those previously described.²¹

¹H NMR (500 MHz, CDCl₃) δ 7.47 (s, 1H), 5.85 (s, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 148.5, 131.5, 126.2, 109.9.

2-bromo-4-chloro-6-methoxyphenol (28)

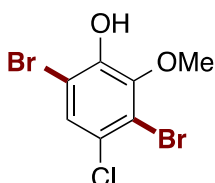


The following compound was obtained according to the general procedure C, by using 4-chloro-6-methoxyphenol in 28% of yield as white solid. The spectroscopic data for this compound match with those previously described.²²

¹H NMR (500 MHz, CDCl₃) δ 7.11(s, 1H), 6.81 (s, 1H), 5.87 (s, 1H), 3.90(s, 3H).

¹³C NMR (125MHz, CDCl₃) 146.1, 143.1, 125.7, 116.6, 112.4, 111.4, 56.4.

2,3-bromo-4-chloro-6-methoxyphenol (29)

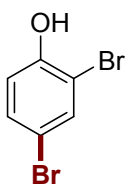


The following compound was obtained according to the general procedure C, by using 4-chloro-6-methoxyphenol in 10% yield as yellowish solid.

¹H-NMR (400 MHz, CDCl₃) δ 6.69 (s, 1H), 6.06 (s 1H), 3.92 (s, 3H).

¹³CNMR (125MHz, CDCl₃) δ 146.1, 143.1, 125.7, 116.6, 112.4, 111.4, 56.6.

2,4-dibromophenol (30)

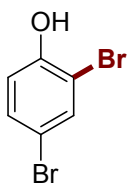


The following compound was obtained according to the general procedure C, by using 2-bromophenol in 35% of yield as colorless solid. The spectroscopic data for this compound match with those previously described.¹⁹

¹H NMR (400 MHz, CDCl₃) δ 7.60(s, 1H), 7.33(d, *J* = 8.54 Hz, 1H), 6.92 (d, *J* = 8.70 Hz, 1H), 5.57(s, 1H).

¹³C NMR (125MHz, CDCl₃) 151.5, 134.0, 132.1, 117.4, 112.4, 110.2.

2,4-dibromophenol (31)

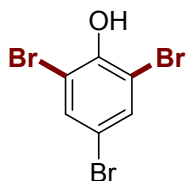


The following compound was obtained according to the general procedure C, by using 4-bromophenol in 28% of yield as colorless solid. The spectroscopic data for this compound match with those previously described.¹⁹

¹H-NMR (400 MHz, CDCl₃) δ 7.60(s, 1H), 7.33(d, *J* = 8.54 Hz, 1H), 6.92 (d, *J* = 8.70 Hz, 1H), 5.57(s, 1H).

¹³C-NMR (125MHz, CDCl₃) 151.5, 134.0, 132.1, 117.4, 112.4, 110.2.

2,4,6-tribromophenol (32)

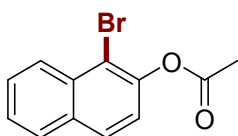


The following compound was obtained according to the general procedure C, by using 4-bromophenol in 8% of yield as colorless solid. The spectroscopic data for this compound match with those previously described.¹⁹

¹H NMR (400 MHz, CDCl₃) δ 7.61(s, 2H), 5.90(s, 1H).

¹³C NMR (125MHz, CDCl₃) 149.2, 134.1, 112.4, 110.4.

1-bromonaphthalen-2-yl-acetate (33)

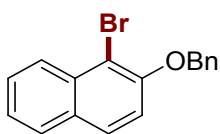


The following compound was obtained according to the general procedure A, by using naphthalen-2-yl-acetate in 72% of yield as yellowish liquid. The spectroscopic data for this compound match with those previously described.²³

¹H NMR (500 MHz, CDCl₃) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.41 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.31 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.07 (dd, *J* = 10.2, 5.7 Hz, 1H), 2.25 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 168.7, 146.3, 132.7, 132.4, 128.8, 128.2, 127.8, 127.0, 126.4, 121.8, 115.1, 20.9.

2-(benzyloxy)-1-bromonaphthalene (34)

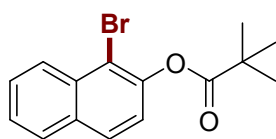


The following compound was obtained according to the general procedure D, by using 2-(benzyloxy)-naphthalene in 62% of yield as white solid. The spectroscopic data for this compound match with those previously described.²⁴

¹H NMR (400 MHz, CDCl₃) δ 8.17 (d, *J* = 8.6 Hz, 1H), 7.77–7.62 (m, 2H), 7.48 (dd, *J* = 19.4, 7.6 Hz, 3H), 7.32 (t, *J* = 7.6 Hz, 3H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.22–7.17 (m, 1H), 5.23 (s, 2H).

¹³C NMR (101 MHz, CDCl₃) δ 153.5, 136.7, 133.1, 130.8, 128.8, 128.6, 128.5, 128.2, 127.7, 127.2, 126.3, 124.5, 115.6, 110.1, 71.8.

1-bromonaphthalen-2-yl-pivalate (35)

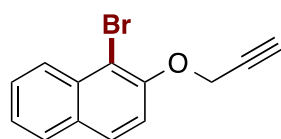


The following compound was obtained according to the general procedure D, by using naphthalen-2-yl-pivalate in 75% of yield as white solid. The spectroscopic data for this compound match with those previously described.²⁵

¹H NMR (500 MHz,) δ 8.14 (d, J = 8.5 Hz, 1H), 7.71 (t, J = 9.2 Hz, 2H), 7.48 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.44 – 7.34 (m, 1H), 7.09 (d, J = 8.8 Hz, 1H), 1.34 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 176.2, 146.6, 132.7, 132.3, 128.7, 128.2, 127.7, 126.9, 126.2, 121.9, 115.0, 39.4, 27.2.

1-bromo-2-(prop-2-yn-1-yloxy)naphthalene (36)

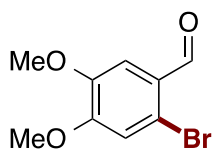


The following compound was obtained according to the general procedure D, by using 2-(prop-2-yn-1-yloxy)naphthalene in 62% of yield as white solid.

¹H NMR (500 MHz, CDCl₃) δ 8.25 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.7 Hz, 1H), 7.44 (d, J = 7.0 Hz, 1H), 7.41 (d, J = 9.0 Hz, 1H), 4.91 (d, J = 2.4 Hz, 2H), 2.55 (t, J = 2.4 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 152.2, 133.2, 130.6, 128.9, 128.2, 127.9, 126.5, 125.0, 116.0, 110.6, 78.4, 76.3, 58.0.

2-Bromo-4,5-dimethoxybenzaldehyde (37)

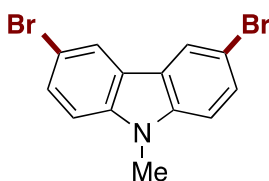


The following compound was obtained according to the general procedure D, by using 3,4-dimethoxybenzaldehyde in 55% of yield as white solid. The spectroscopic data for this compound match with those previously described²

^1H NMR (500 MHz, CDCl_3) δ 10.22 (s, 1H), 7.42 (s, 1H), 7.06 (s, 1H), 3.96 (s, 3H), 3.92 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 190.8, 154.5, 148.9, 126.5, 120.4, 115.4, 110.4, 56.5, 56.1.

3,6-dibromo-9-methyl-9H-carbazole (38)

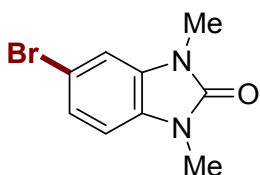


The following compound was obtained according to the a modified general procedure D by using 2.4 equiv of PIDA and 4.8 equiv of AlBr_3 , by using 9-methyl-9H-carbazole in 62% of yield as white solid. The spectroscopic data for this compound match with those previously described.²⁶

^1H NMR (500 MHz, CDCl_3) δ 8.14 (d, $J = 1.2$ Hz, 2H), 7.57 (dd, $J = 8.7, 1.7$ Hz, 2H), 7.27 (d, $J = 10.0$ Hz, 2H), 3.82 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 140.0, 129.2, 123.5, 123.3, 112.2, 110.3, 29.5.

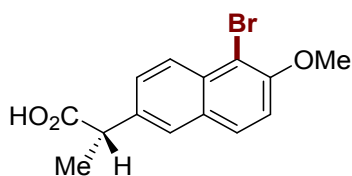
5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (39)



The following compound was obtained according to the general procedure D, by using 1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one in 36% of yield as brown solid. The spectroscopic data for this compound match with those previously described.²⁷

^1H NMR (400 MHz, CDCl_3) δ 7.21 (dd, $J = 8.2, 1.7$ Hz, 1H), 6.83 (d, $J = 8.3$ Hz, 1H), 7.11 (s, 1H), 3.40 (s, 6H).

(S)-2-(5-bromo-6-methoxynaphthalen-2-yl) propanoic acid. (40)

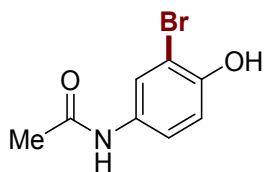


The following compound was obtained according to the general procedure A, by using (*S*)-2-(6-methoxynaphthalen-2-yl) propanoic acid sodium salt in 93 % yield as white solid. The spectroscopic data for this compound match with those previously described.²⁸

¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 9.0 Hz, 1H), 7.63 (s, 1H), 7.46 (dd, *J* = 8.8, 1.5 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 2H), 3.95 (s, 3H), 3.84 (q, *J* = 7.1 Hz, 1H), 1.53 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 153.8, 135.6, 132.4, 129.7, 128.8, 127.6, 126.7, 126.4, 113.9, 108.5, 60.0, 57.0, 51.2, 44.9.

Br-paracetamol (41)

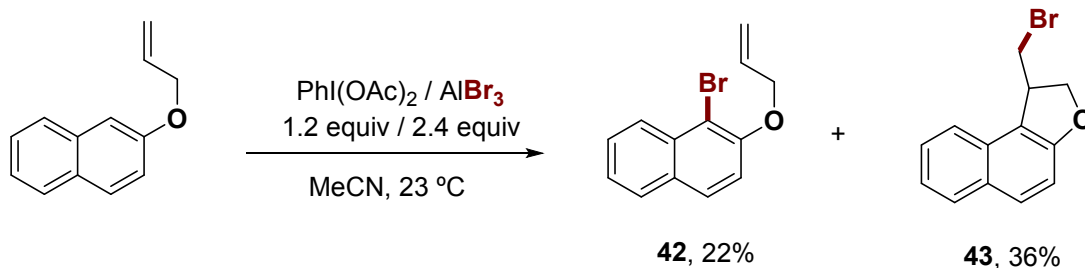


The following compound was obtained according to the general procedure A, by using *N*-(3-bromo-4-hydroxyphenyl) acetamide sodium salt in 65 % yield as white solid. The spectroscopic data for this compound match with those previously described.²⁹

¹H NMR (500 MHz,) 8.21 (s, 1H), 7.77 (s, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 6.93 (d, *J* = 8.7, 1H), 2.18 (s, 3H).

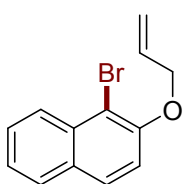
¹³C NMR (126 MHz, CH₃CN+D₂O) δ 171.1, 152.3, 126.7, 123.0, 122.9, 118.9, 111.5, 25.8.

Equation 1.



The following mixture of compounds **42** and **43** was obtained according to the general procedure A, by using 2-(allyloxy) naphthalene as starting material.

2-(allyloxy)-1-bromonaphthalene (**42**)

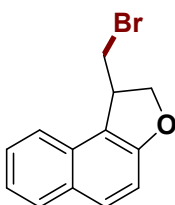


The following compound was obtained in 22 % yield as white solid. The spectroscopic data for this compound match with those previously described.³⁰

¹H NMR (500 MHz, CDCl₃) δ 8.26 (d, *J* = 8.6 Hz, 1H), 7.81 (d, *J* = 8.9 Hz, 2H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 9.4 Hz, 1H), 6.15 (dq, *J* = 10.2, 4.9 Hz, 1H), 5.55 (d, *J* = 17.2 Hz, 1H), 5.36 (d, *J* = 10.6 Hz, 1H), 4.79 (d, *J* = 3.7 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 152.9, 133.2, 132.9, 130.0, 128.7, 128.0, 127.6, 126.3, 124.4, 117.8, 115.5, 109.8, 70.7.

1-(bromomethyl)-1,2-dihydronaphthol[2,1-*b*] furan (**43**)

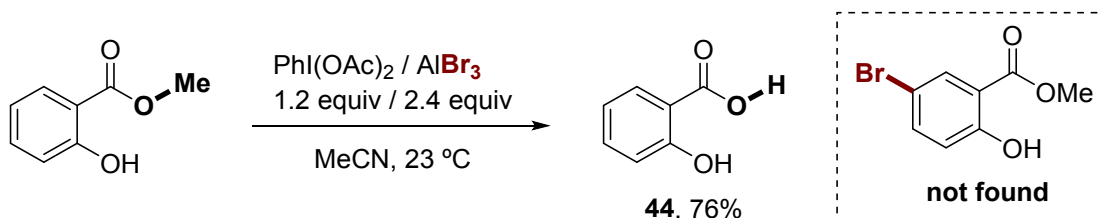


The following compound was obtained in 36% of yield as white solid. The spectroscopic data for this compound match with those previously described.³¹

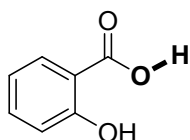
¹H NMR (500 MHz, CDCl₃) δ 8.16 (d, *J* = 8.5 Hz, 1H), 7.72 (q, *J* = 8.8 Hz, 2H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.22 – 7.16 (m, 1H), 4.58 – 4.49 (m, 1H), 4.44 (dq, *J* = 9.4, 4.8 Hz, 2H), 4.10 – 4.01 (m, 1H), 3.95 (dd, *J* = 10.2, 3.6 Hz, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 152.3, 133.1, 130.4, 129.1, 128.0, 127.9, 126.4, 124.9, 115.7, 110.6, 71.2, 47.5, 33.1.

Equation 2.



2-hydroxybenzoic acid (44)



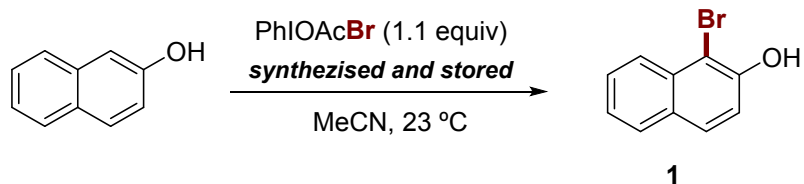
The following compound was obtained according to the general procedure A, by using methyl 2-hydroxybenzoate as starting material in 76% yield as white solid. The spectroscopic data for this compound match with those previously described.³²

^1H NMR (500 MHz, CDCl_3) δ 10.36 (s, 1H), 7.94 (dd, $J = 8.0, 1.7$ Hz, 1H), 7.54 (ddd, $J = 8.8, 7.2, 1.7$ Hz, 1H), 7.26 (s, 1H), 7.02 (dd, $J = 8.4, 0.8$ Hz, 1H), 6.99 -6.90 (m, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 174.9, 162.2, 137.0, 130.9, 119.6, 117.8, 111.2.

Scheme 4.

Evaluation of the thermal stability and reactivity for the proposed brominating active species PhIOAcBr . We carried out a procedure for the isolation of the proposed active brominating species. After its synthesis we describe the behavior of the solid obtained in bromination reactions along one month at $4\text{ }^\circ\text{C}$ and $23\text{ }^\circ\text{C}$. The results are summarized.



PhIOAcBr stored at

4 °C	23 °C
------	-------

<i>in situ</i> :	----	93%
one day:	92%	86%
one week:	91%	82%
two weeks:	91%	78%
one month:	90%	75%

Isolated yields are described

The procedure here described was followed to get the proposed active brominating species PhIOAcBr.

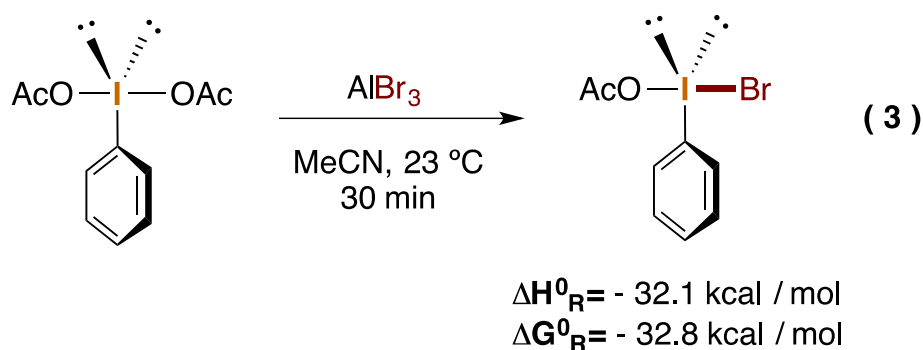
A 100 mL dry round bottom flask, was charged with PIDA (diacetoxy)iodobenzene (100 mg, 0.31 mmol, 1 equiv.) and dry acetonitrile (0.15 M) at 25 °C. After dissolving and obtaining homogeneous mixture, AlBr₃ (182 mg, 0.61 mmol, 2 equiv.) was added and stirring for 10 min. An exothermic reaction is observed on the AlBr₃ addition. A yellow-orange precipitate is observed. The reaction mixture is transferred to a 20 mL Corning® tube and was centrifuged during 10 min at 5 000 rpm. The supernatant is a homogeneous solution, which was separated by decantation, from the solid in the bottom. The supernatant is carefully evaporated without heating and dried to high vacuum. This procedure (98 mg) yields 92% mg of an orange solid that is presumed to be the brominating active species PhIOAcBr.

The half of the solid was kept in the freezer at 4 °C and another half was kept at 23 °C. This solid was used to carry out the bromination reactions of 2-naphthol along one month. The results are summarized in the table next to chemical equation.

3. Theoretical calculations for PhIOAcBr

Equation 3. Computational Study

We carried out the following theoretical calculations to determine the feasibility in the active brominating species formation PhIOAcBr by mixing PIDA and AlBr₃. The results of this calculations are following showed.



Computational Details

We have performed gas-phase geometry optimizations without no symmetry restrictions using the Gaussian16 rev. A.03 program.³³ The new global hybrid meta density-functional M08-HX developed by Truhlar and coworkers was chosen,³⁴ which have shown a broad accuracy for main group chemistry and organometallics in terms of reaction energies. The electronic configurations of the molecules were described with a split-valence basis set of triple- ζ quality with one polarization function, 6-311G*,³⁵⁻³⁶ for all the light atoms, whereas the Los Alamos pseudopotential LANL08d basis set was set up for Br and I atoms.³⁵⁻³⁶ The stationary points were characterized by analytical frequency calculations (all the harmonic frequencies were positive). The reported Gibbs free energies in this work include zero-point energy, thermal and entropic corrections evaluated at 298 K and 1 atm. Also, we performed calculations for including the solvent effect through the PCM model³⁷ using the SMD parameters³⁸ according to the Truhlar's model using acetonitrile as solvent. That way, our composed level of theory can be named as (SMD: acetonitrile)M08-HX/(6-311G*,LANL08d).

Table S1. Cartesian coordinates (xyz) of the optimized geometries calculated at the M08-HX/(6-311G*,LANL08d) level. Coordinates are given in Angstroms.

AlBr₃ + PIDA

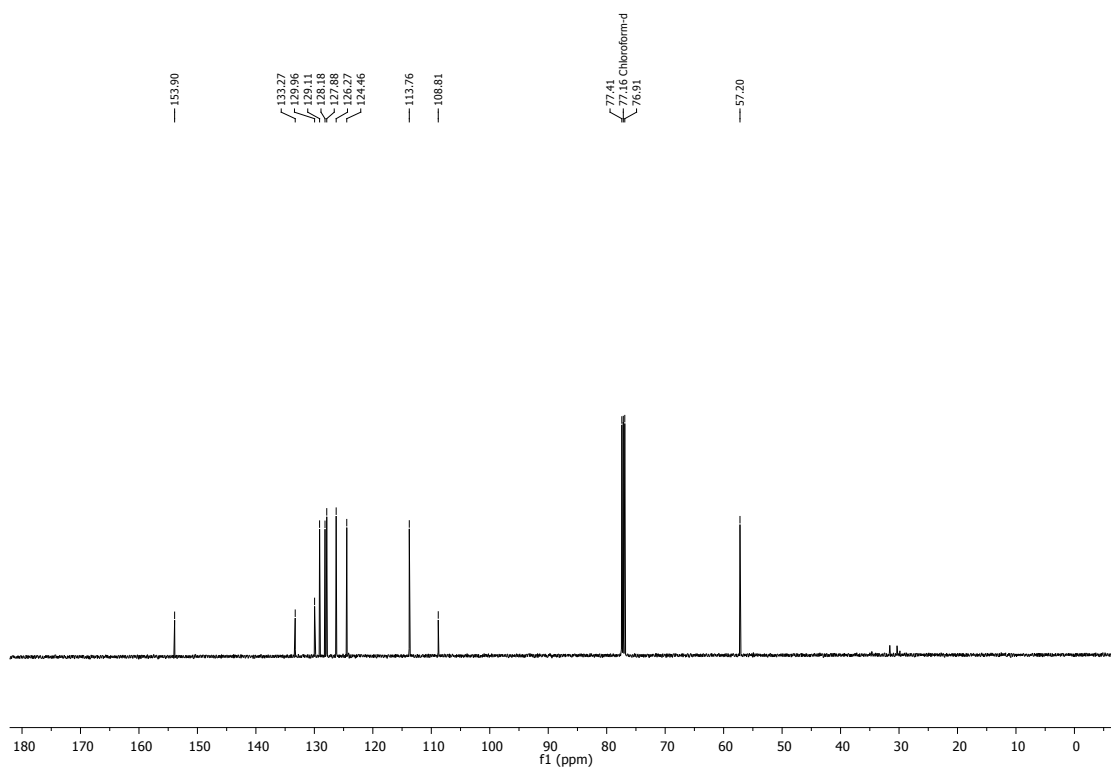
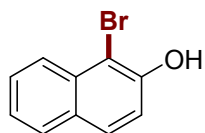
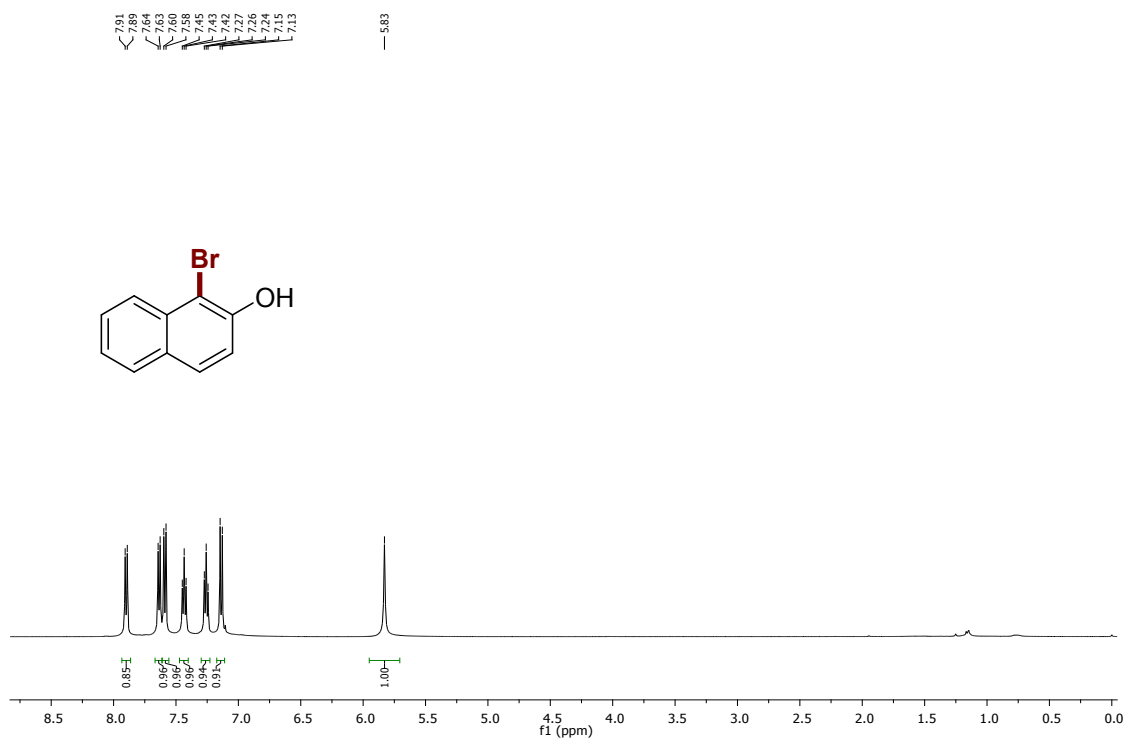
E(scf) = -982.001616831 a.u.

Brominating reagent

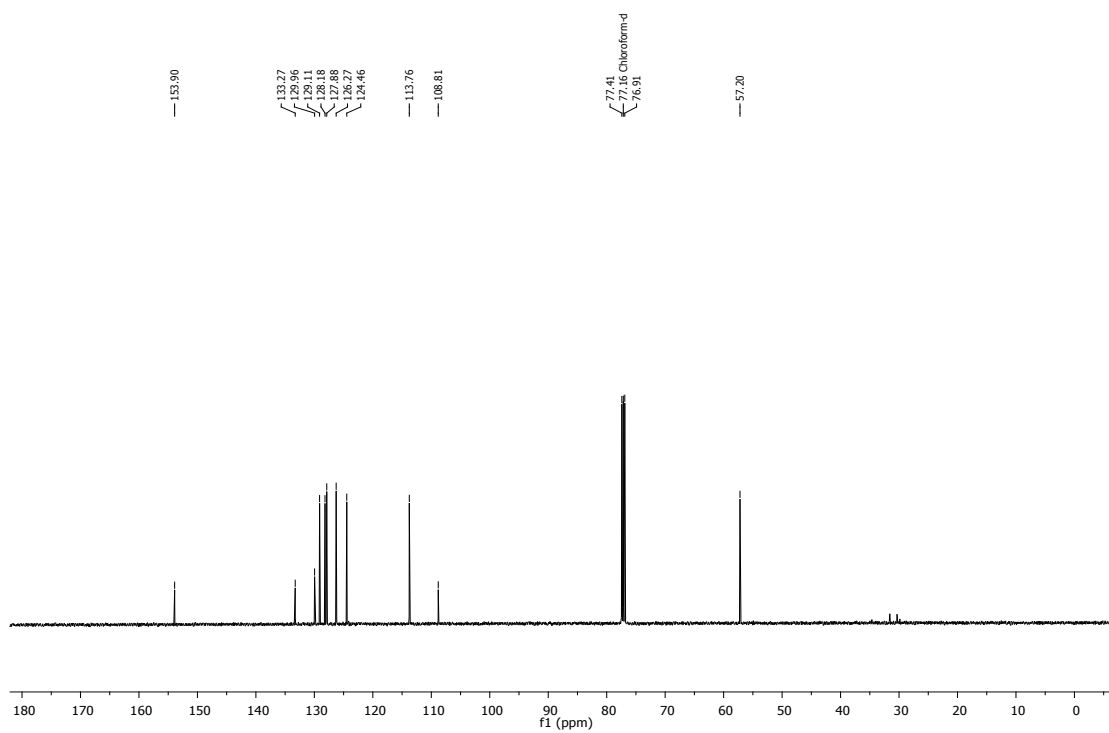
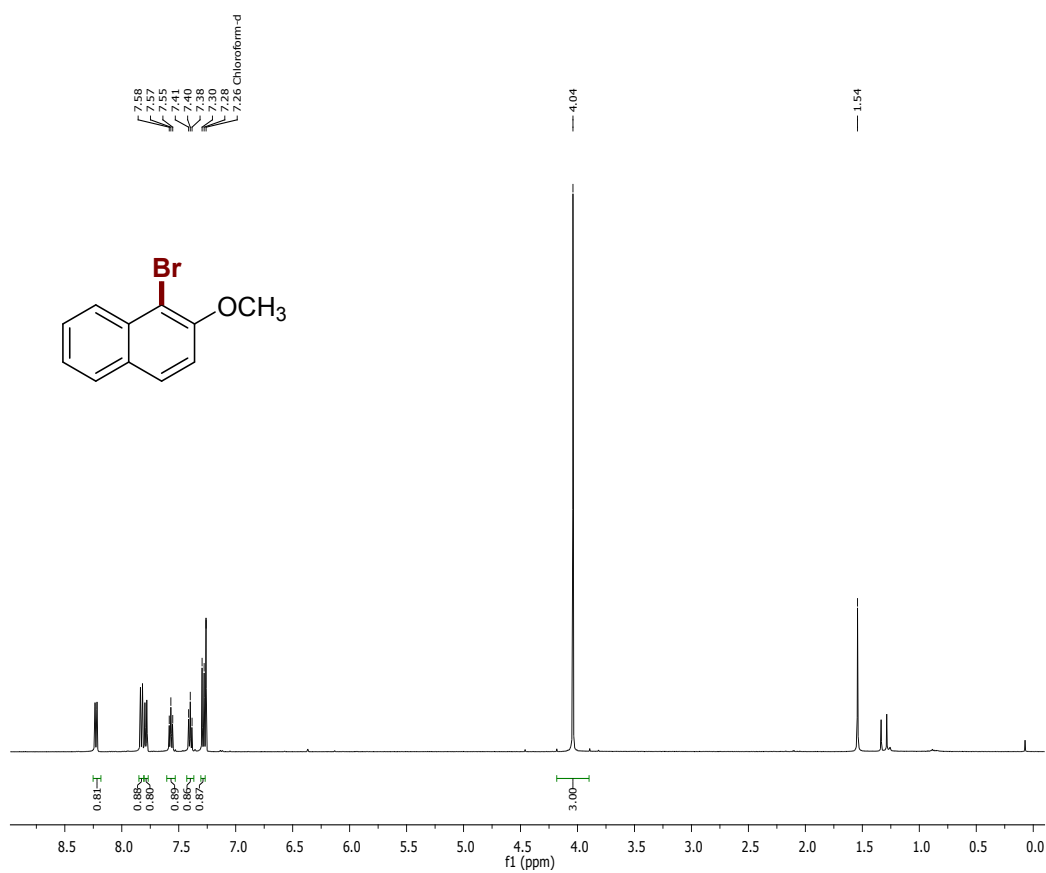
E(scf) = -484.564924519 a.u.

4. Copies of ^1H and ^{13}C Spectra

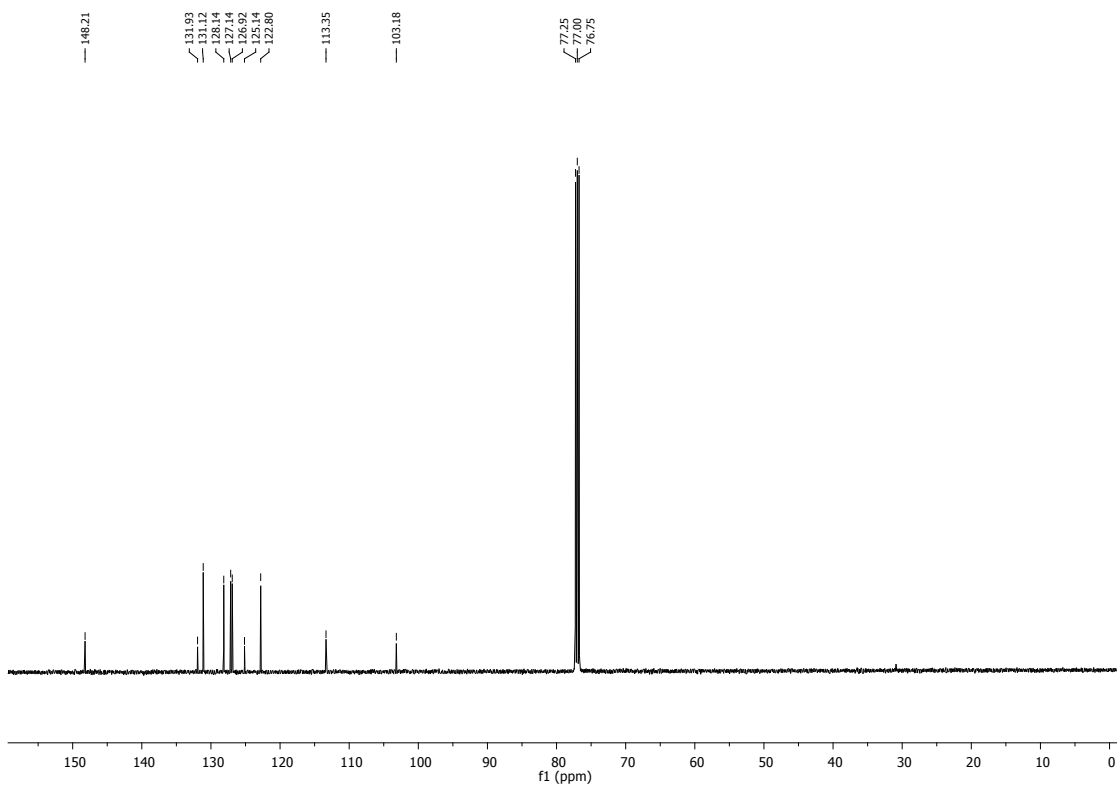
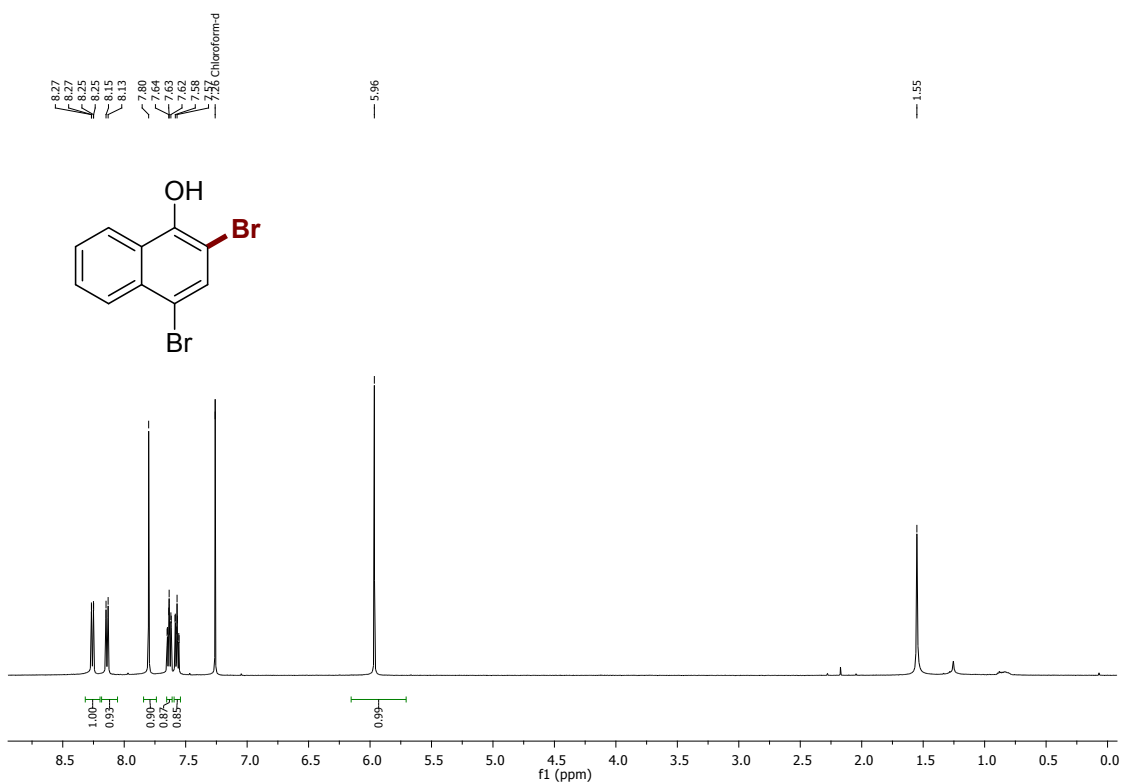
1-bromonaphthalen-2-ol (1)



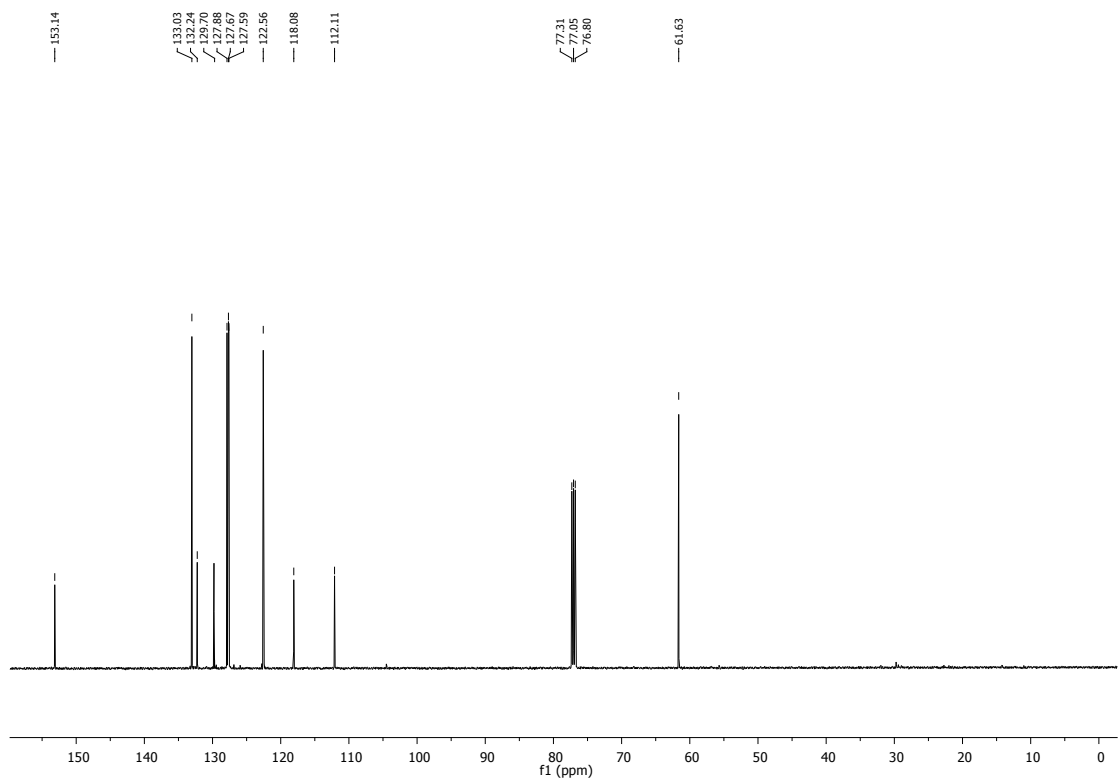
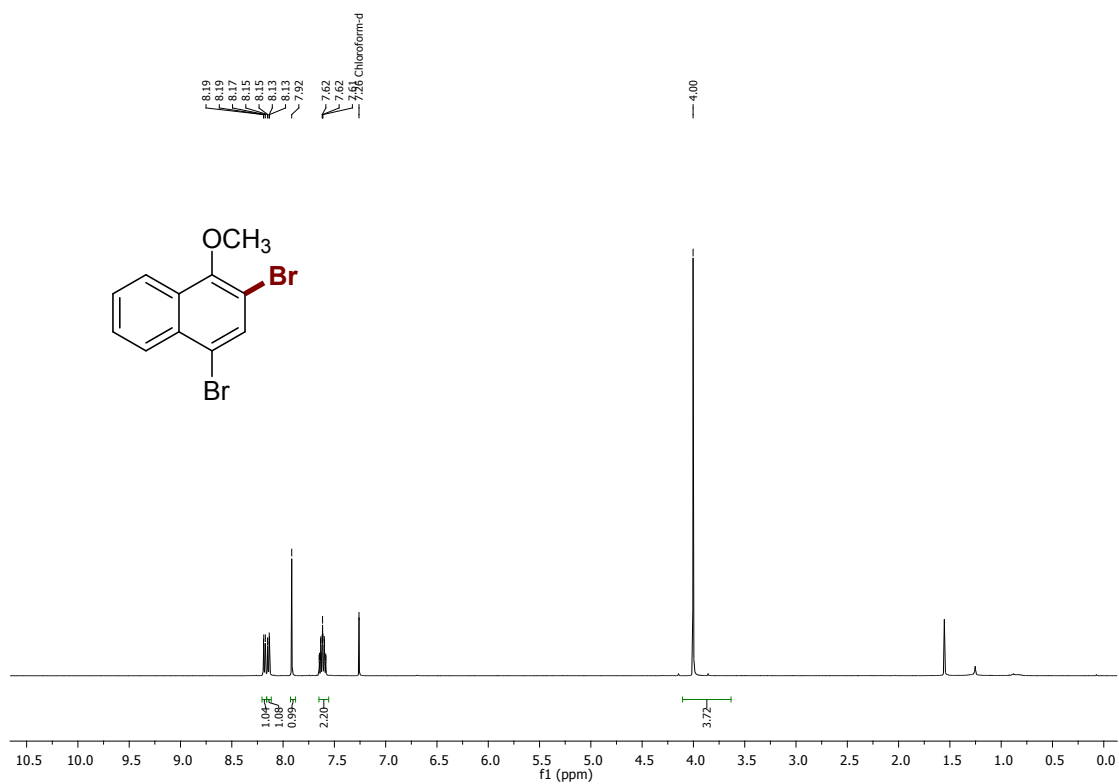
Bromo-2-methoxynaphthalene (2)



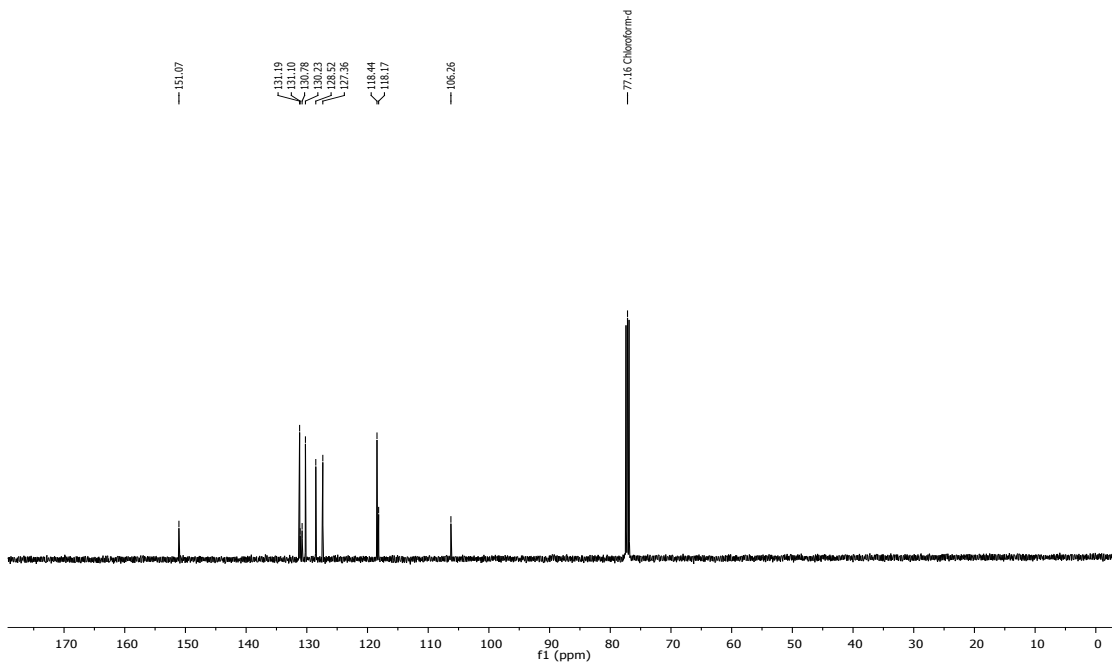
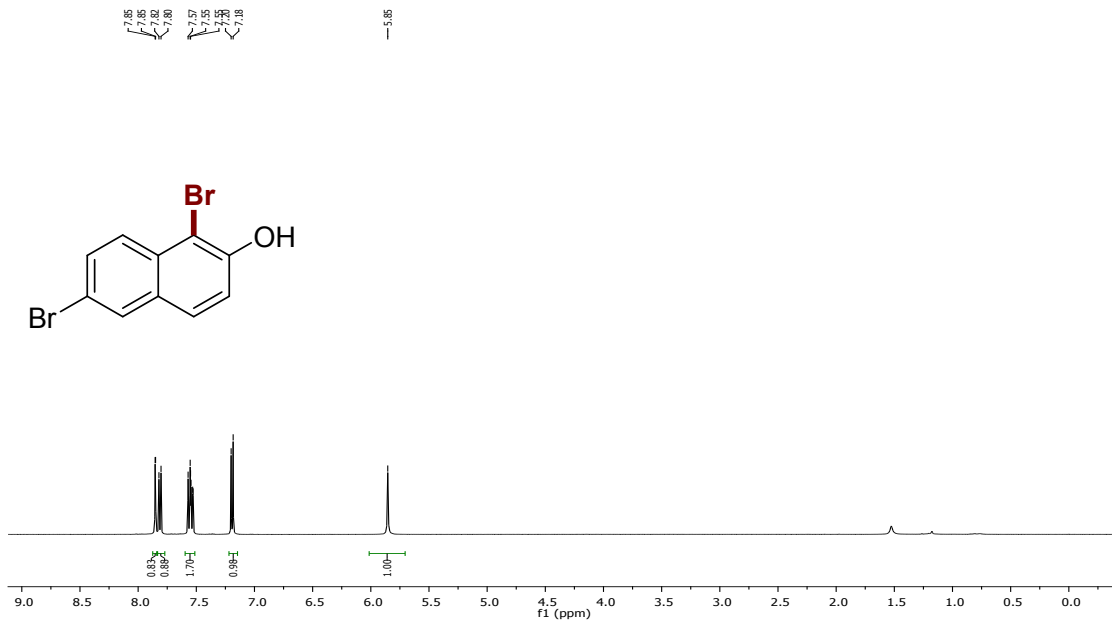
2,4-dibromonaphthalen-1-ol (3)



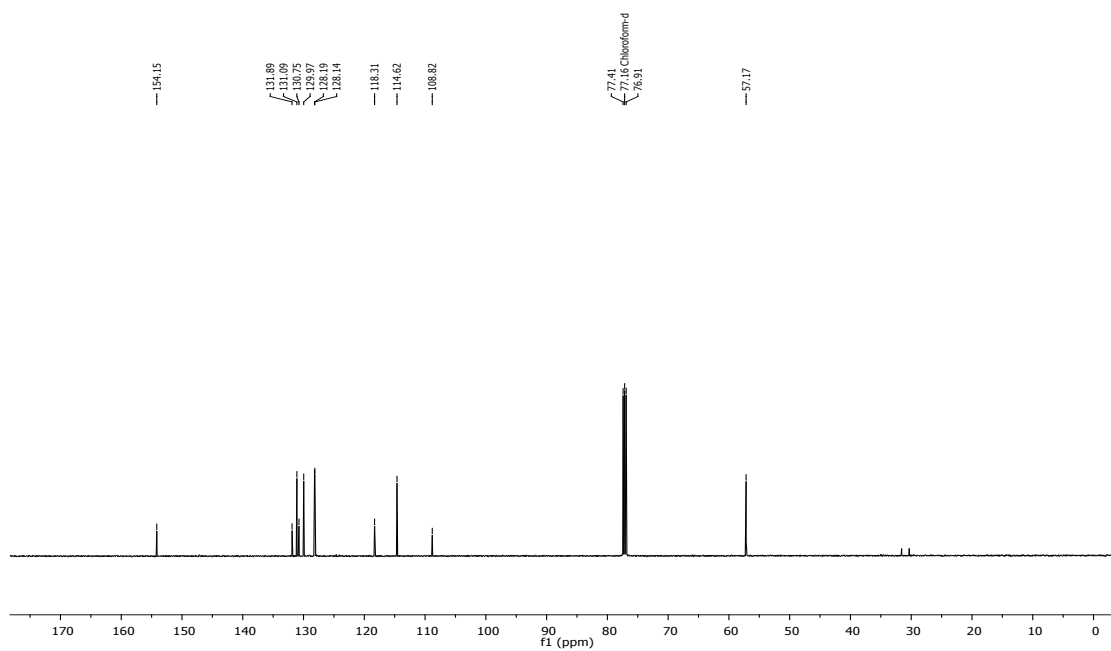
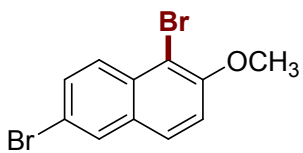
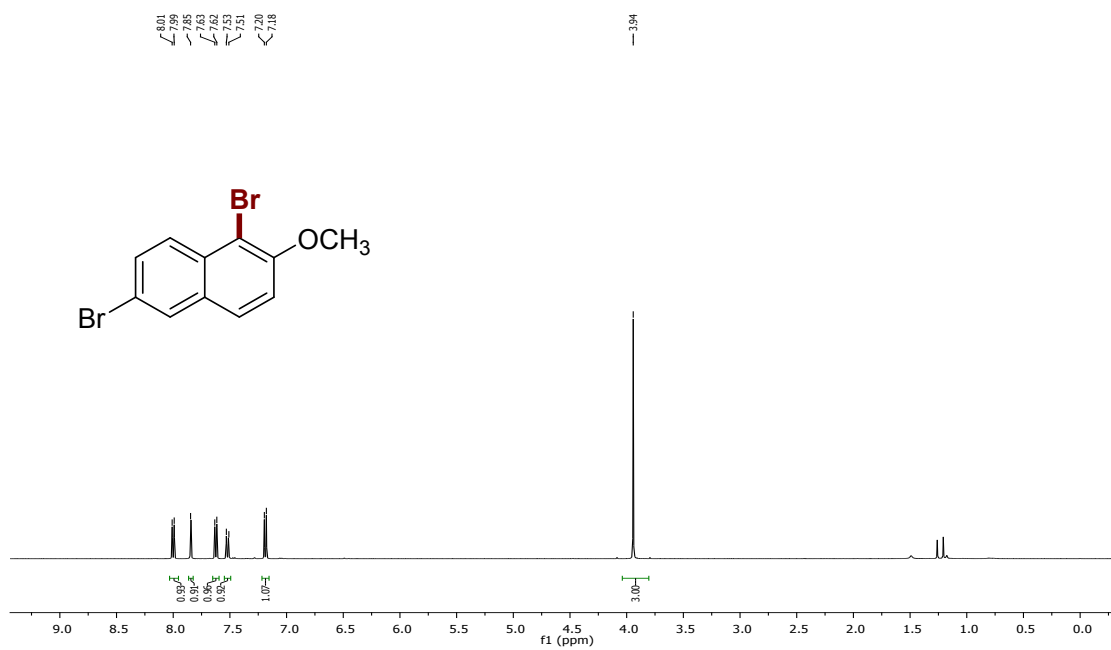
2,4-dibromo-1-methoxynaphthalene (4)



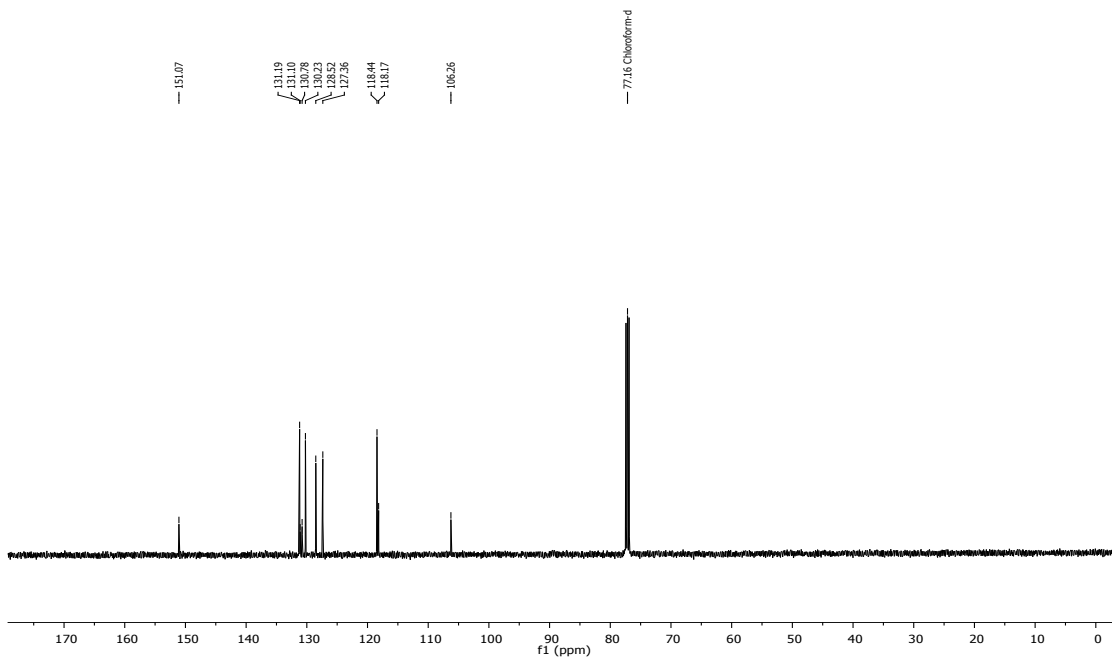
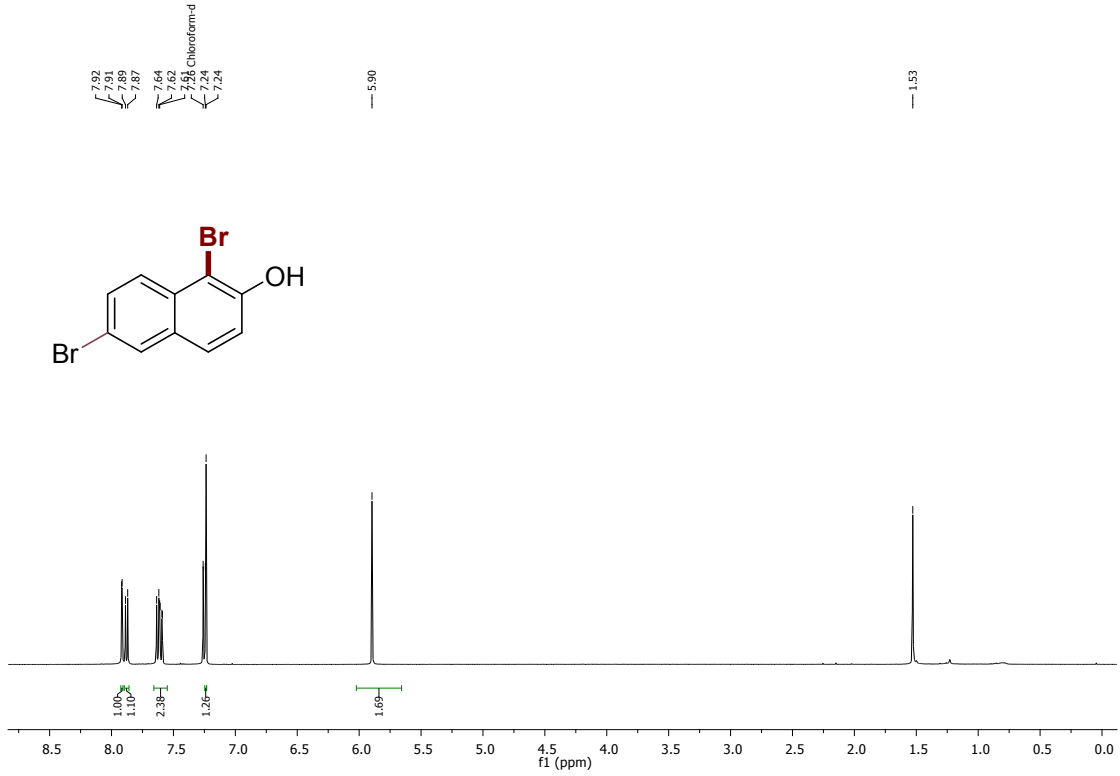
1,6-dibromonaphthalen-2-ol (5)



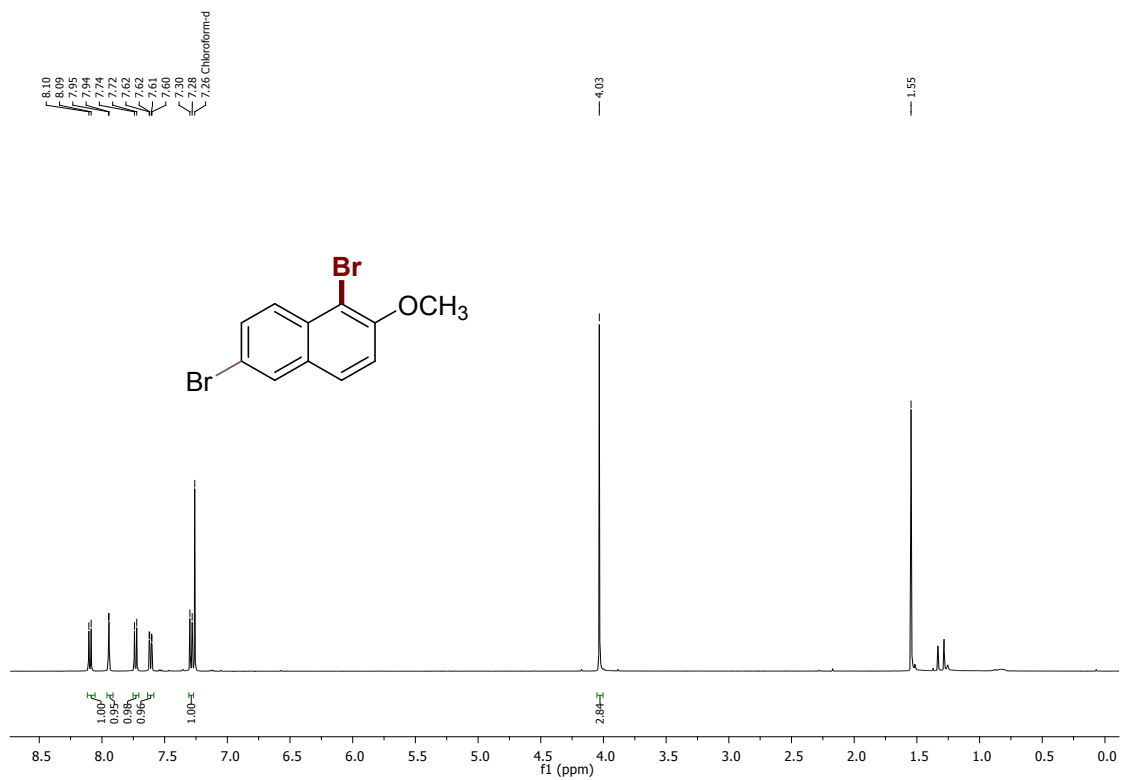
1,6-dibromo-2-methoxynaphthalene (6)

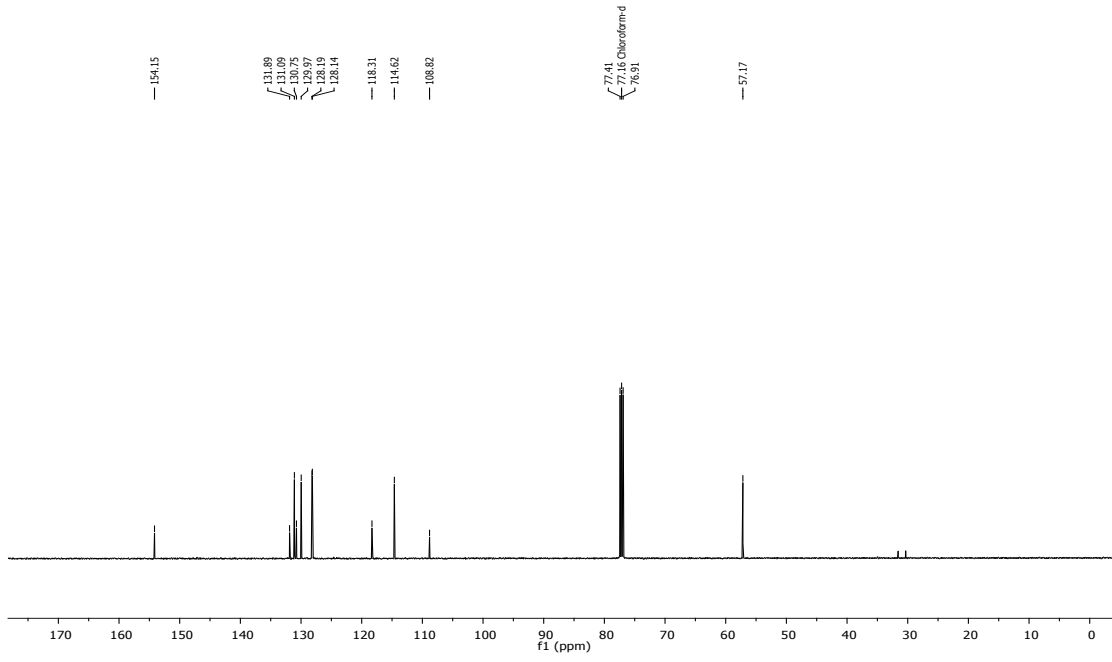


1,6-dibromonaphthalen-2-ol (7)

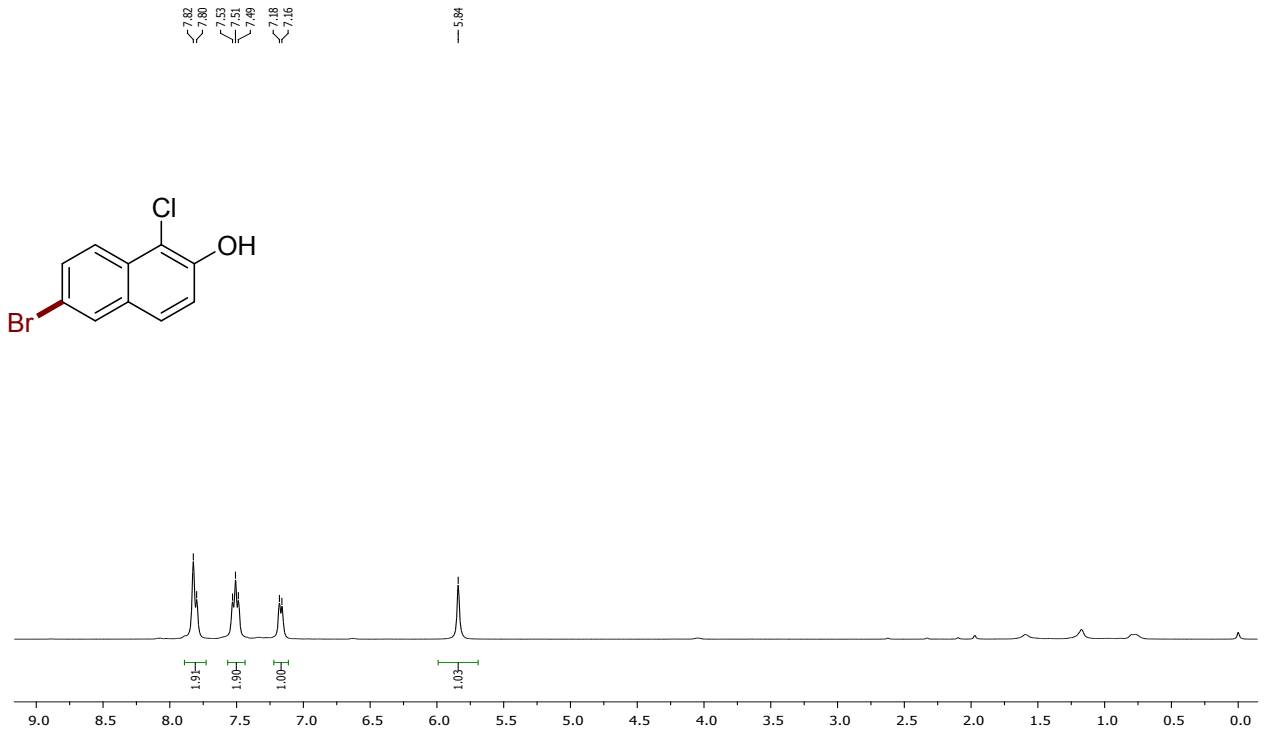


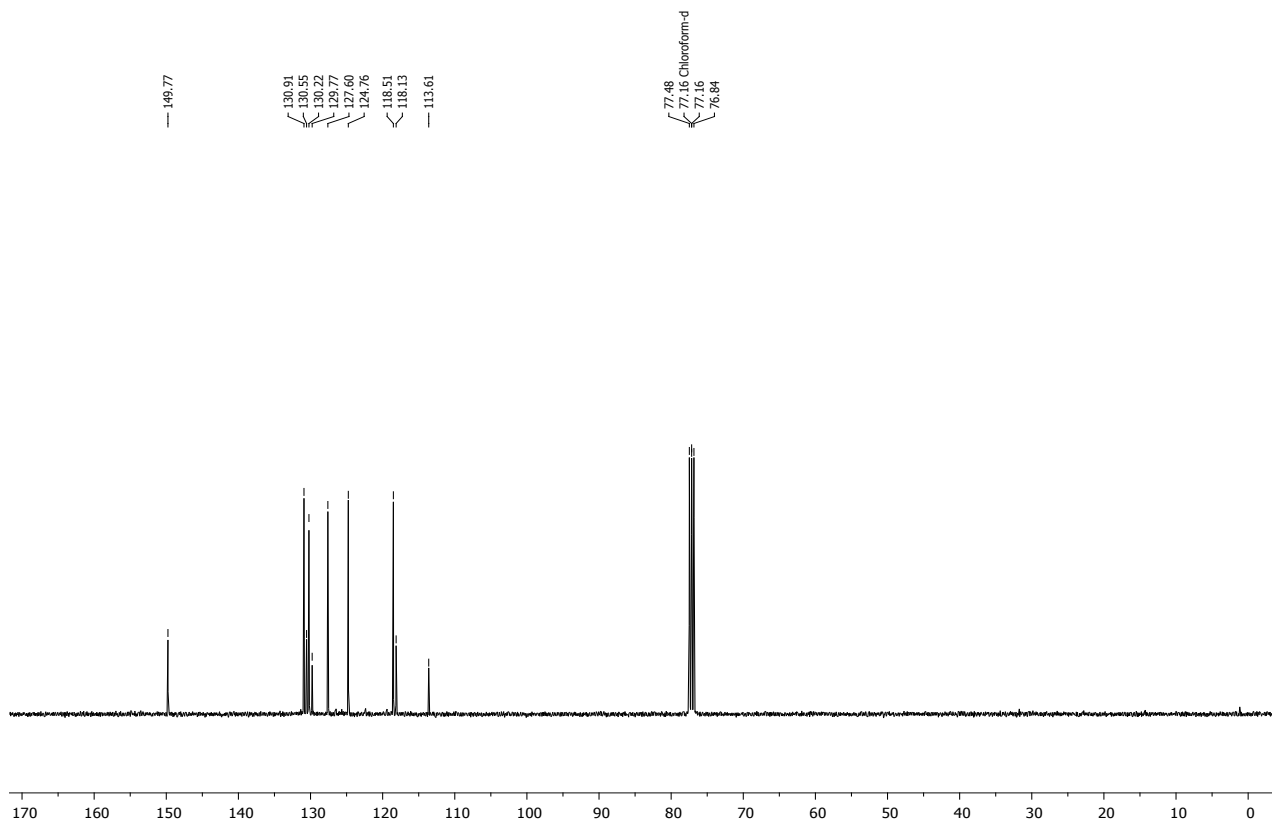
1,6-dibromo-2-methoxynaphthalene (**8**)



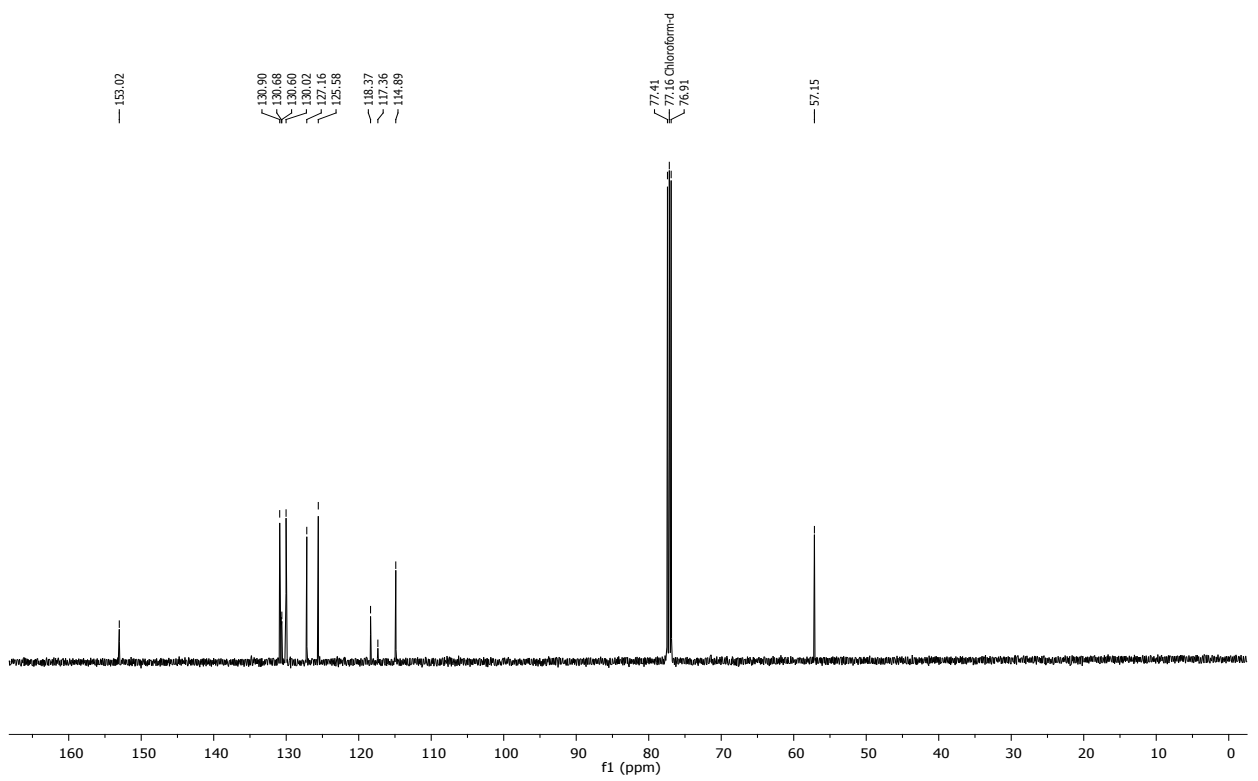
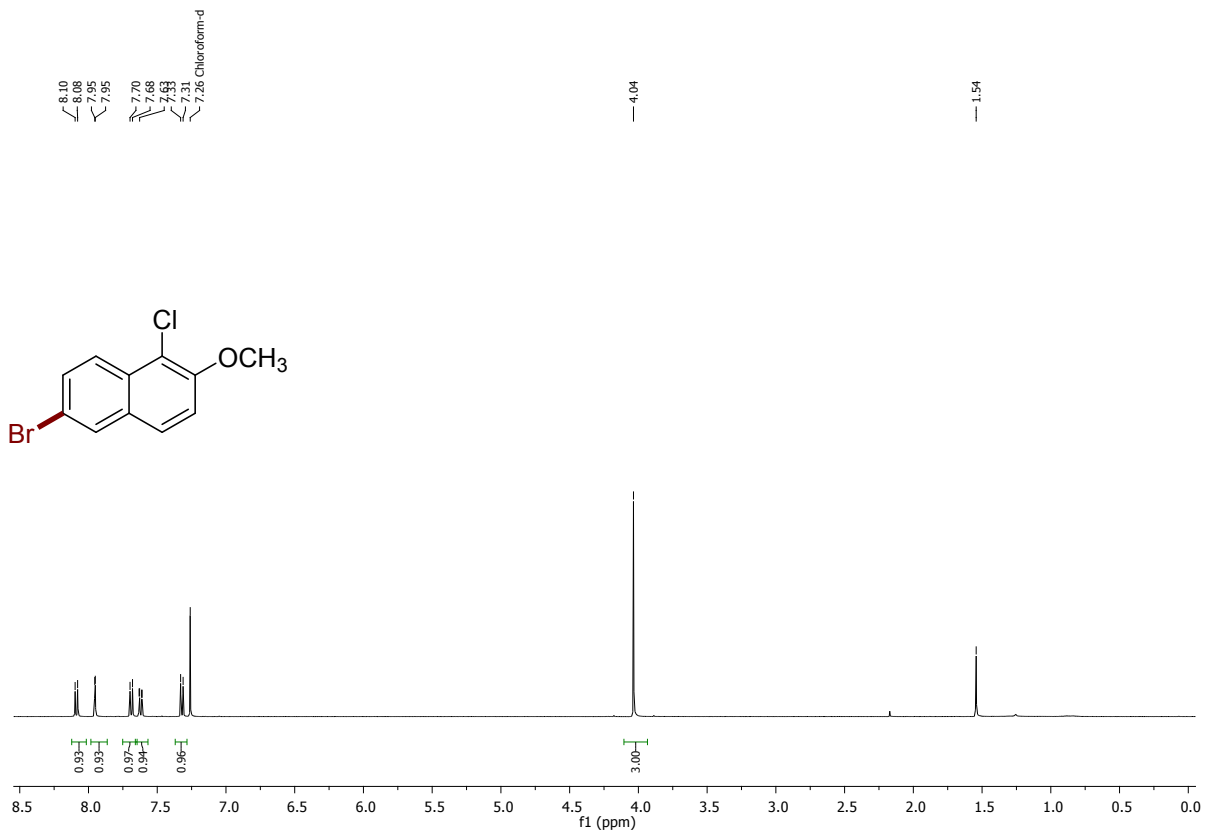


6-bromo-1-chloronaphthalen-2-ol (9)

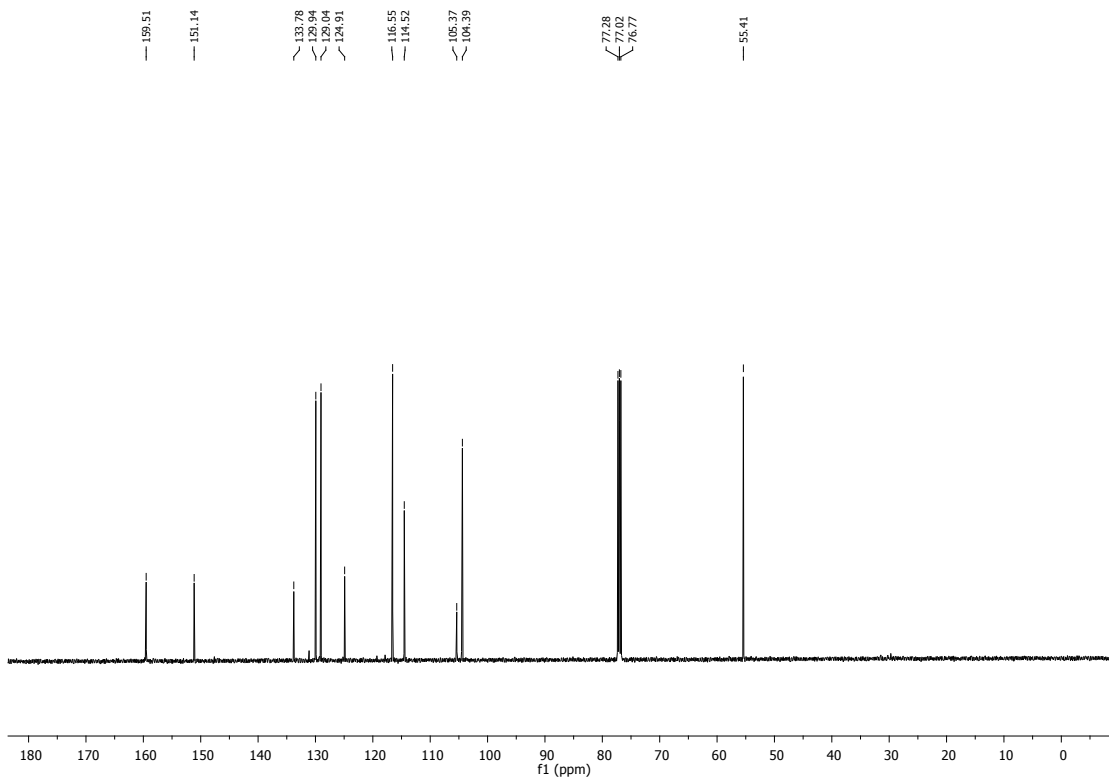
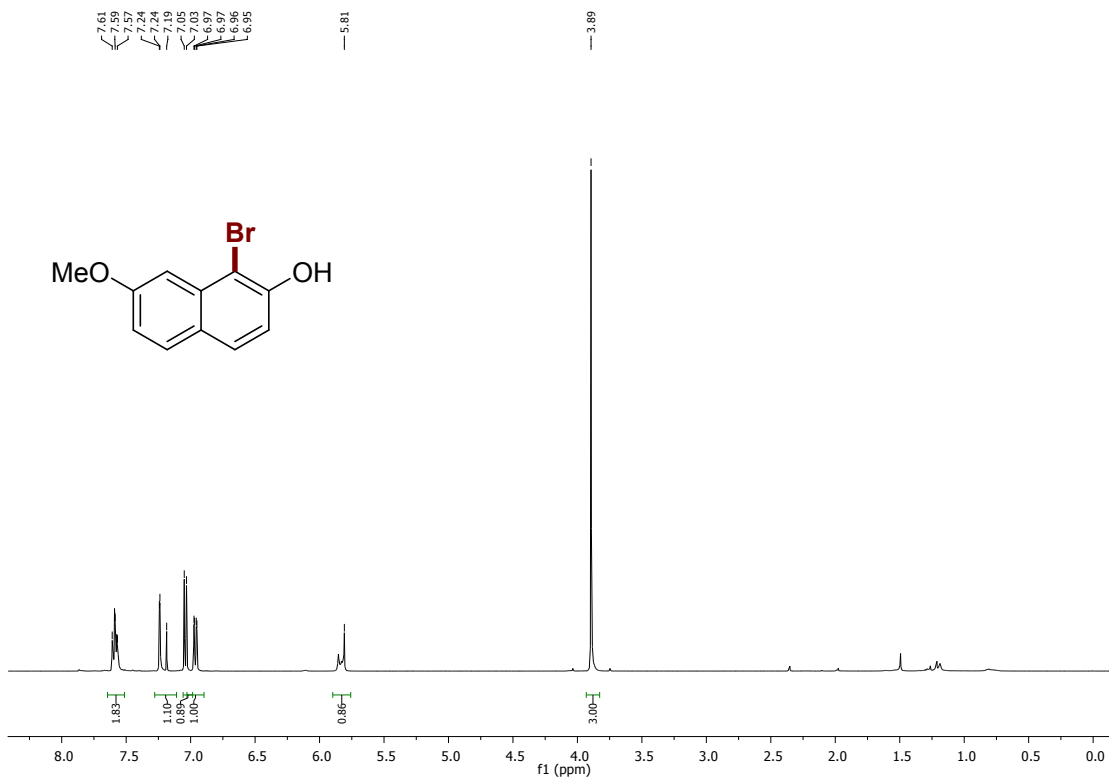




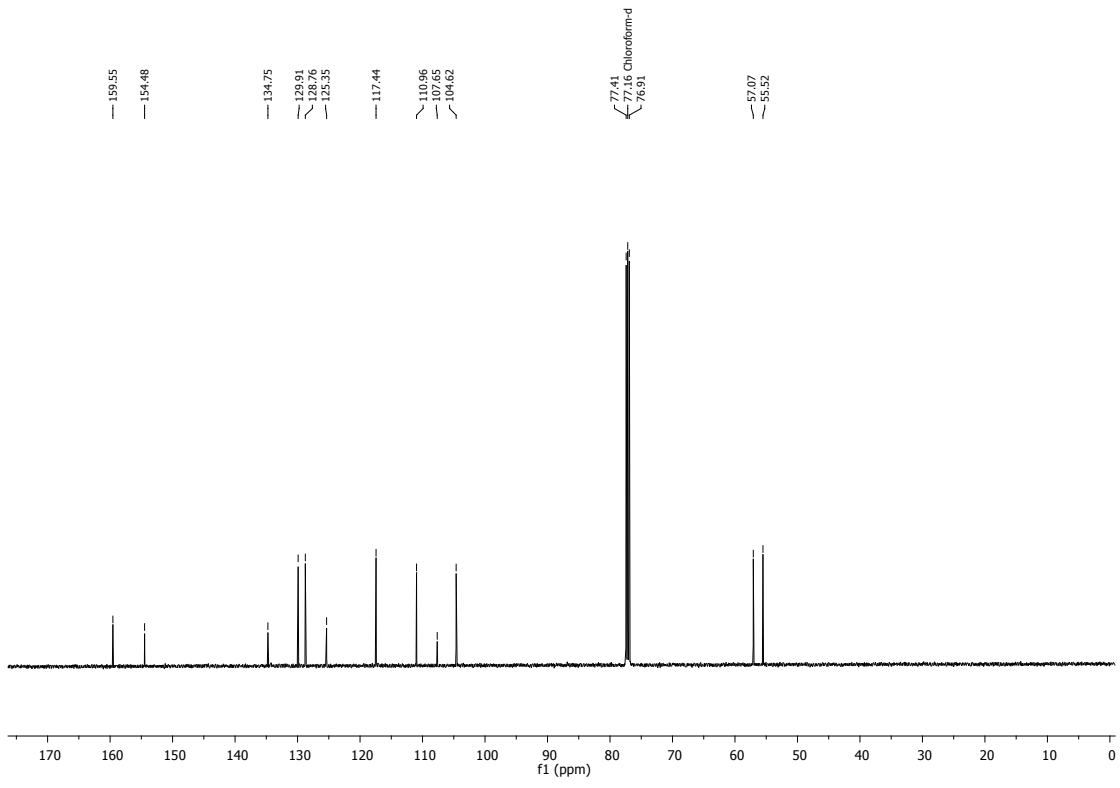
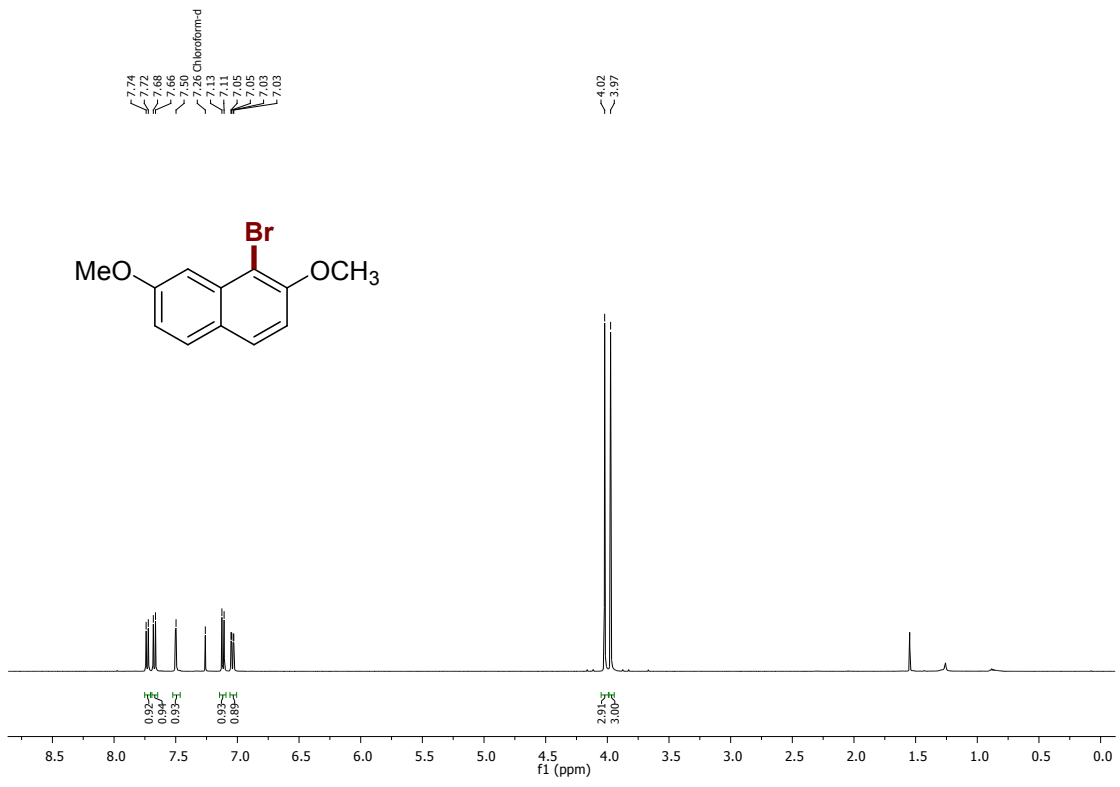
6-bromo-1-chloro-2-methoxynaphthalene (10)



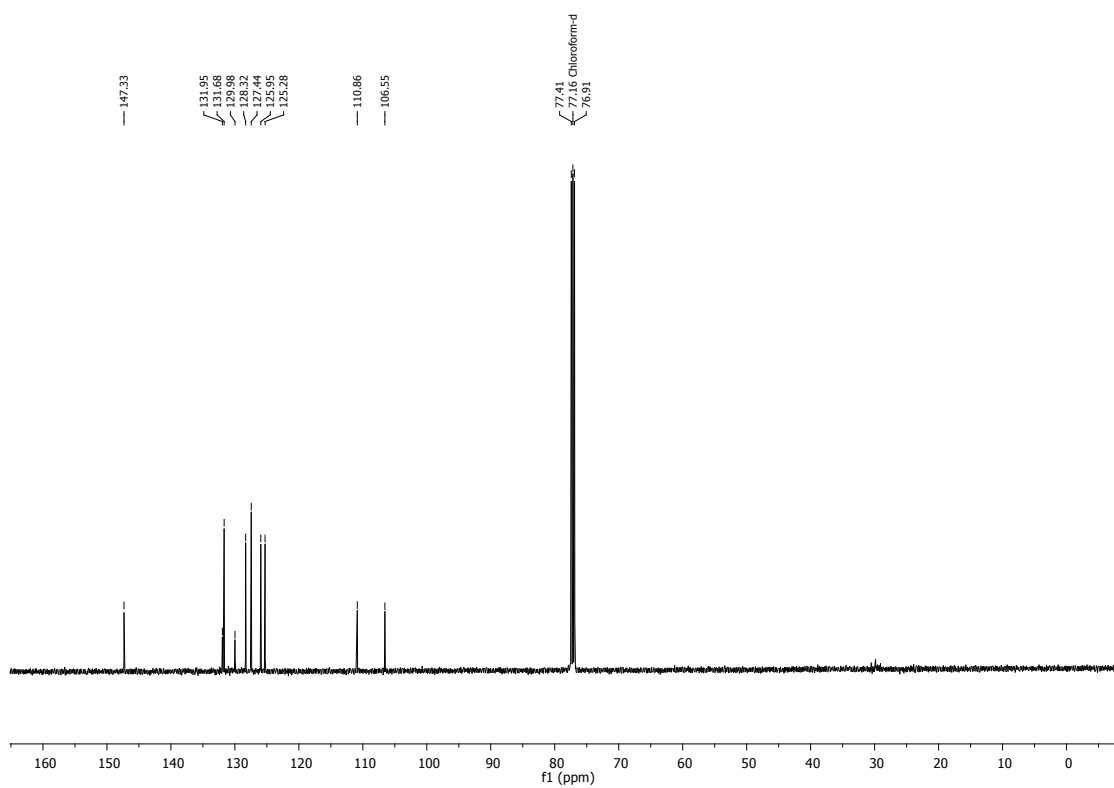
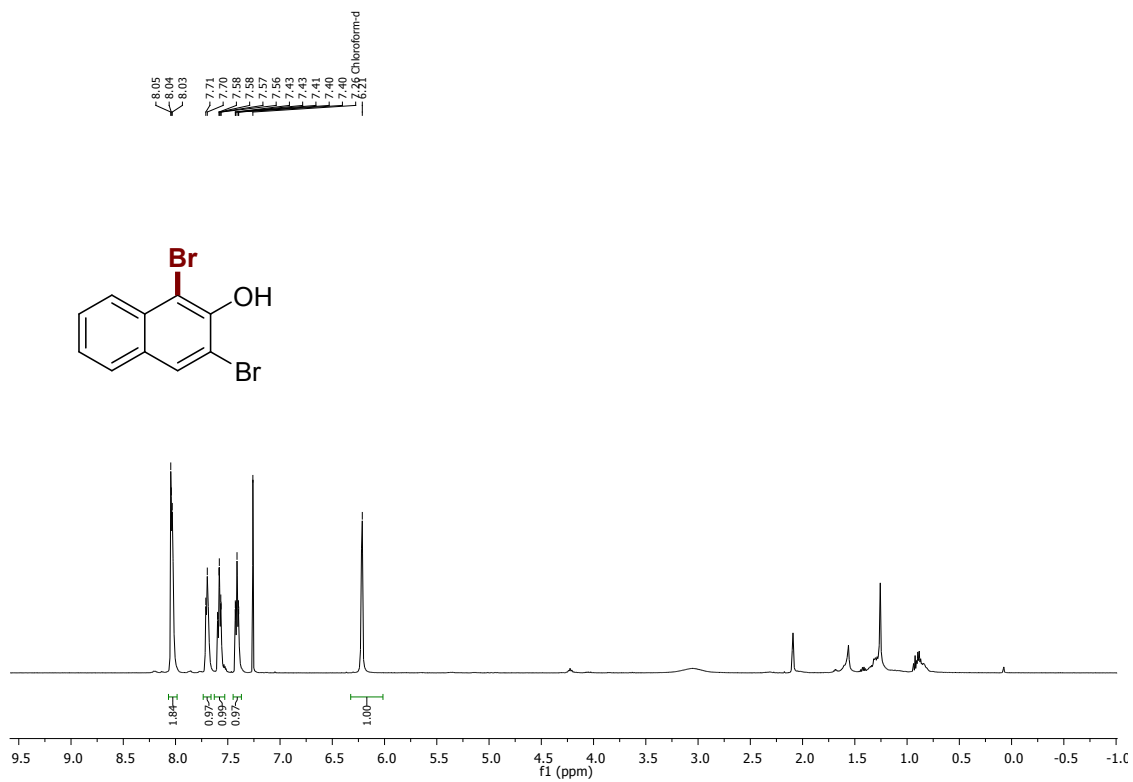
1-bromo-7- methoxynaphthalen-2-ol (**11**)



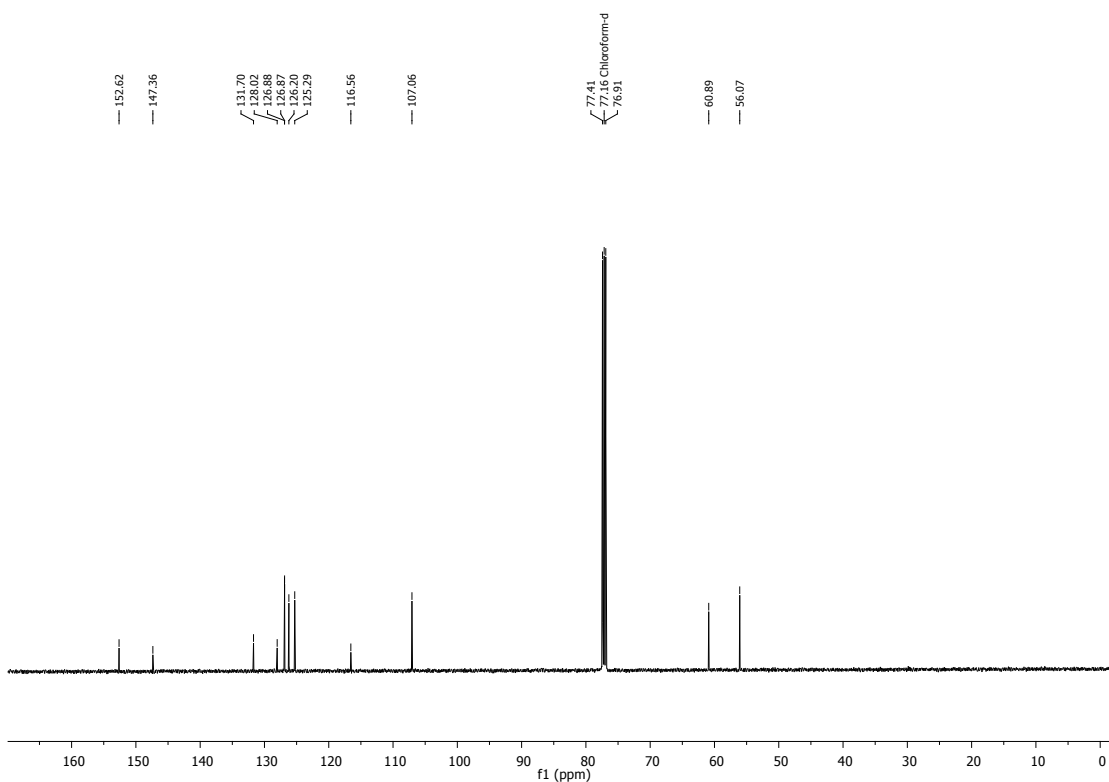
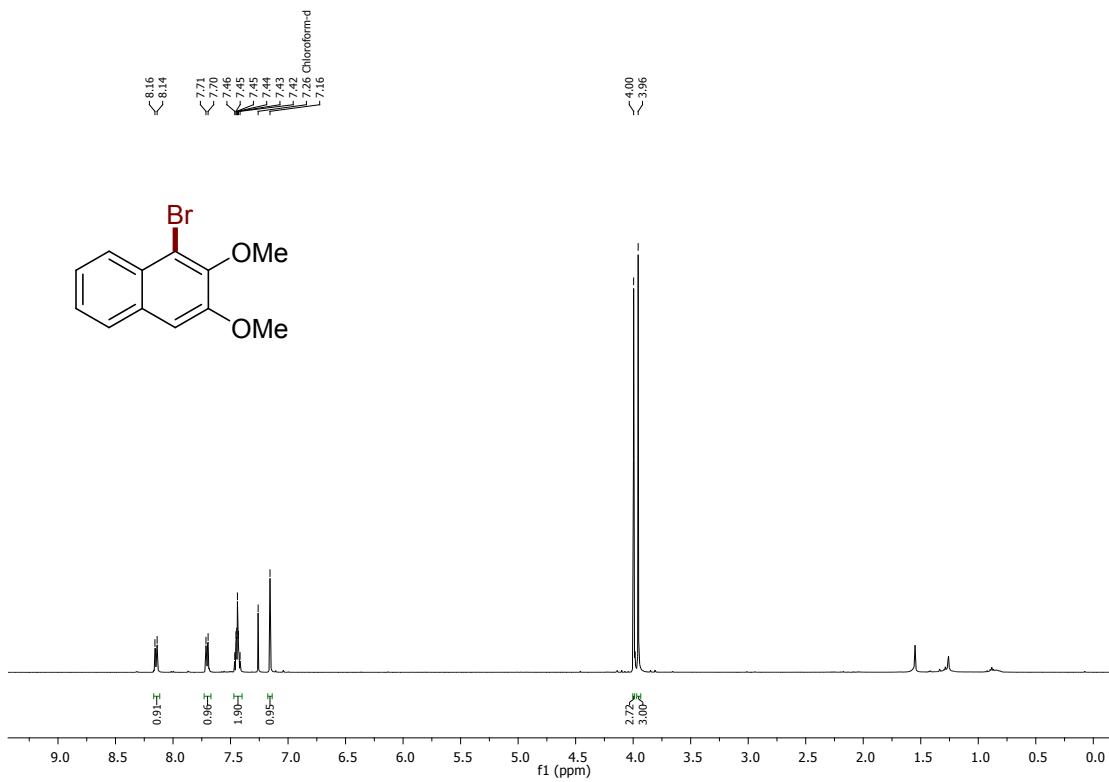
1-Bromo-2,7-methoxynaphthalen (12)



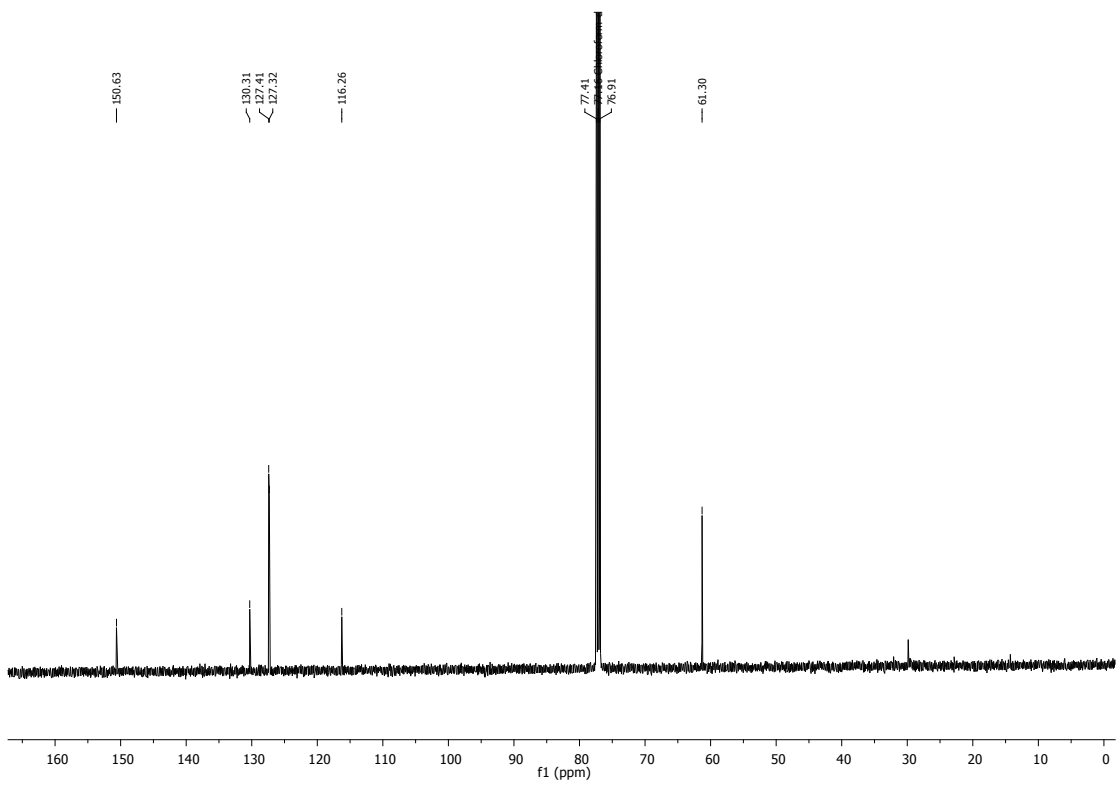
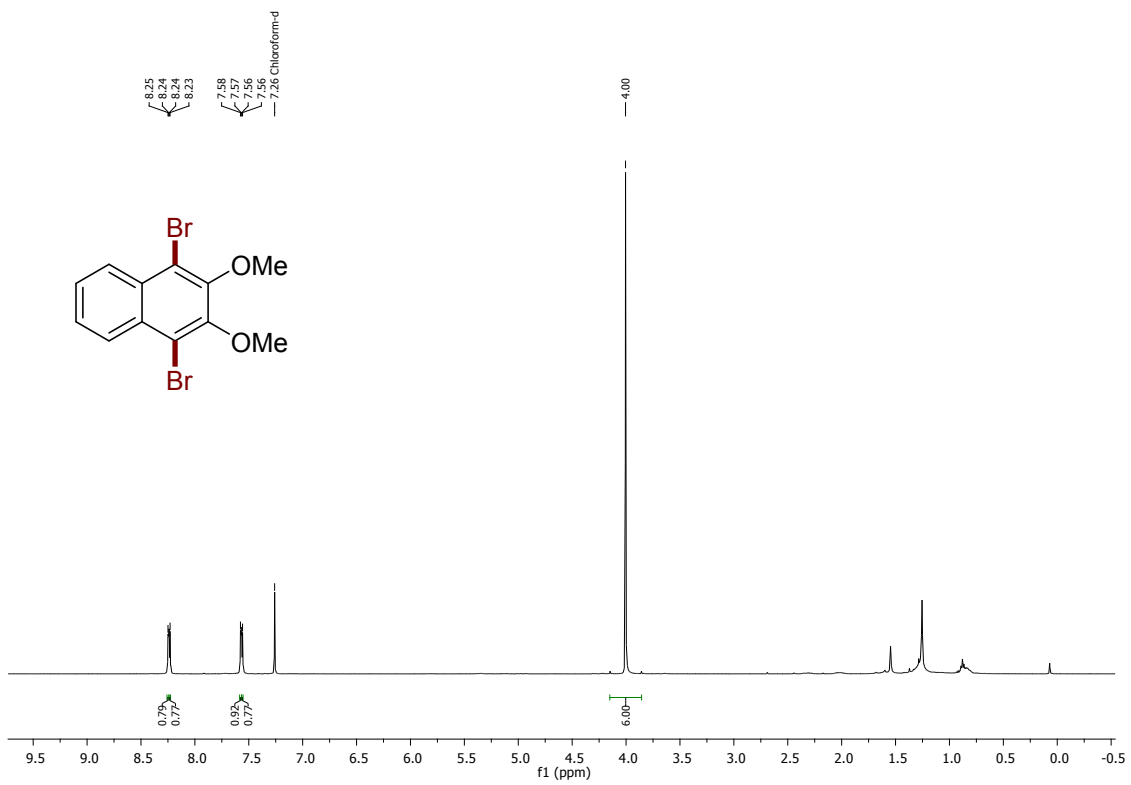
1,3-dibromonaphthalen-2-ol (13)



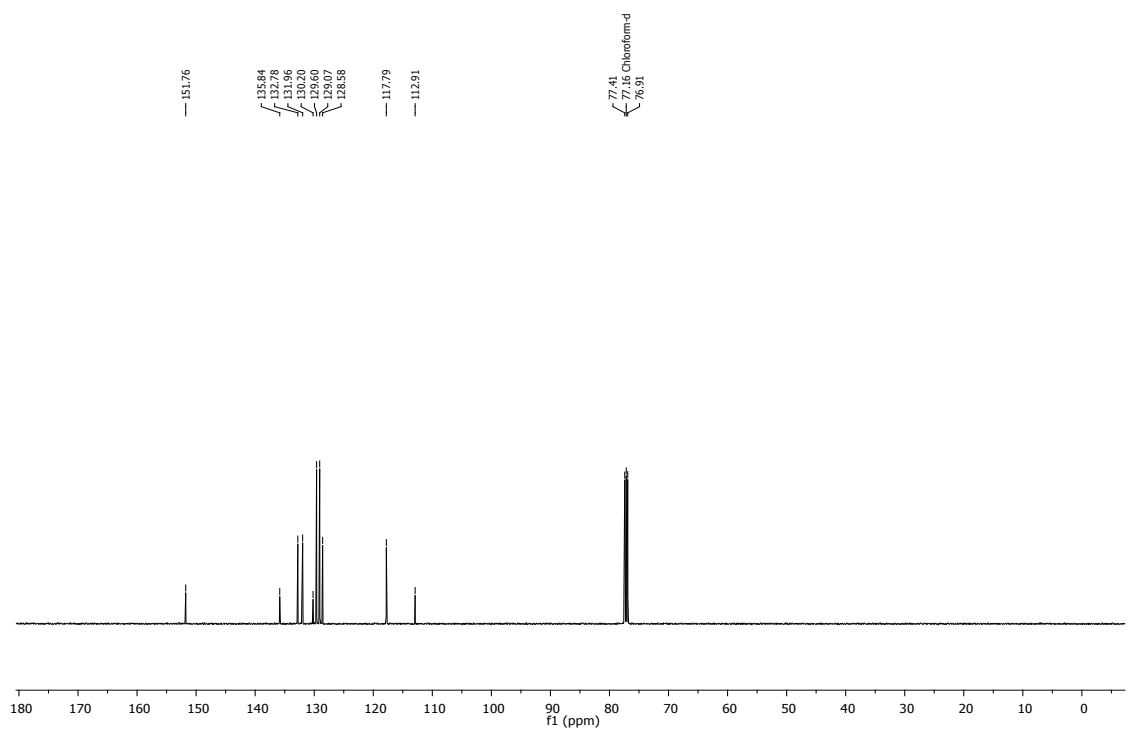
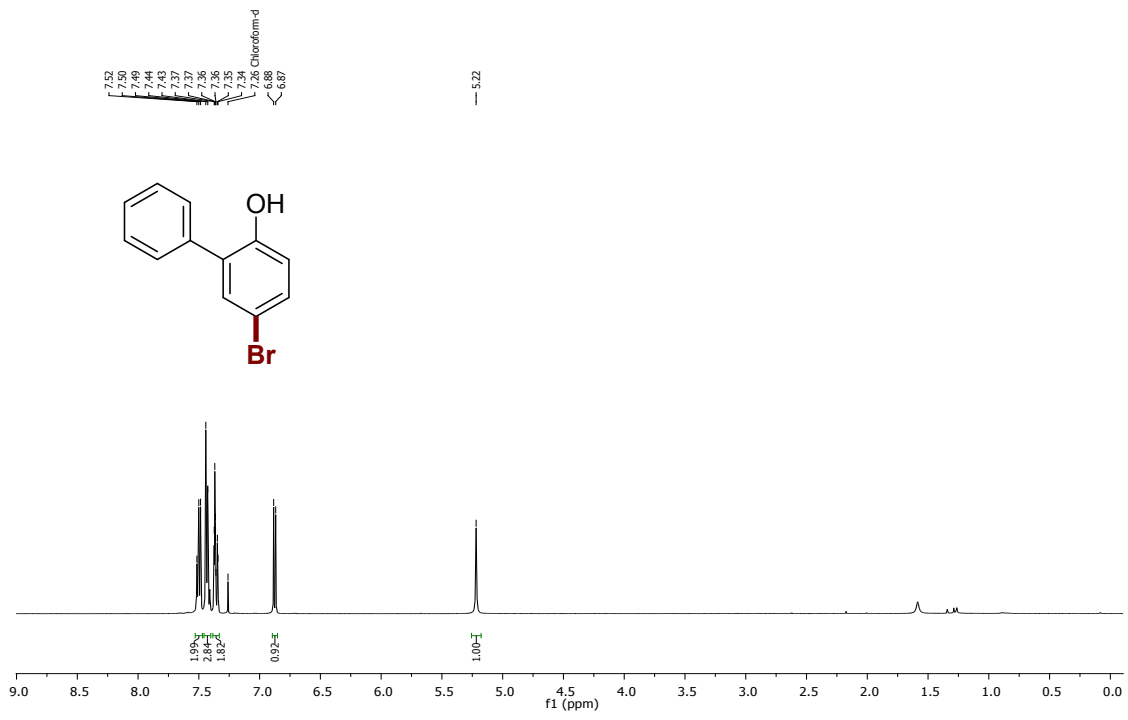
1-bromo-2,3-dimethoxynaphthalene (**14**)



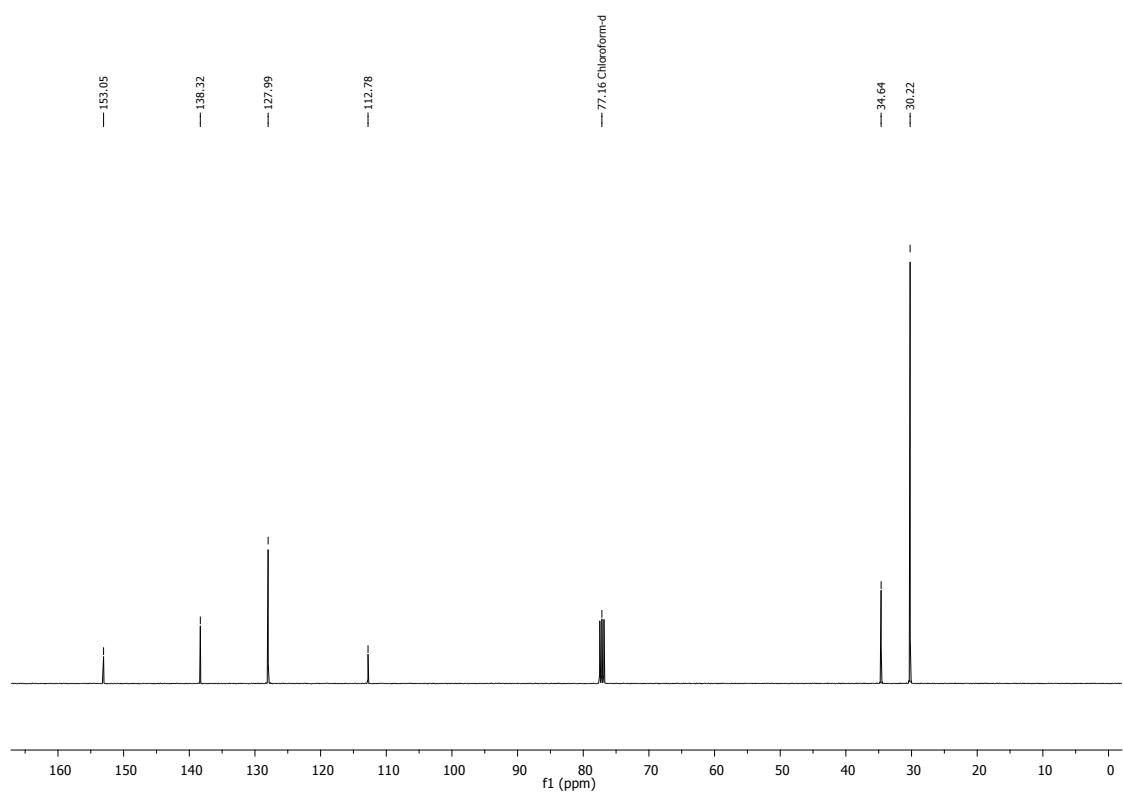
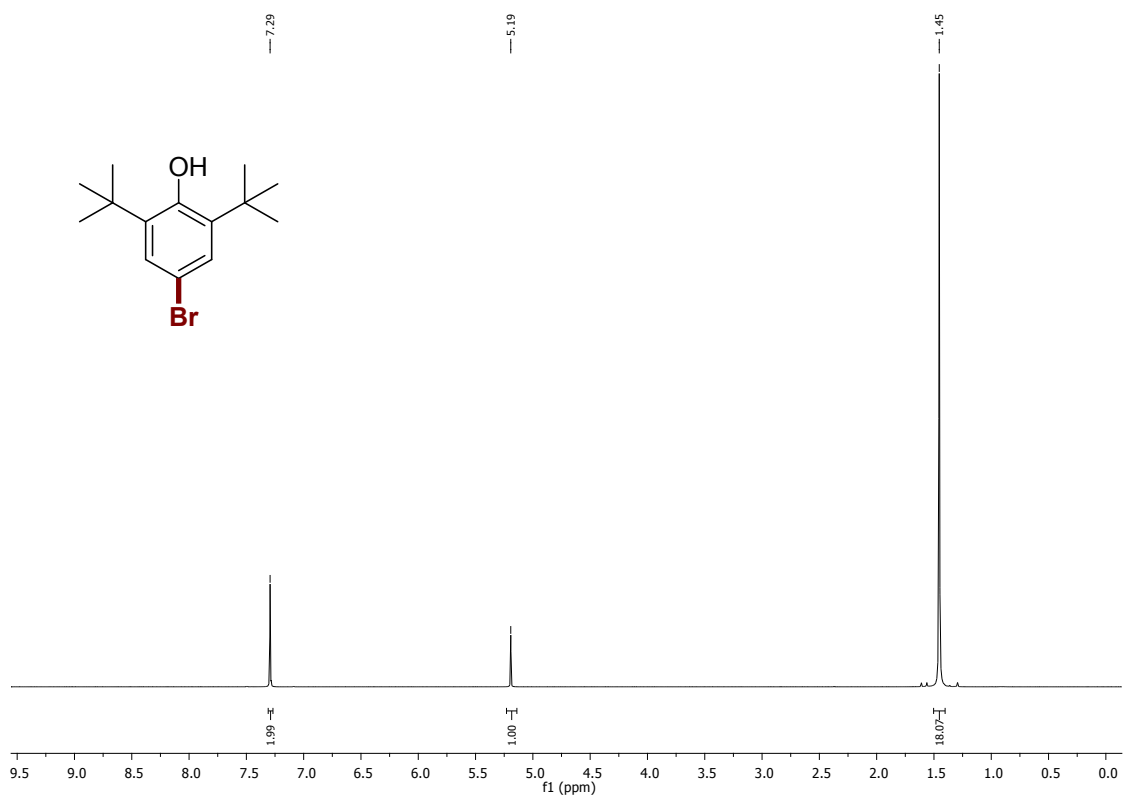
1,4-dibromo-2,3-dimethoxynaphthalene (15)



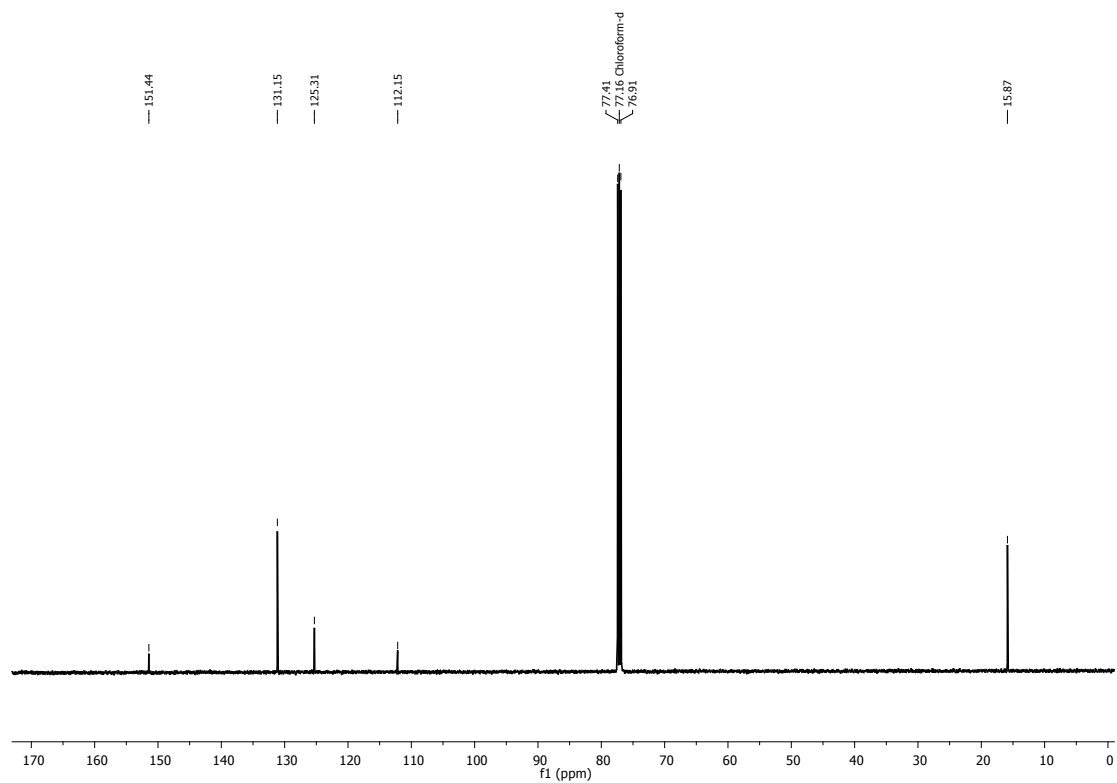
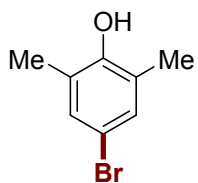
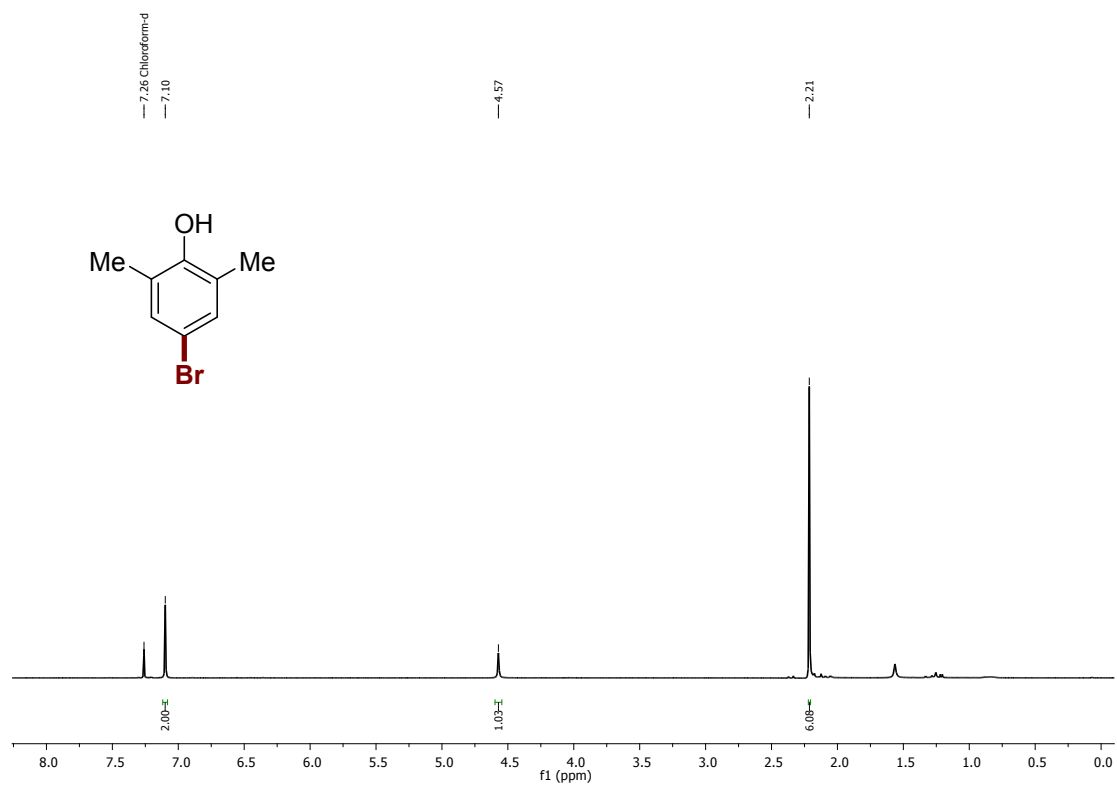
3-bromo-[1,1'-biphenyl]-2-ol (16)



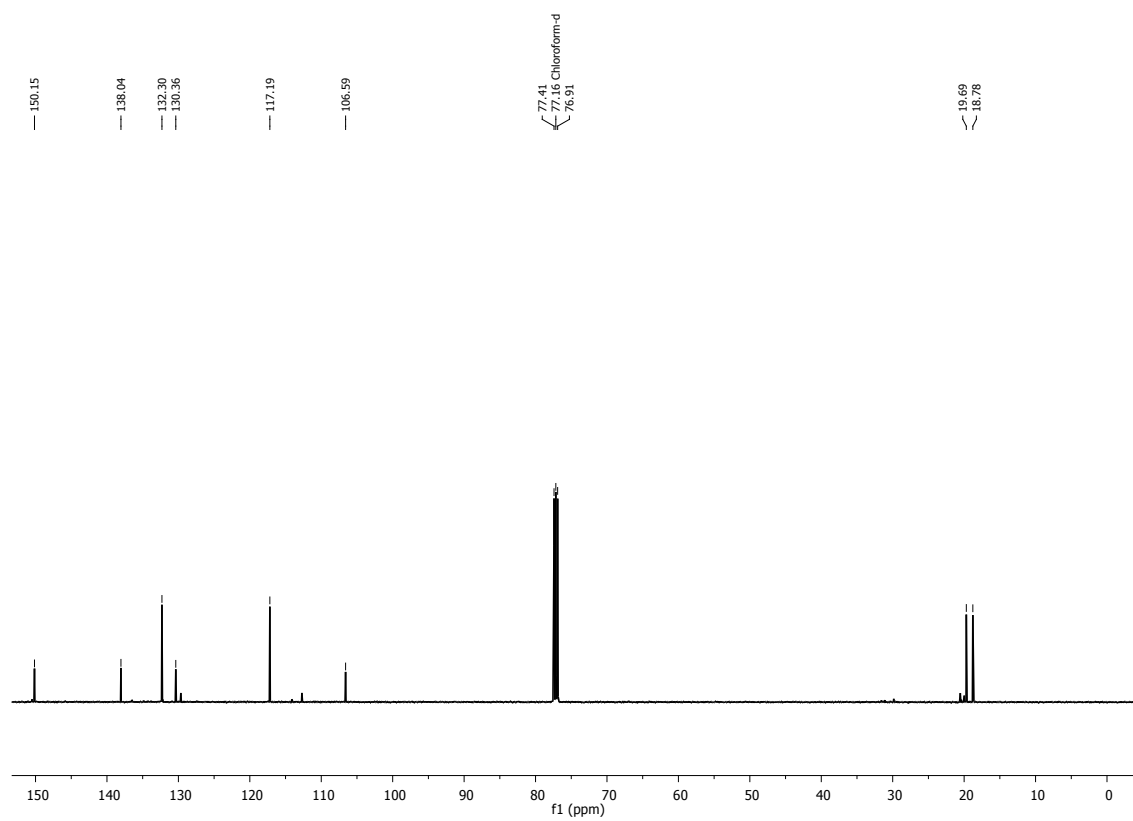
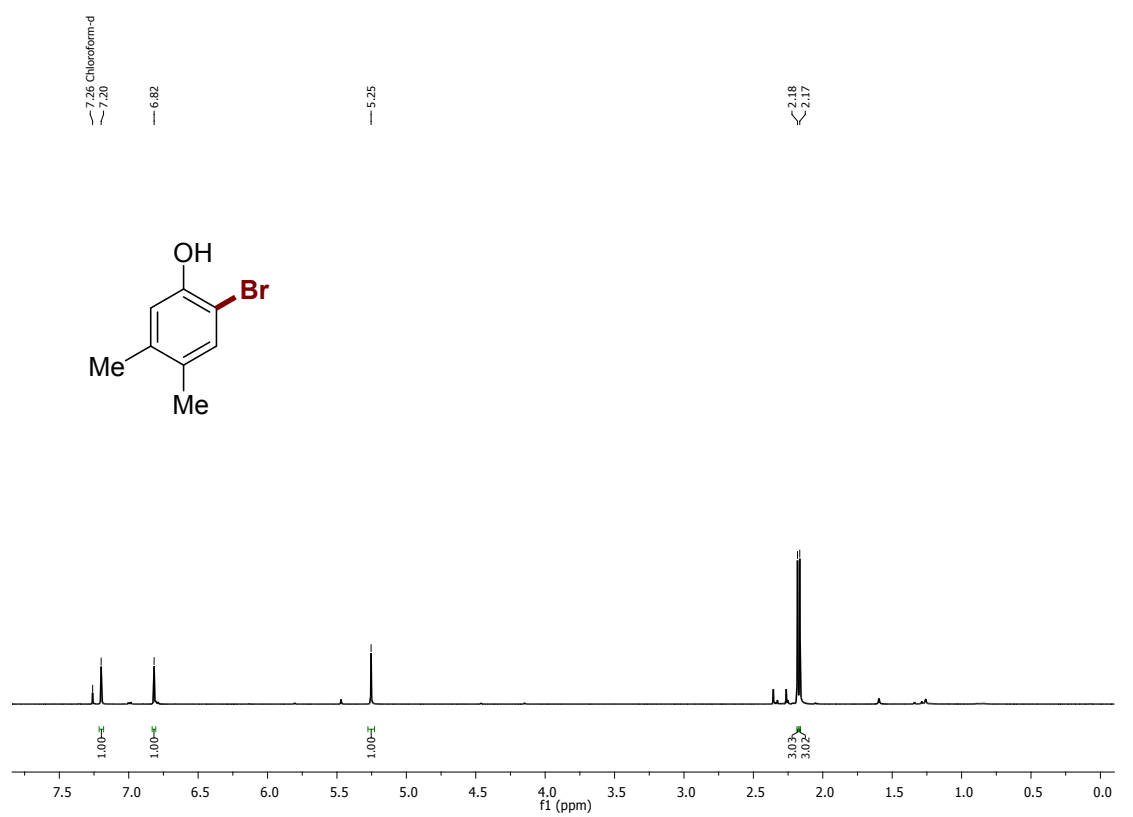
4-bromo-2,6-di-tert-butylphenol (17)



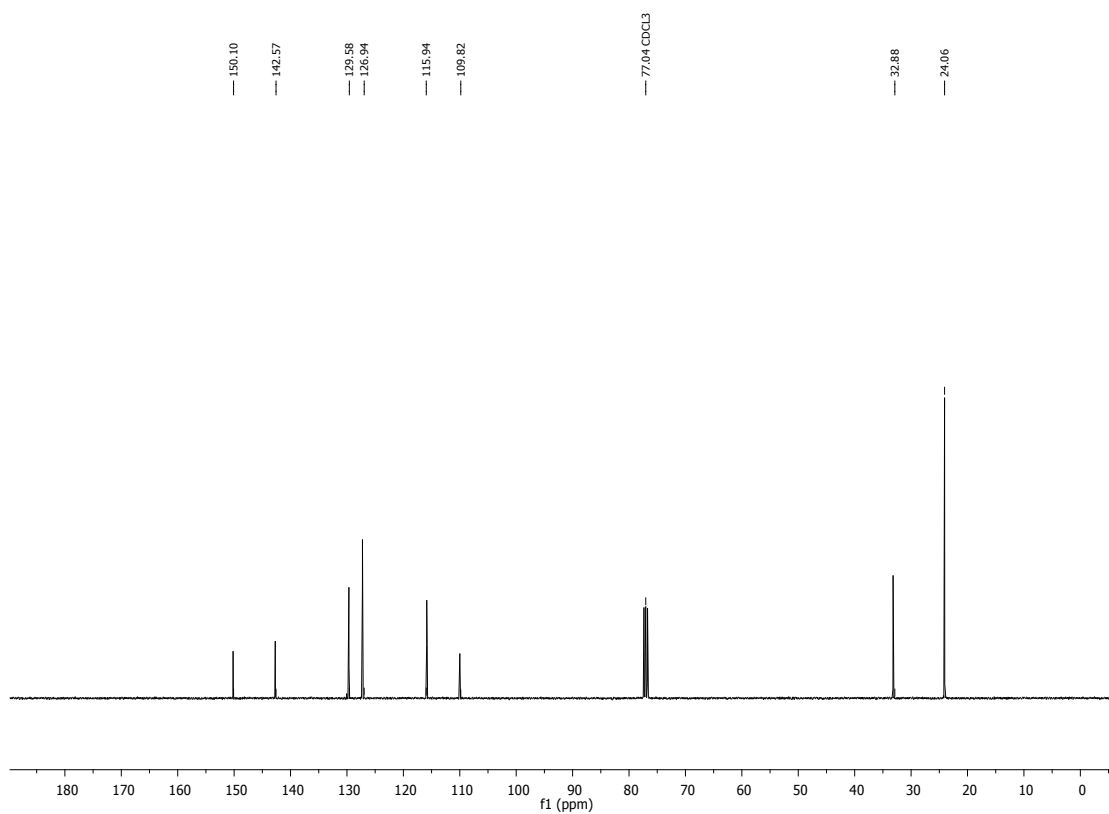
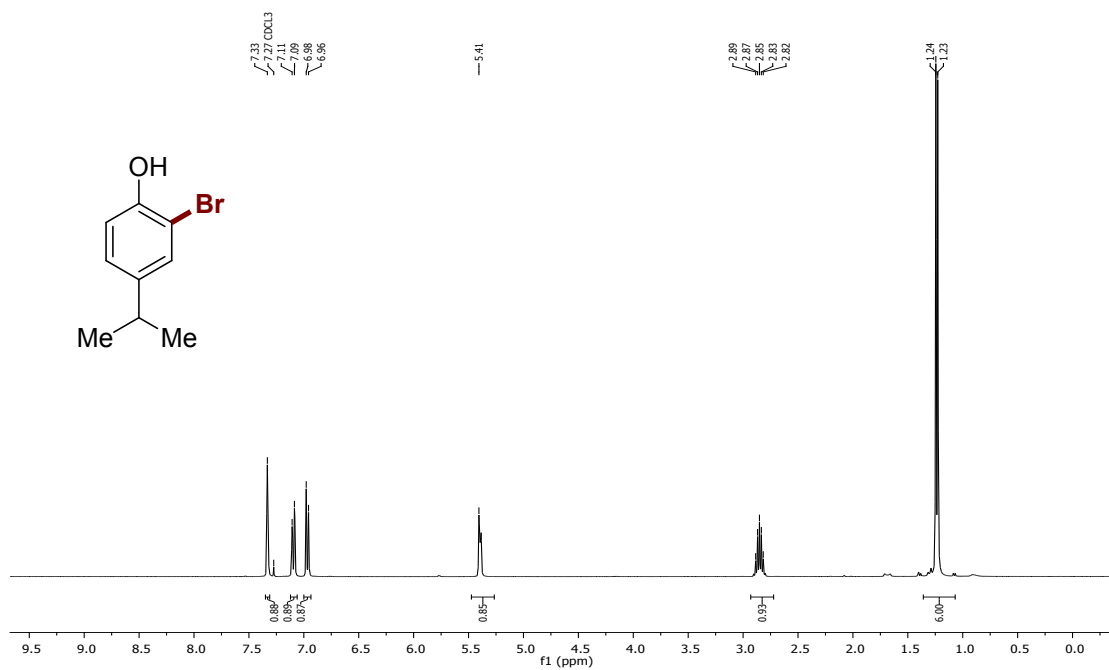
4-bromo-2,6-dimethylphenol (**18**)



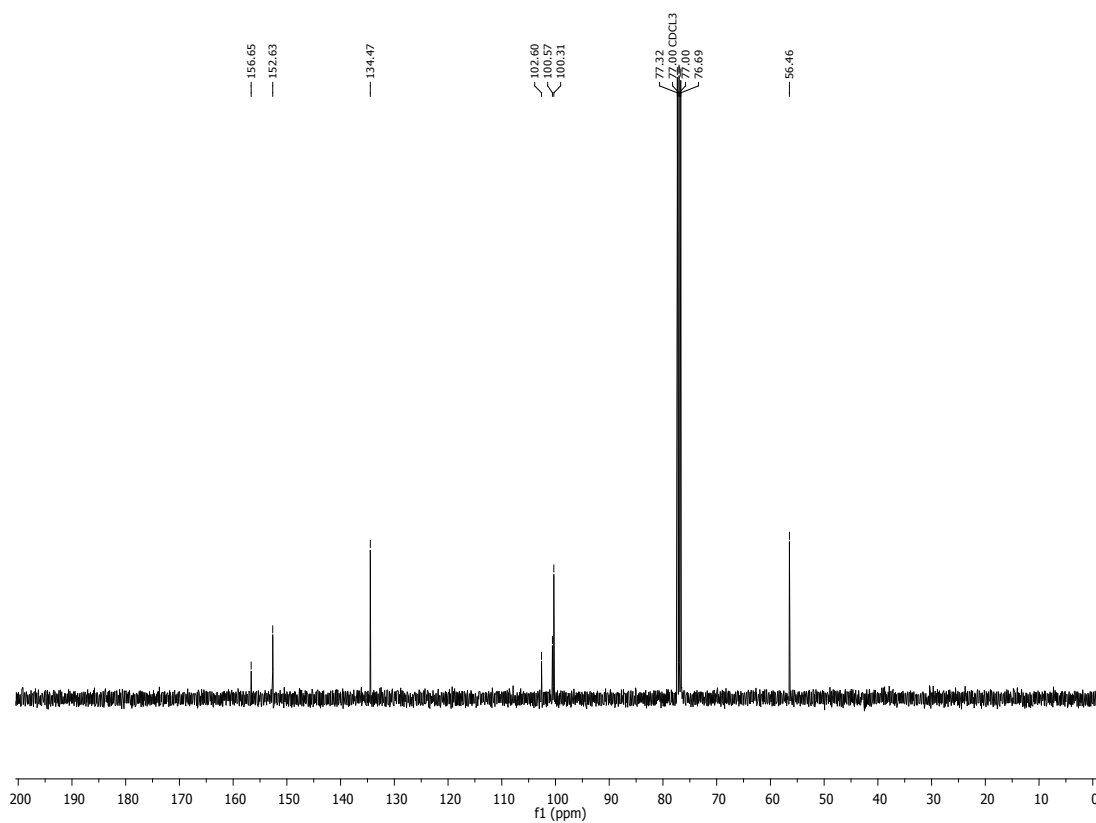
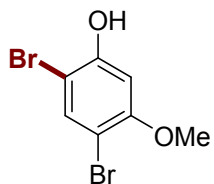
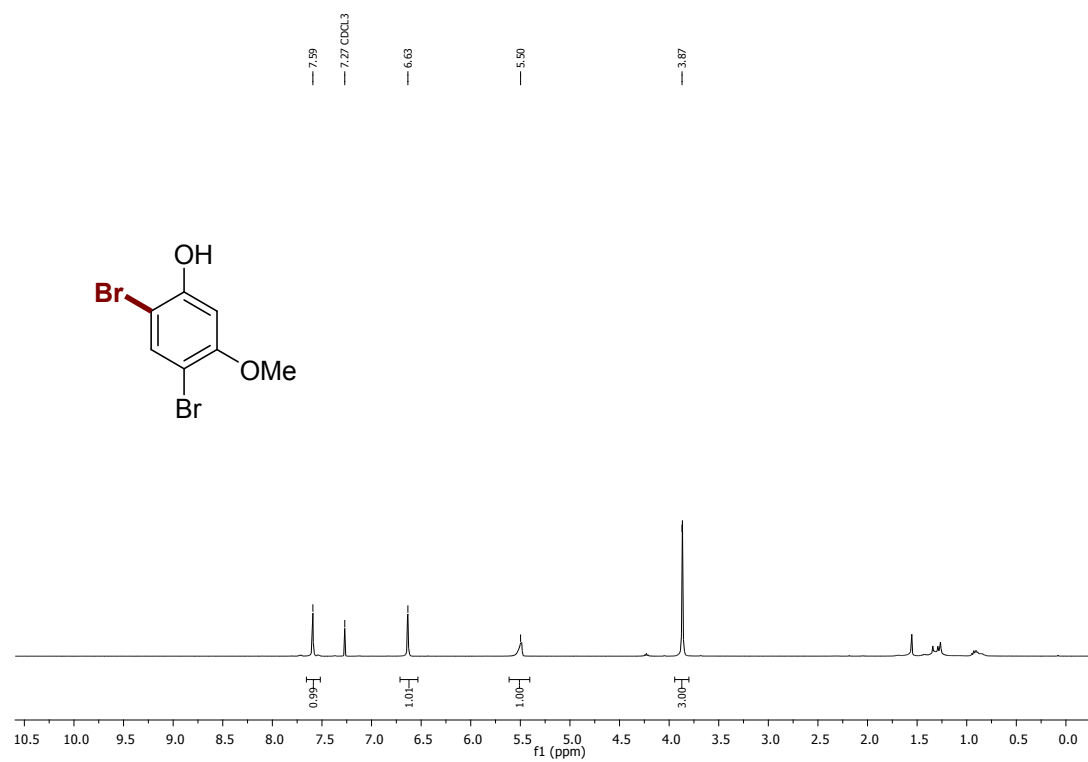
2-bromo-4,5-dimethylphenol (19)



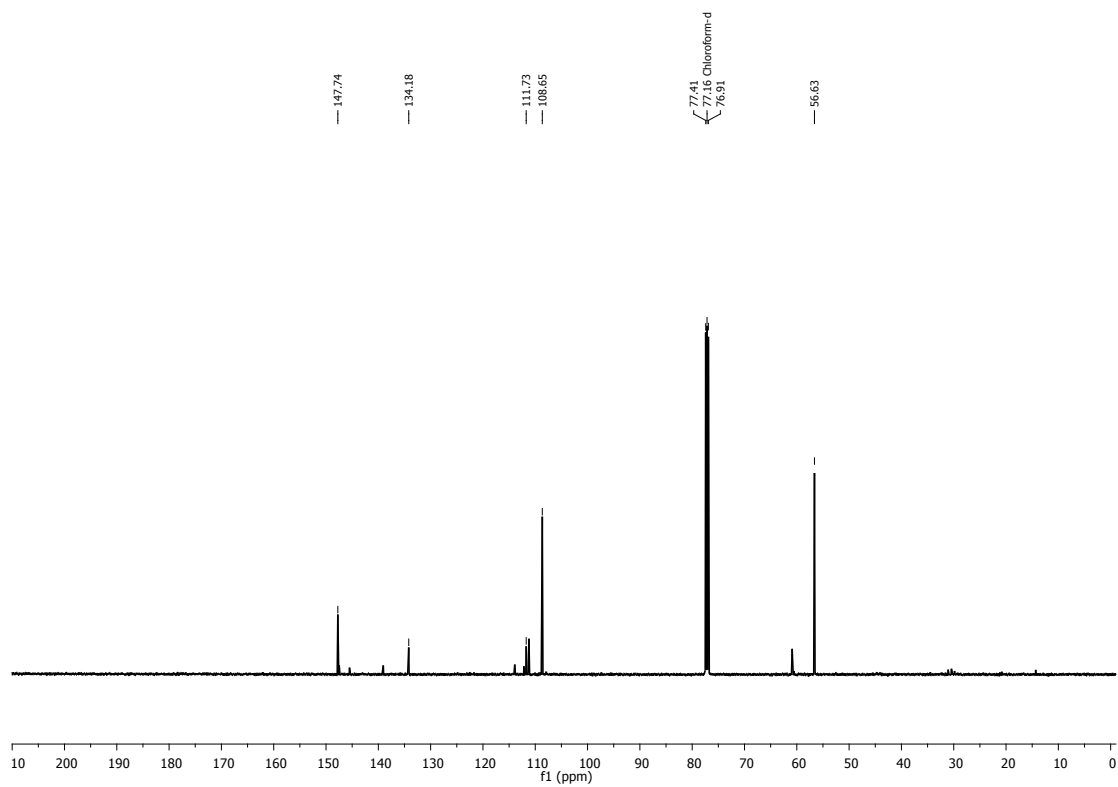
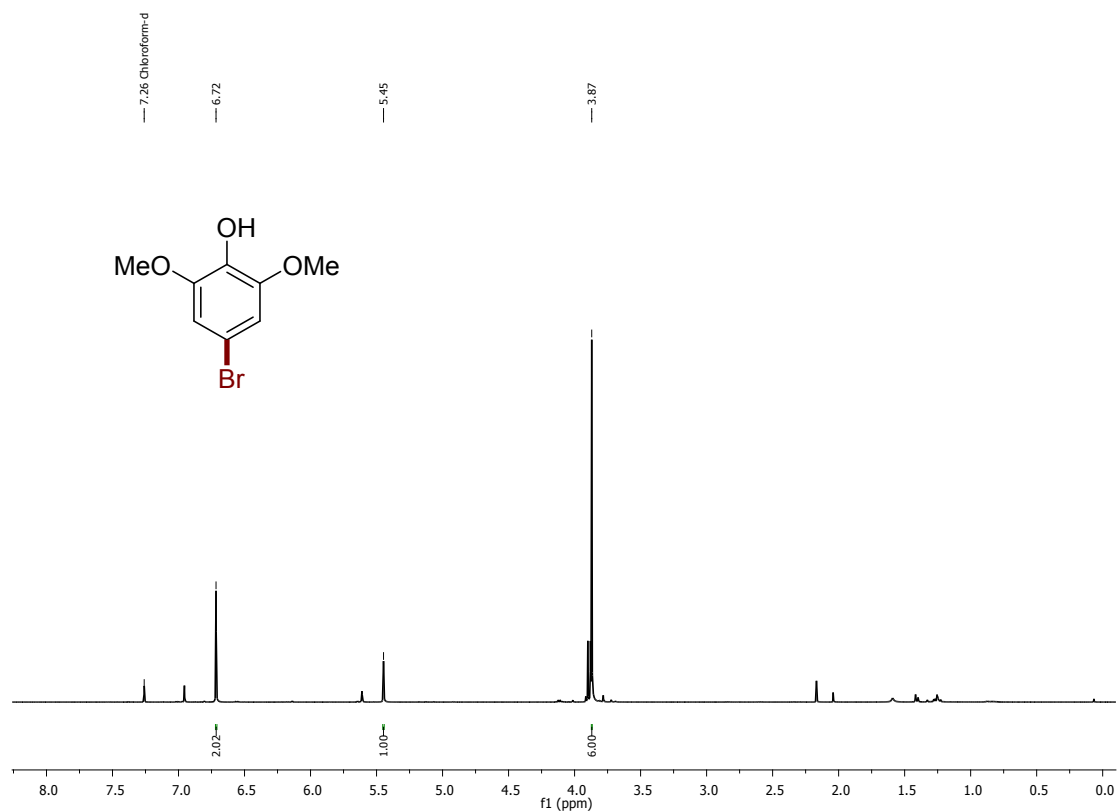
2-bromo-4-isopropylphenol (20)



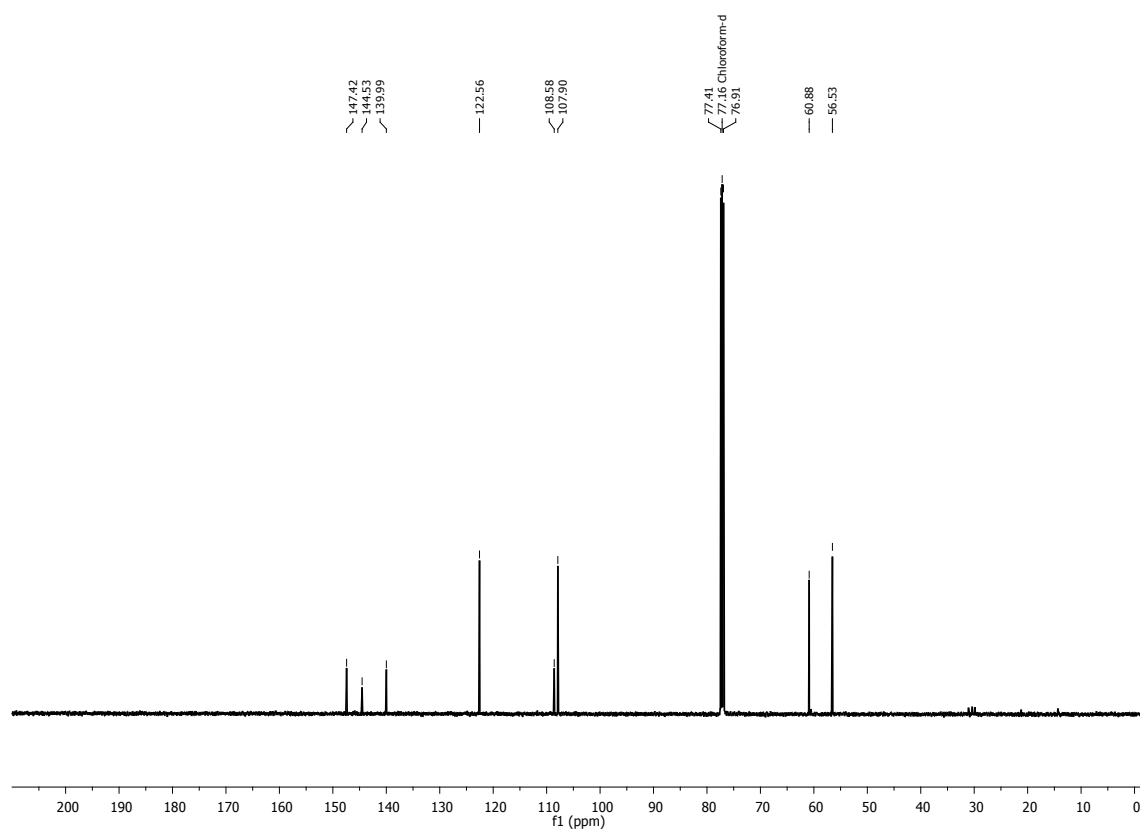
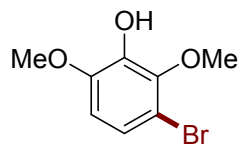
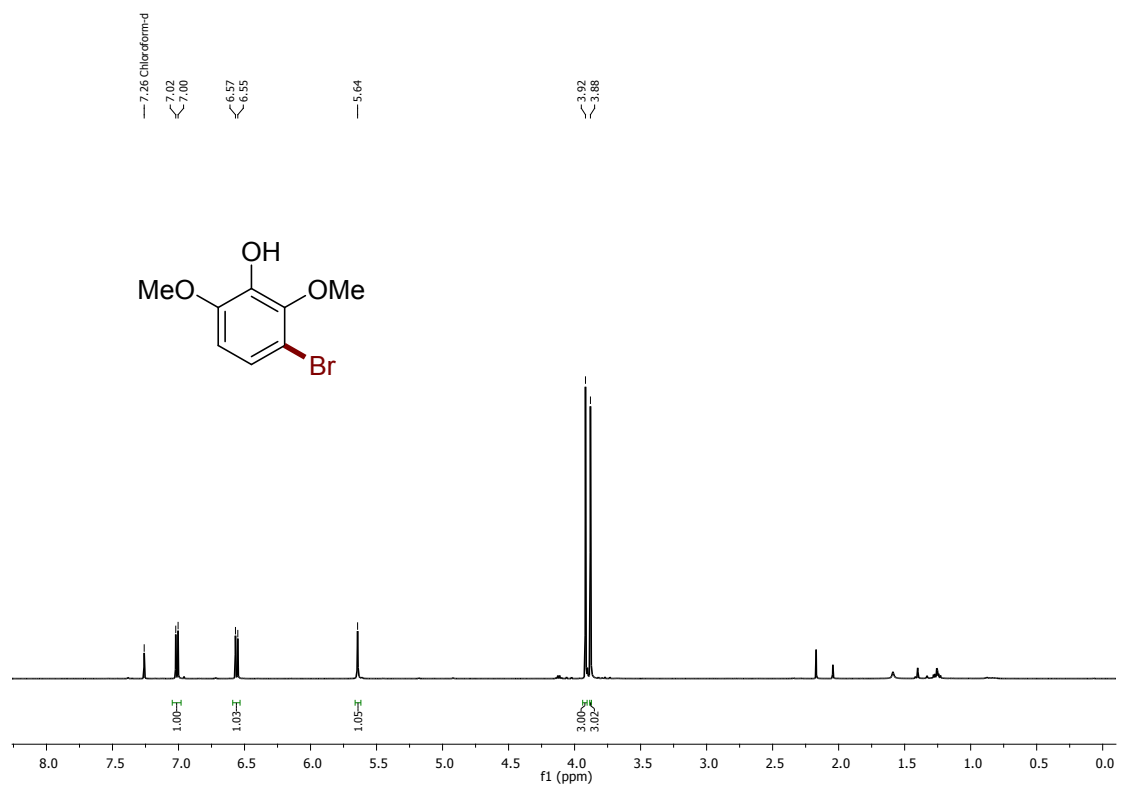
2,4-dibromo-5-methoxyphenol (**21**)



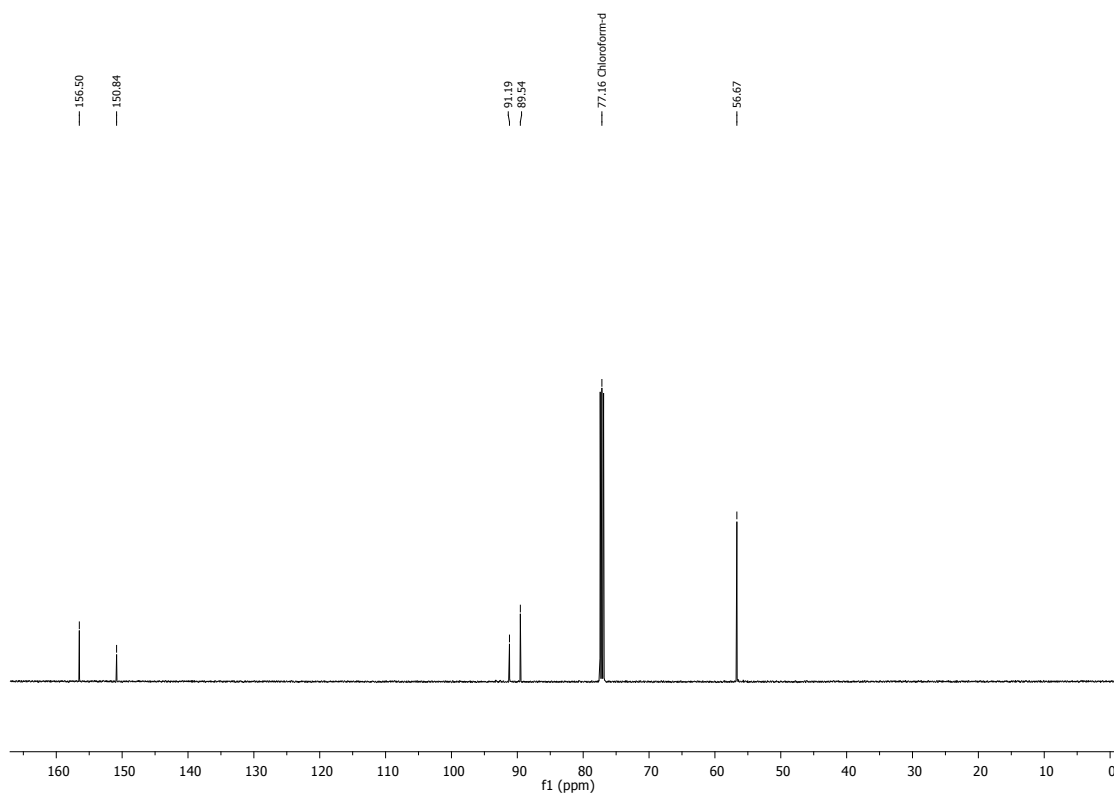
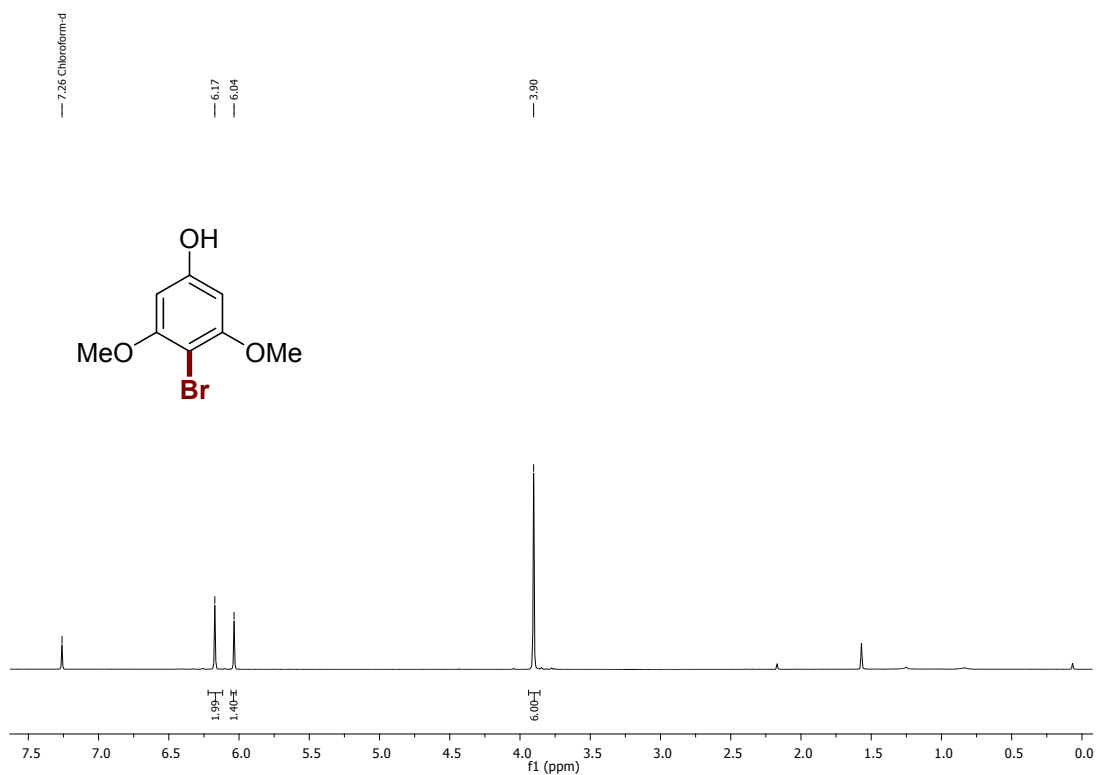
4-bromo-2,6-dimethoxyphenol (22)



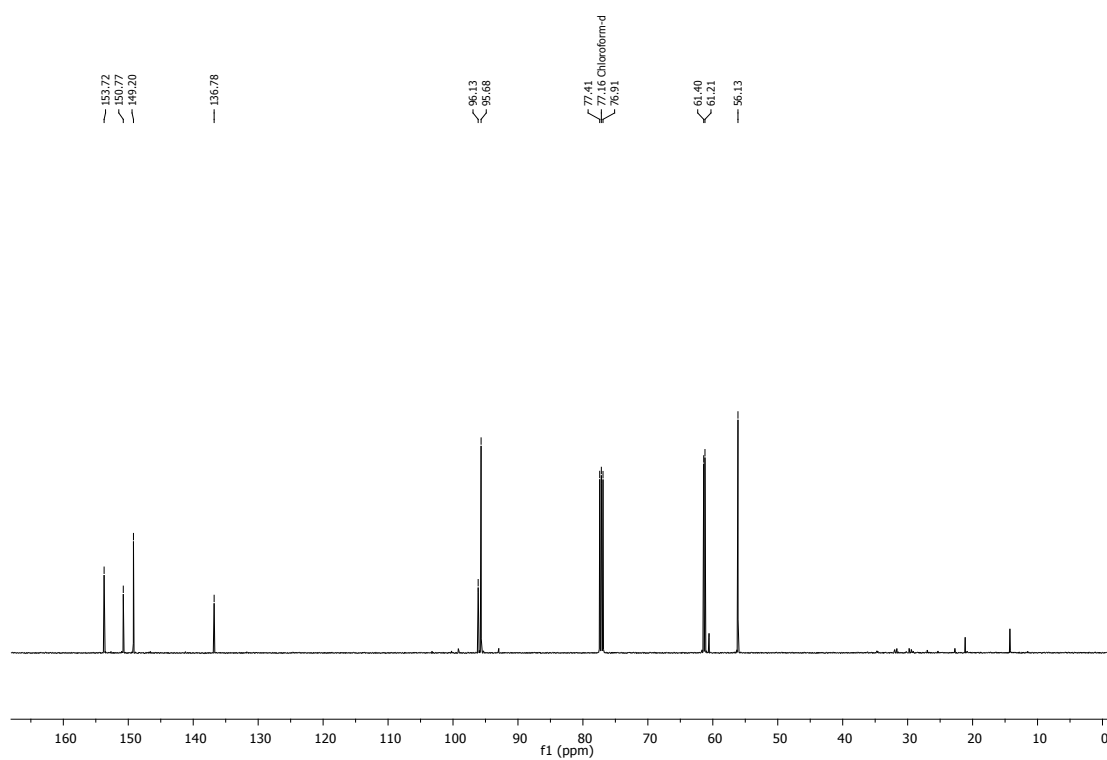
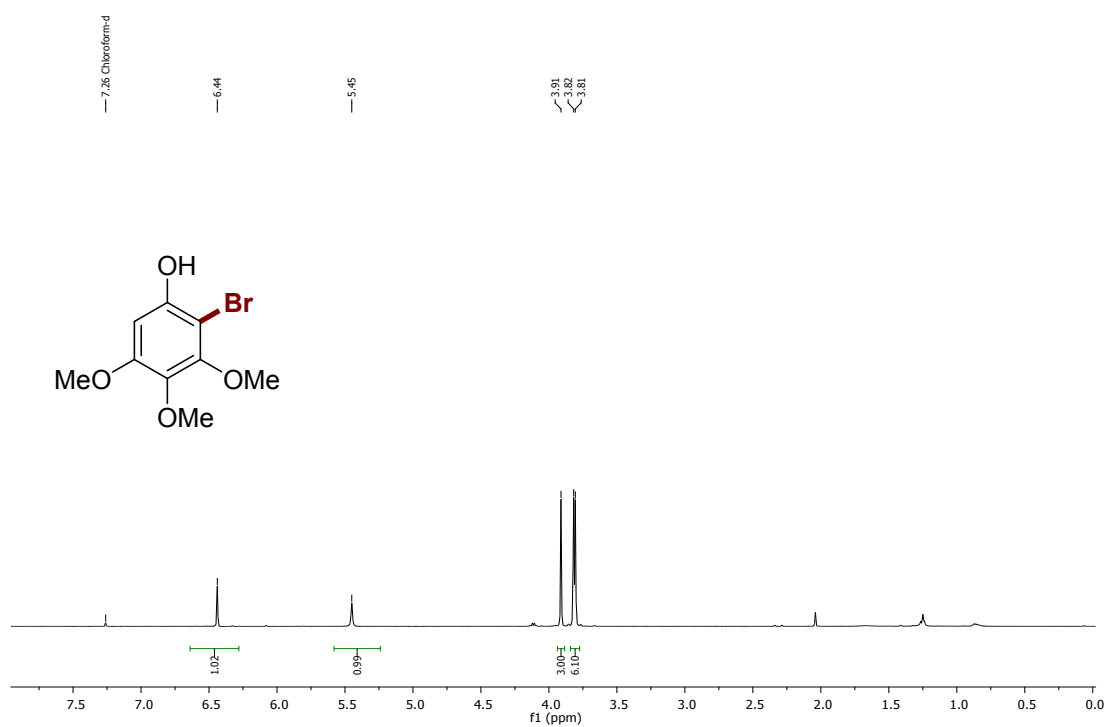
3-bromo-2,6-dimethoxyphenol (**23**)



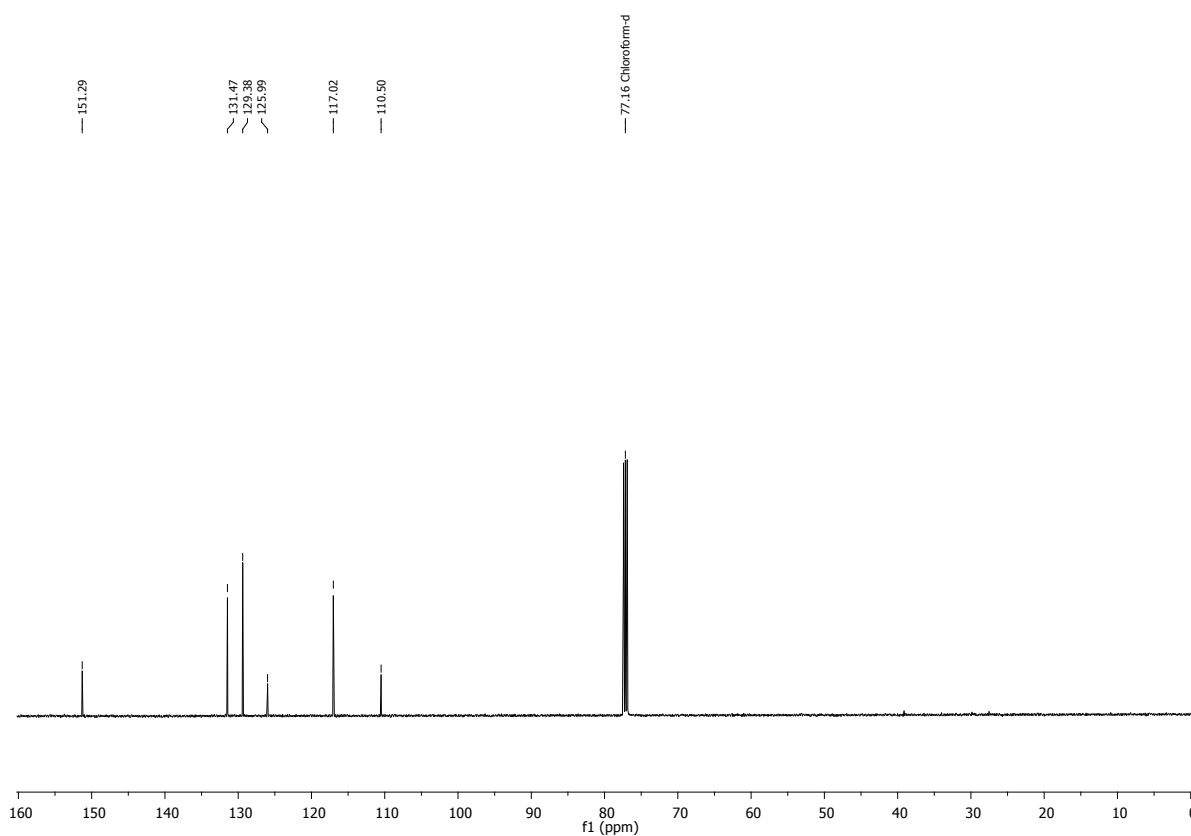
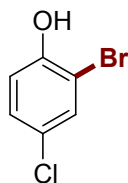
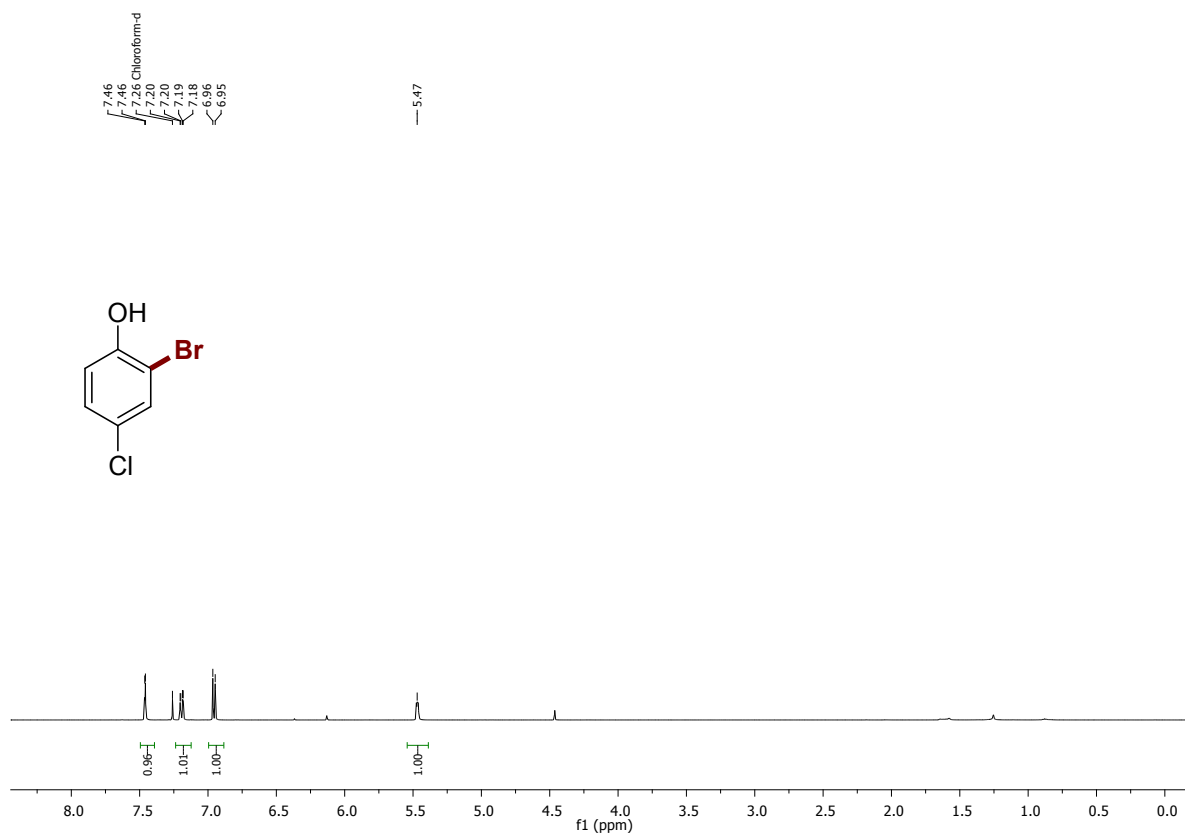
4-bromo-3,5-dimethoxyphenol (**24**)



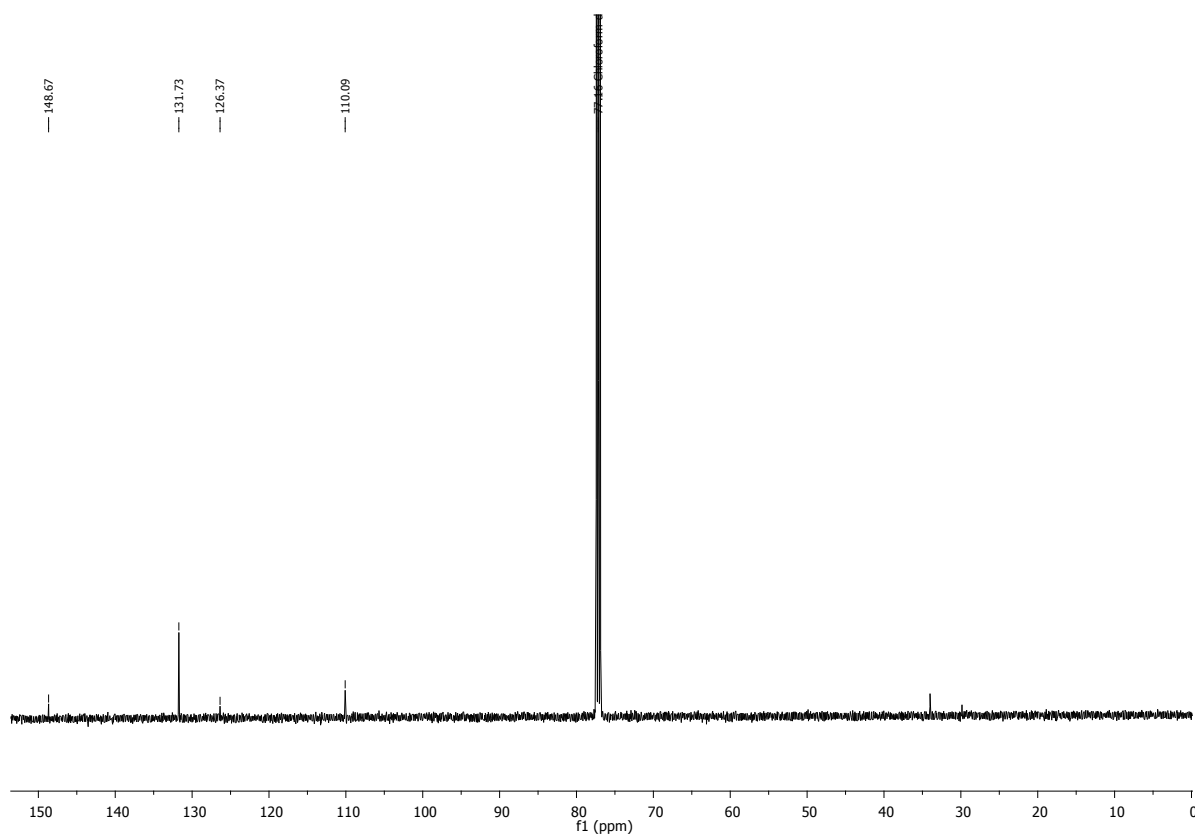
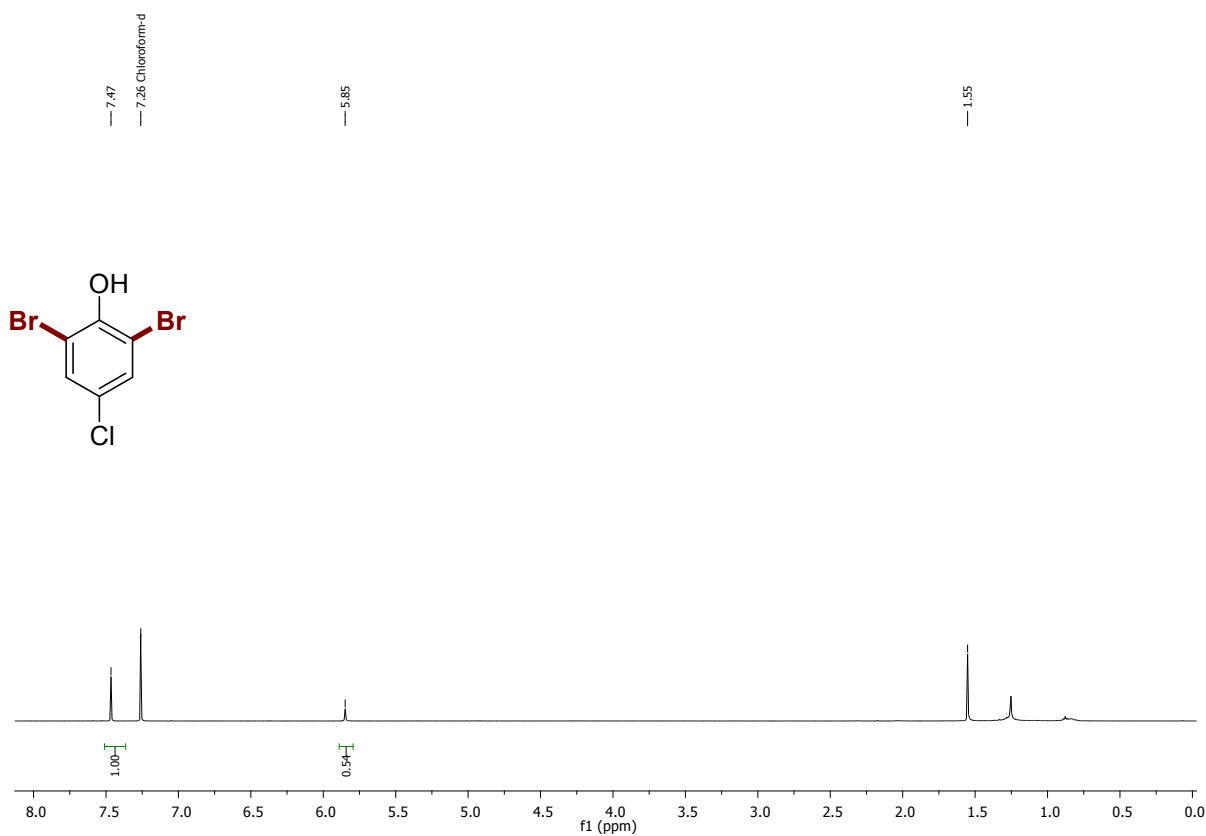
2-bromo-3,4,5-trimethoxyphenol (**25**)



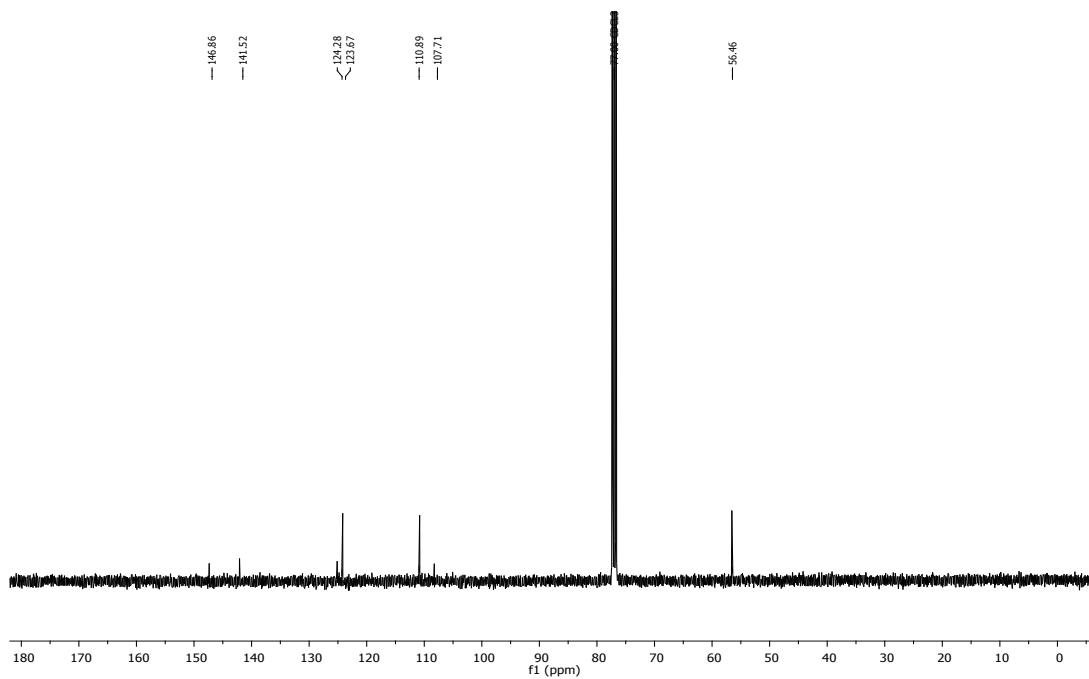
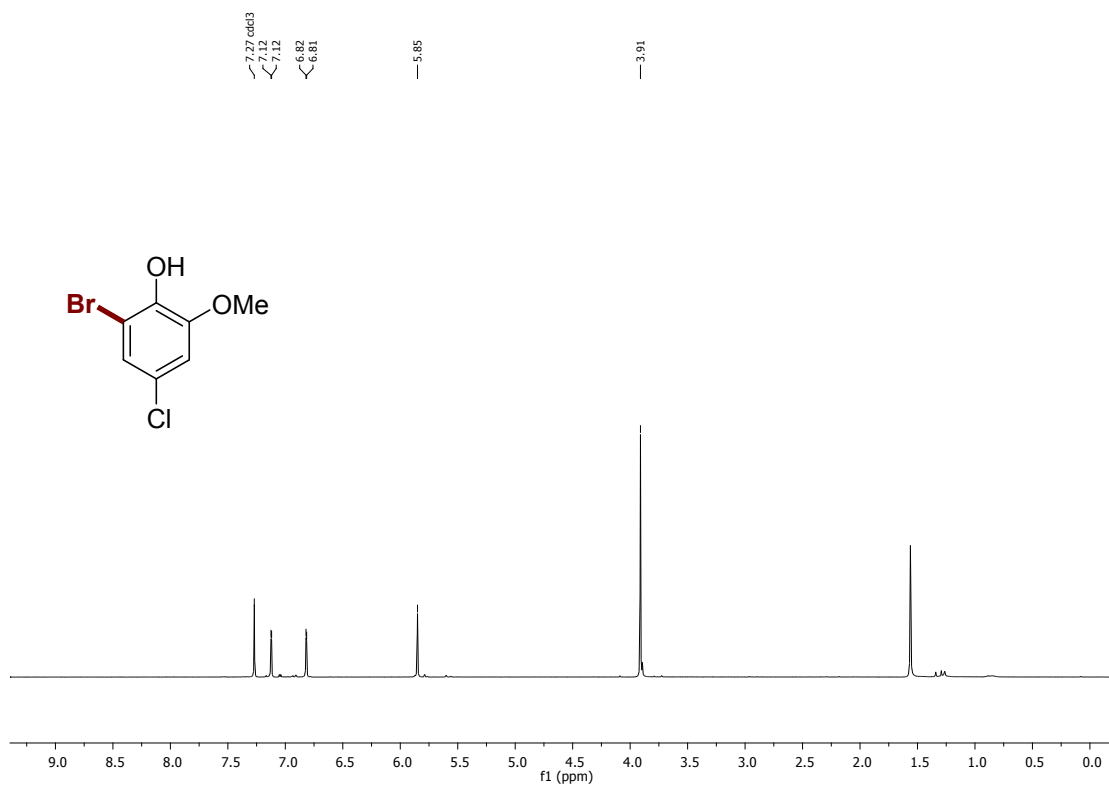
2-bromo-4-chlorophenol (26)



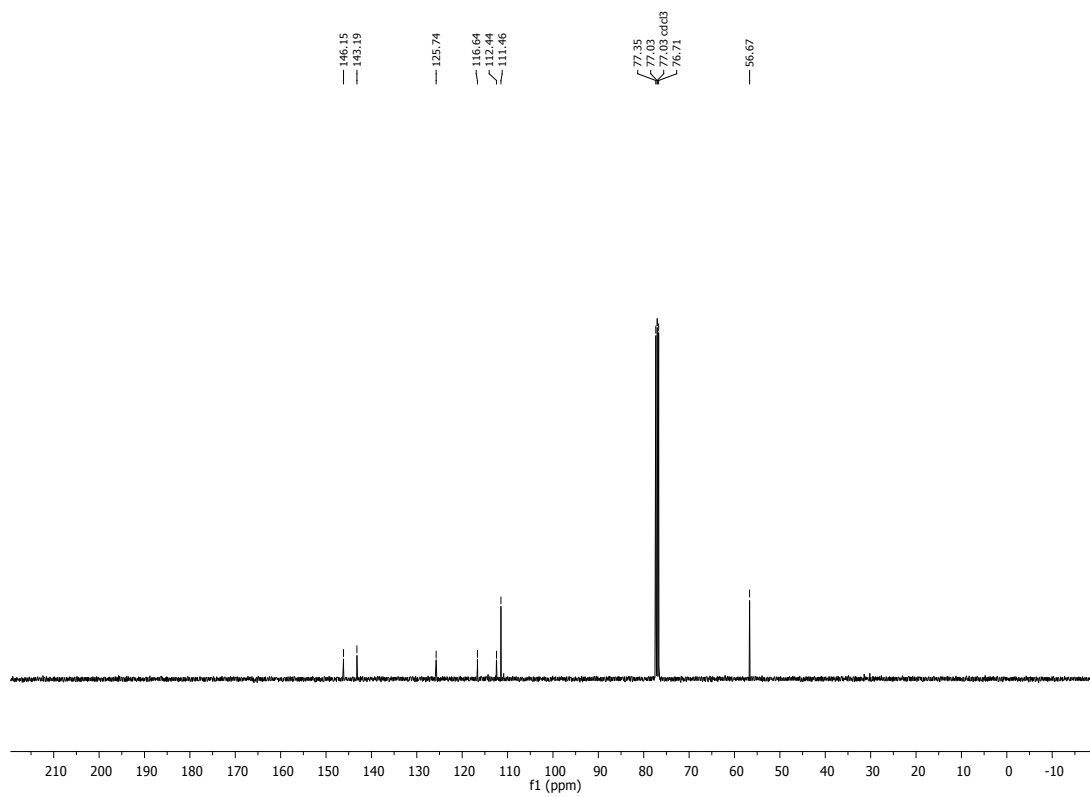
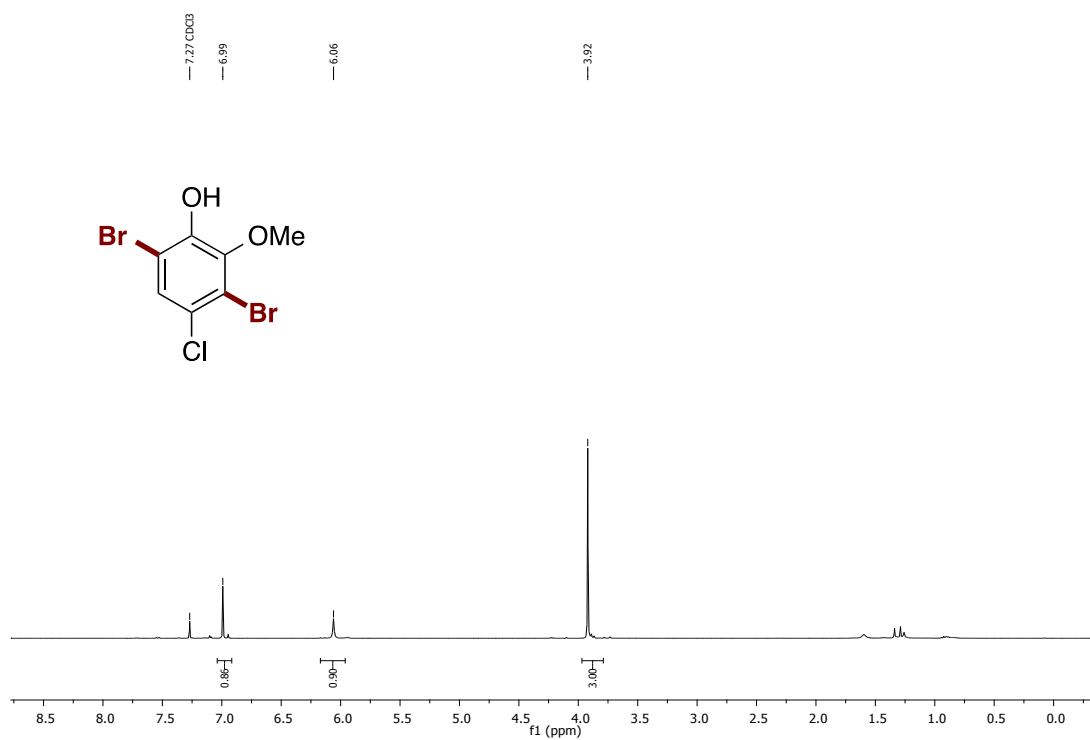
2,6-dibromo-4-chlorophenol (27)



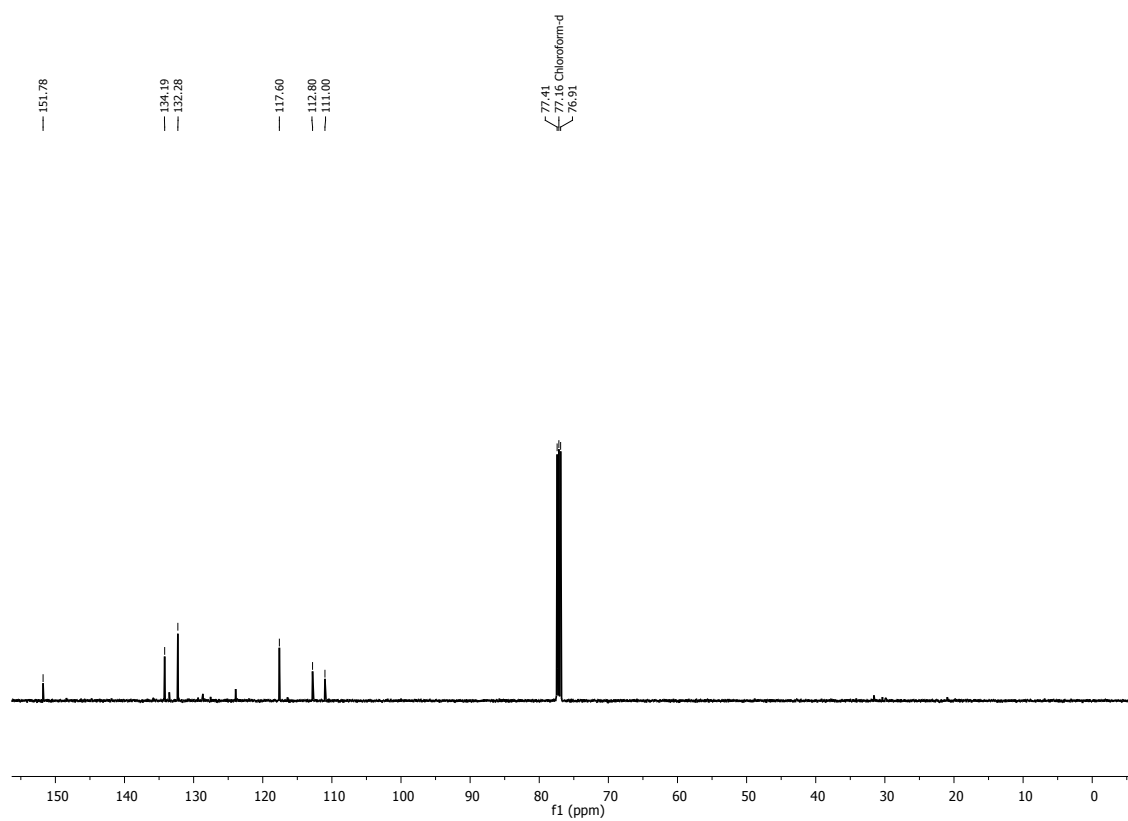
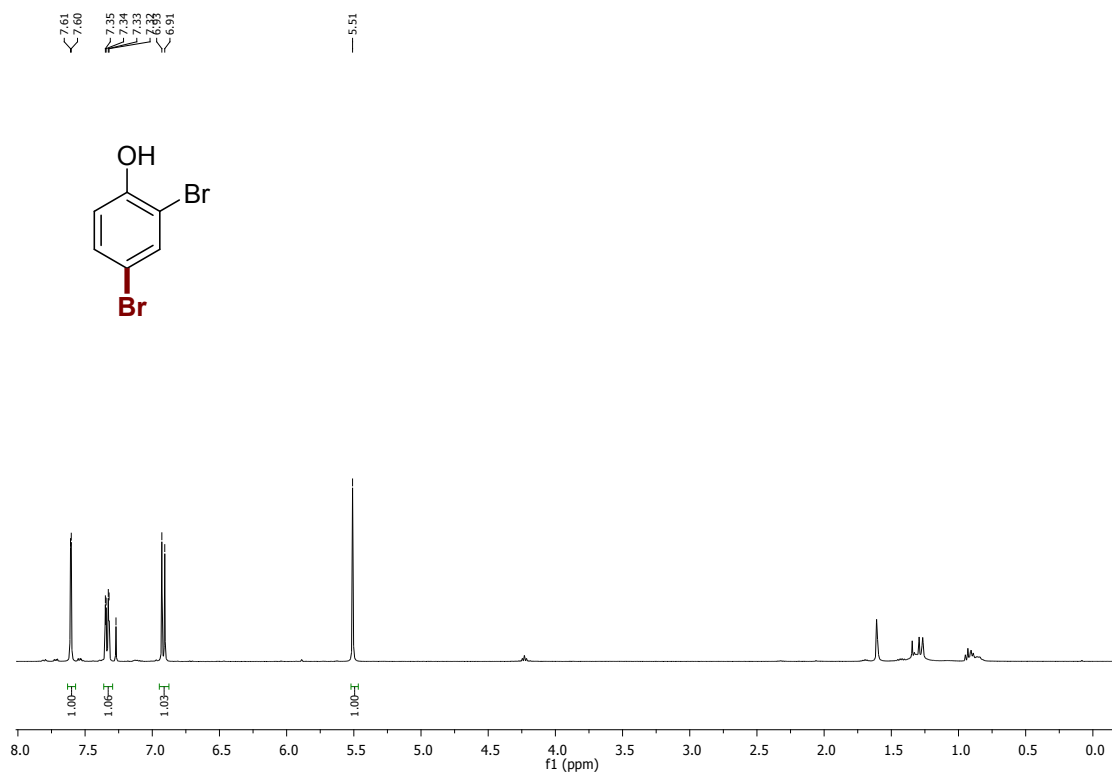
2-bromo-4-chloro-6-methoxyphenol (**28**)



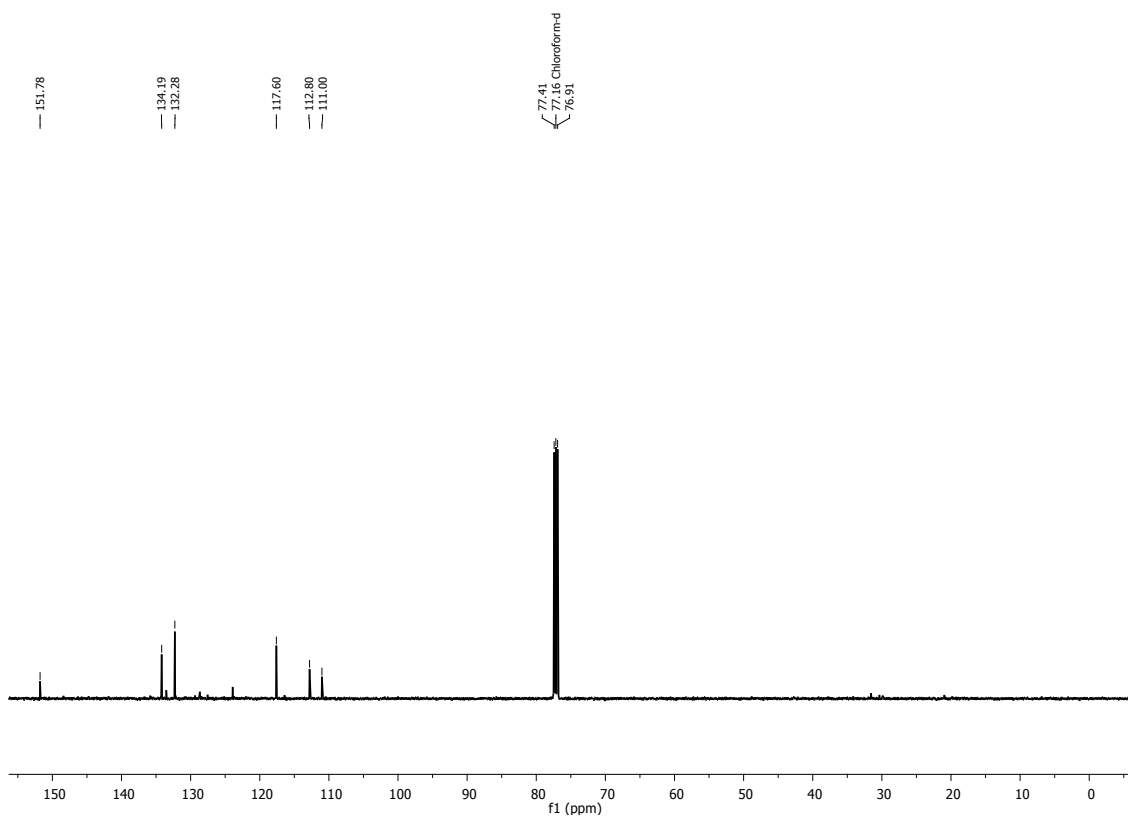
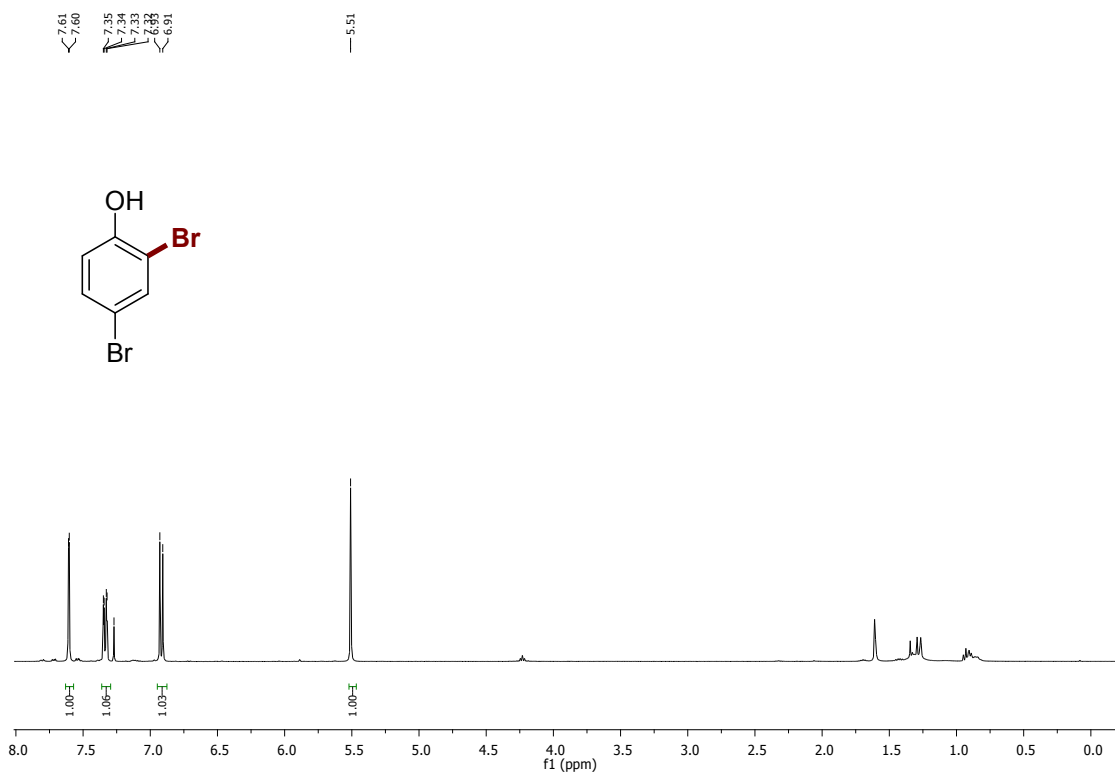
3,6-dibromo-4-chloro-2-methoxyphenol (29)



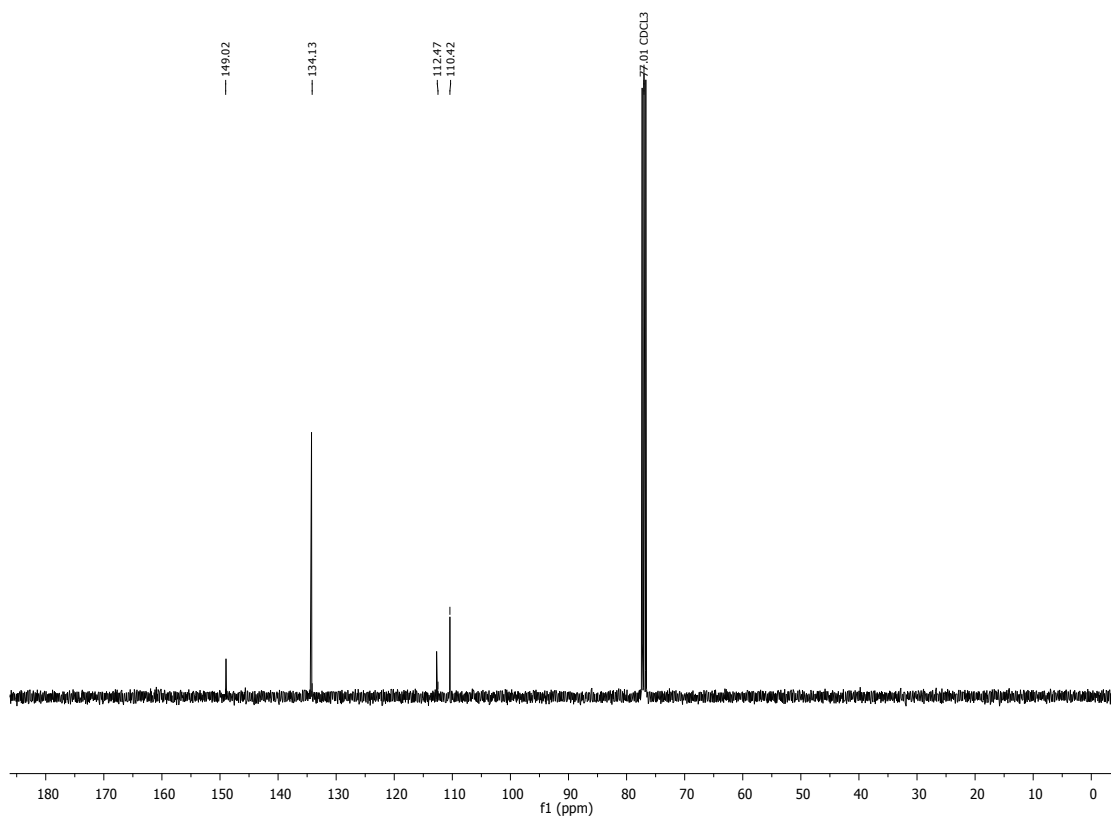
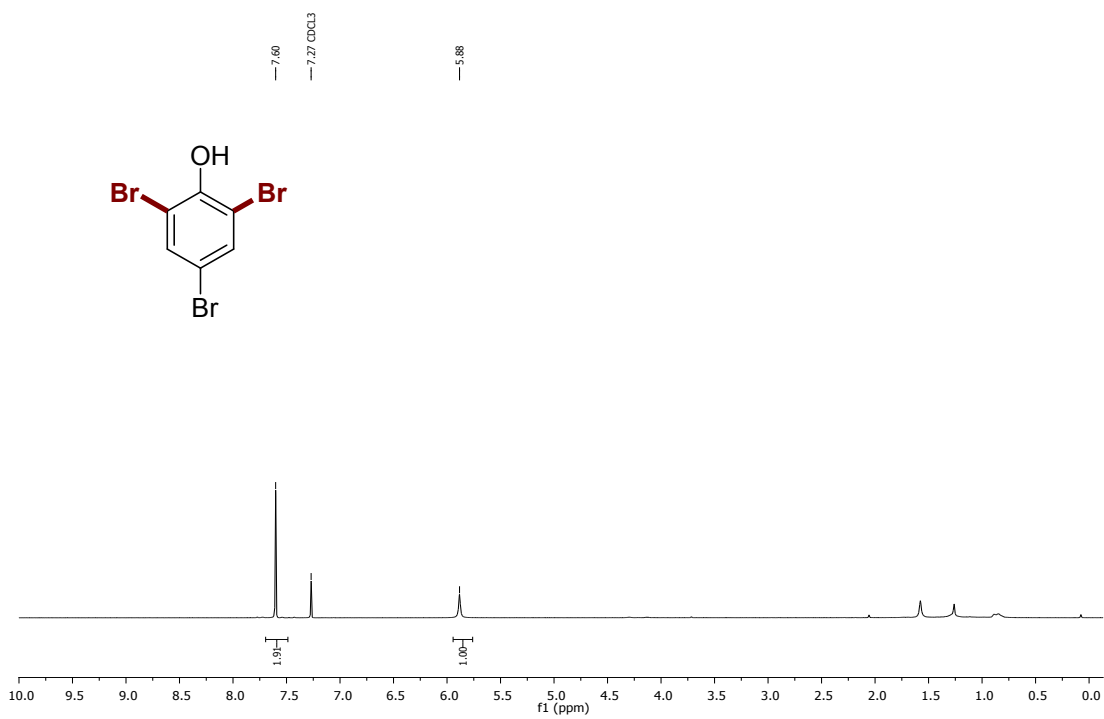
2,4-dibromophenol (30)



2,4-dibromophenol (31)

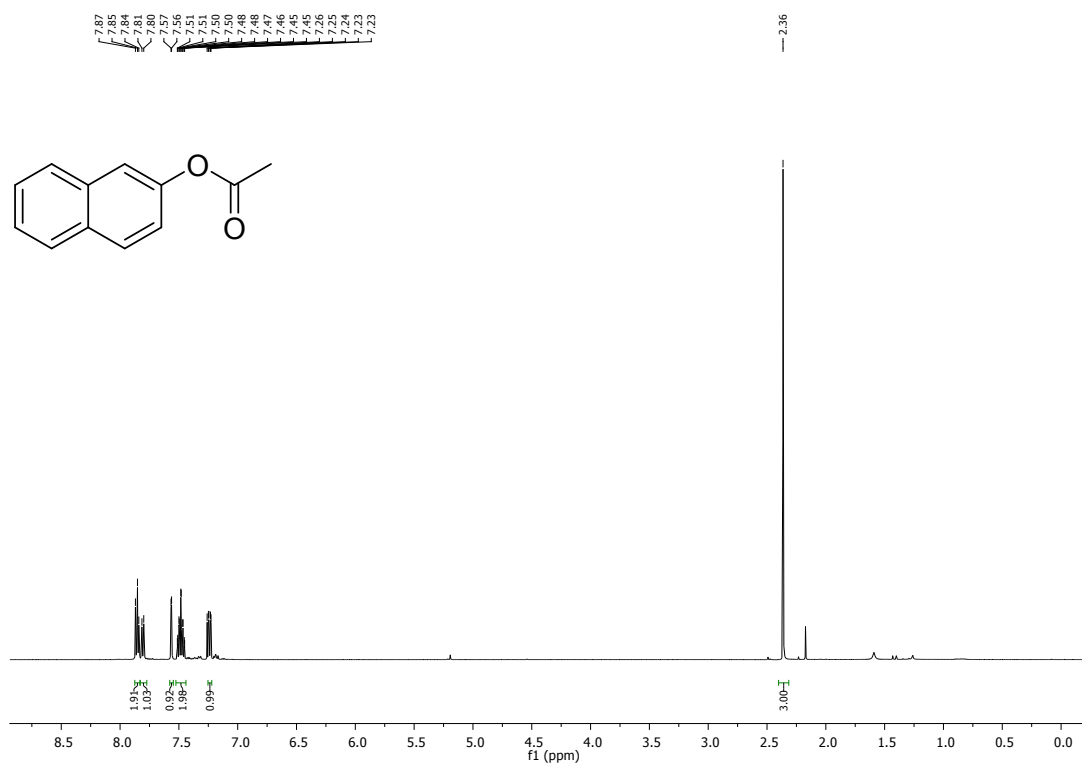


2,4,6-tribromophenol (32)

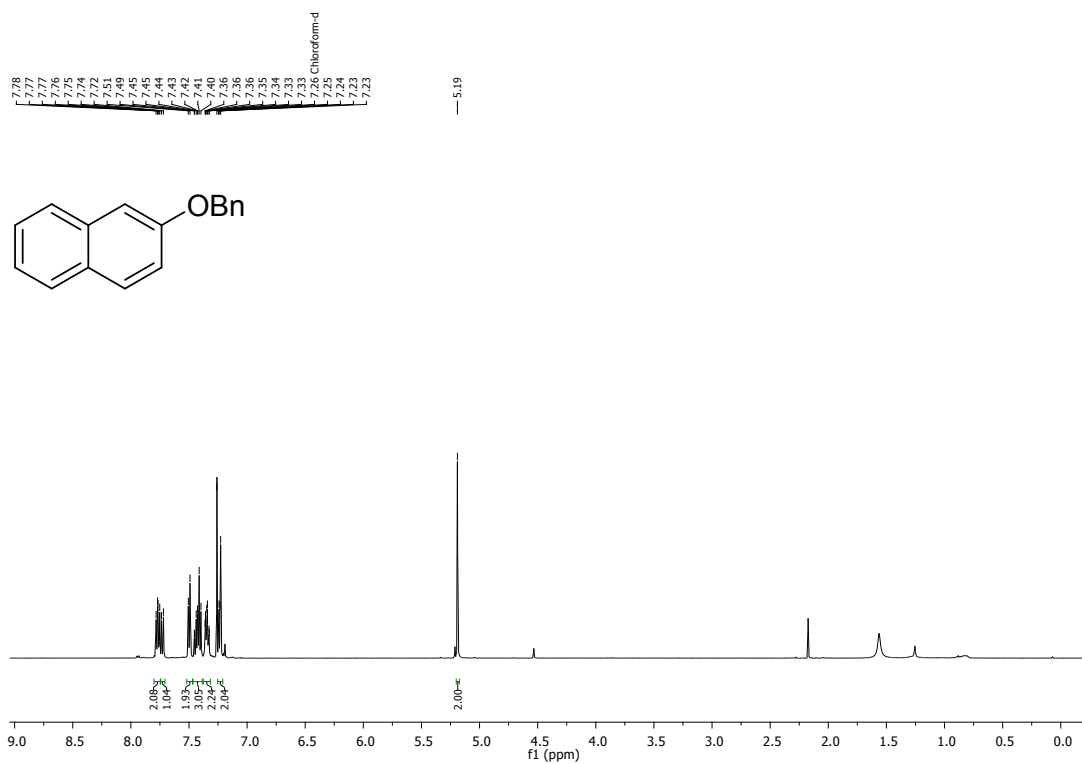


^1H spectra for known starting materials

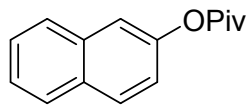
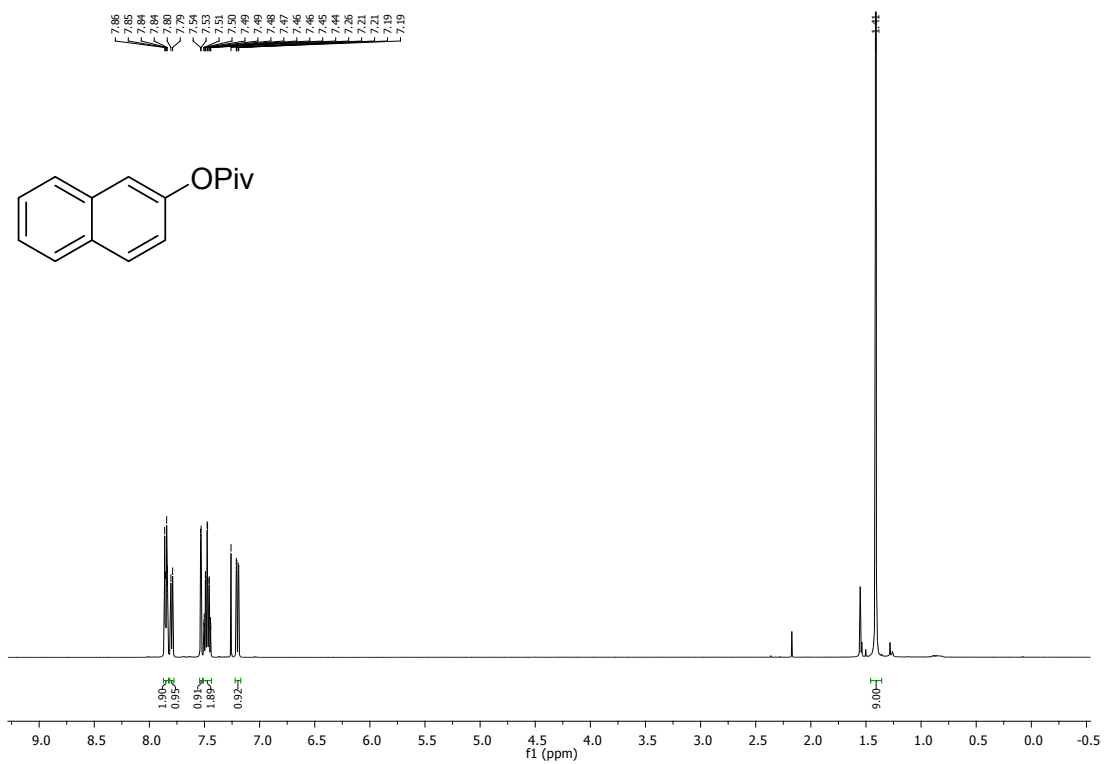
naphthalen-2-yl acetate³⁹



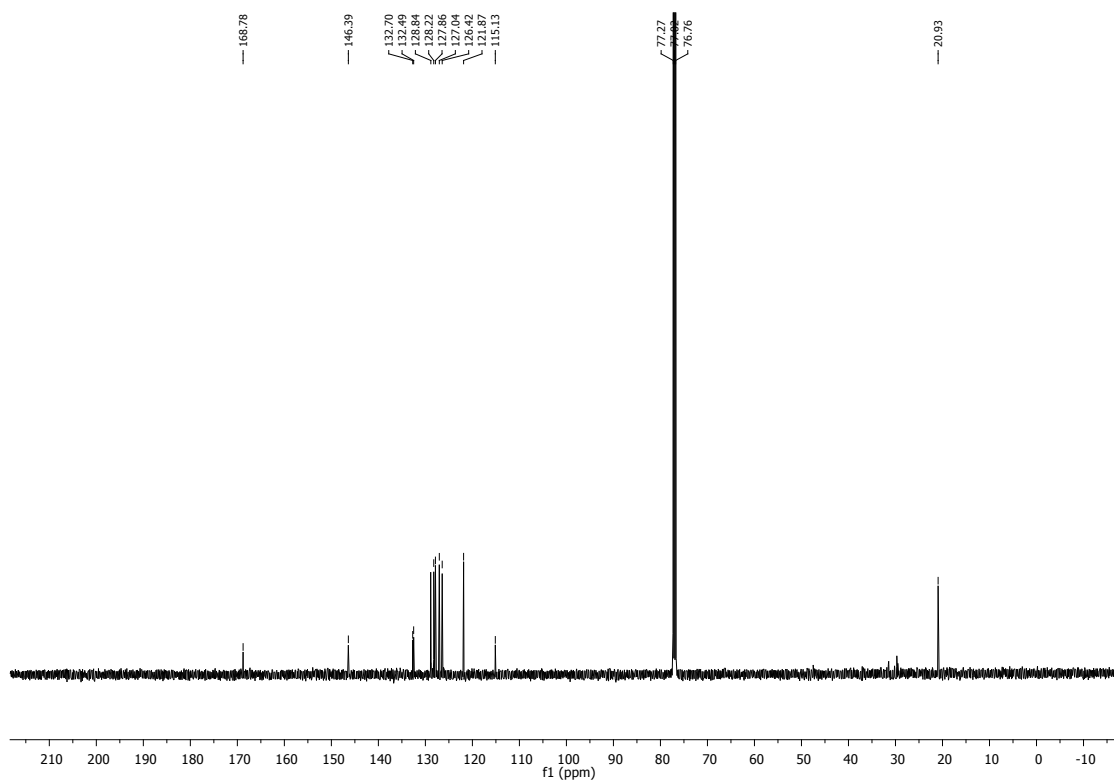
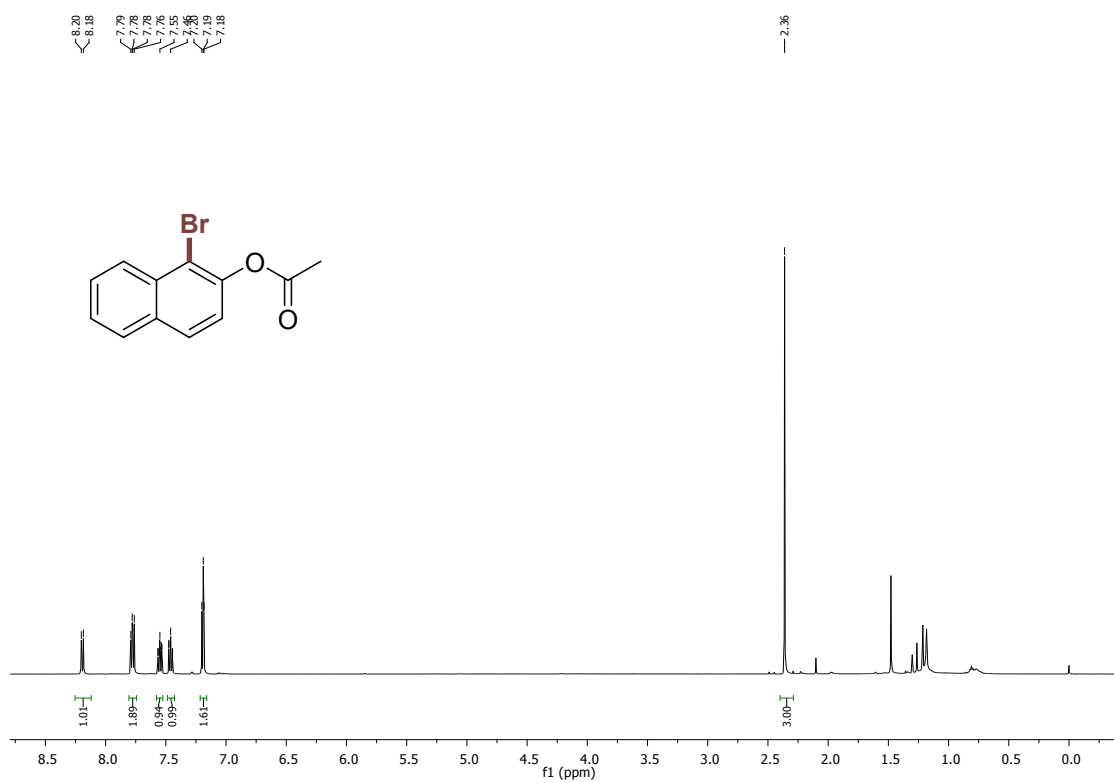
2-(benzyloxy)naphthalene⁴⁰



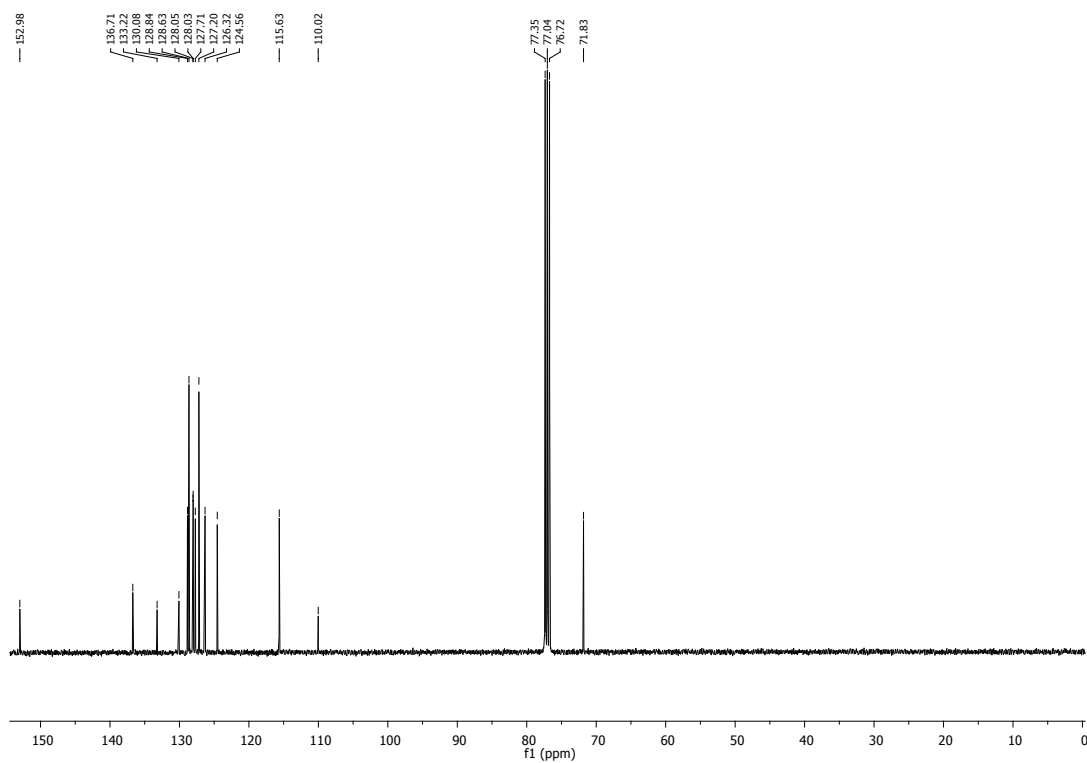
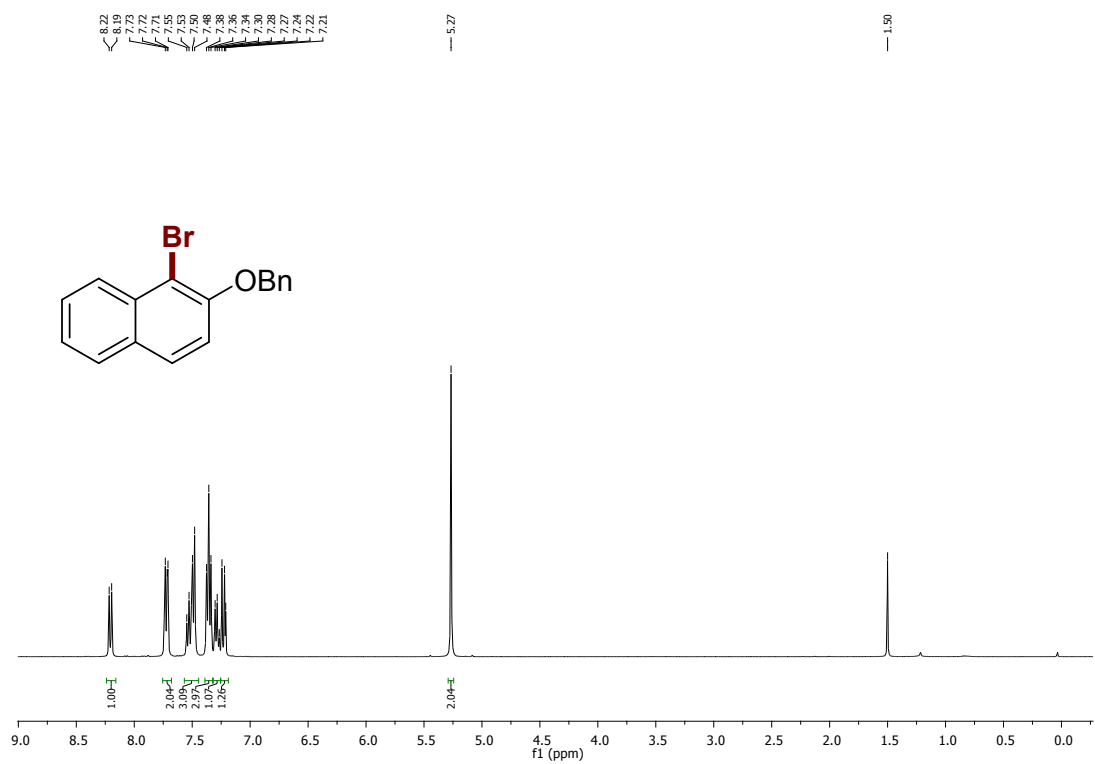
naphthalen-2-yl pivalate⁴¹



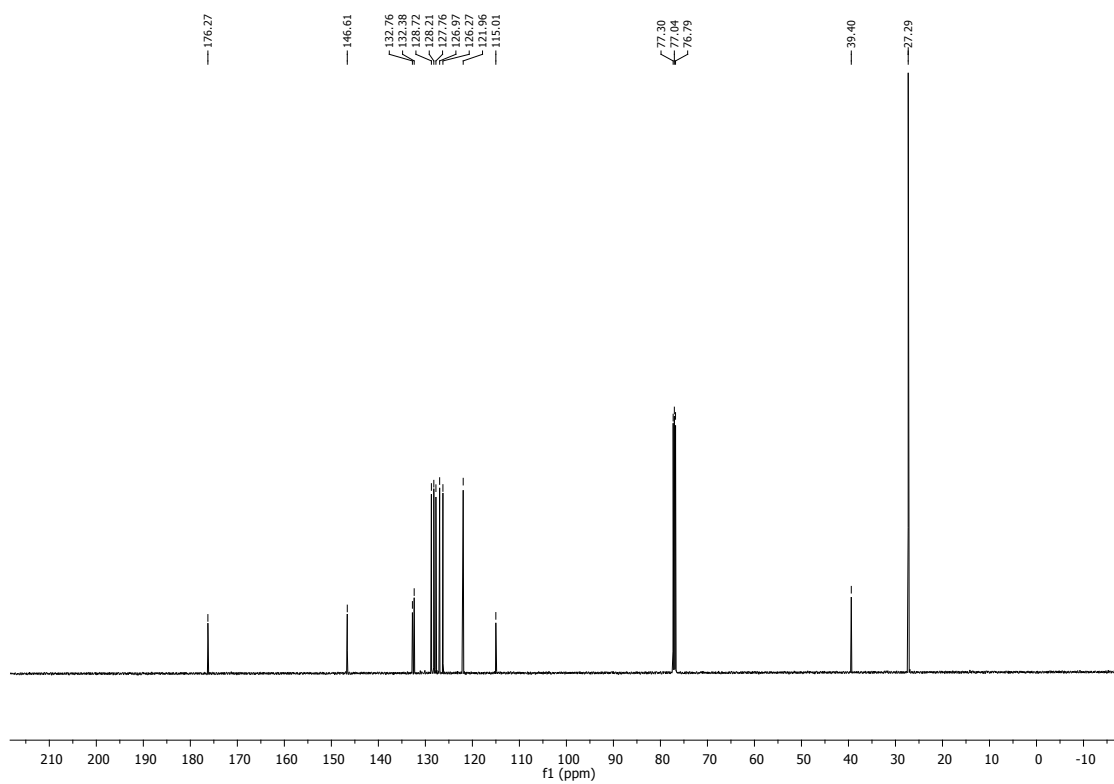
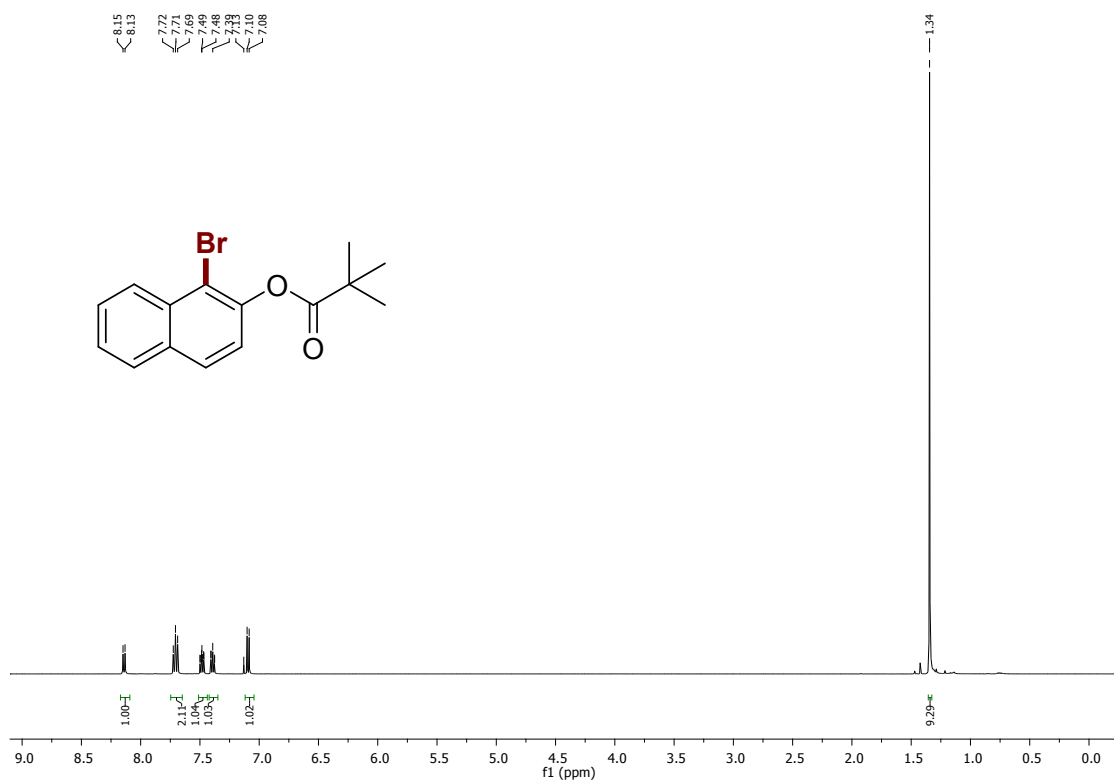
1-bromonaphthalen-2-yl-acetate (33)



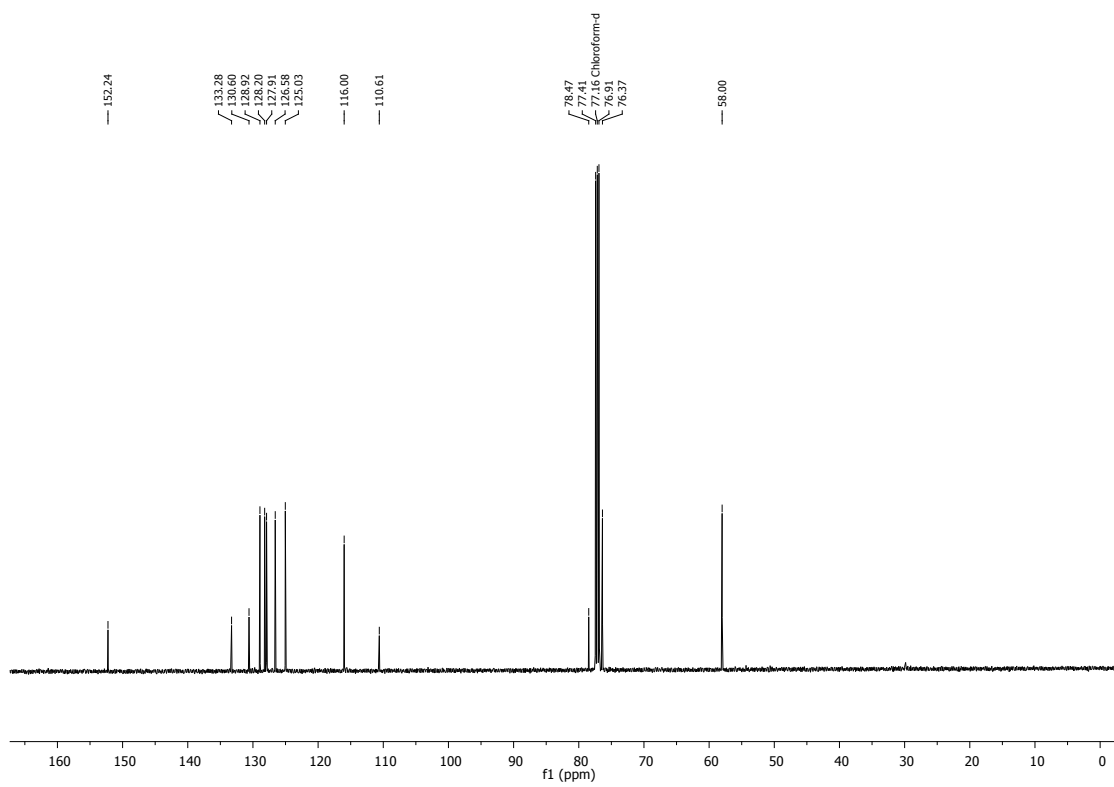
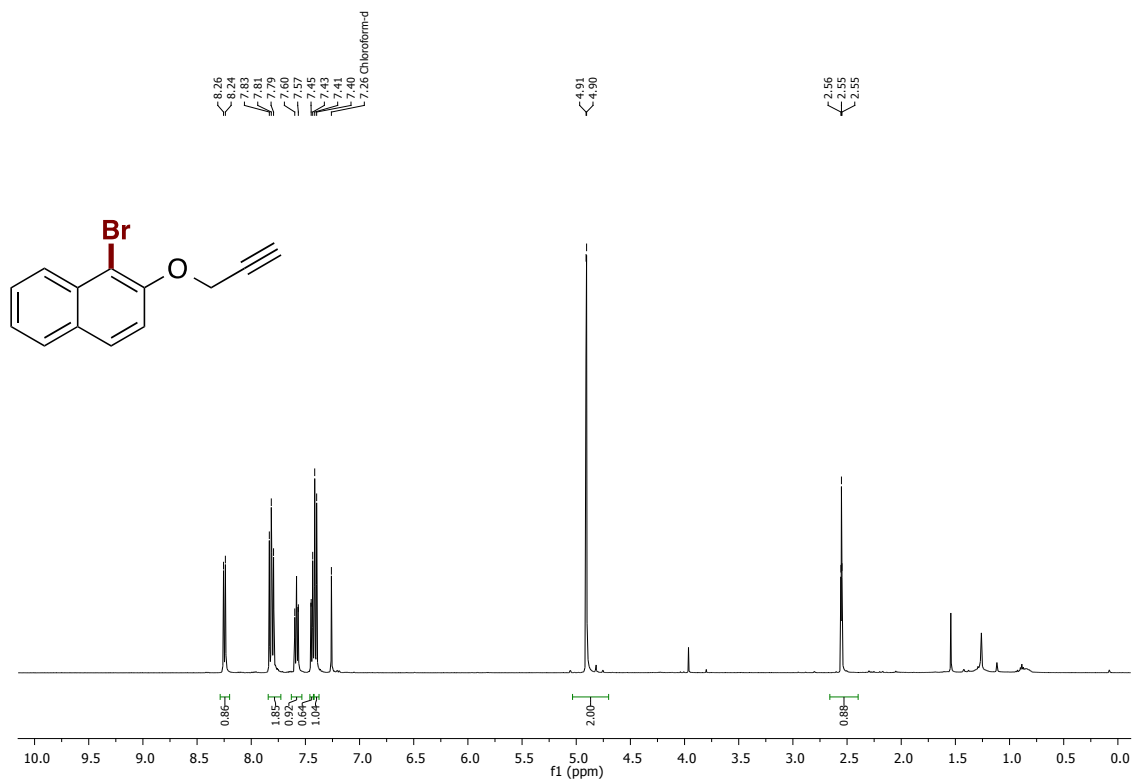
2-(benzyloxy)-1-bromonaphthalene (34)



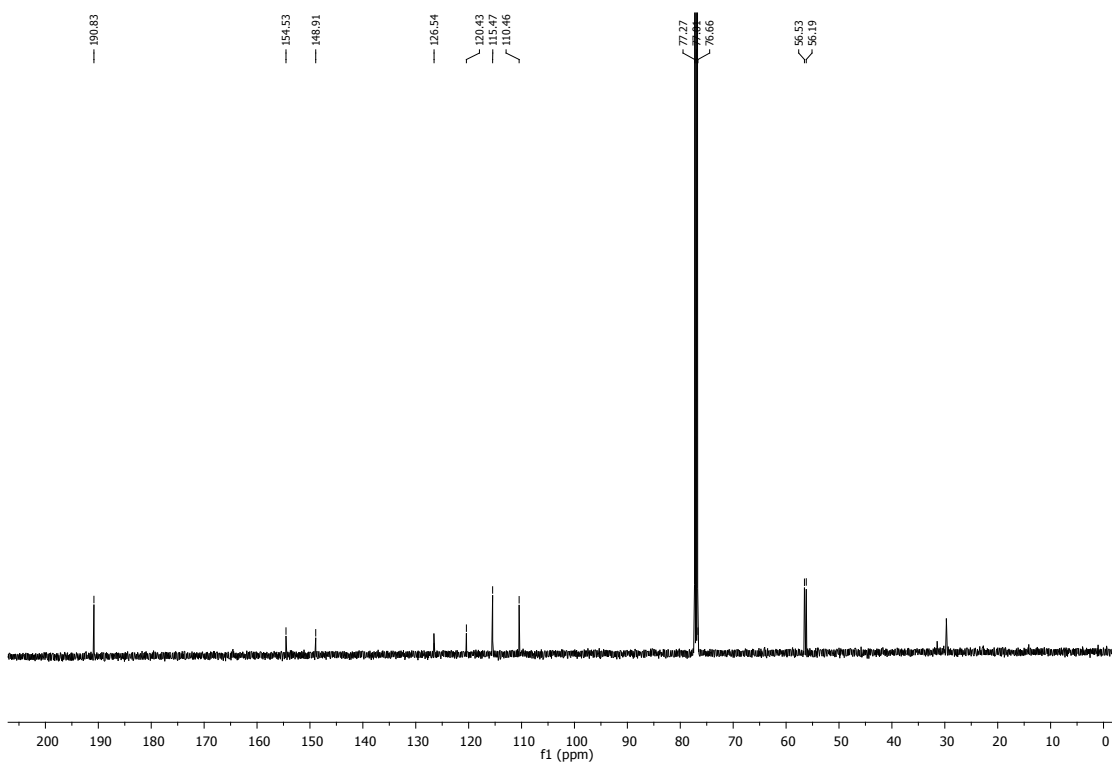
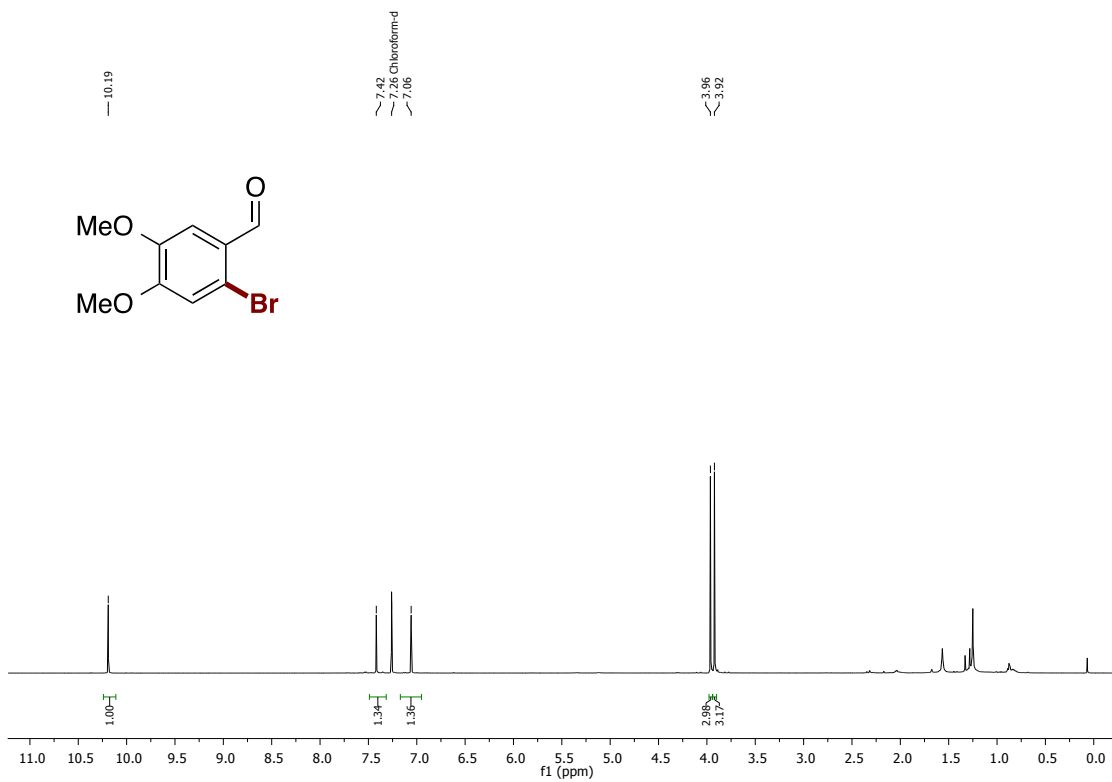
1-bromonaphthalen-2-yl-pivalate (35)



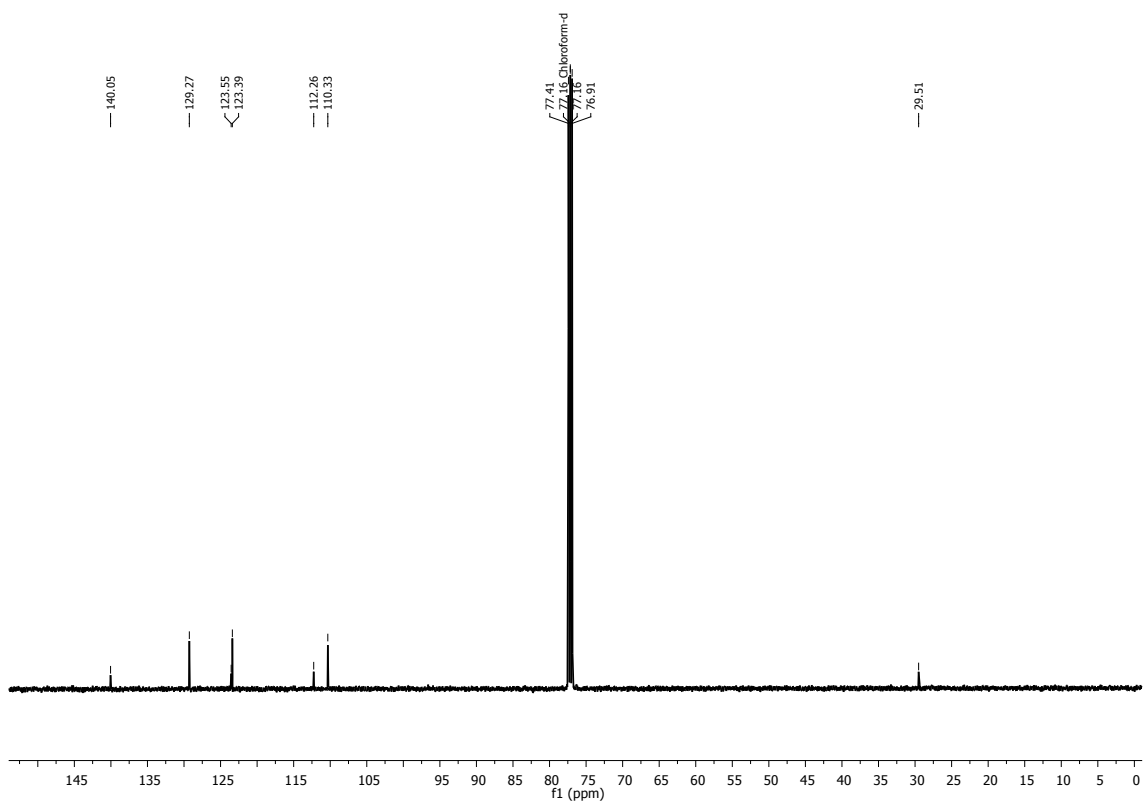
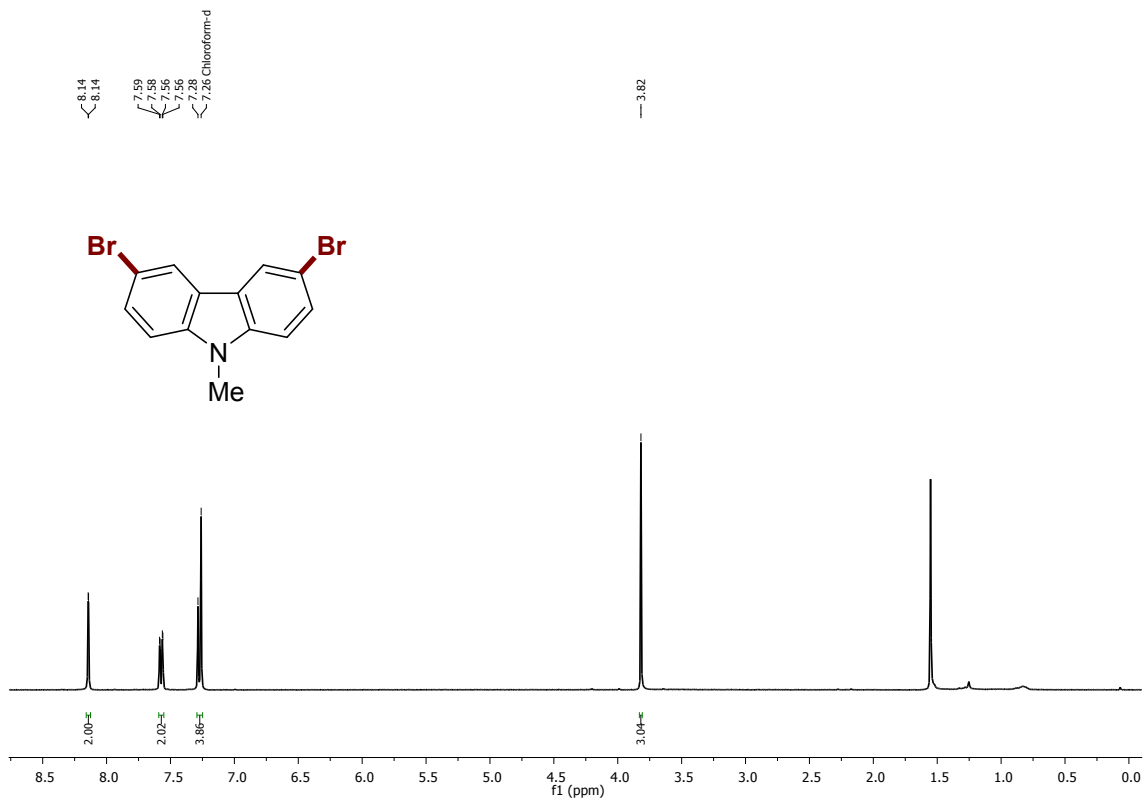
1-bromo-2-(prop-2-yn-1-yloxy)naphthalene (36)



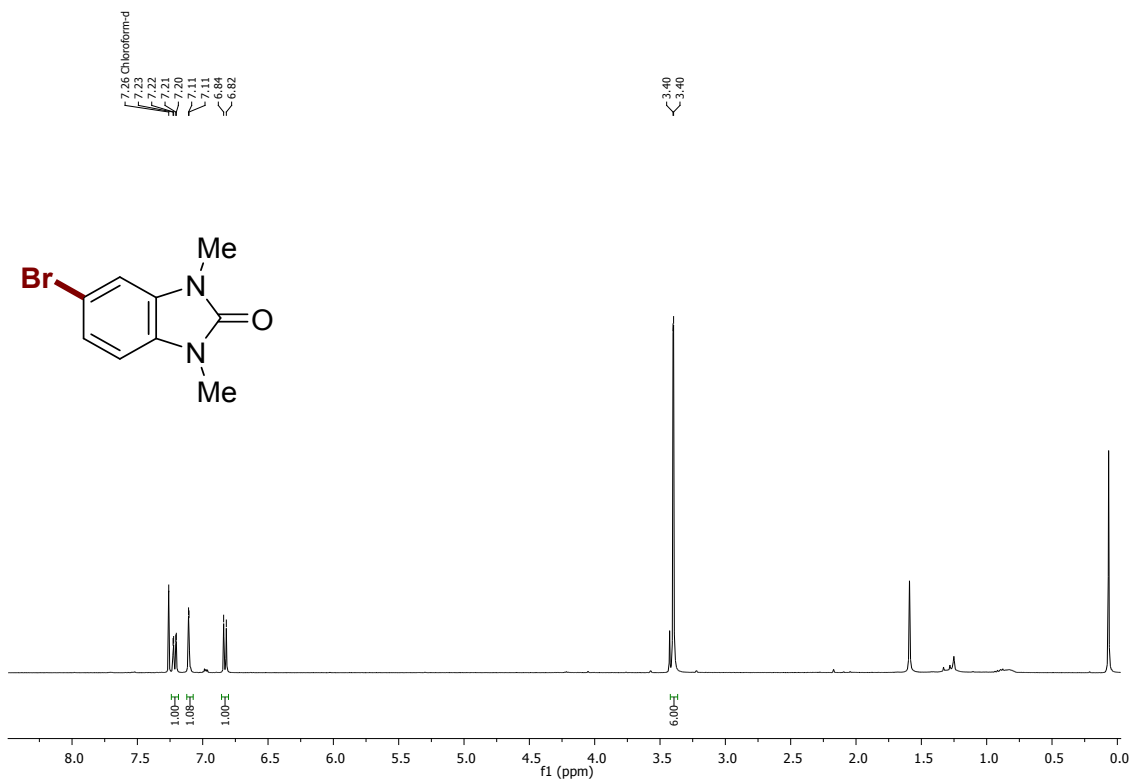
2-Bromo-4,5-dimethoxybenzaldehyde (37)



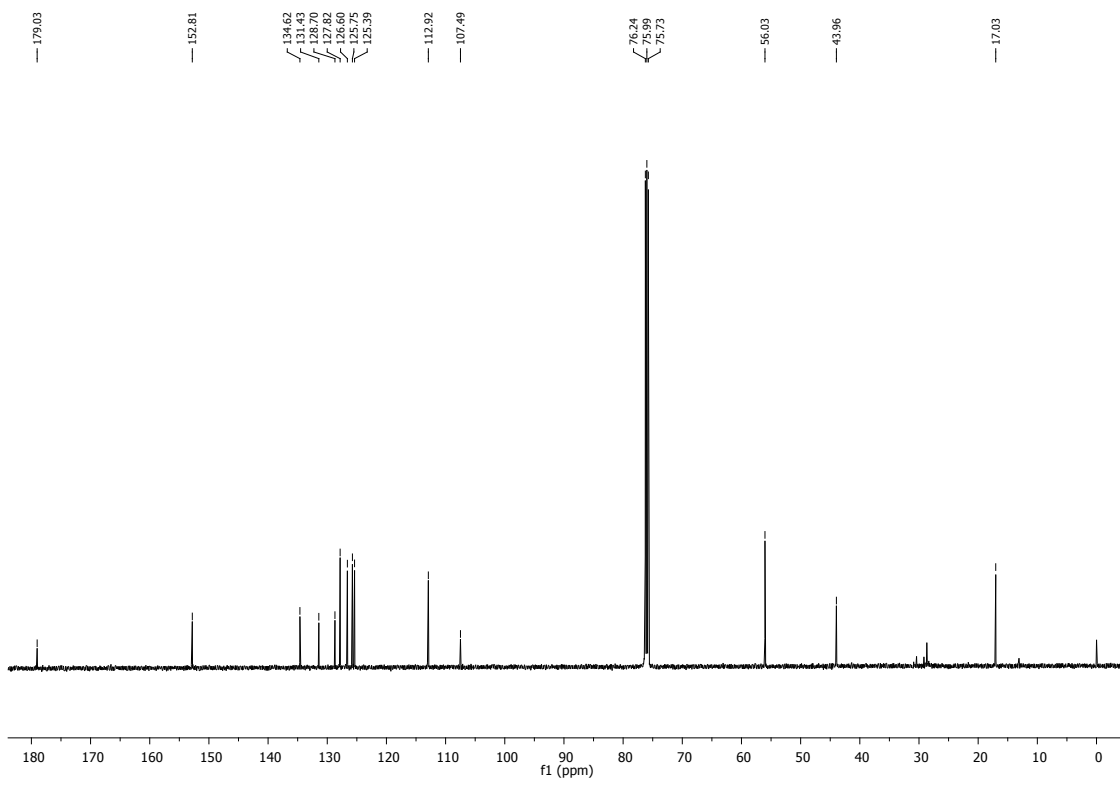
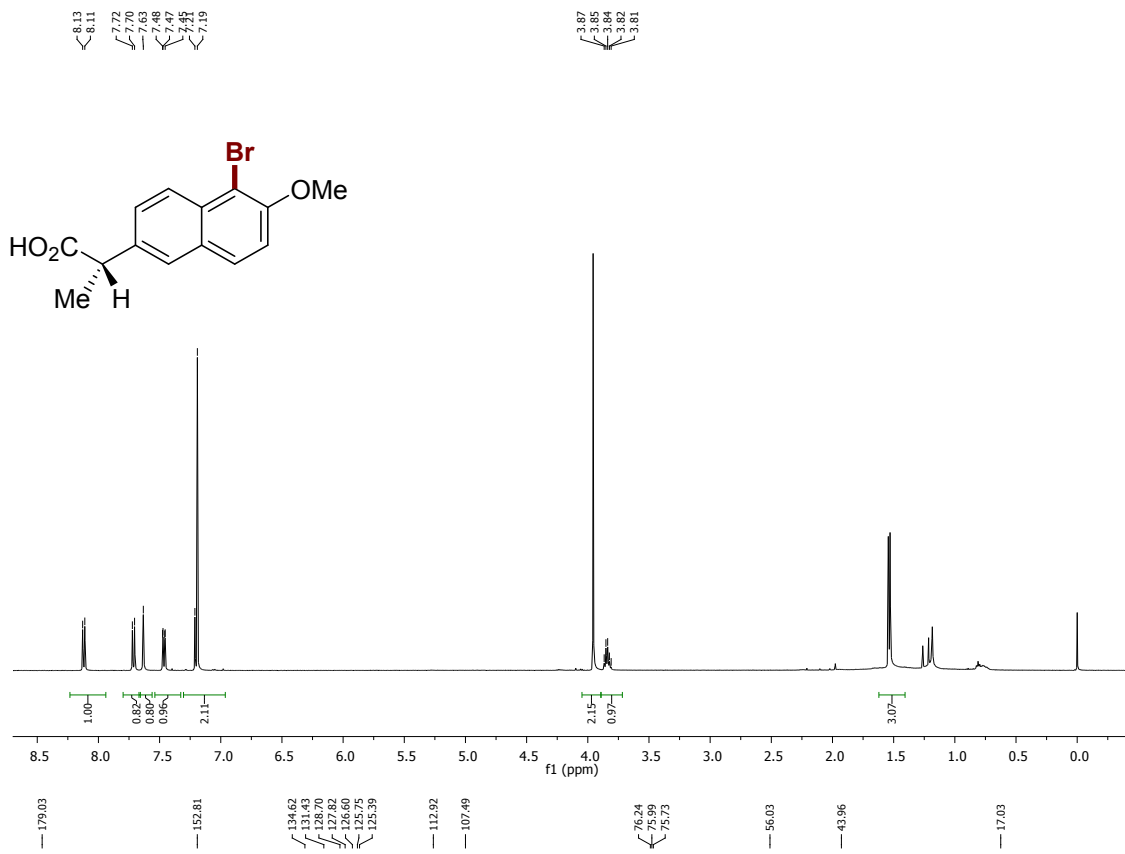
3,6-dibromo-9-methyl-9H-carbazole (**38**)



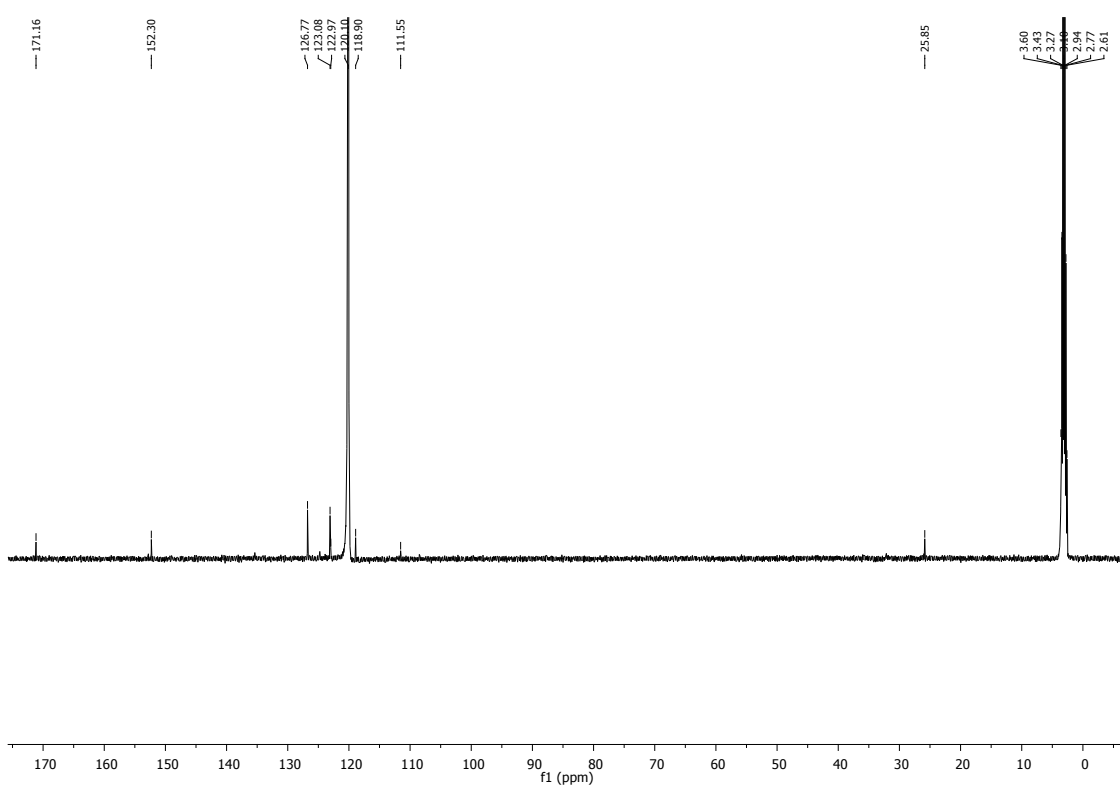
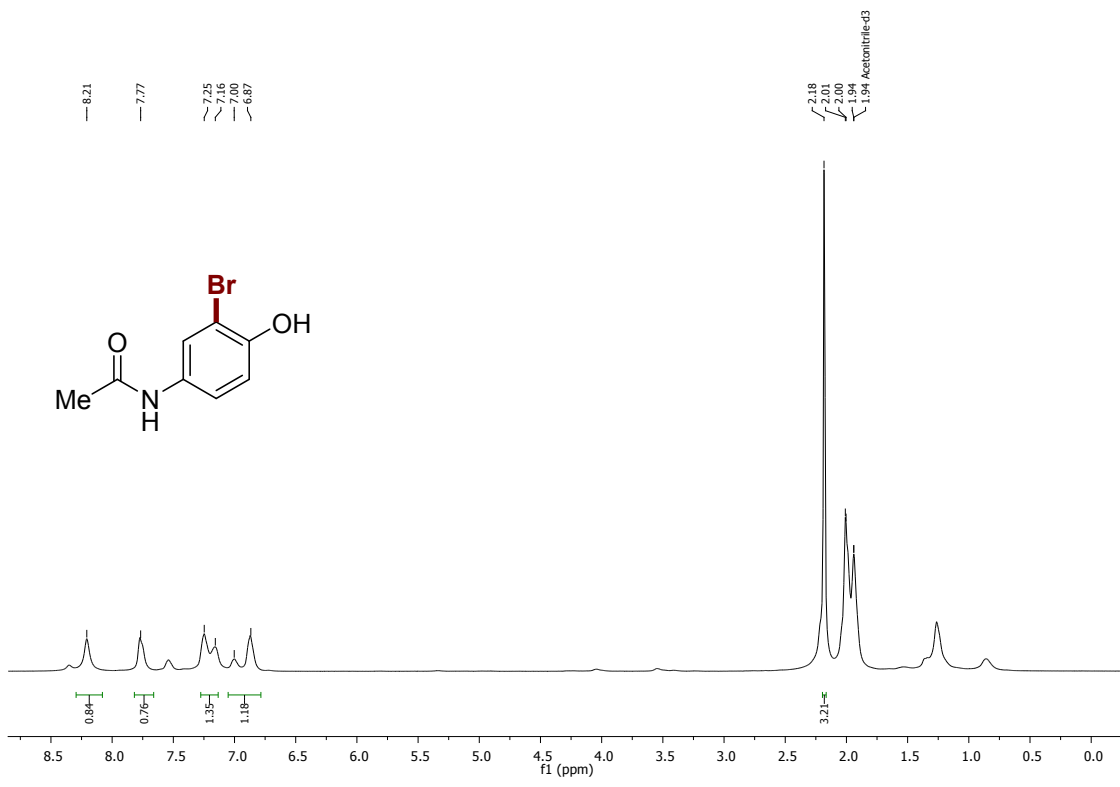
5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (39)



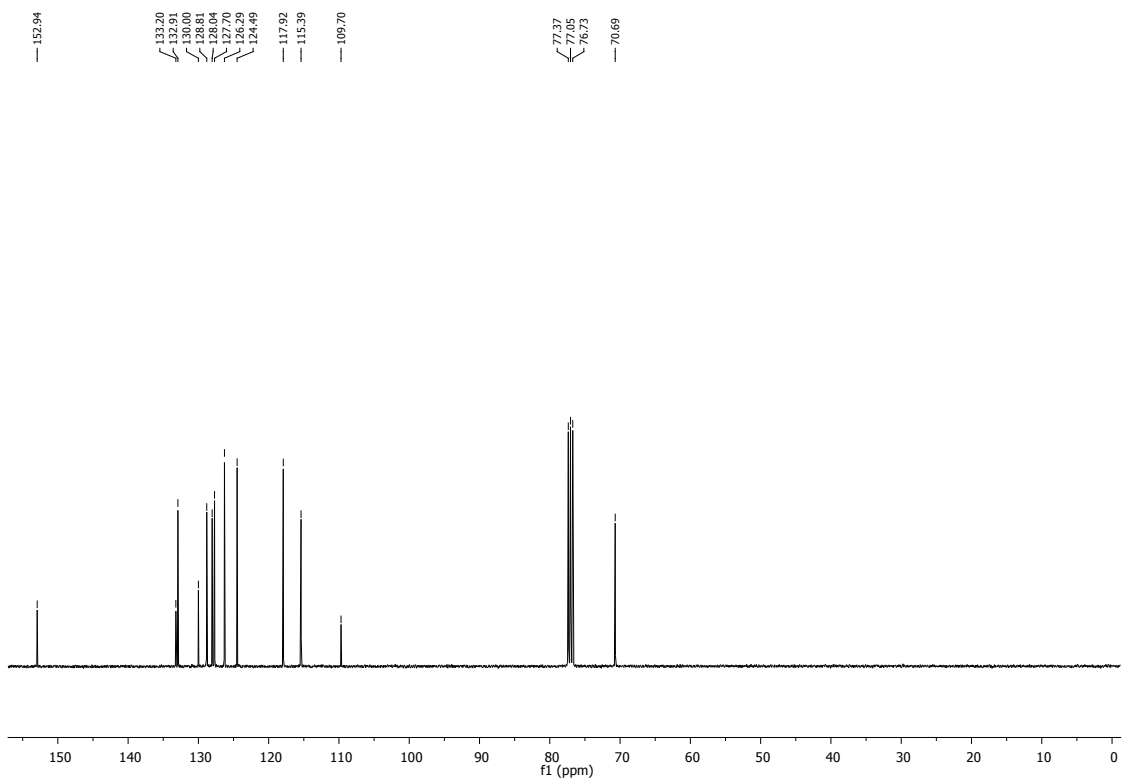
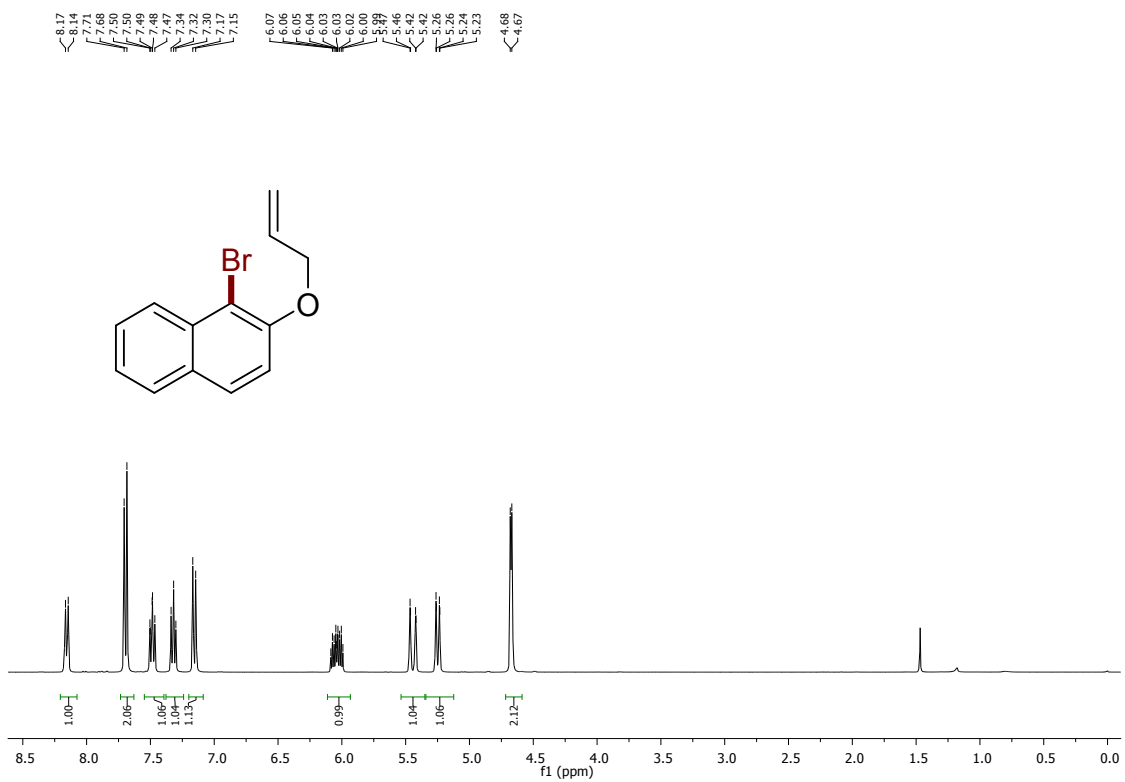
Br-Naproxen (40)



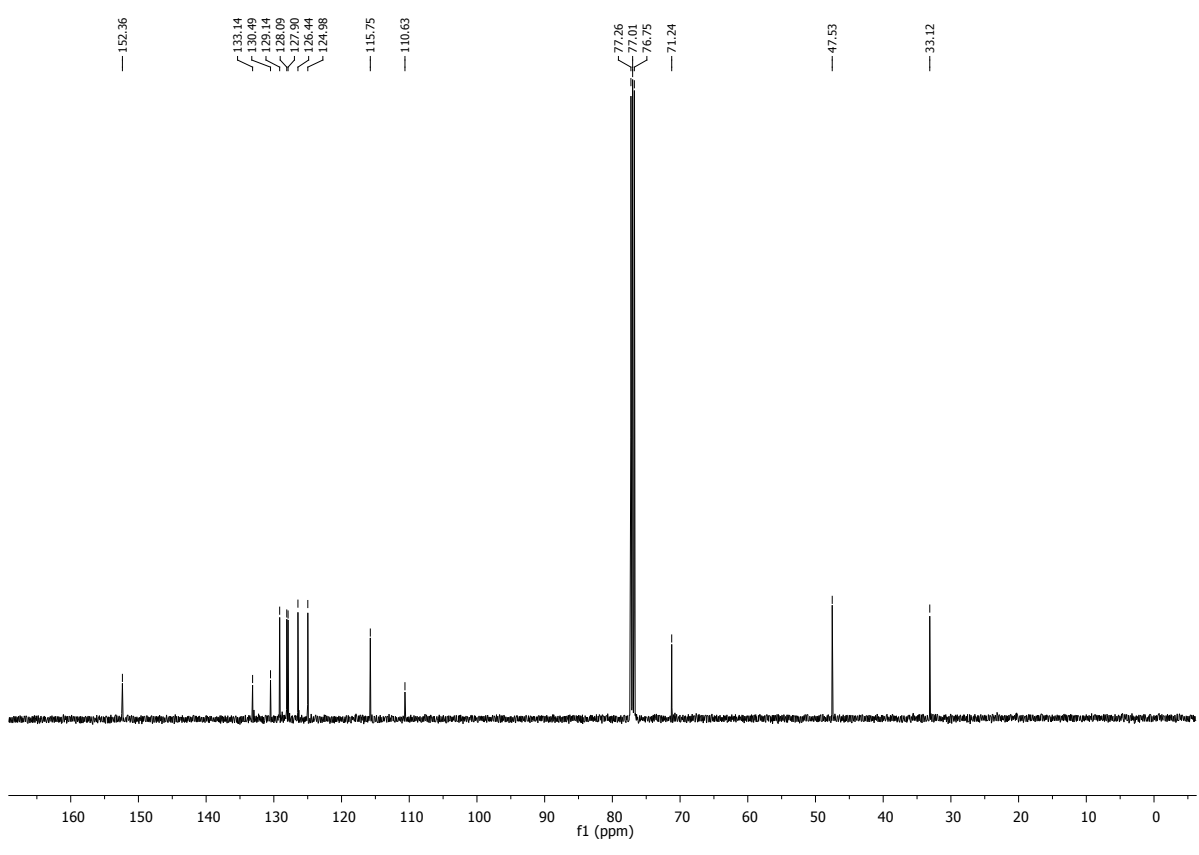
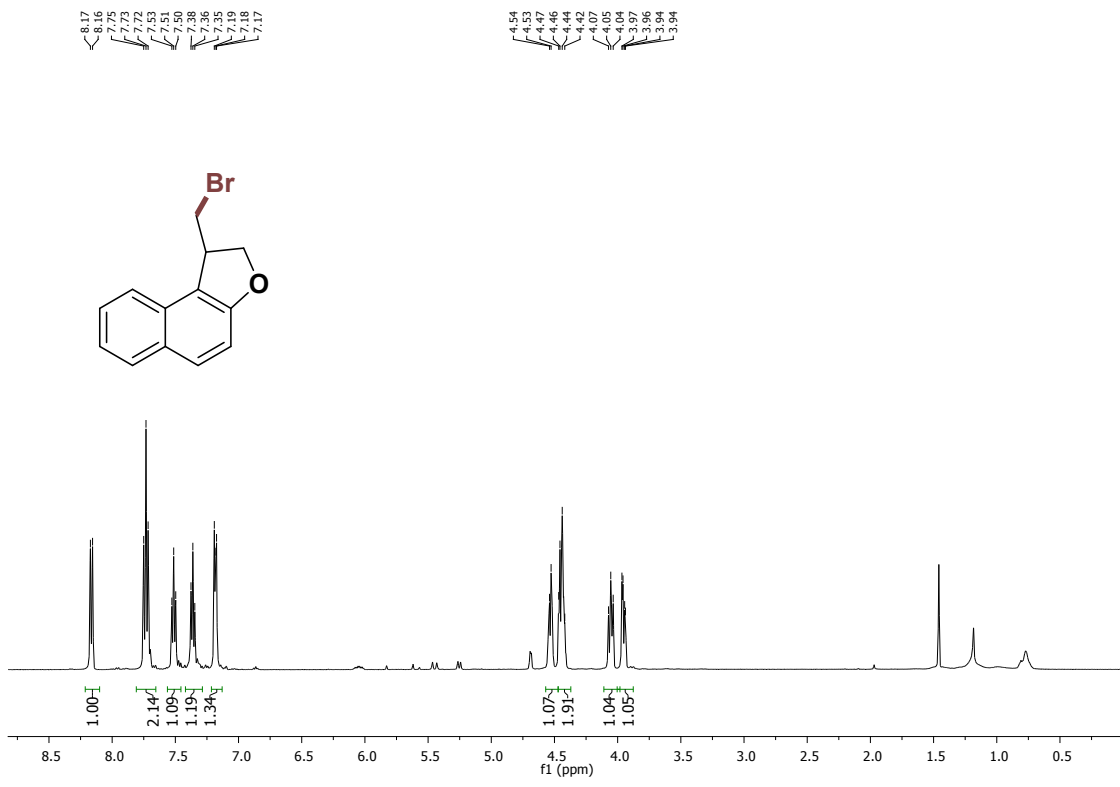
Br-Paracetamol (41)



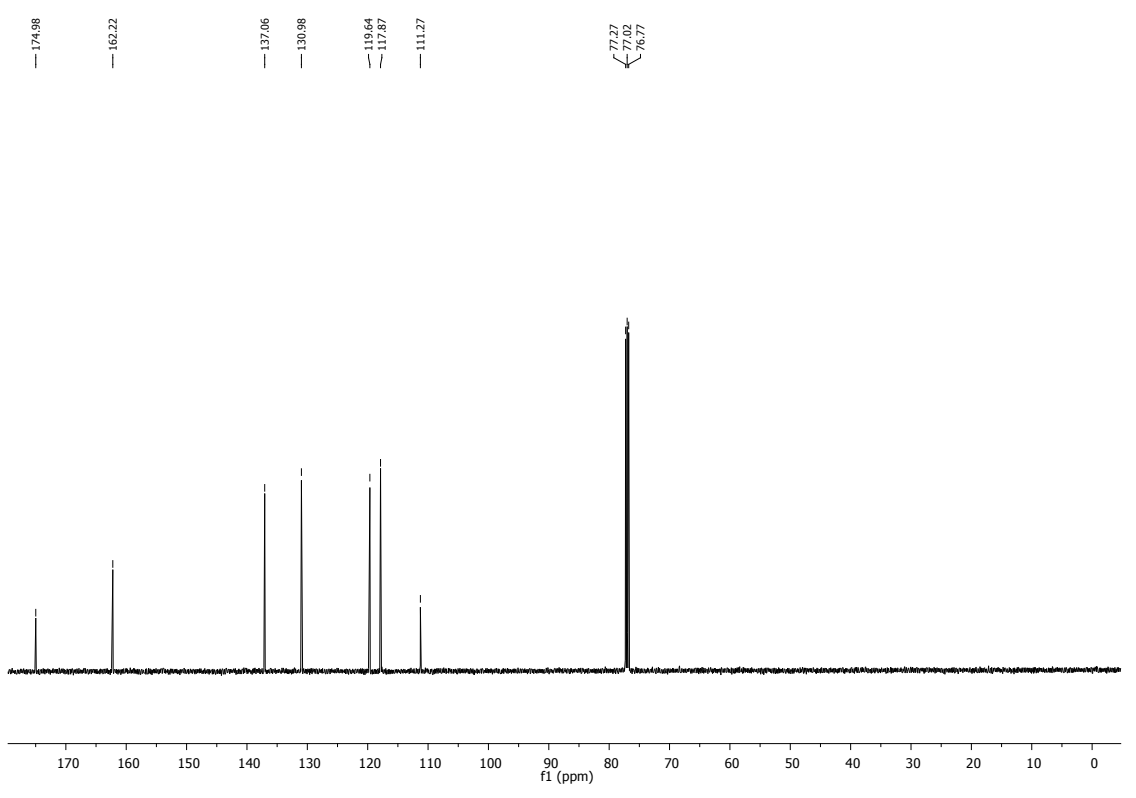
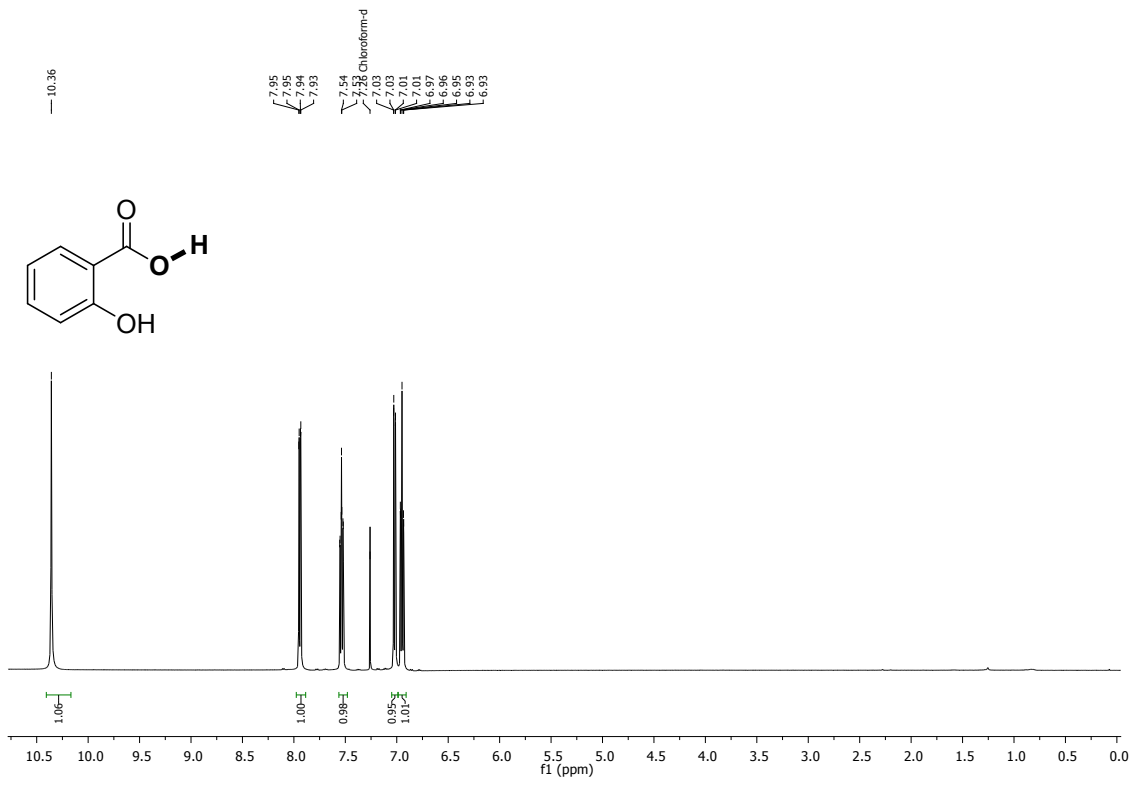
2-(allyloxy)-1-bromonaphthalene (42)



1-(bromomethyl)-1,2-dihydro-2H-benzofuran (**43**)



2-hydroxybenzoic acid (44)



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