Palladium-catalyzed intermolecular tandem cyclization reaction: a highly regioselective synthesis of 3*H*-Spiro[isobenzofuran-1,3′-isochroman] scaffolds

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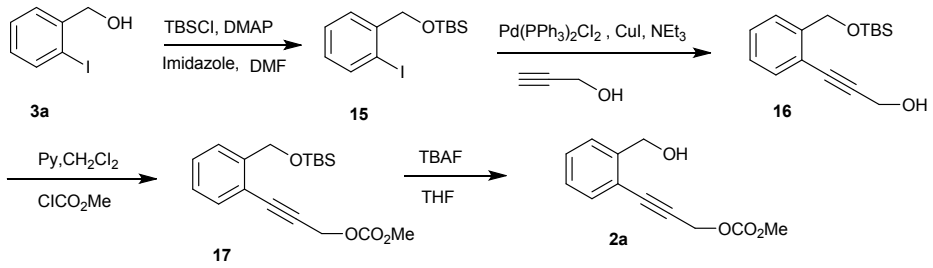
Supporting Information Content:

1. General Information

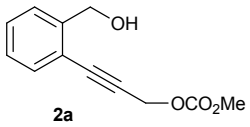
Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried according to standard methods prior to use. For product purification by flash column chromatography, silica gel (200~300 mesh) and light petroleum ether (bp. 60~90 °C) are used. The ^{1}H and ^{13}C NMR data were recorded on Bruker-400 MHz spectrometer at room temperature in $CDCl_3$ or DMSO-d_6 or CD_3COCD_3 solvent. Chemical shifts for protons are reported using residual $CHCl_3$ or DMSO or CD_3COCD_3 as internal reference (δ = 7.27, 2.50, 2.05 ppm). Carbon spectra were referenced to the shift of the ^{13}C signal of $CDCl_3$ (δ = 77.00, 39.52 ppm, 29.84 and 206.26 ppm). Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant (s) in Hz, integration). Data for ^{13}C NMR is reported in terms of chemical shift (δ, ppm). High-resolution mass spectra (HRMS) data were obtained on a Bruker Daltonics APEX II 47e mass spectrometer. Column chromatography was generally performed on silica gel (200-300 mesh) and TLC inspections were on silica gel GF254 plates. Substrates **3a, 3g, 3p** and **3r** were purchased from commercial suppliers and used without further treatment.

2. Preparation of starting materials

2.1 2a-g were prepared following the published literature procedures. [1]

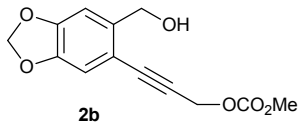


3-(2-(hydroxymethyl)phenyl)prop-2-yn-1-yl methyl carbonate (2a)



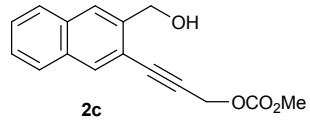
White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.45 (t, J = 6.6 Hz, 2H), 7.39-7.36 (m, 1H), 7.29-7.25 (m, 1H), 4.99 (s, 2H), 4.81 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 143.2, 132.4, 129.2, 127.3, 127.3, 120.0, 86.9, 84.8, 63.6, 56.1, 55.1; FT-IR (KBr, cm^{-1}) 3317, 3231, 3073, 3012, 2985, 2859, 174, 1587, 1448, 1367, 1284, 1264, 1048, 931, 756; HRMS (ESI): m/z calcd for $C_{12}H_{16}NO_4$ $[M+NH_4]^+$ 238.1074, found 238.1072.

3-(6-(Hydroxymethyl)benzo[*d*][1,3]dioxol-5-yl)prop-2-yn-1-yl methyl carbonate (2b)



White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.02 (s, 1H), 6.92 (s, 1H), 6.04 (s, 2H), 5.27-5.24 (t, J = 5.4 Hz, 1H), 5.01 (s, 2H), 4.53-4.52 (d, J = 5.2 Hz, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 154.7, 148.5, 145.8, 140.4, 111.1, 110.9, 107.0, 101.5, 86.4, 84.2, 60.8, 55.9, 55.0; FT-IR (KBr, cm^{-1}) 3316, 3053, 3007, 2956, 2912, 2227, 1747, 1617, 1504, 1488, 1442, 1385, 1369, 1297, 1280, 1266, 1085, 1042, 934, 789; HRMS (ESI): m/z calcd for $C_{13}H_{12}NO_6$ $[M+NH_4]^+$ 282.0972, found 282.0973.

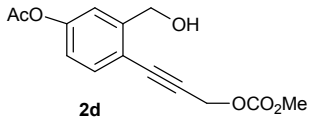
3-(3-(Hydroxymethyl)naphthalen-2-yl)prop-2-yn-1-yl methyl carbonate (2c)



2c

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.07 (s, 1H), 8.00 (s, 1H), 7.93-7.89 (t, J = 8.4 Hz, 2H), 7.56-7.48 (m, 2H), 5.47-5.44 (t, J = 5.6 Hz, 1H), 5.10 (s, 2H), 4.77-4.76 (d, J = 5.6 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 154.7, 140.3, 132.8, 132.0, 131.3, 127.5, 127.4, 127.3, 126.2, 124.4, 117.1, 87.7, 84.1, 61.2, 55.9, 55.1; FT-IR (KBr, cm^{-1}) 3365, 3286, 3055, 2968, 2940, 2858, 2237, 1752, 1630, 1599, 1493, 1447, 1375, 1299, 1274, 1043, 944, 887, 747; HRMS (ESI): m/z calcd for $C_{16}H_{18}NO_4$ $[M+NH_4]^+$ 288.1230, found 288.1229.

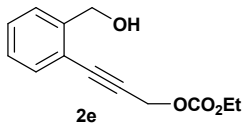
3-(Hydroxymethyl)-4-(3-((methoxycarbonyl)oxy)prop-1-yn-1-yl)phenyl acetate (2d)



2d

Colourless liquid; ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.48-7.42 (m, 2H), 7.13-7.10 (m, 1H), 4.93-4.93 (d, J = 2.1 Hz, 2H), 4.77 (s, 2H), 4.47 (s, 1H), 3.87 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 170.4, 154.5, 152.7, 147.6, 133.8, 120.2, 119.8, 117.7, 89.6, 83.0, 62.3, 55.8, 52.9, 20.5; FT-IR (KBr, cm^{-1}) 3467, 3076, 3011, 2958, 2856, 2232, 1757, 1605, 1578, 1488, 1443, 1374, 1225, 1199, 1152, 1026, 943, 901, 827, 790; HRMS (ESI): m/z calcd for $C_{14}H_{18}NO_6$ $[M+NH_4]^+$ 296.1129, found 296.1130.

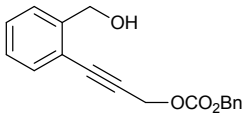
Ethyl (3-(2-(hydroxymethyl)phenyl)prop-2-yn-1-yl) carbonate (2e)



2e

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.56-7.53 (d, J = 7.6 Hz, 1H), 7.44-7.40 (t, J = 7.6 Hz, 2H), 7.27-7.23 (t, J = 7.4 Hz, 1H), 5.32-5.30 (t, J = 5.4 Hz, 1H), 5.03 (s, 2H), 4.63-4.62 (d, J = 4.8 Hz, 2H) 4.20-4.15 (q, J = 7.2 Hz, 2H), 1.25-1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 154.0, 144.5, 131.6, 129.1, 126.6, 126.3, 118.5, 88.0, 83.9, 64.1, 60.9, 55.6, 14.0; FT-IR (KBr, cm^{-1}) 3303, 3067, 2984, 2941, 2227, 1749, 1599, 1480, 1453, 1401, 1379, 1362, 1261, 1039, 1015, 872, 760; HRMS (ESI): m/z calcd for $C_{13}H_{18}NO_4$ $[M+NH_4]^+$ 252.1230, found 252.1229.

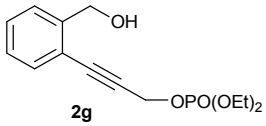
Benzyl (3-(2-(hydroxymethyl)phenyl)prop-2-yn-1-yl) carbonate (2f)



2f

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.56-7.54 (d, J = 7.6 Hz, 1H), 7.44-7.35 (m, 7H), 7.28-7.24 (t, J = 7.2 Hz, 1H), 5.33-5.30 (t, J = 5.6 Hz, 1H), 5.21 (s, 2H), 5.07 (s, 2H), 4.64-4.62 (d, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 154.0, 144.5, 135.2, 131.6, 129.1, 128.5, 128.4, 128.2, 126.6, 126.3, 118.5, 87.9, 84.0, 69.3, 60.9, 55.9; FT-IR (KBr, cm^{-1}) 3309, 3217, 3086, 3033, 2976, 2860, 2242, 2219, 1736, 1638, 1584, 1480, 1453, 1434, 1386, 1279, 1263, 1249, 1048, 991, 928, 913, 756, 694; HRMS (ESI): m/z calcd for $C_{18}H_{20}NO_4$ $[M+NH_4]^+$ 314.1387, found 314.1386.

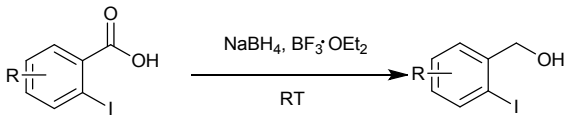
Diethyl (3-(2-(hydroxymethyl)phenyl)prop-2-yn-1-yl) phosphate (2g)



2g

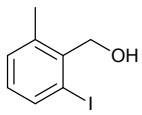
White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.55-7.53 (d, J = 7.6 Hz, 1H), 7.44-7.40 (t, J = 7.6 Hz, 2H), 7.28-7.25 (t, J = 7.6 Hz, 1H), 5.32-5.29 (t, J = 5.6 Hz, 1H), 4.96-4.94 (d, J = 10.8 Hz, 2H), 4.64-4.63 (d, J = 5.6 Hz, 2H), 4.11-4.03 (dt, J = 15.2 Hz, J = 7.2 Hz, 4H), 1.28-1.24 (td, J = 7.0 Hz, J = 0.6 Hz, 6H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 144.4, 131.6, 129.1, 126.7, 126.3, 118.5, 88.5 (d, J = 6 Hz), 84.2, 63.6 (d, J = 6 Hz), 61.0, 55.4 (d, J = 5 Hz), 15.9 (d, J = 6 Hz); FT-IR (KBr, cm^{-1}) 3402, 3066, 2985, 2931, 2231, 1599, 1480, 1449, 1375, 1260, 1165, 1026, 974, 836, 762; HRMS (ESI): m/z calcd for $C_{14}H_{20}O_5P$ $[M+H]^+$ 299.1043, found 299.1044.

2.2 Synthesis of 3b-3f



2-Iodobenzoic acid (2 mmol) was dissolved in THF (10 mL) and cooled to 0 °C. $NaBH_4$ (2.5 mmol, 95mg) and $BF_3{\cdot}OEt_2$ (2.5 mmol, 0.35mL) was slowly added into the stirring solution at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 2 h, monitoring by TLC. Upon completion, the reaction was quenched with water (15 mL) at 0 °C and saturated with K_2CO_3. After extraction with EtOAc (3 × 20 mL), the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc : petroleum = 4:1) to yield the target 2-iodobenzyl alcohol.

(2-Iodo-6-methylphenyl)methanol (3b)

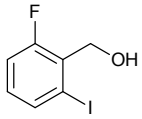


3b

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.22 (d, J = 4.9 Hz, 2H), 7.18-7.15 (q, J = 4.5 Hz, 1H), 4.68 (s, 2H) 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 142.0, 128.9, 128.0, 125.6, 104.6,

70.2, 29.0.

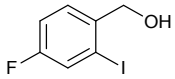
(2-Fluoro-6-iodophenyl)methanol (3c)



3c

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 1H), 7.10–7.05 (m, 1H), 7.04–6.98 (m, 1H), 4.83 (d, J = 2.1 Hz, 2H), 2.1 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 159.2, 135.2 (d, J = 4 Hz), 131.1 (d, J = 9 Hz), 115.9 (d, J = 23 Hz), 100.5 (d, J = 3 Hz), 62.6 (d, J = 4 Hz).

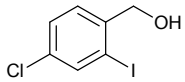
(4-Fluoro-2-iodophenyl)methanol (3d)



3d

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.69-7.67 (dd, J = 2.6 Hz, J = 8.4 Hz, 1H), 7.49-7.45 (dd, J = 6.2 Hz, J = 8.6 Hz, 1H), 7.29-7.24 (td, J = 8.6 Hz, J = 2.6 Hz, 1H), 4.38 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 160.5 (d, J = 245 Hz), 140.0 (d, J = 3 Hz), 128.6 (d, J = 8 Hz), 124.9 (d, J = 24 Hz), 114.9 (d, J = 20 Hz), 96.4 (d, J = 8 Hz), 66.5.

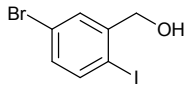
(4-Chloro-2-iodophenyl)methanol (3e)



3e

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.86-7.85 (d, J = 1.8 Hz, 1H), 7.49-7.44 (m, 2H), 5.52 (bs, 1H), 4.38 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 142.9, 137.0, 131.8, 128.6, 128.0, 97.1, 66.7.

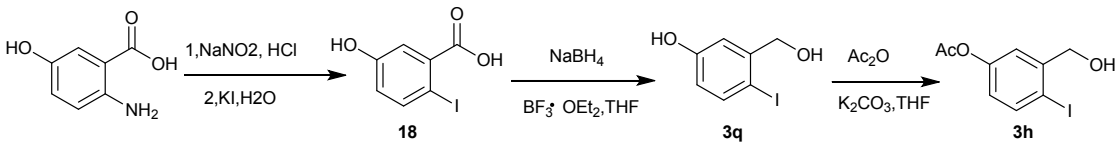
(5-bromo-2-iodophenyl)methanol (3f)



3f

White solid; ^{1}H NMR (400 MHz, d_6-$CDCl_3$) δ 7.66-7.62 (m, 2H), 7.15-7.12 (m, 1H), 4.63 (s, 2H), 2.15 (s, 1H); ^{13}C NMR (100 MHz, d_6-$CDCl_3$) δ 144.5, 14.02, 132.1, 131.0, 94.6, 68.6 .

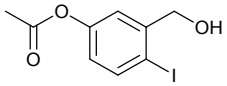
2.3 Synthesis of substituted 3h and 3q



A solution of $NaNO_2$ (2.16 g, 31.3 mmol) in water (10 mL) was added slowly to a cold (0 °C) stirred solution of 2-amino-5-hydroxybenzoic acid (4.0g, 26.1 mmol), concentrated HCl (20 mL) and crushed ice (15 g) in water (40 mL). After addition was completed, the solution was stirred for additional 30

min below 5 °C. A solution of KI (6.62 g, 39.2 mmol) in water (10 mL) was added slowly. The resulting mixture was stirred for 20 min at 0 °C and then heated to 90 °C for 30 minutes to remove all N_2. The mixture was cooled to room temperature and extracted with EtOAc (5 times). The organics were washed with saturated aqueous $NaHSO_3$ (several times) and water, and then dried over anhydrous Na_2SO_4. The solvents were removed under *vacuo* to give **3q** as yellowish red solid, which was used for next step without further purification. **18** (20 mmol) was dissolved in THF (100 mL) and cooled to 0 °C. $NaBH_4$ (30mmol) and $BF_3{\cdot}OEt_2$ (30mmol) was slowly added into the stirring solution at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 2 h, monitoring by TLC. Upon completion, the reaction was quenched with water (100 mL) at 0 °C and saturated with K_2CO_3. After extraction with EtOAc (3 × 200 mL), the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (SiO2; 20% EtOAc in petroleum) to yield the target **3h**

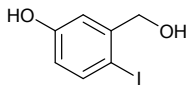
3-(Hydroxymethyl)-4-iodophenyl acetate (3h)



3h

White solid; ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.83-7.81 (d, J = 8.4 Hz, 1H), 7.33-7.32 (d, J = 2.8 Hz, 1H), 6.85-6.82 (dd, J = 8.4 Hz, J = 2.8 Hz, 1H), 4.64-4.62 (t, J = 5.2 Hz, 1H), 4.56-4.55 (d, J = 5.2 Hz, 2H) 2.26 (s, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 169.4, 152.5, 146.3, 140.1, 123.0, 121.9, 91.5, 68.6, 20.9.

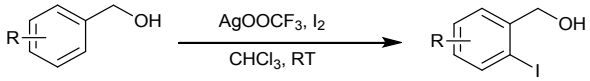
3-(Hydroxymethyl)-4-iodophenol (3q)



3q

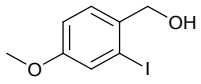
White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.53-7.51 (d, J = 8.4 Hz, 1H), 7.00-6.99 (d, J = 2.9 Hz, 1H), 6.49-6.46 (dd, J = 8.4 Hz, J = 3.0 Hz, 1H), 5.33 (bs, 1H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 144.6, 138.8, 116.1, 115.2, 82.4, 67.1.

2.4 Synthesis of 3i-l and 3n



A solution of I_2 (1.38g, 5.5 mmol) in $CHCl_3$ was dropped into a stirring solution of the benzyl alcohol (5mmol) and silver trifluoroacetate (1.21g, 5.5 mmol) in $CHCl_3$ (20 mL) at room temperature over a period of 10 min. The resulting suspension was stirred for 2 h and monitored by TLC. Upon completion, the mixture was filtered through a layer of silica gel and concentrated in vacuo. The iodinated product was purified through column chromatography

(2-Iodo-4-methoxyphenyl)methanol (3i)

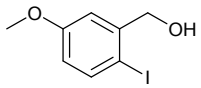


3i

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.7 (s, 1H), 7.29-7.27 (d, J = 8.2 Hz, 1H), 6.95-6.93 (d,

J = 8.4 Hz, 1H), 4.40 (bs, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 156.5, 137.1, 136.8, 127.9, 113.4, 111.1, 61.6, 51.3.

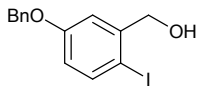
(2-Iodo-5-methoxyphenyl)methanol (3j)



3j

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.64 (d, J = 8.6 Hz, 1H), 7.05-7.04 (d, J = 3 Hz, 1H), 6.60-6.57 (dd, J = 3 Hz, J = 8.6 Hz 1H), 4.60 (s, 2H), 3.79 (s, 3H), 2.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 143.6, 139.5, 115.2, 114.1, 85.3, 69.1, 55.4.

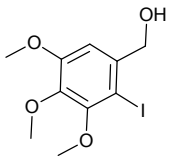
(5-(Benzyloxy)-2-iodophenyl)methanol (3k)



3k

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.67-7.64 (d, J = 8.6 Hz, 1H), 7.45-7.32 (m, 5H), 7.18-7.17 (d, J = 3Hz, 1H), 6.74-6.72 (dd, J = 8.6 Hz, J = 3 Hz, 1H), 5.10 (s, 2H), 4.36 (s, 2H), 3.38 (bs, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 158.8, 144.9, 138.9, 136.8, 128.4, 127.8, 127.6, 115.3, 114.7, 85.1, 69.2, 67.1.

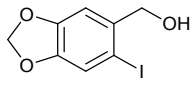
3,4,5-Trimethoxy-2-iodobenzyl alcohol (3l)



3l

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.03 (s, 1H), 5.45 (s, 1H), 4.38-4.37 (d, J = 0.36Hz, 2H), 3.82(s, 3H), 3.75-3.75 (d, J = 0.16Hz, 6H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 153.4, 152.0, 140.3, 139.4, 107.5, 83.4, 67.4, 60.5, 60.4, 55.8.

(6-Iodobenzo[*d*][1,3]dioxol-5-yl)methanol (3n)



3n

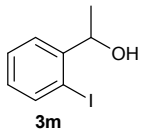
White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.33 (s, 1H), 7.03 (s, 1H), 6.03 (s, 2H), 5.39 (bs, 1H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 148.0, 147.0, 137.3, 117.5, 108.0, 101.5, 84.4, 67.1.

2.5 Synthesis of 3m

2'-Iodoacetophenone (2 mmol, 492mg) was dissolved in THF (10 mL) and cooled to 0 °C. $NaBH_4$ (2.5 mmol, 95mg) and $BF_3{\cdot}OEt_2$ (2.5 mmol, 0.35mL) was slowly added into the stirring solution at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 2 h, monitoring by TLC. Upon completion, the reaction was quenched with water (15 mL) at 0 °C and saturated with K_2CO_3. After extraction with EtOAc (3 × 20 mL), the combined organic phases were dried (Na_2SO_4) and

concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc : petroleum = 4:1) to yield the target **3m**

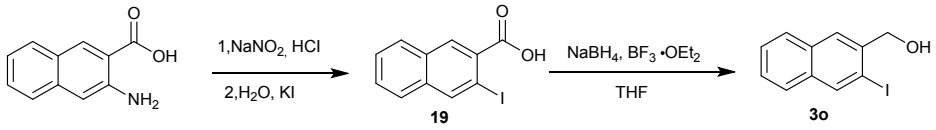
1-(2-Iodophenyl)ethanol (3m)



3m

White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.78-7.76 (dd, J = 7.8 Hz, J = 1 Hz, 1H), 7.56-7.53 (dd, J = 7.8 Hz, J = 1.6 Hz, 1H), 7.42-7.38 (td, J = 7.4 Hz, J = 0.8 Hz, 1H), 7.00-6.96 (td, J = 7.4 Hz, J = 1.6 Hz, 1H), 5.38 (bs, 1H), 4.80-4.76 (q, J = 6.4 Hz, 1H), 1.27-1.25 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 148.8, 138.6, 128.8, 128.4, 126.6, 97.1, 71.8, 24.5.

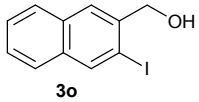
2.6 Synthesis of substituted 2-iodobenzyl alcohol 3o



19 **3o**

A solution of $NaNO_2$ (345 mg, 5.0 mmol) in water (2 mL) was added slowly to a cold (0 °C) stirred solution of 3-amino-2-naphthoic acid (1 g, 4.27 mmol), concentrated HCl (6 mL) and crushed ice (5 g) in water (10 mL). After addition was completed, the solution was stirred for additional 30 min below 5 °C. A solution of KI (1.35 g, 8.0 mmol) in water (4 mL) was added slowly. The resulting mixture was stirred for 5 min at 0 °C and then heated to 90 °C for 30 minutes to remove all N_2. The mixture was cooled to room temperature and extracted with EtOAc (5 times). The organics were washed with saturated aqueous $NaHSO_3$ (several times) and water, and then dried over anhydrous Na_2SO_4. The solvents were removed under *vacuo* to give crude product as reddish yellow solid. The residue **19** (2mmol) was dissolved in THF (10 mL) and cooled to 0 °C. $NaBH_4$ (2.5mmol) and BF_3·OEt_2(2.5mmol) was slowly added into the stirring solution at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 2 h, monitoring by TLC. Upon completion, the reaction was quenched with water (100 mL) at 0 °C and saturated with K_2CO_3. After extraction with EtOAc (3×20 mL), the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography (SiO_2; 20% EtOAc in petroleum) to yield the target **3o**.

(3-Iodonaphthalen-2-yl)methanol (3o)



3o

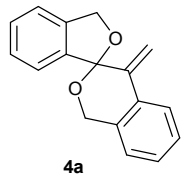
White solid; ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.47 (s, 1H), 7.97 (s, 1H), 7.92-7.90 (d, J = 7.8 Hz, 1H), 7.85-7.83 (d, J = 7.7 Hz, 1H), 7.5-7.48 (m, 2H), 5.53 (bs, 1H), 4.57 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 140.0, 137.6, 133.6, 132.2, 127.6, 126.6, 126.4, 126.2, 125.5, 94.9, 67.3.

3. General procedure for the preparation of 3*H*-Spiro[isobenzofuran-1,3′-isochroman] compounds 4.

To a solution of propargylic compound **2** (1.5 mmol) in DMF (5.0 mL) was added Na_2CO_3 (188 mg, 3mmol). The mixture was stirred for 5 min and $Pd(OAc)_2/P(2\text{-Tol})_3$ (13.4mg, 0.06 mmol, 10 mol %), and aryl halides **3** (0.60 mmol) were added. The resulting mixture was then heated under an argon atmosphere at 120 °C. When the reaction was considered complete as determined by TLC analysis, the reaction mixture was allowed to cool to room temperature and quenched with a saturated aqueous solution of ammonium chloride, and the mixture was extracted with EtOAc. The combined organic extracts were washed with water and saturated brine. The organic layers were dried over Na_2SO_4, filtered. Solvents were evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford spriocyclic compound **4**.

4. Spectra Data of 3*H*-Spiro[isobenzofuran-1, 3′-isochroman] compounds.

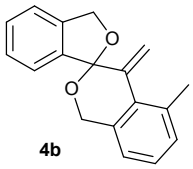
4'-Methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman](4a)



4a

Pale yellow oil; (65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.74 (m, 1H), 7.44-7.27 (m, 6H), 7.14-7.12 (m, 1H), 5.83 (s, 1H), 5.32-5.29 (d, J = 12.8 Hz, 1H), 5.28-5.24 (d, J = 15.0 Hz, 1H), 5.20-5.17 (d, J = 12.8 Hz, 1H), 5.08 (s, 1H), 4.83-4.80 (d, J = 15 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 140.3, 139.8, 134.1, 130.8, 129.2, 127.9, 127.6, 127.2, 124.3, 124.0, 123.7, 121.1, 111.3, 109.6, 71.7, 63.7; FT-IR (KBr, cm^{-1}) 3365, 3069, 3035, 2945, 2860, 1655, 1597, 1578, 1461, 1371, 1230, 1074, 1053, 1006, 959, 760; HRMS (ESI): m/z calcd for $C_{17}H_{15}O_2$ $[M+H]^+$ 251.1067, found 251.1068.

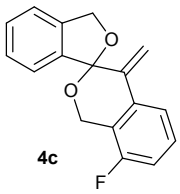
8'-Methyl-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4b)



4b

Pale yellow solid; (57%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.38-7.33 (m, 2H), 7.28-7.19 (m, 3H), 7.12-7.10 (d, J = 7.2 Hz, 1H), 6.76-6.74 (d, J = 7.6 Hz, 1H), 5.63 (s, 1H), 5.51 (s, 1H), 5.19-5.12 (d, J = 13.1 Hz, J = 15.2 Hz, 2H), 4.74-4.71 (d, J = 13.5 Hz, 1H), 4.60-4.57(d, J = 13.5Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 141.3, 141.2, 138.8, 137.9, 134.7, 132.4, 130.2, 128.6, 127.5, 126.9, 122.1, 121.8, 121.4, 117.0, 110.1, 70.9, 64.2, 20.3; FT-IR (KBr, cm^{-1}) 3365, 3071, 3033, 2965, 2860, 1633, 1603, 1460, 1382, 1223, 1058, 1007, 971, 760; HRMS (ESI): m/z calcd for $C_{18}H_{17}O_2$ $[M+H]^+$ 265.1223, found 265.1222.

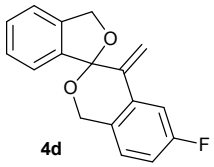
8'-Fluoro-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4c)



4c

White solid; (63%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.67-7.65 (d, J = 7.8 Hz, 1H), 7.48-7.42 (m, 2H), 7.39-7.34 (m, 2H), 7.27-7.25 (d, J = 7.5 Hz, 1H), 7.20-7.15 (t, J = 8.8 Hz, 1H), 5.94 (s, 1H), 5.18-5.15 (d, J = 13.1 Hz, 1H), 5.11-5.07 (d, J = 13.1 Hz, 1H), 5.01-4.97 (d, J = 15.4 Hz, 2H) , 4.92-4.88 (d, J = 15.4 Hz, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 157.7 (d, J = 240 Hz), 140.4, 138.6,138.6, 132.9 (d, J = 5 Hz), 129.2, 128.4 (d, J = 8 Hz), 127.4, 123.5, 121.4, 121.0 (d, J = 17 Hz), 120.1 (d, J = 3 Hz), 114.0 (d, J = 20 Hz), 112.1, 108.3, 71.2, 57.6 (d, J = 5 Hz); FT-IR (KBr, cm^{-1}) 3434, 3106, 3044, 2950, 2864, 1639, 1612, 1575, 1462, 1374, 1239, 1078, 1048, 994, 956, 757; HRMS (ESI): m/z calcd for $C_{17}H_{14}FO_2$ $[M+H]^+$ 269.0972, found 269.0971.

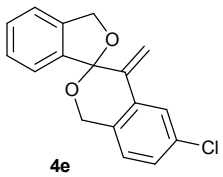
6'-Fluoro-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4d)



4d

White solid; (68%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.67-7.64 (dd, J = 10.6 Hz, J = 2.5 Hz, 1H), 7.45-7.42 (m, 2H), 7.38-7.34 (m, 1H), 7.27-7.21 (m, 2H), 7.19-7.14 (m, 1H), 5.97 (s, 1H), 5.17-5.13 (d, J = 13.1 Hz, 1H), 5.11-5.08 (d, J = 13.1 Hz, 1H), 5.02-4.98 (d, J = 14.9 Hz, 1H), 4.95 (s, 1H), 4.77-4.73 (d, J = 14.9 Hz, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 161.5 (d, J = 240 Hz), 140.3, 139.3, 139.2, 132.6 (d, J = 8 Hz), 130.1 (d, J = 2 Hz), 129.2, 127.5, 126.7 (d, J = 8 Hz), 123.3, 121.4, 115.1 (d, J = 22 Hz), 112.8, 110.3 (d, J = 22 Hz), 108.4, 71.0, 62.1; FT-IR (KBr, cm^{-1}) 3436, 3102, 2921, 2867, 1613, 1585, 1490, 1460, 1365, 1229, 1048, 1001, 959, 768; HRMS (ESI): m/z calcd for $C_{17}H_{14}FO_2$ $[M+H]^+$ 269.0972, found 269.0972.

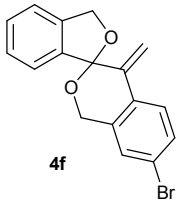
6'-Chloro-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4e)



4e

White solid; (62%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.87-7.87 (d, J = 2 Hz, 1H), 7.46-7.41 (m, 2H), 7.38-7.33 (m, 2H), 7.24-7.21 (m, 2H), 5.98 (s, 1H), 5.16-5.13 (d, J = 13.0 Hz, 1H), 5.10-5.07 (d, J = 13.0 Hz, 1H), 5.01-4.98 (d, J = 15.3 Hz, 1H), 4.94 (s, 1H), 4.78-4.74 (d, J = 15.3 Hz, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 140.3, 139.1, 138.9, 132.8, 132.5, 131.9, 129.2, 127.7, 127.4, 126.5, 123.7, 123.3, 121.3, 112.8, 108.5, 71.1, 62.2; FT-IR (KBr, cm^{-1}) 3433, 3080, 3047, 2927, 2850, 1641, 1593, 1461, 1363, 1225, 1047, 1000, 946, 764; HRMS (ESI): m/z calcd for $C_{17}H_{14}ClO_2$ $[M+H]^+$ 285.0677, found 285.0676.

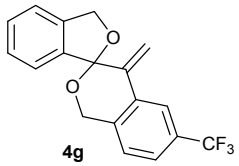
6'-bromo-5'-methylene-3H-spiro[isobenzofuran-1,3'-isochroman] (4f)



4f

White solid; (53%); ^{1}H NMR (400 MHz, d_6-$CDCl_3$) δ 7.59-7.56 (d, J = 8.48 Hz, 1H), 7.42-7.39 (m, 2H), 7.36-7.25 (m, 4H), 5.79 (s, 1H), 5.28-5.25 (d, J = 12.7 Hz, 1H), 5.20-5.13 (m, 2H), 5.07 (s, 1H), 4.75-4.71 (d, J = 15.1 Hz, 1H); ^{13}C NMR (100 MHz, d_6-$CDCl_3$) δ140.3, 139.4, 139.3, 136.0, 130.3, 129.7, 129.3, 127.7, 127.2, 125.8, 123.6, 121.9, 121.1, 111.8, 109.3, 71.8, 63.0; FT-IR (KBr, cm^{-1}) 3394, 3098, 3076, 2892, 2856, 1635, 1590, 1483, 1466, 1406, 1369, 1229, 1047, 994, 954, 759; HRMS (ESI): m/z calcd for $C_{17}H_{14}BrO_2$ $[M+H]^+$ 329.0177, found 329.0178.

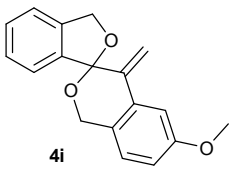
4'-Methylene-6'-(trifluoromethyl)-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4g)



4g

Pale yellow solid; (57%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.03-8.01 (d, J = 8.2 Hz, 1H), 7.65-7.62 (m, 2H), 7.47-7.42 (m, 2H), 7.38-73.4 (td, J = 7.6 Hz, J = 1.8 Hz, 1H), 7.24-7.22 (d, J = 7.6 Hz, 1H), 6.05 (s, 1H), 5.18-5.15 (d, J = 13.2 Hz, 1H), 5.12-5.05 (m, 3 H), 4.90-4.82 (d, J = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 140.3, 139.0, 138.9, 135.0, 134.4, 129.2, 128.0 (d, J = 32 Hz), 127.5, 125.1, 124.1 (d, J = 270 Hz), 123.7 (d, J = 4 Hz), 123.3, 121.7 (d, J = 4 Hz), 121.4, 114.0, 108.6, 71.1, 62.3; FT-IR (KBr, cm^{-1}) 3433, 3086, 3051, 2957, 2879, 1639, 1616, 1579, 1504, 1465, 1363, 1338, 1164, 1116, 1047, 997, 958,759; HRMS (ESI): m/z calcd for $C_{18}H_{14}F_3O_2$ $[M+H]^+$ 319.0640, found 319.0939.

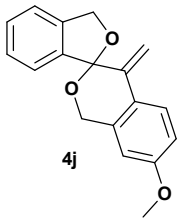
6'-Methoxy-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4i)



4i

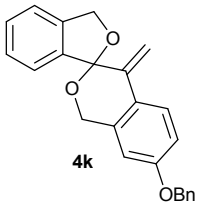
White solid; (65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 744-7.40 (m, 1H), 7.37-7.32 (m, 3H), 7.25-7.24 (d, J = 2.9 Hz, 1H), 7.06-7.04 (d, J = 8.4 Hz, 1H), 6.91-6.89 (d, J = 8.4 Hz, J = 2.5 Hz, 1H), 5.80 (s, 1H), 5.31-5.28 (d, J = 12.7 Hz, 1H), 5.22-5.16 (m, 2H), 5.10 (s, 1H), 4.79-4.75 (d, J = 14.4 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 140.5, 140.3, 139.8, 131.8, 129.0, 127.5, 126.6, 125.4, 123.5, 121.0, 114.7, 111.4, 109.3, 108.4, 71.6, 63.3, 55.3; FT-IR (KBr, cm^{-1}) 3433,3055, 3024, 2909, 2868, 1636, 1605, 1579, 1497, 1462, 1384, 1338, 1233, 1050, 1004, 962, 770; HRMS (ESI): m/z calcd for $C_{18}H_{17}O_3$ $[M+H]^+$ 281.1172, found 281.1174.

7'-Mthoxy-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4j)



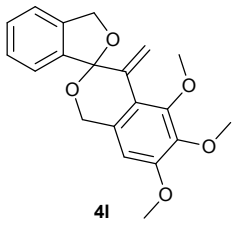
White solid; (63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.66 (d, *J* = 8.7 Hz, 1H), 7.43-7.39 (m, 1H), 7.35-7.32 (m, 3H), 6.89-6.86 (dd, *J* = 8.7 Hz, *J* = 2.6 Hz, 1H), 6.64-6.63 (d, *J* = 2.6 Hz, 1H), 5.69 (s, 1H), 5.30-5.27 (d, *J* = 12.6 Hz, 1H), 5.25-5.21 (d, *J* = 14.7 Hz, 1H), 5.19-5.16 (d, *J* = 12.6 Hz, 1H), 4.94 (s, 1H), 4.79-4.75 (d, *J* = 14.7 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 140.4, 139.8, 139.7, 135.4, 129.1, 127.5, 125.6, 123.6, 123.5, 121.0, 113.9, 109.6, 109.0, 108.3, 71.6, 63.7, 55.2; FT-IR (KBr, cm^{-1}) 3428, 3055, 3012, 2925, 2868, 1632, 1609, 1579, 1498, 1462, 1365, 1249, 1075, 1006, 961, 766; HRMS (ESI): m/z calcd for $C_{18}H_{17}O_3$ $[M+H]^+$ 281.1172, found 281.1174.

7'-(Benzyloxy)-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4k)



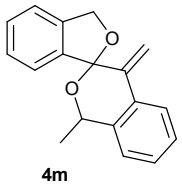
White solid; (60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.67 (d, *J* = 8.7 Hz, 1H), 7.47-7.40 (m, 5H), 7.38-7.33 (m, 4H), 6.97-6.94 (dd, *J* = 8.7 Hz, *J* = 2.4 Hz, 1H), 6.72-6.72 (d, *J* = 2.1 Hz, 1H), 5.70 (s, 1H), 5.31-5.28 (d, *J* = 12.7 Hz, 1H), 5.25-5.21 (d, *J* = 14.9 Hz, 1H), 5.19-5.16 (d, *J* = 12.7 Hz, 1H), 5.11 (s, 2H), 4.95 (s, 1H), 4.78-4.74 (d, *J* = 14.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 140.4, 139.8, 139.7, 136.7, 135.4, 129.1, 128.5, 127.9, 127.5, 127.3, 125.6, 123.8, 123.6, 121.0, 114.7, 109.6, 109.5, 109.2, 71.6, 70.0, 63.7; FT-IR (KBr, cm^{-1}) 3402, 3062, 3033, 2921, 2861, 1607, 1574, 1498, 1382, 1359, 1277, 1244, 1074, 1049, 1005, 958, 758; HRMS (ESI): m/z calcd for $C_{24}H_{21}O_3$ $[M+H]^+$ 357.1485, found 357.1484.

5',6',7'-Trimethoxy-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4l)



Colorless oil; (55%); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.40-7.38 (m, 2H), 7.33-7.30 (m, 2H), 7.20-7.18 (d, J = 7.6 Hz, 1H), 6.67 (s, 1H), 6.21-6.21 (d, J = 1.5 Hz, 1H), 5.18-5.18(d, J = 1.5 Hz, 1H), 5.17-5.08(dd, J = 12.8Hz, J = 21.5 Hz, 2H), 4.97-4.93 (d, J = 14.4 Hz, 1H), 4.62-4.58 (d, J = 14.4 Hz, 1H), 3.87(s, 2H), 3.82(s, 2H), 3.80(s, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 154.1, 153.6, 142.9, 142.1, 141.3, 139.0, 133.0, 129.6, 128.1, 124.2, 121.9, 118.8, 115.7, 111.1, 104.6, 71.9, 64.3, 60.9, 60.2, 56.3. FT-IR (KBr, cm^{-1}) 3455, 2935, 2861, 1655, 1596, 1488, 1461, 1413, 1358, 1337, 1278, 1242, 1118, 1098, 1048, 1013, 958,764; HRMS (ESI): m/z calcd for $C_{24}H_{21}O_3$ $[M+H]^+$ 341.1485, found 341.1484.

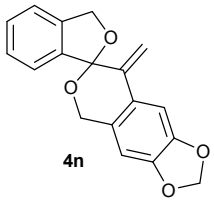
1'-Methyl-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (4m)



4m

Pale yellow solid; (64%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.76-7.72 (m, 1H), 7.43-7.21 (m, 6H), 6.90-6.88 (d, J = 7.6 Hz, 1H), 5.81-5.75 (s, 1H), 5.20-4.85 (m, 4H), 1.53-1.52 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 141.0, 140.9, 140.3, 139.8, 139.7, 139.6, 138.6, 138.3, 130.6, 130.4, 128.9, 128.8, 128.2, 128.0, 127.3, 127.2, 127.1, 127.0, 124.8, 124.3, 124.0, 123.9, 123.5, 122.3, 121.6, 121.2, 110.9, 110.0, 109.0, 107.9, 70.8, 70.2, 67.3, 23.1, 20.4; FT-IR (KBr, cm^{-1}) 3367, 3067, 3032, 2979, 2931, 2864, 1632, 1610, 1576, 1460, 1372, 1234, 1106, 1007, 962, 752; HRMS (ESI): m/z calcd for $C_{18}H_{17}O_2$ $[M+H]^+$ 265.1223, found 265.1224.

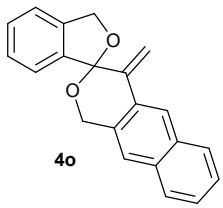
8-Methylene-5,8-dihydro-3'*H*-spiro[[1,3]dioxolo[4,5-*g*]isochromene-7,1'-isobenzofuran] (4n)



4n

Pale red oil; (56%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.39 (m, 1H), 7.37-7.31 (m, 3H), 7.17 (s, 1H), 6.56 (s, 1H), 5.98-5.96 (dd, J = 6.8 Hz, J = 1.2 Hz, 2H), 5.61 (s, 1H), 5.29-5.26 (d, J = 12.7 Hz, 1H), 5.18-5.13 (m, 2H), 4.95 (s, 1H), 4.71-4.67 (d, J = 14.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 147.2, 140.3, 140.1, 139.7, 129.1, 128.4, 127.5, 124.6, 123.6, 121.0, 109.7, 109.3, 104.1, 103.9, 101.0, 71.6, 63.7; FT-IR (KBr, cm^{-1}) 3372, 3037, 2905, 2862, 1625, 1610, 1561, 1501, 1482, 1377, 1355, 1274, 1243, 1089, 1038, 957, 937, 756; HRMS (ESI): m/z calcd for $C_{18}H_{15}O_4$ $[M+H]^+$ 295.0965, found 295.0966.

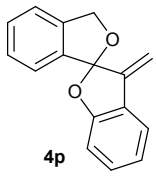
-Methylene-1,4-dihydro-3'*H*-spiro[benzo[*g*]isochromene-3,1'-isobenzofuran] (4o)



4o

Pale yellow solid; (55%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.90-7.87 (m, 1H), 7.82-7.80 (m, 1H), 7.61 (s, 1H), 7.51-7.46 (m, 2H), 7.44-7.40 (m, 1H), 7.35-7.27 (m, 3H), 6.02 (s, 1H), 5.40-5.33 (m, 2H), 5.24-5.21 (d, J = 13.6 Hz, 2H), 4.97-4.94 (d, J = 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ141.5, 140.5, 140.0, 132.8, 132.8, 132.6, 130.2, 129.0, 128.1, 127.6, 127.3, 126.4, 125.8, 123.3, 123.1, 122.5, 121.0, 113.2, 109.9, 71.7, 64.0; FT-IR (KBr, cm^{-1}) 3432, 3047, 2919, 2854, 1638, 1597, 1499, 1460, 1370, 1316, 1229, 1188, 1094, 1048, 1002, 957, 855, 758; HRMS (ESI): m/z calcd for $C_{21}H_{17}O_2$ $[M+H]^+$ 301.1223, found 301.1225.

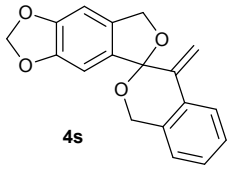
3-Methylene-3*H*,3'*H*-spiro[benzofuran-2,1'-isobenzofuran] (4p)



4p

Pale yellow oil; (20%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.50 (dd, *J* = 7.5 Hz, *J* = 0.72 Hz, 1H), 7.47-7.43 (m, 1H), 7.38-7.34 (m, 2H), 7.31-7.27 (m, 1H), 7.25-7.23 (m, 1H), 7.02-6.98 (td, *J* = 7.5 Hz, *J* = 0.72 Hz, 1H), 6.88-6.86 (d, *J* = 8.0 Hz, 1H), 5.80 (s, 1H), 5.44-5.40 (d, *J* = 12.8 Hz, 1H), 5.27-5.24 (d, *J* = 12.8 Hz, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 146.0, 139.9, 138.5, 130.9, 129.6, 128.2, 124.1, 123.1, 121.1, 121.0, 120.8, 118.9, 110.4, 108.6, 72.6; FT-IR (KBr, cm^{-1}) 3394, 3051, 3034, 2924, 2870, 1645, 1608, 1594, 1463, 1357, 1280, 1267, 1242, 1057, 990, 912, 750; HRMS (ESI): m/z calcd for $C_{16}H_{13}O_2$ $[M+H]^+$ 237.0910, found 237.0908.

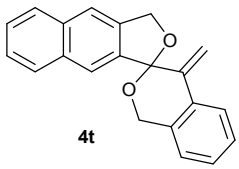
4'-methylene-7*H*-spiro[[1,3]dioxolo[4,5-*f*]isobenzofuran-5,3'-isochroman] (4s)



4s

Pale red oil; (52%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73-7.71 (m, 1H), 7.32-7.27 (m, 2H), 7.14-7.10 (m, 1H), 6.73 (s, 2H), 6.03-5.98 (dd, *J* = 16.6 Hz, *J* = 1.2 Hz, 2H), 5.81 (s, 1H), 5.25-5.17 (m, 2H), 5.11 (s, 1H), 5.08-5.04 (d, *J* = 12.2 Hz, 1H), 4.81-4.77 (d, *J* = 14.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 147.8, 140.4, 134.1, 133.8, 132.9, 130.7, 127.9, 127.1, 124.3, 124.0 1112, 109.6, 104.0, 101.6, 101.2, 71.6, 63.7; FT-IR (KBr, cm^{-1}) 3395, 3066, 3021, 2951, 2899, 2860, 1617, 1600, 1577, 1501, 1478, 1387, 1368, 1278, 1263, 1061, 1032, 1011, 962, 938, 773, 733; HRMS (ESI): m/z calcd for $C_{18}H_{15}O_4$ $[M+H]^+$ 295.0965, found 295.0963.

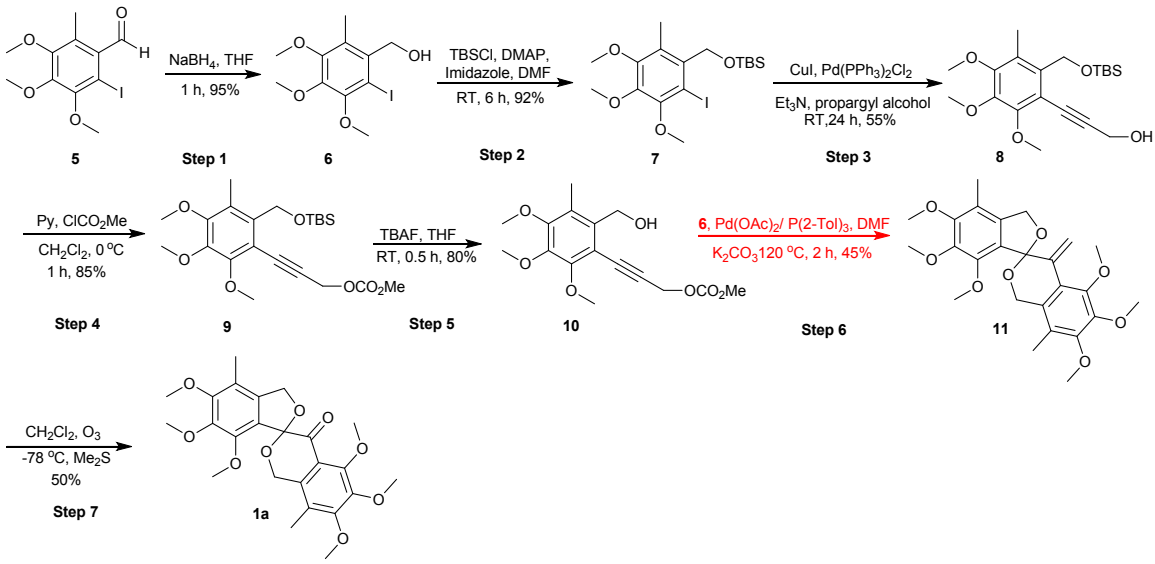
4-Methylene-3'*H*-spiro[isochroman-3,1'-naphtho[2,3 c]furan] (4t)



4t

White solid; (54%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.98-7.95 (m, 2H), 7.91 (s, 1H), 7.85-7.82 (m, 1H), 7.79 (s, 1H), 7.56-7.47 (m, 2H), 7.35-7.33 (m, 2H), 7.22-7.20 (m, 1H), 5.94 (s, 1H), 5.30-5.26 (d, *J* = 13.6 Hz, 1H), 5.25-5.21 (d, *J* = 13.6 Hz, 1H), 5.09-5.05 (d, *J* = 15.1 Hz, 1H), 5.02 (s, 1H), 4.80-4.76 (d, *J* = 15.1 Hz, 1H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 139.9, 138.7, 138.4, 133.9, 133.5, 132.5, 130.4, 128.5, 127.9, 127.7, 127.2, 126.5, 125.8, 124.4, 123.9, 122.3, 119.5, 111.6, 108.2, 70.2, 62.6; FT-IR (KBr, cm^{-1}) 3431, 3057, 2919, 2865, 1629, 1608, 1503, 1486, 1461, 1442, 1370, 1312, 1232, 1209, 1105, 1065, 1050, 1009, 958, 900, 878, 777; HRMS (ESI): m/z calcd for $C_{21}H_{17}O_2$ $[M+H]^+$ 301.1223, found 301.1224.

5. Synthesis of 1a



Step 1

5 (2 mmol, 672 mg) was dissolved in THF (10 mL) and cooled to 0 °C. $NaBH_4$ (2.5 mmol, 95 mg) and $BF_3{\cdot}OEt_2$ (2.5 mmol, 0.35mL) was slowly added into the stirring solution at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 2 h, monitoring by TLC. Upon completion, the reaction was quenched with water (15 mL) at 0 °C and saturated with K_2CO_3. After extraction with EtOAc (3 × 20 mL), the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc : petroleum = 4:1) to yield the target **6** (642 mg, 95%).

Step 2

6 (2 mmol, 676 mg) was dissolved in DMF (2.5mL), DMAP (0.04 mmol, 4.88 mg) and imidazole (2.4mmol, 163 mg) were slowly added into the stirring solution and stirred for 0.5 h. The mixed reaction was then added TBSCl (3 mmol, 450 mg) and stirred for 6 h, monitoring by TLC. Upon completion, the reaction was quenched with water (15 mL) and saturated with K_2CO_3. After extraction with EtOAc (3 × 20 mL), the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc : petroleum = 16:1) to yield the target **7** (832 mg, 92%).

Step 3

To a stirred solution of **7** (4 mmol, 1.8 g), $Pd(PPh_3)_2Cl_2$ (141 mg, 0.2 mmol), CuI (76 mg,0.4 mmol) in NEt_3 (50 mL) was added propargylic alcohol (0.60 mL, 10 mmol) at RT and continued stir for 20 h at the same temperature, water (50 mL) the reaction mixture was diluted with water at the same temperature, and stirring was continued for 30 min. The resulting mixture was extracted with EtOAc (3 × 100 mL). The combined extracts were washed with brine, and the residue upon workup was chromatographed on silica gel with (EtOAc : petroleum = 4:1) as eluent to give the propargylic alcohol **8** (836 mg, 55%).

Step 4

To a stirred solution of propargylic alcohol **8** (2 mmol, 760 mg) and pyridine (4 mmol,0.35 mL) in

CH_2Cl_2 (10 mL) was added dropwise methyl chlorocarbonate (8 mmol, 0.6 mL) at 0 °C, and stirring was continued for 1 h at room temperature. The reaction mixture was diluted with water and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with aqueous NH_4Cl and brine, and the residue upon workup was chromatographed on silica gel with (EtOAc : petroleum = 8:1) as eluent to give the target **9** (745 mg, 85%).

Step 5

To a stirred solution of **9** (2 mmol, 876 mg) in THF (20 mL) was added TBAF (8 mmol, 2.08 g) at room temperature, and stirring was continued for 30 min at the same temperature. The reaction mixture was quenched with 1.0 M HCl, and extracted with EtOAc (3 × 20 mL). The combined extracts were washed with aqueous NH_4Cl and brine, and the residue upon workup was chromatographed on silica gel with (EtOAc : petroleum = 2:1) as eluent to give the target **10** (518 mg, 80%).

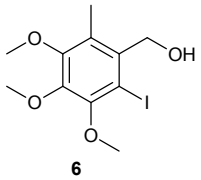
Step 6

To a solution of propargylic compound **10** (1.5 mmol, 486 mg) in DMF (5.0 mL) was added Na_2CO_3 (188 mg, 3 mmol). The mixture was stirred for 5 min and $Pd(OAc)_2/P(2\text{-}Tol)_3$ (13.4mg, 0.06 mmol, 10 mol %), and **6** (0.60 mmol,196 mg) were added. The resulting mixture was then heated under an argon atmosphere at 120 °C. When the reaction was considered complete as determined by TLC analysis, the reaction mixture was allowed to cool to room temperature and quenched with a saturated aqueous solution of ammonium chloride, and the mixture was extracted with EtOAc. The combined organic extracts were washed with water and saturated brine. The organic layers were dried over Na_2SO_4, filtered. Solvents were evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford spriocyclic compound **11** (124 mg, 45%).

Step 7

To a solution of **11** (0.2 mmol, 91.6 mg) in CH_2Cl_2 (10 mL) and the solution was cooled down to −78 °C. O_3 was directed into the solution and TLC was used to indicate the conversion of the substrate every 2 min. After about 10 min, upon complete conversion, the resulting solution was added Me_2S and the solution was allowed to warm up to room temperature and stirred for another 1 h. The resulting solution was concentrated in vacuo and the crude product was purified by column chromatography on silica gel to give the pure product **1a** (46 mg, 50%).

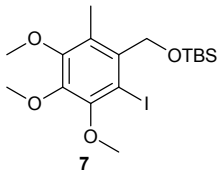
(2-Iodo-3,4,5-trimethoxy-6-methylphenyl)methanol (6)



6

White solid; (95%); ^1H NMR (400 MHz, CD_3COCD_3) δ 4.83 (s, 1H), 4.82 (s, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 153.4, 152.0, 146.5, 129.0, 94.5, 67.4, 61.0, 60.7, 60.7, 12.7 .

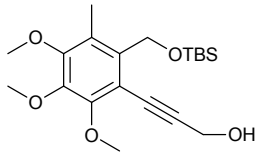
Tert-butyl((2-iodo-3,4,5-trimethoxy-6-methylbenzyl)oxy)dimethylsilane (7)



7

Colorless oil; (92%); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 4.93 (s, 2H), 3.87 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 2.33 (s, 3H), 0.93 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 153.4, 152.0, 146.6, 137.4, 129.1, 94.5, 68.9, 61.0, 60.8, 60.7, 26.3, 18.9, 12.7, -4.8.

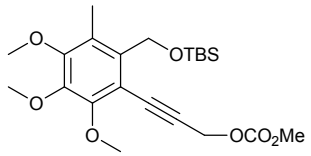
3-(2-(((Tert-butyldimethylsilyl)oxy)methyl)-4,5,6-trimethoxy-3-methylphenyl)prop-2-yn-1-ol (8)



8

Colorless oil; (55%); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 4.89 (s, 2H), 4.49-4.48 (d, J = 5.6 Hz, 2H), 4.34-4.31 (t, J = 5.9 Hz, 1H), 3.85 (s, 6H), 3.81 (s, 3H), 2.26 (s, 3H), 0.89 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 153.8, 153.4, 146.6, 137.3, 128.5, 114.3, 96.5, 79.3, 62.1, 61.2, 61.1, 60.8, 51.2, 26.2, 18.8, 11.9, -5.04.

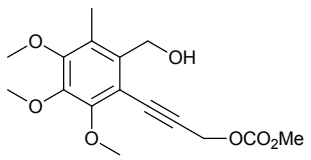
3-(2-(((Tert-butyldimethylsilyl)oxy)methyl)-4,5,6-trimethoxy-3-methylphenyl)prop-2yn-1-ylmethyl carbonate (9)



9

Colorless oil; (85%); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 5.06 (s, 2H), 4.87 (s, 2H), 3.86 (s, 3H) 3.85 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 2.26 (s, 3H), 0.90 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 156.0, 154.2, 154.1, 146.6, 137.6, 128.6, 113.2, 90.4, 82.2, 62.0, 61.4, 61.1, 60.8, 56.7, 55.3, 26.2, 18.8, 11.9, -5.0.

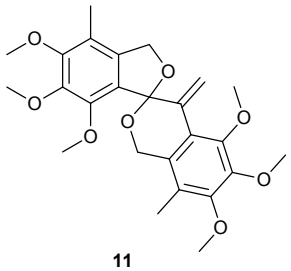
3-(2-(Hydroxymethyl)-4,5,6-trimethoxy-3-methylphenyl)prop-2-yn-1-yl methyl carbonate (10)



10

Colorless oil; (80%); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 5.04 (s, 2H), 4.74 (s, 2H), 3.85 (s, 3H) 3.84 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 156.0, 154.2, 154.0, 146.5, 138.7, 128.3, 113.3, 90.2, 82.2, 61.3, 61.1, 60.8, 60.6, 56.8, 55.3, 11.8.

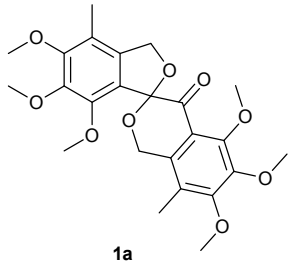
5,5',6,6',7,7'-Hexamethoxy-4,8'-dimethyl-4'-methylene-3*H*-spiro[isobenzofuran-1,3'-isochroman] (11)



11

Colorless oil; (45%); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 6.18-6.18 (d, J = 1.6 Hz, 1H), 5.29-5.29 (d, J = 1.6 Hz, 1H), 5.02 (s, 2H), 4.72-4.71 (d, J = 1.6 Hz, 2H), 3.89 (s, 3H), 3.84 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.58 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 154.1, 151.9, 151.3, 147.6, 146.9, 146.7, 139.1, 135.9, 131.3, 130.2, 122.7, 122.3, 120.1, 116.7, 111.7, 71.4, 61.7, 61.1, 61.0, 60.9, 60.9, 60.8, 60.0, 12.0, 10.5.

5,5',6,6',7,7'-Hexamethoxy-4,8'-dimethyl-3*H*-spiro[isobenzofuran-1,3'-isochroman]-4'-one (1a)



1a

Colorless oil; (50%); ^{1}H NMR (400 MHz, d_6-DMSO) δ 5.14-5.10 (d, *J* = 12.7 Hz, 1H), 5.06-5.02 (d, *J* = 16 Hz, 1H), 5.04-5.01 (d, *J* = 12.7 Hz, 1H), 4.88-4.84 (d, *J* = 16 Hz, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.75 (s, 3H), 3.68 (s, 3H), 2.06 (s, 3H),; ^{13}C NMR (100 MHz, d_6-DMSO) δ 184.9, 156.3, 153.4, 153.4, 146.2, 145.3, 136.6, 135.1, 125.3, 121.9, 119.1, 118.1, 108.0, 72.6, 61.2, 61.0, 60.8, 60.7, 60.5, 60.4, 12.012.0, 10.2.

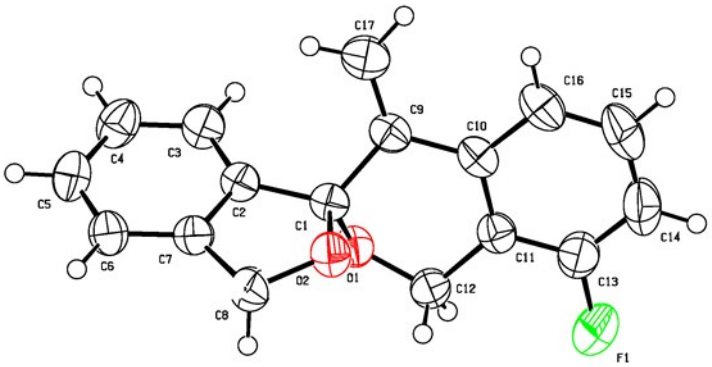
6. Reference

1. M. Yoshida et al. *Tetrahedron,* 61 (2005), 4381–4393

2. Muhammet Uyanik et al. *J. Am. Chem. Soc.* 2009, *131*, 251–262

3. Yepeng Luan et al. *J. Nat. Prod.* 2014, 77, 1718−172

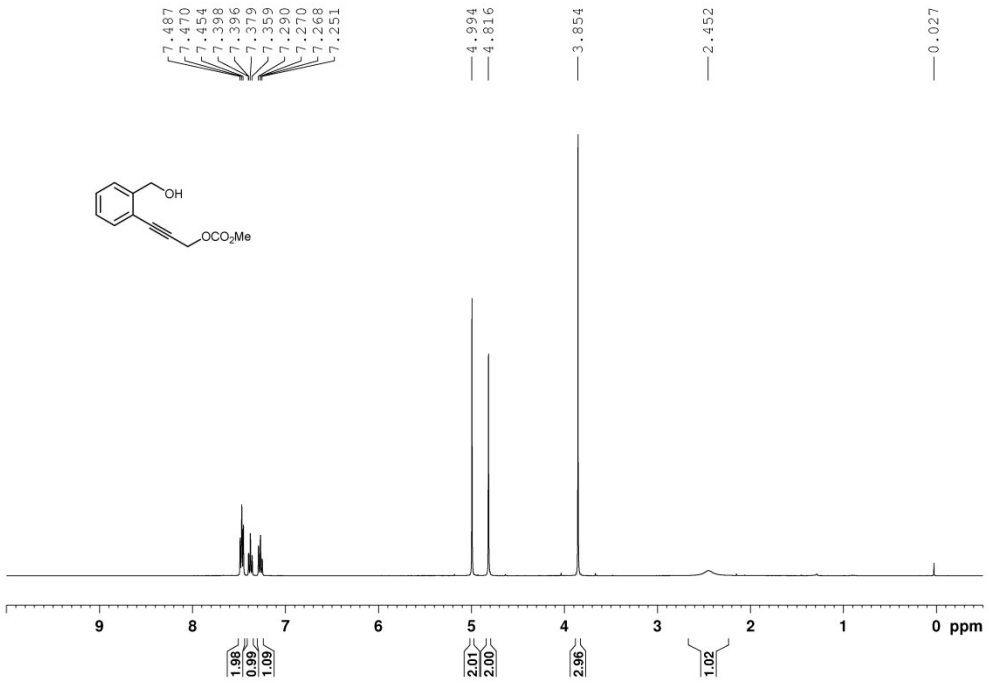
7. Crystallographic data of 4c

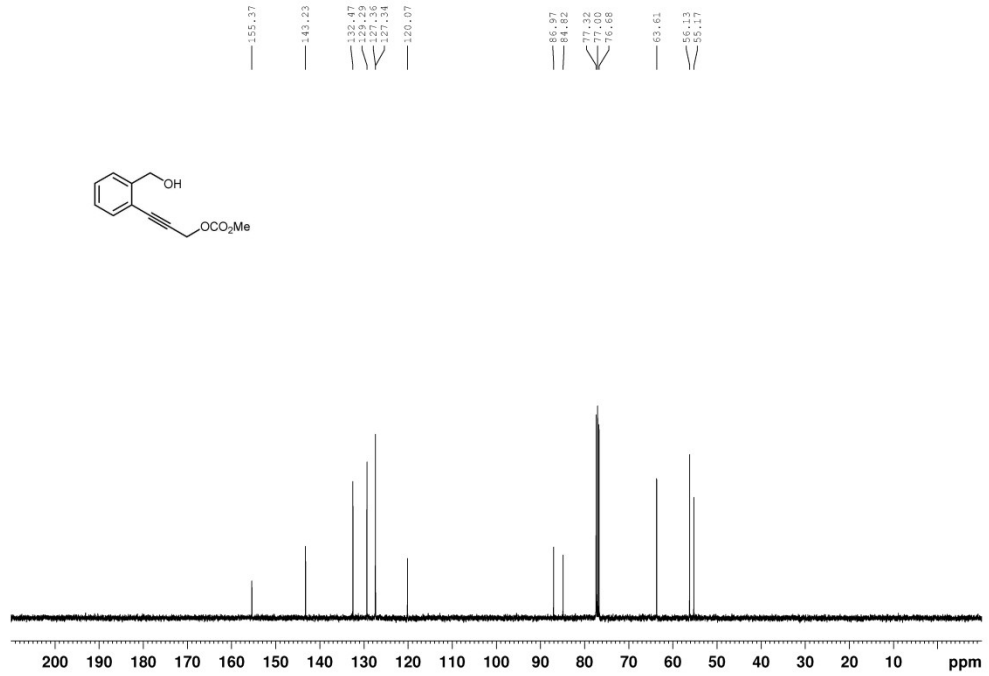


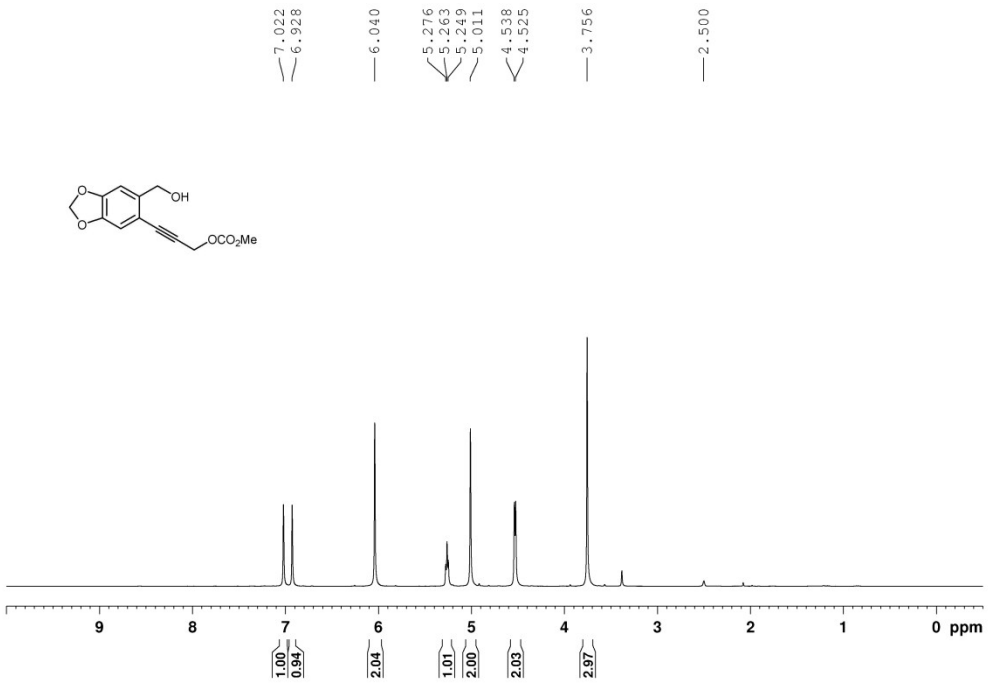
Structure of 4c

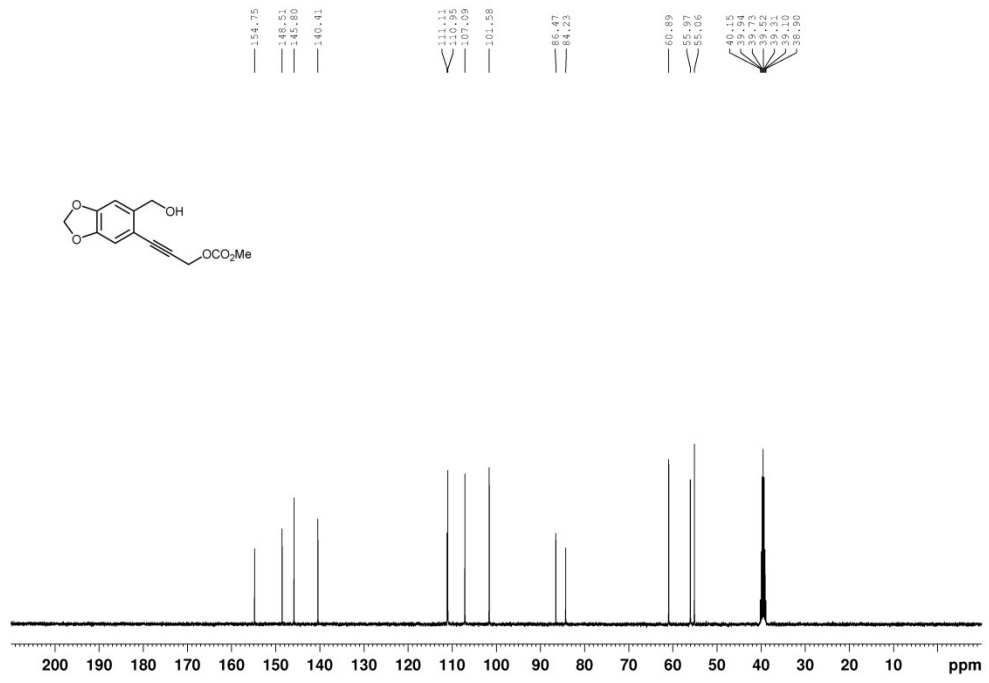
Crystal data	
Moiety formula: C17H13FO2	D_x = 1.347 Mg m−3
M_r = 268.27	Monoclinic, P21/n
Cell: a = 10.848 (2) Å. b = 8.1961 (16) Å c = 15.304 (3) Å, β = 103.597 (3)°	Extinction coefficient: 0.158 (9)
Z = 4	T = 296 K
F(000) = 560	S = 1.00
T_{min} = 0.972, T_{max} = 0.976	h = −12→12
V = 1322.5 (4) Å3	k = −9→9
wR(F2) = 0.123	l = −18→13
Reflections: 2326	R_{int} = 0.048

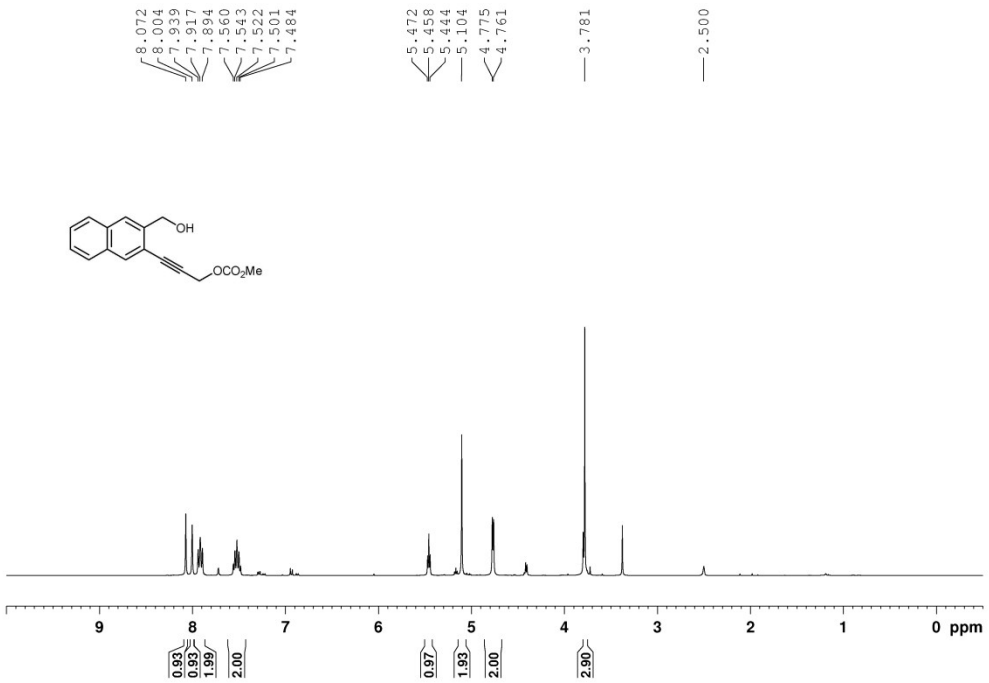
8. Copies of ^{1}H and ^{13}C Spectra

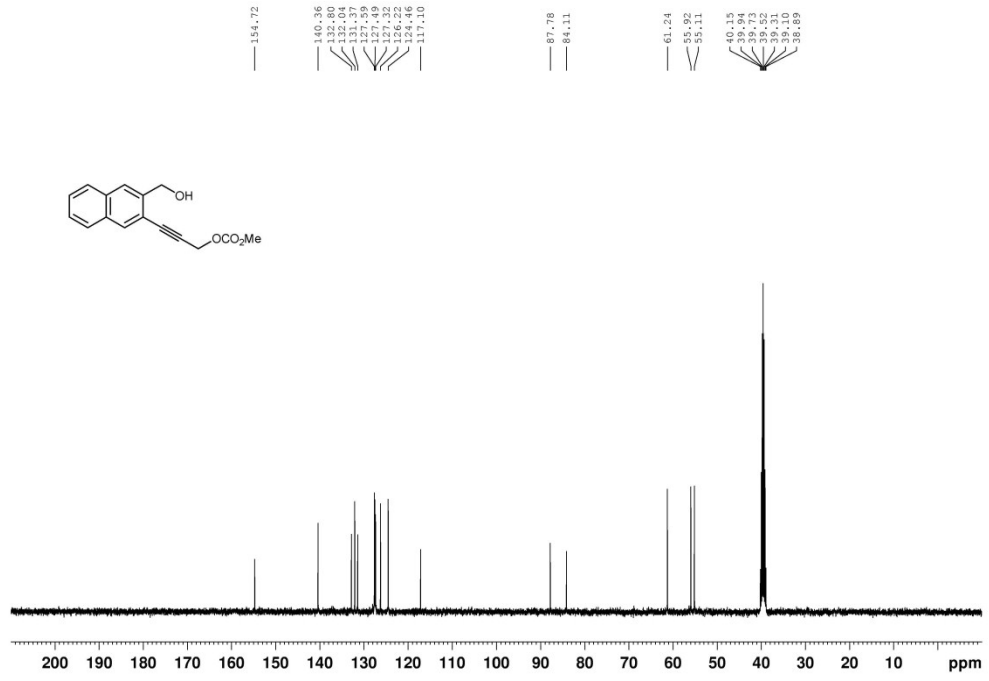


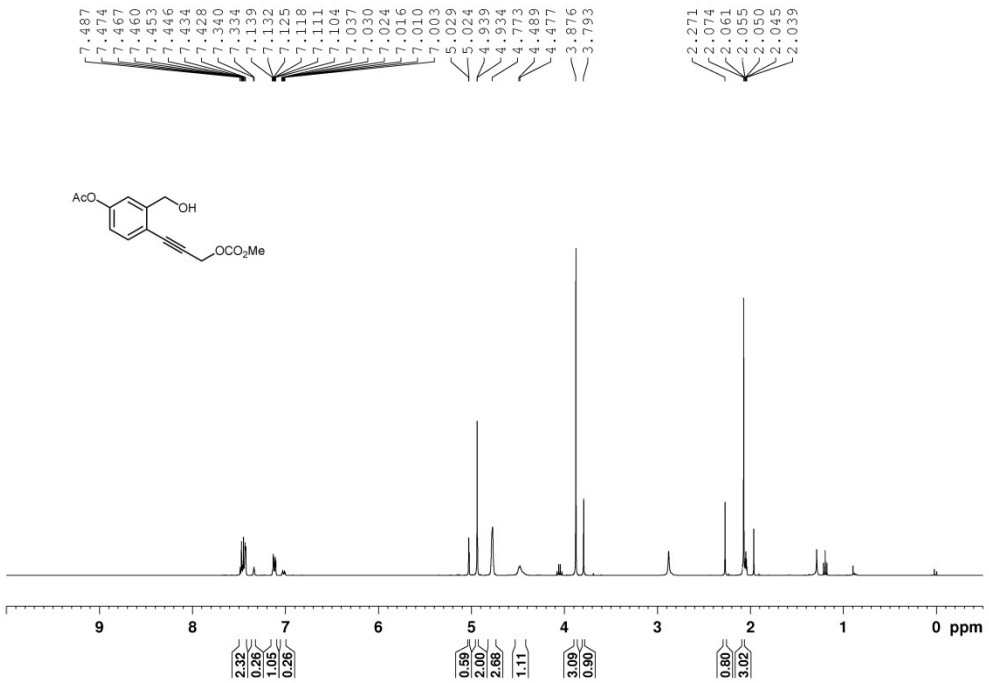


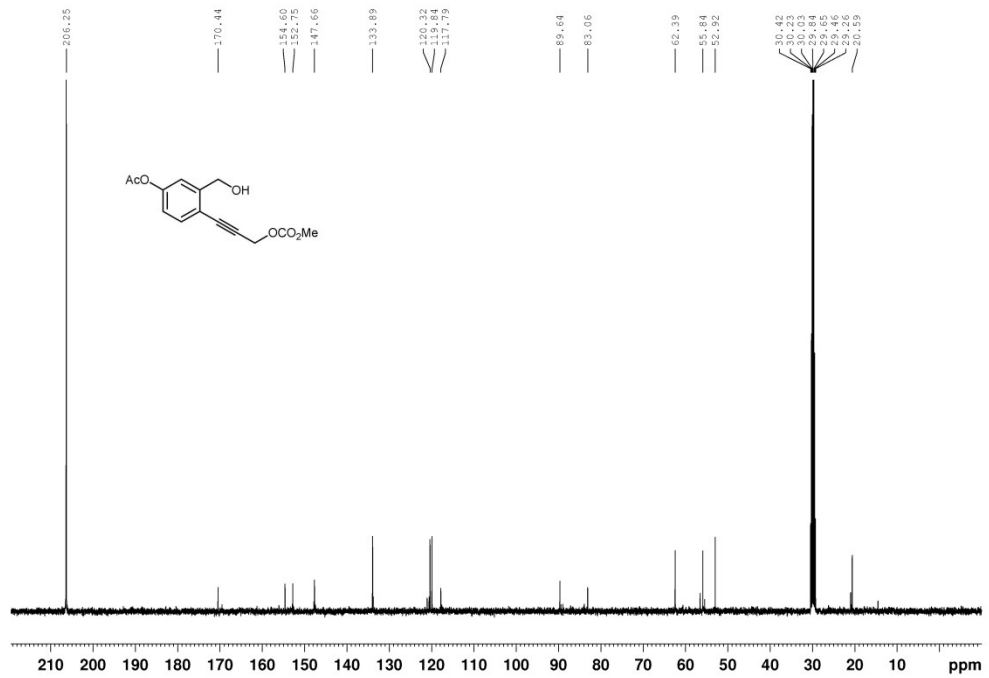

7.022
6.928
6.040
5.276
5.263
5.249
5.011
4.538
4.525
3.756
2.500
OH
OCO2Me
9
8
7
6
5
4
3
2
1
0 ppm
1.00
0.94
2.04
1.01
2.00
2.03
2.97

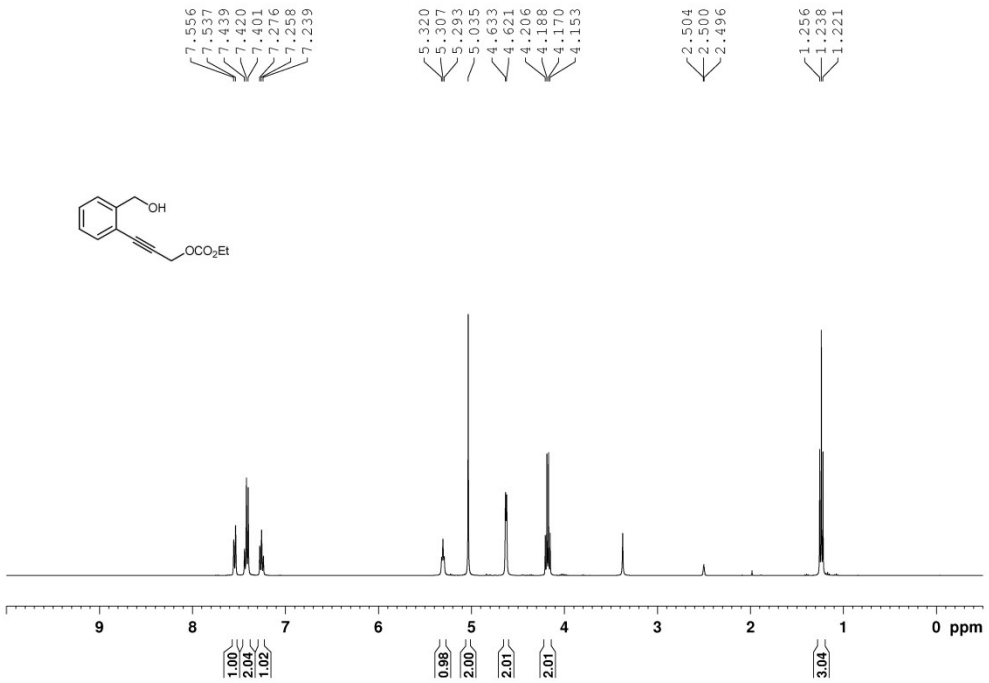

154.75
148.51
145.80
140.41
111.11
110.95
107.09
101.58
86.47
84.23
60.89
55.97
55.06
40.15
39.94
39.73
39.52
39.31
39.10
38.90
OH
OCO2Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.072
8.004
7.939
7.917
7.894
7.560
7.543
7.522
7.501
7.484
5.472
5.458
5.444
5.104
4.775
4.761
3.781
2.500
OH
OCO2Me
9
8
7
6
5
4
3
2
1
0 ppm
0.93
0.93
1.99
2.00
0.97
1.93
2.00
2.90


154.72
140.36
132.80
132.04
131.37
127.59
127.49
127.32
126.22
124.46
117.10
87.78
84.11
61.24
55.92
55.11
40.15
39.94
39.73
39.52
39.31
39.10
38.89
OH
OCO2Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.487
7.474
7.467
7.460
7.453
7.446
7.434
7.428
7.340
7.334
7.139
7.132
7.125
7.118
7.111
7.104
7.037
7.030
7.024
7.016
7.010
7.003
5.029
5.024
4.939
4.934
4.773
4.489
4.477
3.876
3.793
2.271
2.074
2.061
2.055
2.050
2.045
2.039
AcO
OH
OCO2Me
9
8
7
6
5
4
3
2
1
0 ppm
2.32
0.26
1.05
0.26
0.59
2.00
2.68
1.11
3.09
0.90
0.80
3.02


206.25
170.44
154.60
152.75
147.66
133.89
120.32
119.84
117.79
89.64
83.06
62.39
55.84
52.92
30.42
30.23
30.03
29.84
29.65
29.46
29.26
20.59
AcO
OH
OCO2Me
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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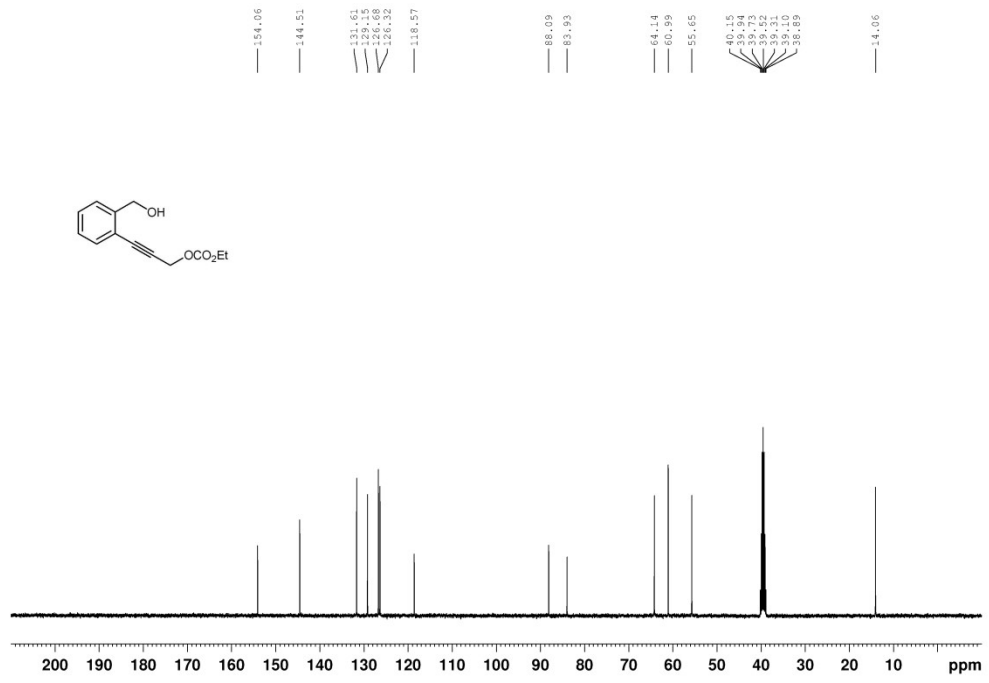
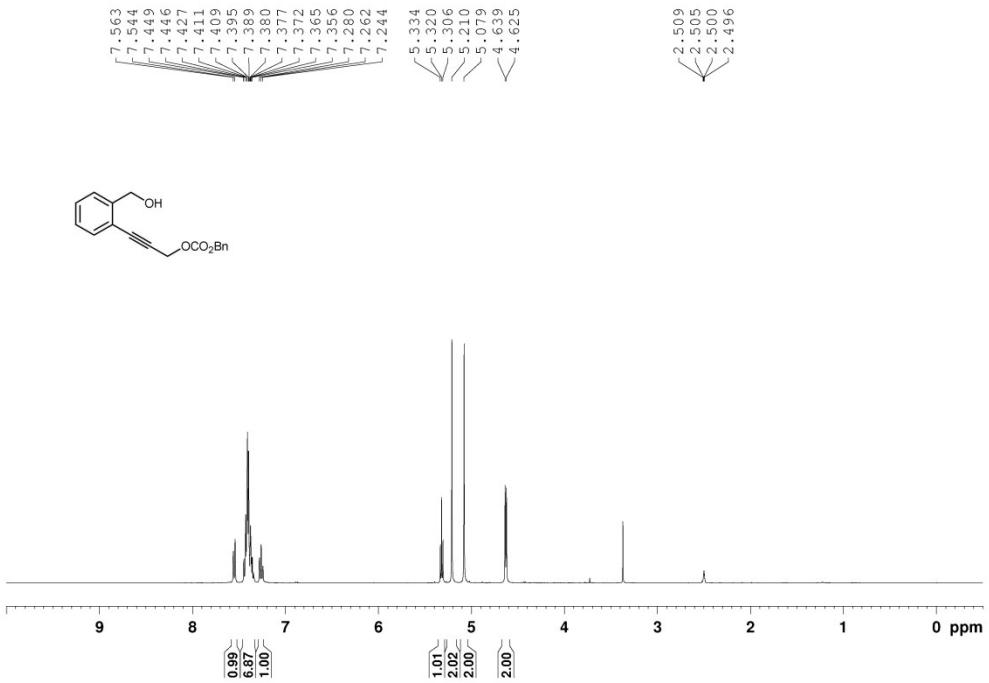
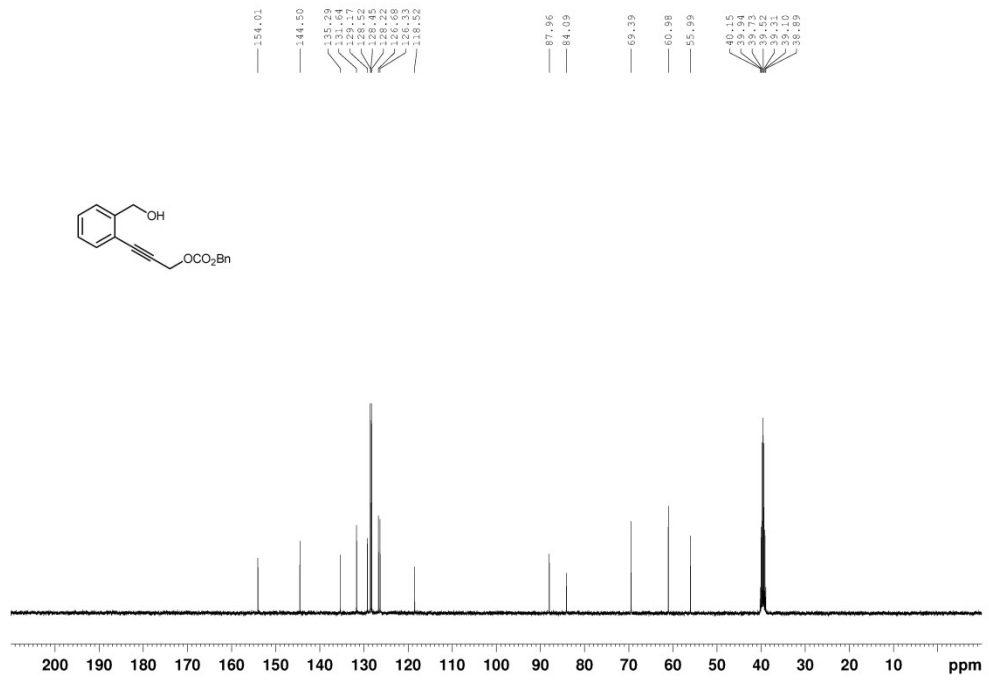
7.537
7.439
7.420
7.401
7.276
7.258
7.239
5.320
5.307
5.293
5.035
4.633
4.621
4.206
4.188
4.170
4.153
2.504
2.500
2.496
1.256
1.238
1.221
OH
OCO2Et
9
8
7
6
5
4
3
2
1
0 ppm
1.00
2.04
1.02
0.98
2.00
2.01
2.01
3.04


154.06
144.51
131.61
129.15
126.68
126.32
118.57
88.09
83.93
64.14
60.99
55.65
40.15
39.94
39.73
39.52
39.31
39.10
38.89
14.06
OH
OCO2Et
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.563
7.544
7.449
7.446
7.427
7.411
7.409
7.395
7.389
7.380
7.377
7.372
7.365
7.356
7.280
7.262
7.244
5.334
5.320
5.306
5.210
5.079
4.639
4.625
2.509
2.505
2.500
2.496
OH
OCO2Bn
9
8
7
6
5
4
3
2
1
0 ppm
0.99
6.87
1.00
1.01
2.02
2.00
2.00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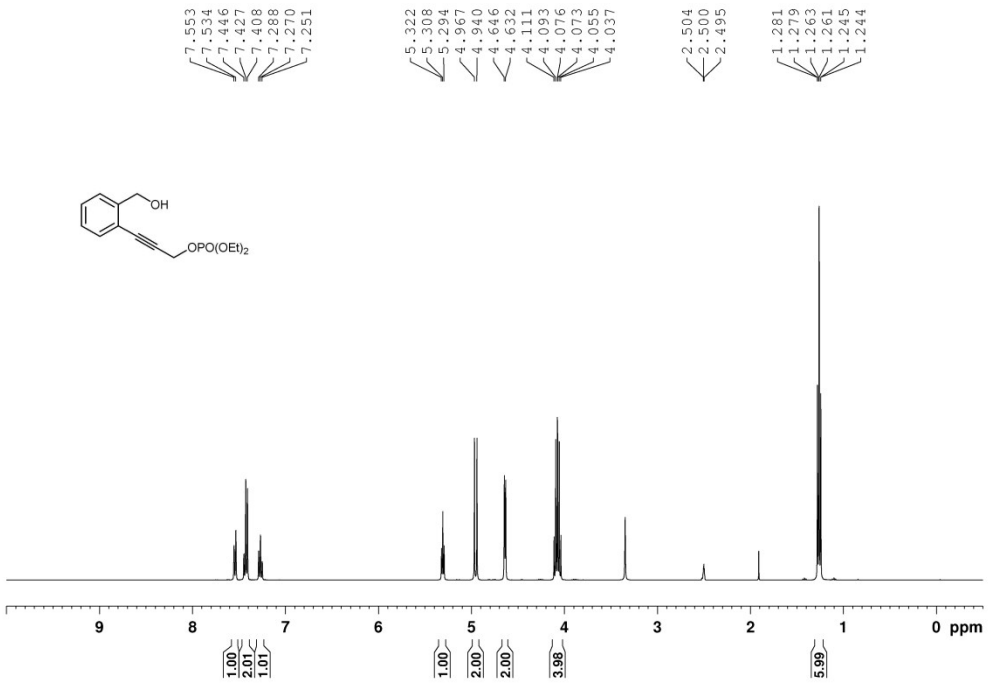
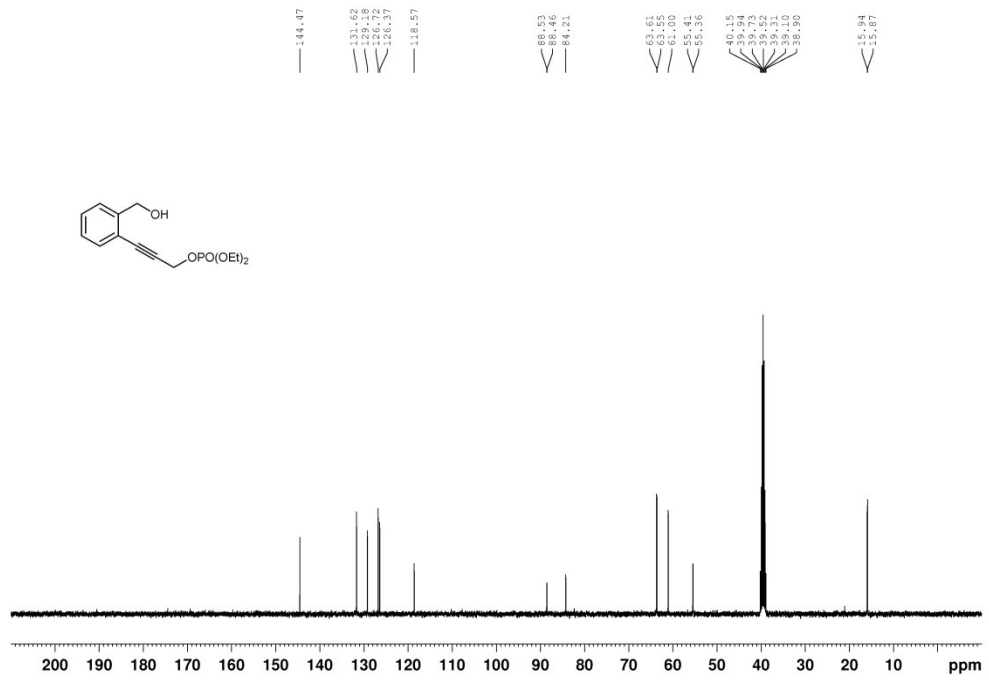
144.50
135.29
131.64
129.17
128.52
128.45
128.22
126.68
126.33
118.52
87.96
84.09
69.39
60.98
55.99
40.15
39.94
39.73
39.52
39.31
39.10
38.89
OH
OCO2Bn
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.553
7.534
7.446
7.427
7.408
7.288
7.270
7.251
5.322
5.308
5.294
4.967
4.940
4.646
4.632
4.111
4.093
4.076
4.073
4.055
4.037
2.504
2.500
2.495
1.281
1.279
1.263
1.261
1.245
1.244
OH
OPO(OEt)2
9
8
7
6
5
4
3
2
1
0 ppm
1.00
2.01
1.01
1.00
2.00
2.00
3.98
5.99


144.47
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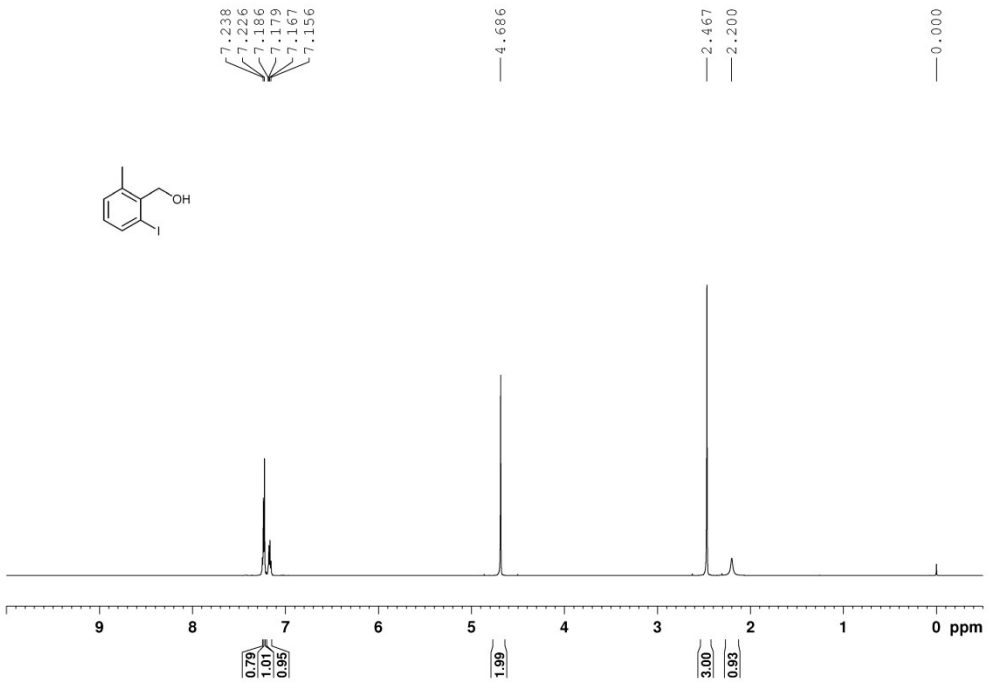
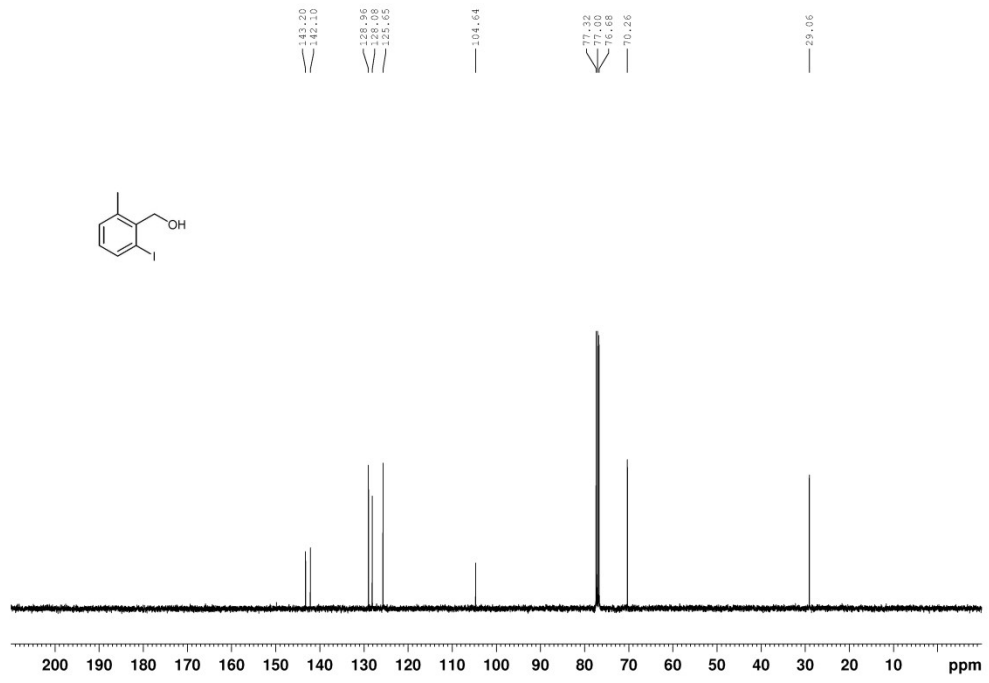
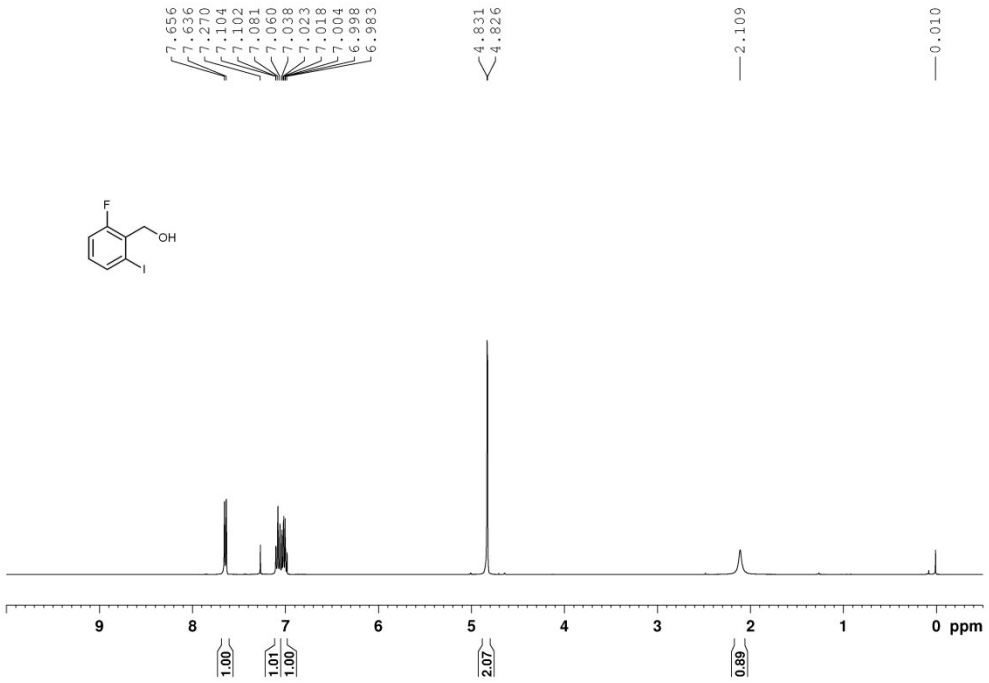
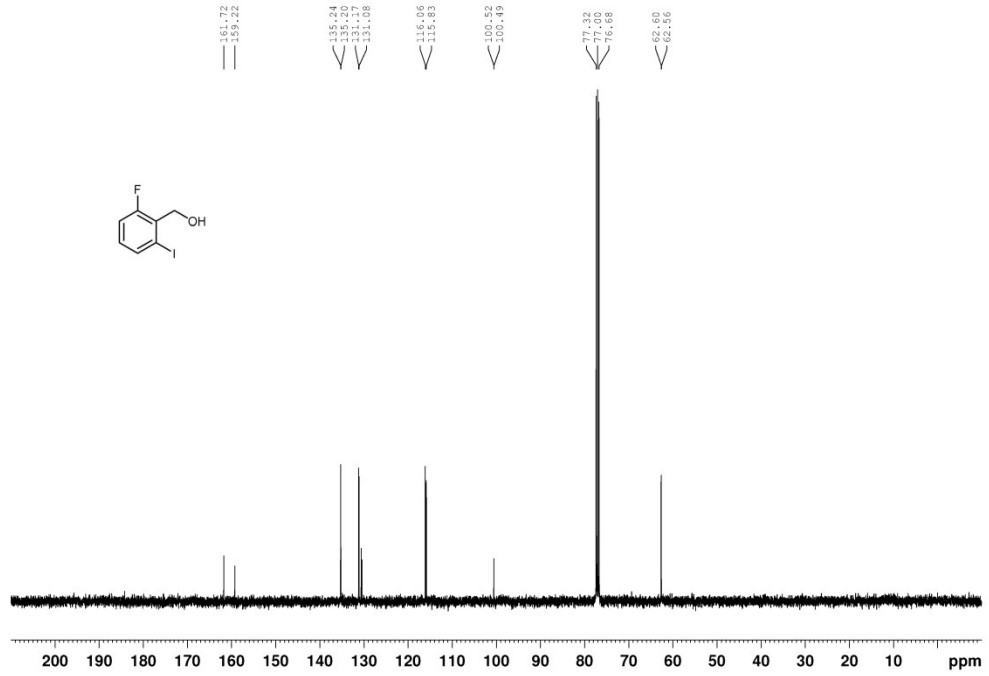
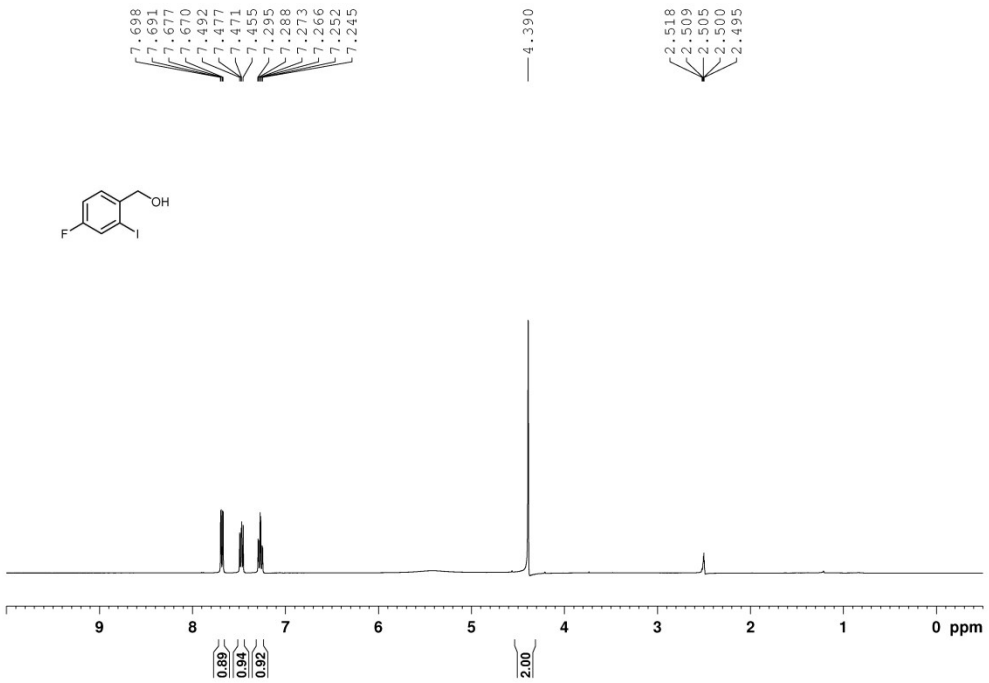
129.18
126.72
126.37
118.57
88.53
86.46
84.21
63.61
63.55
61.00
55.41
55.36
40.15
39.94
39.73
39.52
39.31
39.10
38.90
15.94
15.87
OH
OPO(OEt)2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

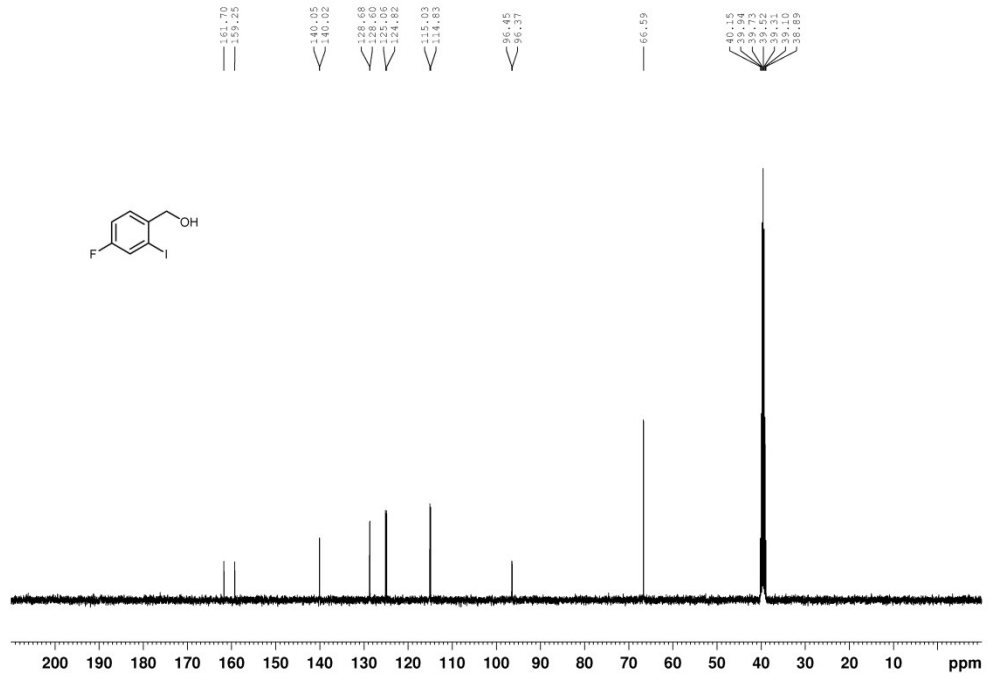

7.238
7.226
7.186
7.179
7.167
7.156
4.686
2.467
2.200
0.000
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.79
1.01
0.95
1.99
3.00
0.93

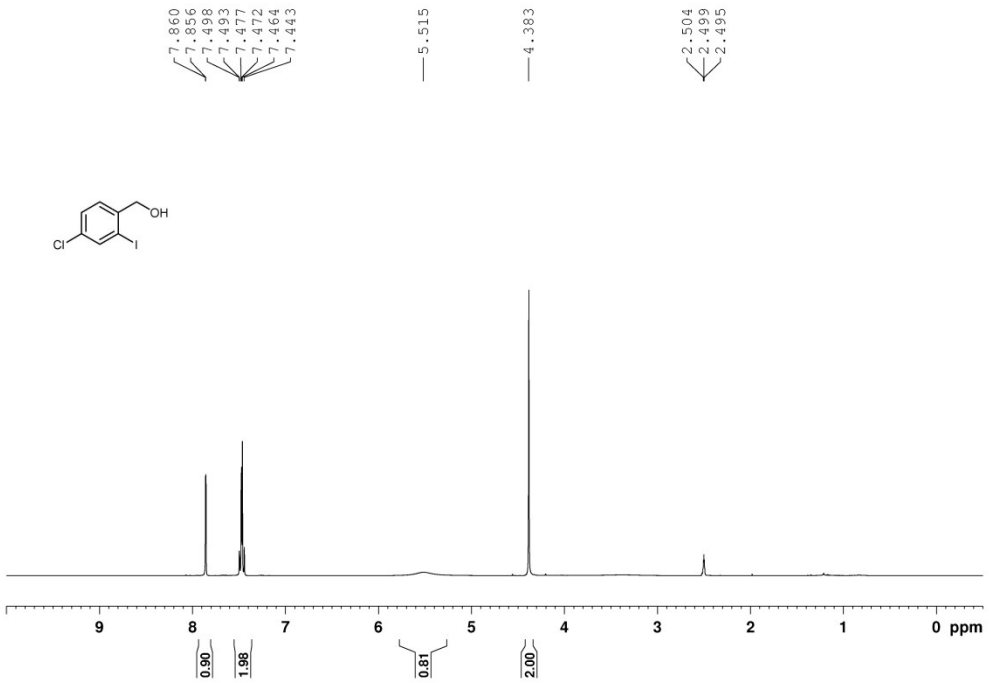

143.20
142.10
128.96
128.08
125.65
104.64
77.32
77.00
76.68
70.26
29.06
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

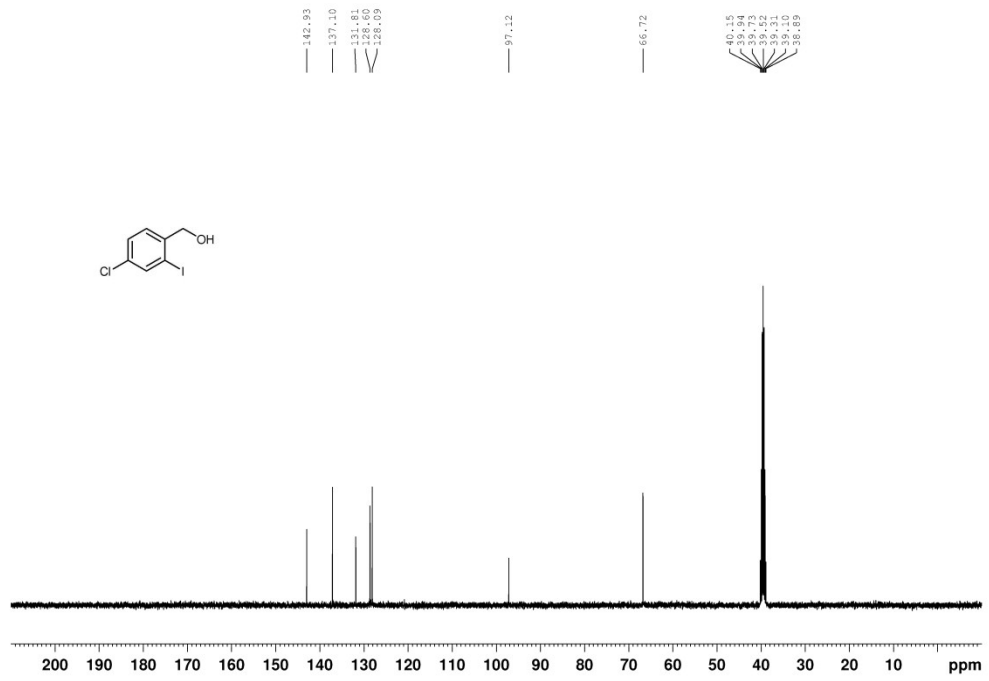

7.656
7.636
7.270
7.104
7.102
7.081
7.060
7.038
7.023
7.018
7.004
6.998
6.983
4.831
4.826
2.109
0.010
F
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
1.00
1.01
1.00
2.07
0.89

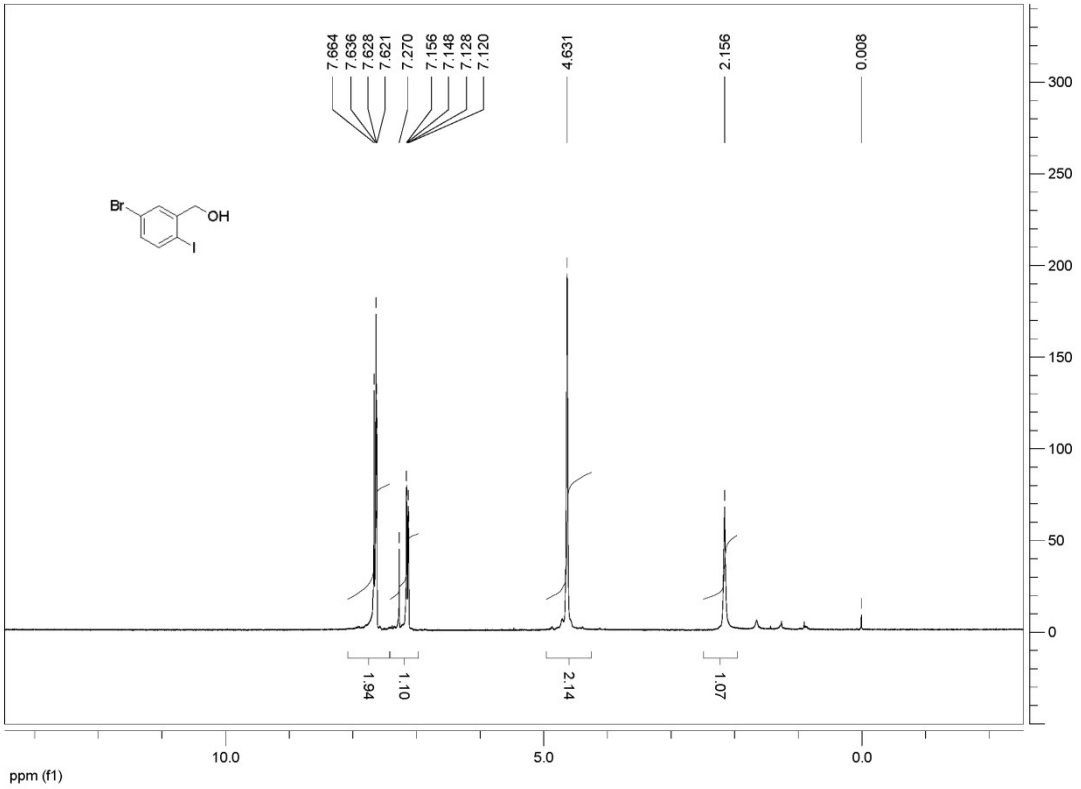

161.72
159.22
135.24
133.50
131.57
131.08
116.06
115.83
100.52
100.49
77.32
77.00
76.68
62.60
62.56
F
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

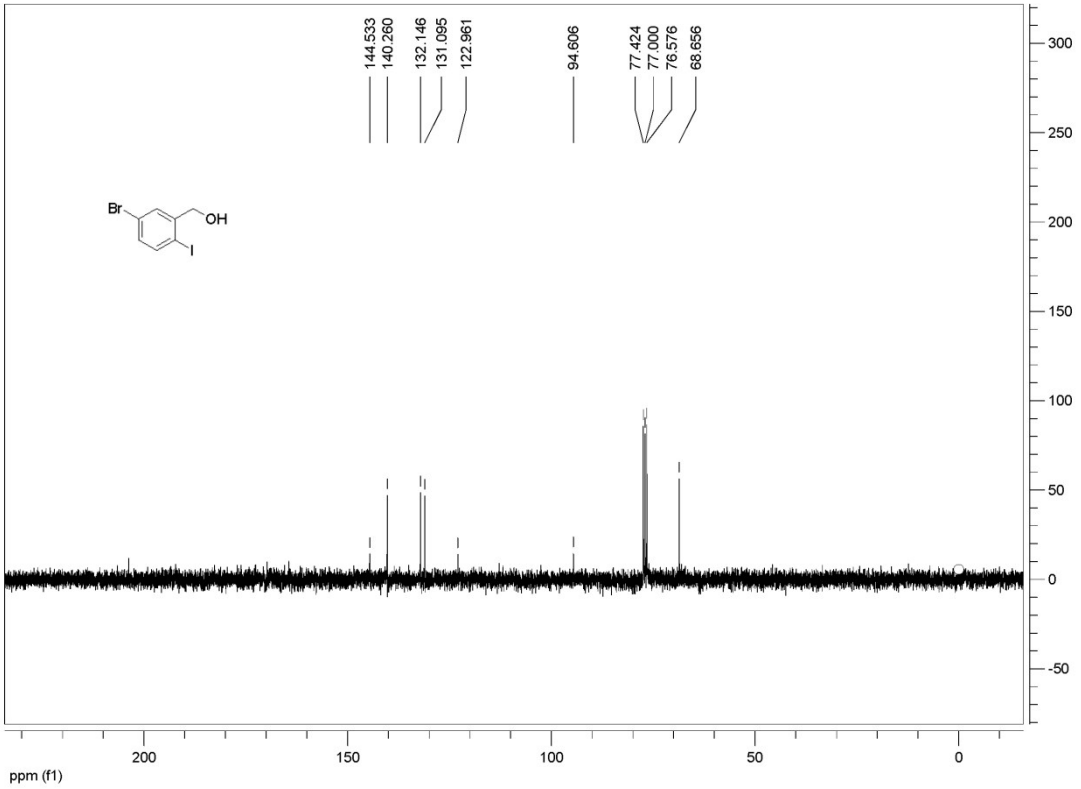

7.698
7.691
7.677
7.670
7.492
7.477
7.471
7.455
7.295
7.288
7.273
7.266
7.252
7.245
4.390
2.518
2.509
2.505
2.500
2.495
OH
F
I
9
8
7
6
5
4
3
2
1
0 ppm
0.89
0.94
0.92
2.00

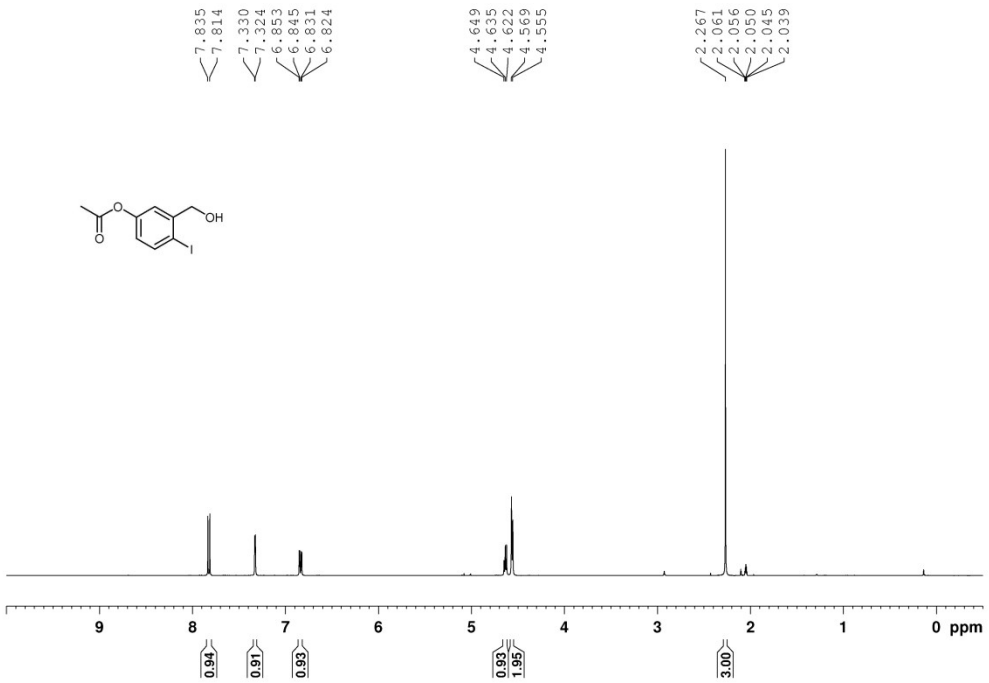

161.70
159.25
140.05
140.02
128.68
128.60
128.50
124.82
115.03
114.83
96.45
96.37
66.59
40.15
39.94
39.73
39.52
39.31
39.10
38.89
OH
F
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

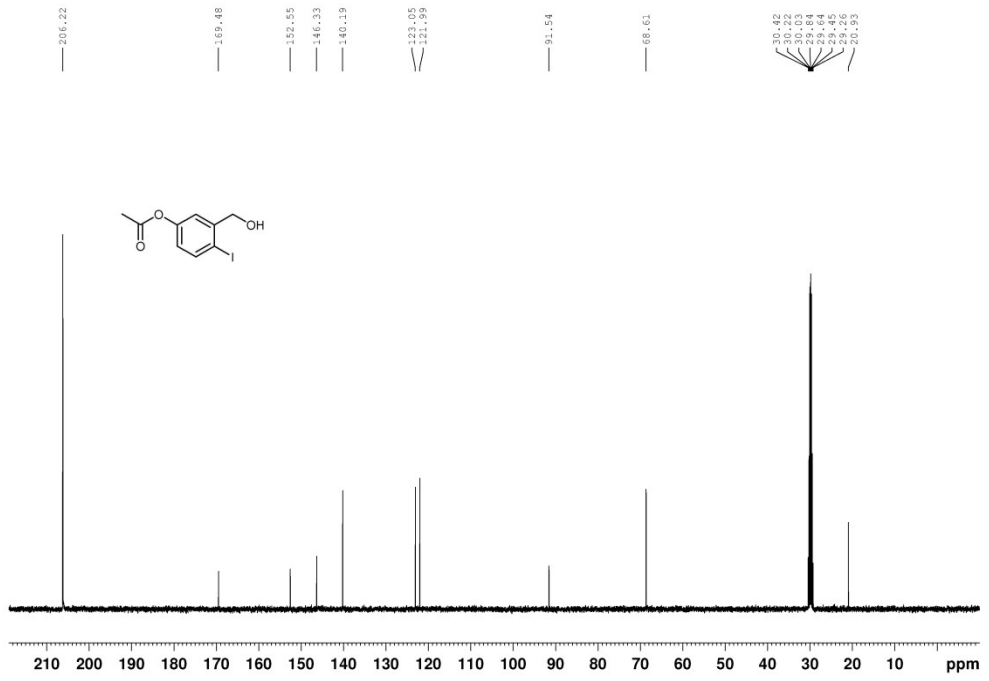

7.860
7.856
7.498
7.493
7.477
7.472
7.464
7.443
5.515
4.383
2.504
2.499
2.495
OH
Cl
I
9
8
7
6
5
4
3
2
1
0 ppm
0.90
1.98
0.81
2.00

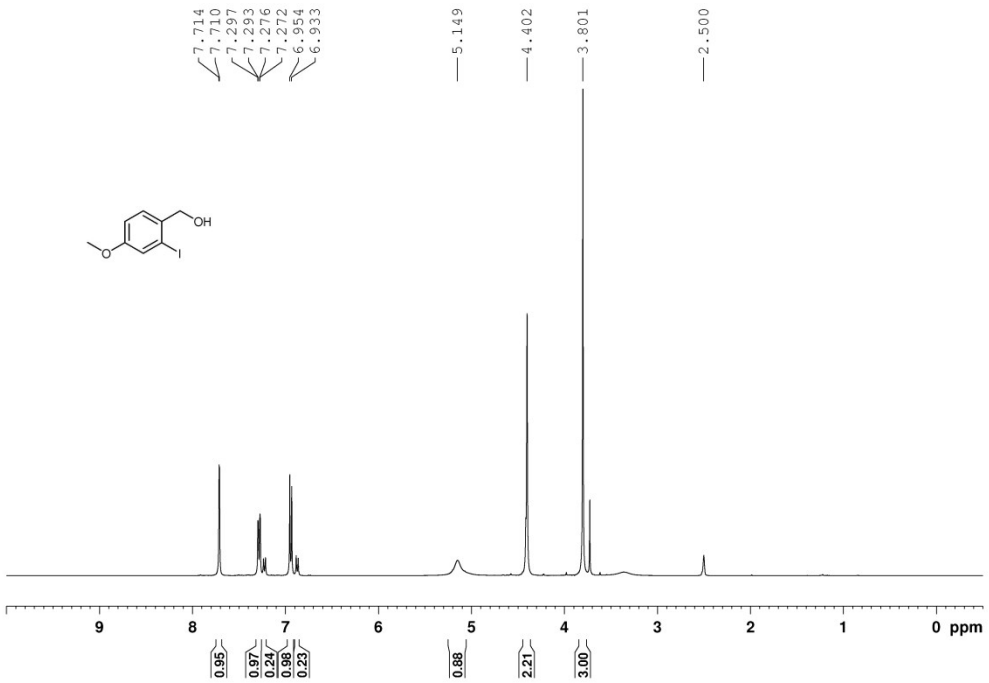

142.93
137.10
131.81
128.60
128.09
97.12
66.72
40.15
39.94
39.73
39.52
39.31
39.10
38.89
OH
Cl
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

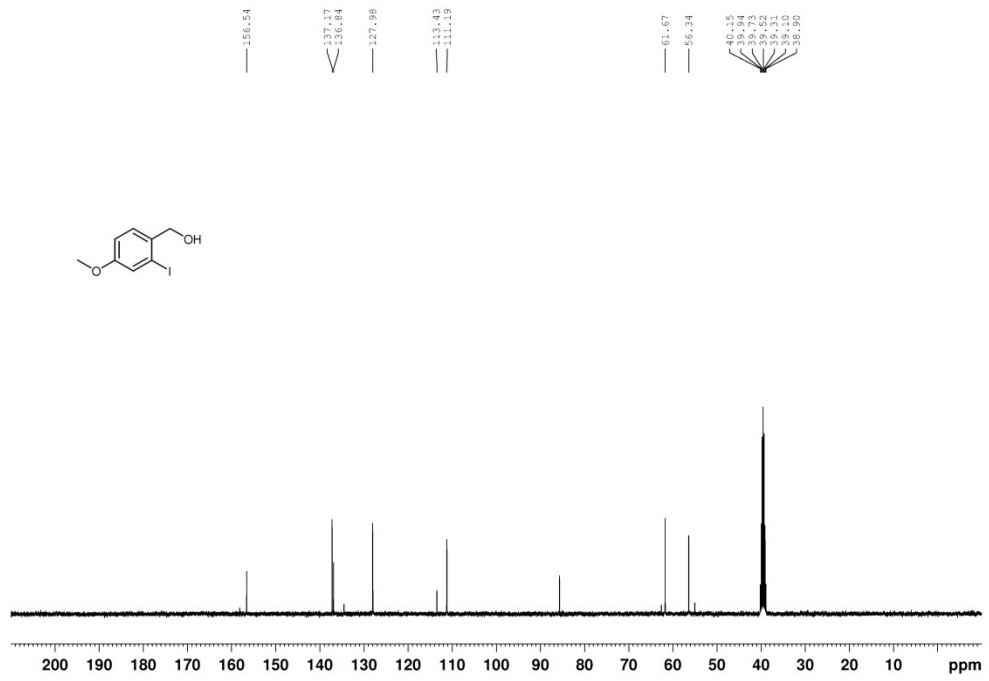

7.664
7.636
7.628
7.621
7.270
7.156
7.148
7.128
7.120
4.631
2.156
0.008
Br
OH
I
1.94
1.10
2.14
1.07
10.0
5.0
0.0
ppm (f1)

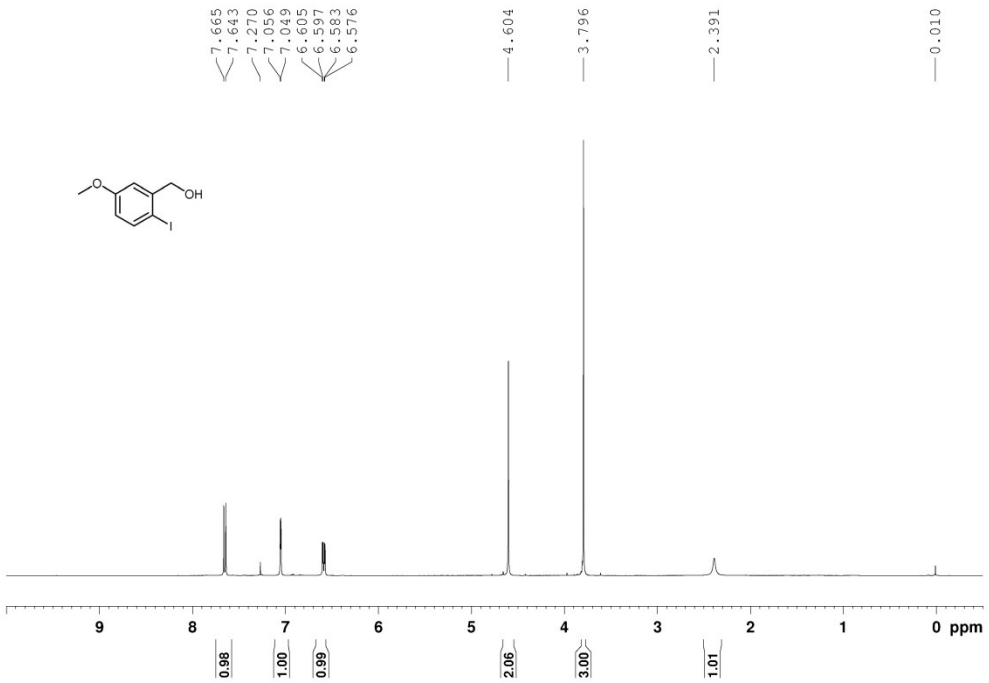

144.533
140.260
132.146
131.095
122.961
94.606
77.424
77.000
76.576
68.656
Br
OH
I
200
150
100
50
0
ppm (f1)

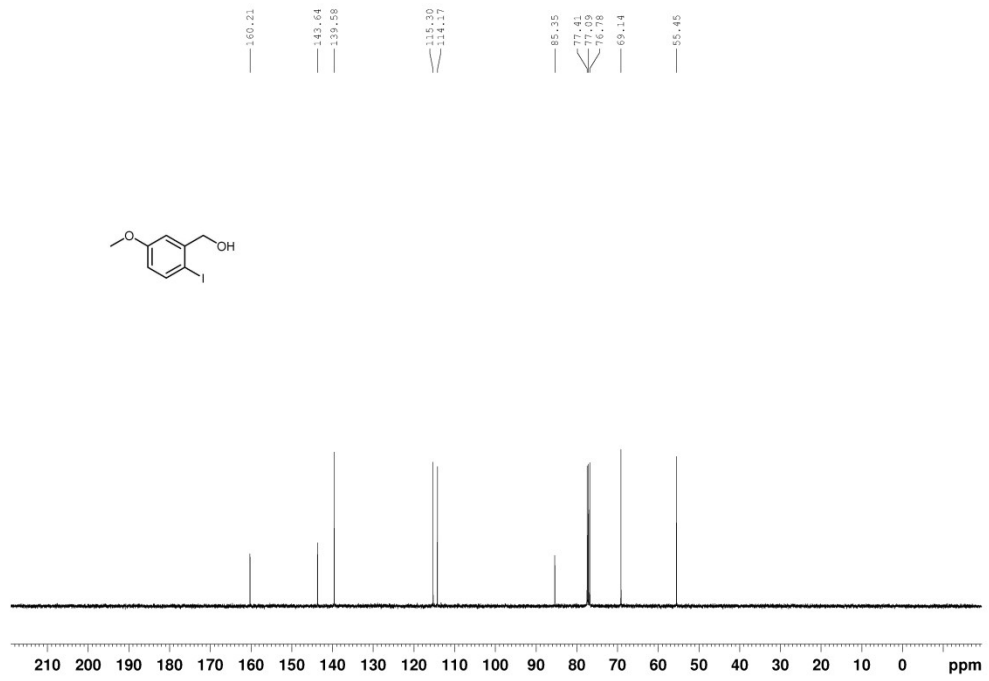

7.835
7.814
7.330
7.324
6.853
6.845
6.831
6.824
4.649
4.635
4.622
4.569
4.555
2.267
2.061
2.056
2.050
2.045
2.039
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.94
0.91
0.93
0.93
1.95
3.00

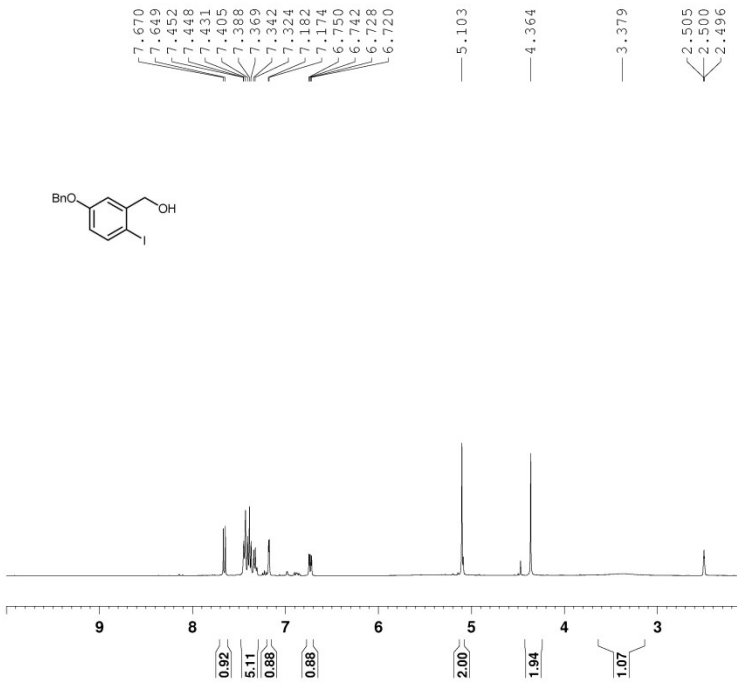

206.22
169.48
152.55
146.33
140.19
123.05
121.99
91.54
68.61
30.42
30.22
30.03
29.84
29.64
29.45
29.26
20.93
OH
I
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

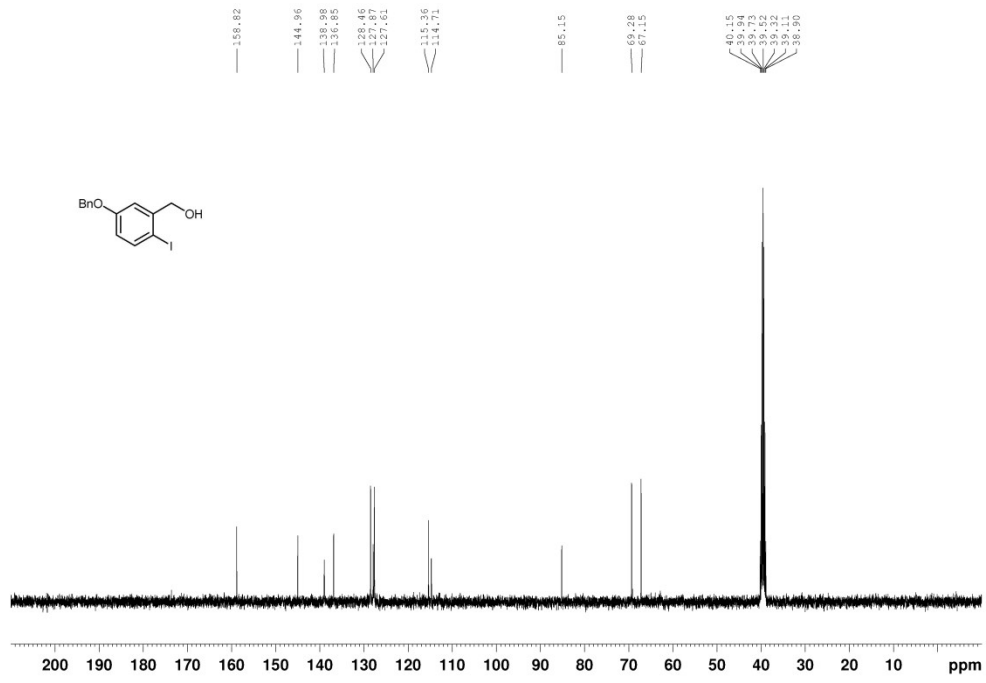

7.714
7.710
7.297
7.293
7.276
7.272
6.954
6.933
5.149
4.402
3.801
2.500
OH
O
I
9
8
7
6
5
4
3
2
1
0 ppm
0.95
0.97
0.24
0.98
0.23
0.88
2.21
3.00

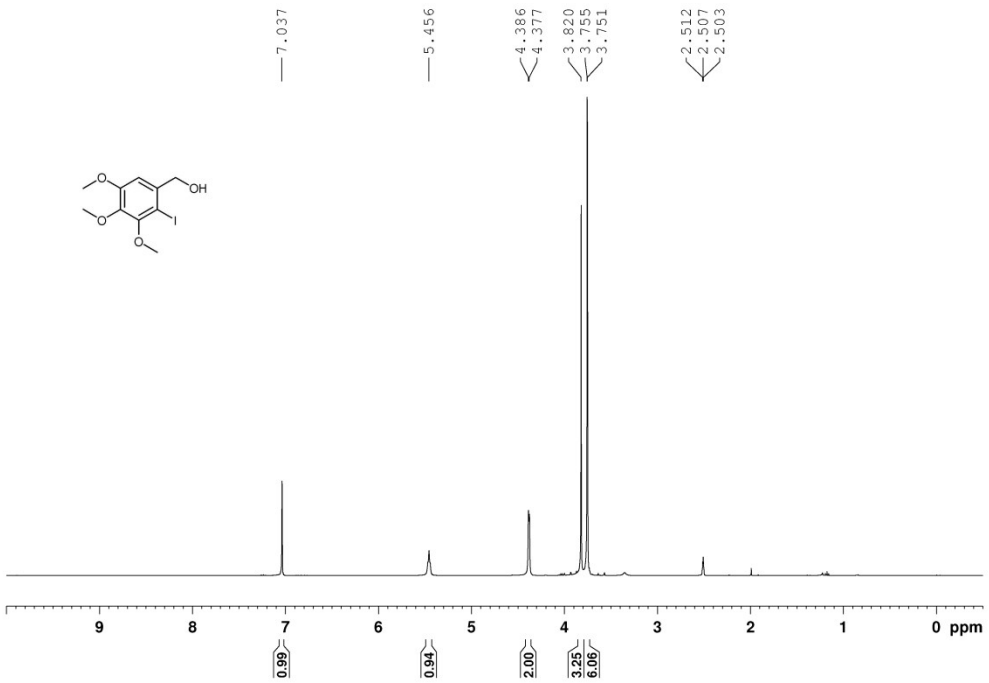

156.54
137.17
136.84
127.98
113.43
111.19
61.67
56.34
40.15
39.94
39.73
39.52
39.31
39.10
38.90
OH
O
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

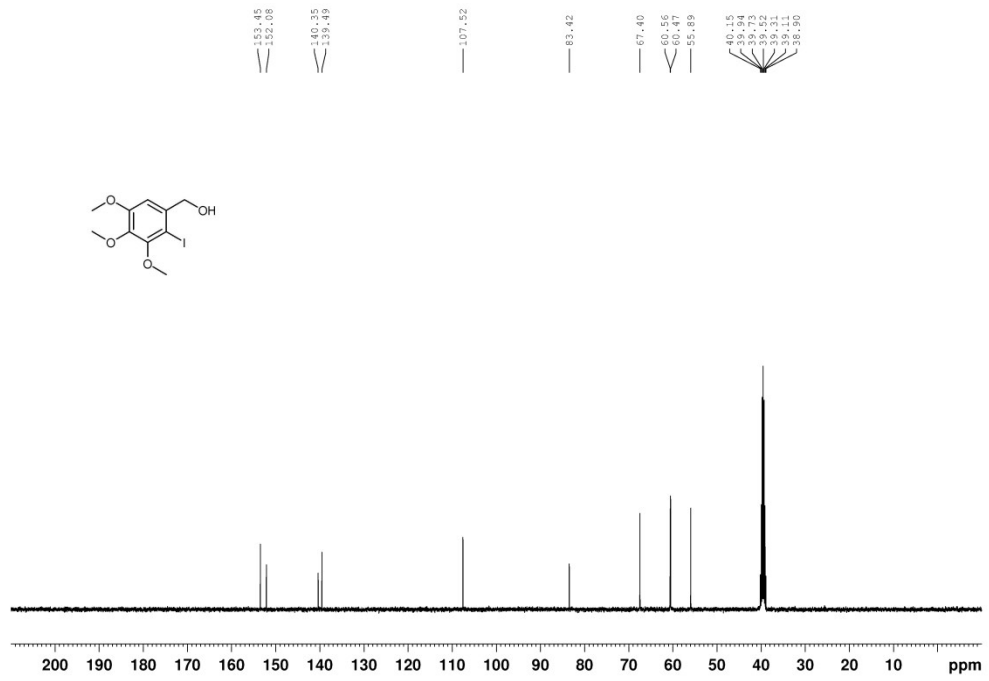

7.665
7.643
7.270
7.056
7.049
6.605
6.597
6.583
6.576
4.604
3.796
2.391
0.010
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.98
1.00
0.99
2.06
3.00
1.01

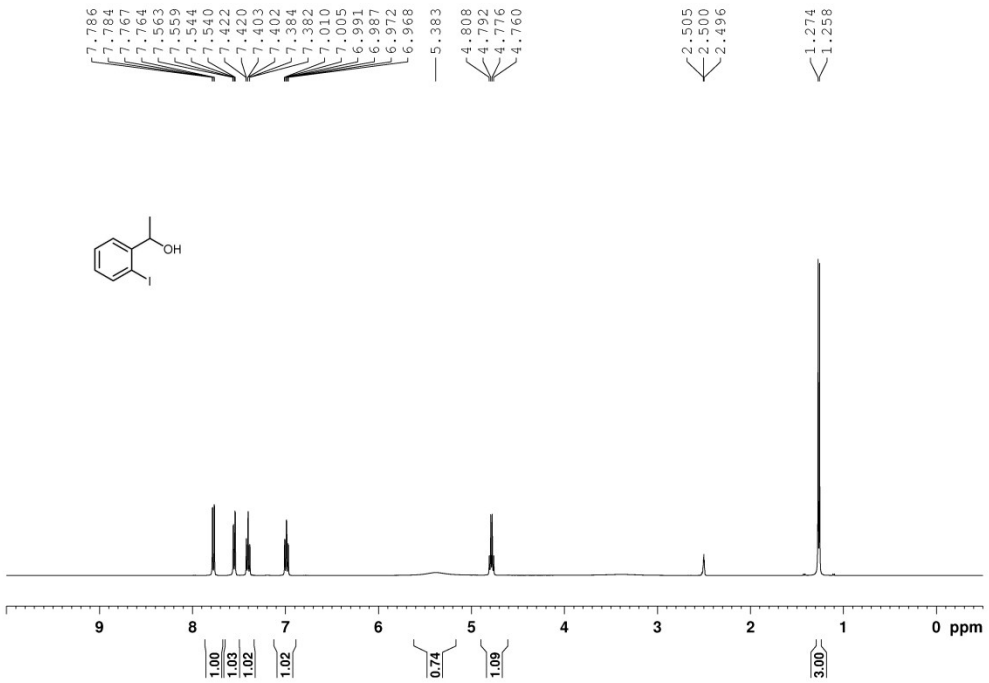

160.21
143.64
139.58
115.30
114.27
85.35
77.41
77.09
76.78
69.14
55.45
OH
I
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

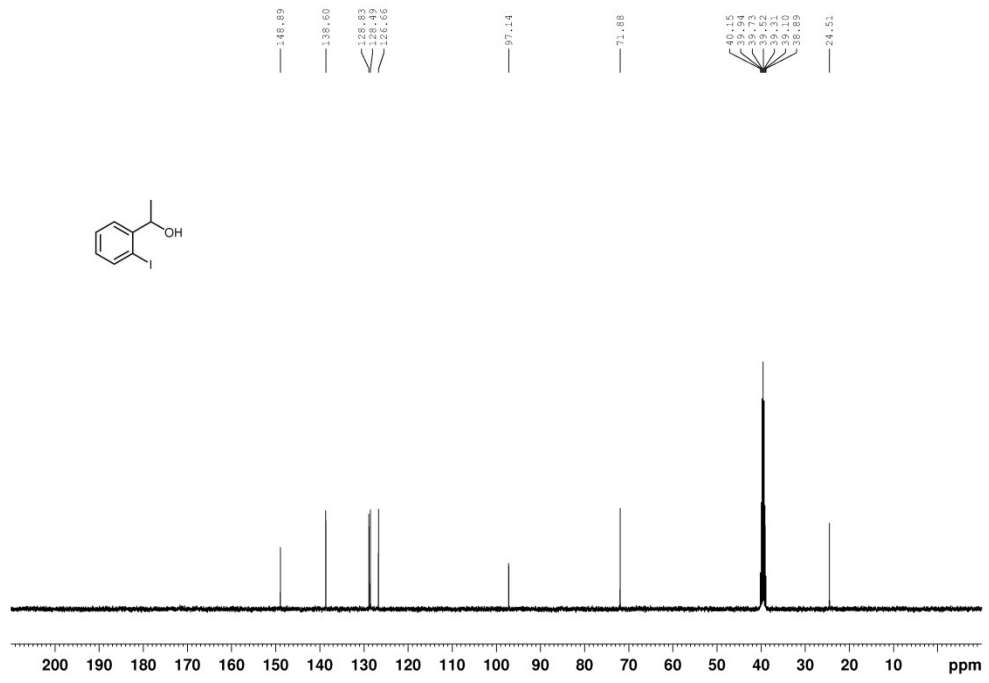

7.670
7.649
7.452
7.448
7.431
7.405
7.388
7.369
7.342
7.324
7.182
7.174
6.750
6.742
6.728
6.720
5.103
4.364
3.379
2.505
2.500
2.496
BnO
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.92
5.11
0.88
0.88
2.00
1.94
1.07

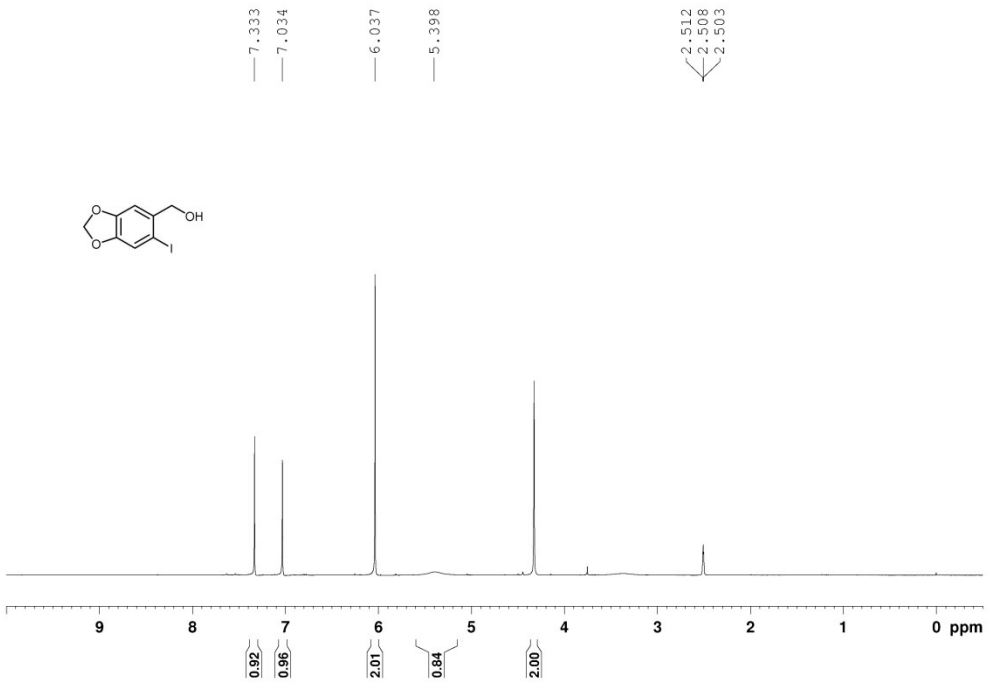

158.82
144.96
138.98
136.85
128.46
127.87
127.61
115.36
114.71
85.15
69.28
67.15
40.15
39.94
39.73
39.52
39.32
39.11
38.90
BnO
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

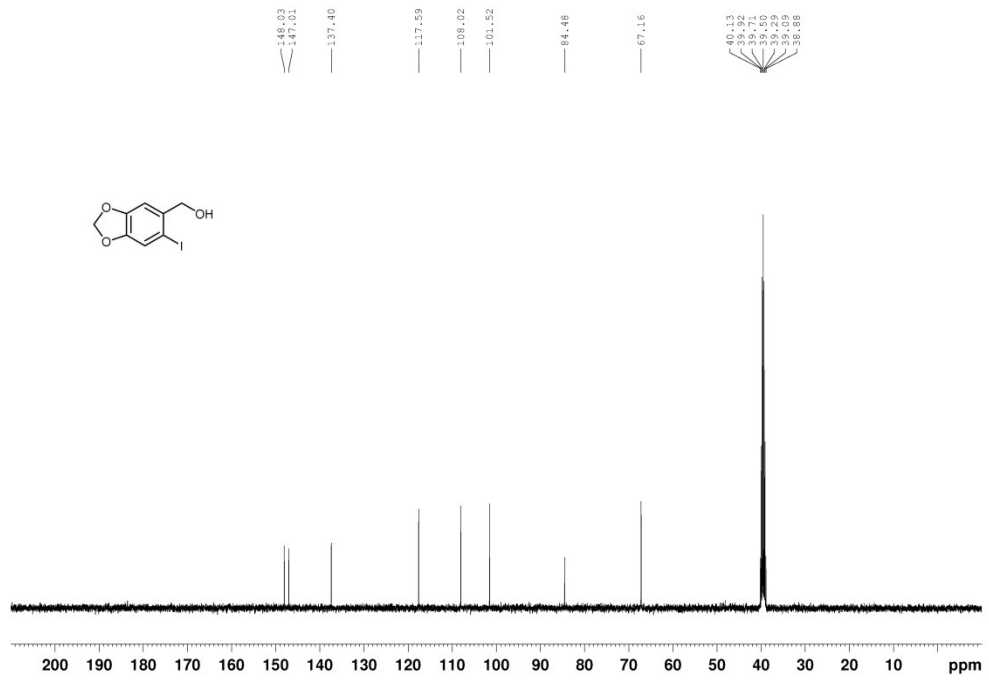

7.037
5.456
4.386
4.377
3.820
3.755
3.751
2.512
2.507
2.503
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.99
0.94
2.00
3.25
6.06

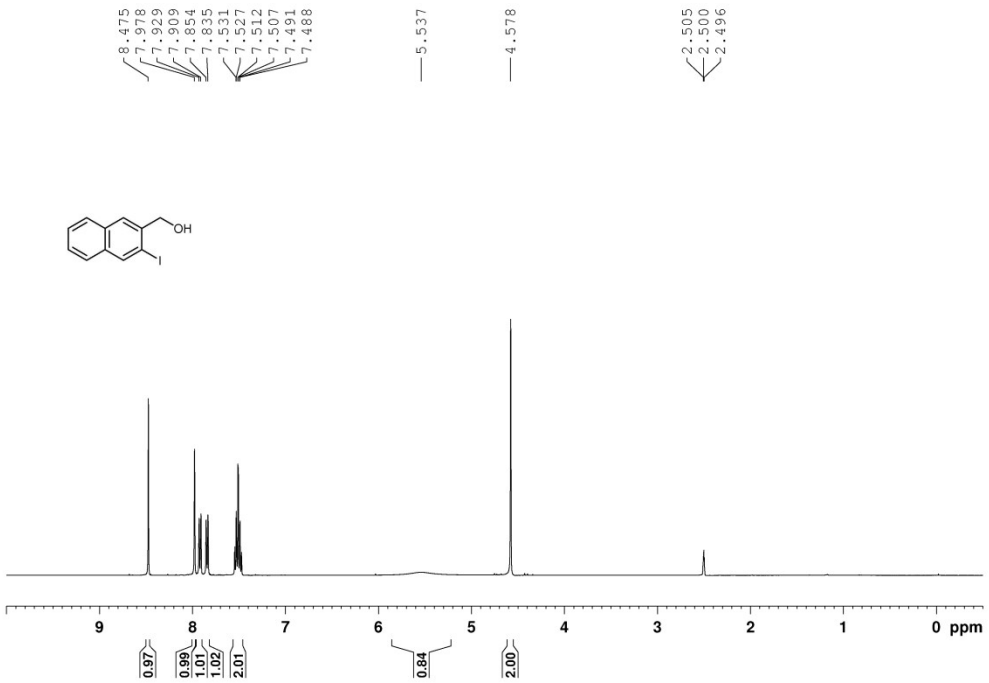

153.45
152.08
140.35
139.49
107.52
83.42
67.40
60.56
60.47
55.89
40.15
39.94
39.73
39.52
39.31
39.11
38.90
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

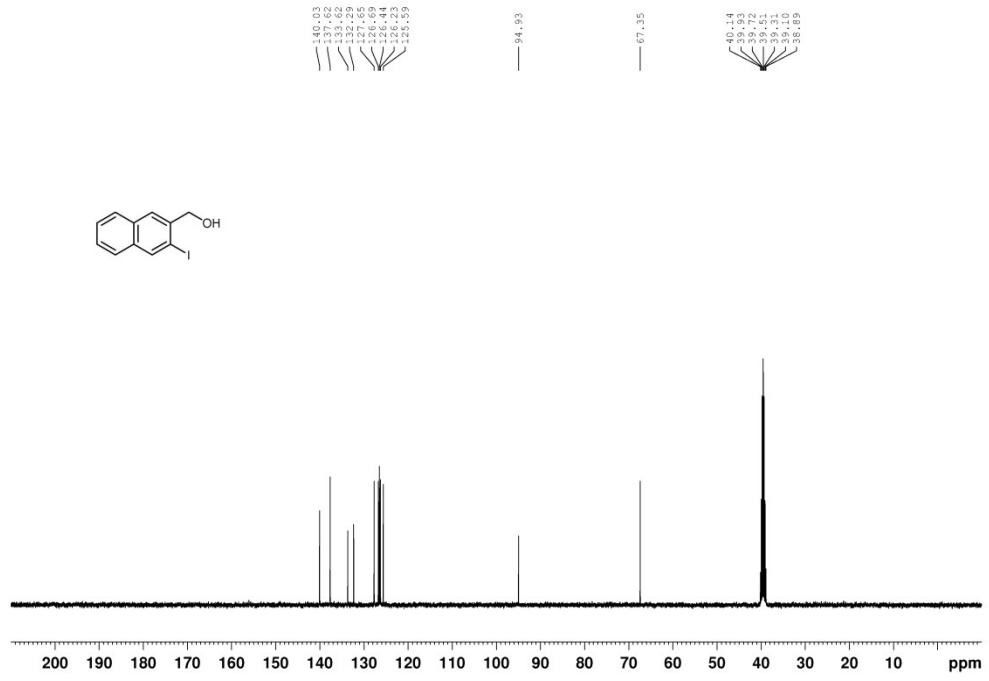

7.786
7.784
7.767
7.764
7.563
7.559
7.544
7.540
7.422
7.420
7.403
7.402
7.384
7.382
7.010
7.005
6.991
6.987
6.972
6.968
5.383
4.808
4.792
4.776
4.760
2.505
2.500
2.496
1.274
1.258
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
1.00
1.03
1.02
1.02
0.74
1.09
3.00

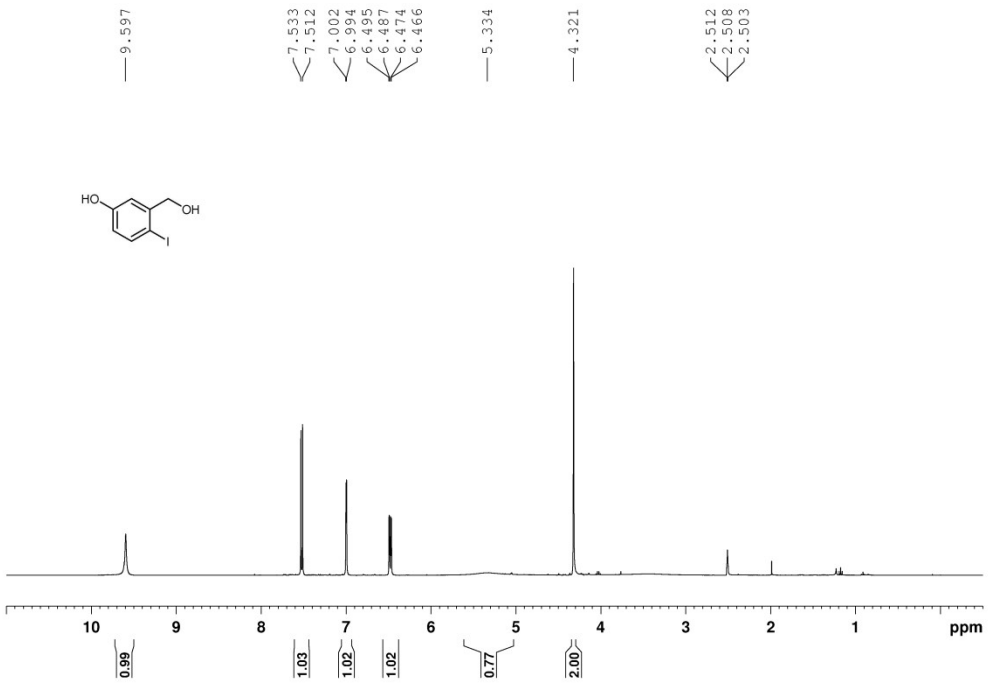

148.89
138.60
128.83
128.49
126.66
97.14
71.88
40.15
39.94
39.73
39.52
39.31
39.10
38.89
24.51
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

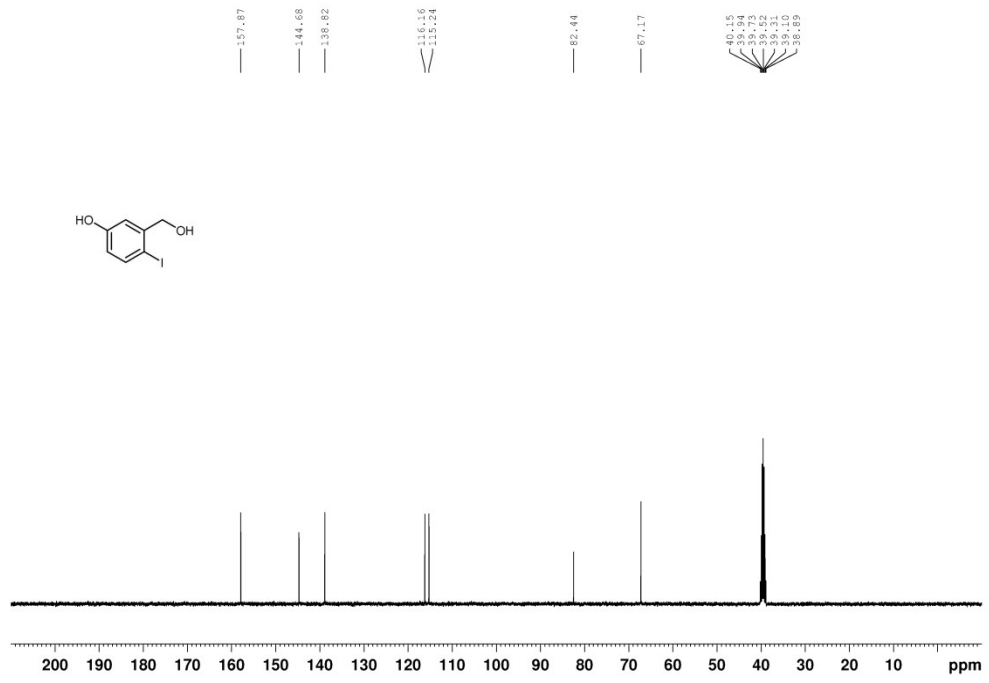

7.333
7.034
6.037
5.398
2.512
2.508
2.503
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.92
0.96
2.01
0.84
2.00

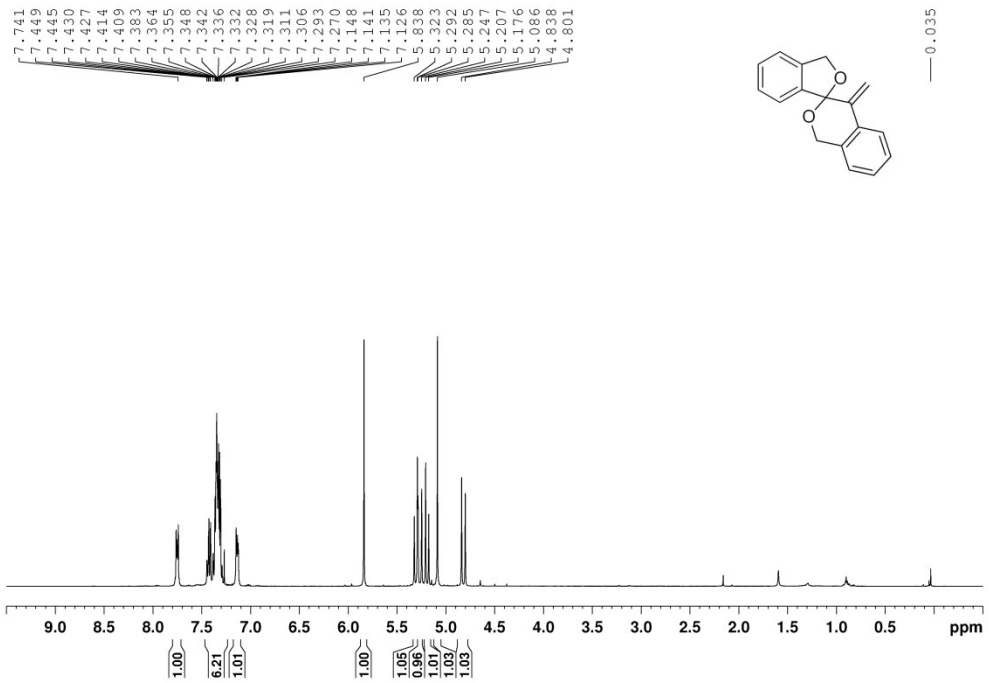

148.03
147.01
137.40
117.59
108.02
101.52
84.48
67.16
40.13
39.92
39.71
39.50
39.29
39.09
38.88
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.475
7.978
7.929
7.909
7.854
7.835
7.531
7.527
7.512
7.507
7.491
7.488
5.537
4.578
2.505
2.500
2.496
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
0.97
0.99
1.01
1.02
2.01
0.84
2.00


140.03
137.62
133.62
132.29
127.65
126.68
126.44
126.23
125.59
94.93
67.35
40.14
39.93
39.72
39.51
39.31
39.10
38.89
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


9.597
7.533
7.512
7.002
6.994
6.495
6.487
6.474
6.466
5.334
4.321
2.512
2.508
2.503
HO
OH
I
10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.03
1.02
1.02
0.77
2.00


157.87
144.68
138.82
116.16
115.24
82.44
67.17
40.15
39.94
39.73
39.52
39.31
39.10
38.89
HO
OH
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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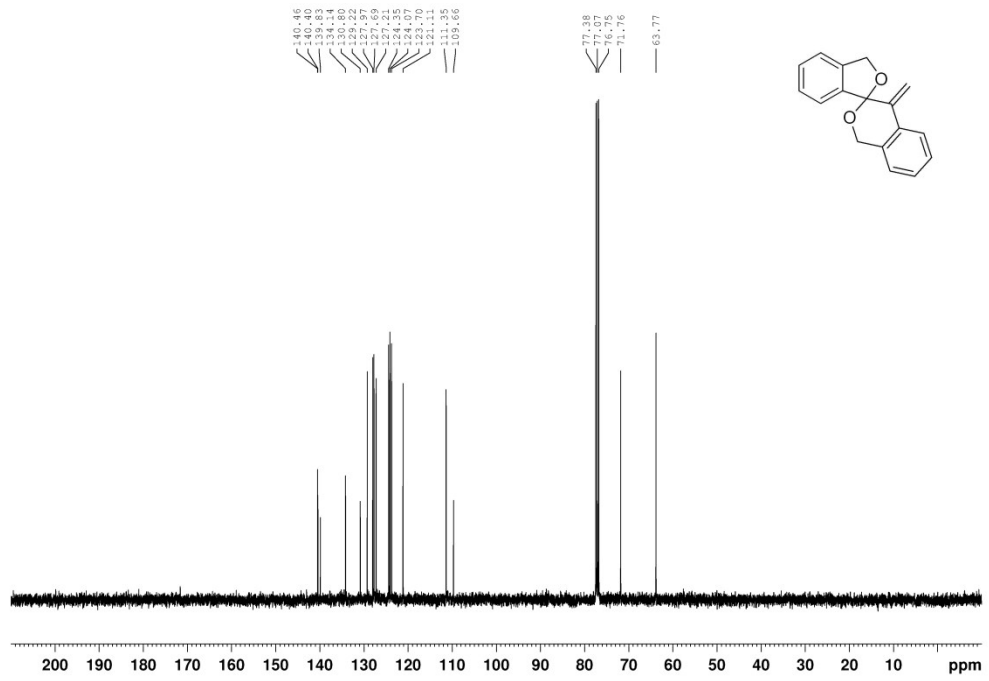
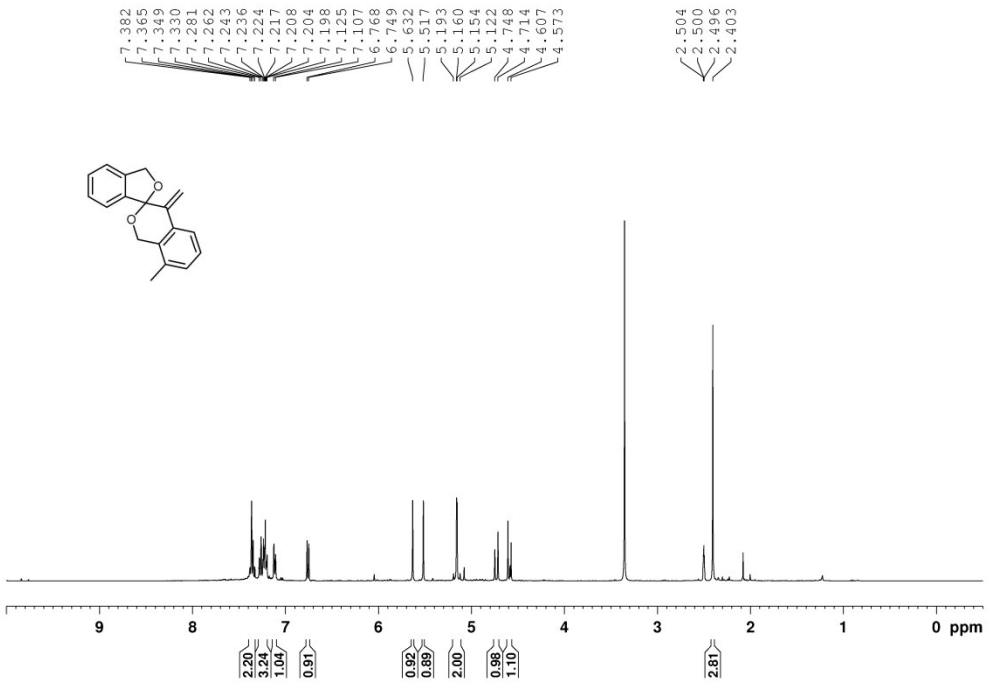
7.445
7.430
7.427
7.414
7.409
7.383
7.364
7.355
7.348
7.342
7.336
7.332
7.328
7.319
7.311
7.306
7.293
7.270
7.148
7.141
7.135
7.126
5.838
5.323
5.292
5.285
5.247
5.207
5.176
5.086
4.838
4.801
0.035
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
6.21
1.01
1.00
1.05
0.96
1.01
1.03
1.03


140.46
140.40
139.83
134.44
130.80
129.22
127.97
127.69
127.21
124.35
124.07
123.70
121.11
111.35
109.86
77.38
77.07
76.75
71.76
63.77
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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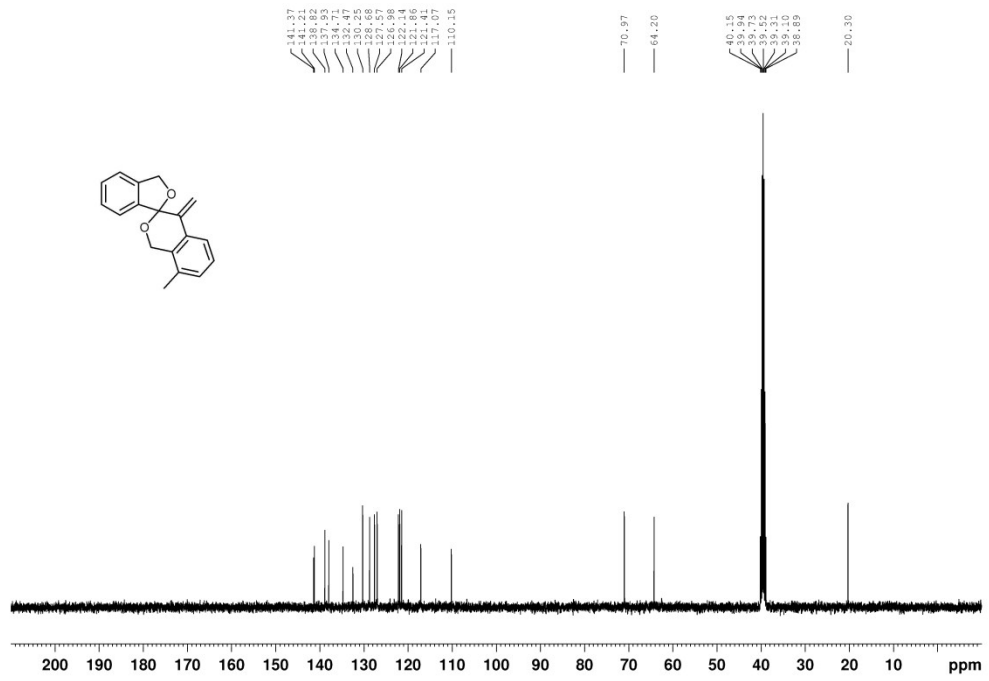
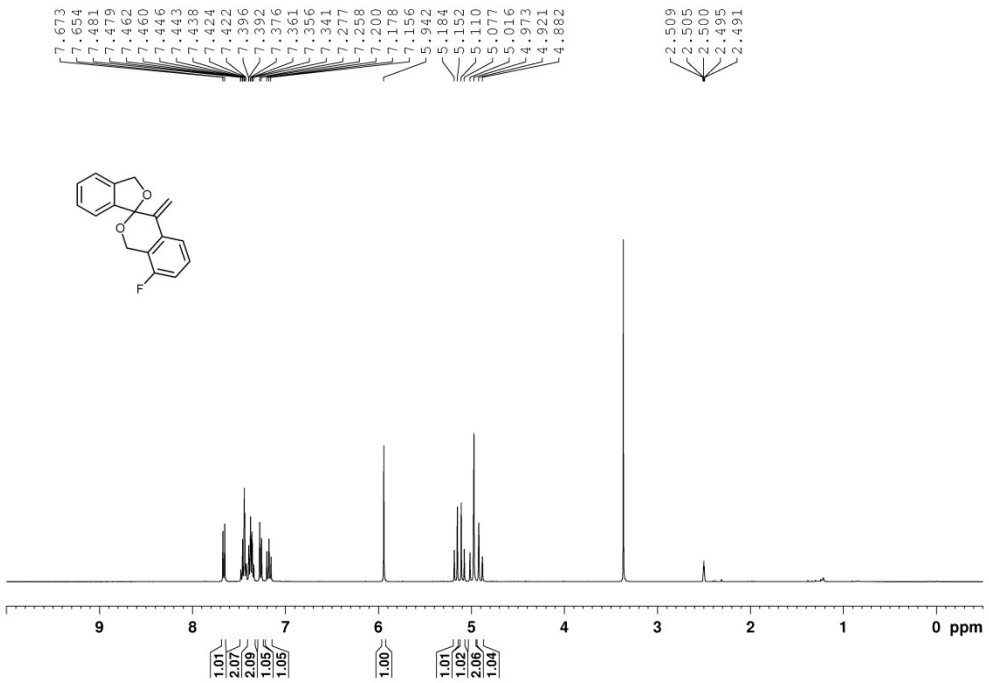
7.330
7.281
7.262
7.243
7.236
7.224
7.217
7.208
7.204
7.198
7.125
7.107
6.768
6.749
5.632
5.517
5.193
5.160
5.154
5.122
4.748
4.714
4.607
4.573
2.504
2.500
2.496
2.403
9
8
7
6
5
4
3
2
1
0 ppm
2.20
3.24
1.04
0.91
0.92
0.89
2.00
0.98
1.10
2.81


141.37
141.21
138.62
137.93
134.71
132.47
130.55
128.68
127.57
126.98
122.14
121.46
121.41
117.07
110.15
70.97
64.20
40.15
39.94
39.73
39.52
39.31
39.10
38.89
20.30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.479
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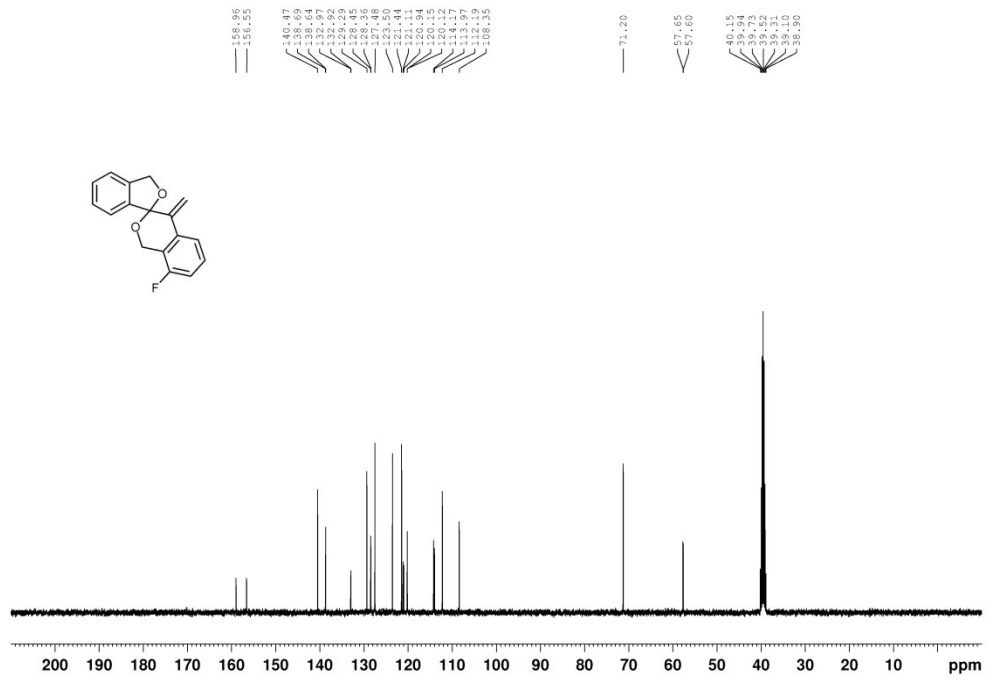
7.460
7.446
7.443
7.438
7.424
7.422
7.396
7.392
7.376
7.361
7.356
7.341
7.277
7.258
7.200
7.178
7.156
5.942
5.184
5.152
5.110
5.077
5.016
4.973
4.921
4.882
2.509
2.505
2.500
2.495
2.491
F
9
8
7
6
5
4
3
2
1
0 ppm
1.01
2.07
2.09
1.05
1.05
1.00
1.01
1.02
2.06
1.04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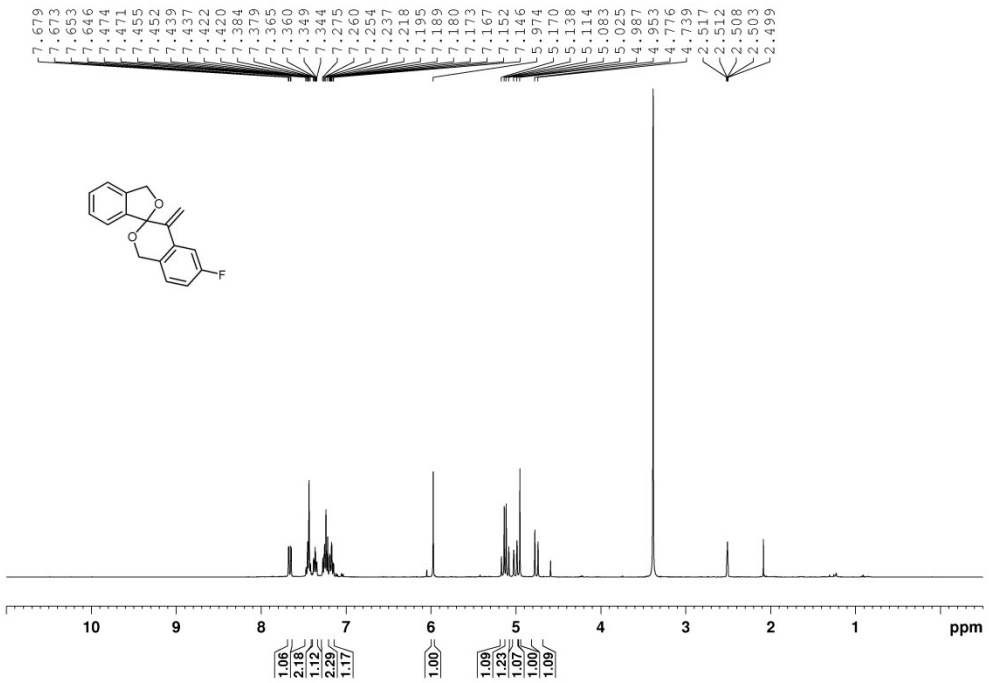
140.47
138.69
138.64
132.97
132.92
128.39
128.45
128.36
127.48
123.60
123.44
121.11
120.94
120.15
120.12
114.17
113.97
112.19
108.35
71.20
57.65
57.60
40.15
39.94
39.73
39.52
39.31
39.10
38.90
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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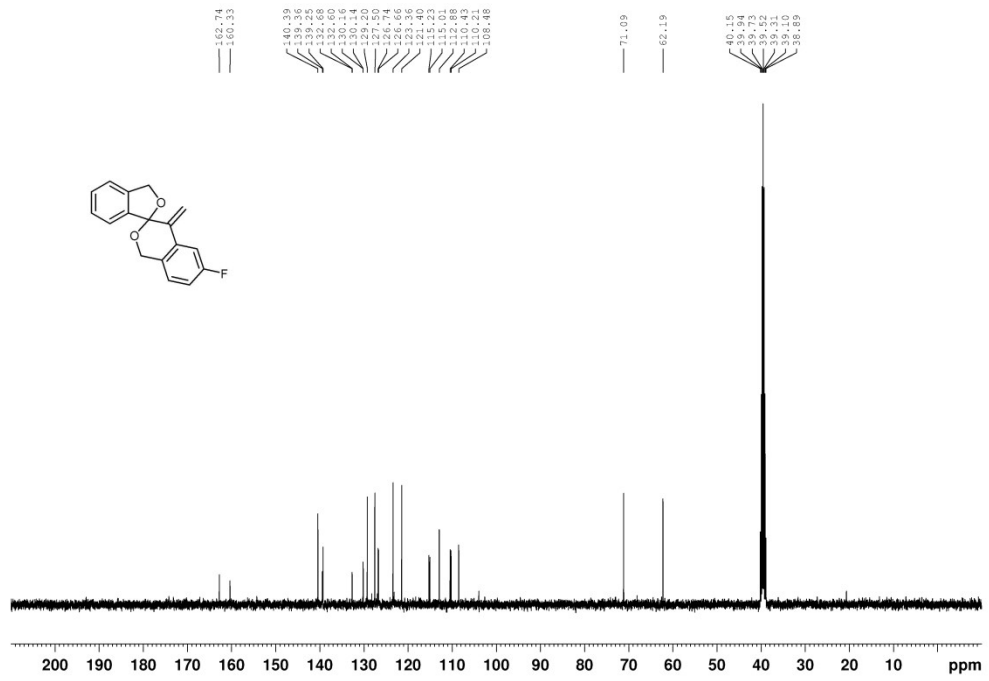
7.471
7.455
7.452
7.439
7.437
7.422
7.420
7.384
7.379
7.365
7.360
7.349
7.344
7.275
7.260
7.254
7.237
7.218
7.195
7.189
7.180
7.173
7.167
7.152
7.146
5.974
5.170
5.138
5.114
5.083
5.025
4.987
4.953
4.776
4.739
2.517
2.512
2.508
2.503
2.499
F
10 9 8 7 6 5 4 3 2 1 ppm
1.06 2.18 1.12 2.29 1.17 1.00 1.09 1.23 1.07 1.00 1.09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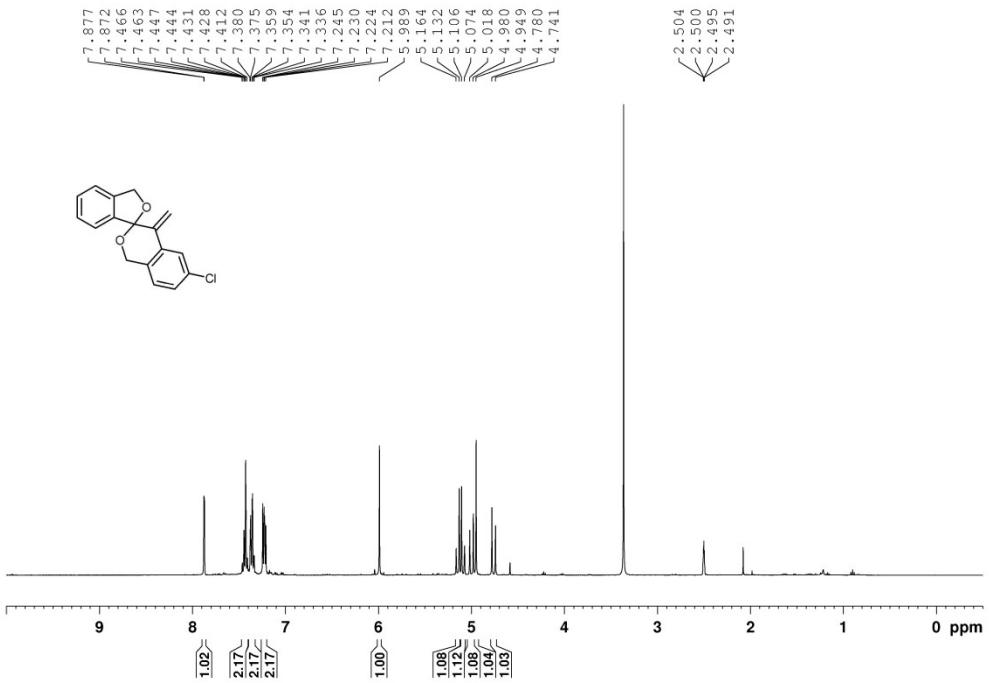
139.36
139.25
132.68
132.60
130.16
130.14
129.20
127.50
126.74
126.66
123.36
121.40
115.23
115.01
113.88
110.43
110.21
108.48
71.09
62.19
40.15
39.94
39.73
39.52
39.31
39.10
38.89
F
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.872
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7.463
7.447
7.444
7.431
7.428
7.412
7.380
7.375
7.359
7.354
7.341
7.336
7.245
7.230
7.224
7.212
5.989
5.164
5.132
5.106
5.074
5.018
4.980
4.949
4.780
4.741
2.504
2.500
2.495
2.491
Cl
9
8
7
6
5
4
3
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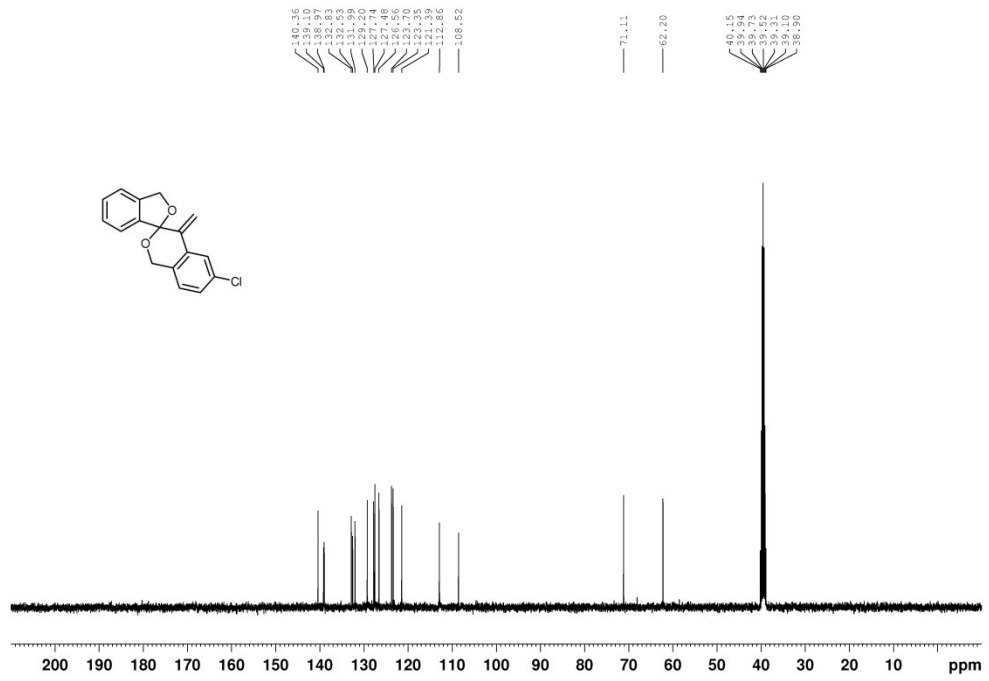
2.17
1.00
1.08
1.12
1.08
1.04
1.03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127.44
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123.35
121.98
112.86
108.52
71.11
62.20
40.15
39.94
39.73
39.52
39.31
39.10
38.90
Cl
200
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150
140
130
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70
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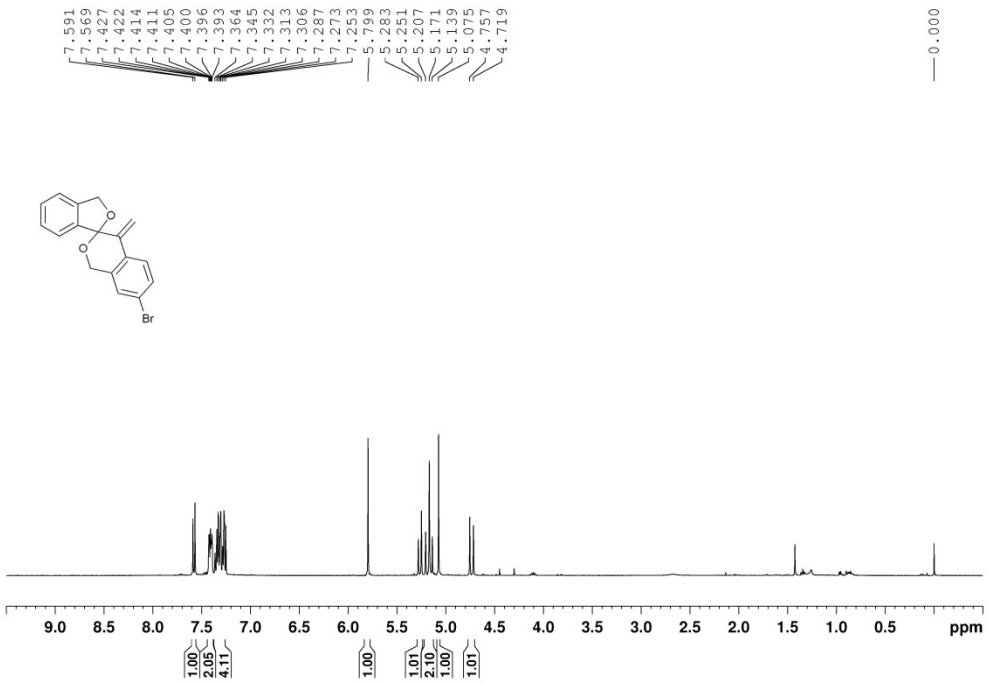
10
ppm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7.400
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7.393
7.364
7.345
7.332
7.313
7.306
7.287
7.273
7.253
5.799
5.283
5.251
5.207
5.171
5.139
5.075
4.757
4.719
0.000
Br
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
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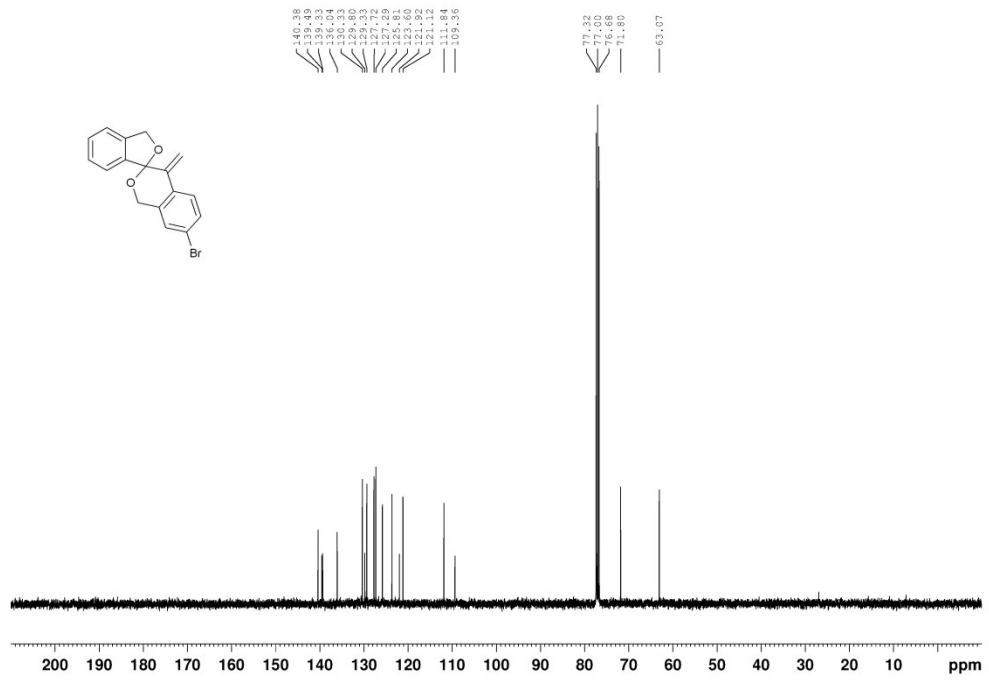
2.05
4.11
1.00
1.01
2.10
1.00
1.01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129.33
127.72
127.09
125.81
123.60
121.92
121.12
111.84
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77.00
76.68
71.80
63.07
Br
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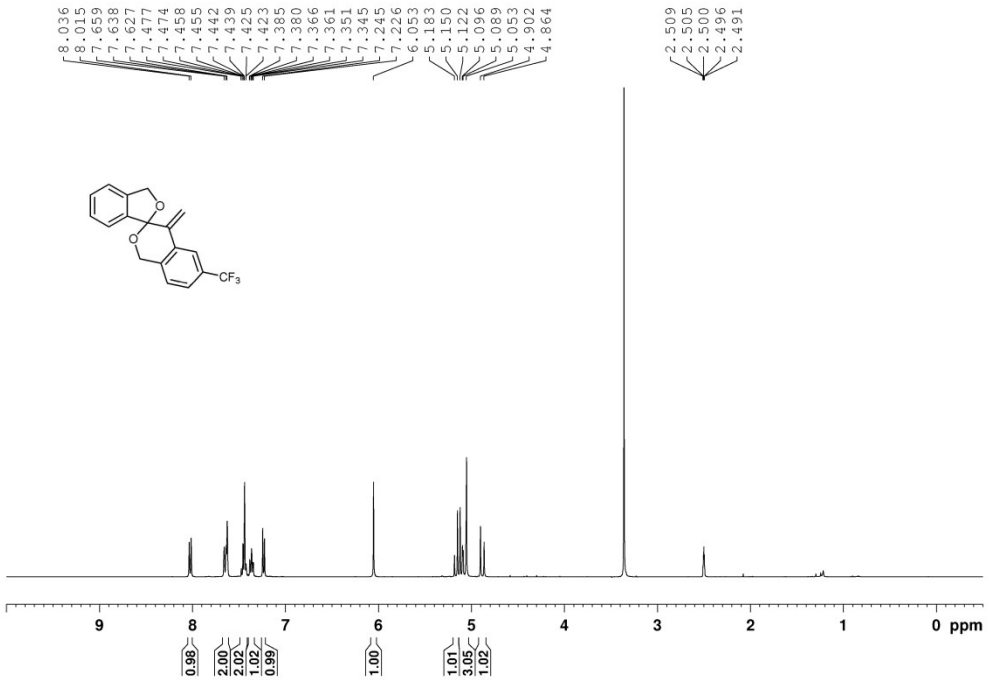
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7.439
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7.423
7.385
7.380
7.366
7.361
7.351
7.345
7.245
7.226
6.053
5.183
5.150
5.122
5.096
5.089
5.053
4.902
4.864
2.509
2.505
2.500
2.496
2.491
CF3
9
8
7
6
5
4
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1.01
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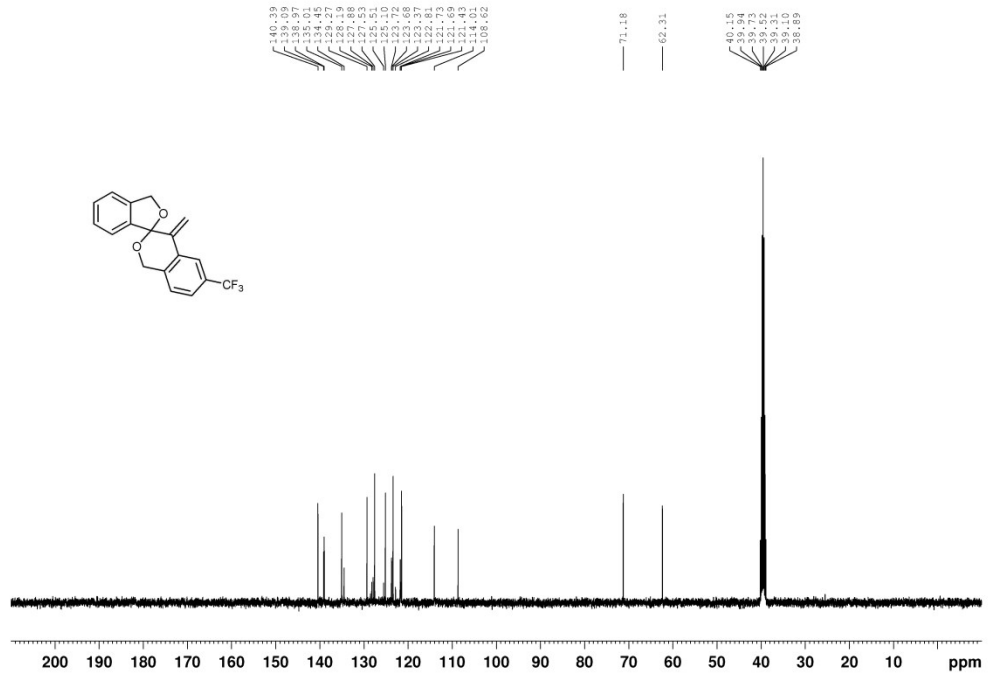
1.02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125.51
125.10
123.72
123.68
123.37
122.91
122.73
121.69
121.43
114.01
108.62
71.18
62.31
40.15
39.94
39.73
39.52
39.31
39.10
38.89
CF3
200
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150
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100
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80
70
60
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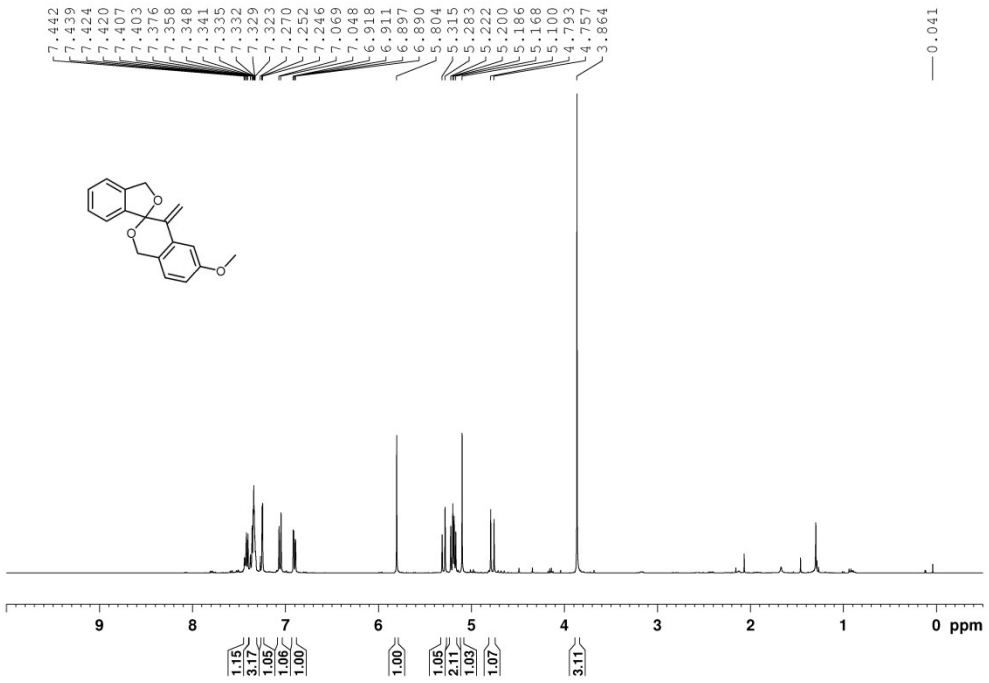
20
10
ppm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7.332
7.329
7.323
7.270
7.252
7.246
7.069
7.048
6.918
6.911
6.897
6.890
5.804
5.315
5.283
5.222
5.200
5.186
5.168
5.100
4.793
4.757
3.864
0.041
9
8
7
6
5
4
3
2
1
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1.05
1.06
1.00
1.00
1.05
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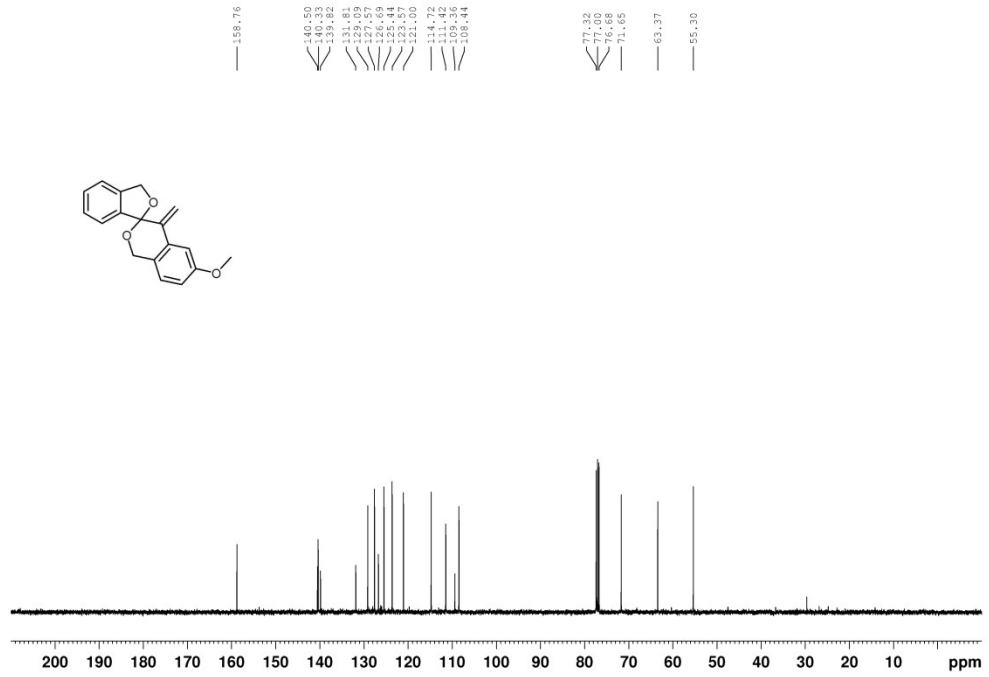
1.03
1.07
3.11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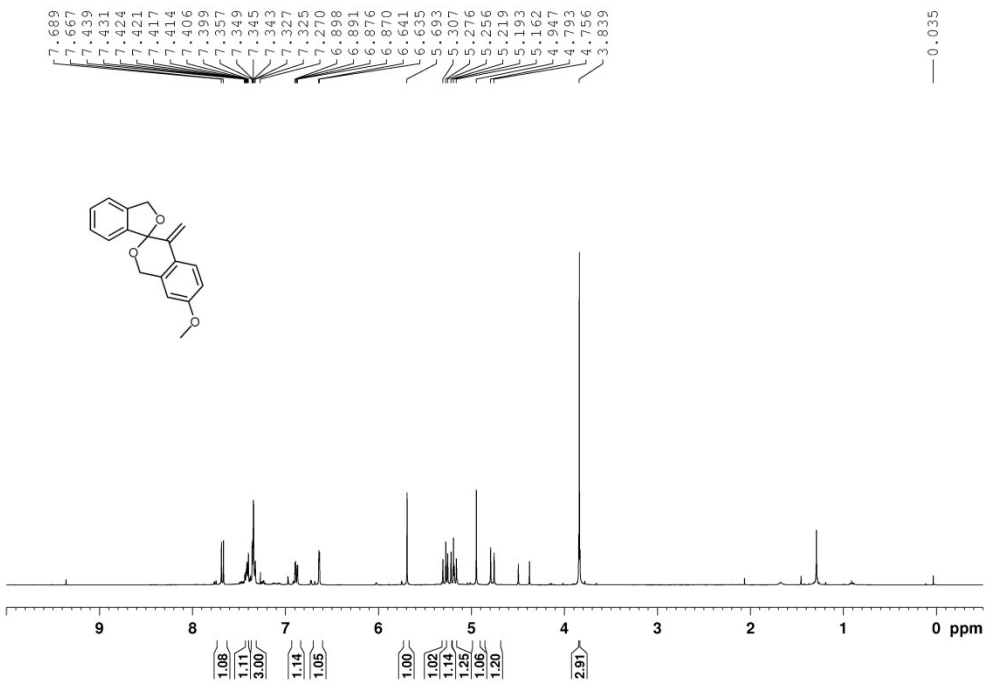
139.82
131.81
129.09
127.57
126.69
125.44
123.57
121.00
114.72
111.32
109.36
108.44
77.32
77.00
76.68
71.65
63.37
55.30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.421
7.417
7.414
7.406
7.399
7.357
7.349
7.345
7.343
7.327
7.325
7.270
6.898
6.891
6.876
6.870
6.641
6.635
5.693
5.307
5.276
5.256
5.219
5.193
5.162
4.947
4.793
4.756
3.839
0.035
9
8
7
6
5
4
3
2
1
0 ppm
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1.14
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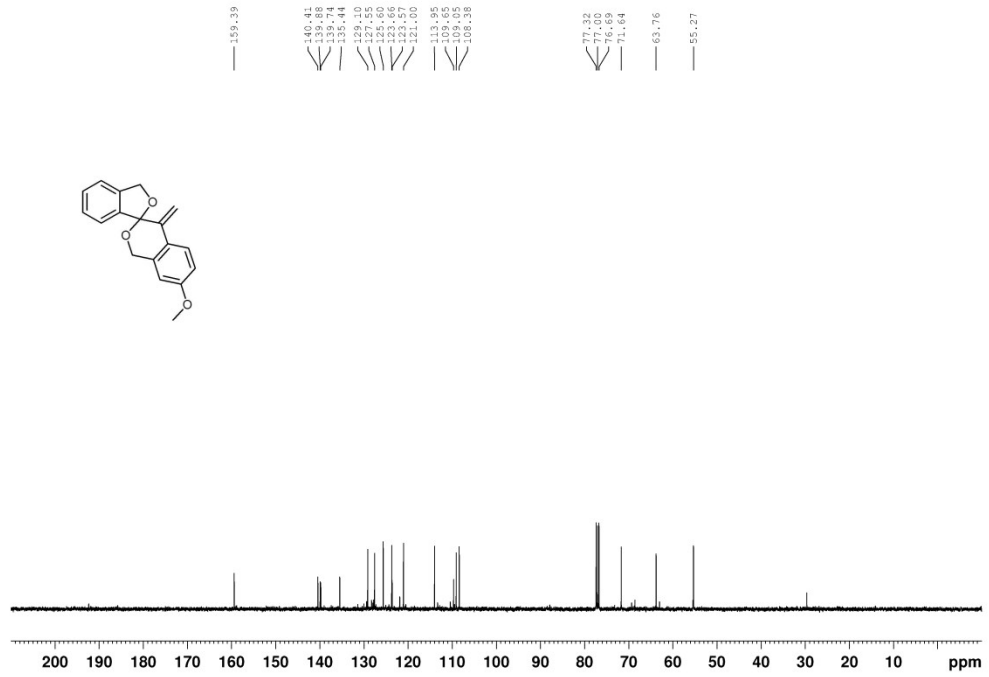
1.06
1.20
2.91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139.74
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129.10
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125.60
123.66
123.57
121.00
113.95
109.65
109.35
108.38
77.32
77.00
76.68
71.64
63.76
55.27
200
190
180
170
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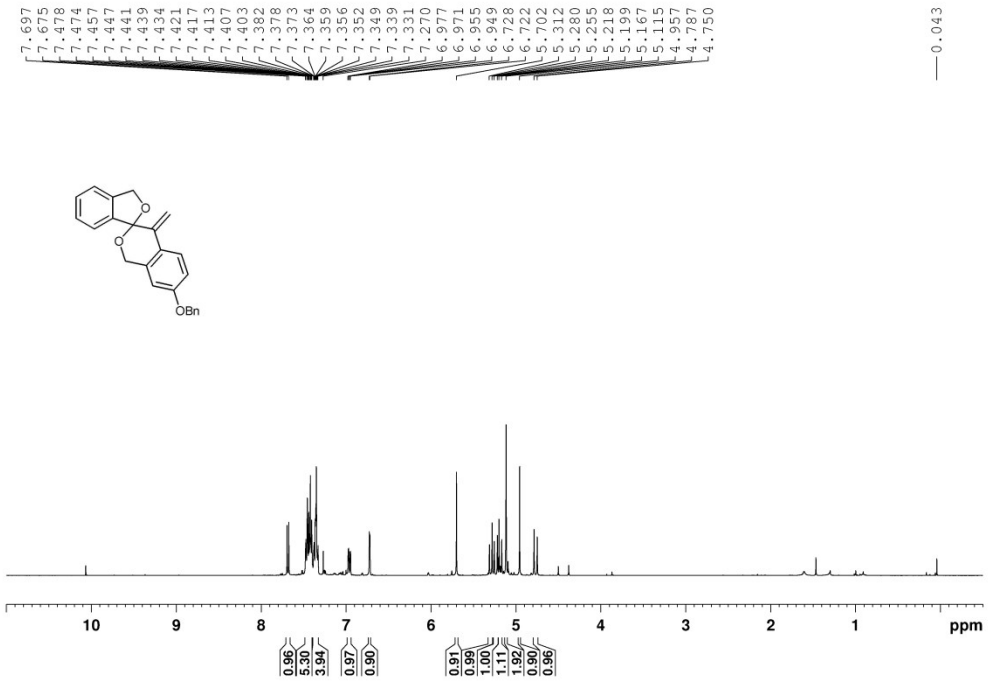
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.407
7.403
7.382
7.378
7.373
7.364
7.359
7.356
7.352
7.349
7.339
7.331
7.270
6.977
6.971
6.955
6.949
6.728
6.722
5.702
5.312
5.280
5.255
5.218
5.199
5.167
5.115
4.957
4.787
4.750
0.043
OBn
10
9
8
7
6
5
4
3
2
1
ppm
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3.94
0.97
0.90
0.91
0.99
1.00
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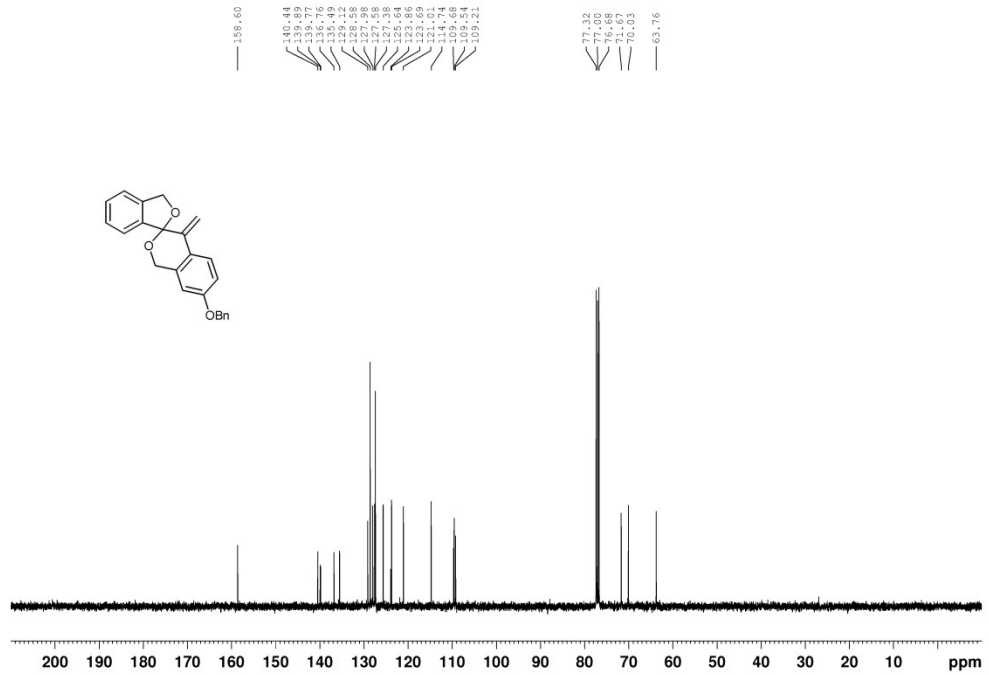
1.92
0.90
0.96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127.28
126.84
123.86
123.69
121.91
121.44
109.68
109.54
109.21
77.32
77.00
76.68
71.67
70.03
63.76
OBn
200
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150
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70
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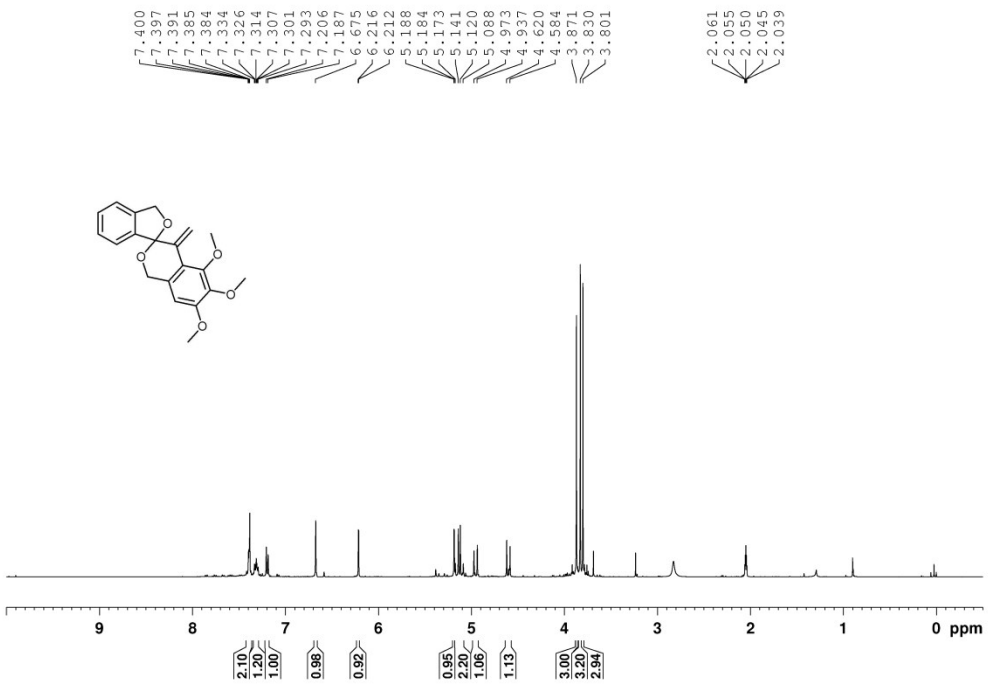
ppm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7.301
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7.187
6.675
6.216
6.212
5.188
5.184
5.173
5.141
5.120
5.088
4.973
4.937
4.620
4.584
3.871
3.830
3.801
2.061
2.055
2.050
2.045
2.039
9
8
7
6
5
4
3
2
1
0 ppm
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1.00
0.98
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0.95
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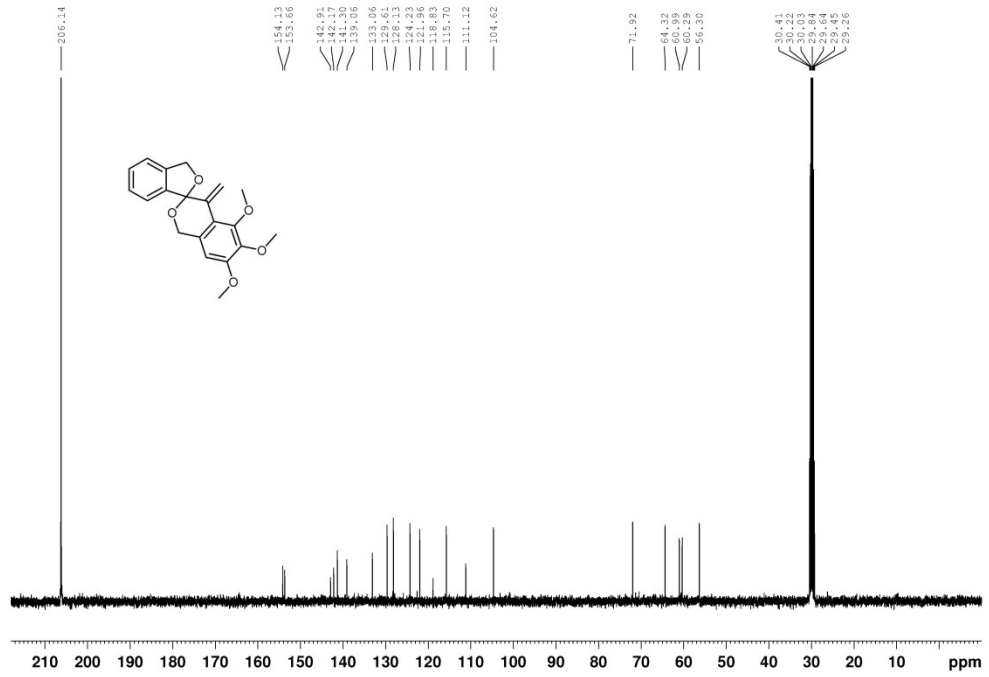
1.06
1.13
3.00
3.20
2.94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133.06
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124.23
121.96
118.83
115.70
111.12
104.62
71.92
64.32
60.99
60.29
56.30
30.41
30.22
30.03
29.84
29.64
29.45
29.26
210
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120
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100
90
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70
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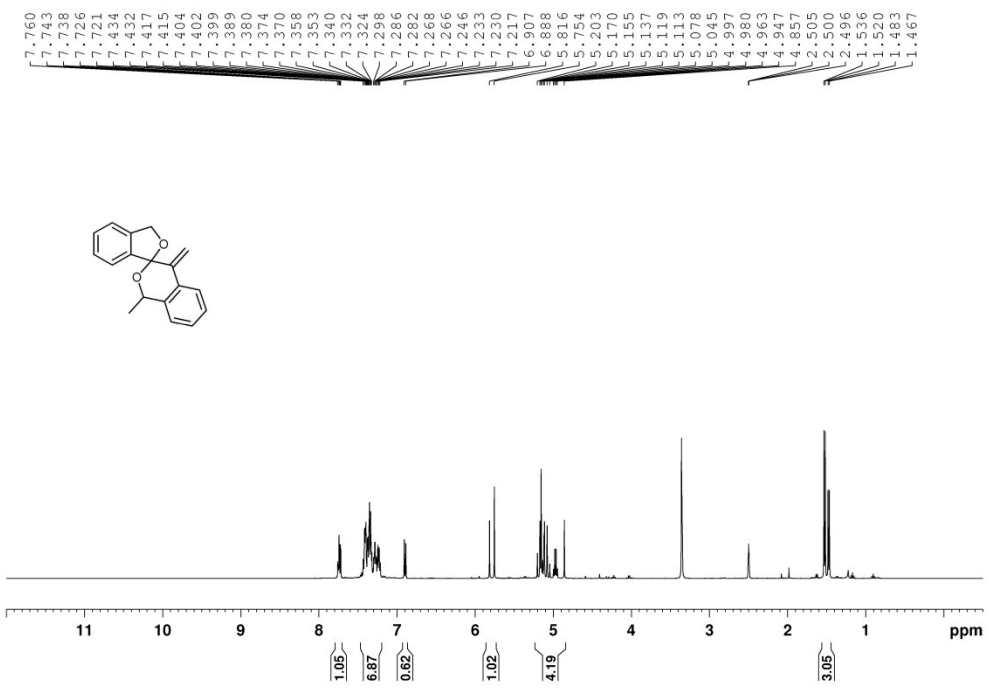
20
10
ppm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7.402
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7.380
7.374
7.370
7.358
7.353
7.340
7.332
7.324
7.298
7.286
7.282
7.268
7.266
7.246
7.233
7.230
7.217
6.907
6.888
5.816
5.754
5.203
5.170
5.155
5.137
5.119
5.113
5.078
5.045
4.997
4.980
4.963
4.947
4.857
2.505
2.500
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1.520
1.483
1.467
11
10
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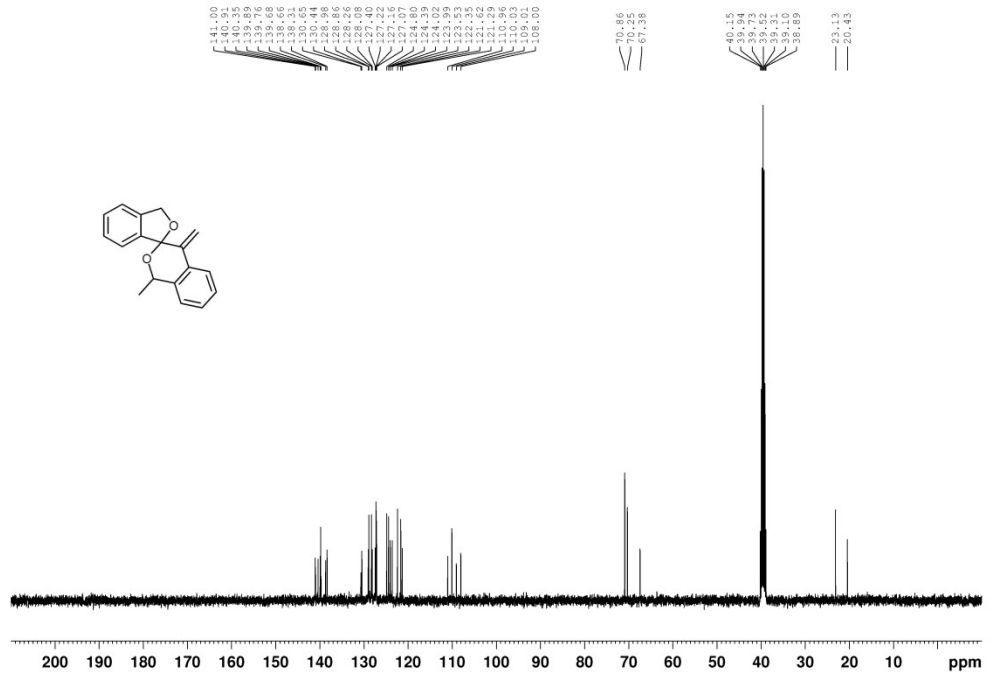
3.05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128.08
127.40
127.22
127.16
127.07
127.00
124.39
124.02
123.99
123.53
123.35
121.62
121.29
110.96
110.03
109.01
108.00
70.86
70.25
67.38
40.15
39.94
39.73
39.52
39.31
39.10
38.89
23.13
20.43
200
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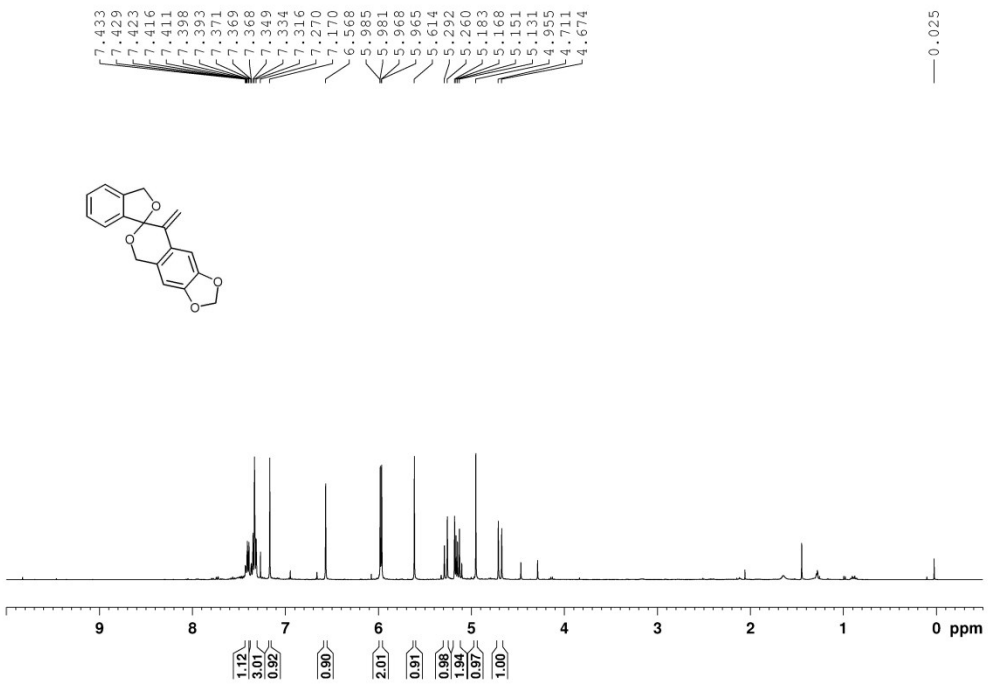
ppm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7.316
7.270
7.170
6.568
5.985
5.981
5.968
5.965
5.614
5.292
5.260
5.183
5.168
5.151
5.131
4.955
4.711
4.674
0.025
9
8
7
6
5
4
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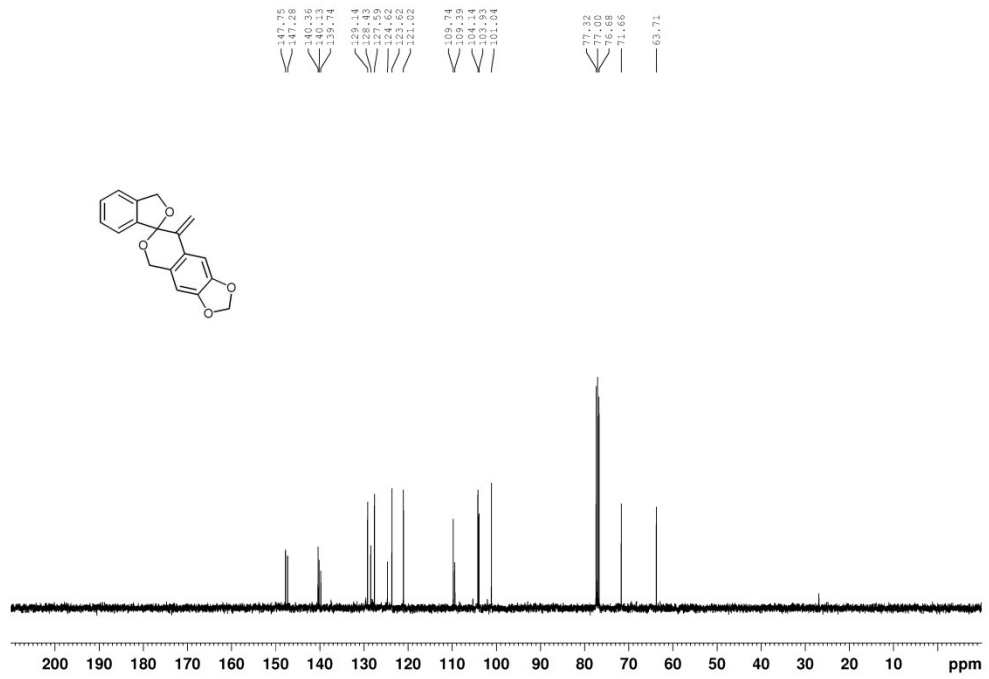
1.00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121.02
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109.39
104.14
103.83
101.04
77.32
77.00
76.68
71.66
63.71
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150
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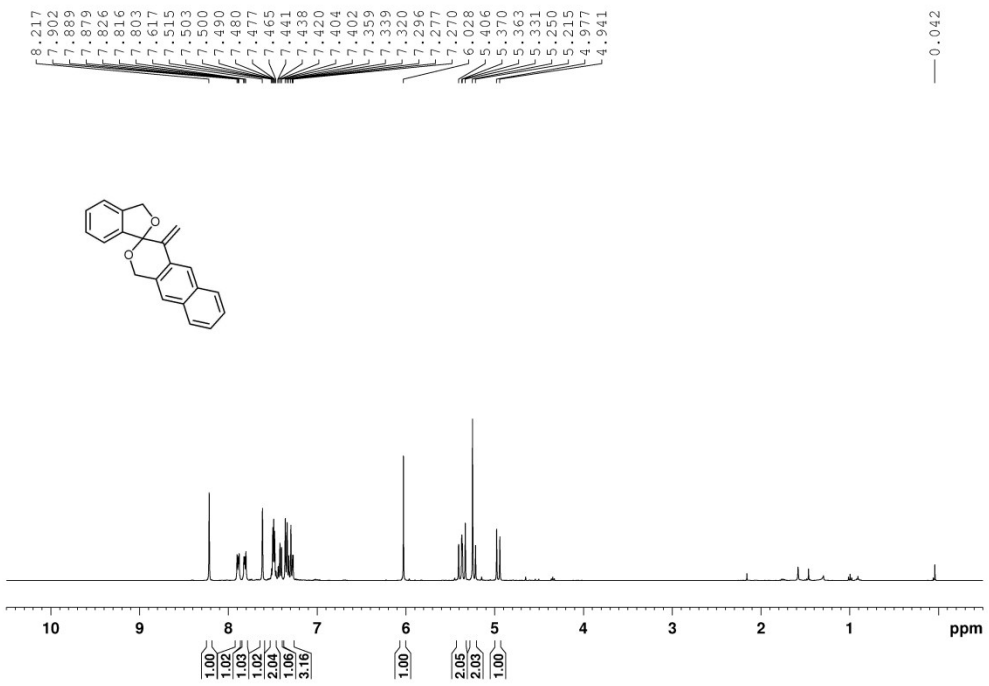
ppm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7.480
7.477
7.465
7.441
7.438
7.420
7.404
7.402
7.359
7.339
7.320
7.296
7.277
7.270
6.028
5.406
5.370
5.363
5.331
5.250
5.215
4.977
4.941
0.042
10
9
8
7
6
5
4
3
2
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1.03
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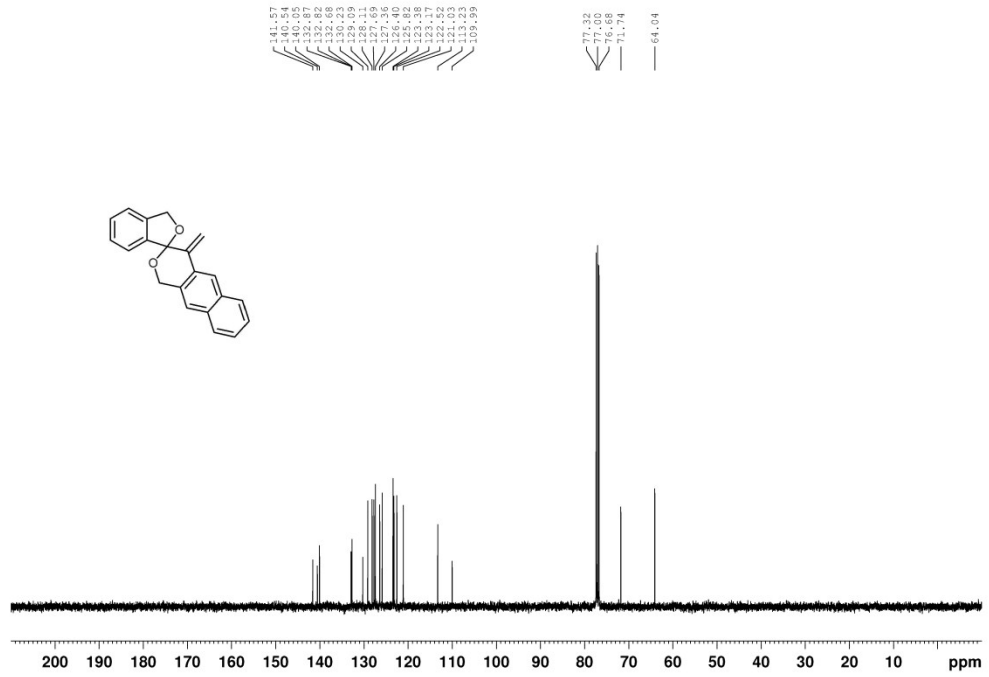
2.03
1.00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127.56
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125.82
123.38
123.17
123.12
121.03
113.23
109.99
77.32
77.00
76.68
71.74
64.04
200
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150
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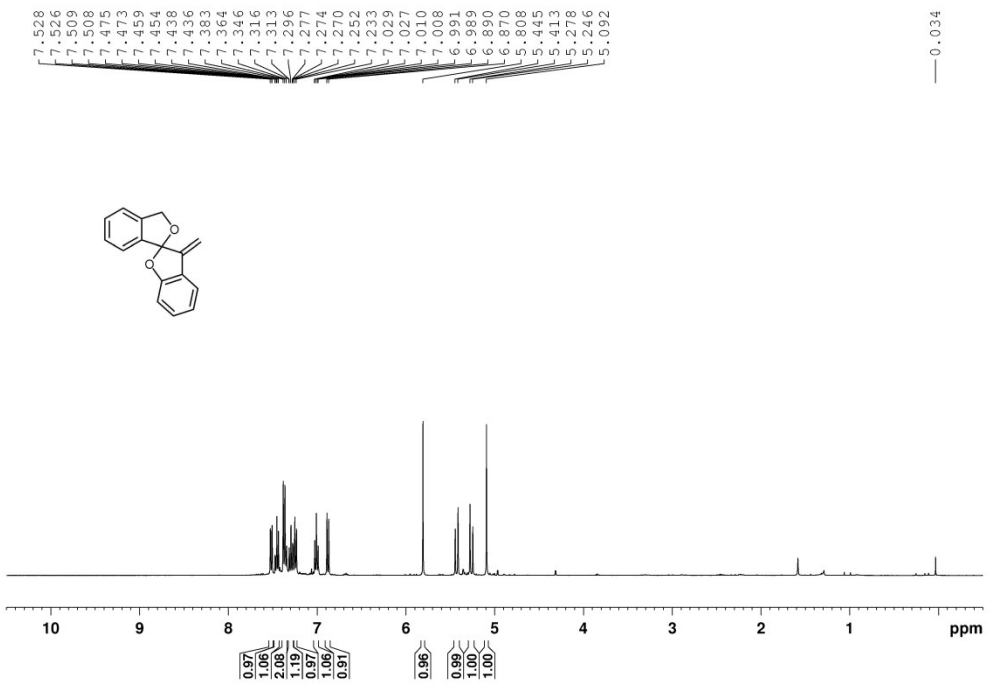
10
ppm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7.346
7.316
7.313
7.296
7.277
7.274
7.270
7.252
7.233
7.029
7.027
7.010
7.008
6.991
6.989
6.890
6.870
5.808
5.445
5.413
5.278
5.246
5.092
0.034
10
9
8
7
6
5
4
3
2
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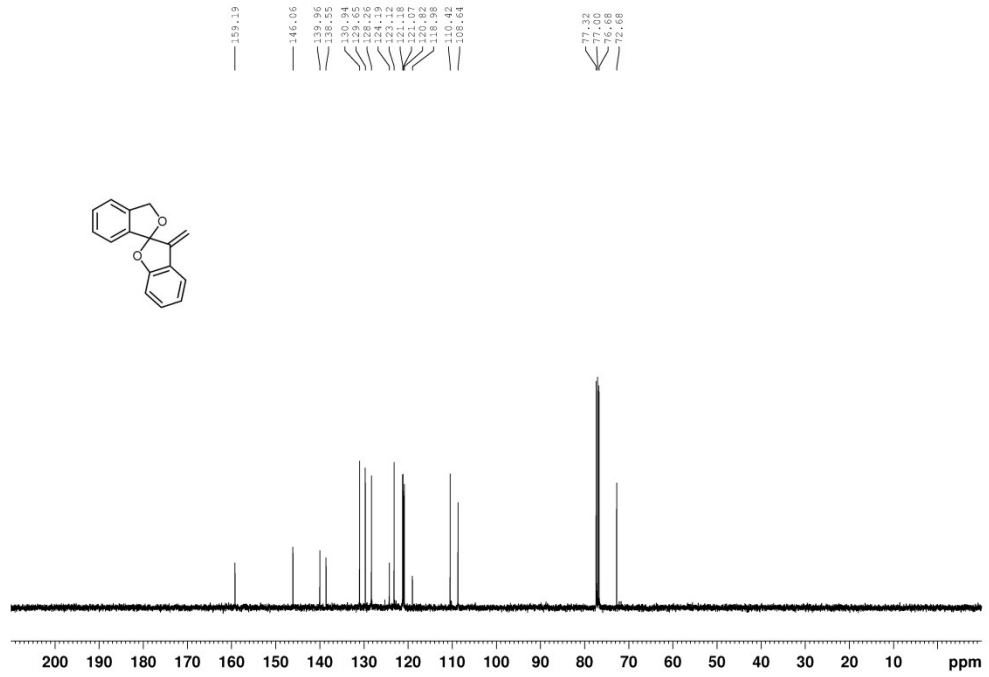
1.00
1.00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124.19
123.12
121.68
121.07
120.82
118.98
110.42
108.64
77.32
77.00
76.68
72.68
200
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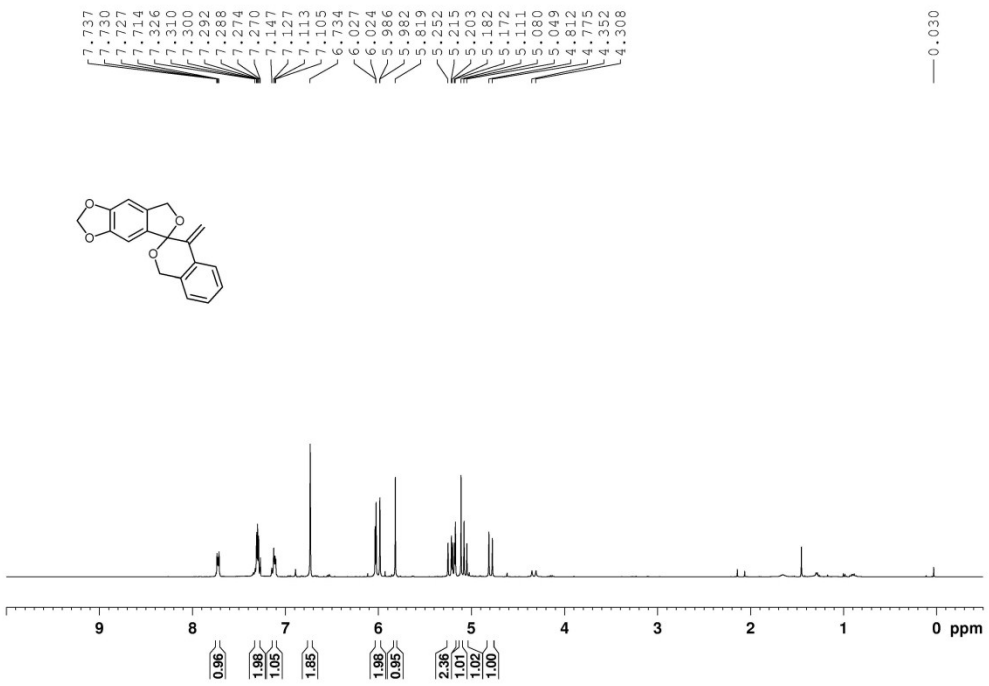
10
ppm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7.292
7.288
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7.113
7.105
6.734
6.027
6.024
5.986
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5.215
5.203
5.182
5.172
5.111
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5.049
4.812
4.775
4.352
4.308
0.030
9
8
7
6
5
4
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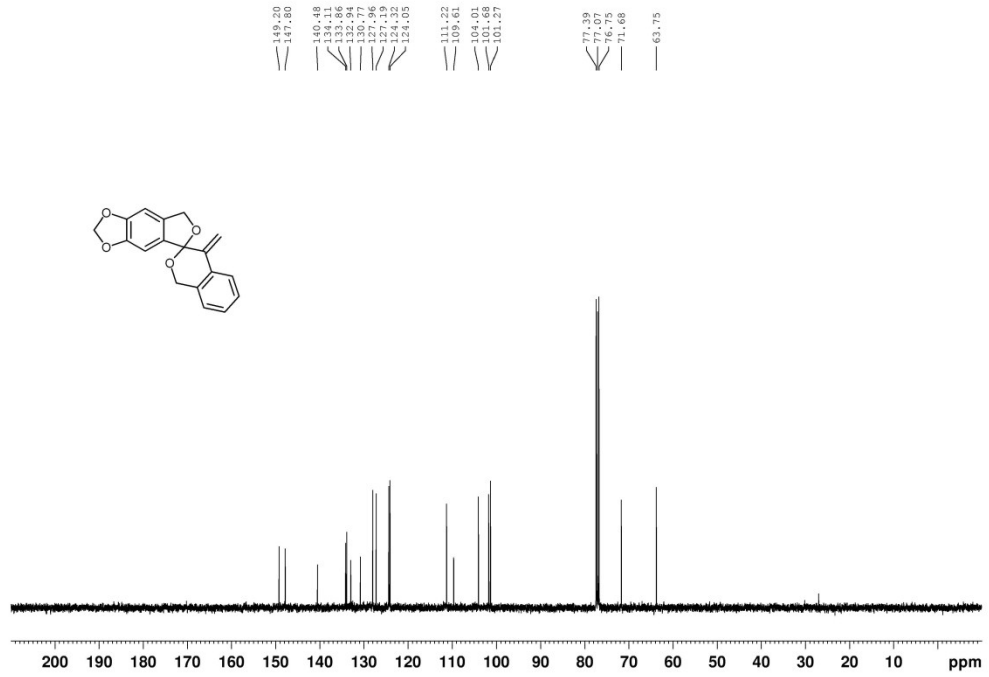
1.02
1.00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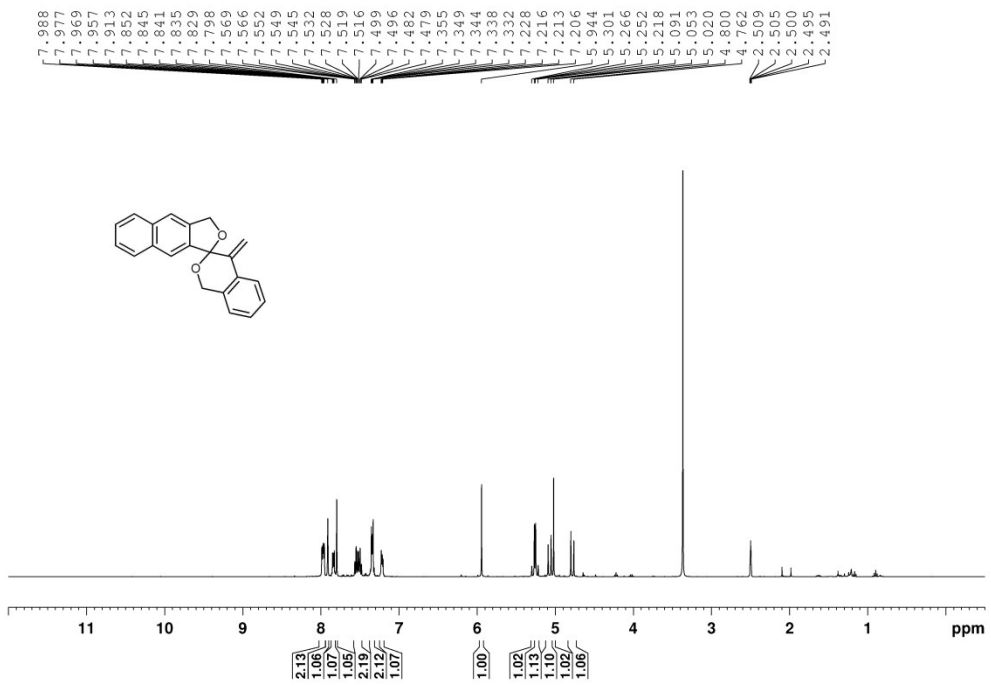
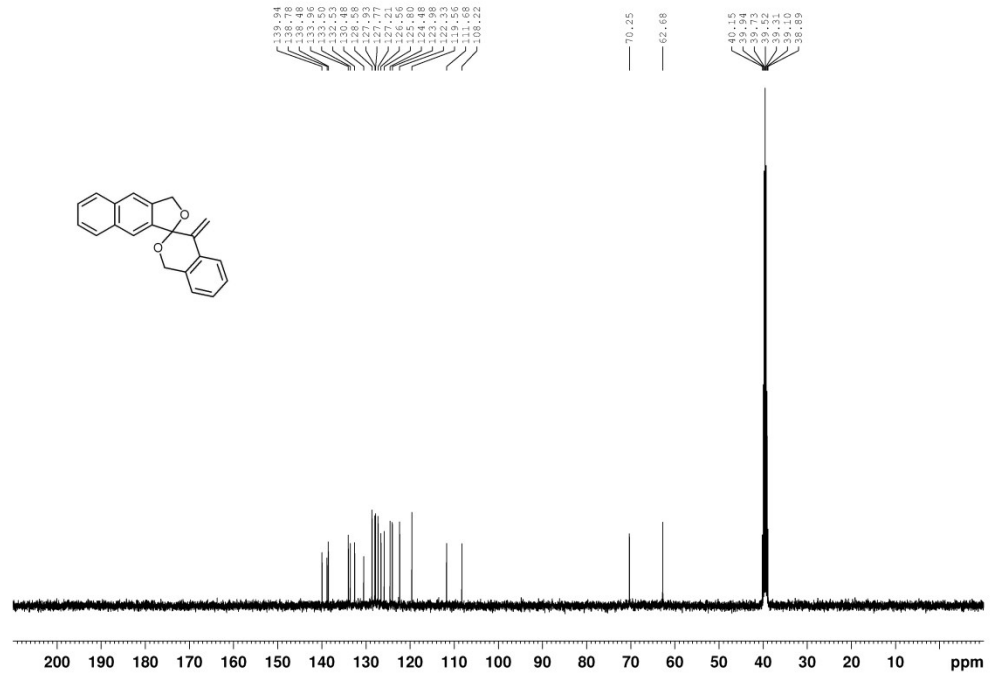
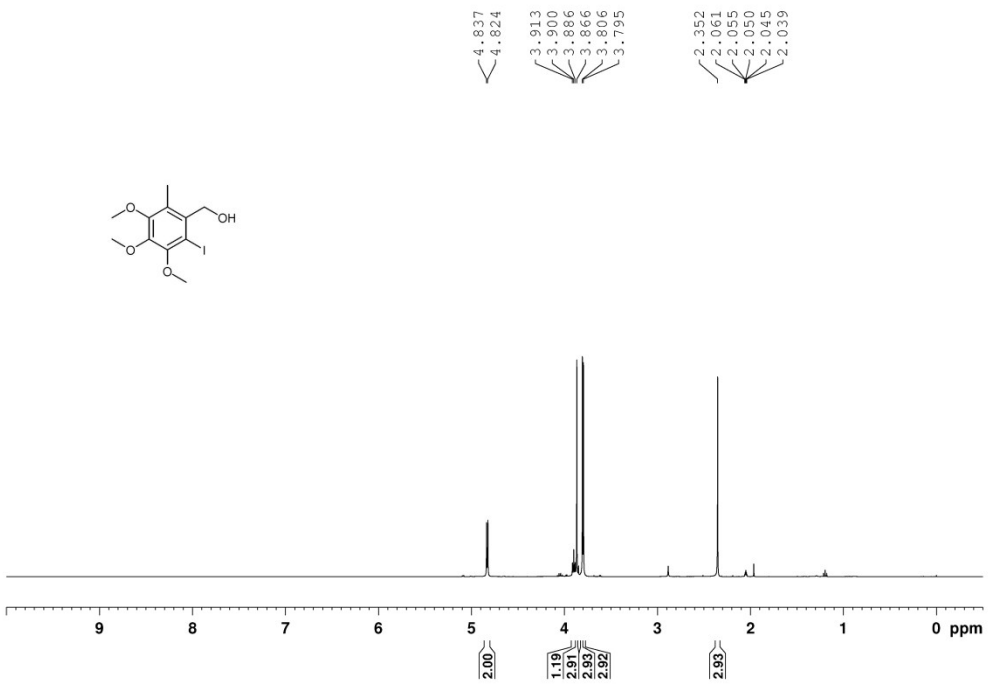
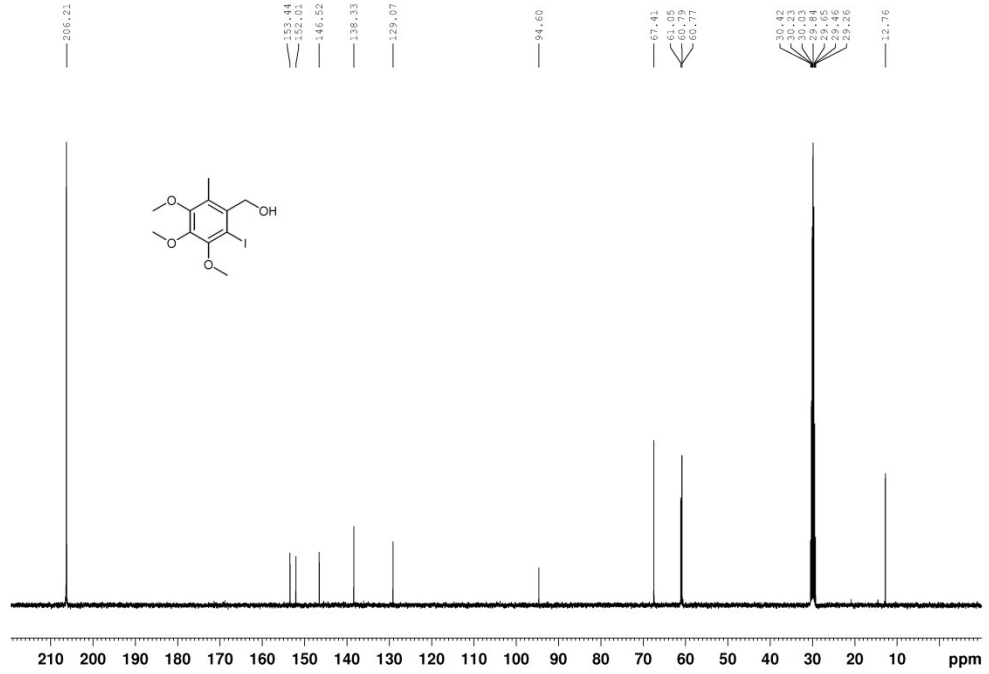
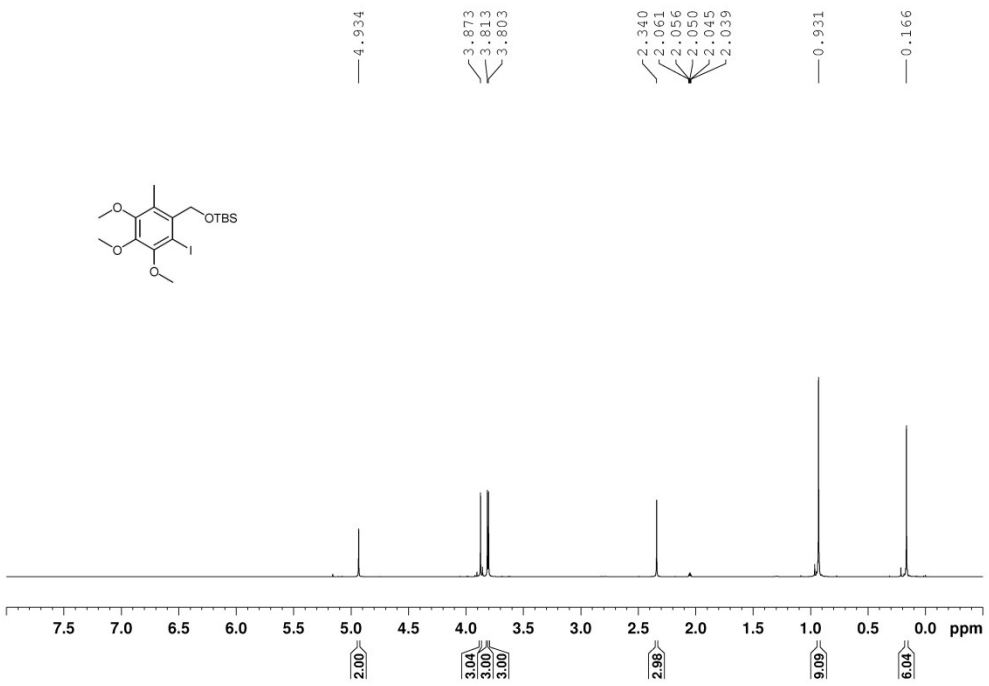
140.48
134.11
133.86
132.94
130.77
128.96
127.19
124.32
124.05
111.22
109.61
104.01
101.68
101.27
77.39
77.07
76.75
71.68
63.75
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

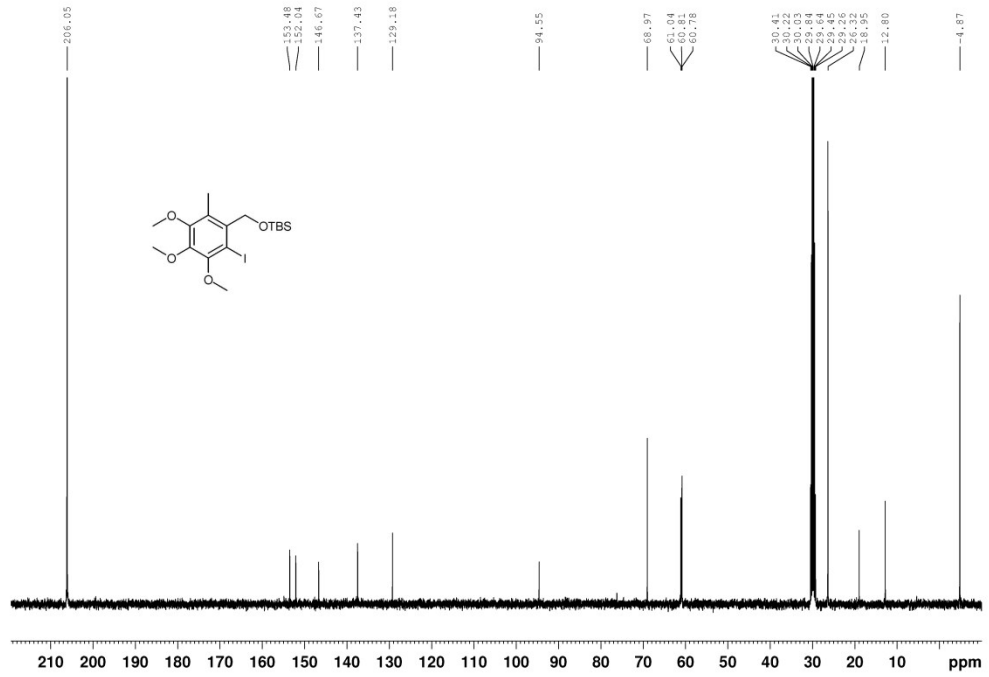

7.988
7.977
7.969
7.957
7.913
7.852
7.845
7.841
7.835
7.829
7.798
7.569
7.566
7.552
7.549
7.545
7.532
7.528
7.519
7.516
7.499
7.496
7.482
7.479
7.355
7.349
7.344
7.338
7.332
7.228
7.216
7.213
7.206
5.944
5.301
5.266
5.252
5.218
5.091
5.053
5.020
4.800
4.762
2.509
2.505
2.500
2.495
2.491
11 10 9 8 7 6 5 4 3 2 1 ppm
2.13 1.06 1.07 1.05 2.19 2.12 1.07 1.00 1.02 1.13 1.10 1.02 1.06

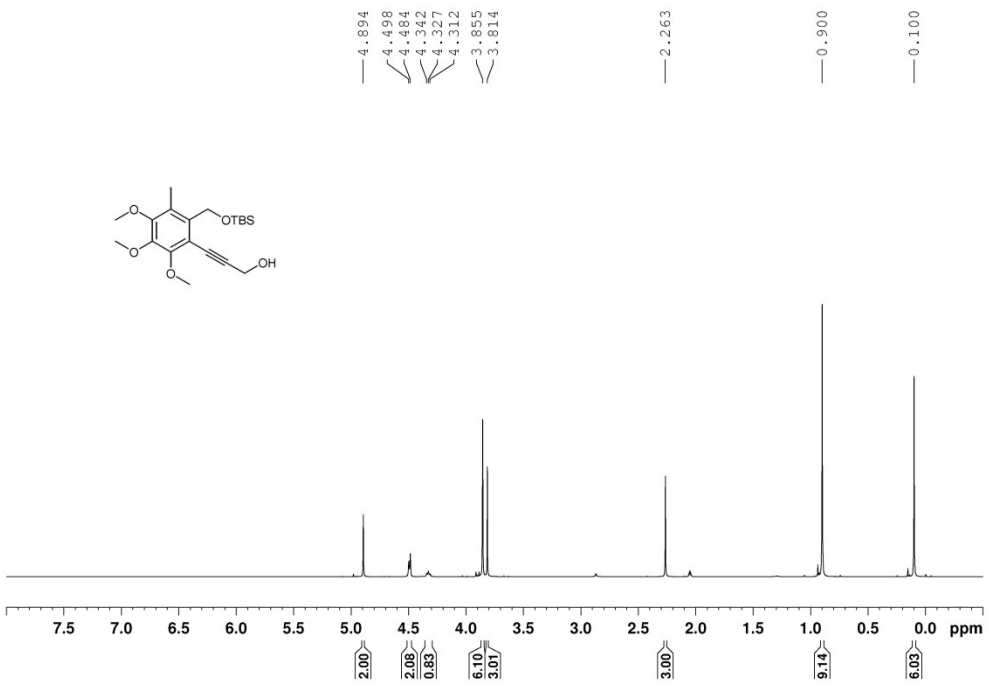

139.94
139.78
138.48
133.96
133.50
130.43
130.18
128.58
127.93
127.77
127.21
126.46
125.80
124.48
123.98
123.53
119.56
111.68
108.22
70.25
62.68
40.15
39.94
39.73
39.52
39.31
39.10
38.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

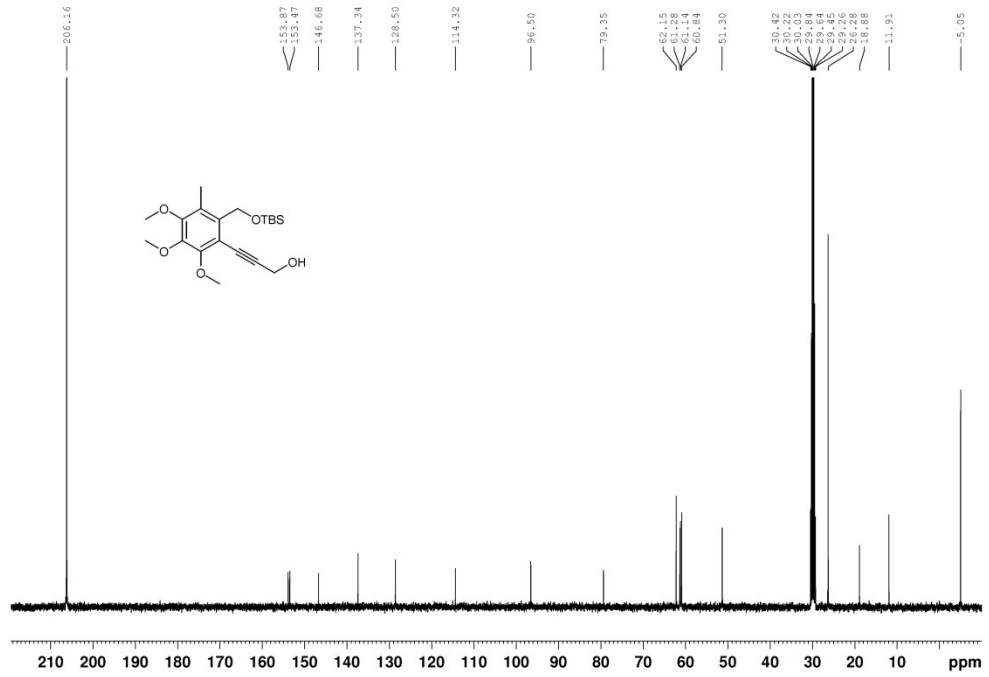

4.837
4.824
3.913
3.900
3.886
3.866
3.806
3.795
2.352
2.061
2.055
2.050
2.045
2.039
OH
I
9
8
7
6
5
4
3
2
1
0 ppm
2.00
1.19
2.91
2.93
2.92
2.93

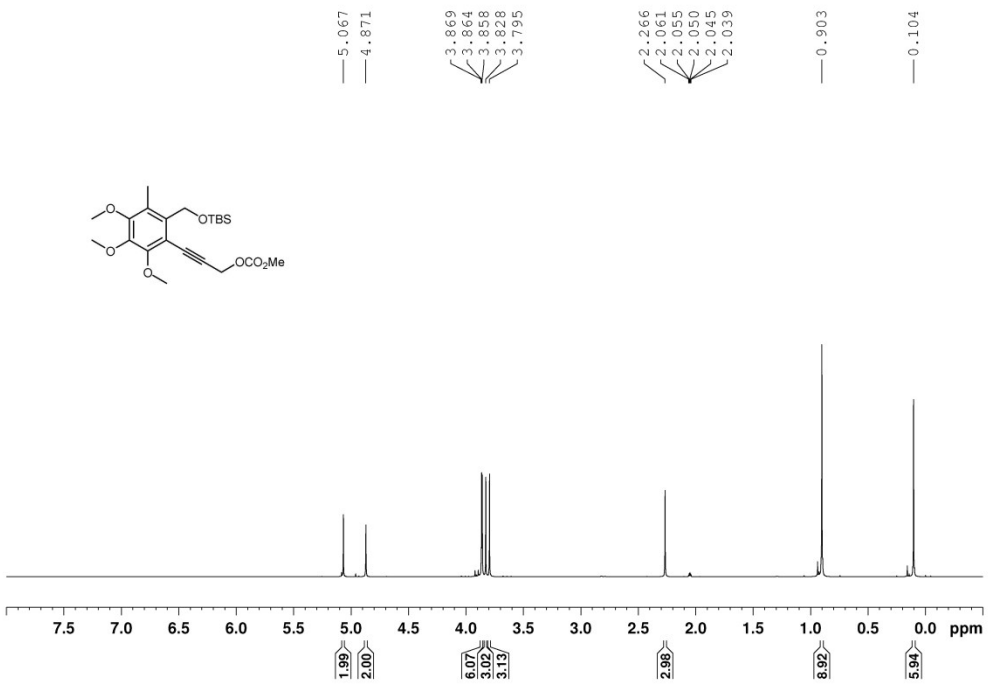

206.21
153.44
152.01
146.52
138.33
129.07
94.60
67.41
61.05
60.79
60.77
30.42
30.23
30.03
29.84
29.65
29.46
29.26
12.76
OH
I
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

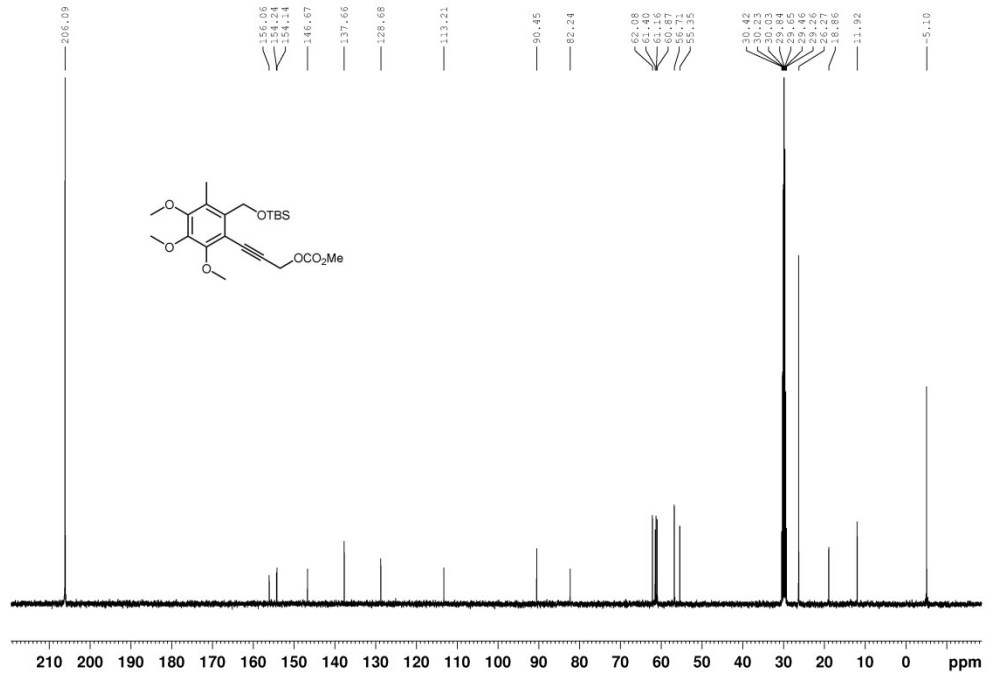

4.934
3.873
3.813
3.803
2.340
2.061
2.056
2.050
2.045
2.039
0.931
0.166
OTBS
I
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
3.04
3.00
3.00
2.98
9.09
6.04

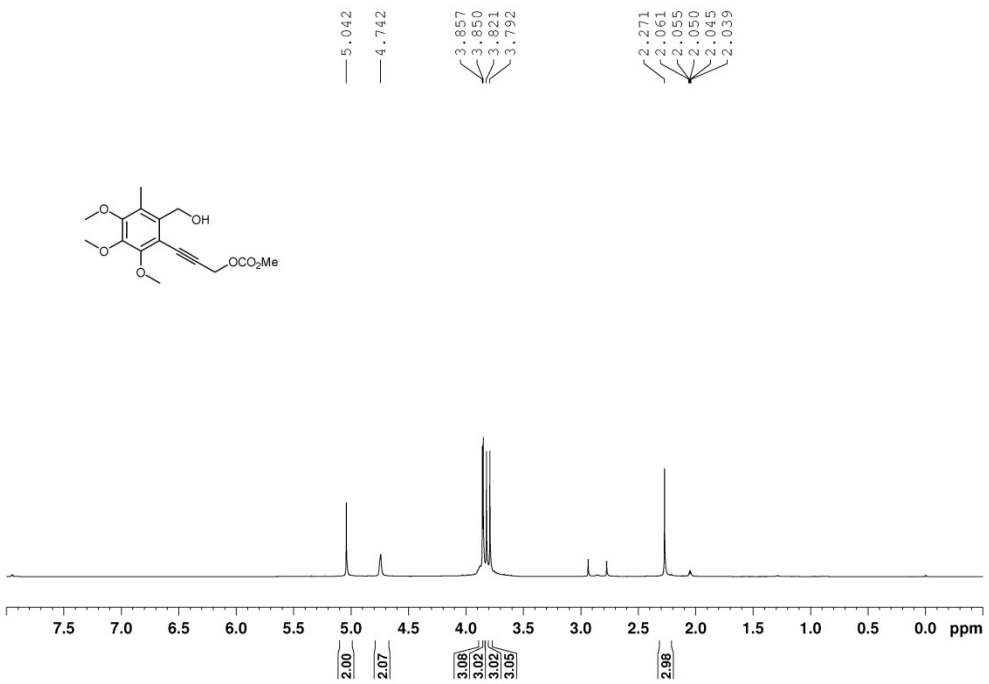

206.05
153.48
152.04
146.67
137.43
129.18
94.55
68.97
61.04
60.81
60.78
30.41
30.22
30.03
29.84
29.64
29.45
29.26
26.32
18.95
-12.80
-4.87
OTBS
I
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

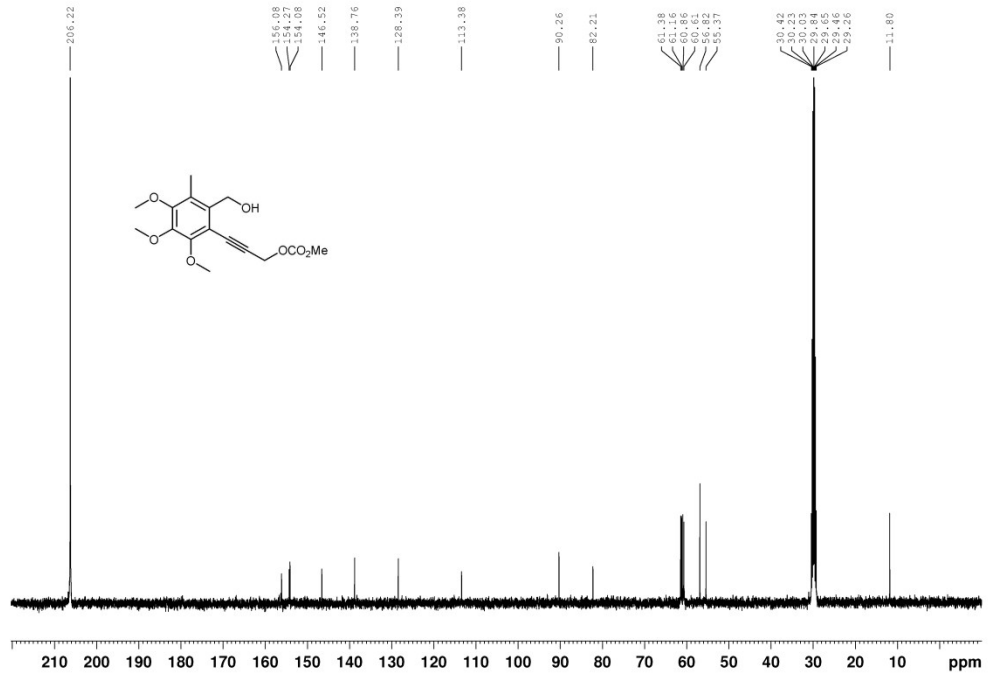

4.894
4.498
4.484
4.342
4.327
4.312
3.855
3.814
2.263
0.900
0.100
OTBS
OH
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
2.08
0.83
6.10
3.01
3.00
9.14
6.03

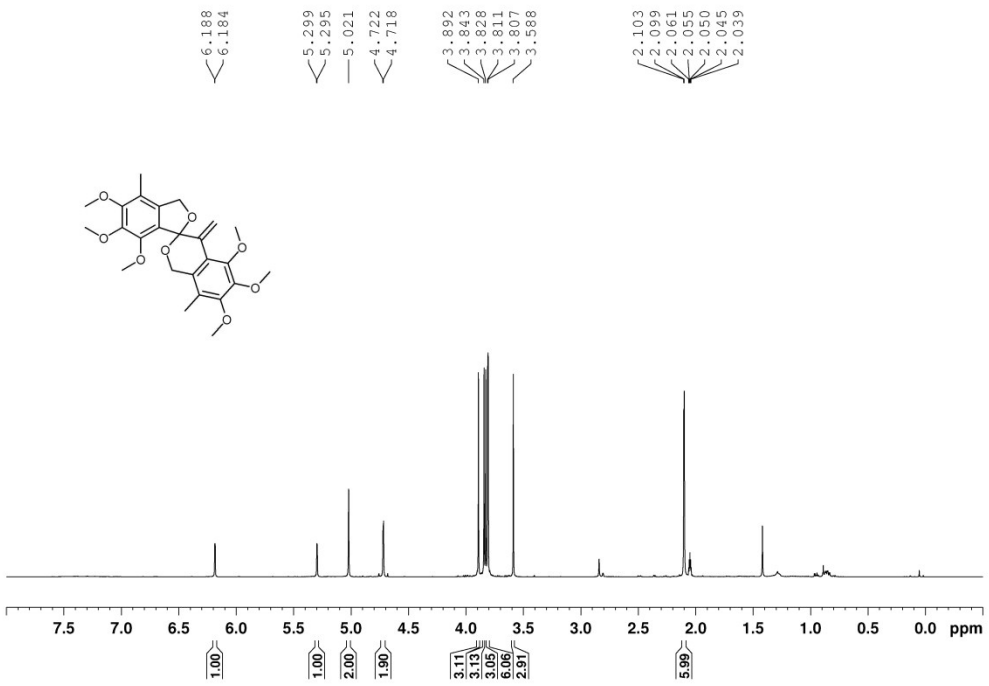

206.16
153.87
153.47
146.68
137.34
128.50
114.32
96.50
79.35
62.15
61.28
61.14
60.84
51.30
30.42
30.22
30.03
29.84
29.64
29.45
29.26
26.28
18.88
11.91
-5.05
OTBS
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

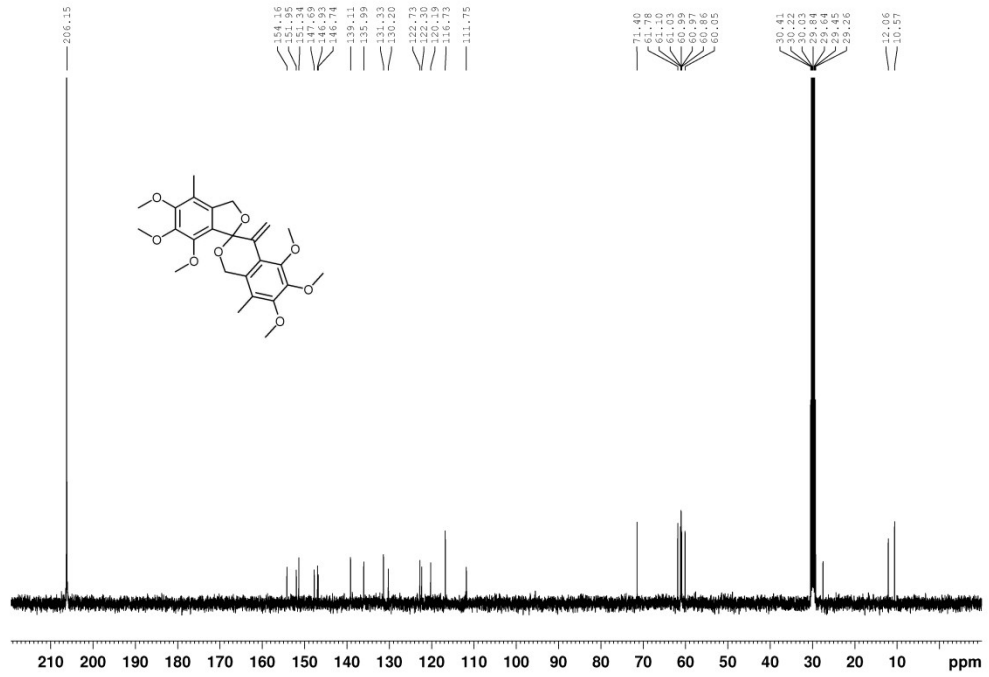

5.067
4.871
3.869
3.864
3.858
3.828
3.795
2.266
2.061
2.055
2.050
2.045
2.039
0.903
0.104
OTBS
OCO2Me
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.99
2.00
6.07
3.02
3.13
2.98
8.92
5.94

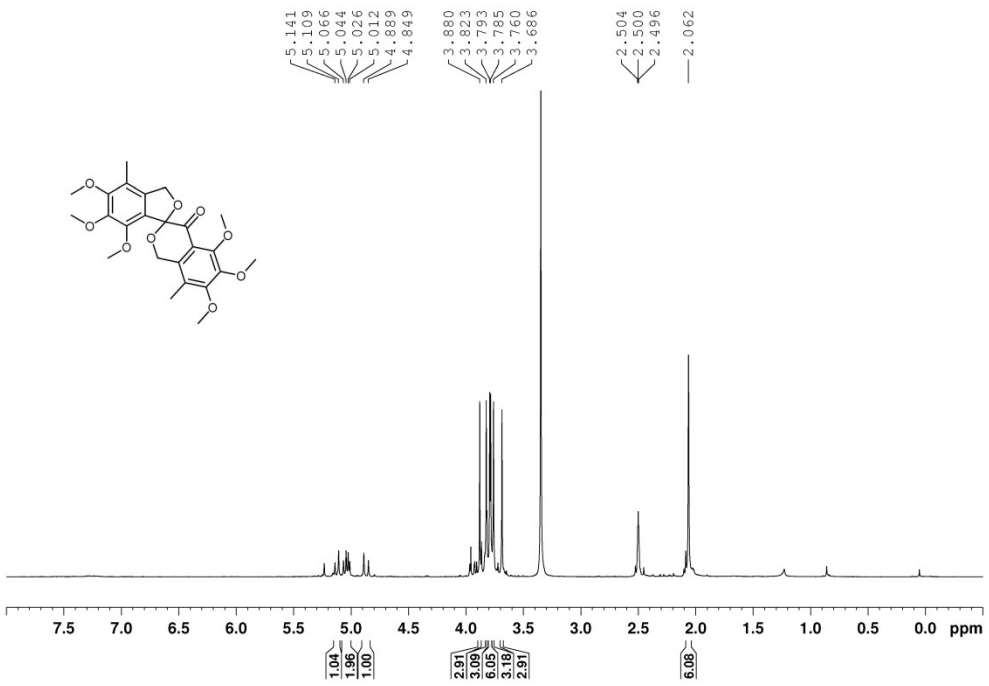

206.09
156.06
154.24
154.14
146.67
137.66
128.68
113.21
90.45
82.24
62.08
61.40
61.16
60.87
56.71
55.35
30.42
30.23
30.03
29.84
29.65
29.46
29.26
26.27
18.86
11.92
-5.10
OTBS
OCO2Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

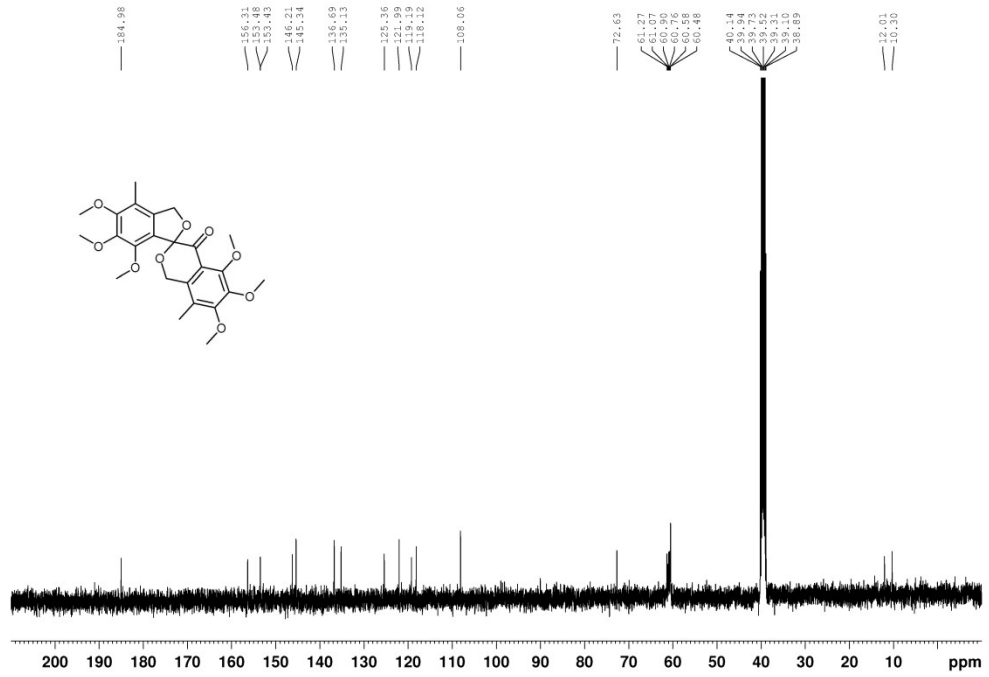

5.042
4.742
3.857
3.850
3.821
3.792
2.271
2.061
2.055
2.050
2.045
2.039
OH
OCO2Me
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
2.07
3.08
3.02
3.02
3.05
2.98


206.22
156.08
154.27
154.08
146.52
138.76
128.39
113.38
90.26
82.21
61.38
61.16
60.86
60.61
56.82
55.37
30.42
30.23
30.03
29.84
29.65
29.46
29.26
11.80
OH
OCO2Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


6.188
6.184
5.299
5.295
5.021
4.722
4.718
3.892
3.843
3.828
3.811
3.807
3.588
2.103
2.099
2.061
2.055
2.050
2.045
2.039
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.00
2.00
1.90
3.11
3.13
3.05
6.06
2.91
5.99


206.15
154.16
151.95
151.34
147.69
146.93
146.74
139.11
135.99
131.33
130.20
122.73
122.30
120.19
116.73
111.75
71.40
61.78
61.10
61.03
60.99
60.97
60.86
60.05
30.41
30.22
30.03
29.84
29.64
29.45
29.26
12.06
10.57
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


5.141
5.109
5.066
5.044
5.026
5.012
4.889
4.849
3.880
3.823
3.793
3.785
3.760
3.686
2.504
2.500
2.496
2.062
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.04
1.96
1.00
2.91
3.09
6.05
3.18
2.91
6.08


184.98
156.31
153.48
153.43
146.21
145.34
136.69
135.13
125.36
121.99
119.19
118.12
108.06
72.63
61.27
61.07
60.90
60.76
60.58
60.48
40.14
39.94
39.73
39.52
39.31
39.10
38.89
12.01
10.30
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm