Supporting Information

For

Synthesis of a 3-(alpha-Styryl)benzo[b]-thiophene Library via Bromocyclization of Alkynes and Palladium Catalyzed Tosylhydrazones Cross-Couplings: Evaluation as Antitubulin Agents

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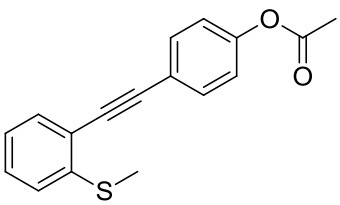
Experimental section general

Commercial reagents were used without further purification unless otherwise stated. All glassware's were oven-dried at 140 °C and all reactions were conducted under an argon atmosphere. Solvents: cyclohexane and ethyl acetate (EtOAc), and dioxane, were dried using the procedures described in D. Perrin Purification of Laboratory Chemicals.[1]

The compounds were all identified by usual physical methods, i.e. ^{1}H NMR, ^{13}C NMR, IR, elemental analysis. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ with a Bruker ARX 400 or Bruker Avance 300 and chemical shifts are reported in ppm. The following abbreviations are used: m (multiplet), s (singlet), br s (broad singlet), d (doublet), t (triplet) dd (doublet of doublet), td (triplet of doublet), q (quadruplet), ddd (doublet of doublet of doublet). IR spectra were measured on a Bruker Vector 22 spectrophotometer (neat, cm^{-1}). Elemental analyses were performed with a Perkin-Elmer 240 analyser. Analytical TLC was performed on Merck precoated silica gel 60F plates with detection by exposure to ultraviolet light (254 nm) and by immersion in a staining solution of 20% phosphomolybdic acid in EtOH or vanillin stain (vanillin, concentrated H_2SO_4, EtOH). Merck silica gel 60 (230-400 mesh) was used for column chromatography. Melting points (m.p.) were recorded on a Büchi B-450 apparatus and were uncorrected.

Analytical data for the selected compounds

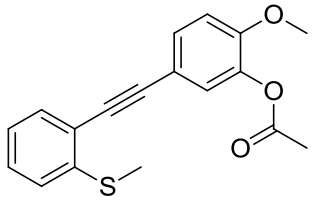
4-((2-(methylthio)phenyl)ethynyl)phenyl acetate (9b)



was prepared according to the general procedure from the alkyne (2-ethynylphenyl)(methyl)sulfane and the 4-iodophenyl acetate. Compound **9b** was obtained

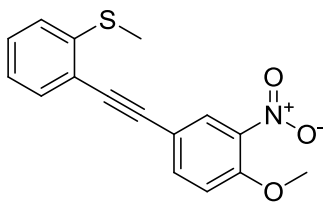
as a brown oil (274 mg, 97% yield); TLC: R_f = 0.50 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 3800, 3646, 1763, 1504, 1433, 1368, 1186, 1163, 1067 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.64 – 7.54 (m, 2H), 7.48 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.35 – 7.26 (m, 1H), 7.22 – 7.12 (m, 1H), 7.12 – 7.06 (m, 3H), 2.51 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2 (C), 150.7 (C), 141.9 (C), 132.9 (2CH), 132.3 (CH), 128.9 (CH), 124.4 (CH), 124,2 (CH), 121.8 (2CH), 121.3 (C), 121.0 (C), 95.1 (C), 87.1 (C), 21.2 (SCH_3), 15.2 (CH_3); HRMS (ESI): for $C_{17}H_{15}O_2S$ $(M + H)^+$: *m/z* calcd 283.0748, found 283.0750.

2-methoxy-5-((2-(methylthio)phenyl)ethynyl)phenyl acetate (9c)



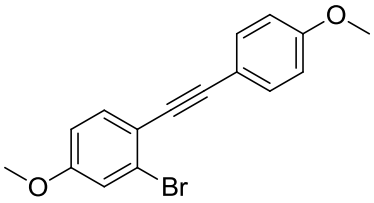
was prepared according general procedure from the alkyne (2-ethynylphenyl)(methyl)sulfane and the 5-iodo-2-methoxyphenyl acetate. Compound **9c** was obtained as a yellow oil (269 mg, 86% yield); TLC: R_f = 0.38 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 3736, 3395, 2067, 1977, 1769, 1613, 1532, 1510, 1434, 1270, 1111, 1018 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.44 (ddd, *J* = 7.3, 5.1, 1.7 Hz, 2H), 7.33 – 7.25 (m, 2H), 7.19 – 7.05 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 3.86 (s, 3H), 2.50 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8 (C), 151.8 (C), 141.7 (C), 139.6 (C), 132.3 (CH), 130.7 (CH), 128.8 (CH), 126.2 (CH), 124.4 (CH), 124.3 (CH), 121.6 (C), 115.9 (C), 112.4 (CH), 95.1 (C), 86.3 (C), 56.1 (OCH_3), 20.8 (SCH_3), 15.3 (CH_3); HRMS (ESI): for $C_{18}H_{17}O_3S$ $(M + H)^+$: *m/z* calcd 313.0854, found 313.0857.

(2-((4-methoxy-3-nitrophenyl)ethynyl)phenyl)(methyl)sulfane (9d)



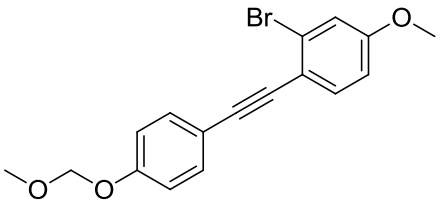
was prepared according general procedure from the alkyne (2-ethynylphenyl)(methyl)sulfane and the 4-iodo-1-methoxy-2-nitrobenzene. Compound **9d** was obtained as a yellow oil (296 mg, 99% yield); TLC: R_f = 0.20 (EtOAc/Cyclohexane, 3/7, SiO_2); IR (neat) 3736, 3395, 2067, 1977, 1769, 1613, 1532, 1510, 1434, 1270, 1111, 1018 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.04 (d, *J* = 2.1 Hz, 1H), 7.71 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.33 (dd, *J* = 8.7, 7.2 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.12 (td, *J* = 7.2, 1.2 Hz, 1H), 7.07 (d, *J* = 8.7 Hz, 1H), 3.99 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.9 (C), 142.0 (C), 137.2 (CH), 132.4 (CH), 129.3 (CH), 128.8 (CH), 124.4 (CH), 124.3 (CH), 120.7 (C), 116.0 (C), 113.7 (CH), 113.2 (C), 93.2 (C), 87.7 (C), 56.8 (OCH_3), 15.2 (SCH_3); HRMS (ESI): for $C_{16}H_{14}NO_3S$ $(M + H)^+$: *m*/*z* calcd 300.0650, found 300.0648.

2-bromo-4-methoxy-1-((4-methoxyphenyl)ethynyl)benzene (9f)



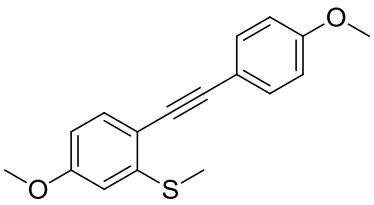
was prepared according general procedure from the alkyne 2-bromo-1-ethynyl-4-methoxybenzene and the 1-iodo-4-methoxybenzene. Compound **9f** was obtained as a brown oil (298 mg, 94% yield); TLC: R_f = 0.30 (EtOAc/Cyclohexane, 5/95, SiO2); IR (neat) 3085, 3065 , 3014, 2940, 2840, 2222, 1893, 1604, 1510, 1462, 1402, 1320, 1153, 1036, 1026 cm^{-1}; ^1H RMN ($CDCl_3$) δ (ppm): 7.50 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.16 (d, *J* = 1.8 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.83 (dd, *J* = 8.7, 1.8 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 159.8 (C), 159.7 (C), 133.8 (CH), 133.1 (2CH), 126.2 (C), 118.0 (C), 117.9 (CH), 115.4 (C), 114.1 (2CH), 113.6 (CH), 92.4 (C), 86.8 (C), 55.7 (OCH_3), 55.4 (OCH_3); HRMS (ESI): for $C_{16}H_{14}BrO$ $(M + H)^+$: *m*/*z* calcd 318.1852, found 318.1850.

2-bromo-4-methoxy-1-((4-(methoxymethoxy)phenyl)ethynyl)-benzene (9g)



was prepared according general procedure from the alkyne 2-bromo-1-ethynyl-4-methoxybenzene and the 1-iodo-4-(methoxymethoxy)benzene. Compound **9g** was obtained as a brown solid (341 mg, 99% yield); m.p = 58-60 °C; TLC: R_f = 0.23 (EtOAc/Cyclohexane, 5/95, SiO_2); IR (neat) 2899, 1605 , 1564, 1510, 1487, 1461, 1439, 1394, 1320, 1285, 1238 , 1223, 1200, 1176, 1151, 1107, 1079, 1032 cm-1; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.49 (d, *J* = 7.8 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.15 (d, *J* = 1.2 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 2H), 6.83 (dd, *J* = 1.2, 8.7 Hz, 1H), 5.19 (s, 2H), 3.81 (s, 3H), 3.48 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 159.6 (C), 157.3 (C), 133.7 (CH), 132.9 (2CH), 126.2 (C), 117.8 (C), 117.7 (CH), 116.6 (C), 116.2 (2CH), 113.5 (CH), 94.3 (OCH_2O), 92.2 (C), 86.9 (C), 56.1 (OCH_3), 55.6 (OCH_3); HRMS (ESI): for $C_{17}H_{16}BrO_3$ $(M + H)^+$: *m*/*z* calcd 347.0283, found 347.0287.

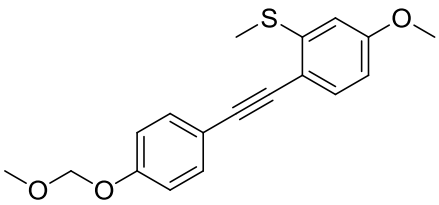
(5-methoxy-2-((4-methoxyphenyl)ethynyl)phenyl)(methyl)-sulfane (9j)



was prepared from the alkyne **9f** (1 mmol). To a solution of **9f** in anhydrous THF (8 mL/mmol) was added at -78 °C *n*-BuLi (2.2 equiv. 1.6 M in THF). The mixture was stirred 1 hour at -78 °C and Me_2S_2 (1.2 mmol) was added. The mixture was stirred 12 hours from -78 °C to room temperature. The mixture was hydrolyzed by a solution saturated of NH_4Cl and extracted by EtOAc. The aqueous layer was washed three times by EtOAc. Organic layers was joined,

washed with water and a saturated solution of NaCl and dried dry by anhydrous $MgSO_4$. The crude product was concentrated under reduce pressure and purified by silica gel chromatography. Compound **9j** was obtained as a yellow oil (182 mg, 64% yield); TLC: R_f = 0.28 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2828, 1604 , 1588, 1552, 1508, 1479, 1462, 1436, 1402, 1289, 1265 , 1223, 1198, 1175, 1149, 1106, 1078, 1057, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.51 (d, *J* = 8.9 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 2H), 6.70 (d, *J* = 2.3 Hz, 1H), 6.63 (dd, *J* = 8.5, 2.4 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 159.8 (C), 159.5 (C), 143.1 (C), 133.2 (CH), 132.8 (2CH), 115.6 (C), 113.9 (2CH), 113.8 (C), 110.5 (CH), 109.2 (CH), 94.4 (C), 85.5 (C), 55.3 (OCH_3), 55.2 (OCH_3), 15.0 (SCH_3); HRMS (ESI): for $C_{17}H_{17}O_2S$ $(M + H)^+$: *m*/*z* calcd 285.3807, found 285.3808.

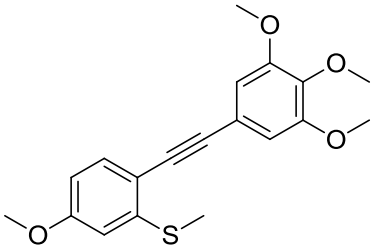
(5-methoxy-2-((4-(methoxymethoxy)phenyl)ethynyl)phenyl)(methyl)sulfane (9k)



was prepared from the alkyne **9g** (1 mmol). To a solution of **9g** in anhydrous THF (8 mL/mmol) was added at -78 °C *n*-BuLi (2.2 equiv., 1.6 M in THF). The mixture was stirred 1 hour at -78 °C and Me_2S_2 (1.2 mmol) was added. The mixture was stirred 12 hours from -78 °C to room temperature. The mixture was hydrolyzed by a solution saturated of NH_4Cl and extracted by EtOAc. The aqueous layer was washed three times by EtOAc. Organic layers was joined, washed with water and a saturated solution of NaCl and dried dry by anhydrous $MgSO_4$. The crude product was concentrated under reduce pressure and purified by silica gel chromatography. Compound **9k** was obtained as a brown oil (242 mg, 77% yield); TLC: Rf = 0.21 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2828, 1604 , 1588, 1552,

1508, 1479, 1462, 1436, 1402, 1289, 1265 , 1223, 1198, 1175, 1149, 1106, 1078, 1057, 1037 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.50 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 2.2 Hz, 1H), 6.62 (dd, *J* = 2.2, 8.5 Hz, 1H), 5.18 (s, 2H), 3.80 (s, 3H), 3.47 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 159.7 (C), 156.9 (C), 143.0 (C), 133.1 (CH), 132.6 (2CH), 118.6 (C), 116.0 (2CH), 113.6 (C), 110.4 (CH), 109.1 (CH), 94.6 (OCH_2O) and (C), 87.5 (C), 55.9 (OCH_3), 55.1 (OCH_3), 14.8 (SCH_3); HRMS (ESI): for $C_{18}H_{19}O_3S$ $(M + H)^+$: *m*/*z* calcd 315.1055, found 315.1060.

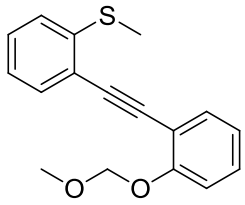
(5-methoxy-2-((3,4,5-trimethoxyphenyl)ethynyl)phenyl)(methyl)sulfane (9m)



was prepared from the 5-((2-bromo-4-methoxyphenyl)ethynyl)-1,2,3-trimethoxybenzene[2] (1 mmol) To a solution of 5-((2-bromo-4-methoxyphenyl)ethynyl)-1,2,3-trimethoxybenzene in anhydrous THF. (8 mL/mmol) was added at -78°C *n*-BuLi (2.2 equiv. 1.6 M in THF). The mixture was stirred 1 hour at -78 °C and Me_2S_2 (2 mmol) was added. The mixture was stirred 12 hours from -78 °C to room temperature. The mixture was hydrolyzed by a solution saturated of NH_4Cl and extracted by EtOAc. The aqueous layer was washed three times by EtOAc. Organic layers was joined, washed with water and a saturated solution of NaCl and dried dry by anhydrous $MgSO_4$. The crude product was concentrated under reduce pressure and purified by silica gel chromatography. Compound **9m** was obtained as a yellow oil (234 mg, 68% yield); TLC: R_f = 0.24 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2964, 2924, 2830, 2014, 1988, 1581, 1496, 1463, 1420, 1414, 1331 , 1283, 1246, 1177, 1157, 1119, 1050, 1002 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.41 (d, *J* = 8.5 Hz, 1H), 6.78 (s, 2H), 6.71 (d, *J* = 2.4 Hz, 1H), 6.65 (dd, *J* = 8.5, 2.4 Hz, 1H), 3.88 (s, 6H), 3.86 (s, 3H), 3.84 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm):

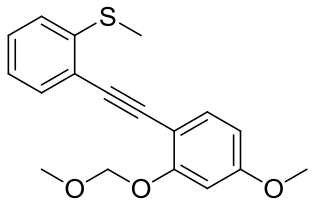
160.2 (C), 153.2 (2C), 143.5 (C), 138.8 (C), 133.6 (CH), 118.7 (C), 113.7 (C), 110.8 (CH), 109.5 (CH), 108.9 (2CH), 94.5 (C), 86.0 (C), 61.1 (OCH_3), 56.3 ($2OCH_3$), 55.5 (OCH_3), 15.2 (SCH_3); HRMS (ESI): for $C_{19}H_{21}O_4S$ $(M + H)^+$: *m*/*z* calcd 345.1161, found 345.1161.

(2-((2-(methoxymethoxy)phenyl)ethynyl)phenyl)(methyl)sulfane (9n)



was prepared according general procedure from the alkyne (2-ethynylphenyl)(methyl)sulfane and the 1-iodo-2-(methoxymethoxy)benzene. Compound **9n** was obtained as a brown oil (276 mg, 97% yield); TLC: R_f = 0.68 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 1583, 1470 , 1403, 1271, 1234, 1200, 1152, 1119, 1082, 1044, 1017 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 7.59 – 7.47 (m, 2H), 7.34 – 7.27 (m, 2H), 7.21 – 7.08 (m, 3H), 7.05 – 6.97 (dt, *J* = 8.3, 4.2 Hz, 1H), 5.31 (s, 2H), 3.55 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 177.9 (C), 167.7 (C), 157.8 (C), 141.7(CH), 133.7 (CH), 132.5 (CH), 129.9 (CH), 128.8 (2CH), 122.1 (CH), 115.6 (CH), 114.2 (C), 95.2 (OCH_2O), 92.3 (C), 91.0 (C), 56.5 (OCH_3), 15.4 (SCH_3); HRMS (ESI): for $C_{17}H_{16}O_2NaS$ $(M + Na)^+$: *m*/*z* calcd 307.0769, found 307.0770.

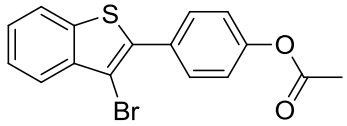
(2-((4-methoxy-2-(methoxymethoxy)phenyl)ethynyl)phenyl)(methyl)sulfane (9o)



was prepared according general procedure from the alkyne (2-ethynylphenyl)(methyl)sulfane and the 1-iodo-4-methoxy-2-(methoxymethoxy)benzene. Compound **9o** was obtained as an orange oil (283 mg, 90% yield); TLC: Rf = 0.53 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 2962, 2919, 2833, 2012, 1984, 1581, 1494,

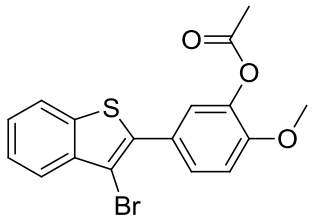
1461, 1430, 1331, 1292, 1187, 1075, 1004 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.62 (d, *J* = 8.7 Hz, 1H), 7.53 – 7.45 (m, 1H), 7.39 – 7.28 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.12 – 7.04 (m, 1H), 6.70 (d, *J* = 2.7 Hz, 1H), 6.39 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.22 (s, 2H), 3.78 (s, 3H), 3.51 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3 (C), 159.1 (C), 141.3 (C), 134.4 (CH), 132.3 (CH), 128.4 (CH), 124.5 (CH), 124.4 (CH), 122.4 (C), 107.5 (CH), 106.5 (C), 102.5 (CH), 95.4 (OCH_2O), 92.5 (C), 89.7 (C), 56.5 (OCH_3), 55.6 (OCH_3), 15.4 (SCH_3); HRMS (ESI): for $C_{18}H_{19}O_3S$ $(M + H)^+$: *m*/*z* calcd 315.1010, found 315.1013.

4-(3-bromobenzo[*b*]thiophen-2-yl)phenyl acetate (10b)



was prepared according to method A. Compound **10b** was obtained as a yellow solid (512 mg, 93% yield); m.p = 136-138 °C TLC: R_f = 0.57 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 2839, 1709 , 1611, 1537, 1530, 1449, 1436, 1367, 1299, 1273, 1247, 1123,1082,1014 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.87 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 169.3 (C), 151.0 (C), 139.1 (C), 137.7 (C), 130.2 (2CH), 130.8 (CH), 130.7 (CH), 125.6 (CH), 125.3 (CH), 123.7 (CH), 122.2 (CH), 121.8 (2CH), 105.2 (C), 21.2 (OCH_3); HRMS (ESI): for $C_{16}H_{11}BrNaO_2S$ $(M + Na)^+$: *m*/*z* calcd 368.9561, found 368.9564.

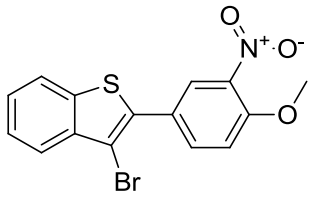
5-(3-bromobenzo[*b*]thiophen-2-yl)-2-methoxyphenyl acetate (10c)



was prepared according to method A. Compound **10c** was obtained as a yellow oil (595 mg, 99% yield); TLC: R_f = 0.41 (EtOAc/Cyclohexane, 3/7, SiO2); IR (neat) 2839, 2359 ,

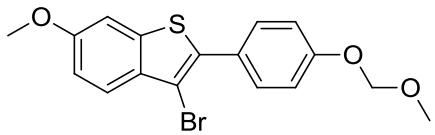
1765, 1711, 1613, 1537, 1500, 1497, 1461, 1435, 1368, 1300, 1267, 1248, 1199, 1162, 1125, 1072, 1029, 1016 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.86 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.63 (dd, *J* = 2.2, 8.5 Hz, 1H), 7.52 (d, *J* = 2.2 Hz, 1H), 7.47 (ddd, *J* = 1.2, 7.1, 8.0 Hz, 1H), 7.39 (ddd, *J* = 1.2, 7.1 , 8.0 Hz, 1H), 7.06 (d, *J* = 8.5 Hz, 1H), 3.90 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 168.8 (C), 151.6 (C), 139.6 (C), 139.2 (C), 137.5 (C), 137.1 (C), 128.3 (CH), 125.7 (C), 125.4 (CH), 125.2 (CH), 124.1 (CH), 123.6 (CH), 122.1 (CH), 112.3 (CH), 104.7 (C), 56.0 (OCH_3), 20.7 (CH_3); HRMS (ESI): for $C_{17}H_{13}BrNaO_3S$ $(M + Na)^+$: *m*/*z* calcd 398.9666, found 398, 9664.

3-bromo-2-(4-methoxy-3-nitrophenyl)benzo[*b*]thiophene (10d)



was prepared according to method A. Compound **10d** was obtained as a yellow solid (576 mg, 99% yield); m.p = 151-153 °C ; TLC: R_f = 0.38 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 2162, 2149 , 1619, 1536, 1434, 1352, 1284, 1020, 1020 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.27 (d, *J* = 2.3 Hz, 1H), 7.94 (dd, *J* = 2.3, 8.8 Hz, 1H), 7.87 (ddd, *J* = 0.6, 1.3, 8.0 Hz, 1H), 7.82 (ddd, *J* = 0.6, 1.3, 7.7 Hz, 1H), 7.50 (ddd, *J* = 1.3, 7.2, 8.0 Hz, 1H), 7.43 (ddd, *J* = 1.3, 7.2, 7.7 Hz, 1H), 7.20 (d, *J* = 8.8 Hz , 1H), 4.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 153.2 (2C), 139.6 (C), 139.0 (C), 137.6 (C), 135.2 (CH), 126.8 (CH), 126.1 (CH), 125.7 (CH), 123.9 (CH), 122.4 (CH), 113.8 (CH), 106.4 (2C), 56.9 (OCH_3); HRMS (ESI): for $C_{15}H_{11}BrNO_3S$ $(M + H)^+$: *m*/*z* calcd 363.9643, found 363.9664.

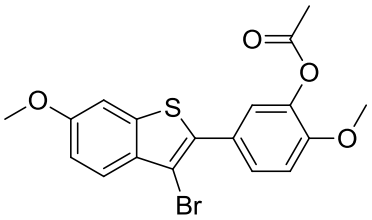
3-bromo-6-methoxy-2-(4-(methoxymethoxy)phenyl)benzo[*b*]thiophene (10g)



was prepared according to method A. Compound **10g** was obtained as a yellow oil (270

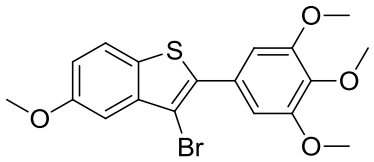
mg, 45% yield); TLC: R_f = 0.29 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2961, 2891 , 2829, 1604, 1561, 1494, 1475, 1436, 1404, 1329, 1263, 1231, 1200, 1177, 1151, 1128, 1112, 1080, 1060, 1031 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.72 (d, *J* = 8.9 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 2.1 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 7.08 (dd, *J* = 8.9, 2.1 Hz, 1H), 5.24 (s, 2H), 3.88 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ (ppm): 158.2 (C), 157.4 (C), 138.7 (C), 135.2 (C), 133.2 (C), 130.8 (2CH), 126.7 (C), 124.2 (CH), 116.2 (2CH), 115.1 (CH), 104.7 (CH), 103.8 (C), 94.3 (OCH_2O), 56.1 (OCH_3), 55.7 (OCH_3); HRMS (ESI): for $C_{17}H_{16}BrO_3S$ $(M + H)^+$: *m*/*z* calcd 379.0004, found 379, 0006.

5-(3-bromo-6-methoxybenzo[b]thiophen-2-yl)-2-methoxyphenyl acetate (10h)



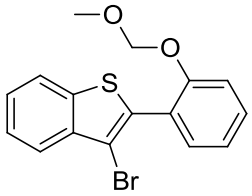
was prepared according to method A from the 2-methoxy-5-((4-methoxy-2-(methylthio)phenyl)ethynyl)phenyl acetate. Compound **10h** was obtained as a colorless oil (364 mg, 90% yield); TLC: R_f = 0.31 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 2837, 1764, 1601, 1538, 1496, 1475, 1368, 1297, 1162, 1028, 1015 cm-1; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.8 Hz, 1H), 7.64 – 7.51 (m, 1H), 7.48 (d, *J* = 2.1 Hz, 1H), 7.25 (d, *J* = 2.1 Hz, 1H), 7.06 (dd, *J* = 13.5, 5.3 Hz, 2H), 3.88 (s, 3H), 3.88 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0 (C), 158.3 (C), 151.4 (C), 139.6 (C), 138.8 (C), 134.3 (C), 133.2 (C), 128.2 (CH), 126.0 (C), 124.4 (CH), 123.9 (CH), 115.3 (CH), 112.4 (CH), 104.7 (CH), 104.2 (C), 56.1 (OCH_3), 55.8 (OCH_3), 20.8 (CH_3); HRMS (ESI): for $C_{18}H_{15}BrNaO_4S$ $(M + Na)^+$: *m*/*z* calcd 428.9772, found 428.9770.

3-bromo-5-methoxy-2-(3,4,5-trimethoxyphenyl)benzo[*b*]thiophene (10i)



was prepared according to method A from compound **9m**. Compound **10i** was obtained as a yellow solid (417 mg, 64% yield); m.p = 130-132 °C; TLC: R_f = 0.67 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat) : 3002, 2938 , 2838, 1606, 1581, 1466, 1452, 1335, 1291, 1237, 1174, 1125, 1029, 1004 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.74 (d, *J* = 8.9 Hz, 1H), 7.27 (d, *J* = 2.3 Hz, 1H), 7.09 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.97 (s, 2H), 3.93 (s, 6H), 3.92 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ (ppm): 158.5 (C), 153.4 (2C), 138.9 (C), 138.6 (C), 135.5 (C), 133.4 (C), 128.7 (C), 124.5 (CH), 115.4 (CH), 107.1 (2CH), 104.9 (CH), 104.3 (C), 61.1 (OCH_3), 56.4 ($2OCH_3$), 55.9 (OCH_3); HRMS (ESI): for $C_{18}H_{18}O_4SBr$ $(M + H)^+$: *m*/*z* calcd 409.0109, found 409.0107.

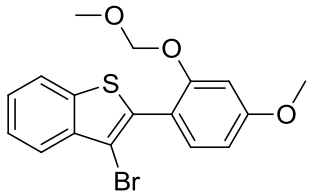
3-bromo-2-(2-(methoxymethoxy)phenyl)benzo[*b*]thiophene (10j)



was prepared according method B from the alkyne (2-((2-(methoxymethoxy)phenyl)ethynyl)phenyl)(methyl)sulfane. Compound **10j** was obtained as an orange oil (342 mg, 98% yield); TLC: Rf = 0.91 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) 3057, 2956, 1482, 1434, 1237, 1198, 1114, 1081, 1046cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.91 – 7.79 (m, 2H), 7.52 – 7.44 (m, 2H), 7.45 – 7.38 (m, 2H), 7.29 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.13 (td, *J* = 7.5, 1.2 Hz, 1H), 5.19 (s, 2H), 3.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3 (C), 138.7 (C), 138.4 (C), 135.5 (C), 132.5 (CH), 130.8 (CH), 125.4 (CH), 125.1 (CH), 123.6 (CH), 122.8 (C), 122.3 (CH), 121.8 (CH), 115.3 (CH), 107.8 (CH), 94.9 (OCH_2O), 56.4 (OCH_3); HRMS (ESI): for $C_{16}H_{13}BrNaO_2S$ $(M + Na)^+$: *m*/*z* calcd

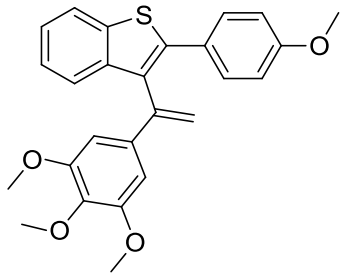
370.9717, found 370.9720.

3-bromo-2-(4-methoxy-2-(methoxymethoxy)phenyl)benzo[*b*]thiophene (10k)



was prepared according to method B from compound **9o**. Compound **10k** was obtained as a brown solid (571 mg, 95% yield); m.p = 83-85 °C; TLC: R_f = 0.47 (EtOAc/Cyclohexane, 5/95, SiO_2); IR (neat): 2958, 2836 , 1609, 1575, 1542, 1493, 1431, 1394, 1310, 1295, 1262, 1249, 1219, 1191, 1077, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): δ 7.89 – 7.77 (m, 2H), 7.47 (td, *J* = 8.0, 7.6, 1.2 Hz, 1H), 7.43 – 7.36 (m, 2H), 6.87 (d, *J* = 2.4 Hz, 1H), 6.67 (dd, *J* = 8.5, 2.4 Hz, 1H), 5.17 (s, 2H), 3.87 (s, 3H), 3.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 161.8 (C), 156.3 (C), 138.7 (C), 138.5 (C), 135.6 (C), 133.1 (CH), 125.2 (CH), 125.0 (CH), 123.5 (CH), 122.2 (CH), 115.2 (C), 107.6 (C), 106.9 (CH), 102.1 (CH), 95.0 (OCH_2O), 56.5 (OCH_3), 55.8 (OCH_3); HRMS (ESI): for $C_{17}H_{15}BrNaO_3S$ $(M + Na)^+$: *m/z* calcd 400.9823, found 400.9821.

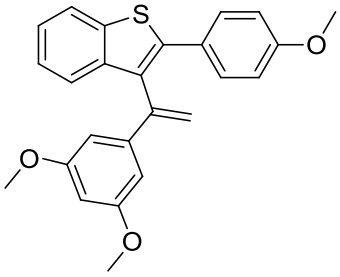
2-(4-methoxyphenyl)-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophene (5a)



was prepared according to the method C from the 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 3-bromo-2-(4-methoxyphenyl)benzo[*b*]thiophene. **5a** was obtained as a yellow oil (416 mg, 96% yield); TLC: R_f = 0.32 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2925, 1607 , 1579, 1500, 1455, 1434, 1412, 1356, 1317, 1292, 1246, 1176, 1124, 1033, 1005 cm^{-1}; ^1H NMR (300 MHz,

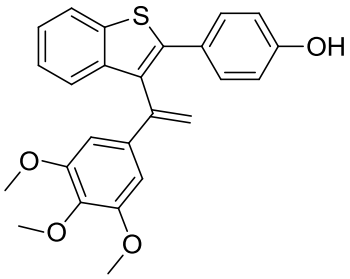
$CDCl_3$) δ (ppm): 7.87 – 7.80 (m, 1H), 7.61 – 7.48 (m, 3H), 7.35 – 7.28 (m, 2H), 6.92 – 6.82 (m, 2H), 6.65 (s, *J* = 1.5 Hz, 2H), 5.98 (s, 1H), 5.34 (s, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.74 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5 (C), 153.1(2C), 142.8(C), 141.1(C), 140.4(2C), 138.3 (C), 135.4 (C), 131.7 (C), 130.2 (2CH), 126.8 (C), 124.4 (CH), 124.3 (CH), 123.4 (CH), 121.9 (CH), 117.5 (CH_2), 113.9 (2CH), 104.0 (2CH), 60.9 (OCH_3), 56.1 ($2OCH_3$), 55.2 (OCH_3); HRMS (ESI): for $C_{26}H_{24}NaO_4S$ $(M + Na)^+$: *m*/*z* calcd 455.1293, found 455.1291.

3-(1-(3,5-dimethoxyphenyl)vinyl)-2-(4-methoxyphenyl)benzo[*b*]thiophene (5b)



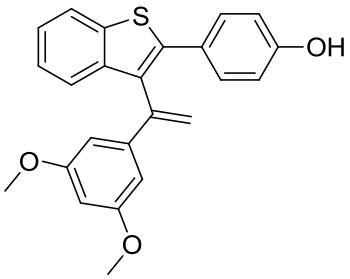
was prepared according to the method C from N'-(1-(3,5-dimethoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide and the 3-bromo-2-(4-methoxyphenyl)benzo[*b*]thiophene. **5b** was obtained as a colorless oil (370 mg, 92% yield); TLC: R_f = 0.19 (EtOAc/Cyclohexane, 5/95, SiO_2); IR (neat): 2837, 1656 , 1589, 1534, 1502, 1454, 1433, 1422, 1355, 1292, 1250, 1204, 1178, 1154, 1112, 1065, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.84 (dd, *J* = 1.3, 6.6 Hz, 1H), 7.58 (d, *J* = 8.9 Hz, 2H), 7.40-7.52 (m, 1H), 7.21-7.37 (m, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 6.62 (d, *J* = 2.2 Hz, 2H), 6.42 (t, *J* = 2.2 Hz, 1H), 6.02 (d, *J* = 1.0 Hz, 1H), 5.34 (d, *J* = 1.0 Hz, 1H), 3.81 (s, 3H), 3.74 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9 (2C), 159.5 (C), 142.9 (C), 142.0 (C), 141.2 (C), 141.0 (C), 138.4 (C), 131.8 (C), 130.3 (C), 126.9 (2CH), 124.4 (C), 124.3 (CH), 123.5 (CH), 121.9 (CH), 118.5 (CH), 114.0 (2CH), 105.1 (2CH), 99.8 (CH), 55.4 ($2OCH_3$), 55.3 (OCH_3); HRMS (ESI): for $C_{25}H_{23}O_3S$ $(M + H)^+$: *m*/*z* calcd 403.1368, found 403.1367.

4-(3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl)phenol (5c)



was prepared according to the method D from 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 4-(3-bromobenzo[*b*]thiophen-2-yl)phenyl acetate. **5c** was obtained as a yellowish oil (314 mg, 75% yield); TLC: R_f = 0.25 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat) : 1610, 1581, 1538, 1503, 1453, 1432, 1357, 1316, 1267, 1204, 1174, 1126, 1001 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.83 (dd, *J* = 1.5, 6.1 Hz, 1H), 7.50 (d, *J* = 7.0 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.27-7.36 (m, 2H), 6.77 (d, *J* = 8.3 Hz, 2H),; 6.62 (s, 2H), 6.06 (s, 1H), 5.95 (s, 1H), 5.32 (s, 1H), 3.84 (s, 3H), 3.71 (s, 6H);^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9 (2C), 153.2 (C), 142.8 (C), 141.2 (C), 140.5 (C), 138.5 (C), 138.1 (C), 135.7 (C), 131.8 (C), 130.5 (2CH), 126.9 (C), 124.5 (CH), 124.4 (CH), 123.5 (CH), 122.0 (CH), 117.6 (CH_2), 115.6 (2CH), 104.2 (2CH), 61.0 (OCH_3), 56.3 ($2OCH_3$); HRMS (ESI): for $C_{25}H_{22}O_4NaS$ $(M + Na)^+$: *m*/*z* calcd 441.1136, found 441.1134.

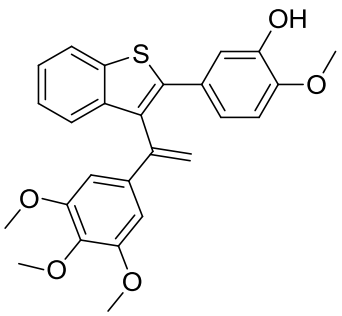
4-(3-(1-(3,5-dimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl)phenol (5d)



was prepared according to the method D from N'-(1-(3,5-dimethoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide and the 4-(3-bromobenzo[b]thiophen-2-yl)phenyl acetate. **5d** was obtained as an orange oil (320 mg, 83% yield); TLC: R_f = 0.21

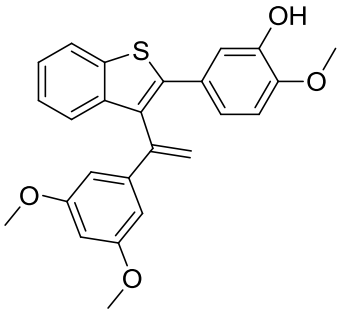
(EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 2839, 1617, 1590, 1514, 1422, 1324, 1253, 1200, 1191, 1011 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.83 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.47-7.51 (m, 1H), 7.19-7.36 (m, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 1.9 Hz, 2H), 6.41 (t, *J* = 1.9 Hz, 1H), 6.00 (s, 1H), 5.54 (s, 1H), 5.33 (s, 1H), 3.73 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9 (2C), 155.6 (C), 142.8 (C), 142.1 (C), 141.2 (C), 140.4 (C), 138.4 (C), 131.9 (C), 130.5 (2CH), 127.0 (C), 124.5 (CH), 124.3 (CH), 123.6 (CH), 122.0 (CH), 118.6 (CH_2), 115.5 (2CH), 105.2 (2CH), 99.9 (CH), 55.5 ($2OCH_3$); HRMS (ESI): for $C_{24}H_{21}O_3S$ $(M + H)^+$: *m*/*z* calcd 389.1211, found 389.1209.

2-methoxy-5-(3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl)phenol (5e)



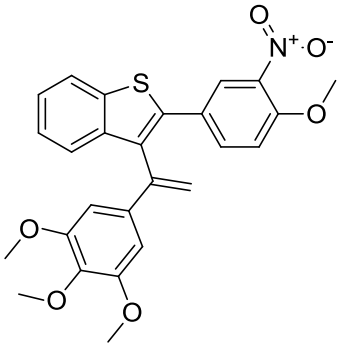
was prepared according to the method D from 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 5-(3-bromobenzo[*b*]thiophen-2-yl)-2-methoxyphenyl acetate. **5e** was obtained as a yellow oil (313 mg, 70% yield); TLC: R_f = 0.25 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 1610, 1581, 1538, 1503, 1453, 1432, 1412, 1357, 1316, 1236, 1174, 1126 , 1001 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.89 – 7.77 (m, 1H), 7.56 – 7.49 (m, 1H), 7.34 – 7.17 (m, 3H), 7.12 – 7.06 (m, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.62 (s, 2H), 6.06 (s, 1H), 5.95 (s, 1H), 5.32 (s, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.71 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1 (2C), 146.6 (C), 145.4 (C), 142.9 (C), 141.2 (C), 140.3 (C), 138.5 (C), 138.1 (C), 135.6 (C), 132.0 (C), 127.8 (2CH), 124.4 (CH), 123.6 (CH), 122.0 (CH), 121.1 (CH_2), 117.6 (CH), 115.4 (CH), 110.5 (CH), 104.1 (2CH), 61.0 (OCH_3), 56.2 ($2OCH_3$), 56.0 (OCH_3); HRMS (ESI): for $C_{26}H_{25}O_5S$ $(M + H)^+$: *m*/*z* calcd 449.1423, found 449.1420.

5-(3-(1-(3,5-dimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl)-2-methoxyphenol (5f)



was prepared according to the method D from N'-(1-(3,5-dimethoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide and the 5-(3-bromobenzo[*b*]thiophen-2-yl)-2-methoxyphenyl acetate. **5f** was obtained as a yellowish oil (306 mg, 72% yield); TLC: R_f = 0.30 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 1589, 1504, 1454, 1424, 1357, 1283, 1263, 1241, 1203, 1154, 1064, 1017 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.87 – 7.76 (m, 1H), 7.54–7.39 (m, 1H), 7.33–7.18 (m, 3H), 7.12 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 2.0 Hz, 2H), 6.38 (s, 1H), 6.00 (s, 1H), 5.62 (s, 1H), 5.34 (s, 1H), 3.86 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9 (2C), 146.6 (C), 145.4 (C), 142.9 (C), 142.1 (C), 141.2 (C), 140.3 (C), 138.5 (C), 132.1 (C), 127.8 (C), 124.4 (CH), 124.3 (CH), 123.6 (CH), 121.9 (CH), 121.2 (CH), 118.5(CH_2), 115.4 (CH), 110.6 (CH), 105.1 (2CH), 99.9 (CH), 56.0 (OCH_3), 55.4 (2OCH_3); HRMS (ESI): for $C_{25}H_{23}O_4S$ $(M + H)^+$: *m*/*z* calcd 419.5127, found 419.5128.

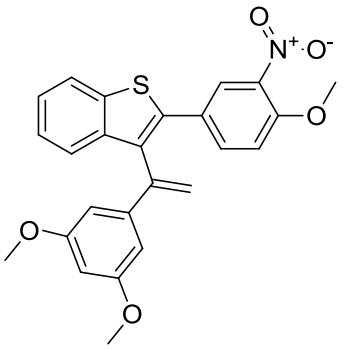
2-(4-methoxy-3-nitrophenyl)-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophene (5g)



was prepared according to the method C from 4-methyl-N'-(1-(3,4,5-

trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 3-bromo-2-(4-methoxy-3-nitrophenyl)benzo[*b*]thiophene. **5g** was obtained as a colorless oil (464 mg, 97% yield); TLC: Rf = 0.29 (EtOAc/Cyclohexane, 3/7, SiO2); IR (neat): 2937, 1579, 1539, 1504, 1457, 1412, 1353, 1278, 1239, 1125, 1006, 1204, 1178, 1154, 1112, 1065, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.10 (d, 1H, *J* = 1.8 Hz), 7.84 (dd, *J* = 1.8, 7.3 Hz, 1H), 7.69 (dd, *J* = 2.2, 8.8 Hz, 1H), 7.64 (m, 1H), 7.32-7.37 (m, 2H), 6.98 (dd, *J* = 1.4, 8.8 Hz, 1H), 6.55 (s, 2H), 6.00 (s, 1H), 5.37 (s, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.71 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2 (2C), 152.4 (C), 142.3 (C), 140.8 (C), 139.2 (C), 138.5 (C), 138.3 (C), 136.2 (C), 135.2 (CH), 134.2 (C), 133.6 (C), 126.9 (CH), 125.9 (CH), 125.1 (CH), 124.8 (CH), 124.0 (CH), 123.7 (CH), 122.1 (CH_2), 113.5 (CH), 104.1 (2CH), 60.8 (OCH_3), 56.6 (OCH_3), 56.1 ($2OCH_3$); HRMS (ESI): for $C_{26}H_{24}NO_6S$ $(M + H)^+$: *m*/*z* calcd 478.1324, found 478.1323.

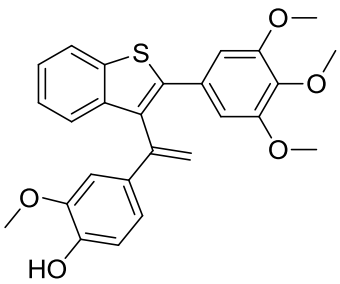
3-(1-(3,5-dimethoxyphenyl)vinyl)-2-(4-methoxy-3-nitrophenyl)benzo[*b*]thiophene (5h)



was prepared according to the method C from N'-(1-(3,5-dimethoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide and the 3-bromo-2-(4-methoxy-3-nitrophenyl)benzo[*b*]thiophene. **5h** was obtained as a yellow oil (350 mg, 78% yield); TLC: R_f = 0.29 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2838, 1688, 1509, 1418, 1333, 1262, 1153, 1009 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.12 (d, *J* = 1.6 Hz, 1H) 7.84 (d, *J* = 7.5 Hz, 1H), 7.72 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.57 (dd, *J* = 1.1, 7.5 Hz, 1H), 7.33 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.51 (d, *J* = 1.5 Hz, 2H), 6.37 (t, *J* = 1.5 Hz, 1H), 6.05 (s, 1H),

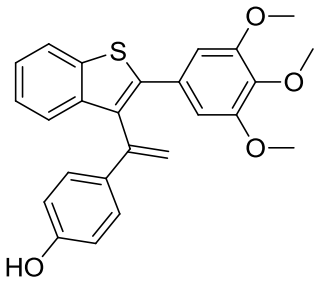
5.37 (s, 1H), 3.92 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (75 MHz, CDCl3) δ 161.0 (2C), 152.5 (C), 142.5 (C), 141.6 (C), 141.0 (C), 139.4 (C), 138.5(C), 137.0 (CH), 134.4 (C), 133.8 (C), 127.0 (CH), 126.0 (CH), 125.1 (CH), 124.9 (CH), 123.8 (CH), 122.1 (CH_2), 119.0 (CH), 113.6 (CH), 105.1 (2CH), 100.0 (CH), 56.7 (OCH_3), 55.4 ($2OCH_3$); HRMS (ESI): for $C_{25}H_{22}NO_5S$ $(M + H)^+$: *m*/*z* calcd 448,1219, found 448.1217.

2-methoxy-4-(1-(2-(3,4,5-trimethoxyphenyl)benzo[b]thiophen-3-yl)vinyl)phenol (5i)



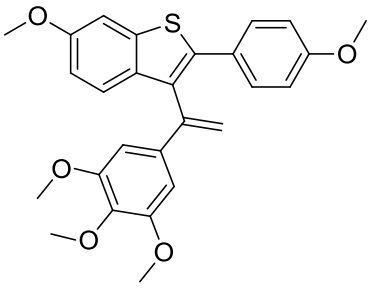
was prepared according to the method D. Compound **5i** was obtained as a yellow solid (389 mg, 86% yield); m.p = 63-64 °C; TLC: Rf = 0.54 (EtOAc/Cyclohexane, 3/7, SiO_2); IR (neat): 3355, 2939, 1581, 1512, 1500, 1464, 1431, 1412, 1355, 1279, 1240, 1127, 1077, 1026, 1002 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.83 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.51 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.31 (ddd, *J* = 8.7, 6.8, 1.6 Hz, 1H), 7.07 (d, *J* = 2.2 Hz, 1H), 6.90 (s, 1H), 6.85 (s, 2H), 6.81 (d, *J* = 2.2 Hz, 1H), 6.70 (d, *J* = 8.7 Hz, 1H), 5.97 (d, *J* = 1.1 Hz, 1H), 5.56 (s, 1H), 5.25 (d, *J* = 1.1 Hz, 1H), 3.84 (s, 3H), 3.84 (s, 3H), 3.73 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.0 (2C), 146.7 (C), 145.7 (C), 142.4 (C), 141.5 (C), 139.9 (C), 138.4 (C), 138.0 (C), 133.2 (C), 132.9 (C), 129.8 (C), 124.6(2CH), 123.6 (CH), 122.0 (CH), 118.7 (CH), 116.1 (CH_2), 112.4 (CH), 110.5 (CH), 106.4 (2CH), 61.0 (OCH_3), 56.1 (OCH_3), 56.1 ($2OCH_3$); HRMS (ESI): for $C_{26}H_{24}O_5NaS$ $(M + Na)^+$: *m*/*z* calcd 471.1242, found 471.1241.

4-(1-(2-(3,4,5-trimethoxyphenyl)benzo[*b*]thiophen-3-yl)vinyl)phenol (5j)



was prepared according to the method D. **5j** was obtained as a yellow solid (385 mg, 92% yield); m.p = 74-75 °C; TLC: R_f = 0.13 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 3356, 1652, 1652, 1607, 1581, 1512, 1497, 1452, 1431, 1410, 1275, 1236, 1218, 1167, 1076, 1022 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.54 (s, 1H), 8.00 (d, *J* = 5.5 Hz, 1H), 7.37 (m, 3H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.85 (s, 2H), 6.68 (d, *J* = 8.7 Hz, 2H), 6.02 (s, 1H), 5.14 (s, 1H), 3.65 (s, 3H), 3.64 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 157.5 (C), 152.6 (2C), 141.8 (2C), 140.8 (C), 138.6 (C), 137.5 (C), 132.8 (C), 129.6 (C), 128.9 (C), 127.2 (2CH), 124.8 (2CH), 122.9 (CH), 122.2 (CH), 115.4 (2CH), 114.6 (CH_2), 105.9 (2CH), 60.0 (OCH_3), 55.6 ($2OCH_3$); HRMS (ESI): for $C_{25}H_{22}O_4NaS$ $(M + Na)^+$: *m*/*z* calcd 441.1136, found 441.1134.

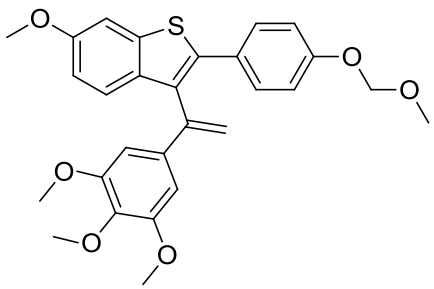
6-methoxy-2-(4-methoxyphenyl)-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophene (5k)



was prepared according to the method C from 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 3-bromo-6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene. **5k** was obtained as a yellow oil (346 mg, 75% yield); TLC: R_f = 0.21 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 2933, 2836, 1612, 1579, 1502, 1412, 1322, 1239, 1176, 1065, 1032, 1003 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.51

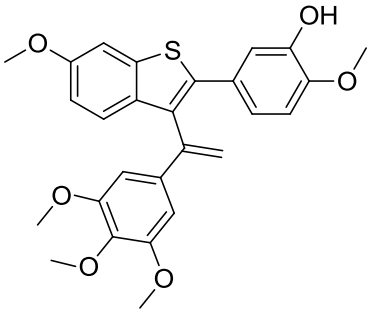
(d, *J* = 8.9 Hz, 2H), 7.36 (d, *J* = 8.9 Hz, 1H), 7.31 (d, *J* = 2.2 Hz, 1H), 6.91 (dd, *J* = 2.2, 8.8 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.62 (s, 2H), 5.93 (s, 1H), 5.30 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.79 (s, 3H), 3.73 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3 (C), 157.5 (C), 153.2 (2C), 143.0 (C), 139.7 (C), 138.1 (C), 137.8 (C), 135.5 (C), 135.3 (C), 131.3 (C), 130.0 (2CH), 127.0 (C), 124.2 (CH), 117.4 (CH_2), 114.3 (CH), 113.9 (2CH), 104.6 (CH), 104.0 (2CH), 61.0 (OCH_3), 56.2 ($2OCH_3$), 55.7 (OCH_3), 55.3 (OCH_3); HRMS (ESI): for $C_{27}H_{26}NaO_5S$ $(M + Na)^+$: *m*/*z* calcd 485.1399, found 485.1387.

6-methoxy-2-(4-(methoxymethoxy)phenyl)-3-(1-(3,4,5-trimethoxyphenyl)vinyl) benzo[*b*]thiophene (5l)



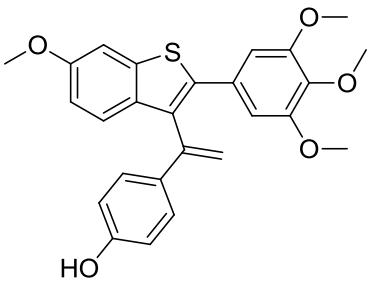
was prepared according to the method C from 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 3-bromo-6-methoxy-2-(4-(methoxymethoxy)phenyl)benzo[*b*]thiophene. **5l** was obtained as a yellow oil (391 mg, 80% yield); TLC: R_f = 0.30 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 3004, 1605, 1579, 1502, 1472, 1436, 1357, 1236, 1152, 1080, 1064, 1035 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.50 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.31 (d, *J* = 2.2 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.90 (dd, *J* = 2.2, 8.8 Hz, 1H), 6.61 (s, 2H), 5.92 (s, 1H), 5.29 (s, 1H), 5.16 (s, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.73 (s, 6H), 3.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5 (C), 156.9 (C), 153.2 (2C), 142.9(C), 139.8 (C), 138.2 (C), 137.6 (C), 135.5 (C), 135.2 (C), 131.6 (C), 130.1 (2CH), 128.2 (C), 124.3 (CH), 117.5 (CH_2), 116.2 (2CH), 114.3 (CH), 104.6 (CH), 104.0 (2CH), 94.4 (OCH_2O), 61.0 ($3OCH_3$), 56.2 (OCH_3), 55.7(OCH_3); HRMS (ESI): for $C_{28}H_{29}O_6S$ $(M + H)^+$: *m*/*z* calcd 493.1685, found 493.1680.

2-methoxy-5-(6-methoxy-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl) phenol (5m)



was prepared according to the method D from 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 5-(3-bromo-6-methoxybenzo[*b*]thiophen-2-yl)-2-methoxyphenyl acetate. **5m** was obtained as a yellowish oil (335 mg, 70% yield); TLC: R_f = 0.11 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 2959, 2936, 1601, 1581, 1538, 1505, 1463, 1412, 1283, 1227, 1264, 1126 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.38 (d, *J* = 8.8 Hz, 1H), 7.30 (d, *J* = 2.0 Hz, 1H), 7.17 (d, *J* = 1.5 Hz, 1H), 7.06 (dd, *J* = 1.5, 8.4 Hz, 1H), 6.90 (dd, *J* = 2.0, 8.8 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.59 (s, 2H), 5.92 (s, 1H), 5.61 (s, 1H), 5.31 (s, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4 (C), 153.0 (2C), 146.3 (C), 145.2 (C), 142.8 (C), 139.7 (C), 137.9 (C), 137.5 (C), 135.5 (C), 135.1 (C), 131.5 (C), 127.8 (C), 124.1 (CH), 120.8 (CH), 117.3 (CH_2), 115.1 (CH), 114.2 (CH), 110.4 (CH), 104.5 (CH), 104.0 (2CH), 60.8 (OCH_3), 56.1 ($2OCH_3$), 55.9 (OCH_3), 55.6 (OCH_3) ; HRMS (ESI): for $C_{27}H_{27}O_6S$ $(M + H)^+$: *m*/*z* calcd 479.1528, found 479.1523.

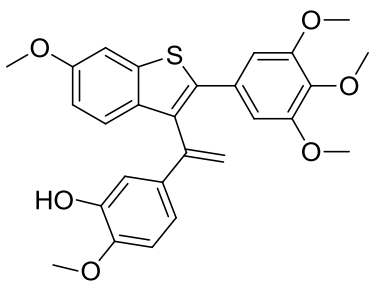
4-(1-(6-methoxy-2-(3,4,5-trimethoxyphenyl)benzo[b]thiophen-3-yl)vinyl)phenol (5n)



was prepared according to the method D. **5n** was obtained as a white solid (296 mg, 66%

yield); m.p = 68-70 °C; TLC: R_f = 0.12 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 3002, 2937, 2035, 1600, 1582, 1535, 1499, 1472, 1434, 1412, 1227, 1174, 1053 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.39 (d, *J* = 8.9 Hz, 1H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 2H), 6.91 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.79 (s, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 5.93 (d, *J* = 1.1 Hz, 1H), 5.21 (d, *J* = 1.1 Hz, 1H) ,3.88 (s, 3H), 3.82 (s, 3H), 3.70 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8 (C), 155.8 (C), 153.0 (2C), 142.5 (C), 139.8 (C), 137.7 (C), 137.1 (C), 135.6 (C), 132.7 (C), 132.2 (C), 130.0 (C), 127.8 (2CH), 124.4 (CH), 115.6 (2CH), 115.3 (CH_2), 114.5 (CH), 106.2 (2CH), 104.7 (CH), 61.0 (OCH_3), 56.1 ($2OCH_3$), 55.8 (OCH_3); HRMS (ESI): for $C_{26}H_{24}O_5NaS$ $(M + Na)^+$: *m*/*z* calcd 471.1242, found 471.1244.

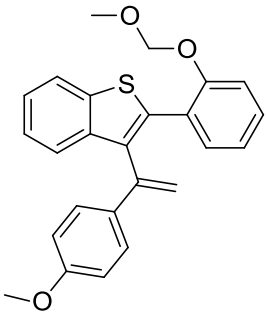
2-methoxy-5-(1-(6-methoxy-2-(3,4,5-trimethoxyphenyl)benzo[*b*]thiophen-3-yl)vinyl)phenol (5o)



was prepared according to the method D. Compound **5o** was obtained as a white solid (311 mg, 65% yield); m.p = 66-67 °C; TLC: R_f = 0.15 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 3001, 2936, 2035, 1599, 1581, 1535, 1502, 1472, 1435, 1412, 1364, 1277, 1229, 1071, 1053, 1025, 1001 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.38 (d, *J* = 8.8 Hz, 1H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.85 – 6.80 (m, 1H), 6.82 (s, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.95 (s, 1H), 5.57 (s, 1H), 5.24 (s, 1H), 3.88 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.73 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7 (C), 153.0 (2C), 146.7 (C), 145.7 (C), 142.6 (C), 139.7 (C), 137.8 (C), 137.1 (C), 135.7 (C), 133.1 (C), 132.5 (C), 130.0 (C), 124.3 (CH), 118.7 (CH), 115.9 (CH_2), 114.4 (CH), 112.4 (CH), 110.5 (CH), 106.1 (2CH), 104.7 (CH), 61.0 (OCH_3), 56.1 ($3OCH_3$), 55.8

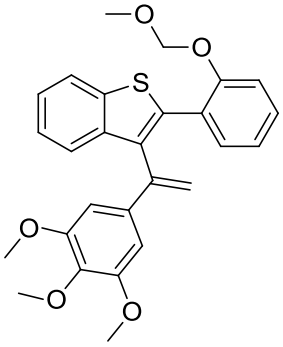
(OCH_3); HRMS (ESI): for $C_{27}H_{26}NaO_6S$ $(M + Na)^+$: *m*/*z* calcd 501.1348, found 501.1341.

2-(2-(methoxymethoxy)phenyl)-3-(1-(4-methoxyphenyl)vinyl)benzo[*b*]thiophene (5p)



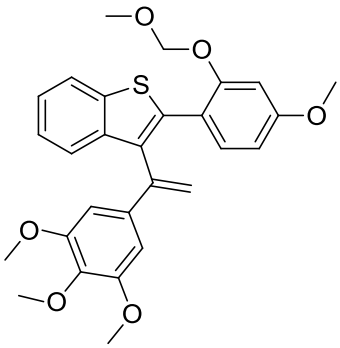
was prepared according to the method A from N'-(1-(4-methoxyphenyl)ethylidene)-4-methylbenzenesulfonohydrazide and the 3-bromo-2-(2-(methoxymethoxy)phenyl)benzo[*b*]thiophene (**10j**). **5p** was obtained as a yellow oil (268 mg, 66% yield); TLC: R_f = 0.73 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 3001, 2858, 2902, 2835, 1590, 1577, 1441, 1423, 1391, 1305, 1254, 1217, 1192, 1152, 1133, 1052, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.85 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.38 – 7.23 (m, 6H), 7.23 – 7.14 (m, 1H), 6.99 (td, *J* = 7.4, 1.1 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.65 (s, 1H), 5.09 (s, 1H), 5.00 (s, 2H), 3.80 (s, 3H), 3.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4 (C), 155.1 (C), 142.3 (C), 139.8 (C), 139.5 (C), 137.3 (C), 135.1 (C), 132.8 (2C), 132.4 (CH), 129.7 (CH), 128.2 (2CH), 124.2 (CH), 124.1 (2CH), 121.9 (CH), 121.5 (CH), 115.3 (CH_2), 114.7 (CH), 113.7 (2CH), 94.5 (OCH_2O), 56.0 (OCH_3), 55.4 (OCH_3); HRMS (ESI): for $C_{25}H_{23}O_3S$ $(M + H)^+$: *m*/*z* calcd 403.1368, found 403.1364.

2-(2-(methoxymethoxy)phenyl)-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophene (5q)



was prepared according to the method C from 4-methyl-N'-(1-(3,4,5-trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 3-bromo-2-(2-(methoxymethoxy)phenyl)benzo[*b*]thiophene. **5q** was obtained as yellow oil (346 mg, 75% yield); TLC: R_f = 0.42 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 2999, 2935, 2662, 1580, 1504, 1453, 1413, 1357, 1316, 1238, 1197, 1153, 1127, 1079 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.85 (d, *J* = 7.9 Hz, 1H), 7.52 – 7.21 (m, 5H), 7.21 – 7.07 (m, 1H), 7.05 – 6.88 (m, 1H), 6.59 (s, 2H), 5.70 (s, 1H), 5.21 (s, 1H), 5.02 (s, 2H), 3.83 (s, 3H), 3.72 (s, 6H), 3.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0 (C), 152.9 (2C), 143.0 (2C), 139.7 (C), 139.5 (C), 138.0 (C), 137.6 (C), 136.2 (C), 134.7 (C), 132.4 (CH), 129.8 (CH), 124.3 (CH), 124.1 (CH), 123.9 (CH), 122.0 (CH), 121.6 (CH), 116.9 (CH_2), 114.8 (CH), 104.6 (2CH), 94.7 (OCH_2O), 61.0 (OCH_3), 56.3 ($2OCH_3$), 56.1 (OCH_3); HRMS (ESI): for $C_{27}H_{26}O_5NaS$ $(M + Na)^+$: *m*/*z* calcd 485.1399, found 485.1401.

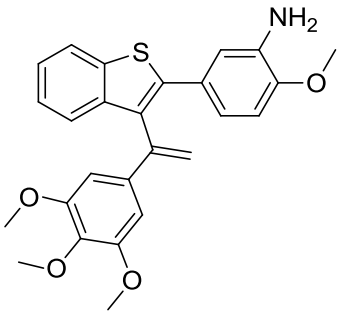
2-(4-methoxy-2-(methoxymethoxy)phenyl)-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophene (5r)



was prepared according to the method C from 4-methyl-N'-(1-(3,4,5-

trimethoxyphenyl)ethylidene)benzenesulfonohydrazide and the 3-bromo-2-(4-methoxy-2-(methoxymethoxy)phenyl)benzo[*b*]thiophene. **5r** was obtained as a yellow oil (411 mg, 83% yield); TLC: R_f = 0.44 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2836, 2154, 2018, 1990, 1611, 1579, 1460, 1413, 1358, 1240, 1221, 1154, 1044, 1005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.82 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.41 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.35 – 7.18 (m, 4H), 6.71 (d, *J* = 2.4 Hz, 1H), 6.58 (s, 2H), 6.51 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.70 (d, *J* = 1.4 Hz, 1H), 5.19 (d, *J* = 1.3 Hz, 1H), 5.00 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.72 (s, 6H), 3.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1 (C), 156.0 (C), 153.0 (2C), 143.1 (C), 139.9 (C), 139.4 (C), 138.1 (C), 137.7 (C), 136.2 (C), 134.3 (C), 132.8 (CH), 124.1 (CH), 124.1 (CH), 123.8 (CH), 121.9 (CH_2), 116.7 (C), 116.5 (CH), 106.6 (2CH), 104.7 (CH), 101.7 (CH), 94.8 (OCH_2O), 61.0 (OCH_3), 56.3 ($2OCH_3$), 56.1 (OCH_3), 55.5 (OCH_3); HRMS (ESI): for $C_{28}H_{28}NaO_6S$ $(M + Na)^+$: *m*/*z* calcd 515.1502, found 515.1498.

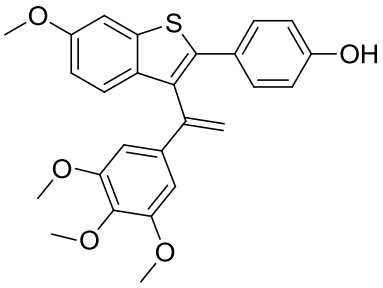
2-methoxy-5-(3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl)aniline (5s)



was prepared from the product **5g**. To a solution of **5g** (0.99 mmol) in 11 mL of EtOH and 4 mL of H_2O were added at room temperature Iron (9.9 mmol) and a drop of concentrated HCl. The mixture was stirred overnight at reflux. After cooling to rt, the mixture was treated by EtOAc, filtrated on celite and concentrated under reduce pressure. The crude product was purified by silica gel chromatography. **5t** was obtained as a colorless oil (420 mg, 90% yield); TLC: R_f = 0.26 (EtOAc/Cyclohexane, 3/7, SiO_2); IR (neat): 2939, 1613, 1581, 1463, 1413, 1369, 1235, 1203, 1026, 1031, 1003 cm^{-1}; ^1H NMR (300 MHz, $(CD_3)_2CO$) δ 7.93 – 7.84 (m, 1H), 7.52 – 7.44 (m, 1H), 7.38 – 7.24 (m, 2H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.91 (dd,

J = 8.3, 2.2 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.69 (s, 2H), 6.04 (d, *J* = 1.3 Hz, 1H), 5.29 (d, *J* = 1.3 Hz, 1H), 4.48 (s, 2H), 3.80 (s, 3H), 3.69 (s, 3H), 3.68 (s, 6H); ^{13}C NMR (75 MHz, $(CD_3)_2CO$) δ 154.2 (2C), 148.0 (C), 144.0 (C), 142.1 (C), 142.0 (C), 139.5 (C), 139.1 (C), 138.5 (C), 136.3 (C), 132.4 (C), 127.8 (C), 125.2 (CH), 125.1 (CH), 123.9 (CH), 122.8 (CH), 118.7 (CH) , 117.8 (CH_2), 115.4 (CH), 111.0 (CH), 105.3 (2CH), 60.5 (CH_3), 56.4 ($2CH_3$), 55.8 (CH3); HRMS (ESI): for $C_{26}H_{26}NO_4S$ (M + H)+: *m*/*z* calcd 448.1583, found 448.1580.

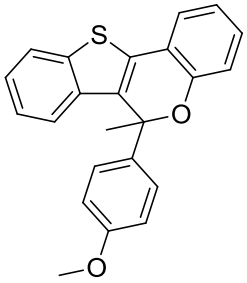
4-(6-methoxy-3-(1-(3,4,5-trimethoxyphenyl)vinyl)benzo[*b*]thiophen-2-yl)phenol (5t)



was prepared from the product **5l**. A solution of **5l** (0.7 mmol) and PTSA (2.1 mmol) in 18 mL of EtOH was stirred overnight at 60°C. After cooling to rt, the mixture was treated by water and extract by EtOAc. The layers are separated. Organic layer was washed with a saturated solution of NaCl, dried with anhydrous $MgSO_4$ and concentrated under reduce pressure. The crude product was purified by silica gel chromatography. **5t** was obtained as a yellow oil (305 mg, 97% yield); TLC: R_f = 0.18 (EtOAc/Cyclohexane, 3/7, SiO_2); IR (neat): 2833, 1610, 1582, 1538, 1503, 1473, 1435, 1413, 1357, 1315, 1238, 1173, 1065, 1035 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.43 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 8.9 Hz, 1H), 7.31 (d, *J* = 2.2 Hz, 1H), 6.90 (dd, *J* = 2.2, 8.9 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.60 (s, 2H), 5.91 (s, 1H), 5.43 (s, 1H), 5.30 (s, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5 (C), 155.6 (C), 153.1 (2C), 142.9 (C), 139.7 (C), 138.0 (C), 137.8 (C), 135.6 (C), 135.3 (C), 131.3 (C), 130.3 (2CH), 127.1 (C), 124.2 (CH), 117.5 (CH_2), 115.5 (2CH), 114.3(CH), 104.7 (CH), 104.0 (2CH), 61.0 (OCH_3), 56.2 ($2OCH_3$),

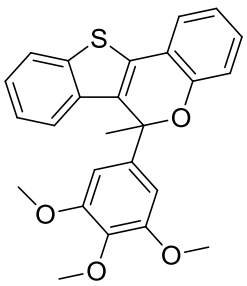
55.8 (OCH_3); HRMS (ESI): for $C_{26}H_{24}NaO_5S$ $(M + Na)^+$: *m*/*z* calcd 471.1242, found 471.1244.

6-(4-methoxyphenyl)-6-methyl-6H-benzo[4,5]thieno[3,2-*c*]chromene (13a)



was prepared according to the general method E from the compound **5p**. **13a** was obtained as a yellow oil (340 mg, 95% yield); TLC: R_f = 0.57 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat):3300, 2951, 1451, 1403, 1115, 1012, 1077, 1003 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.85 – 7.79 (m, 1H), 7.51 (d, *J* = 8.9 Hz, 2H), 7.40 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.29 – 7.11 (m, 3H), 7.08 – 7.02 (m, 1H), 7.01 – 6.92 (m, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6 (C), 151.6 (C), 139.5 (C), 137.5 (C), 136.0 (C), 133.3 (C), 131.8 (C), 130.0 (CH), 128.5 (2CH), 124.6 (CH),124.2 (CH), 123.8 (CH), 123.0 (CH), 122.9 (CH), 121.6 (CH), 119.3 (C), 117.1 (CH), 113.8 (2CH), 82.4 (C), 55.4 (OCH_3), 26.0 (CH_3); HRMS (ESI): for $C_{23}H_{19}O_2S$ $(M + H)^+$: *m*/*z* calcd 359.1106, found 359.1105.

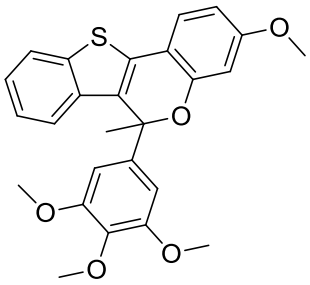
6-methyl-6-(3,4,5-trimethoxyphenyl)-6H-benzo[4,5]thieno[3,2-*c*]chromene (13b)



was prepared according to the general method E from the compound **5q**. **13b** was obtained as a yellow oil (376 mg, 90% yield); TLC: R_f = 0.4 (EtOAc/Cyclohexane, 1/9, SiO_2); IR (neat): 2957, 2923, 2853, 1590, 1553, 1435, 1401, 1290, 1274, 1232, 1198,1152, 1042 cm^-

[1]; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.82 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.40 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.29 – 7.18 (m, 3H), 7.16 – 7.09 (m, 1H), 7.00 (dd, *J* = 11.2, 4.6 Hz, 2H), 6.82 (s, 2H), 3.84 (s, 3H), 3.75 (s, 6H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2 (2C), 151.4 (C), 139.4 (2C), 138.2 (C), 137.5 (C), 133.4 (C), 131.5 (C), 130.1 (CH), 124.8 (CH), 124.3 (CH), 124.0 (CH), 122.9 (2CH), 121.8 (CH), 119.4 (C), 117.2 (CH), 104.8(2CH), 82.8 (C), 60.9 (OCH_3), 56.3 ($2OCH_3$), 26.2 (CH_3); HRMS (ESI): for $C_{25}H_{23}O_4S$ $(M + H)^+$: *m*/*z* calcd 419.1317, found 419.1312.

3-methoxy-6-methyl-6-(3,4,5-trimethoxyphenyl)-6H-benzo[4,5]thieno[3,2-c]chromene (13c)



was prepared according to the general method E from the compound **5r**. **13c** was obtained as a yellow solid (426 mg, 95% yield); mp= 84-85°C; TLC: R_f = 0.54 (EtOAc/Cyclohexane, 2/8, SiO_2); IR (neat): 3334, 3317, 2974, 2928, 2898, 2876, 2360, 2181, 2137, 1929, 1592, 1521, 1421, 1334, 1229, 1089, 1046 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.79 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.31 (d, *J* = 9.0 Hz, 1H), 7.18 (dtd, *J* = 16.4, 7.1, 1.0 Hz, 2H), 7.04 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.81 (s, 2H), 6.59 – 6.53 (m, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 3.75 (s, 6H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6 (C), 153.2 (2C), 152.7 (C), 139.3 (C), 138.9 (C), 138.3 (C), 137.6(C), 133.6 (C), 129.2 (C), 124.8 (CH), 124.7 (CH), 123.8 (CH), 122.8 (CH), 122.5 (CH), 112.6 (C), 108.2 (CH), 104.9 (2CH), 102.6(CH), 83.1 (C), 61.0 (OCH_3), 56.4 ($2OCH_3$), 55.6 (OCH_3), 26.0 (CH_3); HRMS (ESI): for $C_{26}H_{25}O_5S$ $(M + H)^+$: *m*/*z* calcd 449.1423, found 449.1421.

Biology methods

Cell culture and proliferation assay: Cancer cell lines were obtained from the American type Culture Collection (Rockville, USA) and were cultured according to the supplier's instructions. HCT116 colorectal carcinoma cells were grown in RPMI 1640 containing 10% FCS and 1% glutamine. All cell lines were maintained at 37°C in a humidified atmosphere containing 5% CO_2. Cell viability was assessed using Promega CellTiter-Blue reagent according to the manufacturer's instructions. Cells were seeded in 96-well plates (5 X 103 cells per well) containing 50 mL growth medium. After 24 h of culture, the cells were supplemented with 50 mL of the test compound dissolved in DMSO (less than 0.1% in each preparation). After 72 h of incubation, 20 mL of resazurin was added for 2 h before recording fluorescence (λex=560 nm, λem=590 nm) using a Victor microtiter plate fluorimeter (Perkin–Elmer, USA). The IC_{50} value corresponds to the concentration of test compound that caused a decrease of 50% in fluorescence of drug treated cells compared with untreated cells. Experiments were performed in triplicate.

Tubulin binding assay: Sheep brain tubulin was purified according to the method of Shelanski[3] by two cycles of assembly–disassembly and then dissolved in the assembly buffer containing 0.1m MES, 0.5 mm $MgCl_2$, 1mm EGTA and 1 mm GTP (pH 6.6) to give a tubulin concentration of ~2–3 mg/mL. Tubulin assembly was monitored and recorded continuously by turbidimetry at 350 nm in a UV spectrophotometer equipped with a thermostatted cell at 37 °C. The GI_{50} value of each compound was determined as the concentration at which the maximum assembly rate of tubulin was decreased by 50% compared to the rate in the absence of compound. The GI_{50} values for all compounds were compared to the GI_{50} of CA-4, *iso*CA-4 and measured the same day under the same conditions.

Computational methods

X-ray structures of 5 different tubuline cocrystals were retrieved from the PDB[4] (accession codes 1SA0, 1SA1, 3HKC, 3HKD and 3HKE) and prepared using Protein Preparation Wizard workflow from Schrödinger suite,[5] including optimization of the hydrogen bond network and a short minimization with position restraints on heavy atoms using OPLS_2005 force field[6]. Coordinates for compounds **5e**,**k**,**m** were generated using Standardizer from JChem suite v6.3[7] and geometries were refined at the HF/STO-3G level [8] using NWChem v6.1[9]. Ligands were then freely docked in the colchicine binding site located between chains C and D using the ensemble docking procedure available in GOLD v5.2.2[10] over the 5 aligned tubuline structures. CHEMPLP with default parameters was used as an objective function.[11] Structures of complexes were exported, subjected to hydrogen bond network optimization using Protein Preparation Wizard, and loaded in Chimera v1.9[12] for examination (including hydrogen bond detection, close contact analysis and representation of solvent-accessible surface) and depiction.

(1) Armarego, W. L. F.; Chai, C. L. L. In *Purification of Laboratory Chemicals (Sixth Edition)*; Armarego, W. L. F., Chai, C. L. L., Eds.; Butterworth-Heinemann: Oxford, 2009, p 88-444.

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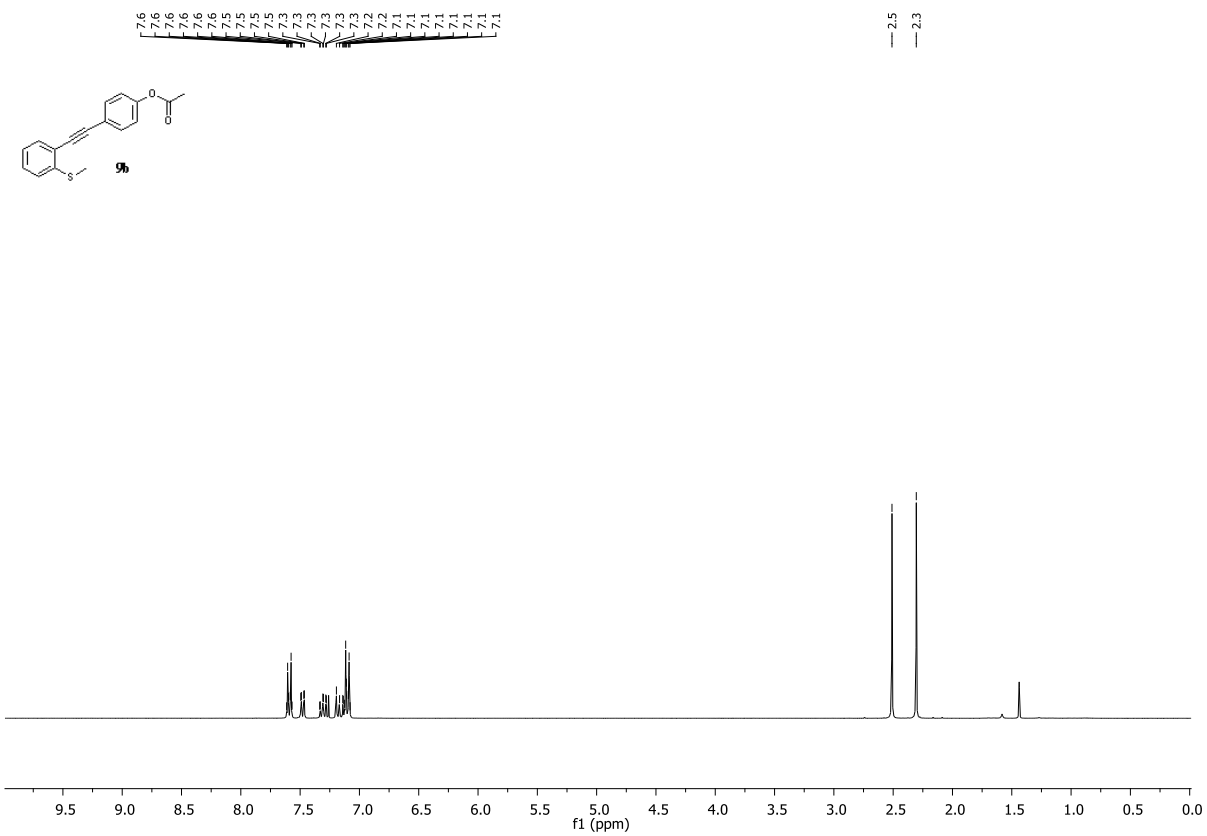
I. ^{1}H and ^{13}C NMR Spectra for Alkynes


7.6
7.6
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7.3
7.3
7.3
7.3
7.2
7.2
7.1
7.1
7.1
7.1
7.1
7.1
7.1
2.5
2.3
O
O
S
9b
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
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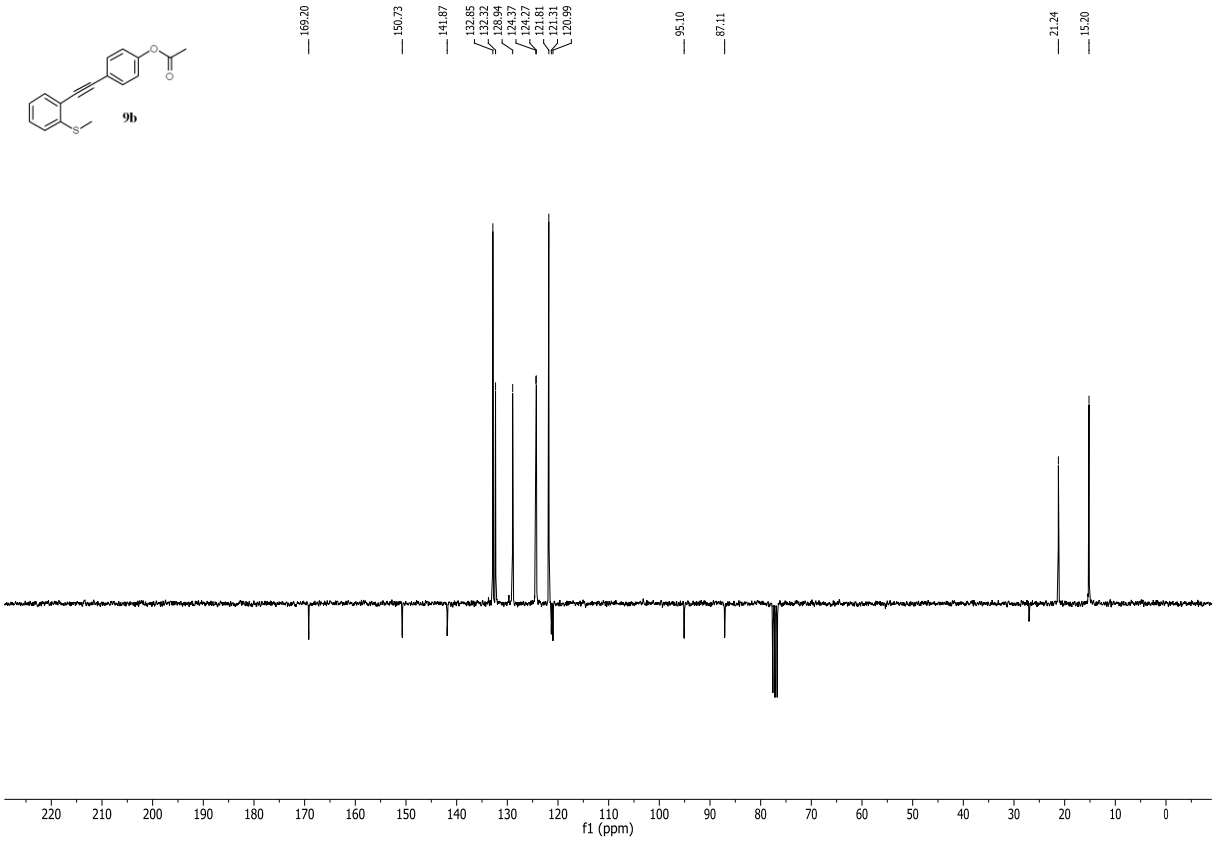
0.0
f1 (ppm)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121.31
120.99
95.10
87.11
21.24
15.20
O
O
S
9b
220
210
200
190
180
170
160
150
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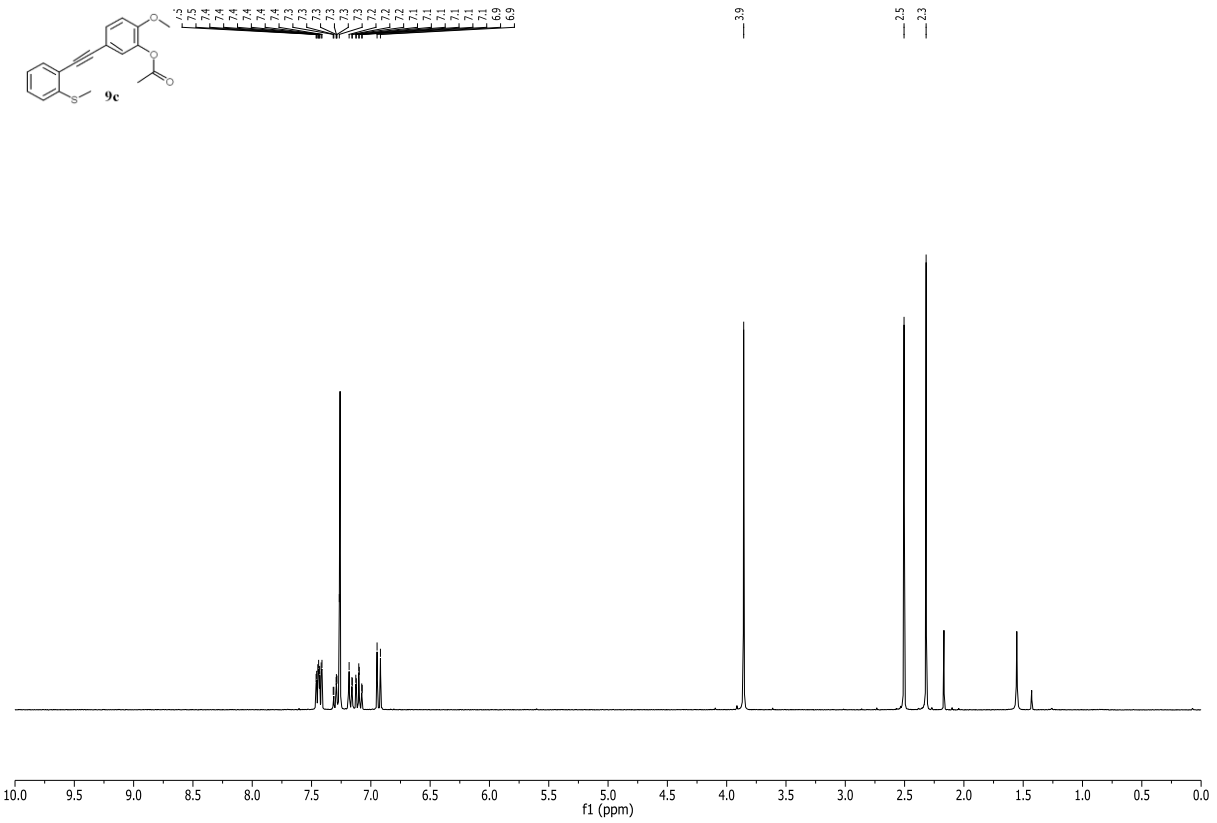
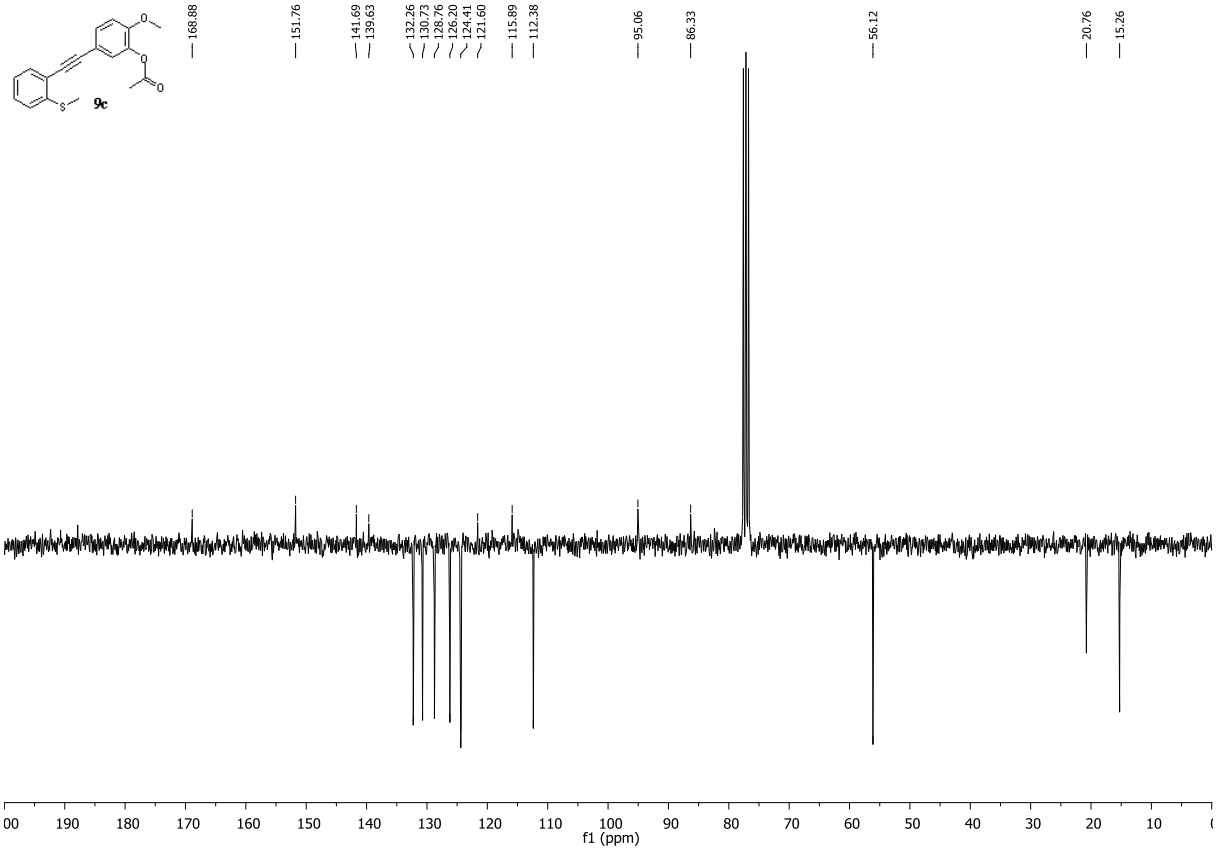
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9c
3.9
2.5
2.3
f1 (ppm)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56.12
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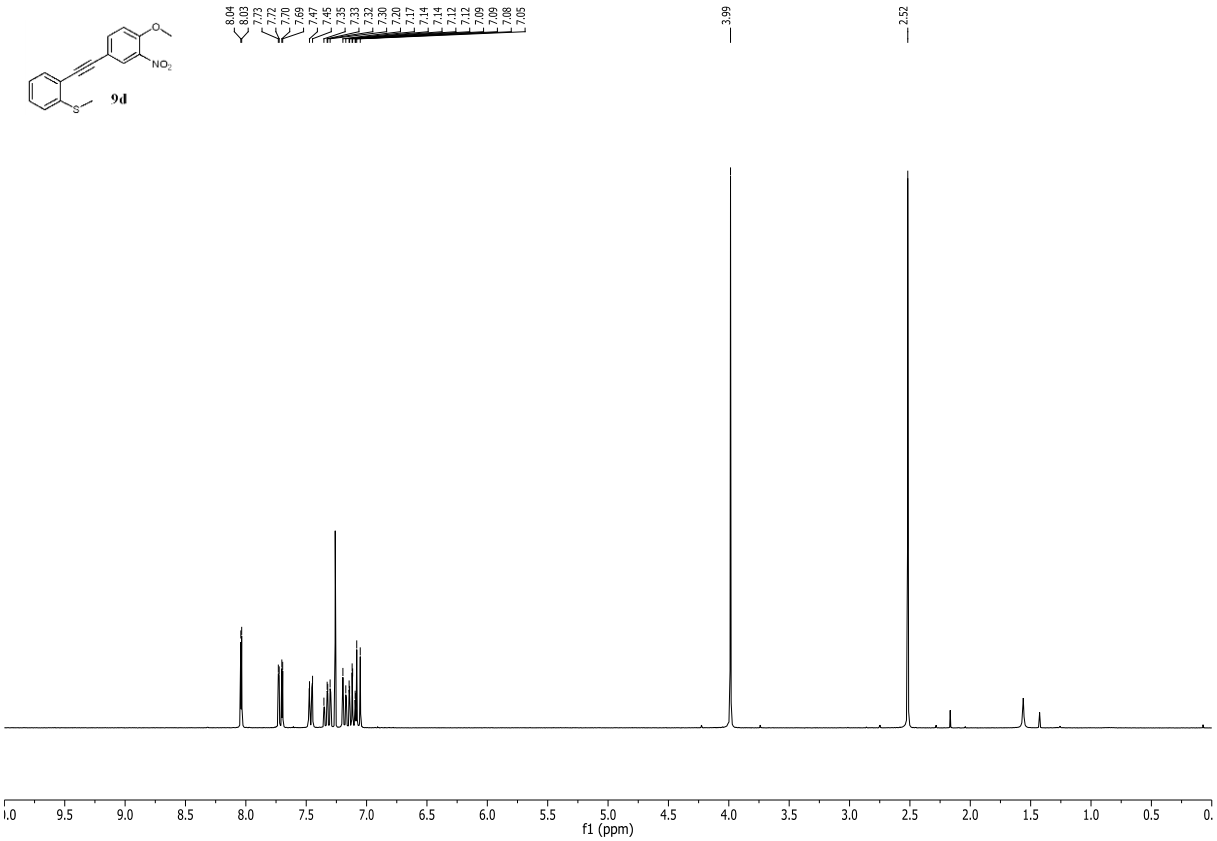
15.26
f1 (ppm)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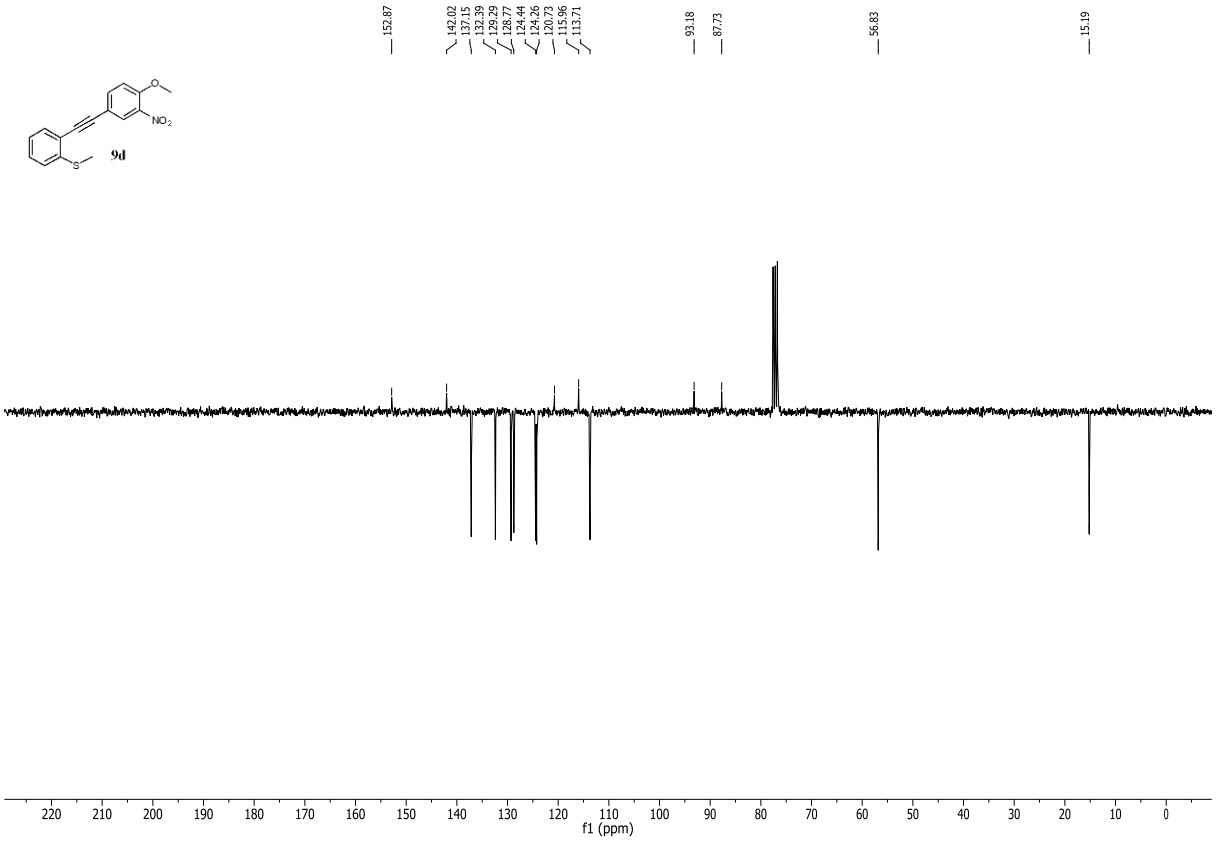
7.20
7.17
7.14
7.12
7.12
7.09
7.09
7.08
7.05
3.99
2.52
O
NO2
S
9d
f1 (ppm)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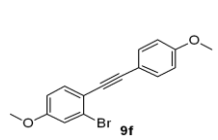
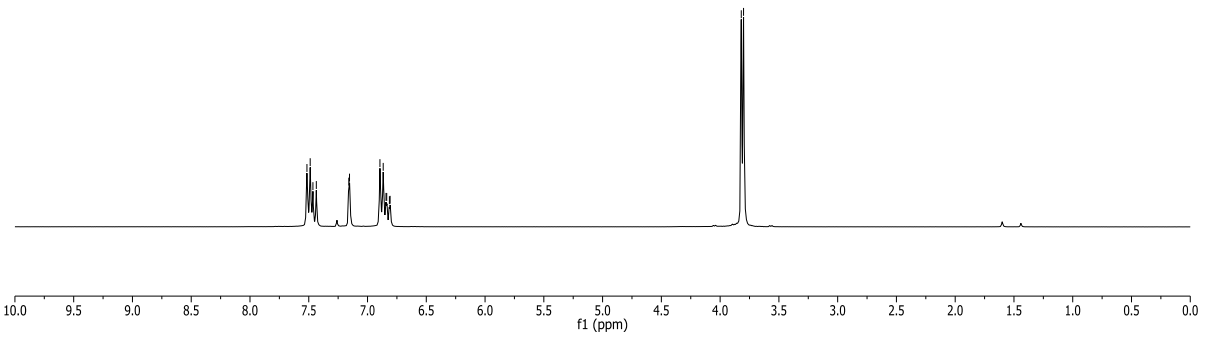
142.02
137.15
132.39
129.29
128.77
124.44
124.26
120.73
115.96
113.71
93.18
87.73
56.83
15.19
O
NO2
S
9d
f1 (ppm)


Br
9f


7.52
7.49
7.46
7.44
7.16
7.15
6.89
6.87
6.84
6.84
6.81
6.81


3.82
3.80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9.0
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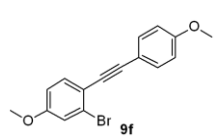
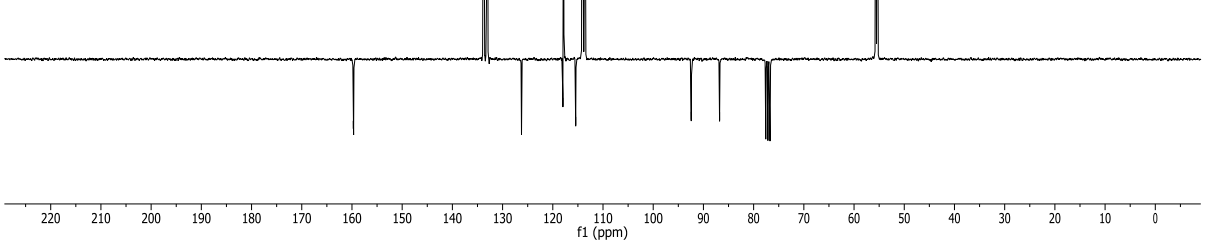
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Br
9f


159.75
133.77
133.06
126.23
117.99
117.86
115.44
114.09
113.61
92.42
86.78
55.67
55.39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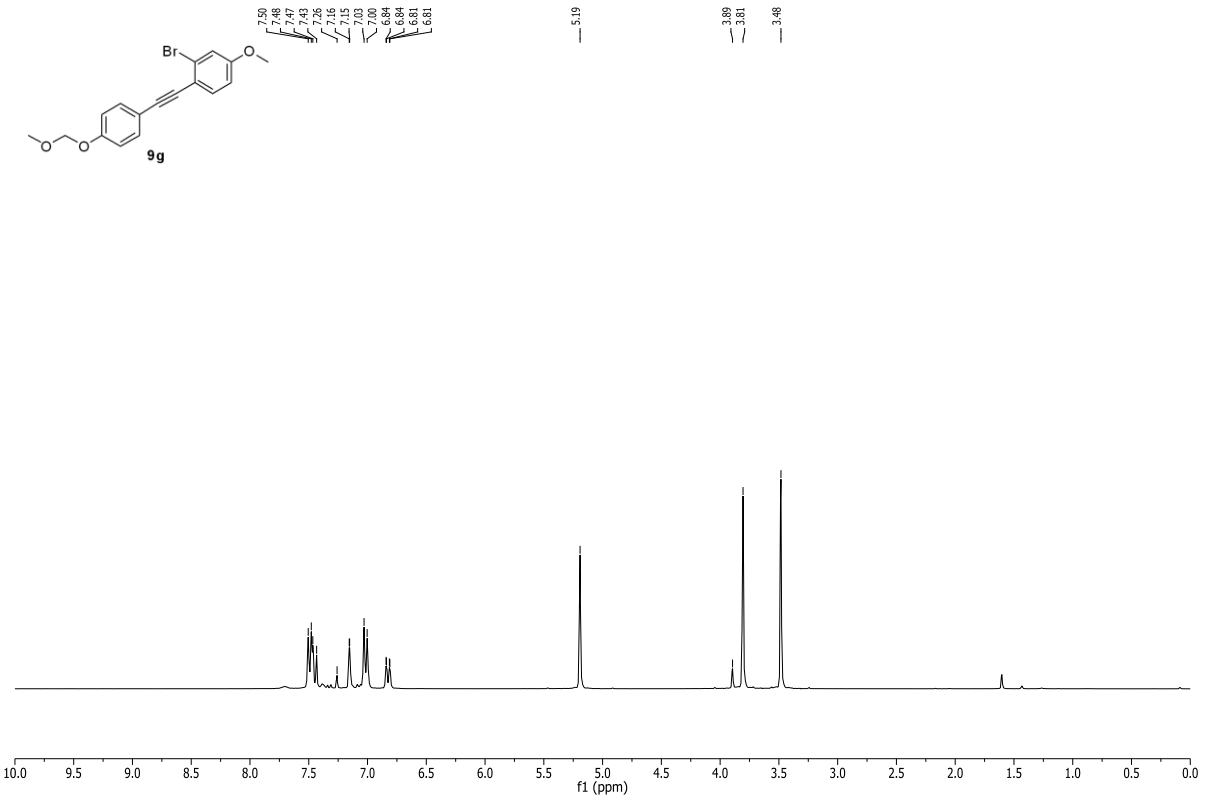
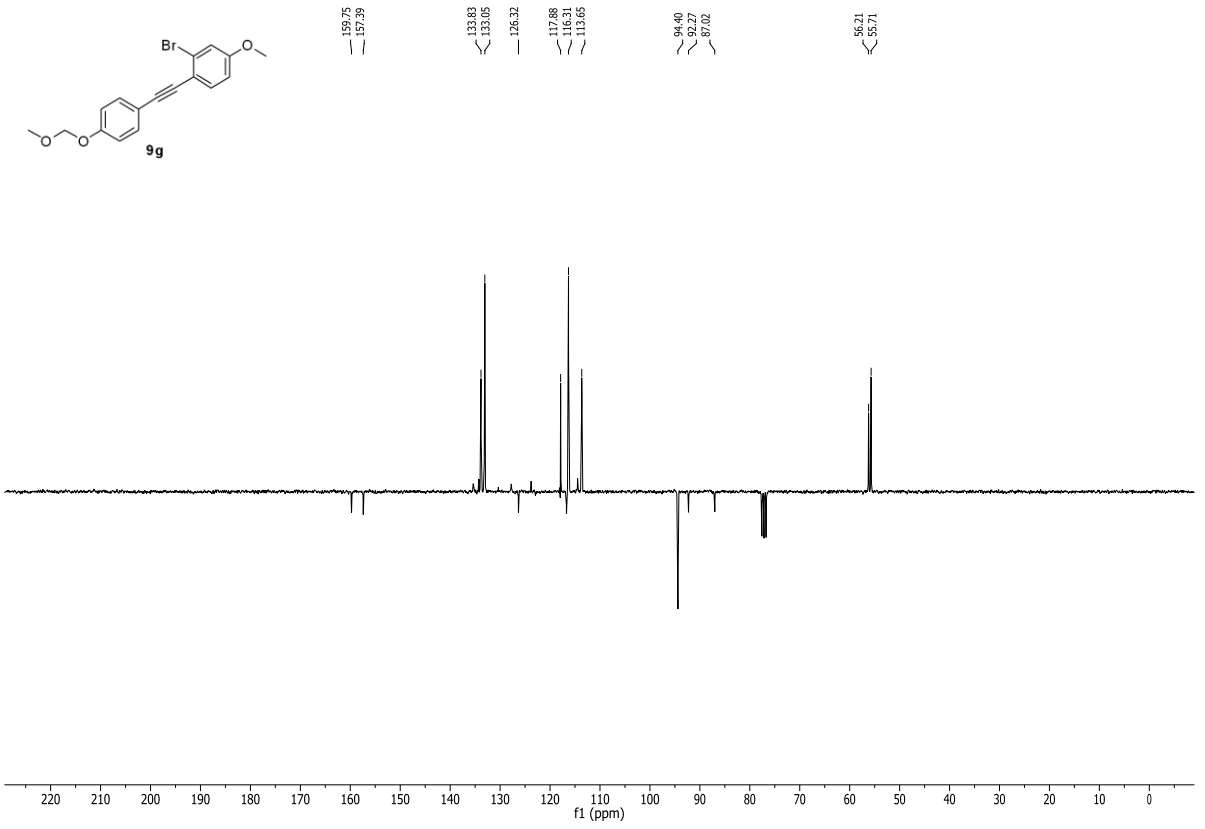
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.50
7.48
7.47
7.43
7.26
7.16
7.15
7.03
7.00
6.84
6.84
6.81
6.81
5.19
3.89
3.81
3.48
Br
O
O
O
9g
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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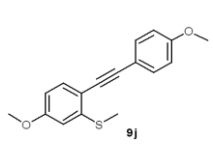
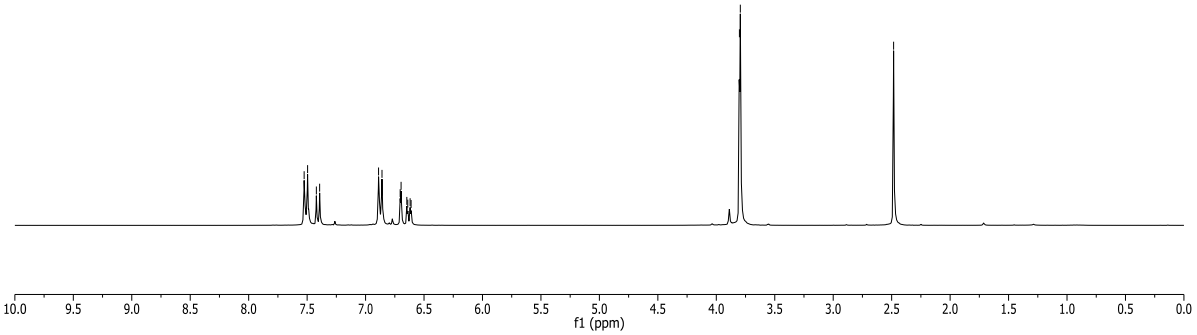
157.39
133.83
133.05
126.32
117.88
116.31
113.65
94.40
92.27
87.02
56.21
55.71
Br
O
O
O
9g
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9j


7.53
7.50
7.42
7.39
6.89
6.86
6.70
6.70
6.65
6.64
6.62
6.61
3.80
3.79
2.48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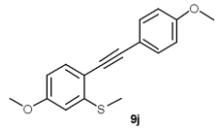
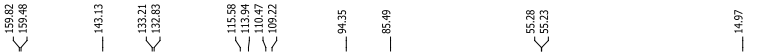
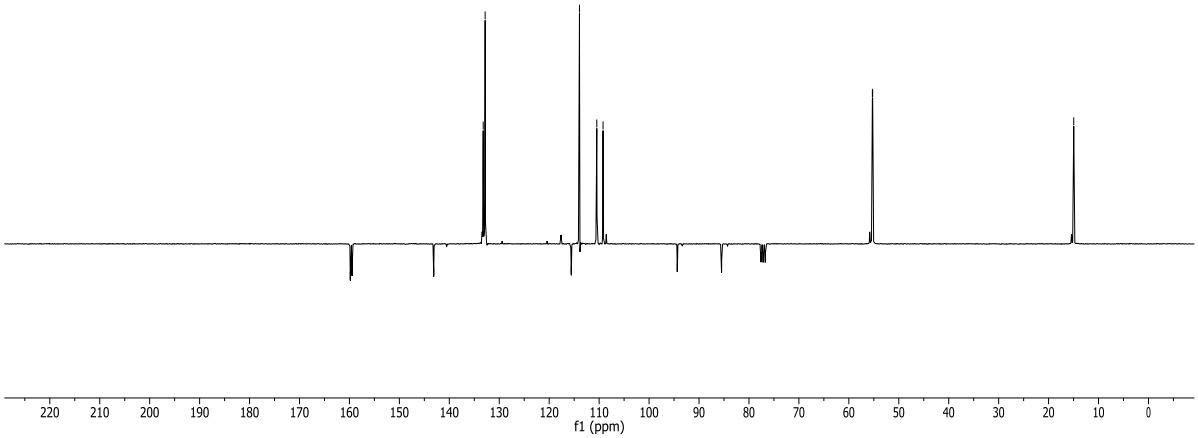
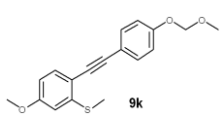
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

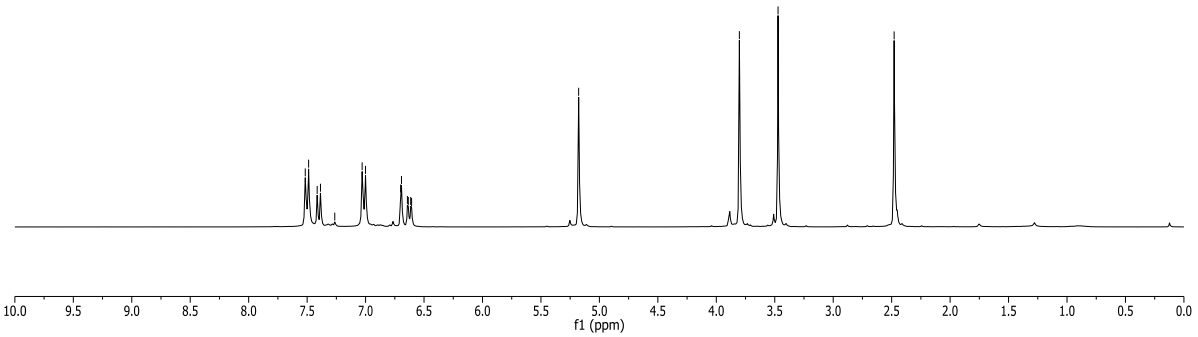

9j


159.82
159.48
143.13
133.21
132.83
115.58
113.94
110.47
109.22
94.35
85.49
55.28
55.23
14.97


220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9k


7.52
7.49
7.41
7.39
7.26
7.03
7.00
6.70
6.69
6.64
6.63
6.61
6.61
5.18
3.80
3.47
2.48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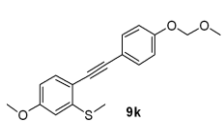
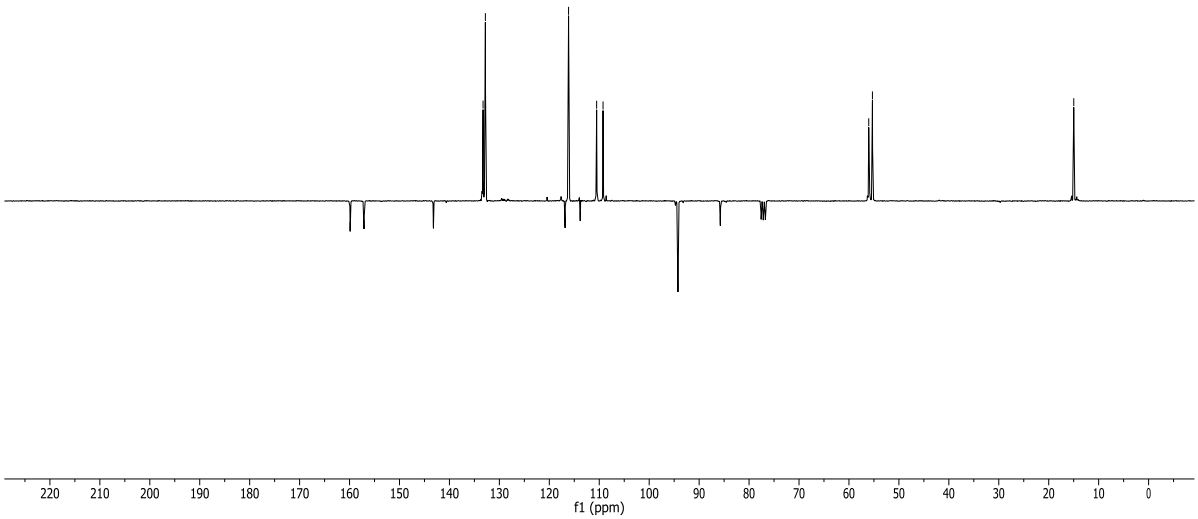
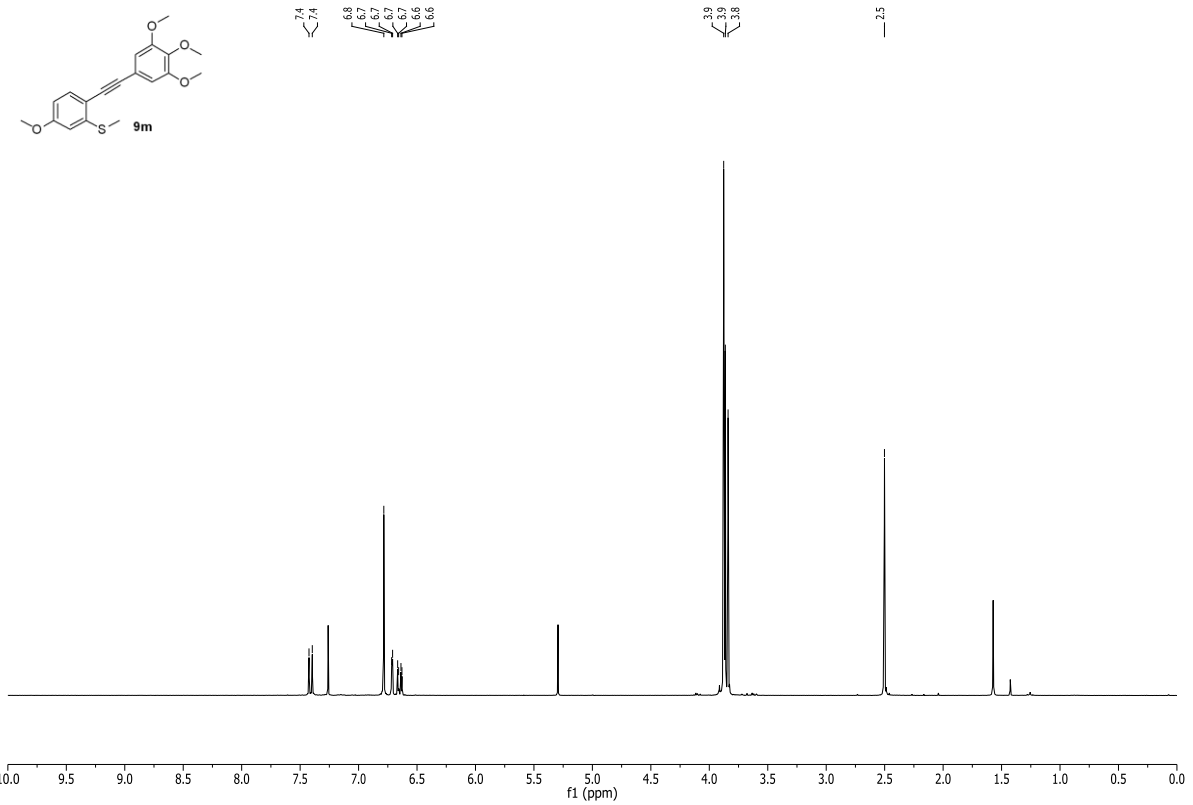
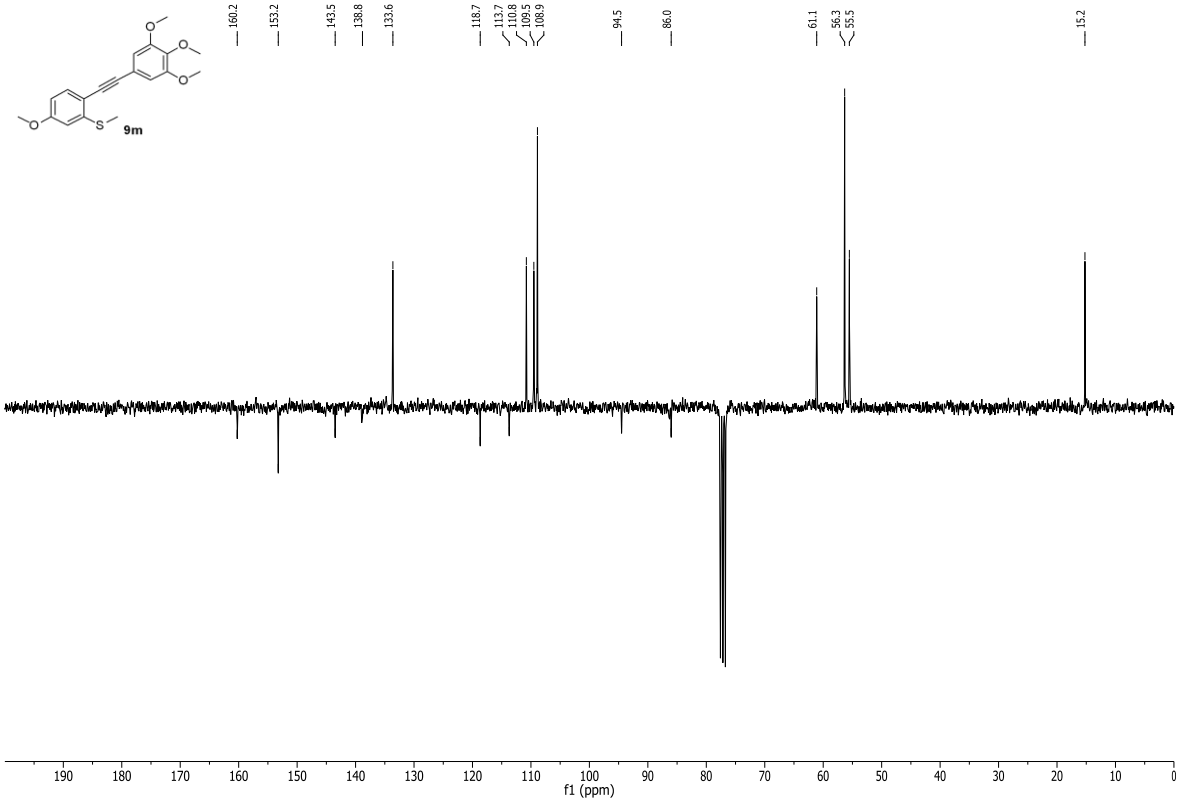
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

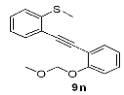

9k


159.88
157.11
143.21
133.27
132.80
116.84
116.14
113.80
110.52
109.24
94.24
85.75
56.04
55.30
14.98

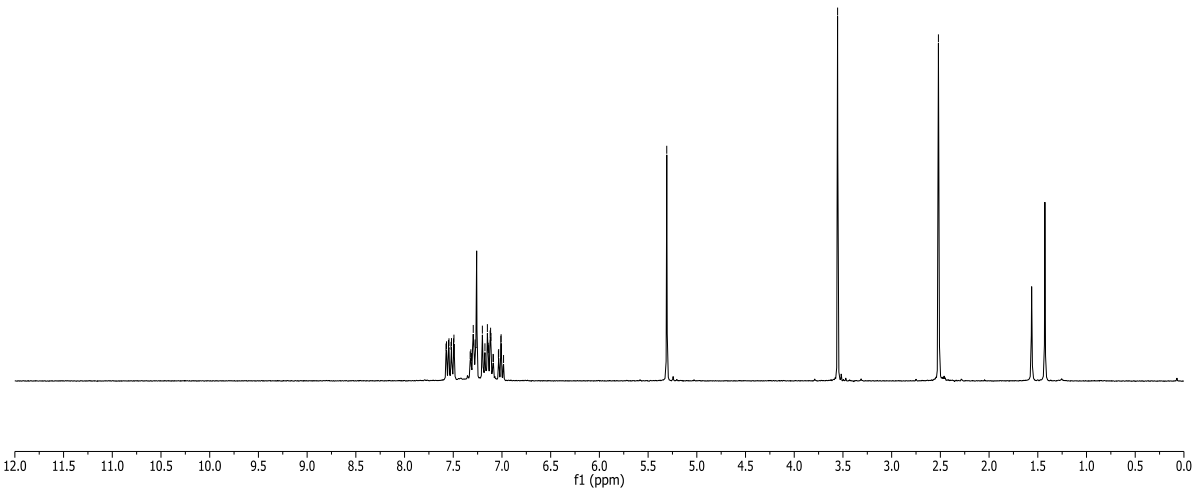

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9m
7.4
7.4
6.8
6.7
6.7
6.7
6.7
6.6
6.6
3.9
3.9
3.8
2.5
f1 (ppm)


9m
160.2
153.2
143.5
138.8
133.6
118.7
113.7
110.8
109.5
108.9
94.5
86.0
61.1
56.3
55.5
15.2
f1 (ppm)


9n


7.57
7.57
7.55
7.54
7.52
7.52
7.50
7.49
7.33
7.32
7.31
7.29
7.28
7.20
7.17
7.15
7.14
7.14
7.12
7.12
7.11
7.09
7.09
7.04
7.03
7.01
7.01
6.98
5.31
3.55
2.52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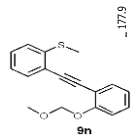
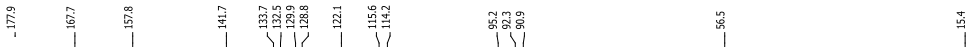
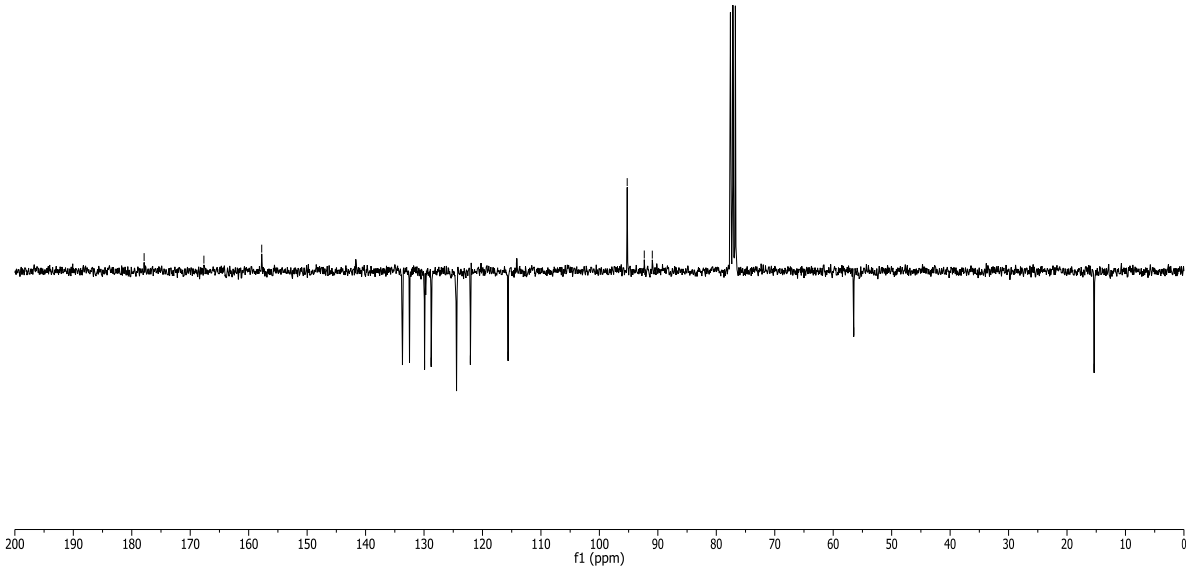
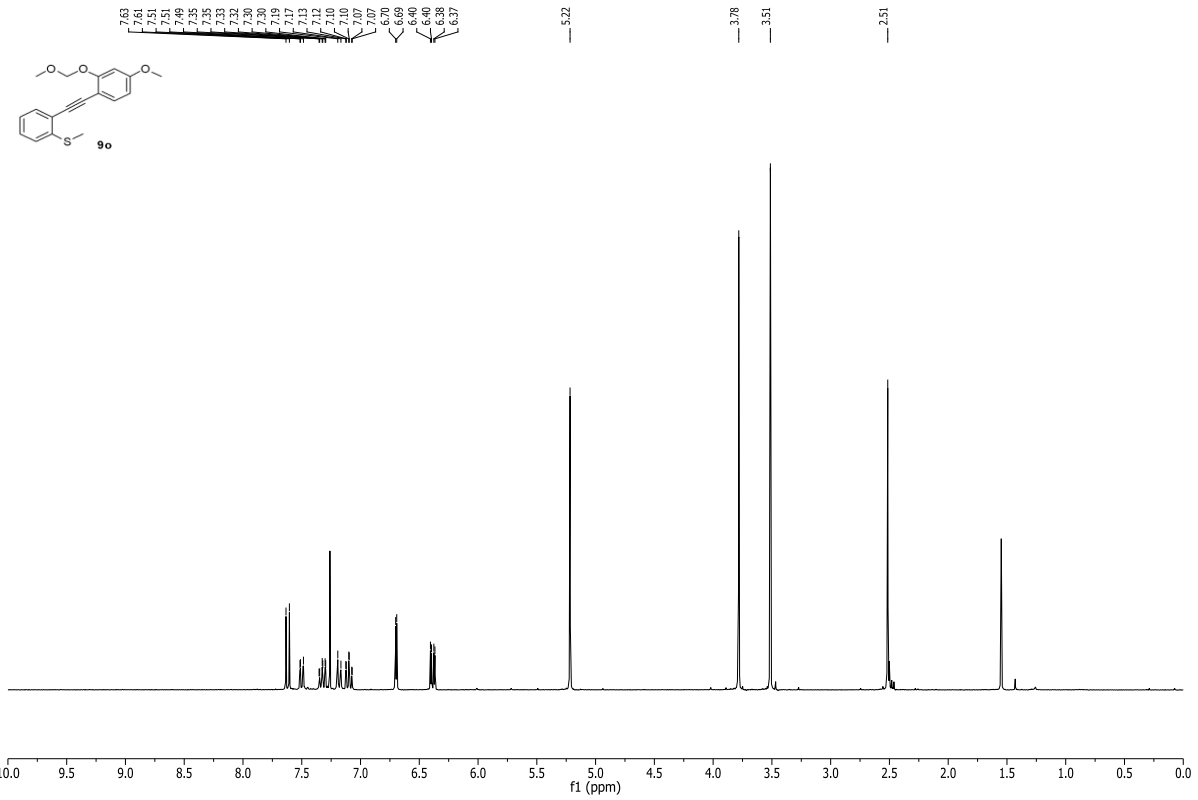
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


9n


177.9
167.7
157.8
141.7
133.7
132.5
129.9
128.8
122.1
115.6
114.2
95.2
92.3
90.9
56.5
15.4


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.61
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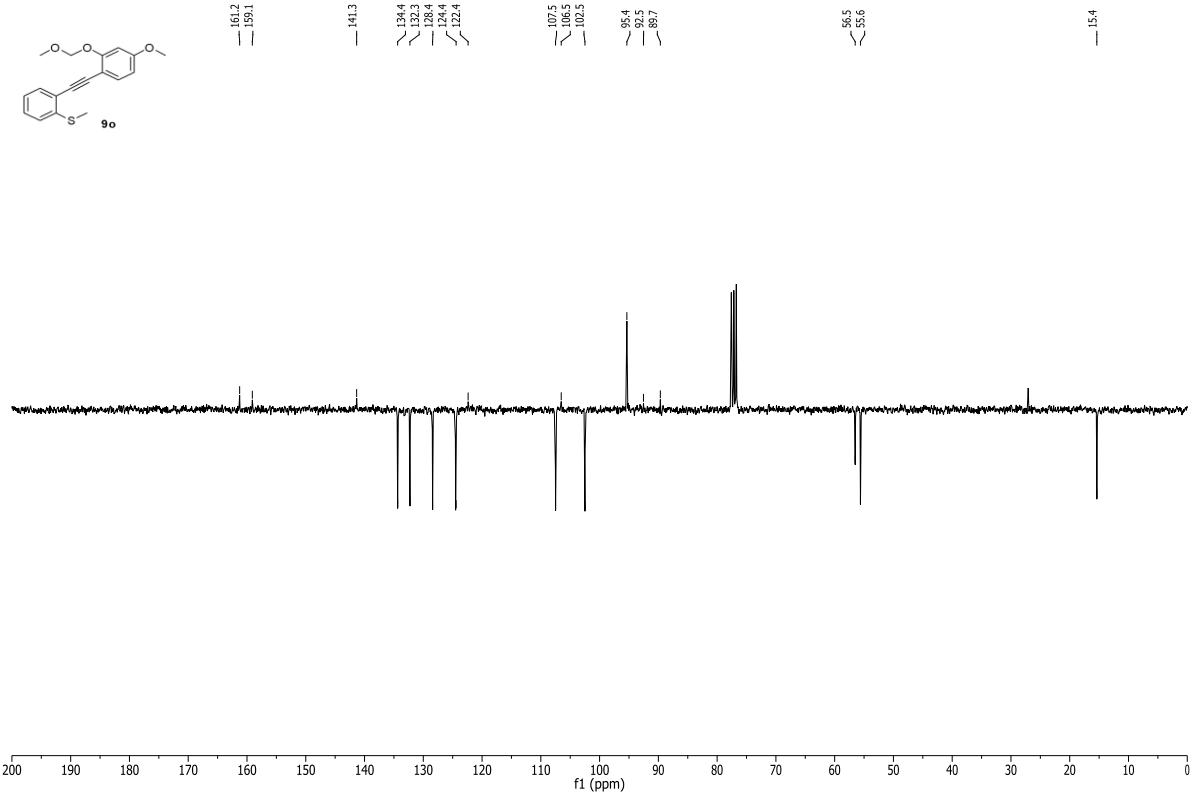
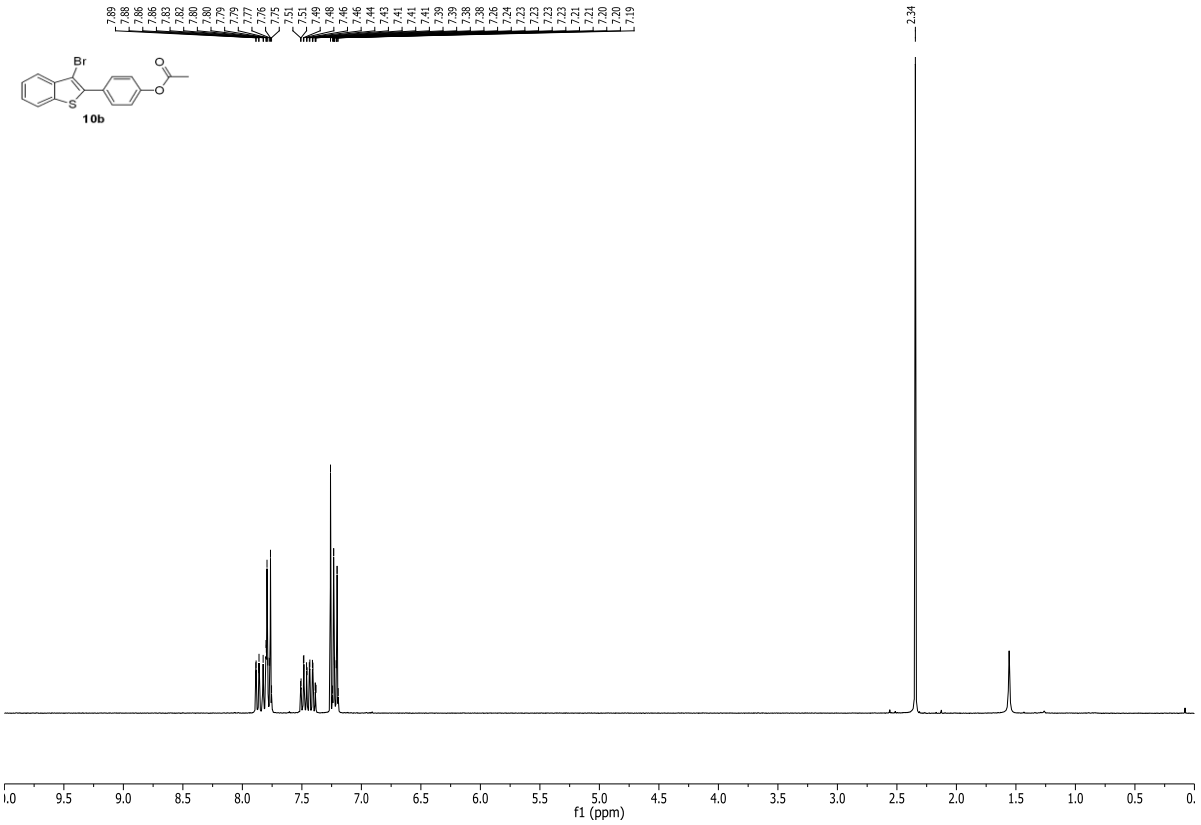
7.51
7.49
7.35
7.35
7.33
7.32
7.30
7.30
7.19
7.17
7.13
7.12
7.10
7.10
7.07
7.07
6.70
6.69
6.40
6.40
6.38
6.37
5.22
3.78
3.51
2.51
9o
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.2
159.1
141.3
134.4
132.3
128.4
124.4
122.4
107.5
106.5
102.5
95.4
92.5
89.7
56.5
55.6
15.4
9o
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

II. ^{1}H and ^{13}C NMR Spectra for 3-bromobenzo[*b*]thiophenes 11b–k


7.89
7.88
7.86
7.86
7.83
7.82
7.80
7.80
7.79
7.79
7.77
7.76
7.75
7.51
7.49
7.48
7.46
7.46
7.44
7.43
7.41
7.41
7.41
7.39
7.39
7.38
7.38
7.26
7.24
7.23
7.23
7.23
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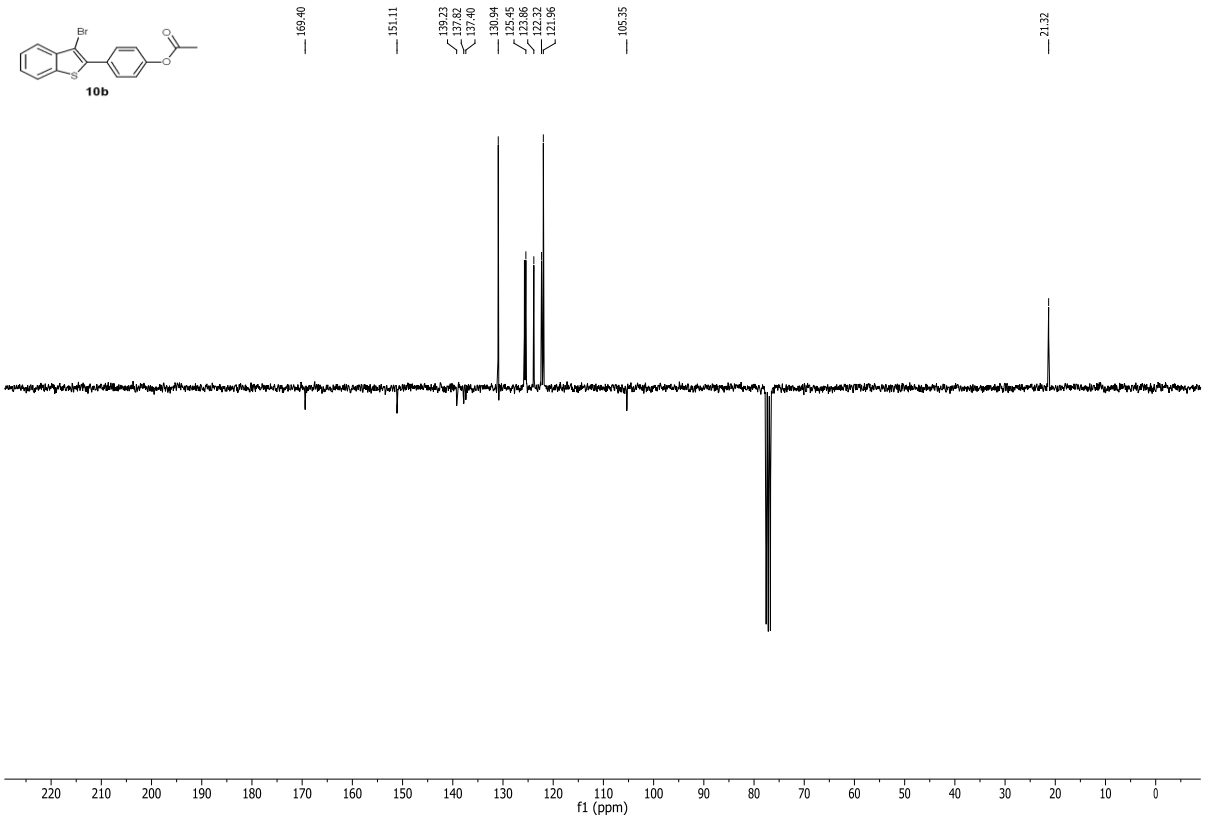
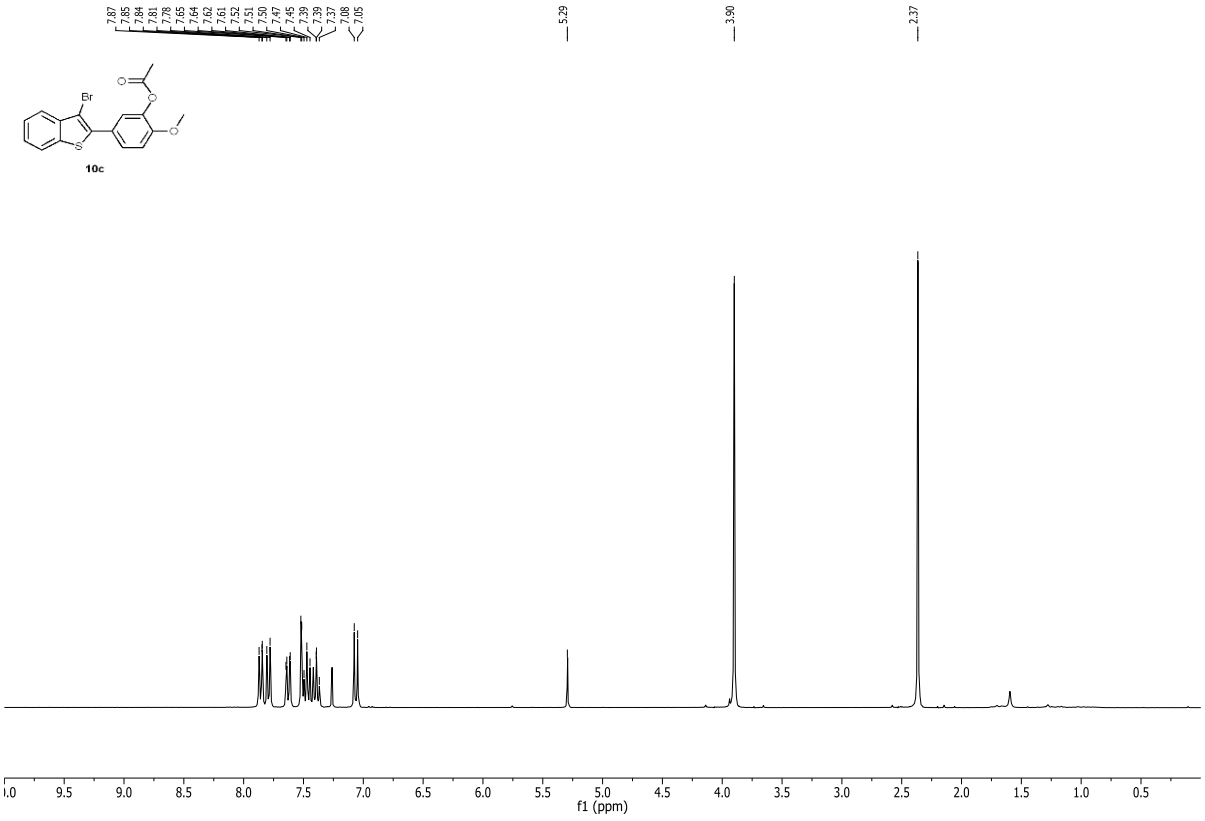
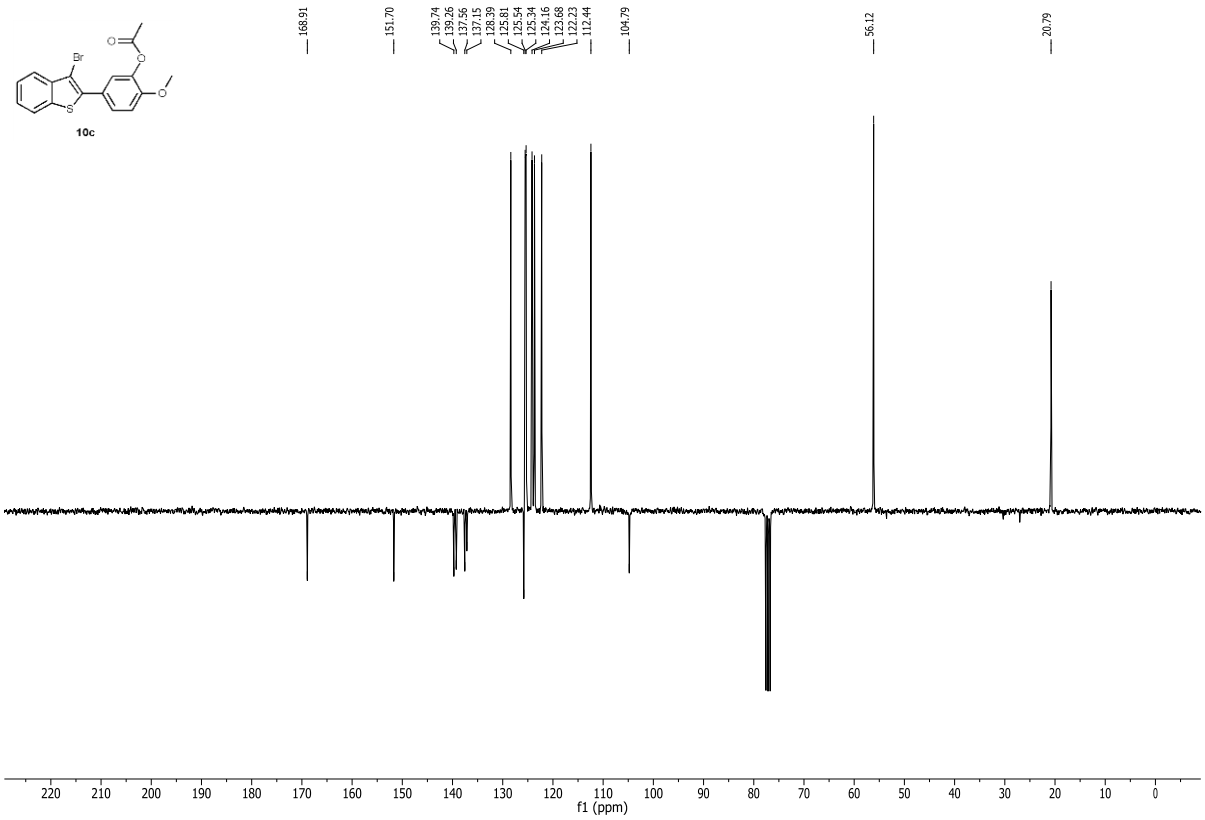
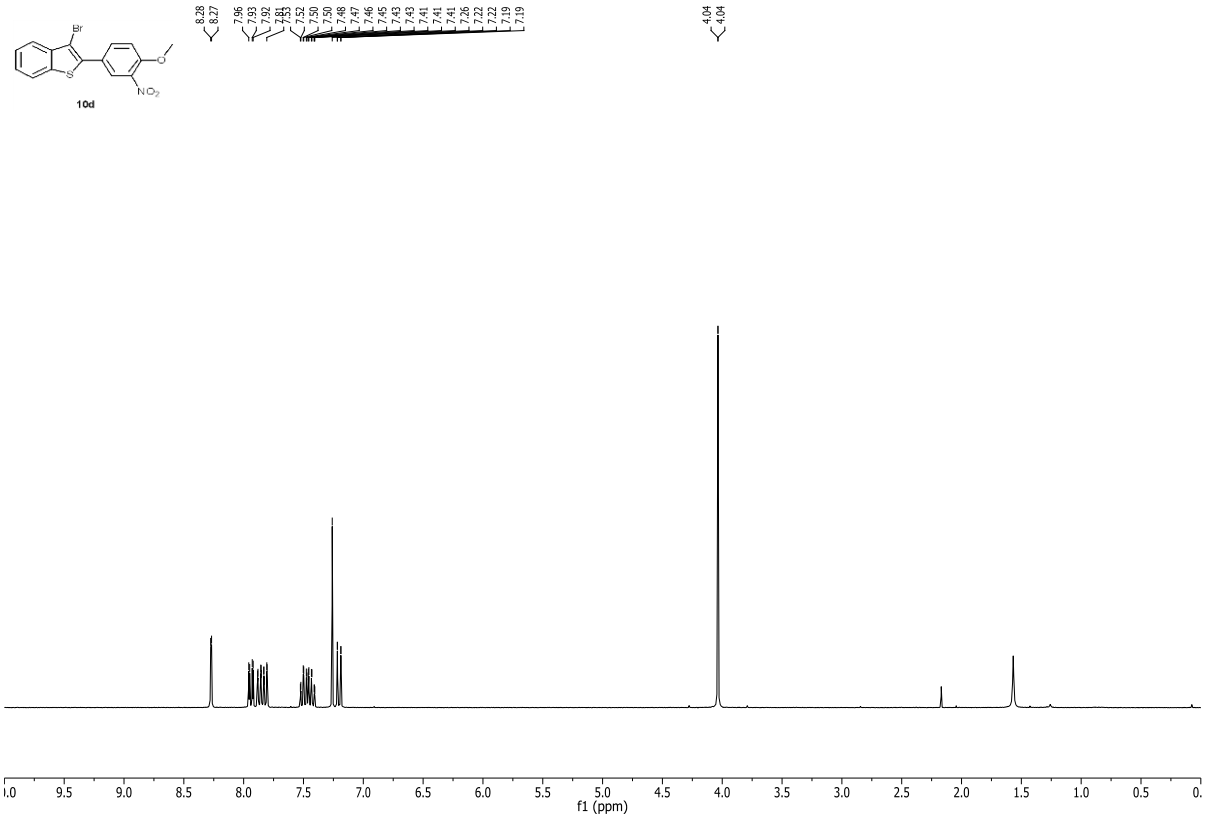
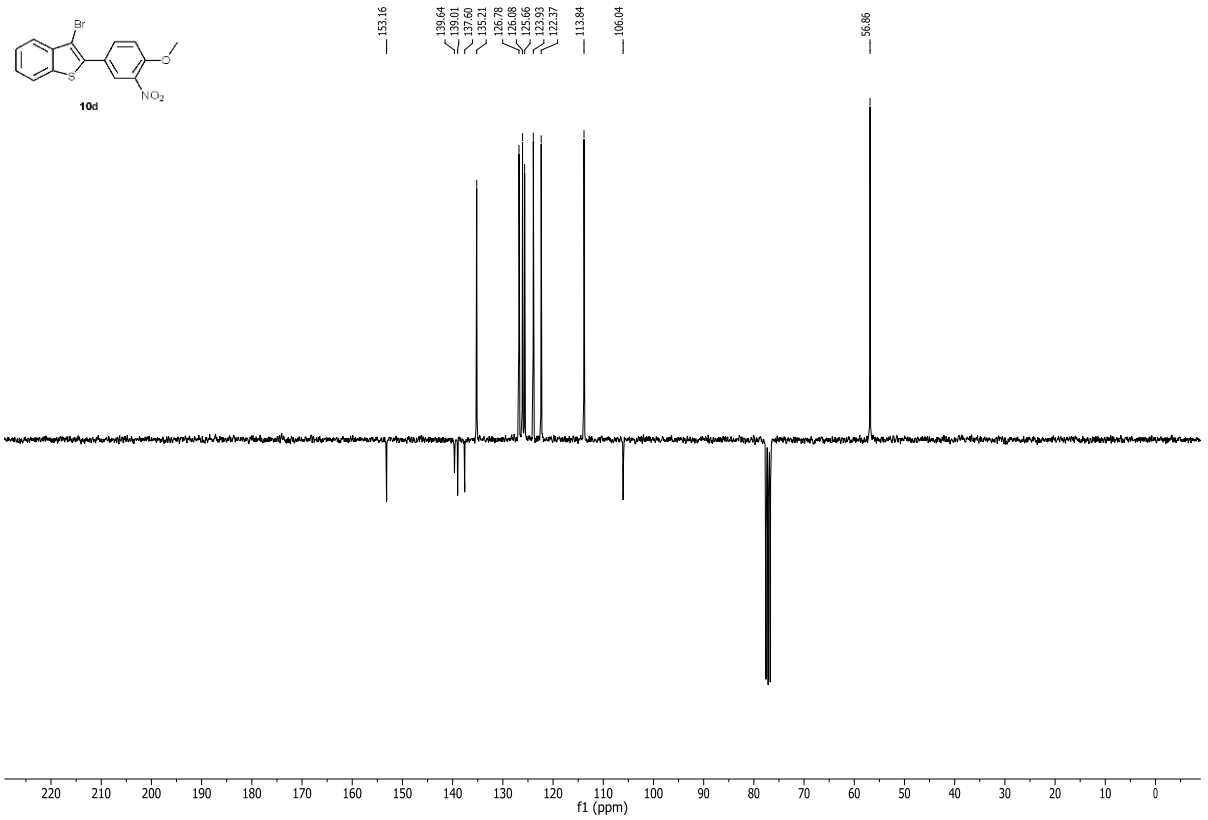
7.21
7.20
7.20
7.19
2.34
Br
S
O
O
10b
f1 (ppm)

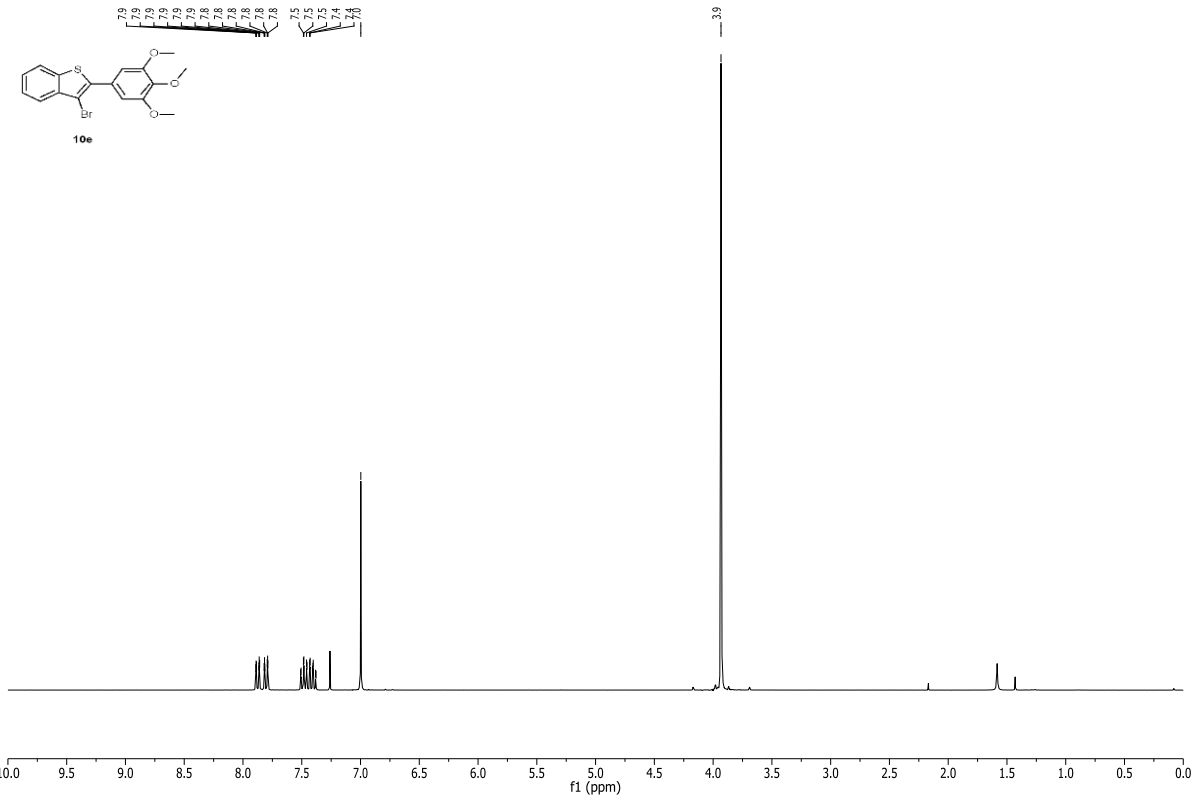

169.40
151.11
139.23
137.82
137.40
130.94
125.45
123.86
122.32
121.96
105.35
21.32
Br
S
O
O
10b
f1 (ppm)

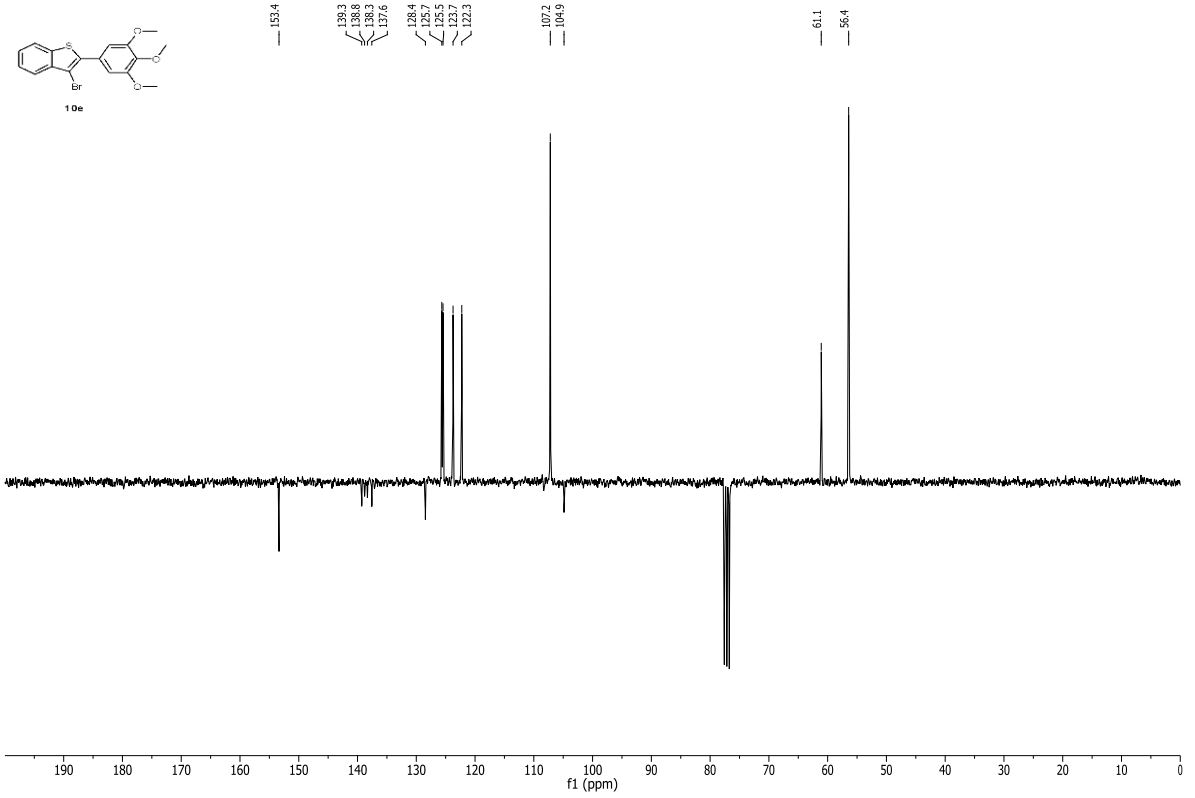

7.87
7.85
7.84
7.81
7.78
7.65
7.64
7.62
7.61
7.52
7.51
7.50
7.47
7.45
7.39
7.39
7.37
7.08
7.05
5.29
3.90
2.37
Br
O
O
O
S
10c
f1 (ppm)

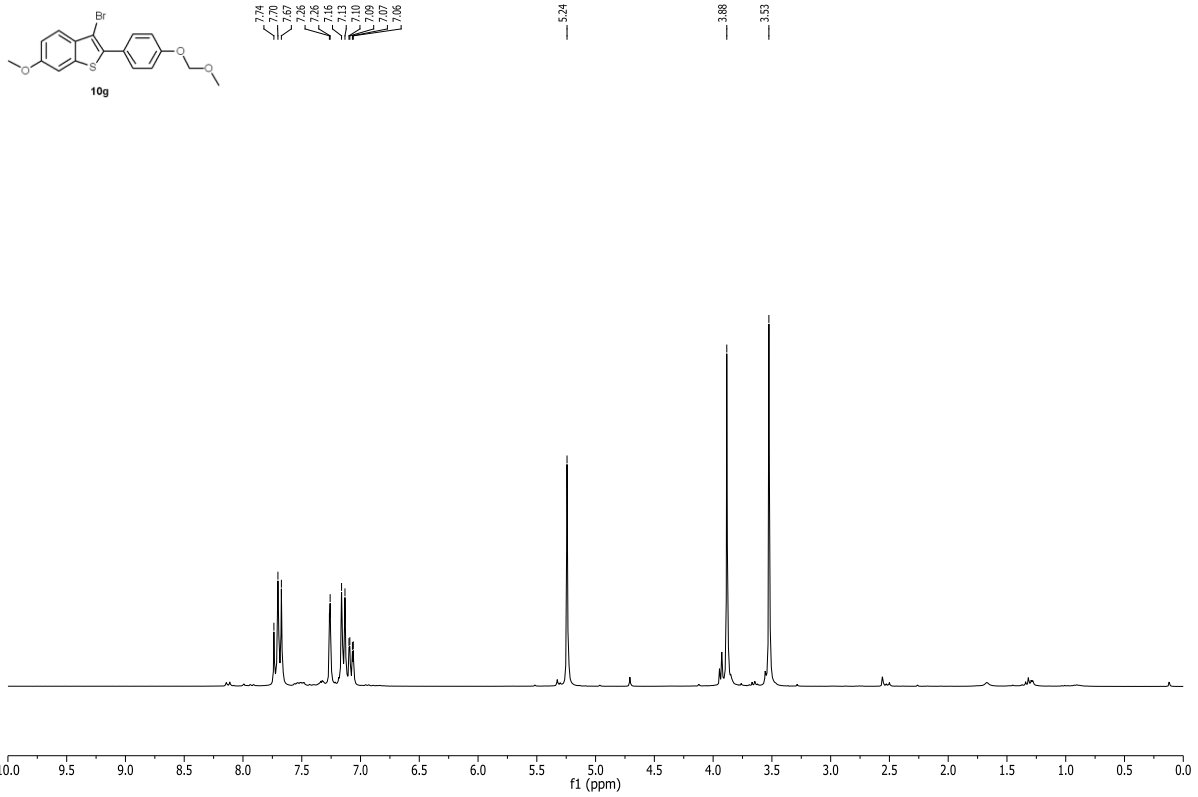

168.91
151.70
139.74
139.26
137.56
137.15
128.39
125.81
125.54
125.34
124.16
123.68
122.23
112.44
104.79
56.12
20.79
Br
O
O
O
S
10c
f1 (ppm)

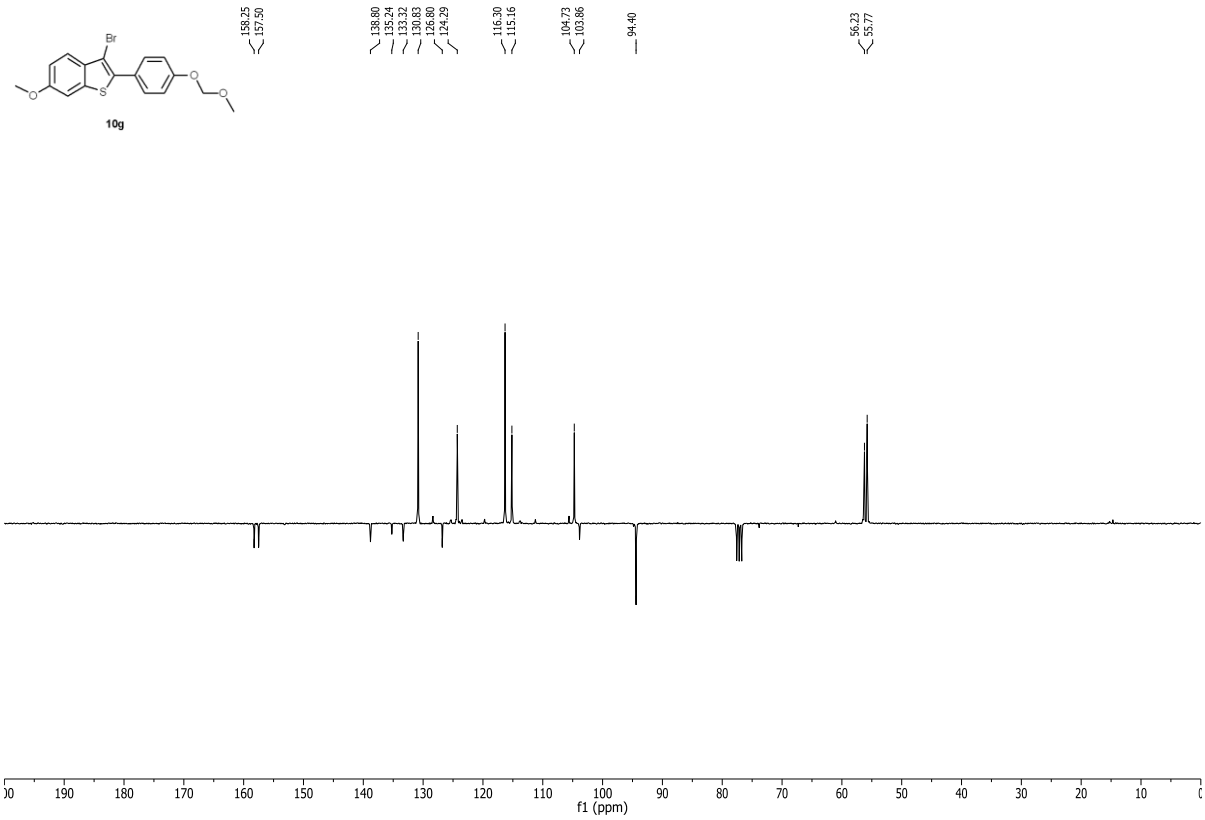

10d
8.28
8.27
7.96
7.93
7.92
7.83
7.52
7.50
7.50
7.48
7.47
7.46
7.45
7.43
7.43
7.41
7.41
7.41
7.26
7.22
7.22
7.19
7.19
4.04
4.04
f1 (ppm)

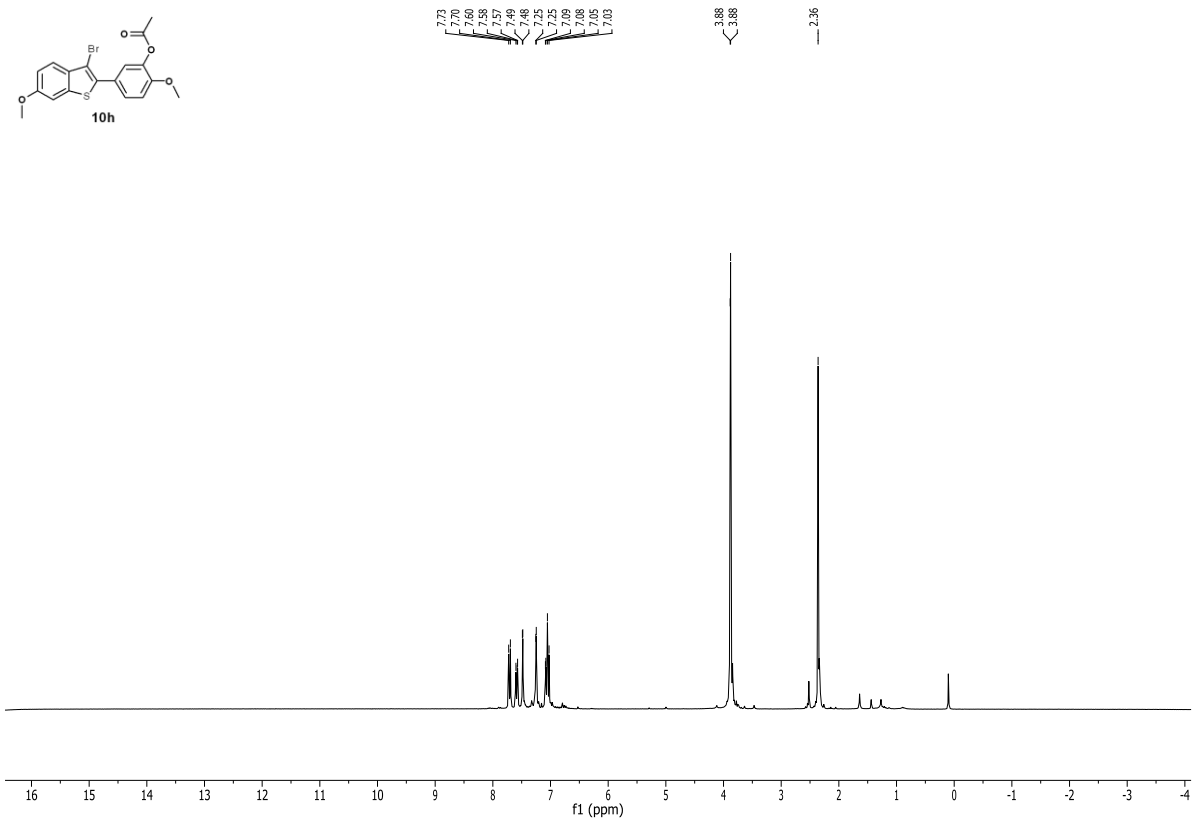

10d
153.16
139.64
139.01
137.60
135.21
126.78
126.08
125.66
123.93
122.37
113.84
106.04
56.86
f1 (ppm)

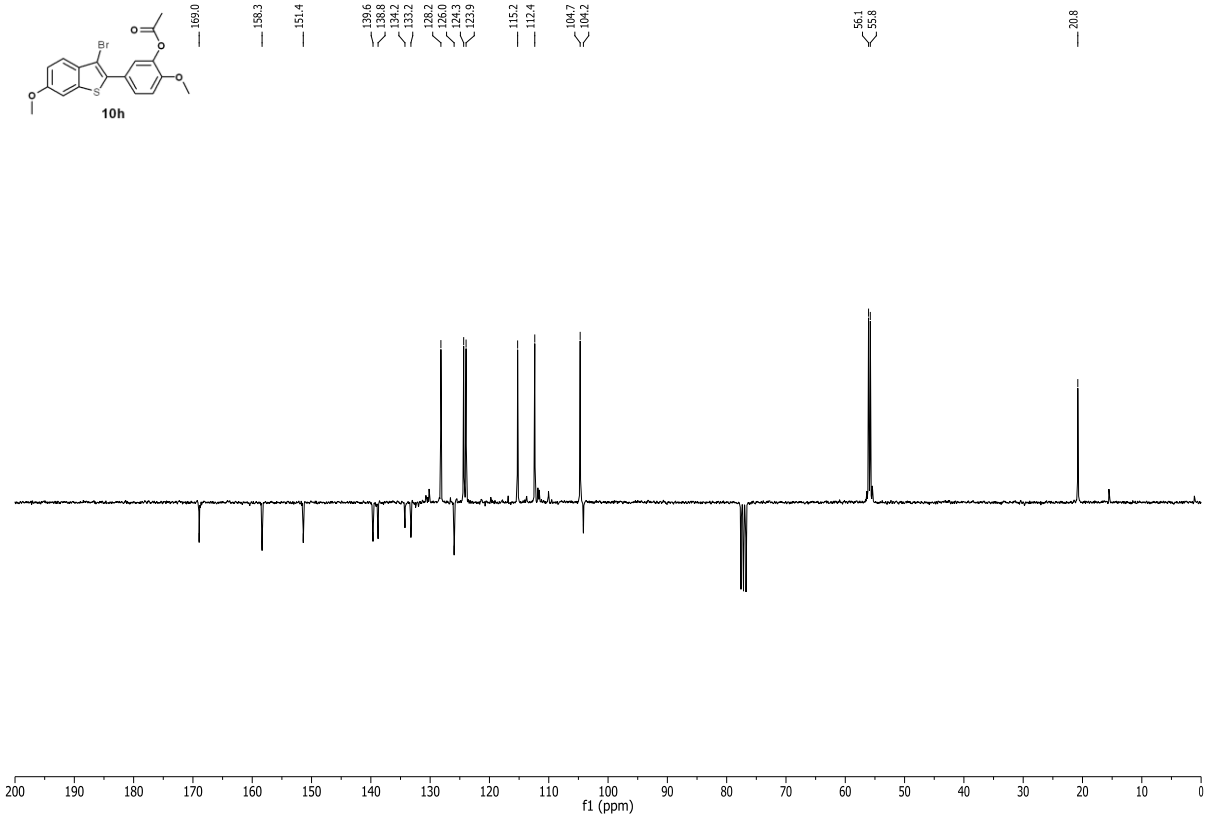

7.9
7.9
7.9
7.9
7.9
7.8
7.8
7.8
7.8
7.8
7.5
7.5
7.5
7.4
7.4
7.0
3.9
10e
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

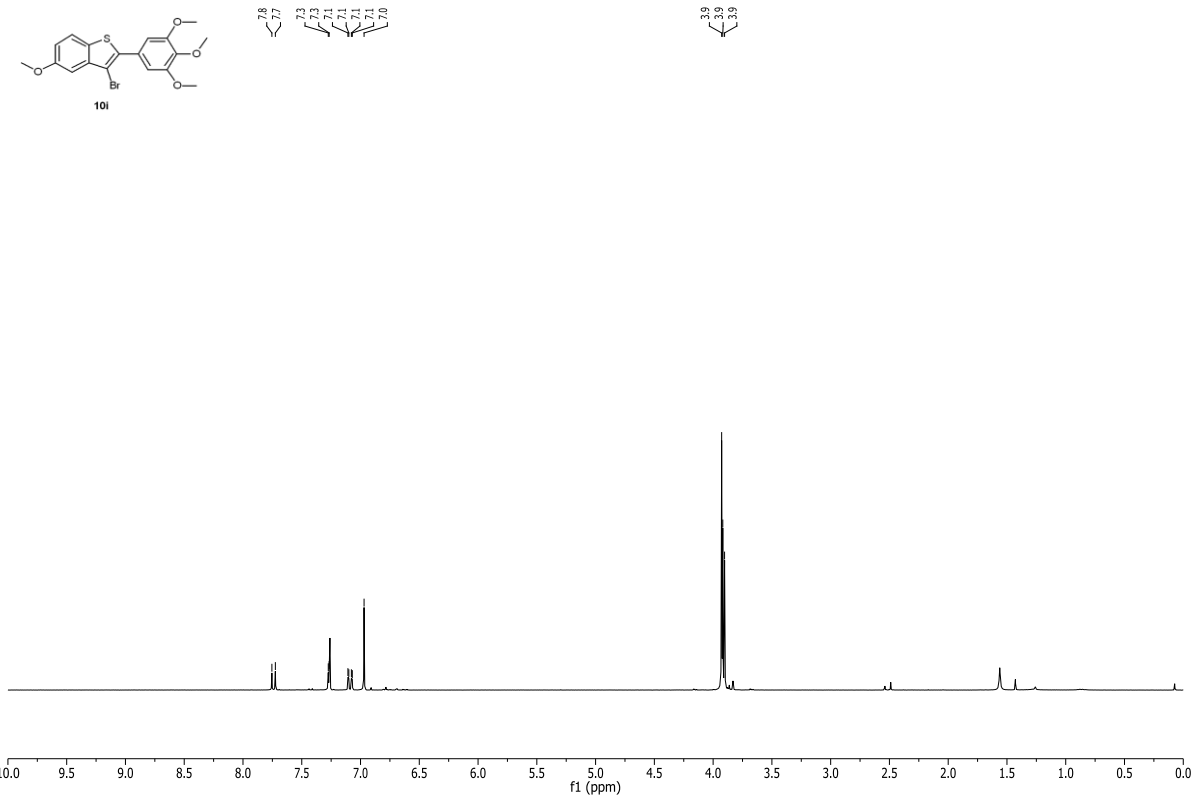

153.4
139.3
138.8
138.3
137.6
128.4
125.7
125.5
123.7
122.3
107.2
104.9
61.1
56.4
10e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

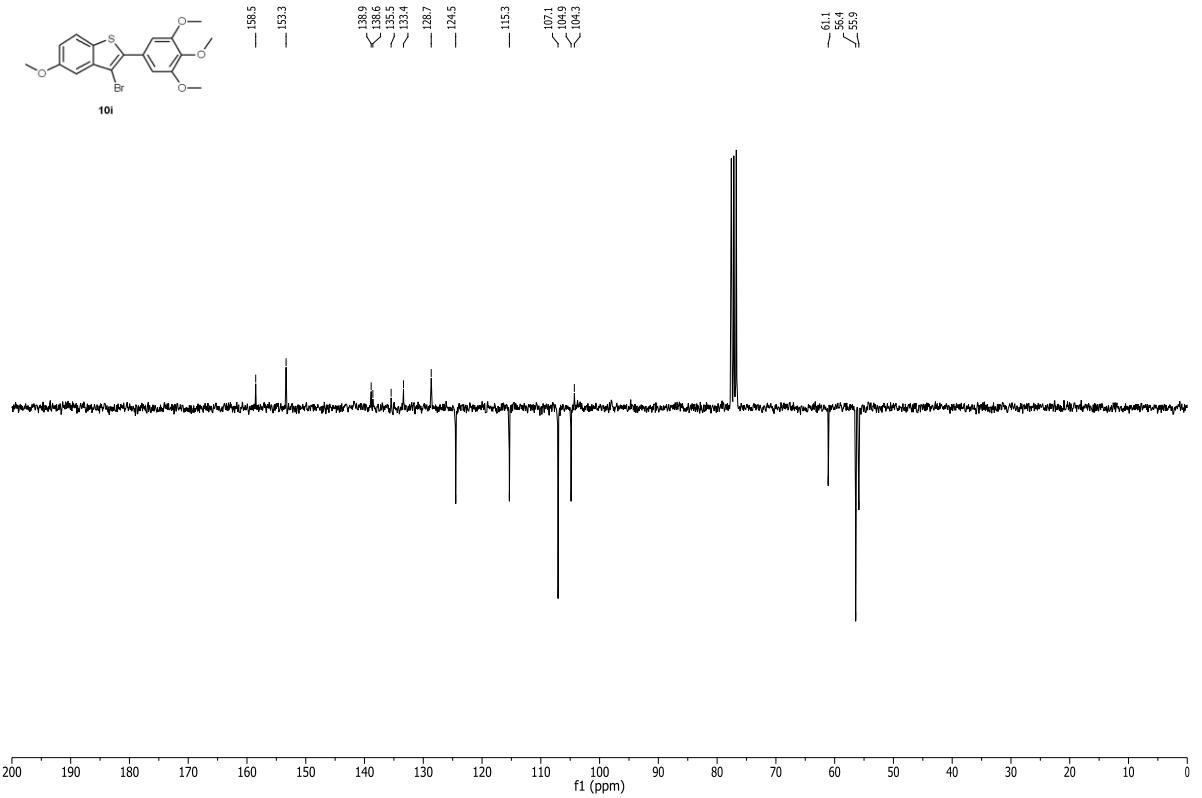

Br
O
S
O
O
10g
7.74
7.70
7.67
7.26
7.26
7.16
7.13
7.10
7.09
7.07
7.06
5.24
3.88
3.53
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

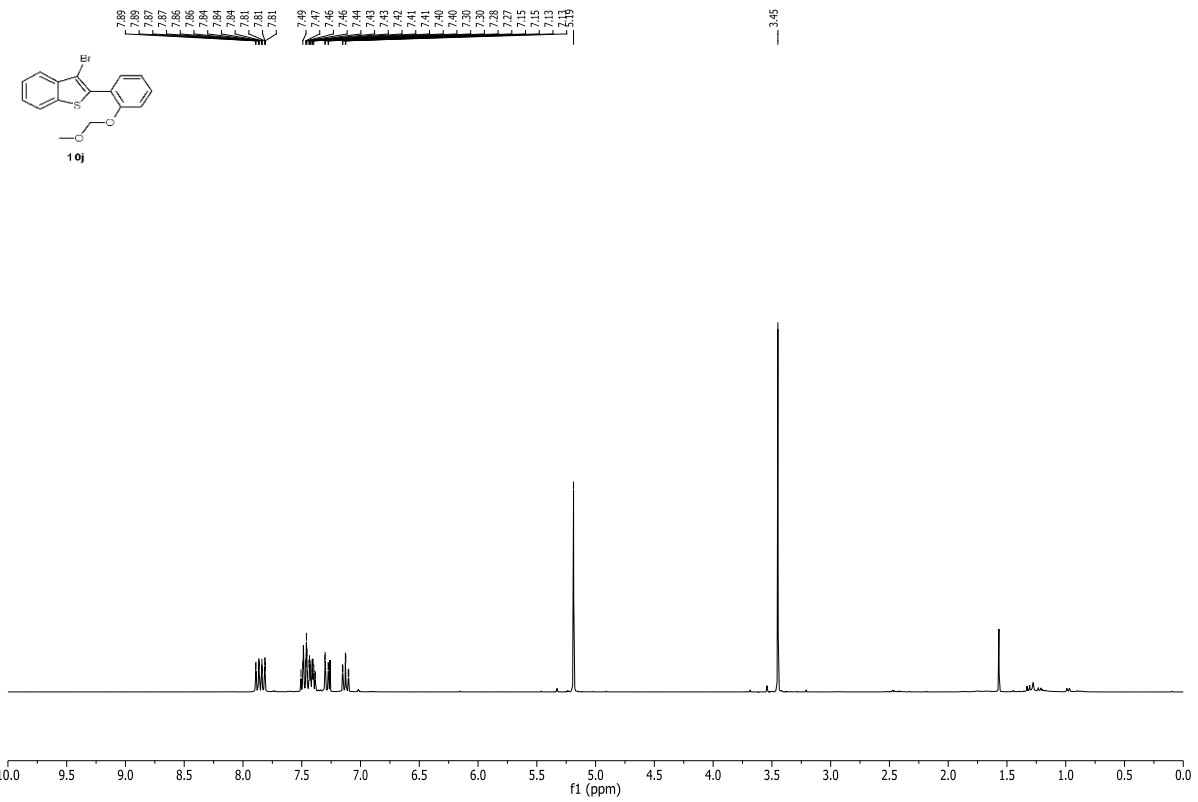

Br
O
S
O
O
10g
158.25
157.50
138.80
135.24
133.72
130.83
126.80
124.29
116.30
115.16
104.73
103.86
94.40
56.23
55.77
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

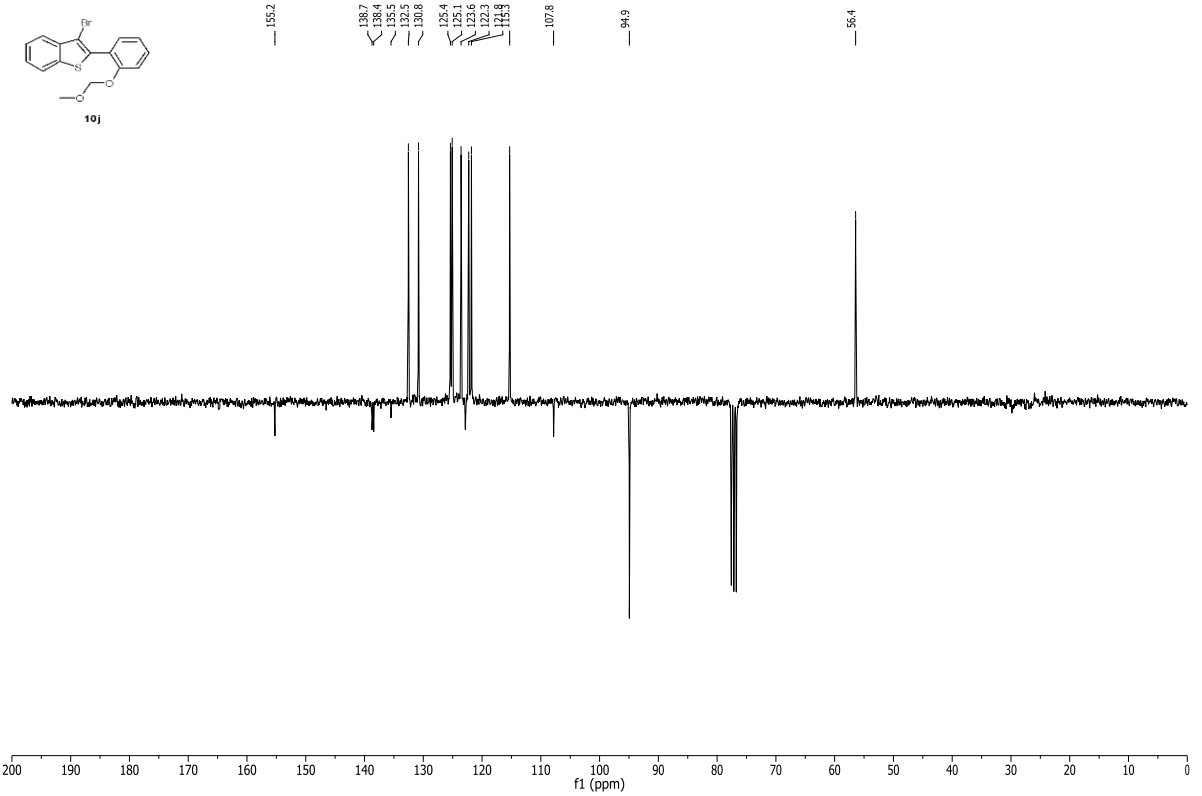

10h
7.73
7.70
7.60
7.58
7.57
7.49
7.48
7.25
7.25
7.09
7.08
7.05
7.03
3.88
3.88
2.36
f1 (ppm)

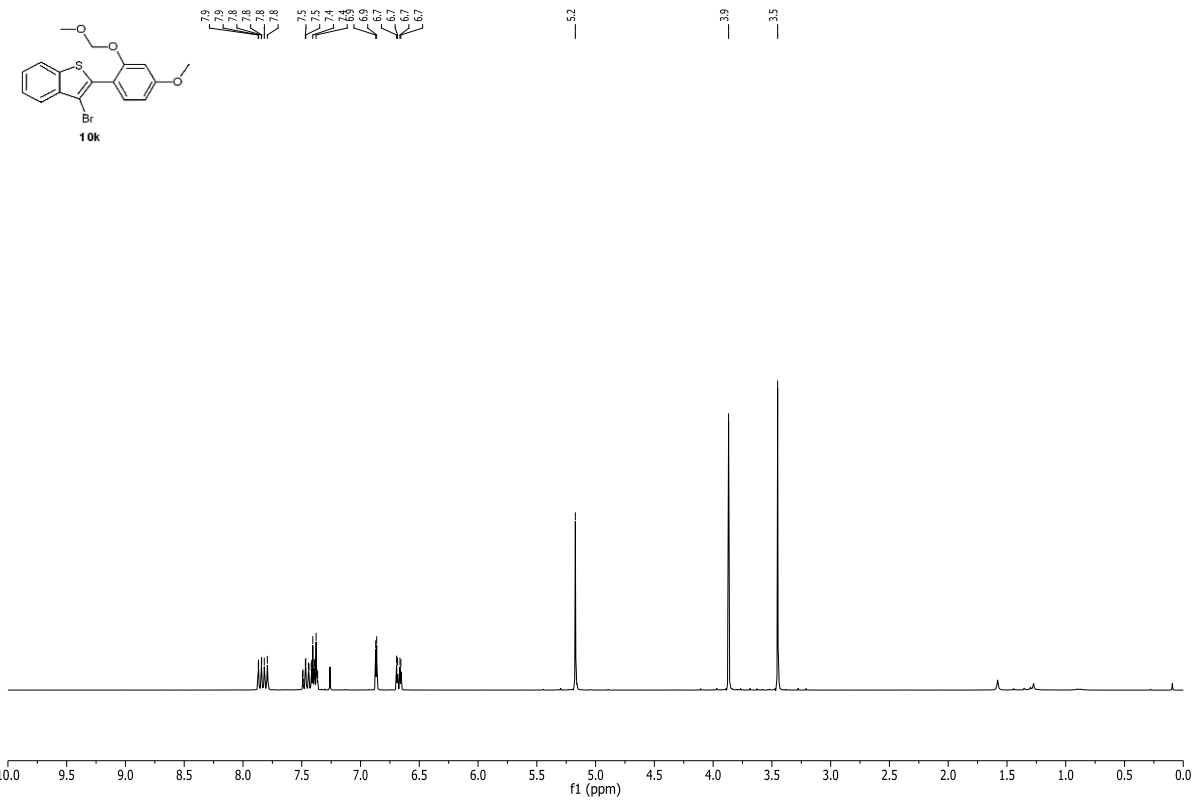

10h
169.0
158.3
151.4
139.6
138.8
134.2
133.2
128.2
126.0
124.3
123.9
115.2
112.4
104.7
104.2
56.1
55.8
20.8
f1 (ppm)

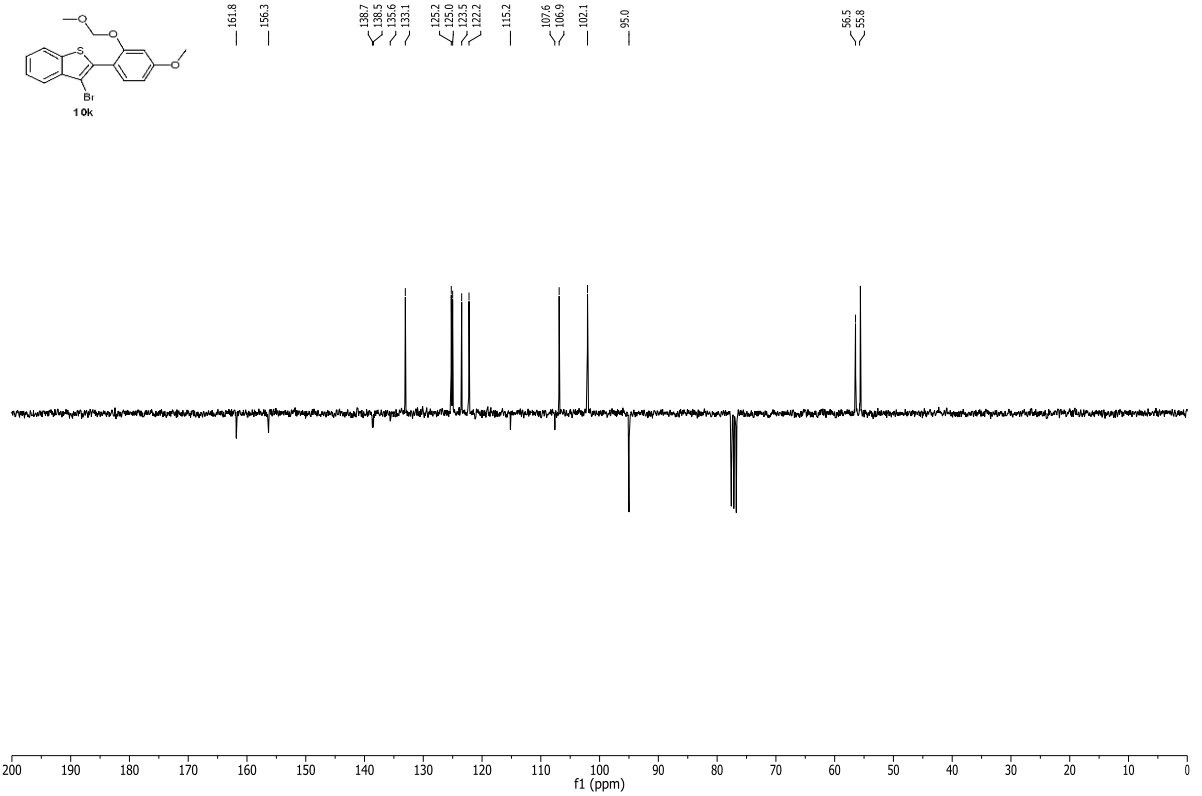

10i
7.8
7.7
7.3
7.3
7.1
7.1
7.1
7.1
7.0
3.9
3.9
3.9
f1 (ppm)


10i
158.5
153.3
138.9
138.6
135.5
133.4
128.7
124.5
115.3
107.1
104.9
104.3
61.1
56.4
55.9
f1 (ppm)

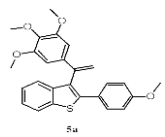

7.89
7.89
7.87
7.87
7.86
7.86
7.84
7.84
7.84
7.81
7.81
7.81
7.49
7.47
7.46
7.46
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.30
7.30
7.28
7.27
7.15
7.15
7.13
5.19
5.19
3.45
Br
O
O
10j
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


155.2
138.7
138.4
135.5
132.5
130.8
125.4
125.1
123.6
122.3
115.3
115.3
107.8
94.9
56.4
Br
O
O
10j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


10k
7.9
7.9
7.8
7.8
7.8
7.8
7.5
7.5
7.4
7.4
6.9
6.9
6.7
6.7
6.7
6.7
5.2
3.9
3.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

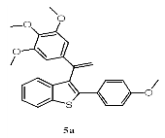

10k
161.8
156.3
138.7
138.5
135.6
133.1
125.2
125.0
123.5
122.2
115.2
107.6
106.9
102.1
95.0
56.5
55.8
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

III. ^{1}H and ^{13}C NMR Spectra for 2-aryl-3(α-styryl)benzo[*b*]thiophene 5a–t



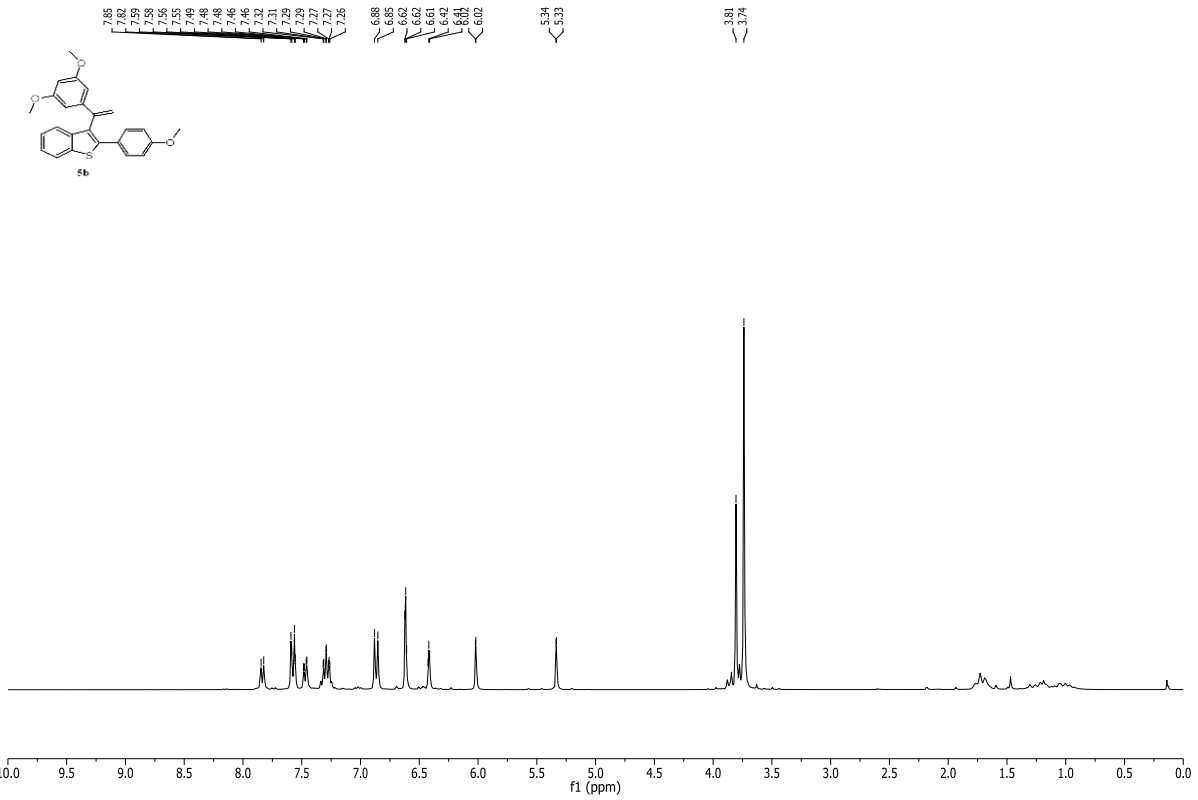
5u

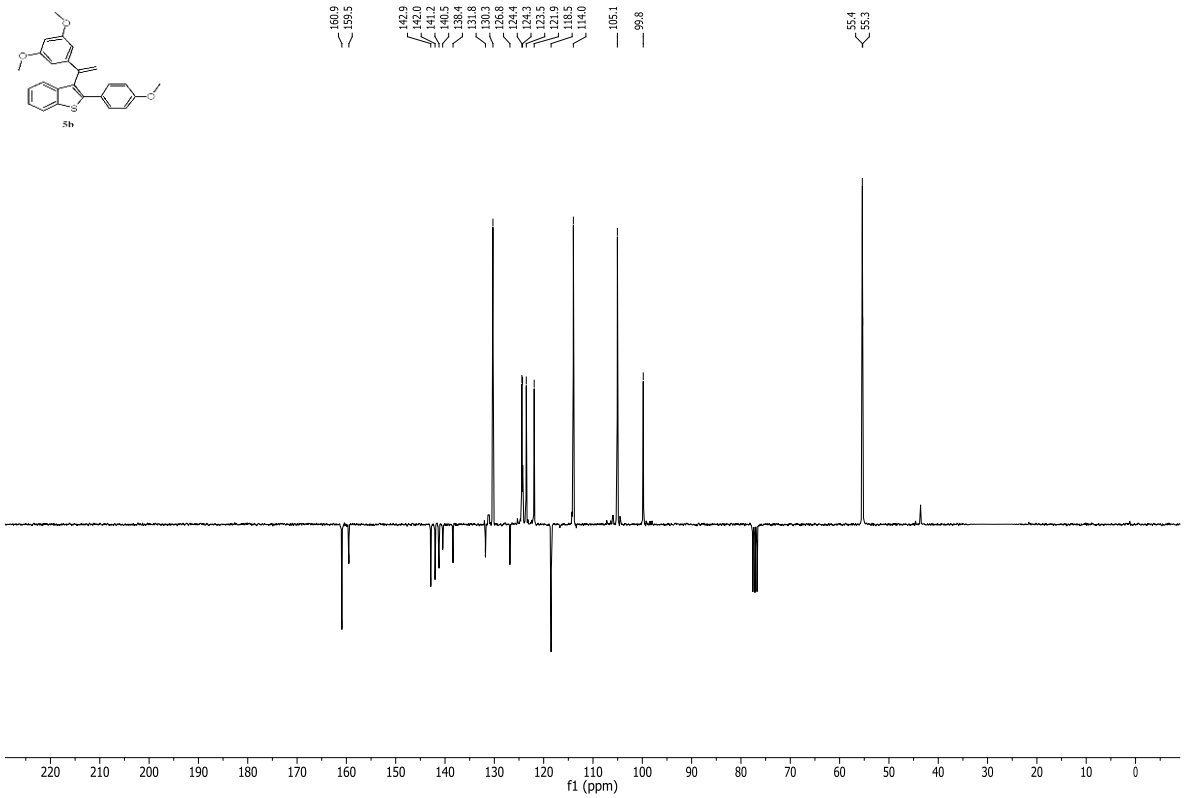
7.85
7.83
7.58
7.55
7.51
7.31
7.29
7.26
6.87
6.85
6.65
5.98
5.34
3.86
3.80
3.74
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

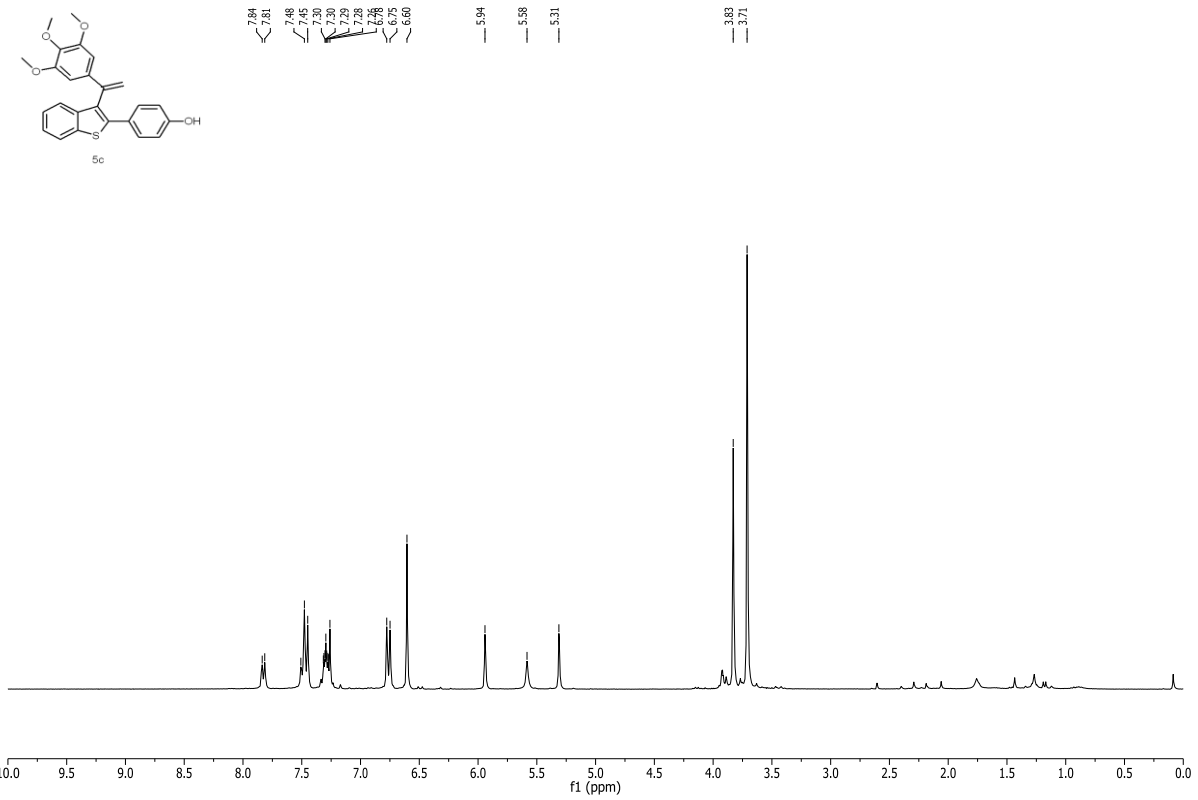


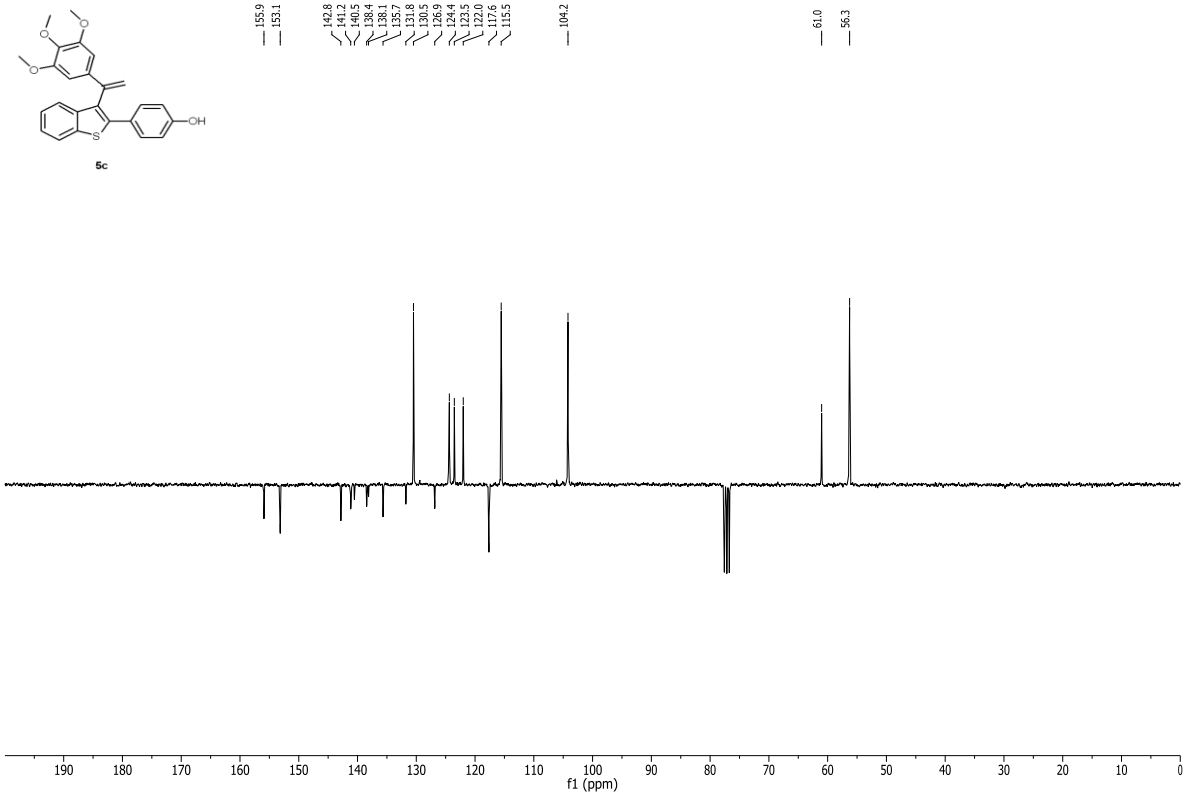
5u

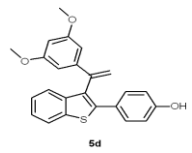
159.46
153.11
142.78
141.08
140.39
138.23
135.41
131.68
130.16
126.76
124.26
123.42
121.89
117.46
113.91
103.97
60.87
56.12
55.23
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.85
7.82
7.59
7.58
7.56
7.55
7.49
7.48
7.48
7.46
7.46
7.32
7.31
7.29
7.29
7.27
7.27
7.26
6.88
6.85
6.62
6.62
6.61
6.42
6.41
6.02
6.02
5.34
5.33
3.81
3.74
5b
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

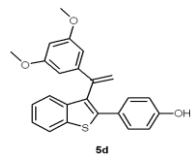

160.9
159.5
142.9
142.0
141.2
140.5
138.4
131.8
130.3
126.8
124.4
124.3
123.5
121.9
118.5
114.0
105.1
99.8
55.4
55.3
5b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.84
7.81
7.48
7.45
7.30
7.30
7.29
7.28
6.75
6.60
5.94
5.58
5.31
3.83
3.71
OH
S
5c
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

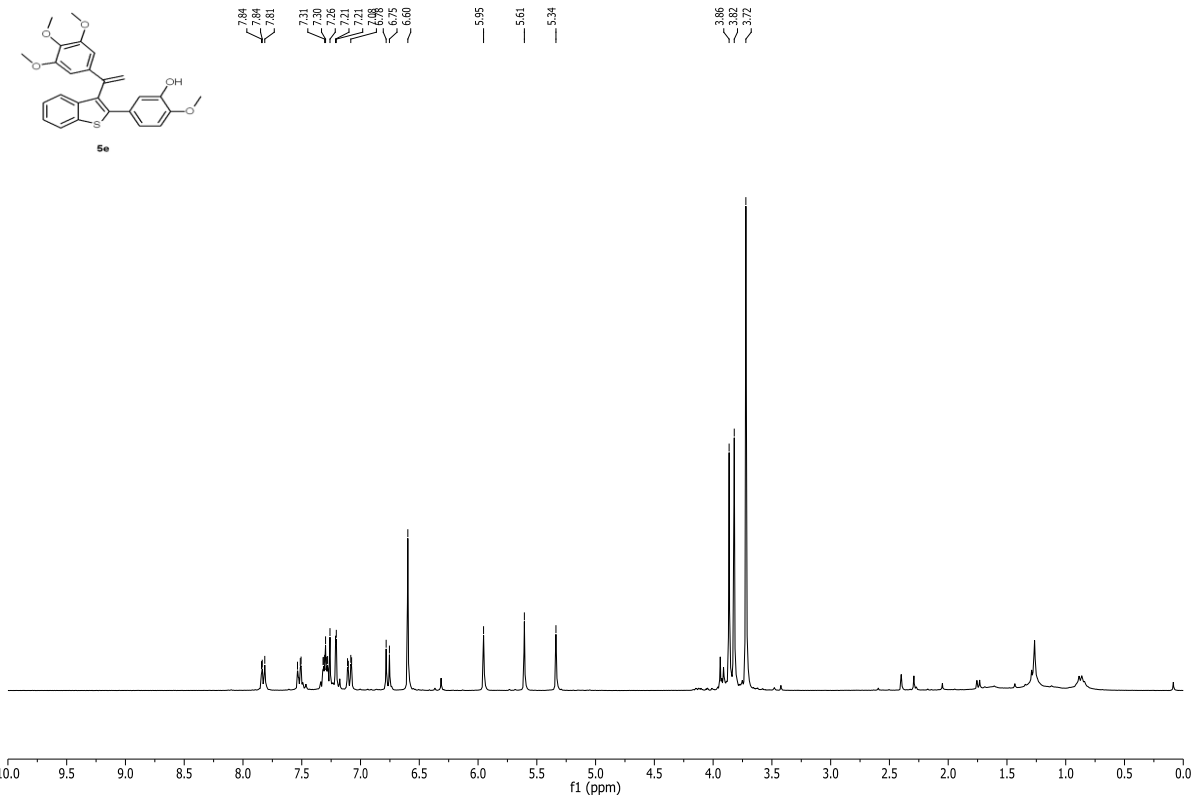

155.9
153.1
142.8
141.2
140.5
138.4
138.1
135.7
131.8
130.5
126.9
124.4
123.5
122.0
117.6
115.5
104.2
61.0
56.3
OH
S
5c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

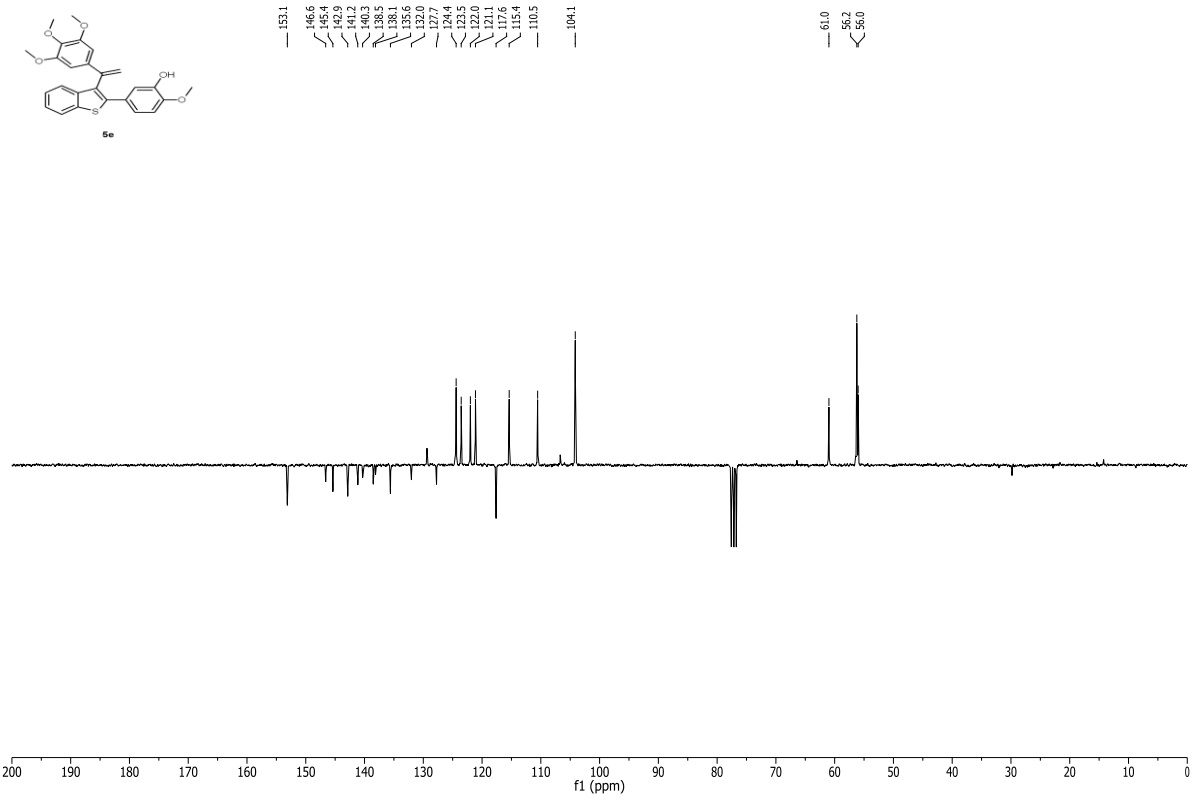

OH
S
5d

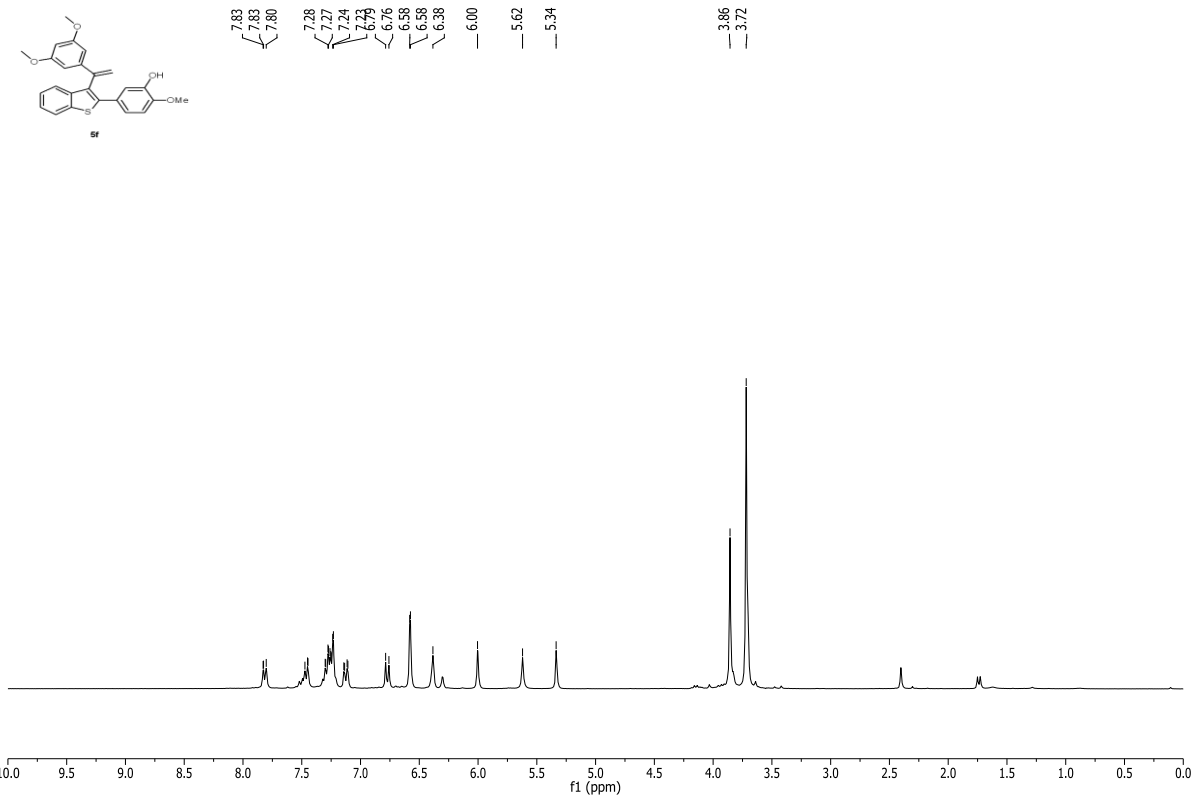
7.83
7.81
7.50
7.47
7.45
7.44
7.30
7.28
6.74
6.59
6.59
6.40
6.00
5.56
5.32
3.72
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

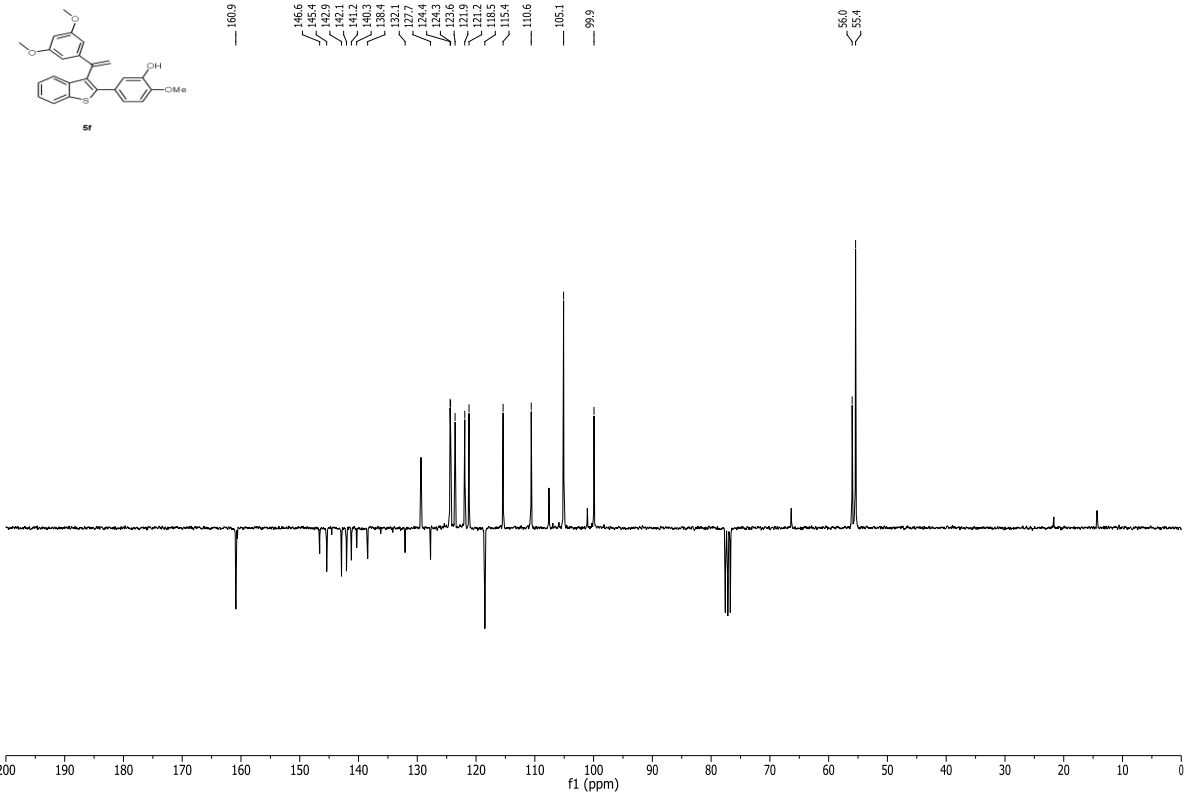

OH
S
5d

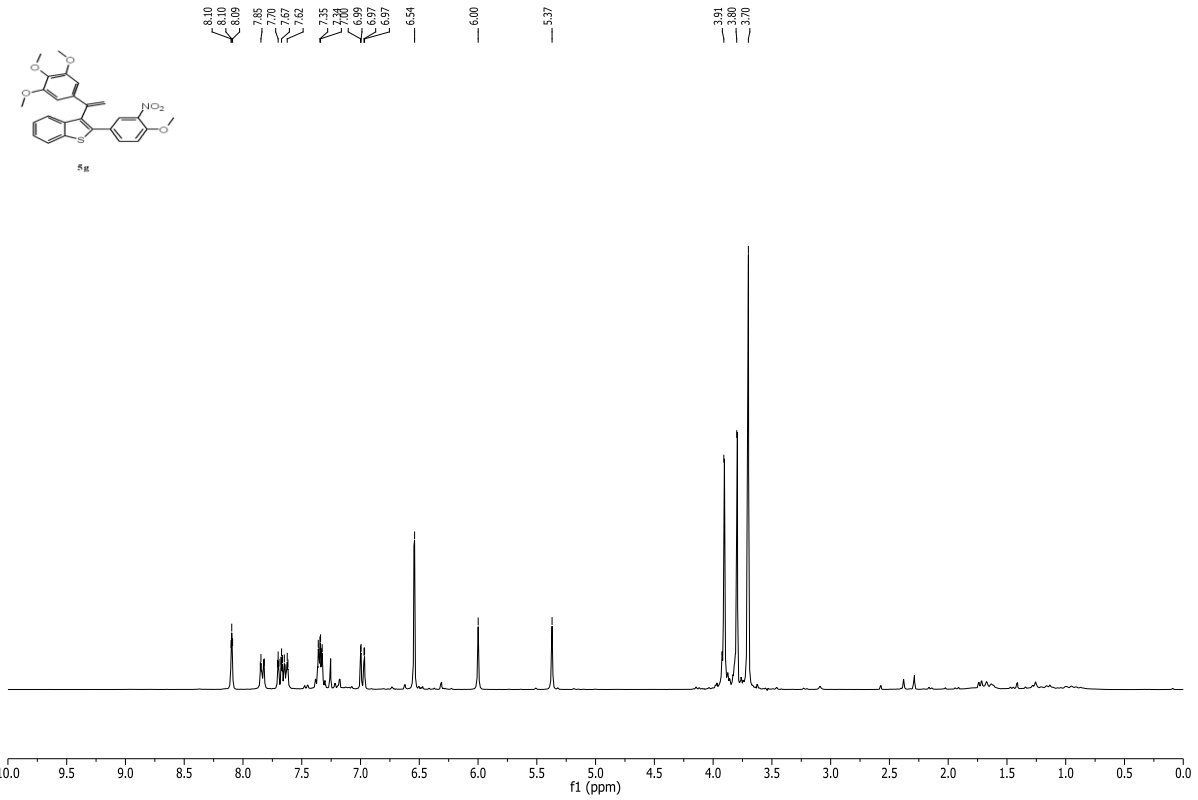
160.9
155.6
142.8
142.1
141.2
140.4
138.4
131.9
130.5
127.0
124.5
124.3
123.5
122.0
118.6
115.5
105.2
99.9
55.5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

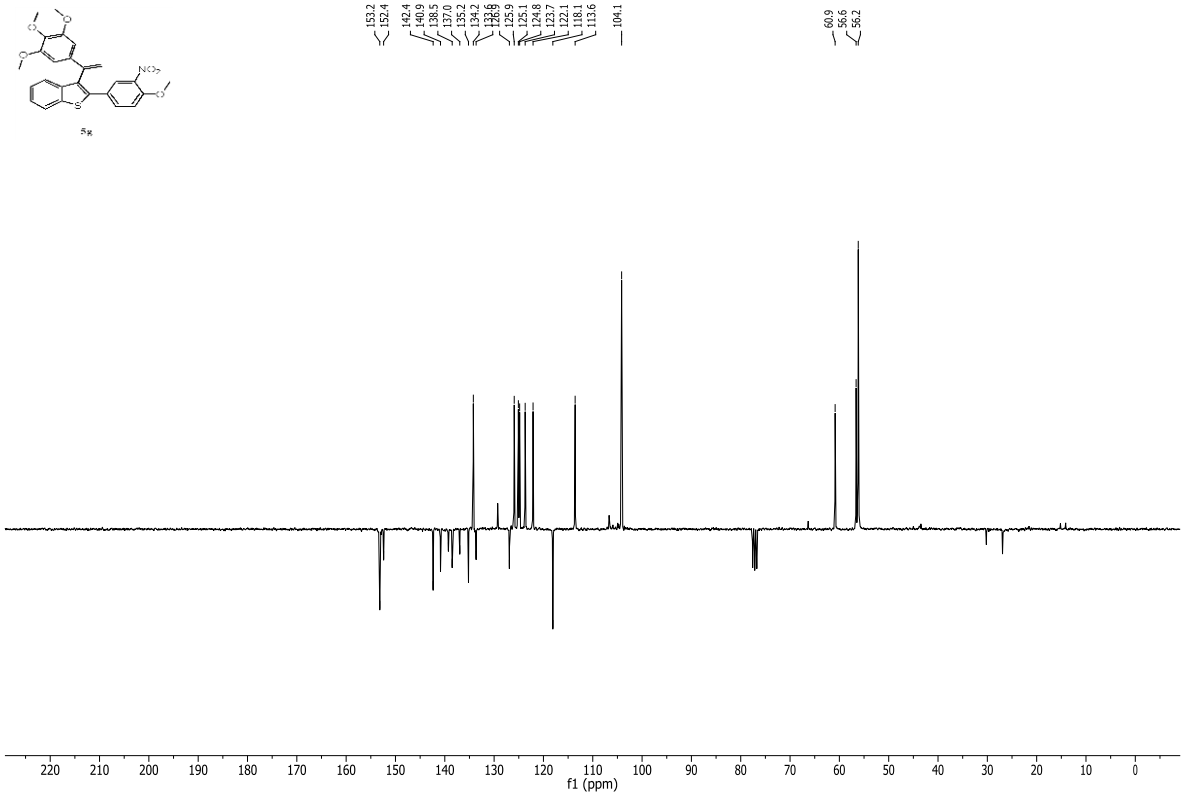

7.84
7.84
7.81
7.31
7.30
7.26
7.21
7.21
6.98
6.96
6.75
6.60
5.95
5.61
5.34
3.86
3.82
3.72
OH
S
5e
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

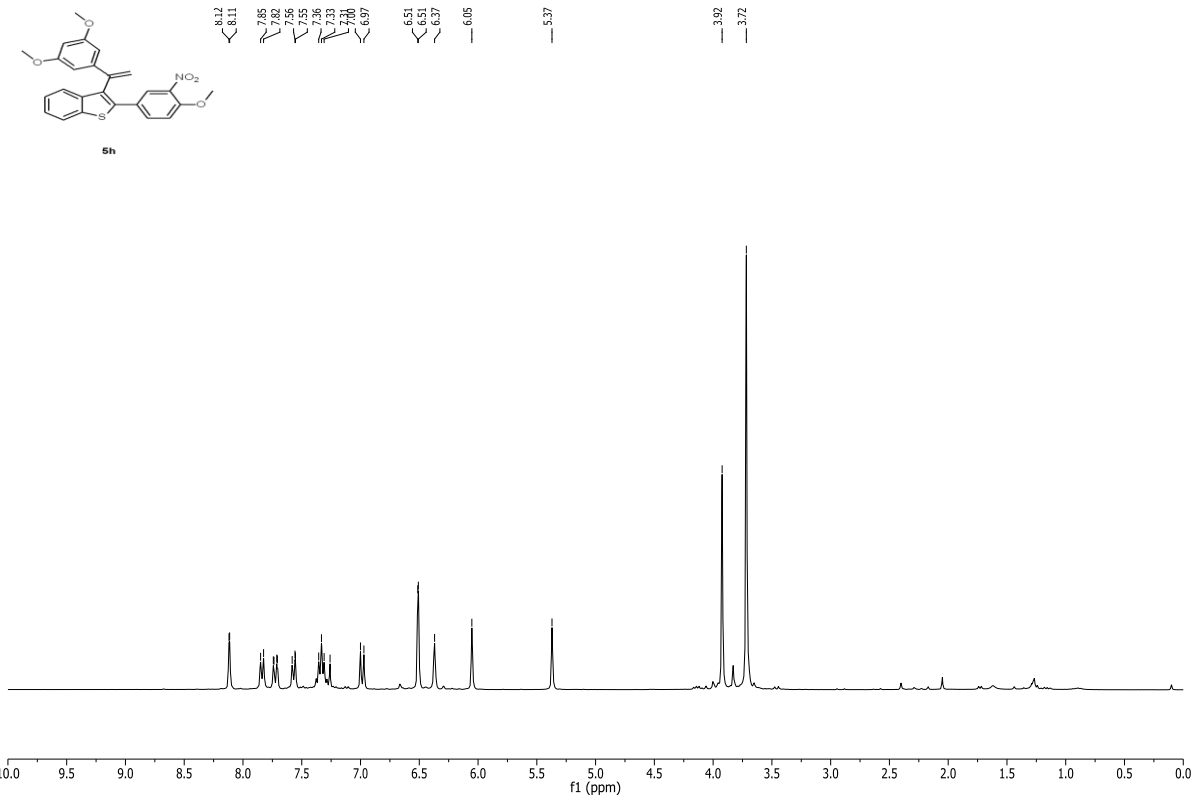

153.1
146.6
145.4
142.9
141.2
140.3
138.5
138.1
135.6
132.0
127.7
124.4
123.5
122.0
121.1
117.6
115.4
110.5
104.1
61.0
56.2
56.0
OH
S
5e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

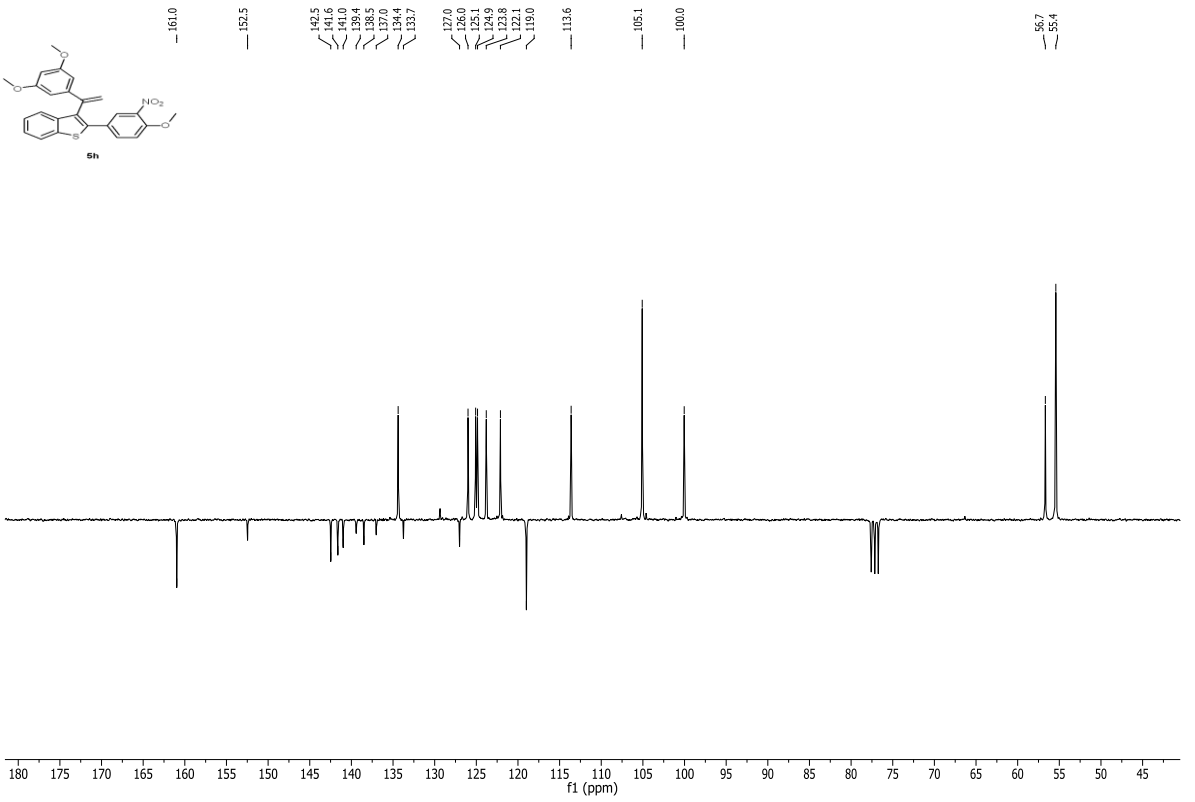

7.83
7.83
7.80
7.28
7.27
7.24
7.23
6.79
6.76
6.58
6.58
6.38
6.00
5.62
5.34
3.86
3.72
OH
OMe
S
5f
f1 (ppm)

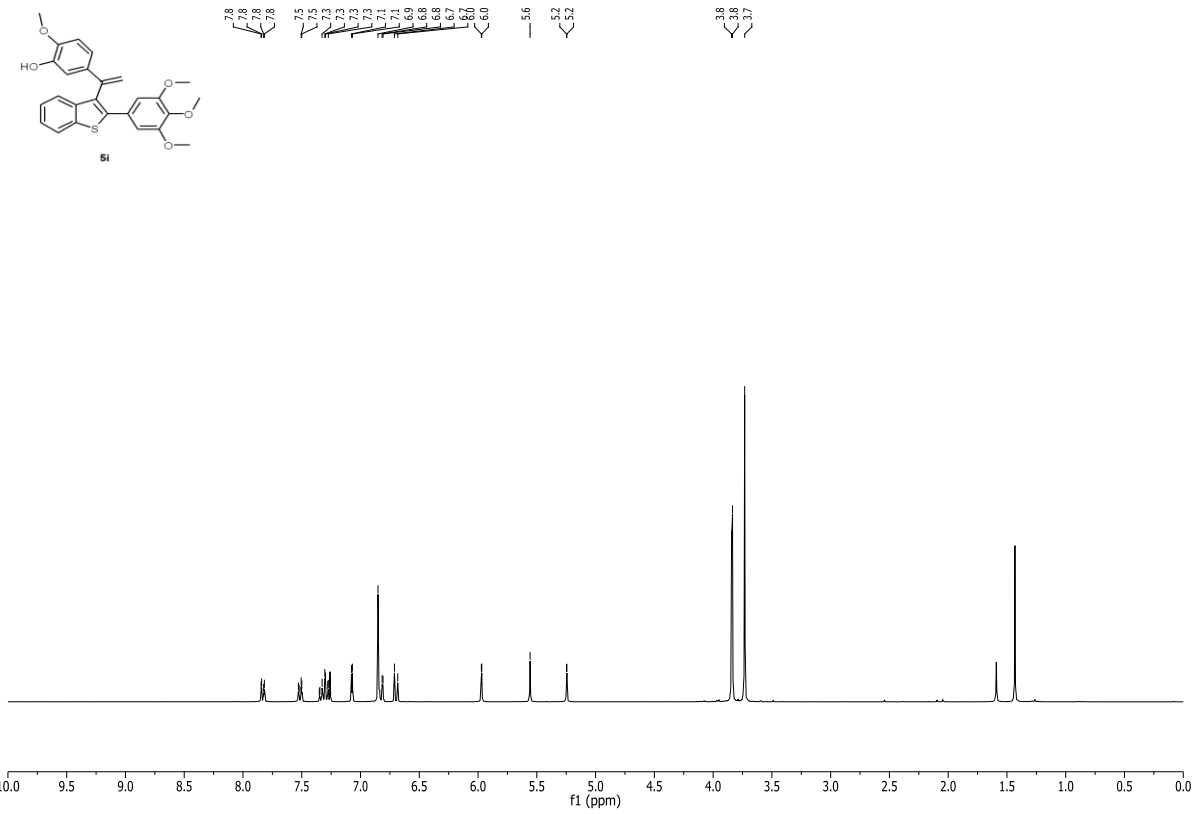

160.9
146.6
145.4
142.9
142.1
141.2
140.3
138.4
132.1
127.7
124.4
124.3
123.6
121.9
121.2
118.5
115.4
110.6
105.1
99.9
56.0
55.4
OH
OMe
S
5f
f1 (ppm)


8.10
8.10
8.09
7.85
7.70
7.67
7.62
7.35
7.34
7.00
6.99
6.97
6.97
6.54
6.00
5.37
3.91
3.90
3.70
NO2
S
5g
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


153.2
152.4
142.4
140.9
138.5
137.0
135.2
134.2
131.6
126.9
125.9
125.1
124.8
123.7
122.1
118.1
113.6
104.1
60.9
56.6
56.2
NO2
S
5g
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.12
8.11
7.85
7.82
7.56
7.55
7.36
7.33
7.31
7.30
6.97
6.51
6.51
6.37
6.05
5.37
3.92
3.72
5h
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.0
152.5
142.5
141.6
141.0
139.4
138.5
137.0
134.4
133.7
127.0
126.0
125.1
124.9
123.8
122.1
119.0
113.6
105.1
100.0
56.7
55.4
5h
180
175
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
f1 (ppm)


7.8
7.8
7.8
7.8
7.5
7.5
7.3
7.3
7.3
7.3
7.3
7.1
7.1
6.9
6.8
6.8
6.7
6.7
6.0
6.0
5.6
5.2
5.2
3.8
3.8
3.7
HO
O
O
O
O
S
5i
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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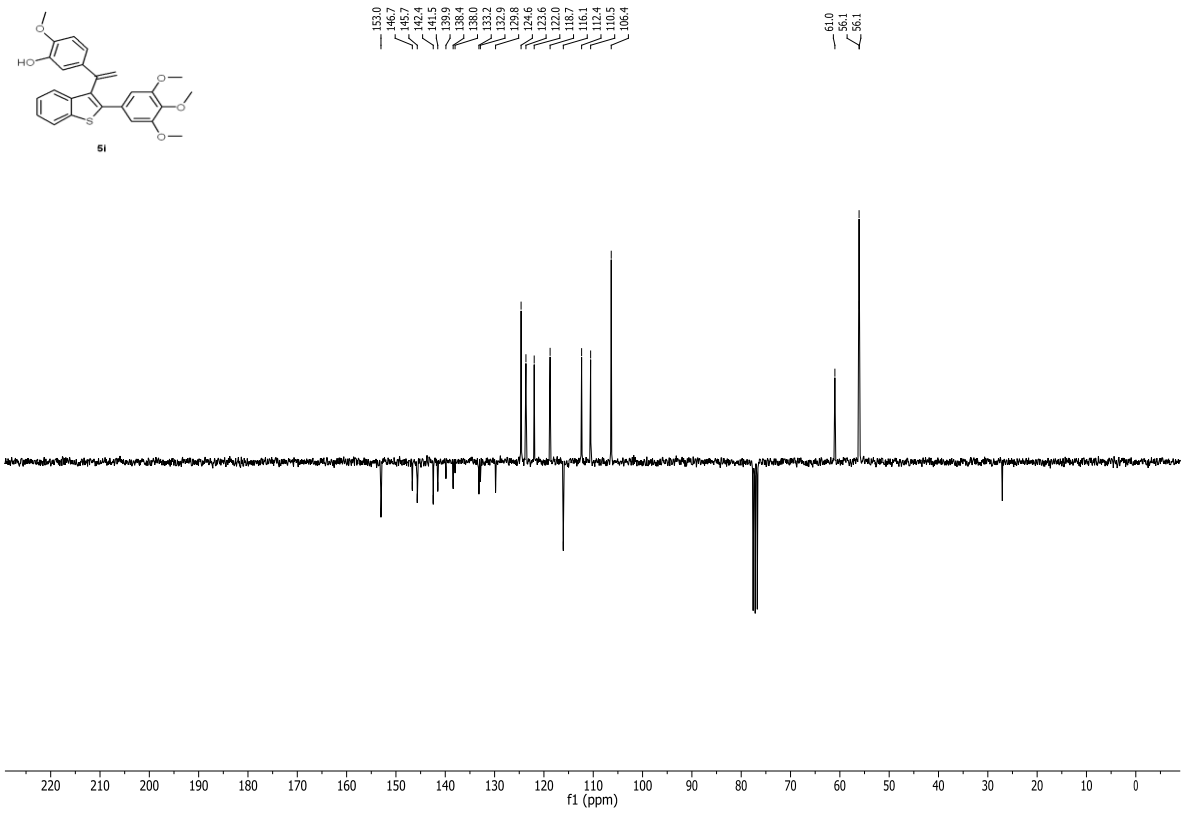
f1 (ppm)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139.9
138.4
138.0
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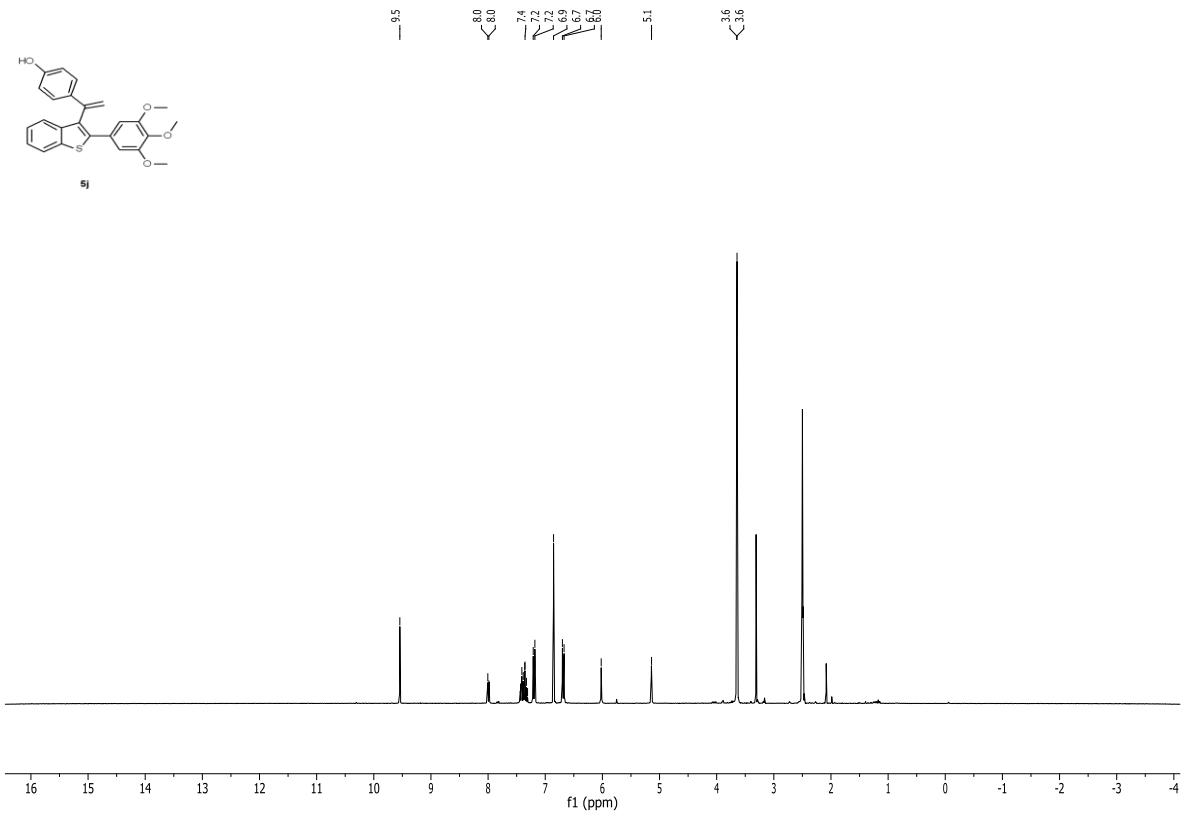
132.9
129.8
124.6
123.6
122.0
118.7
116.1
112.4
110.5
106.4
61.0
56.1
56.1
HO
O
O
O
O
S
5i
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.0
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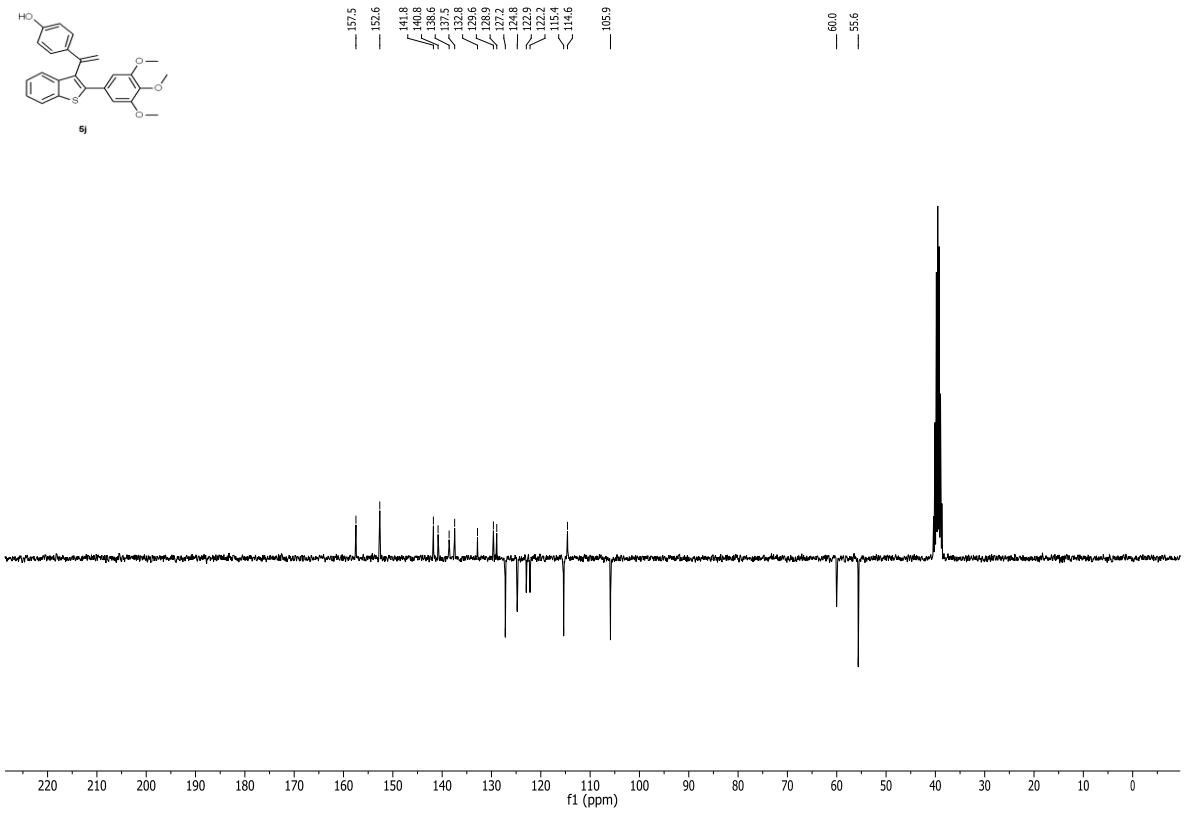
7.2
7.2
6.9
6.7
6.7
6.0
5.1
3.6
3.6
HO
O
O
O
S
5j
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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140.8
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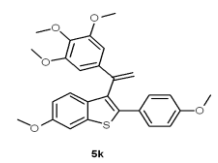
137.5
132.8
129.6
128.9
127.2
124.8
122.9
122.2
115.4
114.6
105.9
60.0
55.6
HO
O
O
O
S
5j
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


5k

7.52
7.49
7.37
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7.31
7.26
6.93
6.92
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6.62
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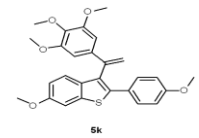
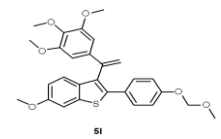
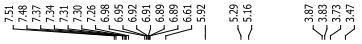
5.30
3.87
3.84
3.79
3.73
f1 (ppm)


5k

159.3
157.4
153.2
142.9
139.7
138.1
137.8
135.5
135.2
131.3
130.0
127.0
124.2
117.4
114.3
113.9
104.6
104.0
61.0
56.2
55.7
55.3
f1 (ppm)

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6.98
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6.89
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5.29
5.16
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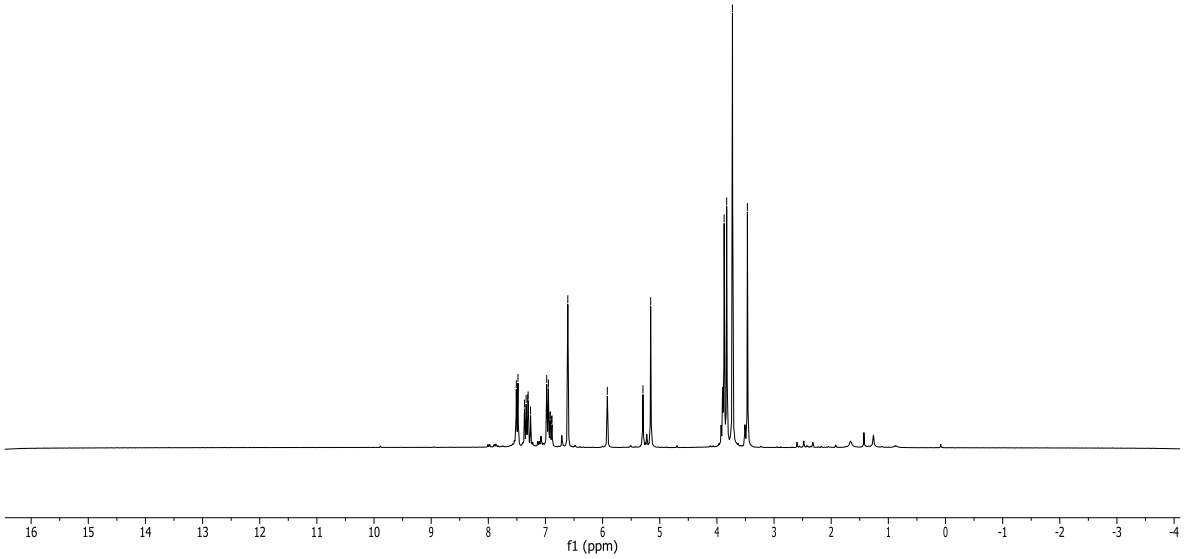
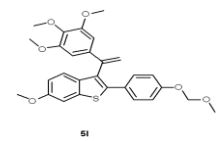
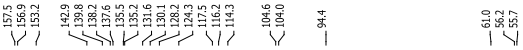
3.83
3.73
3.47


16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

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156.9
153.2
142.9
139.8
138.2
137.6
135.5
135.2
131.6
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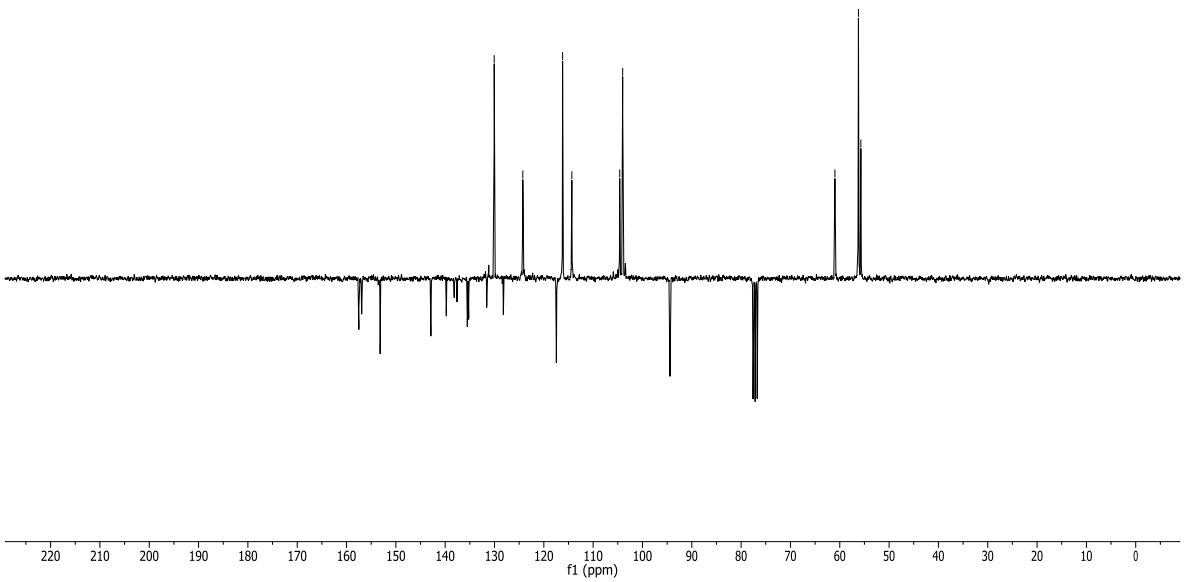
128.2
124.3
117.5
116.2
114.3
104.6
104.0
94.4
61.0
56.2
55.7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210
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180
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110
100
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70
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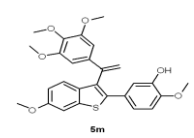
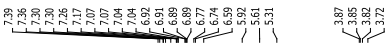
50
40
30
20
10
0
f1 (ppm)


5m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7.17
7.07
7.07
7.04
7.04
6.92
6.91
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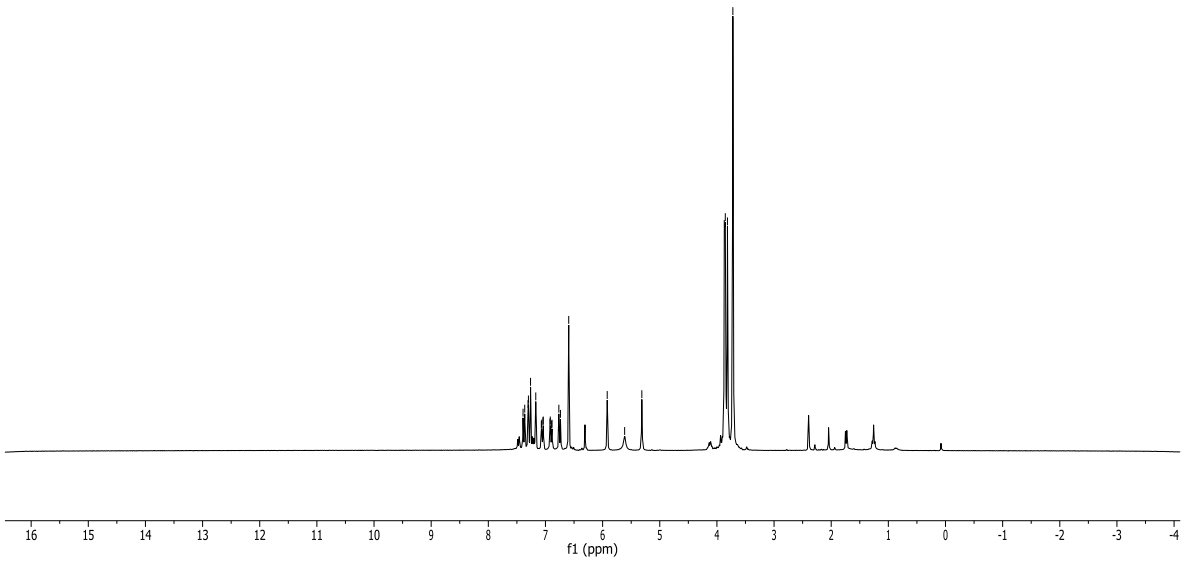
5.61
5.31
3.87
3.85
3.82
3.72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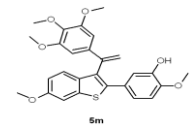
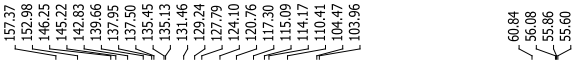
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


5m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135.13
131.46
129.24
127.79
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115.09
114.17
110.41
104.47
103.96
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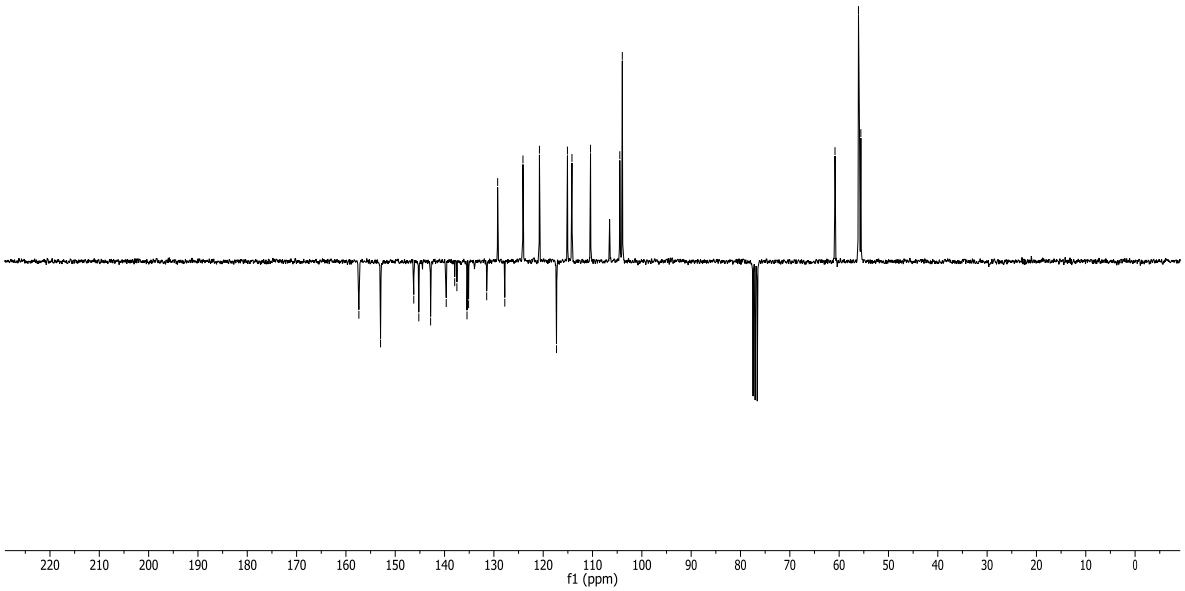
56.08
55.86
55.60


220
210
200
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180
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100
90
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70
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50
40
30
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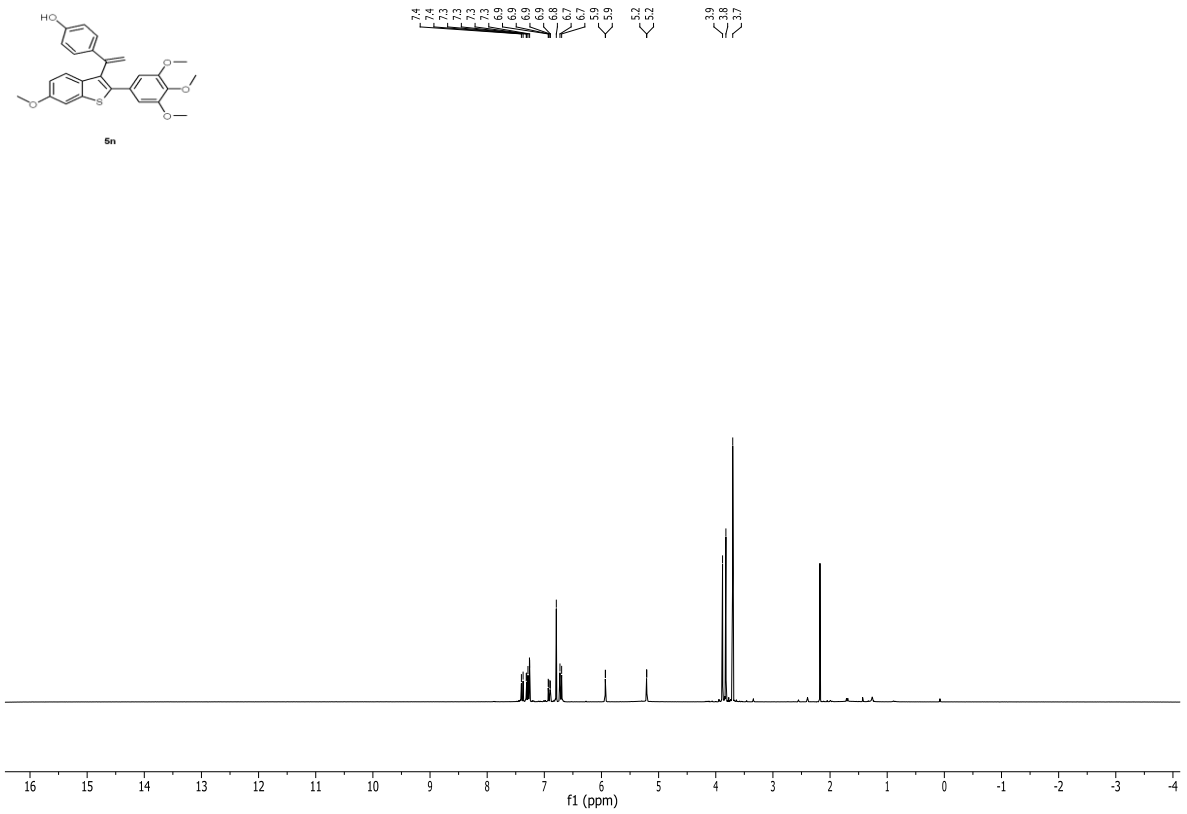
10
0
f1 (ppm)


5n
7.4
7.4
7.3
7.3
7.3
7.3
6.9
6.9
6.9
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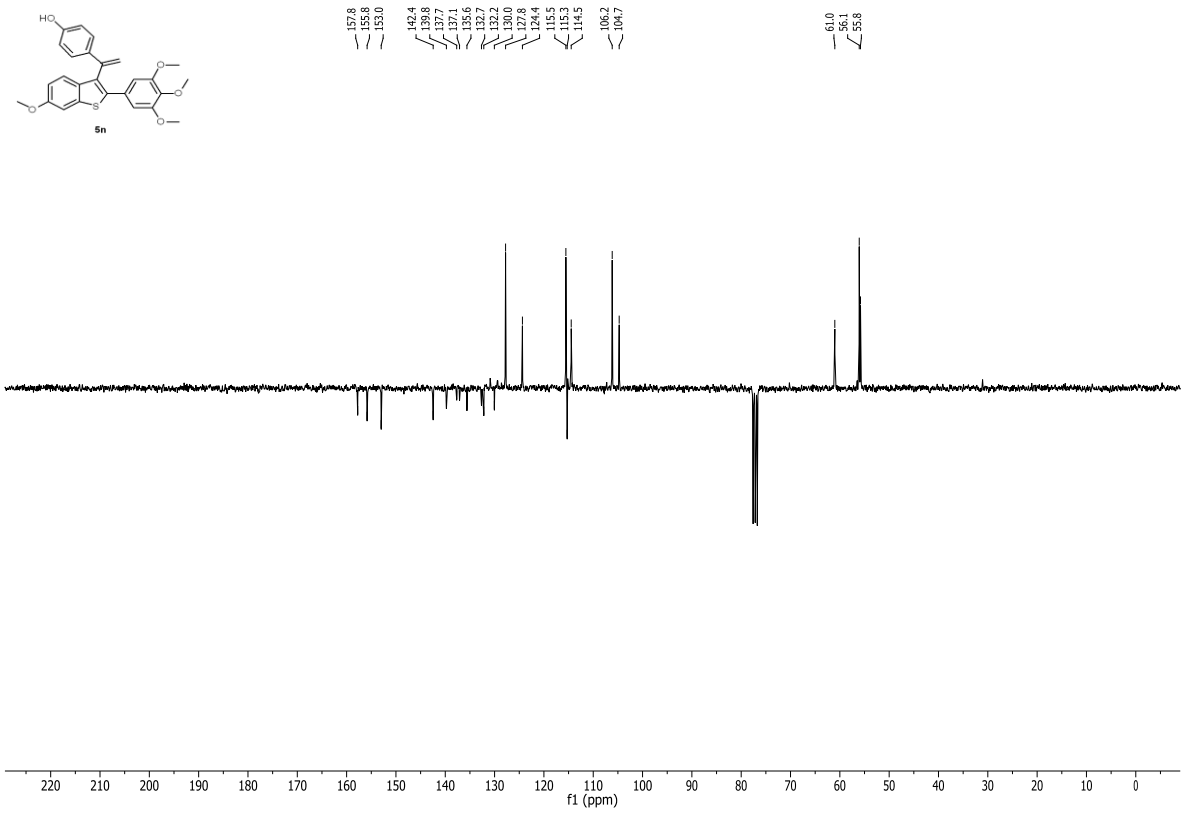
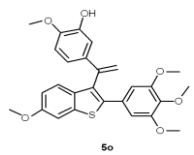
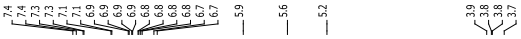
6.7
6.7
5.9
5.9
5.2
5.2
3.9
3.8
3.7
f1 (ppm)


5n
157.8
155.8
153.0
142.4
139.8
137.7
137.1
135.6
132.7
132.2
130.0
127.8
124.4
115.5
115.3
114.5
106.2
104.7
61.0
56.1
55.8
f1 (ppm)


OH
O
O
O
O
S
5o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7.4
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7.3
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7.1
6.9
6.9
6.9
6.9
6.8
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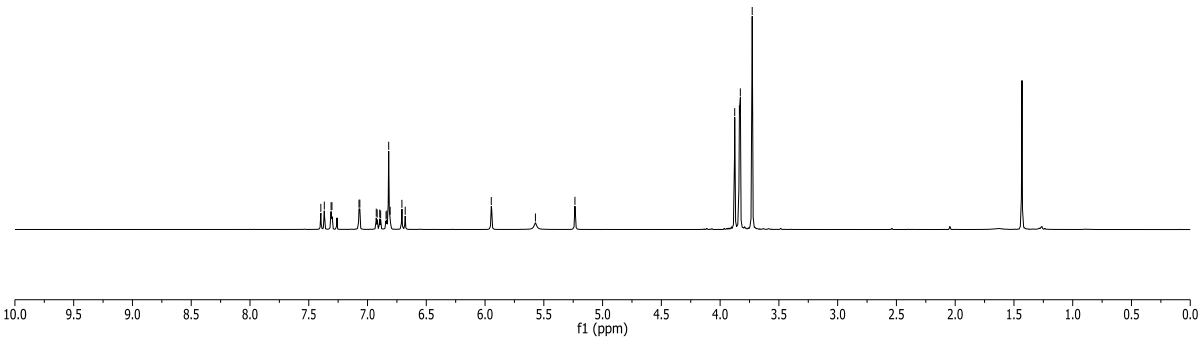
5.6
5.2
3.9
3.8
3.8
3.7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9.0
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7.5
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6.5
6.0
5.5
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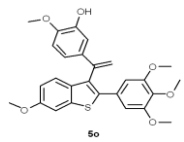
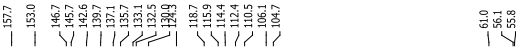
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OH
O
O
O
O
S
5o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135.7
133.1
132.5
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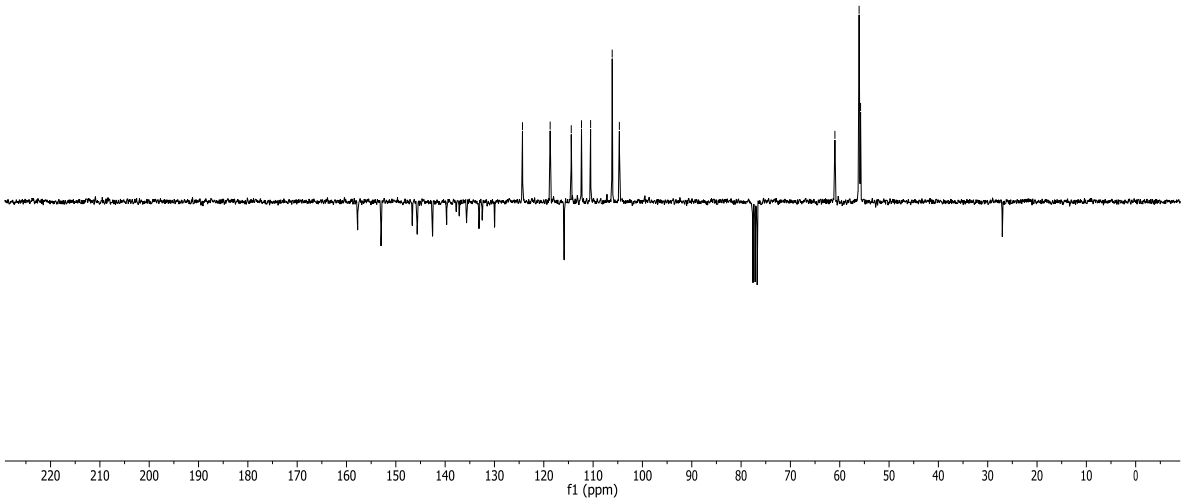
106.1
104.7
61.0
56.1
55.8


220
210
200
190
180
170
160
150
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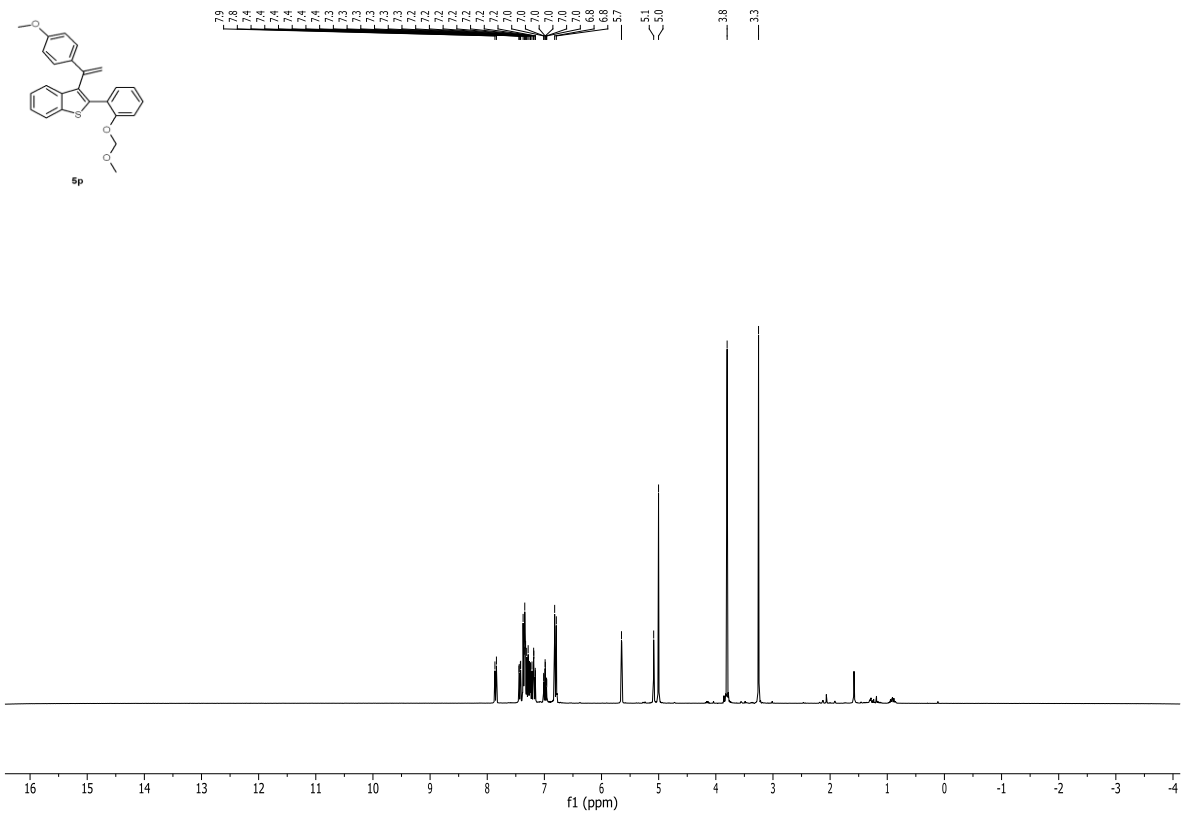
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


5p
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7.4
7.4
7.4
7.4
7.3
7.3
7.3
7.3
7.3
7.2
7.2
7.2
7.2
7.2
7.2
7.2
7.0
7.0
7.0
7.0
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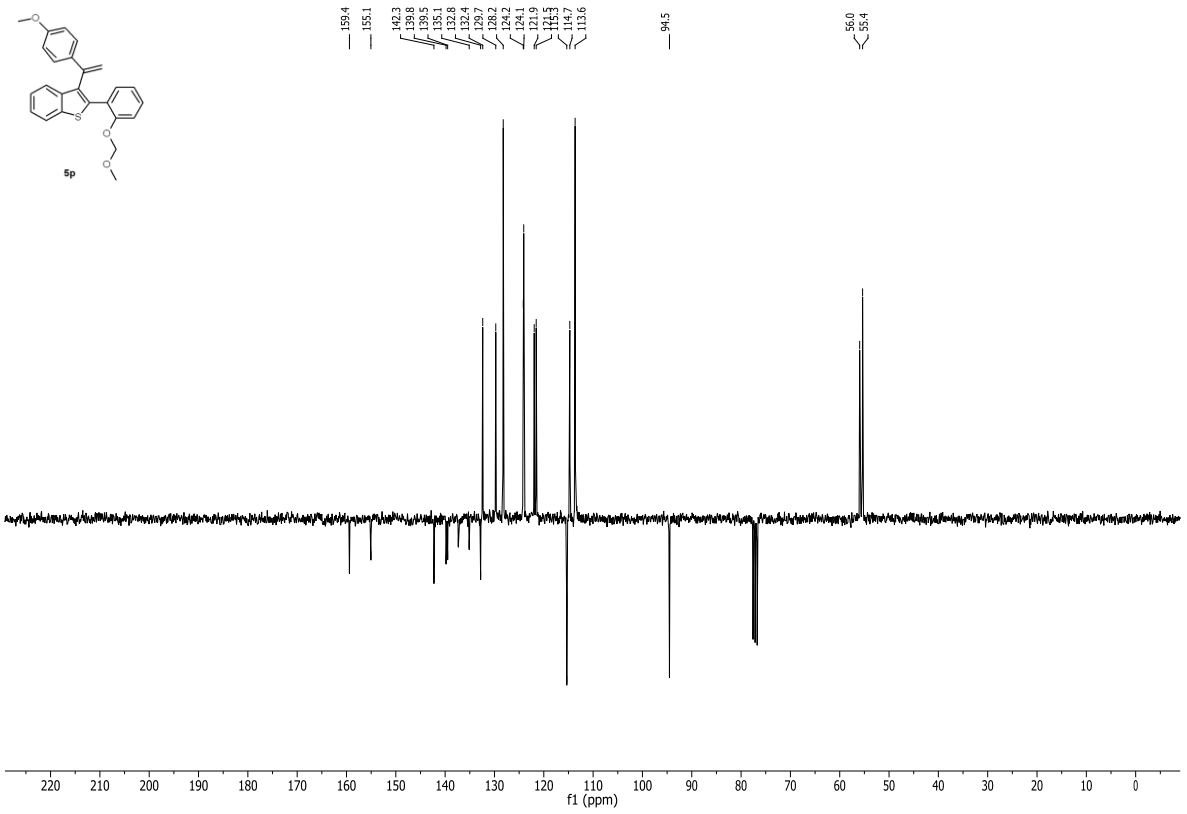
7.0
6.8
6.8
5.7
5.1
5.0
3.8
3.3
f1 (ppm)


5p
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155.1
142.3
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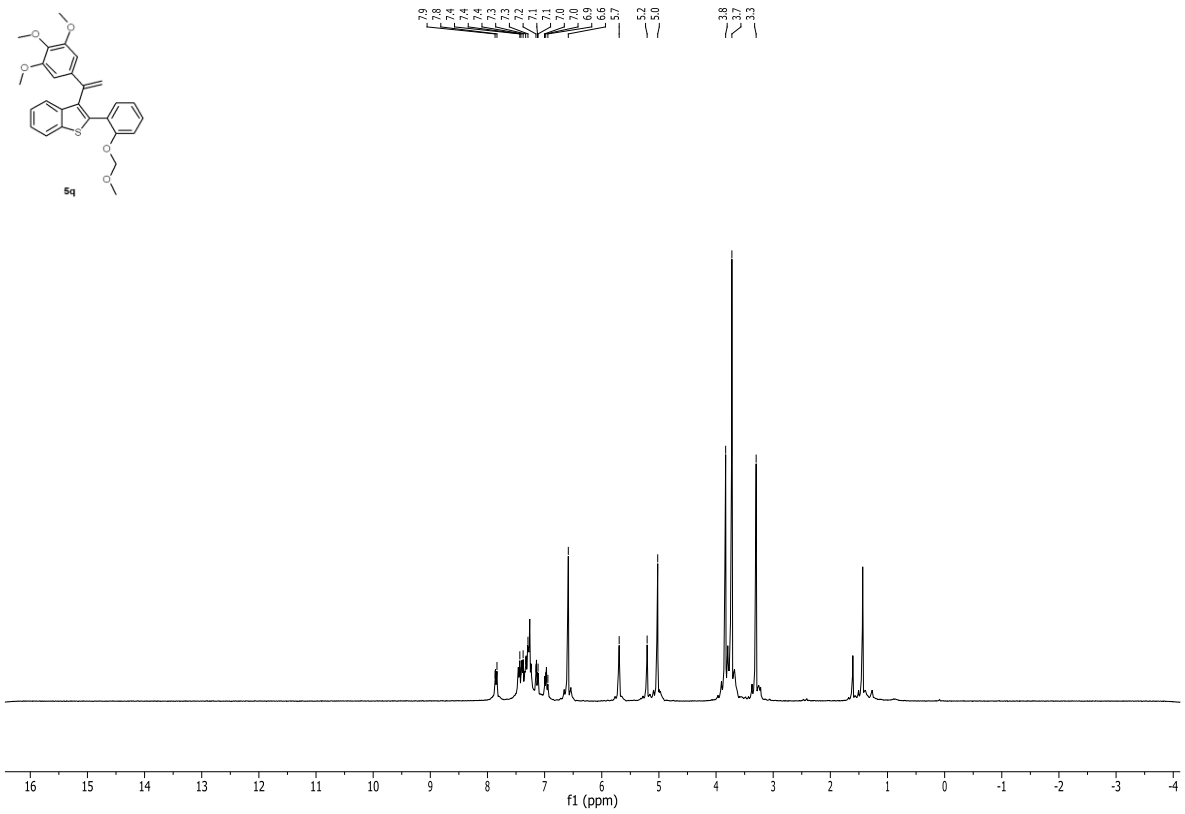
139.5
135.1
132.8
132.4
129.7
128.2
124.2
124.1
121.9
115.5
115.3
114.7
113.6
94.5
56.0
55.4
f1 (ppm)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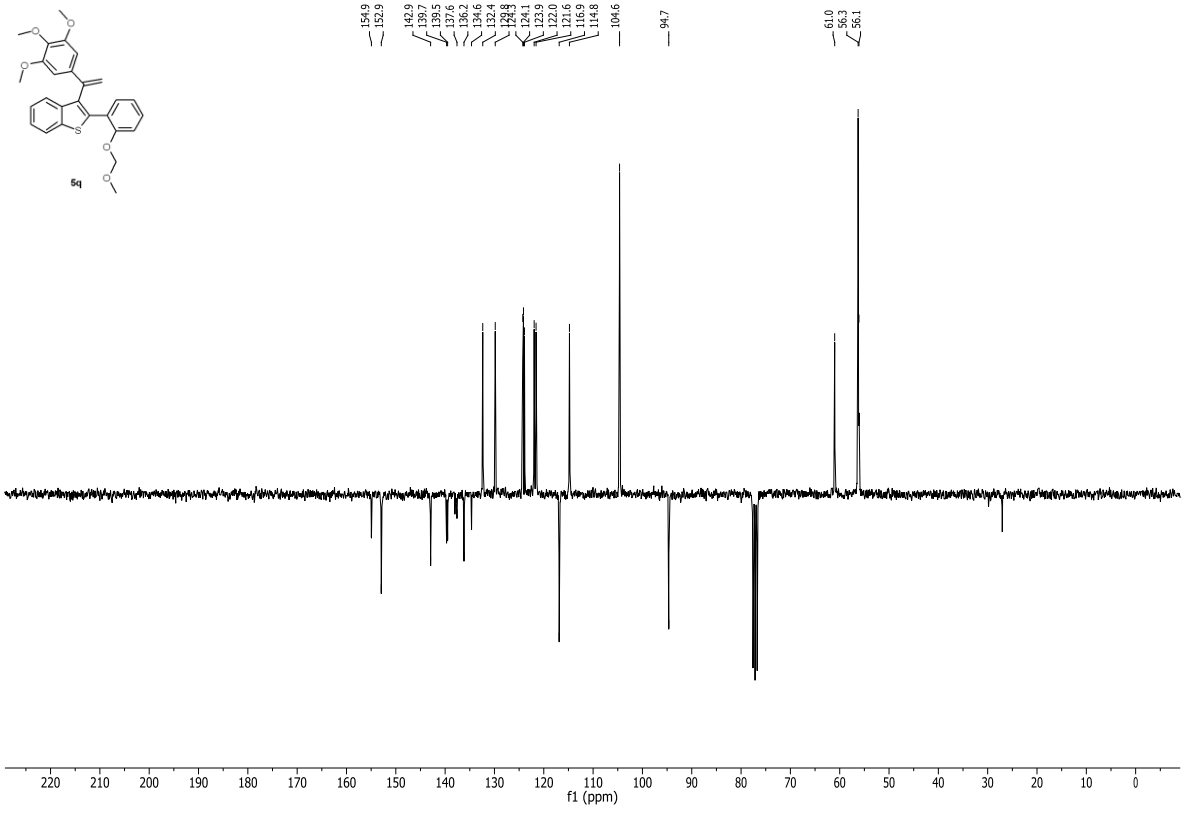
7.4
7.4
7.3
7.3
7.2
7.2
7.1
7.1
7.0
7.0
6.9
6.6
5.7
5.2
5.0
3.8
3.7
3.3
5q
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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152.9
142.9
139.7
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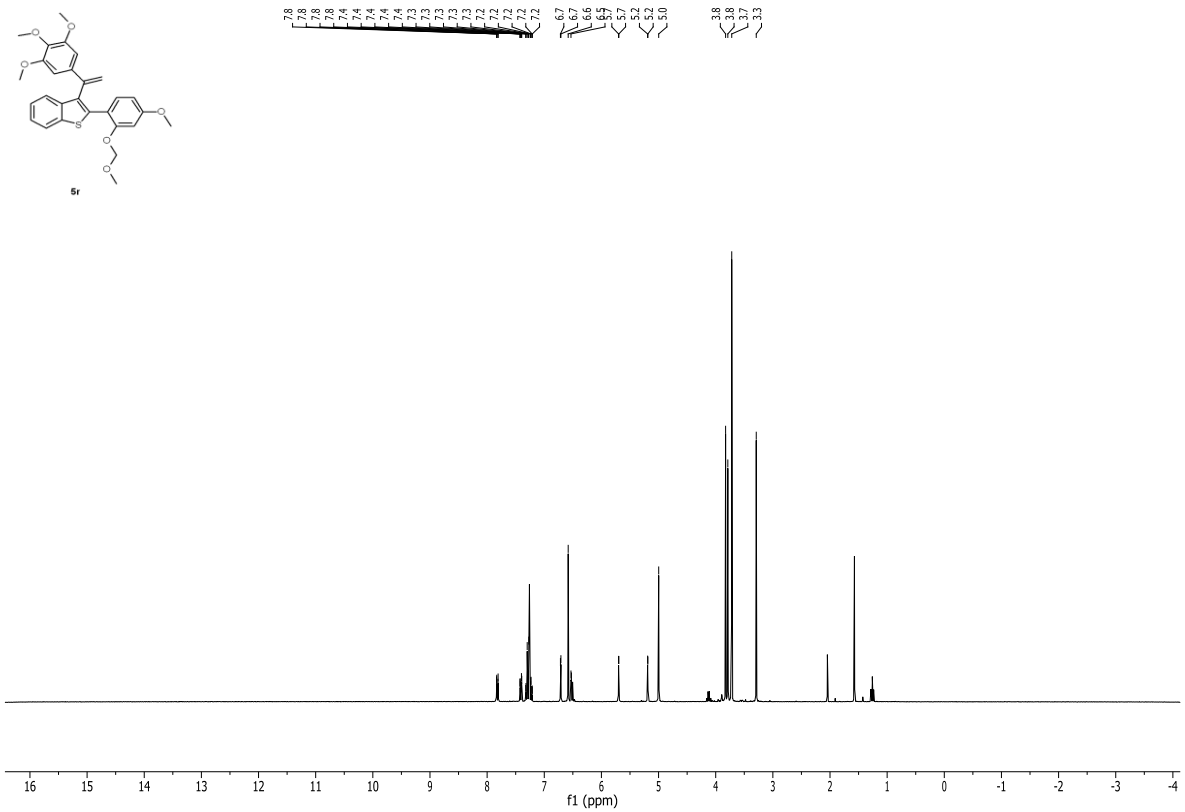
137.6
136.2
134.6
132.4
124.3
124.1
123.9
122.0
121.6
116.9
114.8
104.6
94.7
61.0
56.3
56.1
5q
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.4
7.3
7.3
7.3
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7.2
7.2
7.2
7.2
7.2
6.7
6.7
6.6
6.6
5.7
5.7
5.2
5.2
5.0
3.8
3.8
3.7
3.3
5r
16
15
14
13
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8
7
6
5
4
3
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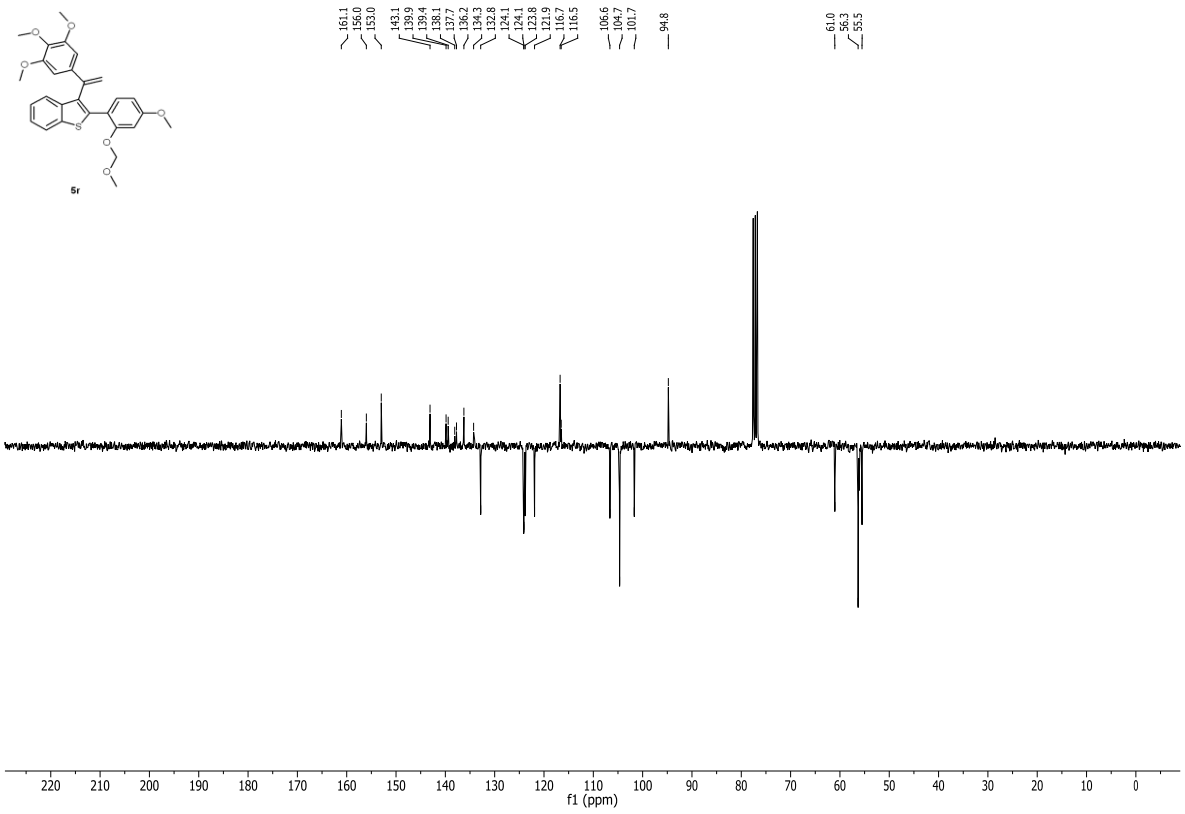
1
0
-1
-2
-3
-4
f1 (ppm)


161.1
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153.0
143.1
139.9
139.4
138.1
137.7
136.2
134.3
132.8
124.1
124.1
123.8
121.9
116.7
116.5
106.6
104.7
101.7
94.8
61.0
56.3
55.5
5r
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
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40
30
20
10
0
f1 (ppm)

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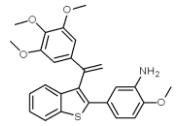
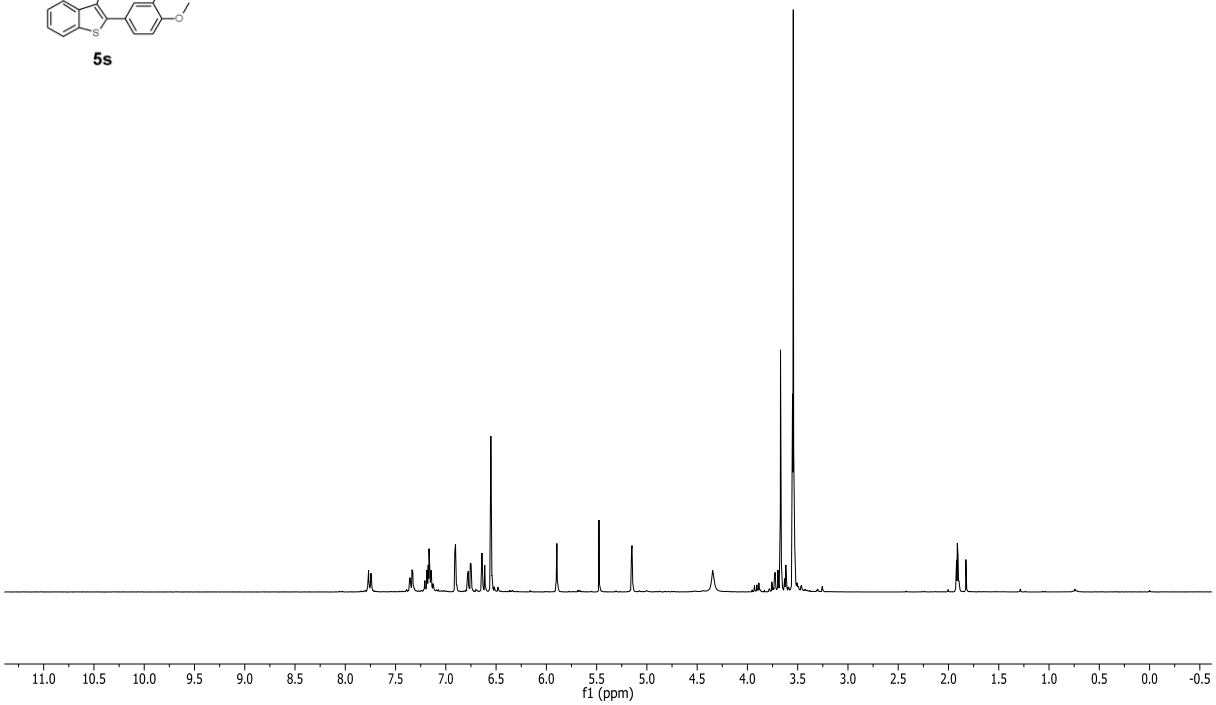
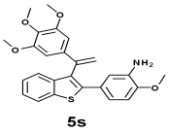


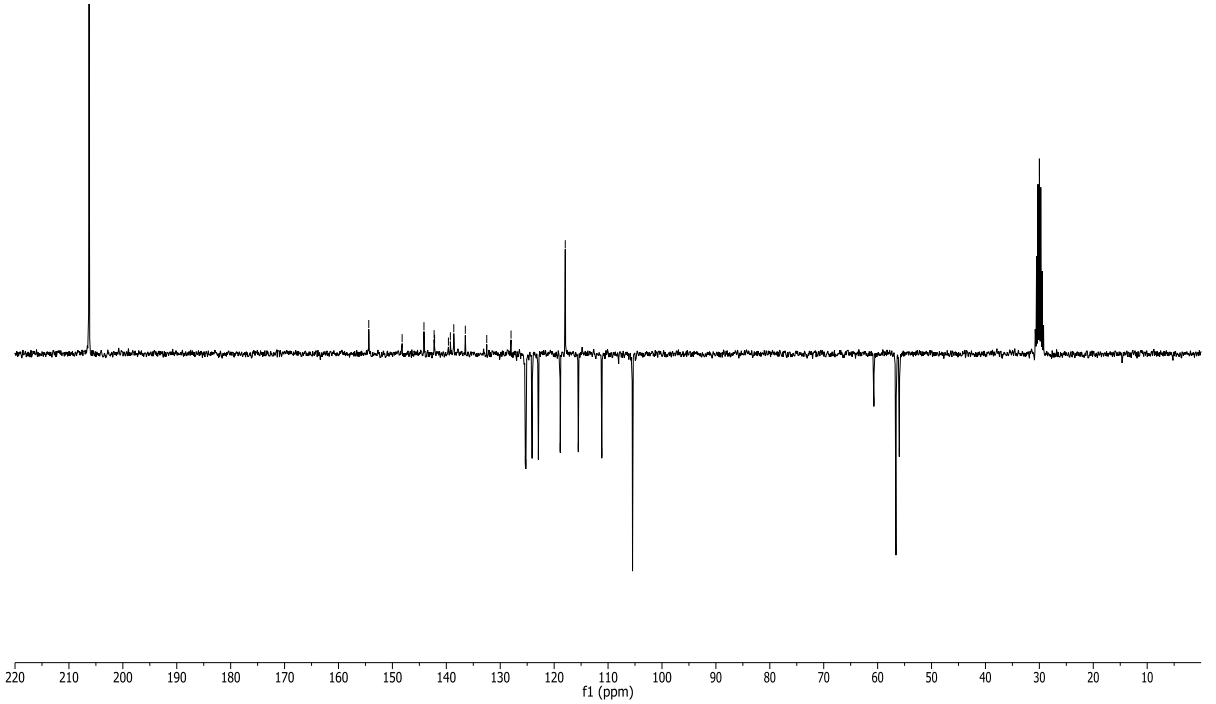
5s

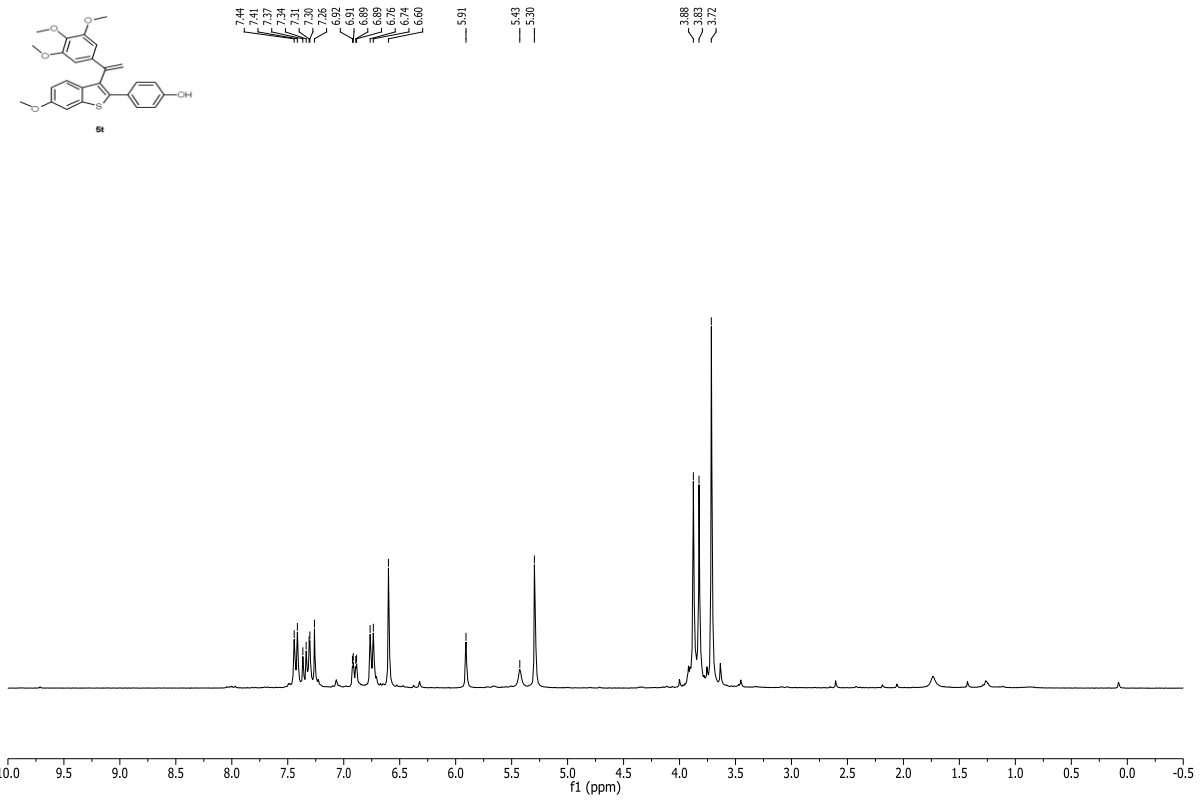




5s

154.4
148.2
144.1
142.3
142.2
139.6
139.3
138.6
136.5
132.5
128.0
125.3
125.2
124.1
122.9
118.9
117.9
115.5
111.2
105.5
60.7
56.6
56.0

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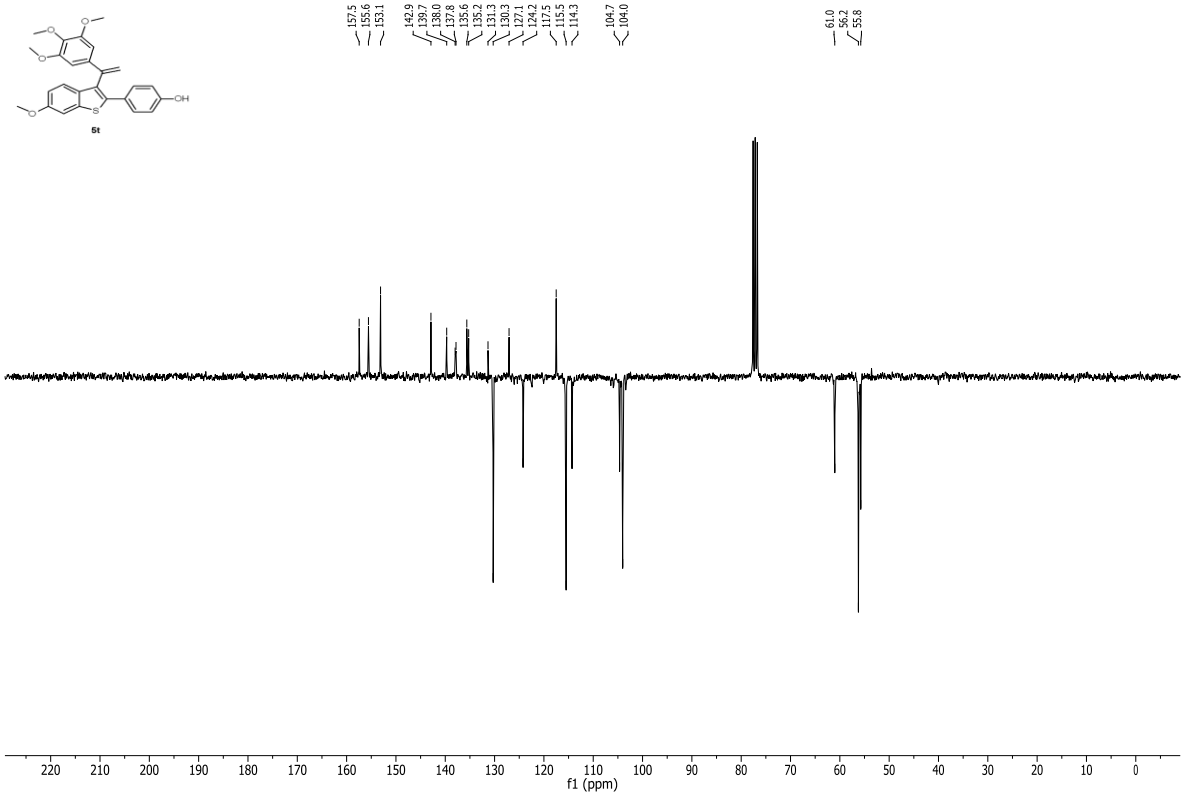
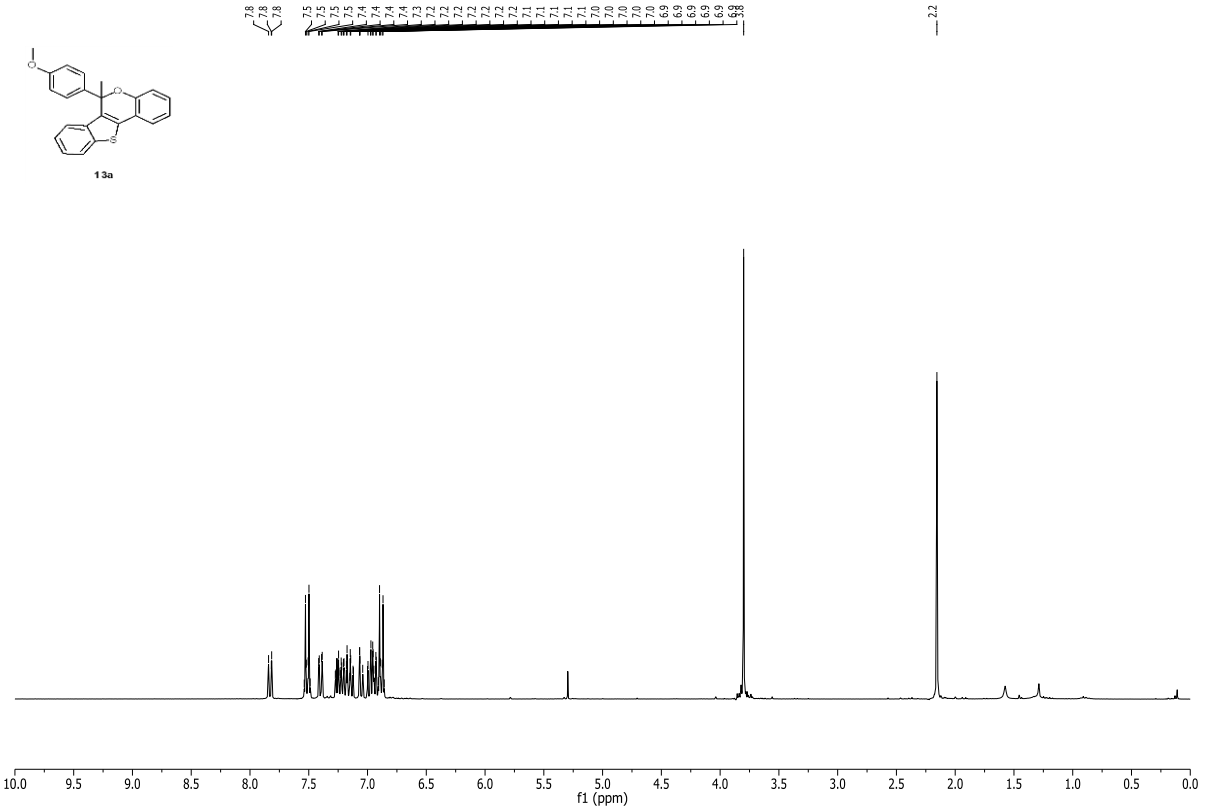
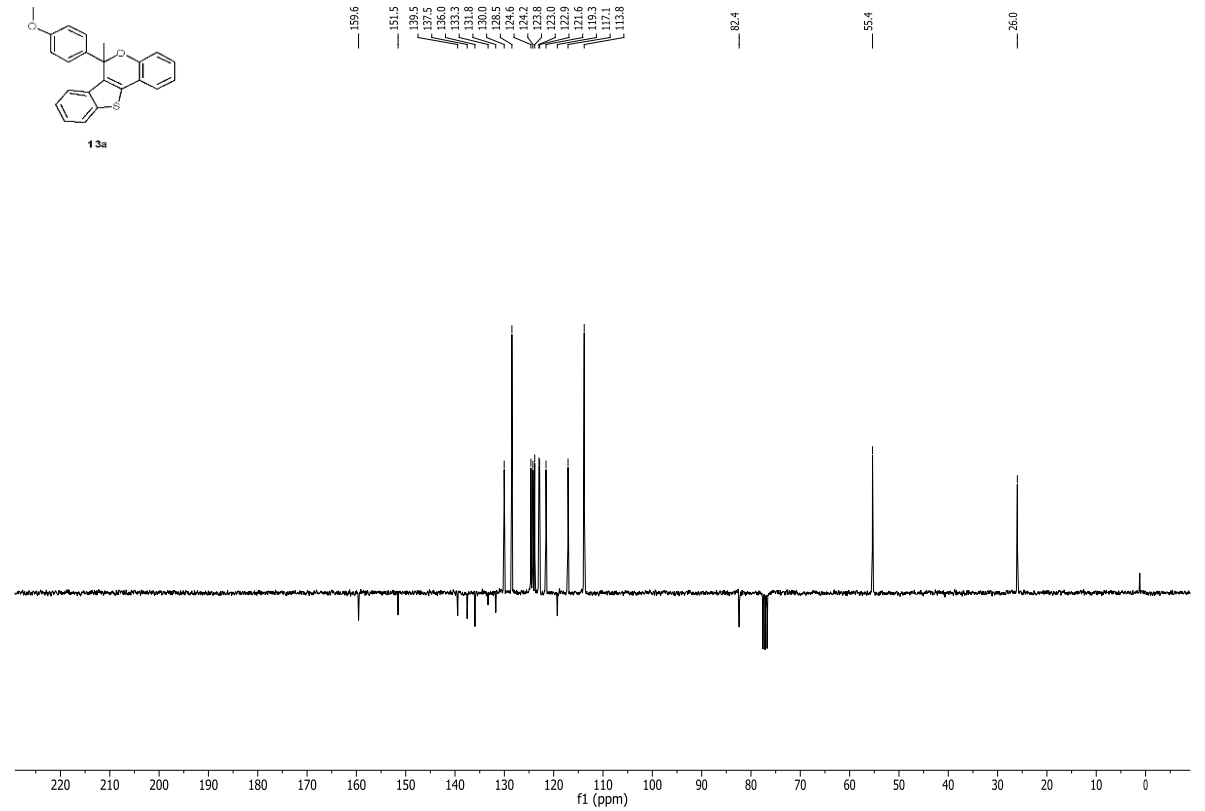
7.30
7.26
6.92
6.91
6.89
6.89
6.76
6.74
6.60
5.91
5.43
5.30
3.88
3.83
3.72
OH
5t
f1 (ppm)

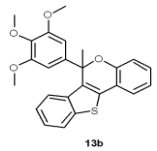

157.5
155.6
153.1
142.9
139.7
138.0
137.8
135.6
135.2
131.3
130.3
127.1
124.2
117.5
115.5
114.3
104.7
104.0
61.0
56.2
55.8
OH
5t
f1 (ppm)

IV. ^{1}H and ^{13}C NMR Spectra for 6-methyl-6-phenyl-6H-benzo[4,5]thieno[3,2-c]chromenes derivatives, 13a-c

4a

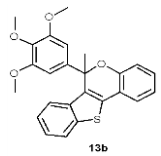






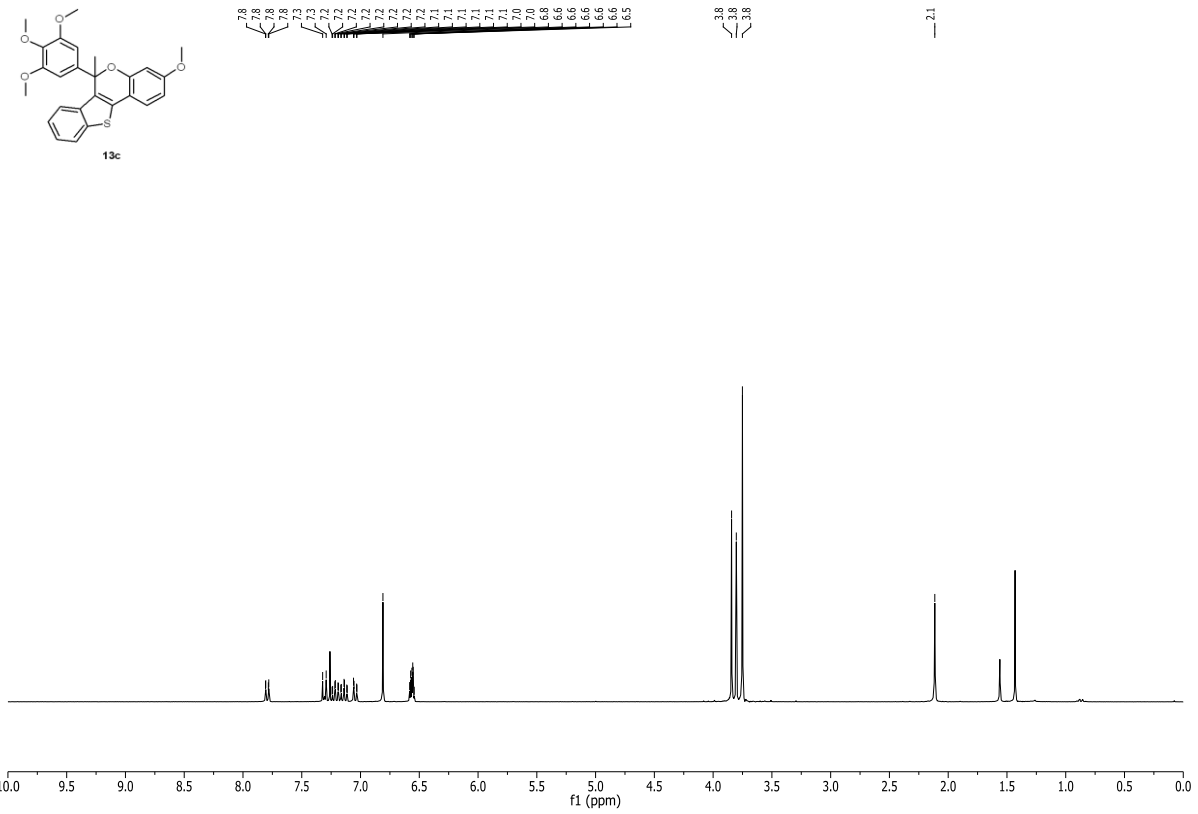
13b

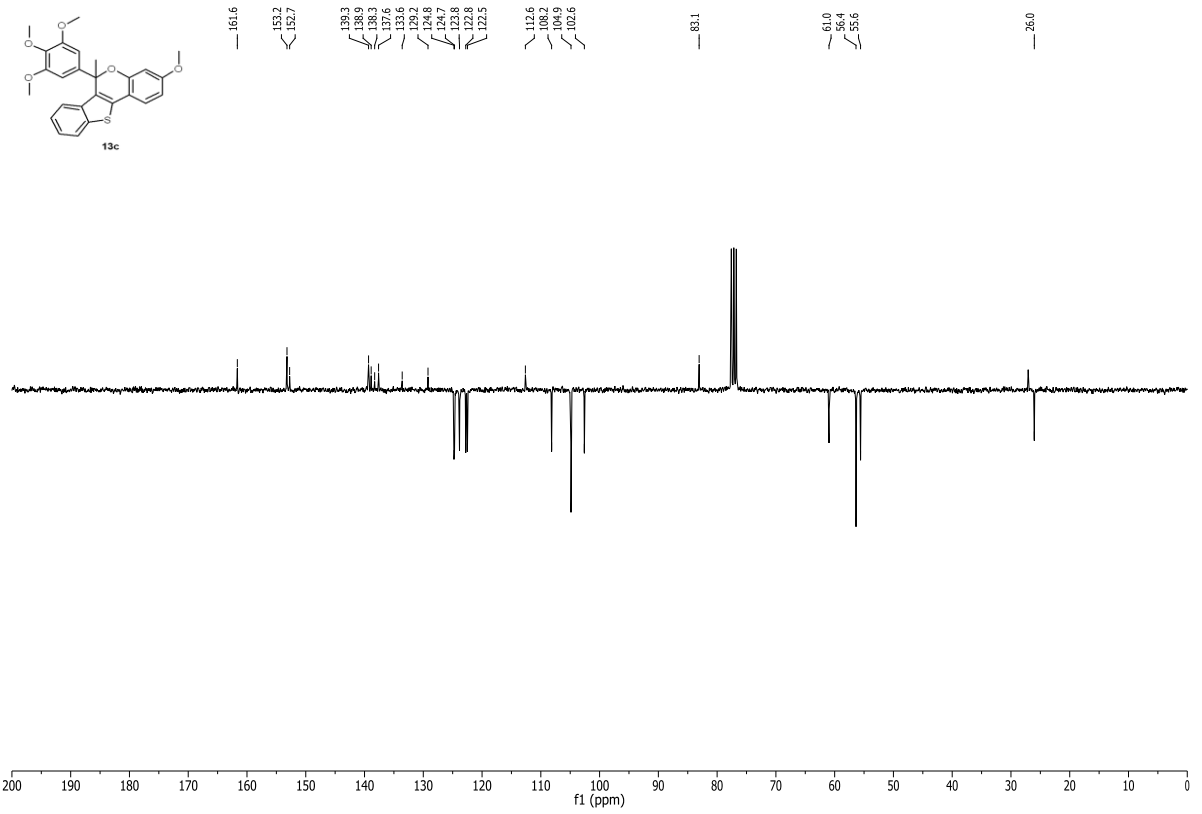
7.8
7.8
7.8
7.8
7.4
7.4
7.4
7.3
7.3
7.2
7.2
7.2
7.2
7.2
7.2
7.1
7.1
7.1
7.1
7.1
7.1
7.0
7.0
7.0
7.0
6.8
3.8
3.7
2.1
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



13b

153.2
151.4
139.4
138.2
137.5
133.4
131.5
130.1
124.8
124.3
123.9
122.9
121.8
119.4
117.2
104.8
82.8
60.9
56.3
26.2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


13c
7.8
7.8
7.8
7.8
7.3
7.3
7.2
7.2
7.2
7.2
7.2
7.2
7.2
7.2
7.2
7.1
7.1
7.1
7.1
7.1
7.1
7.0
7.0
6.8
6.6
6.6
6.6
6.6
6.6
6.5
3.8
3.8
3.8
2.1
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


13c
161.6
153.2
152.7
139.3
138.9
138.3
137.6
133.6
129.2
124.8
124.7
123.8
122.8
122.5
112.6
108.2
104.9
102.6
83.1
61.0
56.4
55.6
26.0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)