Regioselective Benzannulation of Allylic Sulfur Ylides with Ynones: A Rapid Access to substituted Thioanisoles

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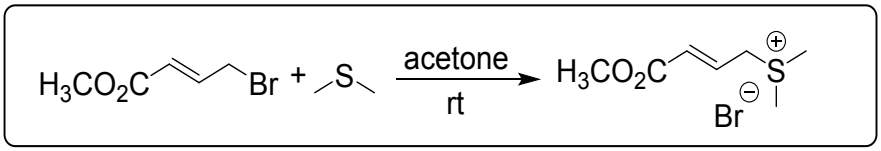
I. General Information and methods.

All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300, 400 or 500 MHz spectrometer for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$ for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using QTof mass spectrometer. Column chromatography was performed with silica gel (100–200 mesh) as the stationary phase. All reactions were monitored by using TLC.

Ynones **1** were prepared following literature procedures.[1] Starting material **2a** was prepared from literature procedures.[2]

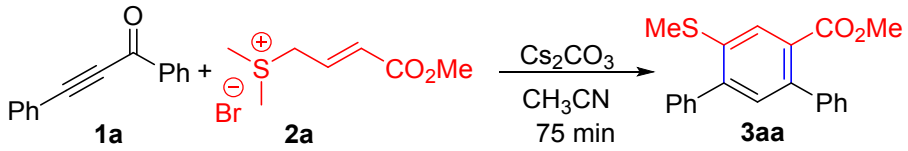
II. General Procedure for the preparation of allylic sulfur ylide (2a):

Starting material **2a** was prepared from literature procedures.[2]



To the mixture of (E)-methyl 4-bromobut-2-enoate (10 mmol) and dimethyl sulphide (5 mL) was added acetone (3 mL). The resulting mixture was stirred at room temperature for 18 h, filtered and was washed with ether before dried in vacuum to get the sulfonium salt **2a** as a white solid.

III. Optimization Studies[a]:



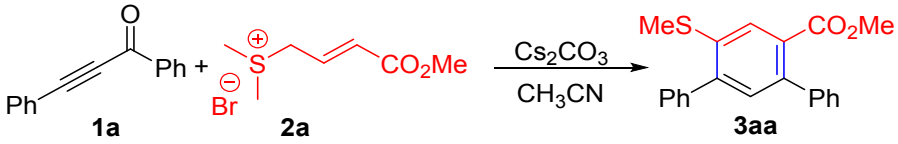
S.No.	Equivalents of **2a**	Conversion to **3aa** & Yield[b] (%)
1	1	50% & 45%
2	1.2	57% & 49%
3	1.5	60% & 59%
4	2	79% & 72%

5	2.5	100% & 80%

[a]Reaction conditions: **1** (0.5 mmol), **2** (1.25 mmol), Cs_2CO_3 (1 mmol) in CH_3CN, at rt, open air. [b]Isolated yield.

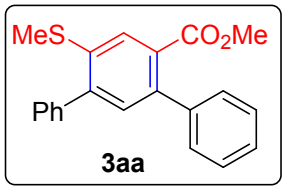
IV. General procedure and chareteristic data of final compounds

(A). General procedure A for the synthesis of final compounds (3) taking Synthesis of 3aa as an Example.

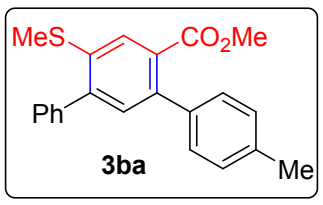


To a 15 mL Schlenk tube was added ynone **1a** (103 mg, 0.5 mmol, 1 equiv), ASY **2a** (300 mg, 1.25 mmol, 2.5 equiv) and Cs_2CO_3 (275 mg, 1 mmol, 2 equiv) in CH_3CN (3 mL) and the reaction mixture was stirred at room temperature under open air until the complete conversion of starting material (75-90 min). After completion of the reaction mixture was diluted with water and was extracted with EtOAc (2 X 10 mL). Combined extracts were washed with brine (10 mL) and were dried over Na_2SO_4. After removal of the solvent under reduced pressure, the crude material was purified on silica gel using 1% EtOAc/hexane to get **3aa** (134 mg, 80%) as yellow solid.

Methyl 6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3aa): 134 mg was obtained from **1a** (103 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 80%; pale yellow solid; mp 90−93 °C; R_f= 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.45 – 7.43 (m, 4H), 7.42 – 7.40 (m, 1H), 7.40 – 7.38 (m, 1H), 7.37 (d, *J* = 0.8 Hz, 1H), 7.35 – 7.31 (m, 3H), 7.26 (d, *J* = 1.3 Hz, 1H), 3.66 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.9, 143.5, 140.6, 139.3, 138.8, 136.8, 132.2, 130.1, 129.1, 128.3, 128.3, 128.1, 127.2, 126.3, 52.1, 16.0; **IR** (KBr) ν 3049, 2970, 2343, 1726, 1296, 1238, 1108, 704 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{19}O_2S$ $[M+H]^+$ 335.1106 found 335.1109.

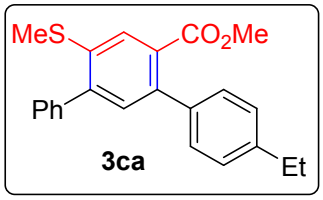


Methyl 4''-methyl-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ba): 132 mg was obtained from **1b** (110 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 76%; yellow sticky gel; R_f= 0.53 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.49 – 7.46 (m, 4H), 7.28 (dd, *J* = 7.9, 3.5 Hz, 3H), 7.26 (d, *J* = 2.1 Hz, 1H), 7.23 (d, *J* = 8.1 Hz, 2H), 3.73 (s, 3H), 2.48 (s, 3H), 2.42 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.0, 143.5, 139.4, 138.8, 137.6, 137.0, 136.5, 132.3, 130.1, 129.1, 128.9, 128.3, 128.2, 128.1, 126.3, 52.1, 21.2, 16.0; **IR** (KBr) ν

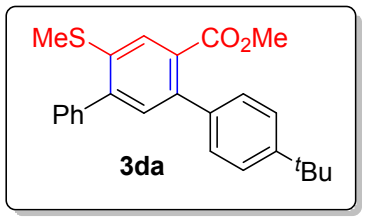


3034, 2944, 1724, 1438, 1295, 1236, 1108, 824, 771, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{22}H_{21}O_2S$ $[M+H]^+$ 349.1262 found 349.1264.

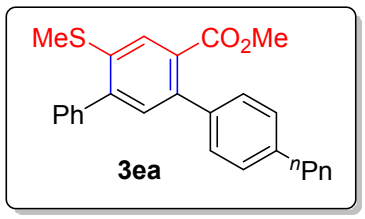
Methyl 4''-ethyl-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ca): 136 mg was obtained from **1c** (117 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 75%; yellow sticky solid; R_f= 0.54 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.37 (dd, *J* = 6.9, 2.6 Hz, 4H), 7.35 – 7.31 (m, 1H), 7.20 – 7.19 (m, 2H), 7.18 – 7.13 (m, 3H), 3.62 (s, 3H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.37 (s, 3H), 1.20 (t, *J* = 7.6 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.0, 142.4, 142.2, 138.4, 137.7, 136.7, 135.4, 131.3, 129.0, 128.0, 127.2, 127.2, 127.0, 126.6, 125.3, 51.1, 27.5, 15.0, 14.4; **IR** (KBr) ν 3049, 2961, 2891, 1725, 1437, 1295, 1236, 1105, 799, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{23}H_{23}O_2S$ $[M+H]^+$ 363.1419 found 363.1430.



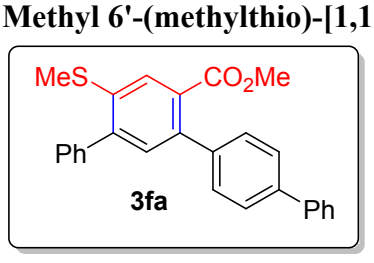
Methyl 4''-(tert-butyl)-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3da): 140 mg was obtained from **1d** (131 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 72%; yellow solid; mp 145-148 °C; R_f= 0.54 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.45 – 7.42 (m, 4H), 7.40 (dd, *J* = 7.1, 3.5 Hz, 3H), 7.27 (d, *J* = 4.1 Hz, 2H), 7.26 (d, *J* = 2.0 Hz, 1H), 3.68 (s, 3H), 2.44 (s, 3H), 1.35 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.1, 150.2, 143.4, 139.4, 138.7, 137.5, 136.5, 132.4, 130.1, 129.1, 128.2, 128.0, 127.8, 126.3, 125.0, 52.1, 34.6, 31.4, 16.0; **IR** (KBr) ν 3033, 2963, 1727, 1544, 1438, 1297, 1239, 778, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{25}H_{27}O_2S$ $[M+H]^+$ 391.1732 found 391.1734.



Methyl 6'-(methylthio)-4''-pentyl-[1,1':3',1''-terphenyl]-4'-carboxylate (3ea): 145 mg was obtained from **1e** (138 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 72%; yellow sticky gel; R_f= 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.44 (dd, *J* = 3.7, 1.7 Hz, 3H), 7.41 (ddd, *J* = 6.0, 3.3, 2.1 Hz, 1H), 7.26 (d, *J* = 1.4 Hz, 2H), 7.25 – 7.23 (m, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 3.67 (s, 3H), 2.65 – 2.61 (m, 2H), 2.44 (s, 3H), 1.64 (dt, *J* = 15.1, 7.5 Hz, 2H), 1.33 (dt, *J* = 9.4, 4.6 Hz, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.1, 143.4, 142.0, 139.4, 138.8, 137.8, 136.5, 132.3, 130.2, 129.1, 128.2, 128.2, 128.1, 126.3, 52.1, 35.6, 31.5, 31.1, 22.6, 16.0, 14.1; **IR** (KBr) ν 3015, 2940, 2861, 1725, 1439, 1371, 1108, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{26}H_{29}O_2S$ $[M+H]^+$ 405.1888 found 405.1891.

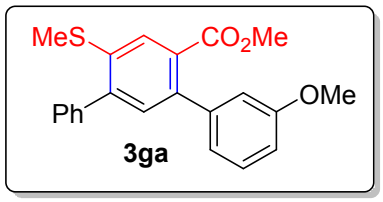


Methyl 6'-(methylthio)-[1,1':3',1'':4'',1'''-quaterphenyl]-4'-carboxylate (3fa): 143 mg was obtained from **1f** (141 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 70%; yellow solid; mp 122-124 °C; R_f= 0.50 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.65 (d, *J* = 1.4 Hz, 1H), 7.63 (dd, *J* = 2.2, 1.4 Hz, 2H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.47 – 7.44 (m, 5H),

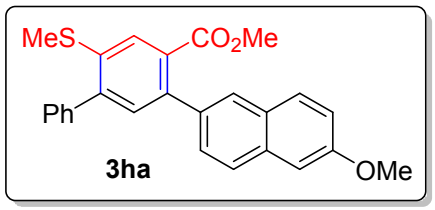


7.42 (t, J = 6.2 Hz, 4H), 7.36 (ddd, J = 7.4, 3.9, 1.2 Hz, 1H), 7.31 (s, 1H), 3.71 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.9, 143.5, 140.7, 140.0, 139.5, 139.3, 138.4, 137.0, 132.3, 130.1, 129.1, 128.8, 128.5, 128.3, 128.1, 127.4, 127.1, 126.8, 126.4, 52.2, 16.0; **IR** (KBr) ν 3233, 3046, 1726, 1438, 1298, 1237, 1109, 764, 702 cm^{-1}; **HRMS** (QToF) calcd for $C_{27}H_{23}O_2S$ $[M+H]^+$ 411.1419 found 411.1422.

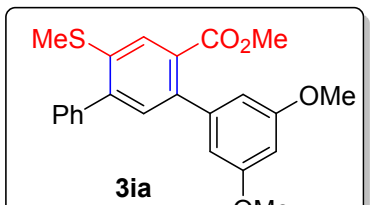
Methyl 3''-methoxy-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ga): 127 mg was obtained from **1g** (118 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 70%; pale yellow sticky solid; R_f = 0.50 (SiO2, EtOAc:Hexane, 9:91); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.46 – 7.43 (m, 4H), 7.42 – 7.39 (m, 1H), 7.29 (dd, J = 9.0, 7.6 Hz, 1H), 7.26 (s, 1H), 6.92 – 6.87 (m, 3H), 3.82 (s, 3H), 3.68 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.9, 159.4, 143.4, 142.0, 139.3, 138.5, 137.0, 132.1, 130.3, 129.1, 128.3, 128.1, 126.2, 120.9, 113.8, 112.9, 55.3, 52.1, 16.0; **IR** (KBr) ν 2962, 2343, 1728, 1598, 1284, 1212, 1060, 703 cm^{-1}; **MASS** (ESI) calcd for $C_{22}H_{21}O_3S$ $[M+H]^+$ 365.12 found 365.11.



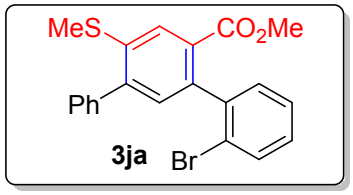
Methyl 5-(6-methoxynaphthalen-2-yl)-2-(methylthio)-[1,1'-biphenyl]-4-carboxylate (3ha): 151 mg was obtained from **1h** (143 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 73%; yellow sticky solid; R_f= 0.45 (SiO2, EtOAc:Hexane, 10:90); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (dd, J = 5.7, 3.3 Hz, 4H), 7.49 – 7.45 (m, 3H), 7.45 – 7.43 (m, 1H), 7.42 – 7.39 (m, 2H), 7.36 (s, 1H), 7.16 (dd, J = 4.8, 2.3 Hz, 2H), 3.94 (s, 3H), 3.63 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.1, 157.8, 143.6, 139.4, 138.7, 136.7, 135.9, 133.6, 132.5, 130.2, 129.6, 129.1, 128.8, 128.3, 128.1, 127.4, 126.7, 126.4, 126.3, 119.0, 105.7, 55.3, 52.1, 16.0; **IR** (KBr) ν 3334, 3005, 2886, 1724, 1542, 1153, 853, 666 cm^{-1}; **HRMS** (QToF) calcd for $C_{26}H_{23}O_3S$ $[M+H]^+$ 415.1368 found 415.1362.



Methyl 3'',5''-dimethoxy-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ia): 152 mg was obtained from **1i** (133 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 77%; light yellow sticky solid; R_f= 0.45 (SiO2, EtOAc:Hexane, 9:91); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.44 (d, J = 4.4 Hz, 4H), 7.42 – 7.39 (m, 1H), 7.27 (s, 1H), 6.48 (d, J = 2.2 Hz, 2H), 6.45 (t, J = 2.2 Hz, 1H), 3.79 (s, 6H), 3.70 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.0, 160.5, 143.3, 142.6, 139.3, 138.4, 137.1, 131.9, 130.4, 129.1, 128.3, 128.1, 126.0, 106.5, 99.6, 55.4, 52.2, 16.0; **IR** (KBr) ν 3033, 2347, 1728, 1593, 1439, 1293, 1109, 784 cm^{-1}; **HRMS** (QToF) calcd for $C_{23}H_{23}O_4S$ $[M+H]^+$ 395.1317 found 395.1307.

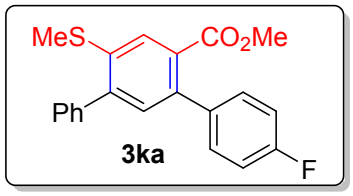


Methyl 2''-bromo-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ja): 144 mg was obtained from **1j** (141 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 70%; yellow sticky solid; R_f= 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ



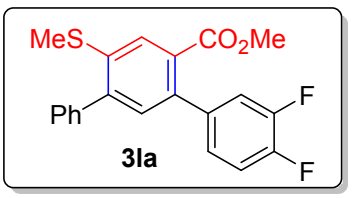
7.89 (s, 1H), 7.61 (dd, J = 8.0, 1.0 Hz, 1H), 7.48 – 7.38 (m, 5H), 7.33 (td, J = 7.5, 1.1 Hz, 1H), 7.26 – 7.24 (m, 1H), 7.21 – 7.17 (m, 1H), 7.12 (s, 1H), 3.68 (s, 3H), 2.47 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.0, 143.7, 142.0, 139.1, 138.5, 137.6, 132.6, 132.1, 130.2, 129.3, 129.1, 128.7, 128.2, 128.2, 127.0, 126.3, 123.2, 52.2, 15.8; **IR** (KBr) ν 3015, 2654, 2451, 1727, 1604, 1272, 1242, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}BrO_2S$ $[M+H]^+$ 413.0211 found 413.0209.

Methyl 4''-fluoro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ka): 125 mg was obtained from **1k** (112 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 71%; pale brownish solid; mp 110-112 °C; R_f = 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.41 (d, J = 4.1 Hz, 5H), 7.25 (dd, J = 8.4, 5.4 Hz, 2H), 7.17 (s, 1H), 7.04 (t, J = 8.6 Hz, 2H), 3.65 (s, 3H), 2.41 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.5, 162.4 (d, J = 247.0 Hz), 160.0, 142.5, 138.2, 136.8, 136.1, 135.6, 131.2 (d, J = 226.0 Hz), 129.0, 128.9, 128.0, 127.2, 127.1, 125.4, 114.1 (d, J = 21.4 Hz), 113.8, 51.1, 14.9; **IR** (KBr) ν 3010, 2882, 2556, 1731, 1591, 1300, 1238, 853, 662 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}FO_2S$ $[M+H]^+$ 353.1012 found 353.0981.



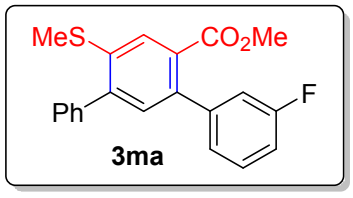
3ka

Methyl 3'',4''-difluoro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3la): 129 mg was obtained from **1l** (121 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 70%; white solid; mp 100-102 °C; R_f = 0.50 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.43 (d, J = 3.8 Hz, 5H), 7.18 (s, 1H), 6.86 – 6.83 (m, 2H), 6.79 (ddd, J = 9.0, 5.6, 2.3 Hz, 1H), 3.73 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.9, 163.9 (d, J = 248.0 Hz), 163.7 (d, J = 248.5 Hz), 161.4, 161.3, 144.1 (t, J = 19.7 Hz), 144.0, 143.9, 143.7, 138.9, 138.3, 136.5, 131.8, 129.7, 129.0, 128.3, 128.3, 126.3, 111.7 (d, J = 25.7 Hz), 111.6 (d, J = 11.9 Hz), 111.5, 111.4, 102.9, 102.6 (t, J = 50.5 Hz), 102.3, 52.3, 15.8; **IR** (KBr) ν 3044, 2961, 2892, 1726, 1254, 1106, 794, 701 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{17}F_2O_2S$ $[M+H]^+$ 371.0917 found 371.0891.



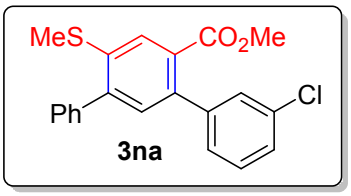
3la

Methyl 3''-fluoro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ma): 123 mg was obtained from **1m** (112 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 70%; yellow sticky solid; R_f = 0.54 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.65 (d, J = 1.4 Hz, 1H), 7.63 (dd, J = 2.2, 1.4 Hz, 2H), 7.62 (d, J = 2.0 Hz, 1H), 7.47 – 7.44 (m, 5H), 7.42 (t, J = 6.2 Hz, 4H), 7.36 (ddd, J = 7.4, 3.9, 1.2 Hz, 1H), 7.31 (s, 1H), 3.71 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.4, 162.7 (d, J = 245.5 Hz), 160.2, 142.5, 141.9, 141.8, 138.1, 136.5, 136.5, 131.0, 128.9, 128.5 (d, J = 8.3 Hz), 128.4, 128.0, 127.2, 127.1, 125.3, 123.2, 123.1, 114.5 (d, J = 22.9 Hz), 114.2, 113.1 (d, J = 21.9 Hz), 112.9, 51.1, 14.8; **IR** (KBr) ν 3028, 2744, 2341, 1729, 1594, 1282, 1242, 1117, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}FO_2S$ $[M+H]^+$ 353.1012 found 353.1006.

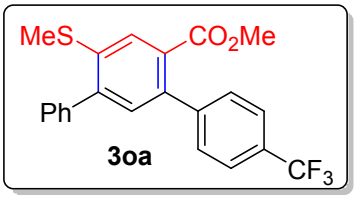


3ma

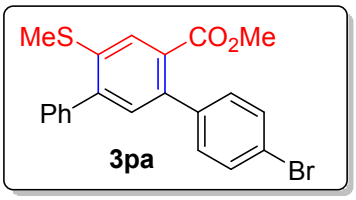
Methyl 3''-chloro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3na): 132 mg was obtained from **1n** (120 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 72%; yellow sticky solid; R_f= 0.53 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.46 – 7.43 (m, 4H), 7.43 – 7.39 (m, 1H), 7.34 (dd, *J* = 1.8, 1.1 Hz, 1H), 7.33 – 7.30 (m, 2H), 7.22 – 7.19 (m, 2H), 3.70 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.3, 143.6, 142.5, 139.1, 137.7, 137.4, 133.9, 132.1, 129.8, 129.2, 129.0, 128.4, 128.3, 128.2, 127.3, 126.7, 126.4, 52.2, 15.9; **IR** (KBr) ν 3034, 2937, 1726, 1592, 1295, 1237, 1107, 785, 702 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}ClO_2S$ $[M+H]^+$ 369.0716 found 369.0686.



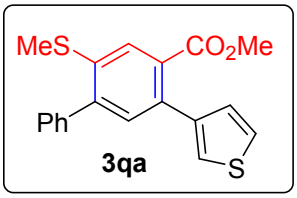
Methyl 6'-(methylthio)-4''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate (3oa): 135 mg was obtained from **1o** (137 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 67%; pale yellow sticky solid; R_f= 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.44 (dd, *J* = 5.3, 3.1 Hz, 6H), 7.43 – 7.40 (m, 1H), 7.21 (s, 1H), 3.69 (s, 3H), 2.47 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.1, 144.5 (d, *J* = 75.8 Hz), 143.7, 139.0, 138.0, 137.5, 132.1, 129.6, 129.5, 129.0, 128.8, 128.3, 128.3, 126.5, 125.6, 125.0 (d, *J* = 3.5 Hz), 124.9, 52.2, 15.9; **IR** (KBr) ν 3046, 2961, 2223, 1727, 1606, 1326, 1240, 1168, 852, 701 cm^{-1}; **MASS** (ESI) calcd for $C_{22}H_{18}F_3O_2S$ $[M+H]^+$ 403.09 found 403.14.



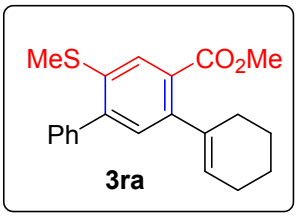
Methyl 4''-bromo-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3pa): 142 mg was obtained from **1p** (141 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 69%; yellow sticky solid; R_f= 0.52 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.53 – 7.50 (m, 2H), 7.45 – 7.43 (m, 4H), 7.43 – 7.40 (m, 1H), 7.21 – 7.19 (m, 3H), 3.70 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.4, 143.6, 139.6, 139.1, 137.6, 137.5, 132.1, 131.2, 130.0, 129.7, 129.0, 128.3, 128.2, 126.4, 121.5, 52.2, 15.9; **IR** (KBr) ν 3040, 2918, 1728, 1557, 1297, 1238, 1111, 776 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}BrO_2S$ $[M+H]^+$ 413.0211 found 413.0186.



Methyl 2-(methylthio)-5-(thiophen-3-yl)-[1,1'-biphenyl]-4-carboxylate (3qa): 115 mg was obtained from **1q** (106 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 68%; yellow sticky solid; R_f= 0.52 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.45 – 7.43 (m, 4H), 7.42 – 7.39 (m, 1H), 7.33 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.30 (s, 1H), 7.25 (dd, *J* = 3.0, 1.3 Hz, 1H), 7.10 (dd, *J* = 5.0, 1.3 Hz, 1H), 3.75 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.9, 143.5, 140.7, 139.3, 136.9, 133.1, 132.0, 130.1, 129.0, 128.4, 128.3, 128.1, 126.1, 125.0, 122.2, 52.2, 15.9; **IR** (KBr) ν 3032, 2928, 1726, 1439, 1293, 1238, 1110, 786 cm^{-1}; **HRMS** (QToF) calcd for $C_{19}H_{17}O_2S_2$ $[M+H]^+$ 341.0670 found 341.0633.

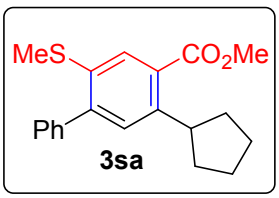


Methyl 6'-(methylthio)-2'',3'',4'',5''-tetrahydro-[1,1':3',1''-terphenyl]-4'-carboxylate (3ra): 98 mg was obtained from **1r** (105 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 58%; yellow sticky gel; R_f= 0.58 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, DMSO) δ 7.64 (s, 1H), 7.43 – 7.41 (m, 4H), 7.39 (dd, *J* = 5.3, 3.3 Hz, 1H), 7.08 (s, 1H), 5.59 (dt, *J* = 5.4, 1.8 Hz, 1H), 3.88 (s, 3H), 2.39 (s, 3H), 2.25 – 2.21 (m, 2H), 2.16 – 2.12 (m, 2H), 1.75 (m, *J* = 6.0, 2.5 Hz, 2H), 1.66 (m, *J* = 6.0, 2.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.7, 143.7, 142.2, 139.6, 138.6, 135.6, 131.2, 129.3, 129.0, 128.2, 127.9, 126.4, 125.3, 52.1, 30.2, 25.6, 23.1, 22.0, 16.0; **IR** (KBr) ν 3033, 2934, 1726, 1292, 1236, 1105 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{23}O_2S$ $[M+H]^+$ 339.1419 found 339.1384.



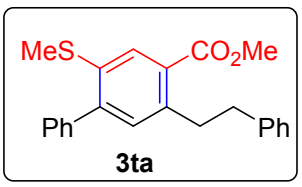
3ra

Methyl 5-cyclopentyl-2-(methylthio)-[1,1'-biphenyl]-4-carboxylate (3sa): 89 mg was obtained from **1s** (99 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 55%; pale yellow liquid; R_f= 0.50 (SiO2, EtOAc:Hexane, 0:100); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.46 – 7.39 (m, 5H), 7.25 (d, *J* = 3.1 Hz, 1H), 3.93 (s, 3H), 3.75 – 3.68 (m, 1H), 2.37 (s, 3H), 2.12 – 2.05 (m, 2H), 1.80 – 1.75 (m, 2H), 1.71 – 1.66 (m, 2H), 1.62 – 1.57 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.6, 144.1, 144.0, 140.0, 134.1, 130.2, 129.1, 128.7, 128.2, 127.9, 126.8, 52.2, 41.4, 34.8, 25.7, 16.2; **IR** (KBr) ν 3033, 1723, 1555, 1463, 1272, 668 cm^{-1}; **MASS** (ESI) calcd for $C_{20}H_{23}O_2S$ $[M+H]^+$ 327.14 found 327.08



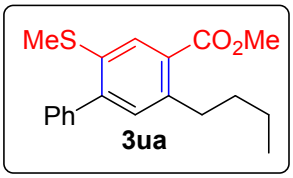
3sa

Methyl 2-(methylthio)-5-phenethyl-[1,1'-biphenyl]-4-carboxylate (3ta): 108 mg was obtained from **1t** (117 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 60%; yellow sticky solid; R_f= 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.44 – 7.38 (m, 3H), 7.37 – 7.34 (m, 2H), 7.28 (dd, *J* = 7.8, 6.9 Hz, 2H), 7.21 (d, *J* = 7.2 Hz, 3H), 7.03 (s, 1H), 3.95 (s, 3H), 3.24 (dd, *J* = 8.9, 7.2 Hz, 2H), 2.91 (dd, *J* = 9.4, 6.7 Hz, 2H), 2.39 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.6, 144.3, 141.8, 140.1, 139.5, 134.9, 133.0, 129.0, 128.8, 128.6, 128.3, 128.1, 128.0, 127.8, 125.9, 52.1, 38.1, 36.4, 16.2; **IR** (KBr) ν 3012, 2936, 2877, 2552, 1723, 1287, 1250, 763, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{23}H_{23}O_2S$ $[M+H]^+$ 363.1419 found 363.1385.



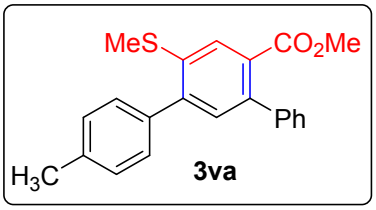
3ta

Methyl 5-butyl-2-(methylthio)-[1,1'-biphenyl]-4-carboxylate (3ua): 84 mg was obtained from **1u** (100 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 53%; yellow liquid; R_f= 0.55 (SiO2, EtOAc:Hexane, 0:100); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.44 – 7.38 (m, 5H), 7.25 (s, 1H), 7.11 (s, 1H), 3.91 (s, 3H), 2.95 – 2.89 (m, 2H), 2.37 (s, 3H), 1.60 (d, *J* = 7.3 Hz, 2H), 1.38 (dd, *J* = 14.7, 7.4 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.8, 144.3, 141.3, 139.7, 134.4, 132.7, 129.0, 128.9, 128.2, 127.9, 127.8, 52.0, 33.9, 33.7, 22.8, 16.2, 14.0; **IR** (KBr) ν 2958, 2886, 1726, 1441, 1288, 1249, 1150, 698 cm^{-1}; **HRMS** (QToF) calcd for $C_{19}H_{23}O_2S$ $[M+H]^+$ 315.1419 found 315.1384.

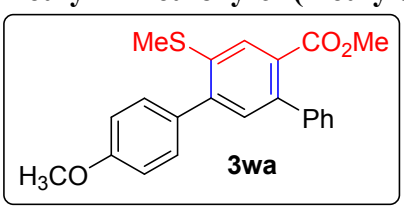


3ua

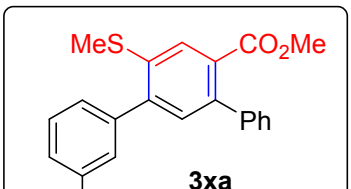
Methyl 4-methyl-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3va): 134 mg was obtained from **1v** (110 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 77%; yellow sticky solid; R_f= 0.53 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.38 (d, *J* = 1.5 Hz, 1H), 7.37 (dd, *J* = 2.2, 1.4 Hz, 1H), 7.35 – 7.34 (m, 1H), 7.33 (t, *J* = 2.2 Hz, 3H), 7.32 (t, *J* = 1.5 Hz, 1H), 7.26 (s, 1H), 7.24 (d, *J* = 3.1 Hz, 2H), 3.66 (s, 3H), 2.45 (s, 3H), 2.40 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.9, 143.5, 140.7, 138.8, 138.0, 136.9, 136.4, 132.2, 129.9, 129.0, 128.9, 128.3, 128.0, 127.2, 126.3, 52.0, 21.3, 16.0; **IR** (KBr) ν 3044, 2935, 1727, 1440, 1298, 1237, 821, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{22}H_{21}O_2S$ $[M+H]^+$ 349.1262 found 349.1256.



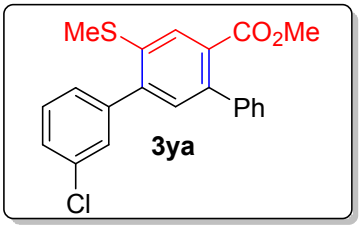
Methyl 4-methoxy-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3wa): 136 mg was obtained from **1w** (118 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 75%; yellow sticky solid; R_f= 0.50 (SiO2, EtOAc:Hexane, 9:91); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.40 – 7.37 (m, 4H), 7.33 (td, *J* = 6.7, 1.4 Hz, 3H), 7.24 (s, 1H), 6.98 – 6.95 (m, 2H), 3.85 (s, 3H), 3.66 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.9, 159.5, 143.2, 140.7, 138.8, 136.9, 132.3, 131.7, 130.3, 129.8, 128.3, 128.0, 127.2, 126.3, 113.7, 55.3, 52.0, 16.0; **IR** (KBr) ν 3016, 2950, 1720, 1604, 1293, 1238, 1105, 761, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{22}H_{21}O_3S$ $[M+H]^+$ 365.1211 found 365.1182.



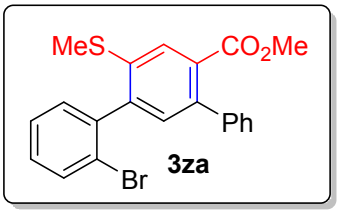
Methyl 3-methoxy-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3xa): 125 mg was obtained from **1x** (118 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 69%; yellow sticky solid; R_f= 0.50 (SiO2, EtOAc:Hexane, 9:91); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.41 – 7.31 (m, 6H), 7.27 (s, 1H), 7.03 (d, J = 7.5 Hz, 1H), 6.99 (s, 1H), 6.94 (d, J = 8.4 Hz, 1H), 3.84 (s, 3H), 3.66 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.9, 159.4, 143.2, 140.6, 140.6, 138.7, 136.9, 132.1, 130.2, 129.3, 128.3, 128.1, 127.2, 126.2, 121.4, 114.6, 113.8, 55.3, 52.1, 16.0; **IR** (KBr) ν 3019, 2966, 1728, 1601, 1294, 761, 703 cm^{-1}; **MASS** (ESI) calcd for $C_{22}H_{21}O_3S$ $[M+H]^+$ 365.12 found 364.95.



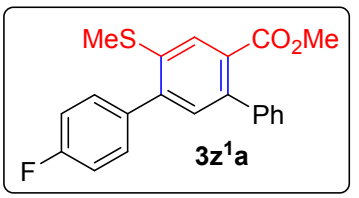
Methyl 3-chloro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3ya): 112 mg was obtained from **1y** (120 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 61%; yellow sticky solid; R_f= 0.54 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.45 – 7.43 (m, 1H), 7.41 – 7.35 (m, 5H), 7.35 – 7.34 (m, 1H), 7.33 (d, J = 1.6 Hz, 1H), 7.31 (t, J = 1.5 Hz, 1H), 7.23 (s, 1H), 3.66 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.7, 141.9, 141.0, 140.3, 138.9, 136.8, 134.2, 132.1, 130.6, 129.5, 129.2, 128.3, 128.2, 128.1, 127.4, 126.4, 52.1, 15.9; **IR** (KBr) ν 3024, 2939, 1727, 1596, 1299, 785, 702 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}ClO_2S$ $[M+H]^+$ 369.0716 found 369.0714.



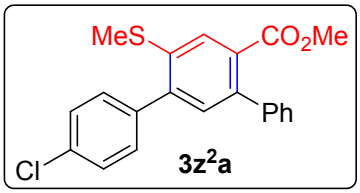
Methyl 2-bromo-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3za): 129 mg was obtained from **1z** (141 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 63%; pale yellow sticky solid; R_f= 0.55 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.68 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.40 – 7.36 (m, 3H), 7.35 – 7.33 (m, 3H), 7.29 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.27 (d, *J* = 0.6 Hz, 1H), 7.19 (s, 1H), 3.67 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.9, 142.4, 140.4, 140.0, 138.6, 137.5, 132.8, 132.1, 131.0, 130.8, 129.7, 128.6, 128.3, 128.1, 127.3, 126.3, 123.4, 52.1, 15.8; **IR** (KBr) ν 3027, 2937, 1729, 1598, 1290, 785, 702 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}BrO_2S$ $[M+H]^+$ 413.0211 found 413.0190.



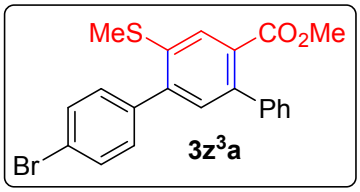
Methyl 4-fluoro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3z^{1}a): 128 mg was obtained from **1z^1** (112 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 73%; yellow sticky solid; R_f= 0.53 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.44 – 7.40 (m, 2H), 7.40 – 7.36 (m, 2H), 7.35 – 7.31 (m, 3H), 7.23 (s, 1H), 7.15 – 7.10 (m, 2H), 3.66 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.8, 163.8 (d, *J* = 247.5 Hz), 161.4, 142.4, 140.5, 138.9, 136.9, 135.3, 132.3, 130.9 (d, *J* = 8.1 Hz), 130.8, 130.3, 128.6, 128.3, 128.1, 127.3, 126.3, 118.7, 115.4 (d, *J* = 21.5 Hz), 115.2, 52.1, 15.9; **IR** (KBr) ν 3225, 2344, 1728, 1517, 1299, 1236, 703 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}FO_2S$ $[M+H]^+$ 353.1012 found 353.1014.



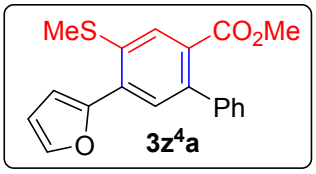
Methyl 4-chloro-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3z^{2}a): 127 mg was obtained from **1z^2** (120 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 69%; yellow solid; mp 110-112 °C; R_f= 0.54 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.41 – 7.39 (m, 5H), 7.38 (t, *J* = 0.9 Hz, 1H), 7.35 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.32 (d, *J* = 1.6 Hz, 1H), 7.31 (t, *J* = 1.5 Hz, 1H), 7.22 (s, 1H), 3.66 (s, 3H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.8, 142.2, 140.4, 138.9, 137.7, 136.8, 134.2, 132.1, 130.5, 128.5, 128.3, 128.1, 127.3, 126.4, 52.1, 15.9; **IR** (KBr) ν 3033, 2957, 1726, 1548, 1298, 1238, 1105, 840 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}ClO_2S$ $[M+H]^+$ 369.0716 found 369.0715.



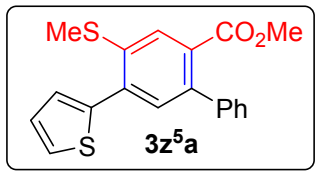
Methyl 4-bromo-6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-carboxylate (3z^{3}a): 125 mg was obtained from **1z^3** (141 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 61%; brownish sticky solid; R_f= 0.54 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.52 (d, *J* = 1.9 Hz, 1H), 7.50 (d, *J* = 2.0 Hz, 1H), 7.45 – 7.42 (m, 5H), 7.21 – 7.18 (m, 3H), 3.70 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, CDCl3) δ 167.4, 142.6, 138.6, 138.1, 136.6, 136.4, 131.0, 130.1, 129.0, 128.7, 128.0, 127.3, 127.2, 125.4, 120.5, 51.1, 14.9; **IR** (KBr) ν 3035, 2351, 1727, 1553, 1302, 1242, 1104, 798, 707 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{18}BrO_2S$ $[M+H]^+$ 413.0211 found 413.0189.



Methyl 5-(furan-2-yl)-4-(methylthio)-[1,1'-biphenyl]-2-carboxylate (3z^{4}a): 115 mg was obtained from **1z^4** (98 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 71%; brownish sticky solid; R_f= 0.51 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.75 (s, 1H), 7.51 (d, *J* = 1.4 Hz, 1H), 7.39 (dd, *J* = 5.8, 1.6 Hz, 2H), 7.34 (dt, *J* = 7.8, 1.7 Hz, 3H), 7.12 (d, *J* = 3.4 Hz, 1H), 6.55 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.65 (s, 3H), 2.59 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.5, 150.6, 142.5, 140.7, 139.1, 134.4, 131.3, 129.5, 129.2, 128.3, 128.0, 127.3, 127.2, 112.0, 111.8, 52.0, 16.1; **IR** (KBr) ν 3024, 2999, 2347, 1724, 1295, 1244, 1111, 792 cm^{-1}; **HRMS** (QToF) calcd for $C_{19}H_{17}O_3S$ $[M+H]^+$ 325.0898 found 325.0864.

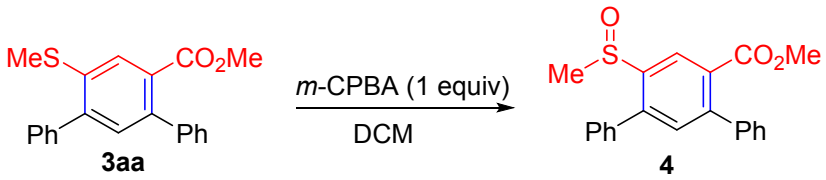


Methyl 4-(methylthio)-5-(thiophen-2-yl)-[1,1'-biphenyl]-2-carboxylate (3z^{5}a): 119 mg was obtained from **1z^5** (106 mg, 0.5 mmol) and **2a** following general procedure **A**. Yield 70%; yellow sticky solid; R_f= 0.52 (SiO2, EtOAc:Hexane, 1:99); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.43 – 7.39 (m, 3H), 7.38 (t, *J* = 1.8 Hz, 1H), 7.37 – 7.35 (m, 2H), 7.34 – 7.31 (m, 2H), 7.12 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.65 (s, 3H), 2.50 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.6, 140.4, 140.0, 138.9, 137.2, 135.9, 132.9, 130.2, 128.3, 128.2, 128.1, 127.3, 127.2, 127.0, 126.6, 52.1, 16.2; **IR** (KBr) ν 3095, 2885, 2352, 1727, 1294, 1244, 1111, 707 cm^{-1}; **HRMS** (QToF) calcd for $C_{19}H_{17}O_2S_2$ $[M+H]^+$ 341.0670 found 341.0637.



V. General Procedure and Characteristic data of derivatives:

(A). General procedure B for the synthesis of derivative (4):

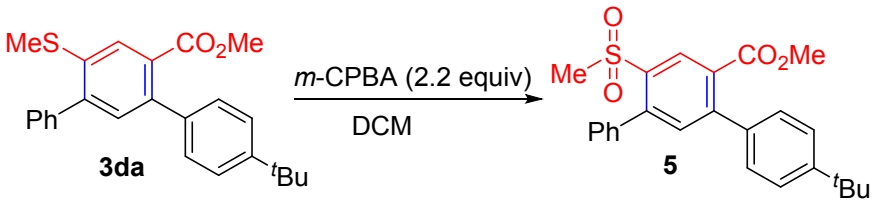


In a 15 mL Schlenk tube, compound **3aa** (167 mg, 0.5 mmol) and *m*-CPBA (86 mg, 0.5 mmol, 1 equiv) were taken in DCM (2.0 mL). The mixture was stirred at room temperature for 25 min and monitored by TLC analysis. Upon completion, the reaction was quenched with saturated $NaHCO_3$ solution (1 mL) and the aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4. After filtration, the solvent was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to get the product **4** as white solid.

Methyl 6'-(methylsulfinyl)-[1,1':3',1''-terphenyl]-4'-carboxylate (4): 157 mg was obtained from **3aa** (167 mg, 0.5 mmol) following general procedure **B**. Yield 90%; white solid; mp 136−138 °C; R_f= 0.50 (SiO2, EtOAc:Hexane, 20:80); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.46 (dd, *J* = 8.6, 6.8 Hz, 3H), 7.43 – 7.41 (m, 4H), 7.40 (dd, *J* = 4.4, 2.2 Hz, 1H), 7.37 (dd, *J* = 4.9, 3.1 Hz, 3H), 3.74 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.6, 144.0, 141.8, 140.9, 138.7, 135.8, 131.9, 130.1, 129.0, 128.6, 128.0, 127.9, 127.9, 127.3,

127.2, 126.9, 124.5, 51.3, 40.5; **IR** (KBr) ν 3154, 3053, 1727, 1300, 1244, 1107, 762, 702 cm^{-1}; **HRMS** (QToF) calcd for $C_{21}H_{19}O_3S_2$ $[M+H]^+$ 351.1055 found 351.1046.

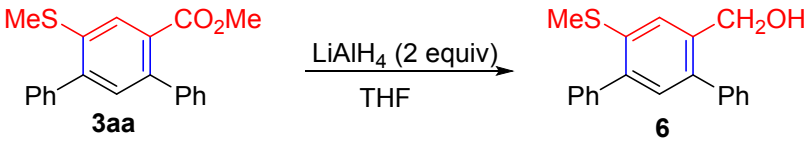
(B). General procedure C for the synthesis of derivative (5):



In a 15 mL Schlenk tube, compound **3da** (100 mg, 0.25 mmol) and *m*-CPBA (95 mg, 0.5 mmol, 1 equiv) were taken in DCM (2.0 mL). The mixture was stirred at room temperature for 45 min and monitored by TLC analysis. Upon completion, the reaction was quenched with saturated $NaHCO_3$ solution (1 mL) and the aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4. After filtration, the solvent was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to get the product **5** as white solid.

Methyl 4''-(tert-butyl)-6'-(methylsulfonyl)-[1,1':3',1''-terphenyl]-4'-carboxylate (5): 95 mg was obtained from **3da** (100 mg, 0.25 mmol) general procedure **C**. Yield 89%; brownish solid; mp 168−171 °C; R_f= 0.50 (SiO2, EtOAc:Hexane, 30:70); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.50 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.47 – 7.44 (m, 4H), 7.42 (d, *J* = 1.8 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 3.76 (s, 3H), 2.67 (s, 3H), 1.35 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.4, 151.5, 146.9, 143.8, 137.8, 137.5, 135.9, 135.3, 130.3, 130.2, 129.9, 128.91, 128.1, 128.0, 125.3, 52.5, 43.4, 34.7, 31.3; **IR** (KBr) ν 3042, 2965, 2889, 1731, 1309, 1247, 1151, 767 cm^{-1}; **HRMS** (QToF) calcd for $C_{25}H_{27}O_4S$ $[M+H]^+$ 423.1630 found 423.1623.

(C). General procedure D for the synthesis of derivative (6):



In a 15 mL Schlenk tube, to the solution of $LiAlH_4$ (38 mg, 1mmol) in dry THF (2.5 mL) at 0 ºC was added compound **3aa** (167 mg, 0.5 mmol) in dry THF (2.5 mL). The mixture was stirred for 1 h and was monitored by TLC analysis. Upon completion, the reaction mixture was quenched using saturated aq. NH_4Cl solution (3 mL), and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic extracts were washed with water and brine, dried over anhydrous Na_2SO_4. After filtration, the solvent was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to get the product **6** as brownish sticky solid.

(6'-(methylthio)-[1,1':3',1''-terphenyl]-4'-yl)methanol (6): 130 mg was obtained from **1x** (167 mg, 0.5 mmol). Yield 85%; brownish sticky solid; R_f= 0.50 (SiO2, EtOAc:Hexane,

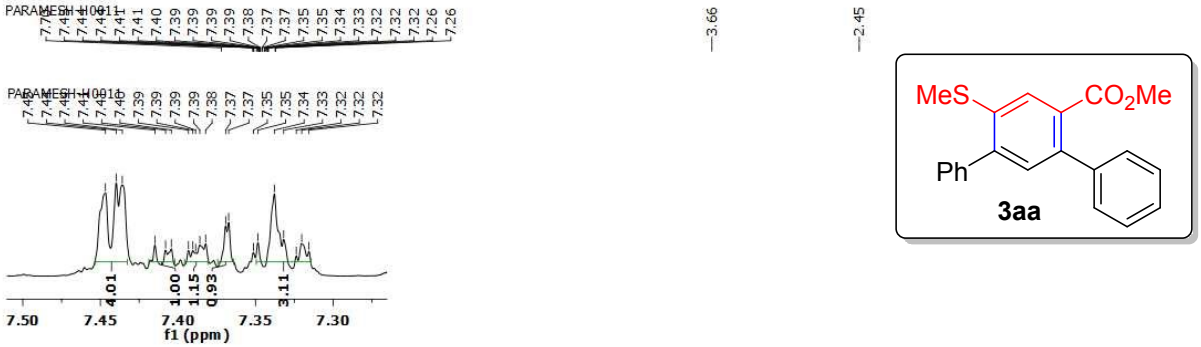
35:65); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.55 – 7.51 (m, 3H), 7.49 (dt, *J* = 3.5, 2.7 Hz, 3H), 7.47 (dd, *J* = 4.8, 2.9 Hz, 3H), 7.46 – 7.43 (m, 2H), 4.77 (s, 2H), 2.51 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 140.2, 140.0, 139.9, 137.7, 137.6, 136.6, 131.7, 129.3, 129.2, 128.3, 128.1, 127.7, 127.3, 125.2, 63.0, 16.1; **IR** (KBr) ν 3411, 3360, 2922, 1444, 1023, 768, 705 cm^{-1}; **HRMS** (QToF) calcd for $C_{20}H_{17}S$ $[M\text{-}OH]^+$ 289.1051 found 289.1010.

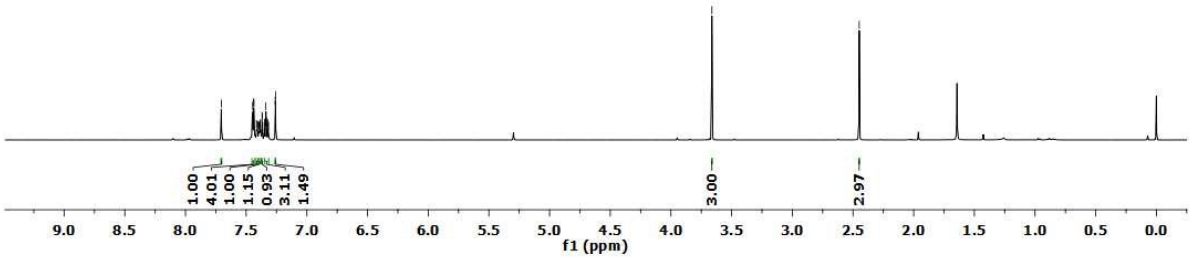
VI. References:

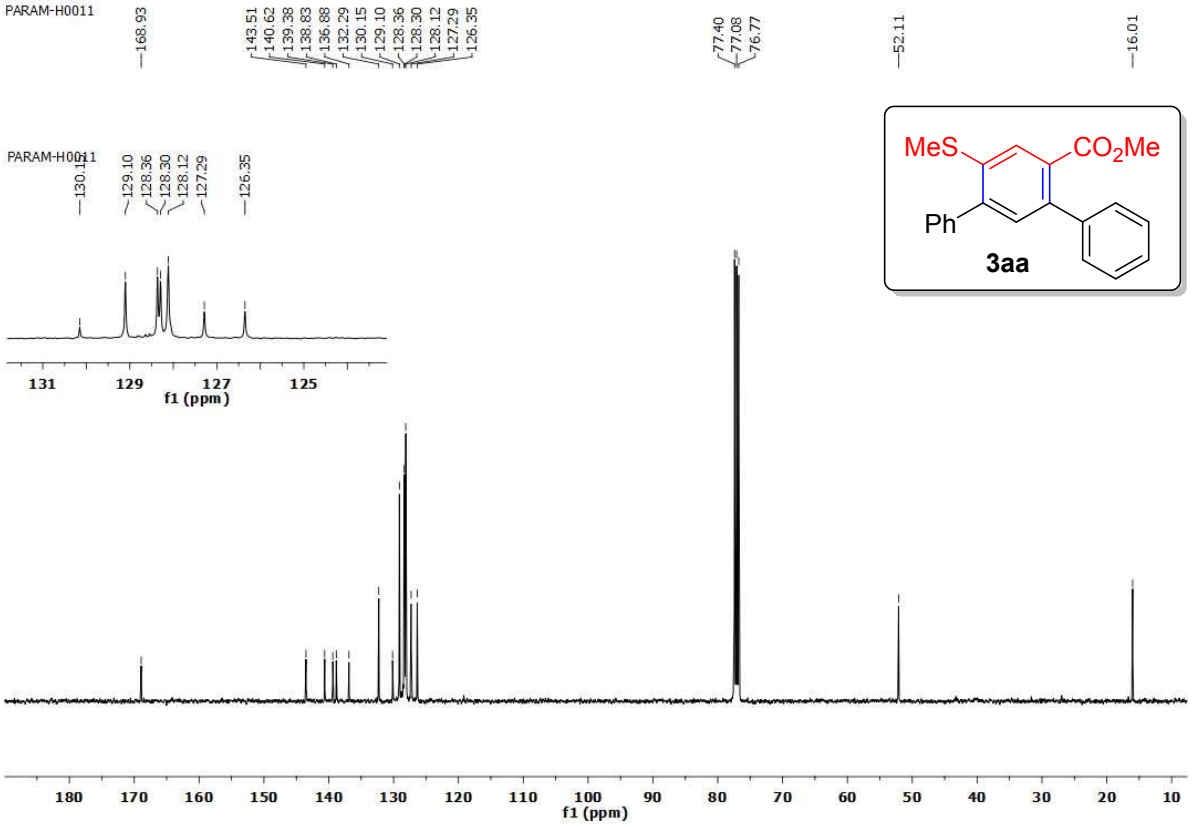
1. (a) S. Cai, K. Yang, D. Z. Wang, *Org. Lett.*, 2014, **16**, 2606; (b) K. Okamoto, T. Shimbayashi, E. Tamura, K. Ohe, *Org. Lett*., 2015, **17**, 5843; (c) C. E. Song, D. Jung, S. Y. Choung, E. J. S. G. RohLee, *Angew. Chem., Int. Ed*., 2004, **43**, 6183; (d) D. Qiana, J. Zhang, *Chem. Commun*., 2012, **48**, 7082; (e) J. Meesin, P. Katrun, C. Pareseecharoen, M. Pohmakotr, V. Reutrakul, D. Soorukram, C. Kuhakarn*, J. Org. Chem*., 2016, **81**, 2744; (f) R. Samineni, J. Madapal, S. Pabbaraja, G. Mehta, *Org. Lett*., 2017, **19**, 6152; (g) S. Singh, R. Samineni, S. Pabbaraja, G. Mehta, *Angew. Chem., Int. Ed*., 2018, **57**, 16847.

2. Q.-G. Wang, X.-M. Deng, B.-H. Zhu, L.-W. Ye, X.-L. Sun, C.-Y. Li, C.-Y. Zhu, Q. Shen, and Y. Tang, *J. Am. Chem. Soc*., 2008, **130**, 5408.

VII. Copies of ^{1}H and ^{13}C NMR spectra





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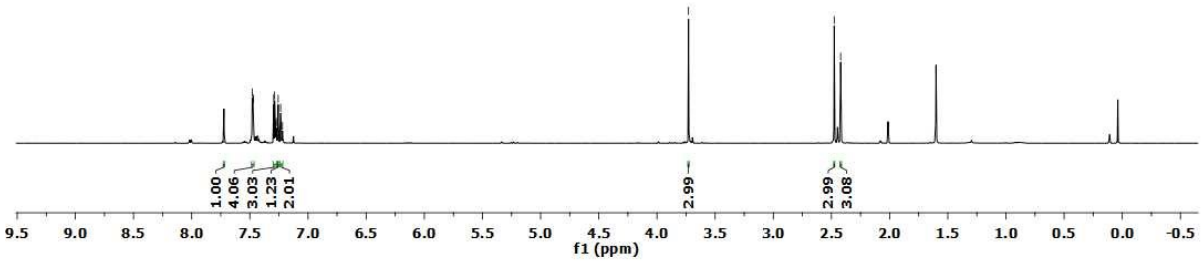
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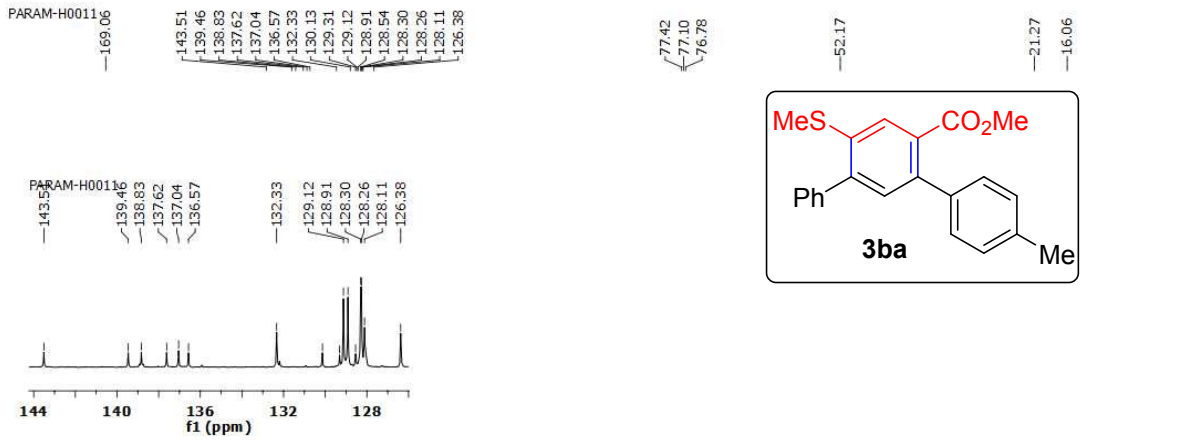
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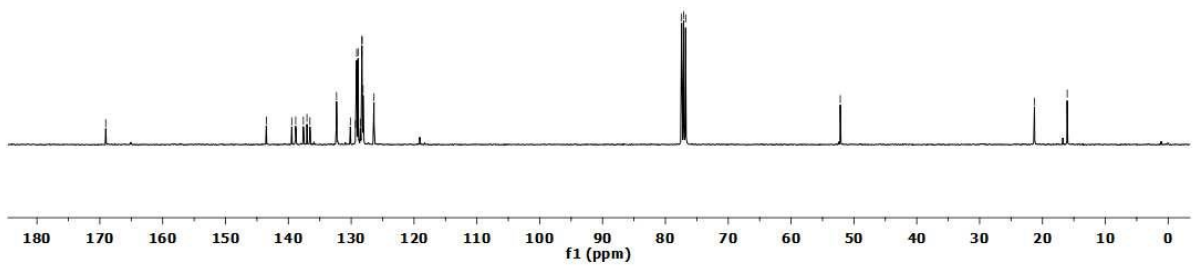
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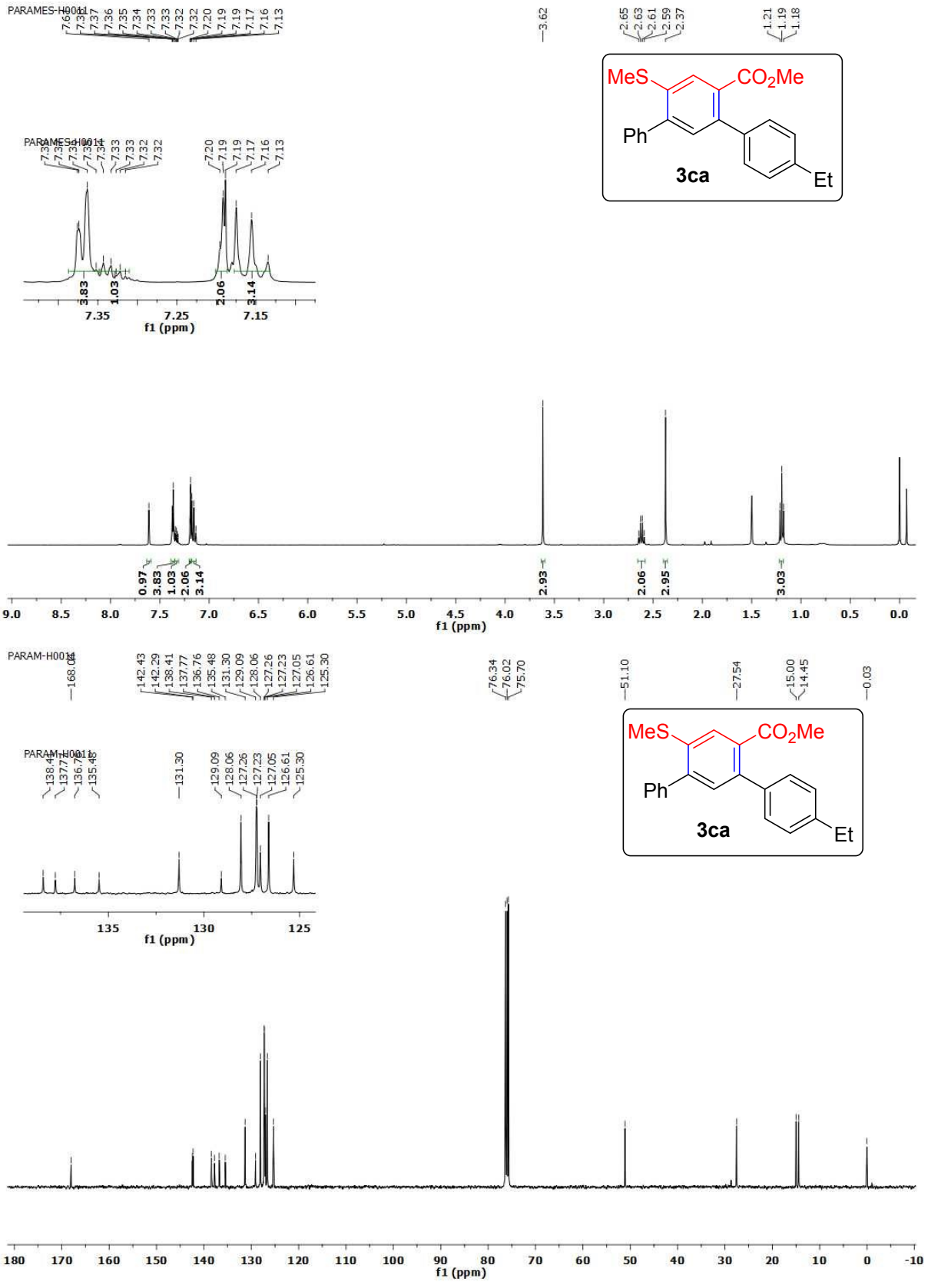
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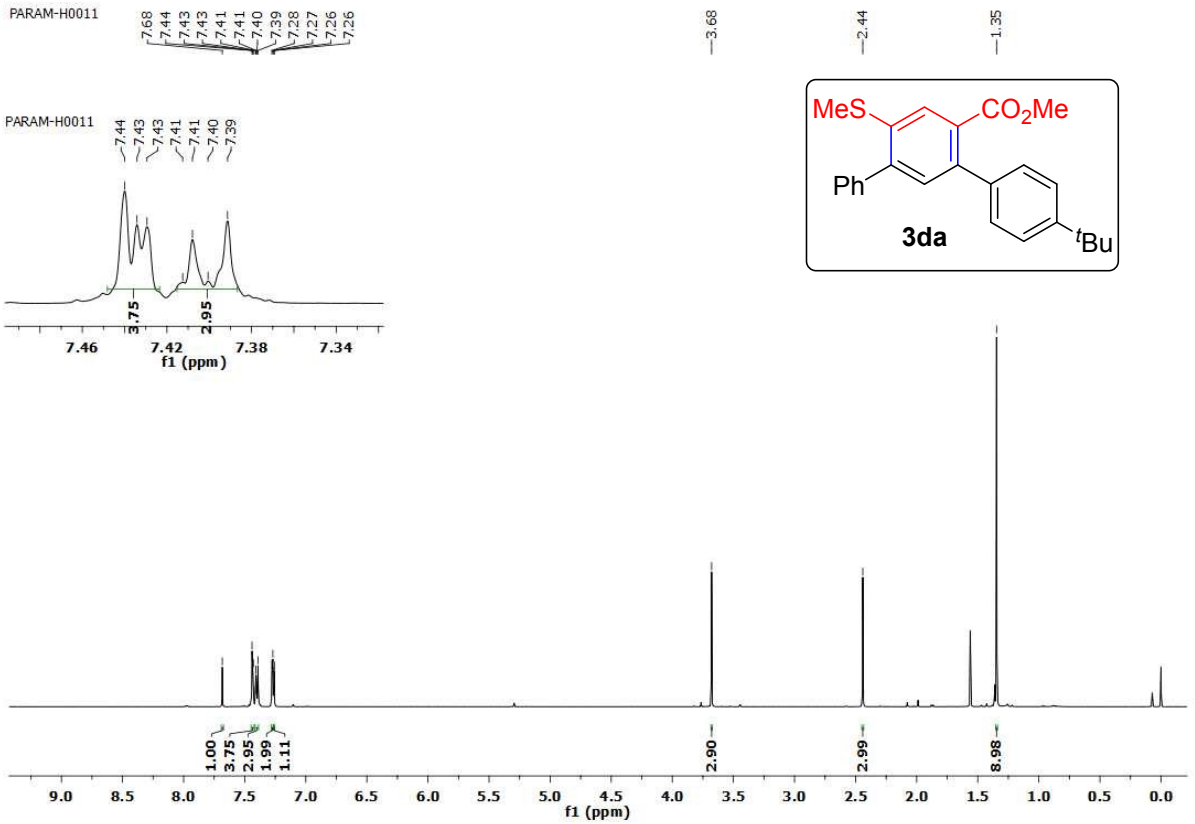
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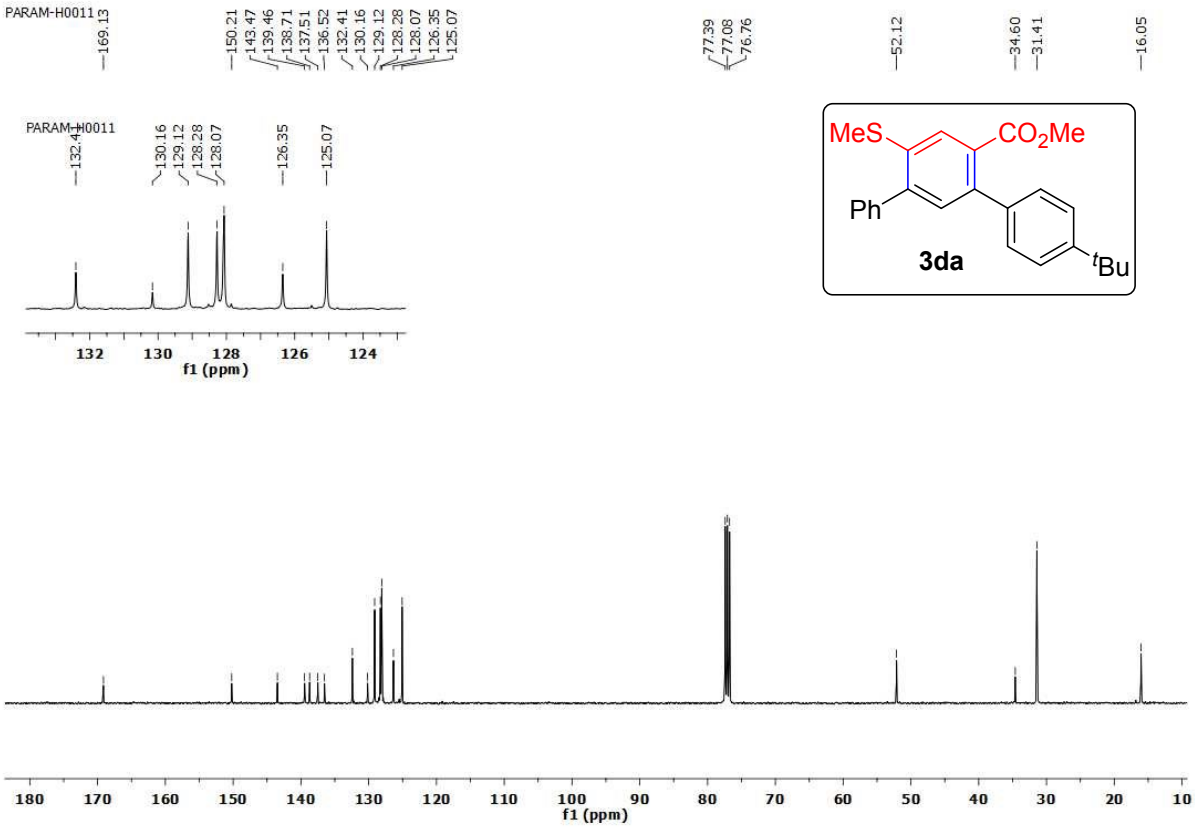
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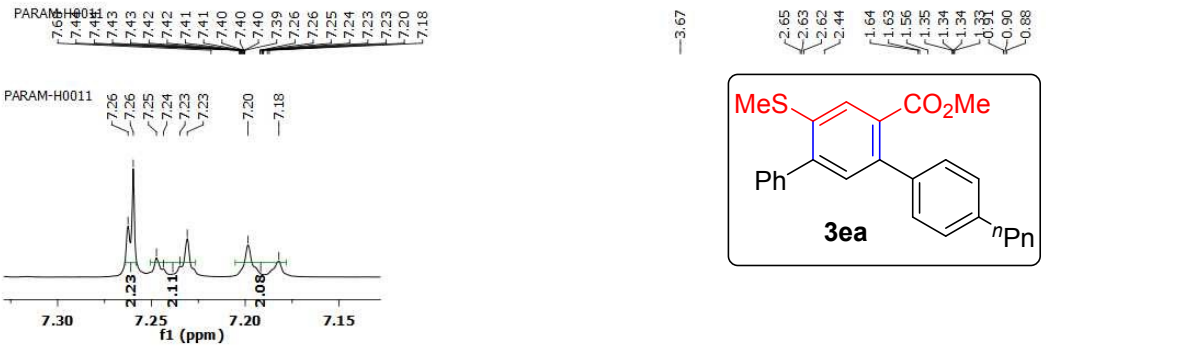
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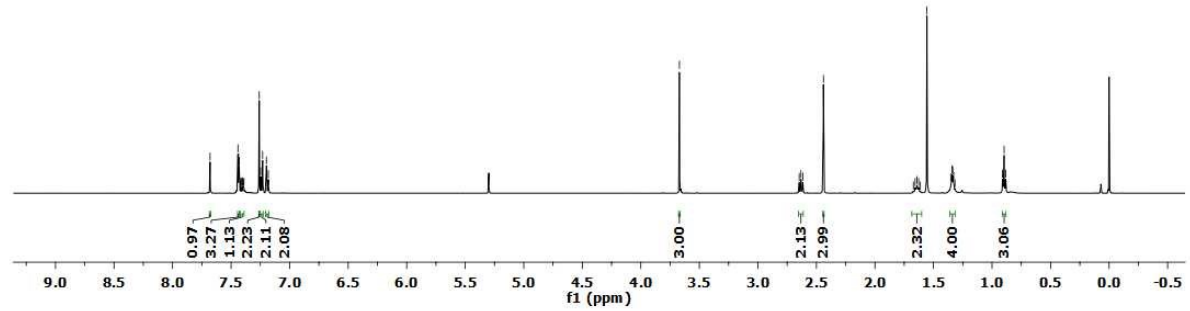
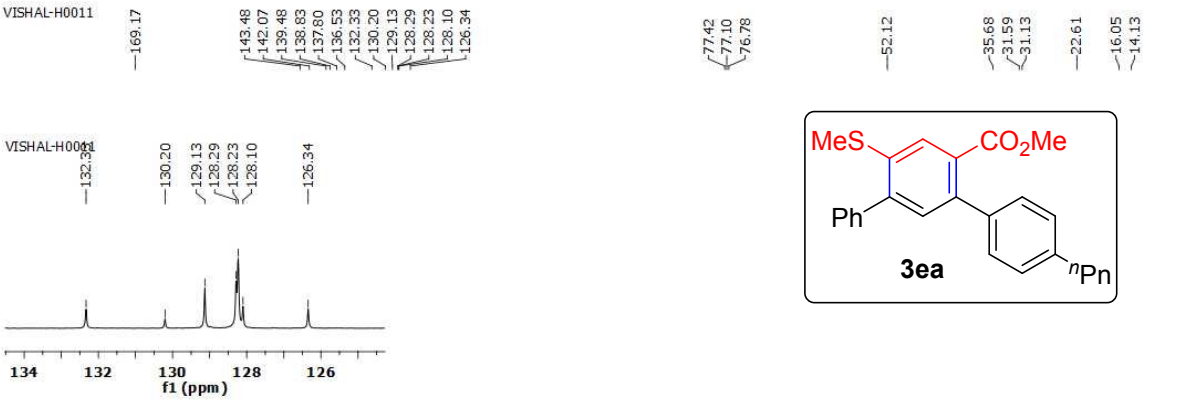
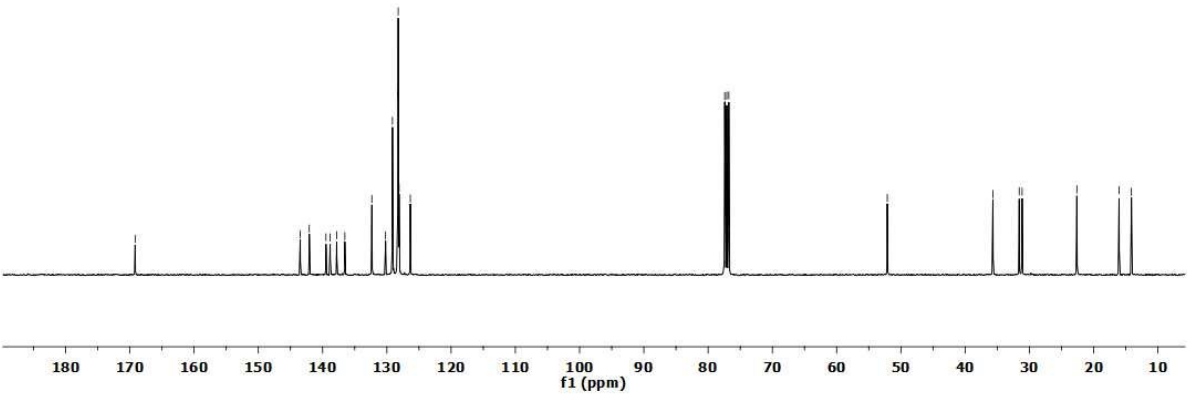
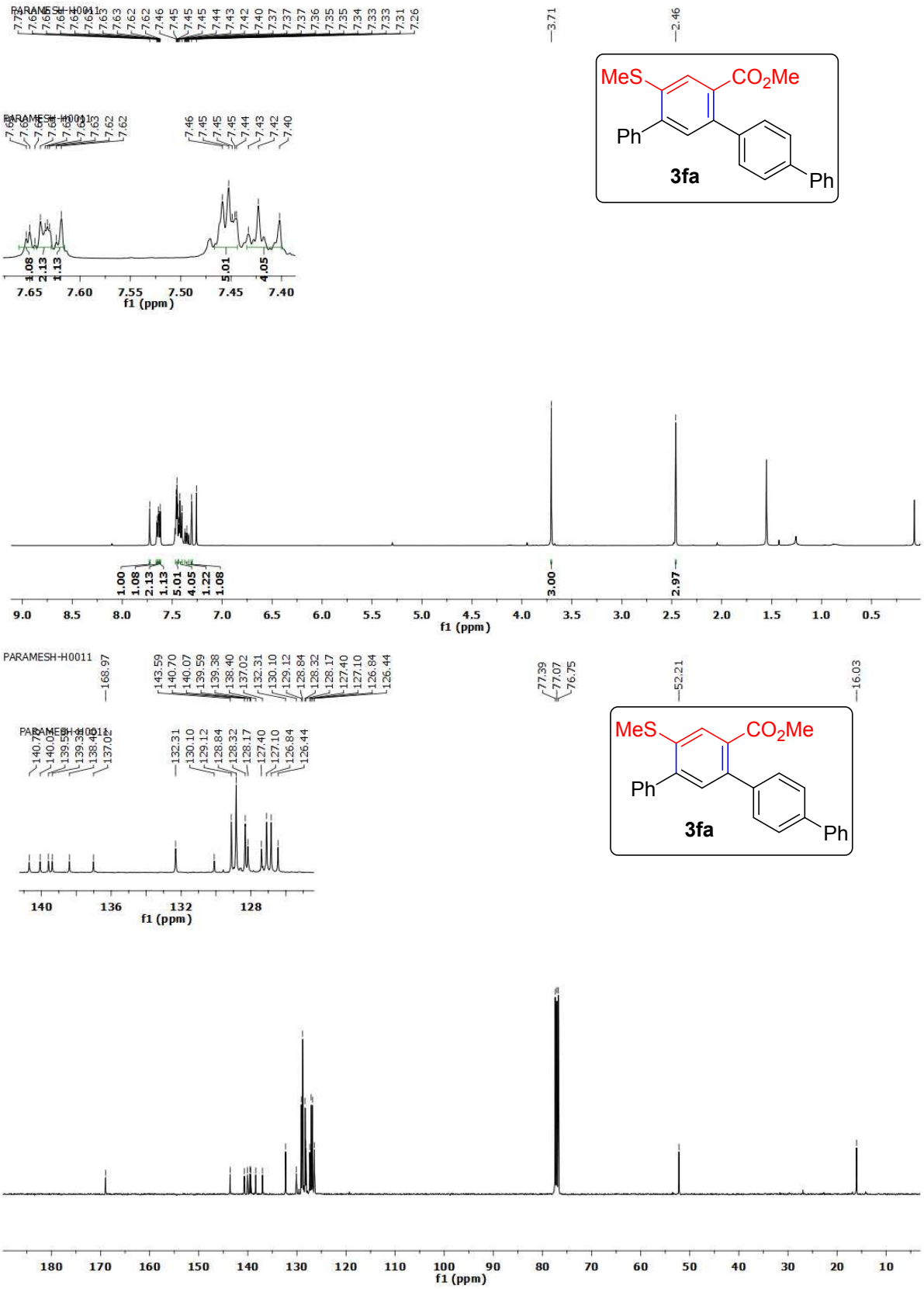
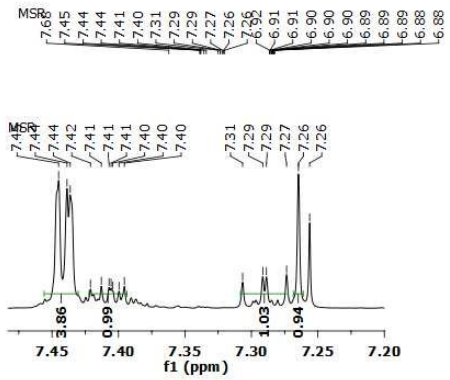
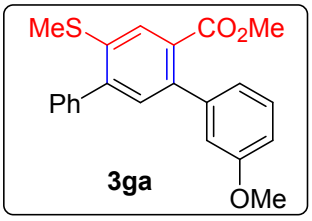

f1 (ppm)

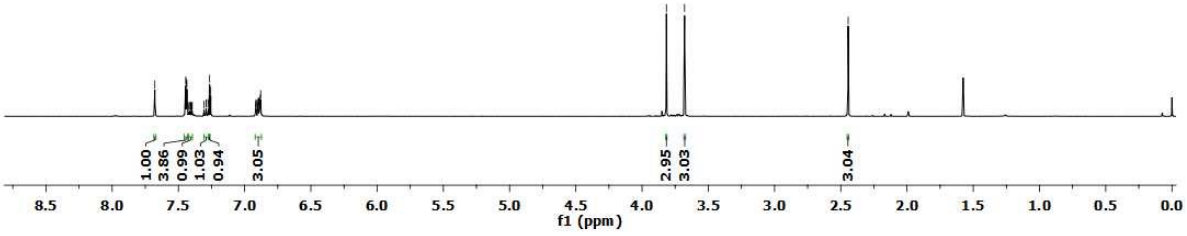

VISHAL-H0011
MeS
CO2Me
Ph
3ea
nPn
f1 (ppm)

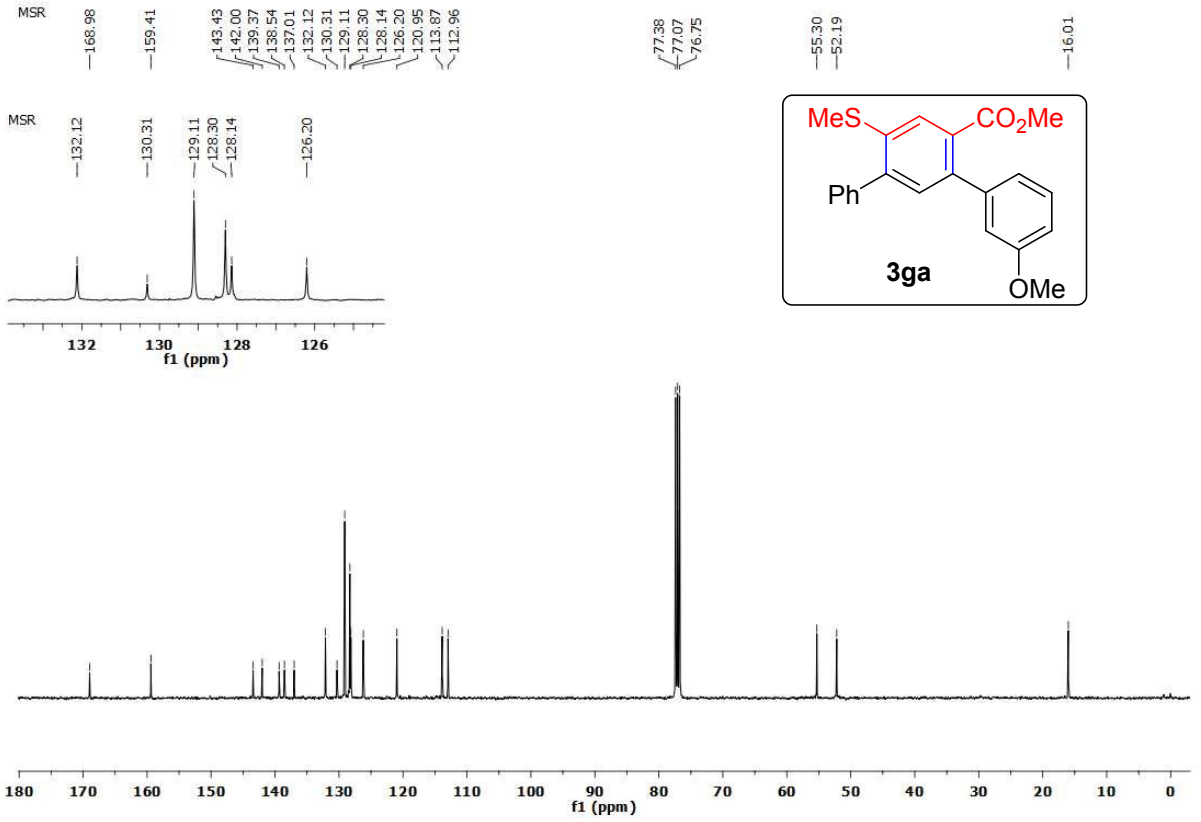

f1 (ppm)


PARAMESH-H0011
3.71
2.46
MeS
CO2Me
Ph
3fa
Ph
1.08
2.13
1.13
5.01
4.05
f1 (ppm)
1.00
1.08
2.13
1.13
5.01
4.05
1.22
1.08
3.00
2.97
f1 (ppm)
PARAMESH-H0011
168.97
143.59
140.70
140.07
139.59
139.38
138.40
137.02
132.31
130.10
129.12
128.84
128.32
128.17
127.40
127.10
126.84
126.44
77.39
77.07
76.75
52.21
16.03
MeS
CO2Me
Ph
3fa
Ph
f1 (ppm)
f1 (ppm)

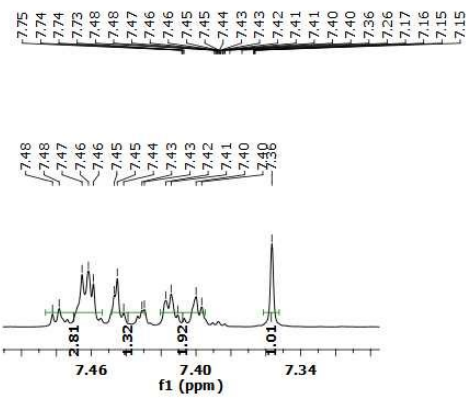

MSR
7.68
7.45
7.44
7.44
7.41
7.40
7.31
7.29
7.29
7.27
7.26
6.92
6.91
6.91
6.90
6.90
6.89
6.89
6.89
6.88
6.88
3.82
3.68
2.44
MSR
3.86
0.99
1.03
0.94
7.45
7.40
7.35
7.30
7.25
7.20
f1 (ppm)

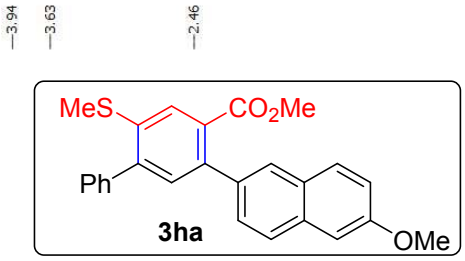

MeS
CO2Me
Ph
3ga
OMe

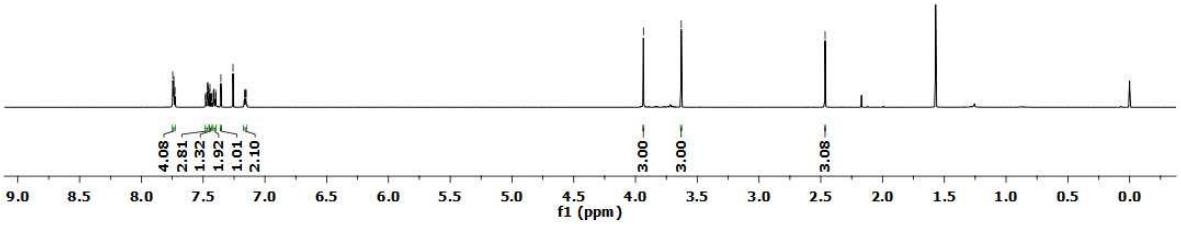

1.00
3.86
0.99
1.03
0.94
3.05
2.95
3.03
3.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

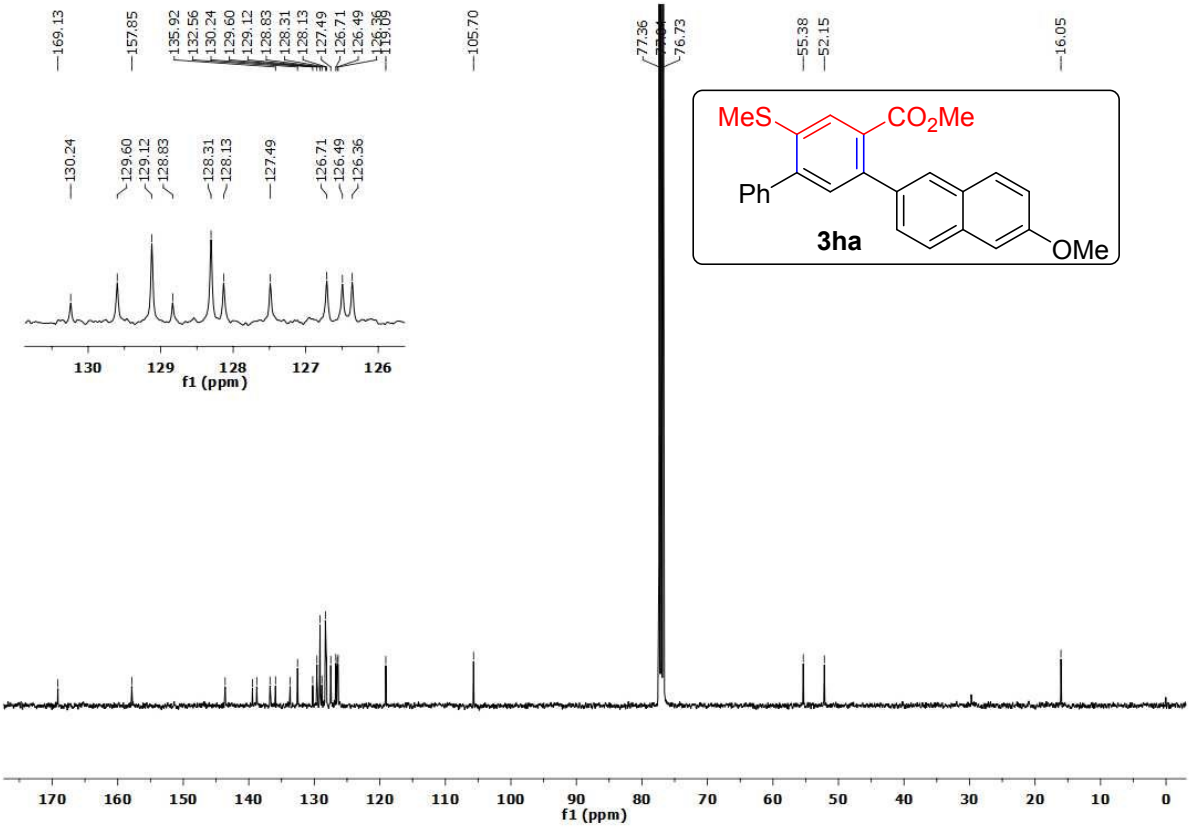

MSR
168.98
159.41
143.43
142.00
139.37
138.54
137.01
132.12
130.31
129.11
128.30
128.14
126.20
120.95
113.87
112.96
77.38
77.07
76.75
55.30
52.19
16.01
MSR
132.12
130.31
129.11
128.30
128.14
126.20
132
130
128
126
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

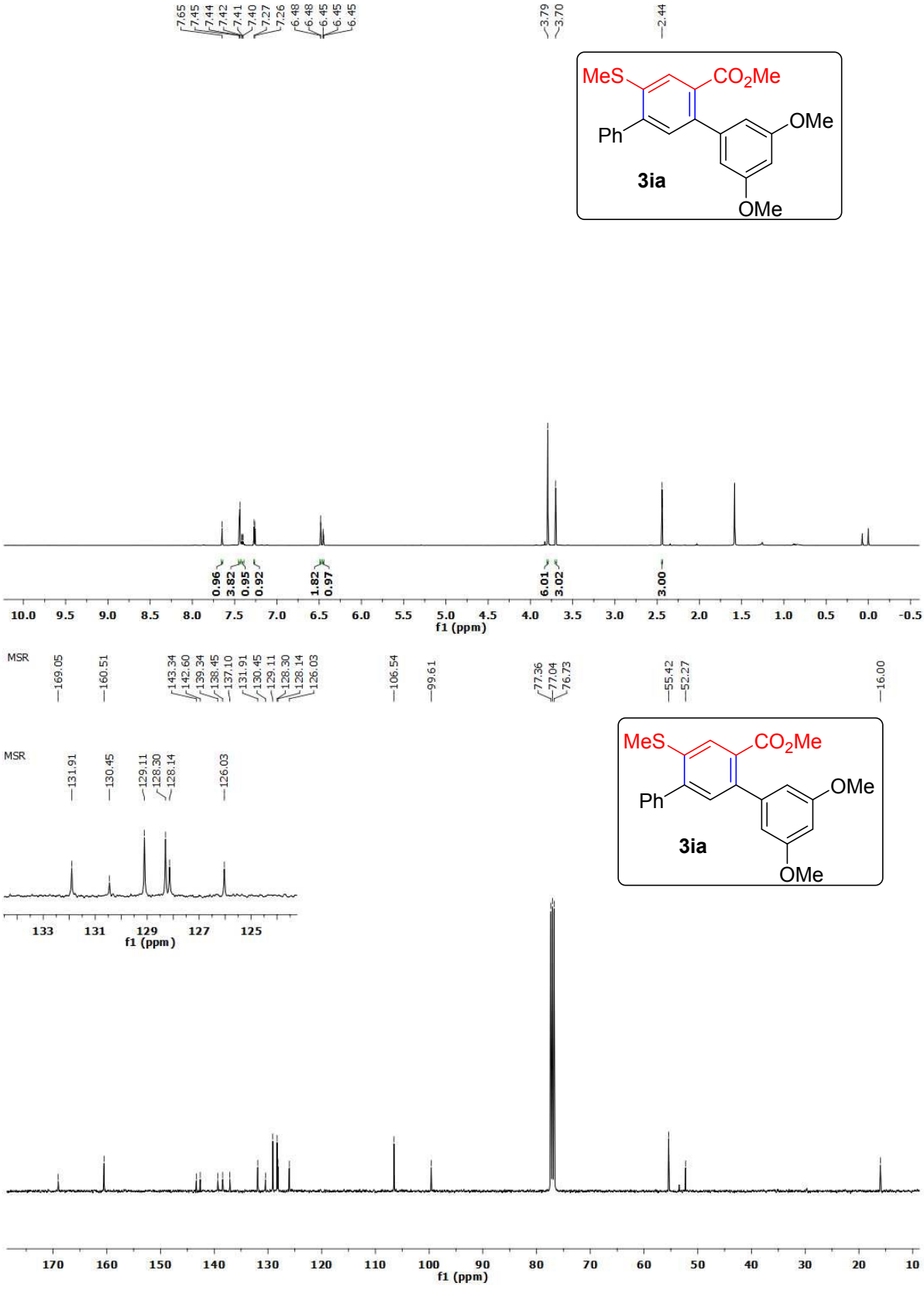
MeS
CO2Me
Ph
3ga
OMe

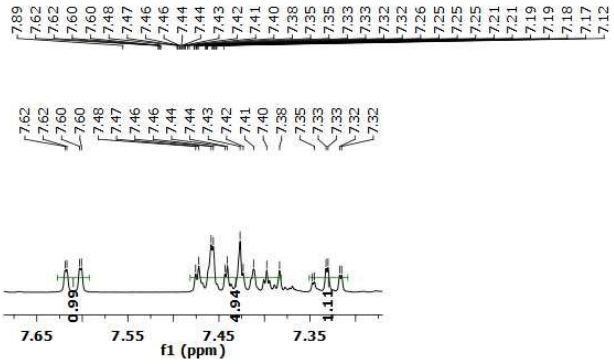

7.75
7.74
7.74
7.73
7.48
7.48
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.36
7.26
7.17
7.16
7.15
7.15
7.48
7.48
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.41
7.40
7.40
2.81
1.32
1.92
1.01
7.46
7.40
7.34
f1 (ppm)

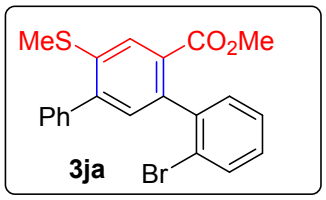

3.94
3.63
2.46
MeS
CO2Me
Ph
3ha
OMe

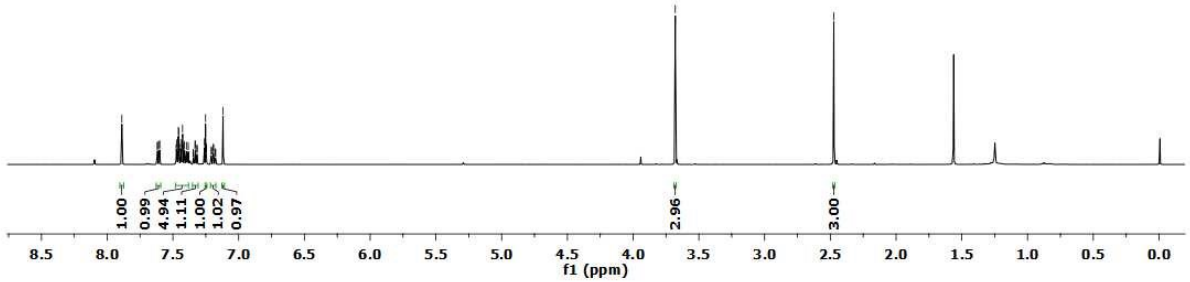

4.08
2.81
1.32
1.92
1.01
2.10
3.00
3.00
3.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

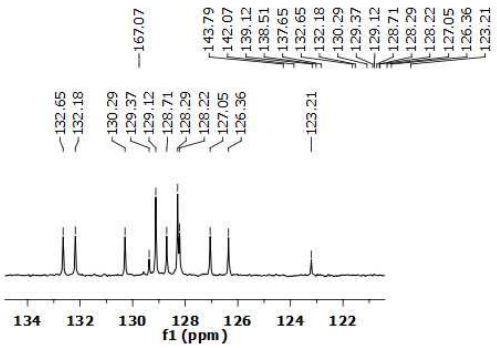

169.13
157.85
135.92
132.56
130.24
129.60
129.12
128.83
128.31
128.13
127.49
126.71
126.49
126.36
105.70
77.36
77.04
76.73
55.38
52.15
16.05
130.24
129.60
129.12
128.83
128.31
128.13
127.49
126.71
126.49
126.36
130
129
128
127
126
f1 (ppm)
MeS
CO2Me
Ph
3ha
OMe
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

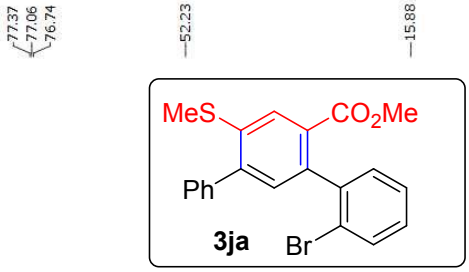

7.65
7.45
7.44
7.42
7.41
7.40
7.27
7.26
6.48
6.45
6.45
6.45
3.79
3.70
2.44
MeS
CO2Me
Ph
OMe
OMe
3ia
0.96
3.82
0.95
0.92
1.82
0.97
6.01
3.02
3.00
f1 (ppm)
MSR
169.05
160.51
143.34
142.60
139.34
138.45
137.10
131.91
130.45
129.11
128.30
128.14
126.03
106.54
99.61
77.36
77.04
76.73
55.42
52.27
16.00
MSR
131.91
130.45
129.11
128.30
128.14
126.03
f1 (ppm)

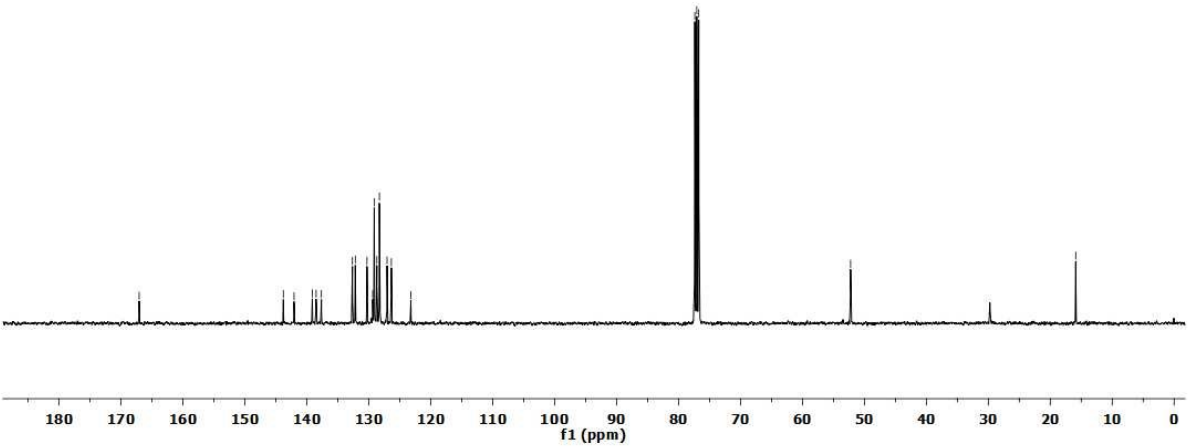

7.89
7.62
7.62
7.60
7.60
7.48
7.47
7.46
7.46
7.44
7.44
7.43
7.42
7.41
7.40
7.38
7.35
7.35
7.33
7.33
7.32
7.32
7.26
7.25
7.25
7.25
7.21
7.21
7.19
7.19
7.18
7.17
7.12
3.68
2.47
0.99
4.94
1.11
7.65
7.55
7.45
7.35
f1 (ppm)

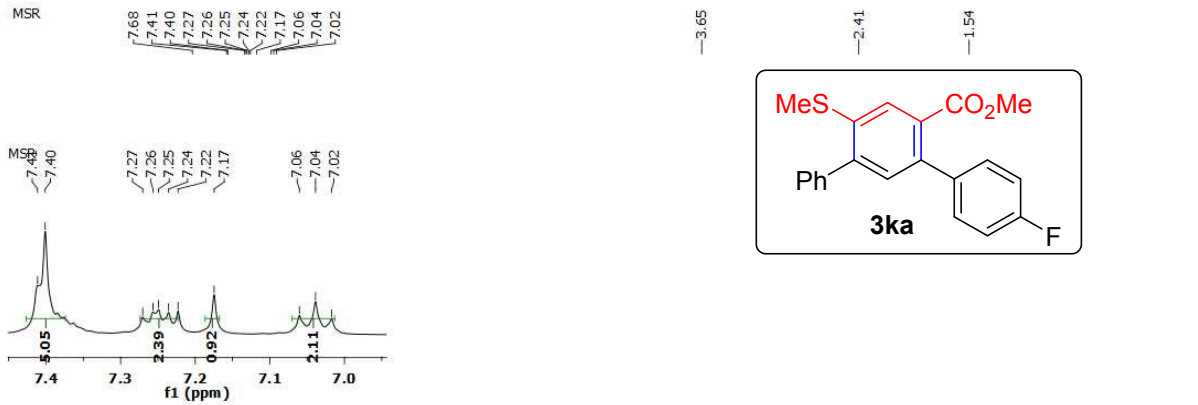

MeS
CO2Me
Ph
3ja
Br

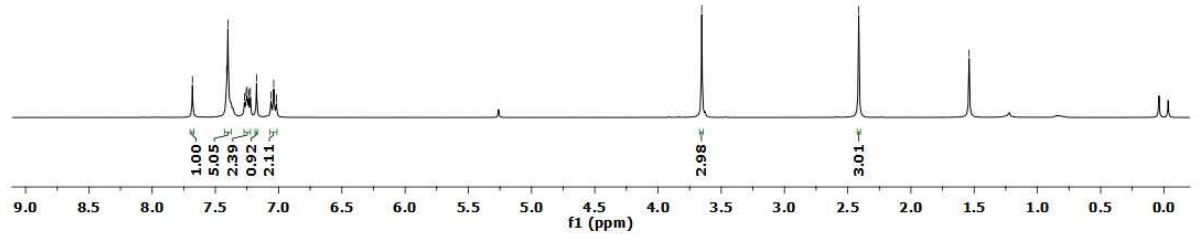

1.00
0.99
4.94
1.11
1.00
1.02
0.97
2.96
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

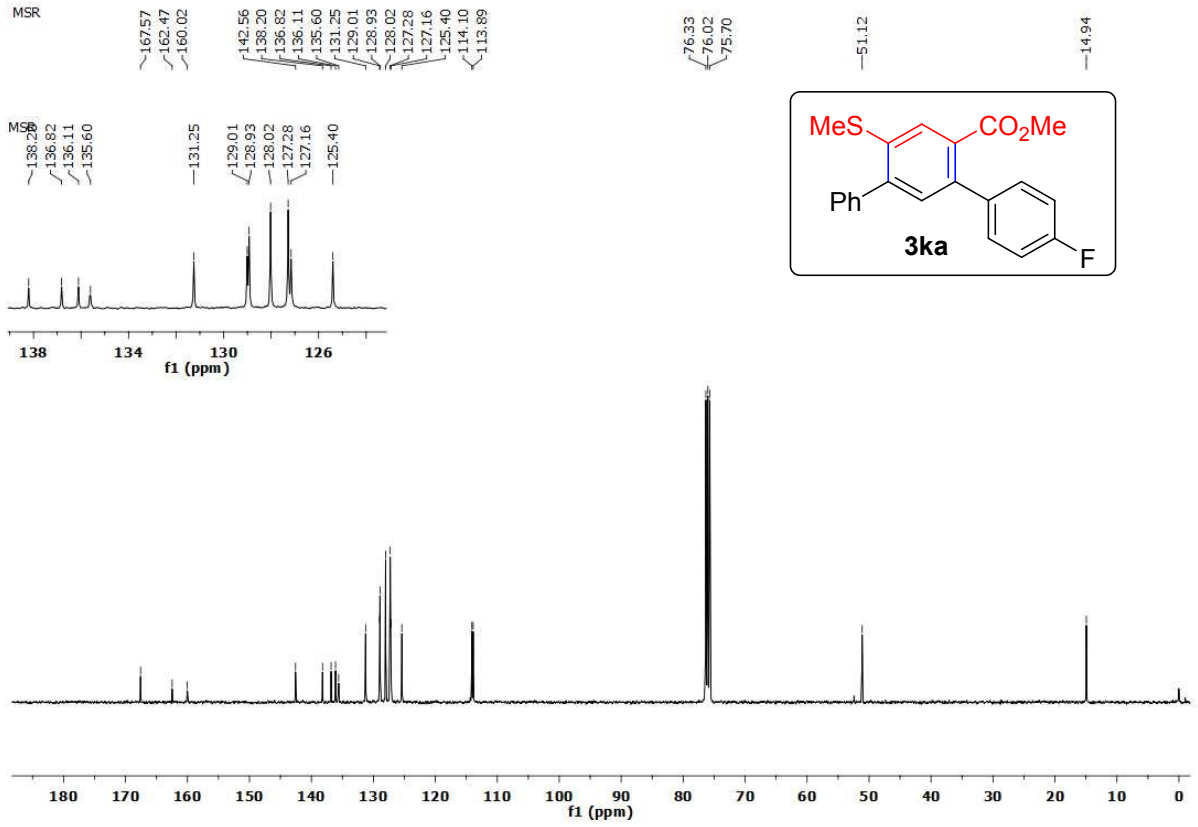

167.07
143.79
142.07
139.12
138.51
137.65
132.65
132.18
130.29
129.37
129.12
128.71
128.29
128.22
127.05
126.36
123.21
134
132
130
128
126
124
122
f1 (ppm)


77.37
77.06
76.74
52.23
15.88
MeS
CO2Me
Ph
3ja
Br

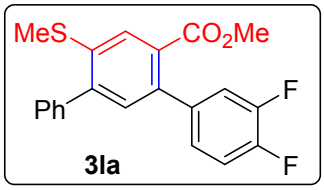

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

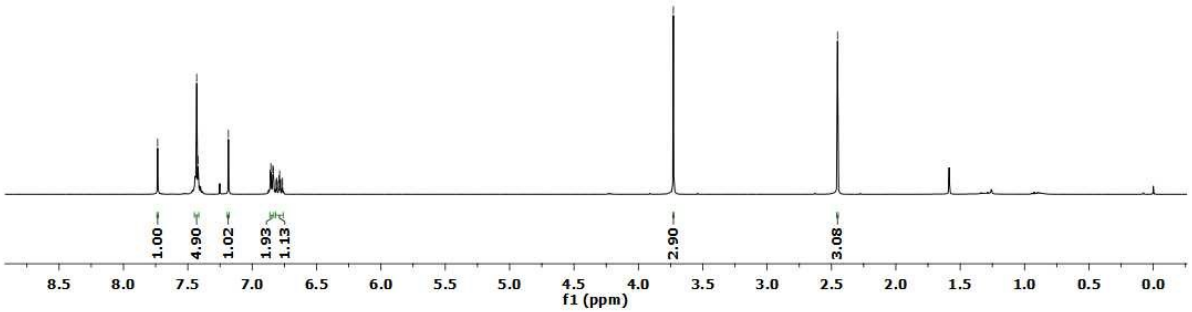

MSR
7.68
7.41
7.40
7.27
7.26
7.25
7.24
7.22
7.17
7.06
7.04
7.02
3.65
2.41
1.54
MeS
CO2Me
Ph
F
3ka
5.05
2.39
0.92
2.11
f1 (ppm)


1.00
5.05
2.39
0.92
2.11
2.98
3.01
f1 (ppm)

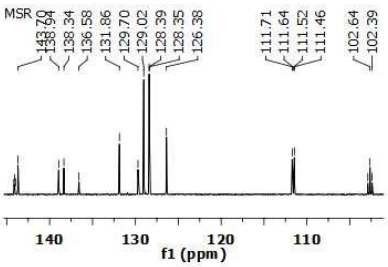

MSR
167.57
162.47
160.02
142.56
138.20
136.82
136.11
135.60
131.25
129.01
128.93
128.02
127.28
127.16
125.40
114.10
113.89
76.33
76.02
75.70
51.12
14.94
MeS
CO2Me
Ph
F
3ka
f1 (ppm)


7.73
7.43
7.42
7.18
6.86
6.86
6.85
6.85
6.84
6.83
6.81
6.81
6.80
6.79
6.79
6.78
6.77
6.76
3.73
2.45


MeS
CO2Me
Ph
F
F
3la


1.00
4.90
1.02
1.93
1.13
2.90
3.08
f1 (ppm)


MSR
167.99
163.90
163.77
161.43
161.30
144.08
143.98
143.70
138.94
138.34
136.58
131.86
129.70
129.02
128.39
128.35
126.38
111.71
111.64
111.52
111.46
102.90
102.64
102.39
77.39
77.07
76.75
52.33
15.87


MSR
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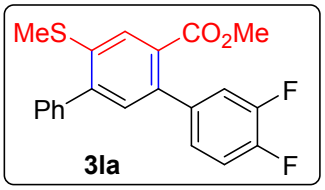
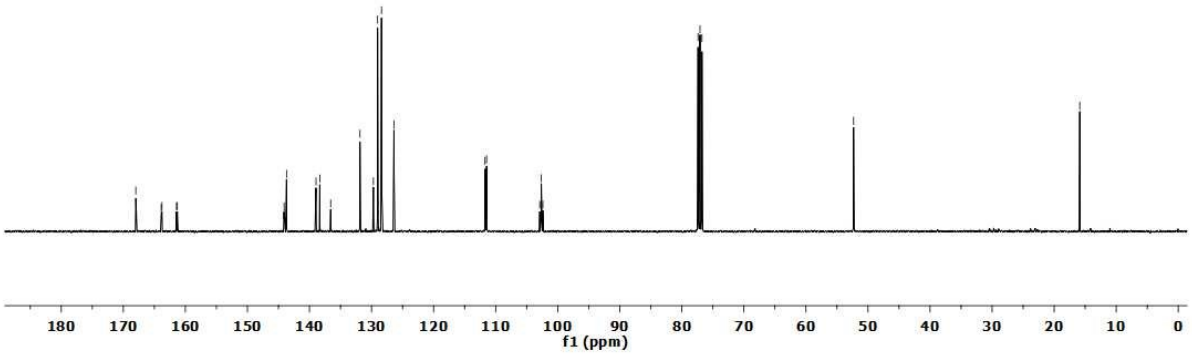
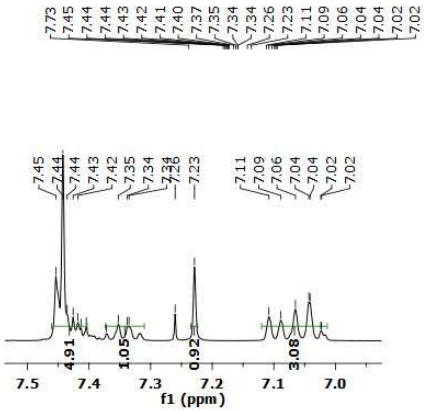
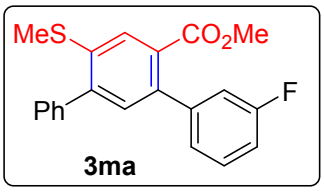
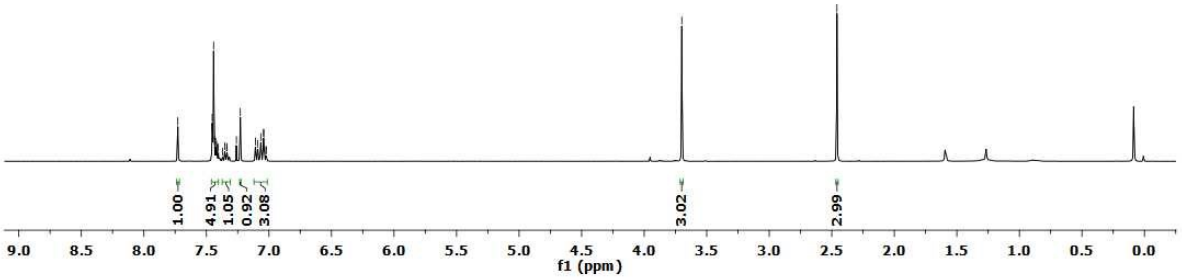
138.34
136.58
131.86
129.70
129.02
128.39
128.35
126.38
111.71
111.64
111.52
111.46
102.64
102.39
f1 (ppm)

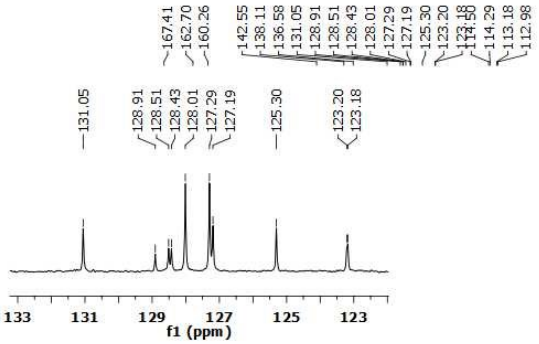

MeS
CO2Me
Ph
F
F
3la


f1 (ppm)

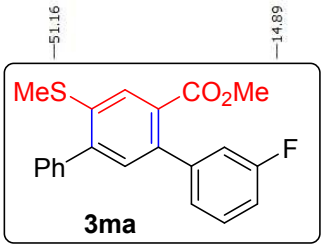

7.73
7.45
7.44
7.44
7.43
7.42
7.41
7.40
7.37
7.35
7.34
7.34
7.26
7.23
7.11
7.09
7.06
7.04
7.04
7.02
7.02
3.70
2.46
7.45
7.44
7.44
7.43
7.42
7.35
7.34
7.23
7.11
7.09
7.06
7.04
7.04
7.02
7.02
4.91
1.05
0.92
3.08
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)

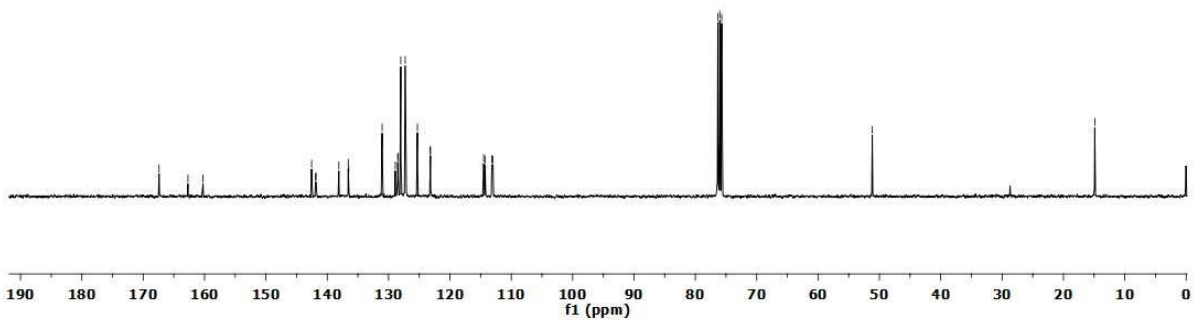

MeS
CO2Me
Ph
F
3ma

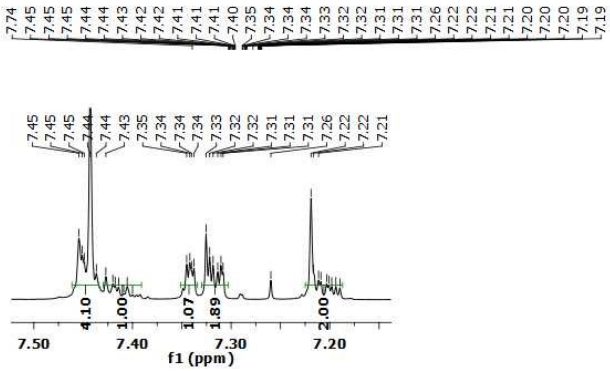

1.00
4.91
1.05
0.92
3.08
3.02
2.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

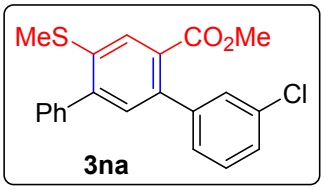

167.41
162.70
160.26
142.55
138.11
136.58
131.05
128.91
128.51
128.43
128.01
127.29
127.19
125.30
123.20
123.18
114.50
114.29
113.18
112.98
131.05
128.91
128.51
128.43
128.01
127.29
127.19
125.30
123.20
123.18
133
131
129
127
125
123
f1 (ppm)

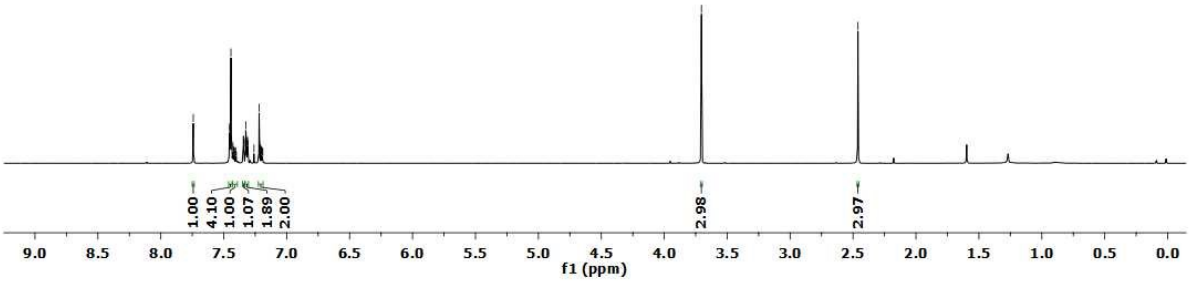

76.34
76.02
75.70

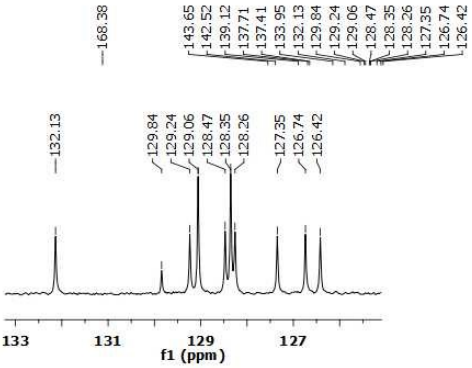

51.16
14.89
MeS
CO2Me
Ph
F
3ma


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


7.74
7.45
7.45
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.41
7.41
7.40
7.35
7.34
7.34
7.34
7.33
7.32
7.32
7.31
7.31
7.31
7.26
7.22
7.22
7.21
7.21
7.20
7.20
7.20
7.19
7.19
3.70
2.46
4.10
1.00
1.07
1.89
2.00
7.50
7.40
7.30
7.20
f1 (ppm)


MeS
CO2Me
Ph
Cl
3na


1.00
4.10
1.00
1.07
1.89
2.00
2.98
2.97
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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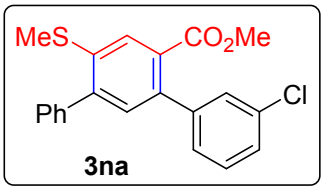
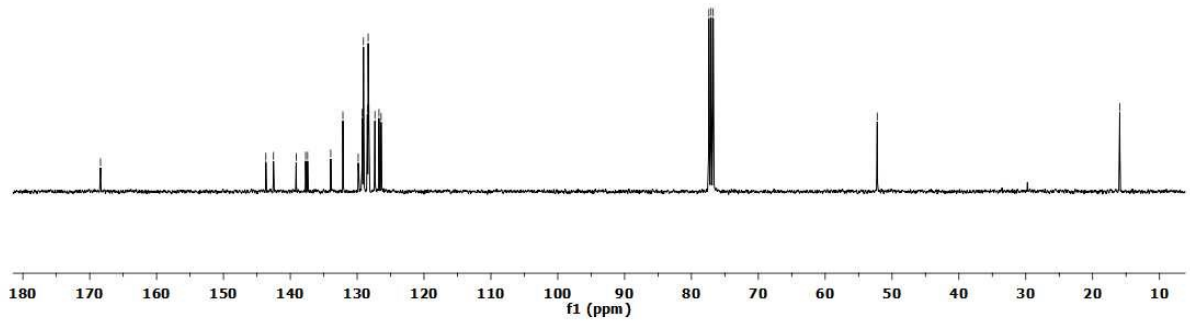
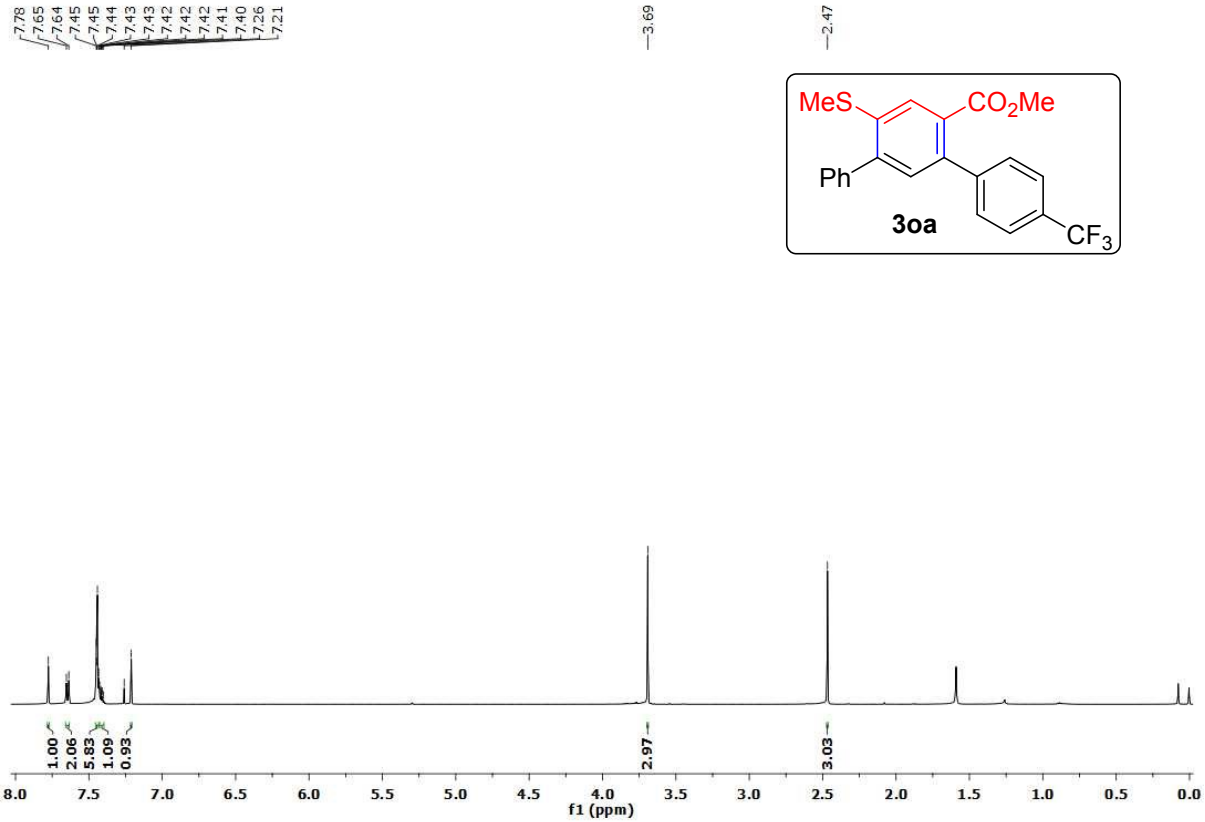
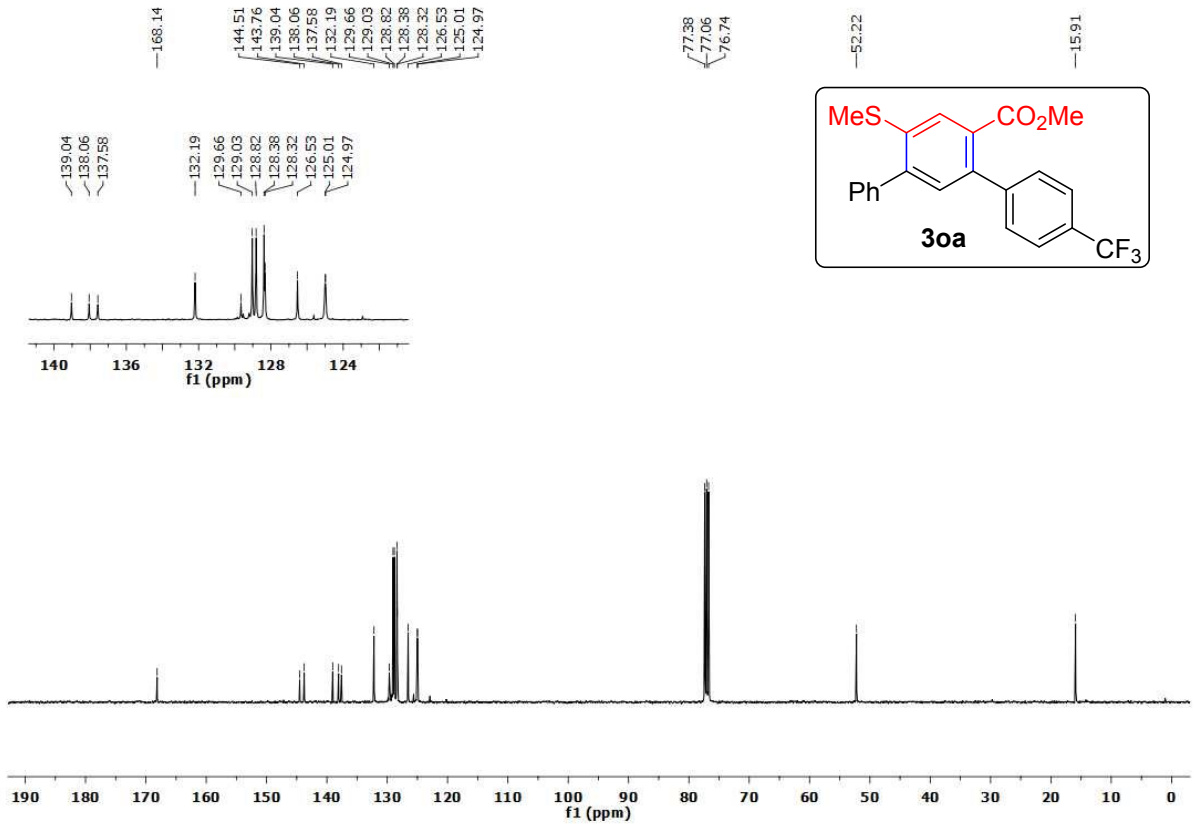
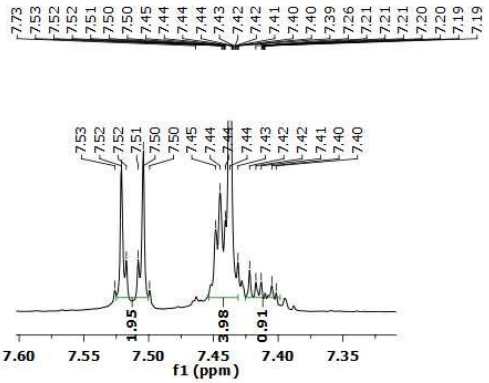
143.65
142.52
139.12
137.71
137.41
133.95
132.13
129.84
129.24
129.06
128.47
128.35
128.26
127.35
126.74
126.42
77.39
77.07
76.75
52.22
15.94
132.13
129.84
129.24
129.06
128.47
128.35
128.26
127.35
126.74
126.42
133
131
129
127
f1 (ppm)

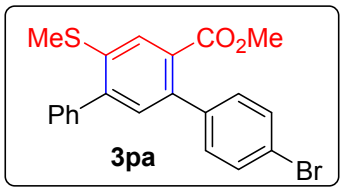

MeS
CO2Me
Ph
Cl
3na

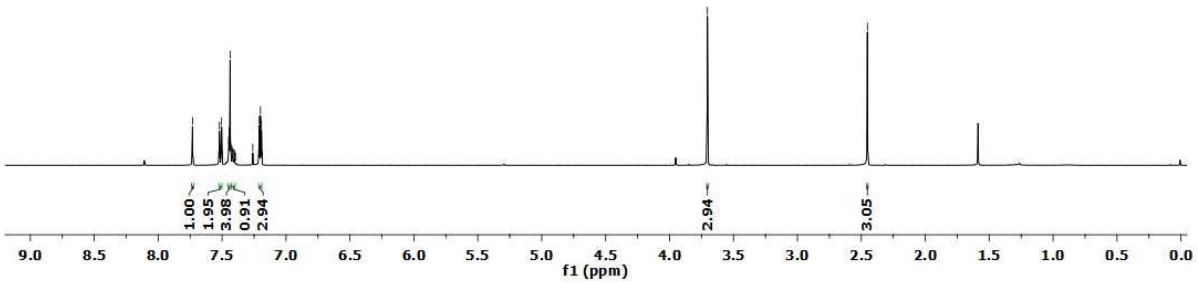

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

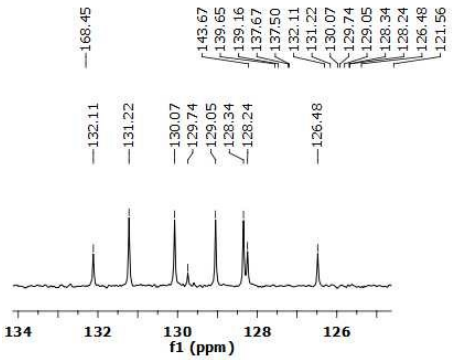

7.78
7.65
7.64
7.45
7.45
7.44
7.43
7.43
7.42
7.42
7.42
7.41
7.40
7.26
7.21
3.69
2.47
MeS
CO2Me
Ph
3oa
CF3
1.00
2.06
5.83
1.09
0.93
2.97
3.03
f1 (ppm)


168.14
144.51
143.76
139.04
138.06
137.58
132.19
129.66
129.03
128.82
128.38
128.32
126.53
125.01
124.97
77.38
77.06
76.74
52.22
15.91
MeS
CO2Me
Ph
3oa
CF3
f1 (ppm)


7.73
7.53
7.52
7.52
7.51
7.50
7.50
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.26
7.21
7.21
7.20
7.20
7.19
7.19
3.70
2.45
1.95
3.98
0.91
7.60
7.55
7.50
7.45
7.40
7.35
f1 (ppm)


MeS
CO2Me
Ph
3pa
Br


1.00
1.95
3.98
0.91
2.94
2.94
3.05
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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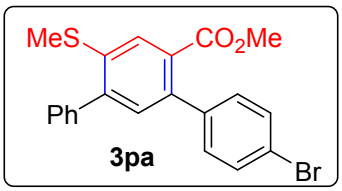
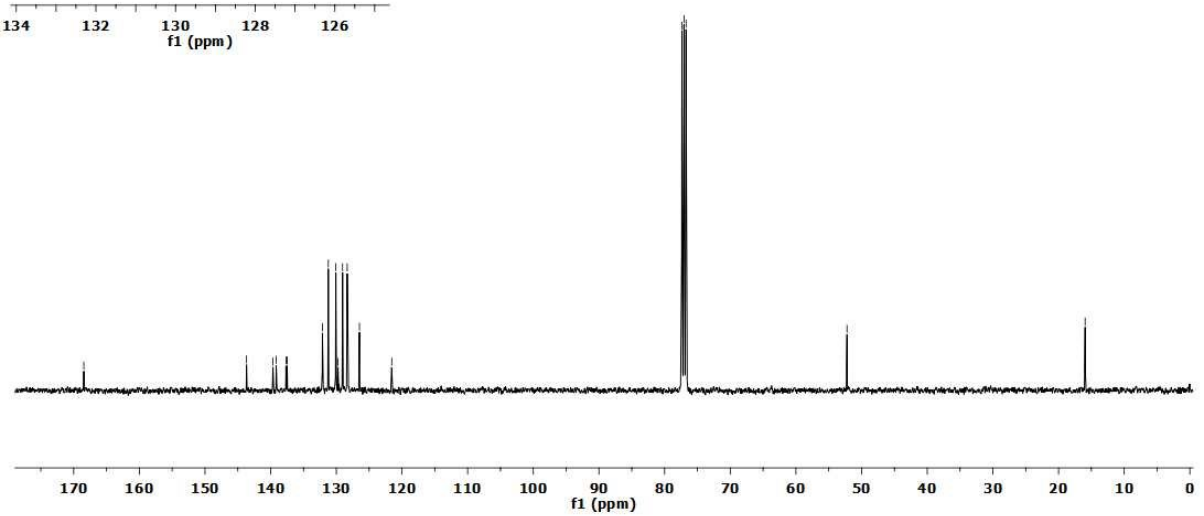
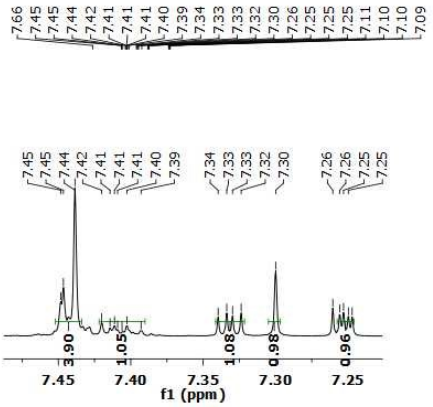
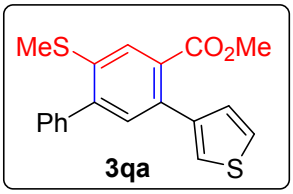
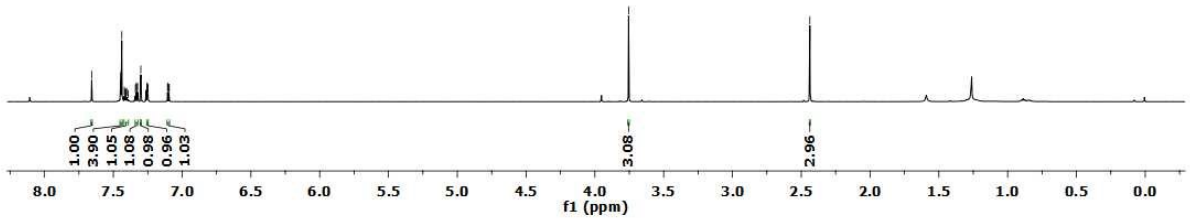
143.67
139.65
139.16
137.67
137.50
132.11
131.22
130.07
129.74
129.05
128.34
128.24
126.48
121.56
77.37
77.05
76.73
52.22
15.95
132.11
131.22
130.07
129.74
129.05
128.34
128.24
126.48
134
132
130
128
126
f1 (ppm)

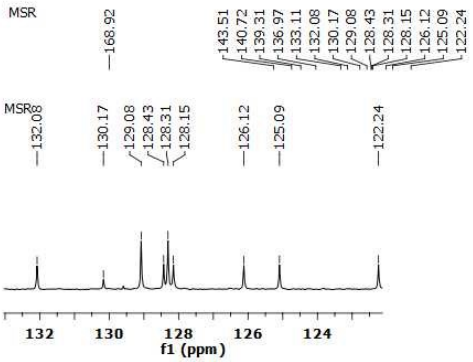

MeS
CO2Me
Ph
3pa
Br

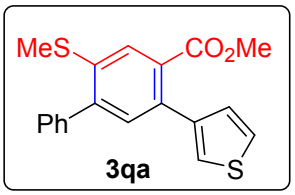

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

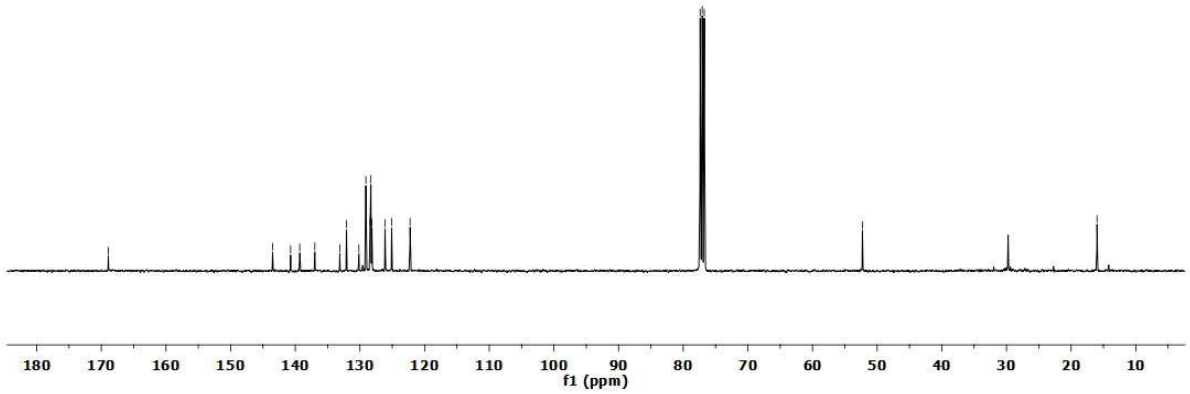

7.66
7.45
7.45
7.44
7.42
7.41
7.41
7.41
7.40
7.39
7.34
7.33
7.33
7.32
7.30
7.26
7.25
7.25
7.11
7.10
7.10
7.09
3.75
2.44
3.90
1.05
1.08
0.98
0.96
7.45
7.40
7.35
7.30
7.25
f1 (ppm)

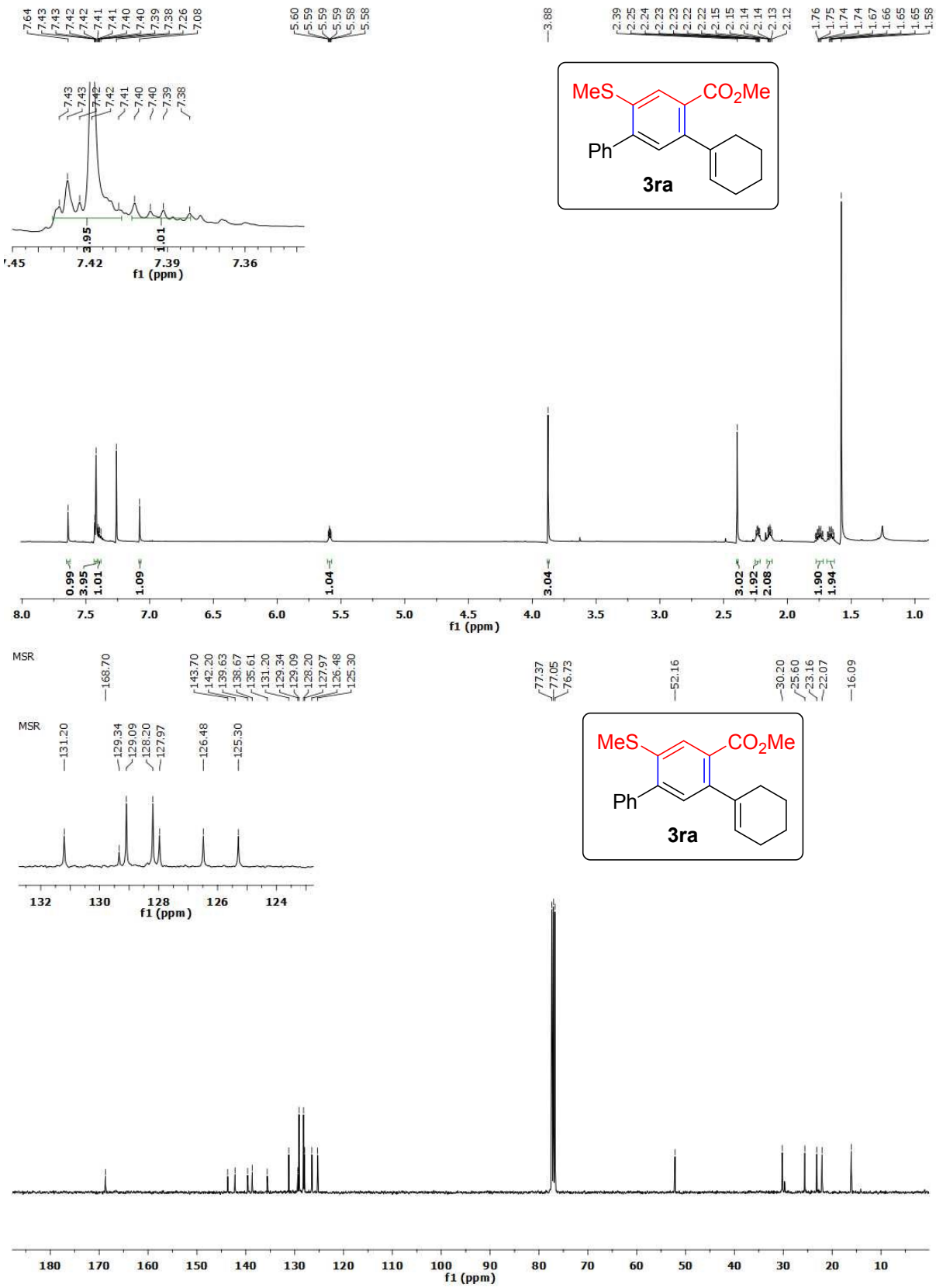

MeS
CO2Me
Ph
S
3qa

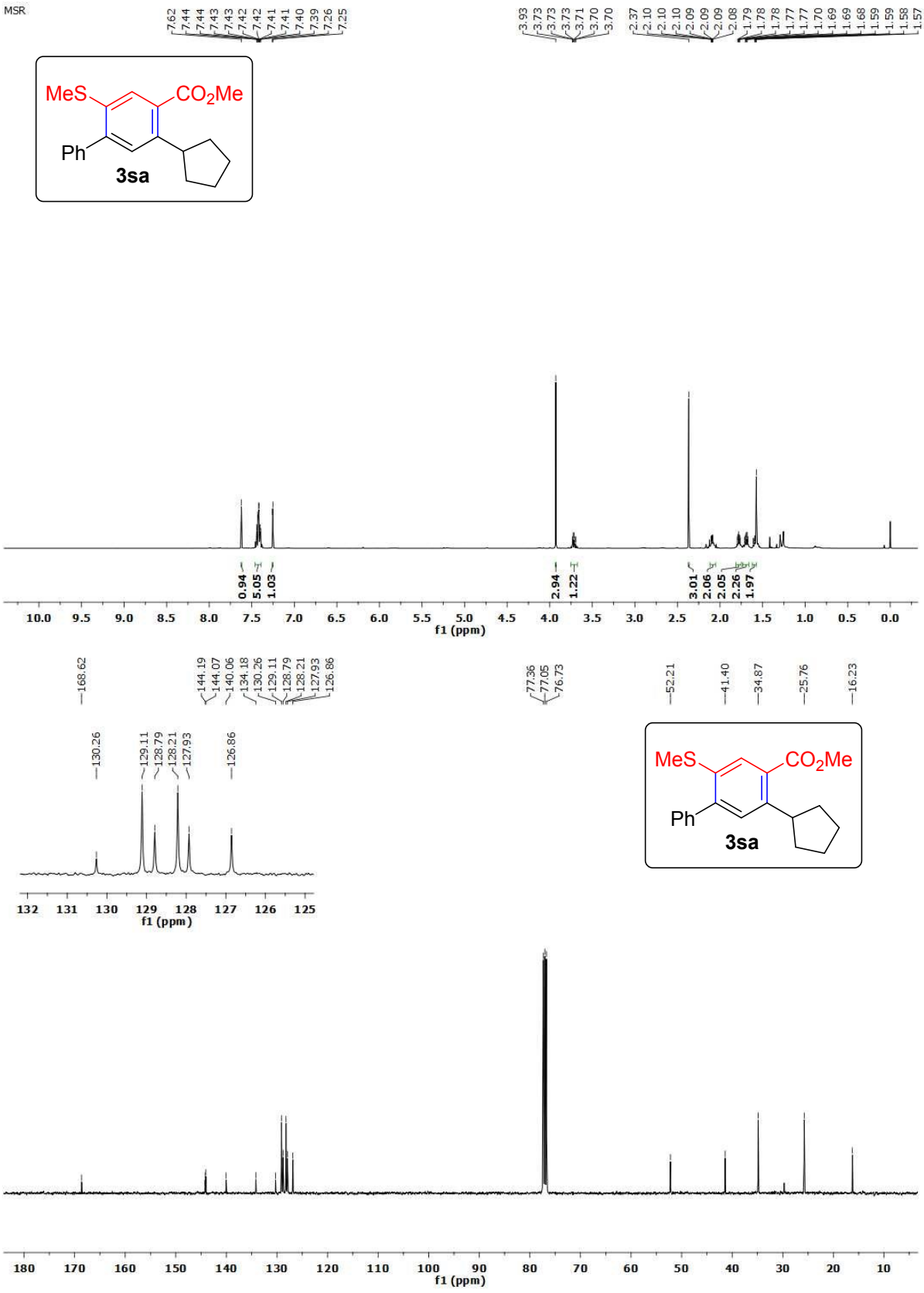

1.00
3.90
1.05
1.08
0.98
0.96
1.03
3.08
2.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

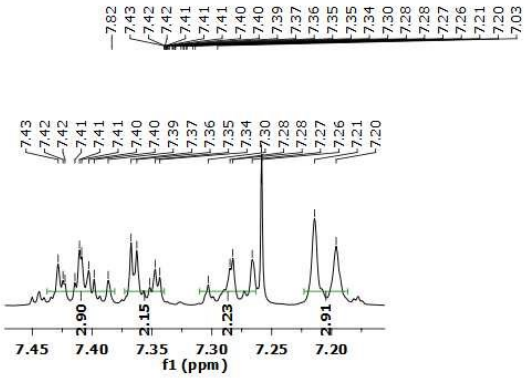

MSR
168.92
143.51
140.72
139.31
136.97
133.11
132.08
130.17
129.08
128.43
128.31
128.15
126.12
125.09
122.24
77.37
77.05
76.74
52.28
15.99
MSR
132.08
130.17
129.08
128.43
128.31
128.15
126.12
125.09
122.24
132
130
128
126
124
f1 (ppm)

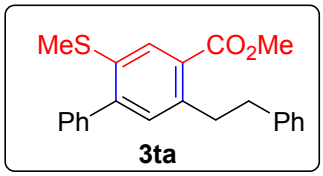

MeS
CO2Me
Ph
S
3qa

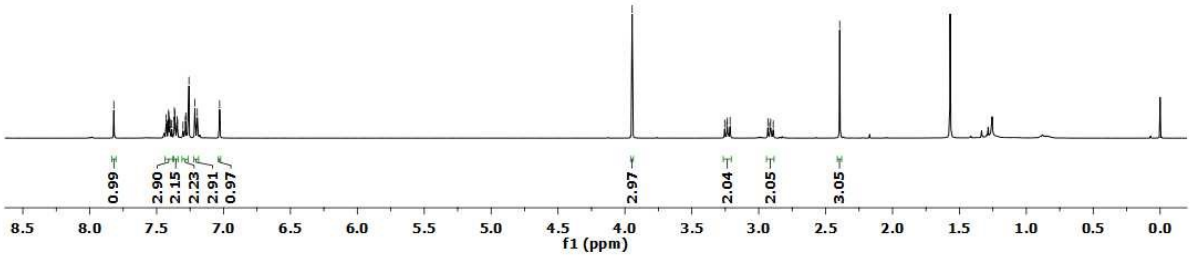

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

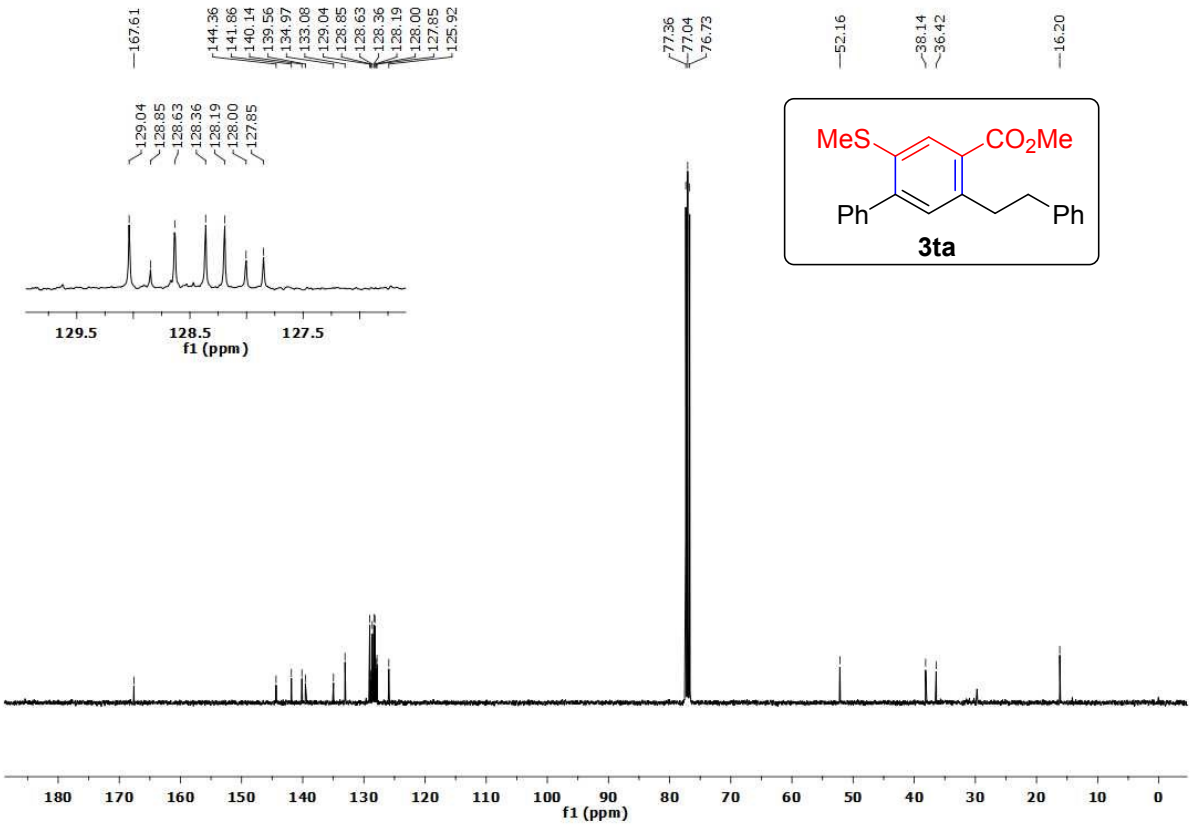

MeS
CO2Me
Ph
3ra
f1 (ppm)
MeS
CO2Me
Ph
3ra
f1 (ppm)


MSR
MeS
CO2Me
Ph
3sa
f1 (ppm)
f1 (ppm)
f1 (ppm)


7.82
7.43
7.42
7.42
7.42
7.41
7.41
7.41
7.40
7.40
7.39
7.37
7.36
7.35
7.35
7.34
7.30
7.28
7.28
7.27
7.26
7.21
7.20
7.03
3.95
3.25
3.24
3.23
3.21
2.93
2.92
2.91
2.89
2.39
2.90
2.15
2.23
2.91
7.45
7.40
7.35
7.30
7.25
7.20
f1 (ppm)

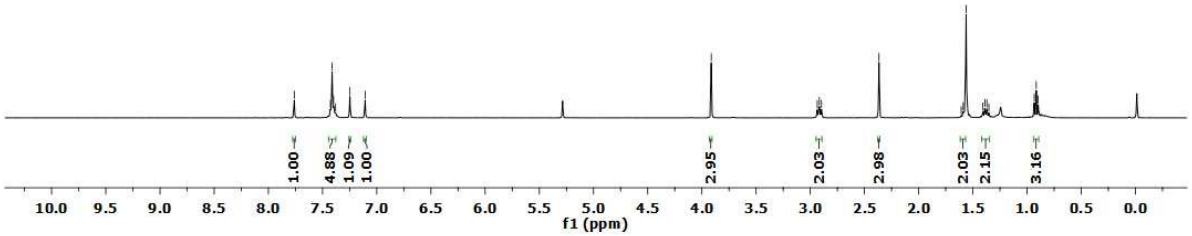

MeS
CO2Me
Ph
Ph
3ta

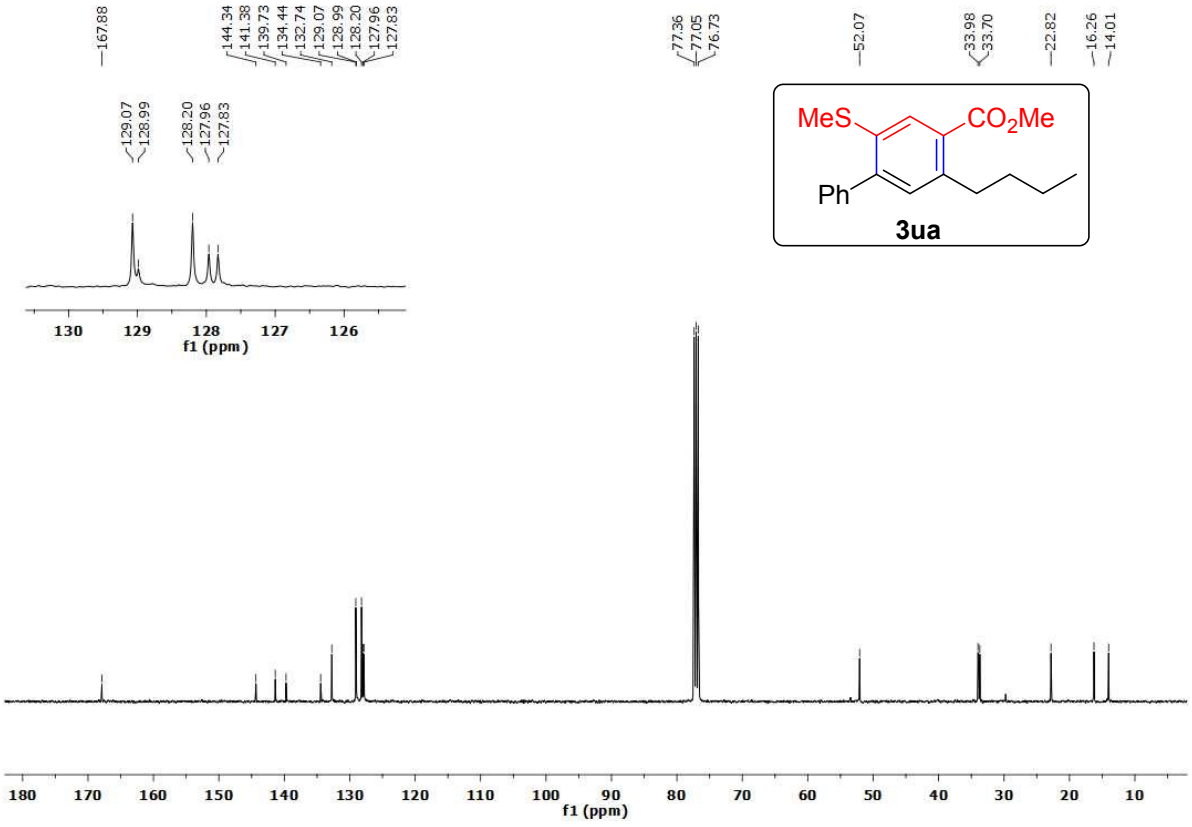

0.99
2.90
2.15
2.23
2.91
0.97
2.97
2.04
2.05
3.05
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

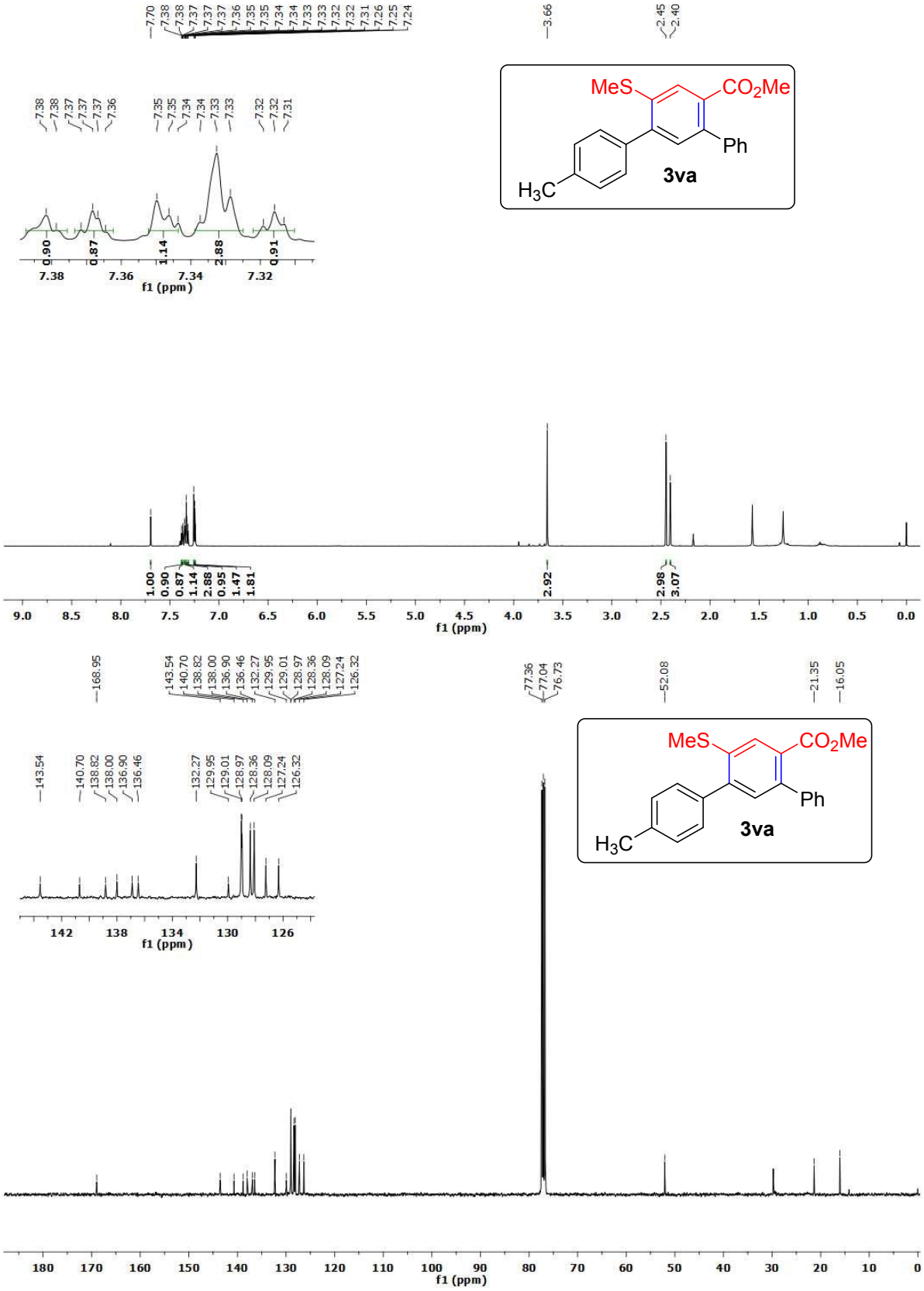

167.61
144.36
141.86
140.14
139.56
134.97
133.08
129.04
128.85
128.63
128.36
128.19
128.00
127.85
125.92
77.36
77.04
76.73
52.16
38.14
36.42
16.20
129.04
128.85
128.63
128.36
128.19
128.00
127.85
129.5
128.5
127.5
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

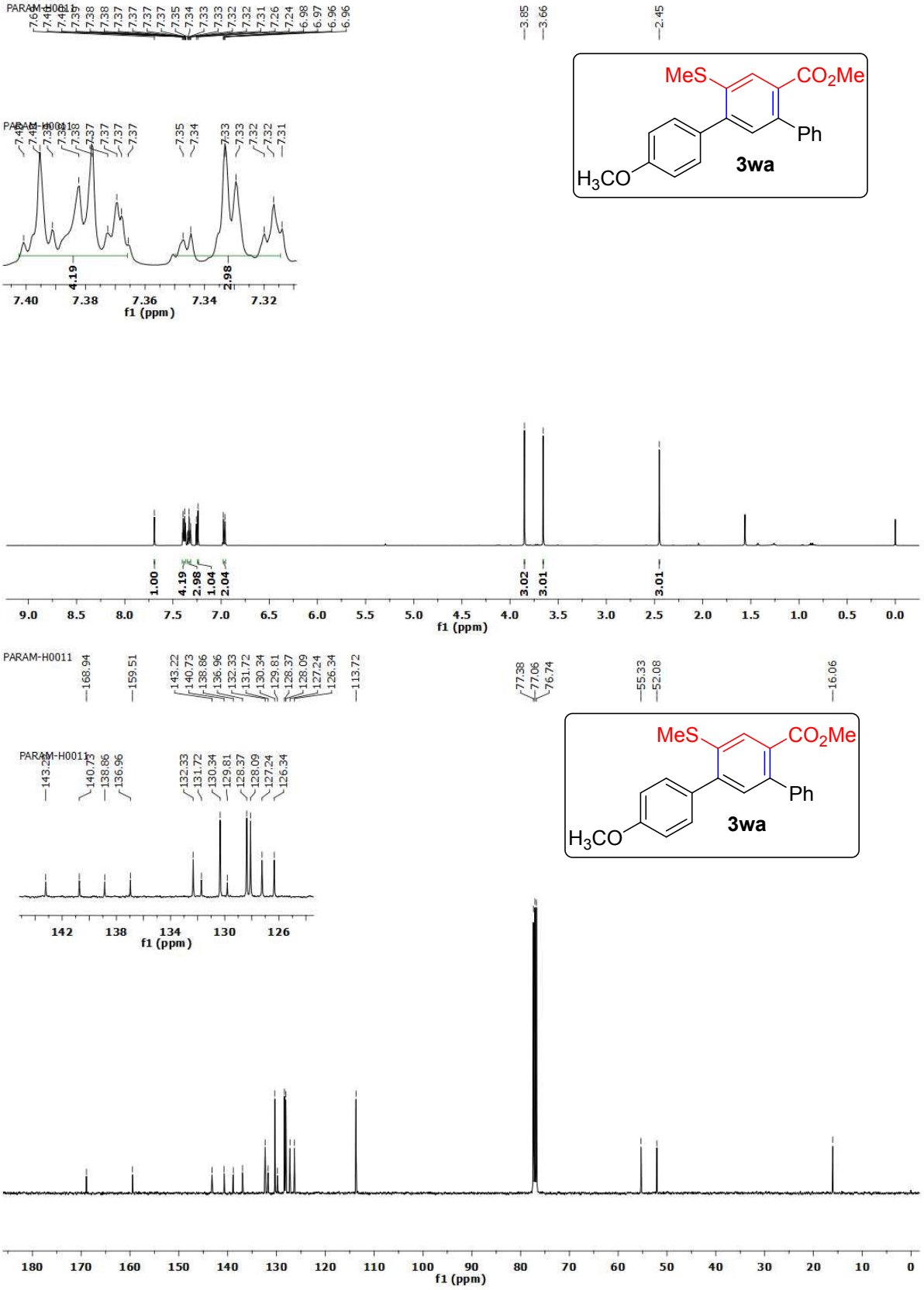
MeS
CO2Me
Ph
Ph
3ta

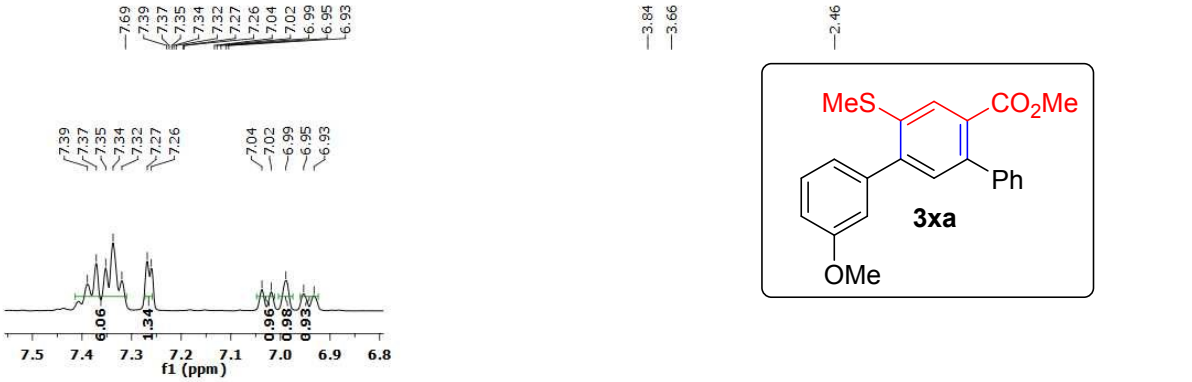

7.76
7.43
7.41
7.40
7.38
7.25
7.11
3.91
2.94
2.92
2.90
2.37
1.59
1.56
1.41
1.39
1.37
0.93
0.91
0.90
MeS
CO2Me
Ph
3ua

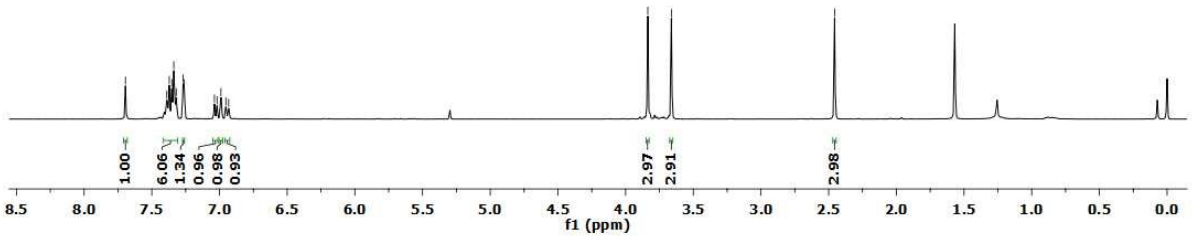

1.00
4.88
1.09
1.00
2.95
2.03
2.98
2.03
2.15
3.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


167.88
144.34
141.38
139.73
134.44
132.74
129.07
128.99
128.20
127.96
127.83
77.36
77.05
76.73
52.07
33.98
33.70
22.82
16.26
14.01
129.07
128.99
128.20
127.96
127.83
130 129 128 127 126
f1 (ppm)
MeS
CO2Me
Ph
3ua
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.70
7.38
7.38
7.37
7.37
7.37
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.31
7.26
7.25
7.24
3.66
2.45
2.40
MeS
CO2Me
Ph
H3C
3va
0.90
0.87
1.14
2.88
0.91
7.38
7.36
7.34
7.32
f1 (ppm)
1.00
0.90
0.87
1.14
2.88
0.95
1.47
1.81
2.92
2.98
3.07
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)
168.95
143.54
140.70
138.82
138.00
136.90
136.46
132.27
129.95
129.01
128.97
128.36
128.09
127.24
126.32
77.36
77.04
76.73
52.08
21.35
16.05
142
138
134
130
126
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


PARAM-H0011
3.85
3.66
2.45
MeS
CO2Me
Ph
H3CO
3wa
4.19
2.98
7.40
7.38
7.36
7.34
7.32
f1 (ppm)
1.00
4.19
2.98
1.04
2.04
3.02
3.01
3.01
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)
PARAM-H0011
168.94
159.51
143.22
140.73
138.86
136.96
132.33
131.72
130.34
129.81
128.37
128.09
127.24
126.34
113.72
77.38
77.06
76.74
55.33
52.08
16.06
MeS
CO2Me
Ph
H3CO
3wa
PARAM-H0011
142
138
134
130
126
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.69
7.39
7.37
7.35
7.34
7.32
7.27
7.26
7.04
7.02
6.99
6.95
6.93
3.84
3.66
2.46
MeS
CO2Me
Ph
3xa
OMe
6.06
1.34
0.96
0.98
0.93
f1 (ppm)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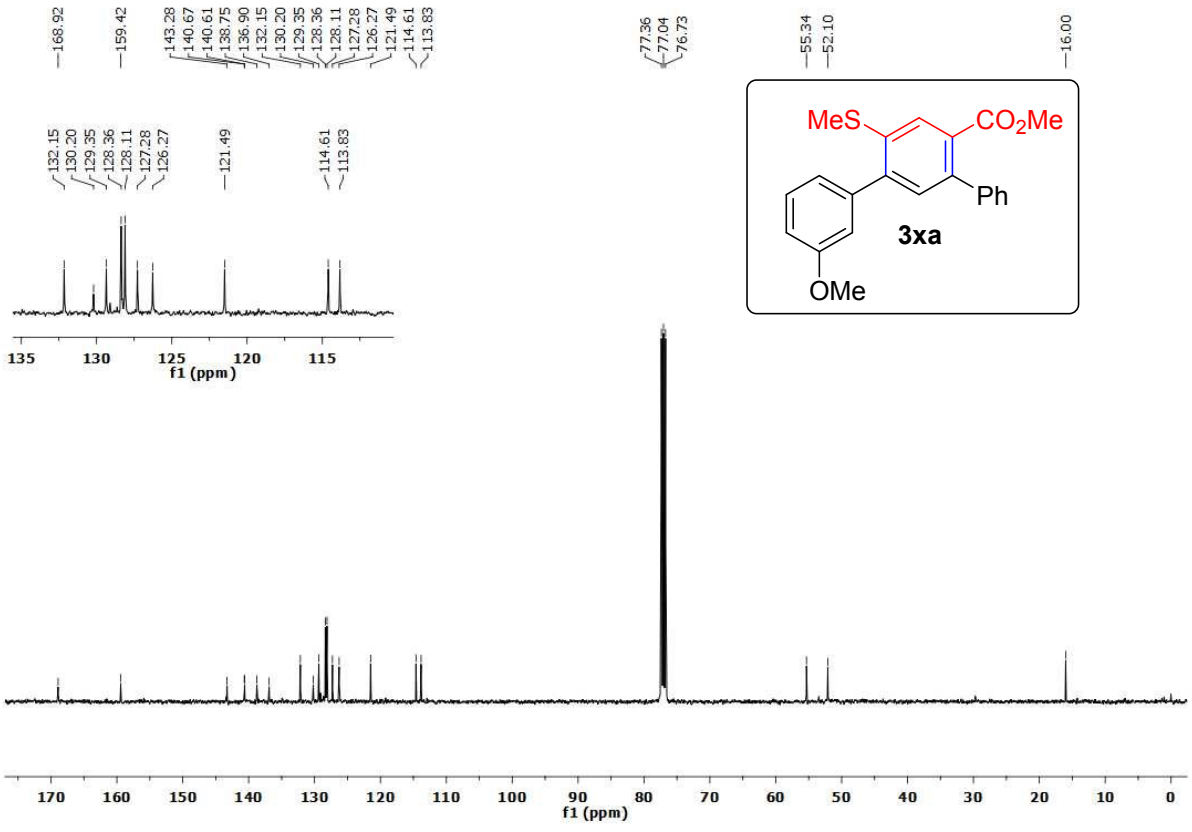
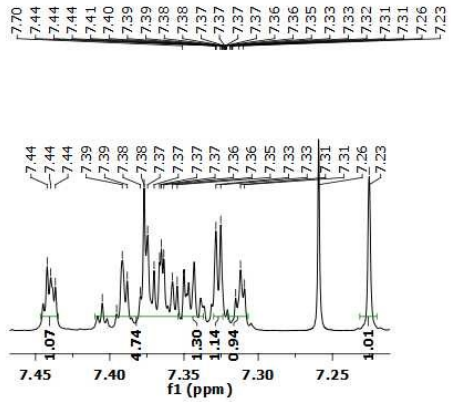
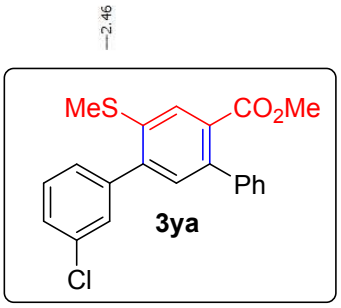
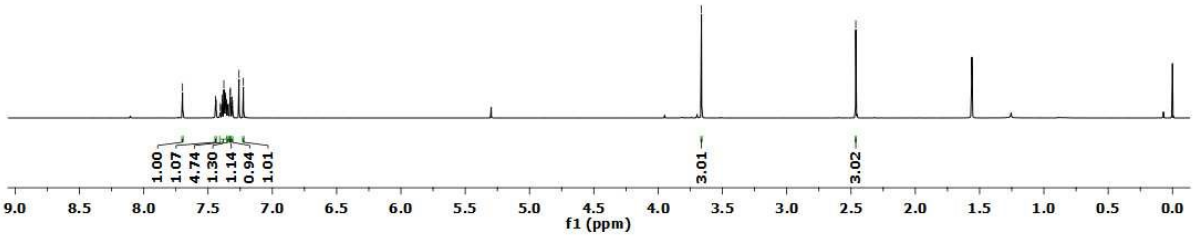
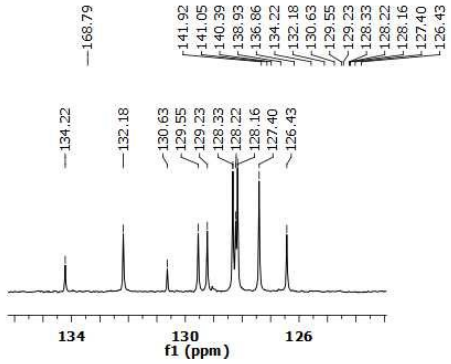
6.06
1.34
0.96
0.98
0.93
2.97
2.91
2.98
f1 (ppm)

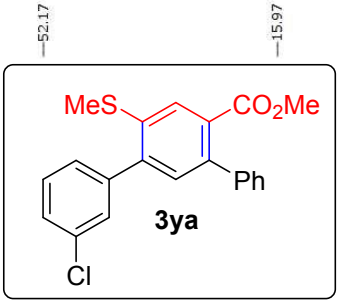

168.92
159.42
143.28
140.67
140.61
138.75
136.90
132.15
130.20
129.35
128.36
128.11
127.28
126.27
121.49
114.61
113.83
77.36
77.04
76.73
55.34
52.10
16.00
MeS
CO2Me
Ph
3xa
OMe
f1 (ppm)

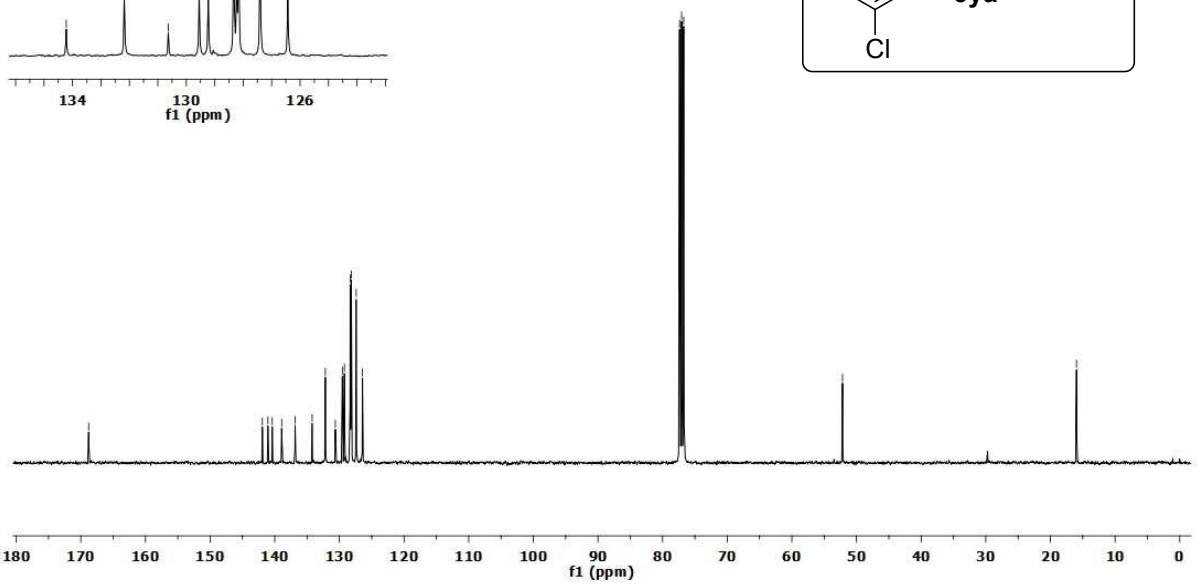

7.70
7.44
7.44
7.44
7.41
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.37
7.37
7.36
7.36
7.35
7.33
7.33
7.32
7.31
7.31
7.26
7.23
7.44
7.44
7.44
7.39
7.39
7.38
7.38
7.37
7.37
7.37
7.37
7.36
7.36
7.35
7.33
7.33
7.31
7.31
7.26
7.23
1.07
4.74
1.30
1.14
0.94
1.01
7.45
7.40
7.35
7.30
7.25
f1 (ppm)

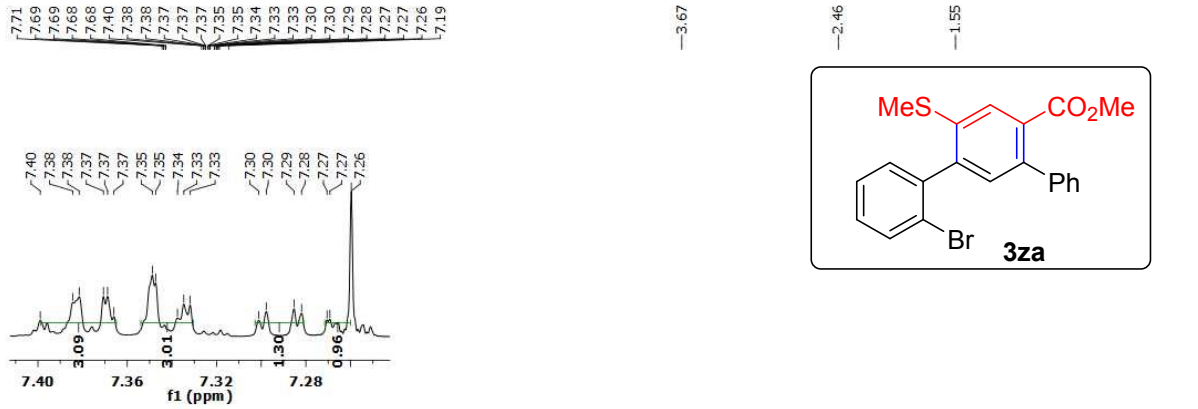

3.66
2.46
MeS
CO2Me
Ph
3ya
Cl

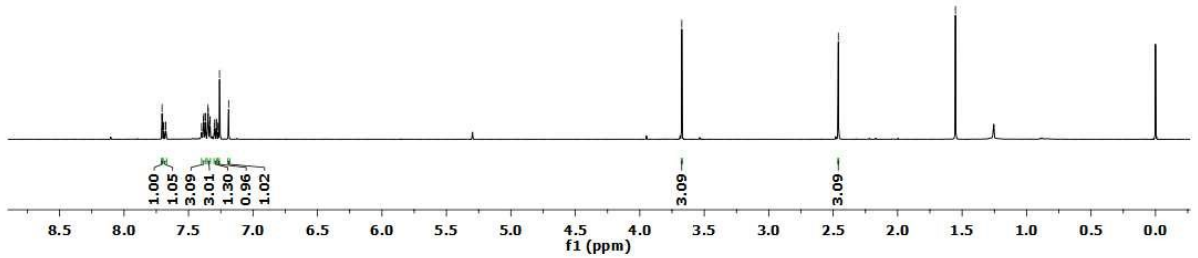

1.00
1.07
4.74
1.30
1.14
0.94
1.01
3.01
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

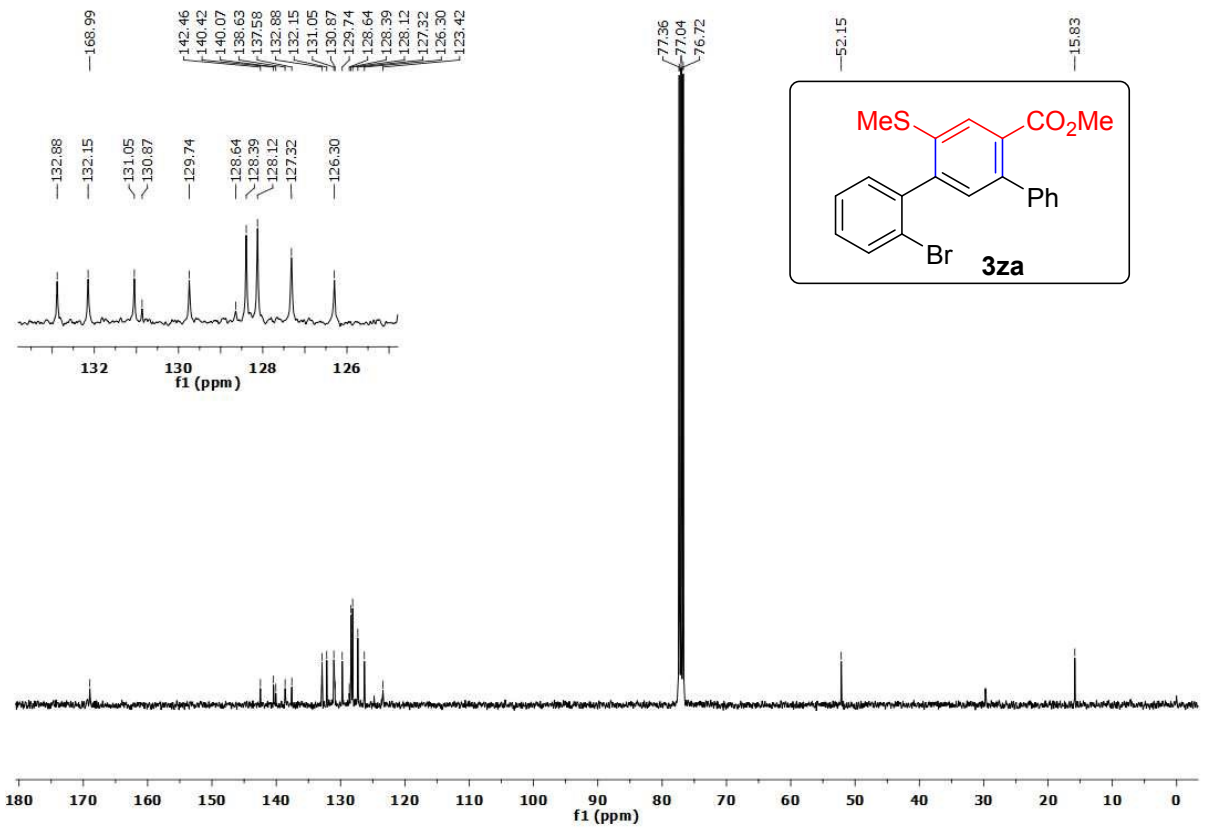

168.79
141.92
141.05
140.39
138.93
136.86
134.22
132.18
130.63
129.55
129.23
128.33
128.22
128.16
127.40
126.43
134.22
132.18
130.63
129.55
129.23
128.33
128.22
128.16
127.40
126.43
134
130
126
f1 (ppm)

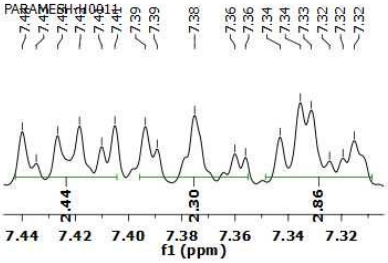

77.38
77.06
76.74
52.17
15.97
MeS
CO2Me
Ph
3ya
Cl

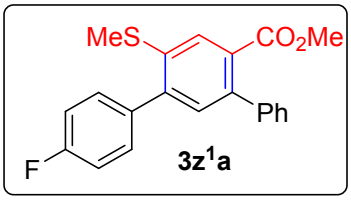

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

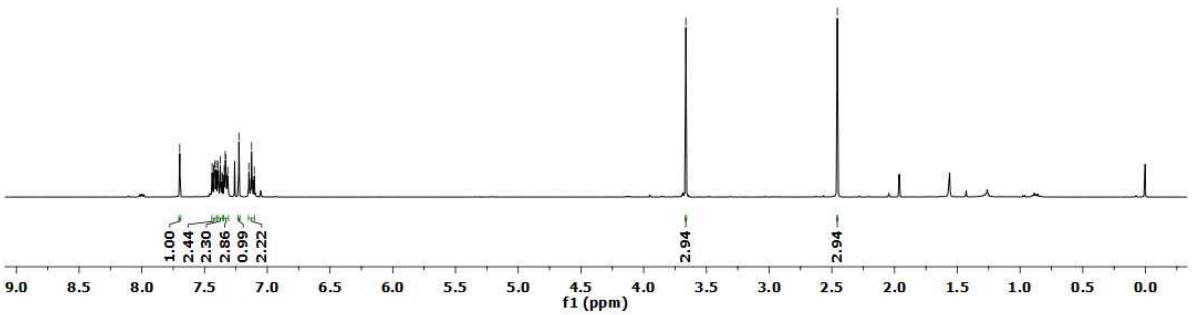

MeS
CO2Me
Ph
Br
3za

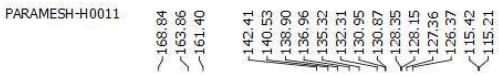


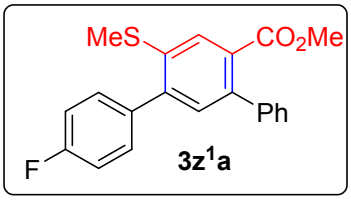

MeS
CO2Me
Ph
Br
3za

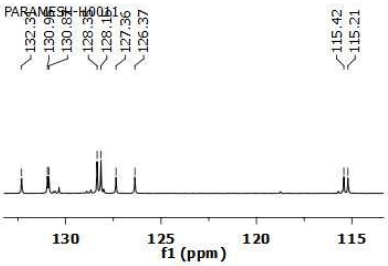

2.44
2.30
2.86
7.44 7.42 7.40 7.38 7.36 7.34 7.32
f1 (ppm)

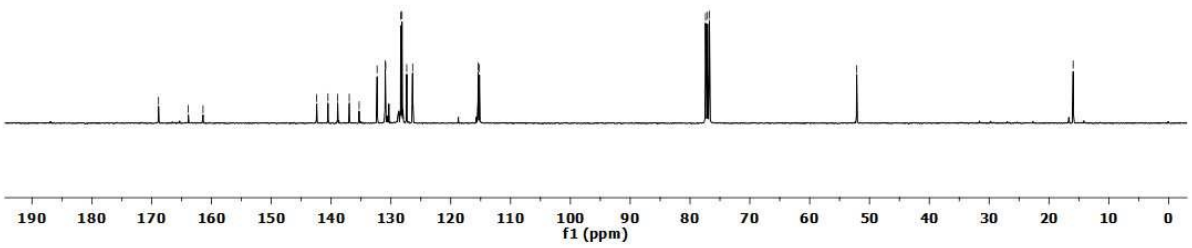

MeS
CO2Me
Ph
F
3z1a

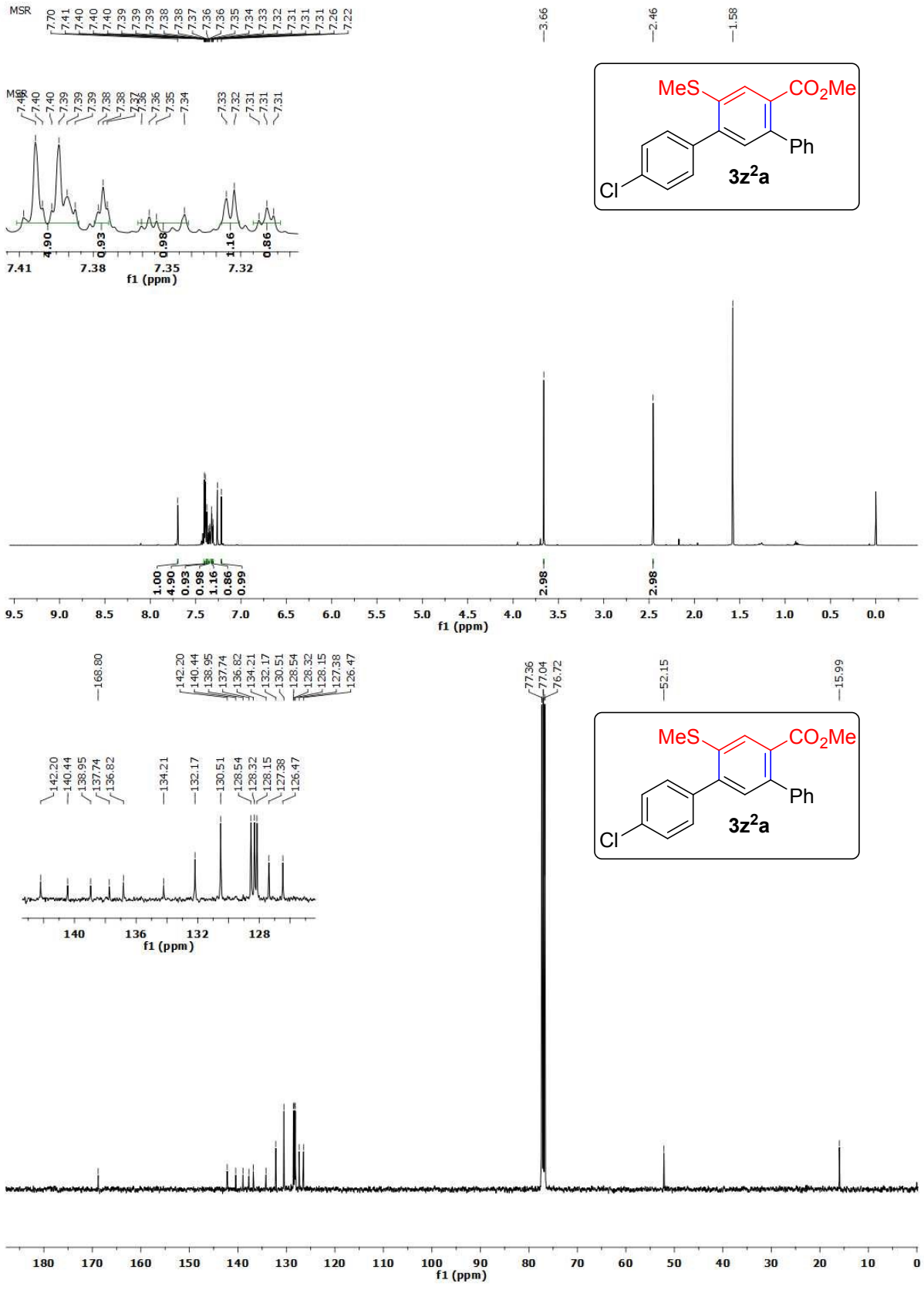

1.00
2.44
2.30
2.86
0.99
2.22
2.94
2.94
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

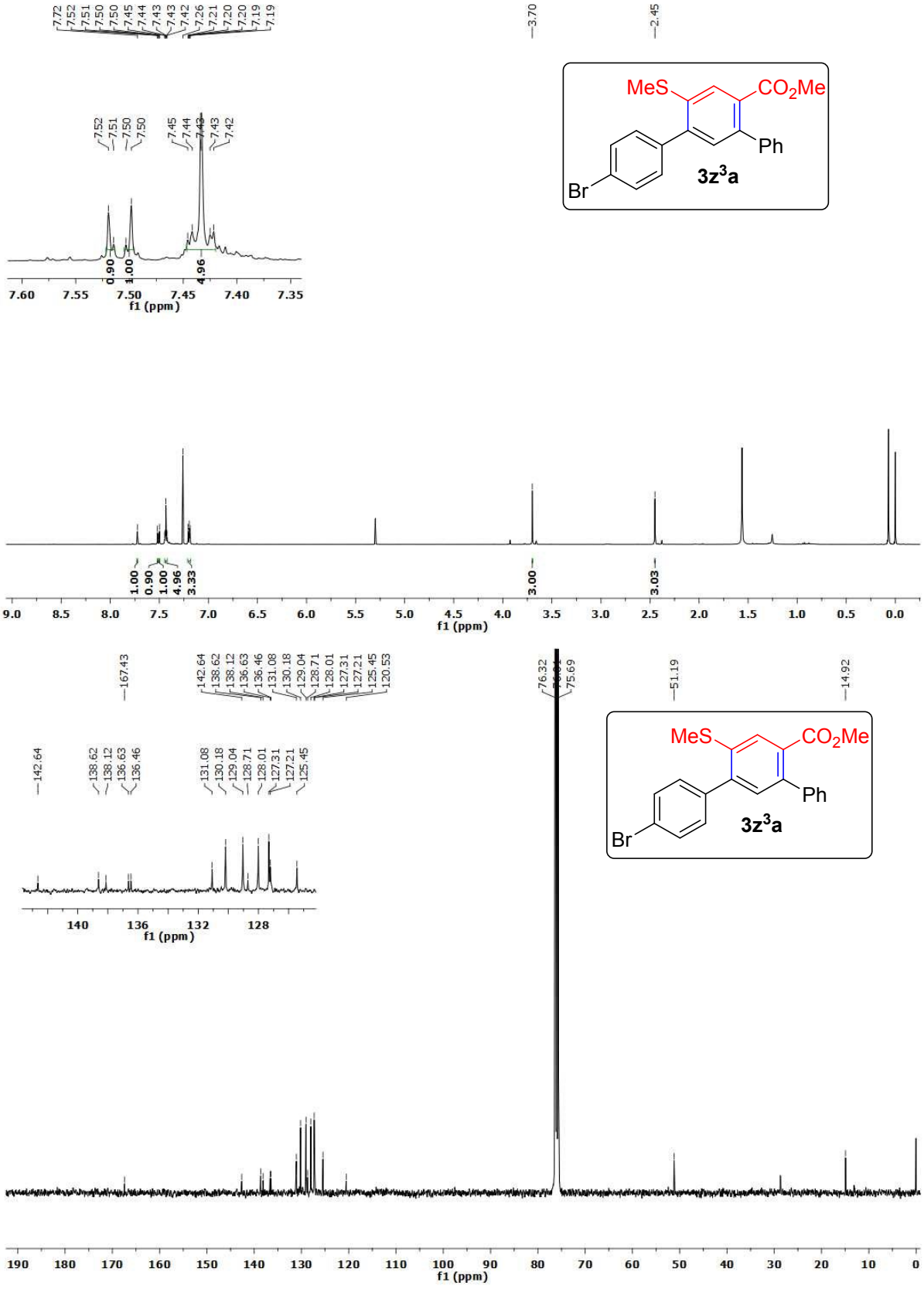


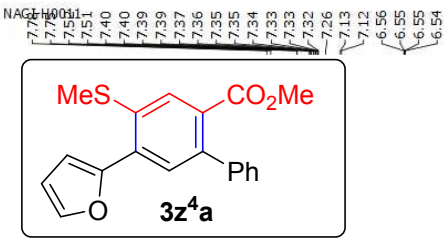

MeS
CO2Me
Ph
F
3z1a

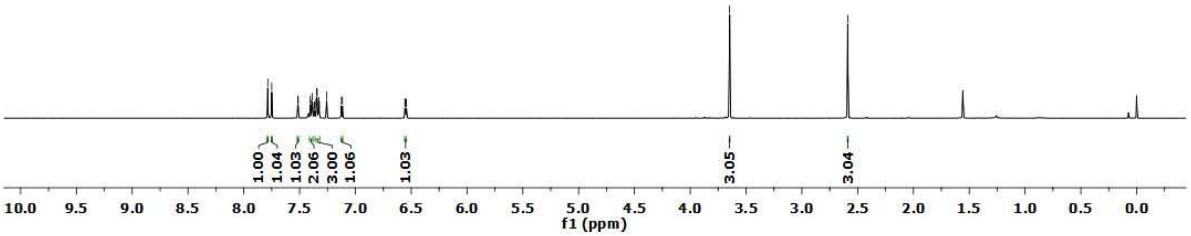

130
125
120
115
f1 (ppm)

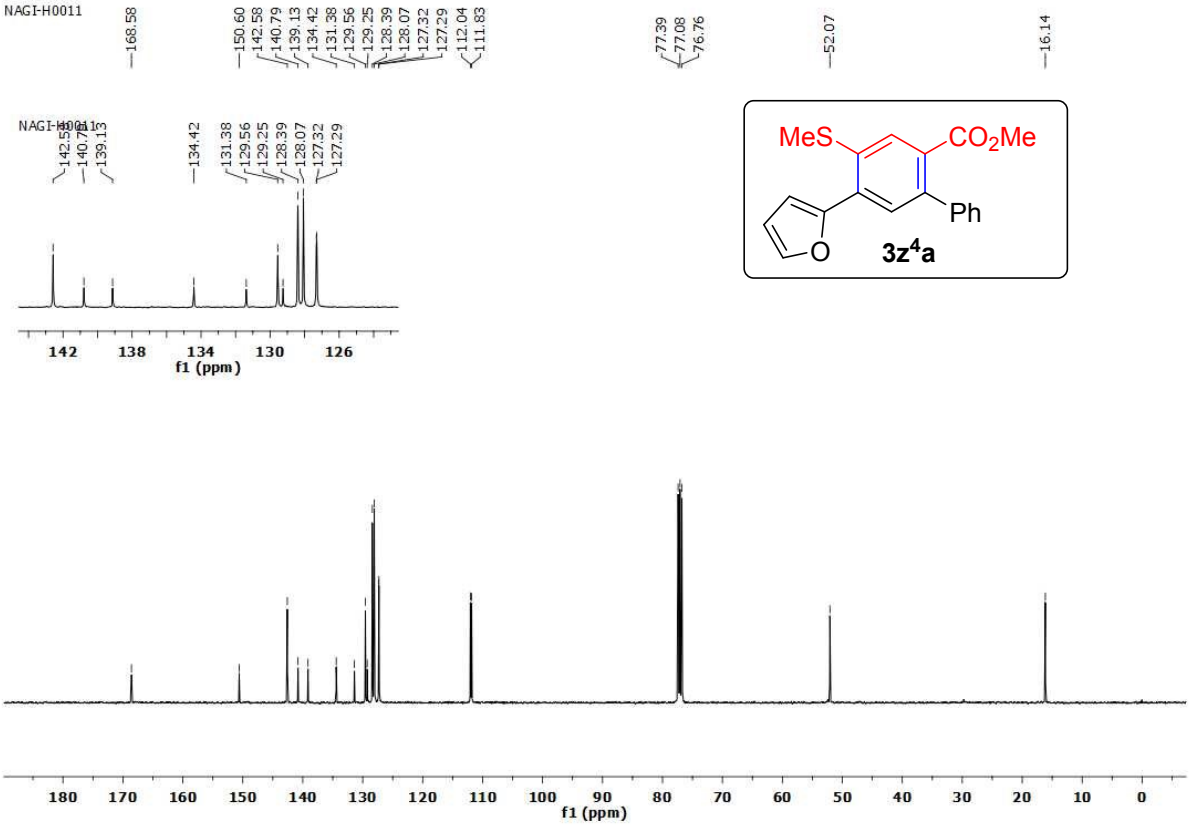

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

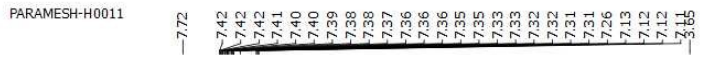

MeS
CO2Me
Ph
Cl
3z2a
f1 (ppm)

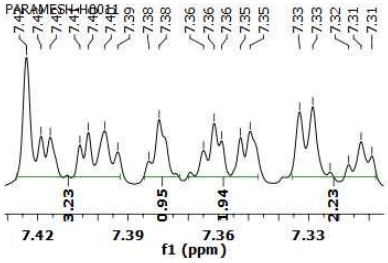

7.72
7.52
7.51
7.50
7.50
7.45
7.44
7.43
7.43
7.42
7.26
7.21
7.20
7.20
7.19
7.19
3.70
2.45
MeS
CO2Me
Ph
Br
3z3a
0.90
1.00
4.96
f1 (ppm)
1.00
0.90
1.00
4.96
3.33
3.00
3.03
167.43
142.64
138.62
138.12
136.63
136.46
131.08
130.18
129.04
128.71
128.01
127.31
127.21
125.45
120.53
76.32
75.69
51.19
14.92

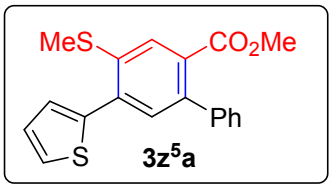

NAGI-H0011
7.77
7.77
7.51
7.51
7.40
7.40
7.39
7.39
7.37
7.36
7.35
7.35
7.34
7.33
7.33
7.32
7.26
7.13
7.12
6.56
6.55
6.55
6.54
3.65
2.59
MeS
CO2Me
Ph
O
3z4a

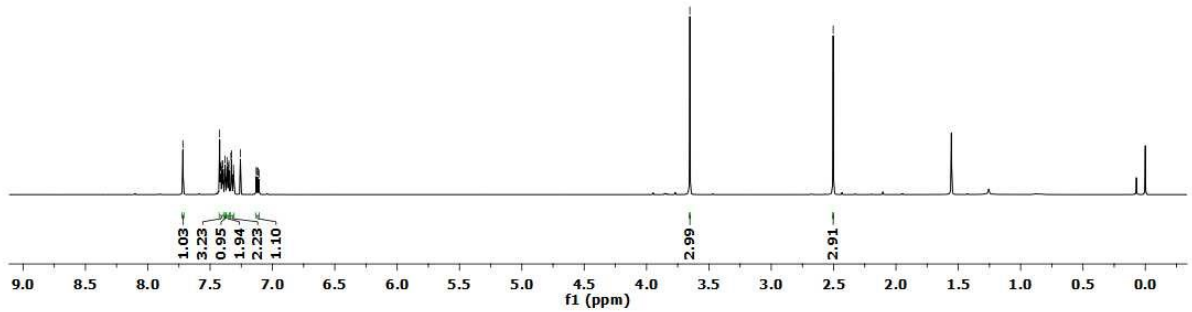

1.00
1.04
1.03
2.06
3.00
1.06
1.03
3.05
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

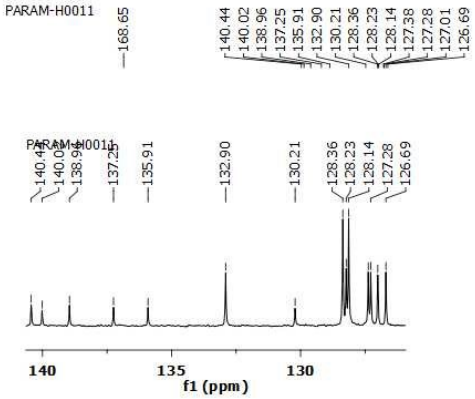

NAGI-H0011
168.58
150.60
142.58
140.79
139.13
134.42
131.38
129.56
129.25
128.39
128.07
127.32
127.29
112.04
111.83
77.39
77.08
76.76
52.07
16.14
NAGI-H0011
142.58
140.79
139.13
134.42
131.38
129.56
129.25
128.39
128.07
127.32
127.29
142
138
134
130
126
f1 (ppm)
MeS
CO2Me
Ph
O
3z4a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

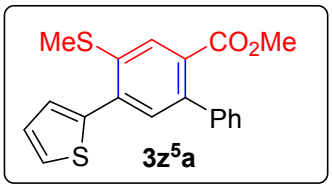

PARAMESH-H0011
7.72
7.42
7.42
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.36
7.36
7.36
7.35
7.33
7.33
7.32
7.31
7.26
7.13
7.12
7.12
7.11
3.65
2.50

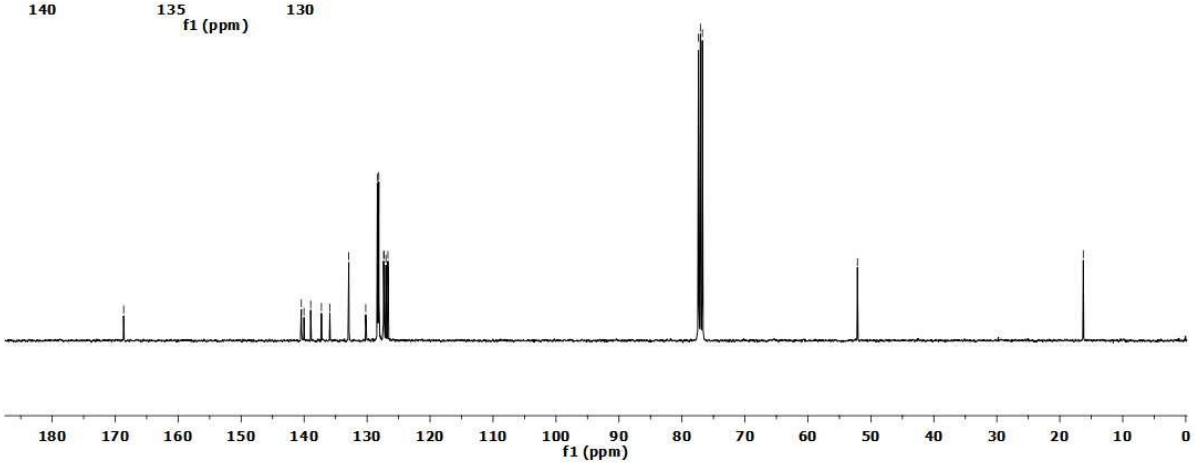

PARAMESH-H0011
7.42
7.42
7.41
7.41
7.41
7.39
7.38
7.38
7.36
7.36
7.36
7.35
7.35
7.33
7.33
7.32
7.31
7.31
3.23
0.95
1.94
2.23
7.42
7.39
7.36
7.33
f1 (ppm)

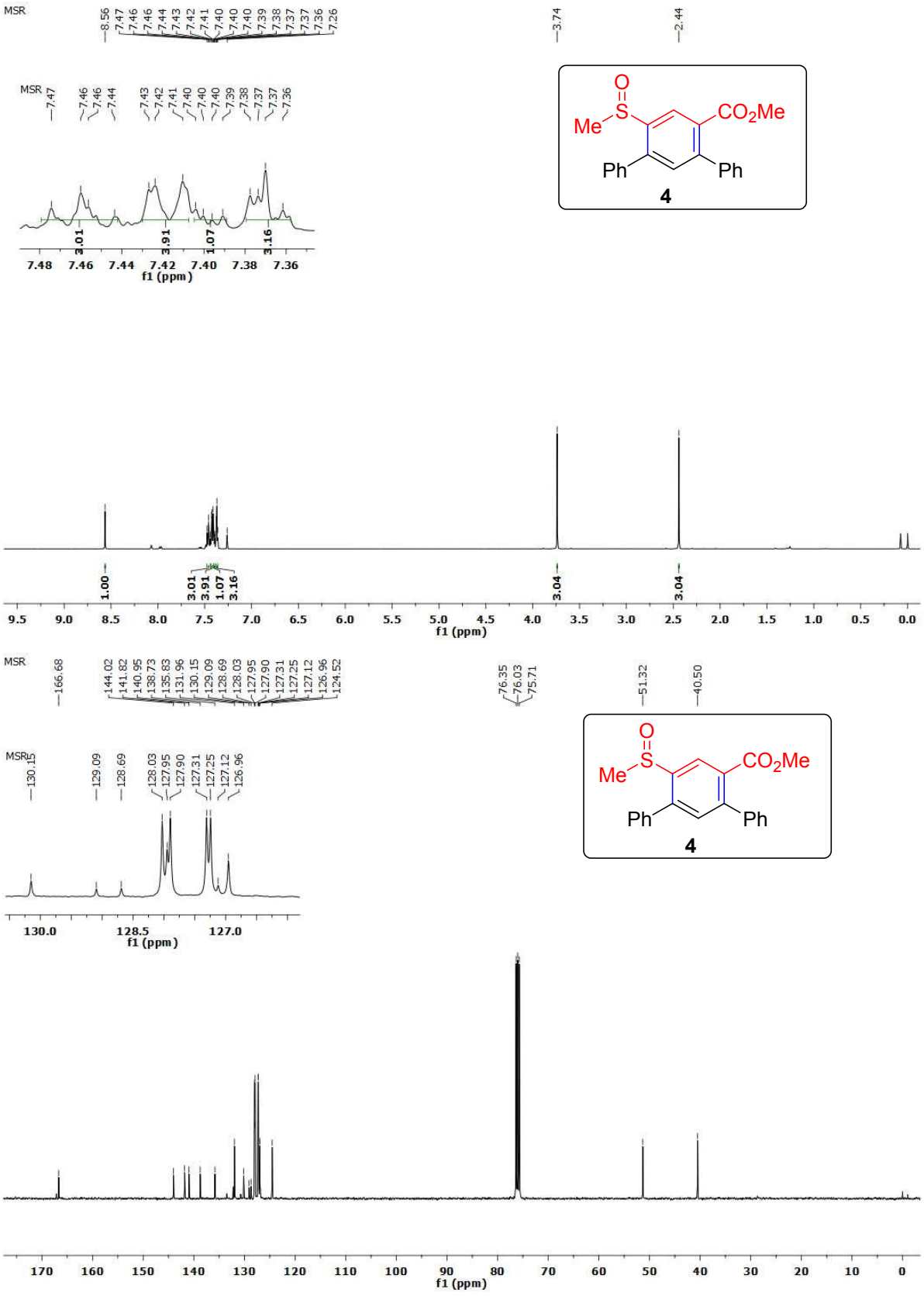

MeS
CO2Me
Ph
S
3z5a

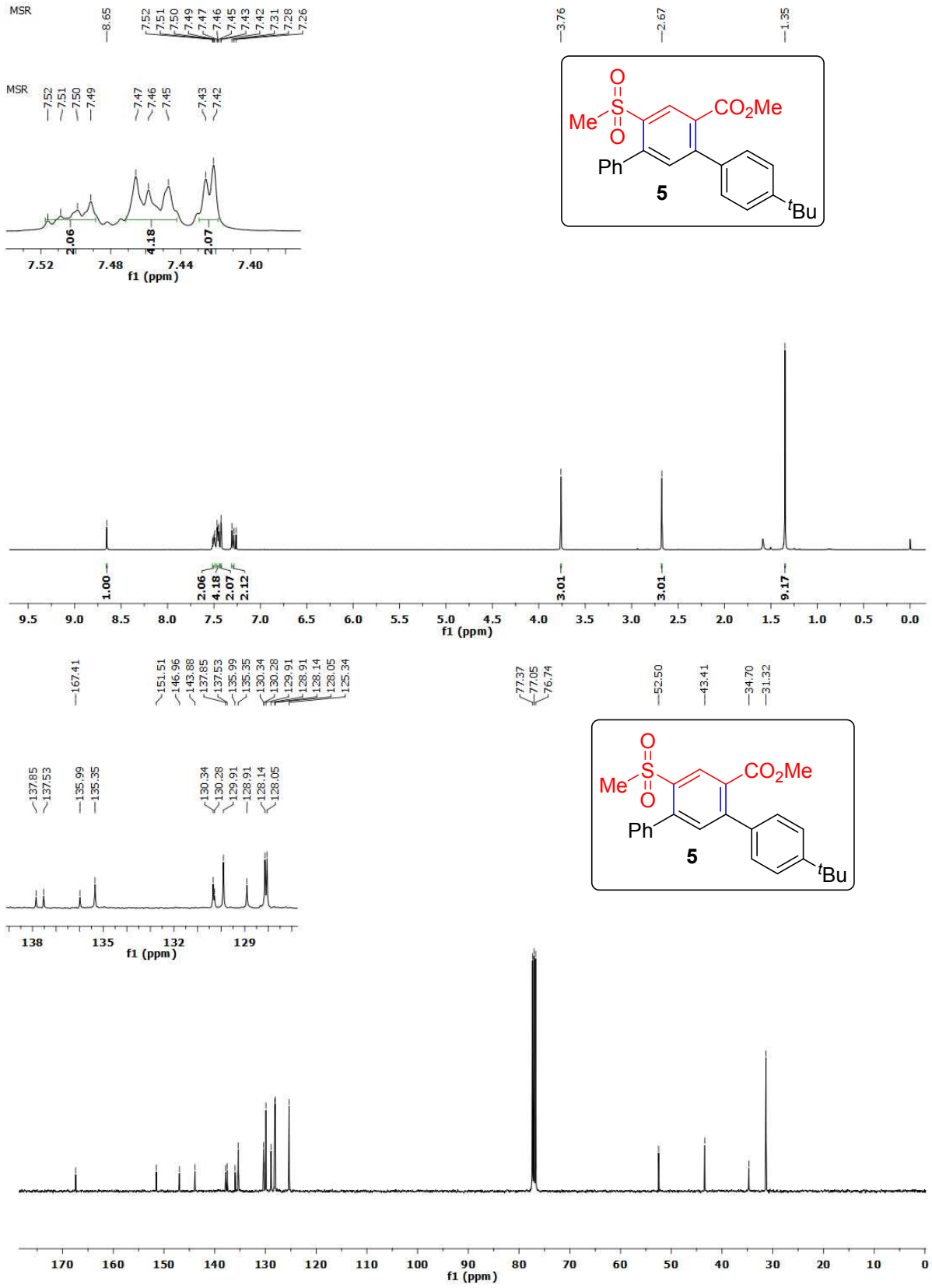

1.03
3.23
0.95
1.94
2.23
1.10
2.99
2.91
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

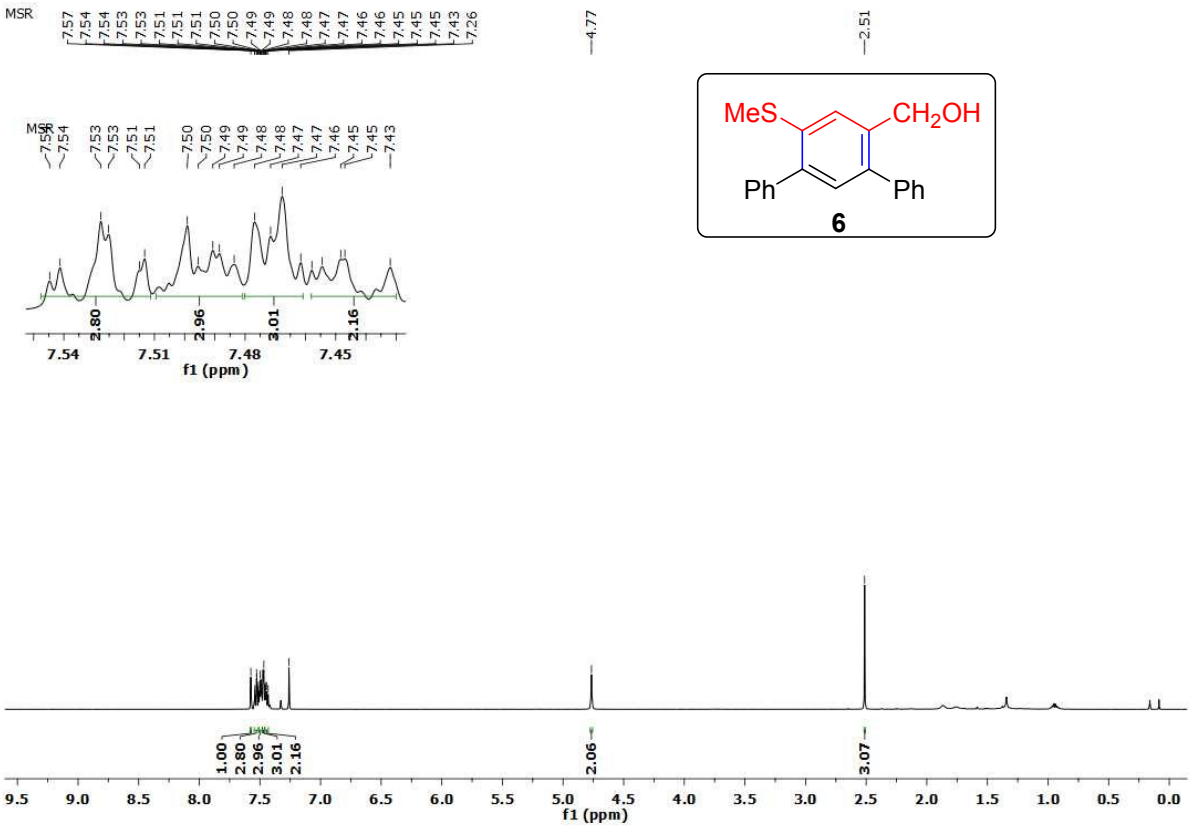

PARAM-H0011
168.65
140.44
140.02
138.96
137.25
135.91
132.90
130.21
128.36
128.23
128.14
127.38
127.28
127.01
126.69
77.38
77.07
76.75
52.13
16.27
140
135
130
f1 (ppm)

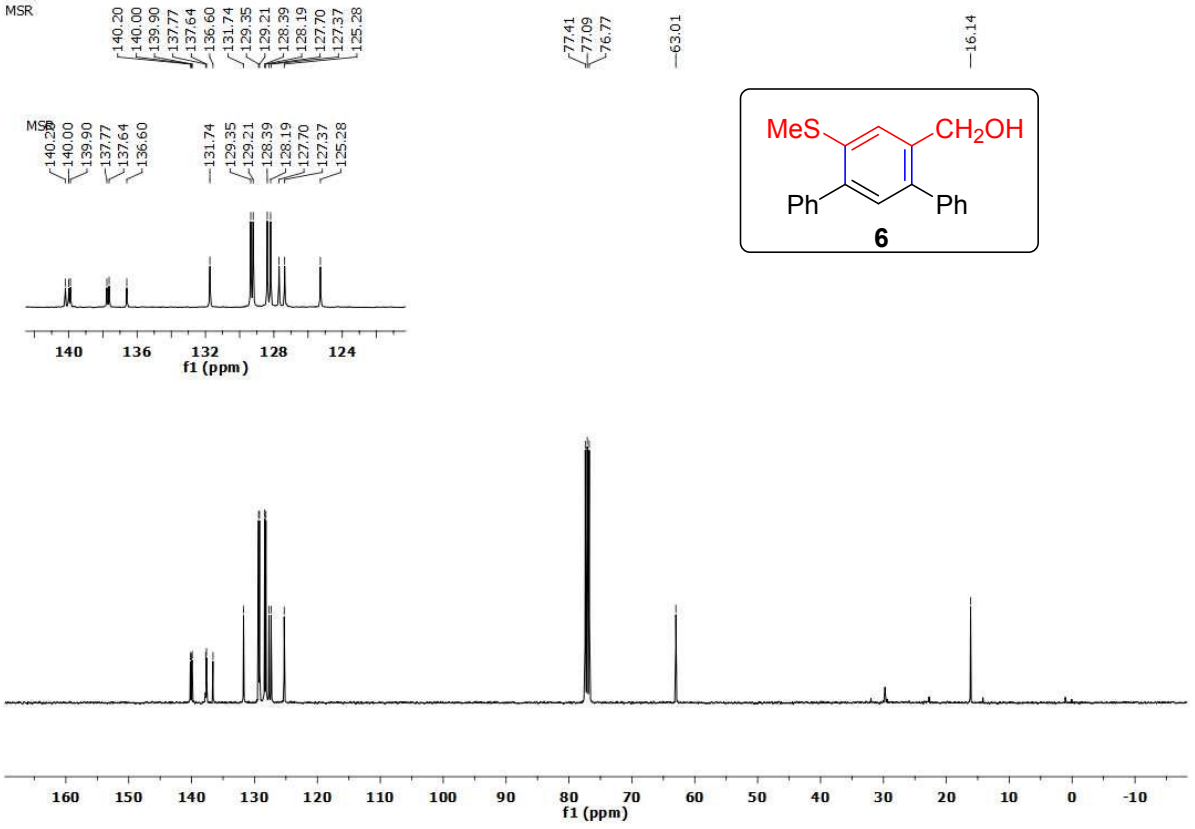

MeS
CO2Me
Ph
S
3z5a


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


MSR
8.56
7.47
7.46
7.46
7.44
7.43
7.42
7.41
7.40
7.40
7.40
7.39
7.38
7.37
7.37
7.36
7.26
3.74
2.44
MSR
7.47
7.46
7.46
7.44
7.43
7.42
7.41
7.40
7.40
7.40
7.39
7.38
7.37
7.37
7.36
3.01
3.91
1.07
3.16
7.48 7.46 7.44 7.42 7.40 7.38 7.36
f1 (ppm)
O
S
Me
CO2Me
Ph
Ph
4
1.00
3.01
3.91
1.07
3.16
3.04
3.04
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)
MSR
166.68
144.02
141.82
140.95
138.73
135.83
131.96
130.15
129.09
128.69
128.03
127.95
127.90
127.31
127.25
127.12
126.96
124.52
76.35
76.03
75.71
51.32
40.50
MSR
130.15
129.09
128.69
128.03
127.95
127.90
127.31
127.25
127.12
126.96
130.0 128.5 127.0
f1 (ppm)
O
S
Me
CO2Me
Ph
Ph
4
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MSR
8.65
7.52
7.51
7.50
7.49
7.47
7.46
7.45
7.43
7.42
7.31
7.28
7.26
3.76
2.67
1.35
MSR
7.52
7.51
7.50
7.49
7.47
7.46
7.45
7.43
7.42
2.06
4.18
2.07
7.52
7.48
7.44
7.40
f1 (ppm)
Me
S
O
O
CO2Me
Ph
5
tBu
1.00
2.06
4.18
2.07
2.12
3.01
3.01
9.17
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)
167.41
151.51
146.96
143.88
137.85
137.53
135.99
135.35
130.34
130.28
129.91
128.91
128.14
128.05
125.34
77.37
77.05
76.74
52.50
43.41
34.70
31.32
137.85
137.53
135.99
135.35
130.34
130.28
129.91
128.91
128.14
128.05
138
135
132
129
f1 (ppm)
Me
S
O
O
CO2Me
Ph
5
tBu
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MSR
7.57 7.54 7.54 7.53 7.53 7.51 7.51 7.51 7.50 7.50 7.49 7.49 7.48 7.48 7.47 7.47 7.46 7.46 7.45 7.45 7.43 7.26
4.77
2.51
MeS
CH2OH
Ph
Ph
6
2.80 2.96 3.01 2.16
7.54 7.51 7.48 7.45
f1 (ppm)
1.00 2.80 2.96 3.01 2.16
2.06
3.07
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)


MSR
140.20 140.00 139.90 137.77 137.64 136.60 131.74 129.35 129.21 128.39 128.19 127.70 127.37 125.28
77.41 77.09 76.77
63.01
16.14
MeS
CH2OH
Ph
Ph
6
140 136 132 128 124
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

VIII. X-ray crystallography data

Crystallographic data

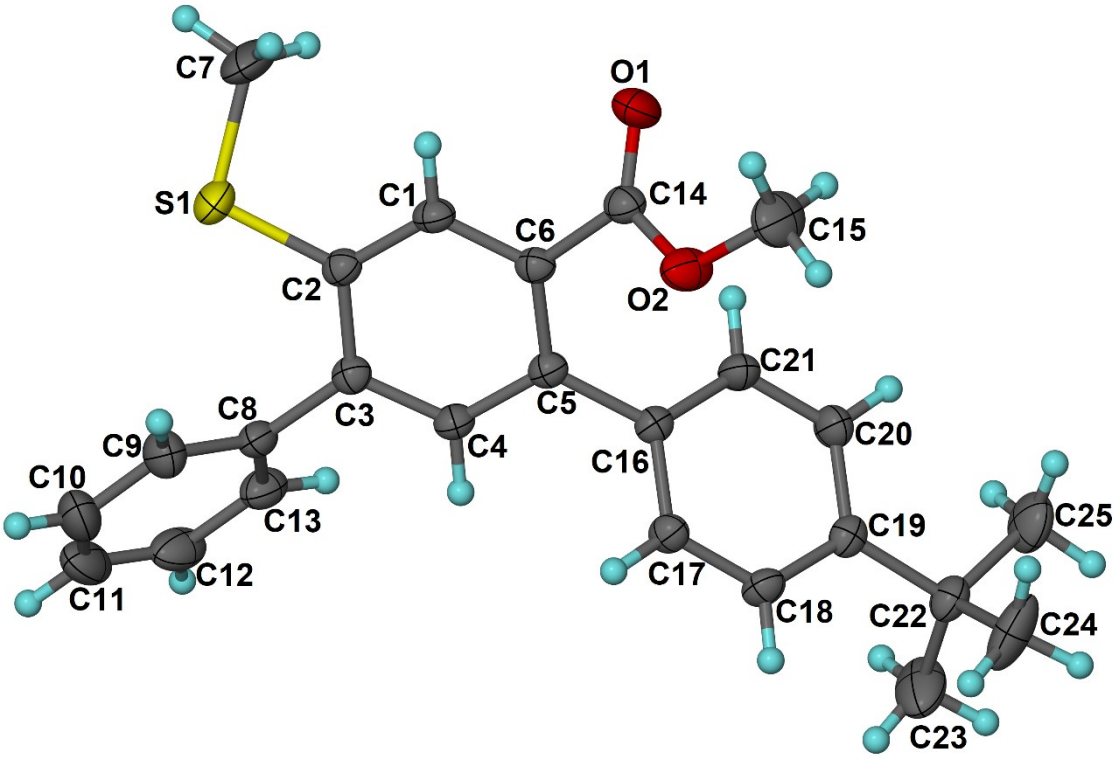


Figure caption: ORTEP diagram of KA959 compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. The t-butyl group was disordered over two sites. Only the major component of the disordered carbon atoms are shown for clarity purpose. CCDC 2020969 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Table 1. Crystallographic details of KA959 compound.

Datablock: KA959_0m

Bond precision: C-C = 0.0034 A Wavelength=0.71073

Cell: a=10.361(5) b=22.362(10) c=10.254(4)
alpha=90 beta=113.650(8) gamma=90
Temperature: 293 K

	Calculated	Reported
Volume	2176.2(17)	2176.3(17)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C25 H26 O2 S	C25 H26 O2 S
Sum formula	C25 H26 O2 S	C25 H26 O2 S
Mr	390.52	390.52
Dx,g cm-3	1.192	1.192
Z	4	4
Mu (mm-1)	0.166	0.166
F000	832.0	832.0
F000'	832.82	
h,k,lmax	12,27,12	12,27,12
Nref	4278	4275
Tmin,Tmax	0.945,0.956	0.633,0.746
Tmin'	0.945	

Correction method= # Reported T Limits: Tmin=0.633 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.999 Theta(max)= 25.998

R(reflections)= 0.0505(3395) wR2(reflections)= 0.1328(4275)

S = 1.051 Npar= 289

Experimental.

Data collection and Structure solution details:

Single crystal X-ray data for KA959 compound were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An Iμs microfocus Mo source (λ=0.71073Å) supplied the multi-mirror monochromated incident X-ray beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 9913 reflections for KA959. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.[2-3] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. The carbon atoms of t-butyl group were disordered over two sites with site occupancies of 0.577(7) for the major component of atoms (C23/C24/C25) and 0.423(7) for the minor component of atoms (C23D/C24D/C25D). DELU and SIMU instructions were used for constraining the anisotropic displacement parameters of disorder carbon atoms during the refinement. **CCDC deposition number 2020969 contain the supplementary crystallographic data for this paper** which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL Version 2014/7, http://shelx.uni-ac.gwdg.de/SHELX/index.php
3. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.
4. A. L. Spek, Acta Cryst. 2009, D65, 148-155.