

Supporting Information

for

Multicomponent Domino Reactions of Hydrazinecarbodithioates: A Concise Access to 3-Substituted 5-Thiol-1,3,4-Thiadiazolines

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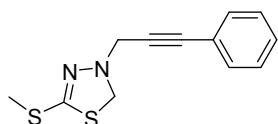
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General Methods

All commercially available reagents were used without purification unless otherwise noted. Column chromatography was performed using silica gel (100–200 mesh). Visualization of the compounds was accomplished with UV light (254 nm) and iodine. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ operating at 400 MHz and 100 MHz, respectively. Proton chemical shifts are reported relative to the residual proton signals of the deuterated solvent CDCl₃ (7.28 ppm) or TMS. Carbon chemical shifts were internally referenced to the deuterated solvent signals in CDCl₃ (77.10 ppm). Chemical shifts are reported in δ (parts per million) values. Coupling constants *J* are reported in Hz. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), and multiple (m). High-resolution mass spectra were recorded on a Liquid Chromatograph Mass Spectrometer (LCMS-IT-TOF).

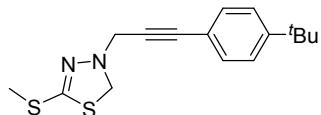
General Procedure for the Synthesis of Compounds (5a-5n). In a 4ml vial along with a stirring bar, hydrazinecarbodithioate (0.5 mmol), formaldehyde solution (37% wt% in water) (1.6 mmol) and propiolic acid (0.4 mmol) was mixed in DCM (1.0 mL). Then the reaction vessel was sealed and heated in an oil-bath for 12 h at a temperature of 60 °C. The resulting reaction mixture was loaded on a silica gel column and flashed with 3–5% ethyl acetate in petroleum ether to afford the desired product **5** as light yellow oil or yellow solid.

General Procedure for the Synthesis of Compounds (6a-6i). In a 4ml vial along with a stirring bar, hydrazinecarbodithioate (0.5 mmol), formaldehyde solution (37% wt% in water) (1.6 mmol) and boronic acid (0.4 mmol) was mixed in DCM (1.0 mL). Then the reaction vessel was sealed and heated in an oil-bath for 12 h at a temperature of 60 °C. The resulting reaction mixture was loaded on a silica gel column and flashed with 2–5% ethyl acetate in petroleum ether to afford the desired product **6** as light yellow oil.



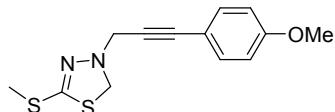
5-(methylthio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole 5a. Light yellow

oil (76.7 mg, 77% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.48 – 7.46 (m, 2H), 7.36 – 7.32 (m, 3H), 4.76 (s, 2H), 4.20 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.4, 131.8, 128.4, 128.3, 122.7, 86.2, 83.4, 61.4, 45.3, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 249.0515, found 249.0515.



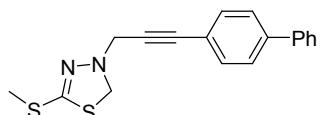
3-(3-(4-tert-butylphenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5b.

Light yellow oil (94.0 mg, 77% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.39 (dd, $J = 21.6, 8.4$ Hz, 4H), 4.76 (s, 2H), 4.20 (s, 2H), 2.56 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.7, 149.2, 131.6, 125.3, 119.7, 86.3, 82.7, 61.4, 45.4, 34.8, 31.2, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 305.1141, found 305.1150.



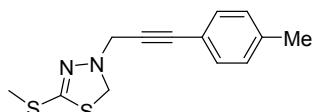
3-(3-(4-methoxyphenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5c.

Light yellow oil (78.1 mg, 70% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.38 (m, 2H), 6.86 – 6.84 (m, 2H), 4.75 (s, 2H), 4.18 (s, 2H), 3.82 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.7, 149.2, 133.2, 114.8, 113.9, 86.0, 81.9, 61.4, 55.3, 45.4, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{OS}_2$ [$\text{M} + \text{H}]^+$ 279.0620, found 279.0626.



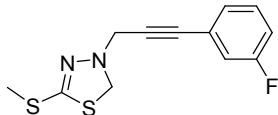
3-(3-(4-phenylphenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5d.

Yellow solid: mp 142–143 °C (92.3 mg, 71% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.64 – 7.54 (m, 6H), 7.50 – 7.47 (m, 2H), 7.42 – 7.38 (m, 1H), 4.79 (s, 2H), 4.25 (s, 2H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.4, 141.2, 140.3, 132.3, 128.9, 127.7, 127.1, 127.0, 121.6, 86.1, 84.2, 61.5, 45.4, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 325.0828, found 325.0818.



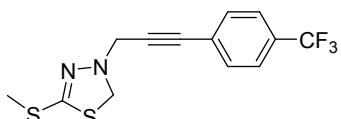
5-(methylthio)-3-(3-p-tolylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole 5e. Yellow solid : mp 205–206 °C (94.7 mg, 90% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.36 (d, $J = 8.0$ Hz,

2H), 7.14 (d, J = 8.0 Hz, 2H), 4.76 (s, 2H), 4.20 (s, 2H), 2.56 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.2, 138.5, 131.7, 129.1, 119.6, 86.3, 82.7, 61.4, 45.3, 21.5, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{S}_2$ [M + H] $^+$ 263.0671, found 263.0672.



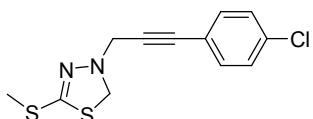
3-(3-(3-fluorophenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5f.

Light yellow oil (80.1 mg, 75% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.32 – 7.22 (m, 2H), 7.17 – 7.14 (m, 1H), 7.07 – 7.02 (m, 1H), 4.74 (s, 2H), 4.19 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.3 (d, J = 245 Hz), 149.6, 129.9, 127.68 (d, J = 3.0 Hz), 124.50 (d, J = 9.4 Hz), 118.6 (d, J = 22 Hz), 115.8 (d, J = 21 Hz), 84.9, 84.5, 61.4, 45.2, 15.9. HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{11}\text{FN}_2\text{S}_2$ [M + H] $^+$ 267.0420, found 267.0413.



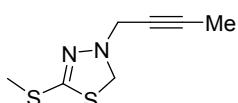
5-(methylthio)-3-(3-(4-(trifluoromethyl)phenyl)prop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole 5g.

Light yellow oil (83.7 mg, 66% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.60 – 7.55 (m, 4H), 4.76 (s, 2H), 4.21 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 132.0, 130.3, 130.0, 126.5, 125.2 (q, J = 3.8 Hz), 122.5, 86.1, 84.8, 61.4, 45.2, 15.9. HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{11}\text{F}_3\text{N}_2\text{S}_2$ [M + H] $^+$ 317.0389, found 317.0391.



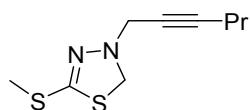
3-(3-(4-chlorophenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5h.

Light yellow oil (98.5 mg, 87% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.38 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 4.73 (s, 2H), 4.18 (s, 2H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.5, 134.5, 133.0, 128.7, 121.2, 85.0, 84.5, 61.4, 45.3, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{11}\text{ClN}_2\text{S}_2$ [M + H] $^+$ 283.0125, found 283.0118.

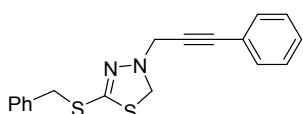


3-(but-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5i. Light yellow oil (28.4 mg, 38% yield); ^1H NMR (400 MHz, CDCl_3) δ 4.67 (s, 2H), 3.93 (s, 2H), 2.55 (s, 3H), 1.87 (t, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.8, 82.1, 73.2, 61.2, 44.8, 15.9, 3.6. HRMS

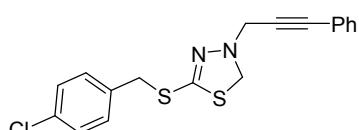
(ESI) m/z calcd for C₇H₁₀N₂S₂ [M + H]⁺ 187.0358, found 187.0364.



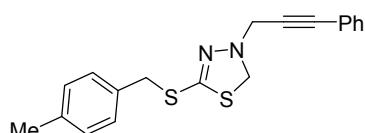
3-(hex-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 5j. Light yellow oil (36.1 mg, 42% yield); ¹H NMR (400 MHz, CDCl₃) δ 4.678 (s, 2H), 3.95 (t, *J* = 2.0 Hz, 2H), 2.54 (s, 3H), 2.23 – 2.19 (m, 2H), 1.57 – 1.51 (m, 2H), 1.01 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 148.7, 86.6, 74.1, 61.3, 44.9, 22.1, 20.8, 15.9, 13.5. HRMS (ESI) m/z calcd for C₉H₁₄N₂S₂ [M + H]⁺ 215.0671, found 215.0676.



5-(benzylthio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole 5l. Light yellow oil (79.3 mg, 61% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.26 (m, 10H), 4.76 (s, 2H), 4.32 (s, 2H), 4.22 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 147.8, 136.6, 131.9, 129.2, 129.1, 128.8, 128.6, 128.5, 128.3, 127.6, 122.7, 86.2, 83.4, 61.4, 45.3, 37.7. HRMS (ESI) m/z calcd for C₁₈H₁₆N₂S₂ [M + H]⁺ 325.0828, found 325.0823.

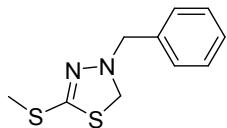


5-(4-chlorobenzylthio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole 5m. Light yellow oil (97.7 mg, 68% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.43 (m, 2H), 7.38 – 7.30 (m, 5H), 7.26 – 7.24 (m, 2H), 4.76 (s, 2H), 4.25 (s, 2H), 4.21 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 147.2, 135.4, 133.4, 131.8, 130.4, 128.7, 128.5, 128.4, 122.6, 86.3, 83.2, 61.4, 45.3, 36.8. HRMS (ESI) m/z calcd for C₁₈H₁₅ClN₂S₂ [M + H]⁺ 359.0438, found 359.0442.

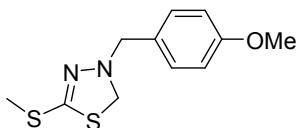


5-((4-methylbenzyl)thio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole 5n. Light yellow oil (63.8 mg, 47% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.45 (m, 2H), 7.35 – 7.28 (m, 5H), 7.28 (d, *J* = 7.6 Hz, 2H), 4.76 (s, 2H), 4.28 (s, 2H), 4.22 (s, 2H), 2.32 (s,

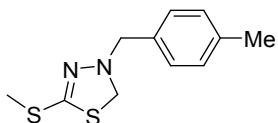
3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.0, 137.3, 133.5, 131.8, 129.3, 129.0, 128.4, 128.3, 122.7, 86.2, 83.4, 61.3, 45.3, 37.5, 21.1. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}$]⁺ 339.0984, found 339.0988.



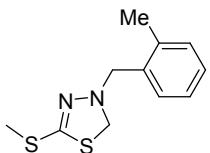
3-benzyl-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6a. Light yellow oil (71.1 mg, 79% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.43 – 7.31 (m, 5H), 4.45 (s, 2H), 4.29 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.2, 136.6, 129.1, 128.6, 127.8, 62.2, 59.9, 15.9. HRMS (ESI) m/z calcd for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}$]⁺ 225.0515, found 225.0520.



3-(4-methoxybenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6b. Light yellow oil (92.8 mg, 91% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.31 (d, $J = 8.4$ Hz, 2H), 6.91 (t, $J = 5.6$ Hz, 2H), 4.42 (s, 2H), 4.21 (s, 2H), 3.82 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.2, 148.1, 130.4, 128.6, 113.9, 62.0, 59.2, 55.3, 15.9. HRMS (ESI) m/z calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{OS}_2$ [$\text{M} + \text{H}$]⁺ 255.0620, found 255.0617.

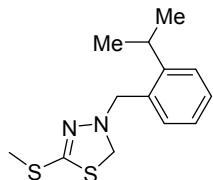


3-(4-methylbenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6c. Light yellow oil (61.2 mg, 64% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.30 (d, $J = 8.0$ Hz, 2H), 7.19 (d, $J = 7.6$ Hz, 2H), 4.44 (s, 2H), 4.25 (s, 2H), 2.56 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.1, 137.4, 133.5, 129.2, 129.1, 62.1, 59.6, 21.2 15.9. HRMS (ESI) m/z calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}$]⁺ 239.0671, found 239.0666.

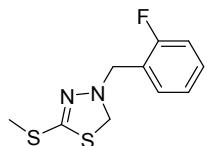


3-(2-methylbenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6d. Light yellow oil (51.6 mg, 54% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.33 (d, $J = 7.2$ Hz, 1H), 7.27 – 7.15

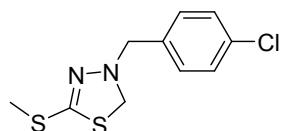
(m, 3H), 4.47 (s, 2H), 4.26 (s, 2H), 2.56 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.3, 137.6, 134.8, 130.5, 129.9, 127.9, 125.9, 62.4, 57.8, 19.3, 15.9. HRMS (ESI) m/z calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 239.0671, found 239.0669.



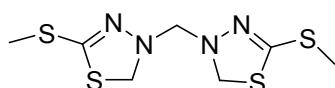
3-(2-isopropylbenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6e. Light yellow oil (42.6 mg, 40% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.38 – 7.30 (m, 3H), 7.20 – 7.16 (m, 1H), 4.45 (s, 2H), 4.30 (s, 2H), 3.50 – 3.43 (m, 1H), 2.57 (s, 3H), 1.28 (m, 3H), 1.27 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.4, 133.1, 130.3, 128.3, 125.7 (d, $J = 11.0$ Hz), 62.2, 57.3, 28.6, 24.0, 16.0. HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 266.0911, found 266.0915.



3-(2-fluorobenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6f. Light yellow oil (22.4 mg, 23% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.50 (t, $J = 7.4$ Hz, 1H), 7.36 – 7.30 (m, 1H), 7.16 (t, $J = 7.4$ Hz, 1H), 7.08 (t, $J = 9.2$ Hz, 1H), 4.53 (s, 2H), 4.34 (s, 2H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.3 (d, $J = 245$ Hz), 148.4, 131.7 (d, $J = 4.0$ Hz), 129.5 (d, $J = 8.0$ Hz), 124.2 (d, $J = 3.6$ Hz), 115.5, 115.2, 62.2, 52.9 (d, $J = 102.0$ Hz), 15.86 (s). HRMS (ESI) m/z calcd for $\text{C}_{10}\text{H}_{11}\text{FN}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 243.0420, found 243.0421.



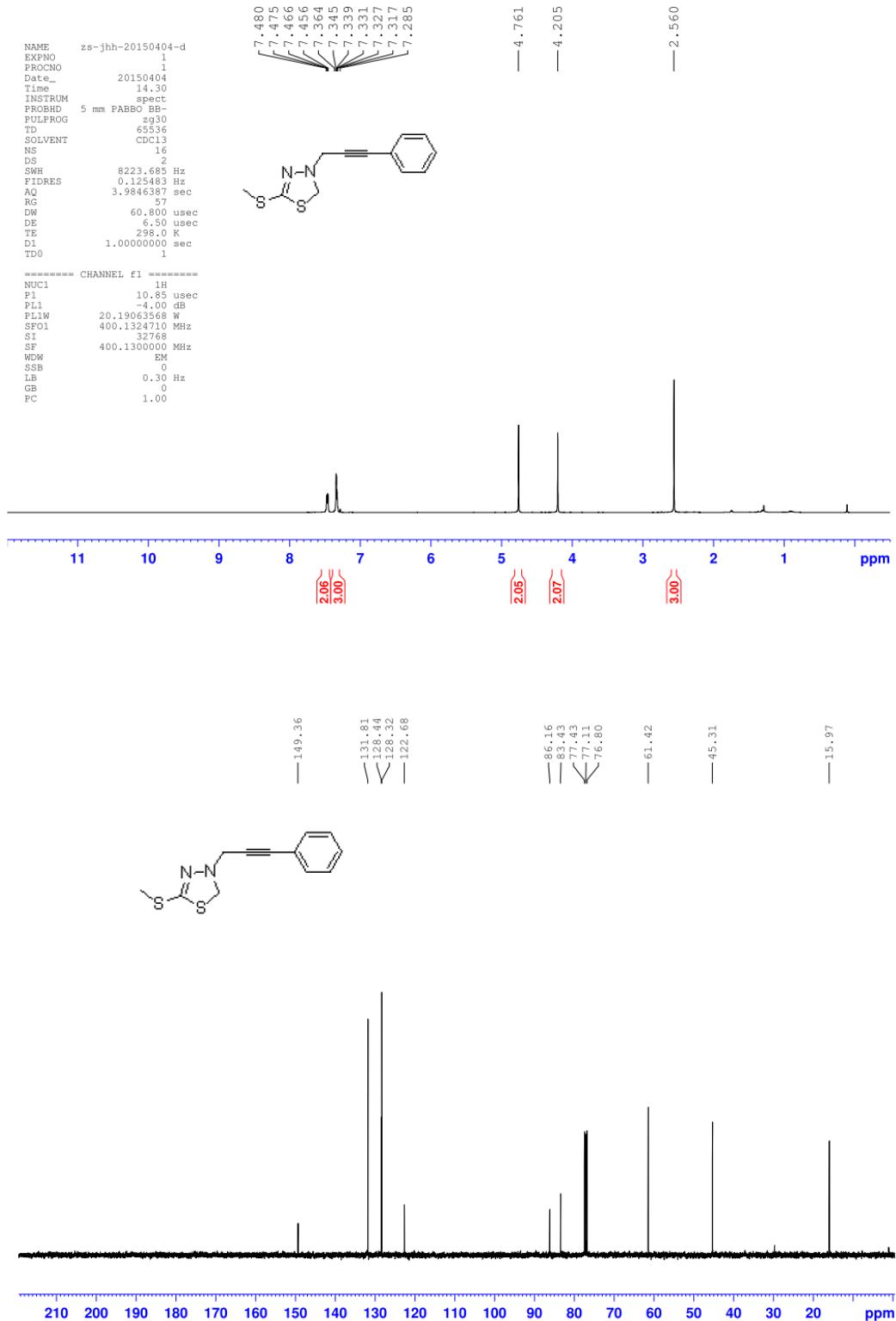
3-(4-chlorobenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole 6g. Light yellow oil (63.2 mg, 61% yield); ^1H NMR (400 MHz, CDCl_3) δ 7.43 – 7.36 (m, 4H), 4.56 (s, 2H), 4.31 (s, 2H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.6, 135.2, 133.6, 130.4, 128.7, 62.2, 59.1, 15.9. HRMS (ESI) m/z calcd for $\text{C}_{10}\text{H}_{11}\text{ClN}_2\text{S}_2$ [$\text{M} + \text{H}]^+$ 259.0125, found 259.0132.



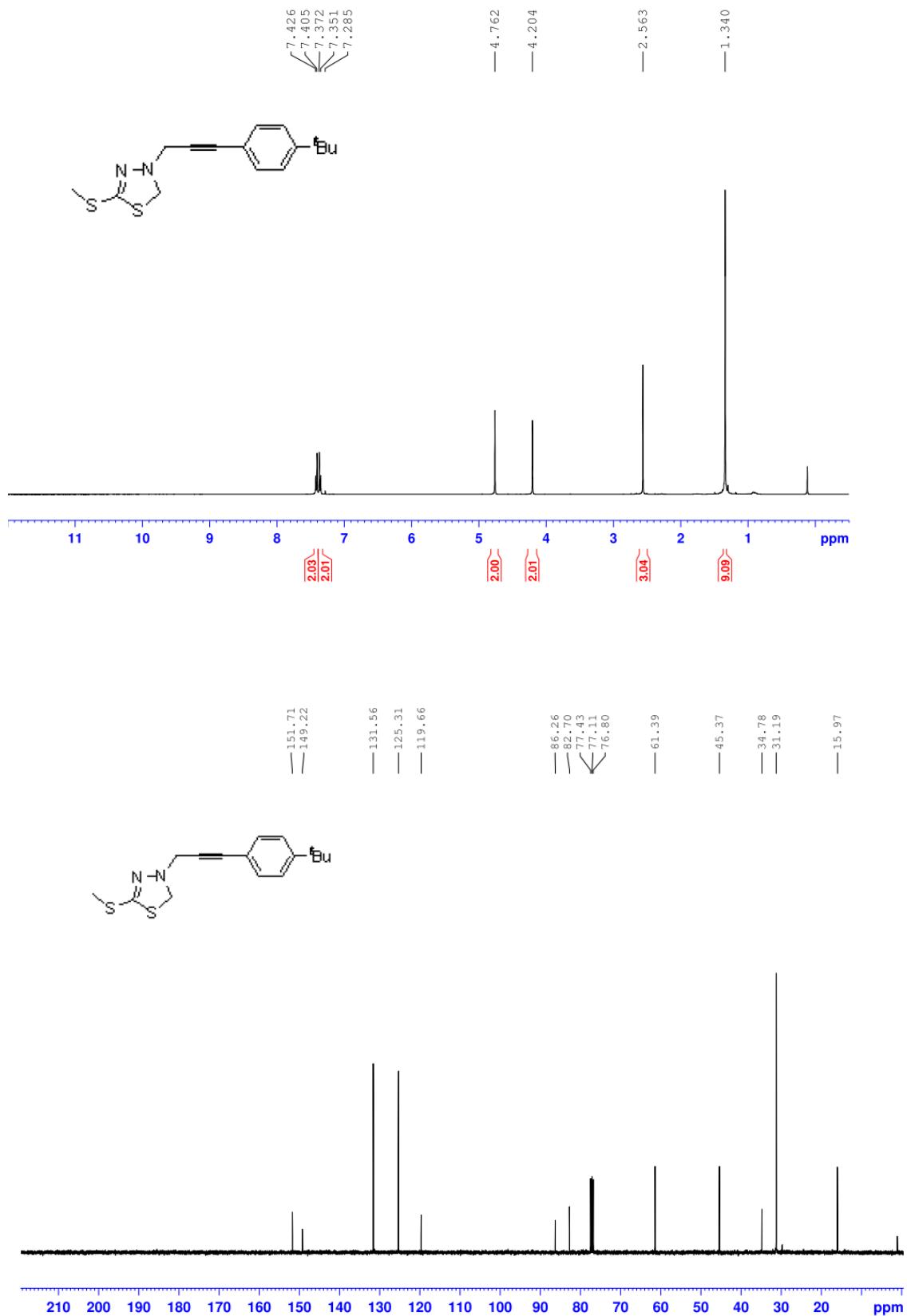
Bis(5-(methylthio)-1,3,4-thiadiazol-3(2H)-yl)methane 7. Light yellow oil (46.0 mg, 66%

yield); ^1H NMR (400 MHz, CDCl_3) δ 4.78 (s, 4H), 4.55 (s, 2H), 2.51 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.6, 72.5, 60.7, 15.9; MS (ESI) m/z : 281.0 $[\text{M} + \text{H}]^+$.

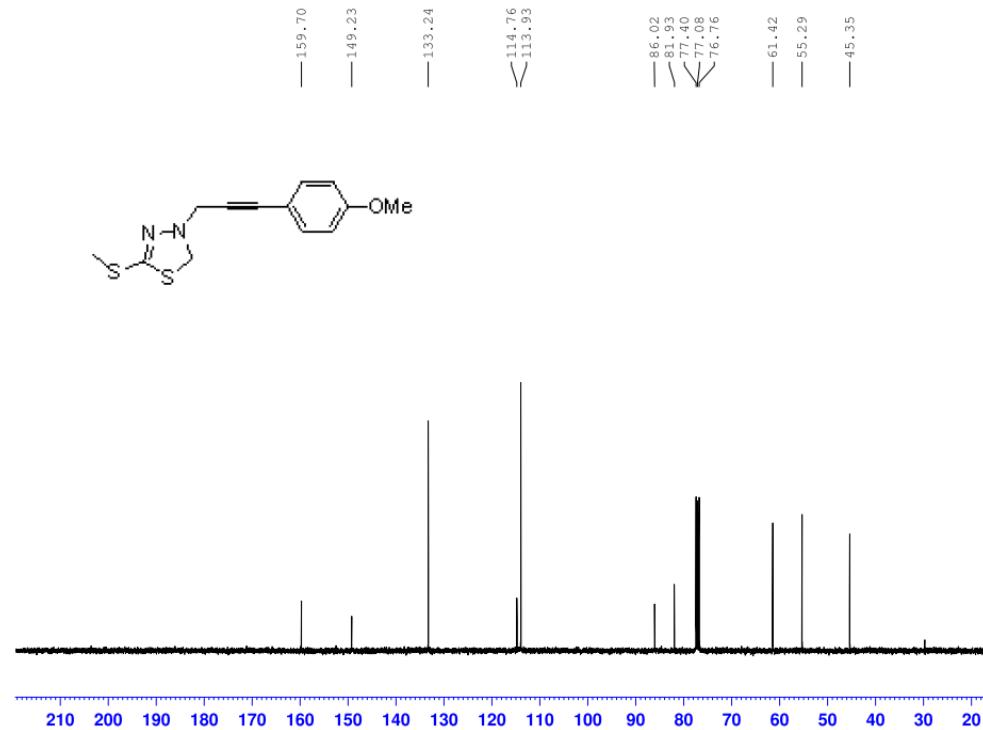
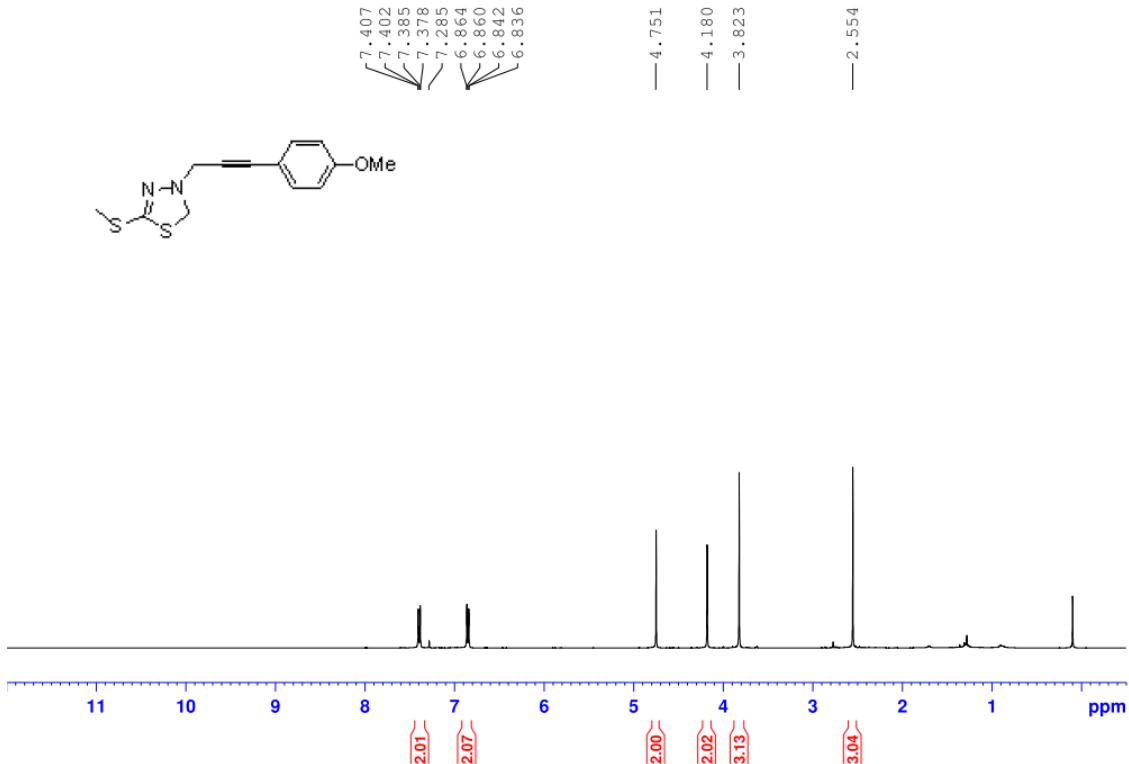
5-(methylthio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole (5a)



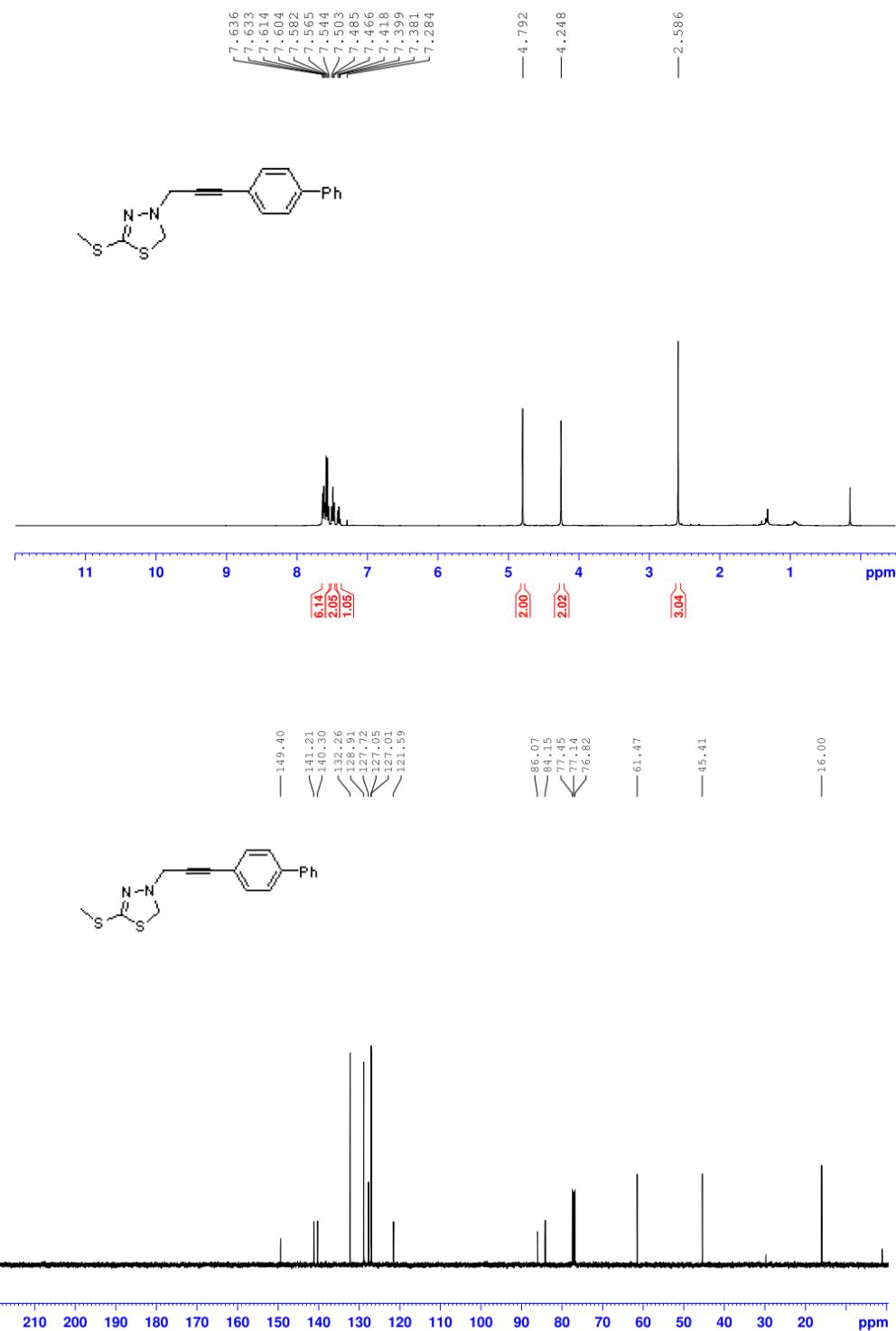
3-(3-(4-tert-butylphenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5b)



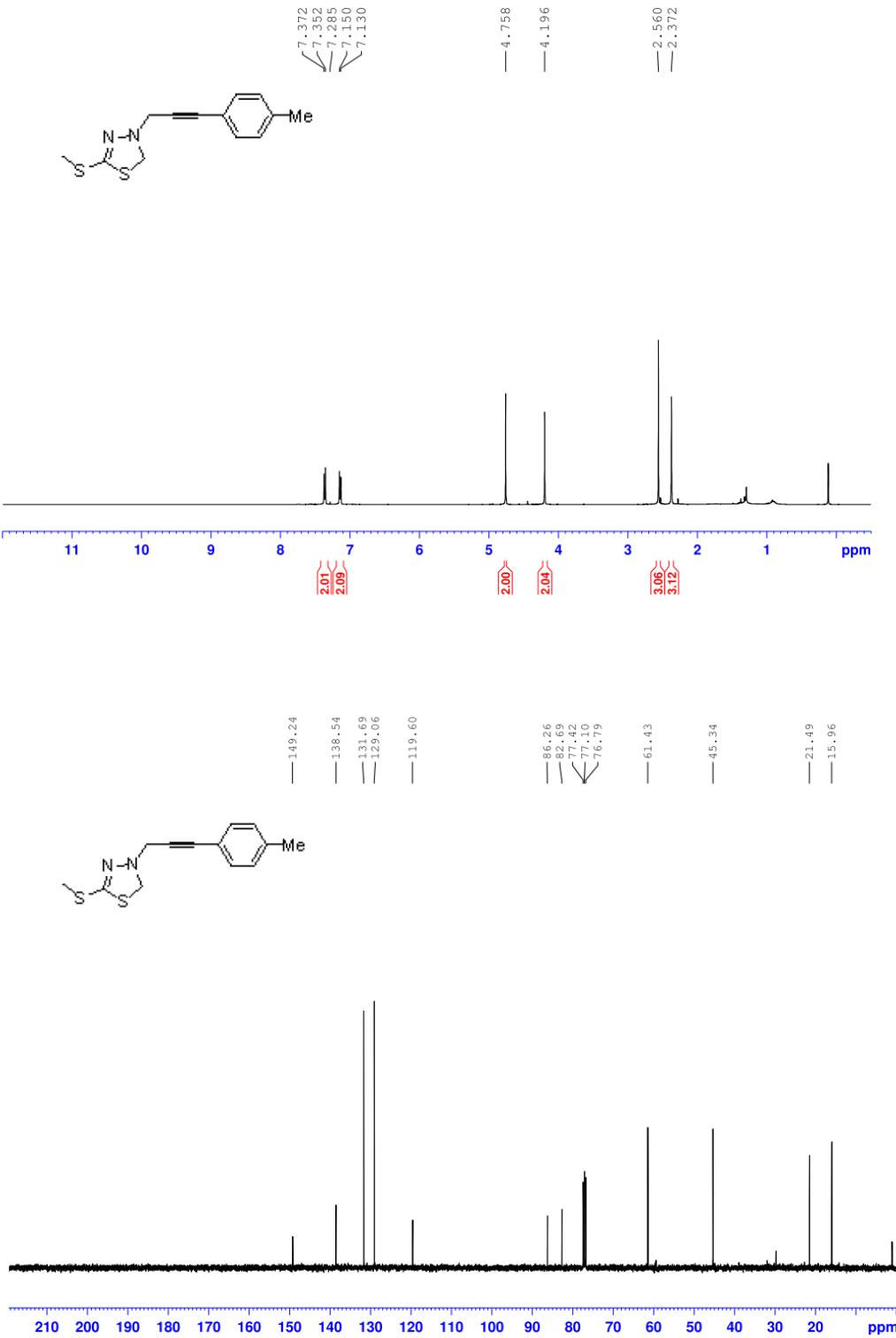
3-(3-(4-methoxyphenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5c)



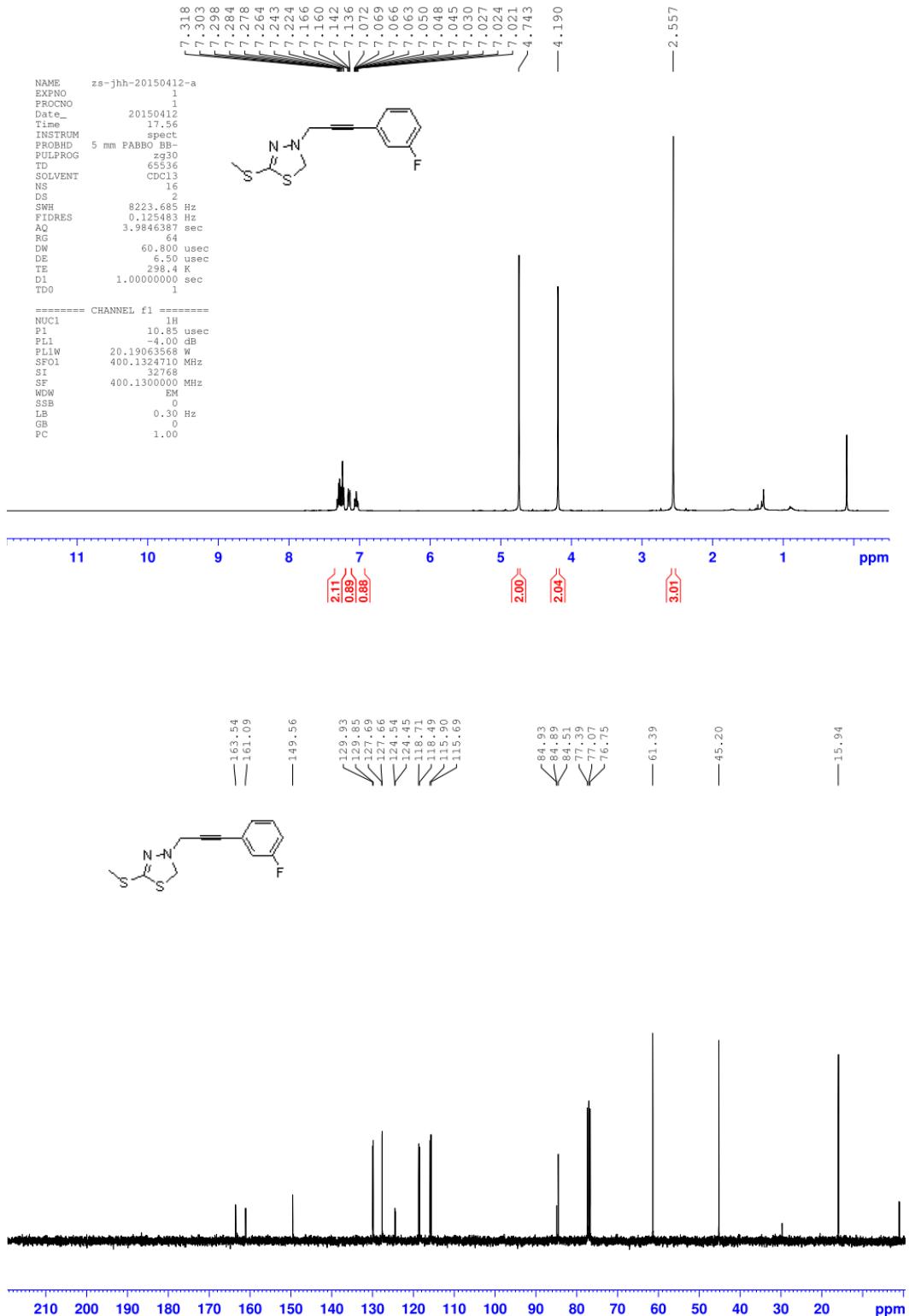
3-(3-(4-phenylphenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5d)



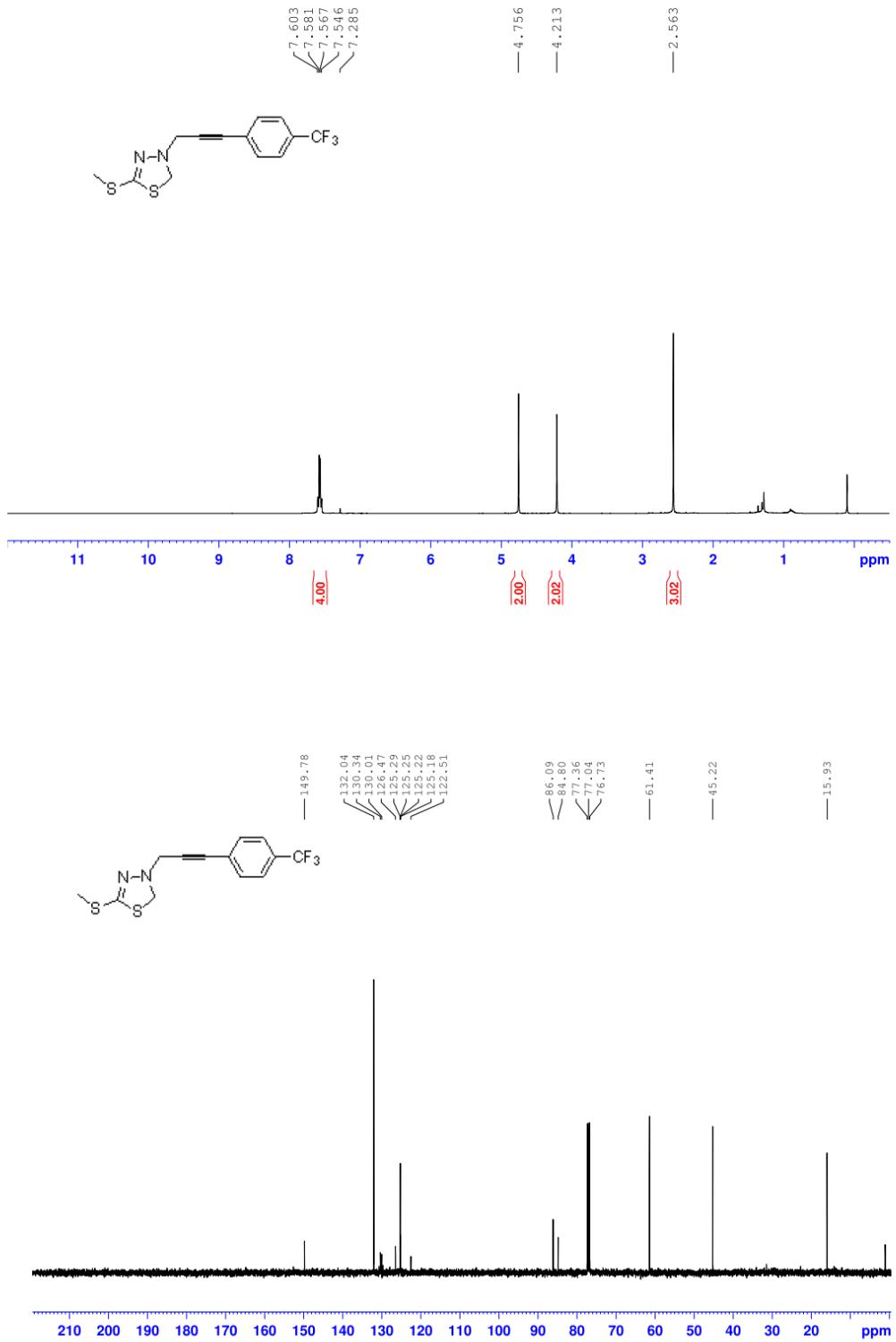
5-(methylthio)-3-(3-p-tolylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole (5e)



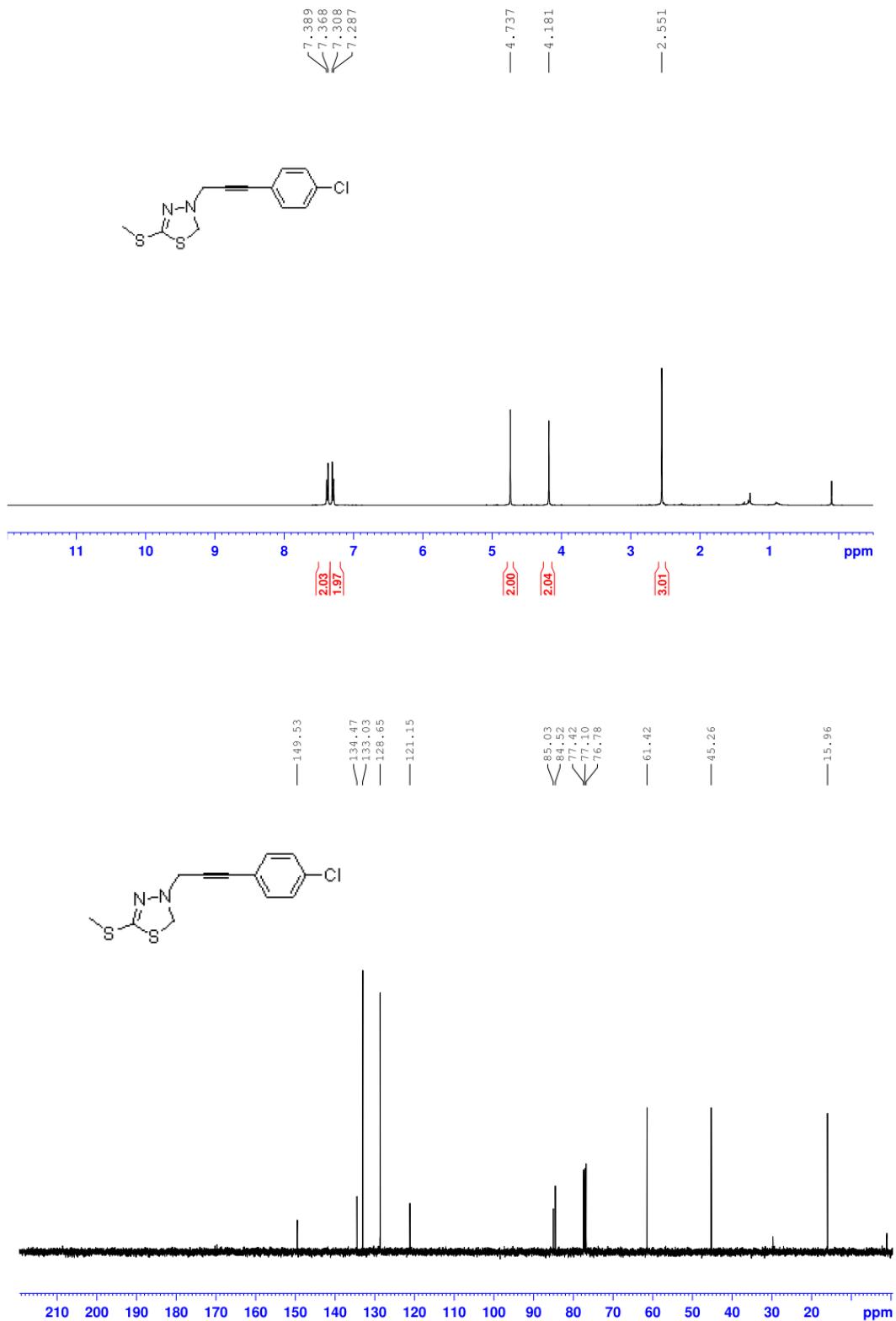
3-(3-(3-fluorophenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5f)



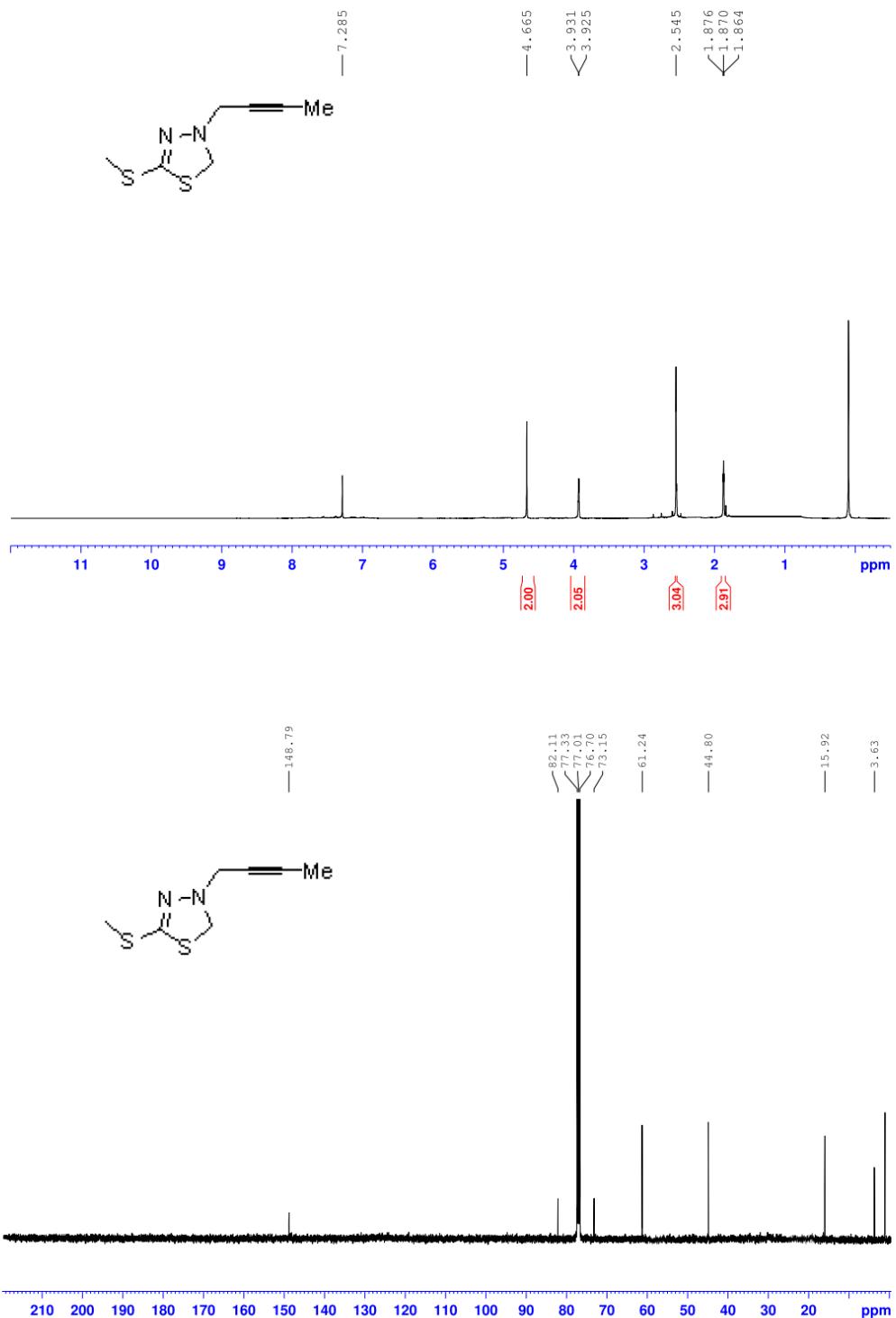
**5-(methylthio)-3-(3-(trifluoromethyl)phenyl)prop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole
(5g)**



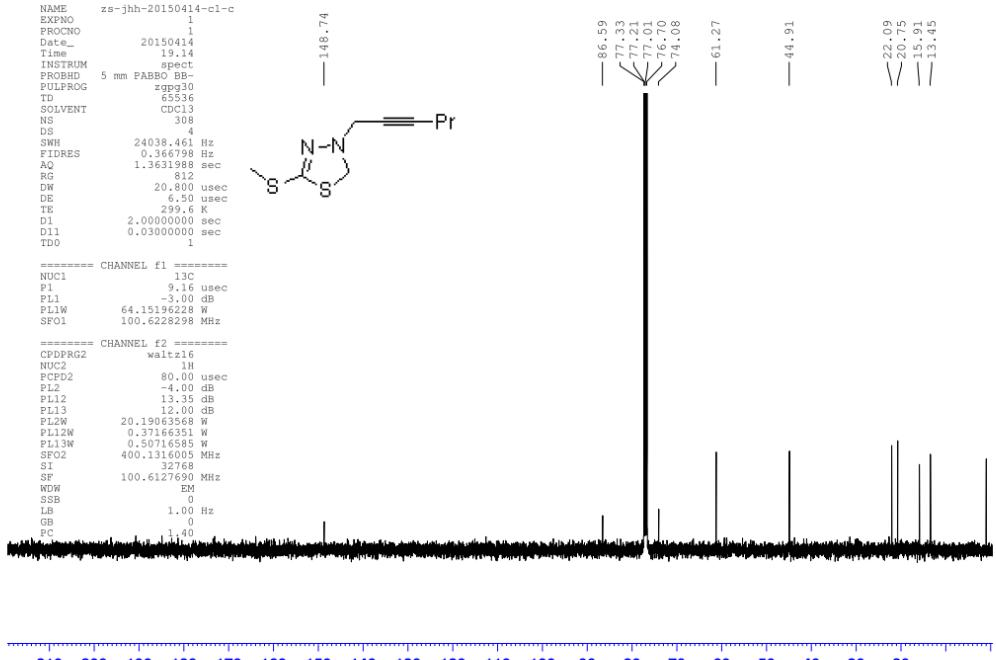
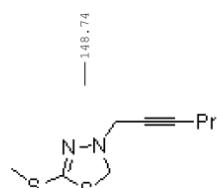
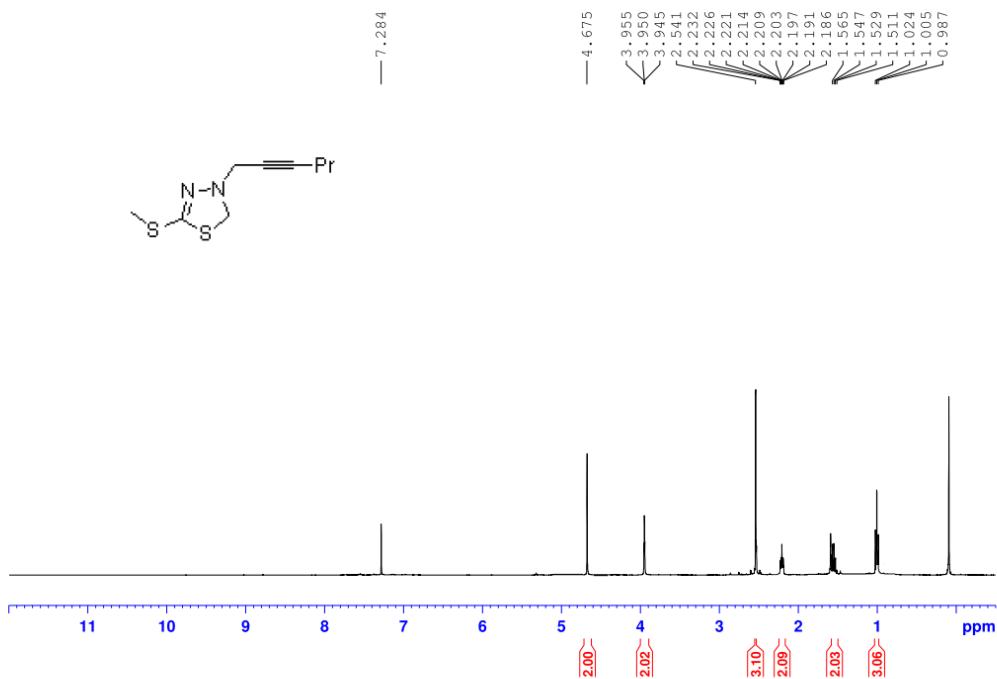
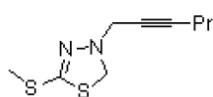
3-(3-(4-chlorophenyl)prop-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5h)



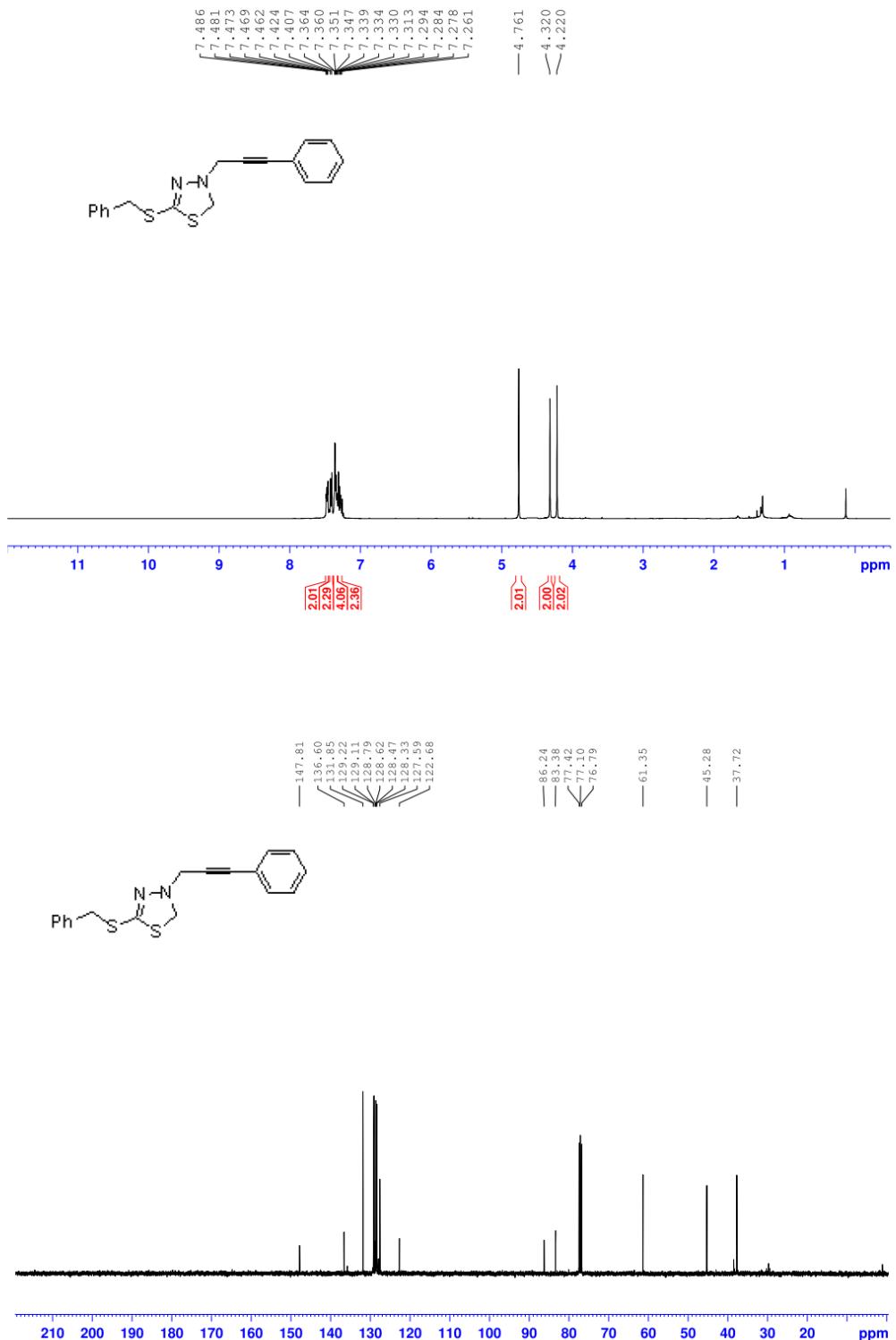
3-(but-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5i)



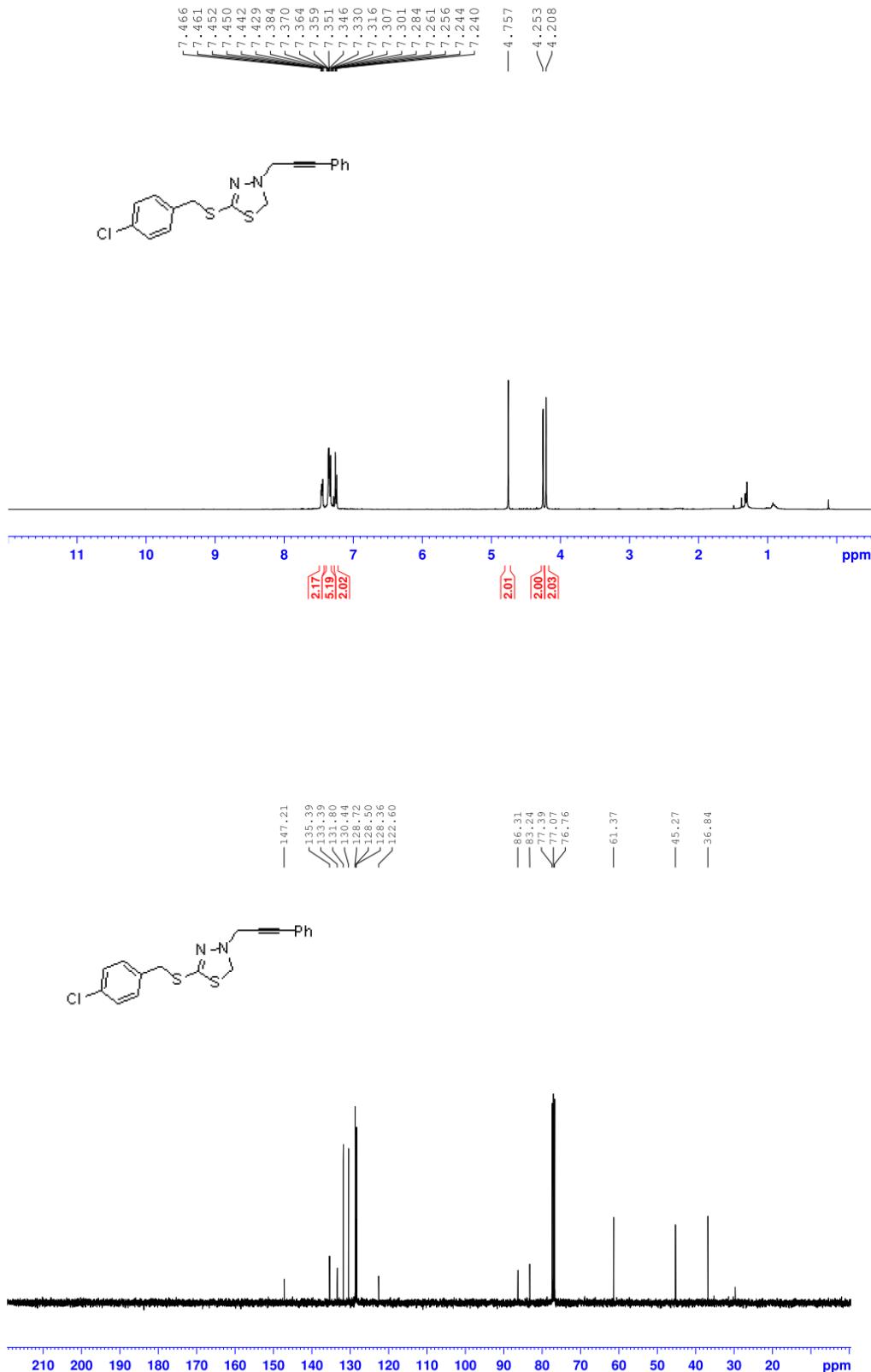
3-(hex-2-ynyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (5j)



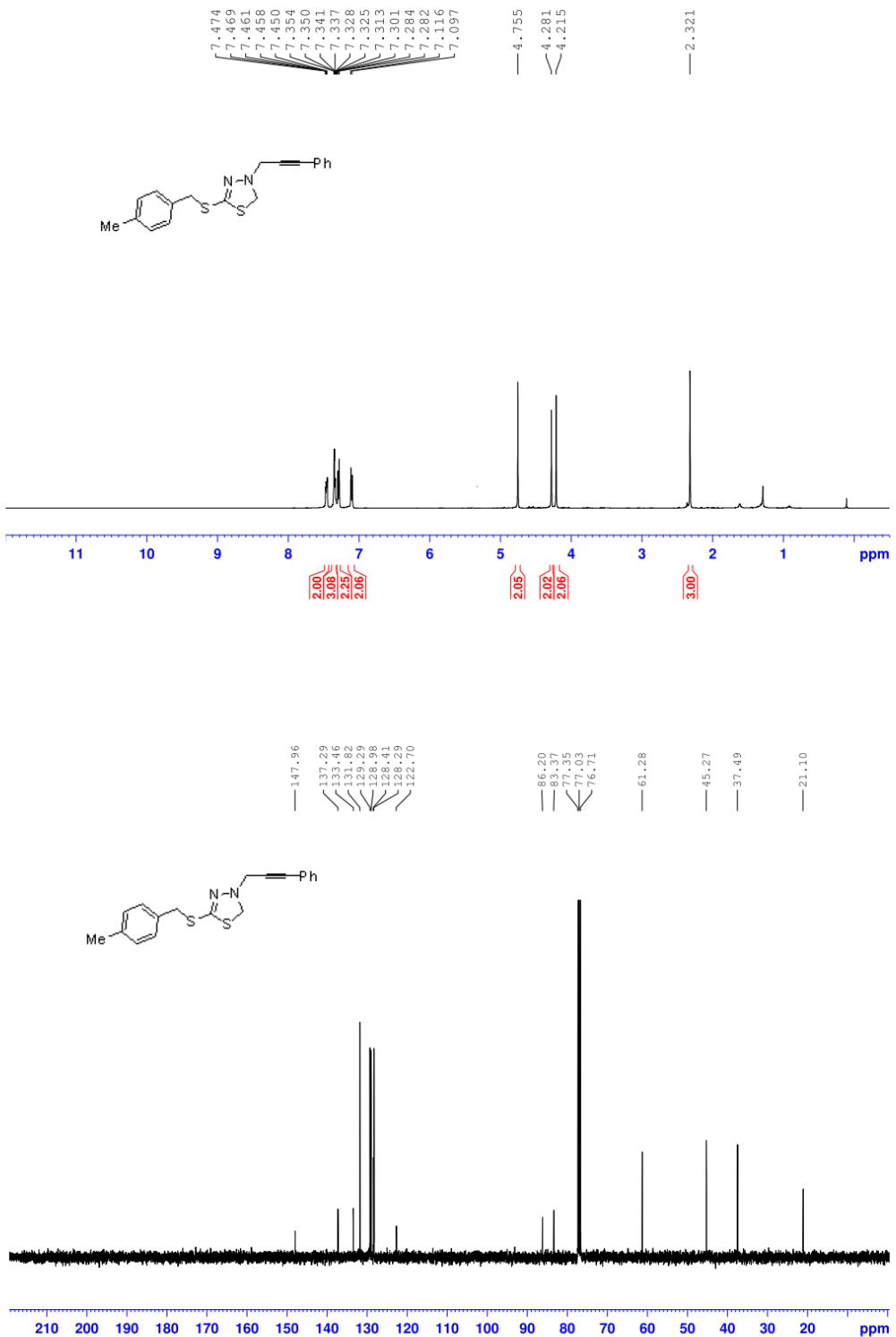
5-(benzylthio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole (5l)



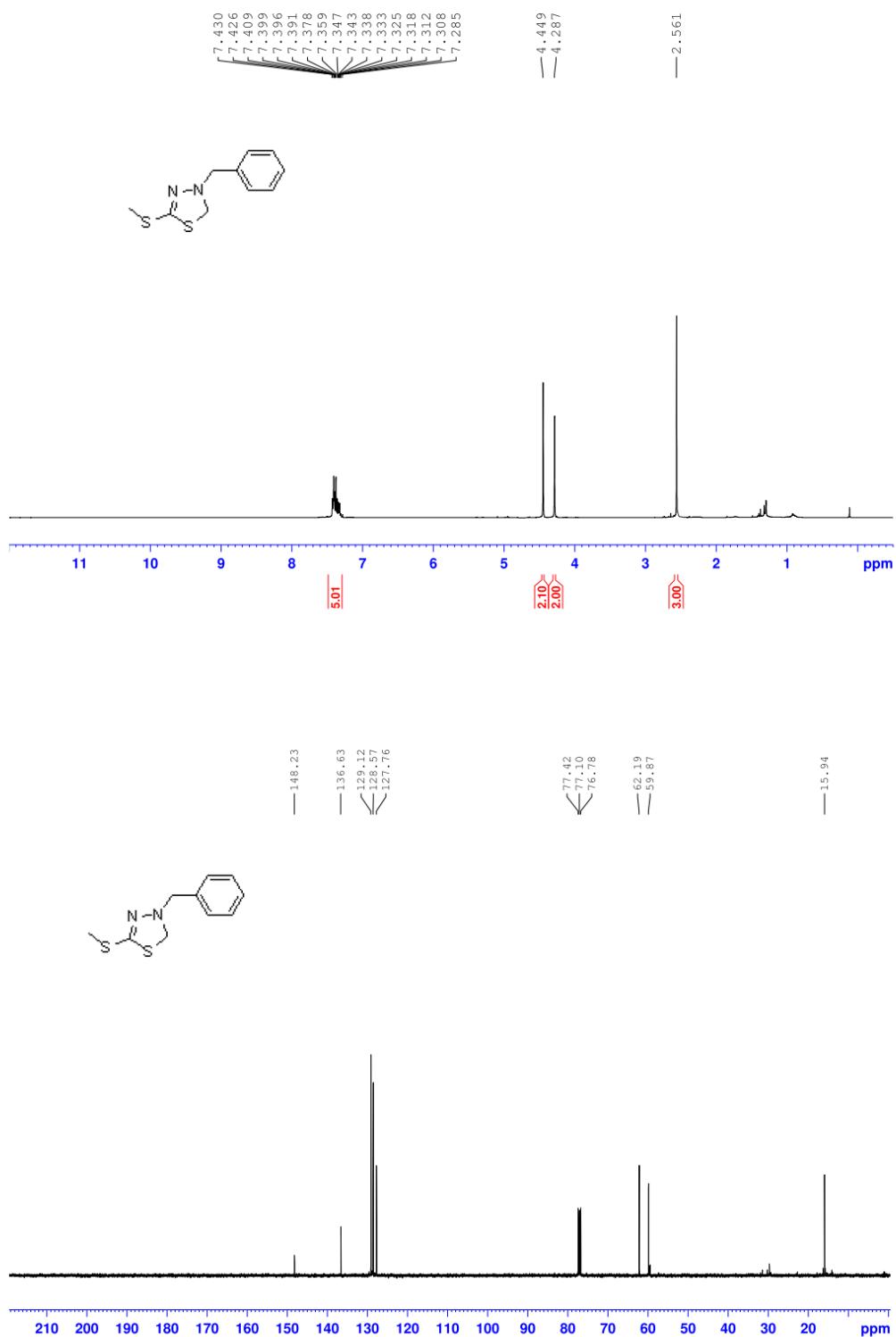
5-(4-chlorobenzylthio)-3-(3-phenylprop-2-ynyl)-2,3-dihydro-1,3,4-thiadiazole (5m)



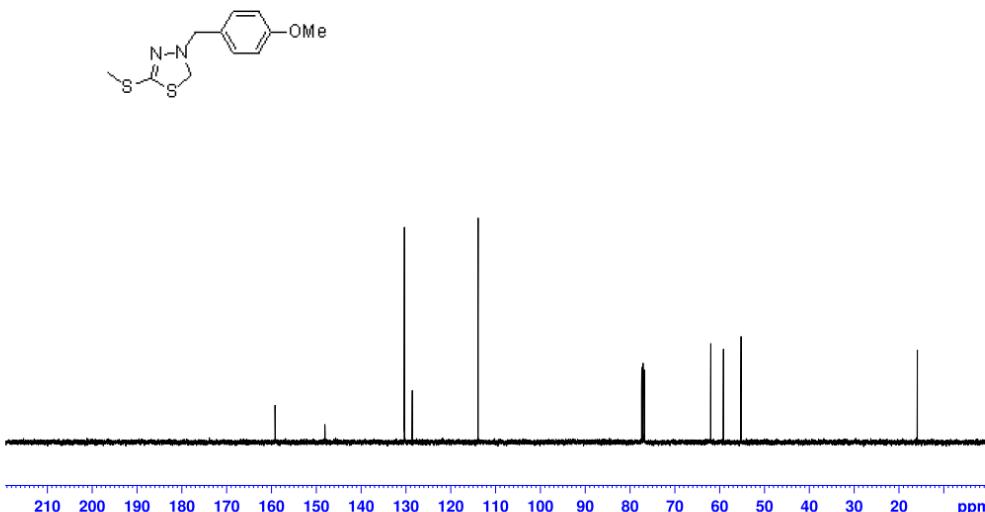
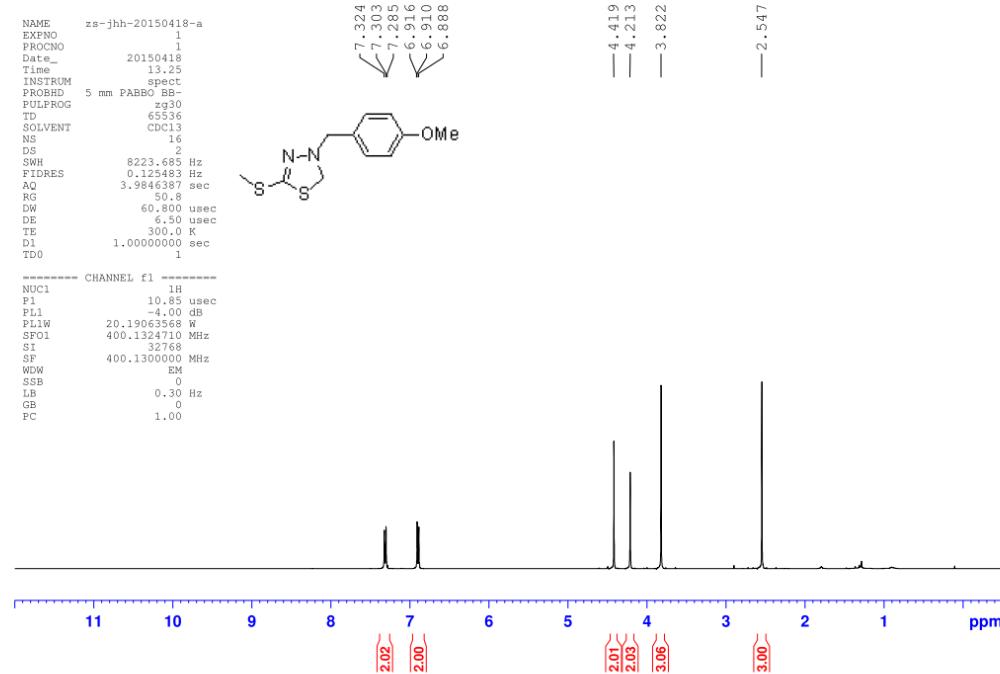
5-((4-methylbenzyl)thio)-3-(3-phenylprop-2-yn-1-yl)-2,3-dihydro-1,3,4-thiadiazole (5n)



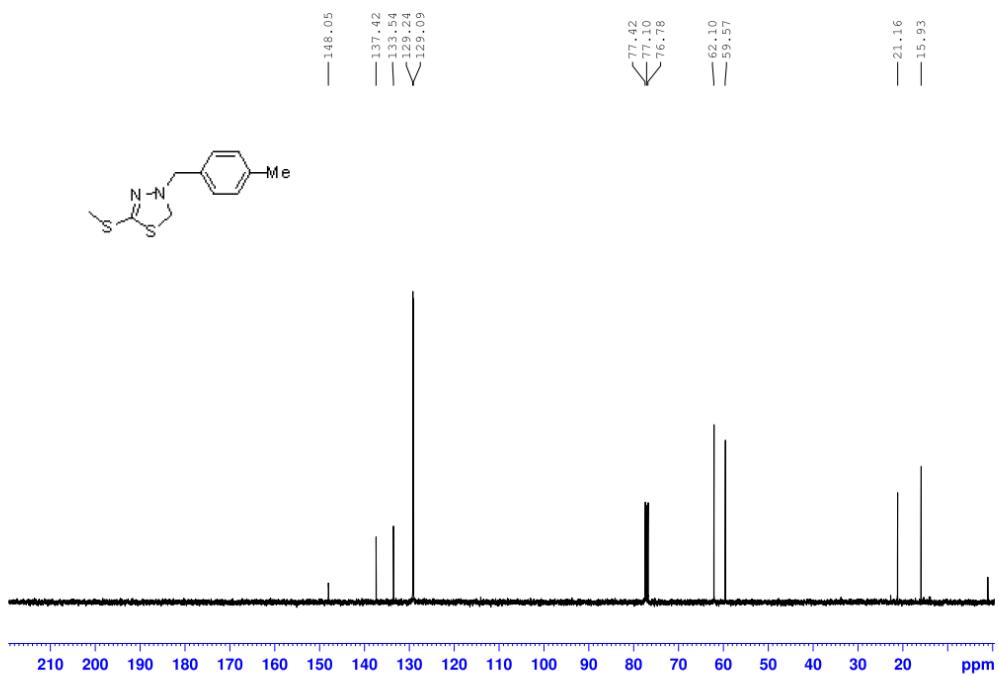
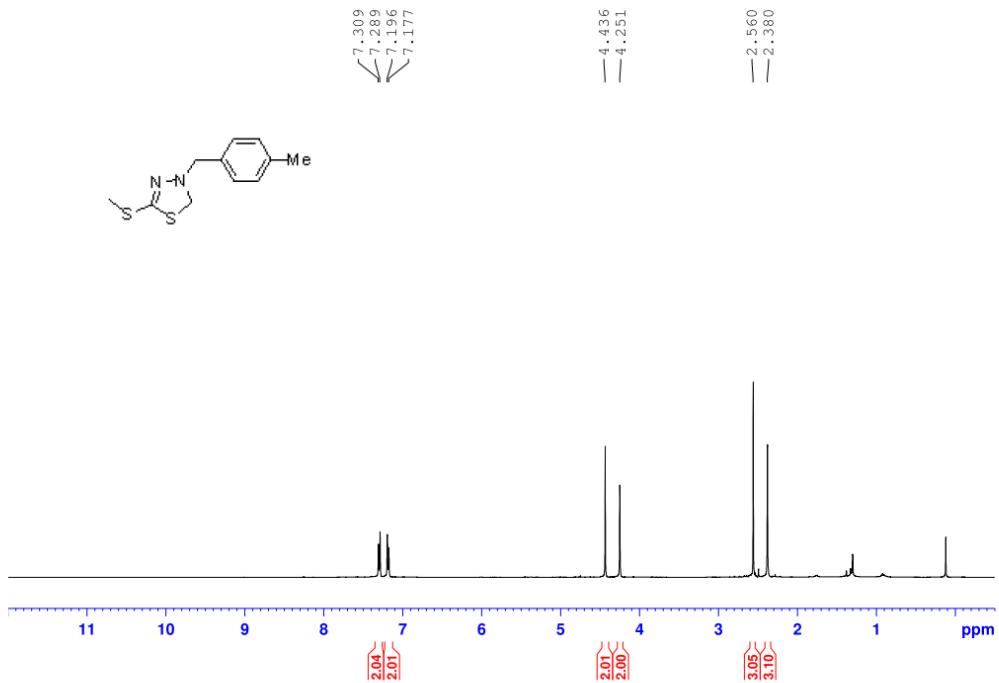
3-benzyl-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6a)



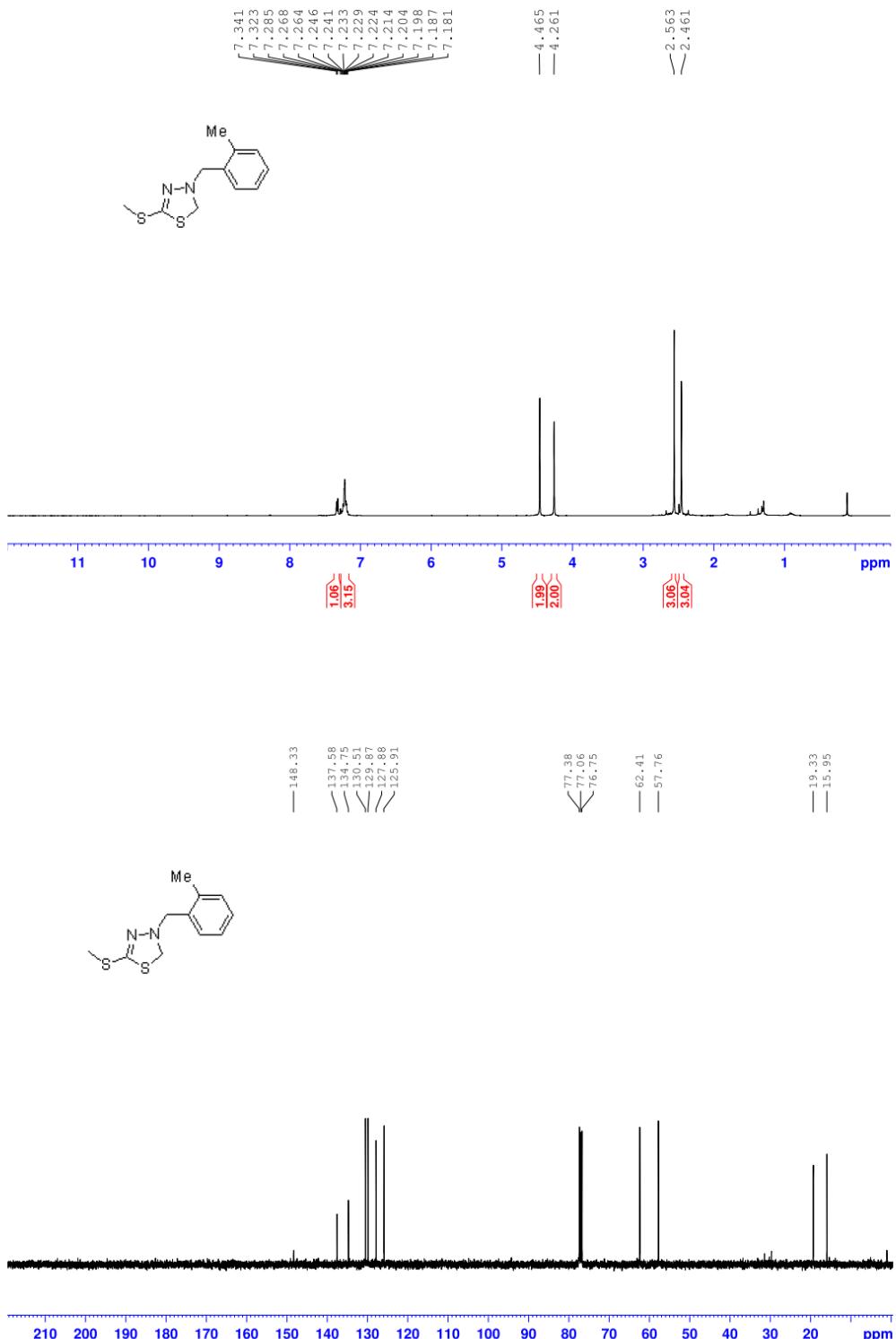
3-(4-methoxybenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6b)



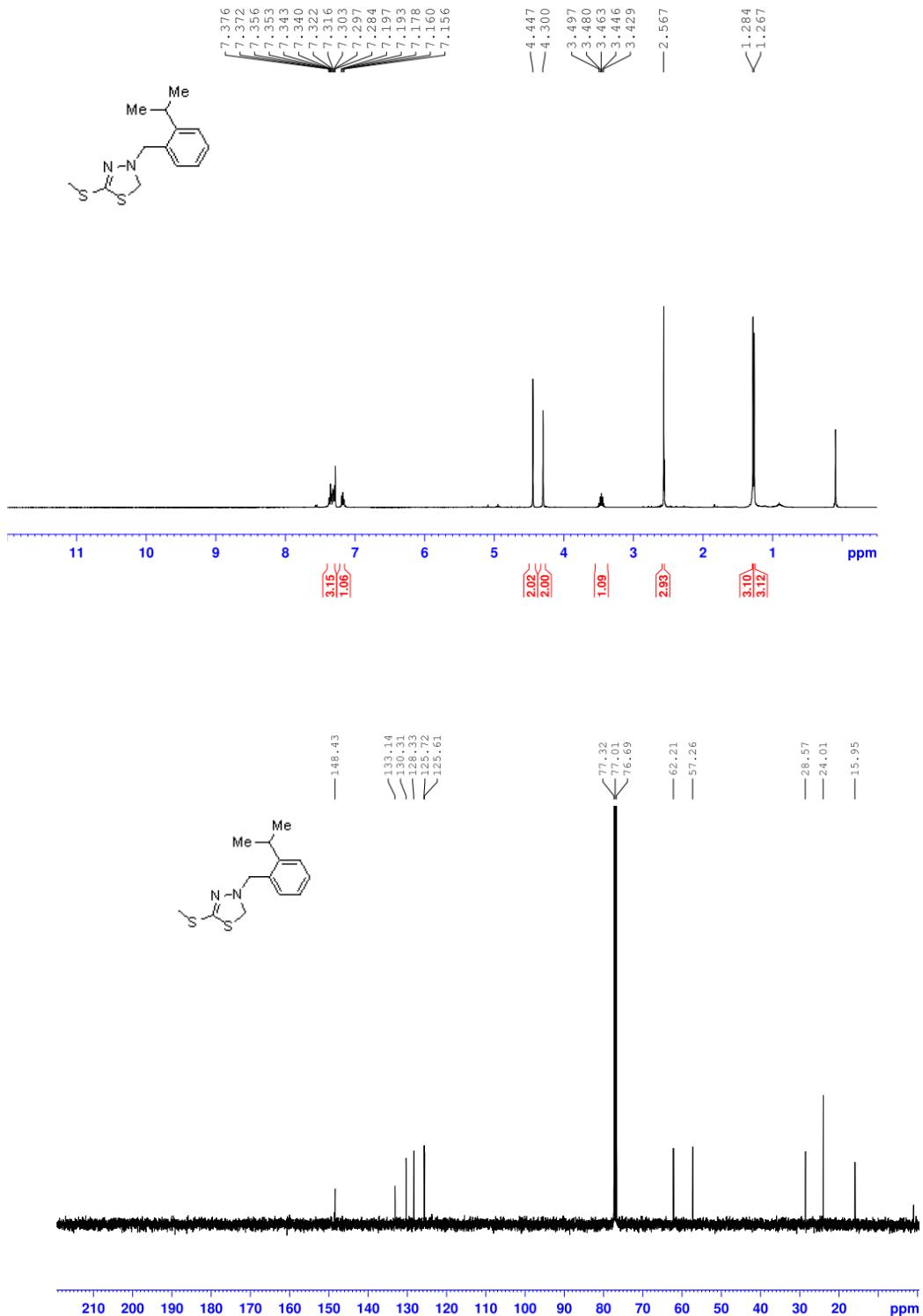
3-(4-methylbenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6c)



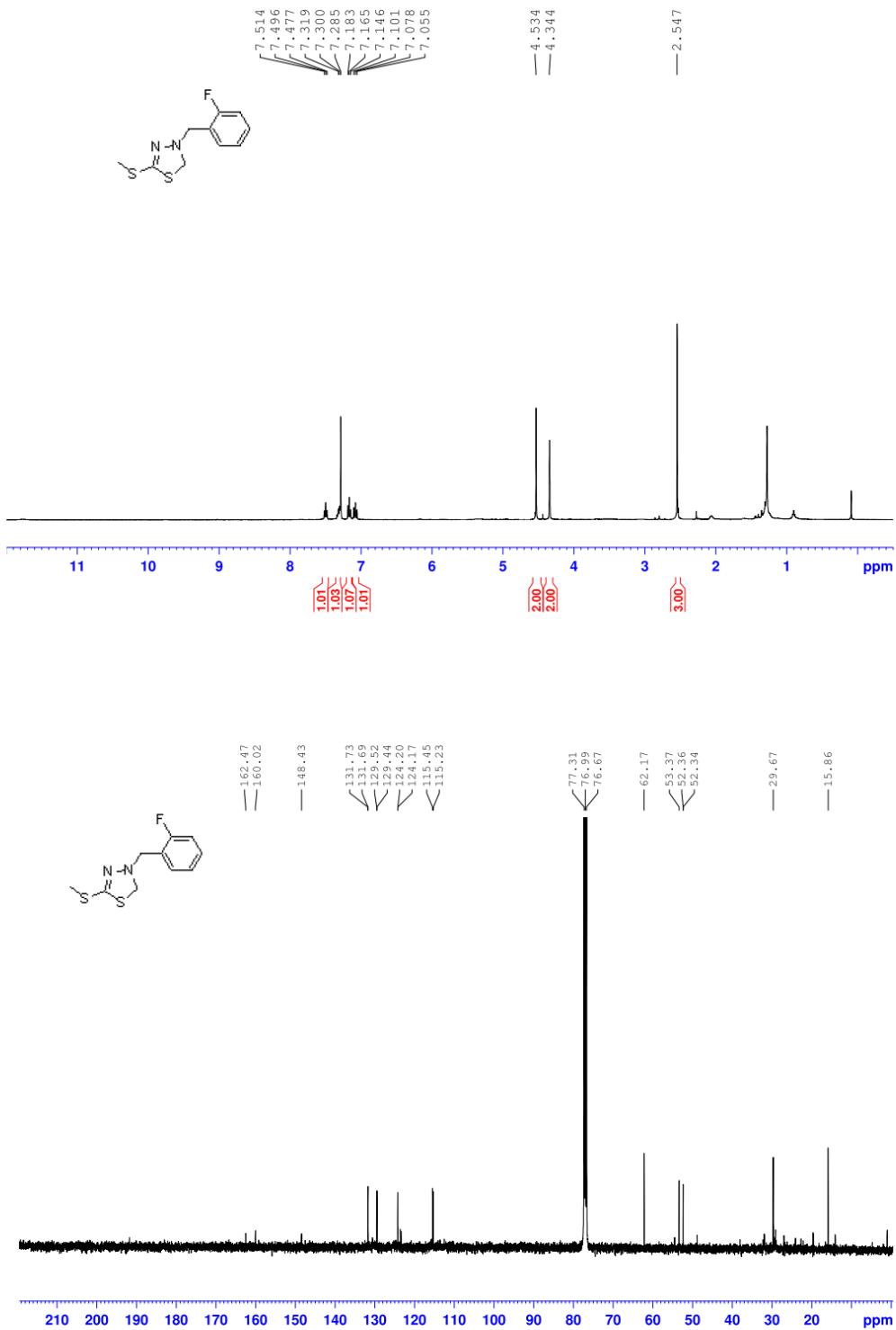
3-(2-methylbenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6d)



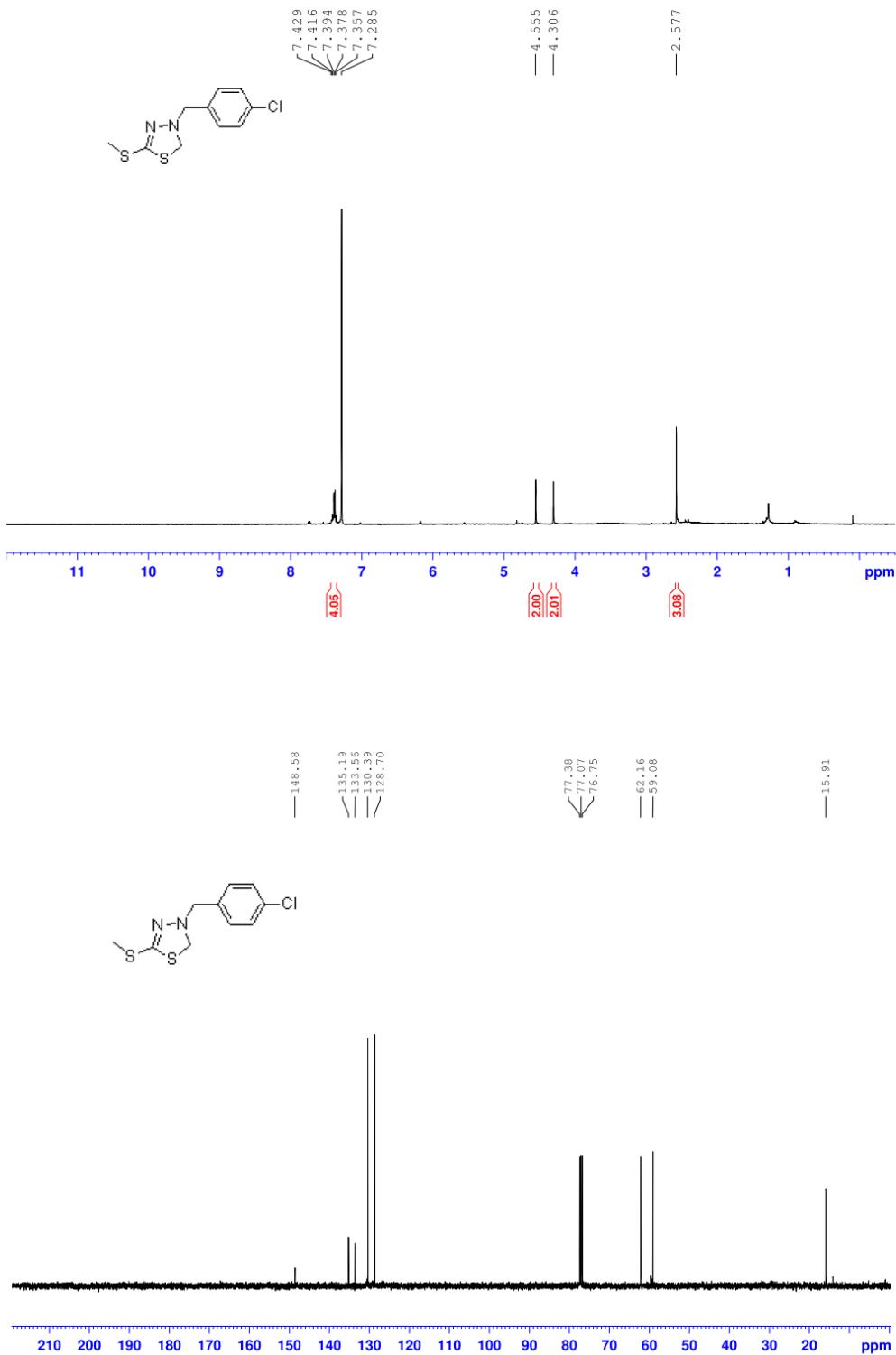
3-(2-isopropylbenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6e)



3-(2-fluorobenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6f)



3-(4-chlorobenzyl)-5-(methylthio)-2,3-dihydro-1,3,4-thiadiazole (6g)



Bis(5-(methylthio)-1,3,4-thiadiazol-2H-yl)methane (7)

