Copper-mediated [3+2] oxidative cyclization of oxime acetate and their utility in formal synthesis of fentiazac

Nitin L. Jadhao,[a,b] Harish B. Musale,[c] J. M. Gajbhiye,[a,b] Vivek T. Humne [c]

[a]Organic Chemistry Division, CSIR-National Chemical Laboratory, Pune, 411008, India

[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India.

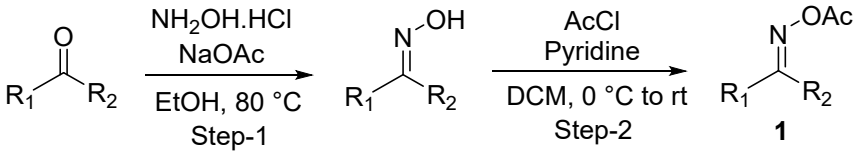
[c]Shri R. R. Lahoti Science College, Morshi, India

Table of content

1. General Information

All new compounds were fully characterized. NMR experiments were performed with 300 MHz, 400 MHz, and 500 MHz spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal reference. *J* values are given in hertz. The ^{1}H and ^{13}C NMR spectra are referenced to the residual solvent signals (7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C in $CDCl_3$, 2.50 ppm for ^{1}H and 39.9 ppm for ^{13}C in DMSO-d_6). IR spectra were recorded by using KBr pellets or neat. TOF and quadruple mass analyzer types were used for the HRMS measurements. Column chromatography was performed on silica gel (100−200 mesh) in glass columns to purify the compounds and visualized with UV light (254 nm), PMA and DNP stain. Commercially available reagents and solvents were used without further purification and were purchased. Melting points were determined using open capillary tubes and are uncorrected.

2. Synthesis of starting material (oxime acetate)



Step 1: A mixture of $NH_2OH{\cdot}HCl$ (5.5 mmol), ketone (5 mmol), and NaOAc (6 mmol) in ethanol (10 mL) was stirred at 80 °C until the full conversion of ketone as determined by TLC. The reaction was cooled to room temperature. After removing most of the solvent under reduced pressure, the reaction mixture was diluted with water and extracted three times with ethyl acetate. The combined organic layer was washed with aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated to give the crude ketoximes for direct use in the next step without further purification.

Step 2: The obtained oximes was dissolved in anhydrous dichloromethane (15 mL). After cooling to 0 °C, pyridine (7.5 mmol) was added. And then the acetyl chloride (6 mmol) was added dropwise. The mixture was stirred at room temperature until the completion of reaction. Water was added and the mixture was extracted three times with dichloromethane. The combined organic layers were washed with dilute hydrochloric acid, aqueous $NaHCO_3$, and brine. After drying with Na_2SO_4, filtering, and evaporating under reduced pressure, the residue was purified by column chromatography (ethyl acetate : petroleum ether = 1 : 10 to 1 : 6) to give the oxime acetates.

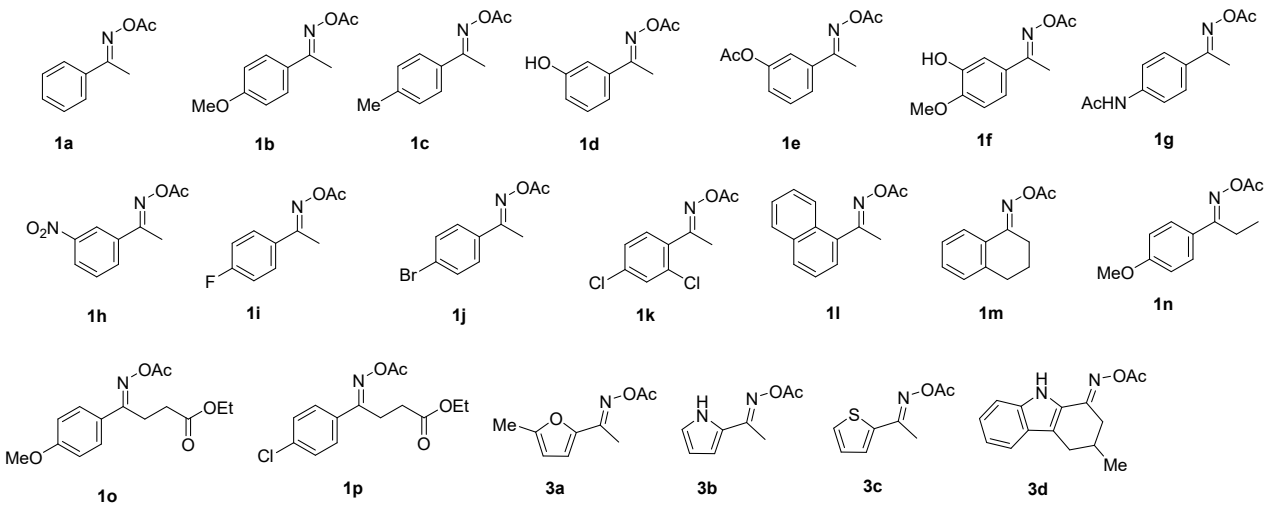


Figure 1. Starting Substrates

Oxime acetate of acetophenone (1a):[1]

White solid, 85%, mp 52-57 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (dd, J_1 = 8.1, J_2 = 1.5 Hz, 2H), 7.47 – 7.36 (m, 3H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 162.4, 134.8, 130.5, 128.5, 127.0, 19.8, 14.4.

Oxime acetate of *p*-methoxyacetophenone (1b):[2]

White solid, 85%, mp 53-55 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 3.82 (s, 3H), 2.34 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 162.0, 161.6, 128.6, 127.1, 114.0, 55.4, 20.0, 14.2.

Oxime acetate of *p*-methylacetophenone (1c):[2]

White solid, 81%, mp 104-106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 2.37 (s, 3H), 2.36 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 162.4, 140.9, 132.0, 129.3, 127.0, 21.4, 20.0, 14.4.

Oxime acetate of m-hydroxylacetophenone (1d):

White solid, 84%, mp 212-215 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.31 (s, 1H), 8.24 (s, 1H), 7.20 (d, J = 7.9 Hz, 1H), 6.92 (t, J = 7.9, 1H), 6.66 (d, J = 7.9 Hz, 1H), 2.39 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 162.0, 161.6, 160.0, 128.6, 128.4, 127.1, 114.0, 26.5, 20.6; HRMS (ESI-qTOF) Calcd for $C_{10}H_{11}NO_3$ $[M+H]^+$, 194.0739, Found 194.0883.

Oxime acetate of meta-o-acetylacetophenone (1e):

White solid, 84%, mp 156-161 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.20 (d, J = 7.9 Hz, 1H), 6.98 (t, J = 7.9, 1H), 6.65 (d, J = 7.9 Hz, 1H), 2.39 (s, 3H), 2.35 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.2, 169.1, 162.0, 161.6, 160.0, 128.6, 128.4, 127.1, 114.0, 26.8, 26.5, 20.6; HRMS (ESI-qTOF) Calcd for $C_{12}H_{13}NO_4$ $[M+H]^+$, 236.0845, Found 236.0932.

Oxime acetate of 3-hydroxyl-4-methoxy-acetophenone (1f):

White solid, 84%, mp 171-174 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.21 (s, 1H), 8.31 (s, 1H), 7.20 (d, J = 7.9 Hz, 1H), 6.98 (t, J = 7.9, 1H), 3.25 (s, 3H), 2.35 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 162.0, 161.6, 160.0, 128.6, 128.4, 127.1, 114.0, 29.8, 26.5, 20.6; HRMS (ESI-qTOF) Calcd for $C_{11}H_{13}NO_4$ $[M+H]^+$, 224.0845, Found 224.0743.

Oxime acetate of 4-*N*-acetyl-acetophenone (1g):[2]

Yellow solid, 84%, mp 212-215 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.22 (s, 1H), 7.76 (d, J = 9.0 Hz, 2H), 7.71 (d, J = 9.1 Hz, 2H), 2.36 (s, 3H), 2.25 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 168.5, 161.8, 141.6, 128.7, 127.6, 118.6, 24.1, 19.7, 13.7.

Oxime acetate of 4-fluoro-acetophenone (1i):[2]

White solid, 82%, mp decomposed ≥ 143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, J_1 = 8.8 Hz, J_2 = 5.4 Hz, 2H), 7.16 - 7.11 (m, 2H), 2.60 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.8, 167.0, 164.5, 161.4, 131.0, 130.9, 129.1, 129.0, 115.7, 115.5, 26.5, 20.6.

Oxime acetate of 4-bromo-acetophenone (1j):[4a,b]

Yellow solid, 84%, mp 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J_1 = 8.8 Hz, J_2 = 5.4 Hz, 2H), 7.3 (d, J_1 = 8.8 Hz , J_2 =5.4 Hz, 2H), 2.60 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.8, 164.5, 161.4, 131.9, 131.9, 129.1, 119.5, 119.5, 26.5, 20.6.

Oxime acetate of 2,4-dichloro-acetophenone (1k):[2]

White solid, 89%, mp 212-215 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51–7.43 (m, 1H), 7.28 (d, J = 8 Hz, 1H), 7.26 (d, J = 8 Hz, 1H), 2.27 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.1, 161.2, 135.3, 135.1, 133.4, 130.9, 129.9, 127.2, 26.5, 20.6.

Oxime acetate of α-tetralone(1m):[5]

Thick liquid, 82%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 7.9 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 7.26 – 7.16 (m, 2H), 2.87 (t, J = 6.6 Hz, 2H), 2.81 (t, J = 6.6 Hz, 2H), 2.26 (s, 3H), 1.93 - 1.81 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.2, 161.3, 140.9, 130.7, 128.9, 128.7, 126.5, 125.5, 29.5, 25.5, 21.3, 19.8.

Oxime acetate of 4-methoxy-propinophenone (1n):[6]

Yellow thick liquid, 82%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.9 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H), 2.83 (q, J = 7.7 Hz, 2H), 2.26 (s, 3H), 1.18 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.3, 166.7, 161.5, 128.7, 128.7, 125.9, 114.0, 55.3, 21.4, 19.9, 11.4.

Oxime acetate of 4-chloro-phenyl-oxo-butyric ester (1p):

Thick liquid, 81%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 6.8 Hz, 2H), 7.39 (d, J = 6.7 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.18 - 3.10 (m, 2H), 2.60 - 2.51 (m, 2H), 2.27 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.6, 168.3, 163.5, 137.0, 131.8, 129.0, 128.6, 60.9, 30.9, 23.4, 19.7, 14.1; HRMS (ESI-qTOF) Calcd for $C_{14}H_{16}ClNO_4$ [M+H]+, 298.0768, Found 298.0891.

Oxime acetate of 5-methyl-2-furanone (3a):[7]

Thick liquid, 76%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.79 (d, J = 3.4 Hz, 1H), 6.09 (dd, J = 3.4, 0.9 Hz, 1H), 2.36 (s, 3H), 2.26 (s, 3H), 2.24 (s, 3H); 13C NMR (101 MHz, $CDCl_3$): δ 168.4, 155.8, 153.8, 146.4, 115.1, 108.0, 19.6, 13.9, 12.9.

Oxime acetate of 2-pyrralone (3b):[8]

White solid, 78%, mp 46-55 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (s, 1H), 6.90 (dt, J_1 = 4.1 Hz, J_2 = 2.0 Hz, 1H), 6.62 – 6.60 (m, 1H), 6.24 (dd, J_1 = 6.2 Hz, J_2 = 2.6 Hz, 1H), 2.28 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.7, 154.8, 125.9, 122.2, 113.5, 109.6, 19.7, 12.8.

Oxime acetate of 2-thionone (3c):

White solid, 80%, mp 128-131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (ddd, J_1 = 6.0 Hz, J_2 = 4.4 Hz, J_3 = 1.0 Hz, 2H), 7.07 (dd, J_1 = 5.1 Hz, J_2 = 3.8 Hz, 1H), 2.40 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.7, 157.7, 137.9, 129.2, 129.1, 127.2, 19.4, 14.1.

3. Representative procedure for the synthesis of 2-aminothiazole (2a-p):

In a 50 mL round bottom flask, oxime acetate (50 mg, 0.28 mmol), copper iodide (26.8 mg, 50 mol%, 0.14 mmol) and potassium persulphate (114.5 mg, 0.42 mmol) was charged with sodium thiocyanate (27.5 mg, 0.33 mmol) in 1,4-dioxane (20 mL). The reaction mixture was allowed to stir at preheated 110 ^{o}C for 3-4 h. The progress of the reaction was checked by TLC. After completion, reaction mixture was immediate filtered in hot condition otherwise impurities are developed in the reaction. Concentrated the reaction mixture under vaccume and purified by column chromatography using eluent (5% to 15% ethyl acetate in pet ether with 0.5 ml TEA) to afforded 2-aminothiazole **(2a-p)**.

4-Phenyl-2-aminothiazole (2a):[9]

White solid; 32 mg; Yield 64%; mp: 148-151 ^{o}C; R_f: 0.5 (8:2:: EA:Pet ether); IR (ν cm^{-1}): 3382 (w), 1610 (s), 1532 (s), 1489 (s), 1040 (s), 837 (s), 730 (s); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, J = 7.6 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.29 (t, J = 7.3 Hz, 1H), 6.72 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.2, 151.3, 134.6, 128.6, 127.7, 126.0, 102.8; HRMS (ESI-qTOF) Calcd for $C_9H_8N_2S$ $[M+H]^+$, 177.0408, Found 177.0818.

4-(4`-Methoxy-phenyl)-2-aminothiazole (2b): [9]

White solid; 32 mg; Yield 64%; mp: 198-201 ^{o}C; R_f: 0.3 (9:1:: EA:Pet ether); IR (ν cm^{-1}): 3438 (w), 3272 (w), 3116 (w), 1625 (s), 1607 (s), 1535 (s), 1492 (s), 1034 (s), 834 (s), 736 (s); ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.71 (d, J = 6.9 Hz, 2H), 7.28 (bs, 2H), 6.94 (d, J = 6.8 Hz, 2H), 6.86 (s, 1H), 3.77 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6): δ 168.8, 159.2, 129.9, 129.9. 127.3, 114.3, 114.3, 114.0, 99.9, 55.5; HRMS (ESI-qTOF) Calcd for $C_{10}H_{10}N_2OS$ $[M+H]^+$, 207.0514, Found 207.0215.

4-(4`-Methyl-phenyl)-2-aminothiazole (2c): [9]

White solid; 32 mg; Yield 64%; mp: 122-125 ^{o}C; R_f : 0.4 (8:2:: EA:Pet ether); IR (ν cm^{-1}): 3451(w), 3296 (w), 3118 (w), 1626 (s), 1536 (s), 1490 (s), 1035 (s), 820 (s), 727 (s); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.67 (d, J = 8.1 Hz, 2H), 7.29 (bs, 2H), 7.18 (d, J = 8.1 Hz, 2H), 6.95 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, DMSO- d_6): δ 168.8, 137.1, 129.5, 129.5, 129.2, 128.5, 125.9, 125.9, 101.2, 21.2; HRMS (ESI-qTOF) Calcd for $C_{10}H_{10}N_2S$ $[M+H]^+$, 191.0565, Found 191.0758.

4-(3`-Hydroxyl-phenyl)-2-aminothiazole (2d): [10]

Brown semi solid; 33 mg; Yield 66%; R_f : 0.1 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 3439 (w), 1661 (w), 1051 (s), 1023 (s), 1003 (s), 821 (s), 758 (s); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.39 (s, 1H), 7.22 - 7.12 (m, 3H), 6.99 (s, 2H), 6.89 (s, 1H), 6.66 (d, J = 7.9 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 168.4, 157.8, 150.4, 136.6, 129.8, 116.8, 114.7, 113.0, 101.8; HRMS (ESI-qTOF) Calcd for $C_9H_8N_2OS$ $[M+H]^+$, 193.0357, Found 193.0923.

4-(3`-*O*-Acetyl-phenyl)-2-aminothiazole (2e):

Yellow solid; 34 mg; Yield 68%; mp: 115-118 ^{o}C; R_f : 0.3 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 3380 (w), 3314 (w), 1700 (s), 1531 (s), 1488 (s), 1041 (s), 829 (s), 741 (s); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.68 (d, J = 7.5 Hz, 1H), 7.51 (s, 1H), 7.39 (t, J = 7.9 Hz, 1H), 7.07 (s, 3H), 7.00 (d, J = 7.8 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 169.6, 168.6, 151.1, 149.2, 136.8, 129.7, 123.4, 120.8, 119.2, 103.0, 21.3; HRMS (ESI-qTOF) Calcd for $C_{11}H_{10}N_2O_2S$ $[M+H]^+$, 235.0463, Found 235.0536.

4-(3`-Hydroxyl-4-methoxy-phenyl)-2-aminothiazole (2f):

Yellow thick liquid; 31 mg; Yield 62%; R_f : 0.5 (8:2:: EA:Pet ether); IR (ν cm^{-1}): 3414 (w), 1659 (w), 1048 (s), 1023 (s), 999 (s), 823 (w), 760 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.00 (s, 1H), 7.33 (d, J = 1.9 Hz, 1H), 7.21 (dd, J = 8.2, 1.9 Hz, 1H), 6.98 (s, 2H), 6.78 (s, 1H), 6.75 (d, J

= 8.2 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 168.3, 150.5, 147.8, 146.4, 127.3, 118.7, 115.7, 110.2, 99.2, 56.0; HRMS (ESI-qTOF) Calcd for $C_{10}H_{10}N_2O_2S$ $[M+H]^+$, 223.0463, Found 223.0761.

4-(4`-*N*-Acetyl-phenyl)-2-aminothiazole (2g):

Brown thick liquid; 33 mg; Yield 66%; R_f : 0.3 (5:5:: EA:Pet ether); IR (ν cm^{-1}): 3439 (w), 1662 (w), 1051 (s), 1023 (s), 1003 (s), 821 (w), 758 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.98 (s, 1H), 7.70 (d, J = 7.8 Hz, 2H), 7.57 (d, J = 7.9 Hz, 2H), 7.00 (s, 2H), 6.87 (s, 1H), 1.99 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 168.7, 168.4, 150.1, 138.8, 130.3, 126.3, 126.3, 119.2, 119.2, 100.4, 21.7; HRMS (ESI-qTOF) Calcd for $C_{11}H_{11}N_3OS$ $[M+H]^+$, 234.0623, Found 234.0231.

4-(3`-Nitro-phenyl)-2-aminothiazole (2h): [9]

Yellow solid; 27 mg; Yield 54%; mp: 189-191 ^{o}C; R_f : 0.4 (6:4:: EA:Pet ether); IR (ν cm^{-1}): 3388 (w), 3314 (w), 1580 (s), 1550 (s), 1600 (s), 1450 (s), 1043 (s), 837 (s), 739 (s); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.63 (t, J = 2.0 Hz, 1H), 8.26 (t, J = 1.0 Hz, 1H), 8.24 (t, J = 1.0 Hz, 1H), 8.11 (dd, J_1 = 8.2 Hz, J_2 =2.4 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 7.34 (s, 1H), 7.24 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 169.0, 148.6, 147.8, 136.8, 131.8, 130.5, 122.1, 120.5, 104.7; HRMS (ESI-qTOF) Calcd for $C_9H_7N_3O_2S$ $[M+H]^+$, 222.0259, Found 222.0332.

4-(4`-Flouro-phenyl)-2-aminothiazole (2i): [9]

Yellow solid; 35 mg; Yield 70%; mp: 111-115 ^{o}C; R_f : 0.1 (9:1:: EA:Pet ether); IR (ν cm^{-1}): 3470 (w), 3305 (w), 3125 (w), 1639 (s), 1532 (s), 1487 (s), 1037 (s), 832 (s), 728 (s); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.86 - 7.80 (m, 2H), 7.19 (t, J = 8.9 Hz, 2H), 7.08 (s, 2H), 6.98 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 168.7, 163.0, 160.6, 149.3, 131.7, 127.9, 115.8; HRMS (ESI-qTOF) Calcd for $C_9H_7FN_2S$ $[M+H]^+$, 195.0314, Found 195.0582.

4-(4`-Bromo-phenyl)-2-aminothiazole (2j): [9]

White solid; 36 mg; Yield 72%; mp: 180-182 °C; R_f : 0.5 (8:2:: EA:Pet ether); IR (ν cm^{-1}): 3427 (w), 3280 (w), 3109 (w), 1632 (s), 1532 (s), 1104 (s), 1067 (s), 1035(s), 907 (s), 725 (w), 694 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.74 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.08 (m, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 173.5, 153.8, 139.3, 136.5, 132.7, 125.3, 107.6; HRMS (ESI-qTOF) Calcd for $C_9H_7BrN_2S$ [M+2], 255.9513, Found 255.9689.

4-(2`,4`-Dichloro-phenyl)-2-aminothiazole (2k):[11]

White solid; 31 mg; Yield 62%; mp: 190-194 °C; R_f : 0.1 (9.5:0.5:: EA:Pet ether); IR (ν cm^{-1}): 3394 (w), 1655 (w), 1047 (s), 1023 (s), 994 (s), 824 (w), 761 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.88 (d, J = 8.5 Hz, 1H), 7.64 (d, J = 2.0 Hz, 1H), 7.46 (dd, J = 8.5, 2.2 Hz, 1H), 7.11 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 167.7, 145.6, 132.8, 132.7, 132.4, 131.7, 130.1, 127.8, 107.4; HRMS (ESI-qTOF) Calcd for $C_9H_6Cl_2N_2S$ $[M+H]^+$, 244.9629, Found 243.9891.

4-(4`-Naphathyl)-2-aminothiazole (2l):[12]

White solid; 36 mg; Yield 72%; mp: 160-164 °C; R_f : 0.55 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 3387 (w), 3030 (w), 1606 (s), 1540 (s), 1490 (s), 1041 (s), 830 (s), 730 (s); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.61 - 9.57 (m, 1H), 9.15 - 9.10 (m, 2H), 8.89 (dd, J_1 = 7.1 Hz, J_2 = 1.2 Hz, 1H), 8.77 - 8.72 (m, 3H), 7.89 (s, 1H), 6.68 (bs, 2H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 162.6, 146.0, 129.1, 128.4, 126.7, 123.8, 123.5, 122.3, 121.4, 121.3, 121.1, 120.5, 101.3; HRMS (ESI-qTOF) Calcd for $C_{13}H_{10}N_2S$ $[M+H]^+$, 227.0565, Found 227.0637.

4,5-Dihydronaphtho[1,2-d]thiazol-2-amine (2m):[13]

Brown semi-solid; 25 mg; Yield 57%; R_f : 0.1 (8:2:: EA:Pet ether); IR (ν cm^{-1}): 3439 (w), 3263 (w), 1599 (w), 1529 (s), 1339 (s), 1062 (s), 763 (s), 739 (s), ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.52 (d, J = 7.5 Hz, 1H), 7.22 – 7.16 (m, 2H), 7.11 (td, J_1 = 7.5 Hz, J_1 = 1.2 Hz, 1H), 6.95 (s, 2H), 2.93 (t, J = 7.9 Hz, 2H), 2.76 (t, J = 7.9 Hz, 2H); ^{13}C NMR (126 MHz, DMSO-d_6): δ 167.0,

144.7, 134.7, 132.1, 128.1, 127.0, 126.6, 122.6, 118.0, 28.5, 20.7; HRMS (ESI-qTOF) Calcd for $C_{11}H_{10}N_2S$ $[M+H]^+$, 203.0565, Found 203.0637.

4-(4`-Methoxy-phenyl)-5-methyl-2-aminothiazole (2n): *[14]*

Yellow semi-solid; 32 mg; Yield 64%; R_f : 0.2 (8:2:: EA:Pet ether); IR (ν cm-1): 3490 (w), 3030 (w), 1635 (w), 1253 (w), 1032 (w), 782 (w); ^{1}H NMR (400 MHz, DMSO-d6): δ 7.38 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 6.54 (s, 2H), 3.72 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, DMSO): δ 165.5, 158.5, 144.1, 129.7, 127.3, 114.6, 114.1, 55.4, 12.1; HRMS (ESI-qTOF) Calcd for $C_{11}H_{12}N_2OS$ $[M+H]^+$, 221.0670, Found 221.0981.

4-(4`-Methoxy-phenyl)- 5-ethylacetate-2-aminothiazole (2o):

Brown semi-solid; 33 mg; Yield 66%; R_f : 0.5 (5:5:: EA:Pet ether); IR (ν cm^{-1}): 2993 (w), 1732 (m), 1611 (w), 1247 (w), 1027 (w), 742 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.45 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 6.92 (s, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.68 (s, 2H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 171.0, 166.4, 159.0, 147.7, 129.7, 129.7, 127.9, 114.1, 114.1, 110.4, 61.1, 55.5, 32.9, 14.4; HRMS (ESI-qTOF) Calcd for $C_{14}H_{16}N_2O_3S$ $[M+H]^+$, 293.0882, Found 293.0954.

4-(4`-Chloro-phenyl)- 5-ethylacetate-2-aminothiazole (2p):

Yellow solid; 35 mg; Yield 70%; mp: 160-164 ^{o}C; R_f : 0.2 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 2993 (w), 1732 (m), 1611 (w), 1250 (w), 1089 (w), 767 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.57 (d, J = 6.8 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 7.02 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.75 (s, 2H), 1.22 (t, J = 7.1 Hz, 3H);^{13}C NMR (101 MHz, DMSO-d_6): δ 175.5, 171.4, 151.3, 138.9, 137.0, 134.9, 134.9, 133.5, 133.5, 117.2, 65.9, 37.5, 19.2; HRMS (ESI-qTOF) Calcd for $C_{13}H_{13}ClN_2O_2S$ $[M+H]^+$, 297.0386, Found 297.0459.

4-(2`-Methyl-furan)-2-aminothiazole (4a):

Yellow thick liquid; 31 mg; Yield 62%; R_f : 0.6 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 2990 (w), 1620 (w), 1250 (w), 1030 (w), 731 (w); ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.08 (s, 2H), 6.60 (s, 1H), 6.39 (d, J = 3.1 Hz, 1H), 6.12 (d, J = 3.1 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6): δ 168.9, 151.3, 149.5, 142.3, 107.9, 107.2, 99.7, 14.1; HRMS (ESI-qTOF) Calcd for $C_8H_8N_2OS$ $[M+H]^+$, 181.0357, Found 181.0218.

4-Pyrrole-2-aminothiazole (4b):

White solid; 32 mg; Yield 64%; mp: 155-161 ^{o}C**;** R_f : 0.4 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 2999 (w), 1600 (w), 1212 (w), 1034 (w), 679 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.95 (s, 1H), 6.90 (s, 2H), 6.70 (dd, J = 4.2, 2.6 Hz, 1H), 6.52 (s, 1H), 6.30-6.27 (m, 1H), 6.01 (dd, J = 5.8, 2.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.2, 149.5, 133.3, 123.3, 113.4, 110.9, 101.2; HRMS (ESI-qTOF) Calcd for $C_7H_7N_3S$ $[M+H]^+$, 166.0361, Found 166.0433.

4-Thiophene-2-aminothiazole (4c):*[12]*

Yellow liquid; 32 mg; Yield 64%; R_f : 0.4 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 2999 (w), 1612(w), 1257 (w), 1030 (w), 756 (w); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.41-7.36 (m, 2H), 7.13 (s, 2H), 7.04 (dd, J_1 = 5.0 Hz, J_2 = 3.6 Hz, 1H), 6.84 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 168.7, 144.8, 139.5, 128.2, 125.0, 123.1, 100.2; HRMS (ESI-qTOF) Calcd for $C_7H_6N_2S_2$ $[M+H]^+$, 182.9972, Found 182.8135.

4-Methyl-10*H*-thiazolo[4,5-a]carbazol-2-amine (4d):

White solid; 32 mg; Yield 65%; mp: 180-186 ^{o}C R_f : 0.2 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 3400 (s), 3032 (w), 1612(s), 1224 (s), 1032 (s), 678 (s); ^{1}H NMR (500 MHz, DMSO- d_6): δ 11.34 (s, 1H), 8.02 (d, J = 7.7 Hz, 1H), 7.62 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.43 (s, 2H), 7.32 (t, J = 7.3 Hz, 1H), 7.11 (t, J = 7.3 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (126 MHz, DMSO- d_6): δ 166.5, 140.0,

137.2, 129.7, 128.0, 125.0, 123.3, 121.3, 120.9, 120.0, 118.8, 113.5, 111.7, 21.3; HRMS (ESI-qTOF) Calcd for $C_{14}H_{11}N_3S$ $[M+H]^+$, 254.0674, Found 254.0992.

4. Representative procedure for the synthesis of substrate 7 (Sandmeyer reaction):

In 50 mL round bottom flask, $CuBr_2$ (0.278 g, 1.25 mmol) was added in acetonitrile (12 mL). Cool the reaction mixture at 0 ℃. Then, t-butyronitrile (0.148 mL, 1.48 mmol) was added at 0 ℃ and allowed to stir for 10 min. Thereafter, substrate **2q** (0.200 g, 1.13 mmol) was dissolve in acetonitrile (2 mL) and added to reaction mixture at 0 ℃ in portionwise (do not remove ice cold condition). The progress of the reaction was checked by TLC after 2h. Pour the reaction mixture into crushed ice and keep at 5 ℃ for 12 h. The solid product was separated and purified by column chromatography (1% to 3% Ethyl acetate in per-ether) to afforded product **7**.

4-(4`-Chloro-phenyl)- 5-ethylacetate-2-bromothiazole (7):

Yellow thick liquid; 194 mg; Yield 71%; R_f : 0.8 (7:3:: EA:Pet ether); IR (ν cm^{-1}): 3030 (w), 2991(w), 1710 (s), 1600(s), 1580 (s), 1224 (s), 1032 (s), 678 (s); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.60 (d, J = 8.6 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 4.17 - 4.05 (m, 4H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 170.0, 151.1, 135.0, 133.6, 132.3, 130.5, 130.5, 130.3, 129.1, 129.1, 61.7, 32.5, 14.5; HRMS (ESI-qTOF) Calcd for $C_{13}H_{11}BrClNO_2S$ $[M+2]^+$, 360.9382, Found 360.9430.

5. Representative procedure for the synthesis of substrate 8 (Sukuzi coupling):

The substrate **7** (0.050 g, 0.28 mmol), phenyl boronic acid (0.052g, 0.42 mmol), $Pd_2(dba)_3$ (10 mol%), X-Phos (20 mol%) and sodium carbonate (0.060 g, 0.56 mmol) was added in acetonitrile:water (5 ml). The reaction mixture was degased under argon atmosphere. Allow to stir the reaction mixture for 24 h at 80 ℃. The process of the reaction was checked by TLC.

Concentrated under vacuum and purified by column chromatography (2% Ethyl acetate in per-ether) to afforded product **8**.

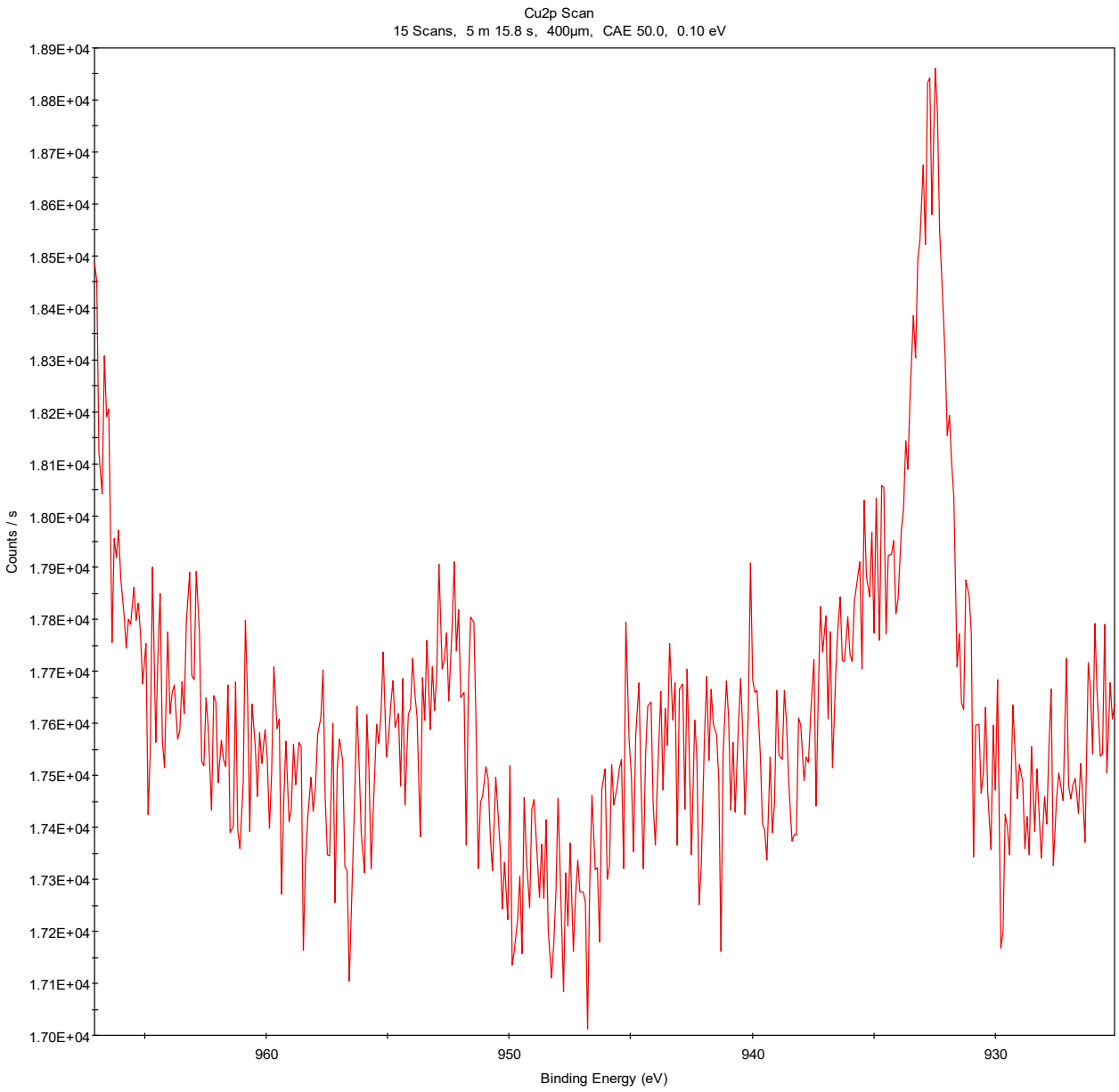
4-(4`-Chloro-phenyl)- 5-ethylacetate-2-phenylthiazole (8):

White solid; 41 mg; Yield 62%; R_f : 0.7 (9:1:: EA:Pet ether); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (dd, J = 16.3, 8.6 Hz, 1H), 7.79 – 7.69 (m, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.49 - 7.39 (m, 5H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.95 (d, *J* = 4.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.0, 166.2, 152.8, 130.2, 130.1, 129.3, 128.9, 128.9, 128.8, 128.8, 128.7, 128.4, 127.2, 127.1, 126.4, 126.4, 61.6, 33.2, 14.1; HRMS (ESI-qTOF) Calcd for $C_{19}H_{16}ClNO_2S$ $[M+H]^+$, 358.0590, Found 358.0666.

6. Mechanism investigation

6 .1 XPS study

In a 50 mL round bottom flask, oxime acetate (50 mg, 0.028 mmol), copper iodide (26.8 mg, 0.014 mmol) and potassium persulphate (114.5 mg, 0.042 mmol) was charged with sodium thiocyanate (27.5 mg, 0.033 mmol) in 1,4-dioxane (20 mL). The reaction mixture was allowed to stir at preheated 110 ℃ for 3-4 h. The progress of the reaction was checked by TLC. After completion, reaction mixture was immediate filtered in hot condition. The obtained residue was used for XPS study. The X-ray photoelectron spectroscopy (XPS) analysis indicates that the oxidation state of Cu is +1.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1.88E+04
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1.85E+04
1.84E+04
1.83E+04
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1.81E+04
1.80E+04
1.79E+04
1.78E+04
1.77E+04
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1.75E+04
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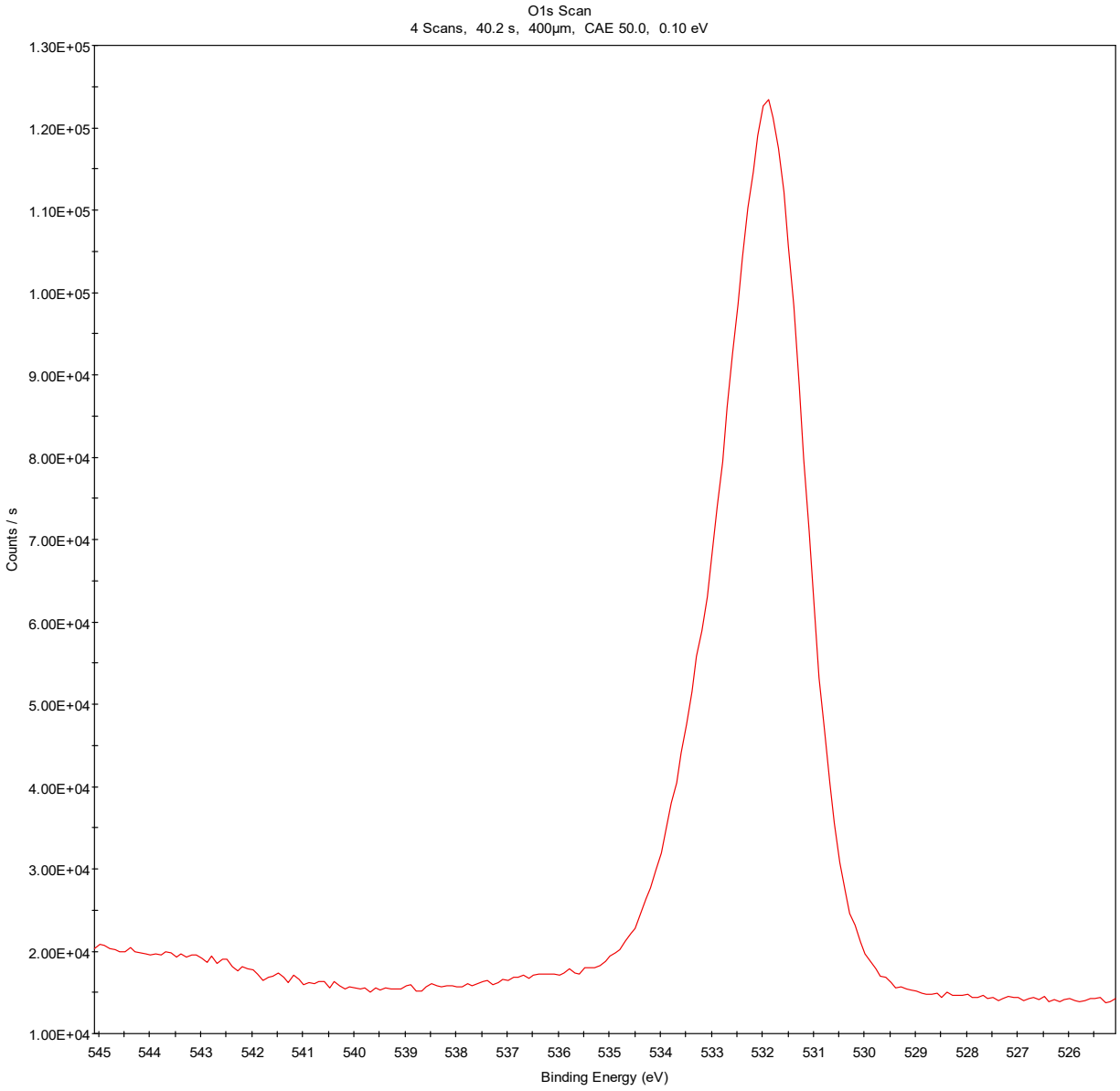
1.70E+04
960
950
940
930
Binding Energy (eV)


O1s Scan
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1.10E+05
1.00E+05
9.00E+04
8.00E+04
7.00E+04
6.00E+04
5.00E+04
4.00E+04
3.00E+04
2.00E+04
1.00E+04
Counts / s
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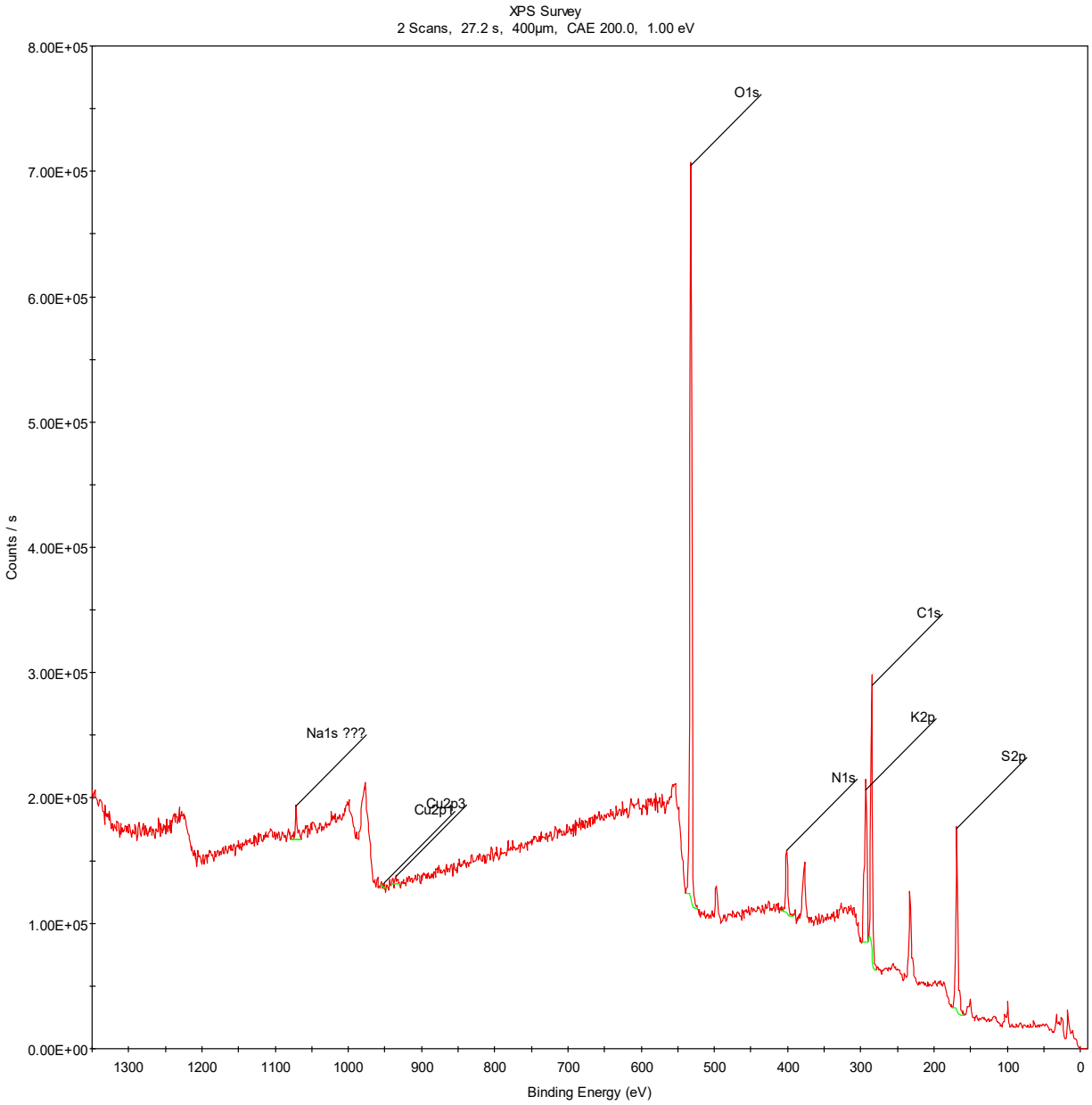
Binding Energy (eV)


XPS Survey
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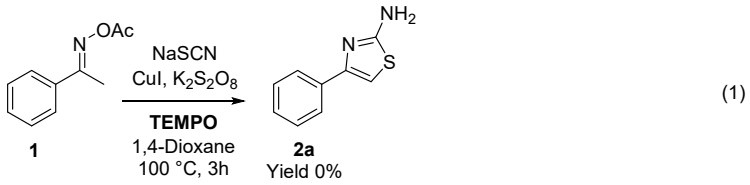
4.00E+05
3.00E+05
2.00E+05
1.00E+05
0.00E+00
Counts / s
O1s
C1s
K2p
S2p
N1s
Na1s ???
Cu2p3
Cu2p1
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Binding Energy (eV)

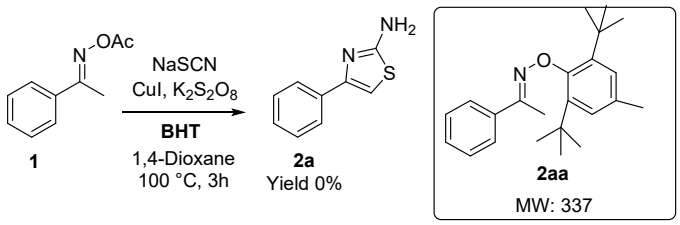
6.2 Trapping experiment with TEMPO and BHT free radical

Two experiments were designed to rationalize the free reaction pathway. The radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and BHT was added to the standard conditions. No desired product **2a** was obtained; instead, **2aa** was detected in GCMS.

HRMS (ESI) m/z [M + 1]+ calcd for $C_{23}H_{31}NO$: 337.2406; found: 337.0659.



(1)



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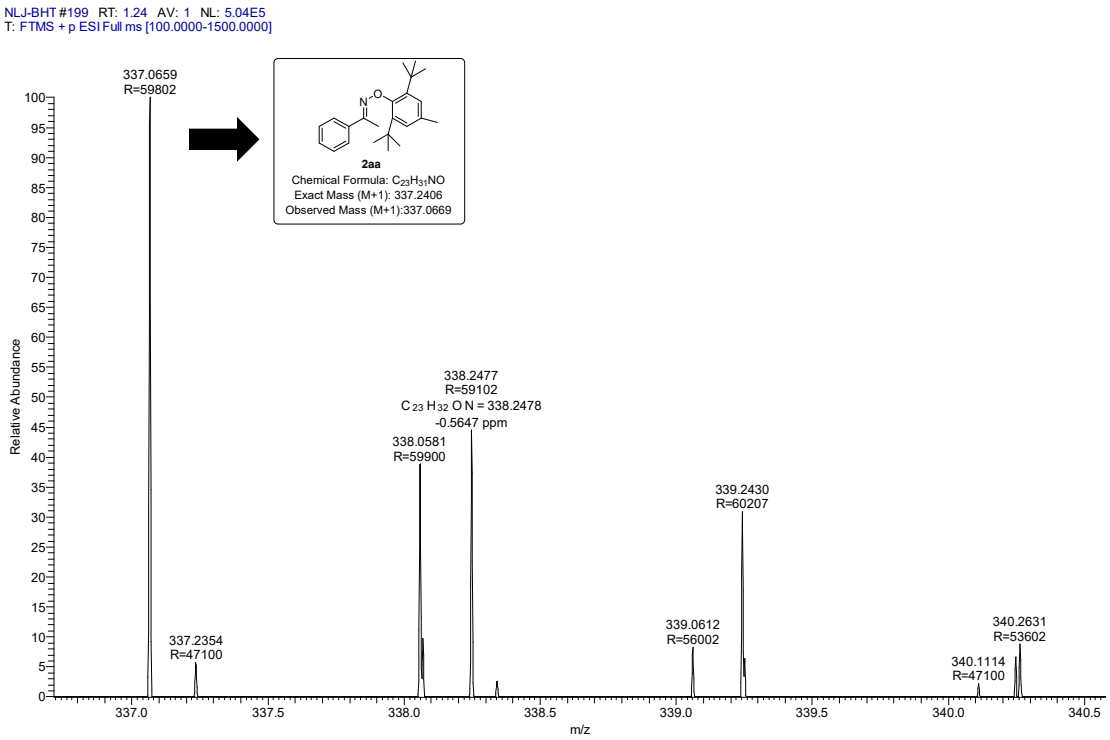

Figure 2. HRMS

6.3 Cyclic voltammetry studies

Substrate redox potentials were determined using CV with the following method in figure 1. S5Cyclic voltammetry was conducted on an Autolab PGSTAT100 (Metrohm) using a 3-electrode cell configuration. A glassy carbon working electrode was employed alongside a platinum flag counter electrode and a silver pseudo-reference electrode. These values were converted to a saturated calomel electrode (SCE) scale. 5 mM oxime solutions were freshly prepared in acetonitrile along with 0.1M supporting electrolyte (tetrabutylammonium tetrafluoroborate). Nitrogen was passed through the sample between measurements to avoid the deleterious influence of oxygen reduction, either directly or through indirect reaction with the oxime-derived species. Samples were examined at 4 different scan rates 0.05 Vs -1 – 2.00 Vs -1.

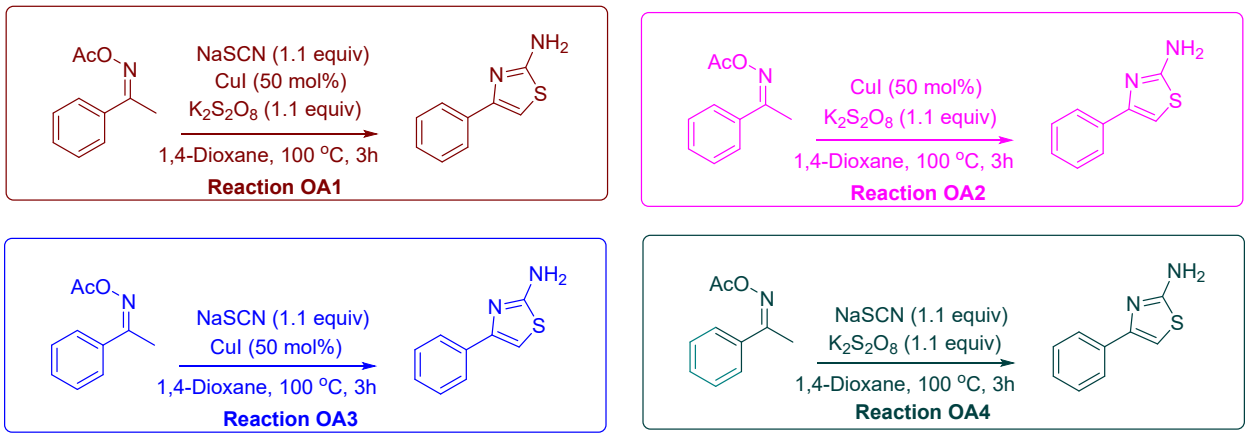

Fig 3. Different conditions used for cyclic voltammetry study

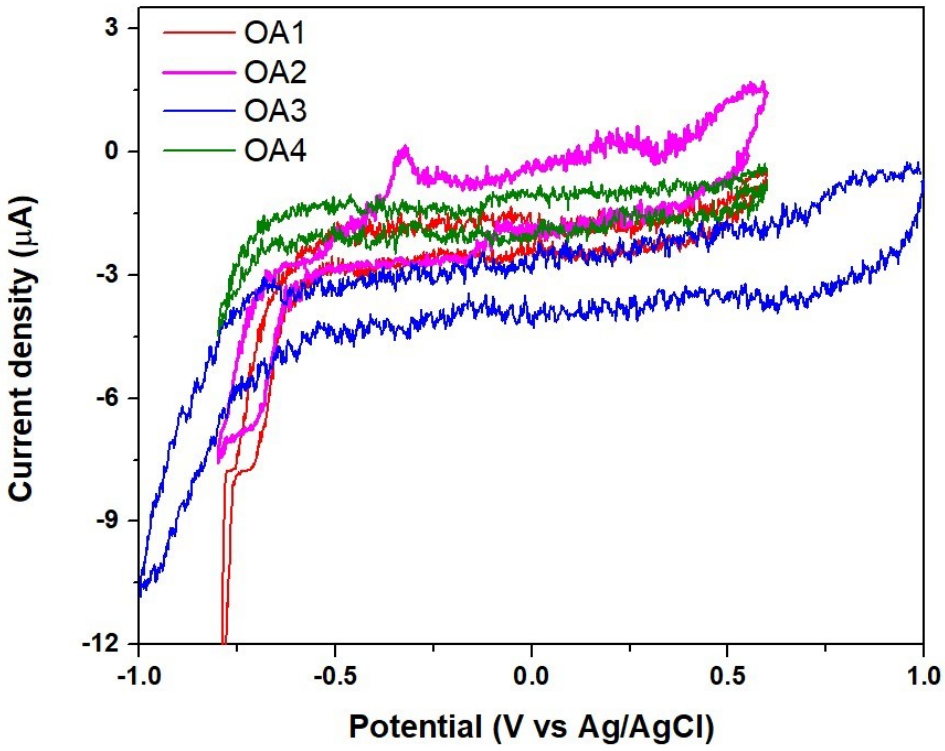

Fig 4. Cyclic voltragrams of reactants and their mixtures in a 0.1M supporting electrolyte (tetrabutylammonium tetrafluoroborate).solution in ACN scan rate 0.1 V/s starting potential 0.5 V glass carbon (6mm diameter working electrode). Platinum plate (counter electrode). Ag/ AgCl (saturated KCl, reference electrode).

7. References

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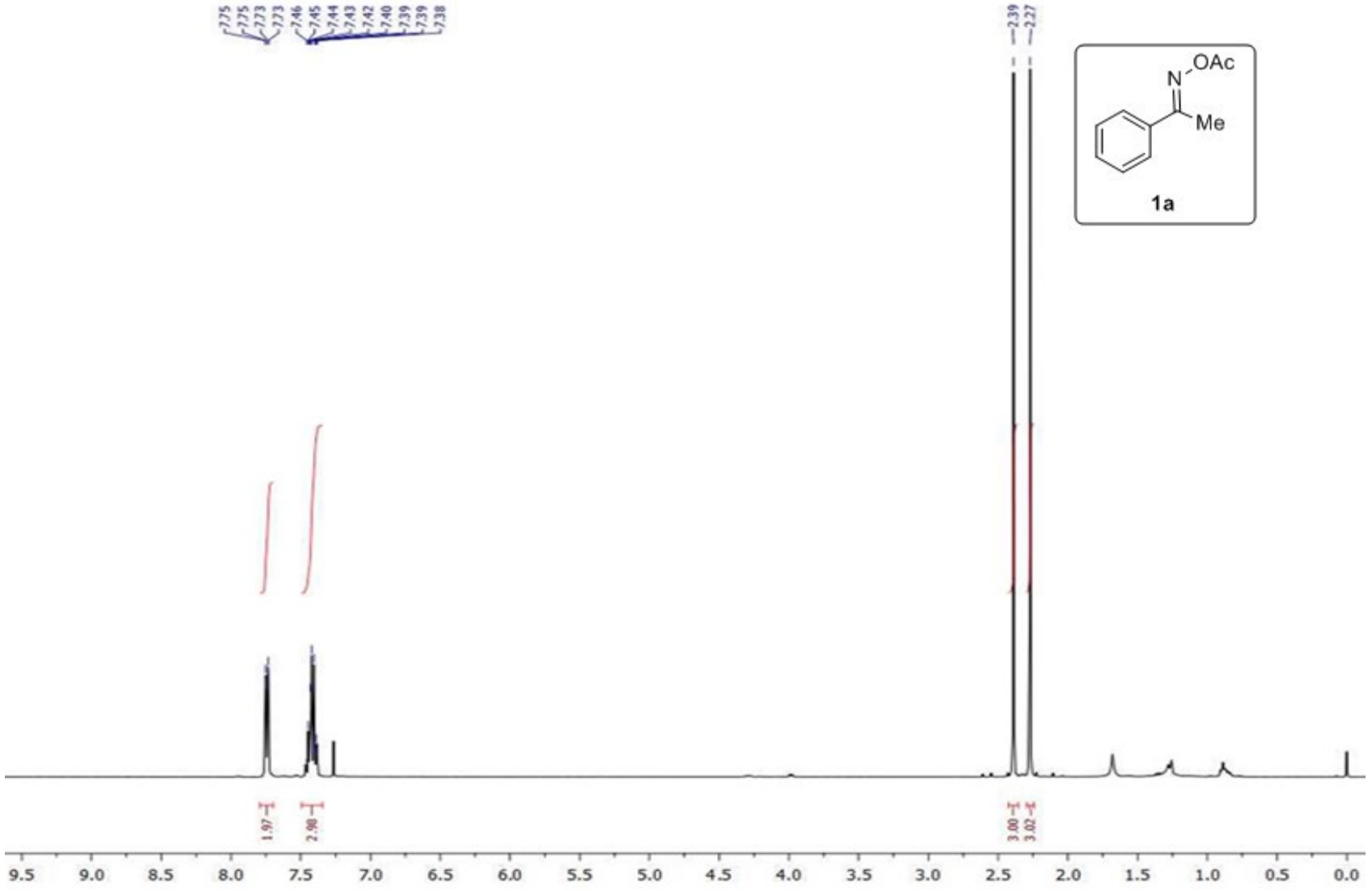
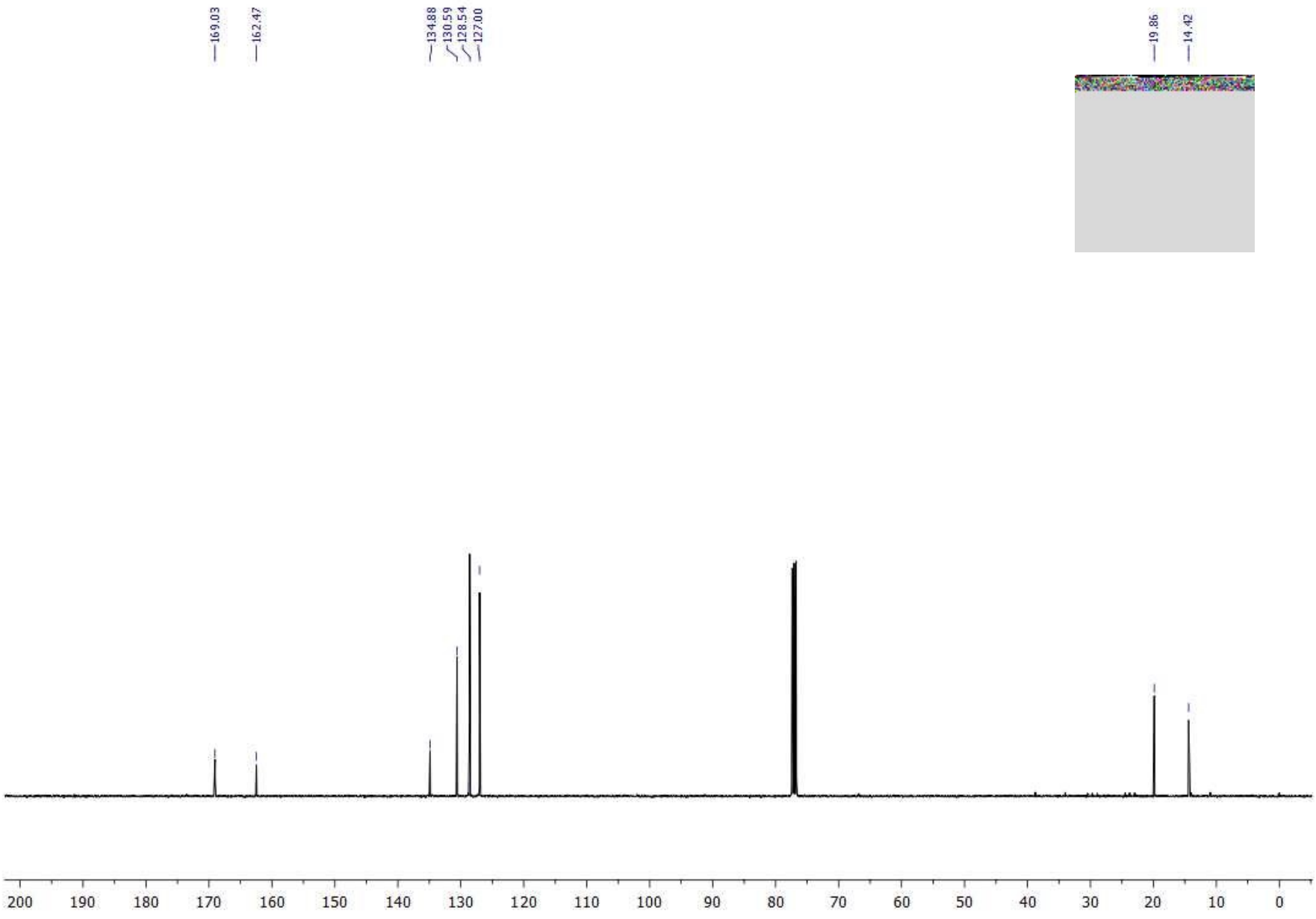
8. ^{1}H and ^{13}C spectrum of starting substrates

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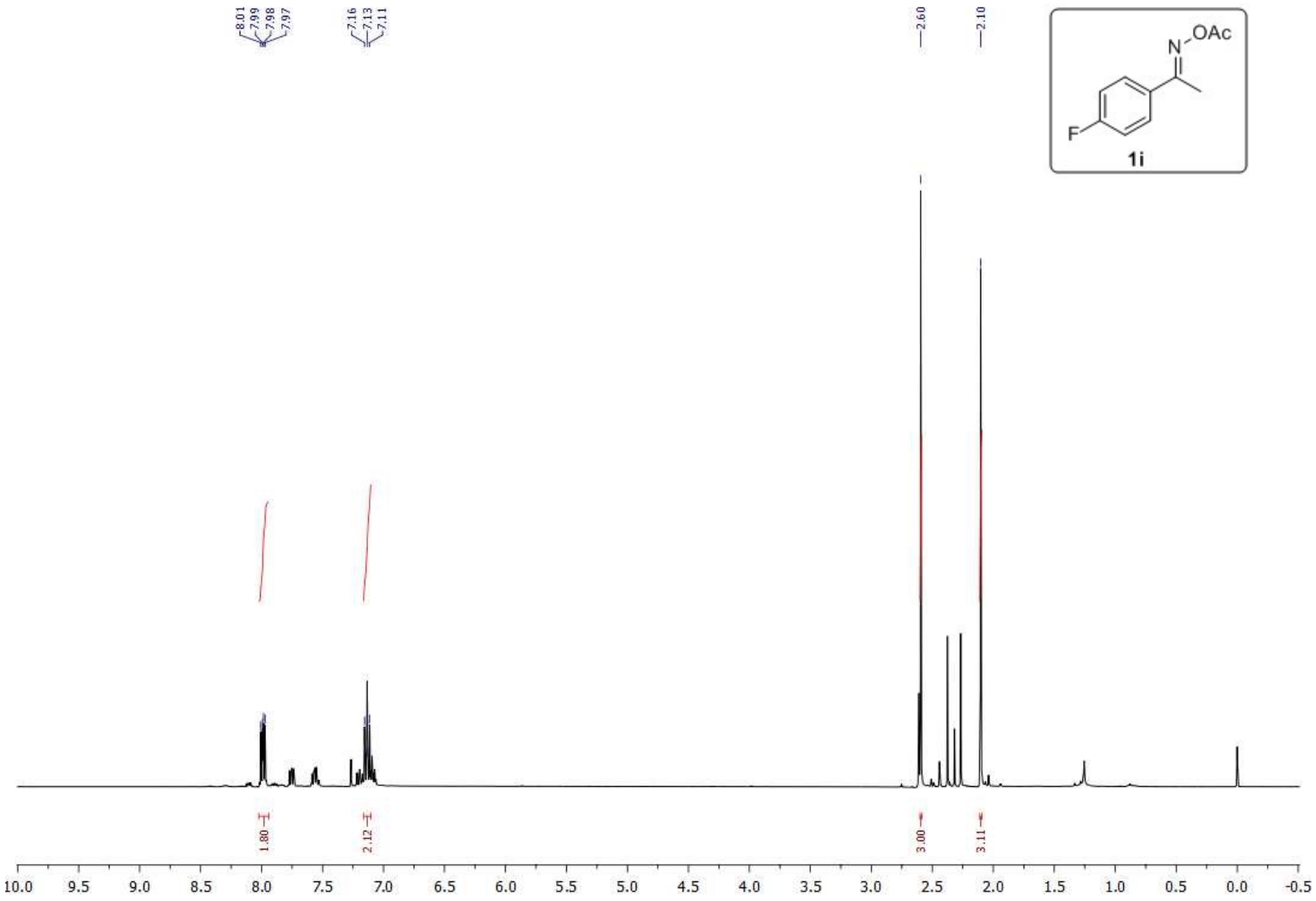
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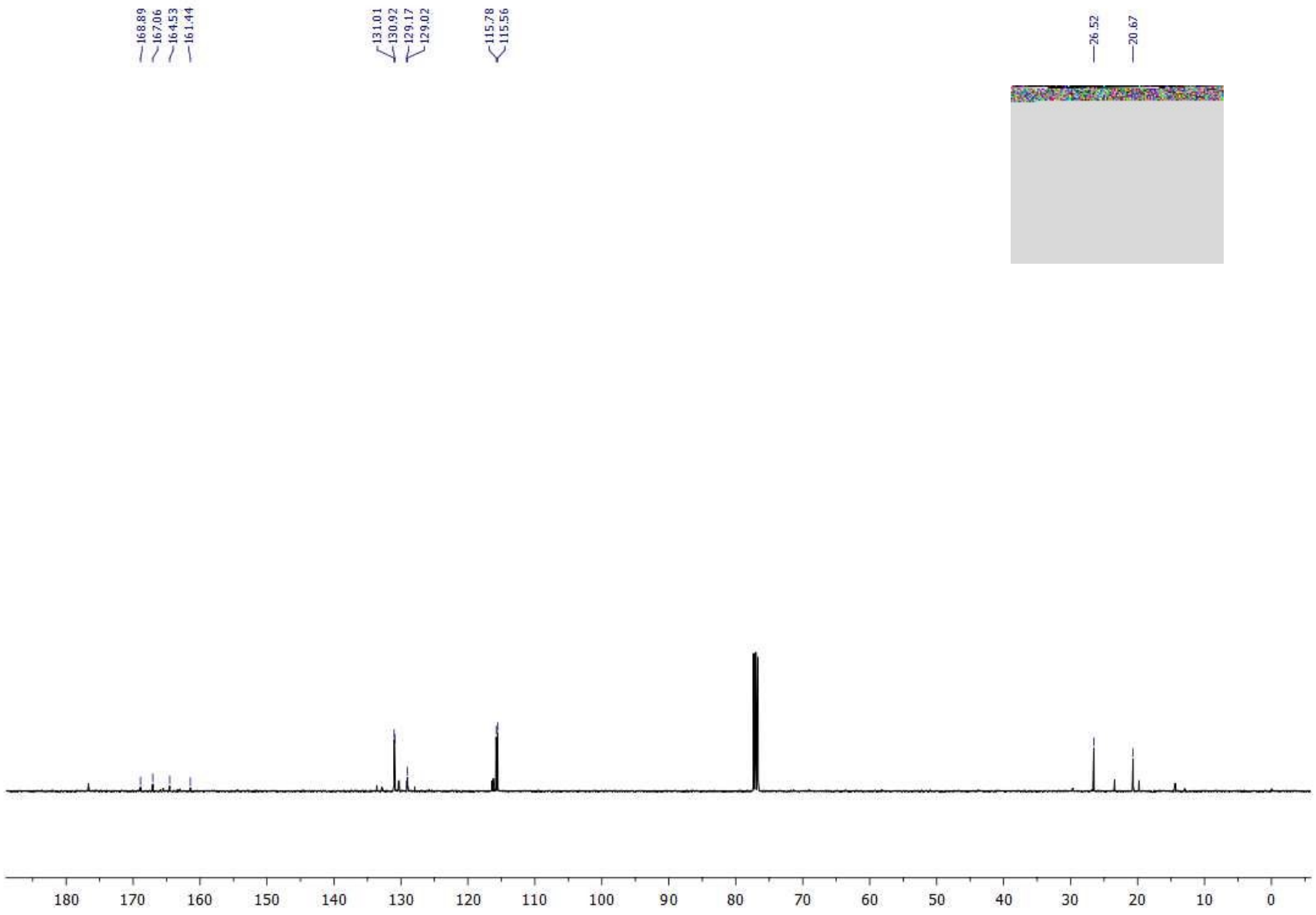
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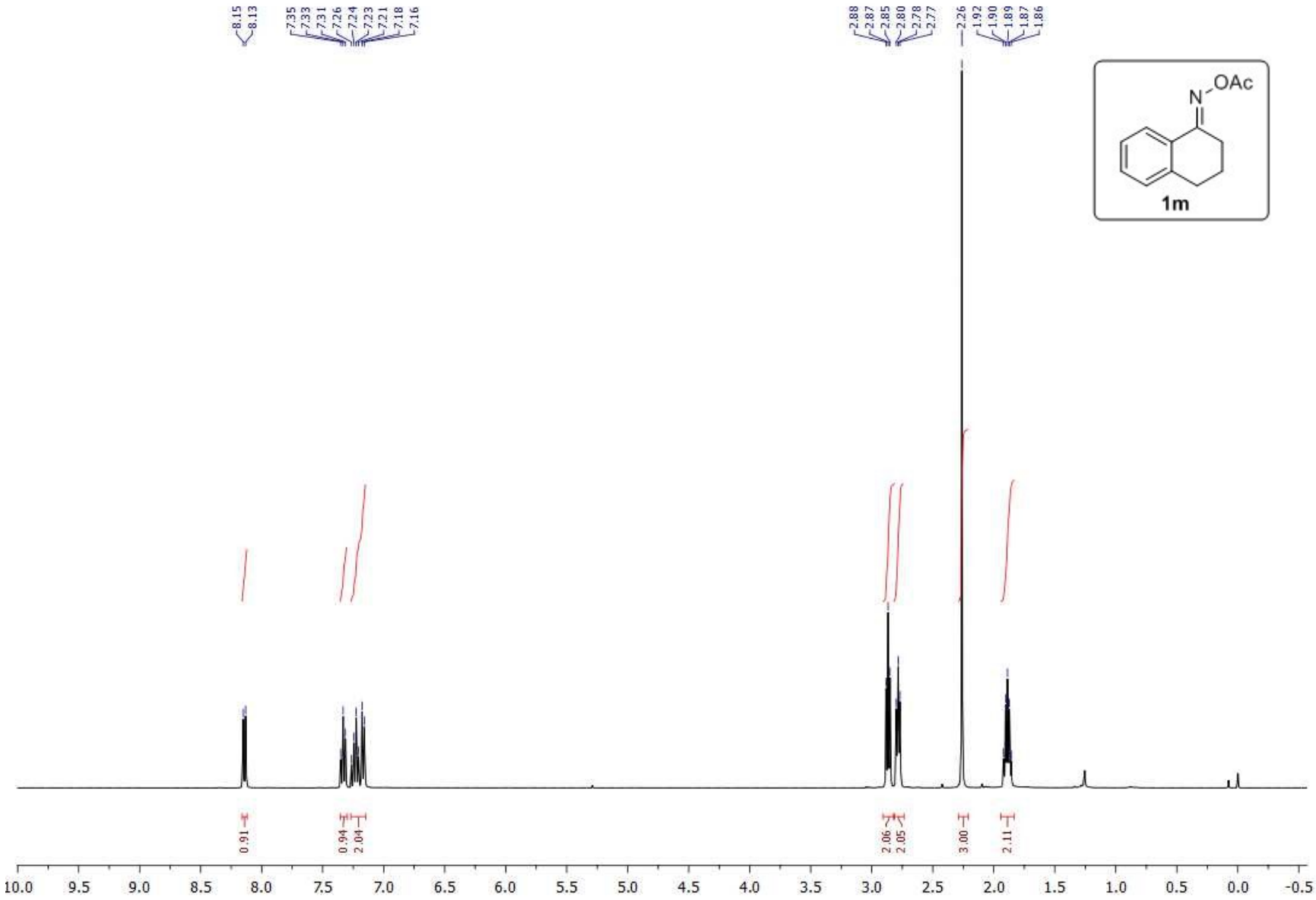
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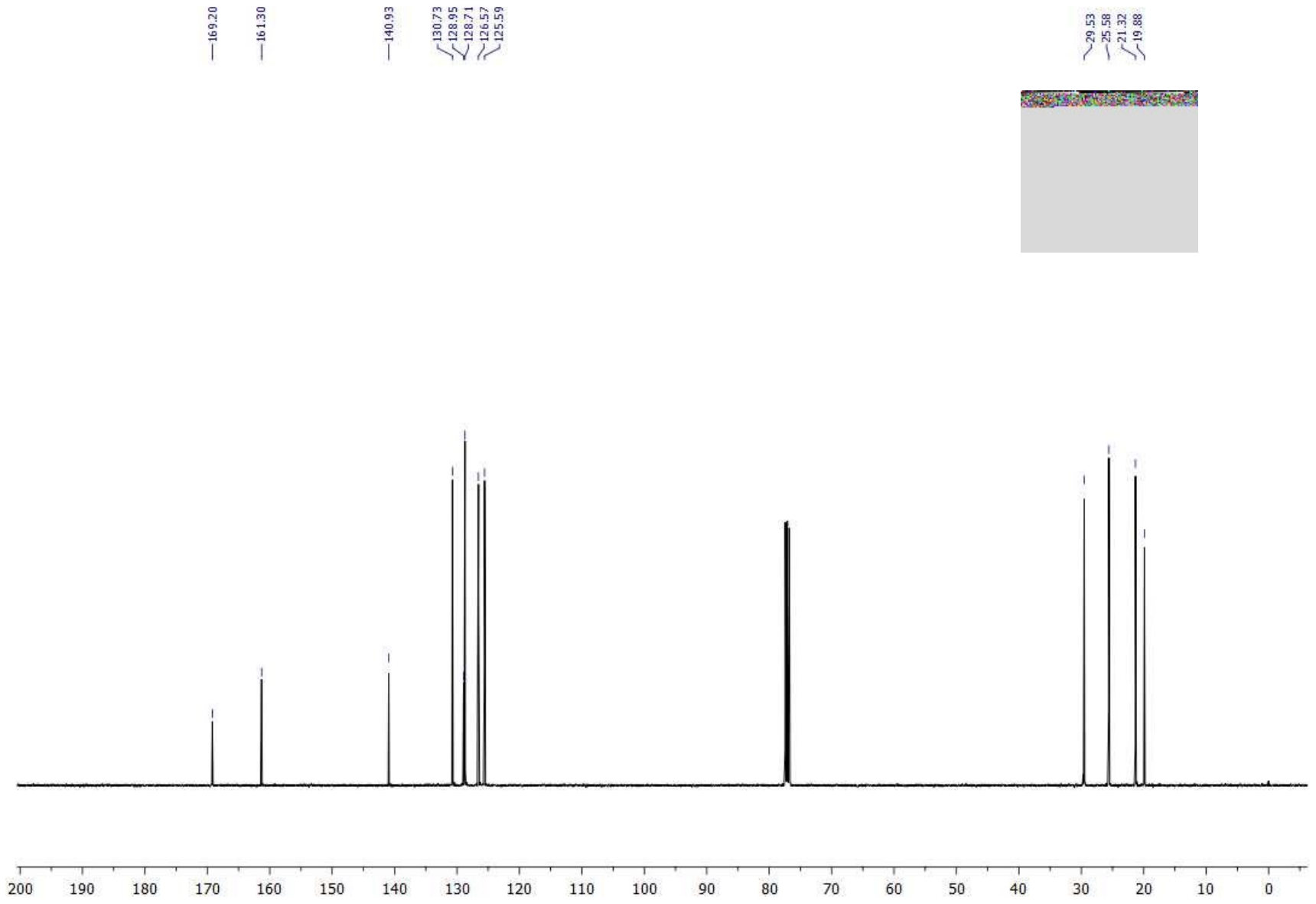
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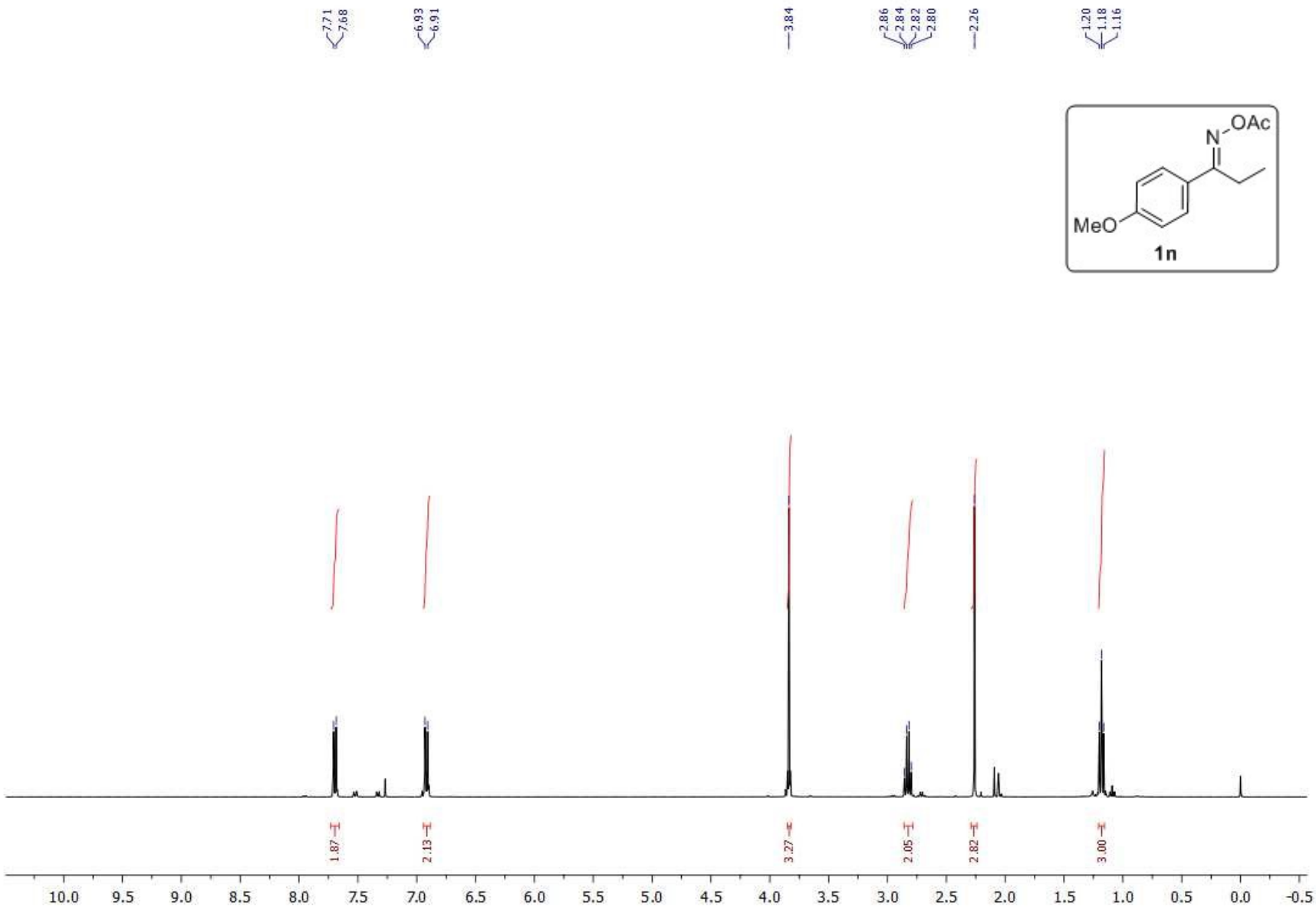
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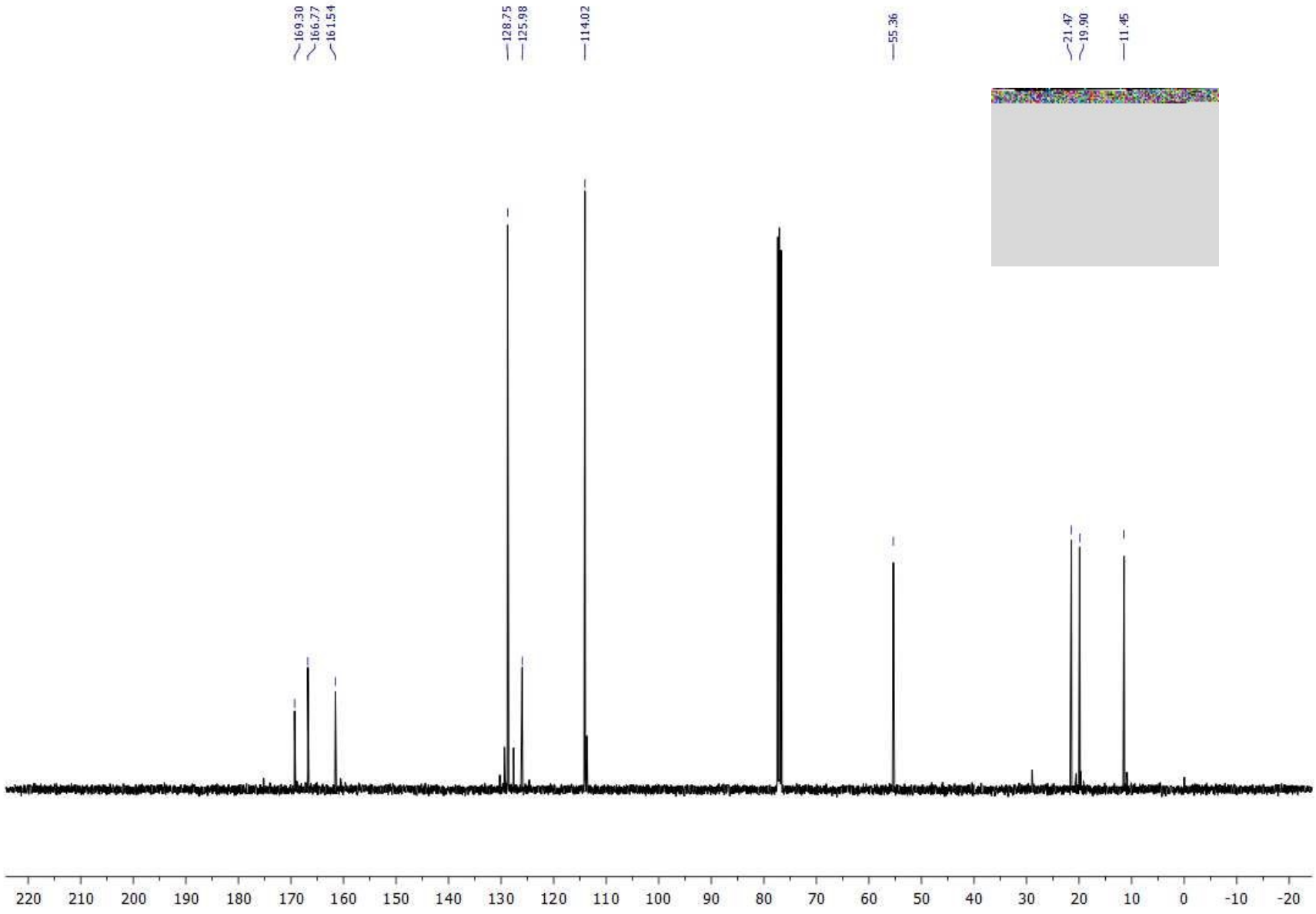
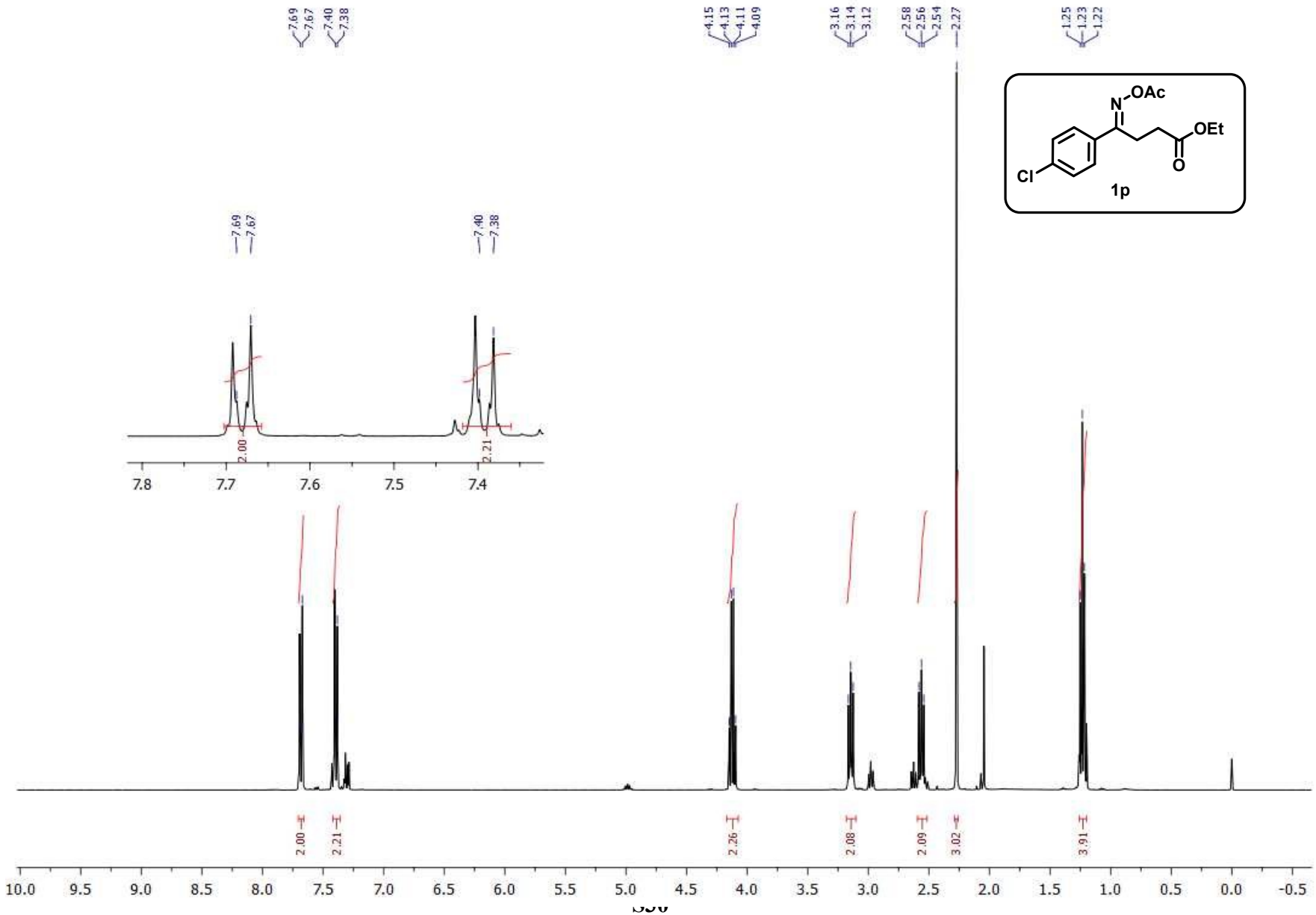
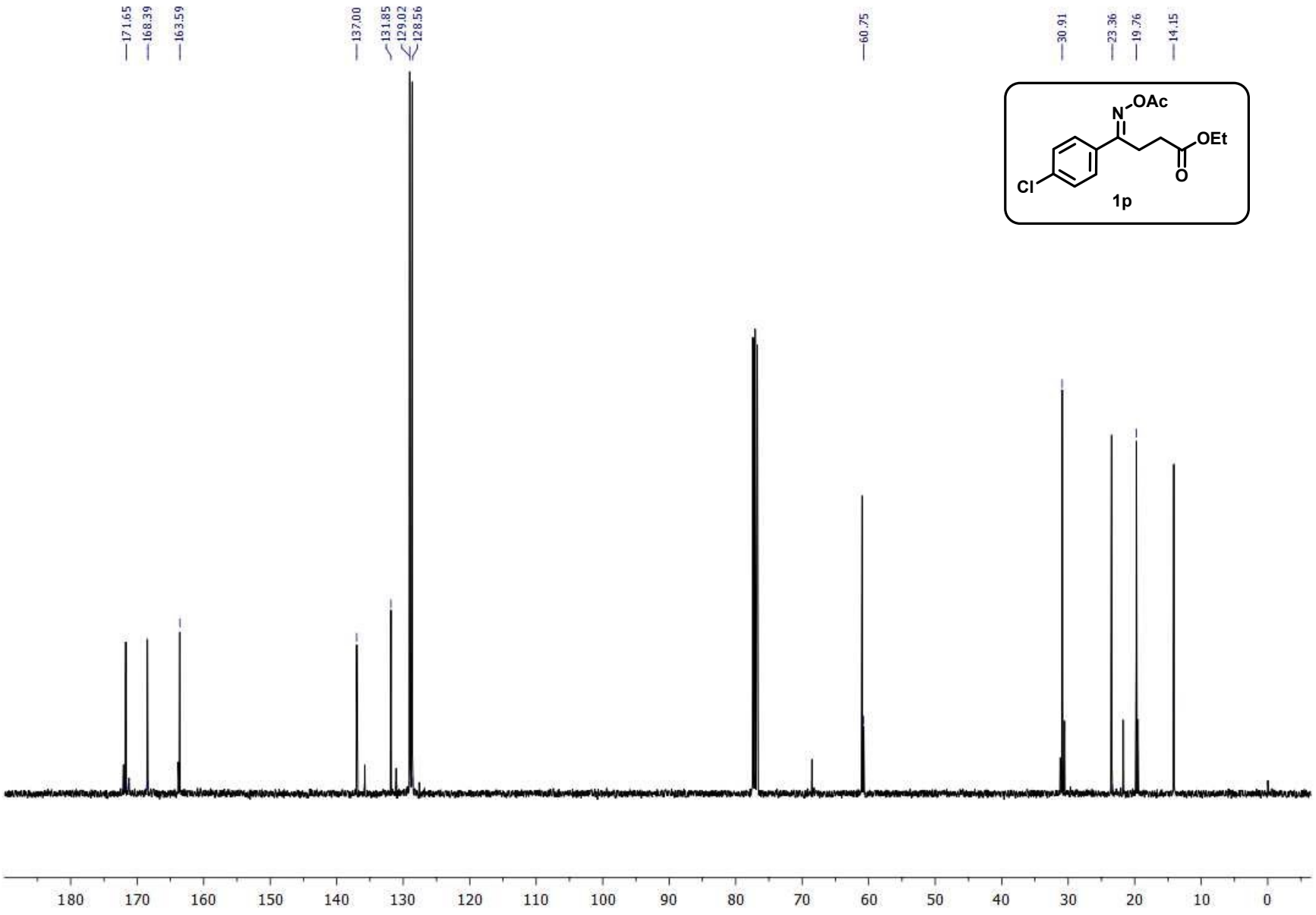
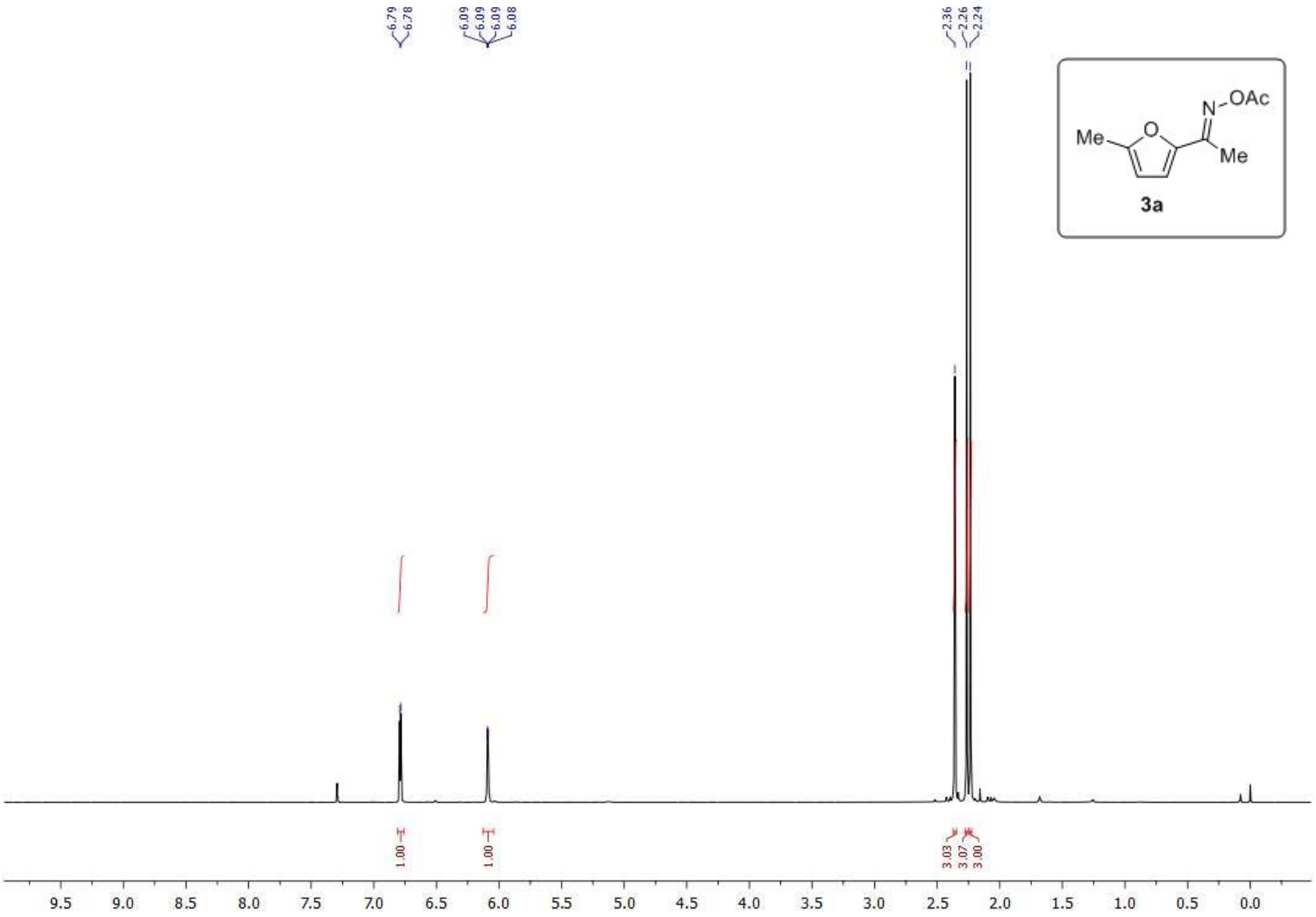
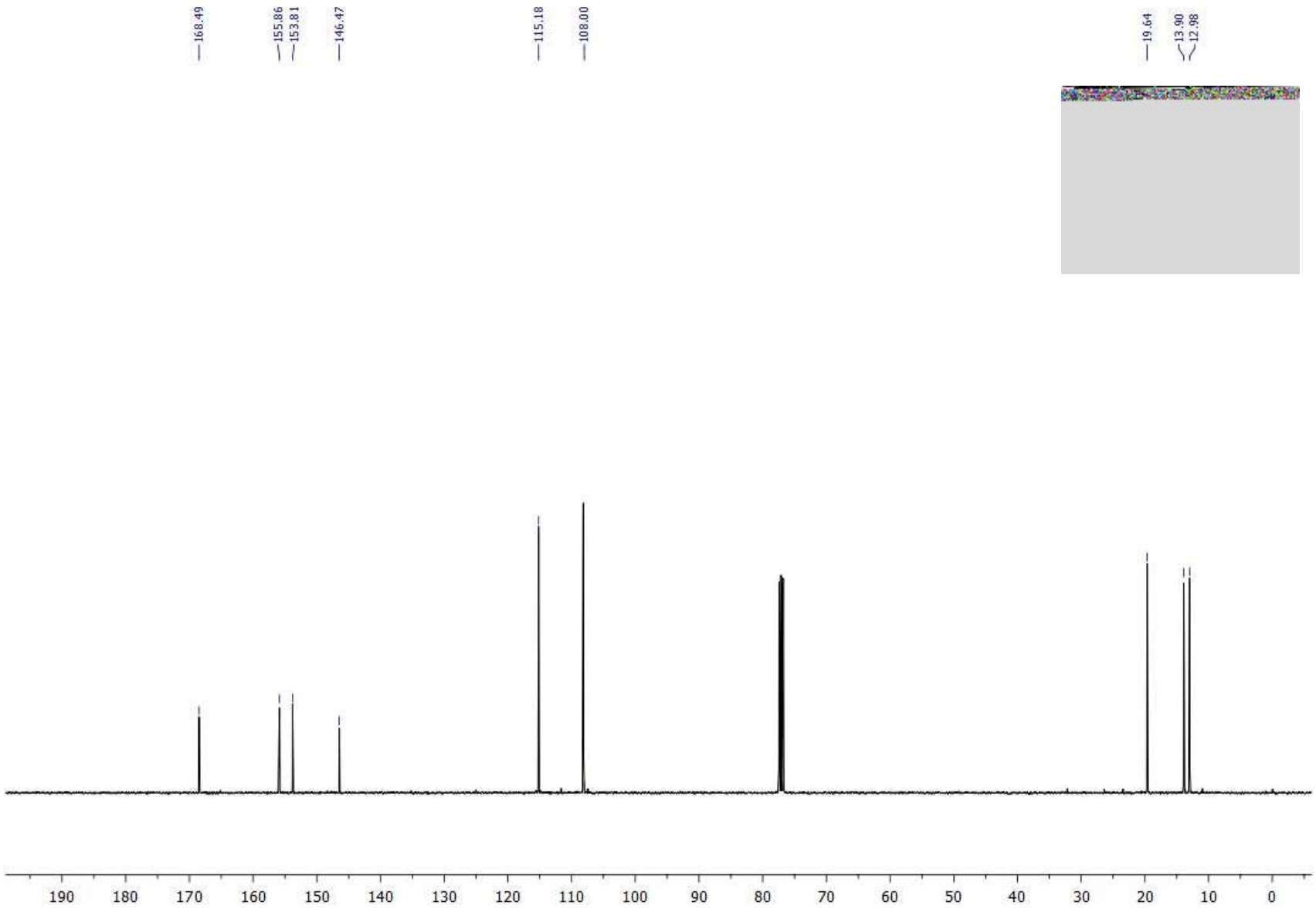
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

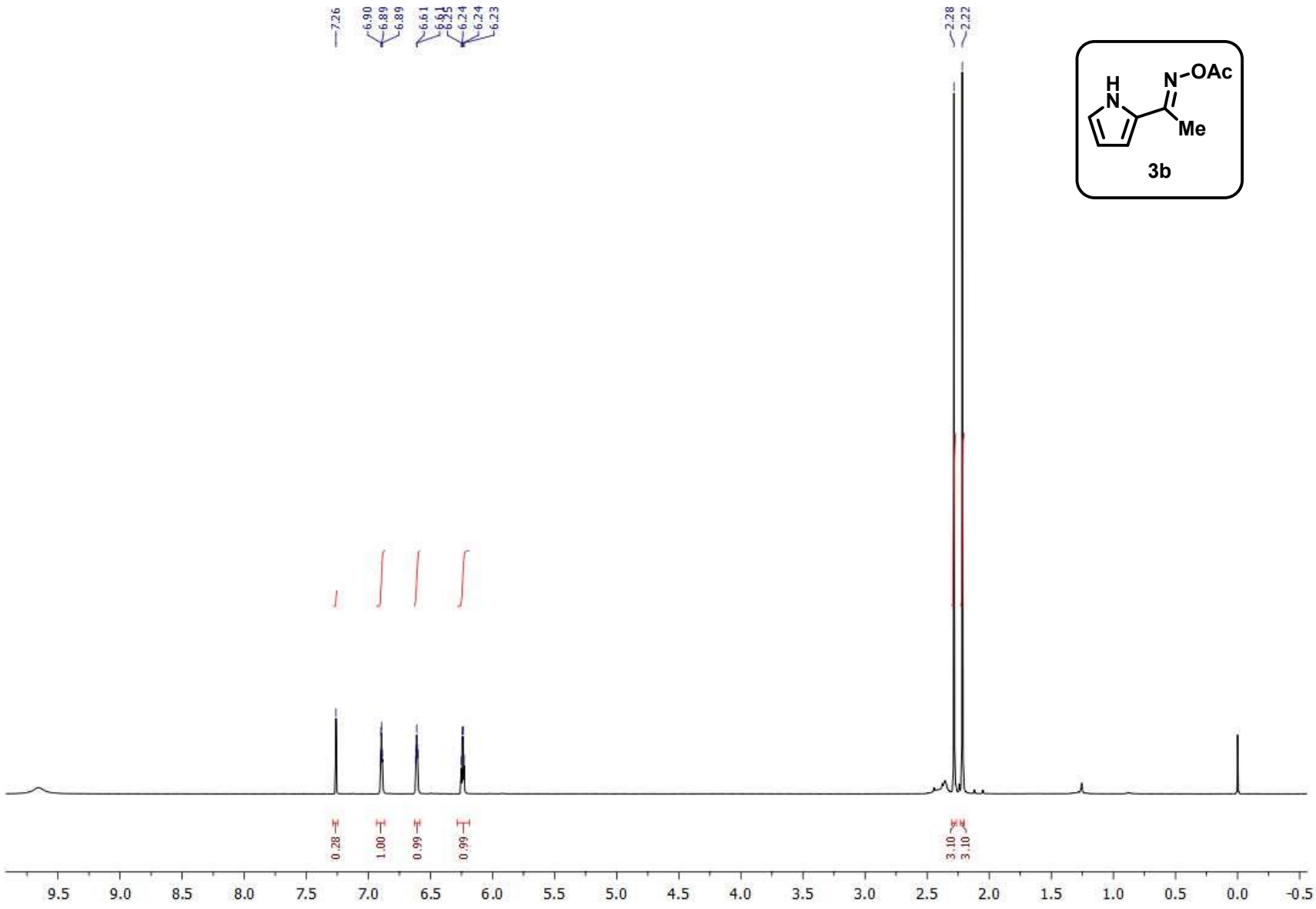

169.30
166.77
161.54
128.75
125.98
114.02
55.36
21.47
19.90
11.45
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

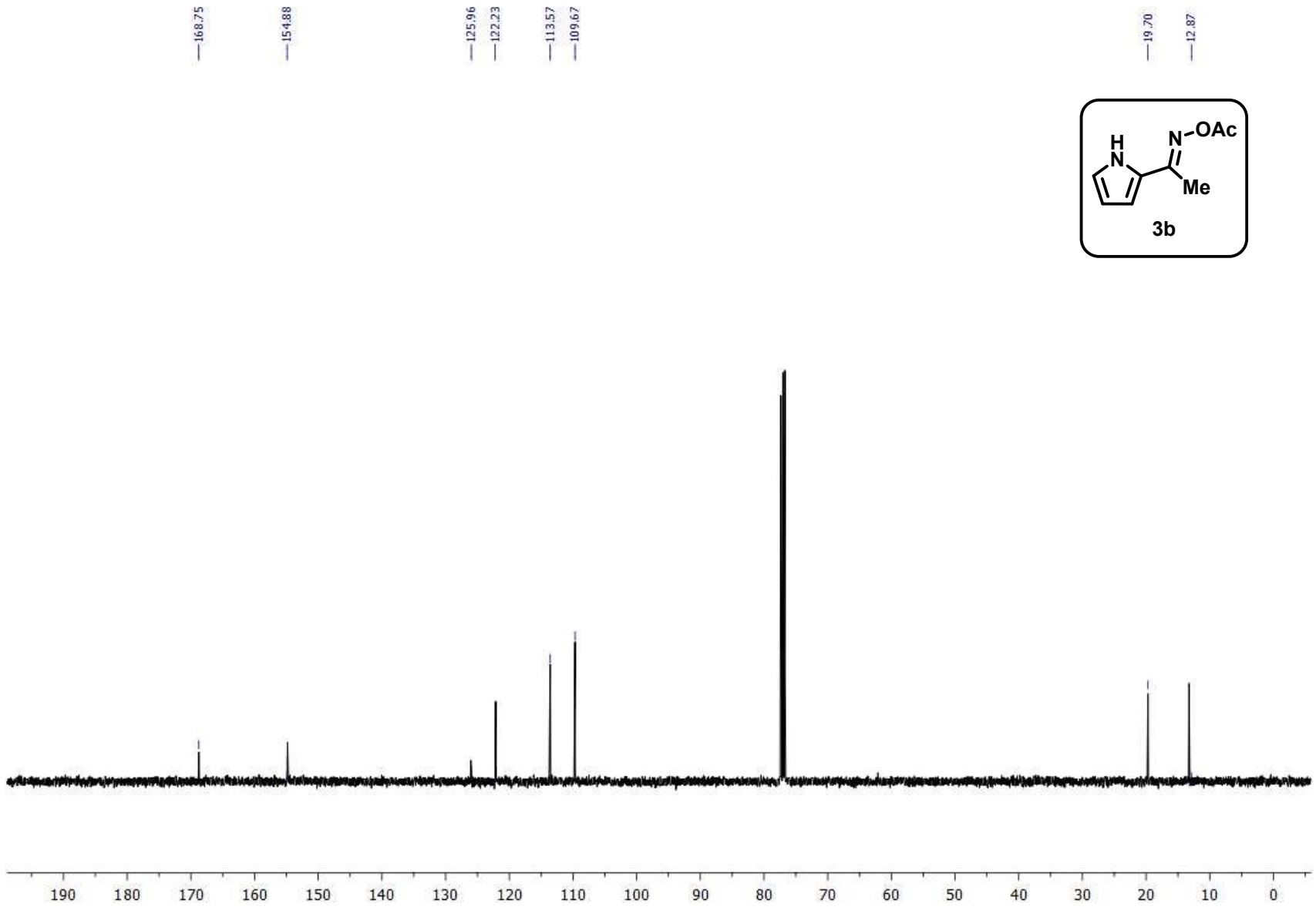

7.69
7.67
7.40
7.38
4.15
4.13
4.11
4.09
3.16
3.14
3.12
2.58
2.56
2.54
2.27
1.25
1.23
1.22
OAc
N
OEt
O
Cl
1p
2.00
2.21
2.26
2.08
2.09
3.02
3.91
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
7.8
7.7
7.6
7.5
7.4

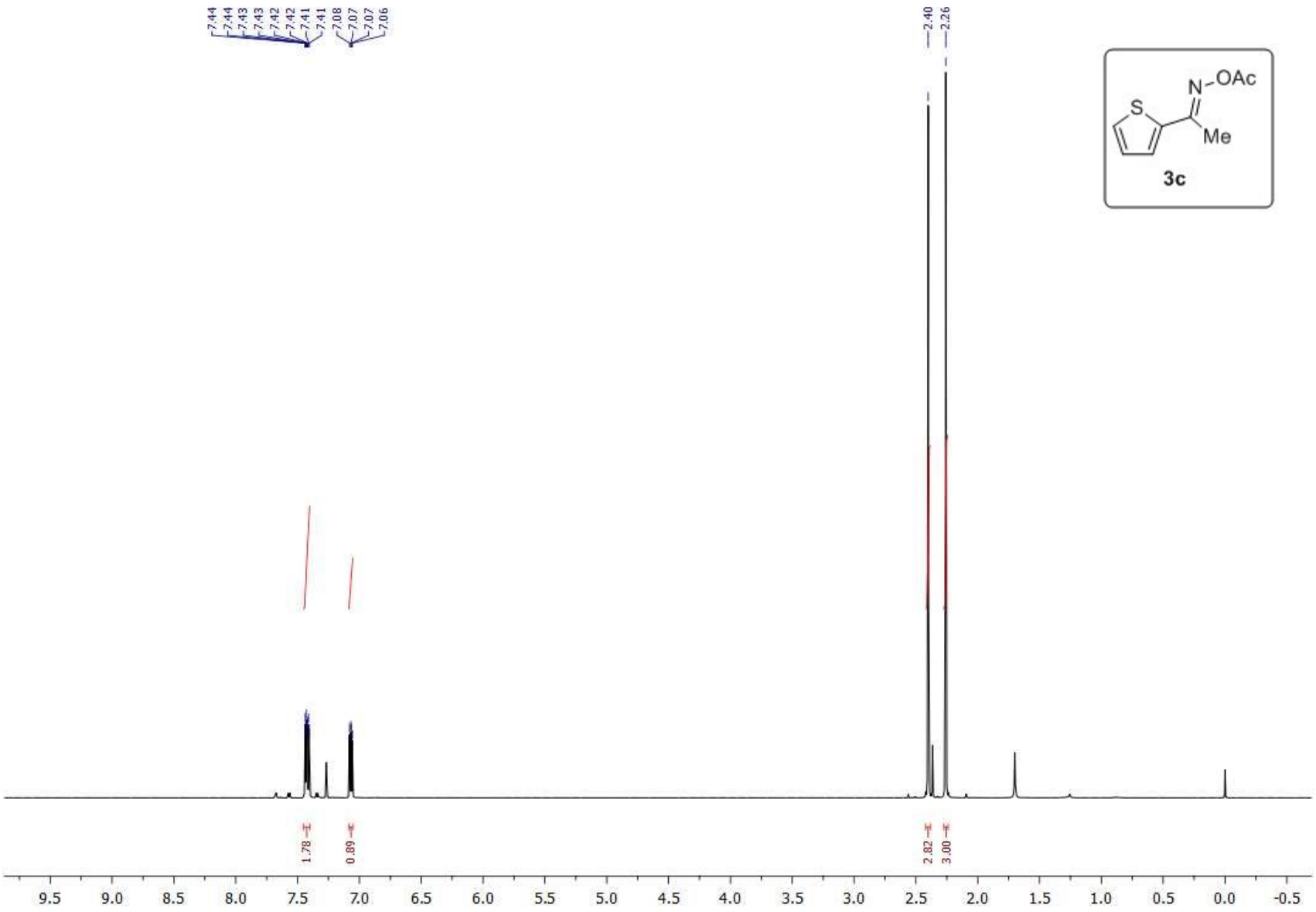

171.65
168.39
163.59
137.00
131.85
129.02
128.56
60.75
30.91
23.36
19.76
14.15
N
OAc
OEt
O
Cl
1p
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

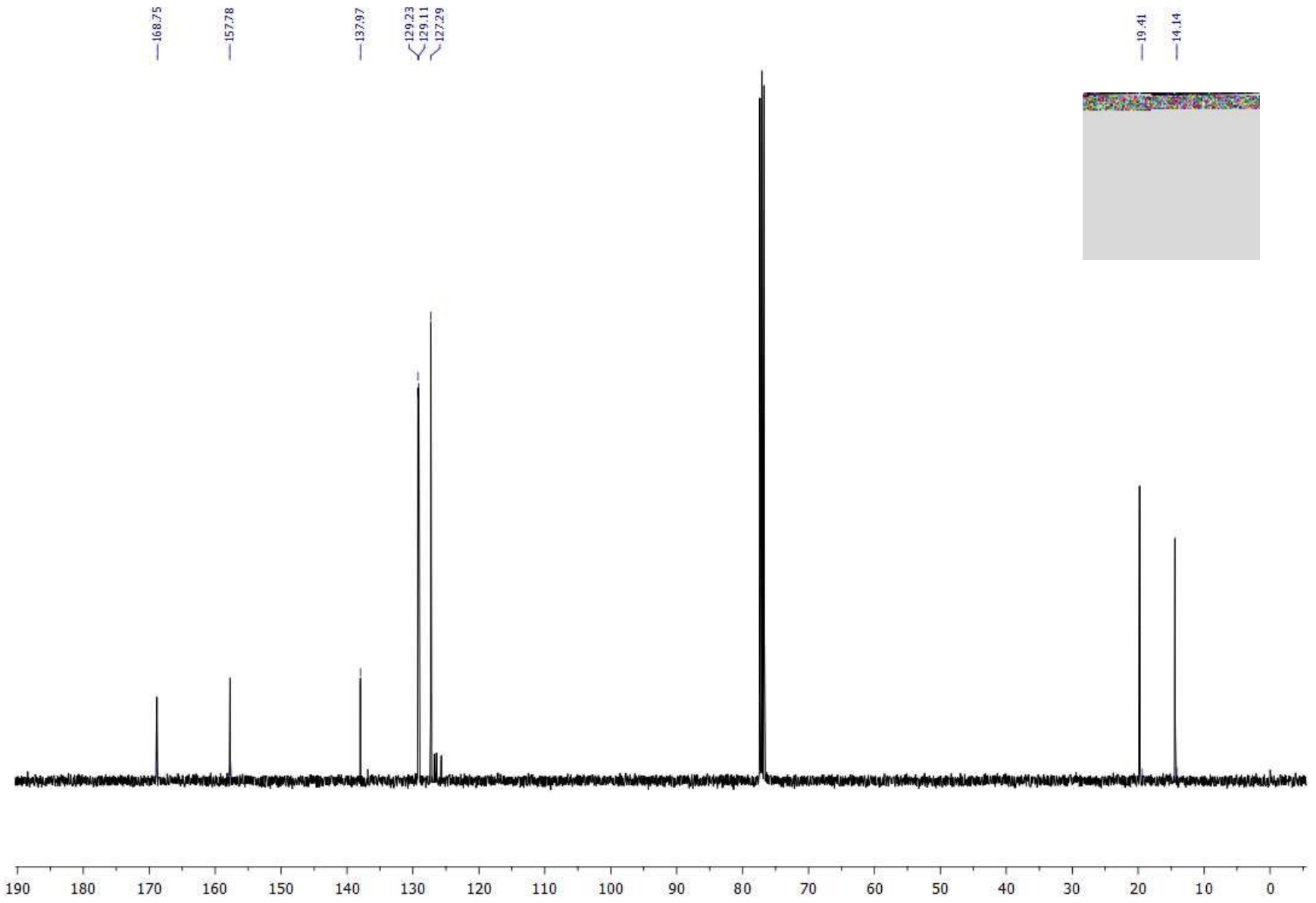

6.79
6.78
6.09
6.09
6.09
6.08
2.36
2.26
2.24
Me
O
N
OAc
Me
3a
1.00
1.00
3.03
3.07
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


168.49
155.86
153.81
146.47
115.18
108.00
19.64
13.90
12.98
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

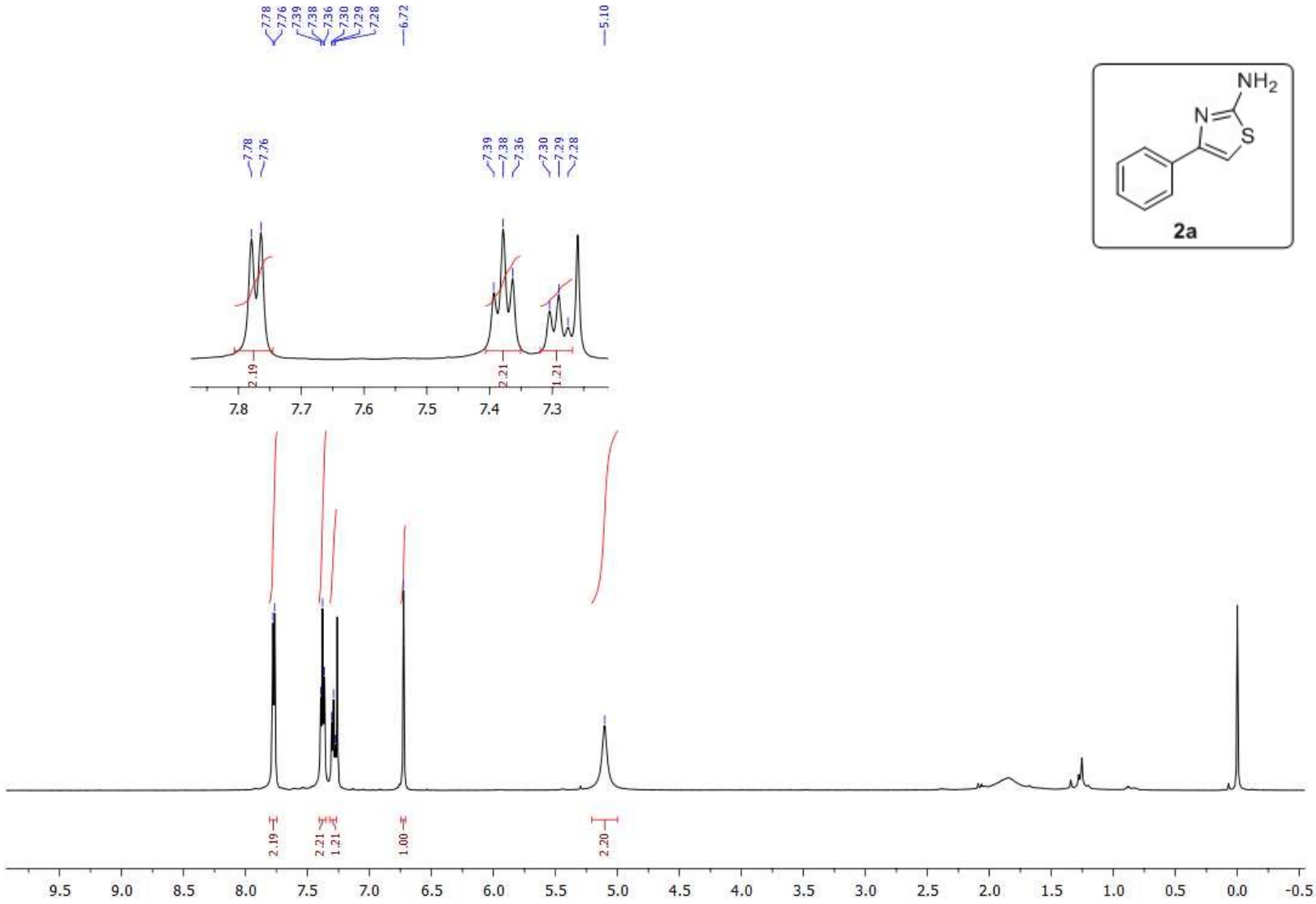

7.26
6.90
6.89
6.89
6.61
6.24
6.24
6.23
2.28
2.22
H
N
N-OAc
Me
3b
0.28
1.00
0.99
0.99
3.10
3.10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

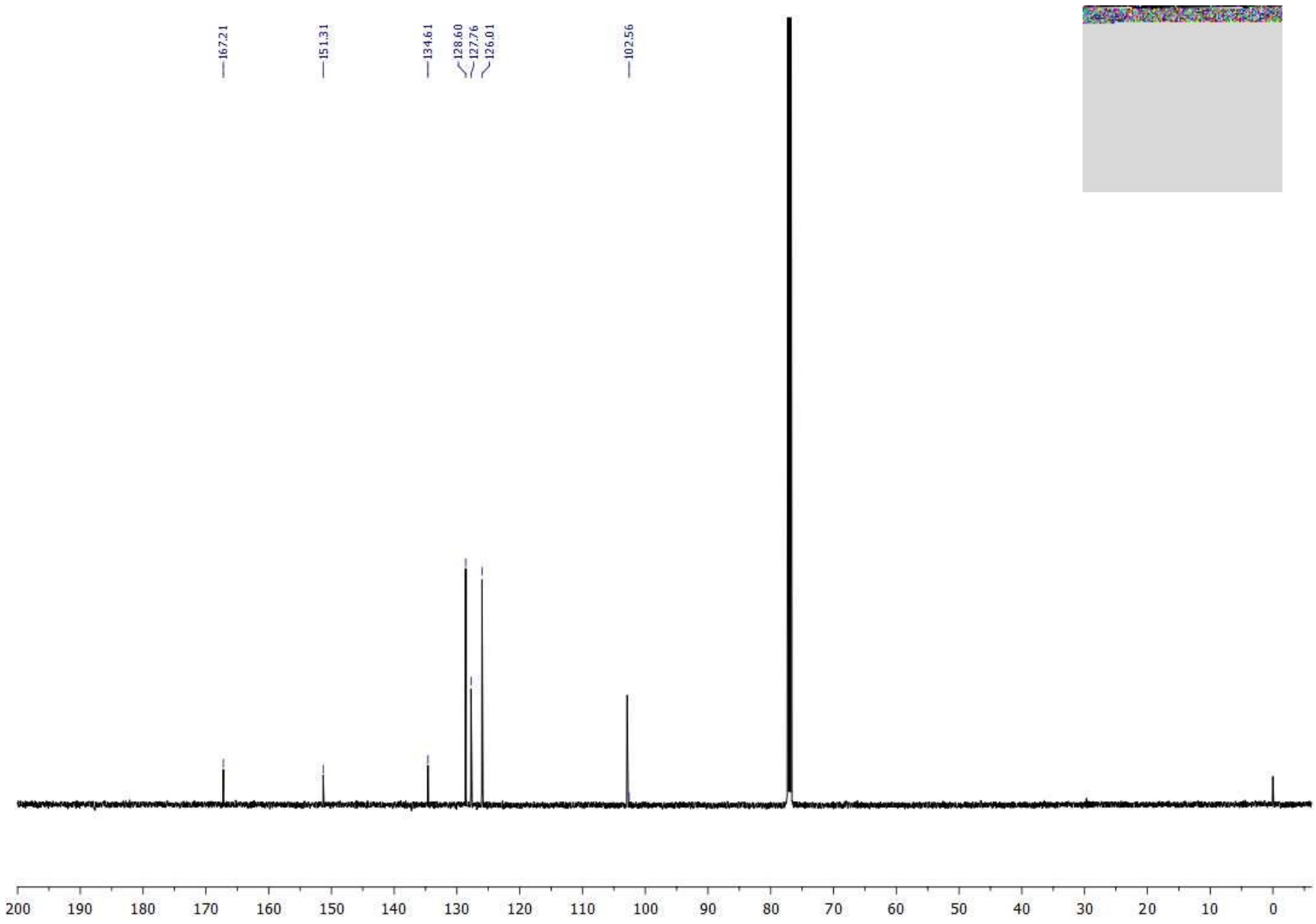

168.75
154.88
125.96
122.23
113.57
109.67
19.70
12.87
H
N
N
OAc
Me
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

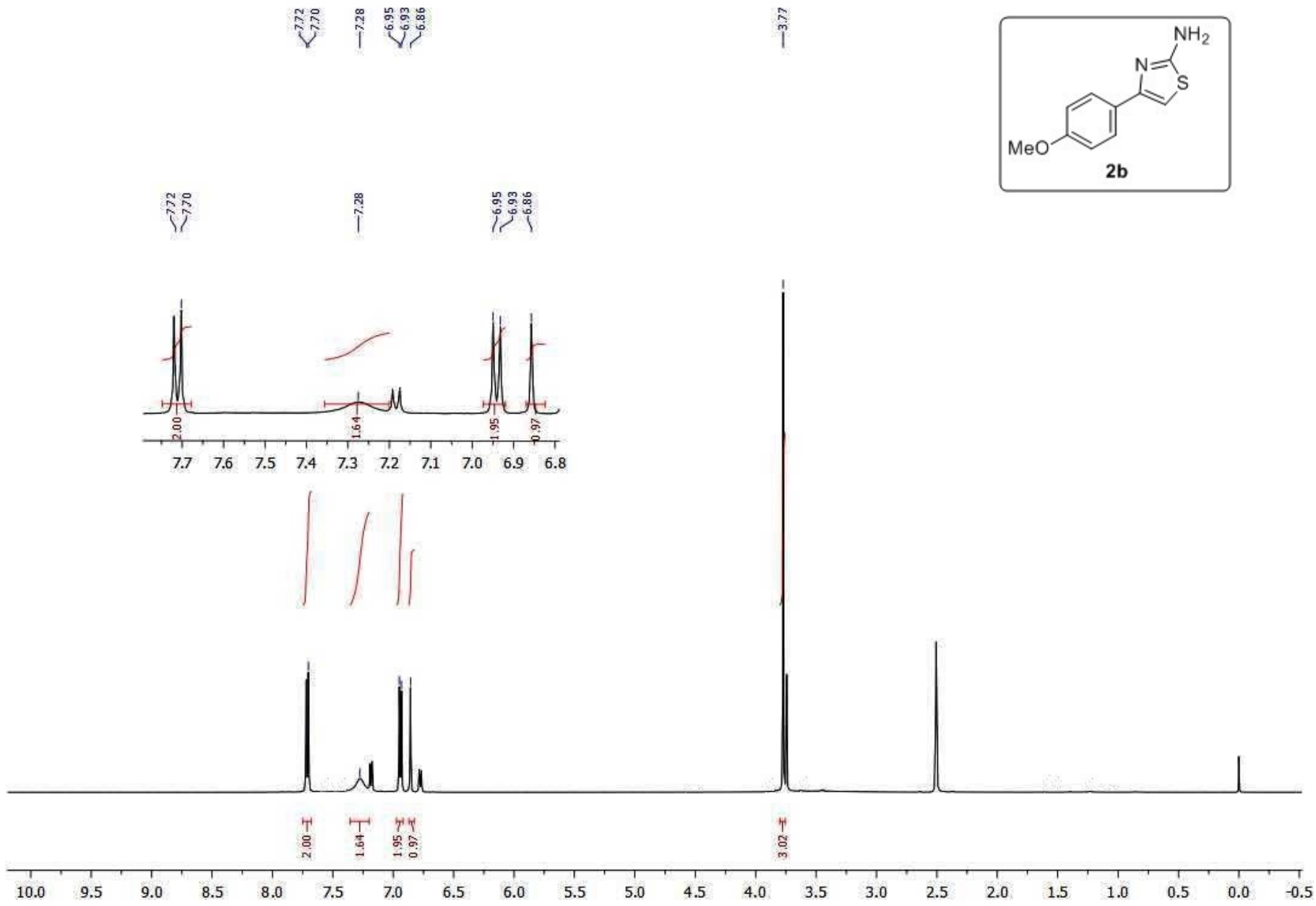

7.44
7.44
7.43
7.43
7.42
7.42
7.41
7.41
7.08
7.07
7.07
7.06
2.40
2.26
N-OAc
S
Me
3c
1.78
0.89
2.82
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

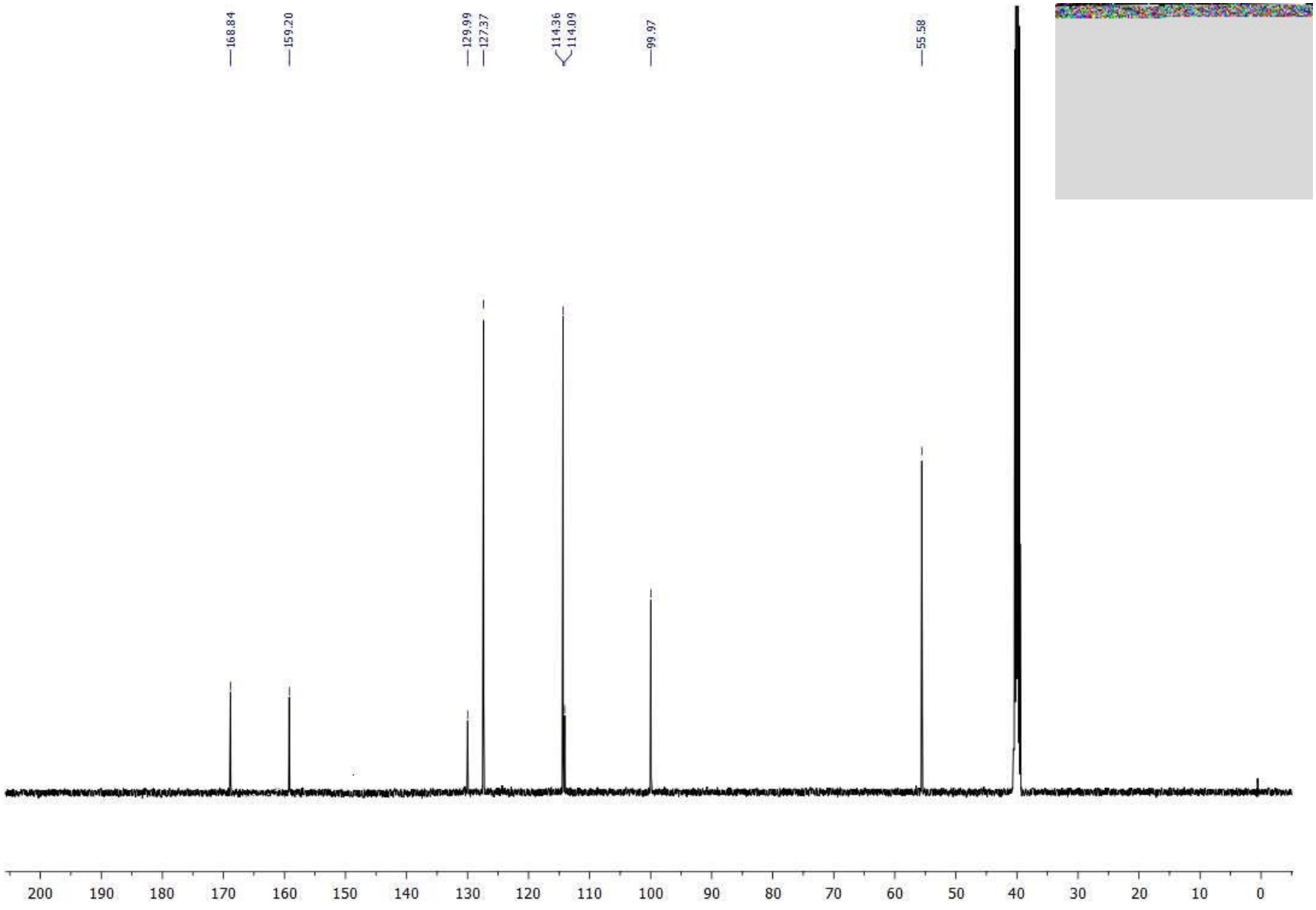

168.75
157.78
137.97
129.23
129.11
127.29
19.41
14.14
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

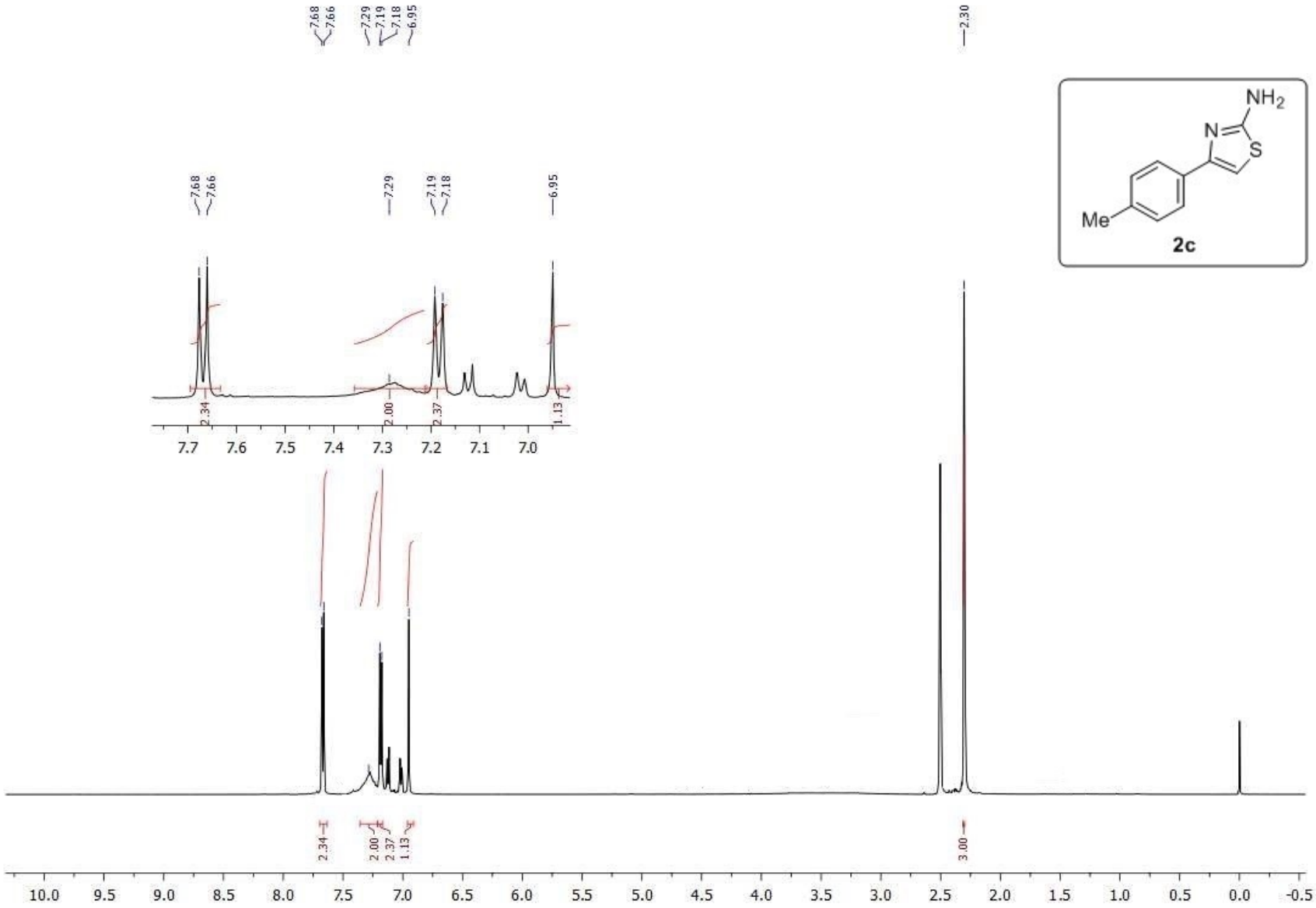
9. ^{1}H, ^{13}C and HRMS of products

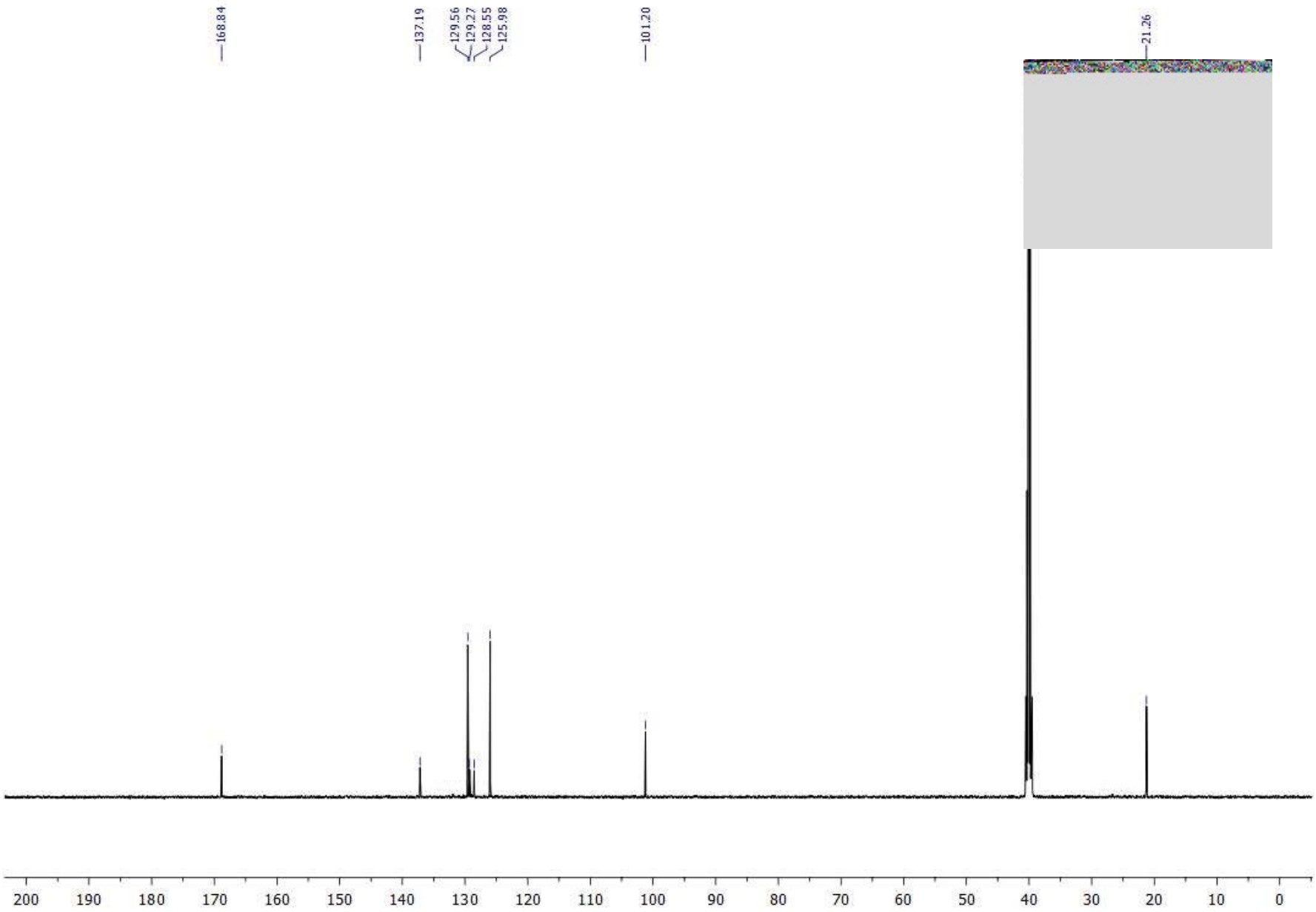


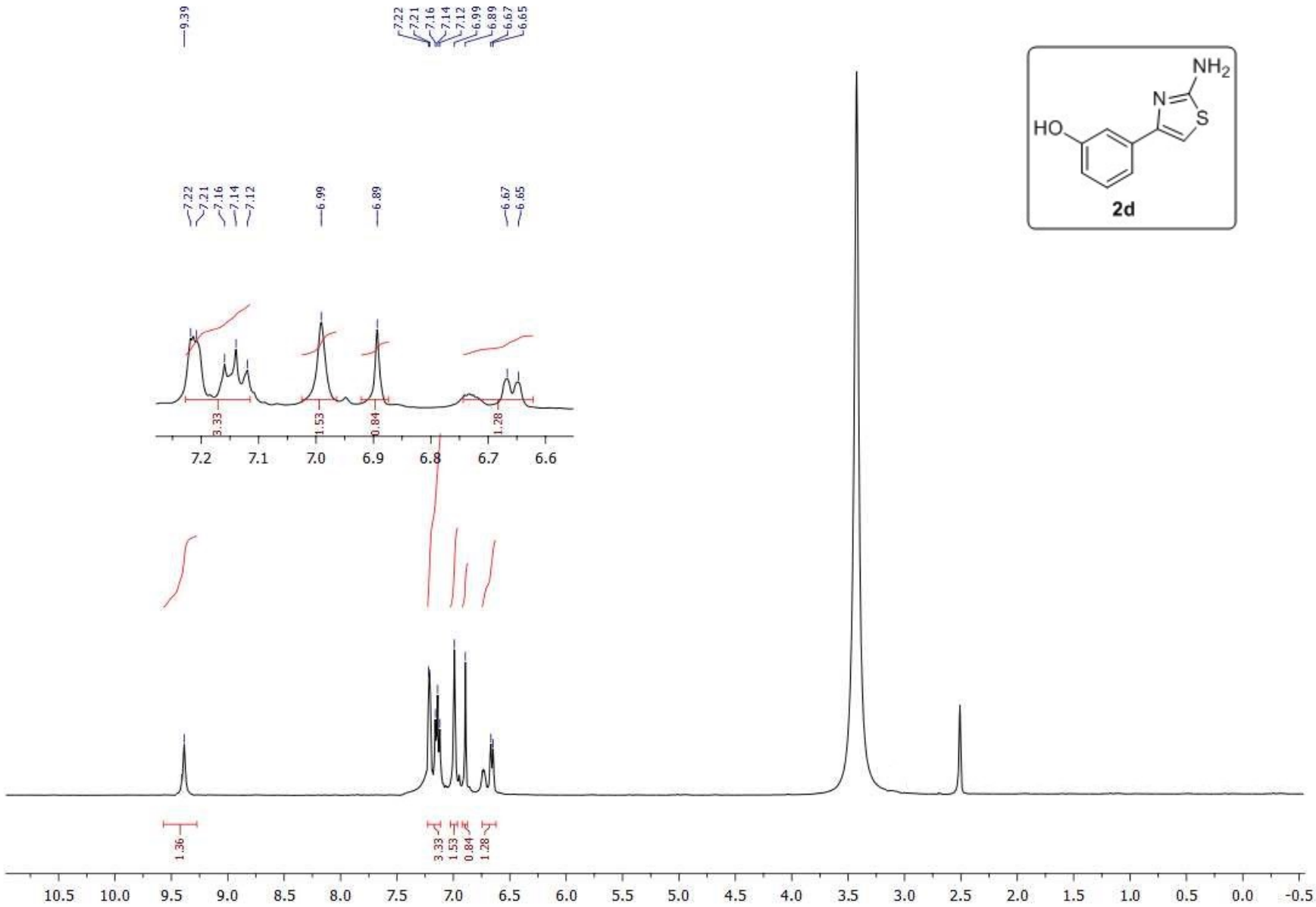

167.21
151.31
134.61
128.60
127.76
126.01
102.56
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

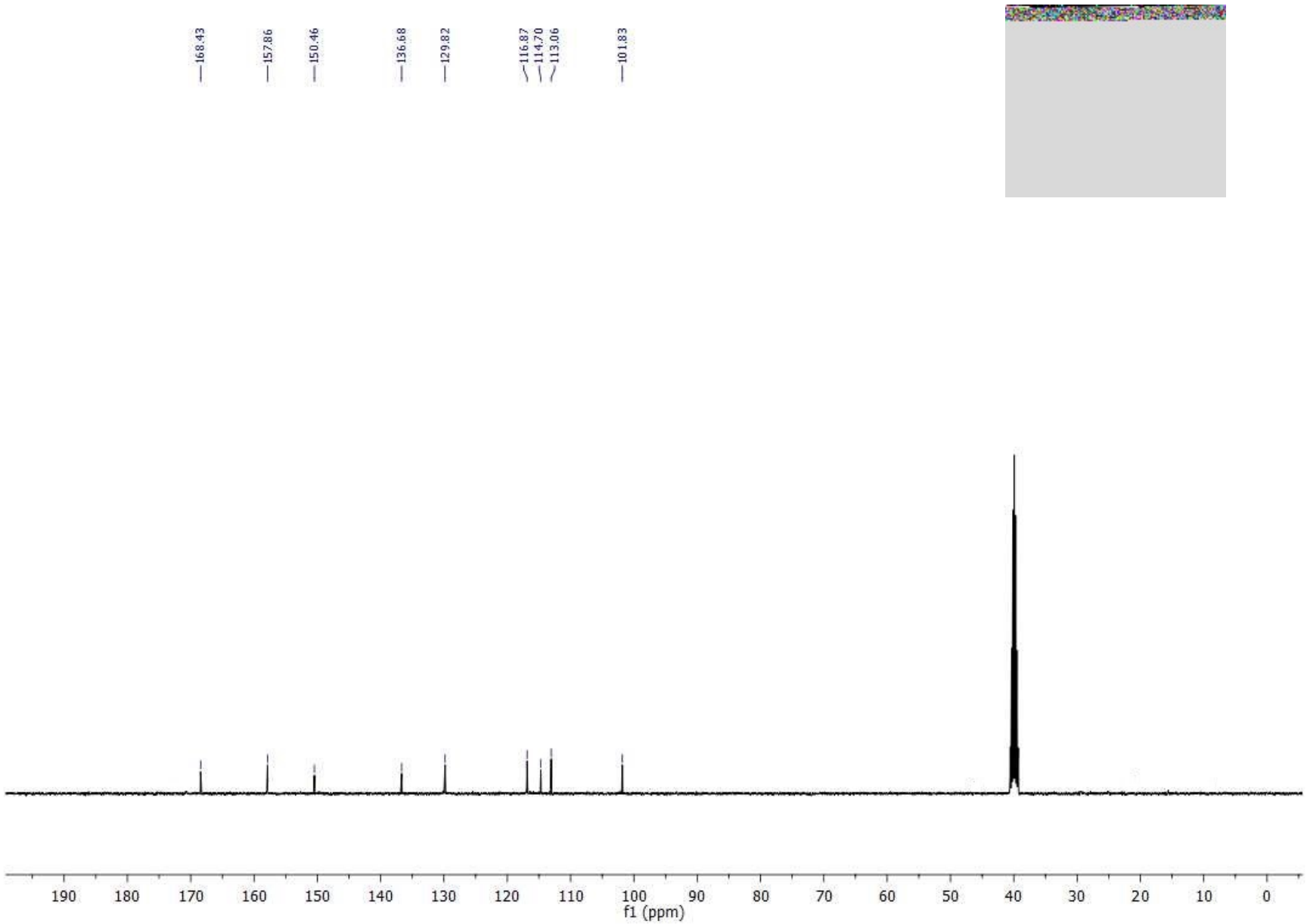

7.72
7.70
7.28
6.95
6.93
6.86
3.77
NH2
N
S
MeO
2b
2.00
1.64
1.95
0.97
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

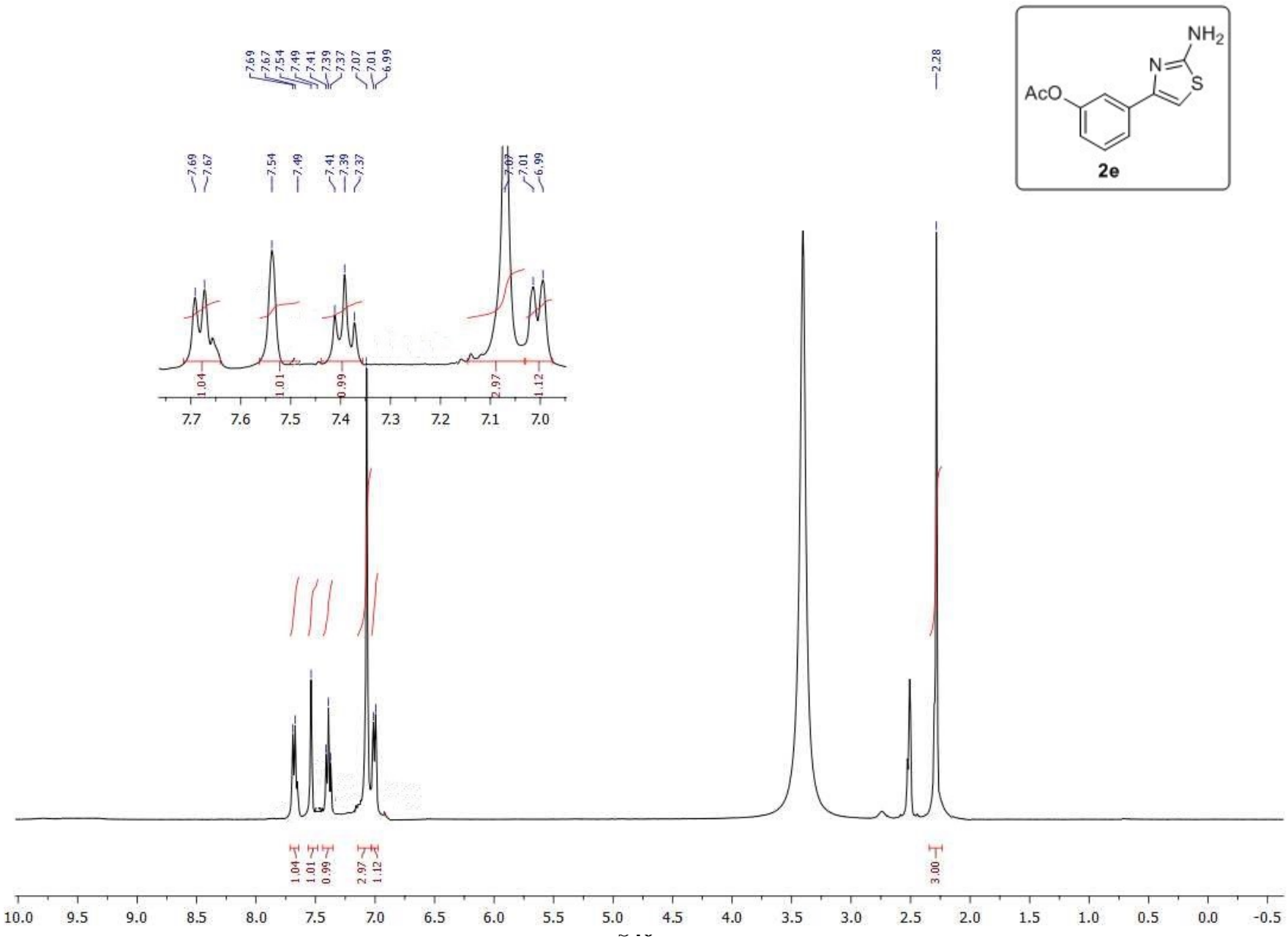

168.84
159.20
129.99
127.37
114.36
114.09
99.97
55.58
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

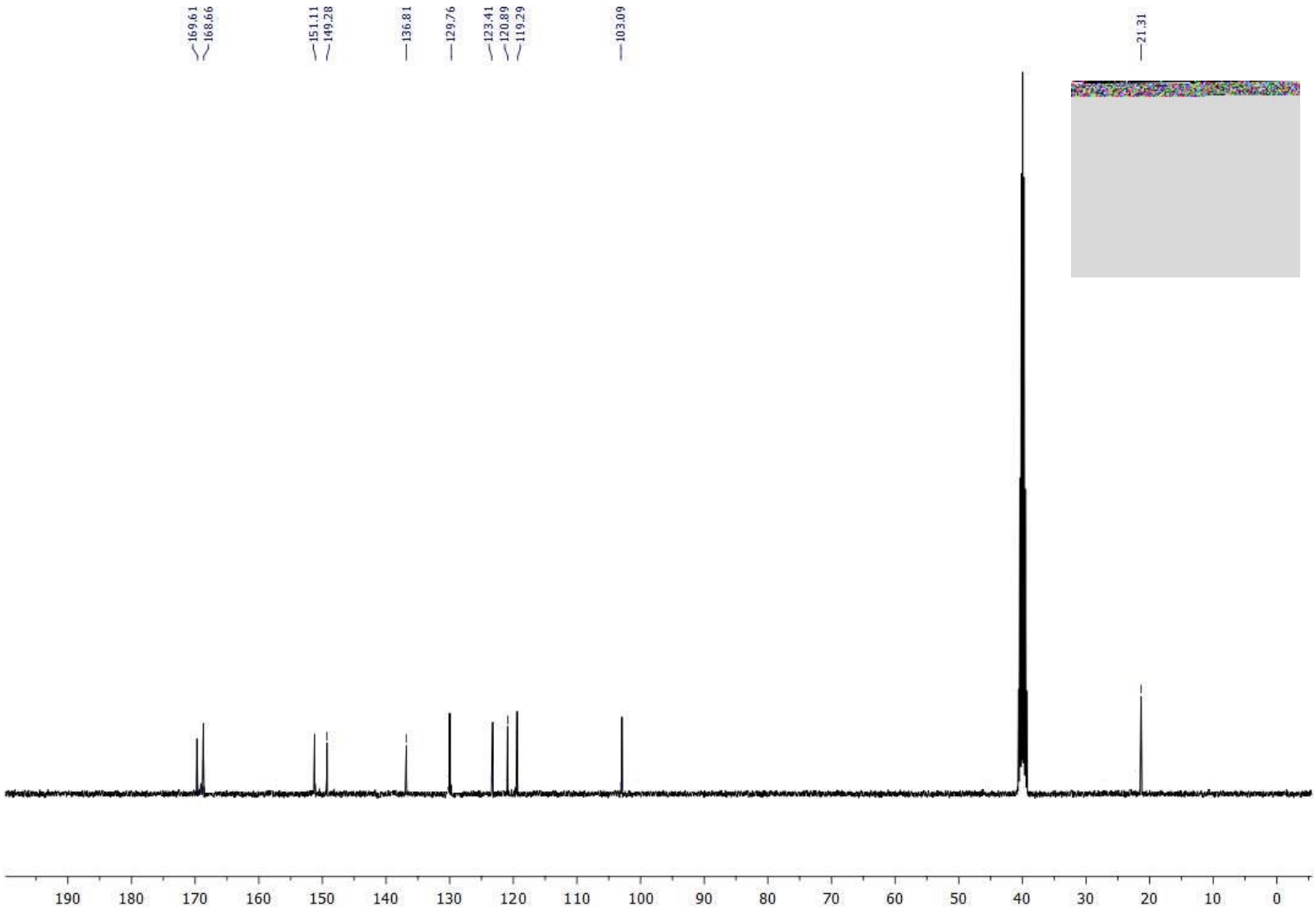

7.68
7.66
7.29
7.19
7.18
6.95
2.30
NH2
N
S
Me
2c
2.34
2.00
2.37
1.13
3.00

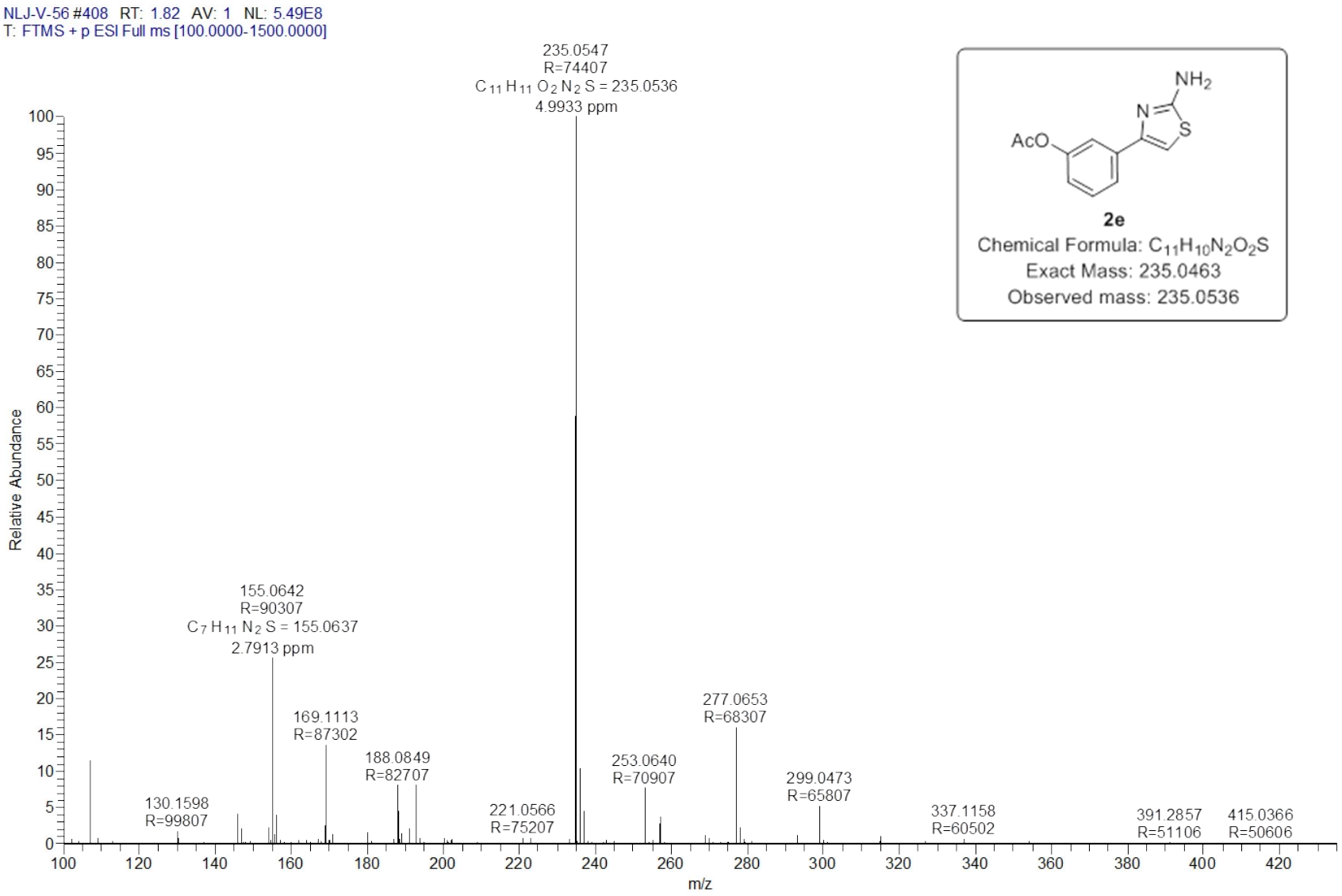

168.84
137.19
129.56
129.27
128.55
125.98
101.20
21.26
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

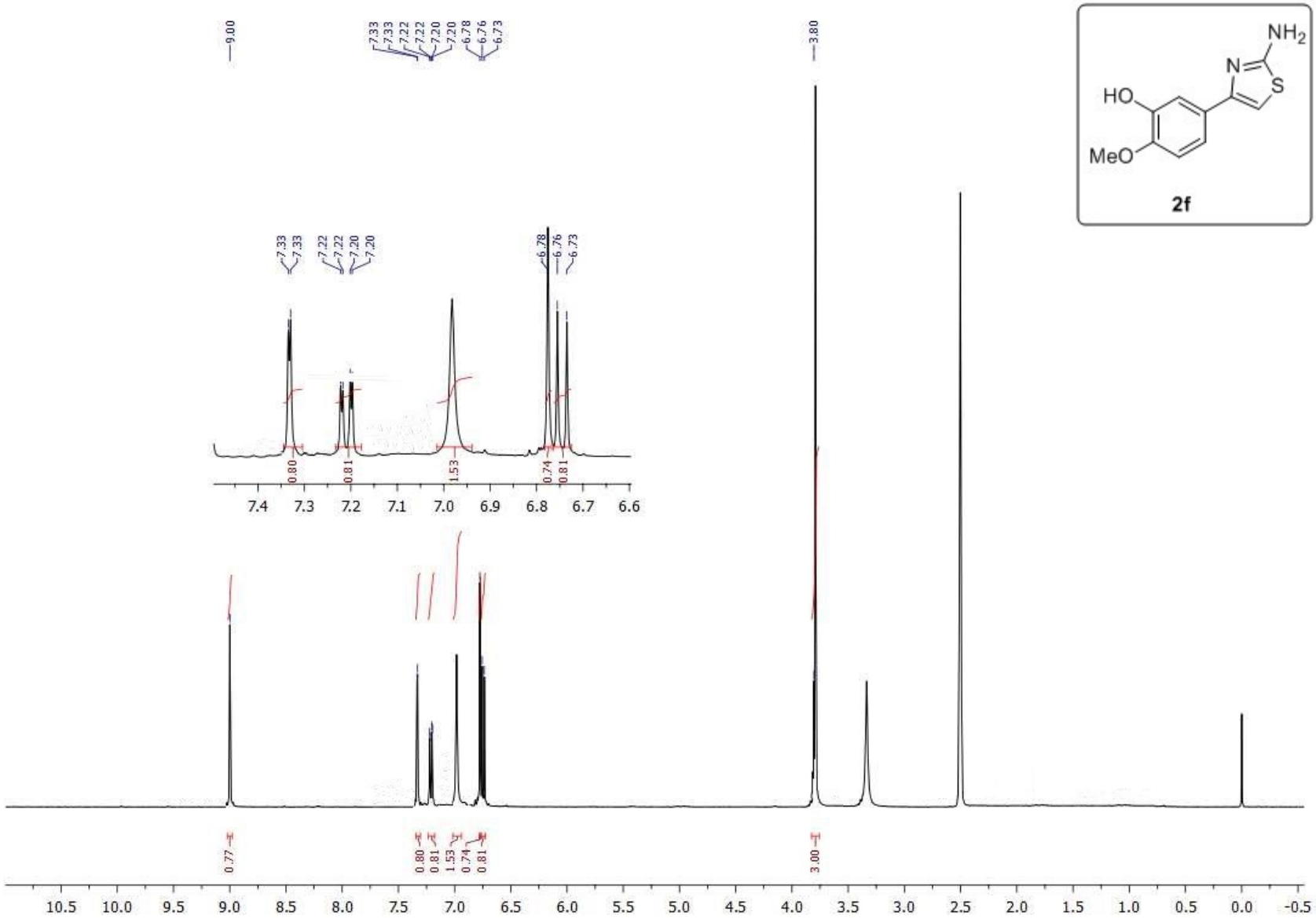

9.39
7.22
7.21
7.16
7.14
7.12
6.99
6.89
6.67
6.65
NH2
N
S
HO
2d
3.33
1.53
0.84
1.28
1.36

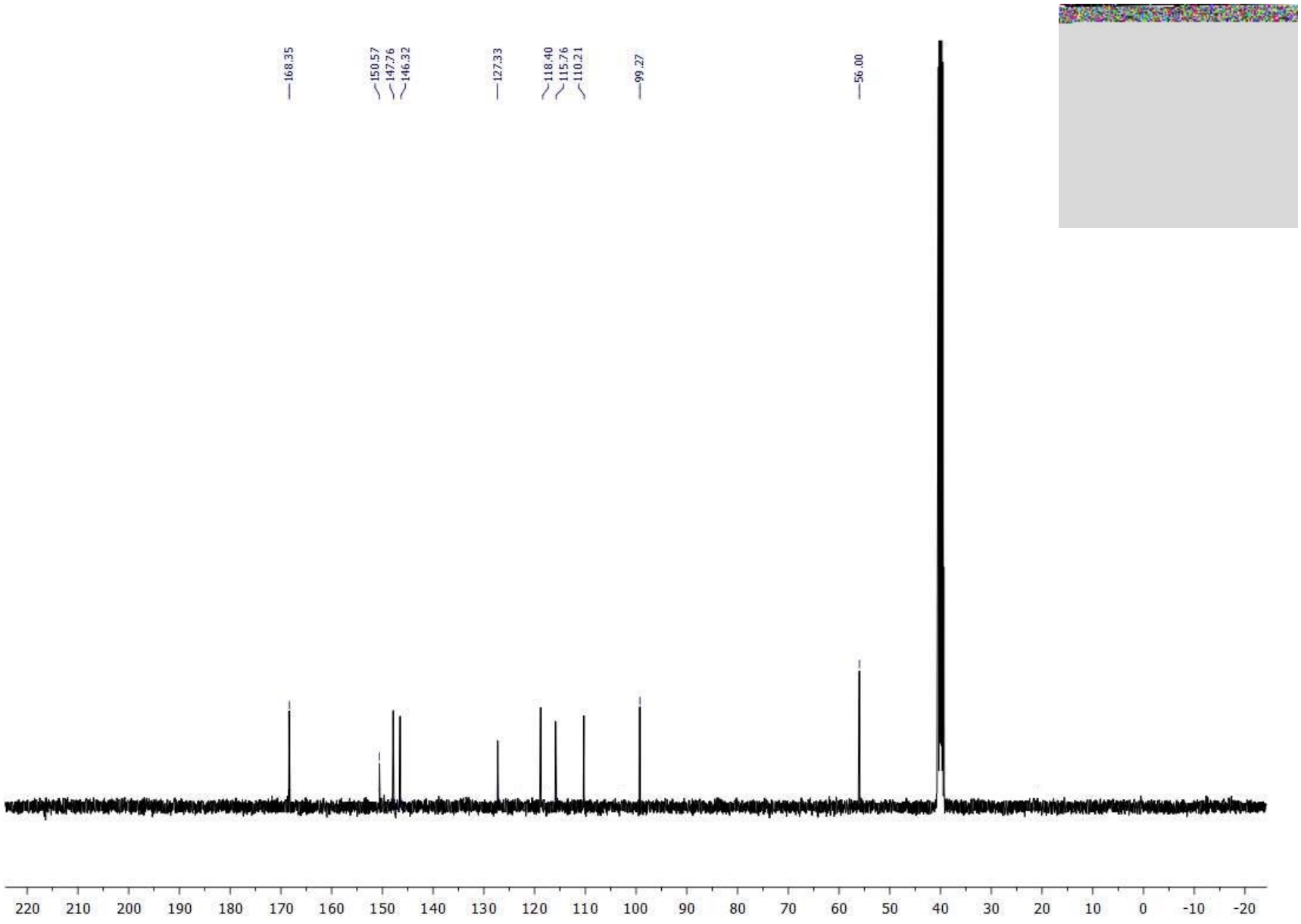

168.43
157.86
150.46
136.68
129.82
116.87
114.70
113.06
101.83
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

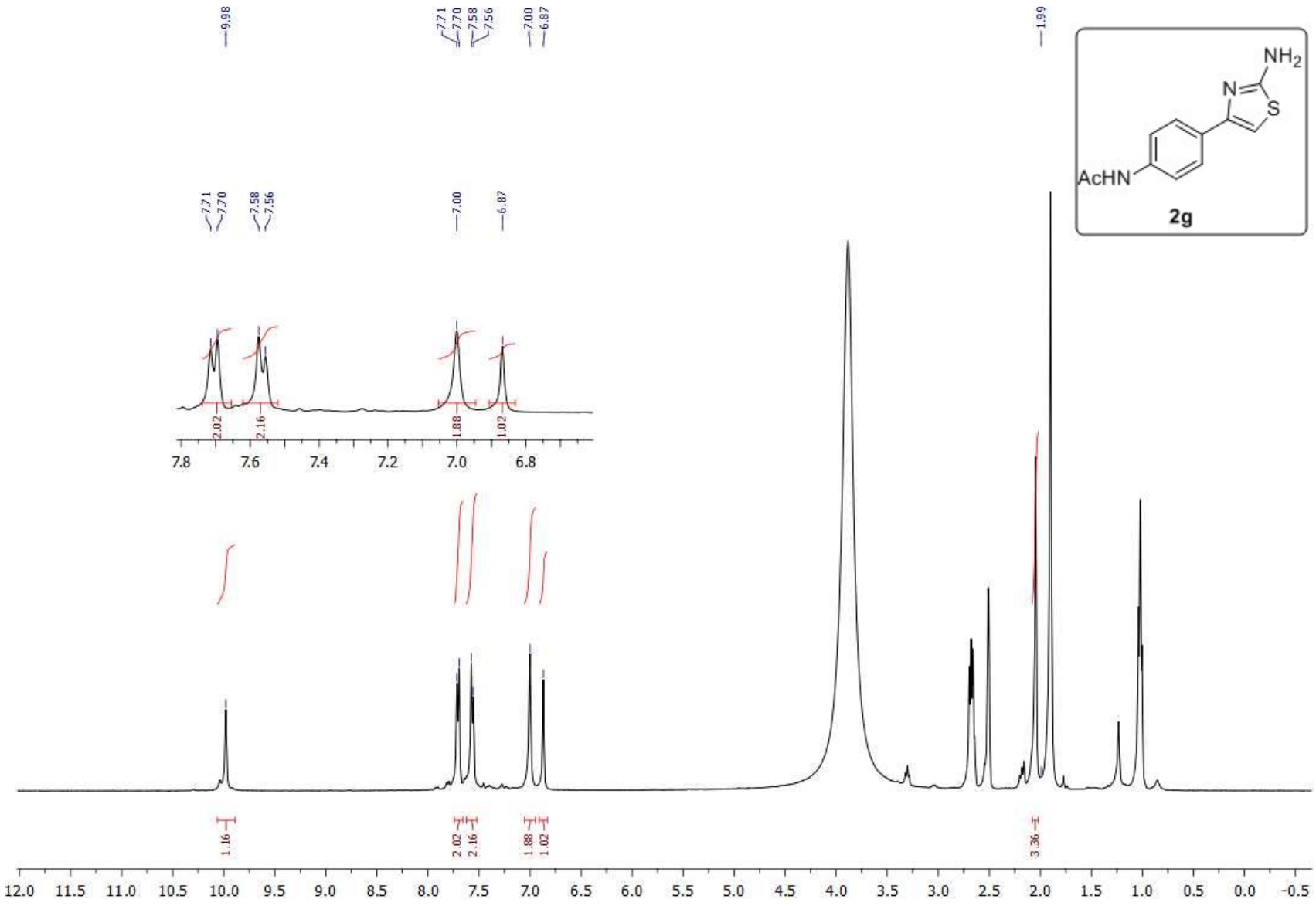

NH2
N
S
AcO
2e
7.69
7.67
7.54
7.49
7.41
7.39
7.37
7.07
7.01
6.99
2.28
1.04
1.01
0.99
2.97
1.12
3.00

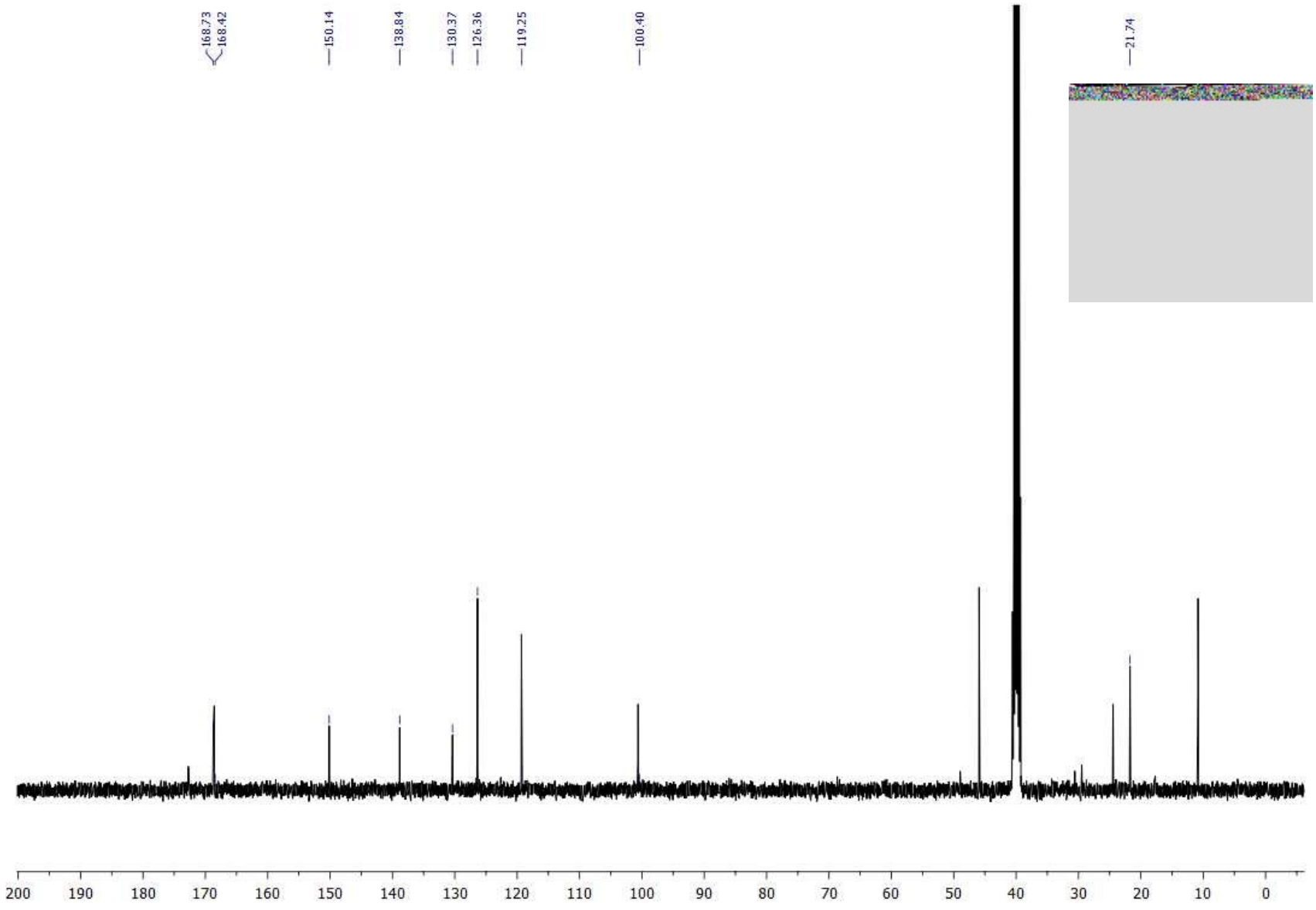

169.61
168.66
151.11
149.28
136.81
129.76
123.41
120.89
119.29
103.09
21.31
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

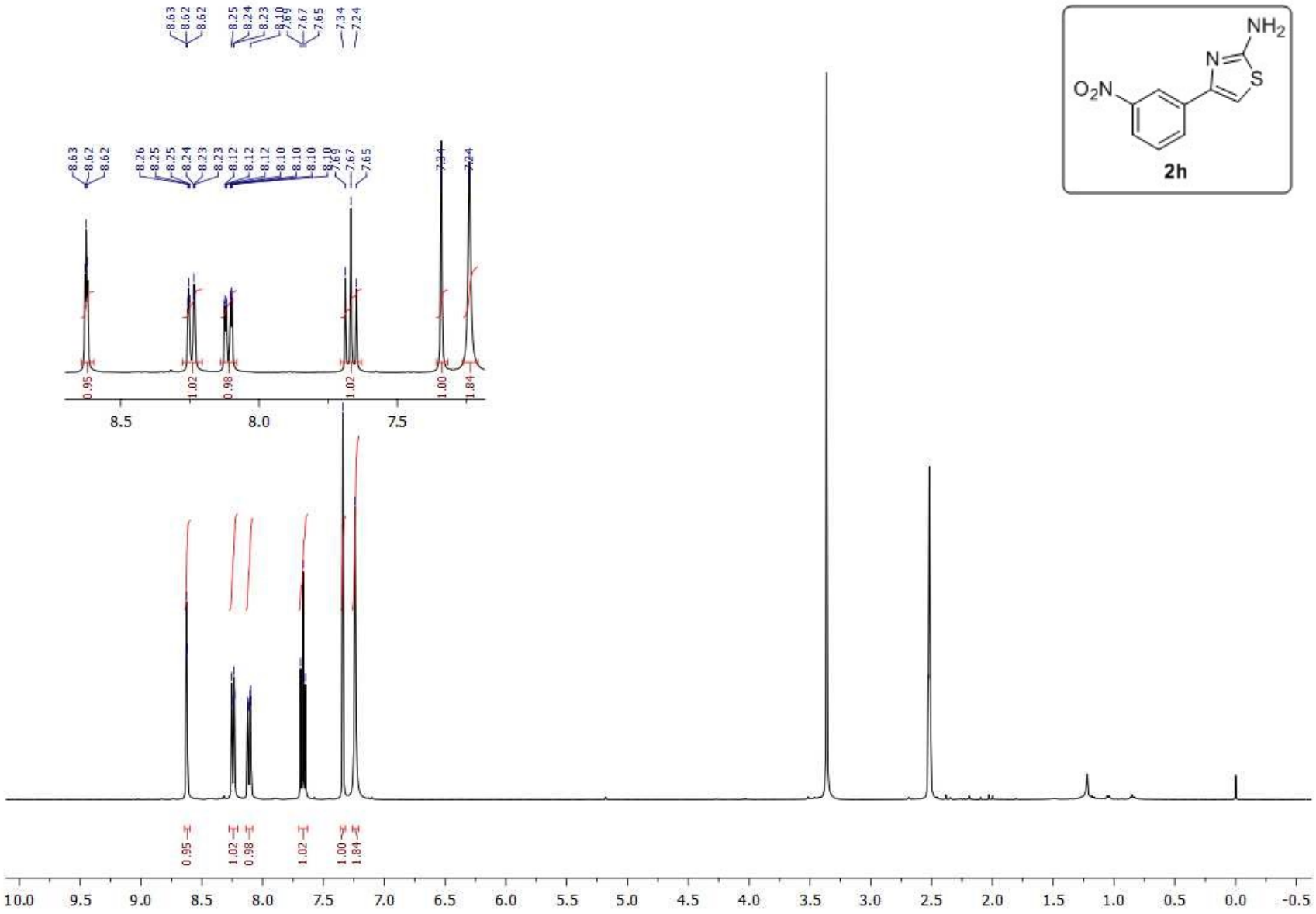

NLJ-V-56 #408 RT: 1.82 AV: 1 NL: 5.49E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]
235.0547
R=74407
C 11 H 11 O 2 N 2 S = 235.0536
4.9933 ppm
155.0642
R=90307
C 7 H 11 N 2 S = 155.0637
2.7913 ppm
169.1113
R=87302
188.0849
R=82707
130.1598
R=99807
221.0566
R=75207
253.0640
R=70907
277.0653
R=68307
299.0473
R=65807
337.1158
R=60502
391.2857
R=51106
415.0366
R=50606
Relative Abundance
m/z
NH2
N
S
AcO
2e
Chemical Formula: C11H10N2O2S
Exact Mass: 235.0463
Observed mass: 235.0536

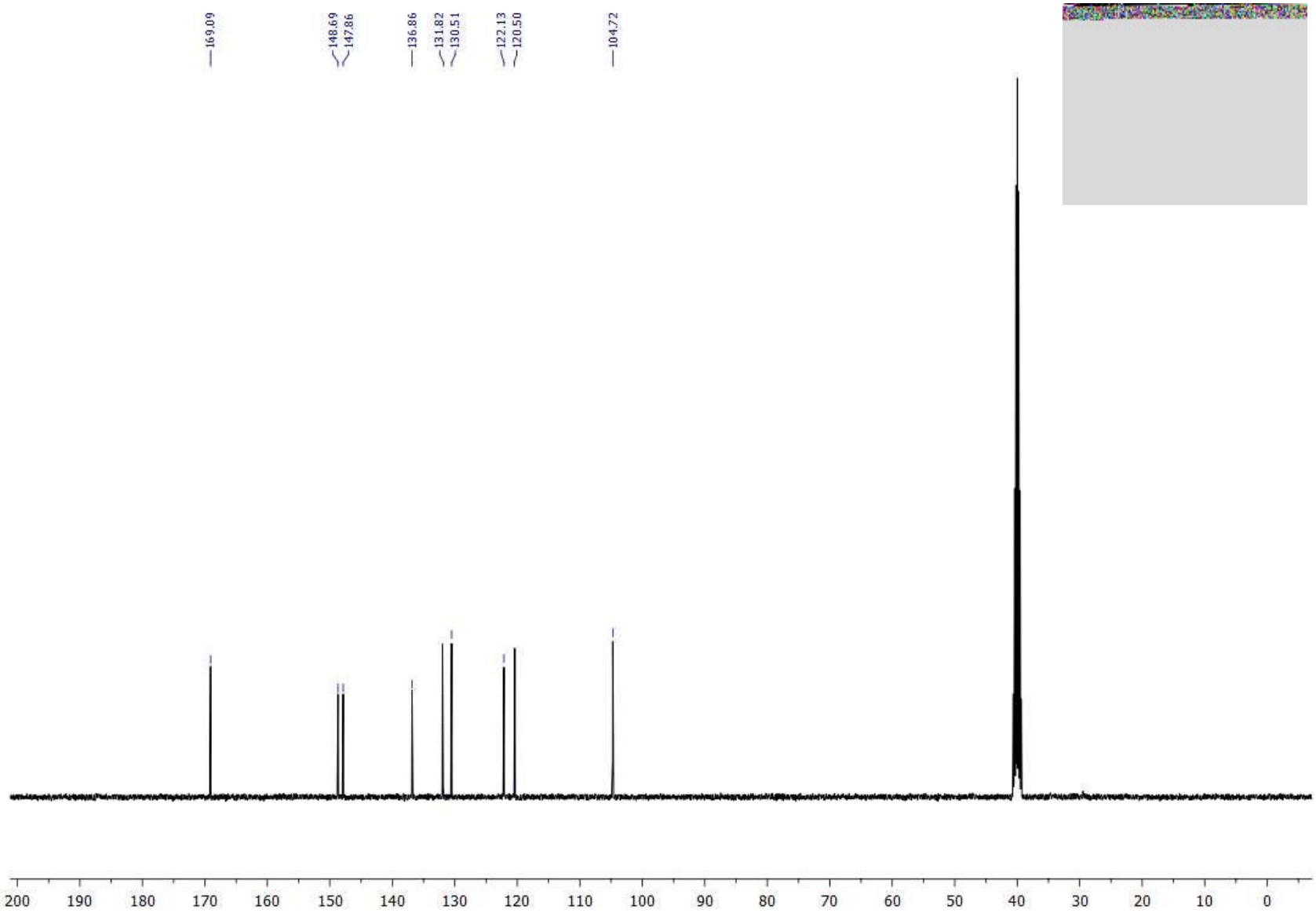

9.00
7.33
7.33
7.22
7.22
7.20
7.20
6.78
6.76
6.73
3.80
NH2
N
S
HO
MeO
2f
0.80
0.81
1.53
0.74
0.81
0.77
3.00

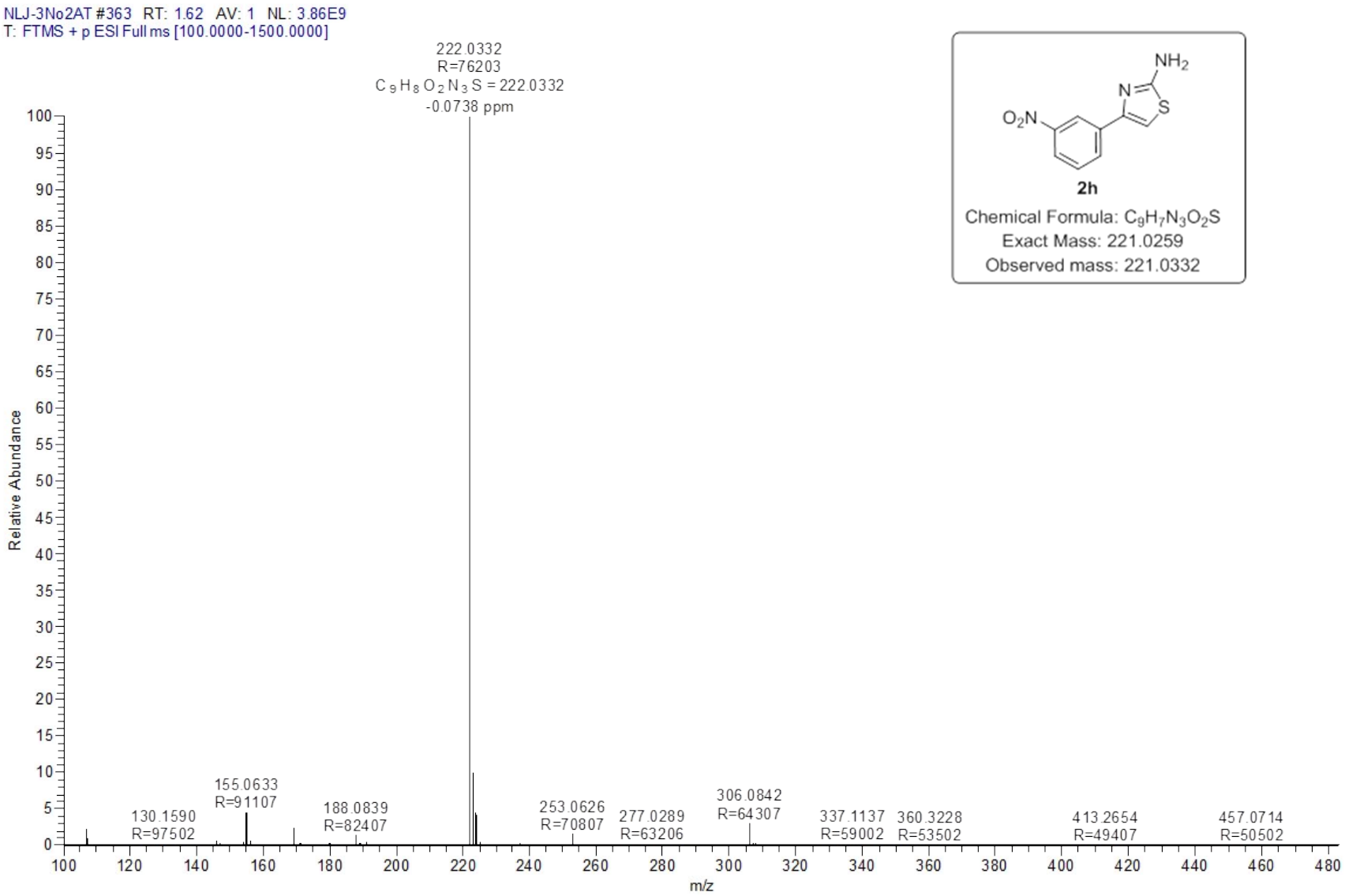

168.35
150.57
147.76
146.32
127.33
118.40
115.76
110.21
99.27
56.00
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

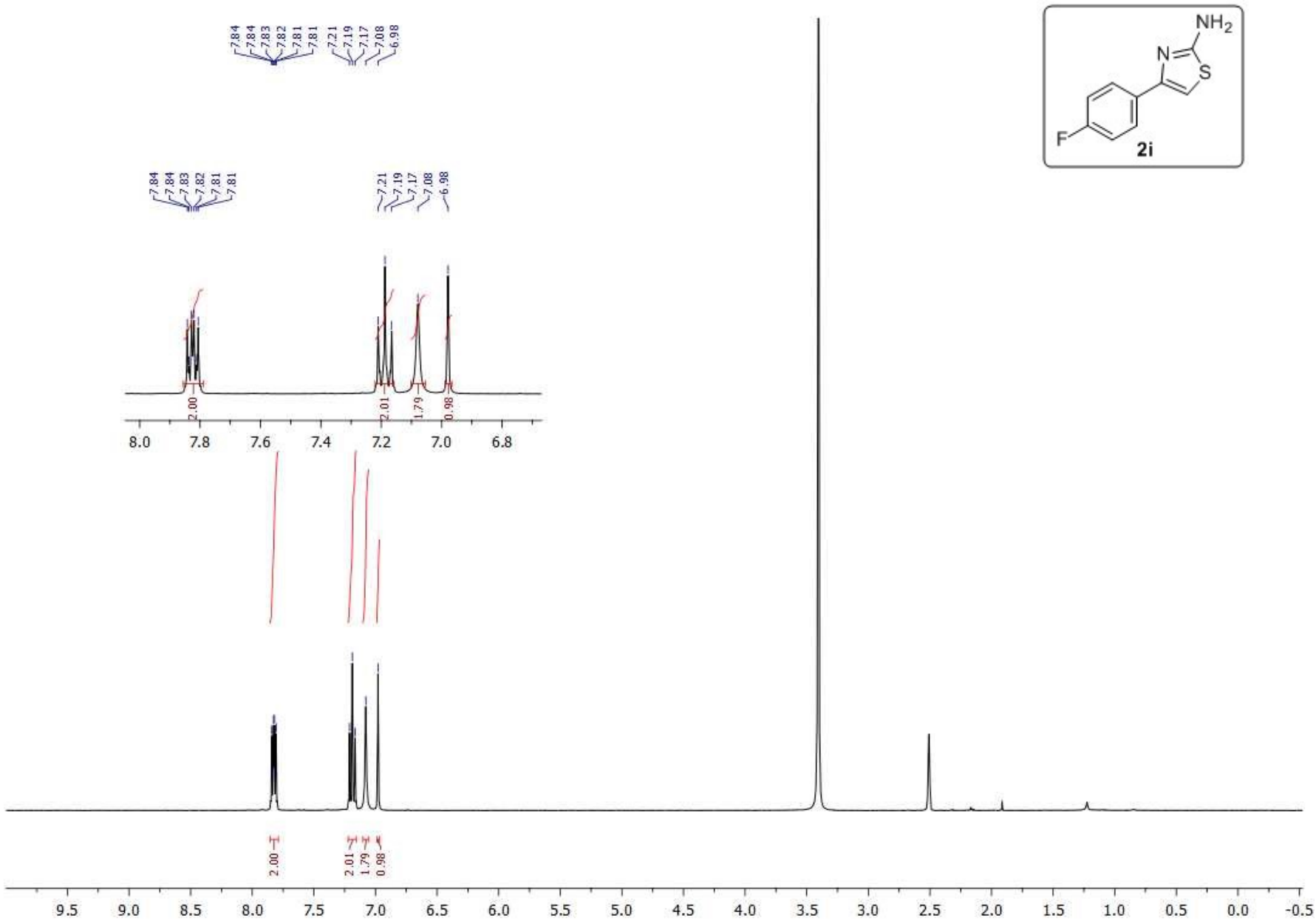

9.98
7.71
7.70
7.58
7.56
7.00
6.87
1.99
NH2
N
S
AcHN
2g
2.02
2.16
1.88
1.02
3.36

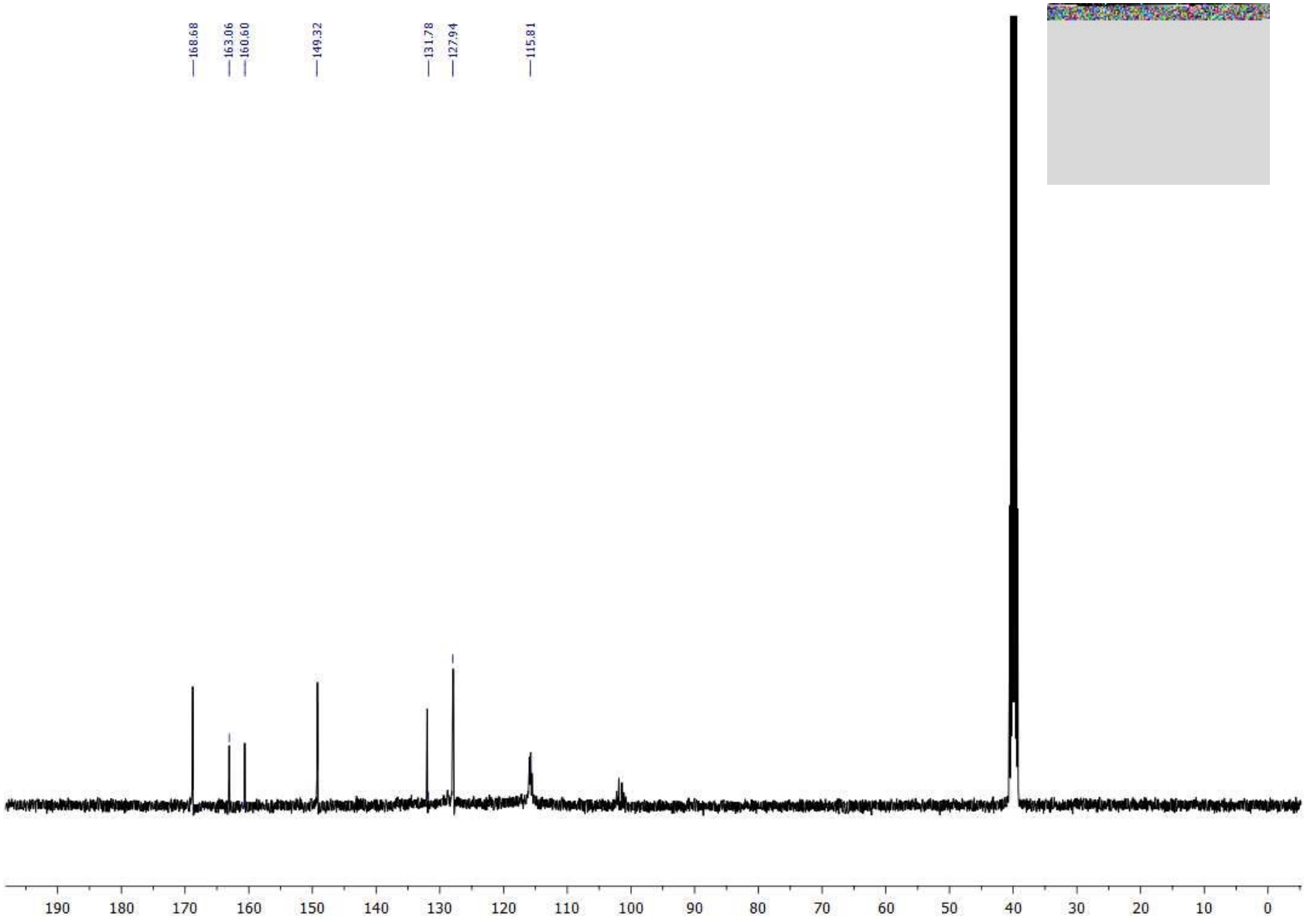

168.73
168.42
150.14
138.84
130.37
126.36
119.25
100.40
21.74
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

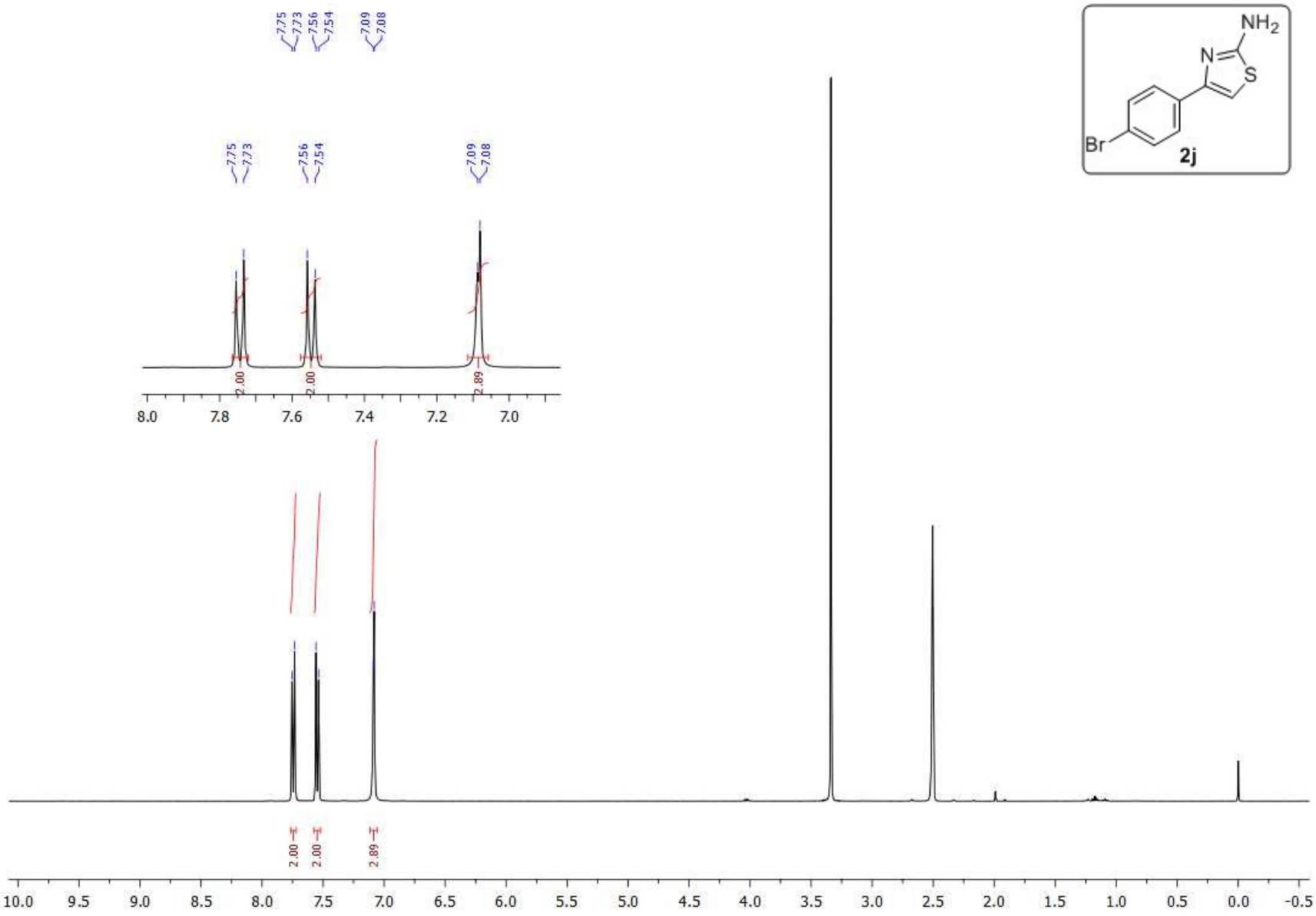

2h

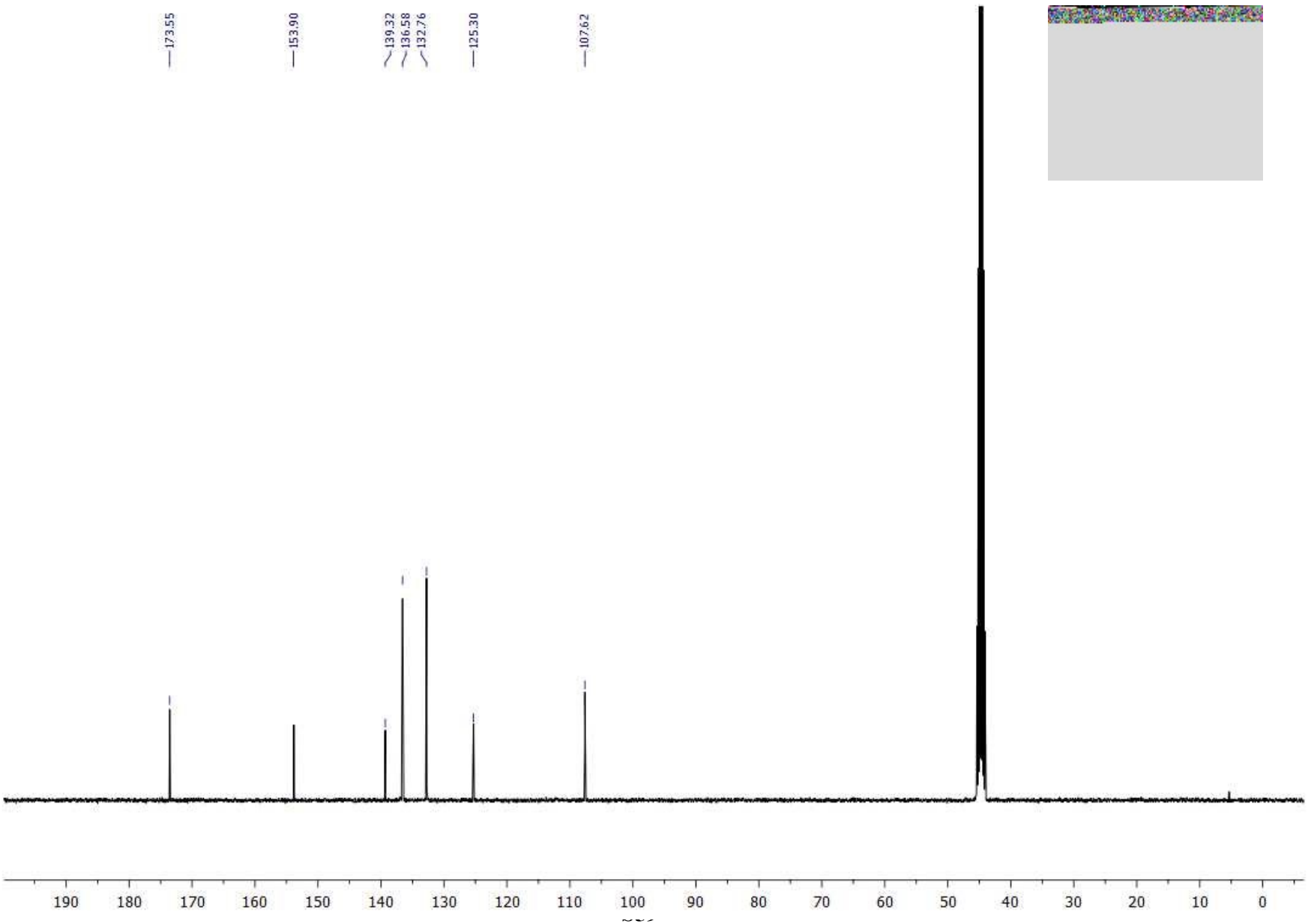

169.09
148.69
147.86
136.86
131.82
130.51
122.13
120.50
104.72
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

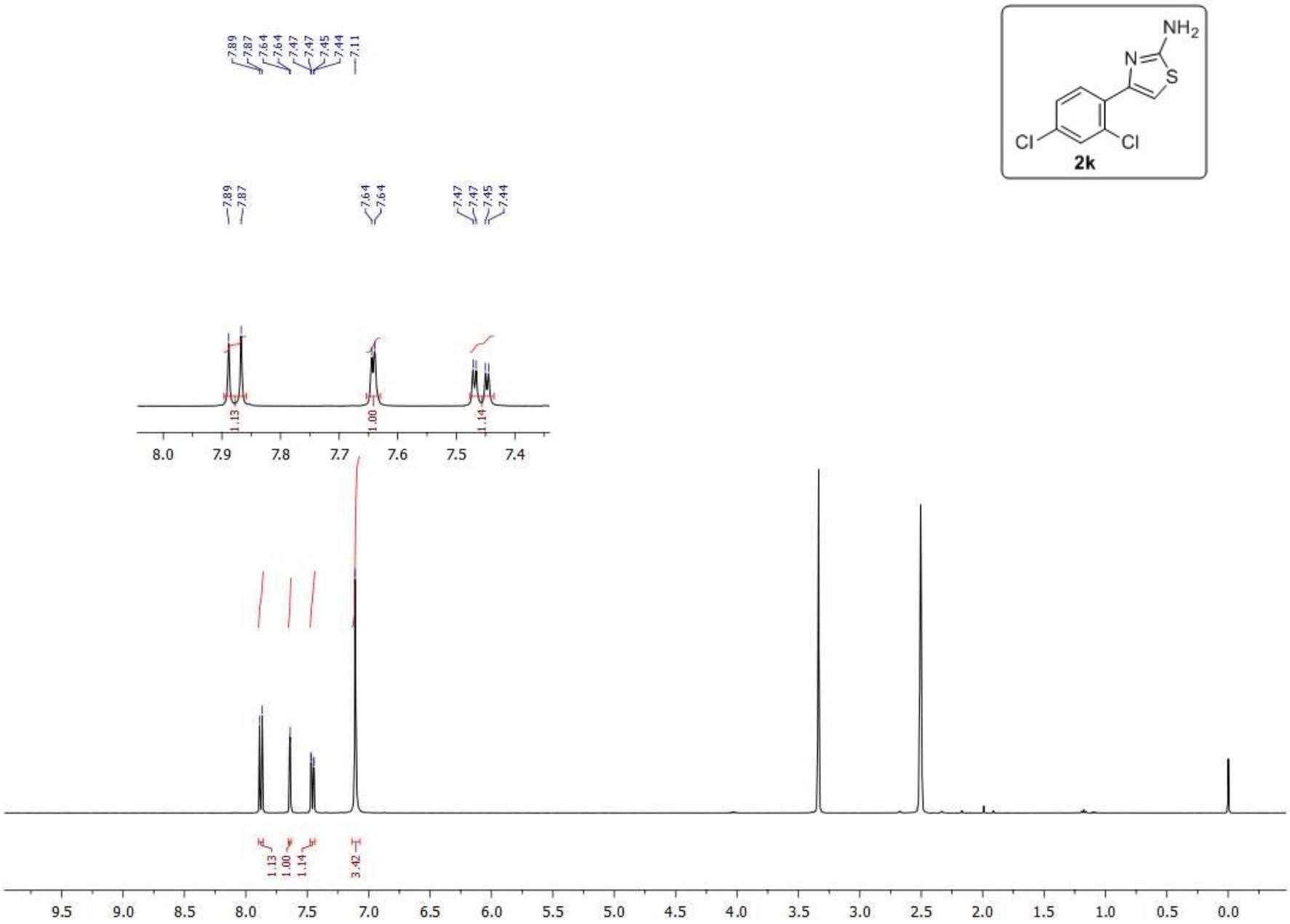

NLJ-3No2AT #363 RT: 1.62 AV: 1 NL: 3.86E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
222.0332
R=76203
C 9 H 8 O 2 N 3 S = 222.0332
-0.0738 ppm
Relative Abundance
m/z
130.1590
R=97502
155.0633
R=91107
188.0839
R=82407
253.0626
R=70807
277.0289
R=63206
306.0842
R=64307
337.1137
R=59002
360.3228
R=53502
413.2654
R=49407
457.0714
R=50502
2h
Chemical Formula: C9H7N3O2S
Exact Mass: 221.0259
Observed mass: 221.0332

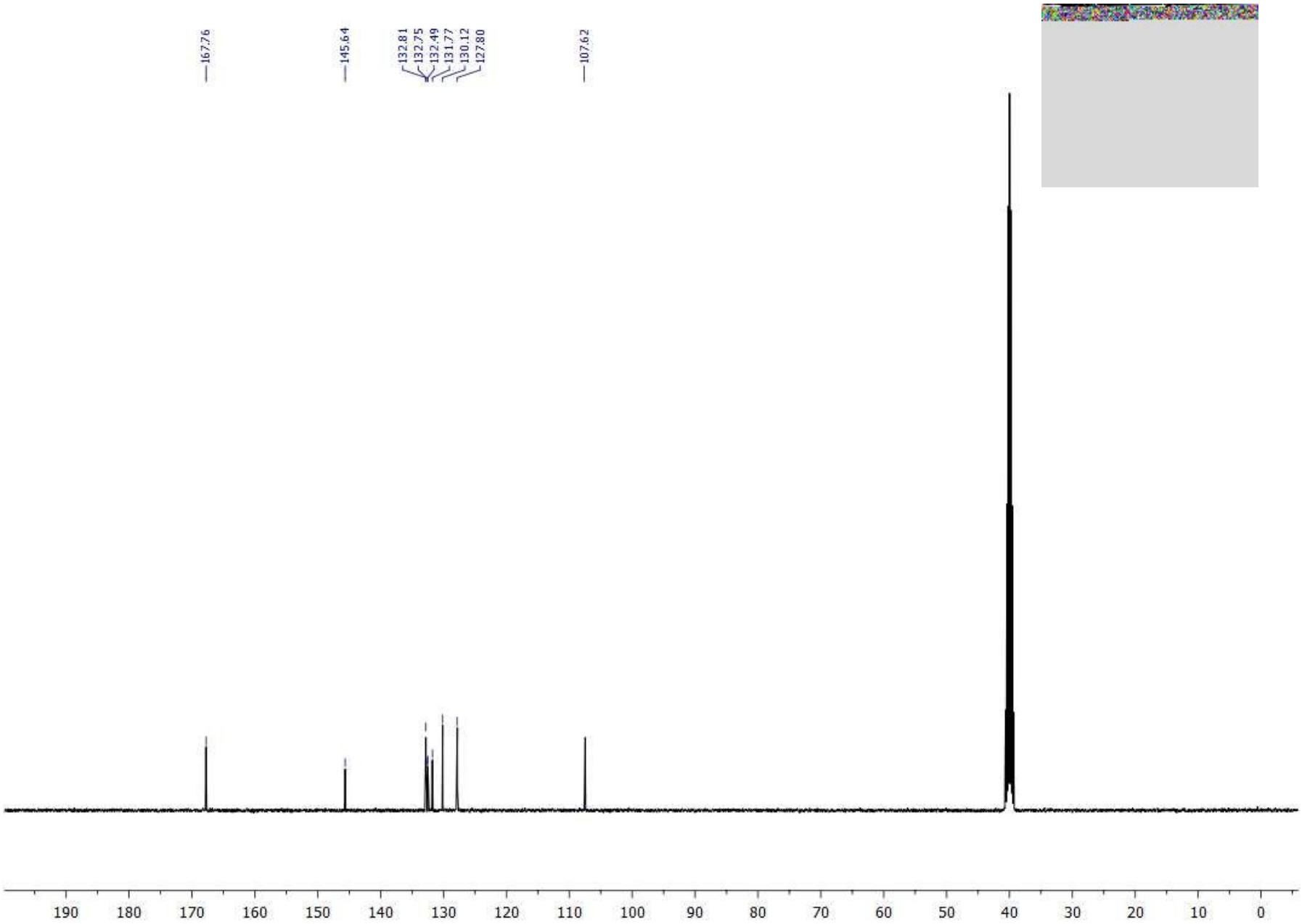

7.84
7.84
7.83
7.82
7.81
7.81
7.21
7.19
7.17
7.08
6.98
2.00
2.01
1.79
0.98
8.0
7.8
7.6
7.4
7.2
7.0
6.8
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
NH2
N
S
F
2i

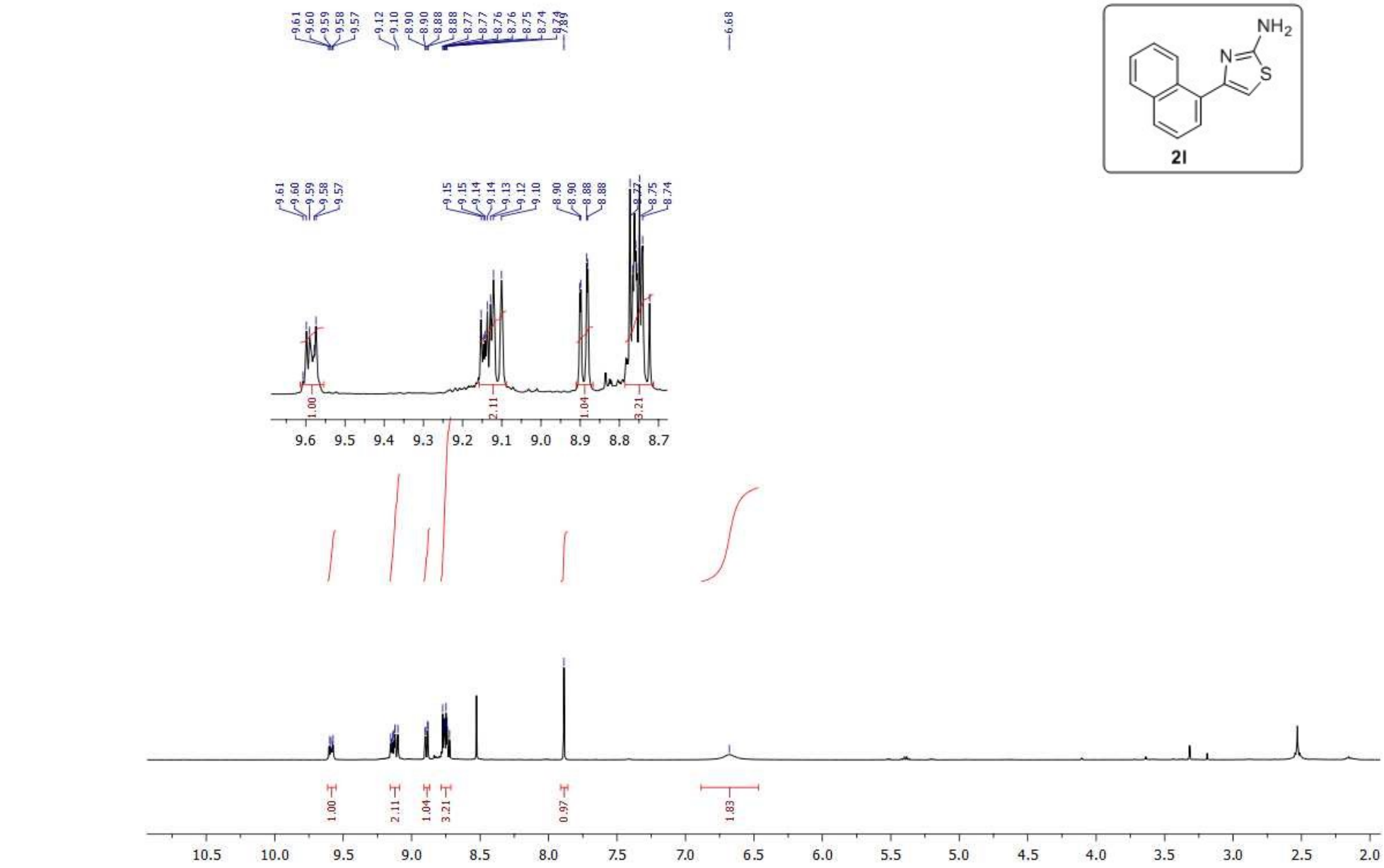

168.68
163.06
160.60
149.32
131.78
127.94
115.81
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

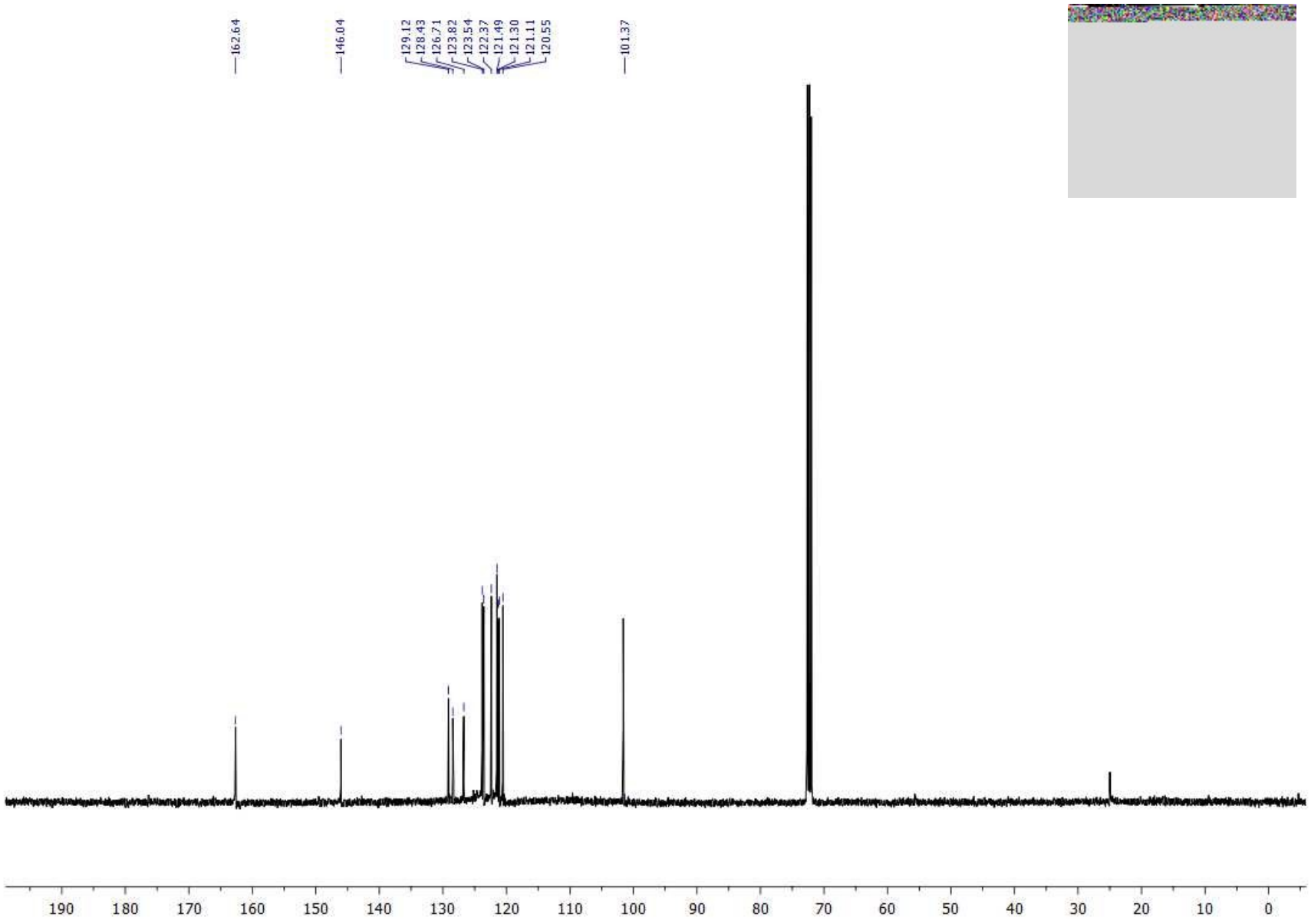

7.75
7.73
7.56
7.54
7.09
7.08
2.00
2.00
2.89
8.0
7.8
7.6
7.4
7.2
7.0
NH2
N
S
Br
2j
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

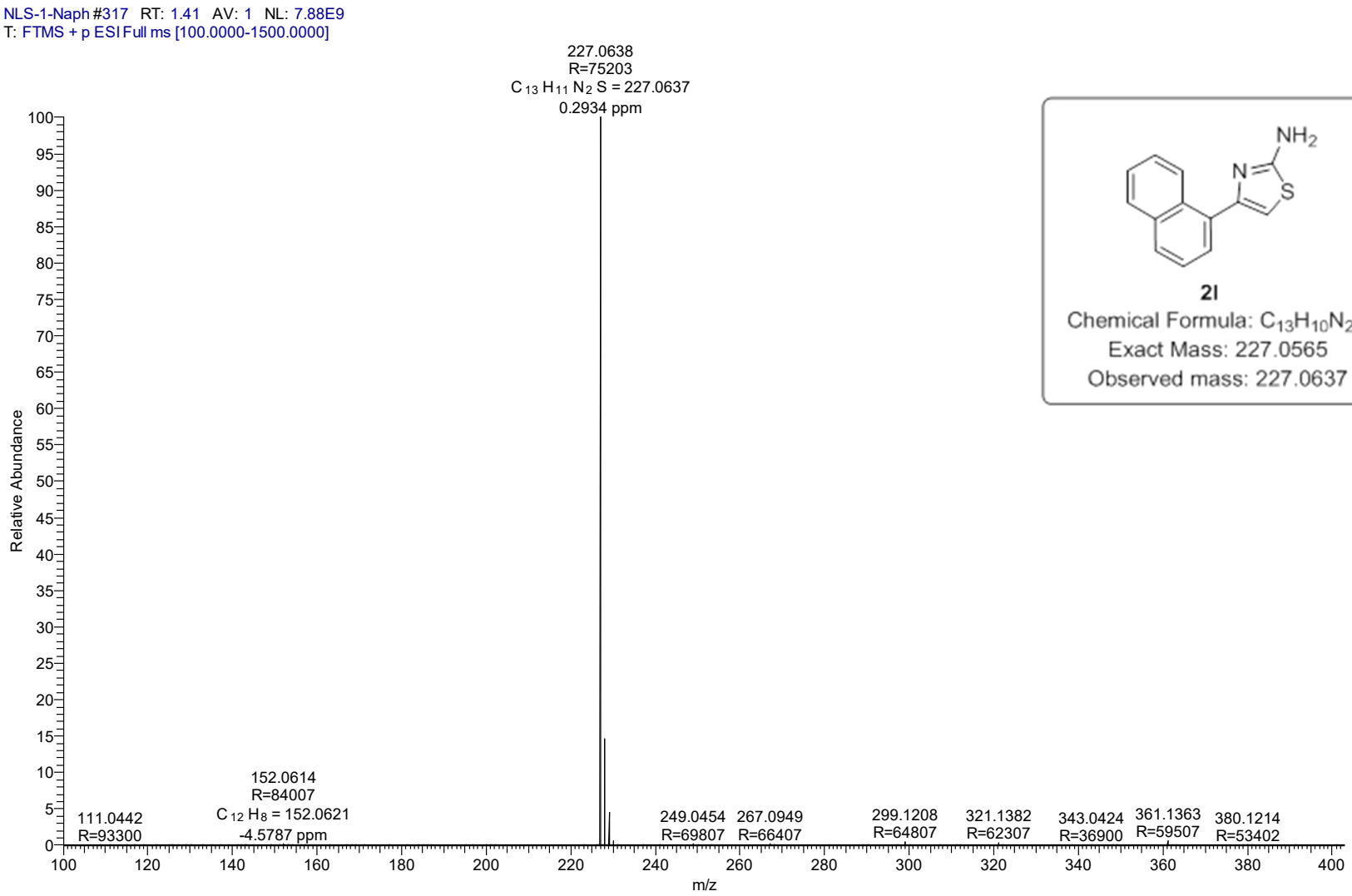

173.55
153.90
139.32
136.58
132.76
125.30
107.62
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

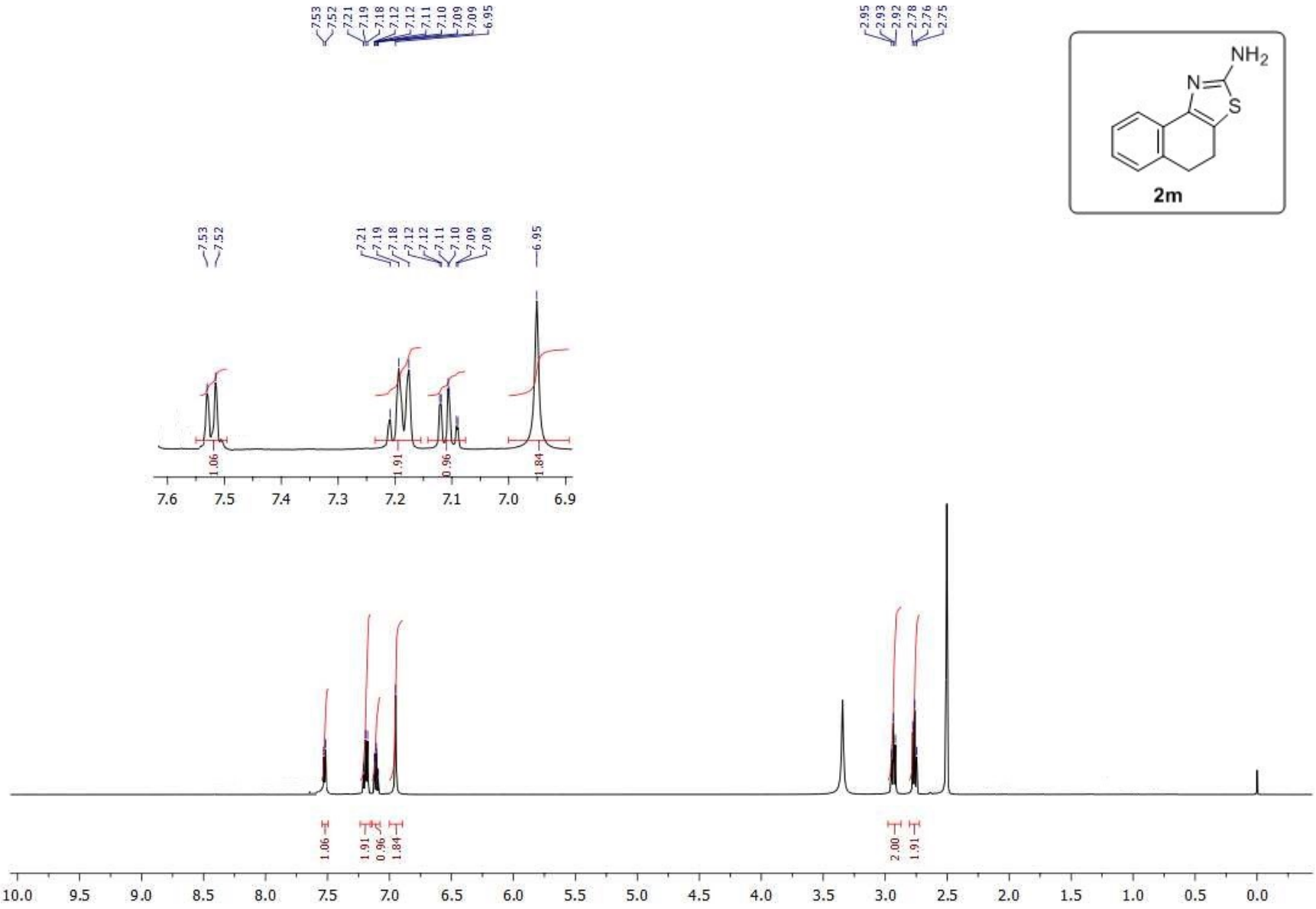

7.89
7.87
7.64
7.64
7.47
7.47
7.45
7.44
7.11
1.13
1.00
1.14
3.42
NH2
N
S
Cl
Cl
2k

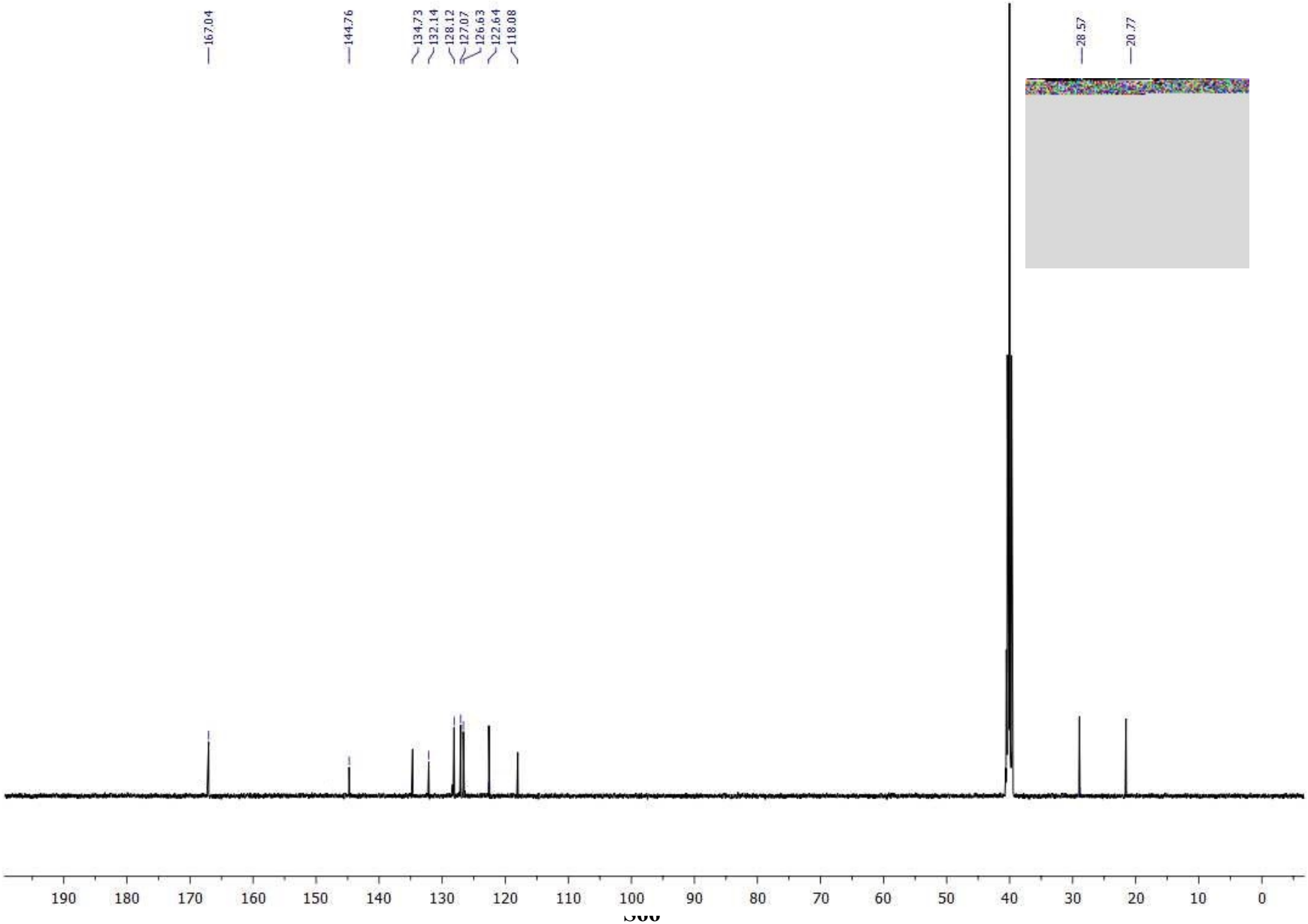

167.76
145.64
132.81
132.75
132.49
131.77
130.12
127.80
107.62
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

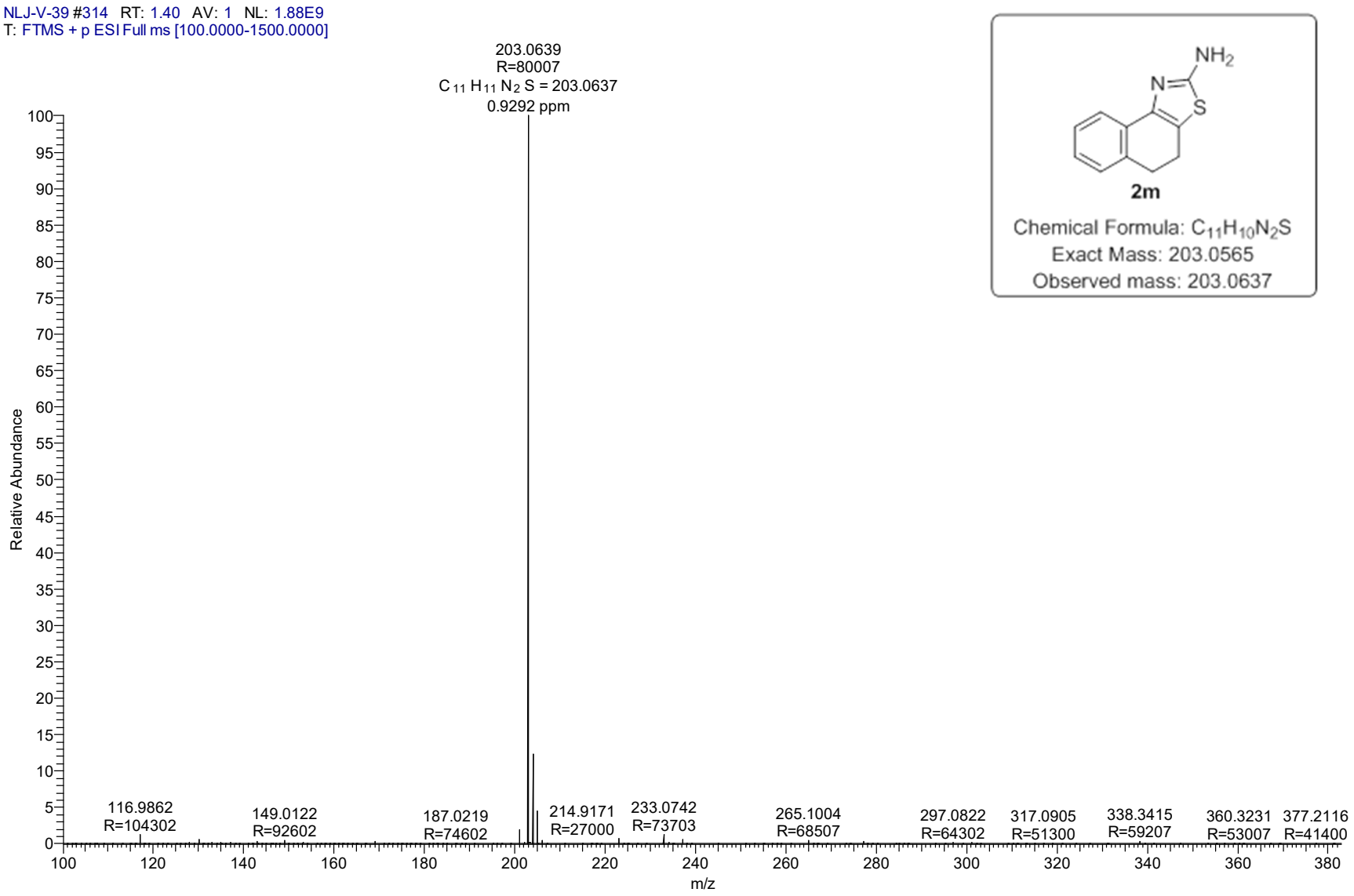

NH2
N
S
2l

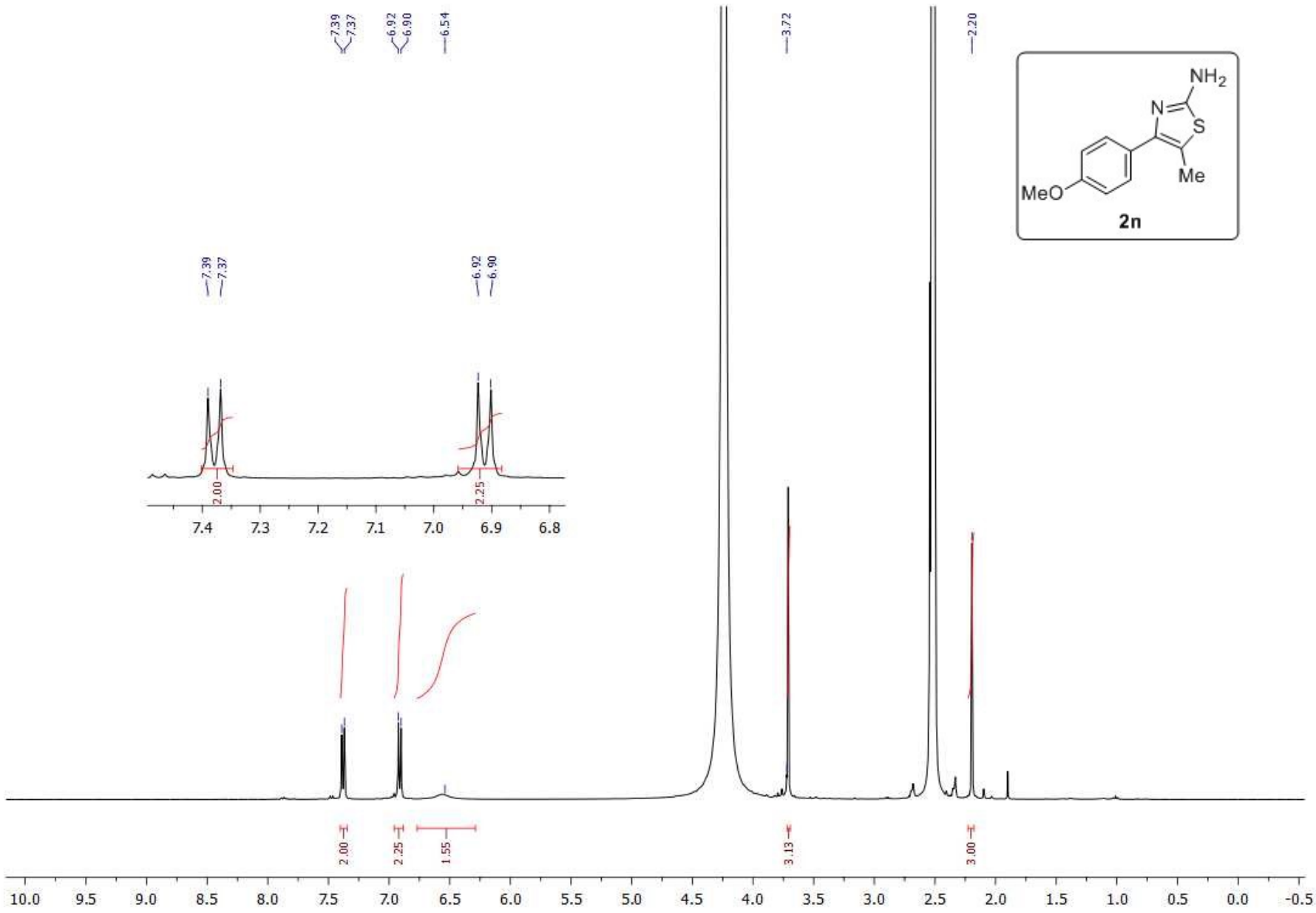

162.64
146.04
129.12
128.43
126.71
123.82
123.54
122.37
121.49
121.30
121.11
120.55
101.37
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

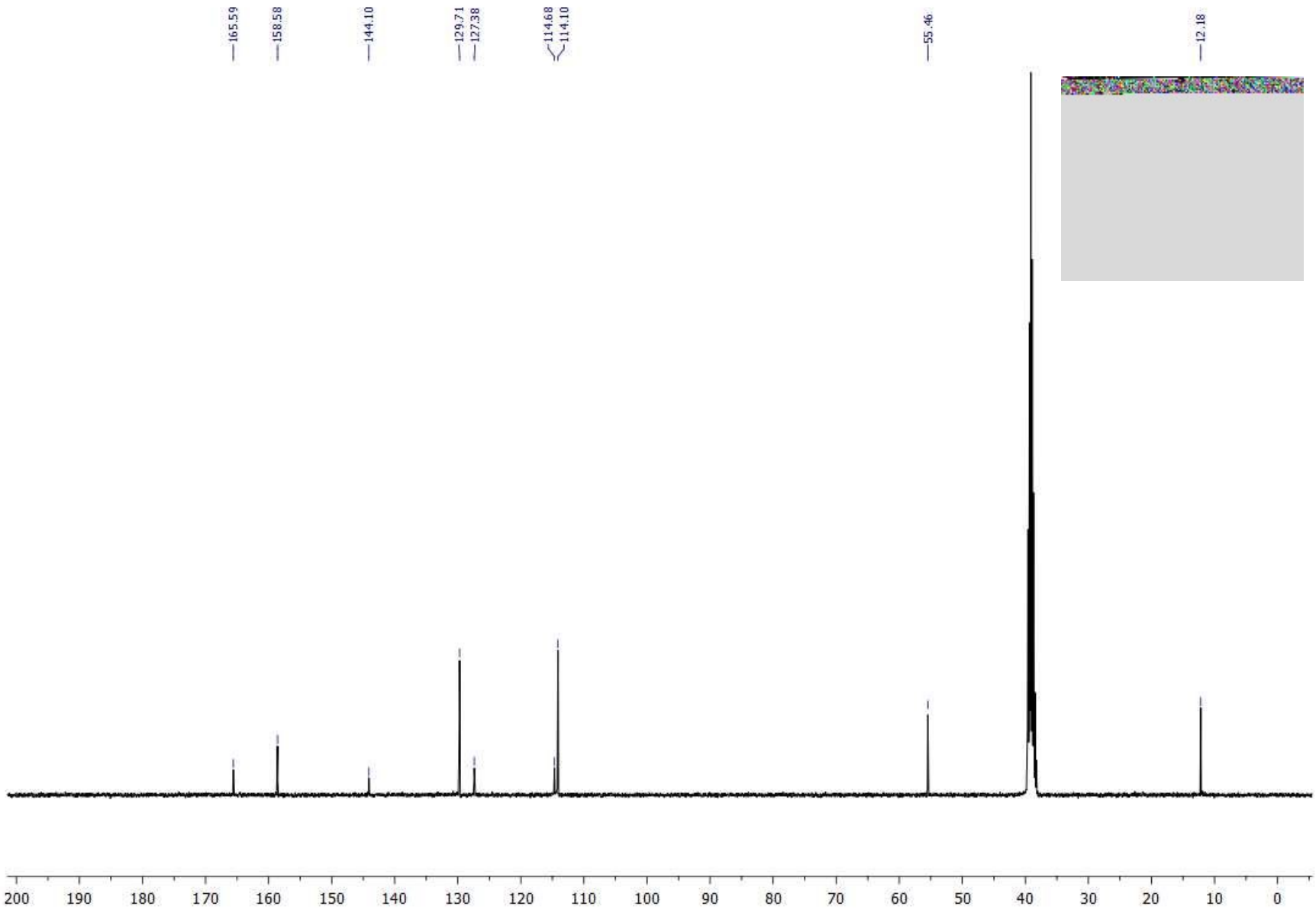

NLS-1-Naph #317 RT: 1.41 AV: 1 NL: 7.88E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
227.0638
R=75203
C 13 H 11 N 2 S = 227.0637
0.2934 ppm
Relative Abundance
m/z
111.0442
R=93300
152.0614
R=84007
C 12 H 8 = 152.0621
-4.5787 ppm
249.0454
R=69807
267.0949
R=66407
299.1208
R=64807
321.1382
R=62307
343.0424
R=36900
361.1363
R=59507
380.1214
R=53402
NH2
N
S
2l
Chemical Formula: C13H10N2S
Exact Mass: 227.0565
Observed mass: 227.0637

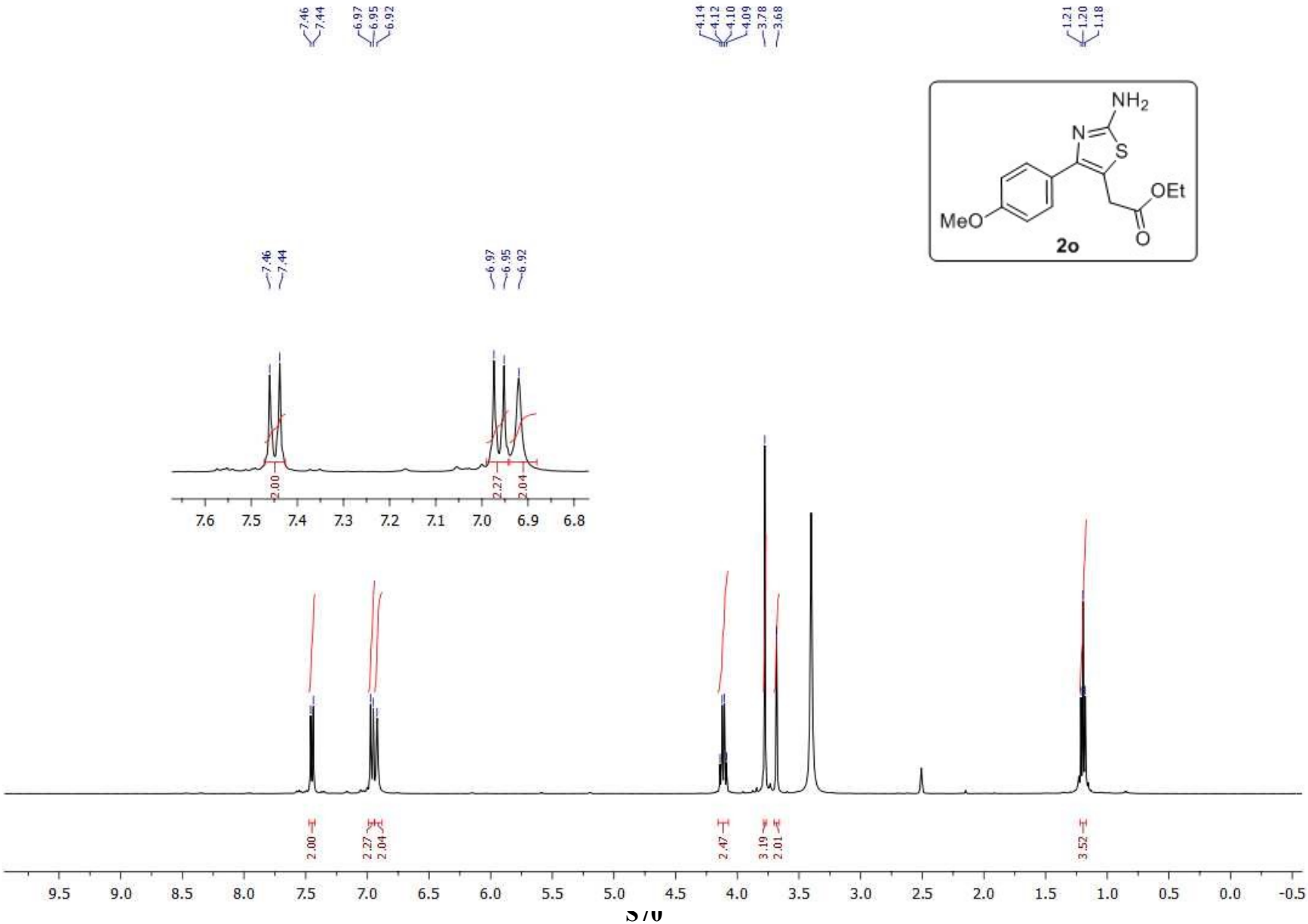

7.53
7.52
7.21
7.19
7.18
7.12
7.12
7.11
7.10
7.09
7.09
6.95
2.95
2.93
2.92
2.78
2.76
2.75
NH2
N
S
2m
1.06
1.91
0.96
1.84
2.00
1.91
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

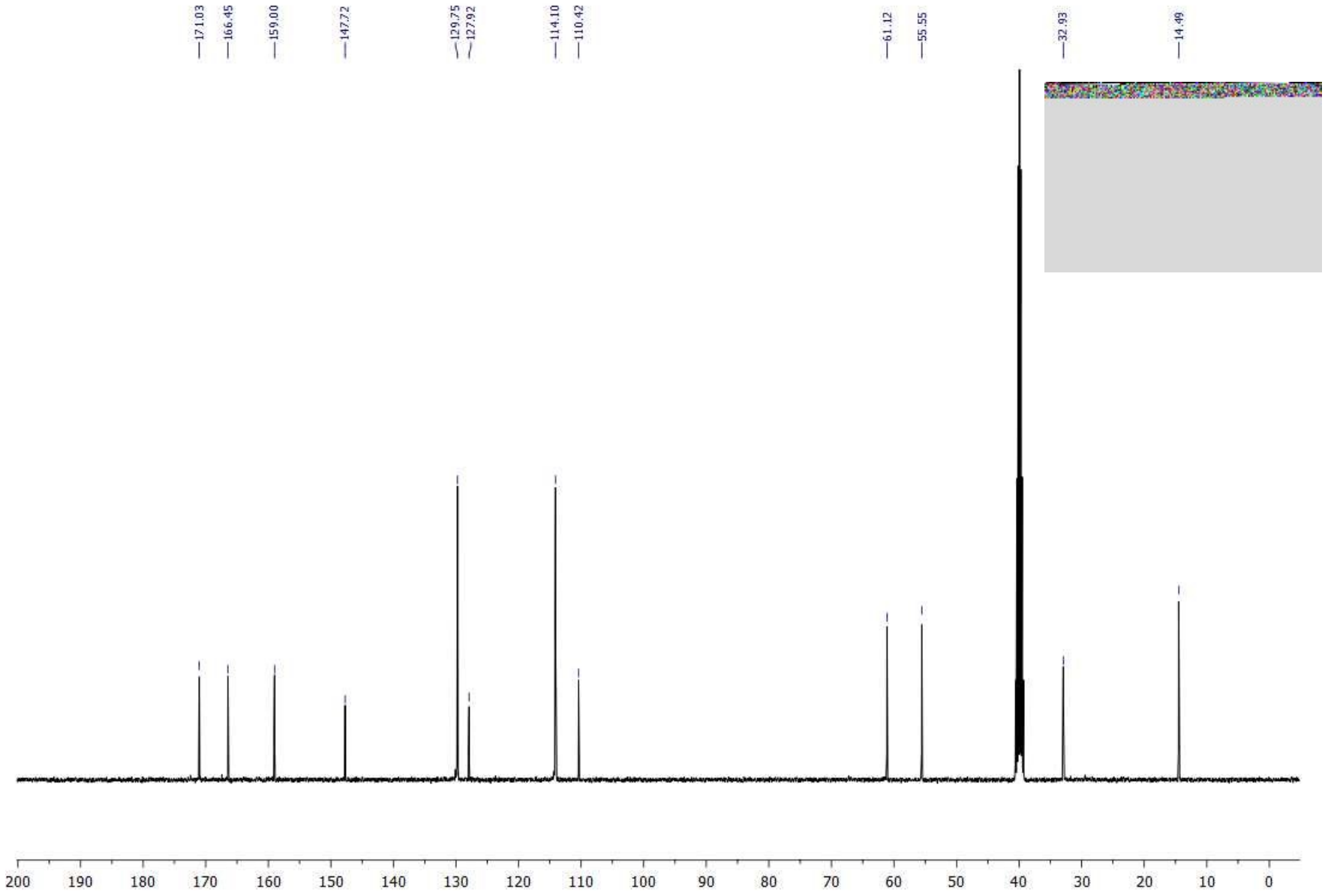

167.04
144.76
134.73
132.14
128.12
127.07
126.63
122.64
118.08
28.57
20.77
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

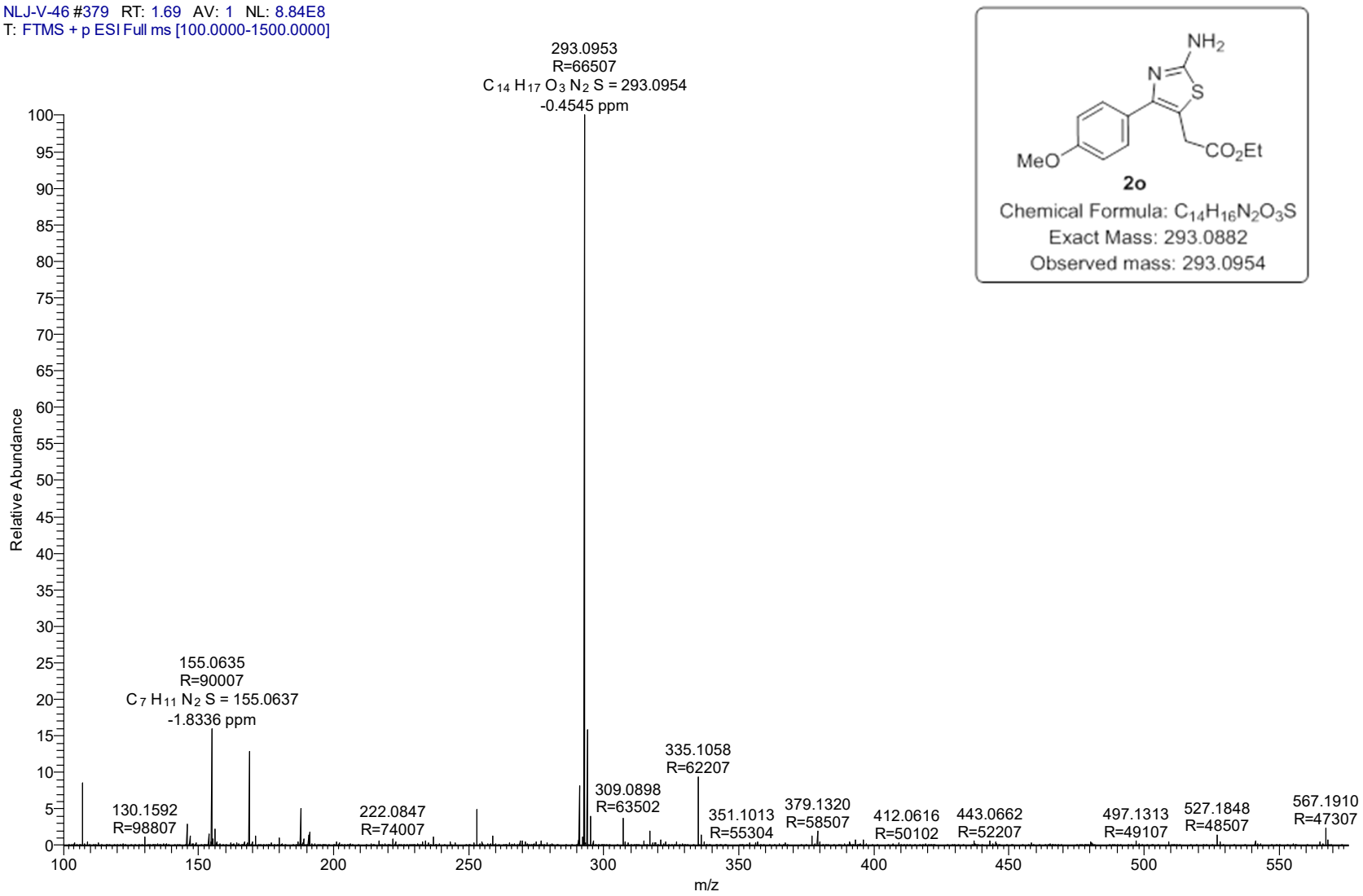

NLJ-V-39 #314 RT: 1.40 AV: 1 NL: 1.88E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
203.0639
R=80007
C 11 H 11 N 2 S = 203.0637
0.9292 ppm
NH2
N
S
2m
Chemical Formula: C11H10N2S
Exact Mass: 203.0565
Observed mass: 203.0637
Relative Abundance
m/z
116.9862
R=104302
149.0122
R=92602
187.0219
R=74602
214.9171
R=27000
233.0742
R=73703
265.1004
R=68507
297.0822
R=64302
317.0905
R=51300
338.3415
R=59207
360.3231
R=53007
377.2116
R=41400

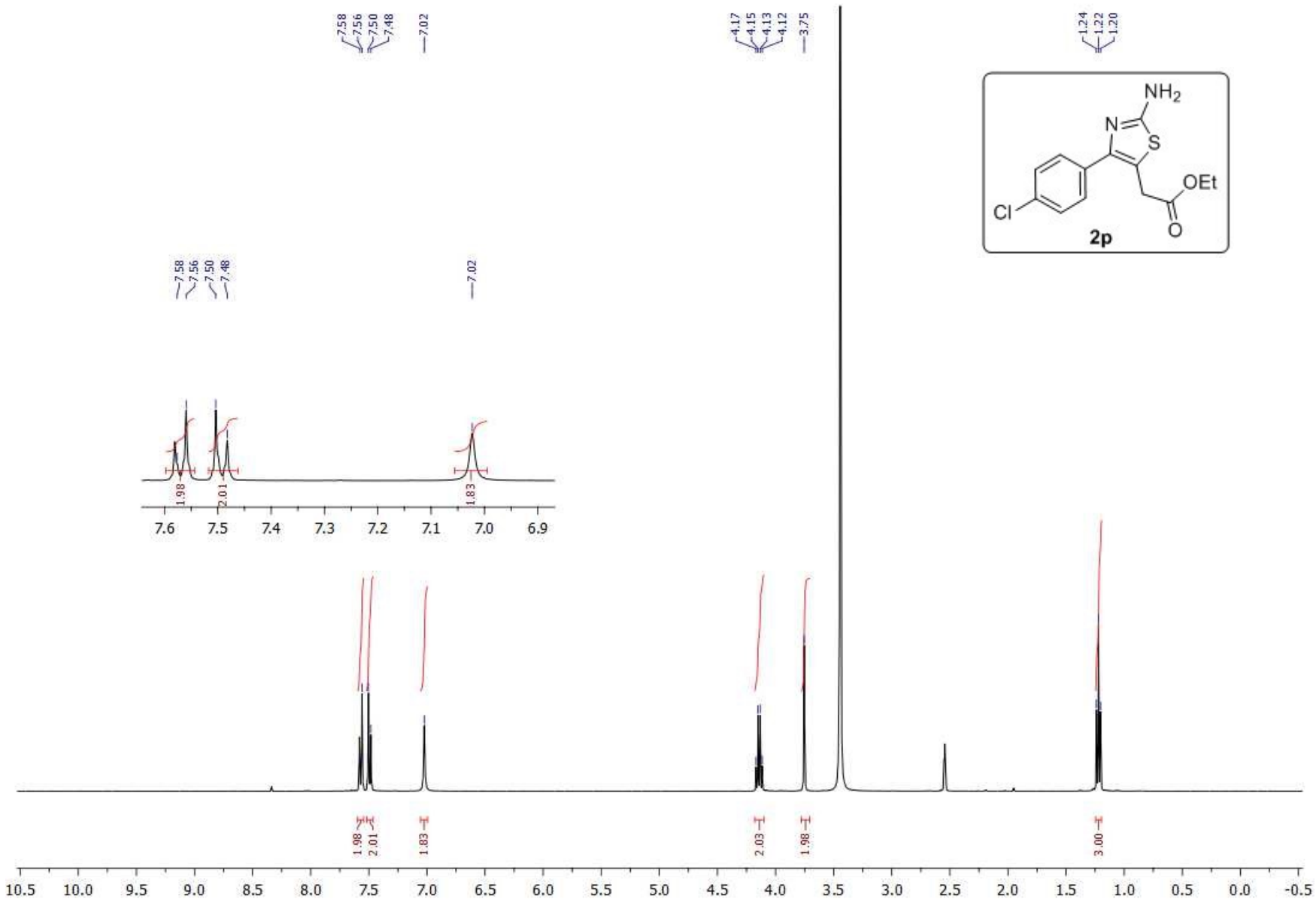

7.39
7.37
6.92
6.90
6.54
3.72
2.20
NH2
N
S
Me
MeO
2n
2.00
2.25
7.4
7.3
7.2
7.1
7.0
6.9
6.8
1.55
3.13
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

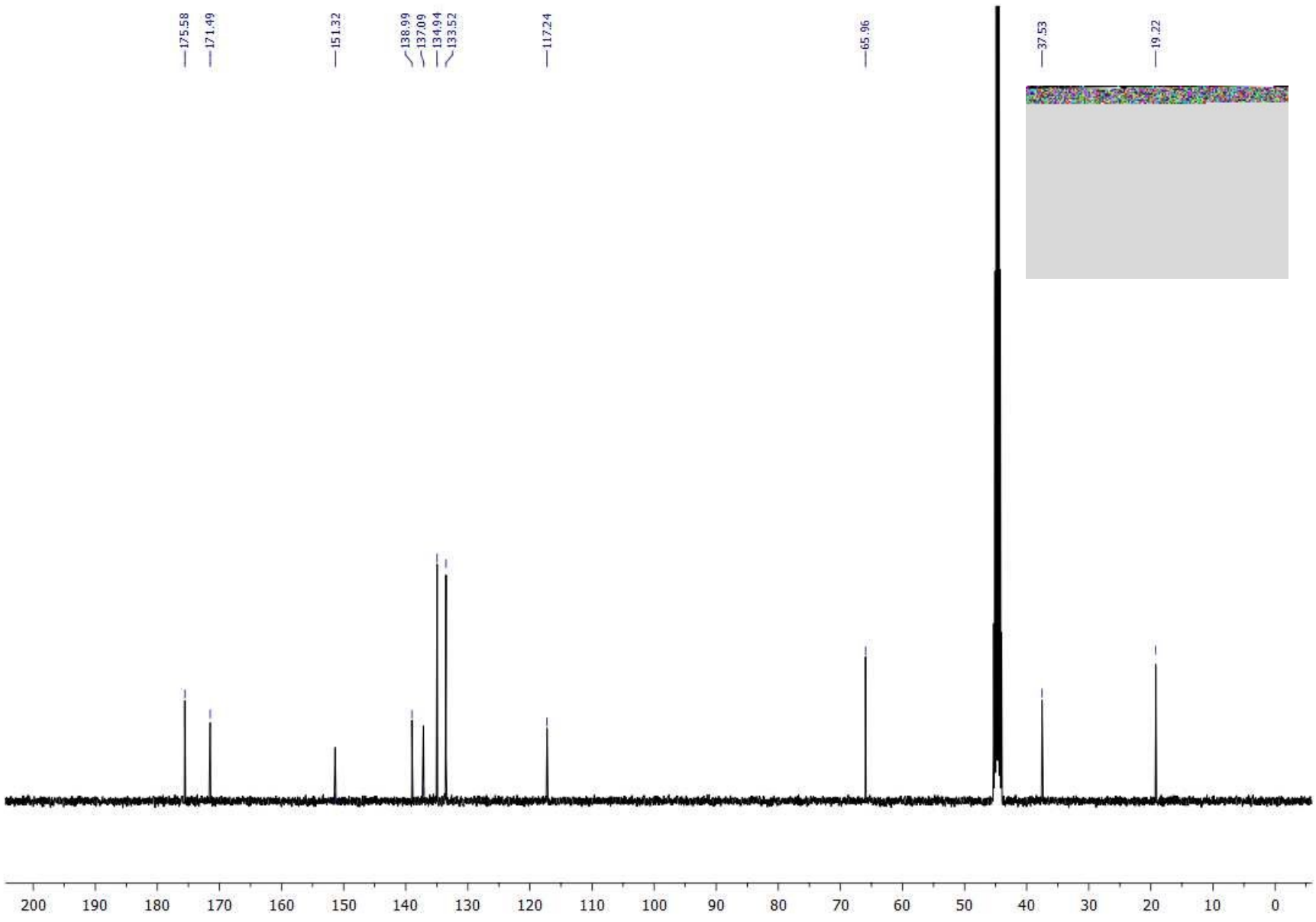

165.59
158.58
144.10
129.71
127.38
114.68
114.10
55.46
12.18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

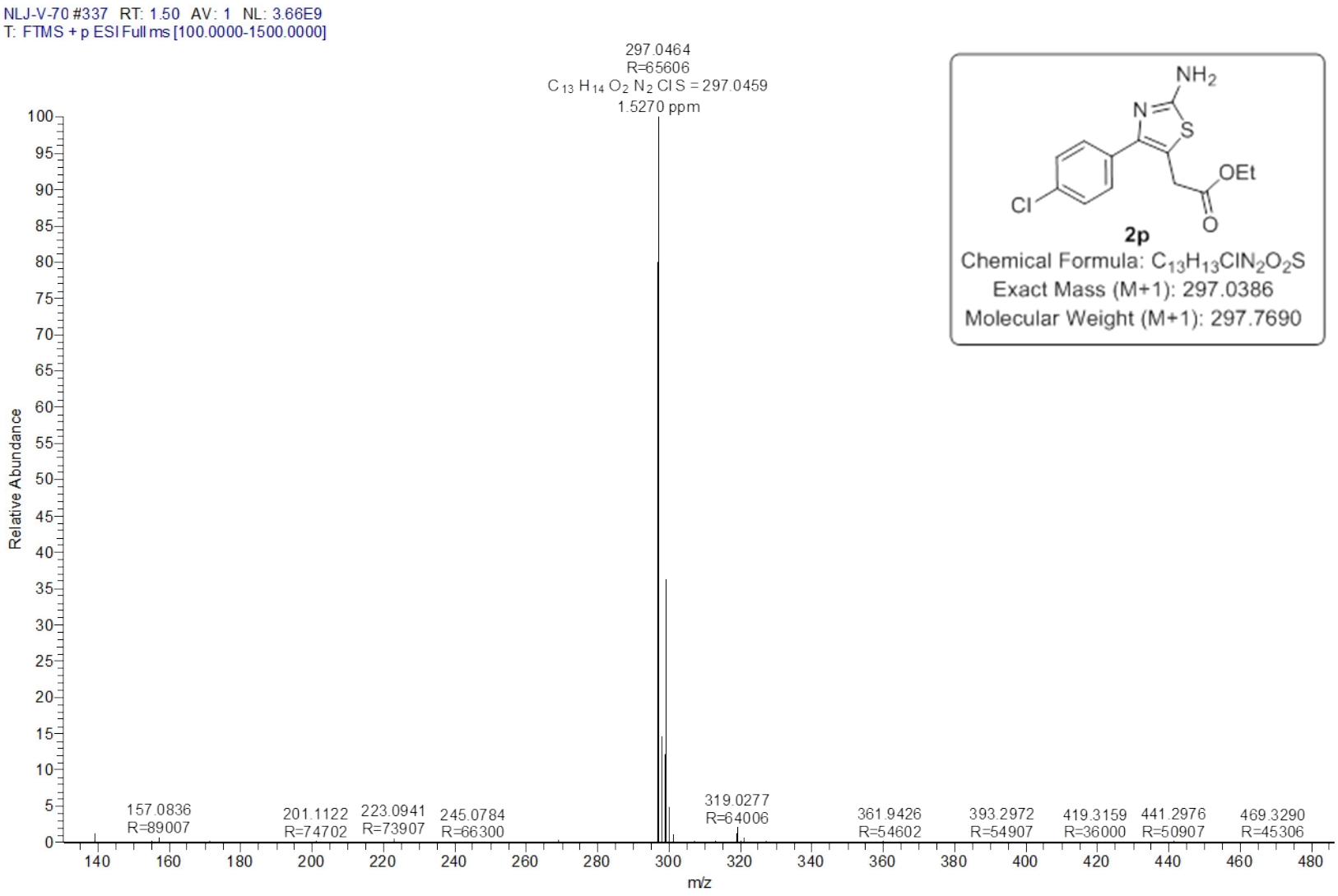

7.46
7.44
6.97
6.95
6.92
4.14
4.12
4.10
4.09
3.78
3.68
1.21
1.20
1.18
NH2
N
S
OEt
MeO
O
2o
2.00
2.27
2.04
2.47
3.19
2.01
3.52

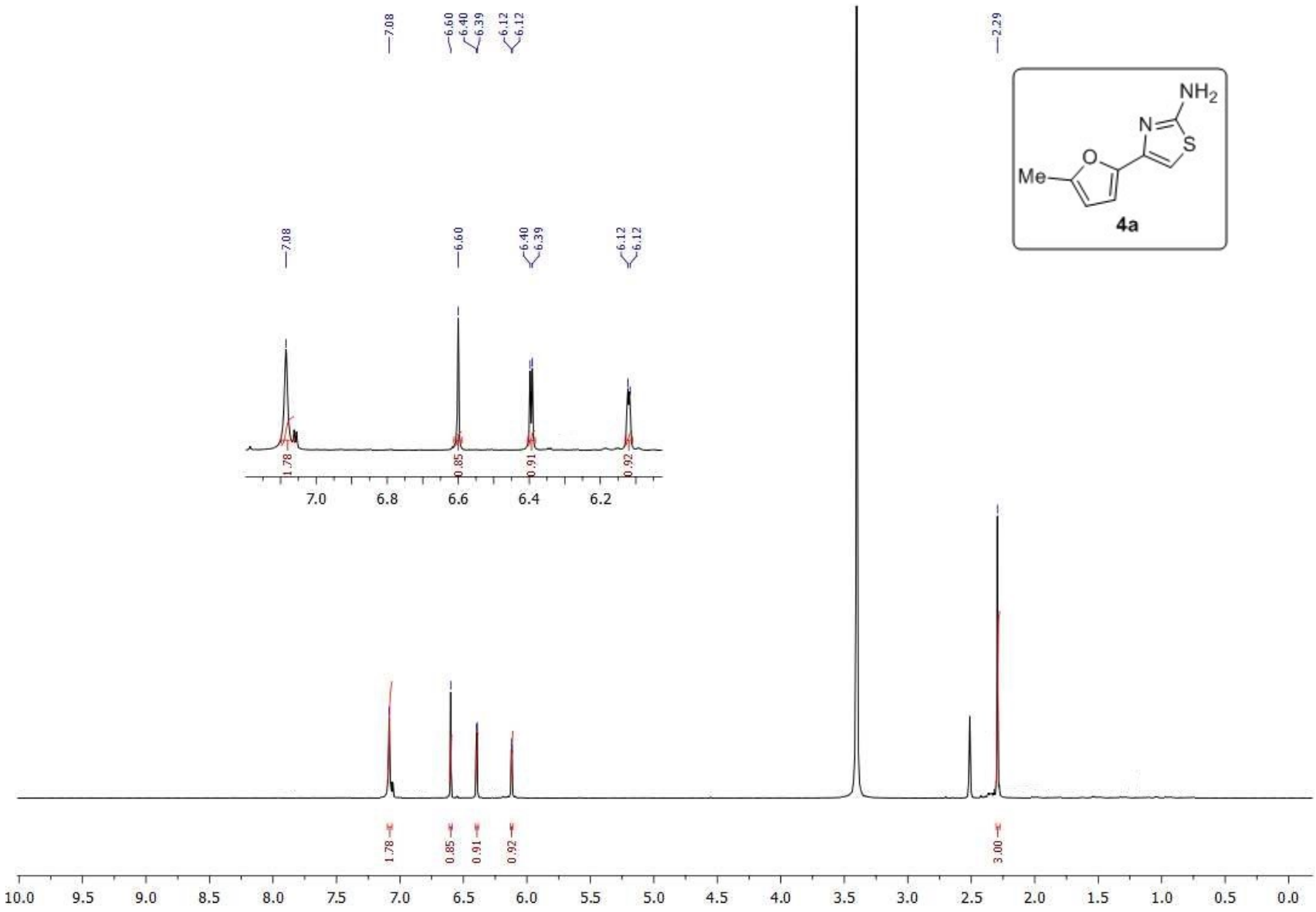

171.03
166.45
159.00
147.72
129.75
127.92
114.10
110.42
61.12
55.55
32.93
14.49
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

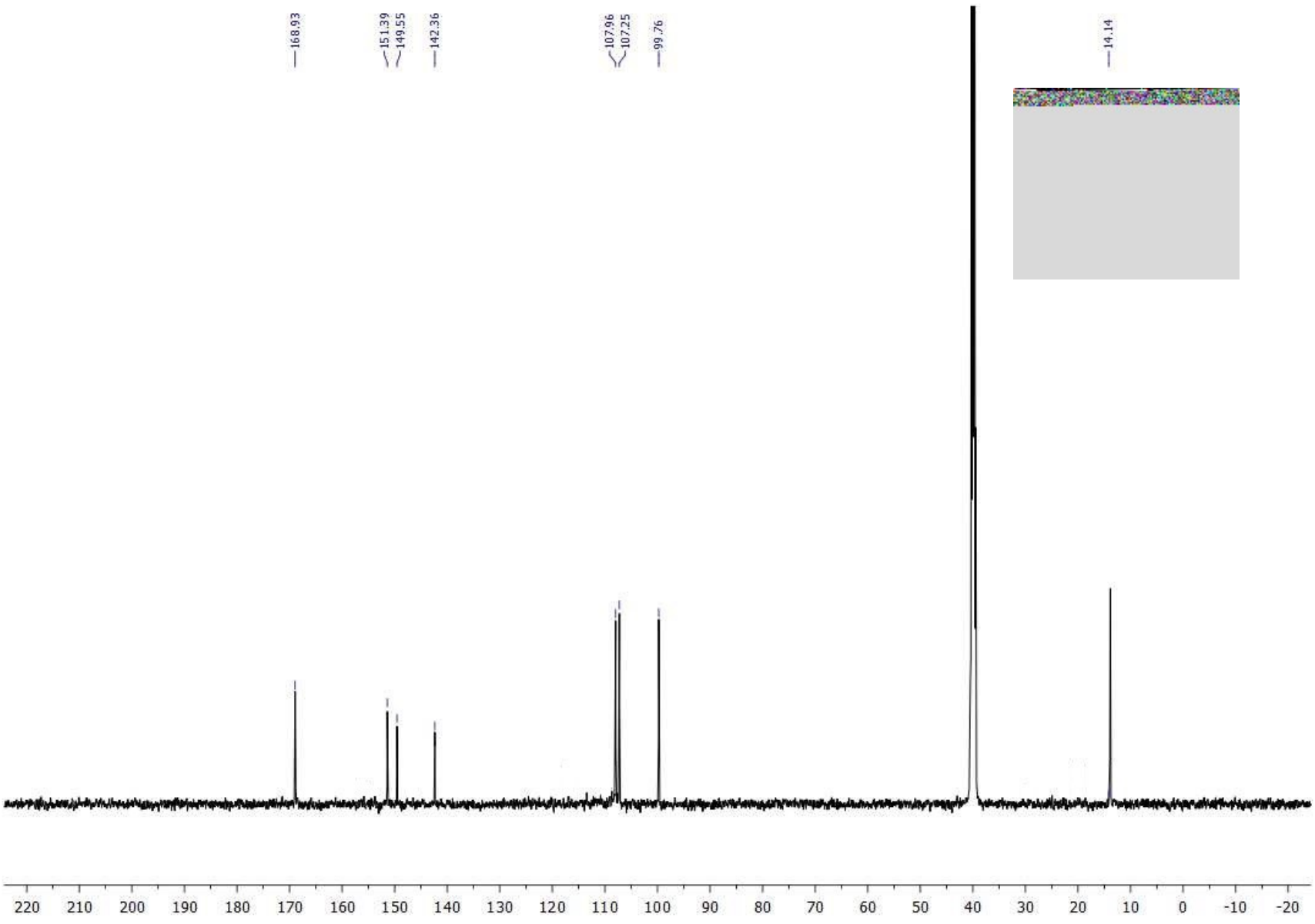

NLJ-V-46 #379 RT: 1.69 AV: 1 NL: 8.84E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]
293.0953
R=66507
C 14 H 17 O 3 N 2 S = 293.0954
-0.4545 ppm
155.0635
R=90007
C 7 H 11 N 2 S = 155.0637
-1.8336 ppm
130.1592
R=98807
222.0847
R=74007
309.0898
R=63502
335.1058
R=62207
351.1013
R=55304
379.1320
R=58507
412.0616
R=50102
443.0662
R=52207
497.1313
R=49107
527.1848
R=48507
567.1910
R=47307
Relative Abundance
m/z
NH2
N
S
MeO
CO2Et
2o
Chemical Formula: C14H16N2O3S
Exact Mass: 293.0882
Observed mass: 293.0954

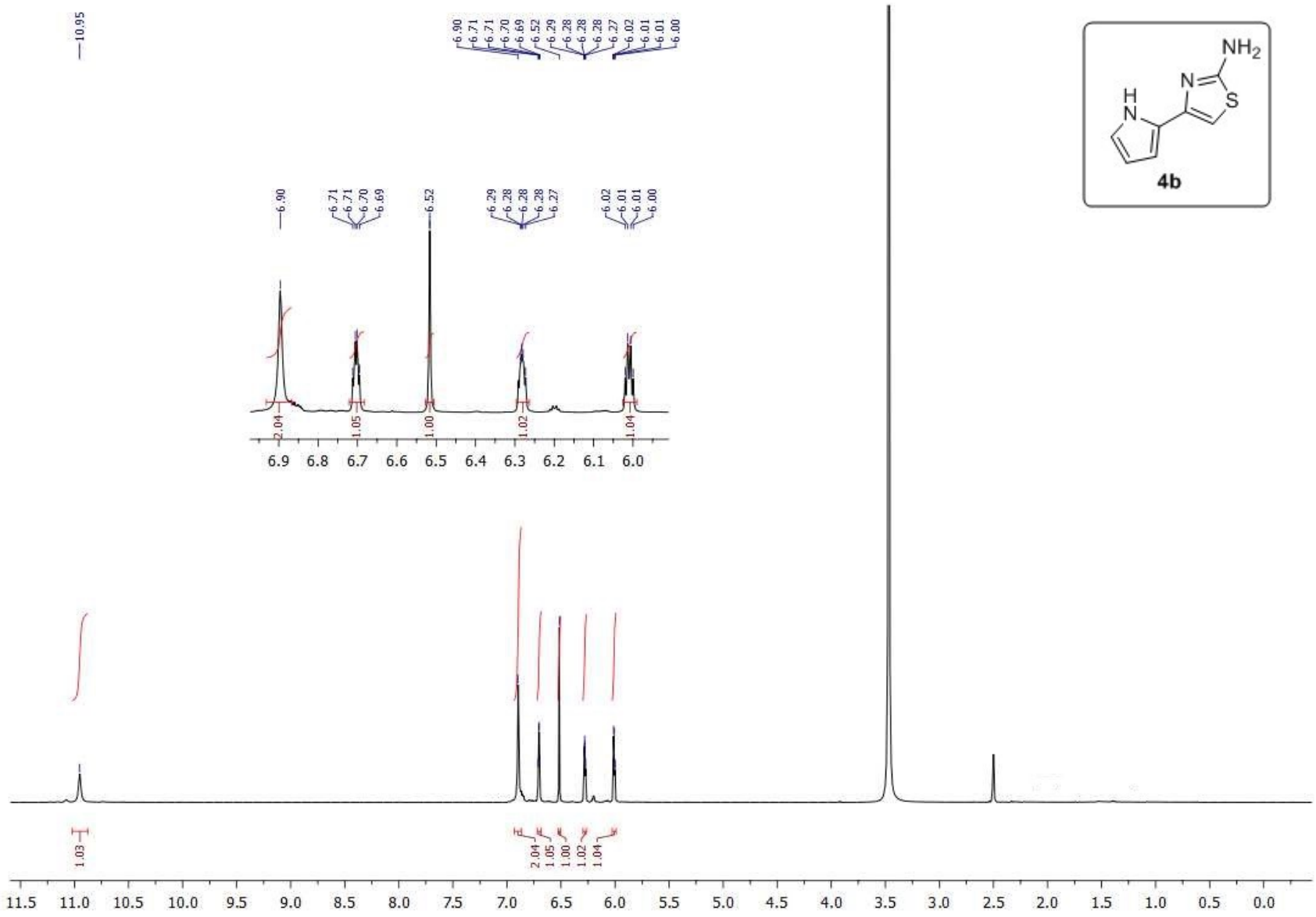

7.58
7.56
7.50
7.48
7.02
4.17
4.15
4.13
4.12
3.75
1.24
1.22
1.20
NH2
N
S
OEt
Cl
O
2p
1.98
2.01
1.83
2.03
1.98
3.00

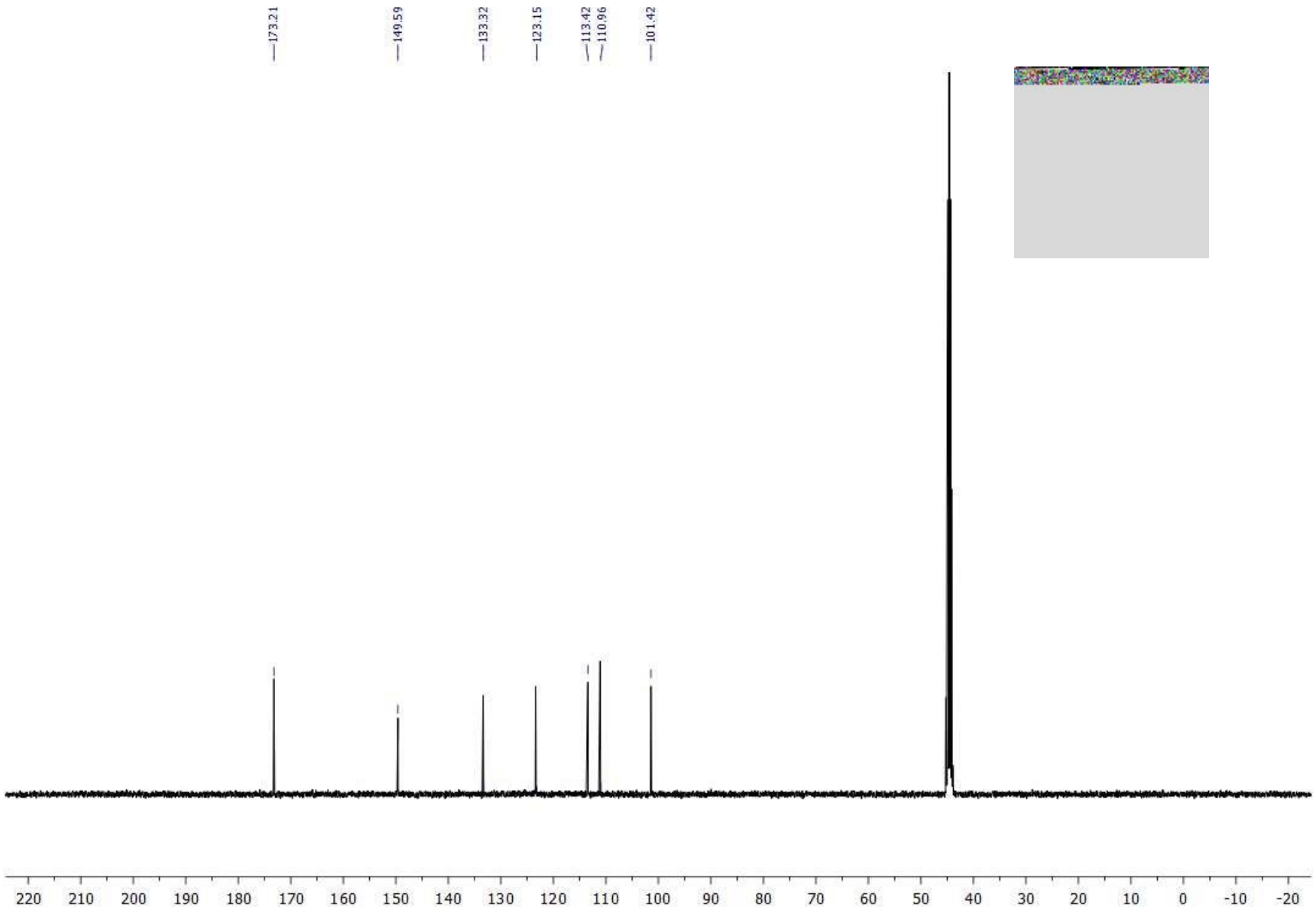

175.58
171.49
151.32
138.99
137.09
134.94
133.52
117.24
65.96
37.53
19.22
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

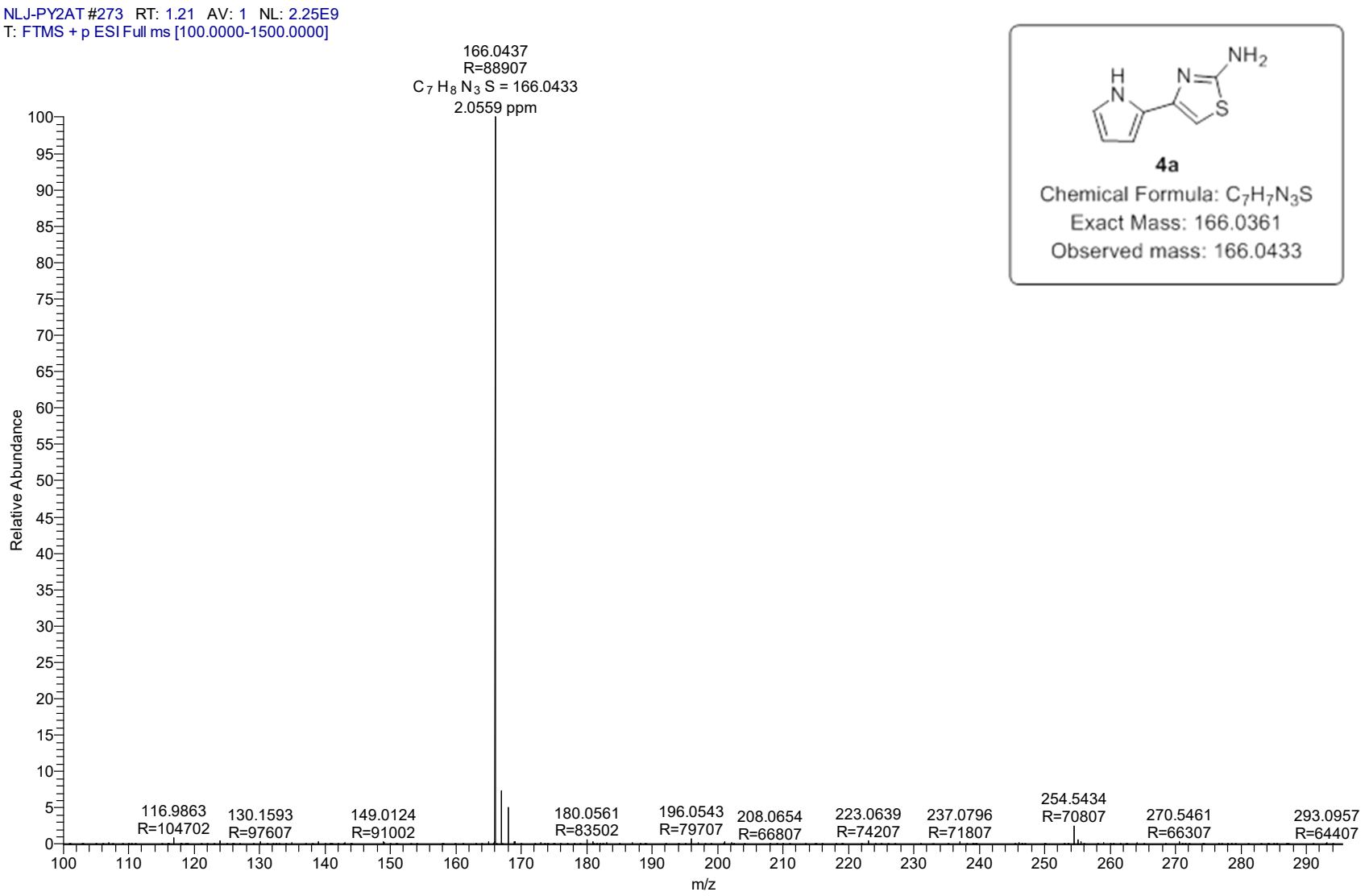

NLJ-V-70 #337 RT: 1.50 AV: 1 NL: 3.66E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
297.0464
R=65606
C13 H14 O2 N2 Cl S = 297.0459
1.5270 ppm
Relative Abundance
m/z
157.0836
R=89007
201.1122
R=74702
223.0941
R=73907
245.0784
R=66300
319.0277
R=64006
361.9426
R=54602
393.2972
R=54907
419.3159
R=36000
441.2976
R=50907
469.3290
R=45306
NH2
N
S
OEt
Cl
O
2p
Chemical Formula: C13H13ClN2O2S
Exact Mass (M+1): 297.0386
Molecular Weight (M+1): 297.7690

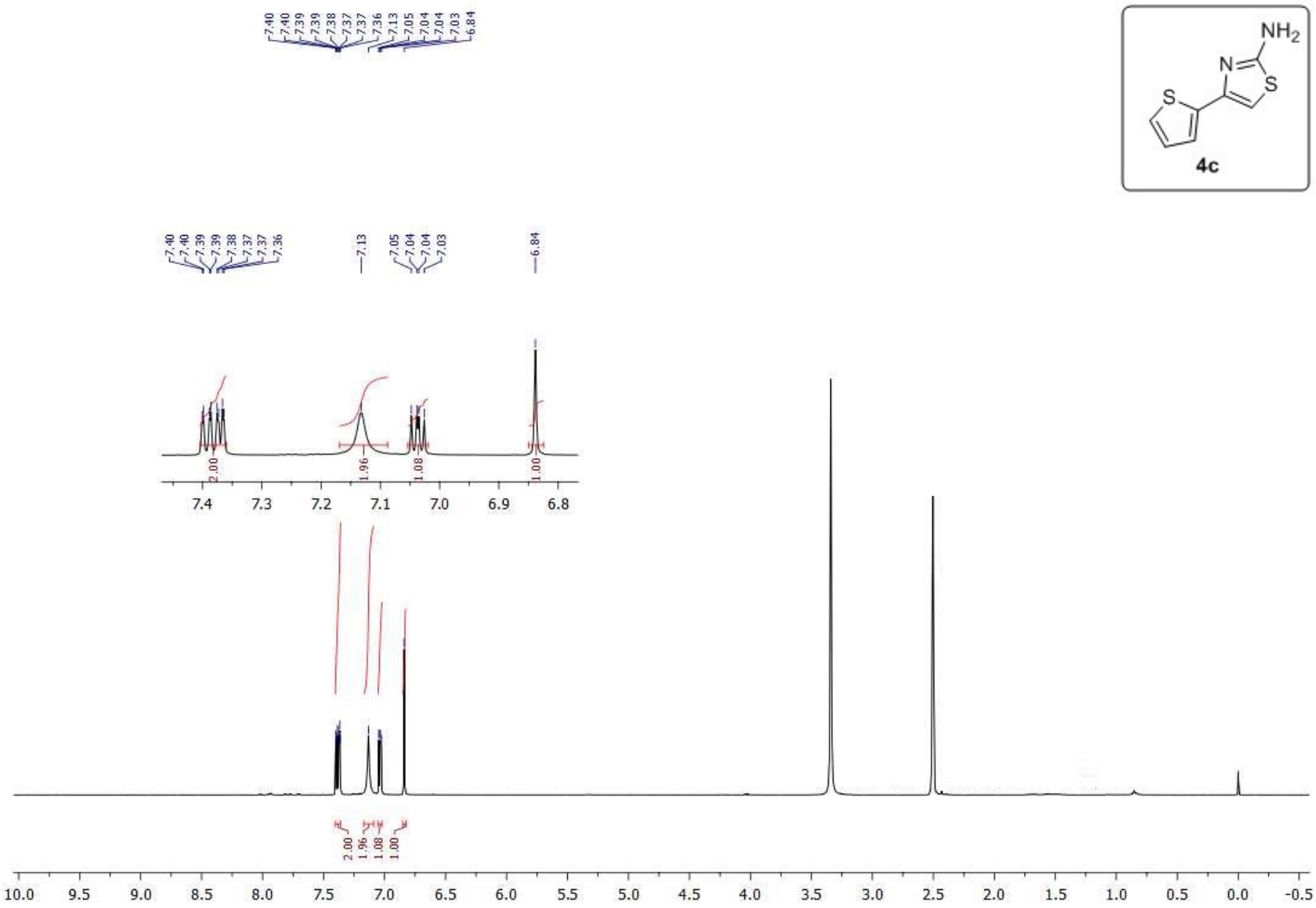

7.08
6.60
6.40
6.39
6.12
6.12
2.29
NH2
N
S
O
Me
4a
1.78
0.85
0.91
0.92
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

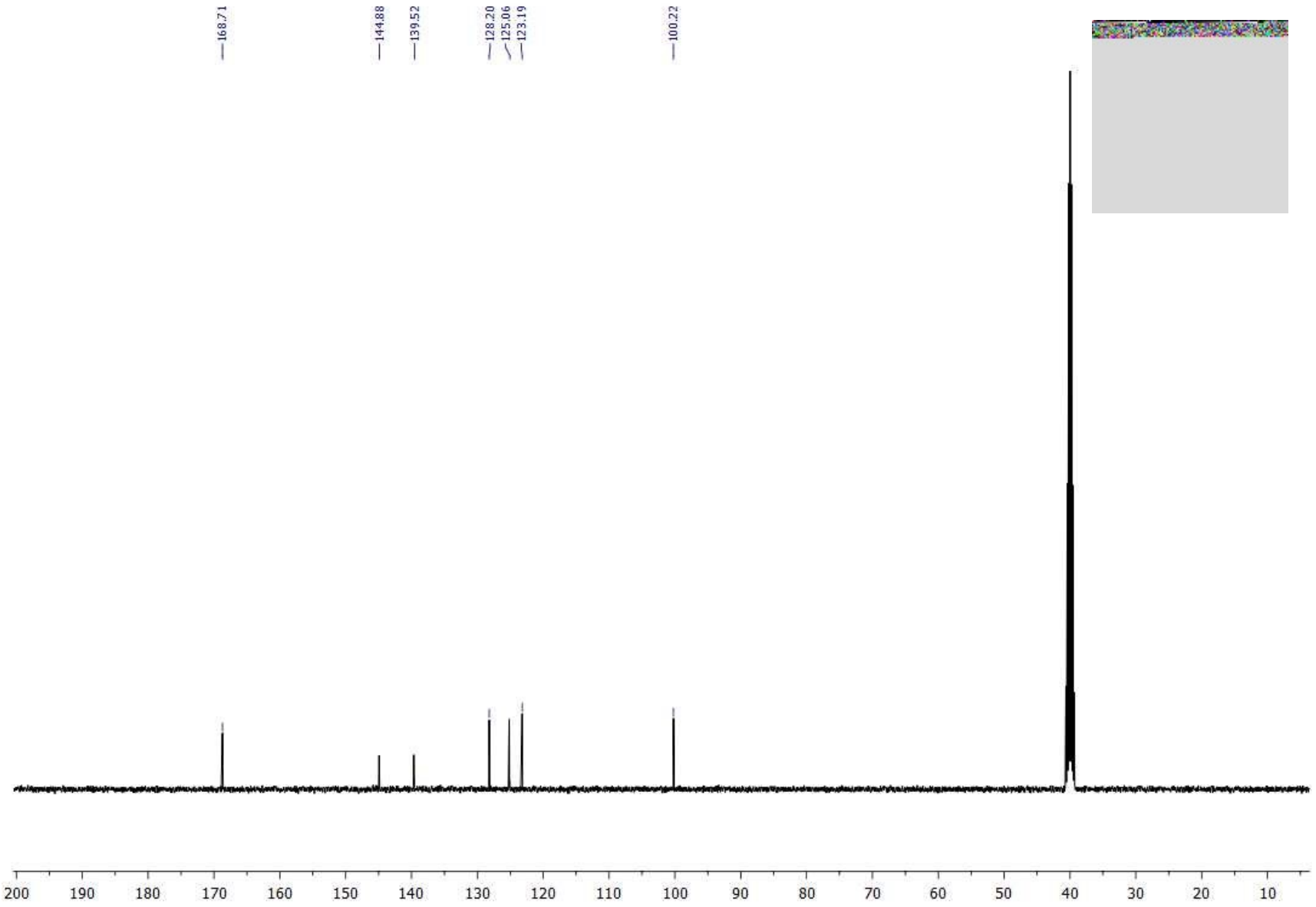

168.93
151.39
149.55
142.36
107.96
107.25
99.76
14.14
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

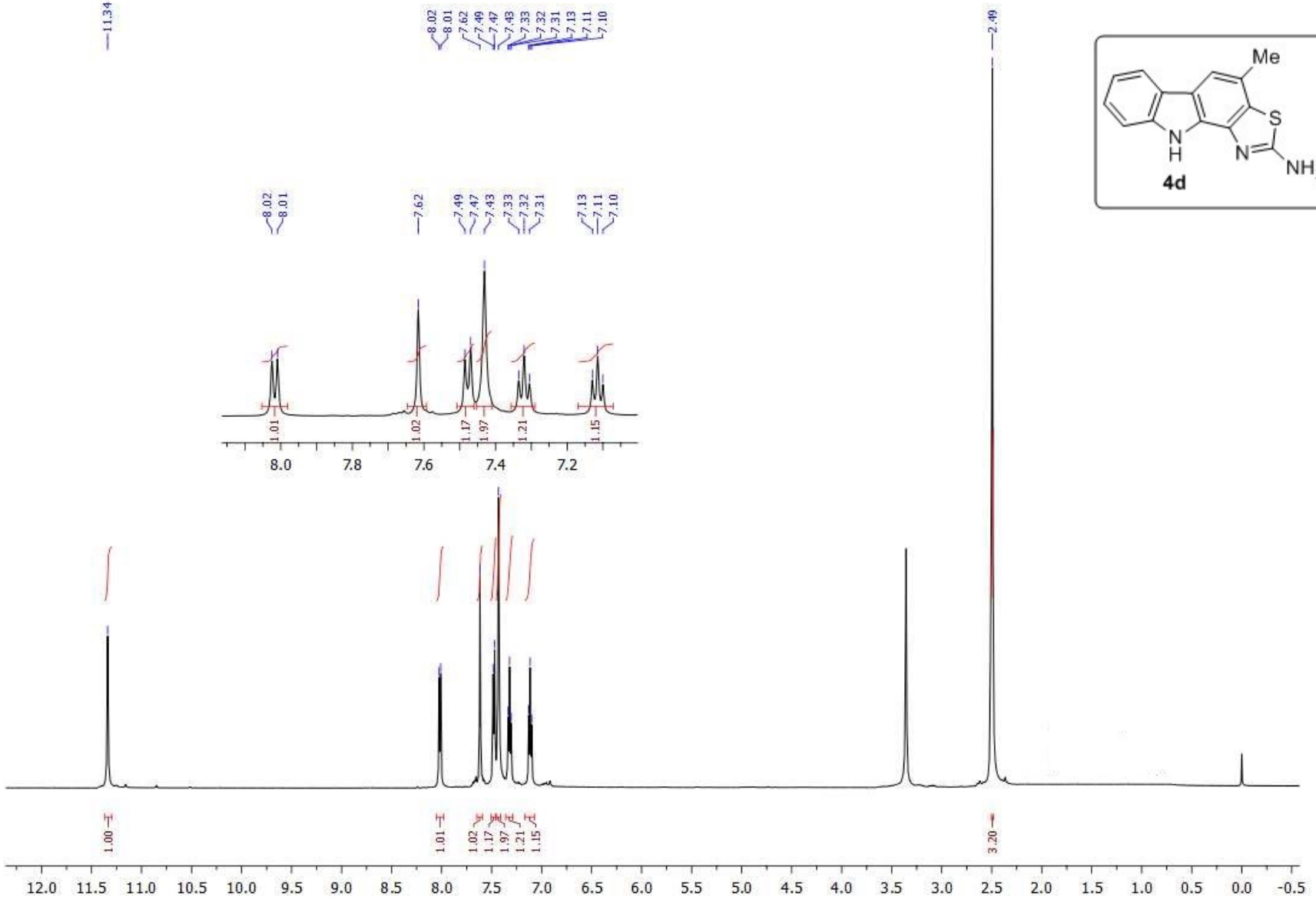

10.95
6.90
6.71
6.71
6.70
6.69
6.52
6.29
6.28
6.28
6.28
6.27
6.02
6.01
6.01
6.00
NH2
N
S
H
N
4b
2.04
1.05
1.00
1.02
1.04
1.03
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0

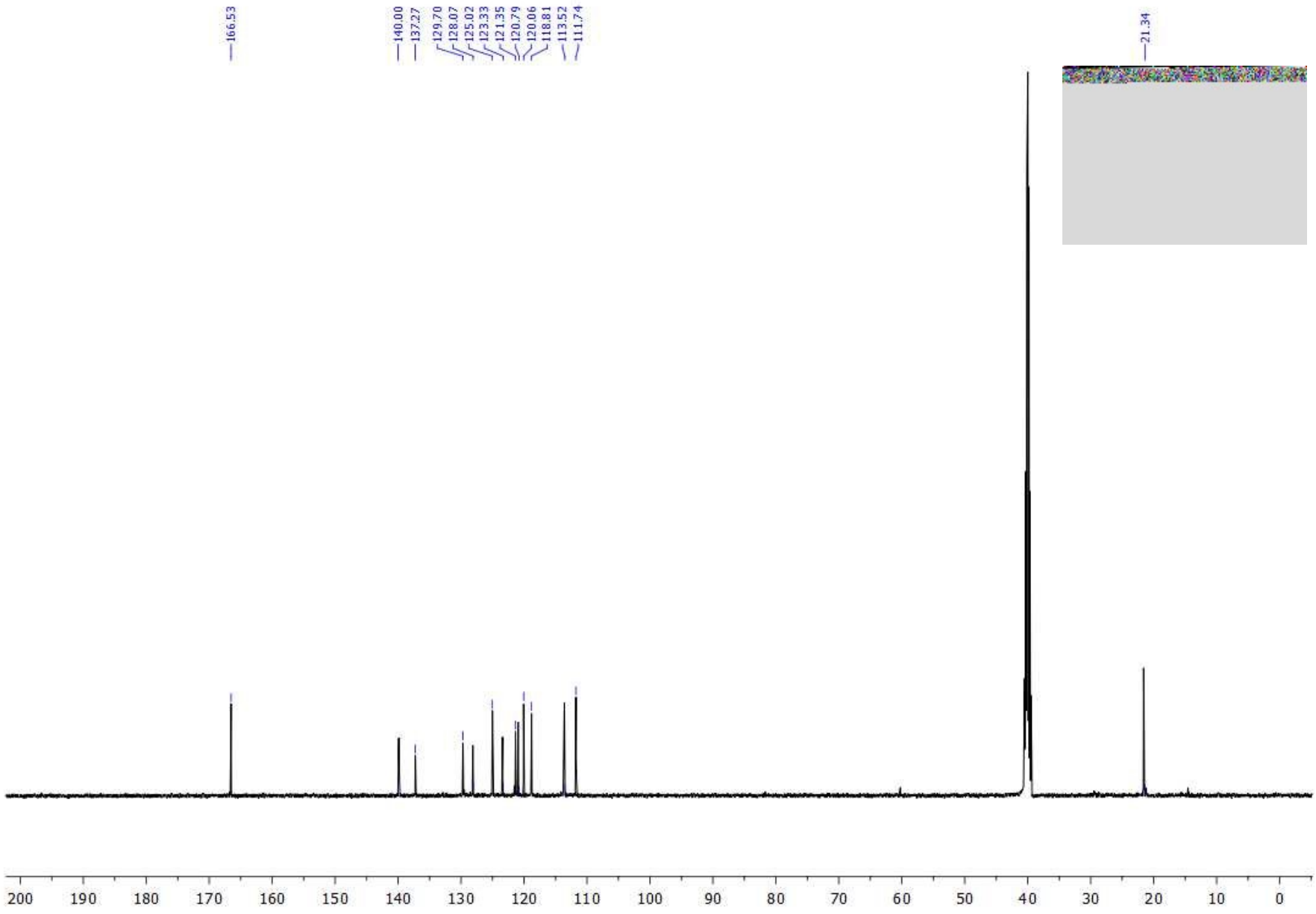

173.21
149.59
133.32
123.15
113.42
110.96
101.42
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20

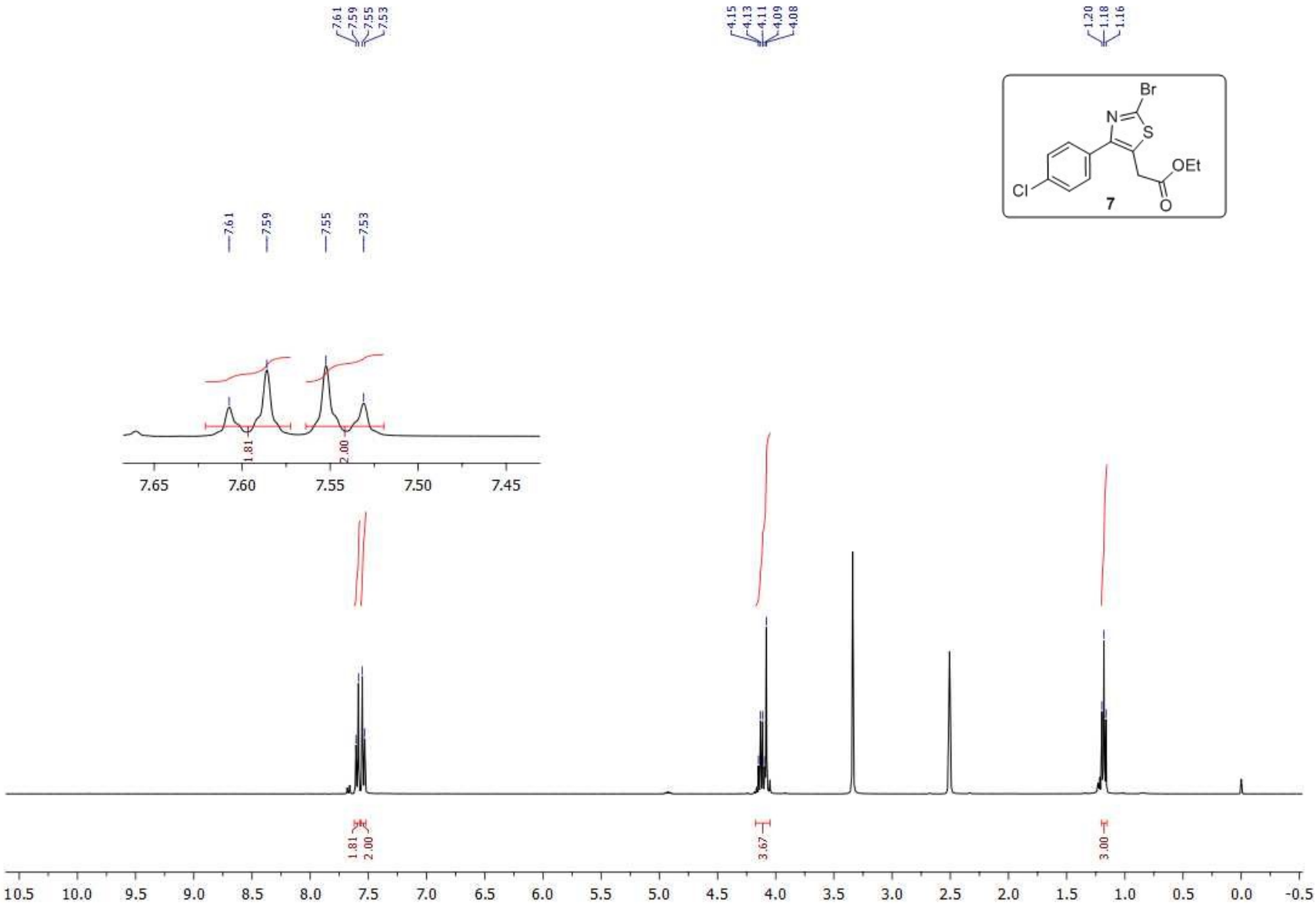

NLJ-PY2AT #273 RT: 1.21 AV: 1 NL: 2.25E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
166.0437
R=88907
C 7 H 8 N 3 S = 166.0433
2.0559 ppm
Relative Abundance
m/z
116.9863
R=104702
130.1593
R=97607
149.0124
R=91002
180.0561
R=83502
196.0543
R=79707
208.0654
R=66807
223.0639
R=74207
237.0796
R=71807
254.5434
R=70807
270.5461
R=66307
293.0957
R=64407
4a
Chemical Formula: C7H7N3S
Exact Mass: 166.0361
Observed mass: 166.0433

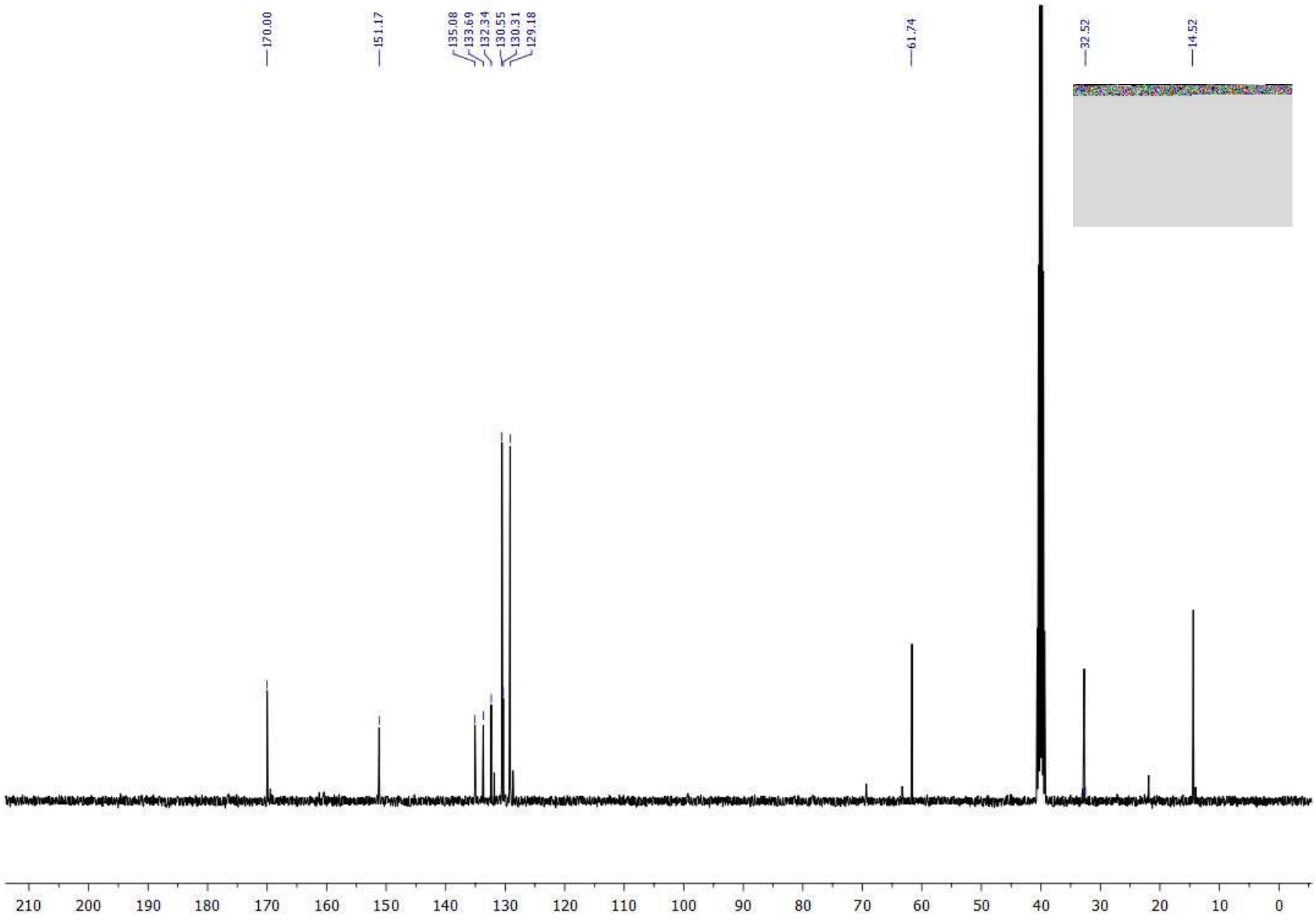

7.40
7.40
7.39
7.39
7.38
7.37
7.37
7.36
7.13
7.05
7.04
7.04
7.03
6.84
NH2
N
S
S
4c
2.00
1.96
1.08
1.00
7.4
7.3
7.2
7.1
7.0
6.9
6.8
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

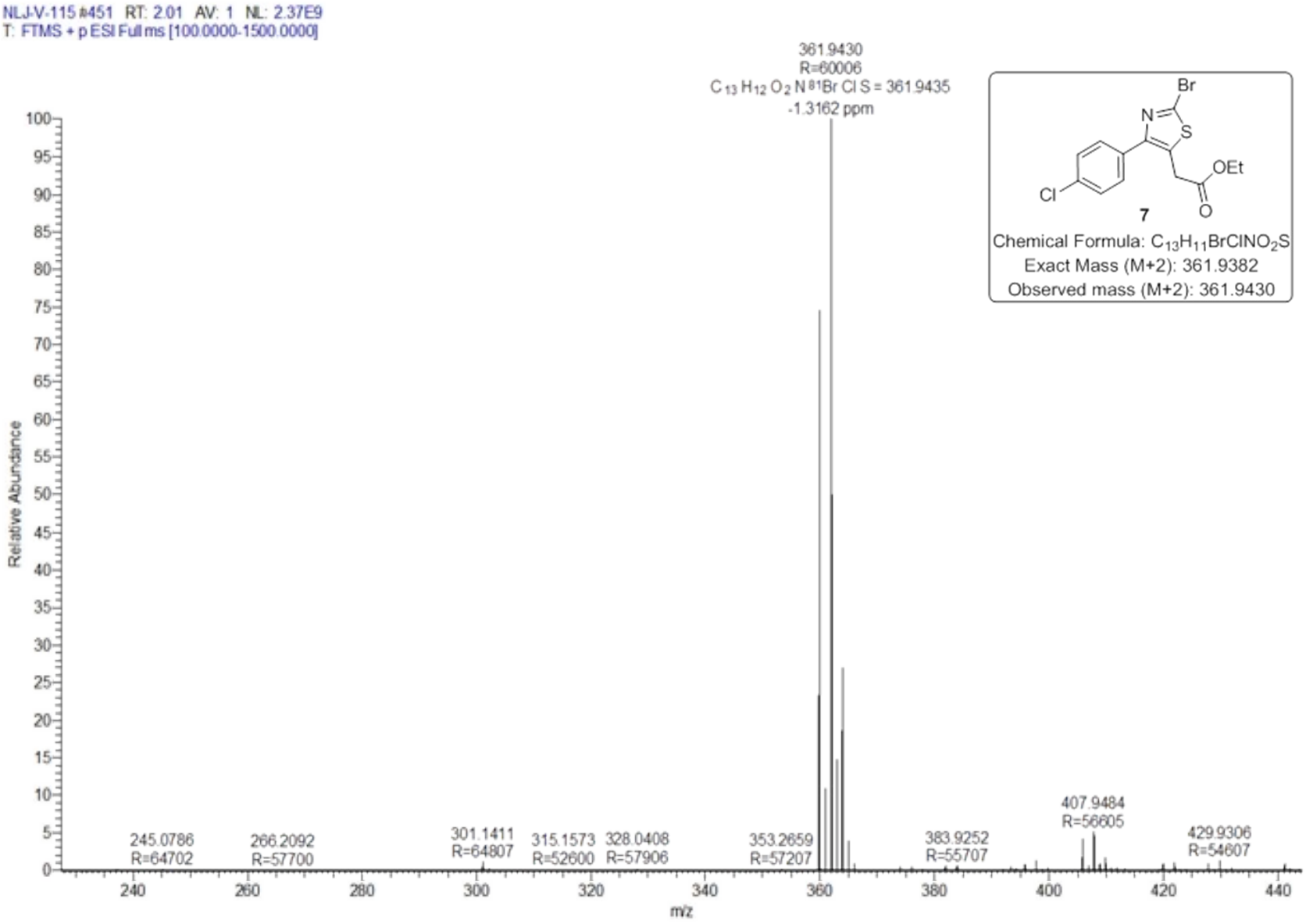

168.71
144.88
139.52
128.20
125.06
123.19
100.22
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

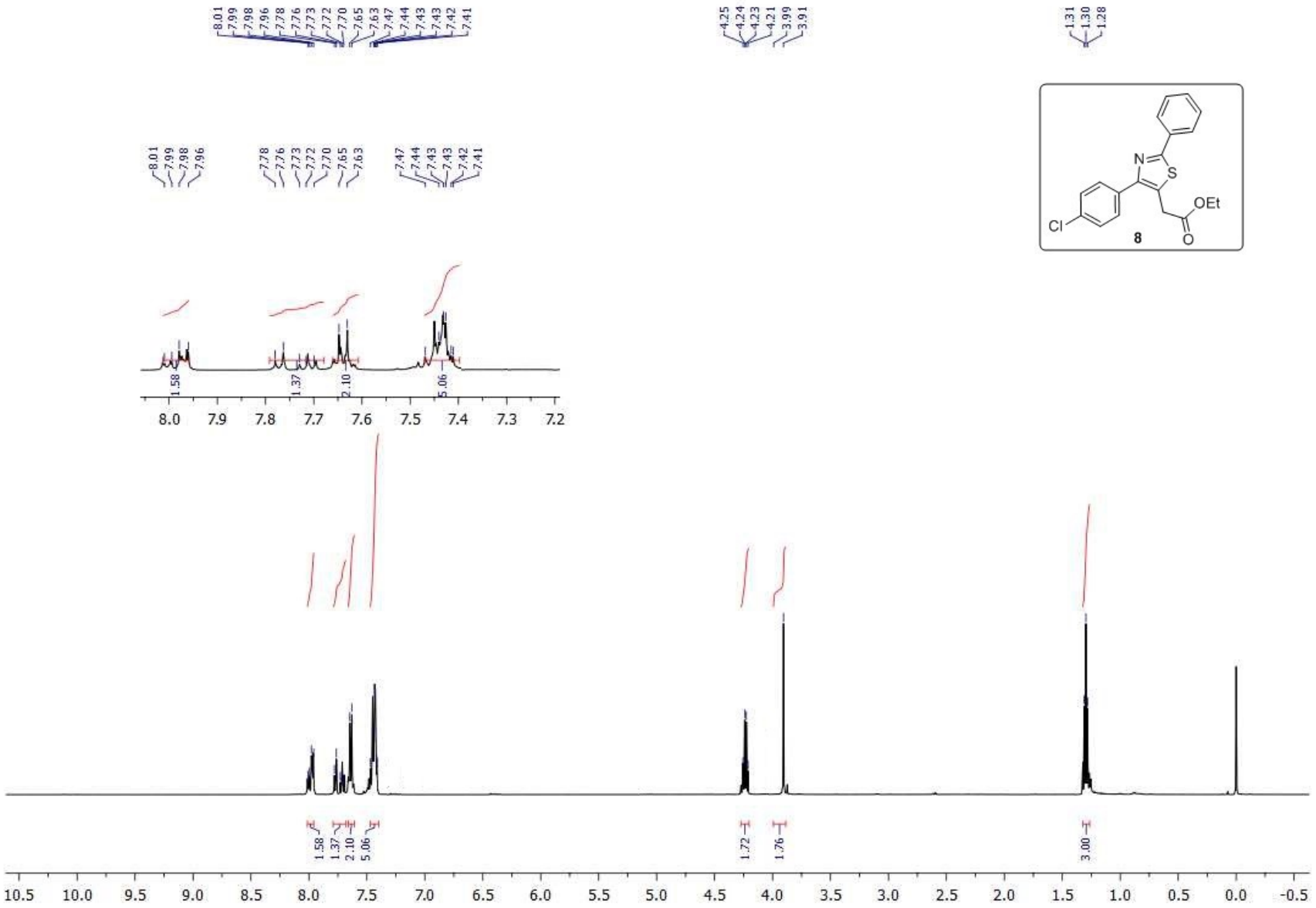

11.34
8.02
8.01
7.62
7.49
7.47
7.43
7.33
7.32
7.31
7.13
7.11
7.10
2.49
Me
S
N
H
N
NH2
4d
1.01
1.02
1.17
1.97
1.21
1.15
3.20
8.0
7.8
7.6
7.4
7.2
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

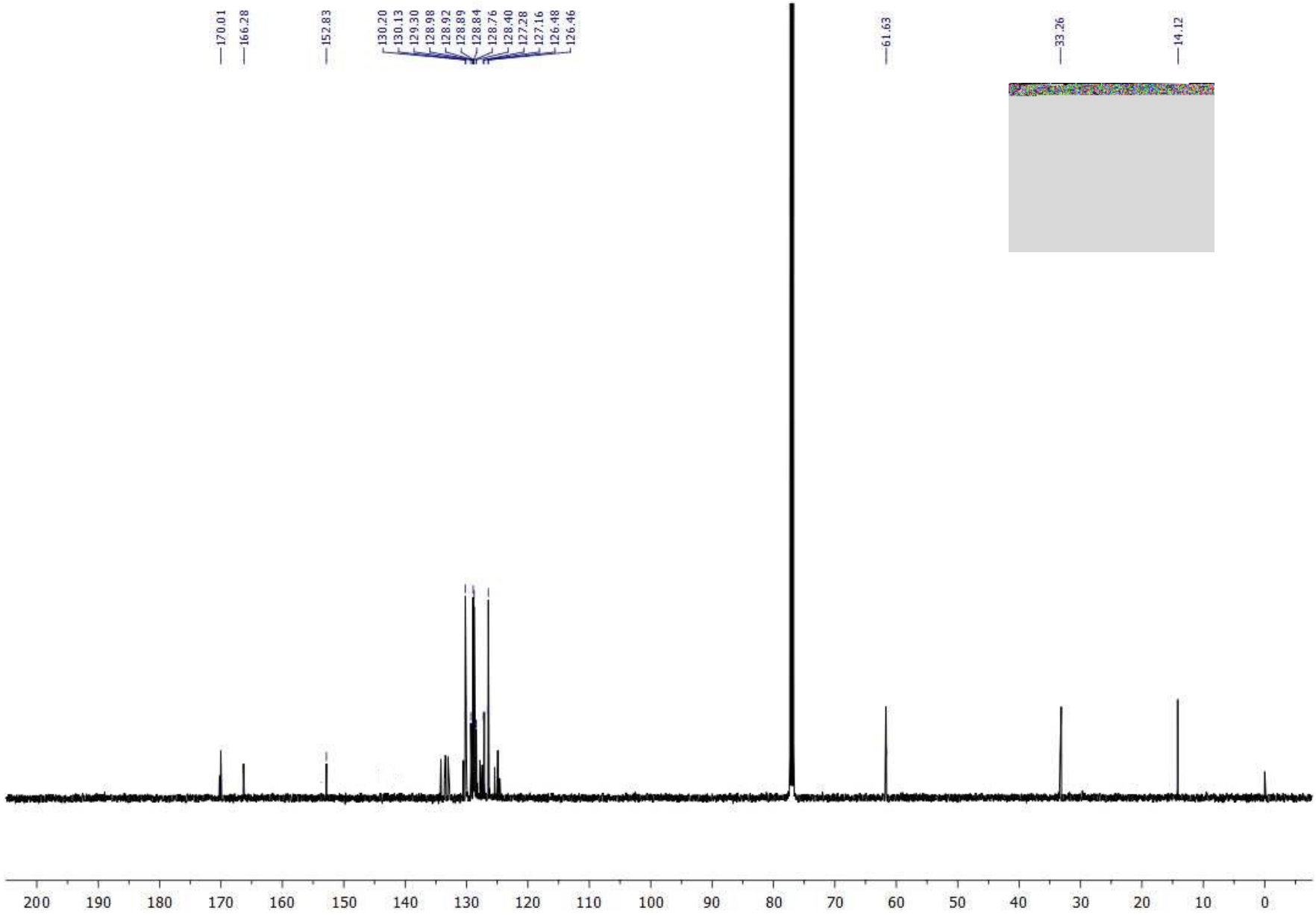

166.53
140.00
137.27
129.70
128.07
125.02
123.33
121.35
120.79
120.06
118.81
113.52
111.74
21.34
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

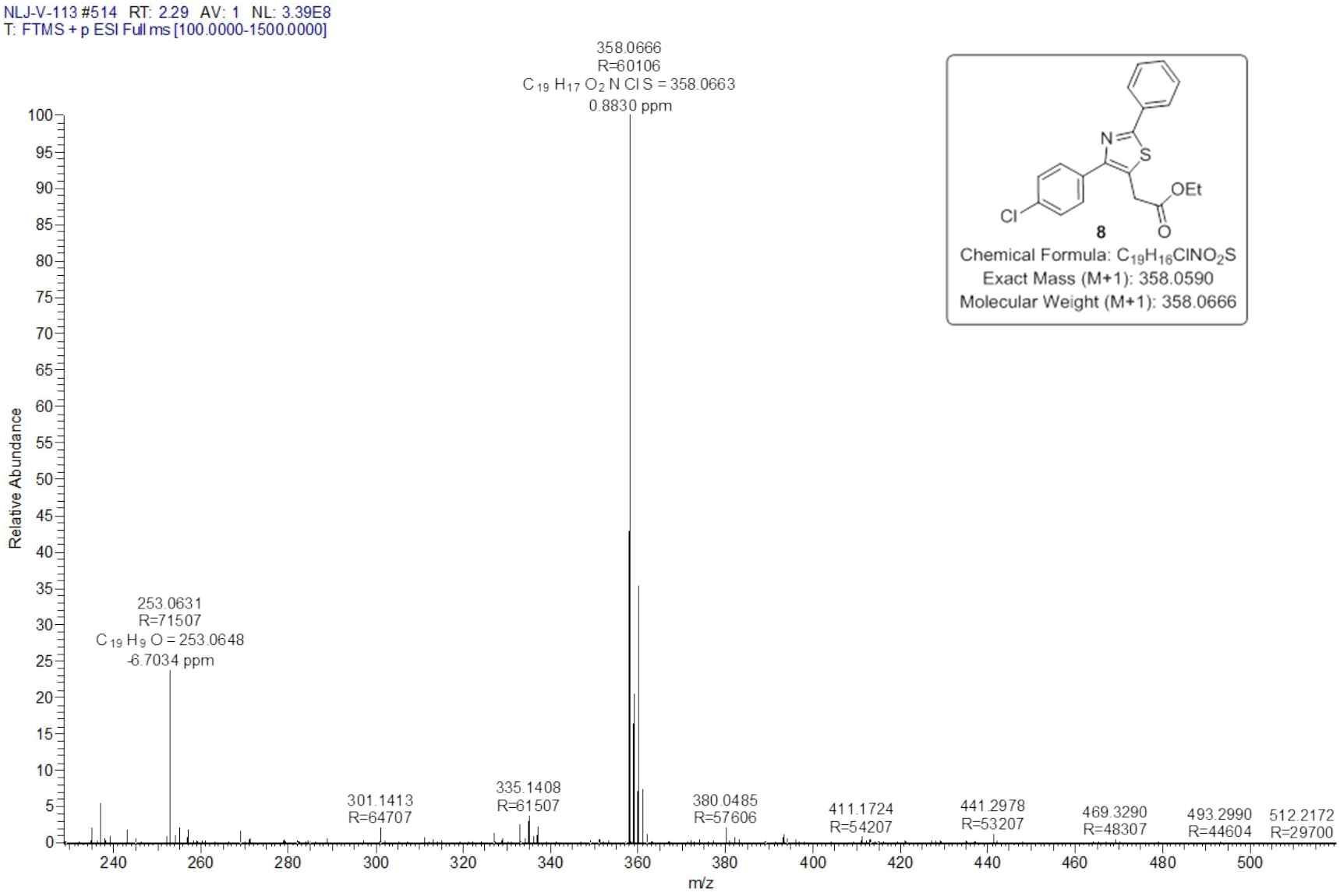

7.61
7.59
7.55
7.53
4.15
4.13
4.11
4.09
4.08
1.20
1.18
1.16
Br
N
S
OEt
Cl
O
7
1.81
2.00
3.67
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


170.00
151.17
135.08
133.69
132.34
130.55
130.31
129.18
61.74
32.52
14.52
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


NLJ-V-115 #451 RT: 2.01 AV: 1 NL: 2.37E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
361.9430
R=60006
C 13 H 12 O 2 N 81Br Cl S = 361.9435
-1.3162 ppm
Br
N
S
OEt
Cl
O
7
Chemical Formula: C13H11BrClNO2S
Exact Mass (M+2): 361.9382
Observed mass (M+2): 361.9430
Relative Abundance
m/z
245.0786
R=64702
266.2092
R=57700
301.1411
R=64807
315.1573
R=52600
328.0408
R=57906
353.2659
R=57207
383.9252
R=55707
407.9484
R=56605
429.9306
R=54607


8.01
7.99
7.98
7.96
7.78
7.76
7.73
7.72
7.70
7.65
7.63
7.47
7.44
7.43
7.43
7.42
7.41
4.25
4.24
4.23
4.21
3.99
3.91
1.31
1.30
1.28
N
S
OEt
Cl
O
8
1.58
1.37
2.10
5.06
1.72
1.76
3.00


170.01
166.28
152.83
130.20
130.13
129.30
128.98
128.92
128.89
128.84
128.76
128.40
127.28
127.16
126.48
126.46
61.63
33.26
14.12
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


NLJ-V-113 #514 RT: 2.29 AV: 1 NL: 3.39E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]
358.0666
R=60106
C 19 H17 O2 N Cl S = 358.0663
0.8830 ppm
253.0631
R=71507
C 19 H9 O = 253.0648
-6.7034 ppm
301.1413
R=64707
335.1408
R=61507
380.0485
R=57606
411.1724
R=54207
441.2978
R=53207
469.3290
R=48307
493.2990
R=44604
512.2172
R=29700
Relative Abundance
m/z
N
S
OEt
Cl
O
8
Chemical Formula: C19H16ClNO2S
Exact Mass (M+1): 358.0590
Molecular Weight (M+1): 358.0666