BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Supporting Information

for

Synthesis of 5-arylidenerhodanines in L-proline-based deep eutectic solvent

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Experimental procedures, characterization of compounds, copies of NMR spectra and HRMS spectra

HRMS analysis

Samples of products **3e** and **3j** were respectively dissolved in 1 mL ethanol (ethanol HPLC grade 99.9%, Carlo Erba Reagents) for a final concentration of 1 µg/mL, to be characterized by FT-ICR MS (FT-ICR MS 7T, SolariX 2xR, Bruker Daltonics, Bremen, Germany) with electrospray ionization (ESI - Bruker Daltonics), in negative-ion detection mode. Both, ion source and instrument parameters were optimized via software FTMS-Control V2.3.0 (Bruker Daltonics). Prior to acquisition, the mass spectrometer was externally calibrated and ICR detection cell was shimmed and gated using direct introduction of a 0.1 mg/mL sodium trifluoroacetate solution. The sample solution was infused into the source at a 3 µL/min flow rate and the capillary voltage was set at 3.7 kV. The drying gas temperature and flow rate were kept at 200 °C and 4 L/min, respectively, and the nebulizer pressure at 0.5 bar. The mass spectra resulted from the accumulation of 20 scans over a *m*/*z* 107.5–1500 range and with a 4 megaword time-domain. A mass resolution of 450 000 was achieved at *m*/*z* 300. Molecular formulae were assigned by SmartFormula Editor (Bruker Daltonics) with a ±1 ppm mass accuracy window. Theoretical mass specta, with the isotopic distribution, were also used to confirm the molecular assignment.

(*Z*)-5-(4-Hydroxy-3-methoxybenzylidene)-2-thioxothiazolidin-4-one (3a). Yellow solid obtained after 1 h at 60 °C in 94% yield. Mp = 219 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.84 (s, 3H, OCH_3), 6.94 (d, 1H, J = 8,4 Hz), 7.10 (dd, 1H, J = 8,4 Hz and 2 Hz), 7.16 (d, 1H, J = 2 Hz), 7.56 (s, 1H, =CH), 10.06 (br s, 1H, OH), 13.72 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 195.7, 169.8, 149.9, 148.1, 132.5, 125.0, 124.4, 121.4, 116.3, 114.3, 55.6.

(5-Methylfurfurylidene)-2-thioxothiazolidin-4-one (3b). Yellow solid obtained after 1 h at 60 °C in 92% yield. Mp = 210 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.41 (s, 3H, CH_3), 6.44 (m, 1H), 7.10 (d, 1H, *J* = 3.6 Hz), 7.42 (s, 1H, =CH), 13.62 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 196.6, 169.0, 158.5, 148.2, 121.8, 121.2, 117.8, 110.8, 13.8.

(*Z*)-5-(3-Hydroxy-4-methoxybenzylidene)-2-thioxothiazolidin-4-one (3c). Light yellow solid obtained after 1 h at 60 °C in 92% yield. Mp = 227 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.84 (s, 3H, OCH_3), 7.01 (d, 1H, *J* = 2 Hz), 7.06–7.12 (m, 2H), 7.49 (s, 1H, =CH), 9.55 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 195.7, 169.6, 150.5, 147.1, 132.3, 125.7, 124.4, 122.1, 116.0, 112.6, 55.7.

(*Z*)-5-(3,4-Dihydroxybenzylidene)-2-thioxothiazolidin-4-one (3d). Ochre yellow solid obtained after 1 h at 60 °C in 83% yield (3 h = 99% yield). Mp = 303 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 6.87 (d, 1H, *J* = 8.4 Hz), 6.98–6.99 (m, 2H), 7.46 (s, 1H, =CH), 9.54 (br s, 1H, OH), 9.96 (br s, 1H, OH), 13.69 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 196.2, 170.2, 149.7, 146.5, 133.2, 125.4, 124.9, 121.3, 117.1, 116.9.

(*Z*)-5-(2-Hydroxy-5-methoxybenzylidene)-2-thioxothiazolidin-4-one (3e). Orange solid obtained after 1 h at 60 °C in 63% yield. Mp = 220 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.72 (s, 3H, OCH_3), 6.76 (d, 1H, *J* = 2.8 Hz), 6.89 (d, 1H, *J* = 8.8 Hz), 6.97 (dd, 1H, *J* = 8.8 and 2.8 Hz), 7.79 (s, 1H, =CH), 10.30 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 196.1, 169.8, 152.5, 151.9, 127.4, 124.4, 120.2, 119.9, 117.5, 112.5, 55.7. HRMS–ESI$^-$ (*m*/*z*): $[M]^-$ calcd for $C_{11}H_8NO_3S_2$, 266.998464; found, 266.998482.

(*Z*)-5-(3-Nitrobenzylidene)-2-thioxothiazolidin-4-one (3f). Yellow solid obtained after 1 h at 60 °C in 79% yield. Mp = 237 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.76 (s, 1H, =CH),

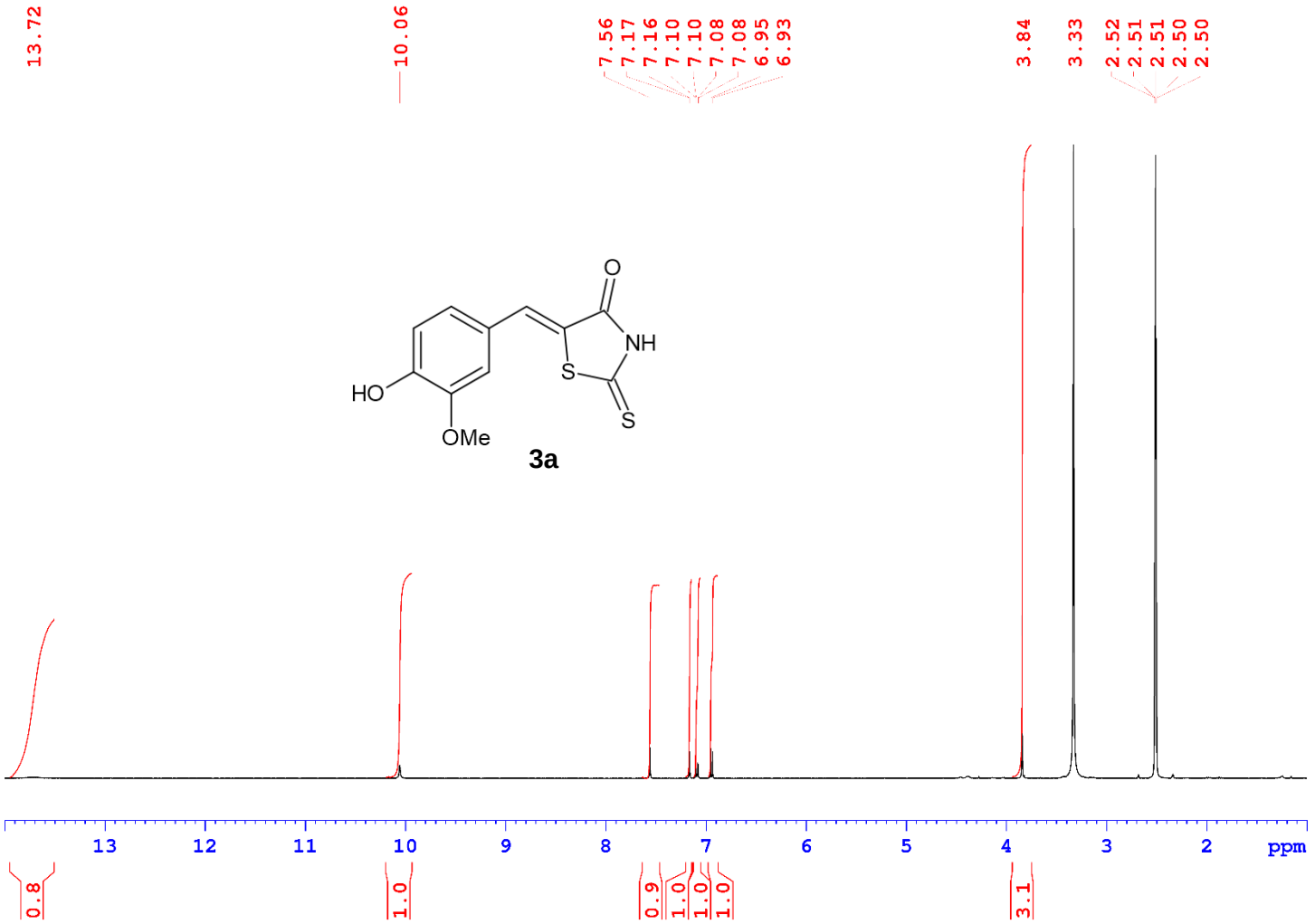
7.81 (t, 1H, J = 8 Hz)), 7.99 (d, 1H, J = 7.6 Hz), 8.29 (m, 1H), 8.42 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 195.7, 170.2, 148.4, 135.7, 134.9, 131.0, 129.3, 128.4, 124.7, 124.5.

(*Z*)-5-(2-Naphthalen-2-ylmethylene)-2-thioxothiazolidin-4-one (3g). Yellow solid obtained after 24 h at 60 °C in 85% yield. Mp = 258 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.60–7.64 (m, 3H), 7.77 (s, 1H), 7.99 (d, 1H, J = 1.2 and 7.6 Hz), 8.04–8.08 (m, 2H), 8.19 (s, 1H);^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 196.1, 170.0, 133.4, 132.9, 131.6, 131.5, 130.7, 129.2, 128.9, 128.3, 127.8, 127.3, 126.3, 126.2.

(*Z*)-5-(1*H*-Pyrrol-2-ylmethylene)-2-thioxothiazolidin-4-one (3h). Orange solid obtained after 1 h at 60 °C in 86% yield. Mp = 259 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 6.40 (m, 1H), 6.53 (m, 1H), 7.27 (d, 1H, J = 1.2 Hz), 7.50 (s, 1H, =CH), 11.80 (br s, 1H, NH), 13.54 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 194.9, 169.4, 127.3, 125.8, 121.9, 117.1, 115.0, 112.8.

(*Z*)-5-(4-Hydroxy-3-methoxybenzylidene)-4-oxo-2-thioxo-1,3-thiazolidin-3-yl)acetic acid (3i). Yellow solid obtained after 1 h at 60 °C in 72% yield. Mp = 249 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.85 (s, 3H, OCH_3), 4.67 (s, 2H, NCH_2), 6.97 (d, 1H, J = 8.4 Hz), 7.17 (dd, 1H, J = 8.4 Hz and 2 Hz), 7.23 (d, 1H, J = 2 Hz), 7.79 (s, 1H, =CH), 10.23 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 193.1, 167.5, 166.6, 150.5, 148.2, 134.7, 125.5, 124.3, 117.5, 116.5, 114.7, 55.7, 45.5.

(*Z*)-5-(5-Hydroxymethylfurfurylidene)-2-thioxothiazolidin-4-one (3j). Ochre yellow solid obtained after 1 h at 60 °C in 72% yield. Mp = 149 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 4.49 (s, 2H), 5.52 (br s, 1H, OH), 6.58 (d, 1H, J = 3.6 Hz), 7.11 (d, 1H, J = 3.6 Hz), 7.44 (s, 1H, =CH), 13.62 (br s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 196.8, 169.1, 161.2, 148.8, 121.8, 121.0, 117.8, 110.9, 56.0. HRMS–ESI$^-$ (*m*/*z*): [M]$^-$ calcd for $C_9H_6NO_3S_2$, 240.982814; found, 240.982805.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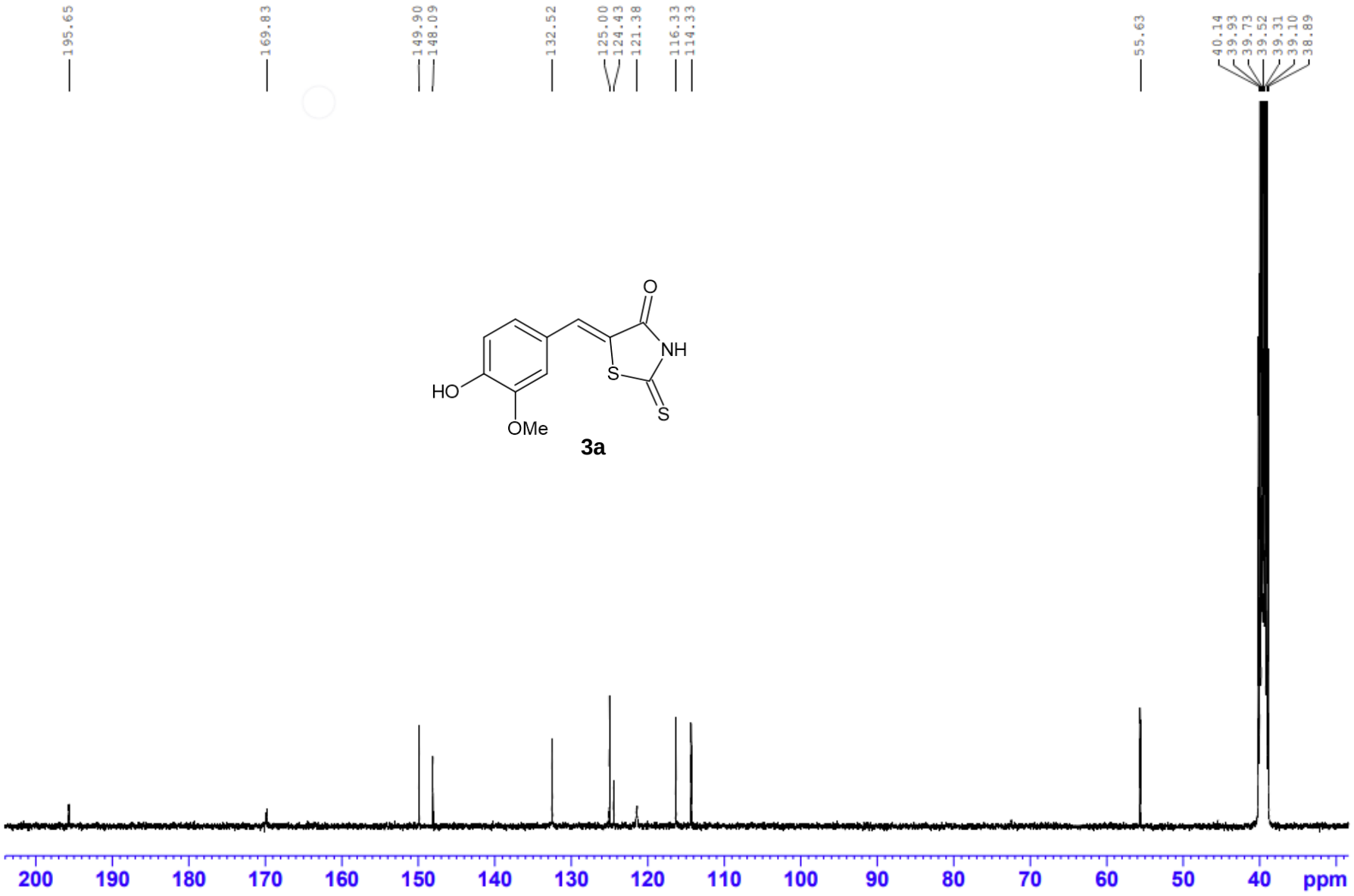
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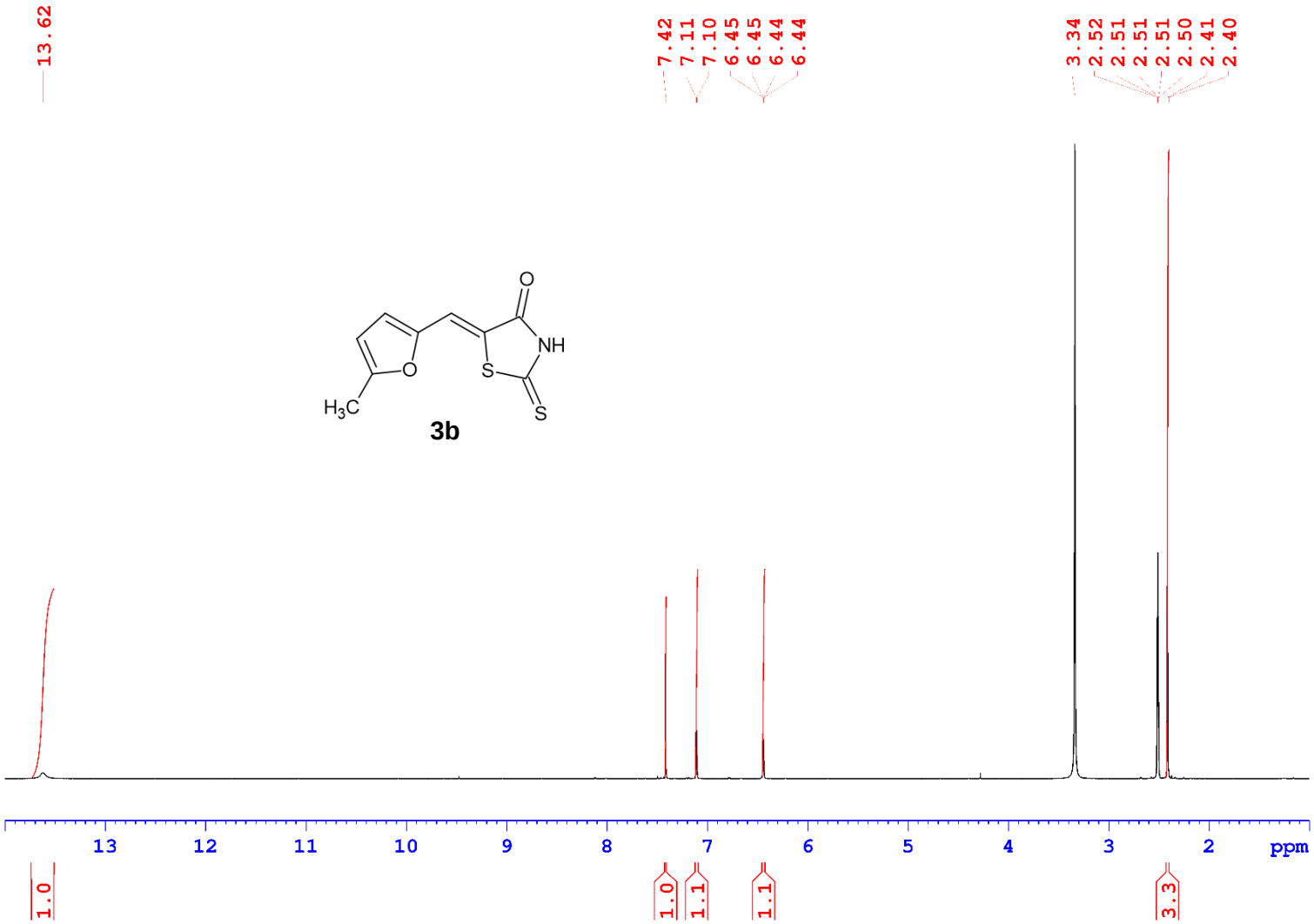
3a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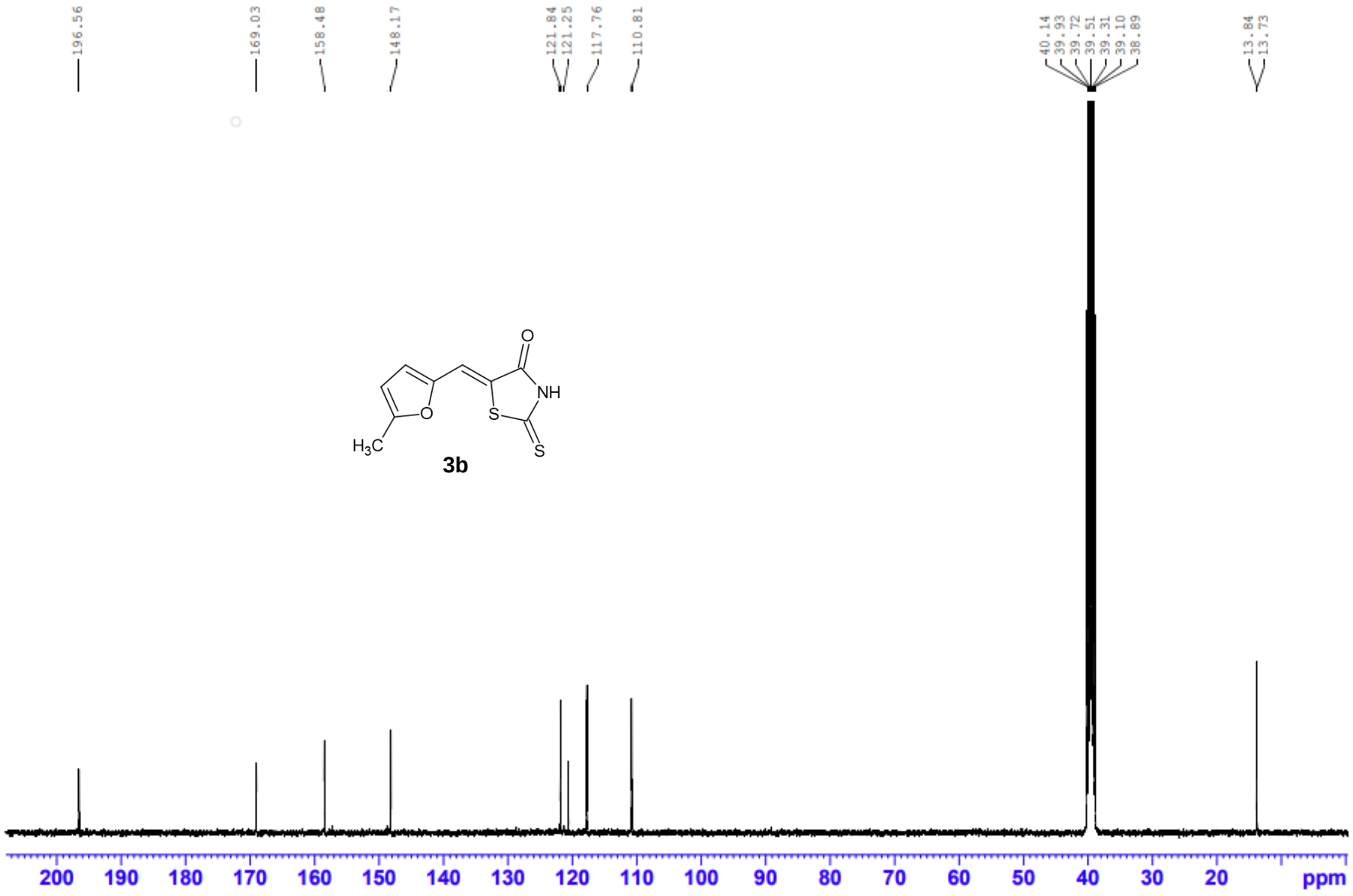
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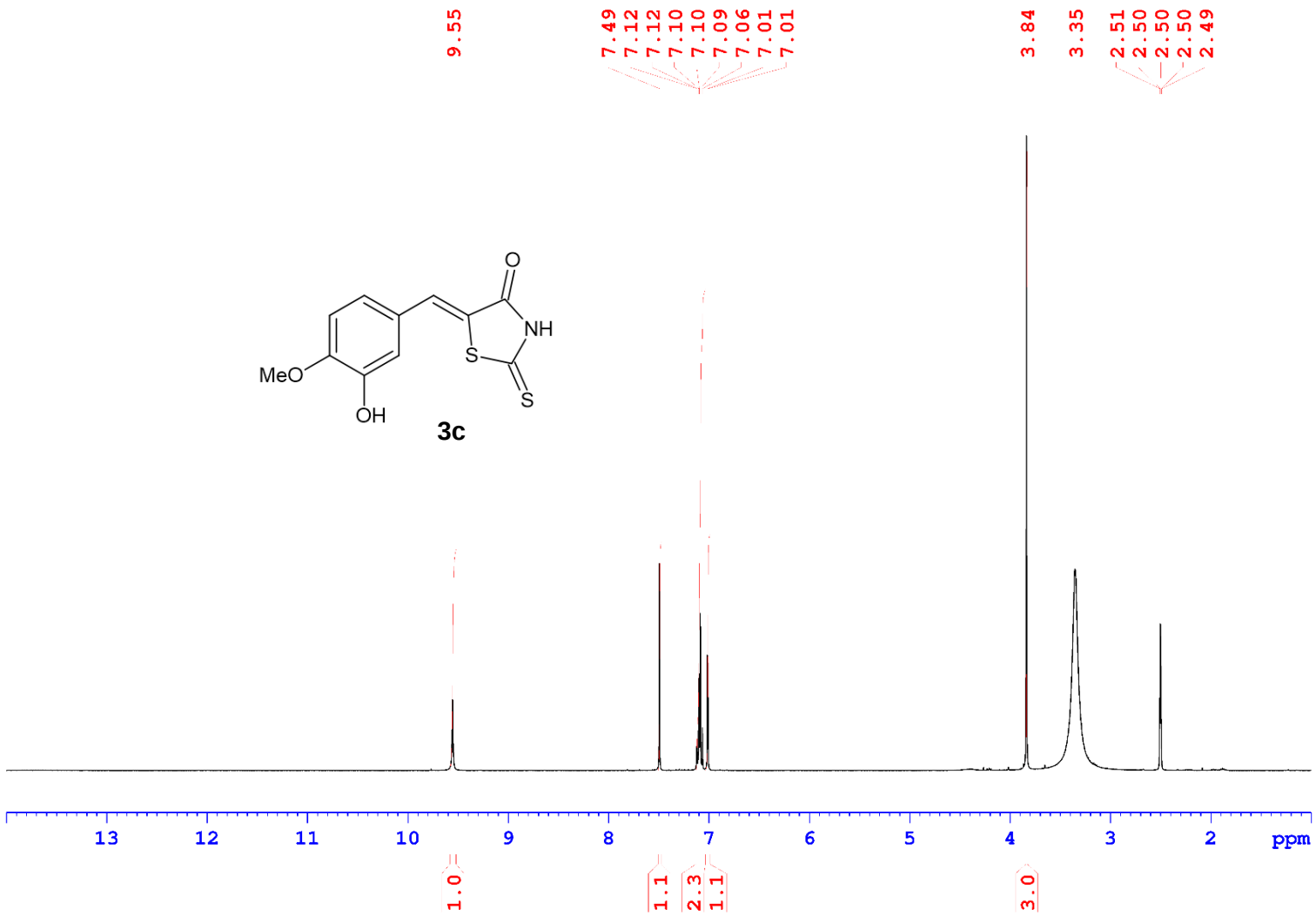
3b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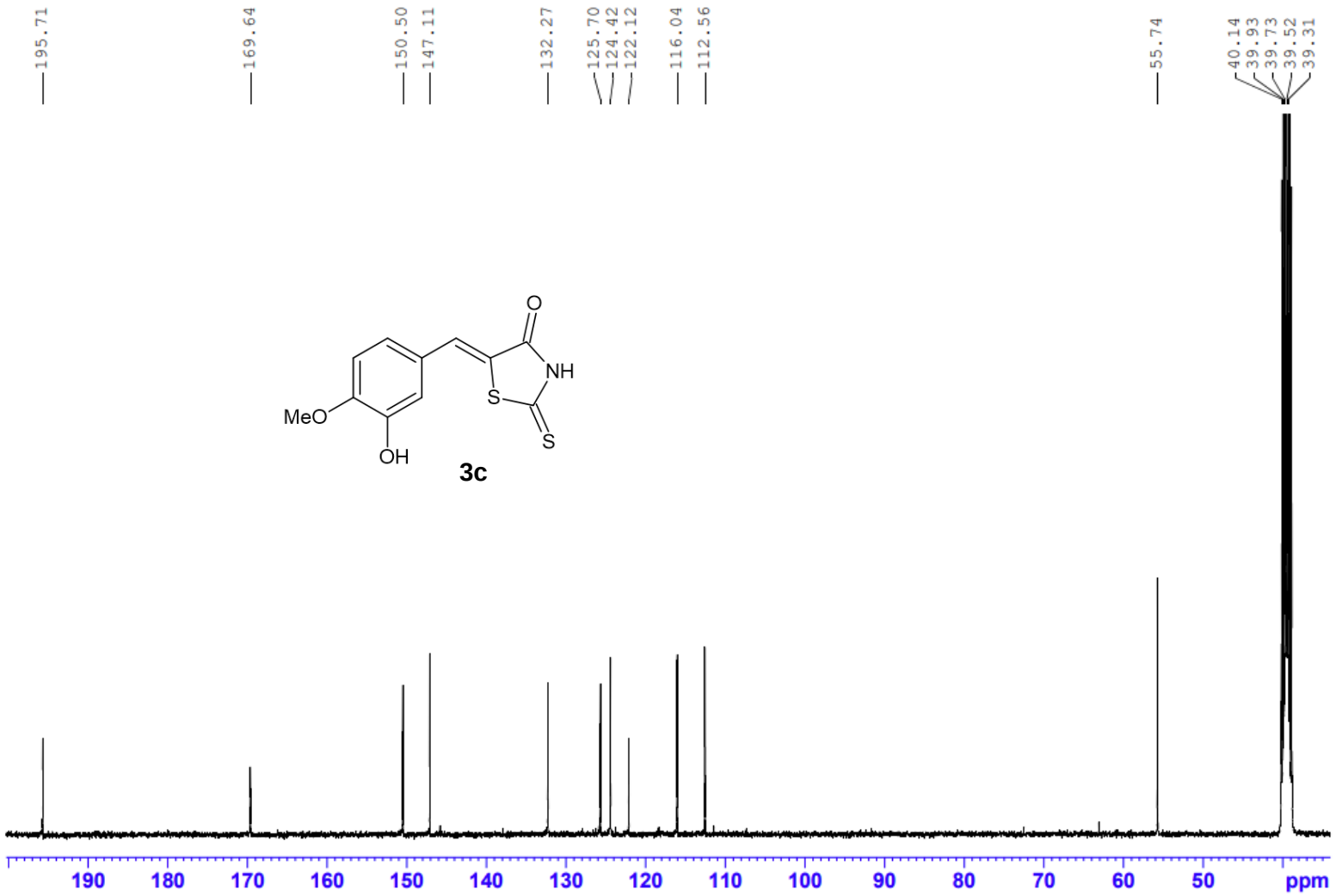
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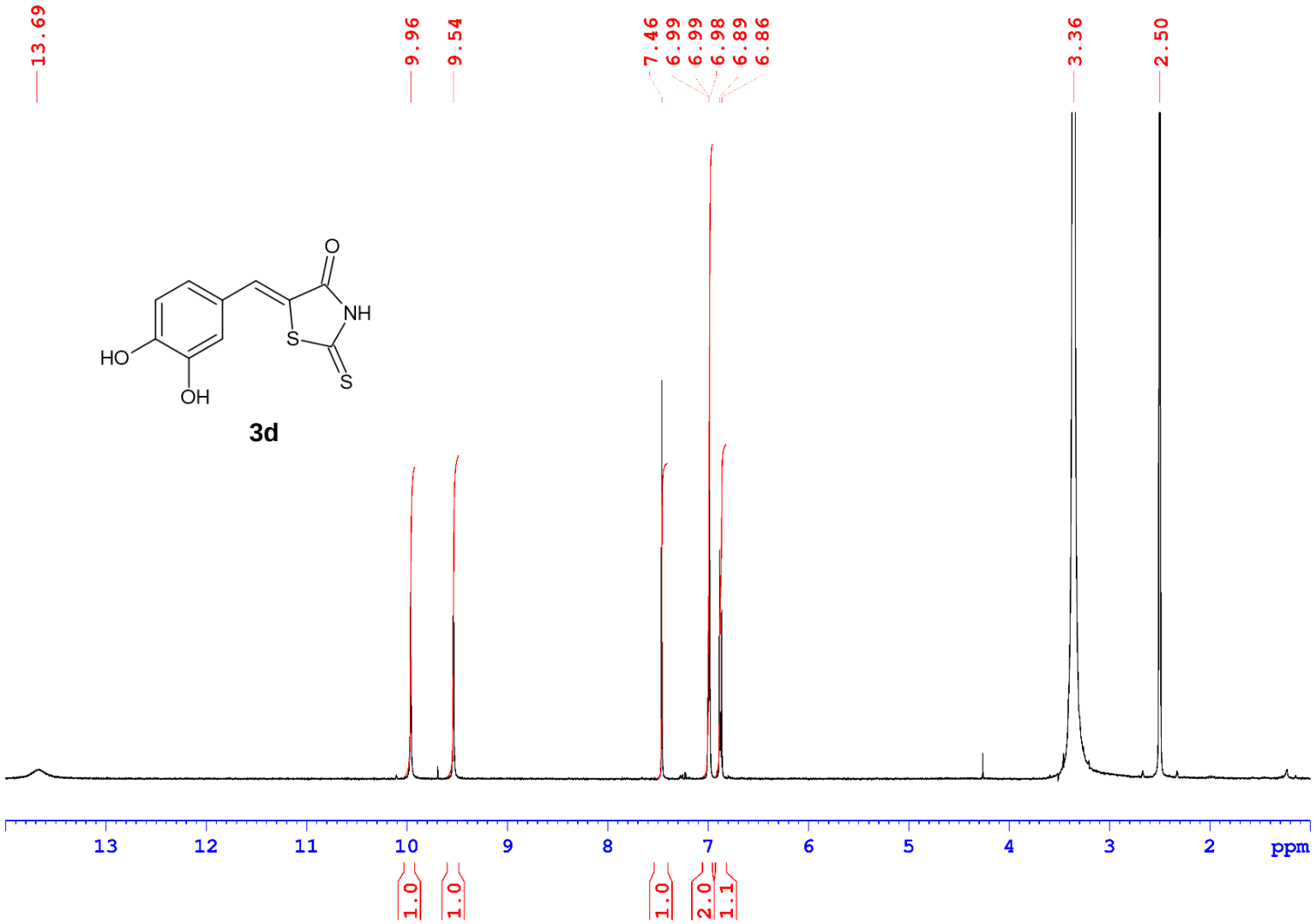
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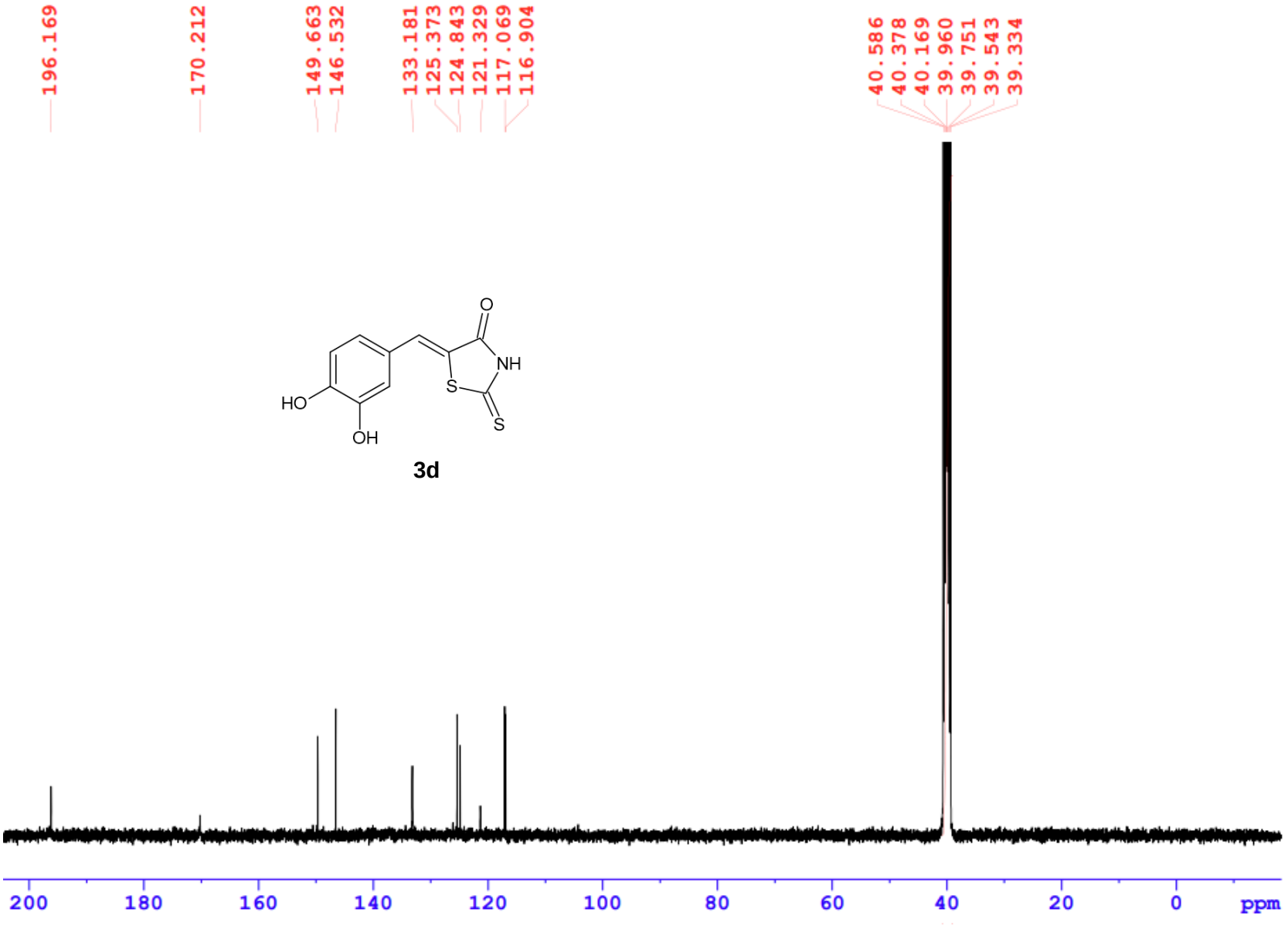
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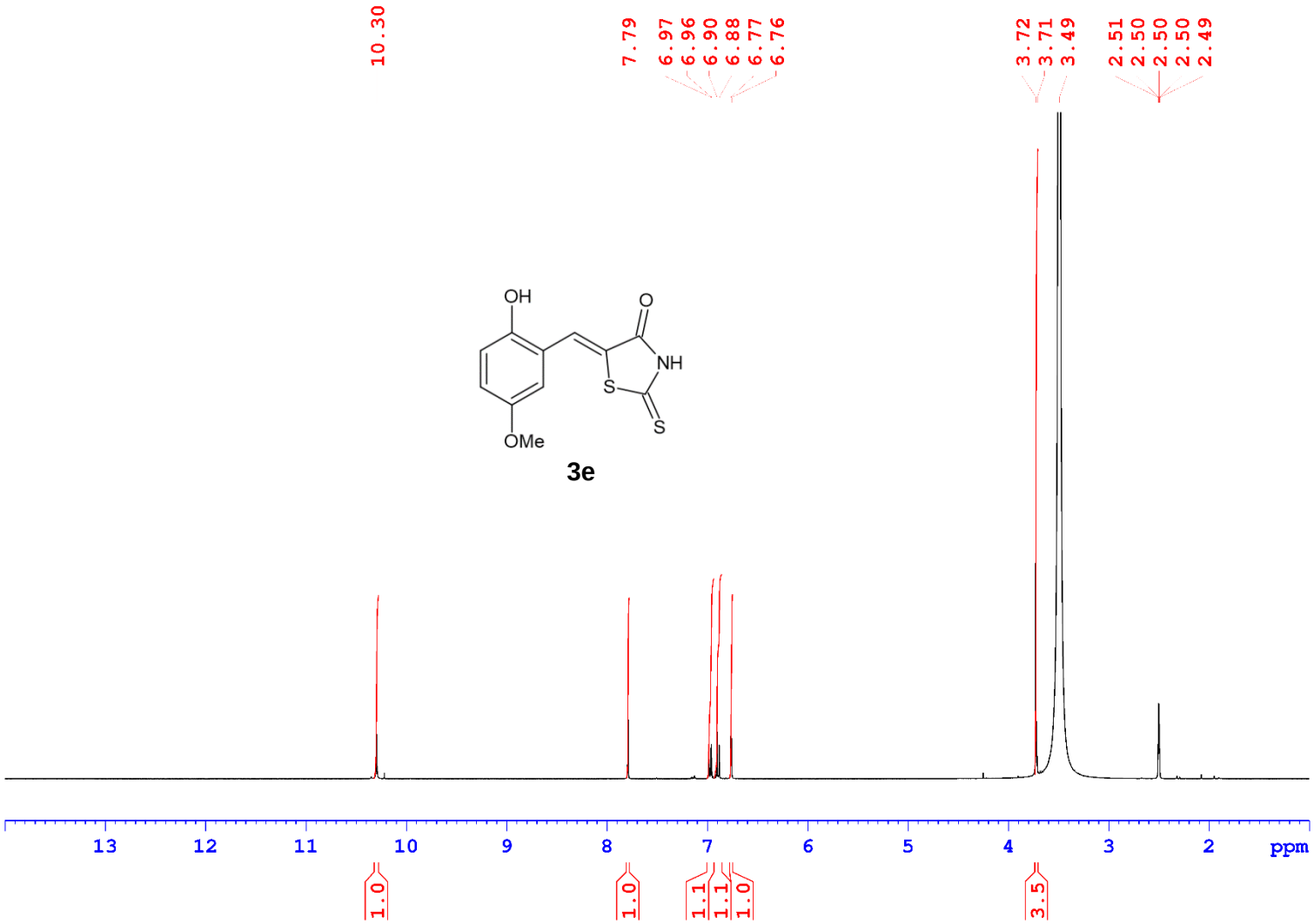
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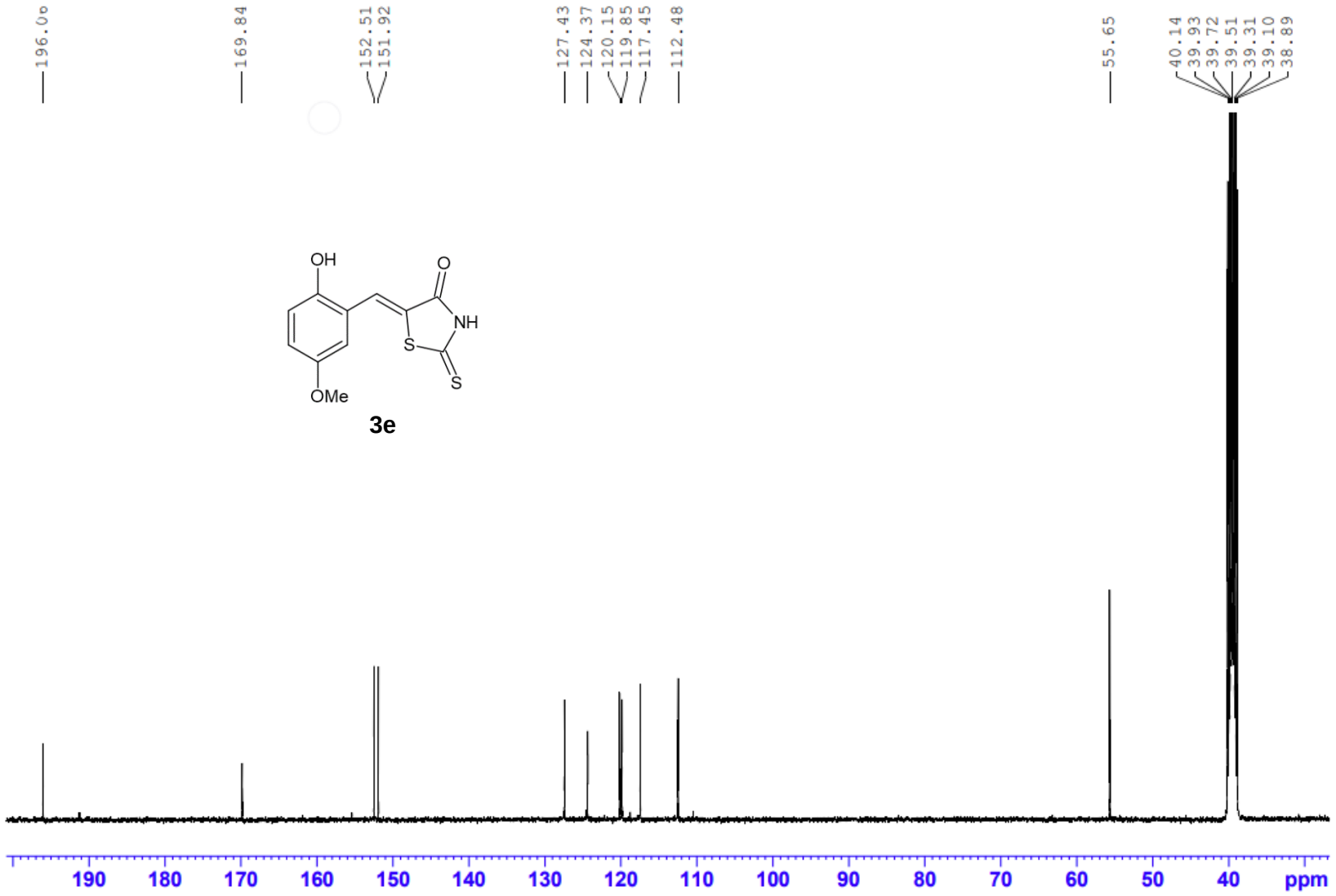
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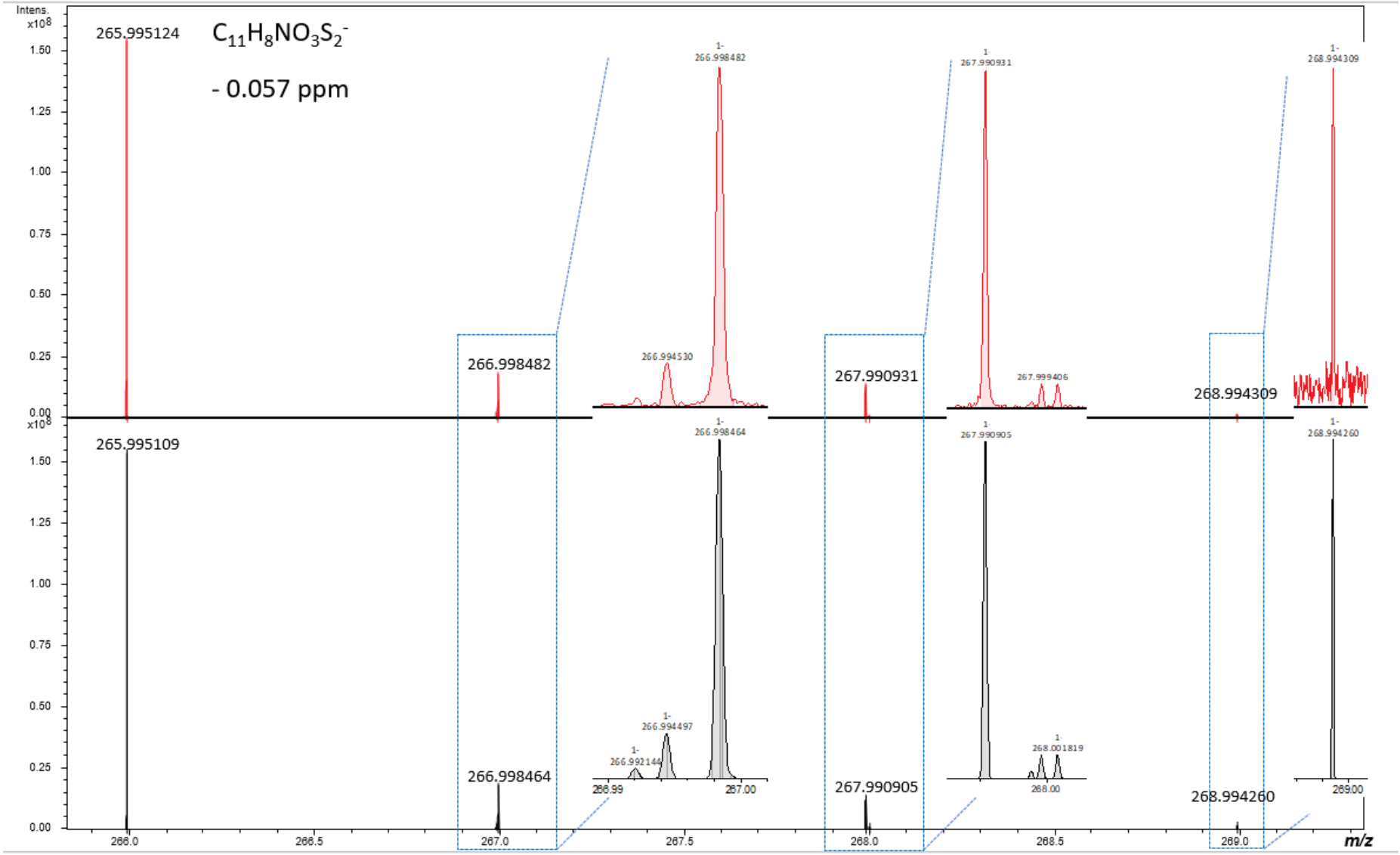
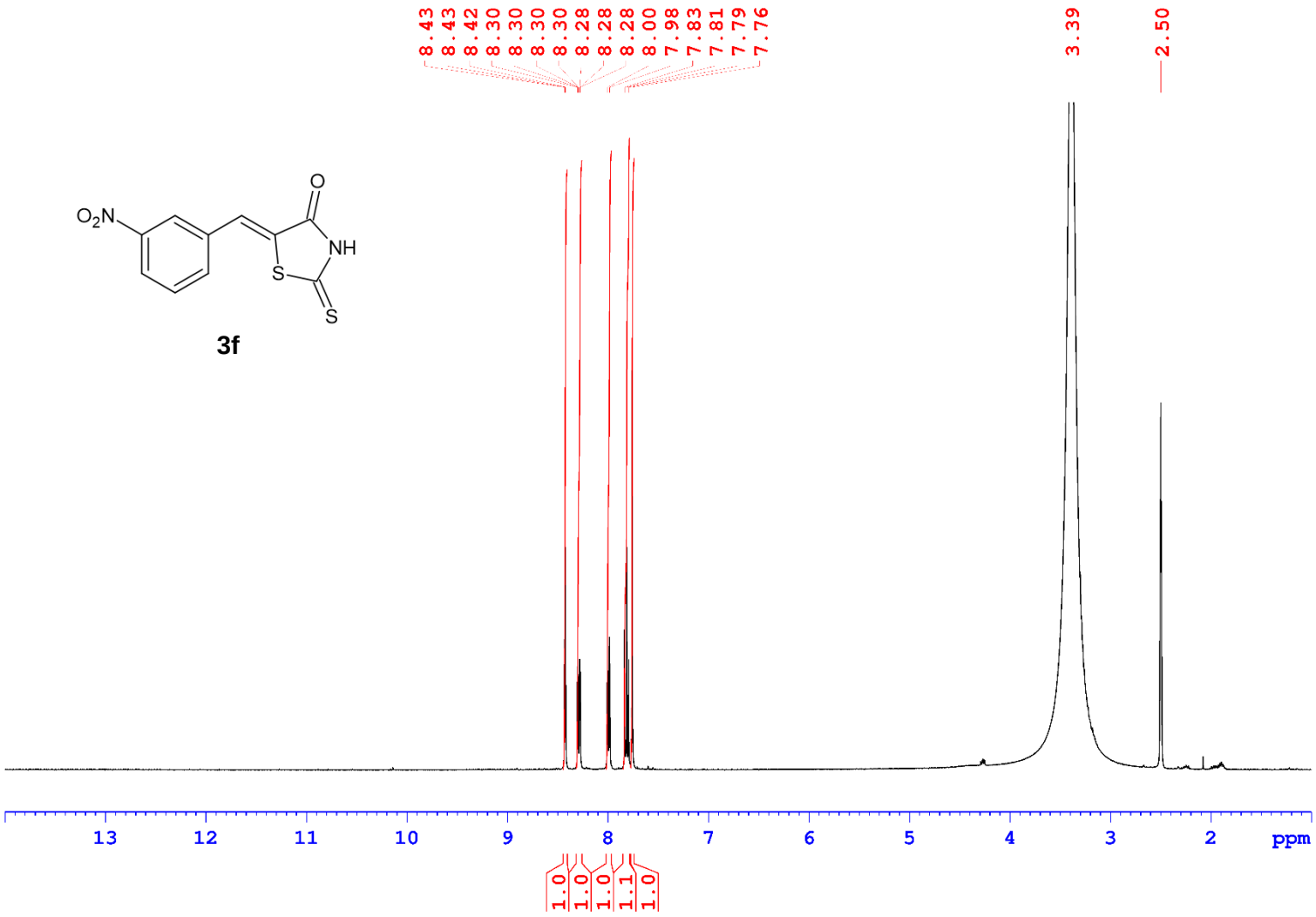
3e



Experimental (red) and theoretical (black) isotopic distributions for 3e [$C_{11}H_8NO_3S_2$]$^-$ ion detected by ESI (-) FT-ICR MS.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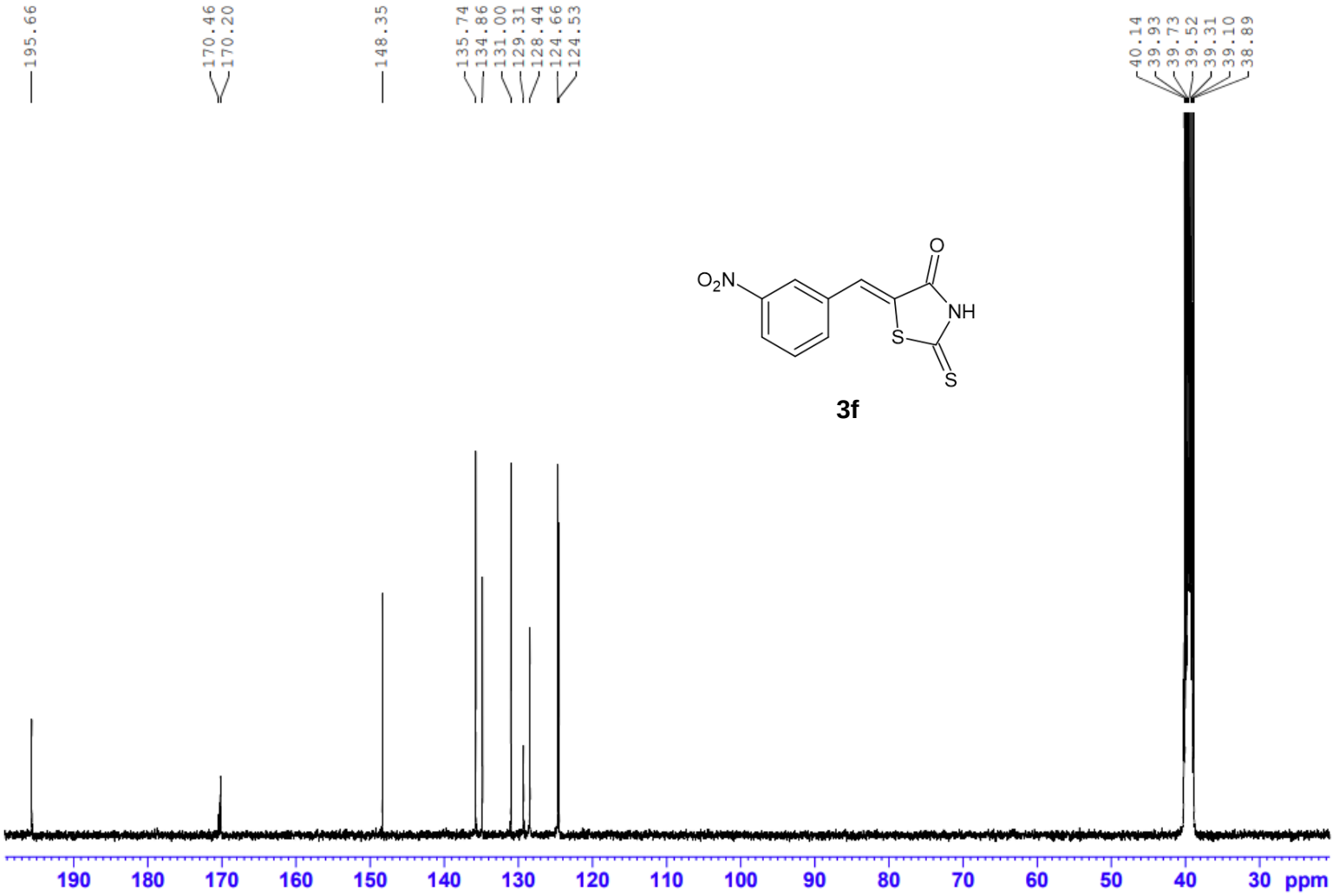
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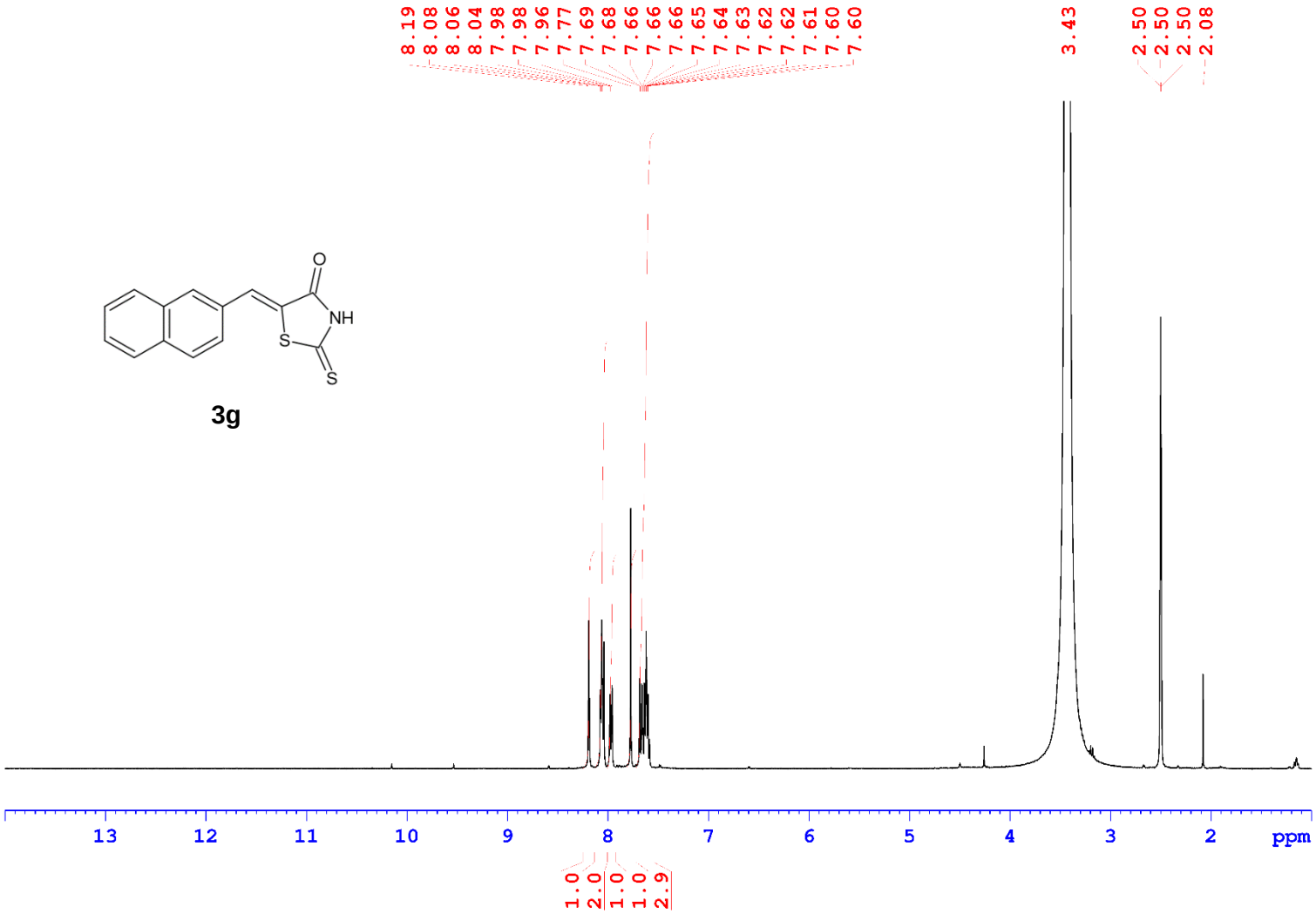
3f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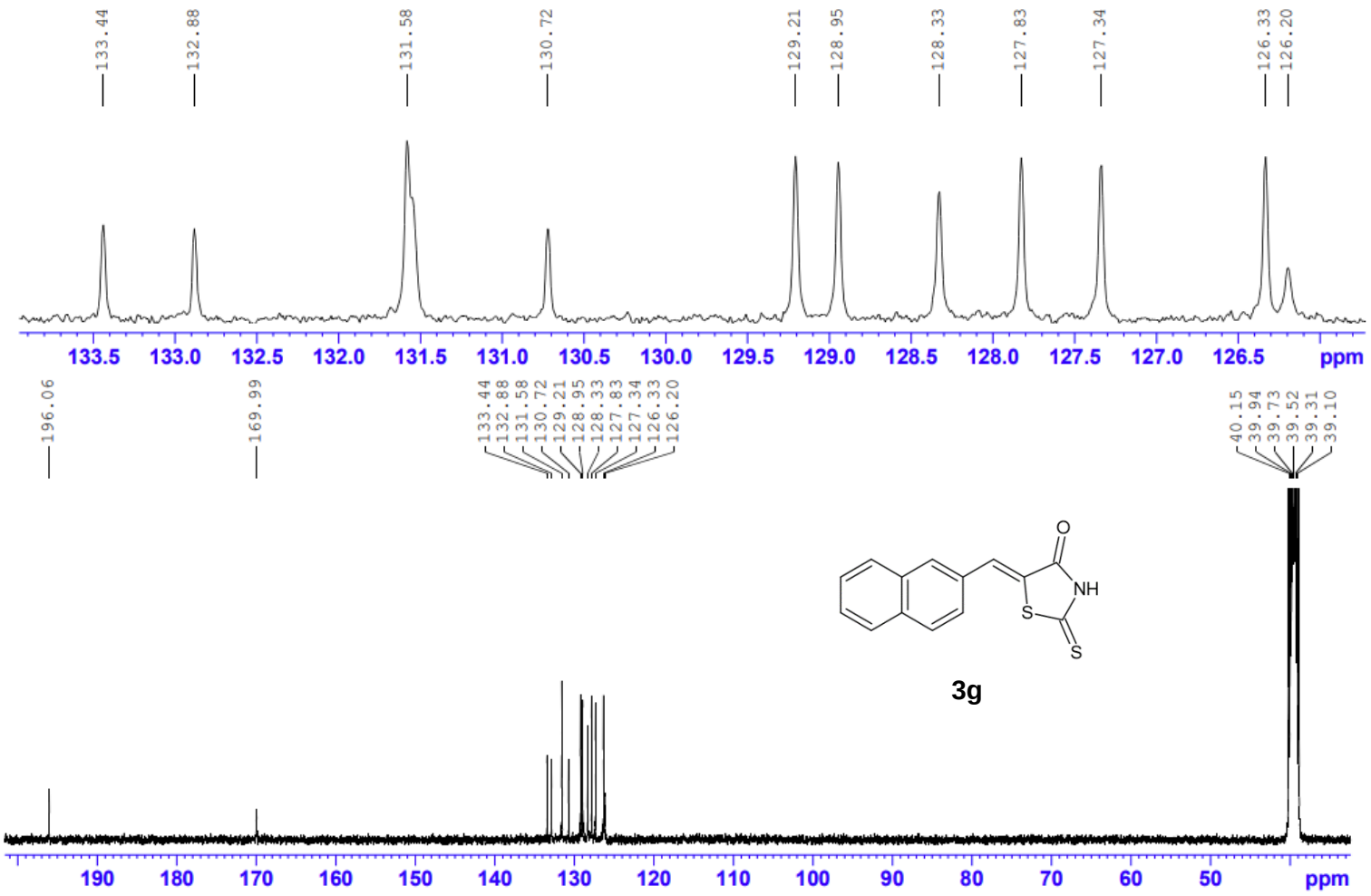
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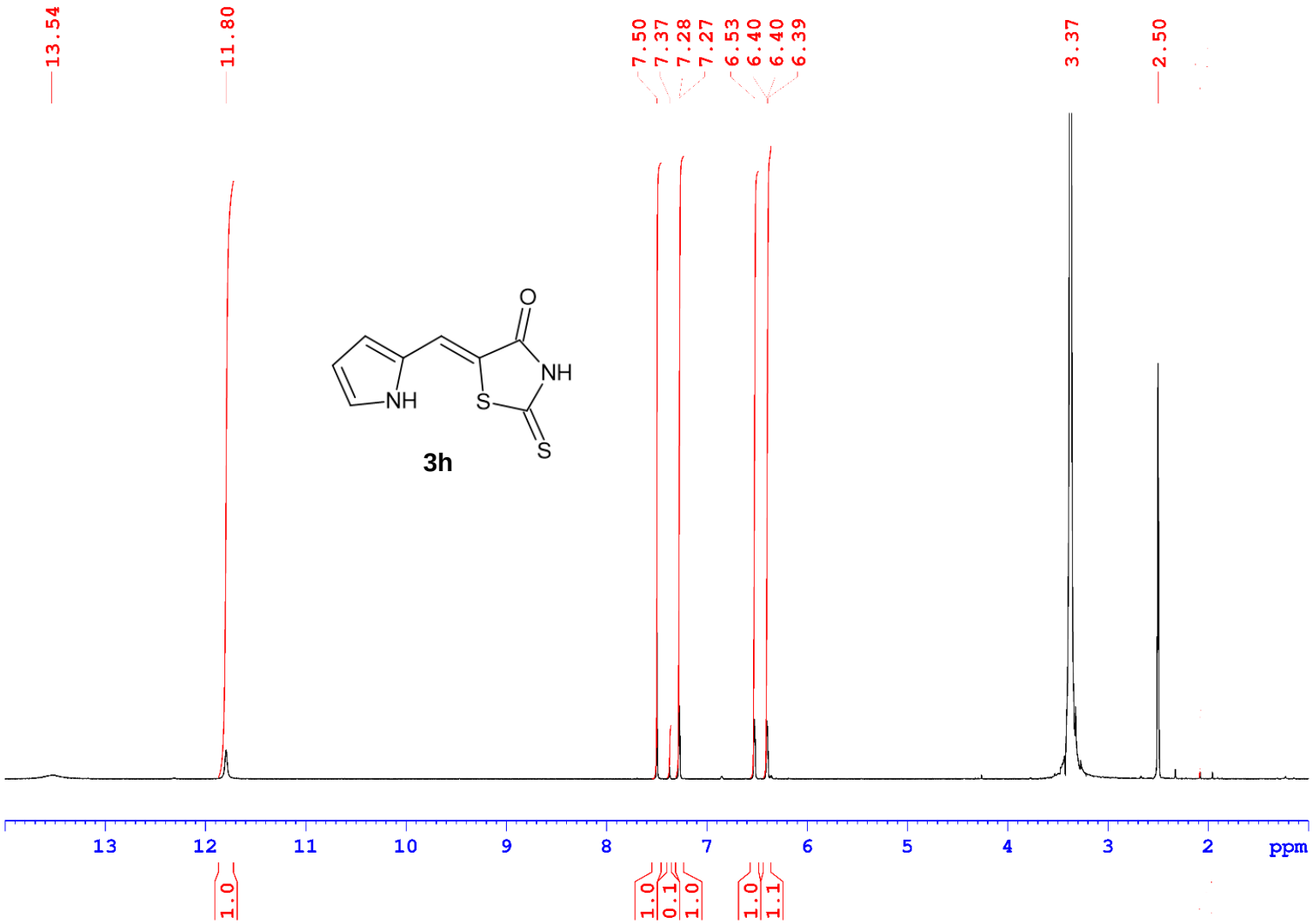
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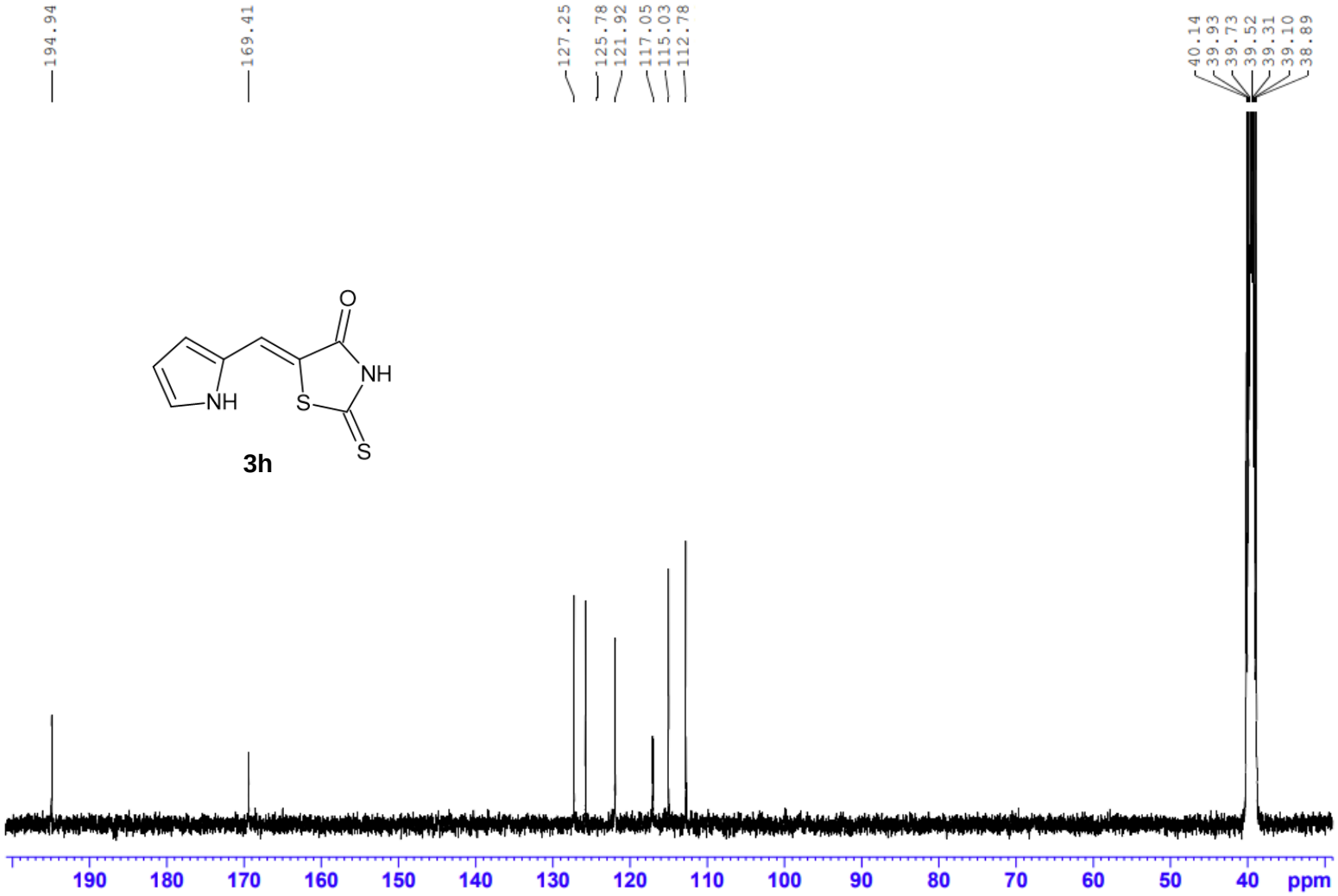
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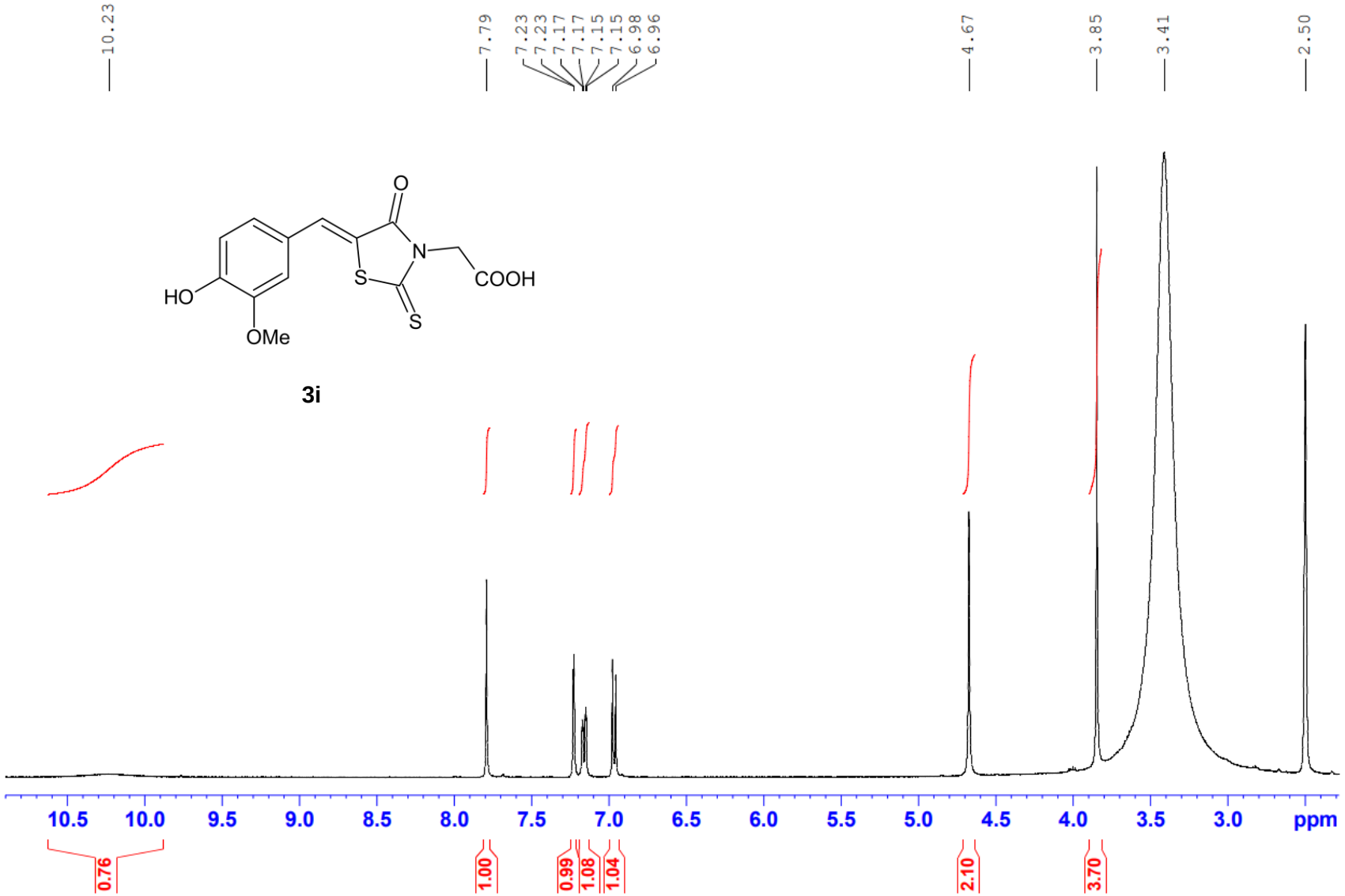
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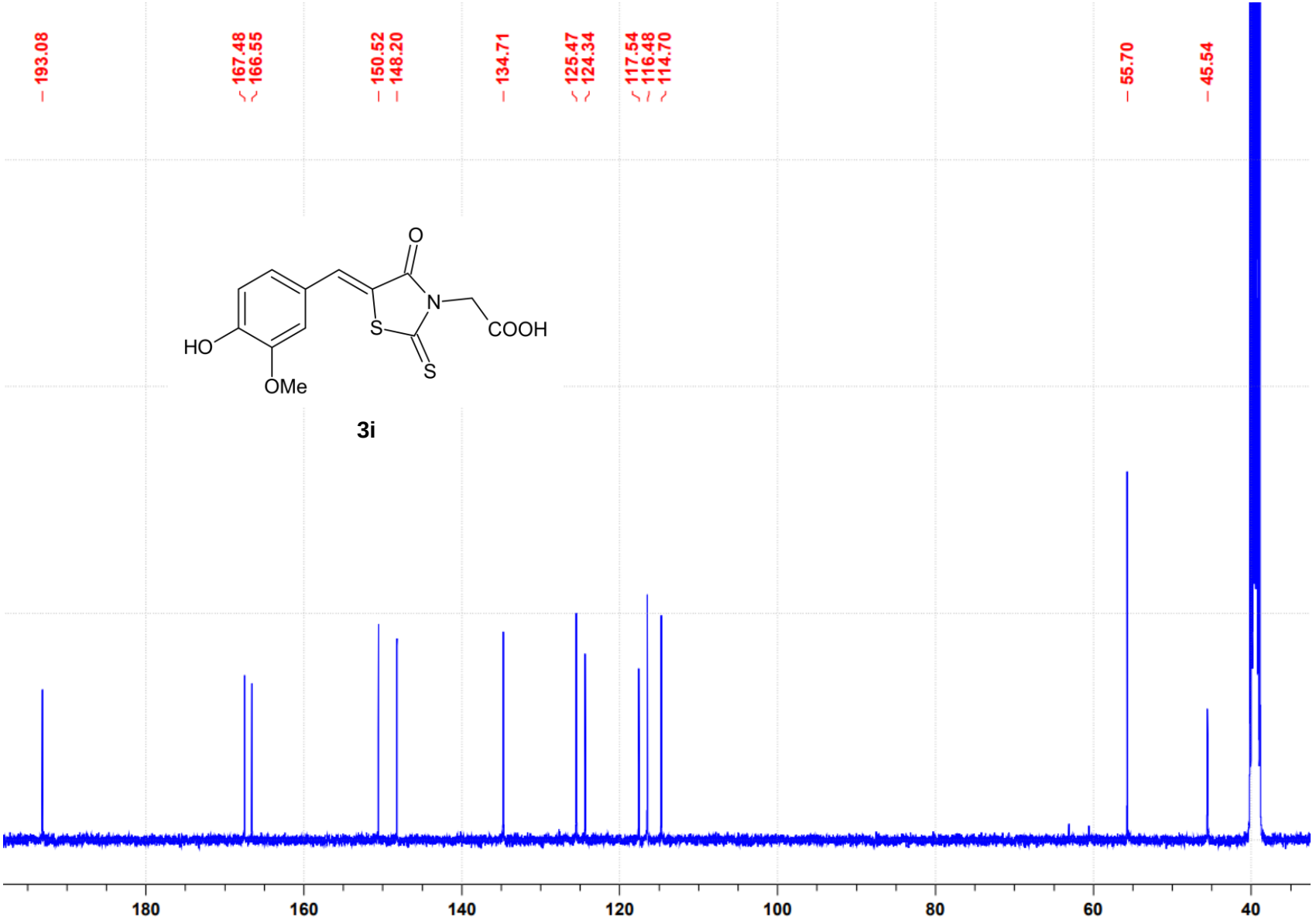
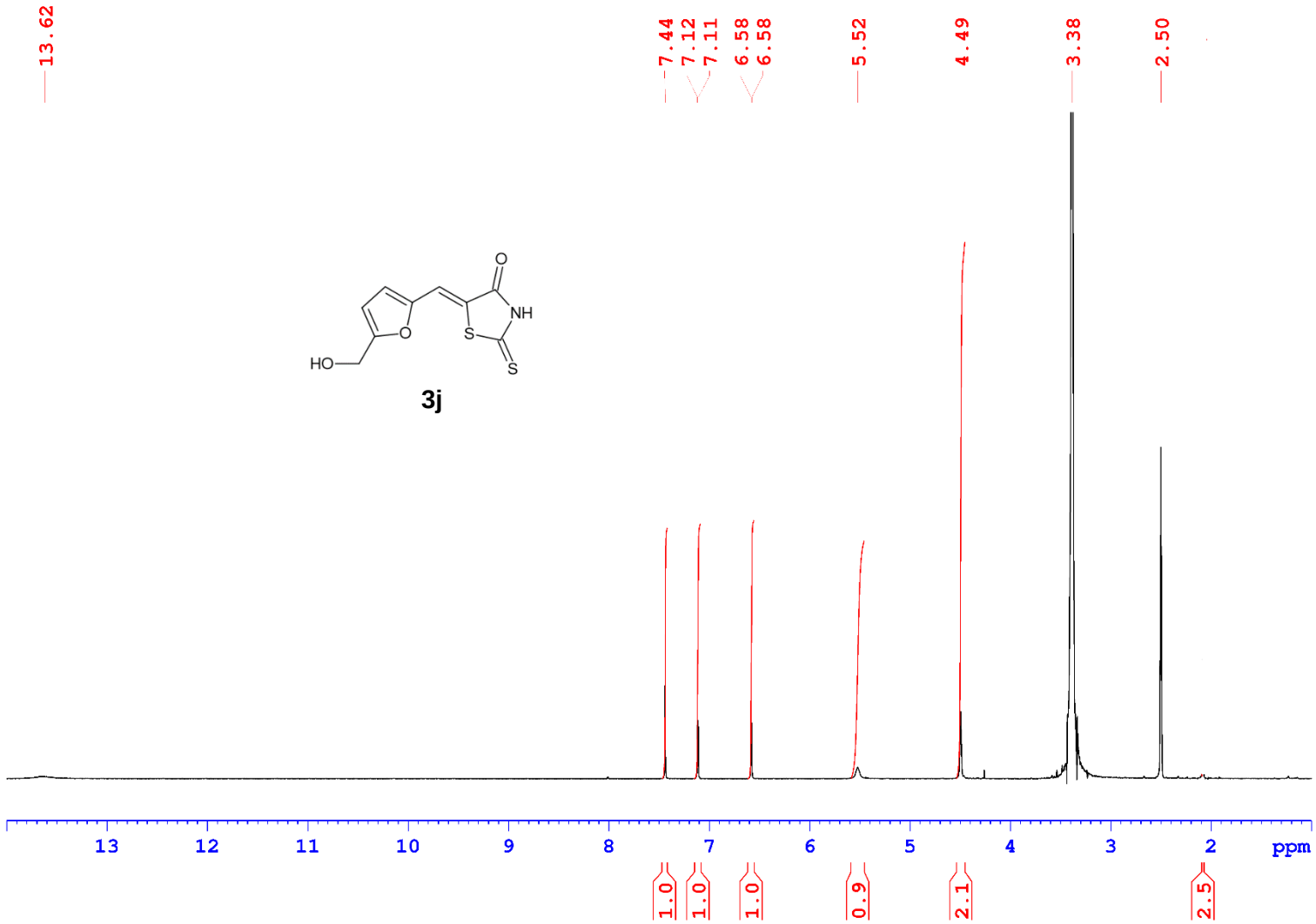
3.70

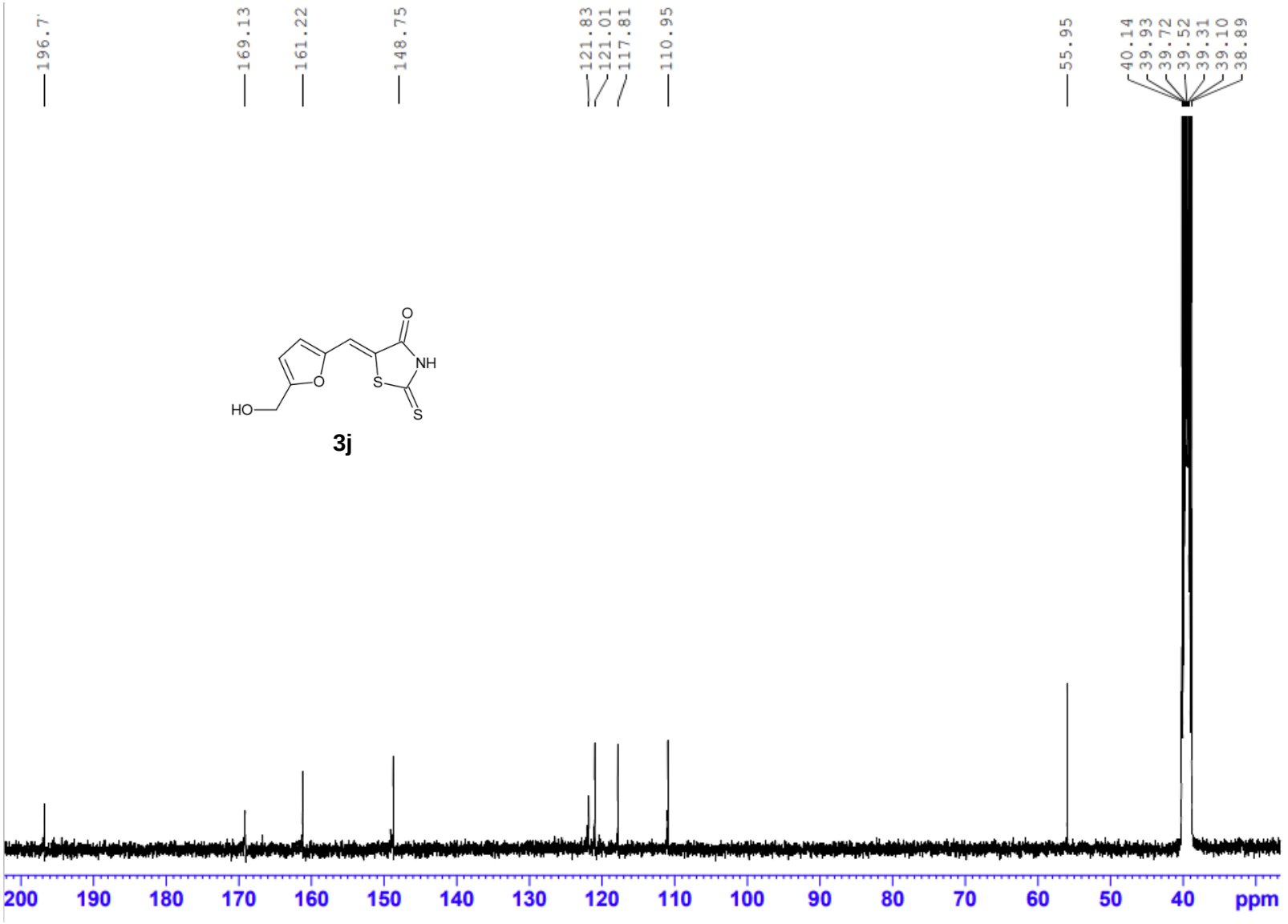
3i


193.08
167.48
166.55
150.52
148.20
134.71
125.47
124.34
117.54
116.48
114.70
55.70
45.54
O
N
S
S
COOH
HO
OMe
180
160
140
120
100
80
60
40

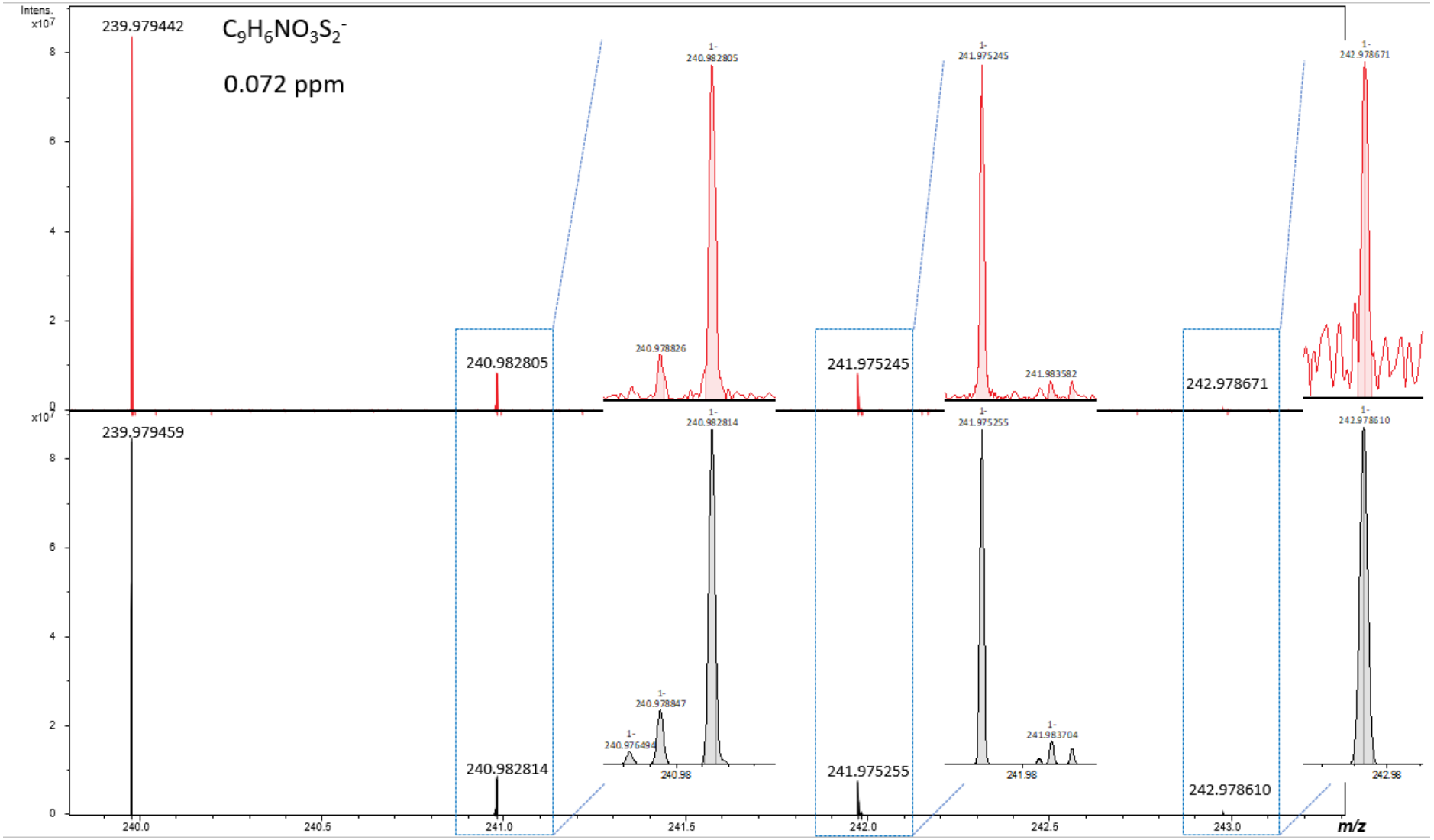
3i


13.62
7.44
7.12
7.11
6.58
6.58
5.52
4.49
3.38
2.50
O
NH
S
S
O
HO
13
12
11
10
9
8
7
6
5
4
3
2
ppm
1.0
1.0
1.0
0.9
2.1
2.5

3j


196.7'
169.13
161.22
148.75
121.83
121.01
117.81
110.95
55.95
40.14
39.93
39.72
39.52
39.31
39.10
38.89
O
NH
S
S
O
HO
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
ppm

3j



Experimental (red) and theoretical (black) isotopic distributions for **3j** $[C_9H_6NO_3S_2]^-$ ion detected by ESI(−) FT-ICR MS.