Electronic Supplementary Information for

Site-Selective C(sp^3)–H Amination of Thioamide with Anthranils under Cp^*Co^{III} Catalysis

Rui-Hua Liu,[a] Qi-Chao Shan,[a] Xu-Hong Hu,*[a] and Teck-Peng Loh*[ab]

[a] Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, China.

[b] Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore.

E-mail: ias_xhhu@njtech.edu.cn; teckpeng@ntu.edu.sg

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General Information

Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification.

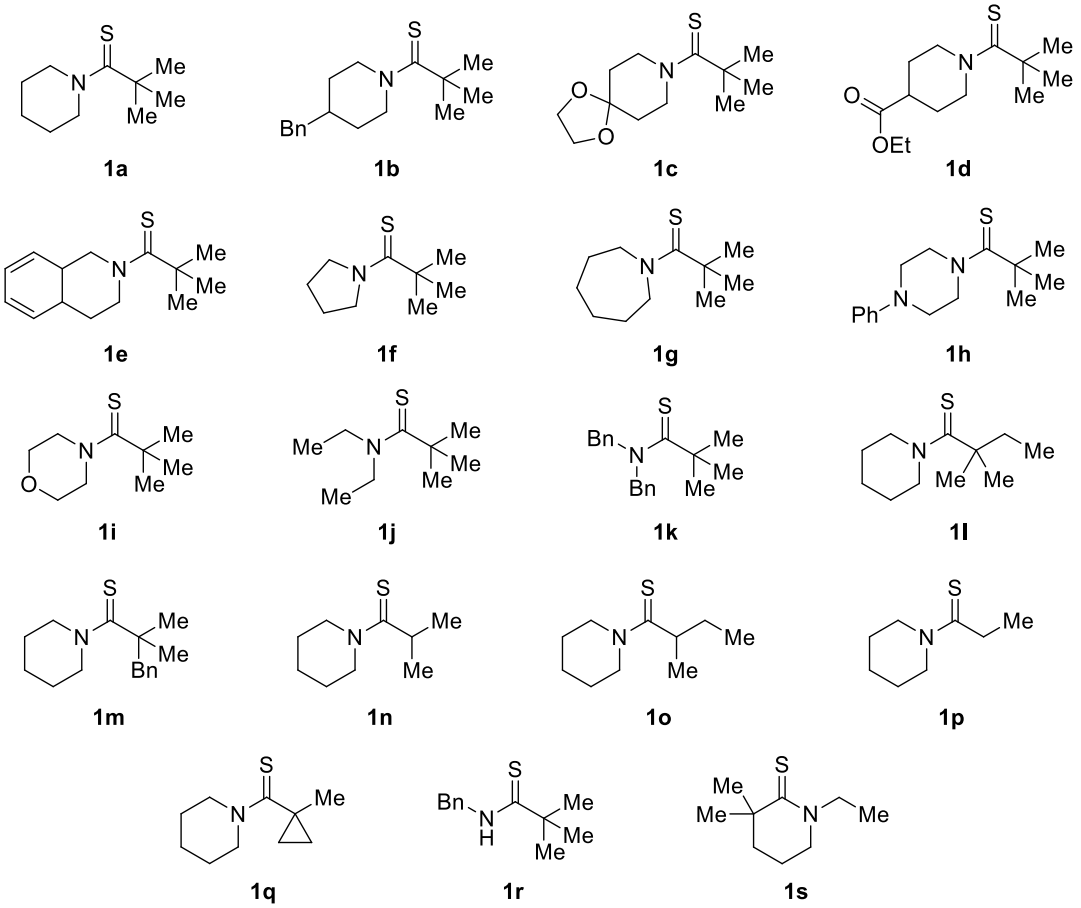
Thin layer chromatography was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm.

Flash chromatography was performed using 200-300 mesh silica gel with the indicated solvent system.

^{1}H NMR and ^{13}C NMR spectra were recorded at 25 ℃ on Bruker Advance 400M Hz NMR and JEOL 400M Hz spectrometers ($CDCl_3$ as solvent). Chemical shifts for 1H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of $SiMe_4$ (δ 0.00 singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); dt (doublet of triplets); m (multiplet); brs (broad single) and etc. Coupling constants are reported as a J value in Hz. ^{13}C NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe4 (δ 0.0) and relative to the signal of chloroform-*d* (δ 77 triplet). High resolution mass spectral analysis (HRMS) was performed on Waters-XEVOG2Q-TOF (Waters Corporation).

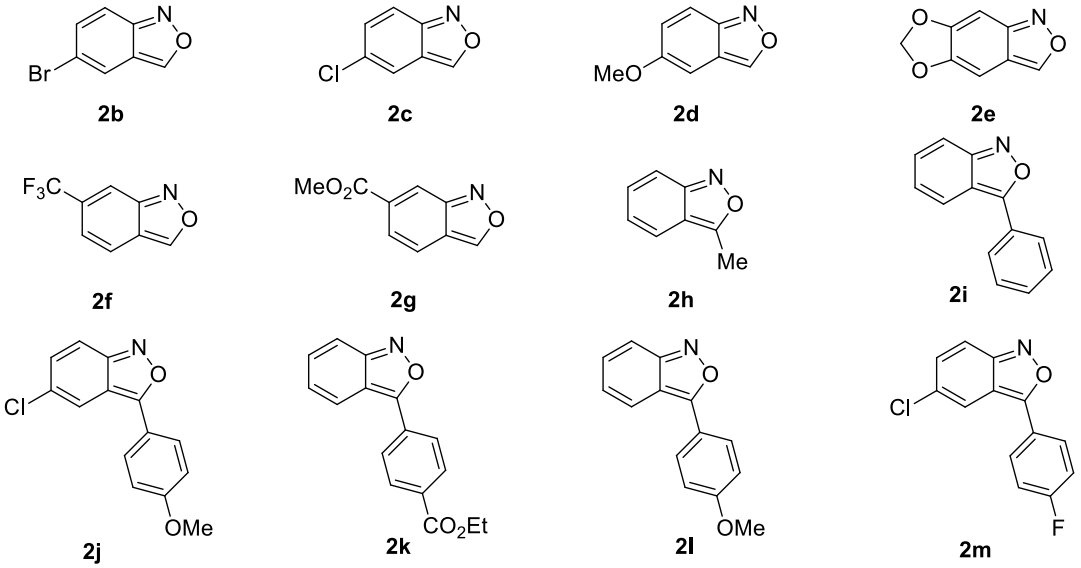
2. Experimental sections

2.1 Methods for the synthesis of thioamides 1a-s



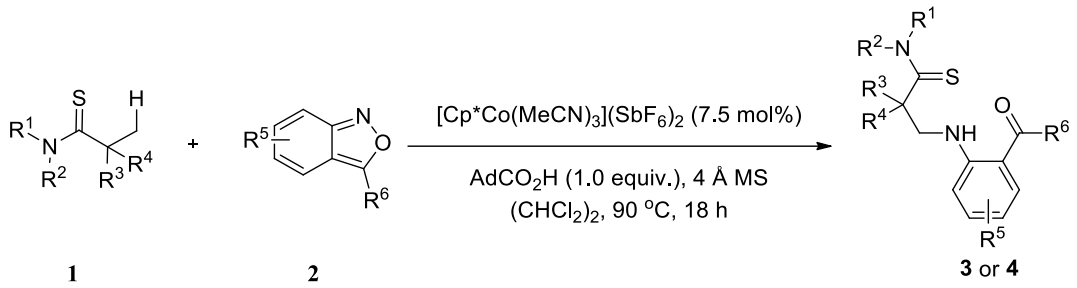
Compounds **1a-r**,[1] and **1s**[2] were prepared according to the previously described methods.

2.2 Methods for the synthesis of anthranils 2b-m



Compounds **2b-g**,[3] **2h**,[4] **2i**,[5] and **2j-m**[6] were prepared according to the previously described methods.

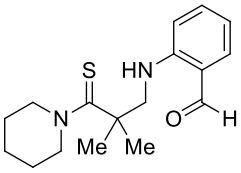
2.3 Typical procedure: the synthesis of products 3 and 4



A 4 mL screw-cap vial was charged with thioamide **1** (2.0 equiv., 0.3 mmol), anthranil **2** (1.0 equiv., 0.15 mmol), $[Cp^*Co(MeCN)_3](SbF_6)_2$ (8.9 mg, 0.01125 mmol), $AdCO_2H$ (27.0 mg, 0.15 mmol), 4 Å MS (60 mg), and $(CHCl_2)_2$ (1.5 mL). The vial was carefully blown with nitrogen for 30 seconds and placed into preheated oil bath at 90 ℃ with stirring for 18 h. After cooling down, the reaction mixture was quenched with sat. $NaHCO_3$ and extracted with DCM. The combined organic layers were washed with sat. NaCl, dried over Na_2SO_4, evaporated in vacuo and the resultant residue was purified by flash chromatography (PE/EtOAc) on silica gel to afford the compound **3** or **4**.

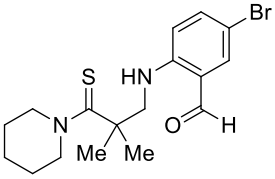
2.4 NMR data of products 3 and 4

2-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)benzaldehyde (3a)



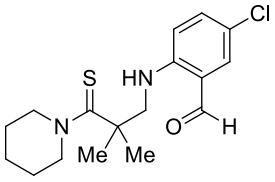
Following typical procedure, **3a** was obtained as a yellow solid (33.8 mg, 0.111 mmol, 74%). mp: 83.8 – 84.2 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.82 (s, 1H), 8.80 (brs, 1H), 7.44 (dd, J = 7.7, 1.7 Hz, 1H), 7.36 (t, J = 7.8 Hz, 1H), 6.79 (d, J = 8.6 Hz, 1H), 6.65 (t, J = 7.4 Hz, 1H), 4.12 (brs, 4H), 3.71 (d, J = 6.0 Hz, 2H), 1.72 – 1.69 (m, 6H), 1.48 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.11, 193.69, 151.21, 136.80, 135.77, 118.48, 114.51, 110.87, 55.45, 54.02, 47.90 × 2, 26.15, 25.81 × 2, 24.27 × 2. HRMS (ESI): m/z calculated for $C_{17}H_{25}N_2OS$ $[M + H]^+$: 305.1688, found: 305.1689.

5-Bromo-2-((2,2-dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)benzaldehyde (3b)



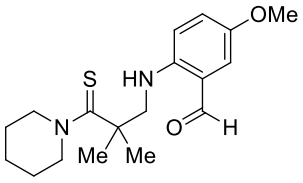
Following typical procedure, **3b** was obtained as a yellow solid (53.7 mg, 0.140 mmol, 93%). mp: 77.5 – 79.2 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.74 (s, 1H), 8.82 (brs, 1H), 7.39 (d, J = 2.6 Hz, 1H), 7.29 (dd, J = 9.0, 2.4 Hz, 1H), 6.76 (d, J = 9.1 Hz, 1H), 4.11 (brs, 4H), 3.70 (d, J = 6.1 Hz, 2H), 1.72 – 1.69 (m, 6H), 1.45 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.78, 192.47, 149.72, 135.70, 135.26, 119.03, 118.81, 112.73, 56.00, 54.04, 47.96 × 2, 26.14, 25.53 × 2, 24.25 × 2. HRMS (ESI): m/z calculated for $C_{17}H_{24}{}^{79}BrN_2OS$ $[M + H]^+$: 383.0793, found: 383.0794.

5-Chloro-2-((2,2-dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)benzaldehyde (3c)



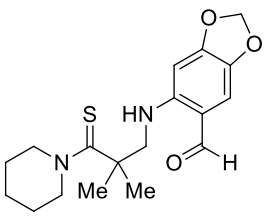
Following typical procedure, **3c** was obtained as a yellow oil (46.8 mg, 0.138 mmol, 92%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.84 (brs, 1H), 7.52 (d, J = 2.5 Hz, 1H), 7.40 (dd, J = 9.1, 2.5 Hz, 1H), 6.71 (d, J = 9.0 Hz, 1H), 4.11 (brs, 4H), 3.69 (d, J = 6.1 Hz, 2H), 1.72 – 1.69 (m, 6H), 1.45 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.71, 192.41, 150.00, 138.34, 138.29, 119.70, 113.11, 105.21, 55.94, 54.03, 47.96 × 2, 26.12, 25.48 × 2, 24.22 × 2. HRMS (ESI): m/z calculated for $C_{17}H_{24}{}^{35}ClN_2OS$ $[M + H]^+$: 339.1298, found: 339.1291.

2-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)-5-methoxybenzaldehyde (3d)



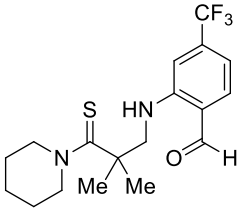
Following typical procedure, **3d** was obtained as a yellow oil (34.1 mg, 0.102 mmol, 68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 8.50 (brs, 1H), 7.06 (dd, J = 9.2, 3.0 Hz, 1H), 6.95 (d, J = 3.0 Hz, 1H), 6.77 (d, J = 9.2 Hz, 1H), 4.12 (brs, 4H), 3.79 (s, 3H), 3.68 (d, J = 6.1 Hz, 2H), 1.72 – 1.69 (m, 6H), 1.47 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.25, 192.98, 149.30, 146.79, 125.21, 117.91, 117.84, 112.55, 56.03, 55.81, 54.02, 47.95 × 2, 26.14, 25.93 × 2, 24.27 × 2. HRMS (ESI): m/z calculated for $C_{18}H_{27}N_2O_3S$ $[M + H]^+$: 335.1793, found: 335.1789.

5-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)benzo[*d*][1,3]dioxole-4-carbaldehyde (3e)



Following typical procedure, **3e** was obtained as a yellow solid (27.2 mg, 0.078 mmol, 52%). mp: 160.9 – 161.8 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.53 (s, 1H), 9.22 (brs, 1H), 6.79 (s, 1H), 6.33 (s, 1H), 5.92 (s, 2H), 4.13 – 4.11 (m, 4H), 3.66 (d, J = 5.9 Hz, 2H), 1.72 – 1.69 (m, 6H), 1.47 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.10, 190.09, 154.85, 151.08, 137.87, 112.48, 111.35, 101.31, 91.33, 56.18, 54.00, 47.73 × 2, 26.12, 25.70 × 2, 24.26 × 2. HRMS (ESI): m/z calculated for $C_{18}H_{25}N_2OS$ $[M + H]^+$: 349.1586, found: 349.1585.

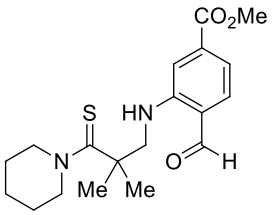
2-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)-4-(trifluoromethyl)benzaldehyde (3f)



Following typical procedure, **3f** was obtained as a green oil (41.3 mg, 0.111 mmol, 74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.88 (s, 1H), 9.01 (brs, 1H), 7.56 (d, J = 8.0 Hz, 1H), 6.99 (s, 1H), 6.85 (dd, J = 8.0, 1.5 Hz, 1H), 4.12 (brs, 4H), 3.73 (d, J = 6.0 Hz, 2H), 1.80 – 1.67 (m, 6H), 1.47 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.43, 193.30, 150.67, 137.45, 136.61 (q, $J_{C\text{-}F}$ = 32.0 Hz), 123.66 (d, $J_{C\text{-}F}$ = 273.5 Hz), 119.96 (q, $J_{C\text{-}F}$ = 1.3 Hz), 110.45 (q, $J_{C\text{-}F}$ = 3.9 Hz), 107.90 (q, $J_{C\text{-}F}$ = 4.3 Hz), 55.98, 54.06, 48.05, 26.13, 25.58, 24.23. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.75.

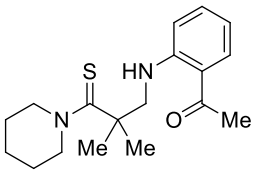
HRMS (ESI): m/z calculated for $C_{18}H_{24}F_3N_2OS$ $[M + H]^+$: 373.1561, found: 373.1560.

Methyl 3-((2,2-dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)-4-formylbenzoate (3g)



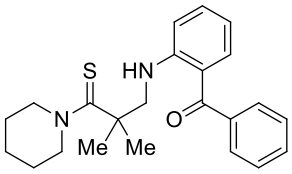
Following typical procedure, **3g** was obtained as a green oil (49.5 mg, 0.137 mmol, 91%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.90 (s, 1H), 8.89 (brs, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.45 (s, 1H), 7.24 (dd, *J* = 8.0, 1.4 Hz, 1H), 4.13 (brs, 4H), 3.93 (s, 3H), 3.76 (d, *J* = 6.1 Hz, 2H), 1.77 – 1.67 (m, 6H), 1.48 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.61, 193.51, 166.75, 150.59, 136.77, 135.84, 120.52, 114.61, 112.42, 55.64, 54.02, 52.42, 48.11 × 2, 26.10, 25.78 × 2, 24.21 × 2. HRMS (ESI): m/z calculated for $C_{19}H_{27}N_2O_3S$ $[M + H]^+$: 363.1742, found: 363.1747.

1-(2-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)phenyl)ethanone (3h)



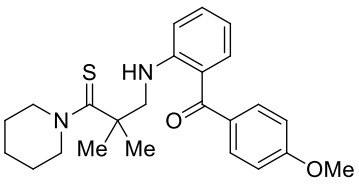
Following a modified procedure, as the reaction was run for 12 h, **3h** was obtained as a yellow oil (32.0 mg, 0.101 mmol, 67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.31 (brs, 1H), 7.74 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.34 (ddd, *J* = 8.6, 6.9, 1.6 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.56 (t, *J* = 7.1 Hz, 1H), 4.13 (brs, 4H), 3.66 (d, *J* = 5.7 Hz, 2H), 2.58 (s, 3H), 1.78 – 1.66 (m, 6H), 1.50 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.48, 200.73, 151.61, 135.11, 132.93, 117.68, 113.79, 111.81, 55.56, 54.14, 47.81 × 2, 28.00, 26.40, 26.26 × 2, 24.41 × 2. HRMS (ESI): m/z calculated for $C_{18}H_{27}N_2OS$ $[M + H]^+$: 319.1844, found: 319.1848.

(2-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)phenyl)(phenyl)methanone (3i)



Following a modified procedure, as the reaction was run for 24 h, **3i** was obtained as a yellow oil (40.5 mg, 0.107 mmol, 71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.02 (brs, 1H), 7.61 (d, *J* = 6.9 Hz, 2H), 7.45 (dt, *J* = 18.6, 6.5 Hz, 4H), 7.36 (t, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 6.50 (t, *J* = 7.5 Hz, 1H), 4.13 (brs, 4H), 3.73 (d, *J* = 5.7 Hz, 2H), 1.72 – 1.69 (m, 6H), 1.53 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.32, 199.14, 152.25, 140.60, 135.61, 134.94, 130.61, 129.07 × 2, 127.92 × 2, 117.34, 113.43, 111.66, 55.83, 54.02, 47.73 × 2, 26.14, 26.02 × 2, 24.28 × 2. HRMS (ESI): m/z calculated for $C_{23}H_{29}N_2OS$ $[M + H]^+$: 381.2001, found: 381.1998.

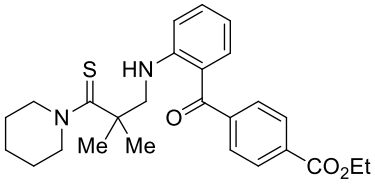
(2-((2,2-Dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)phenyl)(4-methoxyphenyl)methanon e (3j)



Following a modified procedure, as the reaction was run for 24 h, **3j** was obtained as a yellow oil (43.7 mg, 0.107 mmol, 71%). ^{1}H NMR

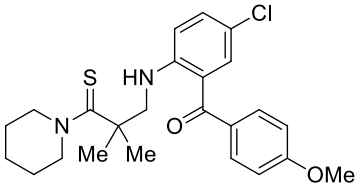
(400 MHz, Chloroform-*d*) δ 8.68 (brs, 1H), 7.64 (d, *J* = 8.9 Hz, 2H), 7.49 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.35 (ddd, *J* = 8.7, 7.0, 1.7 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.86 (dd, *J* = 8.7, 1.0 Hz, 1H), 6.52 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.12 (brs, 4H), 3.87 (s, 3H), 3.69 (d, *J* = 5.7 Hz, 2H), 1.71 – 1.68 (m, 6H), 1.51 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.45, 197.96, 161.94, 151.85, 135.06, 134.41, 132.94, 131.62 × 2, 118.07, 113.46, 113.22 × 2, 111.63, 55.81, 55.40, 54.00, 47.78 × 2, 26.12 × 3, 24.28 × 2. HRMS (ESI): m/z calculated for $C_{24}H_{31}N_2O_2S$ $[M + H]^+$: 411.2106, found: 411.2107.

Ethyl 4-(2-((2,2-dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)benzoyl)benzoate (3k)



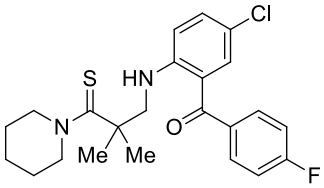
Following a modified procedure, as the reaction was run for 24 h, **3k** was obtained as a yellow oil (55.0 mg, 0.122 mmol, 81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.16 (brs, 1H), 8.11 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.35 (m, 2H), 6.89 (d, *J* = 8.6 Hz, 1H), 6.48 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.13 (brs, 4H), 3.75 (d, *J* = 5.8 Hz, 2H), 1.72 – 1.70 (m, 6H), 1.53 (s, 6H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.09, 198.15, 166.04, 152.44, 144.55, 135.48, 135.38, 131.89, 129.17 × 2, 128.71 × 2, 116.79, 113.53, 111.80, 61.23, 55.94, 54.01, 47.77, 38.53, 36.35, 27.75, 26.13, 25.91, 24.25, 14.28. HRMS (ESI): m/z calculated for $C_{26}H_{33}N_2O_3S$ $[M + H]^+$: 453.2212, found: 453.2213.

(5-Chloro-2-((2,2-dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)phenyl)(4-methoxyphenyl) methanone (3l)



Following a modified procedure, as the reaction was run for 24 h, **3l** was obtained as a yellow oil (61.4 mg, 0.138 mmol, 92%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 (brs, 1H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 2.6 Hz, 1H), 7.28 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 9.1 Hz, 1H), 4.11 (brs, 4H), 3.88 (s, 3H), 3.67 (d, *J* = 5.8 Hz, 2H), 1.75 – 1.66 (m, 6H), 1.48 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.07, 196.75, 162.29, 150.27, 134.09, 133.62, 132.15, 131.64 × 2, 118.94, 117.92, 113.44 × 2, 113.21, 56.34, 55.43, 54.00, 47.83 × 2, 26.11, 25.85 × 2, 24.24 × 2. HRMS (ESI): m/z calculated for $C_{24}H_{30}{}^{35}ClN_2O_2S$ $[M + H]^+$: 445.1717, found: 445.1720.

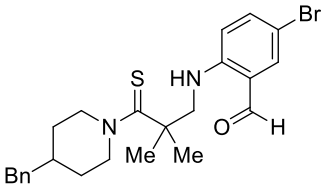
(5-Chloro-2-((2,2-dimethyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)phenyl)(4-fluorophenyl)met hanone (3m)



Following a modified procedure, as the reaction was run for 24 h, **3m** was obtained as a yellow oil (46.8 mg, 0.108 mmol, 72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.85 (brs, 1H), 7.64 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.38 (d, *J* = 2.6 Hz, 1H), 7.29 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.14 (t, *J* =

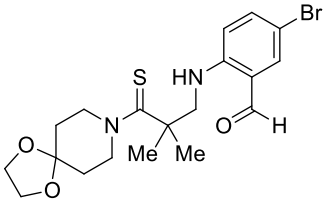
8.6 Hz, 2H), 6.83 (d, *J* = 9.2 Hz, 1H), 4.12 (brs, 4H), 3.70 (d, *J* = 5.9 Hz, 2H), 1.72 – 1.70 (m, 6H), 1.49 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.86, 196.44, 165.73, 163.23, 150.61, 135.94 (d, $J_{C\text{-}F}$ = 3.3 Hz), 134.73, 133.72, 131.59 × 2 (d, $J_{C\text{-}F}$ = 8.9 Hz), 117.99 (d, $J_{C\text{-}F}$ = 14.4 Hz), 115.27 × 2 (d, $J_{C\text{-}F}$ = 21.8 Hz), 113.42, 56.46, 54.03, 47.87 × 2, 26.13, 25.73 × 2, 24.24 × 2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -107.96. HRMS (ESI): m/z calculated for $C_{23}H_{27}{}^{35}ClFN_2OS$ $[M + H]^+$: 433.1517, found: 433.1515.

2-((3-(4-Benzylpiperidin-1-yl)-2,2-dimethyl-3-thioxopropyl)amino)-5-bromobenzaldehyde (4a)



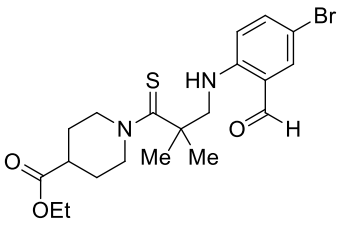
Following typical procedure, **4a** was obtained as a yellow oil (59.6 mg, 0.126 mmol, 84%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.84 (brs, 1H), 7.52 (d, *J* = 2.5 Hz, 1H), 7.40 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.25 – 7.18 (m, 1H), 7.15 – 7.10 (m, 2H), 6.70 (d, *J* = 9.1 Hz, 1H), 5.12 (brs, 2H), 3.68 (d, *J* = 6.1 Hz, 2H), 3.07 (t, *J* = 12.4 Hz, 2H), 2.55 (d, *J* = 7.3 Hz, 2H), 1.96 – 1.88 (m, 1H), 1.78 (d, *J* = 13.6 Hz, 2H), 1.44 (s, 6H), 1.37 – 1.28 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.90, 192.39, 149.95, 139.67, 138.33, 138.28, 128.95 × 2, 128.33 × 2, 126.13, 119.68, 113.09, 105.22, 55.92, 53.08, 48.01 × 2, 42.51, 38.05 × 2, 32.17, 25.51 × 2. HRMS (ESI): m/z calculated for $C_{24}H_{30}{}^{79}BrN_2OS$ $[M + H]^+$: 473.1262, found: 473.1262.

5-Bromo-2-((2,2-dimethyl-3-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-3-thioxopropyl)amino)benzal dehyde (4b)



Following typical procedure, **4b** was obtained as a yellow oil (35.8 mg, 0.081 mmol, 54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.84 (brs, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 7.40 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.71 (d, *J* = 9.1 Hz, 1H), 4.24 (brs, 4H), 4.00 (s, 4H), 3.69 (d, *J* = 6.1 Hz, 2H), 1.86 – 1.78 (m, 4H), 1.45 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.75, 192.47, 149.94, 138.37, 138.31, 119.70, 113.04, 106.49, 105.29, 64.60 × 2, 55.89, 50.53, 48.08 × 2, 35.15 × 2, 25.50 × 2. HRMS (ESI): m/z calculated for $C_{19}H_{26}{}^{35}BrN_2O_3S$ $[M + H]^+$: 441.0848, found: 441.0847.

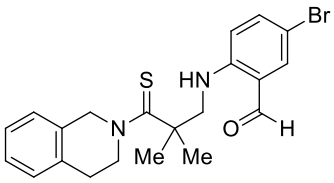
Ethyl 1-(3-((4-bromo-2-formylphenyl)amino)-2,2-dimethylpropanethioyl)piperidine-4-Carboxylate (4c)



Following typical procedure, **4c** was obtained as a yellow oil (41.0 mg, 0.090 mmol, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.85 (brs, 1H), 7.53 (d, *J* = 2.3 Hz, 1H), 7.41 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.71 (d, *J* = 9.1 Hz, 1H), 4.85 (brs, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.69 (d, *J* = 6.1 Hz, 2H), 3.53 – 3.46 (m, 2H), 2.72 – 2.66 (m, 1H), 2.08 – 1.99 (m, 2H), 1.93 – 1.83 (m, 2H), 1.45 (s, 6H), 1.26 (t, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz,

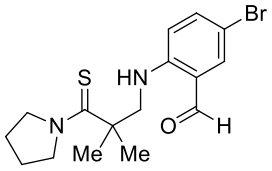
Chloroform-*d*) δ 208.75, 192.46, 173.77, 149.93, 138.36, 138.31, 119.67, 113.06, 105.27, 60.81, 55.93, 51.83, 48.12 × 2, 40.32, 28.09 × 2, 25.42 × 2, 14.17. HRMS (ESI): m/z calculated for $C_{20}H_{28}{}^{79}BrN_2O_3S$ $[M + H]^+$: 455.1004, found: 455.1001.

5-Bromo-2-((2,2-dimethyl-3-(1,4,4a,8a-tetrahydroisoquinolin-2(3H)-yl)-3-thioxopropyl)amino)benzaldehyde (4d)



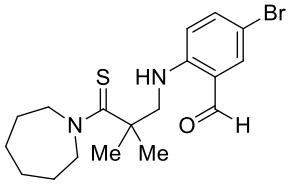
Following typical procedure, **4d** was obtained as a green oil (40.1 mg, 0.093 mmol, 62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.70 (s, 1H), 8.82 (brs, 1H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.38 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.23 – 7.19 (m, 2H), 7.19 – 7.10 (m, 2H), 6.71 (d, *J* = 9.1 Hz, 1H), 5.17 (s, 2H), 4.30 (t, *J* = 5.8 Hz, 2H), 3.72 (d, *J* = 6.1 Hz, 2H), 3.01 (t, *J* = 5.9 Hz, 2H), 1.51 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 208.42, 192.44, 149.90, 138.32, 138.26, 132.50, 128.34, 127.17, 126.66, 126.18, 119.73, 113.12, 105.37, 55.86, 55.12 × 2, 55.09, 48.24 × 2, 25.78 × 2. HRMS (ESI): m/z calculated for $C_{21}H_{24}{}^{79}BrN_2OS$ $[M + H]^+$: 431.0793, found: 431.0793.

5-Bromo-2-((2,2-dimethyl-3-(pyrrolidin-1-yl)-3-thioxopropyl)amino)benzaldehyde (4e)



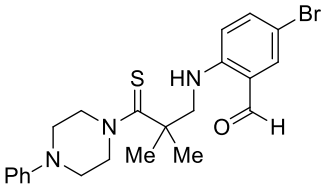
Following a modified procedure, as the reaction was run at 80 ℃, **4e** was obtained as a yellow oil (27.7 mg, 0.075 mmol, 50%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.72 (s, 1H), 8.73 (brs, 1H), 7.52 (d, *J* = 2.5 Hz, 1H), 7.40 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.75 (d, *J* = 9.1 Hz, 1H), 3.96 (t, *J* = 7.1 Hz, 2H), 3.80 (t, *J* = 6.6 Hz, 2H), 3.71 (d, *J* = 6.2 Hz, 2H), 2.00 (dd, *J* = 13.6, 6.8 Hz, 2H), 1.91 – 1.83 (m, 2H), 1.47 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 205.11, 192.52, 150.00, 138.32, 138.26, 119.66, 113.31, 105.42, 55.49, 48.63, 38.63, 36.39, 27.81, 27.54, 25.46, 23.05. HRMS (ESI): m/z calculated for $C_{16}H_{22}{}^{79}BrN_2OS$ $[M + H]^+$: 369.0636, found: 369.0633.

2-((3-(Azepan-1-yl)-2,2-dimethyl-3-thioxopropyl)amino)-5-bromobenzaldehyde (4f)



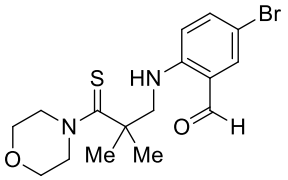
Following typical procedure, **4f** was obtained as a yellow oil (50.1 mg, 0.126 mmol, 84%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.81 (brs, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 7.40 (ddd, *J* = 9.1, 2.4, 0.6 Hz, 1H), 6.70 (d, *J* = 9.1 Hz, 1H), 4.04 (brs, 4H), 3.69 (d, *J* = 6.0 Hz, 2H), 1.88 (brs, 4H), 1.61 – 1.58 (m, 4H), 1.47 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.36, 192.35, 149.95, 138.29, 138.25, 119.70, 113.10, 105.23, 56.12 × 2, 48.09 × 2, 25.94 × 6. HRMS (ESI): m/z calculated for $C_{18}H_{26}{}^{79}BrN_2OS$ $[M + H]^+$: 397.0949, found: 397.0950.

5-Bromo-2-((2,2-dimethyl-3-(4-phenylpiperazin-1-yl)-3-thioxopropyl)amino)benzaldehyde (4g)



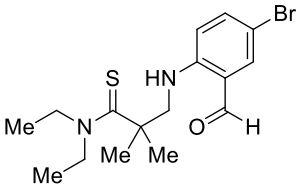
Following typical procedure, **4g** was obtained as a yellow solid (49.7 mg, 0.108 mmol, 72%). mp: 136.5 – 137.9 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.84 (brs, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 7.41 (ddd, *J* = 9.1, 2.5, 0.6 Hz, 1H), 7.32 – 7.26 (m, 2H), 6.96 – 6.87 (m, 3H), 6.72 (d, *J* = 9.1 Hz, 1H), 4.34 (t, *J* = 5.2 Hz, 4H), 3.71 (d, *J* = 6.1 Hz, 2H), 3.36 – 3.24 (m, 4H), 1.49 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.37, 192.50, 150.14, 149.94, 138.40, 138.35, 129.30 × 2, 120.53, 119.77, 116.07 × 2, 113.07, 105.43, 55.94, 52.21 × 2, 48.95, 48.16 × 2, 25.75 × 2. HRMS (ESI): m/z calculated for $C_{22}H_{27}{}^{79}BrN_3OS$ $[M + H]^+$: 460.1058, found: 460.1055.

5-Bromo-2-((2,2-dimethyl-3-morpholino-3-thioxopropyl)amino)benzaldehyde (4h)



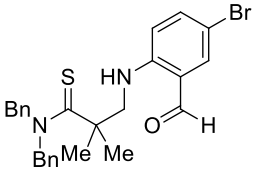
Following a modified procedure, as the reaction was run for 24 h, **4h** was obtained as a yellow solid (31.2 mg, 0.081 mmol, 54%). mp: 100.6 – 102.7 ℃. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.82 (brs, 1H), 7.53 (t, *J* = 1.7 Hz, 1H), 7.41 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.71 (d, *J* = 9.1 Hz, 1H), 4.20 (brs, 4H), 3.80 – 3.74 (m, 4H), 3.69 (d, *J* = 6.1 Hz, 2H), 1.45 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 209.54, 192.49, 149.91, 138.40, 138.36, 119.78, 113.04, 105.46, 66.54 × 2, 55.95, 53.19 × 2, 48.07, 25.67 × 2. HRMS (ESI): m/z calculated for $C_{16}H_{22}{}^{79}BrN_2O_2S$ $[M + H]^+$: 385.0585, found: 385.0585.

3-((4-Bromo-2-formylphenyl)amino)-N,N-diethyl-2,2-dimethylpropanethioamide (4i)



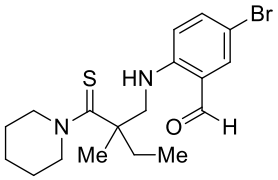
Following typical procedure, **4i** was obtained as a yellow oil (47.9 mg, 0.129 mmol, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.82 (brs, 1H), 7.52 (dd, *J* = 2.5, 0.9 Hz, 1H), 7.39 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.71 (d, *J* = 9.1 Hz, 1H), 3.90 (brs, 4H), 3.69 (d, *J* = 6.0 Hz, 2H), 1.44 (s, 6H), 1.28 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.29, 192.35, 149.95, 138.30, 138.25, 119.67, 113.11, 105.19, 56.15 × 2, 48.05 × 2, 25.76 × 4. HRMS (ESI): m/z calculated for $C_{16}H_{24}{}^{79}BrN_2OS$ $[M + H]^+$: 371.0793, found: 371.0796.

***N*,*N*-Dibenzyl-3-((4-bromo-2-formylphenyl)amino)-2,2-dimethylpropane thioamide (4j)**



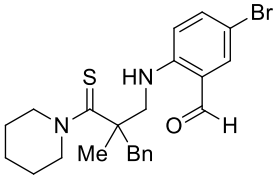
Following typical procedure, **4j** was obtained as a yellow oil (45.3 mg, 0.092 mmol, 61%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.77 (s, 1H), 8.92 (brs, 1H), 7.55 (s, 1H), 7.42 – 7.27 (m, 7H), 7.12 (d, *J* = 7.2 Hz, 4H), 6.66 (d, *J* = 9.1 Hz, 1H), 5.34 (s, 2H), 5.04 (s, 2H), 3.78 (d, *J* = 5.9 Hz, 2H), 1.53 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 211.59, 192.48, 149.88, 138.32 × 3, 138.27 × 3, 135.47, 128.84 × 4, 119.67 × 4, 113.07, 105.31, 56.24, 48.60 × 3, 25.90 × 2. HRMS (ESI): m/z calculated for $C_{26}H_{28}{}^{79}BrN_2OS$ $[M + H]^+$: 495.1106, found: 495.1100.

5-Bromo-2-((2-methyl-2-(piperidine-1-carbonothioyl)butyl)amino)benzaldehyde (4k)



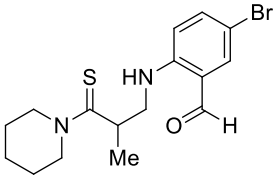
Following typical procedure, **4k** was obtained as a yellow oil (44.7 mg, 0.113 mmol, 75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.74 (brs, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 7.40 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.73 (d, *J* = 9.1 Hz, 1H), 4.13 (brs, 4H), 3.84 (dd, *J* = 13.1, 5.4 Hz, 1H), 3.64 (dd, *J* = 13.1, 6.5 Hz, 1H), 1.85 (q, *J* = 7.5 Hz, 2H), 1.79 – 1.65 (m, 6H), 1.44 (s, 3H), 0.94 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 206.76, 192.41, 150.04, 138.32, 138.27, 119.67, 113.09, 105.20, 53.93, 53.15, 51.37 × 2, 30.11, 26.16, 24.23 × 2, 24.05, 9.24. HRMS (ESI): m/z calculated for $C_{18}H_{26}{}^{79}BrN_2OS$ $[M + H]^+$: 397.0949, found: 397.0948.

2-((2-Benzyl-2-methyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)-5-bromobenzaldehyde (4l)



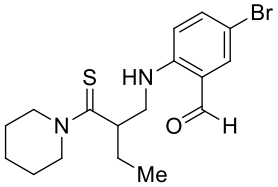
Following typical procedure, **4l** was obtained as a yellow oil (59.3 mg, 0.129 mmol, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.74 (brs, 1H), 7.51 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.29 – 7.21 (m, 3H), 7.16 (dd, *J* = 7.6, 1.8 Hz, 2H), 6.53 (d, *J* = 9.1 Hz, 1H), 4.24 – 4.00 (m, 4H), 3.96 (dd, *J* = 12.7, 5.2 Hz, 1H), 3.40 (dd, *J* = 12.7, 6.4 Hz, 1H), 3.27 – 3.05 (m, 2H), 1.71 – 1.67 (m, 6H), 1.47 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.33, 192.44, 149.81, 138.27, 138.23, 136.57, 130.22 ×2, 128.25 ×2, 126.92, 119.70, 113.21, 105.36, 54.39, 54.29, 52.55 × 2, 43.56, 26.10, 24.16×2, 23.35. HRMS (ESI): m/z calculated for $C_{23}H_{28}{}^{79}BrN_2OS$ $[M + H]^+$: 459.1106, found: 459.1103.

5-Bromo-2-((2-methyl-3-(piperidin-1-yl)-3-thioxopropyl)amino)benzaldehyde (4m)



Following typical procedure, **4m** was obtained as a yellow solid (48.8 mg, 0.132 mmol, 88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.71 (s, 1H), 8.41 (brs, 1H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.42 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.70 (d, *J* = 9.1 Hz, 1H), 4.45 – 4.16 (m, 2H), 3.85 – 3.78 (m, 1H), 3.78 – 3.67 (m, 2H), 3.49 – 3.32 (m, 2H), 1.75 – 1.66 (m, 4H), 1.60 – 1.55 (m, 2H), 1.29 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 204.49, 192.56, 149.40, 138.39, 138.25, 119.57, 113.13, 105.81, 51.86, 50.62, 49.08, 41.29, 27.10, 25.39, 24.35, 19.23. HRMS (ESI): m/z calculated for $C_{16}H_{22}{}^{79}BrN_2OS$ $[M + H]^+$: 369.0636, found: 369.0634.

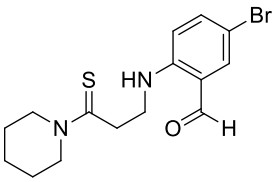
5-Bromo-2-((2-(piperidine-1-carbonothioyl)butyl)amino)benzaldehyde (4n)



Following a modified procedure, as the reaction was run at 70 ℃, **4n** was obtained as a yellow oil (38.5 mg, 0.101 mmol, 67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.70 (s, 1H), 8.34 (brs, 1H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.43

(dd, *J* = 9.0, 2.4 Hz, 1H), 6.70 (d, *J* = 9.0 Hz, 1H), 4.34 (q, *J* = 5.0 Hz, 2H), 3.87 – 3.79 (m, 1H), 3.77 (t, *J* = 5.5 Hz, 2H), 3.45 (ddd, *J* = 13.0, 6.3, 4.9 Hz, 1H), 3.35 – 3.28 (m, 1H), 2.01 – 1.90 (m, 1H), 1.81 – 1.63 (m, 5H), 1.54 (q, *J* = 5.7 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 204.03, 192.54, 149.33, 138.43, 138.25, 119.53, 113.13, 105.84, 52.26, 50.91, 48.32, 48.25, 27.53, 27.09, 25.61, 24.38, 11.70. HRMS (ESI): m/z calculated for $C_{17}H_{24}{}^{79}BrN_2OS$ $[M + H]^+$: 383.0793, found: 383.0791.

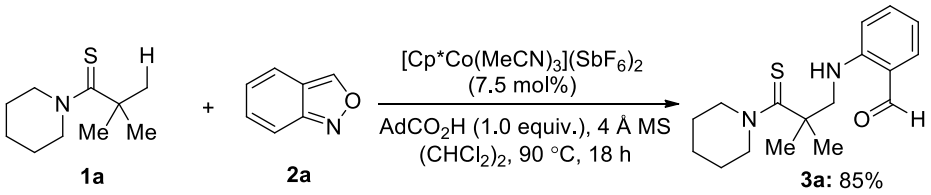
5-Bromo-2-((3-(piperidin-1-yl)-3-thioxopropyl)amino)benzaldehyde (4o)



Following a modified procedure, as the reaction was run with 10 mol % cobalt catalyst at 100 ℃, **4o** was obtained as a yellow oil (15.5 mg, 0.044 mmol, 29%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 8.46 (brs, 1H), 7.56 (d, *J* = 2.4 Hz, 1H), 7.47 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.78 (d, *J* = 9.0 Hz, 1H), 4.28 (t, *J* = 5.0 Hz, 2H), 3.80 – 3.73 (m, 2H), 3.72 – 3.67 (m, 2H), 3.15 – 3.02 (m, 2H), 1.77 – 1.66 (m, 4H), 1.64 – 1.59 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.13, 192.79, 149.12, 138.64, 138.34, 119.68, 113.14, 106.21, 51.46, 50.98, 42.18, 41.24, 26.82, 25.29, 24.07. HRMS (ESI): m/z calculated for $C_{15}H_{20}{}^{79}BrN_2OS$ $[M + H]^+$: 355.0480, found: 355.0483.

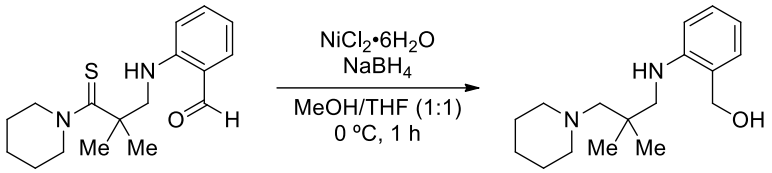
3. Derivatization of the product

3.1 Large scale synthesis of 3a



A 100 mL Schlenk flask was charged with thioamide **1a** (0.3707 g, 2.0 equiv., 2 mmol), anthranil **2a** (0.1191 g, 1.0 equiv., 1 mmol), $[Cp^*Co(MeCN)_3](SbF_6)_2$ (59.2 mg, 0.075 equiv., 0.075 mmol), $AdCO_2H$ (0.1802 g, 1.0 equiv., 1 mmol), 4 Å MS (0.40 g), and $(CHCl_2)_2$ (10 mL). the mixture was stirred at 90 ℃ with stirring for 18 h under N_2. After cooling down, the reaction mixture was quenched with sat. $NaHCO_3$ and extracted with DCM. The combined organic layers were washed with sat. NaCl, dried with Na_2SO_4, evaporated in vacuo. The resulting residue was directly purified by column chromatography to give **3a** as a yellow solid (0.2588 g, 0.85 mmol, 85%).

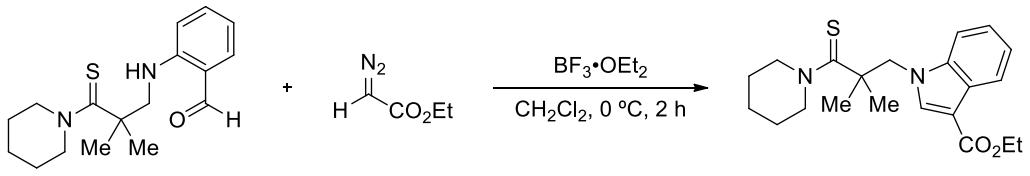
3.2 Synthesis of compound 5



3a **5**: 80%

To a solution of thioamide **3a** (50.0 mg, 1.0 equiv., 0.164 mmol) and $NiCl_2{\cdot}6H_2O$ (304.0 mg, 7.8 equiv., 1.28 mmol) in MeOH/THF (1:1, 40 mL) at 0 °C was added $NaBH_4$ (142 mg, 22.8 equiv., 3.75 mmol) slowly in portionwise. The reaction mixture was then stirred at 0 °C for 1 h. Upon completion, the mixture was warmed to room temperature and concentrated in vacuo. DCM was subsequently added to the black crude residue and filtered over a pad of celite. The filtrate was collected and the solvent was removed in vacuo. The crude mixture was purified by column chromatography to give **5** as a colorless oil (36.0 mg, 0.13 mmol, 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (td, J = 7.5, 1H), 7.11 (dd, J = 7.2, 1H), 6.71 – 6.62 (m, 2H), 4.70 (s, 2H), 2.99 (s, 2H), 2.46 (s, 4H), 2.24 (s, 2H), 1.59 – 1.53 (m, 4H), 1.41 – 1.38 (m, 2H), 0.99 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.84, 129.42, 128.76, 124.54, 115.81, 110.23, 68.93, 64.37, 57.32 × 2, 53.59, 35.81 × 2, 26.26, 25.05 × 2, 23.91. HRMS (ESI): m/z calculated for $C_{17}H_{29}N_2O$ $[M + H]^+$: 277.2280, found: 277.2285.

3.3 Synthesis of compound 6

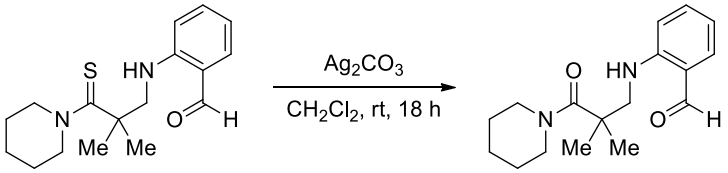


3a **6**: 28%

To an oven-dried sealed tube charged with thioamide **3a** (45.7 mg, 1.0 equiv., 0.15 mmol) and ethyl 2-diazoacetate (85.6 mg, 5.0 equiv., 0.75 mmol), DCM (2 mL) were added under N_2 at 0 ℃, then $BF_3{\cdot}OEt_2$ (31.9 mg, 1.5 equiv., 0.225 mmol) was added. The reaction mixture was allowed to stir at 0 ℃ for 2 h. The reaction mixture was quenched with sat. $NaHCO_3$ (30 mL) and the mixture was extracted with DCM. The combined organic layers were washed with sat. NaCl, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography to give **6** as a yellow oil (15.6 mg, 0.042 mmol, 28%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 – 8.14 (m, 1H), 7.98 (s, 1H), 7.44 – 7.34 (m, 1H), 7.29 – 7.23 (m, 2H), 4.41 (s, 2H), 4.40 – 4.34 (q, J = 6.8, 2H), 3.58 – 3.50 (m, 4H), 1.65 (d, J = 5.3 Hz, 2H), 1.55 (t, J = 5.5 Hz, 4H), 1.42 (t, J = 7.1 Hz, 3H), 1.32 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.72, 165.23, 138.25, 136.14, 126.23, 122.57, 121.57,

121.55, 110.58, 107.66, 59.65, 55.24, 46.35, 44.76 × 2, 26.02 × 2, 24.51, 23.84 × 2, 14.56. HRMS (ESI): m/z calculated for $C_{21}H_{29}N_2O_2S$ $[M + H]^+$: 373.1950, found: 373.1950.

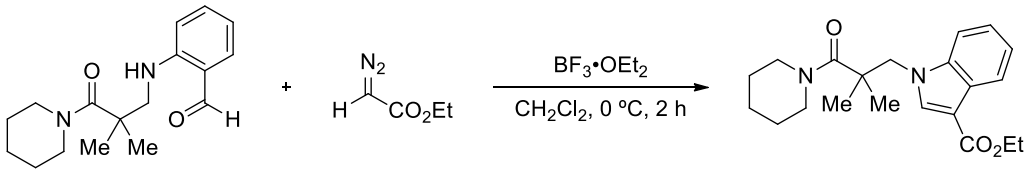
3.4 Synthesis of compound 7



3a **7**: 91%

To a solution of thioamide **3a** (49.0 mg, 1.0 equiv., 0.161 mmol) in DCM (2 mL) was added Ag_2CO_3 (133.0 mg, 3.0 equiv., 0.483 mmol). The reaction was then stirred at room temperature for 18 h. After that, the mixture was filtered over a pad of celite and concentrated in vacuo. The crude mixture was purified by column chromatography to give **7** as a yellow oil (42.4 mg, 0.147 mmol, 91%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.81 (s, 1H), 8.67 (s, 1H), 7.43 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.39 – 7.32 (m, 1H), 6.77 (d, *J* = 8.6 Hz, 1H), 6.64 (t, *J* = 7.4 Hz, 1H), 3.64 – 3.53 (m, 4H), 3.44 (d, *J* = 6.0 Hz, 2H), 1.65 (q, *J* = 6.2, 5.5 Hz, 2H), 1.56 (p, *J* = 5.6 Hz, 4H), 1.37 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.60, 174.03, 151.28, 136.71, 135.66, 118.34, 114.34, 110.65, 52.40, 46.13, 43.41 × 2, 26.03 × 2, 24.58, 23.61 × 2. HRMS (ESI): m/z calculated for $C_{17}H_{25}N_2O_2$ $[M + H]^+$: 289.1916, found: 289.1911.

3.5 Synthesis of compound 9



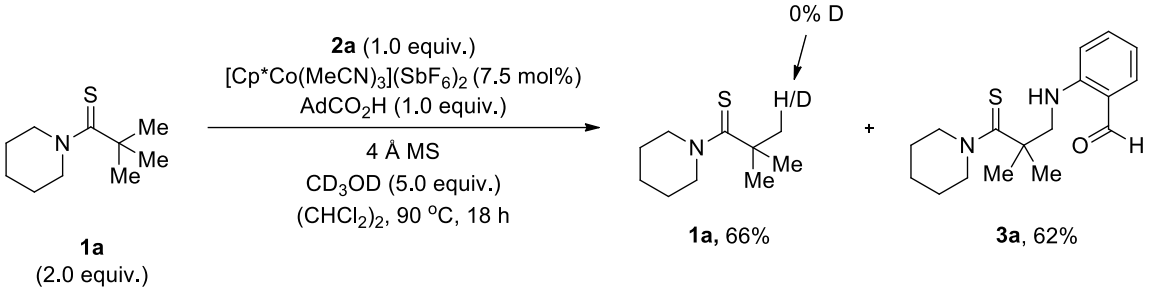
7 **9**: 50%

To an oven-dried sealed tube charged with amide **7** (43.3 mg, 1.0 equiv., 0.15 mmol) and ethyl 2-diazoacetate (85.6 mg, 5.0 equiv., 0.75 mmol), CH_2Cl_2 (2 mL) were added under N_2 at 0 ℃, then $BF_3 \cdot OEt_2$ (31.9 mg, 1.5 equiv., 0.225 mmol) was added. The reaction mixture was allowed to stir at 0 ℃ for 2 h. The reaction mixture was quenched with sat. $NaHCO_3$ (30 mL) and the mixture was extracted with DCM. The combined organic layers were washed with sat. NaCl, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography to give **9** as a yellow oil (26.7 mg, 0.075 mmol, 50%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 – 8.15 (m, 1H),

7.99 (s, 1H), 7.42 – 7.34 (m, 1H), 7.29 – 7.21 (m, 2H), 4.41 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.60 – 3.46 (m, 4H), 1.68 – 1.60 (m, 2H), 1.59 – 1.51 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.32 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.71, 165.23, 138.25, 136.13, 126.23, 122.57, 121.57, 121.55, 110.58, 107.65, 59.64, 55.25, 46.44, 44.76 × 2, 26.02 × 2, 24.51, 23.83 × 2, 14.56. HRMS (ESI): m/z calculated for $C_{21}H_{29}N_2O_3$ $[M + H]^+$: 357.2178, found: 357.2178.

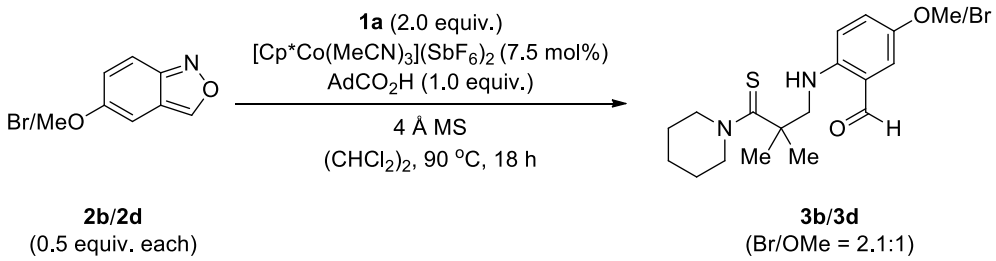
3.6 Mechanistic studies

3.6.1 Deuterium-labeling experiment



A 4 mL screw-cap vial was charged with **2a** (17.9 mg, 0.15 mmol, 1.0 equiv.), **1a** (55.6 mg, 0.3 mmol, 2.0 equiv.), $[Cp^*Co(MeCN)_3](SbF_6)_2$ (8.9 mg, 0.01125 mmol), $AdCO_2H$ (27.0 mg, 0.15 mmol), 4 Å MS (60 mg), CD_3OD (5 equiv.) and $(CHCl_2)_2$ (1.5 mL). The vial was carefully blown with nitrogen for 30 seconds and placed into preheated oil bath at 90 ℃ with stirring for 18 h. After cooling down, the reaction mixture was quenched with sat. $NaHCO_3$ and extracted with DCM. The combined organic layers were washed with sat. NaCl, dried with Na_2SO_4, evaporated in vacuo and the resultant residue was purified by flash chromatography (PE/EtOAc) to recover **1a** (36.7 mg, 0.198 mmol, 66%) and produce **3a** (28.2 mg, 0.093 mmol, 62%).

3.6.2 Competition experiment



A 4 mL screw-cap vial was charged with **2b**/**2d** (0.5 equiv. each, 0.075 mmol), **1a** (55.6 mg, 0.3 mmol, 2.0 equiv.), $[Cp^*Co(MeCN)_3](SbF_6)_2$ (8.9 mg, 0.01125 mmol), $AdCO_2H$ (27.0 mg, 0.15 mmol), 4 Å MS (60 mg), and $(CHCl_2)_2$ (1.5 mL). The vial was carefully blown with nitrogen for 30 seconds and placed into preheated oil bath at 90 ℃ with stirring for 18 h. After cooling down, the reaction mixture was quenched with sat. $NaHCO_3$ and extracted with DCM. The combined organic layers were

washed with sat. NaCl, dried with Na_2SO_4, evaporated in vacuo and the resultant residue was purified by flash chromatography (PE/EtOAc) to yield **3b** (25.0 mg, 0.065 mmol, 87%) and **3d** (10.6 mg, 0.032 mmol, 42%).

4. References

1 P. W. Tan, A. M. Mak, M. B. Sullivan, D. J. Dixon and J. Seayad, *Angew. Chem., Int. Ed*., 2017, **56**, 16550–16554.

2 X. Xing, N. R. O'Connor and B. M. Stoltz, *Angew. Chem., Int. Ed*., 2015, **54**, 11186–11190.

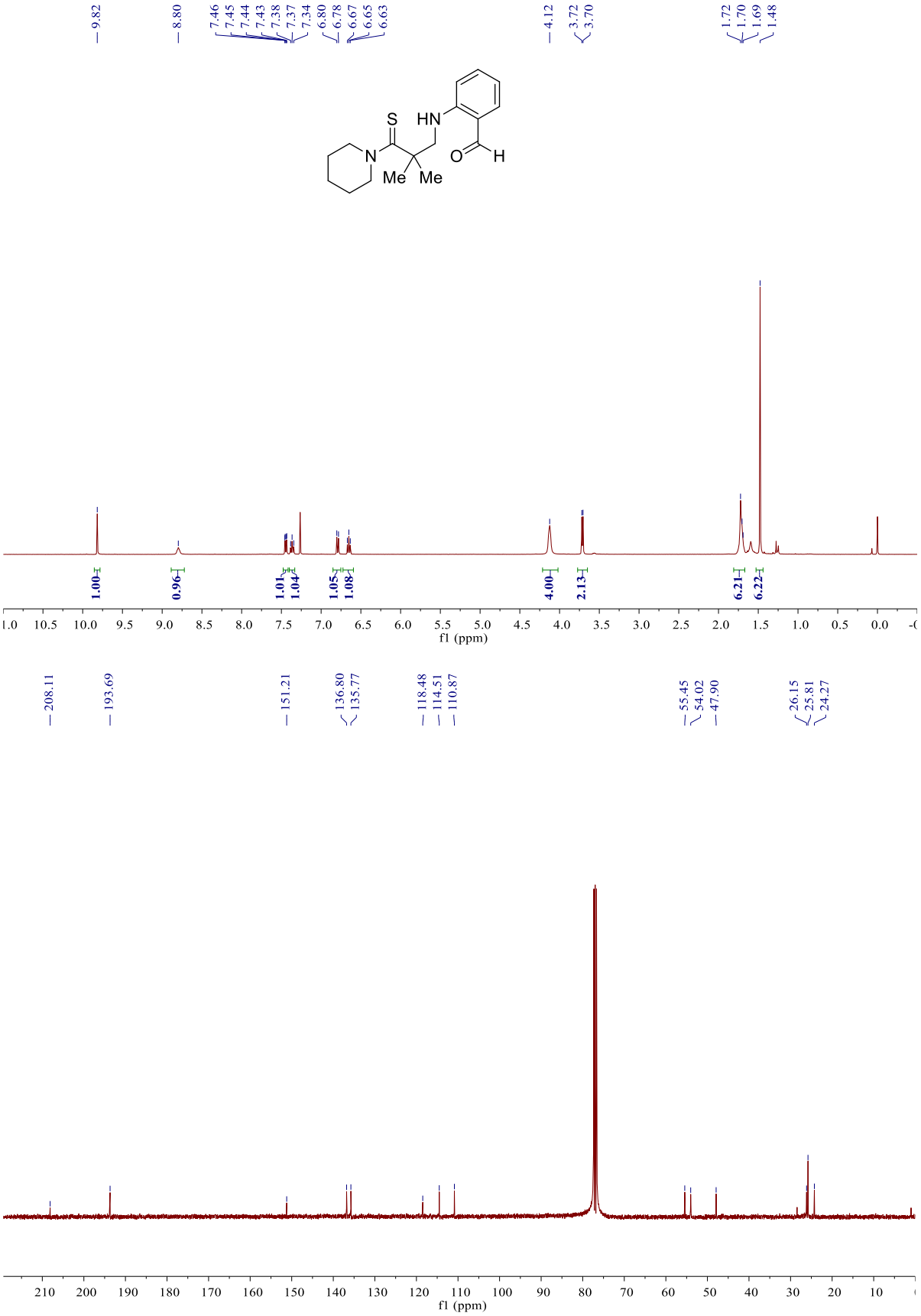
3 H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2016, **55**, 794–797.

4 R. Han, K. I. Son, G. H. Ahn, Y. M. Jun, B. M. Lee, Y. Park and B. H. Kim, *Tetrahedron Lett.*, 2006, **47**, 7295–7299.

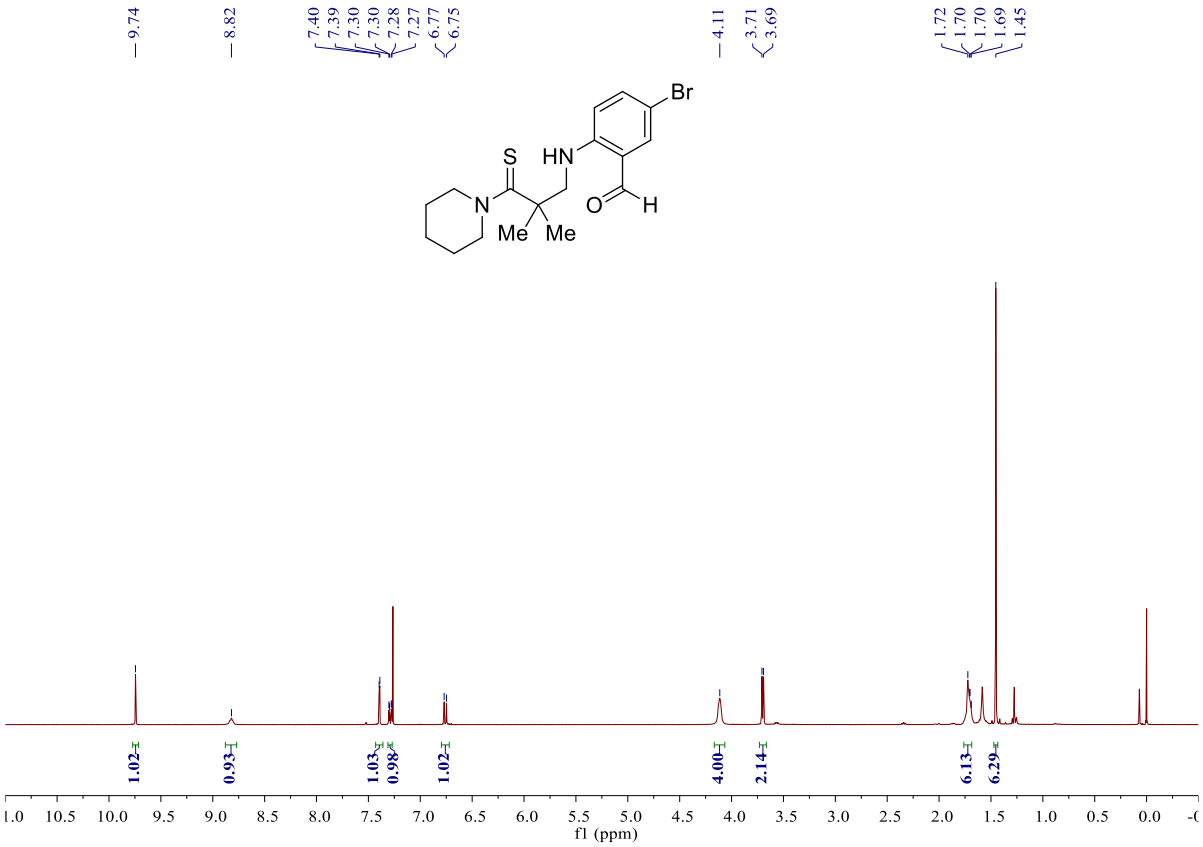
5 D. Zhao, Q. Shen and J.-X. Li, *Adv. Synth. Catal.*, 2015, **357**, 339–344.

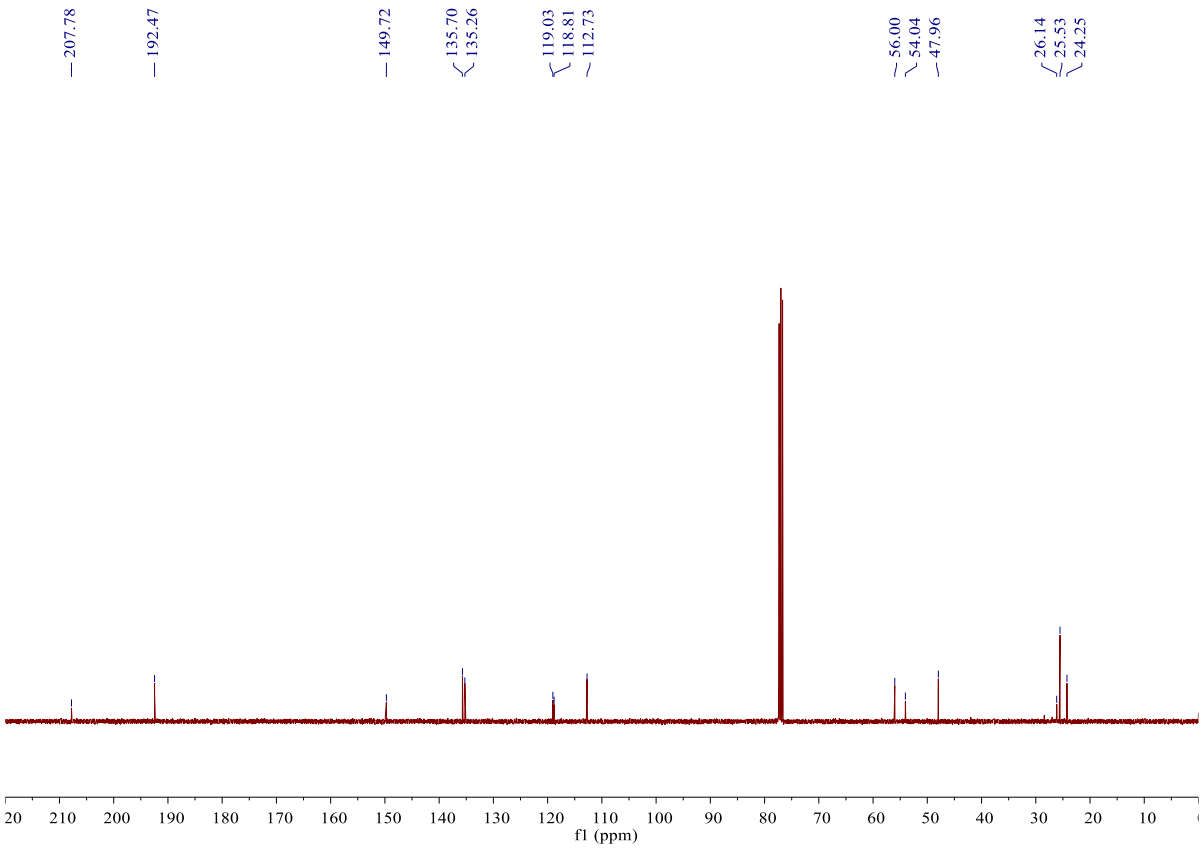
6 H. Li, J. Jie, S. Wu, X. Yang and H. Xu, *Org. Chem. Front.*, 2017, **4**, 250–254.

5. NMR spectra of products

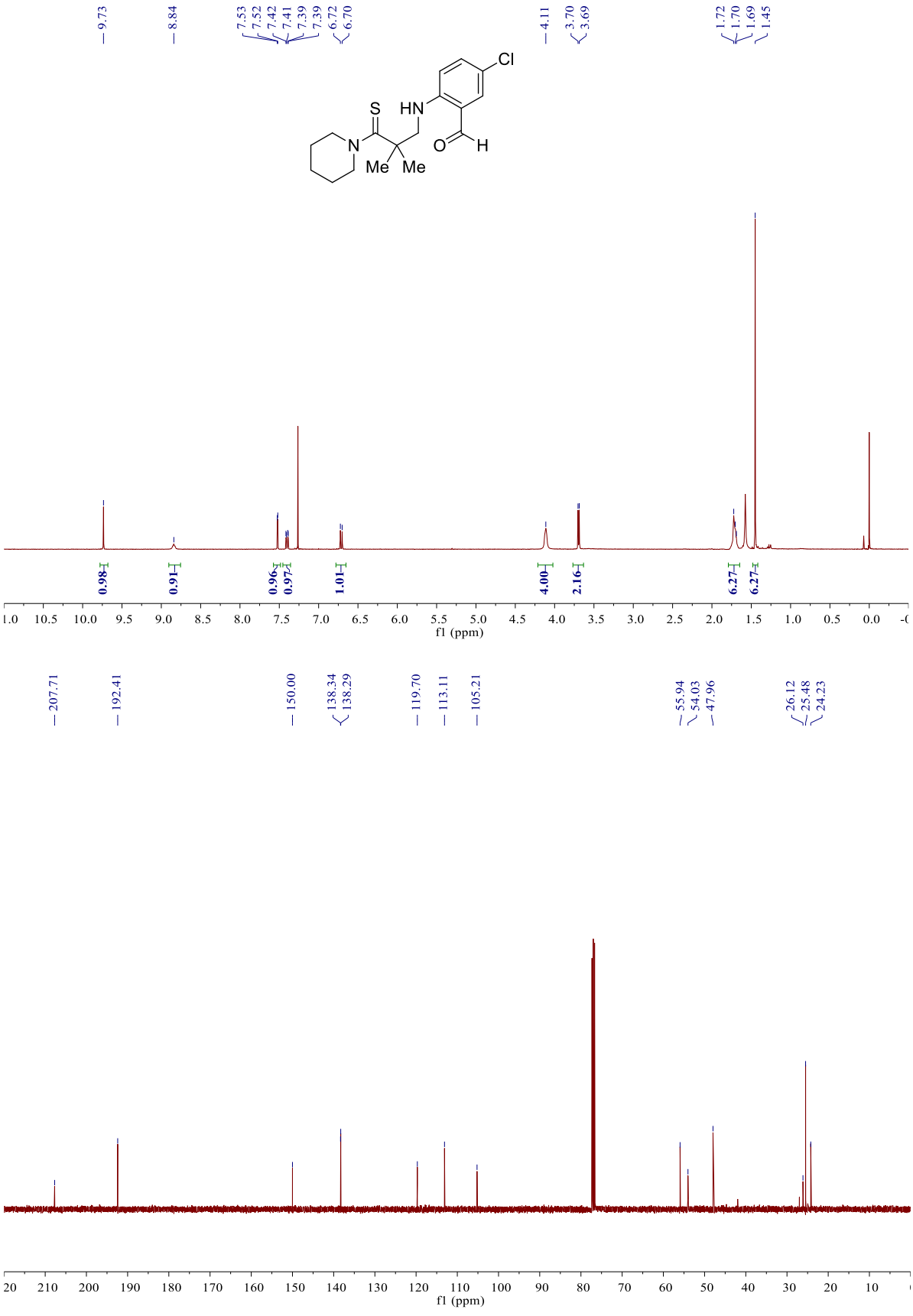


^{1}H and ^{13}C NMR spectra for product 3a ($CDCl_3$)

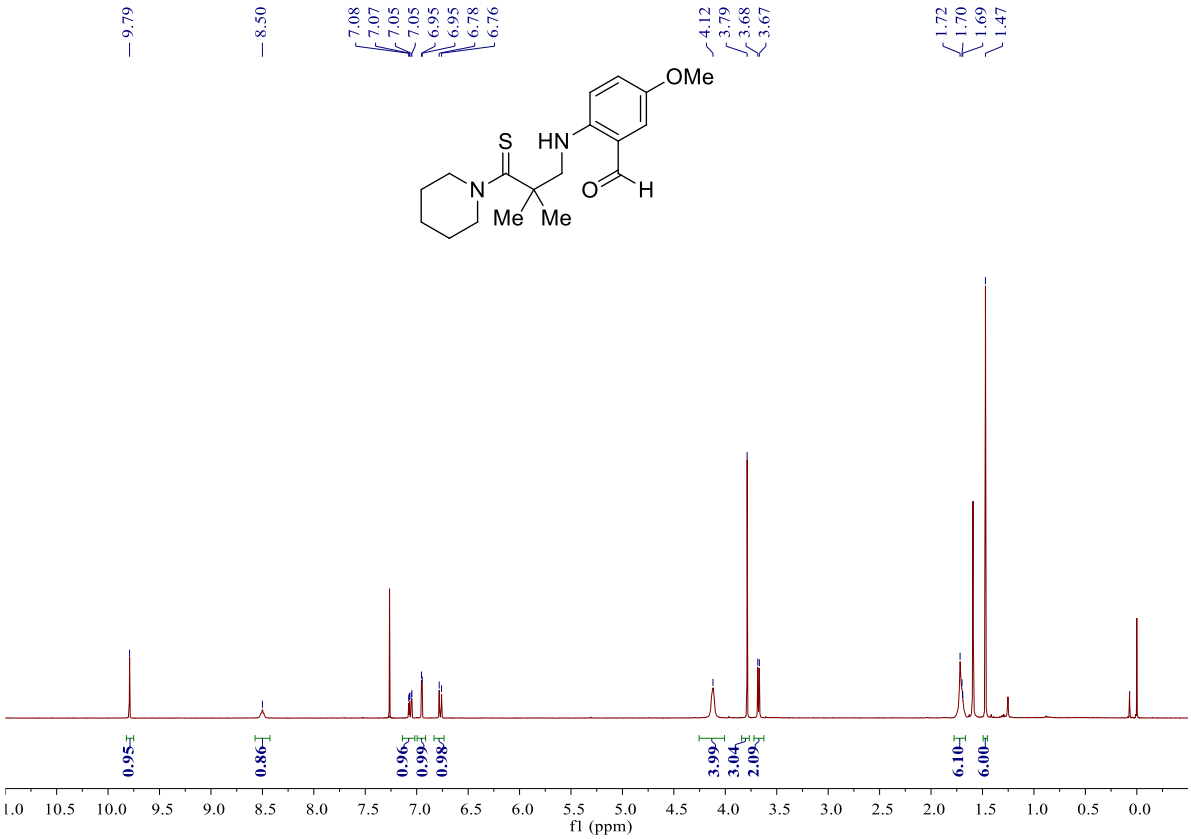


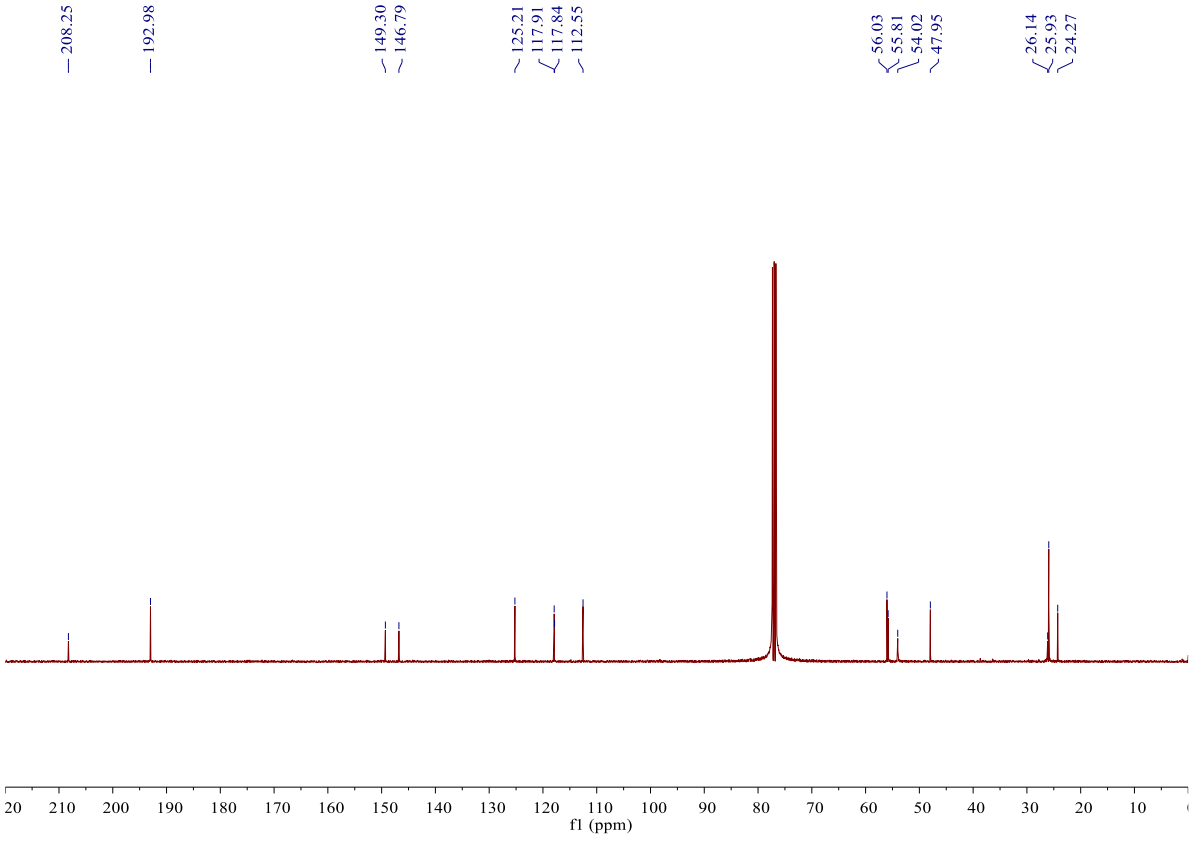


^{1}H and ^{13}C NMR spectra for product 3b ($CDCl_3$)

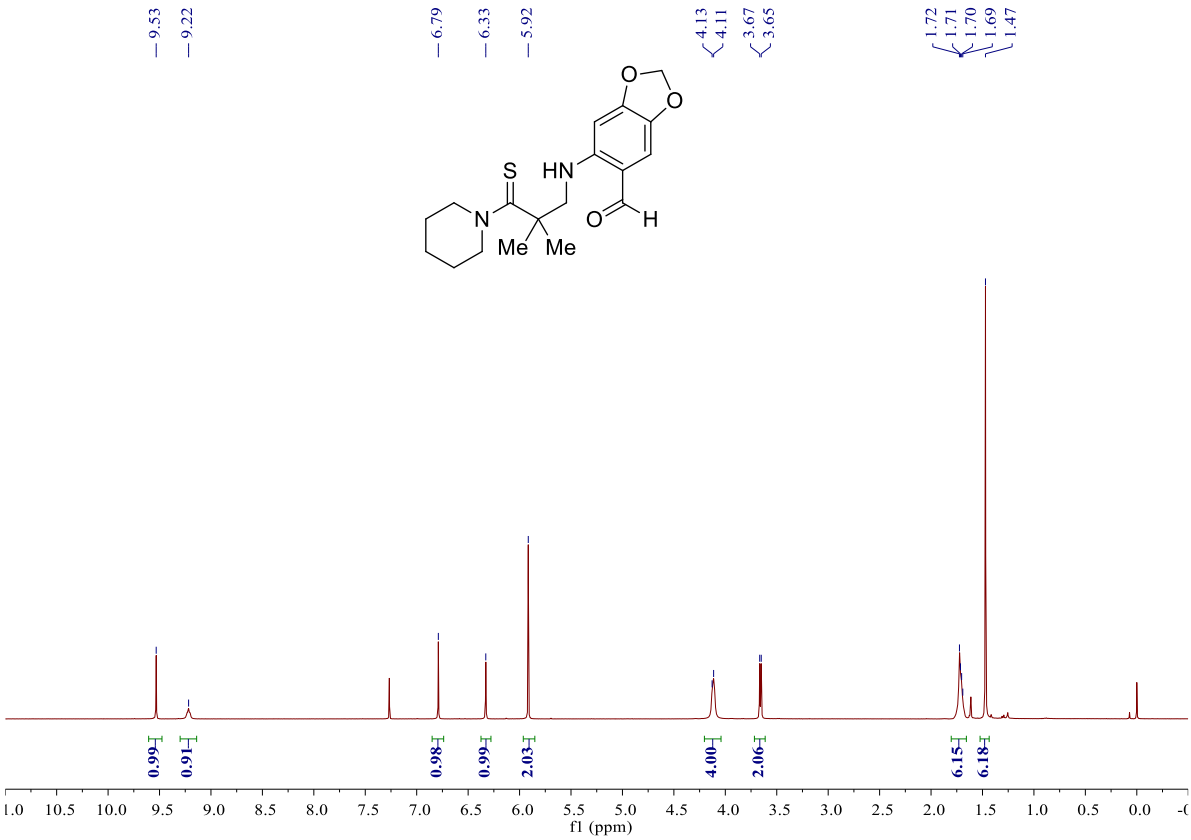


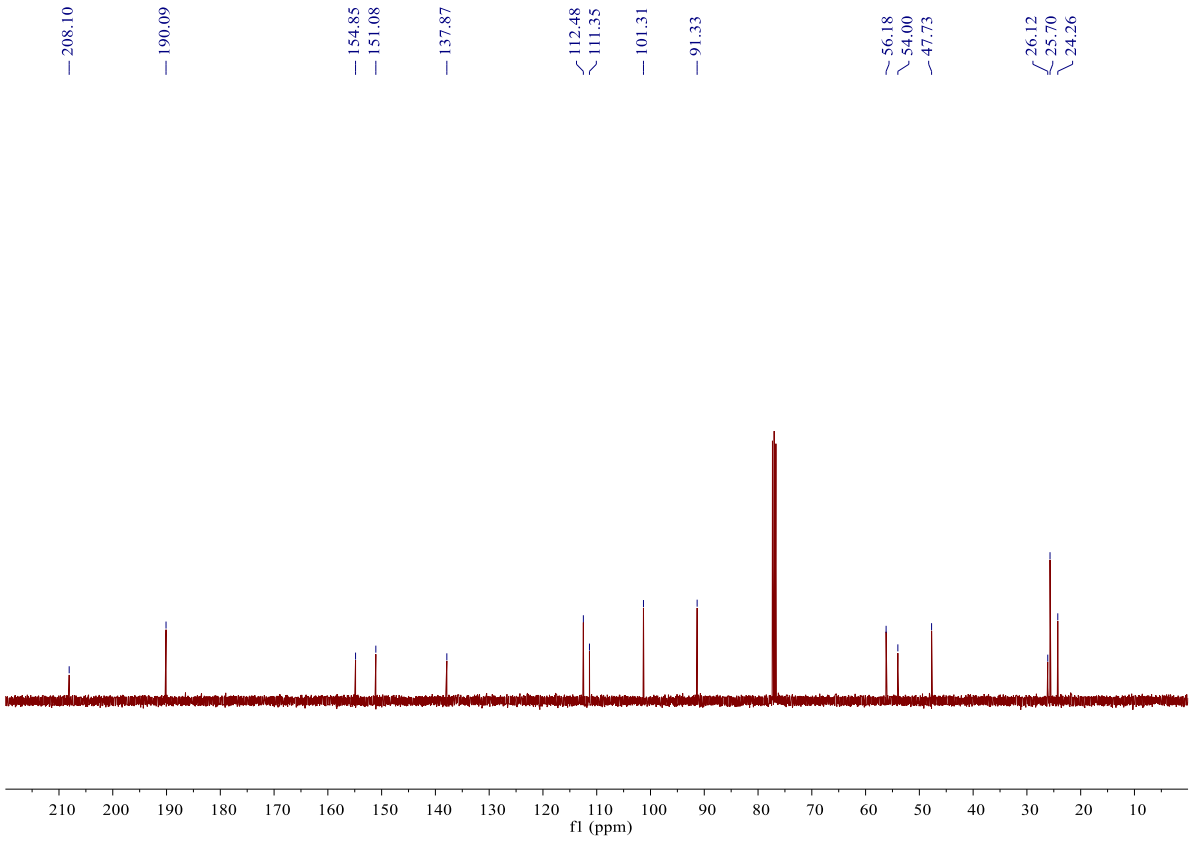
^{1}H and ^{13}C NMR spectra for product 3c ($CDCl_3$)



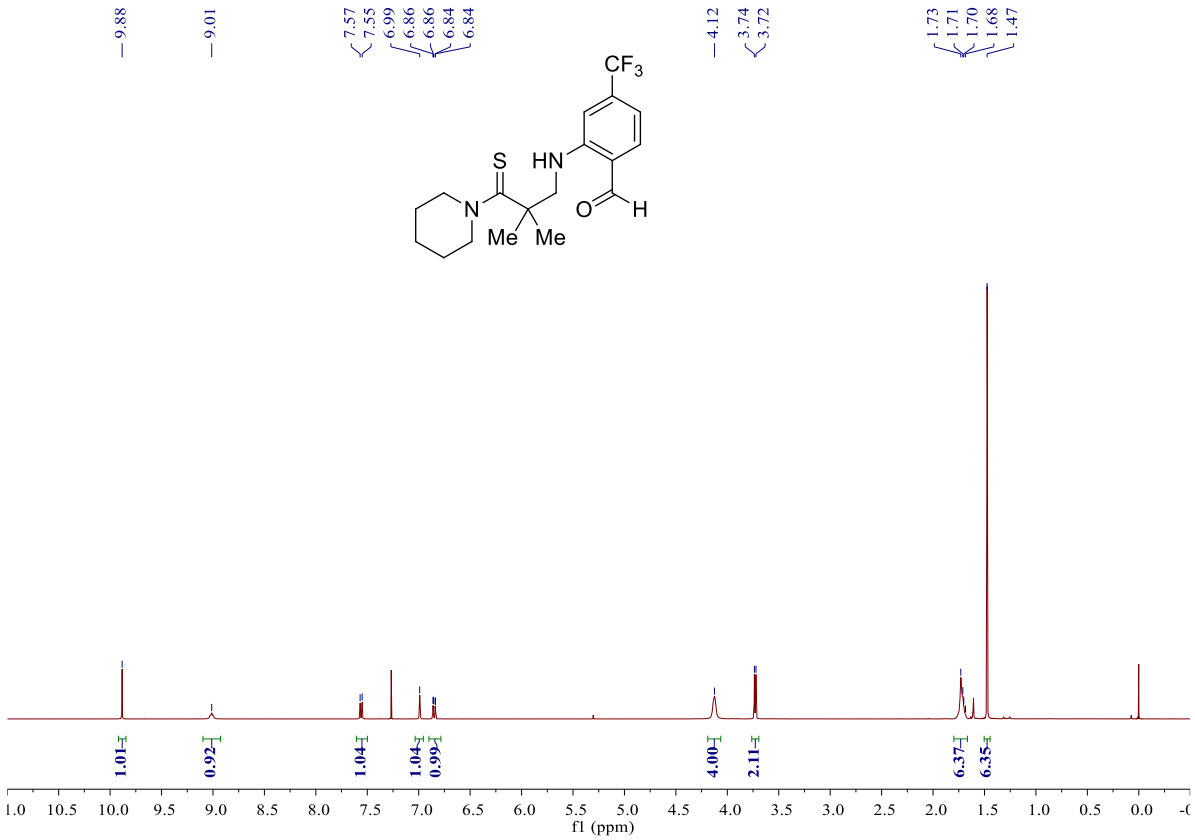


^{1}H and ^{13}C NMR spectra for product 3d ($CDCl_3$)





^{1}H and ^{13}C NMR spectra for product 3e ($CDCl_3$)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6.84
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4.12
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3.72
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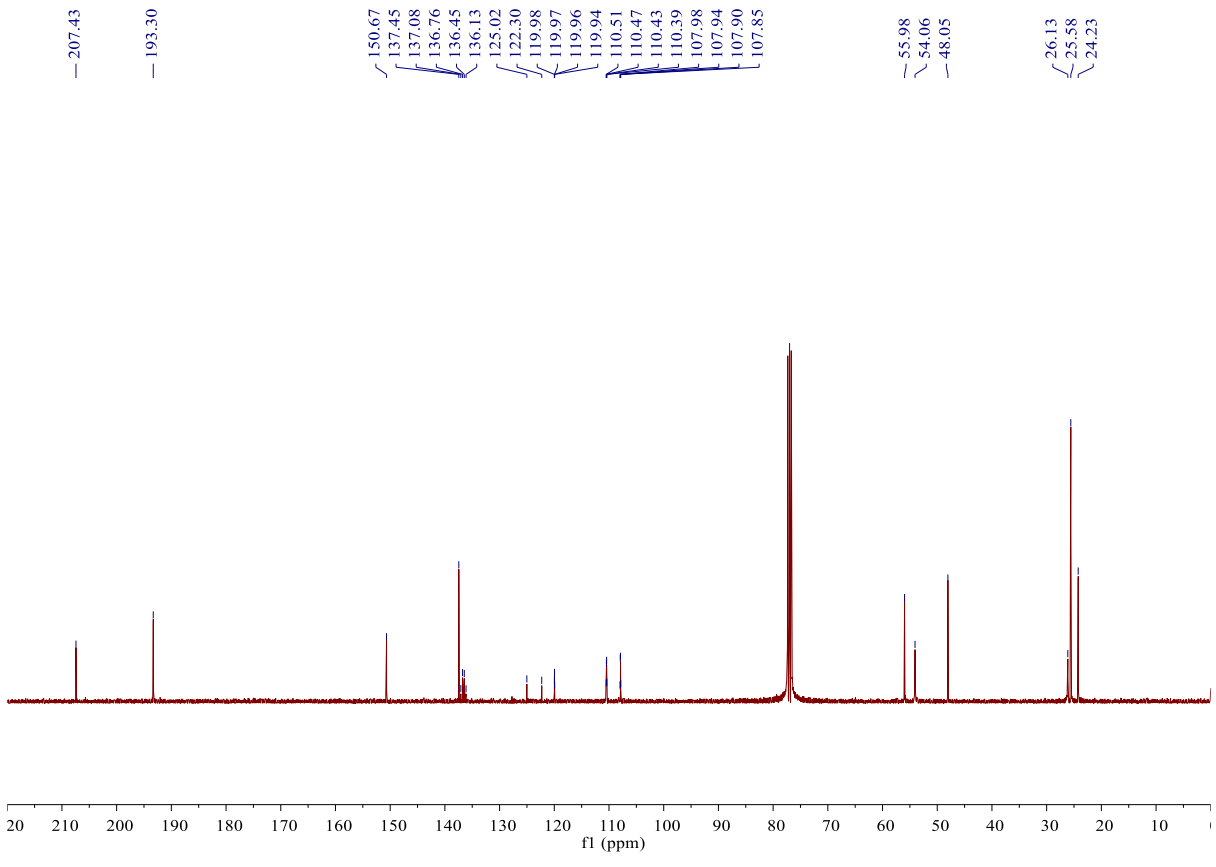
1.71
1.70
1.68
1.47
CF3
S
HN
N
O
H
Me
Me
1.01
0.92
1.04
1.04
0.99
4.00
2.11
6.37
6.35
fl (ppm)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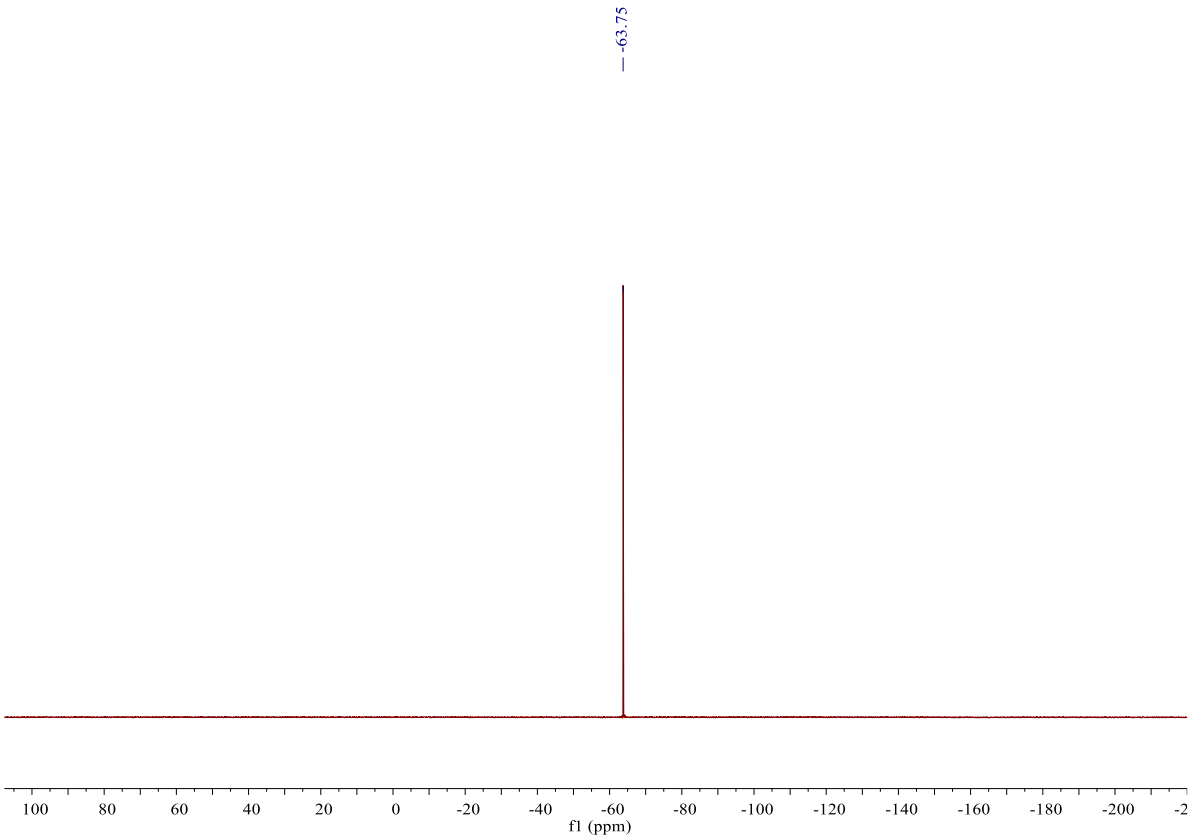
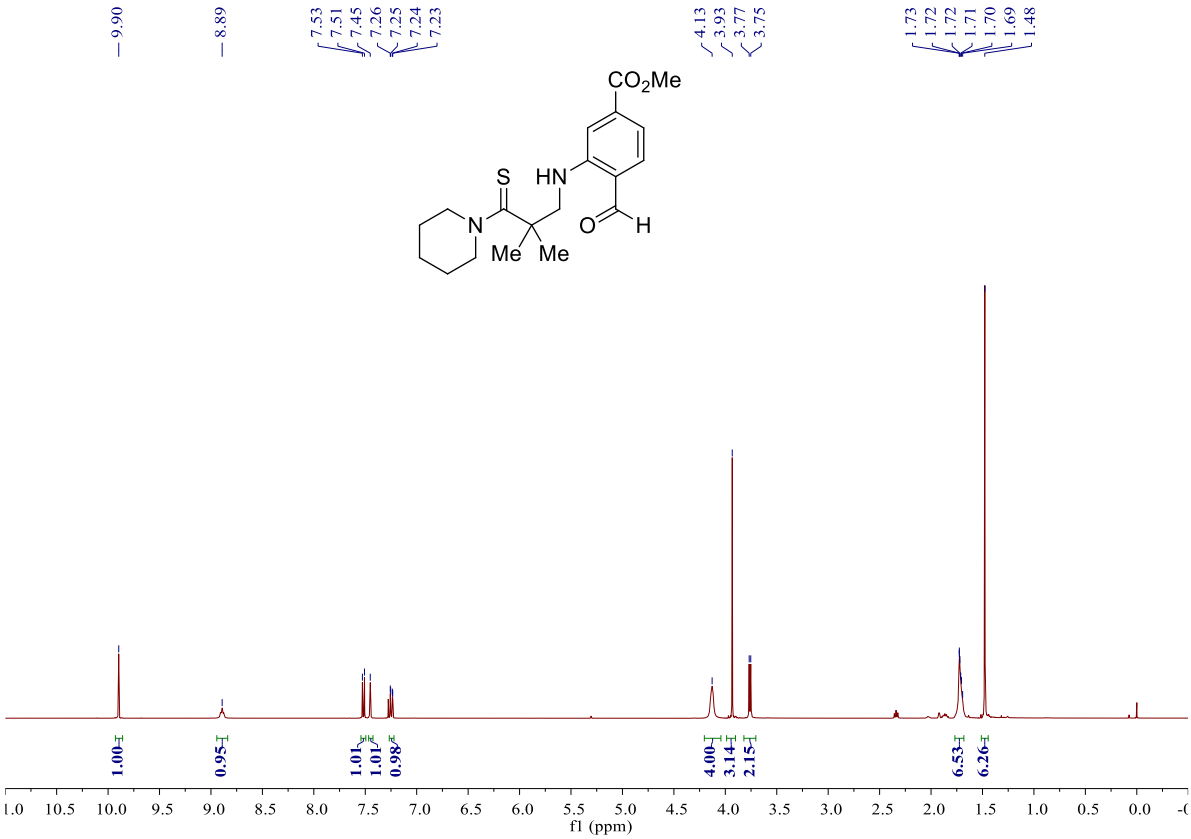
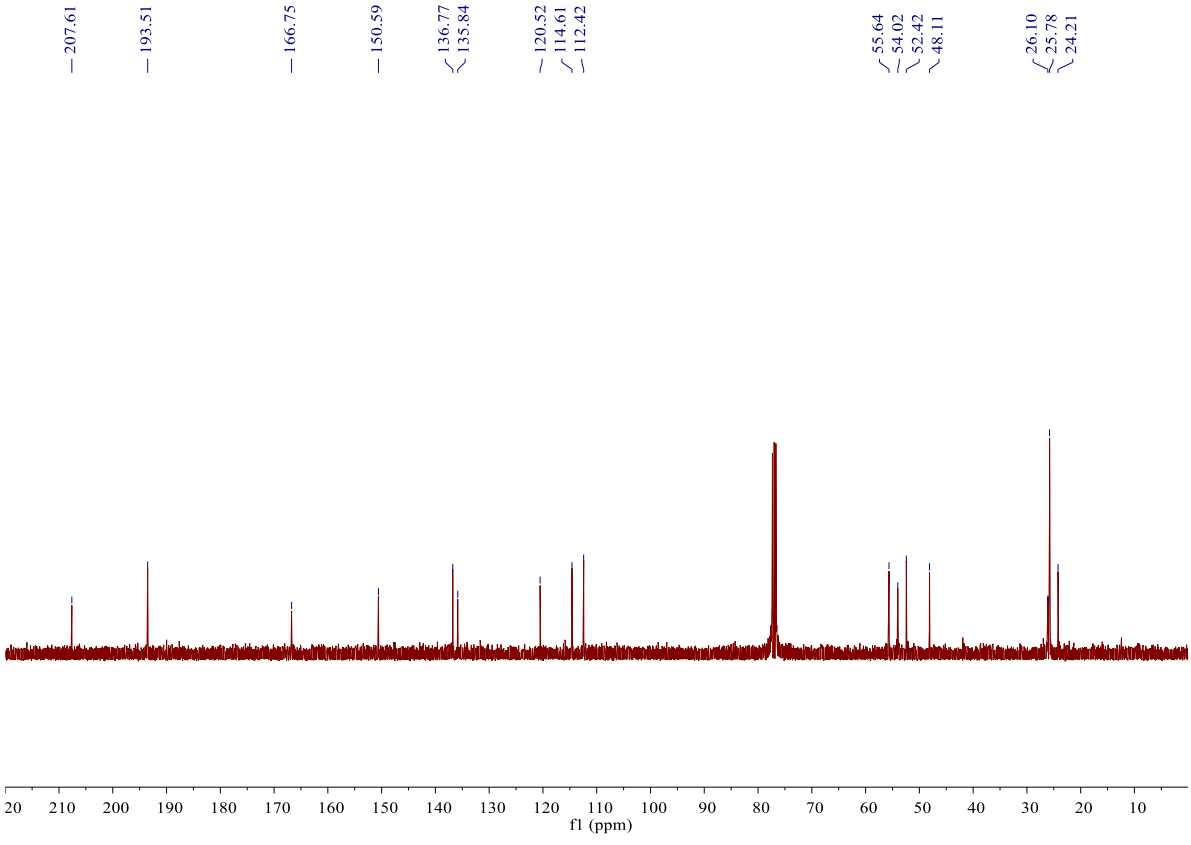
24.23
fl (ppm)

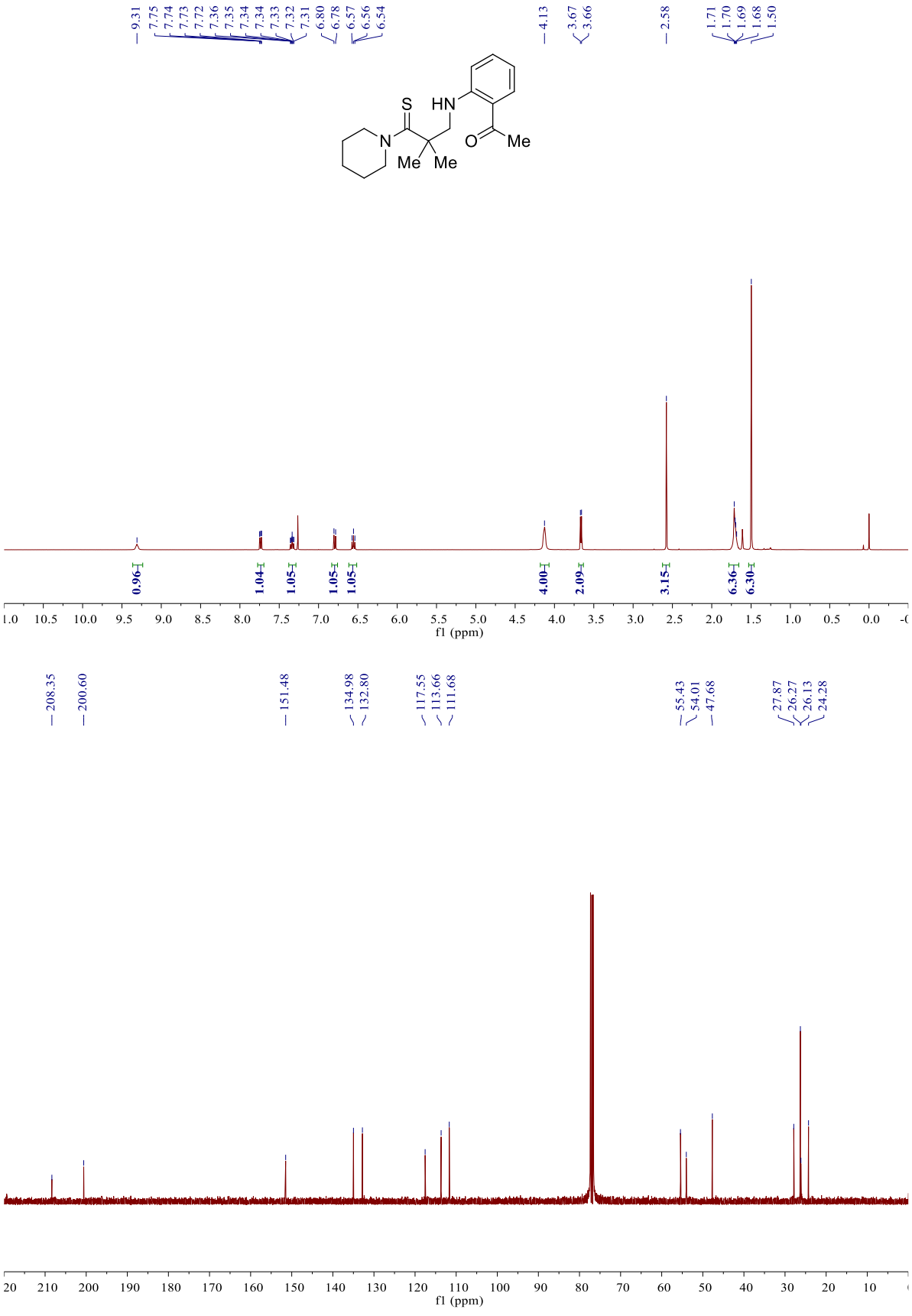


^{1}H , ^{19}F, and ^{13}C NMR spectra for product 3f ($CDCl_3$)

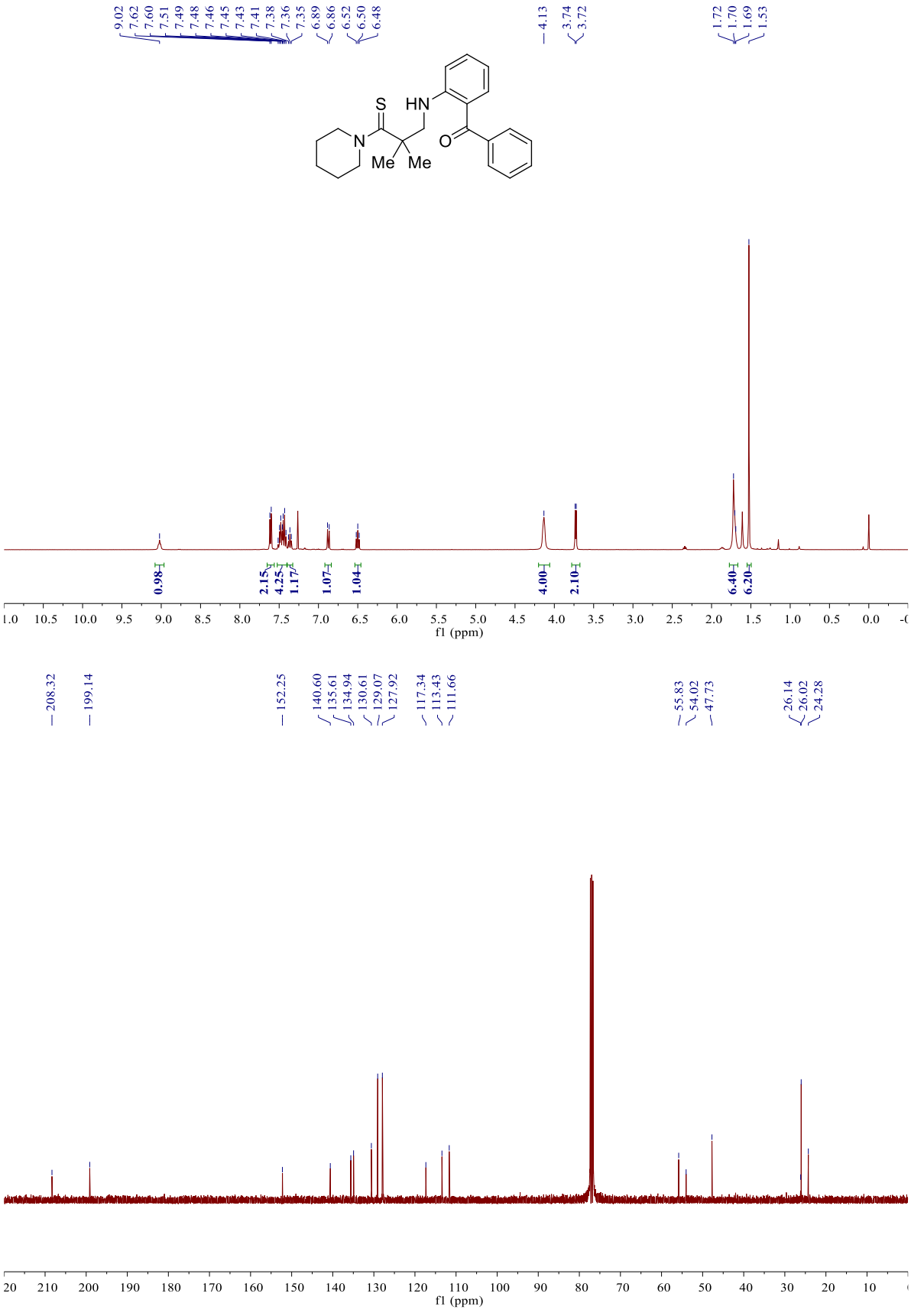




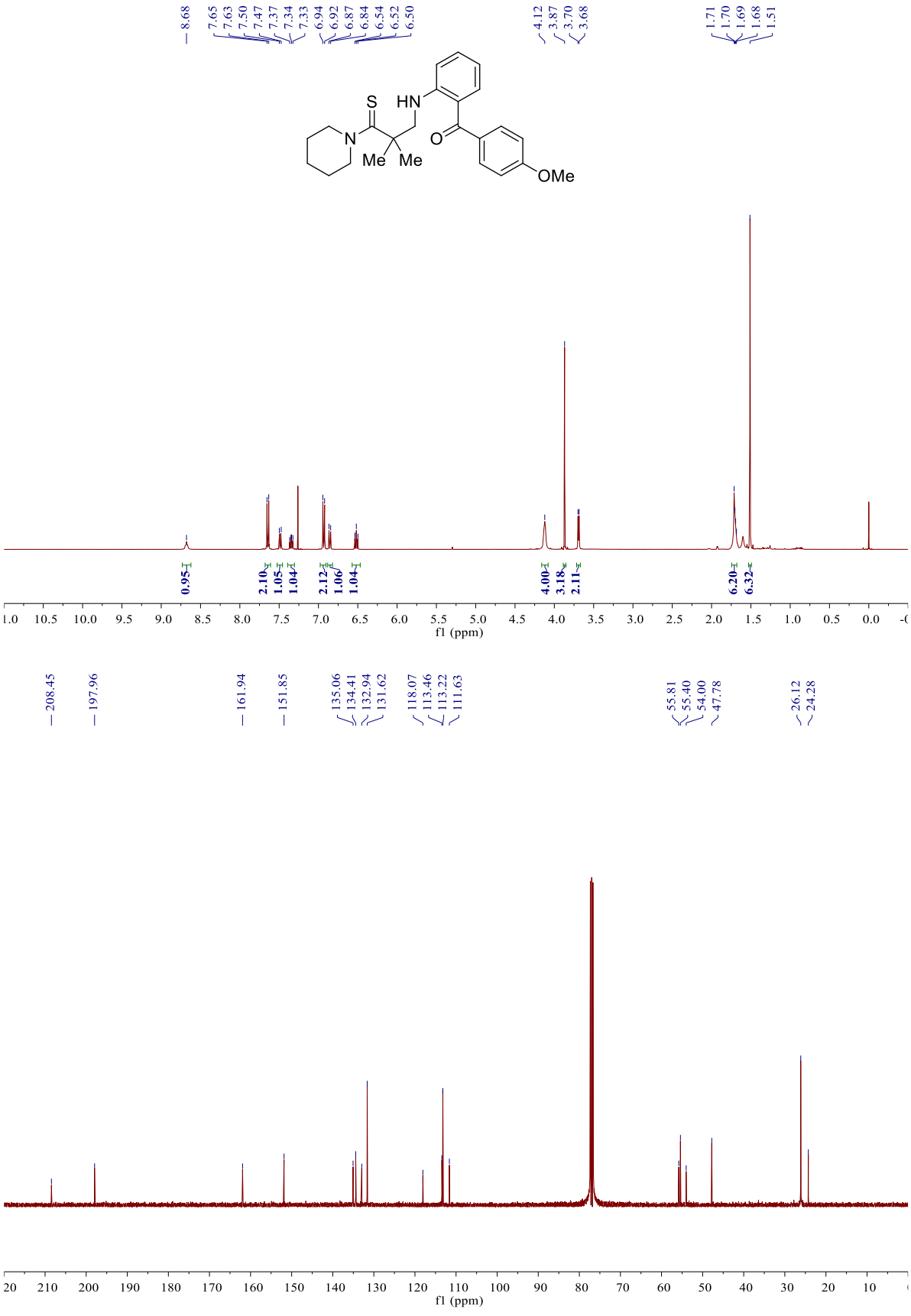
^{1}H and ^{13}C NMR spectra for product 3g ($CDCl_3$)



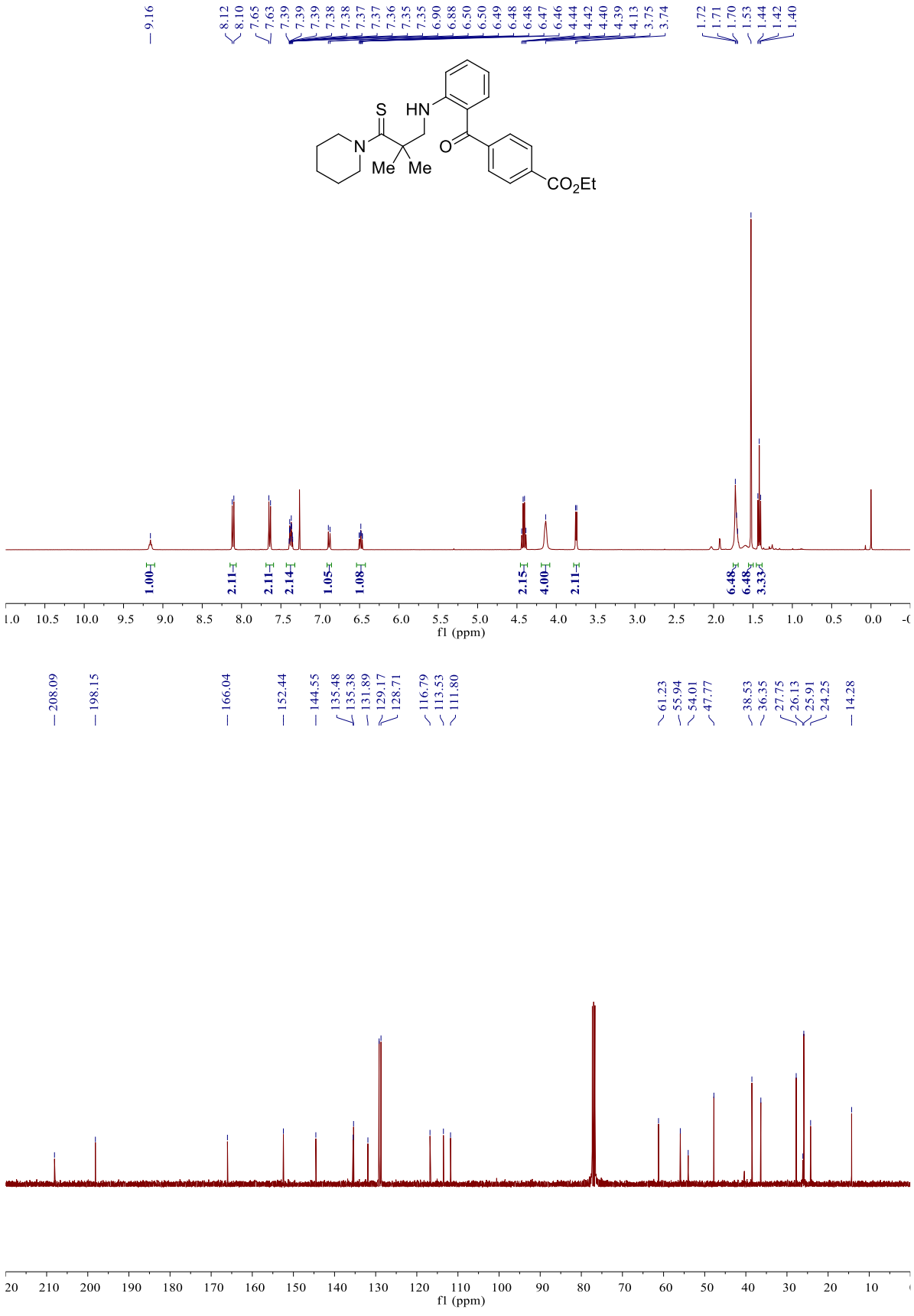
^{1}H and ^{13}C NMR spectra for product 3h ($CDCl_3$)



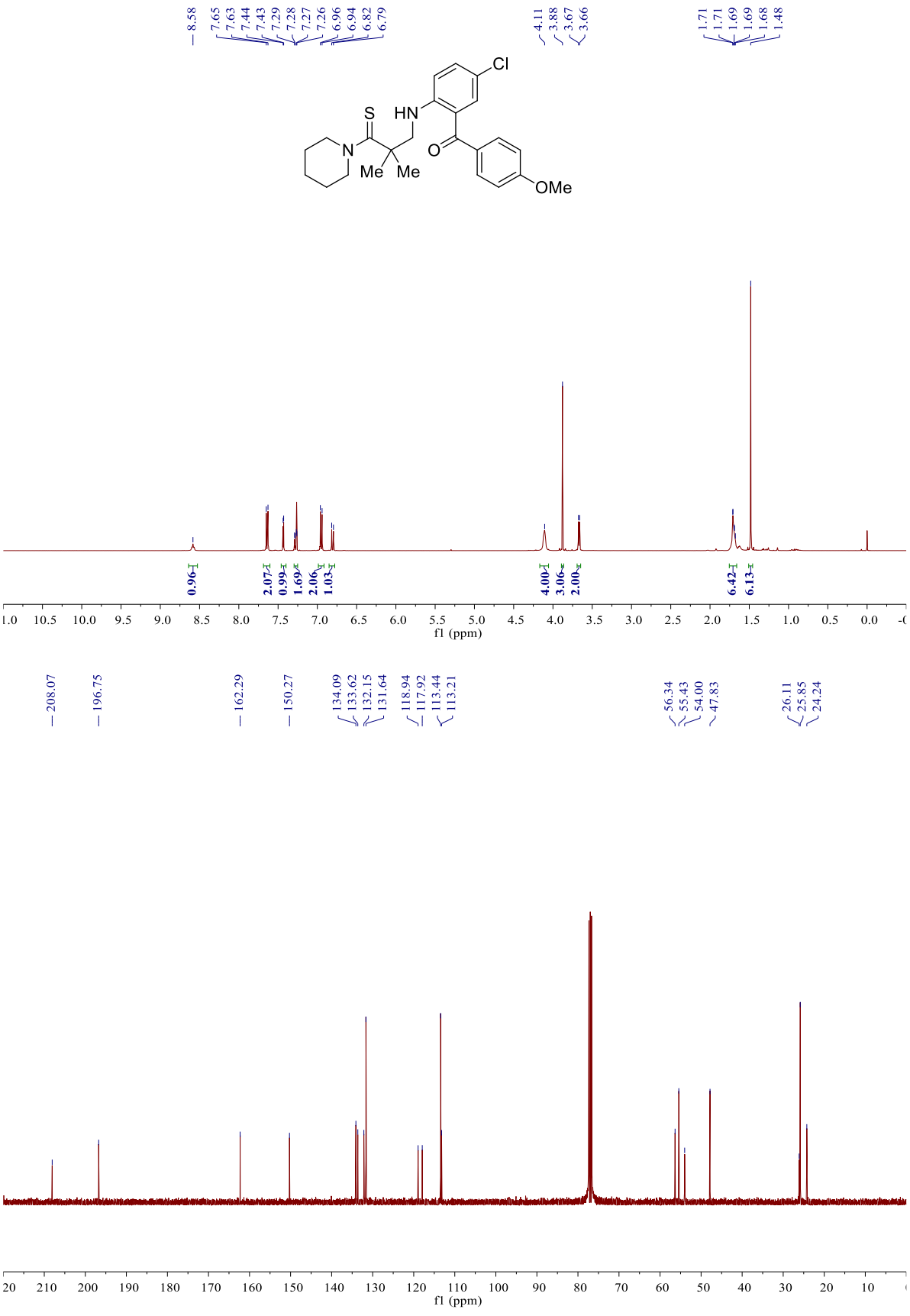
^{1}H and ^{13}C NMR spectra for product 3i ($CDCl_3$)



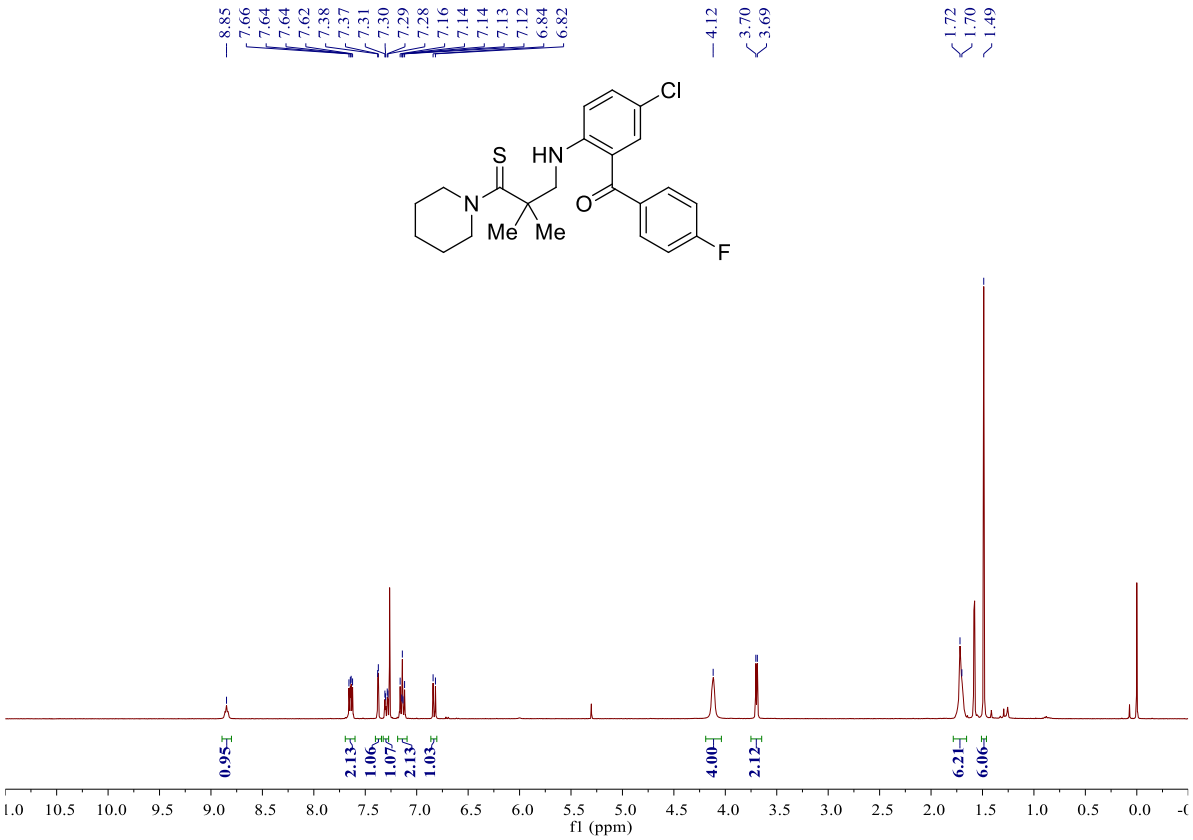
^{1}H and ^{13}C NMR spectra for product 3j ($CDCl_3$)



^{1}H and ^{13}C NMR spectra for product 3k ($CDCl_3$)



^{1}H and ^{13}C NMR spectra for product 3l ($CDCl_3$)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6.82
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3.70
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1.70
1.49
Cl
S
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N
O
Me
Me
F
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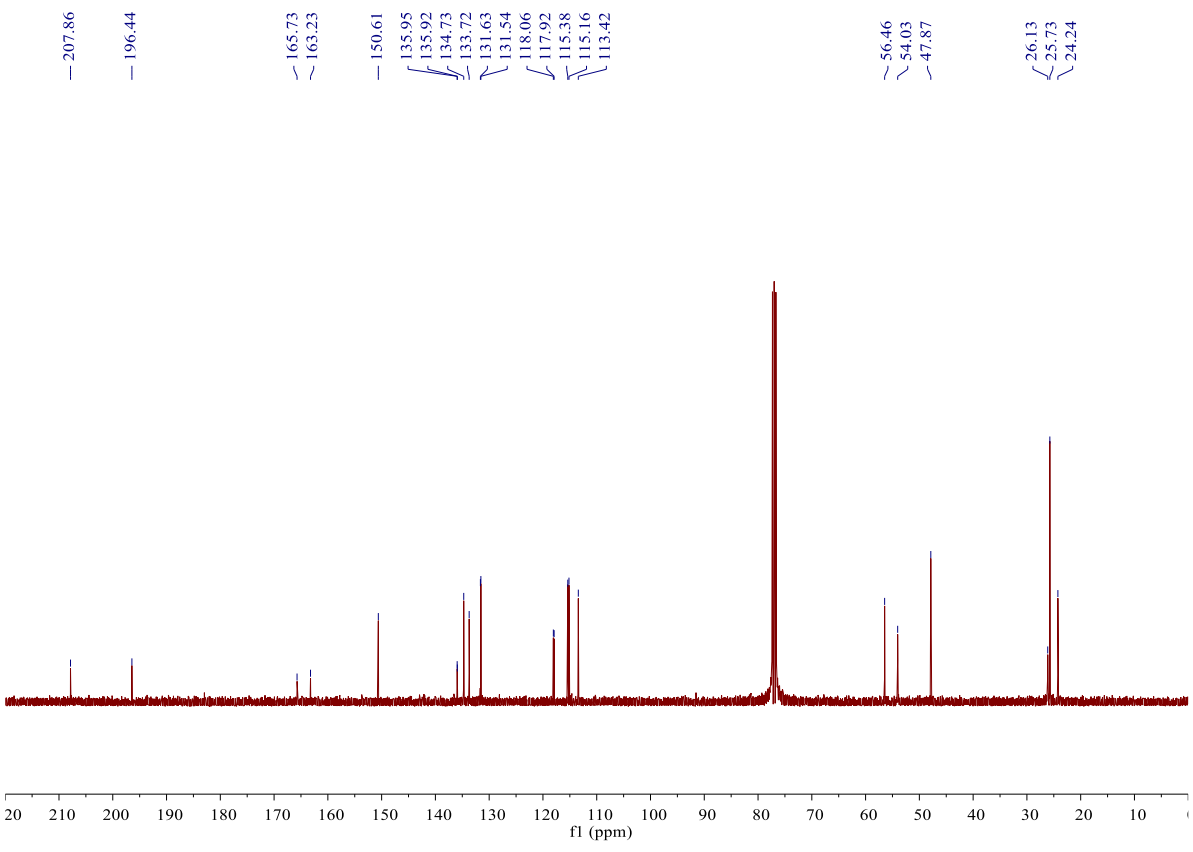
6.21
6.06
fl (ppm)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150.61
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131.63
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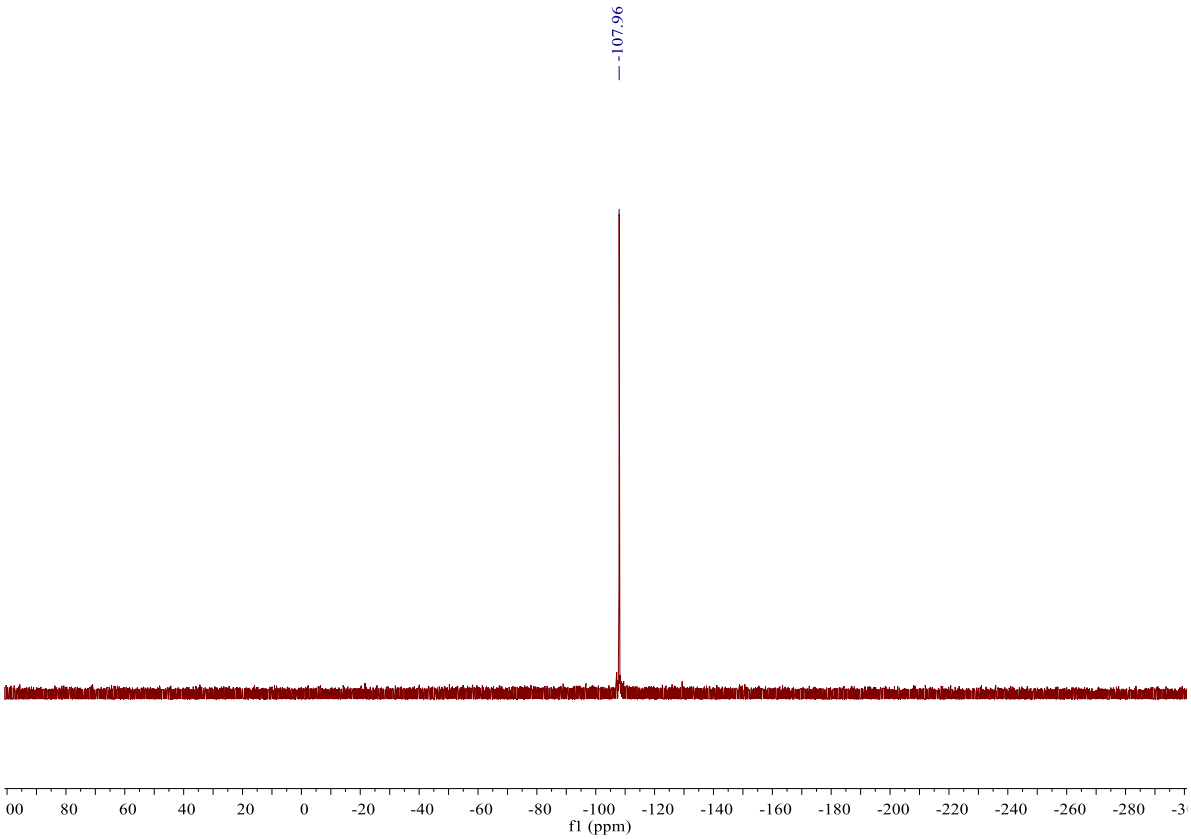
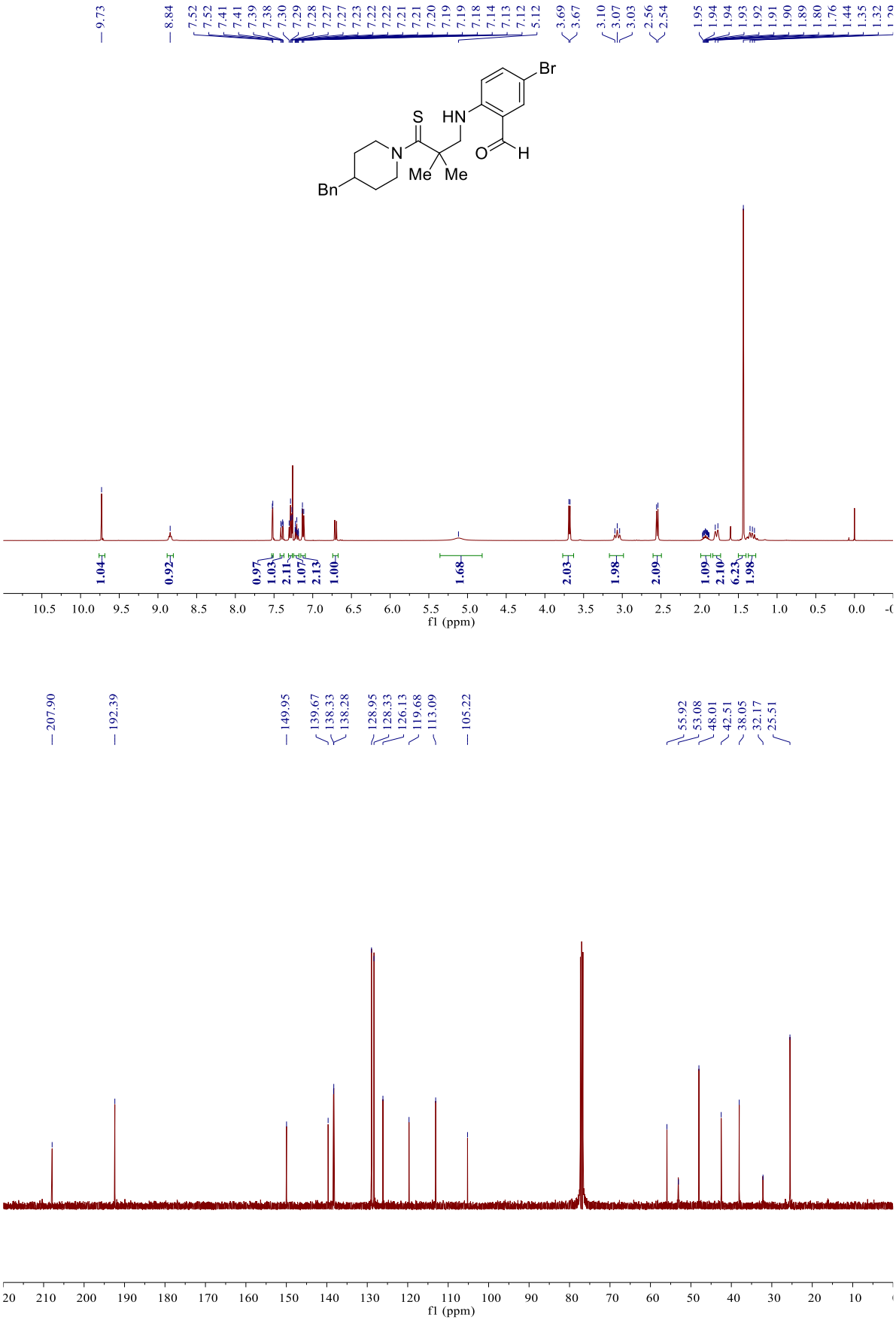
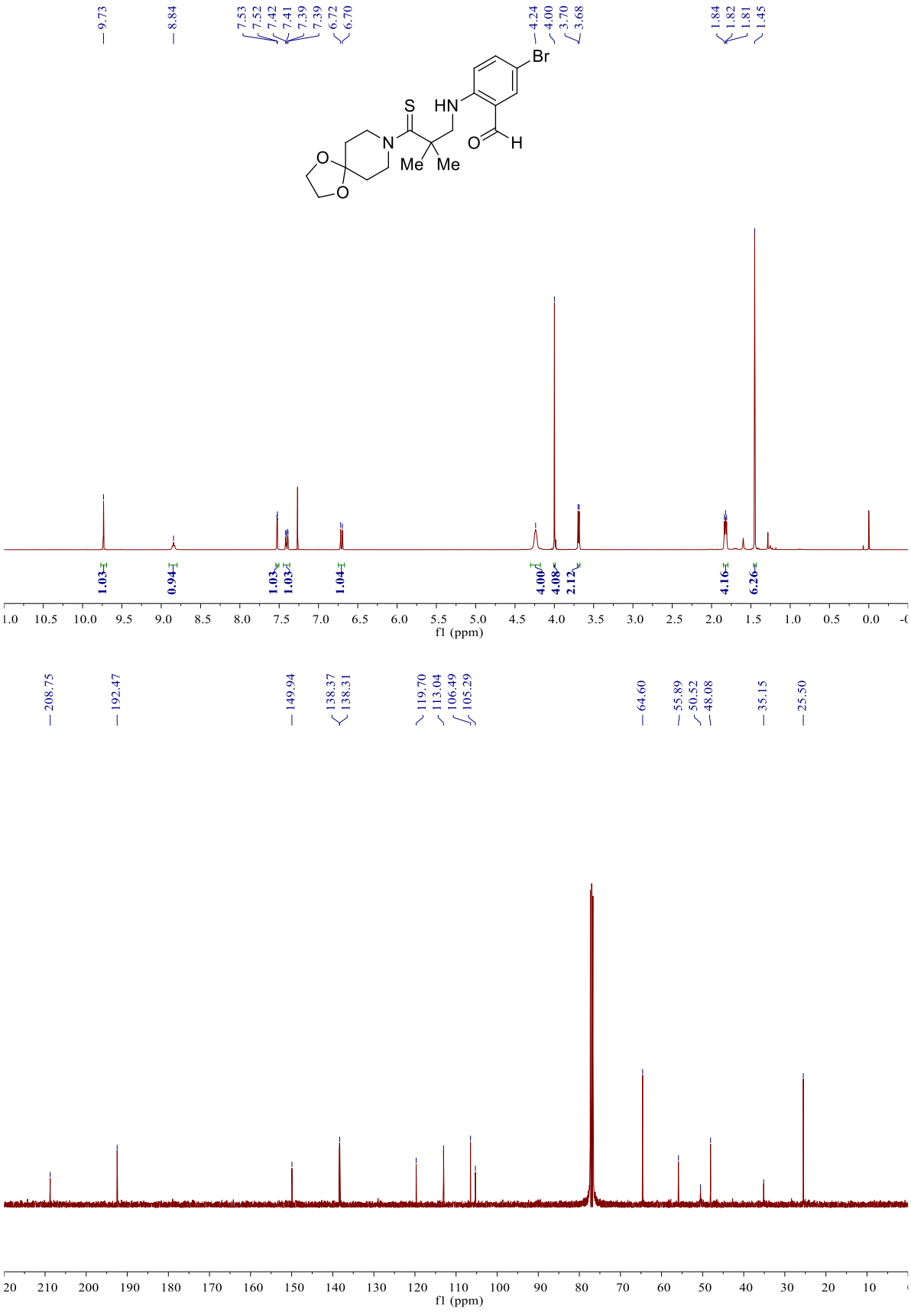
115.38
115.16
113.42
56.46
54.03
47.87
26.13
25.73
24.24
fl (ppm)



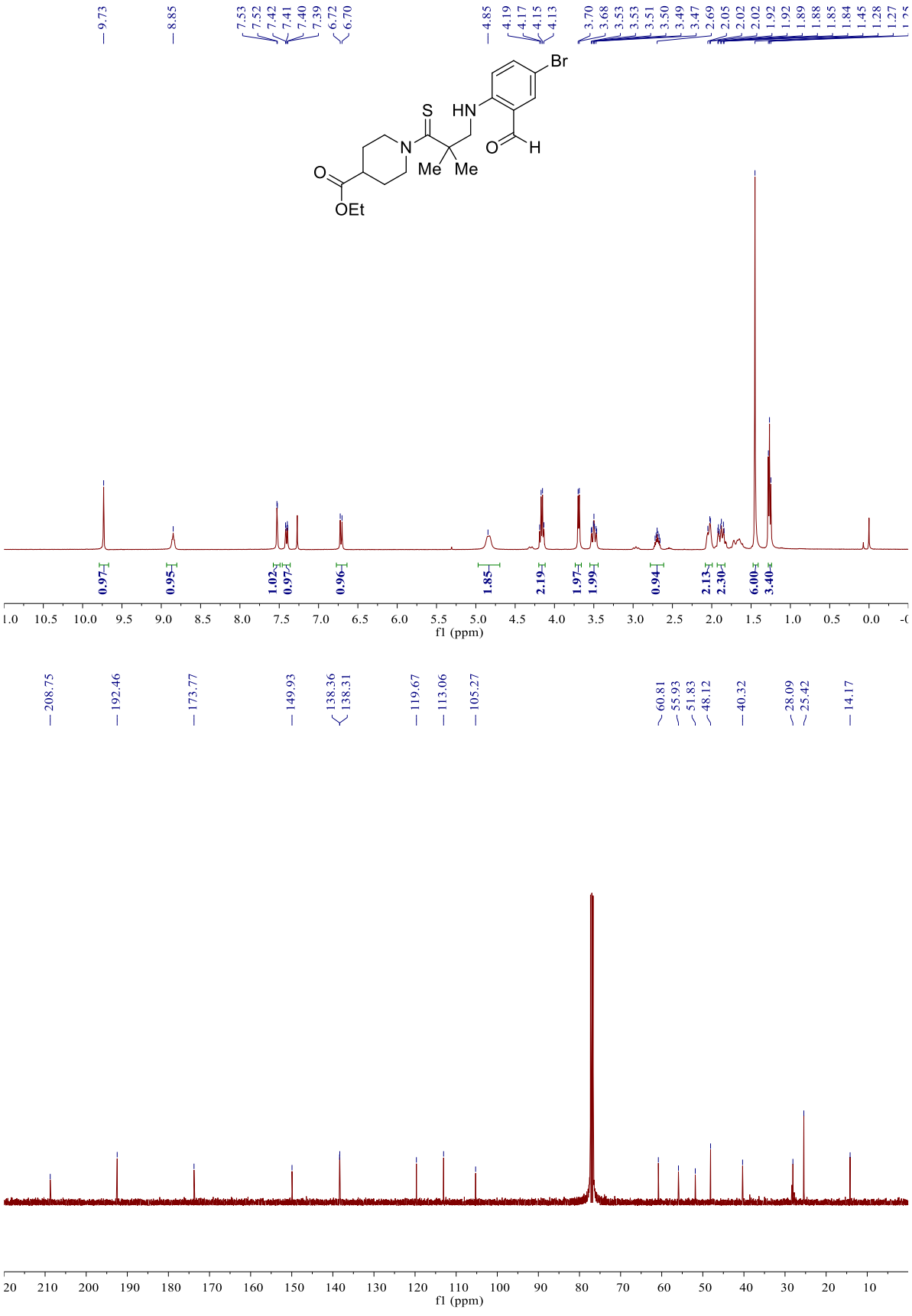
^{1}H, ^{19}F, and ^{13}C NMR spectra for product 3m ($CDCl_3$)



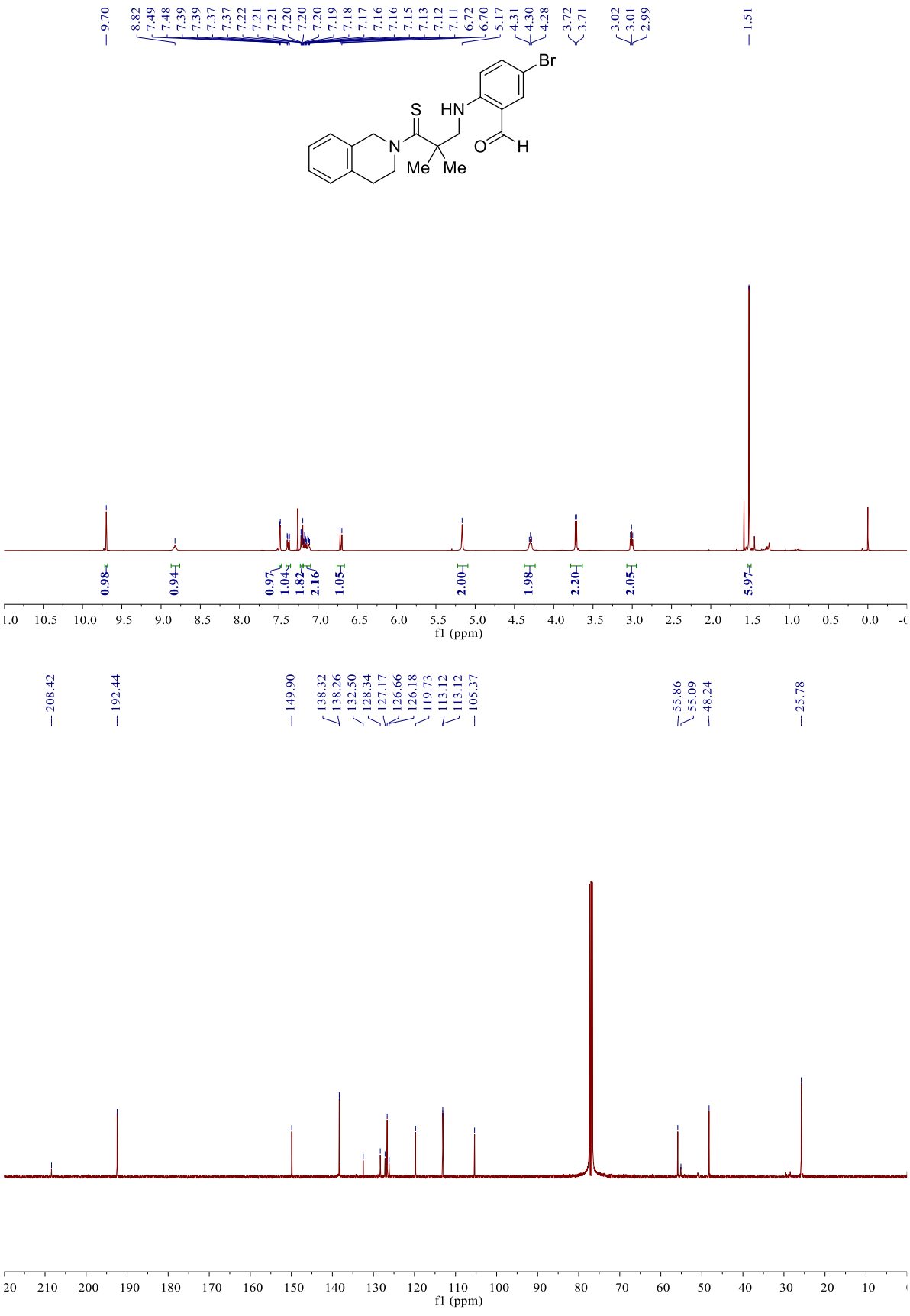
^{1}H and ^{13}C NMR spectra for product 4a ($CDCl_3$)



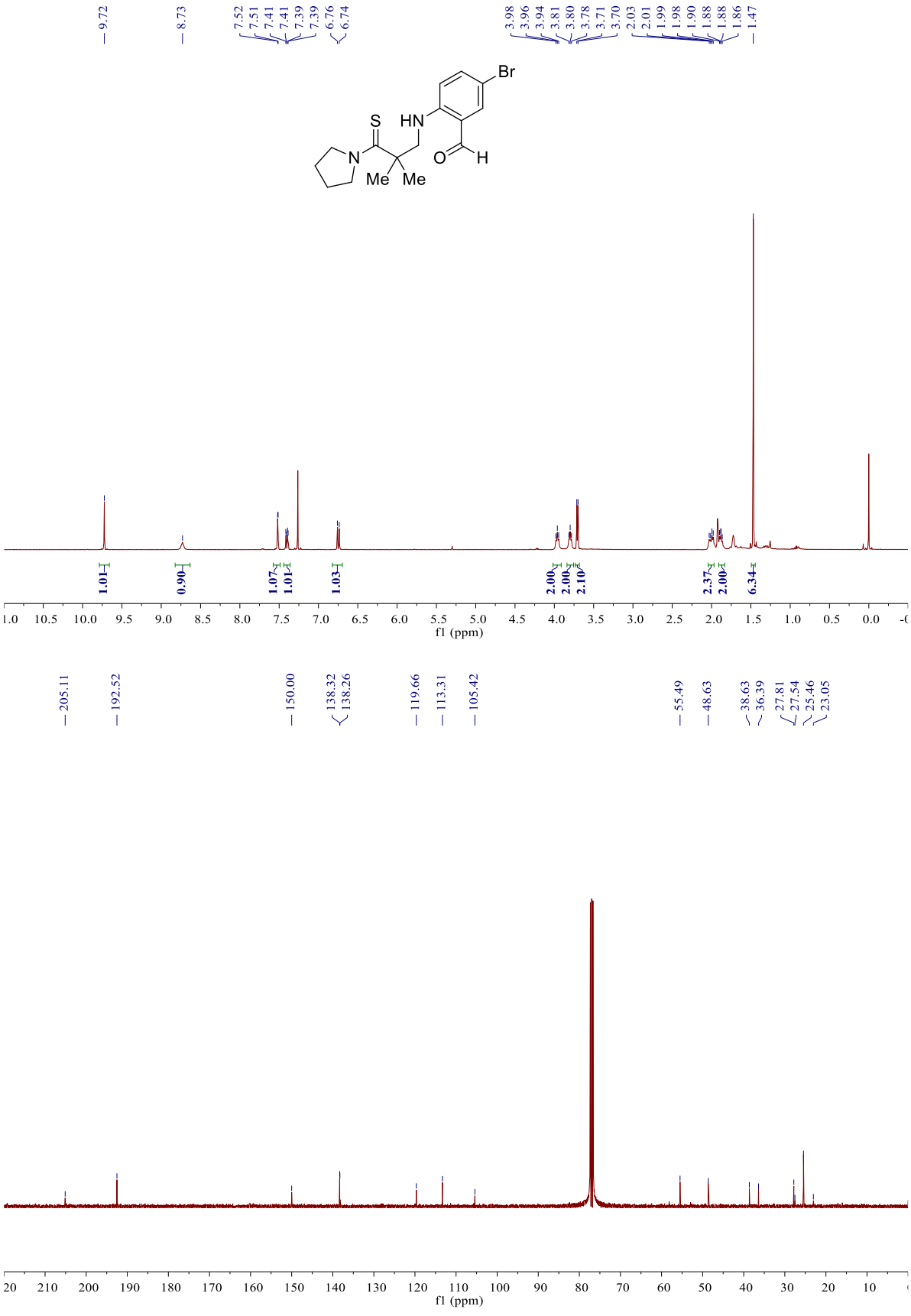
^{1}H and ^{13}C NMR spectra for product 4b ($CDCl_3$)



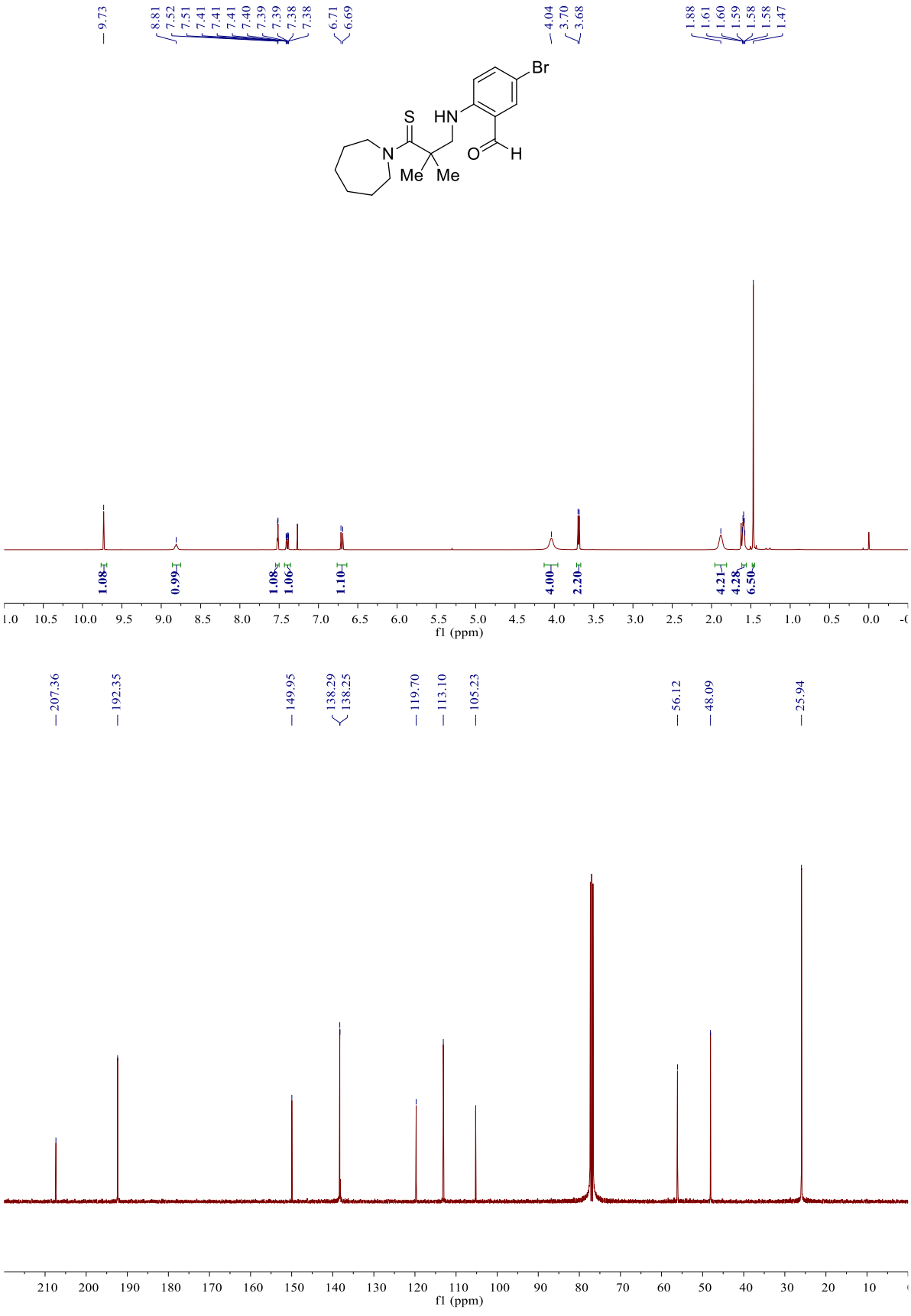
^{1}H and ^{13}C NMR spectra for product 4c ($CDCl_3$)



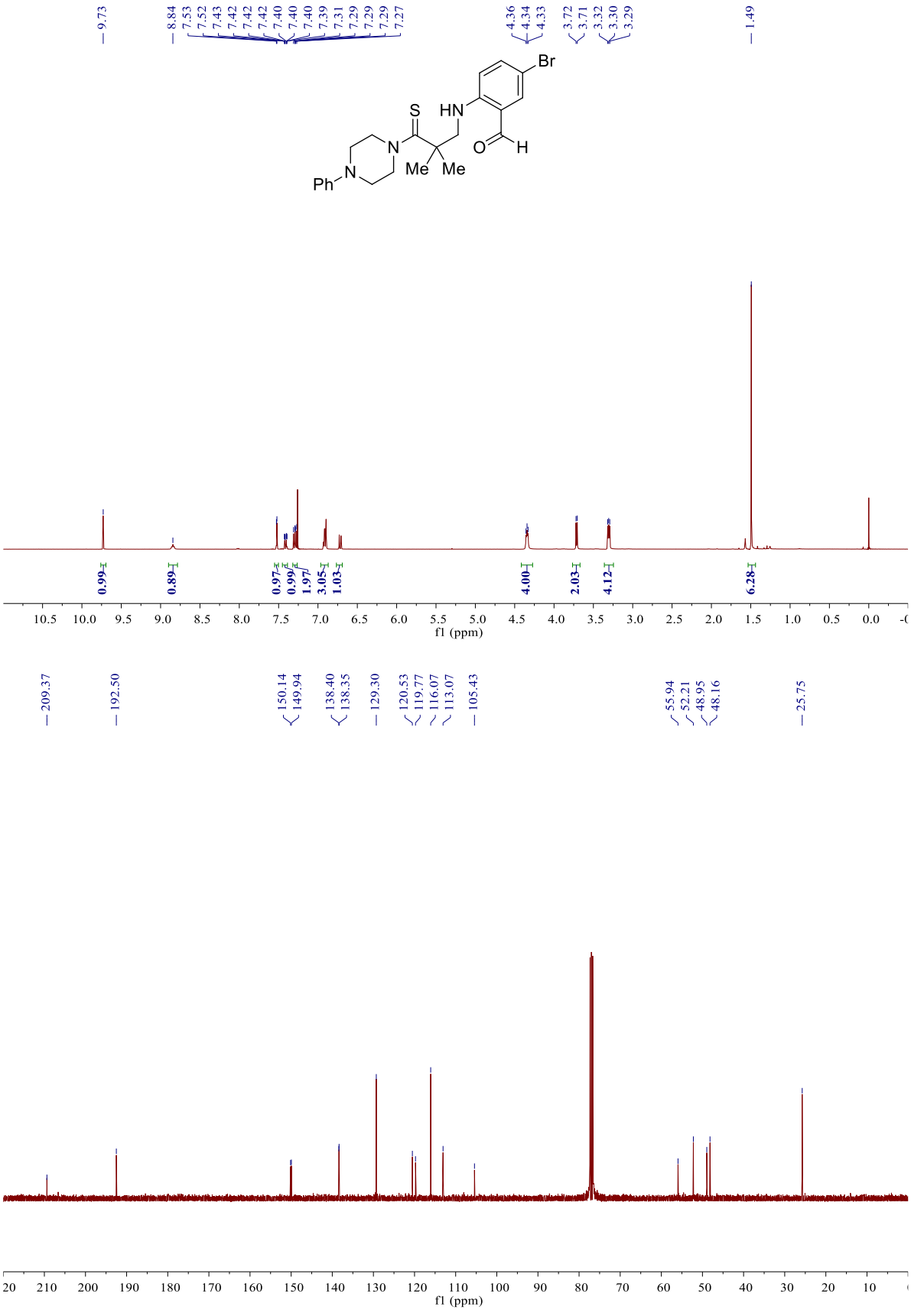
^{1}H and ^{13}C NMR spectra for product 4d ($CDCl_3$)



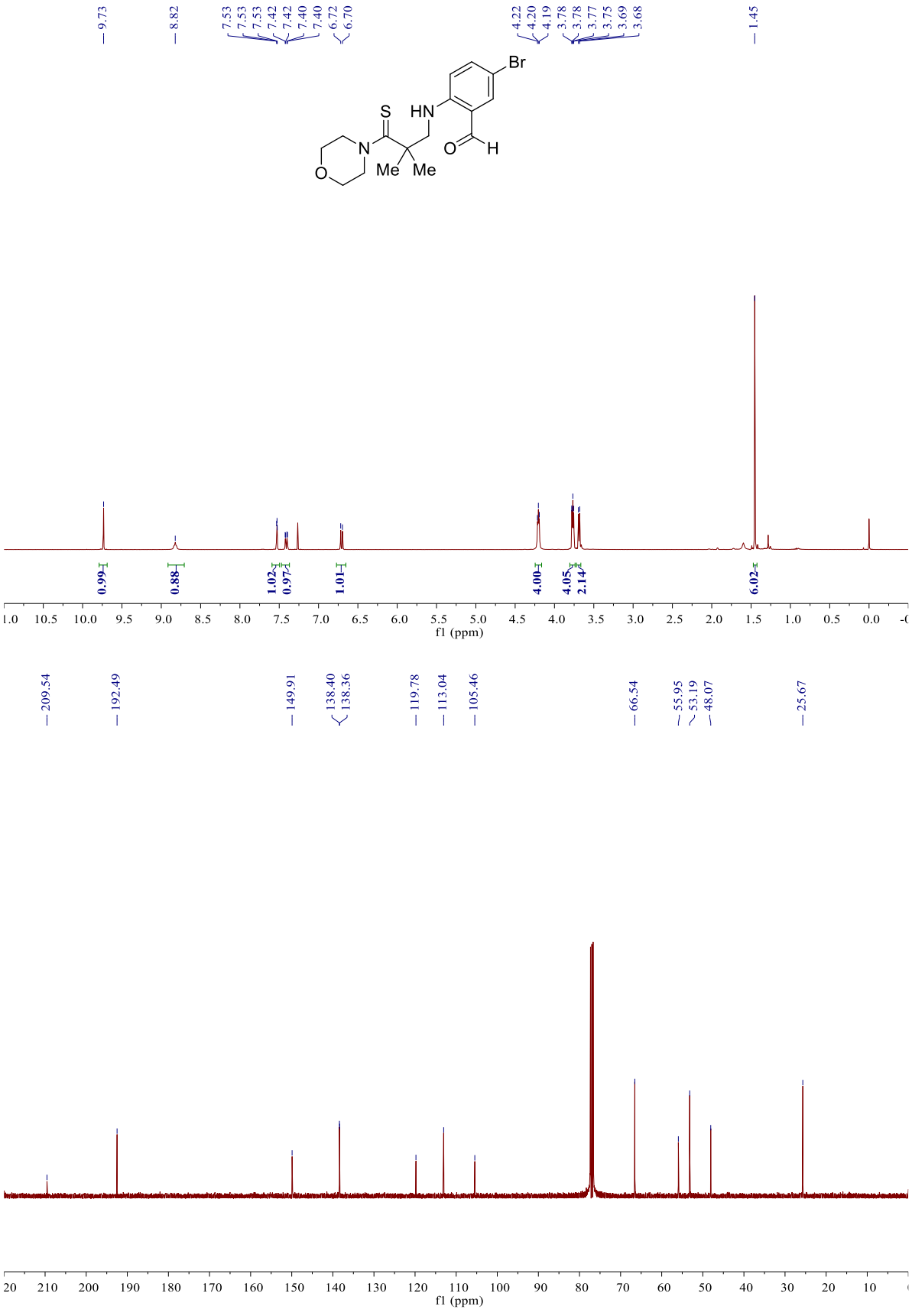
^{1}H and ^{13}C NMR spectra for product 4e ($CDCl_3$)



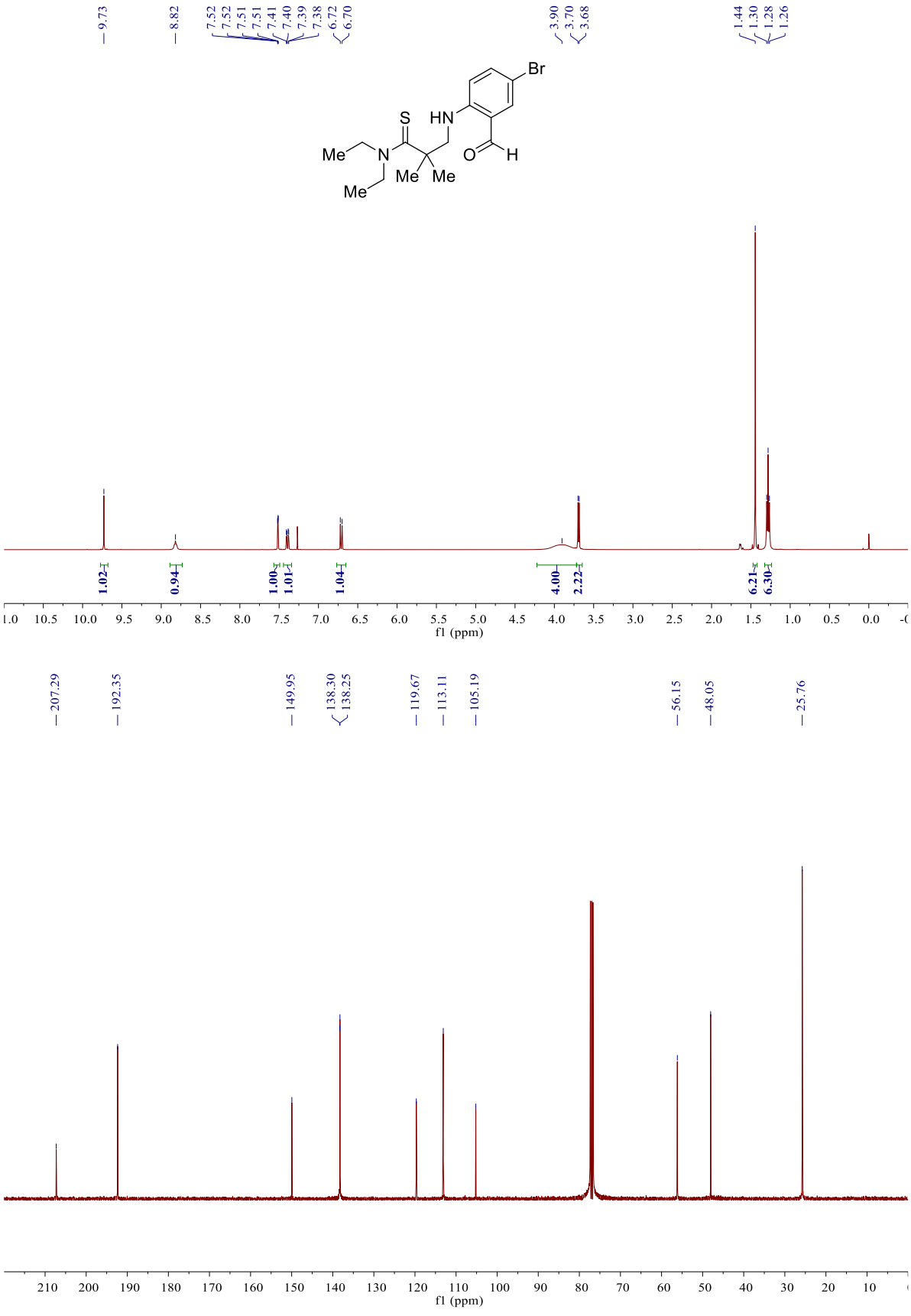
^{1}H and ^{13}C NMR spectra for product 4f ($CDCl_3$)



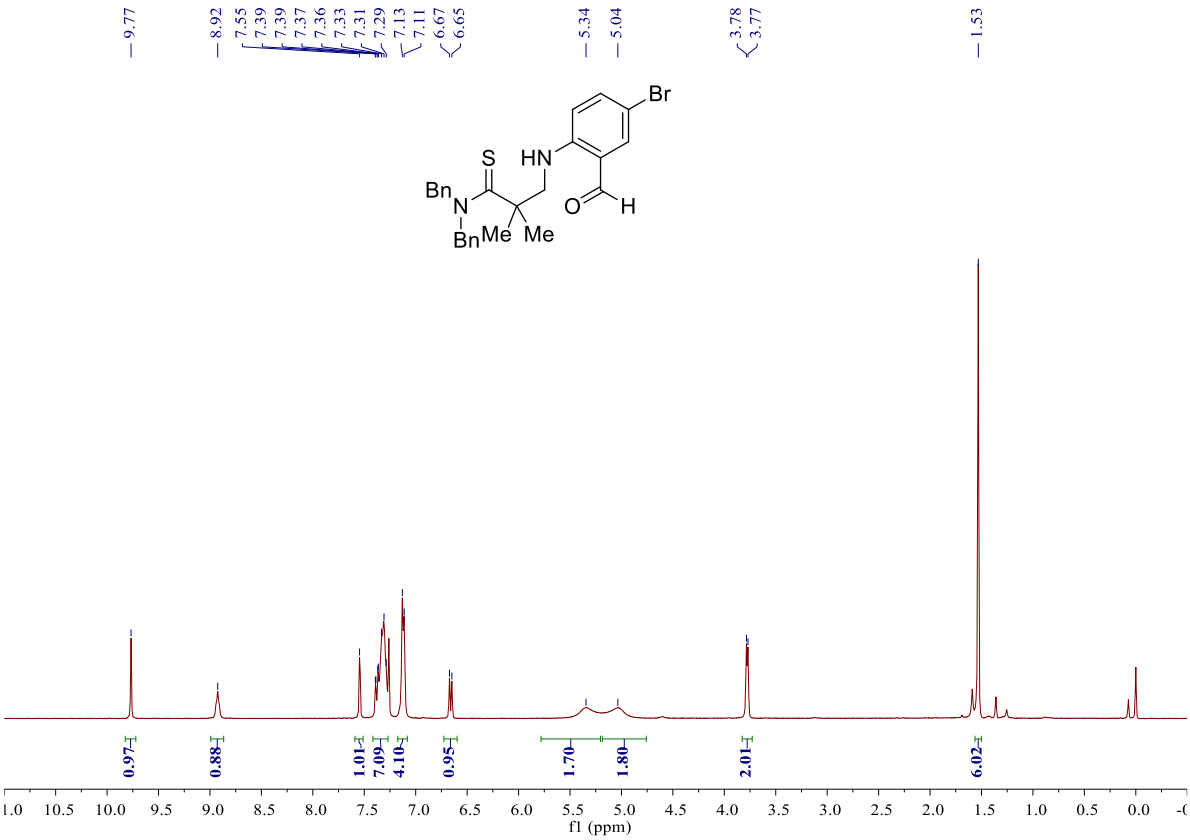
^{1}H and ^{13}C NMR spectra for product 4g ($CDCl_3$)

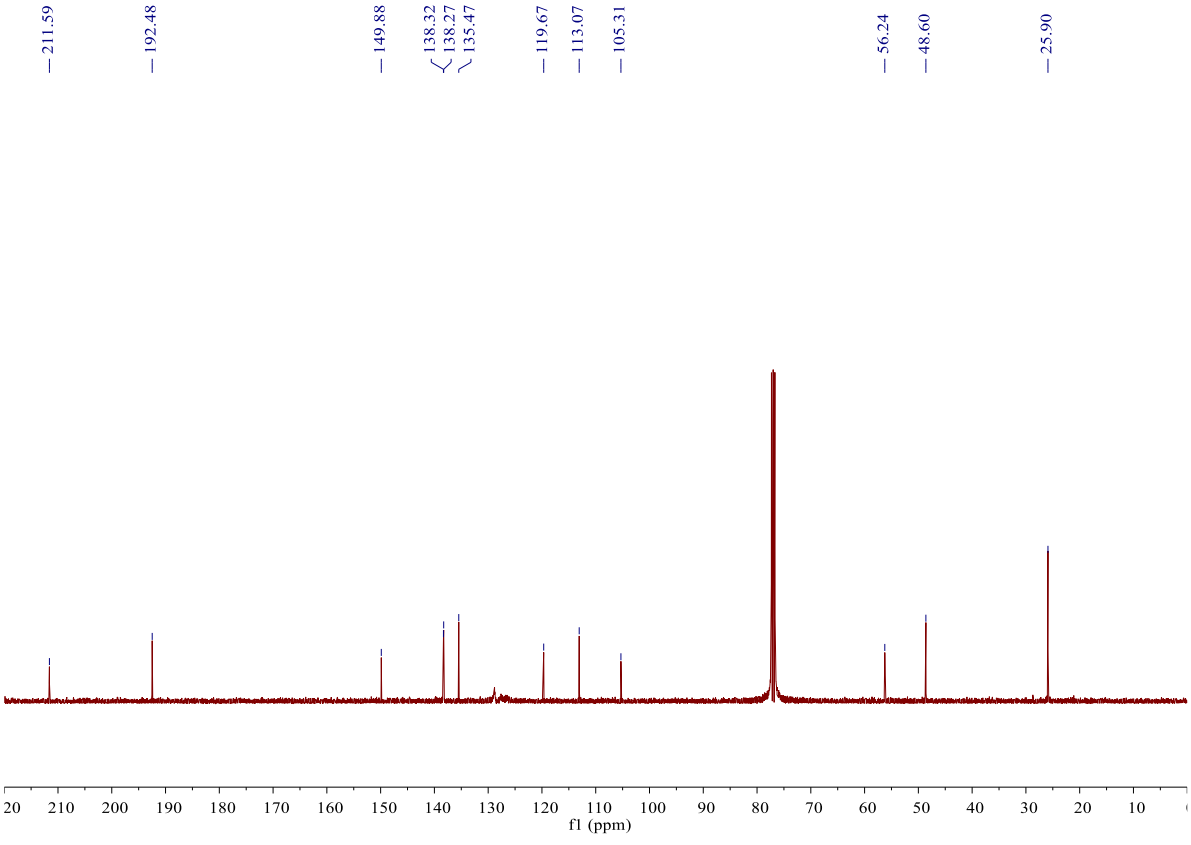


^{1}H and ^{13}C NMR spectra for product 4h ($CDCl_3$)

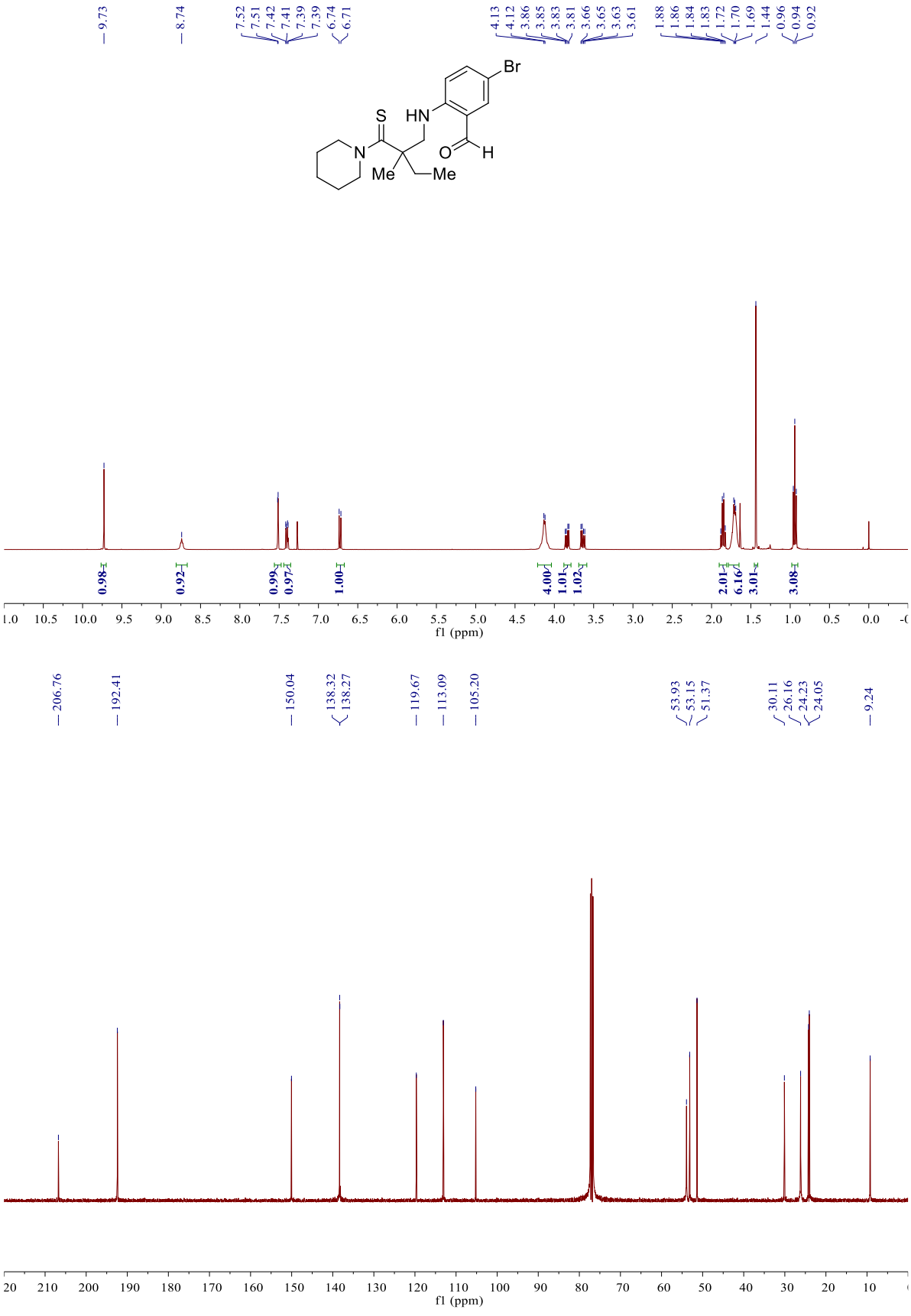


^{1}H and ^{13}C NMR spectra for product 4i ($CDCl_3$)

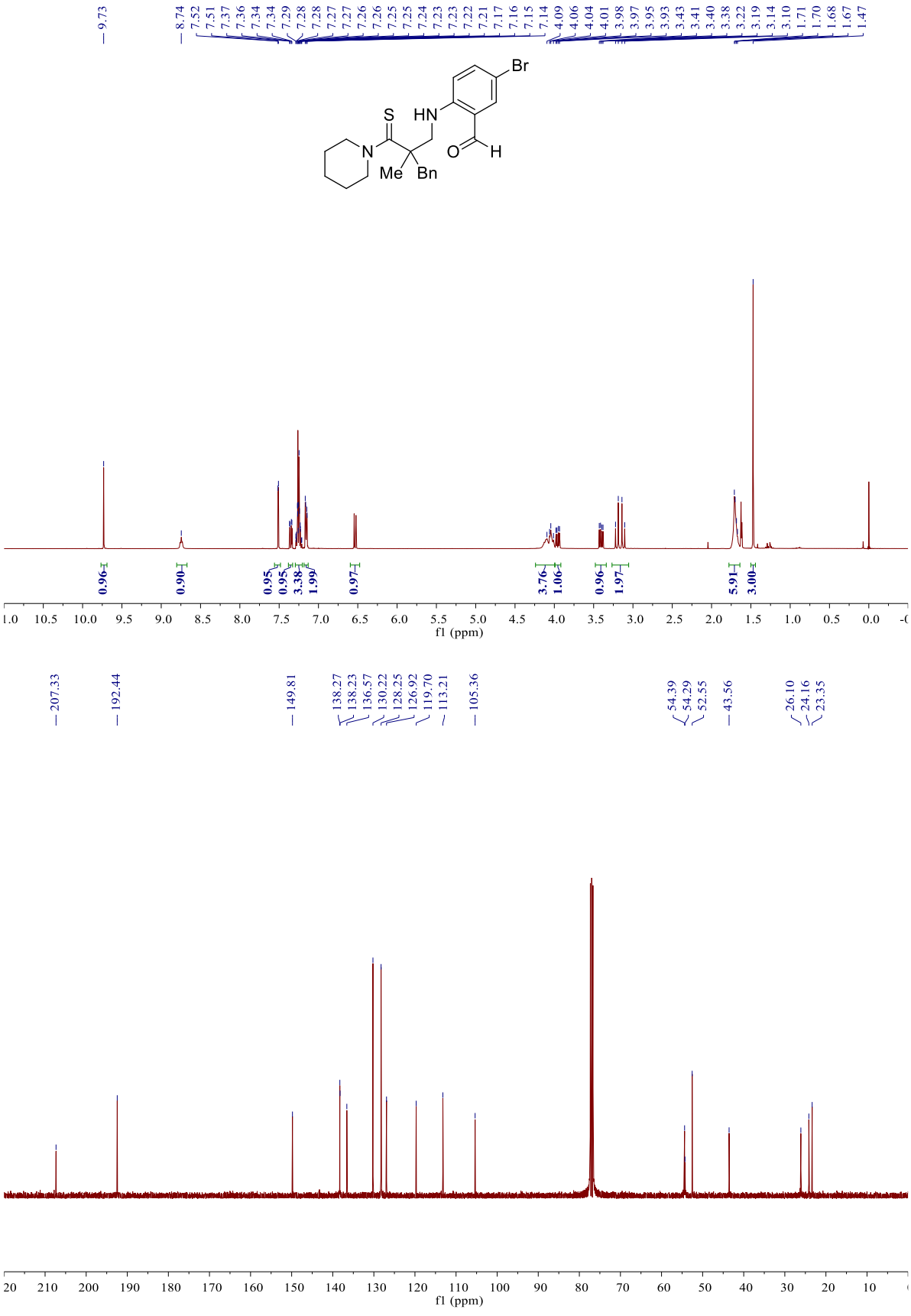




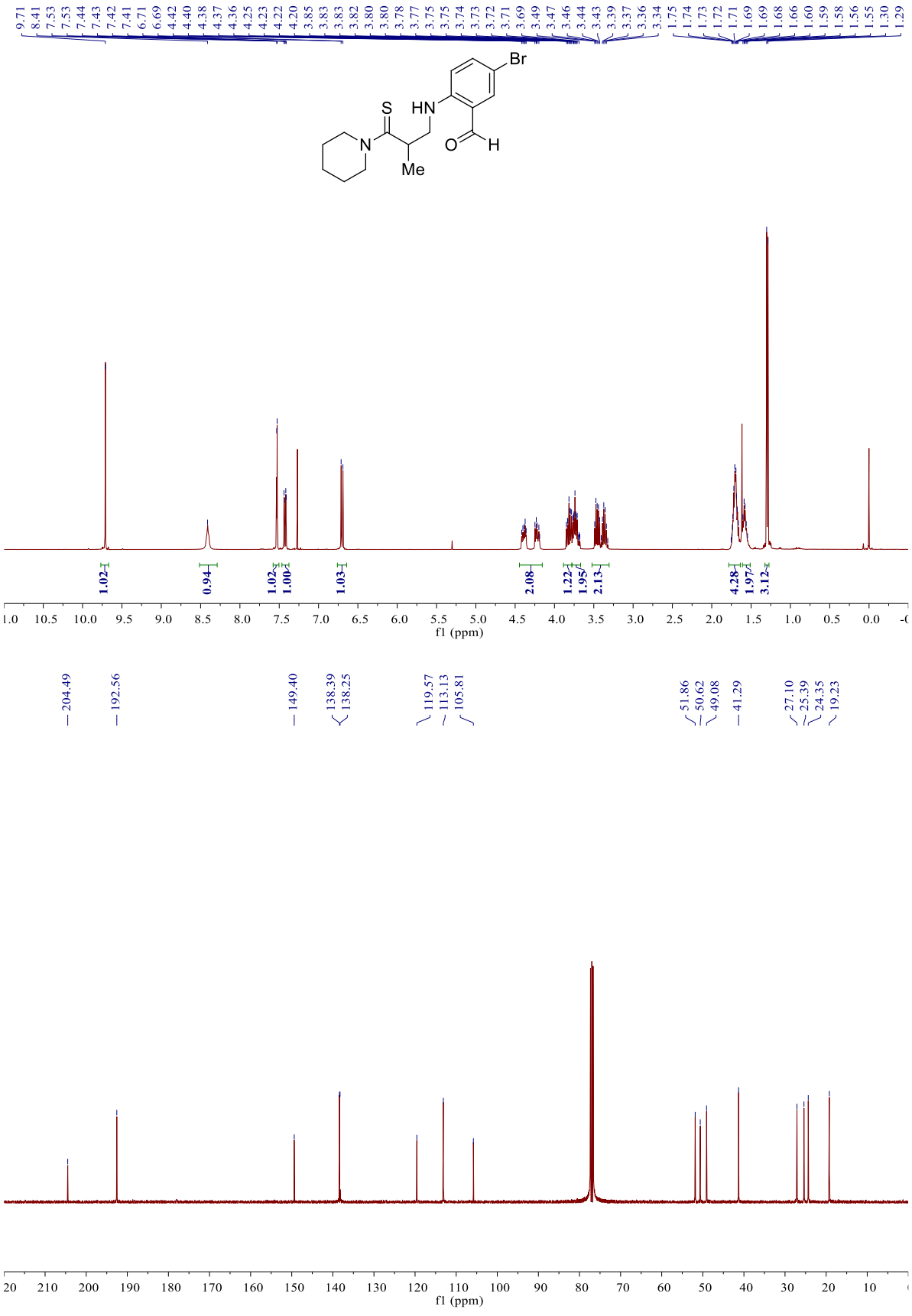
^{1}H and ^{13}C NMR spectra for product 4j ($CDCl_3$)



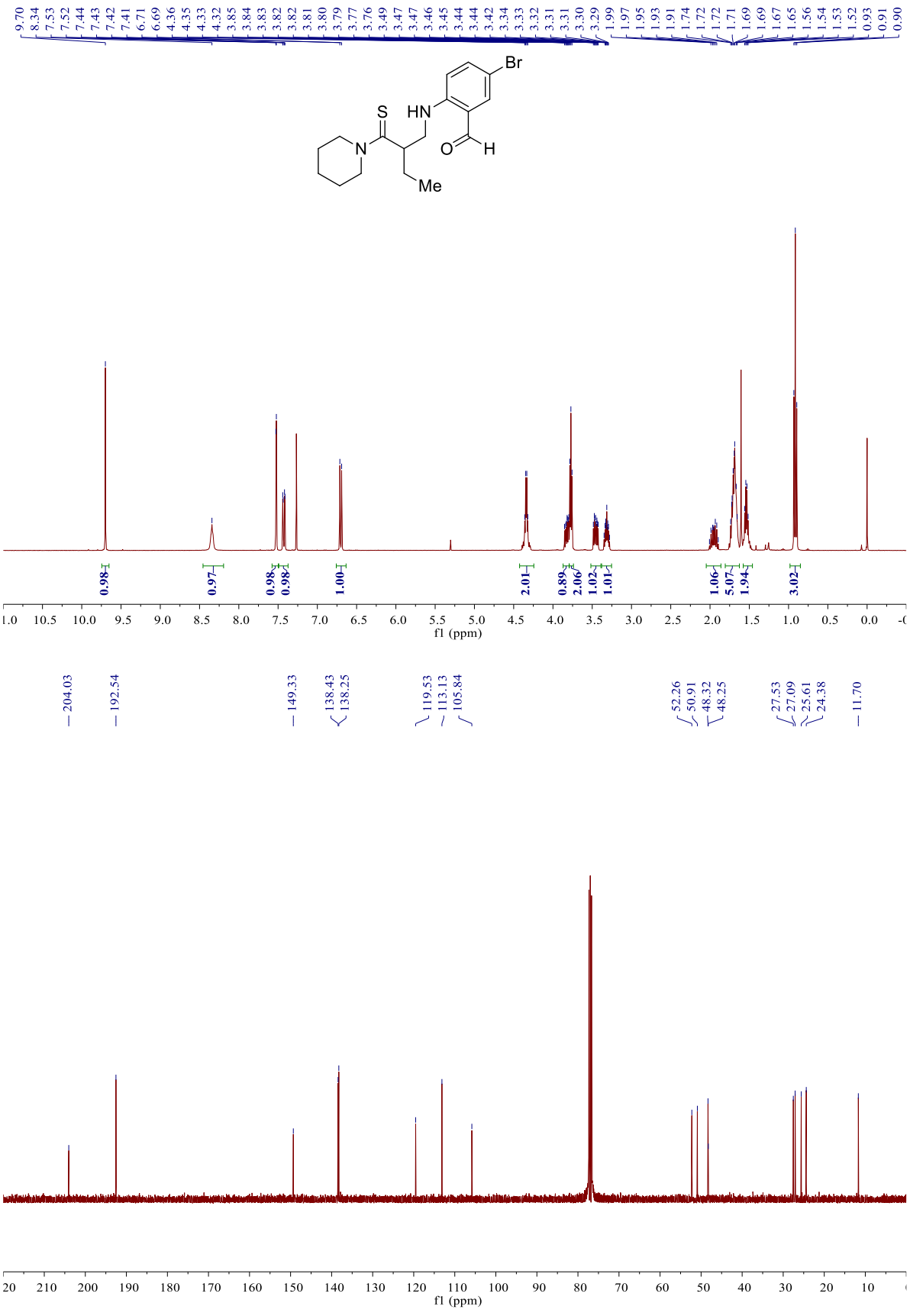
^{1}H and ^{13}C NMR spectra for product 4k ($CDCl_3$)



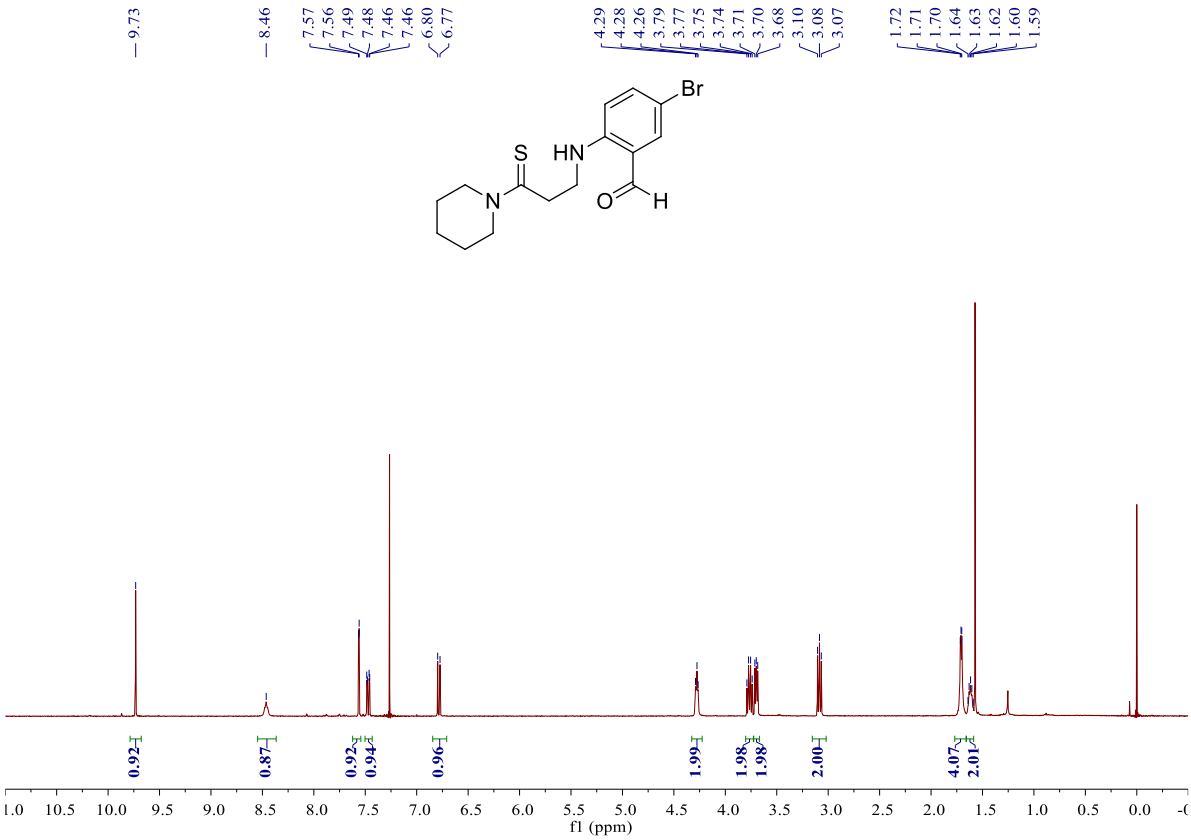
^{1}H and ^{13}C NMR spectra for product 4l ($CDCl_3$)

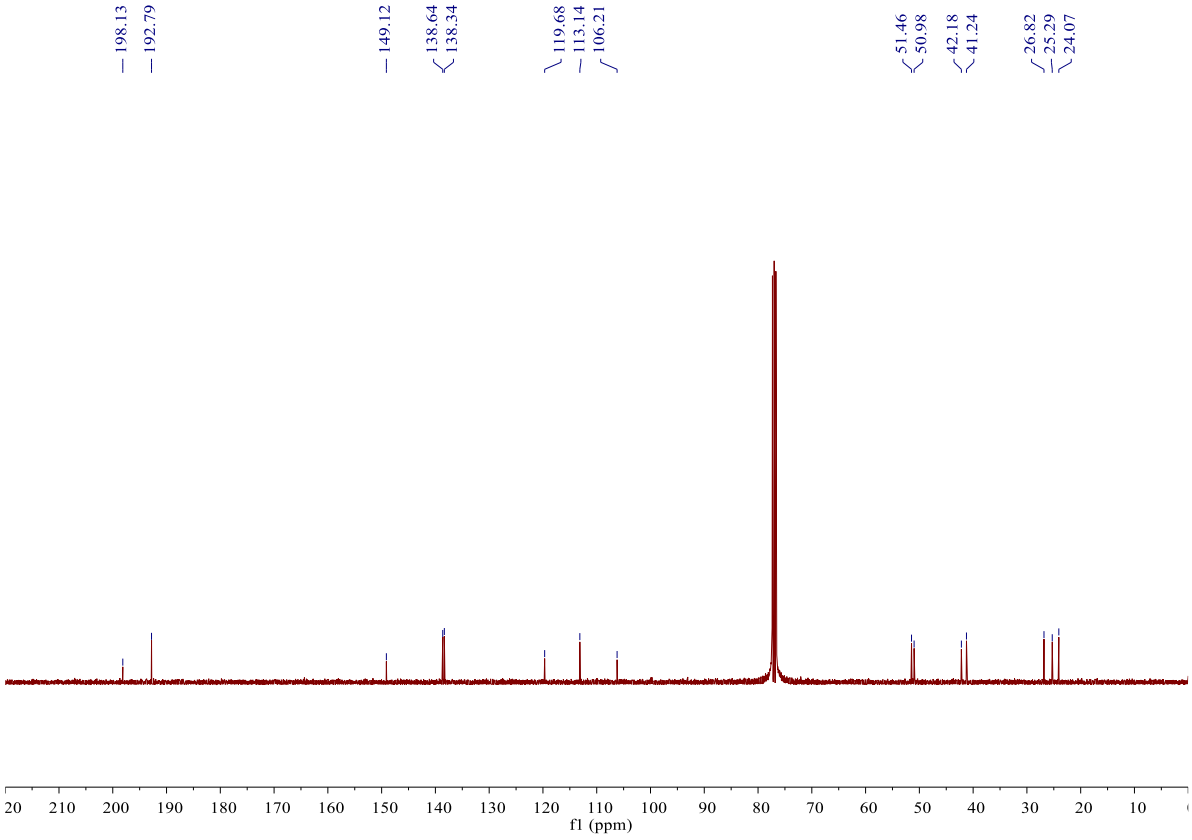


^{1}H and ^{13}C NMR spectra for product 4m ($CDCl_3$)

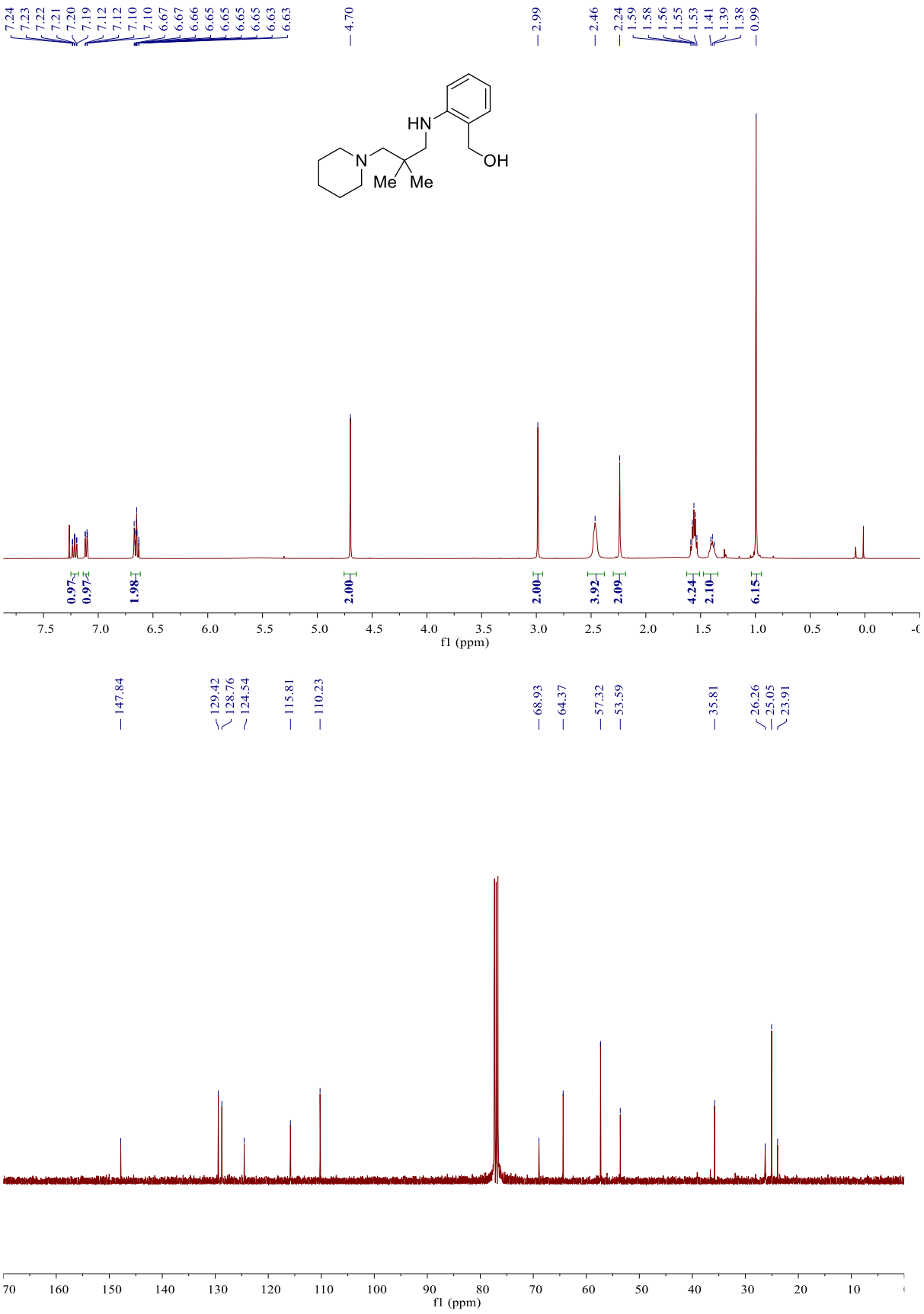


^{1}H and ^{13}C NMR spectra for product 4n ($CDCl_3$)

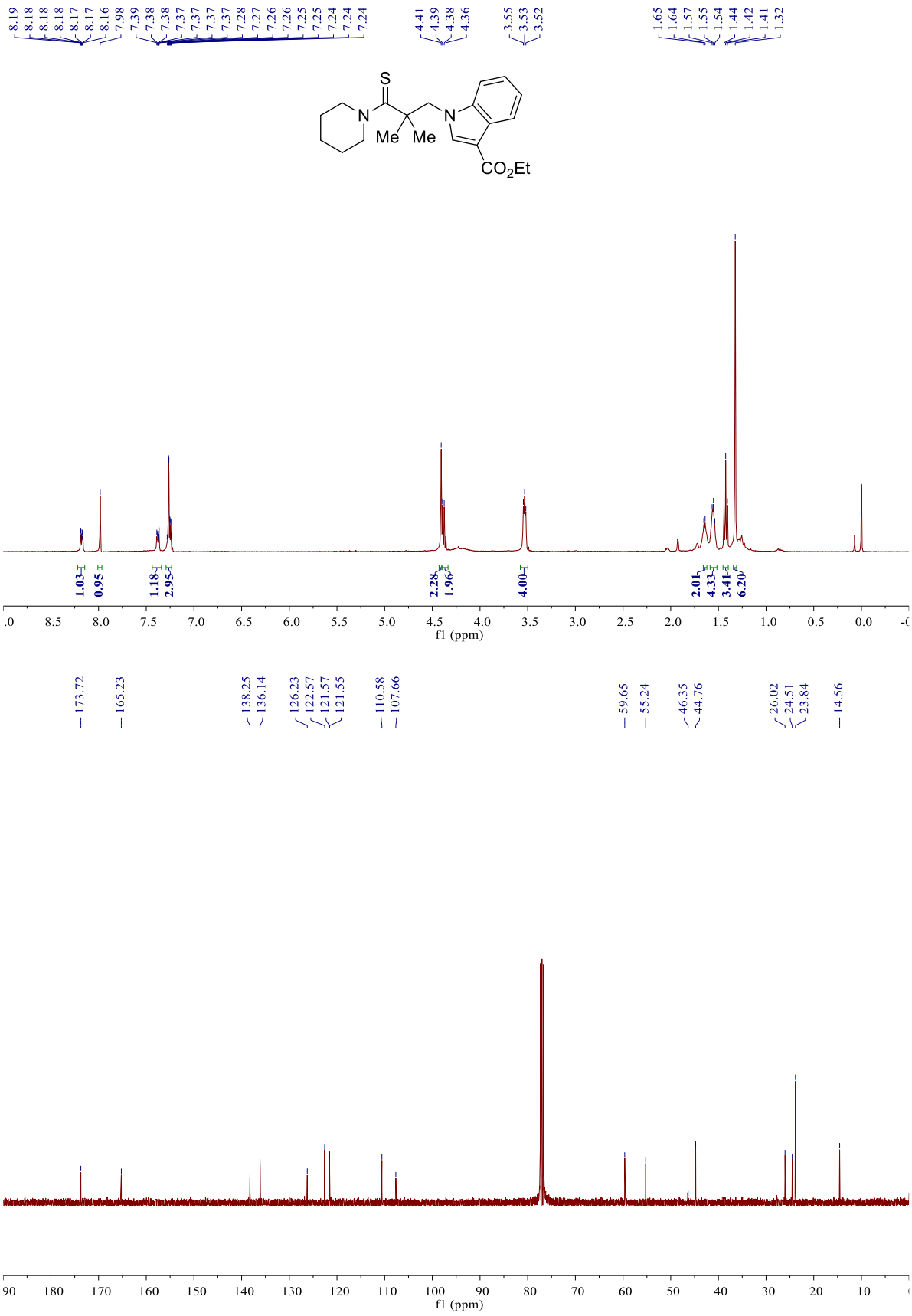




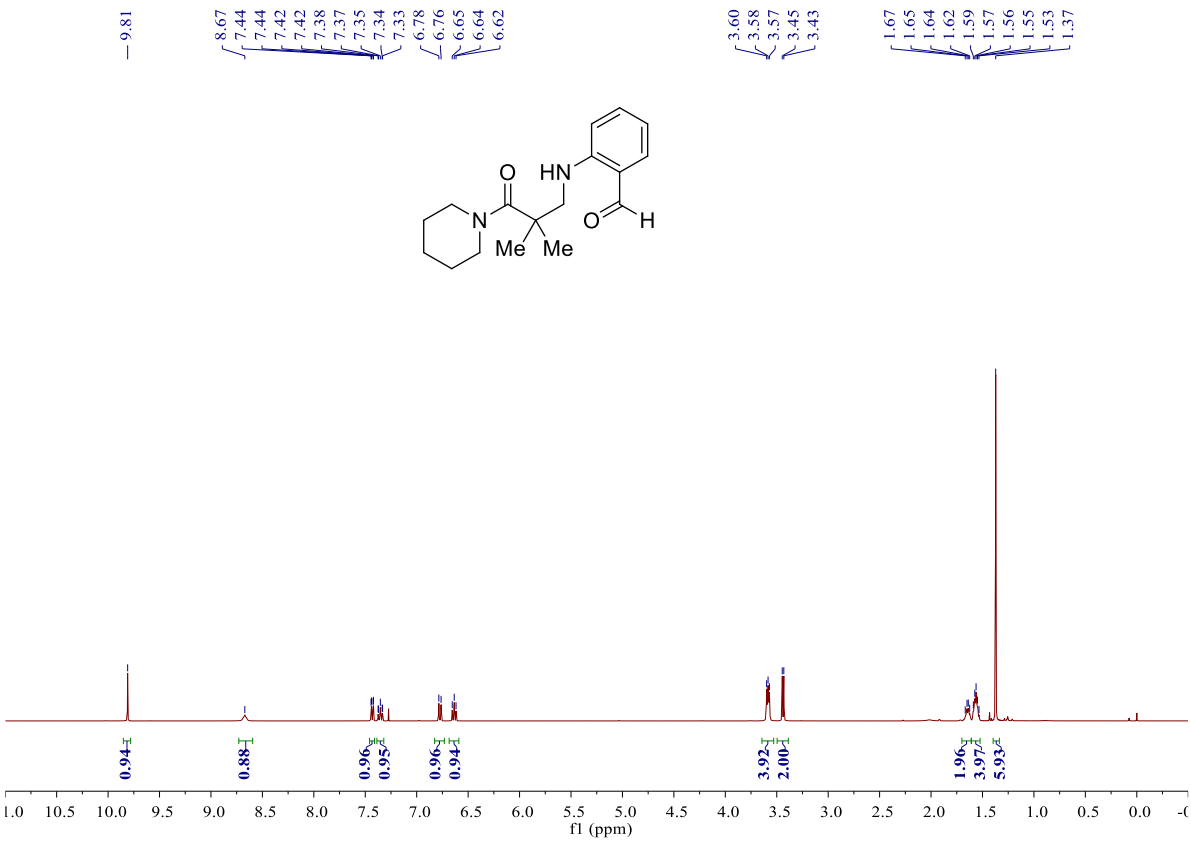
^{1}H and ^{13}C NMR spectra for product 4o ($CDCl_3$)

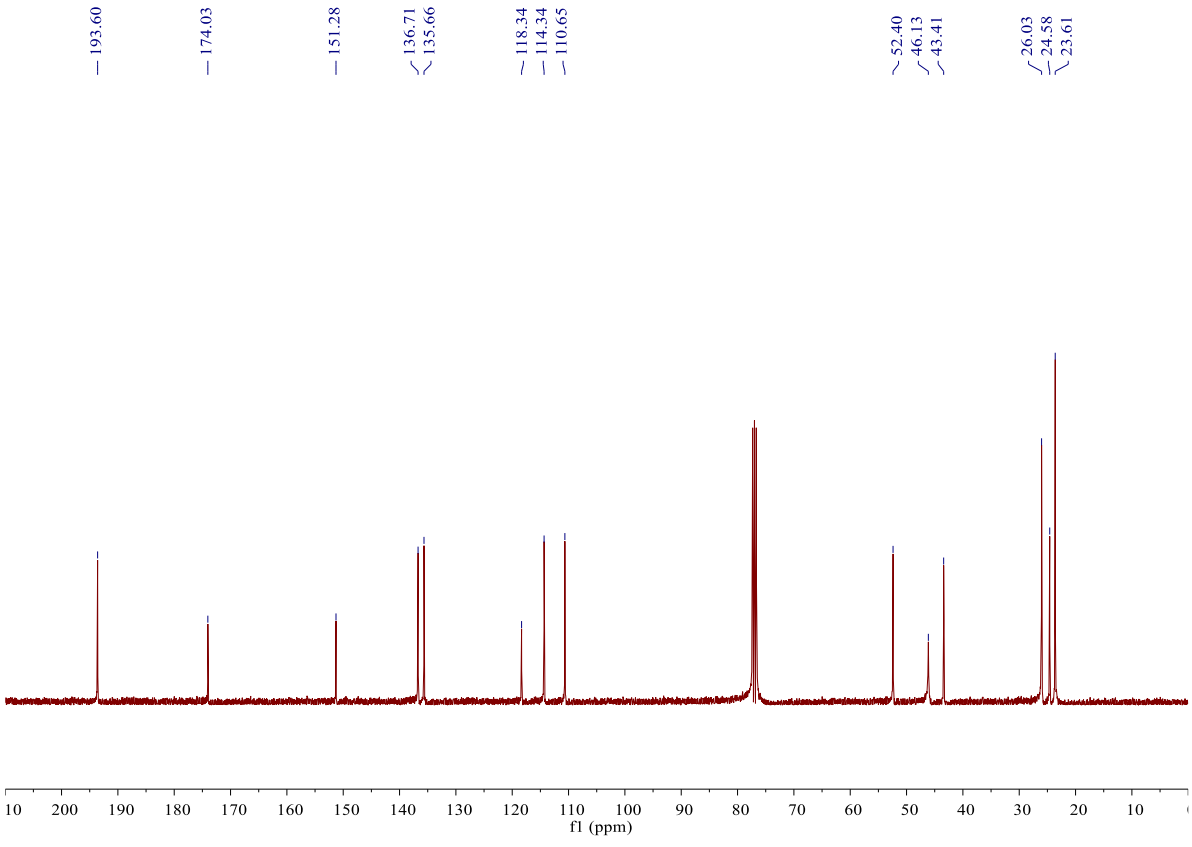


^{1}H and ^{13}C NMR spectra for product 5 ($CDCl_3$)

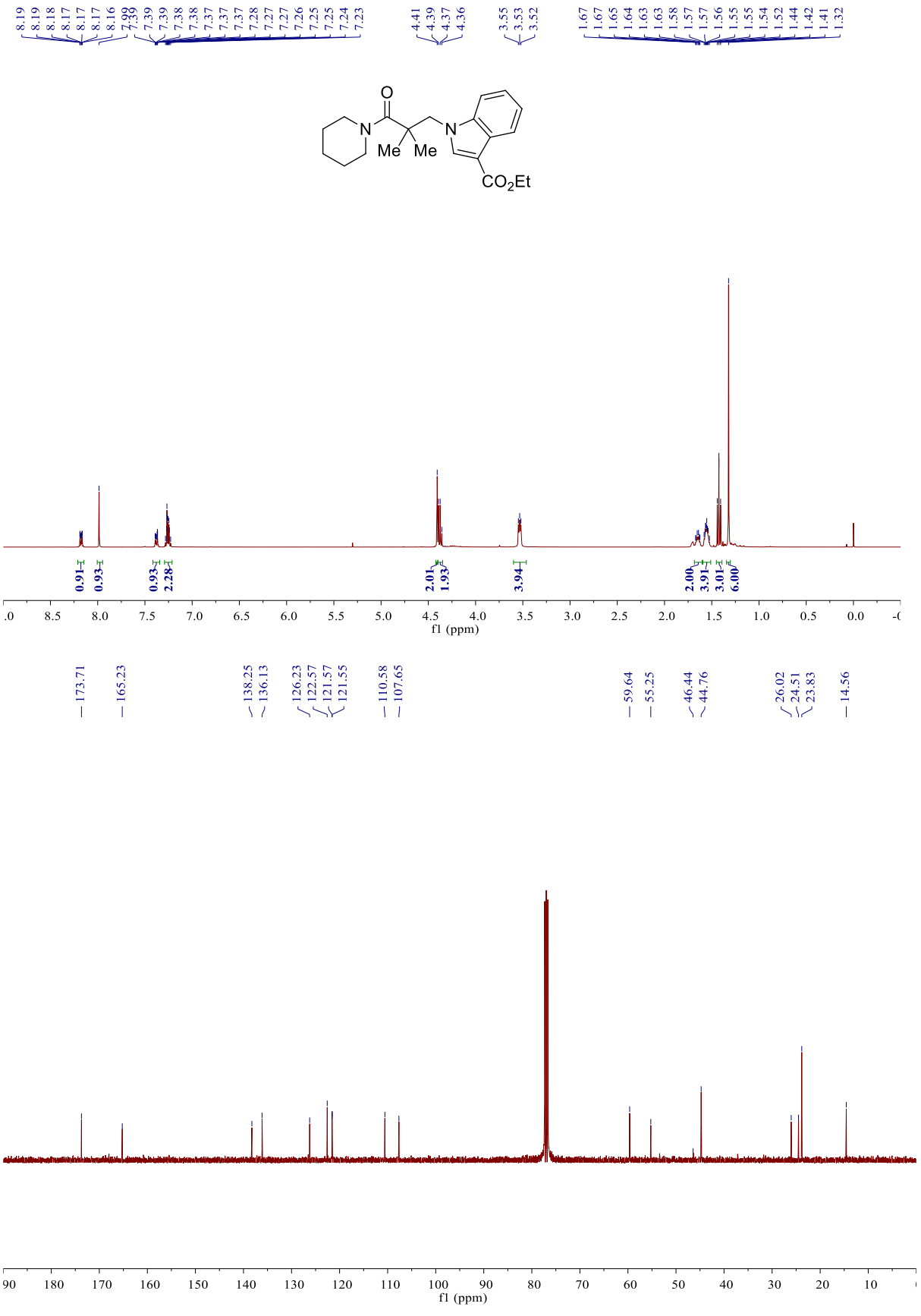


^{1}H and ^{13}C NMR spectra for product 6 ($CDCl_3$)





^{1}H and ^{13}C NMR spectra for product 7 ($CDCl_3$)



^{1}H and ^{13}C NMR spectra for product 9 ($CDCl_3$)