Electronic Supplementary Information

A Simple and Robust Preparation of *N*-Acetylindoxyls: Precursors for Indigogenic Substrates

Michael N. Gandy,[†] Lindsay T. Byrne,[‡] and Keith A. Stubbs*,[†]

[†]*School of Chemistry and Biochemistry, The University of Western Australia, 35 Stirling Highway, Crawley, Western Australia, Australia, 6009*

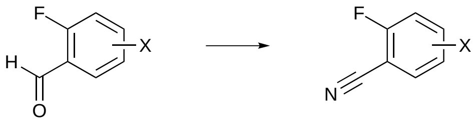
[‡]*Centre for Microscopy, Characterisation and Analysis, The University of Western Australia, 35 Stirling Highway, Crawley, Western Australia, Australia, 6009*

Email: keith.stubbs@uwa.edu.au

Table of contents

General methods

Thin layer chromatography (TLC) was conducted on Merck Kieselgel 60 F_{254} silica plates and visualised under shortwave UV light (254 nm). Infrared spectra were recorded for solid samples using a PerkinElmer Spectrum One Fourier transform infrared spectrometer fitted with an ATR attachment. ^{1}H- and ^{13}C-nuclear magnetic resonance spectra were obtained using a Bruker AV-500 spectrometer (500 MHz for ^{1}H or 125 MHz for ^{13}C) or Bruker Avance 600 spectrometer (600 MHz for ^{1}H or 150 MHz for ^{13}C). Each sample was dissolved in the specified deuterated solvent and each spectrum was calibrated using the residual solvent peak as follows: $CDCl_3$ (δ 7.26 for ^{1}H and δ 77.0 for ^{13}C); DMSO-d_6 (δ 2.50 for ^{1}H and δ 39.5 for ^{13}C). High resolution mass spectra were acquired using a Waters liquid chromatograph premier mass spectrometer. Samples were ionised using the atmospheric-pressure chemical ionisation technique (APCI) and all spectra were acquired in positive ionisation mode. For novel compounds, microanalyses were performed by Robertson Microlit, Ledgewood NJ.



General procedure for the preparation of benzonitriles (11, 16 and 22)

Following a literature procedure previously used to synthesise other nitriles,[1] to a solution of the appropriate aldehyde **12**, **15** or **21** (30.0 mmol) in formic acid (60 mL) was added hydroxylamine hydrochloride (40.0 mmol). The solution was heated at reflux for 6 h under an atmosphere of air. The mixture was then allowed to cool then diluted with ice/water (200 mL). The precipitate was then collected and the filter cake washed with water (200 mL), to give the corresponding benzonitrile **11**, **16** or **22** with yields in the range of 84–89%.

2-Chloro-6-fluorobenzonitrile (11)

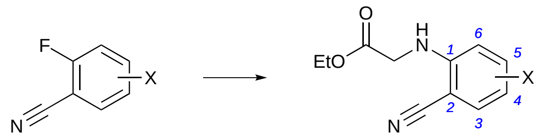
White solid (4.10 g, 89%). R_f (1:4 EtOAc/hexanes): 0.63. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2241 (m, C≡N). ^1H NMR (600 MHz, $CDCl_3$): δ 7.49 (ddd [app dt], J = 8.2, 8.2, 6.1 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.16 (dd [app t] J = 8.2, 8.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.8 (d, J = 261 Hz), 137.9 (d, J = 2.0 Hz), 134.8 (d, J = 9.4 Hz), 125.8 (d, J = 3.6 Hz), 114.6 (d, J = 19.8 Hz), 111.1, 103.4 (d, J = 17.8 Hz). HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_7H_3ClFNNa$ 177.9836; found, 177.9824.

3-Bromo-6-fluorobenzonitrile (16)

White solid (5.10 g, 85%). R_f (1:4 EtOAc/hexanes): 0.68. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2236 (m, C≡N). ^1H NMR (600 MHz, $CDCl_3$): δ 7.76–7.74 (m [app dd], 1H), 7.73–7.70 (m [app ddd], 1H), 7.13 (dd [app t], J = 9.0, 9.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.2 (d, J = 260 Hz), 138.1 (d, J = 8.1 Hz), 135.7, 118.2 (d, J = 20.8 Hz), 117.0 (d, J = 3.9 Hz), 112.4, 103.4 (d, J = 16.8 Hz). HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_7H_3BrFNNa$ 221.9331; found, 221.9321.

4-Chloro-2-fluorobenzonitrile (22)

White solid (3.90 g, 84%). R_f (1:4 EtOAc/hexanes): 0.55. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2242 (m, C≡N). ^1H NMR (600 MHz, $CDCl_3$): δ 7.60–7.56 (m, 1H), 7.29–7.25 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.0 (d, J = 263 Hz), 141.0 (d, J = 9.8 Hz), 134.0, 125.6 (d, J = 3.8 Hz), 117.6 (d, J = 22.3 Hz), 113.1, 100.2 (d, J = 15.5 Hz). HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_7H_3ClFNNa$ 177.9836; found, 177.9829.



General procedure for the preparation of ethyl glycinates (10, 17 and 20)

To a stirring solution of the appropriate benzonitrile **11**, **16** or **22** (20.0 mmol) in DMSO (50 mL) was added glycine ethyl ester hydrochloride (5.58 g, 40.0 mmol) and NEt_3 (10.2 mL, 100 mmol). The flask was stoppered and the mixture was heated at 110 °C (3 h). The reaction mixture was allowed to cool then diluted with water (500 mL) and cooled in an ice bath. The product was collected by filtration to give the corresponding ethyl glycinate **10**, **17** or **20** with yields in the range of 68–76%.

Ethyl [(3-chloro-2-cyanophenyl)amino]acetate (10)

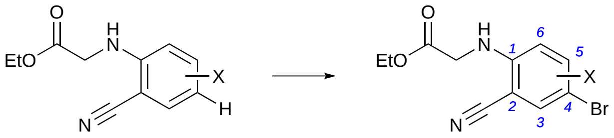
White solid (3.20 g, 68%). R_f (1:4 EtOAc/hexanes): 0.50. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2241 (m, C≡N), 1743 (s, C=O). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.39 (dd [app t], *J* = 8.0, 8.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.69–6.62 (m, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 4.07 (d, *J* = 6.0 Hz, 2H), 1.20 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 170.0, 152.2, 135.6, 134.9, 116.8, 115.1, 110.3, 95.1, 60.7, 44.2, 14.1. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{12}ClN_2O_2$ 239.0587; found, 239.0587.

Ethyl [(4-bromo-2-cyanophenyl)amino]acetate (17)

White solid (4.30 g, 76%). R_f (1:4 EtOAc/hexanes): 0.38. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2223 (m, C≡N), 1745 (s, C=O). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.72 (d, *J* = 2.4 Hz, 1H), 7.53 (dd, *J* = 9.0 2.4 Hz, 1H), 6.63 (d, *J* = 9.0 Hz, 1H), 6.56 (t, *J* = 6.1 Hz, 1H), 4.12 (q, *J* = 6.1 Hz, 2H), 4.04 (d, *J* = 6.2 Hz, 2H), 1.19 (t, *J* = 6.2 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 170.1, 149.6, 137.0, 134.6, 116.5, 113.8, 106.3, 96.4, 60.7, 44.1, 14.1. HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{11}BrN_2O_2Na$ 304.9902; found, 304.9913.

Ethyl [(5-chloro-2-cyanophenyl)amino]acetate (20)

White solid (3.40 g, 72%). R_f (1:4 EtOAc/hexanes): 0.61. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2217 (m, C≡N), 1733 (s, C=O). ^{1}H NMR (600 MHz, DMSO-d_6): δ 7.53 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 1.8 Hz, 1H), 6.73 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.63 (t, *J* = 6.6 Hz, 1H), 4.12 (q, *J* = 6.6 Hz, 2H), 4.08 (d, *J* = 6.6 Hz, 2H), 1.20 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 170.1, 151.2, 139.5, 134.7, 117.1, 116.6, 111.3, 93.6, 60.6, 44.0, 14.1. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{12}ClN_2O_2$ 239.0587; found, 239.0583.



General procedure for the preparation of bromine-substituted ethyl glycinates (13 and 23)

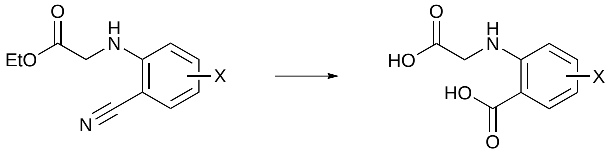
Using a method used to brominate other anilines,[2] to a stirring suspension of the appropriate ethyl glycinate **10** or **20** (7.60 mmol) in AcOH (16 mL) was added ammonium bromide (780 mg, 8.00 mmol) then 30% H_2O_2 (820 µL, 8.00 mmol) dropwise over 5 min and the mixture was then stirred at room temperature (24 h). The mixture was diluted with water and cooled in an ice bath and the resulting solid collected by filtration to give the corresponding ethyl glycinate **13** or **23** with yields in the range of 76–81%.

Ethyl [(4-bromo-3-chloro-2-cyanophenyl)amino]acetate (13)

White solid (1.80 g, 76%). R_f (1:4 EtOAc/hexanes): 0.36. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2217 (m, C≡N), 1730 (s, C=O). ^1H NMR (600 MHz, DMSO-d_6): δ 7.68 (d, J = 9.2 Hz, 1H), 6.82 (t, J = 5.8 Hz, 1H), 6.65 (d, J = 9.2 Hz, 1H), 4.13 (q, J = 7.0 Hz, 2H), 4.09 (d, J = 6.0 Hz, 2H), 1.20 (t, J = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 169.8, 151.5, 138.0, 135.1, 114.8, 112.4, 106.8, 96.5, 60.7, 44.2, 14.1. HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_{11}H_{10}BrClN_2O_2Na$ 338.9512; found, 338.9513. Anal. calcd for $C_{11}H_{10}BrClN_2O_2$: C, 41.60; H, 3.17; N, 8.82; found: C, 41.68; H, 3.19; N, 8.89.

Ethyl [(4-bromo-5-chloro-2-cyanophenyl)amino]acetate (23)

White solid (2.00 g, 81%). R_f (1:4 EtOAc/hexanes): 0.36. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 2220 (m, C≡N), 1734 (s, C=O). ^1H NMR (600 MHz, DMSO-d_6): δ 7.95 (s, 1H), 7.01 (s, 1H), 6.76 (t, J = 6.0 Hz, 1H), 4.13 (q, J = 7.2 Hz, 2H), 4.09 (d, J = 6.0 Hz, 2H), 1.20 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 169.9, 150.3, 139.4, 137.0, 115.9, 113.2, 106.2, 95.4, 60.7, 44.1, 14.1. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{11}BrClN_2O_2$ 316.9692; found, 316.9686. Anal. calcd for $C_{11}H_{10}BrClN_2O_2$: C, 41.60; H, 3.17; N, 8.82; found: C, 41.63; H, 3.27; N, 8.87.



General procedure for the preparation of dicarboxylic acids (9, 18, 24 and 25)

To a 30% w/w KOH solution (25 mL) was added the appropriate ethyl glycinate **13**, **17**, **20** or **23** (5.0 mmol) and the mixture was stirred at 120 °C (2 h). The mixture was then diluted with H_2O (5 mL) and the solution was heated at 120 °C (12 h). The reaction was diluted with 2 M HCl (75 mL) and cooled in an ice bath. The resulting precipitate was collected by filtration to give the corresponding dicarboxylic acid **9**, **18**, **24** or **25** with yields in the range of 89–95%.

3-Bromo-6-[(carboxymethyl)amino]-2-chlorobenzoic acid (9)

Pale green solid (1.40 g, 89%). R_f (8:6:1 $CHCl_3$/EtOAc/AcOH): 0.14. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1680 (s, C=O), 1646 (s, C=O). ^1H NMR (600 MHz, DMSO-d_6): δ 13.2 (br s, 1H), 7.53 (d, J = 9.0 Hz, 1H), 6.49 (d, J = 9.0 Hz, 1H), 6.01 (br s, 1H), 3.89 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 171.7, 166.9, 145.7, 134.5, 130.3, 120.1, 111.9, 107.6, 44.4. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_9H_8BrClNO_4$ 307.9325; found, 307.9332.

5-Bromo-2-[(carboxymethyl)amino]benzoic acid (18)

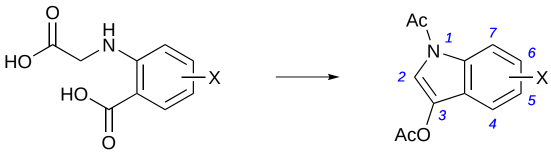
Pale green solid (1.30 g, 92%). R_f (8:6:1 $CHCl_3$/EtOAc/AcOH): 0.39. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1717 (s, C=O). ^1H NMR (600 MHz, DMSO-d_6): δ 8.12 (br s, 1H), 7.86 (d, J = 2.4 Hz, 1H), 7.48 (dd, J = 9.0, 2.4 Hz, 1H), 6.59 (d, J = 9.0 Hz, 1H), 3.99 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 171.5, 168.5, 149.1, 136.7, 133.4, 114.2, 112.2, 105.2, 44.2. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_9H_9BrNO_4$ 273.9715; found, 273.9717.

2-[(Carboxymethyl)amino]-4-chlorobenzoic acid (24)

Pale green solid (1.00 g, 92%). R_f (8:6:1 $CHCl_3$/EtOAc/AcOH): 0.42. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1706 (s, C=O). ^1H NMR (600 MHz, DMSO-d_6): δ 12.8 (br s, 1H), 8.25 (br s, 1H), 7.79 (d, J = 8.4 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 6.62 (dd, J = 8.4, 2.4 Hz, 1H), 4.02 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 171.5, 169.1, 150.9, 139.2, 133.4, 114.7, 111.1, 109.5, 44.2. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_9H_9ClNO_4$ 230.0220; found, 230.0219.

5-Bromo-2-[(carboxymethyl)amino]-4-chlorobenzoic acid (25)

Pale green solid (1.50 g, 95%). R_f (8:6:1 $CHCl_3$/EtOAc/AcOH): 0.36. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1716 (s, C=O), 1649 (s, C=O). ^1H NMR (600 MHz, DMSO-d_6): δ 8.20 (br s, 1H), 8.00 (s, 1H), 6.88 (s, 1H), 4.03 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 171.3, 168.0, 149.8, 138.8, 135.7, 113.4, 111.4, 104.7, 44.2. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_9H_8BrClNO_4$ 307.9325; found, 307.9304.



General procedure for the preparation of *N*-acetylindoxyl acetates (14, 19, 26 and 27)

Following a modified procedure,[3] to a stirring suspension of the appropriate dicarboxylic acid **9**, **18**, **24** or **25** (8.00 mmol) in Ac_2O (10 mL) was added sodium acetate (32 mmol) and the mixture was then stirred at reflux (1 h). The mixture was then cooled and poured into of ice/water (ca 35 g) and cooled in an ice bath. The resulting precipitate was collected by filtration to give the corresponding indoxyl acetate **14**, **19**, **26** or **27** with yields in the range of 86–91%.

1-Acetyl-5-bromo-4-chloro-1*H*-indol-3-yl acetate (14)

White solid (2.30 g, 86%). R_f (1:4 EtOAc/hexanes): 0.24. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1770 (s, C=O), 1712 (s, C=O). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.27 (d, J = 9.0 Hz, 1H), 8.04 (s, 1H), 7.69 (d, J = 9.0 Hz, 1H), 2.62 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 169.6, 169.4, 133.0, 131.4, 130.0, 123.0, 122.5, 119.8, 117.3, 116.5, 23.7, 20.5. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{10}BrClNO_3$ 329.9533; found, 329.9544.

1-Acetyl-5-bromo-1*H*-indol-3-yl acetate (19)

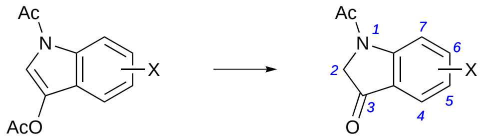
White solid (2.10 g, 91%). R_f (1:4 EtOAc/hexanes): 0.33. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1753 (s, C=O), 1713 (s, C=O). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.29 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H), 7.77 (d, J = 1.8 Hz, 1H), 7.53 (dd, J = 8.0, 1.8 Hz, 1H), 2.61 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 169.5, 168.4, 132.5, 131.4, 128.2, 125.6, 120.5, 117.9, 117.5, 116.0, 23.6, 20.5. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{11}BrNO_3$ 295.9922; found, 295.9941.

1-Acetyl-6-chloro-1*H*-indol-3-yl acetate (26)

White solid (1.70 g, 87%). R_f (1:4 EtOAc/hexanes): 0.32. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1756 (s, C=O), 1703 (s, C=O). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.37 (d, J = 1.8 Hz, 1H), 7.93 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.36 (dd, J = 8.4, 1.8 Hz, 1H), 2.62 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 169.7, 168.2, 133.1, 132.7, 130.2, 123.8, 122.5, 119.4, 116.7, 115.8, 23.6, 20.5. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{11}ClNO_3$ 252.0427; found, 252.0448.

1-Acetyl-5-bromo-6-chloro-1*H*-indol-3-yl acetate (27)

White solid (2.30 g, 88%). R_f (1:4 EtOAc/hexanes): 0.26. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1757 (s, C=O), 1710 (s, C=O). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.53 (s, 1H), 8.01 (s, 1H), 8.00 (s, 1H), 2.62 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 169.7, 168.3, 132.1, 131.8, 129.7, 124.2, 122.7, 118.3, 117.3, 116.1, 23.6, 20.5. HRMS (APCI) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{10}BrClNO_3$ 329.9533; found, 329.9557.



General procedure for the preparation of *N*-acetylindoxyls (1–4)

To a solution of sulfuric acid (80% w/w, 5 mL) was added the appropriate indoxyl acetate **14**, **19**, **26** or **27** (200 mg) and the mixture was stirred at room temperature (45 min). The mixture was then poured into ice/water (ca 10 g) and cooled in an ice bath. The resulting solid was collected by filtration to give the corresponding *N*-acetylindoxyl **1**, **2**, **3** or **4** with yields in the range of 84–89%.

N-Acetyl-5-bromo-4-chloroindoxyl (IUPAC name: 1-Acetyl-5-bromo-4-chloroindolin-3-one) (1)

White solid (150 mg, 86%). R_f (2:3 EtOAc/hexanes): 0.26. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1715 (s, C=O), 1682 (s, C=O). ^1H NMR (600 MHz, $CDCl_3$): δ 8.39 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 4.35 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 190.6, 168.1, 154.0, 140.8, 131.7, 122.7, 118.9, 117.7, 56.4, 24.3. HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_7BrClNO_2Na$ 309.9246; found, 309.9251.

1-Acetyl-5-bromoindolin-3-one (2)

White solid (152 mg, 89%). R_f (2:3 EtOAc/hexanes): 0.25. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1714 (s, C=O), 1671 (s, C=O). ^1H NMR (600 MHz, $CDCl_3$): δ 8.45 (d, J = 9.0 Hz, 1H), 7.83 (br s, 1H), 7.72 (dd, J = 9.0, 2.4 Hz, 1H), 4.31 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.1, 168.0, 152.4, 139.8, 126.5, 126.3, 120.2, 117.3, 56.2, 24.1. HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_8BrNO_2Na$ 275.9636; found, 275.9629.

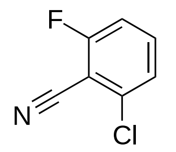
1-Acetyl-6-chloroindolin-3-one (3)

White solid (140 mg, 84%). R_f (2:3 EtOAc/hexanes): 0.26. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1720 (s, C=O), 1667 (s, C=O). ^1H NMR (600 MHz, $CDCl_3$): δ 8.60 (br s, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.18 (dd, J = 7.8, 1.8 Hz, 1H), 4.30 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.2, 168.2, 154.1, 143.9, 124.9, 124.5, 123.2, 118.8, 56.3, 24.2. HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_8ClNO_2Na$ 232.0141; found, 232.0149.

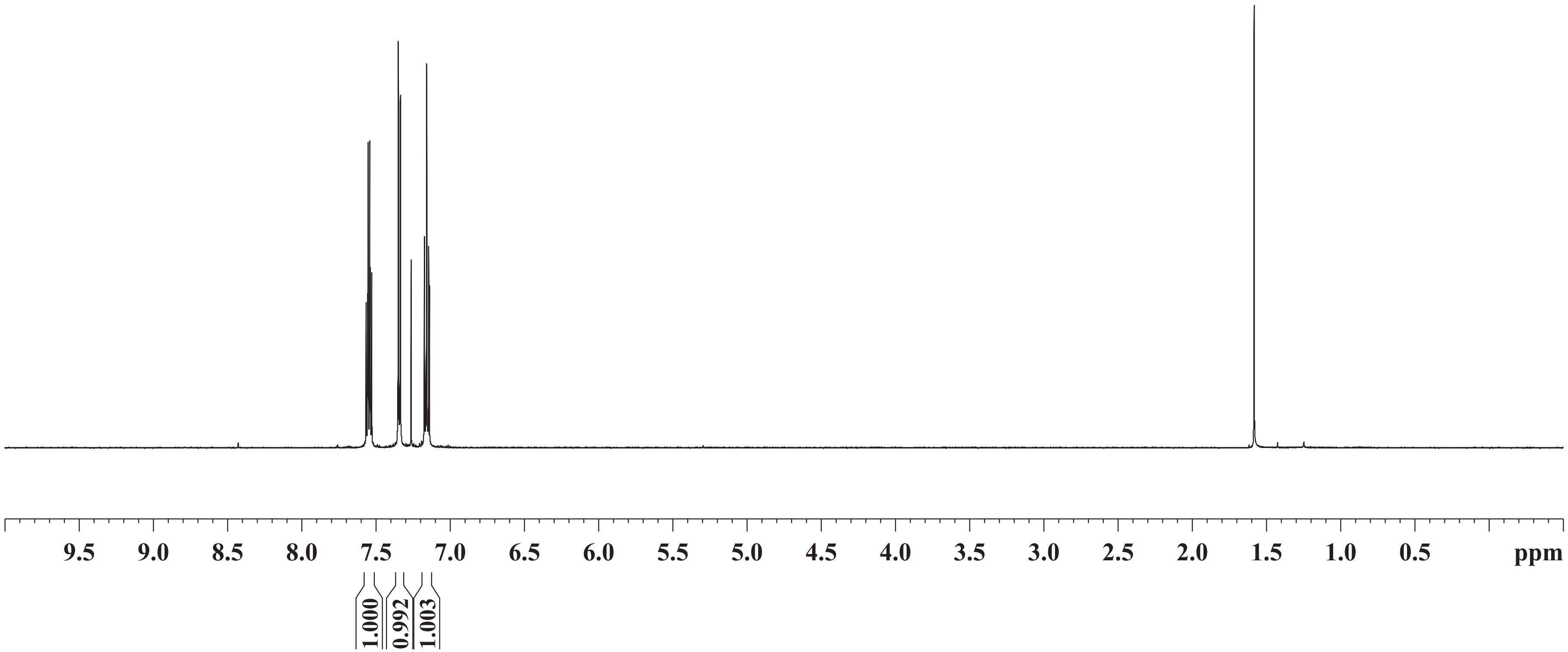
1-Acetyl-5-bromo-6-chloroindolin-3-one (4)

White solid (154 mg, 88%). R_f (2:3 EtOAc/hexanes): 0.26. IR (ATR) $\bar{\nu}_{max}$ (cm^{-1}): 1718 (s, C=O), 1668 (s, C=O). ^1H NMR (600 MHz, $CDCl_3$): δ 8.75 (s, 1H), 7.97 (s, 1H), 4.32 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 192.0, 168.1, 152.3, 143.5, 128.0, 124.6, 120.3, 118.0, 56.3, 24.1. HRMS (APCI) *m/z*: $[M+Na]^+$ calcd for $C_{10}H_7BrClNO_2Na$ 309.9246; found, 309.9243.

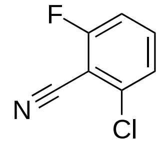
^{1}H NMR (600 MHz, $CDCl_3$)



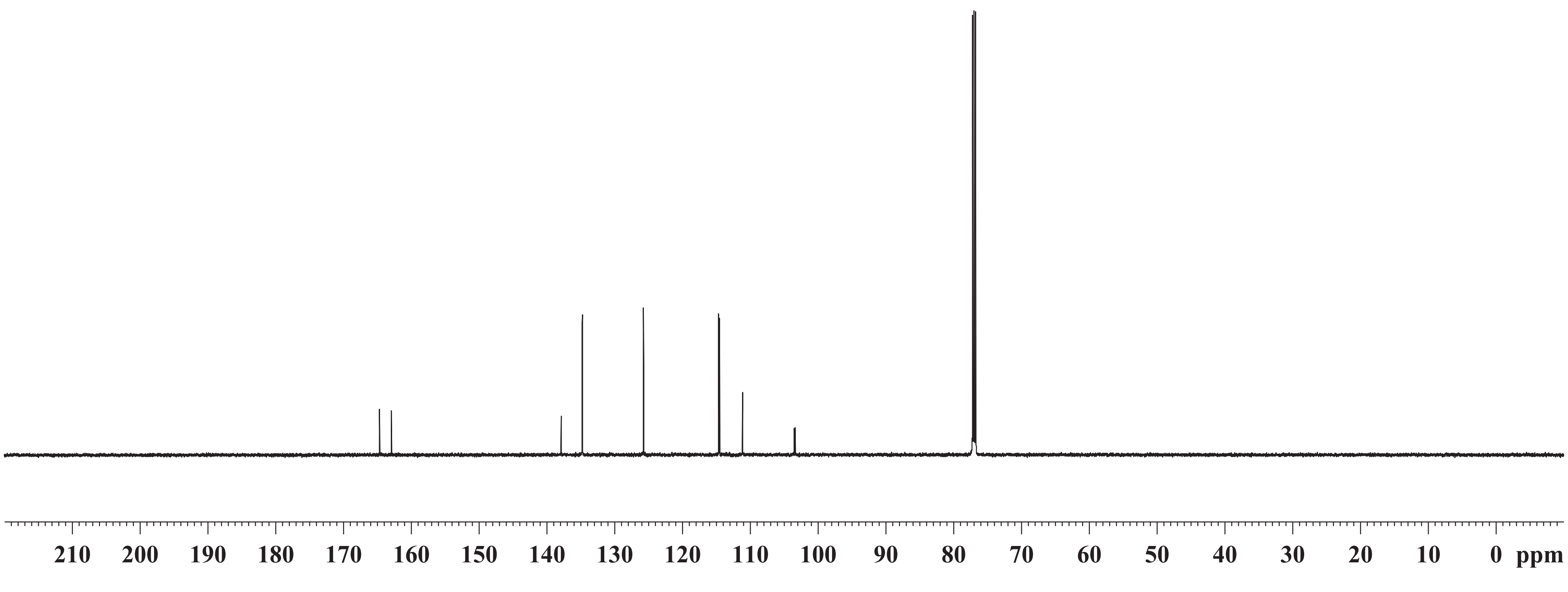
11



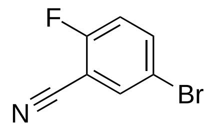
^{13}C NMR (150 MHz, $CDCl_3$)



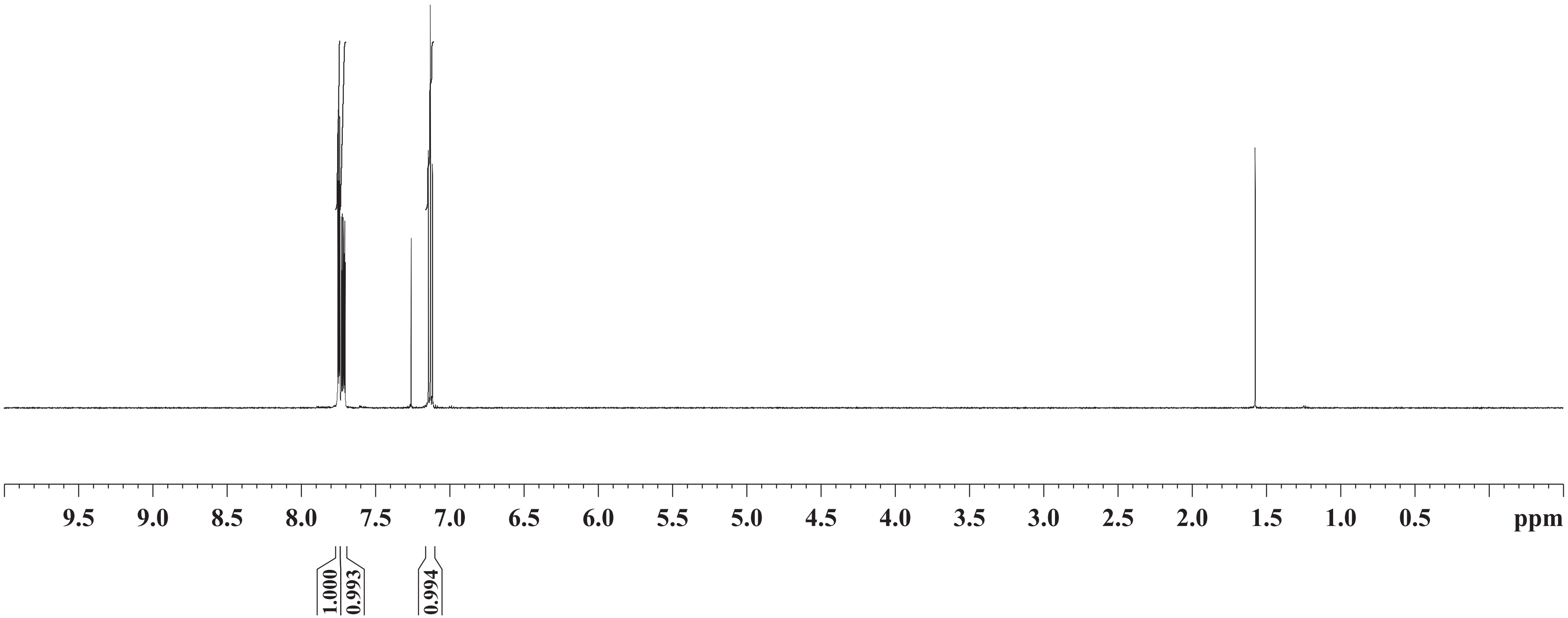
11



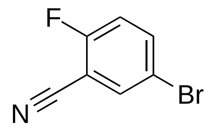
^{1}H NMR (600 MHz, $CDCl_3$)



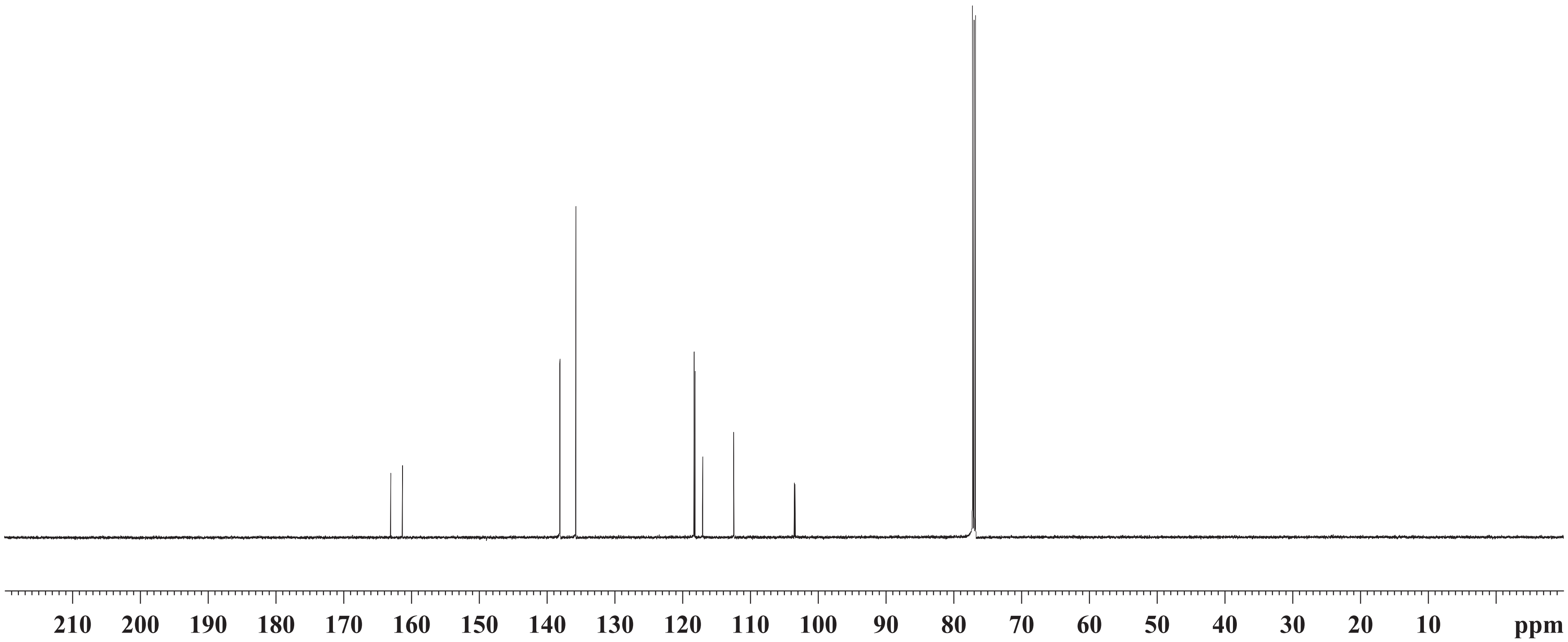
16



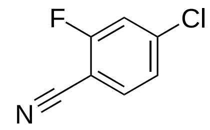
^{13}C NMR (150 MHz, $CDCl_3$)



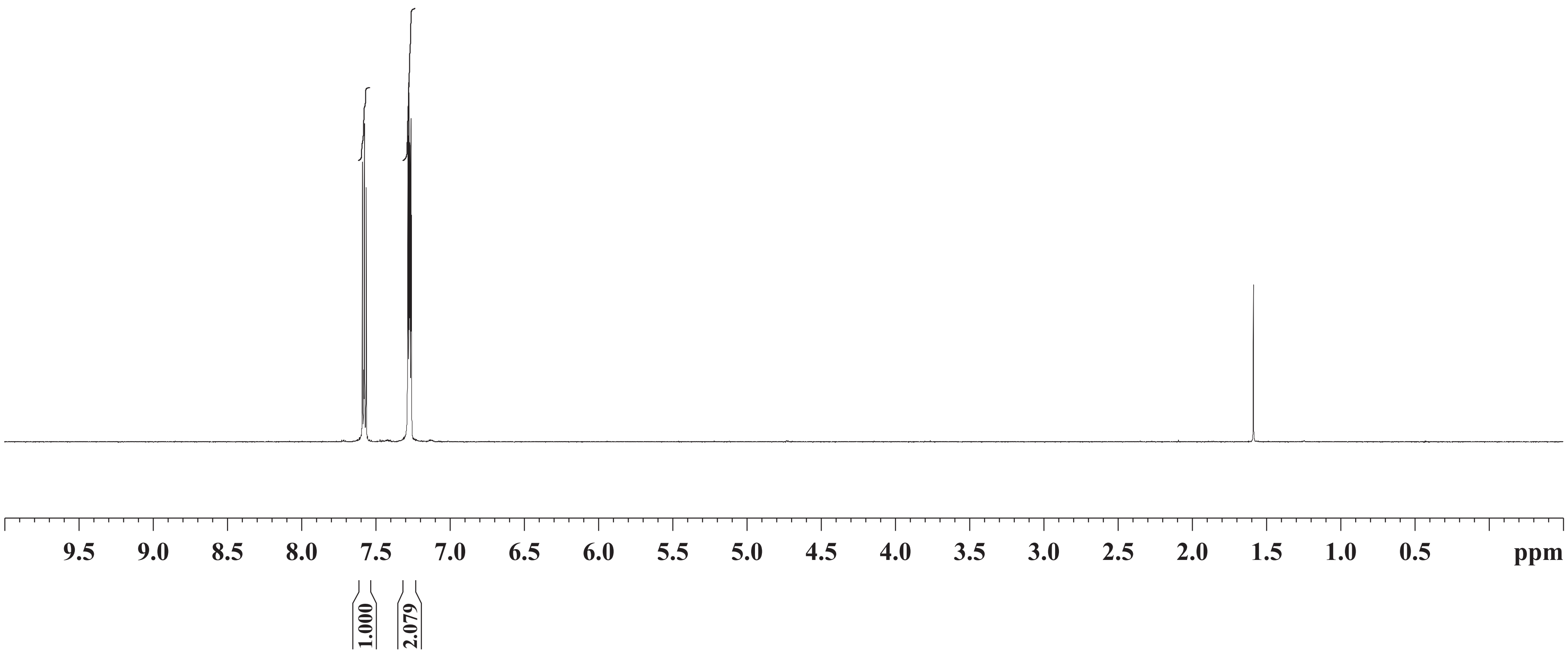
16



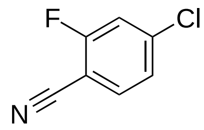
^{1}H NMR (600 MHz, $CDCl_3$)



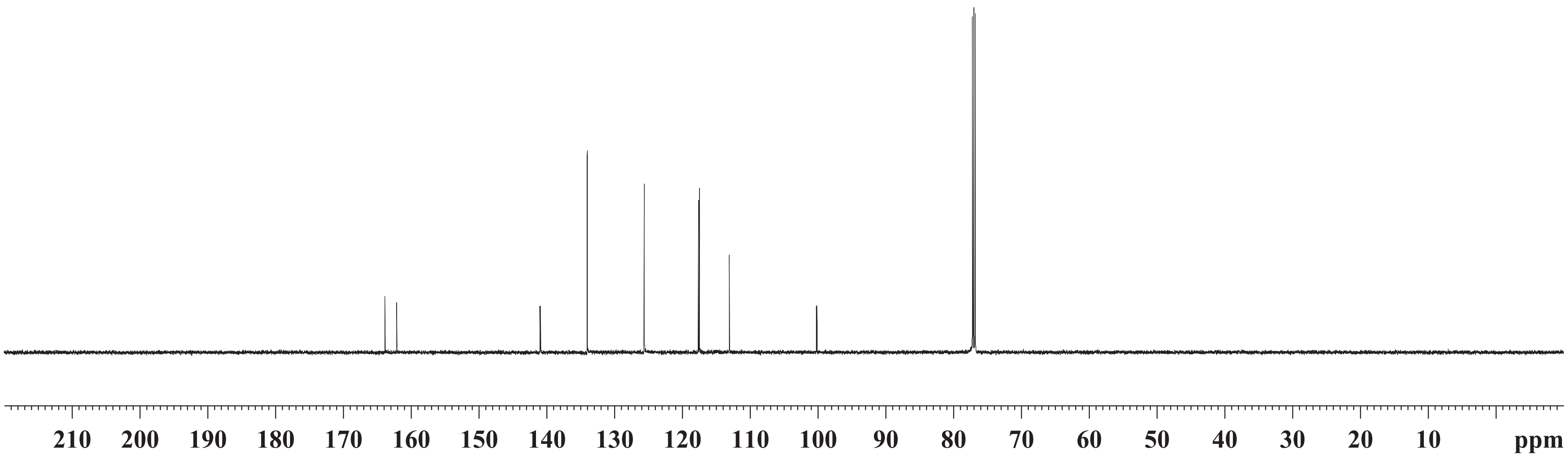
22



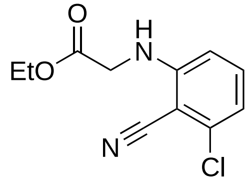
^{13}C NMR (150 MHz, $CDCl_3$)



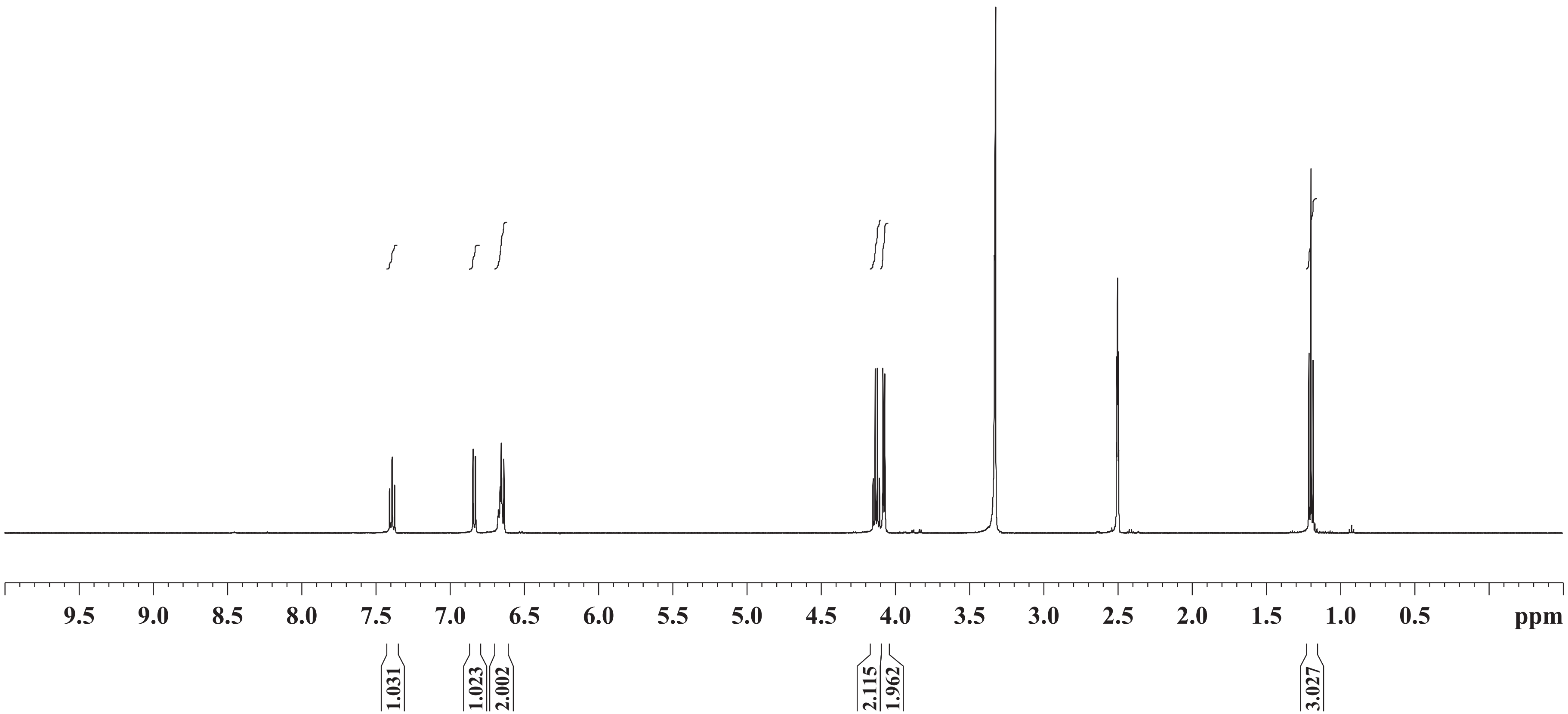
22



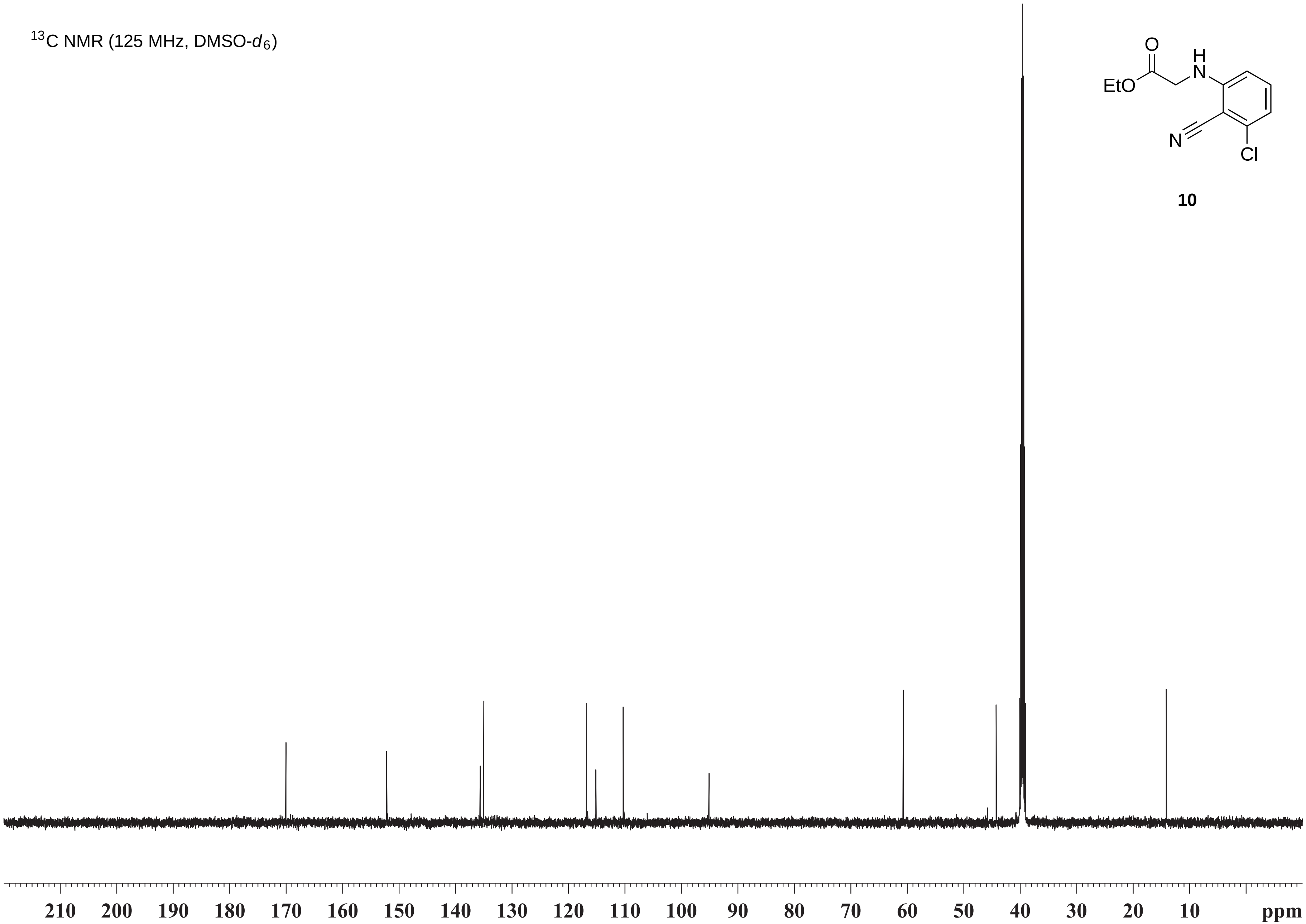
^{1}H NMR (500 MHz, DMSO-d_6)

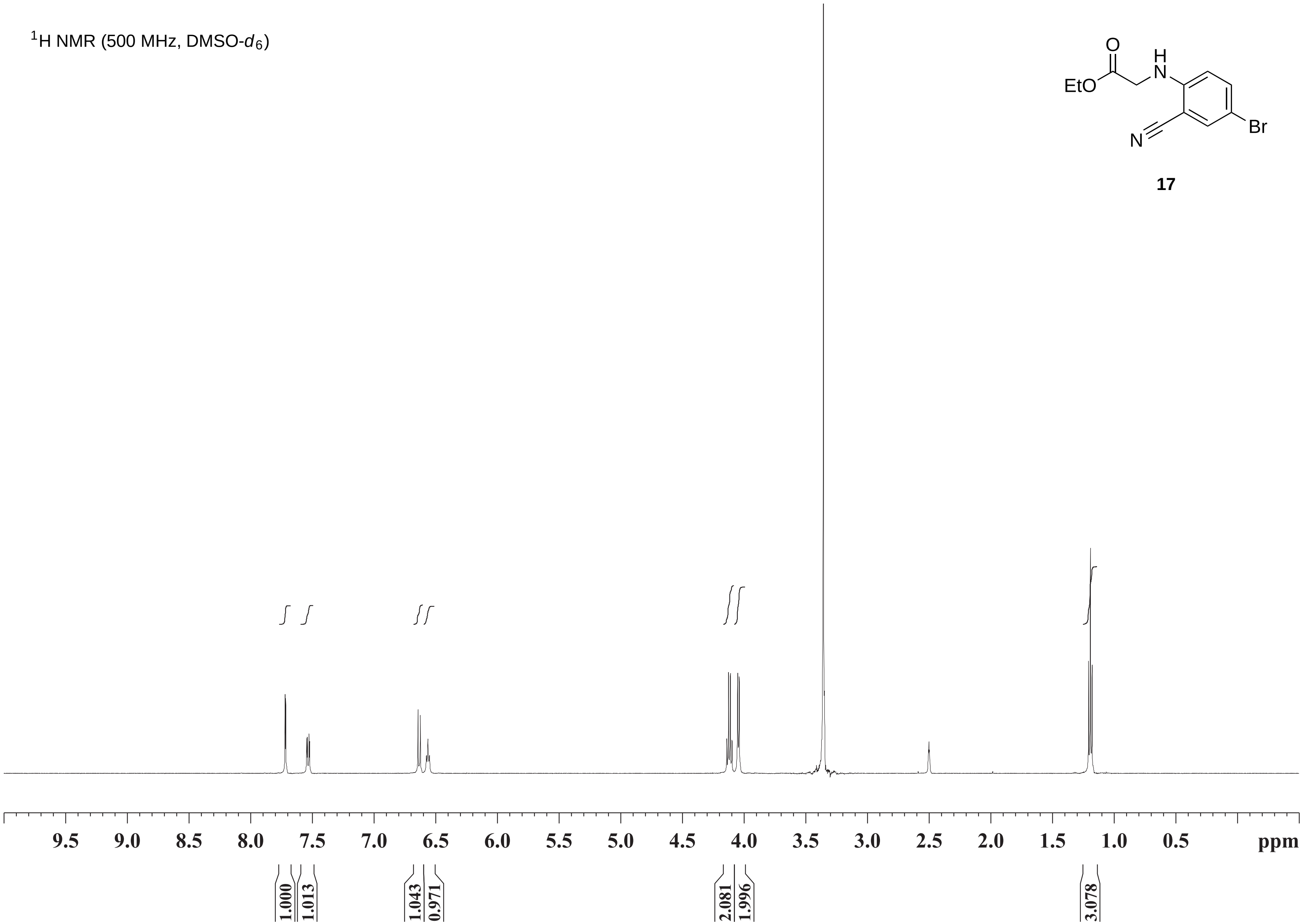


10



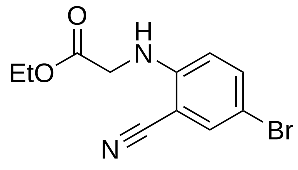
^{13}C NMR (125 MHz, DMSO-d_6)



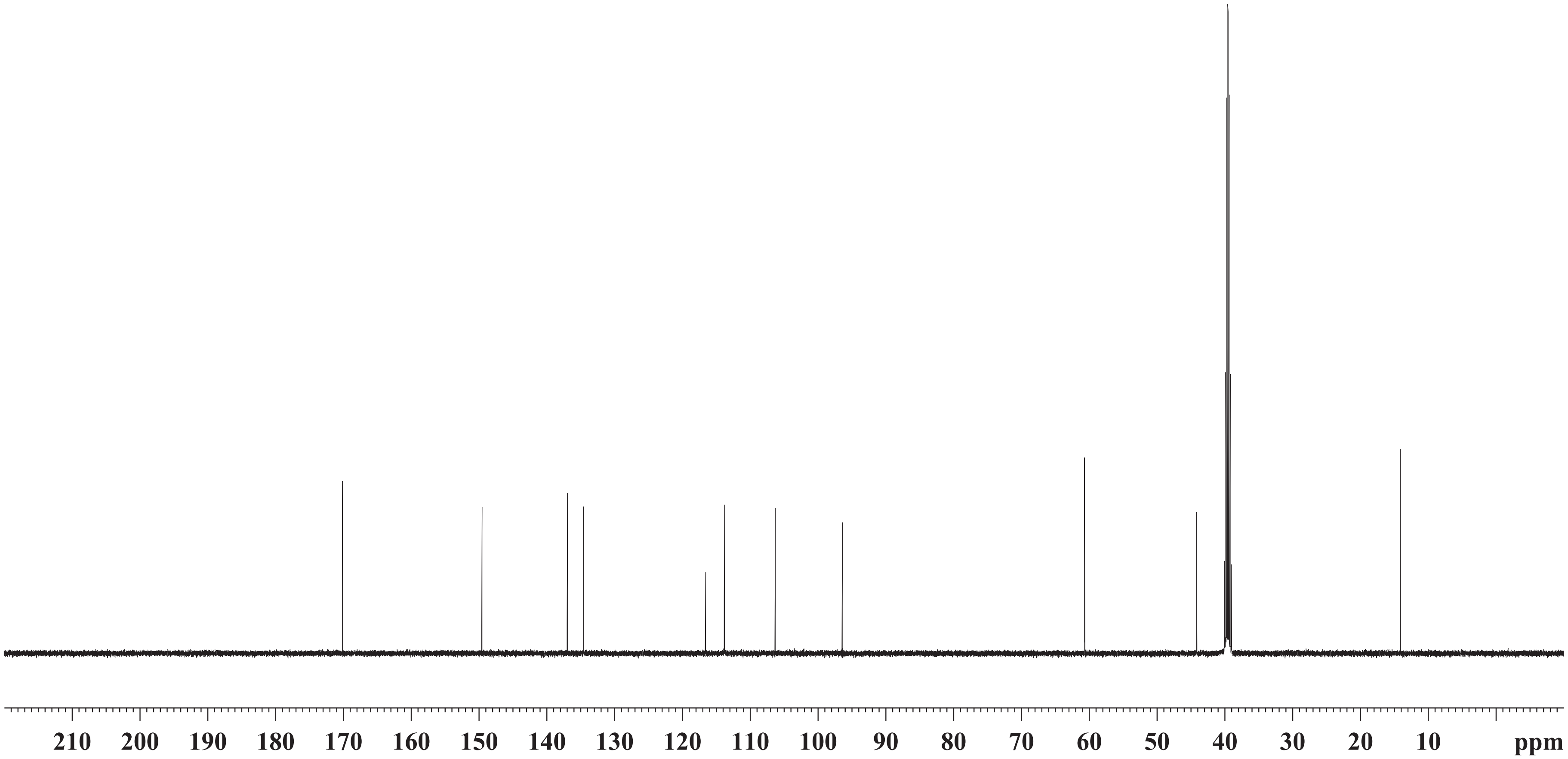


^{1}H NMR (500 MHz, DMSO-d_6)
EtO
O
H
N
N
Br
17
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.000
1.013
1.043
0.971
2.081
1.996
3.078

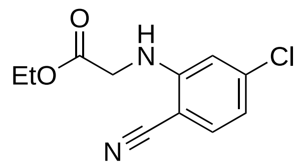
^{13}C NMR (125 MHz, DMSO-d_6)



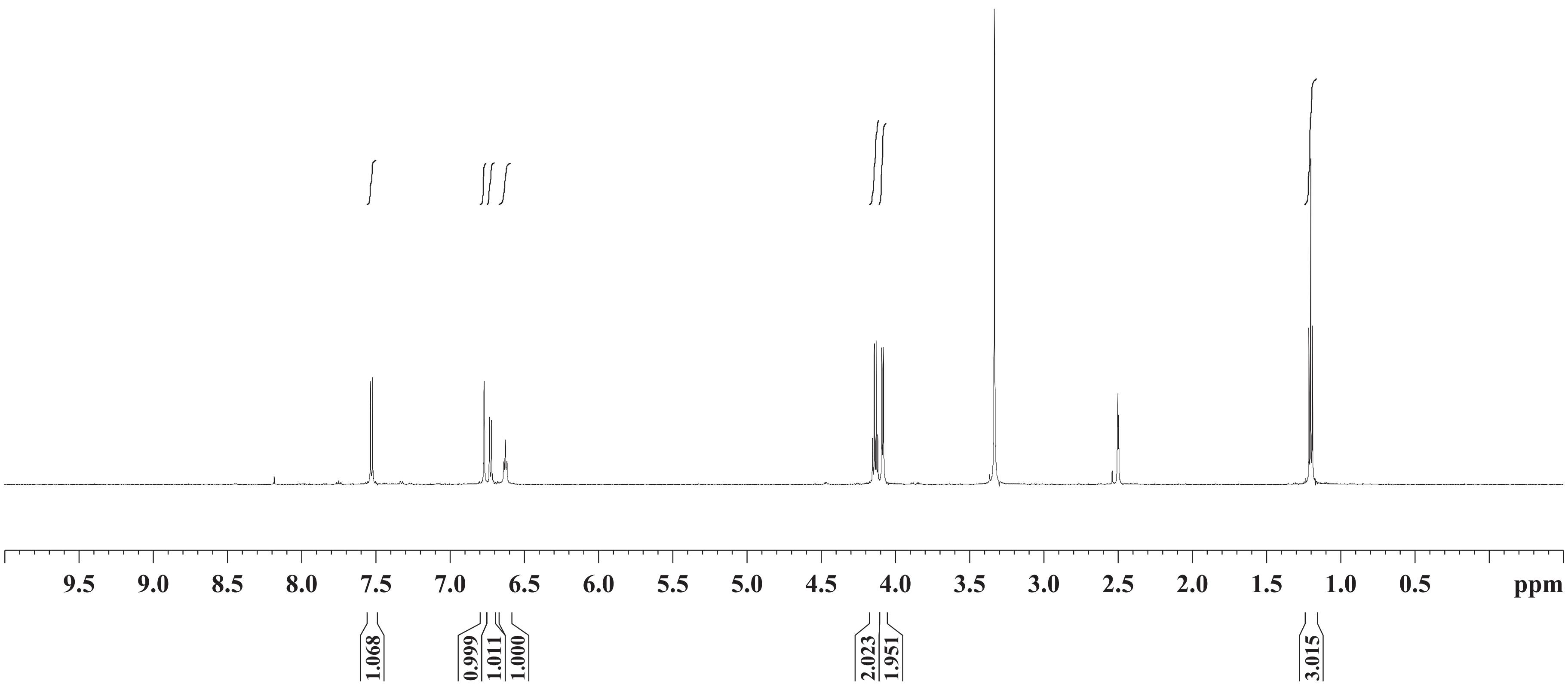
17



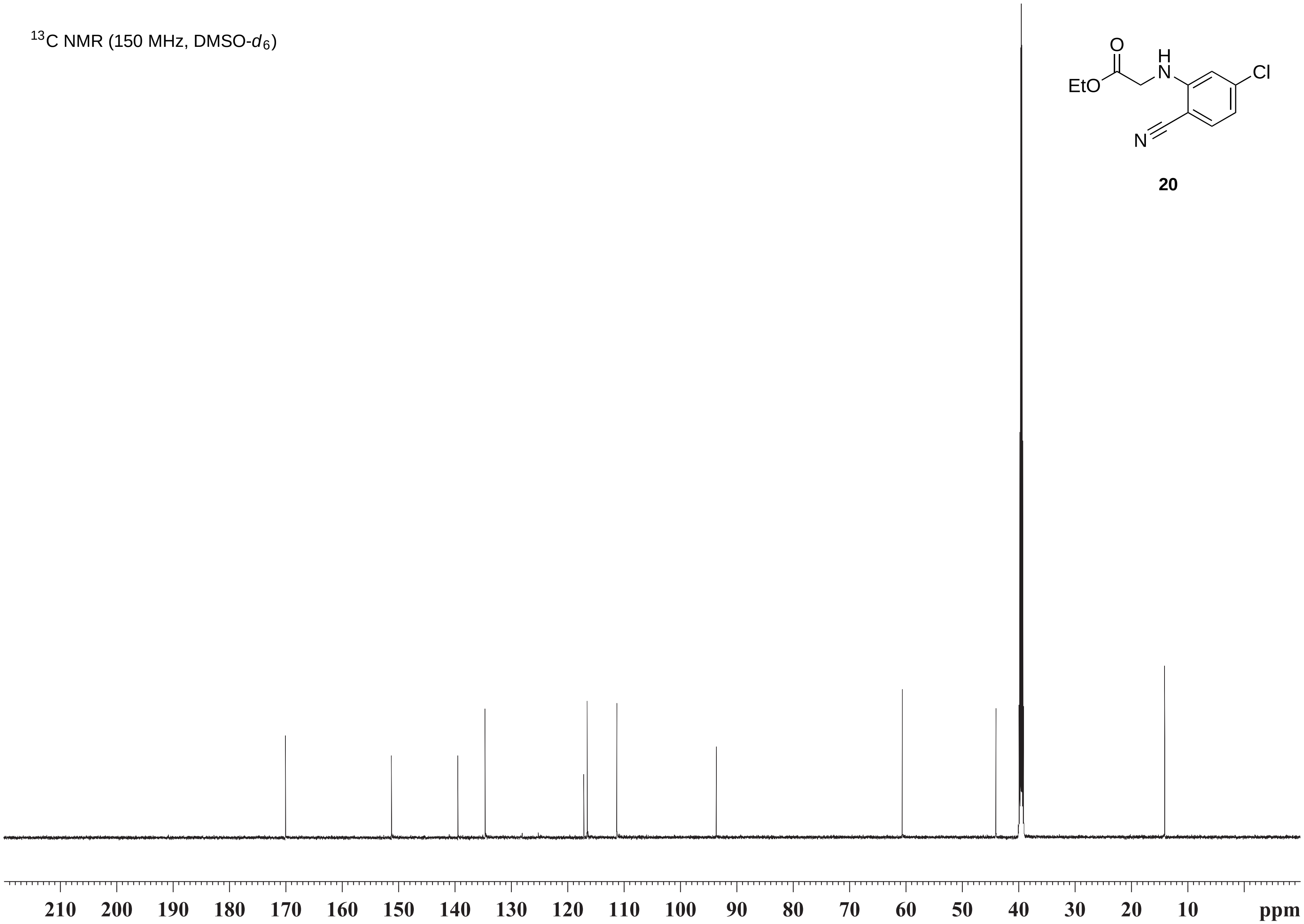
^{1}H NMR (600 MHz, DMSO-d_6)



20

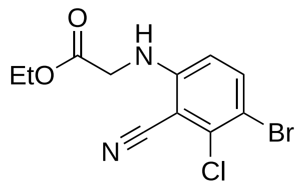


^{13}C NMR (150 MHz, DMSO-d_6)

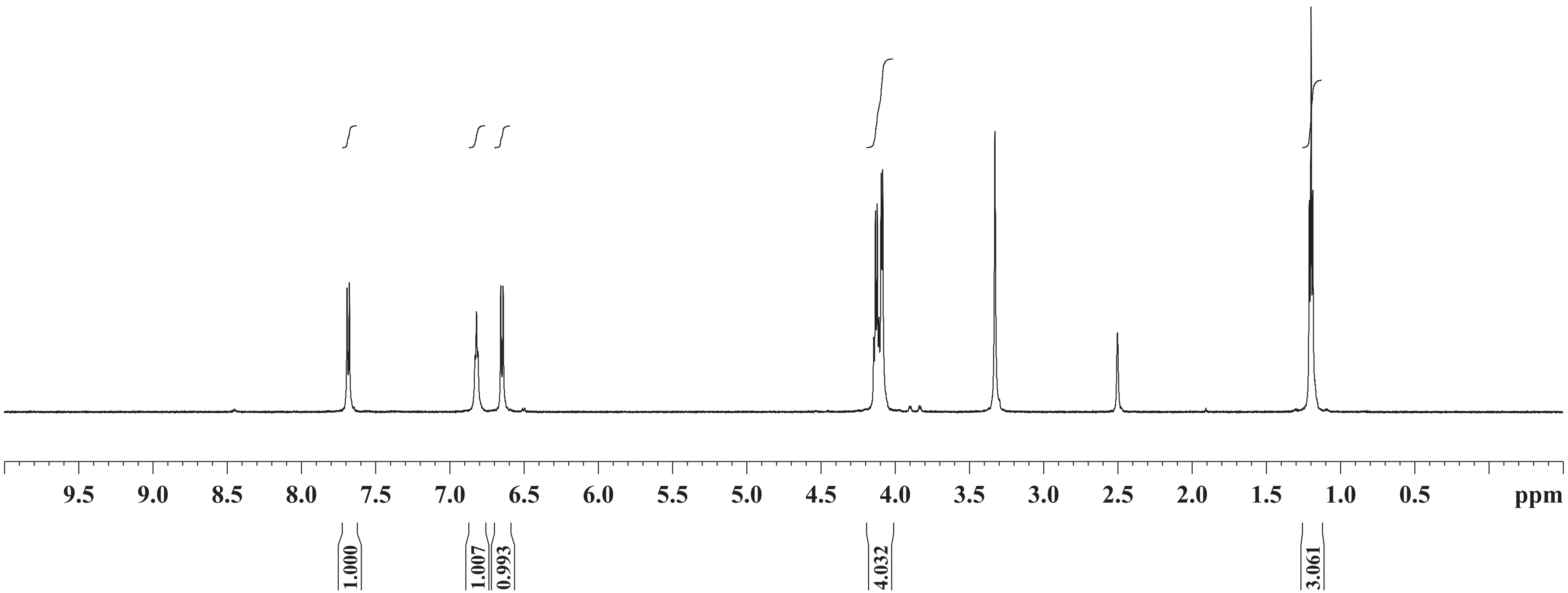


20

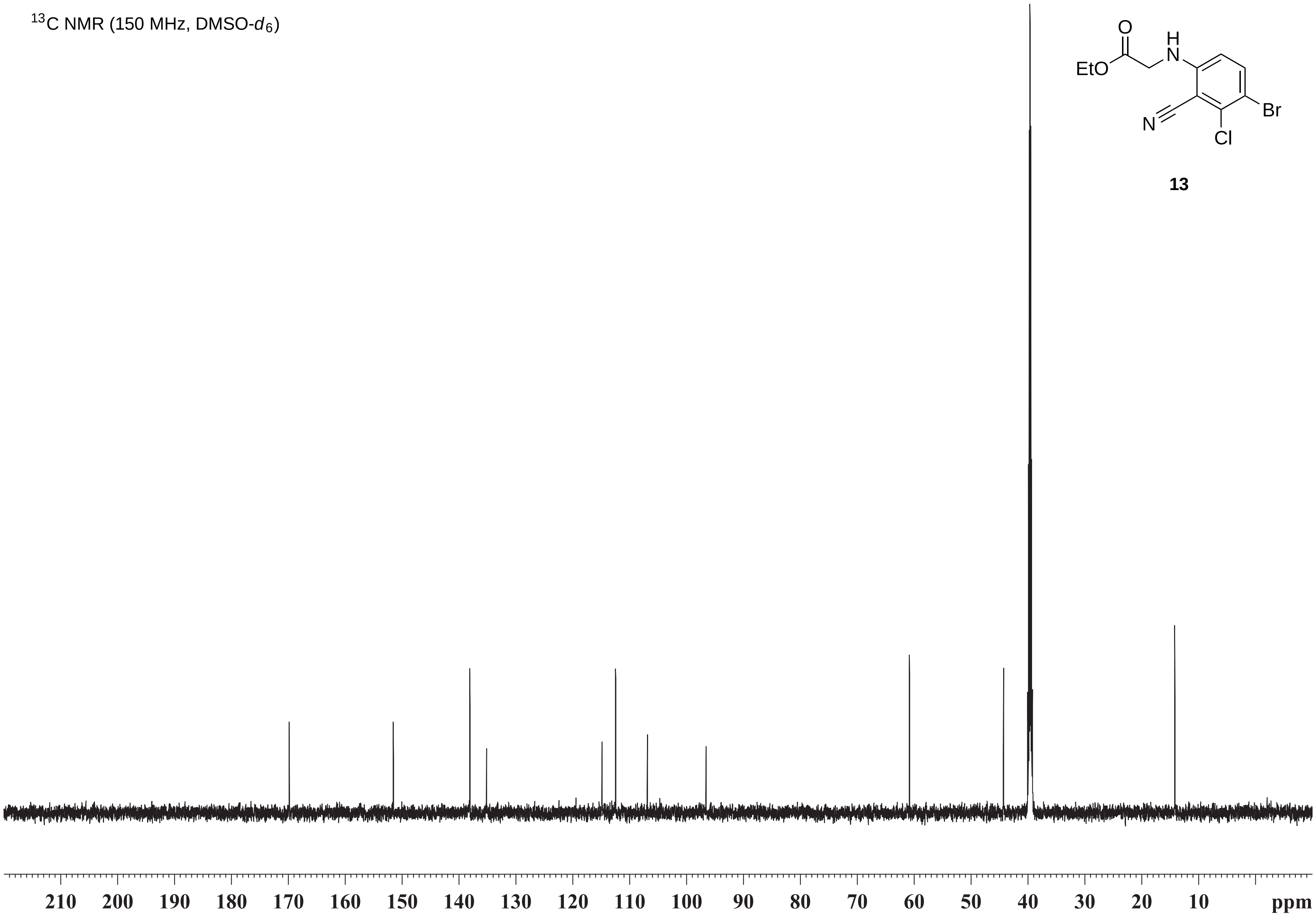
[1]H NMR (600 MHz, DMSO-d_6)



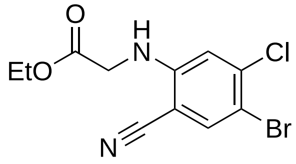
13



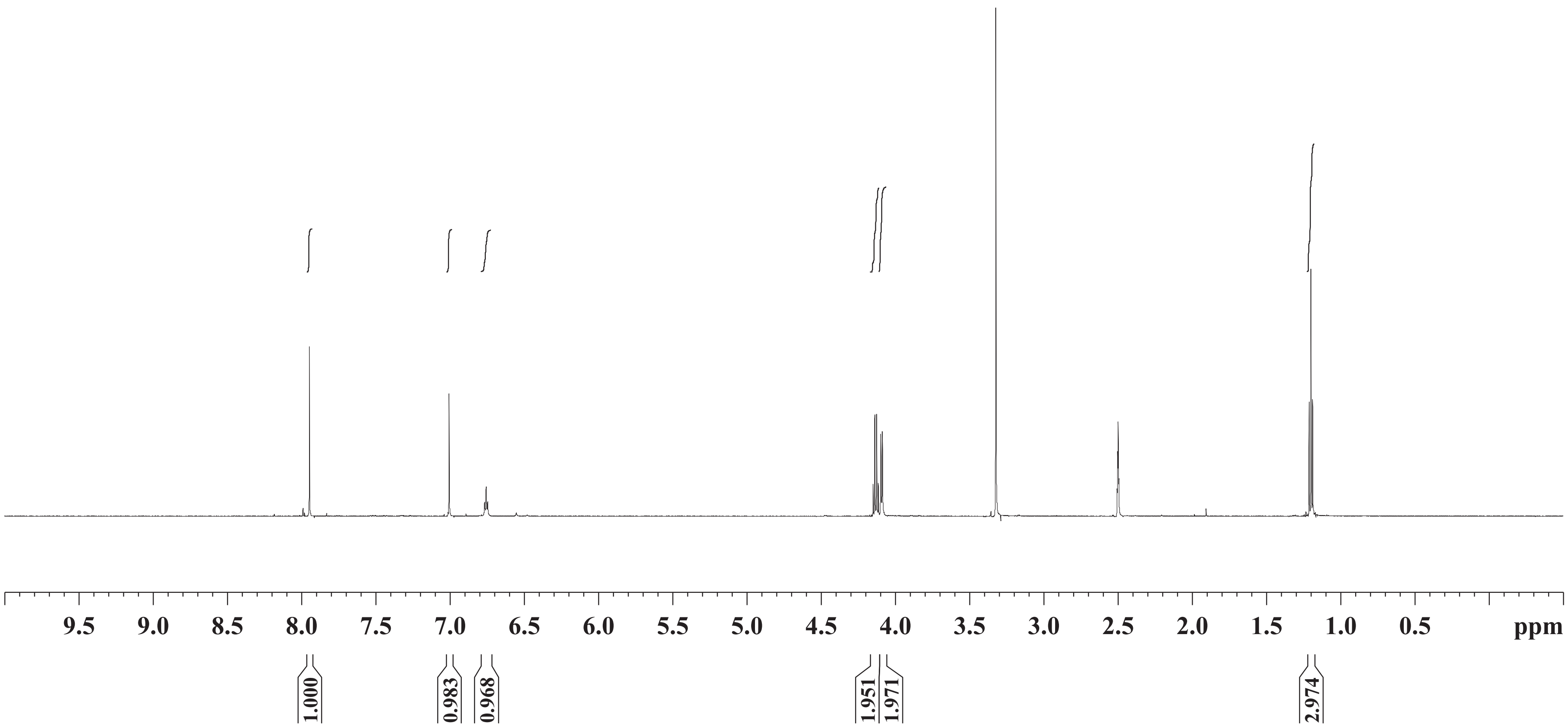
^{13}C NMR (150 MHz, DMSO-d_6)



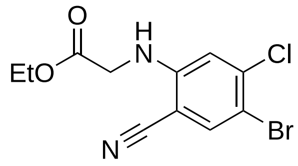
^1H NMR (600 MHz, DMSO-d_6)



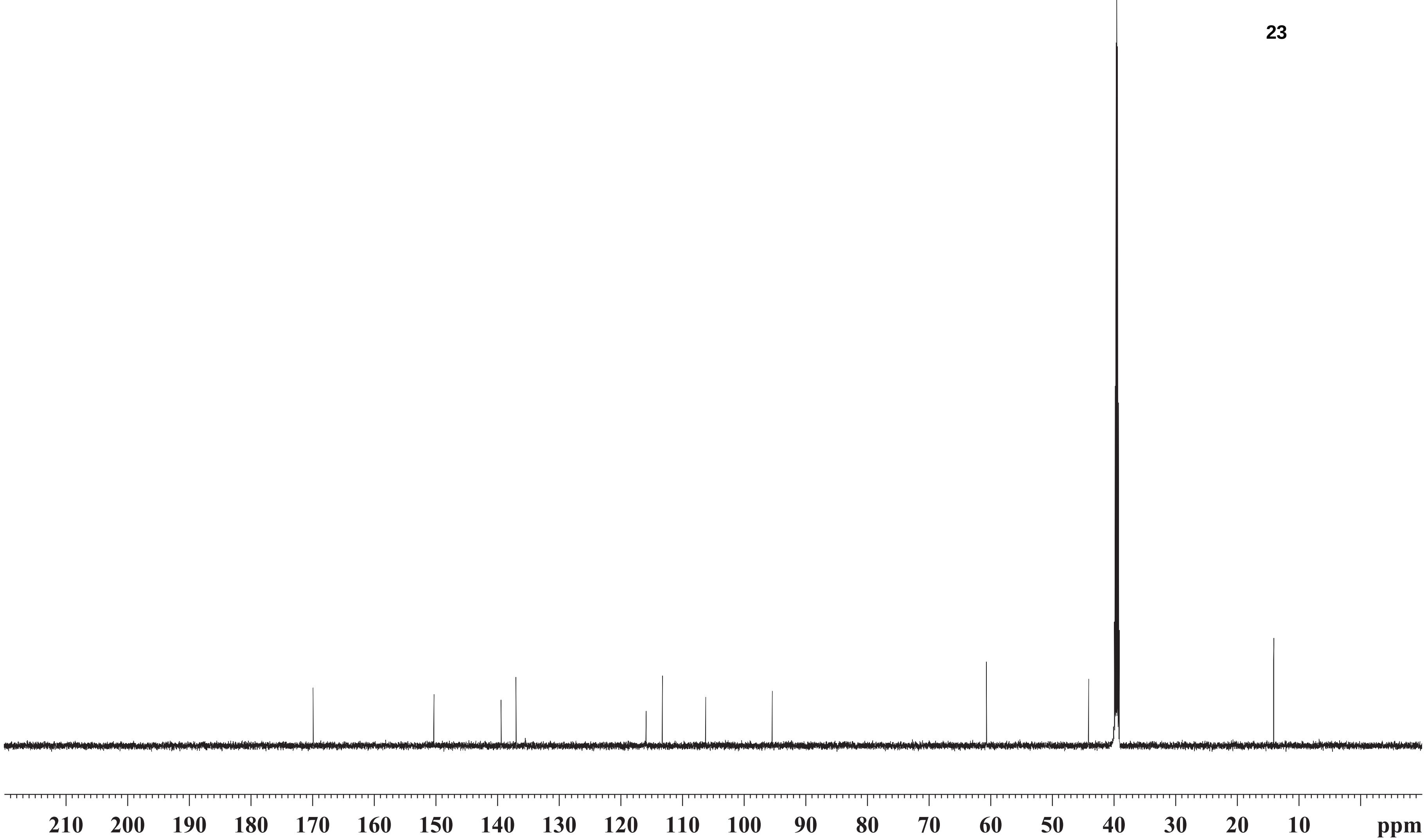
23



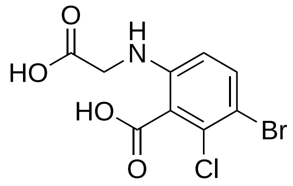
^{13}C NMR (150 MHz, DMSO-d_6)



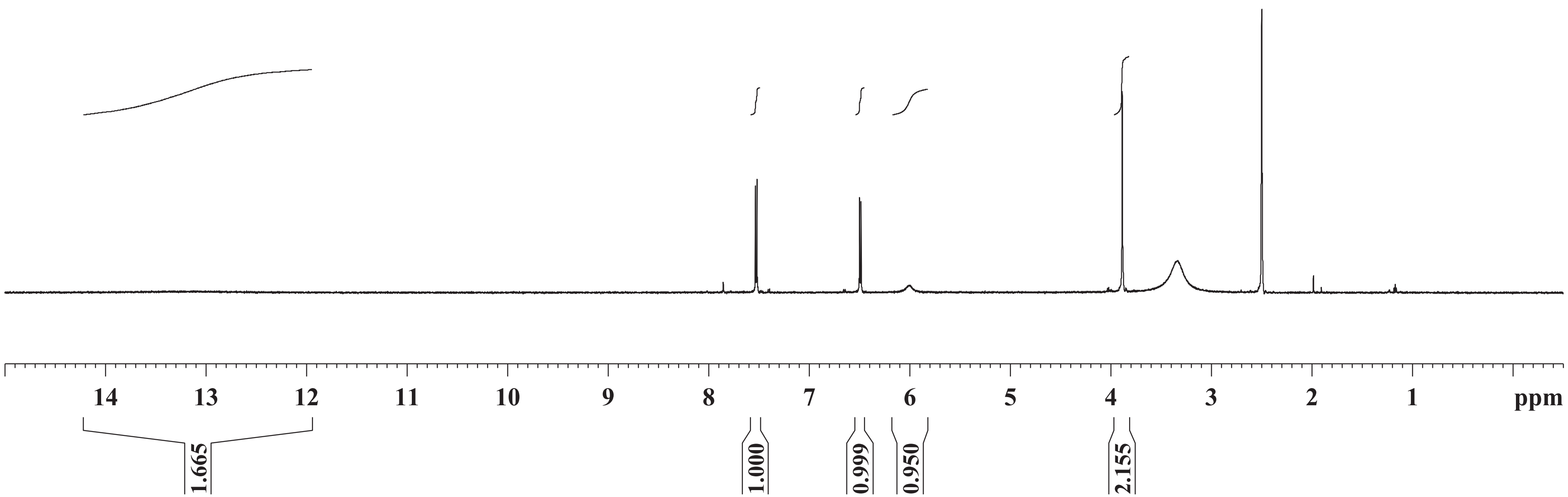
23



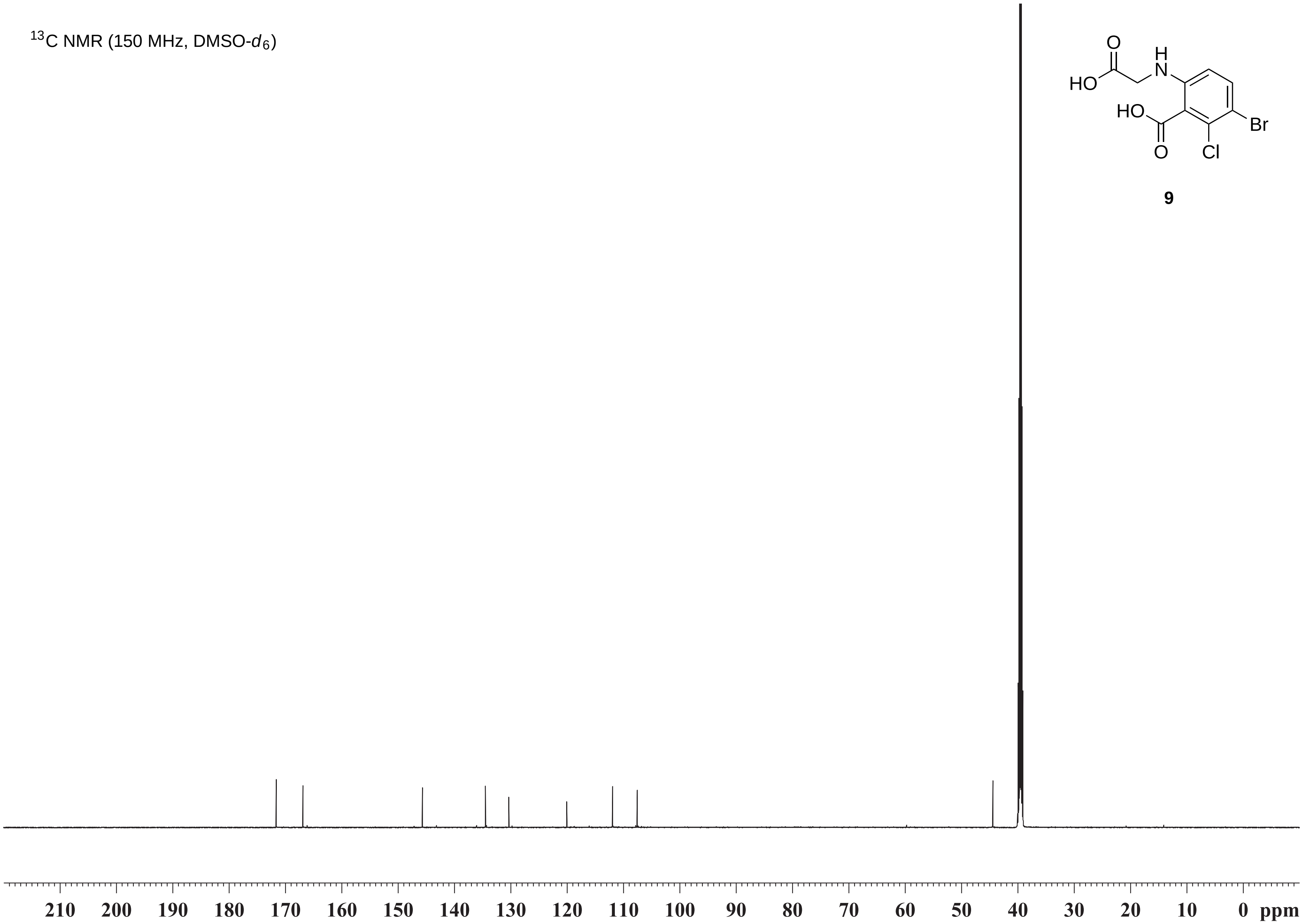
^{1}H NMR (600 MHz, DMSO-d_6)



9

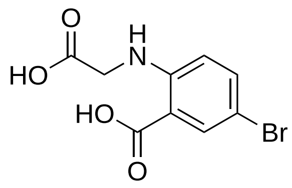


^{13}C NMR (150 MHz, DMSO-d_6)

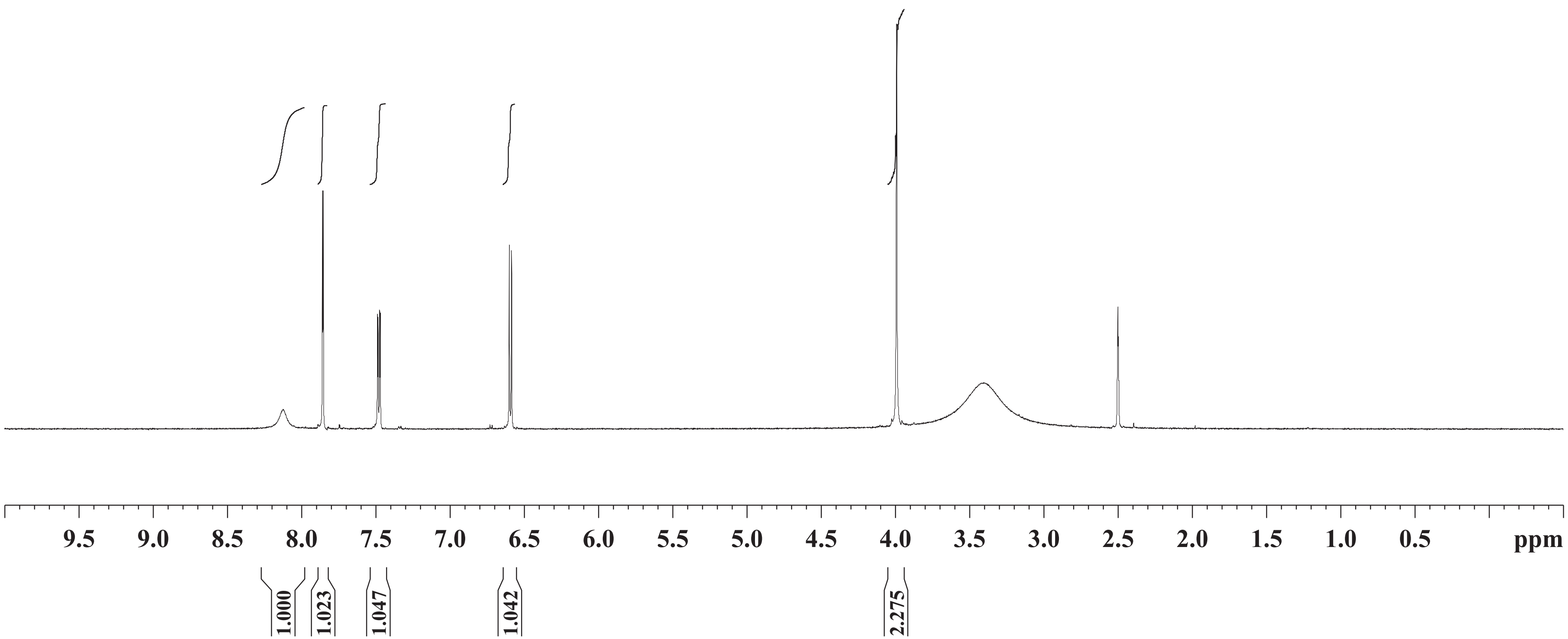


9

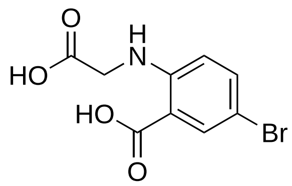
^{1}H NMR (600 MHz, DMSO-d_6)



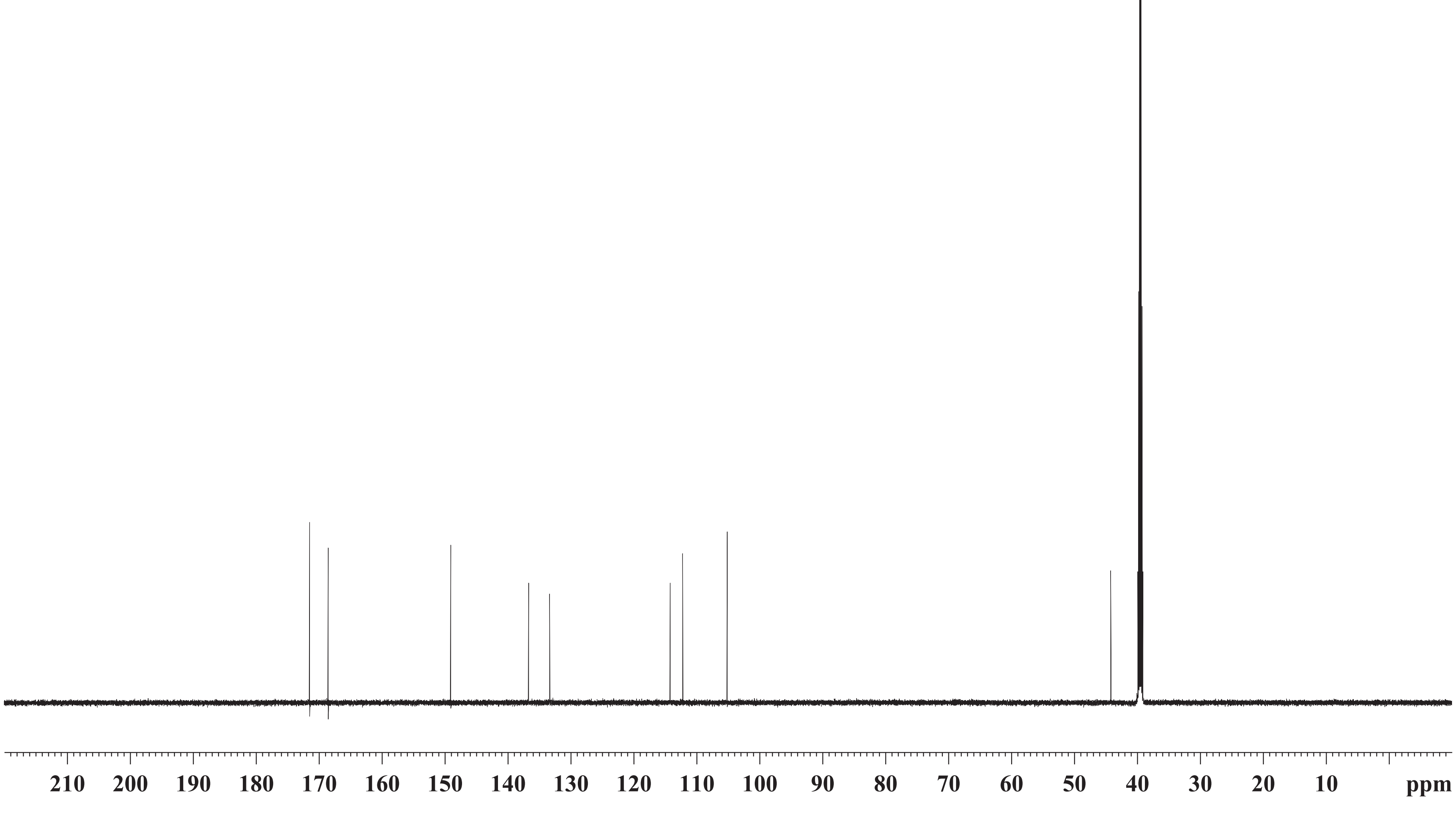
18



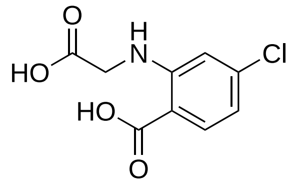
^{13}C NMR (150 MHz, DMSO-d_6)



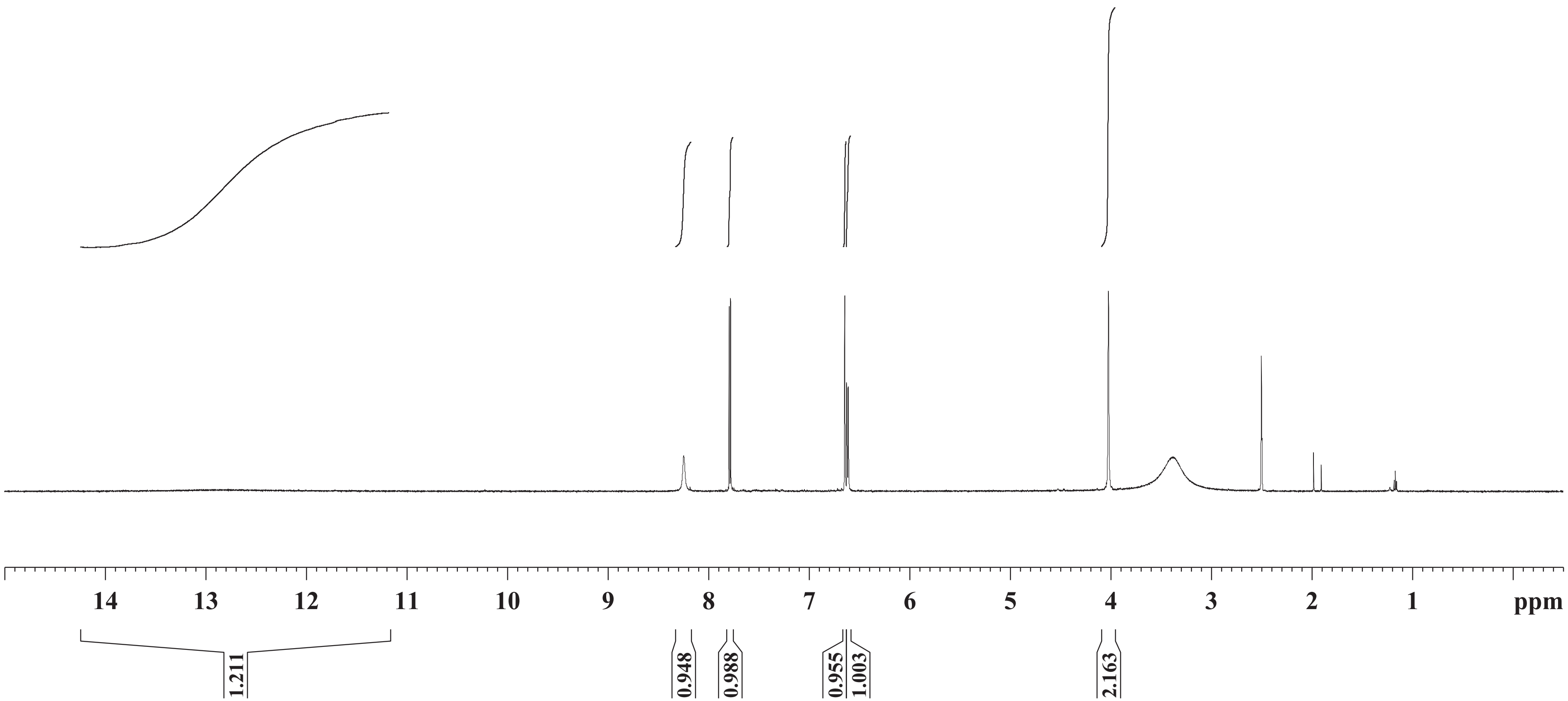
18



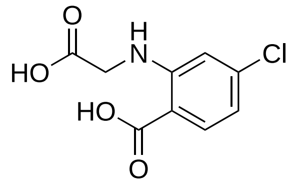
^{1}H NMR (600 MHz, DMSO-d_6)



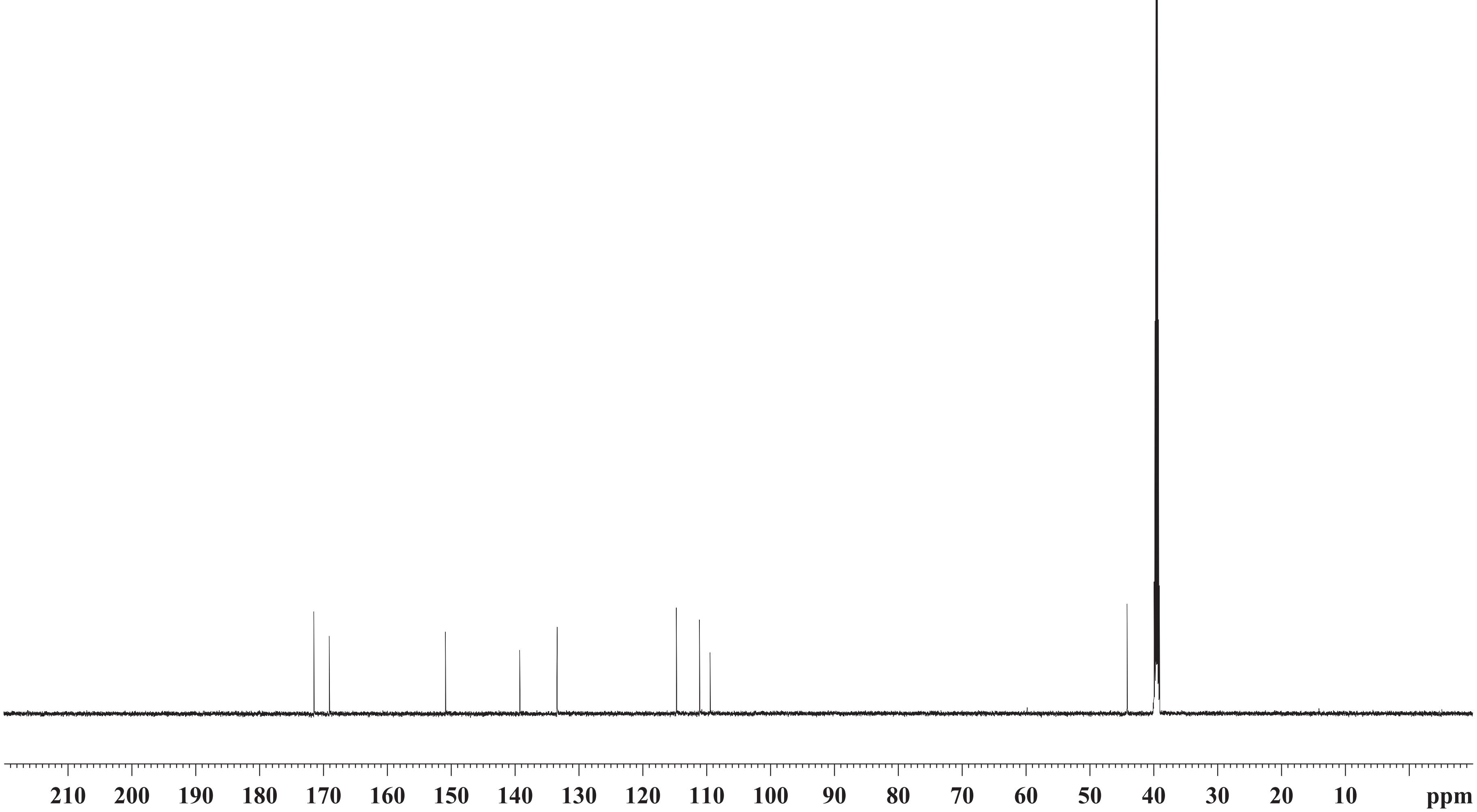
24



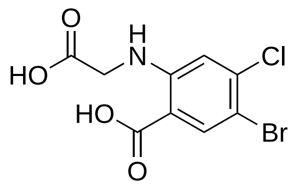
^{13}C NMR (150 MHz, DMSO-d_6)



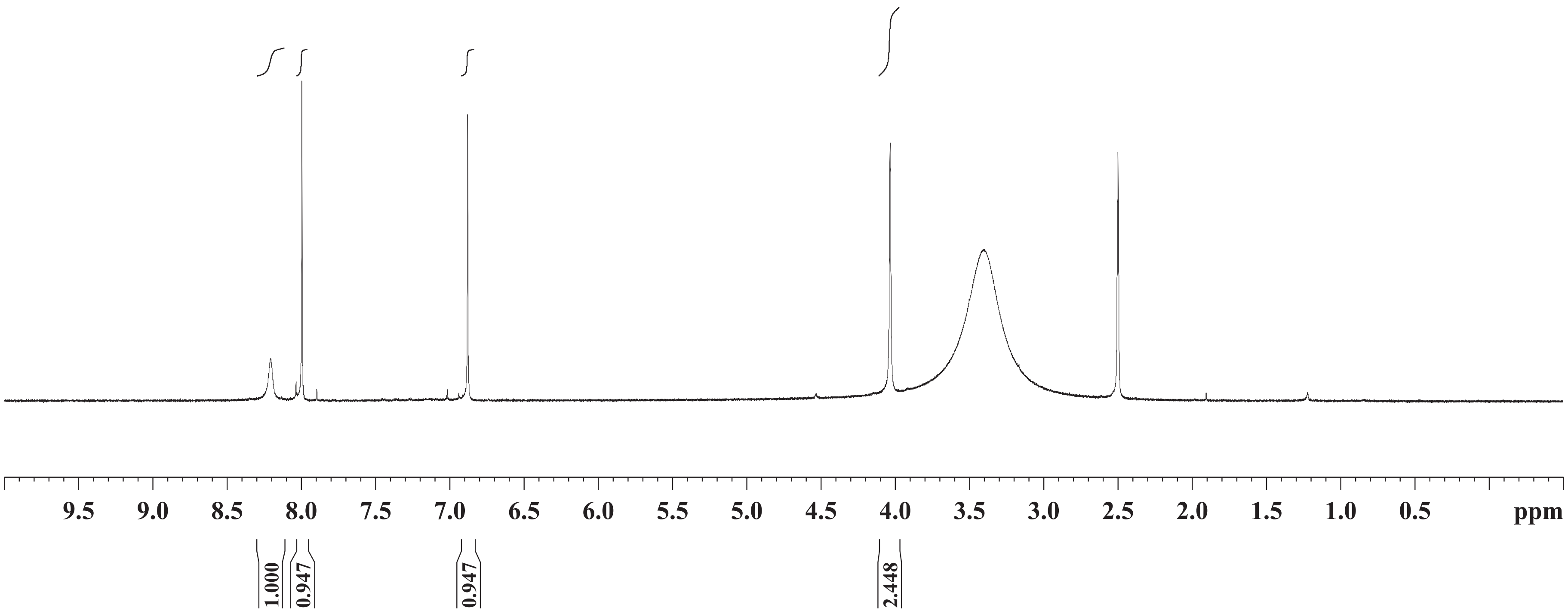
24



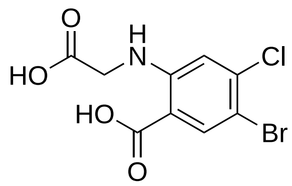
^{1}H NMR (600 MHz, DMSO-d_6)



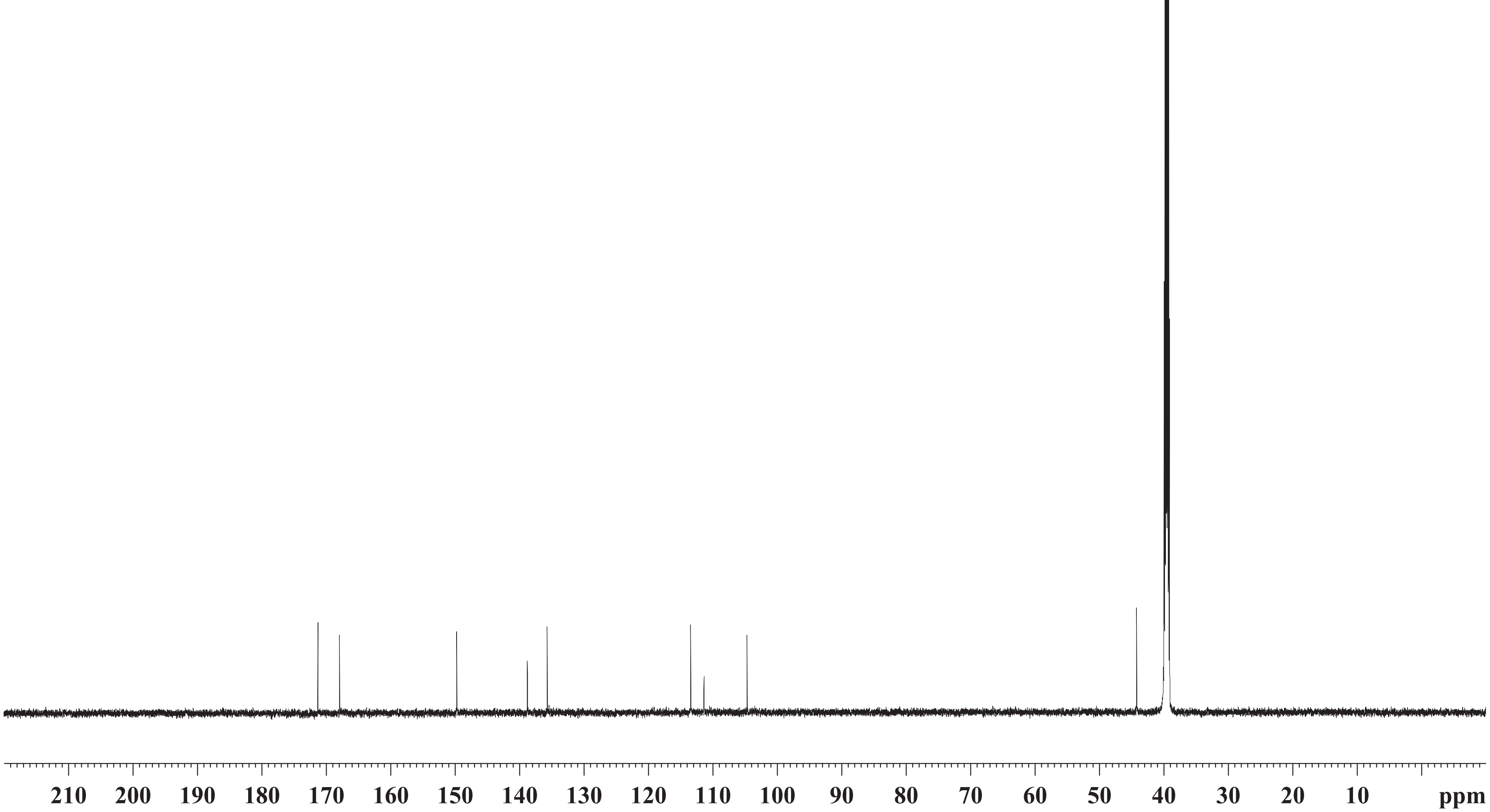
25



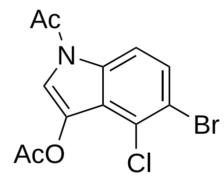
^{13}C NMR (150 MHz, DMSO-d_6)



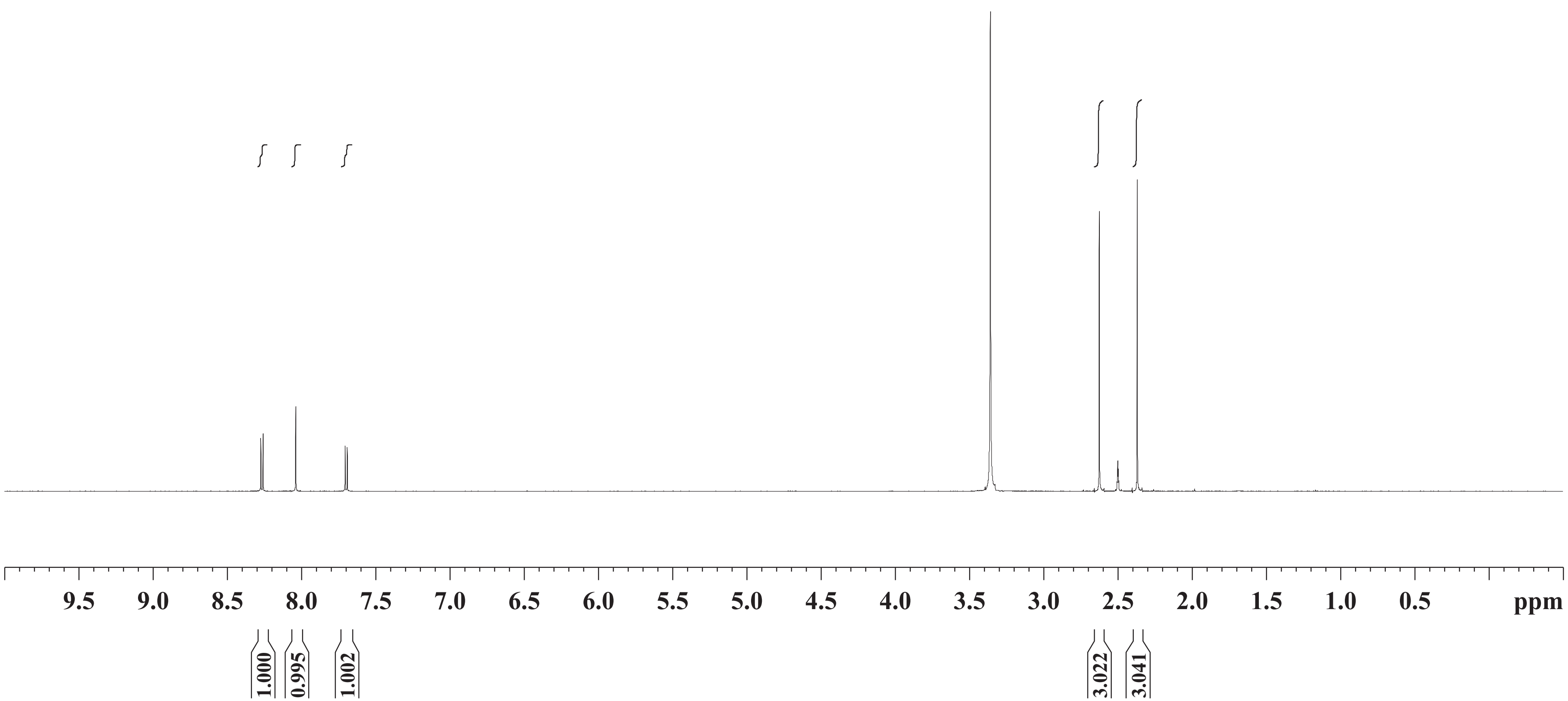
25



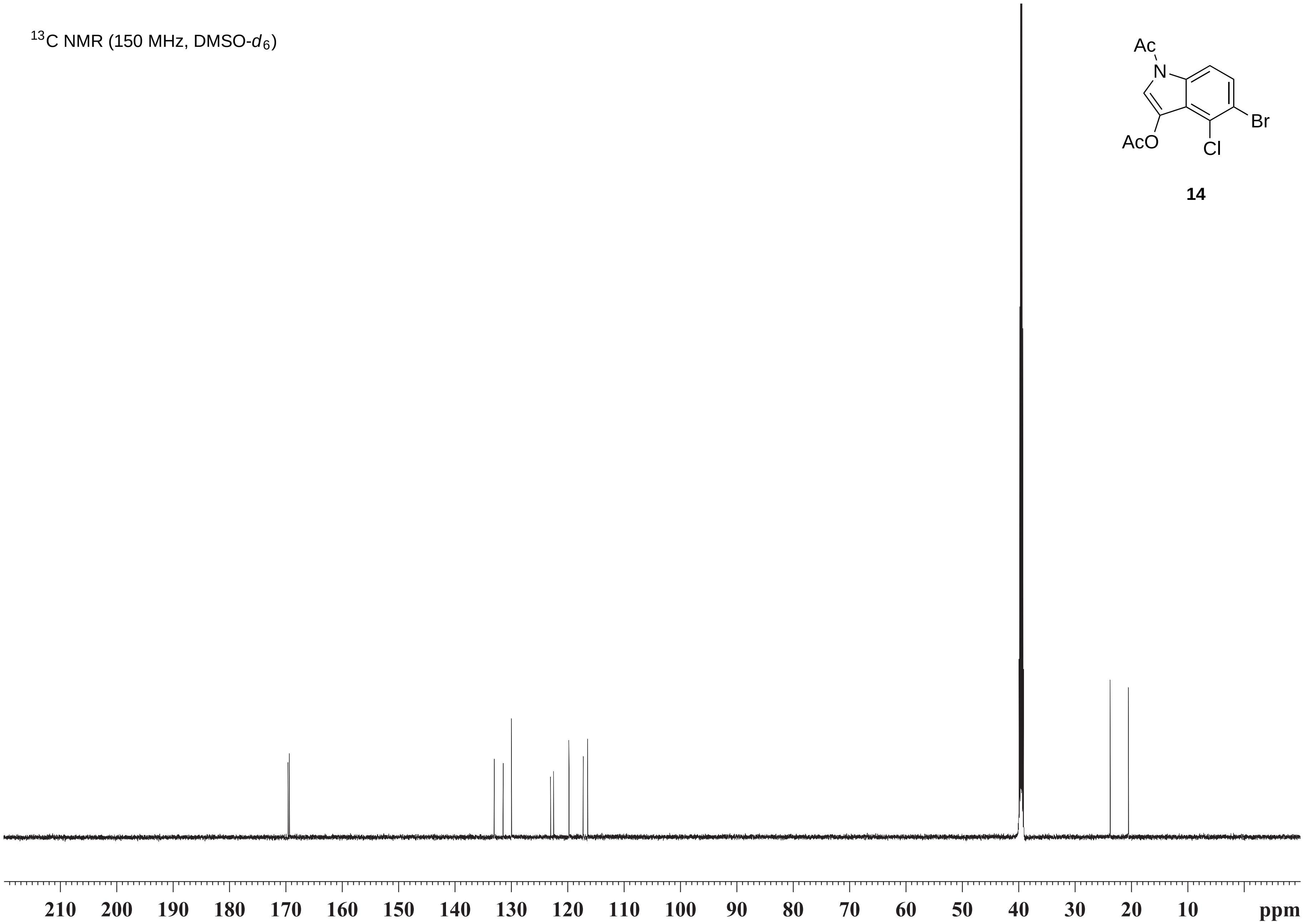
^{1}H NMR (600 MHz, DMSO-d_6)



14

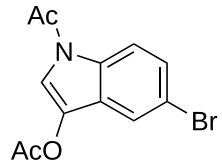


^{13}C NMR (150 MHz, DMSO-d_6)

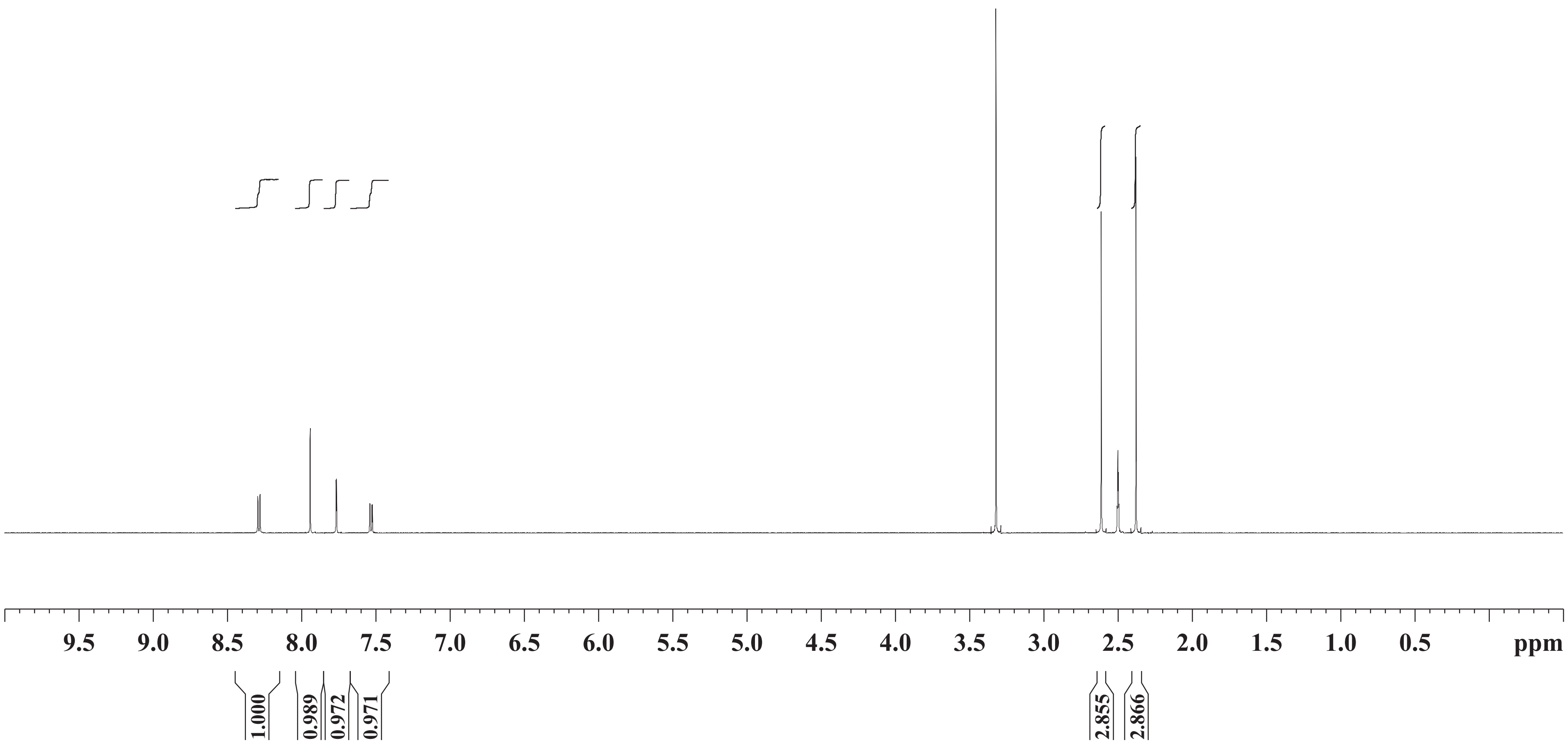


14

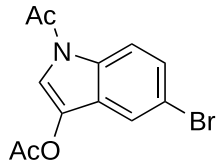
^{1}H NMR (600 MHz, DMSO-d_6)



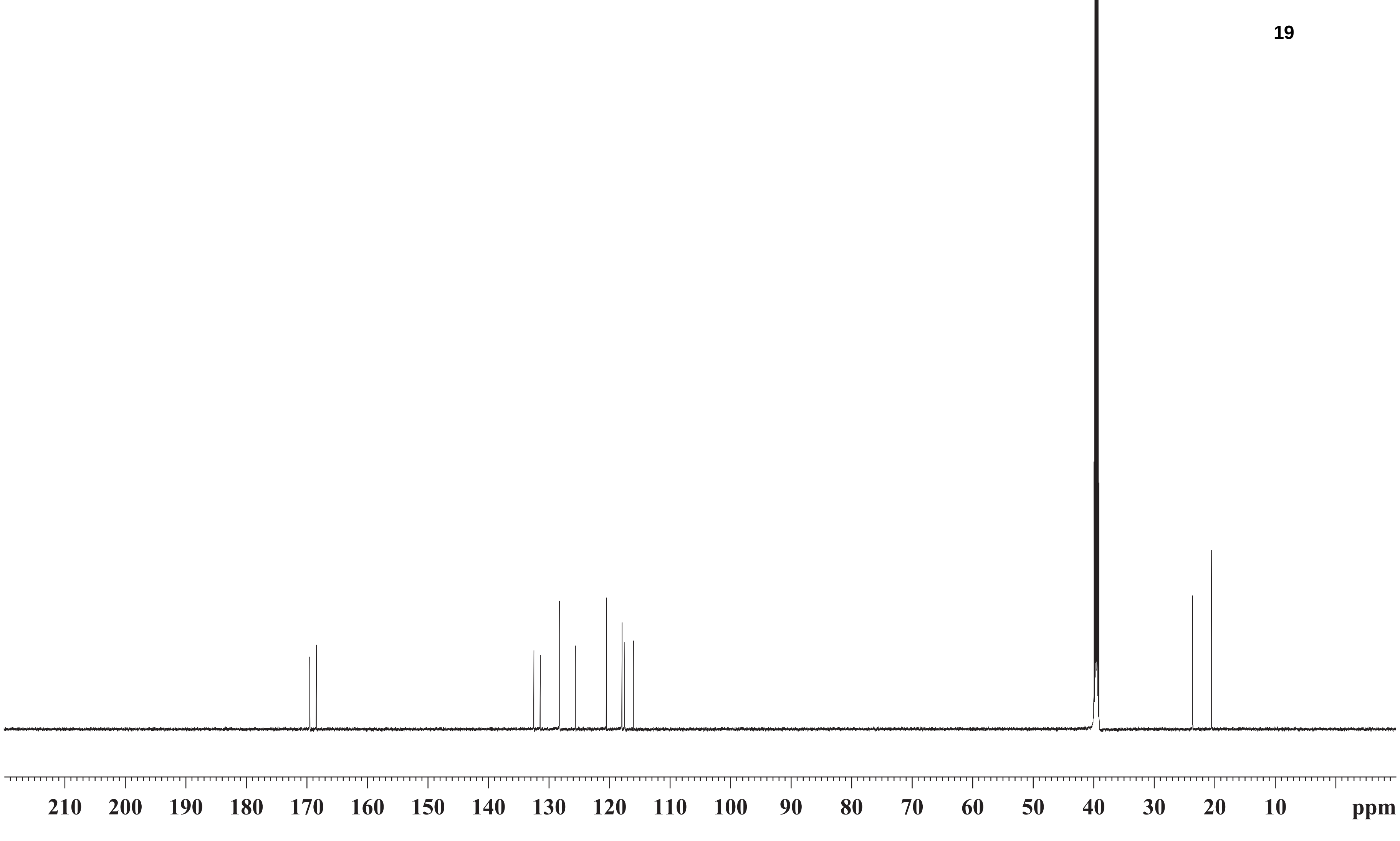
19



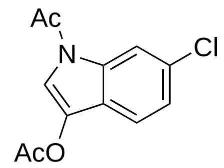
^{13}C NMR (150 MHz, DMSO-d_6)



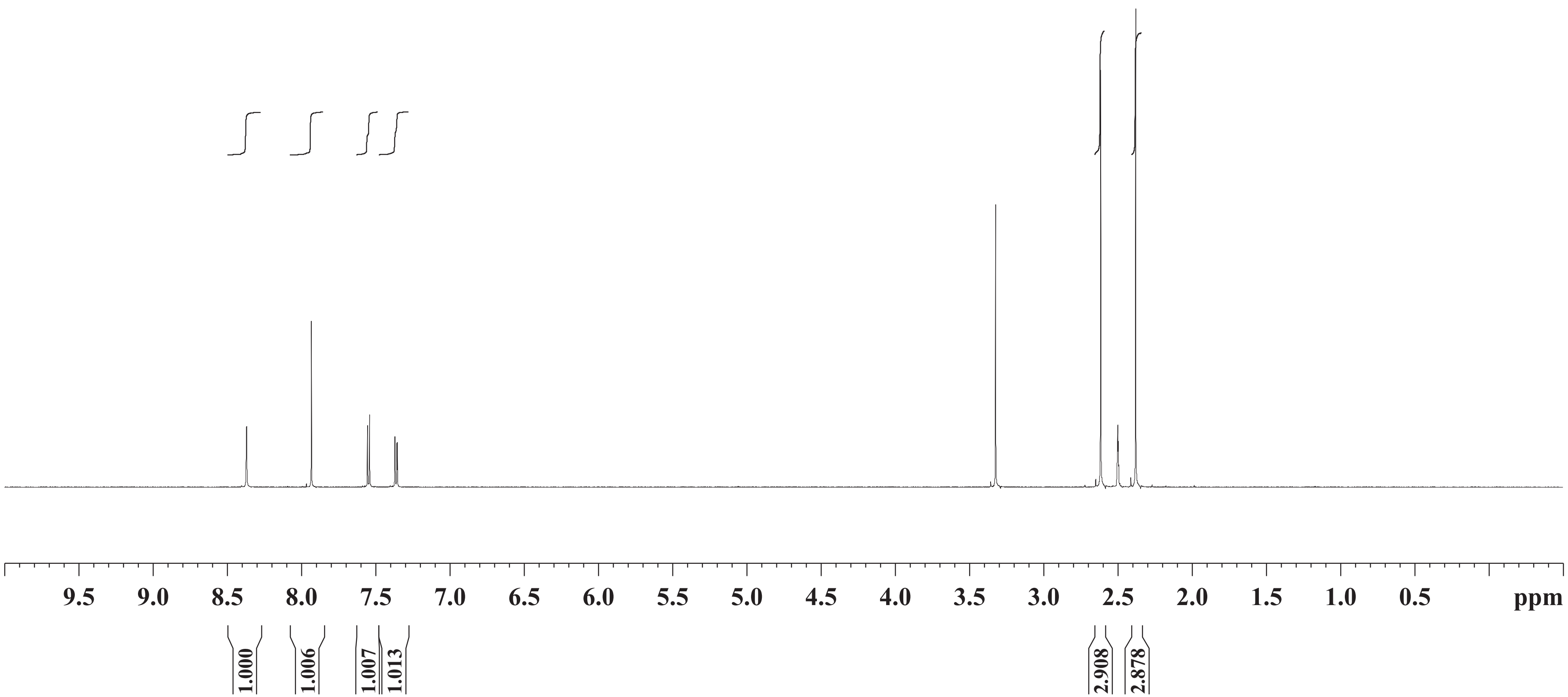
19



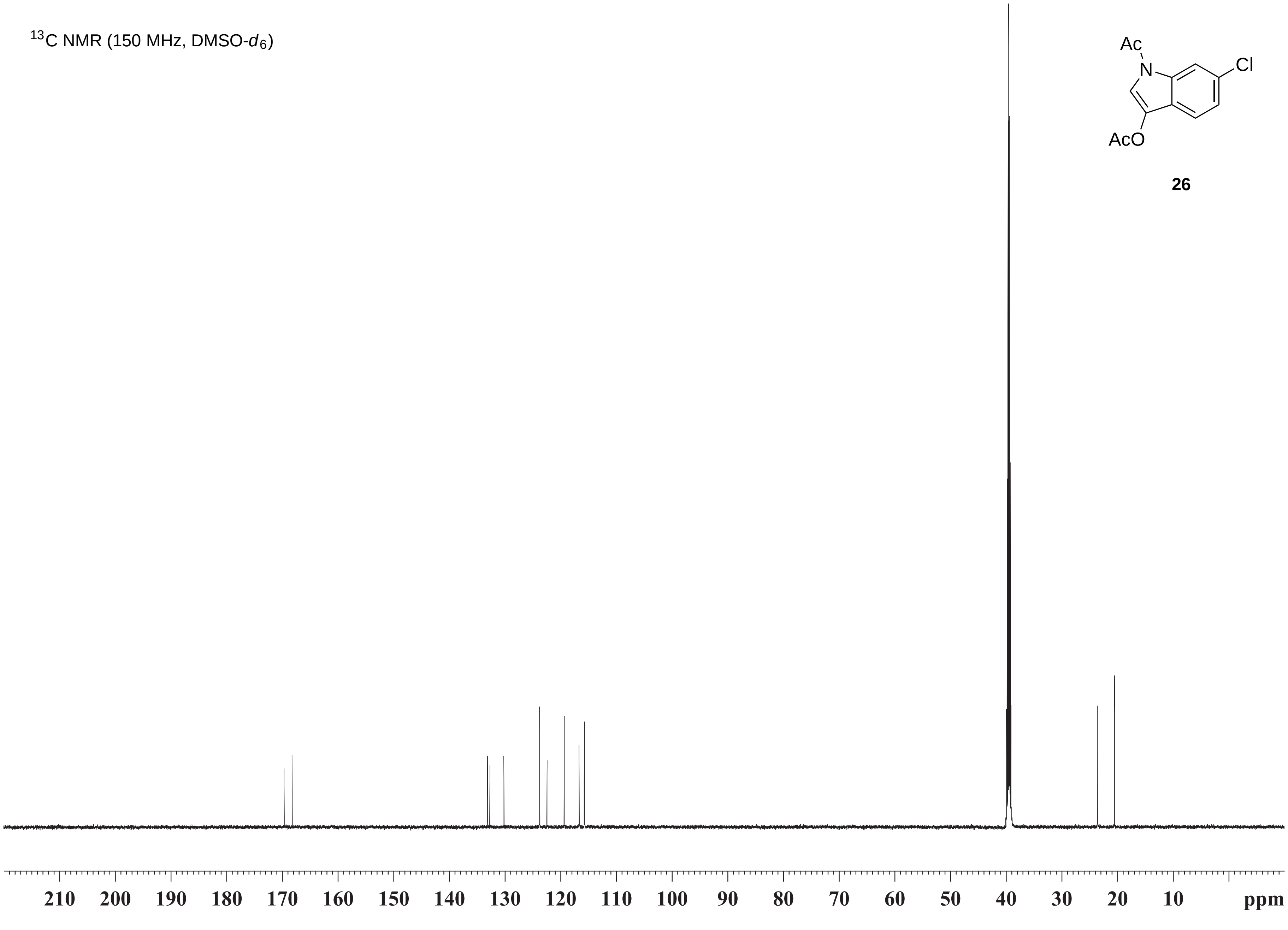
^{1}H NMR (600 MHz, DMSO-d_6)



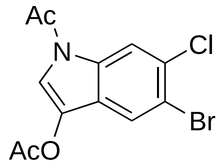
26



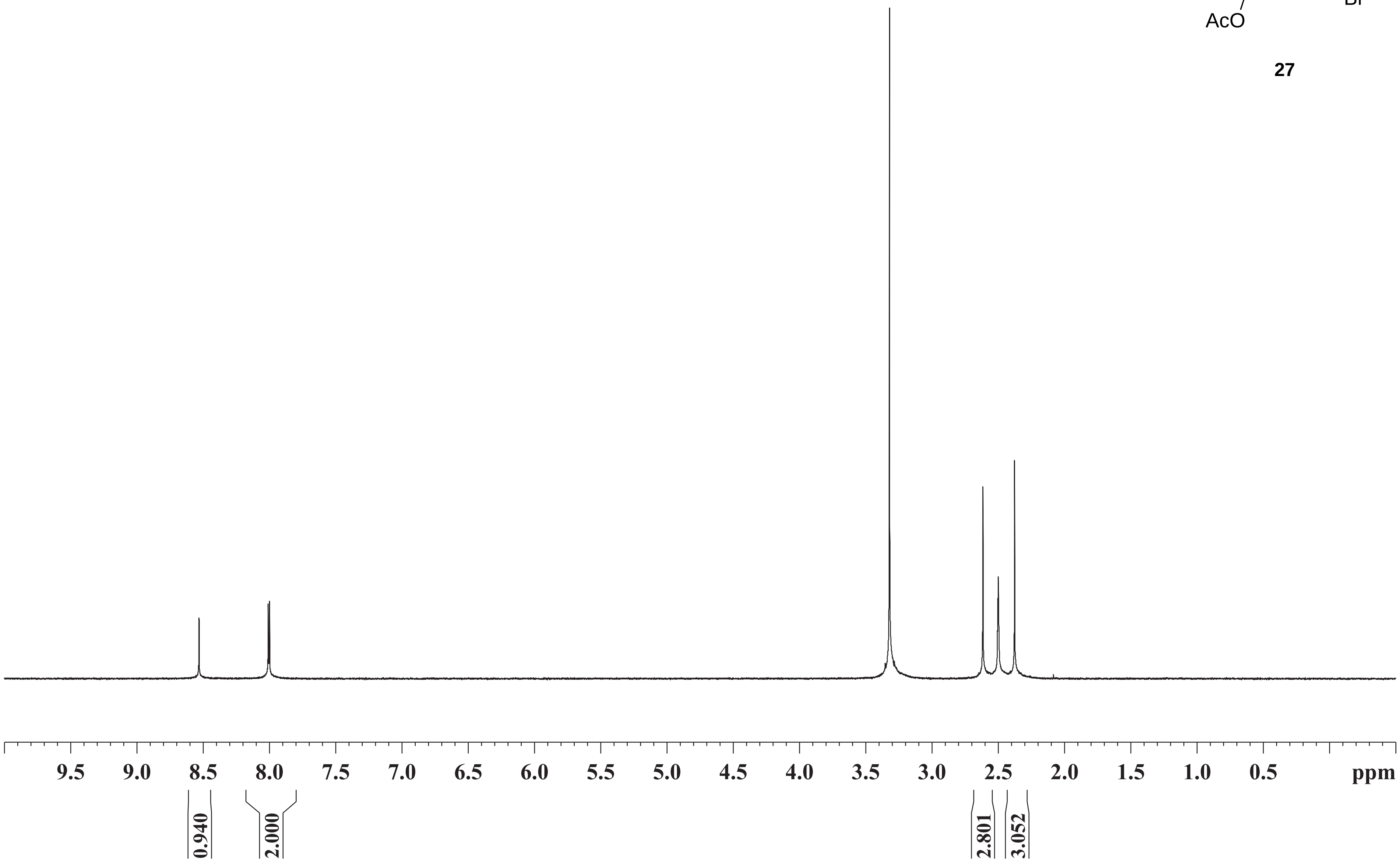
^{13}C NMR (150 MHz, DMSO-d_6)



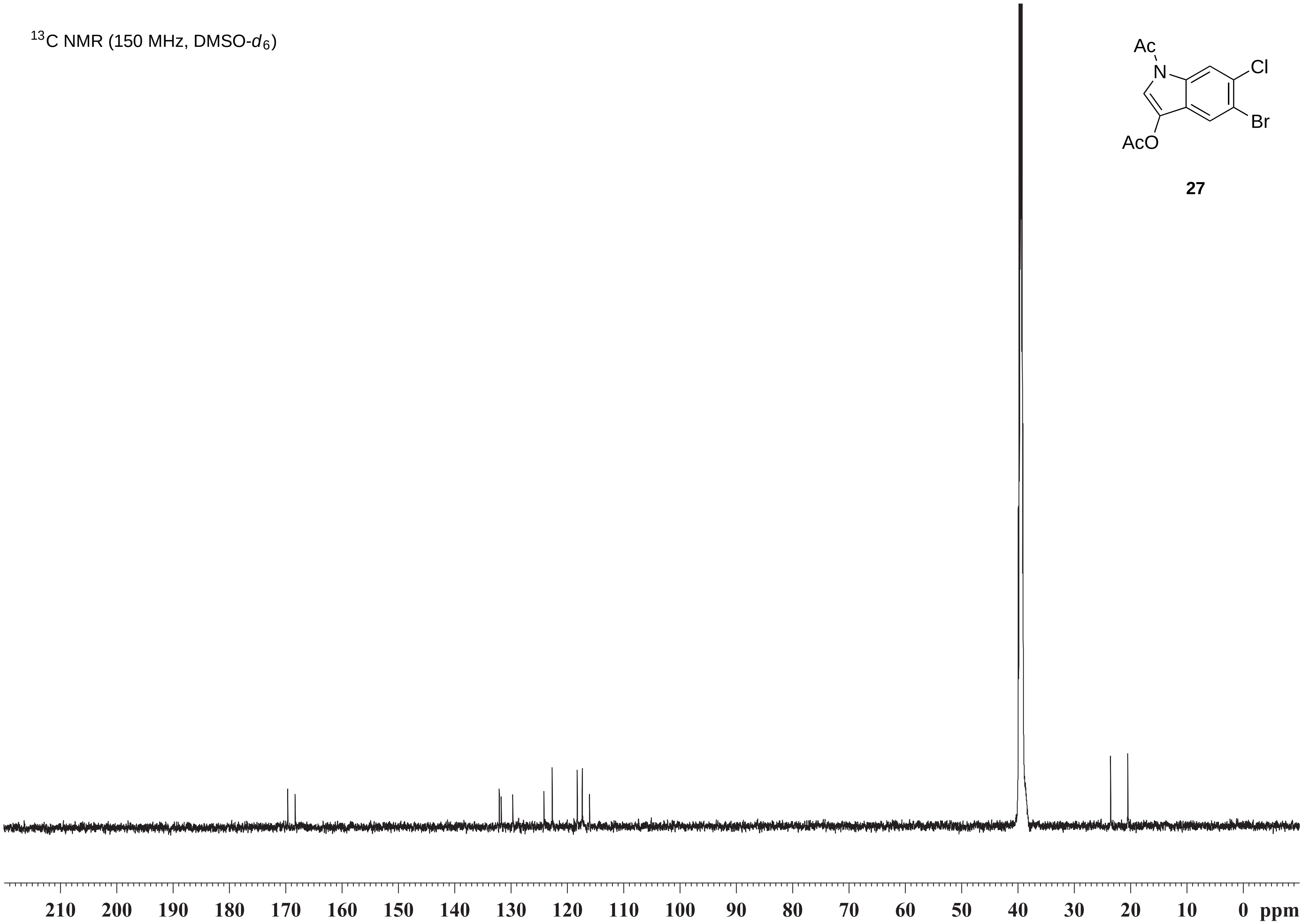
^1H NMR (600 MHz, DMSO-d_6)



27

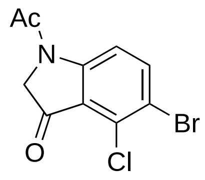


^{13}C NMR (150 MHz, DMSO-d_6)

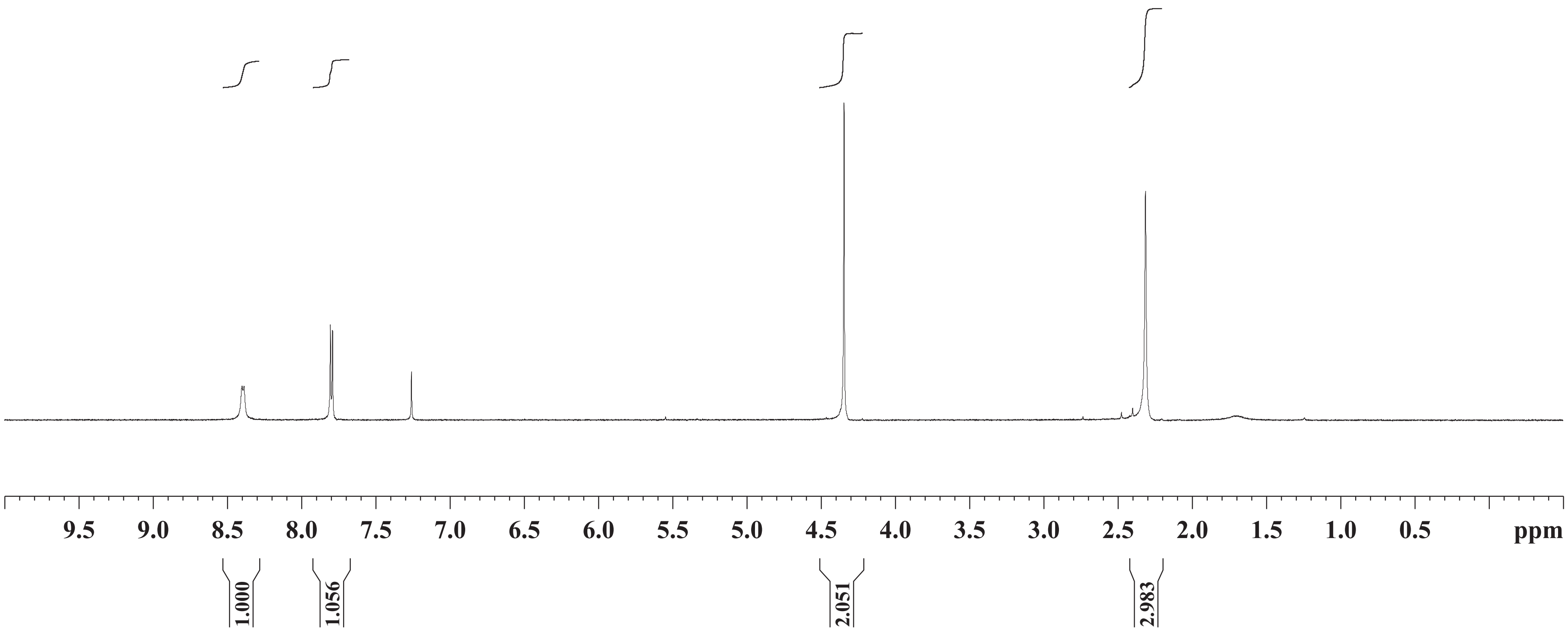


27

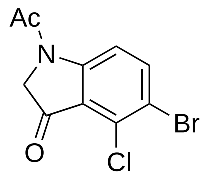
^{1}H NMR (600 MHz, $CDCl_3$)



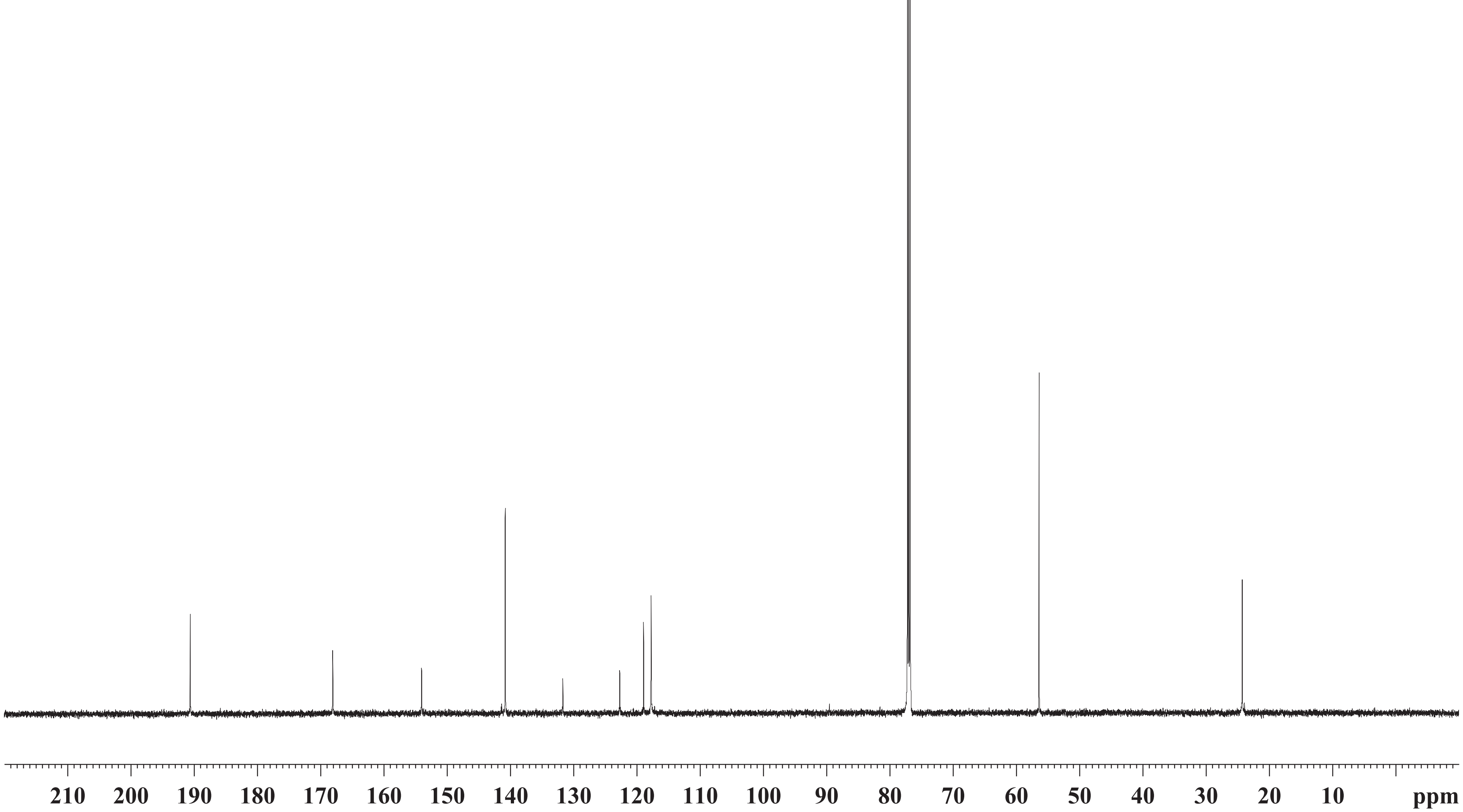
1



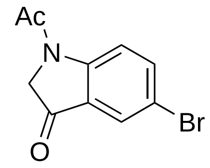
^{13}C NMR (150 MHz, $CDCl_3$)



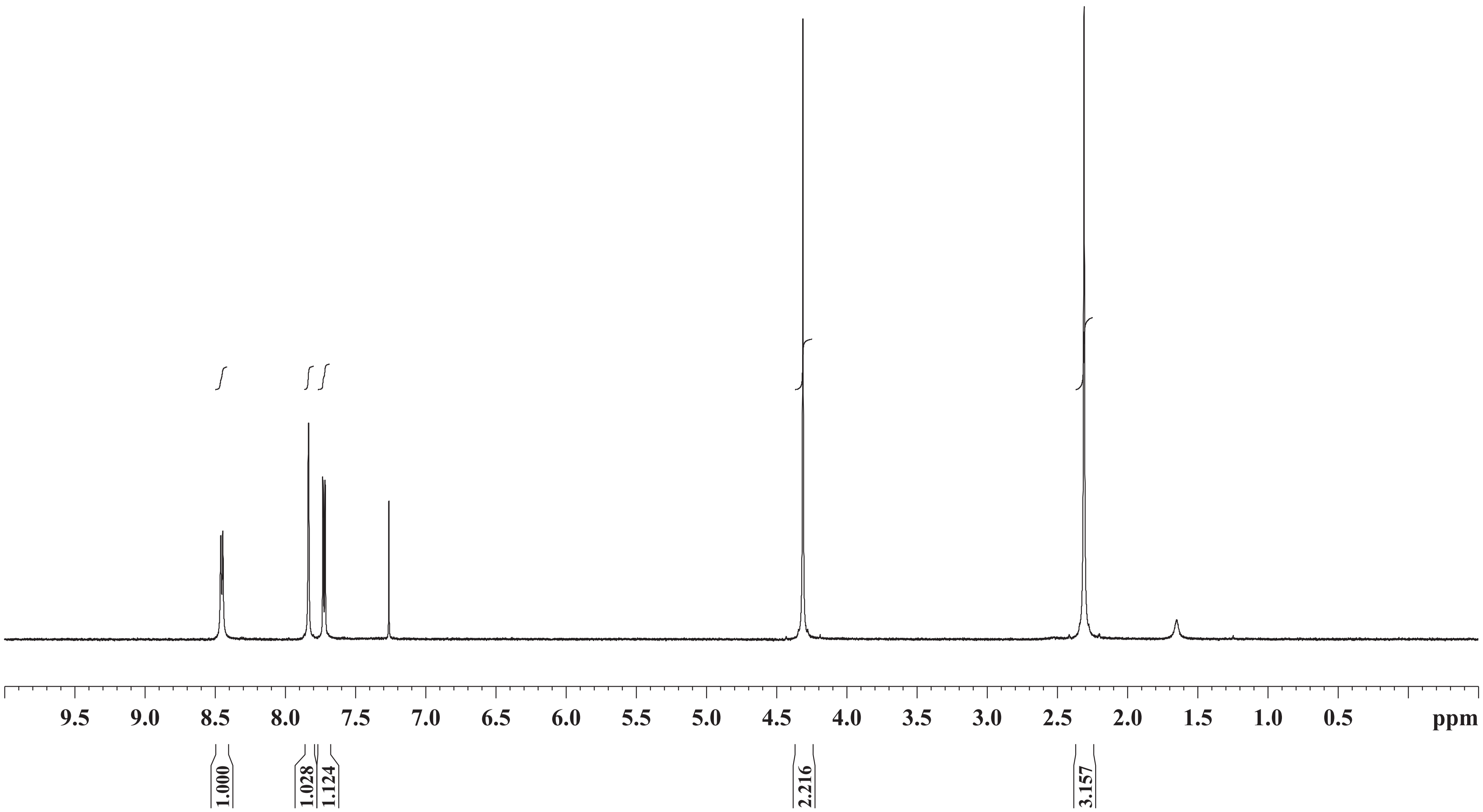
1



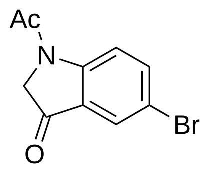
^{1}H NMR (600 MHz, $CDCl_3$)



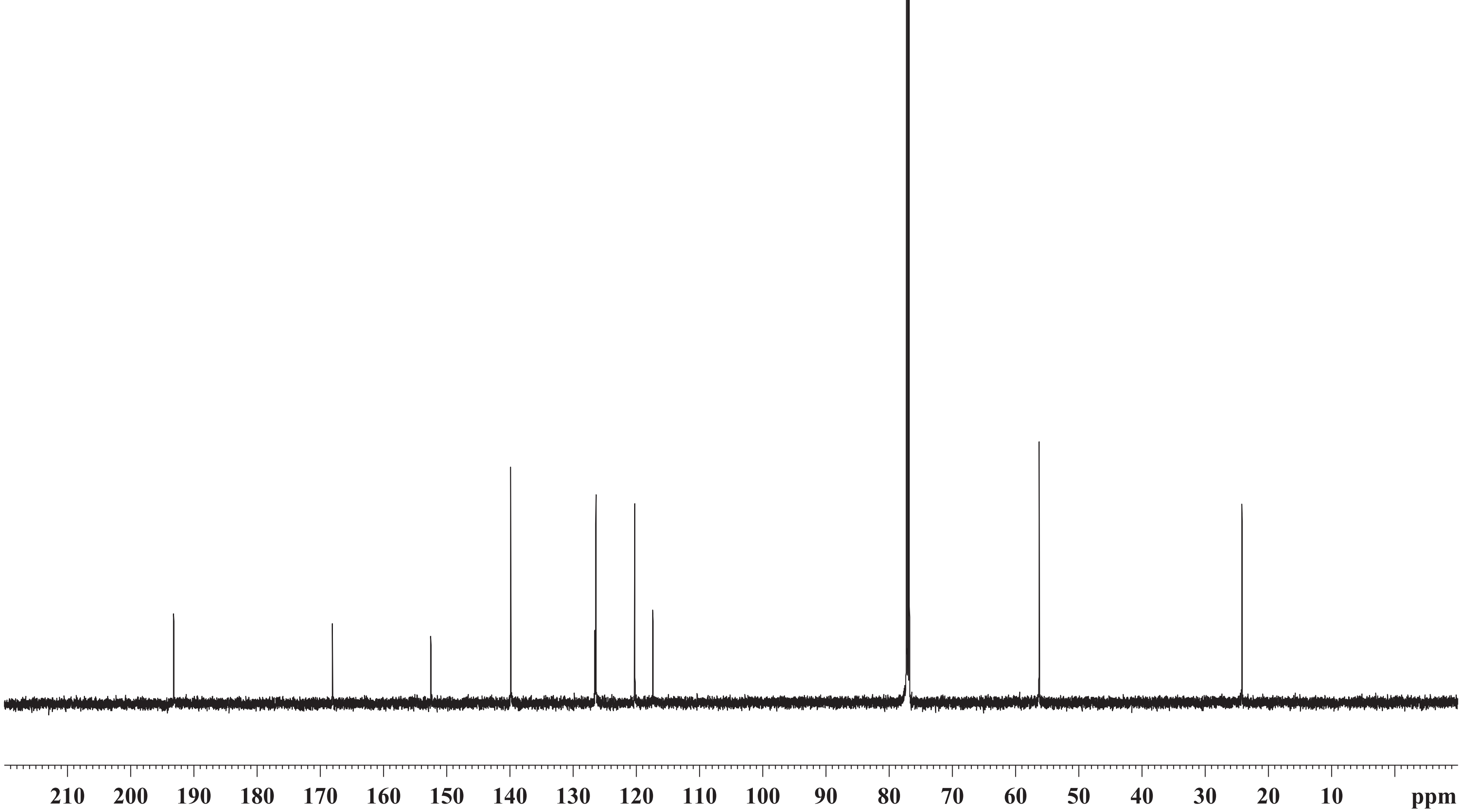
2



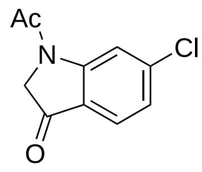
^{13}C NMR (150 MHz, $CDCl_3$)



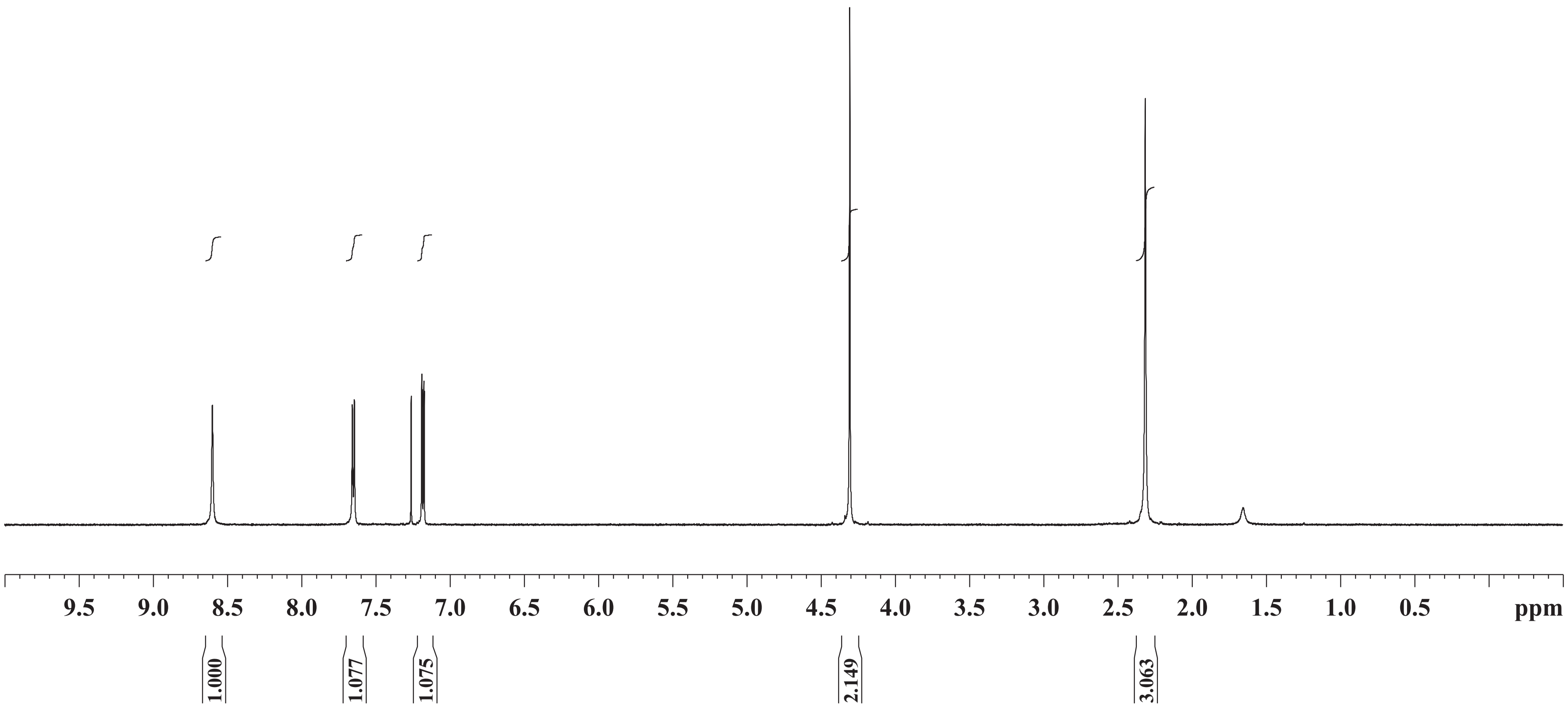
2

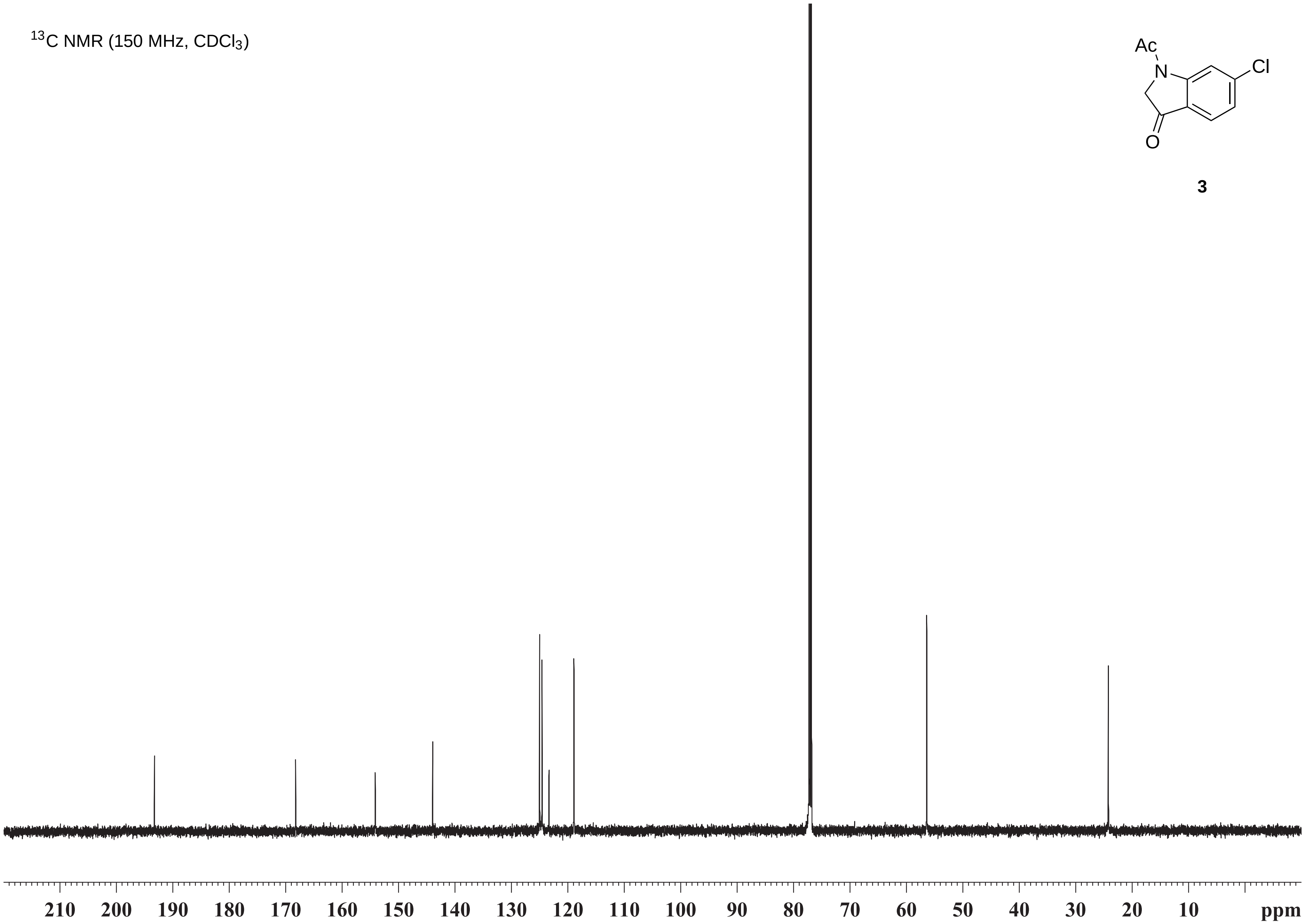


^{1}H NMR (600 MHz, $CDCl_3$)



3

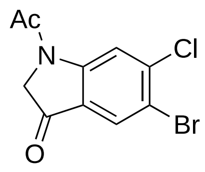




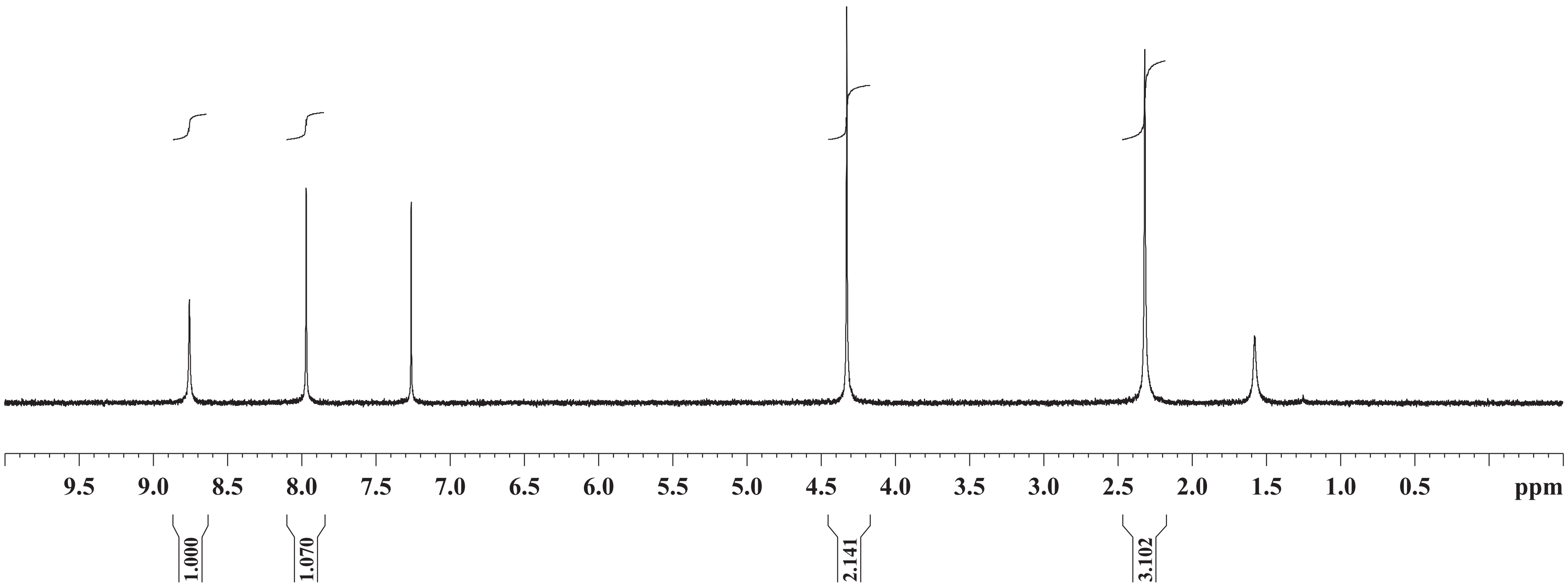
^{13}C NMR (150 MHz, $CDCl_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Ac
N
Cl
O

3

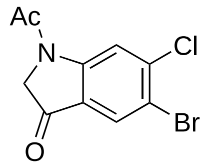
^{1}H NMR (600 MHz, $CDCl_3$)



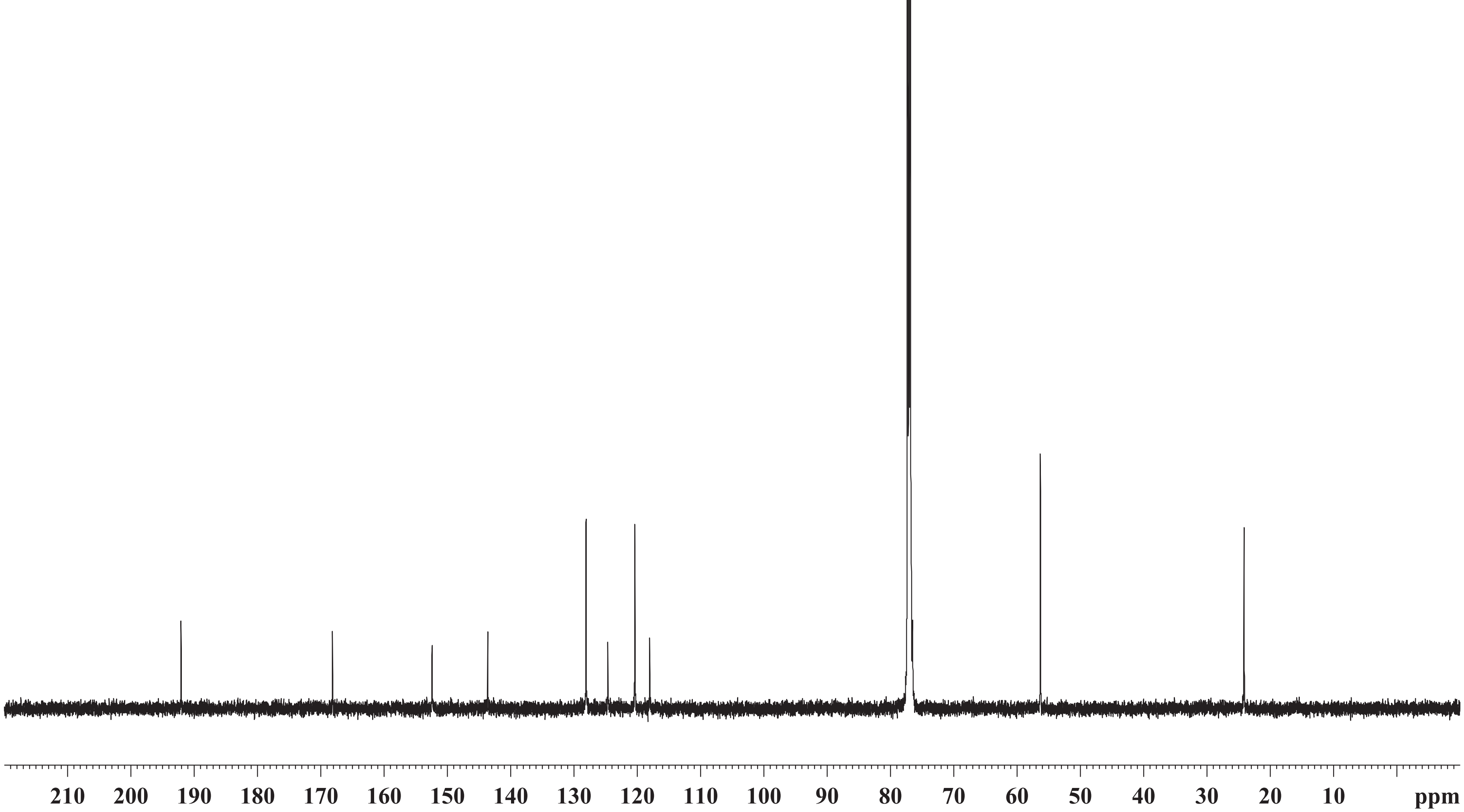
4



13C NMR (150 MHz, $CDCl_3$)



4



References

[1] G. A. Olah and T. Keumi, *Synthesis*, 1979, 112.

[2] S. J. Kulkarni, K. V. Raghavan, K. V. V. K. Mohan, N. Narender and P. Srinivasu, *Synth. Commun.*, 2004, **34**, 2143.

[3] J. C. Rodríguez-Domínguez, A. Balbuzano-Deus, M. A. López-López and G. Kirsch, *J. Heterocycl. Chem.*, 2007, **44**, 273.