A highly efficient and green synthesis of 3,4-dihydropyrimidin-2-ones in low melting mixtures

Sangram Gore,[a,b] Sundarababu Baskaran*[a] and Burkhard Koenig*[b]

Supporting Information

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General Information

^{1}H NMR spectra were recorded on 300 MHz and 400 MHz. ^{13}C NMR spectra were recorded on 75 and 100 MHz. Chemical shifts are expressed in δ units relative to tetramethylsilane (TMS) signal as internal reference in DMSO-d_6, $CDCl_3$ or MeOD. FT-IR spectra's were recorded in $CHCl_3$, or neat. Column chromatography was performed on silica gel (60-120 mesh) using ethyl acetate and hexane as eluent.

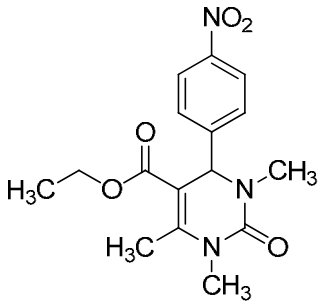
General Procedure for the formation of 3,4-dihydropyrimidin-2-ones:

In a typical experiment, 1.5 g of L-(+)-tartaric acid-DMU (30:70) mixture was heated to 70 ^{o}C to obtain a clear melt. To this melt, 1 mmol of aldehyde and 1 mmol of ethyl acetoacetate were added at 70 ^{o}C. The reaction was monitored by thin layer chromatography. The reaction mixture was quenched by adding water while still hot. The reaction mixture was cooled to room temperature and the solid separated was filtered out and washed with water (3 × 5 mL), dried under vacuum and recrystallized from ethanol to afford pure product.

Experimental Section

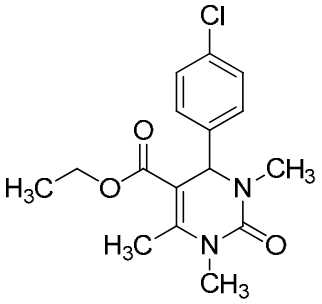
Spectral data of the 3,4-dihydropyrimidin-2-ones and thiones obtained by the condensation of aldehydes, 1,3-dicarbonyls and urea:

2a. Ethyl 1,3,6-trimethyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



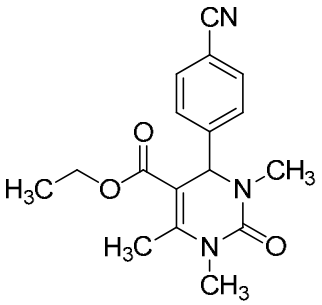
Yellow solid; Yield 96%; M.p. 104-106 ^{o}C; IR (neat): 1725, 1609, 1523 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, 3H, *J* = 6.9 Hz), 2.49 (s, 3H), 2.93 (s, 3H), 3.27 (s, 3H), 4.16 (q, 2H, *J* = 6.6 Hz), 5.36 (s, 1H), 7.40 (d, 2H, *J* = 8.7 Hz), 8.16 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 16.8, 31.2, 34.7, 60.4, 60.5, 102.6, 124.0, 127.5, 147.6, 148.3, 150.4, 153.5, 165.6; HRMS, calcd. for (M^{+}+1) 334.1403, found 334.1415.

2b. Ethyl 4-(4-chlorophenyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



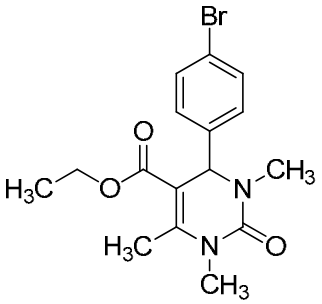
Pale yellow oil; Yield 90%; IR (neat): 1664, 1596 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.23 (t, 3H, *J* = 6.9 Hz), 2.46 (s, 3H), 2.88 (s, 3H), 3.24 (s, 3H), 4.11 (q, 2H, *J* = 7.2 Hz), 5.20 (s, 1H), 7.12–7.17 (m, 2H), 7.23 (s, 1H), 7.33(s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 16.7, 31.1, 34.5, 60.3, 60.4, 103.3, 128.0, 128.8, 133.6, 139.6, 149.6, 153.6, 165.8; HRMS, calcd. for $C_{16}H_{19}ClN_2O_3$ (M^+) 322.1084, found 322.1087.

2c. Ethyl 4-(4-cyanophenyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



Pale yellow solid; Yield 97%; M.p. 85-87 ^oC; IR (neat): 2110, 1687, 1606 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.21 (t, 3H, *J* = 6.9 Hz), 2.45 (s, 3H), 2.88 (s, 3H), 3.23 (s, 3H), 4.10 (q, 2H, *J* = 6.9 Hz), 5.27 (s, 1H), 7.28–7.34 (m, 2H), 7.55 (d, 2H, *J* = 8.1); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 16.8, 31.2, 34.6, 60.4, 60.6, 102.6, 111.8, 118.6, 127.4, 132.6, 146.3, 150.2, 153.5, 165.6; HRMS, calcd. for $C_{17}H_{19}N_3O_3$ (M^+) 313.1426, found 313.1424.

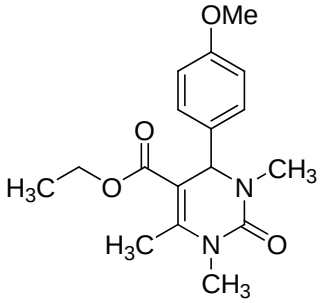
2d. Ethyl 4-(4-bromophenyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



Pale yellow solid; Yield 84%; M.p. 65-66 ^oC; IR (neat): 1684, 1611 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.47 (s, 3H), 2.89 (s, 3H), 3.25 (s, 3H), 4.09–4.17 (m, 2H), 5.20 (s, 1H), 7.07–7.12 (m, 2H), 7.39–7.43 (m, 2H); ^{13}C NMR (75 MHz,

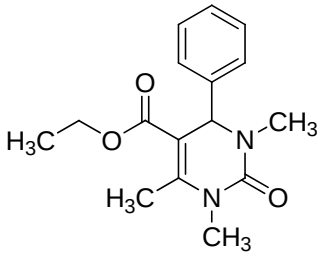
$CDCl_3$): δ 14.3, 16.7, 31.2, 34.5, 60.3, 60.4, 103.2, 121.8, 128.4, 131.8, 140.1, 149.6, 153.7, 165.8; HRMS, calcd. for $C_{16}H_{19}BrN_2O_3$ (M^+) 366.0579, found 366.0575.

2e. Ethyl 4-(4-methoxyphenyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



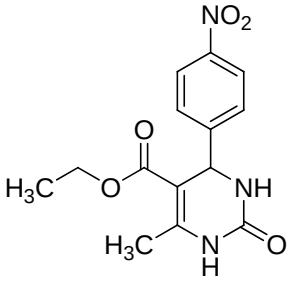
Yellow solid, Yield 98%; M.p. 82–84 ^oC; IR (neat): 1690, 1635 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.21 (t, 3H, J = 7.2 Hz), 2.46 (s, 3H), 2.87 (s, 3H), 3.24 (s, 3H), 3.75 (s, 3H), 4.06–4.14 (m, 2H), 5.16 (s, 1H), 6.77–6.81 (m, 2H), 7.11–7.14 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 16.7, 31.1, 34.3, 55.3, 60.2, 60.4, 103.8, 113.9, 127.9, 133.2, 149.0, 153.8, 159.2, 166.1; HRMS, calcd. for $C_{17}H_{22}N_2O_4$ (M^+) 318.1580, found 318.1577.

2f. Ethyl 1,3,6-trimethyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



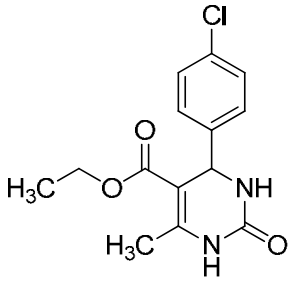
Colorless solid, Yield 97%; M.p. 52-54 ^oC; IR (neat): 3217, 1705, 1618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (m, 3H), 2.48 (s, 3H), 2.91 (s, 3H), 3.26 (s, 3H), 4.08–4.18 (m, 2H), 5.24 (s, 1H), 7.19–7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 16.7, 31.1, 34.5, 60.2, 60.9, 103.6, 126.7, 127.9, 128.7, 141.1, 149.3, 153.9, 166.0; HRMS, calcd. for $C_{16}H_{21}N_2O_3$ (M^++1) 289.1552, found 289.1561.

3a. Ethyl 6-methyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



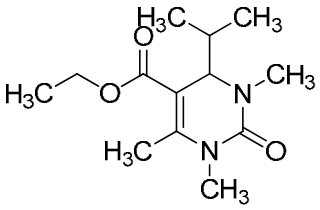
Colorless solid; Yield 91%; M.p. 212–213 ^{o}C; IR (neat): 3105, 1707, 1600, 1522, 1043 cm^{-1}; ^{1}H NMR (300 MHz, DMSO–d_6): δ 1.09 (t, 3H, *J* = 6.9 Hz), 2.26 (s, 3H), 3.98 (q, 2H, *J* = 7.2 Hz), 5.27 (d, 1H, *J* = 3.3 Hz), 7.49–7.52 (m, 2H), 7.89–7.91 (m, 1H), 8.20–8.23 (m, 2H), 9.36 (s, 1H); ^{13}C NMR (75 MHz, DMSO–d_6): δ 14.0, 17.8, 53.6, 59.3, 98.1, 123.8, 127.6, 146.6, 149.3, 151.7, 151.9, 154.9, 165.0; HRMS, calcd. for $C_{14}H_{16}N_3O_5$ (M^++1) 306.1090, found 306.1085.

3b. Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



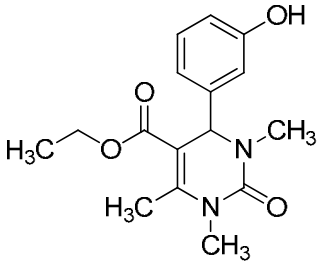
Solid; Yield 83%; M.p. 212-214 ^{o}C; IR (neat): 3243, 1713, 1664 cm^{-1}; ^{1}H NMR (300 MHz, MeOD): δ 1.15 (t, 3H, *J* = 7.2 Hz), 2.33 (s, 3H), 4.10 (q, 2H, *J* = 7.8 Hz), 5.30 (s, 1H), 7.26–7.33 (m, 4H); ^{13}C NMR (75 MHz, MeOD): δ 14.6, 18.2, 55.8, 61.2, 101.7, 129.4, 129.7, 134.5, 144.7, 149.4, 167.4; HRMS, calcd. for $C_{14}H_{16}N_2O_3Cl$ (M^++1) 295.0849, found 295.0854.

5a. Ethyl 4-isopropyl-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



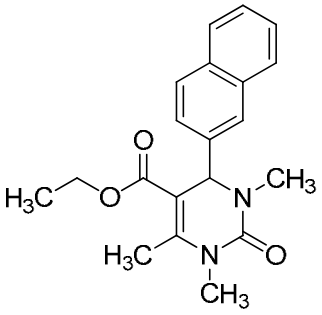
Colorless oil; Yield 98%; IR (neat): 1671, 1213 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (dd, 6H, *J* = 6.8, 2.8 Hz), 1.28 (t, 2H, *J* = 8.0 Hz), 1.82-1.95 (m, 1H), 2.39 (s, 3H), 3.04 (s, 3H), 3.12 (s, 3H), 4.09–4.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 16.4, 18.3, 18.8, 31.0, 33.8, 37.1, 60.1, 62.5, 102.4, 149.6, 154.7, 166.9; HRMS, calcd. for $C_{13}H_{23}N_2O_3$ (M^++1) 255.1709, found 255.1700.

7a. Ethyl 4-(3-hydroxyphenyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



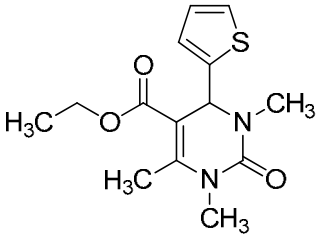
Colorless solid; Yield 92%; M.p. 161-163 ^{o}C; IR (neat): 1665, 1597, 1036 cm^{-1}; ^{1}H NMR (300 MHz, MeOD): δ 1.22 (t, 3H, *J* = 6.9 Hz), 2.50 (s, 3H), 2.87 (s, 3H), 3.24 (s, 3H), 4.10 (q, 2H, *J* = 6.9 Hz), 5.20 (s, 1H), 6.67–6.72 (m, 3H), 7.08–7.14 (m, 1H); ^{13}C NMR (75 MHz, MeOD): δ 14.6, 16.7, 31.4, 34.8, 61.4, 62.2, 105.2, 114.5, 116.1, 119.0, 130.8, 143.7, 150.6, 155.7, 159.0, 167.4; HRMS, calcd. for $C_{16}H_{21}N_2O_4$ (M^++1) 305.1501, found 305.1504.

9a. Ethyl 1,3,6-trimethyl-4-(naphthalen-2-yl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



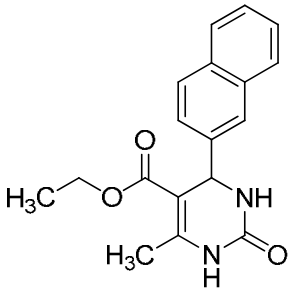
Colorless oil; Yield 93%; IR (neat): 1681, 1623 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, 3H, *J* = 6.9 Hz), 2.40 (s, 3H), 2.96 (s, 3H), 3.31 (s, 3H), 4.14 (q, 2H, *J* = 7.2 Hz), 5.42 (s, 1H), 7.34–7.48 (m, 3H), 7.64 (bs, 1H), 7.76–7.84 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 16.8, 31.1, 34.6, 60.2, 61.2, 103.5, 124.6, 125.6, 126.0, 126.3, 127.7, 128.0, 128.8, 133.0, 133.1, 138.3, 149.4, 153.9, 166.1; HRMS, calcd. For $C_{20}H_{22}N_2O_3$ (M^+) 338.1630, found 338.1629.

11a. Ethyl 1,3,6-trimethyl-2-oxo-4-(thiophen-2-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



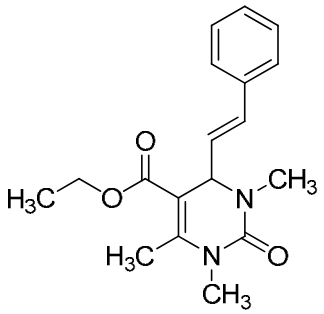
Pale yellow oil; Yield 99%; IR (neat): 1680, 1643 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, 3H, *J* = 6.9 Hz), 2.47 (s, 3H), 2.99 (s, 3H), 3.22 (s, 3H), 4.12–4.21 (m, 2H), 5.49 (s, 1H), 6.85–6.89 (m, 2H), 7.14 (dd, 2H, *J* = 4.5, 1.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 16.4, 31.1, 34.6, 56.3, 60.3, 103.8, 124.5, 124.8, 126.5, 143.8, 150.0, 153.9, 165.5; HRMS, calcd. for $C_{14}H_{18}N_2O_3S$ (M^+) 294.1038, found 294.1036.

12a. Ethyl 6-methyl-4-(naphthalen-2-yl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



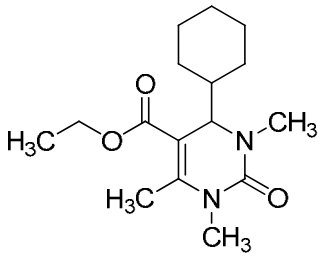
Colorless solid; Yield 70%; M.p. 243-244 ^{o}C; IR (neat): 3240, 1697, 1645, 1091 cm^{-1}; ^{1}H NMR (300 MHz, MeOD): δ 1.12 (t, 3H, *J* = 7.2 Hz), 2.37 (s, 3H), 4.03 (q, 2H, *J* = 7.2 Hz), 5.49 (s, 1H), 7.43–7.49 (m, 3H), 7.71 (d, 1H, *J* = 1.5 Hz), 7.79–7.83 (m, 3H); ^{13}C NMR (75 MHz, MeOD): δ 14.6, 18.3, 56.7, 61.1, 102.0, 125.8, 126.5, 127.1, 127.3, 128.7, 129.1, 129.7, 134.5, 134.8, 136.5, 143.0, 149.2, 167.6; HRMS, calcd. for $C_{18}H_{19}N_2O_3$ (M^++1) 311.1396, found 311.1399.

14a. (*E*)-Ethyl 1,3,6-trimethyl-2-oxo-4-styryl-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



Colorless oil; Yield 72%; IR (neat): 1671, 1038 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.31 (t, 3H, *J* = 7.2 Hz), 2.47, (s, 3H), 3.02 (s, 3H), 3.22 (s, 3H), 4.10–4.26 (m, 2H), 4.78 (d, 1H, *J* = 7.2 Hz), 6.02 (dd, 1H, *J* = 15.6, 6.8 Hz), 6.39 (d, 1H, *J* = 15.6 Hz), 7.20–7.43 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 16.6, 31.2, 34.5, 56.0, 60.3, 101.8, 125.5, 126.7, 128.0, 128.7, 130.6, 136.4, 150.2, 154.3, 165.9; HRMS, calcd. for $C_{18}H_{23}N_2O_3$ (M^++1) 315.1709, found 315.1709.

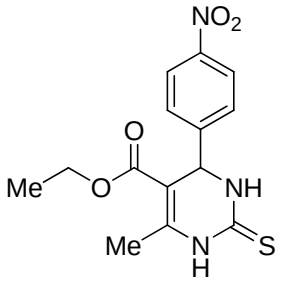
16a. Ethyl 4-cyclohexyl-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



Colorless solid; Yield 95%; M.p. 57-60 ^{o}C; IR (neat): 1671, 1626, 1457 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80–1.18 (m, 5H), 1.27 (t, 3H, *J* = 7.2 Hz), 1.45–1.55 (m, 2H), 1.55–1.64 (m, 2H), 1.64–1.74 (m, 2H), 2.38 (s, 3H), 3.02 (s, 3H), 3.11 (s, 3H), 4.09–4.22 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 16.4, 26.2, 26.3, 26.4, 28.6, 29.0,

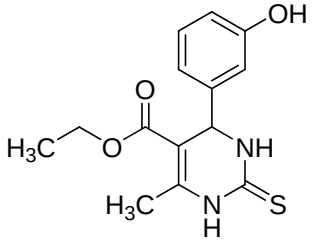
31.0, 37.2, 43.9, 60.1, 61.9, 102.6, 149.5, 154.8, 166.9; HRMS, calcd. for $C_{12}H_{21}N_2O_4$ (M^++1) 295.2022, found 295.2020.

17a. Ethyl 6-methyl-4-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



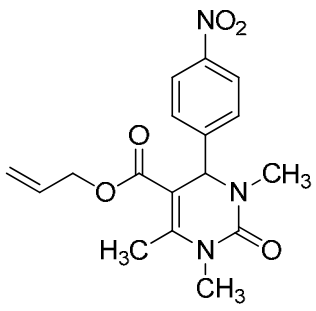
Solid; Yield 85%; M.p. 106–108 ºC; IR (neat): 3106, 1705, 1609, 1527 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.20 (t, 3H, *J* = 6.9 Hz), 2.38, (s, 3H), 4.08–4.15 (m, 2H), 5.51 (d, 1H, *J* = 2.1 Hz), 7.47 (d, 2H, *J* = 8.7 Hz), 7,92 (s, 1H), 8.17 (d, 2H, *J* = 8.7 Hz), 8.27 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 18.6, 55.4, 61.0, 102.2, 124.3, 127.8, 128.4, 143.7, 147.8, 148.9, 164.9; HRMS, calcd. for $C_{14}H_{16}N_3O_4S$ (M^++1) 322.0862, found 302.0859.

18a. Ethyl 4-(3-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



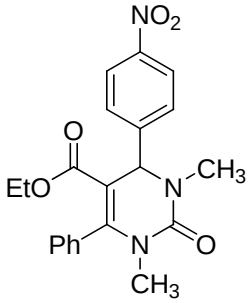
Pale yellow solid; Yield 86%; M.p. 186-188 ^oC; IR (neat): 3384, 1680, 1638, 1589 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.18 (t, 3H, *J* = 8.4 Hz), 2.33 (s, 3H), 4.05–4.14 (m, 2H), 5.34 (s, 1H), 6.72–6.82 (m, 3H), 7.11–7.17 (m, 1H), 7.61 (s, 1H), 7.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2, 18.5, 55.9, 60.7, 102.9, 113.7, 115.6, 118.9, 130.2, 142.8, 143.7, 143.8, 156.2, 165.4; HRMS, calcd. for $C_{14}H_{17}N_2O_3S$ (M^++1) 293.00960, found 293.0965.

20a. Allyl 1,3,6-trimethyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



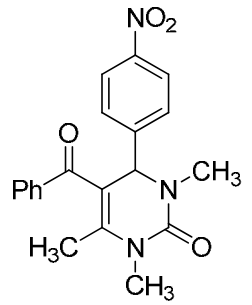
Pale yellow solid; Yield 83%; M.p. 213-215 ^{o}C; IR (neat): 1706, 1602, 1532 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.46 (s, 3H), 2.88 (s, 3H), 3.23 (s, 3H), 4.55 (d, 2H, *J* = 5.7 Hz), 5.15–5.22 (m, 2H), 5.34 (s, 1H), 5.77–5.91 (m, 1H), 7.36 (d, 2H, *J* = 9.0 Hz), 8.09 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.8, 31.2, 34.7, 60.3, 65.2, 102.1, 118.6, 124.0, 127.6, 128.3, 132.1, 147.5, 148.2, 150.9, 153.4, 165.2; HRMS, calcd. for $C_{17}H_{20}N_3O_5$ (M^++1) 346.1403, found 346.1419.

22a. Ethyl 1,3-dimethyl-4-(4-nitrophenyl)-2-oxo-6-phenyl-1,2,3,4 tetrahydropyrimidine-5-carboxylate



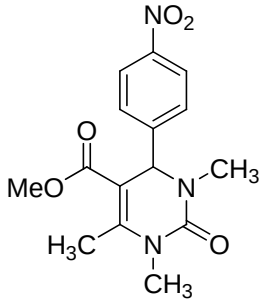
Pale yellow solid; Yield 94%; M.p. 159-161 ^{o}C; IR (neat): 1674, 1600, 1522 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (t, 2H, *J* = 6.8 Hz), 2.86, (s, 3H), 3.02 (s, 3H), 3.79 (t, 2H, *J* = 6.4 Hz), 5.47 (s, 1H), 7.02–7.22 (m, 2H), 7.32–7.49 (m, 3H), 7.57 (d, 2H, *J* = 8.4 Hz), 8.22 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5, 33.5, 34.9, 60.3, 60.7, 103.6, 124.3, 127.3, 127.5, 128.4, 128.6, 129.0, 129.2, 134.6, 147.8, 148.4, 151.5, 153.9, 165.4; HRMS, calcd. for $C_{12}H_{22}N_3O_5$ (M^++1) 396.1559, found 396.1555.

24a. 5-Benzoyl-1,3,6-trimethyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one:



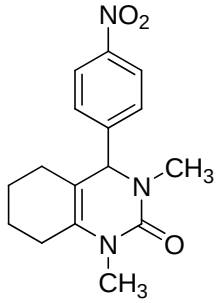
Yellow solid; Yield 95%; M.p. 158-160 ^{o}C; IR (neat): 1667, 1623 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.80 (s, 3H,), 3.0 (s, 3H), 3.24 (s, 3H), 5.55 (s, 1H), 7.35–7.42 (m, 5H), 7.48–7.53 (m, 2H), 8.13–8.16 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.0, 31.1, 34.9, 61.3, 112.2, 124.3, 127.0, 128.3, 128.9, 132.4, 140.5, 145.9, 147.6, 147.9, 153.8, 195.3; HRMS, calcd. for $C_{20}H_{20}N_3O_4$ (M^++1) 366.1454, found 366.1447.

26a. Methyl 1,3,6-trimethyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



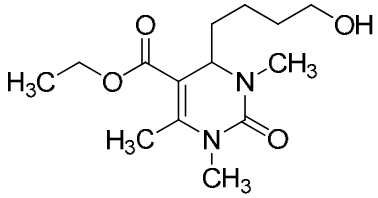
Pale yellow solid; Yield 97%; M.p. 142-144 ^{o}C; IR (neat): 1671, 1521, 1026 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H), 2.91 (s, 3H), 3.25 (s, 3H), 3.68 (s, 3H), 5.34 (s, 1H), 7.37 (d, 2H, J = 8.0 Hz), 8.09–8.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.8, 31.3, 34.7, 51.5, 60.3, 102.3, 124.1, 127.5, 147.5, 148.2, 150.7, 153.5, 166.0; HRMS, calcd. for $C_{15}H_{18}N_3O_5$ (M^++1) 320.1246, found 320.1255.

28a. 1,3-Dimethyl-4-(4-nitrophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-one:



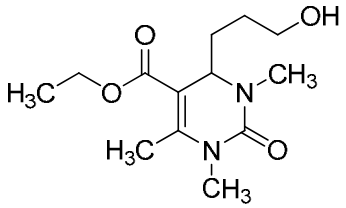
Yellow oil; Yield 70%; IR (neat): 1621cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38–1.47 (m, 1H), 1.57–1.69 (m, 4H), 1.85–1.92 (m, 1H), 2.21–2.27 (m, 2H), 2.77 (s, 3H), 3.15 (s, 3H), 4.54 (s, 1H), 7.35–7.40 (m, 2H), 8.16–8.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7, 22.5, 25.4, 25.9, 29.5, 34.1, 66.6, 106.6, 124.1, 127.7, 131.5, 147.7, 148.7, 154.1; HRMS, calcd. for $C_{16}H_{20}N_3O_3$ (M^++1) 302.1505, found 302.1511.

30a. Ethyl 4-(4-hydroxybutyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



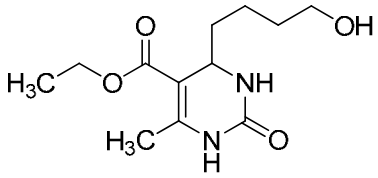
Colorless oil; Yield 97%; IR (neat): 3432, 1661, 1465 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24–1.37 (m, 5H), 1.48–1.58 (m, 4H), 1.77–1.84 (s, 1H) 2.41 (s, 3H), 3.0 (s, 3H), 3.15 (s, 3H), 3.58 (t, 2H, J = 6.4 Hz), 4.12–4.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 16.5, 21.2, 31.1, 32.9, 33.2, 35.4, 56.9, 60.2, 62.7, 103.3, 150.1, 154.5, 166.4; HRMS, calcd. for $C_{14}H_{25}N_2O_4$ (M^++1) 285.1814, found 285.1813.

32a. Ethyl 4-(3-hydroxypropyl)-1,3,6-trimethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:

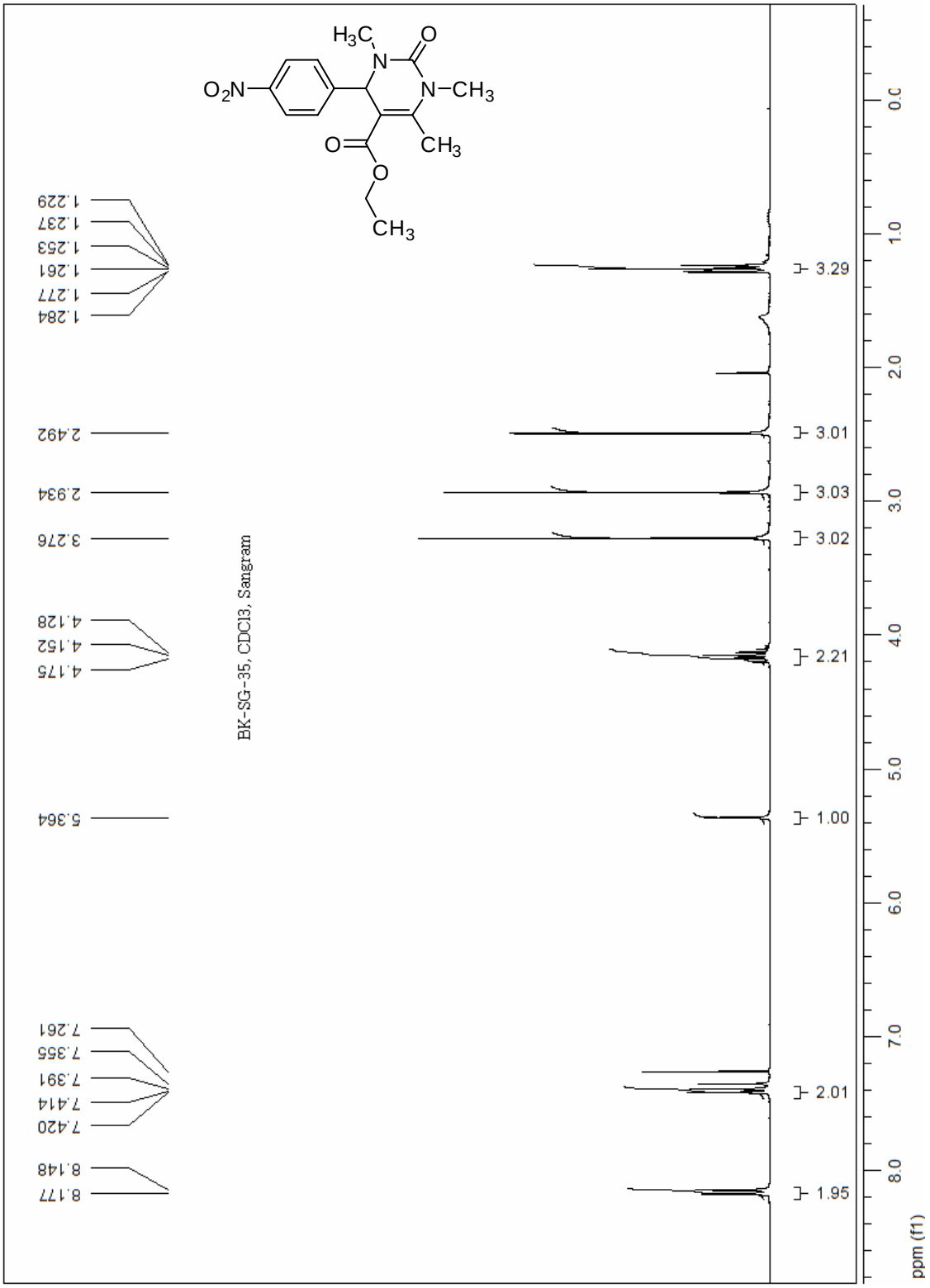


Colorless solid; Yield 94%; M.p. 49-51 ^{o}C; IR (neat): 3243, 1664, 1060 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (t, 3H, *J* = 7.2 Hz), 1.40–1.62, (m, 4H), 1.91–1.99 (s, 1H), 2.41 (s, 3H), 2.99 (s, 3H), 3.14 (s, 3H), 3.57 (t, 3H, *J* = 6.4 Hz), 4.11–4.20 (m, 2H), 4.27 (t, 2H, *J* = 5.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 16.5, 27.8, 29.6, 31.1, 35.2, 56.7, 60.2, 62.8, 102.9, 150.2, 154.4, 166.4; HRMS, calcd. for $C_{13}H_{23}N_2O_4$ (M^++1) 271.1658, found 271.1653.

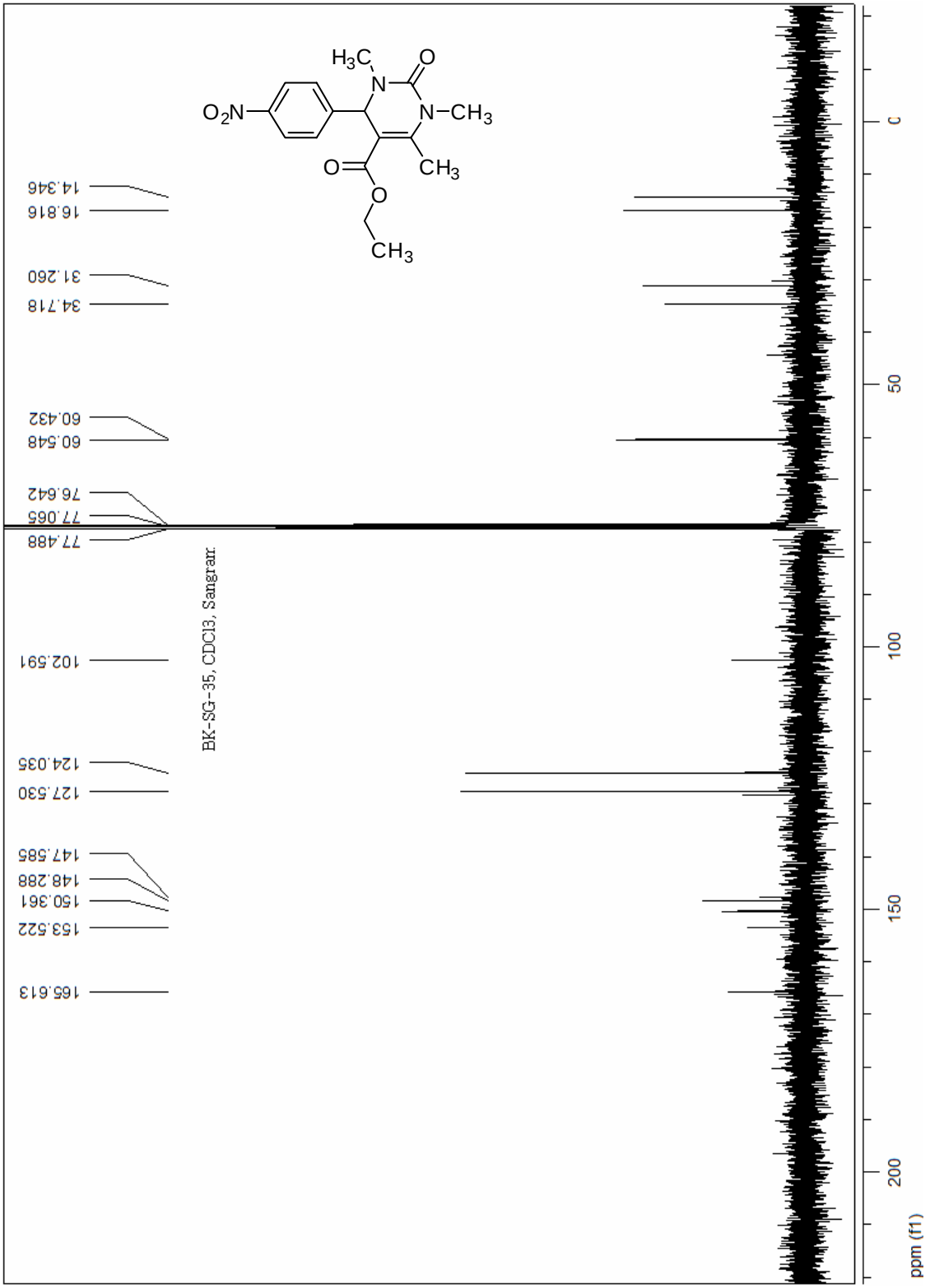
33a. Ethyl 4-(4-hydroxybutyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:



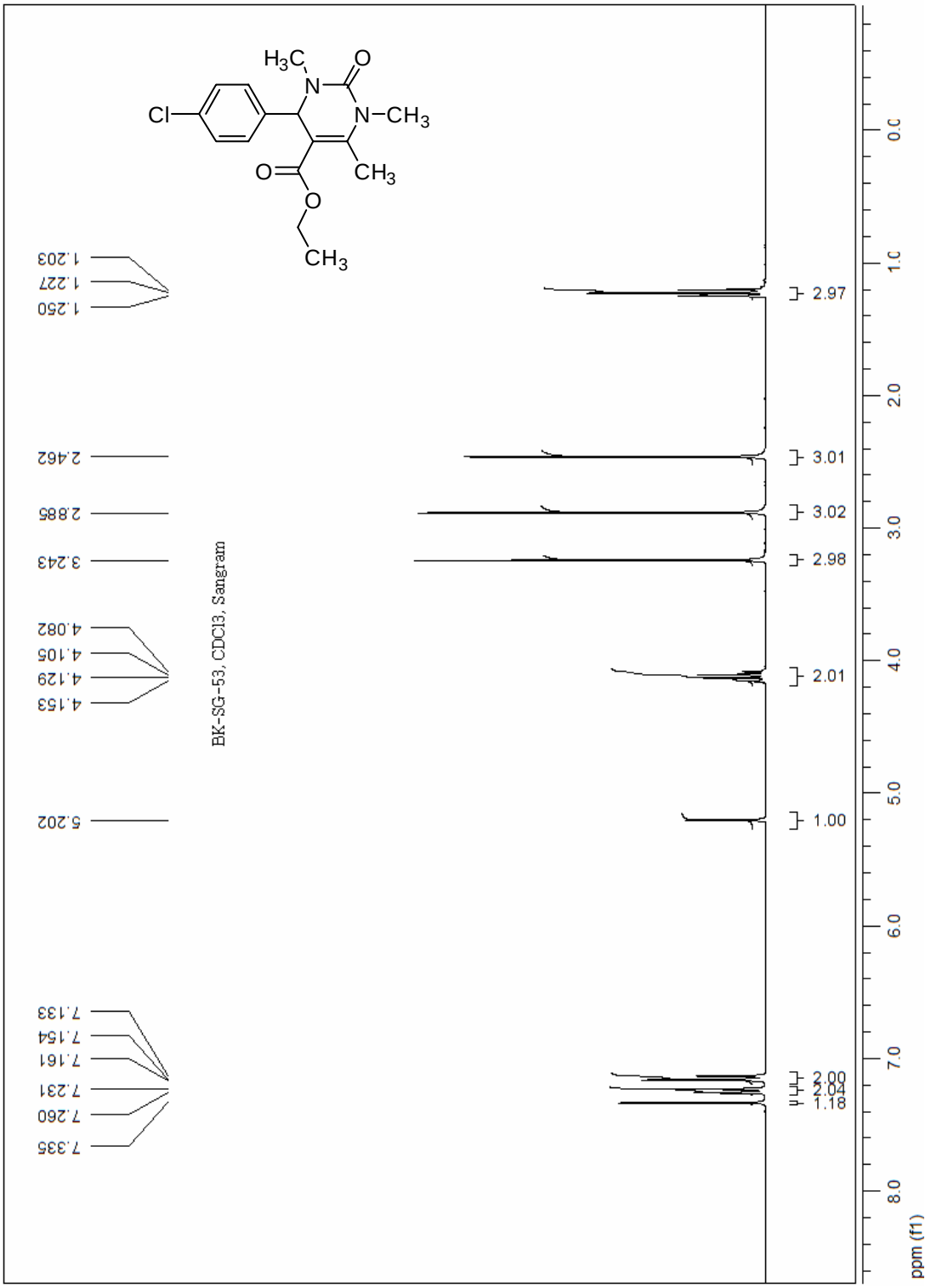
Colorless solid; Yield 87%; M.p. 140-142 ^{o}C; IR (neat): 3420, 1696, 1087 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (t, 3H, *J* = 7.2 Hz), 1.40–1.68, (m, 6H), 2.26 (s, 3H), 2.47 (s, 1H), 3.14 (s, 1H), 3.54–3.70 (m, 2H), 4.09–4.22 (m, 2H), 4.27–4.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 18.6, 20.7, 32.0, 36.5, 51.1, 60.1, 62.4, 101.7, 146.9, 155.1, 166.1; HRMS, calcd. for $C_{12}H_{21}N_2O_4$ (M^++1) 257.1501, found 257.1503.



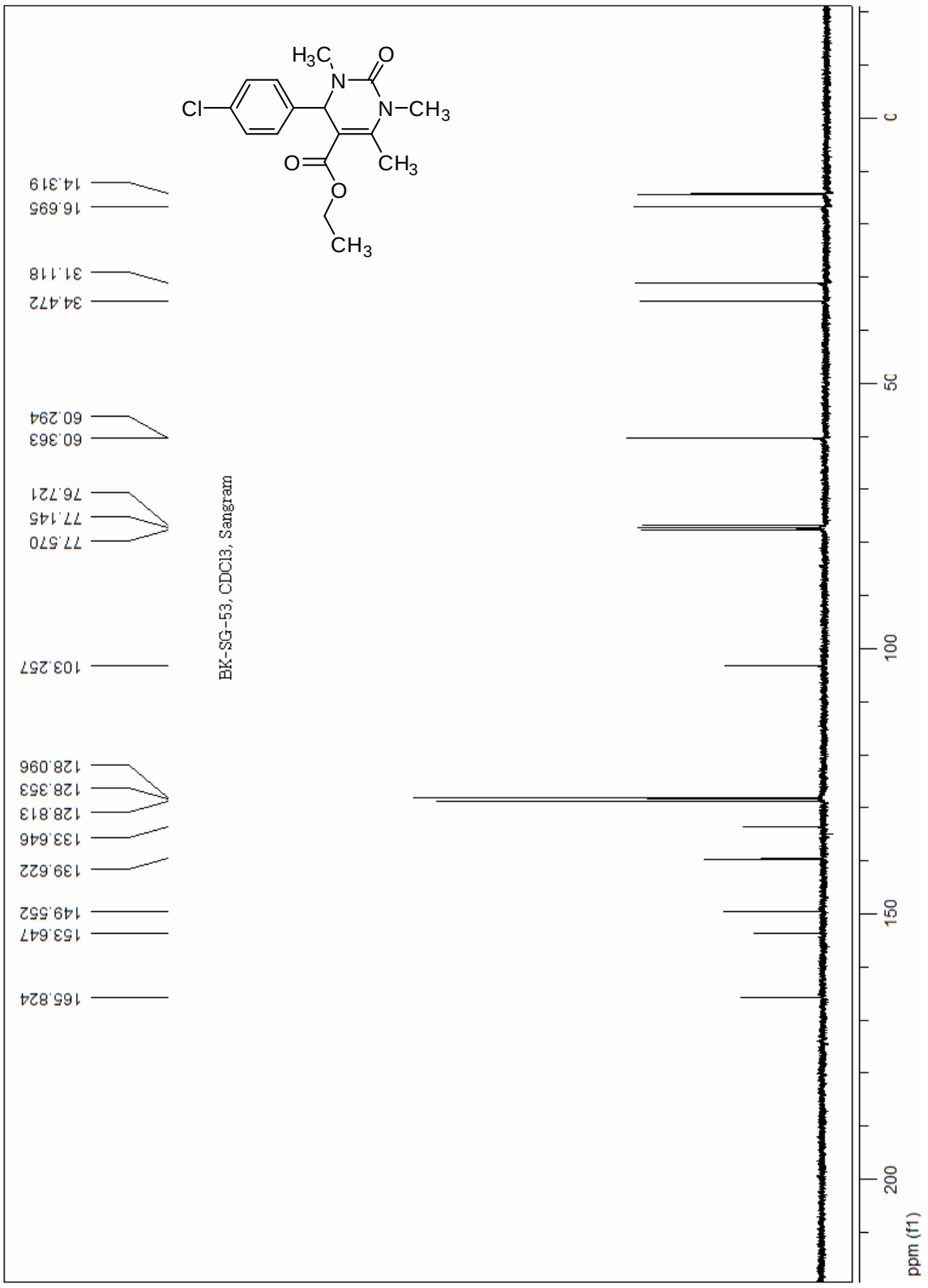
^{1}H NMR spectra of compound **2a**



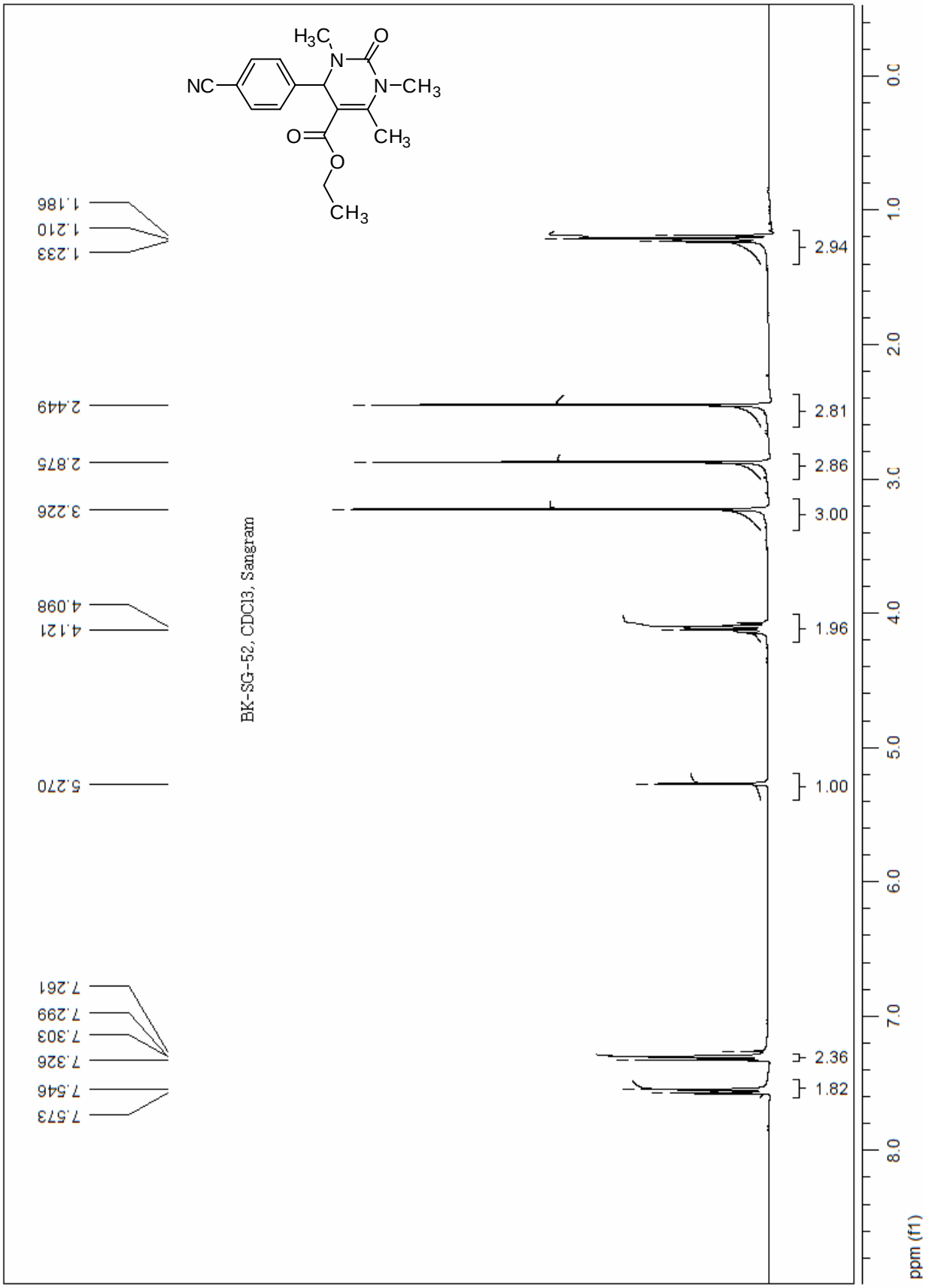
^{13}C NMR spectra of compound **2a**



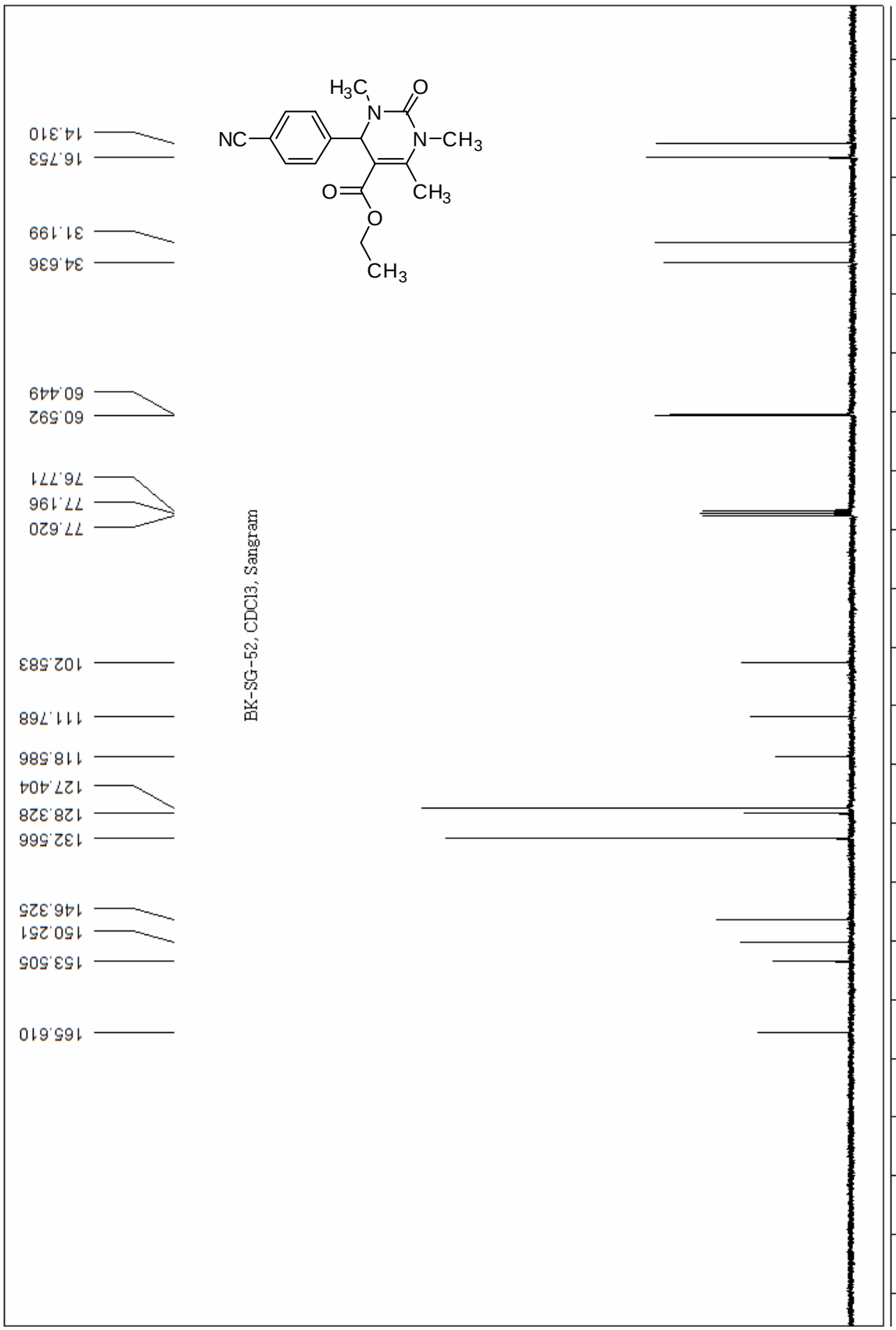
^{1}H NMR spectra of compound **2b**



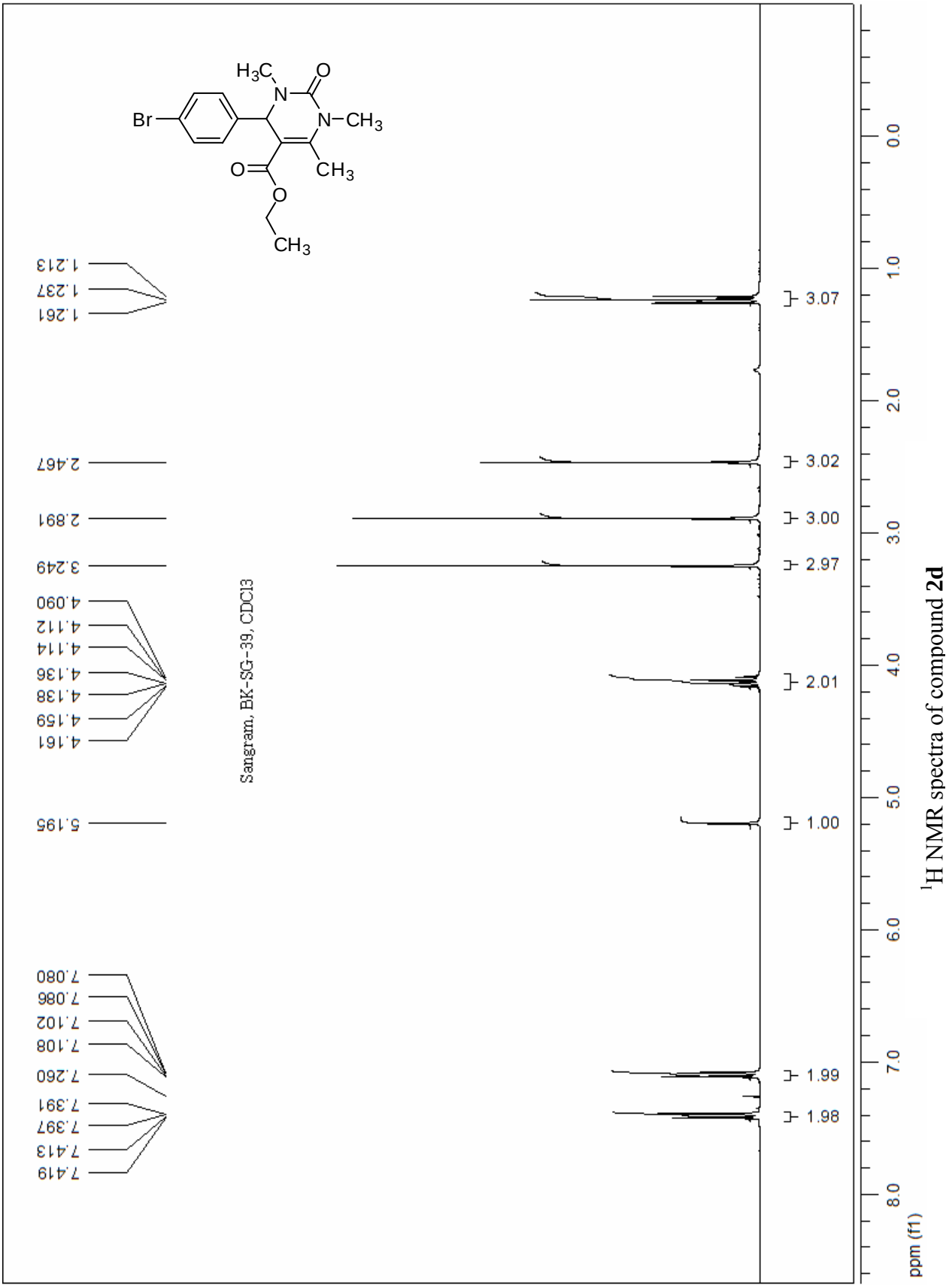
^{13}C NMR spectra of compound **2b**



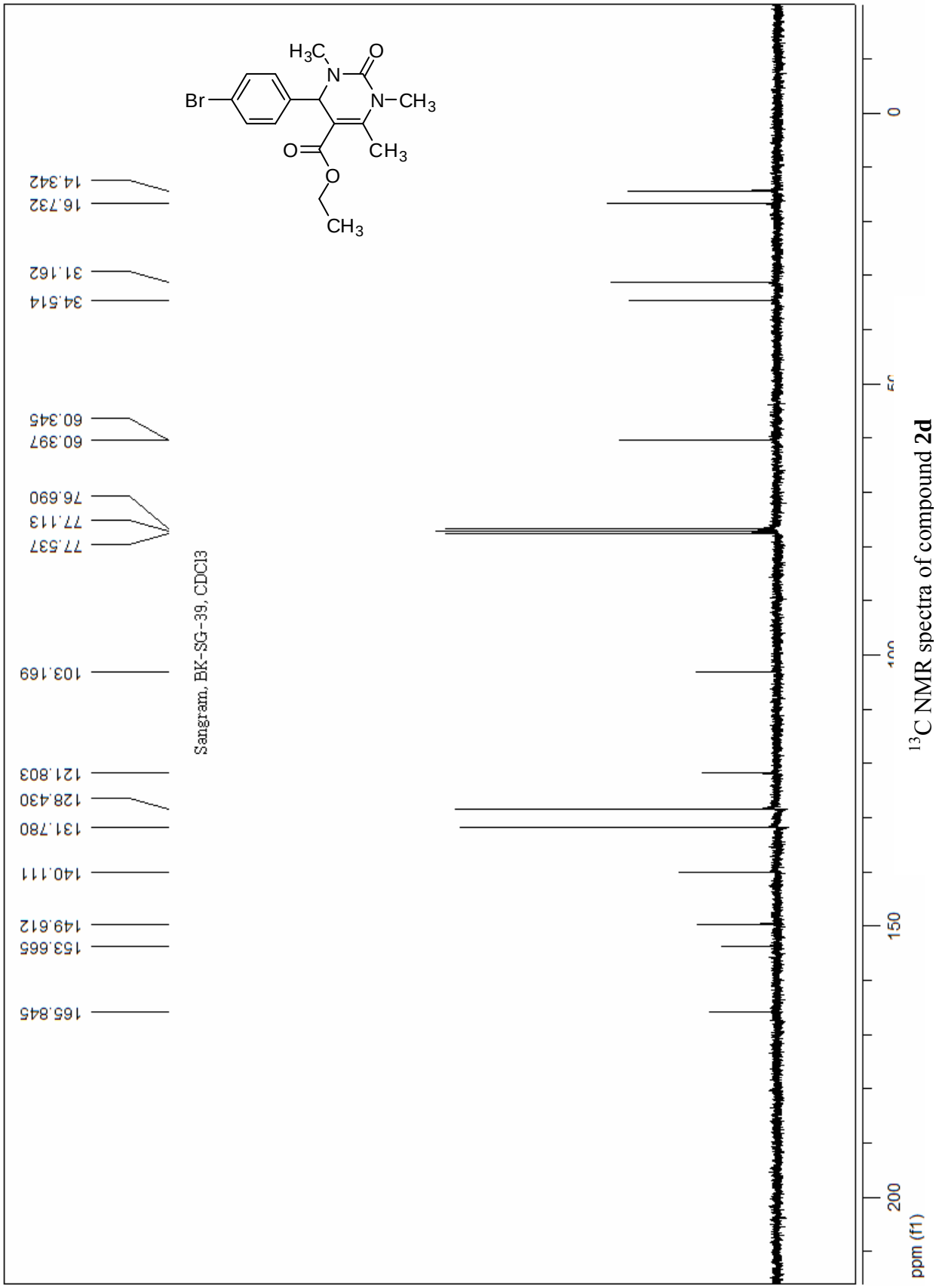
^{1}H NMR spectra of compound **2c**



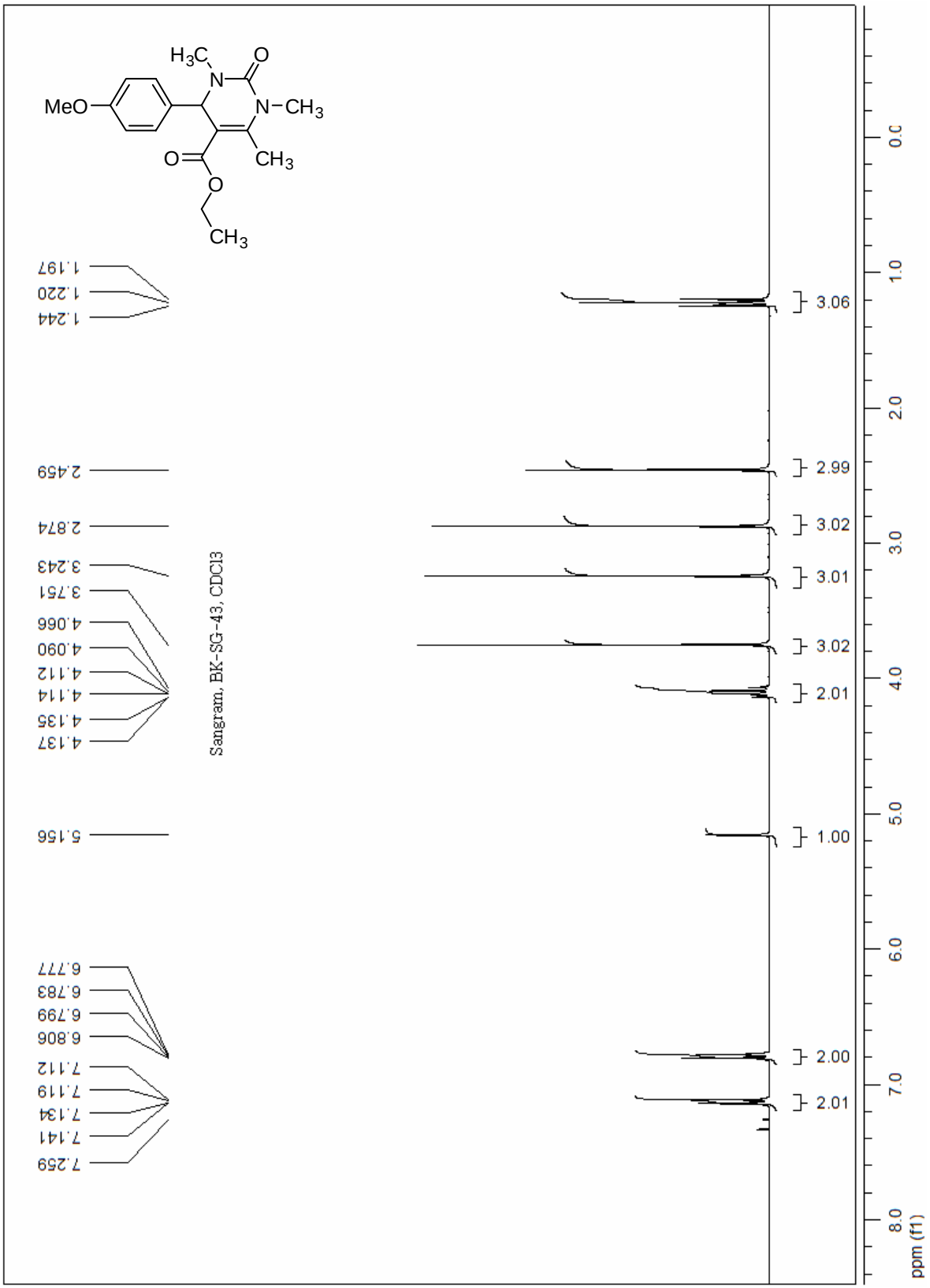
^{13}C NMR spectra of compound **2c**



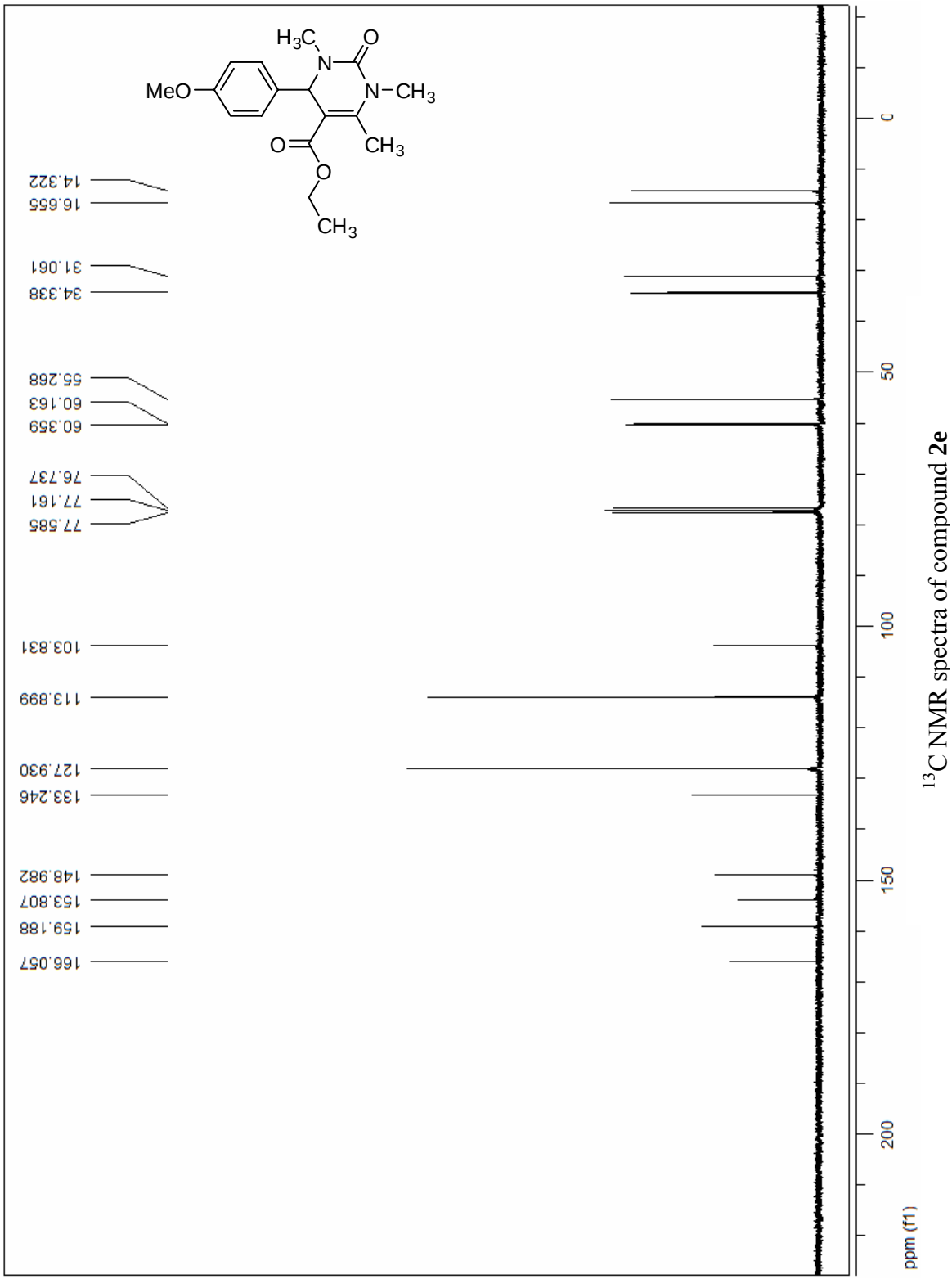
^{1}H NMR spectra of compound **2d**



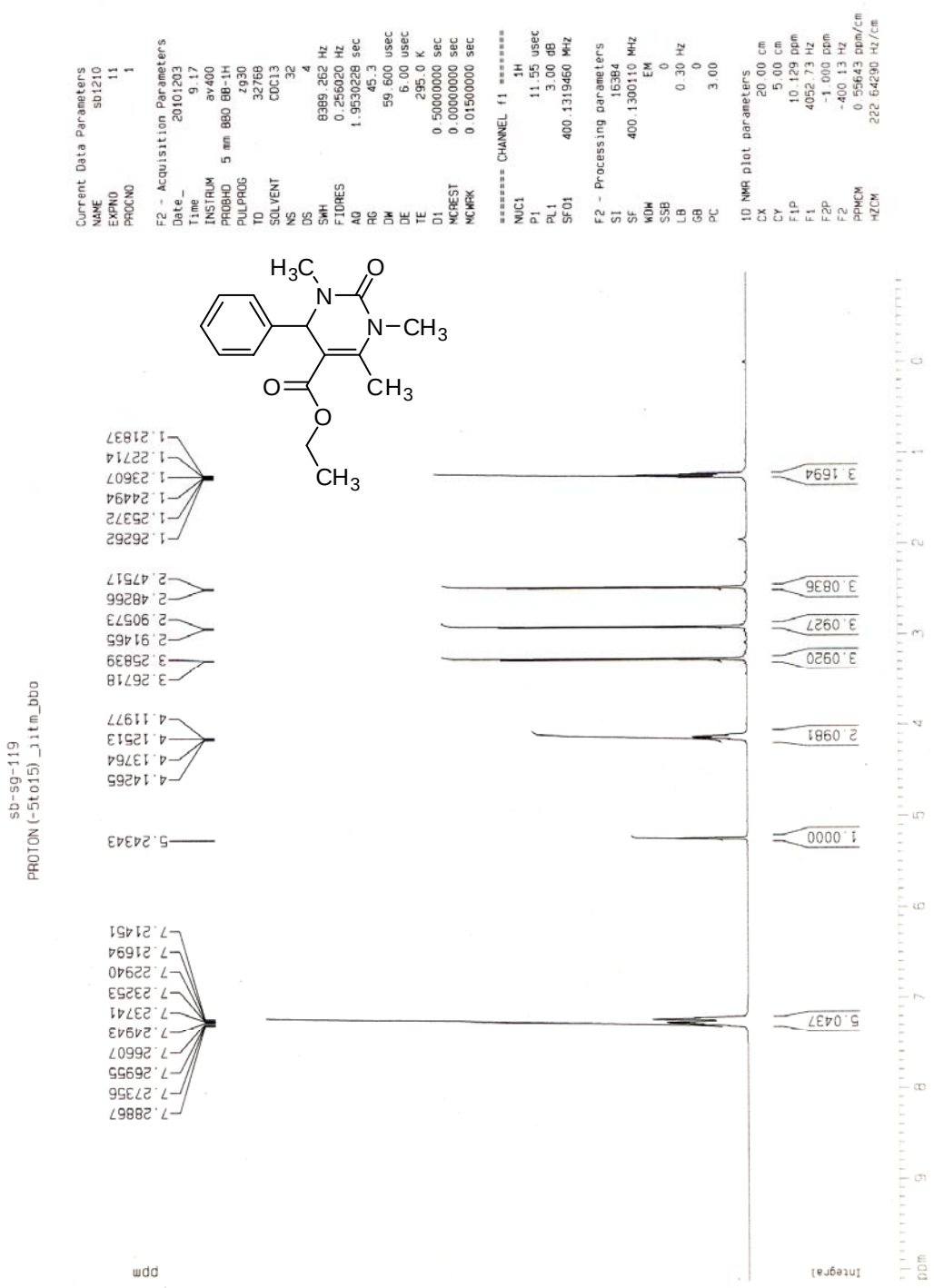
^{13}C NMR spectra of compound **2d**



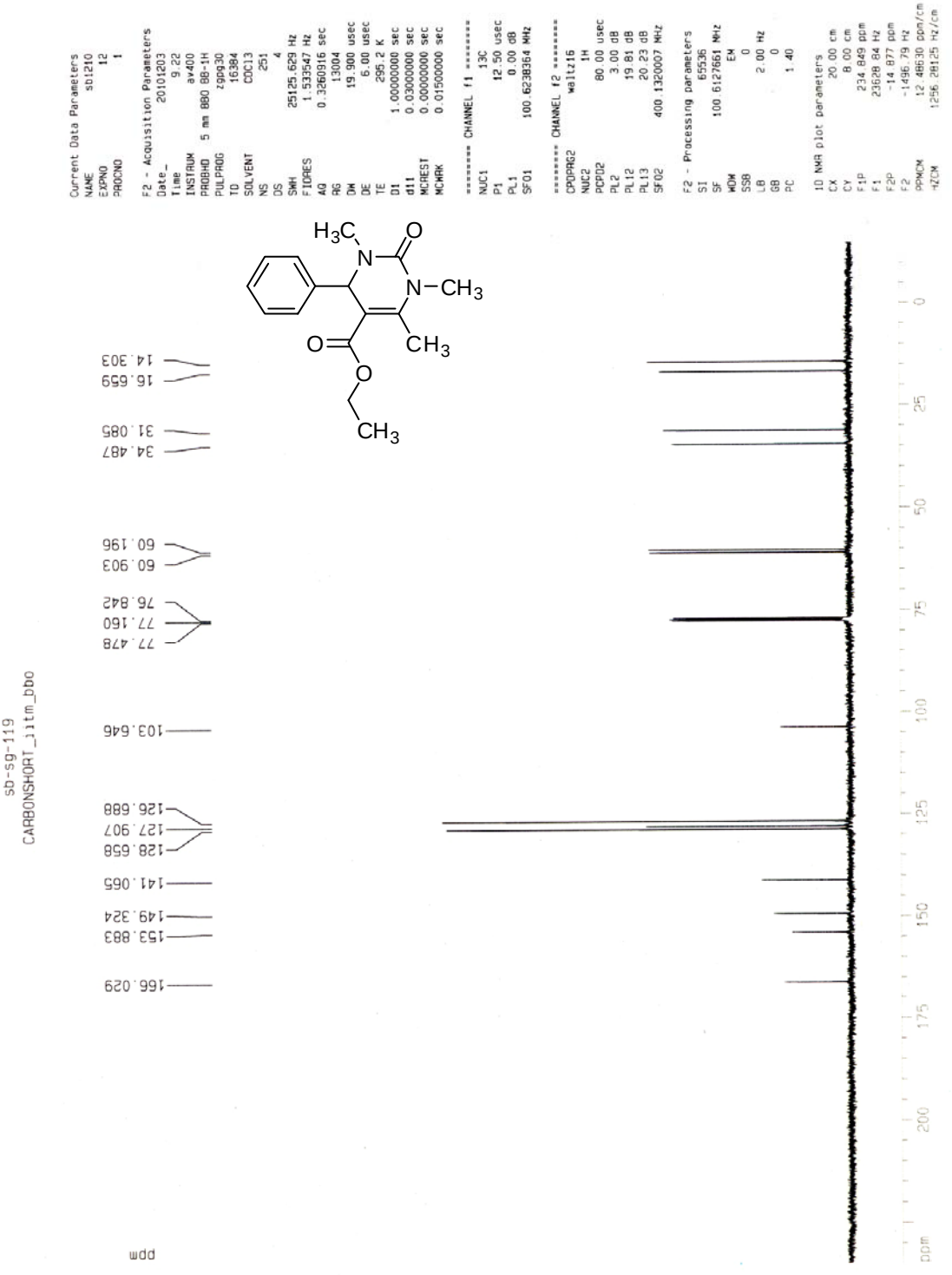
^{1}H NMR spectra of compound **2e**



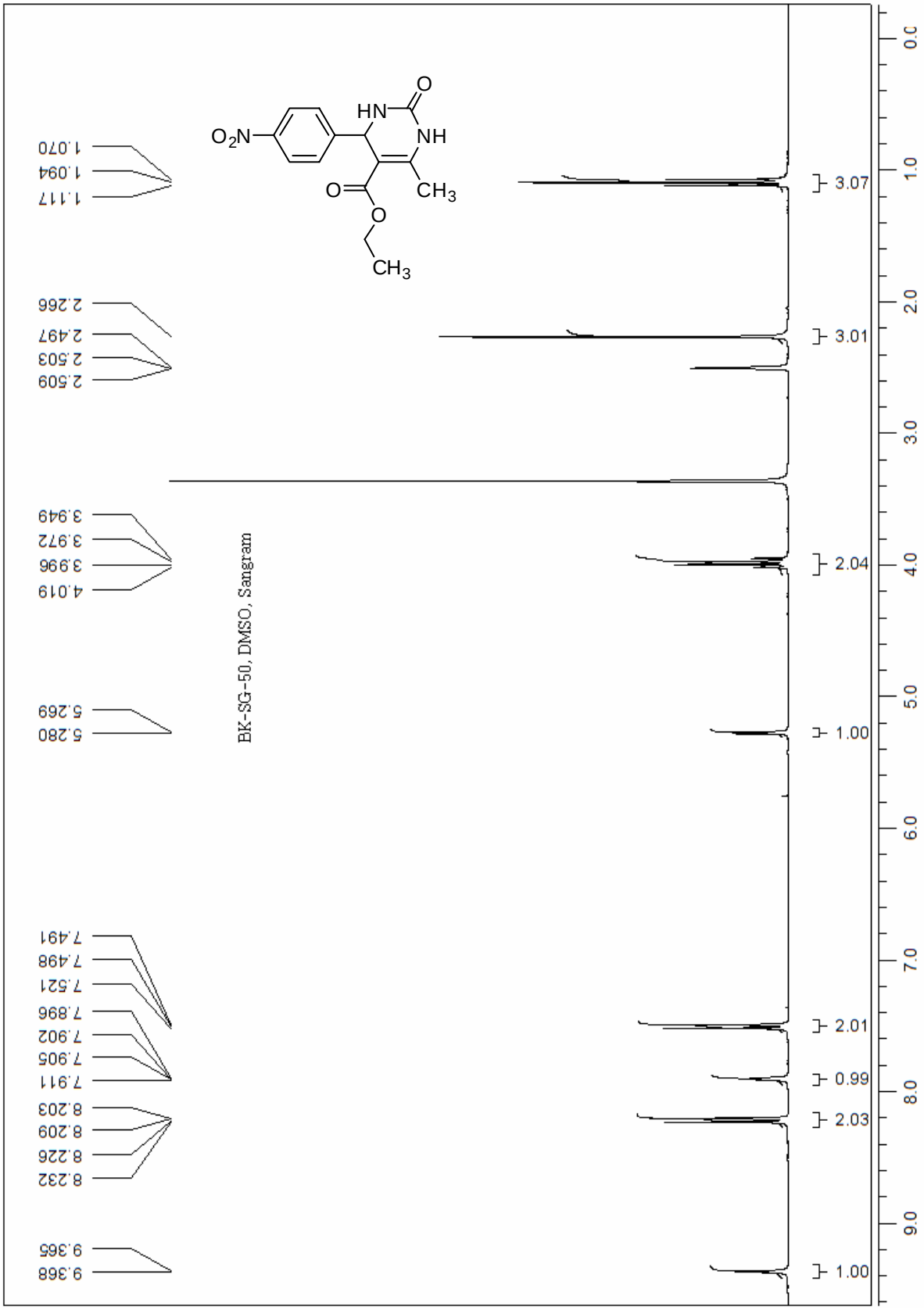
^{13}C NMR spectra of compound **2e**



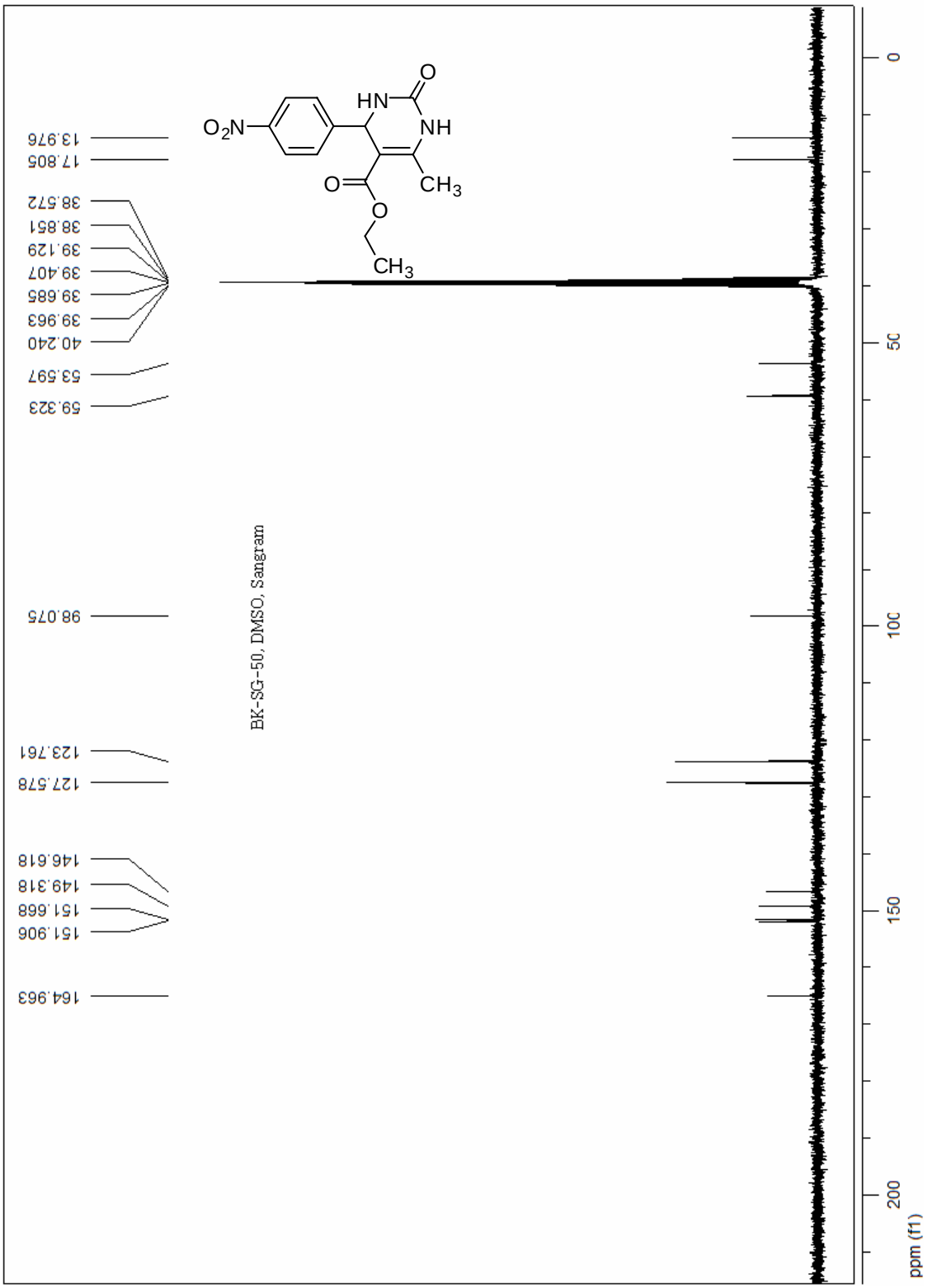
^{1}H NMR spectra of compound **2f**



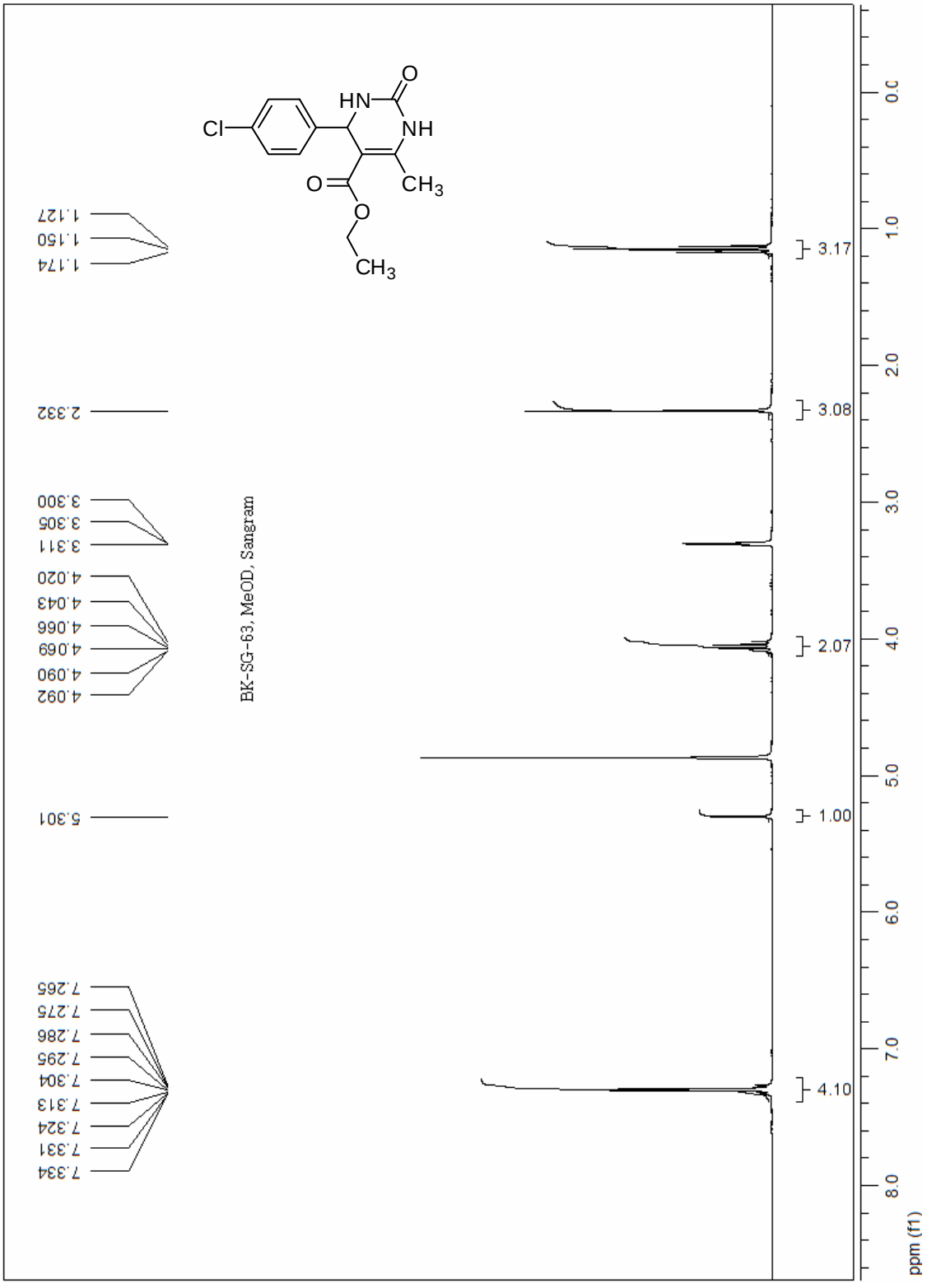
^{13}C NMR spectra of compound **2f**



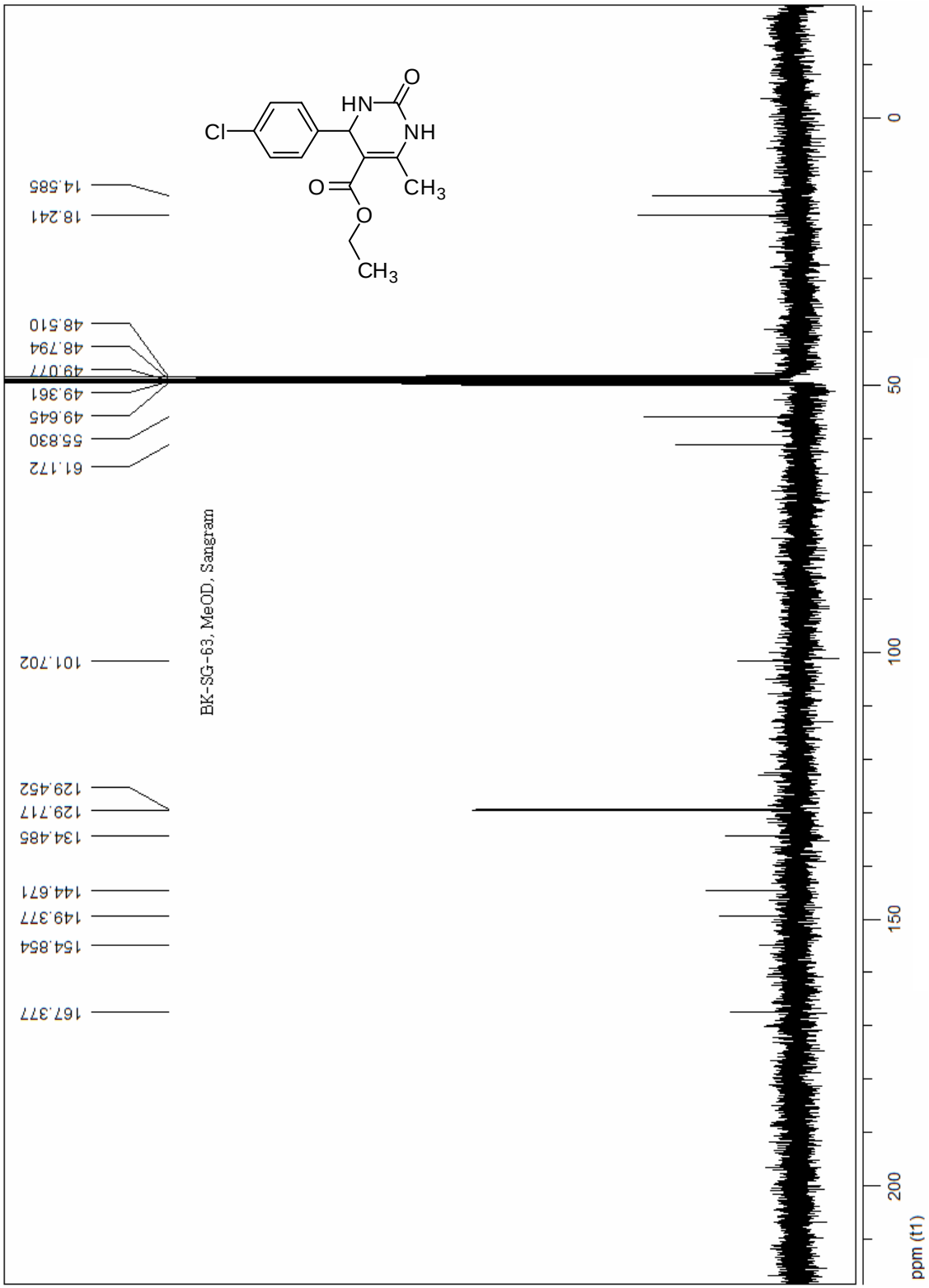
^{1}H NMR spectra of compound **3a**



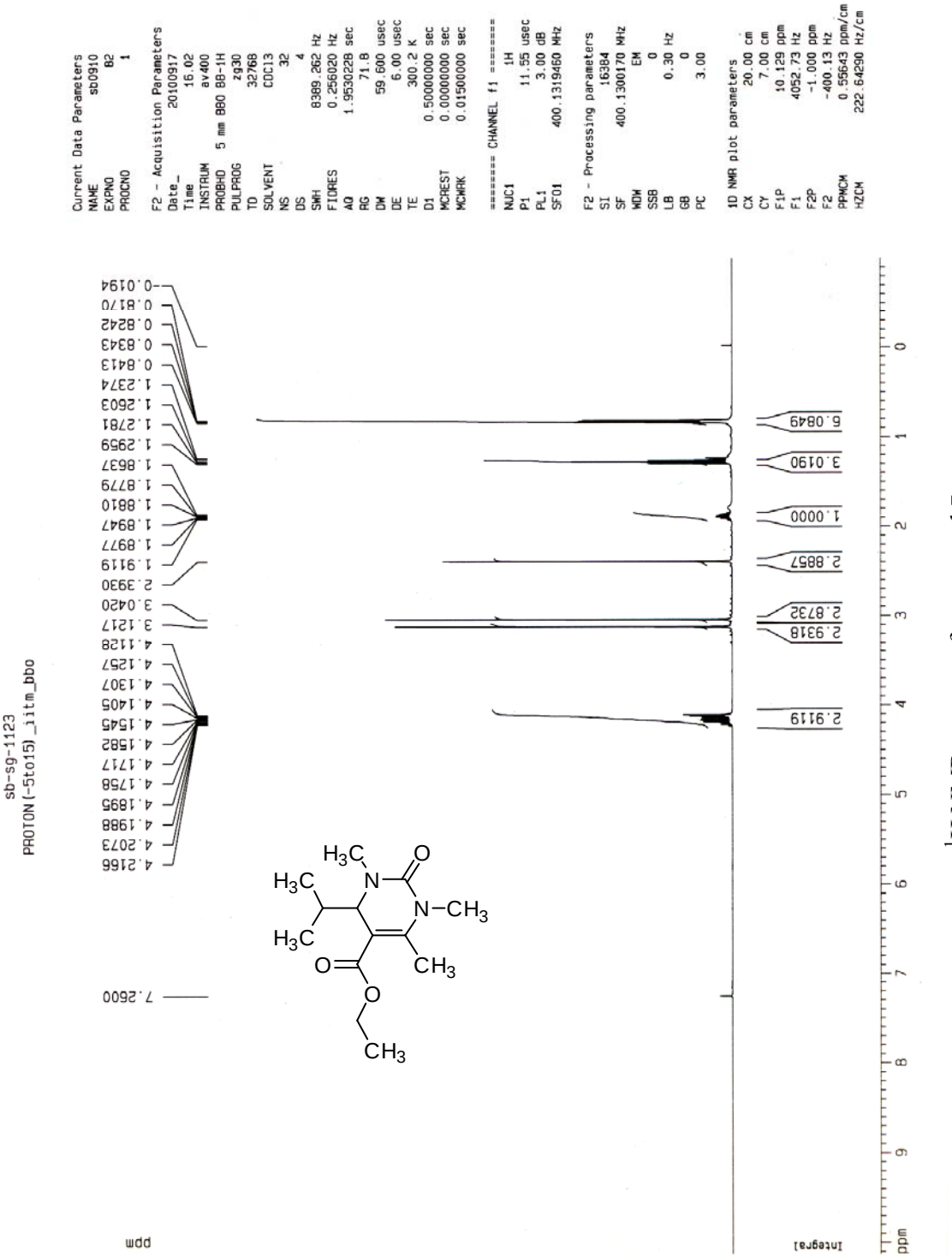
^{13}C NMR spectra of compound **3a**



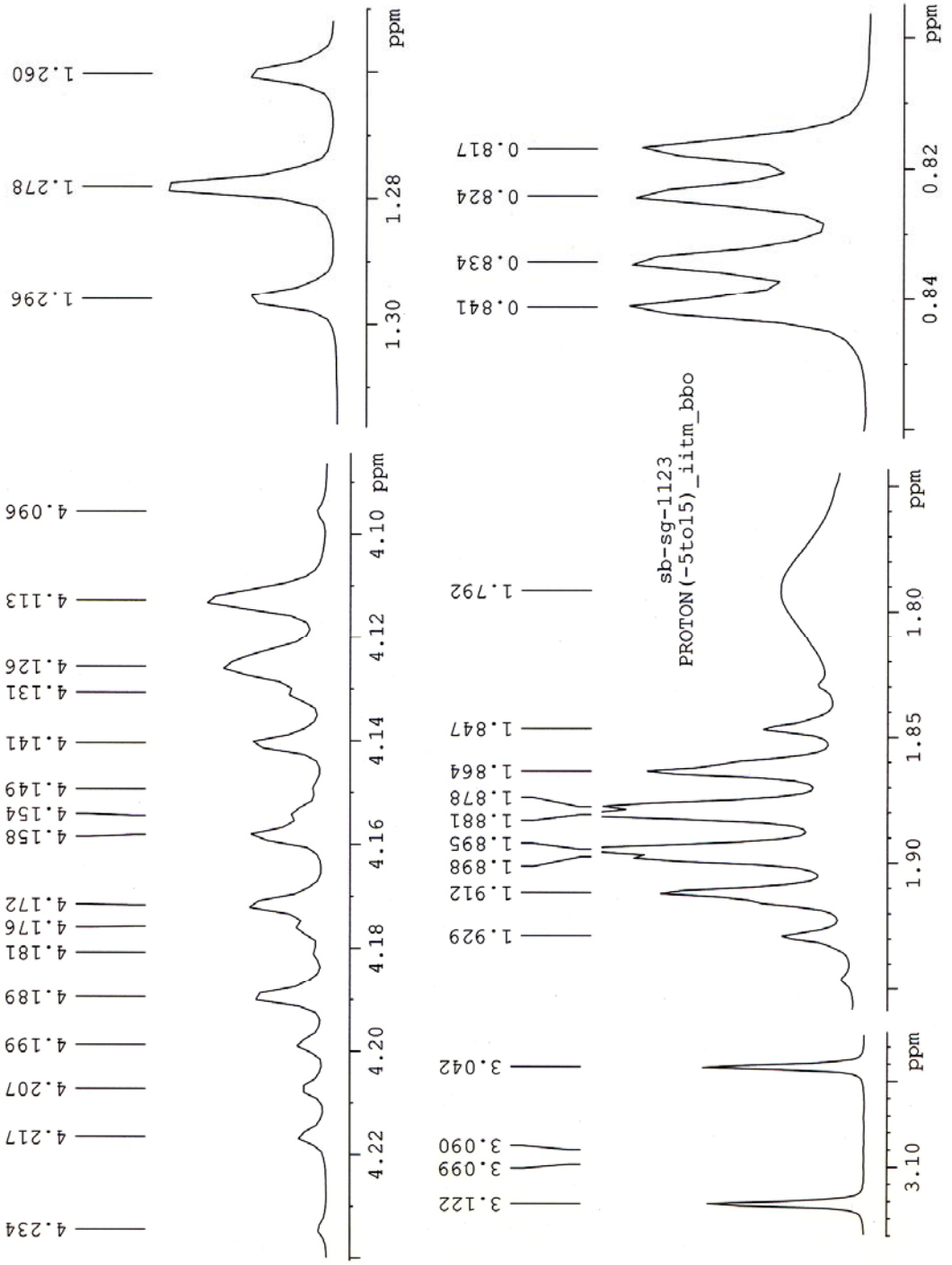
^{1}H NMR spectra of compound **3b**



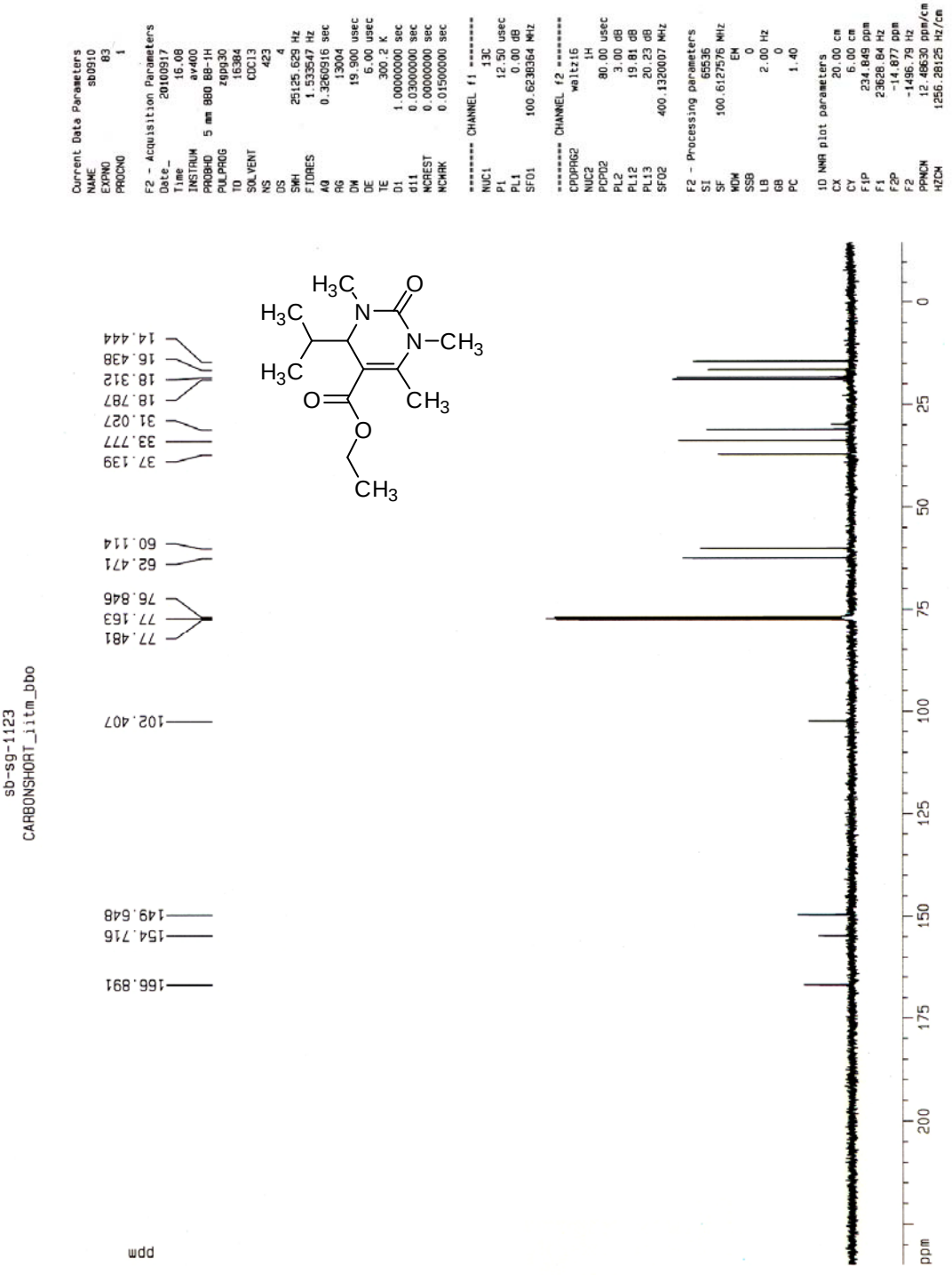
^{13}C NMR spectra of compound **3b**



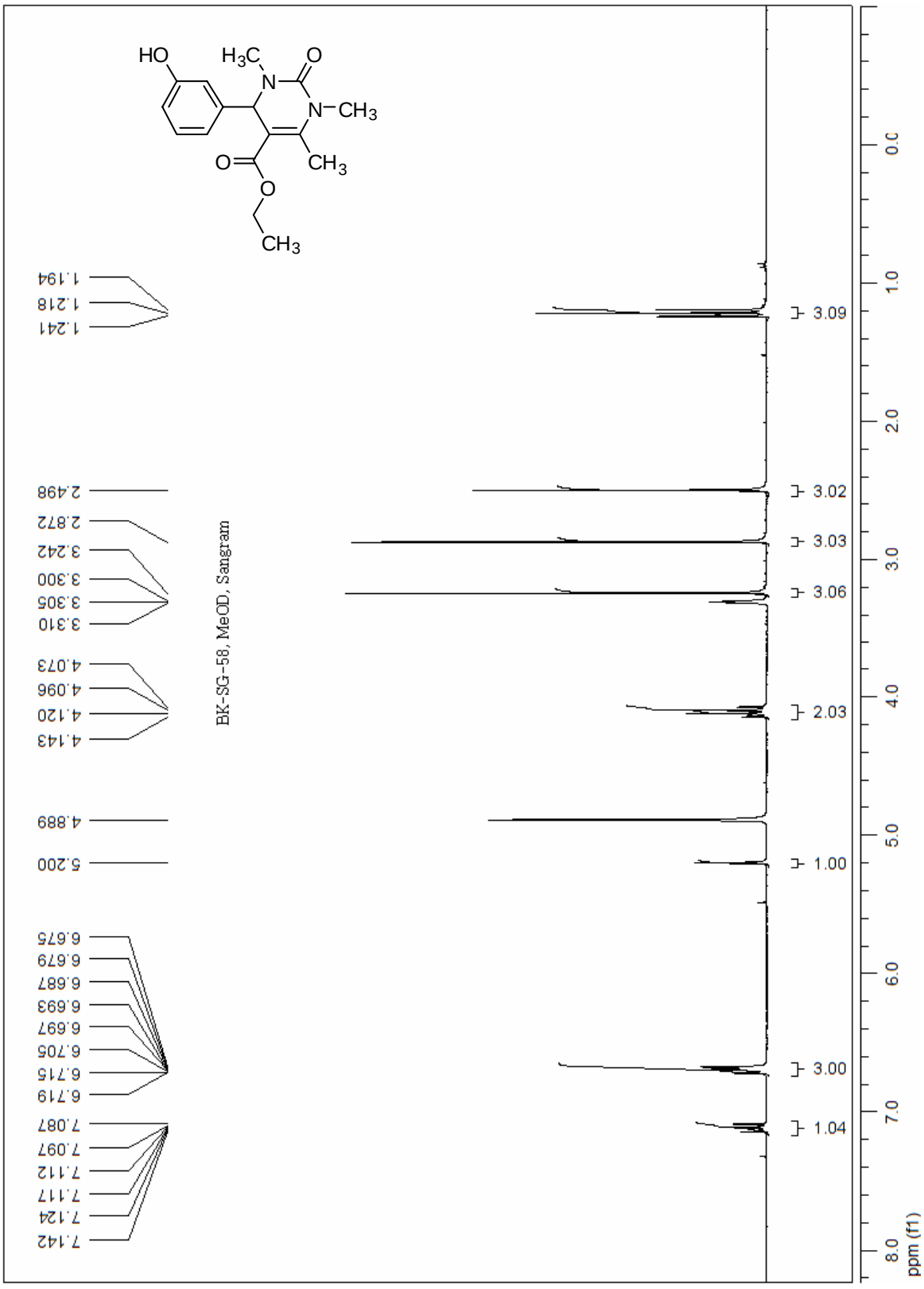
^{1}H NMR spectra of compound **5a**



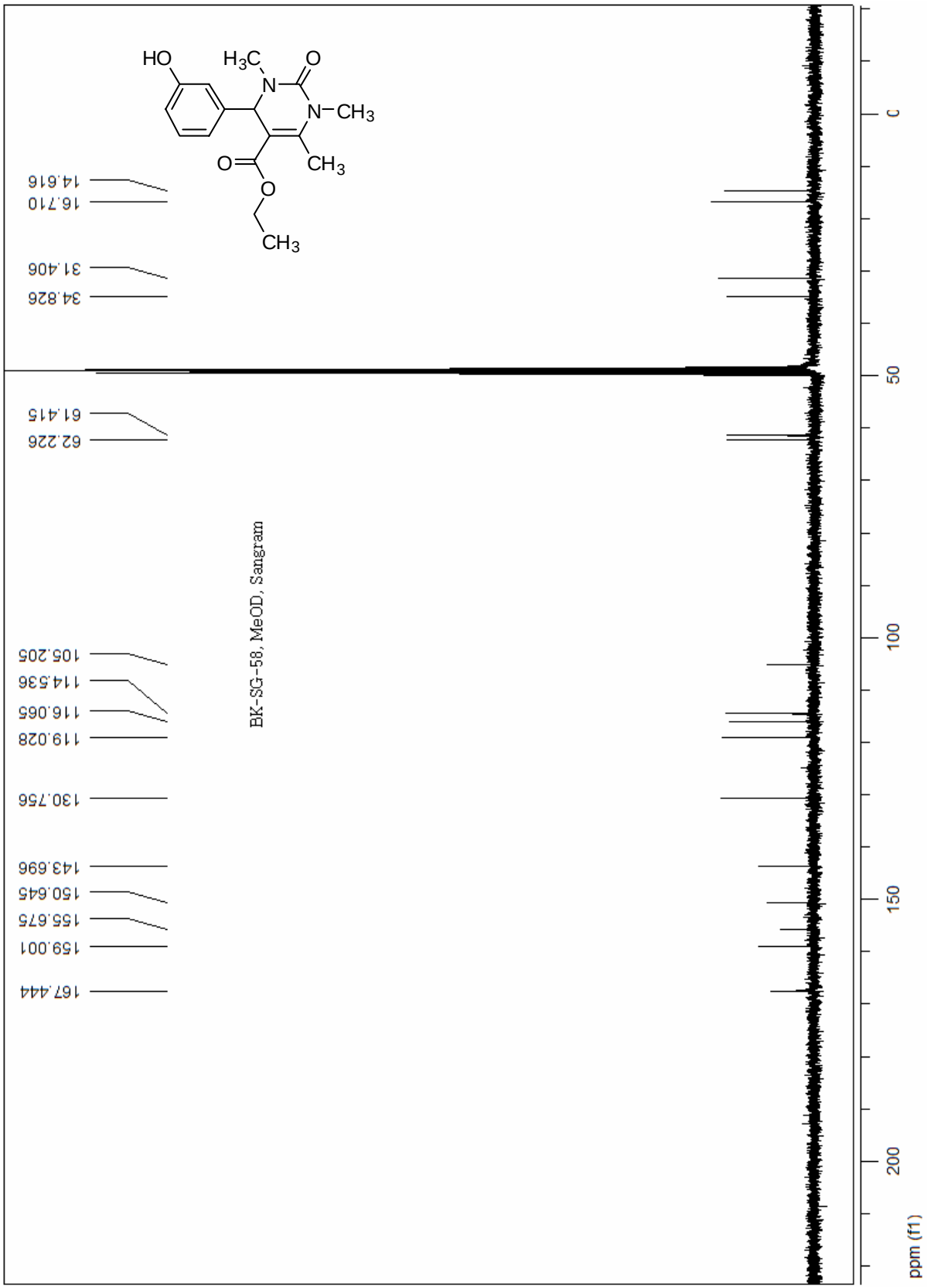
Expanded ^{1}H NMR spectra of compound **5a**



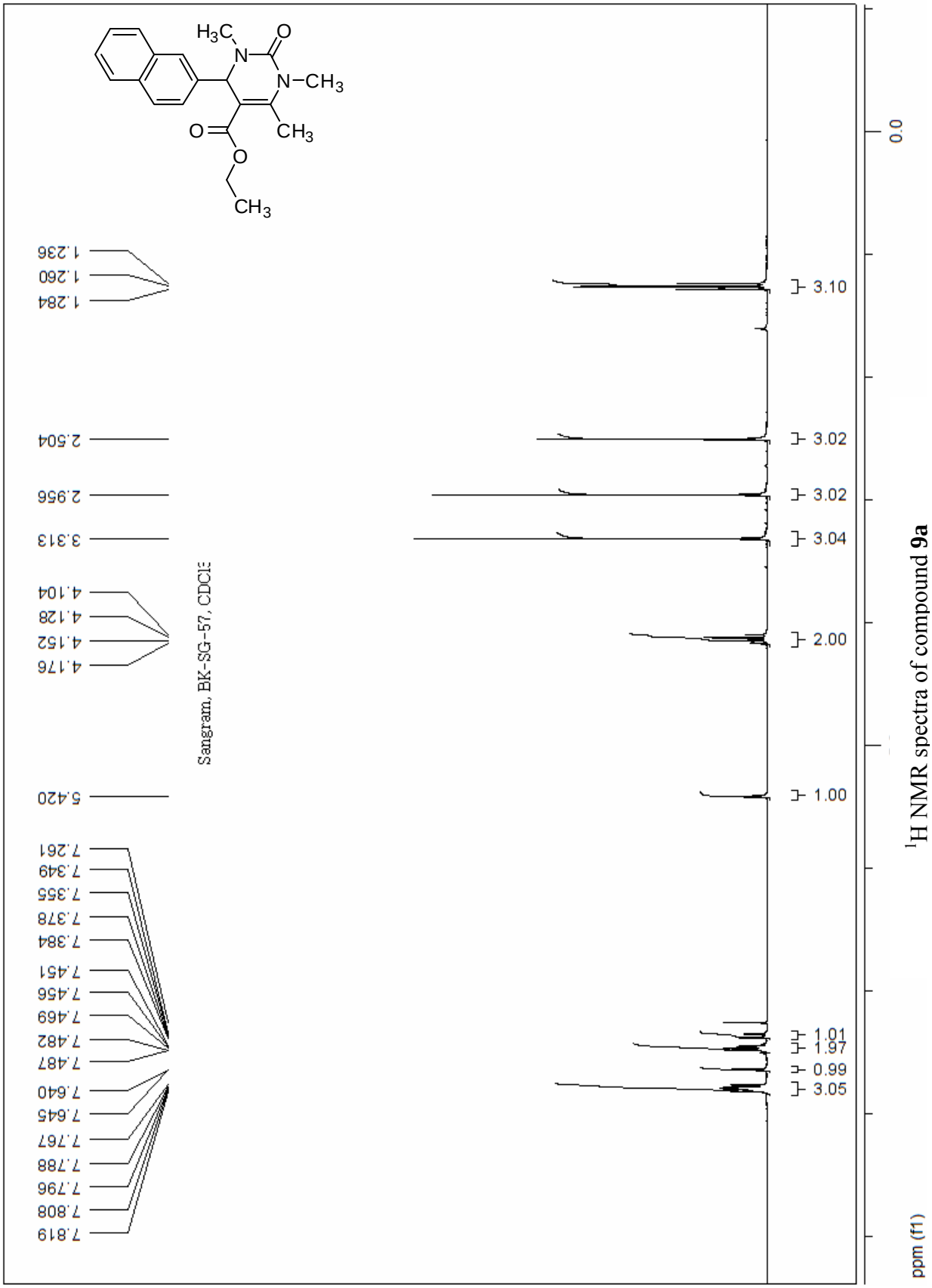
^{13}C NMR spectra of compound **5a**



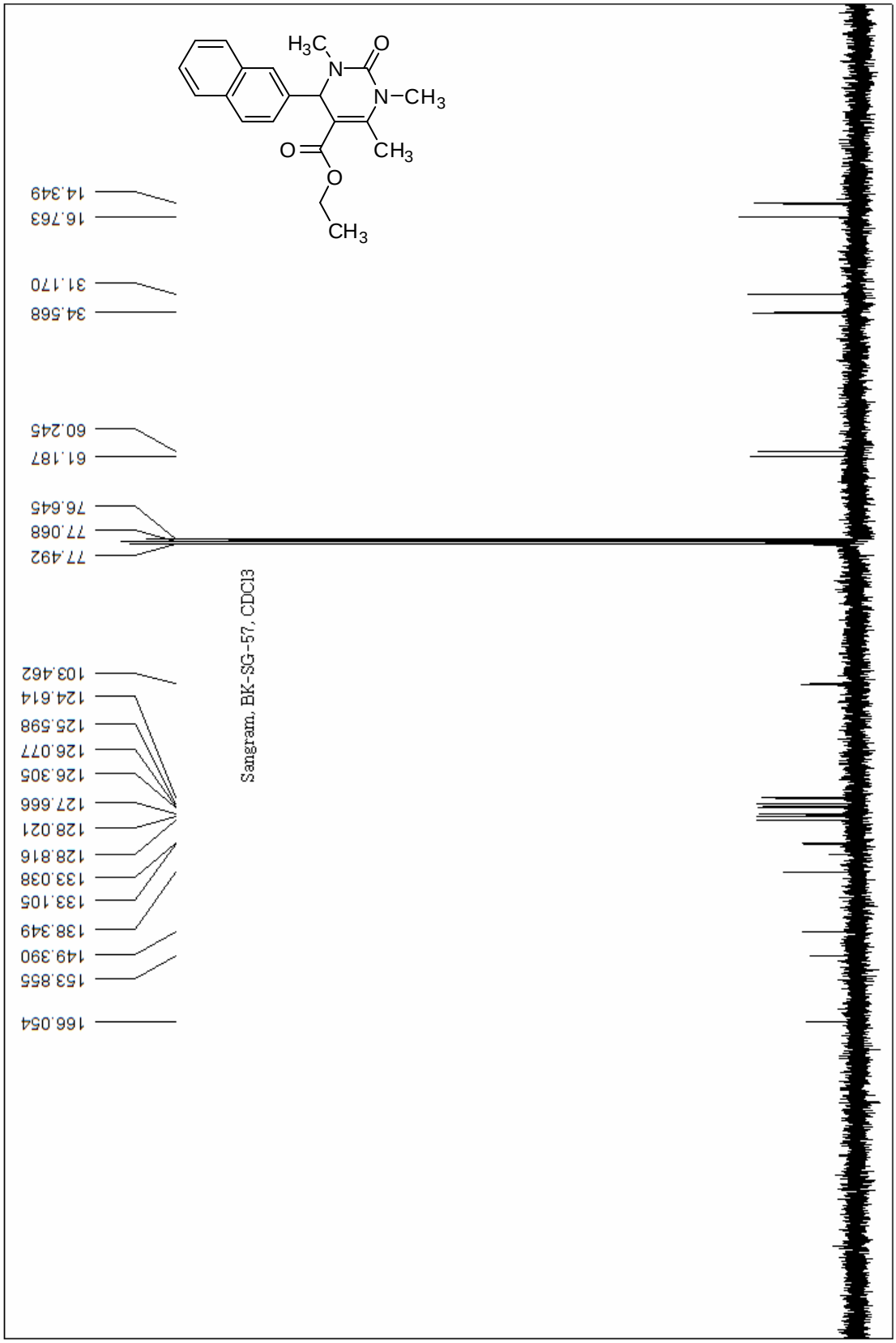
^{1}H NMR spectra of compound **7a**



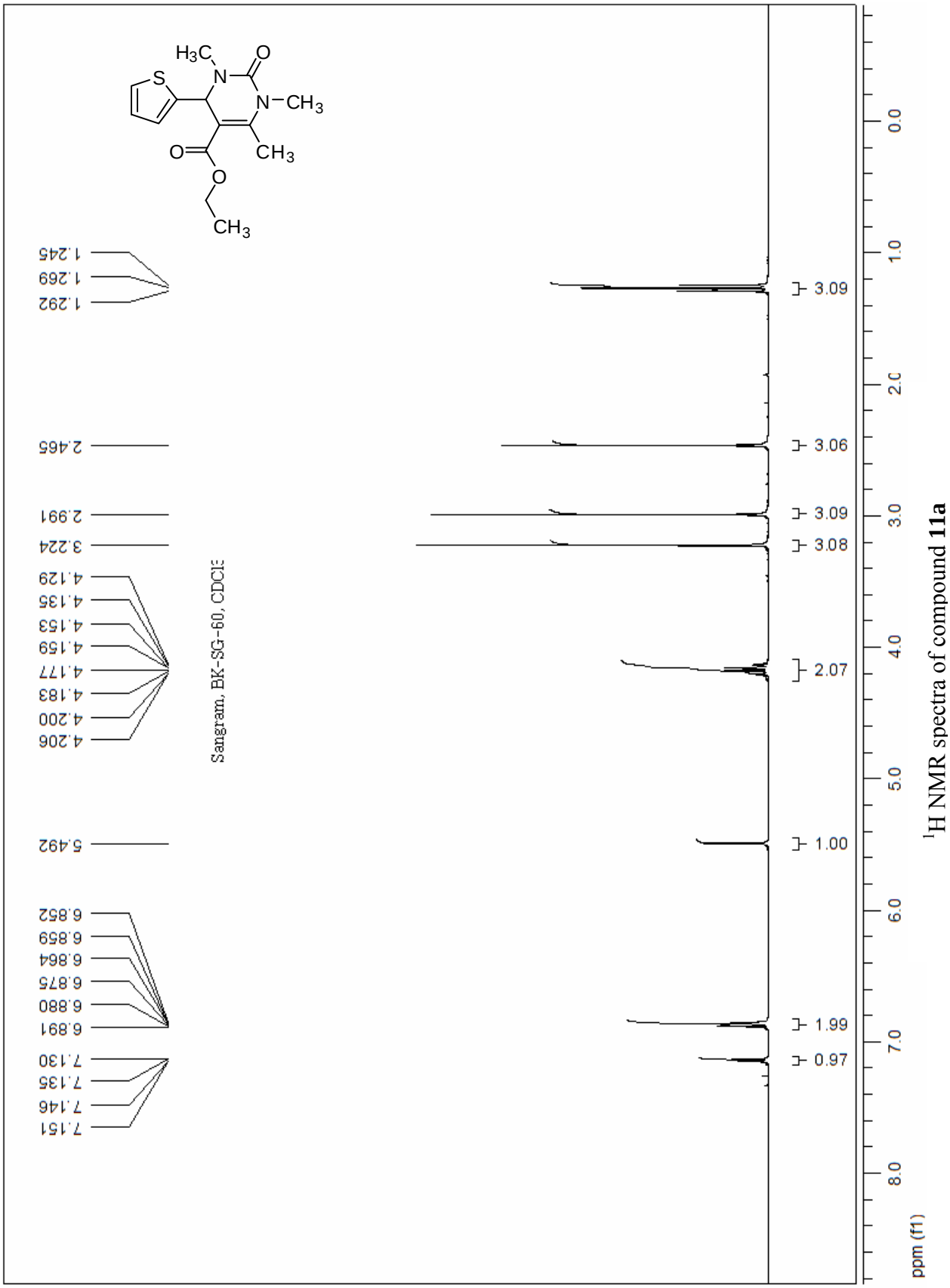
^{13}C NMR spectra of compound **7a**



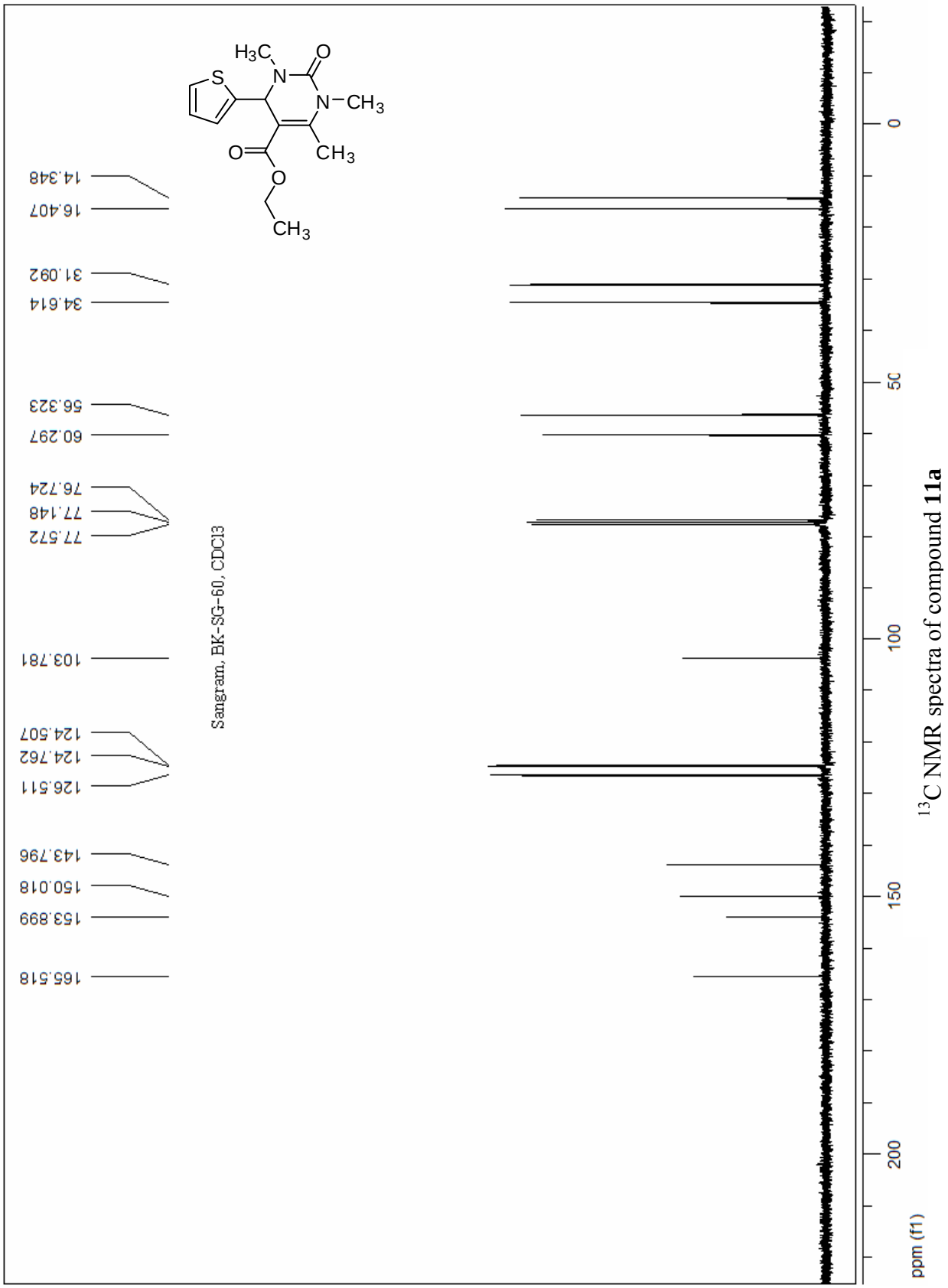
^{1}H NMR spectra of compound **9a**



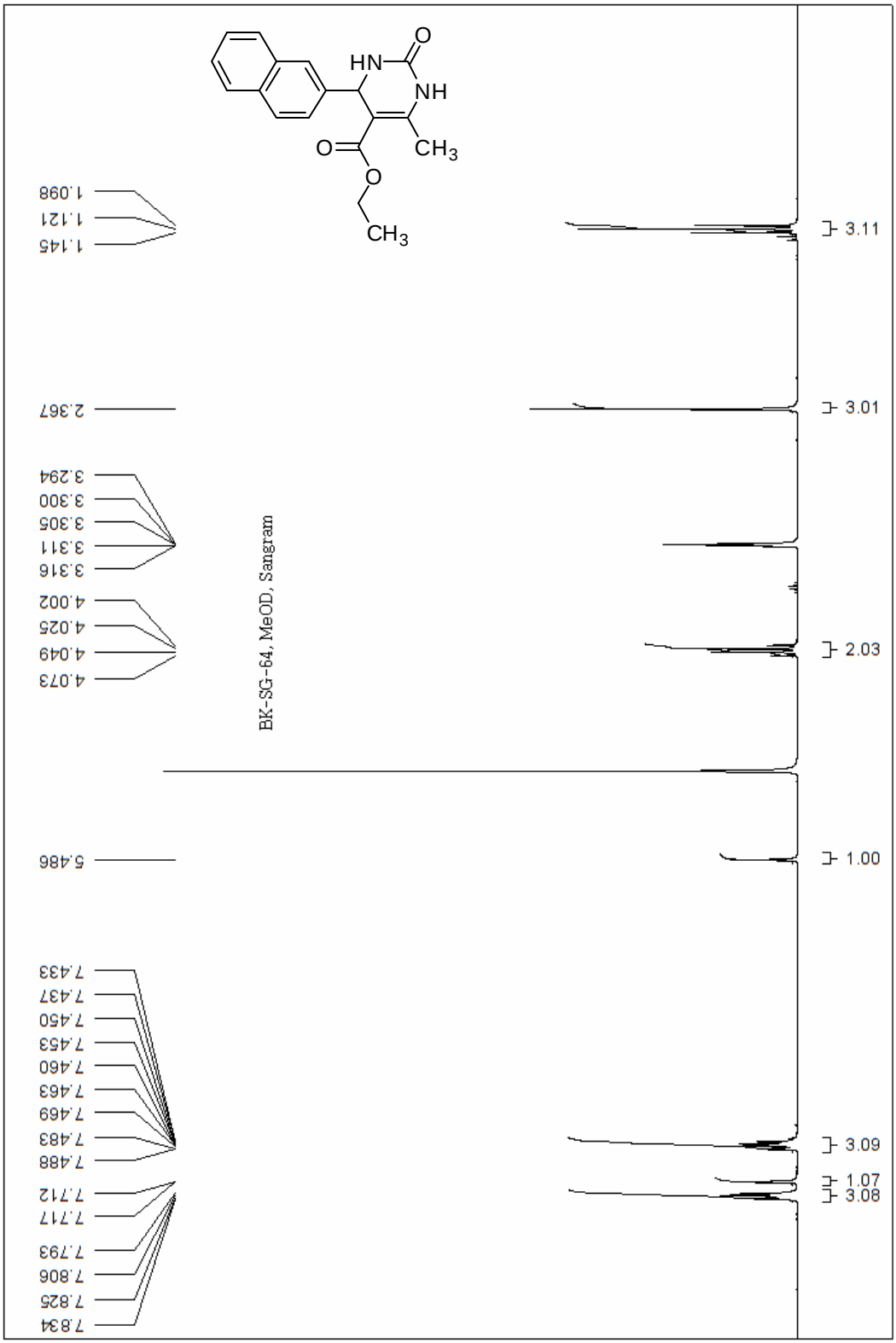
^{13}C NMR spectra of compound **9a**



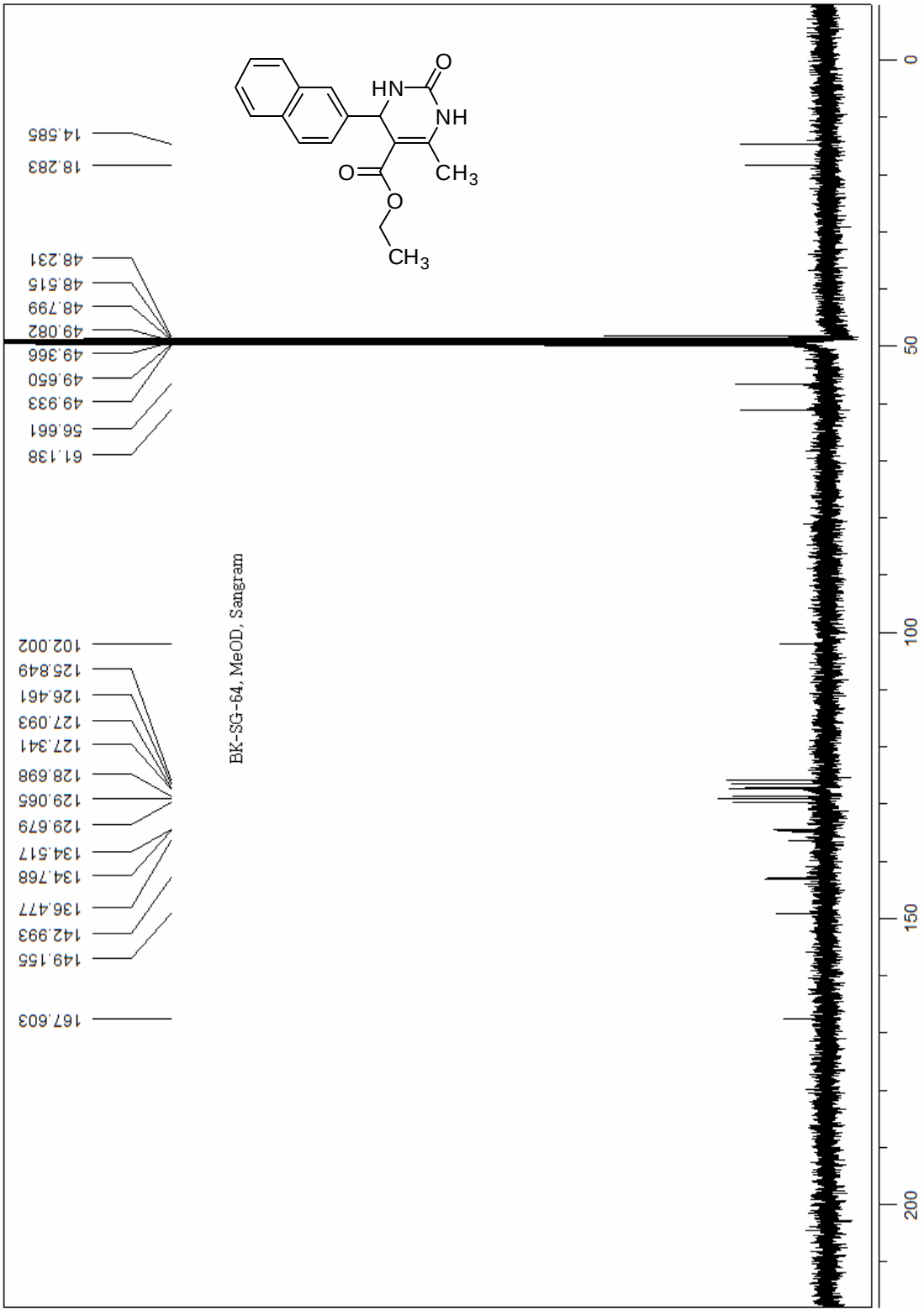
^{1}H NMR spectra of compound **11a**



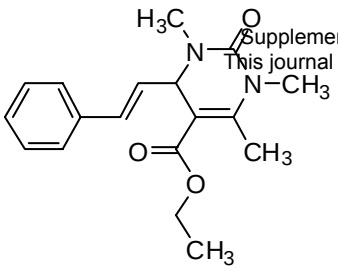
^{13}C NMR spectra of compound **11a**

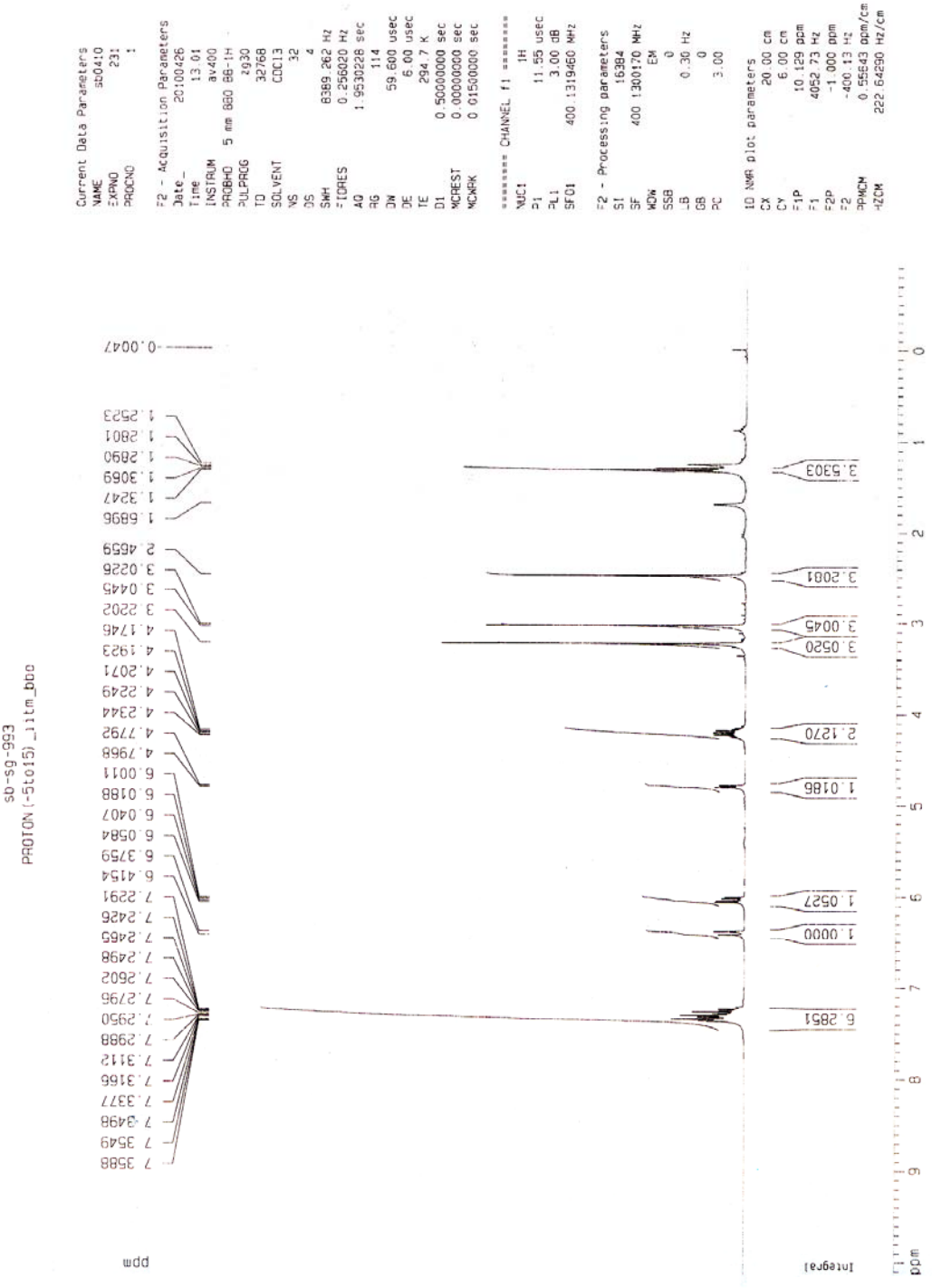


^{1}H NMR spectra of compound **12a**

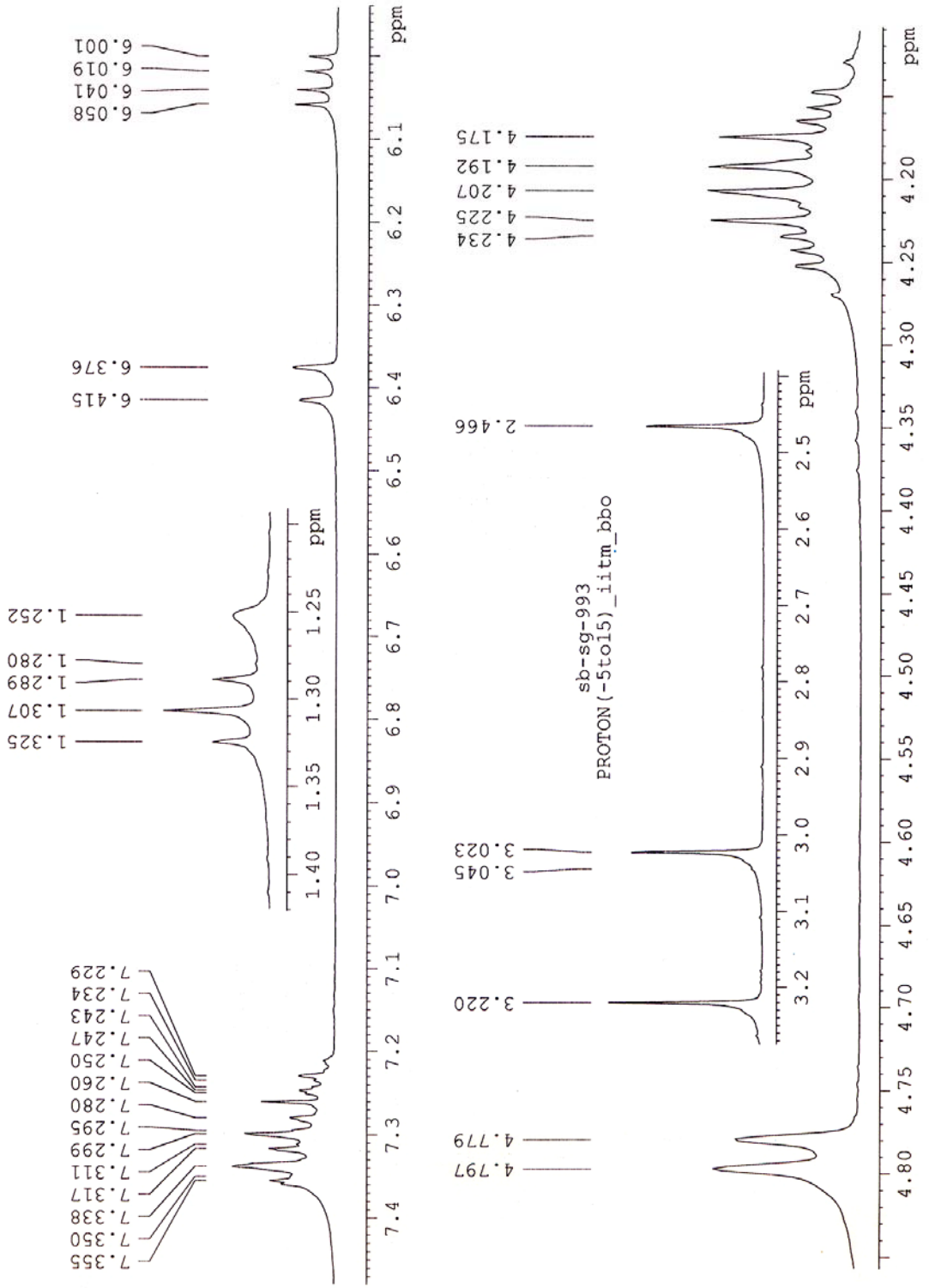


^{13}C NMR spectra of compound **12a**

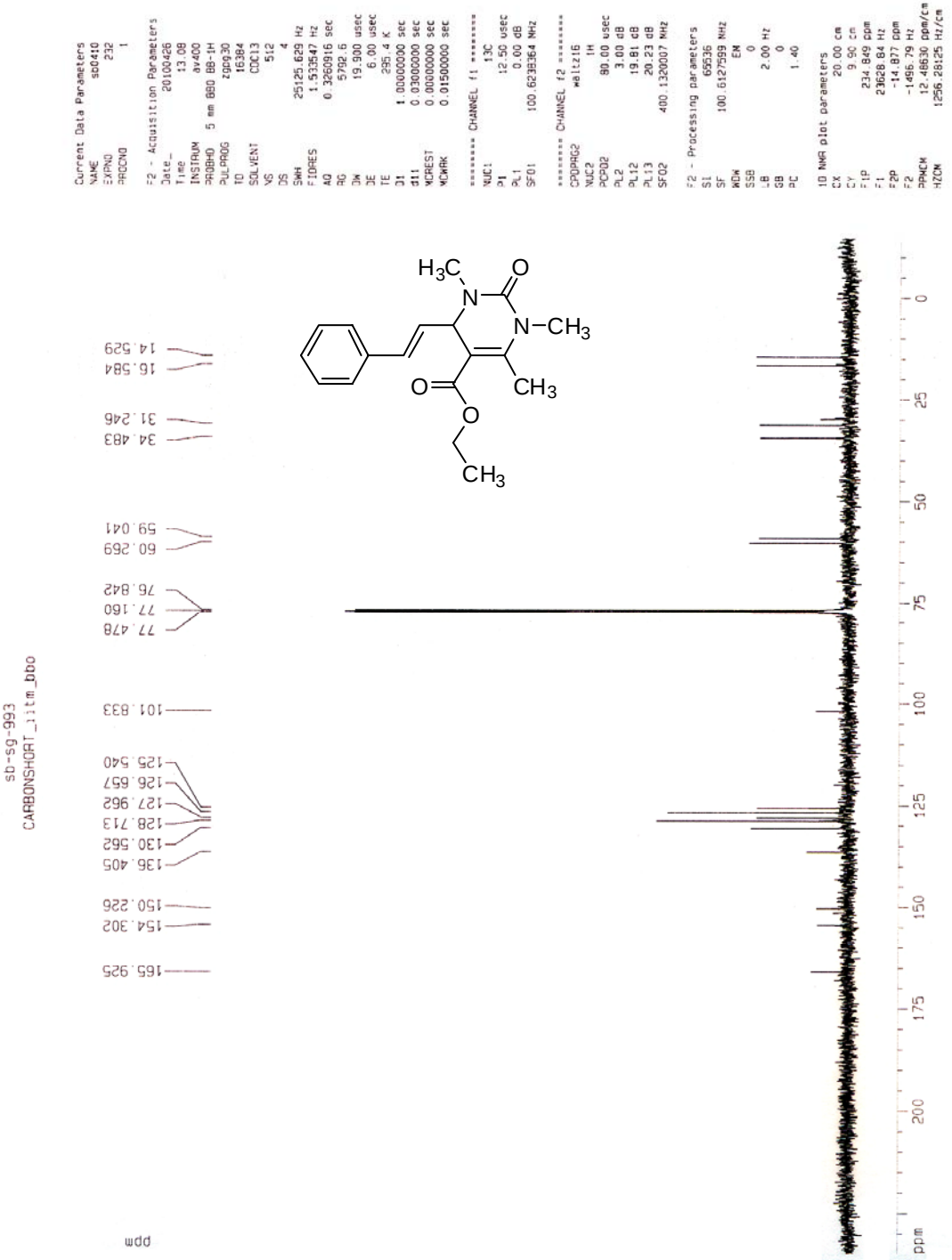




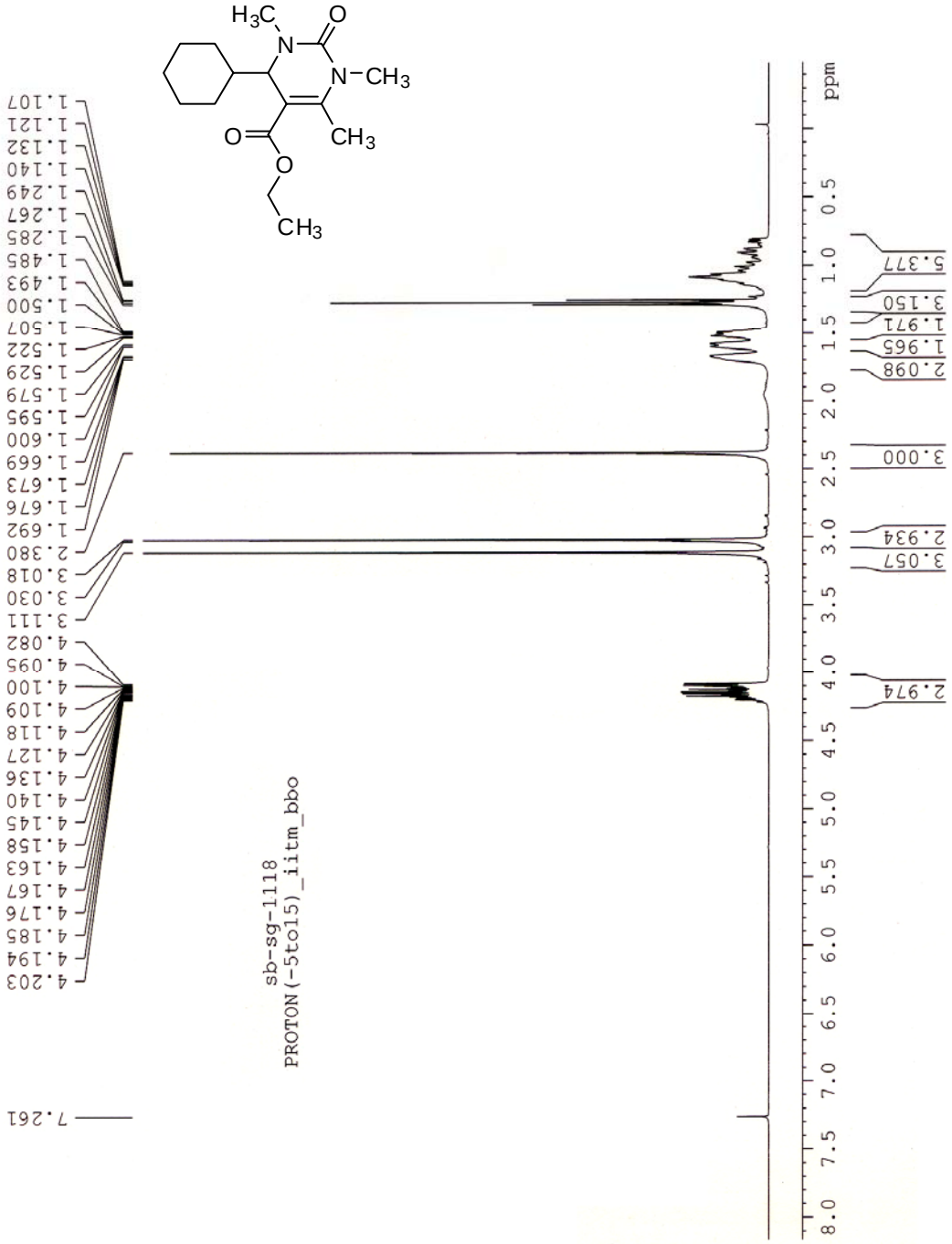
^{1}H NMR spectra of compound **14a**



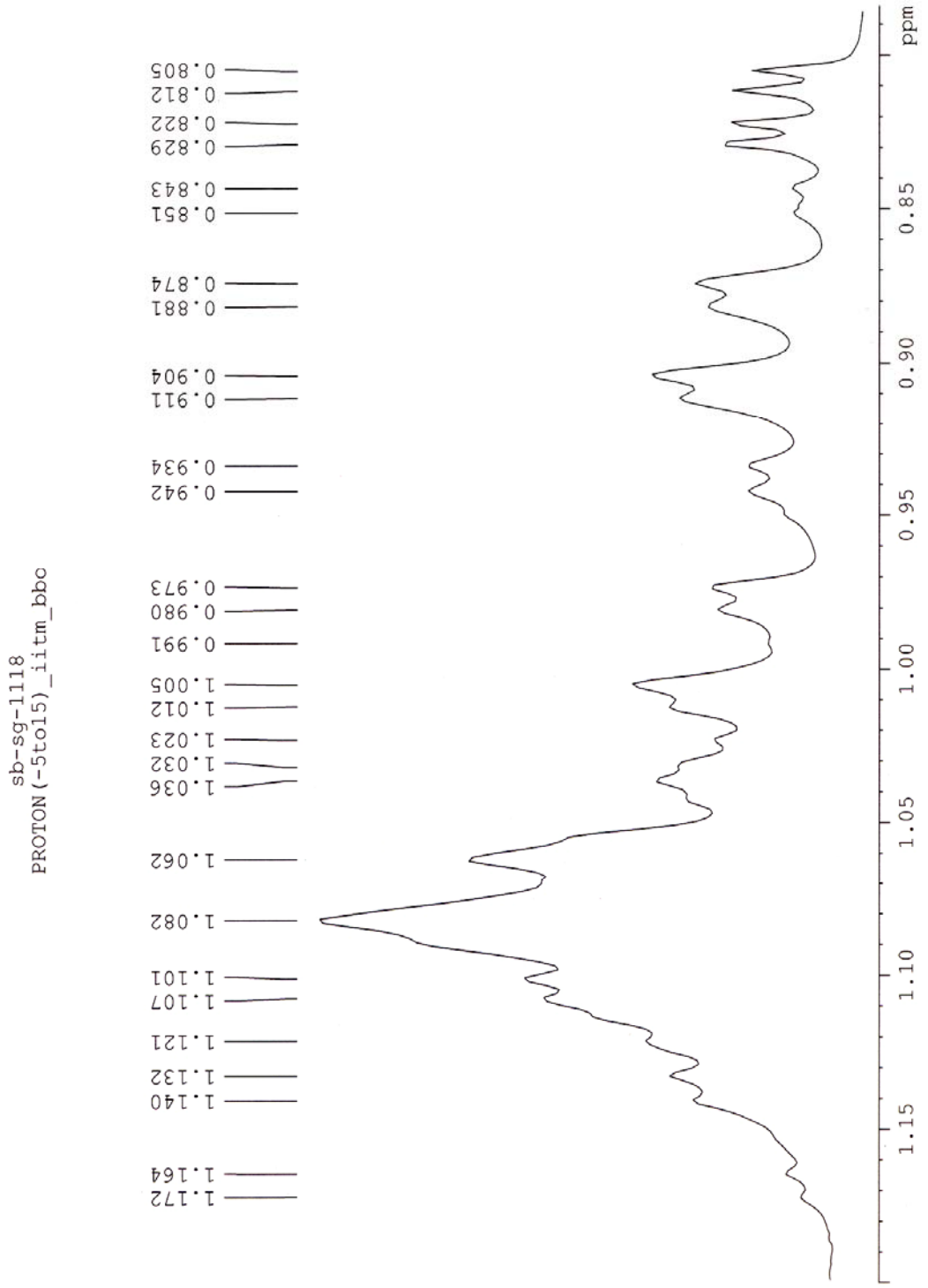
Expanded ^{1}H NMR spectra of compound **14a**



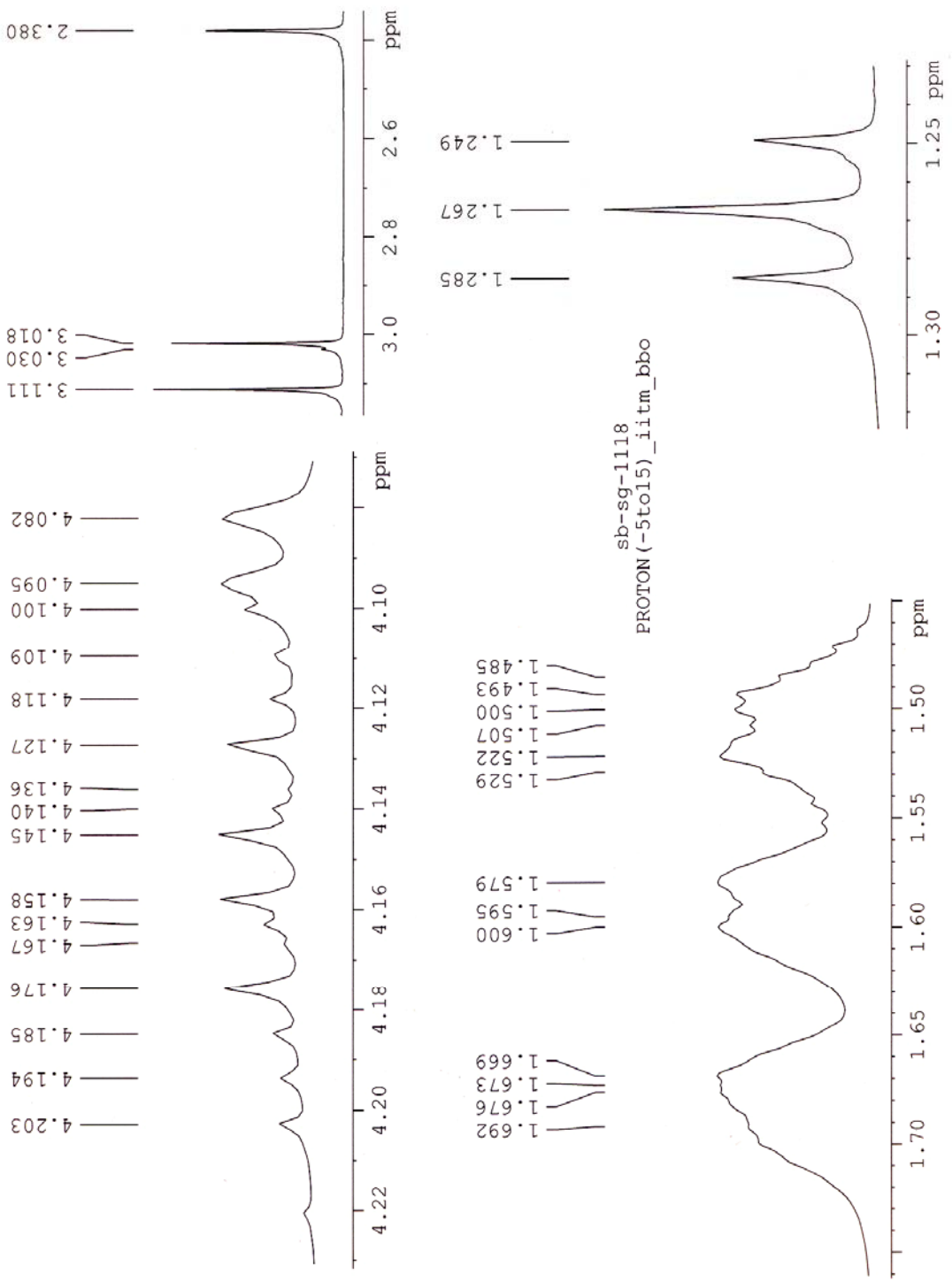
^{13}C NMR spectra of compound **14a**



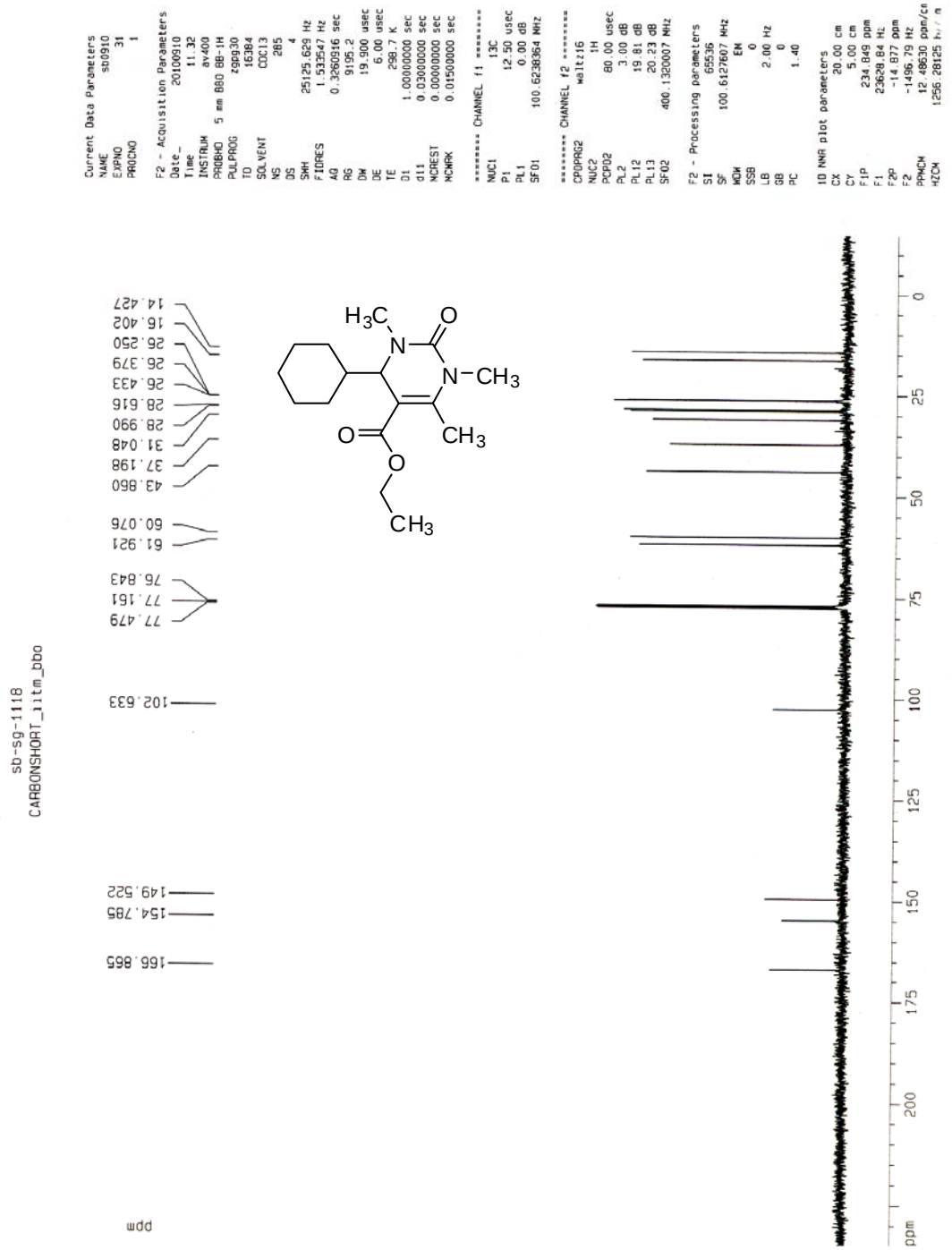
^{1}H NMR spectra of compound **16a**



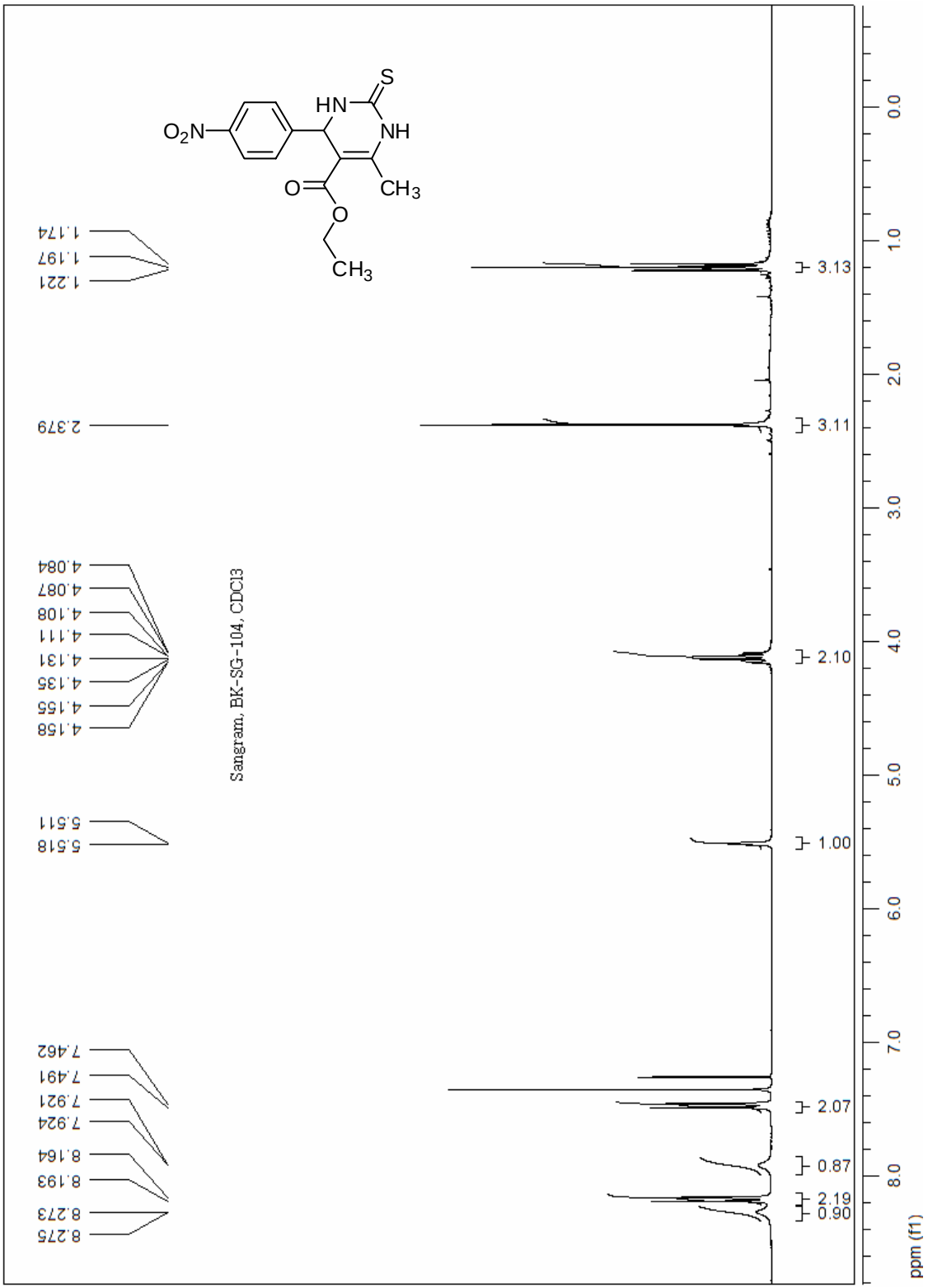
Expanded ^{1}H NMR spectra of compound **16a**



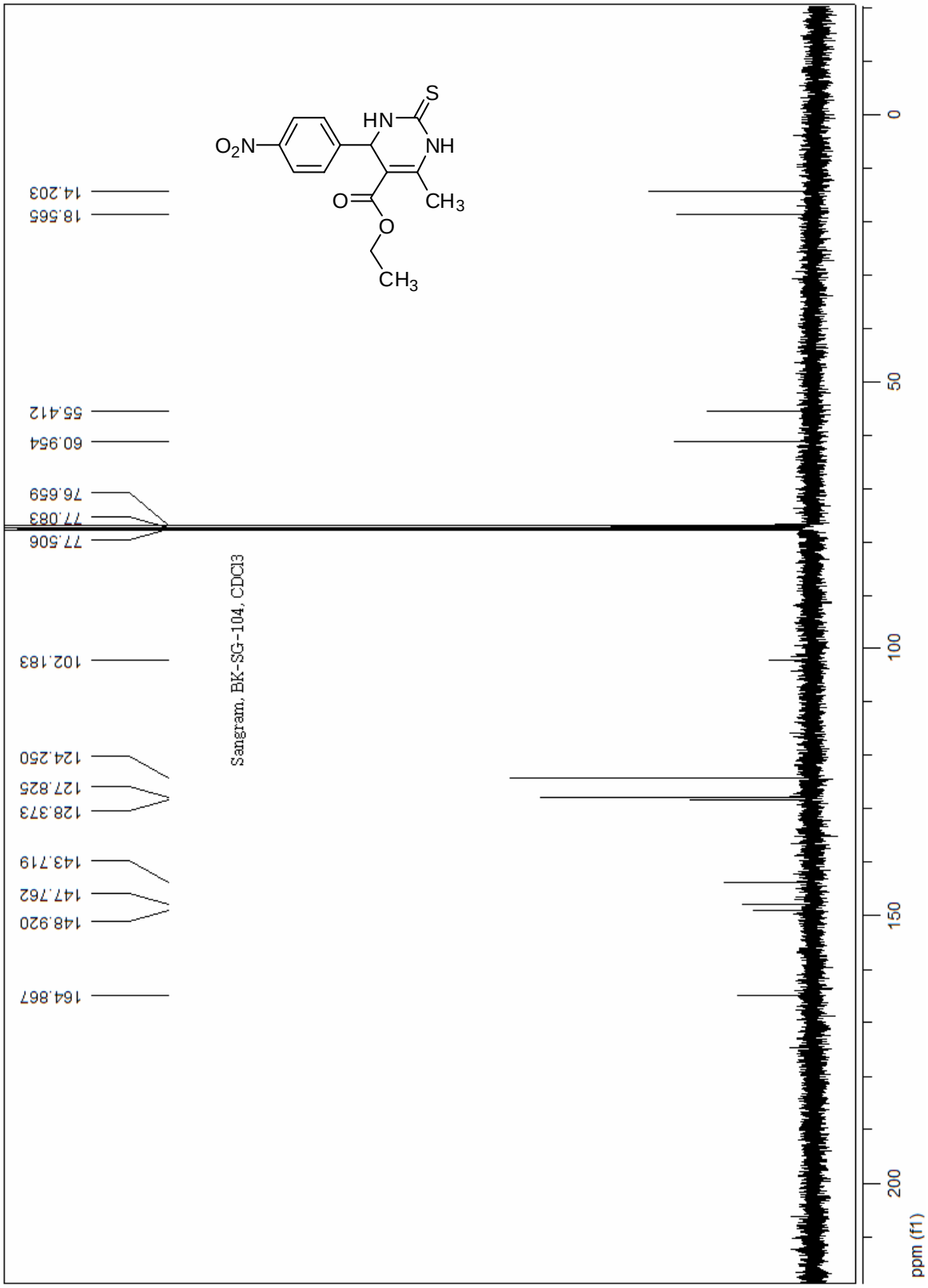
Expanded ^{1}H NMR spectra of compound **16a**



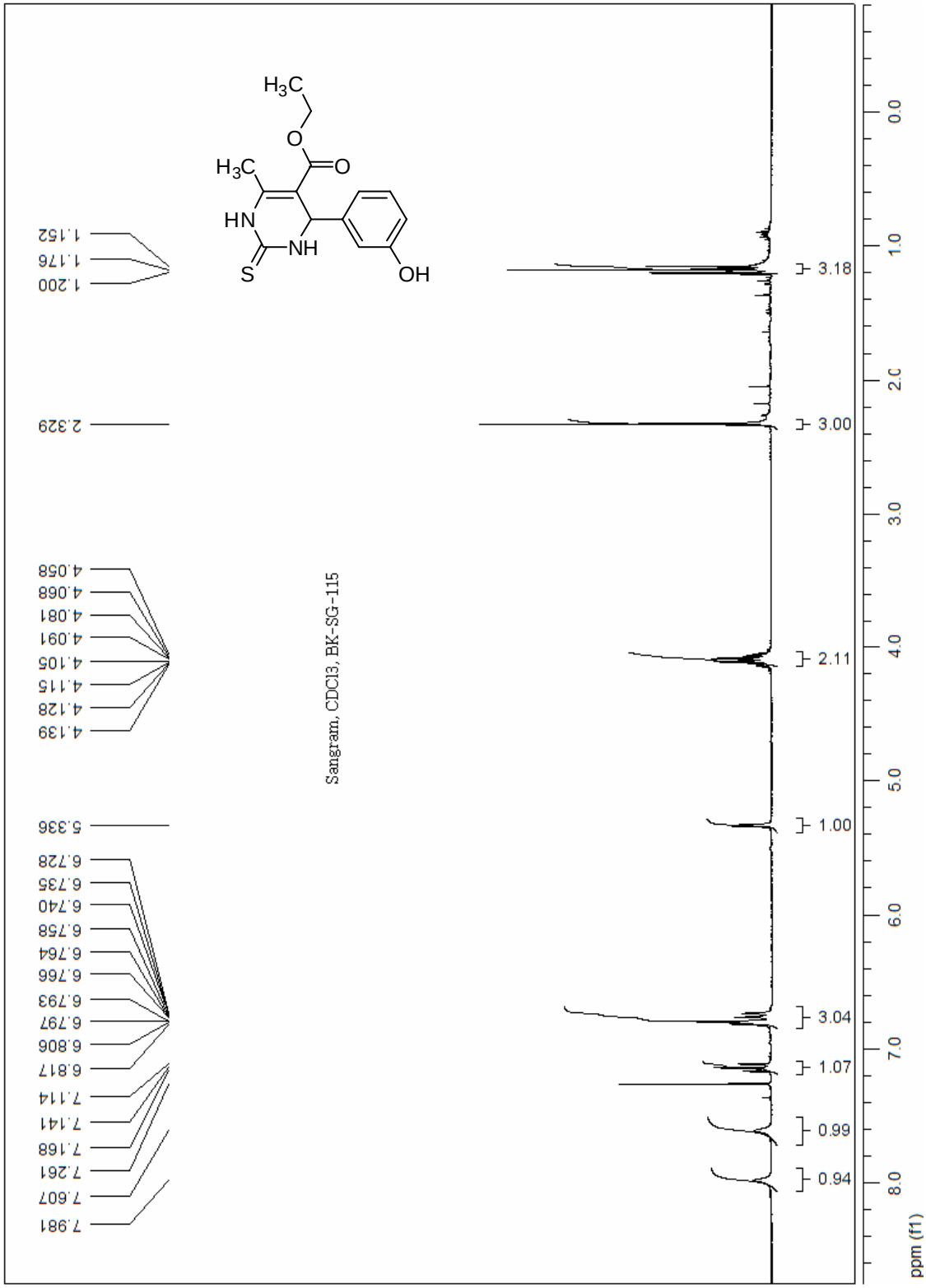
^{13}C NMR spectra of compound **16a**



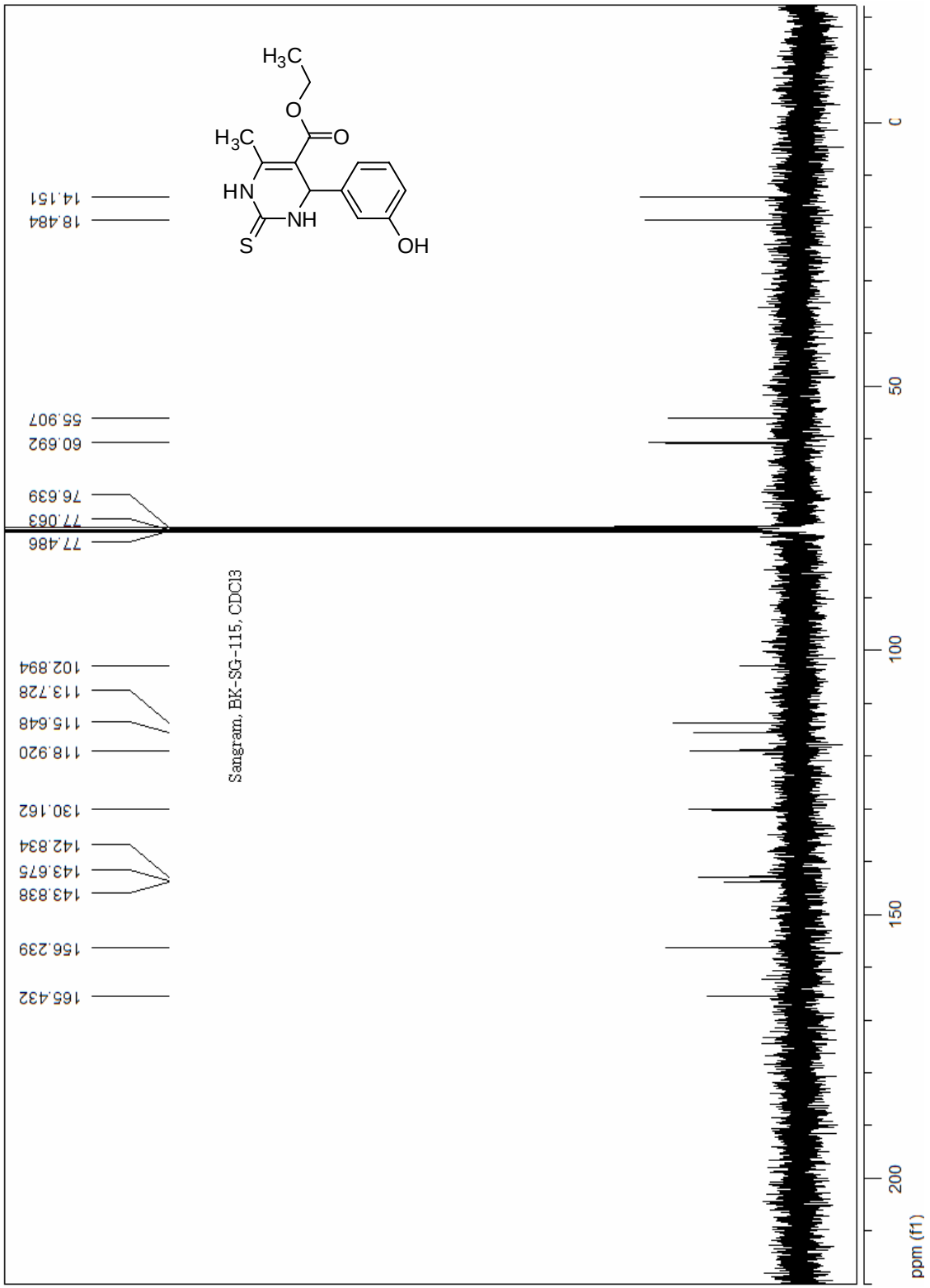
^{1}H NMR spectra of compound **17a**



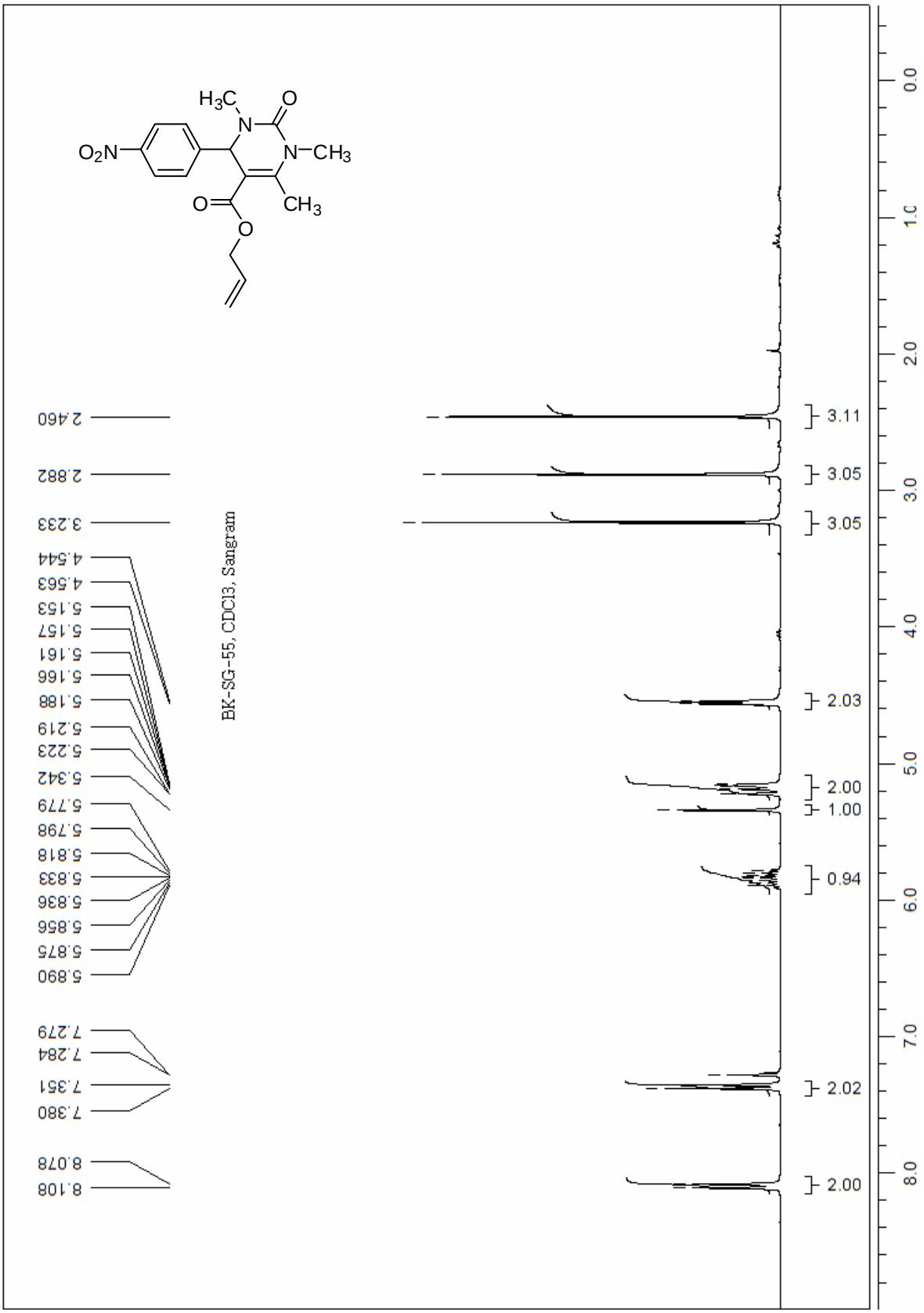
^{13}C NMR spectra of compound **17a**



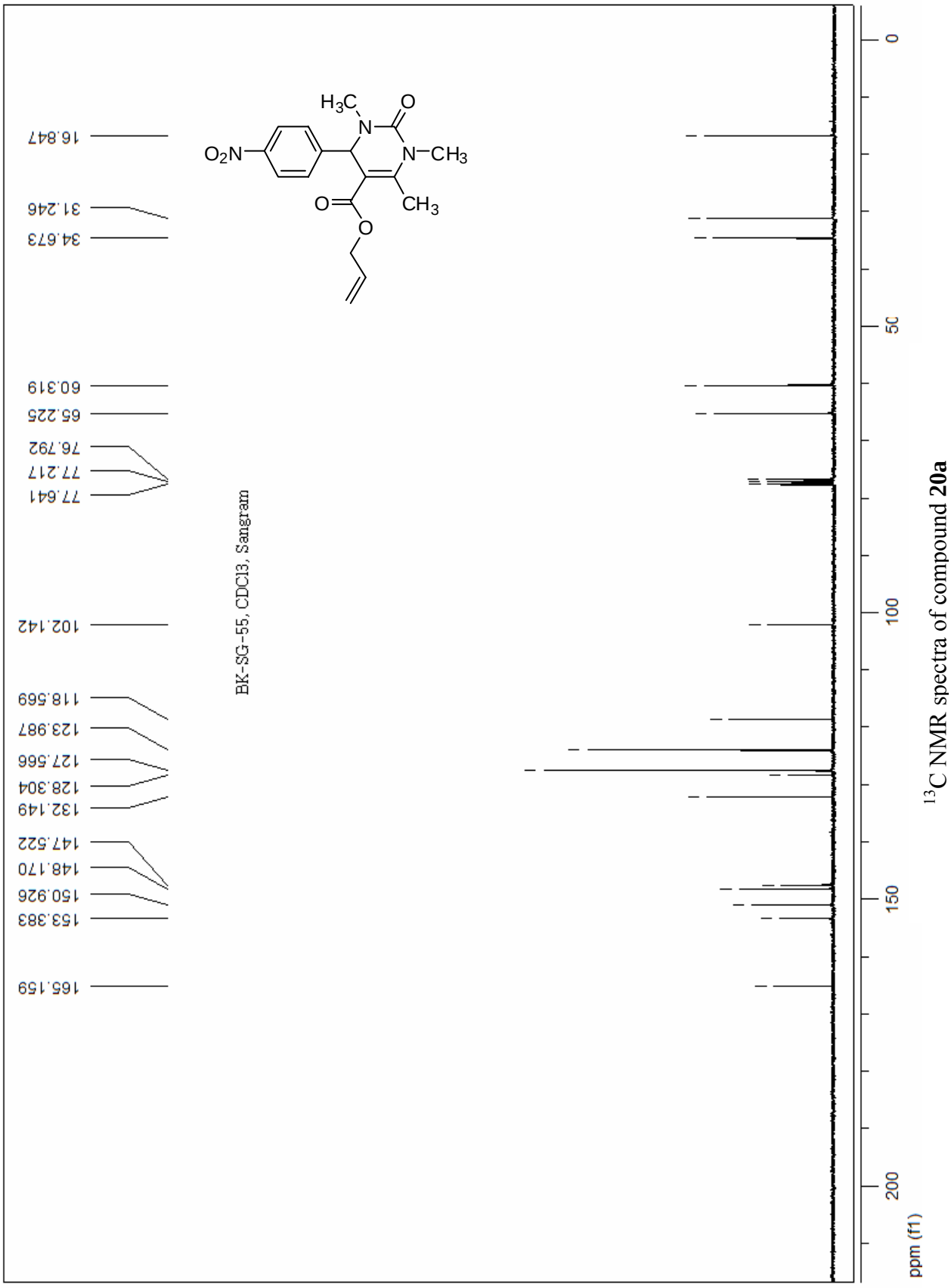
^{1}H NMR spectra of compound **18a**



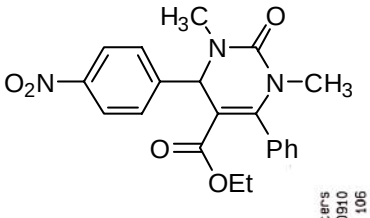
^{13}C NMR spectra of compound **18a**

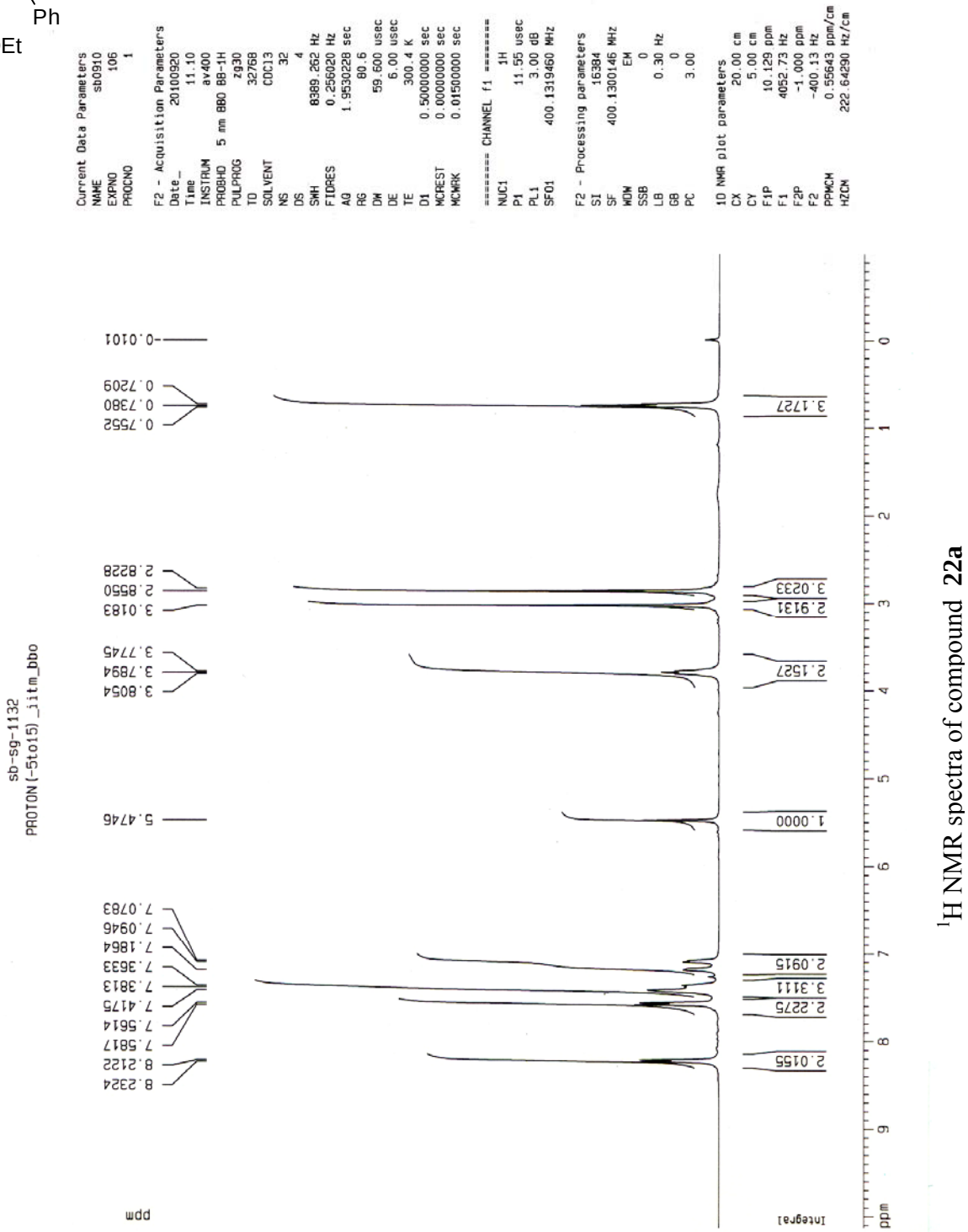


^{1}H NMR spectra of compound **20a**

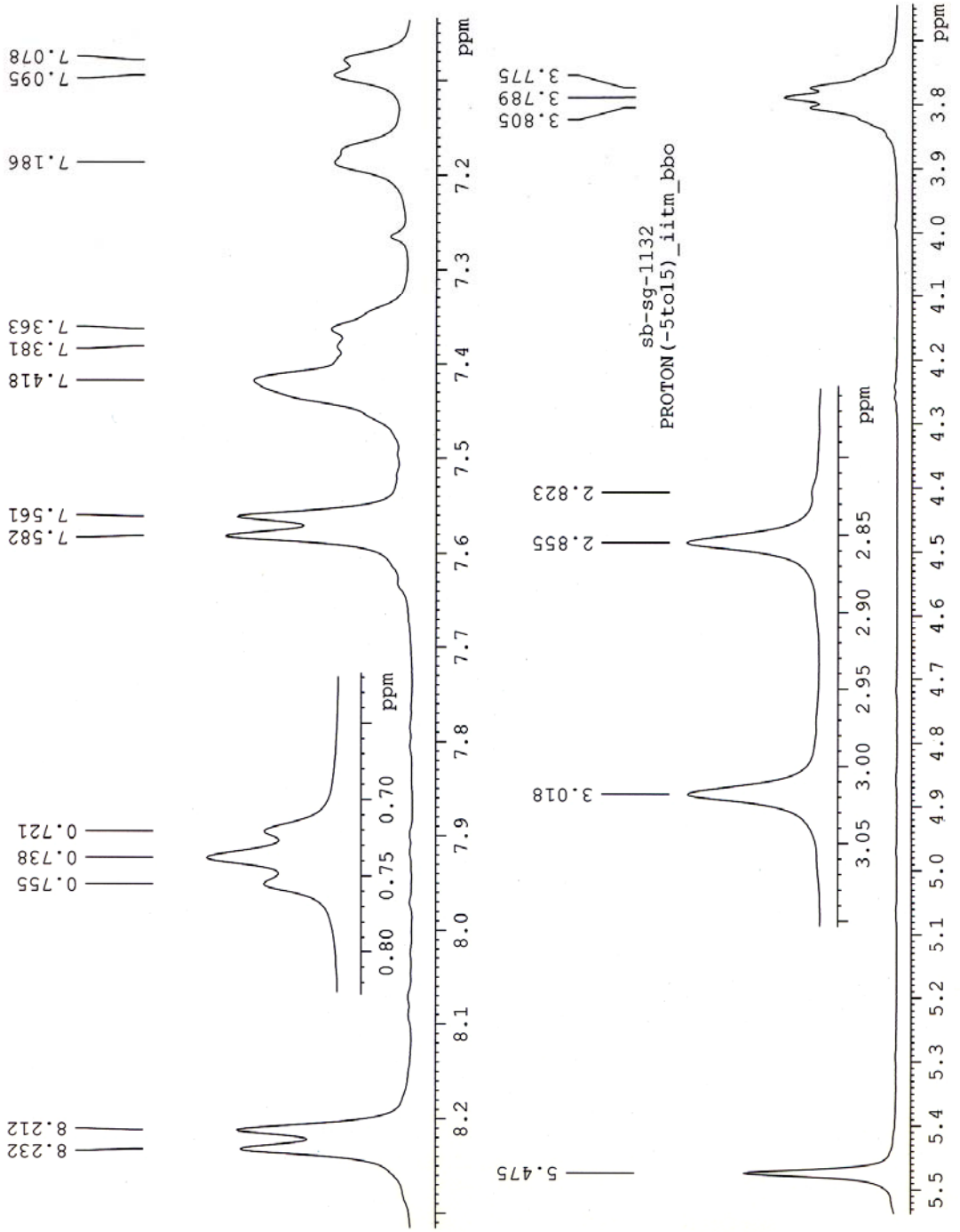


^{13}C NMR spectra of compound **20a**

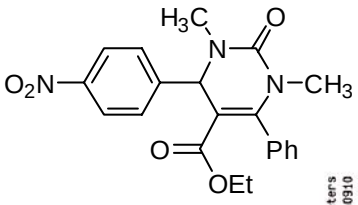


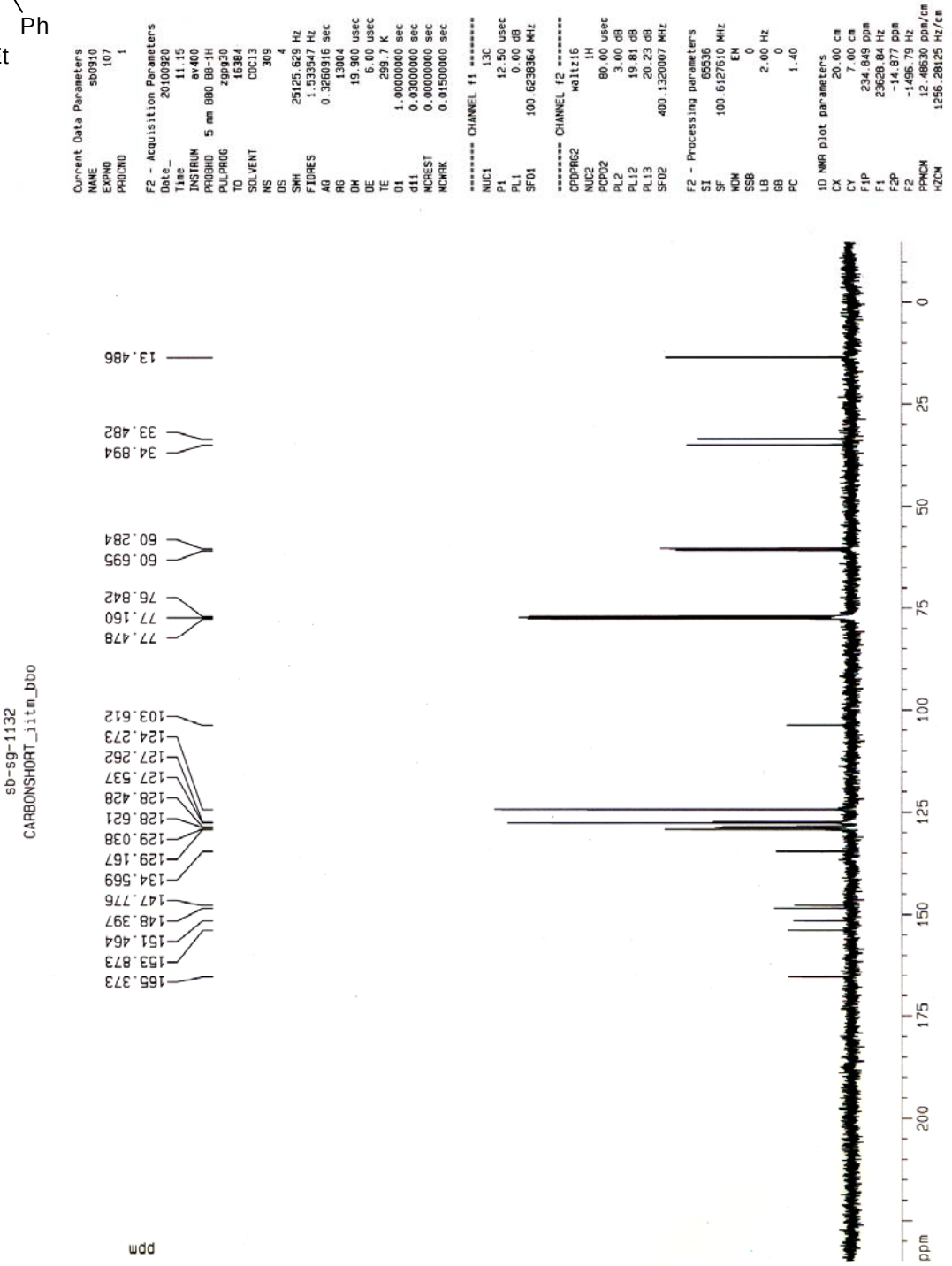


^{1}H NMR spectra of compound **22a**

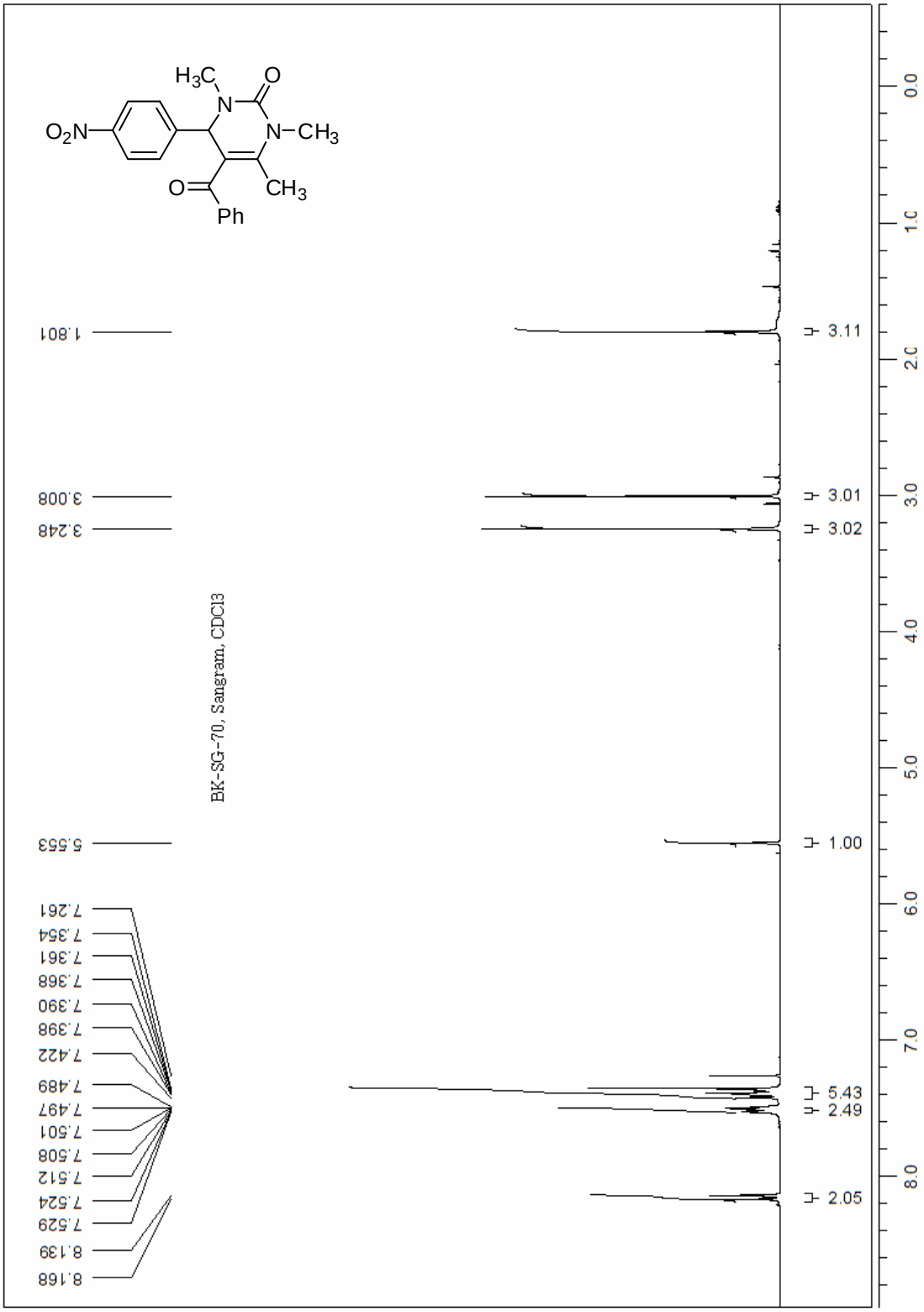


Expanded ^{1}H NMR spectra of compound **22a**

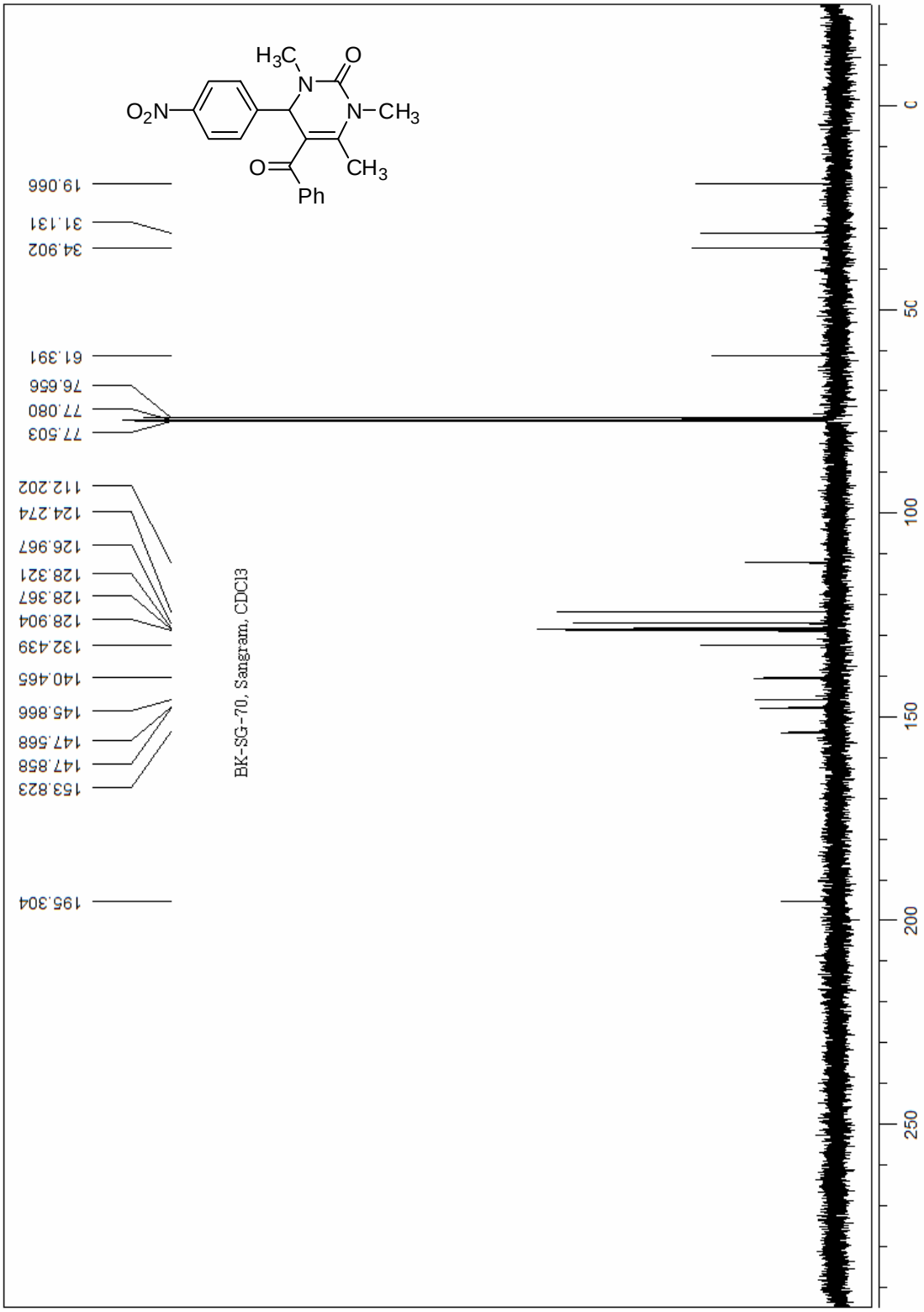




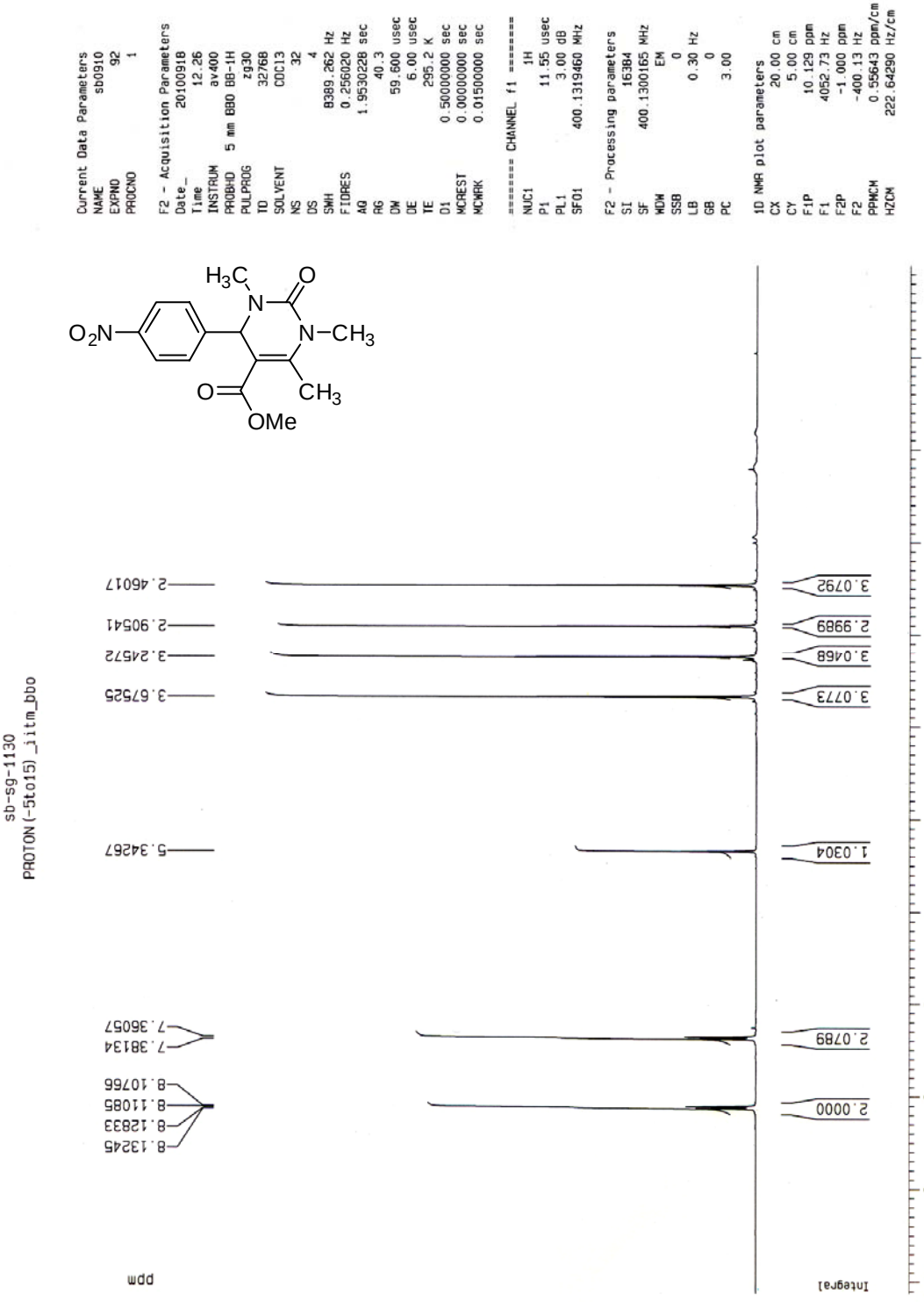
^{13}C NMR spectra of compound **22a**



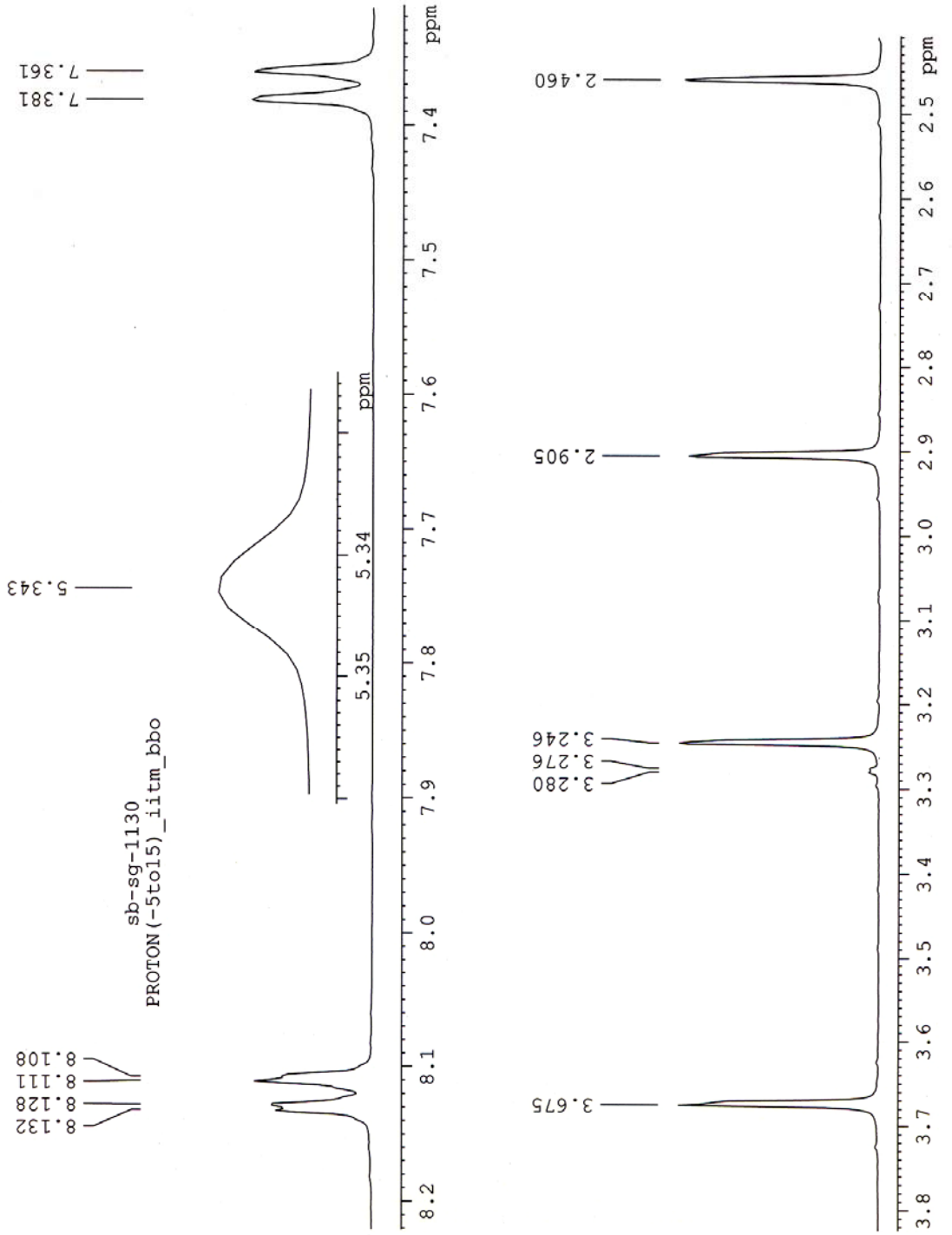
^{1}H NMR spectra of compound **24a**



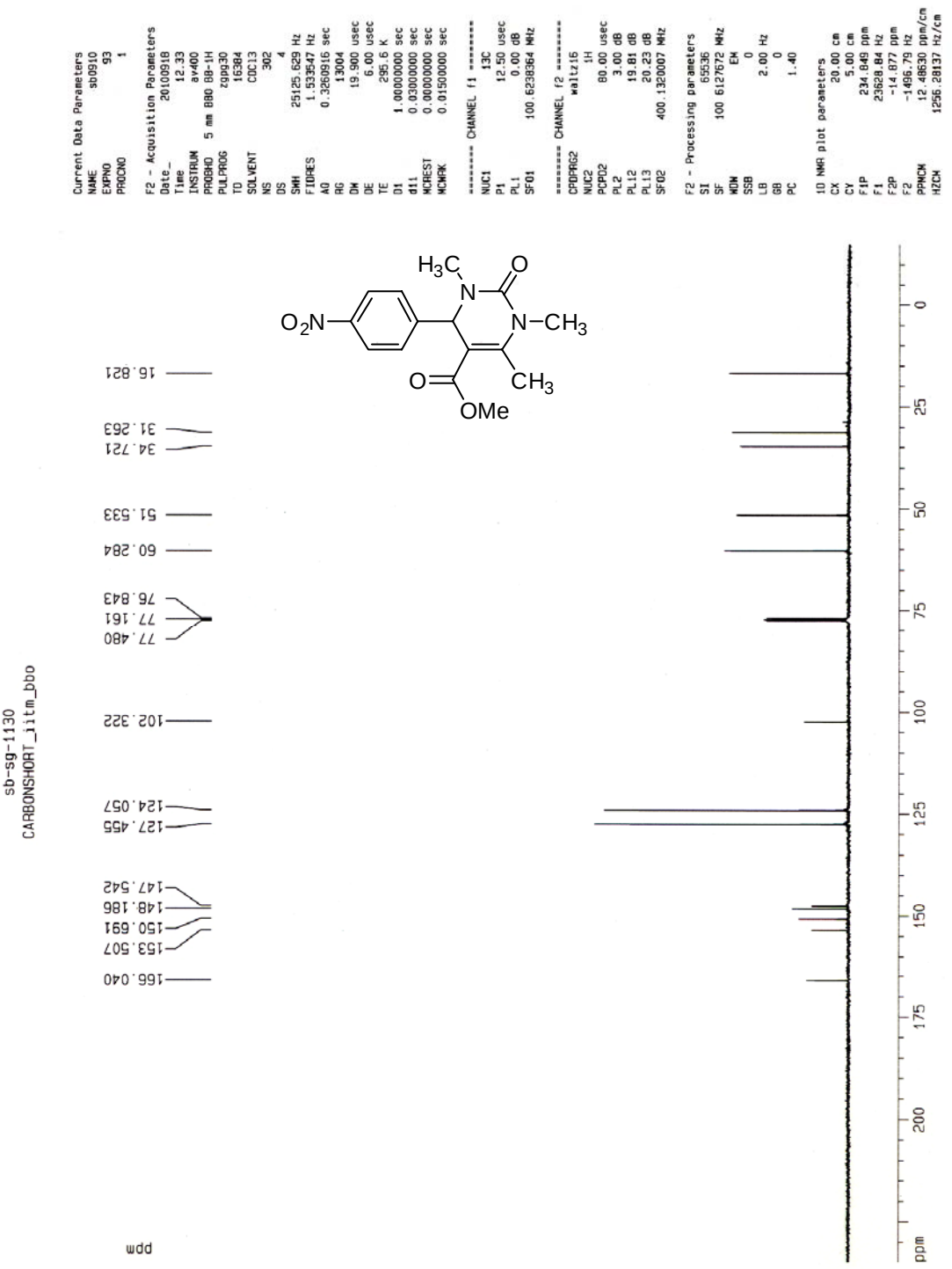
^{13}C NMR spectra of compound **24a**



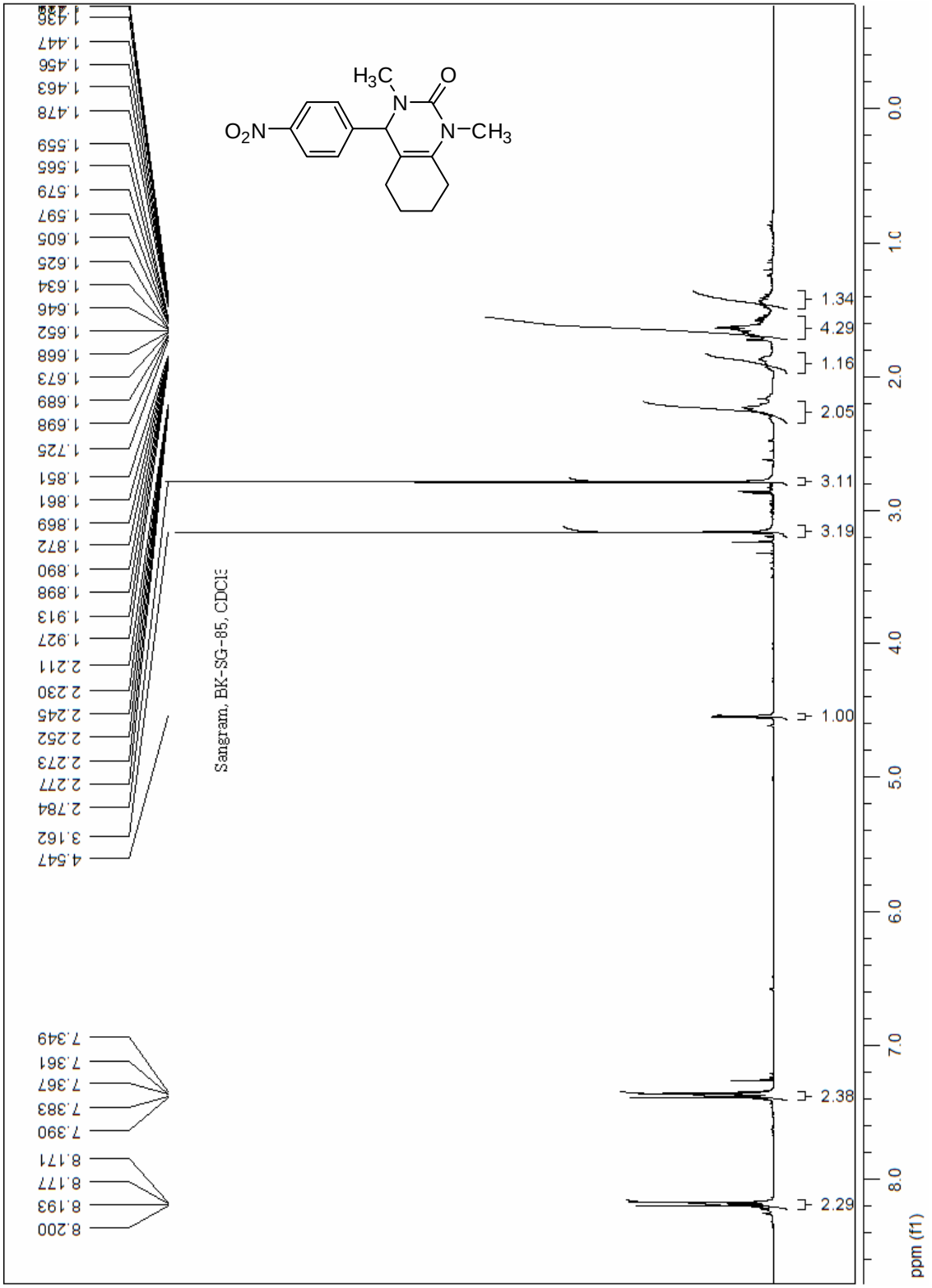
^{1}H NMR spectra of compound **26a**



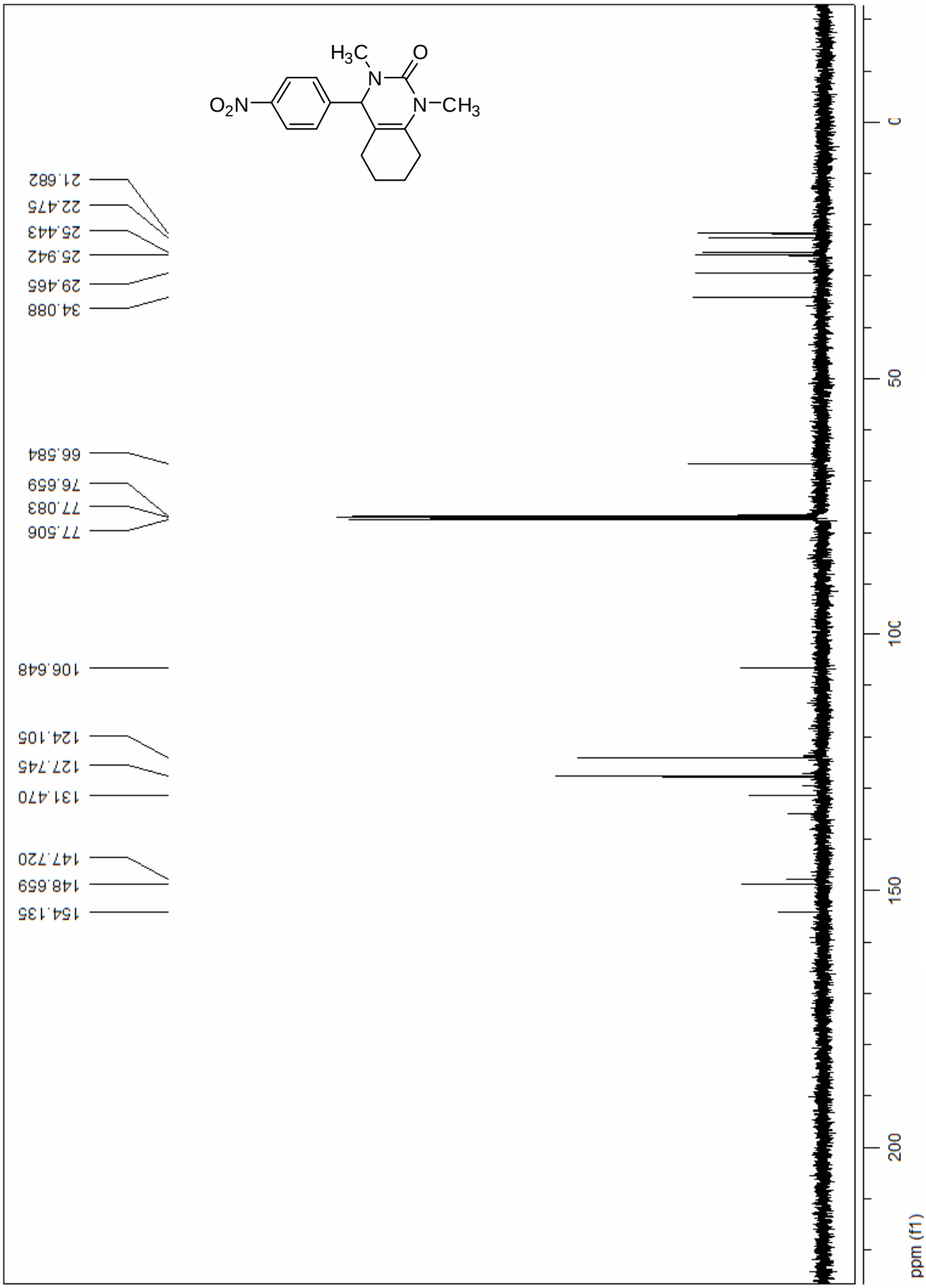
Expanded ^{1}H NMR spectra of compound **26a**



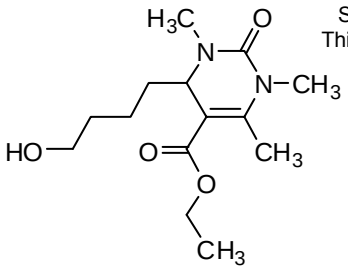
^{13}C NMR spectra of compound **26a**

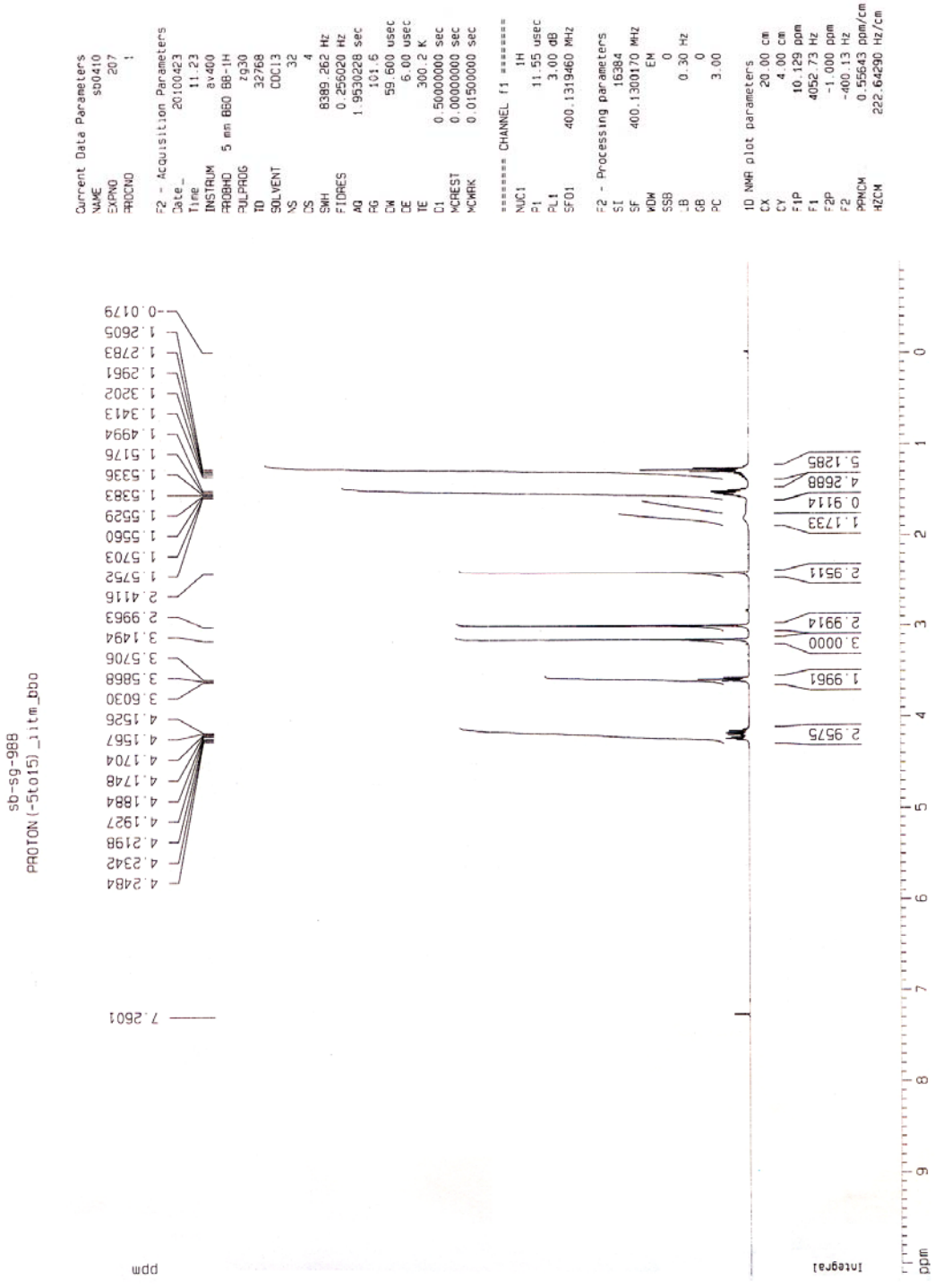


^{1}H NMR spectra of compound **28a**

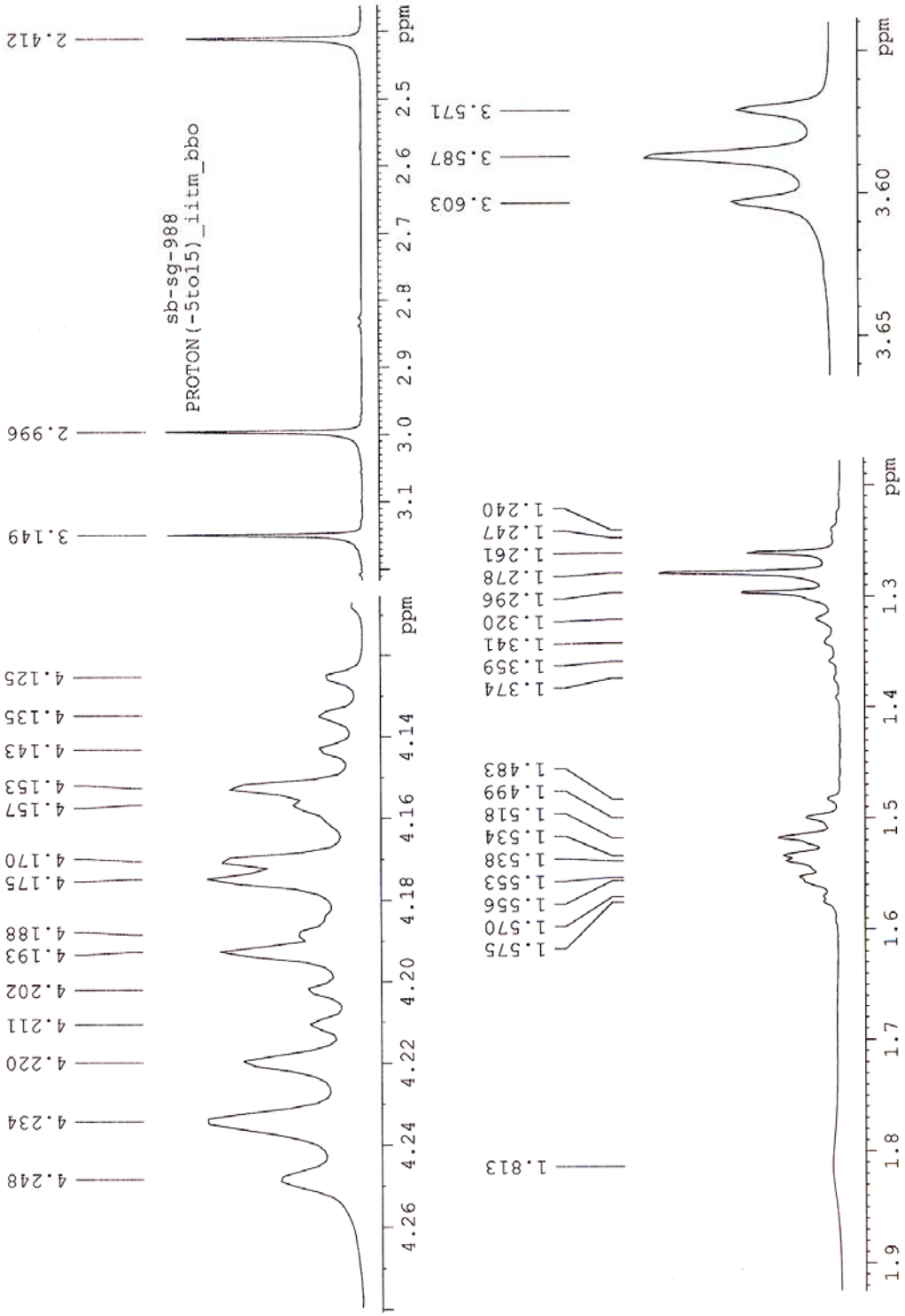


^{13}C NMR spectra of compound **28a**

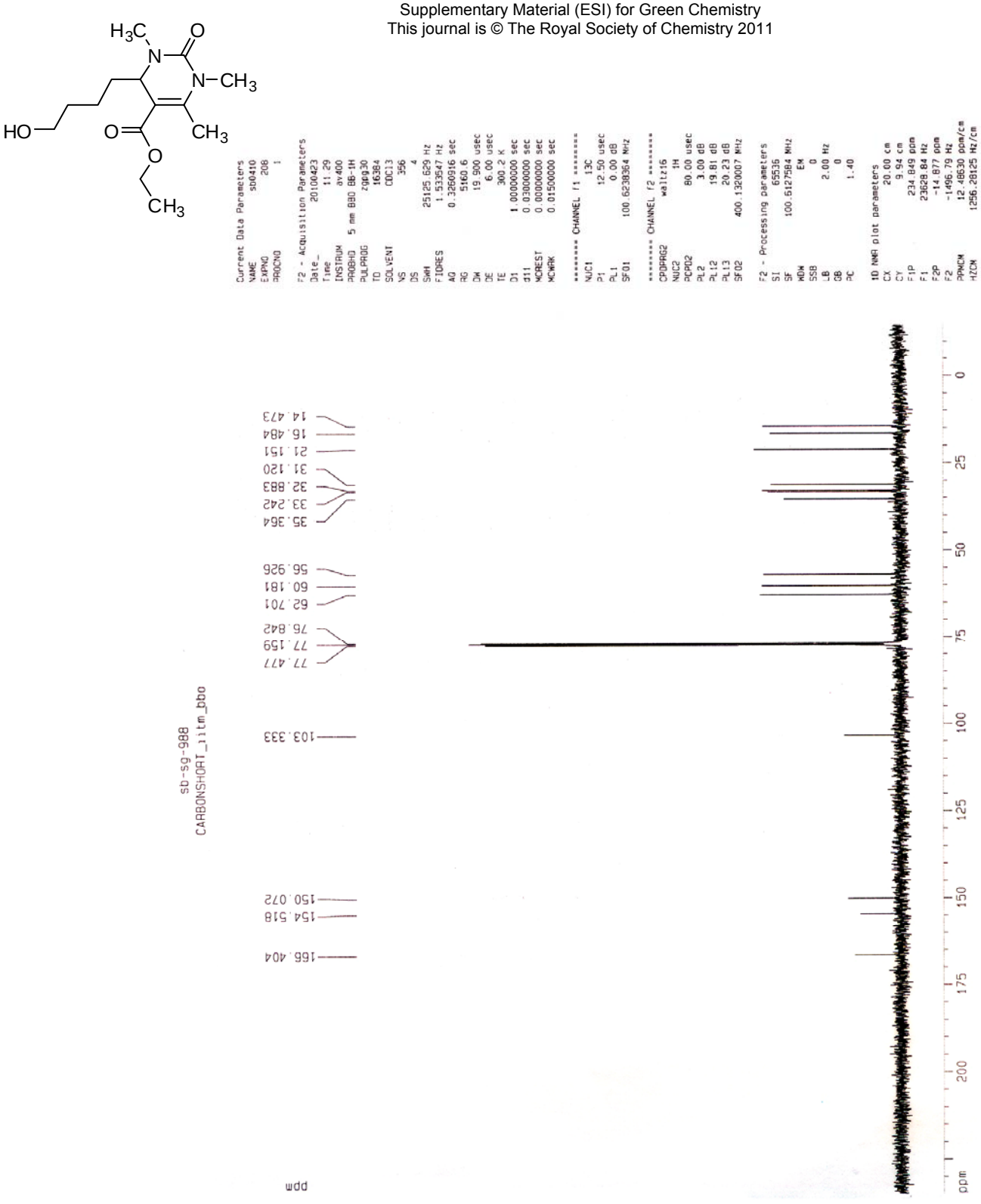




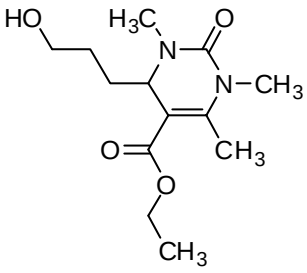
^{1}H NMR spectra of compound **30a**

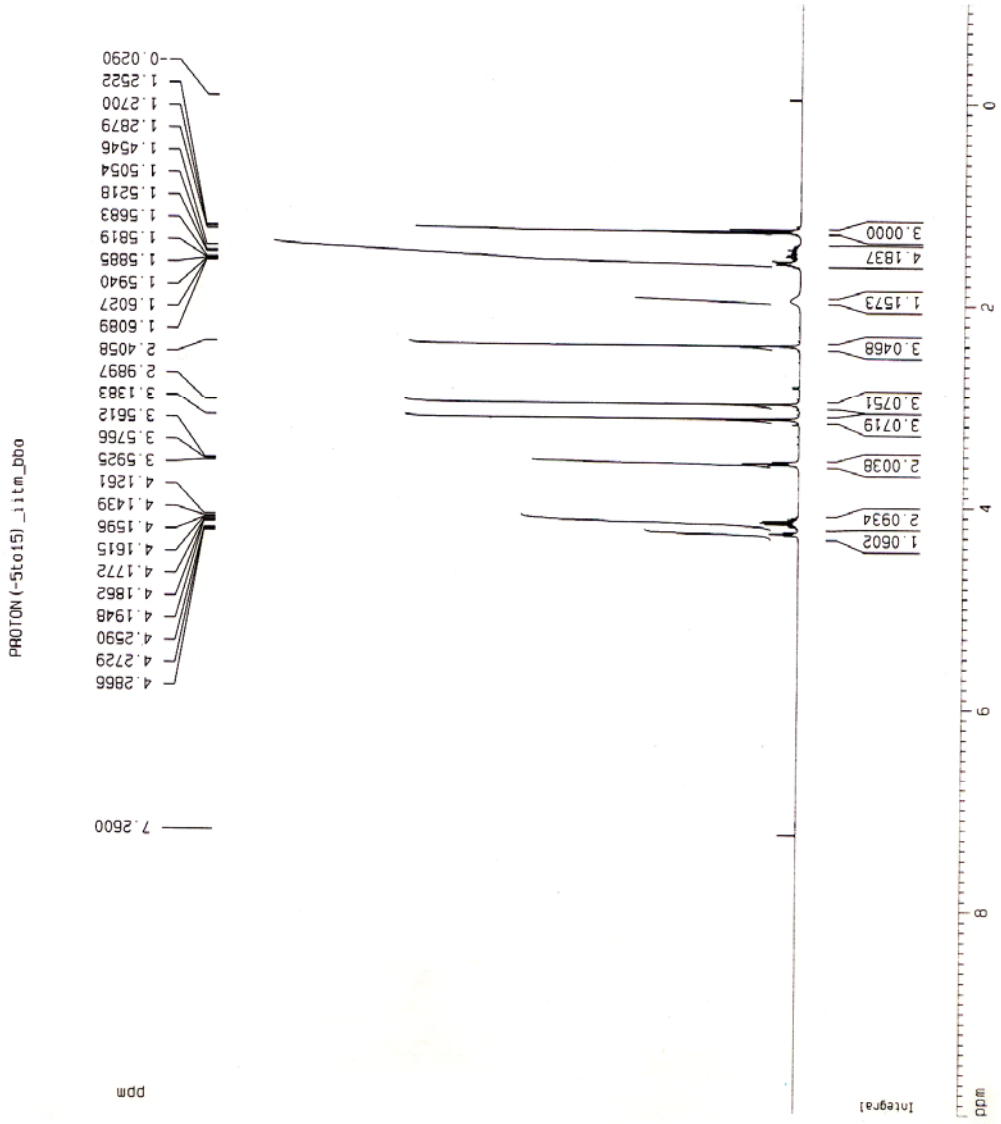


Expanded ^{1}H NMR spectra of compound **30a**

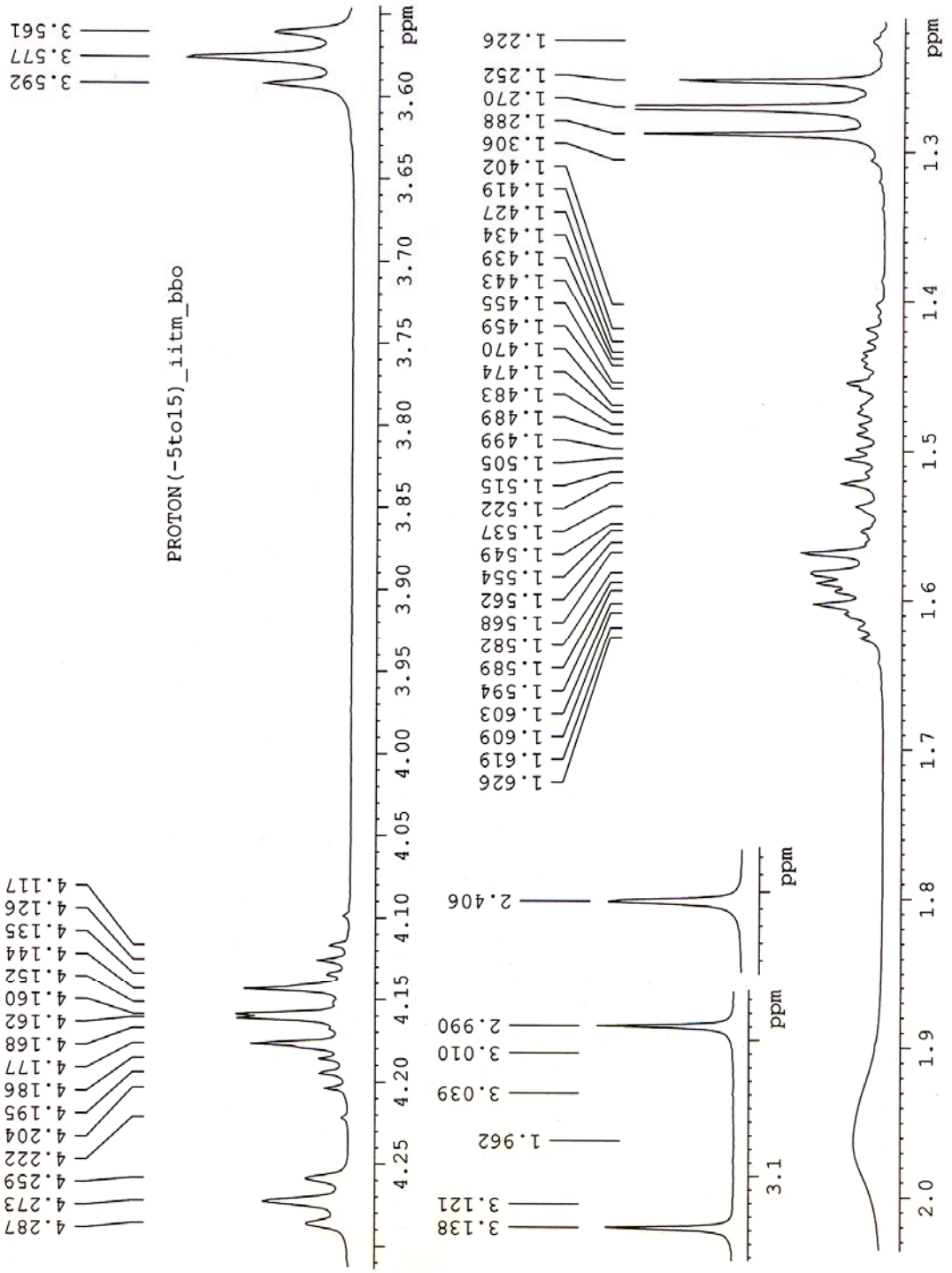


^{13}C NMR spectra of compound **30a**

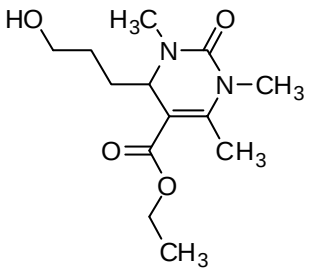


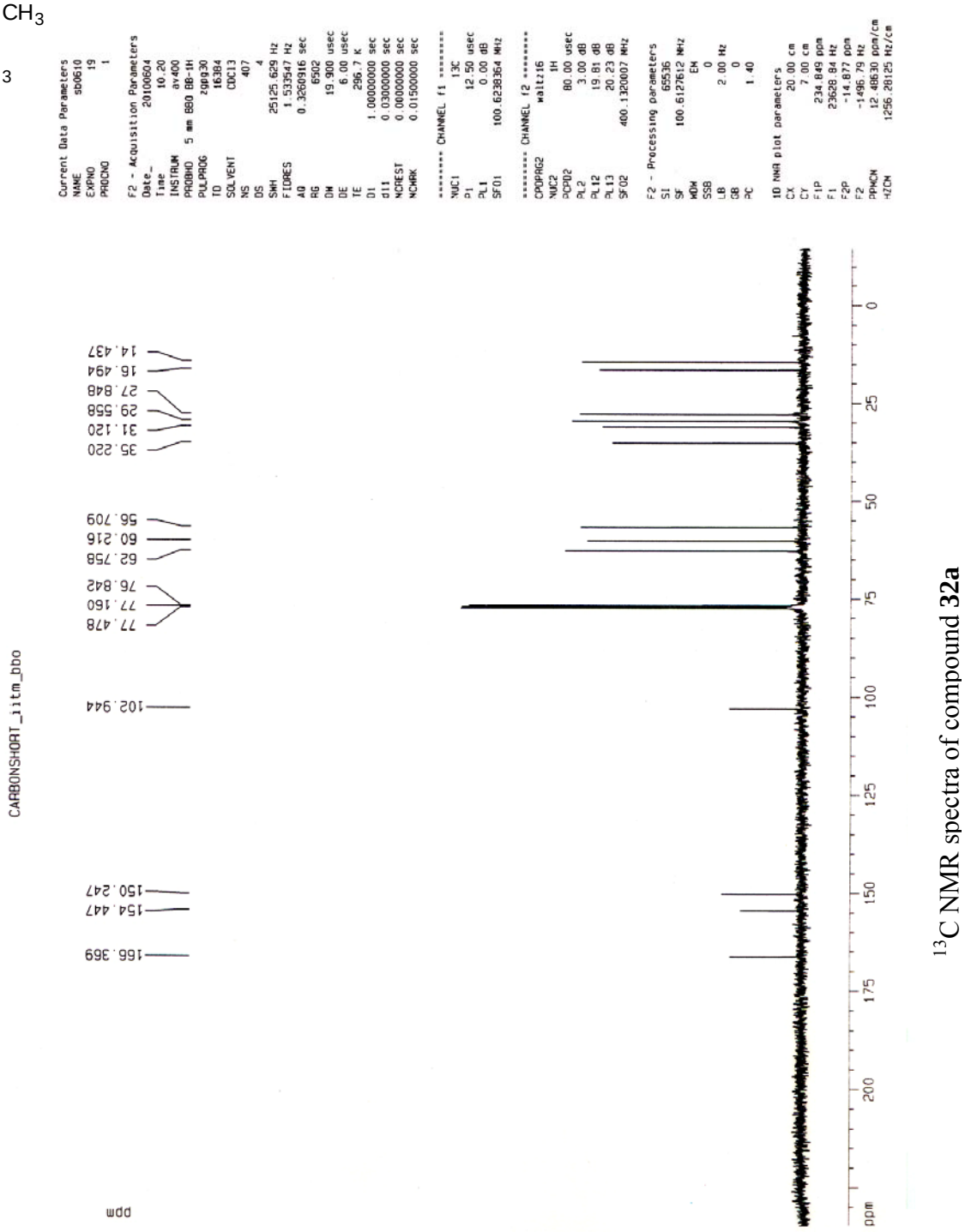


^{1}H NMR spectra of compound **32a**

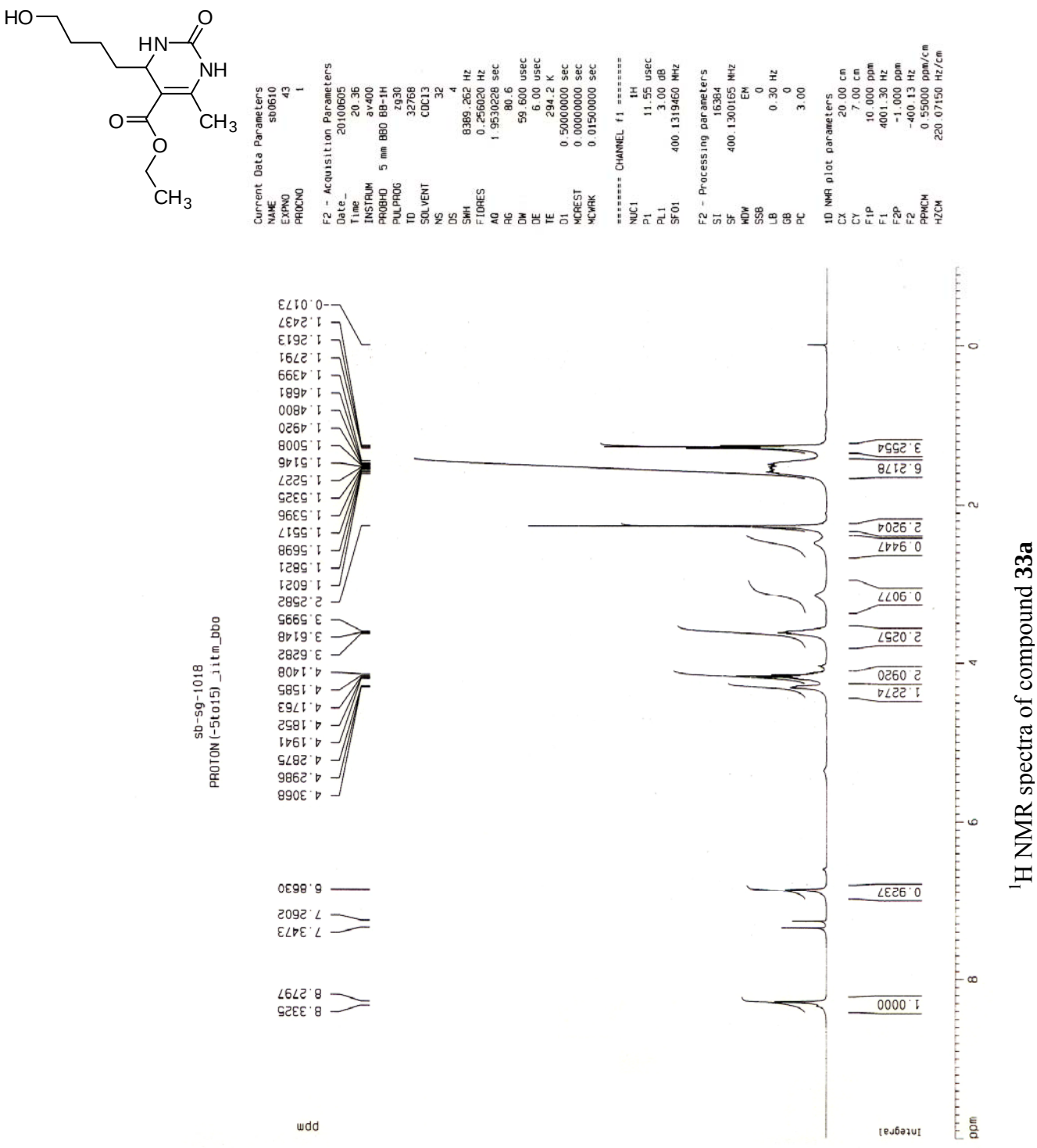


Expanded ^{1}H NMR spectra of compound **32a**

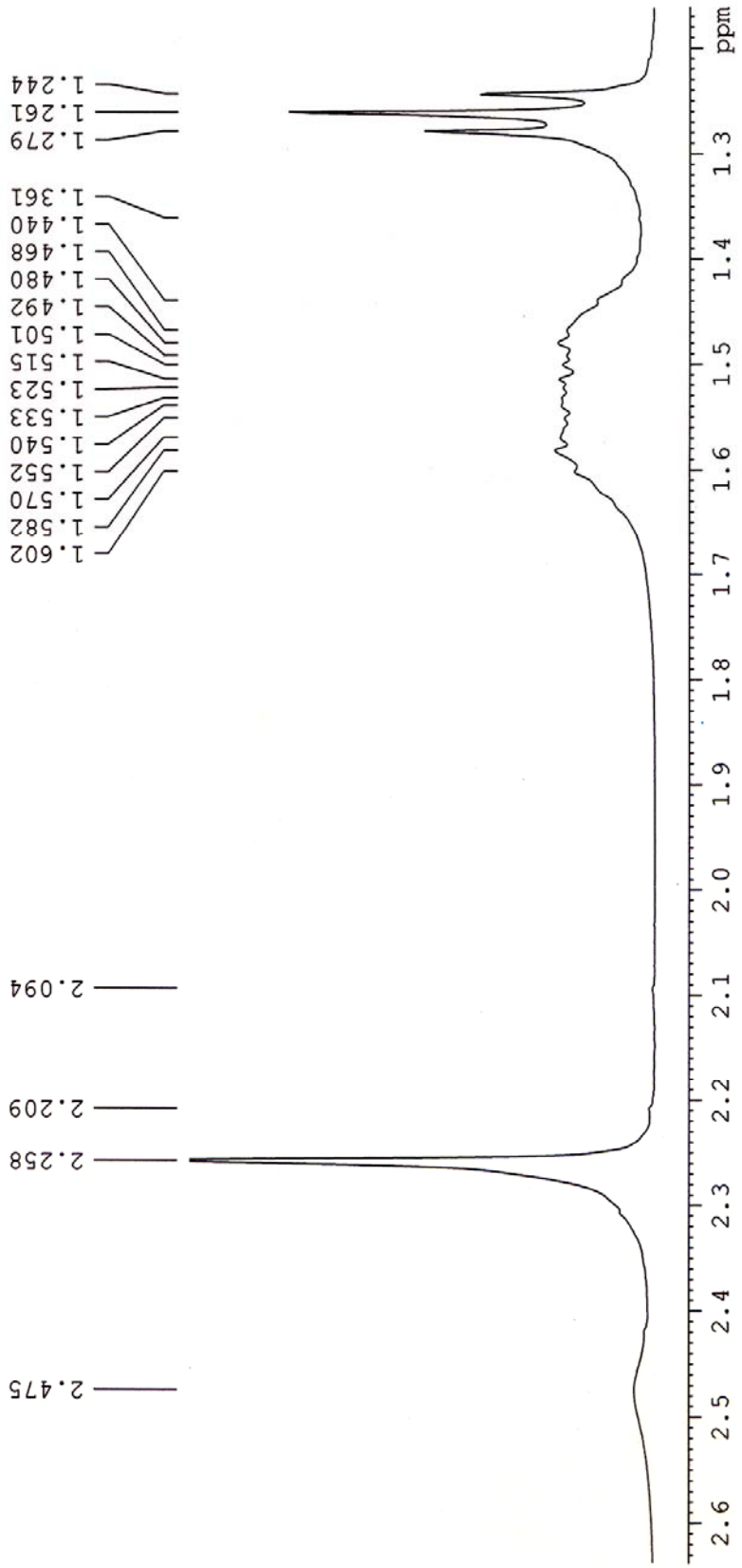




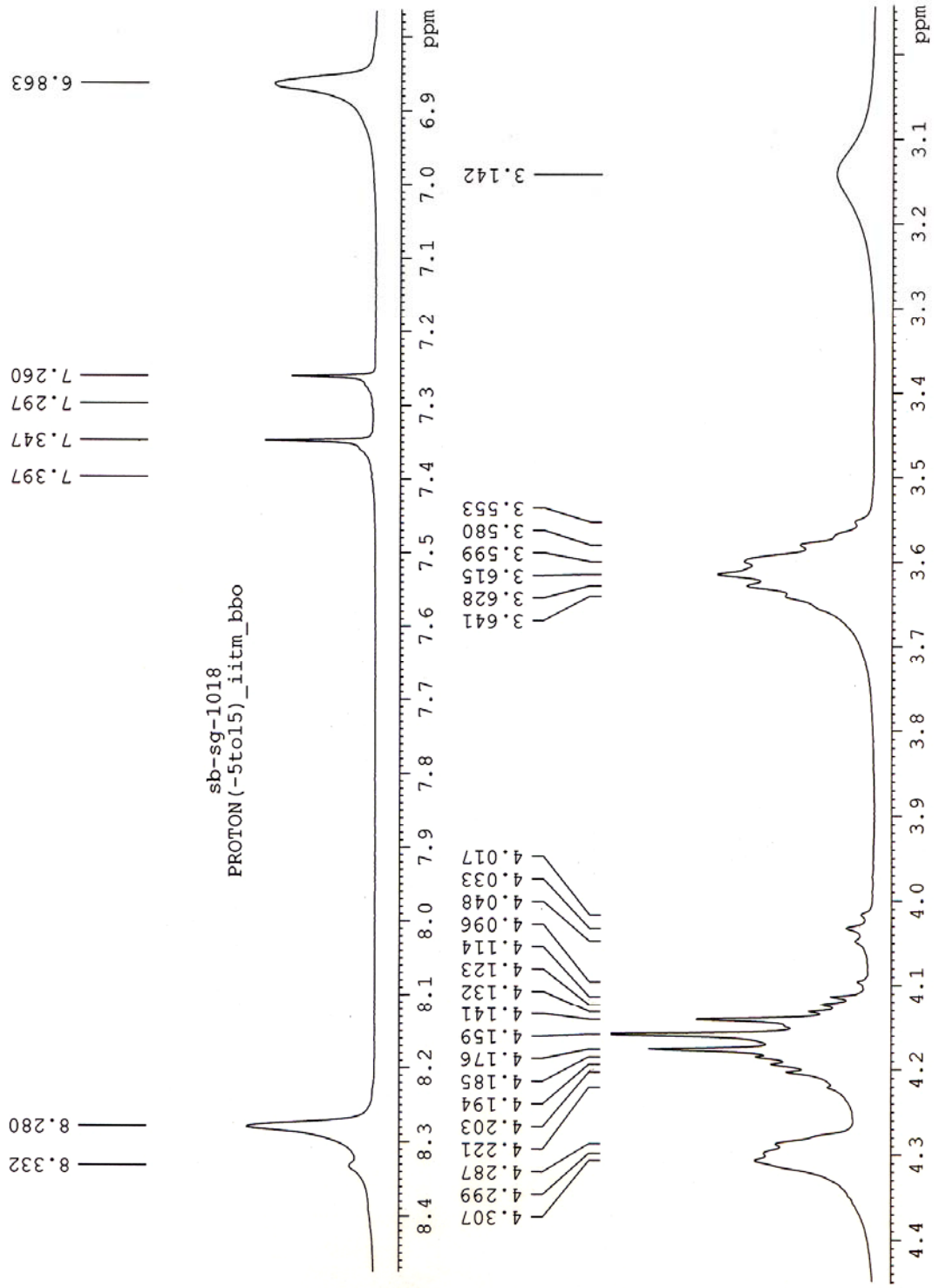
^{13}C NMR spectra of compound **32a**



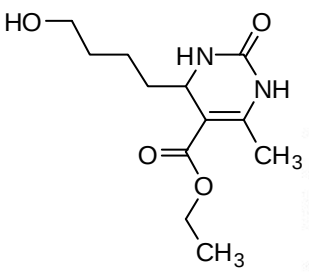
^{1}H NMR spectra of compound **33a**

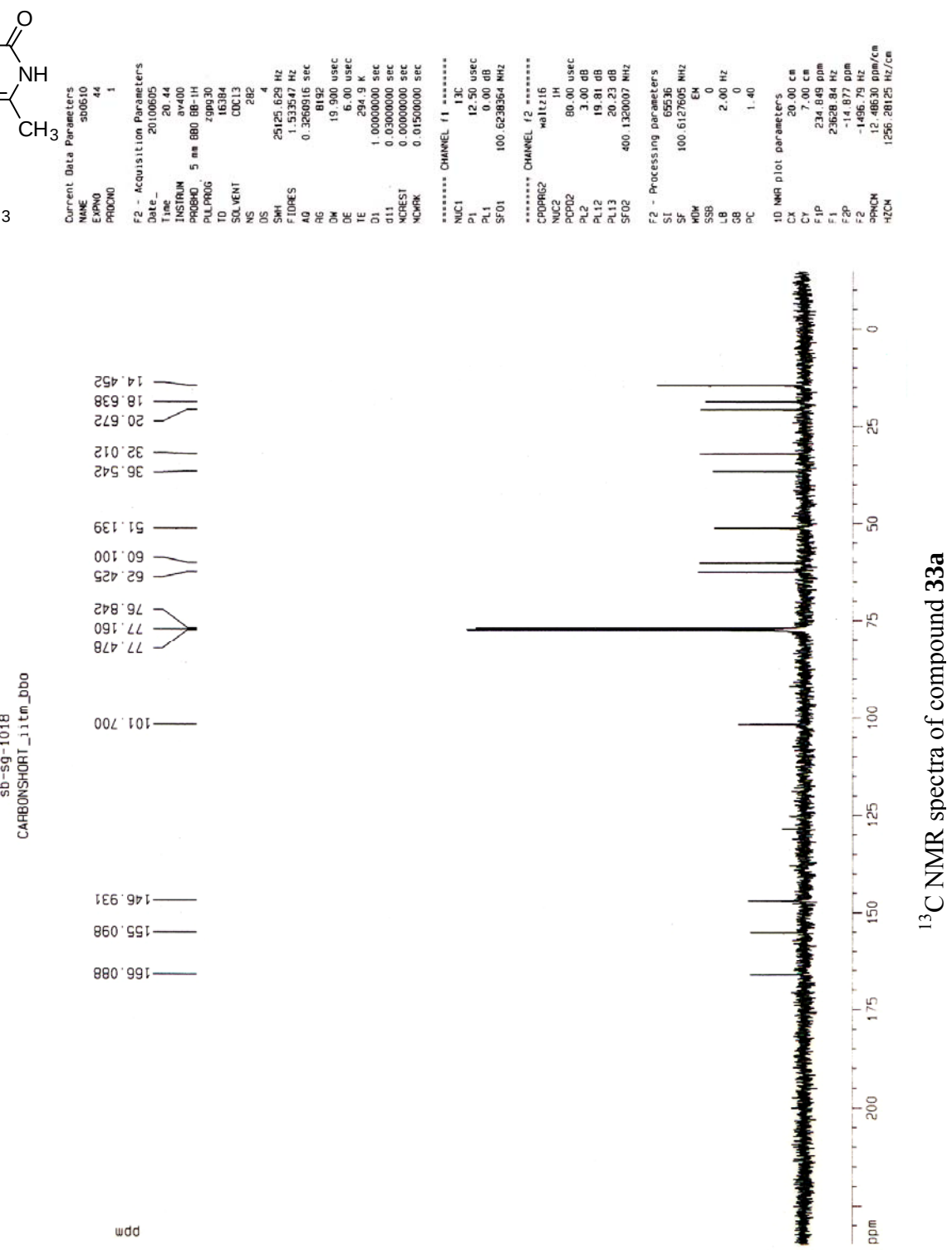


Expanded ^{1}H NMR spectra of compound **33a**



Expanded ^{1}H NMR spectra of compound **33a**





^{13}C NMR spectra of compound **33a**