



Supporting Information

for

Synthesis of 5-unsubstituted dihydropyrimidinone-4-carboxylates from deep eutectic mixtures

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Experimental procedures, characterization of products, copies of NMR spectra

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General information

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

Experimental section

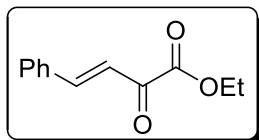
Preparation of β,γ -unsaturated ketoesters:

To a stirred solution of aldehyde (10 mmol), pyruvic acid (10 mmol) in MeOH (15 mL) at 0 °C was added KOH (15 mmol) in MeOH (5 mL) dropwise over 10 minutes. The reaction mixture was allowed to warm to room temperature. After completion of the reaction monitored by TLC, the reaction mixture was filtered over a Buchner funnel. The residue was washed with cold MeOH (10 mL) and acidified with 1N HCl and extracted with EtOAc (10 mL $\times$ 3). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum to give pure β,γ -unsaturated ketoacid in good yield.

To a stirred solution of β,γ -unsaturated ketoacid (10 mmol) in alcohol (25 mL) at 0 °C was added thionyl chloride (12 mmol) dropwise. The resultant reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated under vacuum and the crude reaction mass was quenched with saturated NaHCO_3 solution. The aqueous layer was extracted with ethyl acetate (10 mL $\times$ 3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude compound was purified using column chromatography over silica gel to give pure β,γ -unsaturated ketoester in good yield.

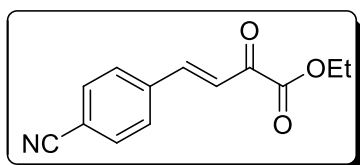
Characterization data for the β,γ -unsaturated ketoesters:

1. (E)-Ethyl 2-oxo-4-phenylbut-3-enoate (7) [1]:



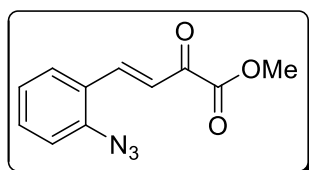
Yellow oil; Yield 80%; ^1H NMR (400 MHz, CDCl_3): δ 1.30 (t, 3H, $J = 7.2$ Hz), 4.29 (q, 2H, $J = 6.8$ Hz), 7.21–7.25 (m, 1H), 7.28–7.36 (m, 3H), 7.51 (d, 1H, $J = 7.6$ Hz), 7.74 (d, 1H, $J = 16.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.1, 62.6, 120.7, 129.1, 129.2, 131.7, 134.1, 148.5, 162.3, 183.0; HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 227.0684, found 227.0694.

2. (E)-Ethyl 4-(4-cyanophenyl)-2-oxobut-3-enoate (9) [2]:



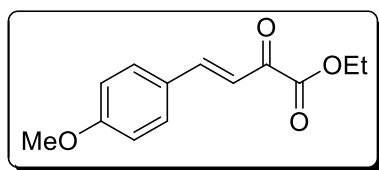
Yellow oil; Yield 78%; ^1H NMR (400 MHz, CDCl_3): δ 1.41 (t, 3H, $J = 7.2$ Hz), 4.40 (q, 2H, $J = 7.2$ Hz), 7.46 (d, 1H, $J = 16.0$ Hz), 7.72 (bs, 4H), 7.83 (d, 1H, $J = 16.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 63.0, 114.6, 118.3, 123.5, 129.3, 132.9, 138.3, 145.5, 161.7, 182.3.

3. (E)-Methyl 4-(2-azidophenyl)-2-oxobut-3-enoate (23):



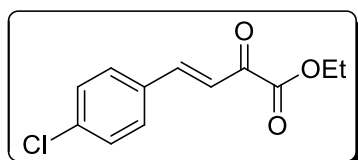
Yellow solid; Yield 51%; ^1H NMR (400 MHz, CDCl_3): δ 3.94 (s, 3H), 7.14–7.25 (m, 2H), 7.38 (d, 1H, $J = 16.4$ Hz), 7.44–7.55 (m, 1H), 7.69 (dd, 1H, $J = 7.6, 0.8$ Hz), 8.13 (d, 1H, $J = 16.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 53.2, 119.1, 121.8, 125.1, 125.6, 128.8, 132.8, 140.6, 142.8, 162.7, 182.6; HRMS calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_3\text{O}_3$ ($\text{M}^+ + \text{H}$) 232.0722, found 232.0712.

4. (E)-Ethyl 4-(4-methoxyphenyl)-2-oxobut-3-enoate (11) [1]:



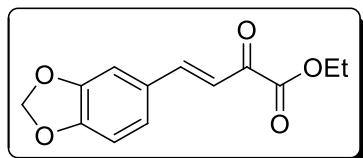
Yellow solid; Yield 84%; ^1H NMR (400 MHz, CDCl_3): δ 1.38 (dt, 3H, $J = 7.2, 0.8$ Hz), 3.82 (s, 3H), 4.36 (dq, 2H, $J = 7.2, 0.8$ Hz), 6.87–6.93 (m, 2H), 7.21 (dd, 1H, $J = 16.0, 1.6$ Hz), 7.56 (d, 2H, $J = 7.6$ Hz), 7.80 (d, 1H, $J = 16.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.1, 55.5, 62.5, 114.6, 118.1, 126.8, 131.1, 148.4, 162.5, 162.6, 182.7; HRMS calcd. for $\text{C}_{13}\text{H}_{15}\text{O}_4$ ($\text{M}^+ + \text{H}$) 235.0970, found 235.0977.

5. (E)-Ethyl 4-(4-chlorophenyl)-2-oxobut-3-enoate (25) [1]:



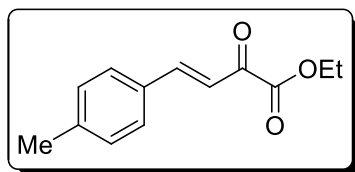
Yellow solid; Yield 73%; ^1H NMR (400 MHz, CDCl_3): δ 1.34 (t, 3H, $J = 7.2$ Hz), 4.32 (q, 2H, $J = 7.2$ Hz), 7.29–7.36 (m, 3H), 7.50 (d, 2H, $J = 8.4$ Hz), 7.74 (d, 1H, $J = 16.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 62.8, 121.0, 129.6, 130.3, 132.6, 137.8, 147.0, 162.1, 182.7; HRMS calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_3\text{Cl}$ ($\text{M}^+ + \text{H}$) 239.0475, found 239.0477.

6. (E)-Ethyl 4-(benzo[d][1,3]dioxol-5-yl)-2-oxobut-3-enoate (13) [1]:



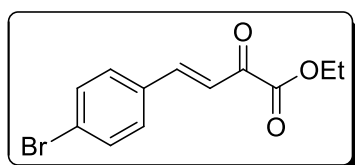
Yellow solid; Yield 48%; ^1H NMR (400 MHz, CDCl_3): δ 1.44 (t, 3H, $J = 6.8$ Hz), 4.42 (q, 2H, $J = 7.2$ Hz), 6.08 (s, 2H), 6.88 (d, 1H, $J = 7.2$ Hz), 7.15–7.20 (m, 2H), 7.27 (d, 1H, $J = 17.2$ Hz), 7.81 (d, 1H, $J = 16.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 62.6, 102.0, 107.0, 108.9, 118.6, 126.7, 128.7, 148.4, 148.7, 151.1, 162.5, 182.7; HRMS calcd. for $\text{C}_{13}\text{H}_{13}\text{O}_5$ ($\text{M}^+ + \text{H}$) 249.0763, found 249.0758.

7. (E)-Ethyl 2-oxo-4-*p*-tolylbut-3-enoate (15) [1]:



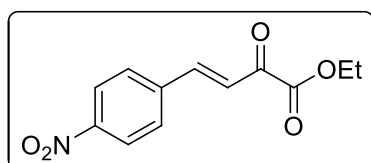
Yellow oil; Yield 88%; ^1H NMR (400 MHz, CDCl_3): δ 1.40 (t, 3H, $J = 7.2$ Hz), 2.38 (s, 3H), 4.38 (q, 2H, $J = 6.8$ Hz), 7.22 (d, 2H, $J = 8.0$ Hz), 7.31 (d, 1H, $J = 16.4$ Hz), 7.52 (d, 2H, $J = 8.4$ Hz), 7.83 (d, 1H, $J = 16.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 21.7, 62.5, 119.6, 129.2, 129.9, 131.4, 142.6, 148.7, 162.4, 183.0; HRMS calcd. for $\text{C}_{13}\text{H}_{14}\text{O}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 241.0841, found 241.0849.

8. (E)-Ethyl 4-(4-bromophenyl)-2-oxobut-3-enoate (19) [1]:



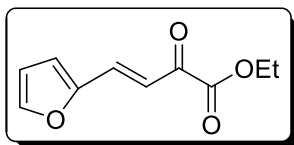
Yellow solid; Yield 69%; ^1H NMR (400 MHz, CDCl_3): δ 1.41 (t, 3H, $J = 7.2$ Hz), 4.39 (q, 2H, $J = 6.8$ Hz), 7.36 (d, 1H, $J = 16.0$ Hz), 7.49 (d, 2H, $J = 8.4$ Hz), 7.56 (d, 2H, $J = 8.4$ Hz), 7.79 (d, 1H, $J = 16.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 62.8, 121.0, 126.3, 130.4, 132.5, 133.0, 147.0, 162.1, 182.7; HRMS calcd. for $\text{C}_{12}\text{H}_{11}\text{O}_3\text{BrNa}$ ($\text{M}^+ + \text{Na}$) 304.9789, found 304.9800.

9. (E)-Ethyl 4-(4-nitrophenyl)-2-oxobut-3-enoate (17) [3]:



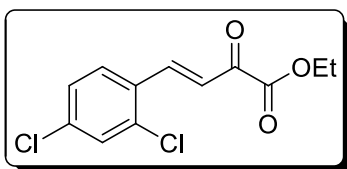
Yellow solid; Yield 75%; ^1H NMR (400 MHz, CDCl_3): δ 1.41 (t, 3H, $J = 6.8$ Hz), 4.40 (q, 2H, $J = 7.2$ Hz), 7.48 (d, 1H, $J = 16.0$ Hz), 7.62–7.82 (m, 2H), 7.87 (d, 1H, $J = 16.0$ Hz), 8.27 (d, 1H, $J = 8.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 63.0, 124.1, 124.4, 129.6, 140.1, 144.9, 149.2, 161.7, 182.3; HRMS calcd. for $\text{C}_{12}\text{H}_{11}\text{NO}_5\text{Na}$ ($\text{M}^+ + \text{Na}$) 272.0535, found 272.0525.

10. (E)-Ethyl 4-(furan-2-yl)-2-oxobut-3-enoate (21) [4]:



Yellow solid; Yield 65%; ^1H NMR (400 MHz, CDCl_3): δ 1.40 (t, 3H, $J = 7.2$ Hz), 4.37 (q, 2H, $J = 7.2$ Hz), 6.54 (dd, 1H, $J = 2.8, 1.6$ Hz), 6.82 (d, 1H, $J = 3.6$ Hz), 7.22 (d, 1H, $J = 15.6$ Hz), 7.55–7.65 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 62.6, 113.3, 118.2, 118.7, 133.7, 146.5, 151.2, 162.2, 182.5; HRMS calcd. for $\text{C}_{10}\text{H}_{10}\text{O}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 217.0477, found 217.0482.

11. (E)-Ethyl 4-(2,4-dichlorophenyl)-2-oxobut-3-enoate (27) [1]:



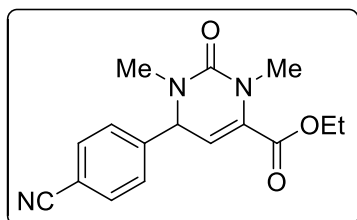
Yellow solid; Yield 45%; ^1H NMR (400 MHz, CDCl_3): δ 1.34 (t, 3H, $J = 6.8$ Hz), 4.32 (q, 2H, $J = 6.8$ Hz), 7.20–7.25 (m, 2H), 7.38 (d, 1H, $J = 2.0$ Hz), 8.11 (d, 1H, $J = 16.4$ Hz), 8.61 (d, 1H, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.1, 62.8, 123.0, 127.8, 128.7, 130.3, 130.9, 136.8, 137.7, 142.5, 161.9, 182.5; HRMS calcd. for $\text{C}_{12}\text{H}_{11}\text{O}_3\text{Cl}_2$ ($\text{M}^+ + \text{H}$) 273.0085, found 273.0082.

General procedure for the formation of 5-unsubstituted dihydropyrimidinones:

Under conditions closely related to [5], 1.5 g of L-(+)-tartaric acid-DMU (30:70) mixture was heated to 70 °C to obtain a clear melt. To the melt, 1 mmol of β,γ -unsaturated ketoester was added at 70 °C. The reaction was monitored by thin layer chromatography. After the completion of reaction, the reaction was quenched by adding water while still hot. The reaction mixture was cooled to room temperature and the aqueous layer was extracted with DCM (3×5 mL) and washed with water (2×5 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude compound was purified using column chromatography over silica gel to afford pure 5-unsubstituted DHPM.

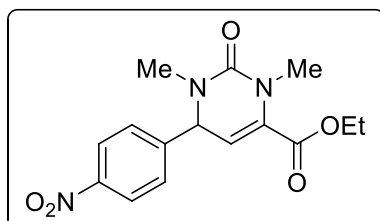
Characterization data for the 5-unsubstituted dihydropyrimidinones:

1. Ethyl 6-(4-cyanophenyl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (10)



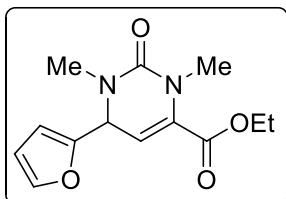
Colorless oil, Yield 88%; IR (neat): 2372, 1729, 1661, 1461, 1264 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.30 (t, 3H, $J = 7.2$ Hz), 2.82 (s, 3H), 3.25 (s, 3H) 4.20–4.27 (m, 2H), 4.98 (d, 1H, $J = 5.6$ Hz), 5.74 (d, 1H, $J = 5.6$ Hz), 7.35 (d, 2H, $J = 8.4$ Hz), 7.68 (d, 2H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 33.1, 34.4, 61.8, 62.0, 109.7, 112.5, 118.5, 127.3, 132.9, 133.2, 145.3, 154.5, 162.4; HRMS calcd. for $\text{C}_{16}\text{H}_{18}\text{N}_3\text{O}_3$ ($\text{M}^+ + \text{H}$) 300.1348, found 300.1362.

2. Ethyl 1,3-dimethyl-6-(4-nitrophenyl)-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (18)



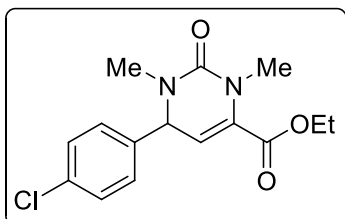
Pale yellow oil; Yield 77%; IR (neat): 2932, 1727, 1661, 1523, 1255, 1090 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.30 (t, 3H, $J = 6.8$ Hz), 2.84 (s, 3H), 3.26 (s, 3H), 4.19–4.29 (m, 2H), 5.05 (d, 1H, $J = 5.6$ Hz), 5.75 (d, 1H, $J = 5.6$ Hz), 7.38–7.43 (m, 2H), 8.22–8.27 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 33.1, 34.5, 61.6, 62.0, 109.5, 124.7, 127.4, 133.1, 147.2, 148.0, 154.4, 162.4. HRMS calcd. for $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_5\text{Na}$ ($\text{M}^+ + \text{Na}$) 342.1066, found 342.1078.

3. Ethyl 6-(furan-2-yl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (22)



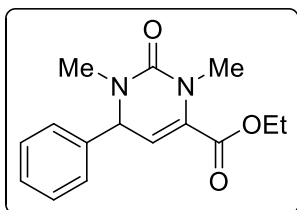
Colorless oil; Yield 60%; IR (neat): 1730, 1660, 1423, 1265, 1092 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.32 (t, 3H, $J = 7.2$ Hz), 2.90 (s, 3H), 3.22 (s, 3H), 4.20–4.31 (m, 2H), 4.92 (d, 1H, $J = 6.0$ Hz), 5.87 (d, 1H, $J = 6.0$ Hz), 6.23 (d, 1H, $J = 3.2$ Hz), 6.32 (dd, 1H, $J = 3.2, 2.0$ Hz), 7.37 (t, 1H, $J = 1.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.1, 33.0, 34.1, 54.6, 61.7, 107.8, 108.7, 110.4, 133.8, 143.1, 151.6, 154.9, 162.5. HRMS calcd. for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_4\text{Na}$ ($\text{M}^+ + \text{Na}$) 287.1008, found 287.1008.

4. Ethyl 6-(4-chlorophenyl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (26)



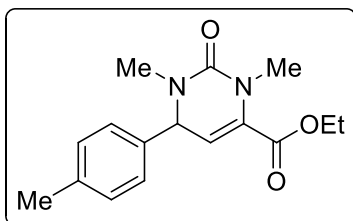
Colorless oil; Yield 85%; IR (neat): 1729, 1661, 1423, 1265, 1091 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.29 (t, 3H, $J = 7.2$ Hz), 2.80 (s, 3H), 3.25 (s, 3H), 4.17–4.30 (m, 2H), 4.89 (d, 1H, $J = 5.6$ Hz), 5.76 (d, 1H, $J = 5.6$ Hz), 7.14–7.18 (m, 2H), 7.32–7.36 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 33.1, 34.2, 61.5, 61.8, 111.0, 128.0, 129.5, 132.3, 134.4, 138.6, 154.6, 162.6. HRMS calcd. for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_3\text{Cl}$ ($\text{M}^+ + \text{H}$) 309.1066, found 309.1009.

5. Ethyl 1,3-dimethyl-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-4-carboxylate (8)



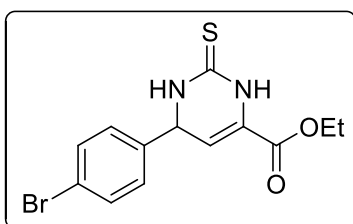
Colorless oil; Yield 83%; IR (neat): 2925, 1715, 1664, 1455, 1248¹; ¹H NMR (400 MHz, CDCl₃): δ 1.30 (t, 3H, J = 7.2 Hz), 2.82 (s, 3H), 3.27 (s, 3H), 4.17–4.30 (m, 2H), 4.91 (d, 1H, J = 5.6 Hz), 5.83 (d, 1H, J = 5.6 Hz), 7.24 (d, 2H, J = 6.8 Hz), 7.30–7.41 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 14.2, 33.1, 34.2, 61.7, 62.1, 111.8, 126.7, 128.6, 129.3, 132.0, 140.0, 154.8, 162.7; HRMS calcd. for C₁₅H₁₉N₂O₃ (M⁺+H) 275.1396, found 275.1405.

6. Ethyl 1,3-dimethyl-2-oxo-6-*p*-tolyl-1,2,3,6-tetrahydropyrimidine-4-carboxylate (16)



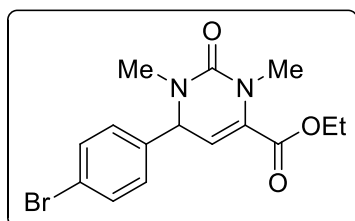
Colorless oil; Yield 84%; IR (neat): 2923, 1727, 1661, 1460, 1086 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.28 (t, 3H, J = 6.8 Hz), 2.34 (s, 3H), 2.80 (s, 3H), 3.25 (s, 3H), 4.15–4.28 (m, 2H), 4.86 (d, 1H, J = 5.6 Hz), 5.81 (d, 1H, J = 5.6 Hz), 7.11 (d, 2H, J = 8.0 Hz), 7.17 (d, 2H, J = 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 14.2, 21.2, 33.0, 34.1, 61.6, 61.8, 112.1, 126.6, 129.9, 131.9, 137.1, 138.4, 154.8, 162.8; HRMS calcd. for C₁₆H₂₁N₂O₃ (M⁺+H) 289.1552, found 289.1552.

7. Ethyl 6-(4-bromophenyl)-1,3-dimethyl-2-thioxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (20A)



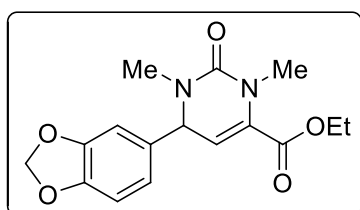
Yellow semisolid; Yield 48%; IR (neat): 1735, 1657, 1586, 1266, 1072 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.32 (t, 3H, $J = 6.8$ Hz), 4.27 (q, 2H, $J = 4.6$ Hz), 4.80 (d, 1H, $J = 6.2$ Hz), 6.34 (d, 1H, $J = 6.0$ Hz), 7.13–7.18 (m, 2H), 7.43–7.48 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.4, 43.0, 61.5, 110.9, 122.5, 129.4, 132.3, 139.2, 140.5, 155.3, 165.3. HRMS calcd. for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_2\text{SBr}$ ($\text{M}^+ + \text{H}$) 340.9959, found 340.9974.

8. Ethyl 6-(4-bromophenyl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (20)



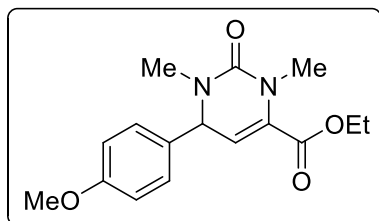
Colorless oil; Yield 70%; IR (neat): 2926 1727, 1662, 1478, 1260 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.28 (t, 3H, $J = 7.2$ Hz), 2.79 (s, 3H), 3.23 (s, 3H), 4.16–4.29 (m, 2H), 4.87 (d, 1H, $J = 5.2$ Hz), 5.75 (d, 1H, $J = 5.2$ Hz), 7.09 (d, 1H, $J = 8.4$ Hz), 7.48 (d, 1H, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.1, 33.0, 34.1, 61.5, 61.8, 110.9, 122.5, 128.3, 132.3, 132.4, 139.1, 154.5, 162.5. HRMS calcd. for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_3\text{Br}_1$ ($\text{M}^+ + \text{H}$) 353.0501, found 353.0500.

9. Ethyl 6-(benzo[d][1,3]dioxol-5-yl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (14)



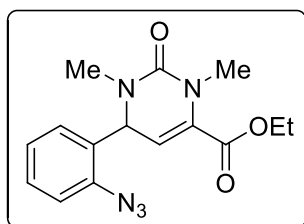
Colorless oil; Yield 71%; IR (neat): 2985, 1726, 1658, 1265 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.29 (t, 3H, $J = 7.2$ Hz), 2.79 (s, 3H), 3.24 (s, 3H), 4.18–4.28 (m, 2H), 4.80 (d, 1H, $J = 5.2$ Hz), 5.77 (d, 1H, $J = 5.6$ Hz), 5.96 (s, 2H), 6.68 (ddd, 2H, $J = 9.6, 1.6$ Hz), 6.76 (d, 1H, $J = 7.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 33.0, 34.0, 61.7, 61.9, 101.4, 107.1, 108.6, 111.7, 120.2, 132.0, 134.0, 147.9, 148.6, 154.6, 162.7. HRMS calcd. for $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}_5$ ($\text{M}^+ + \text{H}$) 319.1294, found 319.1304.

10. Ethyl 6-(4-methoxyphenyl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (12)



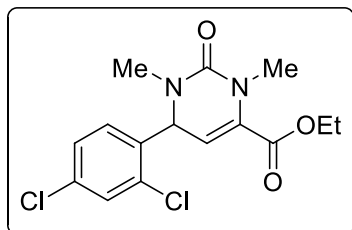
Colorless oil; Yield 87%; IR (neat): 1725, 1646, 1464, 1255 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.29 (t, 3H, $J = 7.2$ Hz), 2.79 (s, 3H), 3.25 (s, 3H), 3.80 (s, 3H), 4.16–4.29 (m, 2H), 4.84 (d, 1H, $J = 5.6$ Hz), 5.80 (d, 1H, $J = 5.6$ Hz), 6.86–6.91 (m, 1H), 7.12–7.18 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 33.1, 34.0, 55.5, 61.5, 61.7, 112.2, 114.5, 128.0, 131.8, 132.1, 154.7, 159.8, 162.8; HRMS calcd. for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_4$ ($\text{M}^+ + \text{H}$) 305.1501, found 305.1496.

11. Ethyl 6-(2-azidophenyl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (24)



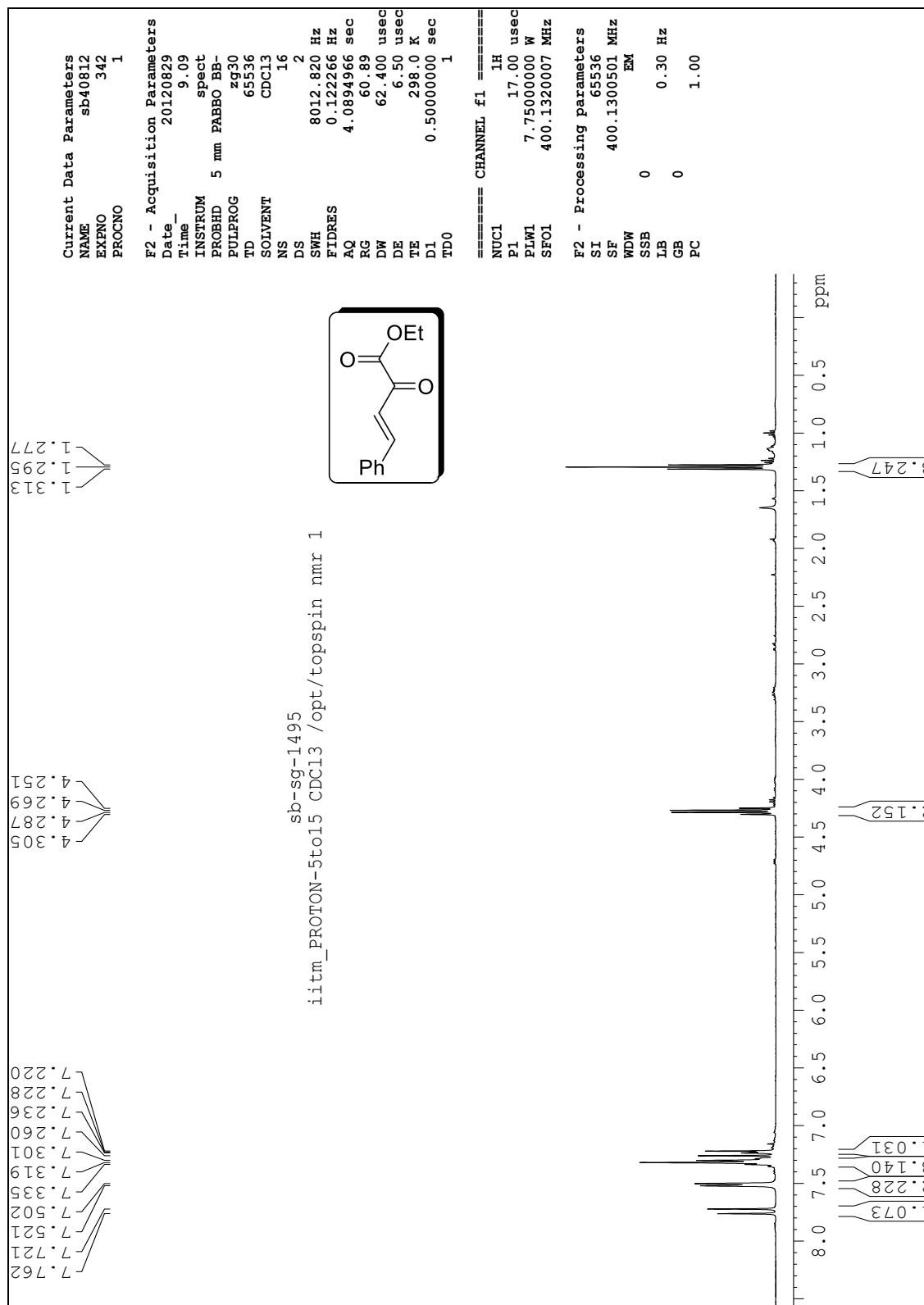
Colorless oil; Yield 53%; IR (neat): 2924, 2124, 1728, 1663, 1260 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 2.83 (s, 3H), 3.23 (s, 3H), 3.77 (s, 3H), 5.24 (d, 1H, $J = 6.0$ Hz), 5.93 (d, 1H, $J = 6.0$ Hz), 7.13–7.20 (m, 3H), 7.31–7.37 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 33.0, 34.4, 52.5, 56.6, 111.3, 118.6, 125.8, 127.3, 129.5, 130.7, 132.1, 136.7, 155.4, 163.1. HRMS calcd. for $\text{C}_{14}\text{H}_{16}\text{N}_5\text{O}_3$ ($\text{M}^+ + \text{H}$) 302.1253, found 302.1243.

12. Ethyl 6-(2,4-dichlorophenyl)-1,3-dimethyl-2-oxo-1,2,3,6-tetrahydropyrimidine-4-carboxylate (28)

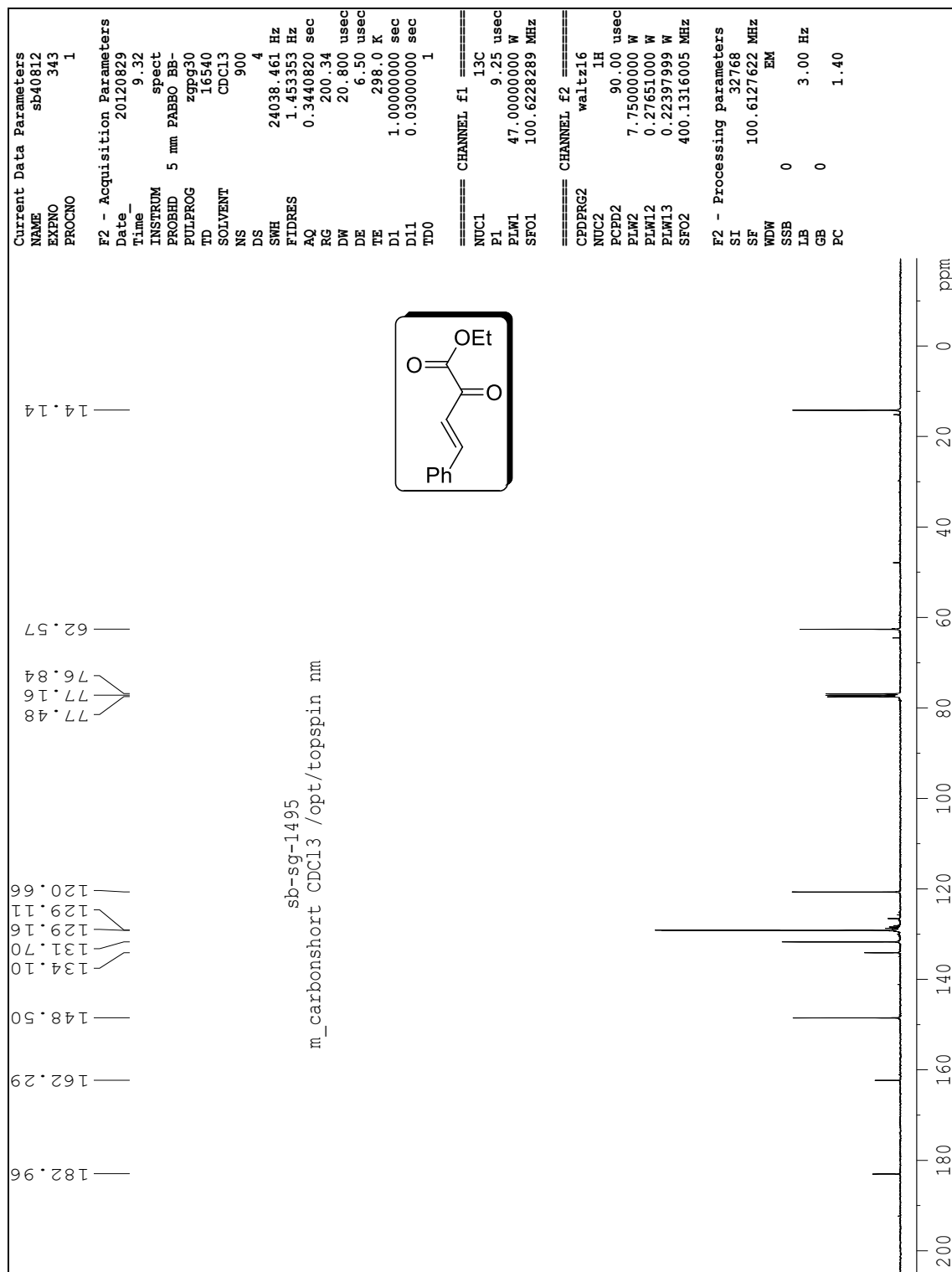


Colorless oil; Yield 51%; IR (neat): 2928, 1729, 1668, 1468, 1255, 1090 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.23 (t, 3H, $J = 7.2$ Hz), 2.78 (s, 3H), 3.17 (s, 3H), 4.10–4.24 (m, 2H), 5.32 (d, 1H, $J = 6.0$ Hz), 5.82 (d, 1H, $J = 6.0$ Hz), 7.07 (d, 1H, $J = 8.0$ Hz), 7.21 (dd, 1H, $J = 8.4$, 2.0 Hz), 7.34 (d, 1H, $J = 2.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 33.0, 34.4, 58.3, 61.9, 109.1, 128.4, 130.0, 132.5, 133.0, 134.7, 135.9, 155.0, 162.5. HRMS calcd. for $\text{C}_{15}\text{H}_{16}\text{Cl}_2\text{N}_2\text{O}_3\text{Na}$ ($\text{M}^+ + \text{Na}$) 365.0436, found 365.0448.

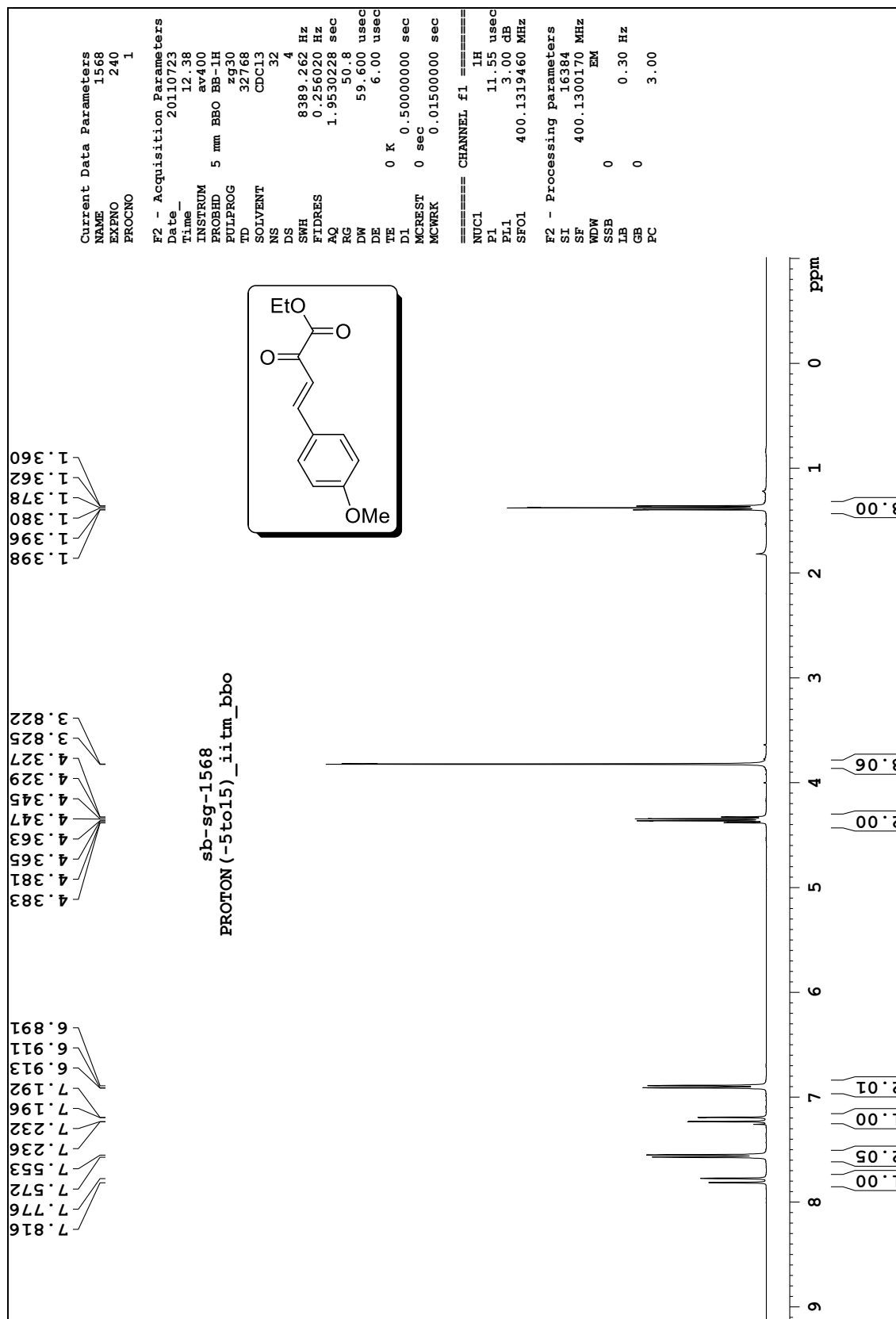
Copies of ¹H NMR and ¹³C NMR spectra



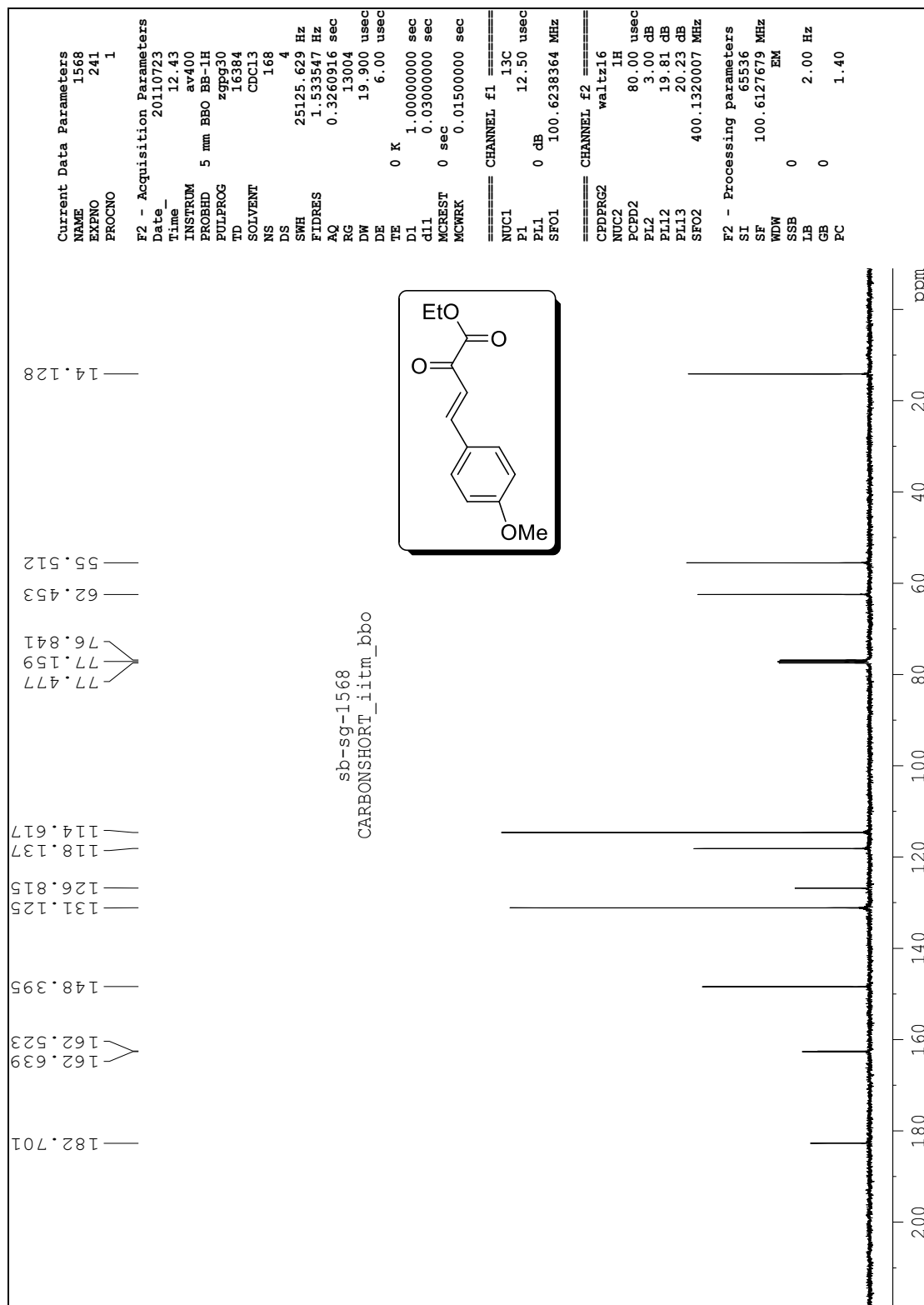
¹H NMR spectrum of compound 7



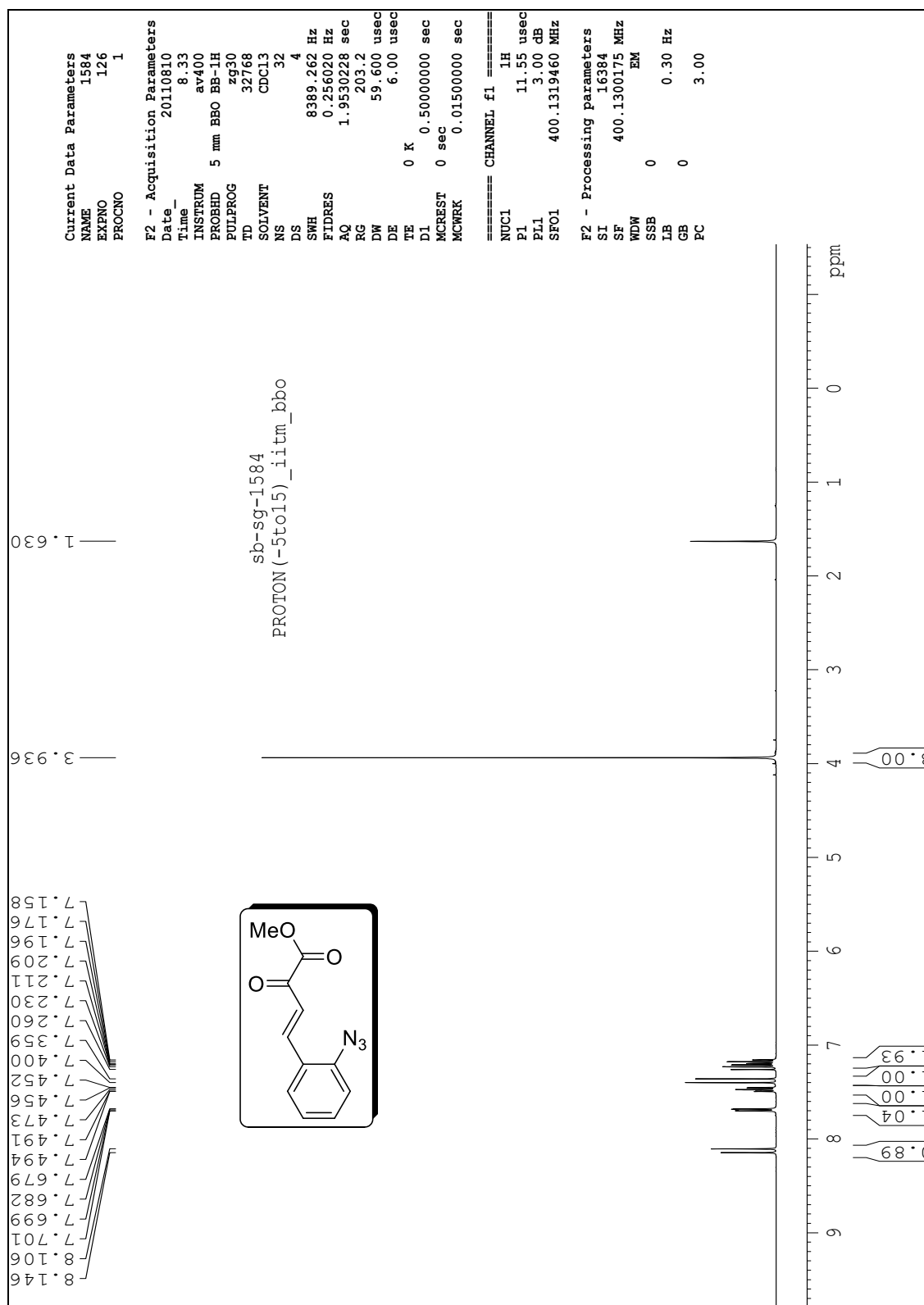
¹³C NMR spectrum of compound 7



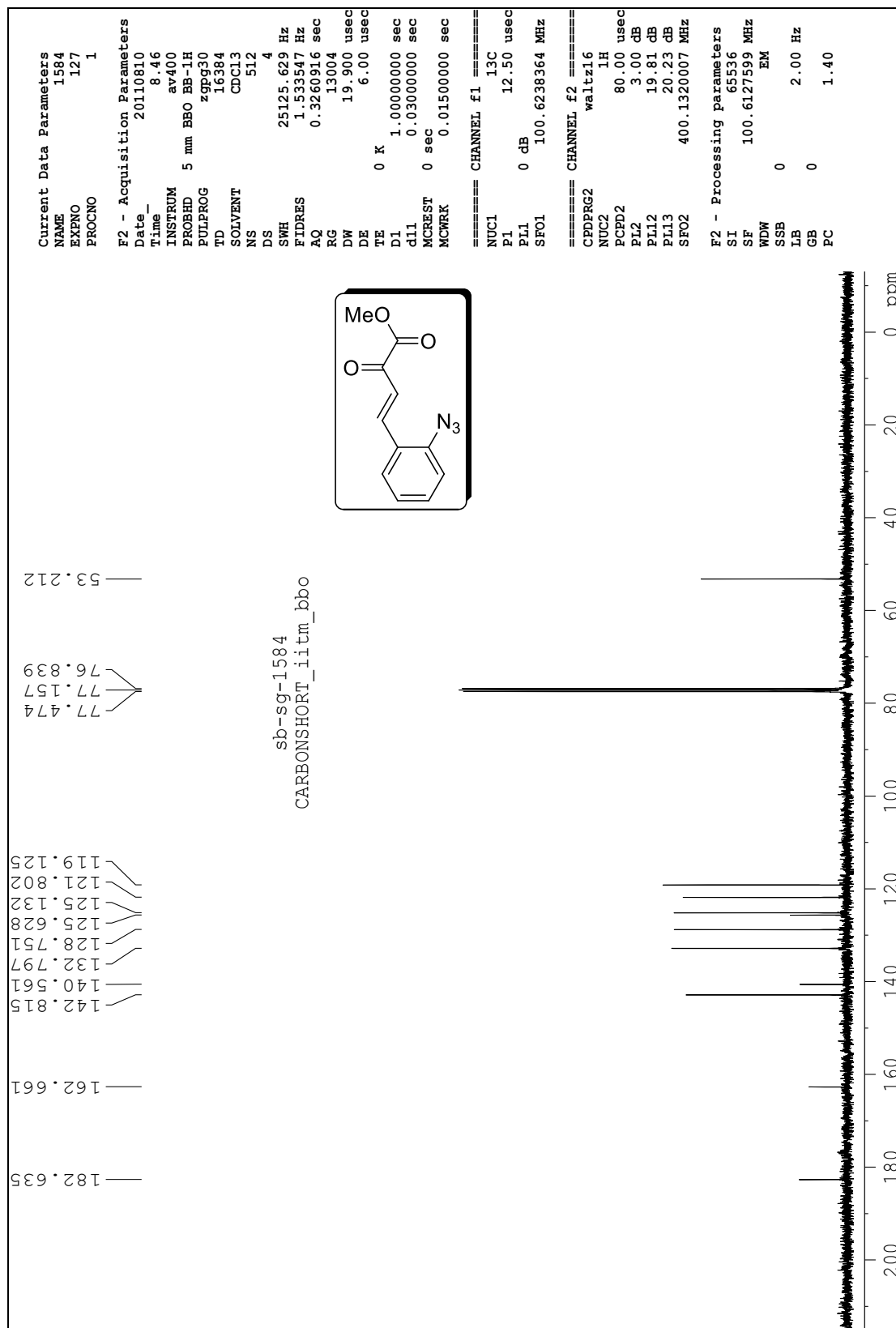
¹H NMR spectrum of compound 11



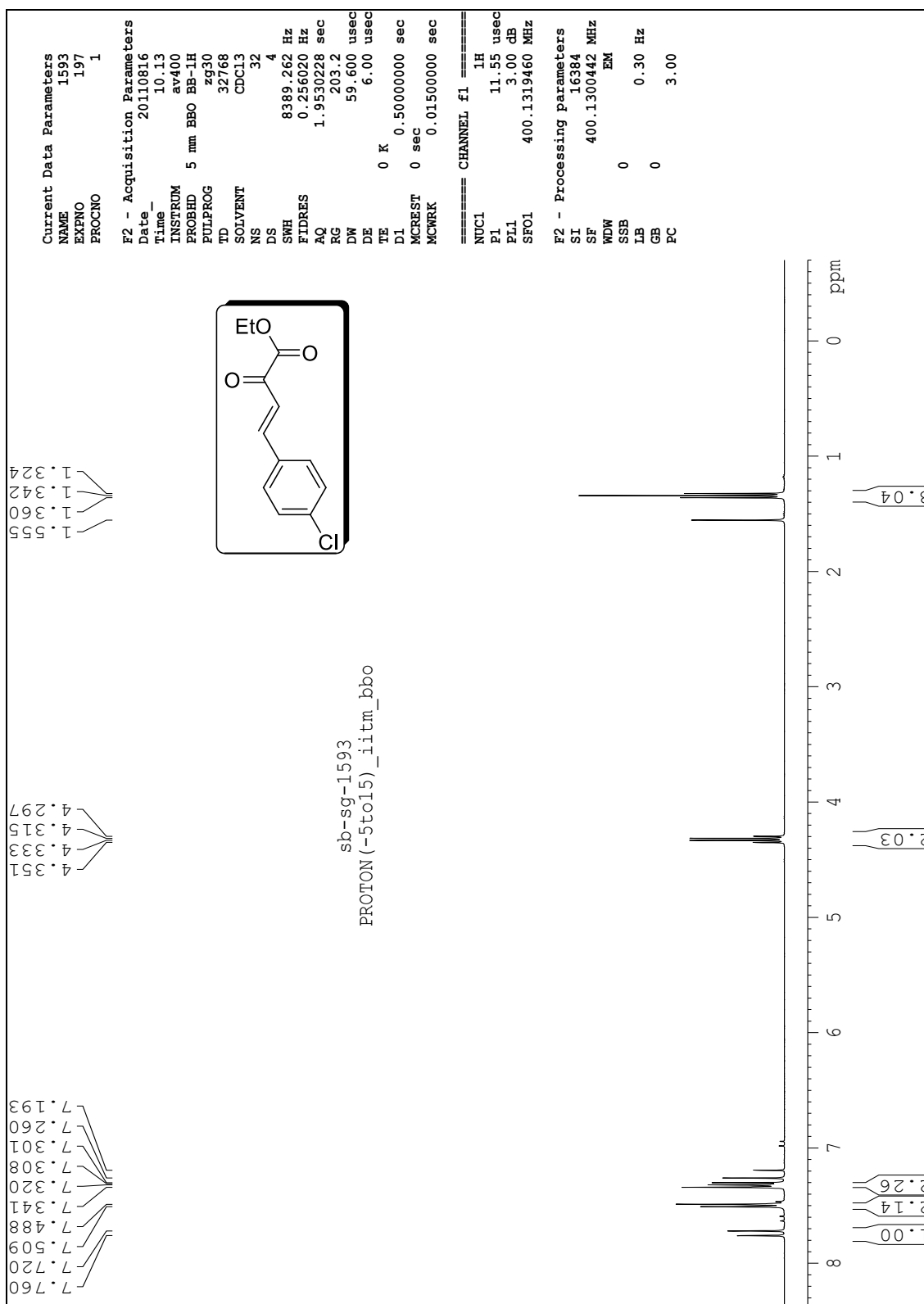
¹³C NMR spectrum of compound 11



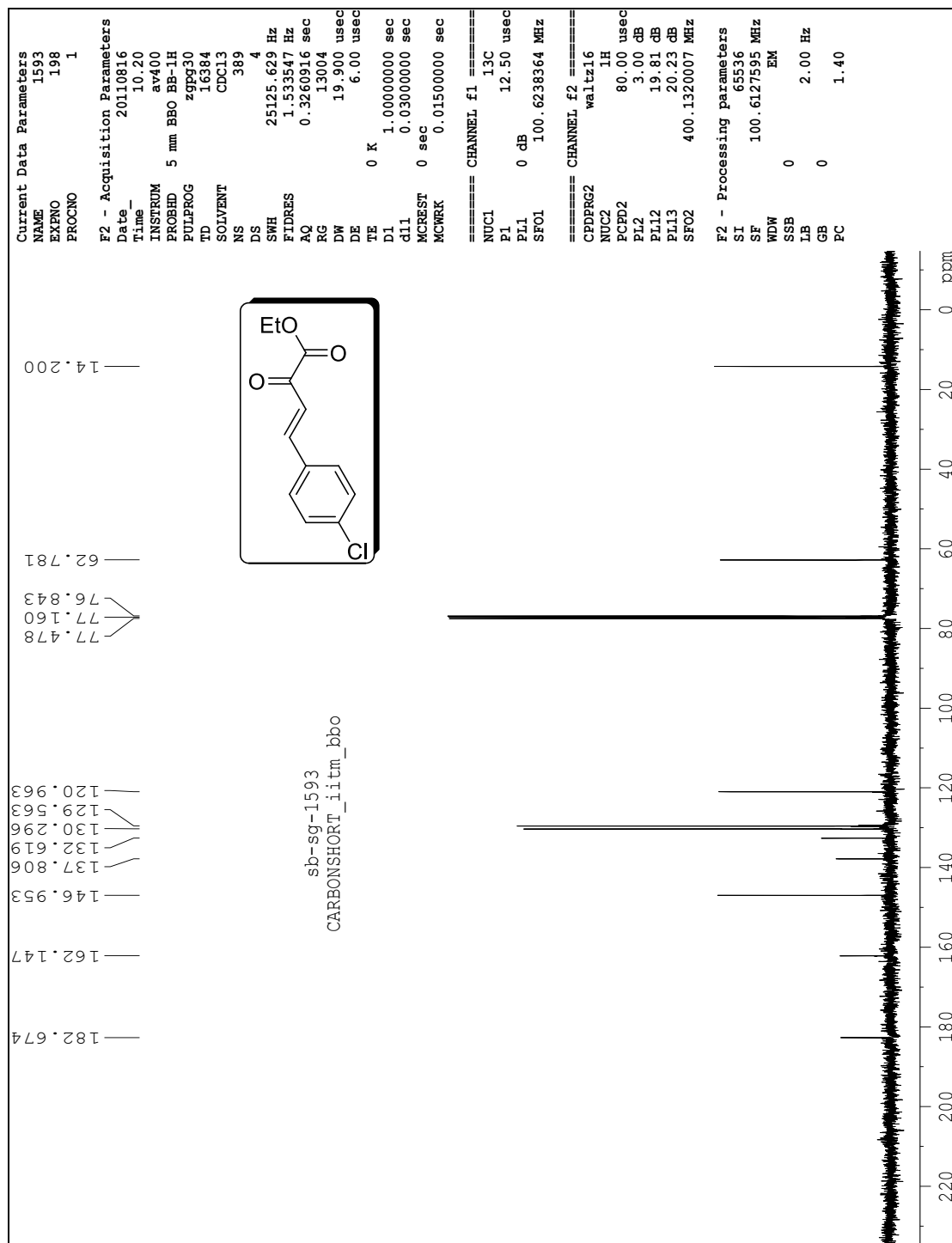
¹H NMR spectrum of compound 23



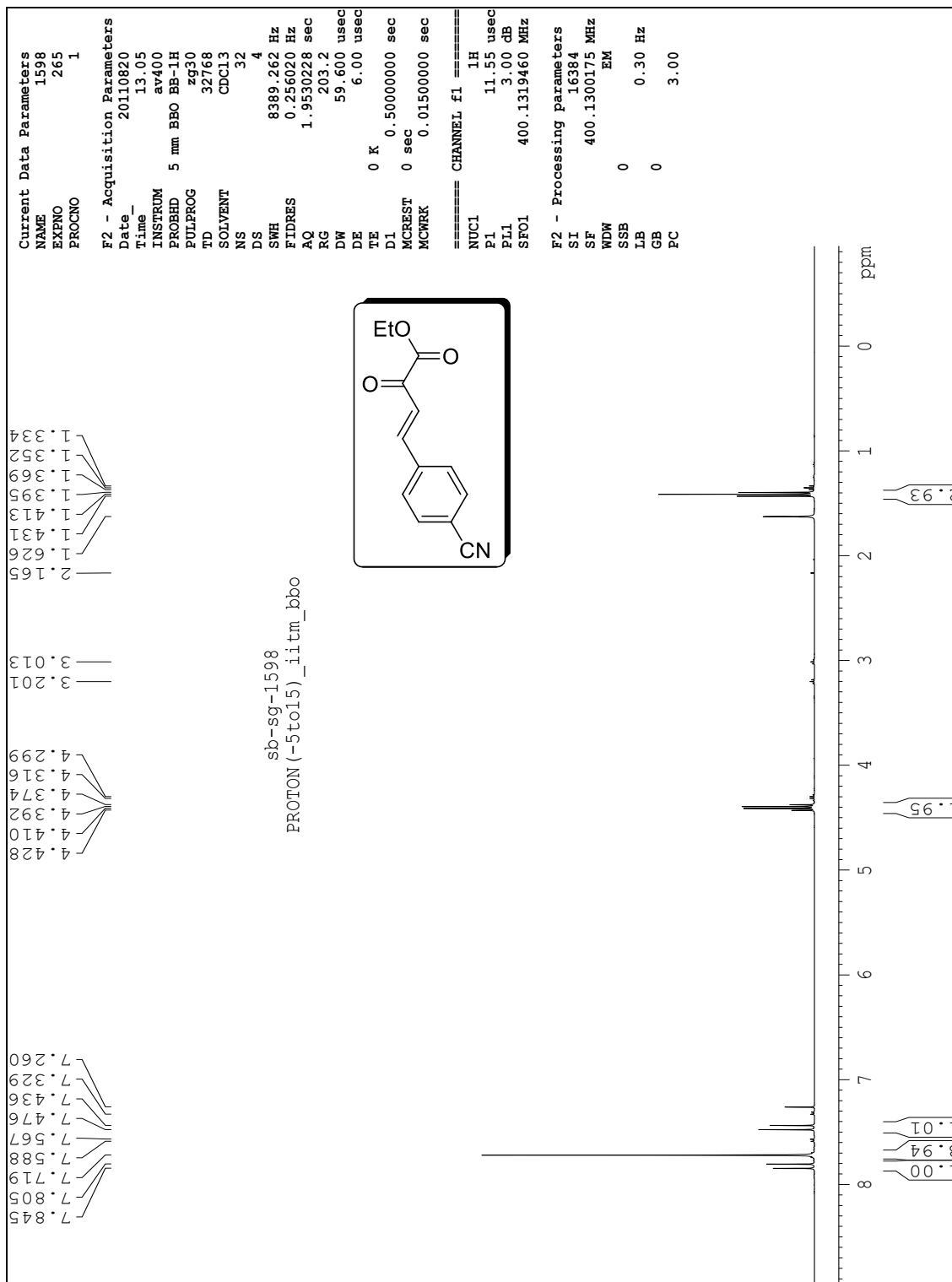
¹³C NMR spectrum of compound 23



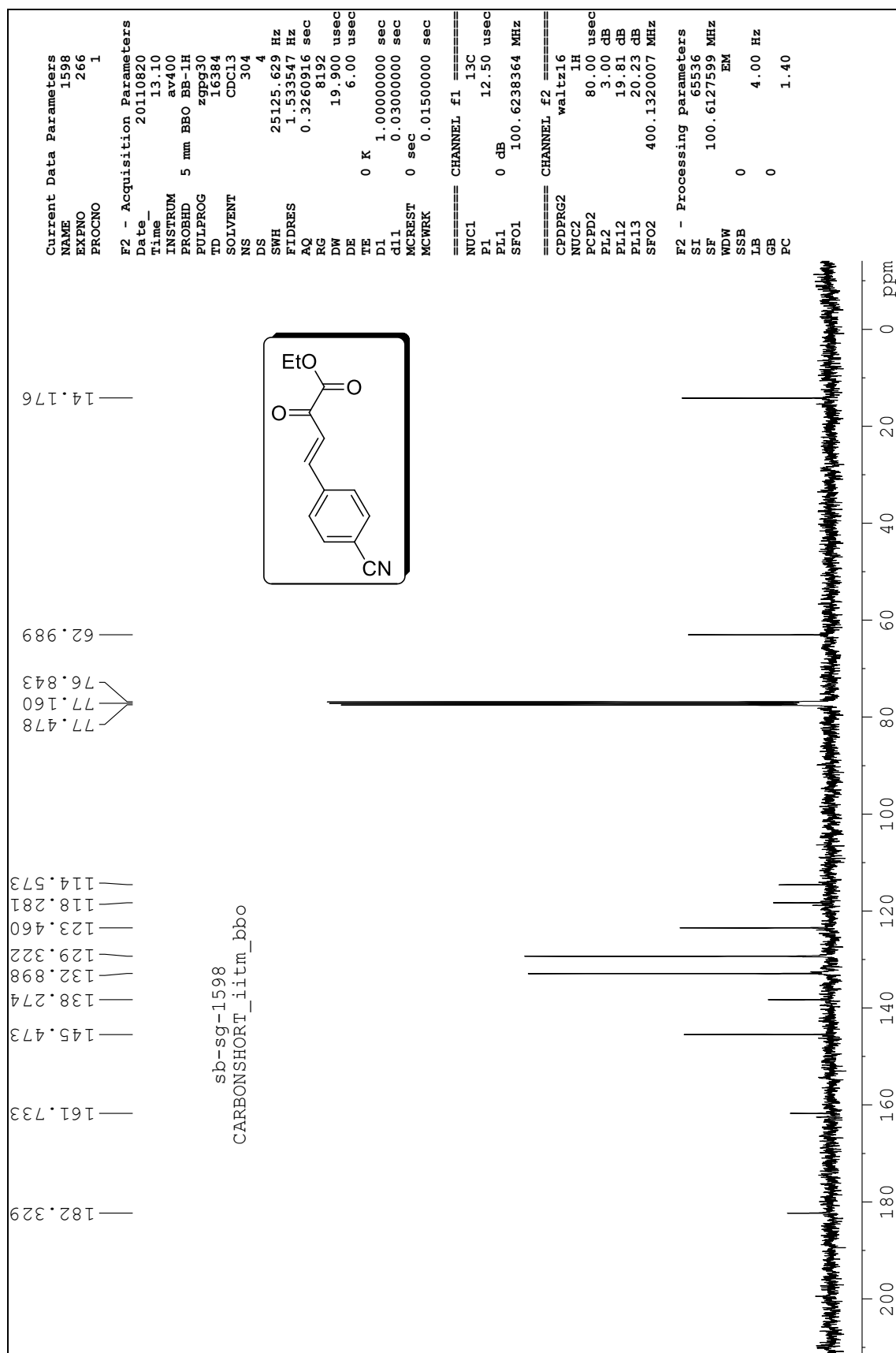
¹H NMR spectrum of compound 25



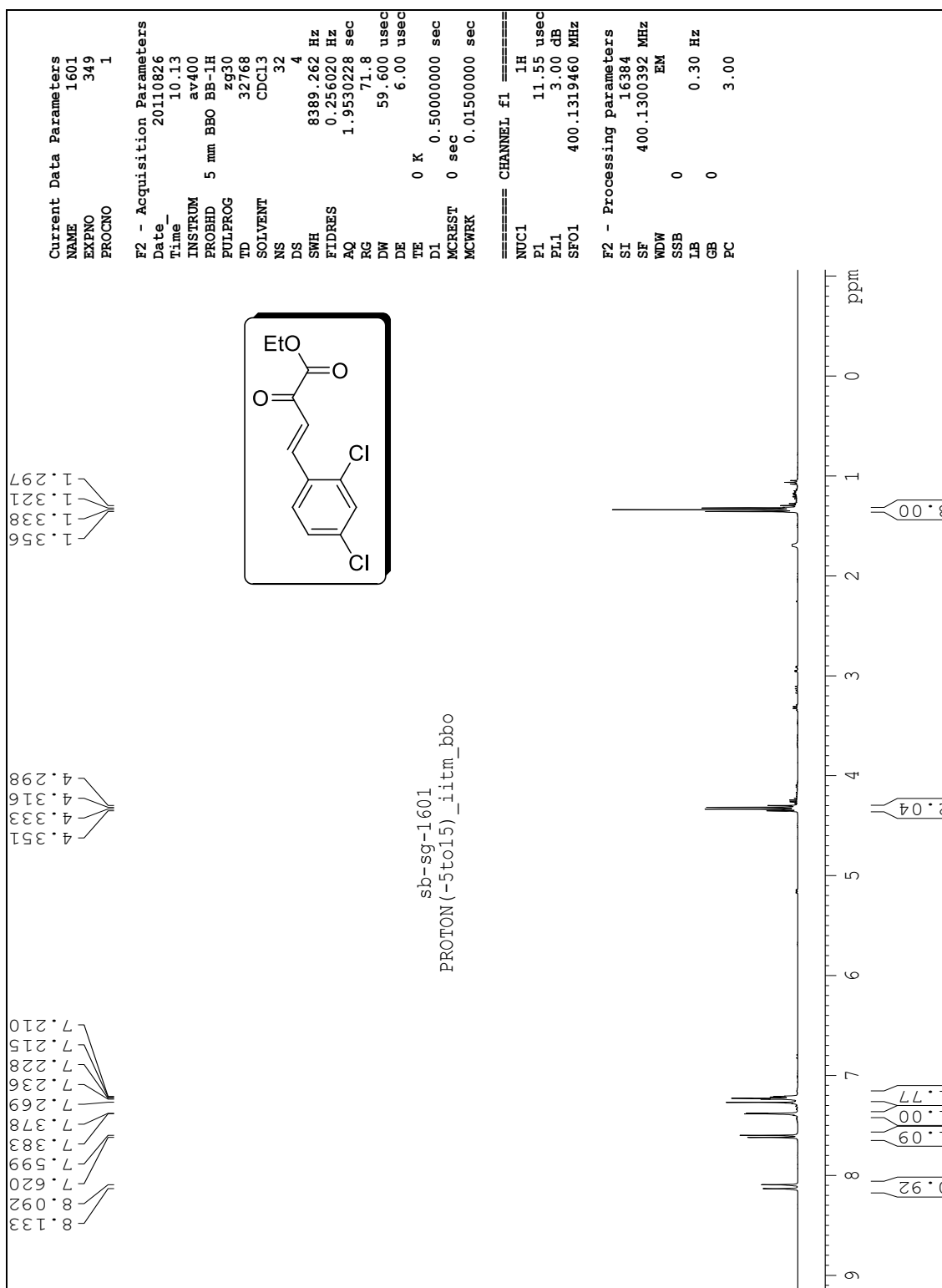
¹³C NMR spectrum of compound 25



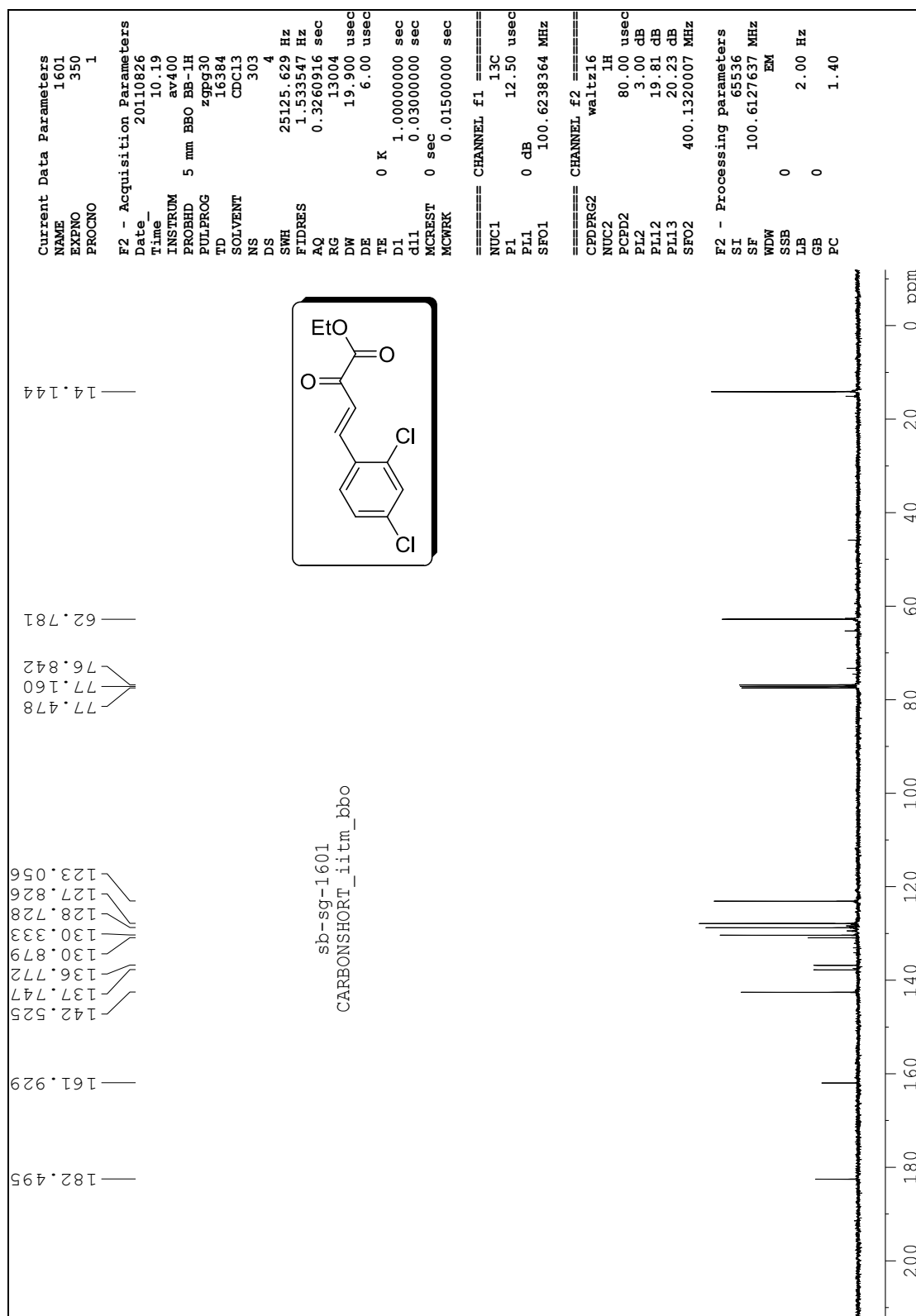
¹H NMR spectrum of compound 9



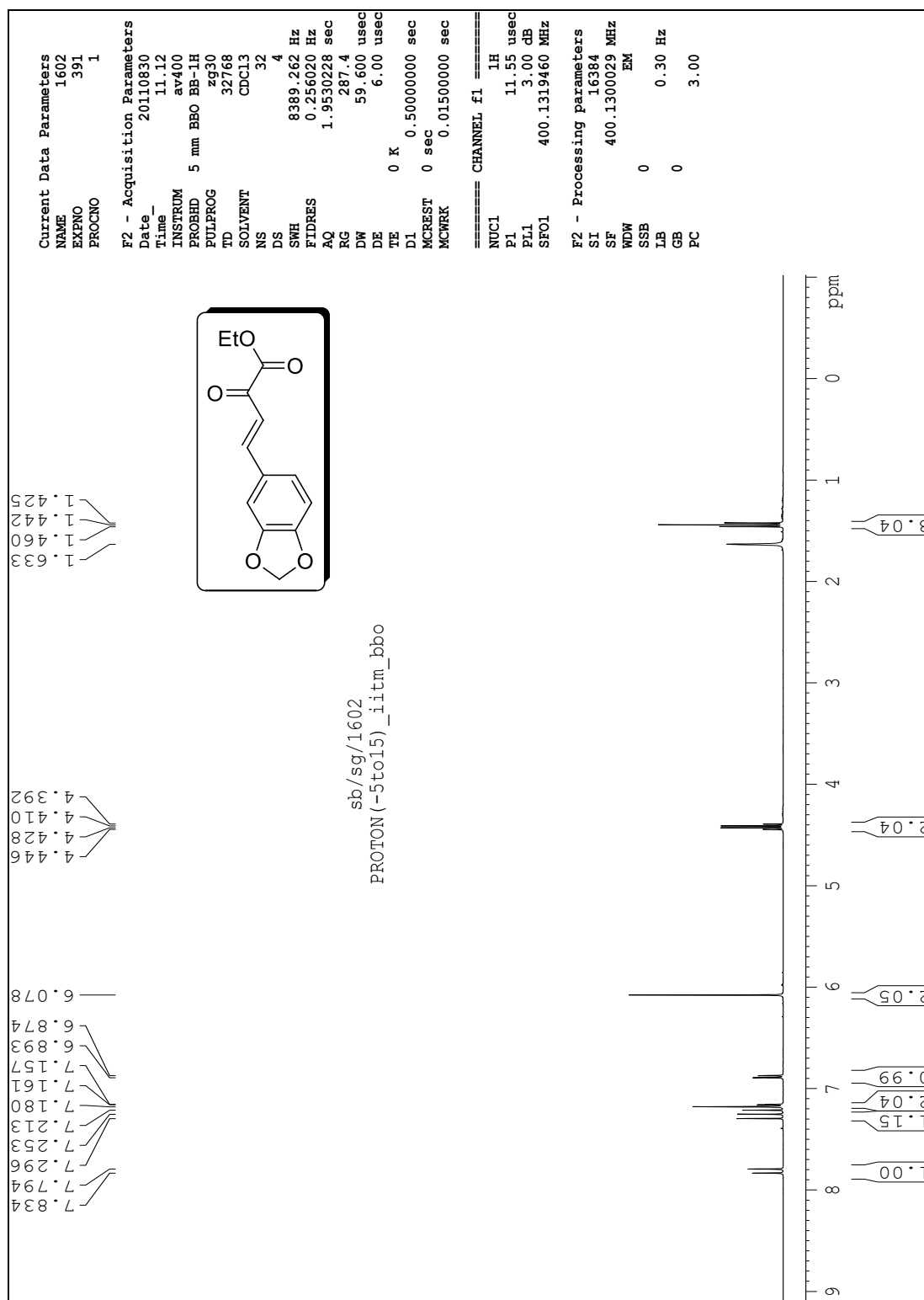
¹³C NMR spectrum of compound **9**



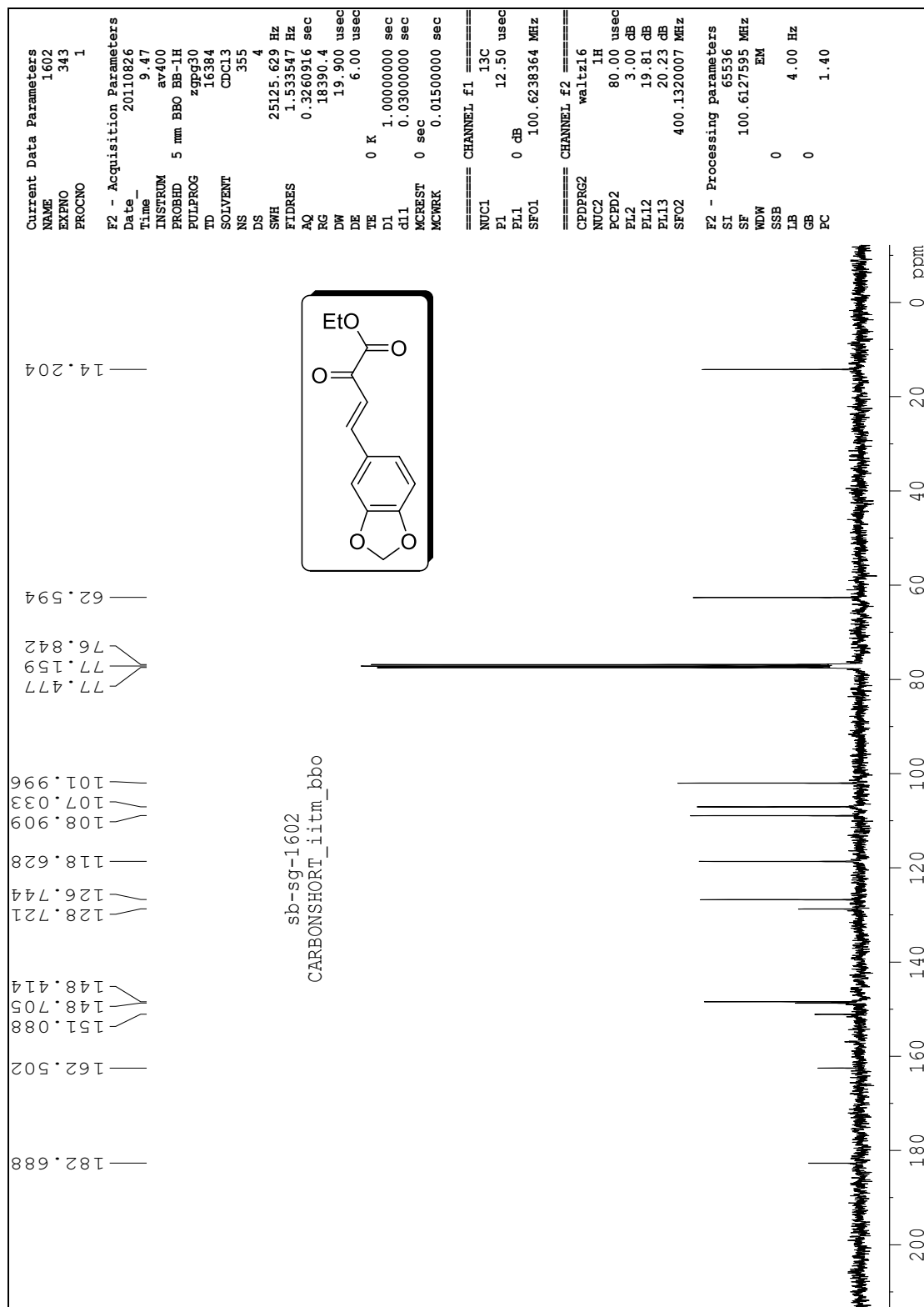
¹H NMR spectrum of compound 27



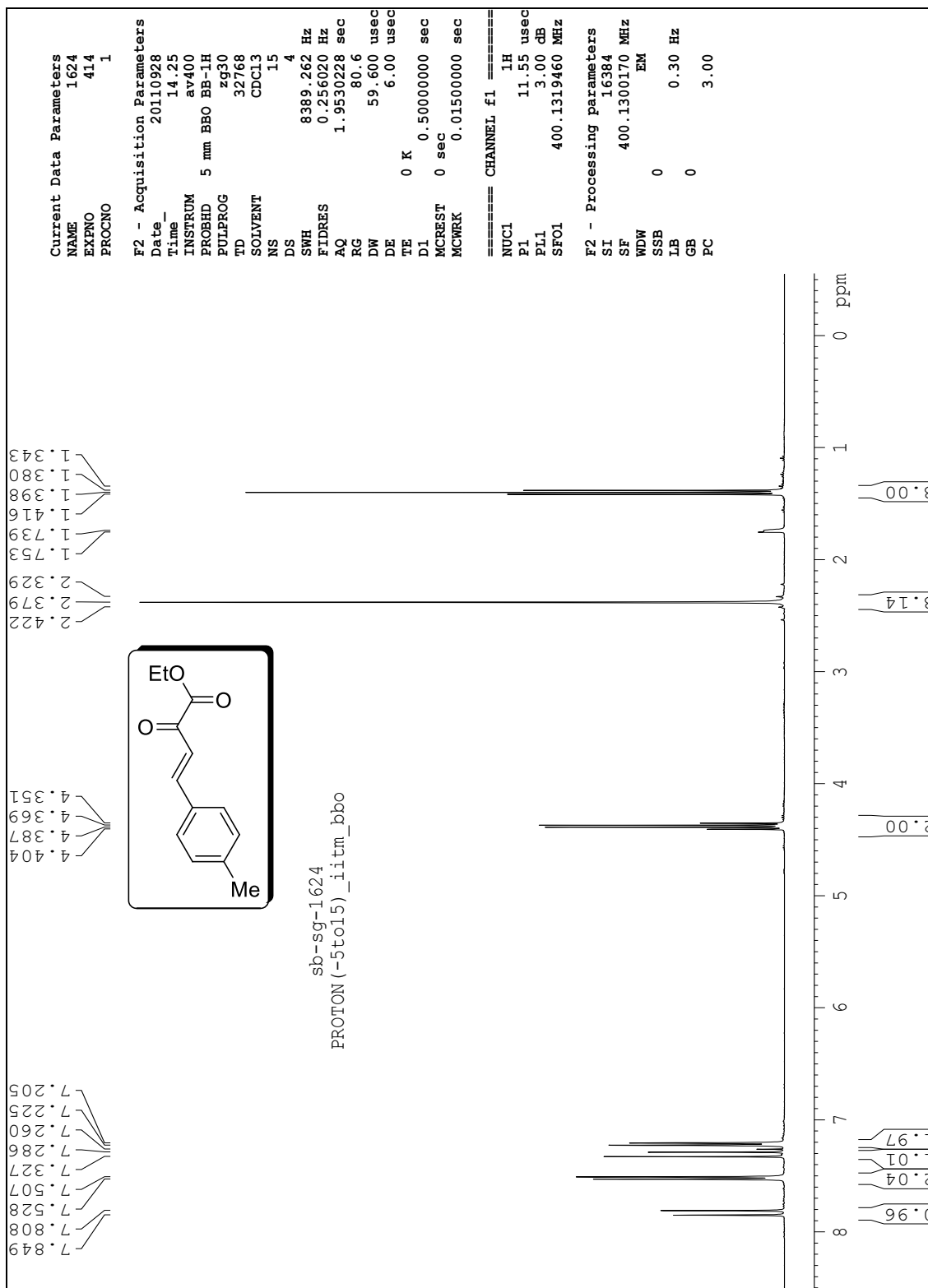
¹³C NMR spectrum of compound 27



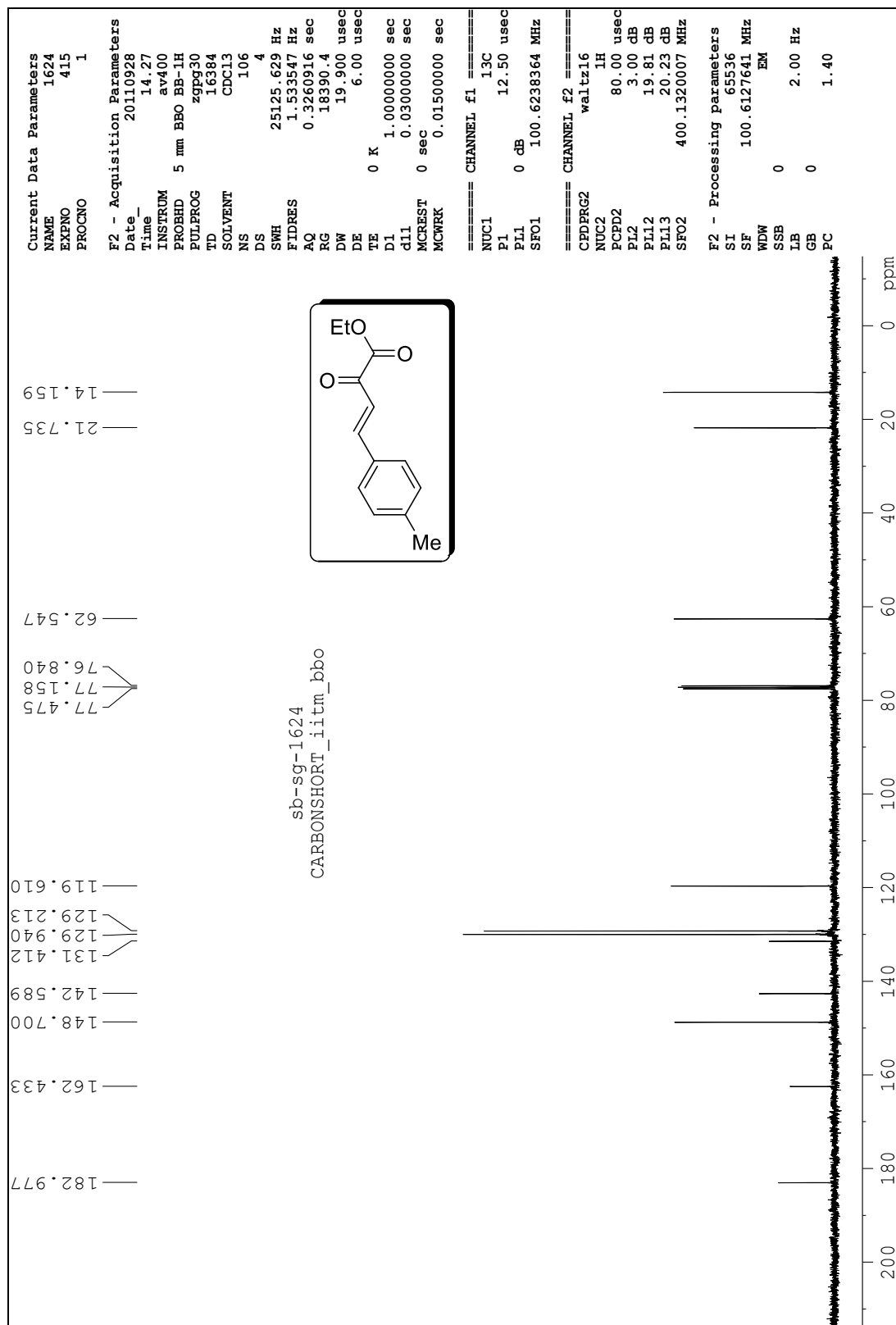
¹H NMR spectrum of compound **13**



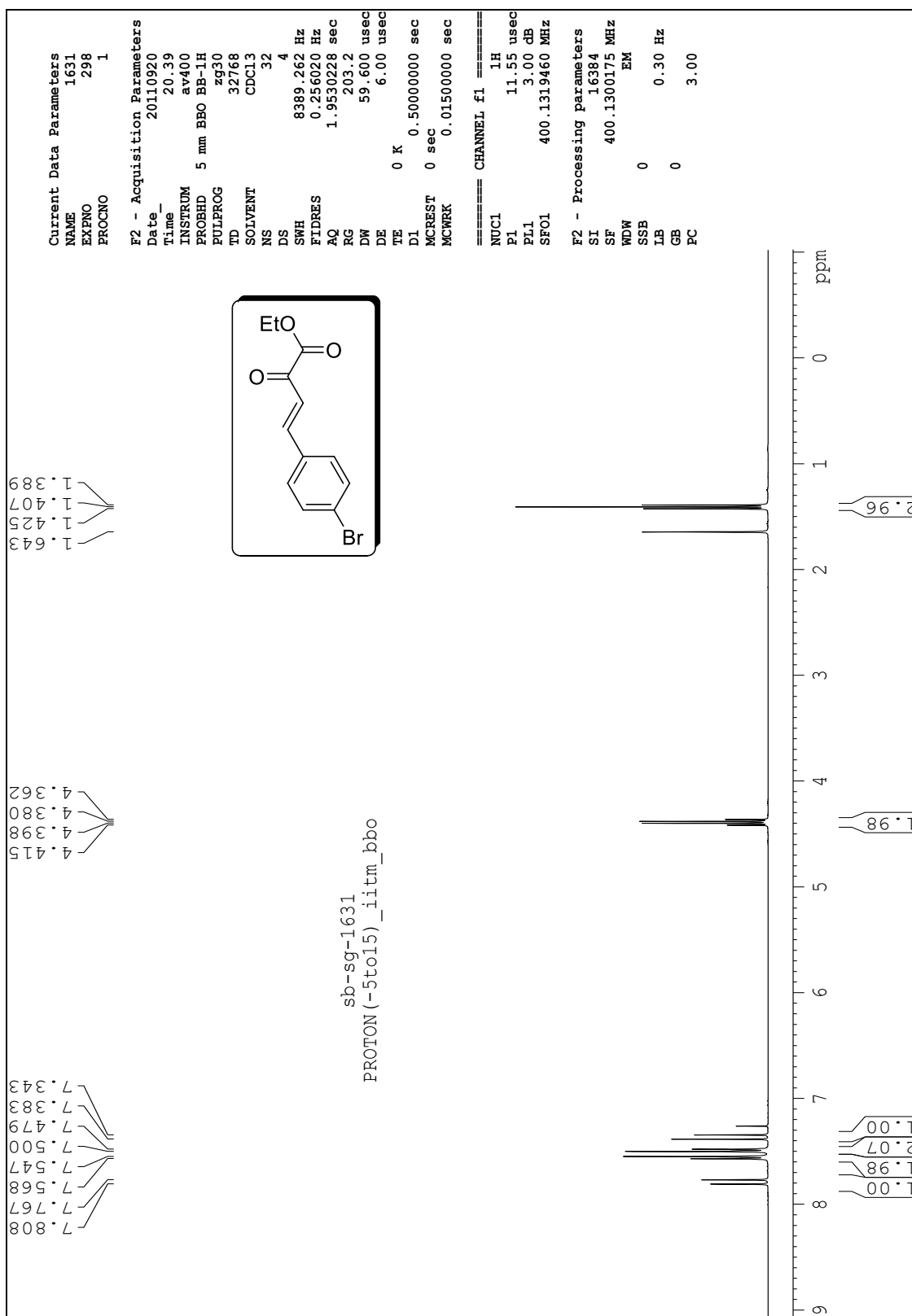
¹³C NMR spectrum of compound 13



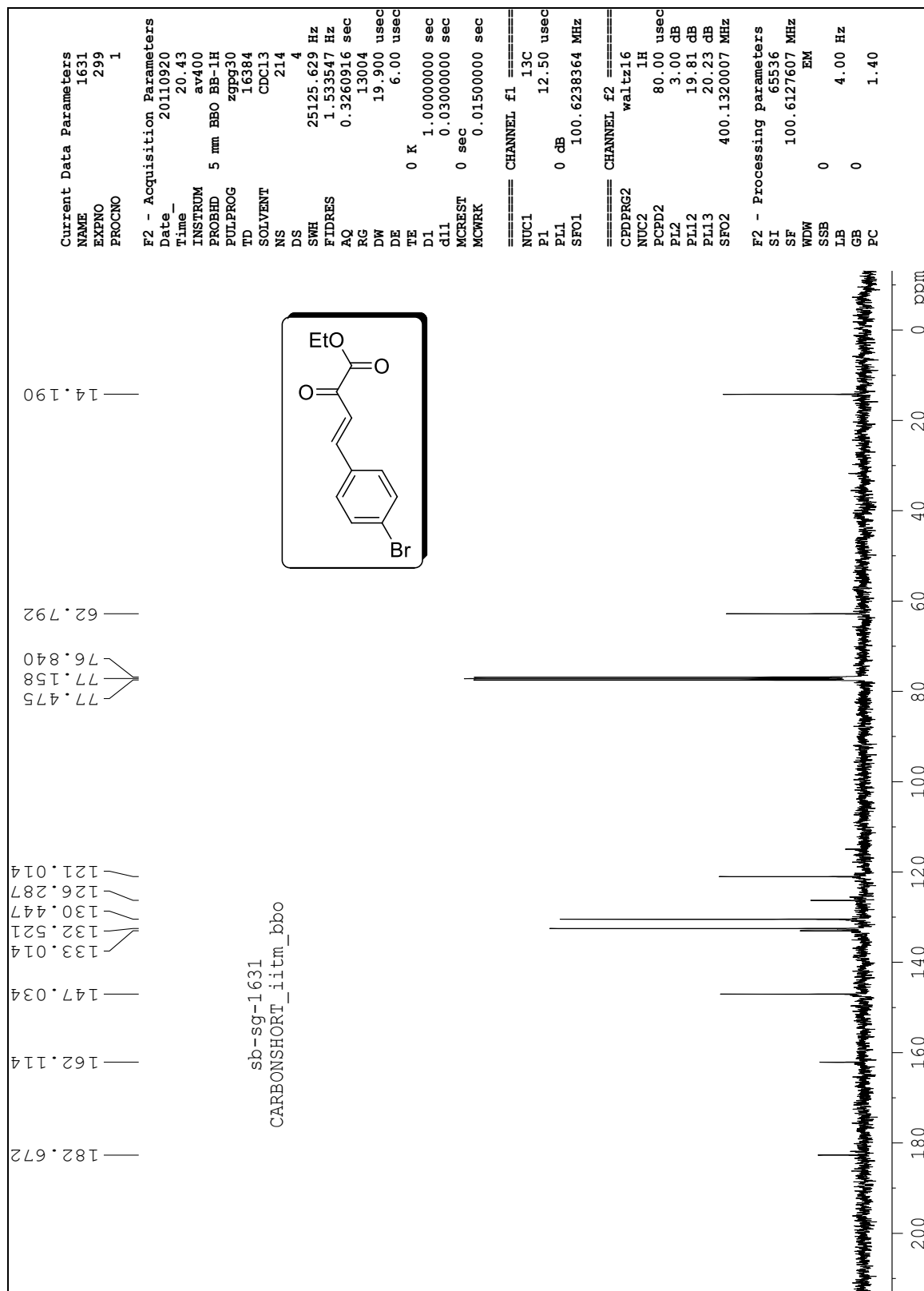
¹H NMR spectrum of compound 15



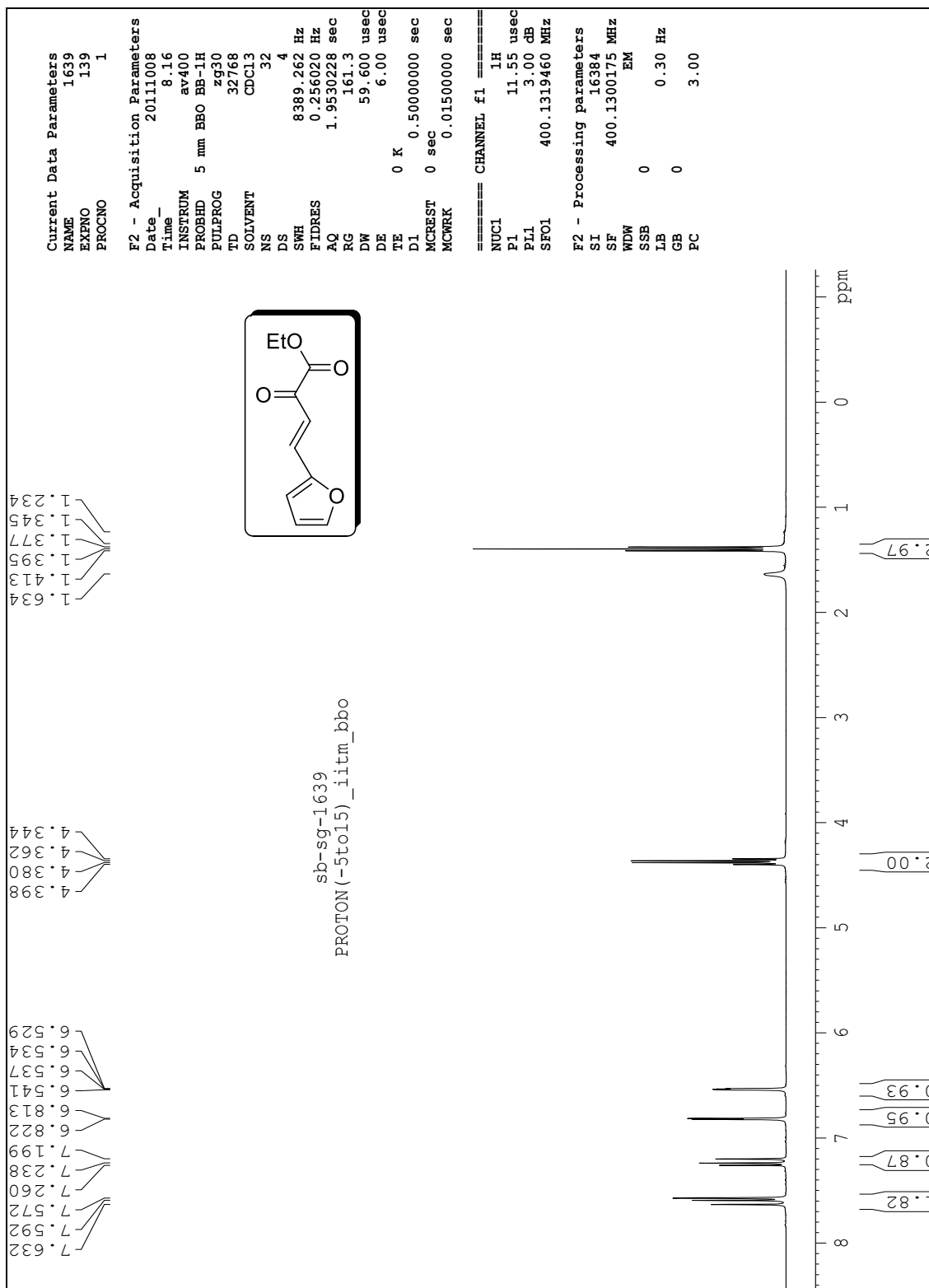
¹³C NMR spectrum of compound **15**



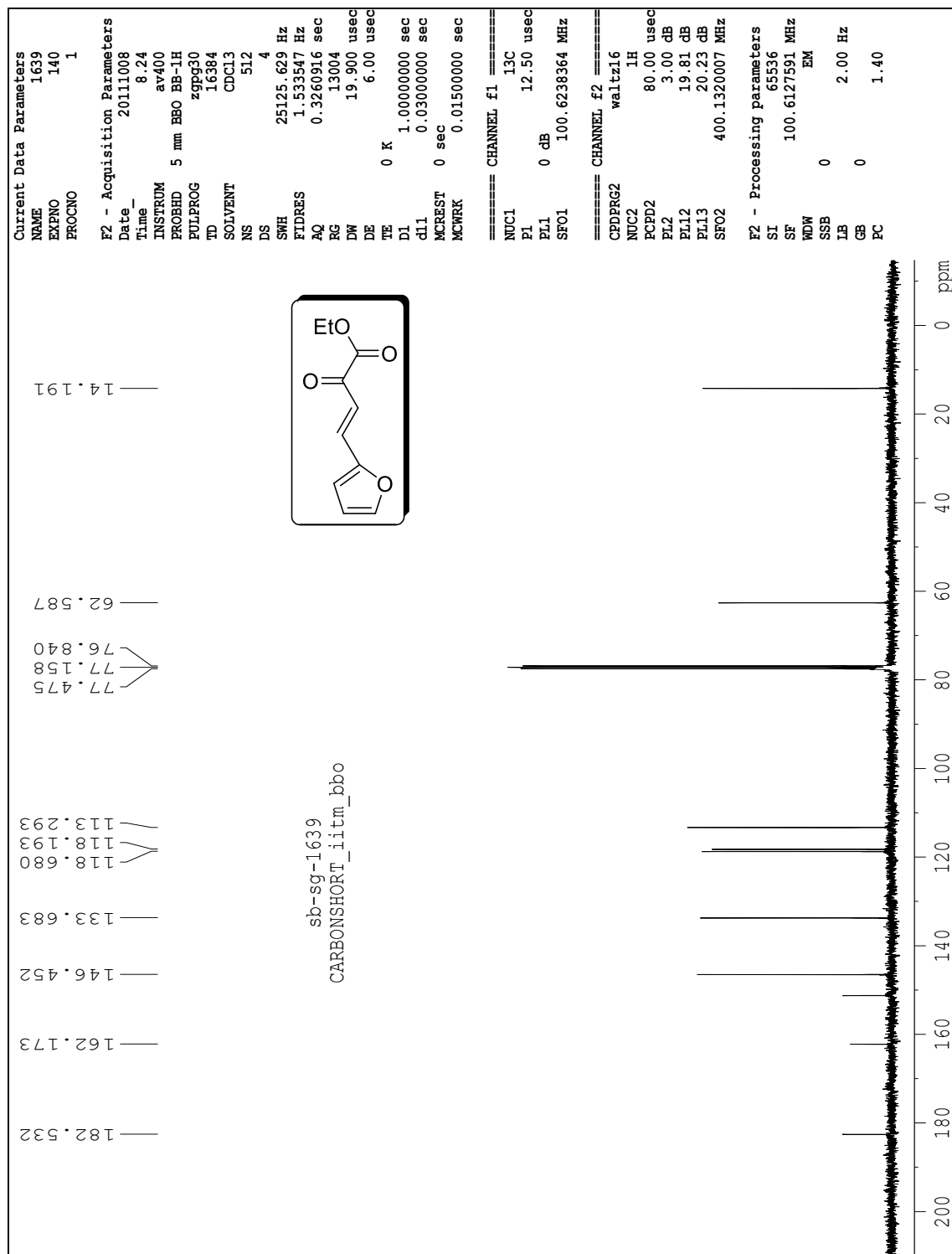
¹H NMR spectrum of compound 19



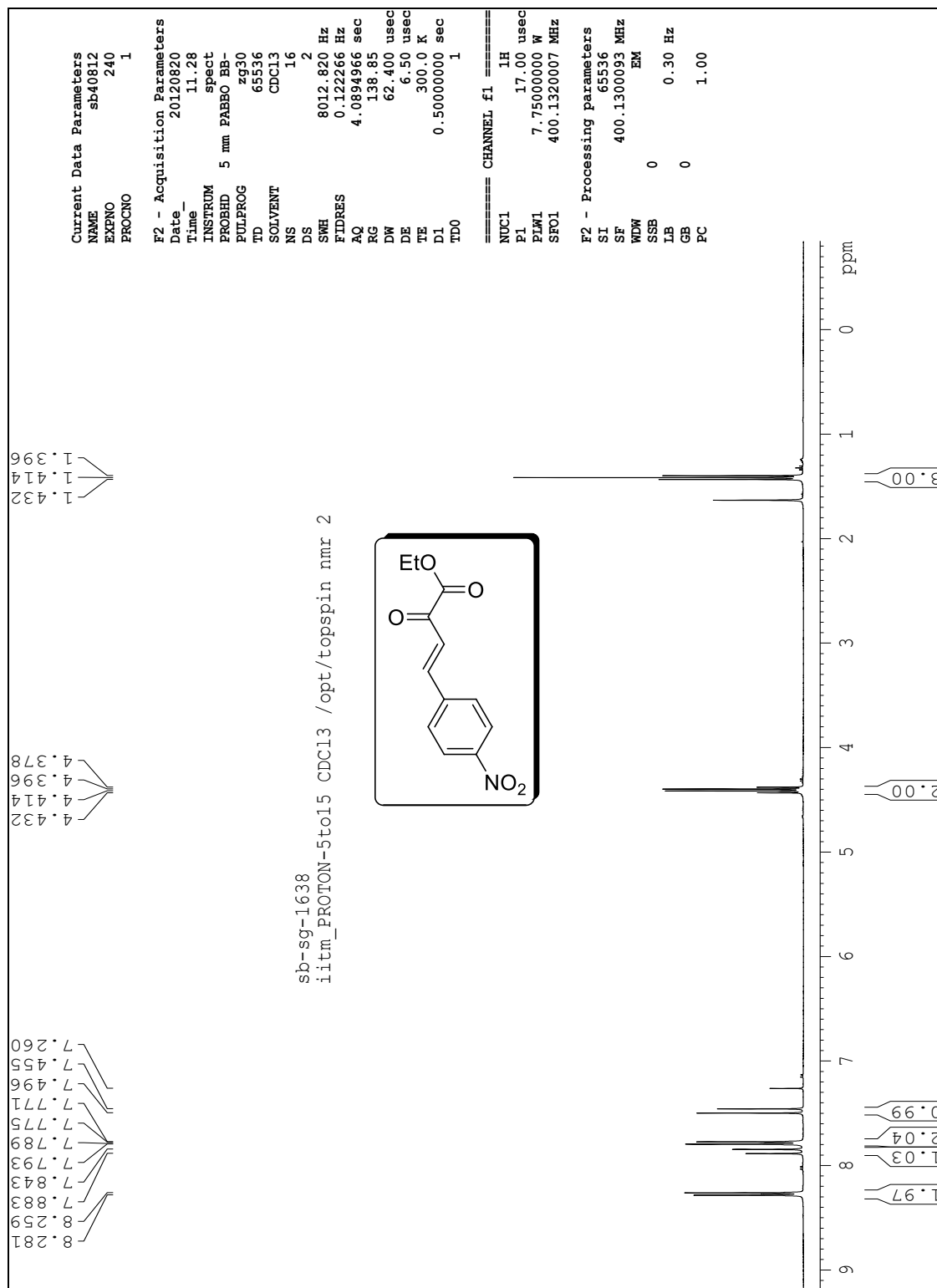
¹³C NMR spectrum of compound **19**



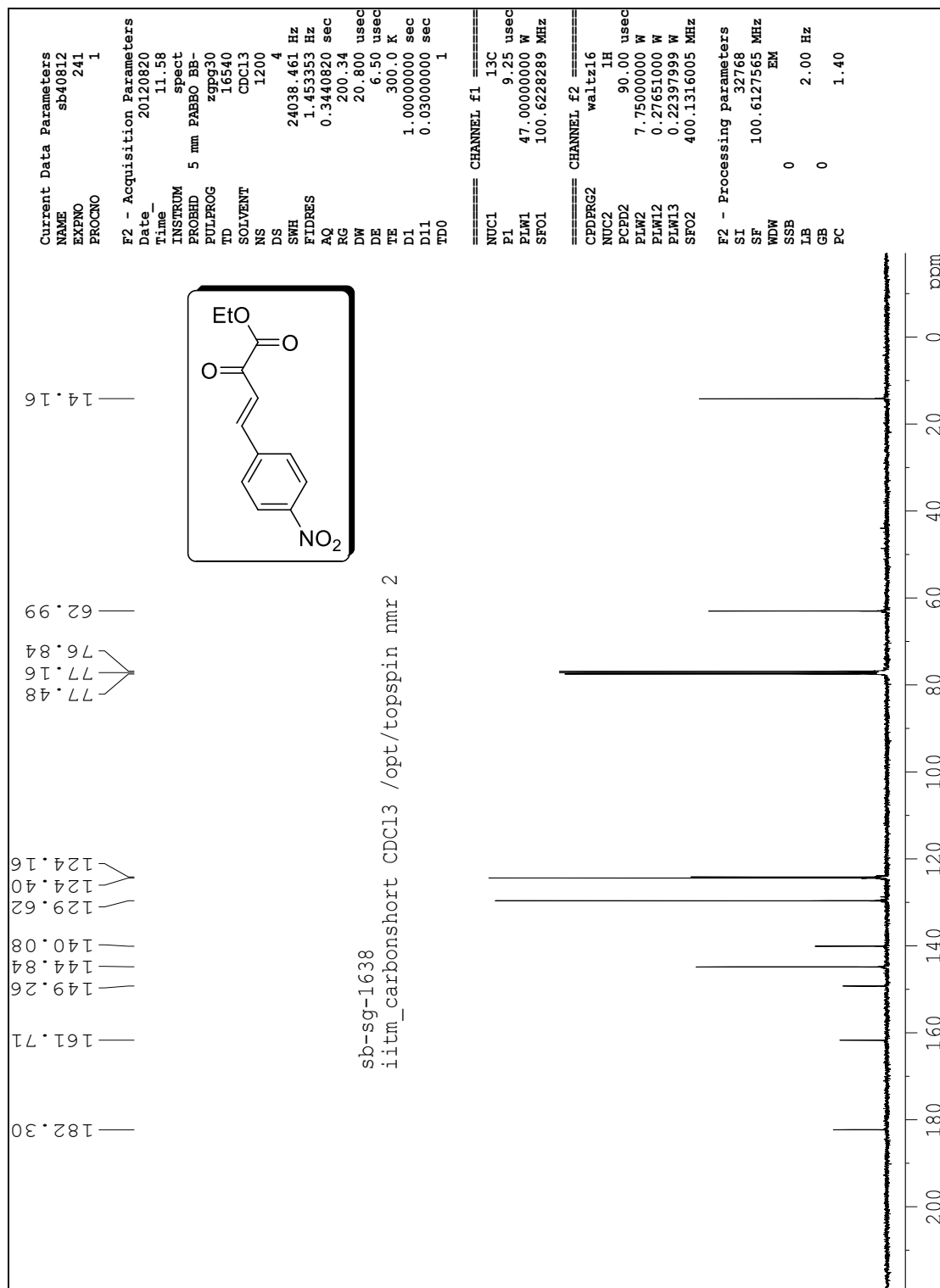
¹H NMR spectrum of compound 21



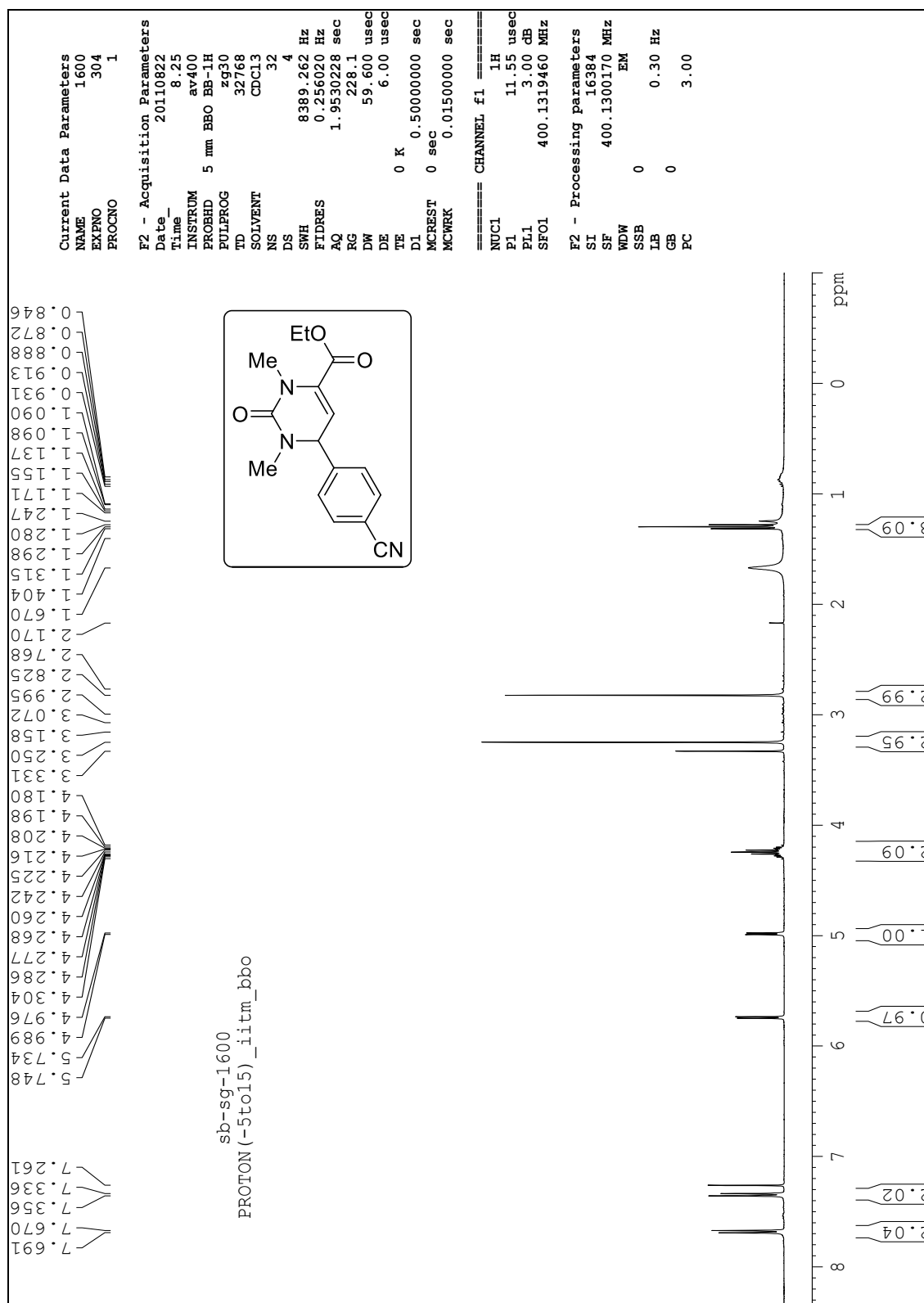
¹³C NMR spectrum of compound 21



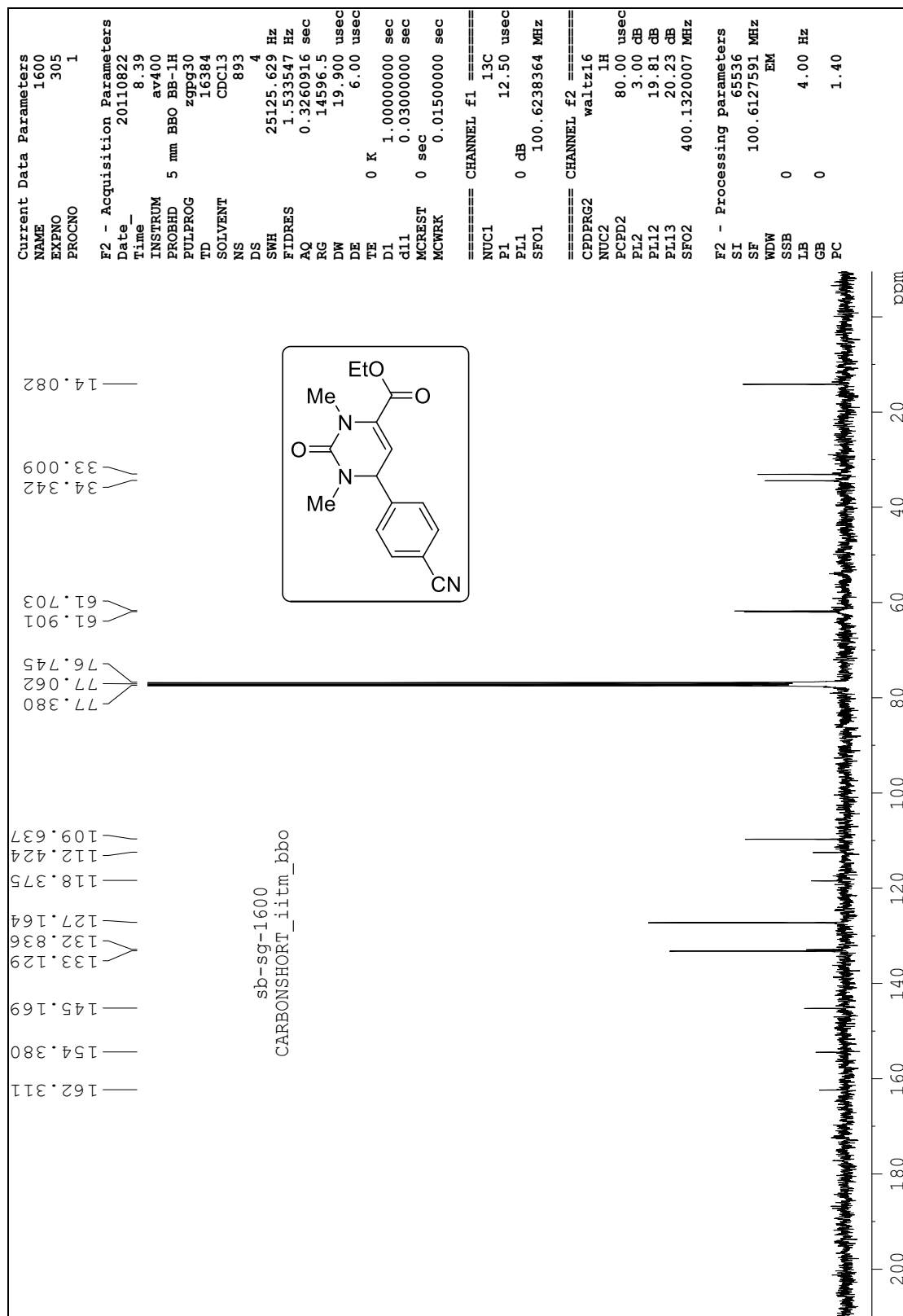
¹H NMR spectrum of compound 17



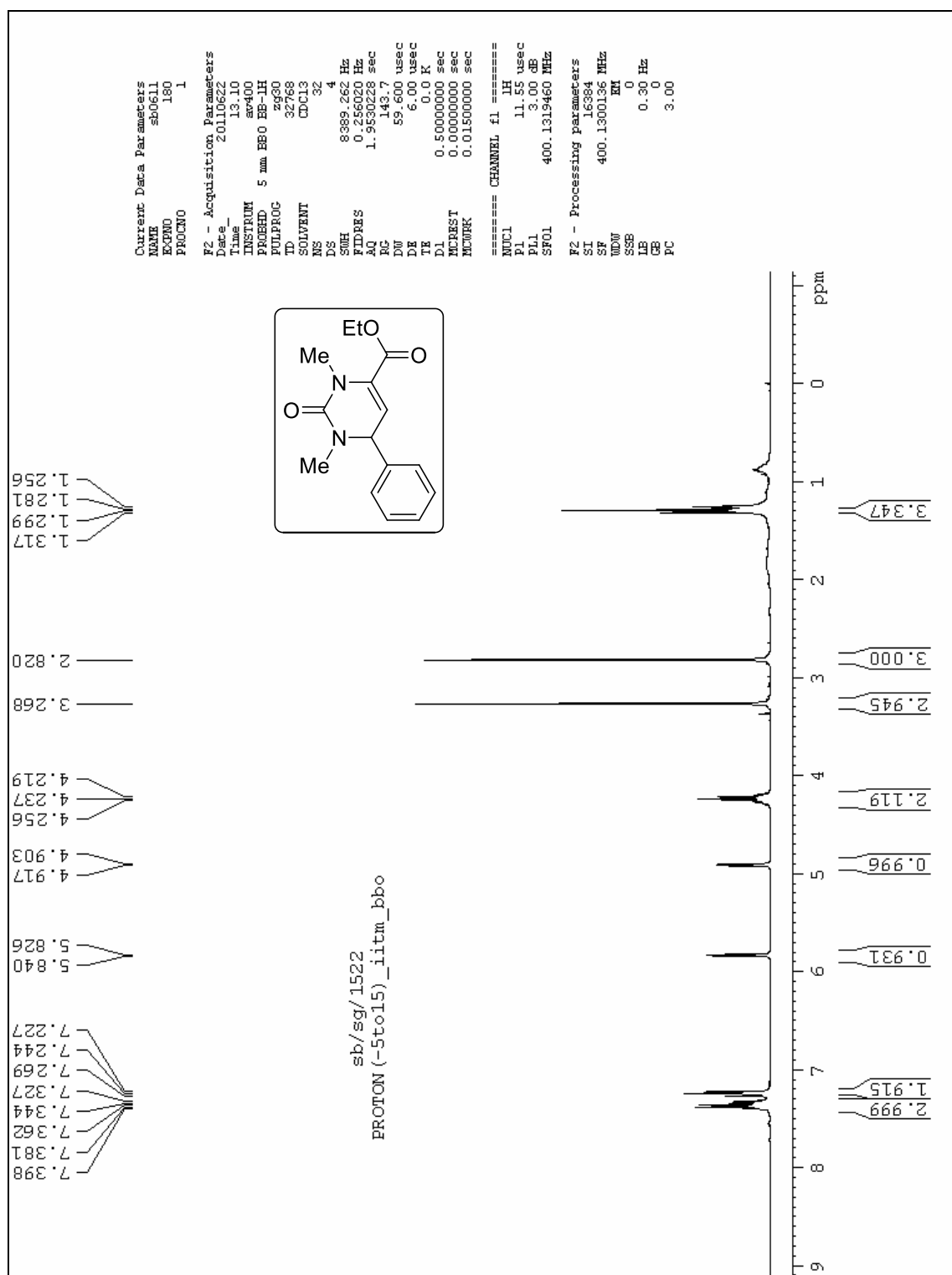
¹³C NMR spectrum of compound 17



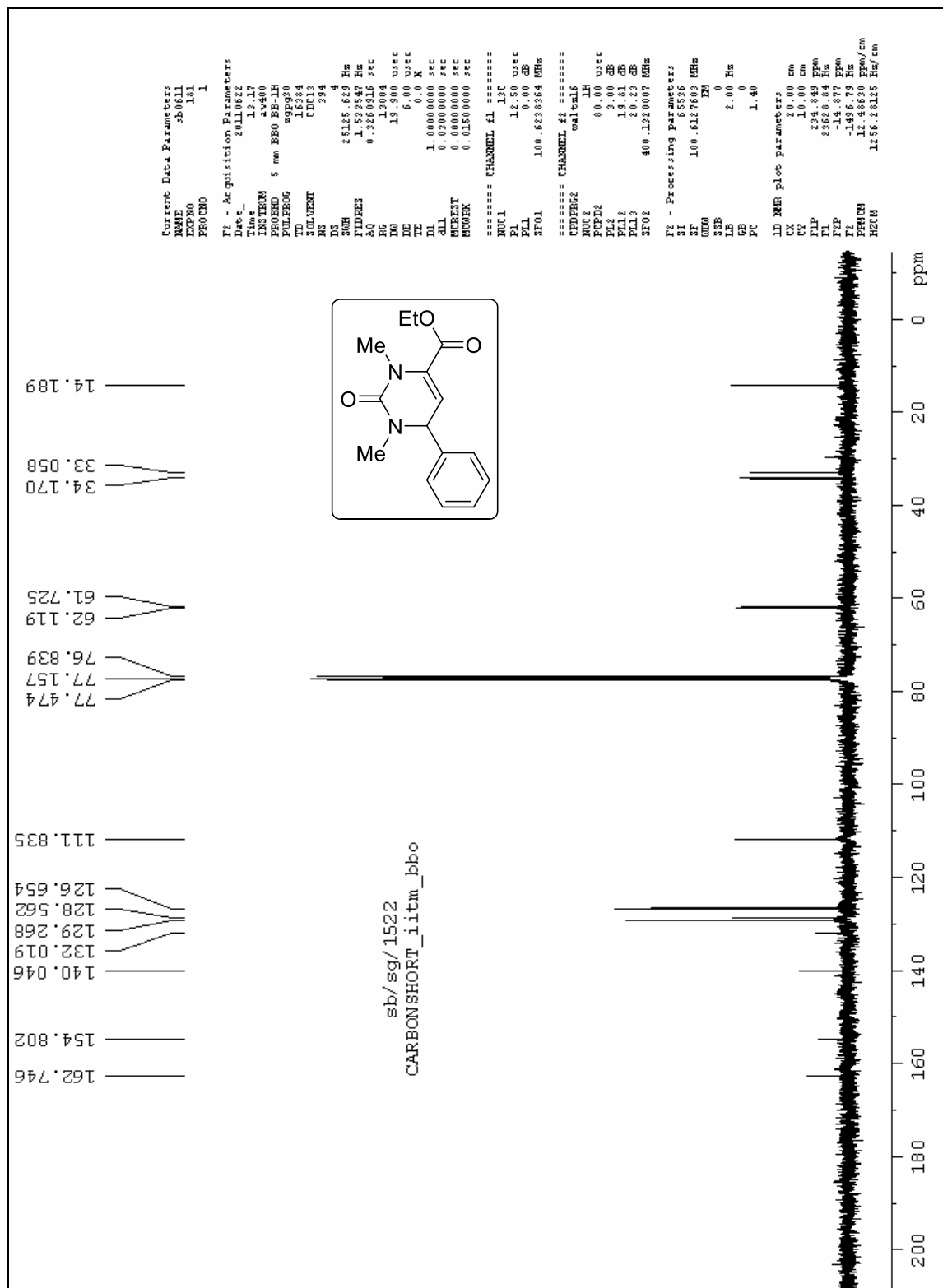
¹H NMR spectrum of compound 10

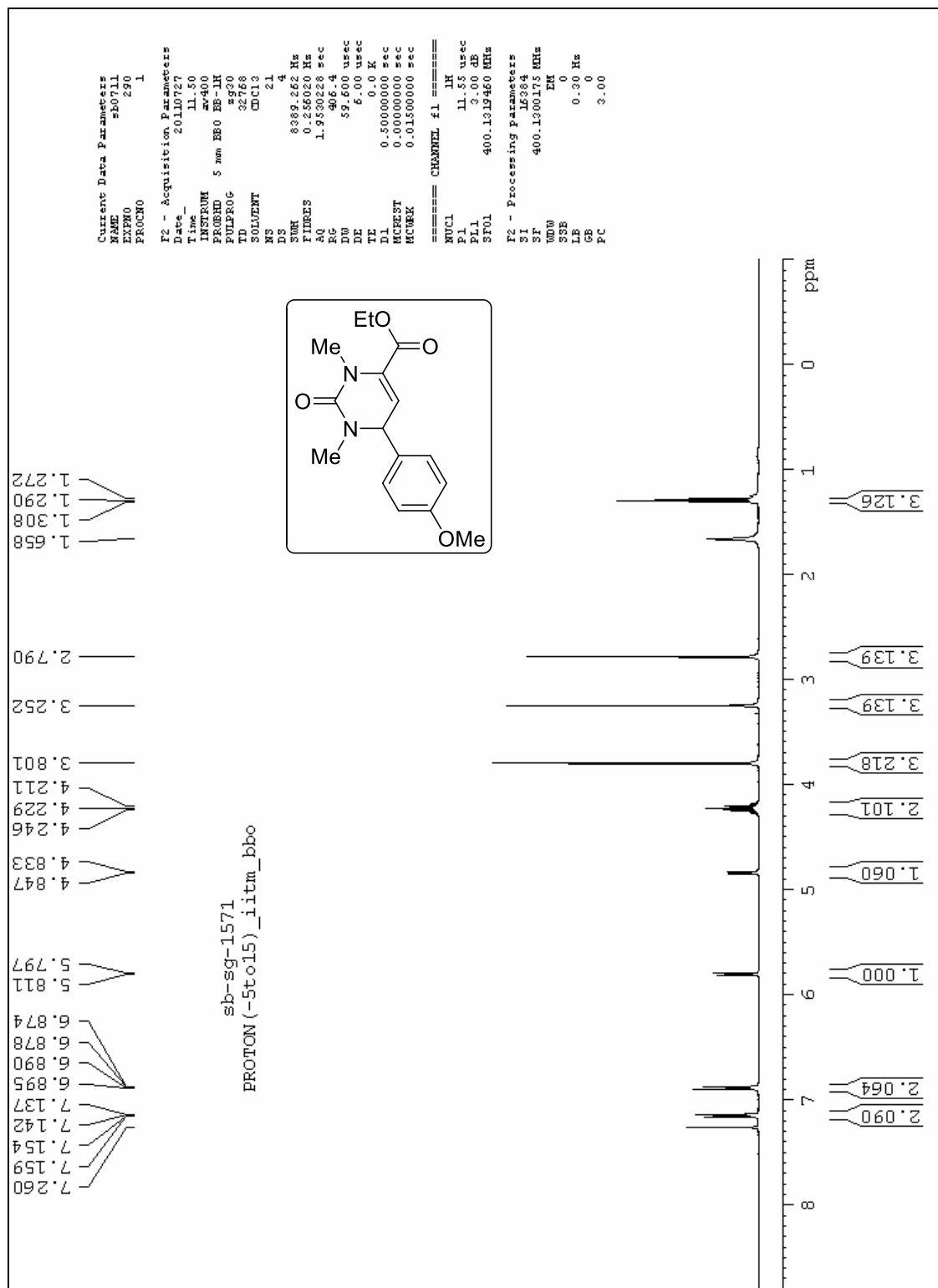


¹³C NMR spectrum of compound 10

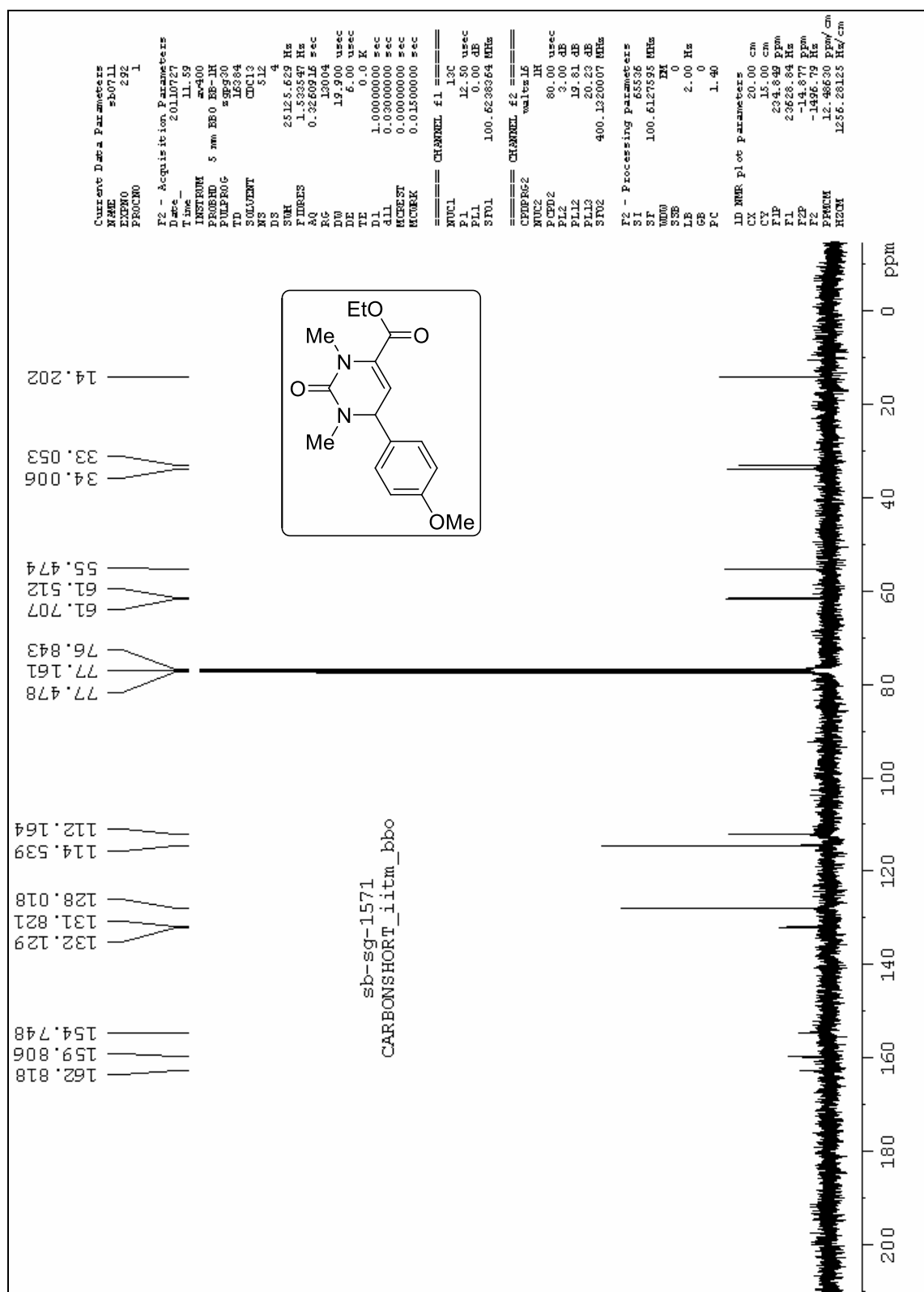


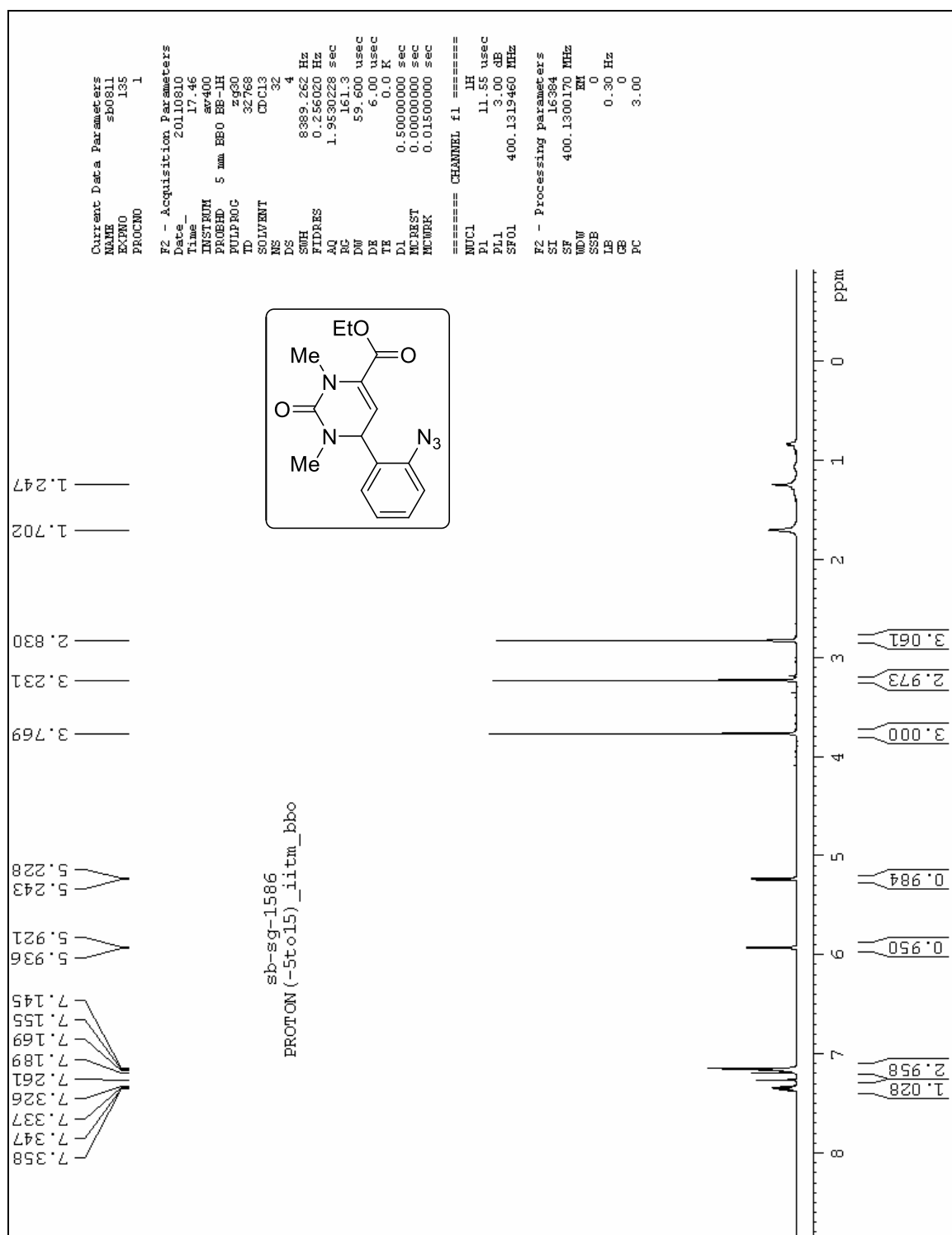
¹H NMR spectrum of compound **8**



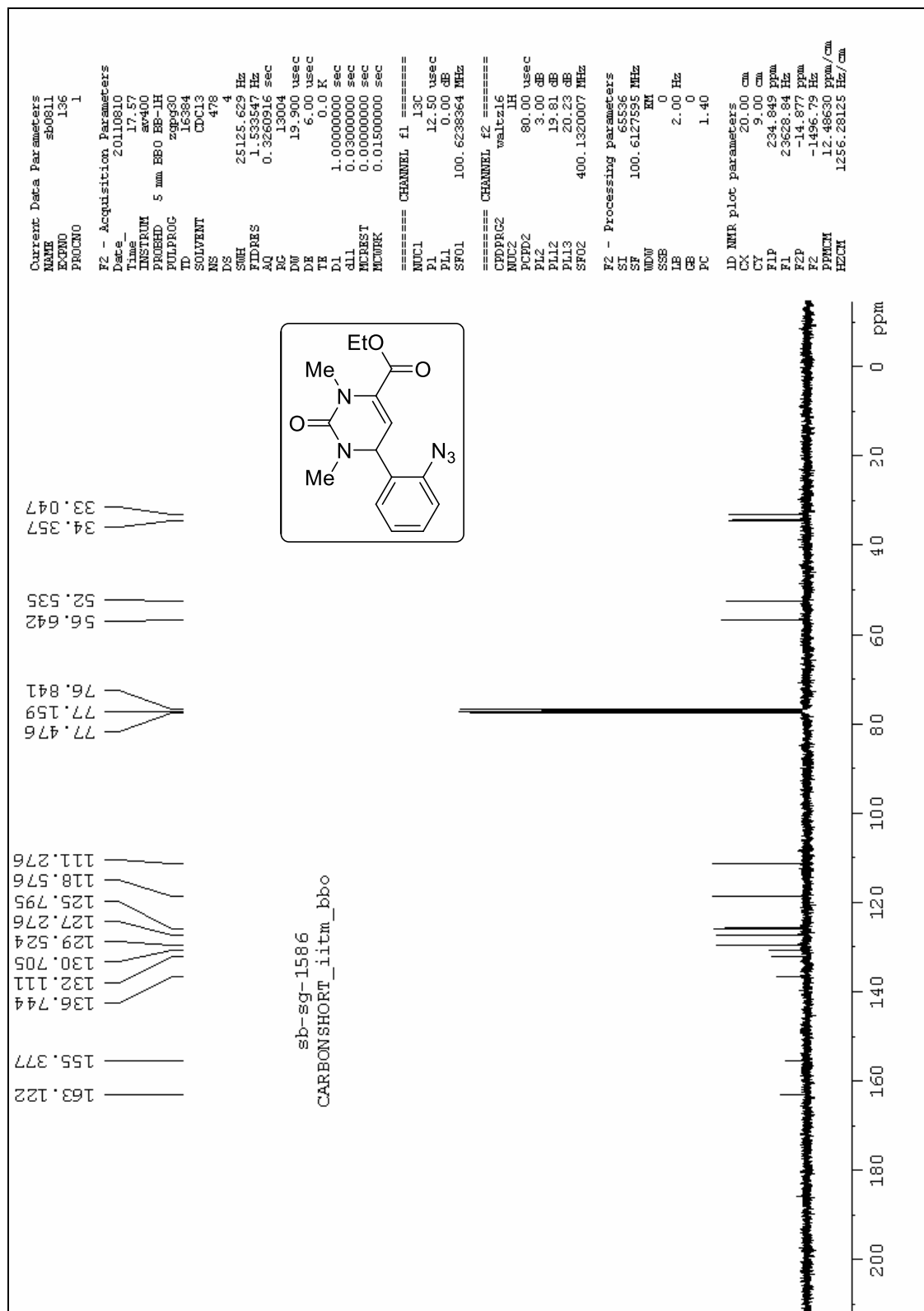


¹H NMR spectrum of compound 12

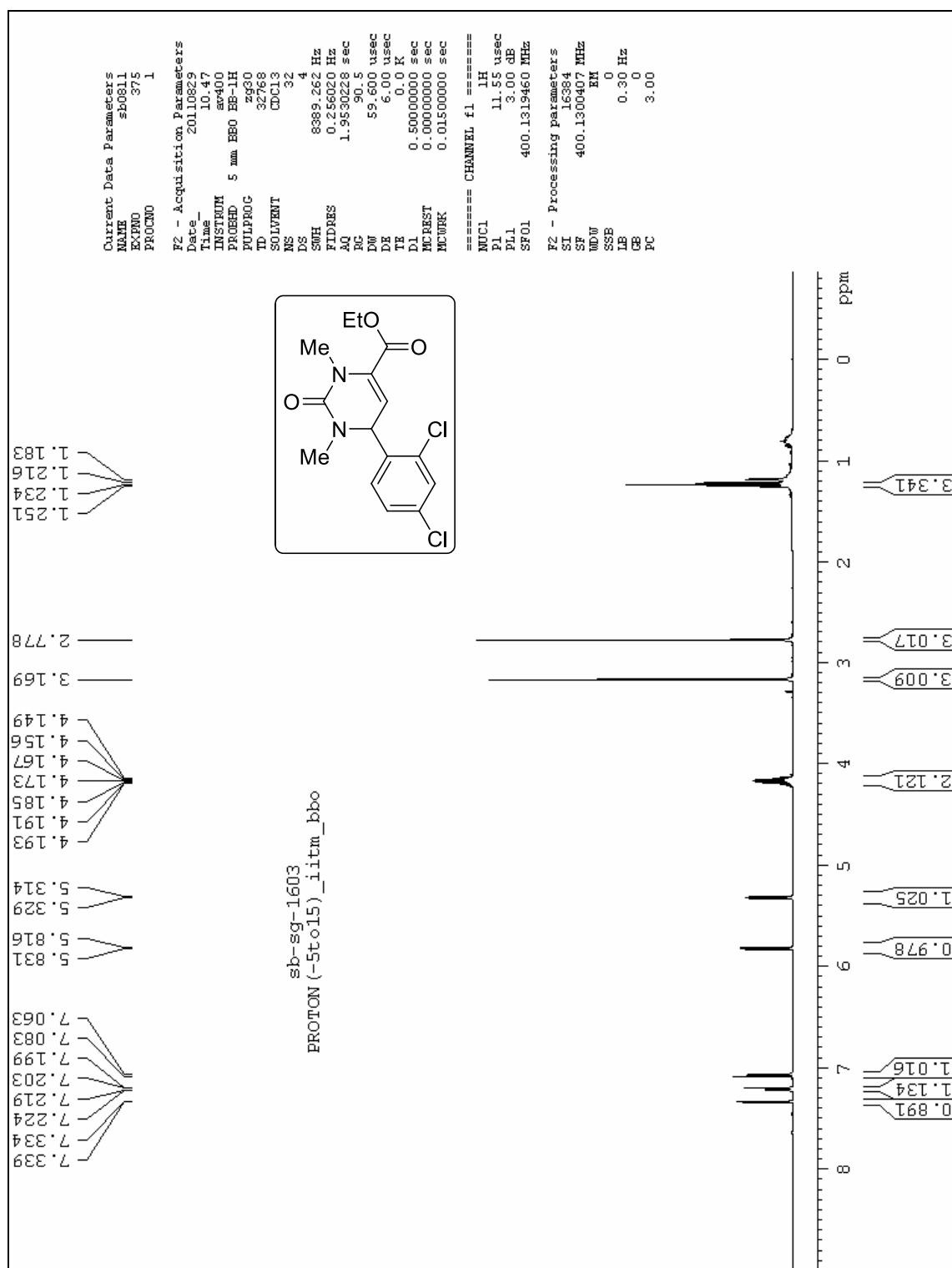




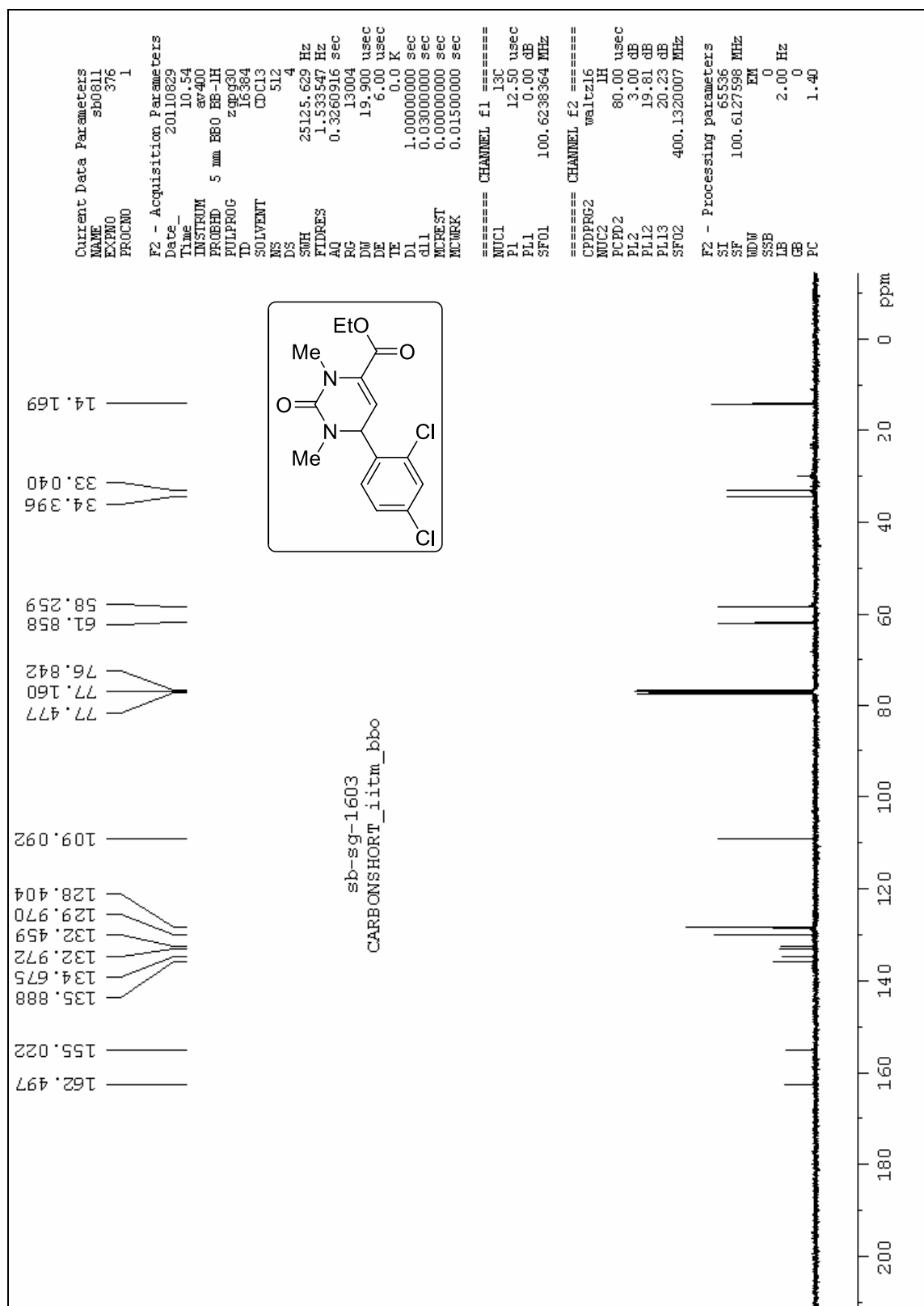
¹H NMR spectrum of compound 24



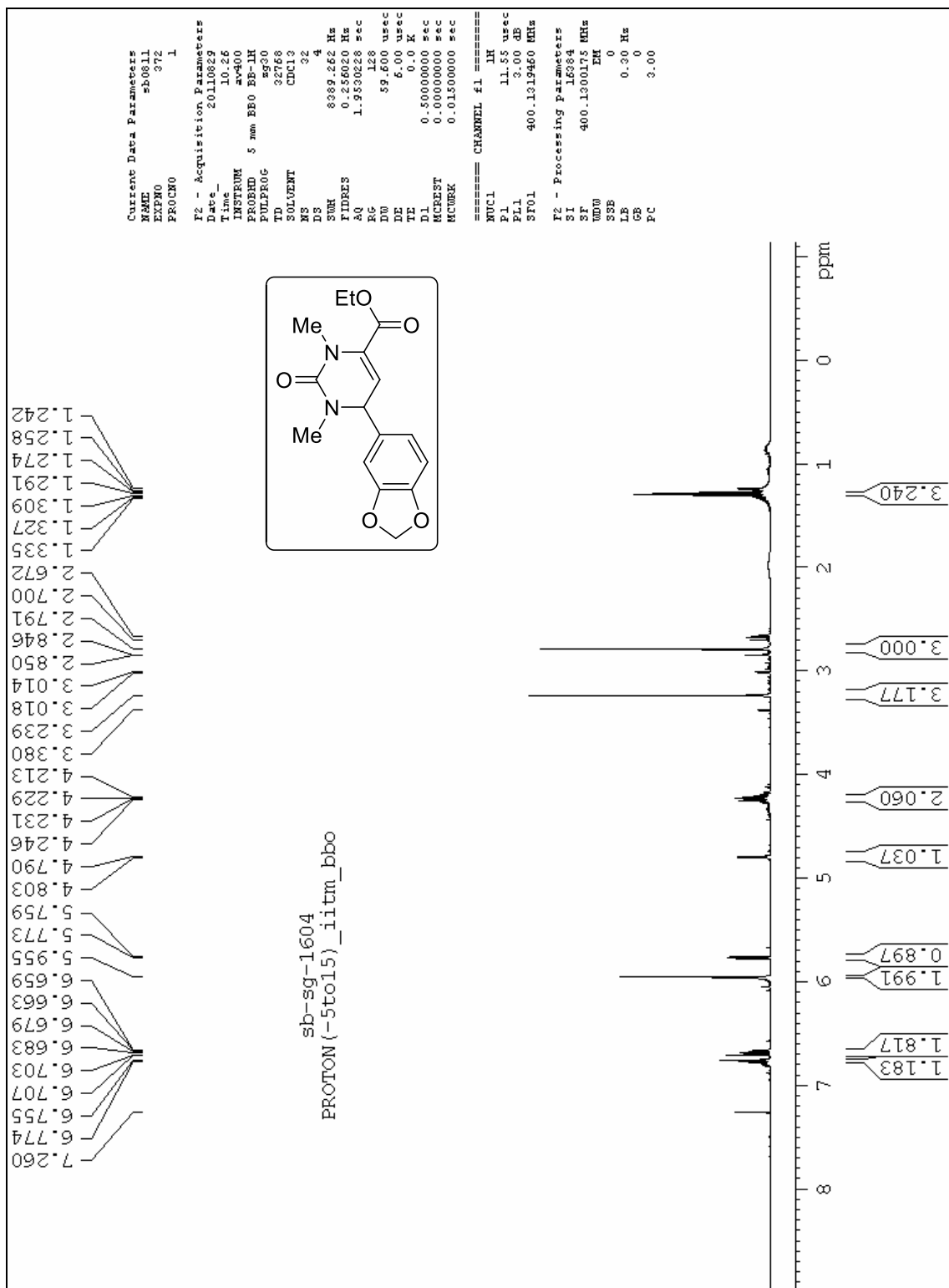
¹³C NMR spectrum of compound 24



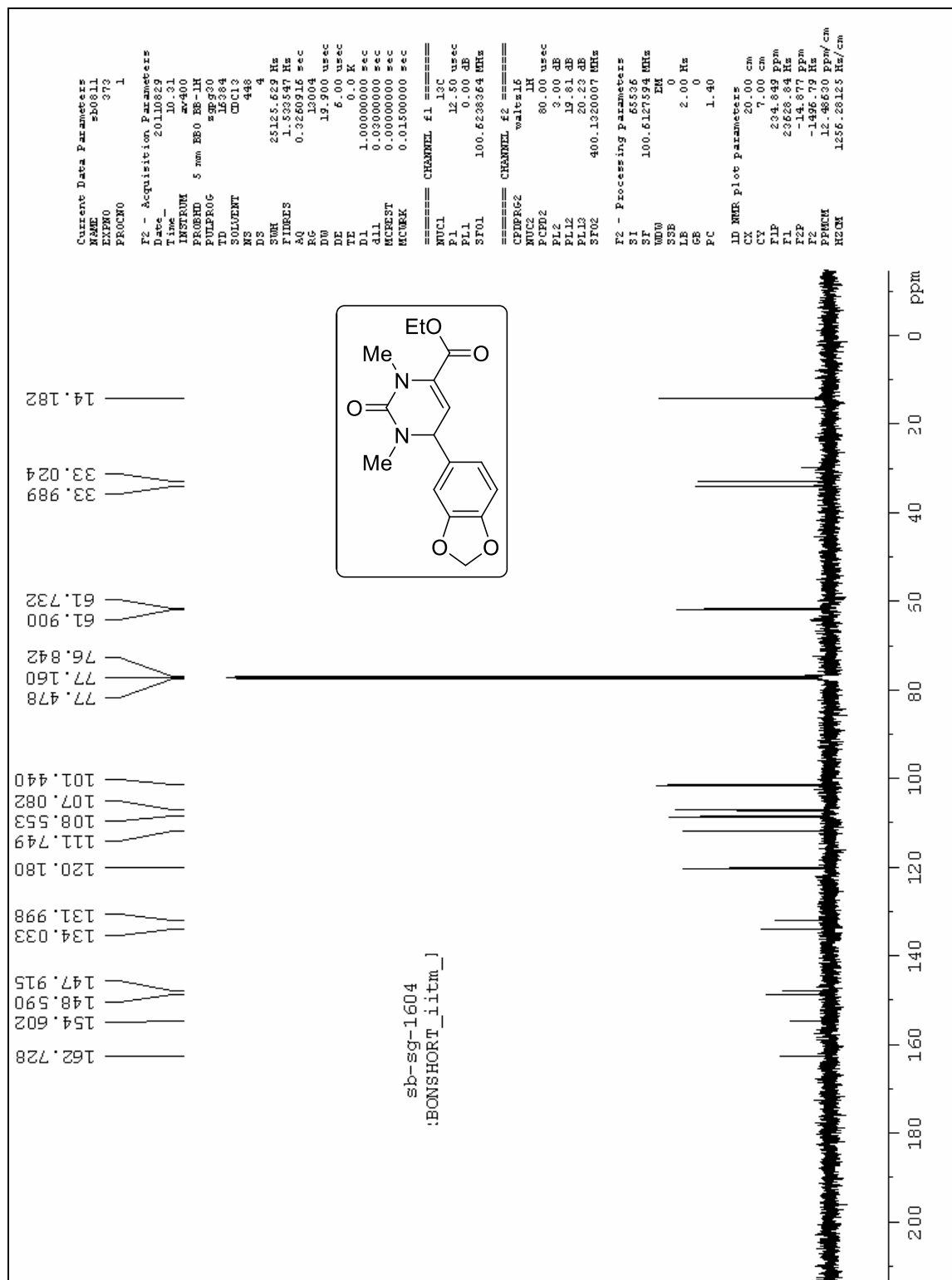
¹H NMR spectrum of compound **28**



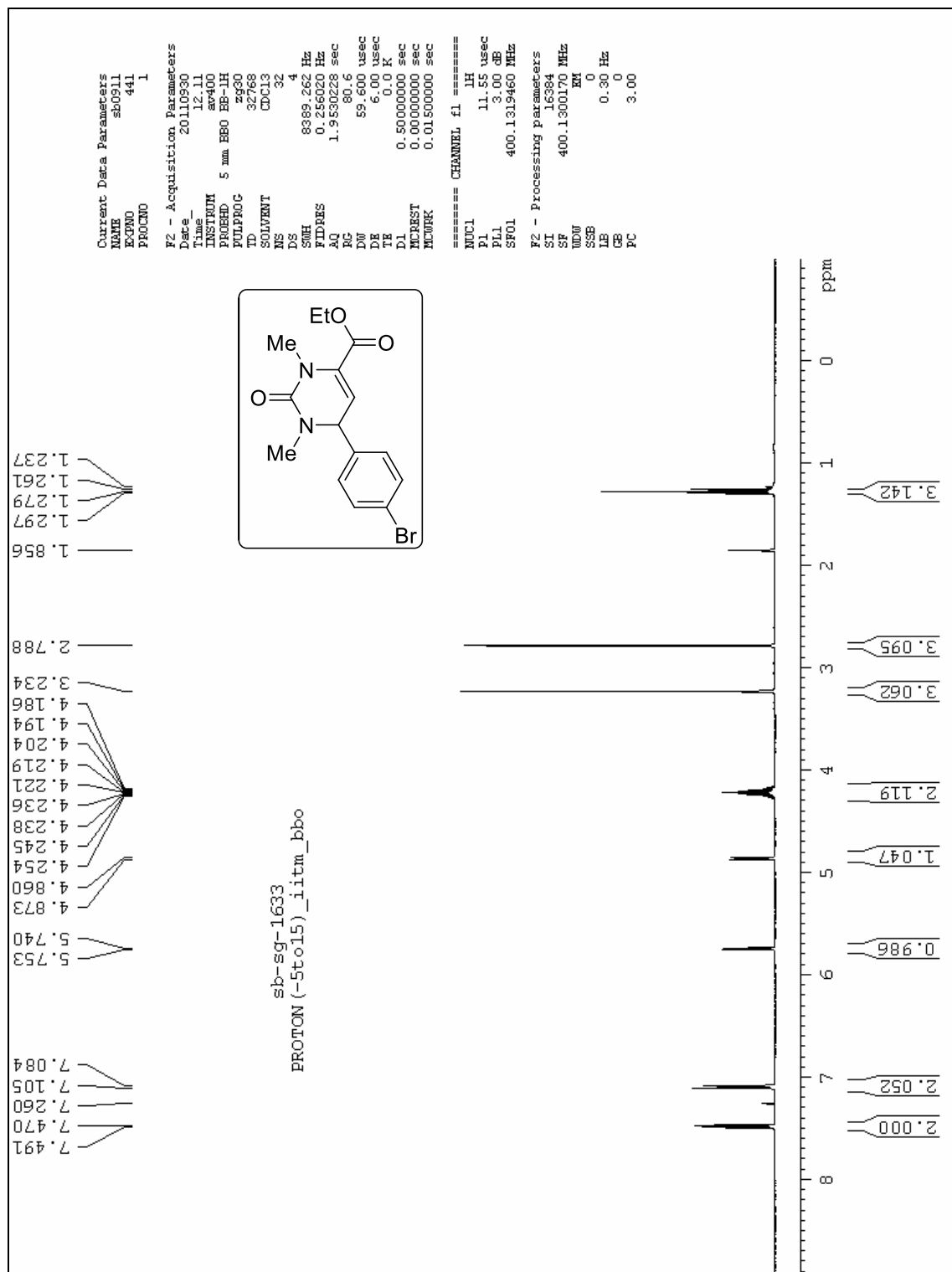
¹³C NMR spectrum of compound **28**



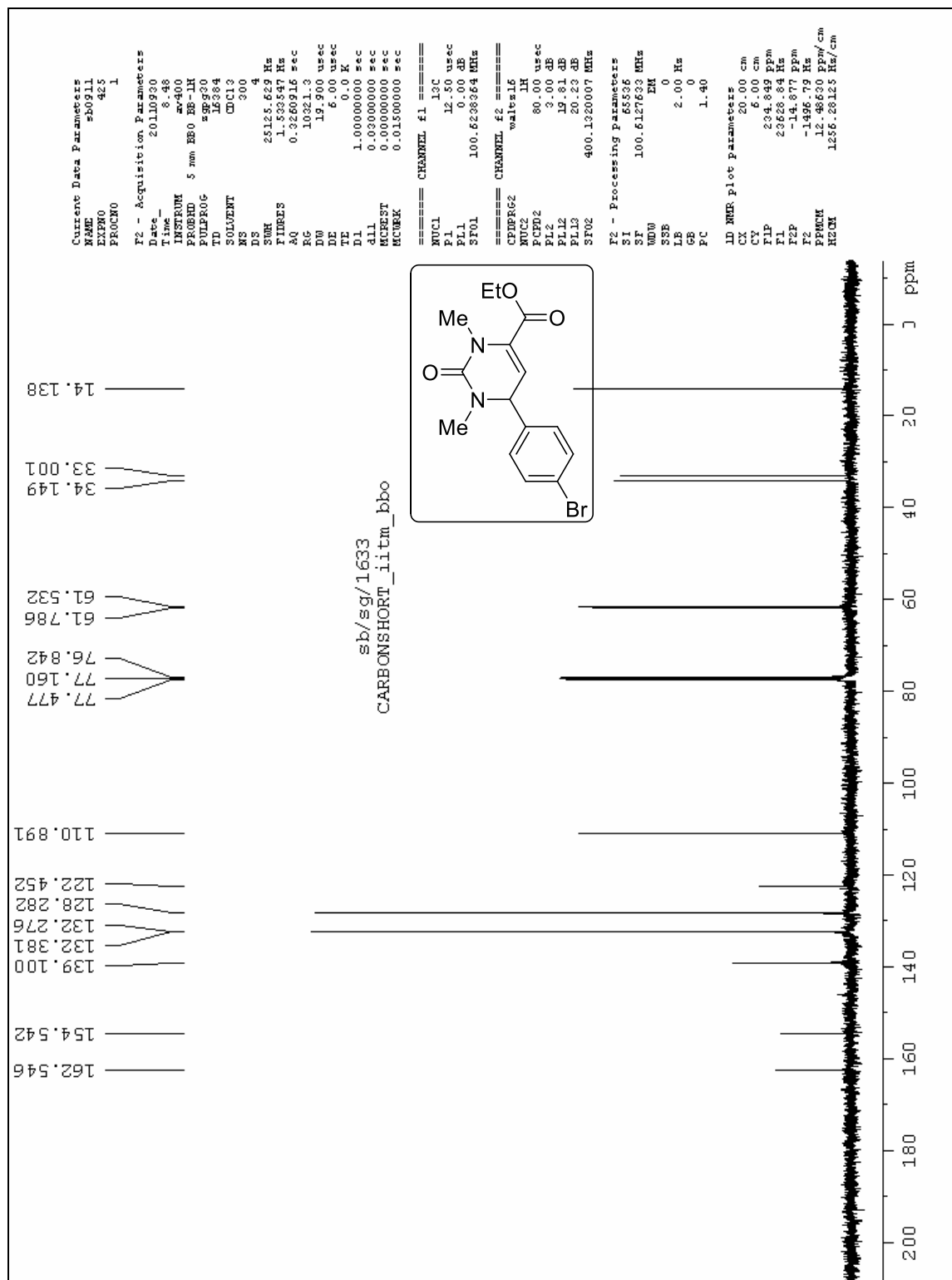
¹H NMR spectrum of compound 14

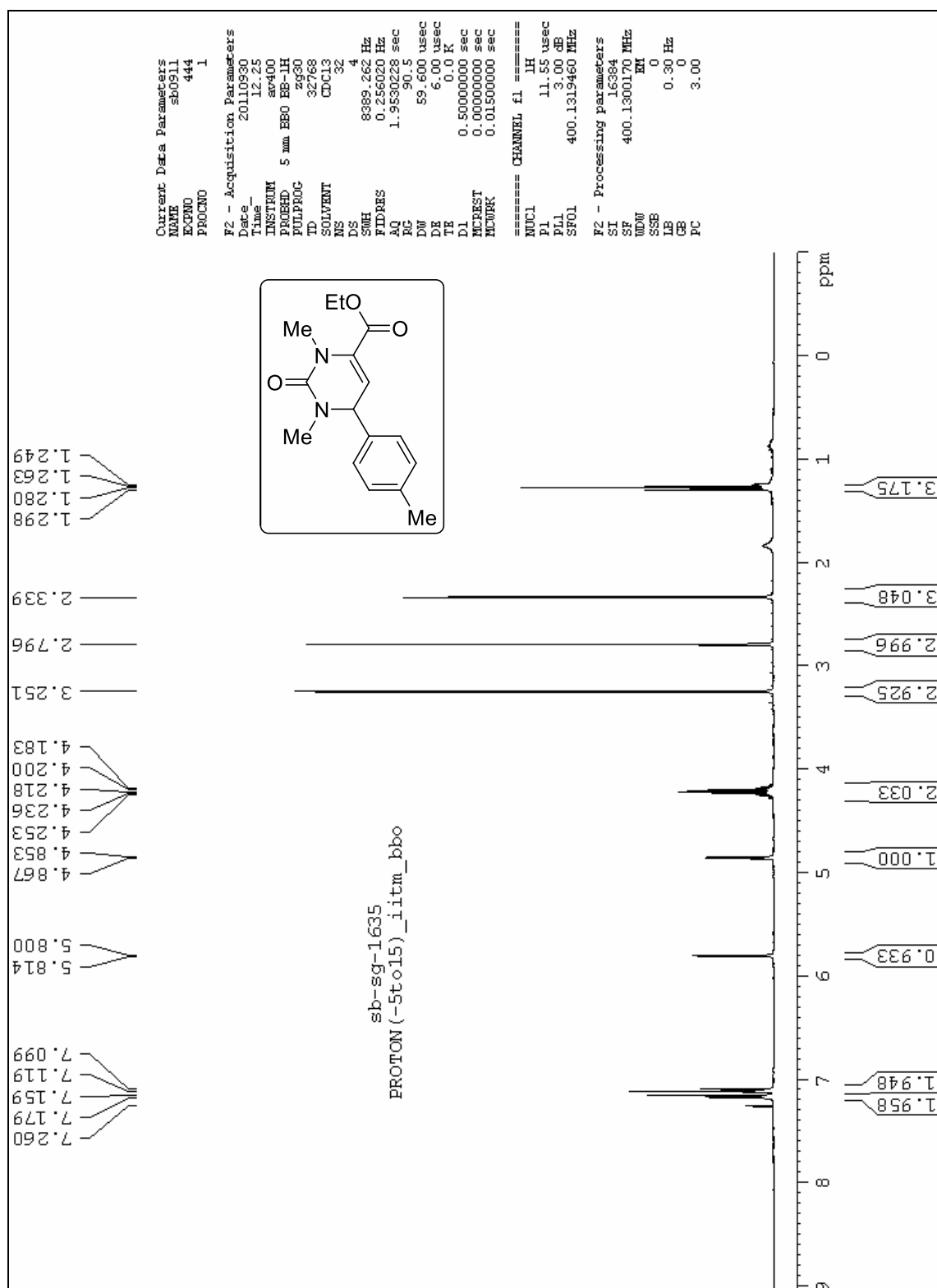


¹³C NMR spectrum of compound **14**

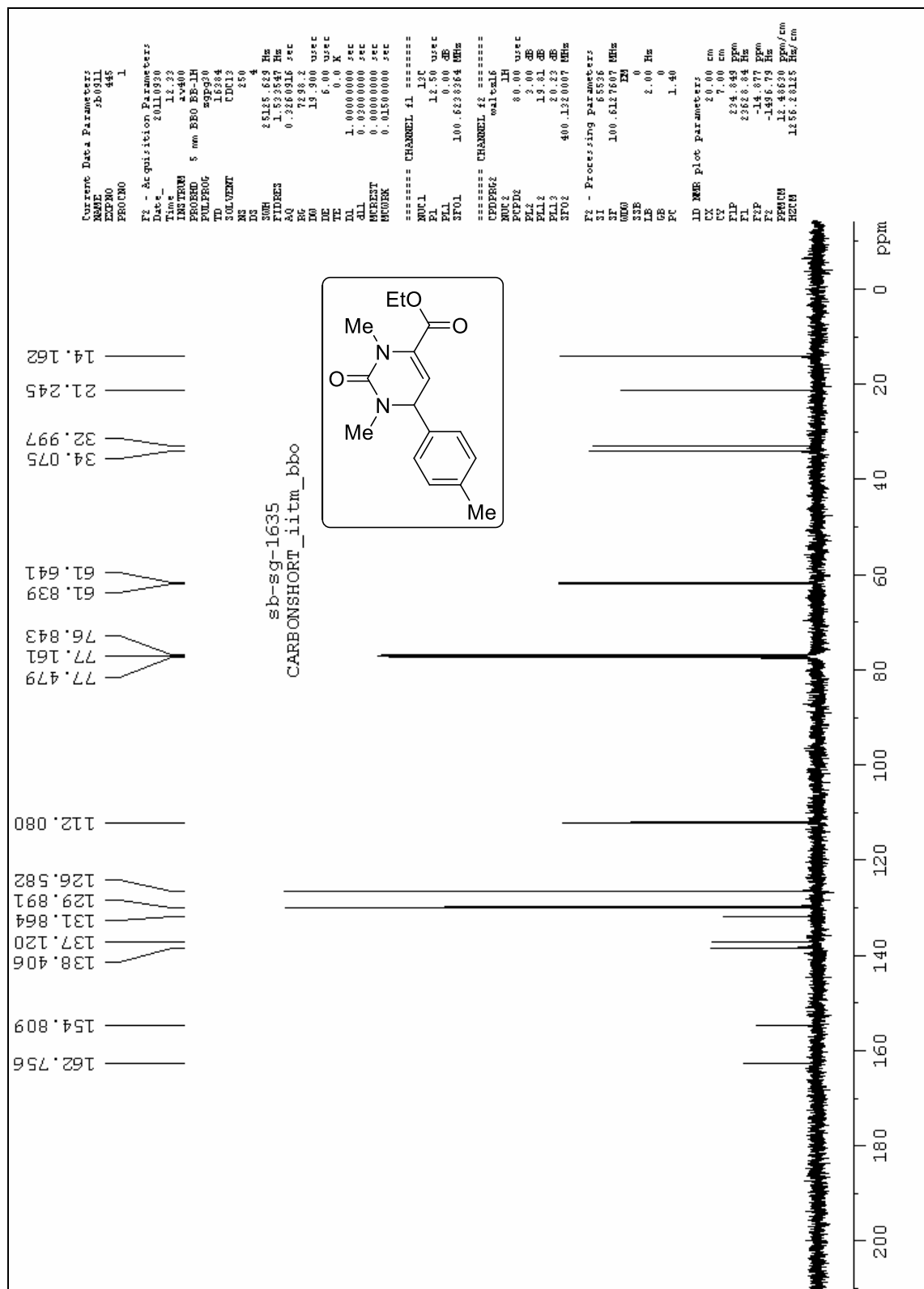


¹H NMR spectrum of compound 20

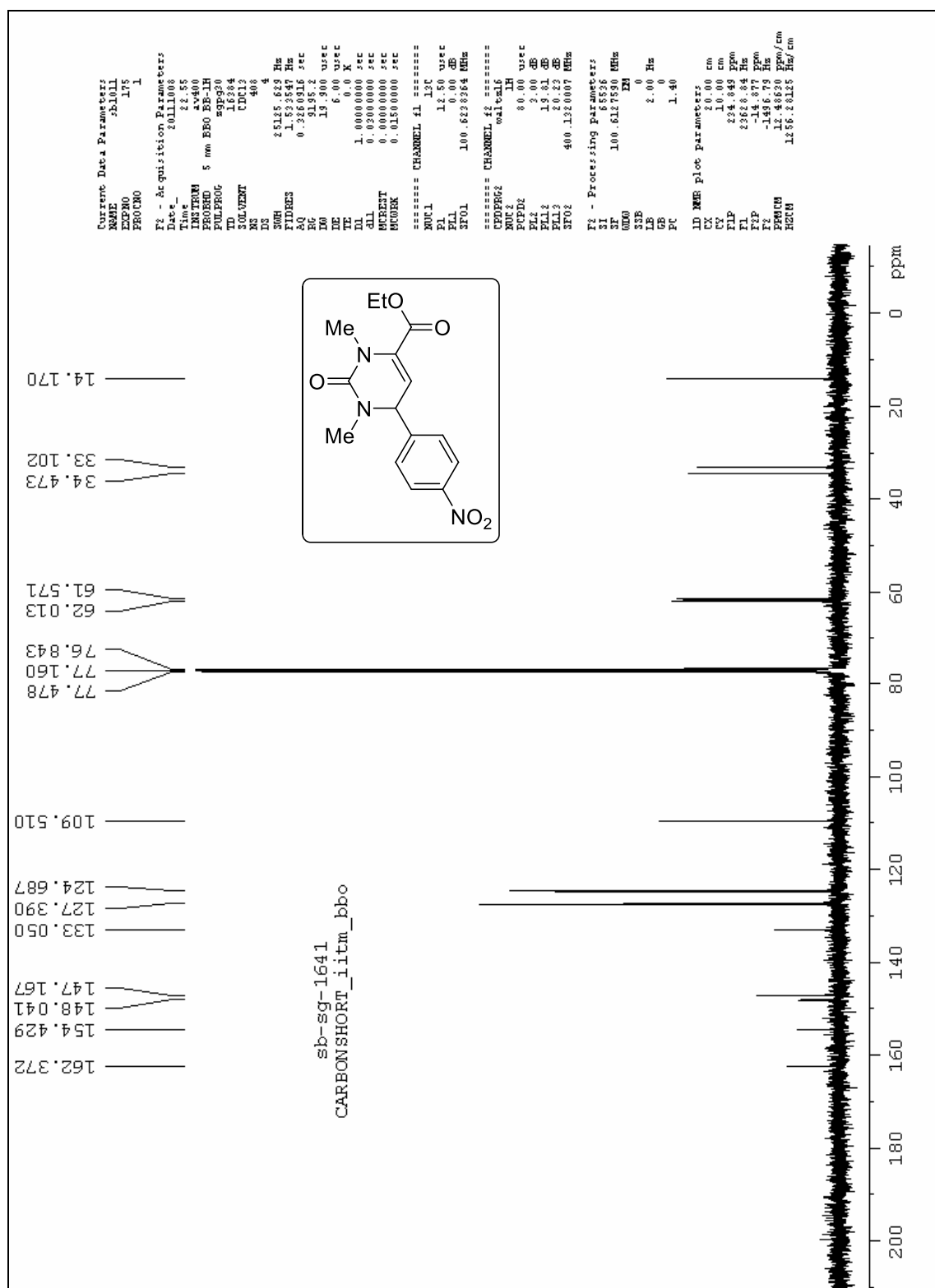
¹³C NMR spectrum of compound 20

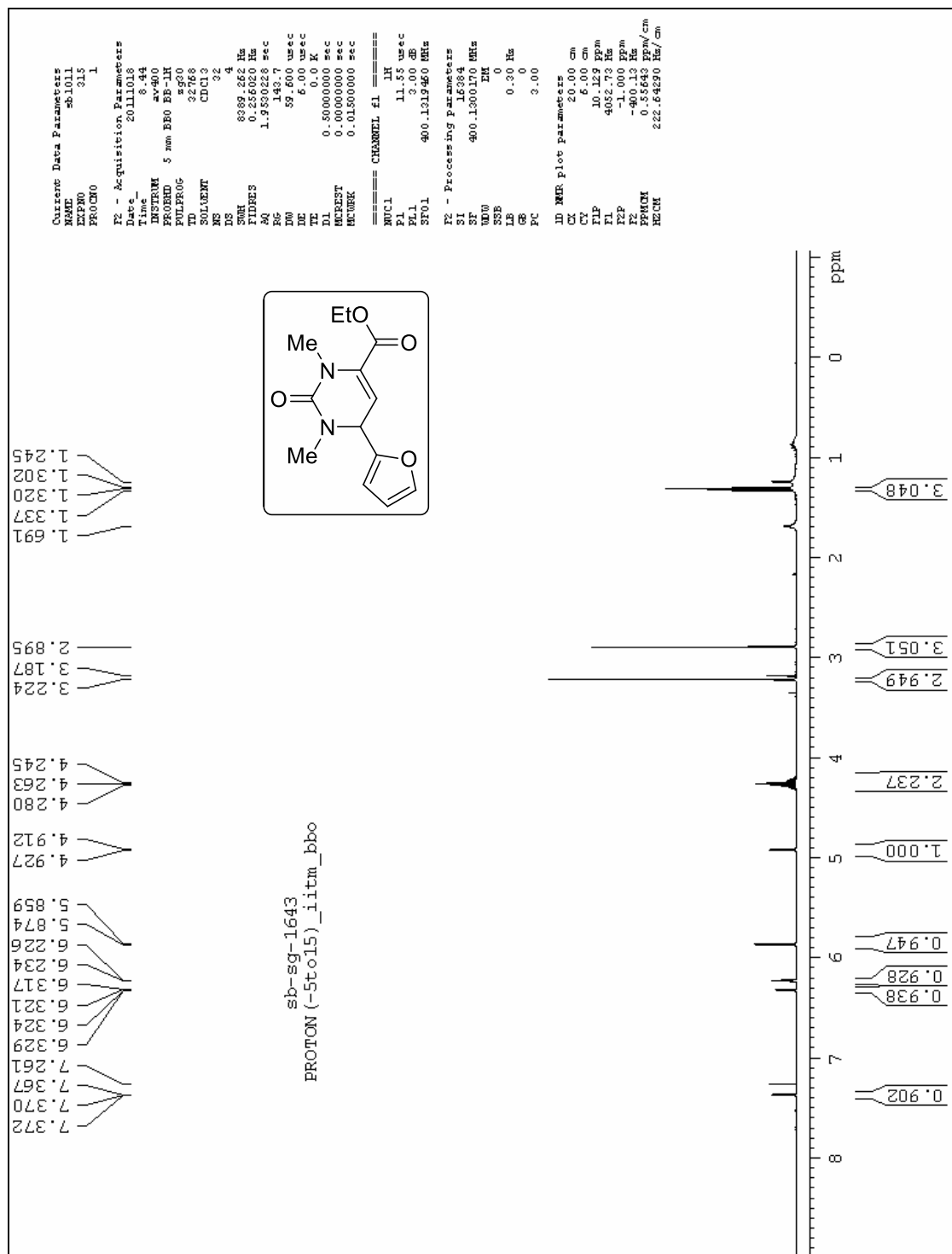


¹H NMR spectrum of compound **16**

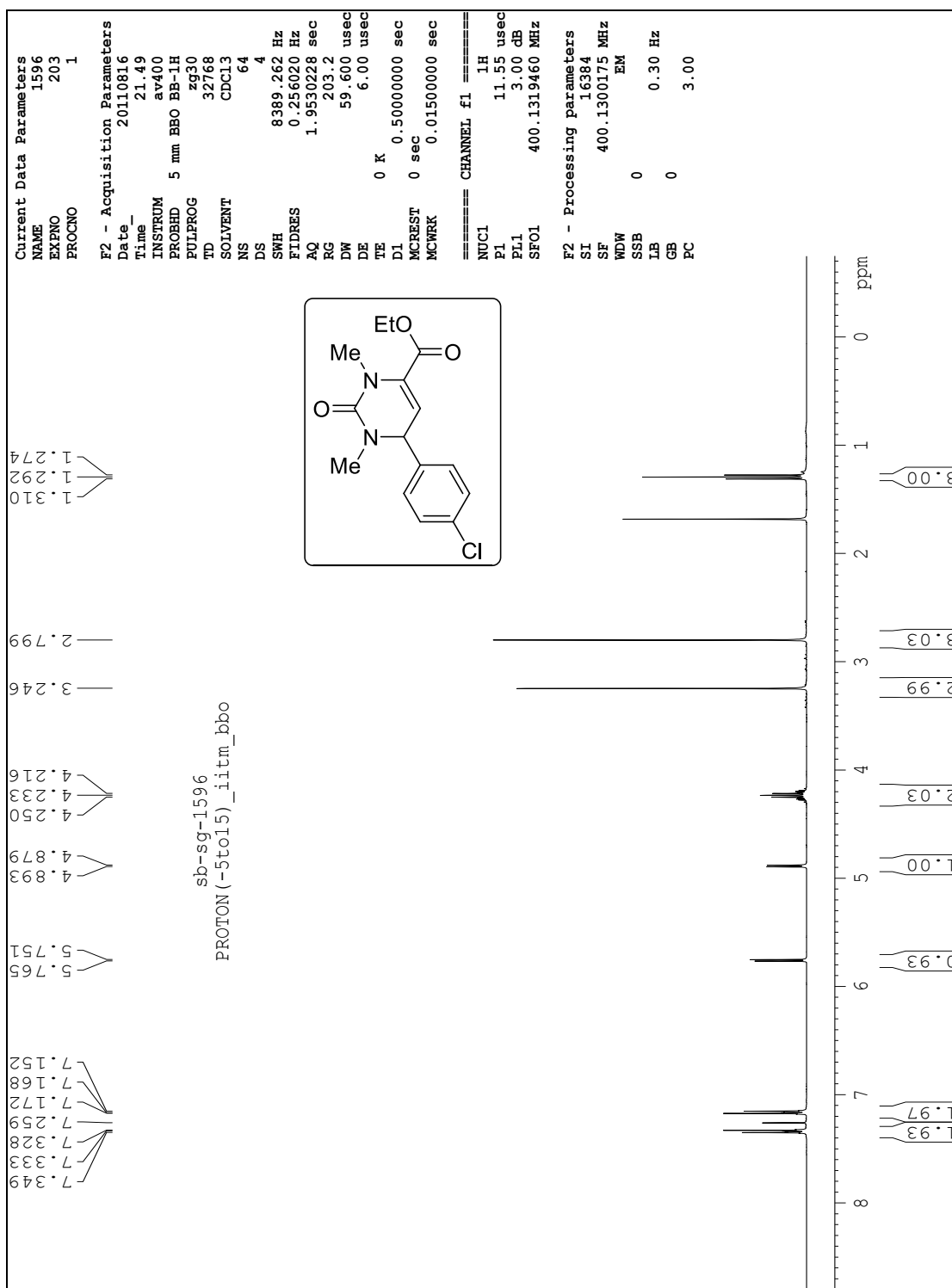


¹³C NMR spectrum of compound 16

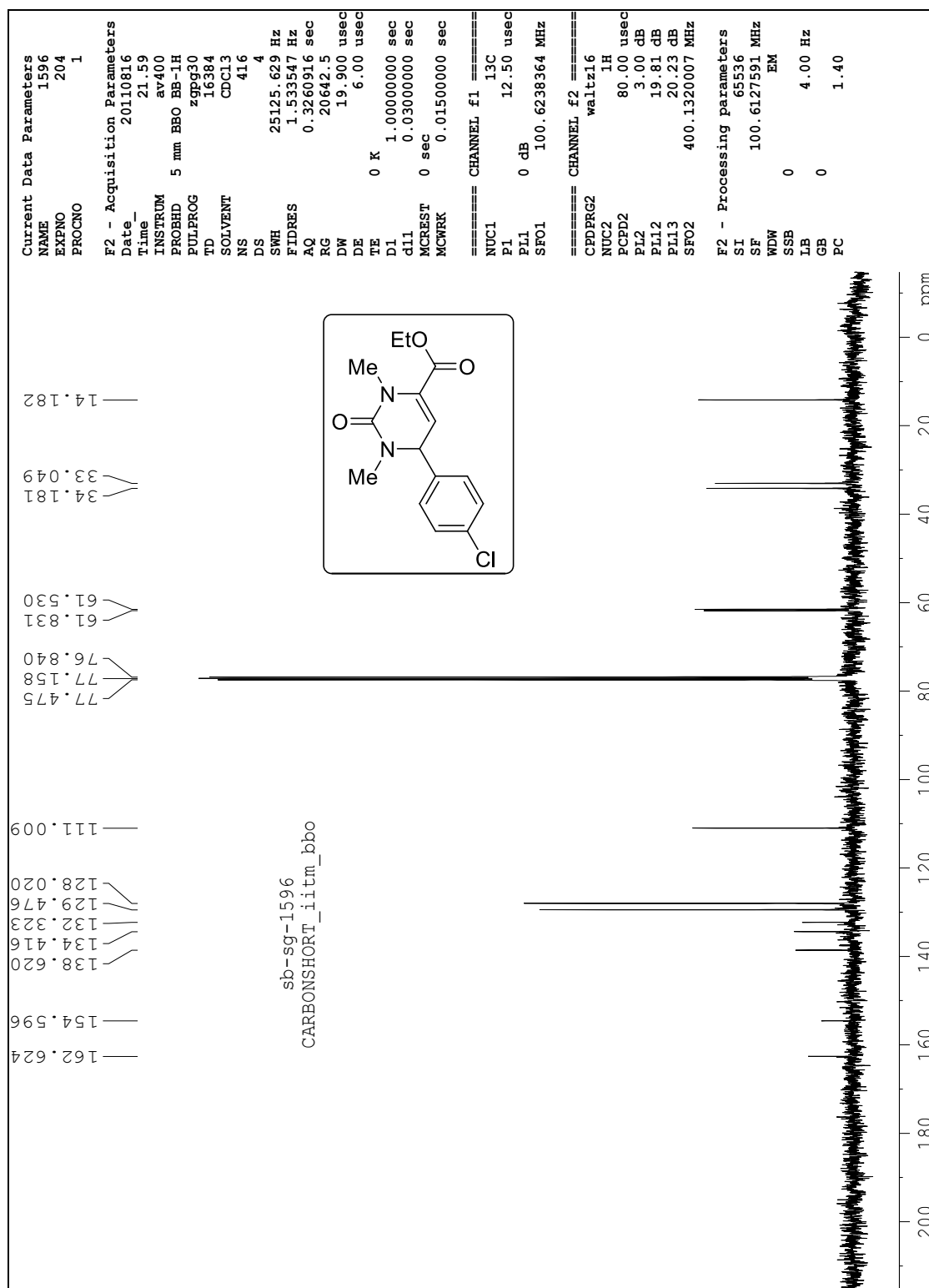




¹H NMR spectrum of compound 22



¹H NMR spectrum of compound 26



¹³C NMR spectrum of compound 26

References

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- [2] Akkari, R., et. al. Substituted pyrazolo[3,4-B]pyridine-6-carboxylic acids and their use. World Patent. WO2017060873A1, April 13, 2017.
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- [4] Halland, N.; Velgaard, T.; Jørgensen, K. A. *J. Org. Chem.* **2003**, *68*, 5067.
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