# Supporting Information

# An Expedient and Divergent Tandem One-Pot Synthesis of Pyrimidin-2,4-diones using the Blaise Reaction Intermediate

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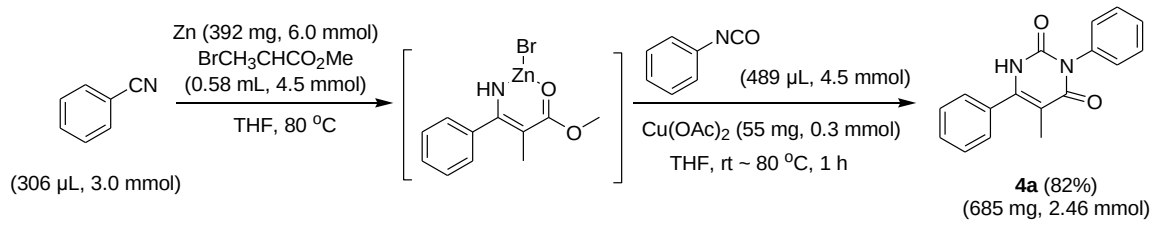
**1. General.** All reactions and manipulations were performed in a nitrogen atmosphere using standard Schelenk techniques. The reaction solvents were distilled prior to used (THF was distilled from sodium benzophenone ketyl). All purchased reagent were used without further purification. Anhydrous solvents were transferred by oven-dried syringe. Flasks were flames dried under a stream of nitrogen. The NMR spectra were recorded at 300 MHz ($^1$H), 75.5 MHz ($^{13}$C) and 282 MHz ($^{19}$F).

**2. Experimental Procedures**

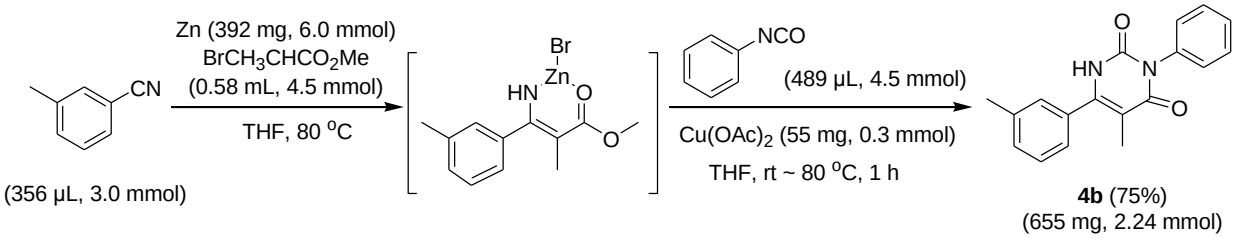
**2-1.** A Typical Procedure for the Synthesis of Pyrimidin-2,4-diones **4a**-**4p**.

5-Methyl-3,6-diphenyl-1*H*-pyrimidine-2,4-dione (**4a**)



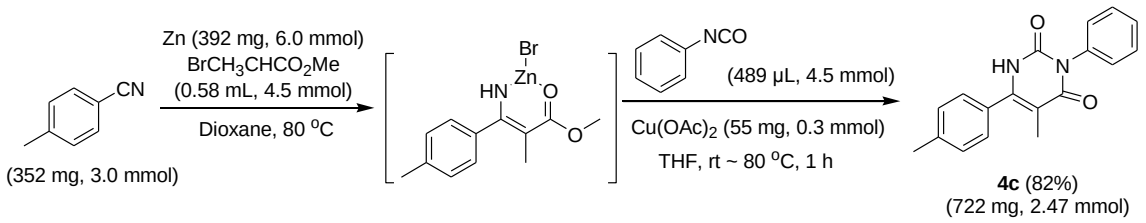

To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 392 mg, 6.0 mmol) in THF (1.0 mL) was added a solution of methanesulfonic acid in THF (1 M, 0.3 mL) at 80 °C bath temperature. After stirring for 10 min, benzonitrile (306 μL, 3.0 mmol) was added all at once. While maintaining THF reflux, methyl 2-bromopropionate (0.58 mL, 4.5 mmol) was added over 1 h using syringe pump, and the reaction mixture was further stirred for 1 h. After cooled to room temperature, to the reaction mixture were added successively $Cu(OAc)_2$ (55 mg, 0.3 mmol and a solution of phenyl isocyanate (489 μL, 4.5 mmol) in THF (1.0 mL). The reaction mixture was refluxed for 1 h, and allowed to cool to room temperature. The reaction was quenched with saturated aqueous $NH_4Cl$ solution, and neutralized with saturated aqueous $Na_2CO_3$ solution. The organic compounds were extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude solid was crystallized with *n*-hexane/ethyl acetate (4/1) to afford pyrimidine-2,4-dione **4a** and the product was further isolated from the residual of filtrates through by column chromatography (*n*-hexane/ethyl acetate = 3/2) to afford **4a** in a combined yield of 82% (685 mg, 2.46 mmol). White solid; mp: 179 - 181 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 7.23 (dd, *J* = 1.5 Hz, *J* = 8.1 Hz, 2H), 7.37 ~ 7.52 (m, 8H), 9.20 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.2, 107.6, 128.3, 128.4, 128.7, 129.0, 129.3, 130.5, 132.5, 134.9, 146.7, 151.8, 164.7 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{17}H_{15}N_2O_2$: 279.1134; Found: 279.1128.

Synthesis of 5-Methyl-3-phenyl-6-*m*-tolyl-1*H*-pyrimidine-2,4-dione (**4b**)



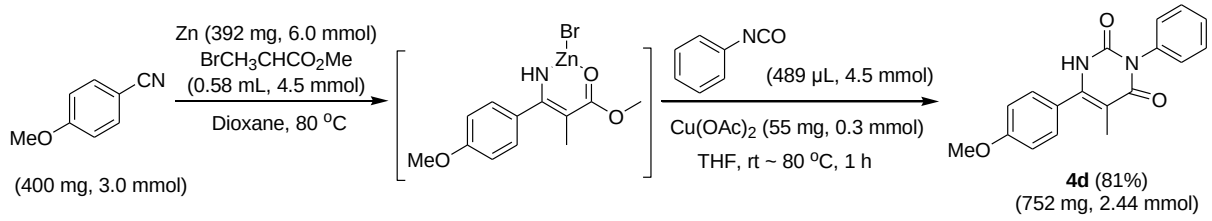

Yield: 75% (655 mg, 2.24 mmol); White solid; mp: 208 - 210 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 2.35 (s, 3H), 7.22 ~ 7.37 (m, 6H), 7.43 ~ 7.52 (m, 3H), 8.56 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.3, 21.4, 107.4, 125.5, 128.4, 128.7 (128.67), 128.7(128.70), 128.8, 129.3, 131.2, 132.5, 135.0, 139.0, 146.9, 151.8, 164.7 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{18}H_{17}N_2O_2$: 293.1290; Found: 293.1285.

5-Methyl-3-phenyl-6-*p*-tolyl-1*H*-pyrimidine-2,4-dione (**4c**)



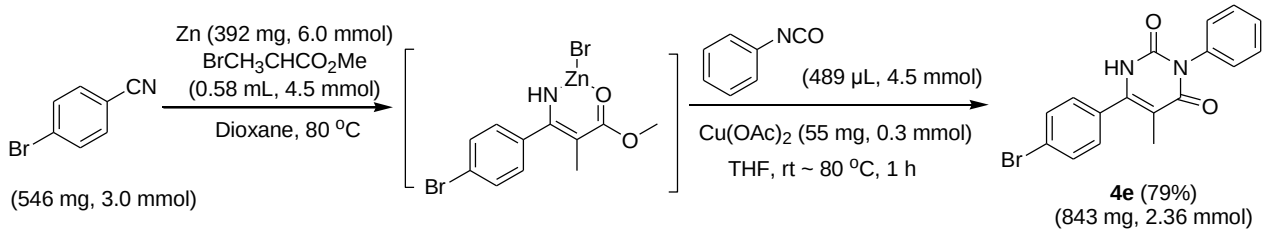

Yield: 82% (722 mg, 2.47 mmol); White solid; mp: 209 - 210 °C; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.42 (s, 3H), 7.23 ~ 7.34 (m, 6H), 7.44 ~ 7.53 (m, 3H), 8.66 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.3, 21.5, 107.3, 128.2, 128.5, 128.6, 129.3, 129.6, 135.0, 140.7, 146.8, 151.8, 164.7 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{18}H_{17}N_2O_2$: 293.1290; Found: 293.1285.

6-(4-Methoxy-phenyl)-5-methyl-3-phenyl-1*H*-pyrimidine-2,4-dione (**4d**)



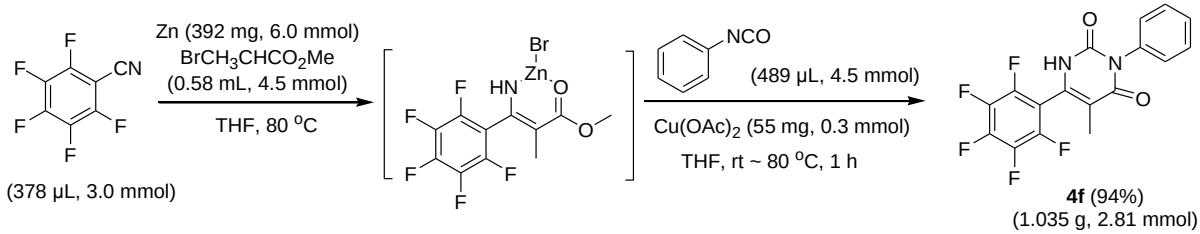

Yield: 81% (752 mg, 2.44 mmol); White solid; mp: 222 - 224 °C; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H), 3.87 (s, 3H), 6.95 (d, *J* = 8.7 Hz, 2H) 7.25 ~ 7.28 (m, 2H), 7.38 ~ 7.54 (m, 5H), 8.50 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.3, 55.5, 107.1, 114.4, 124.7, 128.5, 128.7, 129.4, 129.8, 135.0, 146.5, 151.7, 161.2, 164.8 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{18}H_{16}N_2O_3$: 308.1161; Found: 308.1159.

6-(4-Bromo-phenyl)-5-methyl-3-phenyl-1*H*-pyrimidine-2,4-dione (**4e**)



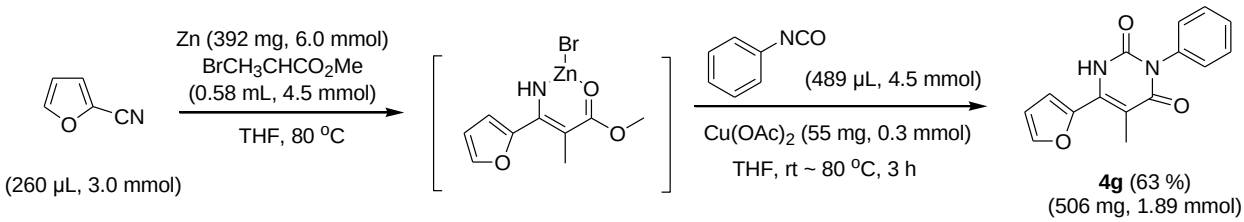

Yield: 79% (843 mg, 2.36 mmol); White solid; mp: 216 - 220 °C; $^{1}$H NMR (300 MHz, DMSO-$d_6$) δ 1.74 (s, 3H), 7.26 (d, *J* = 7.5 Hz, 2H), 7.41 ~ 7.50(m, 5H), 7.72 ~ 7.75 (m, 2H), 11.29 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 11.8, 105.4, 123.4, 128.0, 128.8, 128.9, 130.9, 131.5, 131.7, 135.8, 146.8, 150.6, 164.0 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{17}H_{13}{}^{79}BrN_2O_2$: 356.0160; Found: 356.0157; Cal. for $[M+2]^+$: $C_{17}H_{13}{}^{81}BrN_2O_2$: 358.0140; Found: 358.0124.

5-Methyl-6-pentafluorophenyl-3-phenyl-1*H*-pyrimidine-2,4-dione (**4f**)



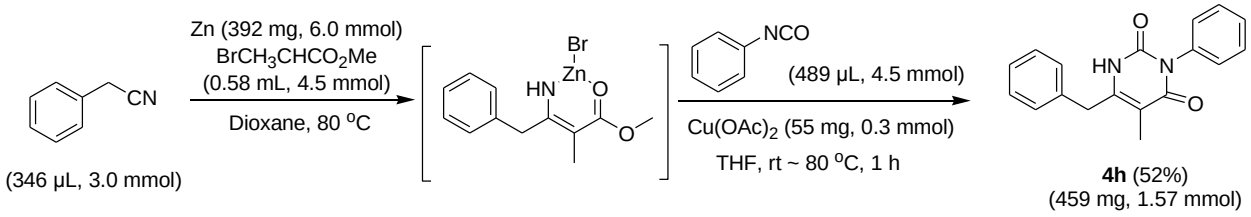
Yield: 94% (1.035 g, 2.81 mmol); White solid; mp: 180 - 184 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.85 (s, 3H), 7.17 ~ 7.20 (m, 2H), 7.46 ~ 7.49 (m, 3H), 10.9 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.1, 113.5, 128.0, 129.1, 129.4, 133.3, 134.1, 152.9, 163.2 ppm; $^{19}$F NMR (282 MHz, $CDCl_3$, $CF_3COOD$ as an internal reference) δ -137.8 (d, *J* = 16.9 Hz, 2F), -149.3 (tt, *J* =14.1 Hz, *J* = 2.8 Hz, 1F), -159.7 (m, 2F) ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{17}H_9F_5N_2O_2$:368.0584; Found: 368.0584.

5-Methyl-6-furanyl-3-phenyl-1*H*-pyrimidine-2,4-dione (**4g)**



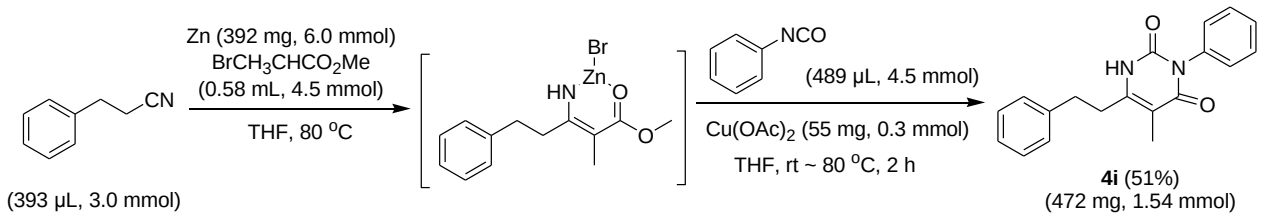

Yield: 63 % ( 506 mg, 1.89 mmol); White solid; mp: 204 - 206 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 2.23 (s, 3H), 6.61 (t, *J* = 1.8 Hz, 1H), 6.98 (d, *J* = 3.3 Hz, 1H), 7.26~7.29 (m, 2H), 7.42~7.56 (m, 4H), 9.12 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 11.8, 105.3, 112.9, 115.7, 128.5, 128.8, 129.3, 135.1, 135.8, 144.7, 144.9, 151.5, 164.6 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{15}H_{12}N_2O_3$: 268.0848; Found: 268.0851.

6-Benzyl-5-methyl-3-phenyl-1*H*-pyrimidine-2,4-dione (**4h**)



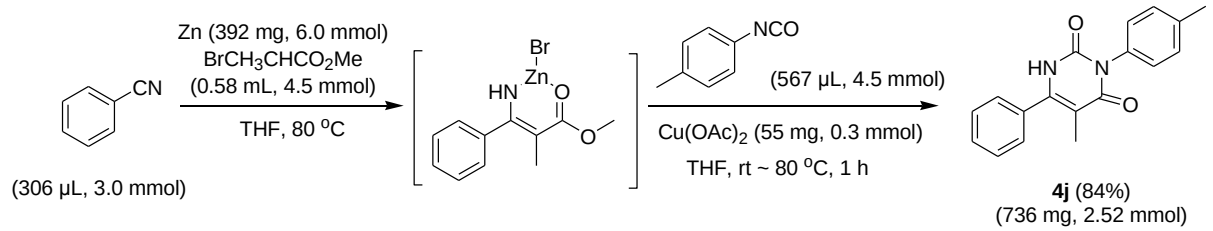

Yield: 52% (459 mg, 1.57 mmol); White solid; mp: 196 - 200 °C; $^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.84 (s, 3H), 3.83 (s, 2H), 7.21 ~ 7.28 (m, 3H), 7.32 ~ 7.47 (m, 7H), 11.25 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 10.5, 35.5, 105.1, 126.8, 127.9, 128.4, 128.7, 128.8, 128.9, 135.9, 136.5, 148.4, 150.8, 164.0 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{18}H_{16}N_2O_2$: 292.1212; Found: 292.1209.

5-Methyl-6-phenethyl-3-phenyl-1*H*-pyrimidine-2,4-dione (**4i**)



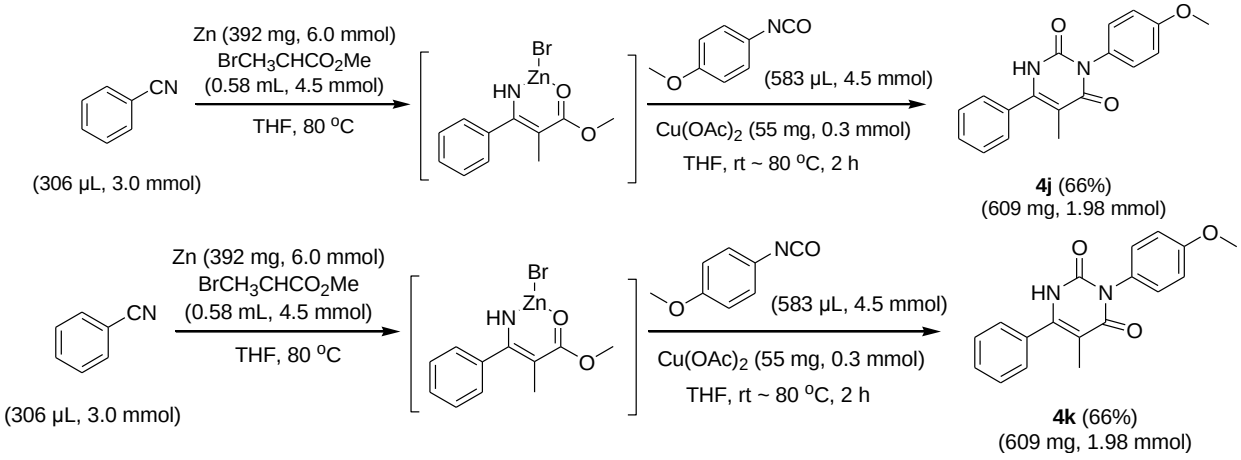

Yield: 51% (472 mg, 1.54 mmol); White solid; mp: 188 - 190 °C; $^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.73 (s, 3H), 2.70 (t, *J* = 7.8 Hz, 2H), 2.87 (t, *J* = 7.8 Hz, 2H), 7.18 ~ 7.25 (m, 2H), 7.31 ~ 7.47 (m, 8H), 11.17 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 10.0, 32.2, 33.2, 104.5, 126.3, 127.9, 128.4, 128.5, 128.8, 128.9, 135.9, 140.4, 149.3, 150.9, 163.9 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{19}H_{18}N_2O_2$: 306.1368; Found: 306.1366.

5-Methyl-6-phenyl-3-*p*-tolyl-1*H*-pyrimidine-2,4-dione (**4j**) (CAS No:95796-77-3)



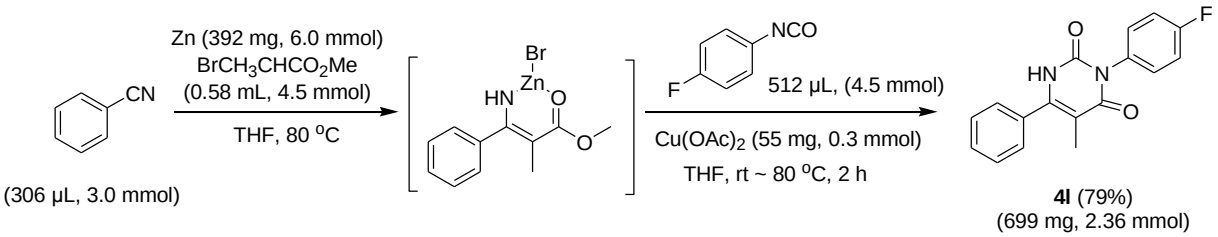

Yield: 84% (736 mg, 2.52 mmol); White solid; mp: 196 - 200 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.96 (s, 3H), 2.41 (s, 3H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.41 ~ 7.47 (m, 5H), 8.96 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.2, 21.4, 107.5, 128.0, 128.2, 129.0, 130.0, 130.4, 132.2, 132.6, 138.6, 146.5, 151.8, 164.8 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{18}H_{17}N_2O_2$: 293.1290; Found: 293.1285.

3-(4-Methoxy-phenyl)-5-methyl-6-phenyl-1*H*-pyrimidine-2,4-dione (**4k**)



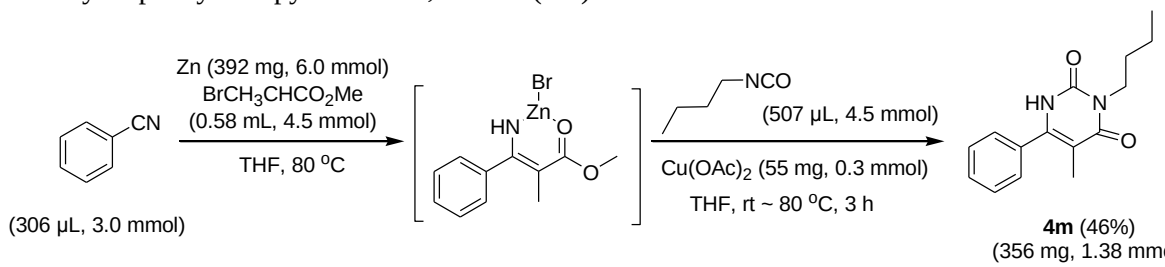

Yield: 66% (609 mg, 1.98 mmol); White solid; mp: 218 - 220 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 3.85 (s, 3H), 6.99 (d, *J* = 9.0 Hz, 2H), 7.16 (d, *J* = 8.7 Hz, 2H), 7.44 ~ 7.48 (m, 5H), 8.73 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.3, 55.6, 107.6, 114.7, 127.4, 128.2, 129.0, 129.4, 130.5, 132.7, 146.5, 151.9, 159.6, 164.9 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{18}H_{17}N_2O_3$: 309.1239; Found: 309.1234.

3-(4-Fluoro-phenyl)-5-methyl-6-phenyl-1*H*-pyrimidine-2,4-dione (**4l**)



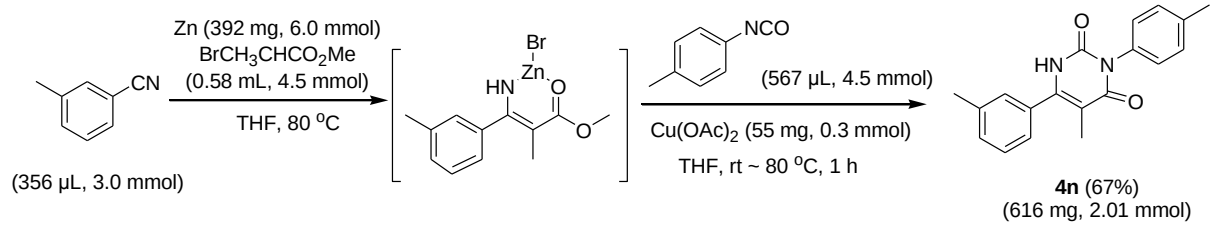

Yield: 79% (699 mg, 2.36 mmol); White solid; mp: 224 - 226 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 7.13 ~ 7.26 (m, 4H), 7.41 ~ 7.52 (m, 5 H), 8.96 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.2, 107.6, 116.2 (d, *J* = 23.4 Hz), 128.3, 129.0, 130.2, 130.3, 130.6 (d, *J* = 3.8 Hz), 132.4, 1468.8, 151.8, 162.4 (d, *J* = 247.6 Hz), 164.6 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{17}H_{14}FN_2O_2$: 297.1039; Found: 297.1034.

3-Butyl-5-methyl-6-phenyl-1*H*-pyrimidine-2,4-dione (**4m**)



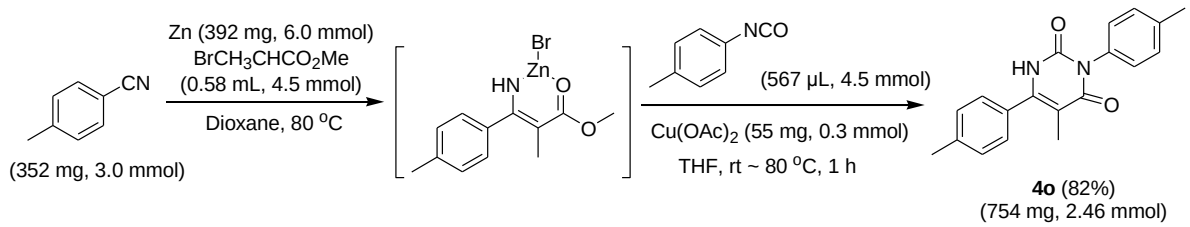

Yield: 46% (356 mg, 1.38 mmol); Pale yellow solid; mp: 114 -118 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.31 ~ 1.39 (m, 2H), 1.53 ~ 1.64 (m, 2H), 1.93 (s, 3H), 3.89 (t, *J* = 7.5 Hz, 2H), 7.42 ~ 7.50 (m, 5H), 9.46 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.2, 13.9, 20.3, 29.8, 40.9, 107.1, 128.4, 128.8, 130.3, 132.7, 146.2, 152.2, 164.6 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{15}H_{18}N_2O_2$: 259.1368; Found: 258.1366.

5-Methyl-6-*m*-tolyl-3-p-tolyl-1*H*-pyrimidine-2,4-dione (**4n**)



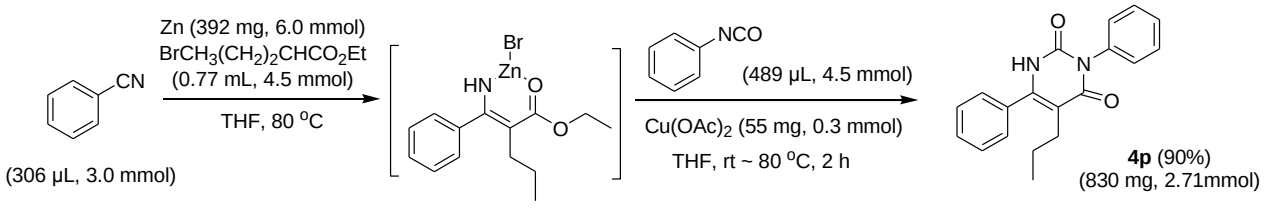

Yield: 67% (616 mg, 2.01 mmol); White solid; mp: 202 - 204 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 2.33 (s, 3H), 2.41 (s, 3H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.21 ~ 7.36 (m, 6H), 8.62 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.3, 21.4, 107.4, 125.4, 128.1, 128.6, 128.9, 130.1, 131.3, 132.3, 132.7, 138.7, 139.1, 146.6, 151.6, 164.9 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{19}H_{19}N_2O_2$: 307.1447; Found: 307.1441.

5-Methyl-3,6-di-*p*-tolyl-1*H*-pyrimidine-2,4-dione (**4o**)



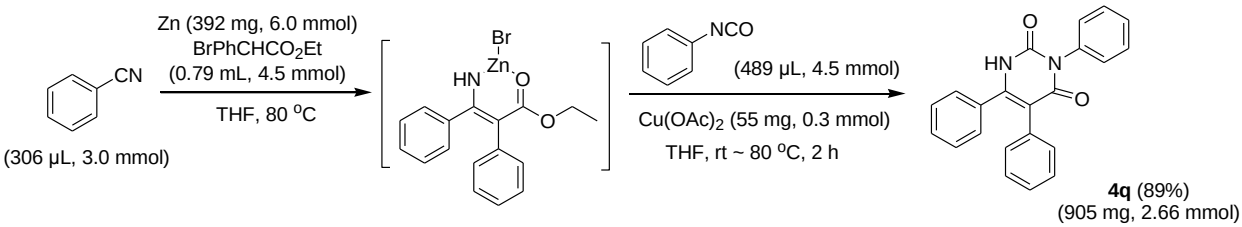

Yield: 82% (754 mg, 2.46 mmol); White solid; mp: 210 - 212 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.42 (s, 3H), 2.42 (s, 3H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.28 ~ 7.36 (m, 6H), 8.32 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 12.3, 21.4, 21.6, 107.3, 128.1(128.09), 128.1(128.13), 129.7, 129.8, 130.0, 132.3, 138.6, 140.7, 146.6, 151.8, 164.8 ppm; HRMS (FAB) *m/z* Cal. for $[M+H]^+$: $C_{19}H_{19}N_2O_2$: 307.1447; Found: 307.1441.

3,6-Diphenyl-5-propyl-1*H*-pyrimidine-2,4-dione (**4p**)



Yield: 90% (830 mg, 2.71 mmol); White solid; mp: 192 - 194 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.5 Hz, 3H), 1.45 ~ 1.57 (m, 2H), 2.30 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 6.6 Hz, 2H), 7.42 ~ 7.51 (m, 8H), 8.63 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 14.2, 22.7, 28.3, 112.3, 128.0, 128.4, 128.6, 128.9, 129.2, 130.3, 132.6, 134.8, 147.3, 151.7, 164.2 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{19}H_{18}N_2O_2$: 306.1368; Found: 306.1365.

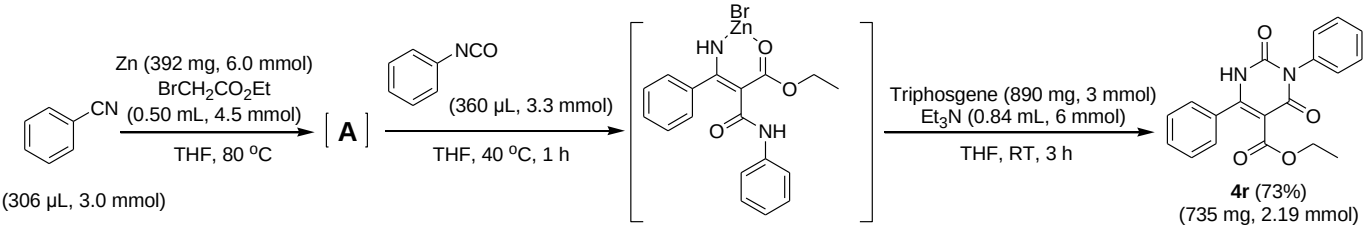
3,5,6-Triphenyl-1*H*-pyrimidine-2,4-dione (**4q**) (CAS No:67566-50-1)




Yield: 89% (905 mg, 2.66 mmol); White solid; mp: 294 - 296 °C; $^1$H NMR (300 MHz, DMSO-$d_6$) δ 7.04 ~ 7.27 (m, 5H), 7.28 ~ 7.52 (m, 10H), 11.55 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 111.5, 126.8, 127.5, 128.1, 128.9(128.87), 128.9(128.93), 129.2, 129.6, 131.5, 132.6, 133.4, 135.8, 149.4, 150.7, 162.9 ppm.

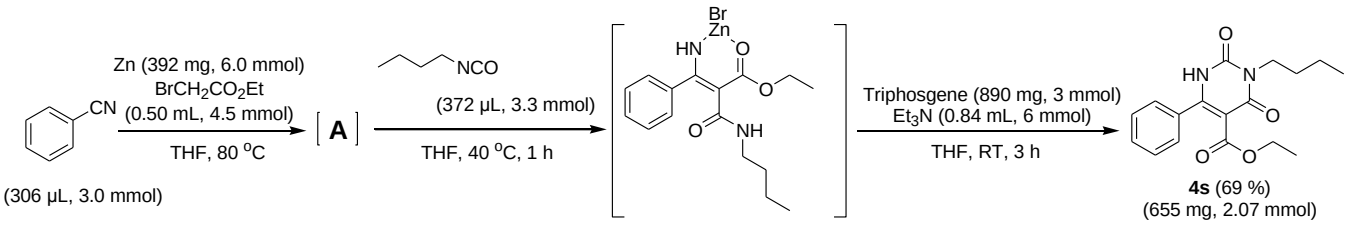
**2-2. A Typical Procedure for the synthesis of pyrimidin-2,4-diones 4r-4u.**

2,4-Dioxo-3,6-diphenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester **(4r)**



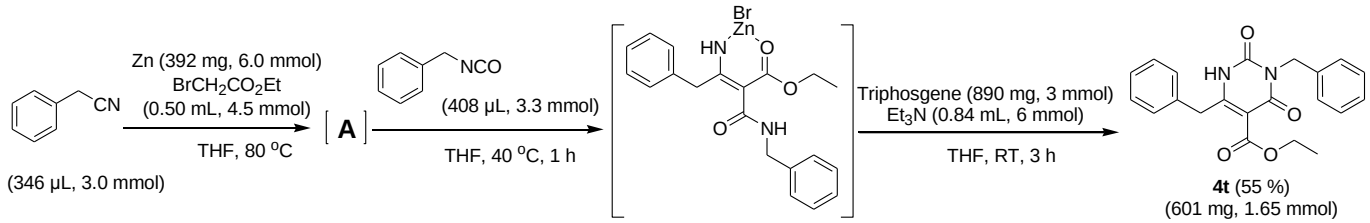

To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 392 mg, 6.0 mmol) in THF (1.0 mL) was added a solution of methanesulfonic acid in THF (1 M, 0.3 mL) at 80 °C bath temperature. After stirring 10 min, to the reaction mixture was added benzonitrile (306 μL, 3.0 mmol) all at once. While maintaining THF reflux, ethyl α-bromoacetate (0.50 mL, 4.5 mmol) was added over 1 h using syringe pump, and the reaction mixture was further stirred for 1 h, and cooled to room temperature. To the reaction mixture was added phenyl isocyanate (360 μL, 3.3 mmol) all at once, and stirred at 40 °C for 1 h. After cool the reaction mixture to 0 °C using ice bath, a solution of triphosgene (890 mg, 3 mmol) in THF (4 mL) was added, and then triethylamine (0.84 mL, 6 mmol) over 30 min using syringe pump. The reaction mixture was stirred at room temperature for 3 h, quenched with saturated aqueous $NH_4Cl$ solution, and neutralized with saturated aqueous $Na_2CO_3$ solution. The organic compounds were extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude solid was solidified with *n*-hexane/ethyl acetate (4/1) to afford pyrimidine-2,4-dione **4r** and the product was further isolated from the residual of the filtrates through by column chromatography (*n*-hexane/ ethyl acetate = 1/1) to give **4r** in a combined yield of 73% (735 mg, 2.19 mmol). White solid; mp: 212 - 214 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.2 Hz, 3H), 4.12 (q, *J* = 6.9 Hz, 2H), 7.21 ~ 7.26 (m, 2H), 7.32 ~ 7.51 (m, 8H), 9.64 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 13.7, 61.8, 107.9, 127.4, 128.3, 129.0(128.95), 129.0(129.02), 129.3, 131.1, 131.6, 133.8, 151.3, 151.4, 160.4, 164.0 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{19}H_{16}N_2O_4$: 336.1110; Found: 336.1113.

3-Butyl-2,4-dioxo-6-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester (**4s**)




Yield: 69% (655 mg, 2.07 mmol);White solid; mp: 156 - 158 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.5 Hz, 3H), 1.04 (t, *J* = 7.5 Hz, 3H), 1.33 (m, 2H), 1.59 (m, 2H), 3.87 (t, *J* = 7.5 Hz, 2H), 4.12 (q, *J* = 7.5 Hz, 2H), 7.45 ~ 7.54 (m, 5H), 10.0 (s , 1H) ppm; $^{13}$C NMR (75.5 MHz, CDCl3) δ 13.7, 20.2, 29.4, 40.8, 61.6, 107.5, 127.5, 128.8, 131.3, 131.4, 151.0, 151.9, 160.4, 164,2 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$ : $C_{17}H_{20}N_2O_4$ : 316.1423. Found: 316.1422.

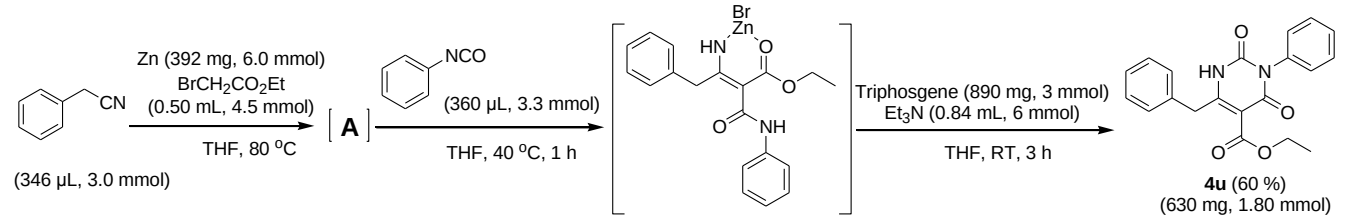
3,6-Dibenzyl-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester (**4t**)




Yield: 55% (601 mg, 1.65 mmol); White solid; mp : 186 - 188 °C ; $^1$H NMR (75.5 MHz, $CDCl_3$) δ 1.34 (t, *J* = 7.2 Hz, 3H), 3.94 (s, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 5.06 (s, 2H), 7.26 ~ 7.29 (m, 8H), 7.42 ~ 7.45 (m, 2H), 9.92 (s, 1H) ppm; $^{13}$C NMR (300 MHz, $CDCl_3$) δ 14.3, 37.1, 44.3, 62.0, 107.5, 128.0, 128.6, 129.1, 129.2, 134.2, 136.1, 152.2, 153.8, 160.2, 164.4 ppm; ; HRMS (EI) *m/z* Cal. for $[M]^+$ : $C_{21}H_{20}N_2O_4$ : 364.1423. Found: 364.1427.

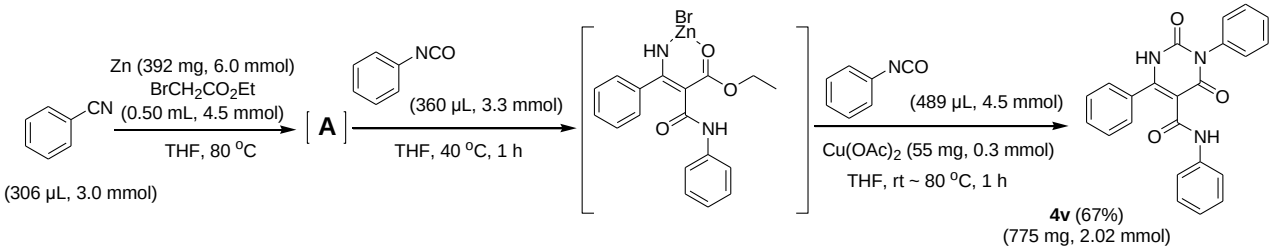
.

3-Benzyl-2,4-dioxo-6-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester (**4u**)



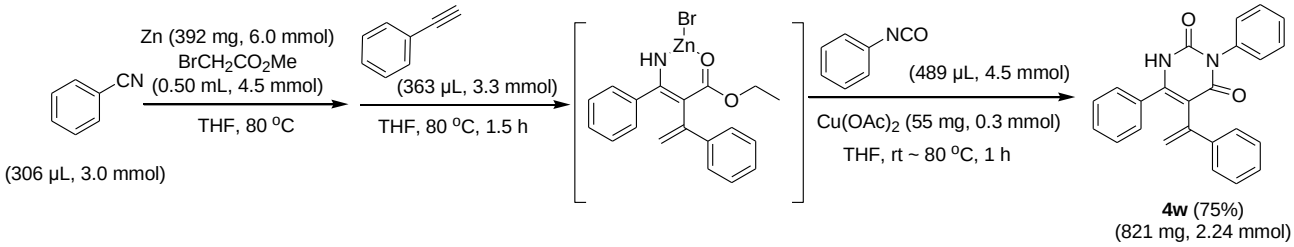

Yield: 60 % (630 mg, 1.80 mmol); White solid; mp: 216 -2 18 °C ; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.34 (t, *J* = 7.1 Hz, 3H), 3.88 (s, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 7.18~7.31 (m, 7H), 7.43 ~ 7.54 (m, 3H), 9.74 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 14.2, 37.0, 62.0, 107.7, 127.9, 128.4, 129.0, 129.1, 129.4, 129.5, 134.0, 151.8, 154.5, 160.3, 164.4 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$ : $C_{20}H_{18}N_2O_4$: 350.1267. Found: 350.1267.

**2-3.** 2,4-Dioxo-3,6-diphenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid phenylamide (**4v**)




To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 392 mg, 6.0 mmol) in THF (1.0 mL) was added a solution of methanesulfonic acid in THF (1 M, 0.3 mL) at 80 °C bath temperature. After stirring 10 min at THF reflux, to the reaction mixture was added benzonitrile (306 μL, 3.0 mmol) all at once. While maintaining THF reflux, ethyl α-bromoacetate (0.50 mL, 4.5 mmol) was added over 1 h using syringe pump, and the reaction mixture was further stirred for 1 h. The reaction mixture was cooled to room temperature, and added phenyl isocyanate (360 μL, 3.3 mmol). After stirring at 40 °C for 1 h, the reaction mixture was cooled to room temperature. To the reaction mixture, $Cu(OAc)_2$ (55 mg, 0.3 mmol) and a solution of phenyl isocyanate (489 μL, 4.5 mmol) in THF (1.0 mL) were added successively. After stirring at 80 °C for 1 h, the reaction mixture was cooled to room temperature, quenched with saturated aqueous $NH_4Cl$ solution, and neutralized with saturated aqueous $Na_2CO_3$ solution. The organic compounds were extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was crystalized with *n*-hexane/ethyl acetate (4/1) to afford pyrimidine-2,4-dione **4v** and the product was further isolated from the residual of the filtrates through by column chromatography (*n*-hexane/ethyl acetate = 1/1) to afford **4v** in a combined yield of 67% (775 mg, 2.02 mmol). White solid; mp: 236 - 240 °C; $^1$H NMR (300 MHz, DMSO-$d_6$) δ 7.01 (t, $J$ = 7.5 Hz, 1H), 7.21 ~ 7.33 (m, 4H), 7.42 ~ 7.61 (m, 10H), 10.31 (s, 1H), 11.79 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 119.6, 124.0, 128.2, 128.4, 128.8, 128.9, 129.0, 129.1, 129.2, 129.5, 131.1, 132.1, 132.1, 135.5, 139.3, 150.9, 161.9, 162.0 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{23}H_{17}N_3O_3$: 383.1270; Found: 383.1267.

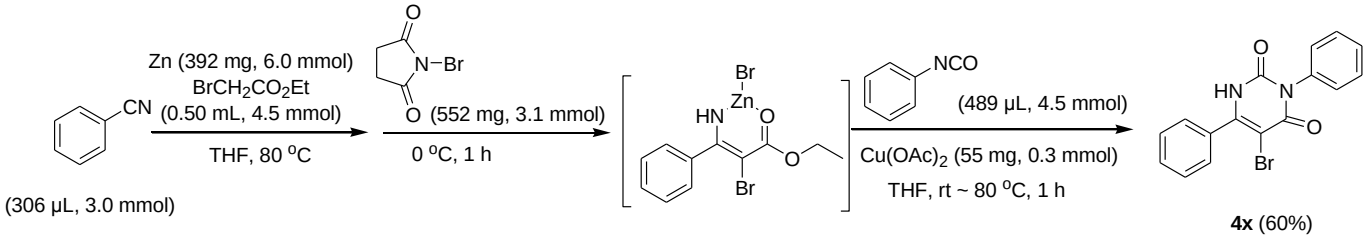
**2-4.** 3,6-Diphenyl-5-(1-phenyl-vinyl)-1*H*-pyrimidine-2,4-dione (**4w**)




To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 392 mg, 6.0 mmol) in THF (1.0 mL) was added a solution of methanesulfonic acid in THF (1 M, 0.3 mL) at 80 °C bath temperature. After stirring 10 min at THF reflux, to the reaction mixture was added benzonitrile (306 μL, 3.0 mmol) all at once. While maintaining THF reflux, ethyl α-bromoacetate (0.50 mL, 4.5 mmol) was added over 1 h using syringe pump, and the reaction mixture was further stirred for 1 h. To this reaction mixture, phenylacetylene (363 μL, 3.3 mmol) was added. After 1.5 h stirring at THF reflux, the reaction mixture was cooled to room temperature, and $Cu(OAc)_2$ (55 mg, 0.3 mmol) and a solution of phenyl isocyanate (489 μL, 4.5 mmol) in THF (1.0 mL) were successively added. After stirring at THF reflux for 30 min, the reaction mixture was cooled to room temperature, quenched with saturated aqueous $NH_4Cl$ solution, and neutralized with saturated aqueous $Na_2CO_3$ solution. The organic compounds were extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried with anhydrous $MgSO_4$, filtered,

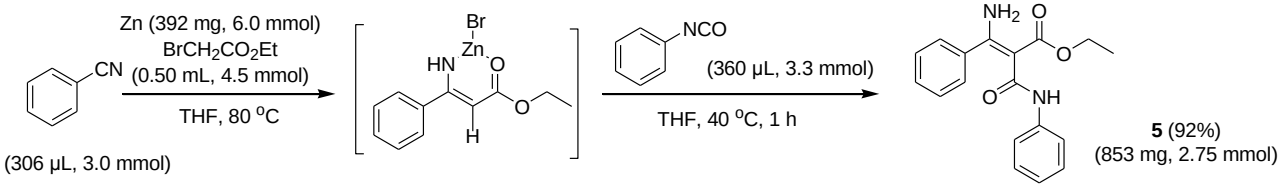
and concentrated under reduced pressure. The crude solid was washed with *n*-hexane/ethyl acetate (4/1) to afford pyrimidine-2,4-dione **4w** and the product was further isolated from the residual of the filtrates through by column chromatography (*n*-hexane/ethyl acetate = 1/1) to afford **4w** in a combined yield of 75% (821 mg, 2.24 mmol). White solid; mp: 226 - 228 °C; $^1$H NMR (300 MHz, $CDCl_3$) δ 5.11 (s, 1H), 5.68 (s, 1H), 7.23 ~ 7.48 (m, 15H), 9.02 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 113.2, 120.3, 126.1, 127.8, 127.9, 128.5, 128.6, 128.8, 128.9, 129.3, 130.7, 132.5, 134.5, 140.2, 140.6, 148.7, 151.6, 162.9 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{24}H_{18}N_2O_2$: 366.1368; Found: 366.1365.

**2-5.** Synthesis of 5-Bromo-3,6-diphenyl-1*H*-pyrimidine-2,4-dione (**4x**)




To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 392 mg, 6.0 mmol) in THF (1.0 mL) was added a solution of methanesulfonic acid in THF (1 M, 0.3 mL) at 80 °C bath temperature. After stirring for 10 min at THF reflux, benzonitrile (306 μL, 3.0 mmol) was added all at once. While maintaining THF reflux, ethyl α-bromoacetate (0.50 mL, 4.5 mmol) was added over 1 h using syringe pump, and the reaction mixture was further stirred for 1 h. The reaction mixture was cooled to 0 °C, and then *N*-bomosuccinimide (552 mg, 3.1 mmol) was added. After 1 h stirring at 0 °C, to the reaction mixture was added successively $Cu(OAc)_2$ (55 mg, 0.3 mmol) and a solution of phenyl isocyanate (489 μL, 4.5 mmol) in THF (1.0 mL). The reaction mixture was stirred at THF reflux for 30 min, and allowed to cool to room temperature, quenched with saturated aqueous $NH_4Cl$ solution, and neutralized with saturated aqueous $Na_2CO_3$ solution. The organic compounds were extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude solid was washed with *n*-hexane/ethyl acetate (4/1) to afford pyrimidine-2,4-dione **4x** and the product was further isolated from the residual of the filtrates through by column chromatography (*n*-hexane/ethyl acetate = 1/1) to afford **4x** in a combined yield of 60% (621 mg, 1.81 mmol). White solid; mp: 216 - 220 °C; $^1$H NMR (300 MHz, DMSO-$d_6$) δ 7.32 (d, $J$ = 7.2 Hz, 2H), 7.40 ~ 7.59 (m, 8H), 11.88 (s, 1H) ppm; $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 95.2, 128.3, 128.4, 128.6, 128.7, 129.0, 130.5, 132.7, 135.8, 150.2, 151.1, 159.9 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$: $C_{16}H_{11}{}^{79}BrN_2O_2$: 342.0004; Found: 342.0000.; Cal. for $[M+2]^+$: $C_{17}H_{11}{}^{81}BrN_2O_2$: 343.9983; Found: 343.9983

**2-6.** Synthesis of 3-Amino-3-phenyl-2-phenylcarbamoyl-acrylic acid ethyl ester (**5**)




To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 392 mg, 6.0 mmol) in THF (1.0 mL) was added a solution of methanesulfonic acid in THF (1 M, 0.3 mL) at 80 °C bath temperature. After stirring for 10 min, benzonitrile (306 μL, 3.0 mmol) was added all at once. While maintaining THF reflux, ethyl α-bromoacetate (0.50 mL, 4.5 mmol) was added over 1 h using syringe pump, and the reaction mixture was further stirred for 1 h. The reaction mixture was cooled to room temperature, and phenyl isocyanate (360 μL, 3.3 mmol) was added. The reaction mixture was stirred at 40 °C for 1 h. The reaction was quenched with saturated aqueous $NH_4Cl$ solution,

and the solution was neutralized with saturated aqueous $Na_2CO_3$ solution. The organic compounds were extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude solid was purified by recrystallization (*n*-hexane/ethyl acetate = ca. 4/1) to afford **5**, and the product was further isolated from the residual of filtrates through by column chromatography (*n*-hexane/ethyl acetate = 4/1) to afford 5 in a combined yield of 92% (853 mg, 2.75 mmol). White solid; mp: 126 - 128 $^{o}$C; 0.57 (t, *J* = 7.2 Hz, 3H), 3.71 (q, *J* = 7.2 Hz, 2H), 5.42 (brs, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 7.23 ~ 7.46 (m, 7H), 7.59 (d, *J* = 8.1Hz, 2H), 10.82 (brs, 2H) ppm; $^{13}$C NMR (300 MHz, $CDCl_3$) δ 13.1, 59.9, 92.1, 120.7, 123.6, 126.8, 128.5, 128.9, 129.6, 138.8, 140.6, 167.6, 169.8, 170.7 ppm; HRMS (EI) *m/z* Cal. for $[M]^+$ : $C_{18}H_{18}N_2O_3$ : 310.1317. Found: 310.1315.

Crystal Structure for **4c (CCDC 938319)**

A colorless plate-like specimen of $C_{18}H_{16}N_2O_2$, approximate dimensions 0.100 mm x 0.290 mm x 0.440 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The total exposure time was 9.83 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 25573 reflections to a maximum θ angle of 28.27° (0.75 Å resolution), of which 3644 were independent (average redundancy 7.018, completeness = 99.8%, $R_{int}$ = 1.91%, $R_{sig}$ = 0.92%) and 3365 (92.34%) were greater than $2\sigma(F^2)$. The final cell constants of a = 11.1596(3) Å , b = 9.7432(3) Å , c = 13.8929(4) Å, β = 102.5580(10)°, volume = 1474.44(7) $Å^3$, are based upon the refinement of the XYZ-centroids of 9941 reflections above 20 σ(I) with 5.148° < 2θ < 56.53°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.944. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9627 and 0.9913. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 4 for the formula unit, $C_{18}H_{16}N_2O_2$. The final anisotropic full-matrix least-squares refinement on $F^2$ with 201 variables converged at R1 = 3.95%, for the observed data and wR2 = 10.98% for all data. The goodness-of-fit was 1.061. The largest peak in the final difference electron density synthesis was 0.354 $e^-/Å^3$ and the largest hole was -0.213 $e^-/Å^3$ with an RMS deviation of 0.058 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.317 $g/cm^3$ and F(000), 616 $e^-$.

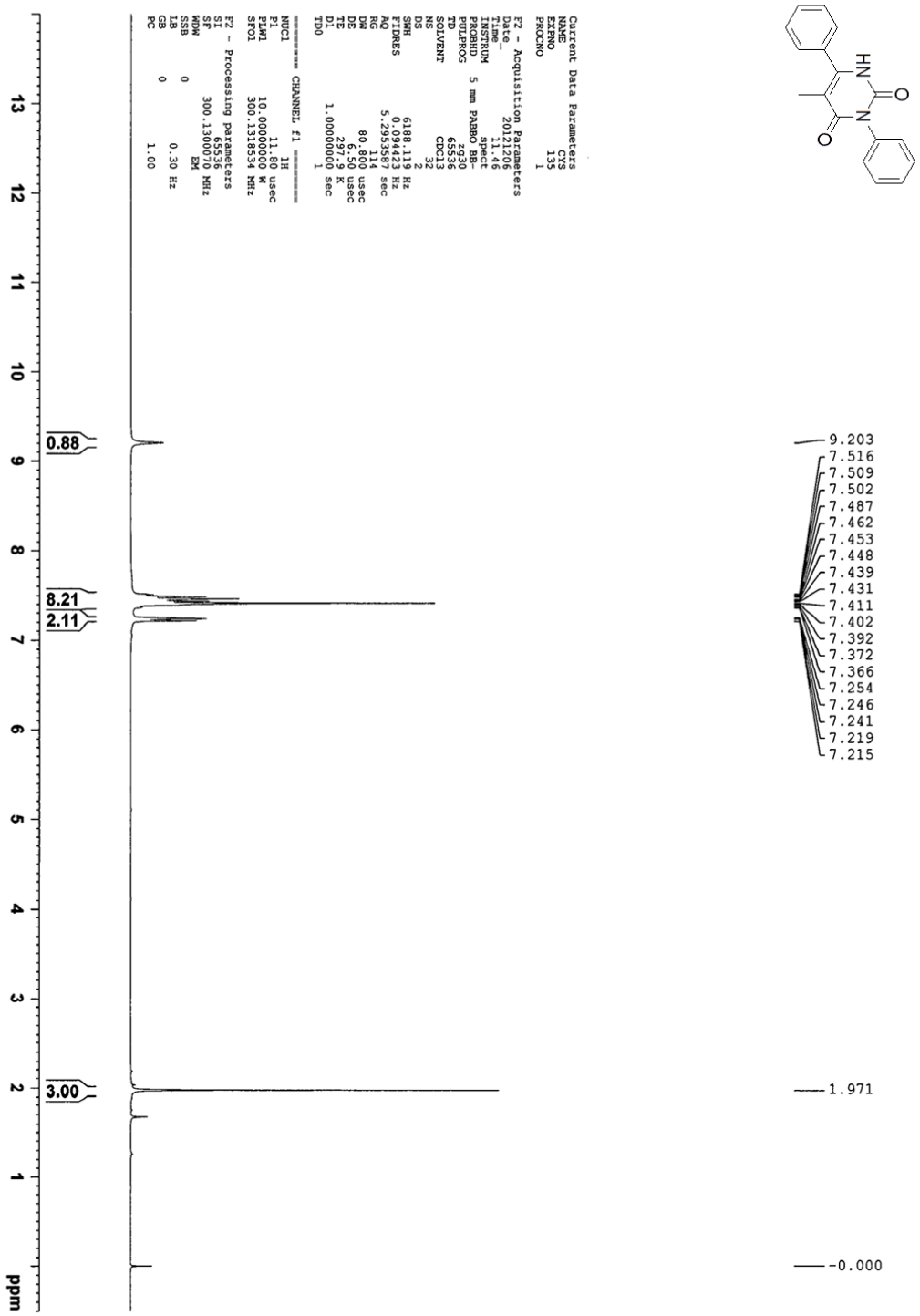
Table S1. Sample and crystal data for **4c.**

| | | |
|---|---|---|
| Chemical formula | $C_{18}H_{16}N_2O_2$ | |
| Formula weight | 292.33 | |
| Temperature | 150(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal size | 0.100 x 0.290 x 0.440 mm | |
| Crystal habit | colorless plate | |
| Crystal system | monoclinic | |
| Space group | P 1 21/c 1 | |
| Unit cell dimensions | a = 11.1596(3) Å | α = 90° |
| | b = 9.7432(3) Å | β = 102.5580(10)° |
| | c = 13.8929(4) Å | γ = 90° |
| Volume | 1474.44(7) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.317 $g/cm^3$ | |
| Absorption coefficient | 0.087 $mm^{-1}$ | |
| F(000) | 616 | |

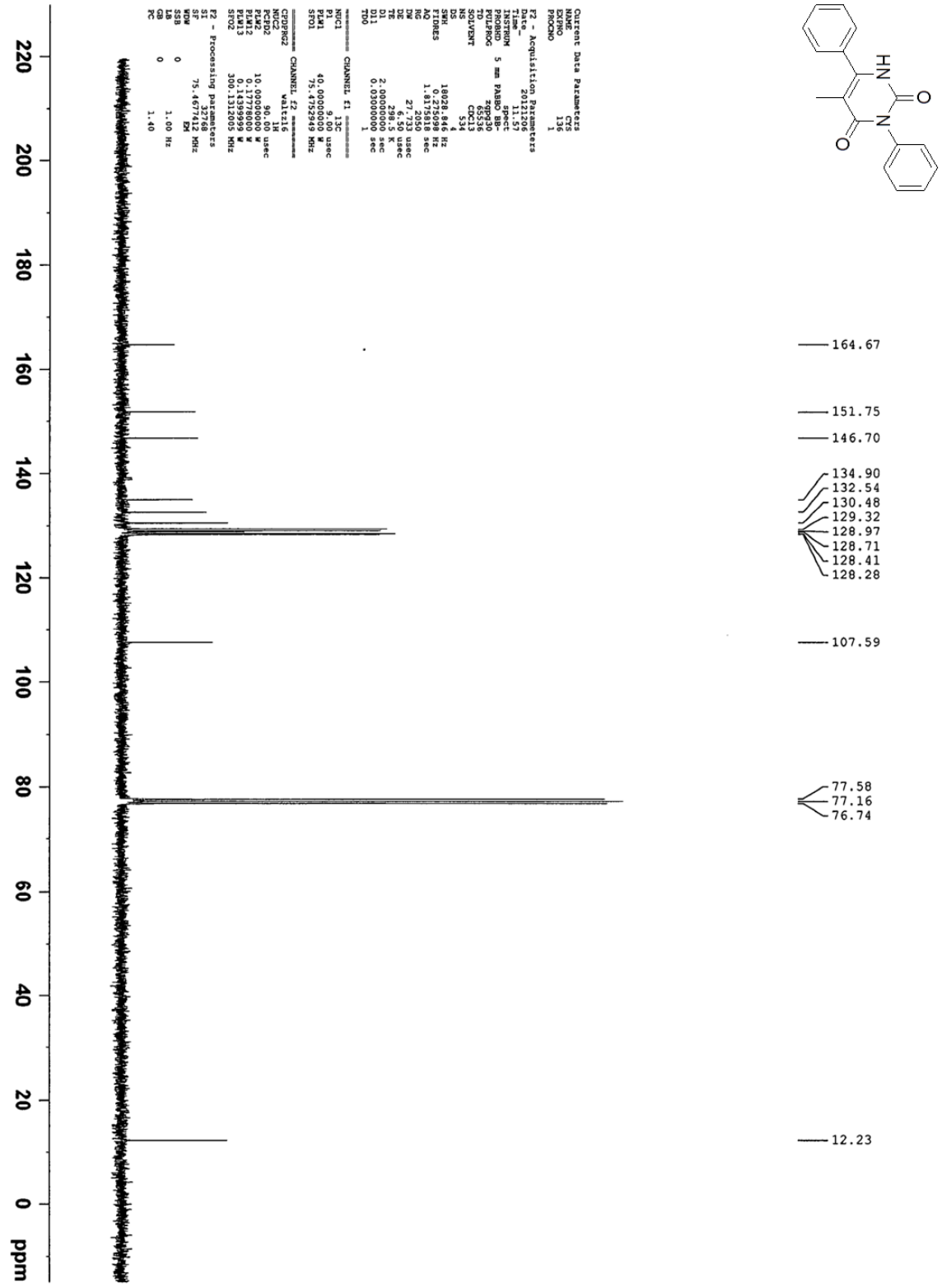
Table S2. Data collection and structure refinement for **4c.**

| | |
|---|---|
| Theta range for data collection | 1.87 to 28.27° |
| Index ranges | -14<=h<=14, -12<=k<=12, -18<=l<=18 |
| Reflections collected | 25573 |
| Independent reflections | 3644 [R(int) = 0.0191] |
| Coverage of independent reflections | 99.8% |
| Absorption correction | multi-scan |
| Max. and min. transmission | 0.9913 and 0.9627 |
| Structure solution technique | direct methods |
| Structure solution program | SHELXS-97 (Sheldrick, 2008) |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Refinement program | SHELXL-97 (Sheldrick, 2008) |
| Function minimized | $\Sigma\, w(F_o^2 - F_c^2)^2$ |
| Data / restraints / parameters | 3644 / 0 / 201 |
| Goodness-of-fit on $F^2$ | 1.061 |
| $\Delta/\sigma_{max}$ | 0.001 |
| Final R indices | 3365 data; I>2σ(I) R1 = 0.0395, wR2 = 0.1071 |
| | all data R1 = 0.0422, wR2 = 0.1098 |
| Weighting scheme | $w=1/[\sigma^2(F_o^2)+(0.0577P)^2+0.5002P]$ where $P=(F_o^2+2F_c^2)/3$ |
| Largest diff. peak and hole | 0.354 and -0.213 eÅ $^{-3}$ |
| R.M.S. deviation from mean | 0.058 eÅ $^{-3}$ |

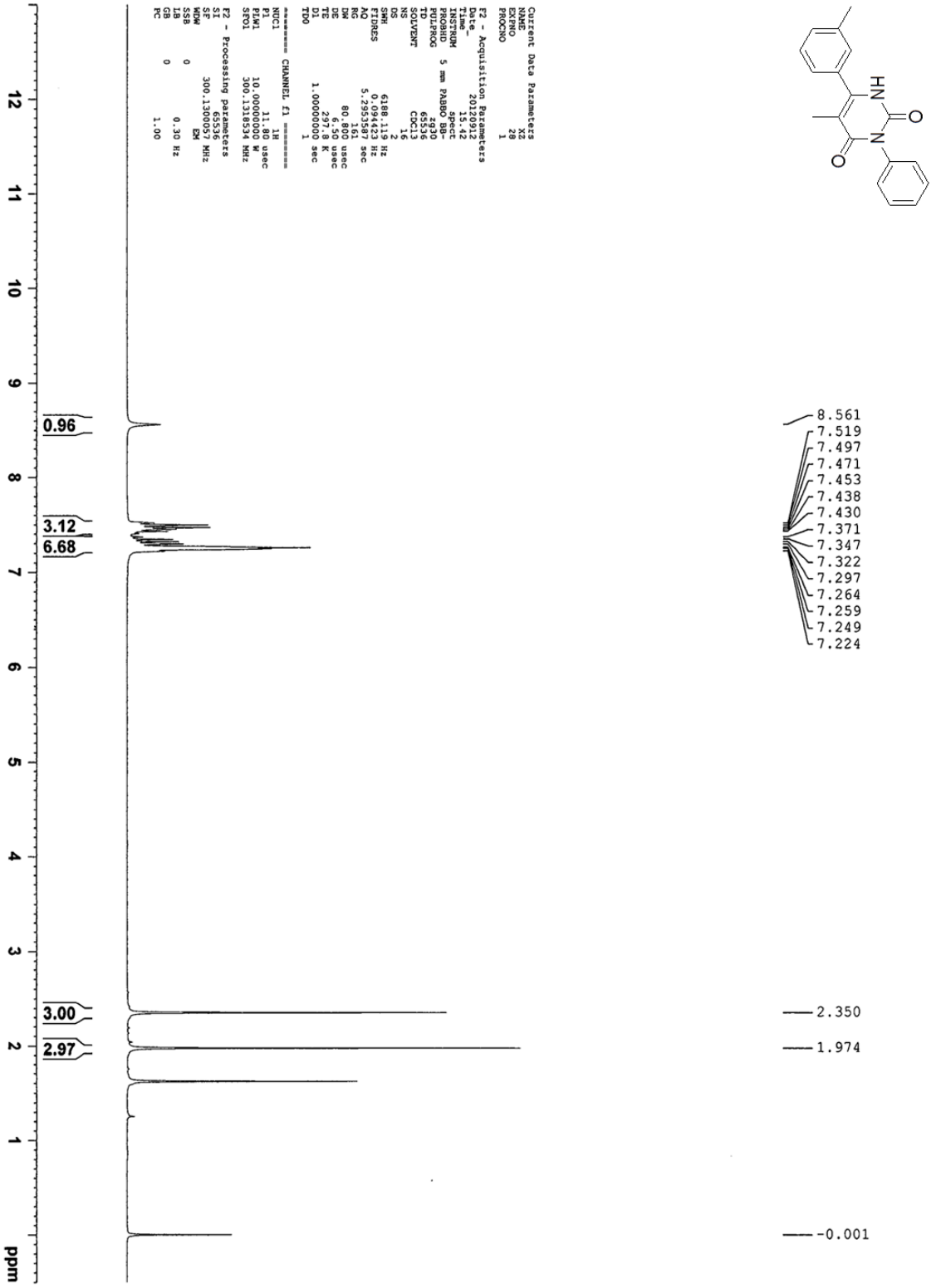
**$^{1}$H Spectrum of 4a in $CDCl_3$**



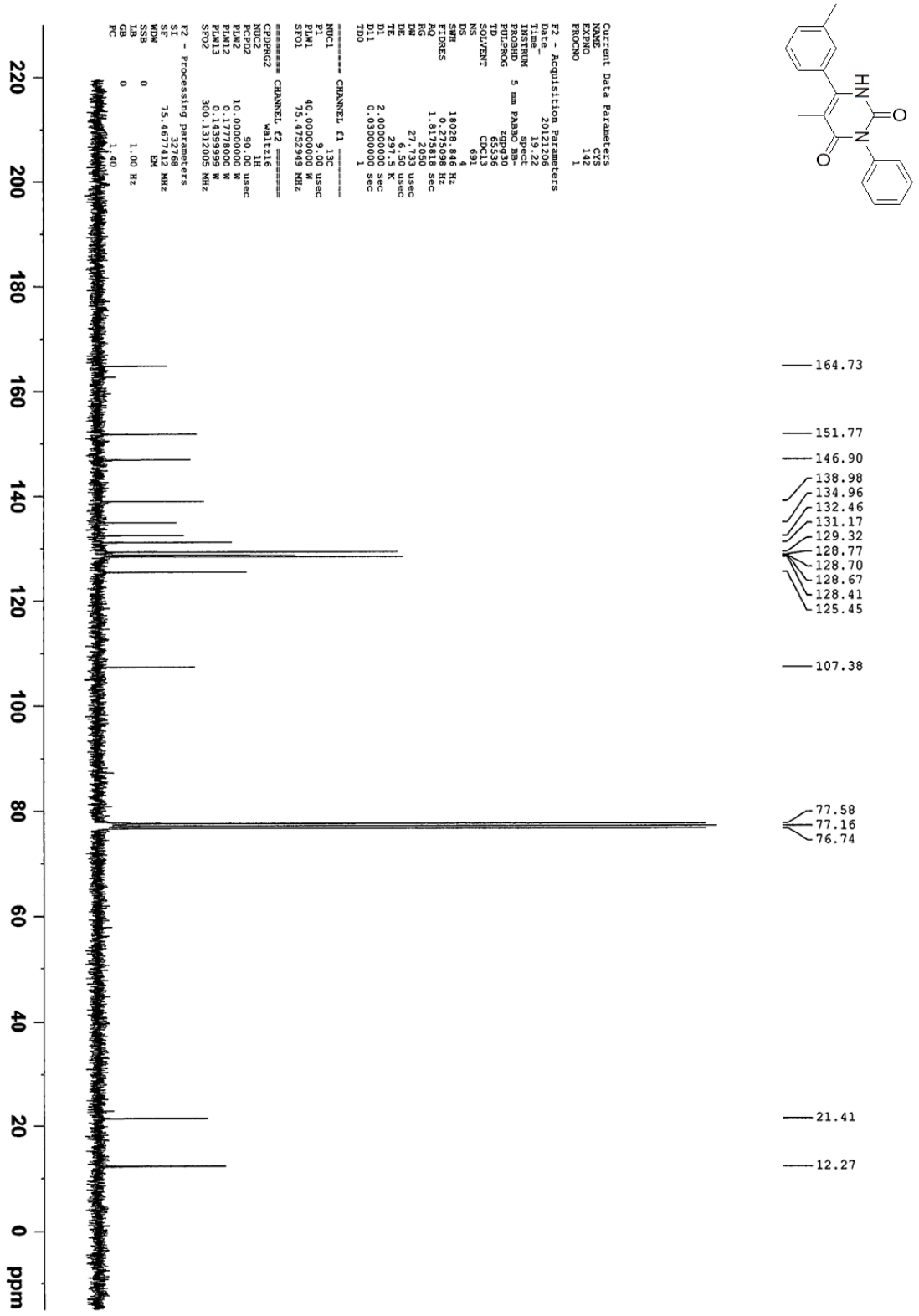
**$^{13}C$ Spectrum of 4a in $CDCl_3$**



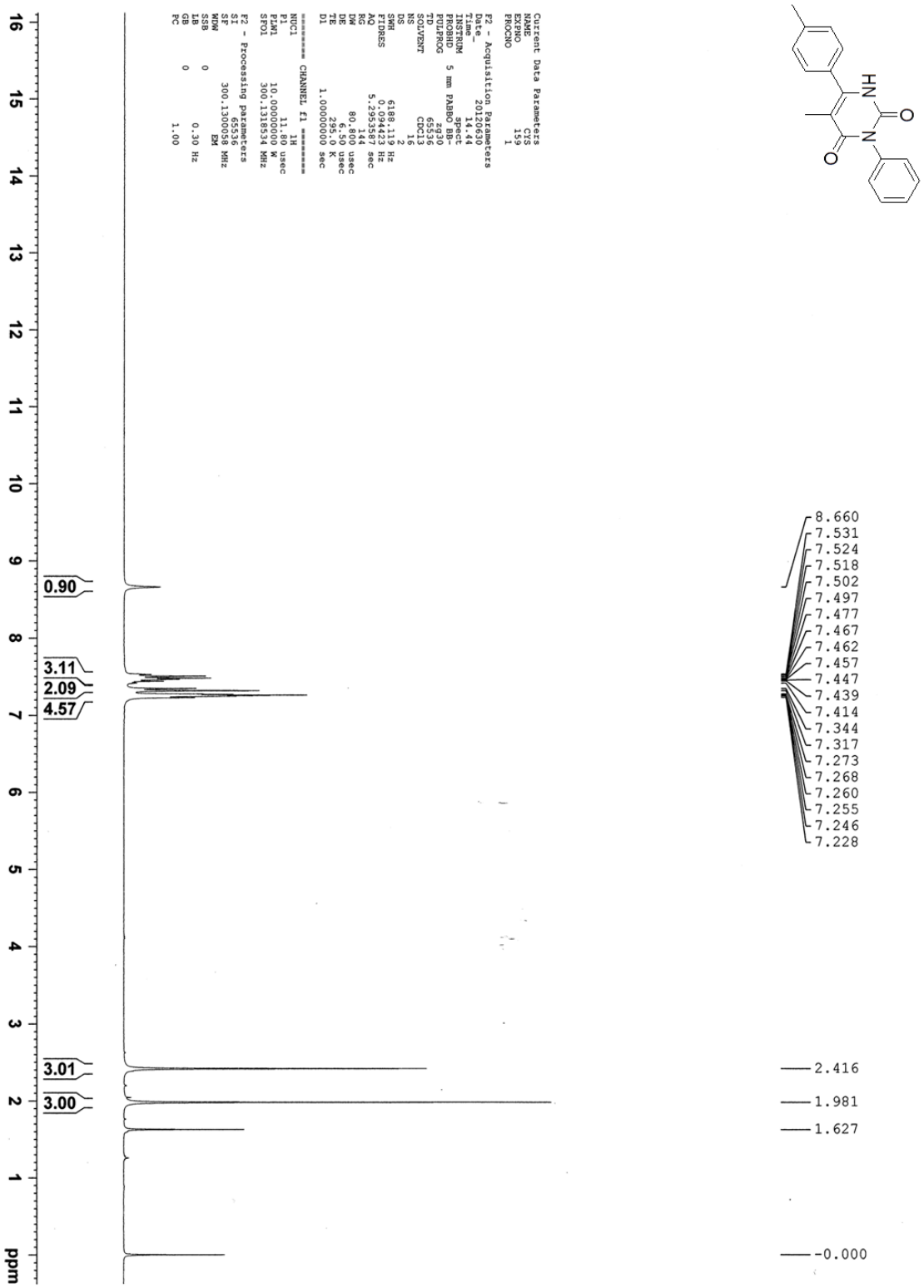
**$^{1}$H Spectrum of 4b in $CDCl_3$**



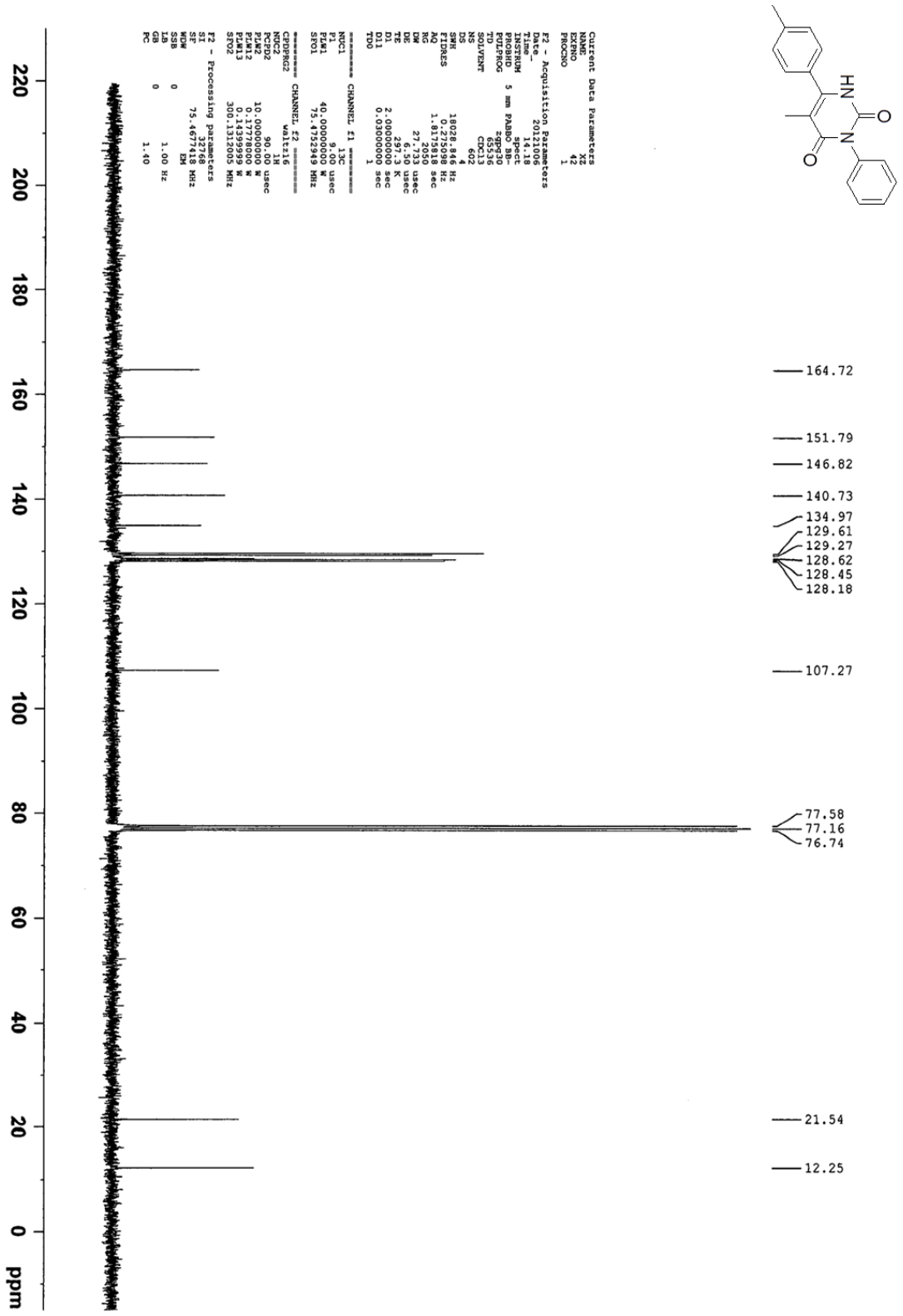
**$^{13}C$ Spectrum of 4b in $CDCl_3$**



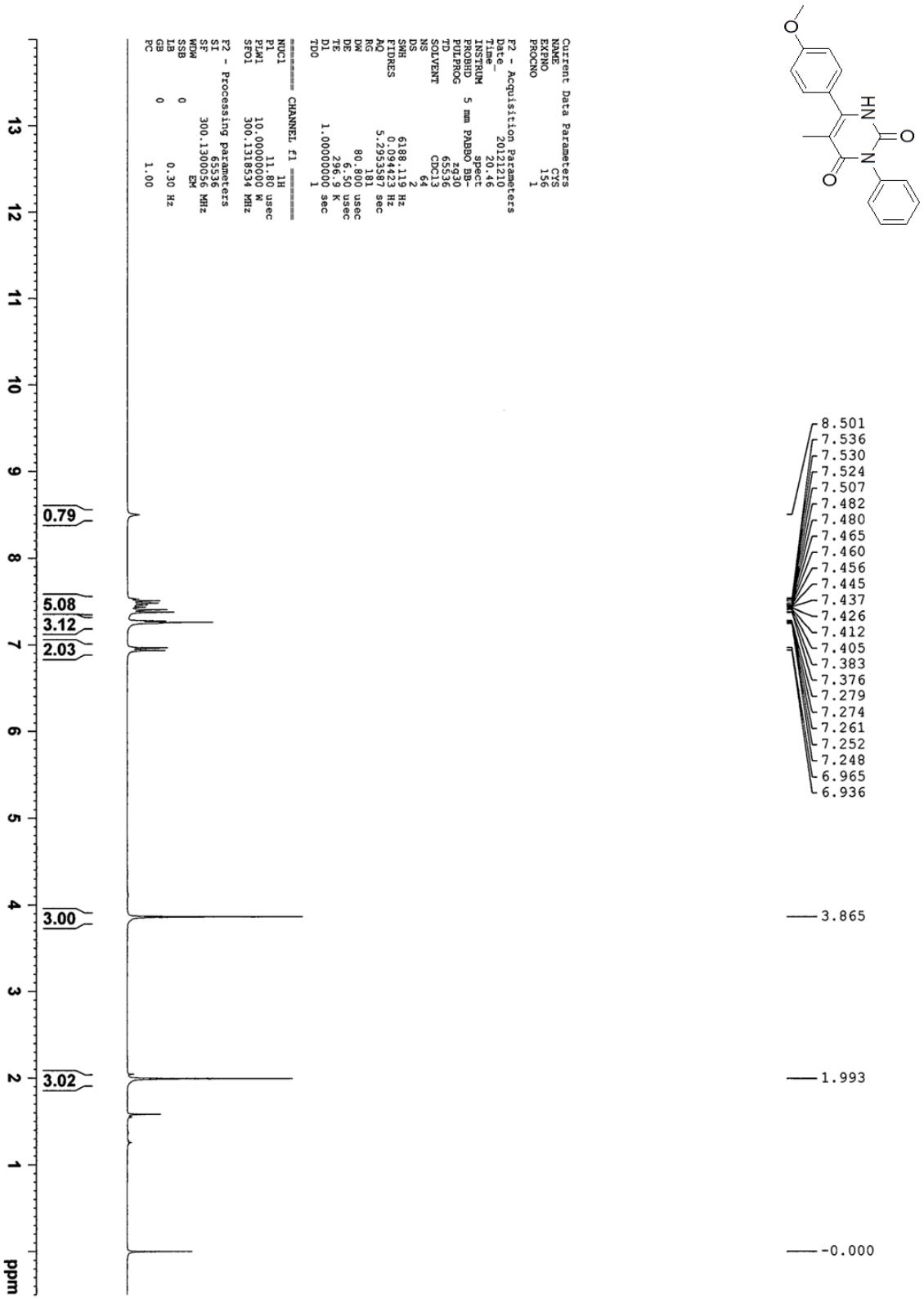
**$^{1}$H Spectrum of 4c in $CDCl_3$**



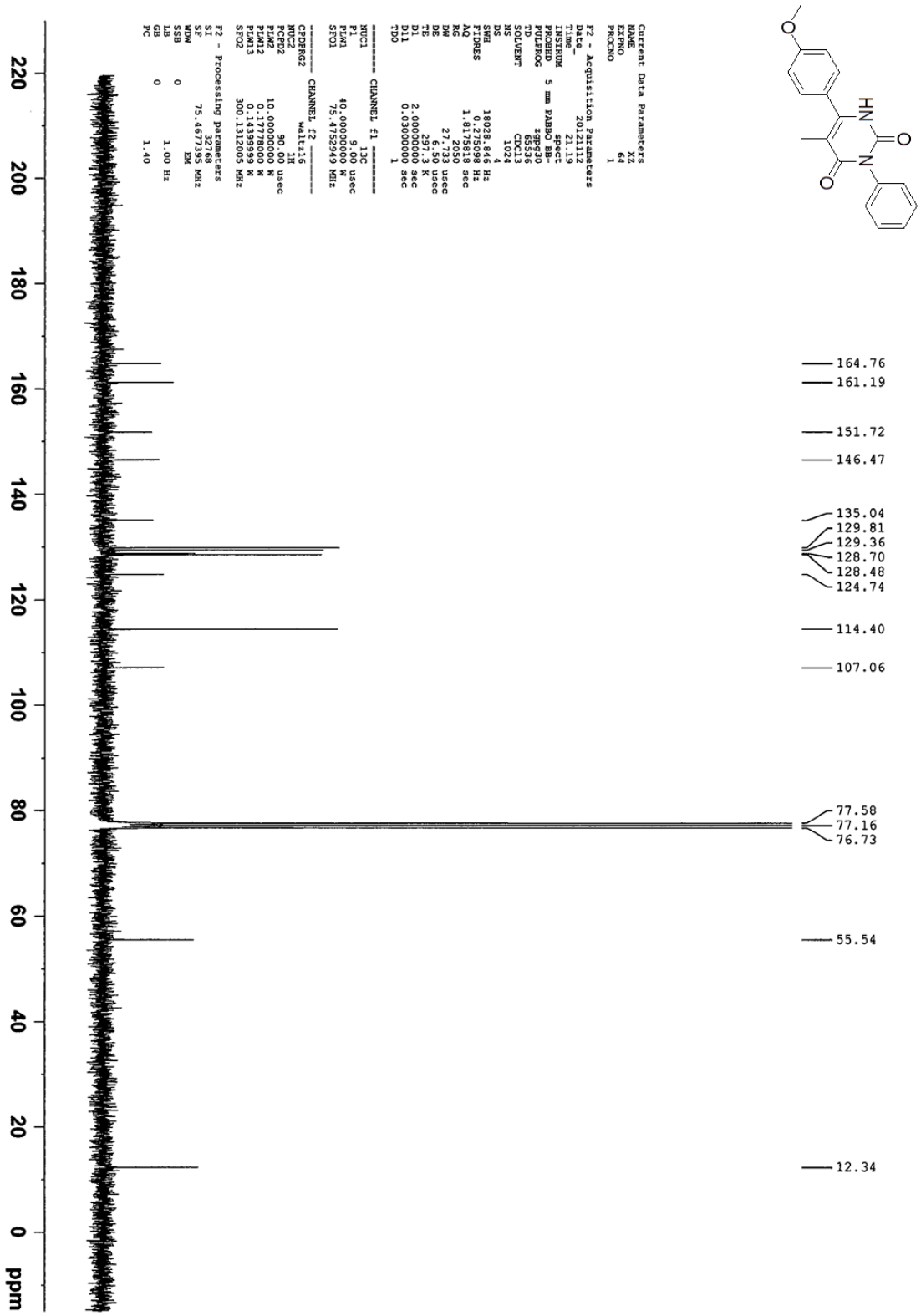
**$^{13}C$ Spectrum of 4c in $CDCl_3$**



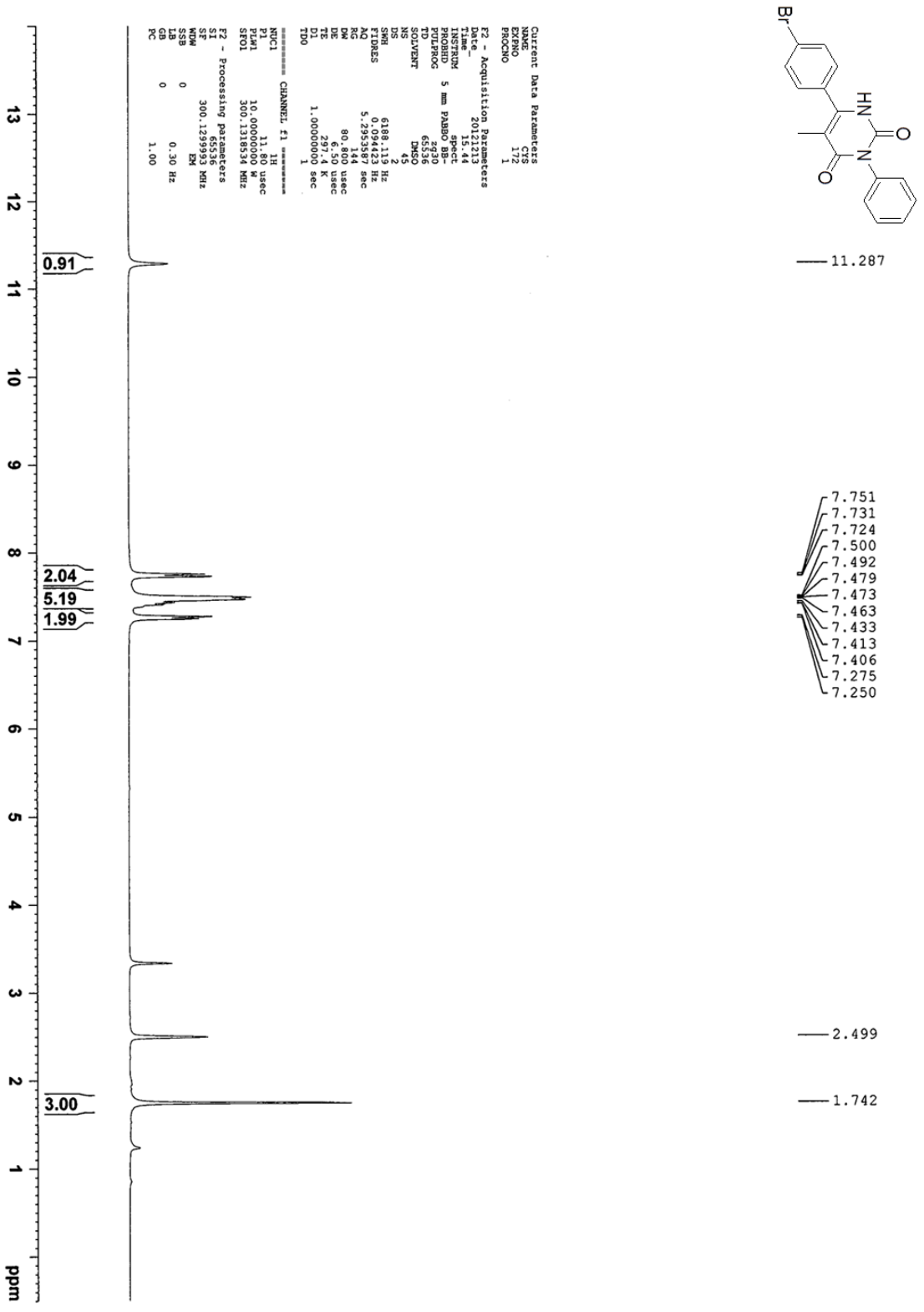
## $^{1}H$ Spectrum of 4d in $CDCl_3$



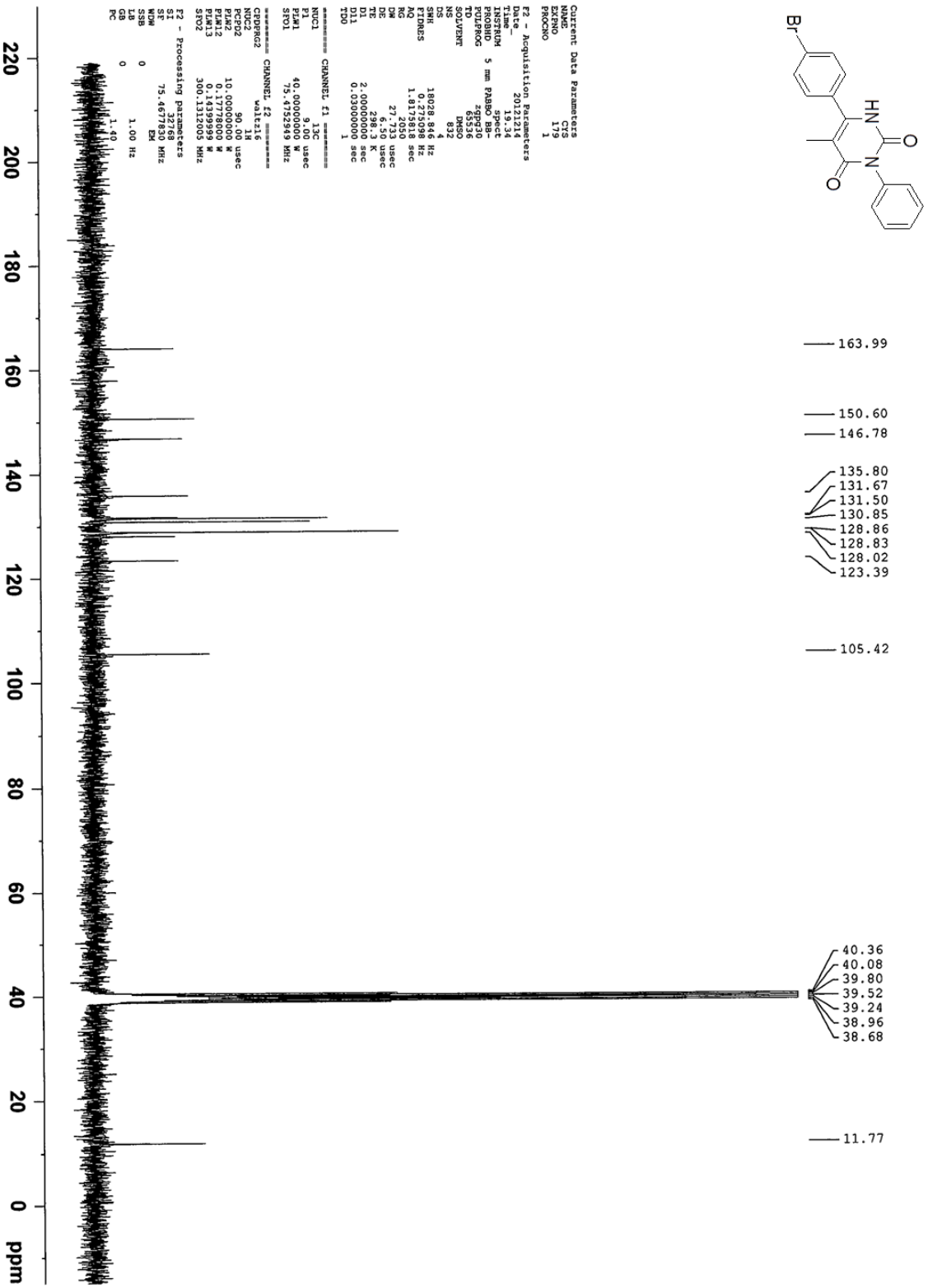
**$^{13}C$ Spectrum of 4d in $CDCl_3$**



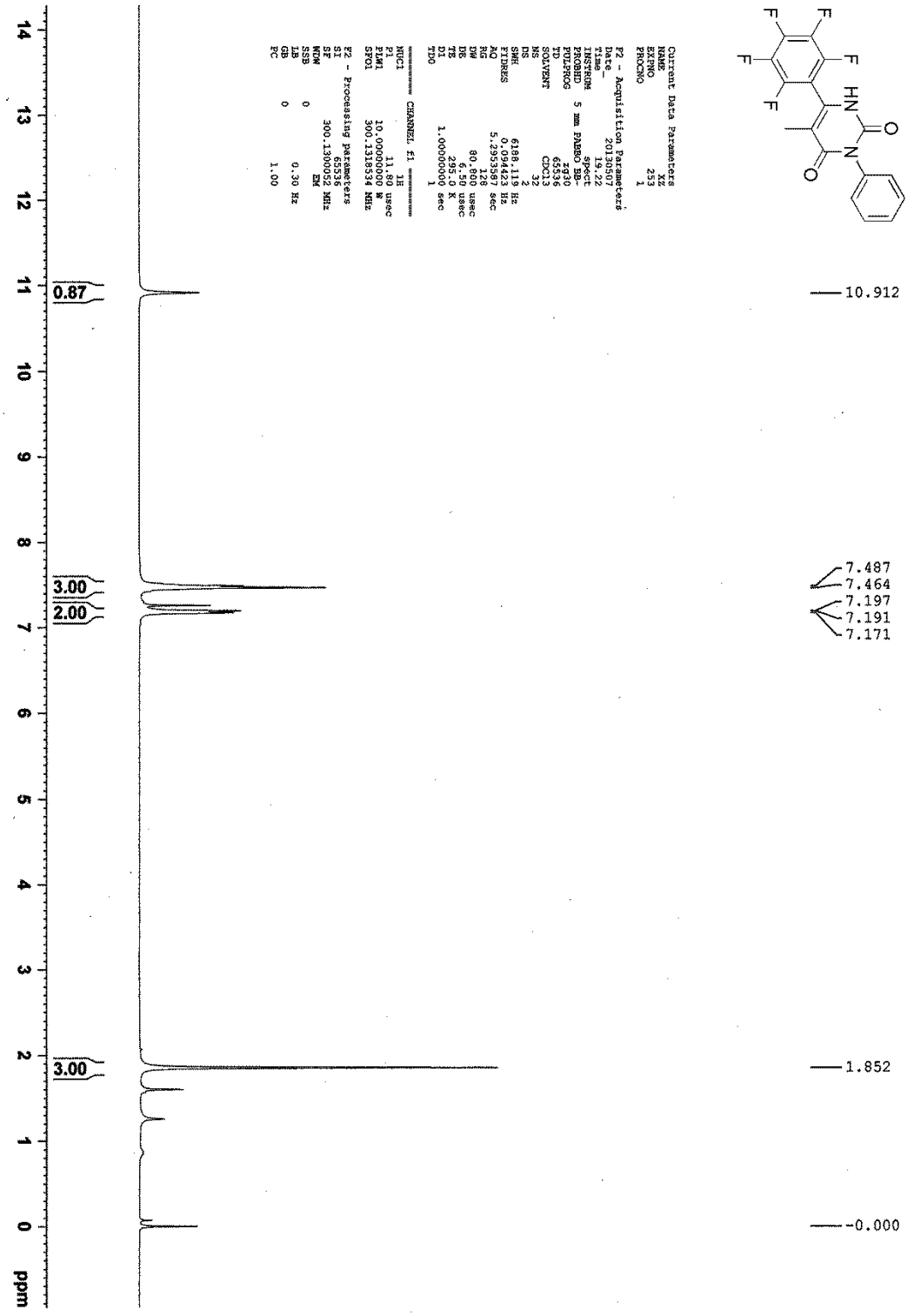
**$^{1}$H Spectrum of 4e in DMSO-$d_6$**



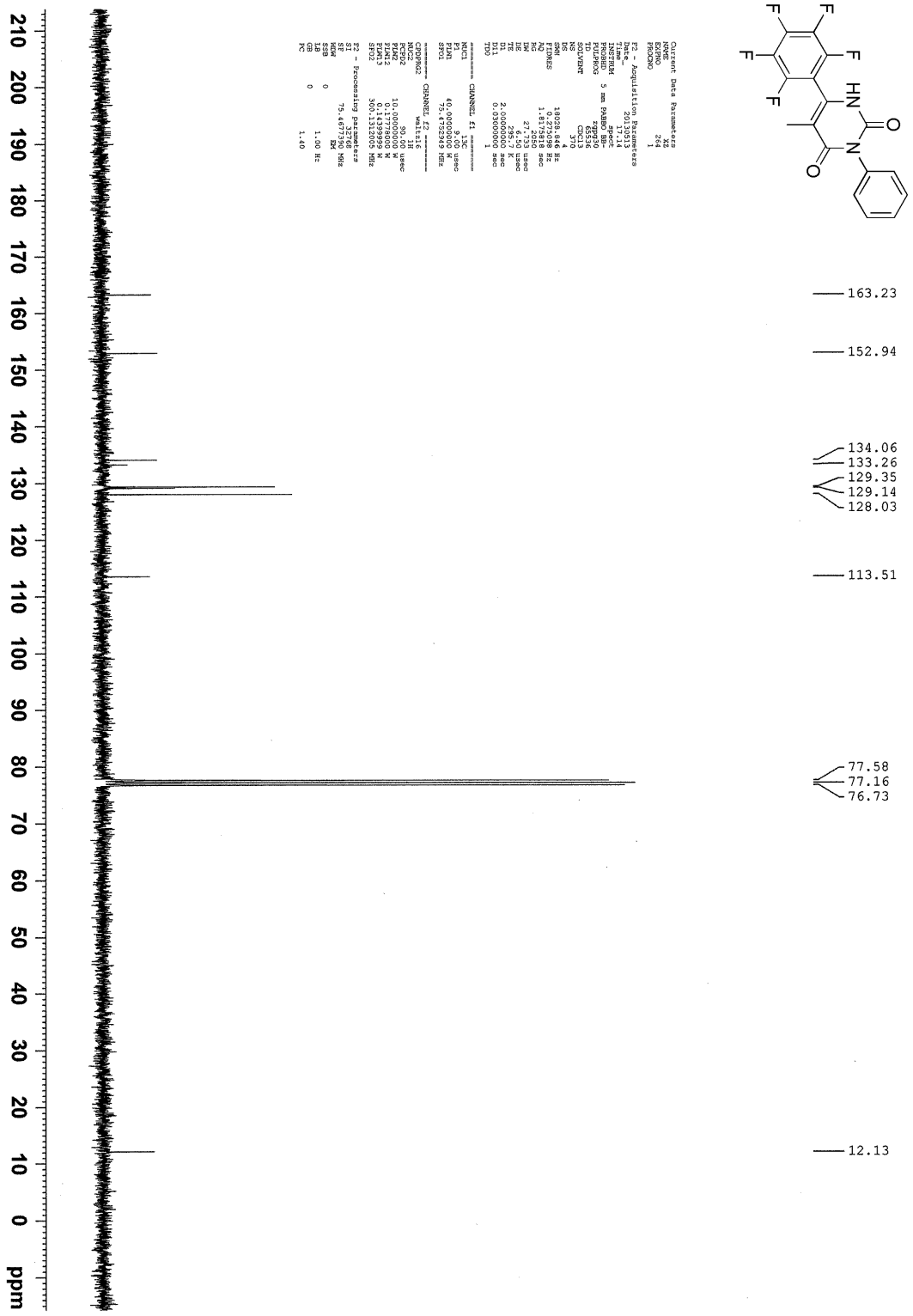
**$^{13}$C Spectrum of 4e in DMSO-$d_6$**



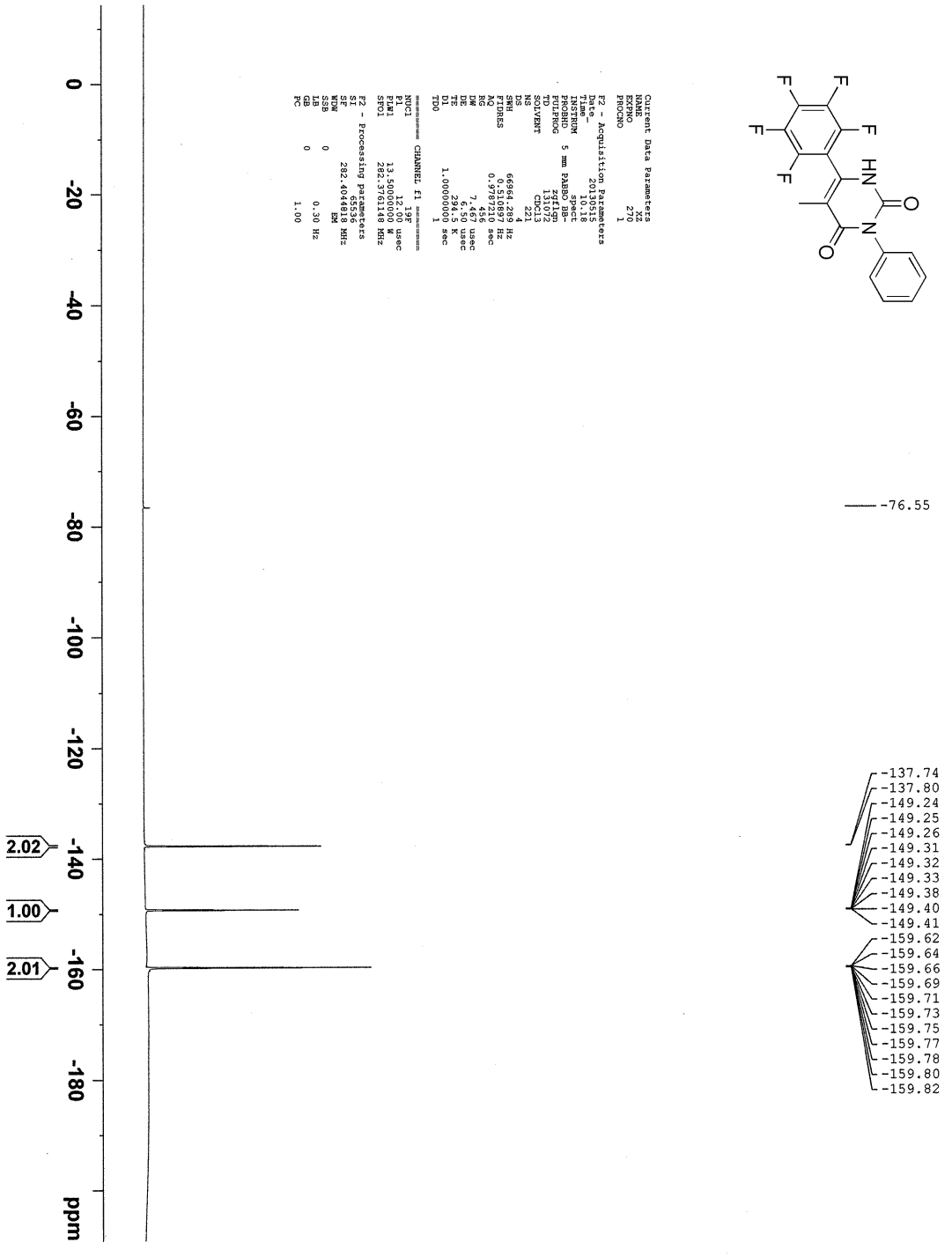
**$^1$H Spectrum of 4f in $CDCl_3$**



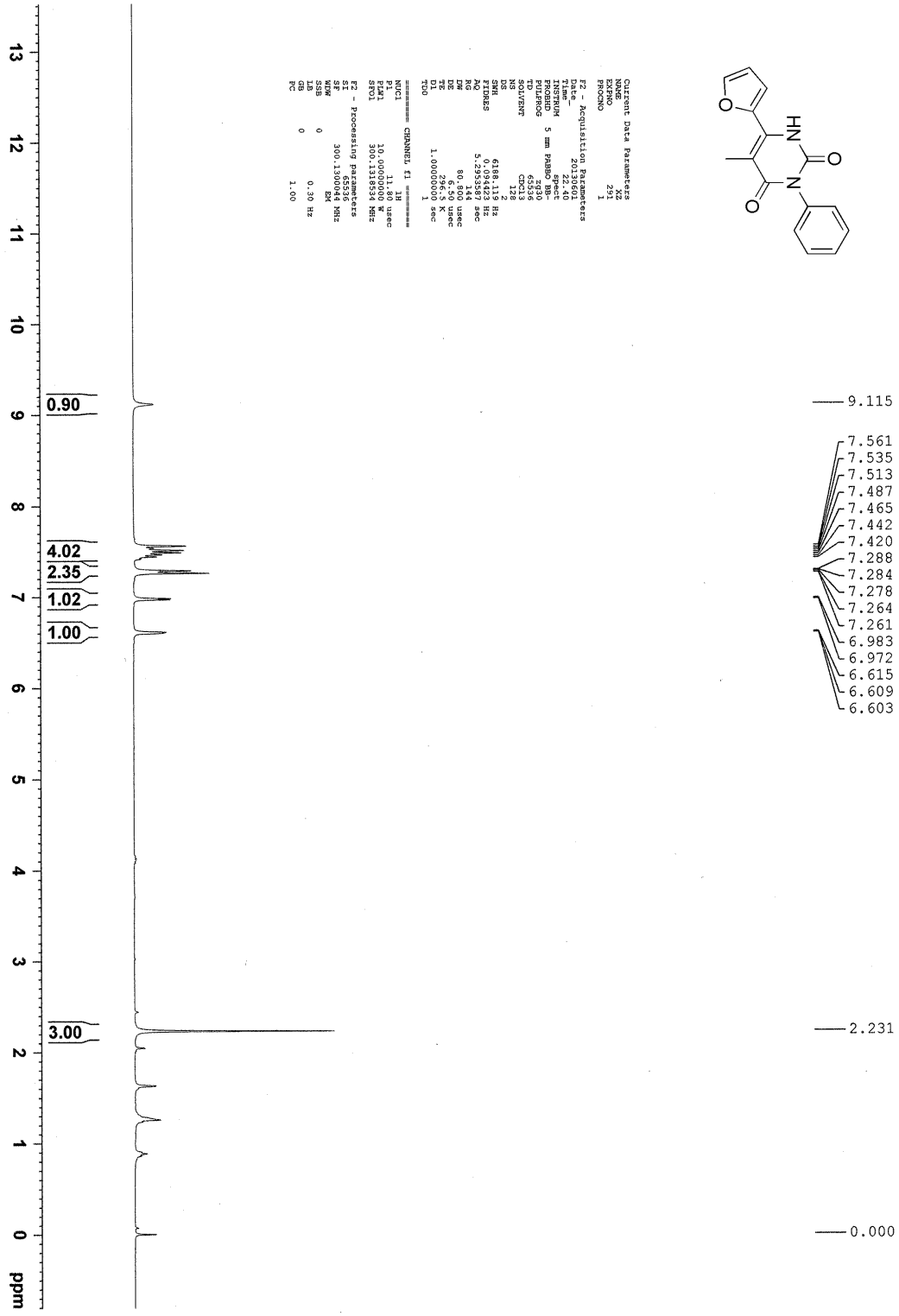
**$^{13}C$ Spectrum of 4f in $CDCl_3$**



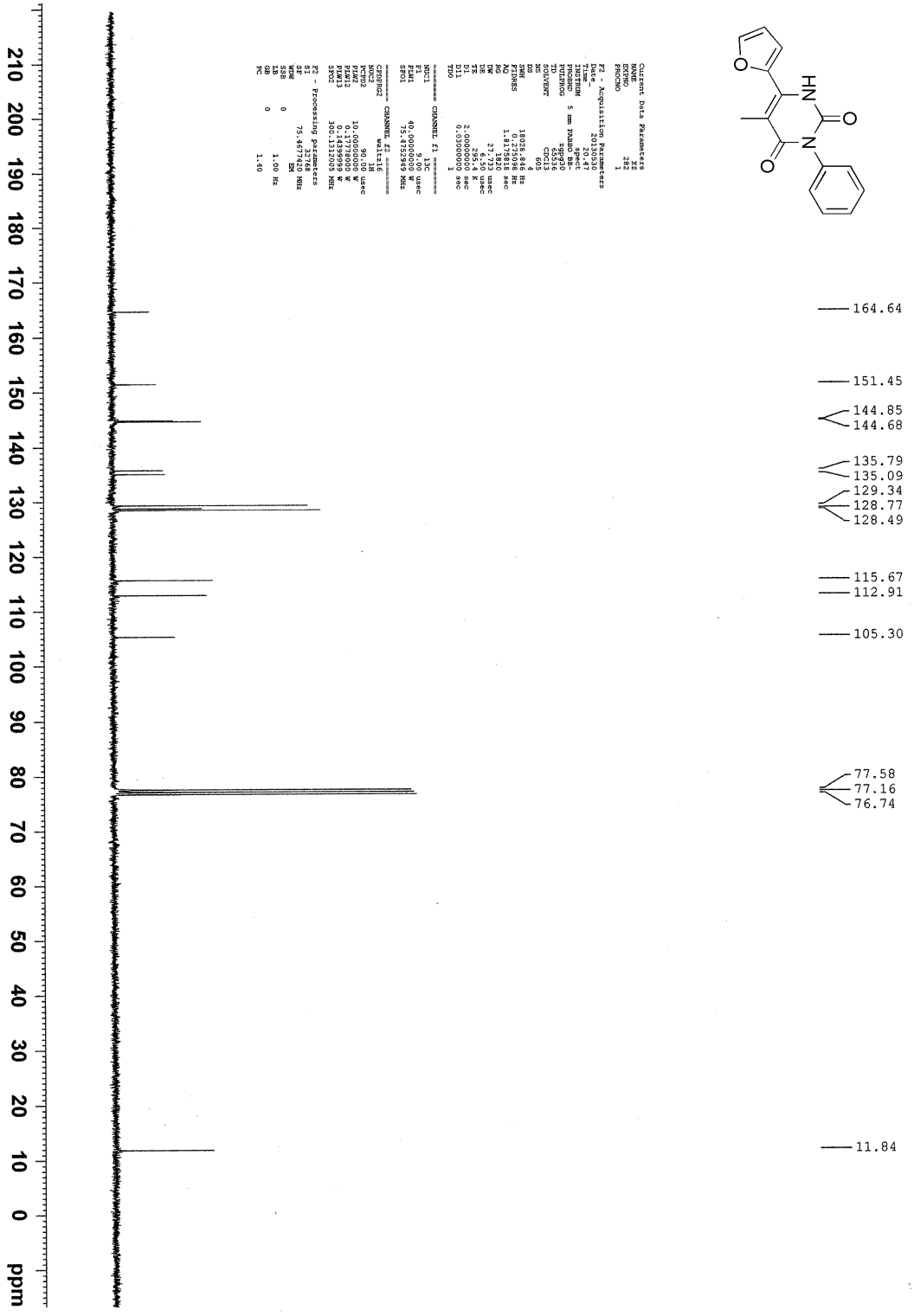
## $^{19}F$ Spectrum of 4f in $CDCl_3$



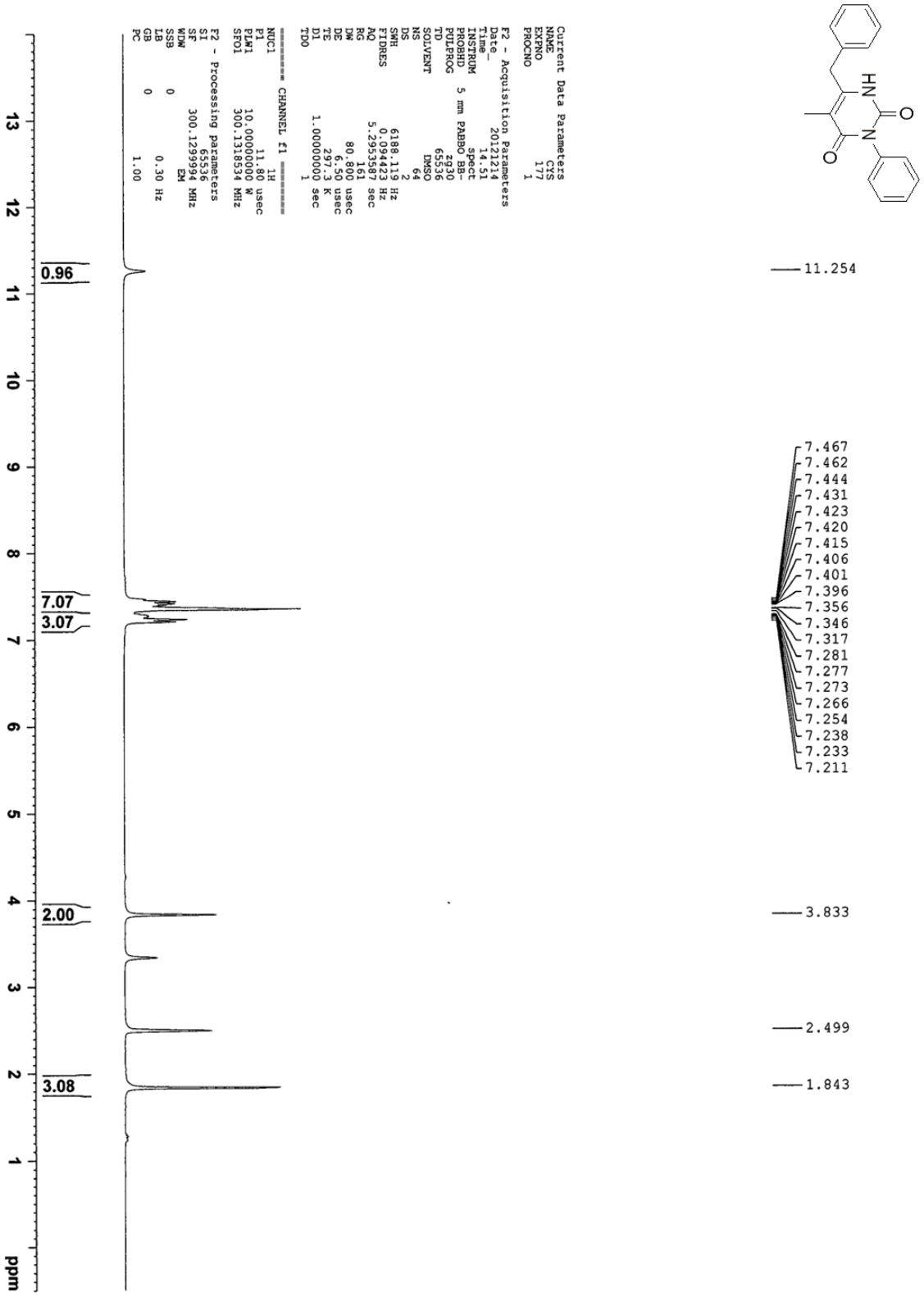
## $^{1}H$ Spectrum of 4g in $CDCl_3$



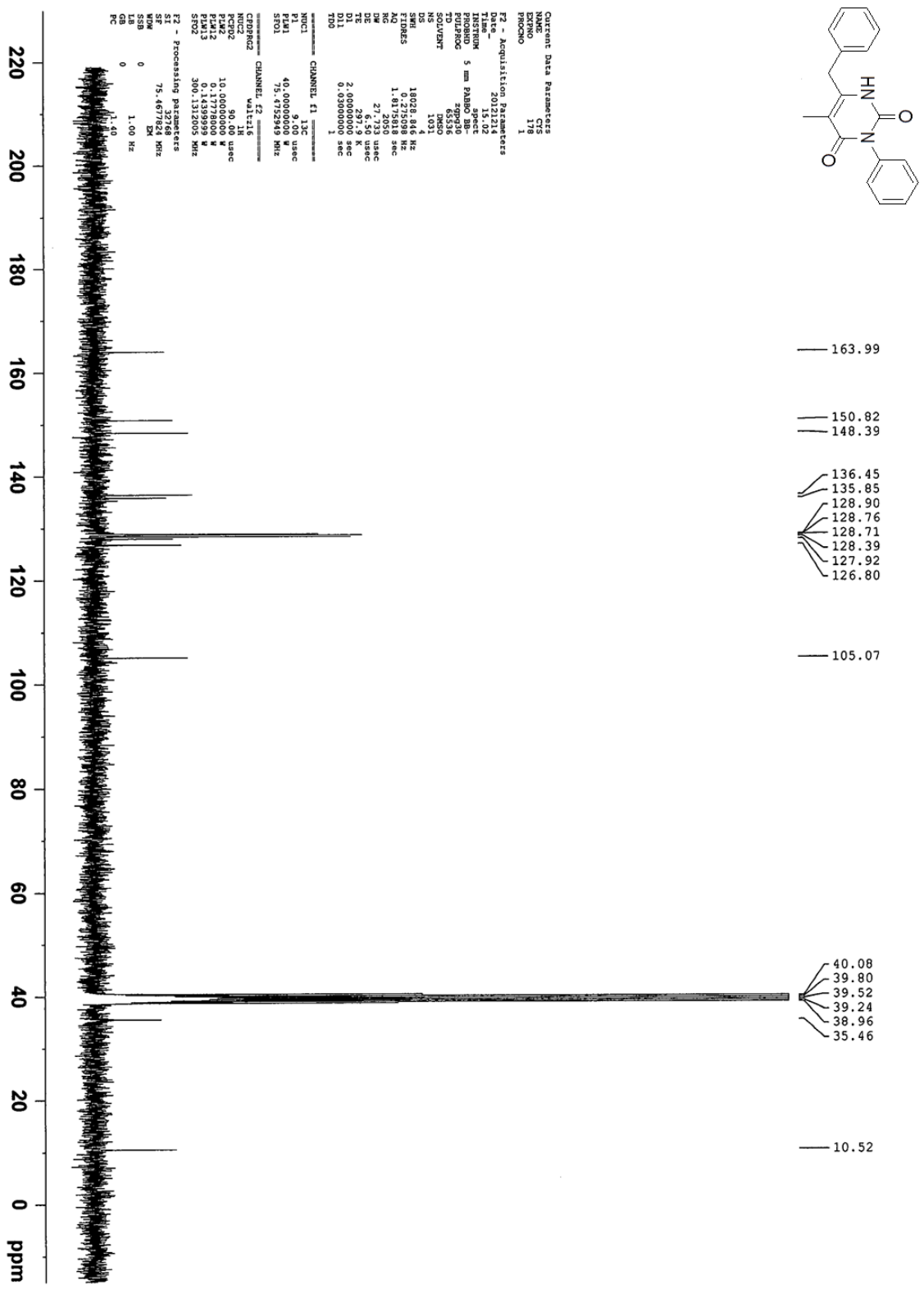
**$^{13}C$ Spectrum of 4g in $CDCl_3$**



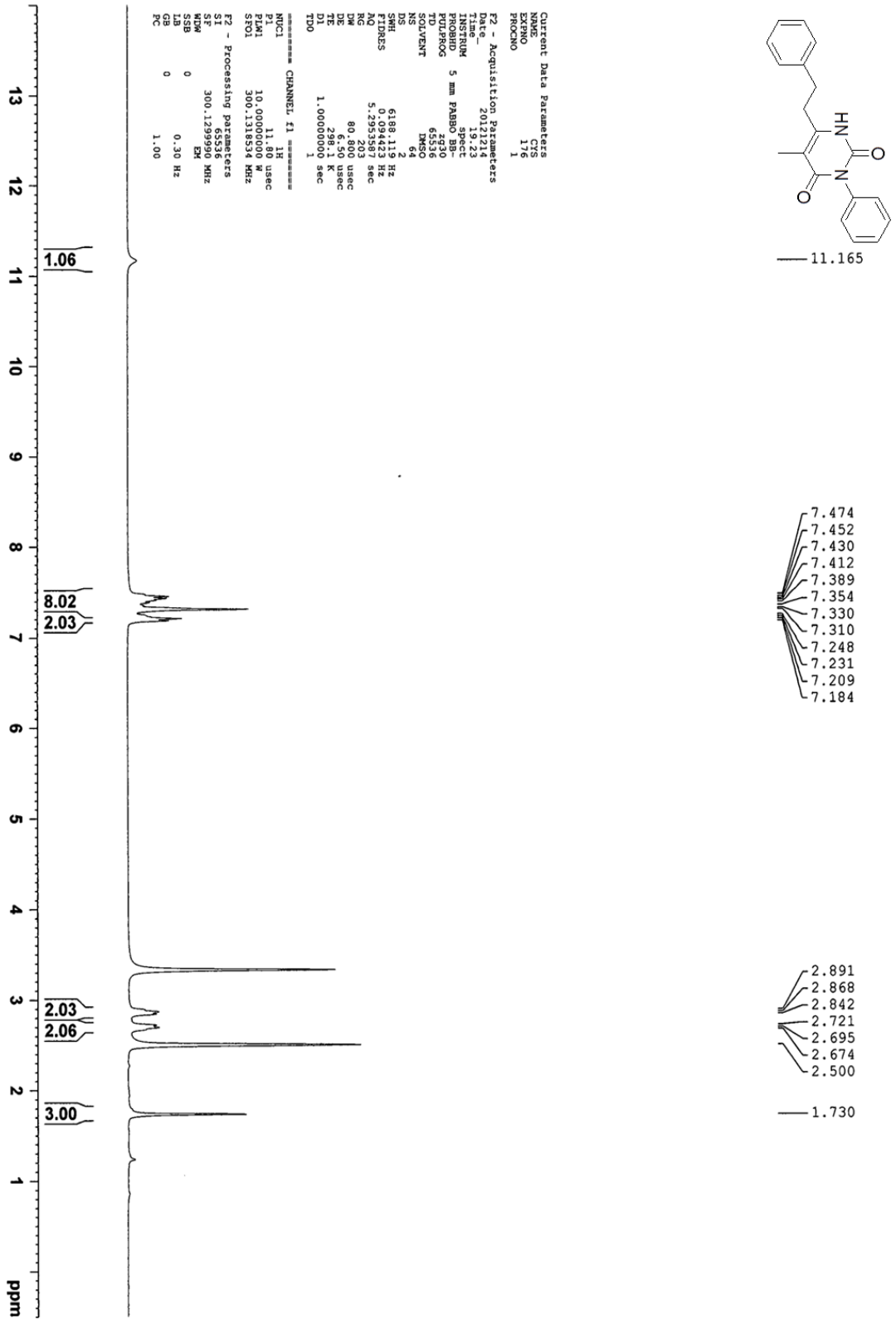
## $^{1}$H Spectrum of 4h in DMSO-$d_6$



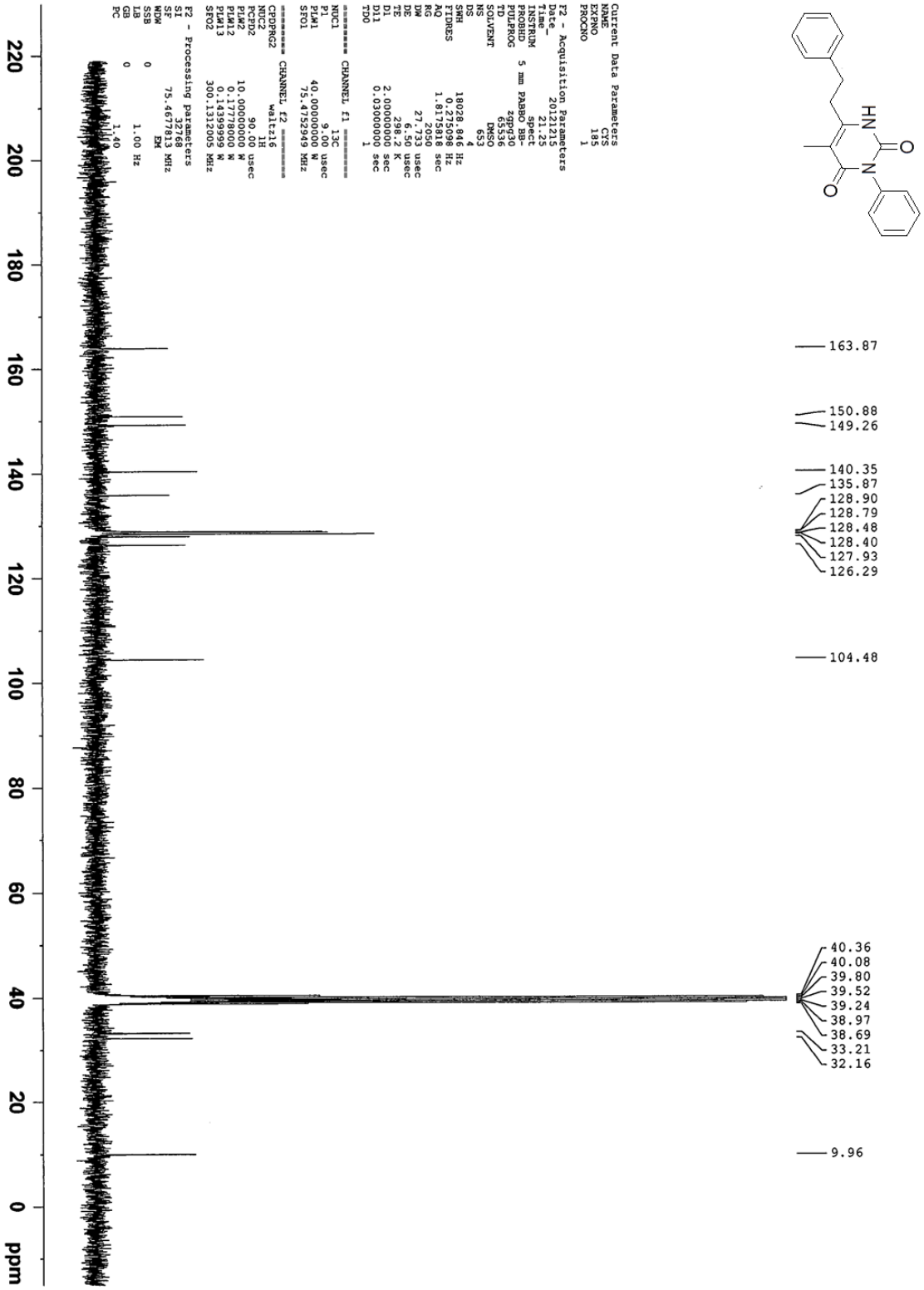
**$^{13}$C Spectrum of 4h in DMSO-$d_6$**



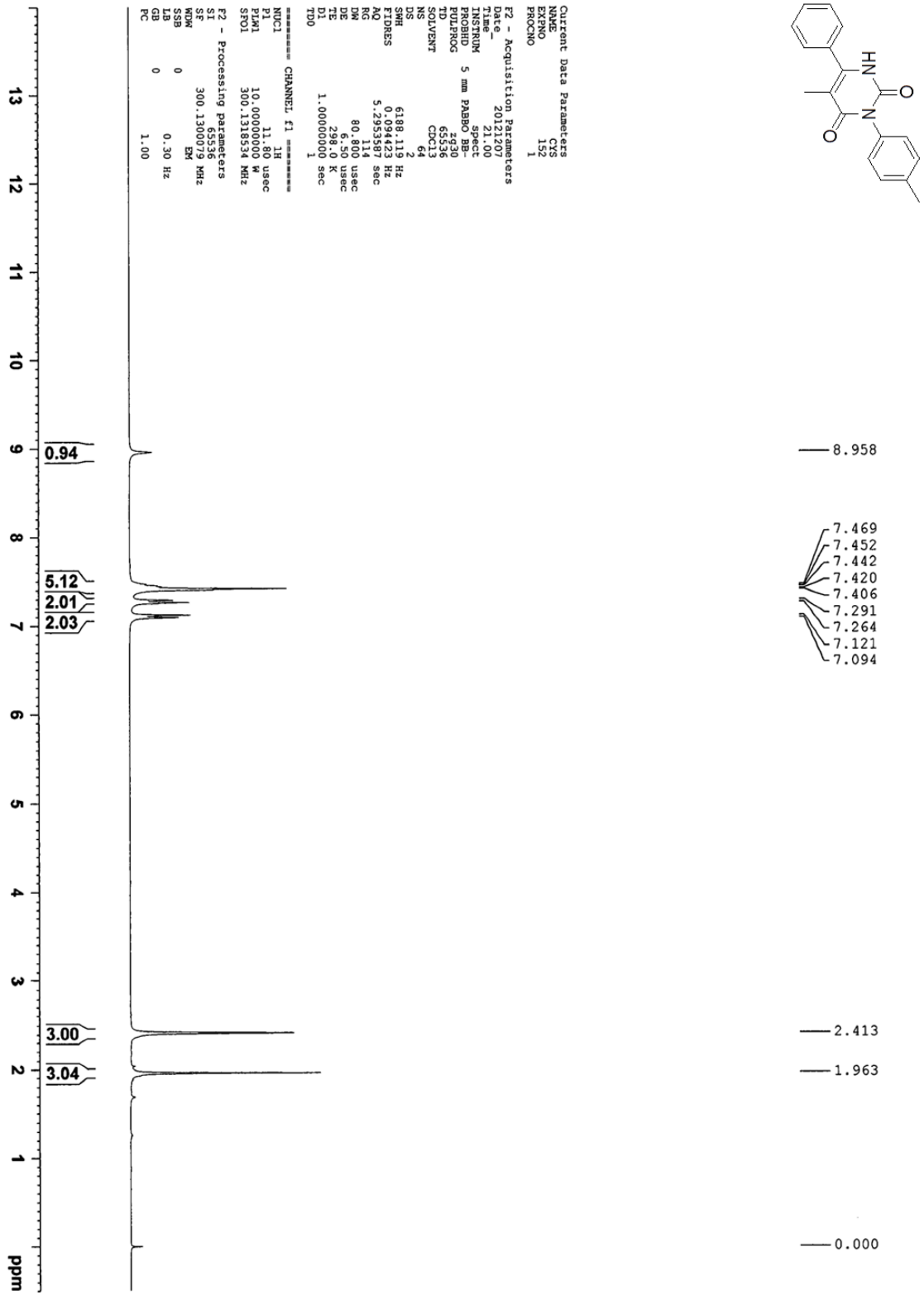
**$^1$H Spectrum of 4i in DMSO-$d_6$**



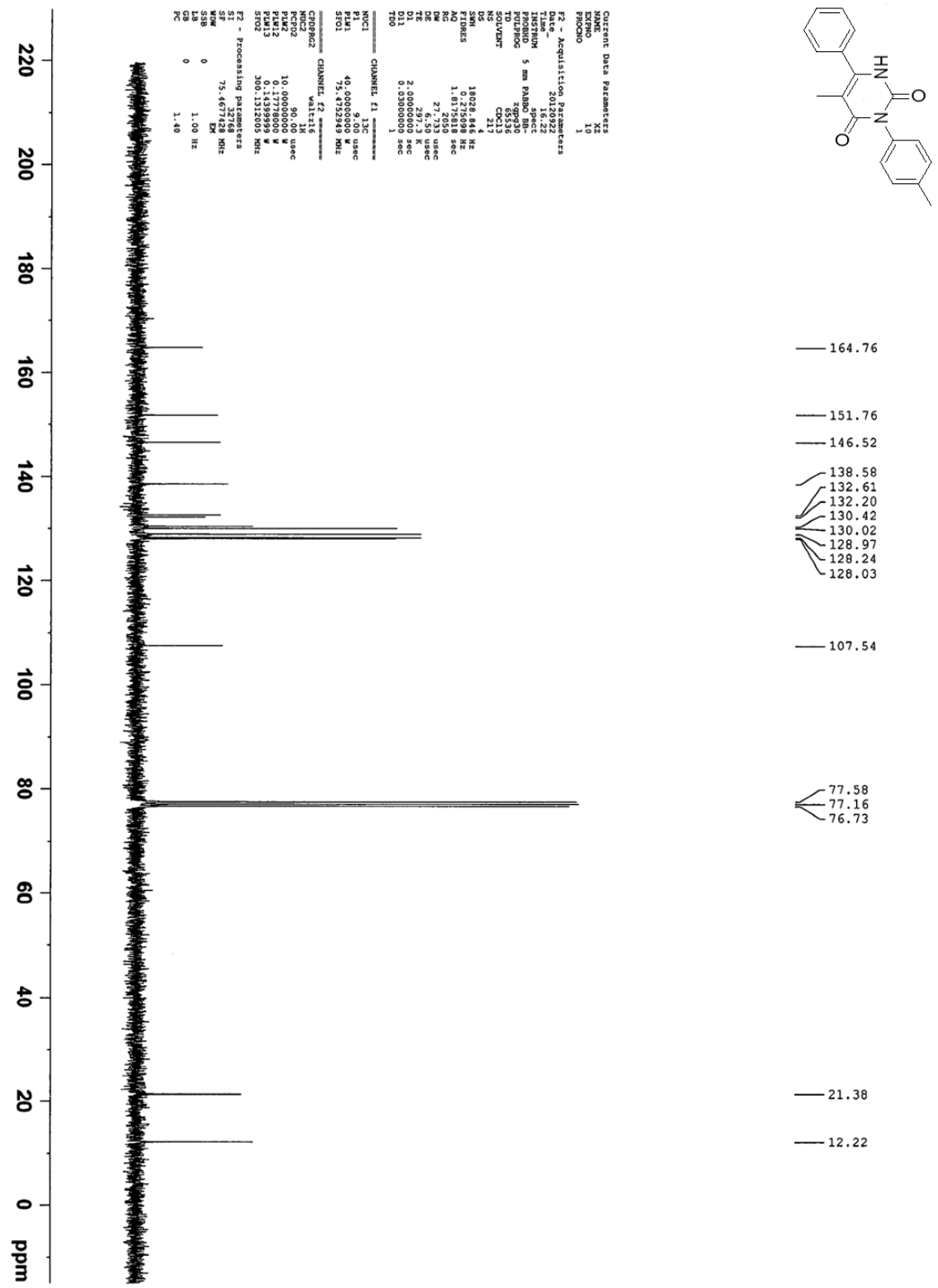
**$^{13}$C Spectrum of 4i in DMSO-$d_6$**



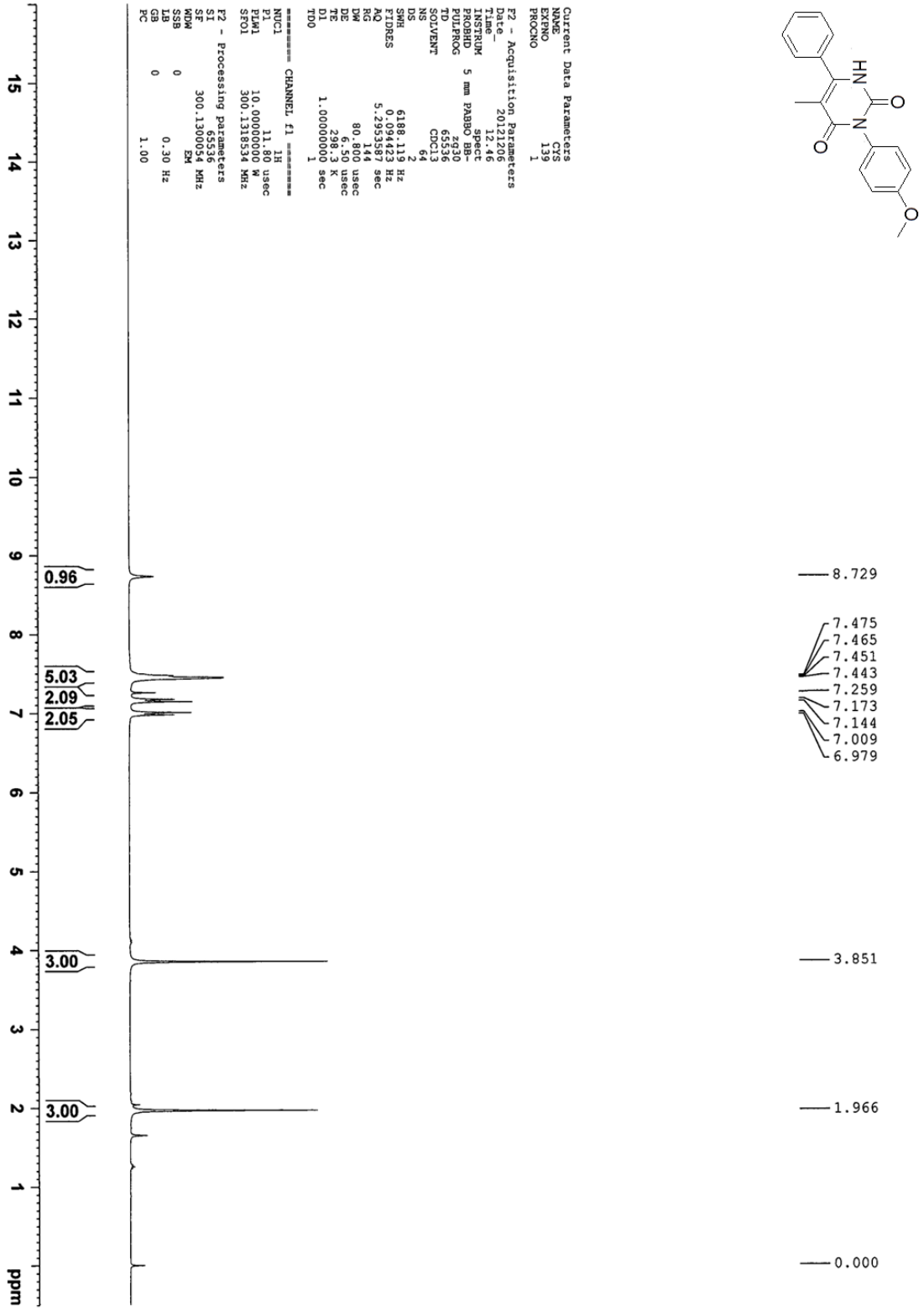
**$^{1}$H Spectrum of 4j in $CDCl_3$**



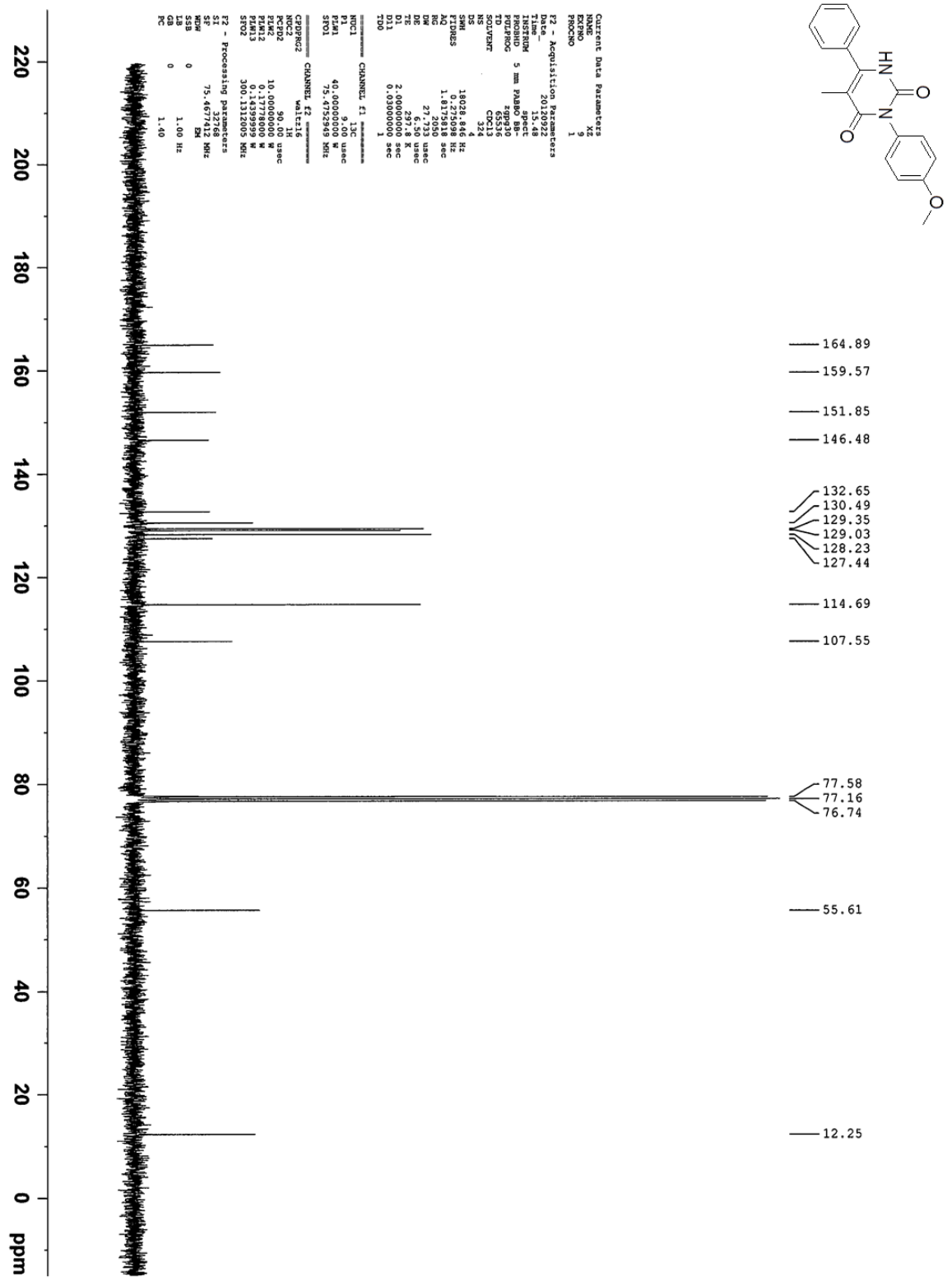
**$^{13}C$ Spectrum of 4j in $CDCl_3$**



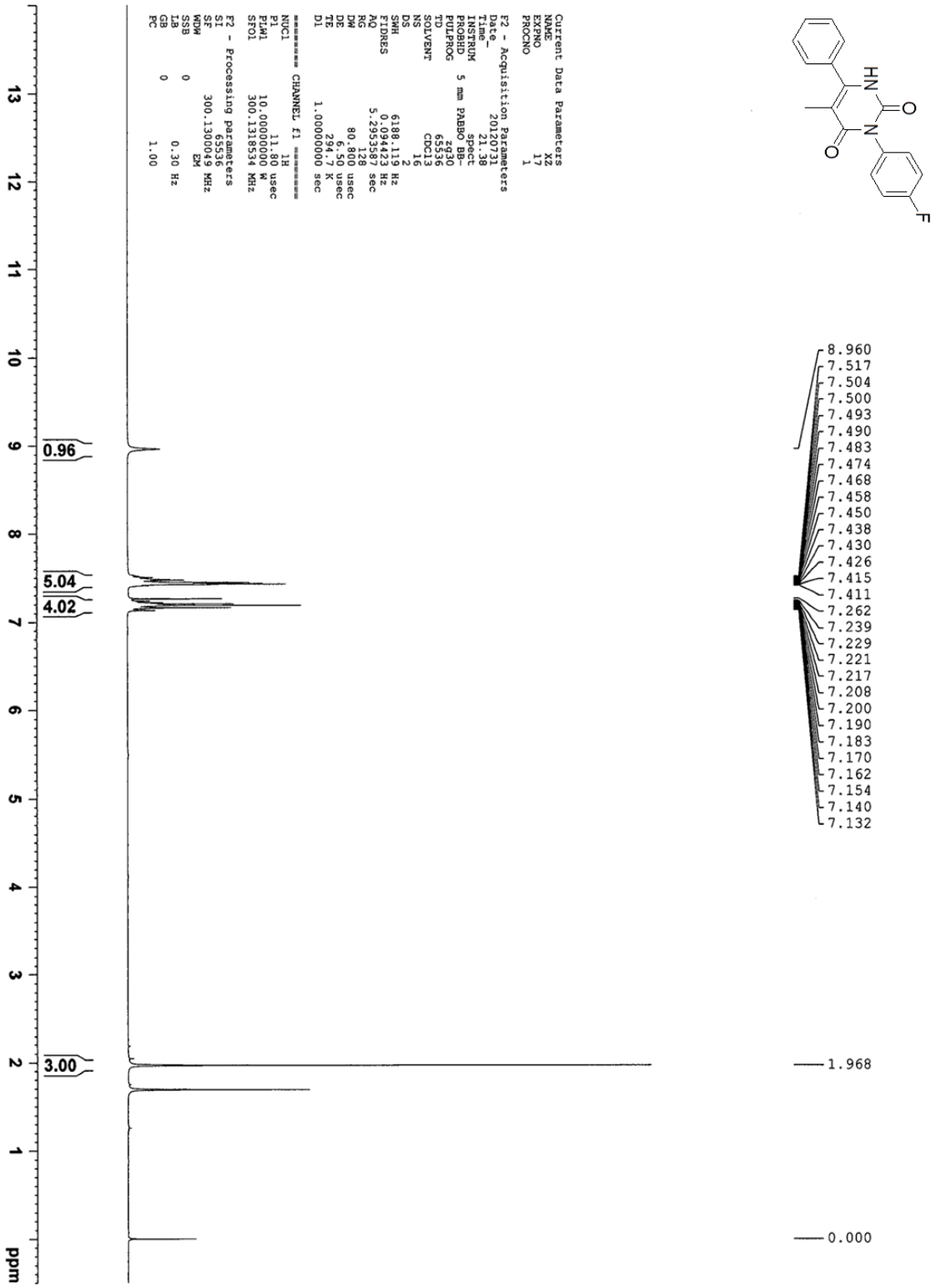
**$^{1}$H Spectrum of 4kin $CDCl_3$**



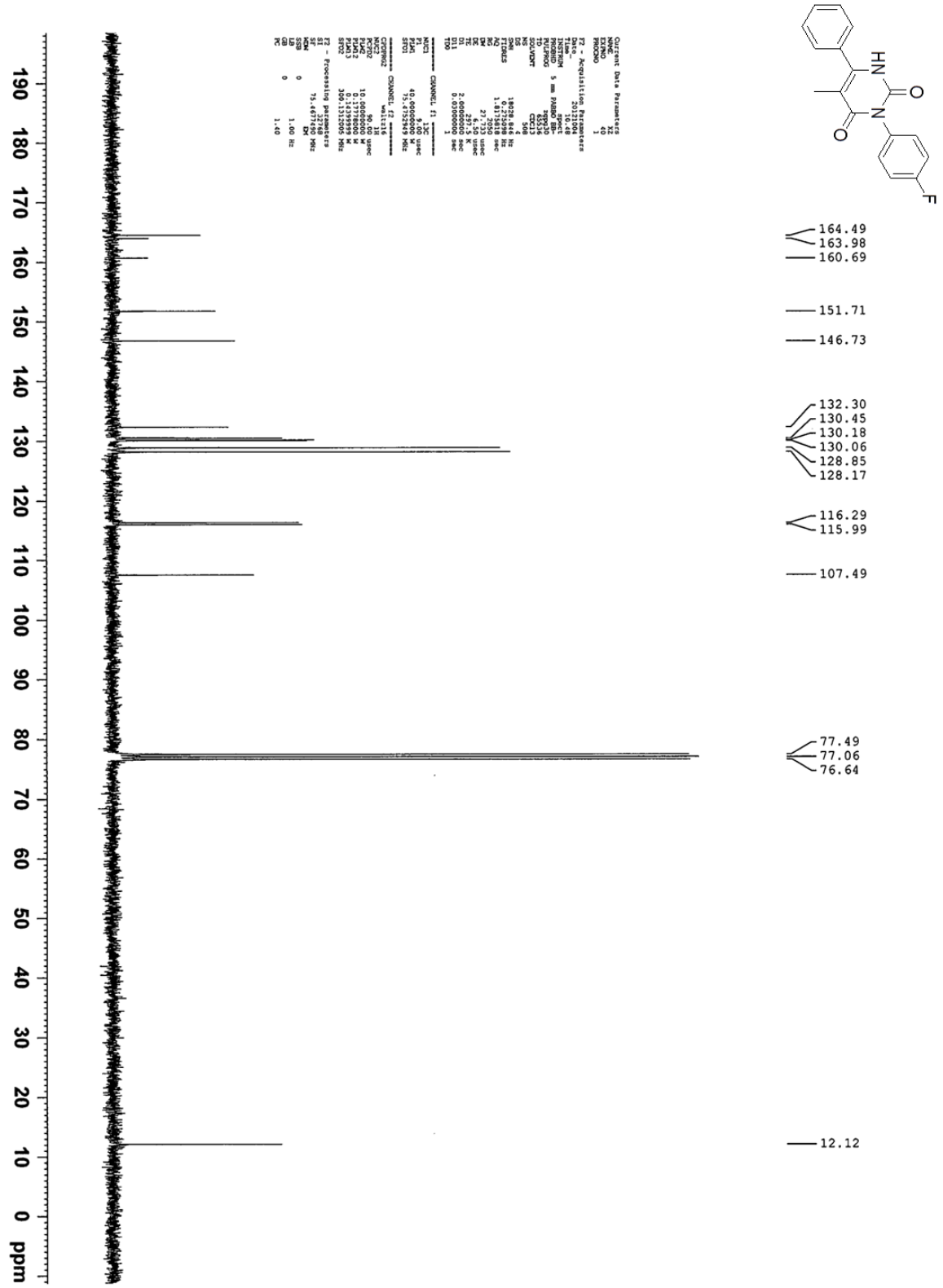
**$^{13}C$ Spectrum of 4k in $CDCl_3$**



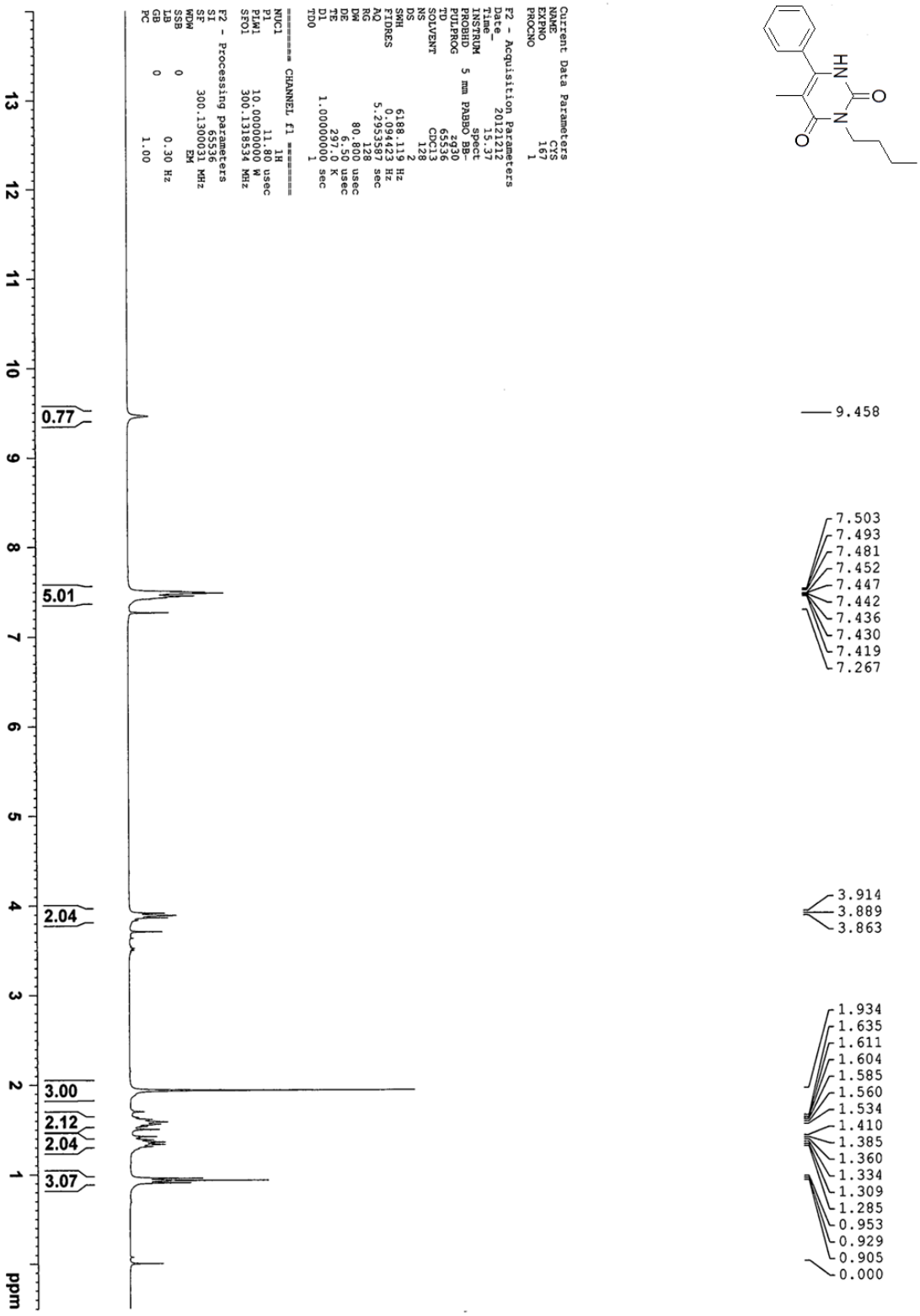
**$^{1}$H Spectrum of 4l in $CDCl_3$**



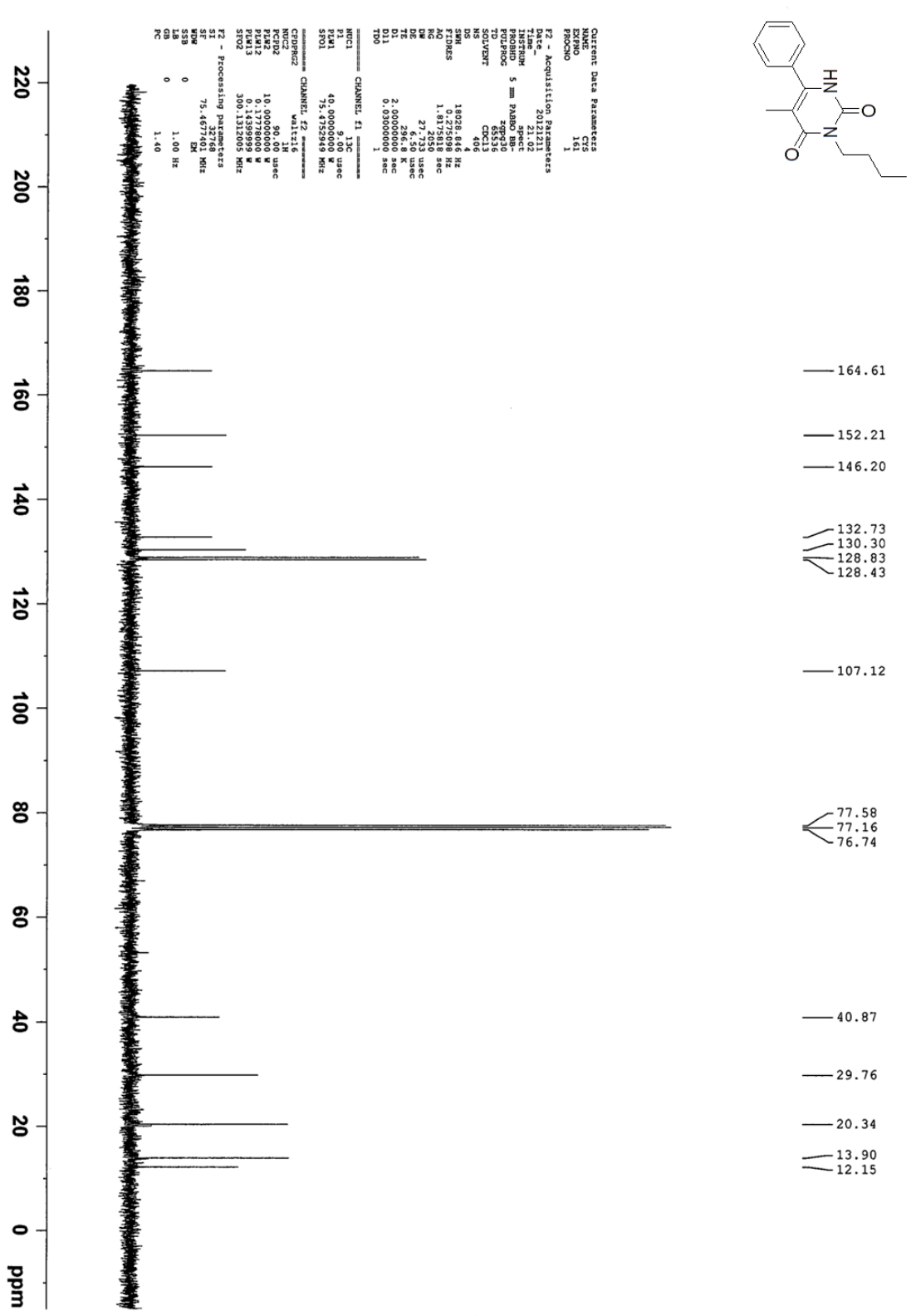
**$^{13}C$ Spectrum of 4l in $CDCl_3$**



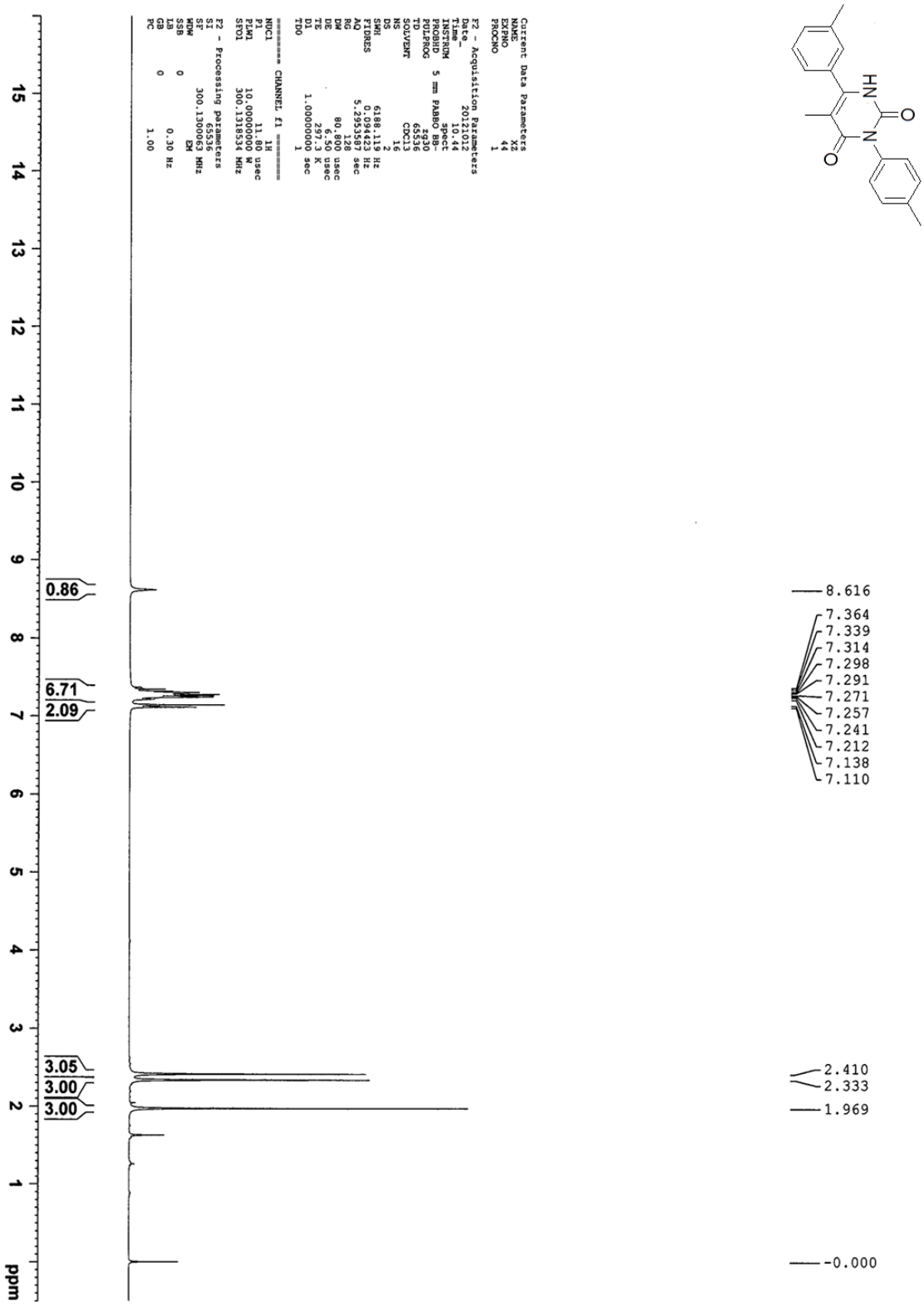
**$^{1}$H Spectrum of 4m in $CDCl_3$**



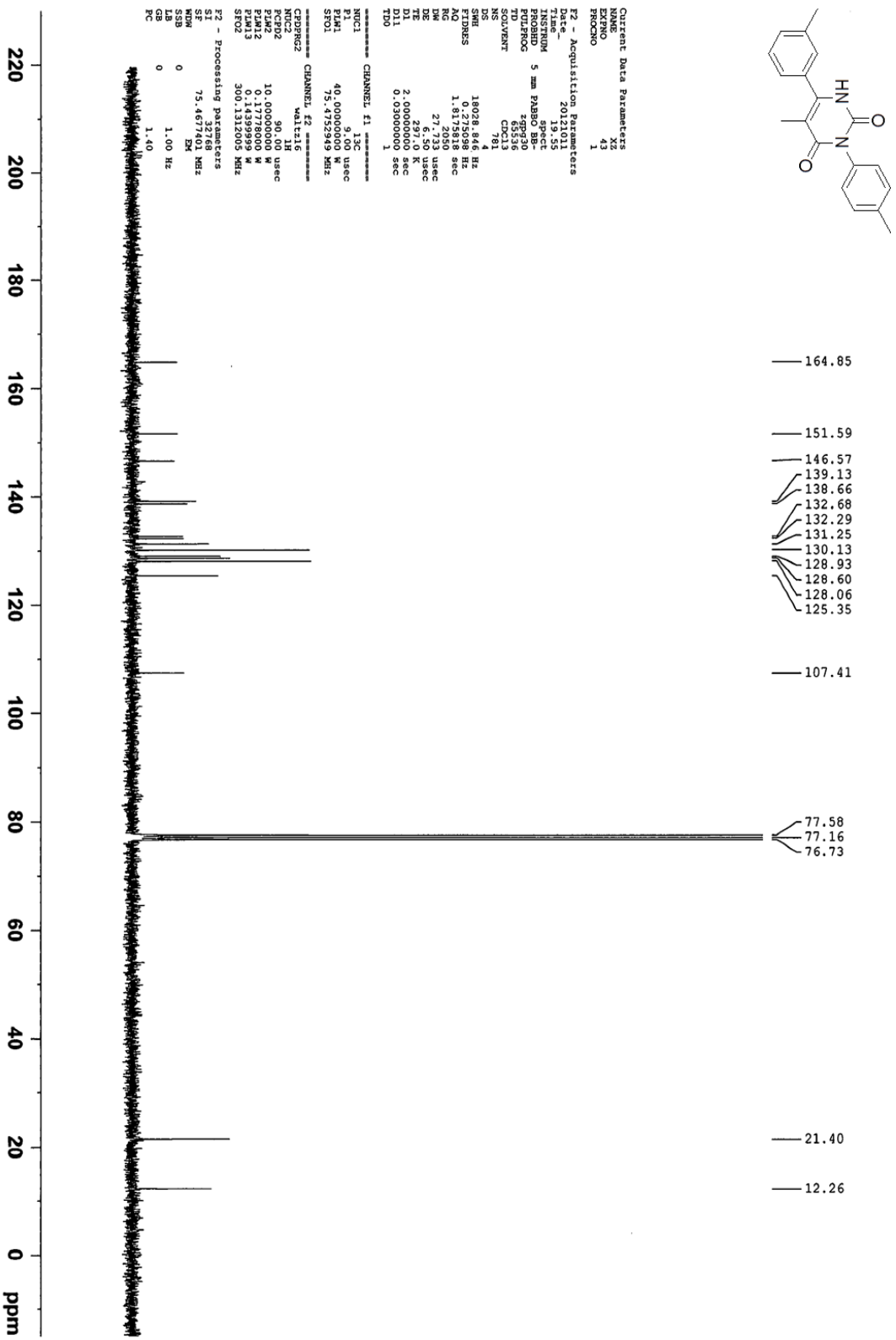
**$^{13}C$ Spectrum of 4m in $CDCl_3$**



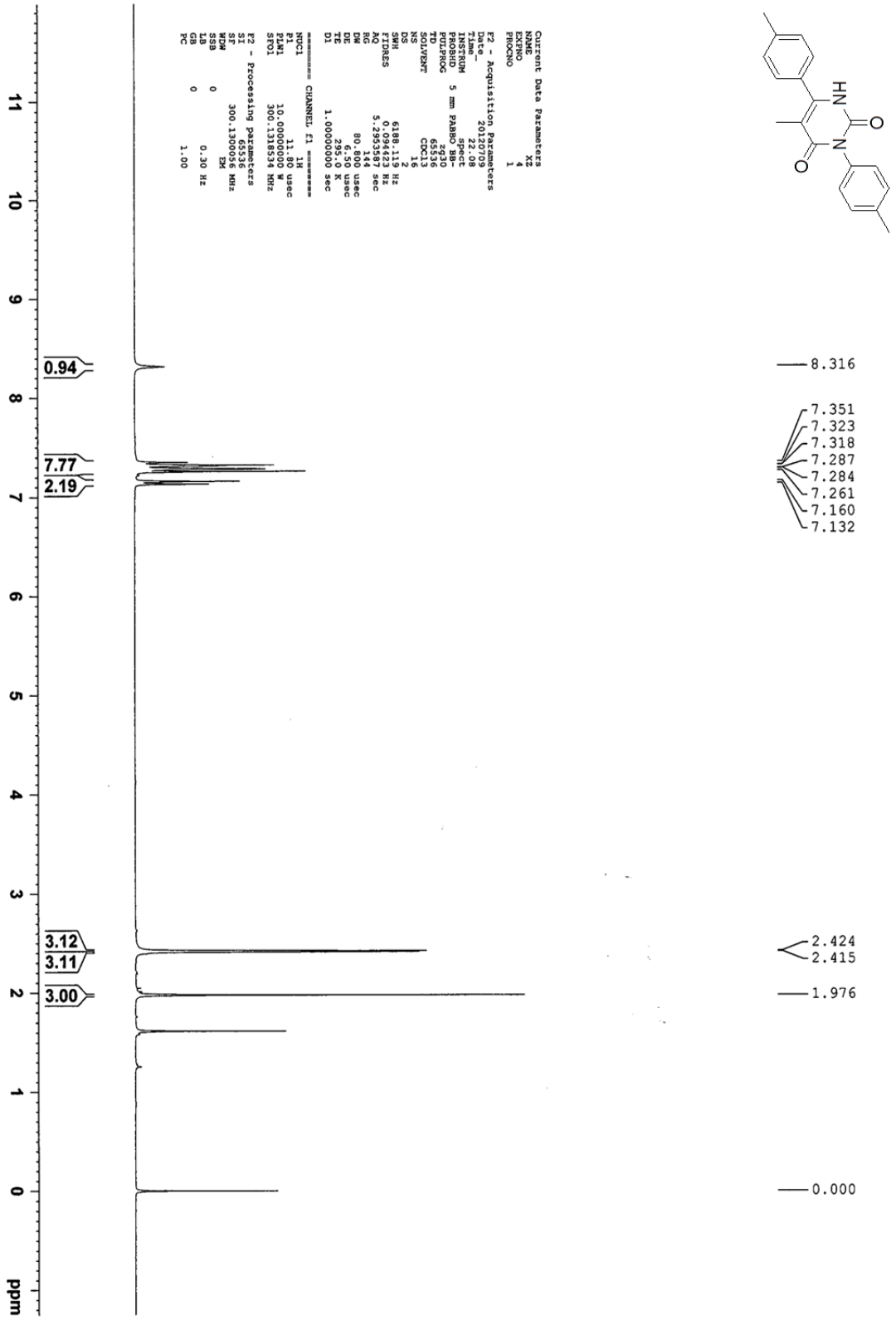
**$^{1}$H Spectrum of 4n in $CDCl_3$**



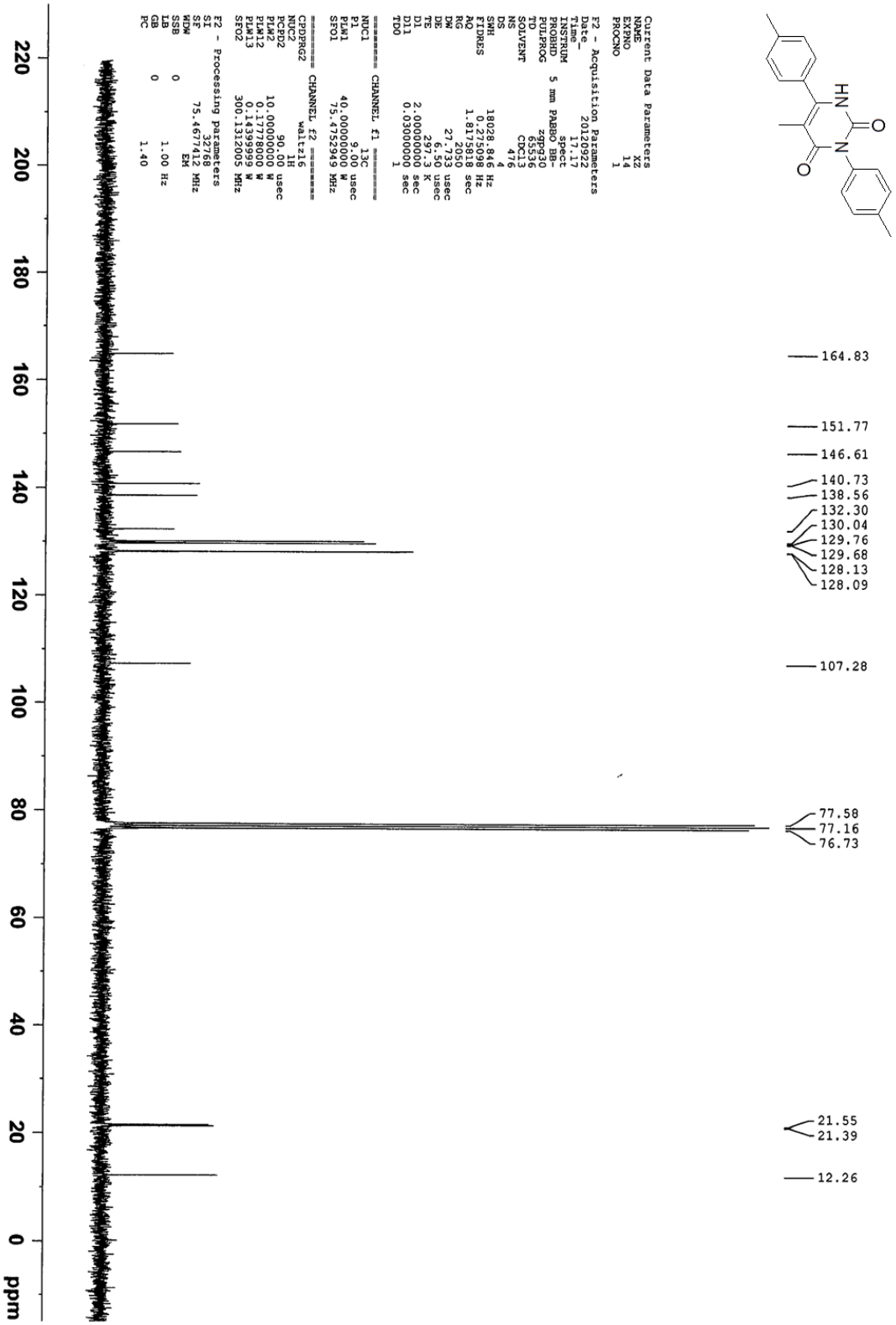
**$^{13}C$ Spectrum of 4n in $CDCl_3$**



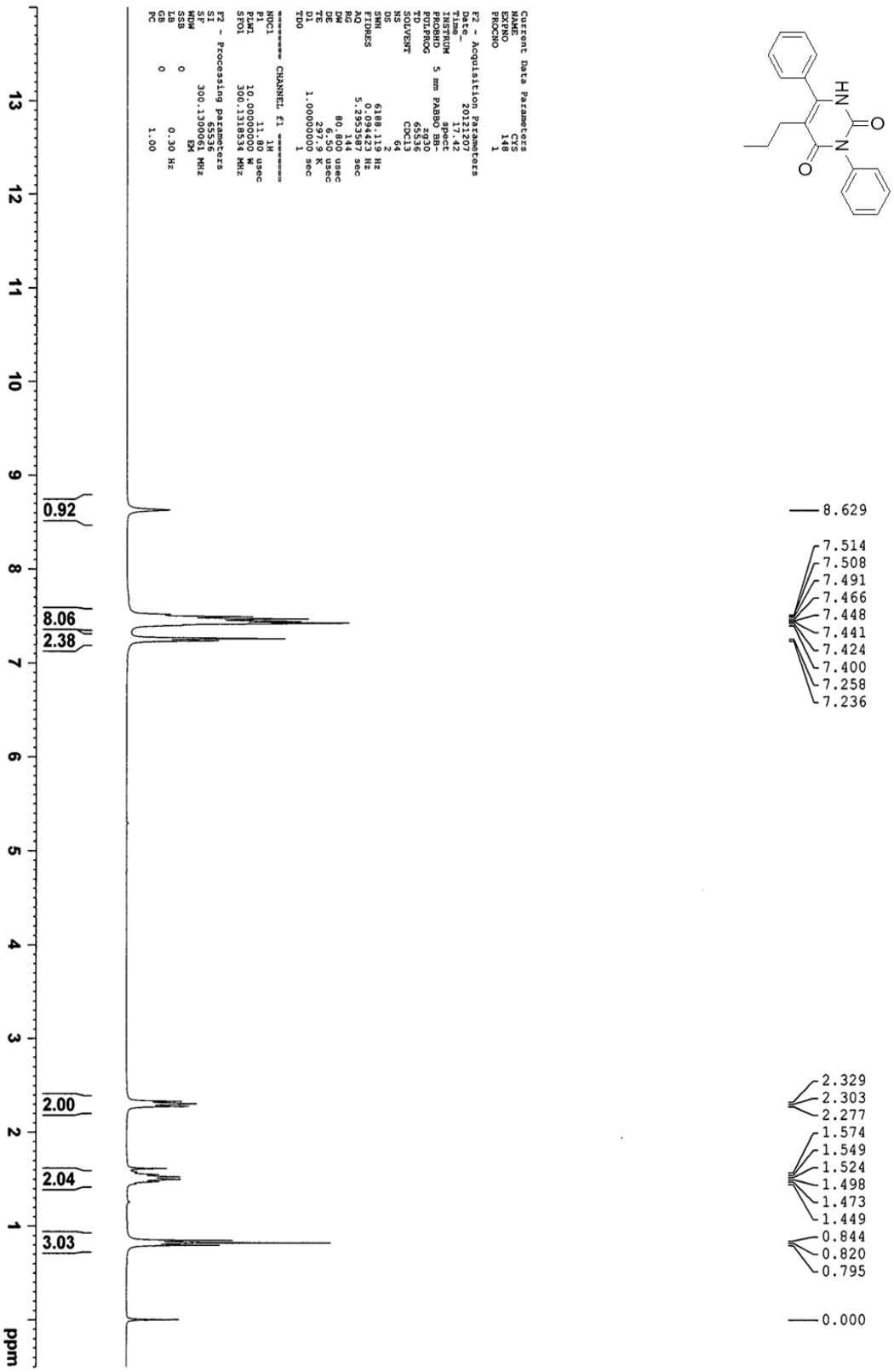
**$^{1}$H Spectrum of 4o in $CDCl_3$**



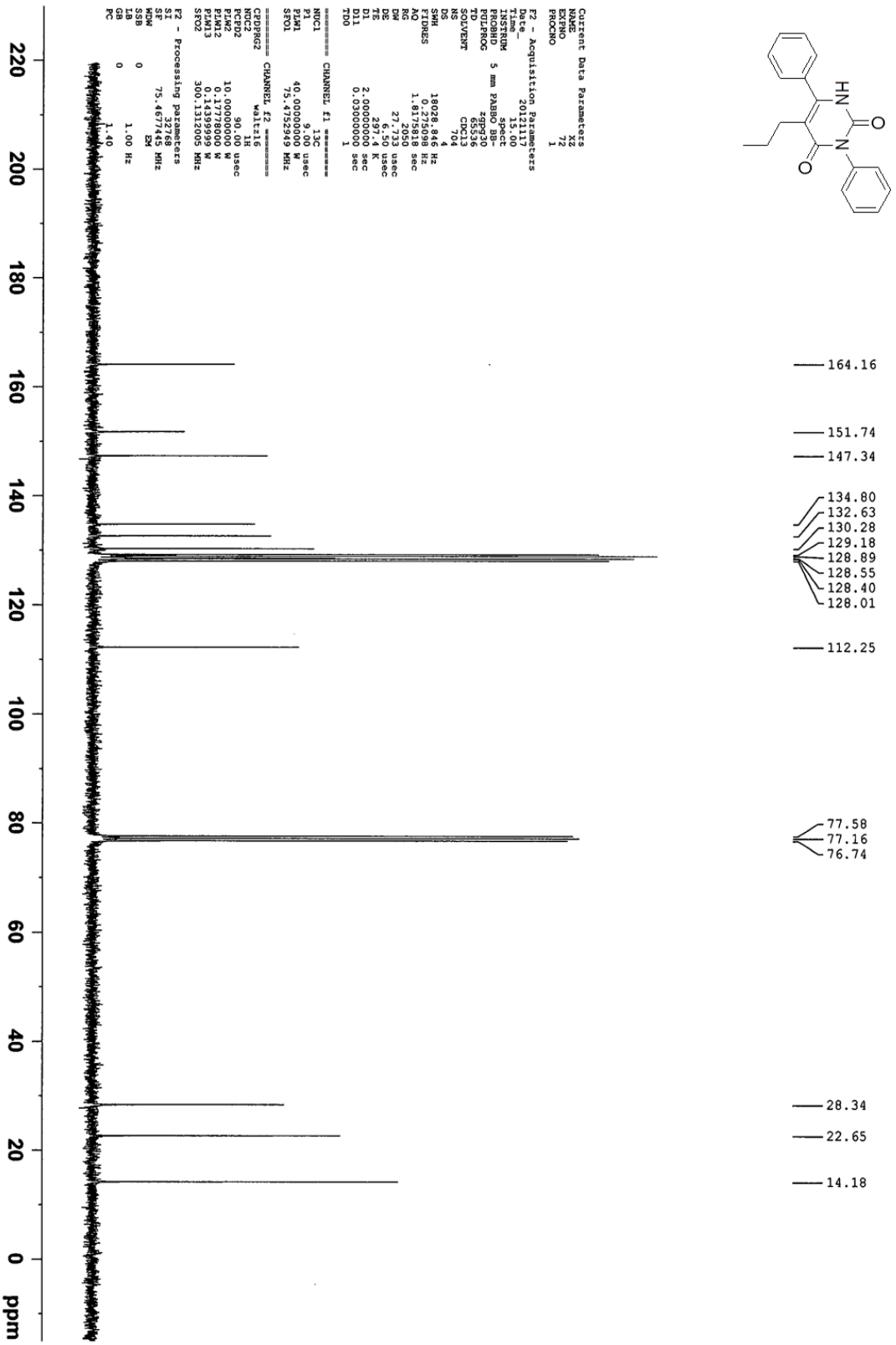
**$^{13}C$ Spectrum of 4o in $CDCl_3$**



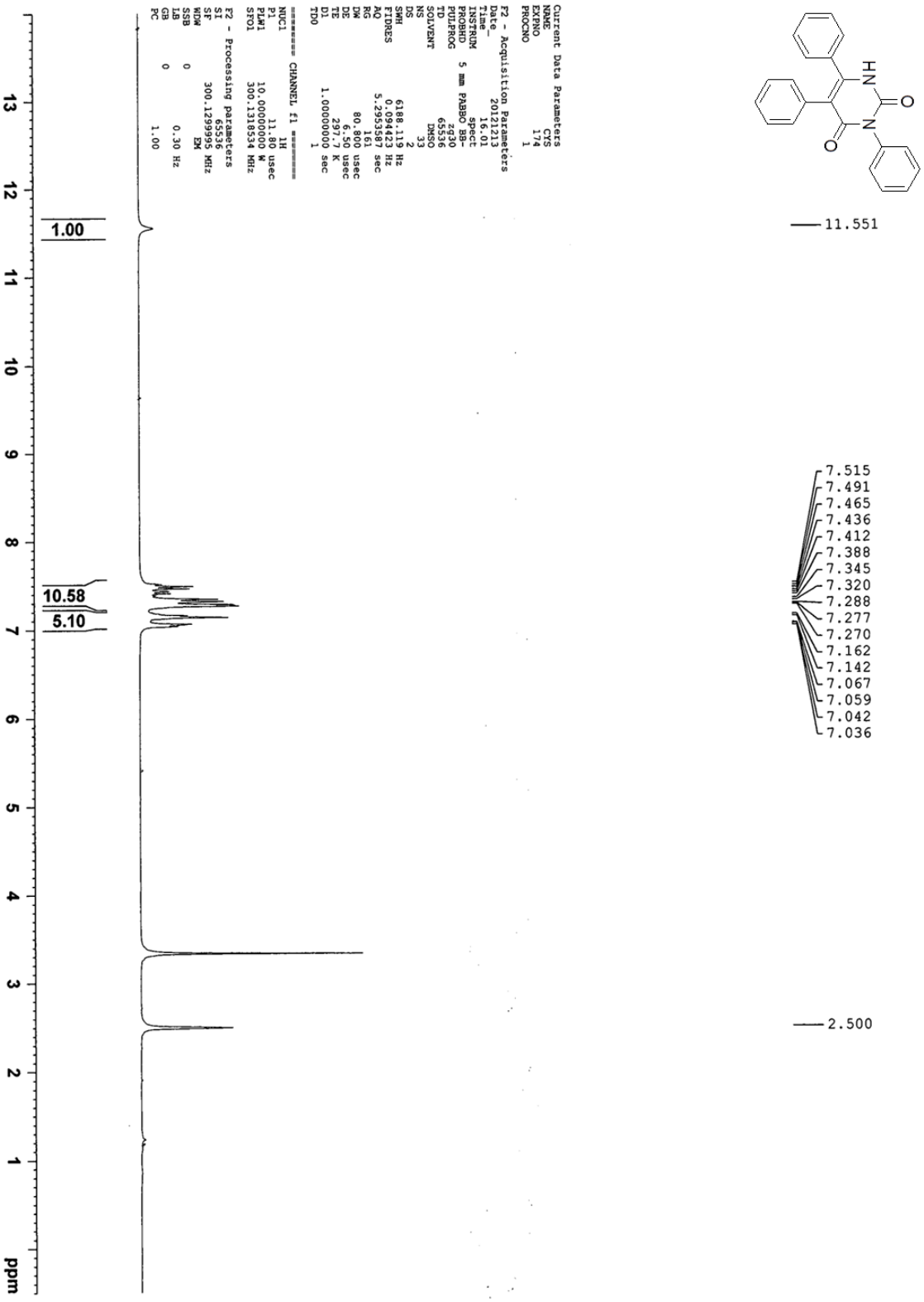
## $^{1}H$ Spectrum of 4p in $CDCl_3$



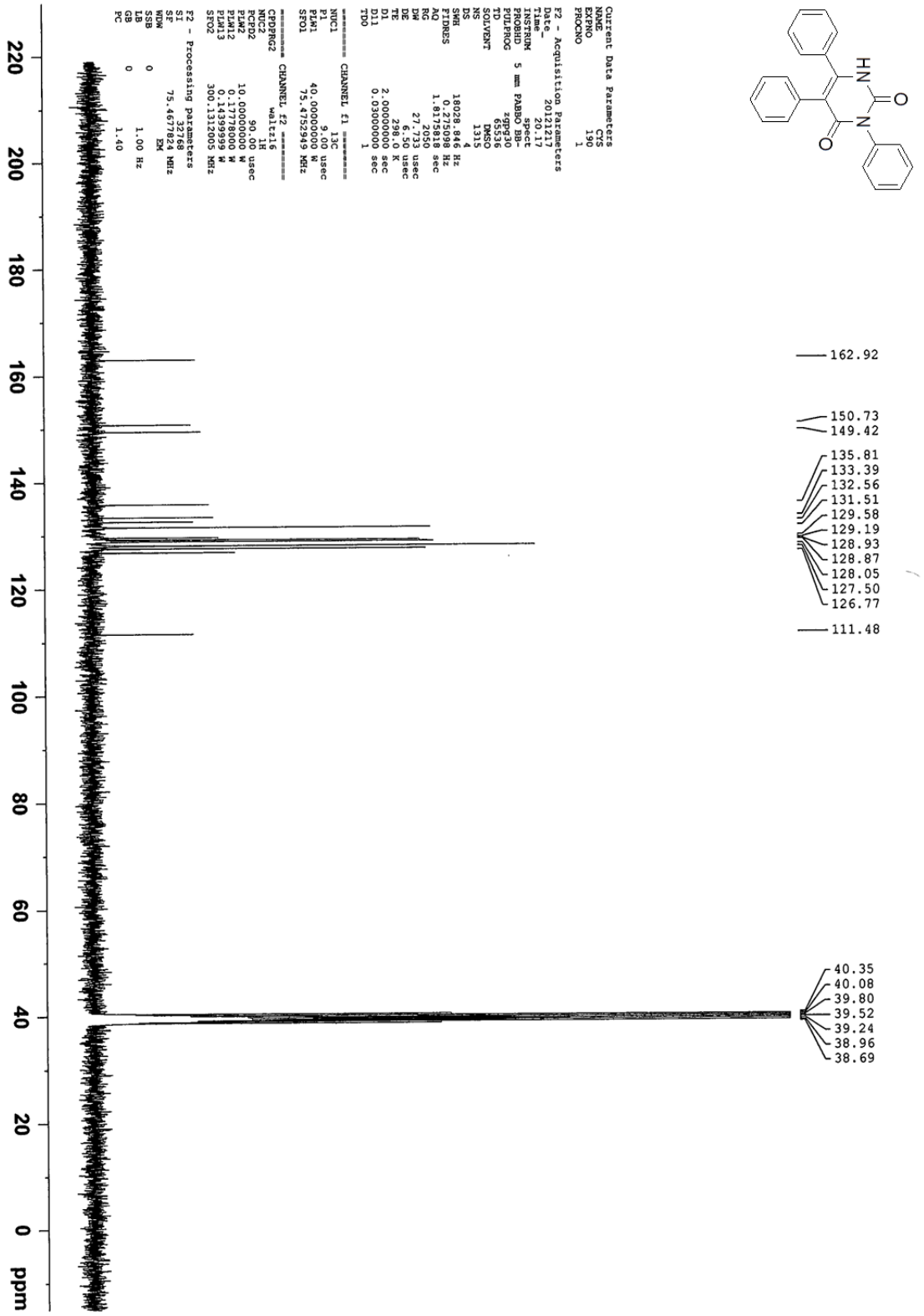
## $^{13}C$ Spectrum of 4p in $CDCl_3$



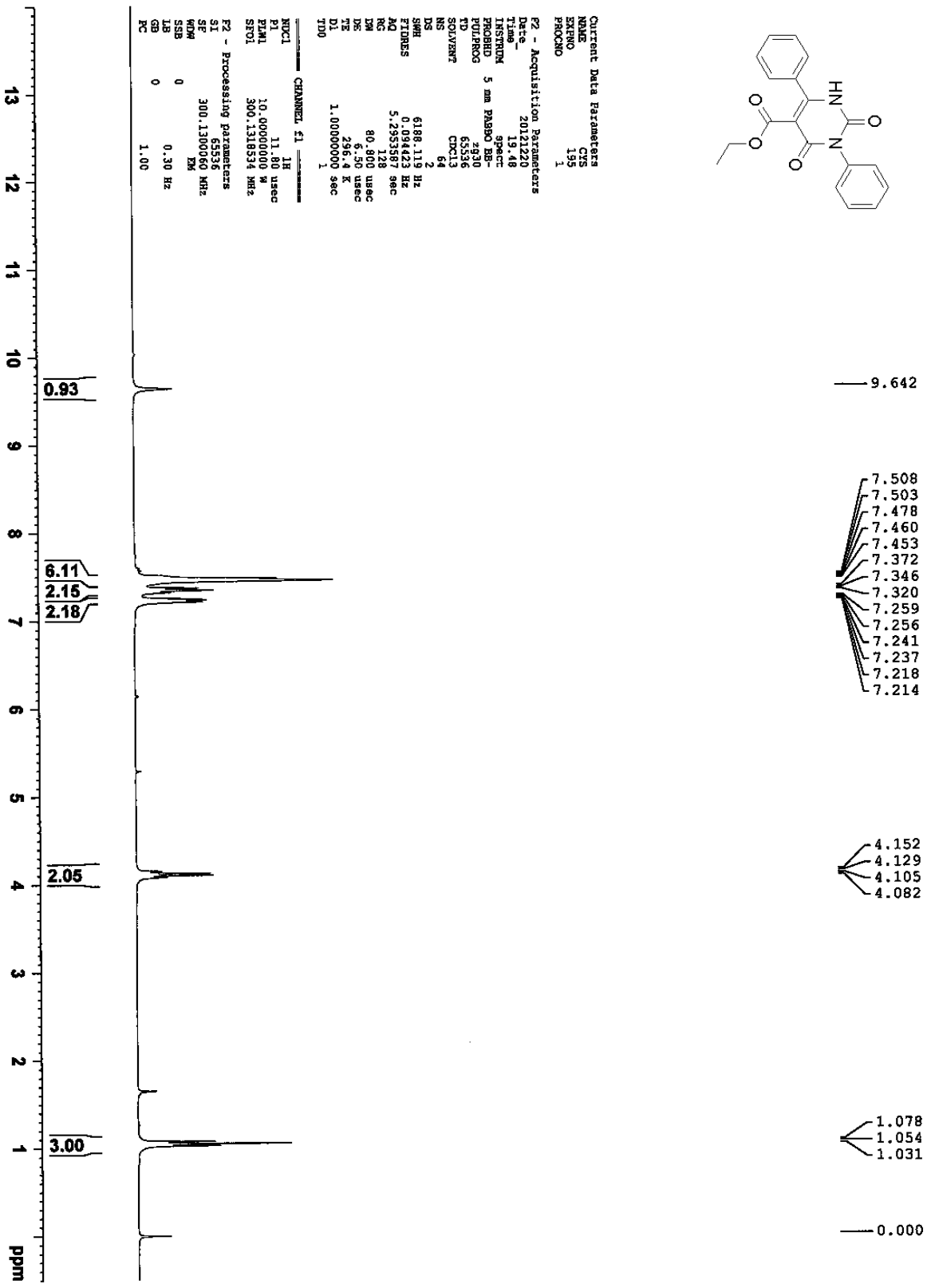
## $^{1}$H Spectrum of 4q in DMSO-$d_6$



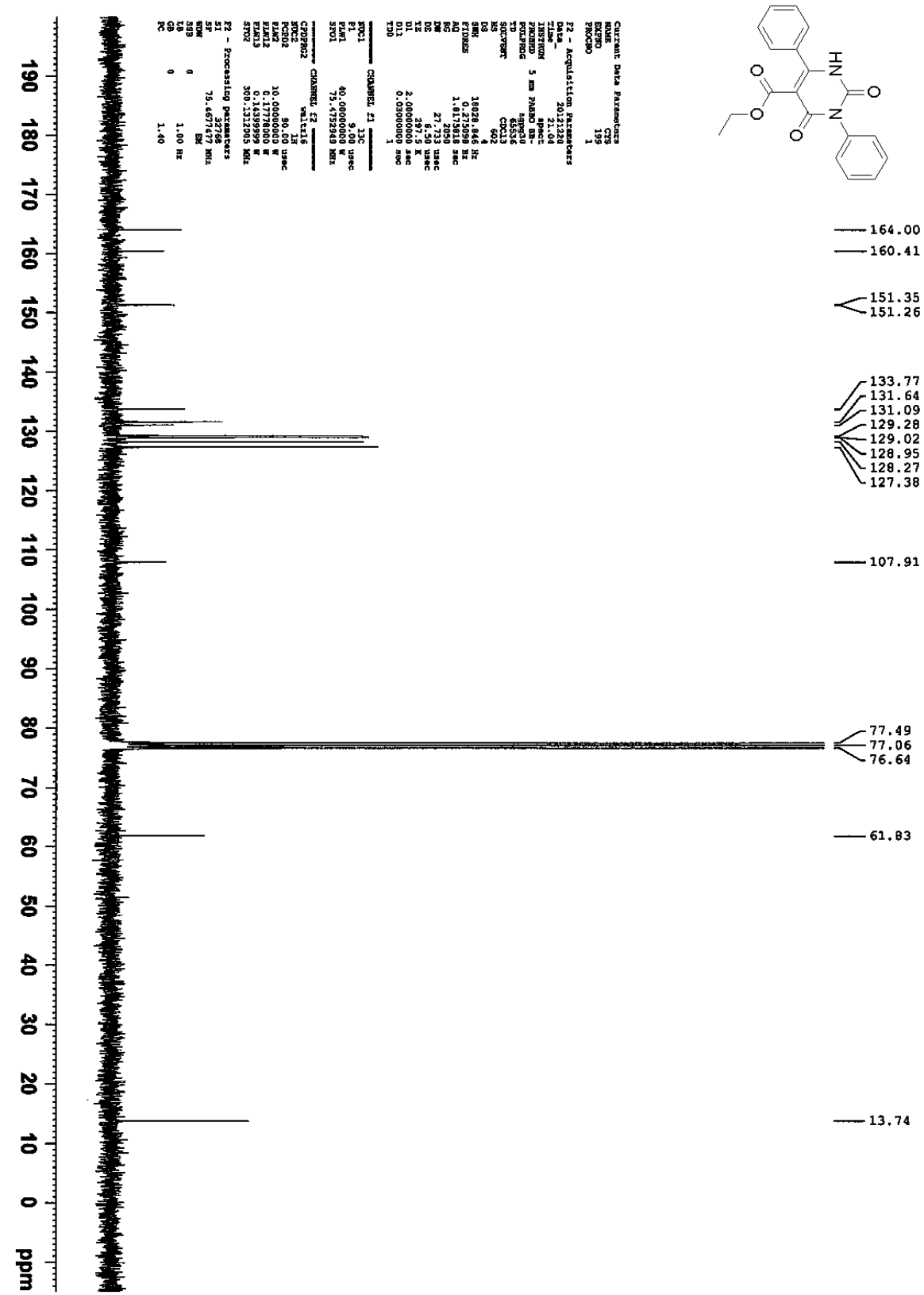
**$^{13}$C Spectrum of 4q in DMSO-$d_6$**



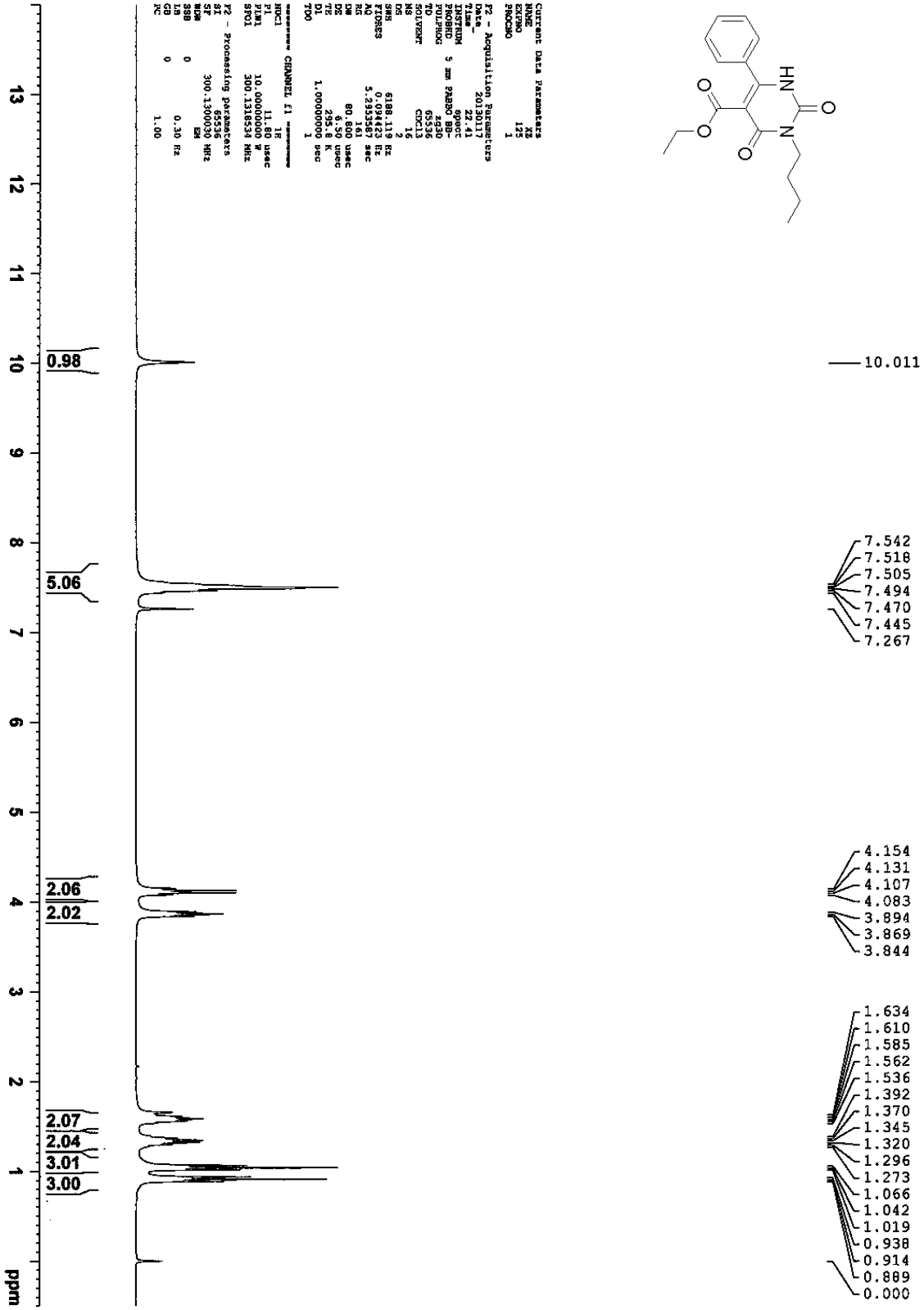
**$^1$H Spectrum of 4r in $CDCl_3$**



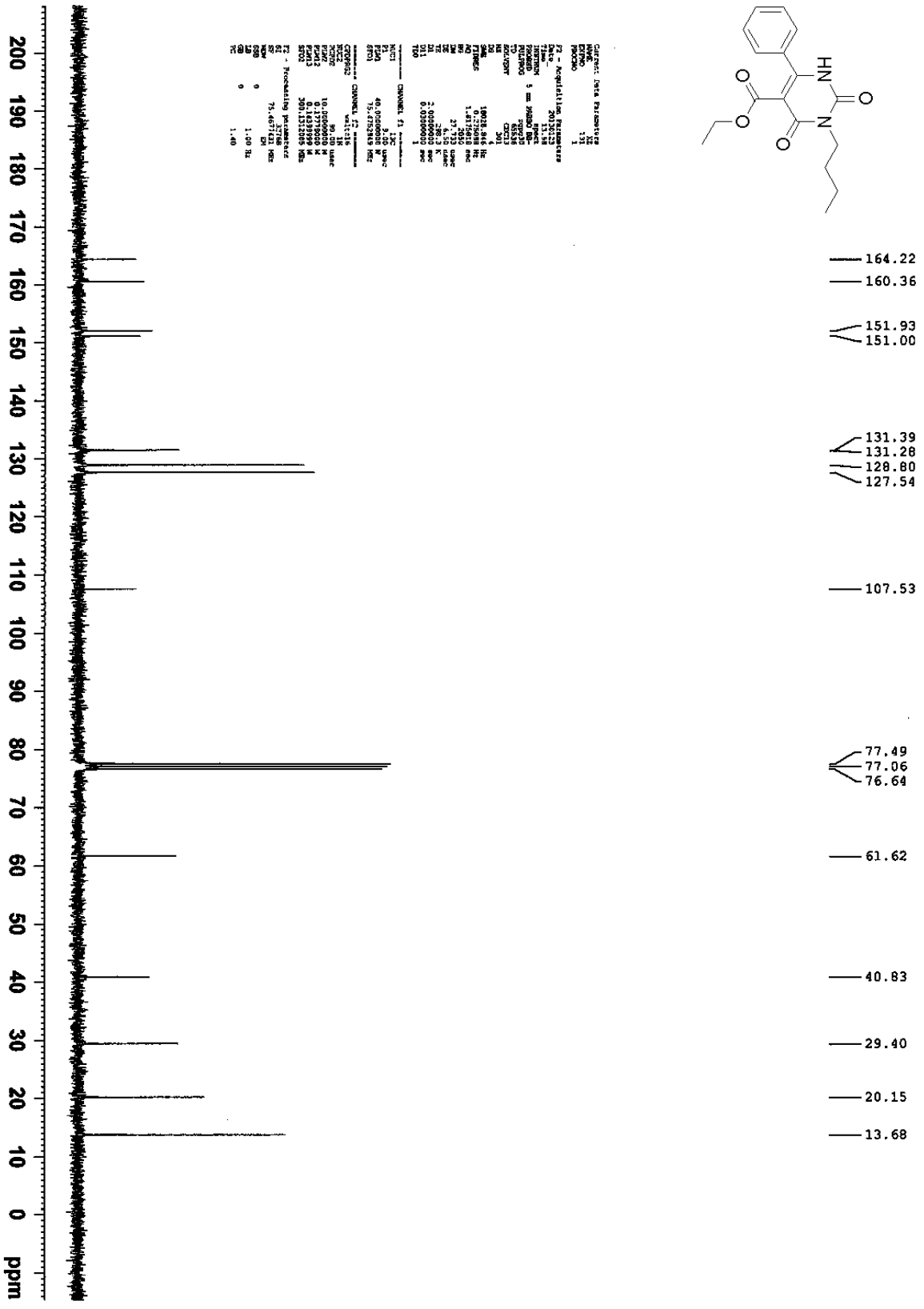
**$^{13}C$ Spectrum of 4r in $CDCl_3$**



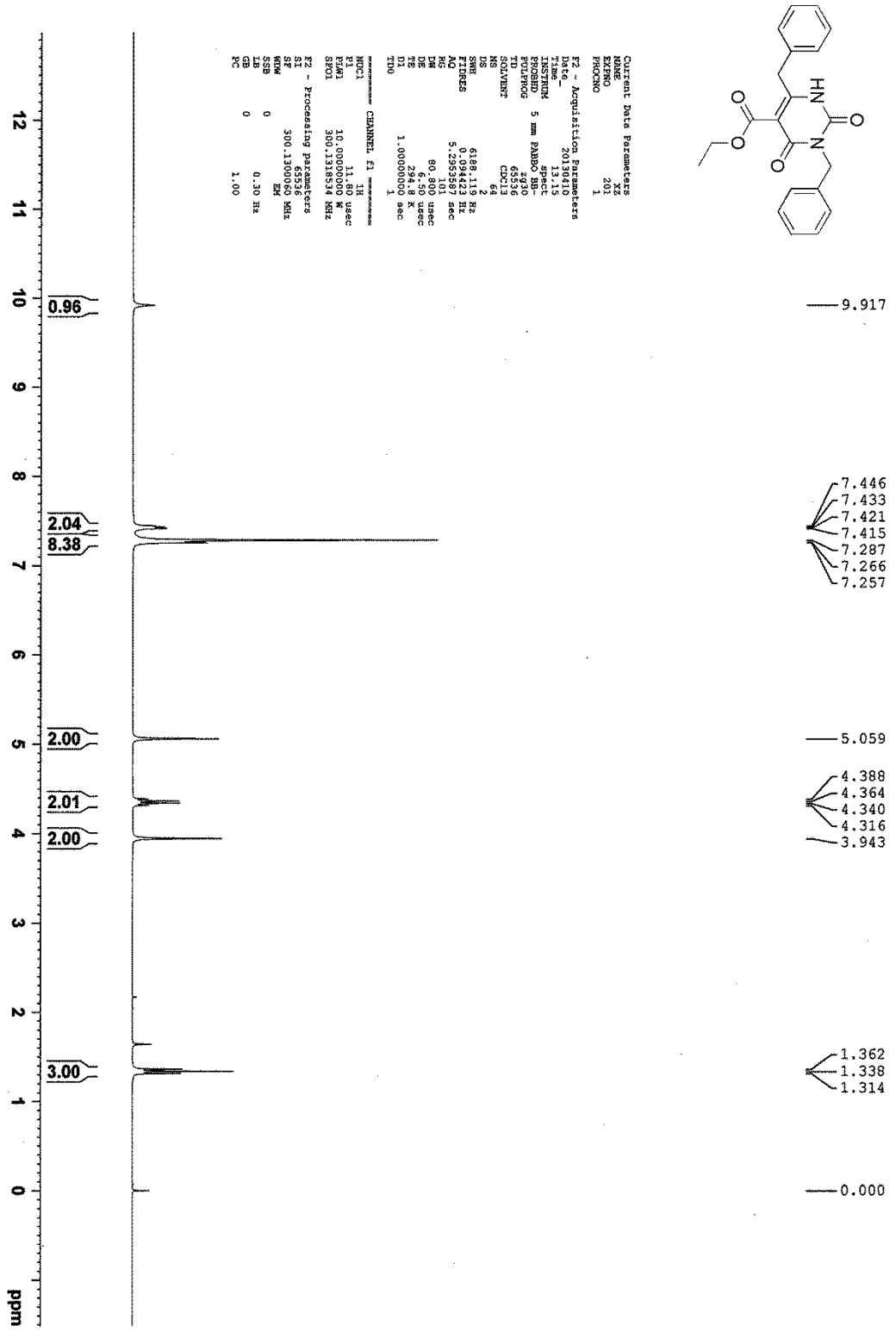
**$^{1}$H Spectrum of 4s in $CDCl_3$**



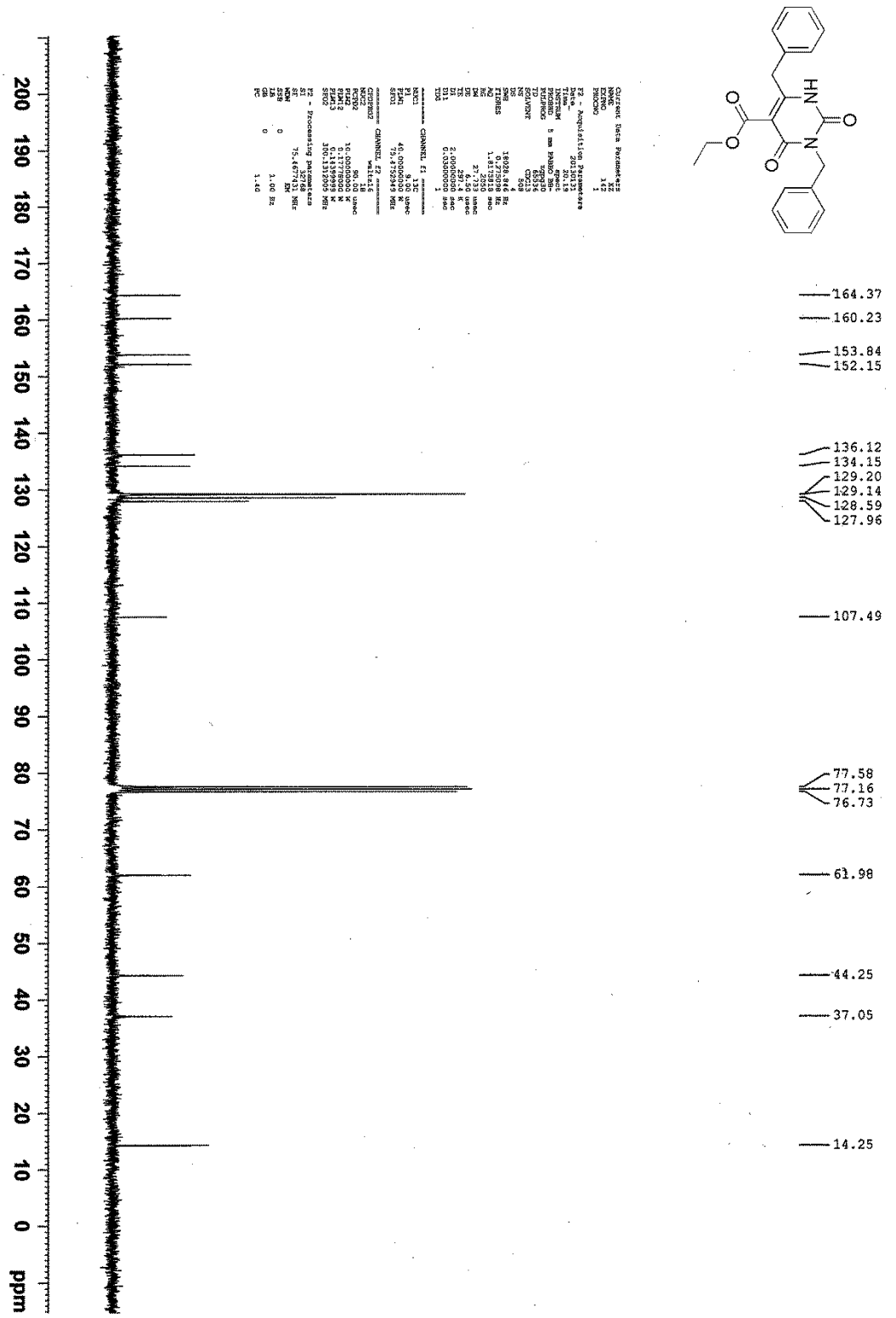
**$^{13}C$ Spectrum of 4s in $CDCl_3$**



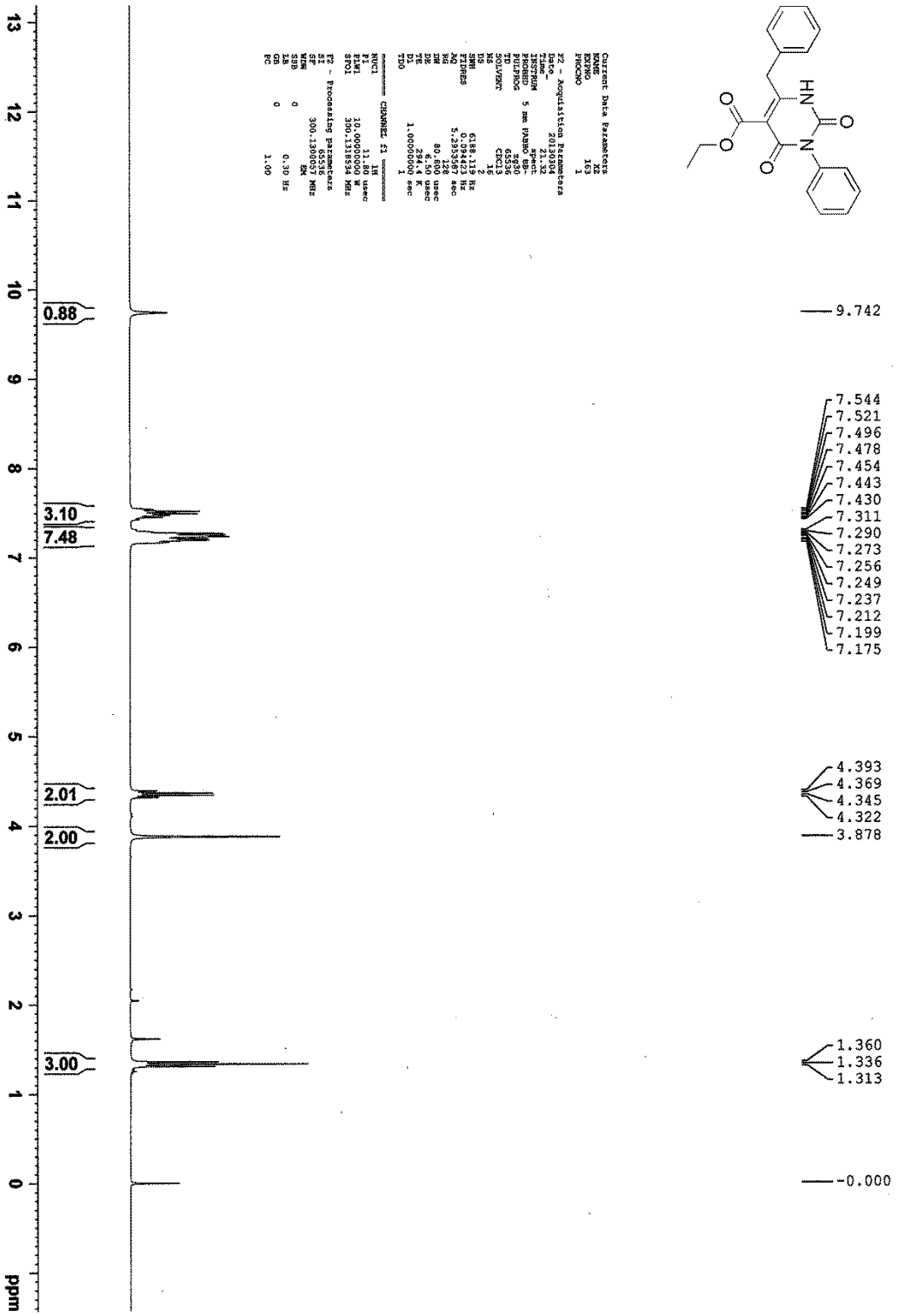
**$^1$H Spectrum of 4t in $CDCl_3$**



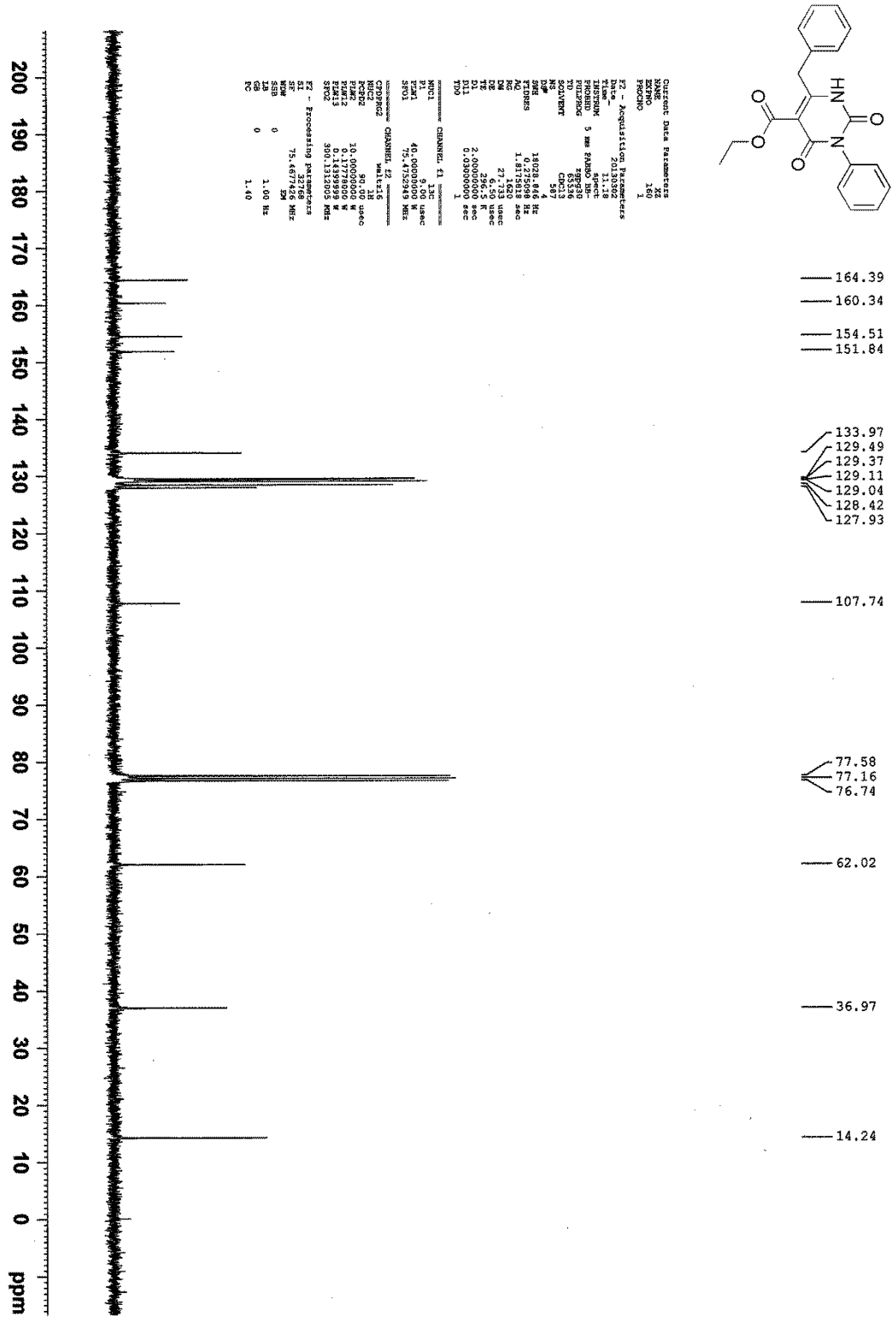
**$^{13}C$ Spectrum of 4t in $CDCl_3$**



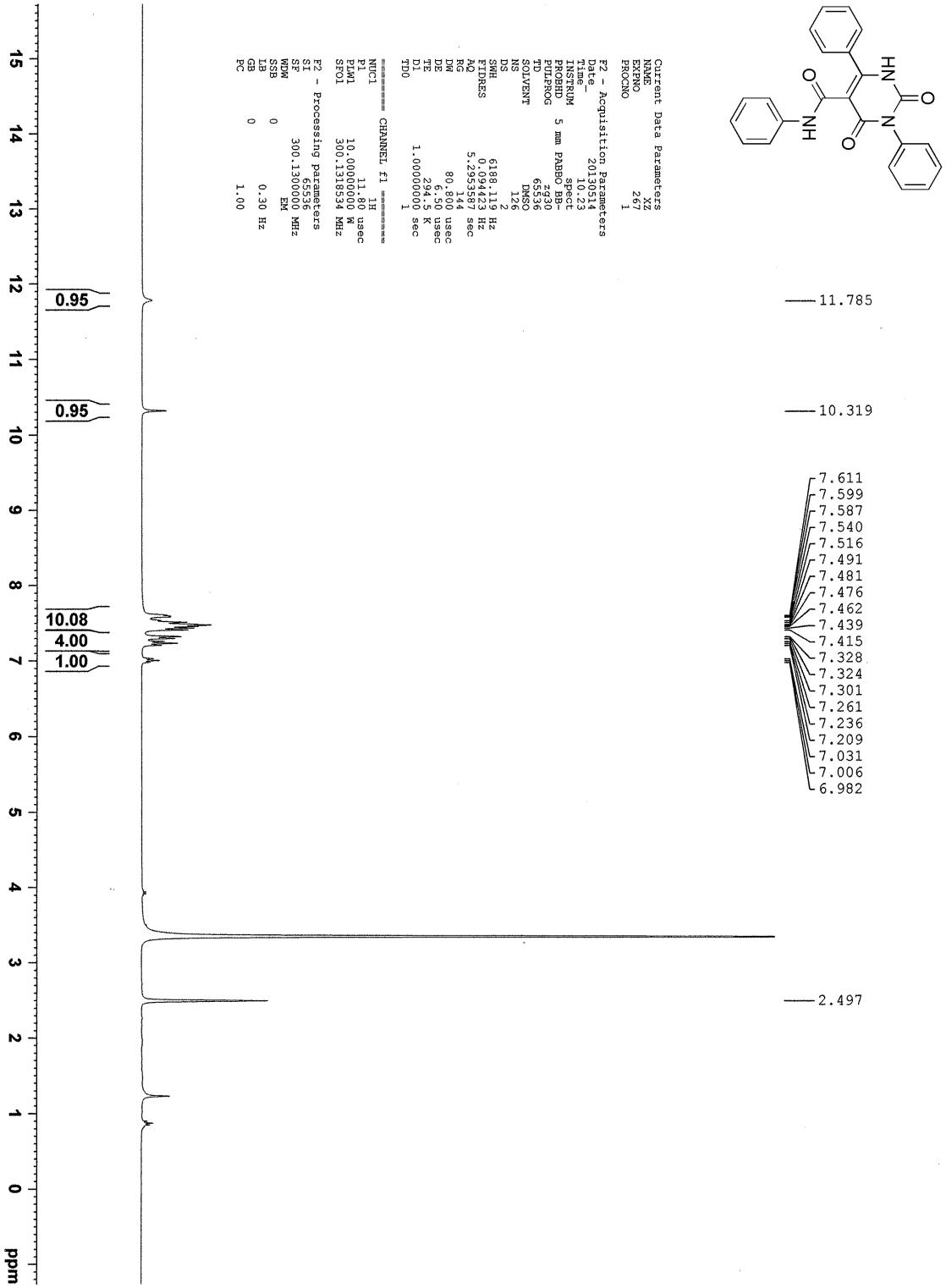
**$^{1}$H Spectrum of 4u in $CDCl_3$**



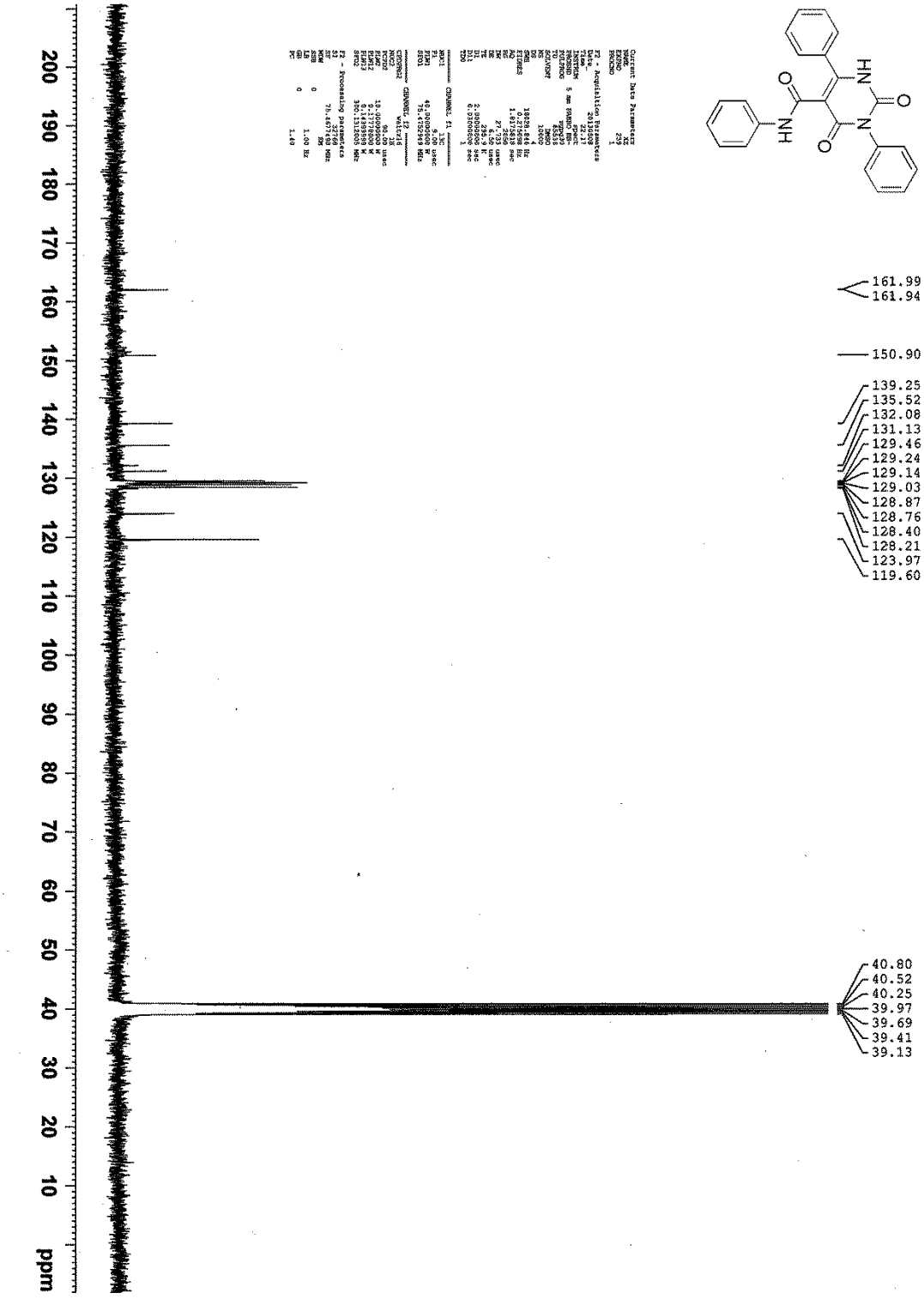
**$^{13}C$ Spectrum of 4u in $CDCl_3$**



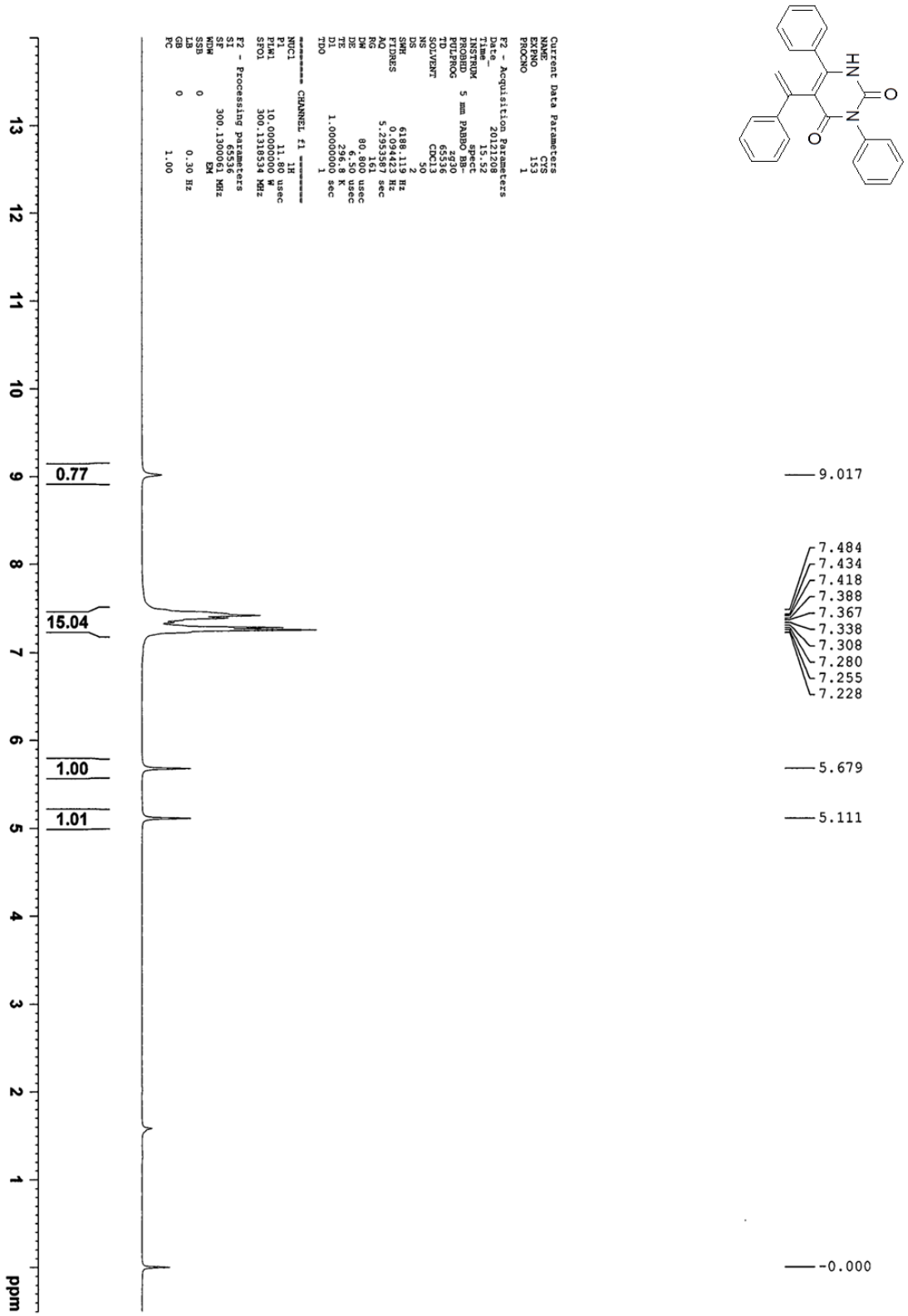
## $^1$H Spectrum of 4v in DMSO-$d_6$



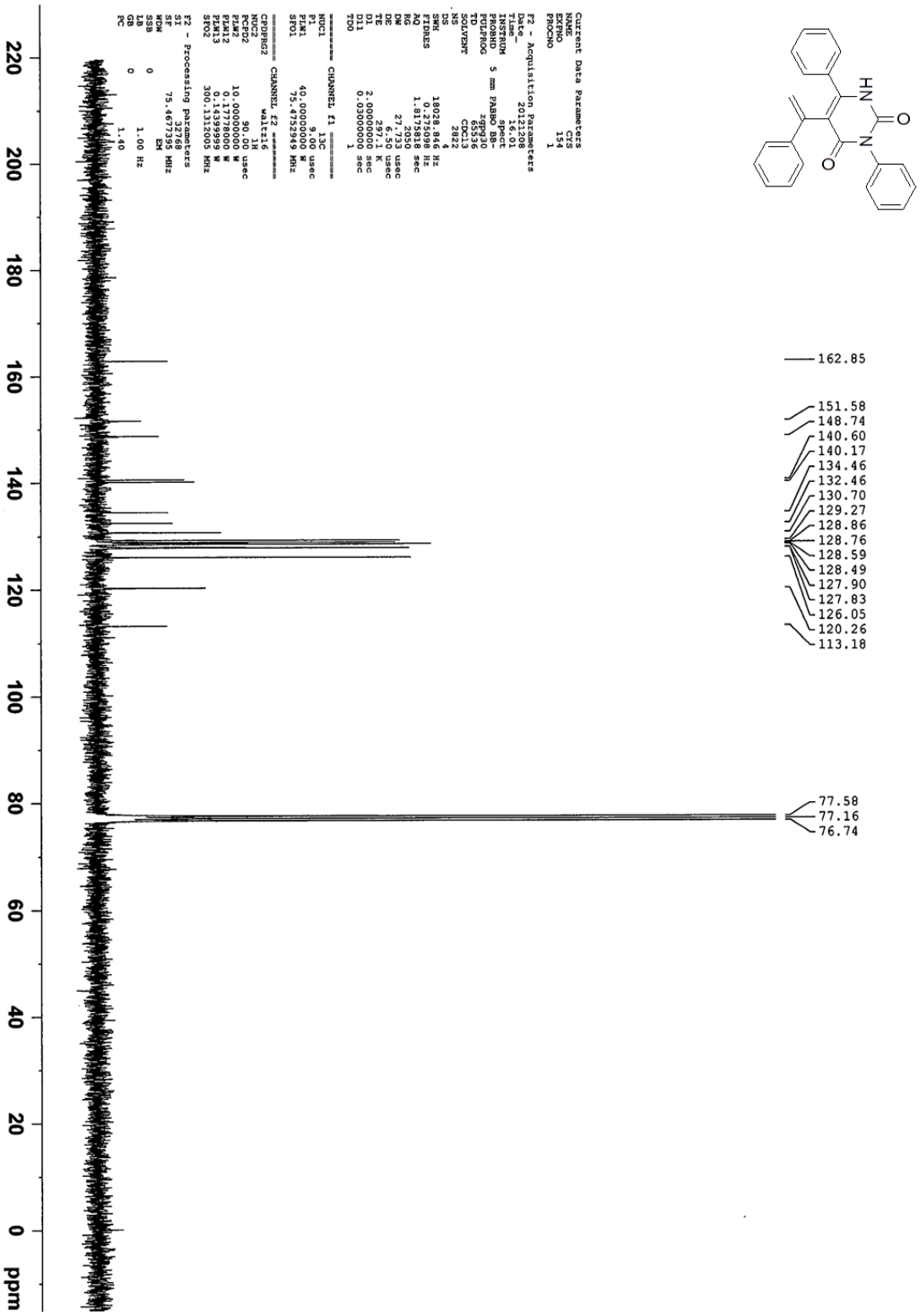
**$^{13}$C Spectrum of 4y in DMSO-$d_6$**



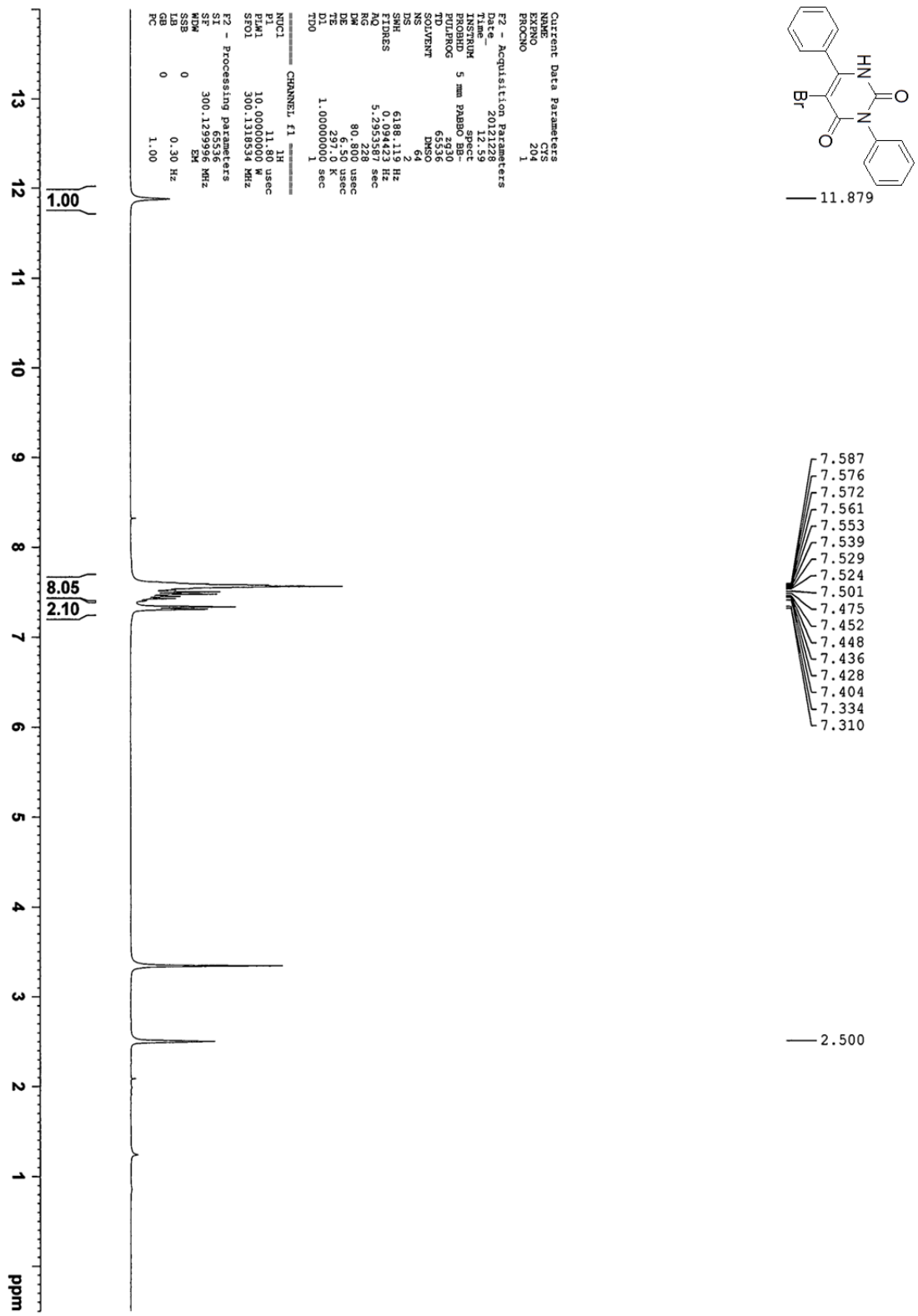
## $^{1}H$ Spectrum of 4w in $CDCl_3$



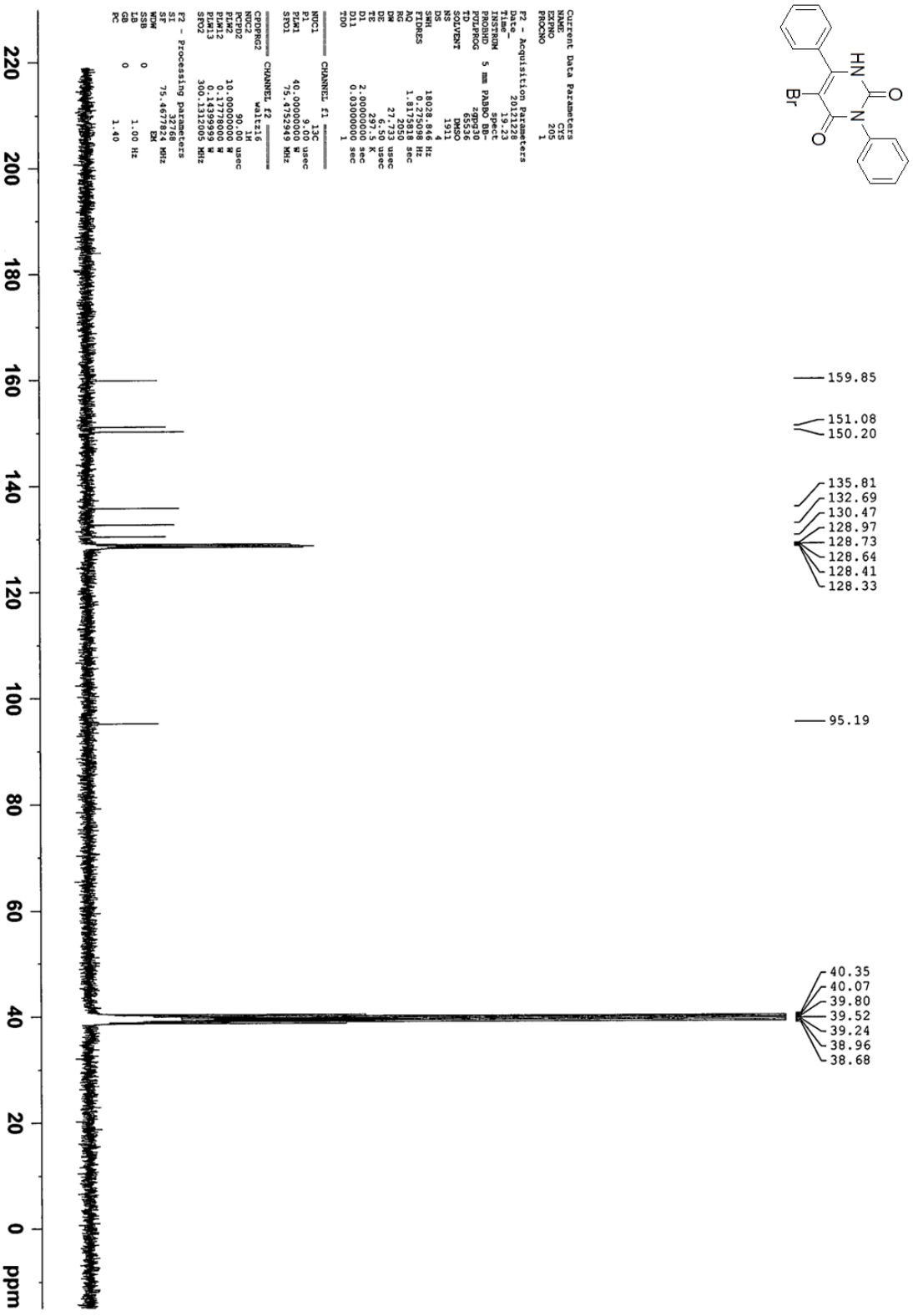
**$^{13}$C Spectrum of 4w in $CDCl_3$**



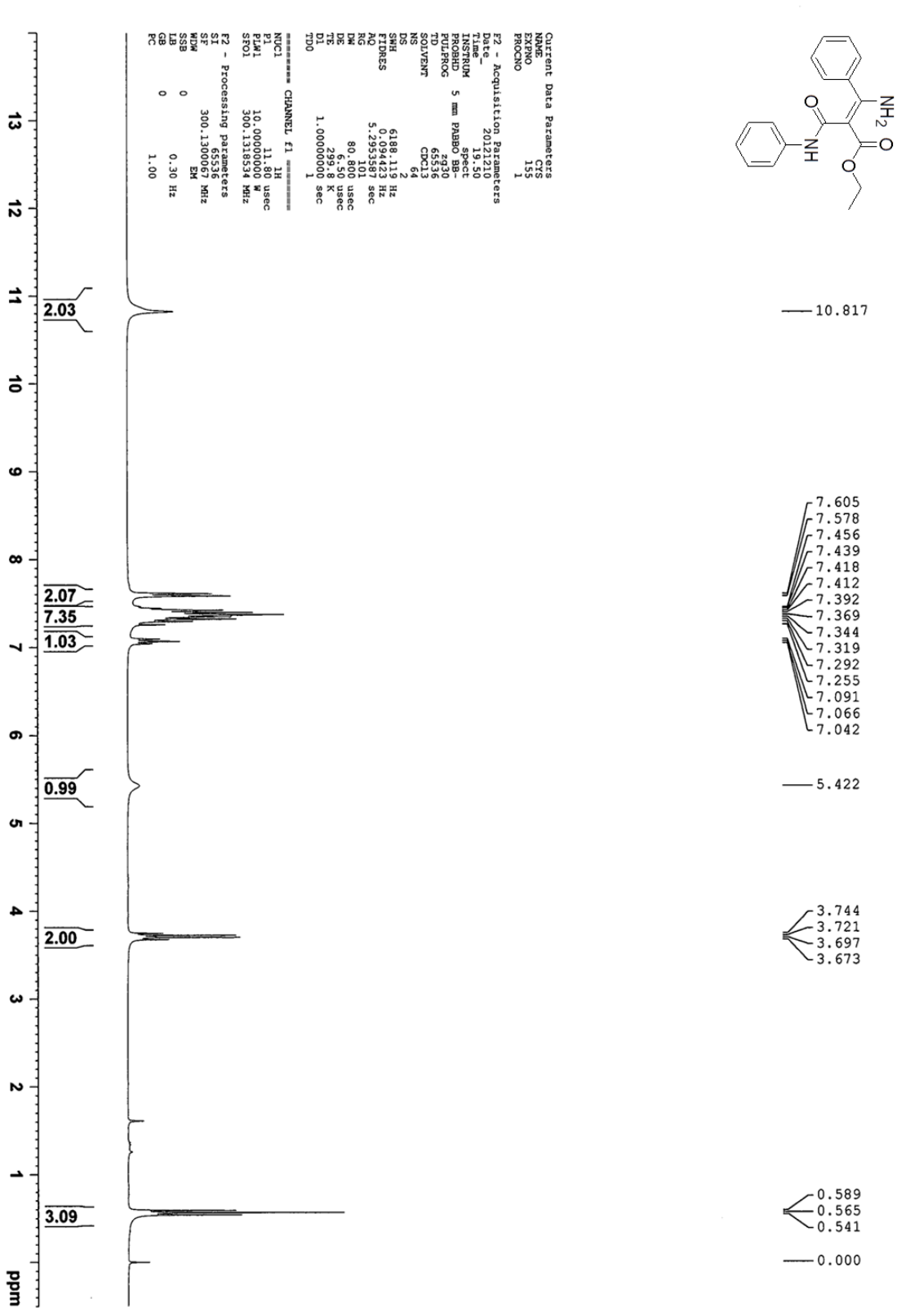
**$^{1}$H Spectrum of 4x in DMSO-$d_6$**



**$^{13}$C Spectrum of 4x in DMSO-$d_6$**



**$^{1}$H Spectrum of 5 in $CDCl_3$**



**$^{13}C$ Spectrum of 5 in $CDCl_3$**