Synthesis of *N*-Acyl-5-Aminopenta-2,4-dienals via Base-Induced Ring-Opening of *N*-Acylated Furfurylamines: Scope and Limitations

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Supporting Information

Contents

***N*-(Furan-2-ylmethyl)acetamide 5a.**[1] To a stirred solution of furfurylamine (950 µL, 10.8 mmol) in pyridine (10 mL) under argon at 0 °C, was added dropwise acetic anhydride (1.10 mL, 11.7 mmol, 1.1 eq). After stirring at room temperature for 1 h, diethyl ether (25 mL) was added. The organic layer was washed with a saturated solution of NH_4Cl (3 × 25 mL), dried ($MgSO_4$) and concentrated in vacuo to afford the acetamide **5a** (987 mg, 66 %) as a yellow amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26 (m, 1 H), 6.69 (br s, 1 H), 6.24 (m, 1 H), 6.13 (m, 1 H), 4.31 (d, J = 5.7 Hz, 2 H), 1.91 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.4 (C), 151.5 (C), 142.0 (CH), 110.4 (CH), 107.2 (CH), 36.4 (CH_2), 22.8 (CH_3); FTIR 3278, 1650, 1538, 731 cm^{-1}; MS (ESI$^+$) *m/z* 162.0 $(M + Na)^+$ 194.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_7H_9NNaO_2$ $(M + Na)^+$ 162.0531, found 162.0524.

***N*-(Furan-2-ylmethyl)-2,2-dimethyl-propionamide 5b.** To a stirred solution of furfurylamine (950 µL, 10.8 mmol, 1.04 eq), and Et_3N (1.45 mL, 10.4 mmol,) in CH_2Cl_2 (25 mL) under argon at 0 °C, was added pivaloyl chloride (1.30 mL, 10.6 mmol, 1.02 eq). The resulting reaction mixture was allowed to warm to ambient temperature and stirred for 2 h. The mixture was washed with saturated NH_4Cl (40 mL) and 5 % aqueous K_2CO_3 (40 mL). The organic layer was separated, dried ($MgSO_4$), concentrated and crystallized from heptane/AcOEt 1/1 to afford the pivalamide **5b** (1.82 g, 97 %) as a yellow solid; mp 34.2–35.2 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27 (dd, J = 1.7, 0.5 Hz, 1 H), 6.24 (dd, J = 3.1, 2.0 Hz, 1 H), 6.16 (br s, 1 H), 6.12 (dd, J = 3.1, 0.5 Hz, 1 H), 4.34 (d, J = 5.7 Hz, 2 H), 1.15 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.2 (C), 151.7 (C), 142.0 (CH), 110.4 (CH), 107.0 (CH), 38.7 (C), 36.6 (CH_2), 27.5 (3 CH_3); FTIR 3344, 1643, 1525, 732 cm^{-1}; MS (ESI$^+$) *m/z* 204.1 $(M + Na)^+$, 236.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{10}H_{15}NNaO_2$ $(M + Na)^+$; 204.1000, found 204.0993.

***N*-(Furan-2-ylmethyl)-4-methoxybenzamide 5c.** Following the procedure reported for the preparation of **5b**, with furfurylamine (950 µL, 10.8 mmol, 1.05 eq), Et_3N (1.45 mL, 10.4 mmol, 1.01 eq) and 4-methoxybenzoyl chloride (1.40 mL, 10.3 mmol), the methoxybenzamide **6c** (2.17 g, 91 %) was obtained as a beige solid; mp 119.5–120.1 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.75 (d, J = 8.6 Hz, 2 H), 7.36 (m, 1 H), 6.90 (d, J = 8.6 Hz, 2 H), 6.43 (br s, 1 H), 6.33 (m, 1 H), 6.28 (m, 1 H), 4.61 (d, J = 5.5 Hz, 2 H), 3.83 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.9 (C), 162.4 (C), 151.6 (C), 142.3 (CH), 129.0 (2 CH), 126.6 (C), 113.8 (2 CH), 110.6 (CH), 107.7 (CH), 55.5 (CH_3), 37.1 (CH_2); FTIR 3306, 1620, 1607, 1573, 1542, 1503, 752 cm^{-1}; MS (ESI$^+$) *m/z* 254.1 $(M + Na)^+$, 286.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{13}H_{13}NNaO_3$ $(M + Na)^+$ 254.0793, found 254.0791.

***N*-(Furan-2-ylmethyl)-4-nitrobenzamide 5d.** Following the procedure reported for the preparation of **5b**, with furfurylamine (950 µL, 10.8 mmol, 1.05 eq), Et_3N (1.45 mL (10.4 mmol, 1.01 eq) and 4-nitrobenzoyl chloride (1.91 g, 10.3 mmol), and crystallization from heptane/AcOEt 60/40, the nitrobenzamide **5d** (2.00 g, 79 %) was obtained as a white powder; mp 145.4–146.2 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27 (d, J = 8.5 Hz, 2 H), 7.94 (d, J = 8.5 Hz, 2 H), 7.38 (m, 1 H), 6.62 (br s, 1 H), 6.35 (m, 2 H), 4.65 (d, J = 5.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.3 (C), 150.5 (C), 149.8 (C), 142.7 (CH), 139.8 (C), 128.4 (2 CH), 124.0 (2 CH), 110.8 (CH), 108.3 (CH), 37.4 (CH_2); FTIR 3330, 1640, 1596, 1541, 1509, 752 cm^{-1}; MS (ESI$^+$) *m/z* 269.1 $(M + Na)^+$, 301.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{12}H_{10}N_2NaO_4$ $(M + Na)^+$ 269.0538, found 269.0530.

***N*-(Furan-2-ylmethyl)-1*H*-pyrrole-2-carboxamide 5e.** To a stirred solution of commercially available 2-trichloroacetylpyrrole (5.01 g, 23.6 mmol) in acetonitrile (50 mL), under argon at room temperature, was added furfurylamine (2.20 mL, 24.9 mmol, 1.05 eq). The

resulting reaction mixture was stirred for 2 days, concentrated and purified by silica gel column chromatography (CH_2Cl_2/acetone 97.5/2.5) to afford the amide **5e** (4.22 g, 94 %) as a pale yellow solid; mp 123.5–124.5 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.45 (br s, 1 H), 8.44 (t, J = 5.8 Hz, 1 H), 7.56 (dd, J = 1.8, 0.8 Hz, 1 H), 6.85 (m, 1 H), 6.81 (m, 1 H), 6.39 (dd, J = 3.2, 1.8 Hz, 1 H), 6.24 (dd, J = 3.2, 0.8 Hz, 1 H), 6.07 (m, 1H), 4.41 (d, J = 5.8 Hz, 2 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 160.4 (C), 152.8 (C), 141.9 (CH), 126.0 (CH), 121.5 (C), 110.5 (CH), 110.2 (CH), 108.6 (CH), 106.7 (CH), 35.3 (CH_2); FTIR 3386, 3278, 1619, 1558, 1519, 1125, 1009, 739 cm^{-1}; MS (ESI$^+$) *m/z* 213.1 (M + Na)$^+$; HRMS (ESI$^+$) calcd for $C_{10}H_{10}N_2NaO_2$ (M + Na)$^+$ 213.0640, found 213.0641.

***N*-(Furan-2-ylmethyl)-1-methyl-1*H*-pyrrole-2-carboxamide 5f** Following the procedure reported for the preparation of **6e**, but with *N*-methyl-2-trichloroacetylpyrrole[2] (1.51 g, 6.67 mmol, 0.96 eq) and furfurylamine (615 µL,6.96 mmol), purification by silica gel column chromatography (pentane/AcOEt 80/20) afforded the amide **5f** (952 mg, 70 %) as a white solid; mp 45.8–46.0 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (dd, J = 1.7, 0.6 Hz, 1 H), 6.71 (dd, J = 2.7, 1.9 Hz, 1 H), 6.55 (dd, J = 3.9, 1.9 Hz, 1 H), 6.32 (dd, J = 3.1, 1.9 Hz, 1 H), 6.26 (dd, J = 3.1, 0.6 Hz, 1 H), 6.21 (br s, 1 H), 6.06 (dd, J = 3.9, 2.7 Hz, 1 H), 4.54 (d, J = 5.6 Hz, 2 H), 3.94 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.7 (C), 151.8 (C), 142.3 (CH), 128.2 (CH), 125.4 (C), 111.9 (CH), 110.5 (CH), 107.4 (CH), 107.3 (CH), 36.9 (CH_2), 36.3 (CH_3); FTIR 3356, 1636, 1511, 1166, 1010, 735 cm^{-1}; MS (ESI$^+$) *m/z* 227.1 (M + Na)$^+$; HRMS (ESI$^+$) calcd for $C_{11}H_{12}N_2NaO_2$ (M + Na)$^+$ 227.0796, found 227.0791.

***N*-Benzyl-2-trichloroacetylpyrrole.[3]** To a stirred suspension of 60% NaH in mineral oil (621 mg, 15.5 mmol, 0.66 eq) (washed twice with diethyl ether) in DMF (15 mL), under argon at room temperature, was added of a solution of 2-trichloroacetylpyrrole (5.0 g, 23.5 mmol) in

DMF5 (mL). At the end of hydrogen evolution, benzyl bromide (3.4 mL, 28.6 mmol, 1.2 eq) was added. After stirring for 2 days, diethyl ether (90 mL) and water (90 mL) were added. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 × 90 mL). The organic layers were combined, washed first with acetic acid (200 mL), then basified to pH 10 with a saturated solution of $NaHCO_3$, dried ($MgSO_4$) and concentrated in vacuo to afford *N*-benzyl-2-trichloroacetylpyrrole (3.44 g, 48 %) as a white solid; mp 49.8–50.9 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58 (dd, J = 4.4, 1.5 Hz, 1 H), 7.28 (m, 3 H), 7.10 (m, 2 H), 7.05 (m, 1 H), 6.29 (dd, J = 4.4, 2.6 Hz, 1 H), 5.56 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7 (C), 137.3 (C), 133.4 (CH), 128.9 (2 CH), 127.9 (CH), 127.0 (2 CH), 124.8 (CH), 121.6 (C), 109.5 (CH), 96.4 (C), 53.6 (CH_2); FTIR 1667, 1403, 1453, 1384, 740, 683 cm^{-1}; MS (IE) *m/z* 300.0 M^+.

1-Benzyl-*N*-(furan-2-ylmethyl)-1*H*-pyrrole-2-carboxamide 5g (3). Following the procedure reported for the preparation of **5e**, but with *N*-benzyl-2-trichloroacetylpyrrole (1.01 g, 3.34 mmol) and furfurylamine (370 µL, 4.18 mmol, 1.25 eq), chromatography on silica gel, eluting with 90:10 pentane/AcOEt, afforded the amide **5g** (592 mg, 63 %) as a white solid; mp 103.3–104.0 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35 (dd, J = 1.8, 0.6 Hz, 1 H), 7.27 (m, 3 H), 7.15 (dd, J = 8.2, 1.7 Hz, 2 H), 6.82 (dd, J = 2.6, 1.8 Hz, 1H), 6.60 (dd, J = 3.9, 1.8 Hz, 1 H), 6.32 (dd, J = 3.0, 1.8 Hz, 1 H), 6.20 (dd, J = 3.0, 0.6 Hz, 1 H), 6.14 (m, 2 H), 5.62 (s, 2 H), 4.52 (d, J = 5.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.6 (C), 151.7 (C), 142.3 (CH), 138.7 (C), 128.7 (2 CH), 127.52 (CH), 127.46 (CH), 127.3 (2 CH), 125.3 (C), 112.4 (CH), 110.6 (CH), 108.0 (CH), 107.4 (CH), 52.0 (CH_2), 36.4 (CH_2); FTIR 3308, 1621, 1540, 1459, 1135, 1020, 735 cm^{-1}; MS (ESI$^+$) *m/z* 281.1 $(M + H)^+$, 303.1 $(M + Na)^+$; HRMS (ESI$^+$) calcd for $C_{17}H_{16}N_2NaO_2$ $(M + Na)^+$ 303.1109, found 303.1102.

2,2,2-Trifluoro-*N*-(furan-2-ylmethyl)acetamide 5h. To a stirred solution of furfurylamine (950 µL, 10.8 mmol, 1.05 eq) and Et_3N (1.90 mL 13.6 mmol, 1.3 eq) in CH_2Cl_2 (10 mL), under argon at -78 °C, was added dropwise TFAA (1.45 mL, 10.4 mmol). The resulting reaction mixture was then allowed to warm to ambient temperature and was treated after 1 h 30 with saturated aqueous $NaHCO_3$. The organic layer was separated, washed first with saturated NH_4Cl then with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated in vacuo to afford the trifluoroacetamide **5h** (1.39 g, 70 %) as an orange solid; mp 31.8–33.0 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38 (m, 1 H), 6.87 (br s, 1 H), 6.34 (m, 1 H), 6.31 (m, 1 H), 4.51 (d, J = 5.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.2 (C, q, J = 37.7 Hz), 148.9 (C), 143.0 (CH), 115.9 (C, q, J = 285.3 Hz), 110.8 (CH), 108.9 (CH), 36.8 (CH_2); FTIR 3296, 1703, 1146, 738 cm^{-1}; MS (ESI$^-$) *m/z* 192.0 $(M - H)^-$; HRMS (ESI$^-$) calcd for $C_7H_5F_3NO_2$ $(M - H)^-$ 192.0272, found 192.0268.

***tert*-Butyl furan-2-ylmethylcarbamate 5i.**[4] To a stirred solution of furfurylamine (950 µL, 10.8 mmol) in CH_2Cl_2 (10 mL) under argon at room temperature, was added Boc_2O (2.47 g, 11.3 mmol, 1.05 eq). The resulting reaction mixture was stirred at room temperature for 2 h. Then, imidazole (3.50 g 51.4 mmol, 4.8 eq) was added and the mixture was stirred for an additional 15 minutes. The mixture was washed with 1 N aqueous HCl (3 × 15 mL) and the organic layer was separated, dried ($MgSO_4$) and concentrated in vacuo to afford the carbamate **5i** (1.19 g, 56 %) as a yellow solid; mp 39.1–40.1 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 1 H), 6.27 (m, 1 H), 6.16 (m, 1 H), 4.98 (br s, 1 H), 4.25 (d, J = 5.6 Hz, 2 H), 1.42 (s, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.7 (C), 152.2 (C), 142.0 (CH), 110.4 (CH), 106.9 (CH), 79.7 (C), 37.7 (CH_2), 28.4 (3 CH_3); FTIR 3342, 1693, 1504, 1247, 1163, 731 cm^{-1}; MS (ESI$^+$) *m/z* 220.1 $(M + Na)^+$, 252.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{10}H_{15}NNaO_3$ $(M + Na)^+$ 220.0950, found 220.0945.

3-(Furan-2-ylmethyl)-1,1-dimethylurea 5j. To a stirred solution of furfurylamine (950 µL, 10.8 mmol, 1.05 eq) and Et_3N (1.90 mL 13.6 mmol, 1.3 eq) in THF (30 mL) under argon at ambient temperature was added a solution of dimethylcarbamoyl chloride (950 µL, 10.3 mmol) in THF (20 mL). The resulting reaction mixture was stirred at 55 °C for 1 h and then allowed to cool to ambient temperature. The precipitate (Et_3N•HCl) was filtered and the mixture was evaporated under reduced pressure to give the urea **5j** (1.37 g, 79 %) as an orange solid; mp 90.0–91.9 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33 (m, 1 H), 6.29 (m, 1 H), 6.20 (m, 1 H), 4.73 (br s, 1 H), 4.39 (d, J = 5.1 Hz, 2 H), 2.89 (s, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.1 (C), 152.9 (C), 142.0 (CH), 110.5 (CH), 107.1 (CH), 38.0 (CH_2), 36.3 (2 CH_3); FTIR 3355, 1621, 1519, 1373, 1345, 753 cm^{-1}; MS (ESI$^+$) *m/z* 191.1 $(M + Na)^+$, 223.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_8H_{12}N_2NaO_2$ $(M + Na)^+$ 191.0796, found 191.0792.

***N*-((3-Methylfuran-2-yl)methyl)benzamide 5k.** To a stirred solution of methyl 3-methyl-2-furoate (499 mg, 3.56 mmol) in formamide (18 mL), under argon at room temperature, was added NaOMe (771 mg, 14.3 mmol, 4.0 eq). The resulting reaction mixture was heated for 45 minutes at 100 °C. It was then cooled to room temperature and ice-cold water (15 mL) and brine (10 mL) were added. The aqueous layer was extracted with ethyl acetate (3 × 30 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated in vacuo to afford the corresponding primary amide,[5] which was dissolved in THF (15 mL). $LiAlH_4$ (340 mg, 8.96 mmol, 2.5 eq) was added and the mixture was heated at 60 °C for 4 h. It was then treated with saturated Na_2SO_4, filtered through a pad of Celite®, washed with $CHCl_3$ and evaporated under reduced pressure to give the amine[5] (301 mg, 2.70 mmol, 76 %) as a yellow oil, which was dissolved in CH_2Cl_2 (10 mL). Benzoyl chloride (380 µL, 3.27 mmol, 1.2 eq) and Et_3N (380 µL, 2.73 mmol, 1.01 eq) were added and the resulting mixture was stirred under argon at room

temperature overnight. The mixture was then treated with saturated NH_4Cl (15 mL) and saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$) concentrated and purified by silica gel column chromatography (pentane/AcOEt 85/15) to yield the amide **5k** (393 mg, 51 %, 3 steps) as a white solid; mp 65.2–66.4 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (m, 2 H), 7.43 (m, 3 H), 7.28 (d, J = 1.9 Hz, 1 H), 6.49 (br s, 1 H), 6.21 (d, J = 1.9 Hz, 1 H), 4.58 (d, J = 5.3 Hz, 2 H), 2.07 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.3 (C), 146.5 (C), 141.5 (CH), 134.4 (C), 131.6 (CH), 128.6 (2 CH), 127.1 (2 CH), 117.4 (C), 113.3 (CH), 35.2 (CH_2), 9.8 (CH_3); FTIR 3300, 1632, 1601, 1538, 1488, 1292, 1107, 694 cm^{-1}; MS (ESI$^+$) *m/z* 238.1 $(M + Na)^+$, 270.1 $(M + Na + MeOH])^+$; HRMS (ESI$^+$) calcd for $C_{13}H_{13}NNaO_2$ $(M + Na)^+$ 238.0844, found 238.0837.

Methyl 4-(4-chlorophenyl)furan-2-carboxylate. 4-(4-chlorophenyl)furan-2-carboxylic acid was prepared according to the literature procedure[6] using 4-bromofuran-2-carboxylic acid[6] (500 mg, 2.62 mmol), 4-chlorophenylboronic acid (430 mg, 2.75 mmol, 1.05 eq), sodium carbonate (501 mg, 4.73 mmol, 1.8 eq) and $Pd(PPh_3)_2Cl_2$ (56 mg 79.8 µmol, 3 mol %). The crude material was then diluted in a mixture toluene/methanol 8/2 (16 mL) and esterified using 2 M trimethylsilyldiazomethane/hexane (1.60 mL, 3.2 mmol, 1.5 eq). After stirring for 2h, the crude material was concentrated and purified by silica gel column chromatography (pentane/Et_2O 95/5) to give the methyl ester (165 mg, 27 %) as a white solid. mp 106.0–106.9 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.82 (d, J = 1.1 Hz, 1 H), 7.43 (m, 1 H), 7.36 (m, 4 H), 3.93 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.1 (C), 145.7 (C), 142.0 (CH), 133.8 (C), 129.6 (C), 129.4 (2 CH), 127.7 (C), 127.3 (2 CH), 116.3 (CH), 52.3 (CH_3); FTIR 1714, 1607, 1592, 1483, 1276, 1263, 811 cm^{-1}; MS (ESI$^+$) *m/z* 259.0 $(M + Na)^+$, 291.0 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{12}H_9{}^{35}ClNaO_3$ $(M + Na)^+$ 259.0138, found 259.0143.

***N*-((4-(4-Chlorophenyl)furan-2-yl)methyl)benzamide 5l.** Following the procedure used for the preparation of the amide **5k**, with the above ester (90 mg, 0.38 mmol), the benzamide **5l** was obtained as a yellow oil (37 mg, 0.12 mmol, 31 %, 3 steps); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.81 (dd, *J* = 7.0, 1.7 Hz, 2 H), 7.62 (d, *J* = 1.1 Hz, 1 H), 7.53–7.27 (m, 7 H), 6.63 (br s, 1 H), 6.57 (br s, 1 H), 4.66 (d, *J* = 7.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.4 (C), 152.8 (C), 138.2 (CH), 134.2 (C), 132.9 (C), 131.8 (CH), 130.8 (C), 129.1 (2 CH), 128.7 (2 CH), 127.2 (2 CH), 127.1 (2 CH), 126.5 (C), 106.9 (CH), 37.2 (CH_2); FTIR 3288, 1624, 1536, 1485, 1287, 823, 698 cm^{-1}; MS (ESI$^+$) *m/z* 334.1 $(M + Na)^+$; HRMS (ESI$^+$) calcd for $C_{18}H_{14}{}^{35}ClNNaO_2$ $(M + Na)^+$ 334.0611, found 334.0595.

***N*-(5-Methyl-furan-2-yl)methyl)benzamide 5m.** Following the procedure reported for the preparation of **6b**, with 5-methylfurfurylamine (1 mL, 8.97 mmol, 1.04 eq), Et_3N (1.25 mL, 8.97 mmol, 1.04 eq) and benzoyl chloride (1.40 mL, 8.61 mmol), the benzamide **5m** (1.72 g, 93 %) was obtained as a yellow solid; mp 66.5–66.7 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.79 (dd, *J* = 6.8, 1.7 Hz, 2 H), 7.42 (m, 3 H), 6.56 (br s, 1 H), 6.14 (d, *J* = 3.0 Hz, 1 H), 5.90 (d, *J* = 3.0 Hz, 1 H), 4.56 (d, *J* = 5.4 Hz, 2 H), 2.26 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ=167.3 (C), 152.1 (C), 149.4 (C), 134.4 (C), 131.6 (CH), 128.6 (2 CH), 127.1 (2 CH), 108.7 (CH), 106.4 (CH), 37.3 (CH_2), 13.6 (CH_3); FTIR 3328, 1642, 1600, 1573, 1541, 1489, 779 cm^{-1}; MS (ESI$^+$) *m/z* 238.1 $(M + Na)^+$, 270.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{13}H_{13}NNaO_2$ $(M + Na)^+$ 238.0844, found 238.0847.

***N*-((1*E*,3*E*)-5-Oxopenta-1,3-dienyl)acetamide 6a.** The general procedure was followed with diisopropylamine (565 µL, 4.03 mmol, 2.80 eq), *n*BuLi (2.5 M/hexanes) (1.70 mL, 4.25 mmol, 2.95 eq) and 201 mg (1.44 mmol) of *N*-(furan-2-ylmethyl)acetamide **5a**. The reaction mixture was allowed to warm from -78 °C to 0 °C over a period of 3 h and turned from orange to

yellow. After treatment A (see Experimental Section), the organic layer was separated dried ($MgSO_4$) concentrated and purified by chromatography on silica gel (CH_2Cl_2/EtOH 95/5) to afford **6a** (12.7 mg, 6 %) as an orange oil; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.61 (br d, J = 10.6 Hz, 1 H), 9.41 (d, J = 8.4 Hz, 1 H), 7.45 (m, 2 H), 6.07 (m, 2 H), 2.01 (s, 3 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 193.1 (C), 168.2 (C), 154.0 (CH), 136.5 (CH), 127.5 (CH), 109.3 (CH), 22.9 (CH_3); MS (ESI$^-$) *m/z* 138.1 (M – H); HRMS (ESI$^-$) calcd for $C_7H_8NO_2$ (M – H)$^-$ 138.0555, found 138.0558.

1-Methyl-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)-1*H*-pyrrole-2-carboxamide 6f. The general procedure was followed with diisopropylamine (1.92 mL, 13.7 mmol, 2.80 eq), *n*BuLi (2.5 M/hexanes) (5.8 mL, 14.5 mmol, 2.96 eq) and 1.0 g (4.90 mmol) of *N*-(furan-2-ylmethyl)-1-methyl-1*H*-pyrrole-2-carboxamide **5f**. The reaction mixture was allowed to warm from -78 °C to -45 °C and turned from red to orange. After treatment A (see Experimental Section) and chromatography on silica gel (CH_2Cl_2/acetone 95/5), **6f** (425 mg, 43 %) was obtained as a red powder; mp 199.3–201.4 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.59 (d, J = 10.9 Hz, 1 H), 9.43 (d, J = 8.1 Hz, 1 H), 7.66 (dd, J = 13.5, 10.9 Hz, 1 H), 7.48 (dd, J = 14.9, 11.4 Hz, 1 H), 7.09 (m, 2 H), 6.29 (dd, J = 13.5, 11.4 Hz, 1 H), 6.13 (dd, J = 3.8, 2.9 Hz, 1 H), 6.04 (dd, J = 14.9, 8.1 Hz, 1 H), 3.88 (s, 3 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 193.0 (C), 158.2 (C), 154.3 (CH), 137.2 (CH), 130.5 (CH), 126.9 (CH), 123.7 (C), 115.2 (CH), 109.4 (CH), 107.4 (CH), 36.5 (CH_3); FTIR 3225, 1674, 1587, 1531, 1165, 1074, 984, 739 cm^{-1}; MS (ESI$^+$) *m/z* 227.1 (M + Na)$^+$, 259.1 (M + Na + MeOH)$^+$; HRMS (ESI$^+$) calcd for $C_{11}H_{12}N_2NaO_2$ (M + Na)$^+$ 227.0796, found 227.0790.

***N*-Benzylidene-1-(furan-2-yl)methylamine 7.** To a stirred solution of benzaldehyde (1.10 mL, 10.8 mmol, 1 eq) in CH_2Cl_2 (10 mL) under argon at ambient temperature, was added

furfurylamine (950 μL, 10.8 mmol) and $MgSO_4$ (2 g). The resulting reaction mixture was stirred at room temperature overnight, filtered and concentrated in vacuo to give the imine **7** (1.02 g, 53 %) as an orange solid; mp 28.7–29.9 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.35 (s, 1 H), 7.80 (dd, J = 7.6, 2.0 Hz, 2 H), 7.42 (m, 4 H), 6.37 (m, 1 H), 6.30 (m, 1 H), 4.78 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.1 (CH), 152.5 (C), 142.3 (CH), 136.1 (C), 131.0 (CH), 128.7 (2 CH), 128.4 (2 CH), 110.5 (CH), 107.6 (CH), 57.3 (CH_2); FTIR 1701, 1643, 1008, 730 cm^{-1}; MS (ESI$^+$) *m/z* 186.1 $(M + H)^+$; HRMS (ESI$^+$) calcd for $C_{12}H_{12}NO$ $(M + H)^+$, 186.0919, found 186.0911.

***N*-(Furan-2-ylmethyl)benzenesulfonamide 8.**[7] To a stirred solution of furfurylamine (950 μL, 10.8 mmol) and Et_3N (1.45 mL, 10.4 mmol, 0.96 eq) in CH_2Cl_2 (25 mL) under argon at 0 °C was added benzenesulfonyl chloride (1.85 mL, 10.8 mmol, 1 eq). The resulting reaction mixture was allowed to warm to ambient temperature and stirred for 2 days. The mixture was washed with water (3 × 25 mL) and the organic layer was separated, dried ($MgSO_4$), concentrated and purified by silica gel column chromatography (CH_2Cl_2/acetone 99/1) to afford the sulfonamide **8** (1.37 g, 56 %) as a yellow solid; mp 83.4–84.0 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83 (m, 2 H), 7.50 (m, 3 H), 7.21 (dd, J = 1.8, 0.4 Hz, 1 H), 6.19 (dd, J = 3.1, 1.8 Hz, 1 H), 6.07 (dd, J = 3.1, 0.4 Hz, 1 H), 5.02 (br t, J = 6.2 Hz, 1 H), 4.19 (d, J = 6.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.5 (C), 142.6 (CH), 140.0 (C), 132.7 (CH), 129.1 (2 CH), 127.2 (2 CH), 110.5 (CH), 108.4 (CH), 40.2 (CH_2); FTIR 3305, 1316, 1153, 747 cm^{-1}; MS (ESI$^+$) *m/z* 260.0 $(M + Na)^+$, 292.1 $(M + Na + MeOH)^+$; HRMS (ESI$^+$) calcd for $C_{11}H_{11}NNaO_3S$ $(M + Na)^+$ 260.0357, found 260.0350.

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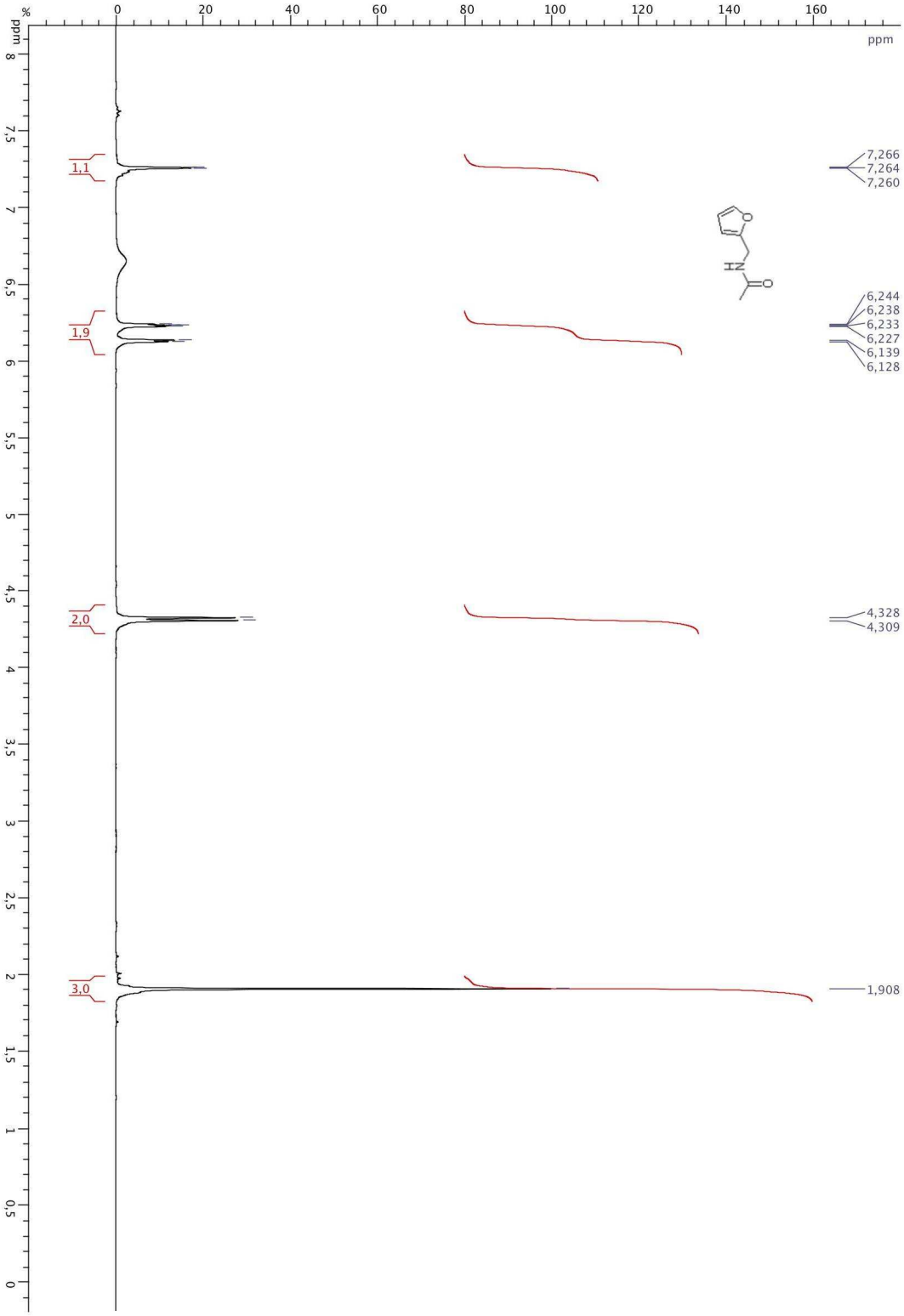
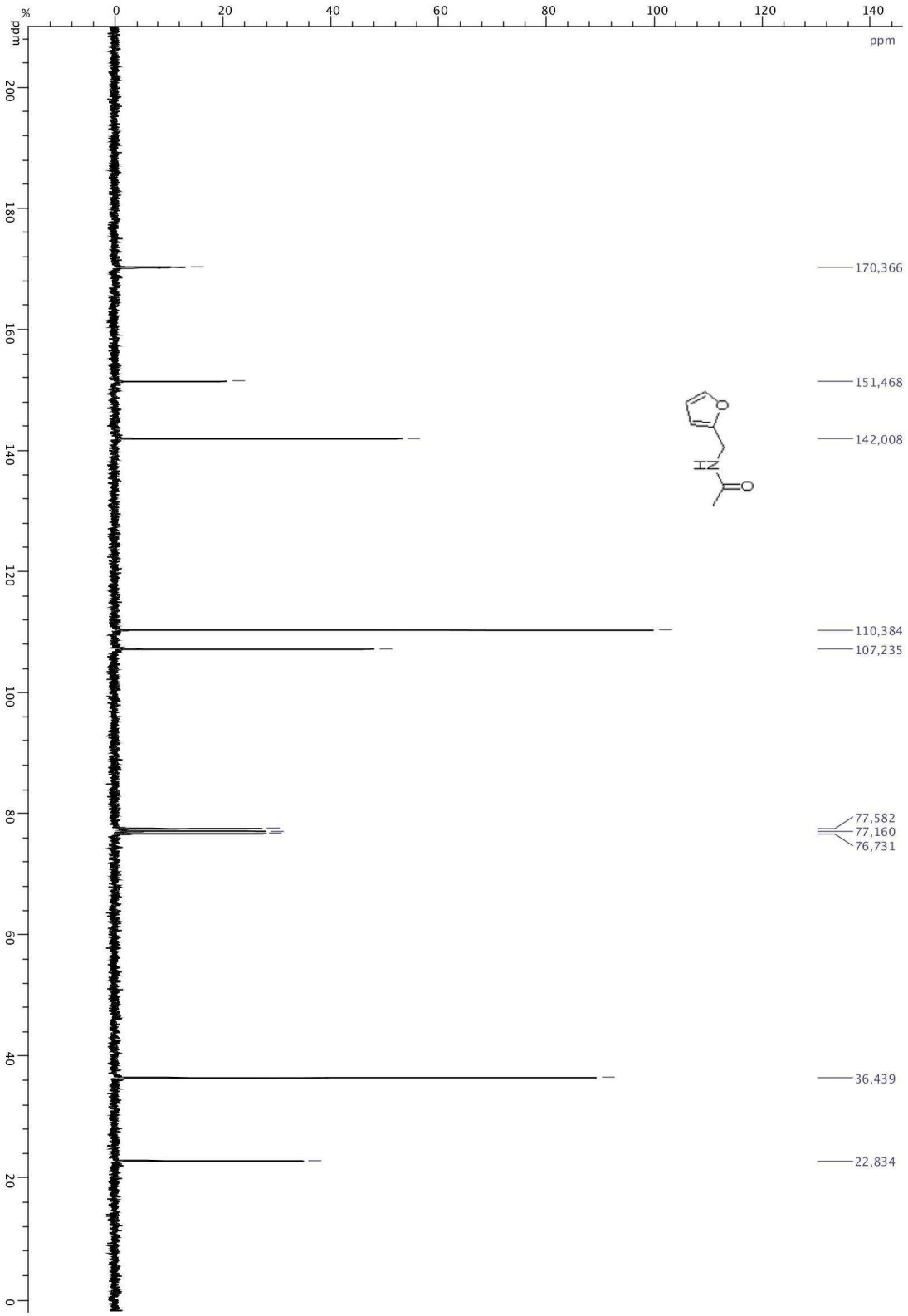
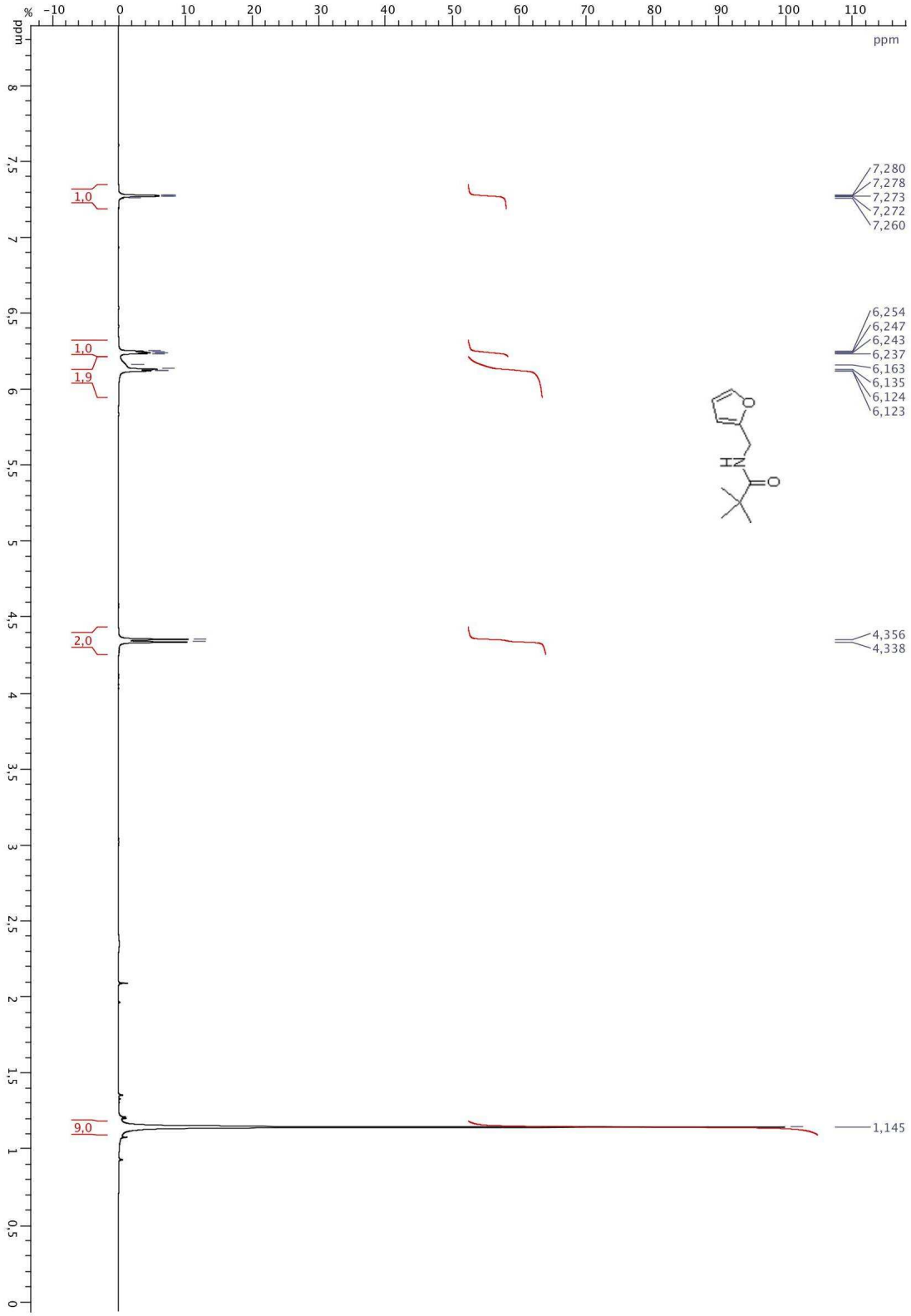
^{1}H NMR of *N*-(furan-2-ylmethyl)acetamide 5a ($CDCl_3$, 300 MHz)



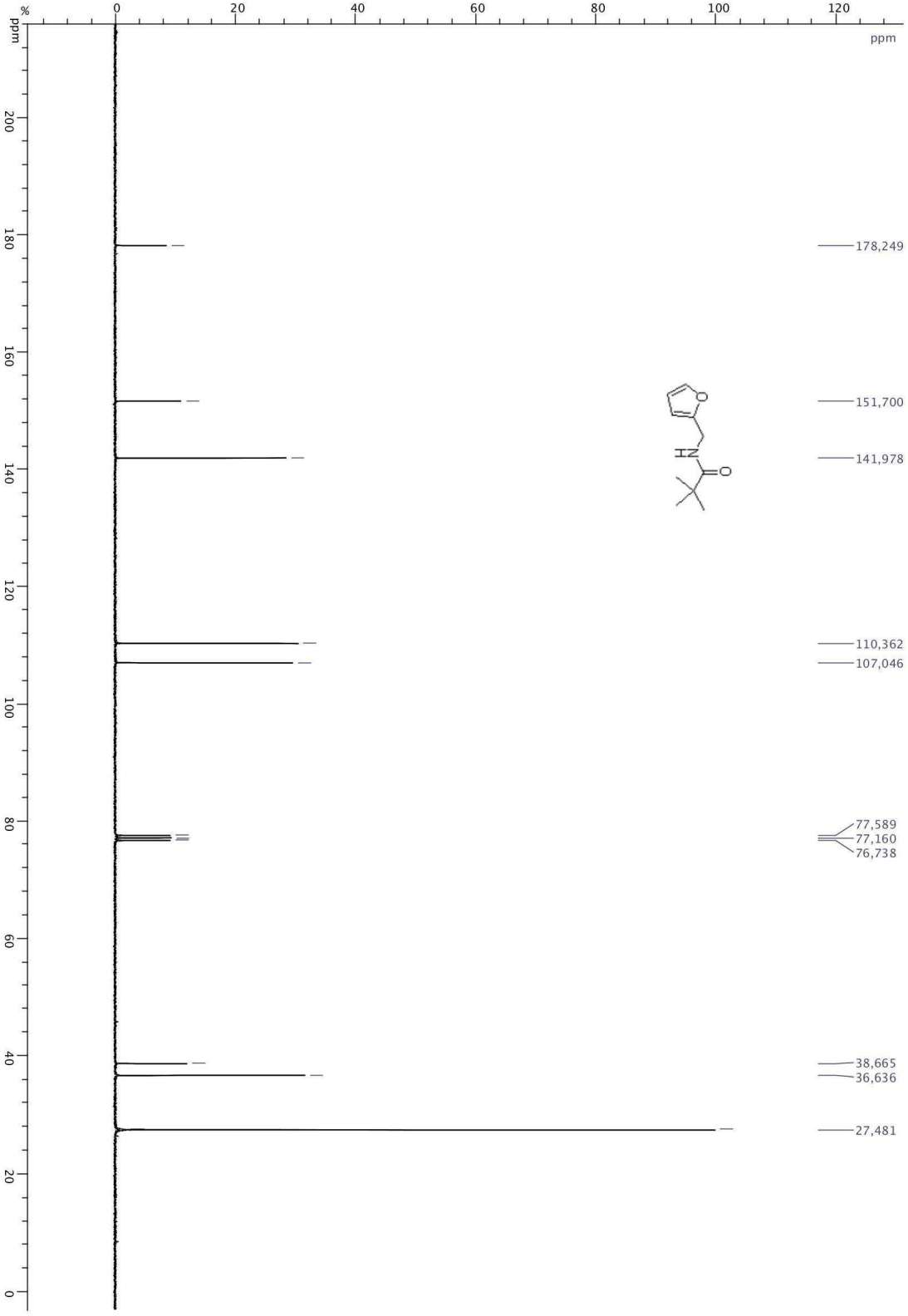
^{13}C NMR of *N*-(furan-2-ylmethyl)acetamide 5a ($CDCl_3$, 75 MHz)



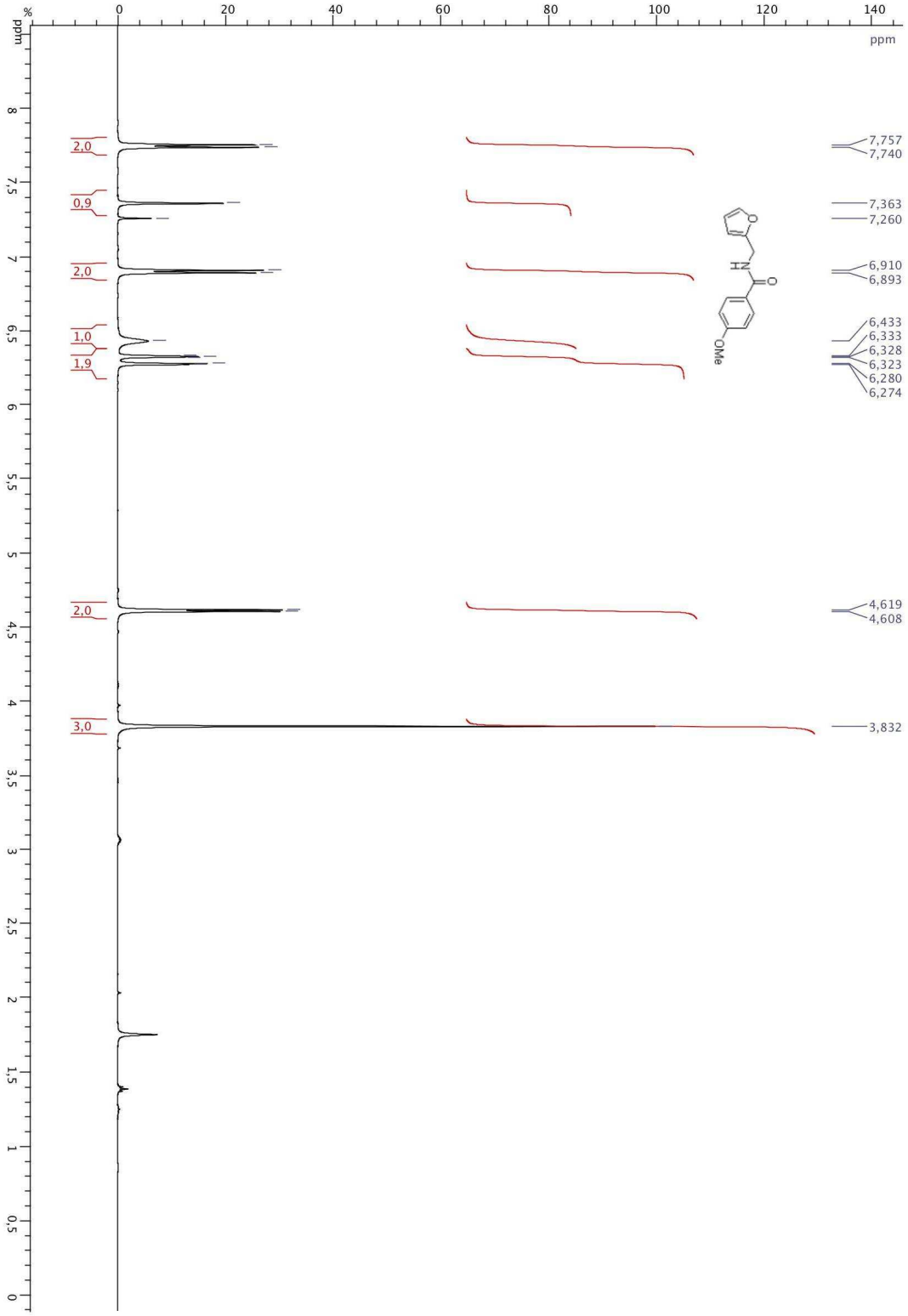
^{1}H NMR of *N*-(furan-2-ylmethyl)-2,2-dimethyl-propionamide 5b ($CDCl_3$, 300 MHz)



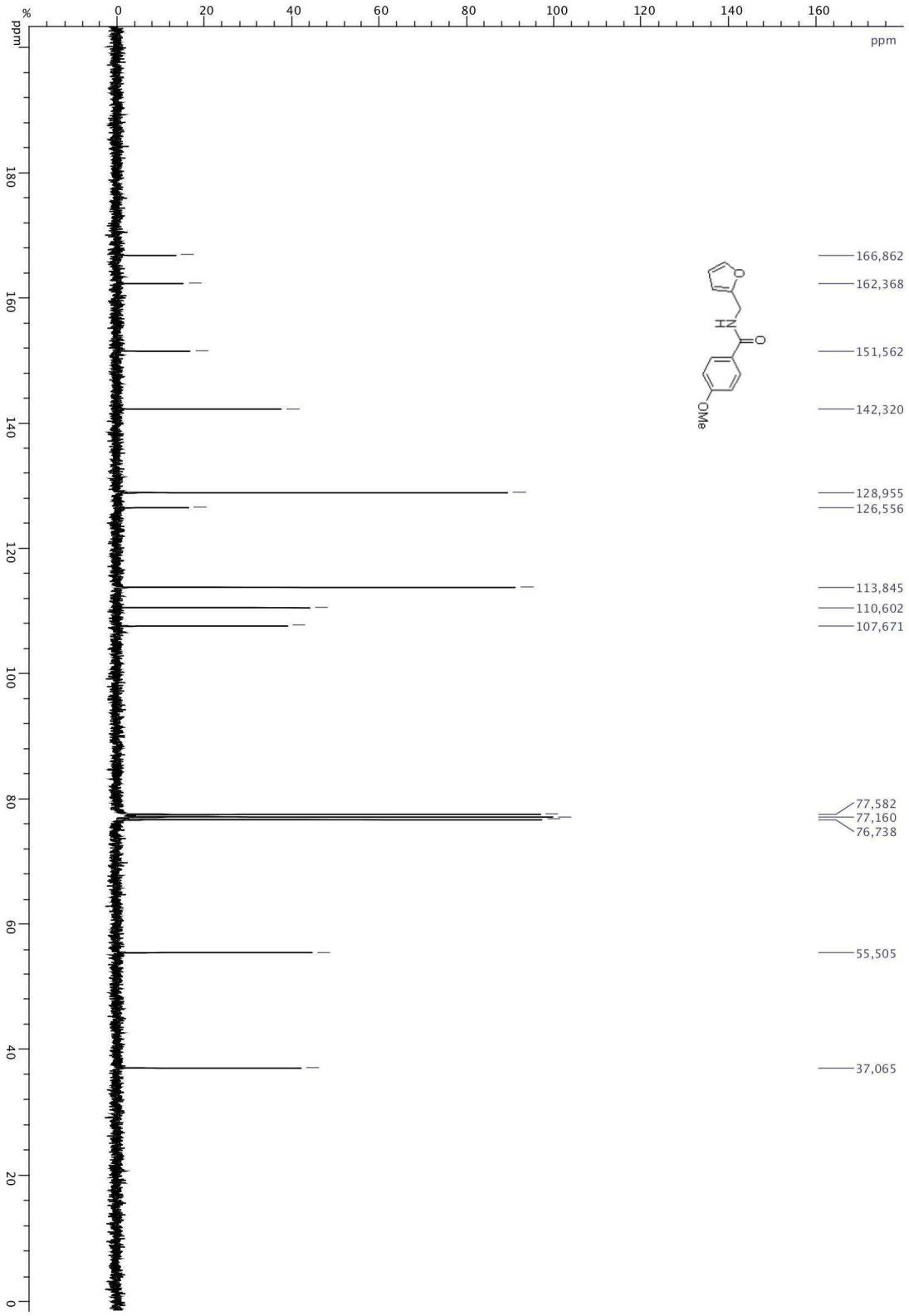
^{13}C NMR of *N*-(furan-2-ylmethyl)-2,2-dimethyl-propionamide 5b ($CDCl_3$, 75 MHz)



^{1}H NMR of *N*-(furan-2-ylmethyl)-4-methoxybenzamide 5c ($CDCl_3$, 300 MHz)



^{13}C NMR of *N*-(furan-2-ylmethyl)-4-methoxybenzamide 5c ($CDCl_3$, 75 MHz)



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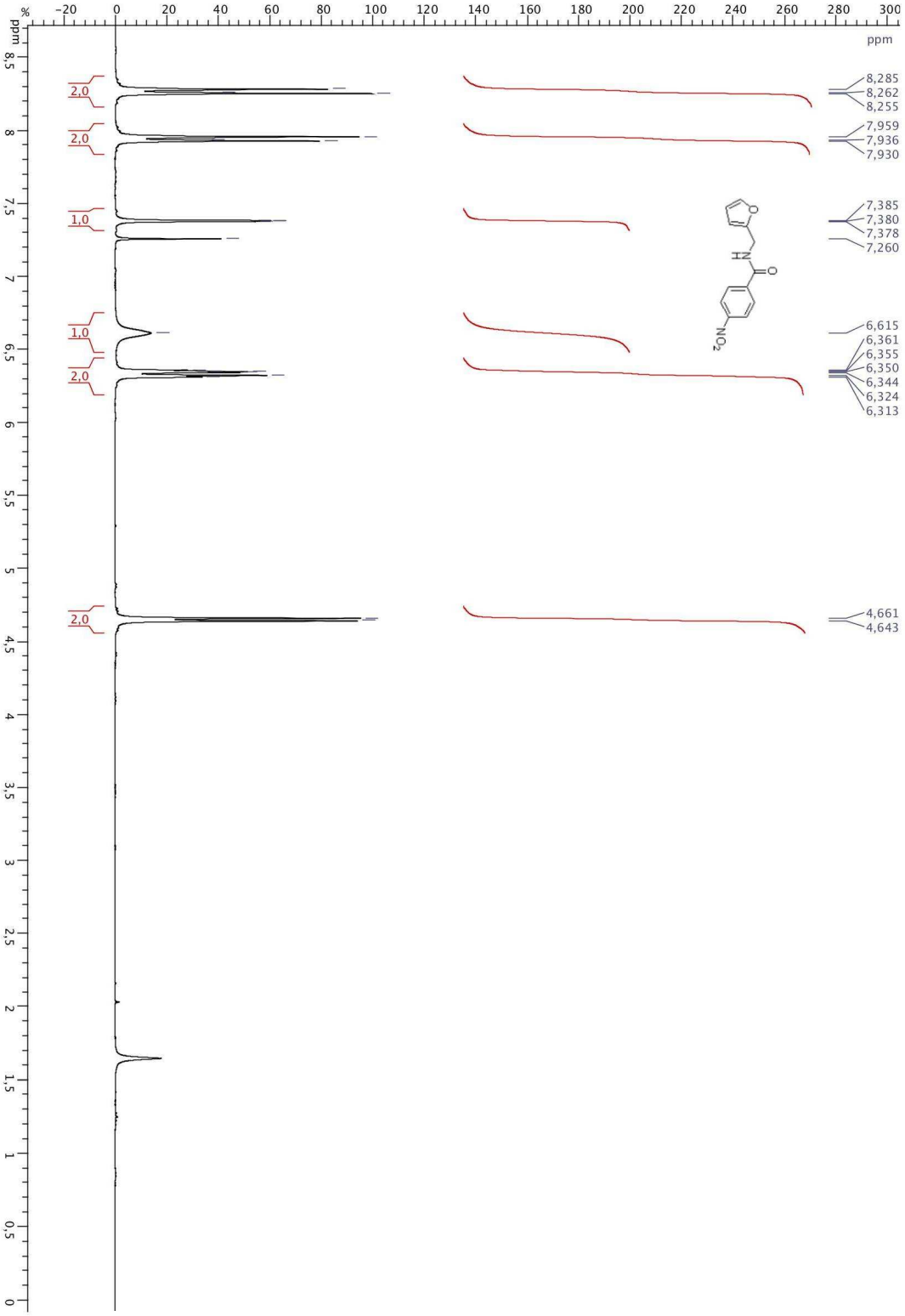
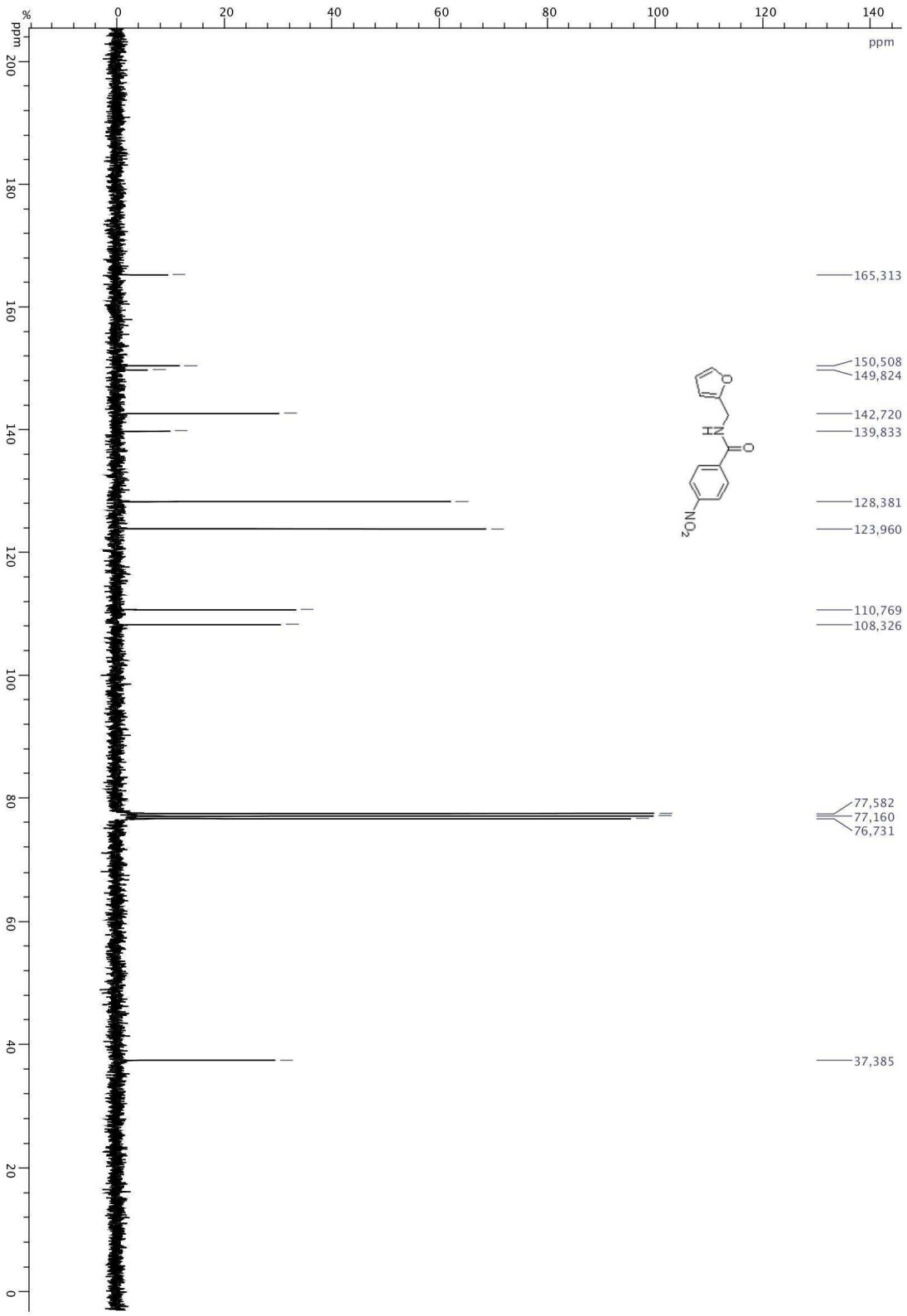
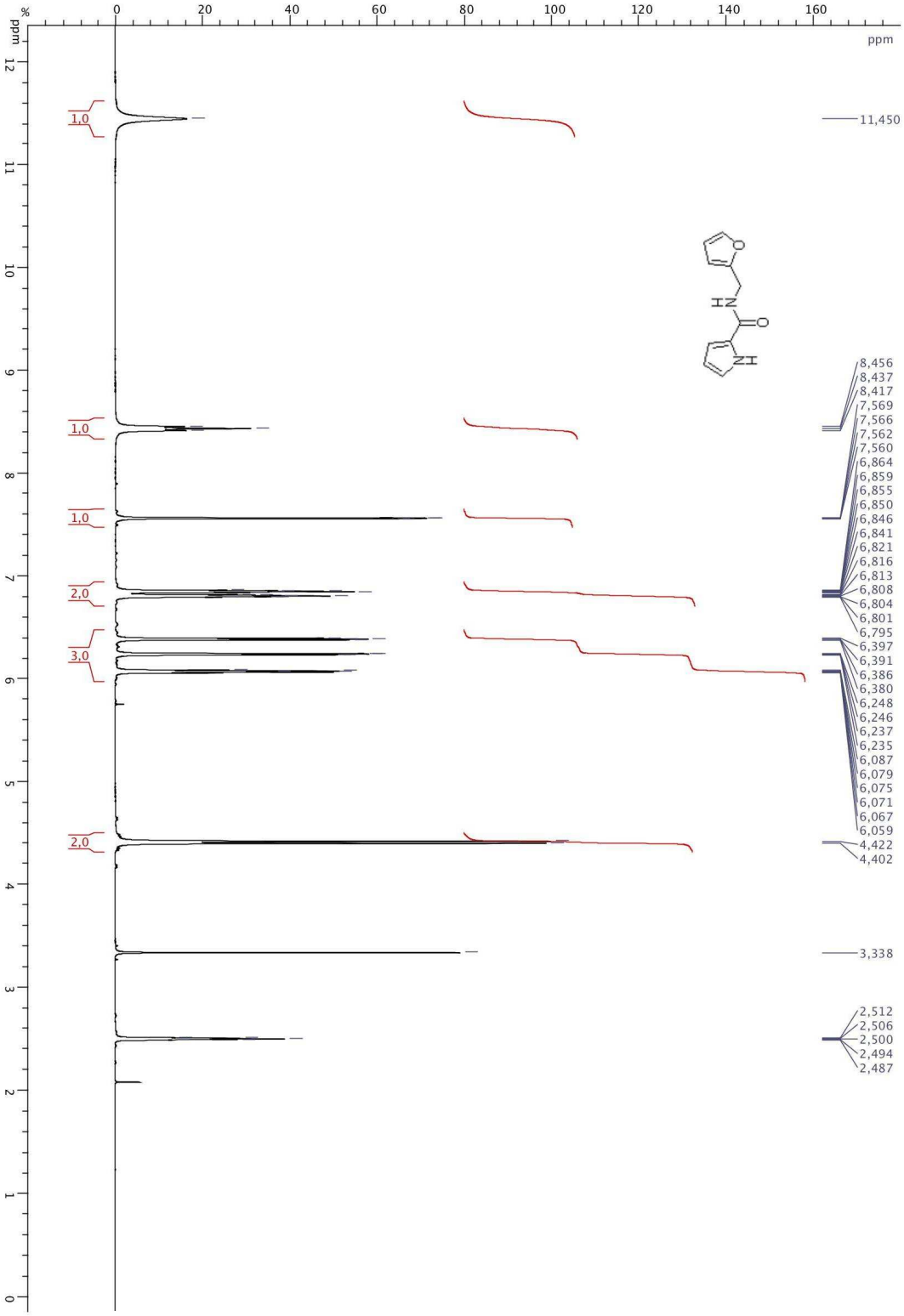


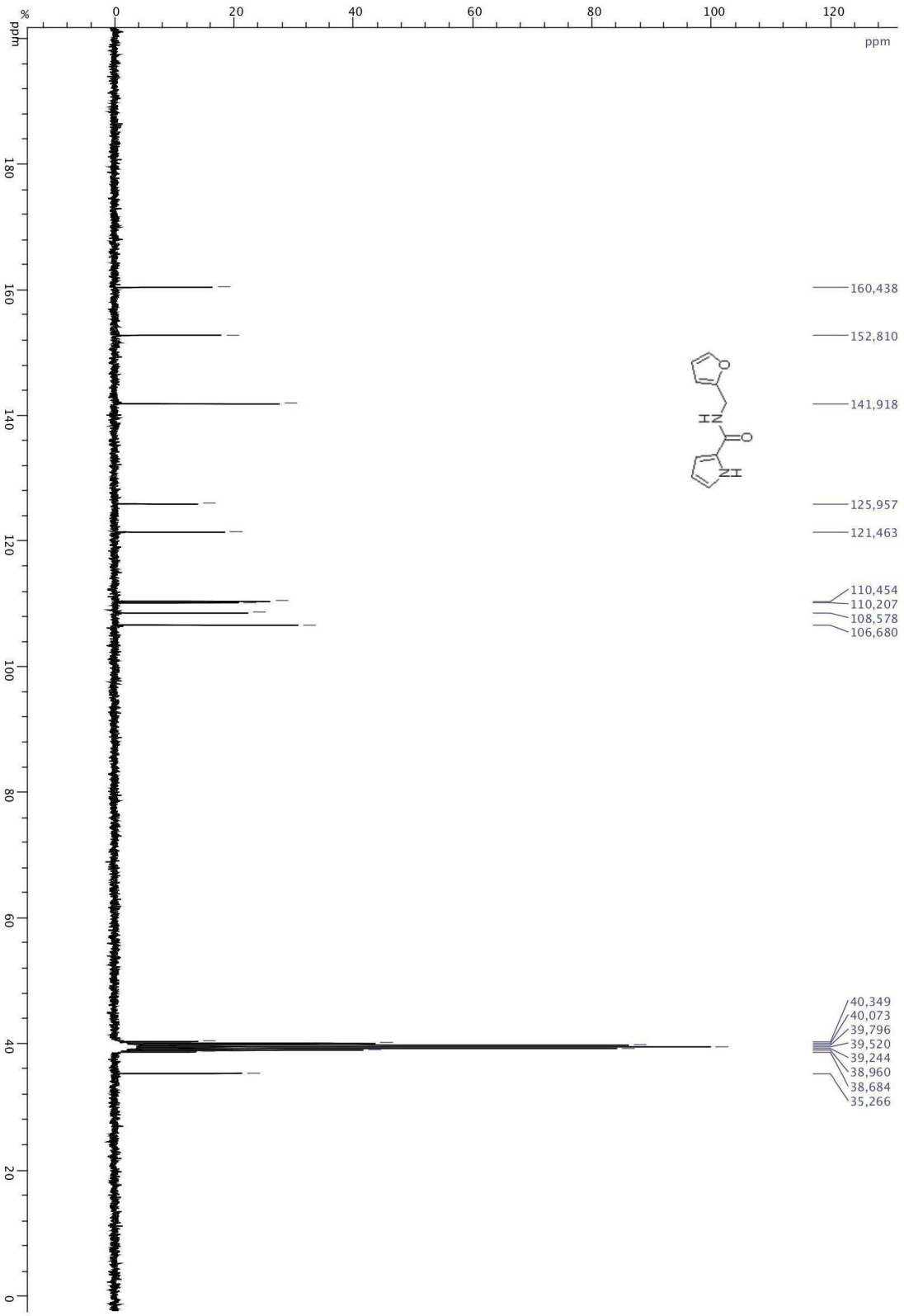
^{13}C NMR of *N*-(furan-2-ylmethyl)-4-nitrobenzamide 5d ($CDCl_3$, 75 MHz)



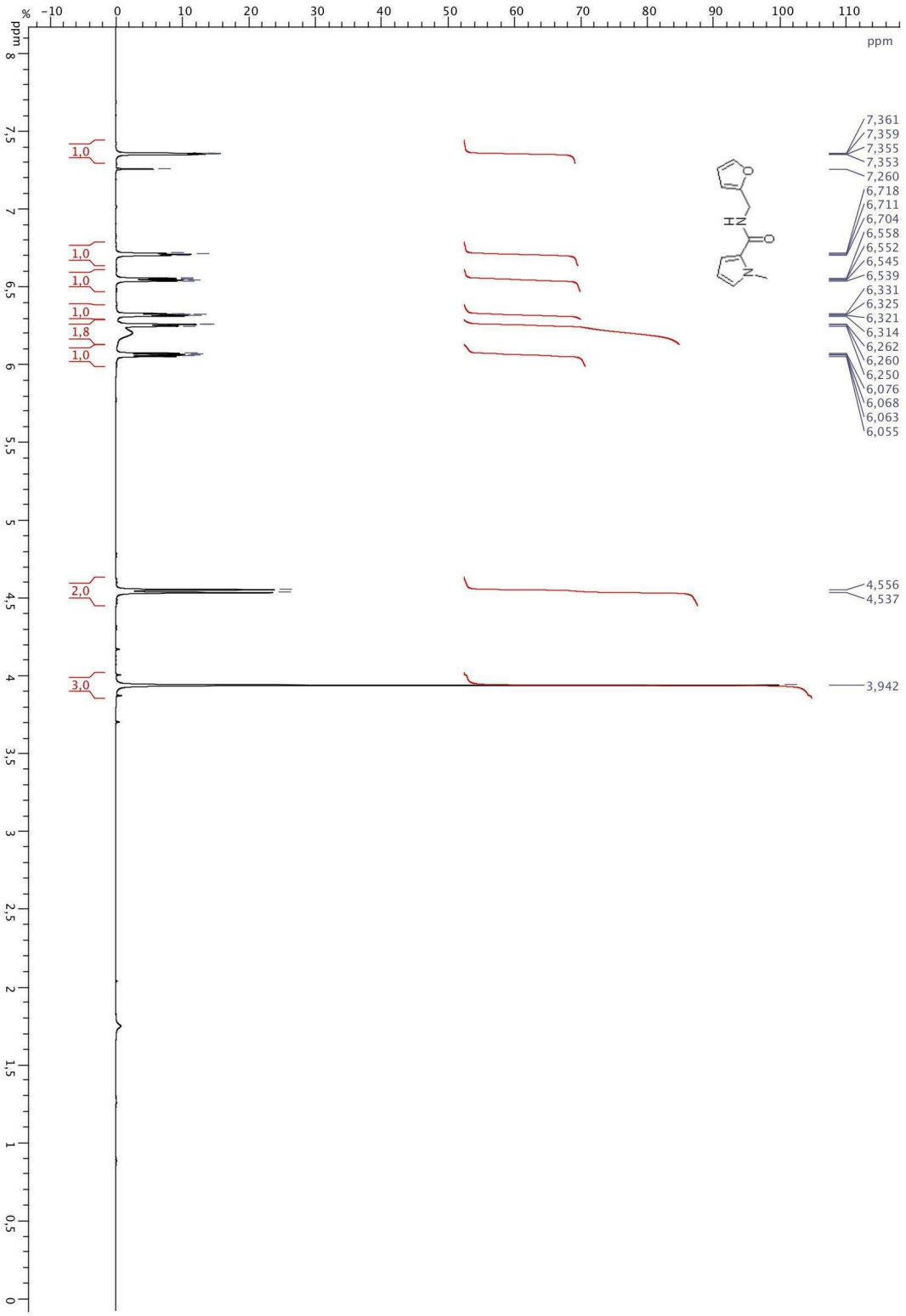
^{1}H NMR of *N*-(furan-2-ylmethyl)-1*H*-pyrrole-2-carboxamide 5e (DMSO-d_6, 300 MHz)



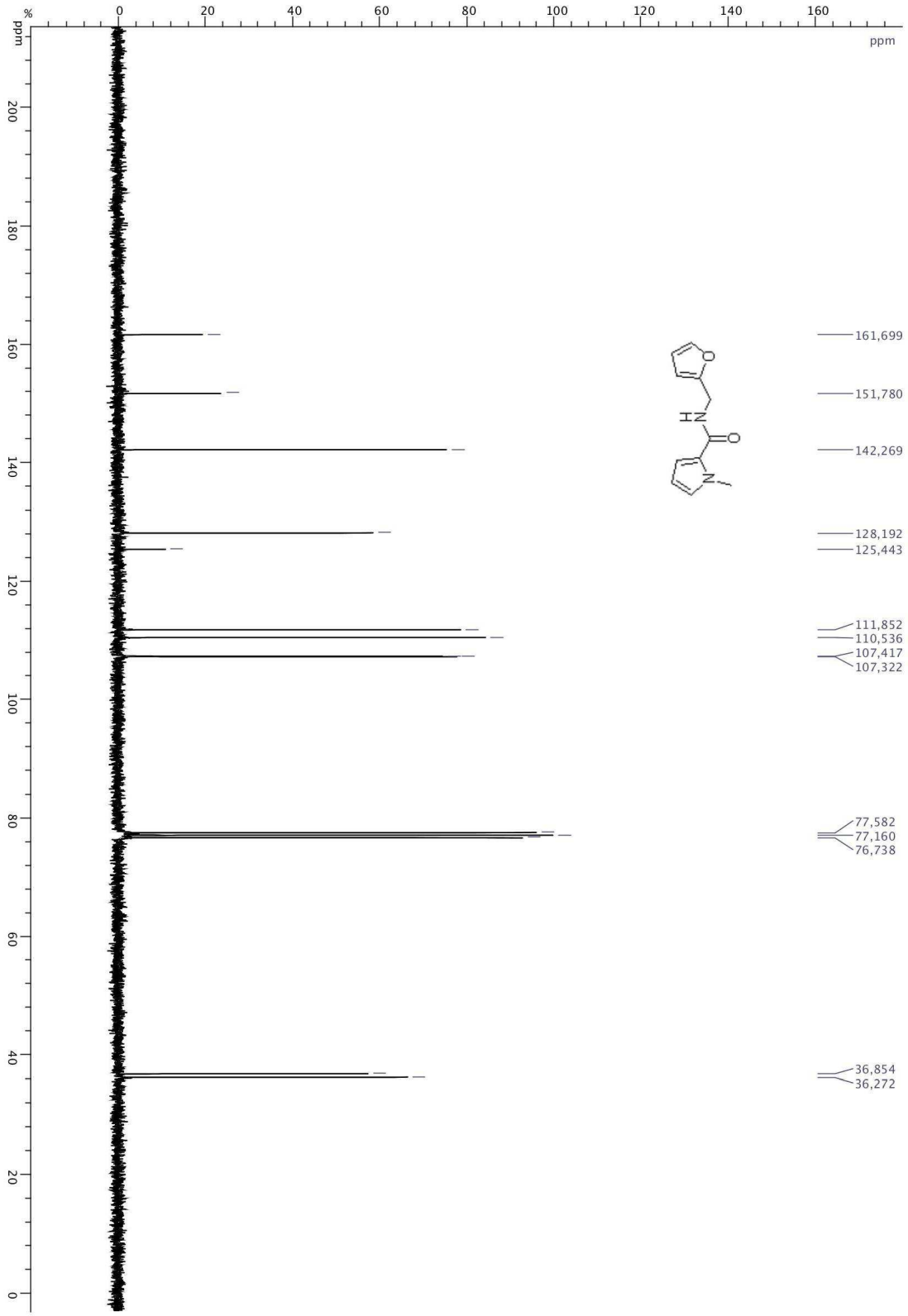
^{13}C NMR of *N*-(furan-2-ylmethyl)-1*H*-pyrrole-2-carboxamide 5e (DMSO-d_6, 75 MHz)



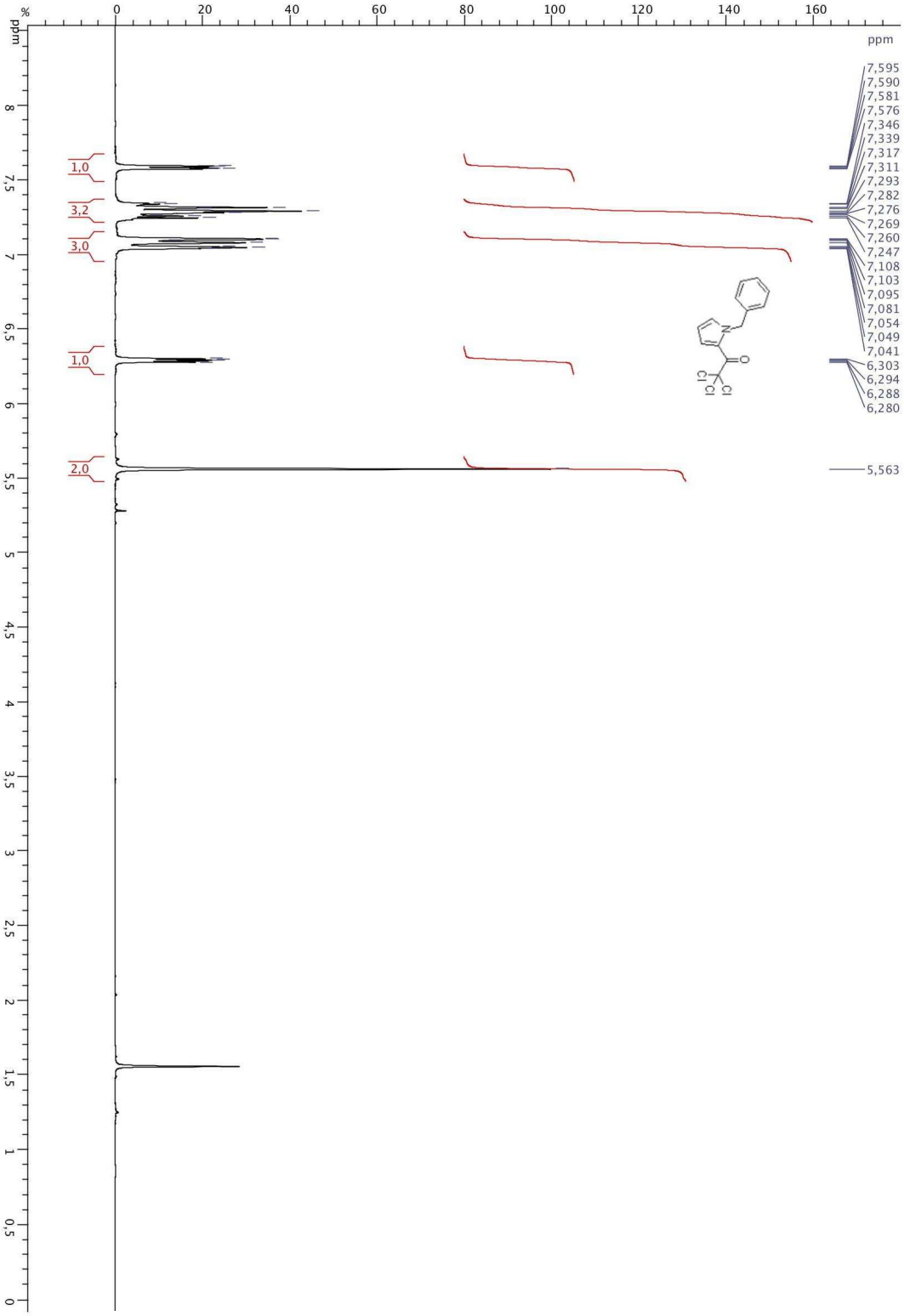
^{1}H NMR of *N*-(furan-2-ylmethyl)-1-methyl-1*H*-pyrrole-2-carboxamide 5f ($CDCl_3$, 300 MHz)



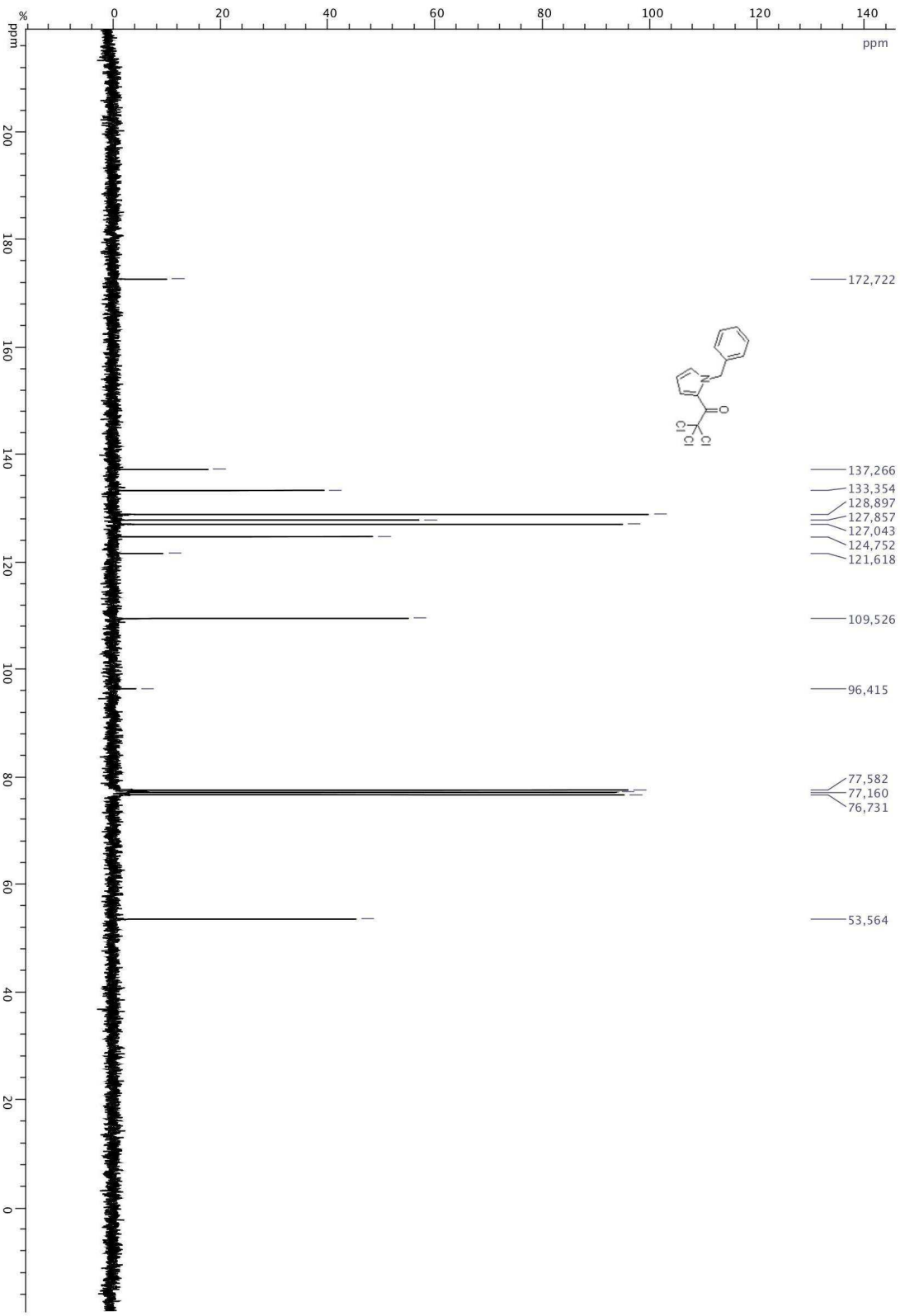
^{13}C NMR of *N*-(furan-2-ylmethyl)-1-methyl-1*H*-pyrrole-2-carboxamide 5f ($CDCl_3$, 75 MHz)



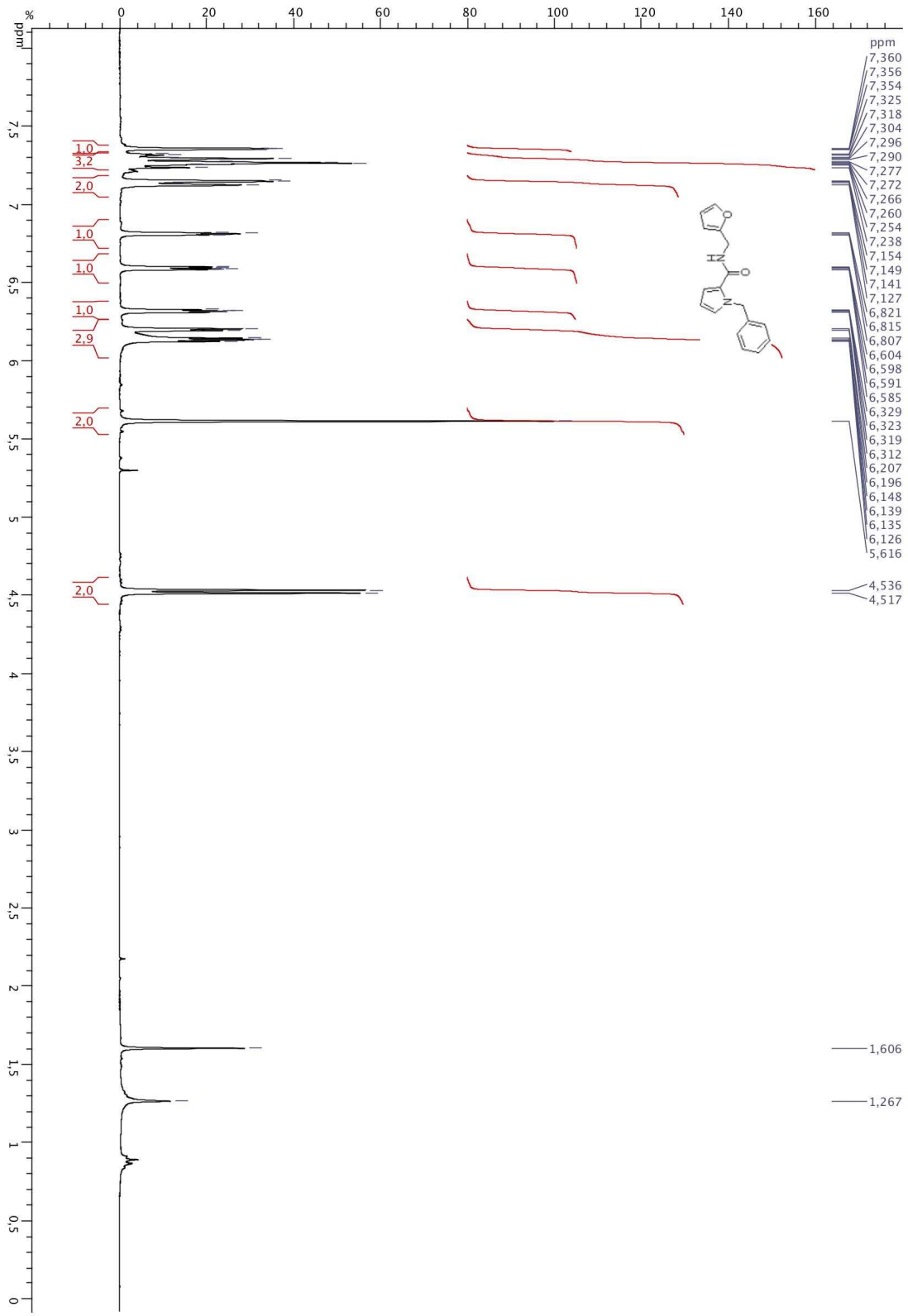
^{1}H NMR of *N*-benzyl-2-trichloroacetylpyrrole ($CDCl_3$, 300 MHz)



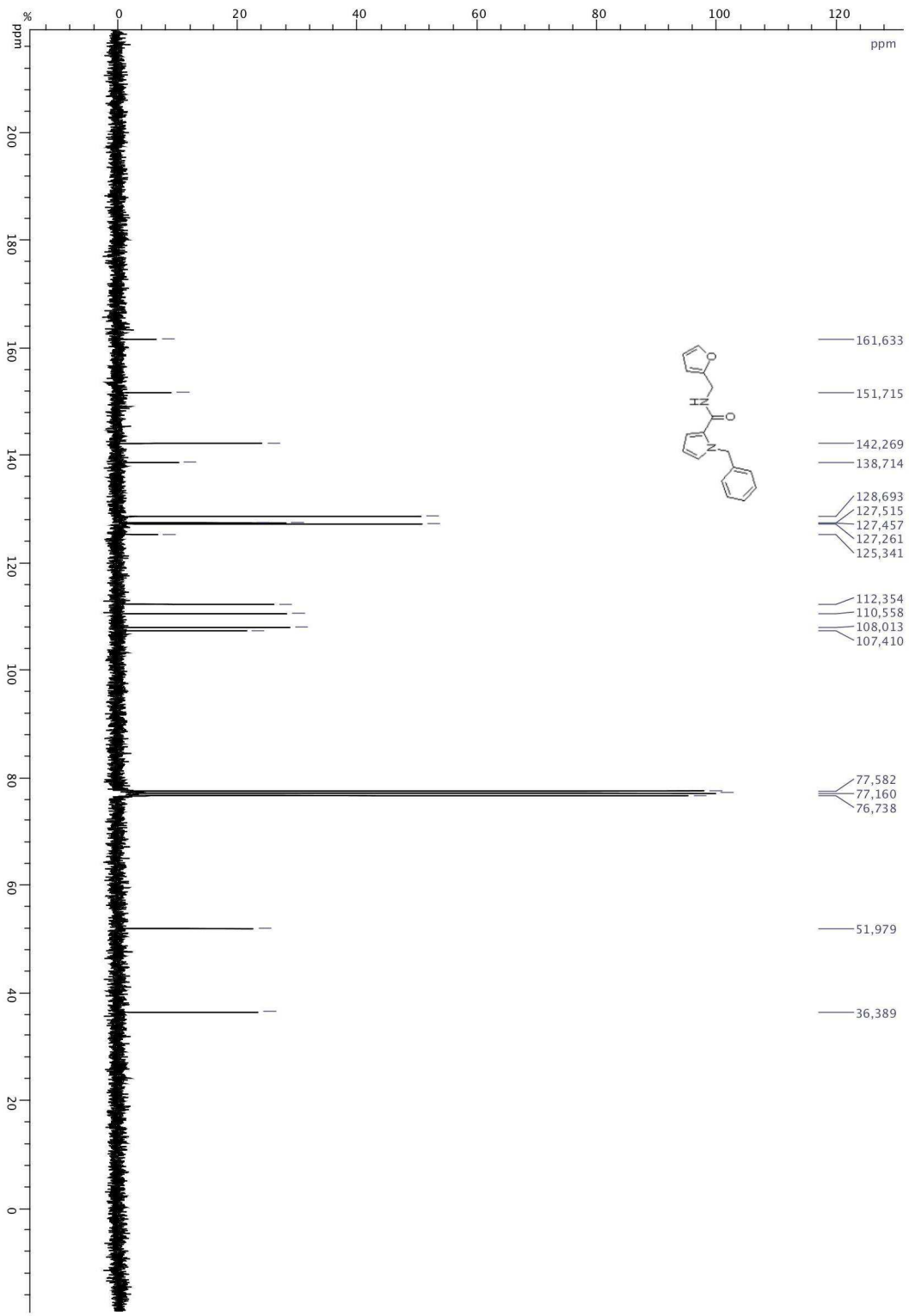
^{13}C NMR of *N*-benzyl-2-trichloroacetylpyrrole ($CDCl_3$, 75 MHz)



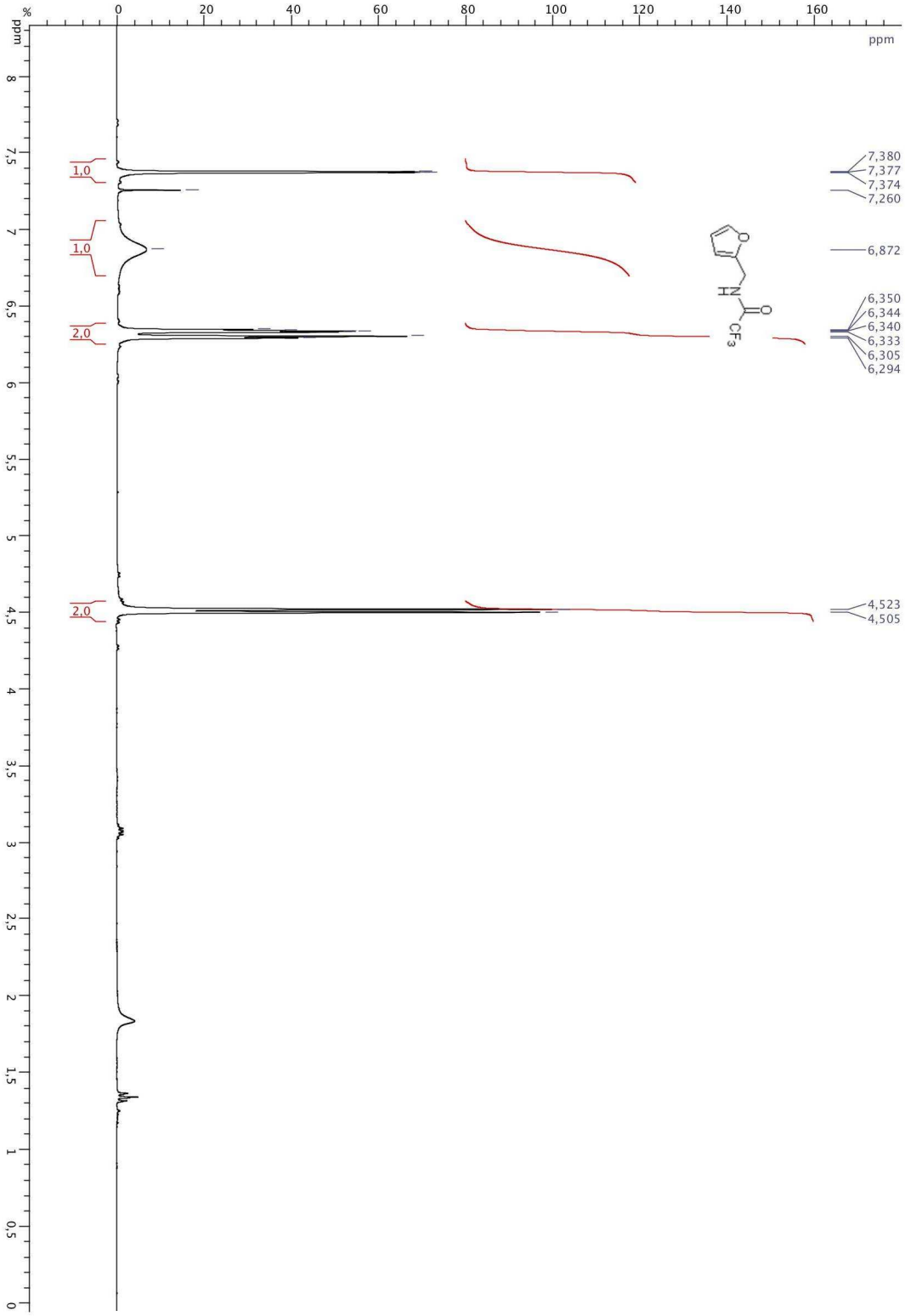
^{1}H NMR of 1-benzyl-*N*-(furan-2-ylmethyl)-1*H*-pyrrole-2-carboxamide 5g (3) ($CDCl_3$, 300 MHz)



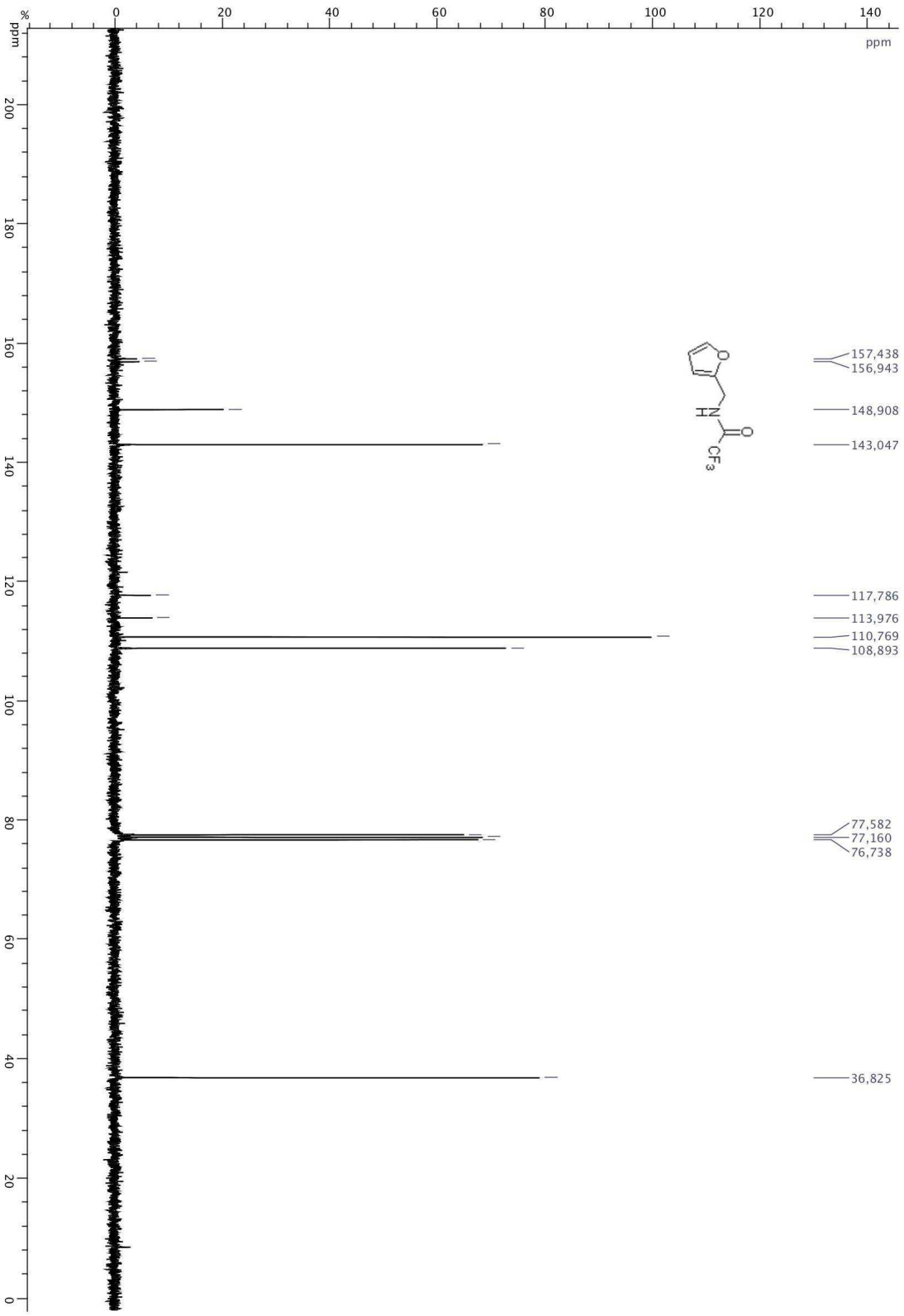
^{13}C NMR of 1-benzyl-*N*-(furan-2-ylmethyl)-1*H*-pyrrole-2-carboxamide 5g (3) ($CDCl_3$, 75 MHz)



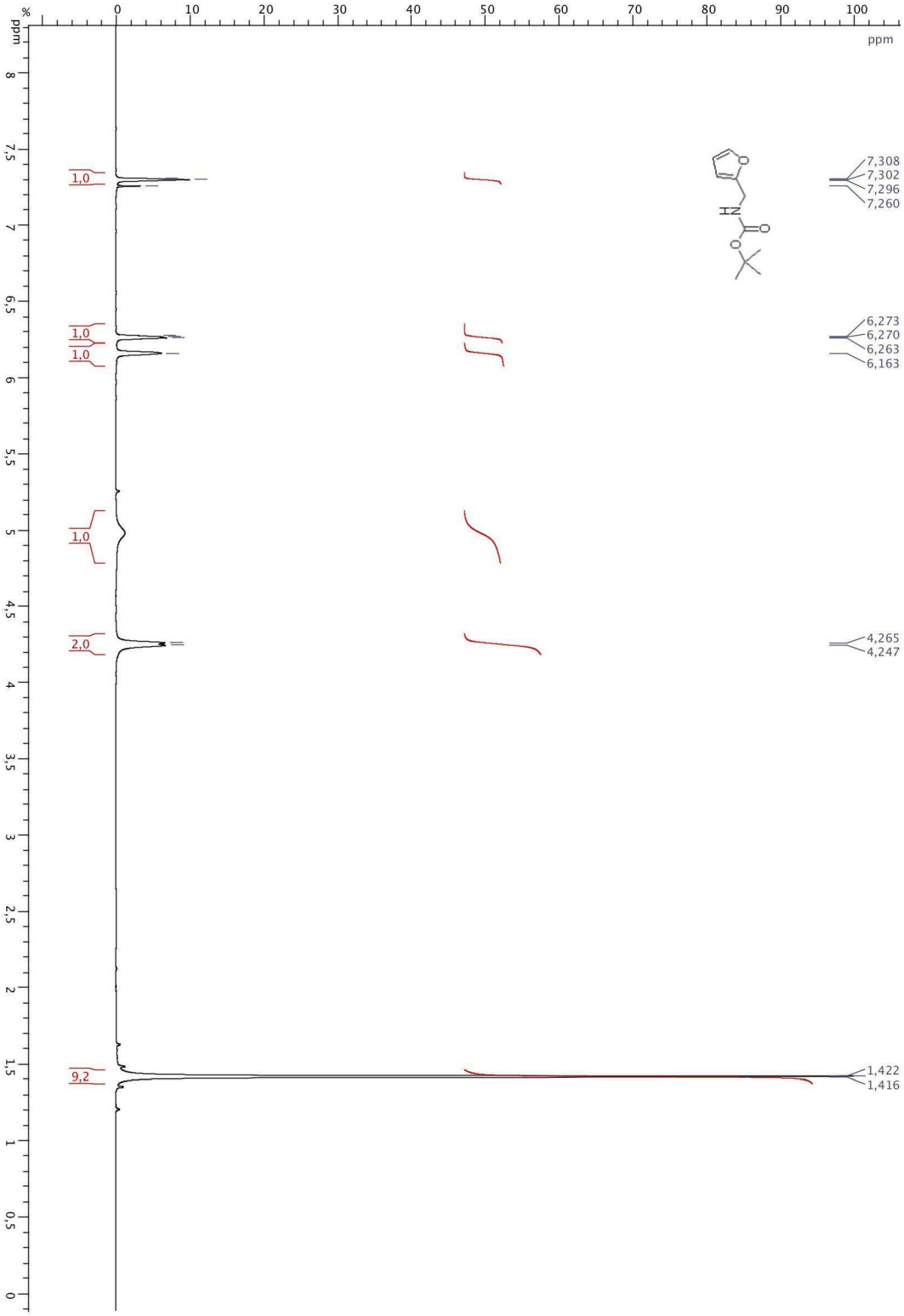
^{1}H NMR of 2,2,2-trifluoro-*N*-(furan-2-ylmethyl)acetamide 5h ($CDCl_3$, 300 MHz)



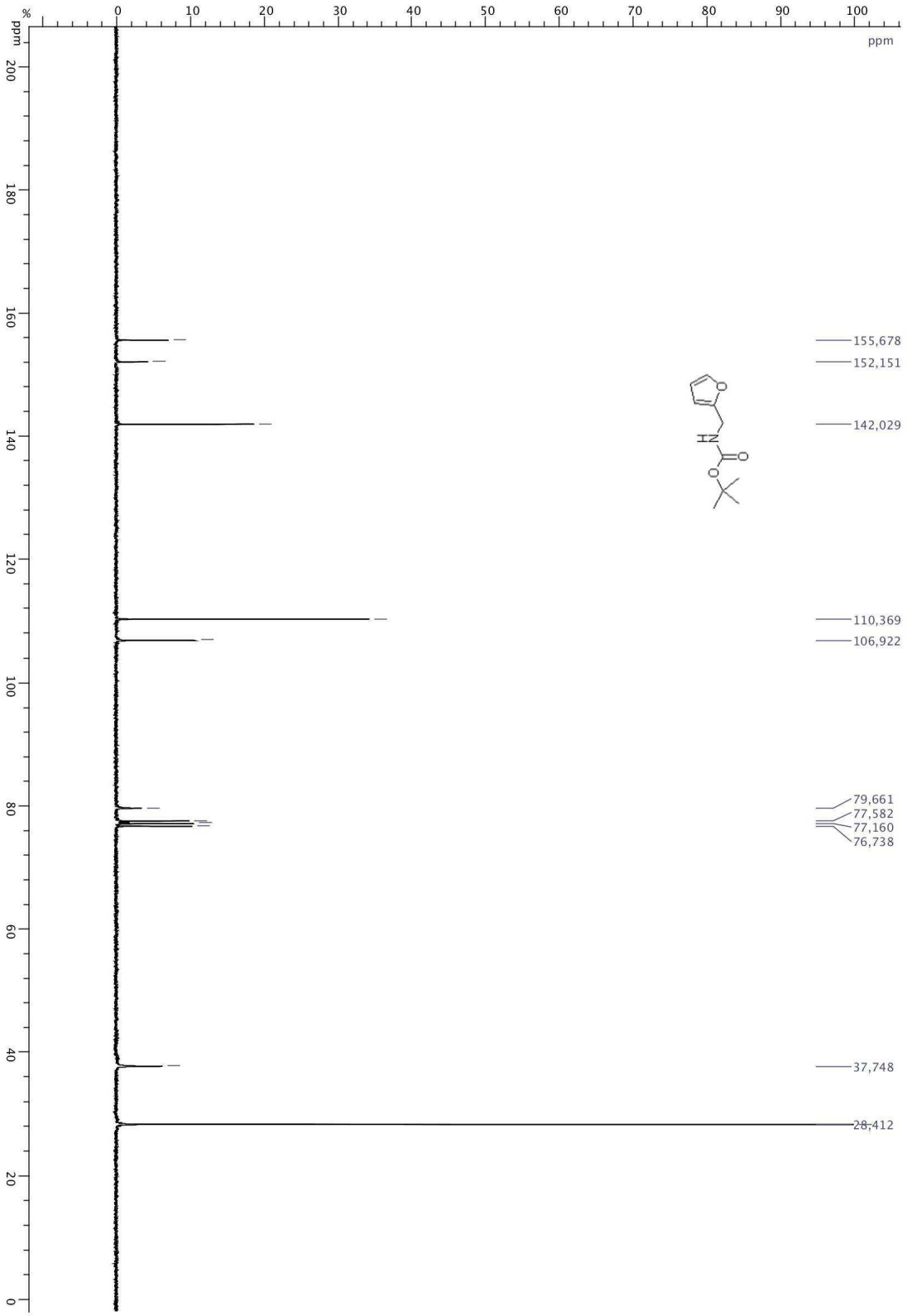
^{13}C NMR of 2,2,2-trifluoro-*N*-(furan-2-ylmethyl)acetamide 5h ($CDCl_3$, 75 MHz)



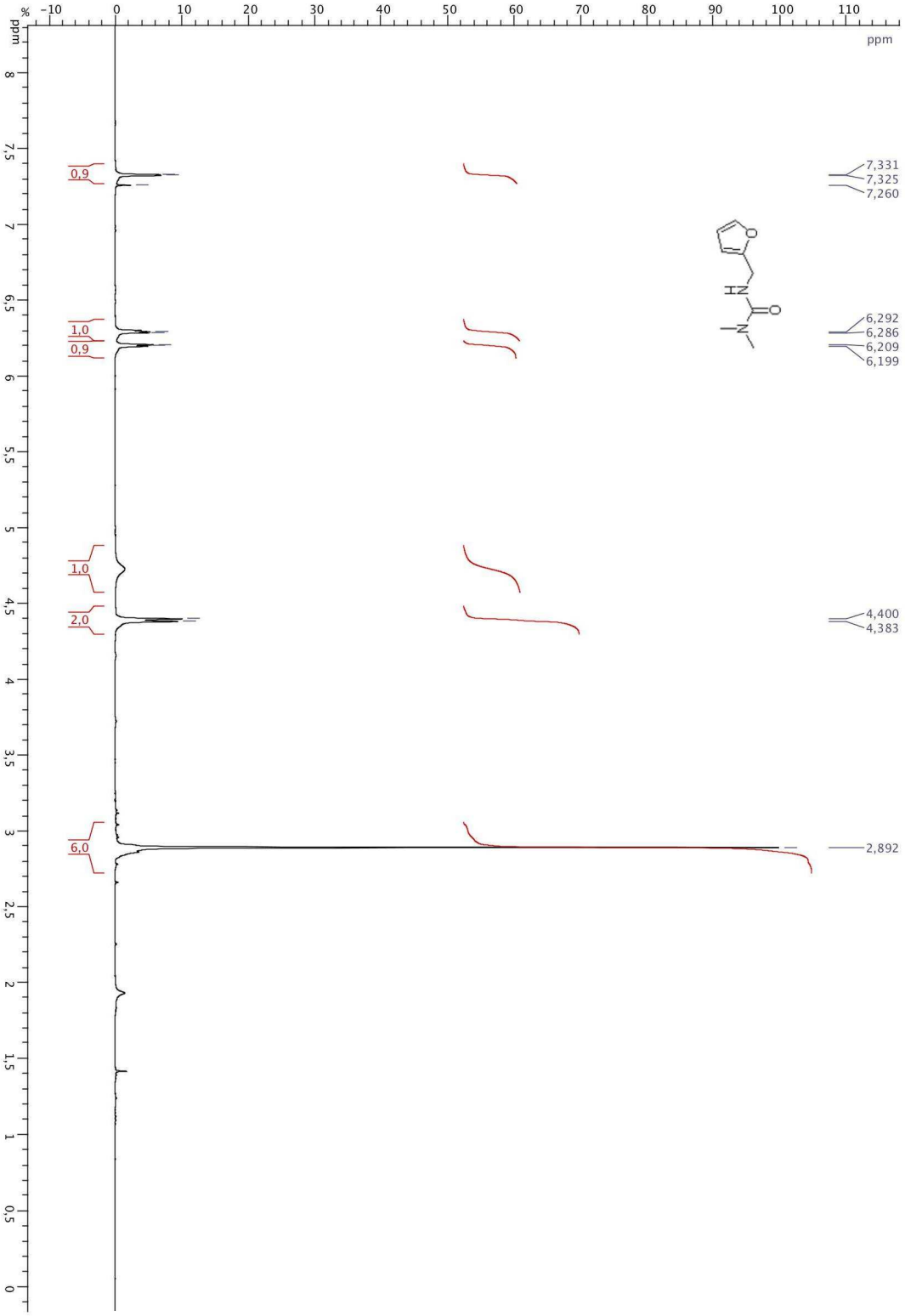
^{1}H NMR of *tert*-butyl furan-2-ylmethylcarbamate 5i ($CDCl_3$, 300 MHz)



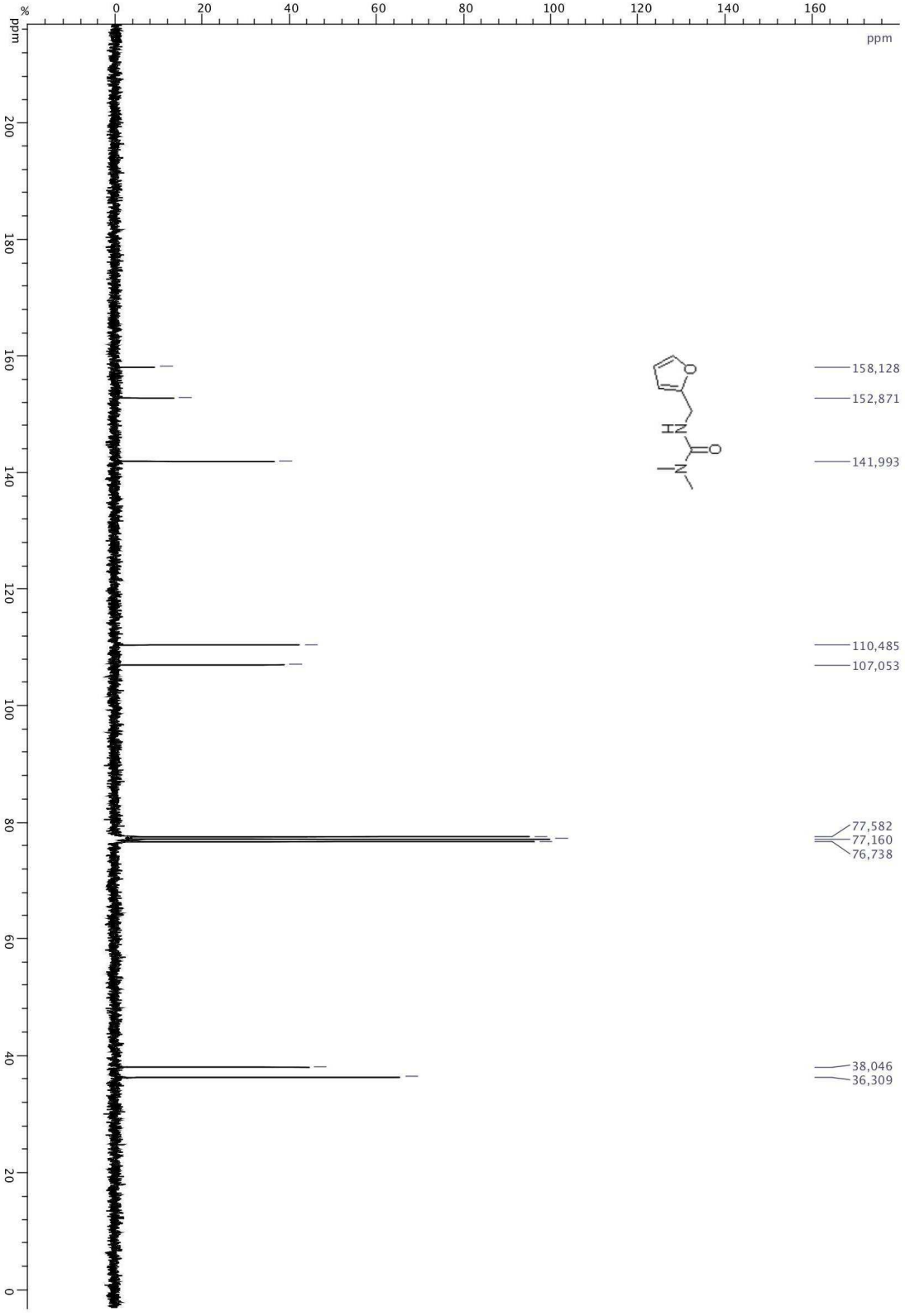
^{13}C NMR of *tert*-butyl furan-2-ylmethylcarbamate 5i ($CDCl_3$, 75 MHz)



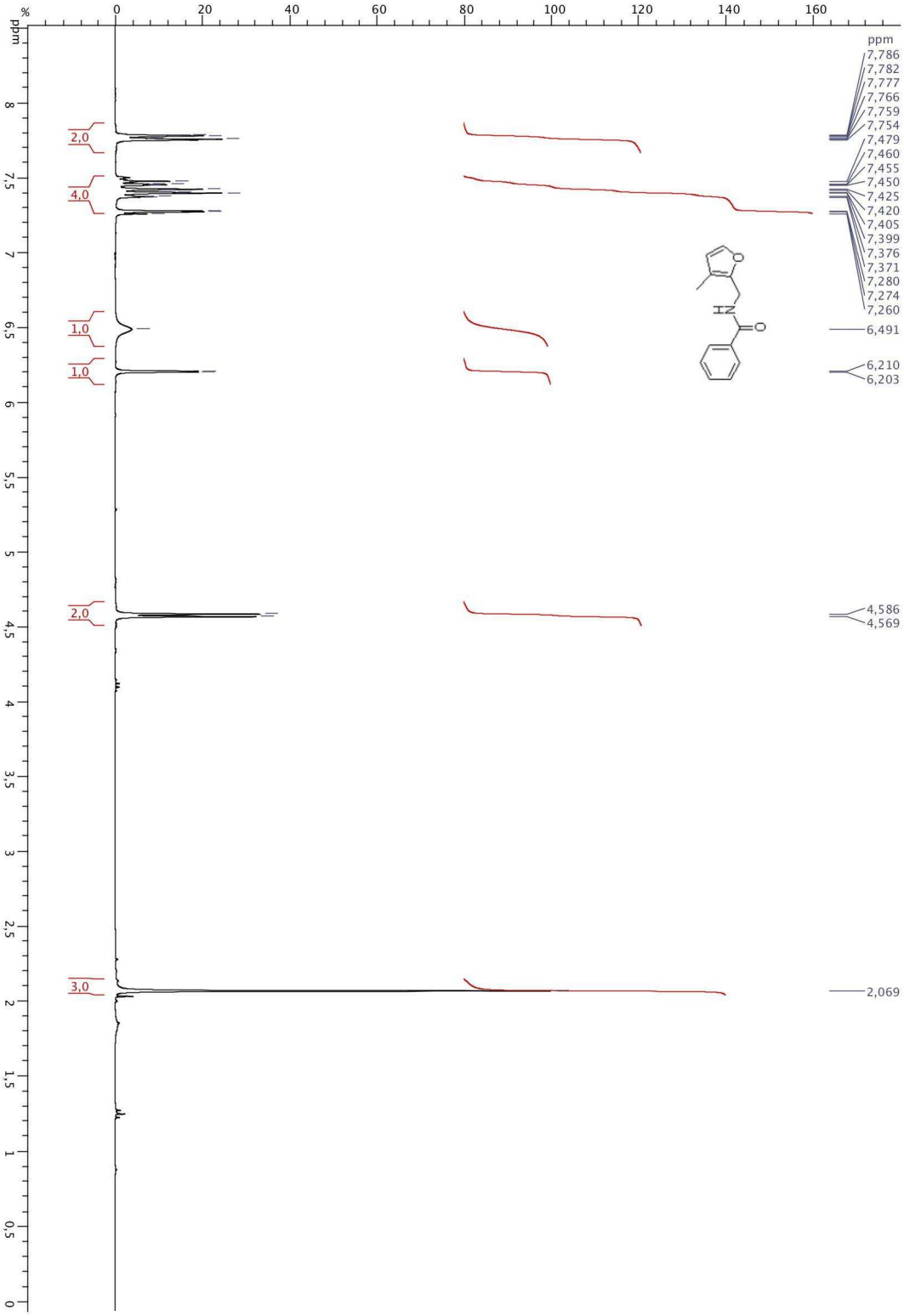
^{1}H NMR of 3-(furan-2-ylmethyl)-1,1-dimethylurea 5j ($CDCl_3$, 300 MHz)



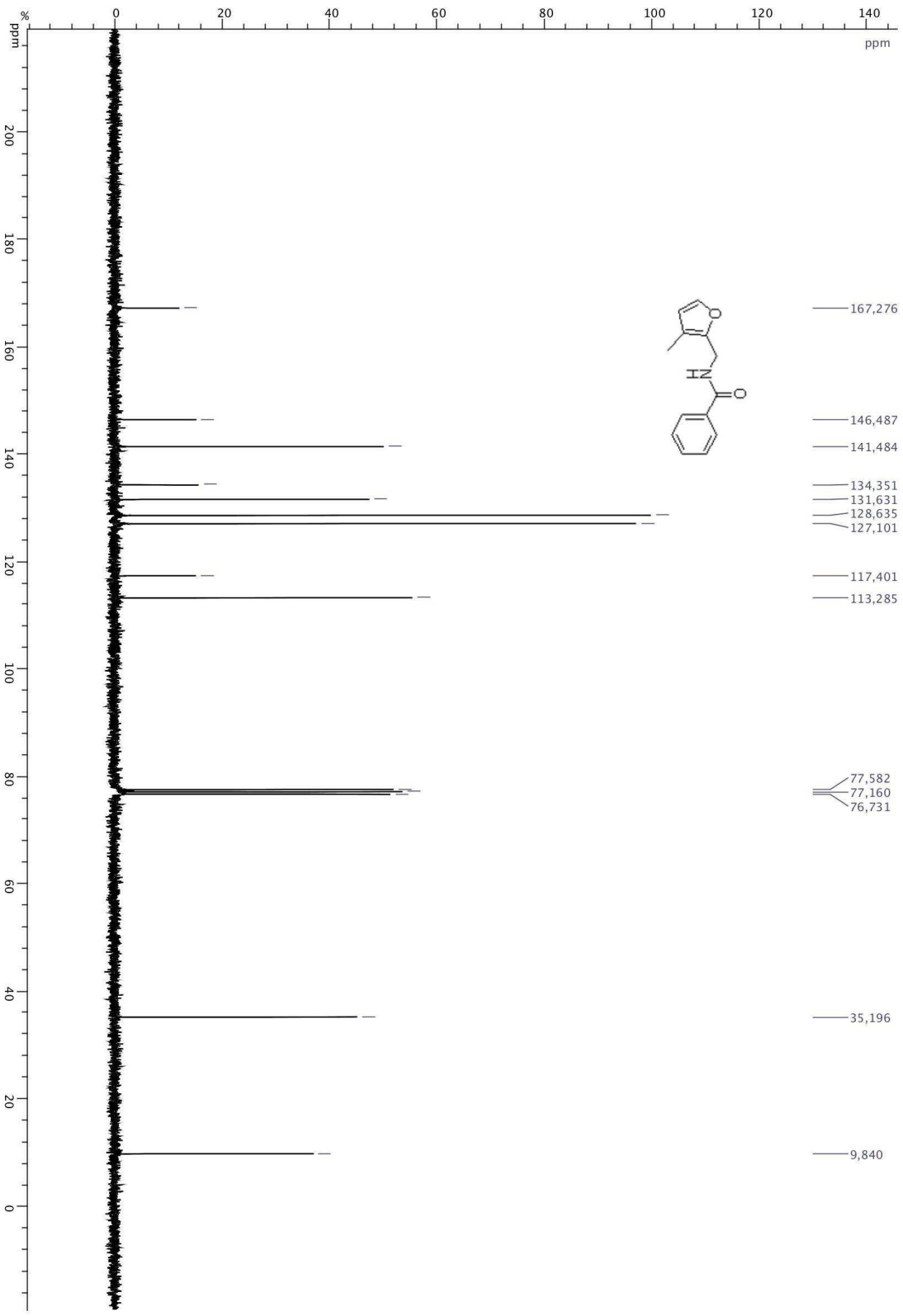
^{13}C NMR of 3-(furan-2-ylmethyl)-1,1-dimethylurea 5j ($CDCl_3$, 75 MHz)



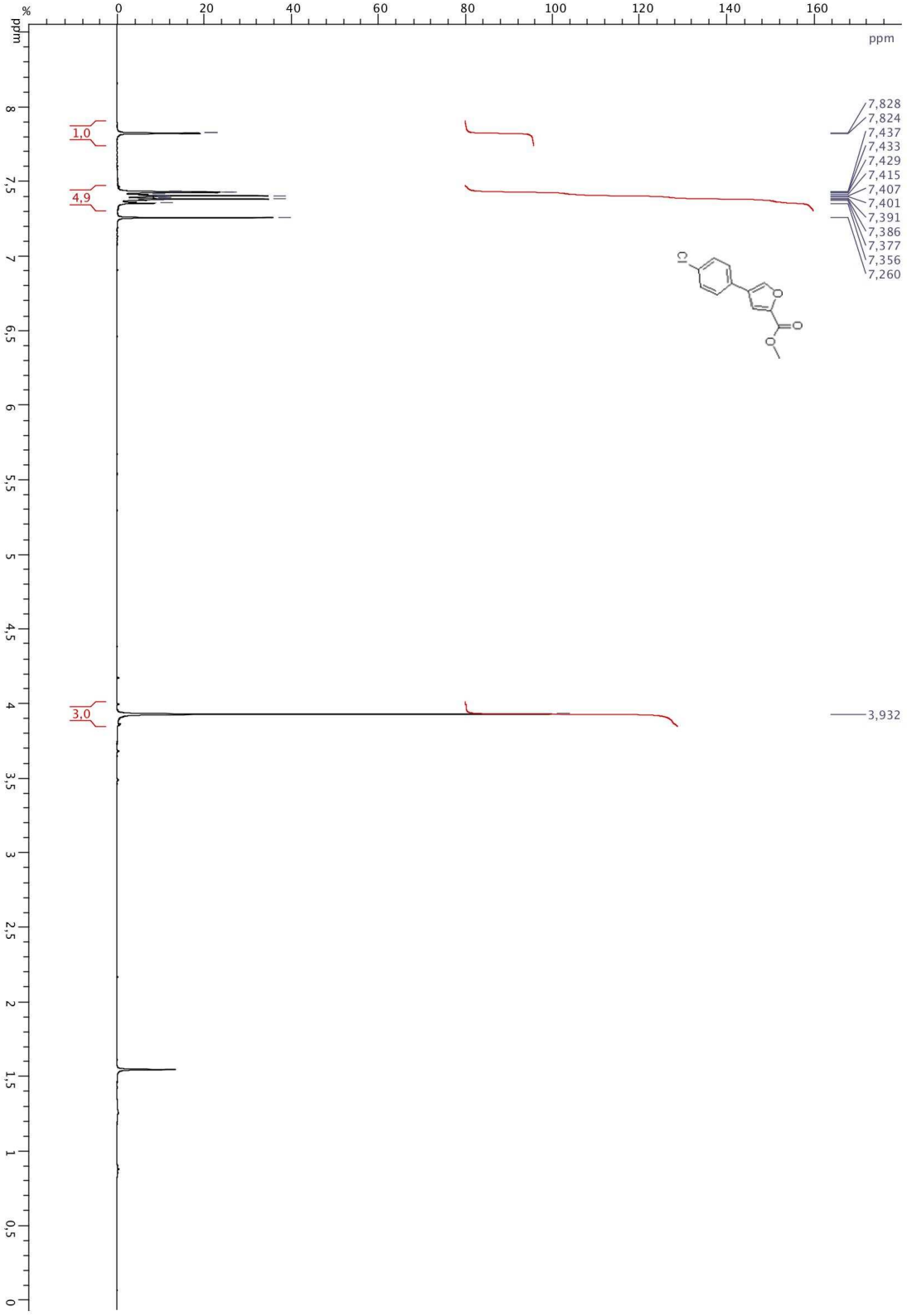
^{1}H NMR of *N*-((3-methylfuran-2-yl)methyl)benzamide 5k ($CDCl_3$, 300 MHz)



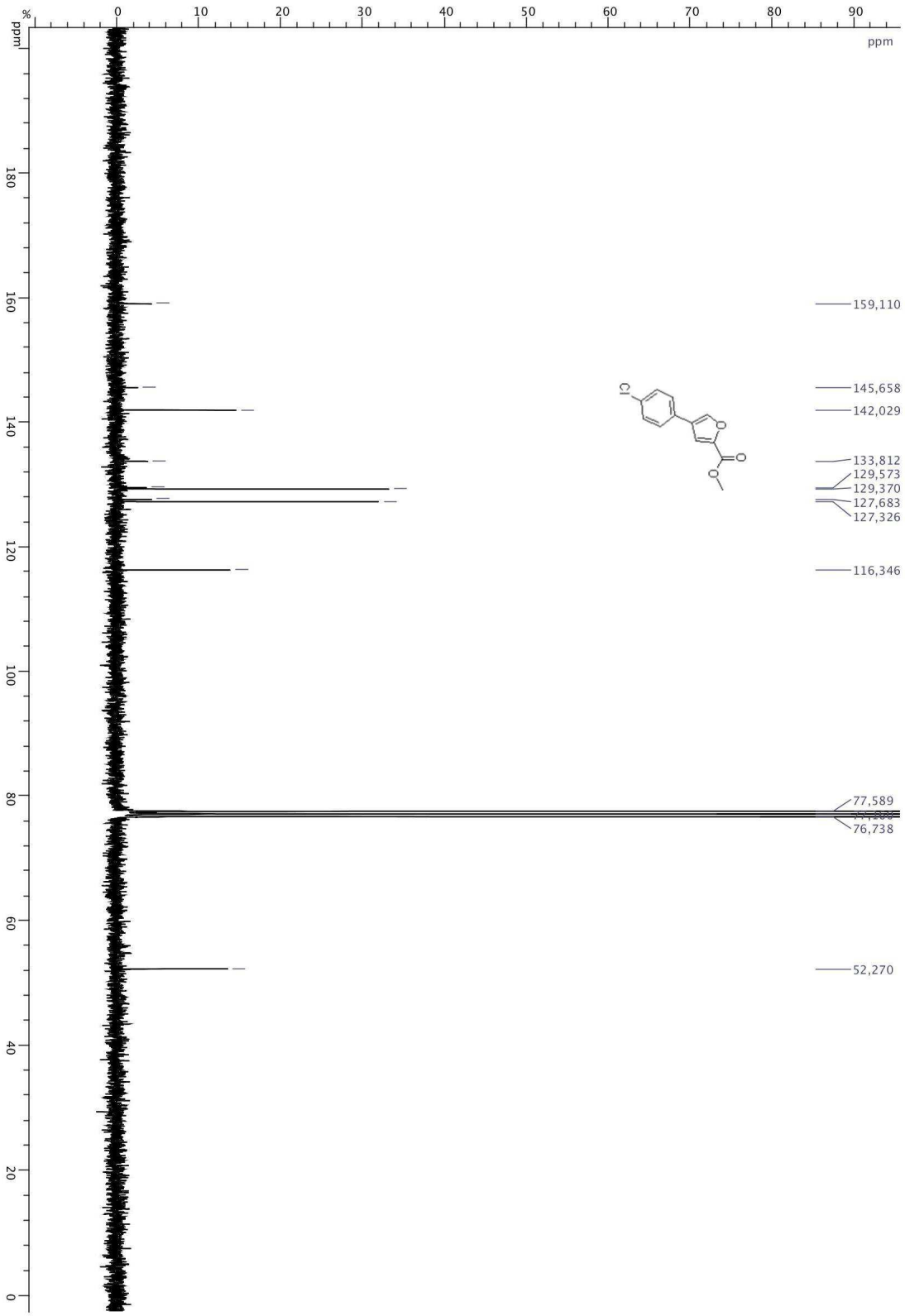
^{13}C NMR of *N*-((3-methylfuran-2-yl)methyl)benzamide 5k ($CDCl_3$, 75 MHz)



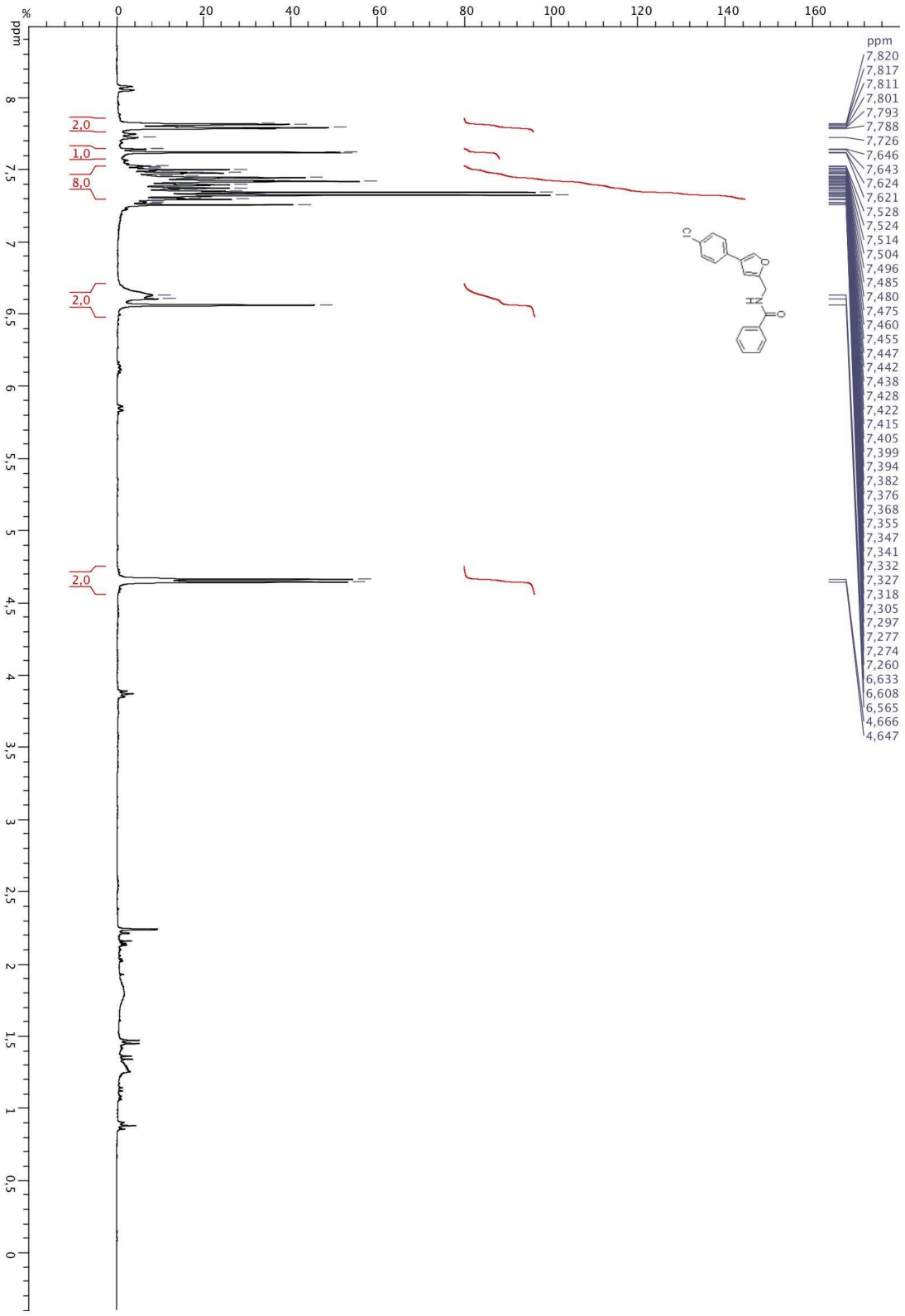
^{1}H NMR of methyl 4-(4-chlorophenyl)furan-2-carboxylate ($CDCl_3$, 300 MHz)



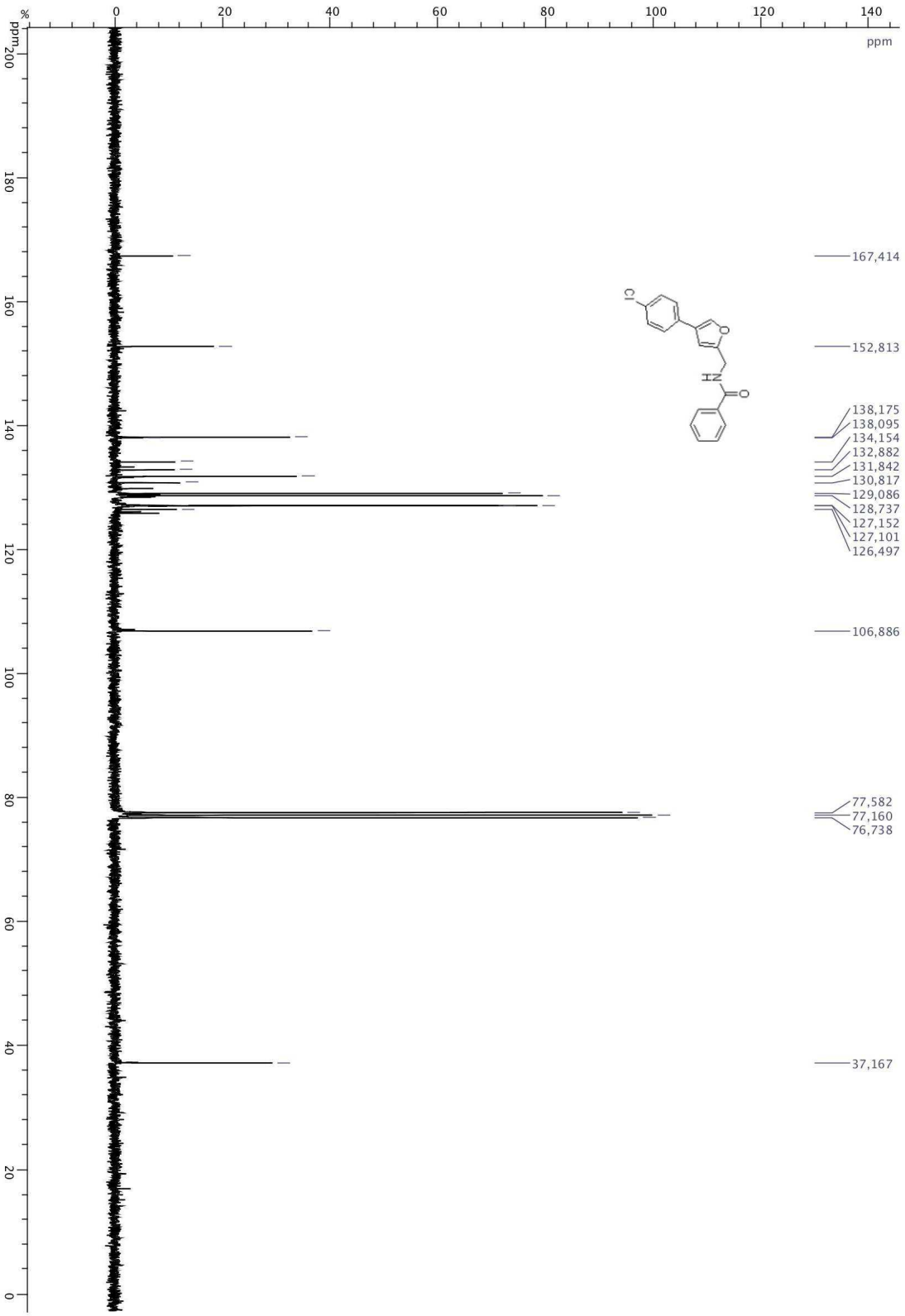
^{13}C NMR of methyl 4-(4-chlorophenyl)furan-2-carboxylate ($CDCl_3$, 75 MHz)



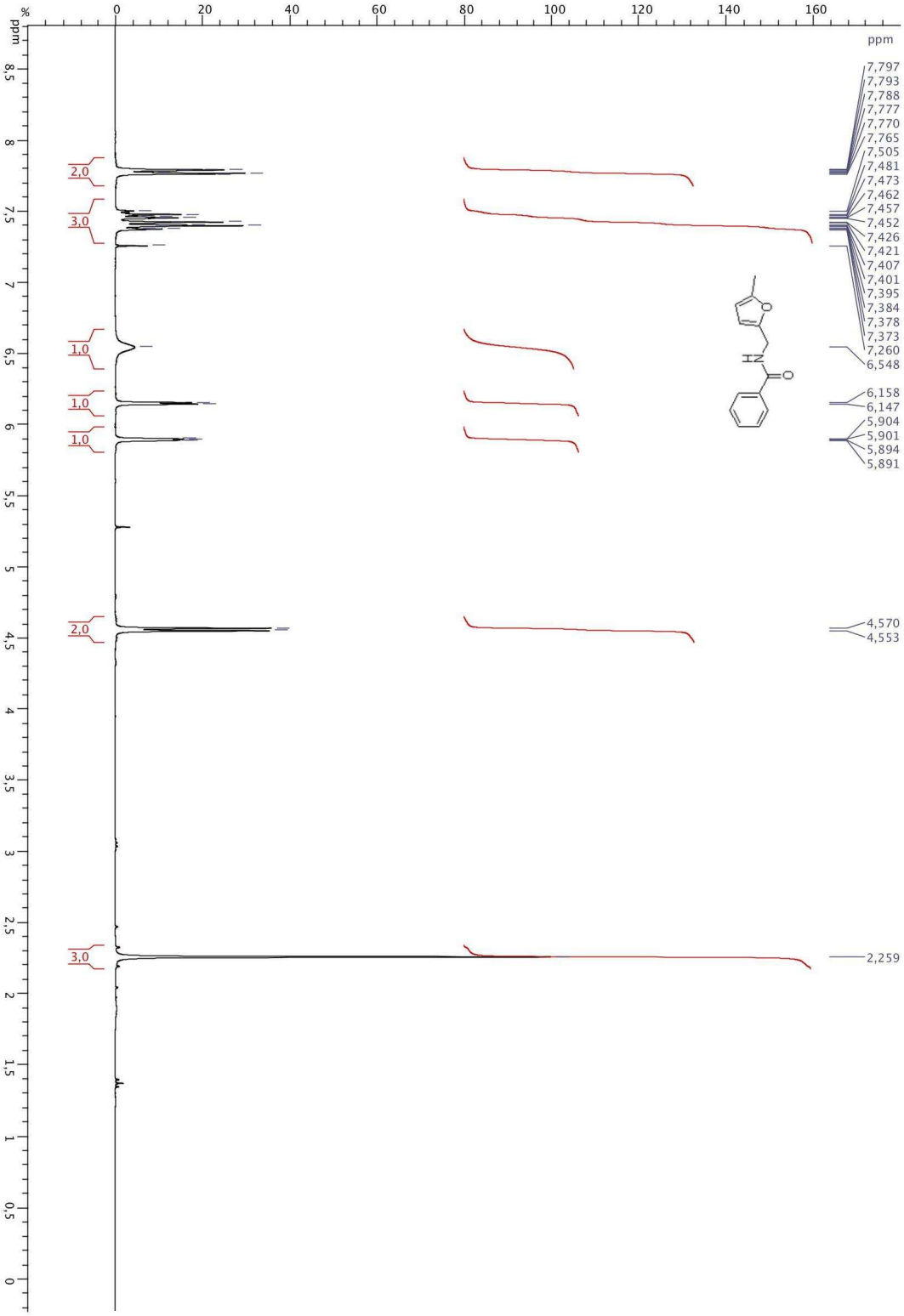
^{1}H NMR of *N*-((4-(4-chlorophenyl)furan-2-yl)methyl)benzamide 5l ($CDCl_3$, 300 MHz)



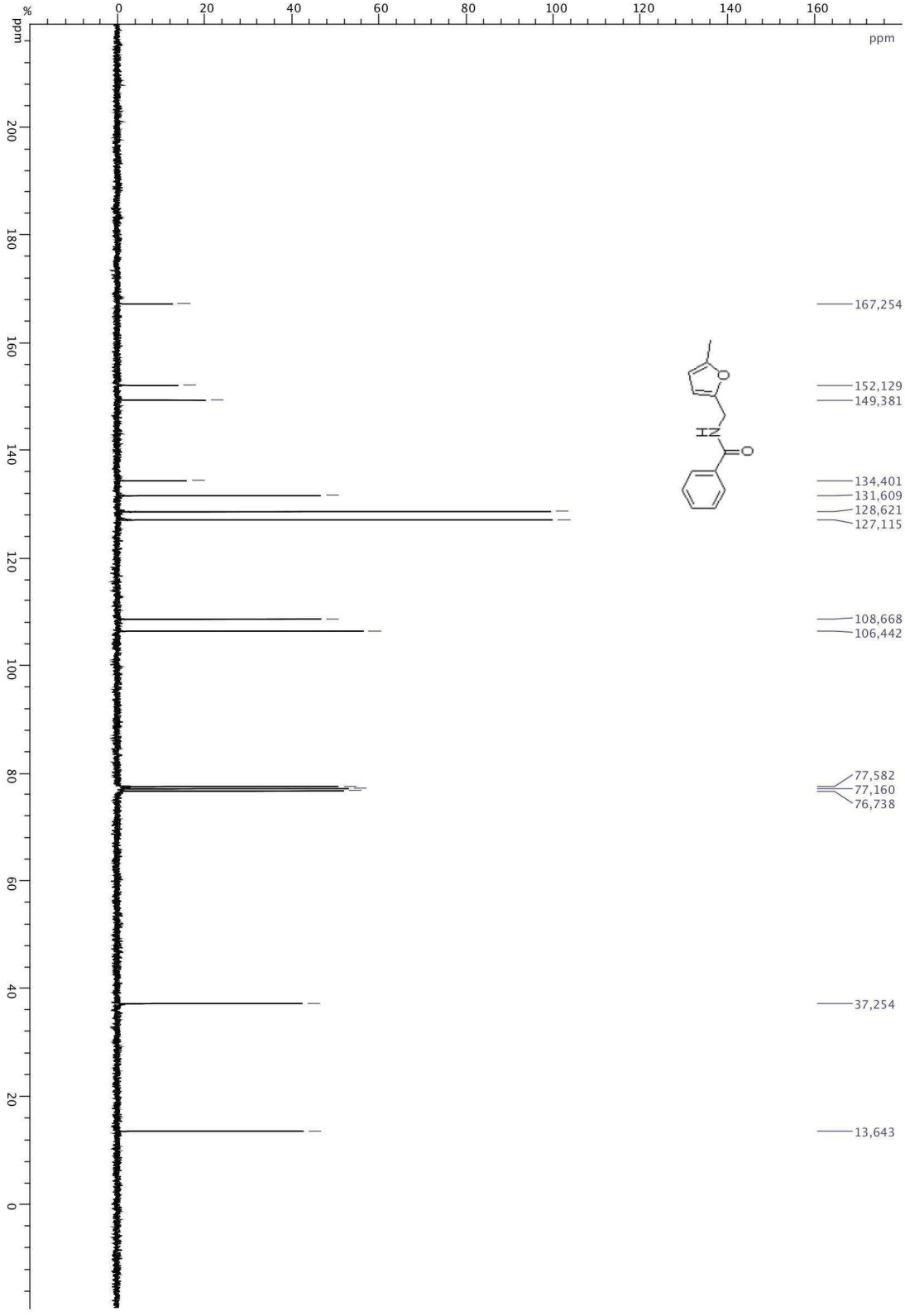
^{13}C NMR of *N*-((4-(4-chlorophenyl)furan-2-yl)methyl)benzamide 5l ($CDCl_3$, 75 MHz)



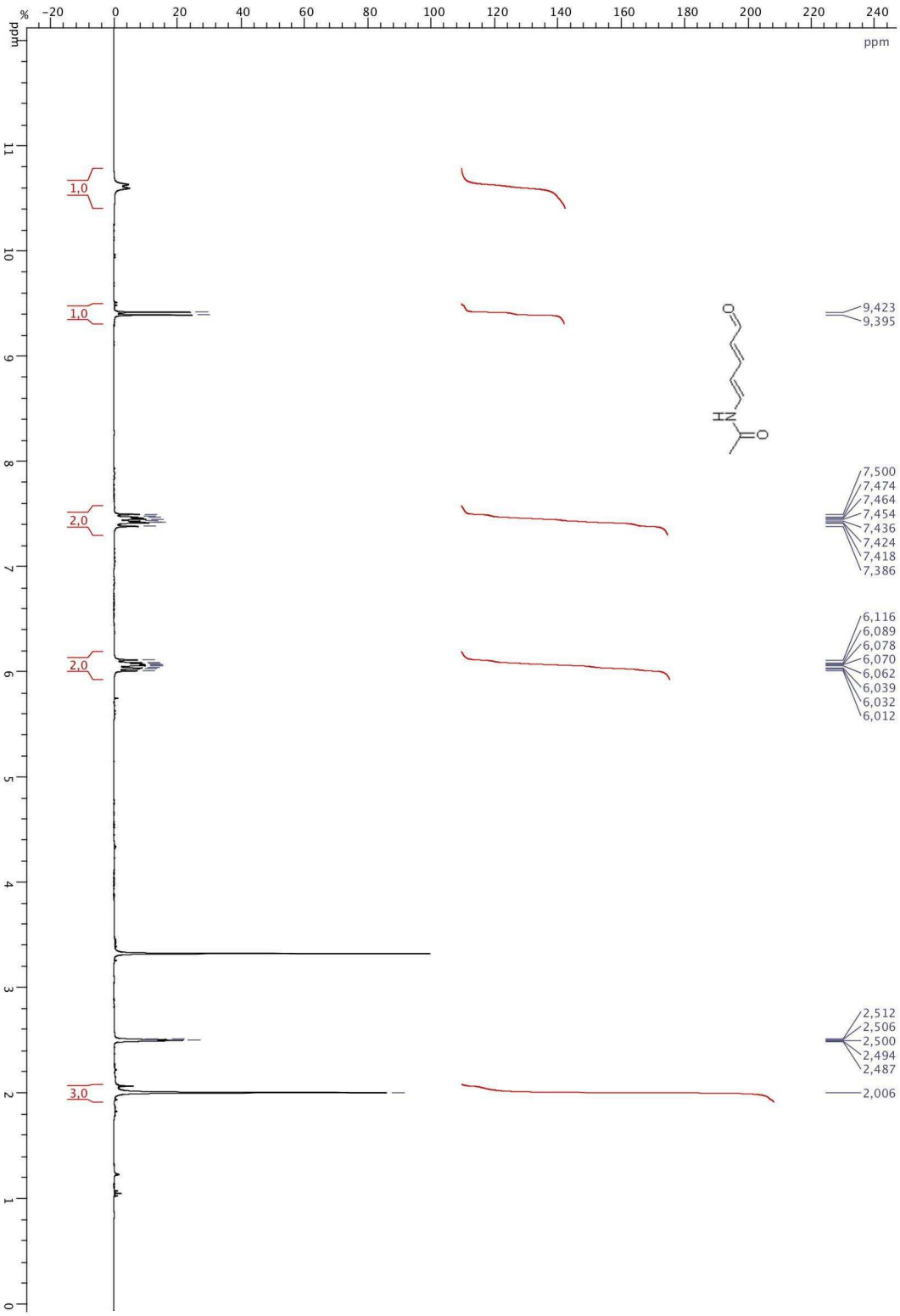
^{1}H NMR of *N*-(5-methyl-furan-2-yl)methyl)benzamide 5m ($CDCl_3$, 300 MHz)



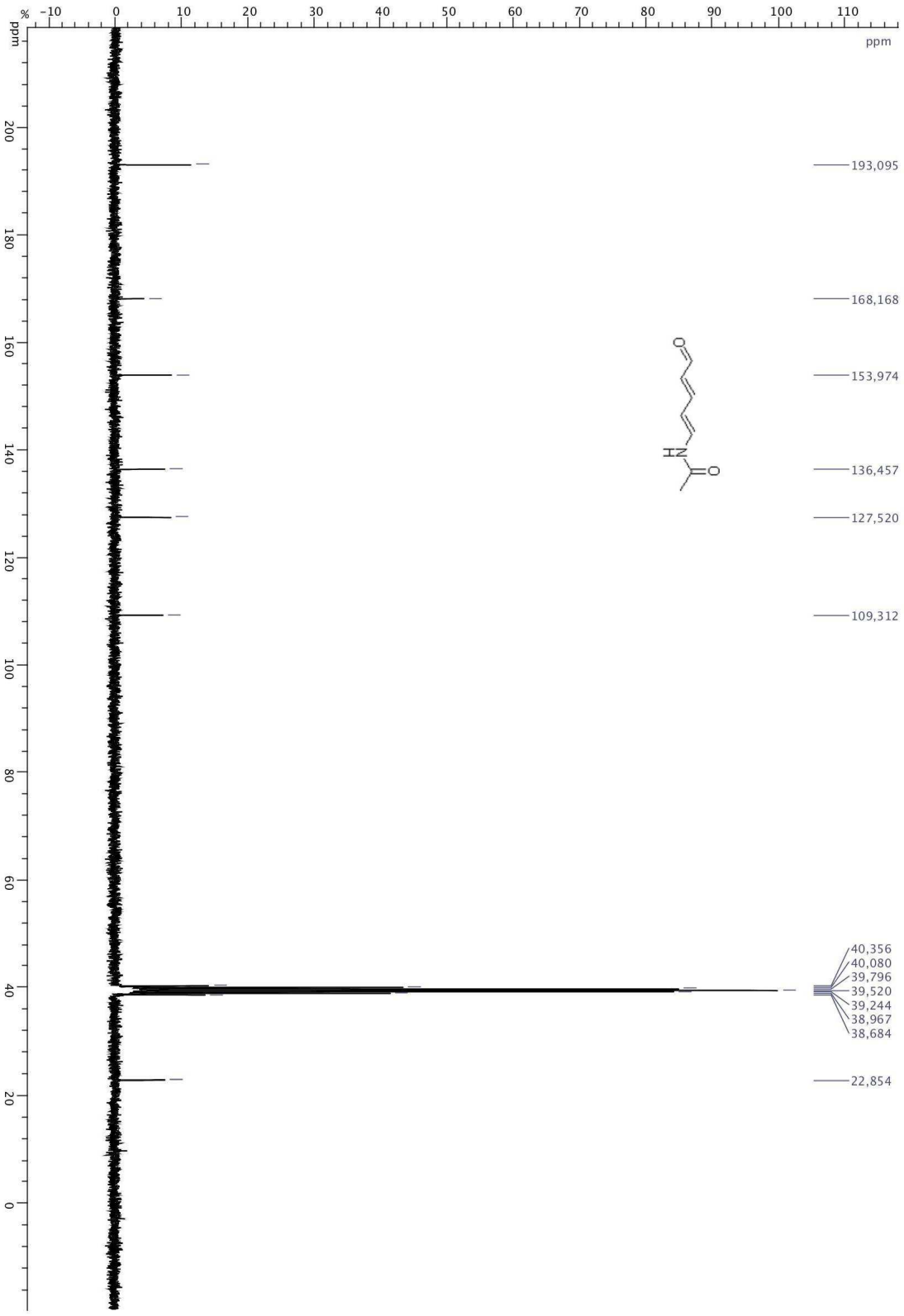
^{13}C NMR of *N*-(5-methyl-furan-2-yl)methyl)benzamide 5m ($CDCl_3$, 75 MHz)



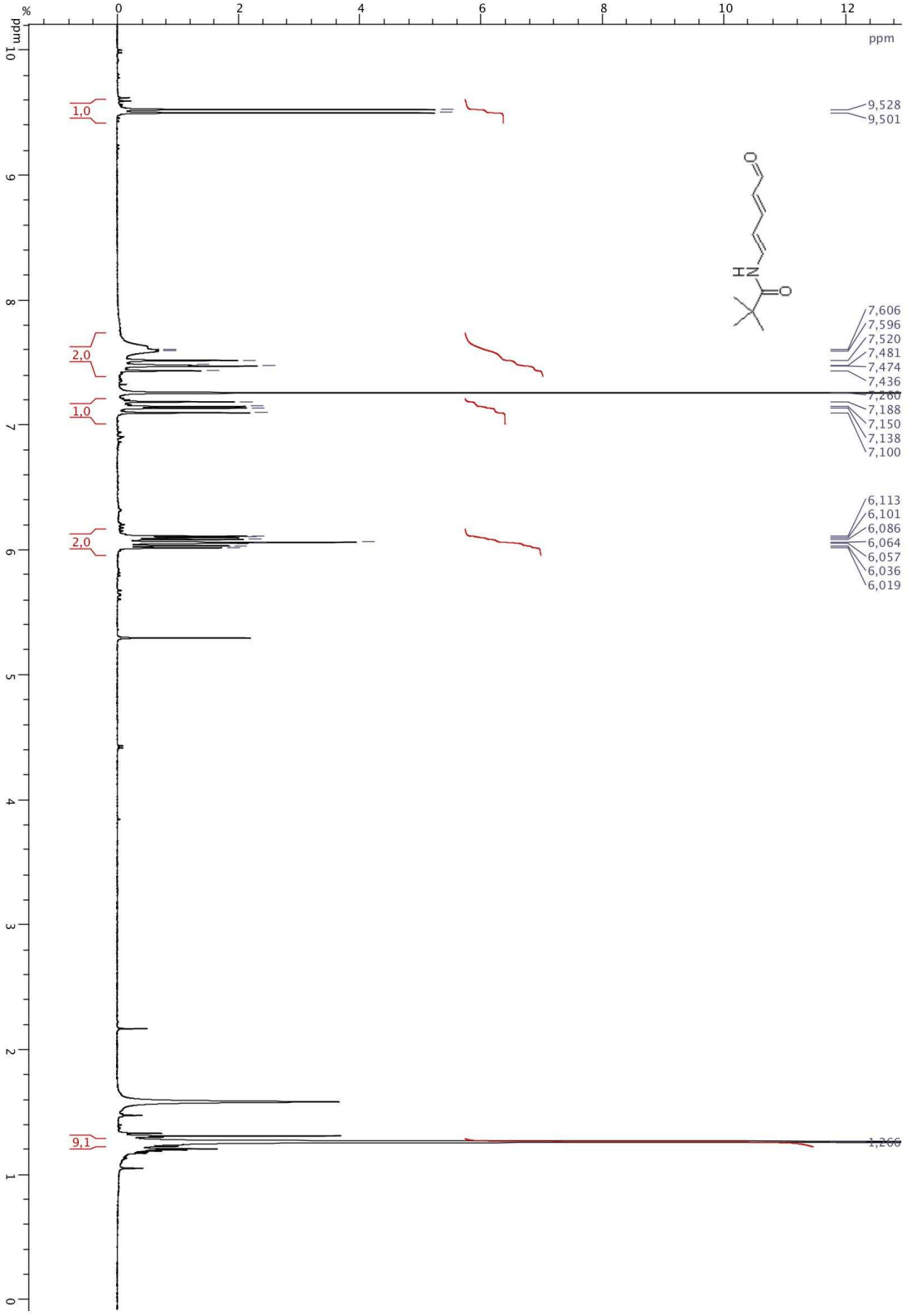
^{1}H NMR of *N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)acetamide 6a (DMSO-d_6, 300 MHz)



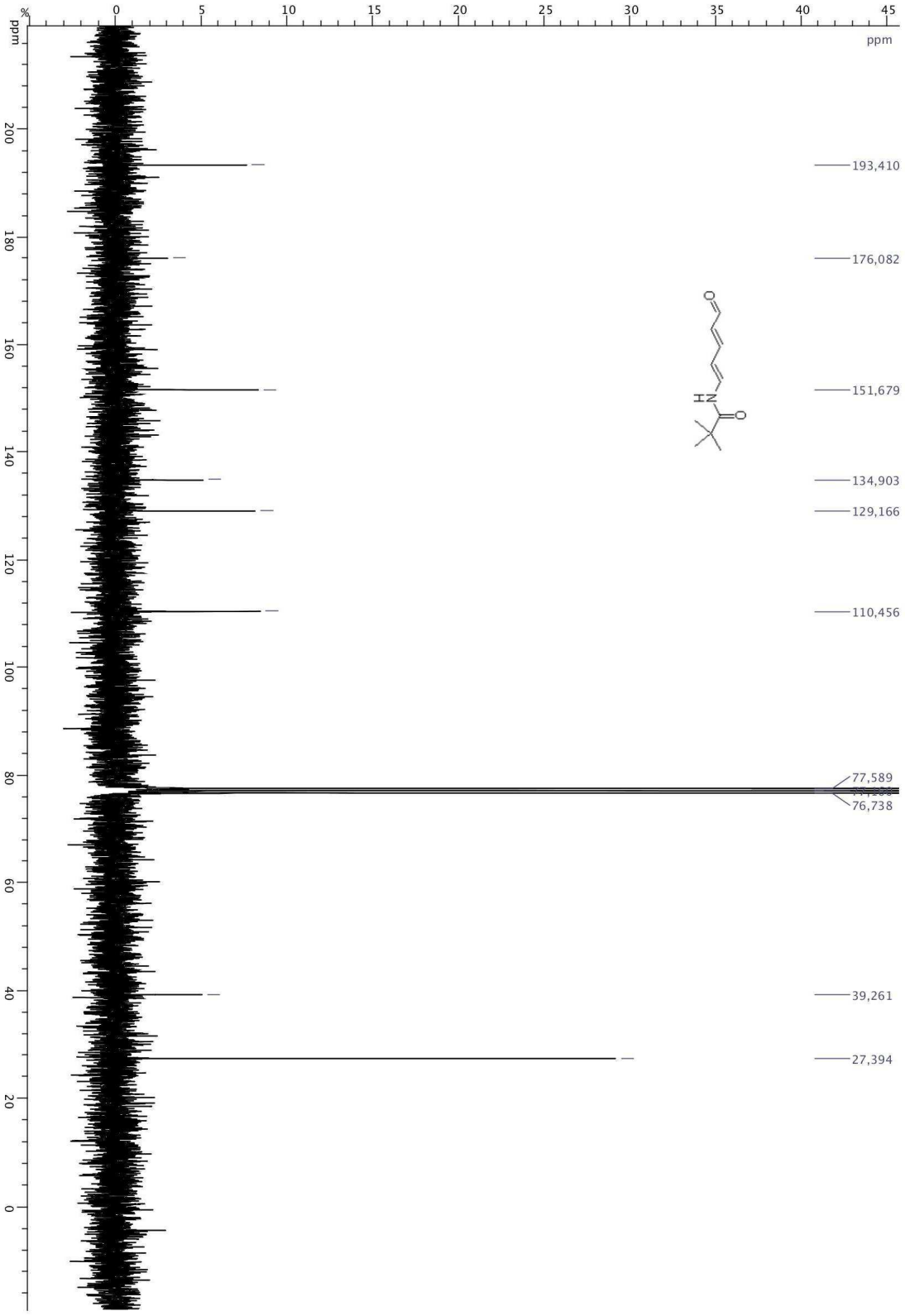
^{13}C NMR of *N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)acetamide 6a (DMSO-d_6, 75 MHz)



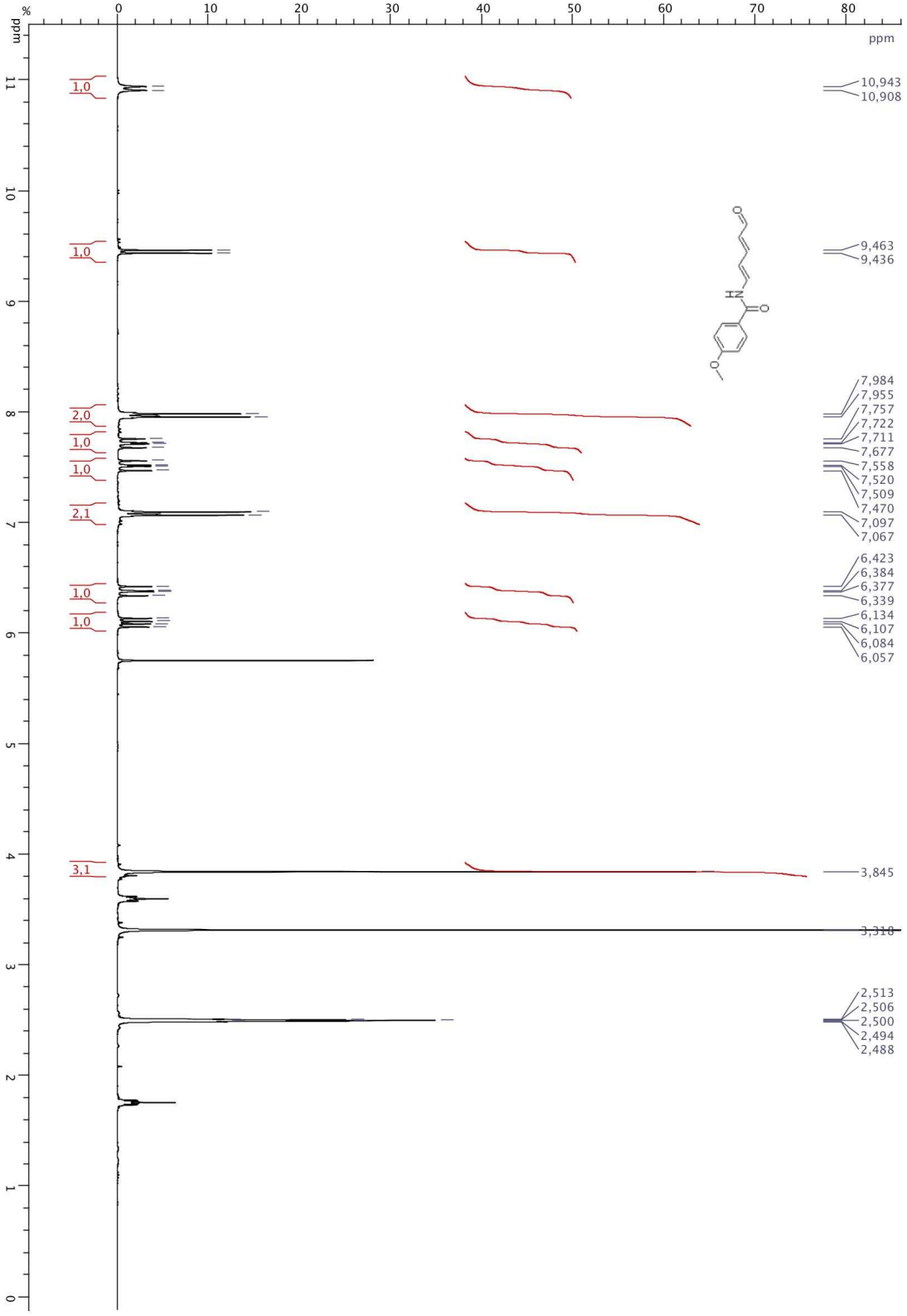
^{1}H NMR of *N*-((1*E*, 3*E*)-5-oxopenta-1,3-dienyl)pivalamide 6b ($CDCl_3$, 300 MHz)



^{13}C NMR of *N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)pivalamide 6b ($CDCl_3$, 75 MHz)

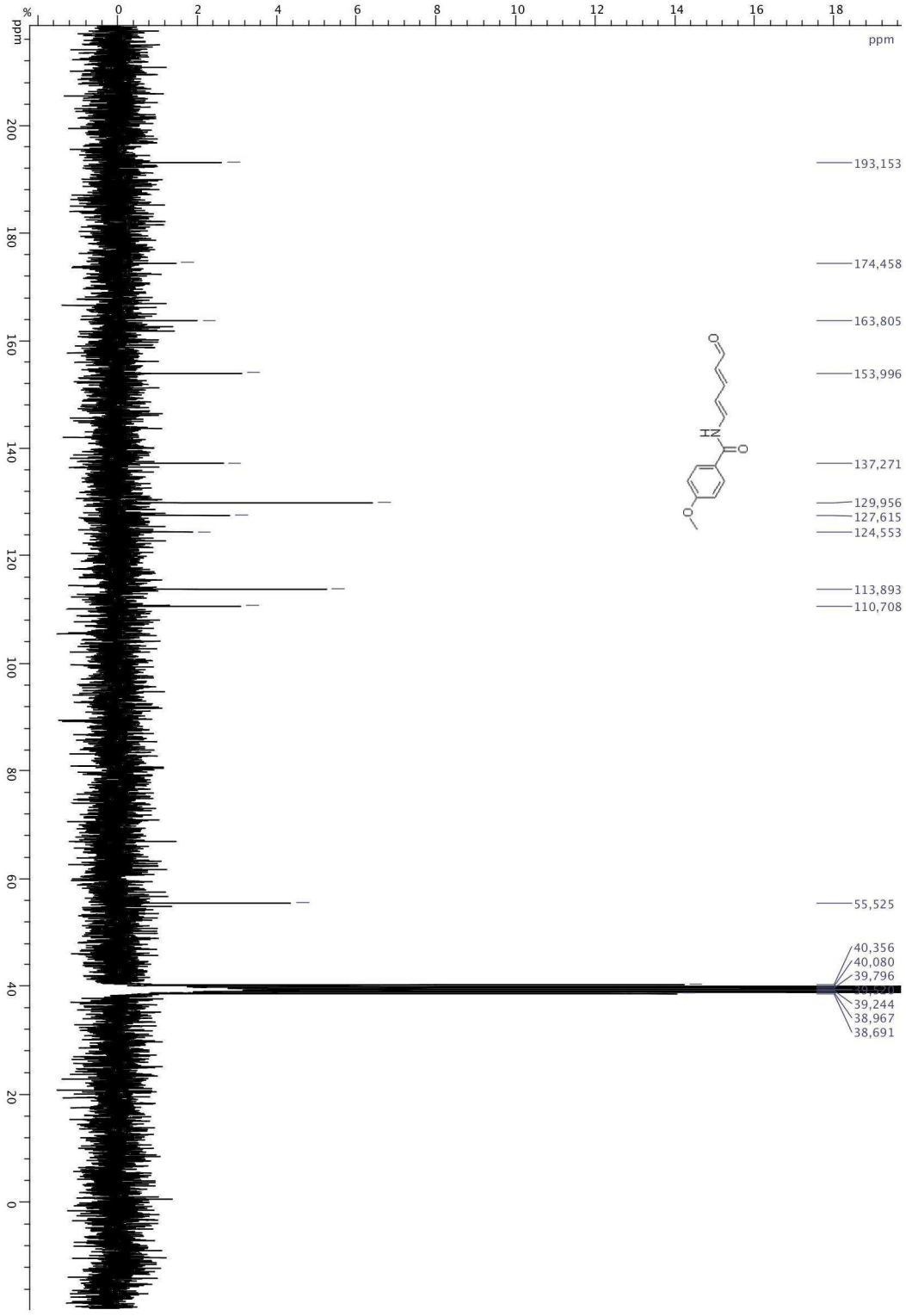


^{1}H NMR of 4-methoxy-*N*-((1*E*, 3*E*)-5-oxopenta-1,3-dienyl)benzamide 6c (DMSO-d_6, 300

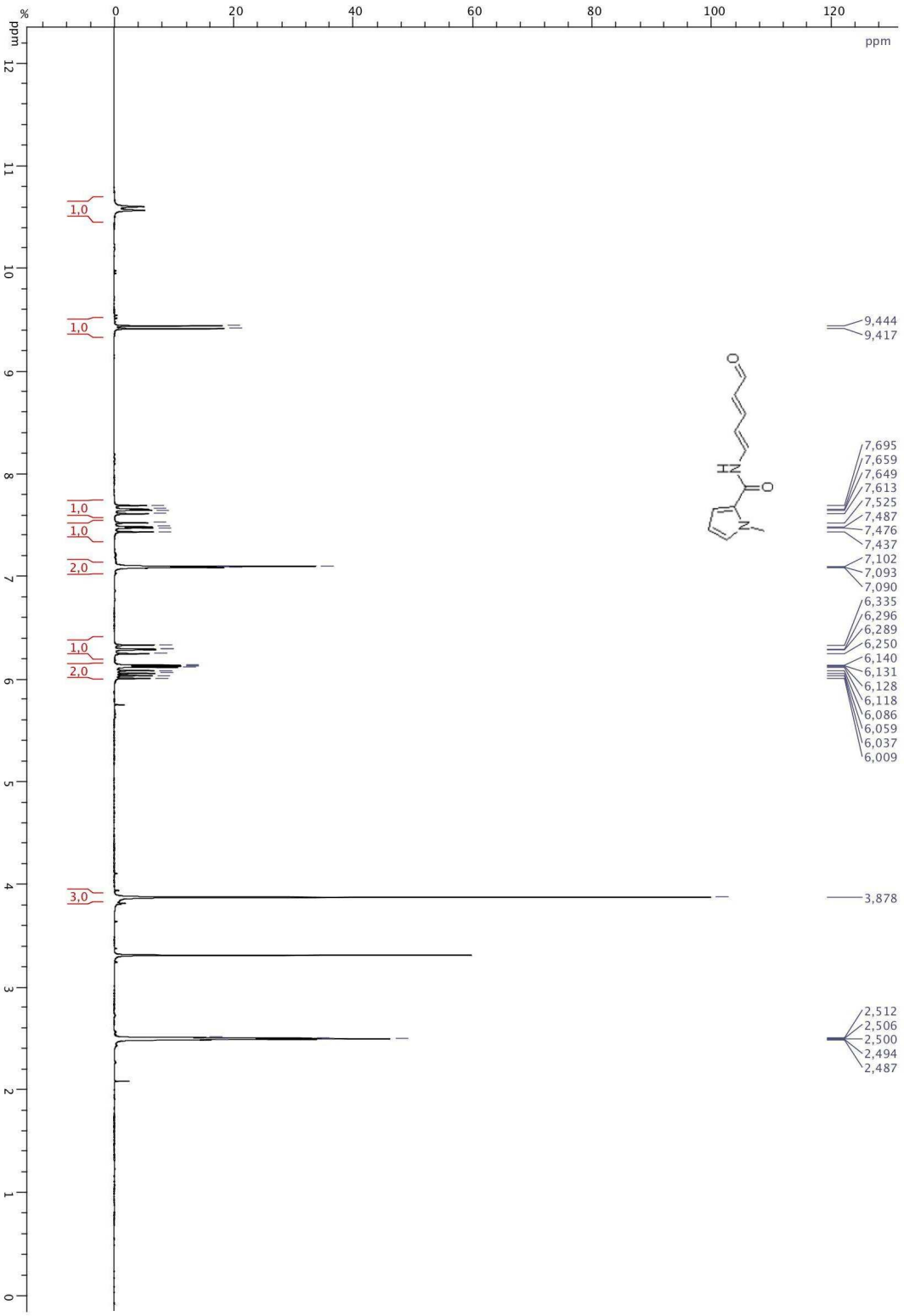


MHz)

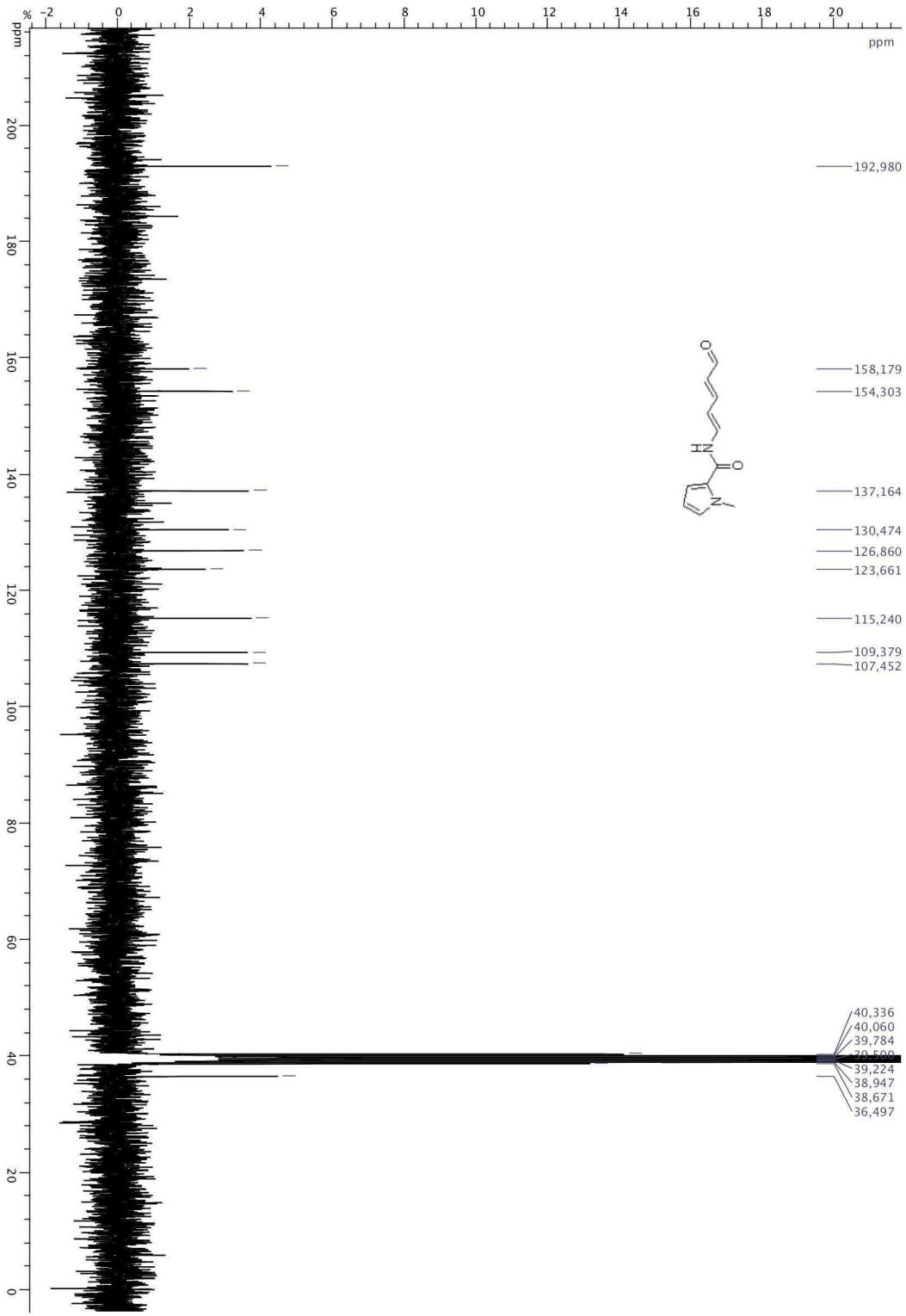
^{13}C NMR of 4-methoxy-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)benzamide 6c (DMSO-d_6, 75 MHz)



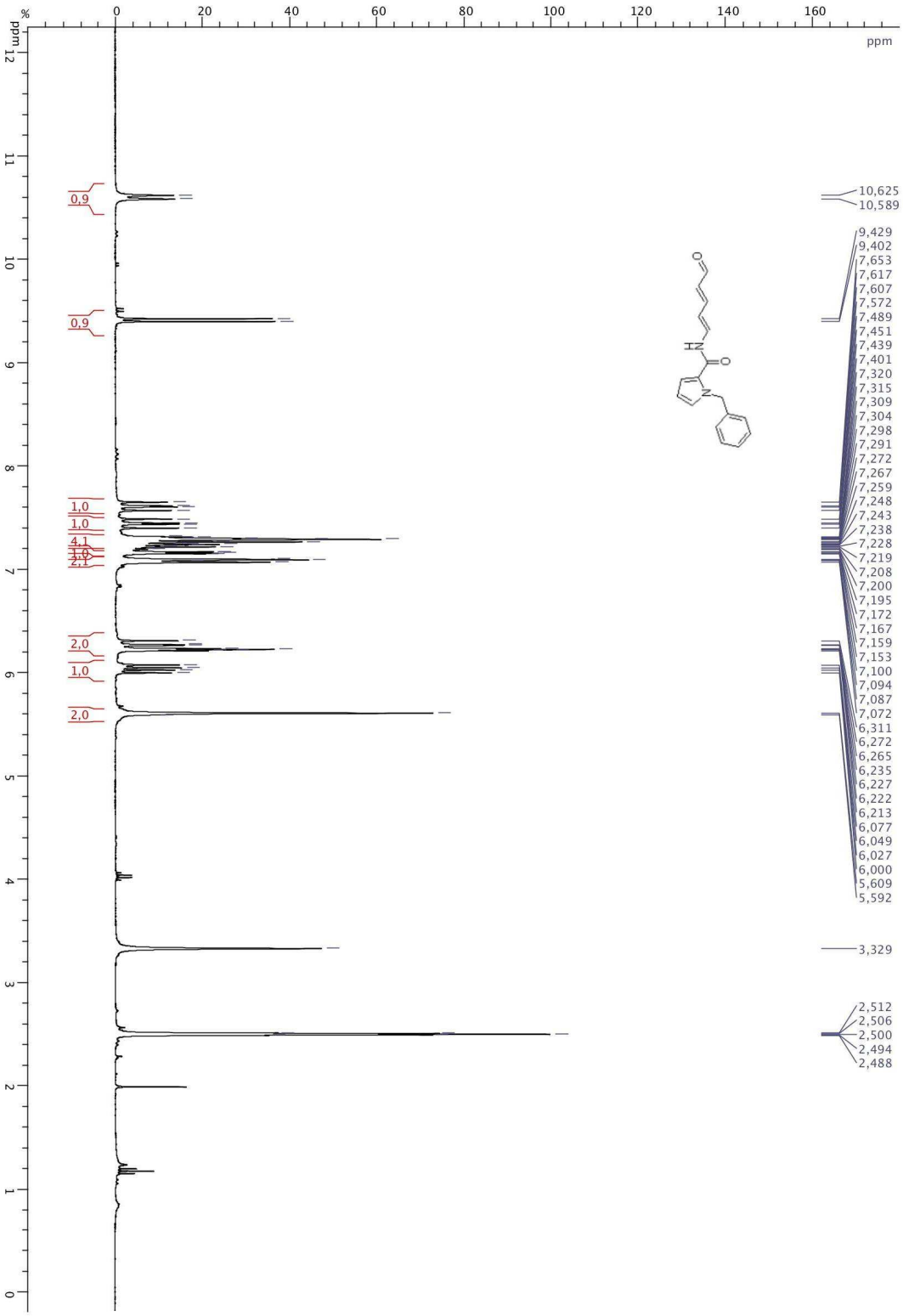
^{1}H NMR of 1-methyl-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)-1*H*-pyrrole-2-carboxamide 6f (DMSO-d_6, 300 MHz)



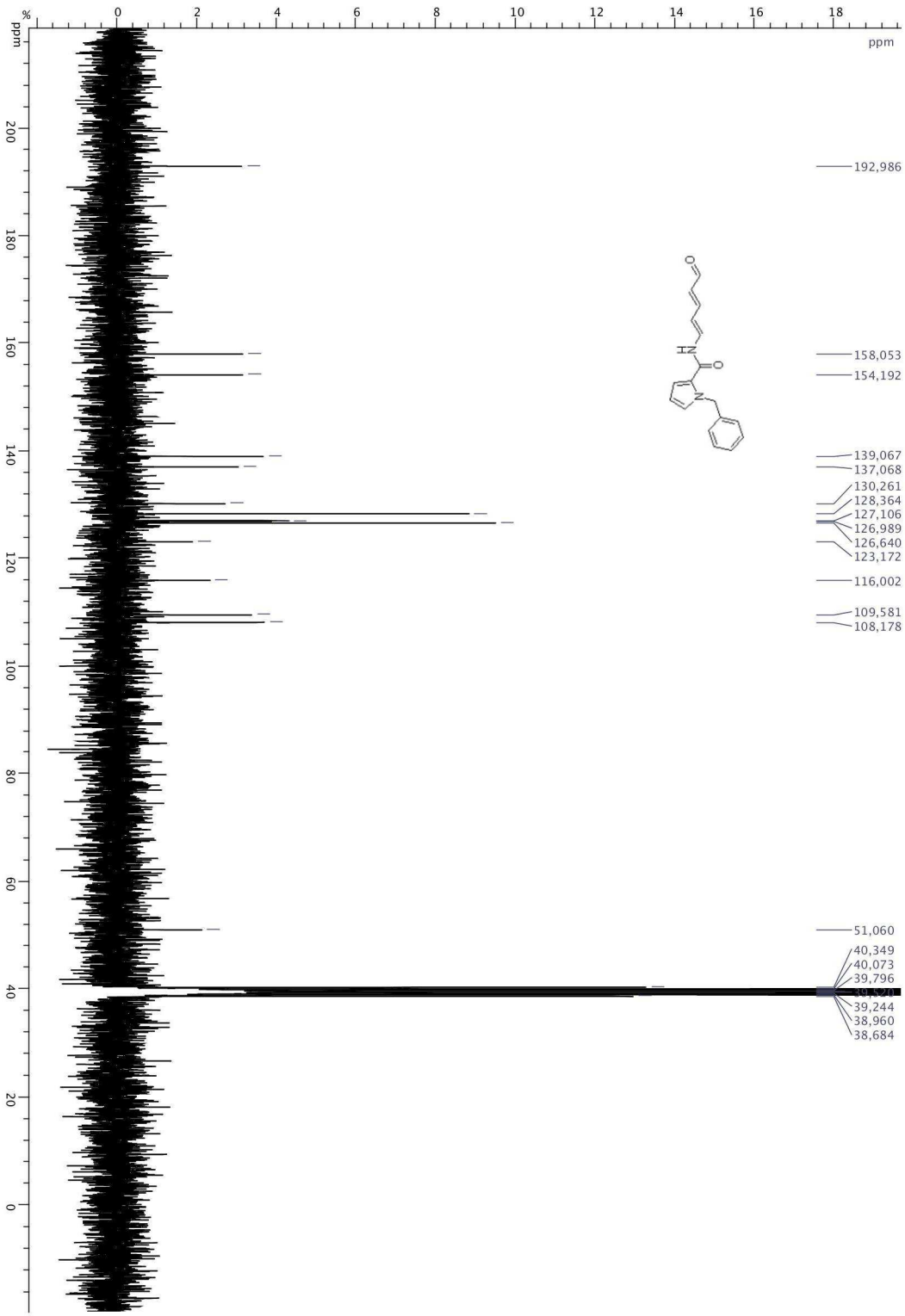
^{13}C NMR of 1-methyl-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)-1*H*-pyrrole-2-carboxamide 6f (DMSO-d_6, 75 MHz)



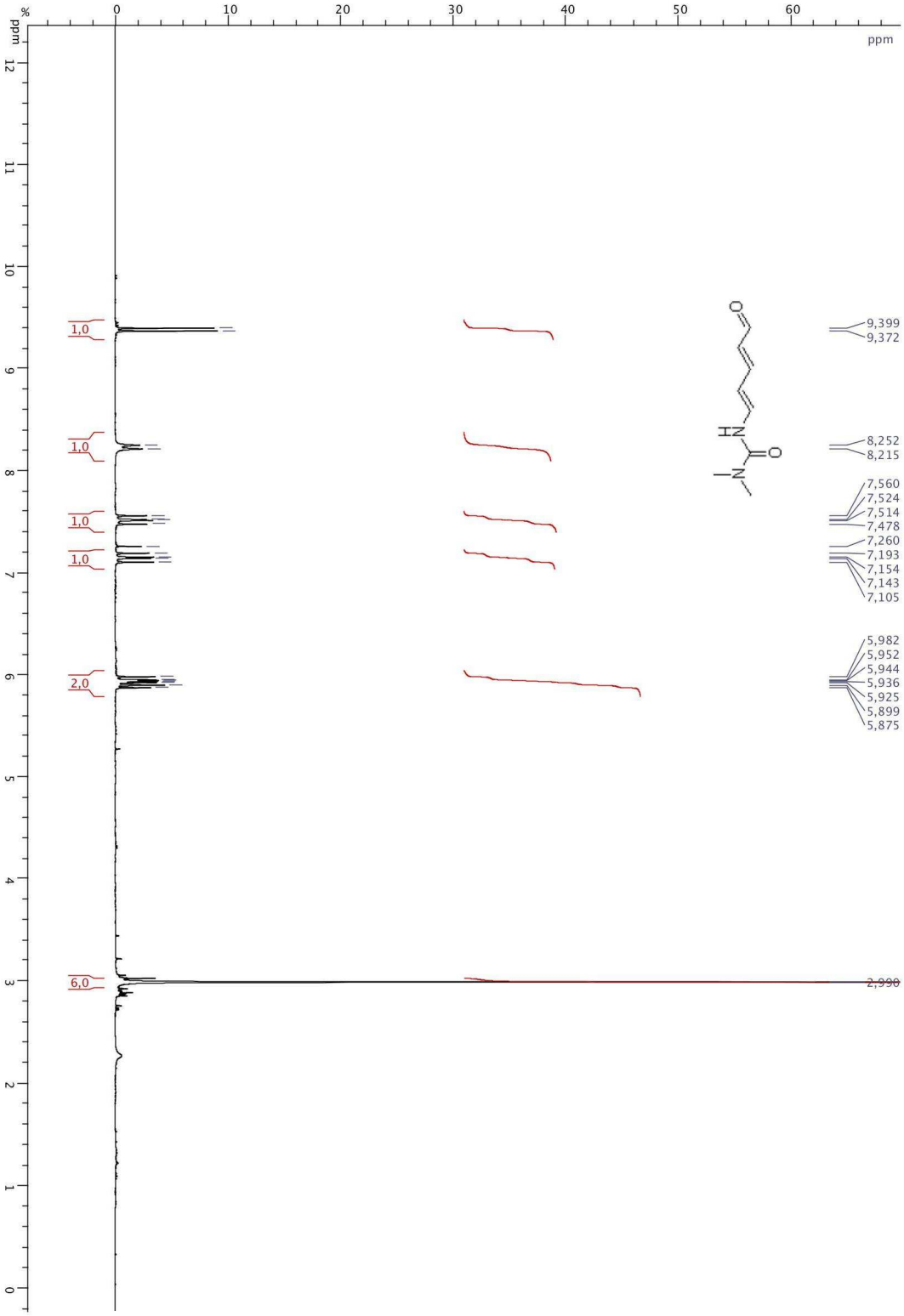
^{1}H NMR of 1-benzyl-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)-1*H*-pyrrole-2-carboxamide 6g (4) (DMSO-d_6, 300 MHz)



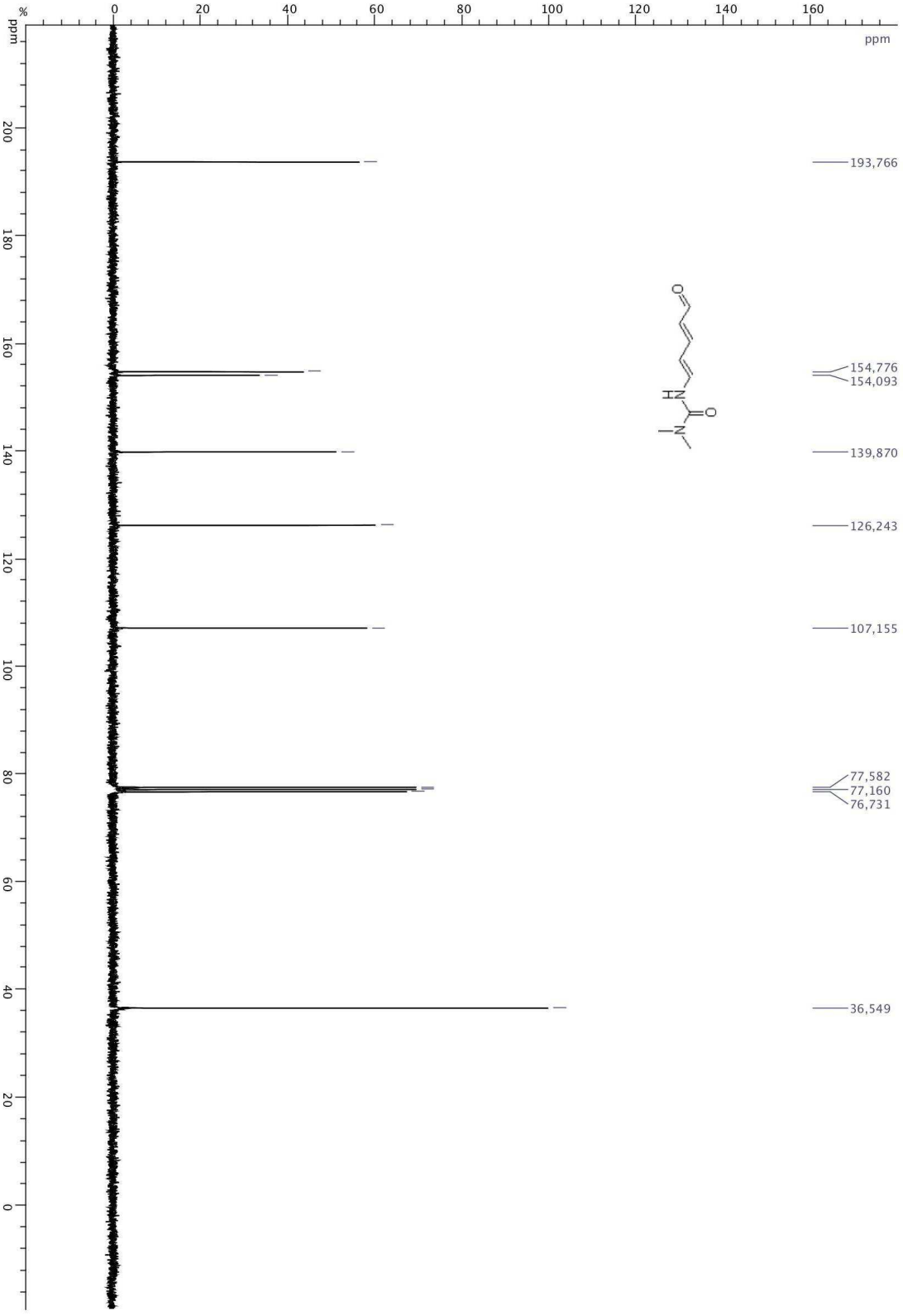
^{13}C NMR of 1-benzyl-*N*-((1*E*,3*E*)-5-oxopenta-1,3-dienyl)-1*H*-pyrrole-2-carboxamide 6g (4) (DMSO-d_6, 75 MHz)



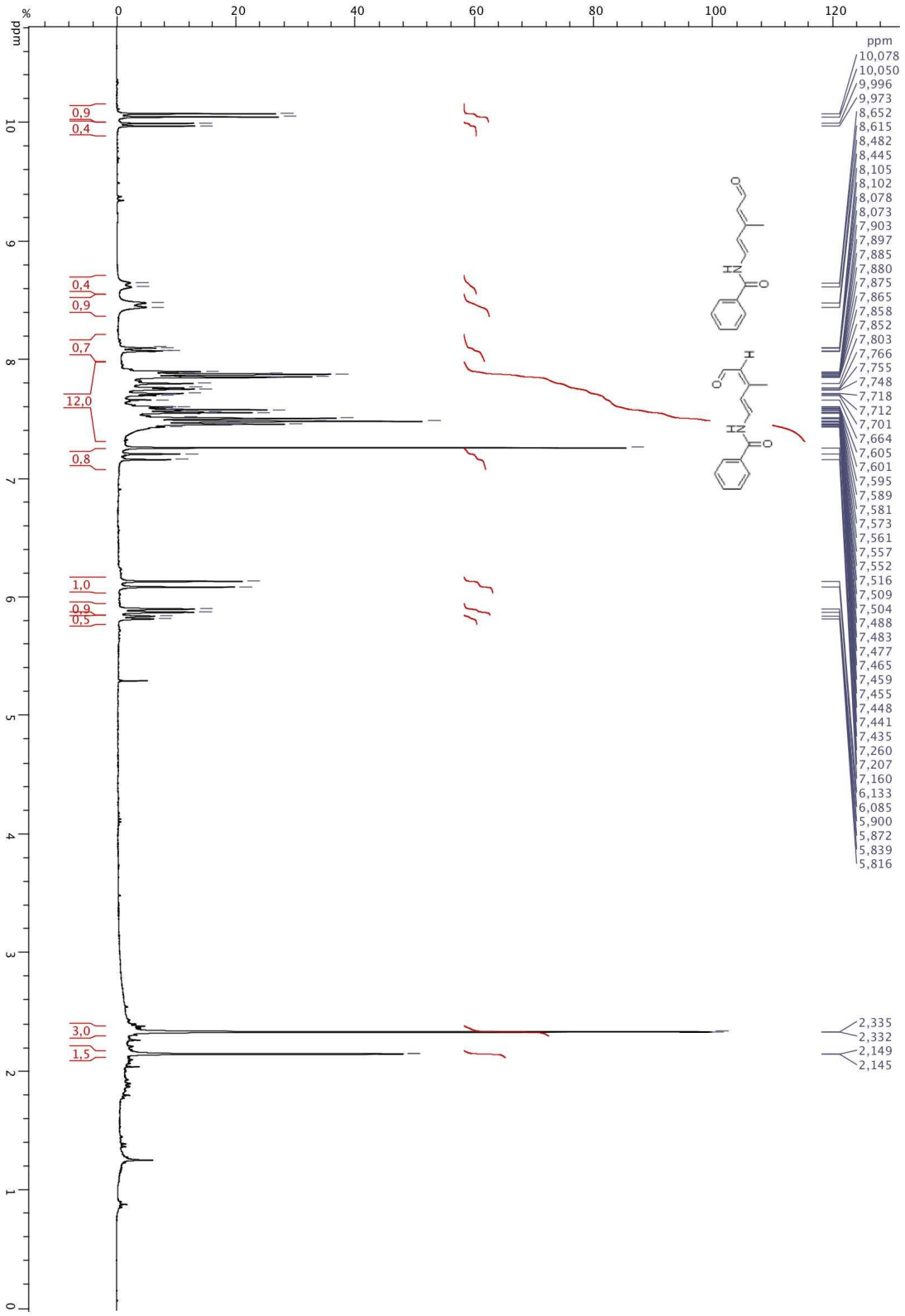
^{1}H NMR of 1,1-dimethyl-3-(1*E*,3*E*)-5-oxopenta-1,3-dienyl)urea 6j ($CDCl_3$, 300 MHz)



^{13}C NMR of 1,1-dimethyl-3-(1*E*,3*E*)-5-oxopenta-1,3-dienyl)urea 6j ($CDCl_3$, 75 MHz)

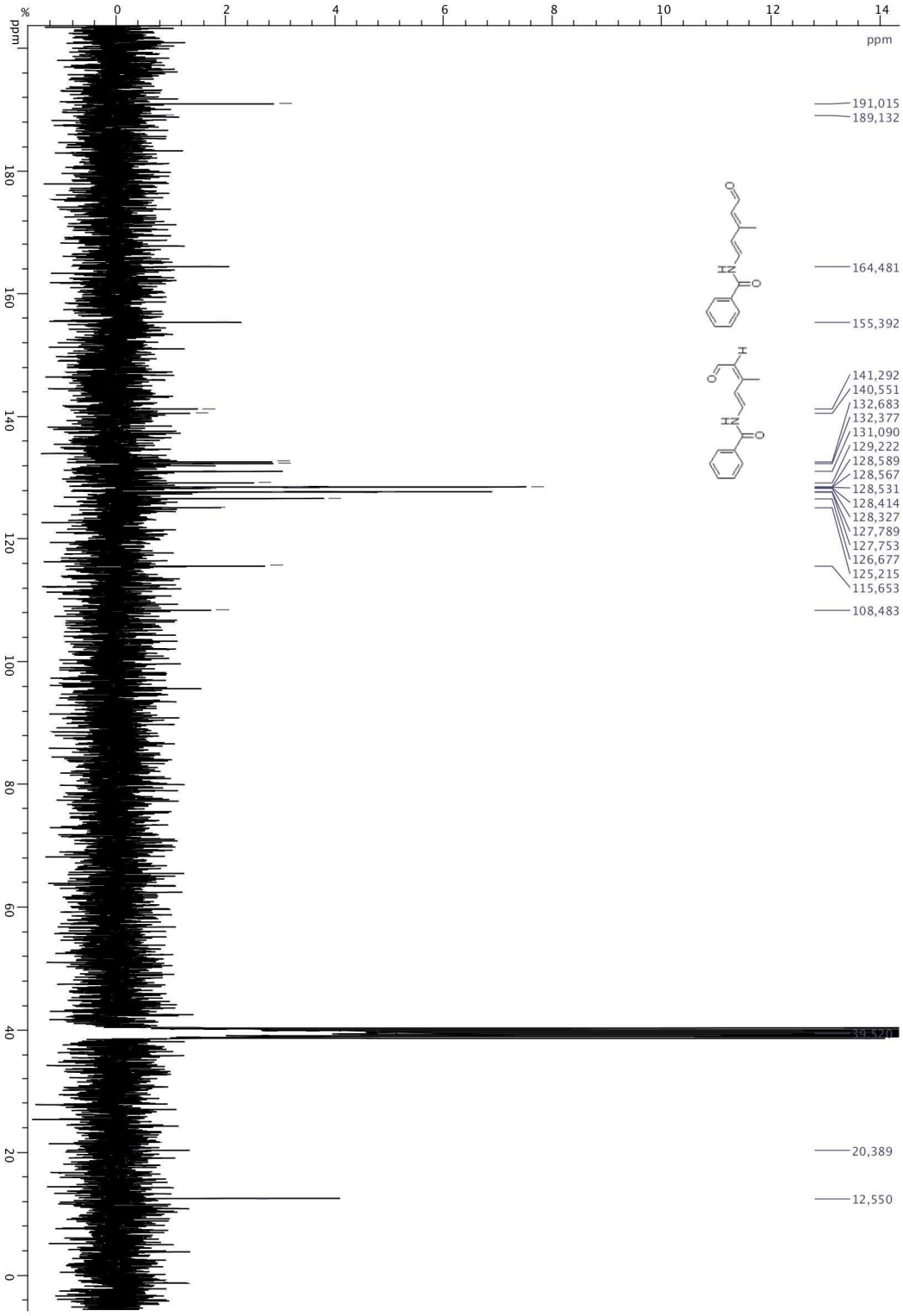


^{1}H NMR of *N*-((1*E*, 3*E/Z*)-3-methyl-5-oxopenta-1,3-dienyl)benzamide (2/1) 6k ($CDCl_3$, 300

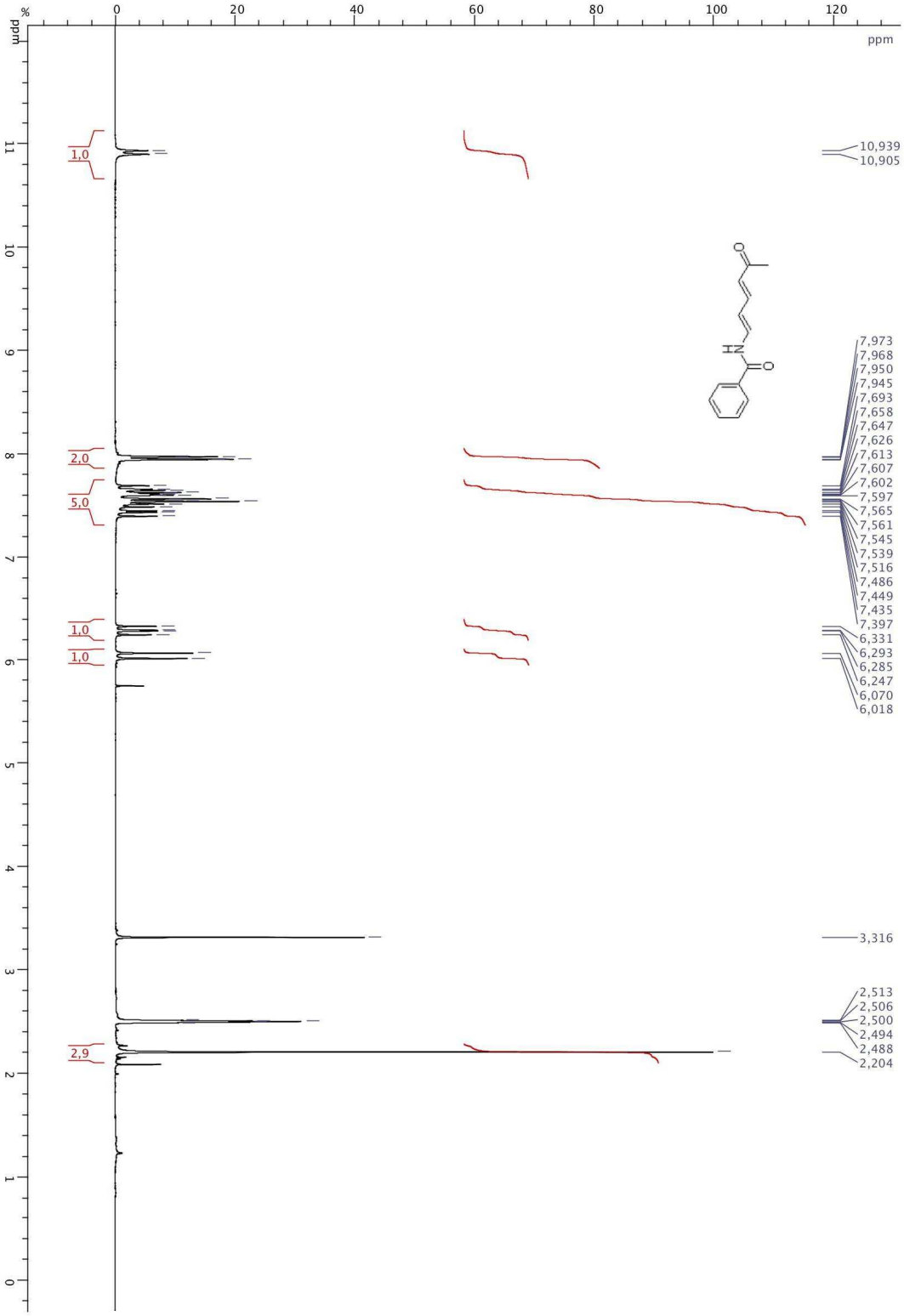


MHz)

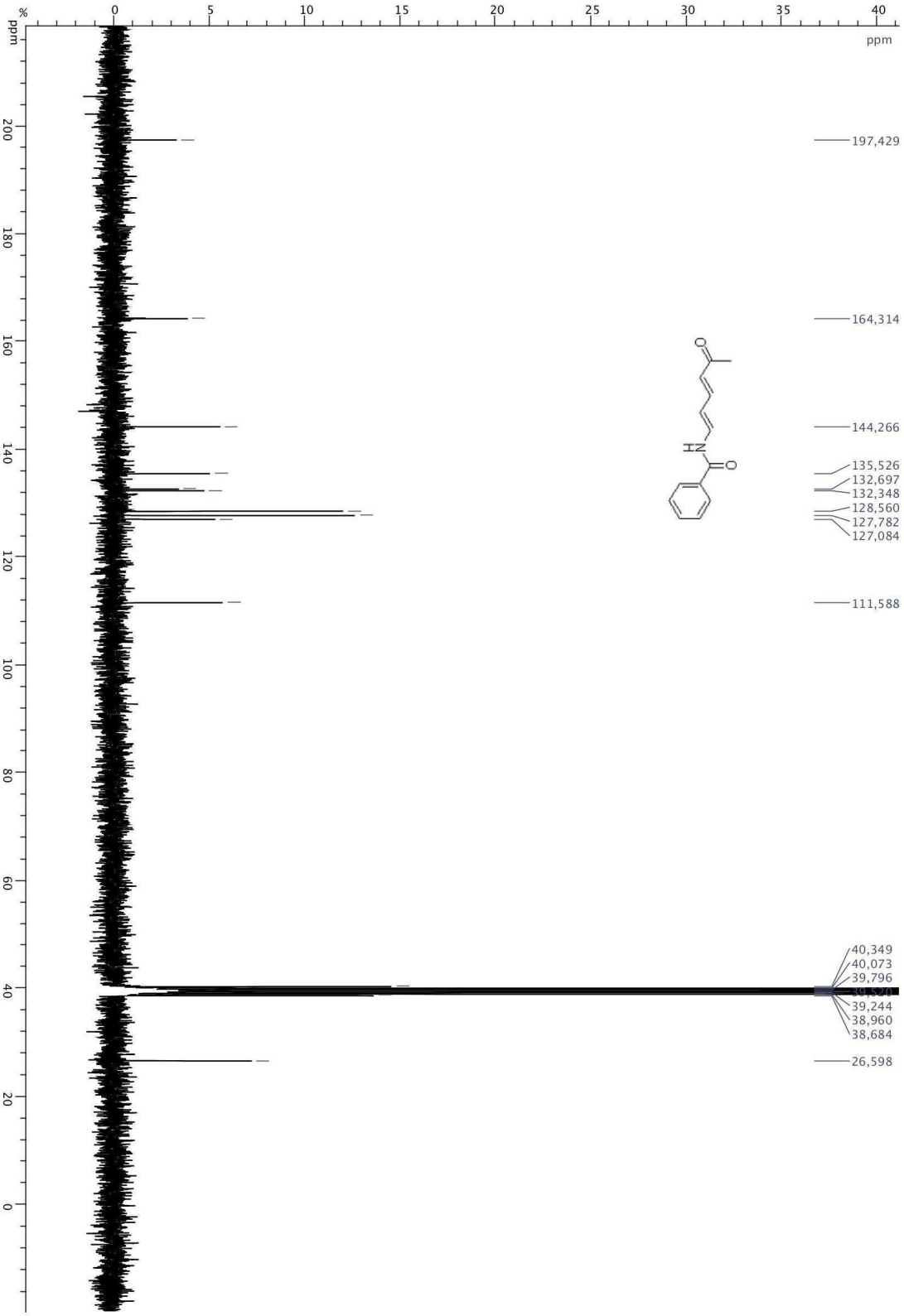
^{13}C NMR of *N*-((1*E*, 3*E/Z*)-3-methyl-5-oxopenta-1,3-dienyl)benzamide (2/1) 6k (DMSO-d_6, 75 MHz)



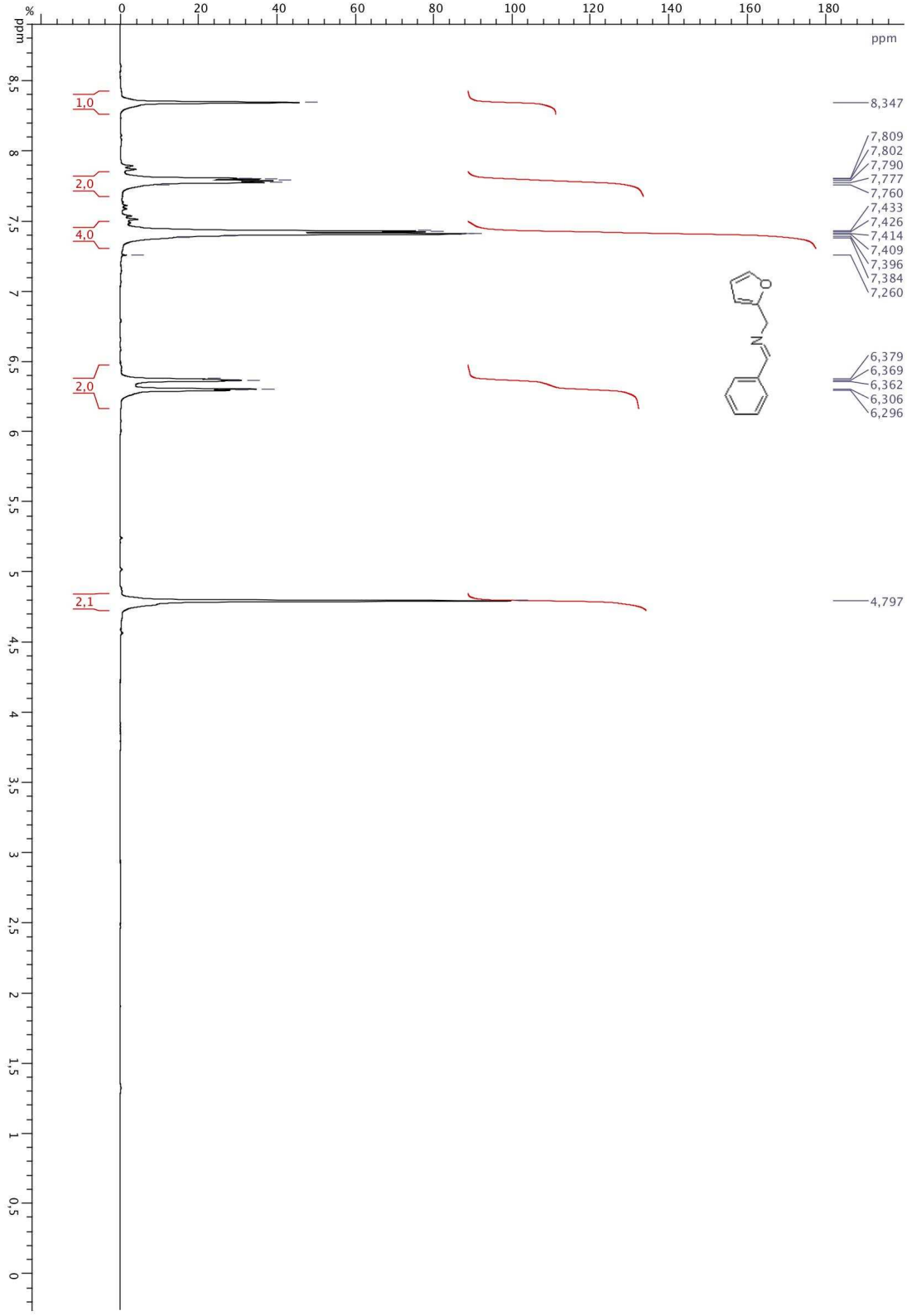
^{1}H NMR of *N*-((1*E*,3*E*)-5-oxohexa-1,3-dienyl)benzamide 6m (DMSO-d_6, 300 MHz)



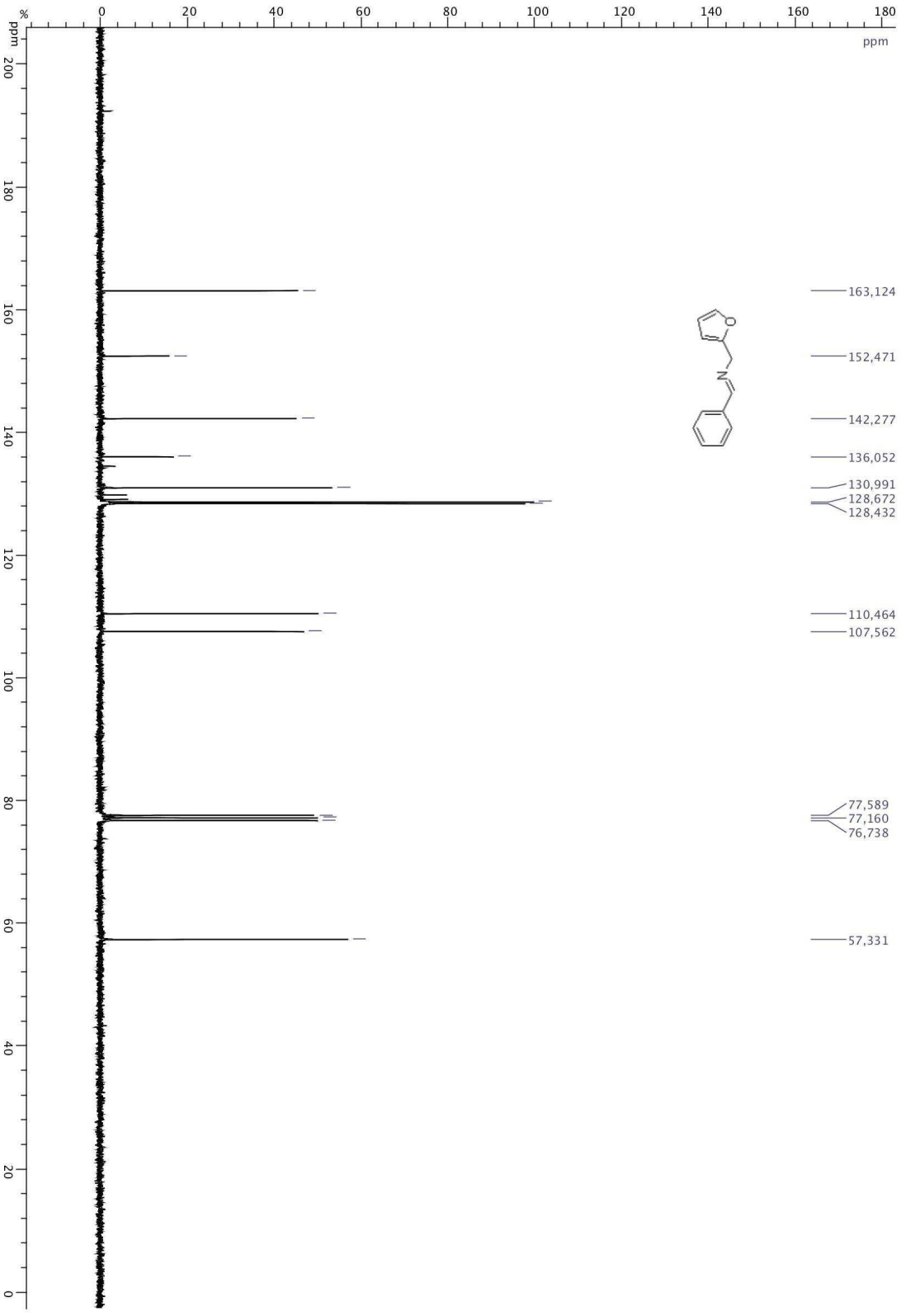
^{13}C NMR of *N*-((1*E*,3*E*)-5-oxohexa-1,3-dienyl)benzamide 6m (DMSO-d_6, 75 MHz)



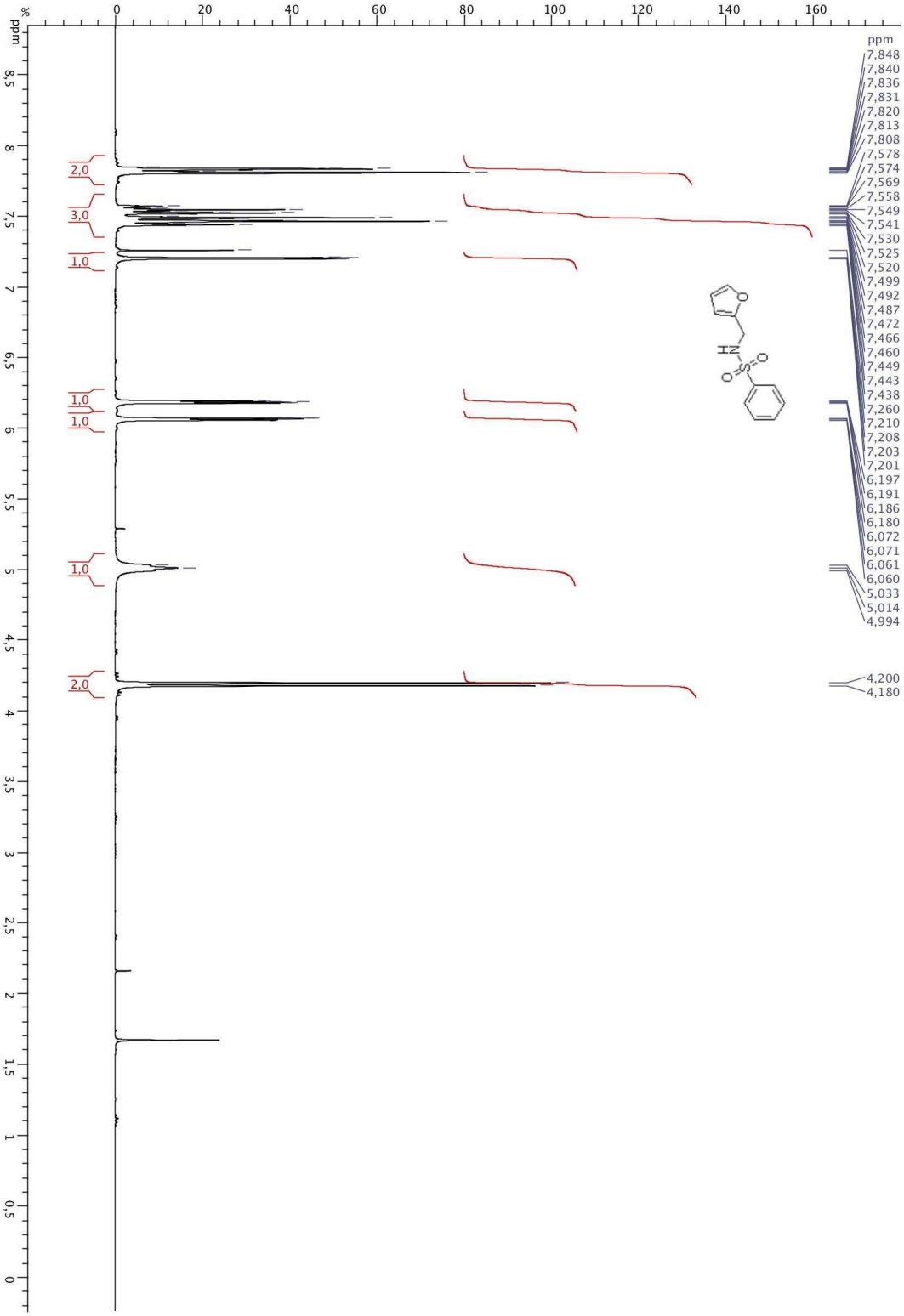
^{1}H NMR of *N*-benzylidene-1-(furan-2-yl)methylamine 7 ($CDCl_3$, 300 MHz)



^{13}C NMR of *N*-benzylidene-1-(furan-2-yl)methylamine 7 ($CDCl_3$, 75 MHz)



^{1}H NMR of *N*-(furan-2-ylmethyl)benzenesulfonamide 8 ($CDCl_3$, 300 MHz)



^{13}C NMR of *N*-(furan-2-ylmethyl)benzenesulfonamide 8 ($CDCl_3$, 75 MHz)