Supporting Information

Transition metal-free synthesis of α-ketoamides from arylmethyl ketones and alkylphosphoramides

Ahalya Behera, Wajid Ali, Manisha Tripathy, Diptimayee Sahoo and Bhisma K. Patel*

Department of Chemistry, Indian Institute of Technology Guwahati

Email: patel@iitg.ernet.in

Contents:

General Information: All the reagents were of commercial grade and purified according to the established procedures. Organic extracts were dried over anhydrous sodium sulphate. Solvents were removed in a rotary evaporator under reduced pressure. Silica gel (60–120 mesh size) was used for the column chromatography. Reactions were monitored by TLC on silica gel 60 F_{254} (0.25 mm). NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^{1}H NMR (400 MHz and 600 MHz) $CDCl_3$ solvent as the internal standard for ^{13}C NMR (100 MHz and 150 MHz). Mass spectra were recorded using ESI mode and APCI mode (Q-TOF MS analyzer). IR spectra were recorded in KBr or neat.

Experiments Performed for Mechanistic Investigation

Control reaction with *N*,*N*-dimethyl-2-oxo-2-phenylacetamide (1a):

A pre-synthesised *N*,*N*-dimethyl-2-oxo-2-phenylacetamide (**1a**) (0.25 mmol), $^{n}Bu_4NI$ (20 mol%, 18.5 mg), HMPA (**1**) (134 mg, 0.75 mmol), chlorobenzene (1 mL), TBHP (70 wt% in H_2O) (6 equiv.) was added to a 10 mL round bottom flask. The flask was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 130 ^{o}C. The progress of the reaction was monitored by TLC. Starting material **1a** remained unchanged even after 24 h without giving any trace of amide product (**1a′**). Thus, ruling out the formation of amide product (**1a′**) via the decomposition of ketoamide (**1a**).

Treatment of phenylglyoxal (A) with hexamethylphosphoramide (1):

An oven-dried round bottom flask was charged with phenylglyoxal (**A**) (67 mg, 0.5 mmol), $^{n}Bu_4NI$ (20 mol%, 37 mg), HMPA (**1**) (268 mg, 1.5 mmol), chlorobenzene (2 mL), TBHP (70 wt% in H_2O) (6 equiv.). The flask was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 130 ^{o}C. The progress of the reaction was monitored by TLC. The reaction after a period of 5 h afforded 62% of benzaldehyde (**B**) and 17% of *N*,*N*-dimethylbenzamide (**1a′**).

Reaction of benzaldehyde (B) with hexamethylphosphoramide (1):

An oven-dried round bottom flask was charged with benzaldehyde (**a**) (53 mg, 0.5 mmol), $^{n}Bu_4NI$ (20mol%, 37 mg), HMPA (**1**) (268 mg, 1.5 mmol), chlorobenzene (2 mL), TBHP (70 wt% in H_2O) (6 equiv.). The flask was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 130 ^{o}C. The reaction progress was monitored by TLC. After completion of the reaction, it was cooled to room temperature. Then the reaction mixture was quenched with saturated $Na_2S_2O_3$ solution and extracted with ethyl acetate. The ethyl acetate layer was dried over anhydrous Na_2SO_4. The solvent was then evaporated under reduced pressure and the residue was purified by column chromatography with an eluent hexane / ethyl acetate (65 / 35) to afford the *N*,*N*-dimethyl benzamide (**1a′**) in an isolated yield of 77%. This confirms the *in situ* generation of benzaldehyde in the reaction medium.

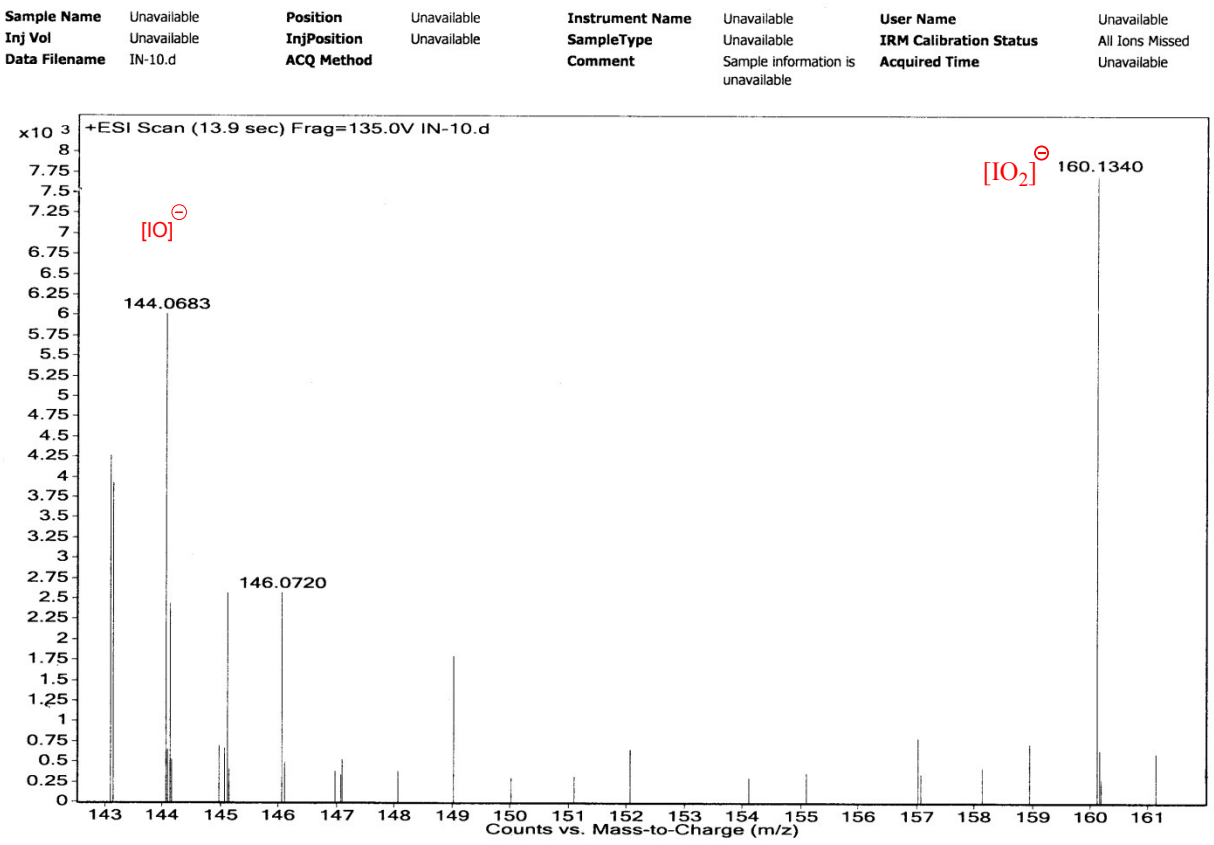
Control experiment with 4′-methyl acetophenone (b) and phenylglyoxal (A):

An equimolar mixture of 4′-methyl acetophenone (**b**) (33.5 mg, 0.25 mmol), phenylglyoxal (**A**) (33.5 mg, 0.25 mmol) and $^{n}Bu_4NI$ (20 mol%, 37 mg), HMPA (**1**) (268 mg, 1.5 mmol), chlorobenzene (2 mL), TBHP (70 wt% in H_2O) (6 equiv.) was placed in an oven-dried round bottom flask. Then it was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 130 ^{o}C. The progress of the reaction was monitored by TLC. The reaction resulted the formation of *N,N*-dimethyl-2-oxo-2-(*p*-tolyl)acetamide (**1b**) in 65% yield. Formation of ketoamide from phenylglyoxal was not observed, thereby ruling out the intermediacy of phenylglyoxal (**A**).

Experimental procedure for the detection of hypervalent iodine species:

An oven-dried round bottom flask was charged with acetophenone (**a**) (60 mg, 0.5 mmol), $^{n}Bu_4NI$ (20mol%, 37 mg), HMPA (**1**) (268 mg, 1.5 mmol), chlorobenzene (2 mL), TBHP (70 wt% in H_2O) (6 equiv.). The flask was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 130 ^{o}C. After 10 minutes, a 10 μL of the reaction mixture was collected and diluted with HPLC grade CH_3CN (1 mL). Then this diluted sample was filtered through a syringe filter having pore size 0.2 μm and was subjected to mass spectral analysis under ESI mode. The peak at 144.0683 and 160.1340 correspond to IO^- and IO_2^- species, respectively as shown below.

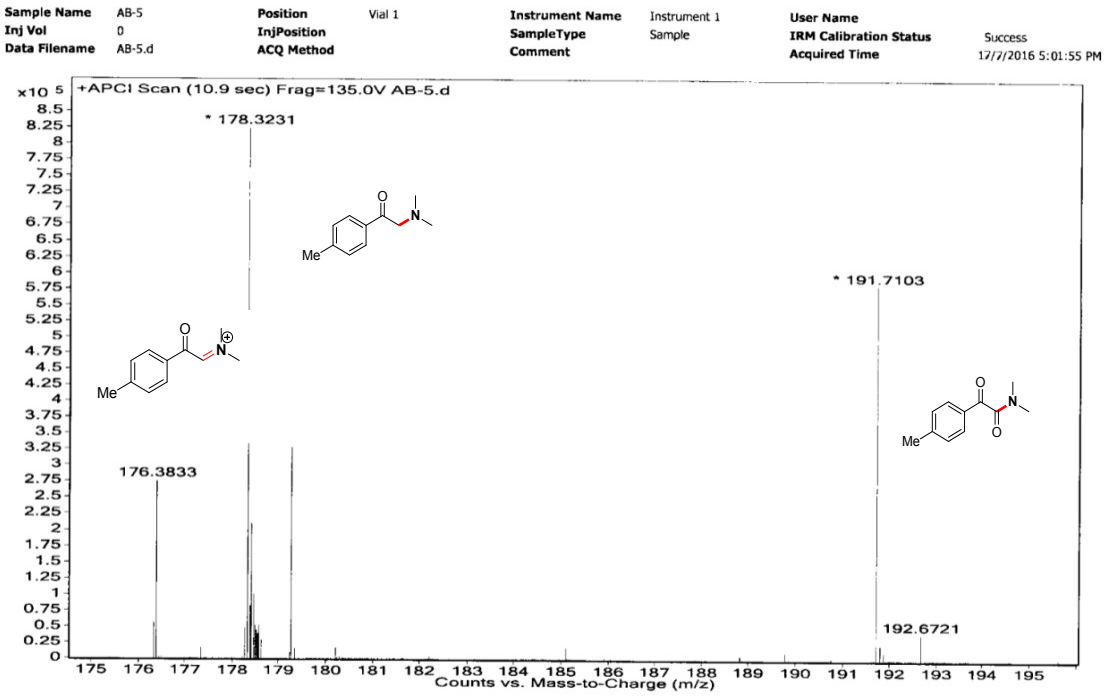
Mass Spectra of quarter-ion of intermediates (I) and (II):



Experimental procedure for the intermediate study:

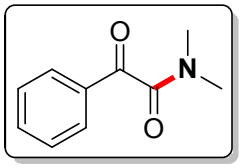
An oven-dried round bottom flask was charged with 4′-methyl acetophenone (**b**) (67 mg, 0.5 mmol), $^{n}Bu_4NI$ (20mol%, 37 mg), HMPA (**1**) (268 mg, 1.5 mmol), chlorobenzene (2 mL), TBHP (70 wt% in H_2O) (6 equiv.). The flask was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 130 ^{o}C. Then small quantities of reaction mixtures were collected in different time intervals such as 5, 10, 15, 20, 30, 45 minutes. Those collecting reaction mixtures are quenched with saturated $Na_2S_2O_3$ solution and extracted with ethyl acetate. From those organic layers, small amount of the worked up reaction mixtures was taken in different vials and diluted with HPLC grade CH_3CN as appropriate for mass samples. Then those diluted mass samples are filtered through mass filter having pore size 0.2 µm. Then the filtered mass samples are recorded in mass machine.

Mass Spectra of intermediates (C) and (D):



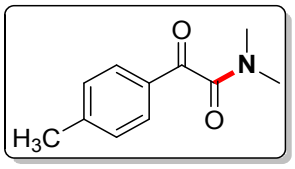
Spectral data

***N,N*-Dimethyl-2-oxo-2-phenylacetamide (1a):**



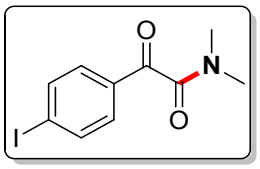
Reddish gummy (63.7 mg, 72% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.95 (s, 3H), 3.11 (s, 3H), 7.48–7.52 (m, 2H), 7.61–7.65 (m, 1H), 7.92–7.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 34.0, 37.1, 129.1, 129.6, 132.9, 134.8, 167.1, 191.9; IR (KBr): 2937, 2814, 1679, 1647, 1597, 1511, 1408, 1247, 1146, 996, 726, 692, 642, 462 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{11}NO_2$ (MH^+) 178.0863; found 178.0858.

***N,N*-Dimethyl-2-oxo-2-(*p*-tolyl)acetamide (1b):**



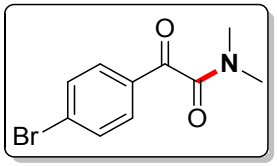
Brownish gummy (74.5 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (s, 3H), 2.95 (s, 3H), 3.11 (s, 3H), 7.31 (d, 2H, *J* = 8.0 Hz), 7.83 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 22.1, 34.2, 37.3, 129.9, 130.0, 130.8, 146.2, 167.4, 191.7; IR (KBr): 2924, 2855, 1718, 1645, 1607, 1456, 1406, 1251, 1146, 998, 756, 618, 474 cm^{-1}; HRMS (ESI): calcd. for $C_{11}H_{13}NO_2$ (MH^+) 192.1019; found 192.1027.

2-(4-Iodophenyl)-*N,N*-dimethyl-2-oxoacetamide (1c):



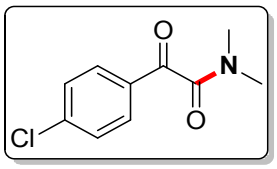
Brownish gummy (106 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.95 (s, 3H), 3.11 (s, 3H), 7.65 (dd, 2H, *J* = 8.4 Hz), 7.88 (dd, 2H, *J* = 8.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.3, 37.3, 103.5, 131.0, 132.6, 138.6, 166.6, 191.1; IR (KBr): 2927, 2851, 1681, 1646, 1581, 1394, 1248, 1146, 1051, 994, 882, 760, 646, 466 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{10}INO_2$ (MH^+) 303.9829; found 303.9831.

2-(4-Bromophenyl)-*N,N*-dimethyl-2-oxoacetamide (1d):



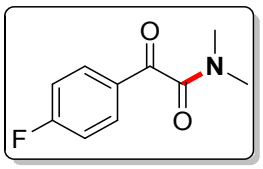
Brownish gummy (82.9 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.96 (s, 3H), 3.11 (s, 3H), 7.65 (d, 2H, *J* = 8.8 Hz), 7.81 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.3, 37.3, 130.4, 131.3, 132.1, 132.6, 166.7, 190.7; IR (KBr): 2926, 2851, 1682, 1648, 1585, 1399, 1247, 1146, 1069, 994, 883, 765, 646, 473 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{10}BrNO_2$ (MH^+) 255.9968; found 255.9972.

2-(4-Chlorophenyl)-*N,N*-dimethyl-2-oxoacetamide (1e):



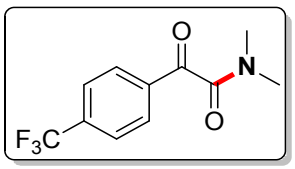
Brownish gummy (62.2 mg, 59% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.96 (s, 3H), 3.12 (s, 3H), 7.49 (d, 2H, *J* = 7.8 Hz), 7.89 (d, 2H, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.3, 37.3, 129.6, 131.3, 131.7, 141.6, 166.7, 190.5; IR (KBr): 2925, 2855, 1682, 1649, 1589, 1401, 1248, 1147, 1089, 995, 846, 768, 691, 472 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{10}ClNO_2$ (MH^+) 212.0473; found 212.0469.

2-(4-Fluorophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1f):



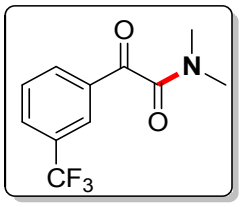
Brownish gummy (52.7 mg, 54% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.97 (s, 3H), 3.11 (s, 3H), 7.16–7.20 (m, 2H), 7.97–8.00 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.3, 37.3, 116.6 (d, *J* = 22.2 Hz), 129.8, 132.7 (d, *J* = 9.6 Hz), 166.0, 166.9, 167.8, 190.2; IR (KBr): 2926, 2855, 1681, 1645, 1598, 1409, 1239, 1146, 996, 853, 773, 612, 506 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{10}FNO_2$ (MH^+) 196.0768; found 196.0764.

***N*,*N*-Dimethyl-2-oxo-2-(4-(trifluoromethyl)phenyl)acetamide (1g):**



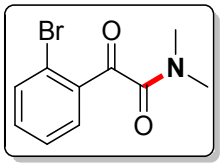
Yellowish gummy (58.8 mg, 48% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.98 (s, 3H), 3.14 (s, 3H), 7.78 (d, 2H, *J* = 7.2 Hz), 8.08 (d, 2H, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.4, 37.3, 124.5, 126.2 (q, *J*= 3.6 Hz), 130.3, 130.6, 135.8, 136.0 (d, *J* = 7.8 Hz), 166.3, 190.4; IR (KBr): 2937, 2867, 1690, 1652, 1409, 1326, 1246, 1131, 1066, 996, 857, 715, 647, 592 cm^{-1}; HRMS (ESI): calcd. for $C_{11}H_{10}F_3NO_2$ (MH^+) 246.0736; found 246.0733.

***N,N*-Dimethyl-2-oxo-2-(3-(trifluoromethyl)phenyl)acetamide (1i):**



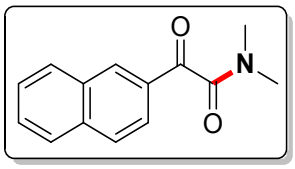
Light yellow liquid (77.2 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.99 (s, 3H), 3.14 (s, 3H), 7.66 (t, 1H, *J* = 8.4 Hz), 7.89 (d, 1H, *J* = 8.0 Hz), 8.14 (d, 1H, *J* = 7.6 Hz), 8.22 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.4, 37.3, 126.6 (q, *J* = 3.4 Hz), 129.2, 129.9, 130.6, 131.2 (t, *J* = 3.6 Hz), 133.2, 134.0, 166.2, 190.1; IR (KBr): 2932, 2855, 1688, 1650, 1407, 1332, 1238, 1131, 1073, 922, 760, 698, 544 cm^{-1}; HRMS (ESI): calcd. for $C_{11}H_{10}F_3NO_2$ (MH^+) 246.0736; found 246.0745.

2-(2-Bromophenyl)-*N,N*-dimethyl-2-oxoacetamide (1j):



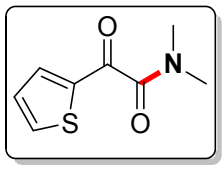
Yellow liquid (66.3 mg, 52% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.08 (s, 3H), 3.09 (s, 3H), 7.42–7.44 (m, 1H), 7.62–7.65 (m, 2H), 7.81–7.83 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.9, 37.5, 121.8, 127.9, 132.9, 134.3, 134.4, 135.6, 166.6, 191.1; IR (KBr): 2931, 2859, 1731, 1681, 2651, 1587, 1434, 1406, 1283, 1154, 1028, 992, 881, 747, 632, 494 cm^{-1}; HRMS (ESI): calcd. for $C_{10}H_{10}BrNO_2$ (MH^+) 255.9968; found 255.9972.

***N,N*-Dimethyl-2-(naphthalen-2-yl)-2-oxoacetamide (1k):**



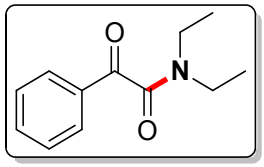
Brownish gummy (94.2 mg, 83% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 3.00 (s, 3H), 3.18 (s, 3H), 7.58 (t, 1H, *J* = 7.2 Hz), 7.65 (t, 1H, *J* = 6.6 Hz), 7.90 (d, 1H, *J* = 8.4 Hz), 7.94–7.98 (m, 2H), 8.03 (d, 1H, *J* = 8.4 Hz), 8.43 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.3, 37.4, 123.9, 127.3, 128.2, 129.3, 129.6, 130.1, 130.6, 132.7, 133.2, 136.6, 167.4, 192.1; IR (KBr): 2924, 2855, 1673, 1644, 1464, 1405, 1282, 1116, 997, 824, 781, 475 cm^{-1}; HRMS (ESI): calcd. for $C_{14}H_{13}NO_2$ (MH^+) 228.1019; found 228.1012.

***N,N*-Dimethyl-2-oxo-2-(thiophen-2-yl)acetamide (1l):**



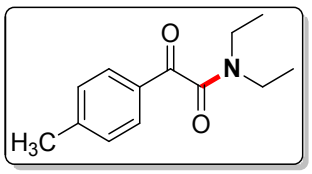
Brownish gummy (64.9 mg, 71% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.04 (s, 3H), 3.10 (s, 3H), 7.17–7.19 (m, 1H), 7.78–7.82 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 34.7, 37.6, 126.9, 129.0, 136.4, 136.6, 166.1, 183.7; IR (KBr): 2926, 2855, 1673, 1649, 1521, 1408, 1253, 1145, 1055, 844, 736, 642, 560 cm^{-1}; HRMS (ESI): calcd. for $C_8H_9NO_2S$ (MH^+) 184.0427; found 184.0422.

***N,N*-Diethyl-2-oxo-2-phenylacetamide (2a):**



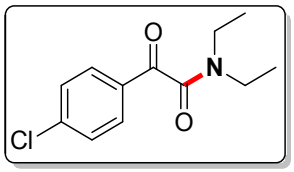
Reddish gummy (69.7 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.15 (t, 3H, J = 7.2 Hz), 1.29 (t, 3H, J = 7.2 Hz), 3.24 (q, 2H, J = 7.2 Hz), 3.56 (q, 2H, J = 7.2 Hz), 7.51 (t, 2H, J = 7.6 Hz), 7.63 (t, 1H, J = 7.6 Hz), 7.94 (d, 2H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.1, 14.3, 39.0, 42.3, 129.2, 129.8, 133.4, 134.8, 166.9, 191.8; IR (KBr) 2977, 2932, 1679, 1638, 1447, 1231, 1145, 1021, 720, 687, 631 cm^{-1}; HRMS (ESI): calcd.for $C_{12}H_{15}NO_2$ (MH^+) 206.1176; found 206.1182.

***N,N*-Diethyl-2-oxo-2-(*p*-tolyl)acetamide (2b):**



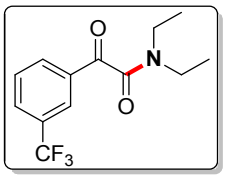
Reddish gummy (64.6 mg, 59% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 1.13 (t, 3H, J = 7.2 Hz), 1.27 (t, 3H, J = 7.2 Hz), 2.42 (s, 3H), 3.22 (q, 2H, J = 7.2 Hz), 3.54 (q, 2H, J = 7.2 Hz), 7.29 (d, 2H, J = 8.4 Hz), 7.82 (d, 2H, J = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 13.0, 14.3, 22.1, 38.9, 42.3, 129.8, 131.0, 146.0, 167.1, 191.5; IR (KBr) 2978, 2937, 1679, 1641, 1448, 1300, 1236, 1145, 1027, 754, 611, 480 cm^{-1}; HRMS (ESI): calcd.for $C_{13}H_{17}NO_2$ (MH^+) 220.1332; found 220.1329.

2-(4-Chlorophenyl)-*N*,*N*-diethyl-2-oxoacetamide (2e):



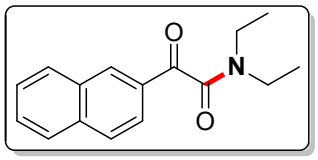
Reddish gummy (88.4 mg, 74% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 1.16 (t, 3H, *J* = 7.2 Hz), 1.28 (t, 3H, *J* = 7.2 Hz), 3.24 (q, 2H, *J* = 7.2 Hz), 3.55 (q, 2H, *J* = 7.2 Hz), 7.48 (d, 2H, *J* = 8.4 Hz), 7.88 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 13.0, 14.4, 39.1, 42.3, 129.6, 131.2, 131.9, 141.4, 166.4, 190.4; IR (KBr) 2978, 2934, 1680, 1641, 1447, 1231, 1145, 1089, 1013, 836, 764, 687, 548 cm^{-1}; HRMS (ESI): calcd.for $C_{12}H_{14}ClNO_2$ (MH^+) 240.0786; found 240.0788.

***N*,*N*-Diethyl-2-oxo-2-(3-(trifluoromethyl)phenyl)acetamide (2i):**



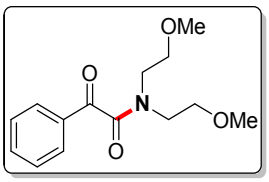
Brownish gummy (110.6 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.18 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 3.6 Hz), 3.26 (q, 2H, *J* = 7.2 Hz), 3.58 (q, 2H, *J* = 7.6 Hz), 7.66 (t, 1H, *J* = 7.6 Hz), 7.88 (d, 1H, *J* = 8.0 Hz), 8.11 (d, 1H, *J* = 8.0 Hz), 8.22 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 13.0, 14.4, 39.3, 42.4, 124.6, 126.5 (q, *J* = 3.6 Hz), 129.9, 131.1 (q, *J* = 2.8 Hz), 131.8, 132.1 (d, *J* = 6.1 Hz), 133.1, 134.1, 166.0, 190.0; IR (KBr) 2927, 2855, 1688, 1642, 1443, 1333, 1216, 1171, 1073, 756, 695, 636 cm^{-1}; HRMS (ESI): calcd.for $C_{13}H_{14}F_3NO_2$ (MH^+) 274.1049; found 274.1050.

***N*,*N*-Diethyl-2-(naphthalen-2-yl)-2-oxoacetamide (2k):**



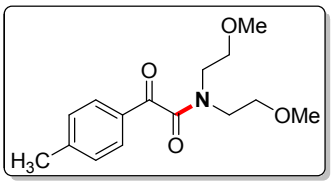
Reddish gummy (89.3 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.16 (t, 3H, *J* = 7.2 Hz), 1.33 (t, 3H, *J* = 7.2 Hz), 3.28 (q, 2H, *J* = 7.2 Hz), 3.62 (q, 2H, *J* = 7.2 Hz), 7.56 (t, 1H, *J* = 7.6 Hz), 7.64 (t, 1H, *J* = 7.6 Hz), 7.89 (d, 1H, *J* = 8.0 Hz), 7.94 (t, 2H, *J* = 10.8 Hz), 8.02 (d, 1H, *J* = 8.8 Hz), 8.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.1, 14.4, 39.1, 42.4, 124.0, 127.3, 128.2, 129.2, 129.5, 130.1, 130.8, 132.6, 133.0, 136.5, 167.0, 191.9; IR (KBr) 2977, 2934, 1674, 1639, 1460, 1359, 1257, 1218, 1190, 869, 651, 475 cm^{-1}; HRMS (ESI): calcd.for $C_{16}H_{17}NO_2$ (MH^+) 256.1332; found 256.1333.

***N,N*-Bis(2-methoxyethyl)-2-oxo-2-phenylacetamide (3a):**



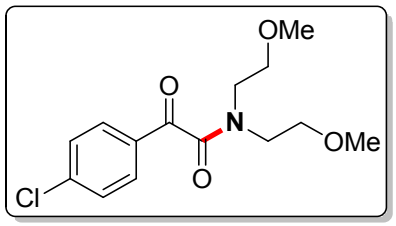
Yellowish gummy (99.4 mg, 75% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 3.11 (s, 3H), 3.38 (s, 3H), 3.43 (t, 2H, *J* = 5.4 Hz), 3.52 (t, 2H, *J* = 5.4 Hz), 3.65 (t, 2H, *J* = 5.4 Hz), 3.77 (t, 2H, *J* = 5.4 Hz), 7.46 (t, 2H, *J* = 7.8 Hz), 7.59 (t, 1H, *J* = 7.8 Hz), 7.94 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 45.4, 48.4, 58.7, 59.0, 70.6, 70.7, 128.8, 130.1, 133.6, 134.5, 167.9, 191.2; IR (KBr) 2927, 2892, 1679, 1640, 1448, 1256, 1190, 1118, 1012, 967, 722 cm^{-1}; HRMS (ESI): calcd.for $C_{14}H_{19}NO_4$ (MH^+) 266.1387; found 266.1395.

***N,N*-Bis(2-methoxyethyl)-2-oxo-2-(*p*-tolyl)acetamide (3b):**



Yellowish gummy (83.9 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (s, 3H), 3.17 (s, 3H), 3.40 (s, 3H), 3.45 (t, 2H, *J* = 5.2 Hz), 3.52 (t, 2H, *J* = 5.2 Hz), 3.67 (t, 2H, *J* = 5.6 Hz), 3.79 (t, 2H, *J* = 5.2 Hz), 7.29 (d, 2H, *J* = 8.0Hz), 7.85 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.2, 45.4, 48.4, 57.9, 58.8, 70.6, 70.9, 129.7, 130.2, 131.2, 145.8, 168.1, 191.1; IR (KBr) 2926, 2855, 1674, 1642, 1448, 1296, 1179, 1118, 1012, 967, 833, 755, 613, 480 cm^{-1}; HRMS (ESI): calcd.for $C_{15}H_{21}NO_4$ (MH^+) 280.1543; found 280.1552.

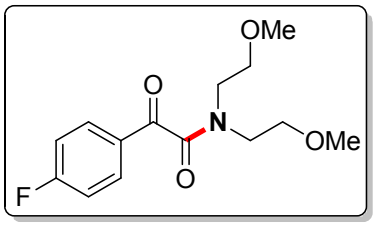
2-(4-Chlorophenyl)-*N,N*-bis(2-methoxyethyl)-2-oxoacetamide (3e):



Yellowish gummy (112.2 mg, 75% yield); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 3.08 (s, 3H), 3.38 (s, 3H), 3.41 (t, 2H, *J* = 5.4 Hz), 3.55 (t, 2H, *J* = 5.4 Hz), 3.64 (t, 2H, *J* = 5.4 Hz), 3.75 (t, 2H, *J* = 5.4 Hz), 7.44 (d, 2H, *J* = 8.4 Hz), 7.89 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 45.5, 48.5, 58.6, 59.1, 70.4, 70.6, 129.1, 131.5, 132.2, 140.9, 167.4,

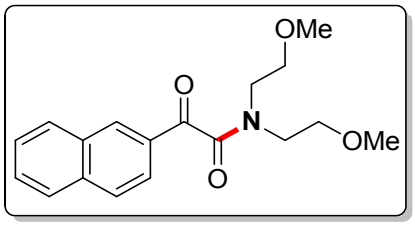
189.6; IR (KBr) 2931, 2891, 1680, 1641, 1487, 1400, 1255, 1192, 1118, 1012, 968, 769, 690, 544, 483 cm^{-1}; HRMS (ESI): calcd.for $C_{14}H_{18}ClNO_4$ (MH^+) 300.0997; found 300.0999.

2-(4-Fluorophenyl)-*N,N*-bis(2-methoxyethyl)-2-oxoacetamide (3f):



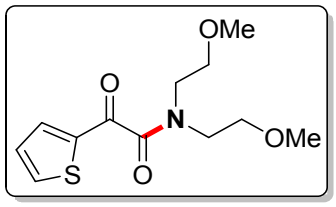
Yellowish gummy (111.8 mg, 79% yield); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.11 (s, 3H), 3.39 (s, 3H), 3.43 (t, 2H, *J* = 5.6 Hz), 3.56 (t, 2H, *J* = 5.2 Hz), 3.65 (t, 2H, *J* = 5.2 Hz), 3.77 (t, 2H, *J* = 5.2 Hz), 7.13–7.17 (m, 2H), 7.98–8.01 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 45.5, 48.5, 58.7, 59.1, 70.5, 70.7, 114.3, 116.1 (d, *J* = 21.9 Hz), 130.3, 133.0 (d, *J* = 9.4 Hz), 165.7, 167.5 (d, *J* = 30.3 Hz), 189.5; IR (KBr) 2926, 2856, 1680, 1642, 1460, 1232, 1119, 1011, 968, 852, 744, 611, 569, 506 cm^{-1}; HRMS (ESI): calcd.for $C_{14}H_{18}FNO_4$ (MH^+) 284.1293; found 284.1301.

***N,N*-Bis(2-methoxyethyl)-2-(naphthalen-2-yl)-2-oxoacetamide (3k):**



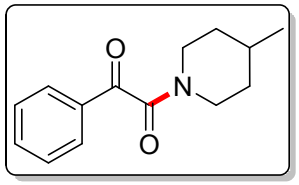
Reddish gummy (113.4 mg, 72% yield); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.12 (s, 3H), 3.45 (s, 3H), 3.48 (d, 2H, *J* = 5.6 Hz), 3.58 (t, 2H, *J* = 5.2 Hz), 3.72 (t, 2H, *J* = 5.2 Hz), 3.85 (t, 2H, *J* = 5.2 Hz), 7.56 (t, 1H, *J* = 7.6 Hz), 7.63 (t, 1H, *J* = 7.6 Hz), 7.90 (t, 1H, *J* = 4.8 Hz), 7.95 (t, 2H, *J* = 8.0 Hz), 8.02 (d, 1H, *J* = 8.4 Hz), 8.49 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 45.4, 48.5, 58.8, 59.2, 70.6, 70.8, 124.3, 127.1, 128.1, 128.8, 129.4, 130.1, 131.0, 132.6, 133.4, 136.4, 168.1, 191.4; IR (KBr) 2924, 2854, 1730, 1637, 1461, 1362, 1263, 1113, 1012, 763, 476 cm^{-1}; HRMS (ESI): calcd.for $C_{18}H_{21}NO_4$ (MH^+) 316.1543; found 316.1538.

***N,N*-Bis(2-methoxyethyl)-2-oxo-2-(thiophen-2-yl)acetamide (3l):**



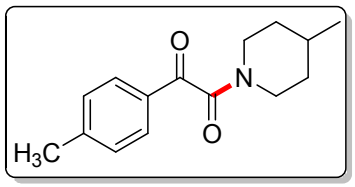
Yellowish gummy (81.3 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.15 (s, 3H), 3.35 (s, 3H), 3.37 (s, 2H), 3.47 (t, 2H, *J* = 5.2 Hz), 3.60–3.65 (m, 2H), 3.75 (t, 2H, *J* = 5.2 Hz), 7.41–7.46 (m, 1H), 7.74 (d, 1H, *J* = 7.2 Hz), 7.81 (d, 1H, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 45.9, 48.6, 58.8, 59.1, 70.6, 70.9, 128.6, 136.1, 136.3, 140.9, 166.8, 183.3; IR (KBr) 3098, 2926, 1739, 1640, 1409, 1255, 1117, 964, 839, 738, 635, 565 cm^{-1}; HRMS (ESI): calcd.for $C_{12}H_{17}NO_4S$ (MH^+) 272.0951; found 272.0950.

1-(4-Methylpiperidin-1-yl)-2-phenylethane-1, 2-dione (4a):



Yellowish gummy (100.5 mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.97 (d, 3H, *J* = 6.4 Hz), 1.09–1.20 (m, 2H), 1.23–1.30 (m, 2H), 1.78–1.81 (m, 1H), 2.76–2.83 (m, 1H), 3.02–3.09 (m, 1H), 3.51–3.54 (m, 1H), 4.61–4.64 (m, 1H), 7.51 (t, 2H, *J* = 8.0 Hz), 7.64 (t, 1H, *J* = 7.6 Hz), 7.94 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.8, 31.4, 33.8, 34.3, 41.7, 46.5, 129.2, 129.7, 133.4, 134.8, 165.6, 192.1; IR (KBr) 2925, 2868, 1679, 1641, 1451, 1372, 1264, 1213, 1142, 1085, 962, 859, 729, 690, 648 cm^{-1}; HRMS (ESI): calcd.for $C_{14}H_{17}NO_2$ (MH^+) 232.1332; found 232.1345.

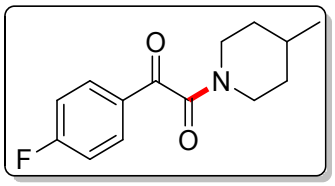
1-(4-Methylpiperidin-1-yl)-2-(*p*-tolyl)ethane-1,2-dione (4b):



Yellowish gummy (88.2 mg, 72% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.97 (d, 3H, *J* = 6.4 Hz), 1.08–1.20 (m, 2H), 1.23–1.29 (m, 2H), 1.79 (d, 1H, *J* = 13.2 Hz), 2.43 (s, 3H), 2.75–2.79 (m, 1H), 3.04–3.08 (m, 1H), 3.51 (d, 1H, *J* = 13.6 Hz), 4.62 (d, 1H, *J* = 13.2 Hz),

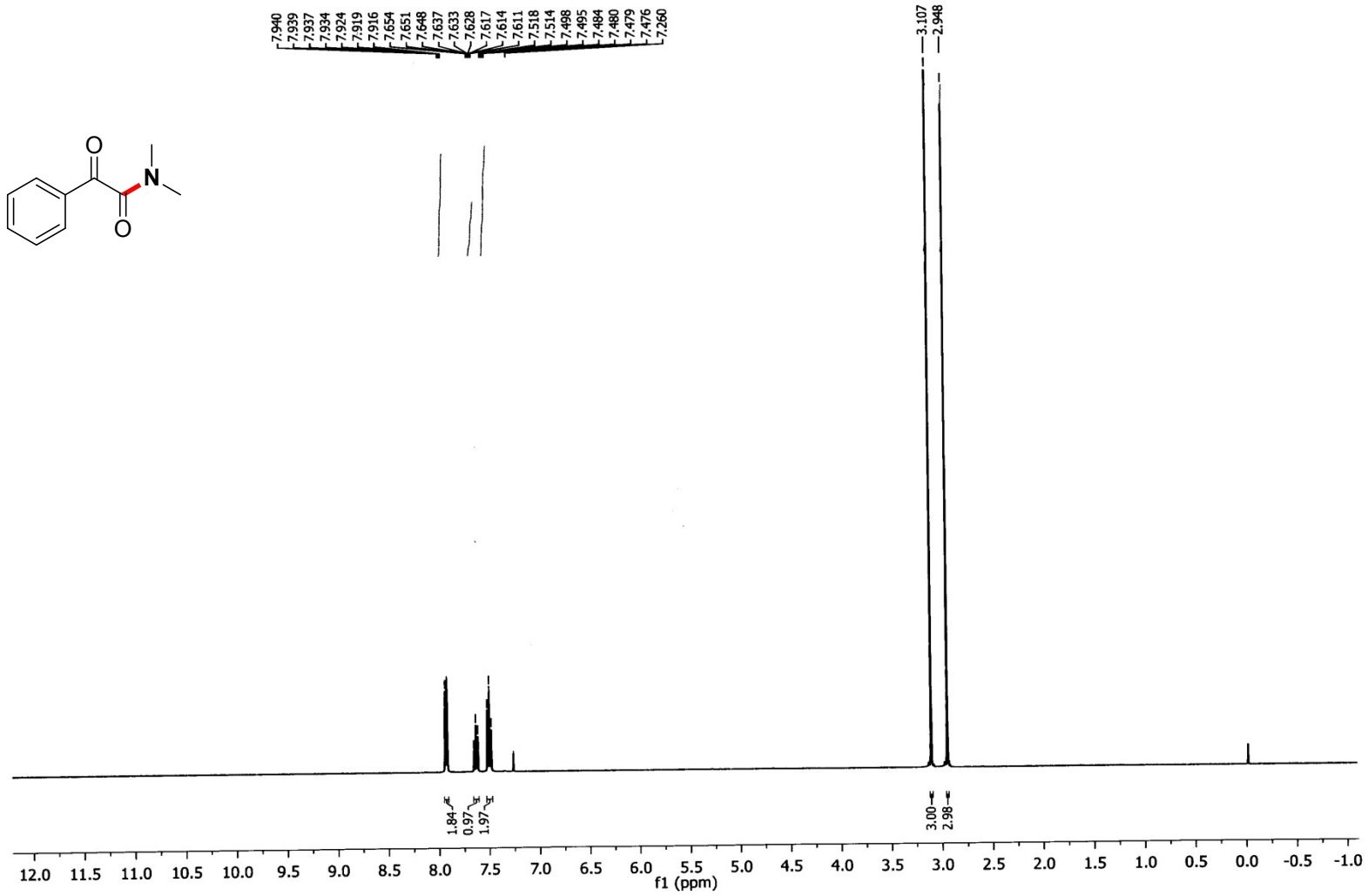
7.30 (d, 2H, *J* = 8.0 Hz), 7.83 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.8, 22.1, 31.3, 33.8, 34.5, 41.7, 46.5, 129.9, 131.1, 146.1, 165.8, 191.9; IR (KBr) 2926, 2869, 1676, 1643, 1453, 1373, 1266, 1216, 1178, 1143, 1086, 962, 865, 755, 693, 614, 480 cm^{-1}; HRMS (ESI): calcd.for $C_{15}H_{19}NO_2$ (MH^+) 246.1489; found 246.1488.

1-(4-Fluorophenyl)-2-(4-methylpiperidin-1-yl)ethane-1,2-dione (4f):

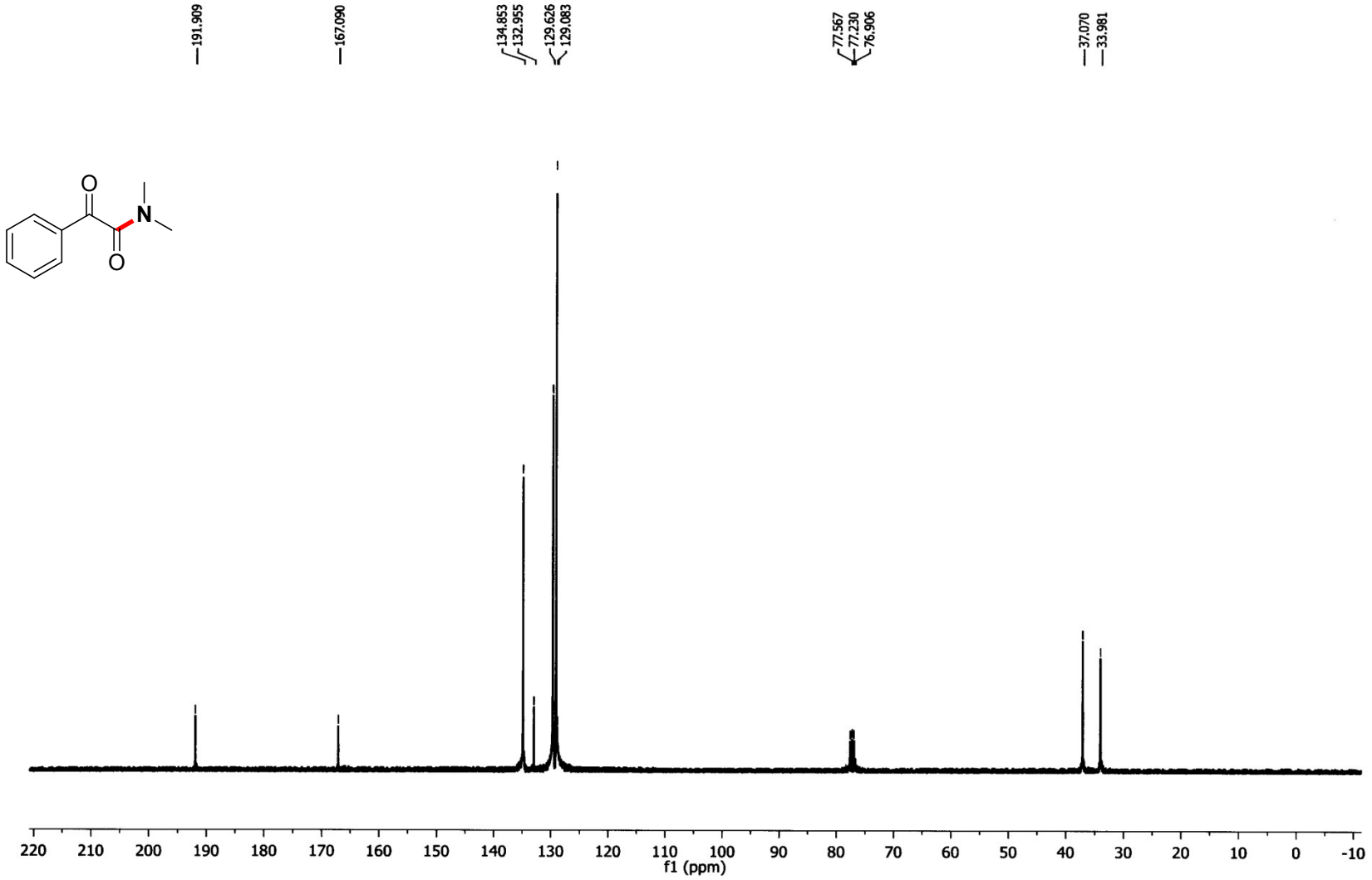


Brownish gummy (100.9 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.98 (d, 3H, *J* = 6.4 Hz), 1.09–1.20 (m, 2H), 1.25 (t, 2H, *J* = 15.2 Hz), 1.80 (d, 1H, *J* = 13.2 Hz), 2.76–2.83 (m, 1H), 3.06–3.09 (m, 1H), 3.52 (d, 1H, *J* = 13.6 Hz), 4.61 (d, 1H, *J* = 13.2 Hz), 7.18 (t, 2H, *J* = 8.8 Hz), 7.96–8.0 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.8, 31.3, 33.8, 34.3, 41.8, 46.6, 116.5 (d, *J* = 22.2 Hz), 130.0, 132.6 (d, *J* = 9.7 Hz), 165.3, 166.0, 167.7, 190.4; IR (KBr) 2925, 2855, 1634, 1510, 1440, 1373, 1308, 1227, 1115, 1088, 970, 760, 577 cm^{-1}; HRMS (ESI): calcd.for $C_{14}H_{16}FNO_2$ (MH^+) 250.1238; found 250.1241.

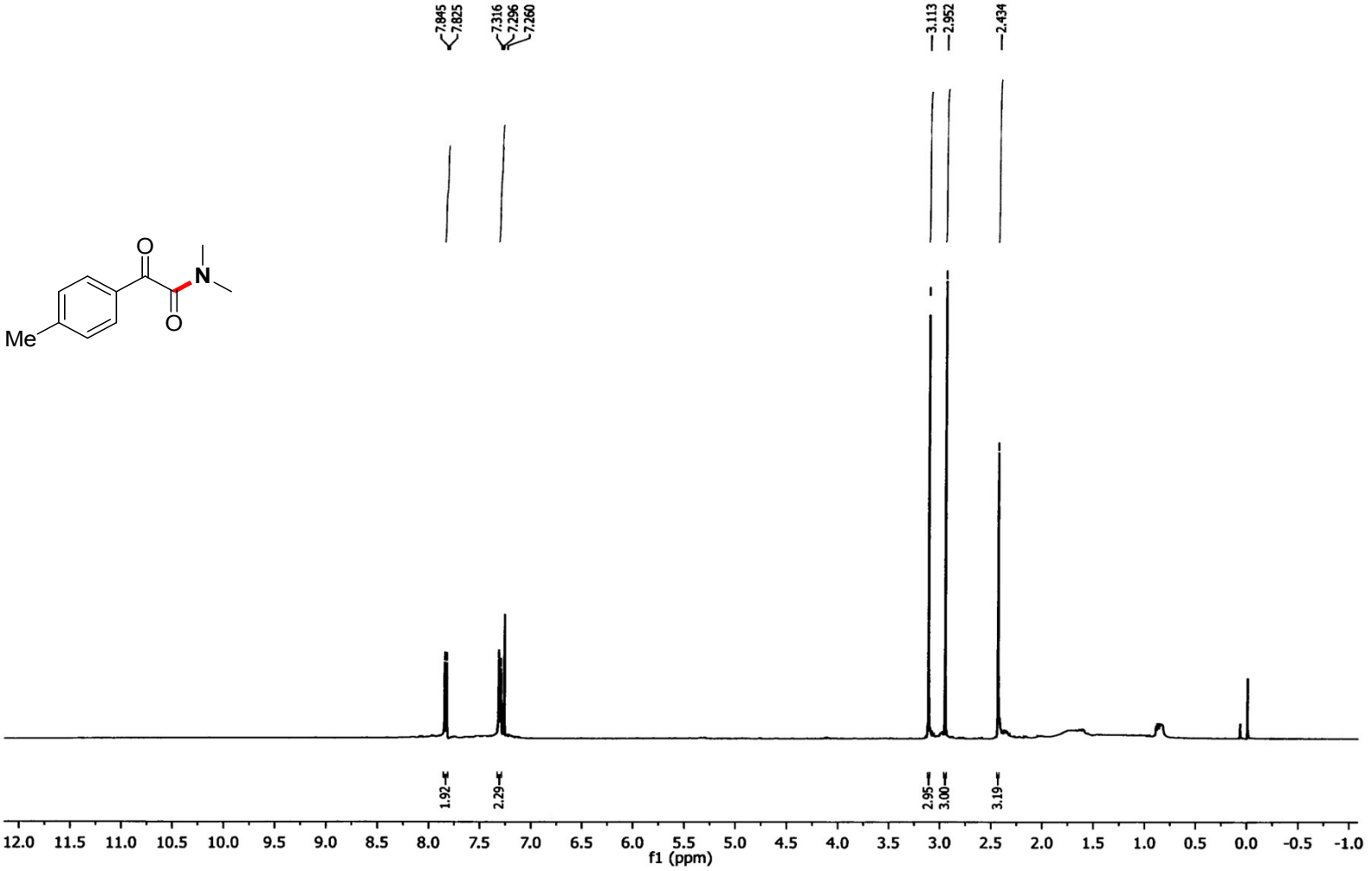
_N,N_-Dimethyl-2-oxo-2-phenylacetamide (1a): ^{1}H NMR (400 MHz, $CDCl_3$)



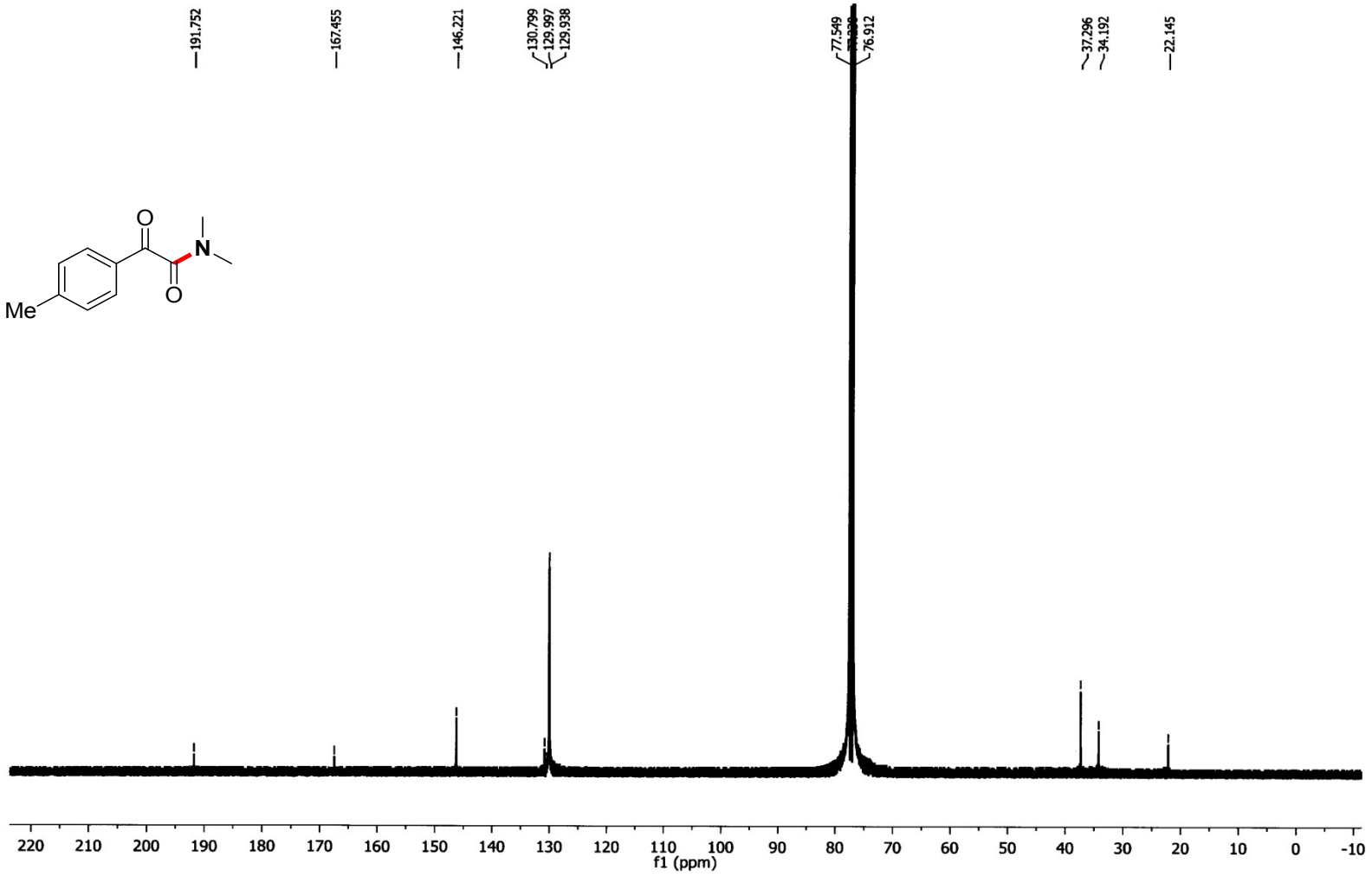
***N,N*-Dimethyl-2-oxo-2-phenylacetamide (1a): ^{13}C NMR (100 MHz, $CDCl_3$)**



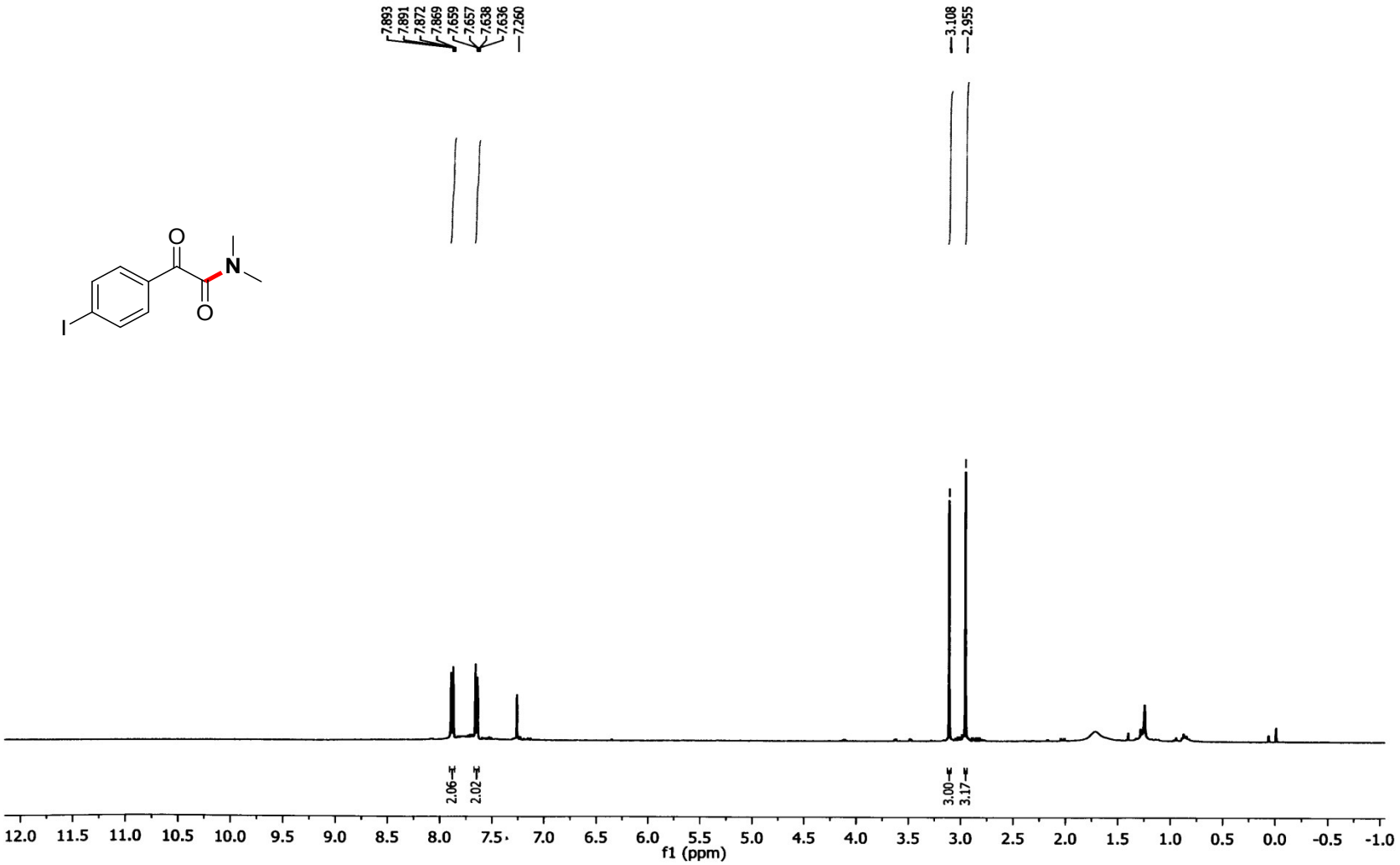
_N_,_N_-Dimethyl-2-oxo-2-(_p_-tolyl)acetamide (1b): ^{1}H NMR (400 MHz, $CDCl_3$)



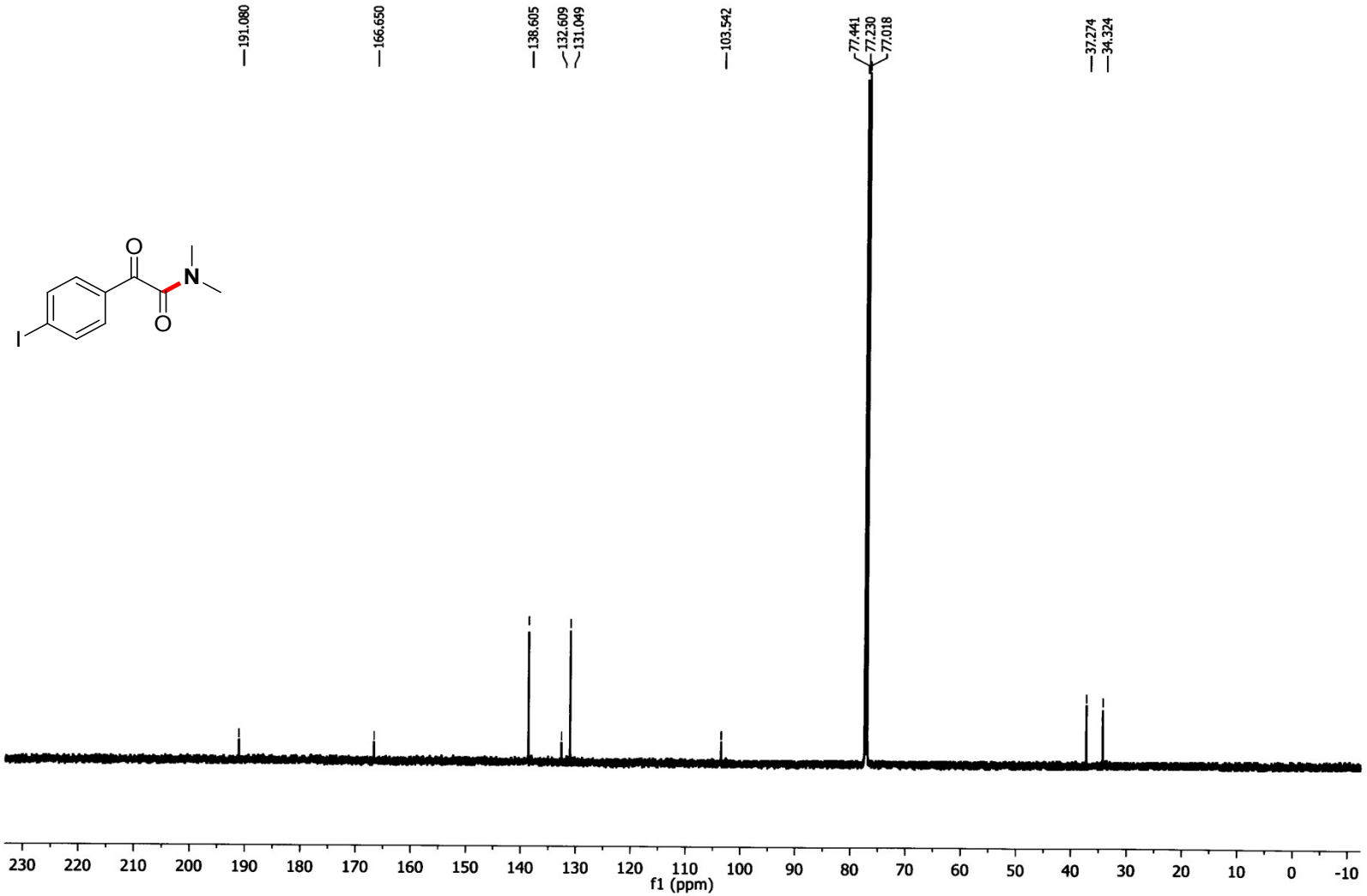
_N_,_N_-Dimethyl-2-oxo-2-(_p_-tolyl)acetamide (1b): ^{13}C NMR (100 MHz, $CDCl_3$)



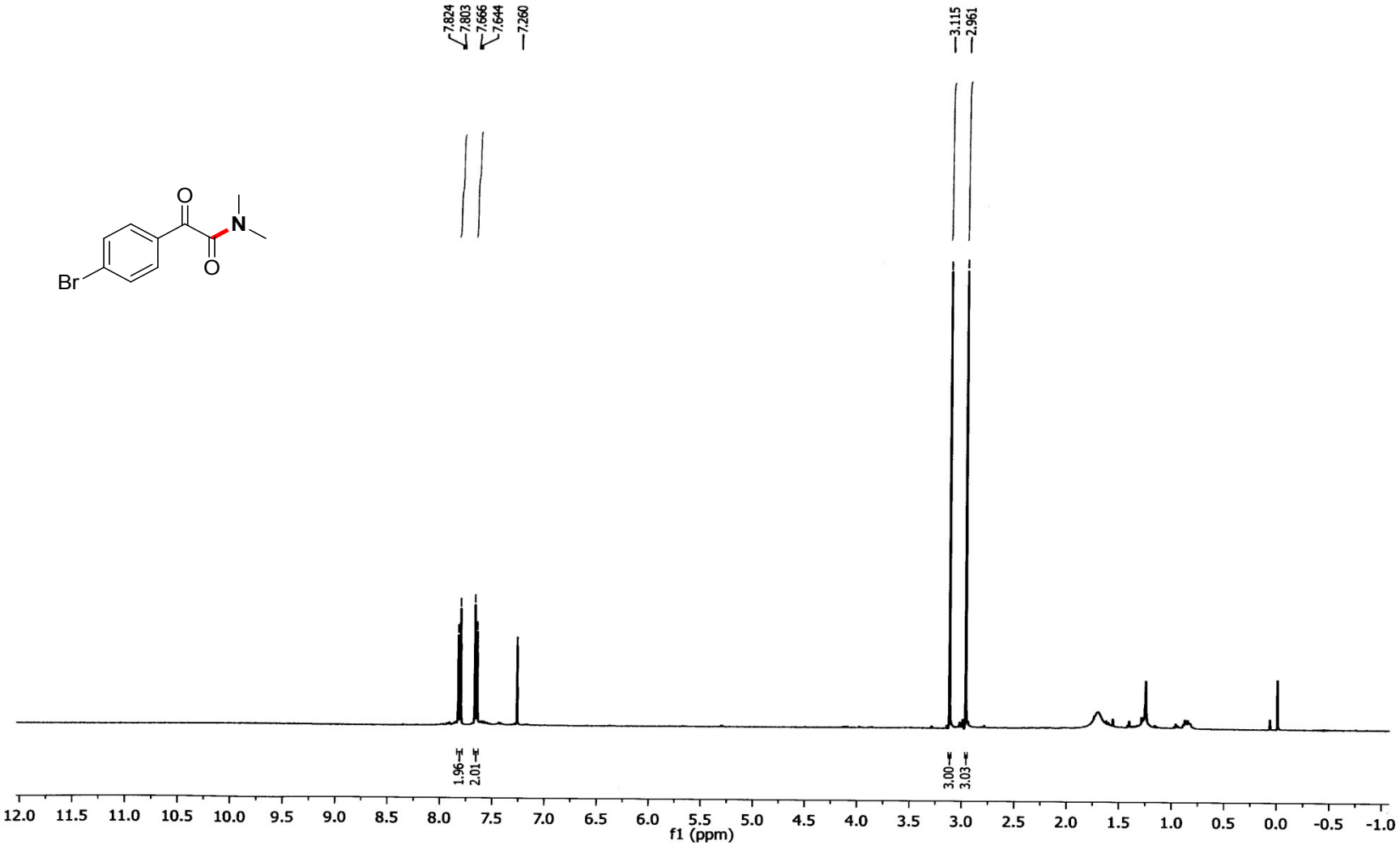
2-(4-Iodophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1c): ^{1}H NMR (400 MHz, $CDCl_3$)



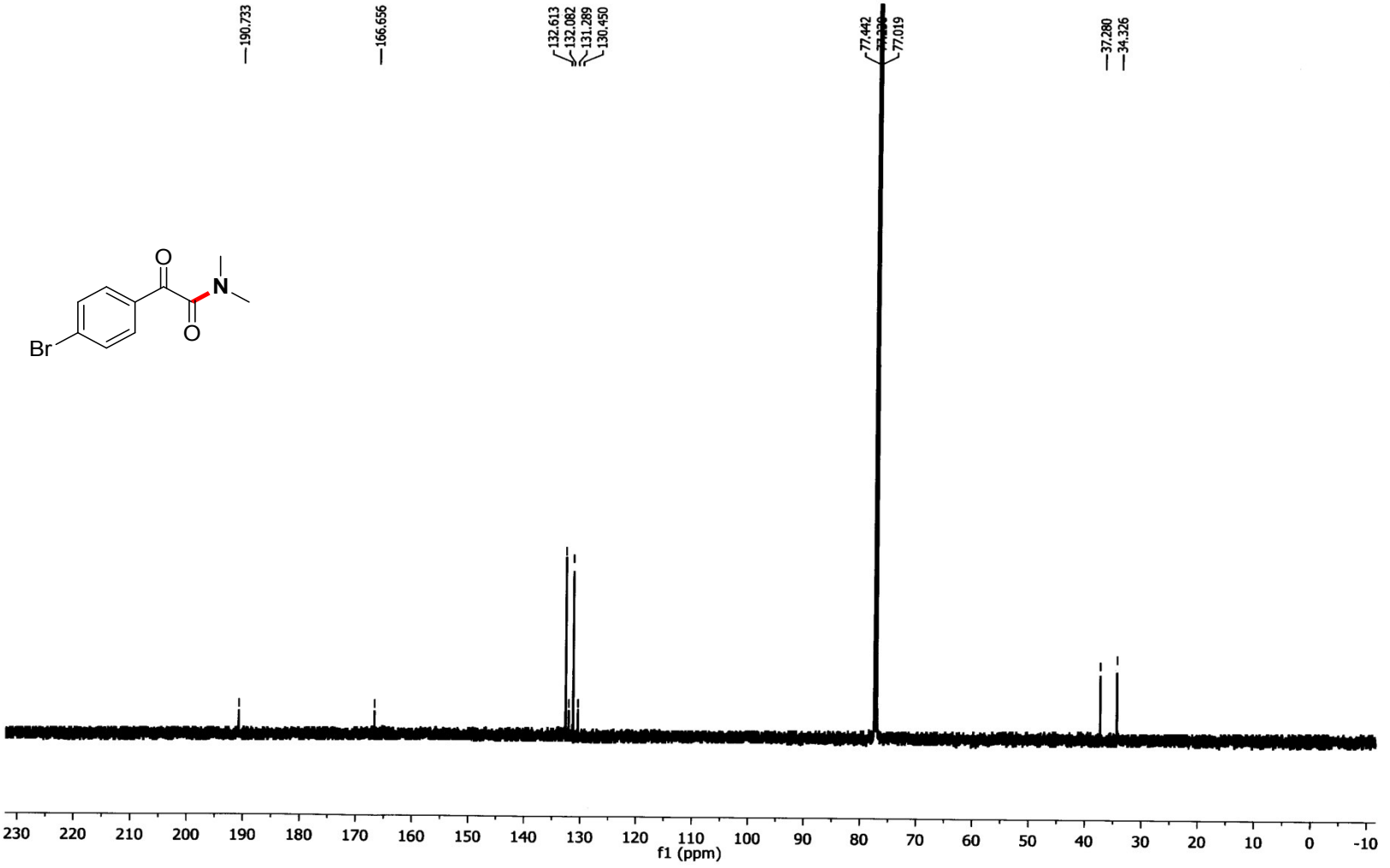
2-(4-Iodophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1c): ^{13}C NMR (150 MHz, $CDCl_3$)



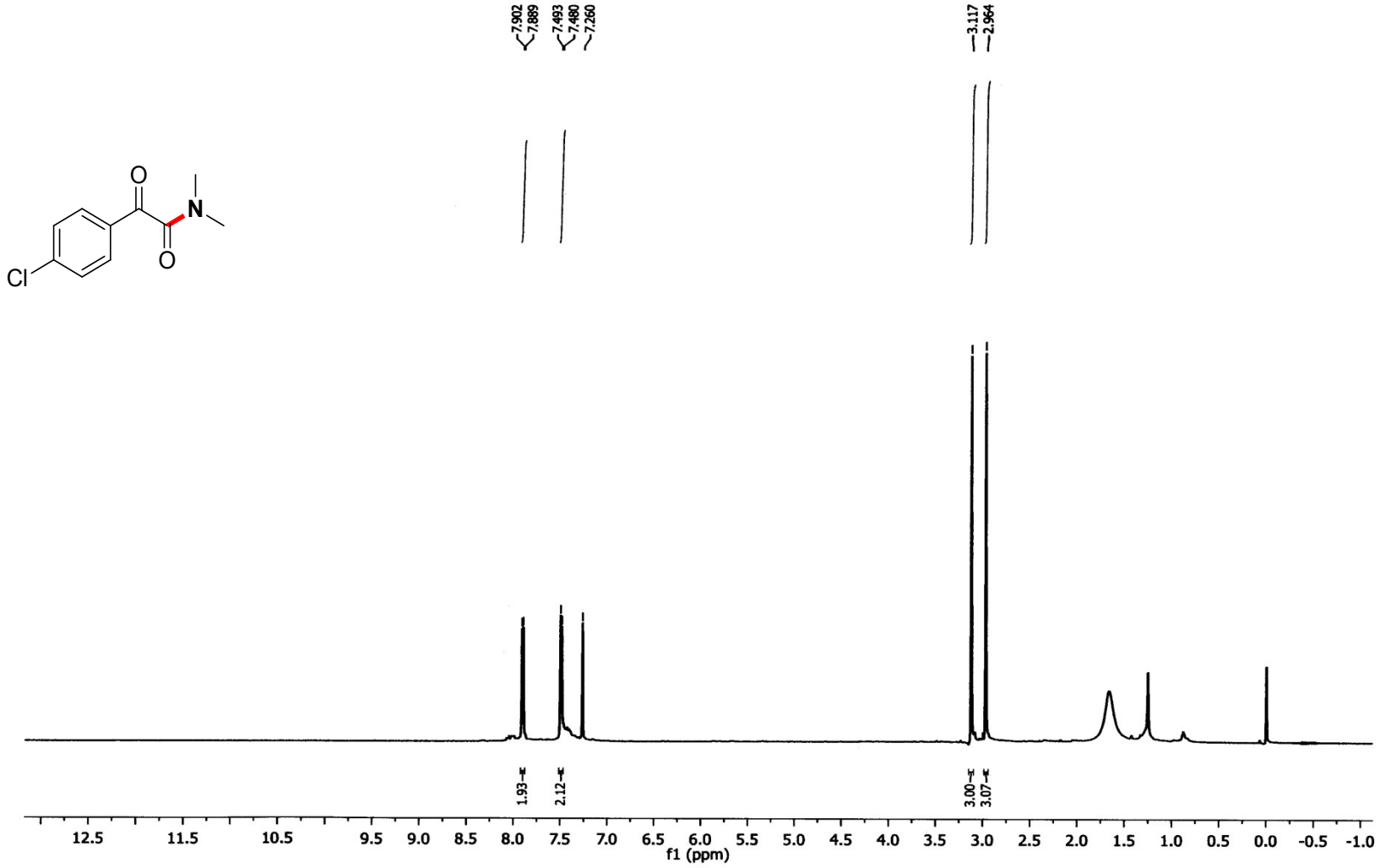
2-(4-Bromophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1d): ^{1}H NMR (400 MHz, $CDCl_3$)



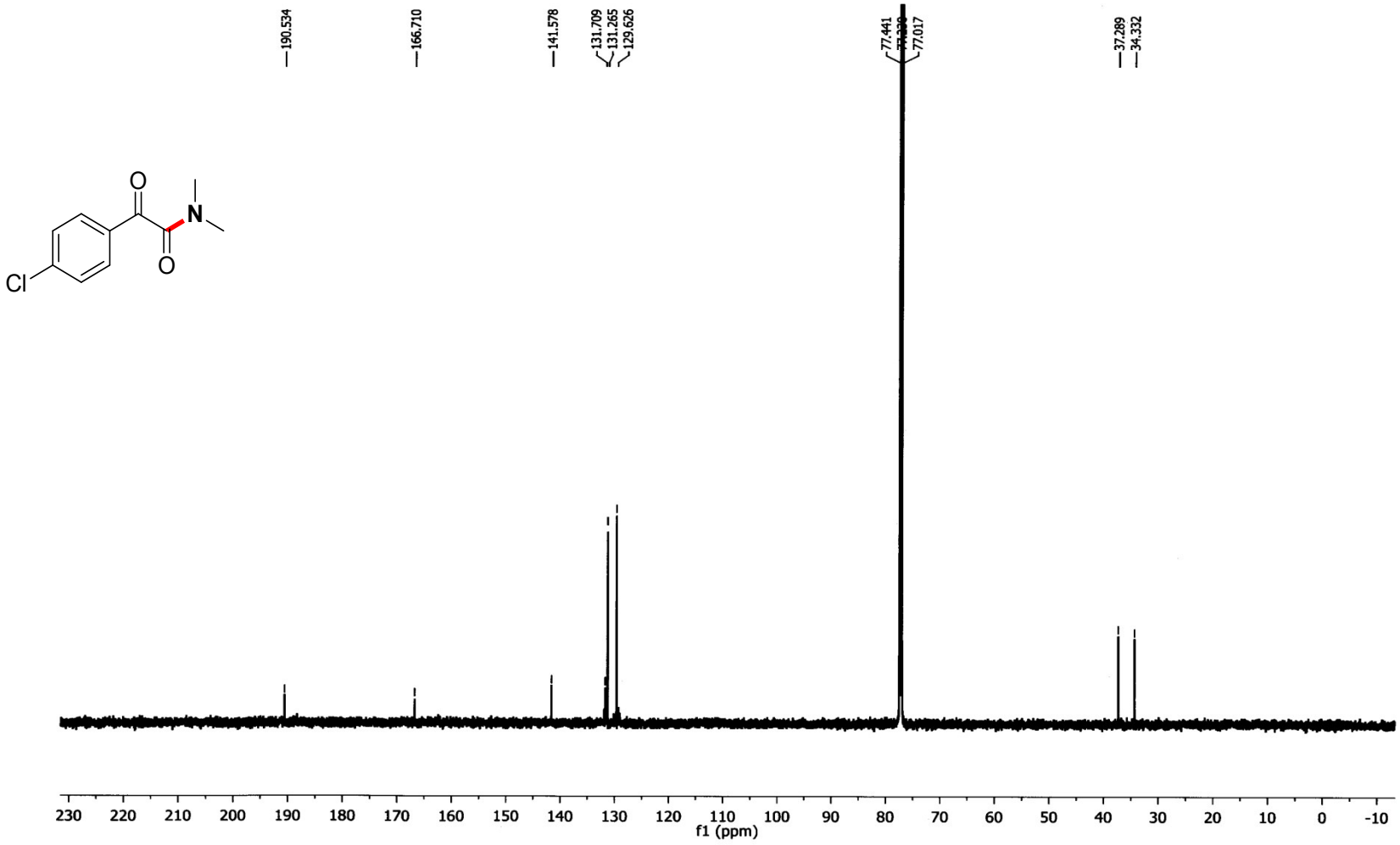
2-(4-Bromophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1d): ^{13}C NMR (150 MHz, $CDCl_3$)



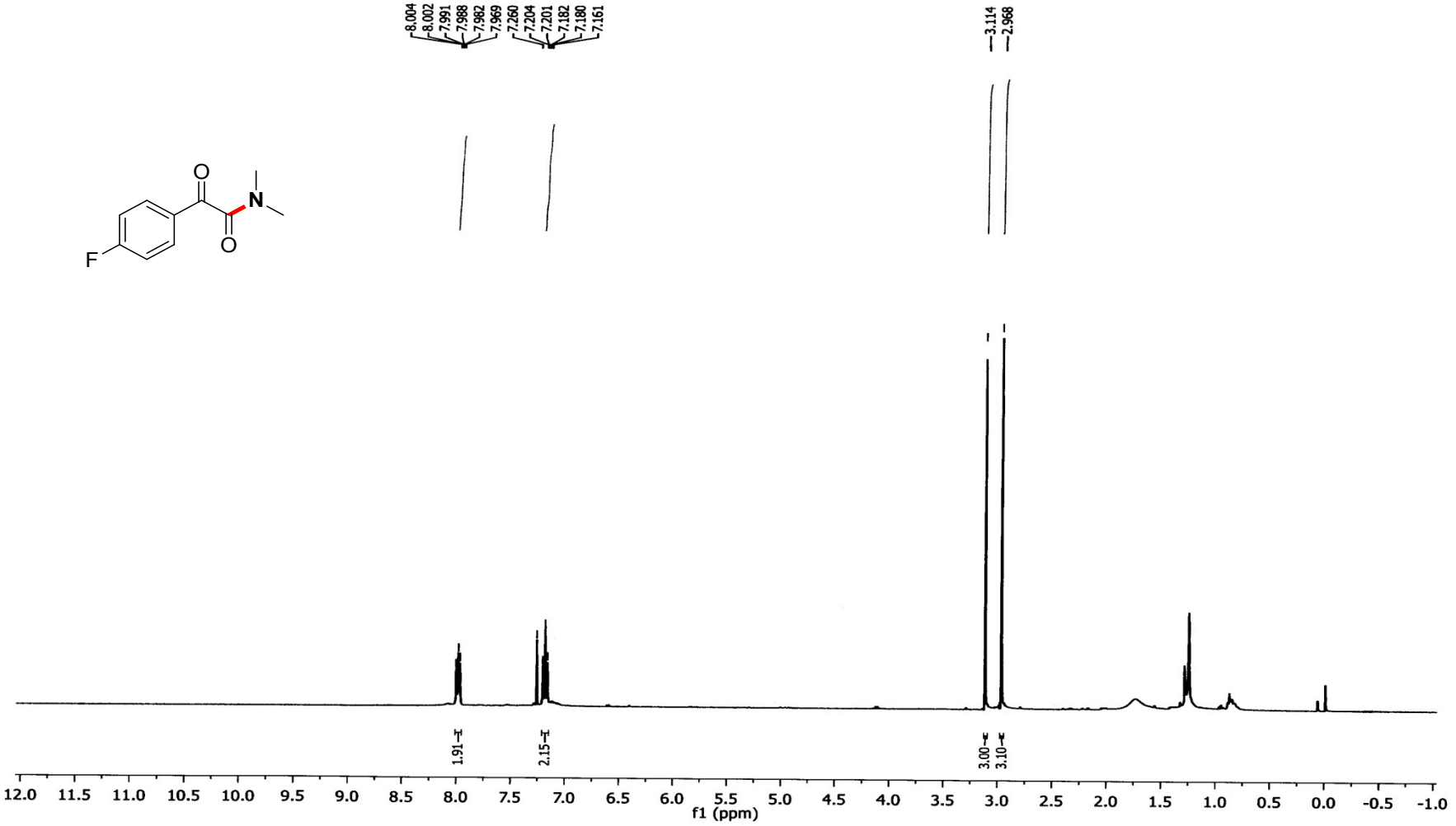
2-(4-Chlorophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1e): ^{1}H NMR (600 MHz, $CDCl_3$)



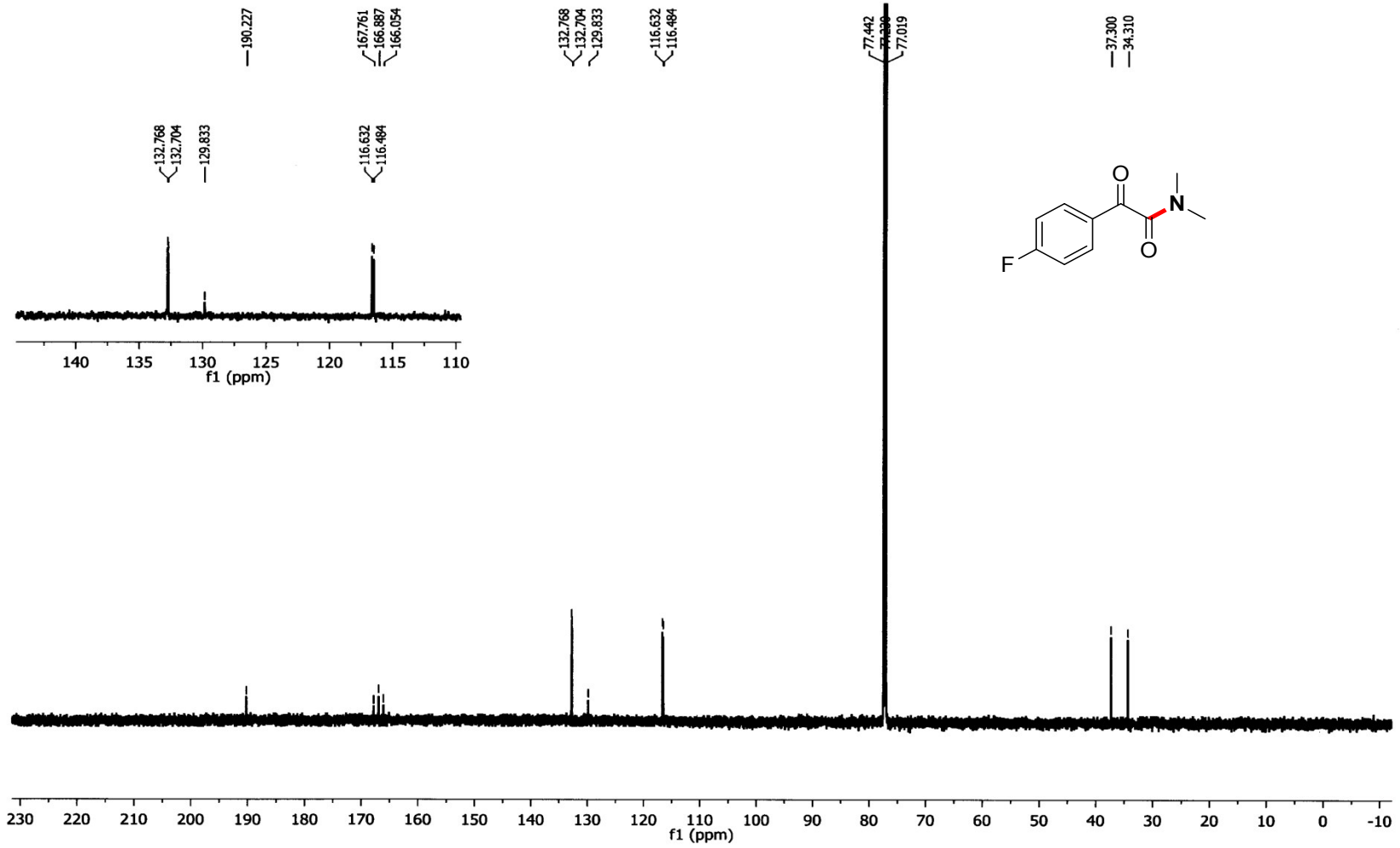
2-(4-Chlorophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1e): ^{13}C NMR (150 MHz, $CDCl_3$)



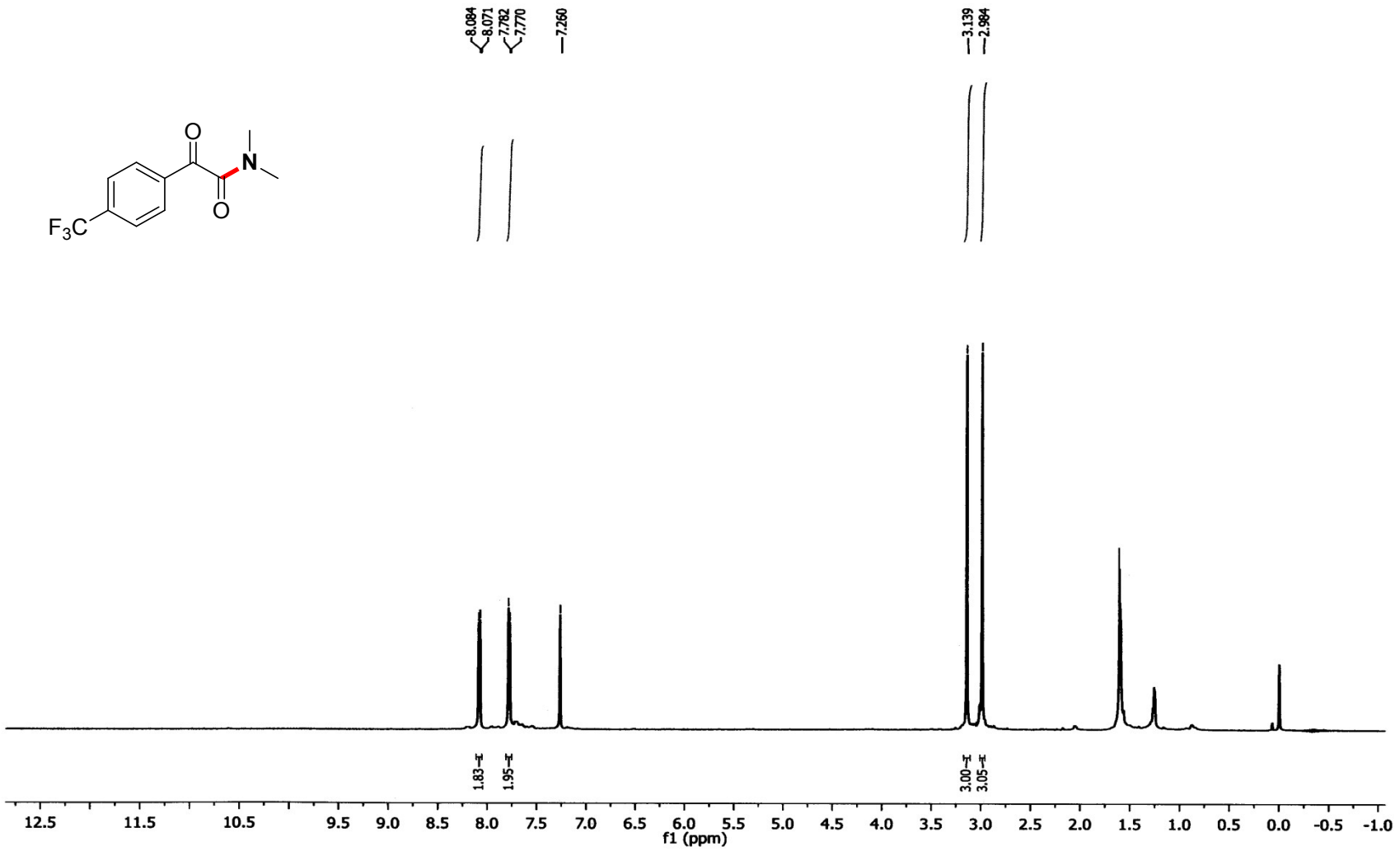
2-(4-Fluorophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1f): ^{1}H NMR (400 MHz, $CDCl_3$)



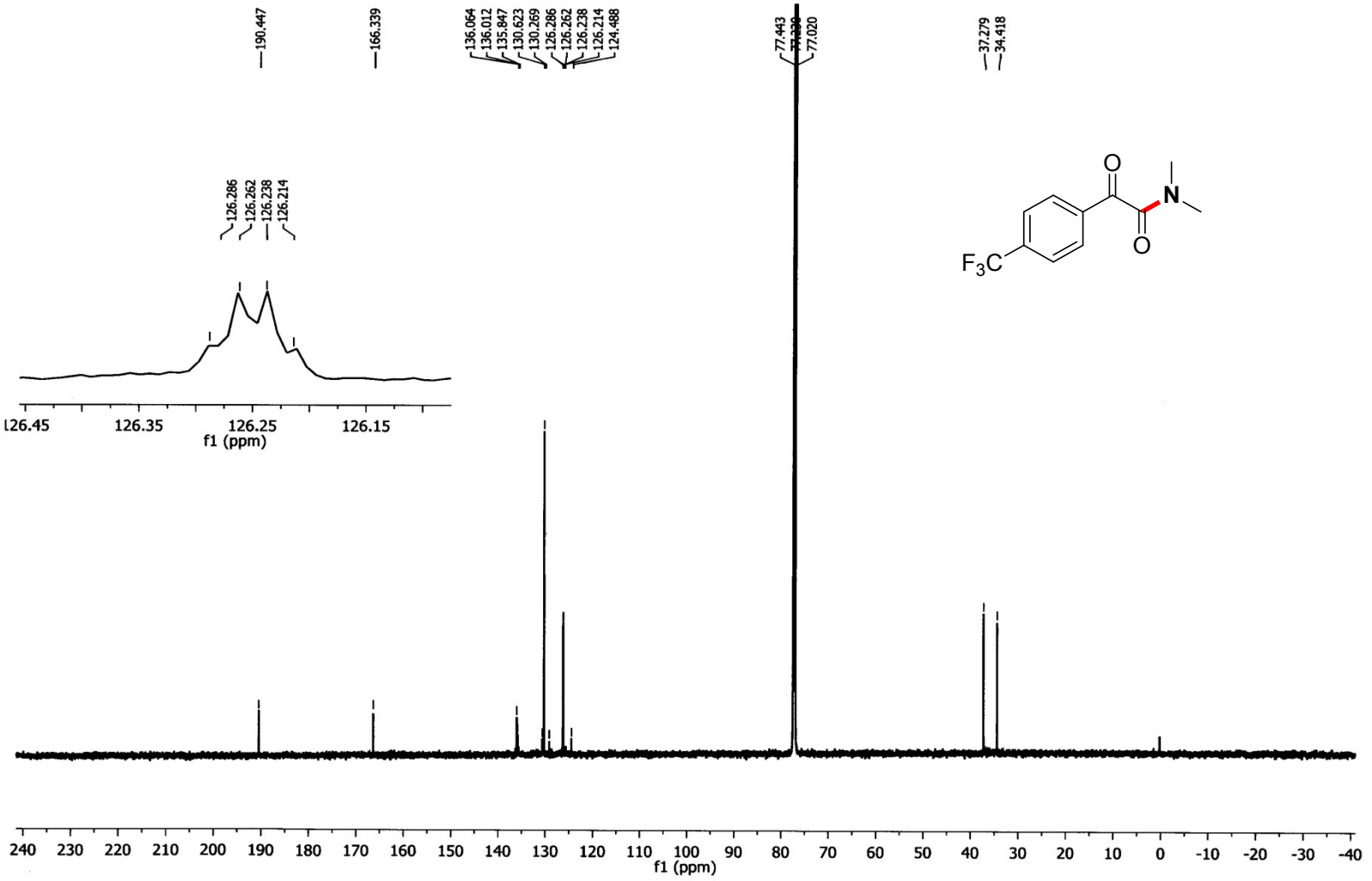
2-(4-Fluorophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1f): ^{13}C NMR (150 MHz, $CDCl_3$)



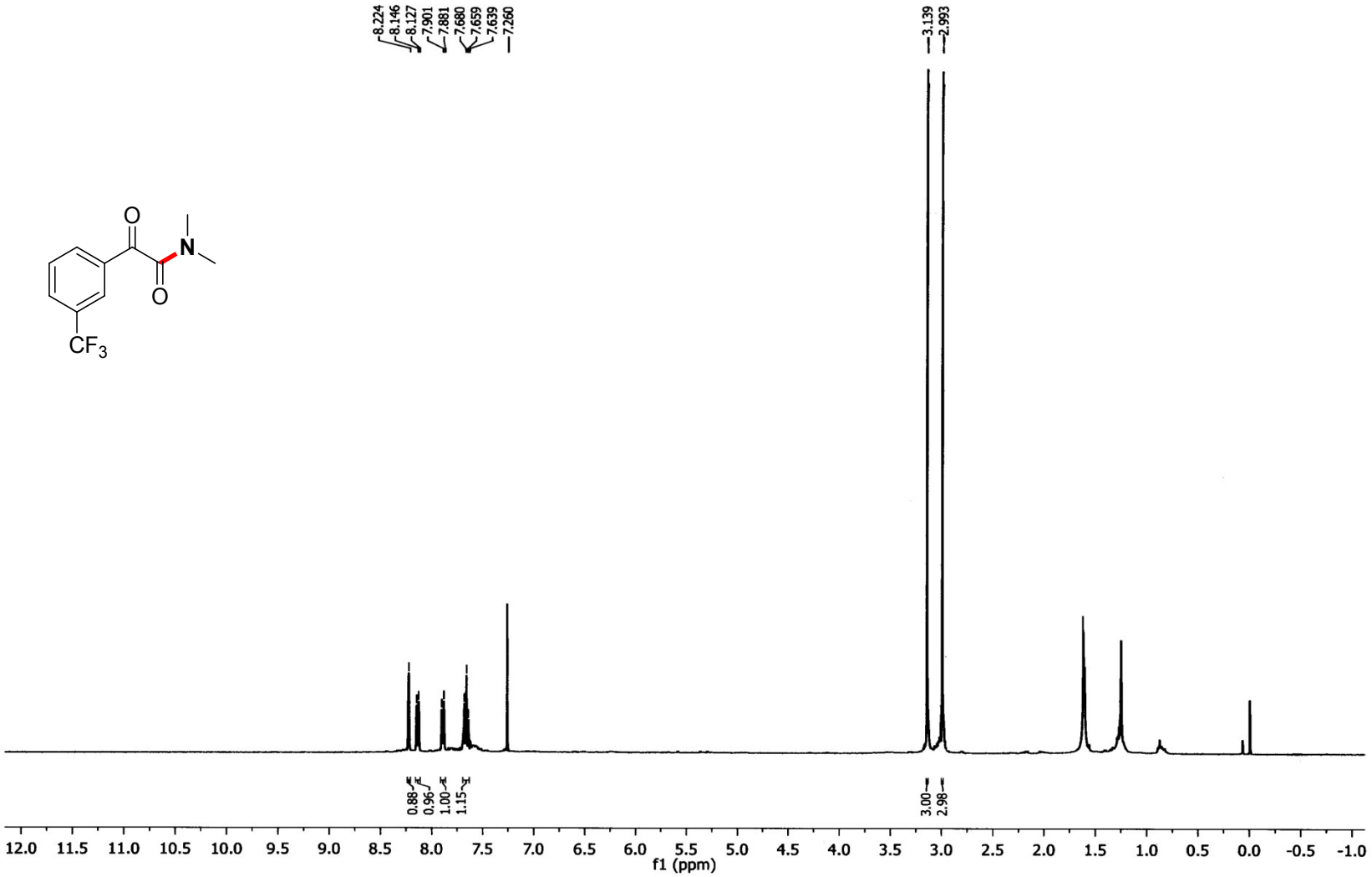
***N,N*-Dimethyl-2-oxo-2-(4-(trifluoromethyl)phenyl)acetamide (1g): ^{1}H NMR (600 MHz, $CDCl_3$)**



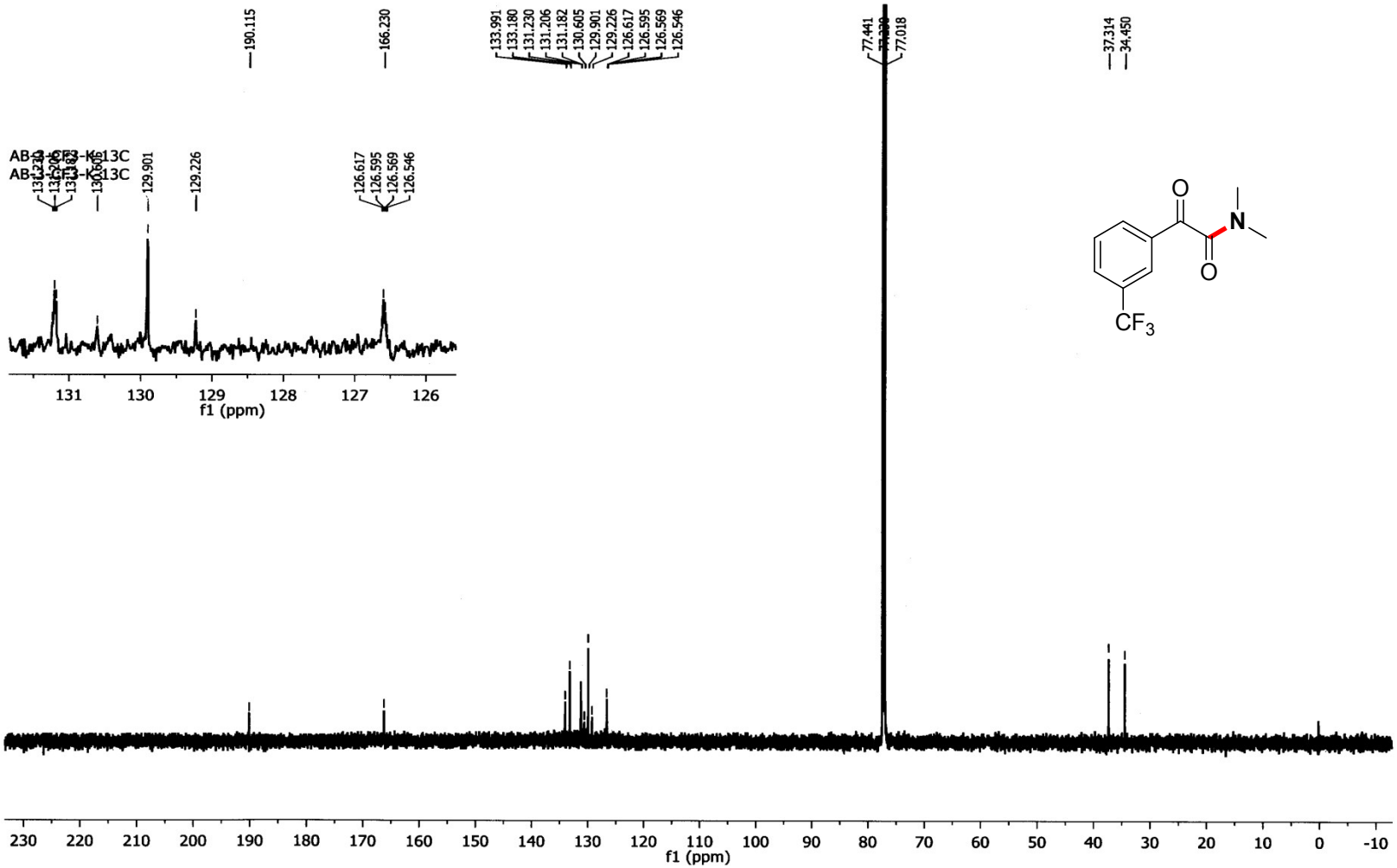
_N,N_-Dimethyl-2-oxo-2-(4-(trifluoromethyl)phenyl)acetamide (1g): ^{13}C NMR (150 MHz, $CDCl_3$)



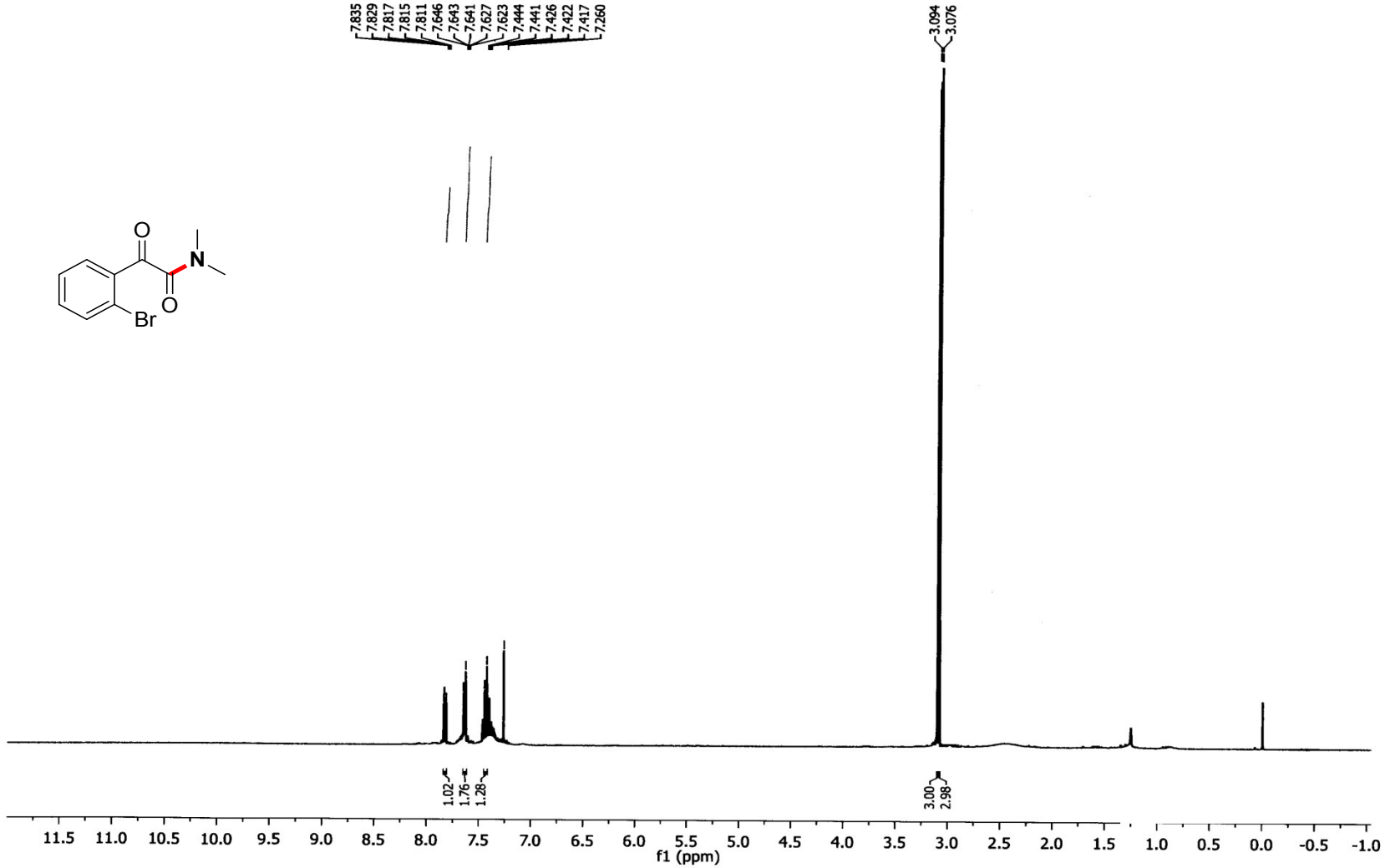
***N,N*-Dimethyl-2-oxo-2-(3-(trifluoromethyl)phenyl)acetamide (1i): ^{1}H NMR (400 MHz, $CDCl_3$)**



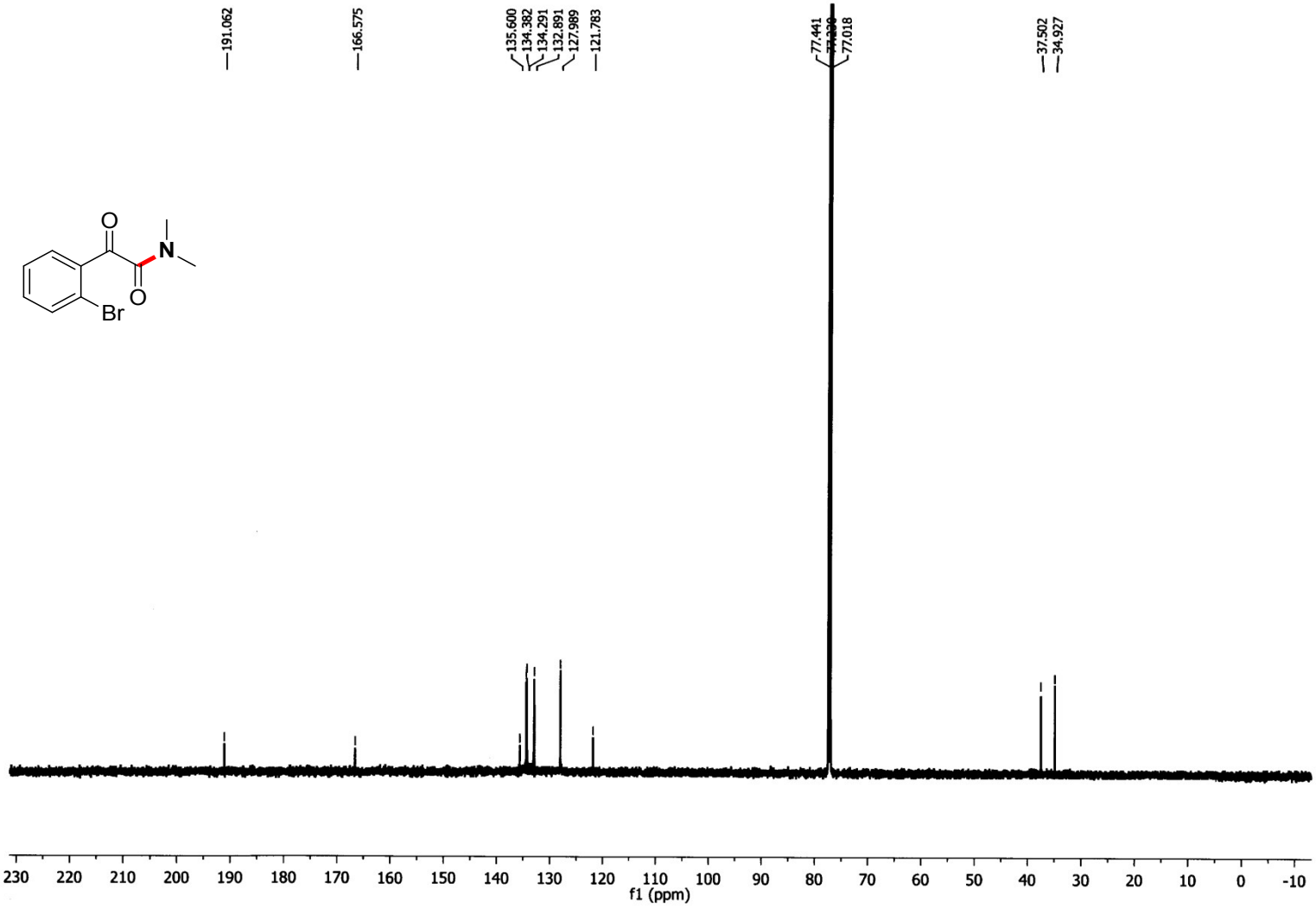
_N,N_-Dimethyl-2-oxo-2-(3-(trifluoromethyl)phenyl)acetamide (1i): ^{13}C NMR (150 MHz, $CDCl_3$)



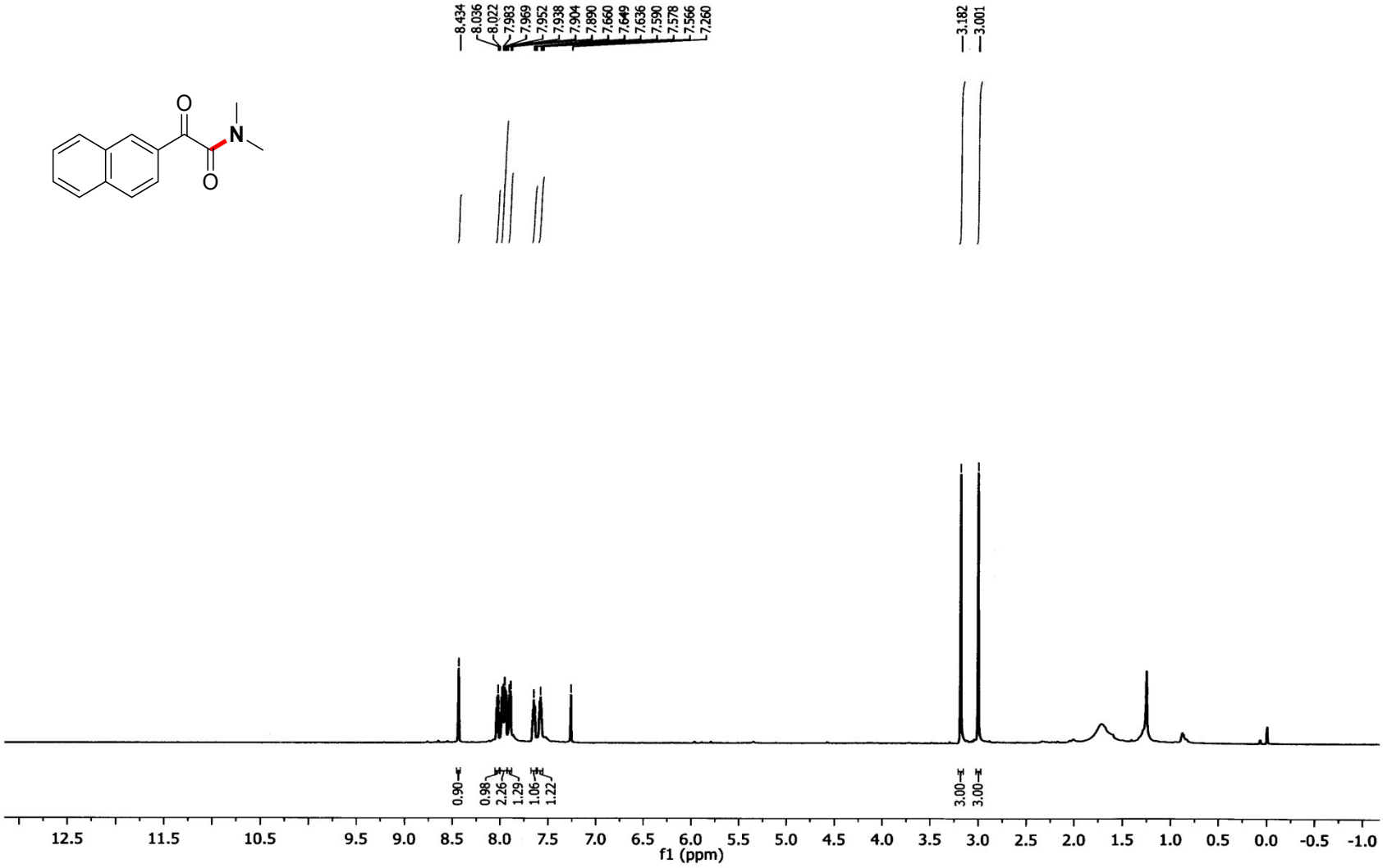
2-(2-Bromophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1j): ^{1}H NMR (400 MHz, $CDCl_3$)



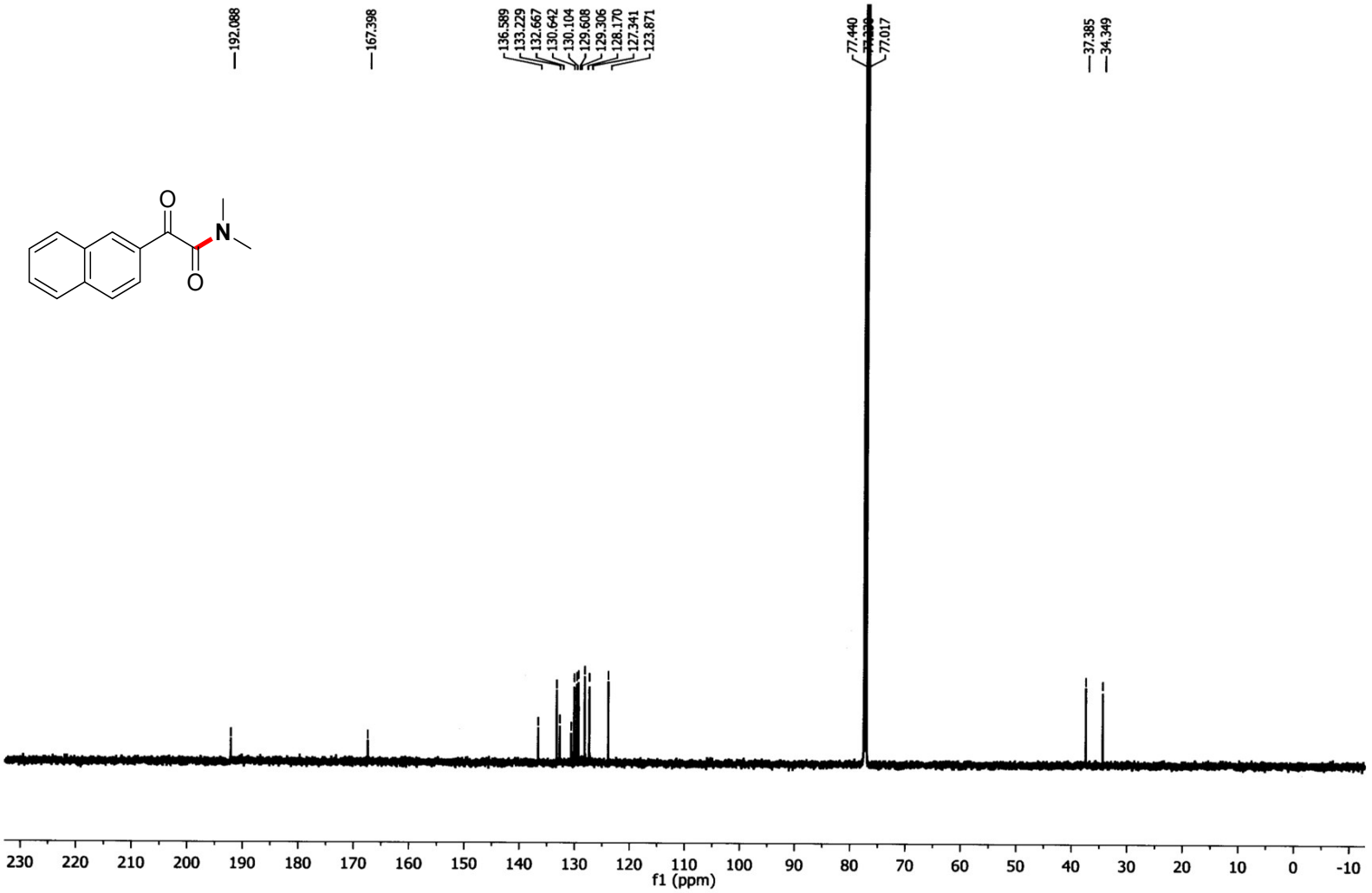
2-(2-Bromophenyl)-*N*,*N*-dimethyl-2-oxoacetamide (1j): ^{13}C NMR (150 MHz, $CDCl_3$)



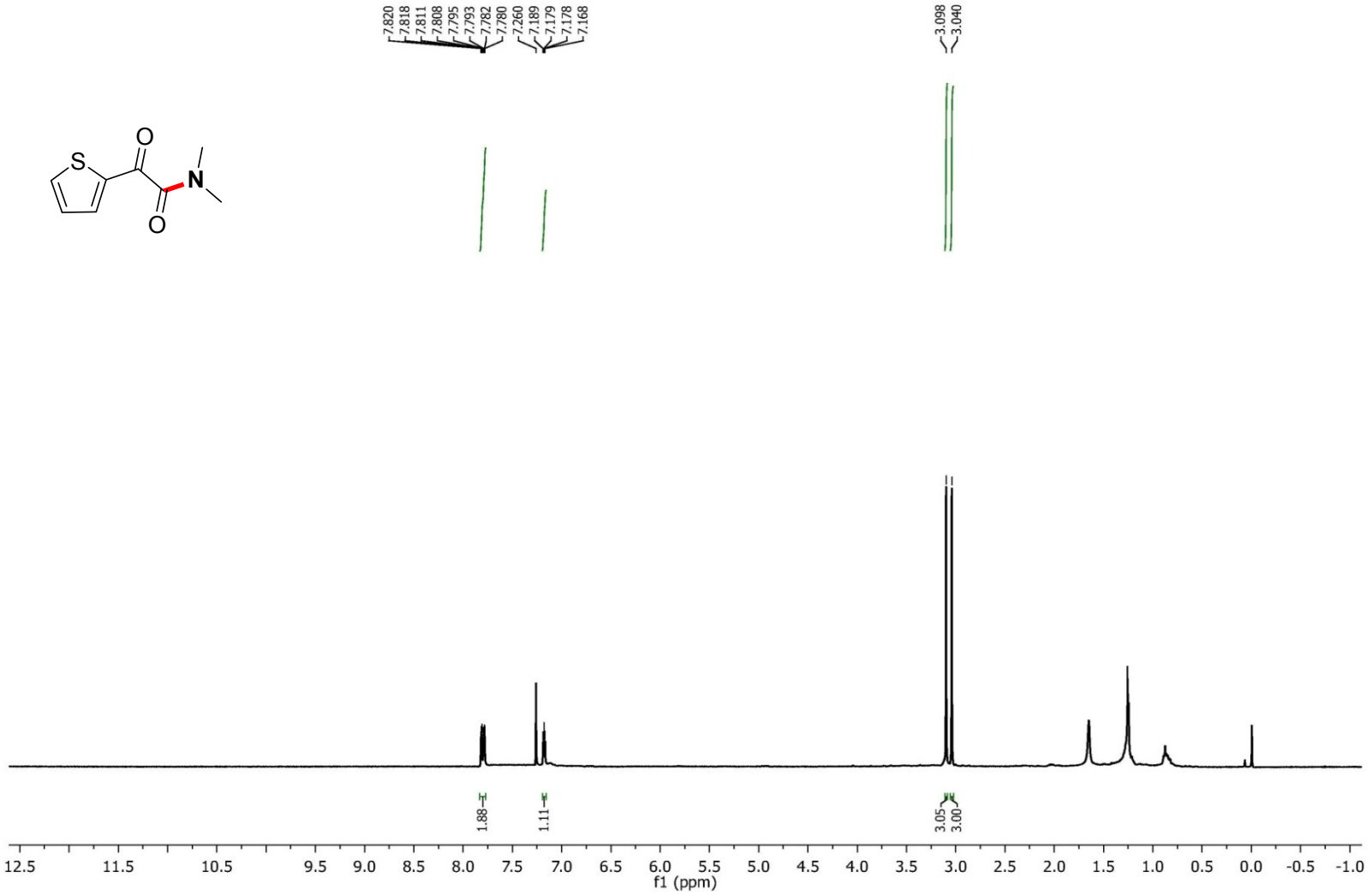
_N,N_-Dimethyl-2-(naphthalen-2-yl)-2-oxoacetamide(1k): ^{1}H NMR (600 MHz, $CDCl_3$)



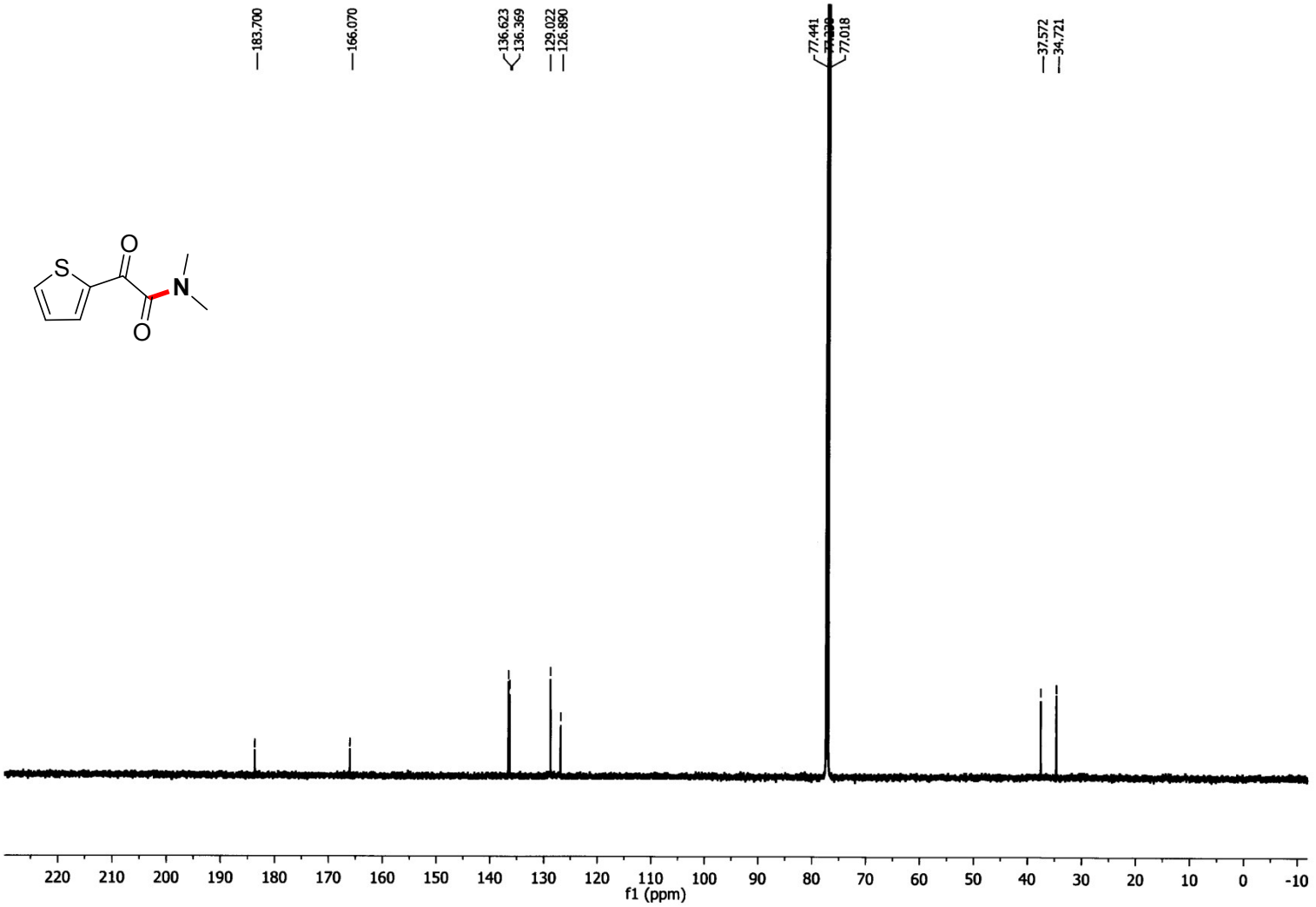
_N,N_-Dimethyl-2-(naphthalen-2-yl)-2-oxoacetamide (1k): ^{13}C NMR (150 MHz, $CDCl_3$)



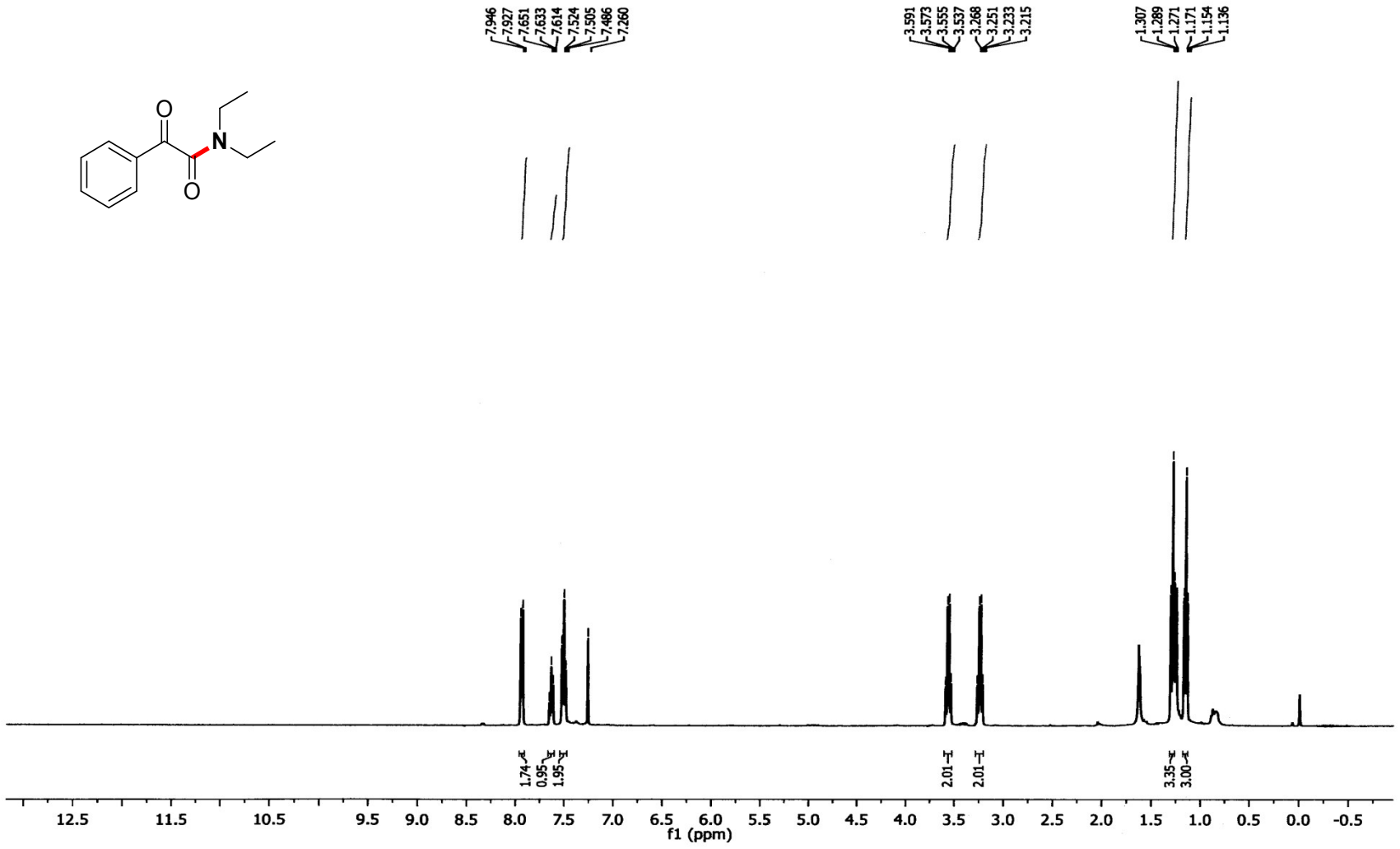
_N,N_-Dimethyl-2-oxo-2-(thiophen-2-yl)acetamide (1l): ^{1}H NMR (400 MHz, $CDCl_3$)



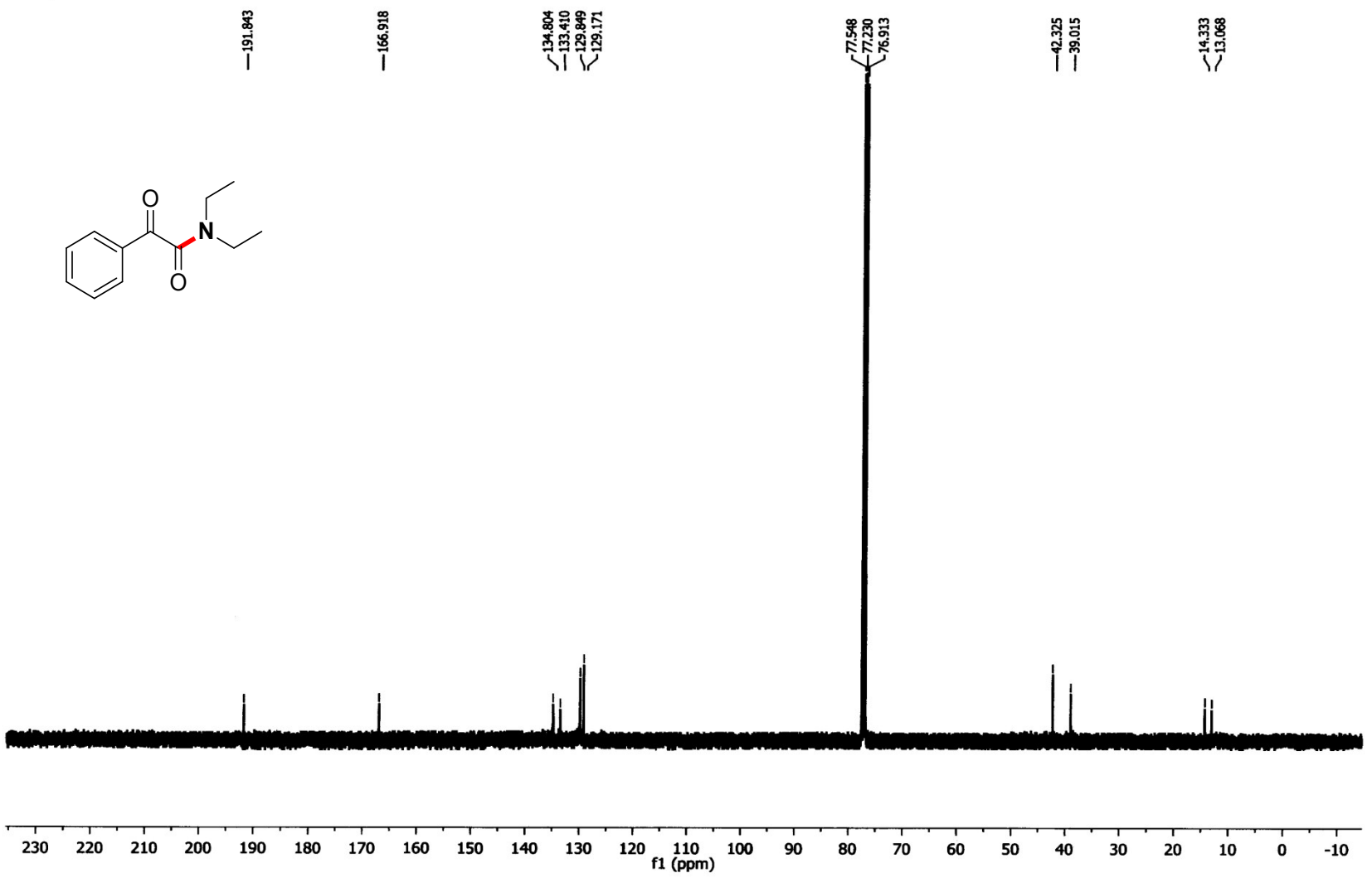
***N,N*-Dimethyl-2-oxo-2-(thiophen-2-yl)acetamide (1l): ^{13}C NMR (150 MHz, $CDCl_3$)**



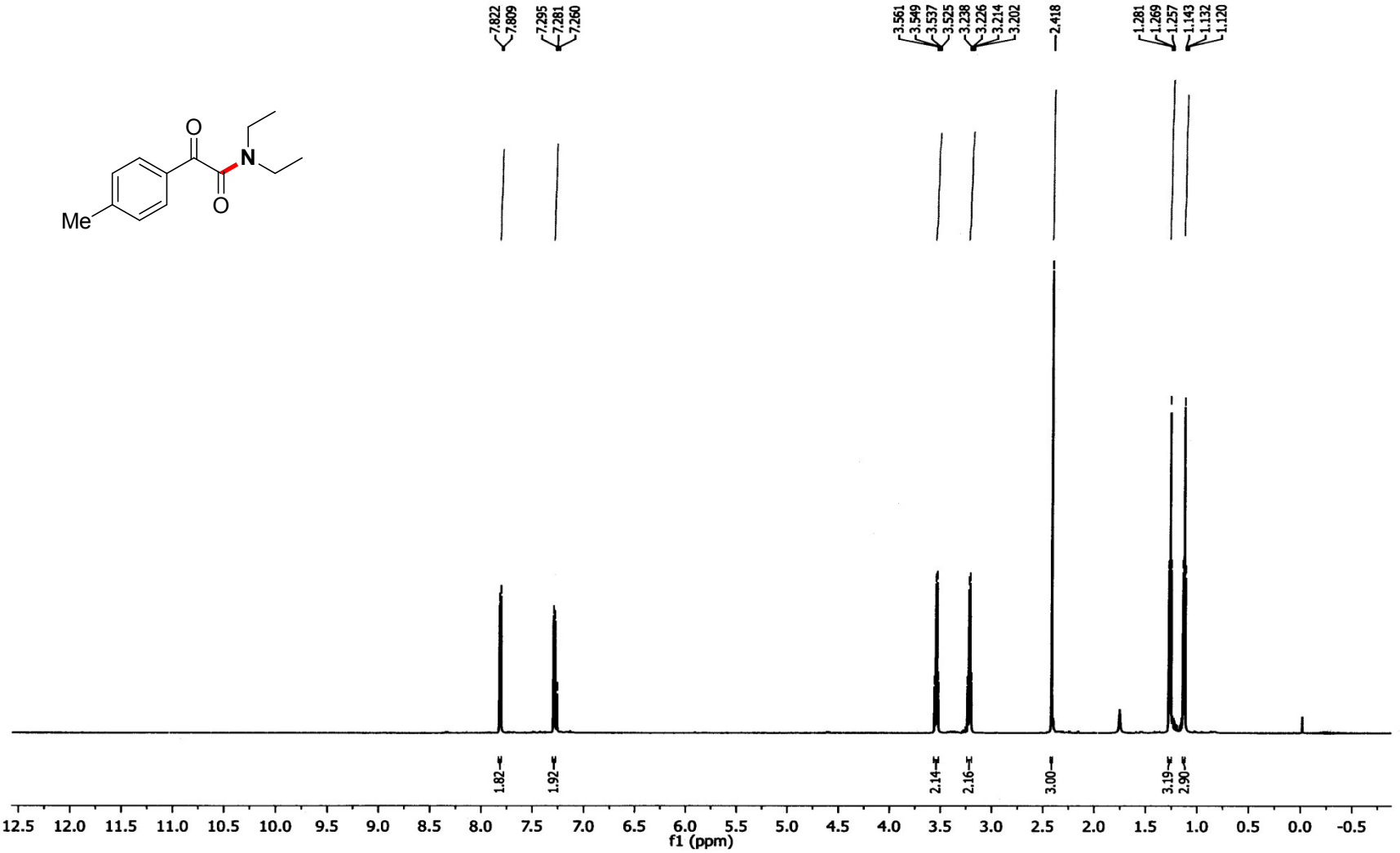
_N_,_N_-Diethyl-2-oxo-2-phenylacetamide (2a): ^{1}H NMR (400 MHz, $CDCl_3$)



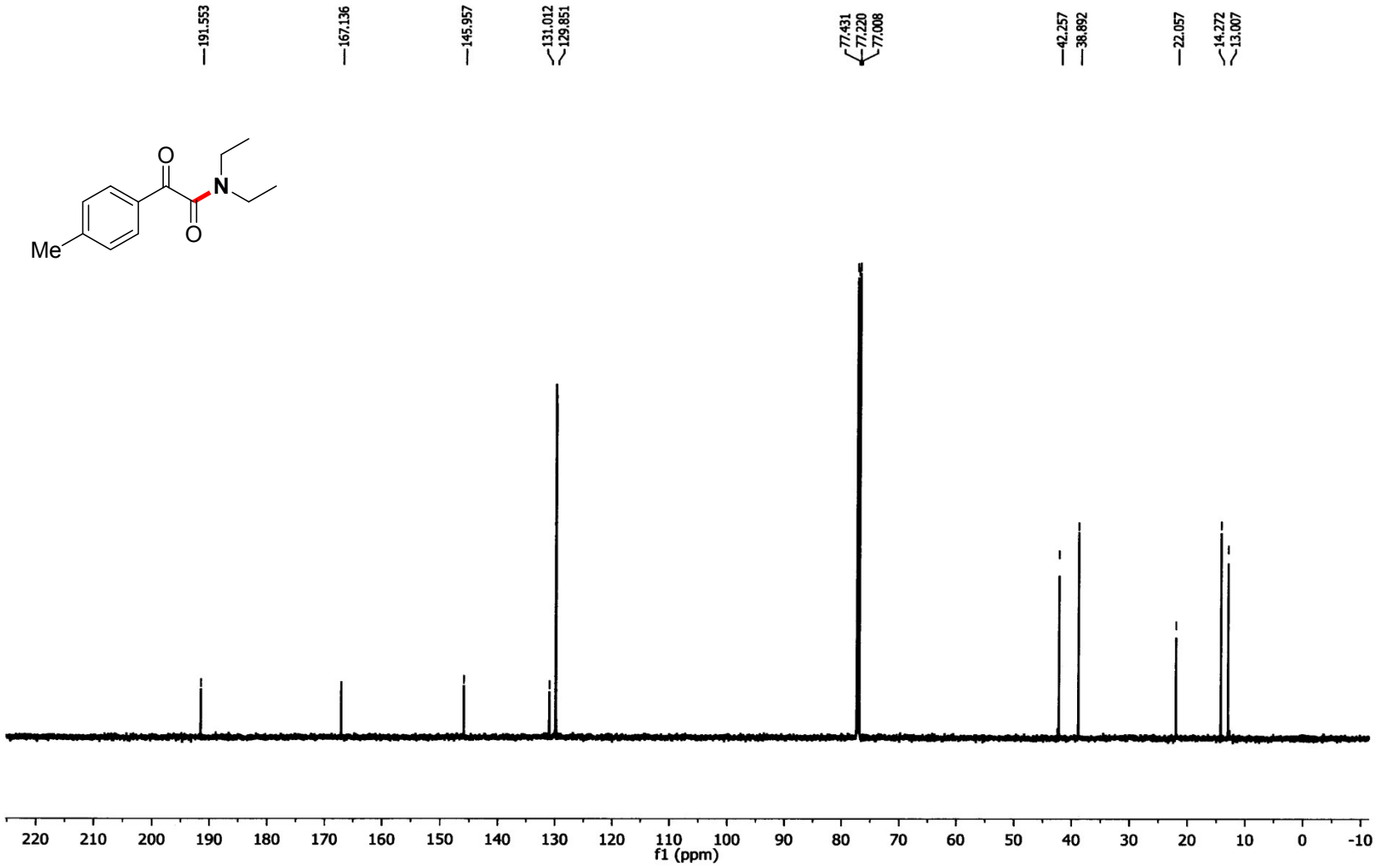
_N_,_N_-Diethyl-2-oxo-2-phenylacetamide (2a): ^{13}C NMR (100 MHz, $CDCl_3$)



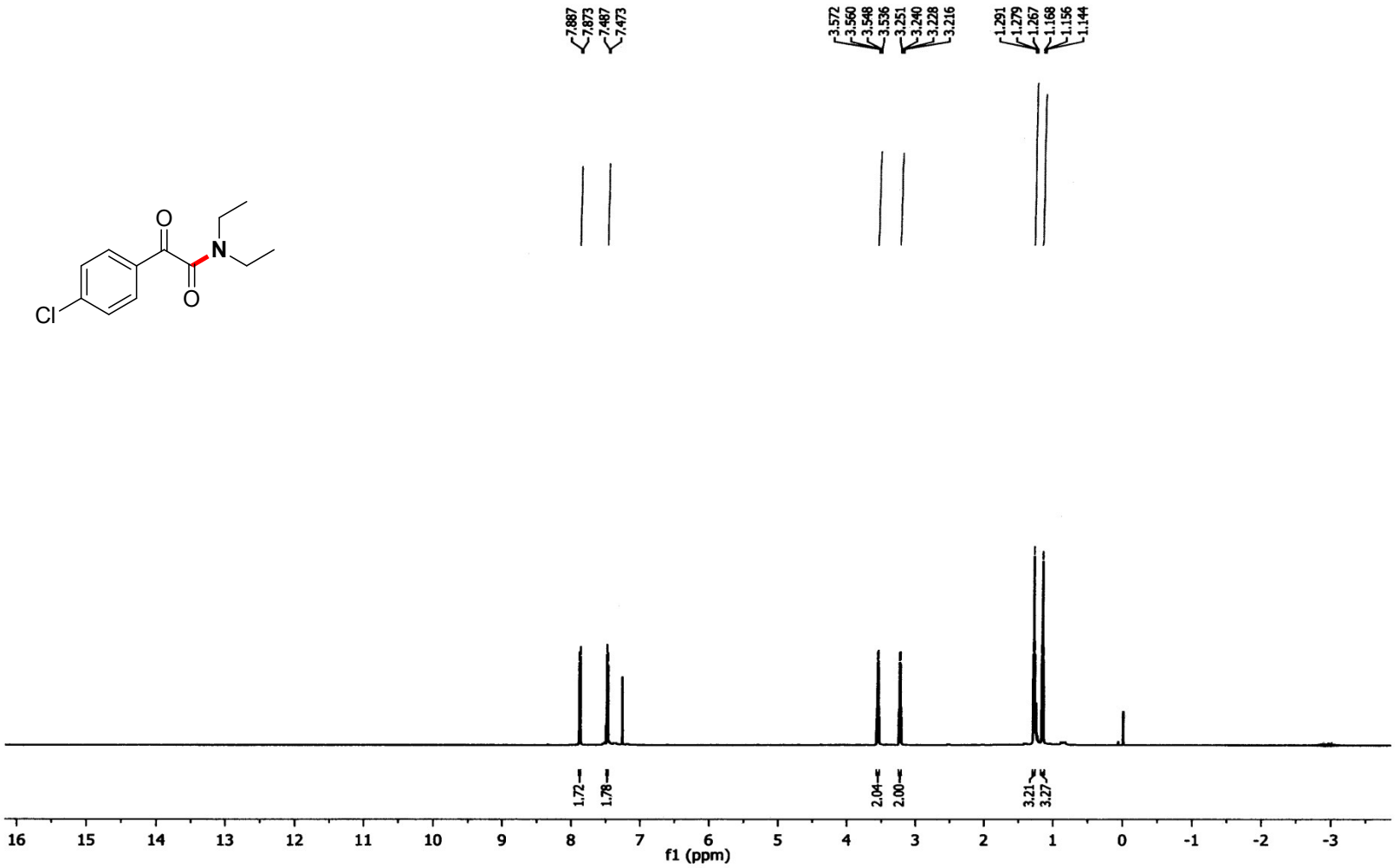
***N*,*N*-Diethyl-2-oxo-2-(*p*-tolyl)acetamide (2b): ^{1}H NMR (600 MHz, $CDCl_3$)**



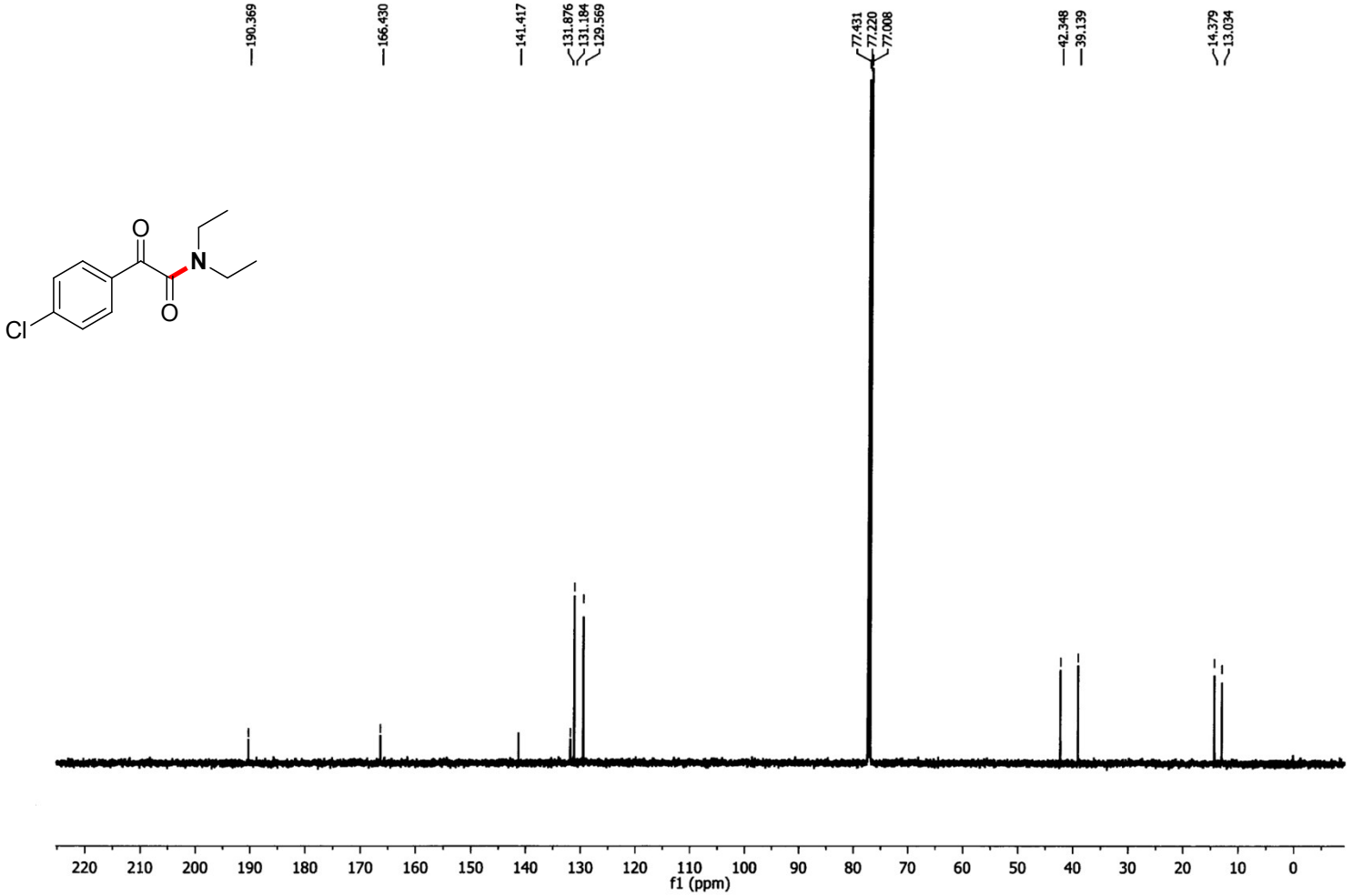
***N*,*N*-Diethyl-2-oxo-2-(*p*-tolyl)acetamide (2b): ^{13}C NMR (150 MHz, $CDCl_3$)**



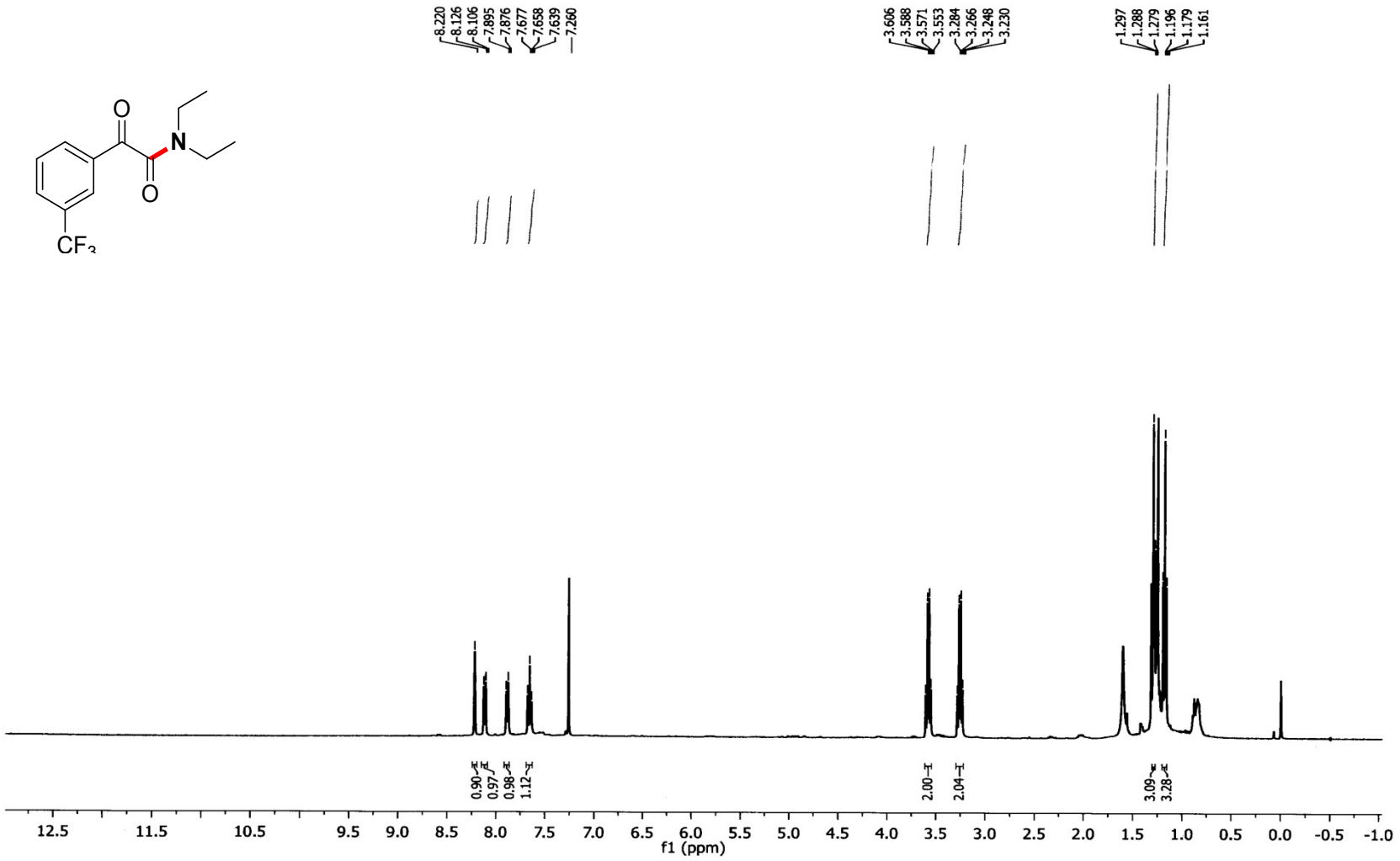
2-(4-Chlorophenyl)-*N*,*N*-diethyl-2-oxoacetamide (2e): ^{1}H NMR (600 MHz, $CDCl_3$)



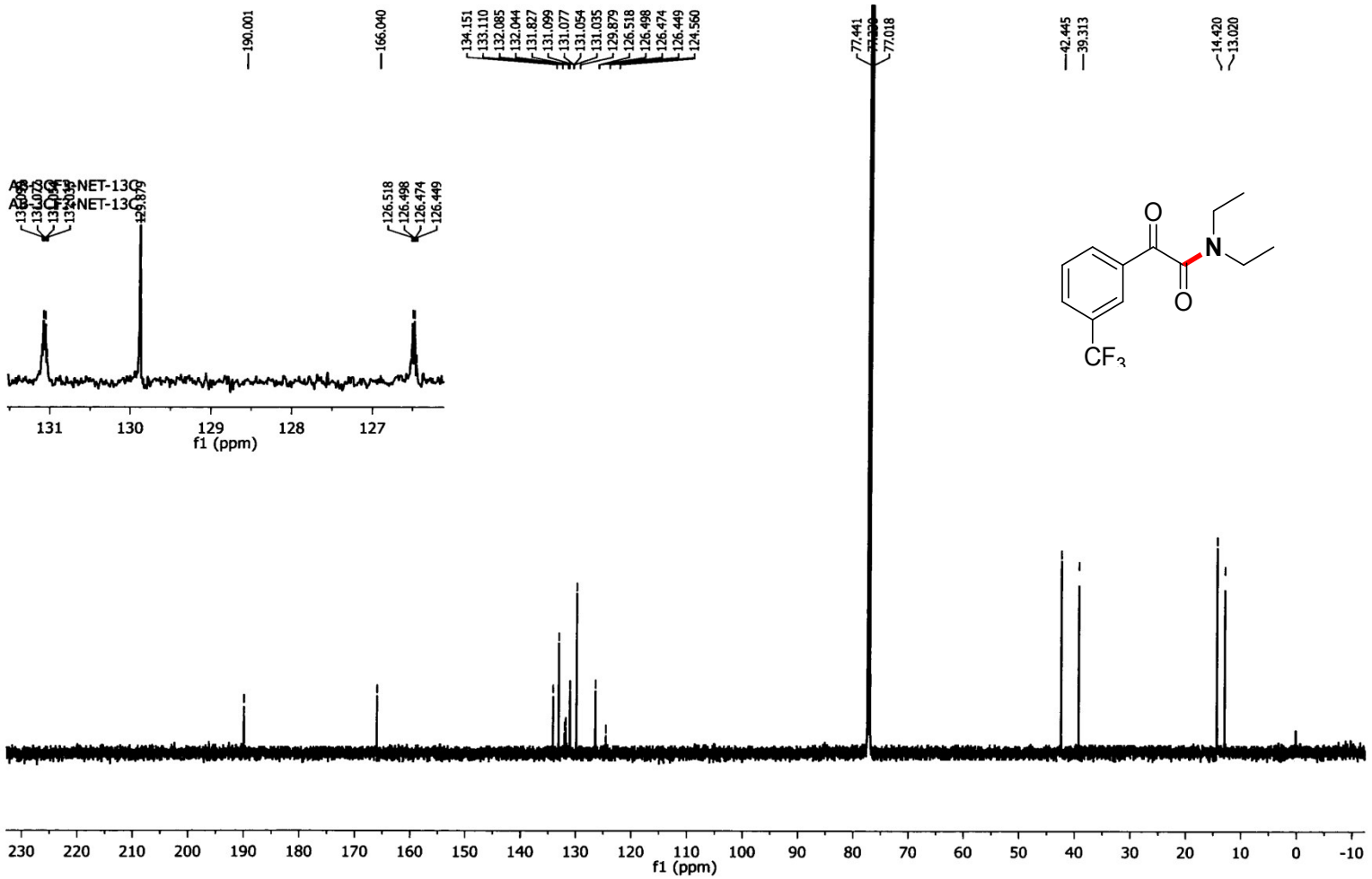
2-(4-Chlorophenyl)-*N*,*N*-diethyl-2-oxoacetamide (2e): ^{13}C NMR (150 MHz, $CDCl_3$)



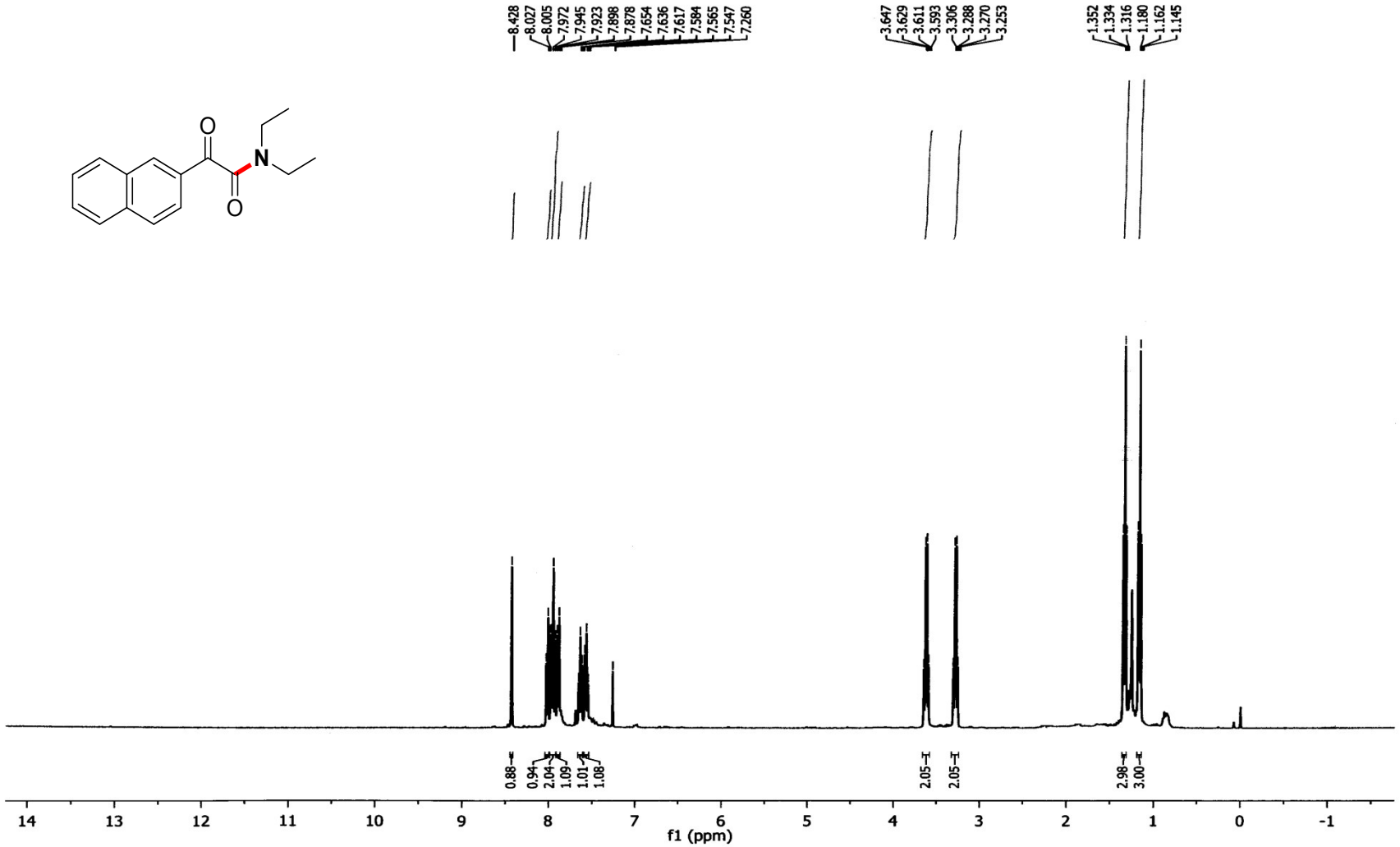
_N_,_N_-Diethyl-2-oxo-2-(3-(trifluoromethyl)phenyl)acetamide (2i): ^{1}H NMR (400 MHz, $CDCl_3$)



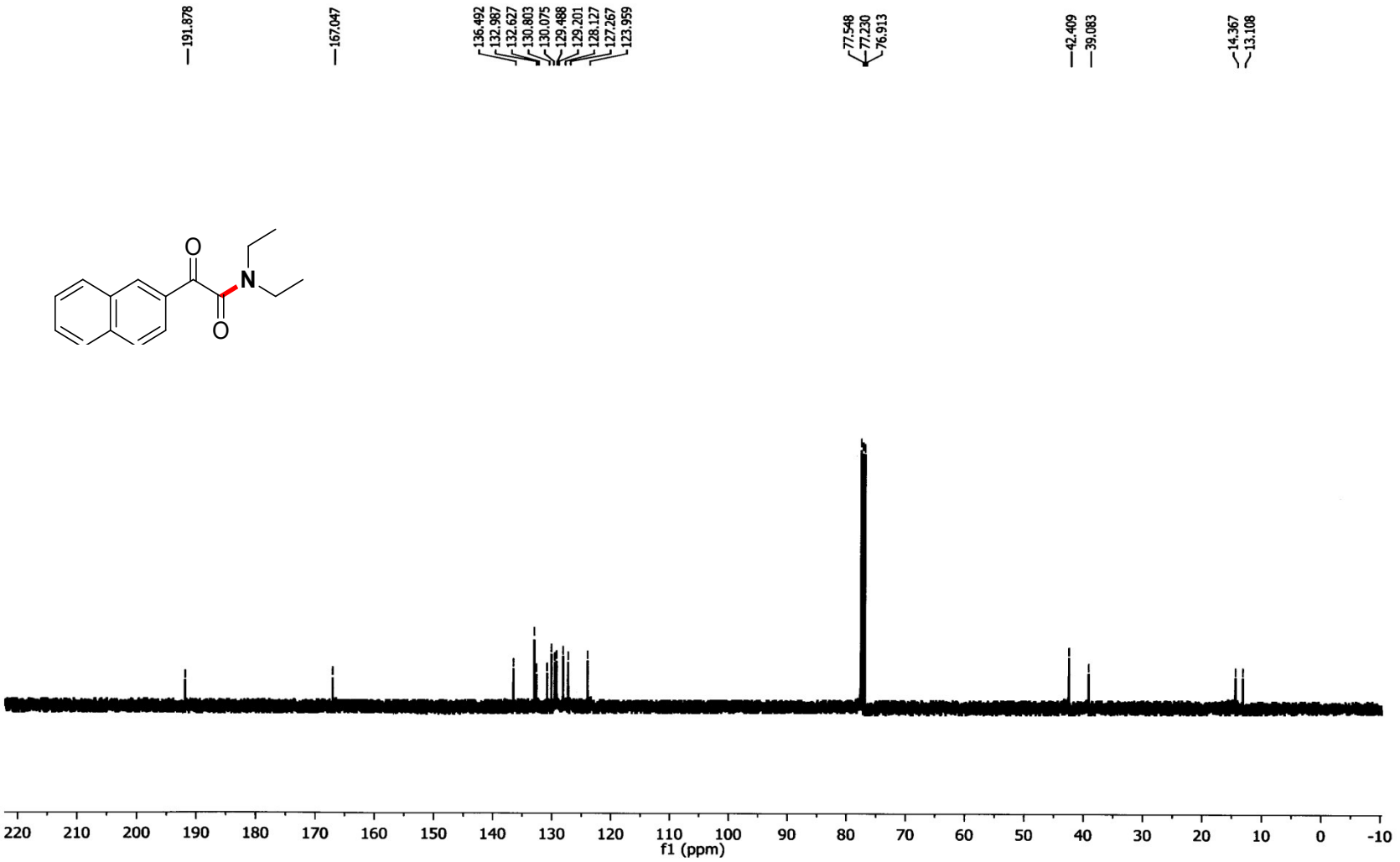
_N_,_N_-Diethyl-2-oxo-2-(3-(trifluoromethyl)phenyl)acetamide (2i): ^{13}C NMR (150 MHz, $CDCl_3$)



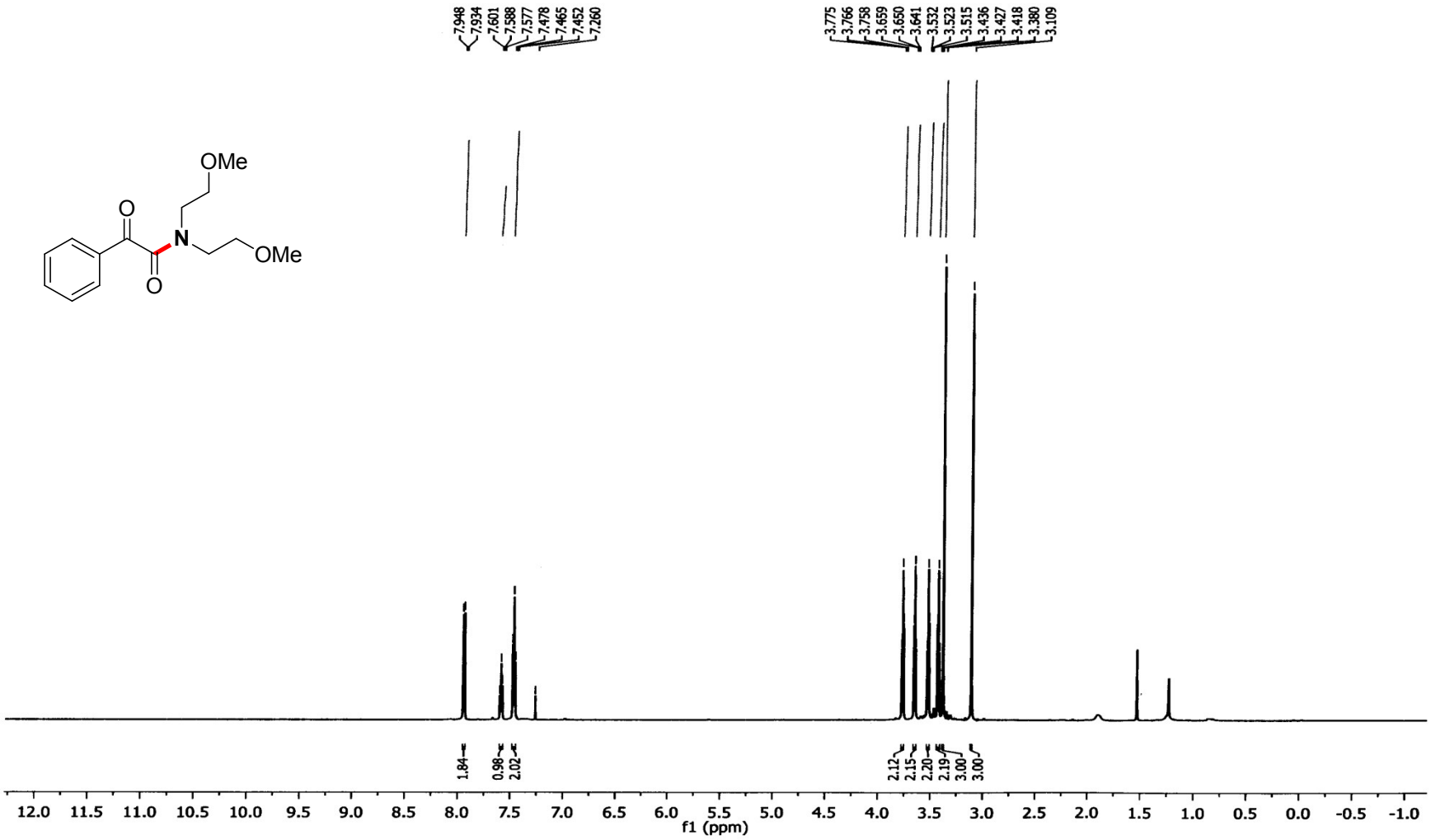
_N_,_N_-Diethyl-2-(naphthalen-2-yl)-2-oxoacetamide (2k): ^{1}H NMR (400 MHz, $CDCl_3$)



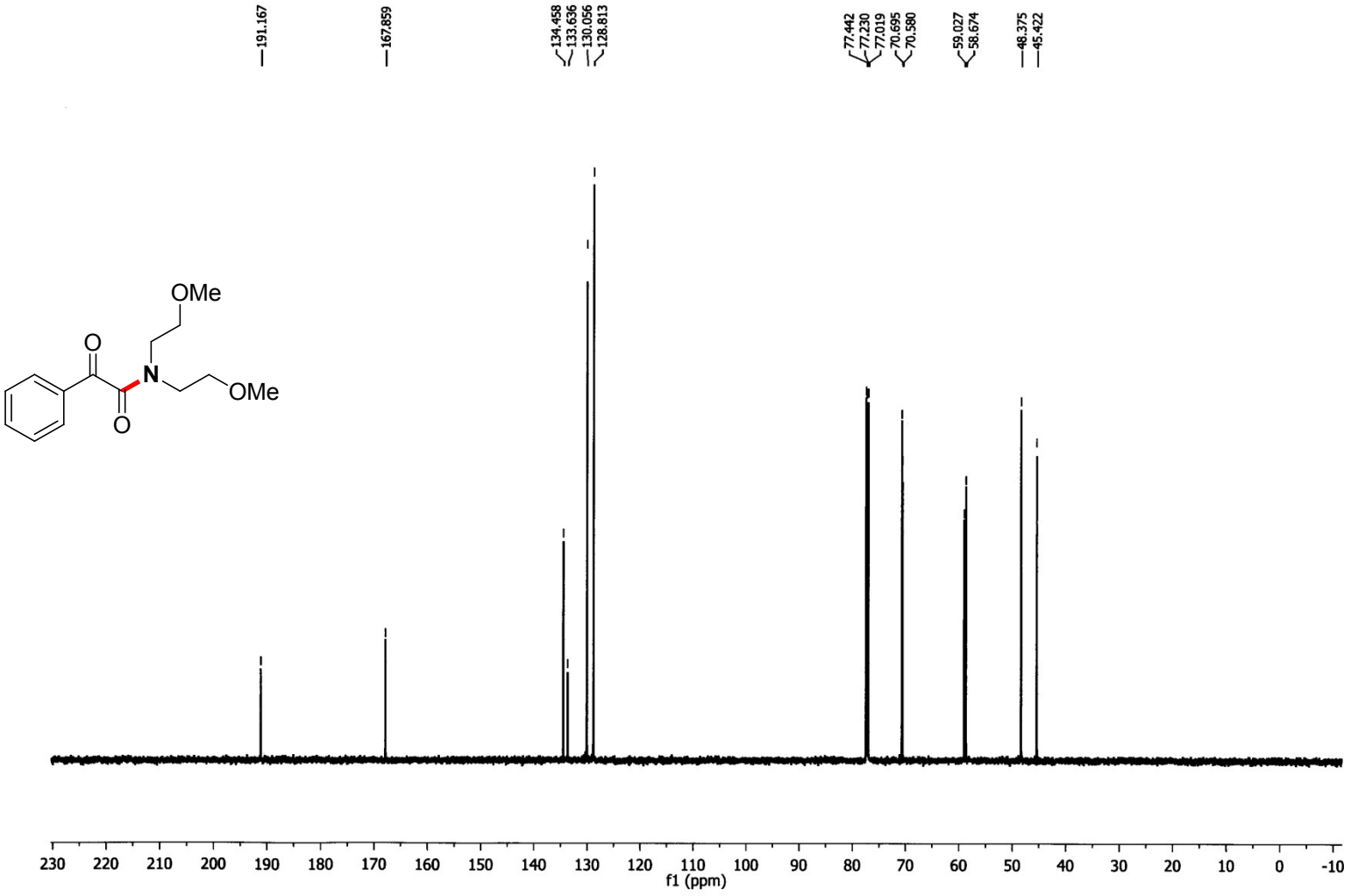
_N_,_N_-Diethyl-2-(naphthalen-2-yl)-2-oxoacetamide (2k): ^{13}C NMR (100 MHz, $CDCl_3$)



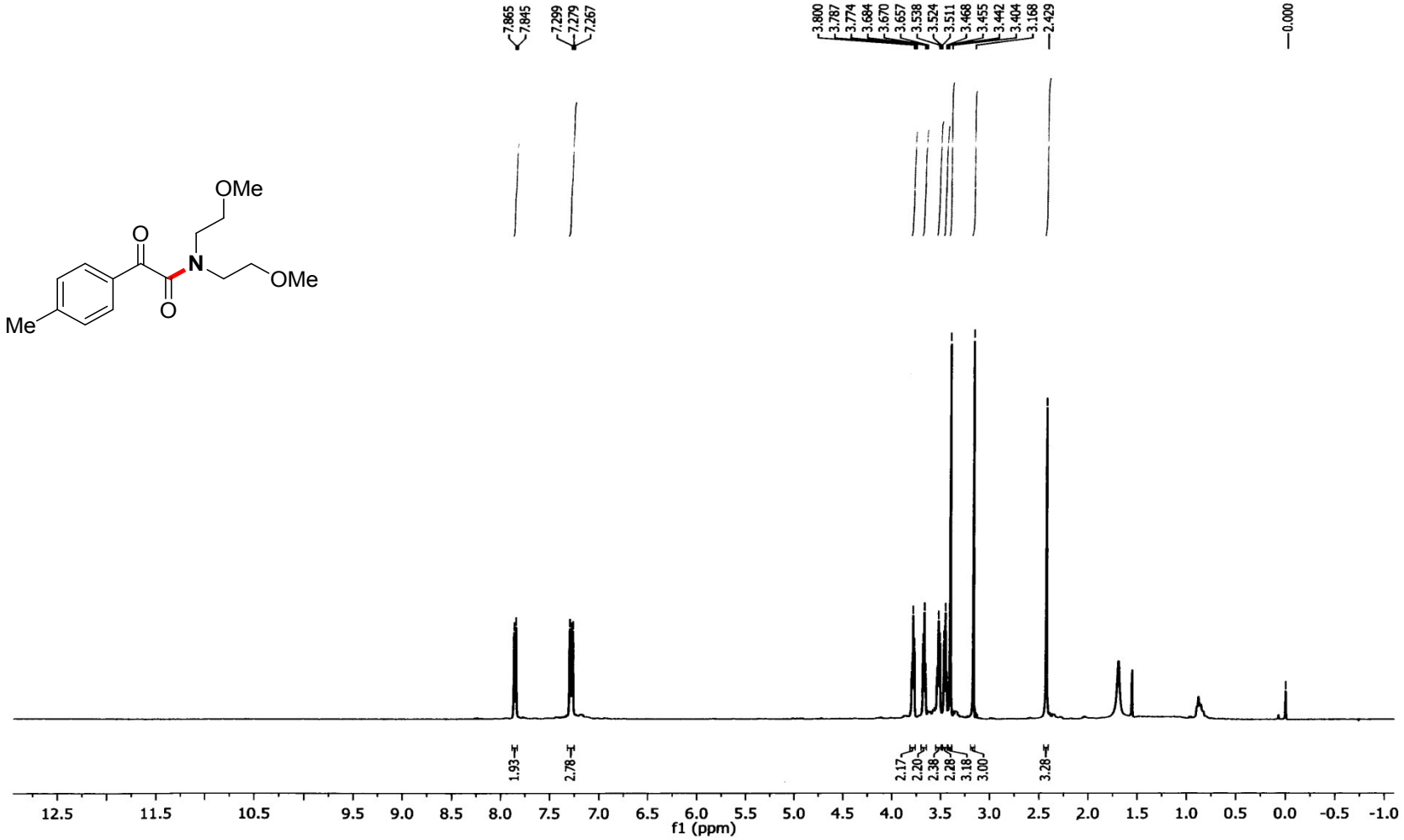
***N*,*N*-Bis (2-methoxyethyl)-2-oxo-2-phenylacetamide (3a): ^{1}H NMR (600 MHz, $CDCl_3$)**



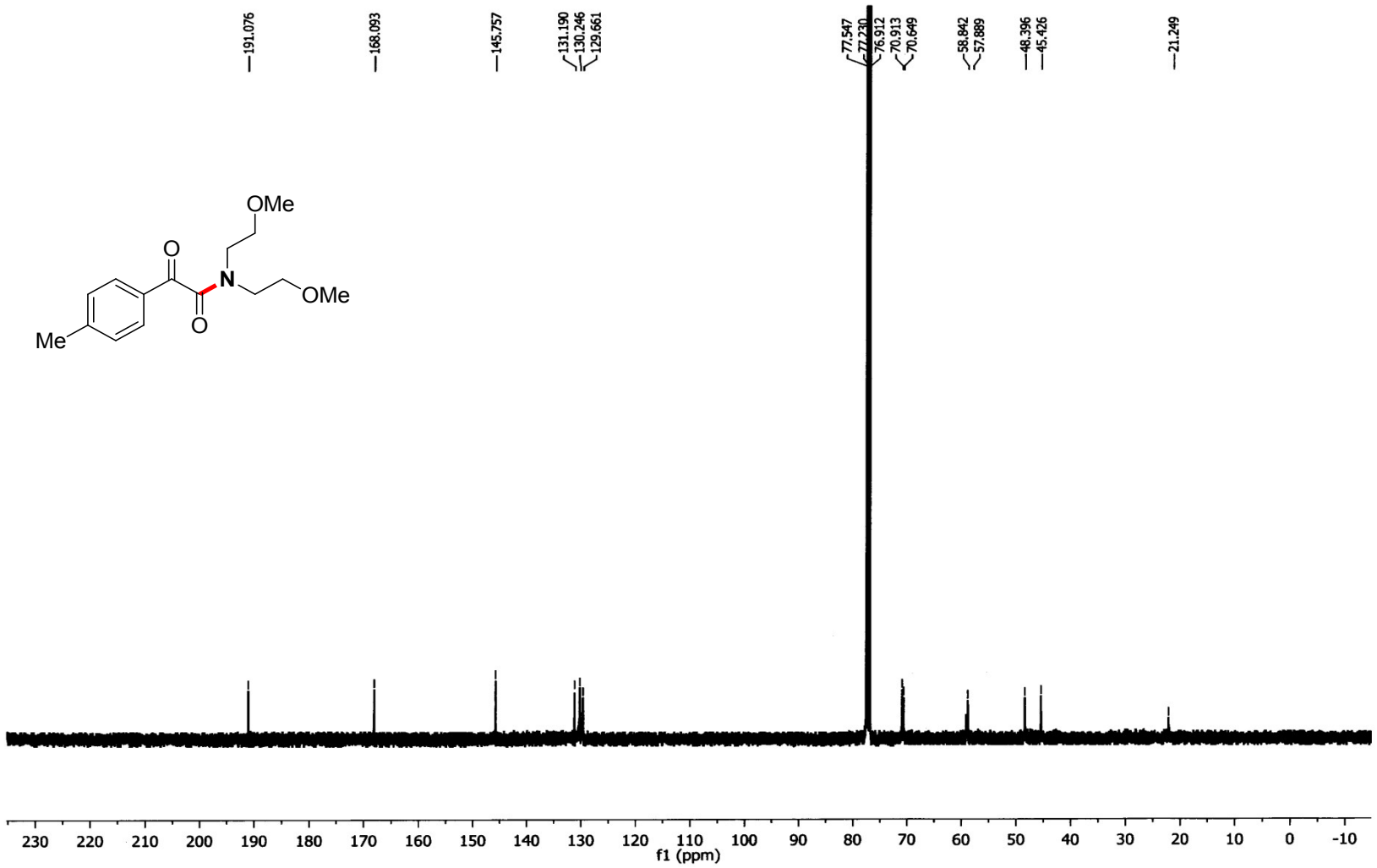
_N_,_N_-Bis(2-methoxyethyl)-2-oxo-2-phenylacetamide (3a): ^{13}C NMR (150 MHz, $CDCl_3$)



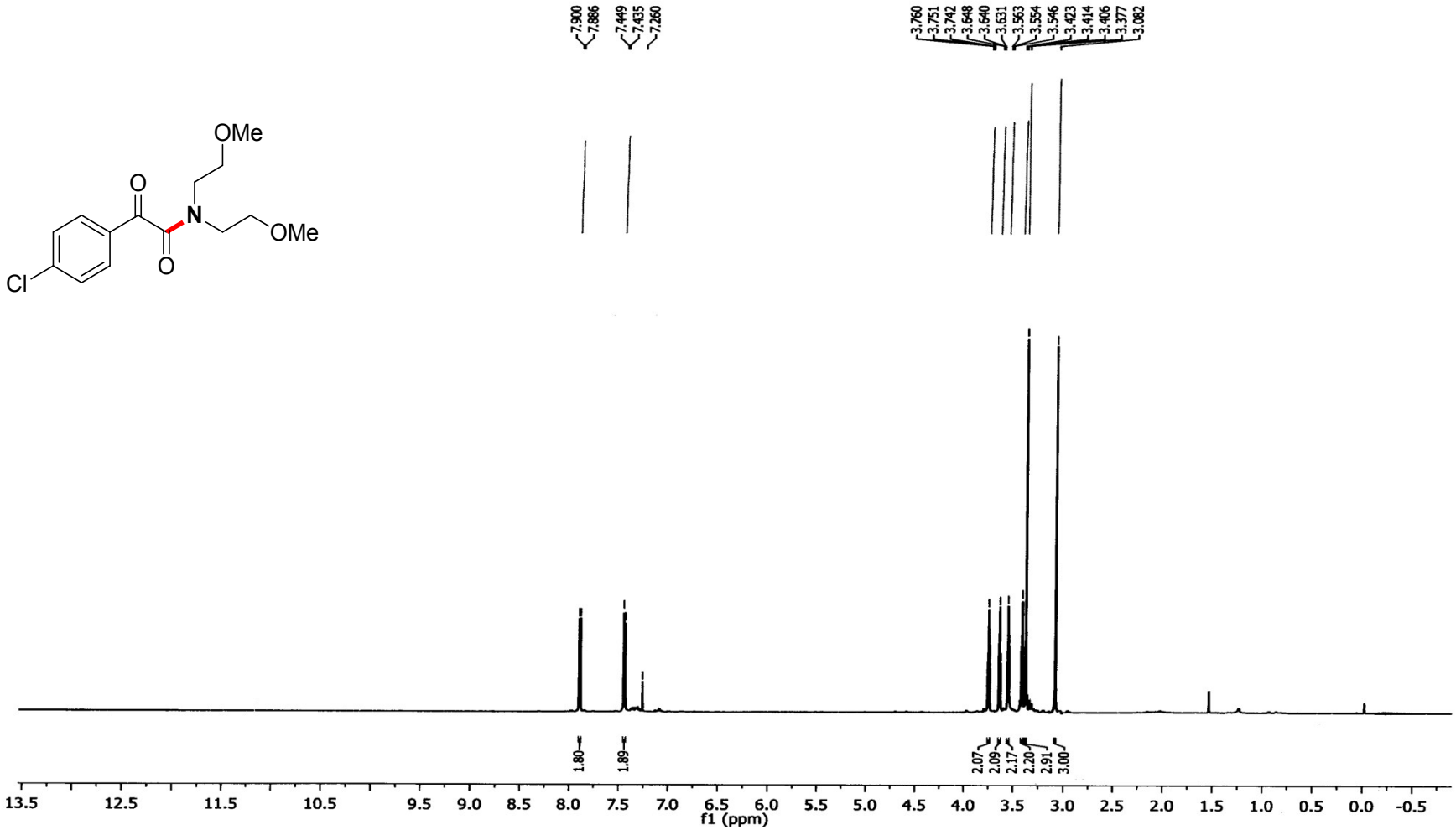
***N*,*N*-Bis(2-methoxyethyl)-2-oxo-2-(*p*-tolyl)acetamide (3b): ^{1}H NMR (400 MHz, $CDCl_3$)**



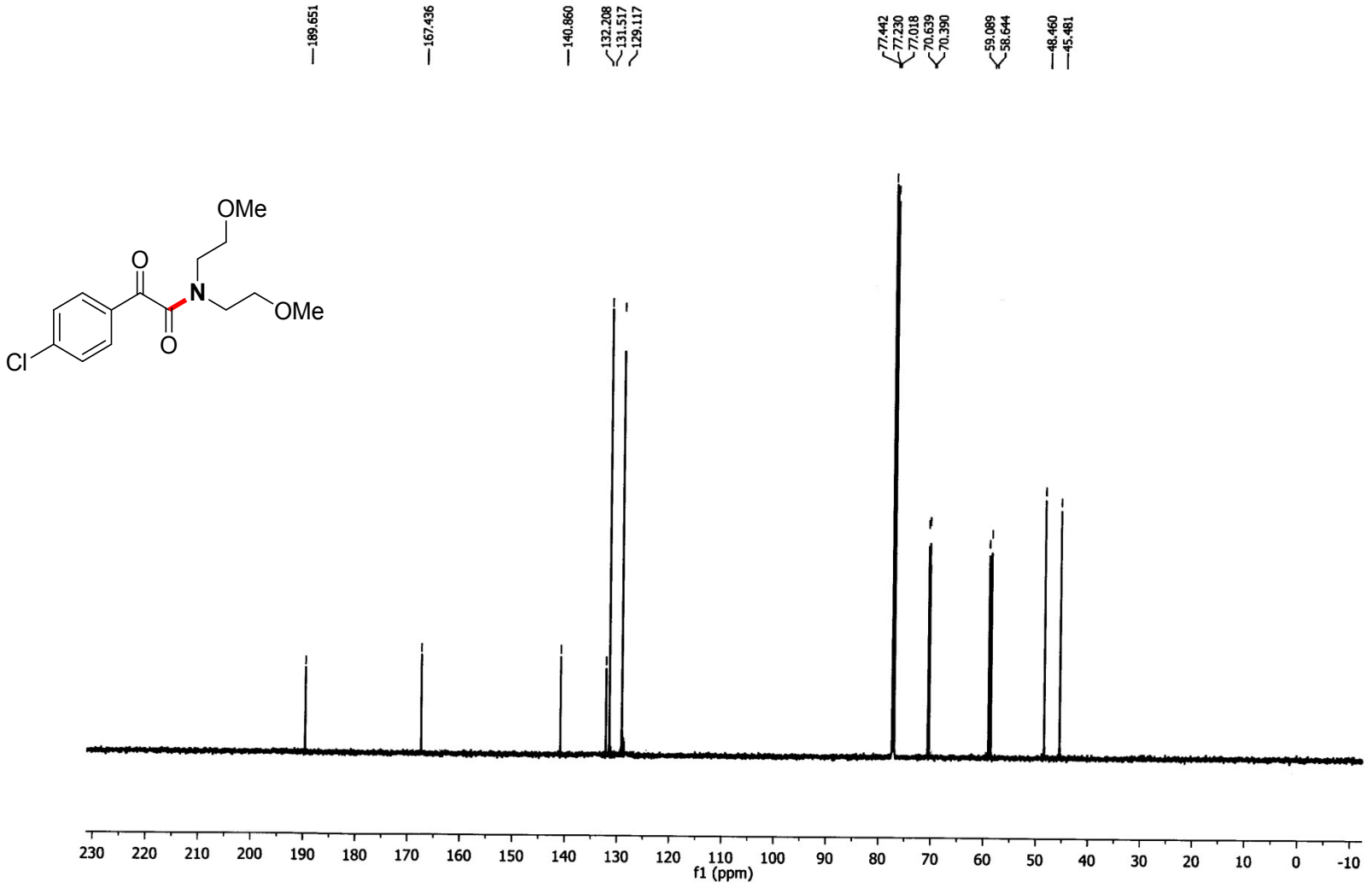
_N_,_N_-Bis(2-methoxyethyl)-2-oxo-2-(_p_-tolyl)acetamide (3b): ^{13}C NMR (150 MHz, $CDCl_3$)



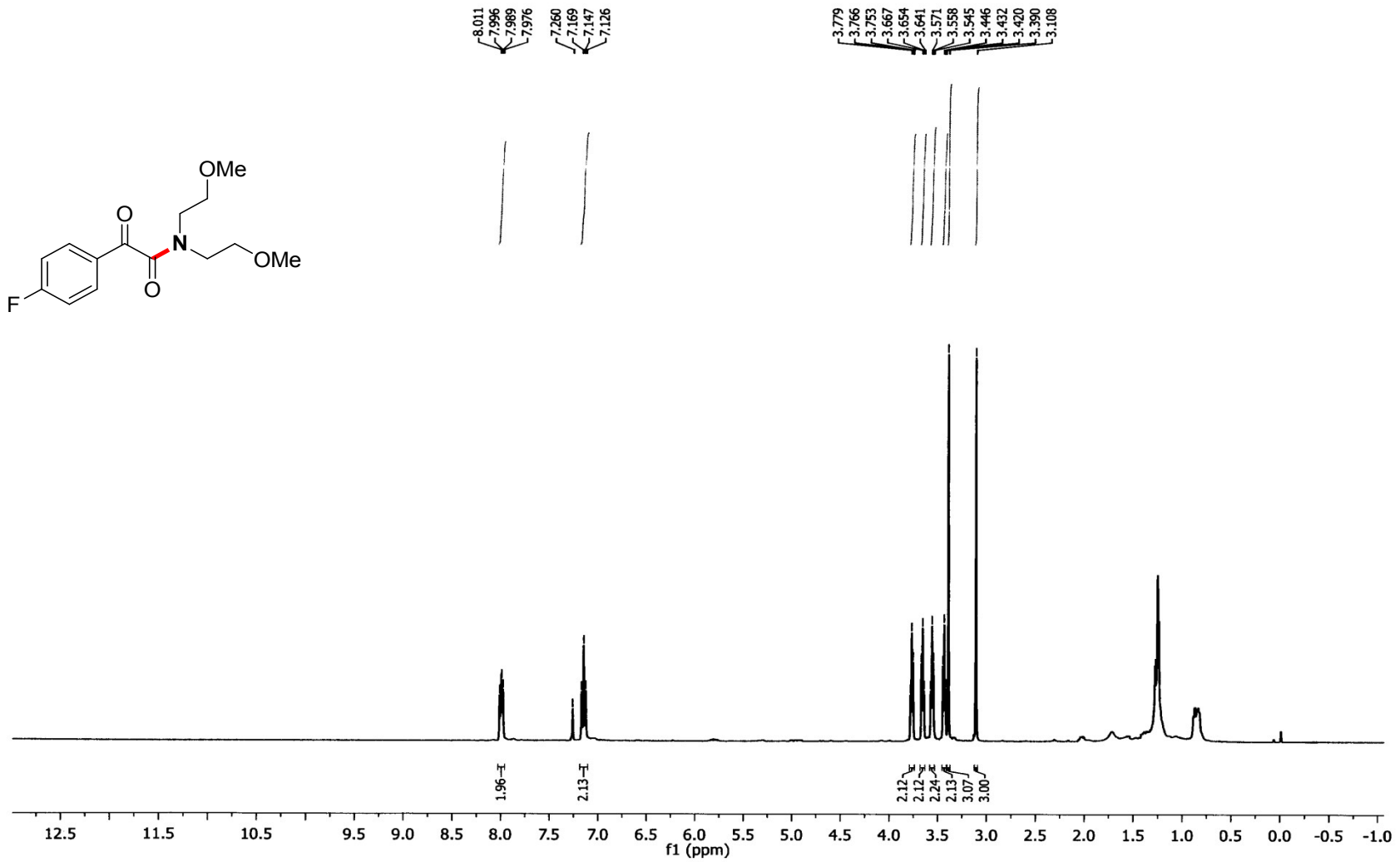
2-(4-Chlorophenyl)-*N*,*N*-bis(2-methoxyethyl)-2-oxoacetamide (3e): ^{1}H NMR (600 MHz, $CDCl_3$)



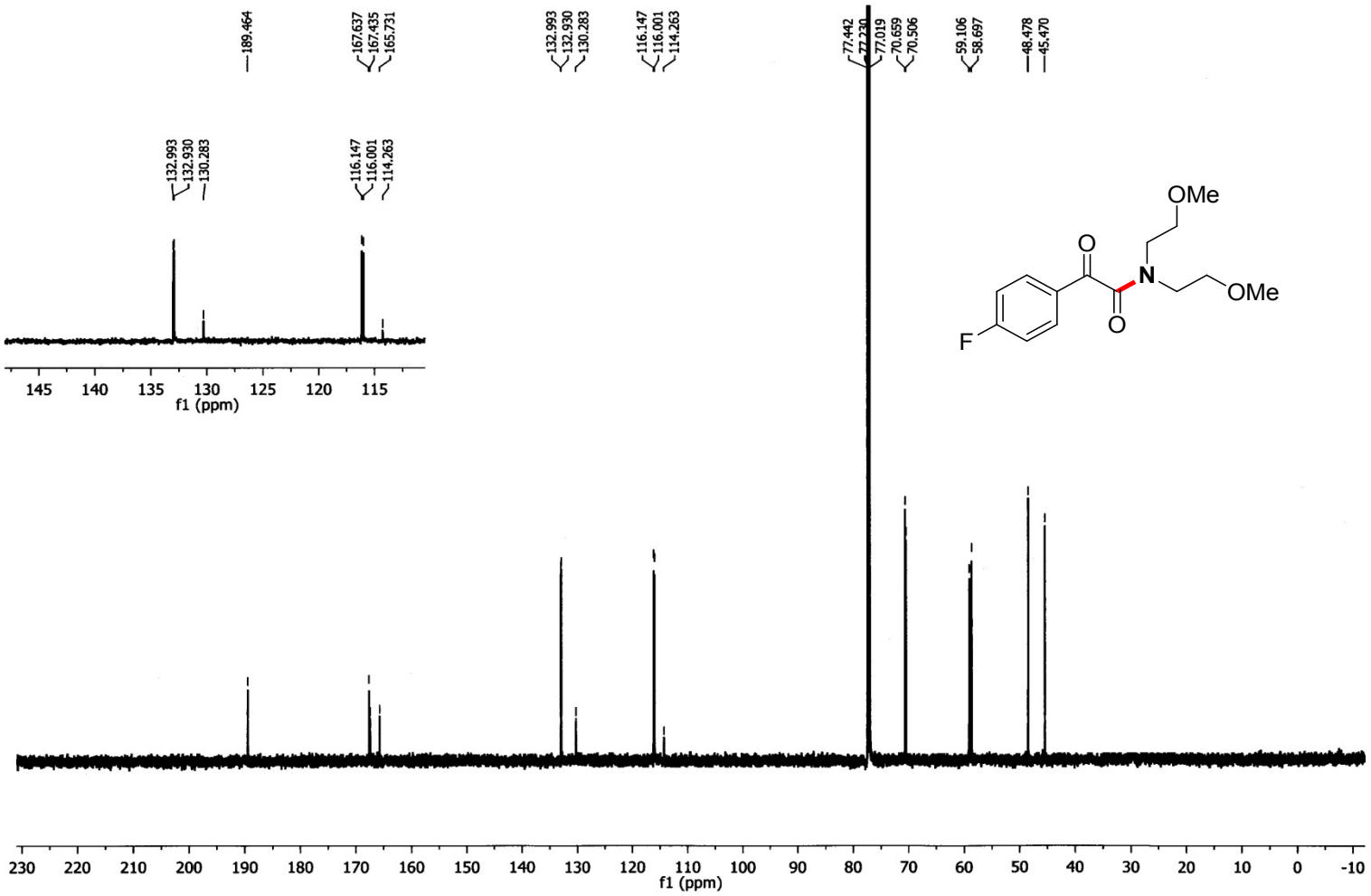
2-(4-Chlorophenyl)-*N*,*N*-bis(2-methoxyethyl)-2-oxoacetamide (3e): ^{13}C NMR (150 MHz, $CDCl_3$)



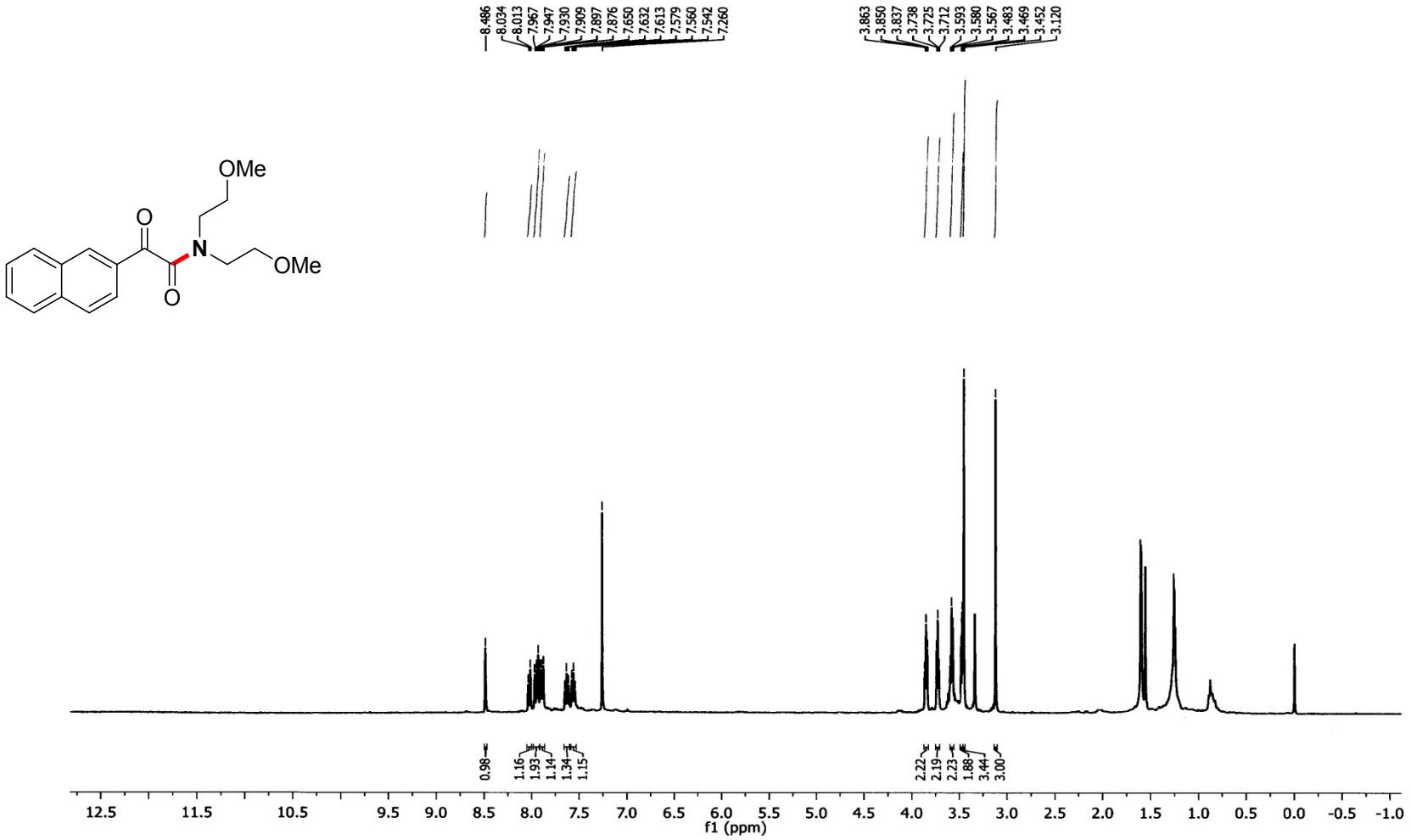
2-(4-Fluorophenyl)-*N*,*N*-bis(2-methoxyethyl)-2-oxoacetamide (3f): ^{1}H NMR (400 MHz, $CDCl_3$)



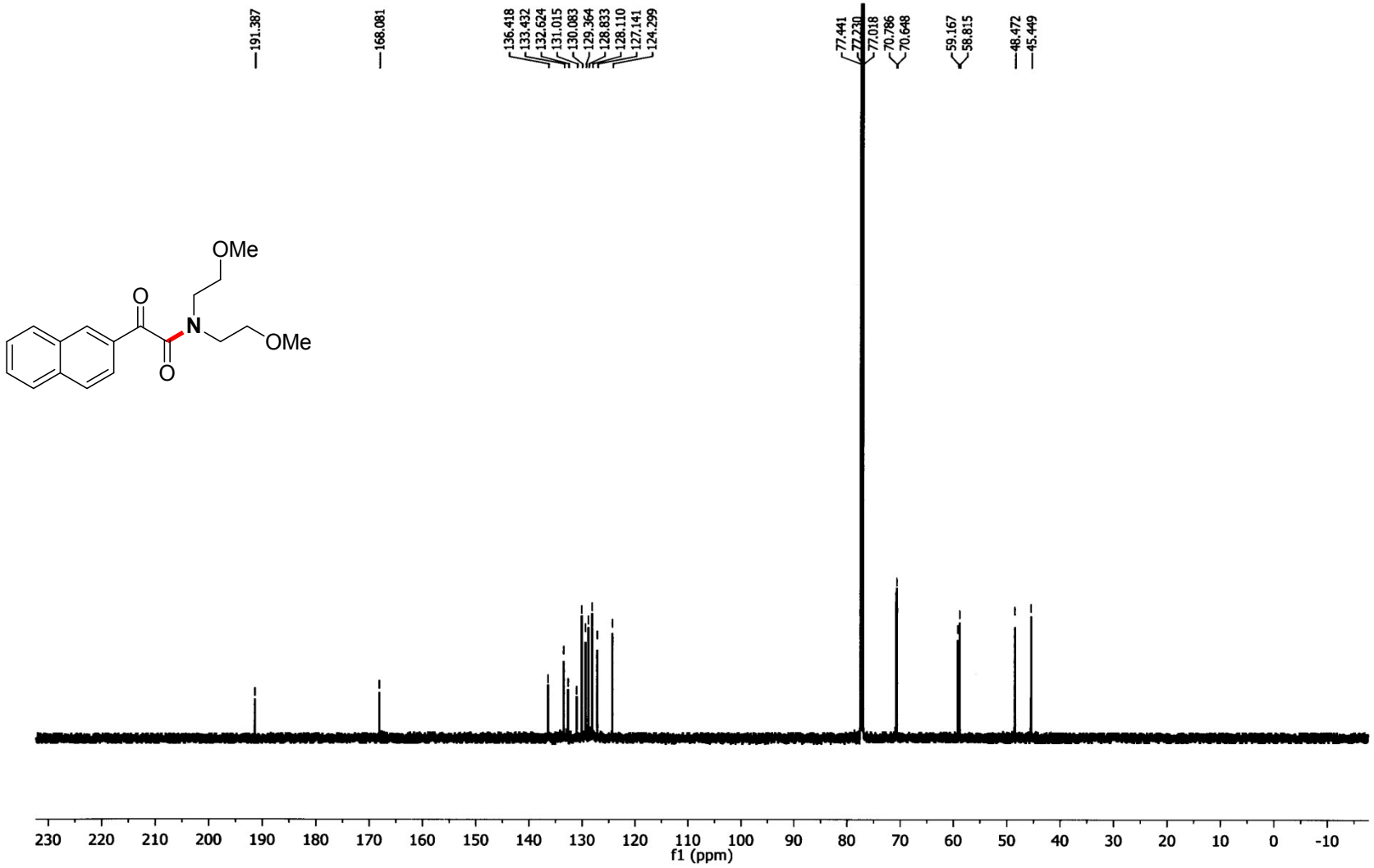
2-(4-Fluorophenyl)-*N*,*N*-bis(2-methoxyethyl)-2-oxoacetamide (3f): ^{13}C NMR (150 MHz, $CDCl_3$)



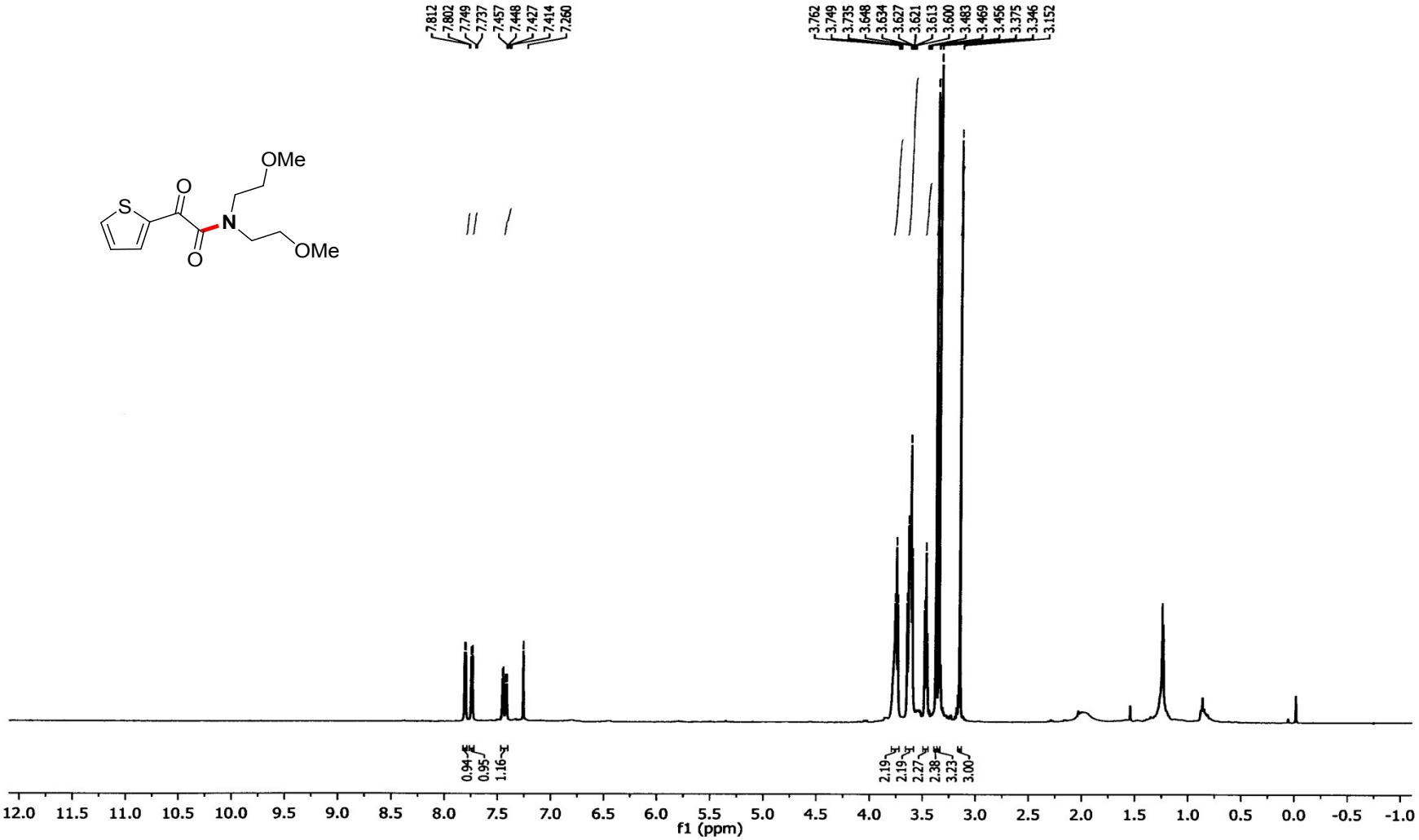
***N*,*N*-bis(2-methoxyethyl)-2-(naphthalen-2-yl)-2-oxoacetamide (3k): ^{1}H NMR (400 MHz, $CDCl_3$)**



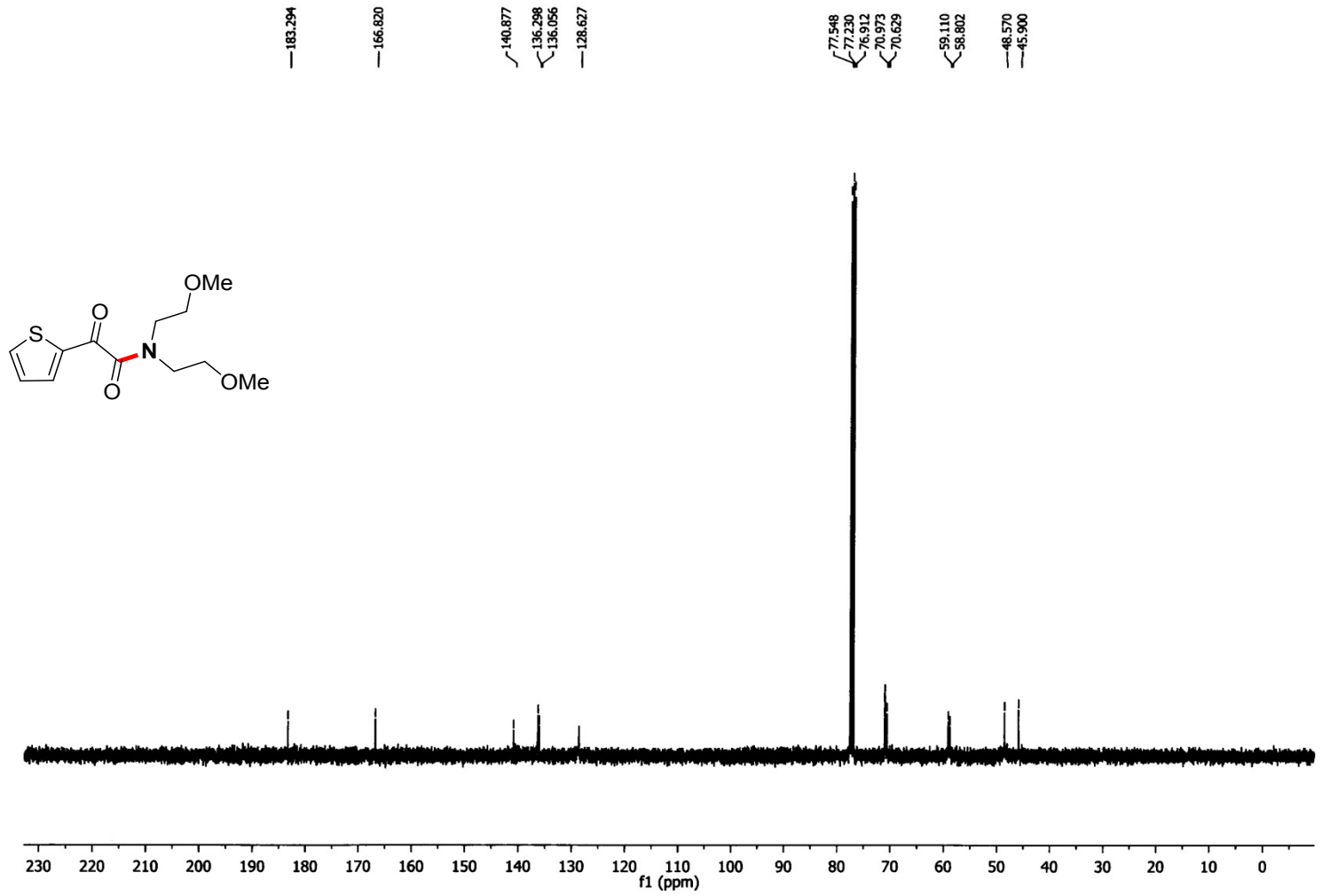
_N_,_N_-Bis(2-methoxyethyl)-2-(naphthalen-2-yl)-2-oxoacetamide (3k): ^{13}C NMR (150 MHz, $CDCl_3$)



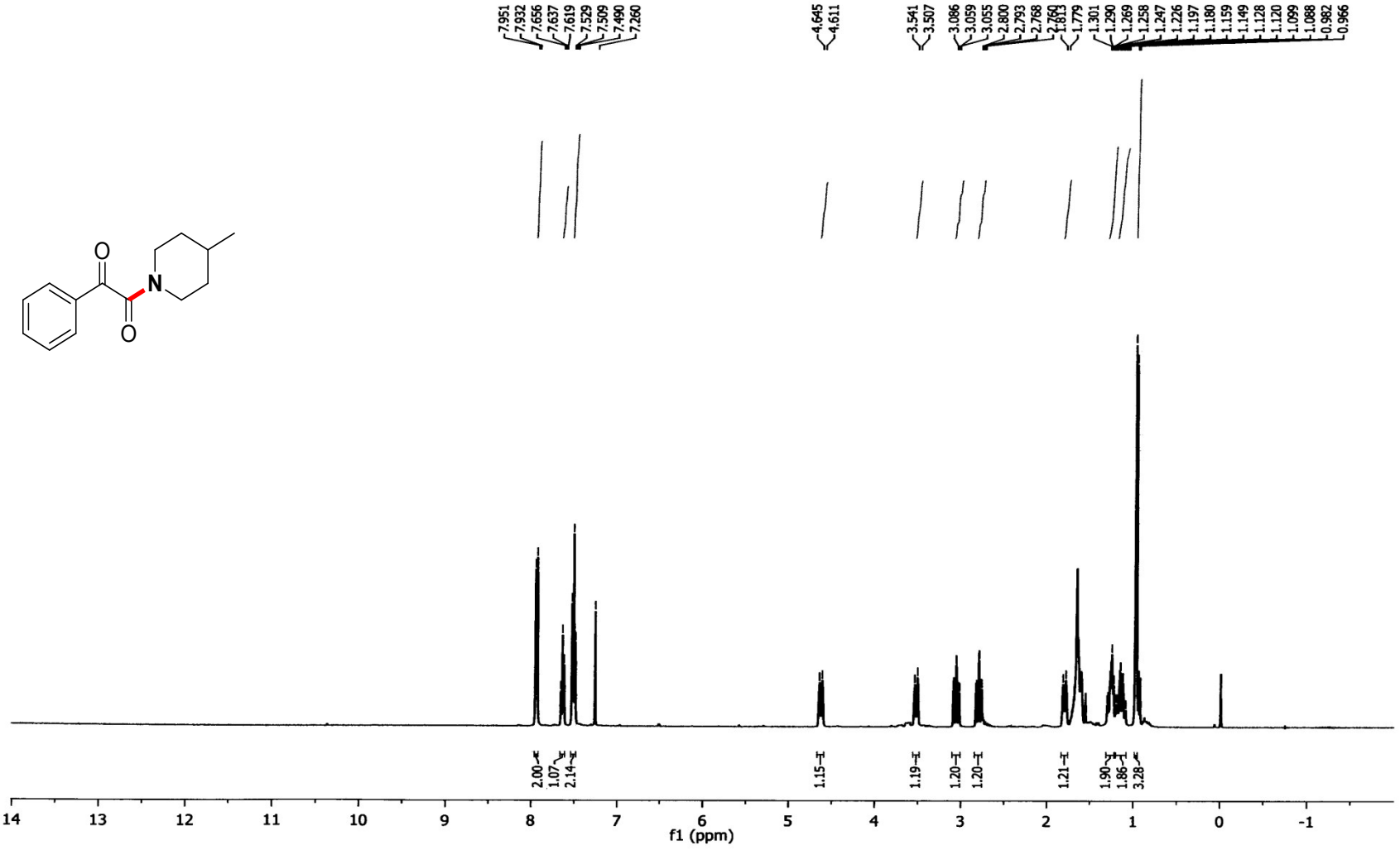
***N*,*N*-Bis(2-methoxyethyl)-2-oxo-2-(thiophen-2-yl)acetamide (3l): ^{1}H NMR (400 MHz, $CDCl_3$)**



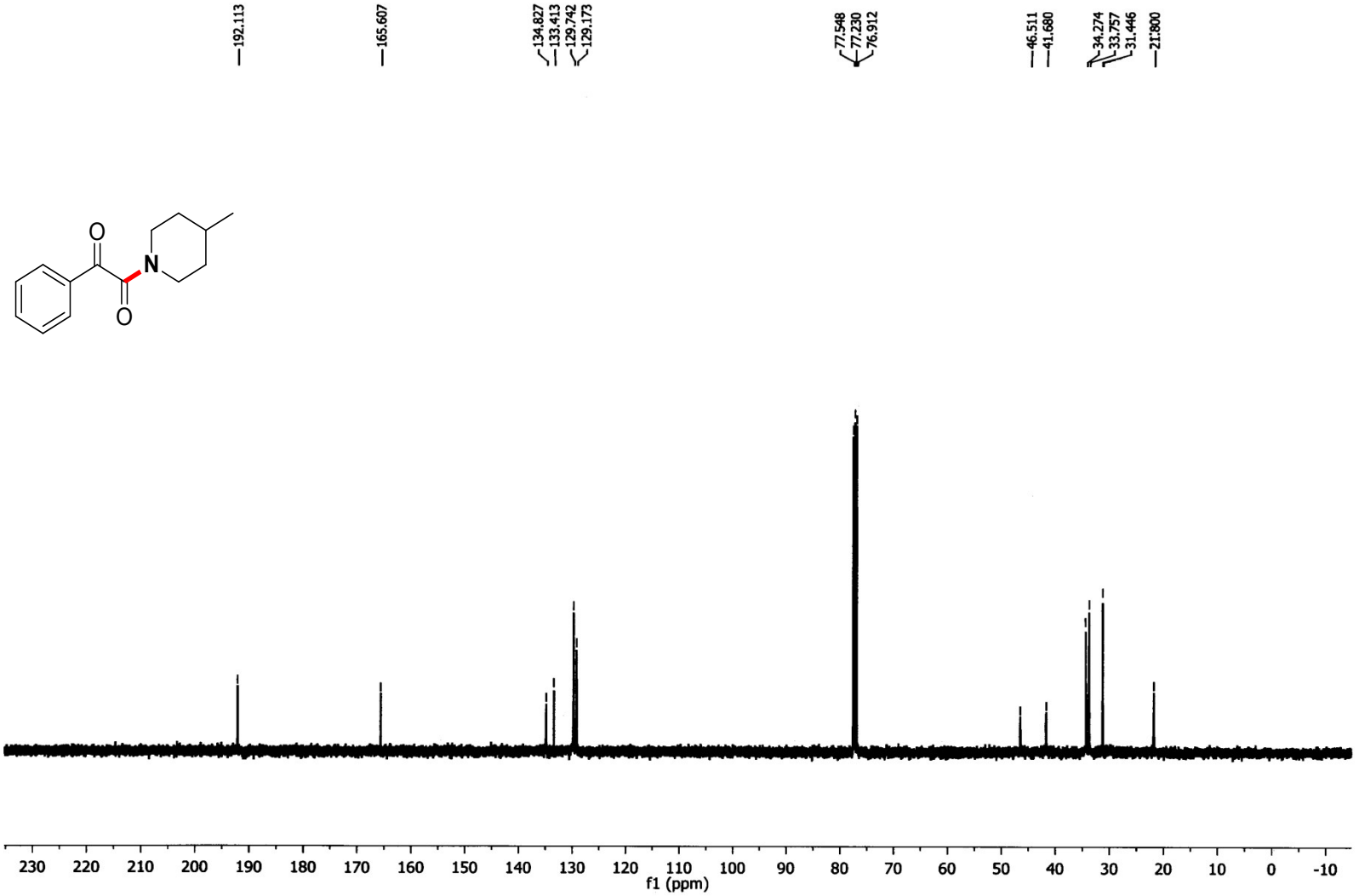
***N*,*N*-Bis(2-methoxyethyl)-2-oxo-2-(thiophen-2-yl)acetamide (3l): ^{13}C NMR (100 MHz, $CDCl_3$)**



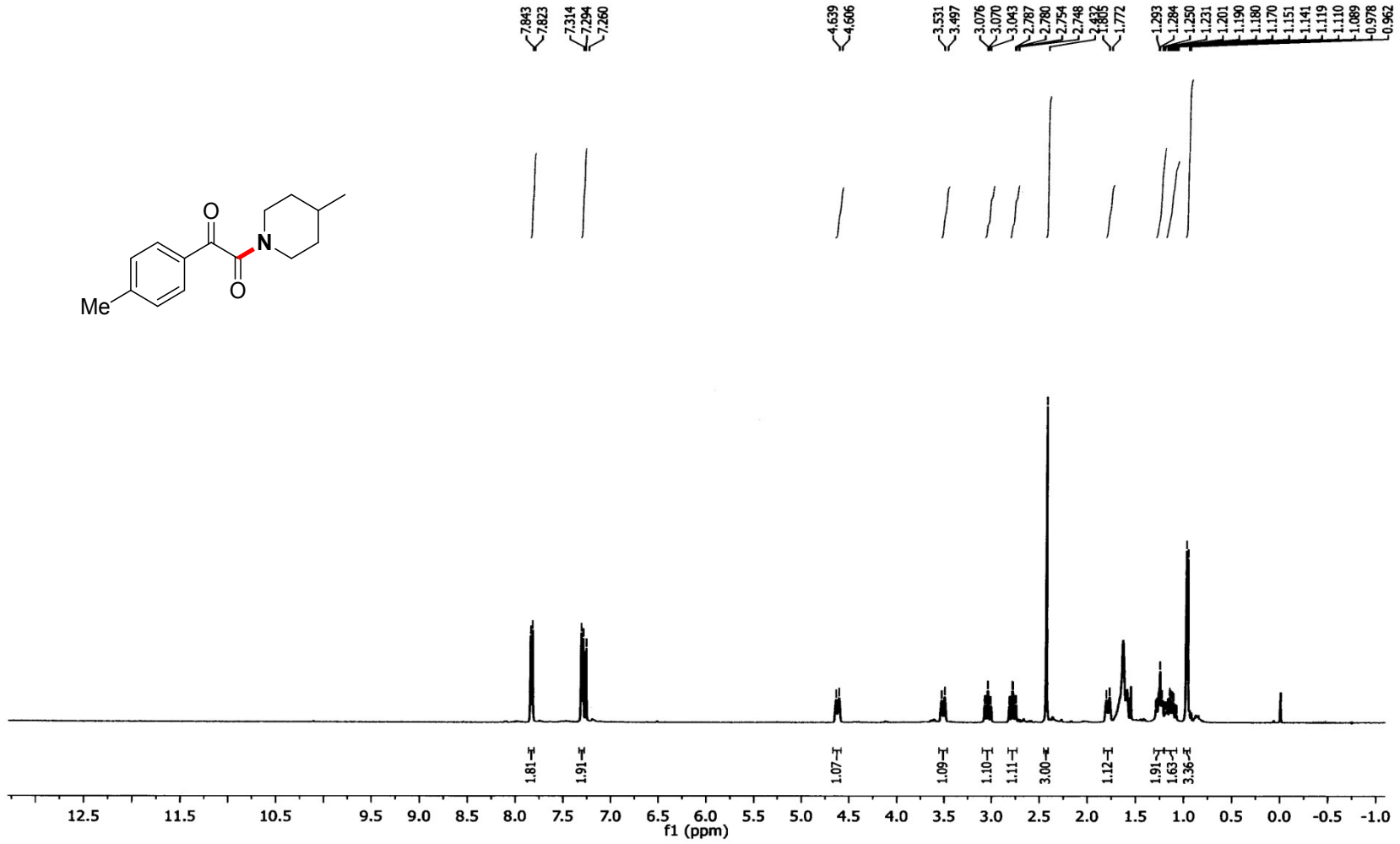
1-(4-Methylpiperidin-1-yl)-2-phenylethane-1, 2-dione (4a): ^{1}H NMR (400 MHz, $CDCl_3$)



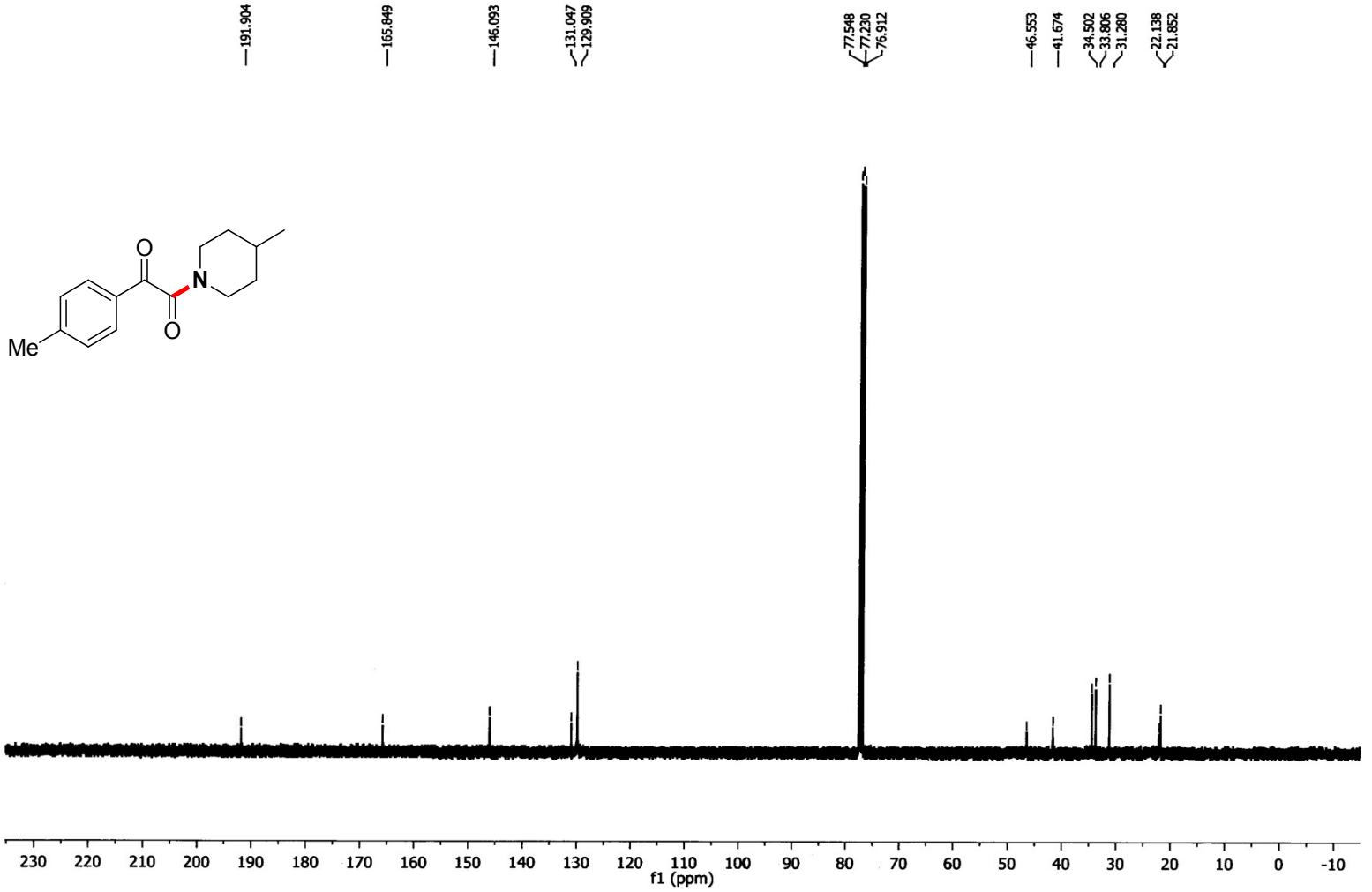
1-(4-Methylpiperidin-1-yl)-2-phenylethane-1,2-dione (4a): ^{13}C NMR (100 MHz, $CDCl_3$)



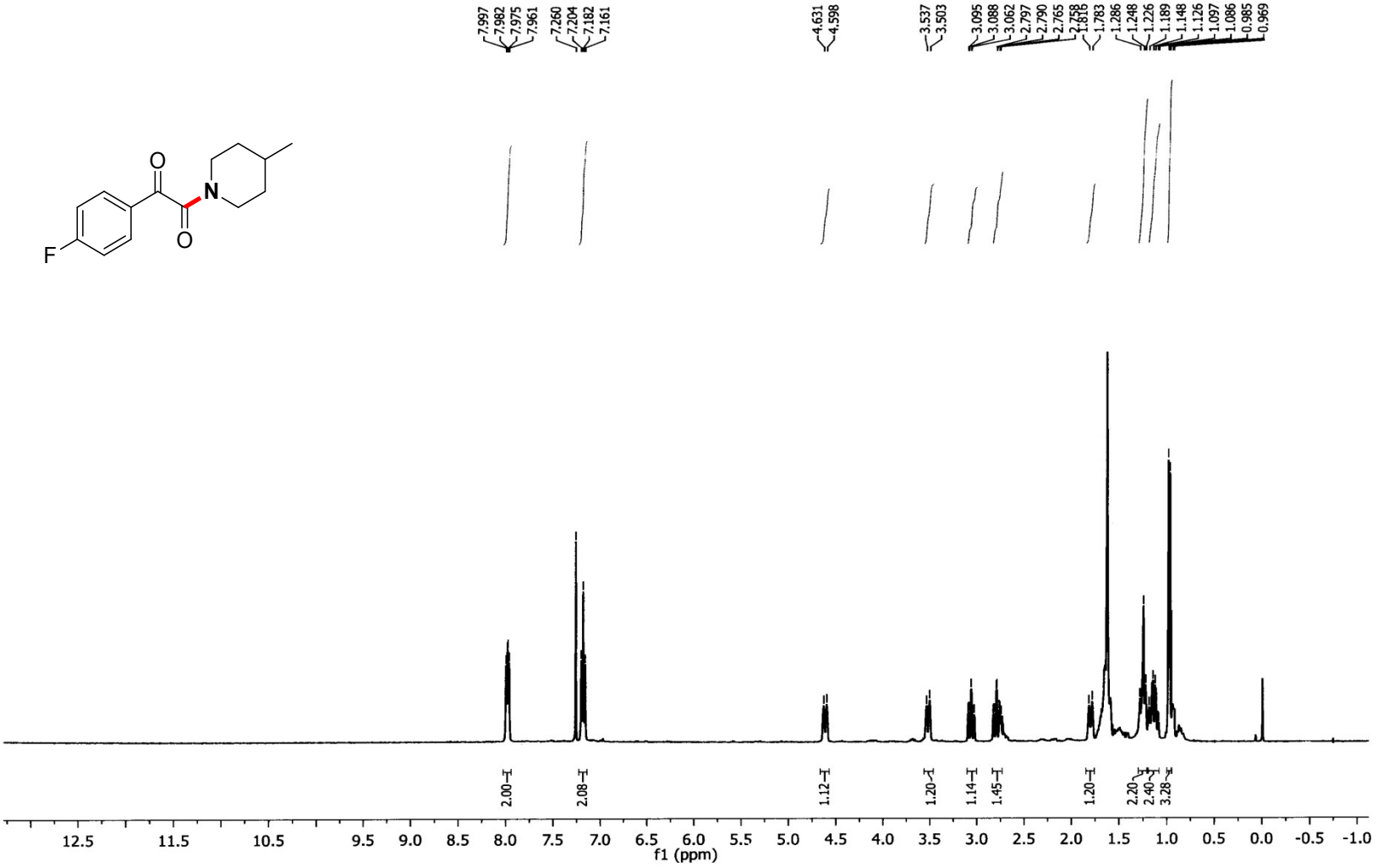
1-(4-Methylpiperidin-1-yl)-2-(*p*-tolyl)ethane-1,2-dione (4b): ^{1}H NMR (400 MHz, $CDCl_3$)



1-(4-Methylpiperidin-1-yl)-2-(*p*-tolyl)ethane-1,2-dione (4b): ^{13}C NMR (100 MHz, $CDCl_3$)



1-(4-Fluorophenyl)-2-(4-methylpiperidin-1-yl)ethane-1,2-dione (4f): ^{1}H NMR (400 MHz, $CDCl_3$)



1-(4-Fluorophenyl)-2-(4-methylpiperidin-1-yl)ethane-1,2-dione (4f): ^{13}C NMR (150 MHz, $CDCl_3$)