SUPPLEMENTARY MATERIAL

Synthesis of chemically diverse esters of 5-aminolevulinic acid for photodynamic therapy via the multicomponent Passerini reaction.

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Synthetic procedures.

_N_-(benzyloxycarbonyl)-5-aminolevulinic acid (2)

5-Aminolevulinic acid (499 mg, 2.98 mmol) was dissolved in 2.5 mL of methanol and cooled in an ice bath. 0.45 mL of benzyloxycarbonyl chloride (Z-Cl) was added, followed by a solution of 0.83 mL of triethylamine in 0.5 mL of methanol, which was added dropwise. After completion of the addition, the reaction mixture was stirred at room temperature for 2 h. The solution was poured into 15 mL of 5% hydrochloric acid. A white precipitated was formed, which was dissolved by adding 40 mL of ethyl acetate. The organic layer was separated, washed with brine (20 mL), water (2 x 20 mL) and finally dried. After evaporation under reduced pressure a crude product was obtained, which was crystallized from ethyl acetate-hexane to yield 67 % of **2** (532 mg).

General procedure for the P-3CR.

To a solution of *N*-(benzyloxycarbonyl)-5-aminolevulinic acid (**2**) in CH_2Cl_2 (0.4 mL / 0.1 mmol of **2**) 1.1 equivalents of formaldehyde (37% aq.) were added, followed by the addition of 1.1 equivalents of the corresponding isocyanide. The mixture was stirred vigorously at room temperature until total disappearance of the acid was observed TLC (usually 24 h). Then, the mixture was concentrated and the residue was purified by silica gel column chromatography, as indicated in each case.

2-(2-ethoxy-2-oxoethylamino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3a)

Compound **3a** was obtained from 42 mg of **2** (0.16 mmol) and ethyl 2-isocyanoacetate. The crude was purified by column chromatography (98:2 CH_2Cl_2-MeOH) to give **3a** (56 mg; 86%) as a colorless syrup; R*f* 0.43 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 7.60-7.49 (m, 5H, Ar), 7.03 (b.s, 1H), 5.82 (b.s, 1H), 5.31 (s, 2H), 4.84 (s, 2H), 4.41-4.38 (m, 4H), 4.27 (d, *J* 5.3 Hz, 2H), 3.04 (t, *J* 6.1 Hz, 2H), 2.93 (t, *J* 6.1 Hz, 2H), 1.44 (t, *J* 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$) 209.6, 171.0, 169.4, 167.2, 128.5, 128.2, 128.1, 67.1, 62.8, 61.7, 50.5, 40.8, 34.5, 27.6, 14.0. HRMS (ESI) calcd for (M+Na) $C_{19}H_{24}N_2NaO_8$: 431.1425. Found: 431.1427.

2-(diethoxyphosphorylmethylamino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3b)

Compound **3b** was obtained from 84 mg of **2** (0.32 mmol) and diethyl (isocyanomethyl)phosphonate. The crude was purified by column chromatography (98:2 CH_2Cl_2-MeOH) to give **3b** (120 mg; 80%) as a colorless syrup; R*f* 0.26 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$) 7.38-7.28 (m, 5H, Ar), 6.84 (b.s, 1H, (CO)-N*H*-CH_2-P), 6.49 (b.s, 1H, O(CO)-N*H*-CH_2), 5.11

(s, 2H, ArC*H*$_2$-O), 4.64 (s, 2H, O-C*H*$_2$-(CO)), 4.17 (d, *J* 5.3 HZ, 2H, NH-C*H*$_2$-(CO)), 4.08 (p, *J* 7.4 Hz, 4H, PO-C*H*$_2$CH$_3$), 3.73 (dd, *J* 6.1, 12.1 Hz, 2H, NH-C*H*$_2$-P), 2.87 (t, *J* 6.1 Hz, 2H, (CO)-C*H*$_2$-CH$_2$-(CO)-O), 2.69 (t, *J* 6.1 Hz, 2H, (CO)-CH$_2$-C*H*$_2$-(CO)-O), 1.27 (t, *J* 7.1 Hz, 6H, PO-CH$_2$C*H*$_3$). ^{13}C-NMR ($CDCl_3$) 205.8 (C=O ketone), 171.1 (C=O)-O), 167.0 (C=O)-NH), 156.7 (O-(C=O)-NH); 136.4, 128.4, 128.1, 128.0 (Ar); 66.9 (Ar-*C*H$_2$-O); 62.81, 62.75, 62.74 (PO-*C*H$_2$CH$_3$; O-*C*H$_2$-(CO)); 50.5 (NH-*C*H$_2$-(CO)); 35.1, 33.8 (NH-*C*H$_2$-P); 34.8((CO)-*C*H$_2$-CH$_2$-(CO)-O), 27.7((CO)-CH$_2$-*C*H$_2$-(CO)-O); 16.33, 16.29 (PO-CH$_2$*C*H$_3$). HRMS (ESI) calcd for (M+H) $C_{20}H_{30}N_2O_9P$: 473.1683. Found: 473.1661.

2-(3,4-dimethoxyphenethylamino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3c)

Compound **3c** was obtained from 40 mg of **2** (0.15 mmol) and 4-(2-isocyanoethyl)-1,2-dimethoxybenzene. The crude was purified by column chromatography (98:2 CH_2Cl_2-MeOH) to give **3c** (59 mg; 81%) as a colorless syrup; R*f* 0.30 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 7.38-7.29 (m, 5H, Ar), 6.78 (d, *J* 7.9 Hz, 1H, Ph(OMe)$_2$), 6.72 (m, 2H, Ph(OMe)$_2$), 6.47 (b.s, 1H, (CO)-N*H*-CH$_2$CH$_2$), 5.40 (b.s, 1H, O-(CO)-N*H*-CH$_2$), 5.10 (s, 2H, Ar-C*H*$_2$-O), 4.58 (s, 2H, O-C*H*$_2$-(CO)), 4.08 (d, *J* 5.4 Hz, 2H, NH-C*H*$_2$-(CO)), 3.85, 3.83 (2s, 6H, Ar-OC*H*$_3$), 3.53 (q, *J* 6.8 Hz, 2H, NH-C*H*$_2$-CH$_2$-Ar), 2.79 (m, 4H, NH-CH$_2$-C*H*$_2$-Ar, (CO)-C*H*$_2$-CH$_2$-(CO)-O), 2.60 (t, *J* 6.1 Hz, 2H, (CO)-CH$_2$-C*H*$_2$-(CO)-O). ^{13}C-NMR ($CDCl_3$): 204.6 (C=O ketone), 171.2 ((C=O)-O), 166.9 ((C=O)-NH), 156.2 (O-(C=O)-NH); 148.9, 147.6, 136.1, 131.3, 128.5, 128.2, 128.1, 120.7, 112.1, 111.3 (Ar), 67.1 (Ar-*C*H$_2$-O), 63.0 (O-*C*H$_2$-(CO)); 55.89, 55.85 (Ar-OCH$_3$); 50.3 (NH-*C*H$_2$-(CO)), 40.6 (NH-*C*H$_2$-CH$_2$-Ar); 35.0, 34.5 ((CO)-*C*H$_2$-CH$_2$-(CO)-O; NH-CH$_2$-*C*H$_2$-Ar); 27.5 ((CO)-CH$_2$-*C*H$_2$-(CO)-O). HRMS (ESI) calcd for (M+H) $C_{25}H_{31}N_2O_8$: 487.2075. Found: 487.2095.

2-(t-butylamino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3d)

Compound **3d** was obtained from 47 mg of **2** (0.18 mmol) and 2-isocyano-2-methylpropane. The crude was purified by column chromatography (100:1 CH_2Cl_2-MeOH) to give **3d** (61 mg; 91%) as a colorless syrup; R*f* 0.43 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 7.35 (m, 5H), 6.03 (b.s, 1H), 5.41 (b.s, 1H), 5.12 (s, 2H), 4.47 (s, 2H), 4.14 (d, *J* 5.2 Hz, 2H), 2.82 (t, *J* 6.1 Hz, 2H), 2.69 (t, *J* 6.1 Hz, 2H), 1.38 (s, 9H). ^{13}C-NMR ($CDCl_3$): 204.4, 171.3, 166.1, 156.3, 136.3, 128.7, 128.4, 128.2, 110.1, 67.2, 63.5, 51.6, 50.6, 34.6, 28.8. HRMS (ESI) calcd for (M+Na) $C_{19}H_{26}N_2O_6Na$: 401.1683. Found: 401.1667.

2-(cyclohexylamino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3e)

Compound **3e** was obtained from 29 mg of **2** (0.11 mmol) and isocyanocyclohexane. The crude was purified by column chromatography (98:2 CH_2Cl_2-MeOH) to give **3e** (35 mg; 80%) as a colorless syrup; R*f* 0.39 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 7.30-7.39 (m, 5H, Ar), 6.23 (d, *J* 7.1

Hz, 1H), 5.38 (b.s, 1H), 5.12 (s, 2H), 4.56 (s, 2H), 4.15 (d, *J* 5.3 Hz, 2H), 3.81 (m, 1H), 2.84 (t, *J* 6.0 Hz, 2H), 2.69 (t, *J* 6.2 Hz, 2H), 1.92 (m,2H), 1.76-1.57 (m, 4H), 1.36 (m, 2H), 1.26-1.12 (m, 2H). ^{13}C-NMR ($CDCl_3$): 203.9, 171.2, 165.3, 128.5, 128.0, 67.2, 63.1, 50.4, 48.1, 34.6, 32.9, 27.6, 25.5, 24.9. HRMS (ESI) calcd for (M+H) $C_{21}H_{29}N_2O_6$: 405.2020. Found: 405.2029.

2-((4-fluorophenyl)amino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3f)

Compound **3f** was obtained from 60 mg of **2** (0.23 mmol) and 1-fluoro-4-isocyanobenzene. The crude was purified by column chromatography (70:0.4 and 50:0.4 CH_2Cl_2-MeOH) to give **3f** (70 mg; 75%) as a colorless syrup; R*f* 0.50 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 8.27 (b.s, 1H), 7.65 (dd, *J* 8.9, 4.8 Hz, 2H), 7.33 (m, 5H), 6.96 (t, *J* 8.5 Hz, 2H), 5.37 (b.s, 1H), 5.08 (s, 2H), 4.72 (s, 2H), 4.13 (d, *J* 5.4 Hz, 2H), 2.90 (t, *J* 6.0 Hz, 2H), 2.71 (t, *J* 6.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$): 206.1, 171.5, 165.4, 160.6, 158.7, 156.4, 136.1, 133.4, 133.3, 128.7, 128.5, 128.2, 122.1, 122.0, 115.8, 115.6, 67.4, 63.1, 50.4, 35.0, 27.9. HRMS (ESI) calcd for (M+H) $C_{21}H_{21}FN_2O_6Na$: 439.1276. Found: 439.1281.

2-(4-tolylamino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3g)

Compound **3g** was obtained from 63 mg of **2** (0.24 mmol) and 1-isocyano-4-methylbenzene. The crude was purified by column chromatography (100:1 CH_2Cl_2-MeOH) to give **3g** (79 mg; 81%) as a colorless syrup; R*f* 0.45 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 8.16 (b.s, 1H, (CO)-N*H*-Ar), 7.54 (d, *J* 8.0 Hz, 2H, Ar(*m*-*H*)-CH_3), 7.33 (m, 5H, Ar), 7.08 (d, *J* 8.0 Hz, 2H, Ar(*o*-*H*)-CH_3), 5.41 (b.s, 1H, (CO)-N*H*-CH_2), 5.08 (s, 2H, Ar-C*H*$_2$-O), 4.70 (s, 2H, O-C*H*$_2$-(CO)), 4.12 (d, *J* 5.3 Hz, 2H, NH-C*H*$_2$-(CO)), 2.86 (t, *J* 6.0 Hz, 2H, (CO)-C*H*$_2$-CH_2-(CO)-O), 2.71 (t, *J* 6.0 Hz, 2H, (CO)-CH_2-C*H*$_2$-(CO)-O), 2.27 (s, 2H, Ar-C*H*$_3$). ^{13}C-NMR ($CDCl_3$): 205.6 (C=O ketone), 171.5 ((C=O)-O), 165.2 ((C=O)-NH), 156.4 (O-(C=O)-NH); 136.2, 134.7, 134.5, 129.6, 128.7, 128.4, 128.2, 120.3 (Ar); 67.3 (Ar-*C*H_2-O), 63.2 (O-*C*H_2-(CO)), 50.5 (NH-*C*H_2-(CO)), 34.9 ((CO)-*C*H_2-CH_2-(CO)-O), 27.9 ((CO)-CH_2-*C*H_2-(CO)-O), 21.0 (Ar-*C*H_3). HRMS (ESI) calcd for (M+H) $C_{22}H_{25}N_2O_6$: 413.1707. Found: 413.17071.

2-((2-(trifluoromethyl)phenyl)amino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3h)

Compound **3h** was obtained from 60 mg of **2** (0.23 mmol) and 1-isocyano-2-(trifluoromethyl)benzene. The crude was purified by column chromatography (100:1 CH_2Cl_2-MeOH) to give **3h** (89 mg; 84%) as a colorless syrup; R*f* 0.50 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 8.36 (b.s, 1H), 8.24 (d, *J* 8.3 Hz, 1H), 7.63 (d, *J* 7.8 Hz, 1H), 7.57 (t, *J* 7.8 Hz, 1H), 7.34 (m, 5H), 7.27 (t, *J* 7.8 Hz, 1H), 5.47 (b.s, 1H), 5.10 (s, 2H), 4.74 (s, 2H), 4.14 (d, *J* 5.1 Hz, 2H), 2.80 (m, 4H). ^{13}C-NMR ($CDCl_3$): 203.7, 170.9, 165.4, 156.3, 136.3, 134.3, 133.2, 128.6, 128.3, 128.2,

126.40, 126.35, 126.31, 126.27, 125.22, 125.15, 124.2, 123.1, 67.2, 63.3, 50.6, 34.3, 27.5. HRMS (ESI) calcd for (M+H) $C_{22}H_{22}F_3N_2O_6$: 467.1425. Found: 467.1420.

2-((4-bromo-2-methylphenyl)amino)-2-oxoethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3i)

Compound **3i** was obtained from 61 mg of **2** (0.23 mmol) and 4-bromo-1-isocyano-2-methylbenzene. The crude was purified by column chromatography (70:0.4 and 50 : 0.4 CH_2Cl_2-MeOH) to give **3i** (94 mg; 84%) as a colorless syrup; R*f* 0.45 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 7.92 (b.s, 1 H, (CO)-N*H*-Ar), 7.61 (d, *J* 8.4 Hz, 1H, Ar), 7.40-7.28 (m, 7H, Ar), 5.37 (b.s, 1H, (CO)-N*H*-CH_2), 5.07 (s, 2H, Ar-C*H*$_2$-O), 4.73 (s, 2H, O-C*H*$_2$-(CO)), 4.10 (d, *J* 5.2 Hz, 2H, O-C*H*$_2$-(CO)), 2.85 (t, *J* 5.9 Hz, 2H, (CO)-C*H*$_2$-CH$_2$-(CO)-O), 2.73 (t, *J* 5.9 Hz, 2H, (CO)-CH$_2$-C*H*$_2$-(CO)-O), 2.23 (s, 3H, Ar-C*H*$_3$). ^{13}C-NMR ($CDCl_3$): 204.8 (C=O ketone), 171.4 ((C=O)-O), 165.4 ((C=O)-NH), 156.3 (O-(C=O)-NH); 136.2, 133.8, 133.4, 132.6, 129.8, 128.7, 128.4, 128.2, 125.3, 119.0 (Ar); 67.3 (Ar-*C*H$_2$-O), 63.5 (O-*C*H$_2$-(CO)), 50.5 (NH-*C*H$_2$-(CO)), 34.6 ((CO)-*C*H$_2$-CH$_2$-(CO)-O), 27.8 ((CO)-CH$_2$-*C*H$_2$-(CO)-O), 17.5 (Ar-*C*H$_3$). HRMS (ESI) calcd for (M+Na) $C_{22}H_{23}BrN_2O_6Na$: 513.0632. Found: 513.0647.

2-oxo-2-(pentadecylamino)ethyl-N-(benzyloxycarbonyl)-5-aminolevulinate (3j)

Compound **3j** was obtained from 39 mg of **2** (0.15 mmol) and 1-isocyanopentadecane. The crude was purified by column chromatography (98:2 CH_2Cl_2-MeOH) to give **3j** (50 mg; 63%) as a colorless syrup; R*f* 0.43 (95:5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 7.40-7.29 (m, 5H, Ar), 6.38 (b.s, 1H), 5.40 (b.s, 1H), 5.12 (s, 2H), 4.58 (s, 2H), 4.14 (d, *J* 4.6 Hz, 2H), 3.29 (q, *J* 6.8 Hz, 2H), 2.83 (t, *J* 5.6 Hz, 2H), 2.69 (t, *J* 5.6 Hz, 2H), 1.73-1.20 (m, 26H), 0.88 (t, *J* 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): 204.5, 171.2, 166.8, 128.3, 128.1, 67.2, 63.1, 50.4, 39.3, 34.6, 31.9, 29.70, 29.66, 29.61, 29.57, 29.42, 29.37, 29.29, 27.6, 26.9, 22.7, 14.1. HRMS (ESI) calcd for (M+H) $C_{30}H_{49}N_2O_6$: 533.3585. Found: 533.3585.

General procedure for the deprotection of the Passerini products.

A stirred suspension of the corresponding intermediates **3a-j**, dissolved in 10:1 MeOH-$CHCl_3$ (3 mL / 0.1 mmol of substrate) and palladium black (0.1 equivalents) was hydrogenated at atmospheric pressure at room temperature. After completion of the reaction (usually for 4 h, controlled by TLC), the mixture was filtered through celite and the solvent was removed *in vacuo*. The crude product was purified by recrystallization or silica gel column chromatography, as indicated in each case.

2-(2-ethoxy-2-oxoethylamino)-2-oxoethyl-5-aminolevulinate (1a)

Compound **1a** was obtained from 40 mg (0.098 mmol) of **3a**. The crude product was purified by recrystallization from CH_2Cl_2 to yield 24 mg of **1a** (90%) as a white solid. Rf 0.08 (93:7 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 4.64 (s, 2H), 4.22 (q, J 7.1 Hz, 2H), 4.03 (d, J 6.5 Hz, 4H), 2.92 (b. dt, J 6.2, 2.0 Hz, 2H), 2.84 (b. dt, J 6.2, 2.0 Hz, 2H), 1.30 (t, J 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 201.4, 171.5, 169.7, 168.3, 62.4, 61.4, 47.0, 40.6, 34.2, 27.2, 13.7. HRMS (ESI) calcd for (M+Na) $C_{11}H_{18}N_2NaO_6$: 297.1057. Found: 297.1048.

2-(diethoxyphosphorylmethylamino)-2-oxoethyl-5-aminolevulinate (1b)

Compound **1b** was obtained from 43 mg (0.092 mmol) of **3b**. The crude product was purified by column chromatography (98:2 and 95:5 CH_2Cl_2-MeOH) to yield 28 mg of **1b** (89%) as a colorless syrup. Rf 0.32 (8:2 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 8.23 (bs, 2H), 4.69 (s, 2H), 4.28 (bs, 2H), 4.15 (m, 4H), 3.85 (bs, 2H), 3.47 (bs, 1H), 3.03 (bs, 2H), 2.85 (bs, 2H), 1.31 (t, J 7.1 Hz, 6H). ^{13}C-NMR ($CDCl_3$): 203.5, 172.6, 168.5, 63.8, 63.7, 63.2, 63.0, 62.95, 62.9, 48.2, 35.3, 35.0, 34.0, 33.8, 32.5, 29.3, 27.8, 16.5. HRMS (ESI) calcd for (M+Na) $C_{12}H_{23}N_2NaO_7P$: 361.1135. Found: 361.1154.

2-(3,4-dimethoxyphenethylamino)-2-oxoethyl-5-aminolevulinate (1c)

Compound **1c** was obtained from 49 mg (0.101 mmol) of **3c**. The crude product was purified by recrystallization from CH_2Cl_2 to yield 22 mg of **1c** (63%) as white solid. Rf 0.09 (93:7 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 6.84 (d, J 8.7 Hz, 1H, Ar), 6.77 (m, 2H, Ar), 4.54 (s, 2H, O-CH_2-(CO)), 4.02 (s, 2H, NH_2-CH_2-(CO)), 3.88 (s, 3H, Ar-OCH_3), 3.86 (s, 3H, Ar-OCH_3), 3.48 (t, J 7.4 Hz, 2H, NH-CH_2-CH_2-Ar), 2.87 (t, J 6.3 Hz, 2H, (CO)-CH_2-CH_2-(CO)O), 2.80 (t, J 7.4 Hz, 2H, NH-CH_2-CH_2-Ar), 2.77 (t, J 6.3 Hz, 2H, (CO)-CH_2-CH_2-(CO)O). ^{13}C-RMN ($CDCl_3$, CD_3OD 9:1): 201.2 (C=O ketone), 171.4 ((C=O)-O), 167.4 ((C=O)-NH); 148.6, 147.3, 131.2, 120.5, 111.9, 111.2 (Ar); 62.6 (O-CH_2-(CO)); 55.6, 55.6 (Ar-OCH_3); 46.9 (NH_2-CH_2-(CO)), 40.5 (NH-CH_2-CH_2-Ar), 34.7 ((CO)-CH_2-CH_2-(CO)-O), 34.1 (NH-CH2-CH2-Ar), 27.1 ((CO)-CH_2-CH_2-(CO)-O). HRMS (ESI) calcd for (M+Na) $C_{17}H_{24}N_2NaO_6$: 375.1527. Found: 375.1510.

2-(t-butylamino)-2-oxoethyl-5-aminolevulinate (1d)

Compound **1d** was obtained from 41 mg (0.108 mmol) of **3d**. The crude product was purified by column chromatography (95:5 and 9:1 CH_2Cl_2-MeOH) to yield 24 mg of **1d** (89%) as a colorless syrup. Rf 0.26 (8:2 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 8.14 (b.s, 2H), 4.64 (b.s, 2H), 4.40 (b.s, 2H), 3.09 (b.s, 2H), 2.85(b.s, 2H), 1.43 (m, 12H). ^{13}C-NMR ($CDCl_3$): 203.2, 172.5, 171.3, 167.1, 166.1, 63.7, 63.5, 51.8, 51.6, 50.7, 48.2, 35.0, 32.3, 29.3, 28.84, 28.79, 28.7, 27.6. HRMS (ESI) calcd for (M+Na) $C_{11}H_{20}N_2NaO_4$: 267.1315. Found: 267.1311.

2-(cyclohexylamino)-2-oxoethyl-5-aminolevulinate (1e)

Compound **1e** was obtained from 27 mg (0.067 mmol) of **3e**. The crude product was purified by recrystallization from CH_2Cl_2 to yield 16 mg of **1e** (90%), as a white solid. Rf 0.39 (9 :5 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 8.25 (b.s, 1H), 4.55 (s, 2H), 4.18 (s, 2H), 3.71 (m, 1H), 3.00-2.73 (m, 6H), 1.87 (m, 2H), 1.74 (m, 2H), 1.63 (m, 1H), 1.40-1.11 (m, 5H). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 202.5, 172.2, 166.7, 63.2, 48.6, 48.5, 47.7, 34.7, 32.71, 32.68, 27.5, 25.4, 25.0. HRMS (ESI) calcd for (M+Na) $C_{13}H_{22}N_2NaO_4$: 293.1472. Found: 293.1466.

2-((4-fluorophenyl)amino)-2-oxoethyl-5-aminolevulinate (1f)

Compound 1f was obtained from 47 mg (0.113 mmol) of 3f. The crude product was purified by recrystallization from CH_2Cl_2 to yield 23 mg of **1f** (73%) as a white solid. Rf 0.20 (85:15 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 7.56 (m, 2H), 7.03 (m, 2H), 4.72 (s, 2H), 4.01 (s, 2H), 2.89 (m, 4H). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 201.0, 171.7, 165.9, 160.2, 158.2, 133.2, 133.1, 121.8, 121.7, 115.0, 114.8, 62.3, 46.7, 33.9, 27.0. HRMS (ESI) calcd for (M+H) $C_{13}H_{16}N_2FO_4$: 283.1089. Found: 283.1098.

2-(4-tolylamino)-2-oxoethyl-5-aminolevulinate (1g)

Compound **1g** was obtained from 55 mg (0.133 mmol) of **3g**. The crude product was purified by recrystallization from CH_2Cl_2 to yield 22 mg of 1g (61%) as a white solid. Rf 0.20 (85:15 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 7.44 (d, J 8.3 Hz, 2H, Ar), 7.13 (d, J 8.3 Hz, 2H, Ar), 4.71 (s, 2H, O-CH_2-(CO)), 4.01 (s, 2H, NH_2-CH_2-(CO)), 2.88 (m, 4H, (CO)-CH_2-CH_2-(CO)-O, (CO)-CH_2-CH_2-(CO)-O), 2.32 (s, 2H, Ar-CH_3). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 201.2 (C=O ketone), 171.7 ((C=O)-O), 165.9 ((C=O)-NH); 134.4, 134.1, 129.0, 120.2 (Ar); 62.5 (O-CH_2-(CO)), 46.8 (NH_2-CH_2-(CO)), 34.0 ((CO)-CH_2-CH_2-(CO)-O), 27.2 ((CO)-CH_2-CH_2-(CO)-O), 20.2 (Ar-CH_3). HRMS (ESI) calcd for (M+H) $C_{14}H_{19}N_2O_4$: 279.1339. Found: 279.1338.

2-((2-(trifluoromethyl)phenyl)amino)-2-oxoethyl-5-aminolevulinate (1h)

Compound **1h** was obtained from 48 mg (0.104 mmol) of **3h**. The crude product was purified by recrystallization from CH_2Cl_2 to yield 29 mg of **1h** (85%) as a white solid. Rf 0.30 (85:15 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 8.01 (d, J 8.2 Hz, 1H), 7.67 (d, J 7.9 Hz, 1H), 7.61 (t, J 7.9 Hz, 1H), 7.35 (t, J 7.7 Hz, 1H), 4.76 (s, 2H), 4.02 (s, 2H), 2.91 (m, 2H), 2.86 (m, 2H). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 201.0, 171.2, 166.1, 133.8, 132.9, 126.31, 126.26, 125.8, 125.7, 63.0, 47.1, 34.3, 27.2. HRMS (ESI) calcd for (M+Na) $C_{14}H_{15}F_3N_2NaO_4$: 355.0876. Found: 355.0881.

2-oxo-2-(pentadecylamino)ethyl-5-aminolevulinate (1j)

Compound **1j** was obtained from 35 mg (0.066 mmol) of **3j**. The crude product was purified by column chromatography (95:5 and 9:1 CH_2Cl_2-MeOH) to yield 14 mg of **1j** (33%), a pale yellow solid. Rf 0.14 (9:1 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$): 4.55 (s, 2H), 4.03 (s, 2H), 3.24 (t, J 7.3 Hz, 2H), 2.89 (t, J 6.3 Hz, 2H), 2.80 (t, J 6.3 Hz, 2H), 1.53 (b.s, 2H), 1.34-1.22 (m, 24H), 0.88 (t, J 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): 201.5, 171.6, 171.4, 167.4, 62.8, 47.1, 39.3, 34.4, 31.8, 29.58, 29.56, 29.54, 29.52, 29.50, 29.48, 29.45, 29.25, 29.22, 29.20, 27.4, 26.83, 26.79, 22.6, 13.9. HRMS (ESI) calcd for (M+H) $C_{22}H_{43}N_2O_4$: 399.3217. Found: 399.3197.

2-((4-bromo-2-methylphenyl)amino)-2-oxoethyl-5-aminolevulinate (1i)

Unexpectedly, when the general procedure deprotection procedure was applied to 67 mg (0.136 mmol) of **3i**, the target compound **1i** was not obtained. After purification of the resulting product by recrystallization from CH_2Cl_2, 40 mg of a white solid was obtained, which was identified as ***2-((2-methylphenyl)amino)-2-oxoethyl-5-aminolevulinate (1k)***. Rf 0.24 (85:15 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 7.42 (dd, 1H, J 7.8; 1.4 Hz, Ar), 7.26-7.13 (m, 3H, Ar), 4.78 (s, 2H, O-CH_2-(CO)), 4.02 (s, 2H, NH_2-CH_2-(CO)), 2.91 (m, 2H, (CO)-CH_2-CH_2-(CO)-O), 2.87 (m, 2H, (CO)-CH_2-CH_2-(CO)-O)), 2.27 (s, 3H, Ar-CH_3). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 201.0 (C=O ketone), 171.7 ((C=O)-O), 166.5 ((C=O)-NH); 134.1, 132.3, 130.3, 126.3, 126.1, 125.0 (Ar); 62.6 (O-CH_2-(CO)), 46.9 (NH_2-CH_2-(CO)), 34.2 ((CO)-CH_2-CH_2-(CO)-O), 27.2 ((CO)-CH_2-CH_2-(CO)-O), 17.1 (Ar-CH_3). HRMS (ESI) calcd for (M+H) $C_{14}H_{19}N_2O_4$: 279.1339. Found: 279.1336.

Compound **1i** was obtained by an alternative procedure: Compound **3i** (20 mg, 0.041 mmol) was dissolved in trifluoroacetic acid and 50 equivalents of thioanisole were slowly added. The mixture was stirred vigorously for 3 hours at room temperature and subsequently the solvents were removed *in vacuo*. CH_2Cl_2 was added and the mixture was evaporated *in vacuo* (3 × 1 mL) to remove any residual TFA. The crude was washed with cyclohexane (2 × 1 mL) and dried *in vacuo* (the flask was heated to 50 °C in a airbath to facilitate evaporation of any residual thioanisole). The crude product was purified by recrystallization from CH_2Cl_2 to yield 15 mg of **1i** (98%) as a white solid. Rf 0.10 (9:1 CH_2Cl_2-MeOH); ^{1}H-NMR ($CDCl_3$, CD_3OD 9:1): 7.41 (d, 1H, J 8.6 Hz, Ar), 7.37 (d, 1H, J 1.9 Hz, Ar), 7.32 (dd, 1H, J 8.6; 2.2 Hz, Ar), 4.73 (s, 2H, O-CH_2-(CO)), 3.96 (s, 2H, NH_2-CH_2-(CO)), 2.89-2.80 (m, 4H, (CO)-CH_2-CH_2-(CO)-O, (CO)-CH_2-CH_2-(CO)-O), 2.24 (s, 3H, Ar-CH_3). ^{13}C-NMR ($CDCl_3$, CD_3OD 9:1): 201.5 (C=O ketone), 171.7 ((C=O)-O), 166.3 ((C=O)-NH); 134.0, 133.6, 133.3, 129.4, 126.2, 119.3 (Ar); 62.9 (O-CH_2-(CO)), 46.9 (NH_2-CH_2-(CO)); 34.2, 27.4 ((CO)-CH_2-CH_2-(CO)-O, (CO)-CH_2-CH_2-(CO)-O); 17.2 (Ar-CH3). HRMS (ESI) calcd for (M+H) $C_{14}H_{18}N_2BrO_4$: 357.0450 Found: 357.0447.

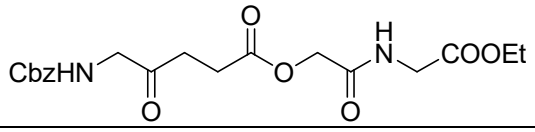
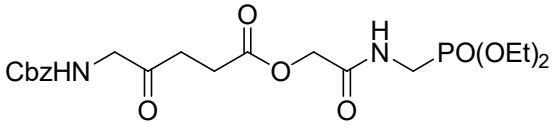
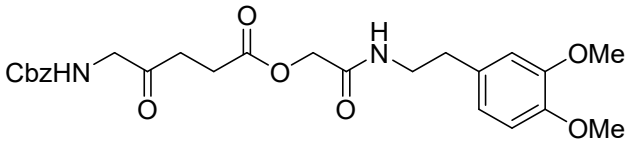
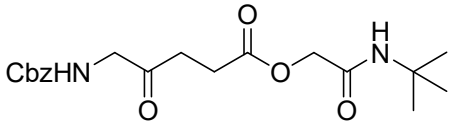
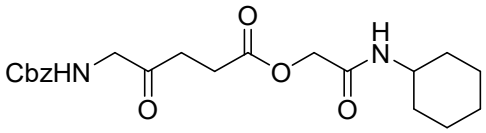
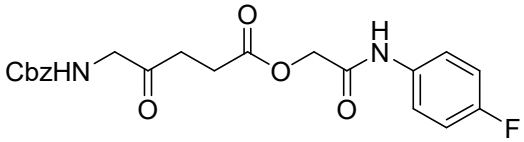
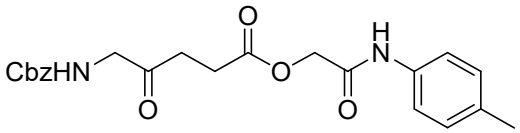
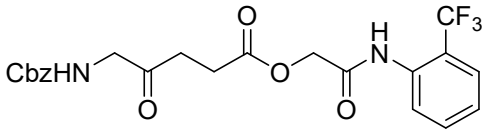
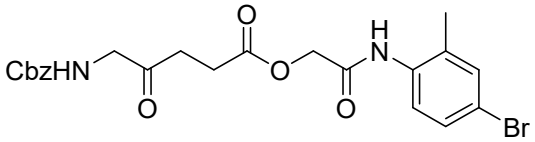
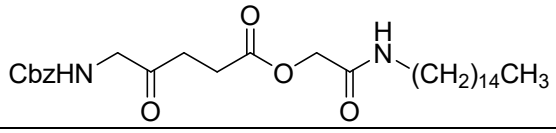
Compound	Structure	logD (pH = 7.4)
3a		0.19
3b		1.07
3c		1.91
3d		1.26
3e		2.01
3f		3.22
3g		3.29
3h		2.71
3i		4.50
3j		6.42

Table S1. Structures of the CBz-protected esters of ALA with their estimated logD.

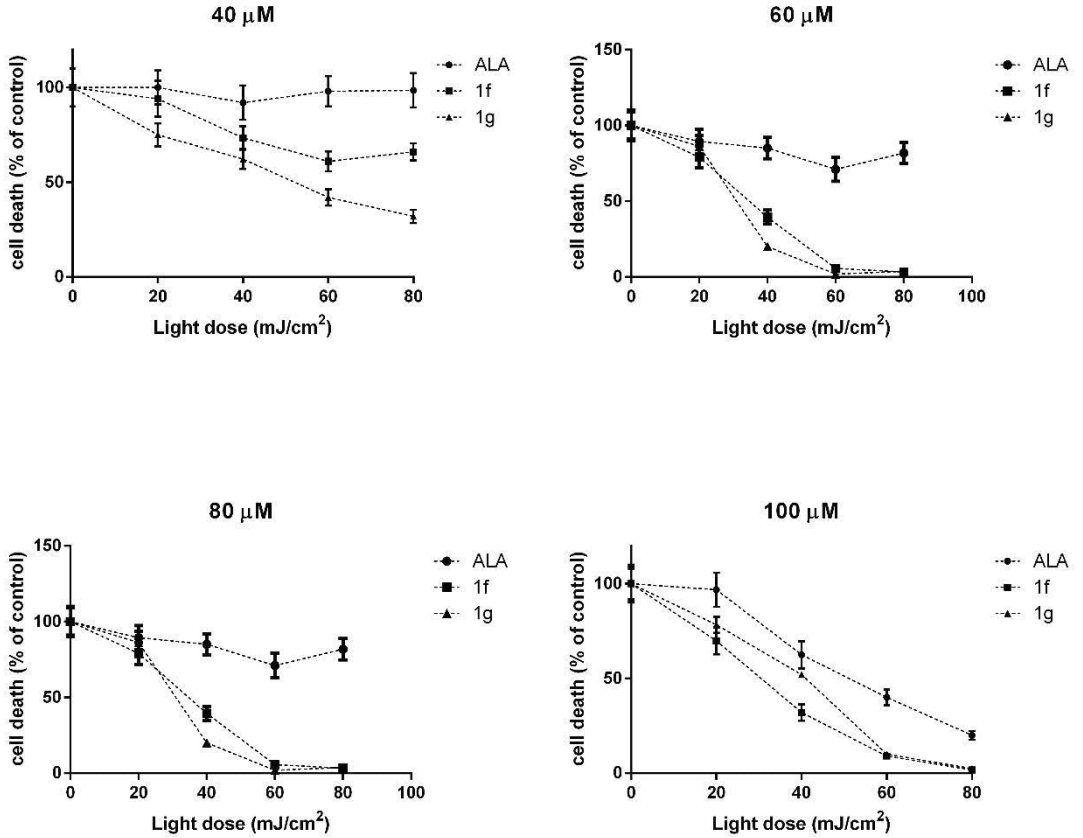
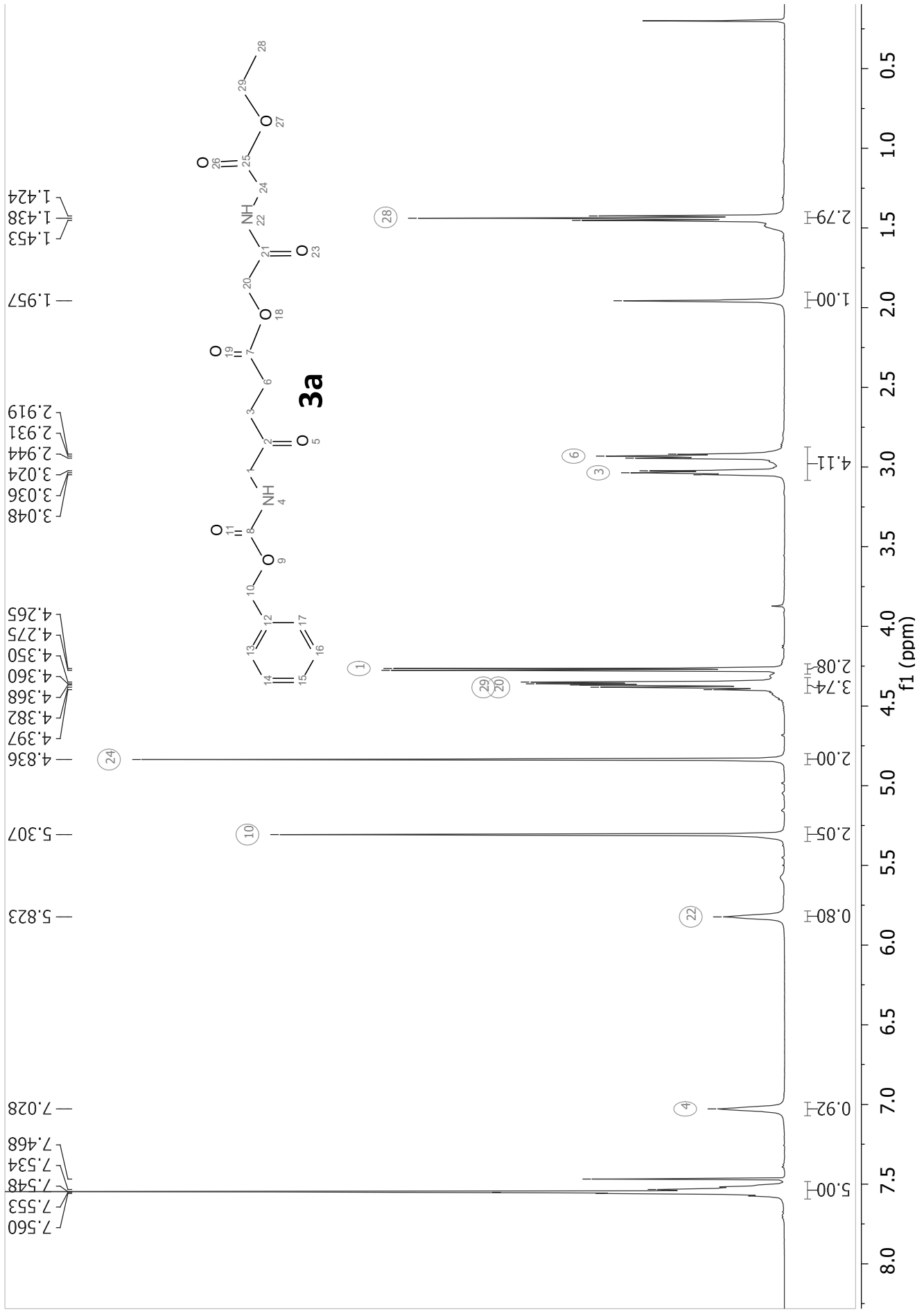
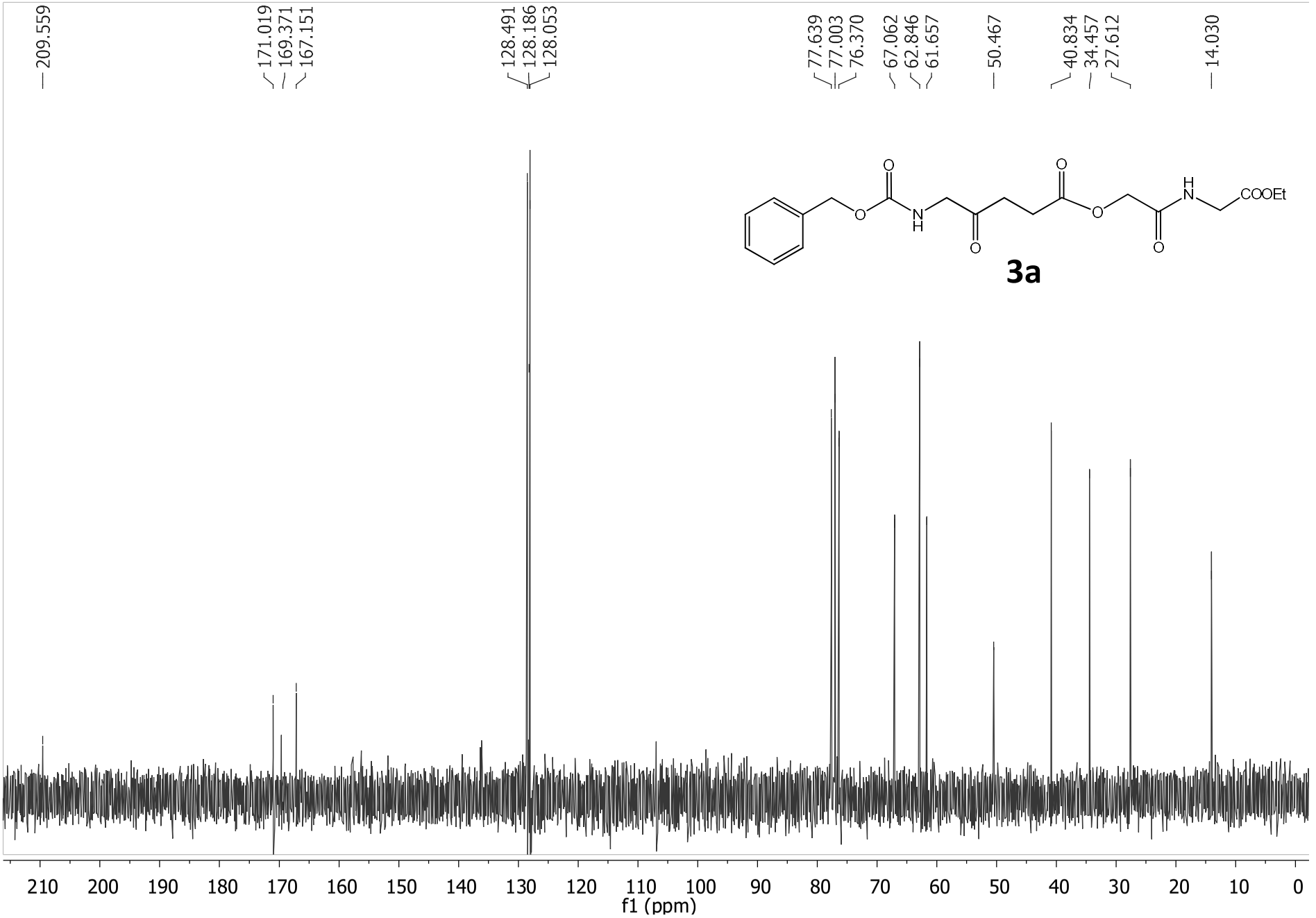


Figure S1. Cell survival after photodynamic treatment for compounds **1f** and **1g**. LM2 cells were incubated with different concentrations of the compounds during 3 h. Afterwards, PDT was performed, and cell viability was evaluated by the MTT assay, as percentage of control non-irradiated cells.

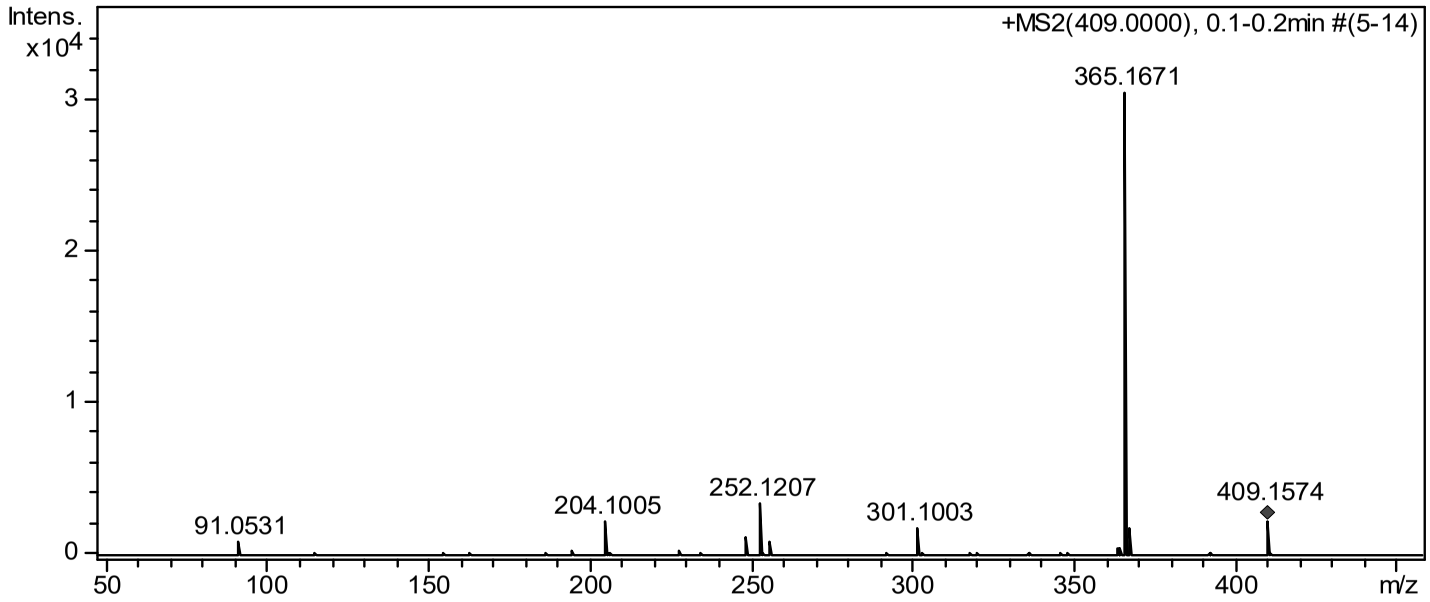
^{1}H-NRM (500 MHz) of compound 2-(2-ethoxy-2-oxoethylamino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3a**)



^{13}C-NRM (50,3 MHz) of compound **3a**

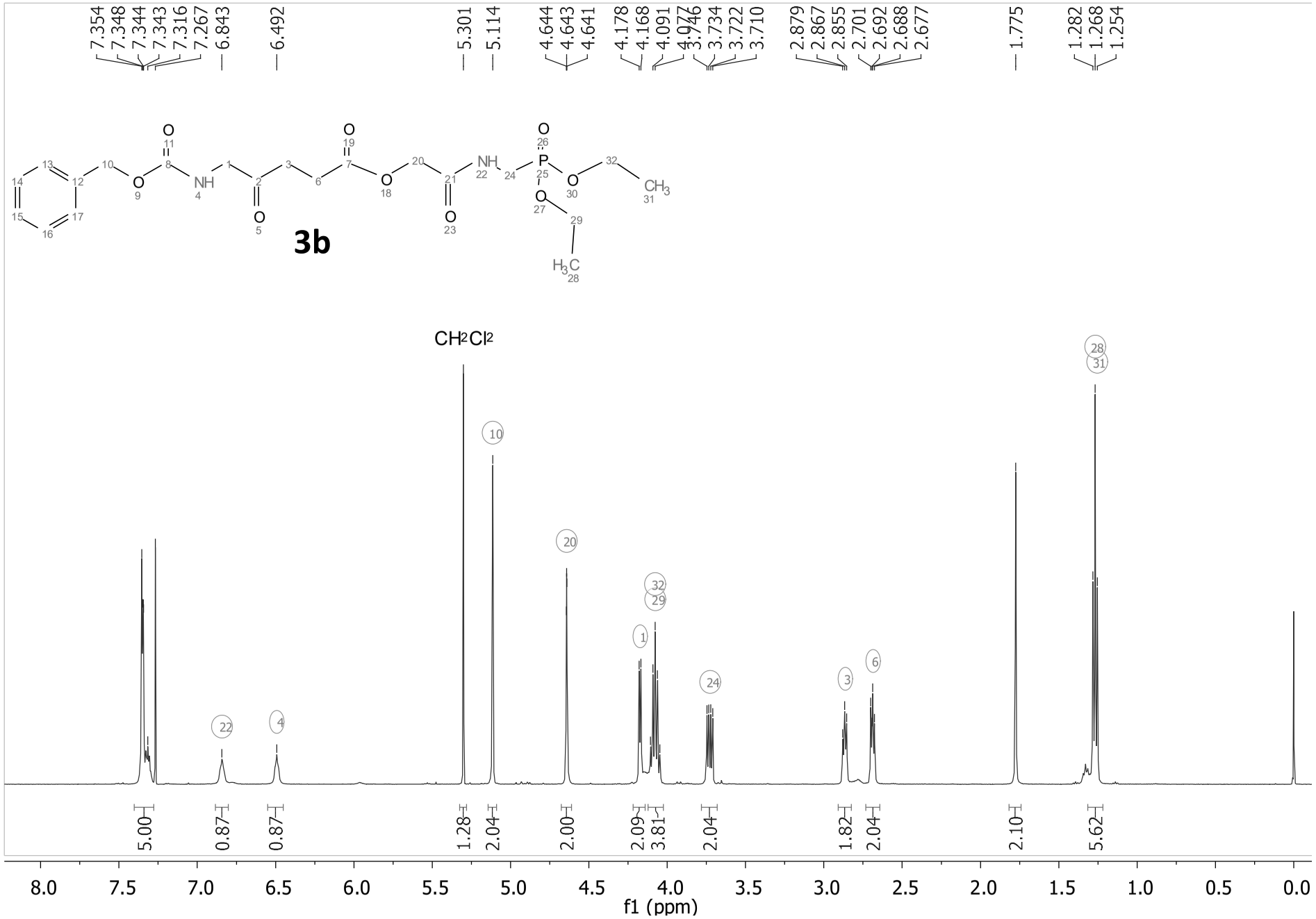


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3a** (collision Energy 10 eV)

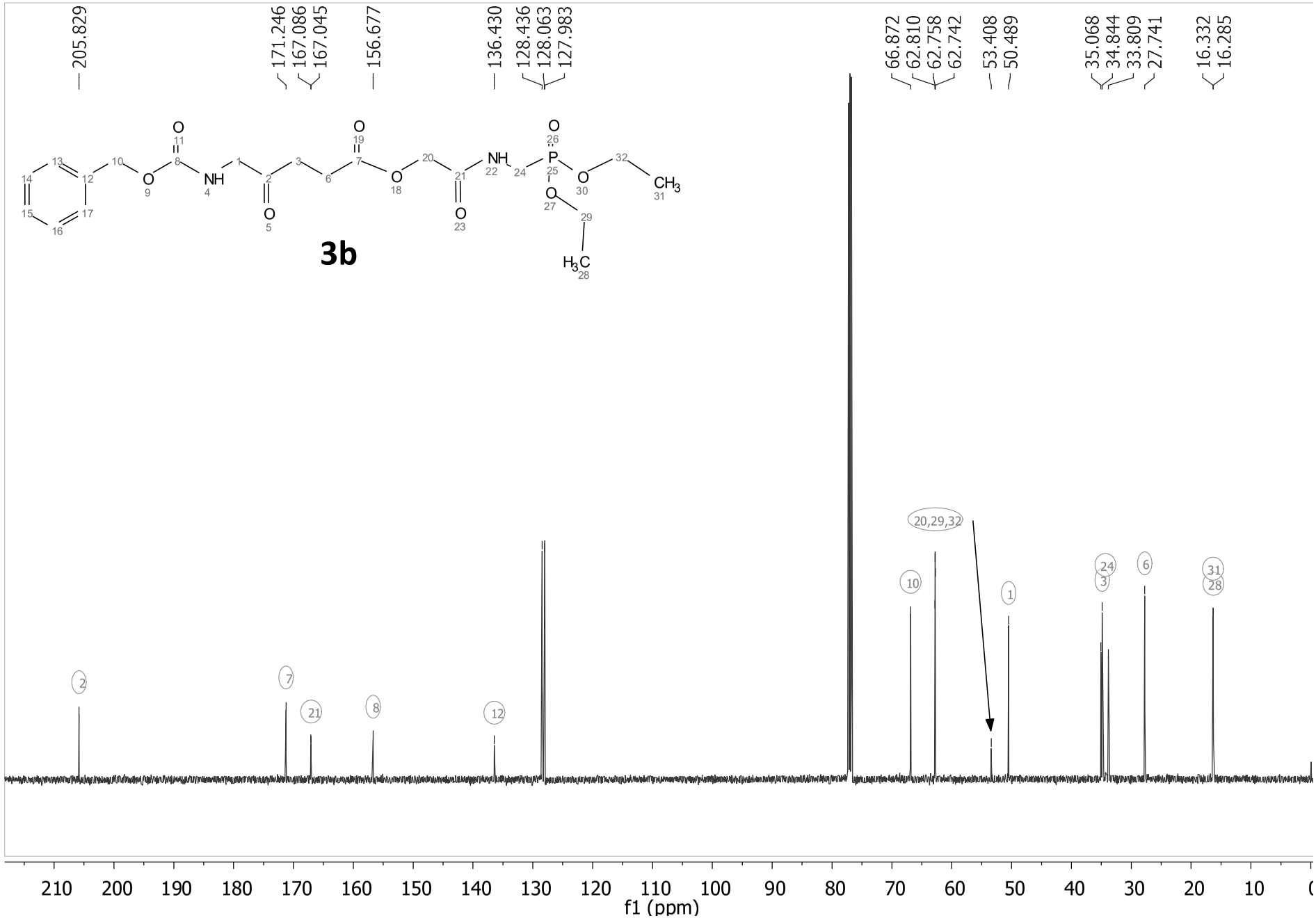


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$	Conf	
204.1005	C 12 H 14 N O 2	204.1019	6.9	6.5	ok	even	id Cy	
252.1207	C 13 H 18 N O 4	252.1230	9.3	5.5	ok	even		
301.1003	C 12 H 17 N 2 O 7	301.1030	8.9	5.5	ok	even	[M+H-BnOH]$^+$	
365.1671	C 18 H 25 N 2 O 6	365.1707	9.8	7.5	ok	even	[M+H-CO_2]$^+$	
409.1574	C 19 H 25 N 2 O 8	409.1605	7.7	8.5	ok	even	[M+H]$^+$	

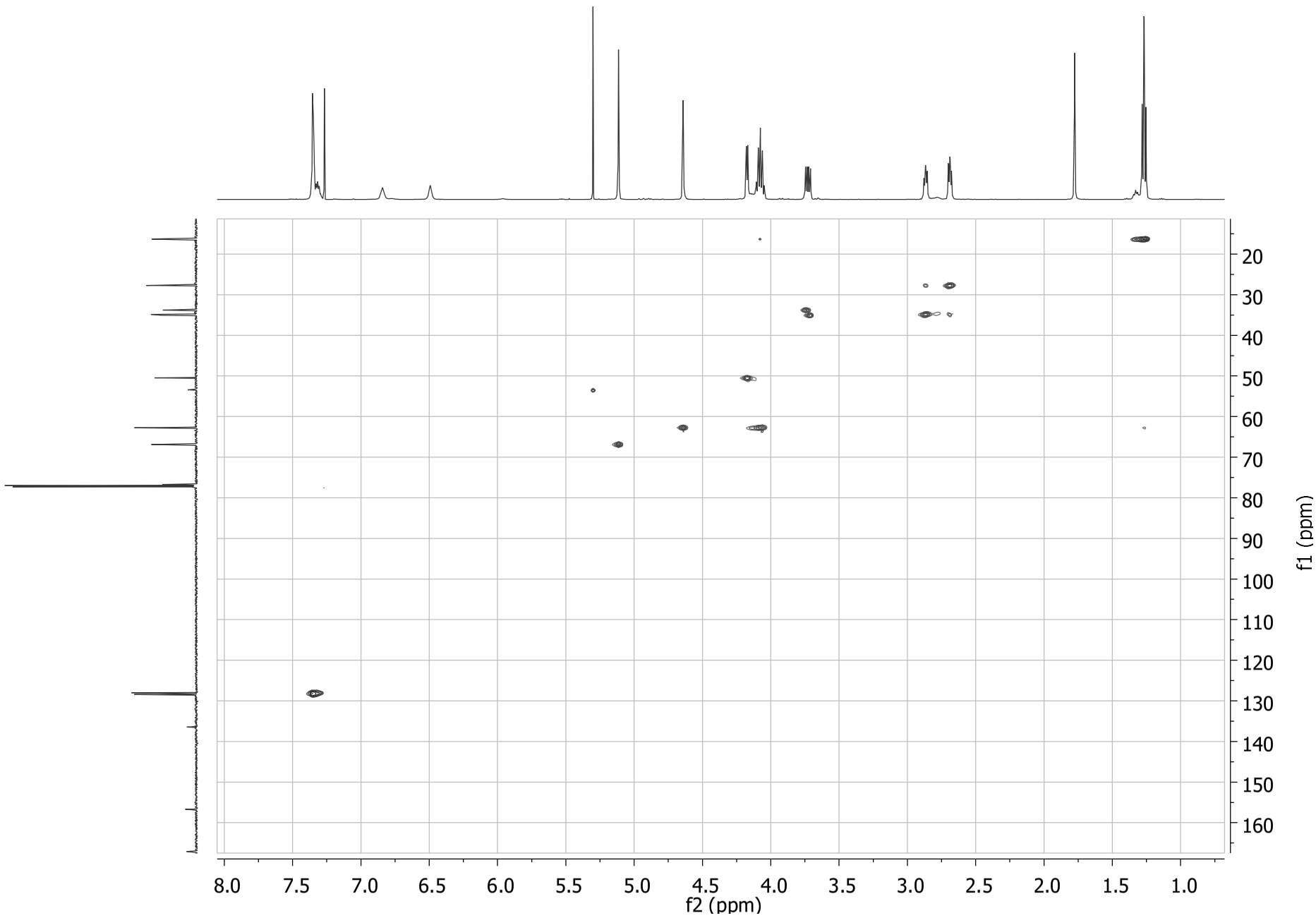
^{1}H-NRM (500 MHz) of compound 2-(diethoxyphosphorylmethylamino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3b**)



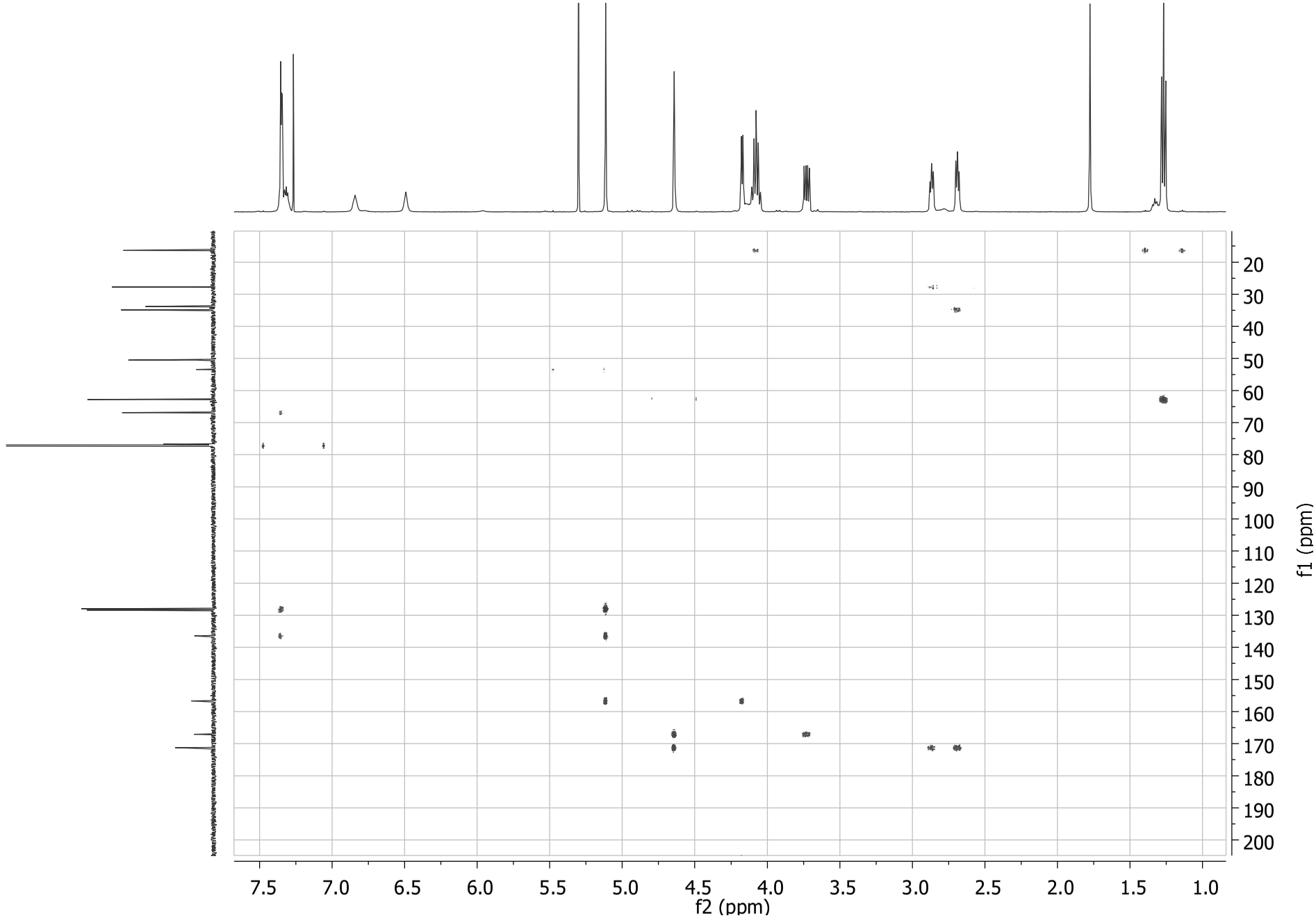
^{13}C-NRM (125,7 MHz) of compound **3b**



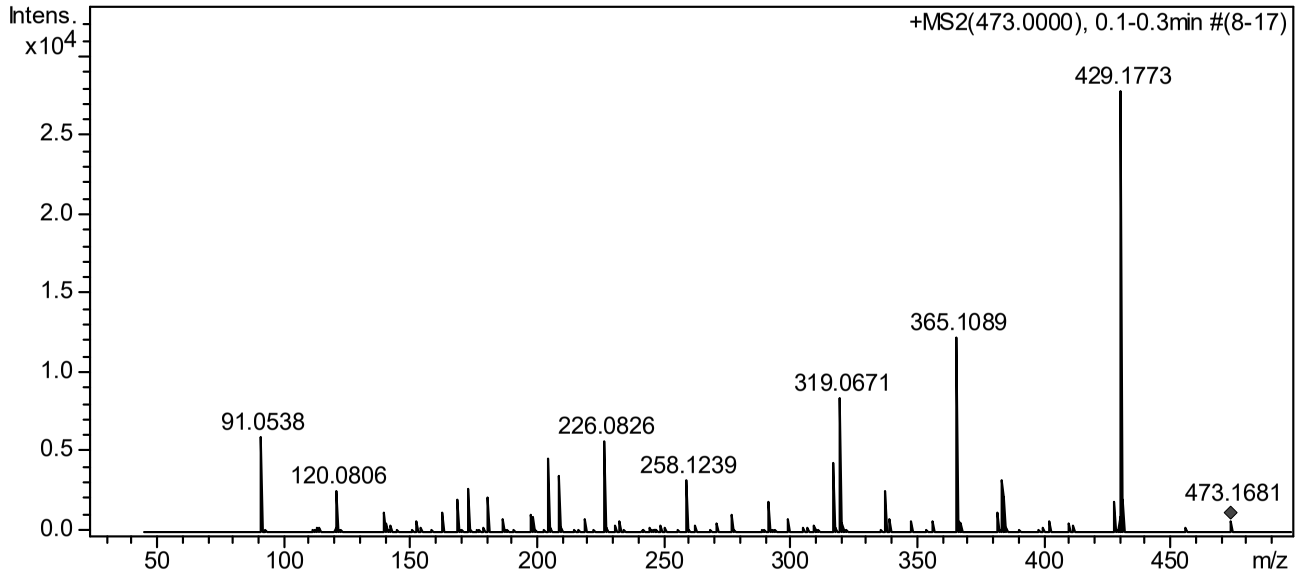
HSQC-DEPT (500 MHz) of compound **3b**



HMBC (500 MHz) of compound **3b**

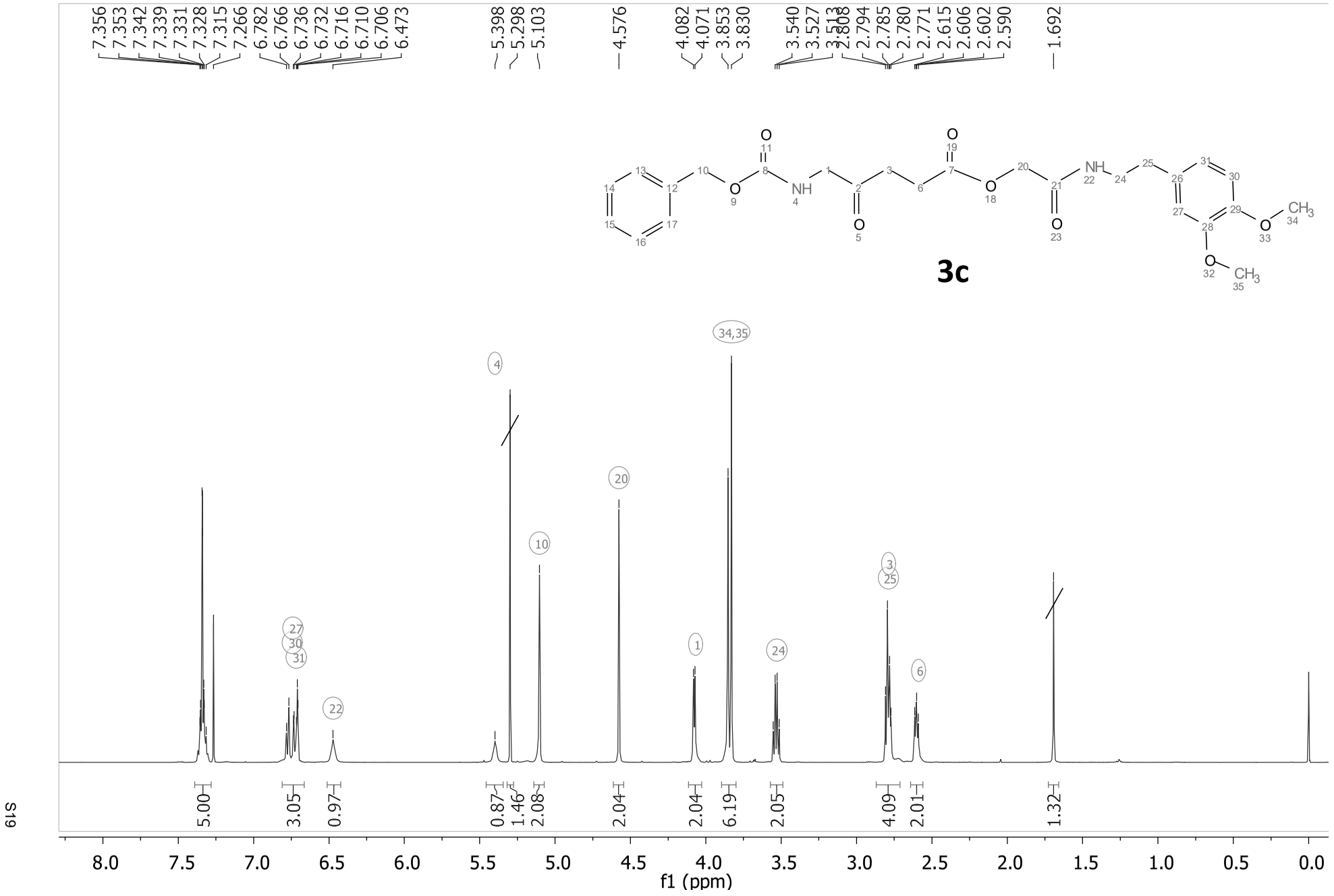


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3b** (collision Energy 10 eV)

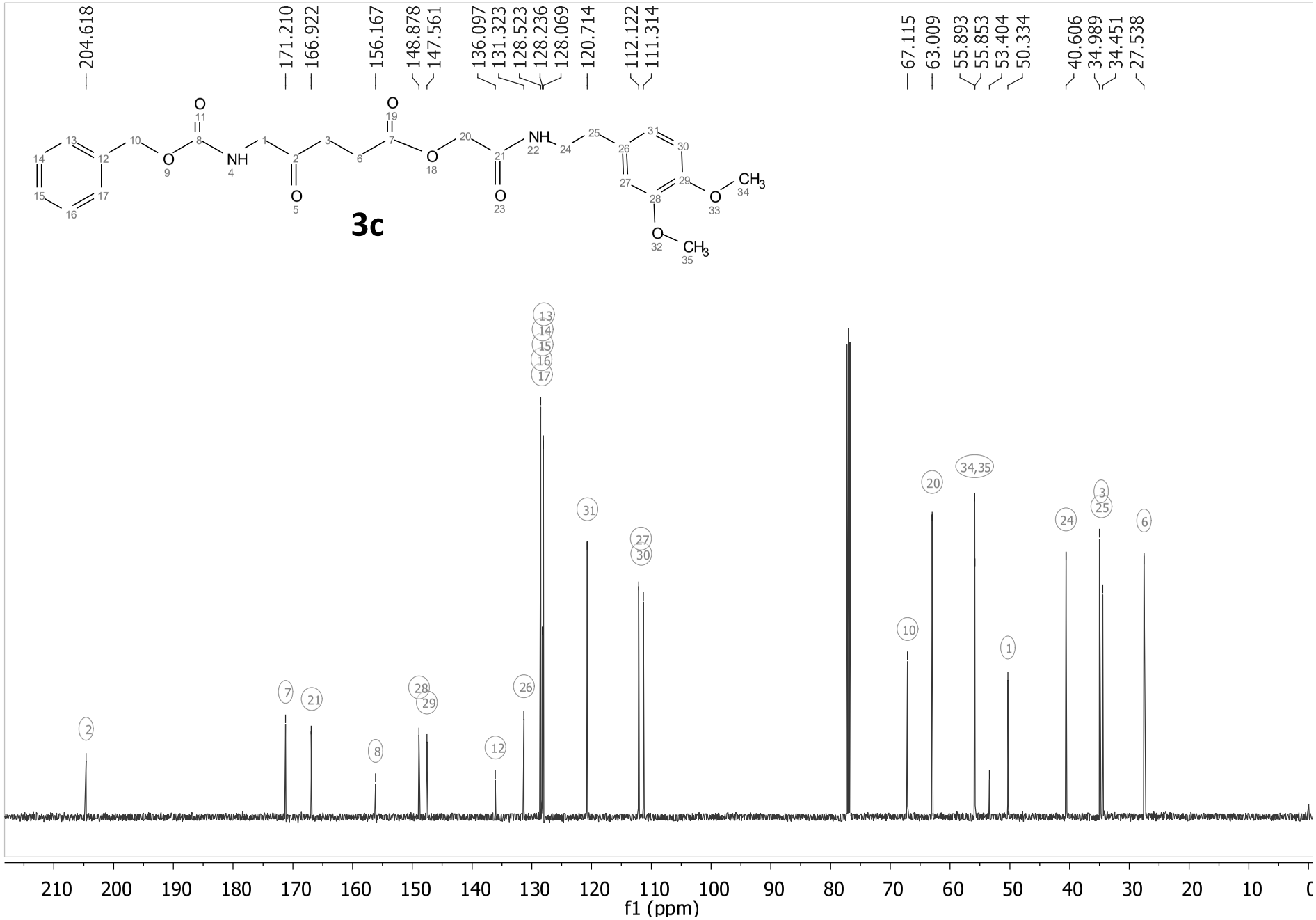


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$	Conf	
91.0538	C 7 H 7		91.0542	4.8	4.5	ok	even	trop$^+$
204.1012	C 12 H 14 N O 2		204.1019	3.4	6.5	ok	even	id anteriores
208.0715	C 7 H 15 N O 4 P		208.0733	8.9	1.5	ok	even	ruptura CO-O→-H_2O
226.0826	C 7 H 17 N O 5 P		226.0839	5.6	0.5	ok	even	ruptura CO-O→
319.0671	C 11 H 16 N 2 O 7 P		319.0690	5.9	5.5	ok	even	[M+H- EtOH-BnOH]$^+$
365.1089	C 13 H 22 N 2 O 8 P		365.1108	5.3	4.5	ok	even	[M+H-BnOH]$^+$
383.1346	C 17 H 24 N 2 O 6 P		383.1366	5.2	7.5	ok	even	[M+H- CO_2- EtOH]$^+$
429.1773	C 19 H 30 N 2 O 7 P		429.1785	2.7	6.5	ok	even	[M+H- CO_2]$^+$

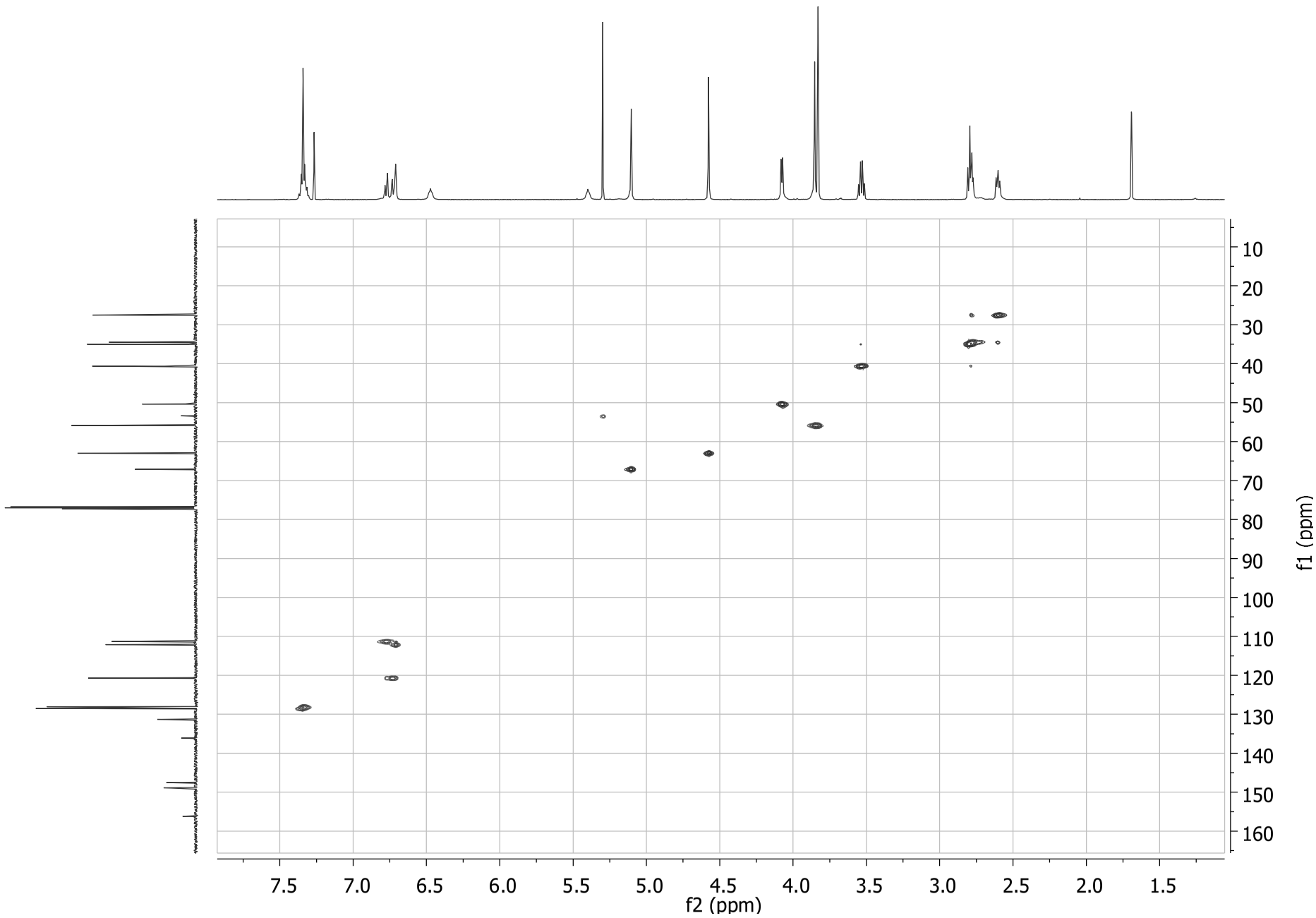
^{1}H-NRM (500 MHz) of compound 2-(3,4-dimethoxyphenethylamino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3c**)



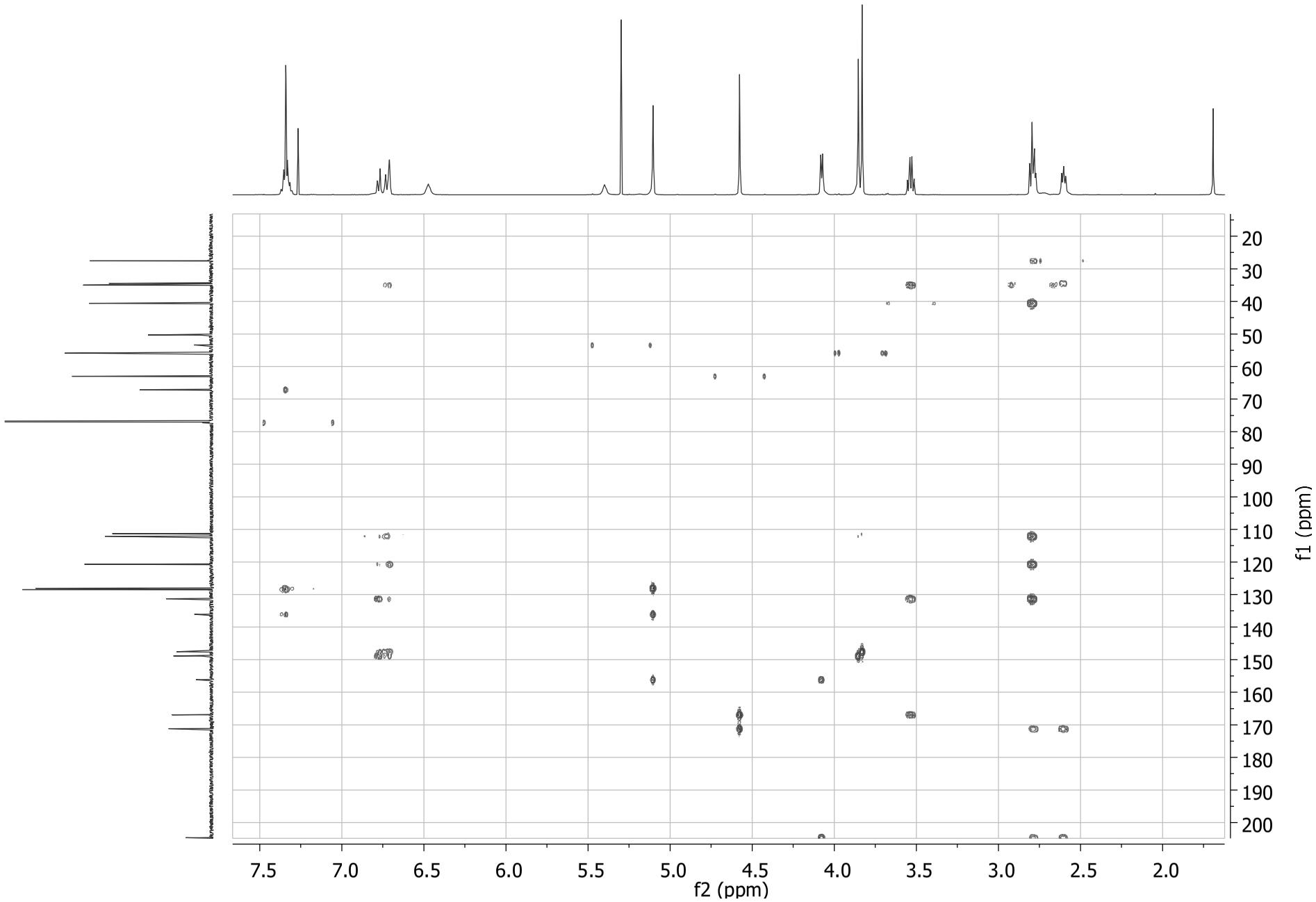
^{13}C-NRM (125,7 MHz) of compound **3c**



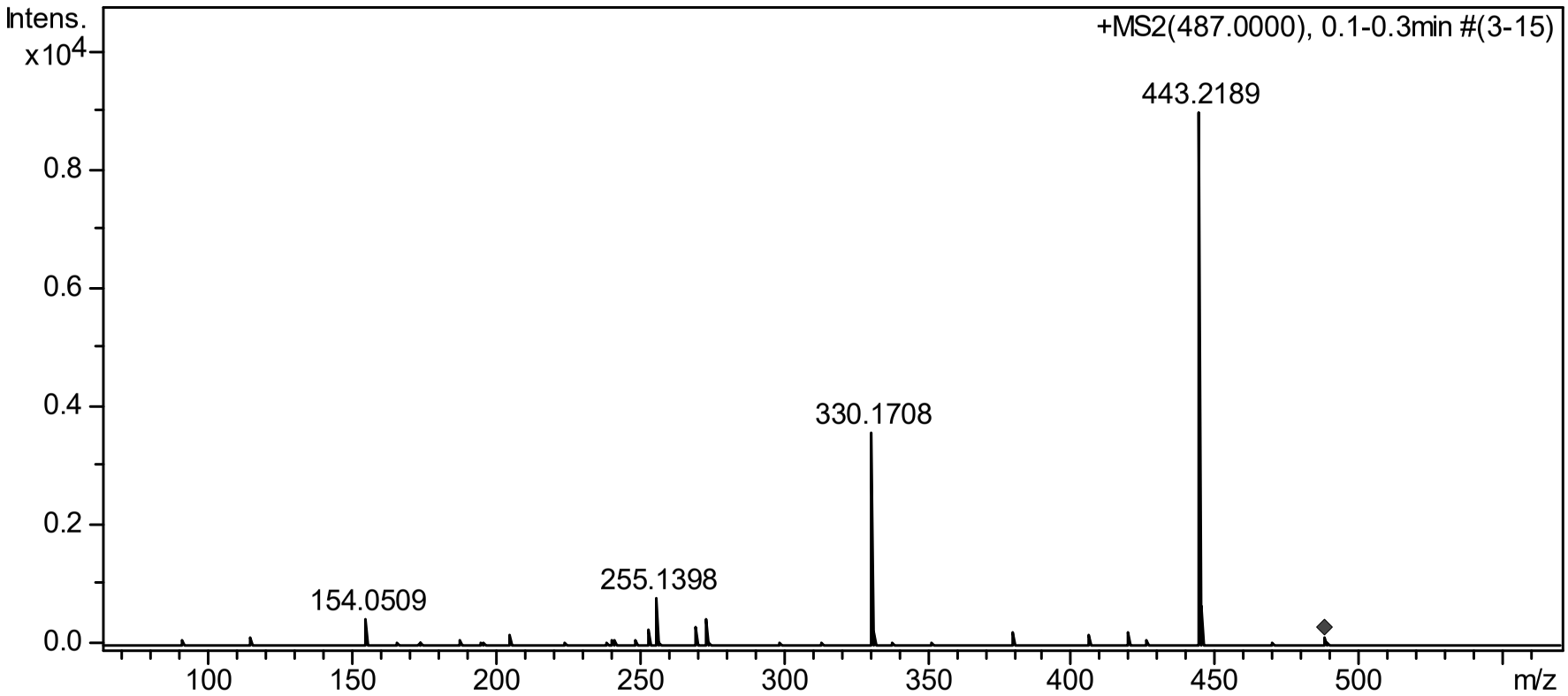
HSQC-DEPT (500 MHz) of compound **3c**



HMBC (500 MHz) of compound **3c**

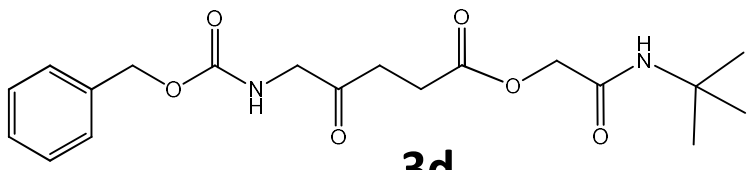


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3c** (collision Energy 10 eV)



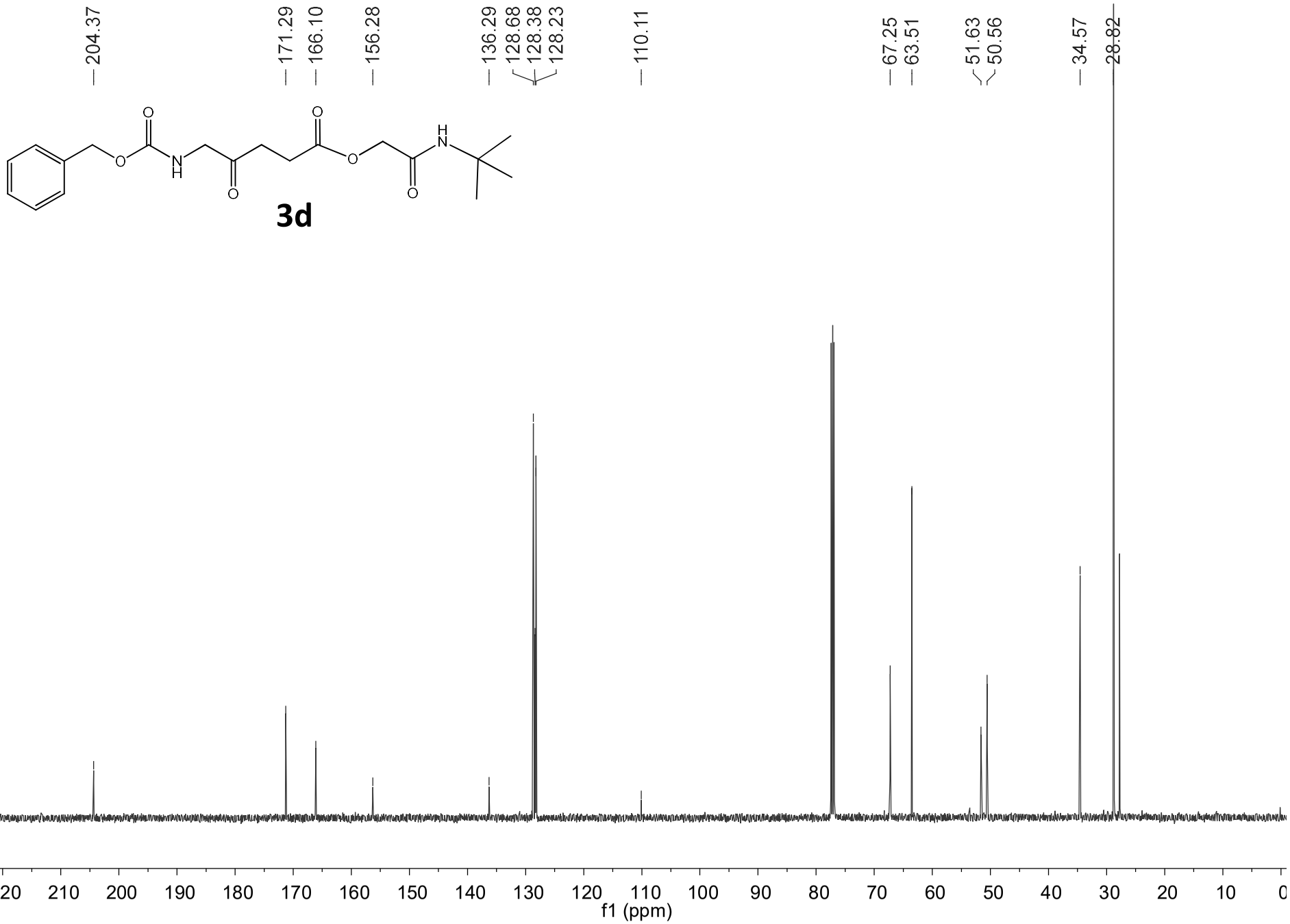
Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	
330.1708	C 19 H 24 N O 4	330.1700	-2.5	8.5	ok	even	
443.2189	C 24 H 31 N 2 O 6	443.2177	-2.7	10.5	ok	even	$[M+H-CO_2]^+$

^{1}H-NRM (500 MHz) of compound 2-(*t*-butylamino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3d**)

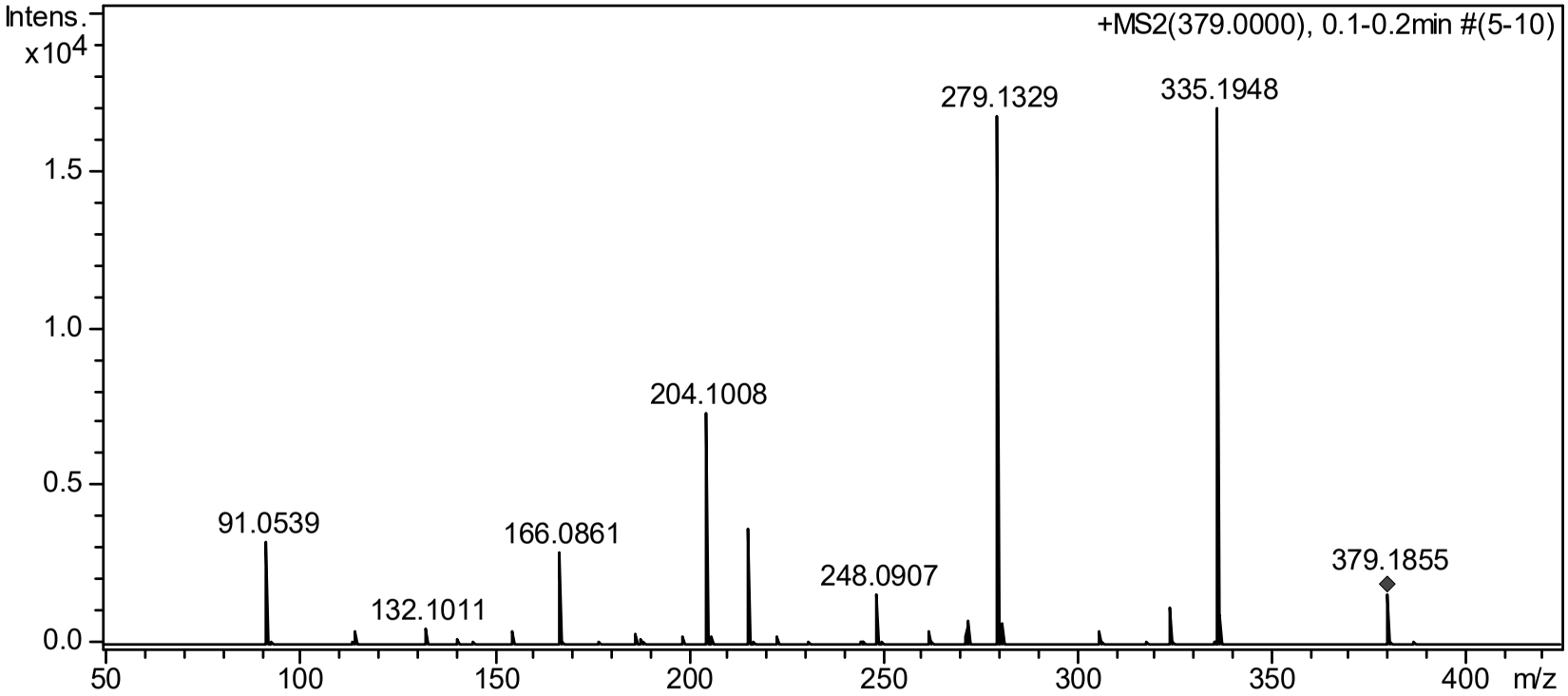


3d

^{13}C-NRM (125,7 MHz) of compound **3d**

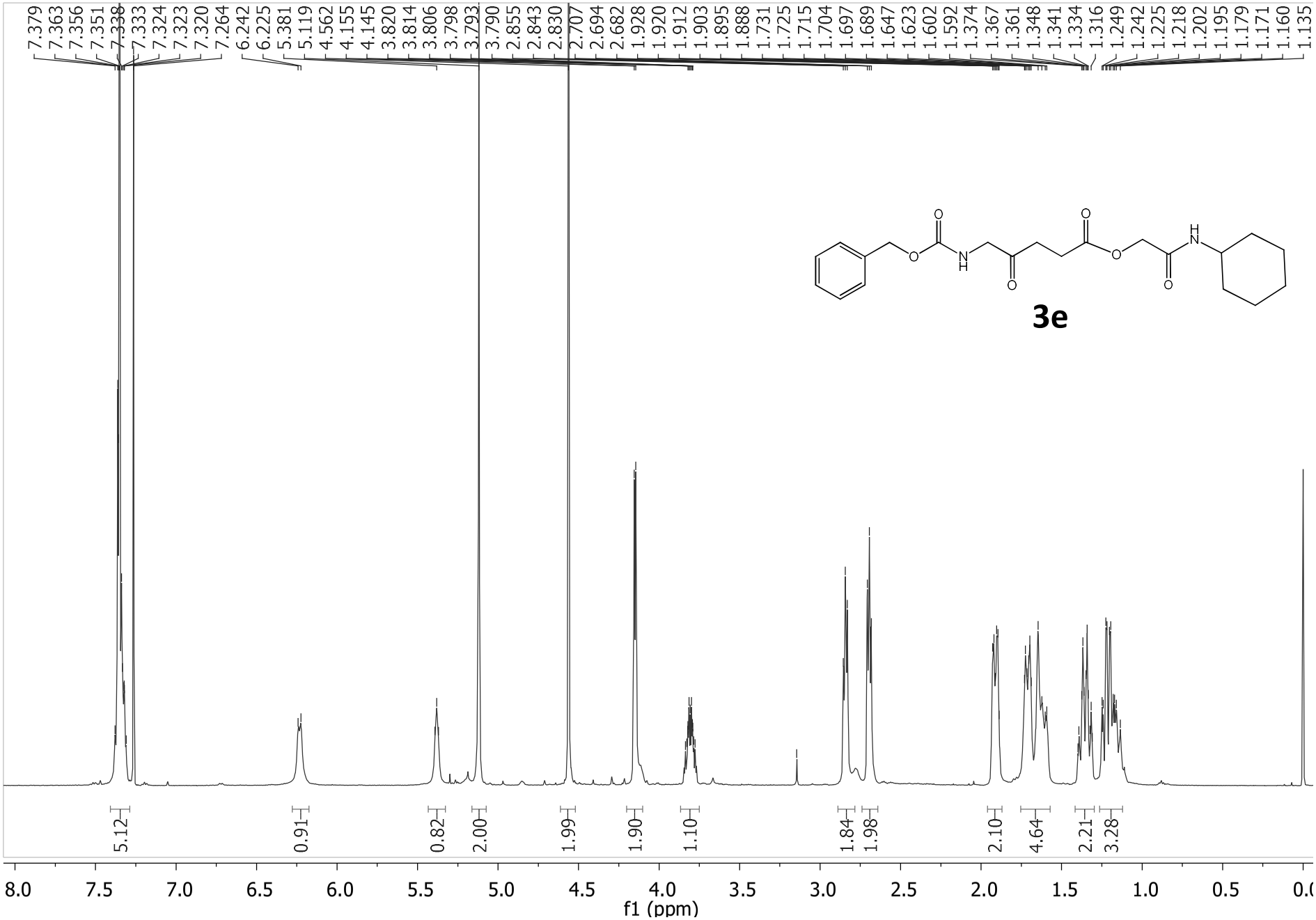


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3d** (collision Energy 10 eV)



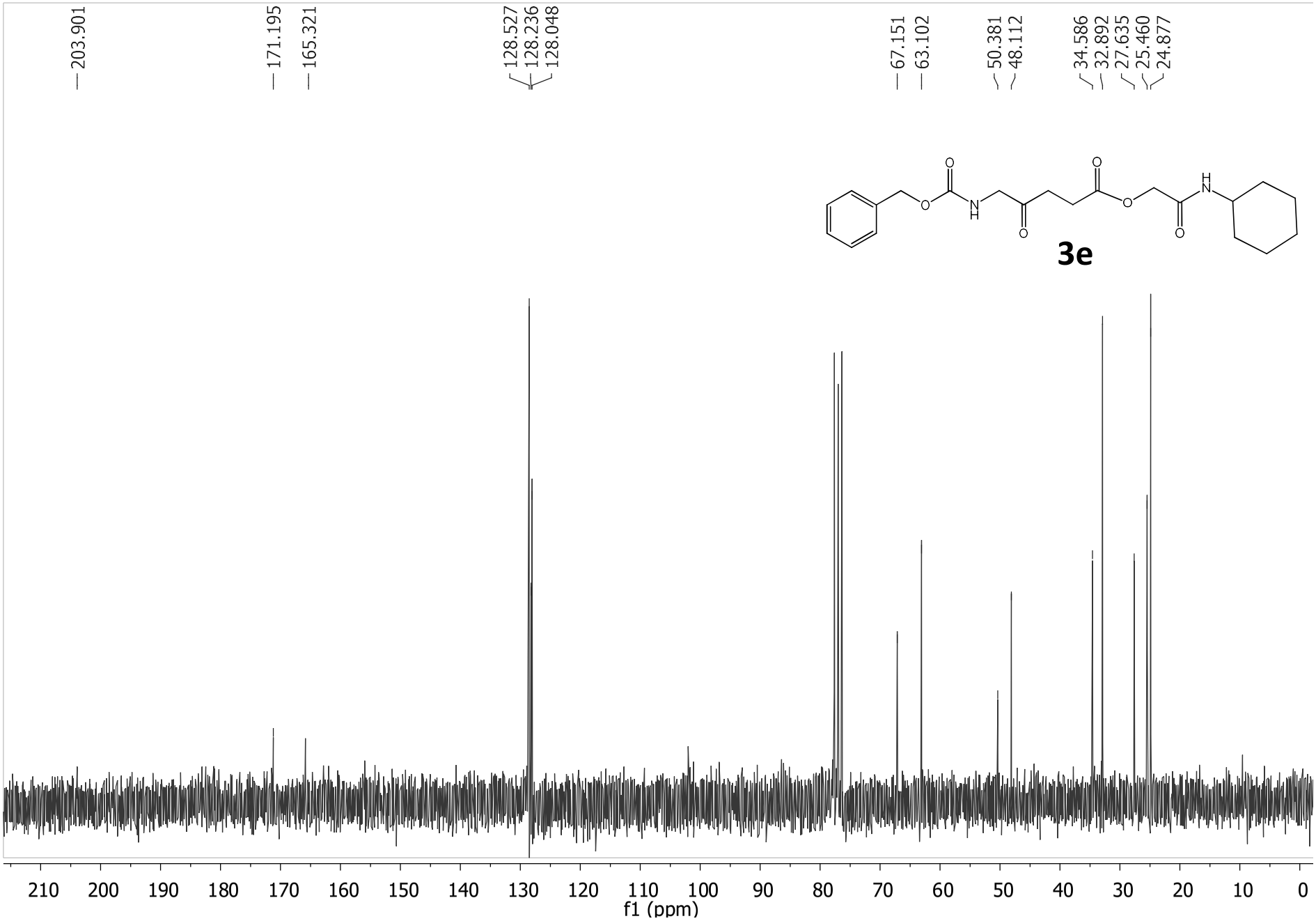
Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	
91.0539	C 7 H 7	91.0542	3.9	4.5	ok	even	trop$^+$
166.0861	C 9 H 12 N O 2	166.0863	0.9	4.5	ok	even	ruptura CO
204.1008	C 12 H 14 N O 2	204.1019	5.2	6.5	ok	even	id anteriores
215.0652	C 8 H 11 N 2 O 5	215.0662	4.9	4.5	ok	even	[M+H-BnOH-propeno]$^+$
279.1329	C 14 H 19 N 2 O 4	279.1339	3.6	6.5	ok	even	[M+H-CO_2-propeno]$^+$
335.1948	C 18 H 27 N 2 O 4	335.1965	5.1	6.5	ok	even	[M+H-CO_2]$^+$

^{1}H-NRM (500 MHz) of compound 2-(cyclohexylamino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3e**)

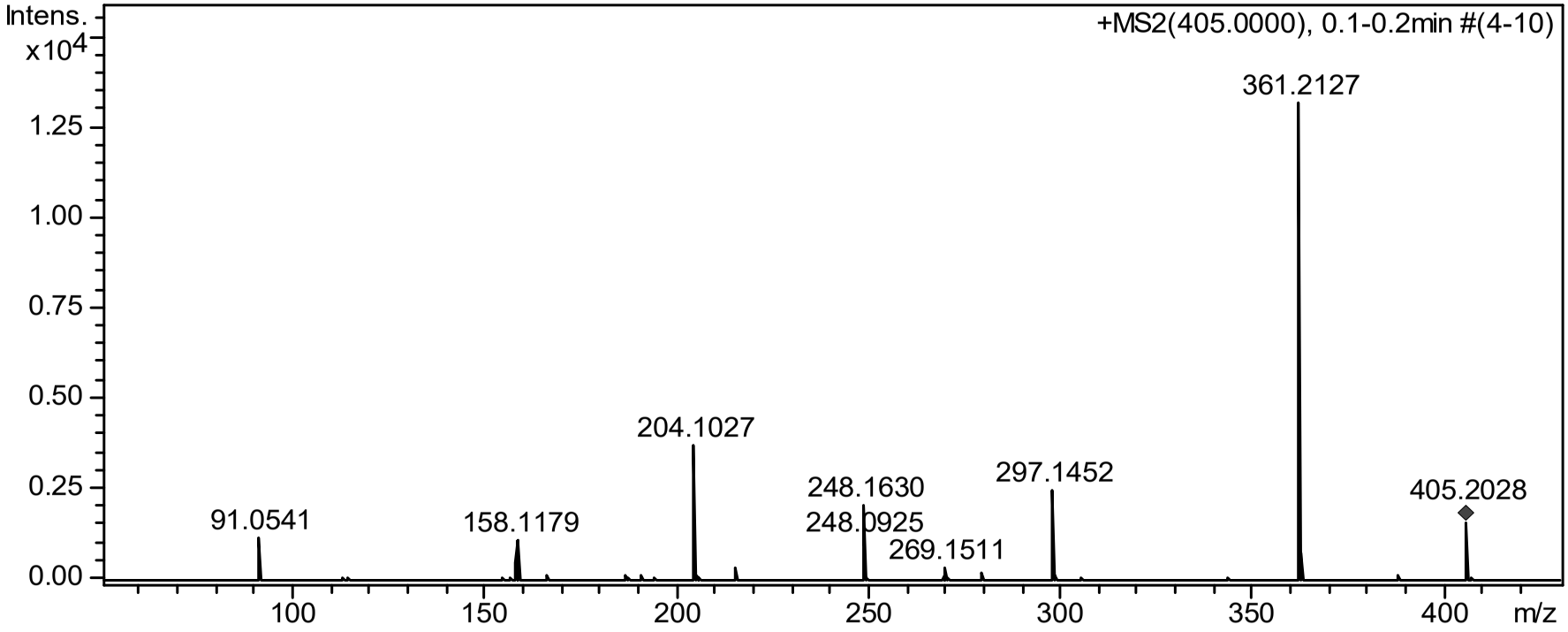


3e

^{13}C-NRM (50,3 MHz) of compound **3e**

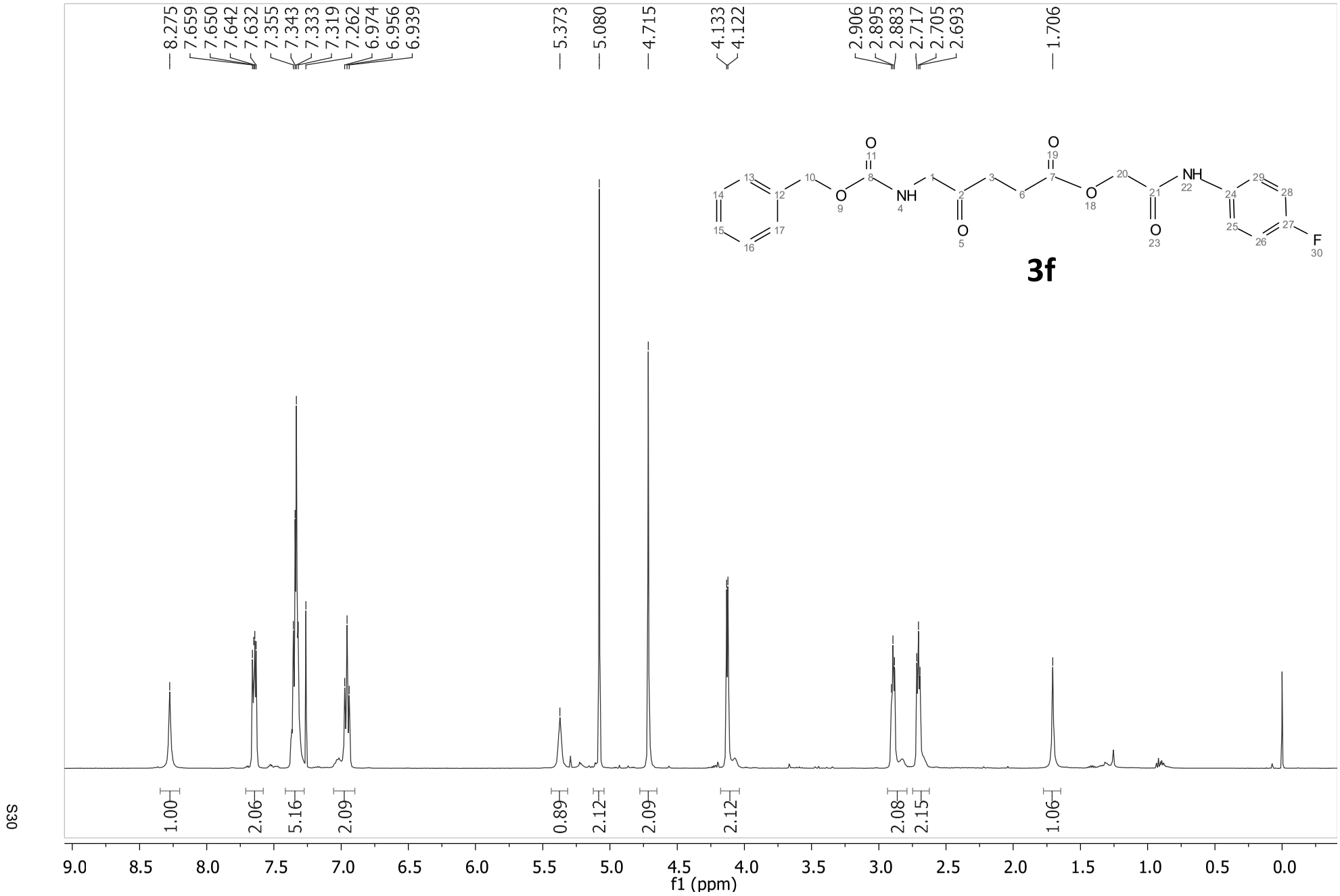


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3e** (collision Energy 10 eV)

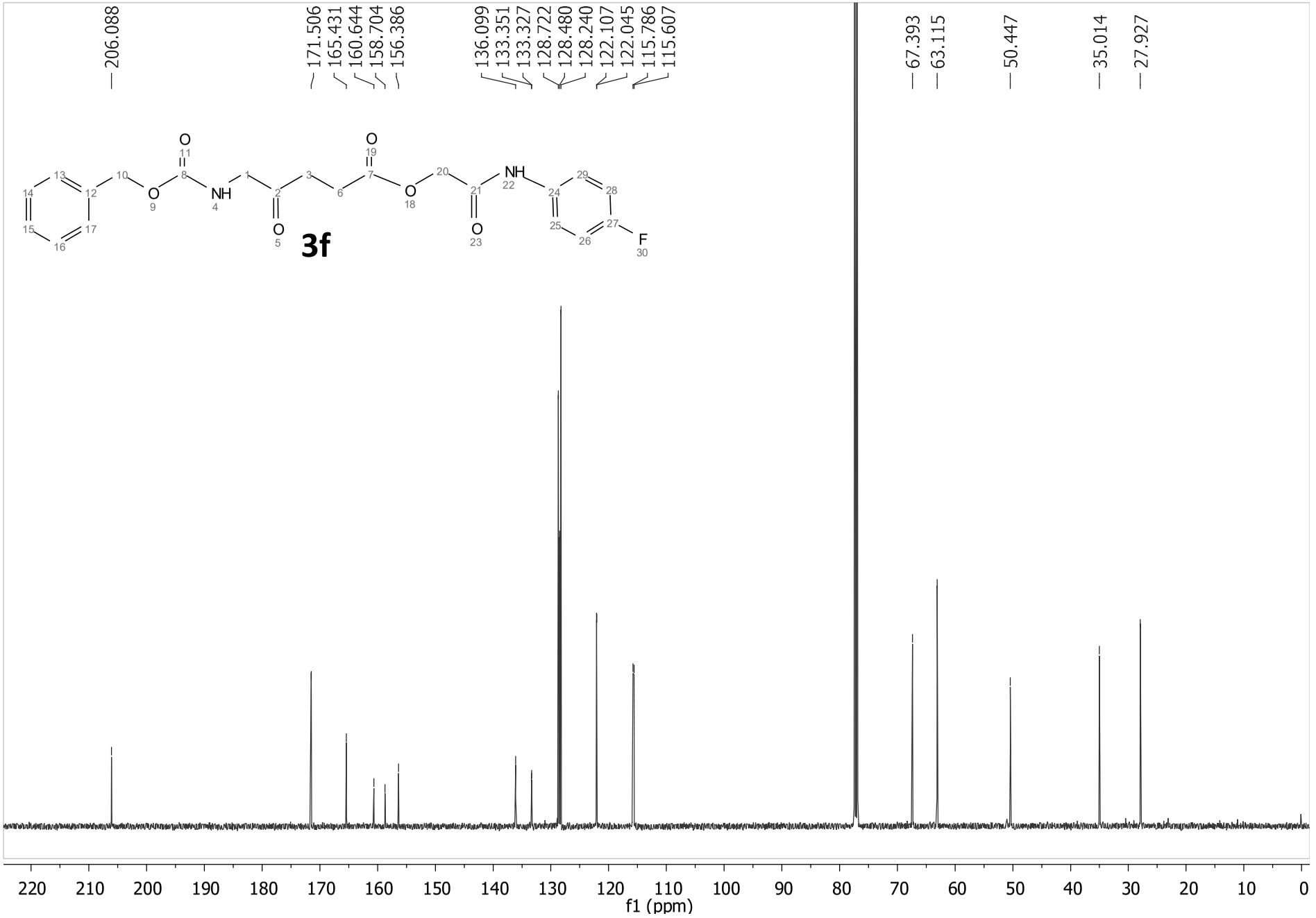


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	
91.0541	C 7 H 7	91.0542	1.3	4.5	ok	even	trop$^+$
158.1179	C 8 H 16 N O 2	158.1176	-2.2	1.5	ok	even	ruptura CO-O→
204.1027	C 12 H 14 N O 2	204.1019	-4.1	6.5	ok	even	m/z 248 – CO_2
248.0925	C13H14NO4	248.0917	3.2				ruptura CO-O←
269.1511	C 13 H 21 N 2 O 4	269.1496	-5.8	4.5	ok	even	[M+H-BnOH-CO]$^+$
297.1452	C 14 H 21 N 2 O 5	297.1445	-2.4	5.5	ok	even	[M+H-BnOH]$^+$
361.2127	C 20 H 29 N 2 O 4	361.2122	-1.3	7.5	ok	even	[M+H-CO_2]$^+$
405.2028	C 21 H 29 N 2 O 6	405.2020	-1.9	8.5	ok	even	[M+H]$^+$

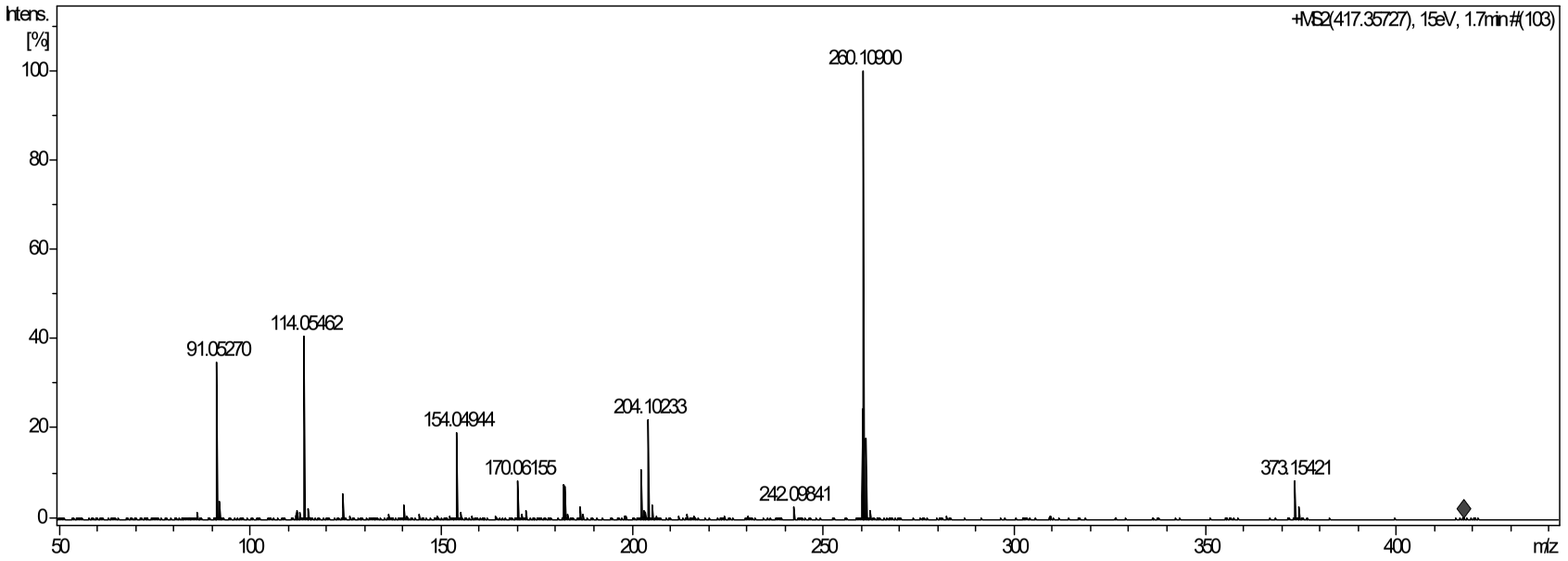
^{1}H-NRM (500 MHz) of compound 2-((4-fluorophenyl)amino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3f**)



^{13}C-NRM (125,7 MHz) of compound **3f**

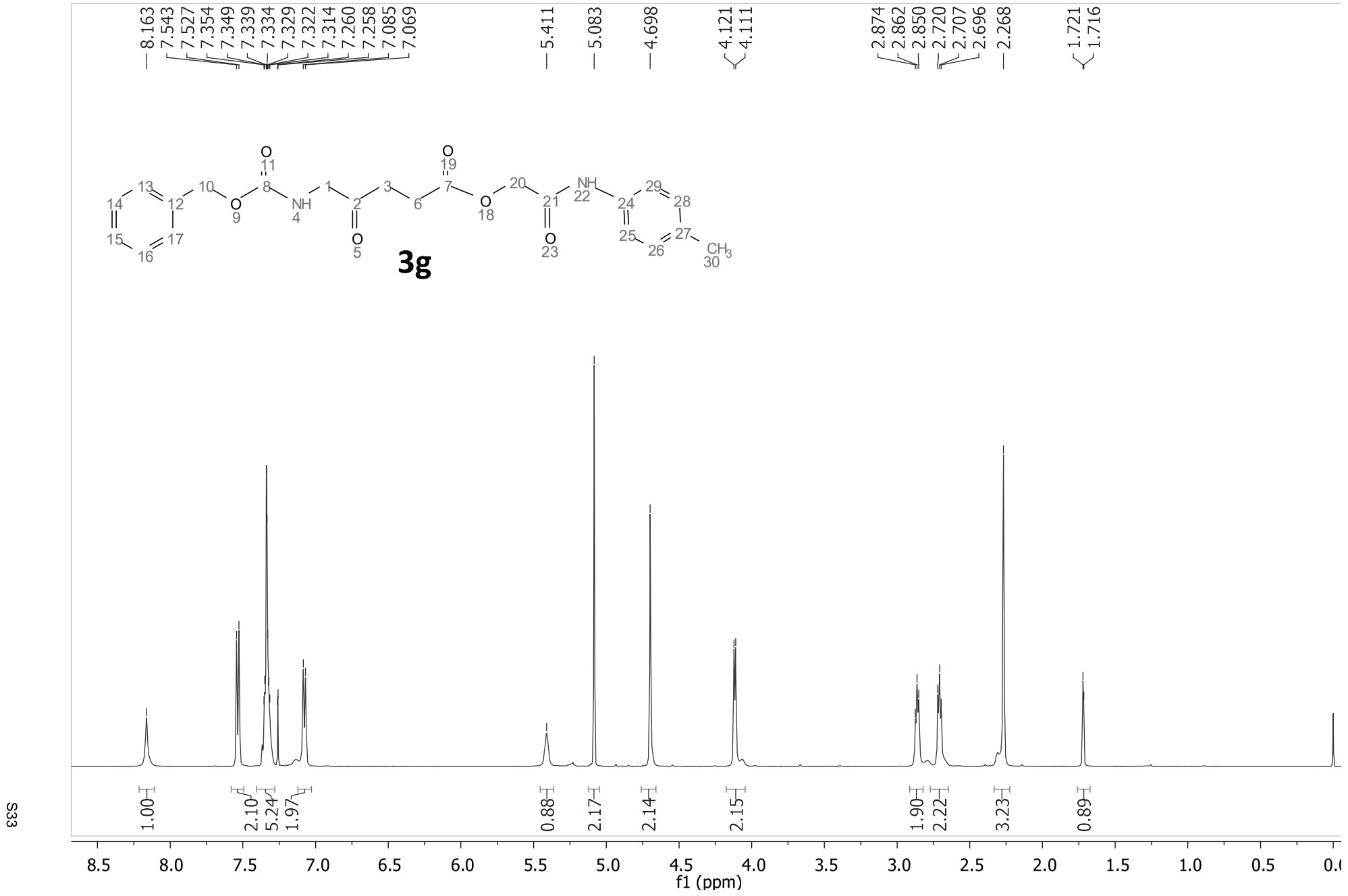


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3f** (collision Energy 10 eV)

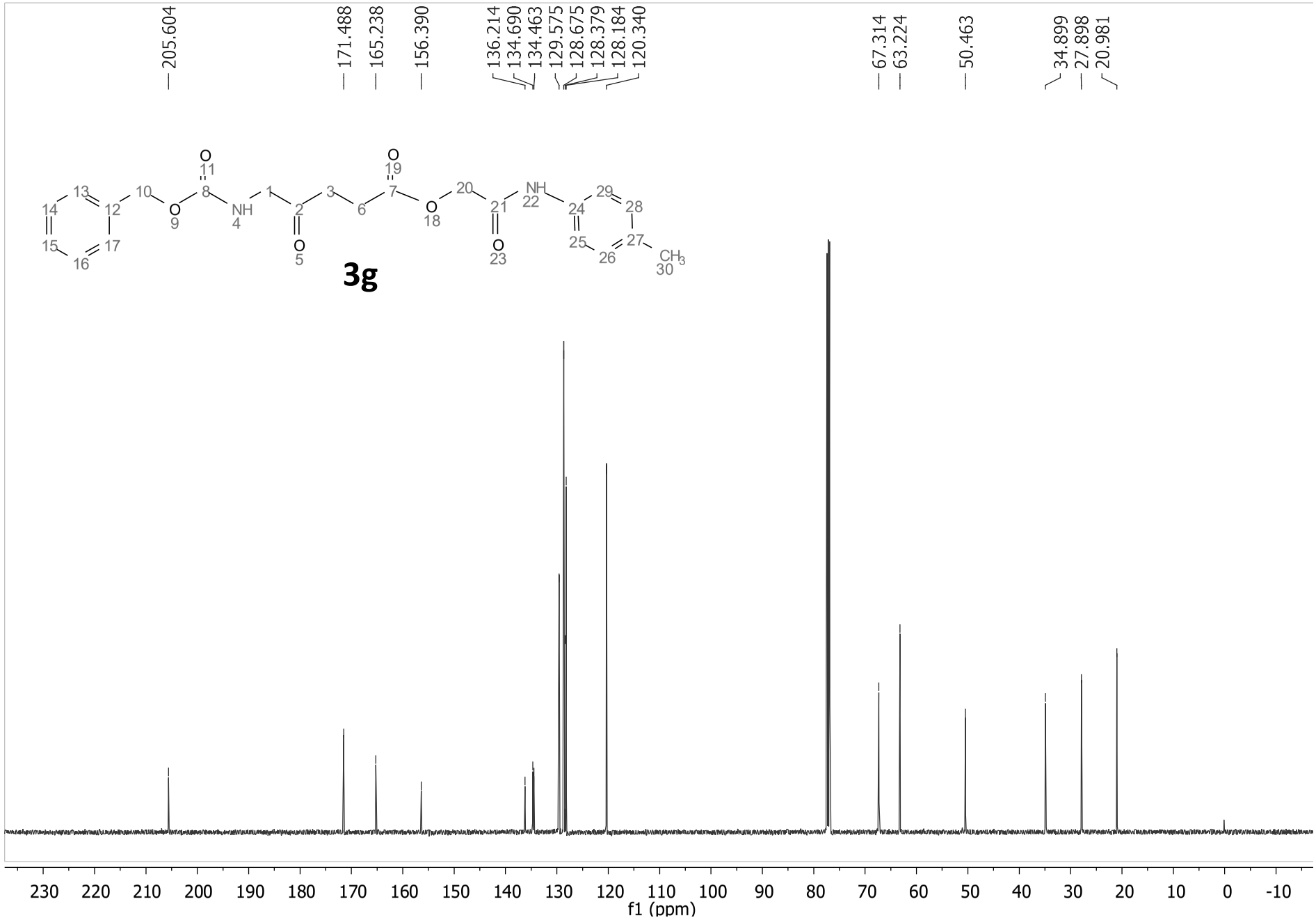


:as. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e¯	Conf	
4.05462	C 5 H 8 N O 2	114.05495	3.0	2.5	ok	even		
4.04944	C 7 H 8 N O 3	154.04987	2.8	4.5	ok	even		
4.10233	C 12 H 14 N O 2	204.10191	-2.1	6.5	ok	even		id ant
0.10900	C 15 H 15 F N O 2	260.10813	-3.3	8.5	ok	even		

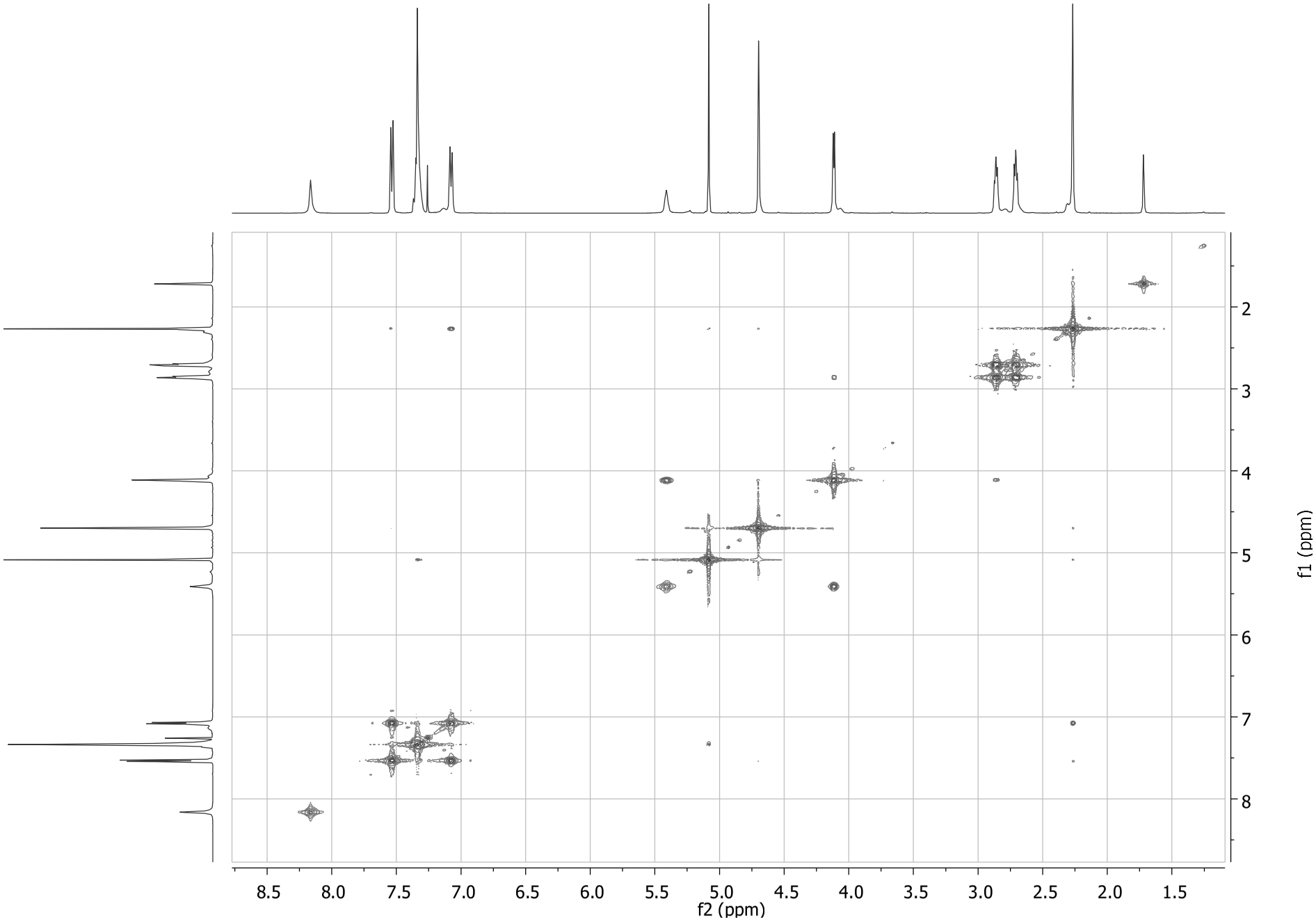
^{1}H-NRM (500 MHz) for compound 2-(4-tolylamino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3g**)



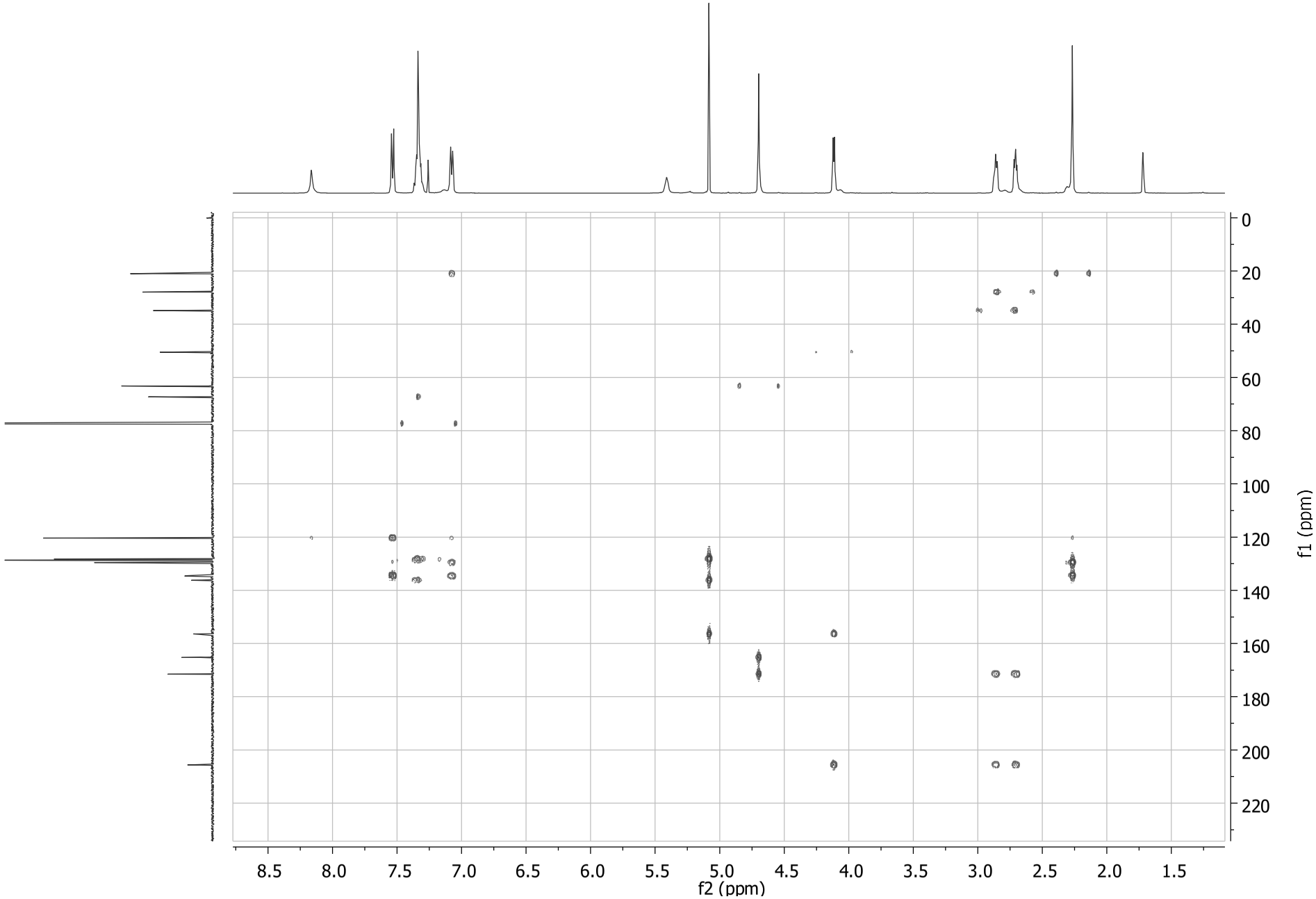
^{13}C-NRM (125,7 MHz) of compound **3g**



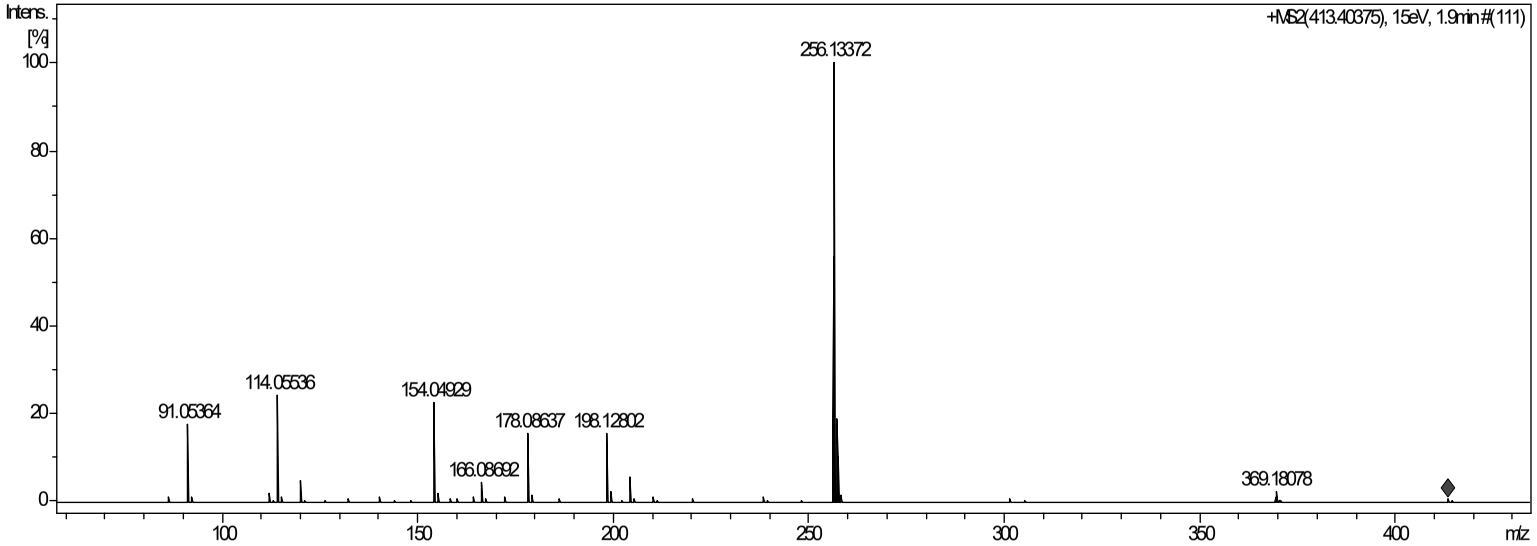
COSY (500 MHz) of compound **3g**



HMBC (500 MHz) of compound **3g**

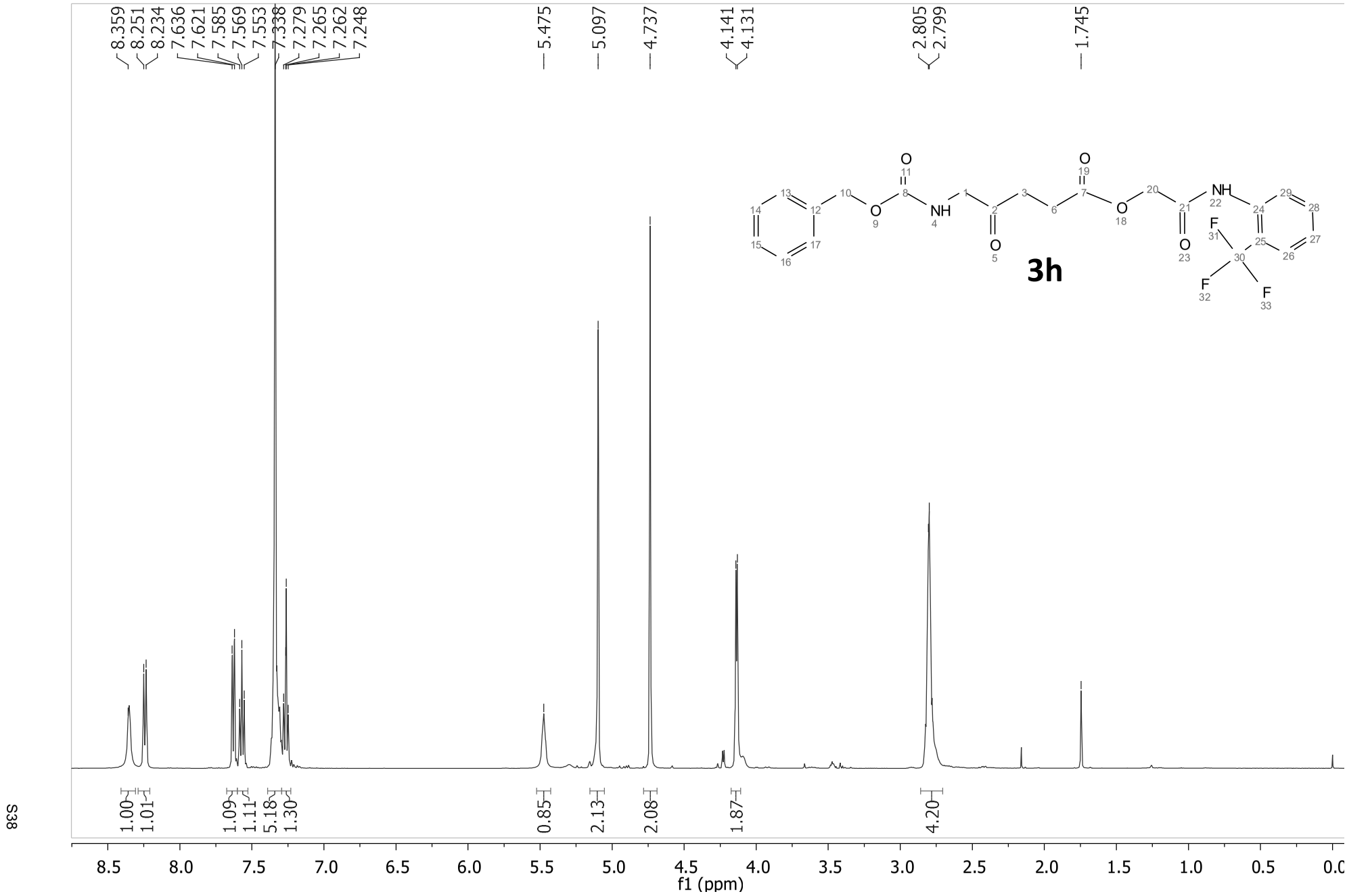


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3g** (collision Energy 10 eV)

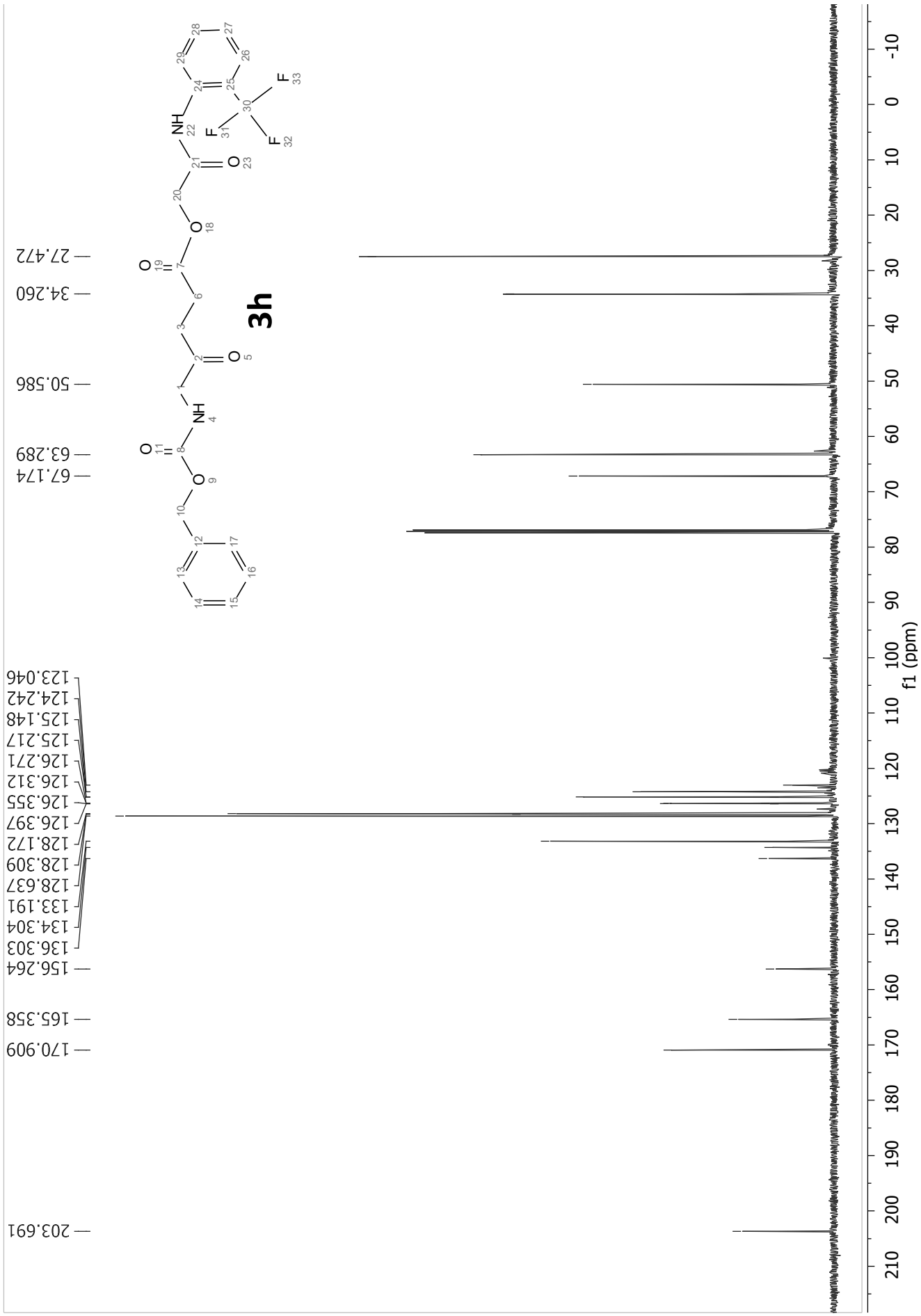


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$	Conf
91.05364	C 7 H 7	91.05423	6.4	4.5	ok	even	
114.05536	C 5 H 8 N O 2	114.05495	-3.5	2.5	ok	even	
154.04929	C 7 H 8 N O 3	154.04987	3.8	4.5	ok	even	X
166.08692	C 9 H 12 N O 2	166.08626	-4.0	4.5	ok	even	α-O Cterm
178.08637	C 10 H 12 N O 2	178.08626	-0.6	5.5	ok	even	
198.12802	C 14 H 16 N	198.12773	-1.5	7.5	ok	even	
204.10108	C 12 H 14 N O 2	204.10191	4.0	6.5	ok	even	369-165
256.13372	C 16 H 18 N O 2	256.13321	-2.0	8.5	ok	even	369-113
369.18078	C 21 H 25 N 2 O 4	369.18088	0.3	10.5	ok	even	-CO2

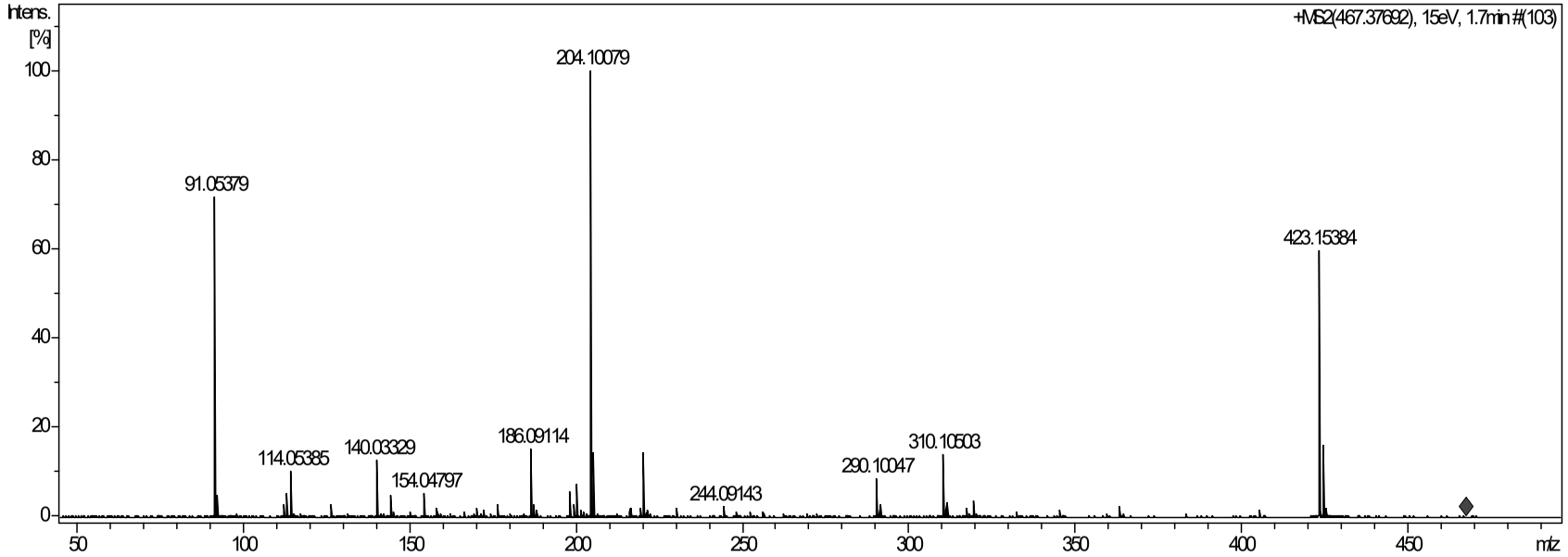
^{1}H-NRM (500 MHz) of compound 2-((2-(trifluoromethyl)phenyl)amino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3h**)



^{13}C-NRM (125,7 MHz) of compound **3h**

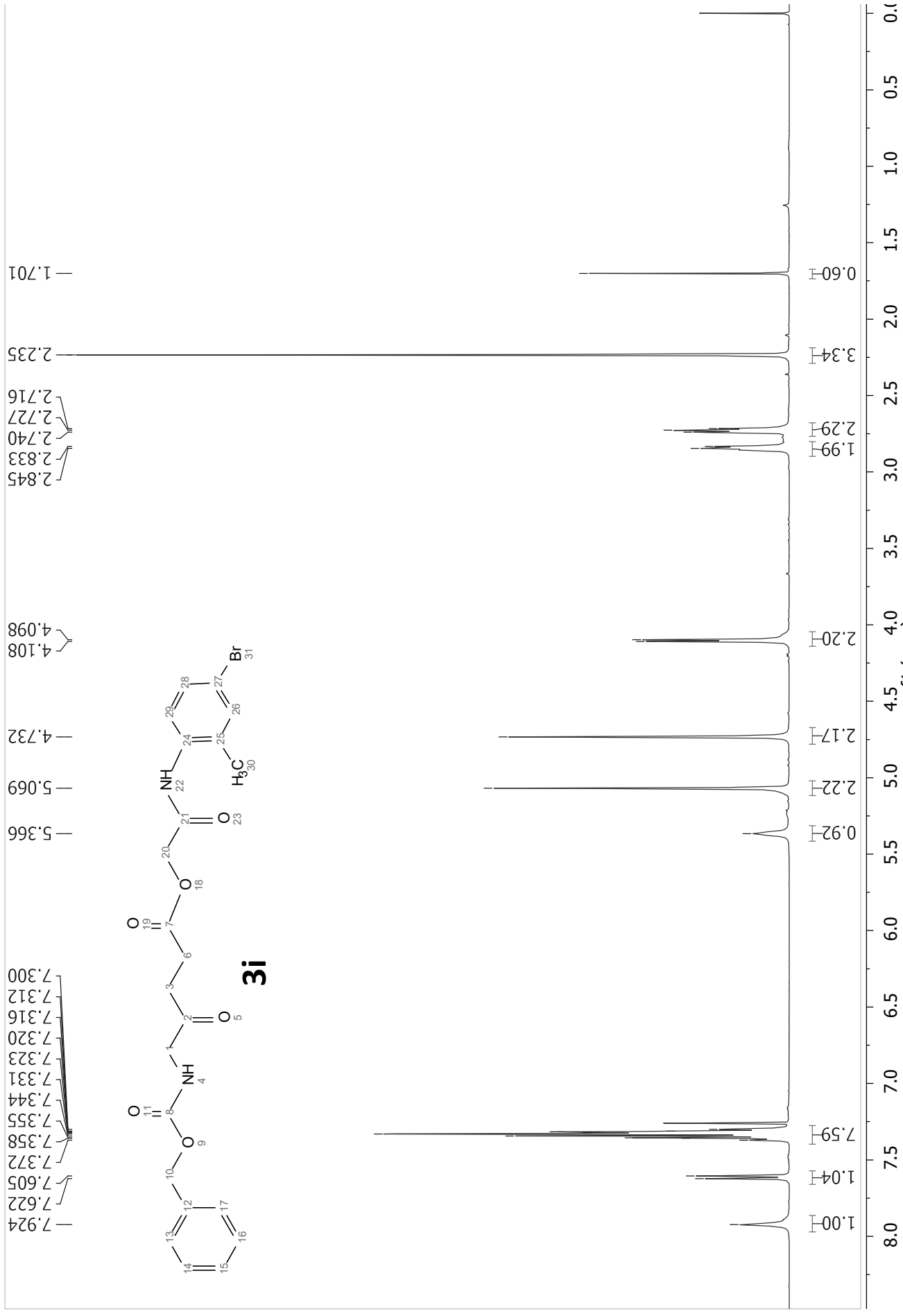


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3h** (collision Energy 10 eV)

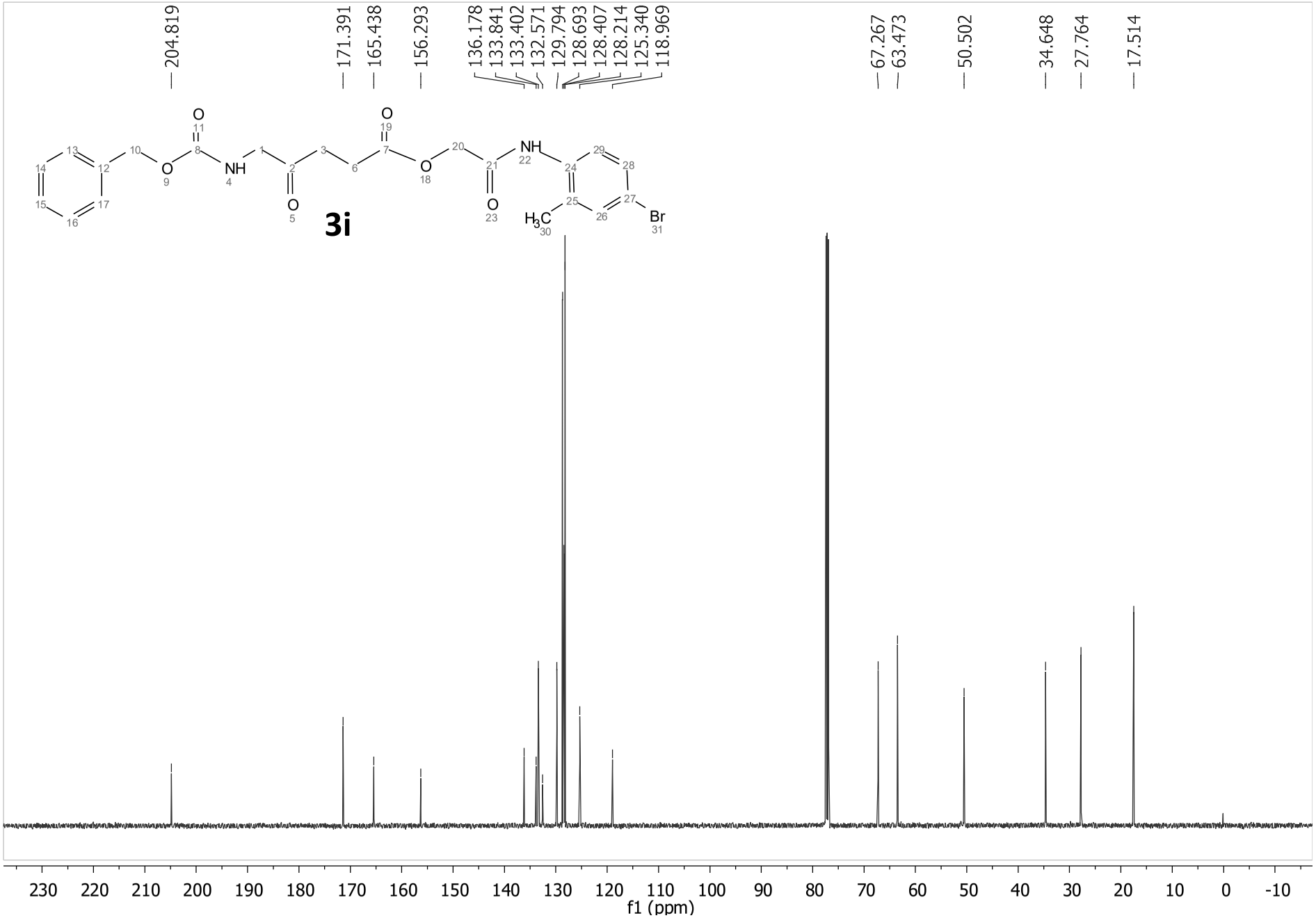


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e¯	Conf	
91.05379	C 7 H 7	91.05423	4.8	4.5	ok	even		
114.05385	C 5 H 8 N O 2	114.05495	9.7	2.5	ok	even		
154.04797	C 7 H 8 N O 3	154.04987	12.3	4.5	ok	even		
186.09114	C 12 H 12 N O	186.09134	1.1	7.5	ok	even		204-H2O
204.10079	C 12 H 14 N O 2	204.10191	5.5	6.5	ok	even		423-219
220.05725	C 9 H 9 F 3 N O 2	220.05799	3.4	4.5	ok	even		α-O Cterm
290.10047	C 16 H 14 F 2 N O 2	290.09871	-6.1	9.5	ok	even		310-HF
310.10503	C 16 H 15 F 3 N O 2	310.10494	-0.3	8.5	ok	even		423-113
423.15384	C 21 H 22 F 3 N 2 O 4	423.15262	-2.9	10.5	ok	even		-CO2

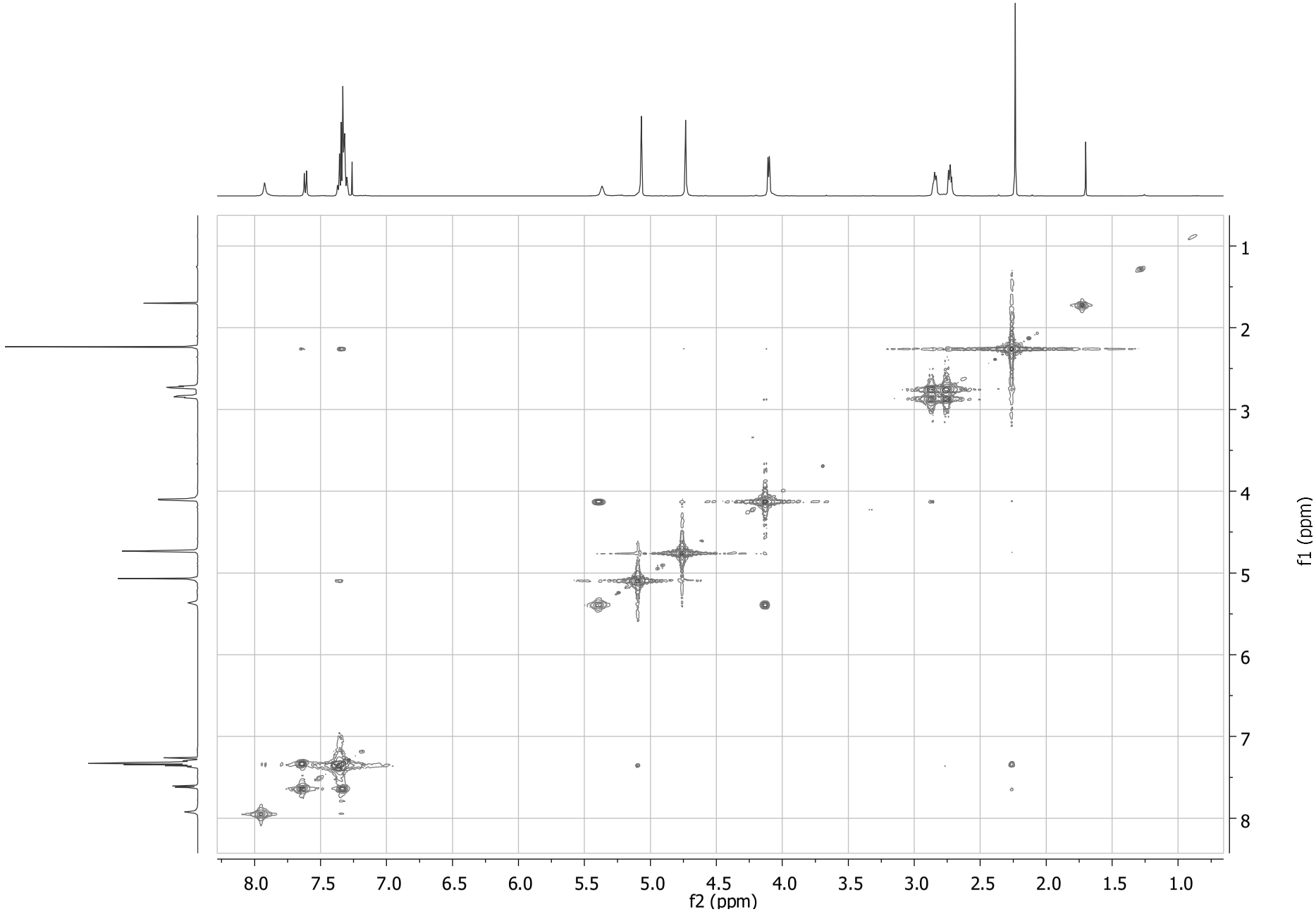
^{1}H-NRM (500 MHz) of compound 2-((4-bromo-2-methylphenyl)amino)-2-oxoethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3i**)



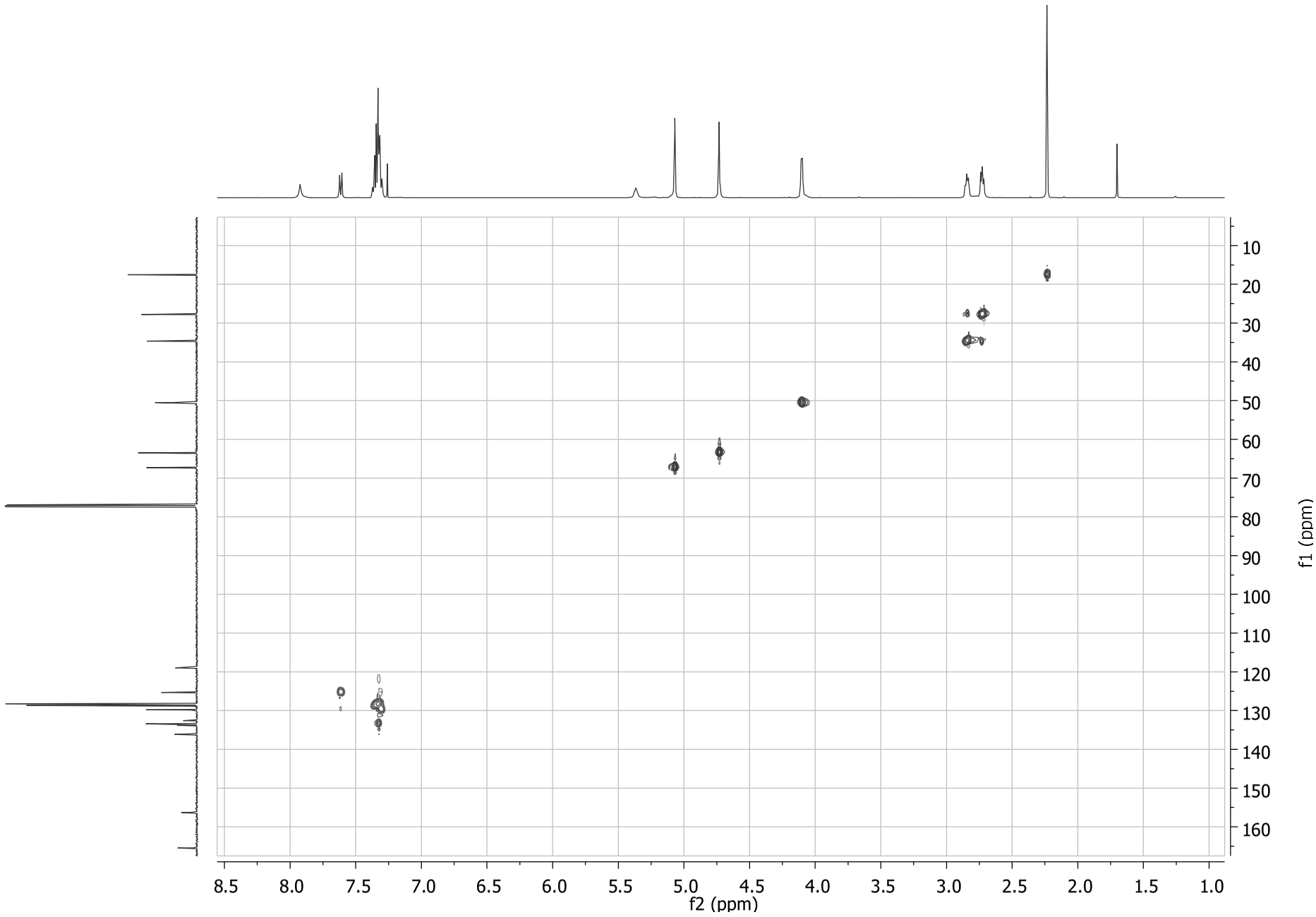
^{13}C-NRM (125,7 MHz) of compound **3i**



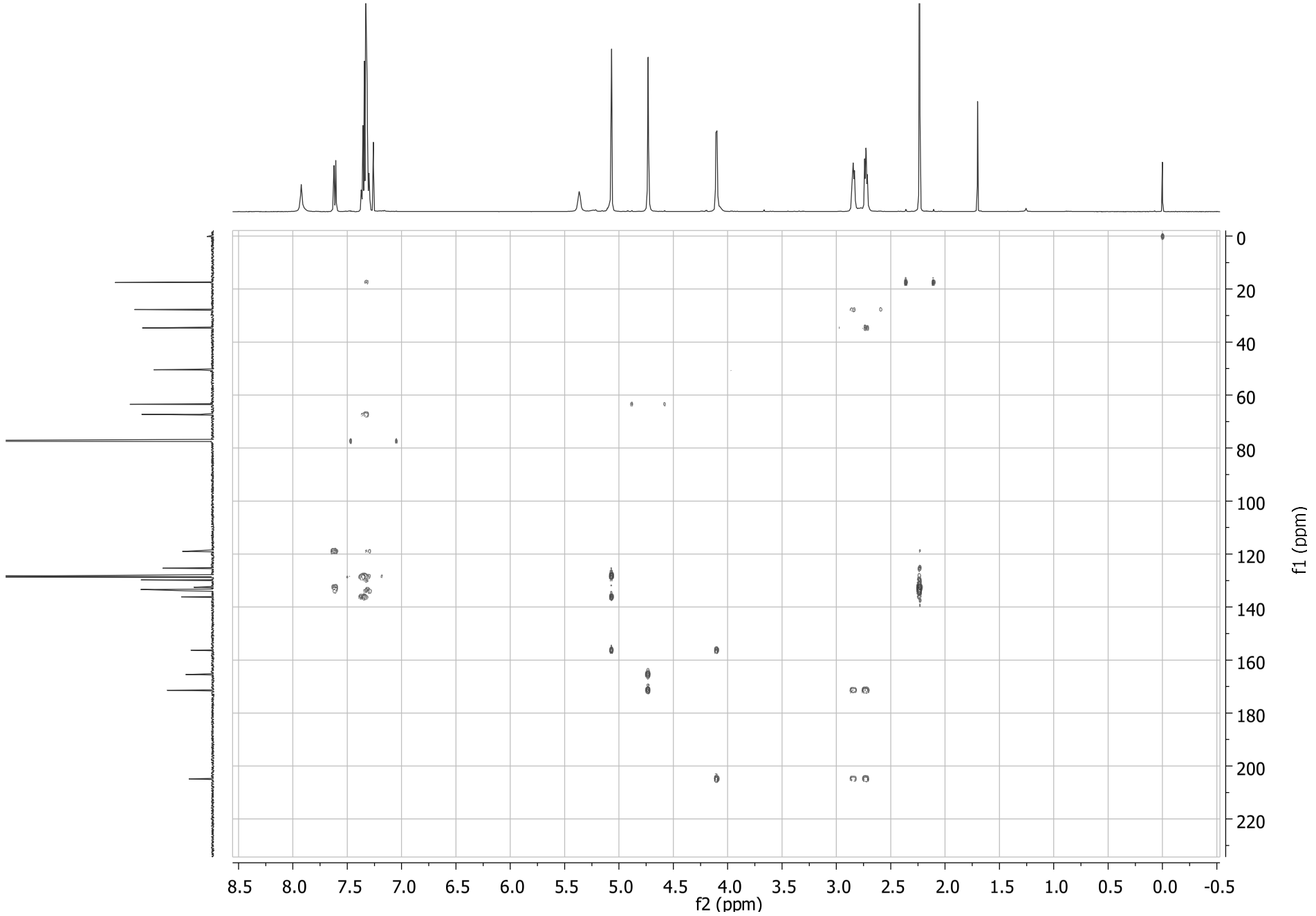
COSY (500 MHz) of compound **3i**



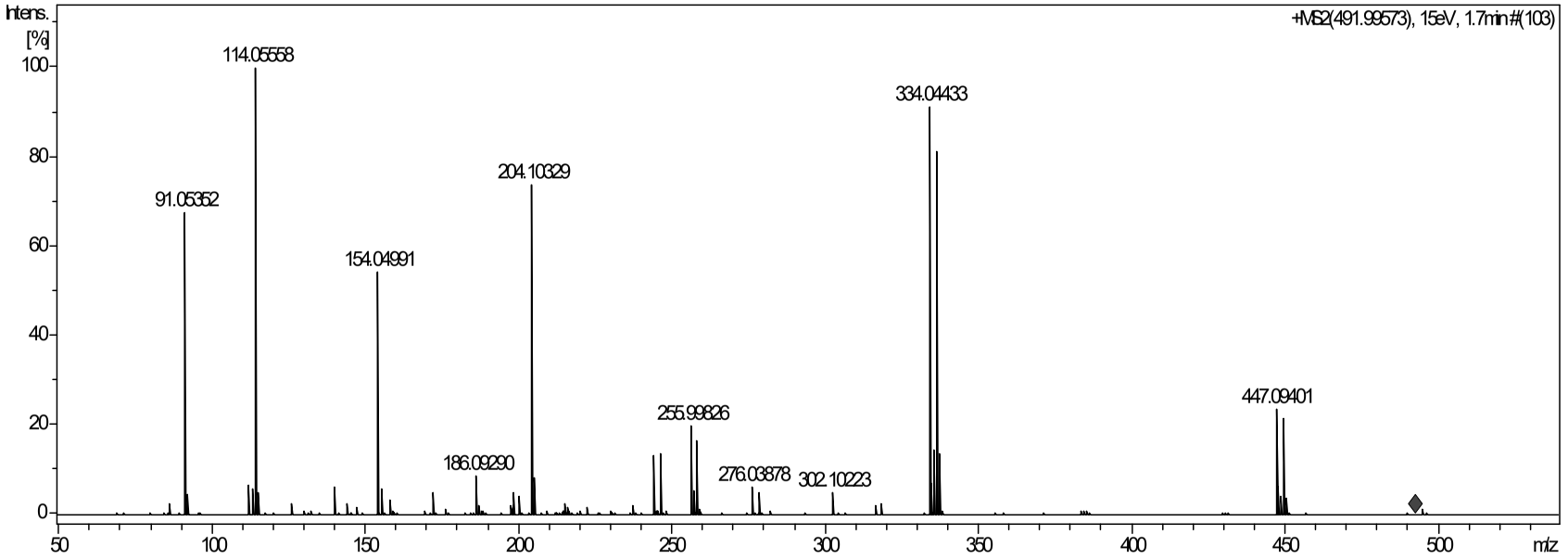
HSQC-DEPT (500 MHz) of compound **3i**



HMBC (500 MHz) of compound **3i**

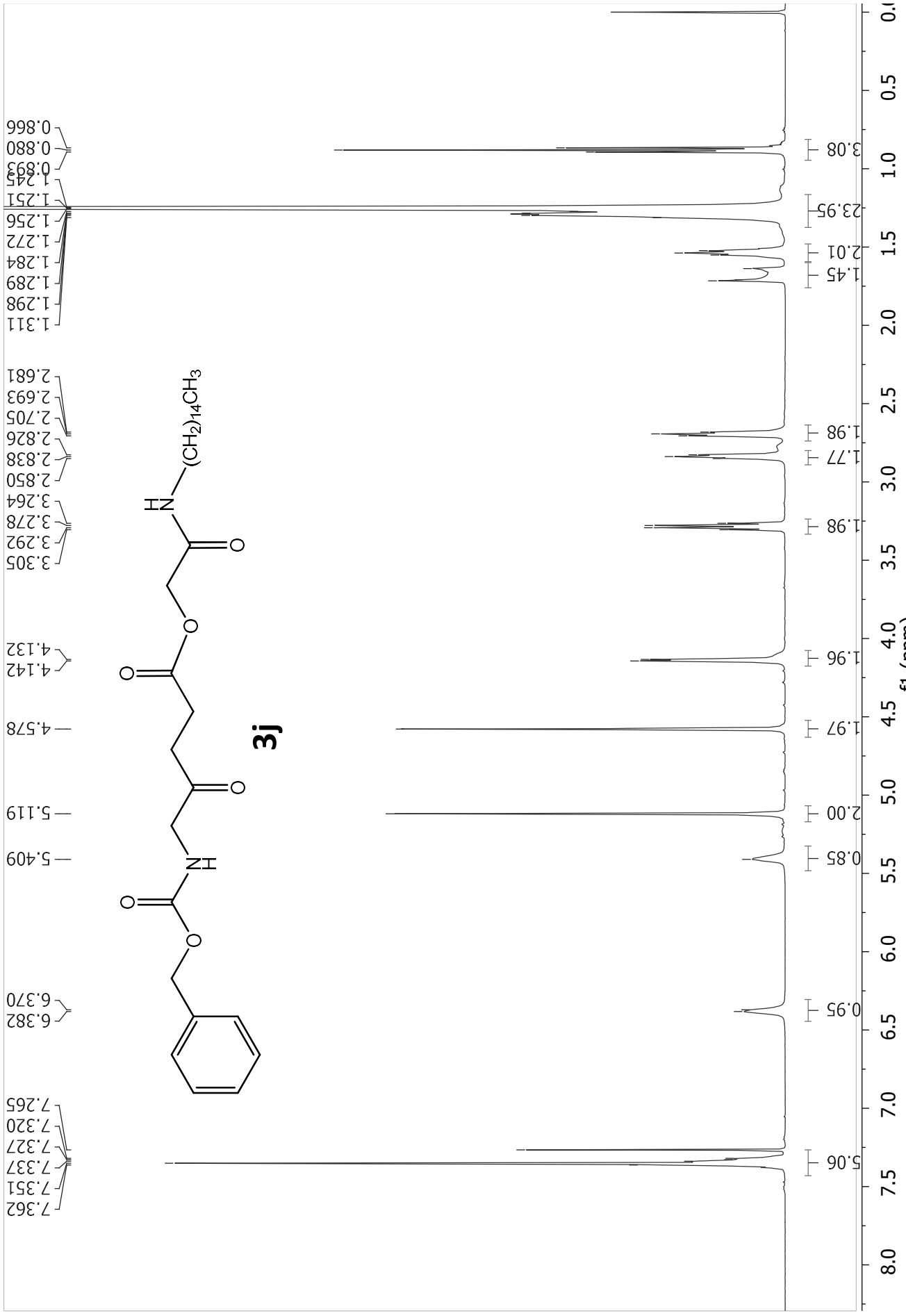


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3i** (collision Energy 10 eV)

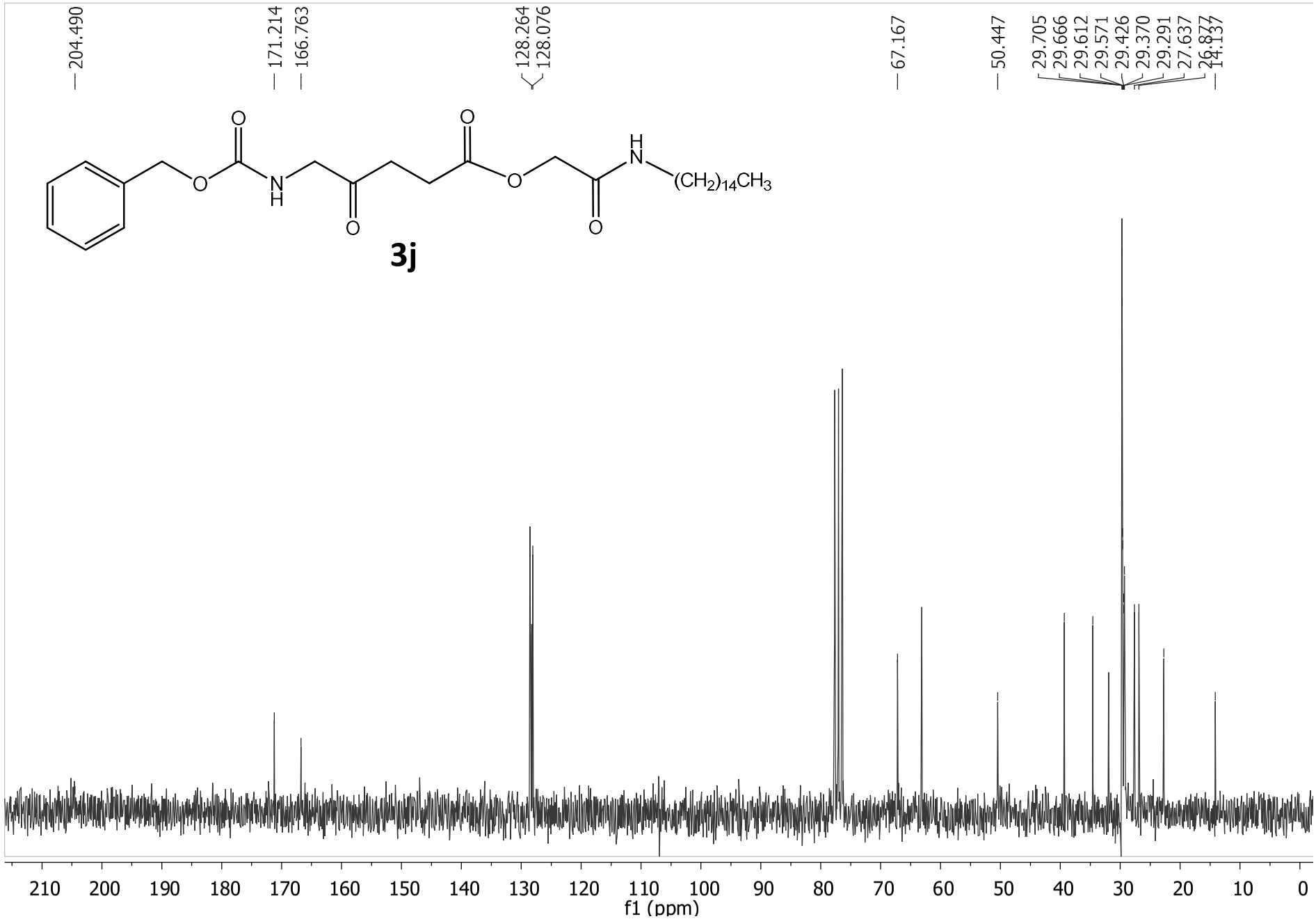


:as. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e¯	Conf	
05352	C 7 H 7	91.05423	7.7	4.5	ok	even		
4.05558	C 5 H 8 N O 2	114.05495	-5.5	2.5	ok	even		
4.04991	C 7 H 8 N O 3	154.04987	-0.3	4.5	ok	even		
6.09290	C 12 H 12 N O	186.09134	-8.4	7.5	ok	even		204-H2O
4.10329	C 12 H 14 N O 2	204.10191	-6.8	6.5	ok	even		id ant
5.99826	C 10 H 11 Br N O 2	255.99677	-5.8	5.5	ok	even		
6.03878	C 14 H 15 Br N	276.03824	-2.0	7.5	ok	even		
4.04433	C 16 H 17 Br N O 2	334.04372	-1.8	8.5	ok	even		447-113
7.09401	C 21 H 24 Br N 2 O 4	447.09140	-5.8	10.5	ok	even		-CO2

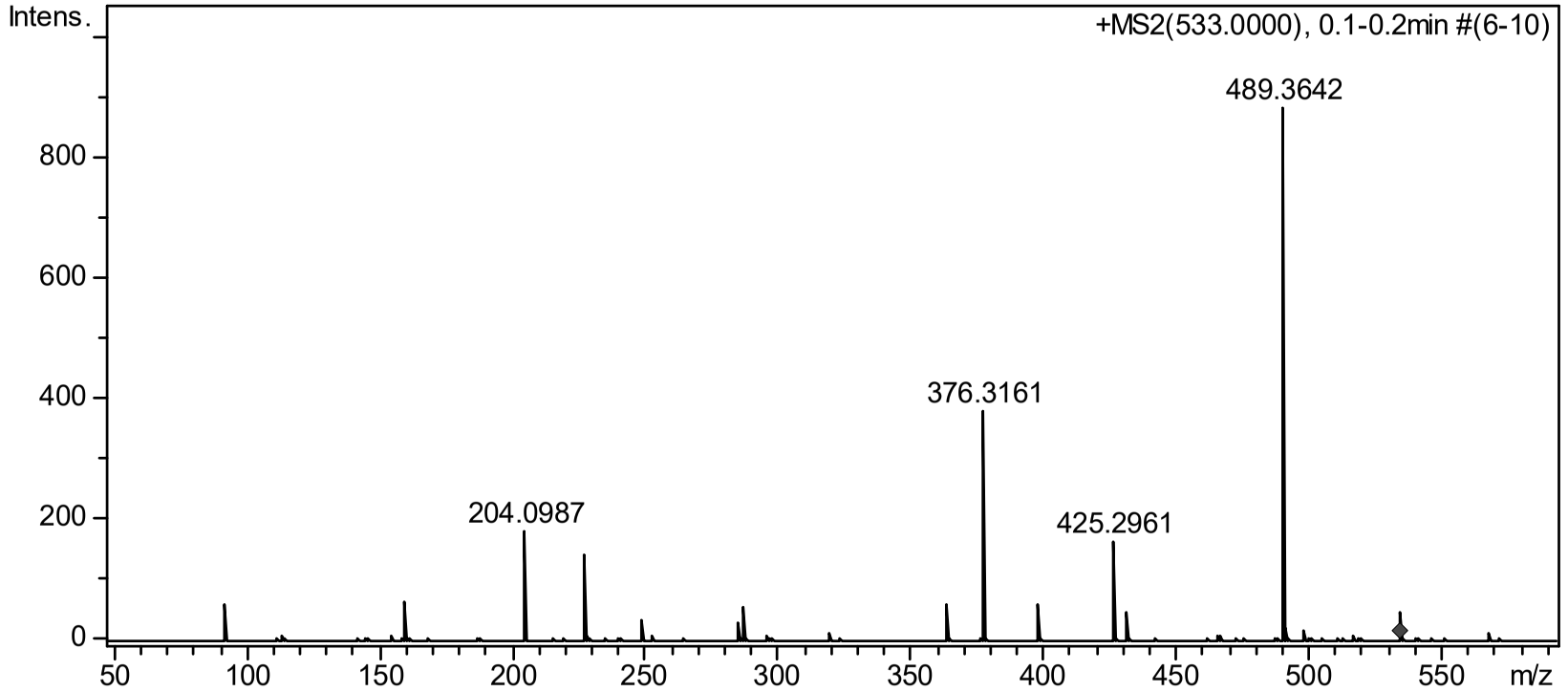
^{1}H-NRM (500 MHz) of compound 2-oxo-2-(pentadecylamino)ethyl-*N*-(benzyloxycarbonyl)-5-aminolevulinate (**3j**)



^{13}C-NRM (50,3 MHz) of compound **3j**

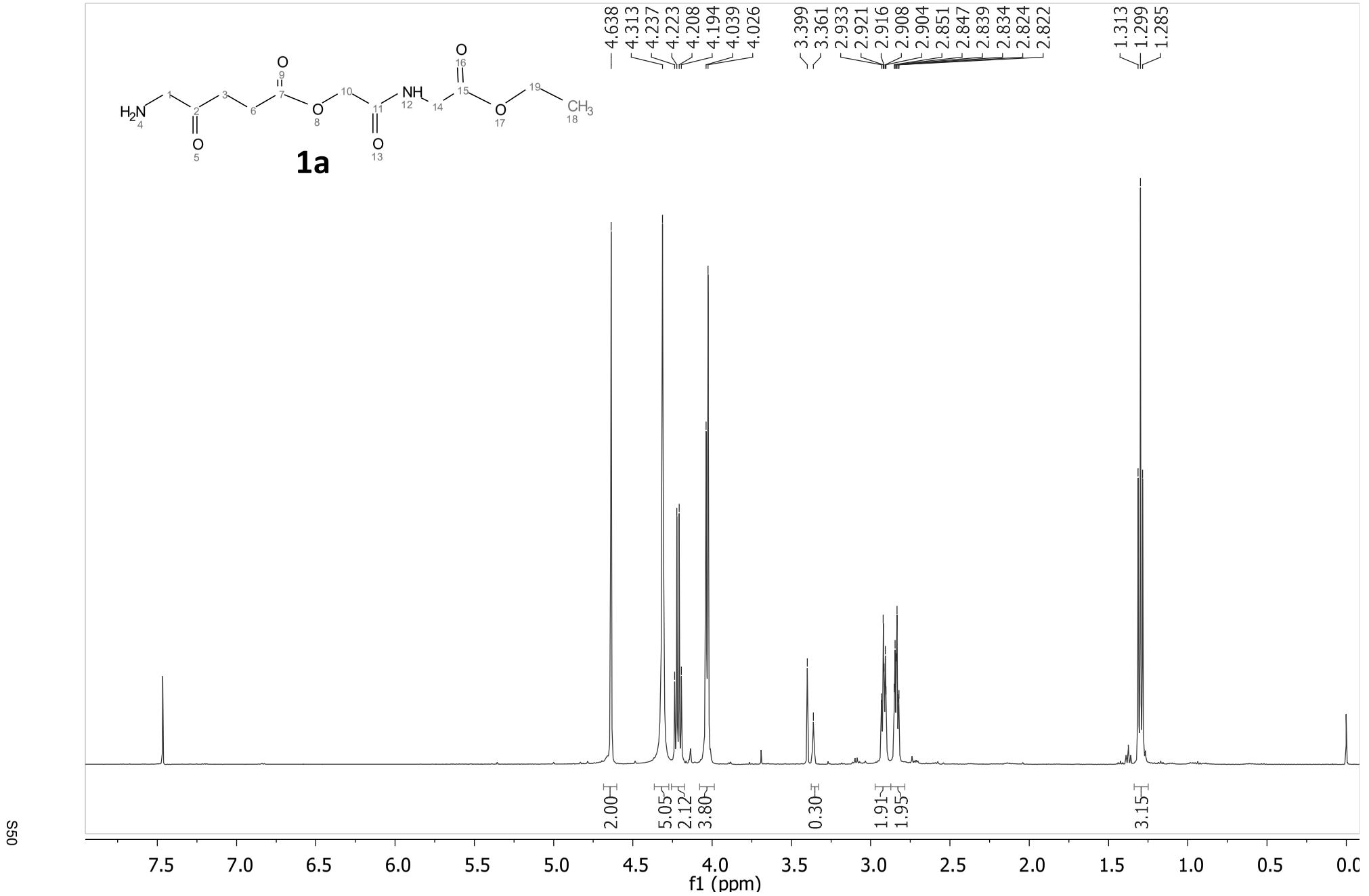


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **3j** (collision Energy 10 eV)

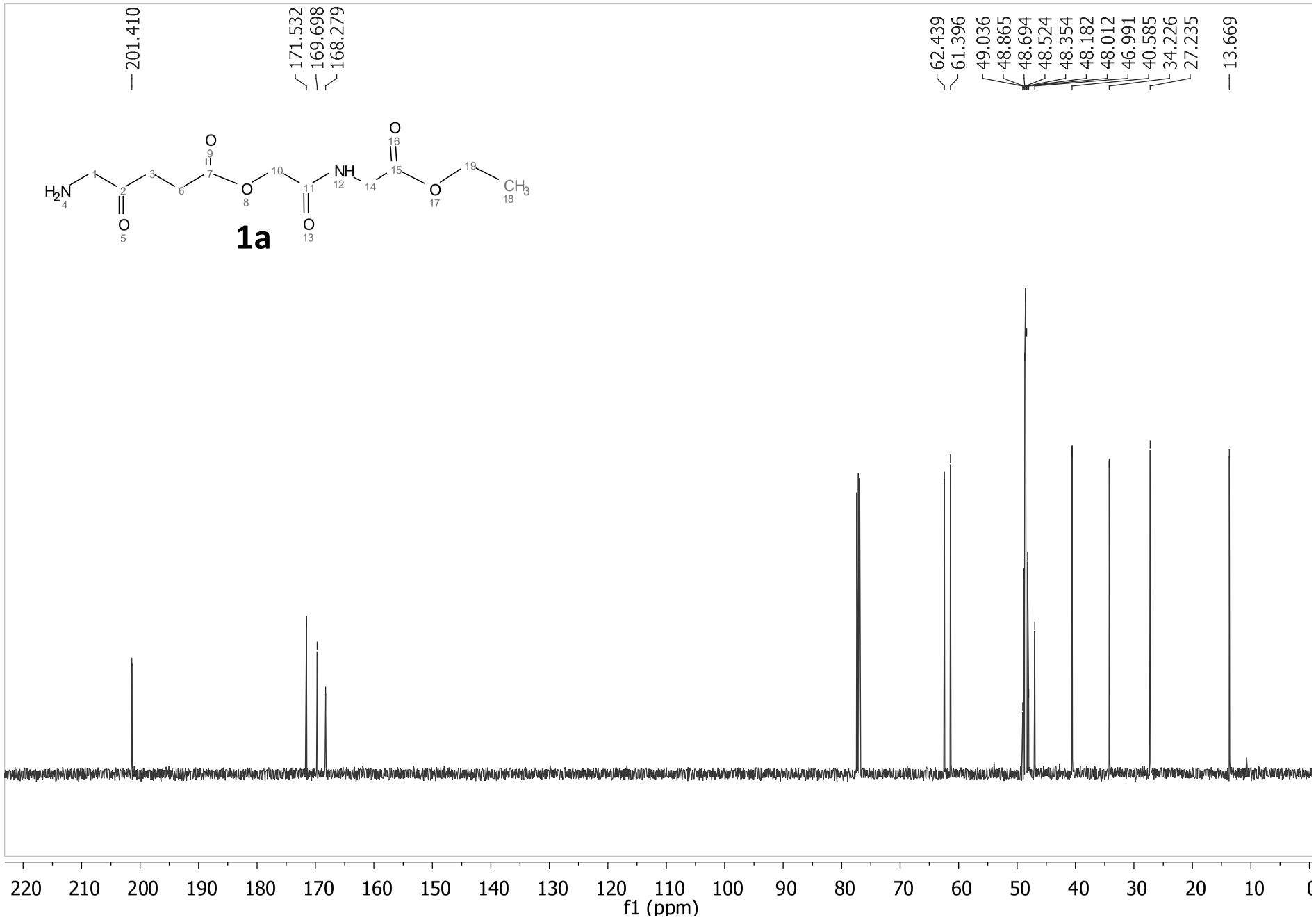


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	
204.0987	C 12 H 14 N O 2	204.1019	-4.1	6.5	ok	even	m/z 248 – CO_2
425.2961	C 23 H 41 N 2 O 5	425.3010	11.6	4.5	ok	even	$[M+H-BnOH]^+$
489.3642	C 29 H 49 N 2 O 4	489.3687	9.1	6.5	ok	even	$[M+H-CO_2]+$

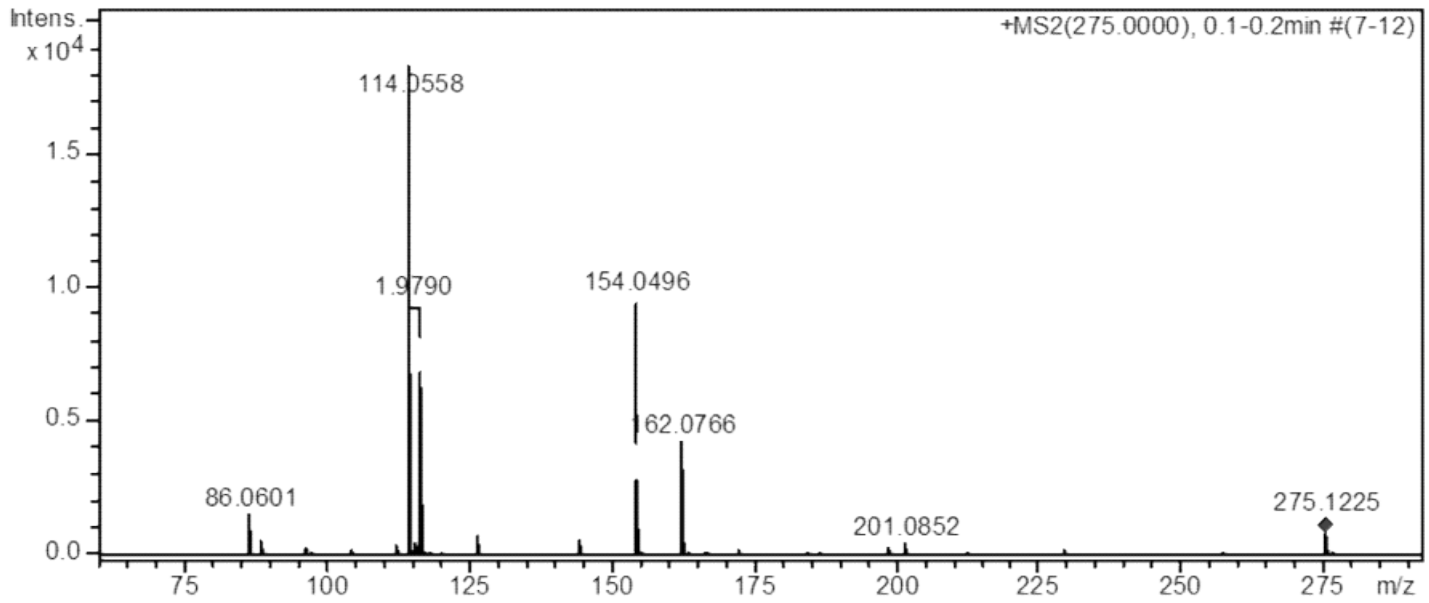
^{1}H-NRM (500 MHz) of compound 2-(2-ethoxy-2-oxoethylamino)-2-oxoethyl-5-aminolevulinate (**1a**)



^{13}C-NRM (125,7 MHz) for compound **1a**

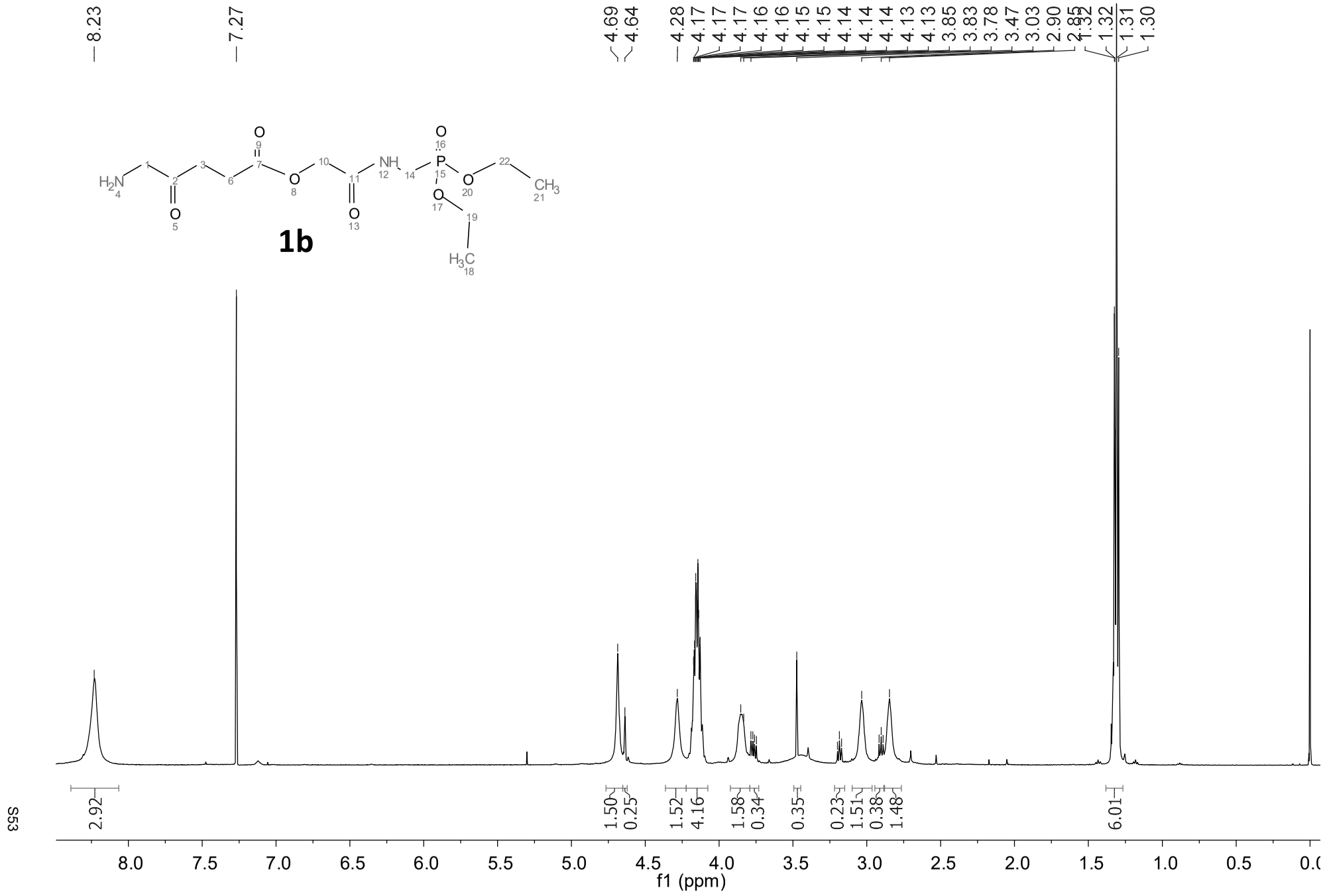


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1a** (collision Energy 10 eV)

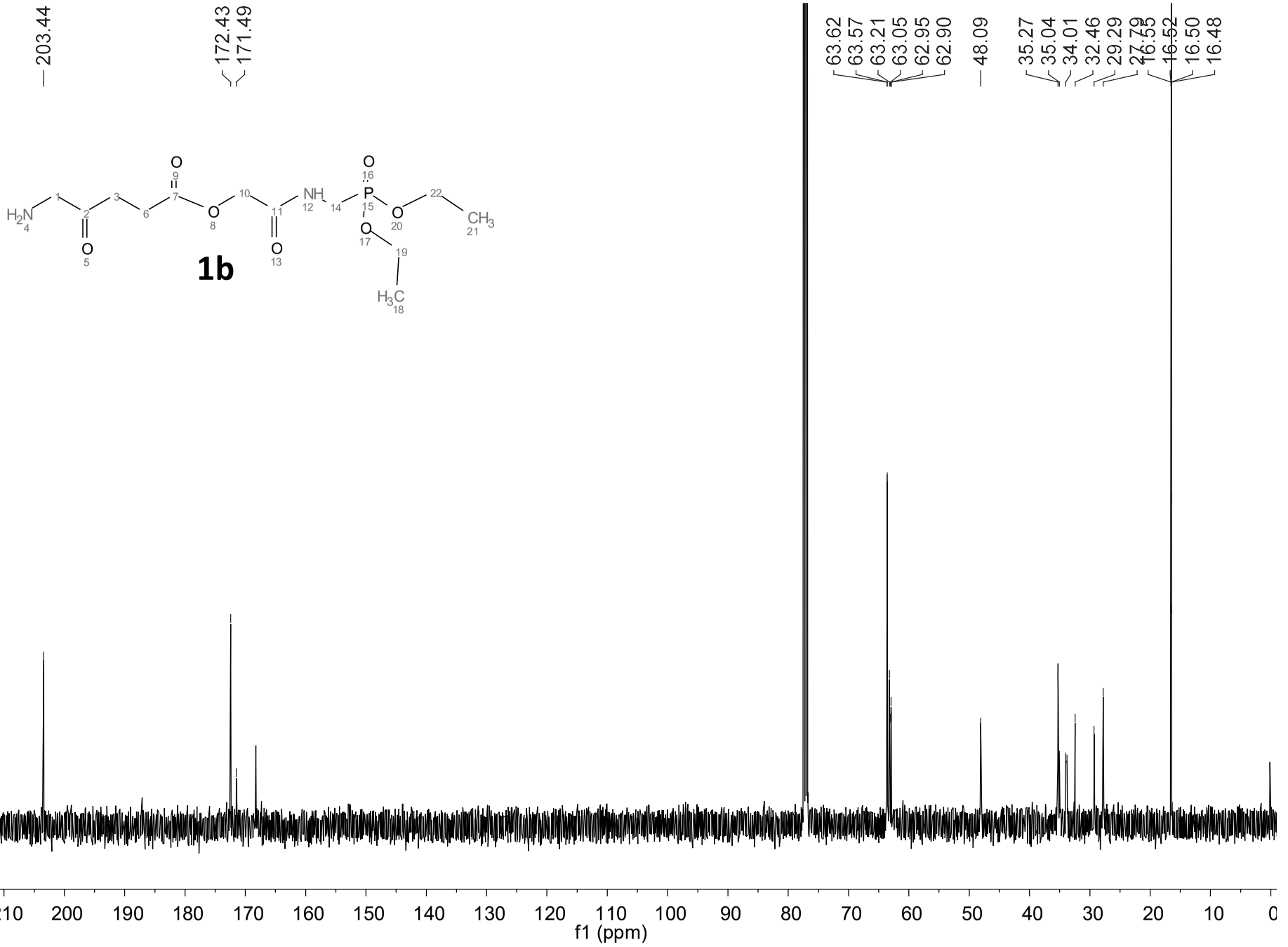


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$	Conf	
86.0601	C 4 H 8 N O	86.0600	-0.5	1.5	ok	even	ruptura αCOO	
88.0392	C 3 H 6 N O 2	88.0393	0.9	1.5	ok	even	ruptura αCON	
114.0558	C 5 H 8 N O 2	114.0550	-7.5	2.5	ok	even	ruptura COO←	
116.0348	C 4 H 6 N O 3	116.0342	-5.4	2.5	ok	even	ruptura CON→	
154.0496	C 7 H 8 N O 3	154.0499	2.0	4.5	ok	even	X	
162.0766	C 6 H 12 N O 4	162.0761	-2.9	1.5	ok	even	ruptura COO→	
275.1225	C 11 H 19 N 2 O 6	275.1238	4.5	3.5	ok	even	[M+H]$^+$	

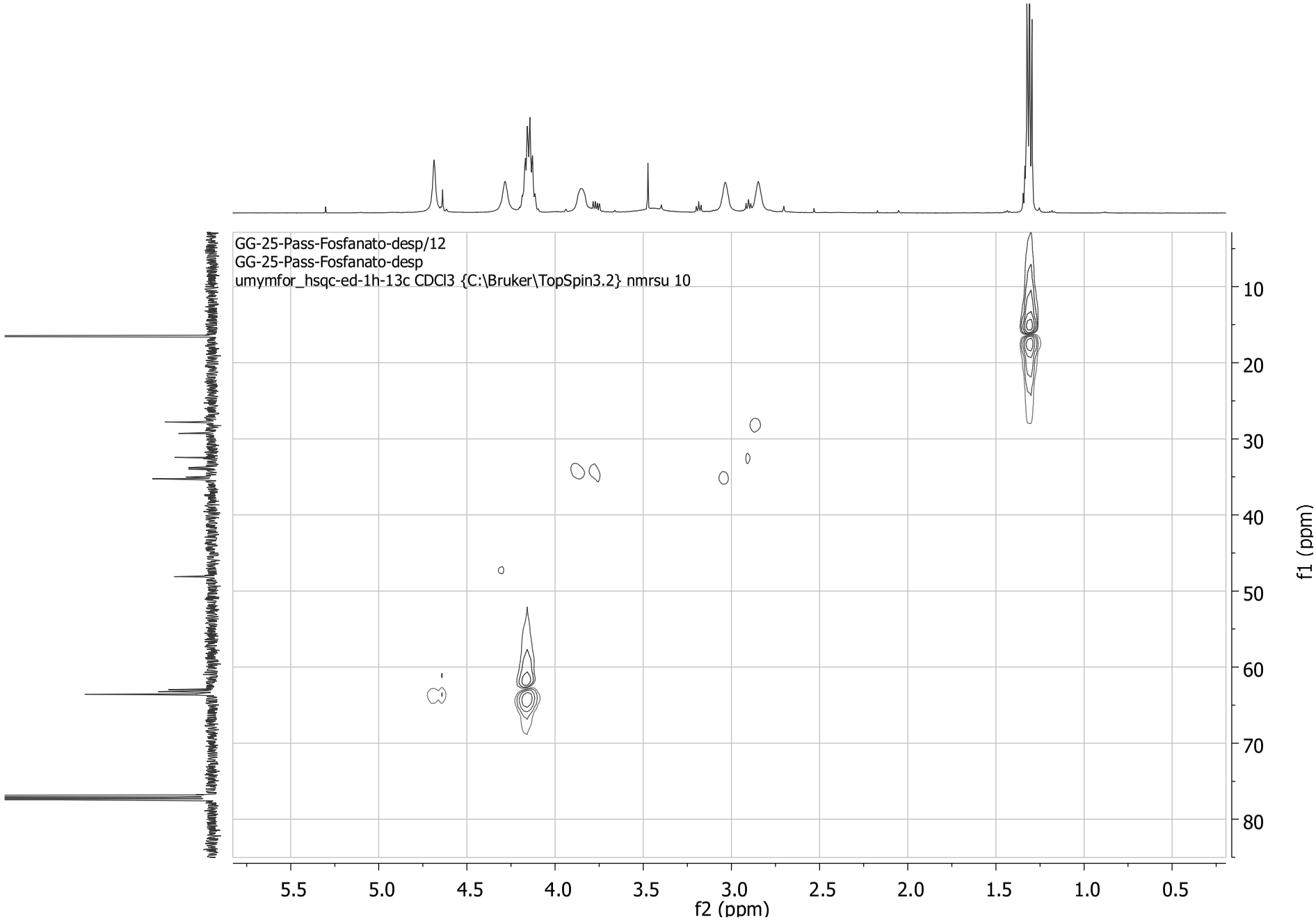
^{1}H-NRM (500 MHz) for compound 2-(diethoxyphosphorylmethylamino)-2-oxoethyl-5-aminolevulinate (**1b**)



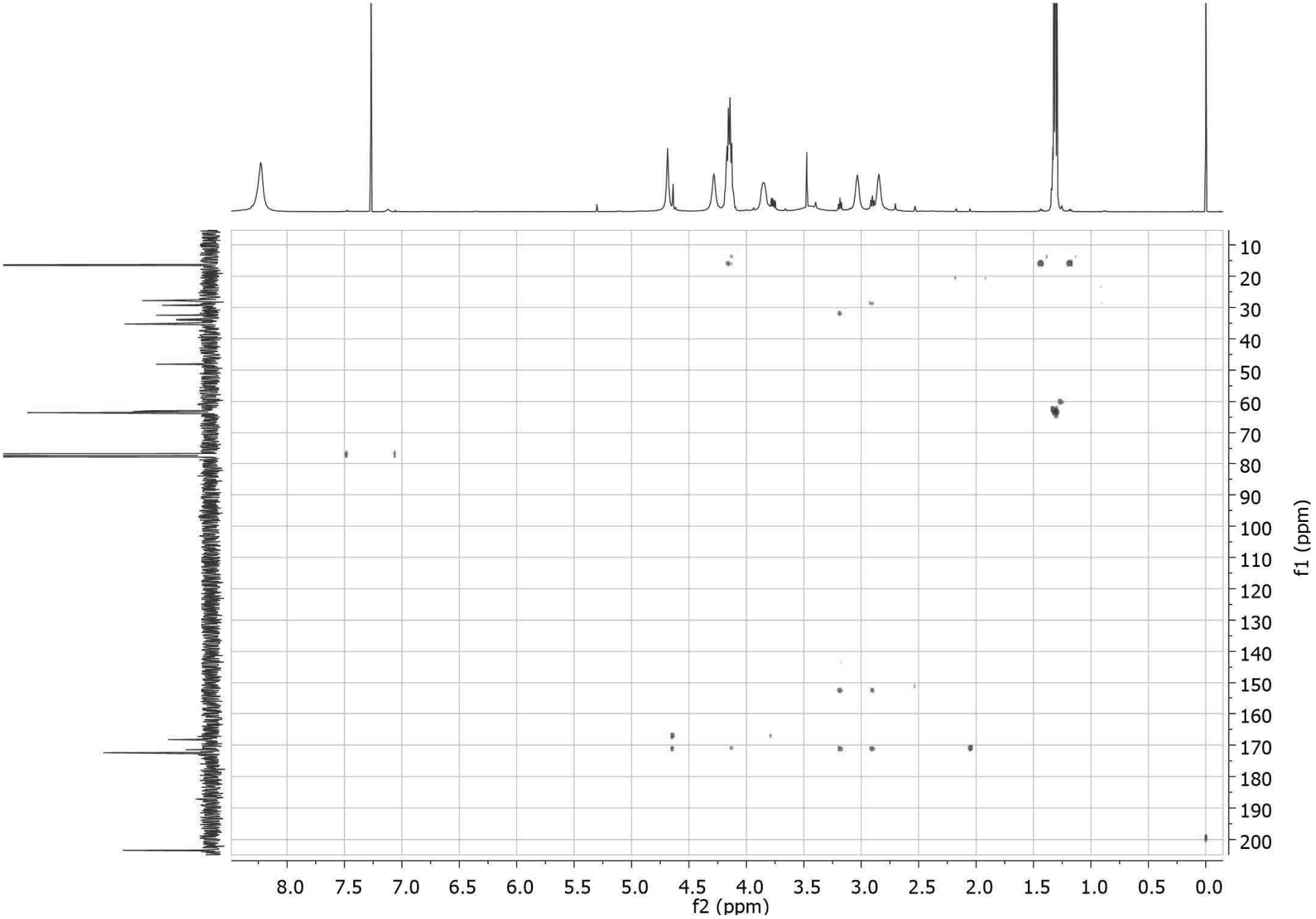
^{13}C-NRM (125,7 MHz) for compound **1b**



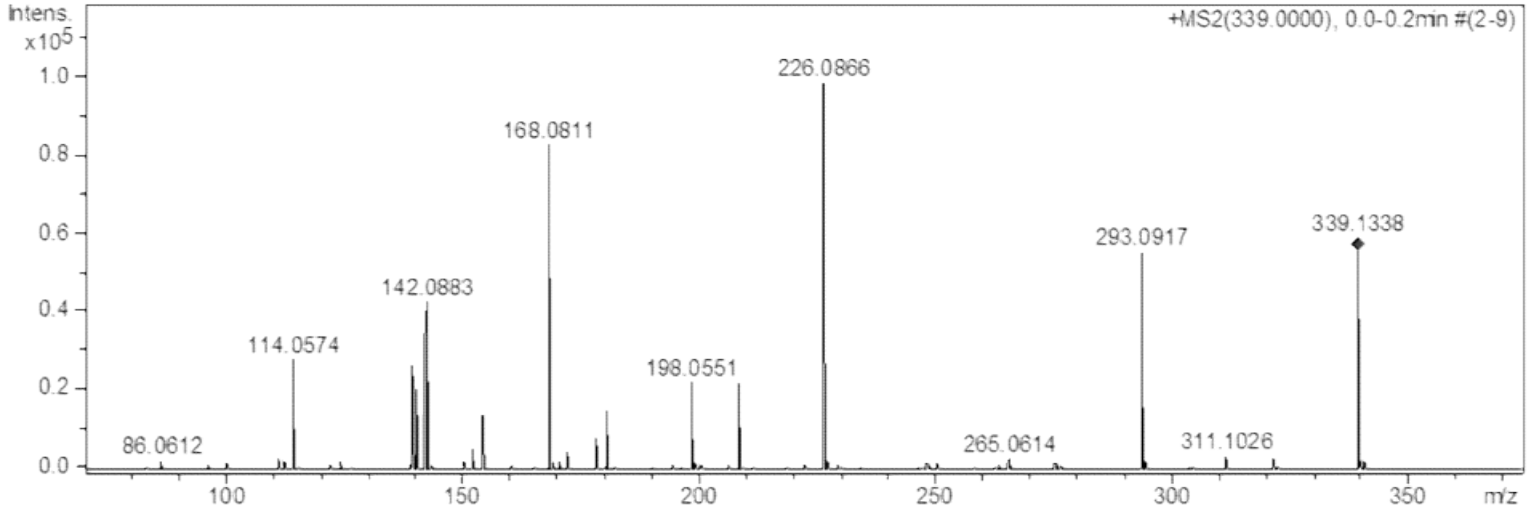
HSQC-DEPT (500 MHz) for compound **1b**



HMBC (500 MHz) for compound **1b**

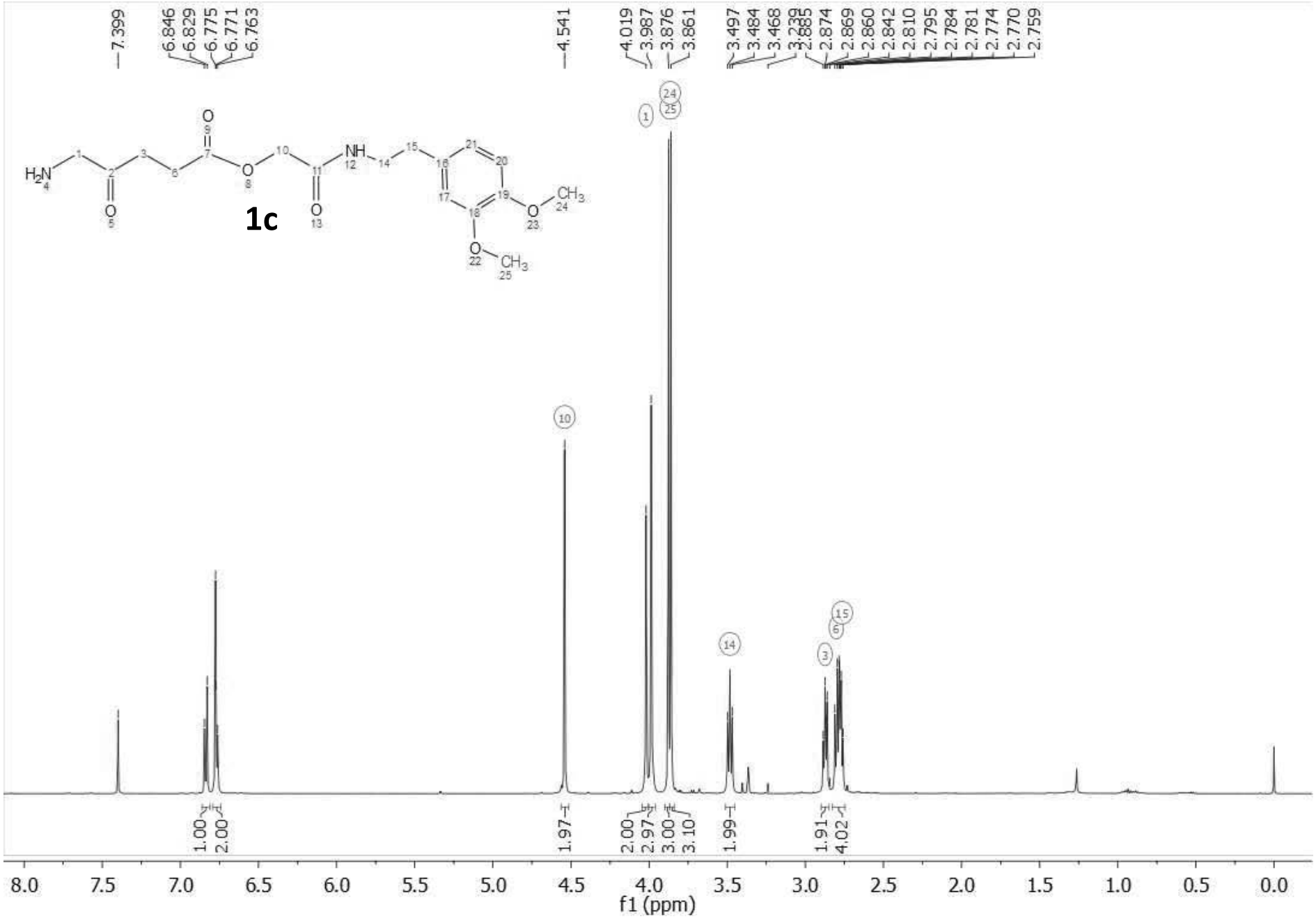


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1b** (collision Energy 10 eV)

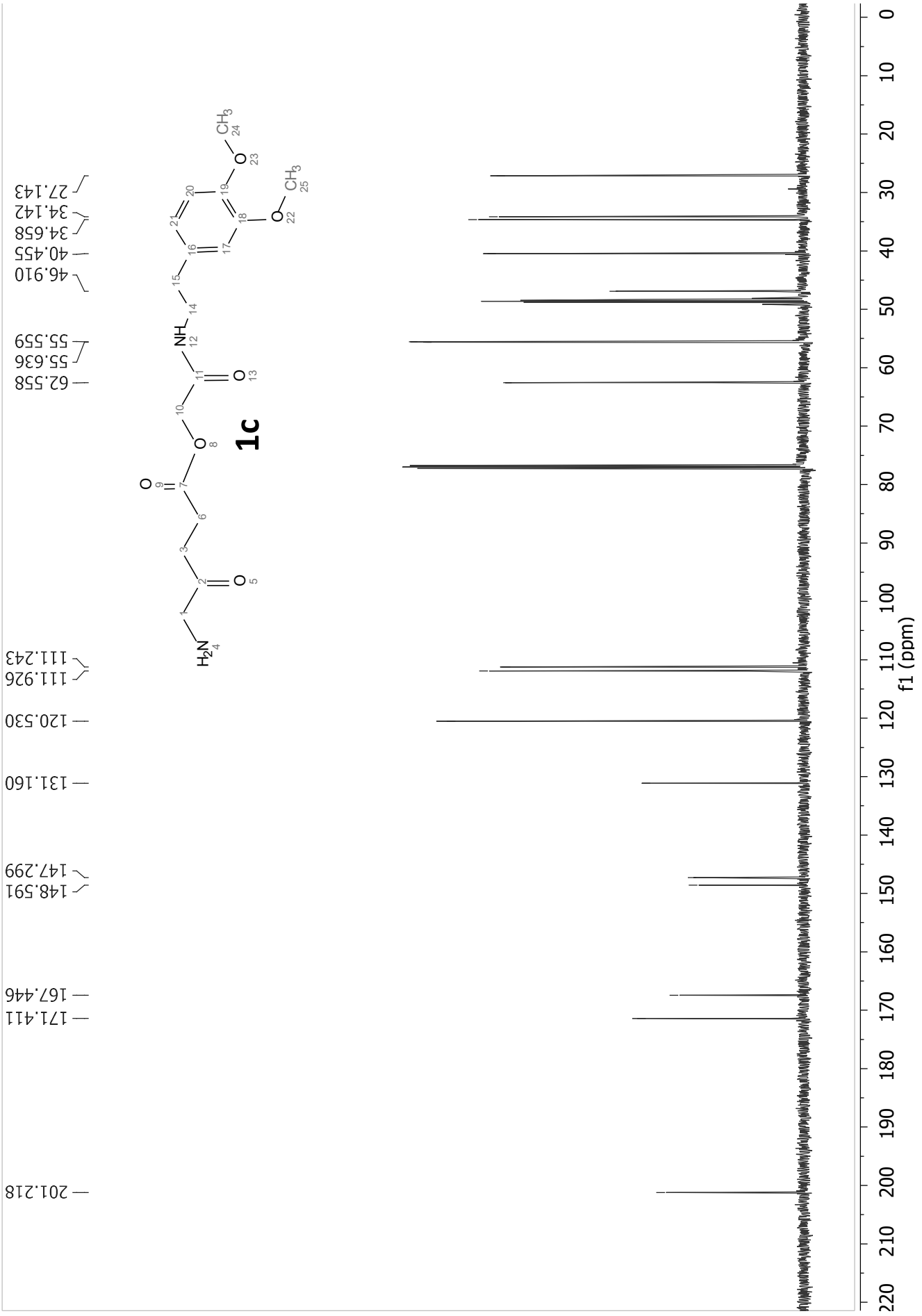


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	
114.0574							
139.0540	C 11 H 7	139.0542	1.4	8.5	ok	even	
	C 7 H 10 N P	139.0545	3.6	4.0	ok	odd	
142.0883	C 7 H 12 N O 2	142.0863	-14.5	2.5	ok	even	
154.0518	C 7 H 8 N O 3	154.0499	-12.8	4.5	ok	even	
168.0811	C 8 H 13 N 2 P	168.0811	0.0	4.0	ok	odd	
	C 12 H 10 N	168.0808	-1.8	8.5	ok	even	
180.0445	C 5 H 11 N O 4 P	180.0420	-13.9	1.5	ok	even	
198.0551	C 5 H 13 N O 5 P	198.0526	-12.7	0.5	ok	even	
208.0756	C 7 H 15 N O 4 P	208.0733	-10.8	1.5	ok	even	
226.0866	C 7 H 17 N O 5 P	226.0839	-12.0	0.5	ok	even	
293.0917	C 10 H 18 N 2 O 6 P	293.0897	-6.9	3.5	ok	even	- EtOH
339.1338	C 12 H 24 N 2 O 7 P	339.1316	-6.4	2.5	ok	even	[M+H]$^+$

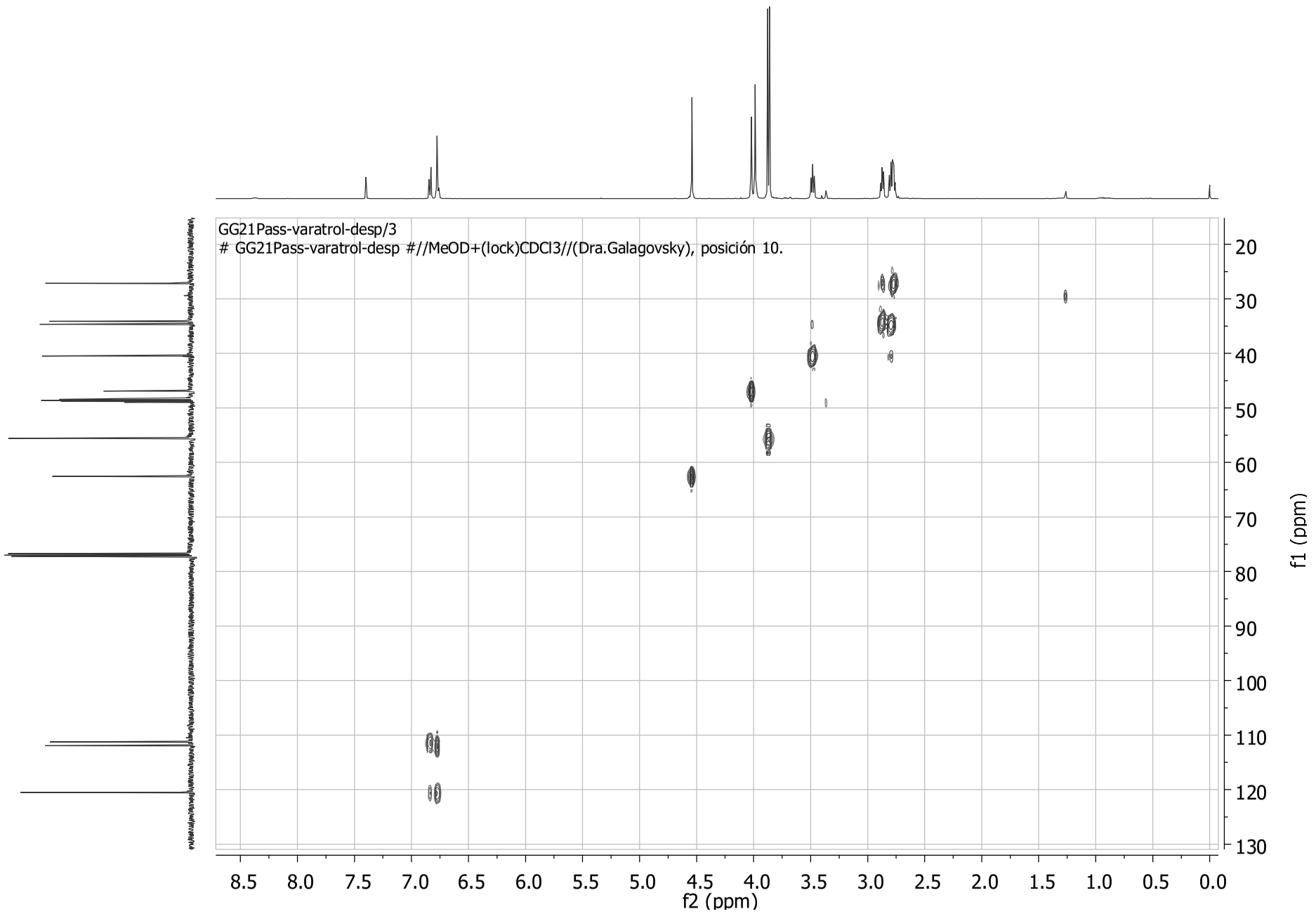
^{1}H-NRM (500 MHz) for compound 2-(3,4-dimethoxyphenethylamino)-2-oxoethyl-5-aminolevulinate (**1c**)



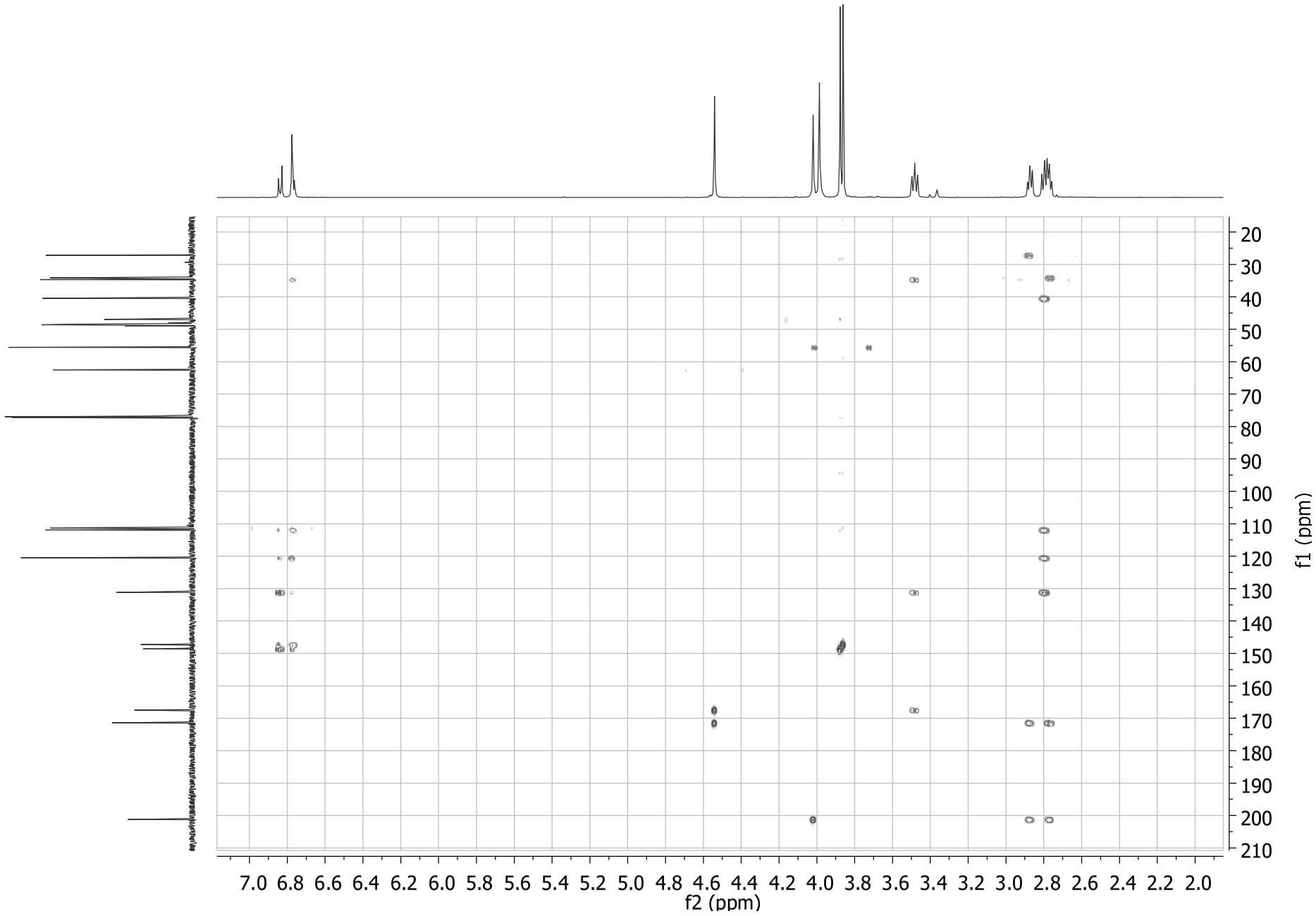
^{13}C-NRM (125,7 MHz) for compound **1c**



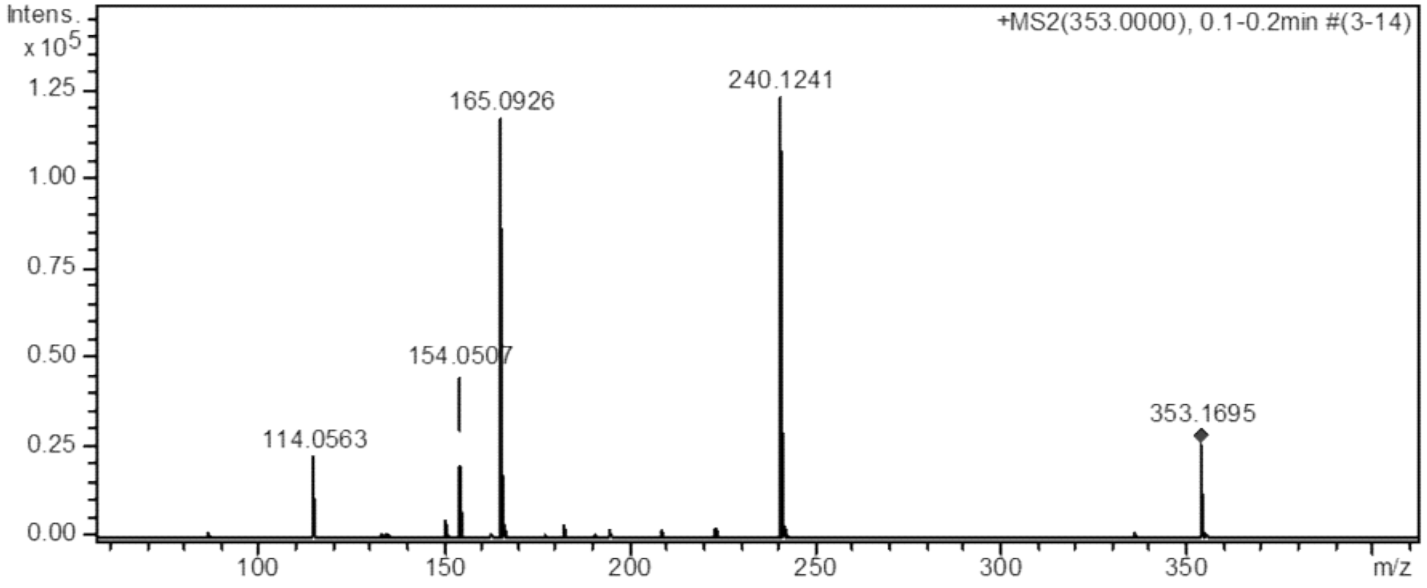
HSQC-DEPT (500 MHz) for compound **1c**



HMBC (500 MHz) for compound **1c**

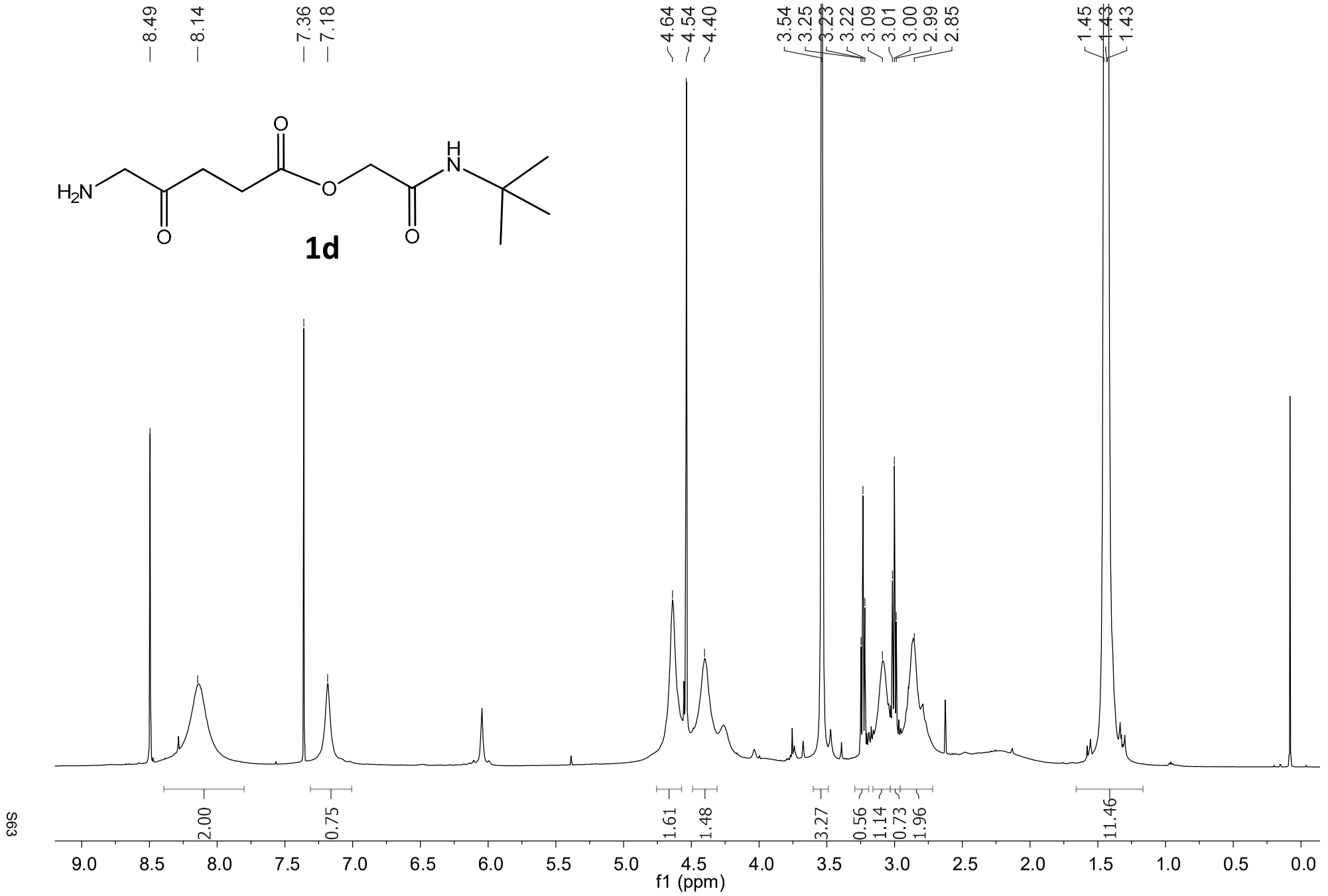


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1c** (collision Energy 15 eV)

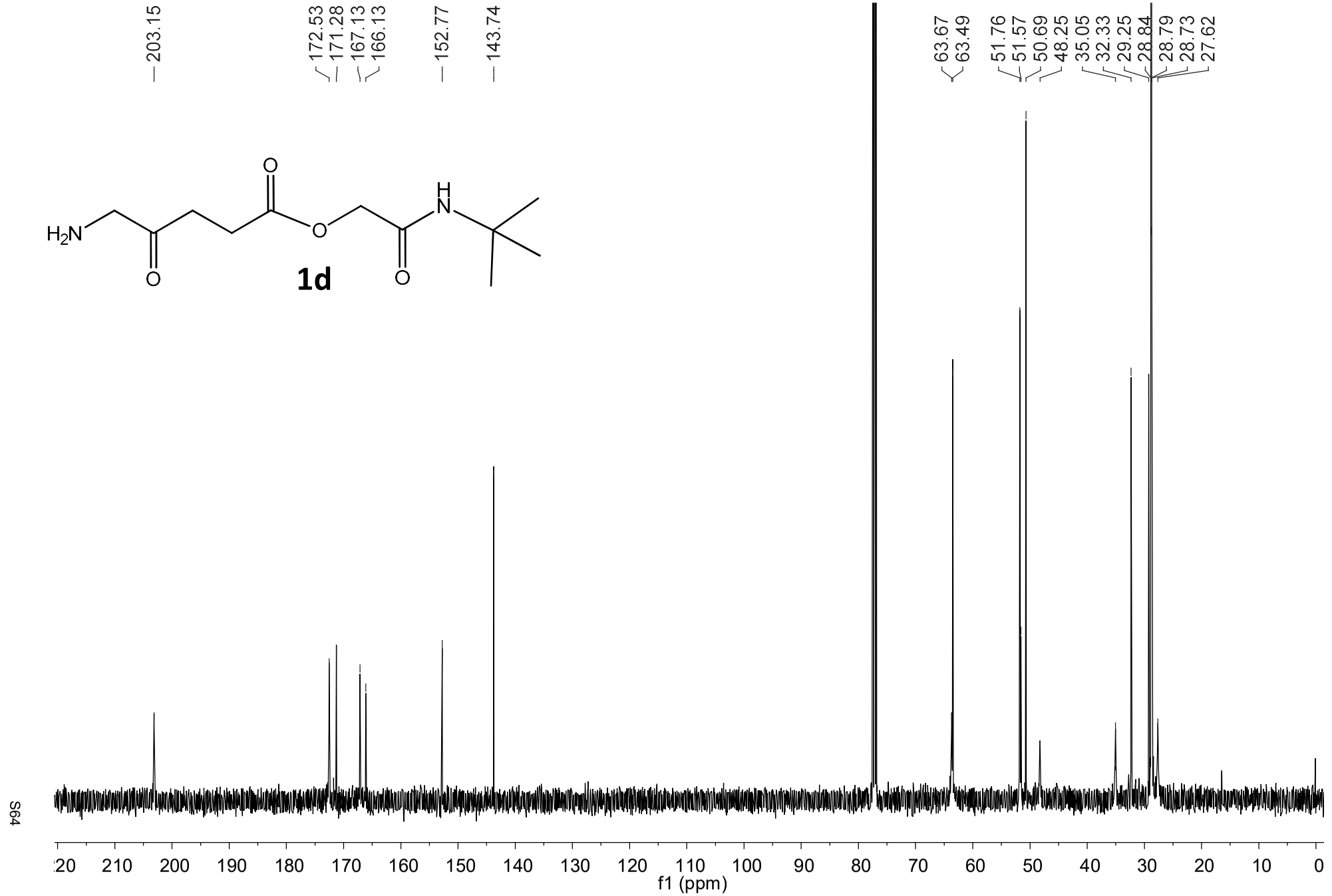


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	
114.0563	C 5 H 8 N O 2	114.0550	-12.1	2.5	ok	even	ruptura CO-O←
154.0507	C 7 H 8 N O 3	154.0499	-5.4	4.5	ok	even	X
165.0926	C 10 H 13 O 2	165.0910	-9.7	4.5	ok	even	ruptura α NH→
240.1241	C 12 H 18 N O 4	240.1230	-4.4	4.5	ok	even	ruptura CO-O→
353.1695	C 17 H 25 N 2 O 6	353.1707	3.4	6.5	ok	even	[M+H]$^+$

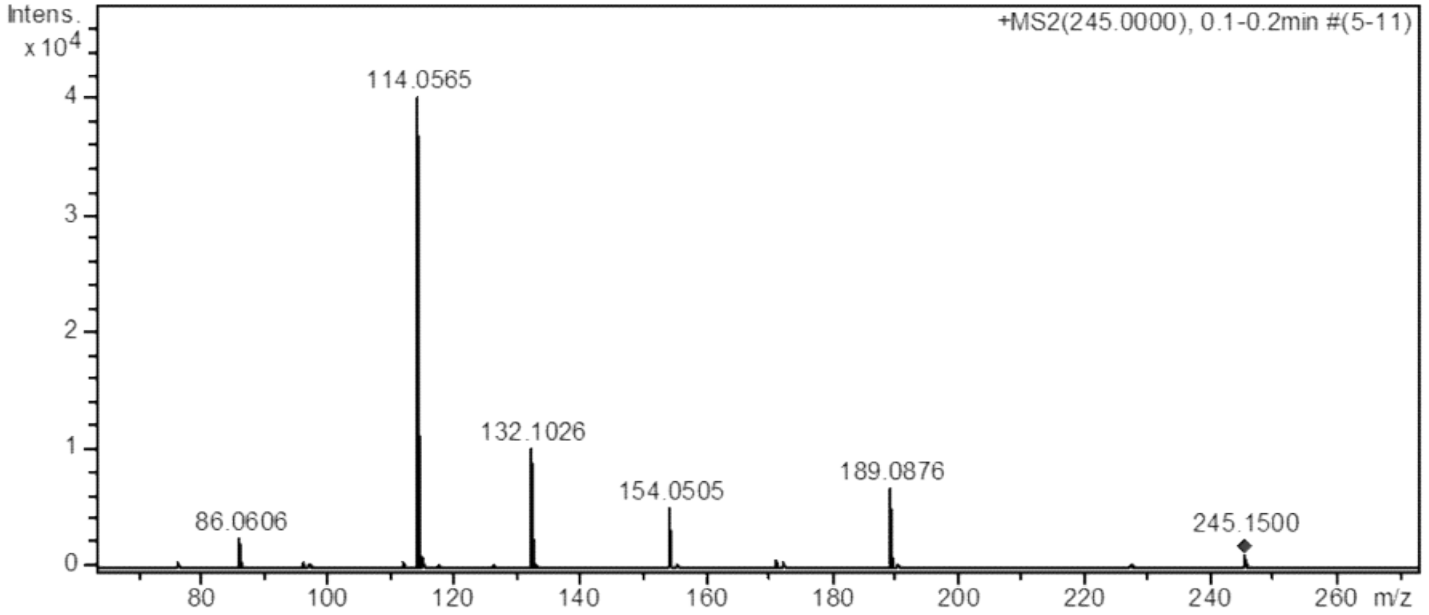
^{1}H-NRM (500 MHz) for compound 2-(*t*-butylamino)-2-oxoethyl-5-aminolevulinate (**1d**)



^{13}C-NRM (125,7 MHz) for compound **1d**

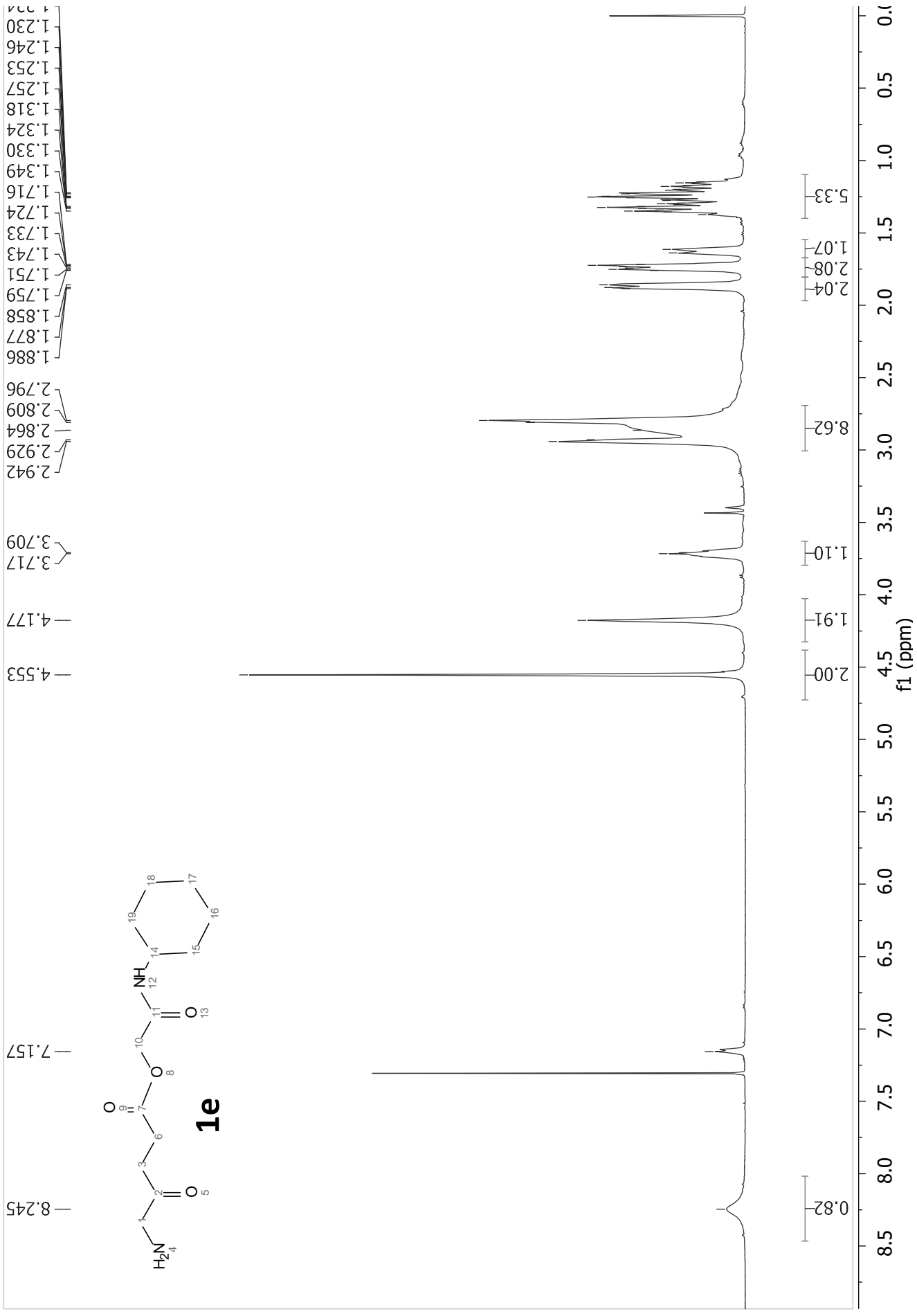


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1d** (collision Energy 15 eV)

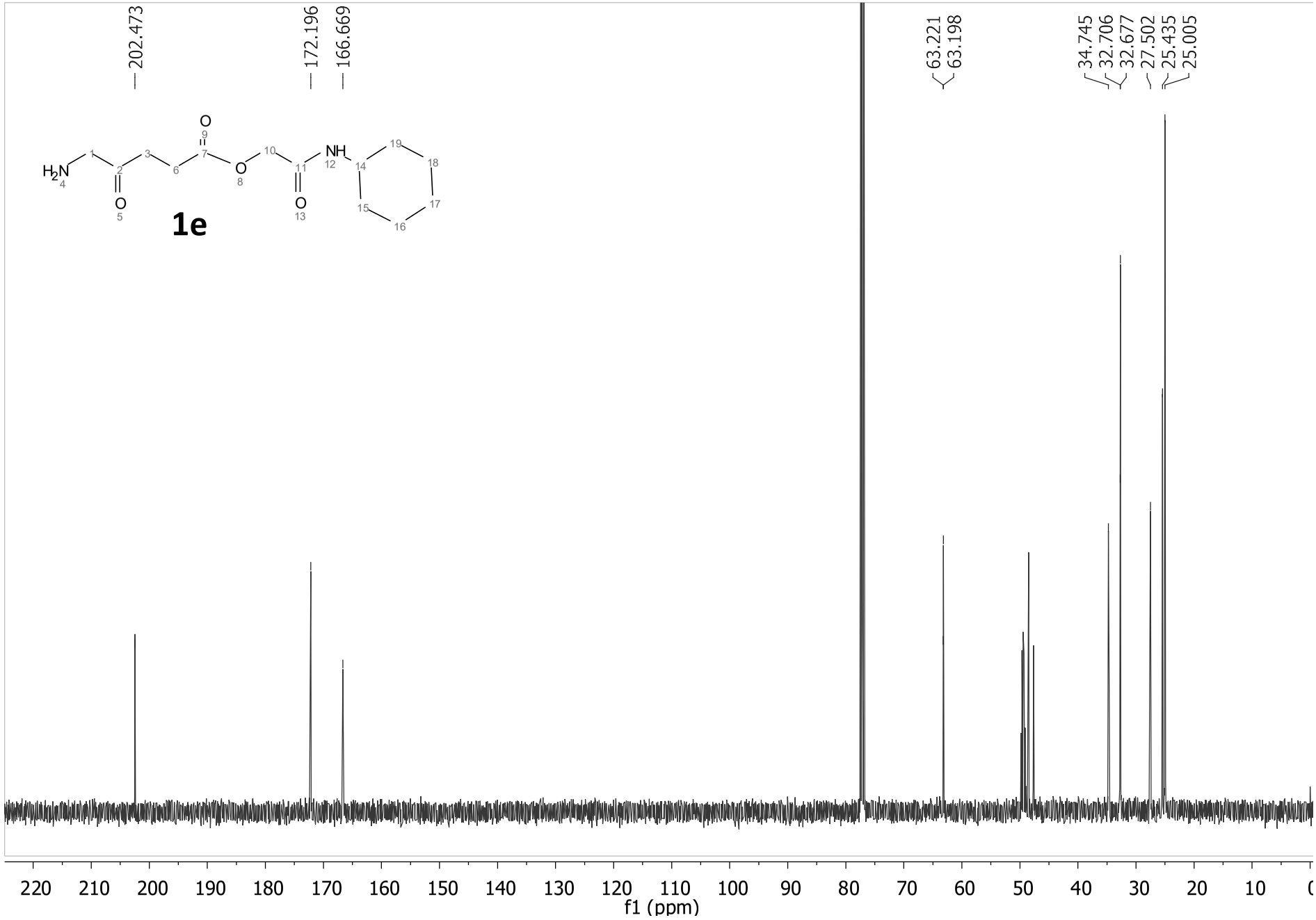


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e⁻ Conf	
114.0565	C 5 H 8 N O 2	114.0550	-14.0	2.5	ok	even	ruptura CO-O←
132.1026	C 6 H 14 N O 2	132.1019	-5.5	0.5	ok	even	ruptura COO→
154.0505	C 7 H 8 N O 3	154.0499	-4.1	4.5	ok	even	X
189.0876	C 7 H 13 N 2 O 4	189.0870	-3.4	2.5	ok	even	$[M+H-C_4H_8]^+$

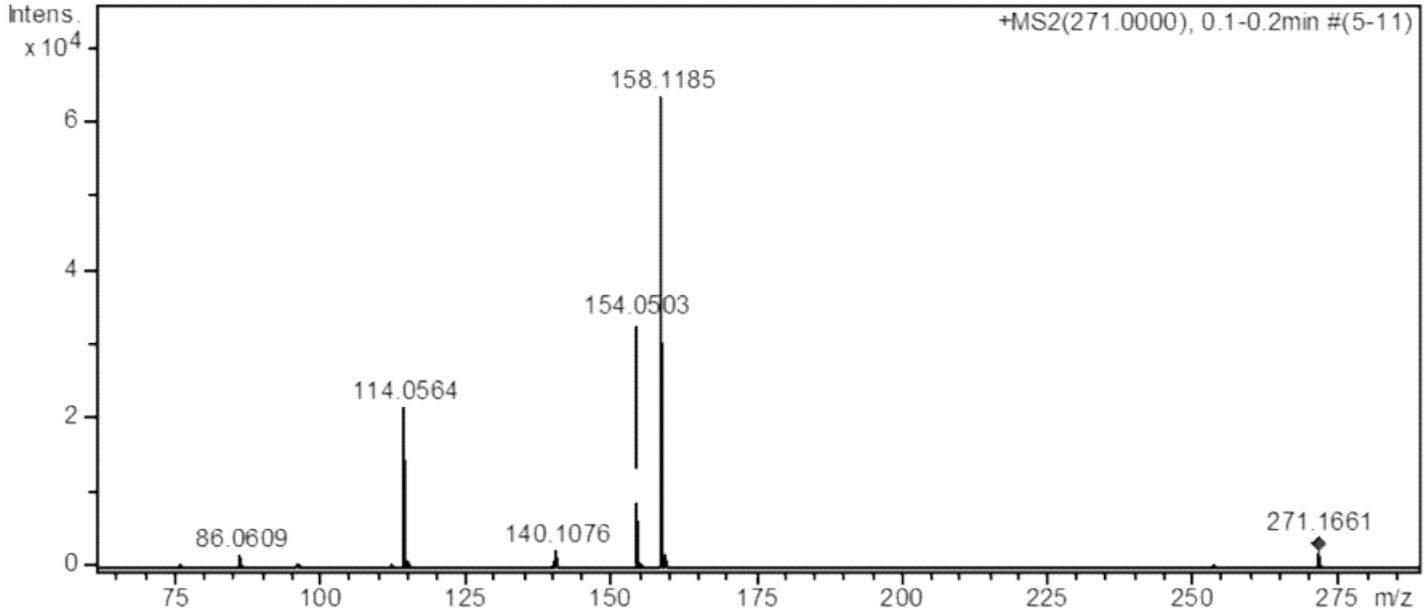
^{1}H-NRM (500 MHz) for compound 2-(cyclohexylamino)-2-oxoethyl-5-aminolevulinate (**1e**)



^{13}C-NRM (125,7 MHz) for compound **1e**

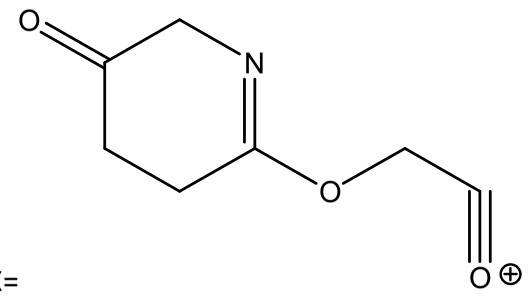


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1e** (collision Energy 15 eV)

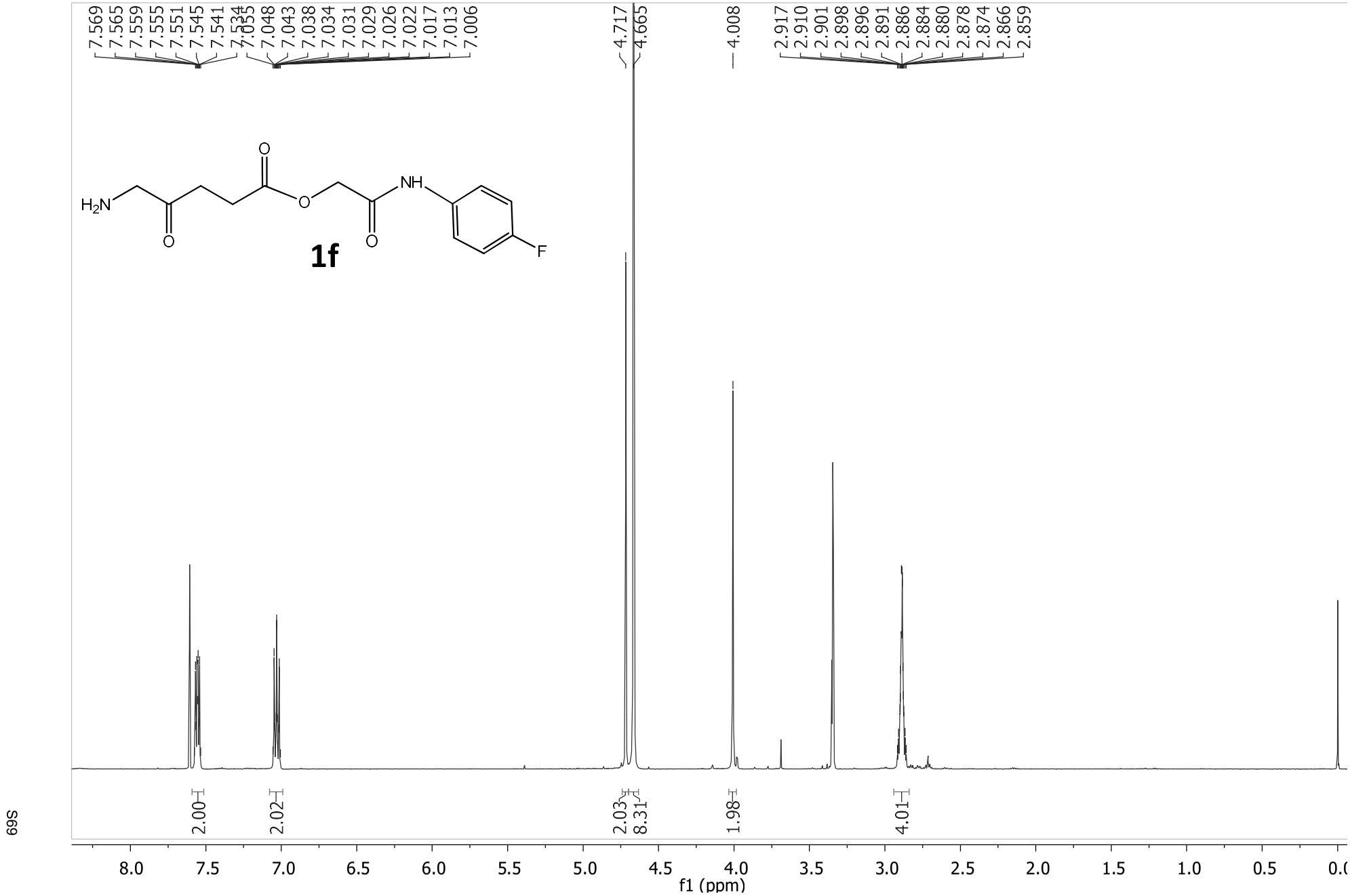


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e⁻ Conf	
114.0564	C 5 H 8 N O 2	114.0550	-12.5	2.5	ok	even	ruptura CO-O←
154.0503	C 7 H 8 N O 3	154.0499	-2.7	4.5	ok	even	X
158.1185	C 8 H 16 N O 2	158.1176	-6.2	1.5	ok	even	ruptura CO-O→

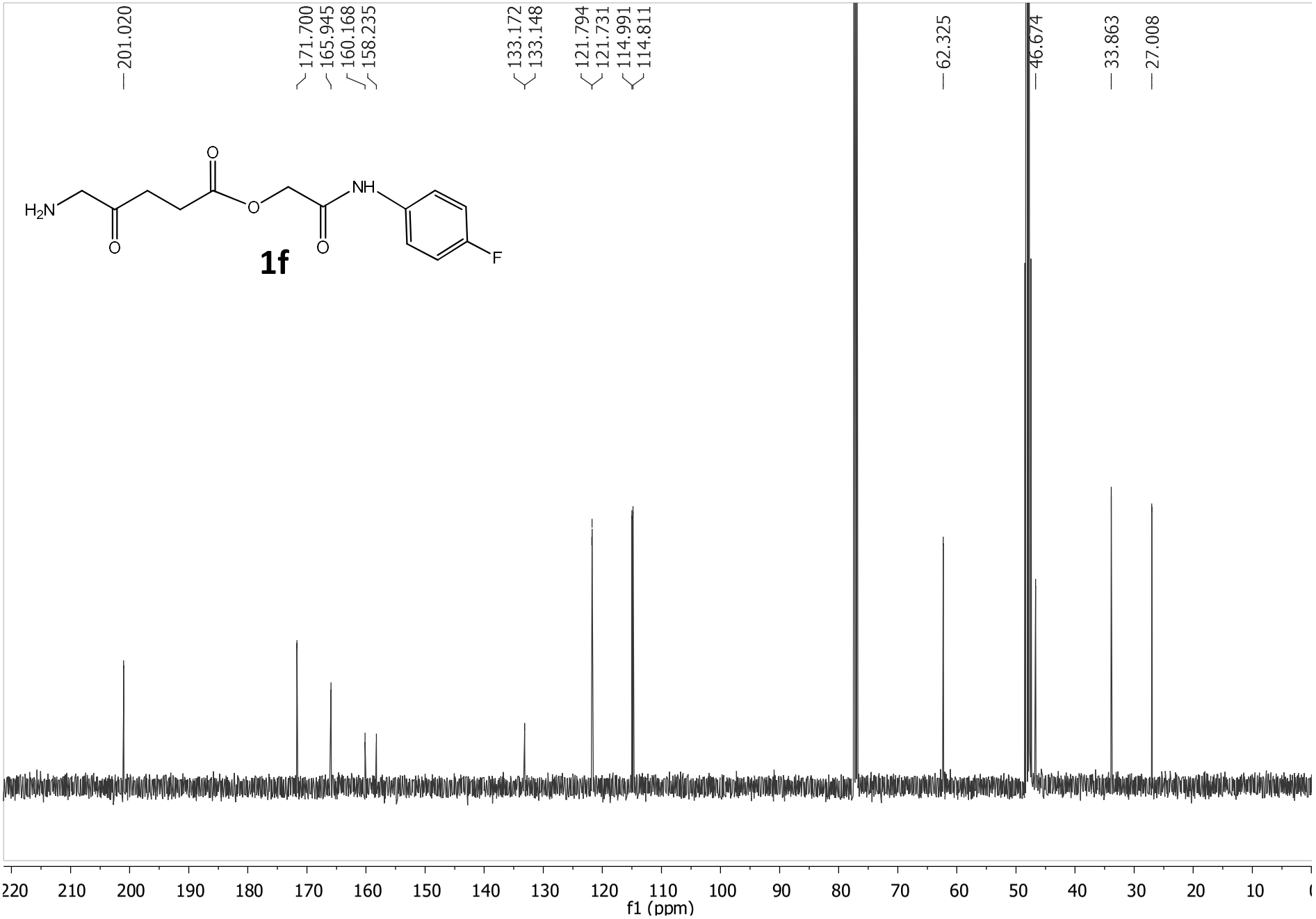
X=



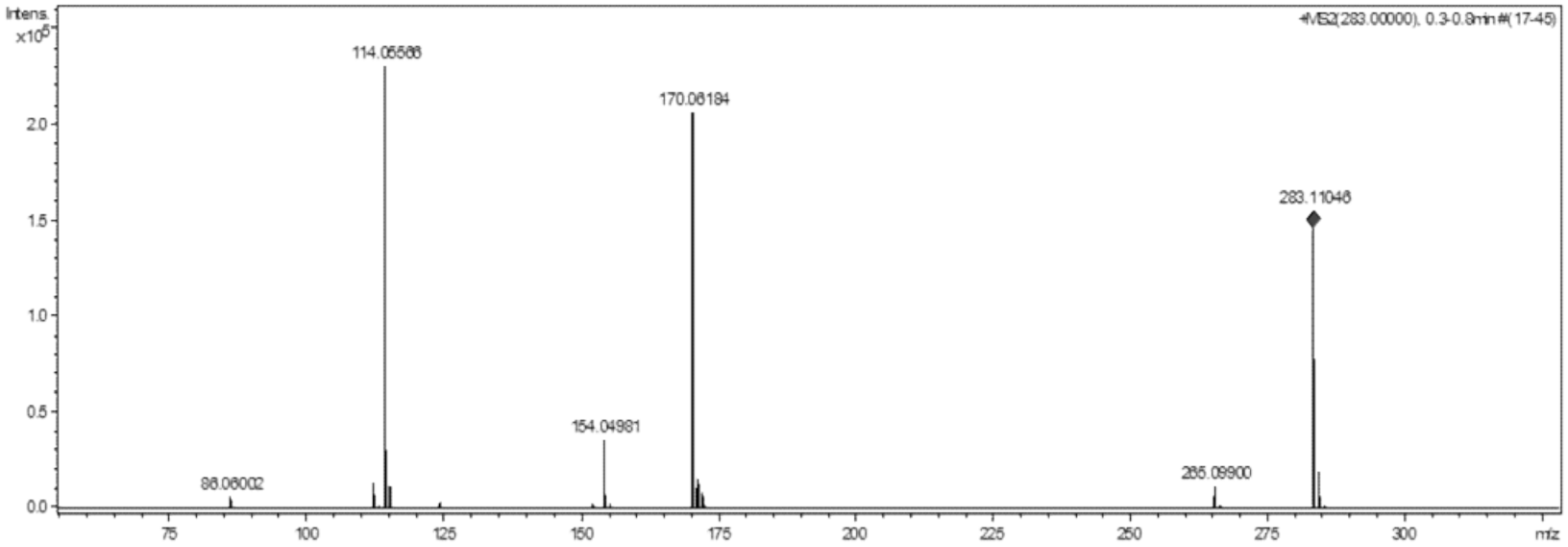
^{1}H-NRM (500 MHz) for compound 2-((4-fluorophenyl)amino)-2-oxoethyl-5-aminolevulinate (**1f**)



^{13}C-NRM (125,7 MHz) for compound **1f**

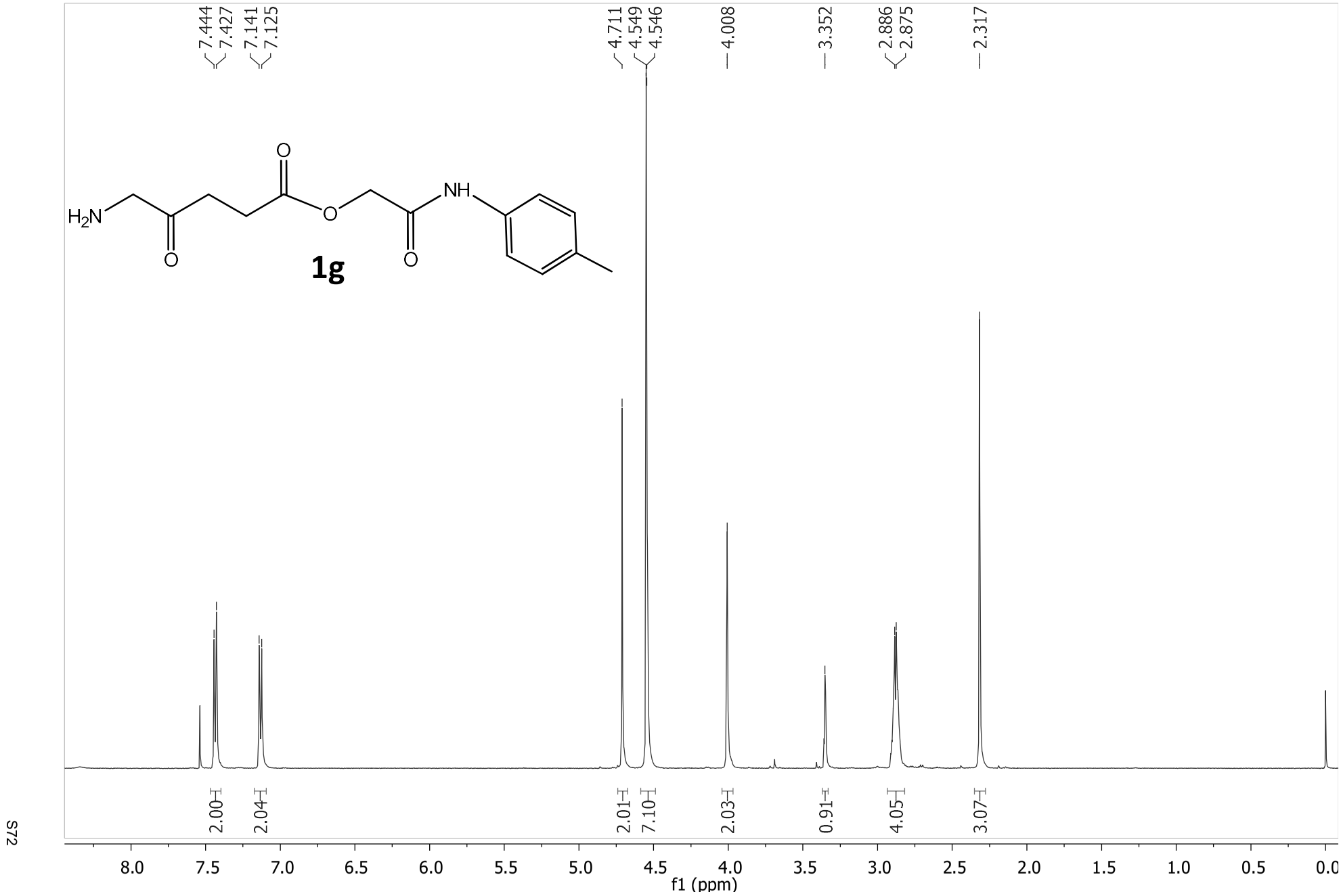


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1f** (collision Energy 10 eV)

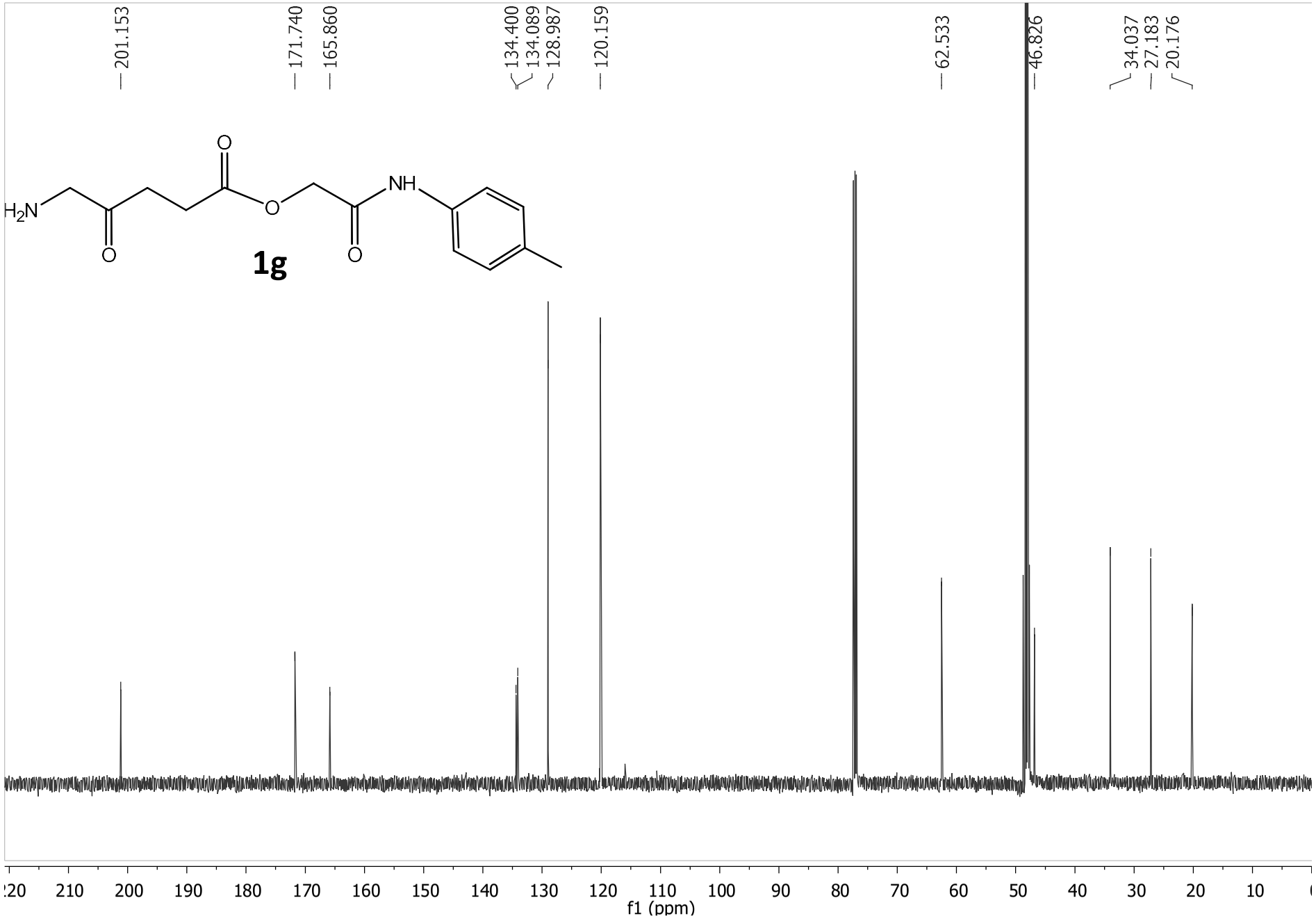


Meas. m/z	Formula	m/z	err [ppm]	e¯ Conf	N-Rule	mSigma
86.06002	C 4 H 8 N O	86.06004	0.3	even	ok	5.2
114.05566	C 5 H 8 N O 2	114.05495	-6.2	even	ok	0.7
154.04981	C 7 H 8 N O 3	154.04987	0.4	even	ok	2.4
170.06184	C 8 H 9 F N O 2	170.06118	-3.9	even	ok	22.5
265.09900	C 13 H 14 F N 2 O 3	265.09830	-2.7	even	ok	10.9

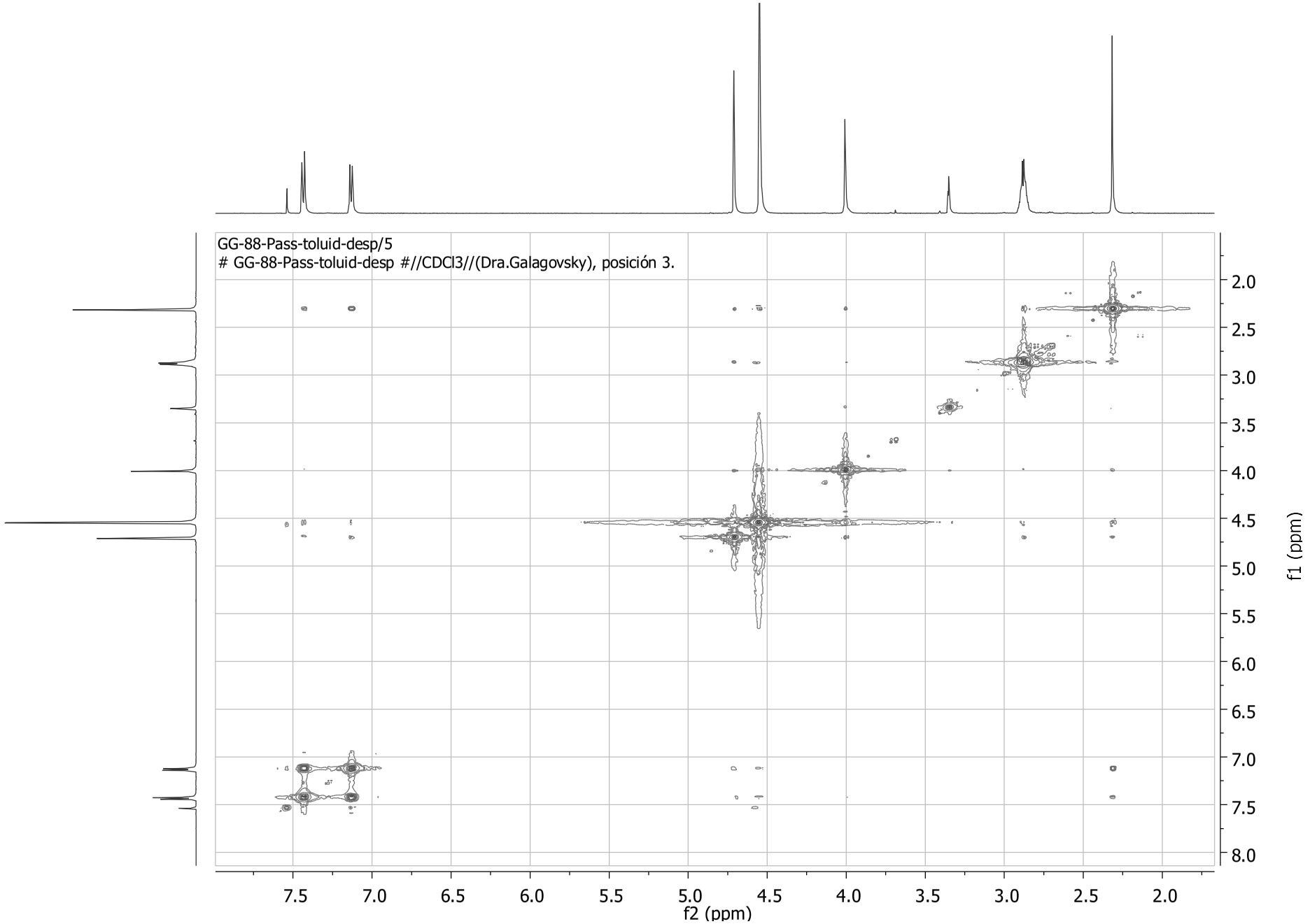
^{1}H-NRM (500 MHz) for compound 2-(4-tolylamino)-2-oxoethyl-5-aminolevulinate (**1g**)



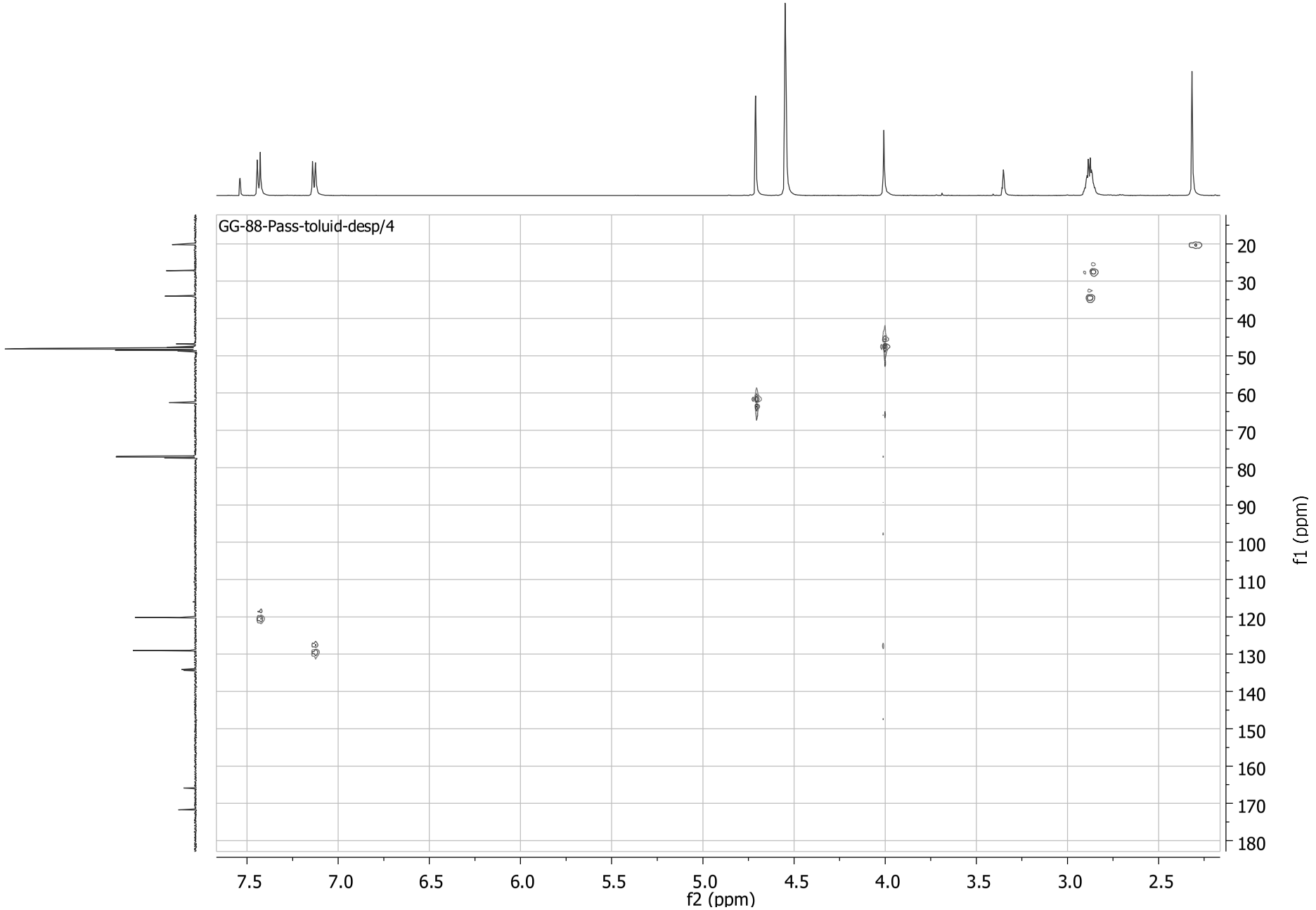
^{13}C-NRM (125,7 MHz) for compound **1g**



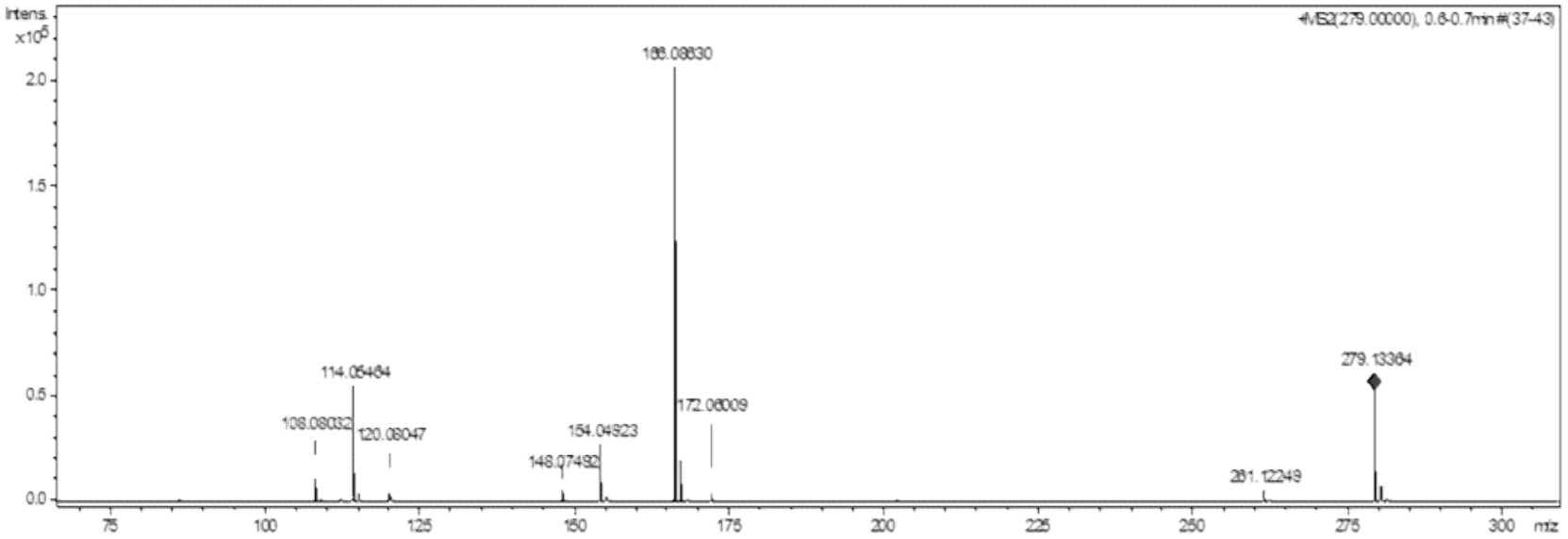
COSY (500 MHz) for compound **1g**



HSQC-DEPT (500 MHz) for compound **1g**

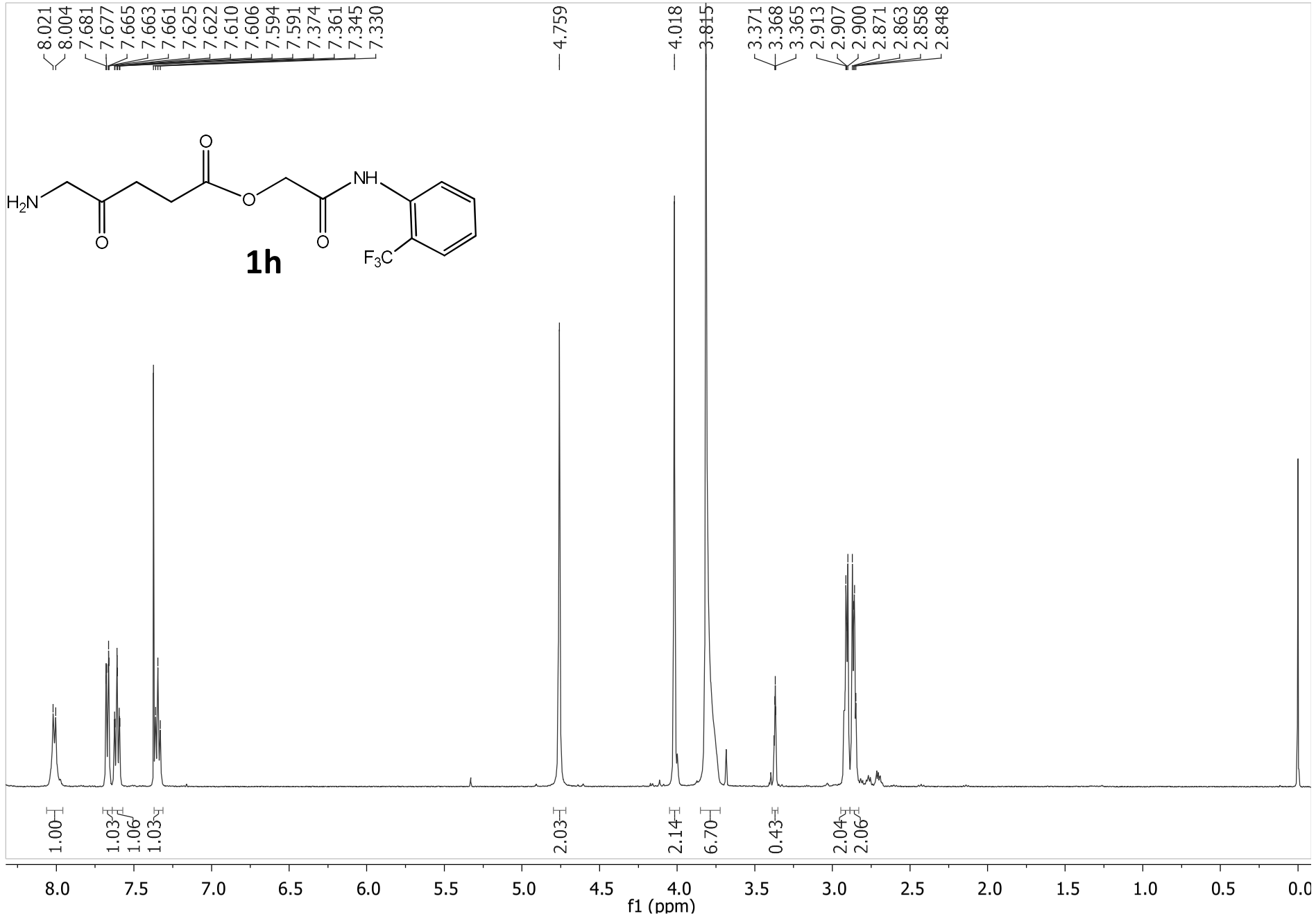


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1g** (collision Energy 10 eV)

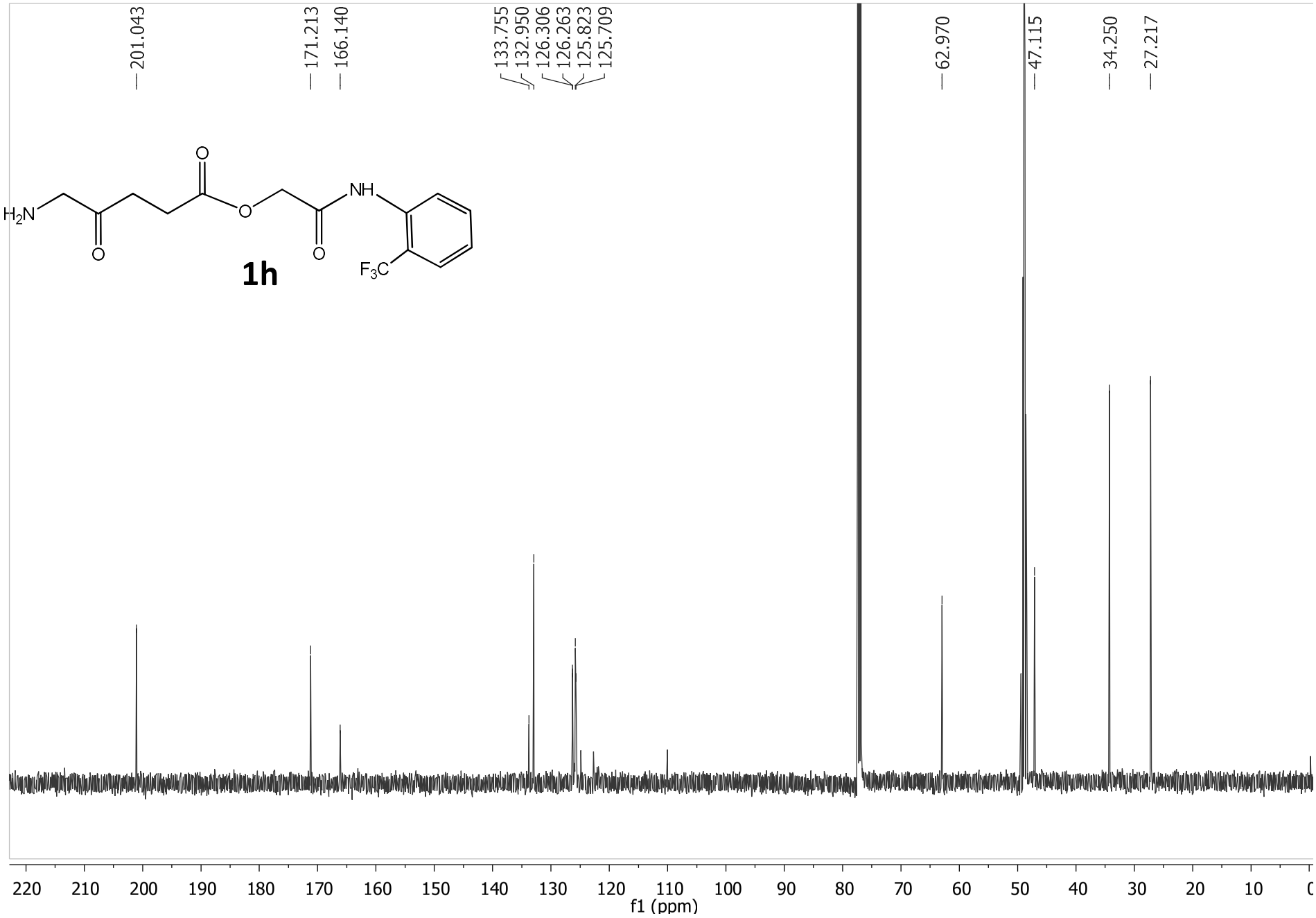


eas. m/z	Formula	m/z	err [ppm]	e¯ Conf	N-Rule	mSigma	
8.08032	C 7 H 10 N	108.08078	4.2	even	ok	5.0	
4.05464	C 5 H 8 N O 2	114.05495	2.7	even	ok	1.7	
0.08047	C 8 H 10 N	120.08078	2.6	even	ok	11.3	
8.07492	C 9 H 10 N O	148.07569	5.2	even	ok	11.4	166-H2O
4.04923	C 7 H 8 N O 3	154.04987	4.2	even	ok	3.3	
6.08630	C 9 H 12 N O 2	166.08626	-0.3	even	ok	3.4	
1.12249	C 14 H 17 N 2 O 3	261.12337	3.3	even	ok	21.4	
279.13364	C 14 H 19 N 2 O 4	279.13393	1.0	even	ok	5.6	

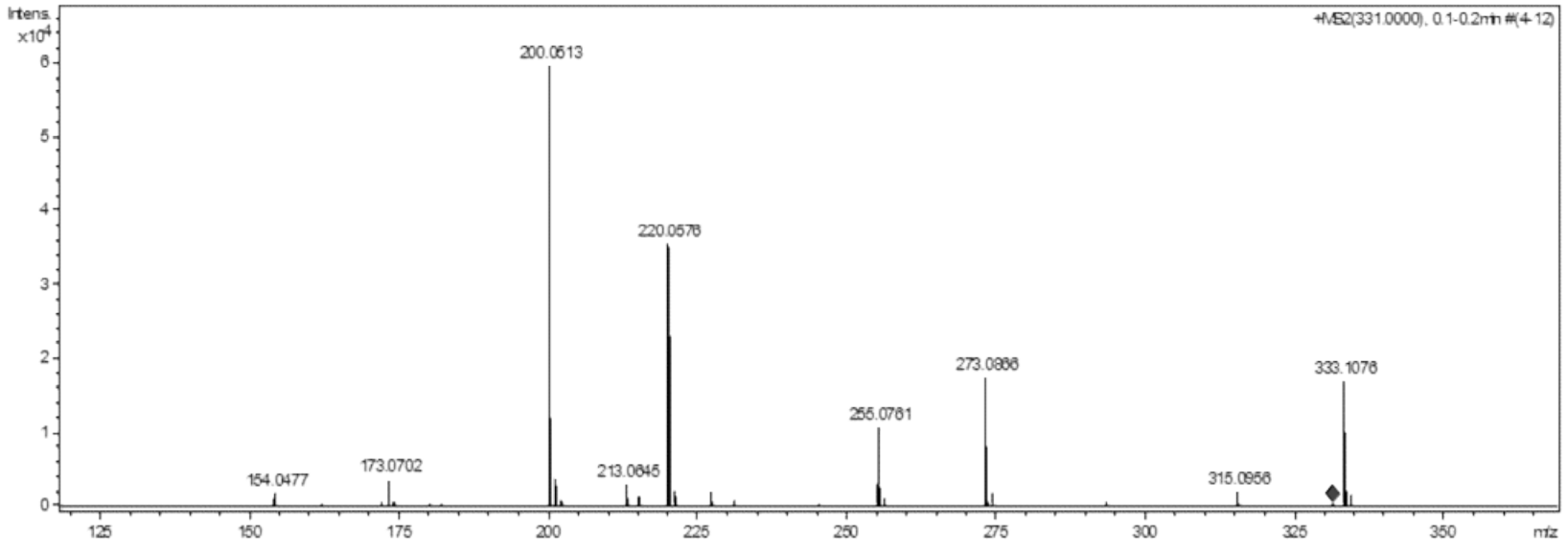
^{1}H-NRM (500 MHz) for compound 2-((2-(trifluoromethyl)phenyl)amino)-2-oxoethyl-5-aminolevulinate (**1h**)



^{13}C-NRM (125,7 MHz) for compound **1h**

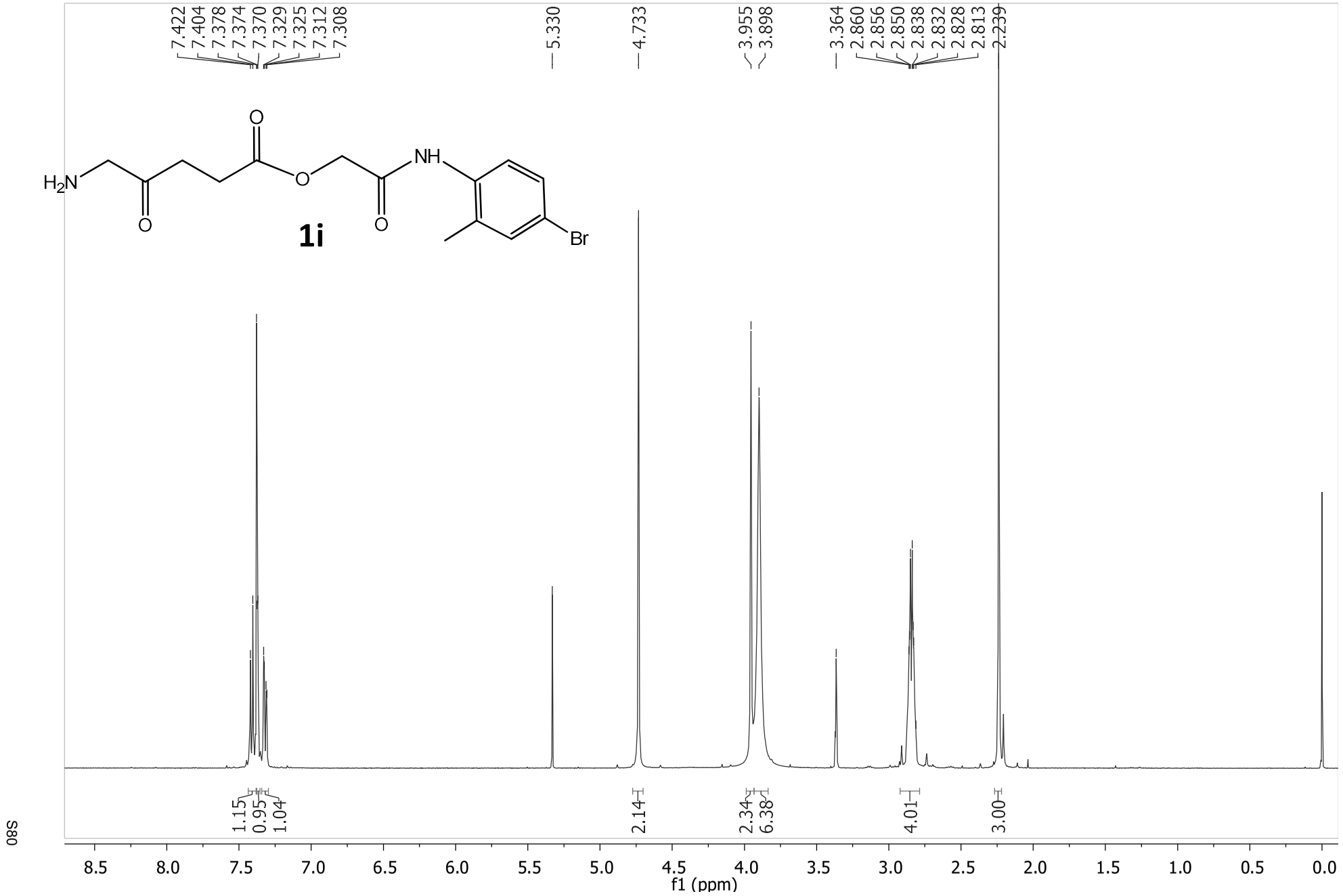


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1h** (collision Energy 10 eV)

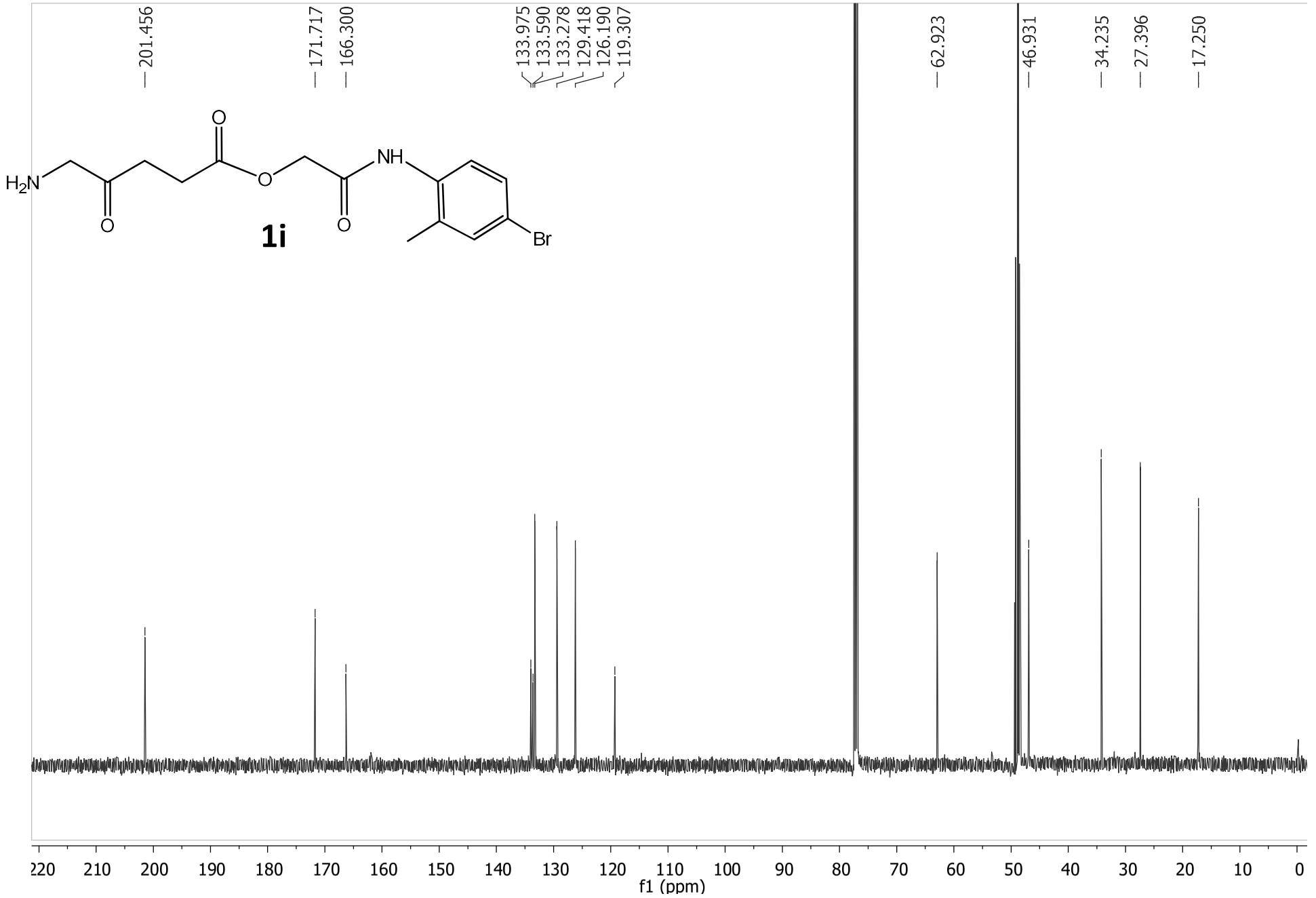


Meas. m/z	Formula	m/z	err [ppm]	rdb	e¯ Conf		N-Rule		
200.0513	C 9 H 8 F 2 N O 2	200.0518	2.3	5.5	even	ok	220-HF		
220.0576	C 9 H 9 F 3 N O 2	220.0580	2.0	4.5	even	ok			
255.0761	C 11 H 12 F N 2 O 4	255.0776	5.7	6.5	even	ok			
	C 12 H 10 F 3 N 2 O	255.0740	-8.3	7.5	even	ok			
	C 14 H 11 N 2 O 3	255.0764	1.3	10.5	even	ok		273-H2O	
273.0866	C 12 H 12 F 3 N 2 O 2	273.0845	-7.7	6.5	even	ok			
	C 14 H 13 N 2 O 4	273.0870	1.3	9.5	even	ok		-3FH?	
315.0956	C 14 H 14 F 3 N 2 O 3	315.0951	-1.7	7.5	even	ok			
333.1076	C 14 H 16 F 3 N 2 O 4	333.1057	-5.8	6.5	even	ok			

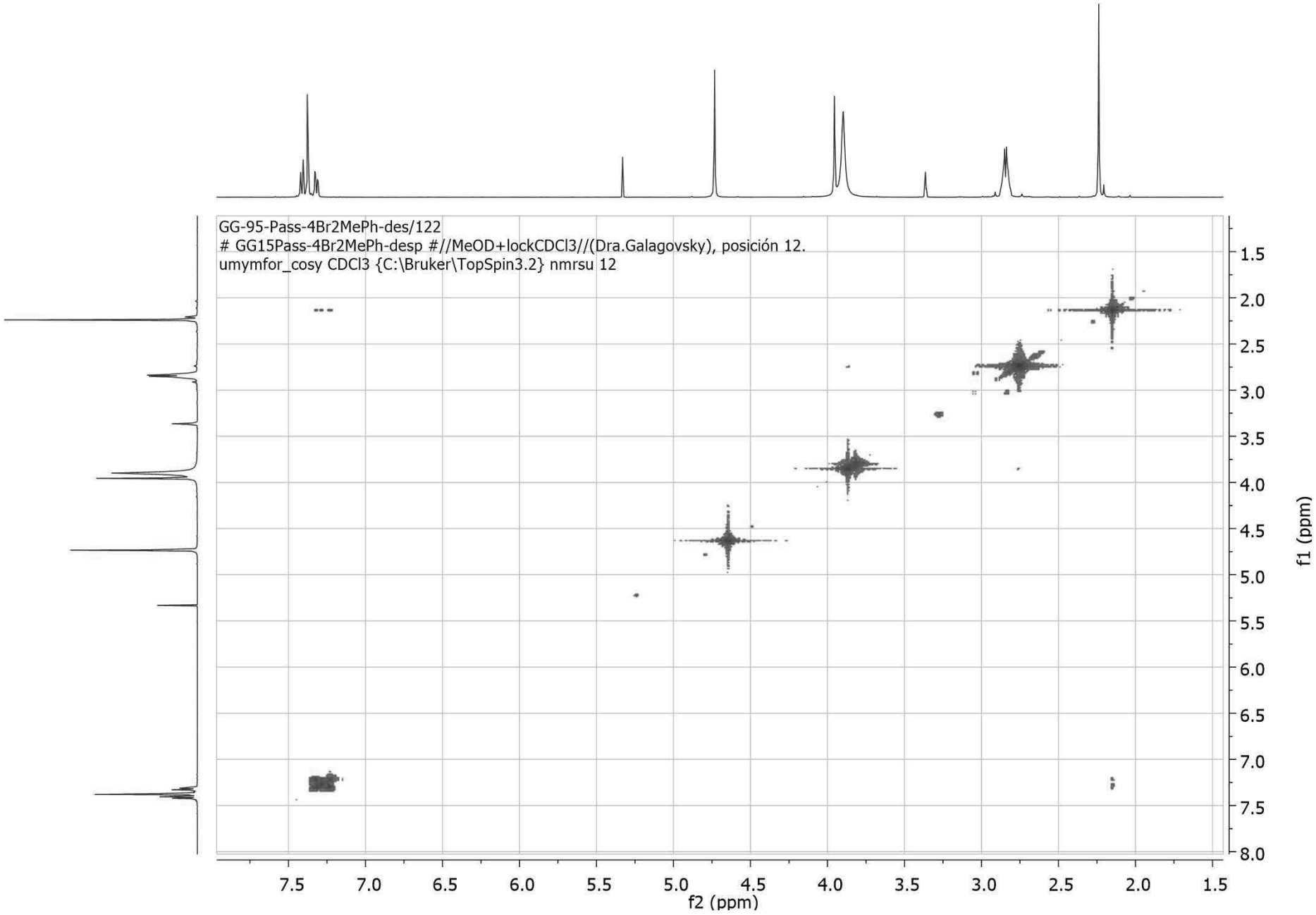
^{1}H-NRM (500 MHz) for compound 2-((4-bromo-2-methylphenyl)amino)-2-oxoethyl-5-aminolevulinate (**1i**)



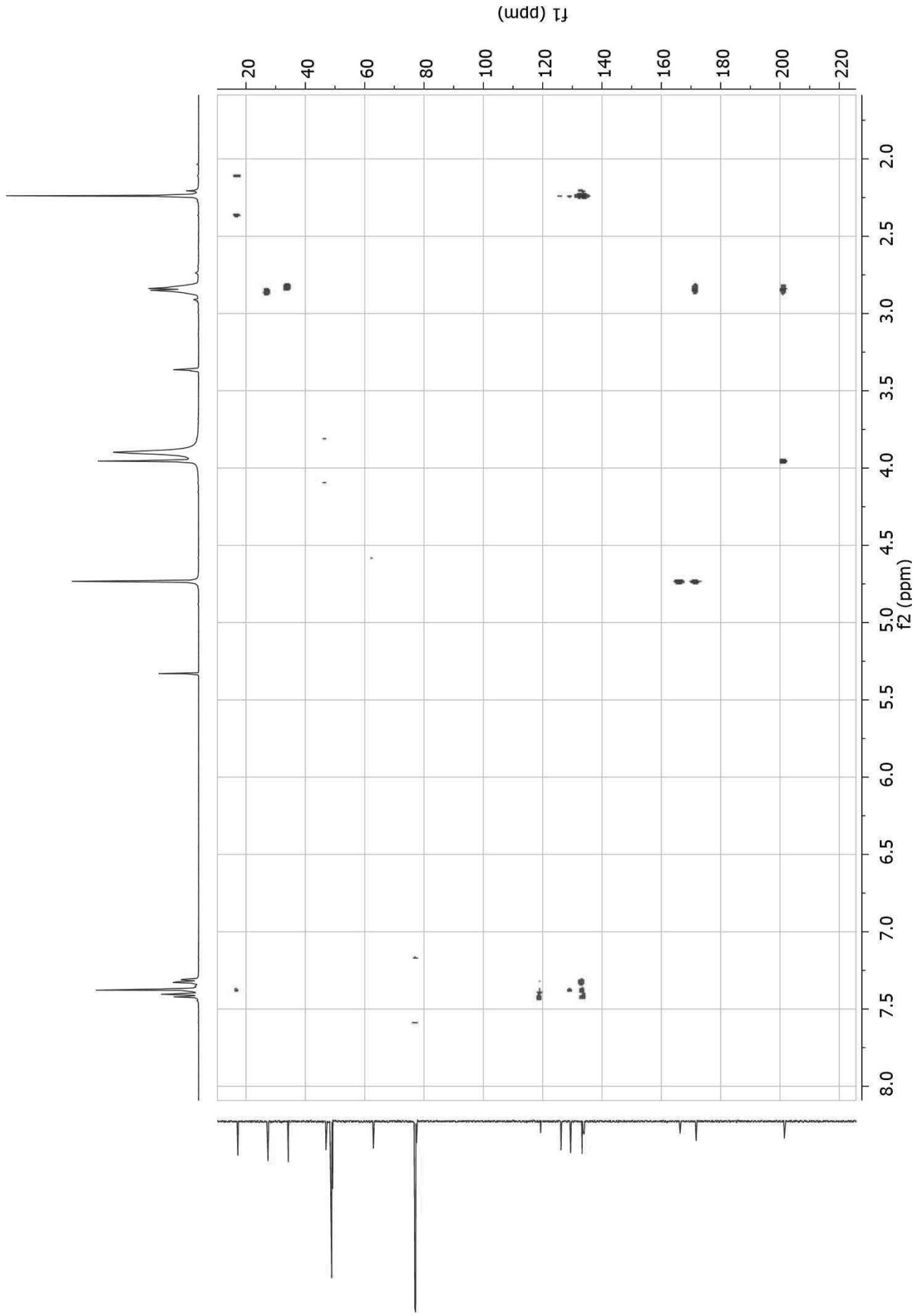
^{13}C-NRM (125,7 MHz) for compound **1i**



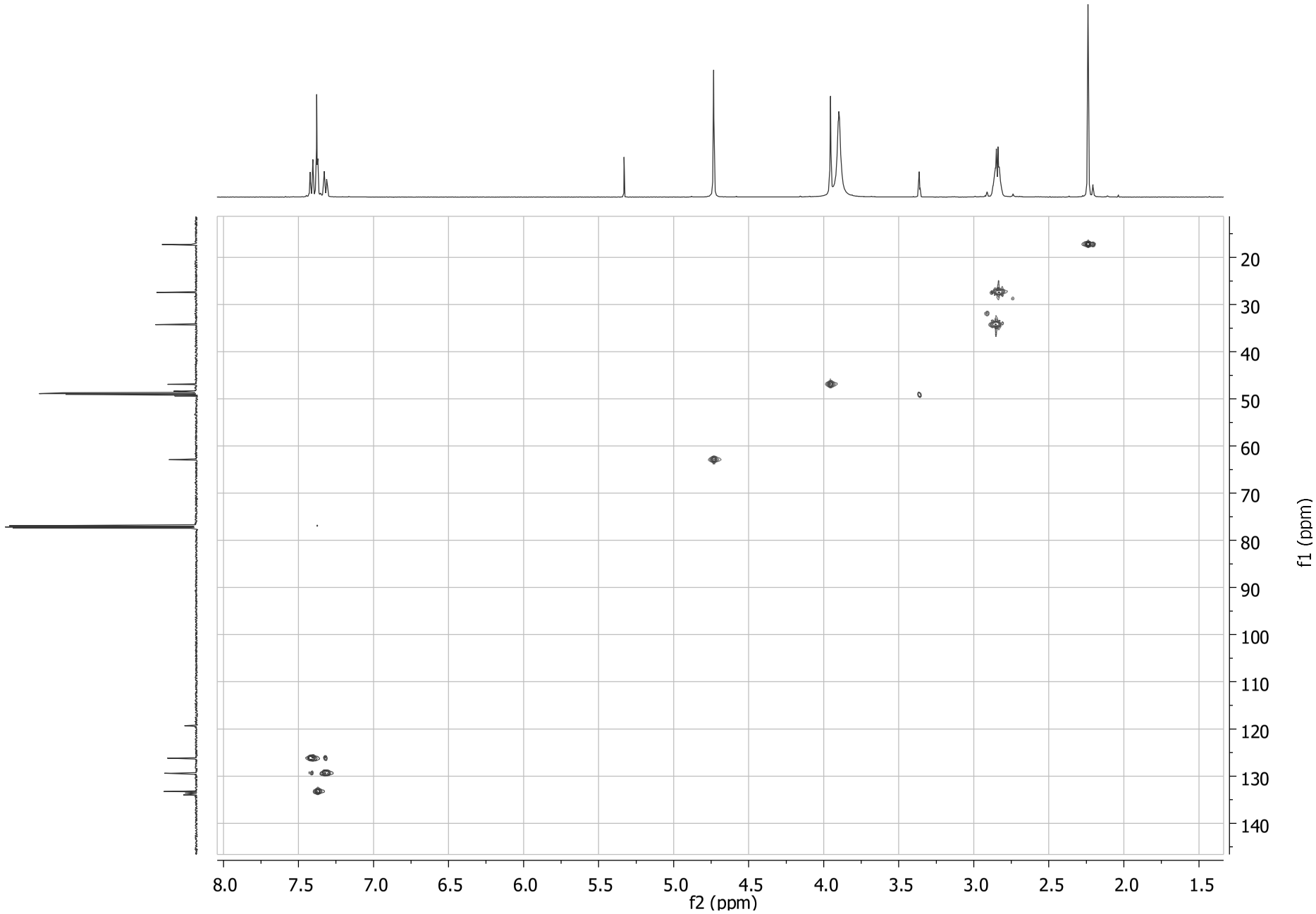
COSY (500 MHz) for compound **1i**



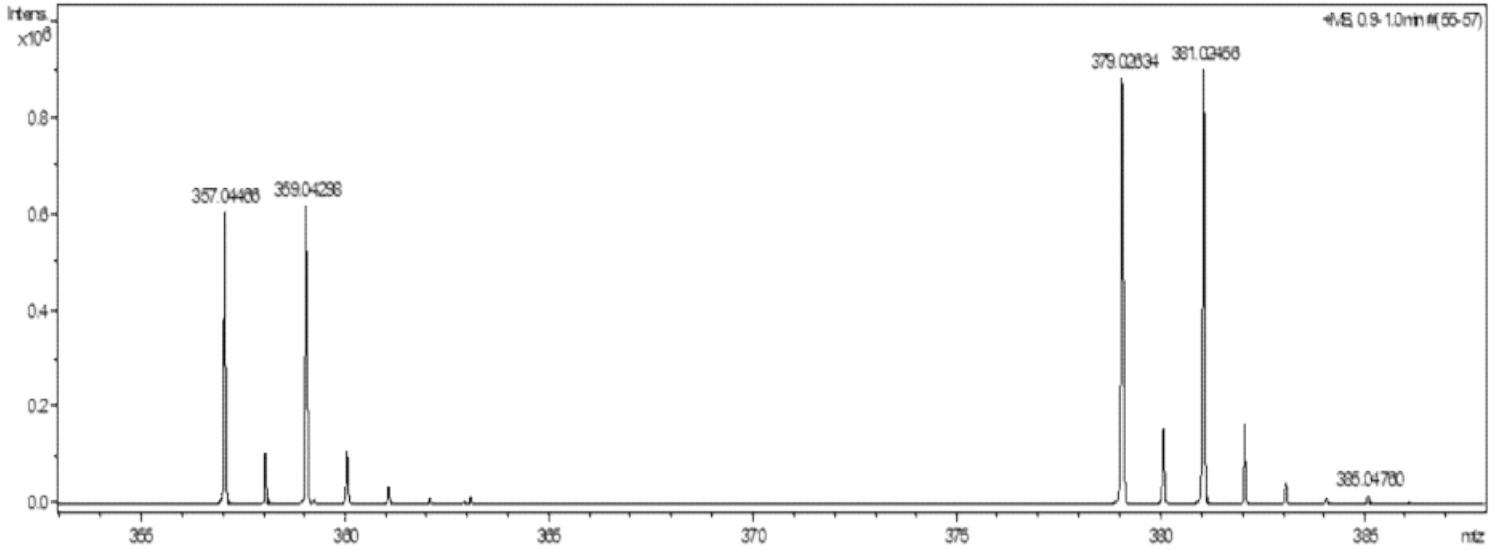
HMBC (500 MHz) for compound **1i**



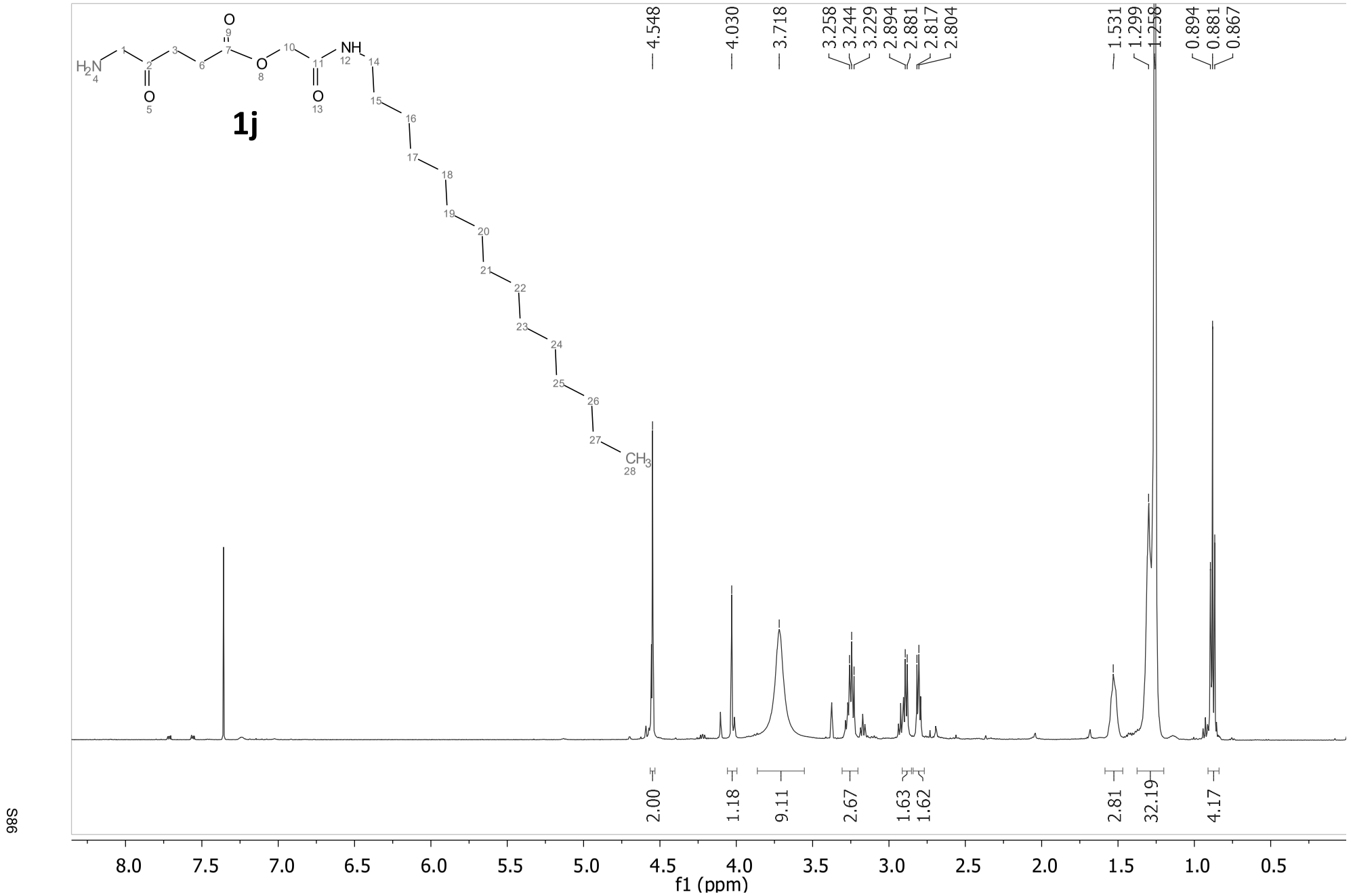
HSQC-DEPT (500 MHz) for compound **1i**



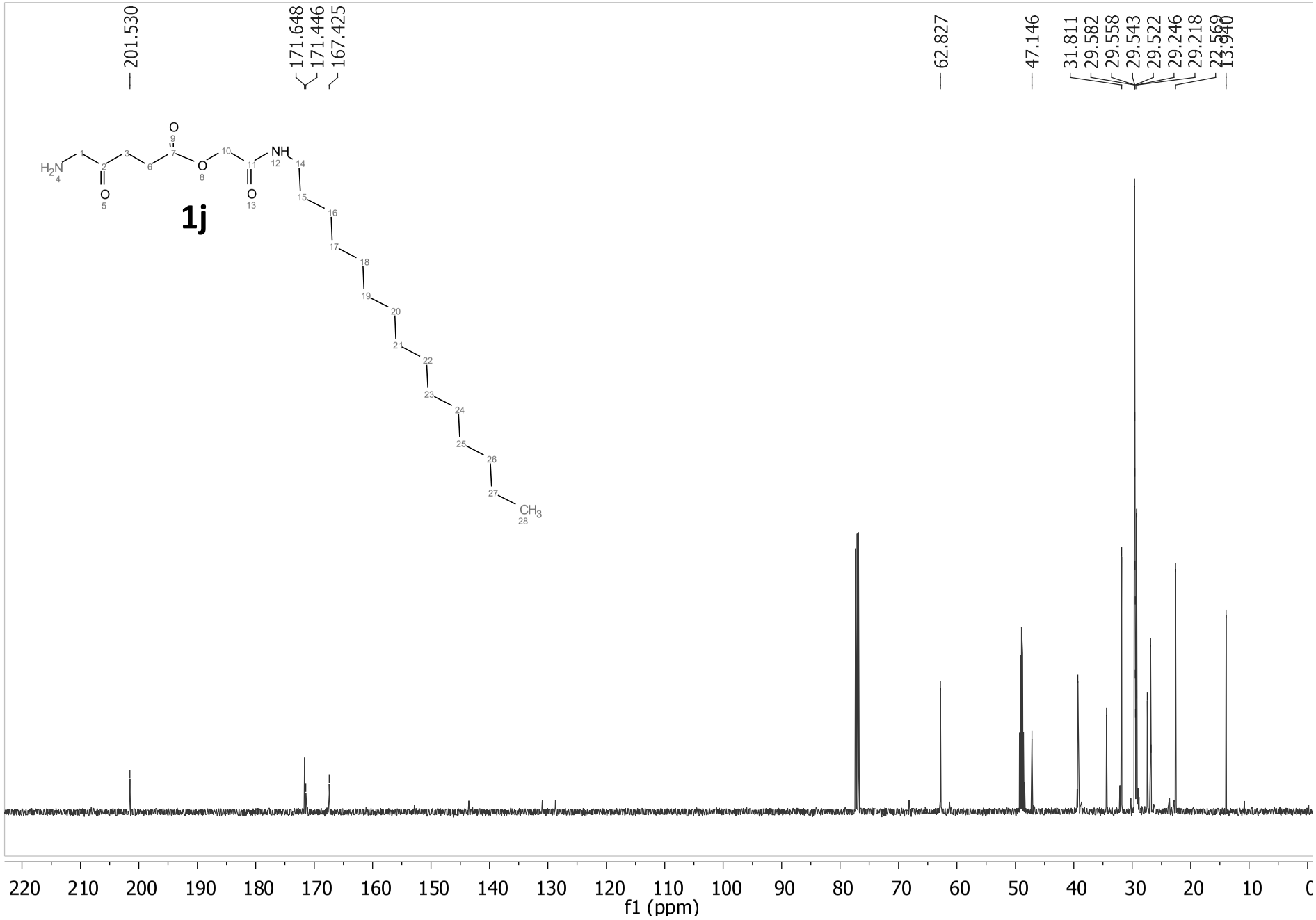
ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1i** (collision Energy 10 eV)



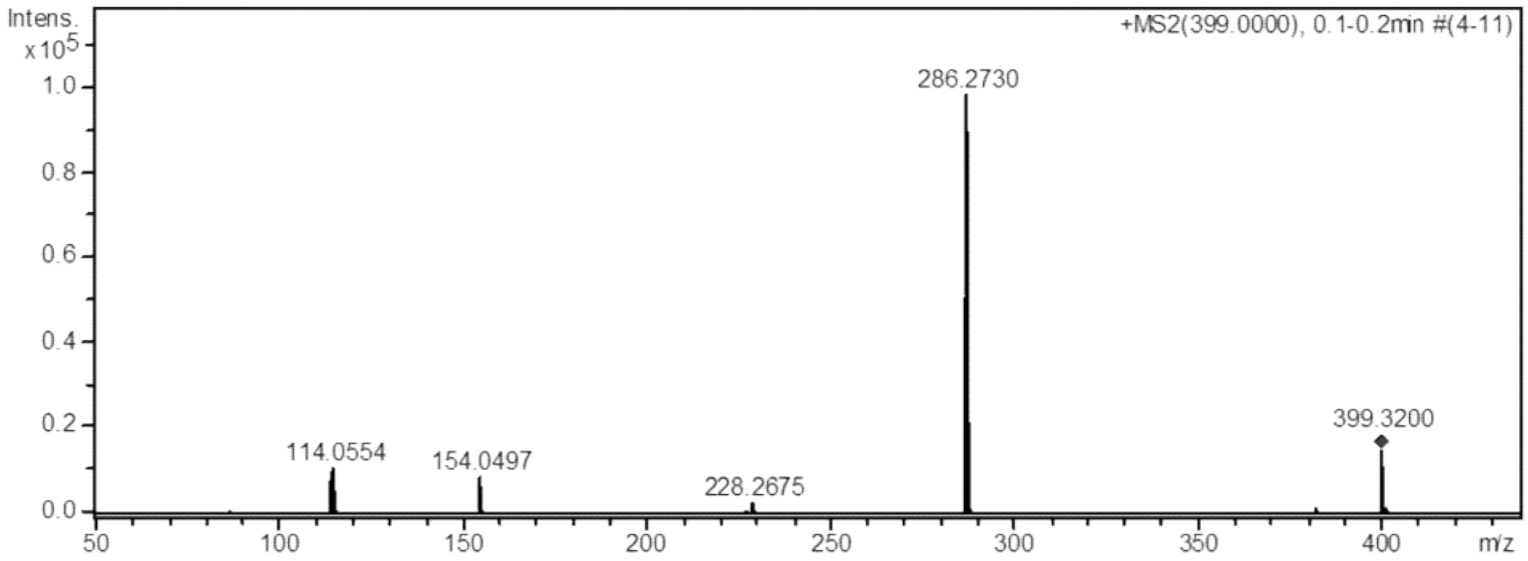
^{1}H-NRM (500 MHz) for compound 2-oxo-2-(pentadecylamino)ethyl-5-aminolevulinate (**1j**)



^{13}C-NRM (125,7 MHz) for compound **1j**

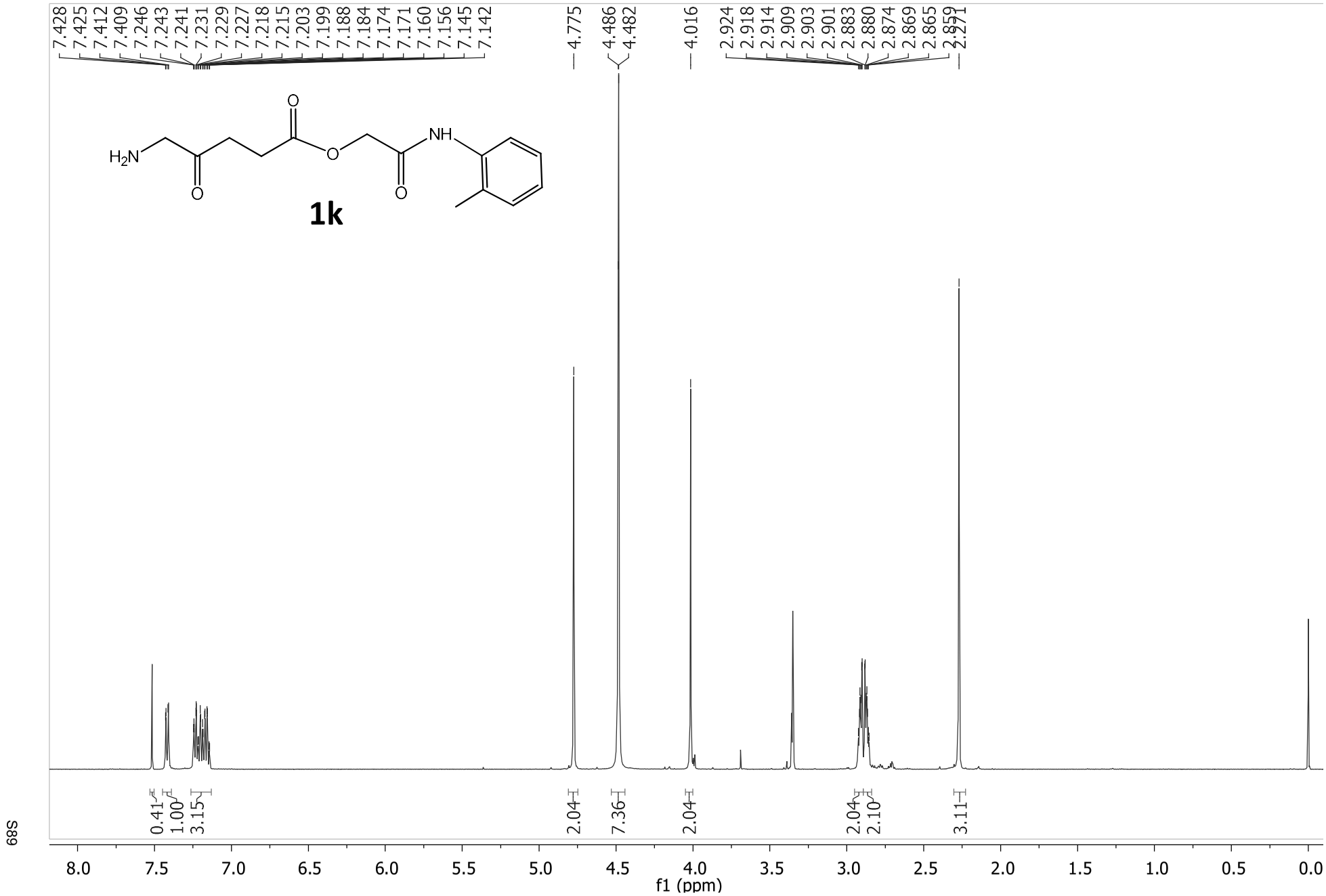


ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1j** (collision Energy 10 eV)

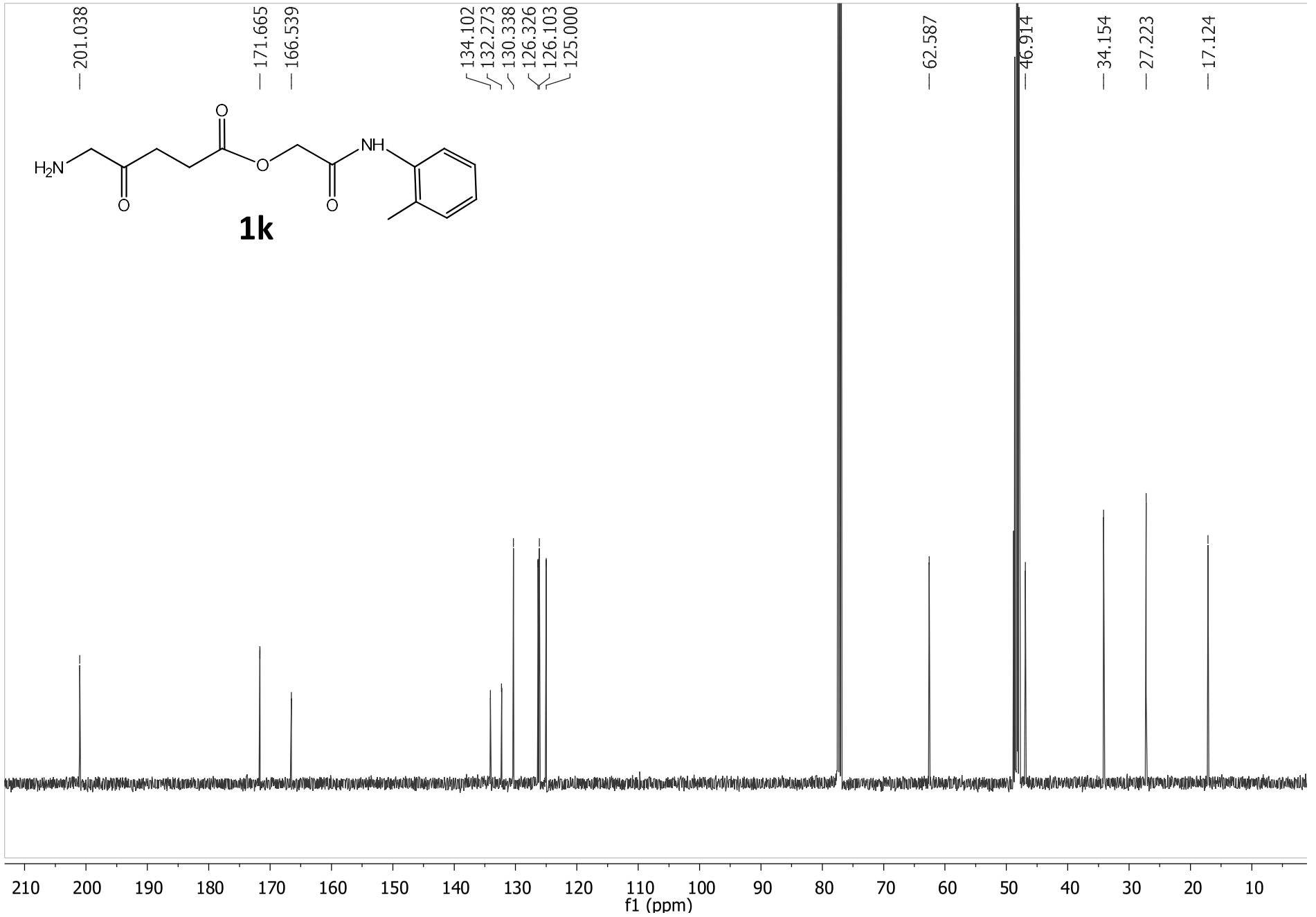


Meas. m/z	Formula	m/z	err [ppm]	rdb	N-Rule	e$^-$ Conf	Asignac.
114.0554	C 5 H 8 N O 2	114.0550	-4.2	2.5	ok	even	ruptura CO-O←
154.0497	C 7 H 8 N O 3	154.0499	0.9	4.5	ok	even	X
228.2675	C 15 H 34 N	228.2686	4.8	-0.5	ok	even	RNH_3^+
286.2730	C 17 H 36 N O 2	286.2741	3.5	0.5	ok	even	ruptura CO-O→
399.3200	C 22 H 43 N 2 O 4	399.3217	4.2	2.5	ok	even	$[M+H]^+$

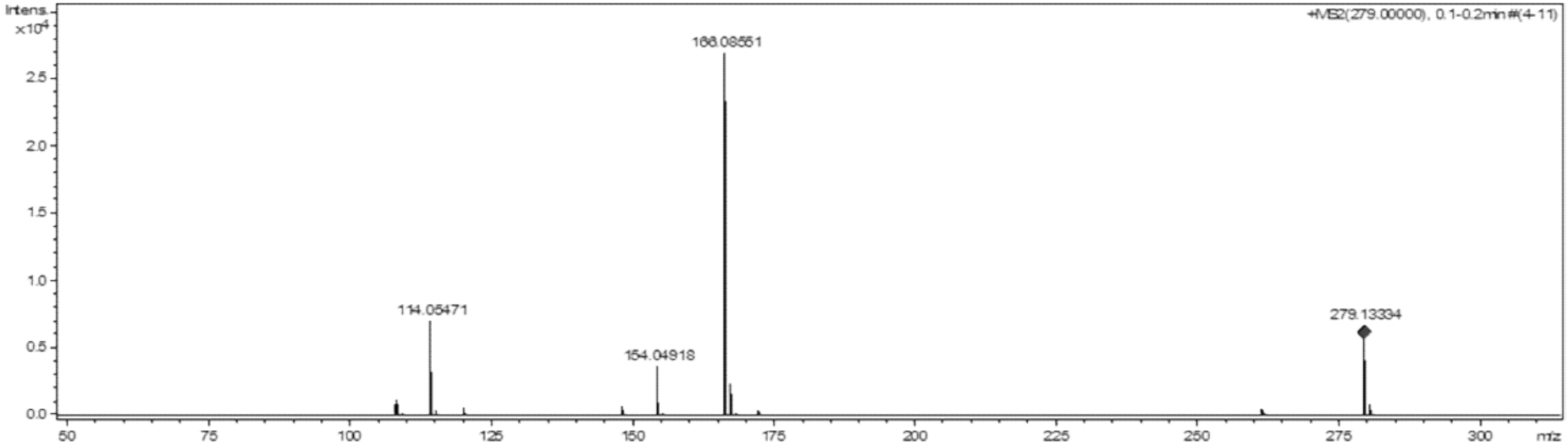
^{1}H-NRM (500 MHz) for compound 2-(2-tolylamino)-2-oxoethyl-5-aminolevulinate (**1k**)



^{13}C-NRM (125,7 MHz) for compound **1k**



ESI MS/MS spectrum of m/z ([M+H]$^+$ cation of compound **1k** (collision Energy 10 eV)



Meas. m/z	Formula	m/z	err [ppm]	e¯ Conf	N-Rule	mSigma
108.08049	C 7 H 10 N	108.08078	2.6	even	ok	12.6
114.05471	C 5 H 8 N O 2	114.05495	2.1	even	ok	4.1
148.07567	C 9 H 10 N O	148.07569	0.2	even	ok	58.4
154.04918	C 7 H 8 N O 3	154.04987	4.5	even	ok	5.5
166.08551	C 9 H 12 N O 2	166.08626	4.5	even	ok	6.5
261.12335	C 14 H 17 N 2 O 3	261.12337	0.1	even	ok	92.3
279.13334	C 14 H 19 N 2 O 4	279.13393	2.1	even	ok	13.0