Electronic Supplementary Material (ESI) for Chemical Communications

Chemoselective alkynylation of *N*-sulfonylamides versus amides and carbamates – Synthesis of tetrahydropyrazines.

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Supplementary information

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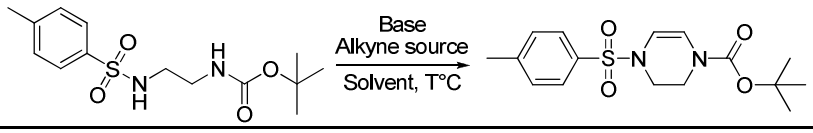
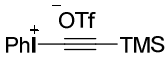
General experimental methods

Infrared (IR) spectra were recorded on a Bruker TENSOR TM 27 (IRFT), wave numbers are indicated in cm^{-1}. NMR spectra were recorded on a Bruker AVANCE 400. ^{1}H NMR were recorded at 400 MHz and data are reported as follows: chemical shift in ppm from tetramethylsilane as an internal standard with the residual solvent peak as an internal indicator ($CDCl_3$ δ: 7.26, DMSO-d6 δ: 2.50), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances, b = broad), integration. ^{13}C NMR spectra were recorded at 100 MHz and the data are reported as follows: chemical shift in ppm from tetramethylsilane as an internal standard with the residual solvent peak as an internal indicator ($CDCl_3$ δ: 77.16). Anhydrous DMF was ordered from Sigma-Aldrich and used as received. TLC was performed on silica gel plates visualized either with a UV lamp (254 nm), or using solution of *p*-anisaldehyde sulfuric acid acetic acid in EtOH followed by heating. Purification was performed on silica gel (Merck-Kieselgel 60, 230-400 mesh). Mass spectra with electronic impact (MS-EI) were recorded on a GC/MS (70 eV). HRMS were performed at the Laboratoire de Spectrométrie de Masse SM3E de l'Université Pierre et Marie Curie de Paris).

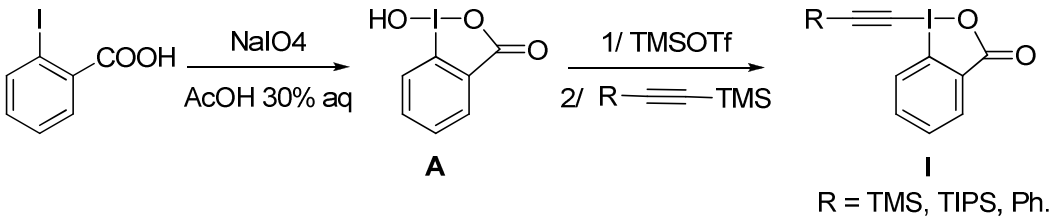
1. Optimization of the conditions for the synthesis of tetrahydropyrazines.



Entry	Solvent	Base	Base equiv	Temperature	Alkyne source	Time	Yield
1	Toluene	tBuOK	2	reflux	TMS-EBX	2h	31%
2	Toluene	tBuOK	4	reflux	TMS-EBX	2h	53%
3	Toluene	tBuOK	4	75 °C	TMS-EBX	2h	0%
4	THF	tBuOK	2	rt	TMS-EBX	2h	17%
5	DMF	tBuOK	2	rt	TMS-EBX	2h	56%
6	**DMF**	**NaH**	**2**	**rt**	**TMS-EBX**	**2h**	**56%**
7	DMF	NaH	2	rt	TIPS-EBX	2h	56%
8	DMF	NaH	2	rt		24h	56%

2. Experimental procedures.

R-ethynyl-1,2-benziodoxol-3(1H)-one (R-EBX) I



According to a reported procedure[1], 2-iodobenzoic acid (1 equiv) was refluxed in 30% v:v aqueous acetic acid (2 mL per mmol) with $NaIO_4$ (1 equiv) for 4 h. Iced water was then added and the mixture was cooled and then filtered. The obtained solid was dried under air to afford benziodoxole **A** in 97% yield.

To a suspension of benziodoxole **A** (1 equiv) in CH_2Cl_2 was added TMSOTf (1.1 equiv) and the mixture was stirred for 1 h in the dark. The TMS-ethynyl reagent (1.1 equiv) was then added and the mixture stirred overnight at r.t in the dark. The solution was then diluted with a saturated aqueous solution of $NaHCO_3$ until it becomes limpid, the organic phase washed with a saturated aqueous solution of $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated under vacuum. If needed, the crude product was recrystallized in acetonitrile to afford R-EBX **I** (R = TMS, 67%; R = TIPS, 73%; R = Ph, 50%) as a white solid.

TMS-EBX (Ia)[1]

Formula: $C_{12}H_{13}IO_2Si$ **Mass:** 344.22 $g.mol^{-1}$

IR (neat): 1602, 1582, 1558, 1436, 1327, 1298, 1249, 1148, 1003, 877, 846, 826, 766, 745, 687, 642, 616 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 8.32 (dd, 1H, *J* = 7.0, 2.1 Hz, ArH), 8.14 (dd, 1H, J = 7.8, 1.3 Hz, ArH), 7.69 (m, 2H, ArH), 0.24 (s, 9H, -TMS).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 167.2, 135.4, 132.8, 131.9, 126.7, 117.4, 115.9, 64.4, 0.3.

MS (EI, 70 eV) *m/z* (abundance): 320 (34), 306 (15), 305 (99), 231 (87), 203 (34), 163 (15), 133 (43), 119 (28), 91 (18), 77 (18), 76 (100), 75 (30), 74 (26), 73 (44), 59 (10), 50 (46).

TIPS-EBX (Ib)[1]

Formula: $C_{18}H_{25}IO_2Si$ **Mass:** 428.38 $g.mol^{-1}$

IR (neat): 2943, 2864, 1615, 1603, 1559, 1461, 1438, 1327, 1294, 1250, 1075, 1017, 993, 882, 830, 745 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 8.37 (m, 1H, ArH), 8.26 (m, 1H, ArH), 7.72 (m, 2H, ArH), 1.1 (m, 21H, -TIPS).

[1] D. Fernandez Gonzalez, J. P. Brandt and J. Waser, *Chem. Eur. J.*, 2010, **16**, 9457-9461.

NMR ^{13}C (100 MHz, $CDCl_3$): δ 166.5, 134.8, 132.5, 131.5, 126, 115.7, 114.2, 64.7, 18.6, 11.2.

Ph-EBX (Ic)[1]

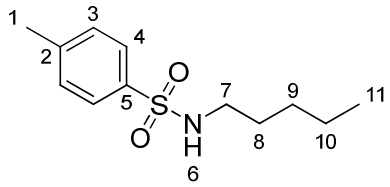
Formula: $C_{15}H_9IO_2$ **Mass:** 348.13 g.mol^{-1}

IR (neat): 3059, 2139, 1616, 1605, 1585, 1557, 1487, 1437, 1330, 1304, 1211, 1147, 1007, 830, 794, 745, 690, 669 cm^{-1}.

NMR ^{1}H (400 MHz, DMSO): δ 8.32 (d, 1H, ^{3}J = 8.3 Hz, ArH), 8.14 (dd, 1H, J = 7.5, 1.7 Hz, ArH), 7.91 (m, 1H, ArH), 7.81 (td, 1H, J = 7.5, 1.0 Hz, ArH), 7.72 (m, 2H, ArH), 7.53 (m, 3H, ArH).

NMR ^{13}C (100 MHz, DMSO): δ 166.2, 135.1, 132.5, 132.0, 131.3, 130.6, 129.0, 137.4, 120.5, 116.3, 104.2, 52.1.

4-Methyl-*N*-pentylbenzenesulfonamide (1)[2]



To a solution of amylamine (435 mg, 5 mmol, 1 equiv) in CH_2Cl_2, was added TsCl (1.045 g, 5.5 mmol, 1.1 equiv) and Et_3N (555 mg, 5.5 mmol, 1.1 equiv) at 0 °C. The mixture was stirred for 5 min at 0 °C, diluted with water and then extracted with CH_2Cl_2. The organic phase was then washed with water and brine, dried over $MgSO_4$, filtered and concentrated under vacuum to give the desired product as a colorless oil (1.031g, 85%).

Formula: $C_{12}H_{19}NO_2S$ **Mass:** 241.11 g.mol^{-1}

IR (neat): 3280, 2957, 2931, 2862, 1599, 1495, 1425, 1322, 1156, 1093, 1020, 900, 814, 707, 660 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.76 (d, 2H, ^{3}J = 8.2 Hz, ArH), 7.31 (d, 2H, ^{3}J = 8.2 Hz, ArH), 4.84 (t, 1H, ^{3}J = 6.2 Hz, -N*H*), 2.91 (m, 2H, CH_2), 2.42 (s, 3H, CH_3), 1.44 (m, 2H, CH_2), 1.23 (m, 4H, $2CH_2$), 0.83 (t, 3H, ^{3}J = 6.7 Hz, CH_3).

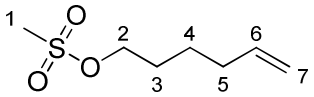
NMR ^{13}C (100 MHz, $CDCl_3$): δ 143.3, 137.0, 129.7, 127.1, 43.2, 29.2, 28.6, 22.1, 21.5, 13.9.

MS (EI, 70 eV) *m/z* (abundance): 241 (8), 184 (68), 172 (12), 156 (8), 155 (91) 92 (11), 91 (100), 86 (12), 65 (25).

Hex-5-enyl methanesulfonate (2a)[3]

[2] T. Nishikata and H. Nagashima, *Angew. Chem. Int. Ed.*, 2012, **51**, 5363-5366.

[3] R. W. Bates and S. Sridhar, *J. Org. Chem.*, 2011, **76**, 5026-5035.



To a solution of hexenol (1 g, 10 mmol, 1 equiv) in CH_2Cl_2 (20 mL) was added MsCl (1.37 g, 12 mmol, 1.2 equiv) and Et_3N (5.05 g, 50 mmol, 5 equiv). The mixture was stirred at rt for 1 h and then water was added to the mixture. The aqueous layer was then extracted 3 times with CH_2Cl_2 and the combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum to afford the product as a yellowish oil (1.97 g, quant.).

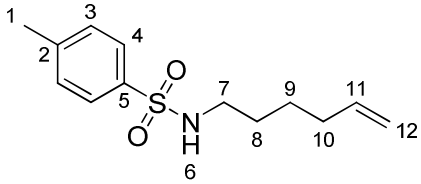
Formula: $C_7H_{14}O_3S$ **Mass:** 178.06 g.mol^{-1}

NMR ^{1}H (400 MHz, $CDCl_3$): δ 5.79 (ddt, 1H, ^3J = 17.1, 10.3, 6.7 Hz, =C*H*R), 4.99 (m, 2H, =CH_2), 4.23 (t, 2H, ^3J = 6.7 Hz), 3.00 (s, 3H, CH_3), 2.05 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 1.52 (m, 2H, CH_2).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 137.9, 115.2, 70.0, 37.3, 33.0, 28.5, 24.6.

MS (EI, 70 eV) *m/z* (abundance): 82 (29), 81 (11), 79 (32), 68 (6), 67 (100), 65 (5), 55 (20), 54 (100), 53 (8).

***N*-(Hex-5-enyl)-4-methylbenzenesulfonamide (2)** [4]



To a suspension of NaH (56 mg, 1.4 mmol, 2.5 equiv, 60% dispersion in mineral oil) in DMF (2 mL) was slowly added tosylamine (287 mg, 1.68 mmol, 3 equiv) in DMF (1 mL) and the mixture stirred for 15 min at rt. A solution of Mesylate **2a** (100 mg, 0.56 mmol, 1 equiv) in DMF (1 mL) was then added to the tosylamide. The mixture was then heated to 80 °C for 2 h before being cooled to rt and quenched with saturated aqueous NH_4Cl solution. The solution was extracted with AcOEt, the organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 80/20) afforded the product as a colorless oil (113 mg, 80%).

Formula: $C_{13}H_{19}NO_2S$ **Mass:** 253.11 g.mol^{-1}

IR (neat): 3279, 2930, 2862, 1640, 1599, 1495, 1424, 1322, 1156, 1093, 995, 909, 814, 706, 660 cm^{-1}.

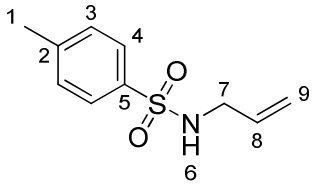
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.76 (d, 2H, ^3J = 8.3 Hz, ArH), 7.30 (d, 2H, ^3J = 8.3 Hz, ArH), 5.71 (ddt, 1H, *J* = 17.1, 10.3, 6.2 Hz, =C*H*R), 4.93 (m, 2H, =CH_2), 4.82 (t, 1H, ^3J = 6.2 Hz, -N*H*), 2.92 (m, 2H, CH_2), 2.42 (s, 3H, *Me*Ph-), 1.98 (m, 2H, CH_2), 1.45 (m, 2H, CH_2), 1.36 (m, 2H, CH_2).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 143.3, 138.1, 137.0, 129.7, 127.1, 114.9, 43.0, 33.1, 28.9, 25.7, 21.5.

MS (EI, 70 eV) *m/z* (abundance): 210 (12), 184 (11), 155 (51), 98 (27), 92 (11), 91 (100), 84 (29), 82 (11), 81 (27), 65 (31).

[4] W. E. Brenzovich,D. Benitez, A. D. Lackner, H. P. Shunatona, E. Tkatchouk, W.A. Goddard and F. D. Toste, *Angew. Chem. Int. Ed.*, 2010, **49**, 5519-5522.

***N*-Allyl-4-methylbenzenesulfonamide (3)**[5]



To a solution of allylamine (571 mg, 10 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was added TsCl (2.09 g, 11 mmol, 1.1 equiv) and Et_3N (1.11g, 11 mmol, 1.1 equiv) and the mixture was stirred at rt. After 15 min water was added and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with water and brine to afford the product as a white solid (2.045 g, 97%).

Formula: $C_{10}H_{13}NO_2S$ **Mass:** 253.11 g.mol^{-1}

mp = 63 °C

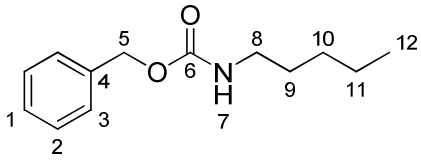
IR (neat): 3247, 2926, 1648, 1595, 1493, 1422, 1318, 1304, 1289, 1158, 1092, 1062, 997, 936, 874, 810, 706, 665, 619 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.77 (d, 2H, ^3J = 8.3 Hz, ArH), 7.31 (d, 2H, ^3J = 8.3 Hz, ArH), 5.71 (ddt, 1H, J = 17.2, 10.2, 5.8 Hz, =C*H*R), 5.16 (m, 1H, =C*H*H), 5.07 (m, 1H, =CH*H*), 5.00 (t, 1H, ^3J = 6.4 Hz, -N*H*), 3.57 (m, 2H, CH_2), 2.42 (s, 3H, *Me*Ph-).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 143.5, 136.9, 133.0, 129.7, 127.2, 117.7, 45.8, 21.5

MS (EI, 70 eV) *m/z* (abundance): 155 (20), 147 (10), 146 (6), 132 (5), 120 (5), 92 (21), 91 (100), 89 (6), 65 (28), 56 (64).

Benzyl pentylcarbamate (4)



To a solution of pentylamine (174 mg, 2 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added carboxybenzyl chloroformate (344 mg, 2.2 mmol, 1.1 equiv) and Et_3N (222 mg, 2.2 mmol, 1.1 equiv). The mixture was stirred overnight at rt and washed with water and brine. The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. The product was obtained as a colorless oil (606 mg, 98%)

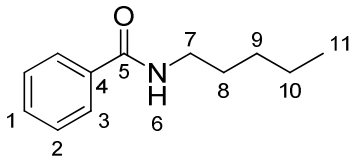
Formula: $C_{13}H_{19}NO_2$ **Mass:** 221.14 g.mol^{-1}

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.33 (m, 5H, ArH), 5.10 (s, 2H, CH_2Ph), 4.76 (bs, 1H, -N*H*), 3.18 (m, 2H, CH_2), 1.48 (m, 2H, CH_2), 1.29 (m, 4H, $2CH_2$), 0.89 (t, 3H, ^3J = 6.9 Hz, CH_3).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.4, 136.7, 128.5, 128.2, 128.1, 66.6, 41.1, 29.7, 28.9, 22.3, 14.0.

[5] M. Yamagishi, K. Nishigai, T. Hata and H. Urabe, *Org. Lett*, 2011, **13**, 4873-4875.

***N*-Pentylbenzamide (5)**[6]



To a solution of pentylamine (174 mg, 2 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was added benzoyl chloride (308 mg, 2.2 mmol, 1.1 equiv) and Et_3N (202 mg, 2.2 mmol, 1.1 equiv). The mixture was stirred at rt for 1 h and washed with water and brine. The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel afforded **5** (403 mg, quant.).

Formula: $C_{12}H_{17}NO$ **Mass:** 191.13 g.mol^{-1}

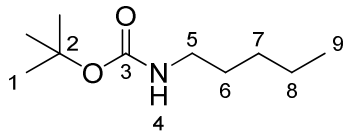
IR (neat): 3333, 3067, 2950, 2925, 2865, 1632, 1579, 1530, 1488, 1330, 1283, 1241, 1151, 1076, 863, 715, 689, 629, 613 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.77 (m, 2H, ArH), 7.44 (m, 3H, ArH), 6.33 (bs, 1H, -N*H*), 3.43 (td, 2H, J = 7.3, 5.8 Hz, H_7), 1.61 (m, 2H, CH_2), 1.35 (m, 4H, $2CH_2$), 0.83 (m, 3H, CH_3).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 167.5, 134.9, 131.3, 128.5, 126.9, 40.1, 29.4, 29.2, 22.4, 14.0.

MS (EI, 70 eV) *m/z* (abundance): 191 (7), 162 (7), 148 (9), 135 (17), 134 (20), 106 (8), 105 (100), 77 (40), 51 (10).

***tert*-Butyl pentylcarbamate (6)**



To a solution of pentylamine (174 mg, 2 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added Boc_2O (479 mg, 2.2 mmol, 1.1 equiv) and Et_3N (202 mg, 2 mmol, 1.1 equiv). The mixture was stirred overnight at rt and was then washed with water and brine. The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel afforded the **6** (225 mg, 60%) as a colorless oil.

Formula: $C_{10}H_{21}NO_2$ **Mass:** 187.15 g.mol^{-1}

IR (neat): 3349, 2960, 2930, 2862, 1688, 1520, 1455, 1391, 1365, 1251, 1170, 1068, 1040, 655, 869, 779, 628 cm^{-1}.

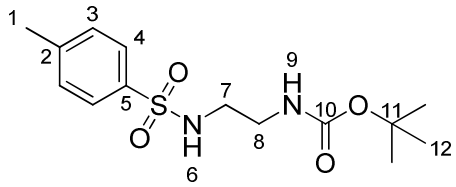
NMR ^{1}H (400 MHz, $CDCl_3$): δ 4.55 (bs, 1H, -N*H*), 3.10 (td, 2H, J = 6.9, 6.9 Hz, CH_2), 1.46 (m, 11H, CH_2 + Boc), 1.31 (m, 4H, $2CH_2$), 0.89 (t, 3H, ^{3}J = 6.9 Hz, CH_3).

[6] E. Petricci, C. Mugnaini, M. Radi, F. Corelli and M. Botta, *J. Org. Chem*, 2004, **69**, 7880-7887.

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.0, 85.16, 40.6, 29.8, 29.0, 28.4, 22.3, 14.0.

MS (EI, 70 eV) *m/z* (abundance): 132 (12), 131 (11), 87 (9), 74 (4), 59 (30), 58 (6), 57 (100).

***tert*-Butyl 2-(4-methylphenylsulfonamido)ethylcarbamate (7)**



To a solution of *N*-(2-aminoethyl)-4-methylbenzenesulfonamide (1.07g, 5 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added Boc_2O (1.2g, 5.5 mmol, 1.5 equiv) and Et_3N (770 µL, 5.5 mmol, 1.5 equiv) and the mixture stirred at rt for 1.5 h. The crude mixture was washed twice with water (2x10 mL). The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 50/50) afforded **7** (1.242 g, 3.95 mmol, 79%) as a white solid.

Formula: $C_{14}H_{22}N_2O_4S$ **Mass:** 314.13 g.mol^{-1}

mp = 120 °C

IR (neat): 3370, 3282, 2980, 2929, 1693, 1598, 1532, 1445, 1364, 1329, 1270, 1250, 1154, 1093, 1052, 976, 899, 816, 778, 661, 629 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.74 (d, 2H, ^{3}J = 8.1 Hz, ArH), 7.29 (d, 2H, ^{3}J = 8.1 Hz, ArH), 5.74 (m, 1H, -N*H*), 5.13 (m, 1H, -N*H*), 3.22 (q_{app}, 2H, ^{3}J = 5.7 Hz, CH_2), 3.02 (q_{app}, 2H, J = 5.7 Hz, CH_2), 2.41 (s, 3H, *Me*Ph-), 1.40 (s, 9H, -*t*Bu).

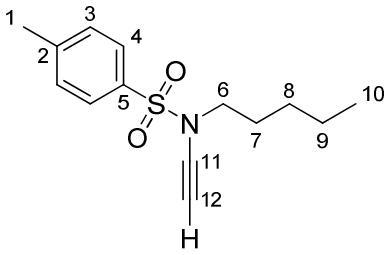
NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.5, 143.4, 136.7, 129.7, 127.0, 79.6, 43.5, 40.2, 28.3, 21.5.

MS (EI, 70 eV) *m/z* (abundance): 184 (21), 155 (41), 103 (74), 92 (13), 91 (62), 65 (18), 59 (17), 57 (100), 56 (20).

Procedure A : Synthesis of ynamides using R-EBX.

To a solution of the considered amine (0.2 mmol, 1 equiv) in DMF (2 mL) at 0 °C was added NaH (8 mg, 0.2 mmol, 1 equiv, 60% dispersion in mineral oil) followed by R-EBX (0.2 mmol, 1 equiv). The reaction mixture was stirred at rt for 2 h then diluted with diethyl ether and washed with water and brine. The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel if needed, afforded the title compound.

***N*-Ethynyl-4-methyl-N-pentylbenzenesulfonamide (8)**



Procedure **A**. 4-Methyl-*N*-pentylbenzenesulfonamide **1** (48.2 mg, 0.2 mmol) was treated with NaH (8 mg, 0.2 mmol, 1 equiv) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 90/10) afforded **8** (44 mg, 83%) as a yellow oil.

Formula: $C_{14}H_{19}NO_2S$ **Mass:** 265.11 g.mol^{-1}

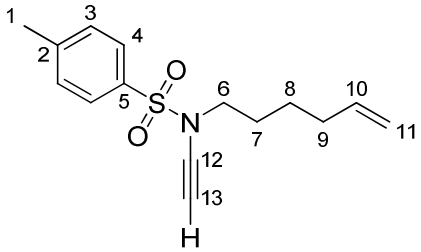
IR (neat): 3287, 2956, 2925, 285, 2134, 1597, 1458, 1362, 1291, 1166, 1090, 1037, 950, 813, 706, 683, 655 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.80 (d, 2H, ^{3}J = 8.3 Hz, ArH), 7.35 (d, 2H, ^{3}J = 8.3 Hz, ArH), 3.29 (m, 2H, CH_2), 2.73 (s, 1H, H_{12}), 2.45 (s, 3H, *Me*Ph-), 1.64 (m, 2H, CH_2), 1.29 (m, 4H, $2CH_2$), 0.87 (m, 3H, CH_3).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 144.7, 134.6, 129.8, 127.6, 76.1, 59.0, 51.2, 28.3, 27.3, 22.1, 21.7, 13.9.

MS (EI, 70 eV) *m/z* (abundance): 265 (0.3), 200 (26), 186 (11), 155 (21), 131 (22), 104 (8), 96 (21), 92 (20), 91 (100), 71 (11), 65 (27), 55 (10).

***N*-Ethynyl-*N*-(hex-5-enyl)-4-methylbenzenesulfonamide (9)**



Procedure **A**. *N*-(Hex-5-enyl)-4-methylbenzenesulfonamide **2** (50.6 mg, 0.2 mmol) was treated with NaH (8 mg, 0.2 mmol, 1 equiv) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 90/10) afforded **9** (51 mg, 93%) as an oil.

Formula: $C_{15}H_{19}NO_2S$ **Mass:** 277.11 g.mol^{-1}

IR (neat): 3297, 2930, 2585, 2132, 1640, 1597, 1442, 1362, 1165, 1090, 993, 911, 813, 706, 983, 657 cm^{-1}.

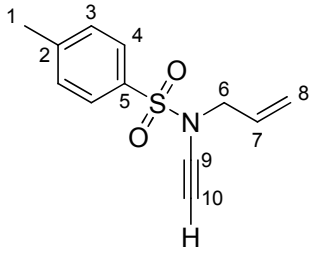
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.80 (d, 2H, ^{3}J = 8.3 Hz, ArH), 7.35 (d, 2H, ^{3}J = 8.3 Hz, ArH), 5.75 (ddt, 1H, *J* = 17.1, 10.2, 6.7 Hz, =C*H*R), 4.97 (m, 2H, $=CH_2$), 3.30 (t, 2H, ^{3}J = 7.2 Hz, CH_2), 2.73 (s, 1H, H_{13}), 2.45 (s, 3H, *Me*Ph-), 2.05 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 1.40 (m, 2H, CH_2).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 144.7, 138.1, 134.6, 129.8, 127.6, 114.9, 76.0, 59.1, 51.0, 33.1, 27.0, 25.3, 21.7.

MS (EI, 70 eV) *m/z* (abundance): 131 (8), 122 (57), 120 (10), 105 (21), 95 (15), 94 (14), 92 (15), 91 (100), 81 (13), 80 (13), 79 (10), 69 (29), 68 (12), 67 (17), 65 (30), 55 (52), 54 (25), 53 (13).

HRMS (ESI): Calculated value for $C_{15}H_{19}NO_2S$ $[M+Na]^+$: 300.10287 ; Obtained: 300.10324

***N*-Allyl-*N*-ethynyl-4-methylbenzenesulfonamide (10)**



Procedure **A**. *N*-Allyl-4-methylbenzenesulfonamide **3** (42.2 mg, 0.2 mmol) was treated with NaH (8 mg, 0.2 mmol, 1 equiv) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 90/10) afforded **9** (35 mg, 74%) as white solid.

Formula: $C_{12}H_{13}NO_2S$ **Mass:** 235.06 g.mol^{-1}

mp = 68 °C

IR (neat): 3271, 2925, 2140, 1594, 1429, 1353, 1295, 1160, 1118, 1087, 1033, 1014, 992, 921, 899, 914, 800, 740, 710, 660, 601 cm^{-1}.

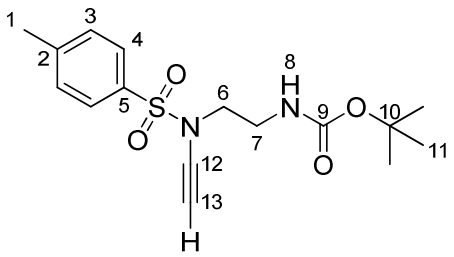
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.81 (d, 2H, ^3J = 8.3 Hz, ArH), 7.36 (d, 2H, ^3J = 8.3 Hz, ArH), 5.72 (ddt, 1H, *J* = 17.1, 10.2, 6.3 Hz, =C*H*R), 5.24 (m, 2H, =CH_2), 3.96 (dt, 2H, *J* = 7.2 Hz, 1.4 Hz, H_6), 2.73 (s, 1H, H_{10}), 2.45 (s, 3H, *Me*Ph-).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 144.9, 134.7, 130.5, 129.8, 127.8, 120.2, 75.5, 59.3, 53.9, 21.7.

MS (EI, 70 eV) *m/z* (abundance): 235 (3), 156 (4), 155 (49), 92 (11), 91 (100), 80 (5), 65 (23), 53 (6).

NMR data are in agreement with those previously reported.[7]

***tert*-Butyl 2-(*N*-ethynyl-4-methylphenylsulfonamido)ethylcarbamate (11)**



[7] D. Brückner, *Tetrahedron*, 2006, **62**, 3809-3814.

Procedure **A**. *tert*-Butyl 2-(4-methylphenylsulfonamido)ethylcarbamate **7** (62.8 mg, 0.2 mmol) was treated with NaH (8 mg, 0.2 mmol, 1 equiv) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 60/40) afforded **11** (59.5 mg, 88%) as a pale yellow oil.

Formula: $C_{16}H_{22}N_2O_4S$ **Mass:** 338.42 g.mol^{-1}

IR (neat): 3293, 2977, 1697, 1597, 1510, 1453, 1364, 1288, 1248, 1160, 1088, 1017, 956, 927, 814, 706, 683, 658 cm^{-1}.

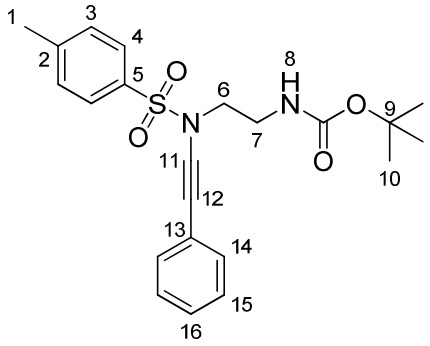
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.80 (d, 2H, ^{3}J = 8.3 Hz, ArH), 7.36 (d, 2H, ^{3}J = 8.3 Hz, ArH), 4.86 (bs, 1H, -N*H*), 3.41 (m, 4H, 2CH_2), 2.77 (s, 1H, H_{13}), 2.46 (s, 3H, *Me*Ph-), 1.44 (s, 9H, Boc).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 155.8, 145.0, 134.2, 129.9, 127.7, 79.7, 75.7, 59.4, 50.9, 38.7, 28.4, 21.7.

MS (EI, 70 eV) *m/z* (abundance): 235 238 (14), 173 (8), 155 (23), 127 (28), 111 (18), 92 (13), 91 (94), 83 (49), 70 (13), 65 (31), 57 (100), 56 (81), 55 (57), 54 (15), 53 (10), 51 (10).

HRMS (ESI): Calculated for $C_{16}H_{24}N_2O_5S$ $[M+H_2O+Na]^+$: 379.1298 ; found: 379.1302.

***tert*-butyl 2-(4-methyl-N-(phenylethynyl)phenylsulfonamido)ethylcarbamate (31)**



Procedure **A**. *tert*-Butyl 2-(4-methylphenylsulfonamido)ethylcarbamate **7** (62.8 mg, 0.2 mmol) was treated with NaH (8 mg, 0.2 mmol, 1 equiv) and Ph-EBX (69.6 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 70/70) afforded **31** (26 mg, 31%) as a yellow oil.

Formula: $C_{22}H_{26}N_2O_4S$ **Mass:** 414.16 g.mol^{-1}

IR (neat): 3413, 2977, 2931, 2236, 1703, 1597, 1507, 1444, 1364, 1271, 1249, 1167, 1089, 971, 912, 813, 754, 731, 691, 675 cm^{-1}.

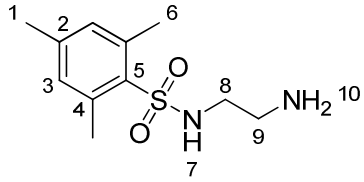
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.84 (d, 2H, ^{3}J = 8.3 Hz, ArH), 7.4-7.33 (m, 4H, ArH), 7.32-7.27 (m, 3H, ArH), 4.93 (bs, 1H, -N*H*), 3.53 (m, 2H, CH_2), 3.45 (m, 2H, CH_2), 2.45 (s, 3H, *Me*Ph-), 1.44 (s, 9H, -*t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 155.8, 144.9, 134.2, 131.4, 129.9, 128.3, 128.0, 127.7, 122.5, 82.0, 79.7, 70.8, 51.4, 39.1, 28.4, 21.7.

MS (EI, 70 eV) *m/z* (abundance): 314 (13), 313 (27), 249 (26), 159 (15), 158 (13), 155 (12), 92 (9), 91 (100), 65 (23).

HRMS (ESI): Calculated for $C_{22}H_{26}N_2O_5S$ $[M+Na]^+$: 437.15055 ; found: 437.15098.

***N*-(2-Aminoethyl)-2,4,6-trimethylbenzenesulfonamide (12a)**



To a solution of ethylenediamine (3 g, 50 mmol, 10 equiv) in CH_2Cl_2 (40 mL) at 0 °C was added 2-mesitylenesulfonyl chloride (1.094 g, 5 mmol, 1 equiv) dropwise. The mixture was stirred at rt for 3 h and washed twice with water. The phases were separated and the organic phase was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford **12a** (1.21 g, quant.) as a white solid.

Formula: $C_{11}H_{18}N_2O_2S$ **Mass:** 242.11 $g.mol^{-1}$

mp = 90 °C

IR (neat): 3349, 3288, 2957, 2935, 2866, 1601, 1562, 1443, 1402, 1350, 1317, 1186, 1152, 1093, 1055, 967, 870, 845, 746, 710, 653 cm^{-1}.

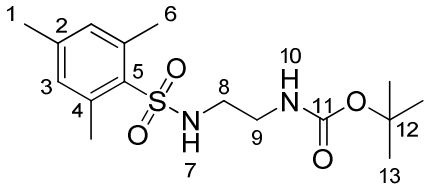
NMR ^{1}H (400 MHz, $CDCl_3$): δ 6.95 (s, 2H, ArH), 2.9 (m, 2H, CH_2), 2.8 (m, 2H, CH_2), 2.64 (s, 6H, $2CH_3$), 2.29 (s, 3H, CH_3).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 142.1, 139, 133.6, 131.9, 44.8, 40.8, 22.9, 20.9.

MS (EI, 70 eV) *m/z* (abundance): 213 (28), 132 (42), 121 (11), 120 (100), 119 (90), 115 (15), 105 (45), 103 (16), 91 (56), 79 (12), 78 (11), 77 (28), 65 (13), 59 (15).

NMR data are in agreement with those previously reported.[8]

3,3-Dimethyl-*N*-(2-(2,4,6-trimethylphenylsulfonamido)ethyl)butanamide (12)[8]



To a solution of *N*-(2-aminoethyl)-2,4,6-trimethylbenzenesulfonamide **12a** (242 mg, 1 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added Boc_2O (240 mg, 1.1 mmol, 1.1 equiv) and Et_3N (111 mg, 1.1 mmol, 1.1 equiv). The mixture was stirred at rt for 4 h and washed with water and brine. The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (PE/AcOEt: 60/40) afforded the product (340 mg, 99%) as an off-white solid.

[8] D. G. Batt, J. J. Petraitis , G. C. Houghton , D. P. Modi , G. A. Cain , M. H. Corjay , S. A. Mousa , P. J. Bouchard , M. S. Forsythe , P. P. Harlow , F. A. Barbera , S. M. Spitz , R. R. Wexler , and Pr. K. Jadhav *J. Med. Chem.* 2000, **47**, 41-58.

Formula: $C_{16}H_{26}N_2O_4S$ **Mass:** 342.16 g.mol^{-1}

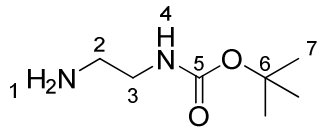
mp = 92 °C

IR (neat): 3387, 3315, 2984, 2962, 2942, 1688, 1601, 1521, 1444, 1428, 1333, 1275, 1254, 1224, 1174, 1157, 1078, 1032, 970, 870, 851, 656, 603 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 6.94 (s, 2H, ArH), 5.48 (bs, 1H, -N*H*), 4.99 (bs, 1H, -N*H*), 3.22 (m, 2H, CH_2), 2.99 (m, 2H, CH_2), 2.62 (s, 6H, $2CH_3$), 2.29 (s, 3H, CH_3), 1.41 (s, 9H, Boc).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.5, 142.2, 139.0, 133.5, 132.0, 79.8, 43.0, 40.3, 28.3, 22.9, 20.9.

***tert*-Butyl 2-aminoethylcarbamate (13a)**[9]



To a solution of ethylenediamine (3g, 50 mmol, 10 equiv) in CH_2Cl_2 at 0 °C was added dropwise a solution of Boc_2O (1.09 g, 5 mmol, 1 equiv) in CH_2Cl_2. The mixture was stirred at rt for 3 h and washed twice with water. The phases were separated and the organic phase was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford **13a** (466 mg, 59%) as a waxy solid.

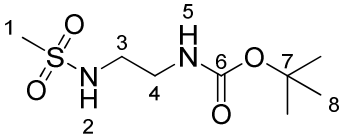
Formula: $C_7H_{16}N_2O_2$ **Mass:** 160.21 g.mol^{-1}

IR (neat): 3358, 2976, 2933, 1684, 1593, 1527, 1454, 1391, 1365, 1274, 1250, 1166, 1040, 655, 670, 781, 627 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 5.1 (bs, 1H, H_4), 3.17 (m, 2H, CH_2), 2.8 (m, 2H, CH_2), 1.45 (s, 9H, -*t*Bu), 1.23 (bs, 2H, -NH_2).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.2, 79.1, 43.4, 41.9, 28.4.

***tert*-Butyl 2-(methylsulfonamido)ethylcarbamate (13)**[9]



To a solution of *tert*-Butyl 2-aminoethylcarbamate **13a** (127 mg, 0.8 mmol, 10 equiv) in CH_2Cl_2 at 0 °C was added MsCl (99 mg, 1.1 mmol, 1.1 equiv). The mixture was stirred at 0 °C for 1 h and at rt overnight. The mixture was washed with water, the aqueous phase extracted with CH_2Cl_2 and the combined organic phases washed with water, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford **13** (197 mg, 83%) as a white solid.

[9] J. J. Soldevila-Barreda, P. C. A. Bruijnincx, A. Habtemariam, G. J. Clarkson, R. J. Deeth and P. J. Sadler, *Organometallics*, 2012, **31**, 5958-5967.

Formula: $C_8H_{18}N_2O_4S$ **Mass:** 238.30 g.mol^{-1}

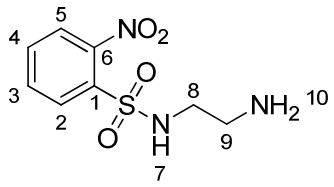
mp = 101 °C

IR (neat): 3357, 3279, 2990, 2934, 1680, 1523, 1446, 1366, 1321, 1308, 1278, 1239, 1143, 1087, 1044, 967, 880, 781, 765, 634 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 5.30 (bs, 1H, –N*H*), 5.1 (bs, 1H, -N*H*), 3.30 (m, 2H, CH_2), 3.25 (m, 2H, CH_2), 2.97 (s, 3H, CH_3), 1.45 (s, 9H, -*t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.6, 79.9, 43.6, 40.7, 40.2, 28.4.

***N*-(2-aminoethyl)-2-nitrobenzenesulfonamide (13'a)[10]**



To a solution of ethylenediamine (3g, 50 mmol, 10 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added dropwise a solution of NsCl (1.1 g, 5 mmol, 1 equiv) in CH_2Cl_2. The mixture was stirred at rt for 3 h and washed twice with water. The phases were separated and the organic phase was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford **13a** (541 mg, 44%) as a waxy yellow oil.

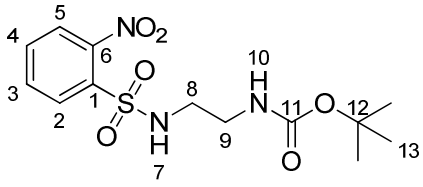
Formula: $C_8H_{11}N_3O_4S$ **Mass:** 245.05 g.mol^{-1}

IR (neat): 3315, 3096, 2876, 1708, 1664, 1593, 1537, 1411, 1361, 1336, 1161, 1125, 1089, 912, 853, 780, 729, 653.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 8.2-8.08 (m, 1H, ArH), 7.9-7.8 (m, 1H, ArH), 7.8-7.7 (m, 2H, ArH), 3.13 (m, 2H, CH_2), 2.99 (bs, 1H, -N*H*), 2.87 (m, 2H, CH_2).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 174.4, 148.1, 133.6, 132.8, 131.1, 125.3, 46.1, 41.0.

***tert*-butyl (2-(2-nitrophenylsulfonamido)ethyl)carbamate (13')[11]**



To a solution of *N*-(2-aminoethyl)-2-nitrobenzenesulfonamide (517 mg, 2.1 mmol, 1 equiv) in CH_2Cl_2 (10 mL) was added Boc_2O (480 mg, 2.2 mmol, 1.05 equiv) and Et_3N (222 mg, 2.2 mmol, 1.05 equiv).

[10] F. Dioury, S. Sambou, E. Guéné, M. Sabatou, C. Ferroud, A. Guy and M. Port, *Tetrahedron*, 2007, **63**, 204-214.

[11] C. Letondor, A. Pordea, N. Humbert, A. Ivanova, S. Mazurek, M. Novic and R. Ward, *J. Am. Chem. Soc.*, 2006, **128**, 8320-8328.

The mixture was stirred overnight at rt and washed with water and brine. The phases were separated and the organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (PE/AcOEt: 60/40) afforded the product (530 mg, 73%) as a waxy yellow oil.

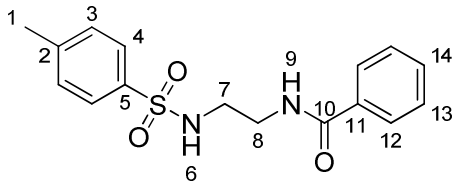
Formula: $C_{13}H_{19}N_3O_6S$ **Mass:** 345.10 g.mol^{-1}

IR (neat): 3338, 2978, 2934, 1687, 1538, 1413, 1364, 1340, 1252, 1161, 1125, 1087, 994, 853, 781, 740, 730, 654.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 8.12 (m, 1H, ArH), 7.86 (m, 1H, ArH), 7.75 (m, 2H, ArH), 5.79 (bs, 1H, -N*H*), 4.92 (bs, 1H, -N*H*), 3.4-3.19 (m, 4H, $2CH_2$), 1.42 (s, 9H, -*t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.2, 148.1, 133.7, 133.5, 132.9, 131.0, 125.4, 79.9, 43.9, 40.4, 28.3.

***N*-(2-(4-Methylphenylsulfonamido)ethyl)benzamide (14)** [12]



To a solution of *N*-(2-aminoethyl)-4-methylbenzenesulfonamide (214 mg, 1 mmol, 1 equiv) in CH_2Cl_2 (5 mL) at 0 °C was added benzoyl chloride (322 mg, 2.3 mmol, 2.3 equiv) and Et_3N (303 mg, 3 mmol, 3 equiv) and the mixture stirred at rt for 4 h. The crude mixture was treated with HCl 10% (10 mL), neutralized with a saturated aqueous solution of $NaHCO_3$ (10 mL) and washed with water (10mL). The organic phase was separated and dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 30/70) afforded **14** (92 mg, 0.29 mmol, 29%) as a white solid.

Formula: $C_{16}H_{18}N_2O_3S$ **Mass:** 318.10 g.mol^{-1}

mp = 128 °C

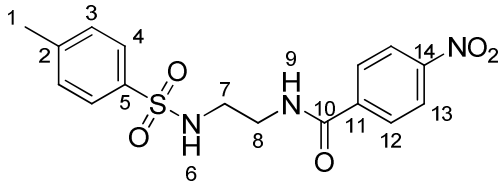
IR (neat): 3263, 3065, 2340, 1644, 1600, 1542, 1486, 1424, 1312, 1239, 1157, 1092, 1025, 957, 846, 810, 699, 659 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.69 (m, 4H, ArH), 7.39 (m, 2H, ArH + -N*H*), 7.29 (m, 2H, ArH), 7.16 (d, 2H, ^3J = 8.1 Hz, ArH), 6.27 (t, 1H, ^3J = 5.8 Hz, -N*H*), 3.51 (q_{app}, 2H, ^3J = 5.6 Hz, CH_2), 3.13 (q_{app}, 2H, ^3J = 5.6 Hz, CH_2), 2.32 (s, 3H, *Me*Ph-).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 168.4, 143.5, 136.6, 133.8, 131.6, 129.8, 128.5, 127.1, 127.0, 42.9, 39.9, 14.2.

***N*-(2-(4-Methylphenylsulfonamido)ethyl)-4-nitrobenzamide (15)**

[12] O. A. Luk'yanov, G. E Pokhvisneva, and T. E Ternikova, *Russ. Chem. Bull.*, 1994, **43**, 1376-1380.



To a solution of *N*-(2-Aminoethyl)-4-methylbenzenesulfonamide (214 mg, 1 mmol, 1 equiv) in CH_2Cl_2 (5 mL) at 0 °C was added 4-nitrobenzoyl chloride (203 mg, 1.1 mmol, 1.1 equiv) and Et_3N (101 mg, 1.1 mmol, 1.1 equiv) and the mixture stirred at rt for 4 h. The crude mixture was treated with a solution of NaOH 1M (10 mL). The organic phase was separated and dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 30/70) afforded **15** (290 mg, 0.80 mmol, 80%) as a white solid.

Formula: $C_{16}H_{17}N_3O_5S$ **Mass:** 363.08 g.mol^{-1}

mp = 128 °C

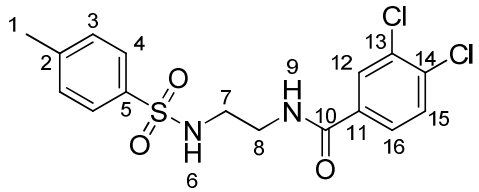
IR (neat): 3295, 3254, 2923, 1675, 1641, 1599, 1543, 1519, 1427, 1345, 1321, 1307, 1225, 1160, 1116, 1090, 1076, 938, 863, 832, 817, 691, 670, 603 cm^{-1}.

NMR ^{1}H (400 MHz, Acetone-d6): δ 8.17 (m, 2H, ArH), 8.04 (bs, 1H, -N*H*), 7.96 (m, 2H, ArH), 7.60 (m, 2H, ArH), 7.21 (m, 2H, ArH), 6.55 (t, 1H, ^{3}J = 6.1 Hz, -N*H*), 3.4 (q_{app}, 2H, ^{3}J = 6.1 Hz, CH_2), 3.03 (q_{app}, 2H, ^{3}J = 6.1 Hz, CH_2), 2.24 (s, 3H, *Me*Ph).

NMR ^{13}C (100 MHz, Acetone-d6): δ 166.2, 150.6, 144.0, 141.3, 139.1, 130.6, 129.6, 127.9, 124.4, 43.6, 41.0, 21.5.

HRMS (ESI): Caculated value for $C_{16}H_{17}O_5N_3S$ $[M+Na]^+$: 386.07811 ; Found: 386.07847.

3,4-Dichloro-*N*-(2-(4-methylphenylsulfonamido)ethyl)benzamide (16)



To a solution of *N*-(2-Aminoethyl)-4-methylbenzenesulfonamide (214 mg, 1 mmol, 1 equiv) in CH_2Cl_2 (5 mL) at 0 °C was added 3,4-Dichlorobenzoyl chloride (230 mg, 1.1 mmol, 1.1 equiv) and Et_3N (101 mg, 1.1 mmol, 1.1 equiv) and the mixture stirred at rt for 4 h. The crude mixture was washed with water (10 mL) and brine (10 mL). The organic phase was separated and dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 40/60) afforded the product (360 mg, 0.93 mmol, 93%) as a white solid.

Formula: $C_{16}H_{16}Cl_2N_2O_3S$ **Mass:** 386.02 g.mol^{-1}

mp = 126 °C

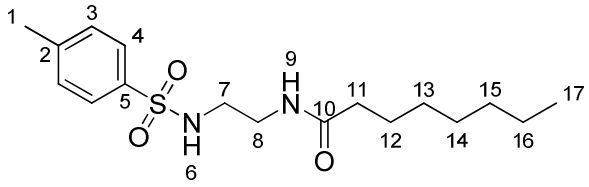
IR (neat): 3414, 3362, 3097, 2865, 1642, 1592, 1543, 1467, 1443, 1375, 1318, 1237, 1152, 1101, 1029, 956, 933, 876, 851, 816, 809, 761, 749, 705, 676, 654 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.83 (d, 1H, ^{3}J = 2.1 Hz, ArH), 7.7 (d, 2H, ^{3}J = 8.2 Hz, ArH), 7.57 (dd, 1H, J = 8.2, 2.1 Hz, ArH), 7.83 (d, 1H, ^{3}J = 8.4 Hz, ArH), 7.24 (m, 3H, ArH), 5.85 (t, 1H, ^{3}J = 6.1 Hz, -N*H*), 3.54 (m, 2H, CH_2), 3.18 (m, 2H, CH_2), 2.39 (s, 3H, *Me*Ph-).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 166.0, 143.9, 136.3, 136.0, 133.6, 132.9, 130.5, 129.9, 129.4, 127.0, 126.2, 42.7, 40.2, 21.5.

HRMS (ESI): Caculated value for $C_{16}H_{16}O_3N_2Cl_2S$ $[M+Na]^+$: 409.01509 ; Found: 409.01578.

***N*-(2-(4-Methylphenylsulfonamido)ethyl)octanamide (17)**



To a solution of *N*-(2-aminoethyl)-4-methylbenzenesulfonamide (214 mg, 1 mmol, 1 equiv) in CH_2Cl_2 (5 mL) at 0 °C was added octanoyl chloride (178 mg, 1.1 mmol, 1.1 equiv) and Et_3N (101 mg, 1.1 mmol, 1.1 equiv) and the mixture stirred at rt for 4 h. The crude mixture was washed with water (10 mL) and brine (10 mL). The organic phase was separated and dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 40/60) afforded the product (211 mg, 0.6 mmol, 60%) as a white solid.

Formula: $C_{17}H_{28}N_2O_3S$ **Mass:** 340.18 $g.mol^{-1}$

mp = 78 °C

IR (neat): 3322, 3271, 2927, 2858, 1651, 1597, 1531, 1470, 1439, 1379, 1324, 1301, 1286, 1214, 1155, 1091, 1074, 1019, 898, 816, 670 cm^{-1}.

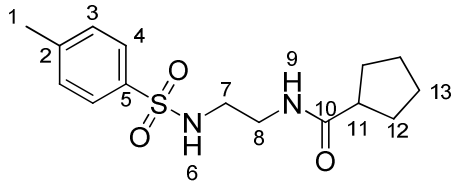
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.74 (d, 2H, ^{3}J = 8.3 Hz, ArH), 7.30 (d, 2H, ^{3}J = 8.3 Hz, ArH), 6.30 (m, 1H, -N*H*), 5.72 (m, 1H, -N*H*), 3.36 (m, 2H, CH_2), 3.06 (m, 2H, CH_2), 2.42 (s, 3H, *Me*Ph-), 2.13 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 1.27 (m, 8H, $4CH_2$), 0.87 (m, 3H, CH_3).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 174.4, 143.6, 136.7, 129.9, 127.0, 43.2, 39.2, 36.6, 31.7, 29.3, 29.0, 25.6, 22.6, 21.5, 14.1.

MS (EI, 70 eV) *m/z* (abundance): 186 (10), 185 (82), 157 (26), 156 (16), 155 (23), 128 (14), 127 (49), 114 (16), 101 (19), 100 (23), 92 (11), 91 (91), 86 (71), 73 (73), 65 (26), 59 (98), 58 (19), 57 (100), 55 (30).

HRMS (ESI): Caculated value for $C_{17}H_{28}O_3N_2S$ $[M+Na]^+$: 363.17128 ; Found: 363.17127.

***N*-(2-(4-Methylphenylsulfonamido)ethyl)cyclopentanecarboxamide (18)**[13]



Following a reported procedure, XTalFluor-E (172 mg, 0.75 mmol, 1.5 equiv) was added at 0 °C to a solution of *N*-(2-Aminoethyl)-4-methylbenzenesulfonamide (214 mg, 1 mmol, 2 equiv) and cyclopentanecarboxylic acid (57 mg, 0.5 mmol, 1 equiv) in THF (8.55 mL). The mixture was stirred at rt for 4 h then quenched with a saturated aqueous solution of Na_2CO_3 and extracted with AcOEt. The organic phase was separated, dried over $MgSO_4$, filtered, concentrated under vacuum and purified over silica gel (EP/AcOEt: 40/60) to afford **18** (113 mg, 0.3 mmol, 60%) as a white solid.

Formula: $C_{15}H_{22}N_2O_3S$ **Mass:** 310.13 g.mol^{-1}

mp = 123 °C

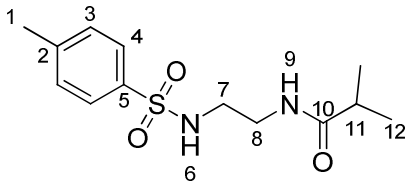
IR (neat): 3270, 2954, 2867, 1650, 1537, 1445, 1377, 1327, 1289, 1237, 1218, 1155, 1090, 1018, 898, 816, 668 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.74 (d, 2H, ^3J = 8.3 Hz, ArH), 7.30 (d, 2H, ^3J = 8.3 Hz, ArH), 6.24 (t, 1H, ^3J = 5.8 Hz, -N*H*), 5.69 (t, 1H, ^3J = 5.8 Hz, -N*H*), 3.36 (td, 2H, J = 5.8 Hz, CH_2), 3.06 (td, 2H, J = 5.8 Hz, CH_2), 2.49 (m, 1H, H_{11}), 2.42 (s, 3H, *Me*Ph-), 1.81 (m, 2H, CH_2), 1.69 (m, 4H, $2CH_2$), 1.55 (m, 2H, CH_2).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 177.5, 143.6, 136.7, 129.8, 127.0, 45.7, 43.4, 39.2, 30.4, 25.9, 21.5.

HRMS (ESI): Caculated value for $C_{15}H_{22}O_3N_2S$ $[M+Na]^+$: 333.12433 ; Found: 333.12402.

***N*-(2-(4-Methylphenylsulfonamido)ethyl)isobutyramide (19)**



To a solution of *N*-(2-aminoethyl)-4-methylbenzenesulfonamide (1.07 g, 5 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added isobutyric acyl chloride (583 mg, 5.5 mmol, 1.1 equiv) and Et_3N (555.5 mg, 1.1 equiv). The mixture was stirred at rt for 3 h and then washed with water (15 mL) and brine (15 mL). The organic phase was separated, dried over $MgSO_4$, filtered and concentrated under vacuum. Purification over silica gel (EP/AcOEt: 50/50) afforded **19** (848 mg, 60%) as a white solid.

Formula: $C_{13}H_{20}N_2O_3S$ **Mass:** 284.12 g.mol^{-1}

[13] A. Orliac, D. Gomez-Pardo, A. Bombrun and J. Cossy, *Org. Lett.,* 2013, ASAP. DOI: 10.1021/ol400045d

mp = 98°C

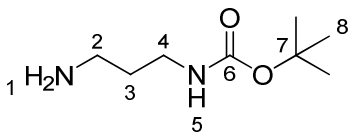
IR (neat): 3306, 2966, 2929, 2872, 1646, 1598, 1547, 1467, 1449, 1433, 1383, 1328, 1248, 1155, 1089, 927, 879, 812, 695, 658 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.74 (d, 2H, ^{3}J = 8.2 Hz, ArH), 7.30 (d, 2H, ^{3}J = 8.2 Hz, ArH), 6.30 (m, 1H, -N*H*), 5.75 (t, 1H, ^{3}J = 5.8 Hz, -N*H*), 3.36 (td, 2H, *J* = 5.8 Hz, CH_2), 3.06 (td, 2H, *J* = 5.8 Hz, CH_2), 2.42 (s, 3H, *Me*Ph-), 2.34 (hept, 1H, ^{3}J = 6.9 Hz, H_{11}), 1.11 (d, 6H, ^{3}J = 6.9 Hz, H_{12}).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 178.2, 143.6, 136.7, 129.8, 127.0, 43.3, 39.1, 35.5, 21.5, 19.5.

MS (EI, 70 eV) *m/z* (abundance): 155 (23), 129 (100), 101 (58), 100 (25), 92 (13), 91 (82), 86 (24), 73 (59), 72 (26), 71 (72), 65 (29), 59 (37), 58 (10).

***tert*-Butyl 3-aminopropylcarbamate (20a)**[14]



To a solution of propane-1,3-diamine (2.96 g, 40 mmol, 20 equiv) in CH_2Cl_2 (1 mL) at 0 °C was added dropwise a solution of Boc_2O (436 mg, 2 mmol, 1 equiv) in CH_2Cl_2 (1 mL). The mixture was stirred at 0 °C for 1 h and at rt for 1 more h. The crude mixture was diluted with CH_2Cl_2 (10 mL) and washed with water (5x20mL). The aqueous phases were combined and back-extracted with CH_2Cl_2 (2x20mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under vacuum to afford **20a** (256 mg, 73%) as a white solid.

Formula: $C_8H_{18}N_2O_2$ **Mass:** 174.13 $g.mol^{-1}$

mp = 103 °C

IR (neat): 3360, 2978, 2938, 2870, 1681, 1586, 1523, 1497, 1366, 1329, 1284, 1269, 1247, 1166, 1053, 1021, 876, 778, 643 cm^{-1}.

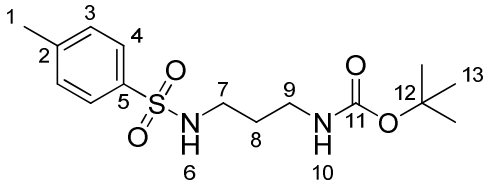
NMR ^{1}H (400 MHz, $CDCl_3$): δ 5.1 (bs, 1H, -N*H*), 3.21 (m, 2H, CH_2), 2.76 (t, 2H, ^{3}J = 6.6 Hz, CH_2), 2.1 (tt, 2H, *J* = 6.6, 6.6 Hz, H_3), 1.44 (s, 9H, *t*Bu), 1.24 (bs, 2H, $-NH_2$).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.1, 79.0, 39.7, 38.4, 33.4, 28.4.

***tert*-butyl 3-(4-methylphenylsulfonamido)propylcarbamate (20)**[15]

[14] D. Oves-Costales, N. Kadi, M. J. Fogg, L. Song, K. S. Wilson, and G. L. Challis, *J. Am. Chem. Soc.* 2007, **129**, 8416-8417.

[15] W.J. Fiedler and M. Hesse, *Helvetica Chimica Acta*, 1993, **76**, 1511-1519.



To a solution of *tert*-butyl 3-aminopropylcarbamate **20a** (222 mg, 1.28 mmol, 1 equiv) in CH_2Cl_2 (3 mL) was added tosyl chloride (291 mg, 1.53 mmol, 1.2 equiv) and triethylamine (154 mg, 1.53 mmol, 1.2 equiv). The mixture was strirred at rt overnight then washed with water (3x10 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to afford **20** (400 mg, 95%) as a white solid.

Formula: $C_{15}H_{24}N_2O_4S$ **Mass:** 328.14 g.mol^{-1}

mp = 112 °C

IR (neat): 3410, 3166, 2969, 2929, 1687, 1599, 1537, 1451, 1363, 1322, 1305, 1279, 1251, 1165, 1152, 1125, 1094, 1062, 1004, 909, 875, 811, 769, 753, 658 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.74 (d, 2H, ^{3}J = 8.2 Hz, ArH), 7.28 (d, 2H, ^{3}J = 8.2 Hz, ArH), 5.72 (m, 1H, -N*H*), 4.78 (m, 1H, -N*H*), 3.16 (m, 2H, CH_2), 2.94 (m, 2H, CH_2), 2.41 (s, 3H, *Me*Ph-), 1.6 (tt, 2H, ^{3}J = 6.9 Hz, 6.9 Hz, H_8), 1.39 (s, 9H, *t*Bu).

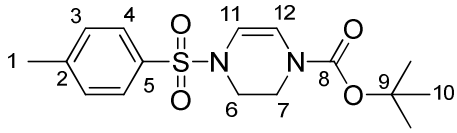
NMR ^{13}C (100 MHz, $CDCl_3$): δ 156.8, 143.2, 137.2, 129.7, 127, 79.5, 39.9, 36.9, 30.2, 28.3, 21.5.

MS (EI, 70 eV) *m/z* (abundance): 227 (6), 212 (35), 156 (5), 155 (53), 92 (10), 91 (100), 89 (6), 65 (23), 56 (13).

Procedure B: the synthesis of tetrahydropyrazines:

To a solution of the diamine (0.2 mmol, 1 equiv) in DMF (2mL) was added at 0 °C NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) followed by TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). The ice-bath was removed and the mixture was stirred at rt for 2 h. The crude mixture was diluted with Et_2O (10 mL) and washed with water (10 mL) and brine (10 mL). The organic phase was separated, dried over $MgSO_4$, filtered and concentrated under vacuum. The desired products were obtained after flash chromatography over silica gel.

***tert*-Butyl 4-tosyl-3,4-dihydropyrazine-1(2H)-carboxylate (21)**



Procedure **B**. *tert*-Butyl 2-(4-methylphenylsulfonamido)ethylcarbamate **7** (62.8 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 70/30) afforded **21** (38 mg, 56%) as a white solid.

Formula: $C_{16}H_{22}N_2O_4S$ **Mass:** 338.13 g.mol^{-1}

mp = 128 °C

IR (neat): 2974, 2924, 1737, 1696, 1656, 1597, 1456, 1383, 1367, 1351, 1308, 1230, 1163, 1119, 1099, 985, 952, 813, 766, 710, 654, 608 cm^{-1}.

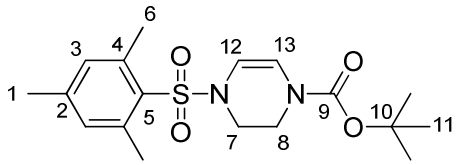
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.68 (m, 2H, ArH), 7.44 (d, 2H, ^{3}J = 8.2 Hz, ArH), 6.32 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 5.99 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 3.48 (m, 2H, CH_2), 3.35 (m, 2H, CH_2), 2.43 (s, 3H, *Me*Ph-), 1.43 (s, 9H, -*t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 151.0, 144.1, 134.2, 129.9, 127.2, 111.7, 106.6, 81.6, 43.2, 39.0, 28.2, 21.6.

MS (EI, 70 eV) *m/z* (abundance): 282 (10), 281 (57), 279 (57), 250 (15), 249 (92), 248 (17), 247 (100), 141 (24), 140 (96), 125 (15), 124 (18), 114 (19), 113 (26), 110 (10), 71 (20), 63 (14).

HRMS (ESI): Caculated value for $C_{16}H_{22}N_2O_4S$ $[M+Na]^+$: 361.11925 ; Found: 361.11922

***tert*-Butyl 4-(mesitylsulfonyl)-3,4-dihydropyrazine-1(2H)-carboxylate (22)**



Procedure **B**. 3,3-Dimethyl-*N*-(2-(2,4,6-trimethylphenylsulfonamido)ethyl) butanamide **12** (68.4 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 70/30) afforded **22** (37 mg, 51%).

Formula: $C_{18}H_{26}N_2O_4S$ **Mass:** 366.16 $g.mol^{-1}$

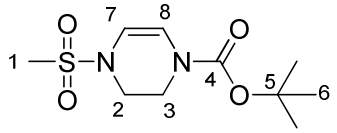
mp = 122 °C

IR (neat): 2977, 2931, 1703, 1604, 1455, 1401, 1364, 1321, 1270, 1234, 1159, 1114, 1059, 1035, 979, 947, 854, 755, 720, 696, 651, 606 cm^{-1}.

NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.08 (s, 2H, H_3), 7.33 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 5.93 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 3.52 (m, 2H, CH_2), 3.37 (m, 2H, CH_2), 2.58 (s, 6H, H_6), 2.30 (s, 3H, *Me*Ph-), 1.45 (s, 9H, -*t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 166.3, 151.3, 143.1, 140.3, 132.2, 109.8, 106.6, 81.5, 42.0, 40.0, 28.2, 23.2, 21.0.

***tert*-Butyl 4-(methylsulfonyl)-3,4-dihydropyrazine-1(2H)-carboxylate (23)**



Procedure **B**. *tert*-Butyl 2-(methylsulfonamido)ethylcarbamate **13** (44.6 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg,

0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 70/30) afforded **23** (14 mg, 26%) as a colorless oil.

Formula: $C_{10}H_{18}N_2O_4S$ **Mass:** 262.09 g.mol^{-1}

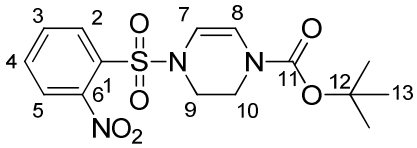
IR (neat): 3140, 2983, 2929, 1690, 1656, 1456, 1401, 1358, 1343, 1312, 1233, 1157, 1047, 962, 944, 860, 767, 730, 674 cm^{-1}.

NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 6.35 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 5.89 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 3.66 (m, 2H, CH_2), 3.59 (m, 2H, CH_2), 2.98 (s, 3H, SO_2-CH_3), 1.49 (s, 9H, *t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 151.2, 111.4, 106.3, 81.8, 43.2, 41.5, 37.3, 28.

MS (EI, 70 eV) *m/z* (abundance): 206 (20), 189 (2), 161 (5), 128 (4), 127 (63), 83 (54), 81 (16), 57 (100), 56 (11), 55 (8), 54 (6).

***tert*-butyl 4-((2-nitrophenyl)sulfonyl)-3,4-dihydropyrazine-1(2H)-carboxylate (23') – mixture of rotamers**



Procedure **B**. *tert*-butyl (2-(2-nitrophenylsulfonamido)ethyl)carbamate **13'** (69 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 70/30) afforded **23'** (25 mg, 38%) as a colorless oil.

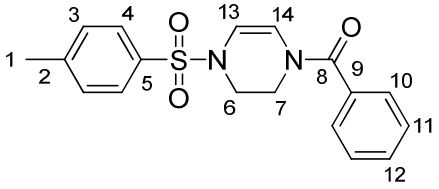
Formula: $C_{15}H_{19}N_3O_6S$ **Mass:** 369.10 g.mol^{-1}

IR (neat): 3126, 2978, 2932, 1703, 1544, 1456, 1403, 1360, 1312, 1276, 1235, 1165, 1119, 1062, 979, 954, 912, 852, 766, 728, 690, 650, 610 cm^{-1}.

NMR ^{1}H (400 MHz, $CDCl_3$): δ 8.00-7.95 (3, 1H, Ar*H*), 7.80-7.70 (m, 2H, Ar*H*), 7.68-7.6 (m, 1H, ArH), 6.55 (d, 0.4H, ^{3}J = 6.6 Hz, =C*H*), 6.39 (d, 0.6H, ^{3}J = 6.6 Hz, =C*H*), 6.06 (d, 0.4H, ^{3}J = 6.6 Hz, =C*H*), 5.96 (d, 0.6H, ^{3}J = 6.6 Hz, =C*H*), 3.70 (m, 2H, CH_2), 3.59 (m, 2H, CH_2), 1.49 (s, 9H, *t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 171.2, 151.0, 148.2, 134.1, 131.2, 130.8, 130.8, 124.2, 124.1, 112.4, 105.4, 81.9, 43.3, 40.0, 28.2.

Phenyl(4-tosyl-3,4-dihydropyrazin-1(2H)-yl)methanone (24)



Procedure **B**. *N*-(2-(4-Methylphenylsulfonamido)ethyl)benzamide **14** (63.6 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8

mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 50/50) afforded **24** (32 mg, 46%) as a white solid.

Formula: $C_{18}H_{18}N_2O_3S$ **Mass:** 342.10 g.mol^{-1}

mp = 120 °C

IR (neat): 2944, 2867, 1632, 1598, 1447, 140, 1382, 1350, 1302, 1275, 1241, 1161, 1099, 1049, 984, 9558, 884, 812, 792, 726, 694, 676, 647 cm^{-1}.

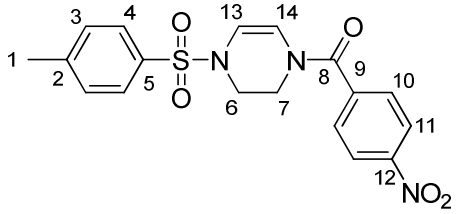
NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.71 (m, 2H, Ar*H*), 7.54-7.39 (m, 7H, Ar*H*), 6.29 (d, 1H, ^{3}J = 6.6 Hz, =C*H*), 6.13 (d, 1H, ^{3}J = 6.6 Hz, =C*H*), 3.62-3.57 (m, 2H, CH_2), 3.57-3.51 (m, 2H, CH_2), 2.44 (s, 3H, CH_3Ph).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 167.7, 144.4, 134.0, 133.6, 130.9, 130.1, 128.5, 128.4, 127.2, 112.6, 108.2, 43.3, 38.3, 21.7

MS (EI, 70 eV) *m/z* (abundance): 342 (5), 187 (17), 106 (8), 105 (100), 91 (9), 81 (4), 77 (23).

HRMS (ESI): Calculated value for $C_{18}H_{18}N_2O_3S$ $[M+Na]^+$: 365.09303 ; Found: 365.09343.

(4-Nitrophenyl)(4-tosyl-3,4-dihydropyrazin-1(2H)-yl)methanone (25)



Procedure **B**. *N*-(2-(4-Methylphenylsulfonamido)ethyl)-4-nitrobenzamide **15** (72.6 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 30/70) afforded **25** (40 mg, 51%) as an orange solid.

Formula: $C_{18}H_{17}N_3O_5S$ **Mass:** 387.08 g.mol^{-1}

mp = 148 °C

IR (neat): 3023, 2922, 1642, 1599, 1522, 1493, 1456, 1409, 1348, 1305, 1269, 1235, 1165, 1101, 988, 958, 919, 848, 815, 738, 707, 692, 657, 618 cm^{-1}.

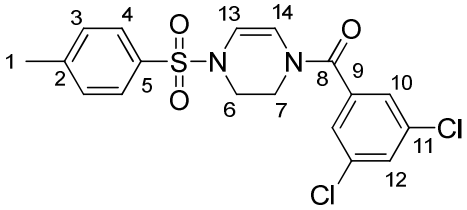
NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 8.21 (m, 2H, Ar*H*), 7.72-7.62 (m, 4H, Ar*H*), 7.42 (d, 2H, ^{3}J = 8.3 Hz, Ar*H*), 6.20 (m, 1H, =C*H*), 6.14 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 3.60-3.55 (m, 2H, CH_2), 3.54-3.50 (m, 2H, CH_2), 2.40 (s, 3H, CH_3Ph).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 165.4, 149.0, 144.6, 139.6, 134.0, 130.1, 129.4, 127.2, 123.8, 110.9, 109.7, 43.1, 38.5, 21.6.

MS (EI, 70 eV) *m/z* (abundance): 220 (29), 206 (16), 205 (100), 177 (11), 145 (13), 121 (5), 95 (8), 91 (9), 81 (13), 67 (9), 57 (45), 55 (10).

HRMS (ESI): Calculated value for $C_{18}H_{17}N_3O_5S$ $[M+Na]^+$: 410.07811 ; Found: 410.07842.

(3,5-Dichlorophenyl)(4-tosyl-3,4-dihydropyrazin-1(2H)-yl)methanone (26)



Procedure **B**. 3,4-Dichloro-*N*-(2-(4-methylphenylsulfonamido)ethyl)benzamide **16** (77.2 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 30/70) afforded **26** (25 mg, 29%) as a pale yellow oil.

Formula: $C_{18}H_{16}Cl_2N_2O_3S$ **Mass:** 410.05 $g.mol^{-1}$

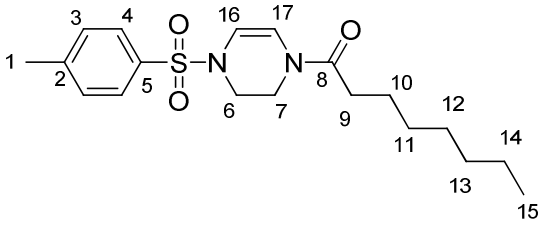
IR (neat): 2920, 2851, 1640, 1595, 1555, 1456, 1405, 1354, 1303, 1232, 1164, 1098, 1033, 995, 960, 892, 814, 749, 710, 696, 659 cm^{-1}.

NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.75-7.6 (m, 4H, Ar*H*), 7.44 (d, 2H, ^3J = 8.2 Hz, Ar*H*), 7.42-7.38 (m, 1H, Ar*H*), 6.25 (m, 1H, =C*H*), 6.15 (d, 1H, ^3J = 6.6 Hz, =C*H*), 3.61-3.56 (m, 2H, CH_2), 3.55-3.48 (m, 2H, CH_2), 2.42 (s, 3H, CH_3Ph).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 165.2, 144.5, 135.5, 134.0, 133.1, 130.6, 130.1, 127.6, 127.2, 111.4, 109.3, 43.2, 38.5, 21.6.

HRMS (ESI): Calculated value for $C_{18}H_{16}Cl_2N_2O_3S$ $[M+Na]^+$: 433.01509 ; Found: 433.01568.

1-(4-Tosyl-3,4-dihydropyrazin-1(2H)-yl)octan-1-one (27)



Procedure **B**. *N*-(2-(4-Methylphenylsulfonamido)ethyl)octanamide **17** (70.8 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 50/50) afforded **27** (51 mg, 67%) as a colorless oil.

Formula: $C_{19}H_{28}N_2O_3S$ **Mass:** 364.18 $g.mol^{-1}$

IR (neat): 2925, 2855, 1648, 1457, 1408, 1354, 1307, 1243, 1165, 1098, 966, 814, 709, 689, 651 cm^{-1}.

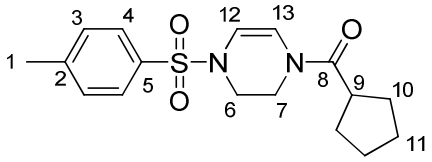
NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.7 (d, 2H, ^3J = 8.2 Hz, Ar*H*), 7.44 (d, 2H, ^3J = 8.2 Hz, Ar*H*), 6.48 (m, 1H, =C*H*), 6.06 (d, 1H, ^3J = 6.7 Hz, =C*H*), 3.55-3.4 (m, 4H, $2CH_2$), 2.42 (s, 3H, CH_3Ph), 1.53 (m, 2H, CH_2), 1.4-1.2 (m, 10H, $5CH_2$), 0.95-0.8 (m, 3H, CH_3).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 169.7, 144.3, 134.1, 130.0, 127.2, 110.6, 108.5, 43.3, 37.4, 32.9, 31.6, 29.2, 29.0, 24.6, 22.6, 21.6, 14.1.

MS (EI, 70 eV) *m/z* (abundance): 364 (4), 209 (4), 127 (4), 91 (6), 84 (6), 83 (100), 57 (19), 55 (5).

HRMS (ESI): Calculated value for $C_{19}H_{28}N_2O_3S$ $[M+Na]^+$: 387.17128 ; Found: 387.17213.

Cyclopentyl(4-tosyl-3,4-dihydropyrazin-1(2H)-yl)methanone (28)



Procedure **B**. *N*-(2-(4-Methylphenylsulfonamido)ethyl)cyclopentanecarboxamide **18** (62 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 50/50) afforded **28** (47 mg, 70%) as a colorless oil.

Formula: $C_{17}H_{22}N_2O_3S$ **Mass:** 334.13 g.mol^{-1}

IR (neat): 3270, 2954, 2867, 1650, 1597, 1536, 1445, 1377, 1327, 1237, 1155, 1090, 1018, 898, 815, 675 cm^{-1}.

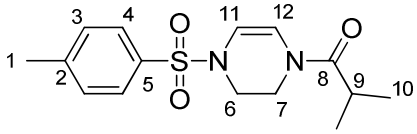
NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.69 (d, 2H, ^3J = 8.2 Hz, Ar*H*), 7.44 (d, 2H, ^3J = 8.2 Hz, Ar*H*), 6.53 (d, 1H, ^3J = 6.8 Hz, =C*H*), 6.06 (d, 1H, ^3J = 6.7 Hz, =C*H*), 3.6-3.4 (m, 4H, $2CH_2$), 2.99 (m, 1H, H_9), 2.42 (s, 3H, CH_3Ph), 1.8-1.5 (m, 8H, H_{10} & H_{11}).

NMR ^{13}C (100 MHz, DMSO-d6, 395K): δ 172.9, 144.3, 134.1, 130.0, 127.2, 110.7, 108.4, 43.4, 41.0, 37.7, 30.0, 26.0, 21.6.

MS (EI, 70 eV) *m/z* (abundance): 334 (5), 179 (14), 97 (23), 91 (11), 84 (6), 83 (100), 69 (59), 65 (4), 55 (4).

HRMS (ESI): Calculated value for $C_{17}H_{22}N_2O_3S$ $[M+Na]^+$: 357.12433 ; Found: 357.12464.

2-Methyl-1-(4-tosyl-3,4-dihydropyrazin-1(2H)-yl)propan-1-one (29)



Following general procedure **B**, *N*-(2-(4-Methylphenylsulfonamido)ethyl)isobutyramide **19** (56.4 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 50/50) afforded **29** (51 mg, 83%) as a colorless oil.

Formula: $C_{15}H_{20}N_2O_3S$ **Mass:** 308.12 g.mol^{-1}

IR (neat): 2972, 2932, 1645, 1596, 1458, 1411, 1354, 1325, 1304, 1242, 1215, 1164, 1087, 1013, 990, 966, 917, 815, 727, 707, 684, 647 cm^{-1}.

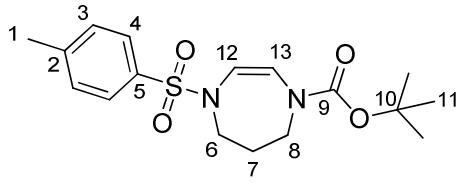
NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.7 (d, 2H, ^{3}J = 8.4 Hz, Ar*H*), 7.44 (d, 2H, ^{3}J = 8.4 Hz, Ar*H*), 6.51 (d, 1H, ^{3}J = 6.8 Hz, =C*H*), 6.08 (d, 1H, ^{3}J = 6.7 Hz, =C*H*), 3.6-3.4 (m, 4H, $2CH_2$), 2.88 (hept, 1H, ^{3}J = 6.8 Hz, H_9), 2.42 (s, 3H, CH_3Ph), 1.2 (d, 6H, ^{3}J = 6.8 Hz, H_{10}).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 173.6, 144.3, 134.1, 130.0, 127.2, 110.3, 108.6, 41.6, 37.6, 30.3, 21.6, 19.0.

MS (EI, 70 eV) *m/z* (abundance): 308 (4), 153 (12), 91 (12), 83 (100), 81 (7), 71 (26), 65 (5).

HRMS (ESI): Calculated value for $C_{15}H_{20}N_2O_3S$ $[M+H]^+$: 309.12674 ; Found: 309.12716.

***tert*-Butyl 4-tosyl-4,5,6,7-tetrahydro-1H-1,4-diazepine-1-carboxylate (30)**



Procedure **B**. *tert*-Butyl 3-(4-methylphenylsulfonamido)propylcarbamate **20** (65.6 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and TMS-EBX (68.8 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt: 70/30) afforded **30** (20 mg, 57%).

Formula: $C_{17}H_{24}N_2O_4S$ **Mass:** 352.14 $g.mol^{-1}$

IR (neat): 2958, 2929, 1700, 1663, 1597, 1456, 1407, 1390, 1376, 1349, 1337, 1311, 1302, 1216, 1158, 1128, 1092, 1064, 1010, 966, 887, 876, 812, 768, 716, 698, 658, 611 cm^{-1}.

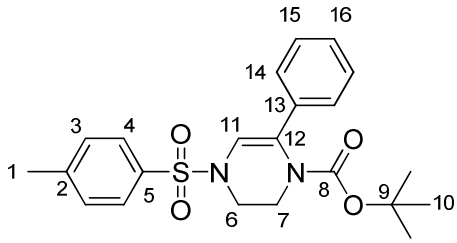
NMR ^{1}H (400 MHz, DMSO-d6, 395K): δ 7.72 (d, 2H, ^{3}J = 8.3 Hz, Ar*H*), 7.44 (d, 2H, ^{3}J = 8.3 Hz, Ar*H*), 6.05 (d, 1H, ^{3}J = 7.2 Hz, =C*H*), 5.82 (d, 1H, ^{3}J = 7.2 Hz, =C*H*), 3.59 (dd, 2H, ^{3}J = 6.2 Hz, CH_2), 3.45 (dd, 2H, ^{3}J = 6.2 Hz, CH_2), 2.43 (s, 3H, CH_3Ph), 1.76 (dddd, 2H, ^{3}J = 6.1 Hz, H_7), 1.43 (s, 9H, *t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 183.5, 152.6, 143.8, 136.0, 129.8, 126.9, 116.6, 112.4, 48.2, 45.2, 42.0, 28.2, 21.6.

MS (EI, 70 eV) *m/z* (abundance): 352 (4), 296 (44), 155 (9), 141 (100), 97 (76), 96 (13), 92 (10), 91 (37), 69 (10), 68 (17), 57 (96), 56 (13).

HRMS (ESI): Calculated value for $C_{17}H_{24}N_2O_4S$ $[M+Na]^+$: 375.13490 ; Found: 375.13534.

***tert*-Butyl 6-phenyl-4-tosyl-3,4-dihydropyrazine-1(2H)-carboxylate (32)**



Procedure **B**. *tert*-Butyl 2-(4-methylphenylsulfonamido)ethylcarbamate **7** (62.8 mg, 0.2 mmol, 1 equiv) was treated with NaH (16 mg, 0.4 mmol, 2 equiv, 60% dispersion in mineral oil) and Ph-EBX (69.6 mg, 0.2 mmol, 1 equiv). Purification over silica gel (EP/AcOEt : 70/30) afforded **32** as the major product along with some inseparable impurities (26 mg, global yield 31%).

Formula: $C_{22}H_{26}N_2O_4S$ **Mass:** 414.16 g.mol^{-1}

IR (neat): 2978, 2931, 2238, 1706, 1669, 1598, 1448, 1366, 1240, 1162, 1090, 1046, 992, 943, 851, 814, 756, 693, 671 cm^{-1}.

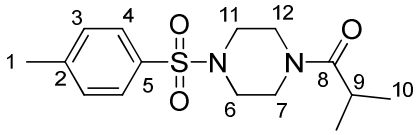
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.77 (m, 2H, ArH), 7.3-7.25 (m, 7H, ArH), 6.65 (s, 1H, =C*H*), 3.68-3.6 (m, 2H, CH_2), 3.58-3.5 (m, 2H, CH_2), 2.39 (s, 3H, *Me*Ph-), 0.95 (s, 9H, -*t*Bu).

NMR ^{13}C (100 MHz, $CDCl_3$): δ 178.4, 144.5, 136.4, 134.2, 132.9, 131.5, 129.8, 128.3, 128.1, 127.8, 105.5, 82.1, 46.1, 44.1, 27.4, 21.6.

MS (EI, 70 eV) *m/z* (abundance): 314 (12), 313 (29), 249 (29), 159 (16), 158 (13), 155 (13), 91 (100), 65 (24).

HRMS (ESI): Calculated value for $C_{22}H_{26}N_2O_4S$ $[M+Na]^+$: 437.15055 ; Found: 437.15116.

2-Methyl-1-(4-tosylpiperazin-1-yl)propan-1-one (33)



To a solution of 2-methyl-1-(4-tosyl-3,4-dihydropyrazin-1(2H)-yl)propan-1-one **29** (61.6 mg, 0.2 mmol, 1 equiv) in EtOH (10 mL) was added Pd/C (42 mg, 20 mol%) and the mixture was stirred under an hydrogen atmosphere (25 bar) for 24 h. After filtration over Celite®, **33** was isolated (53 mg, 85%) as a solid.

Formula: $C_{15}H_{22}N_2O_3S$ **Mass:** 310.13 g.mol^{-1}

mp: 118 °C

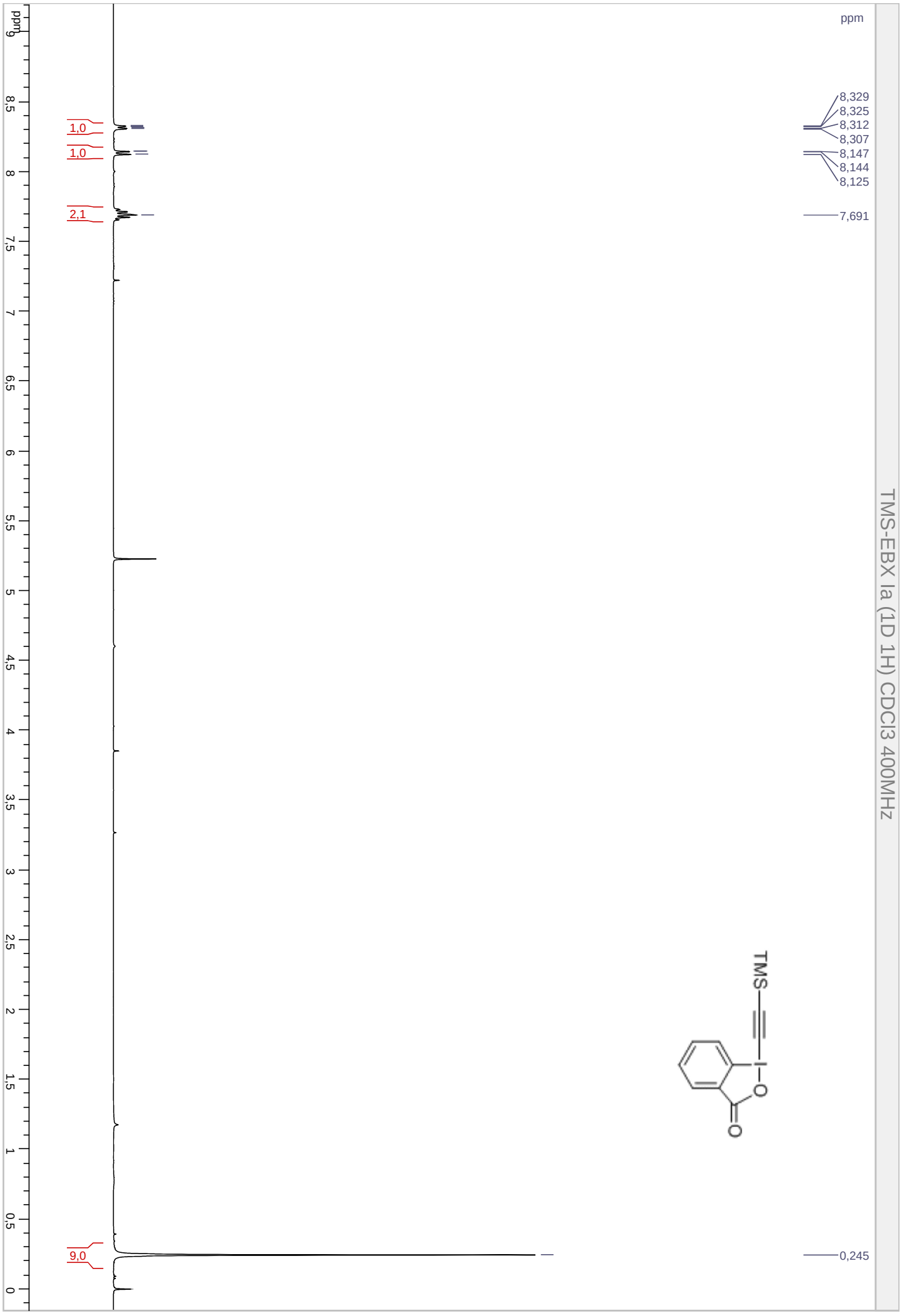
IR (neat): 3306, 2968, 2928, 2856, 1635, 1597, 1473, 1435, 1351, 1272, 1236, 1162, 1117, 1090, 1033, 945, 918, 817, 727, 652 cm^{-1}.

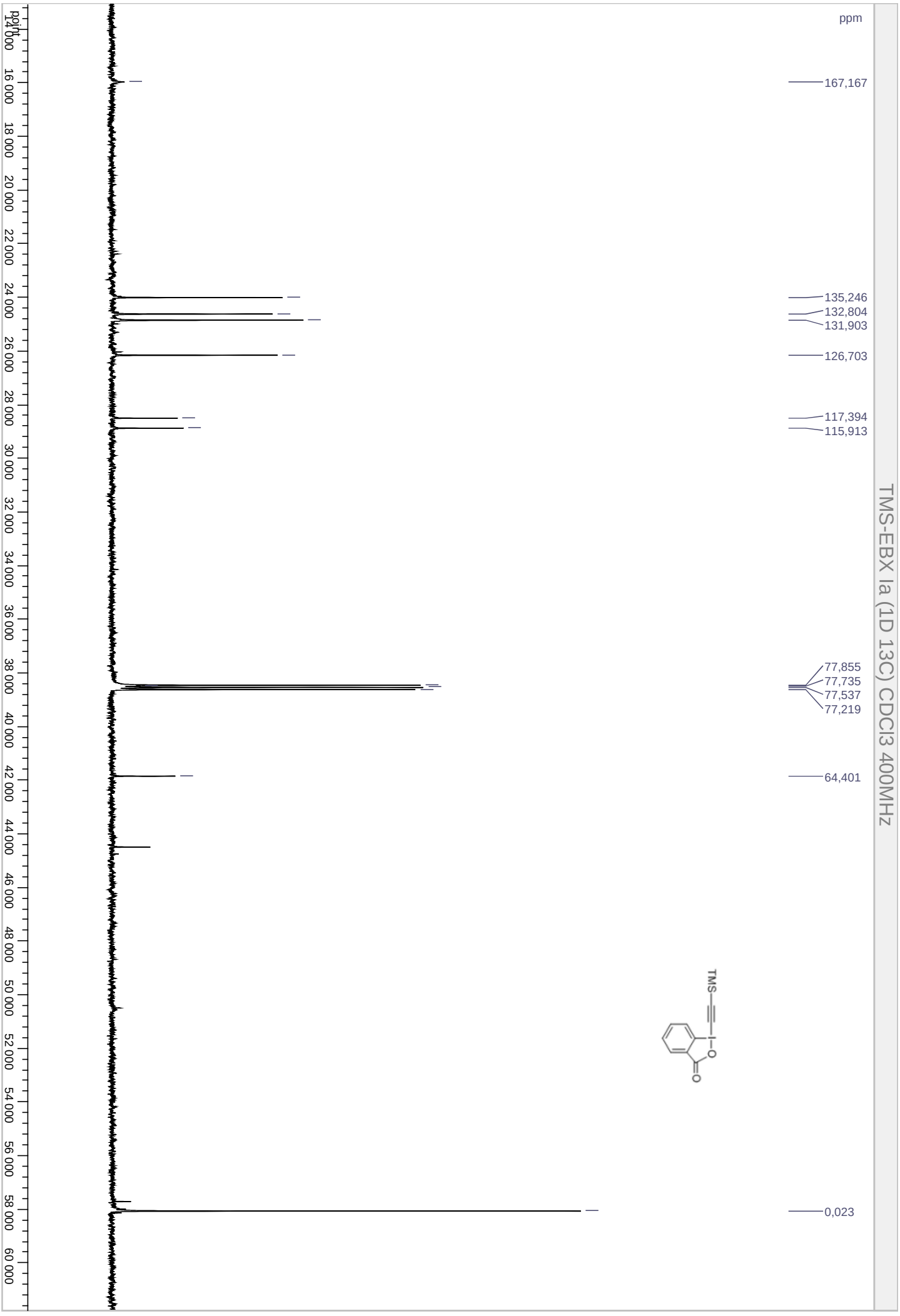
NMR ^{1}H (400 MHz, $CDCl_3$): δ 7.63 (d, 2H, ^{3}J = 8.3 Hz, Ar*H*), 7.34 (d, 2H, ^{3}J = 8.3 Hz, Ar*H*), 3.70 (m, 2H, CH_2), 3.59 (m, 2H, CH_2), 3.05-2.94 (m, 4H, 2 CH_2), 2.69 (hept, 1H, H_9), 2.44 (s, 3H, C*H*$_3$Ph), 1.06 (d, 6H, ^{3}J = 6.8 Hz, H_{10}).

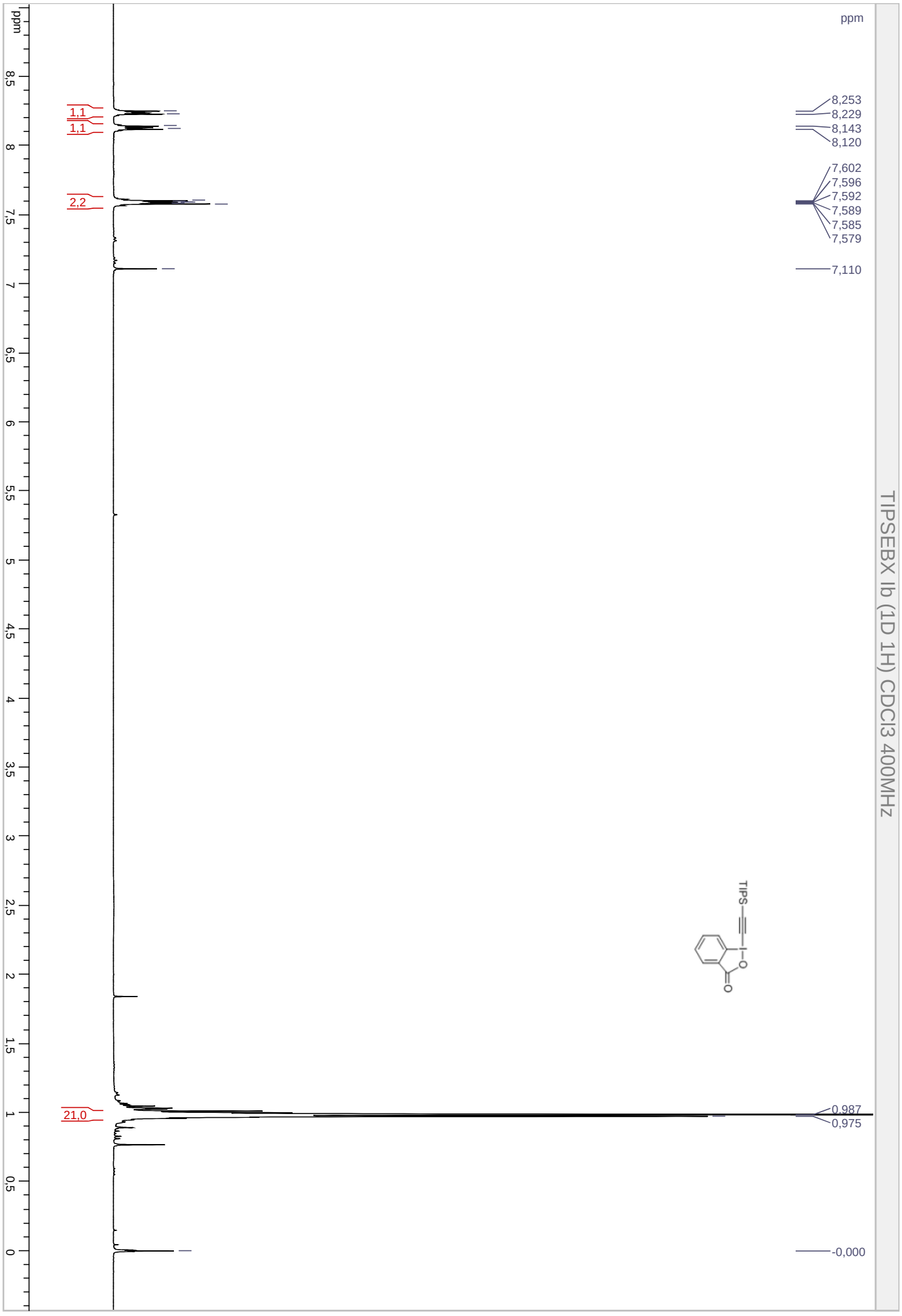
NMR ^{13}C (100 MHz, $CDCl_3$): δ 170.2, 138.9, 127.0, 124.6, 122.5, 41.1, 40.7, 39.6, 35.6, 24.8, 16.3, 14.1.

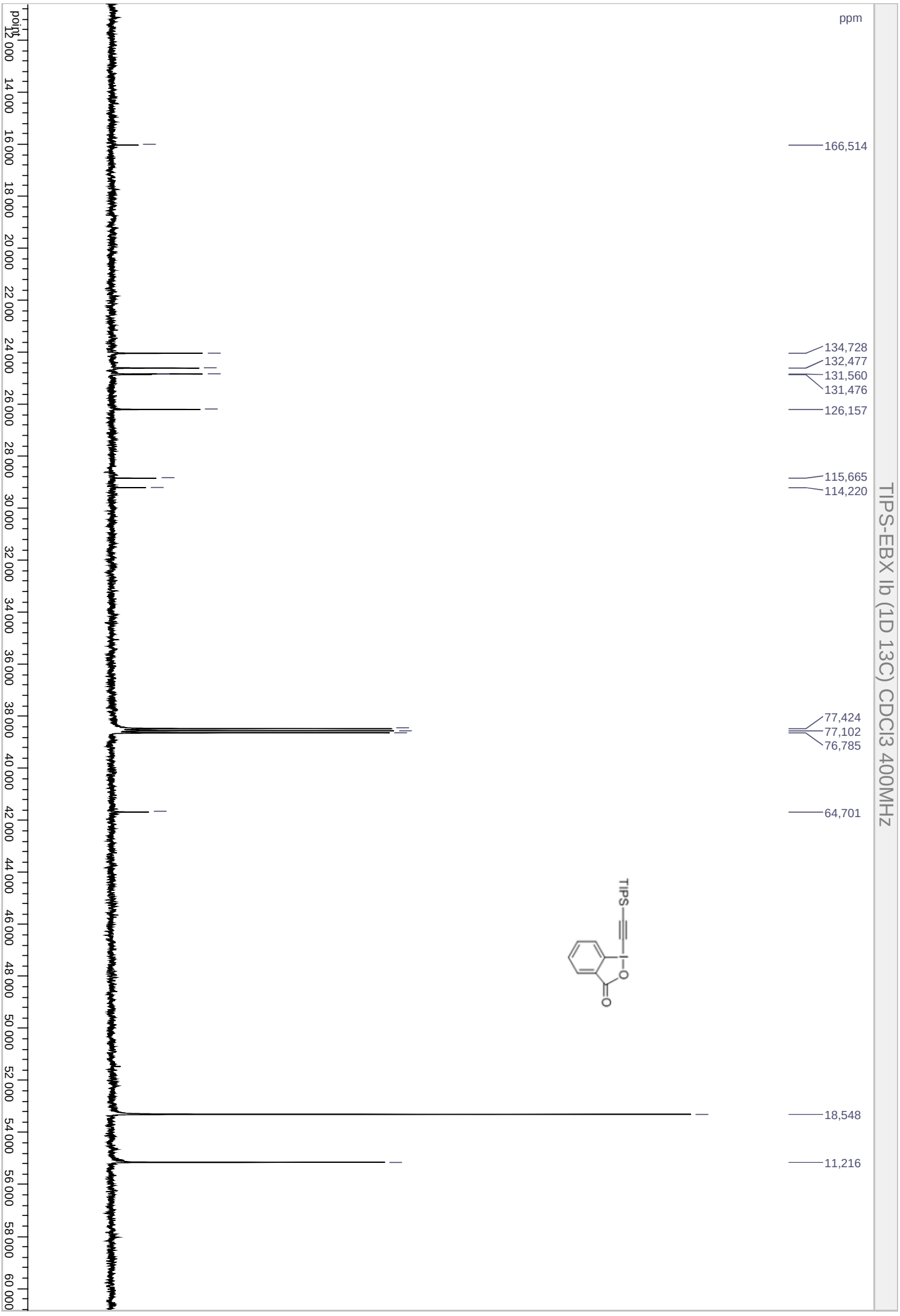
MS (EI, 70 eV) *m/z* (abundance): 310 (1), 156 (8), 155 (88), 91 (23), 85 (100), 71 (20), 65 (7), 56 (18).

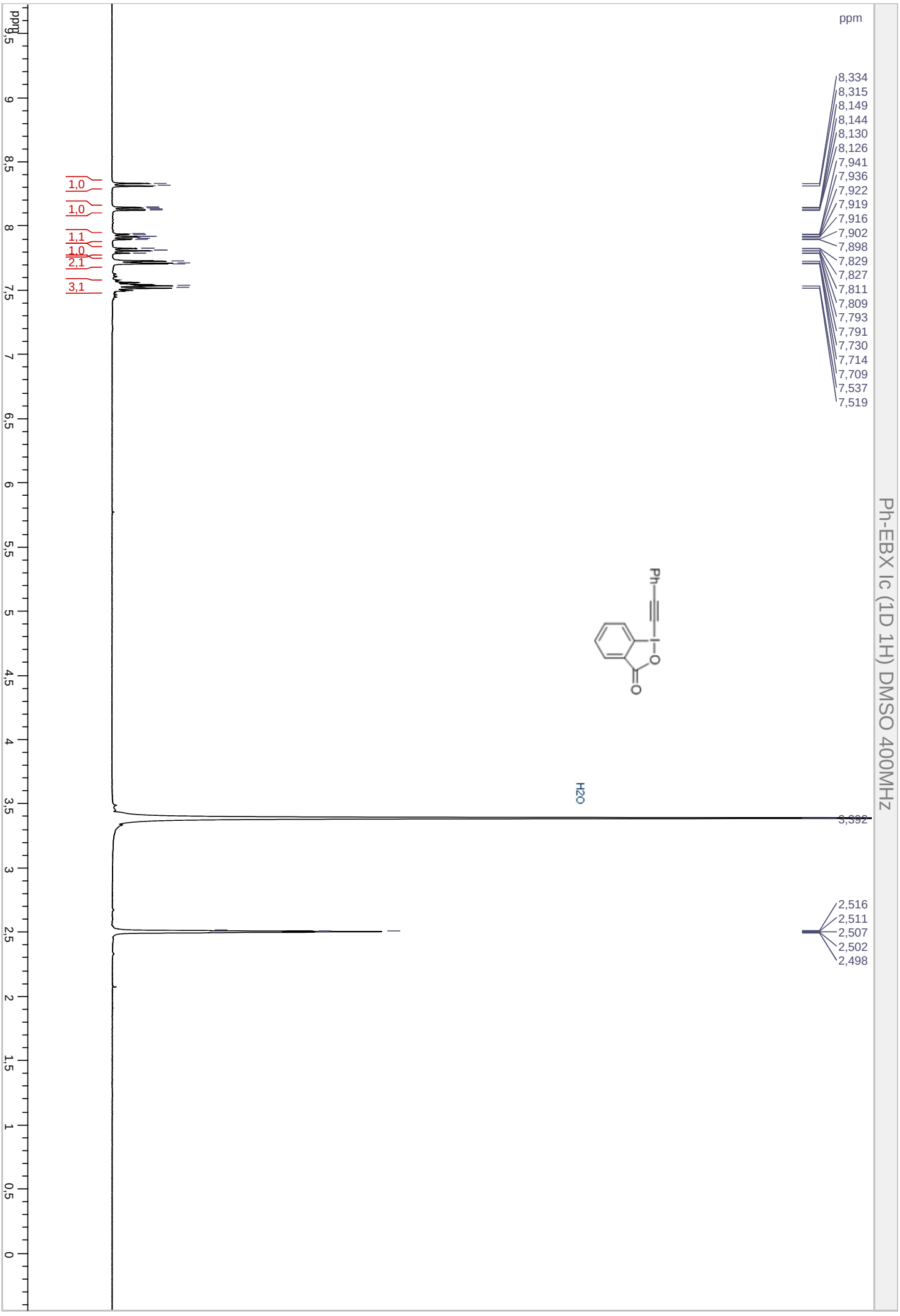
HRMS (ESI): Calculated value for $C_{15}H_{22}N_2O_3S$ $[M+Na]^+$: 333.12433 ; Found: 333.12426.

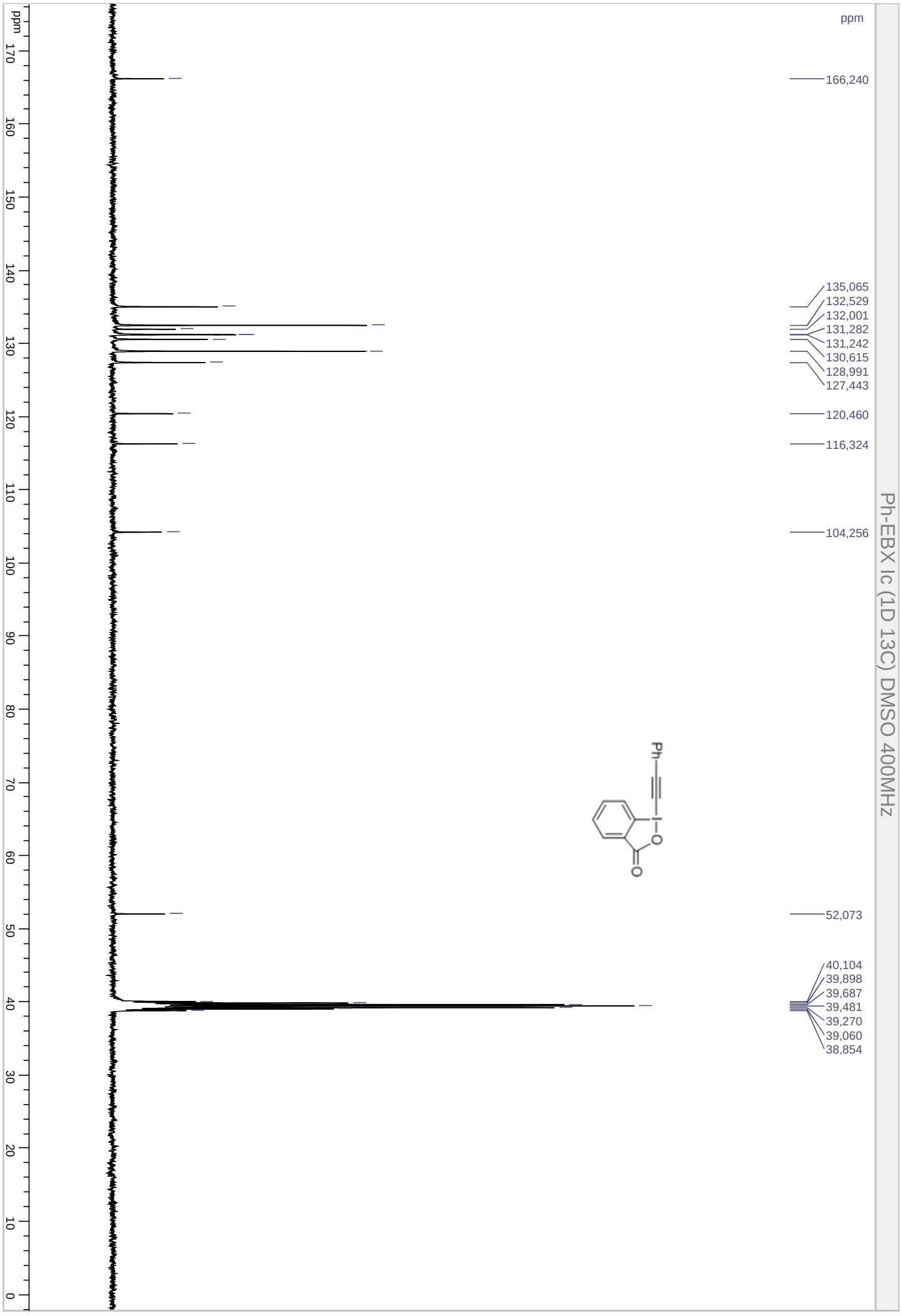


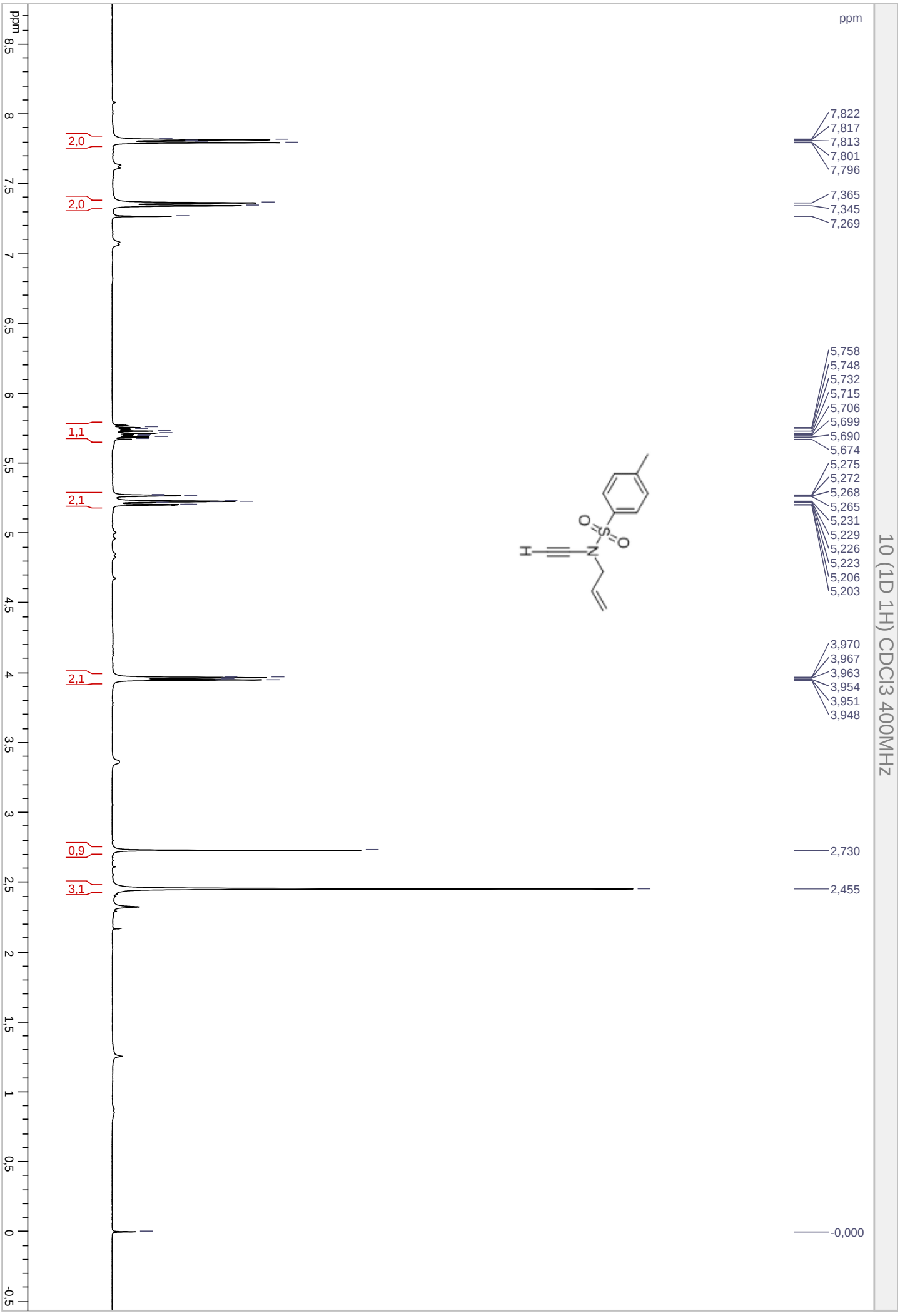








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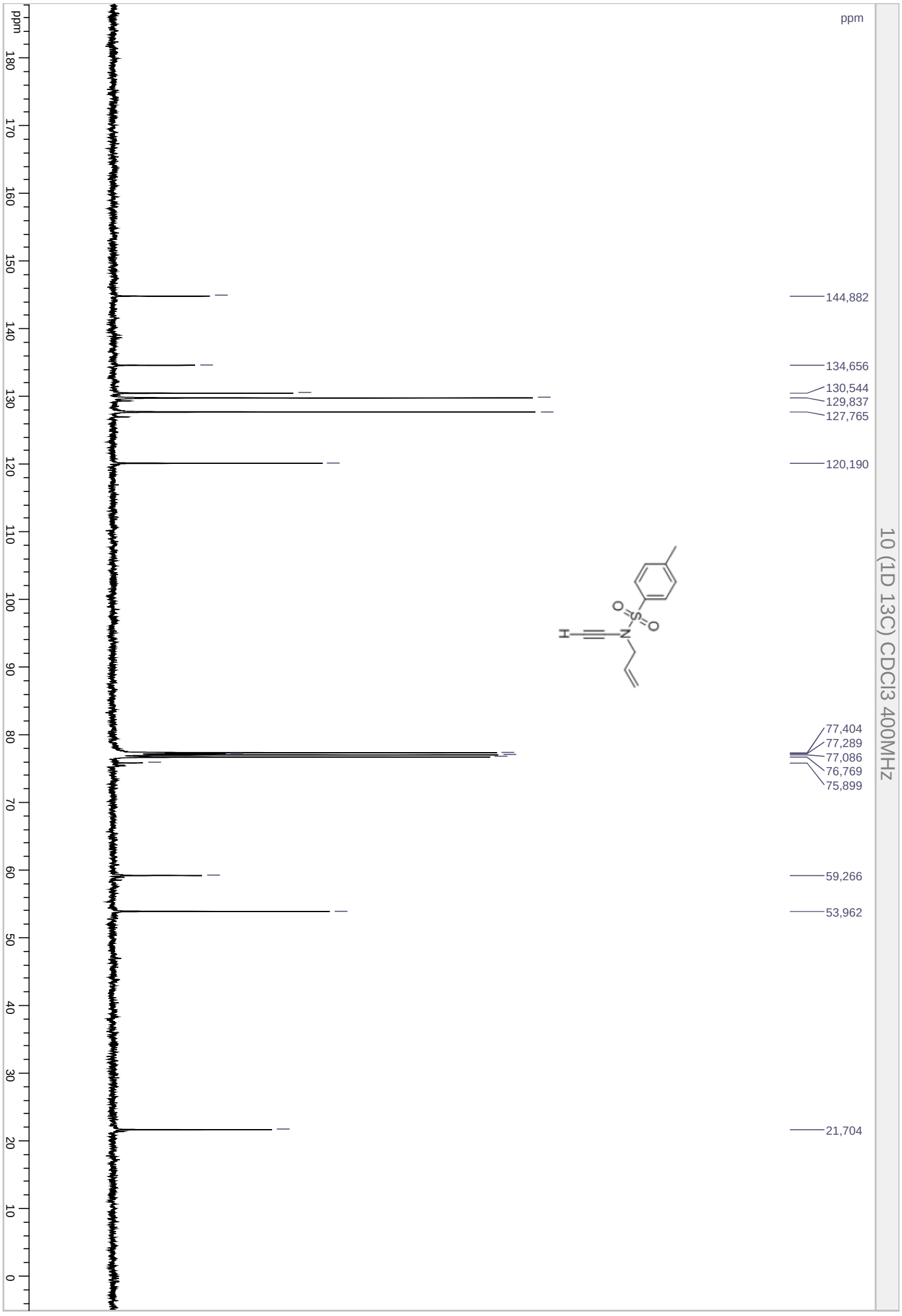

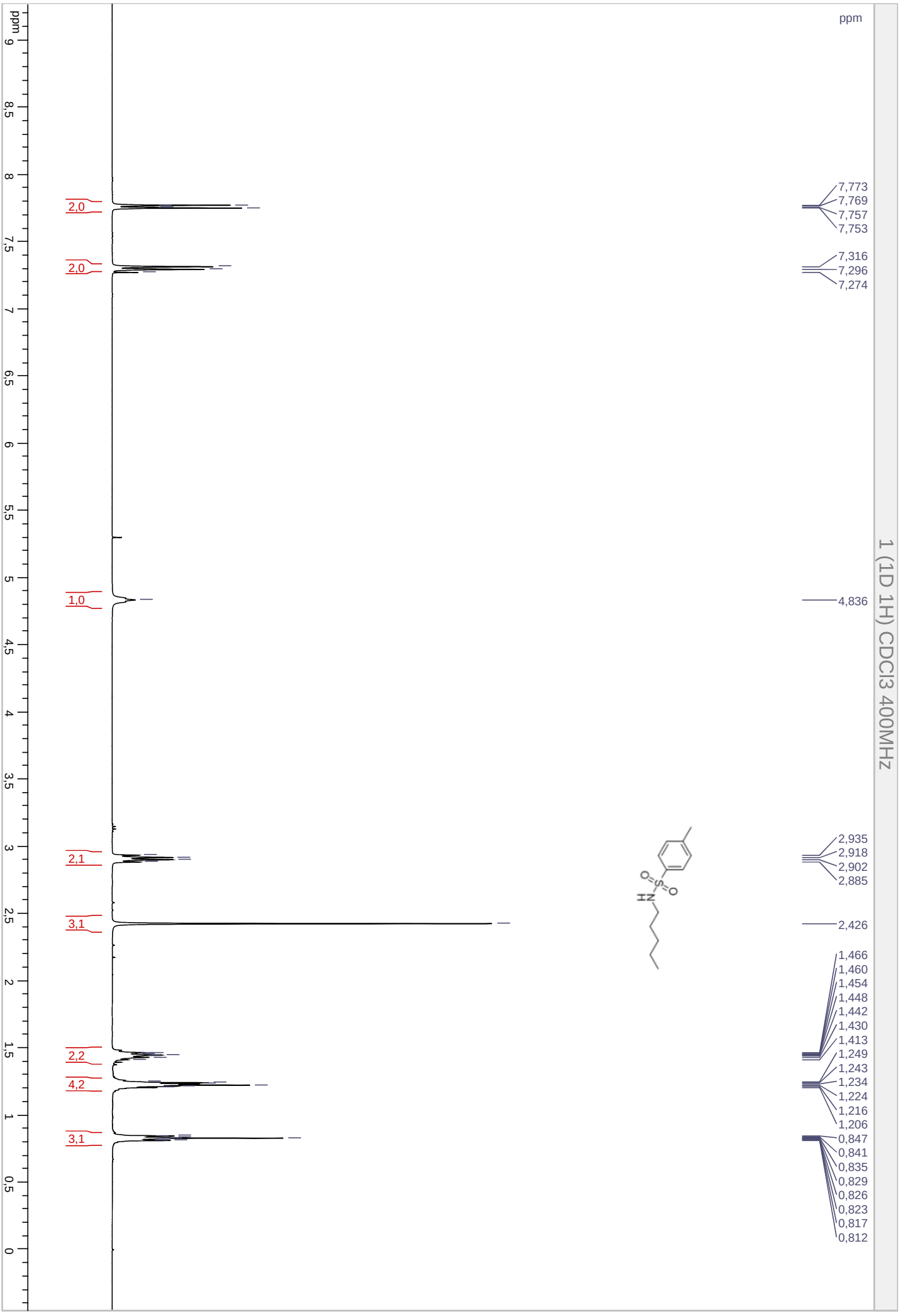

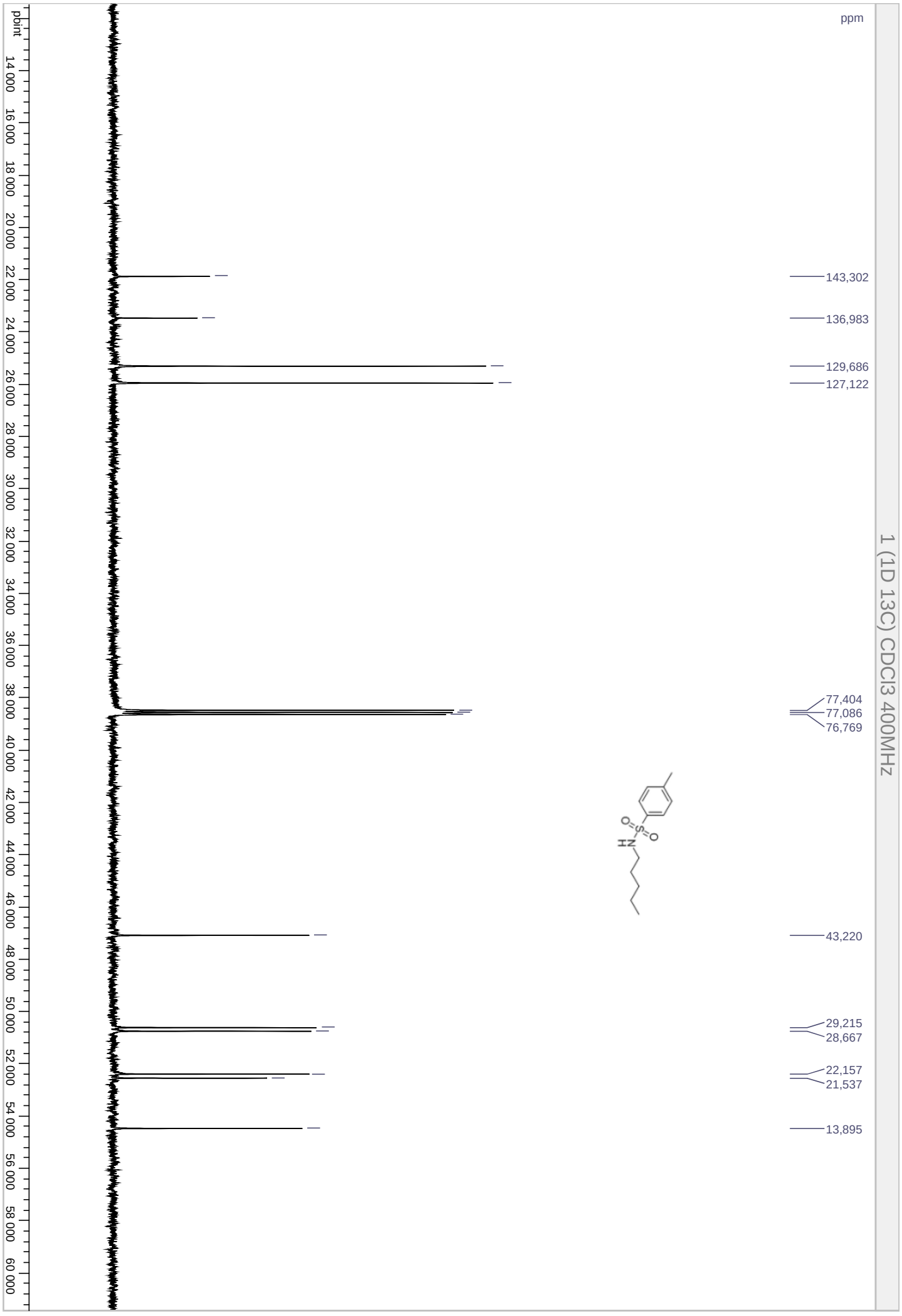

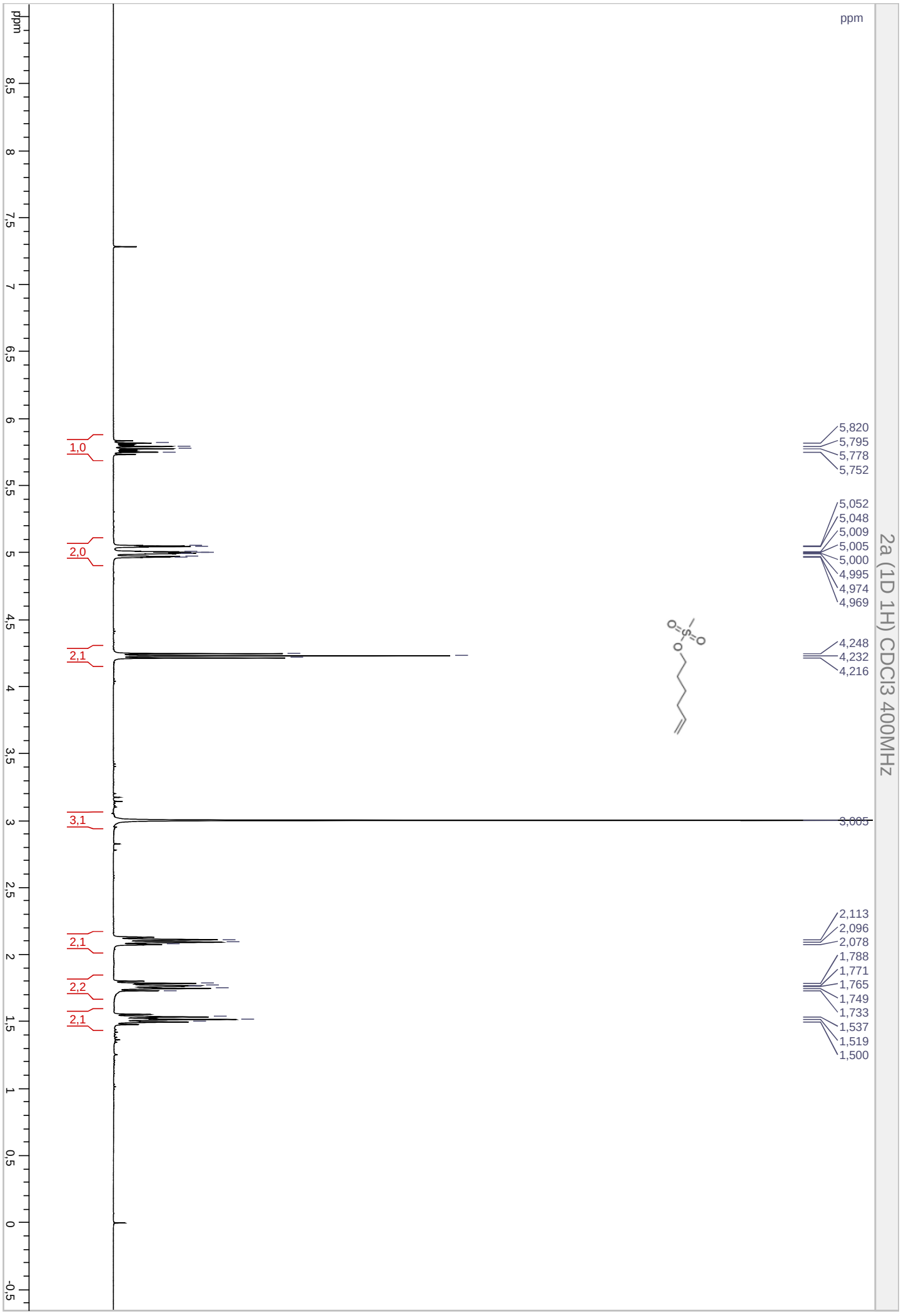

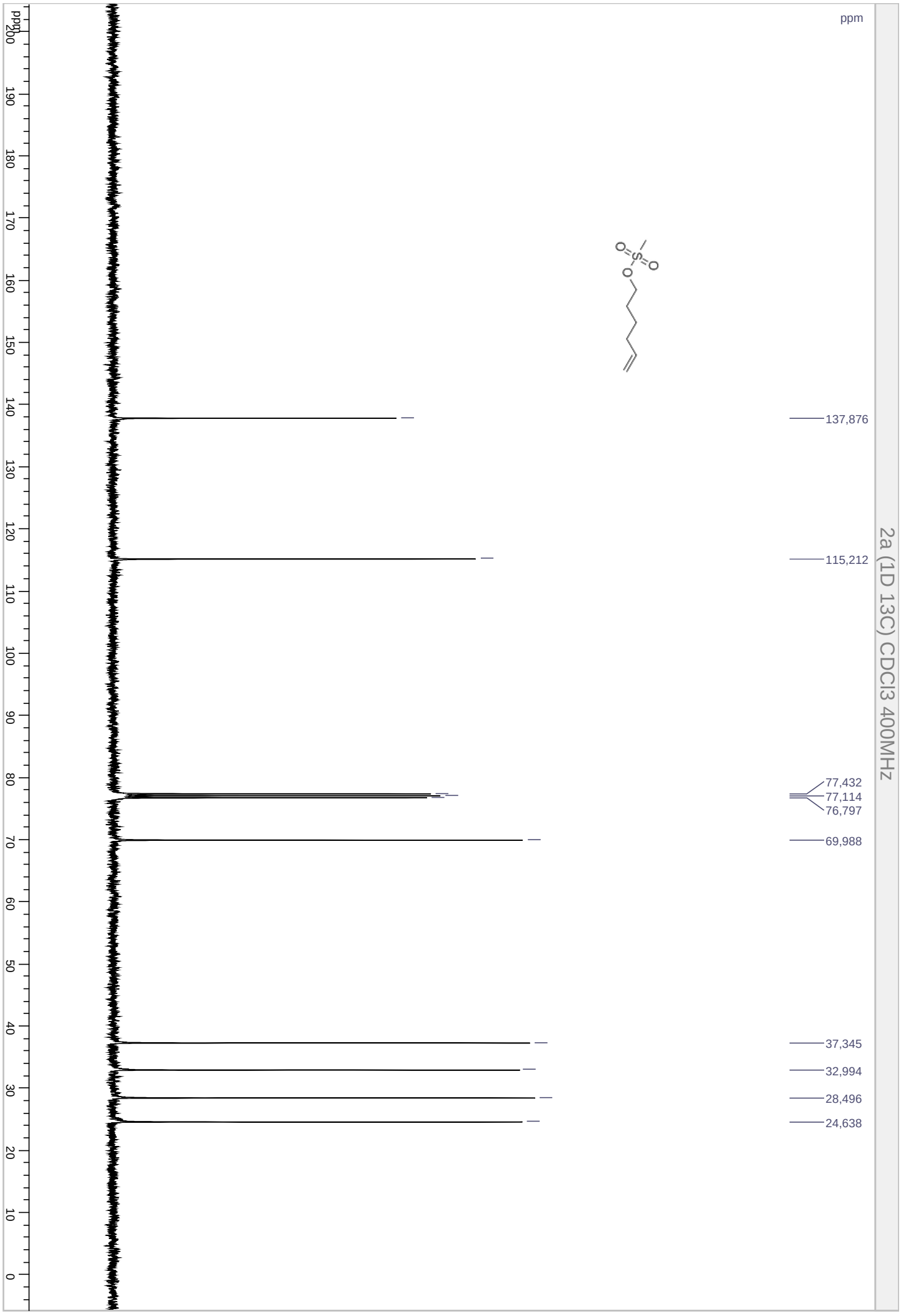

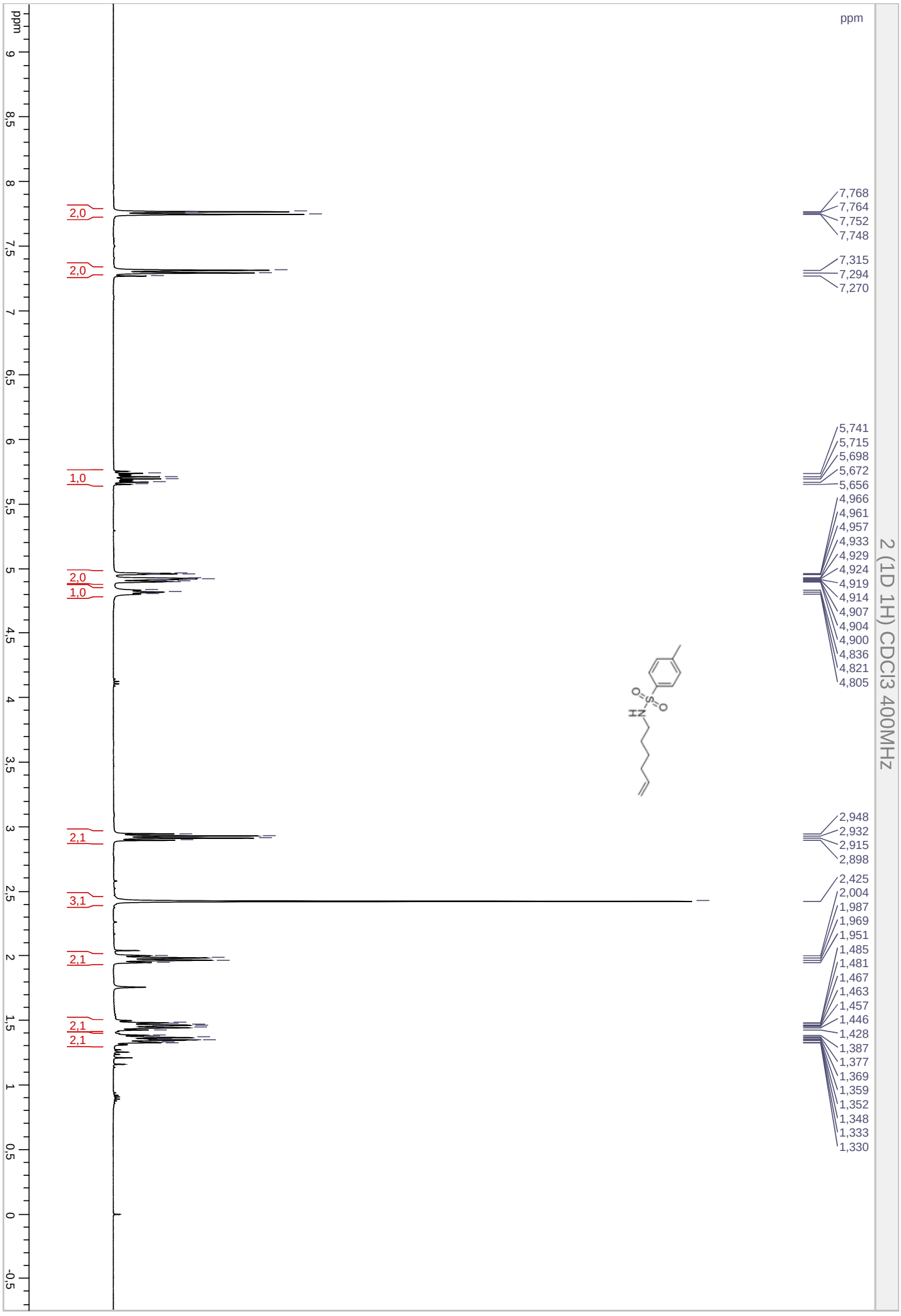

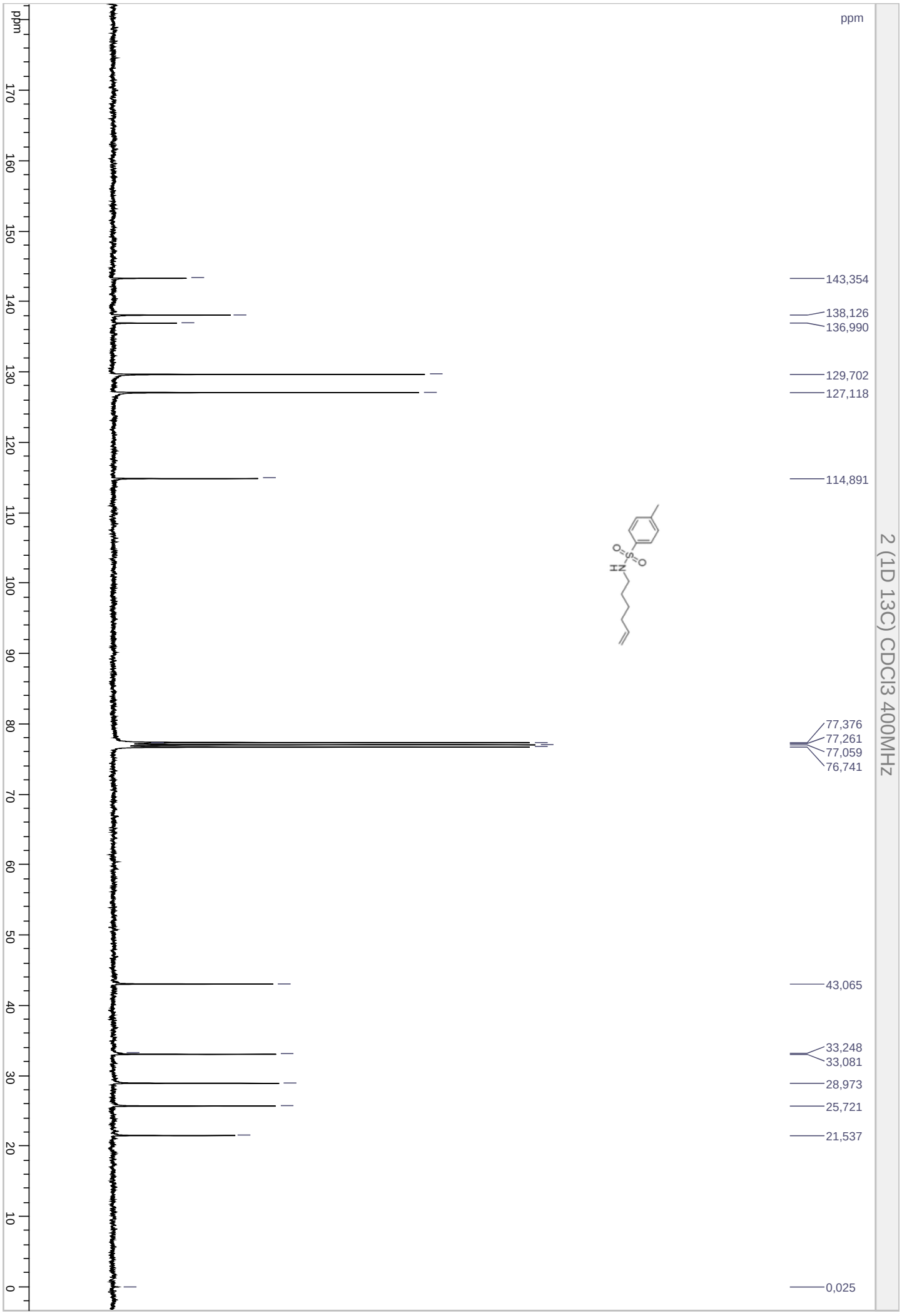

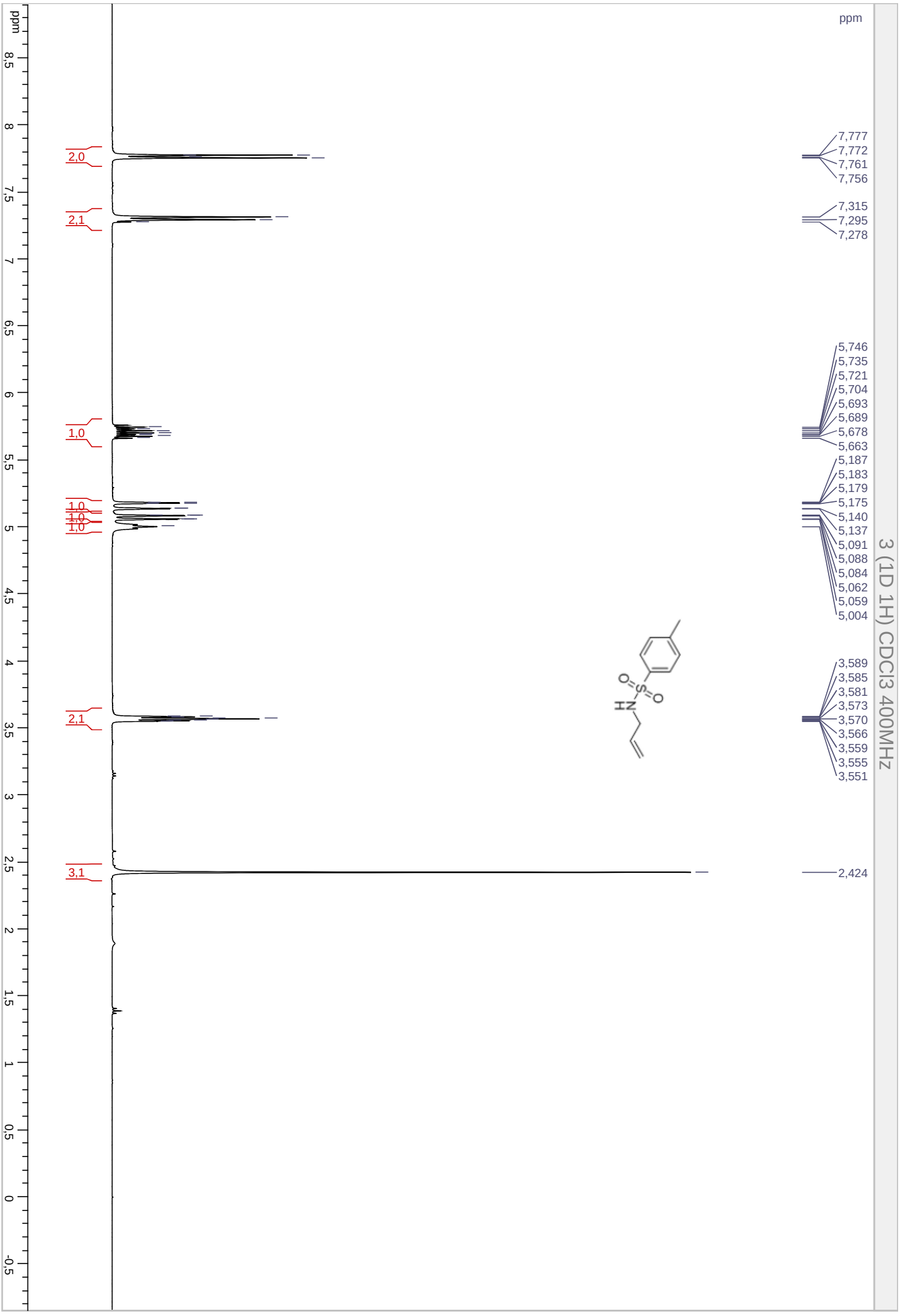

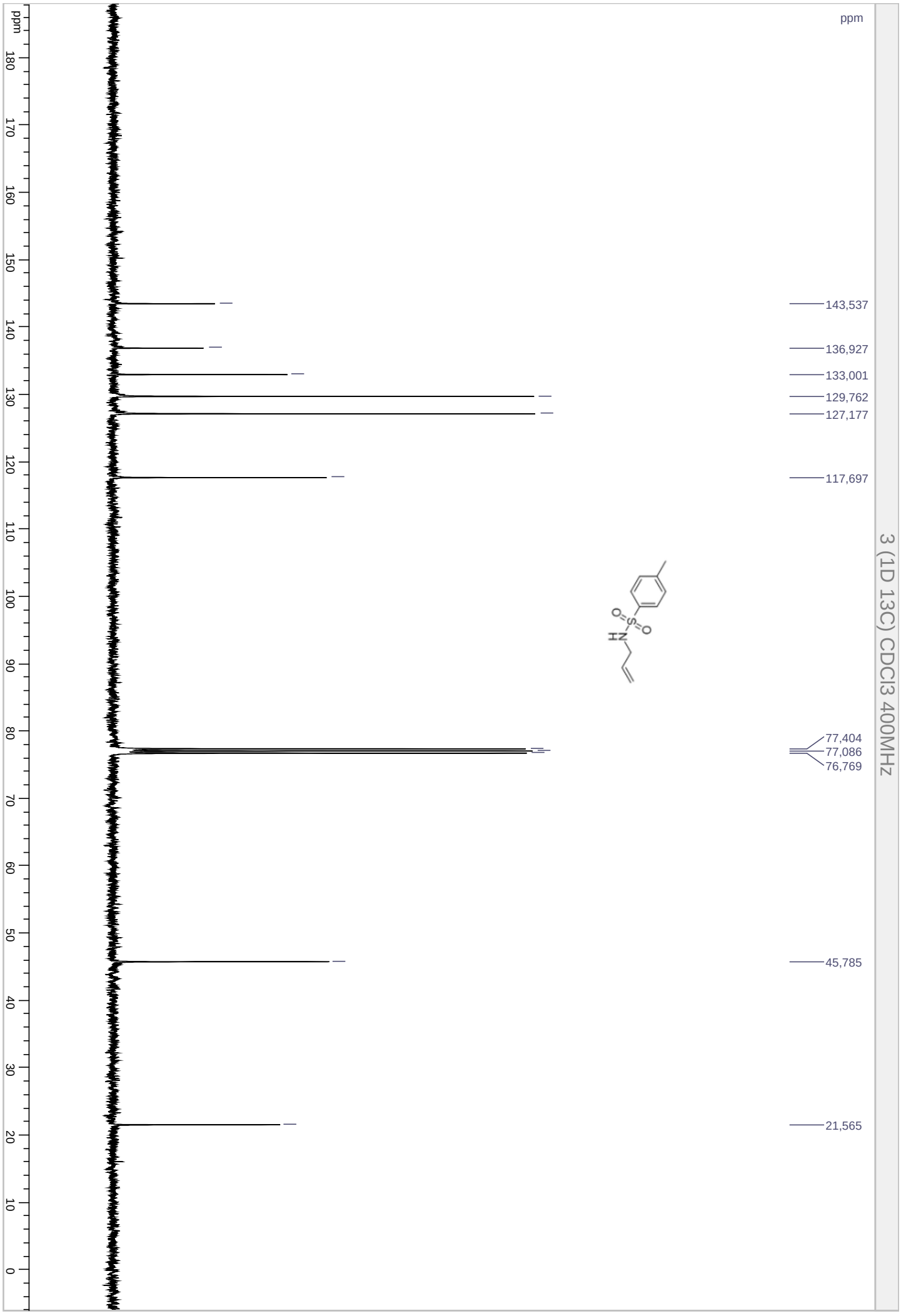

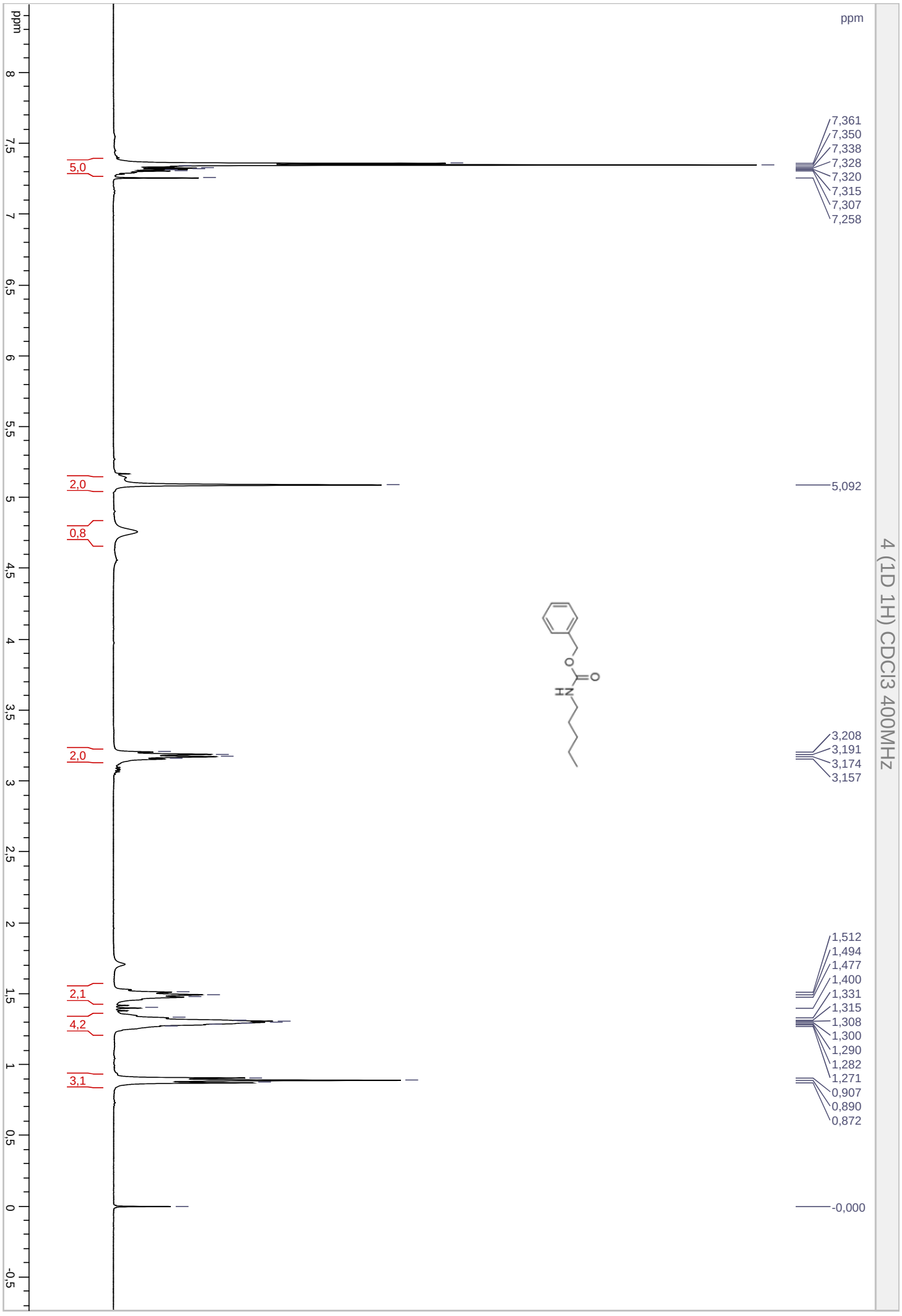

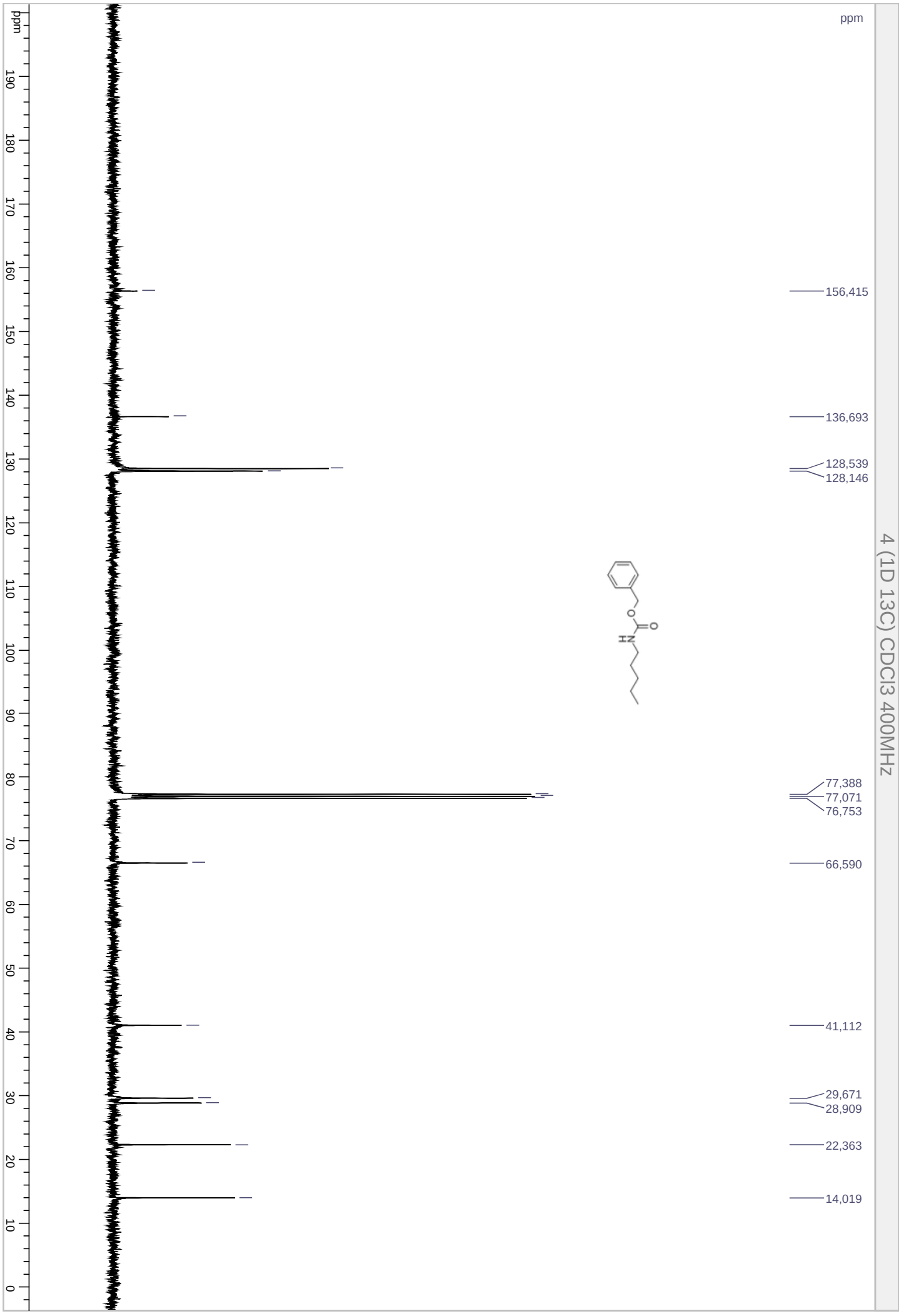

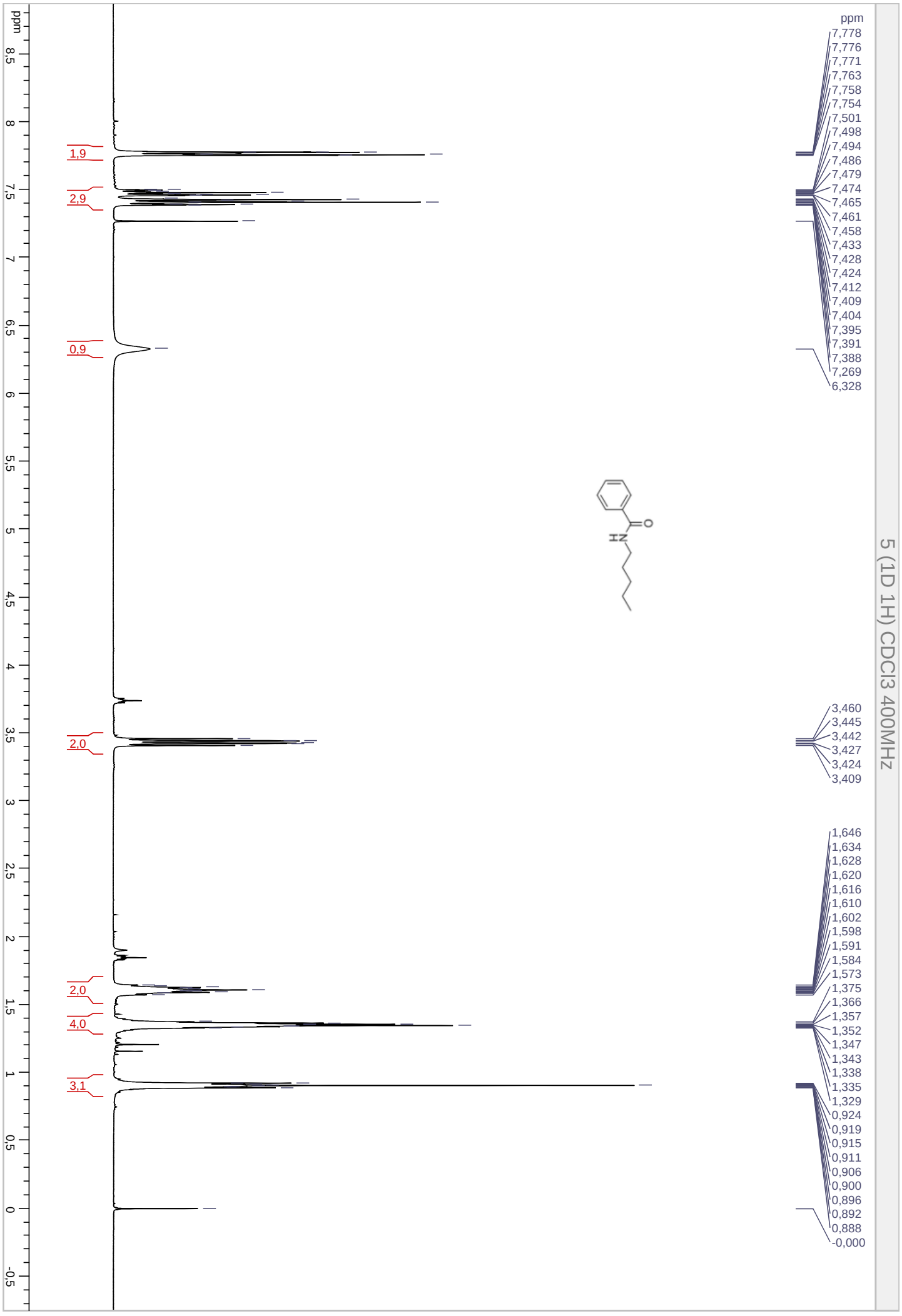

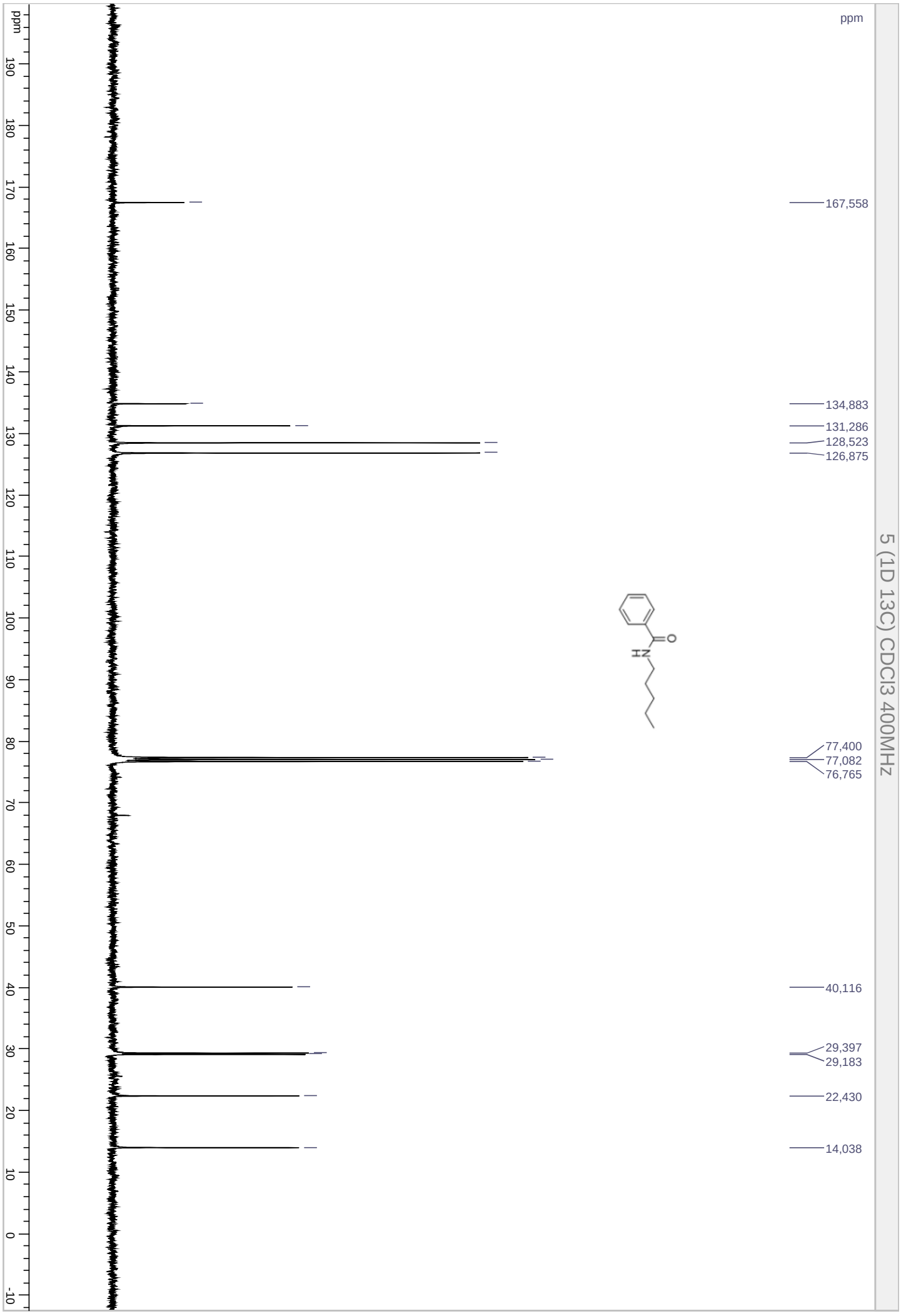

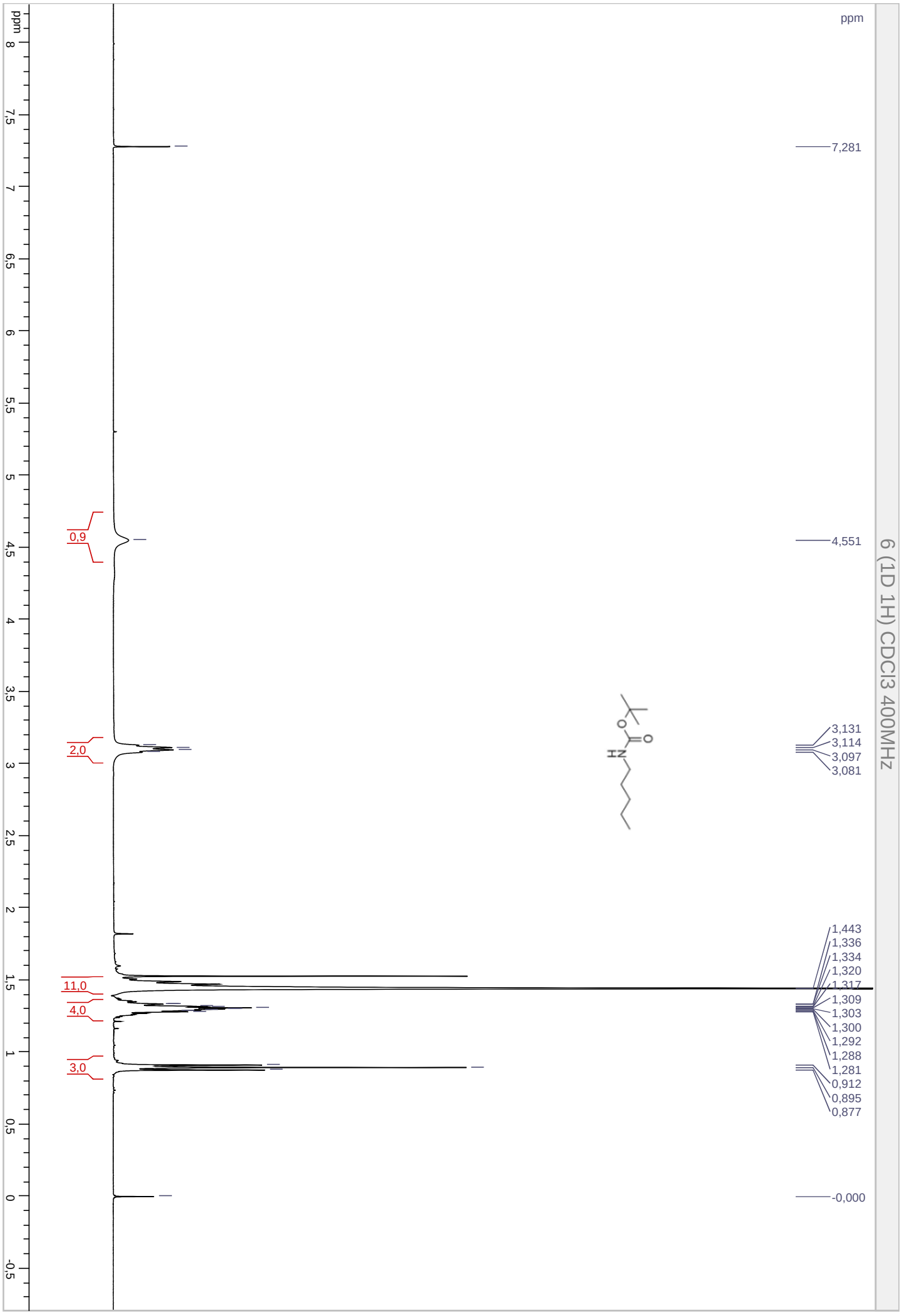

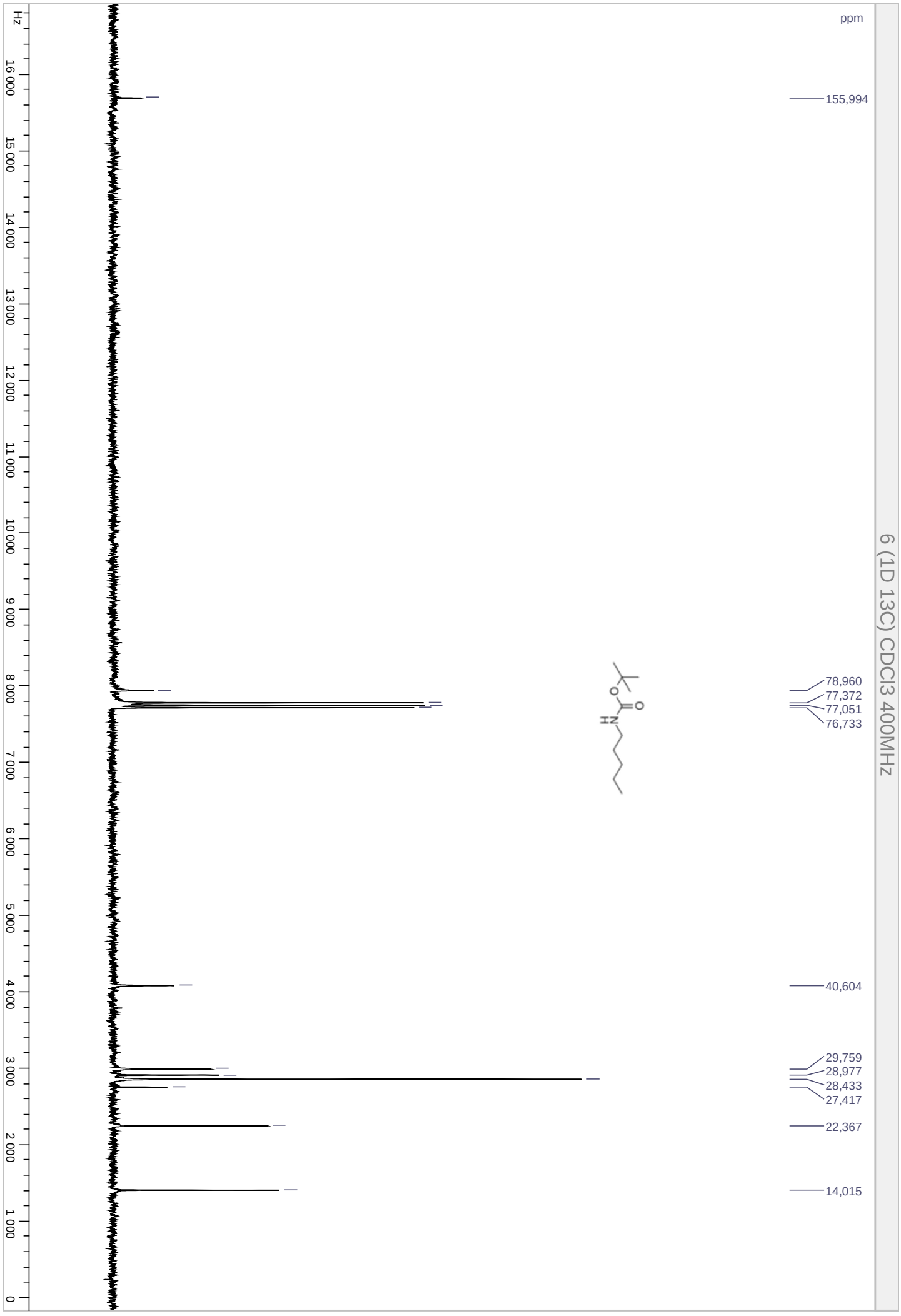

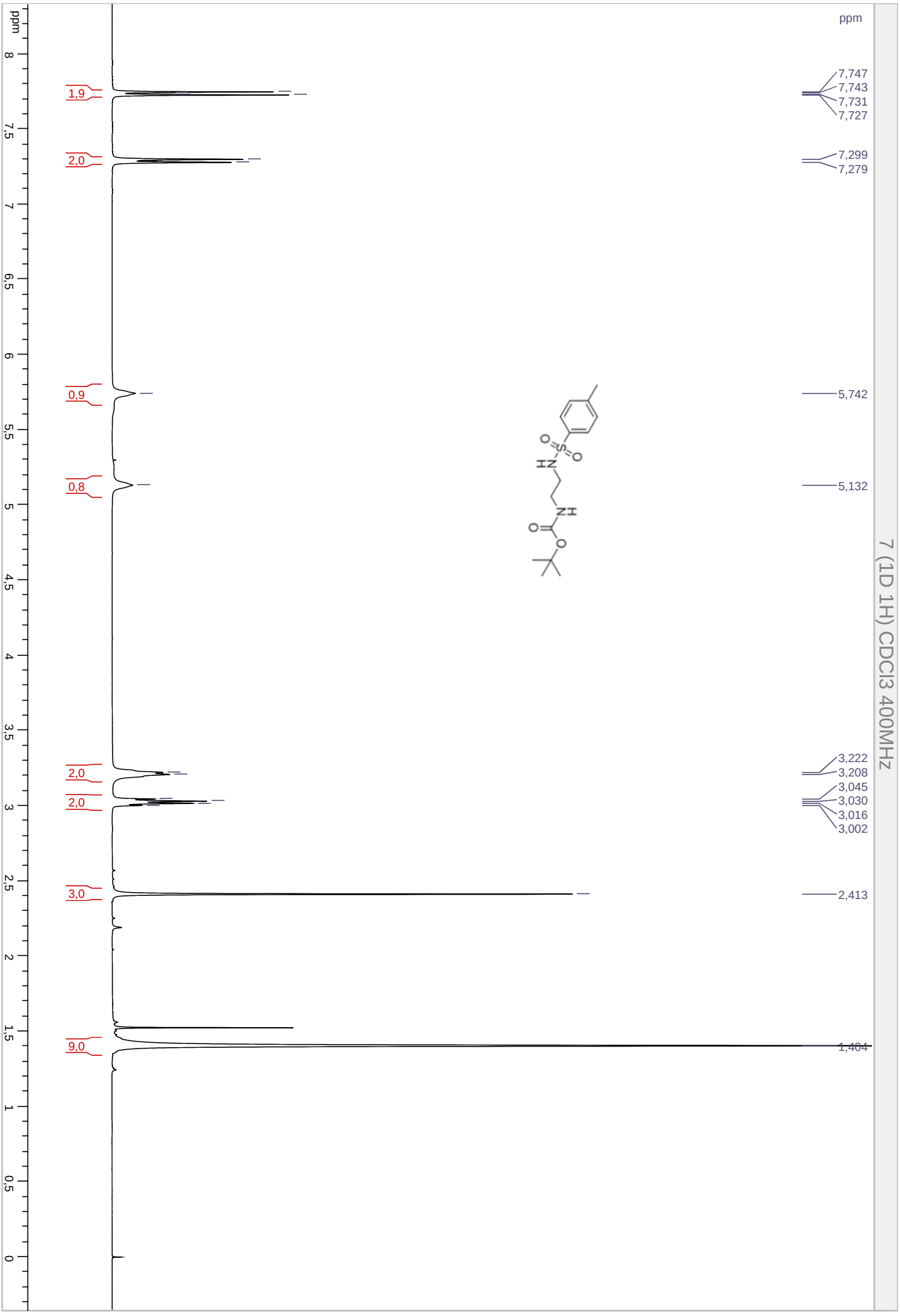

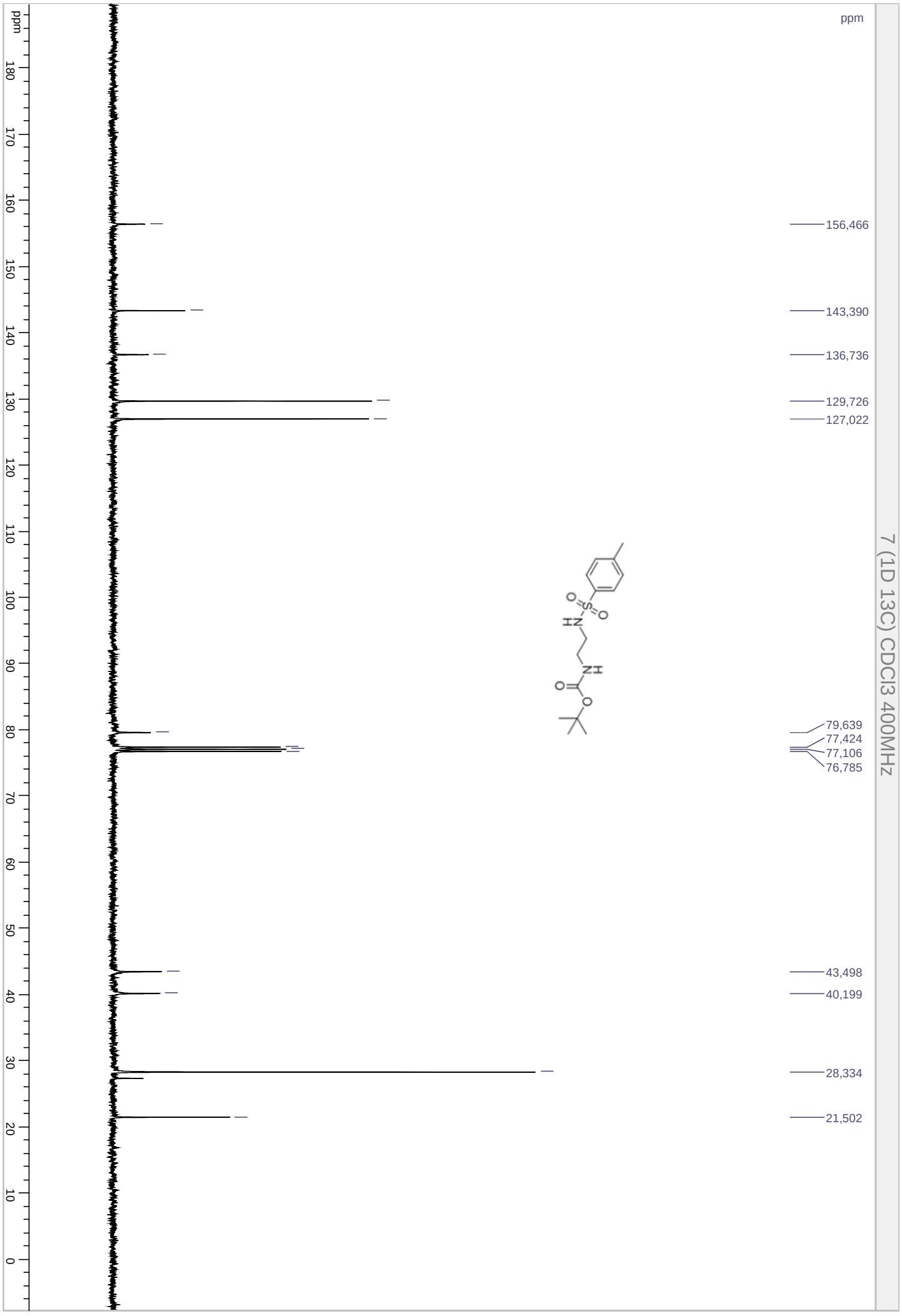

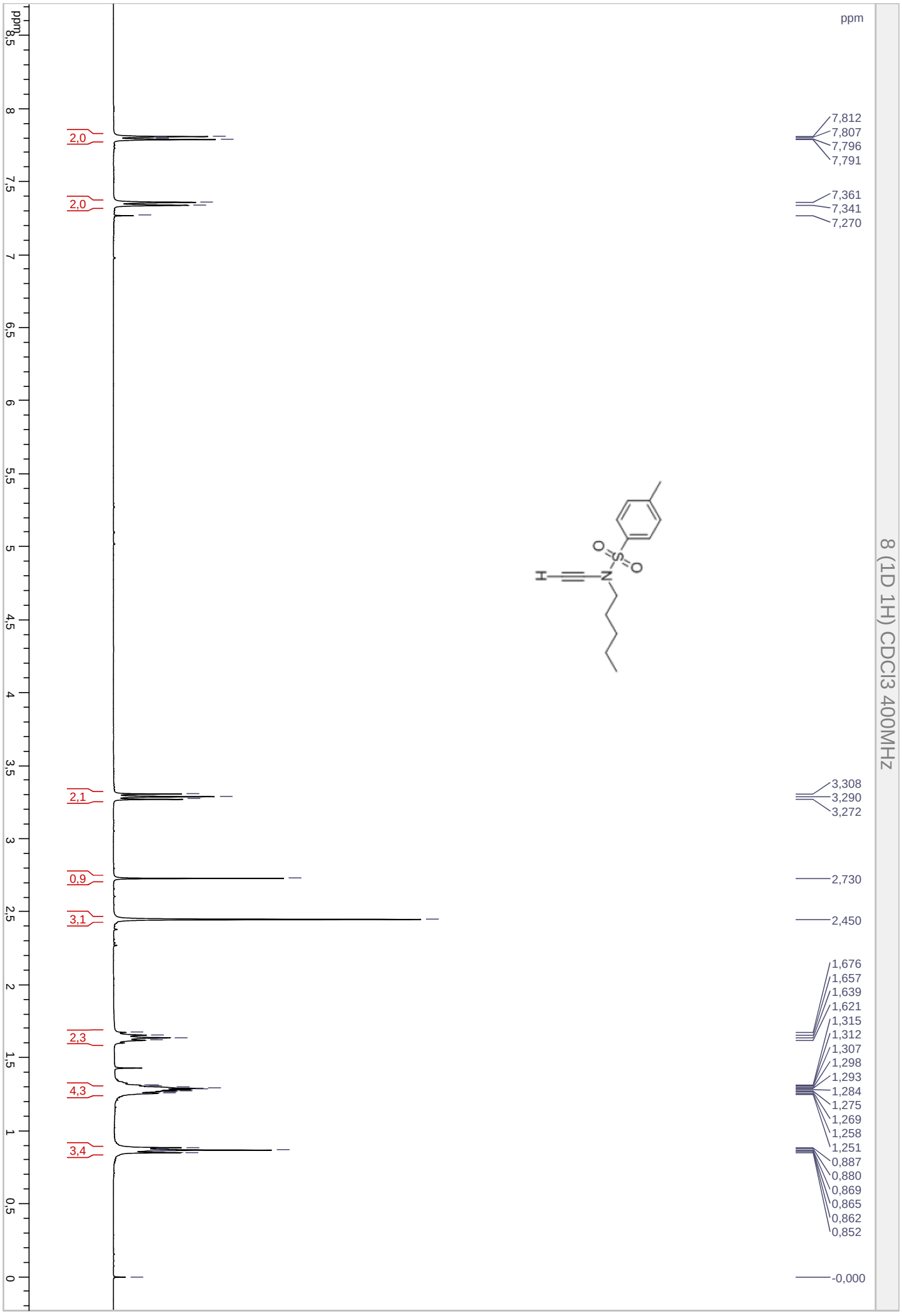
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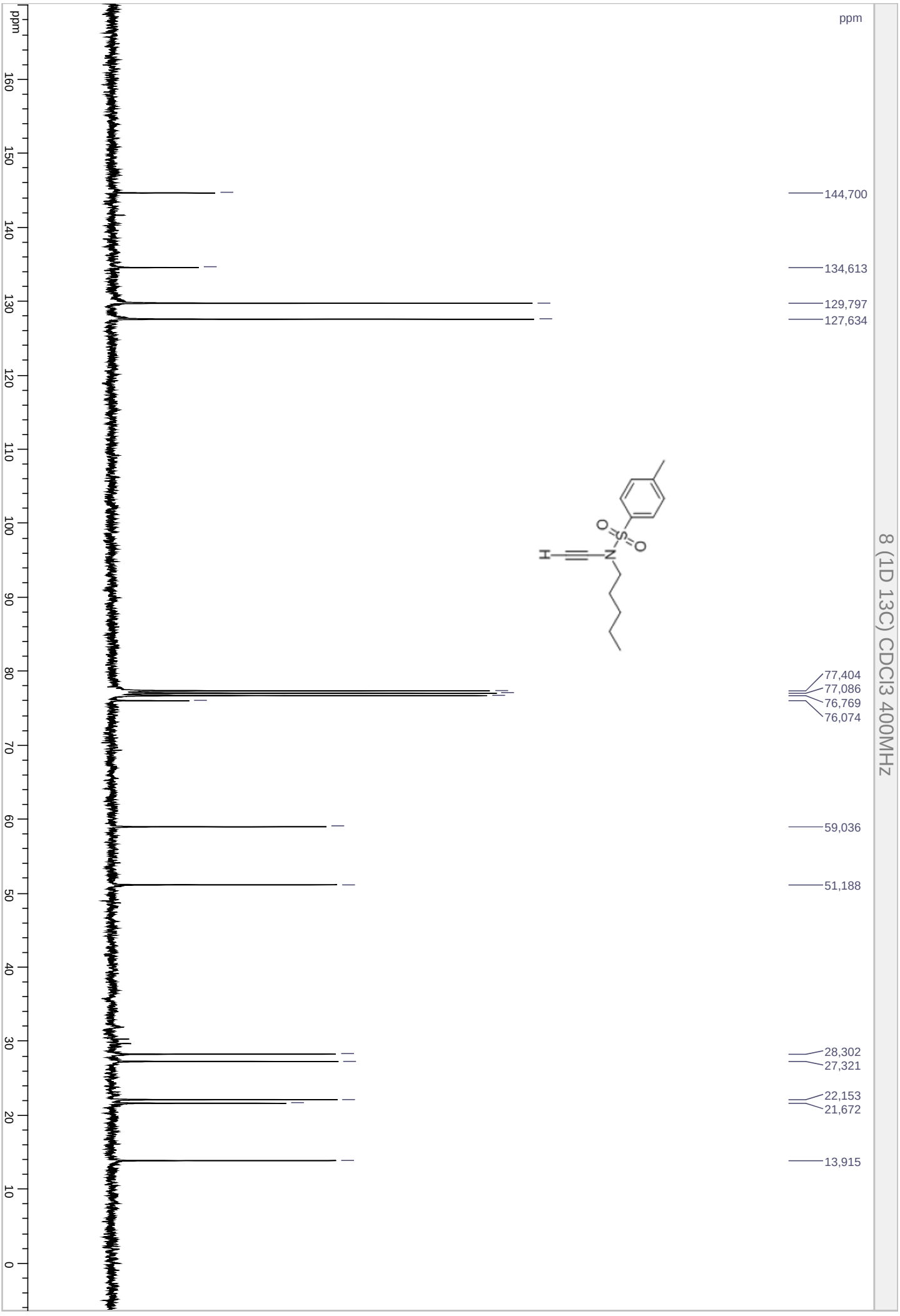

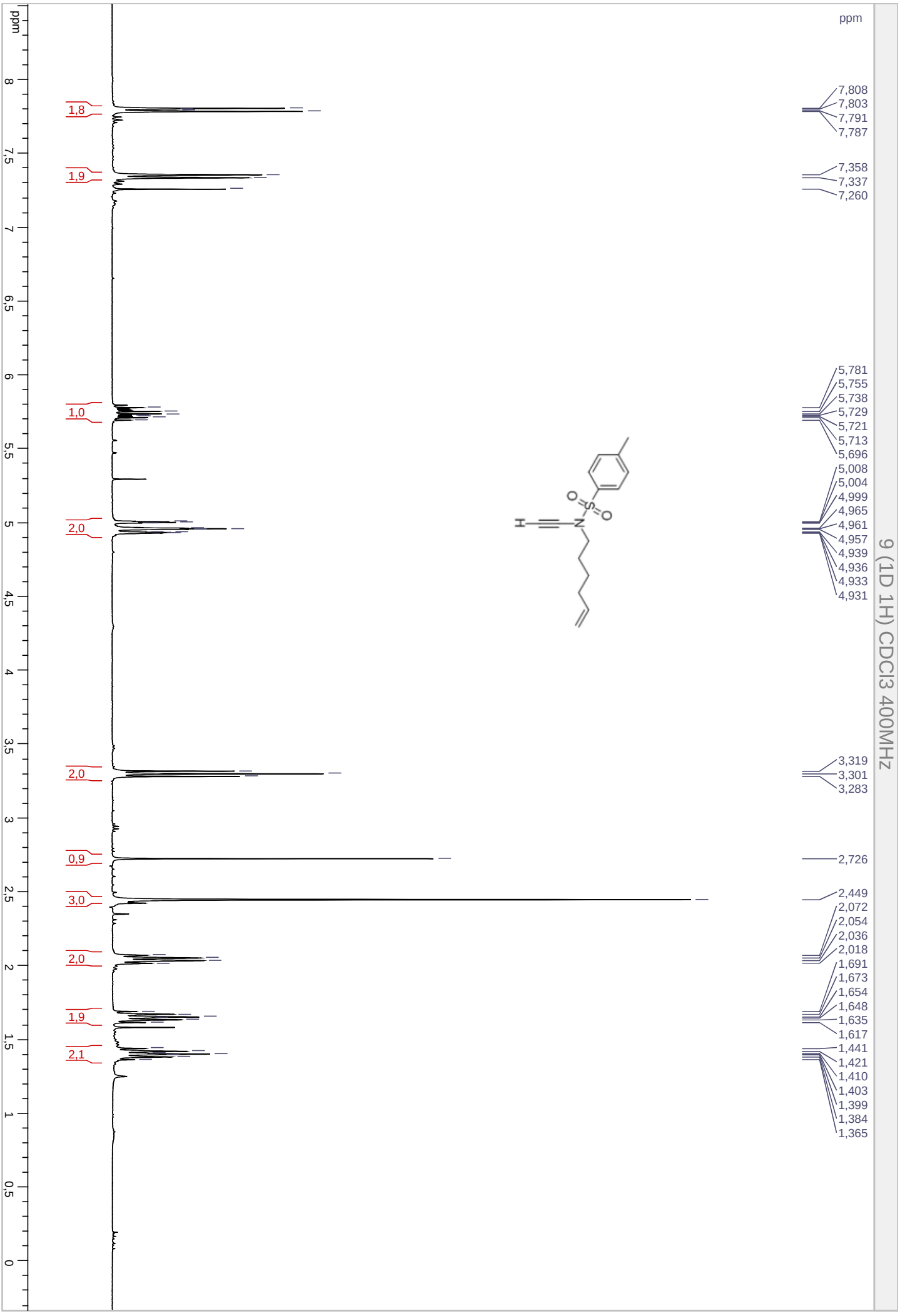

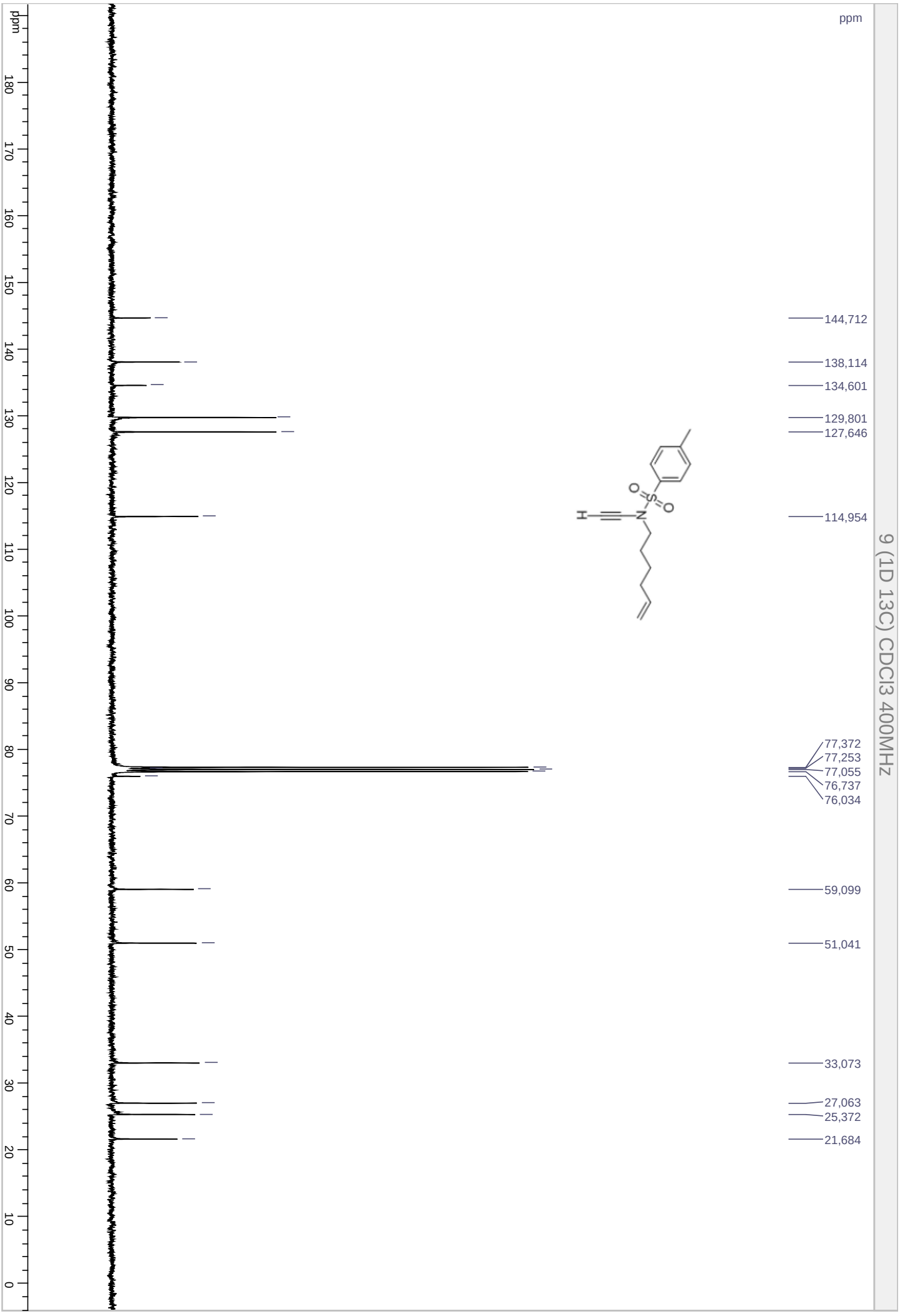

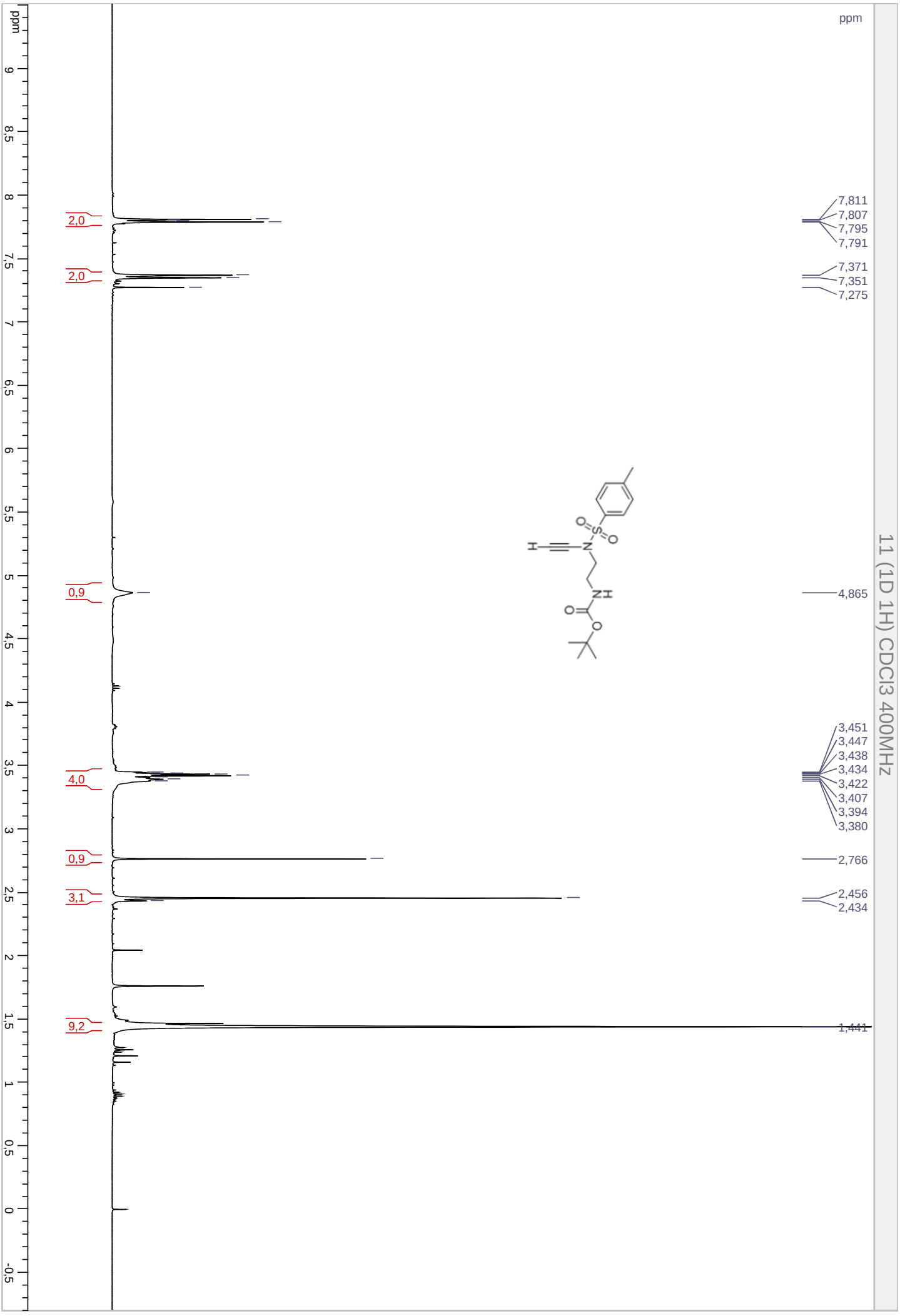

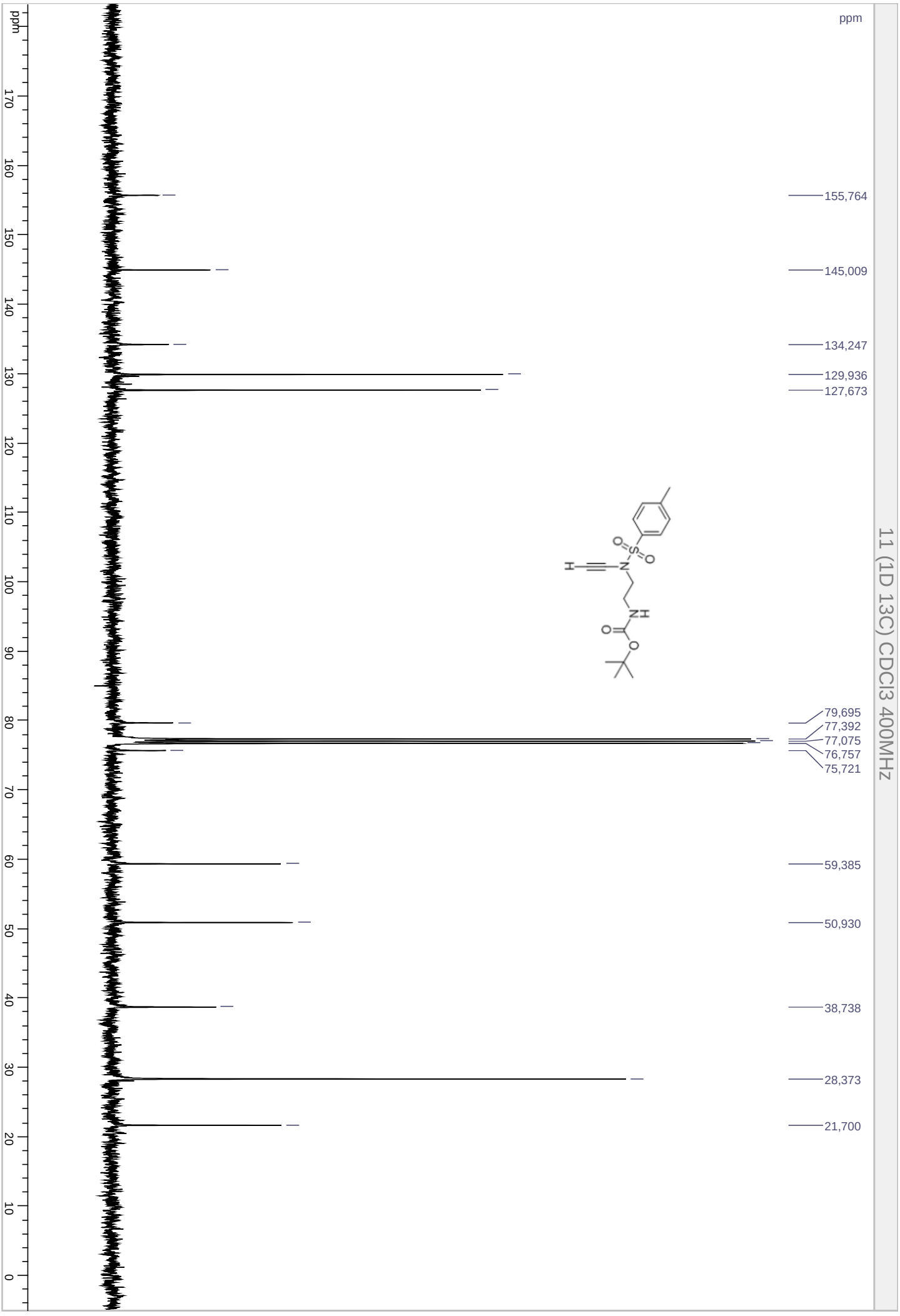

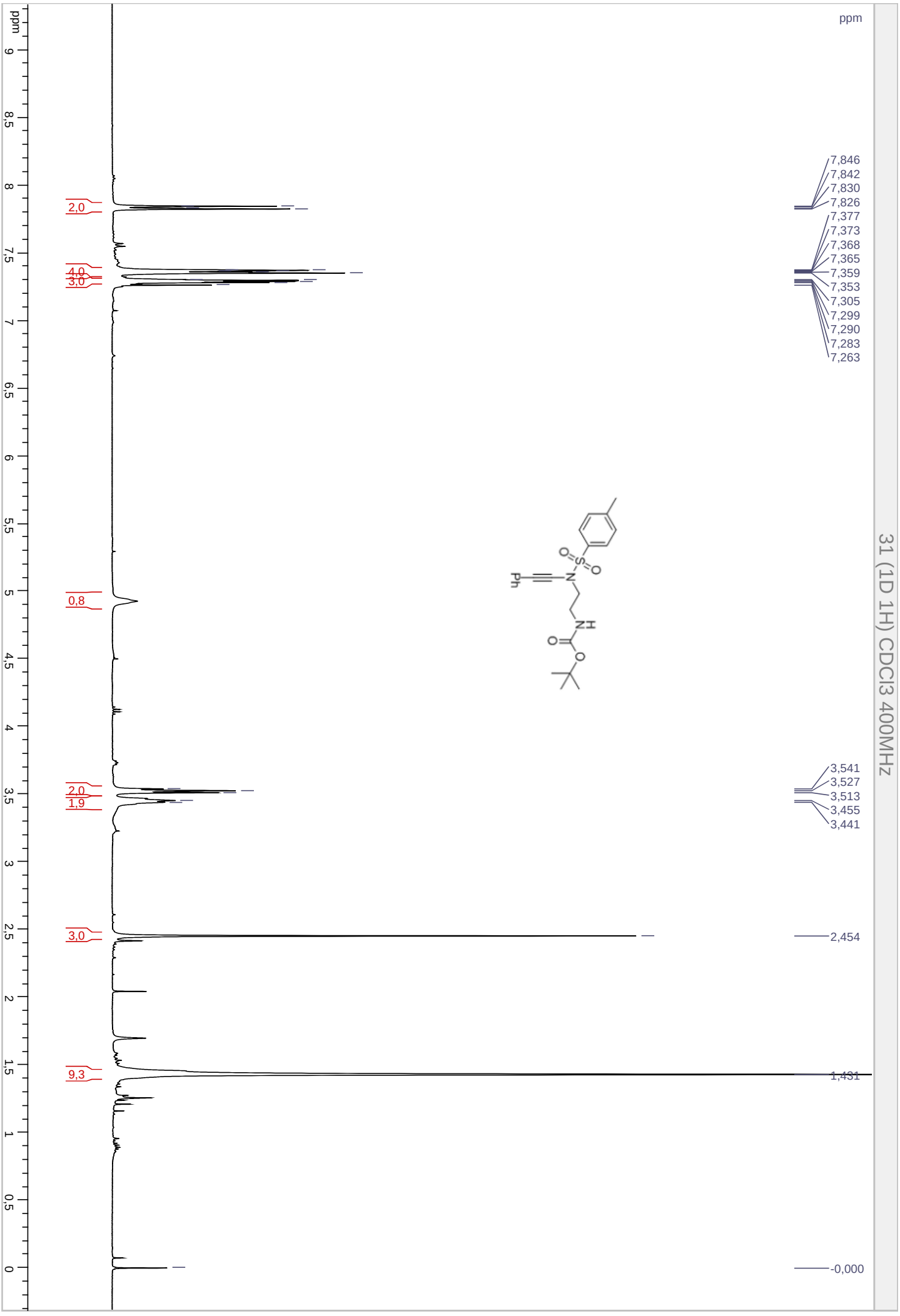

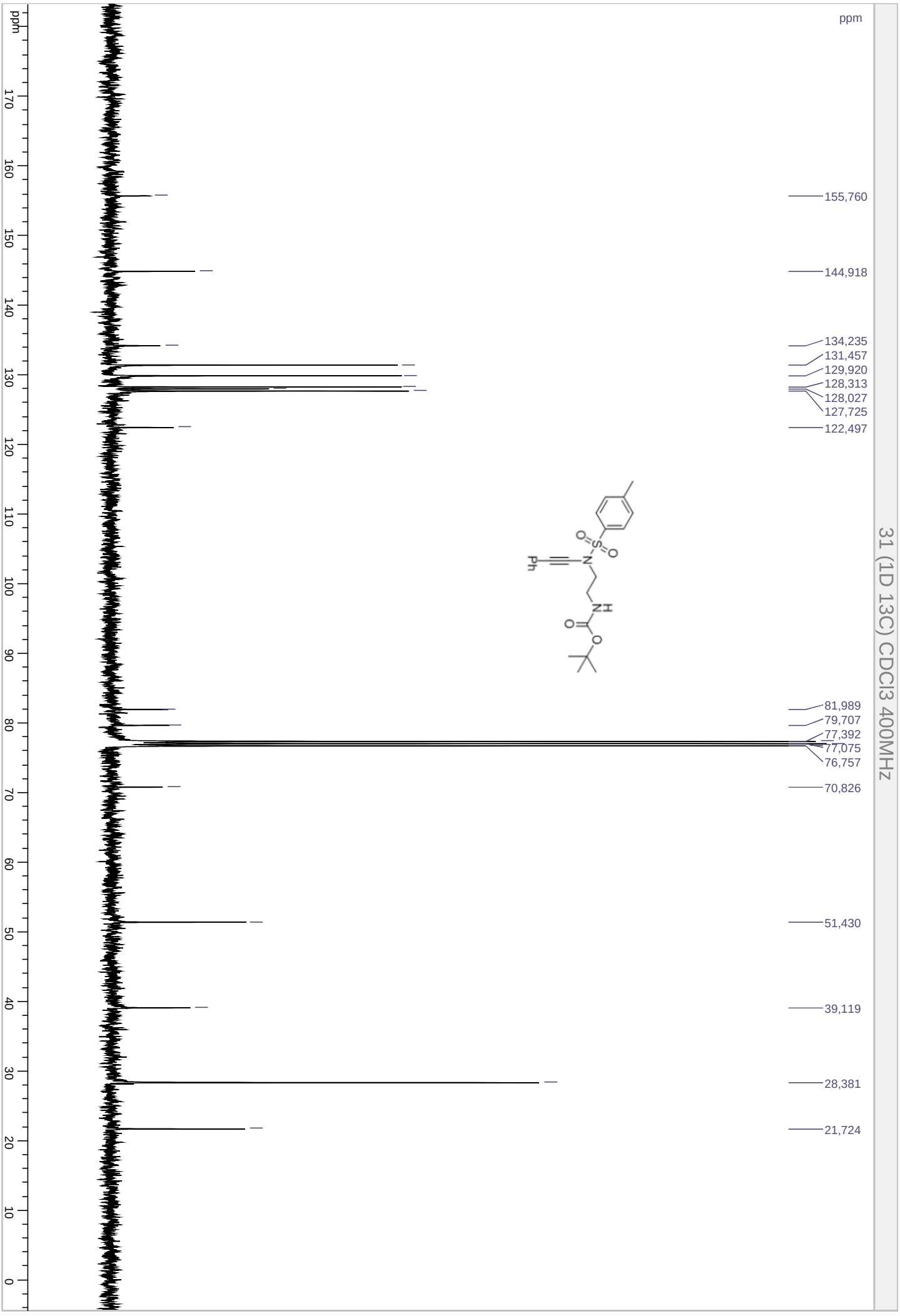

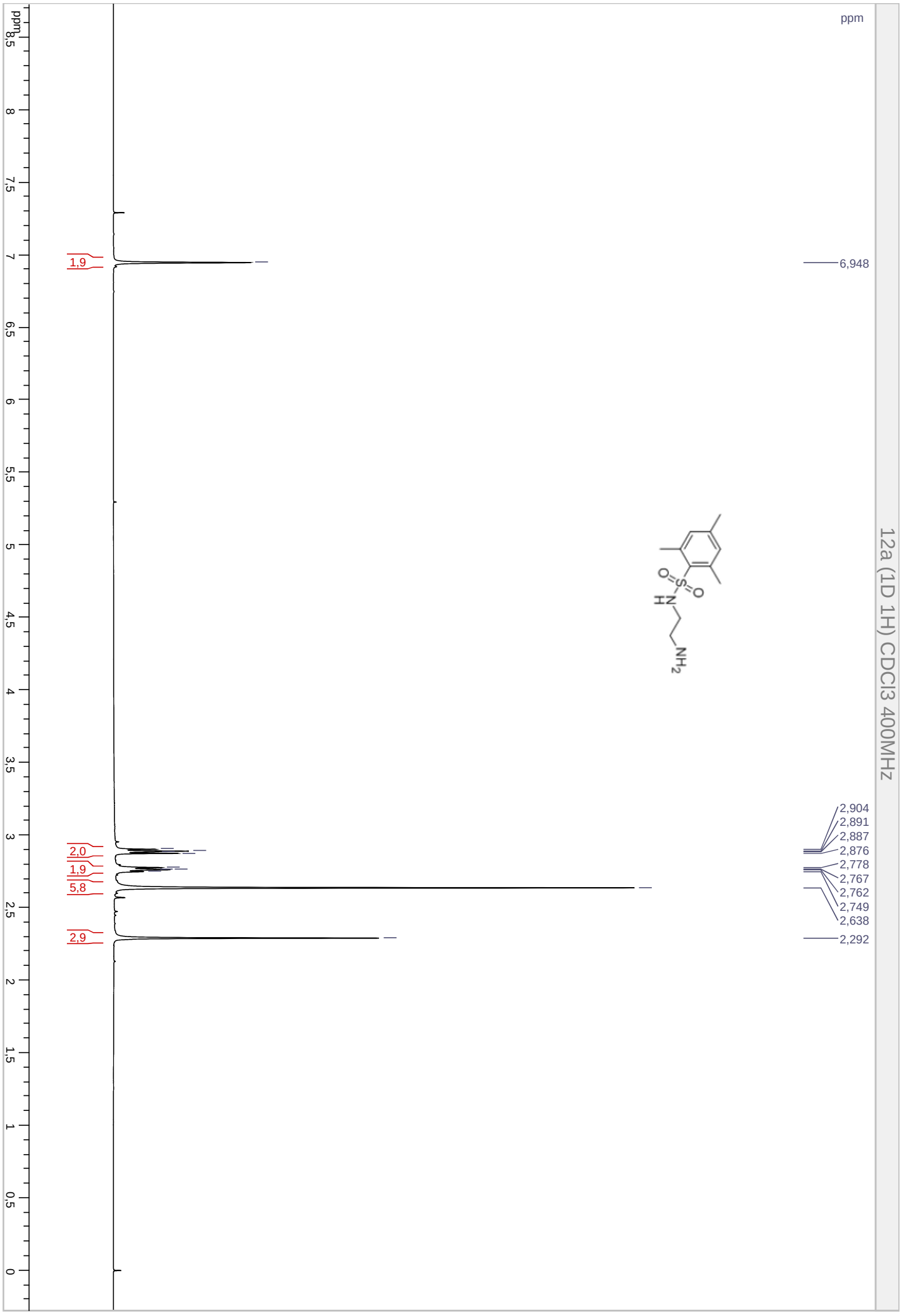

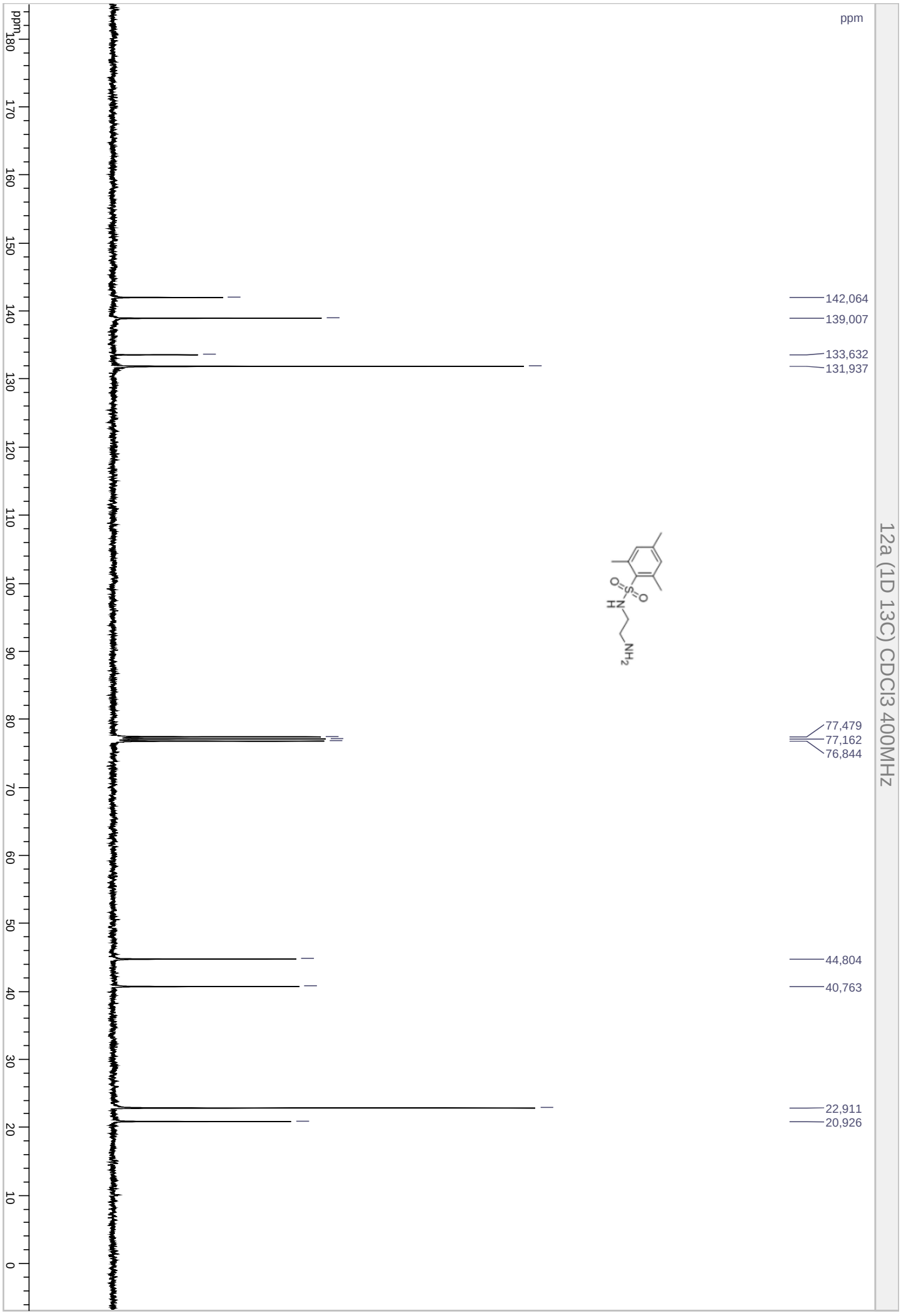

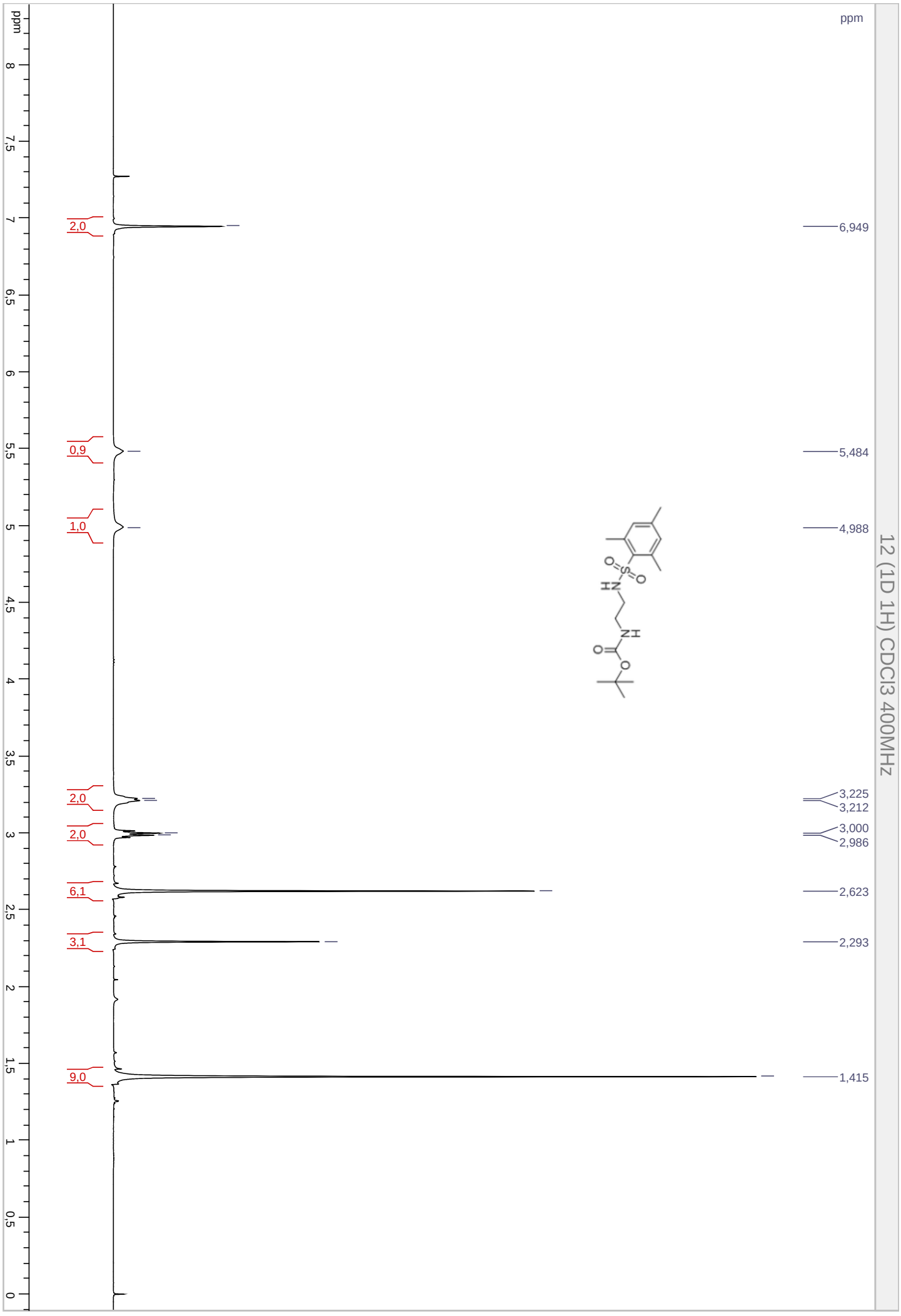

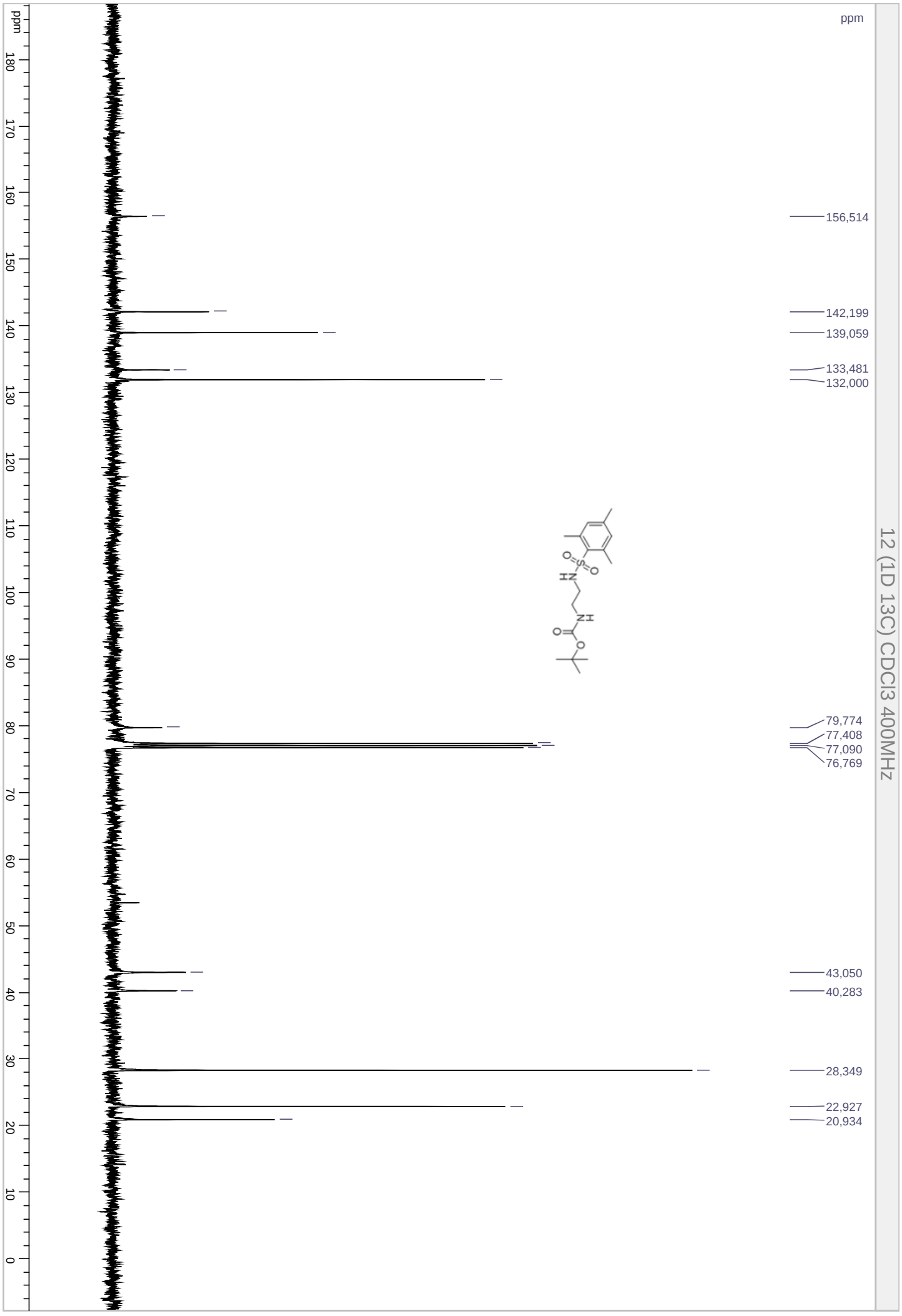

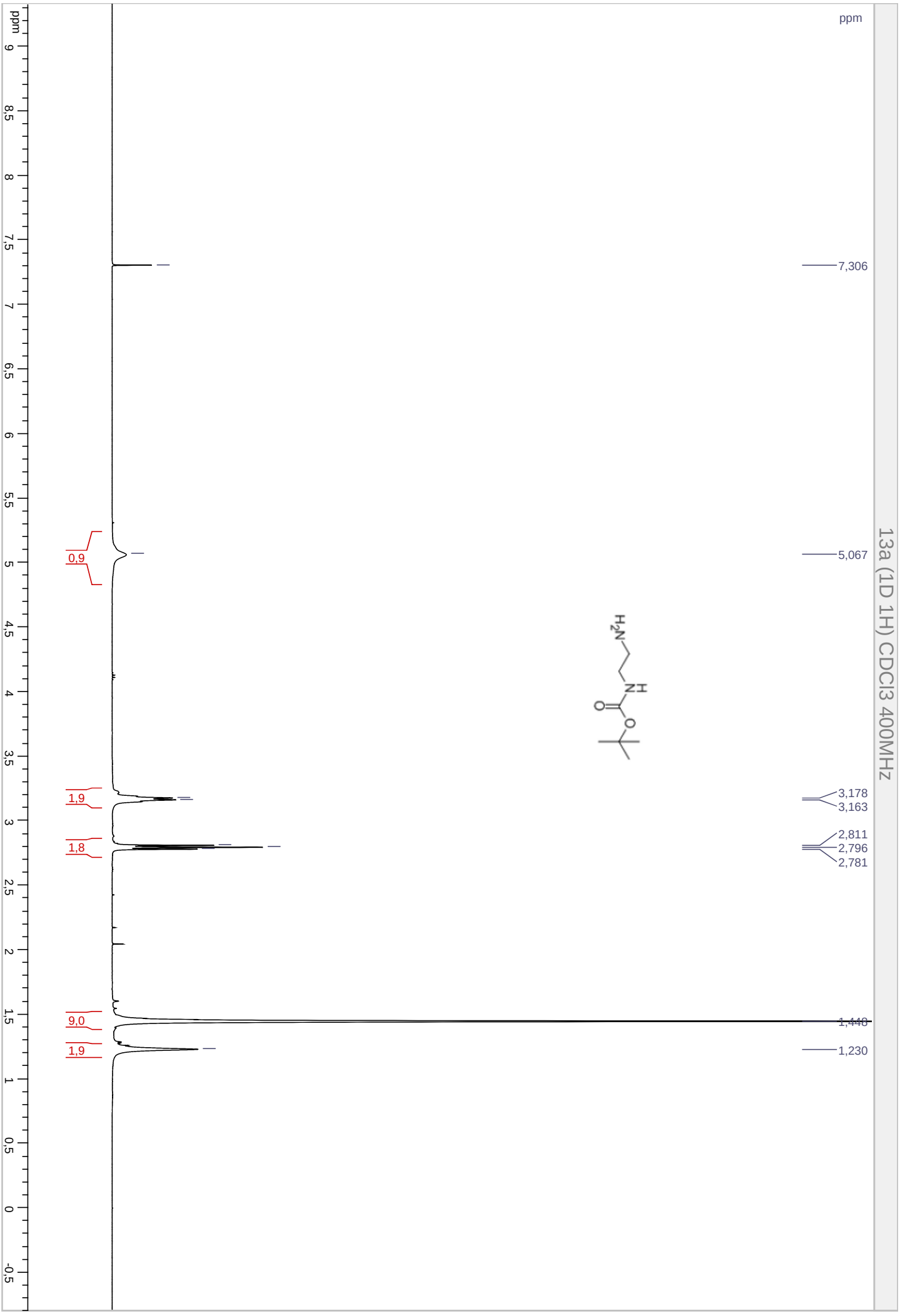
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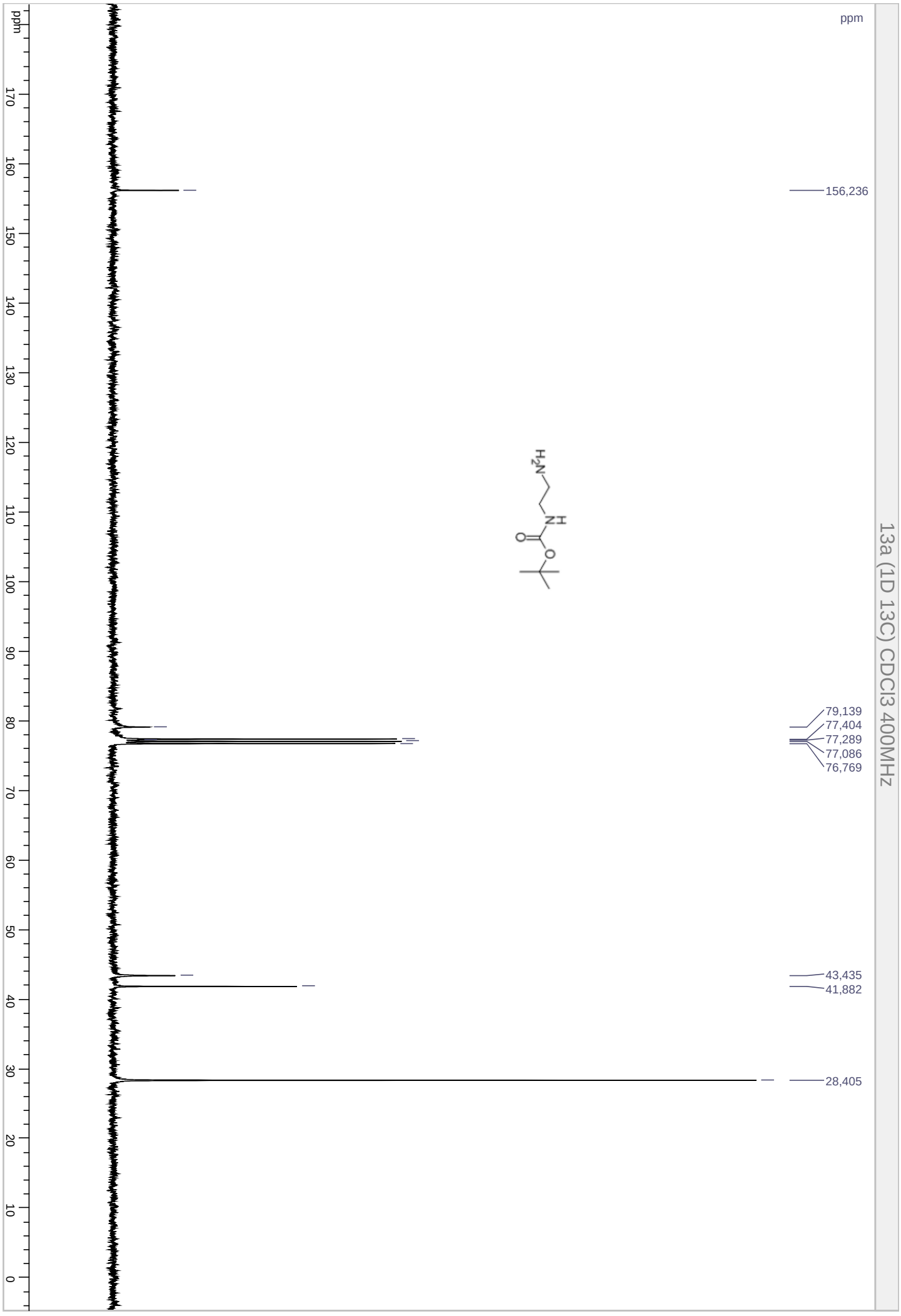

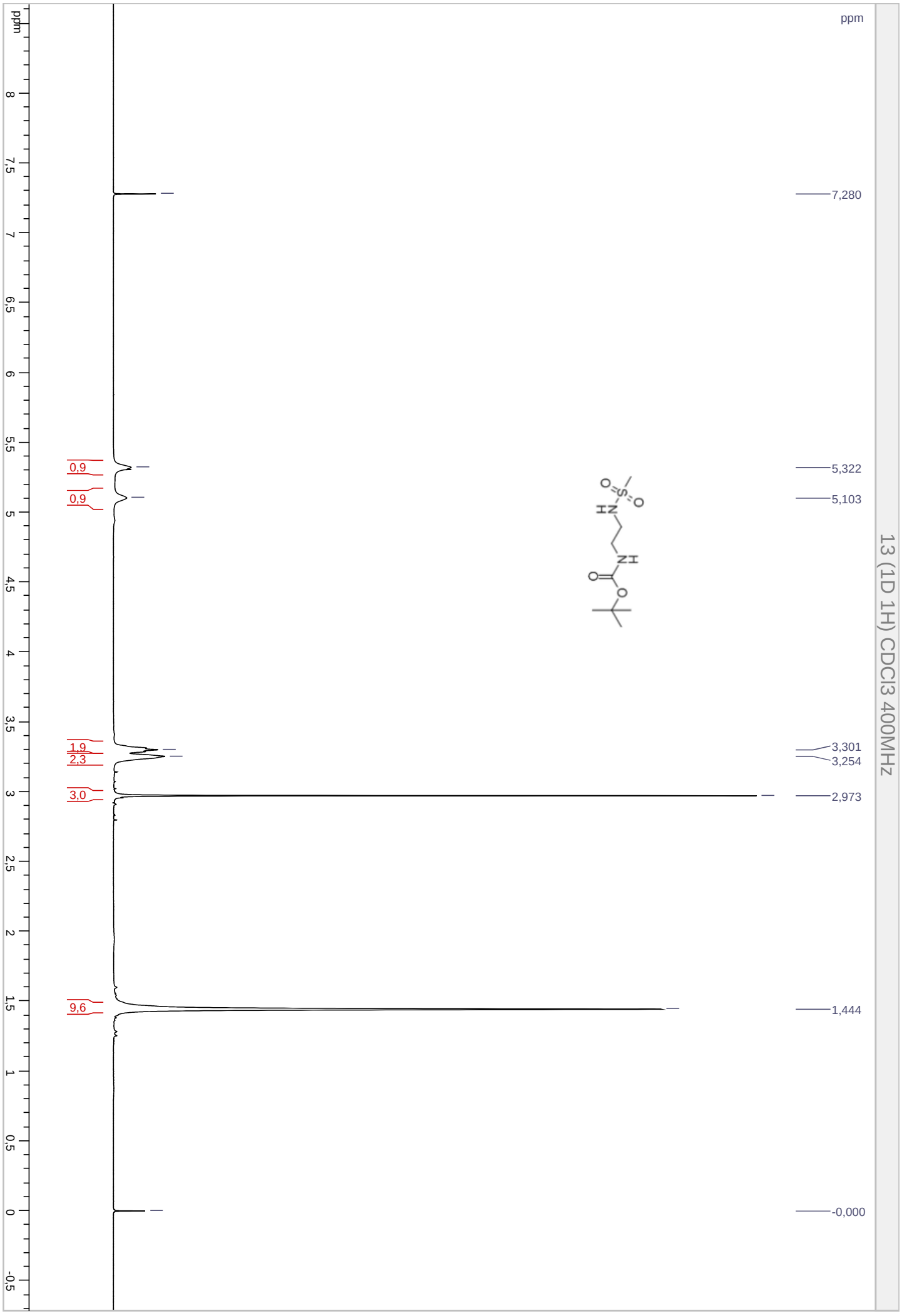

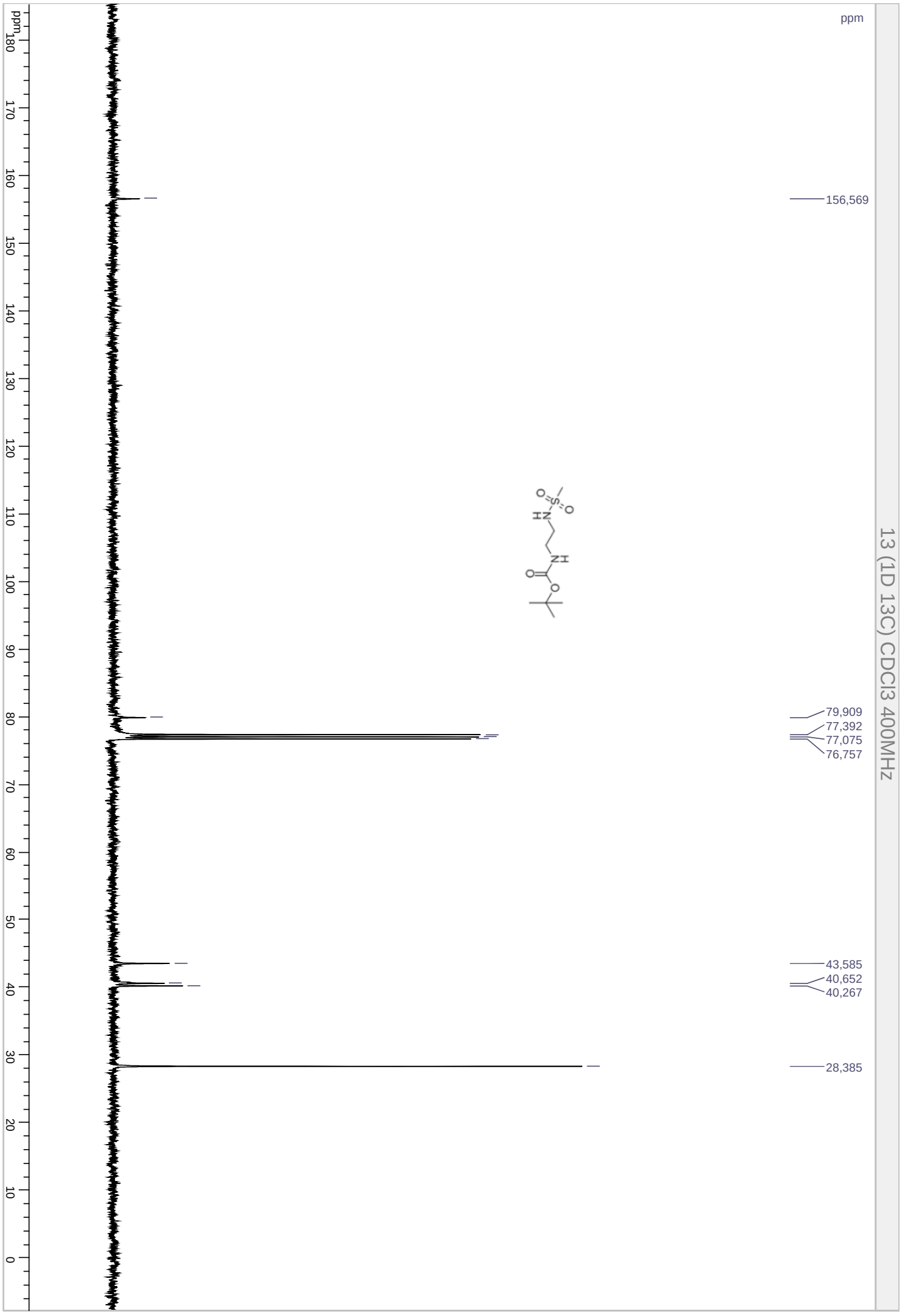

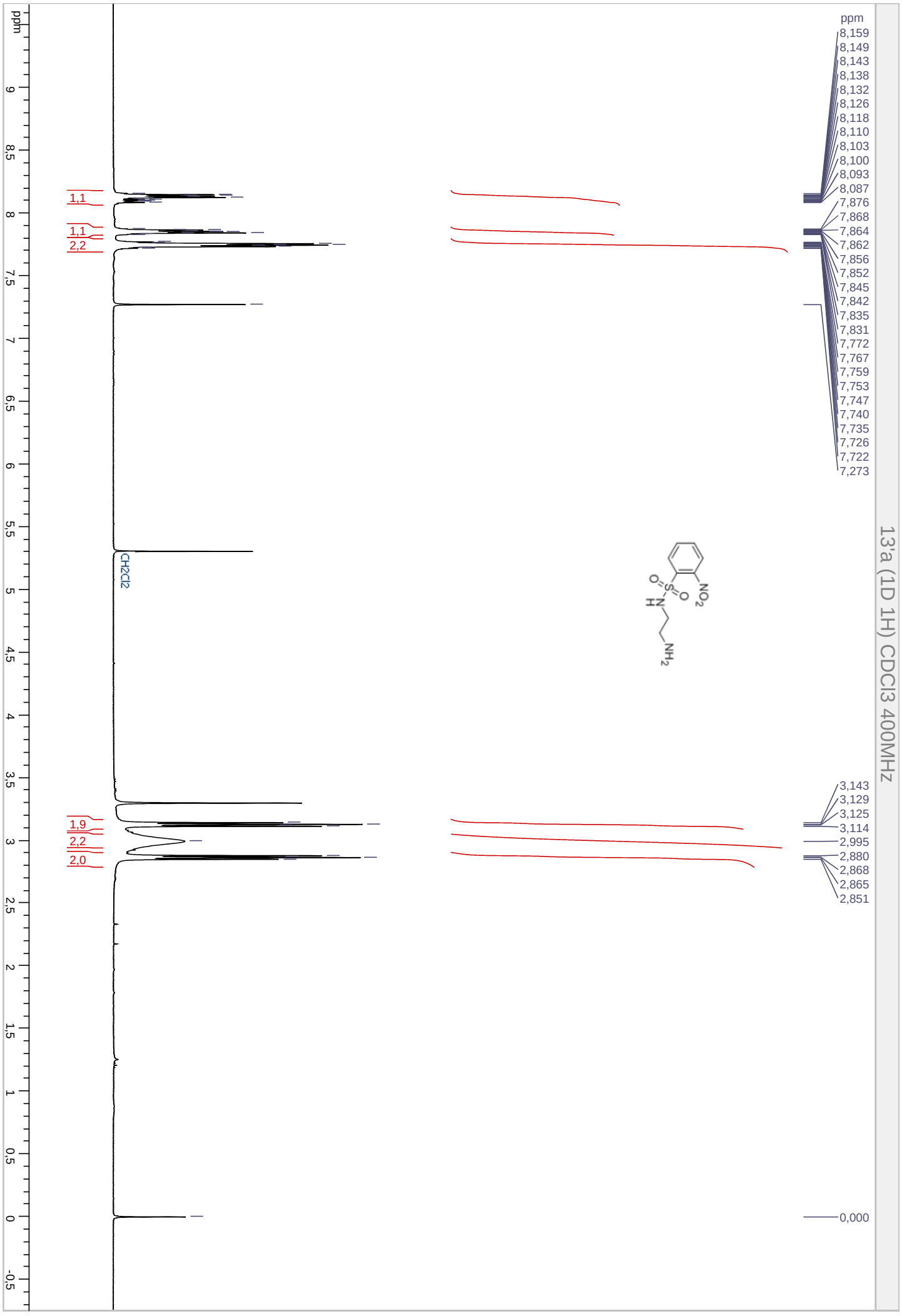

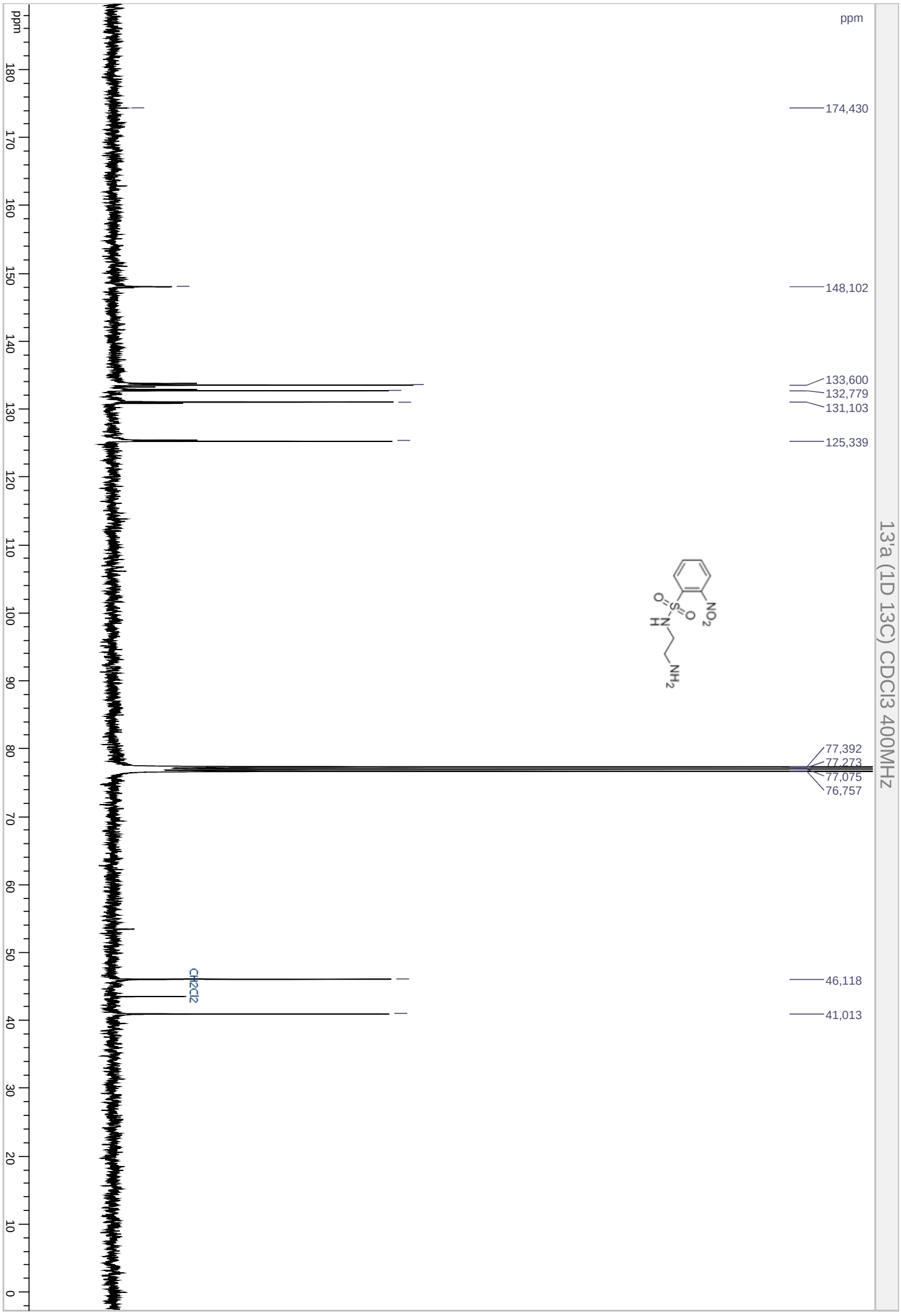

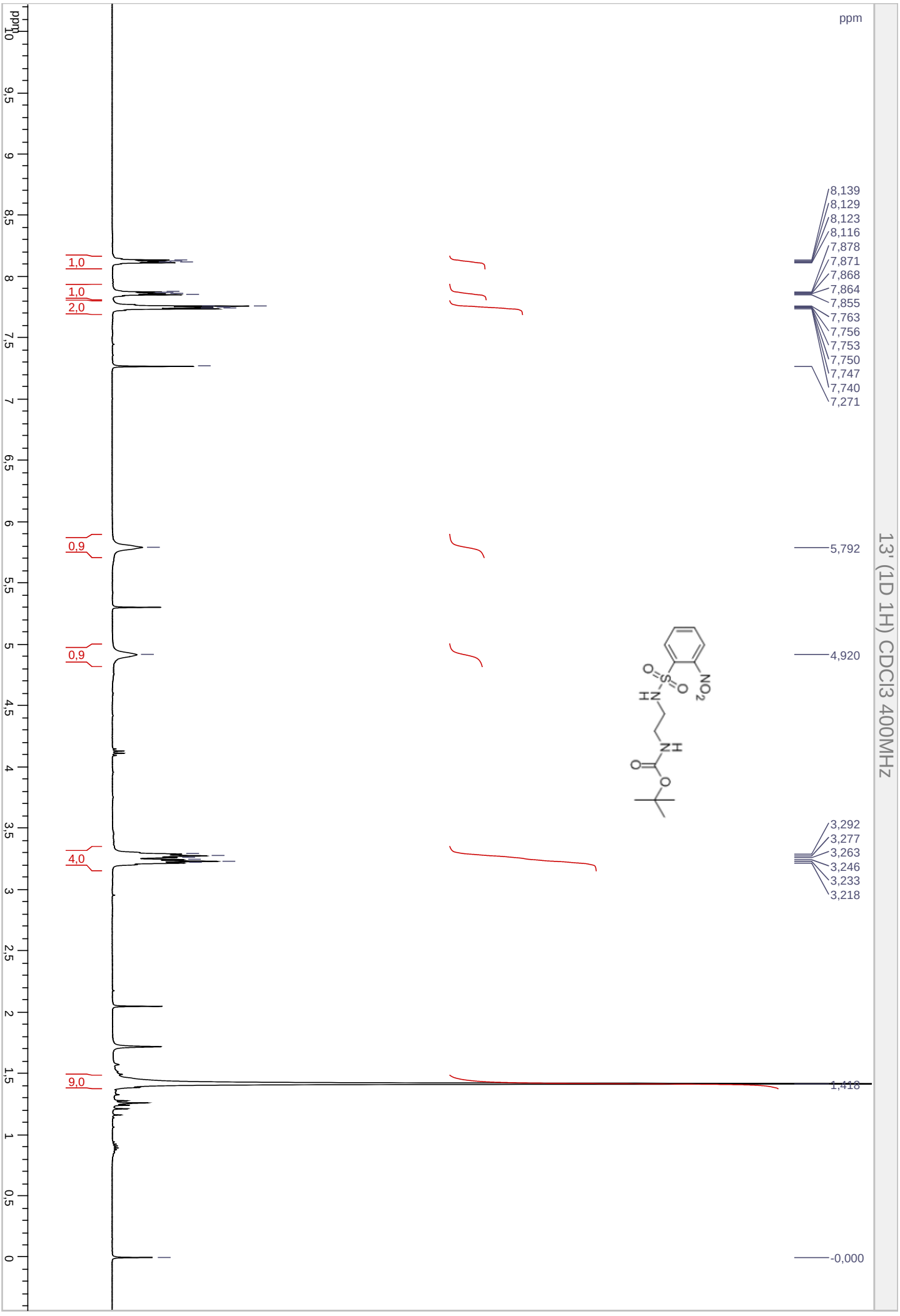

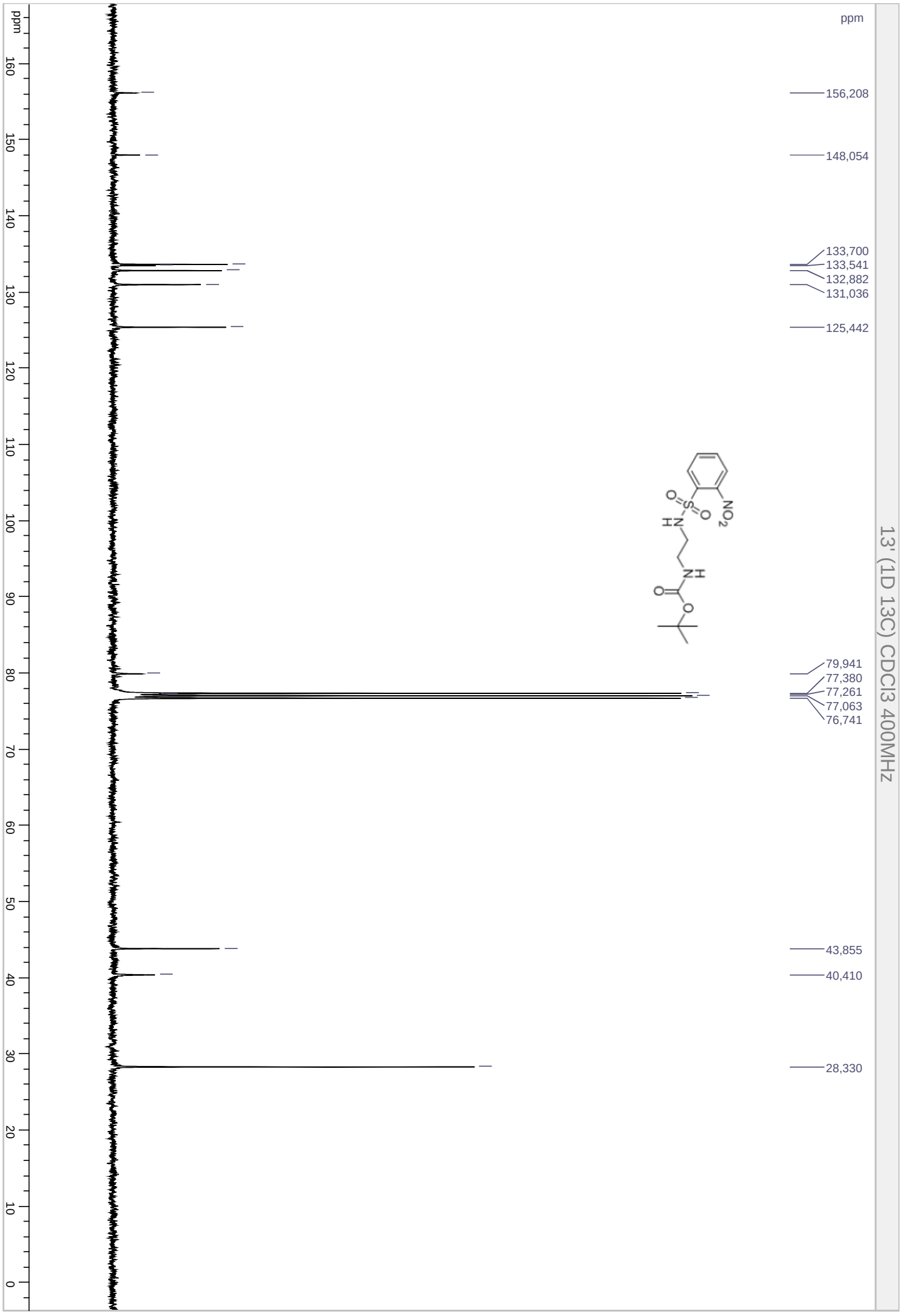

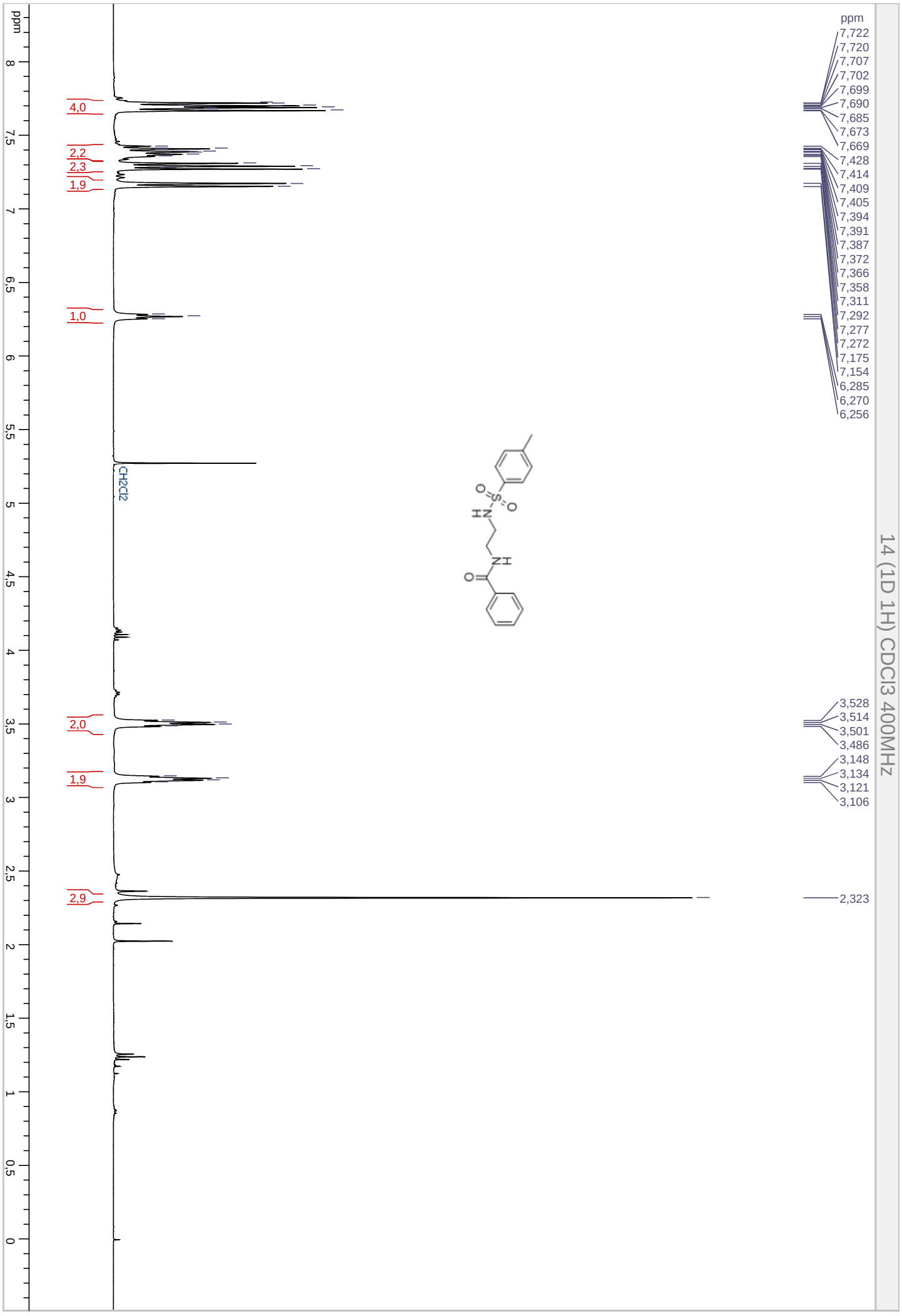

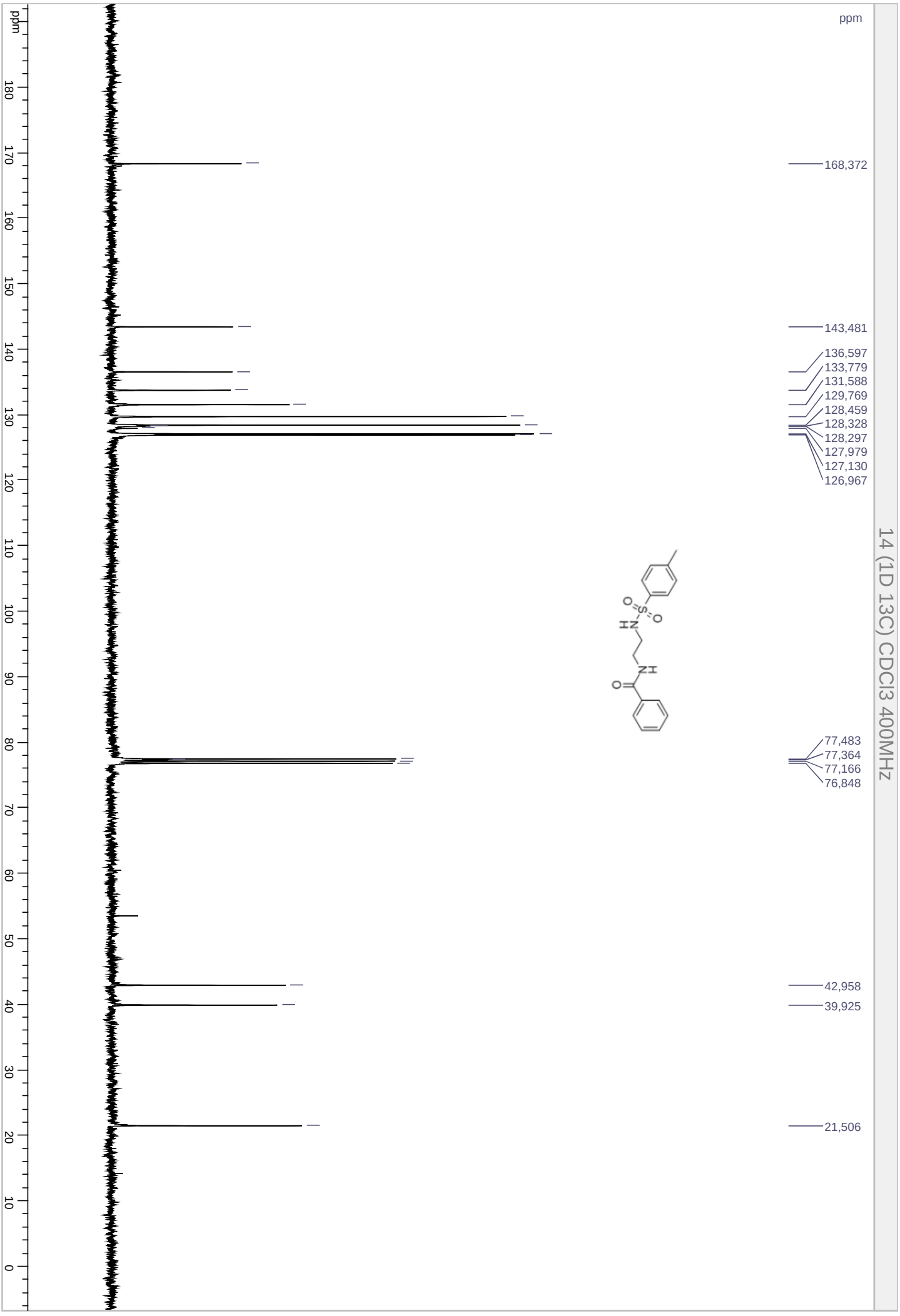

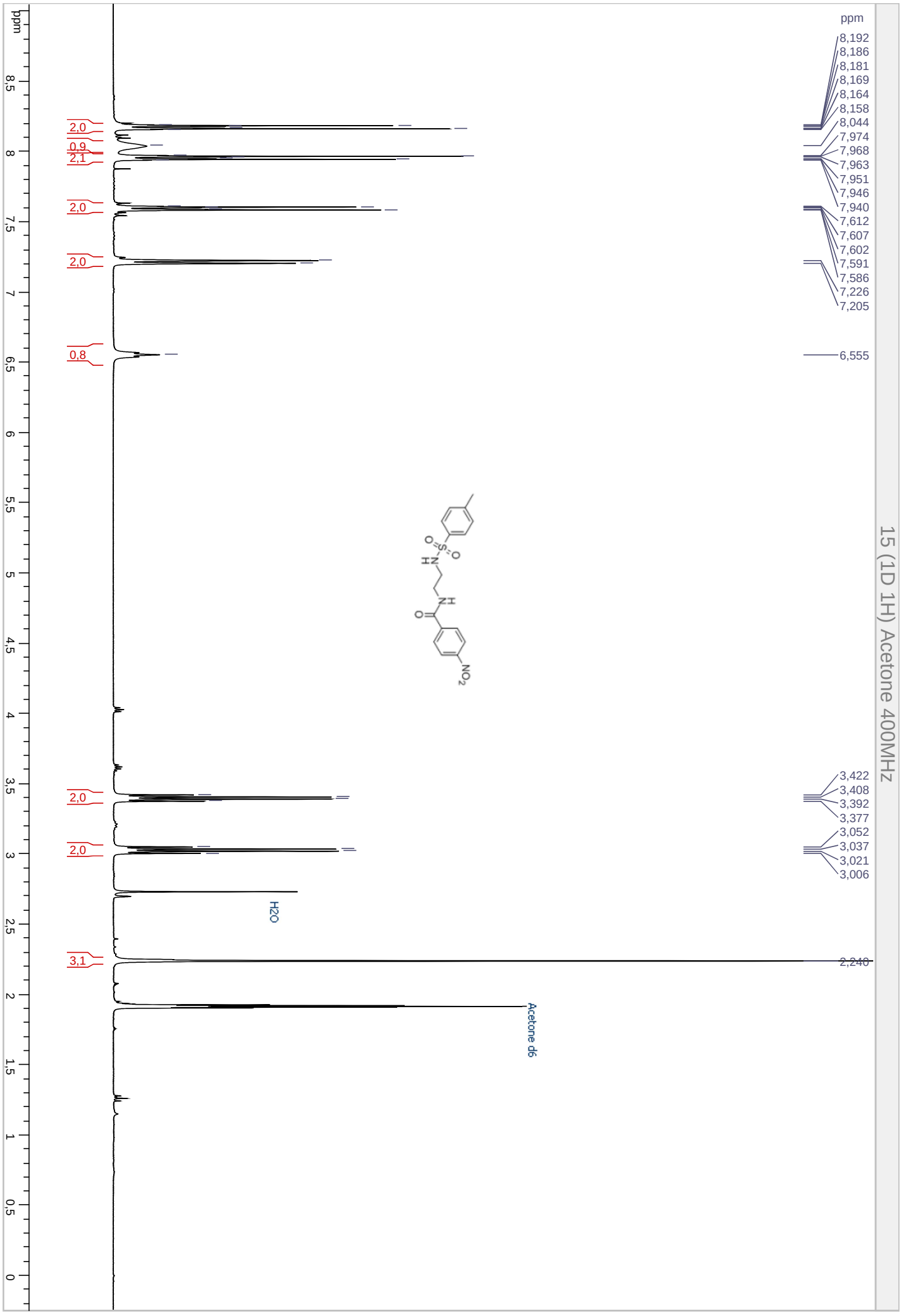

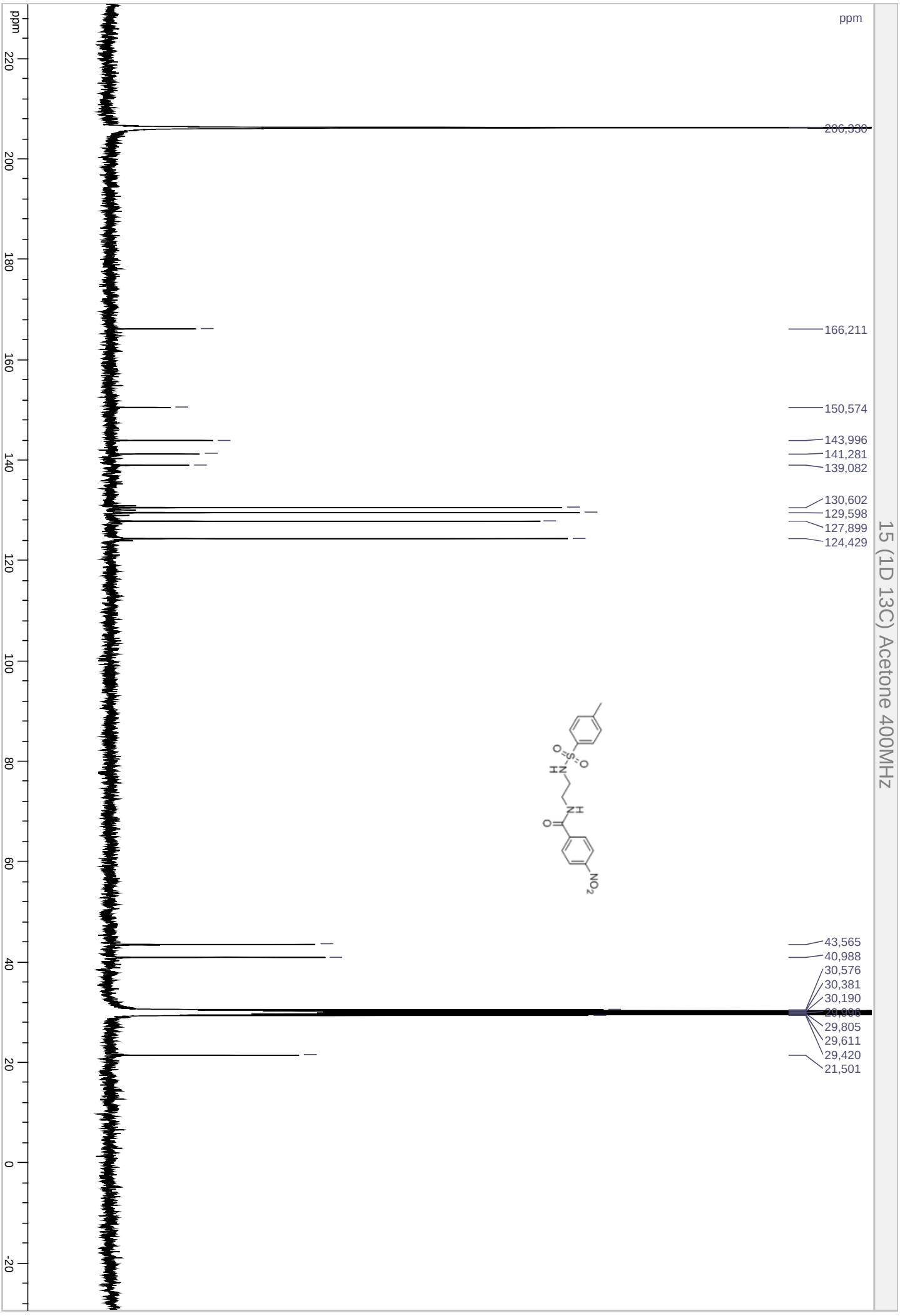
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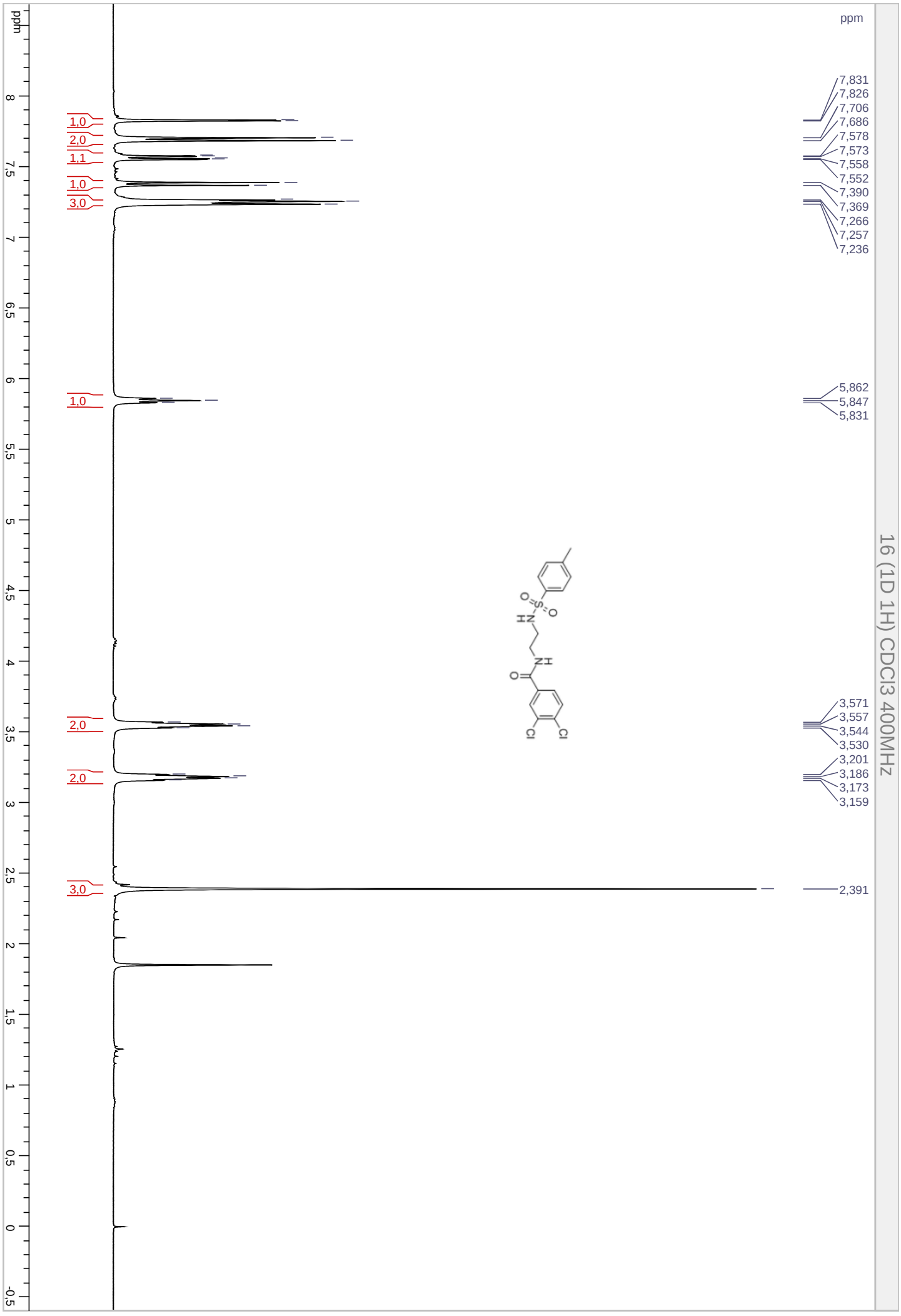
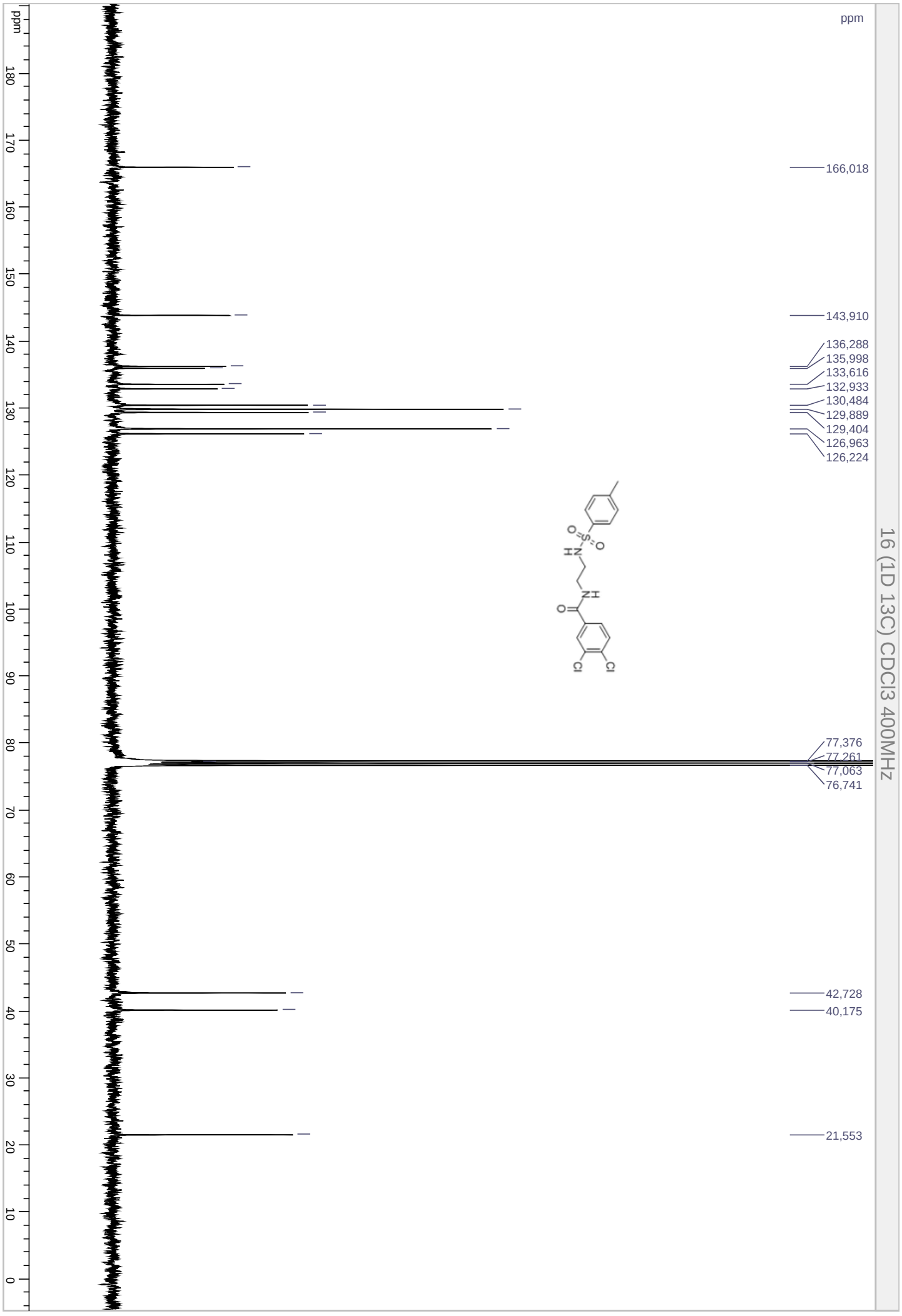
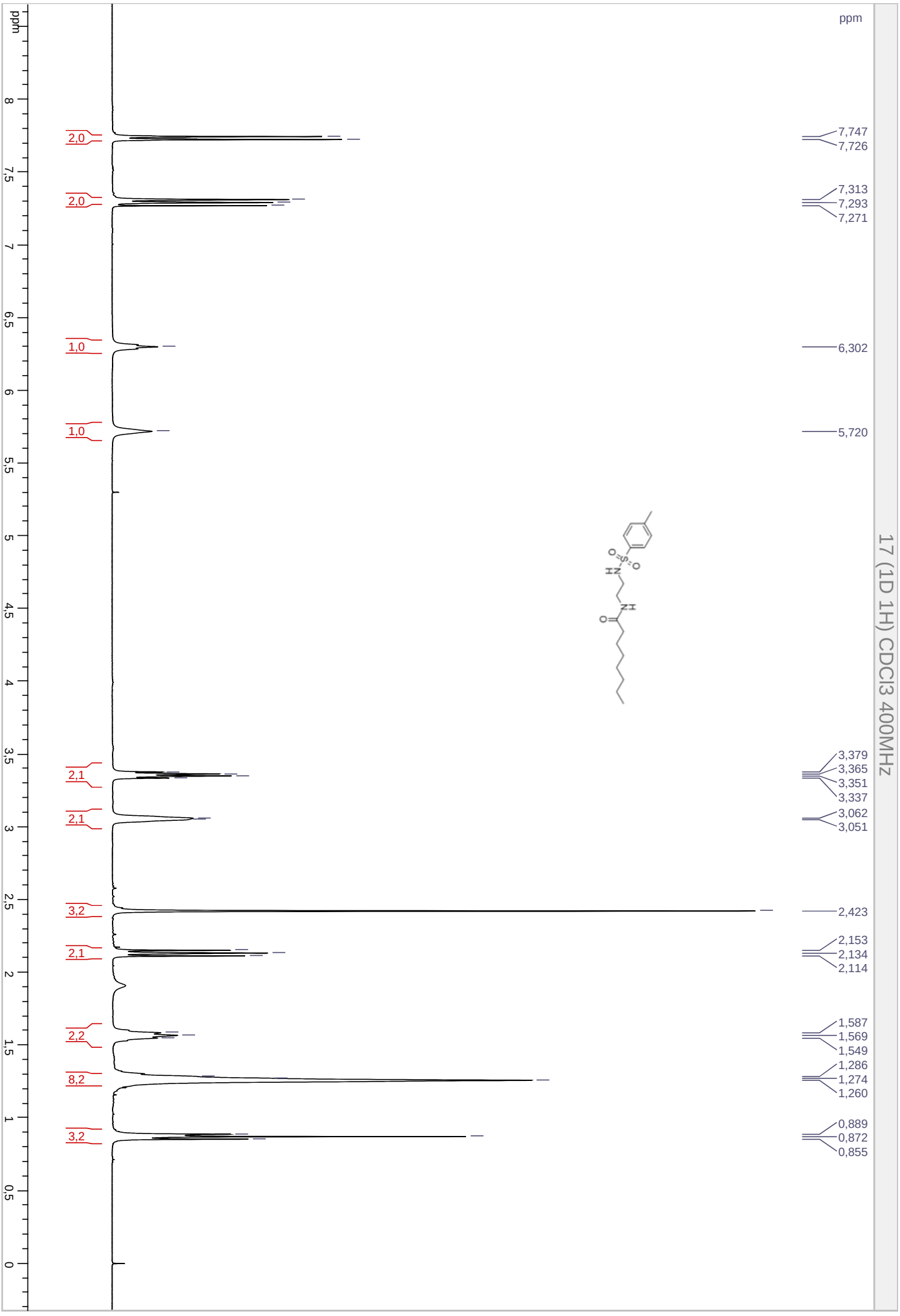
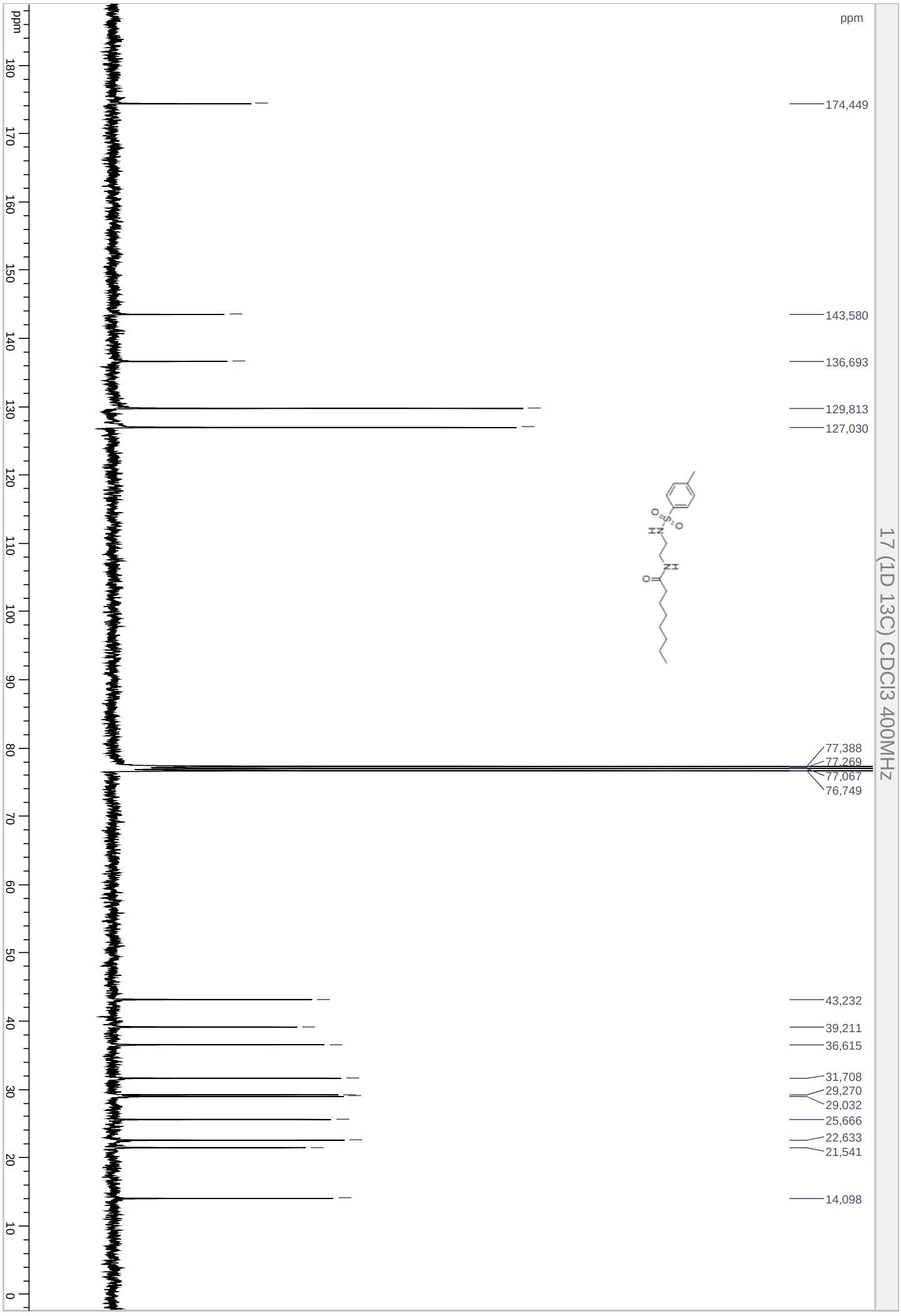
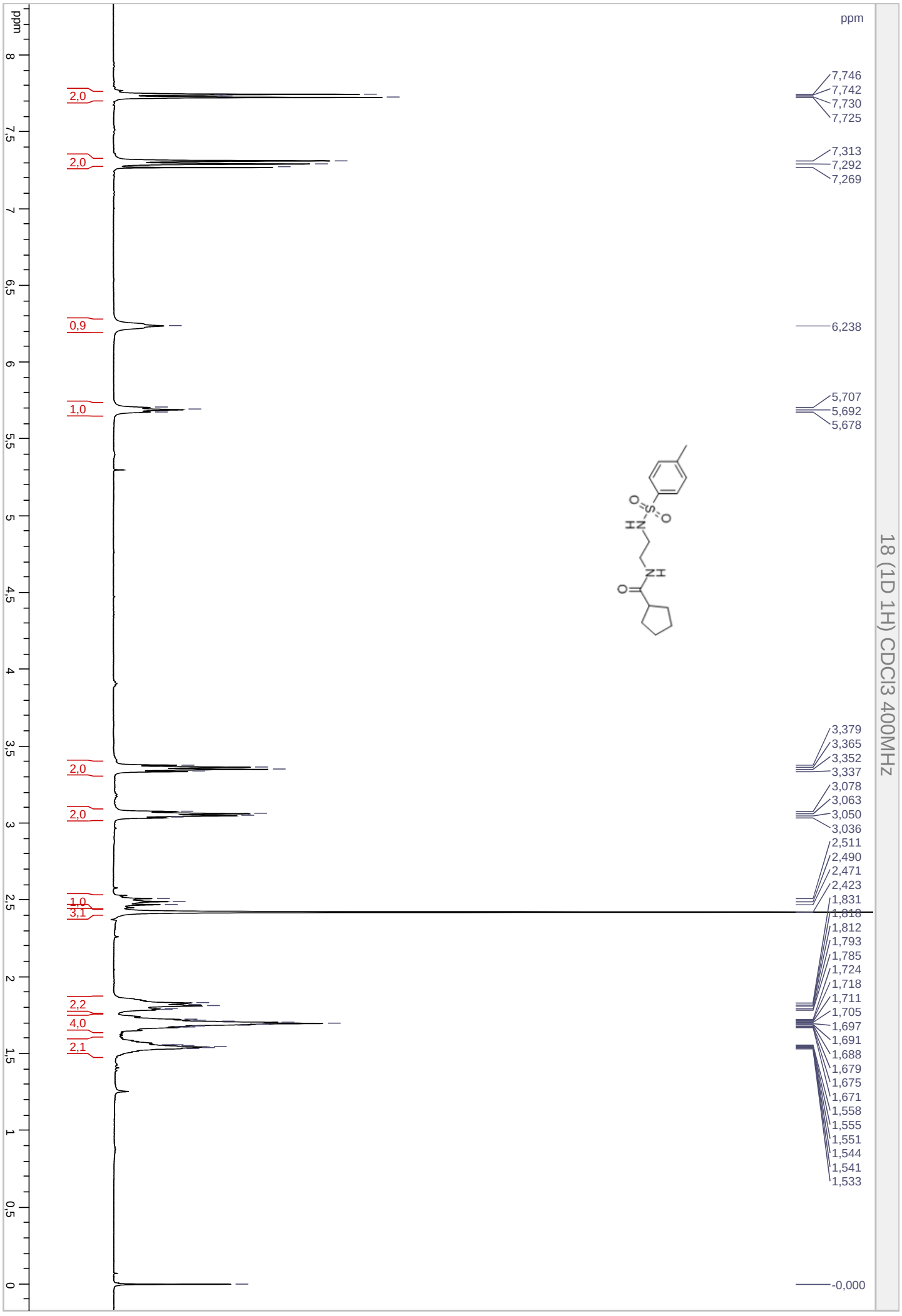
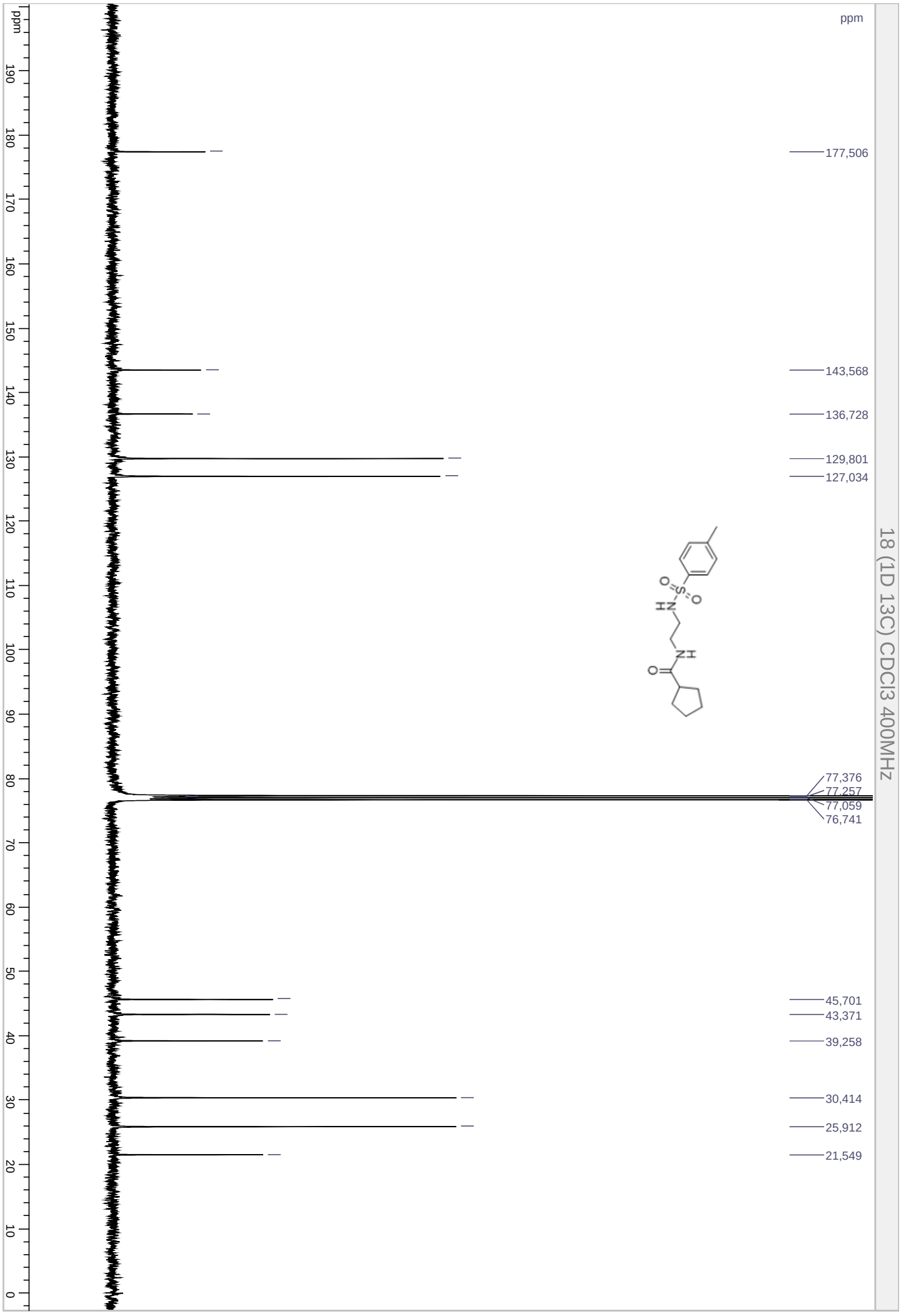


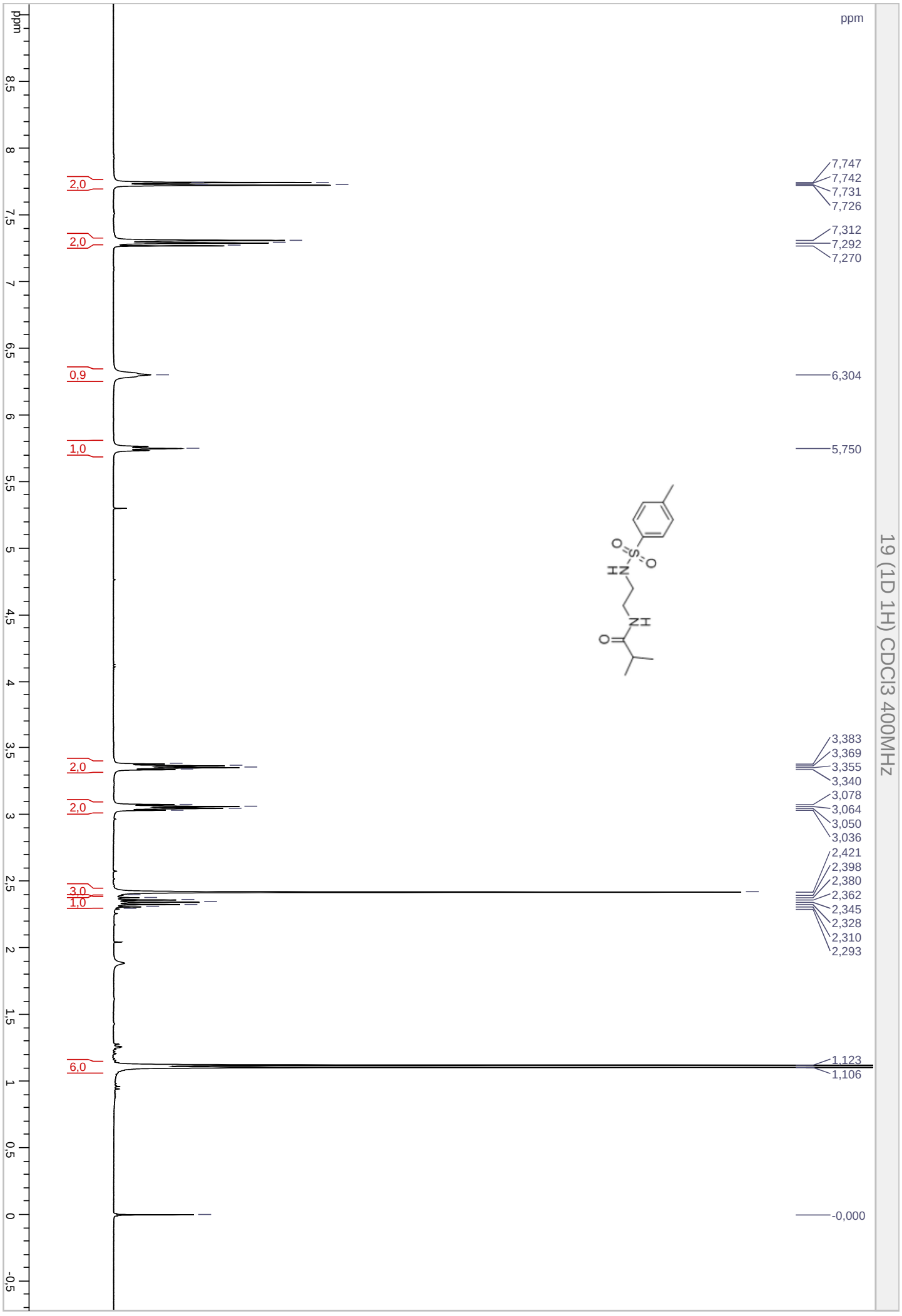


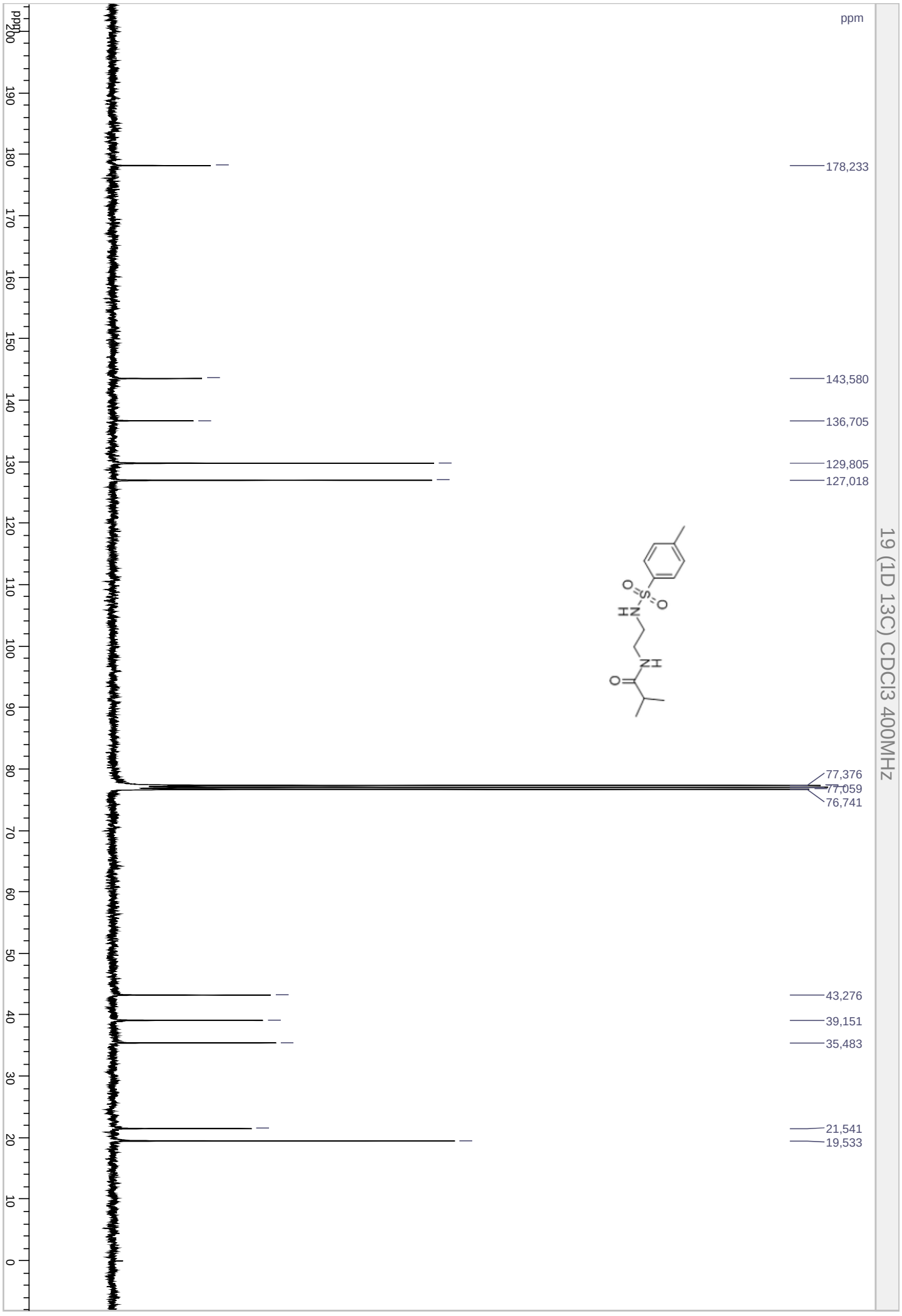


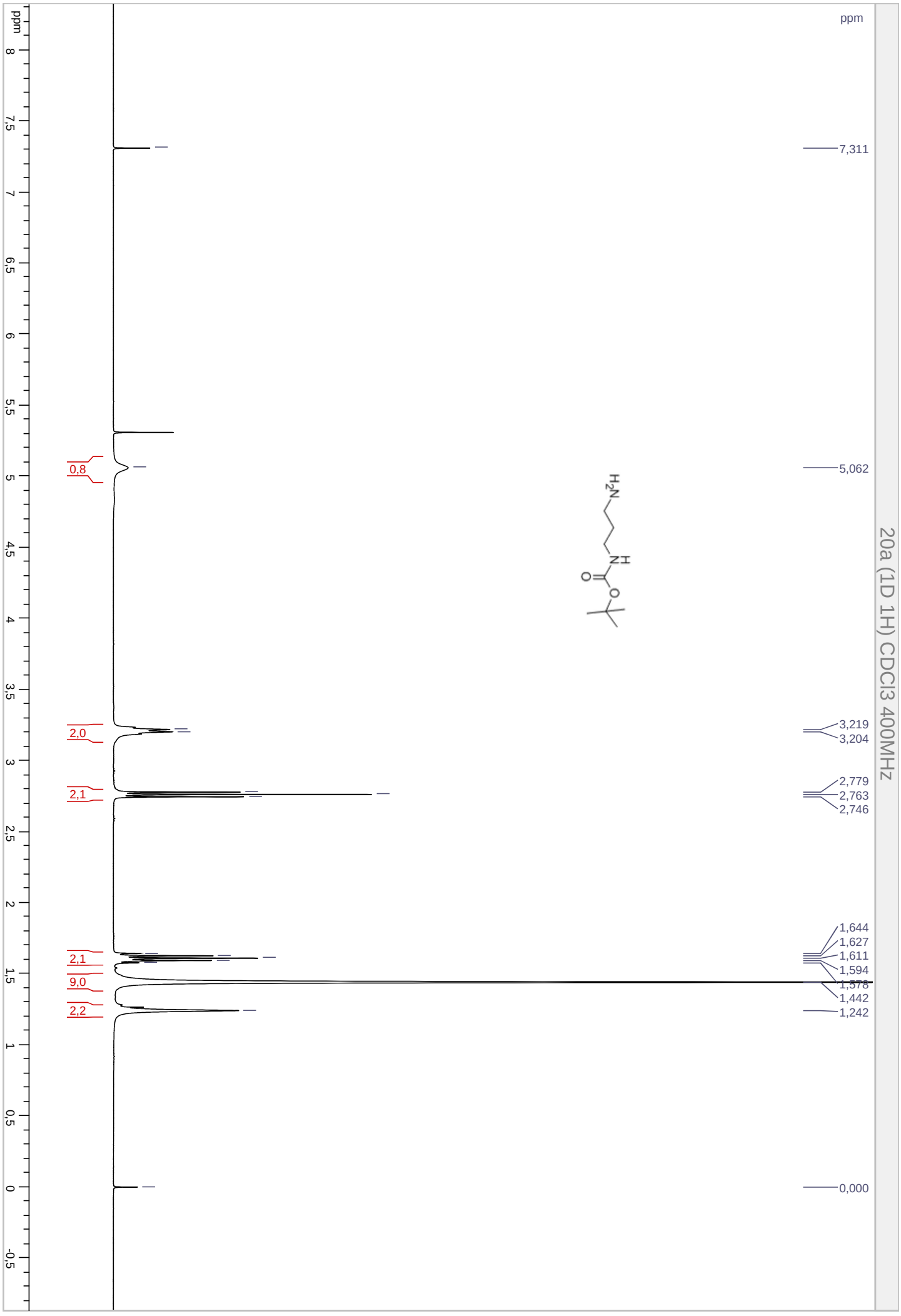


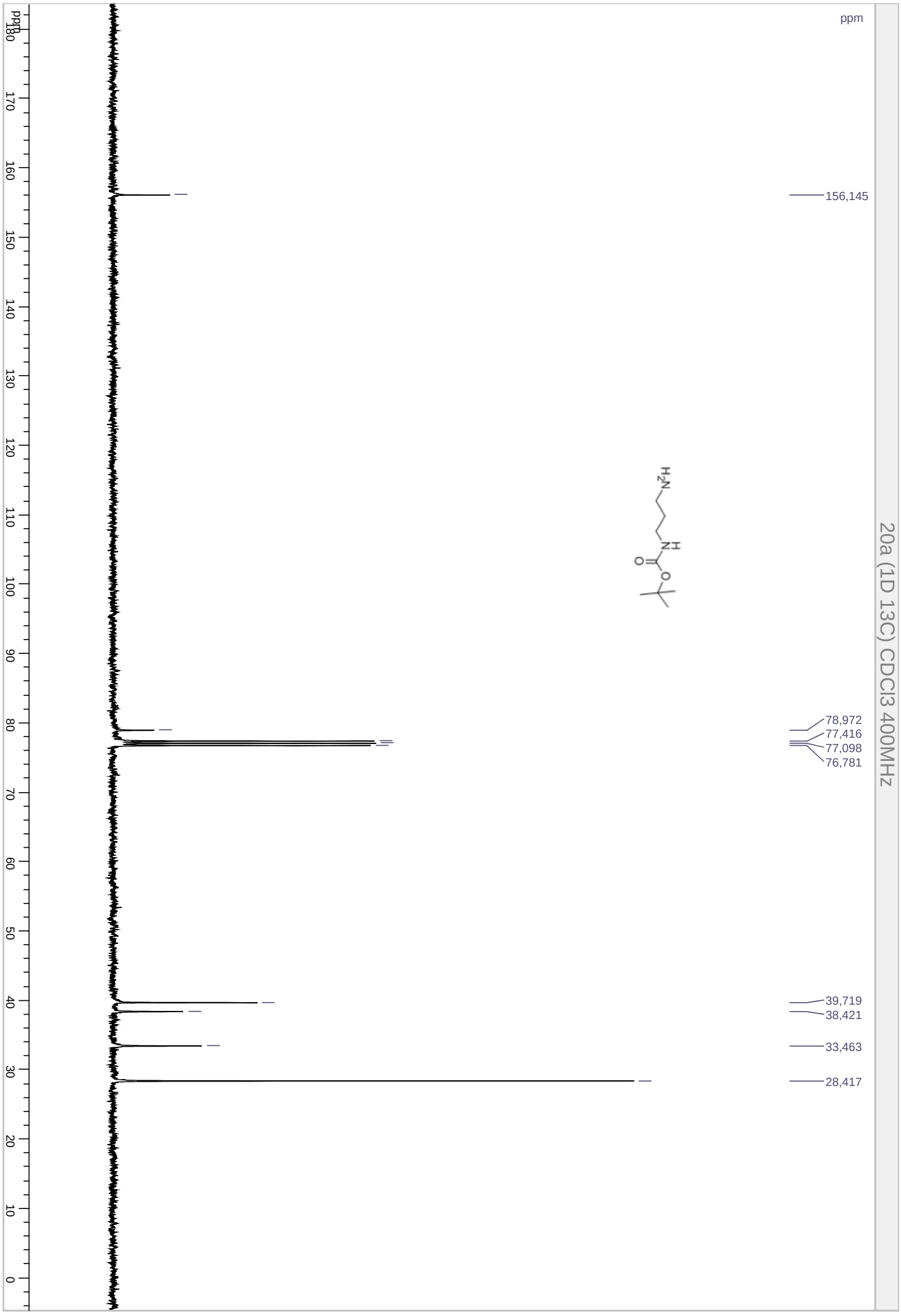


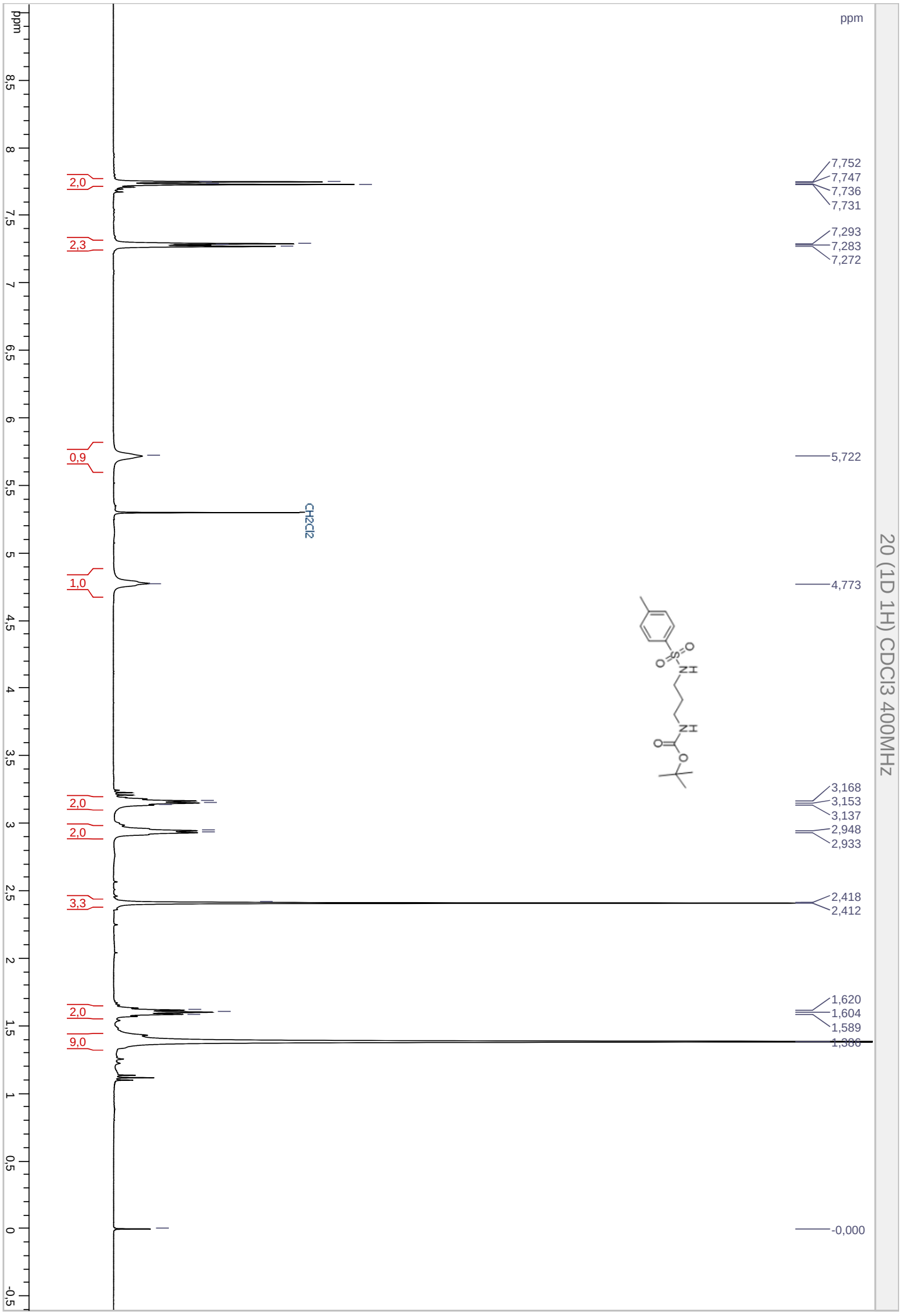


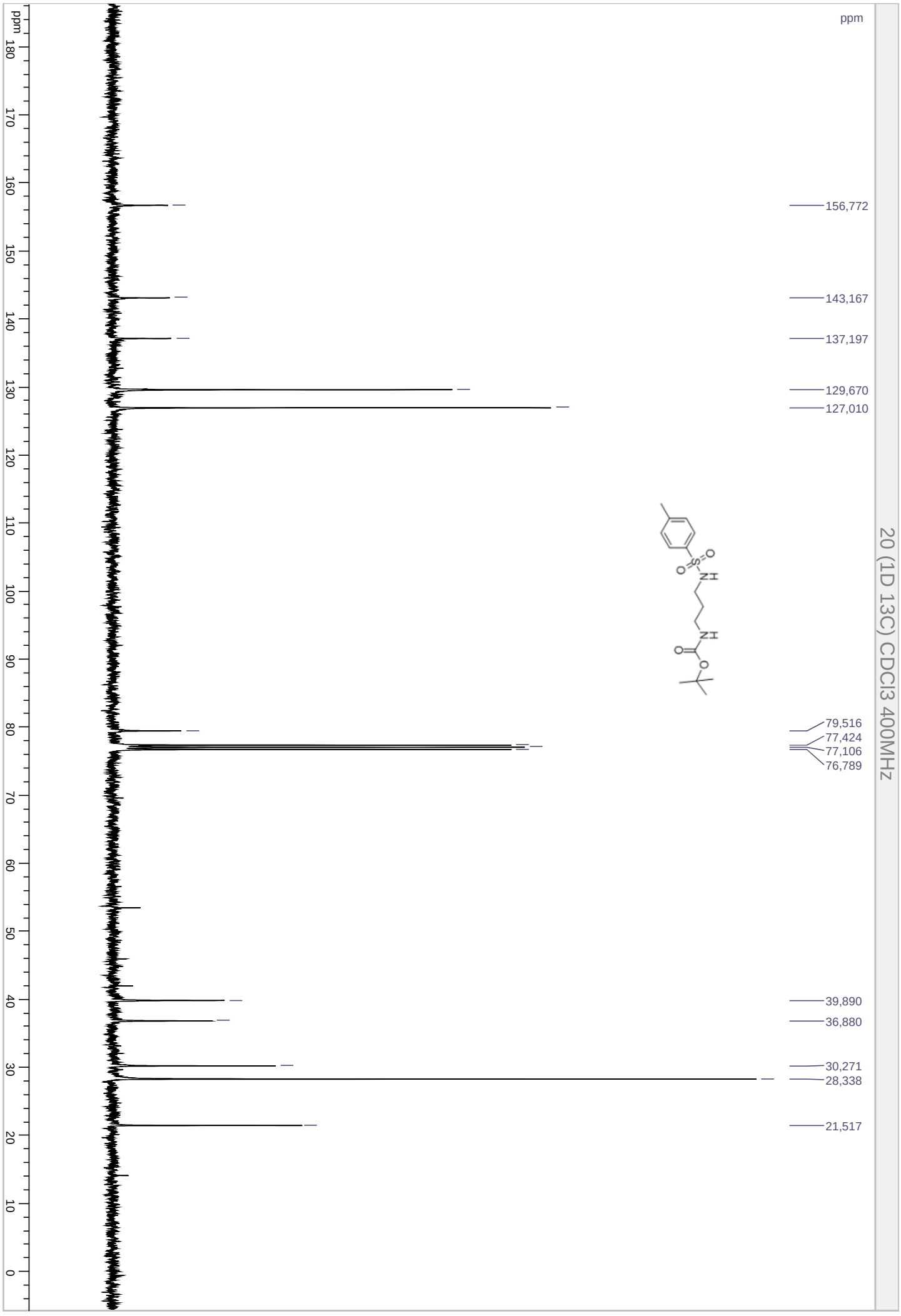


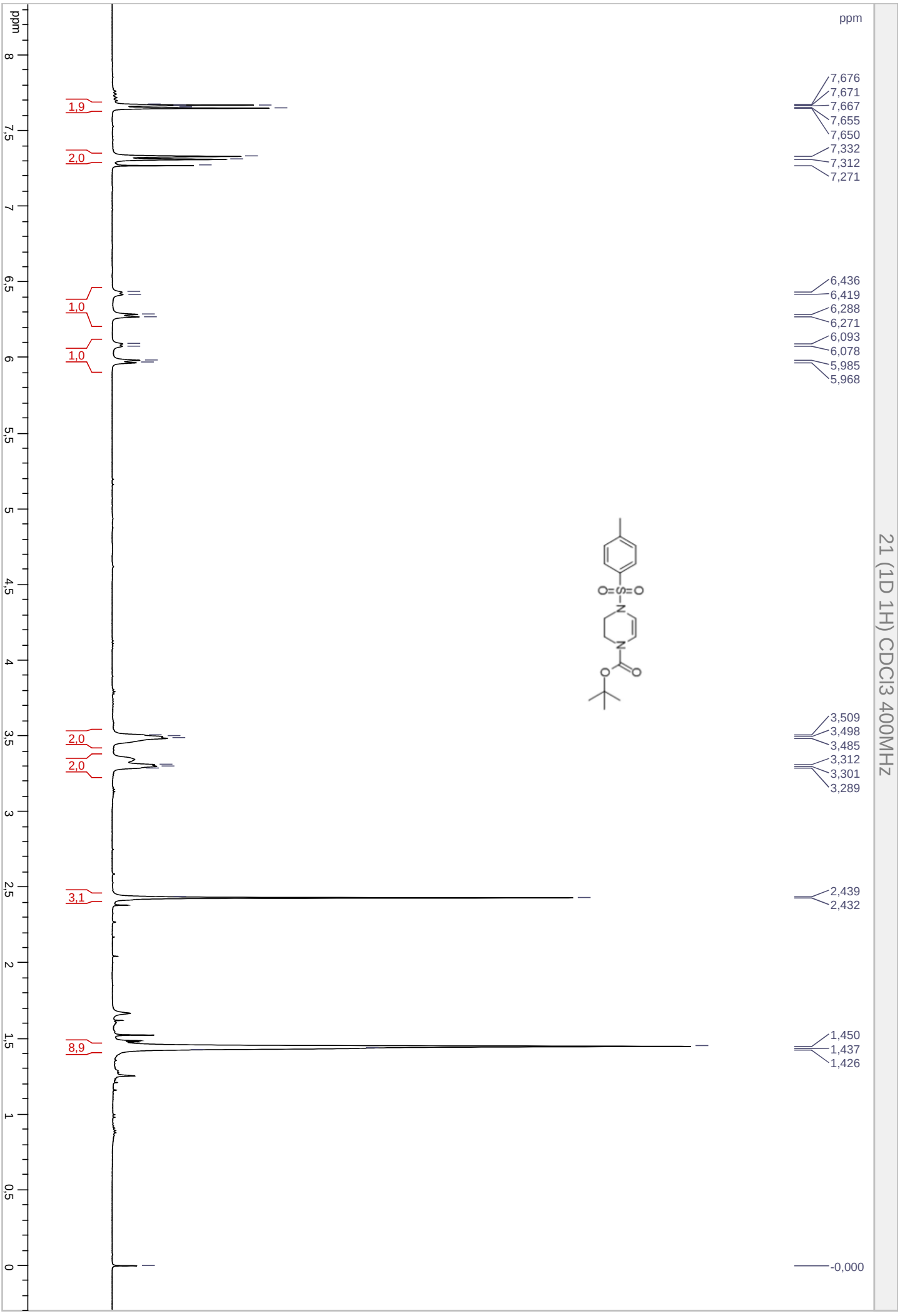


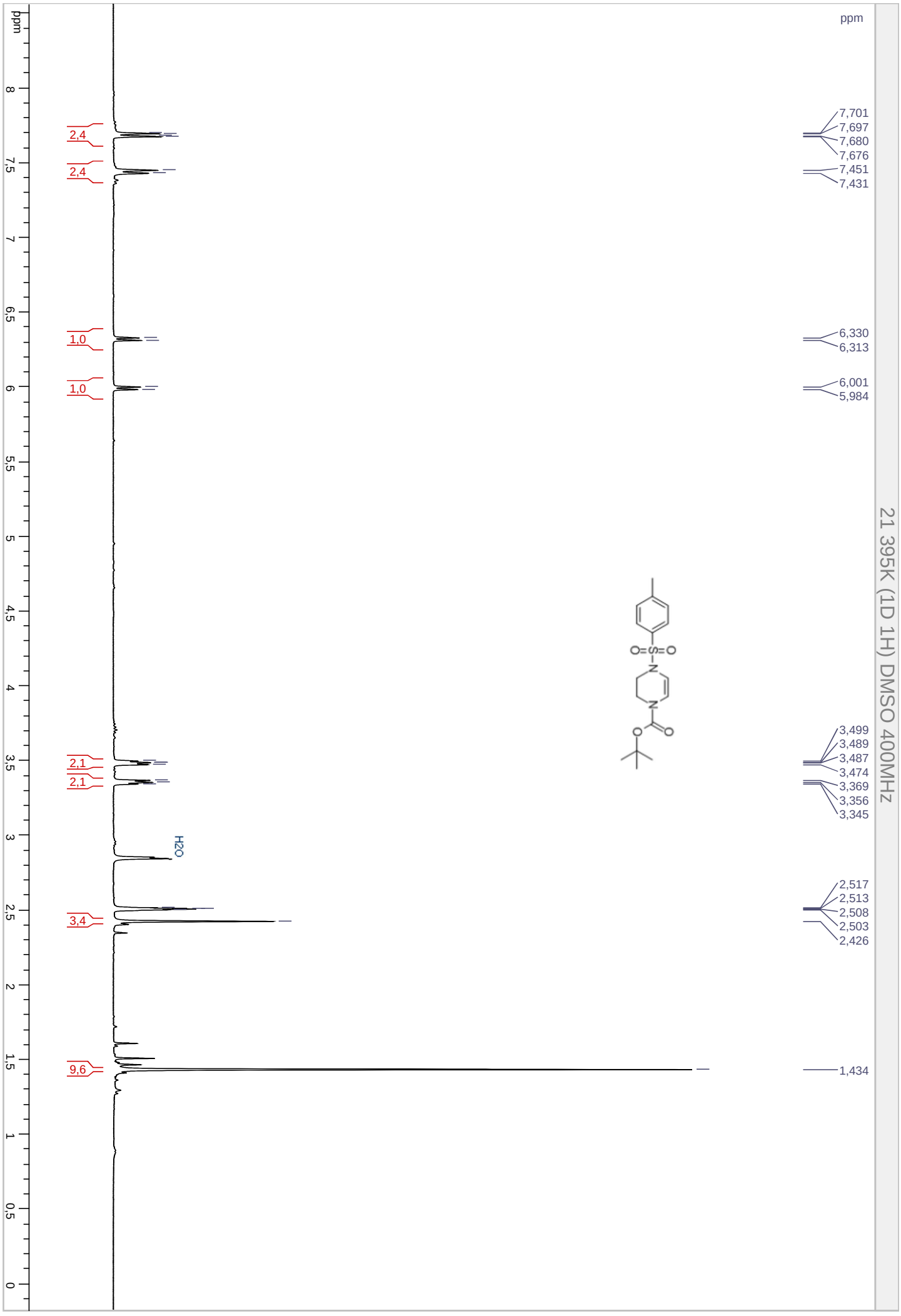


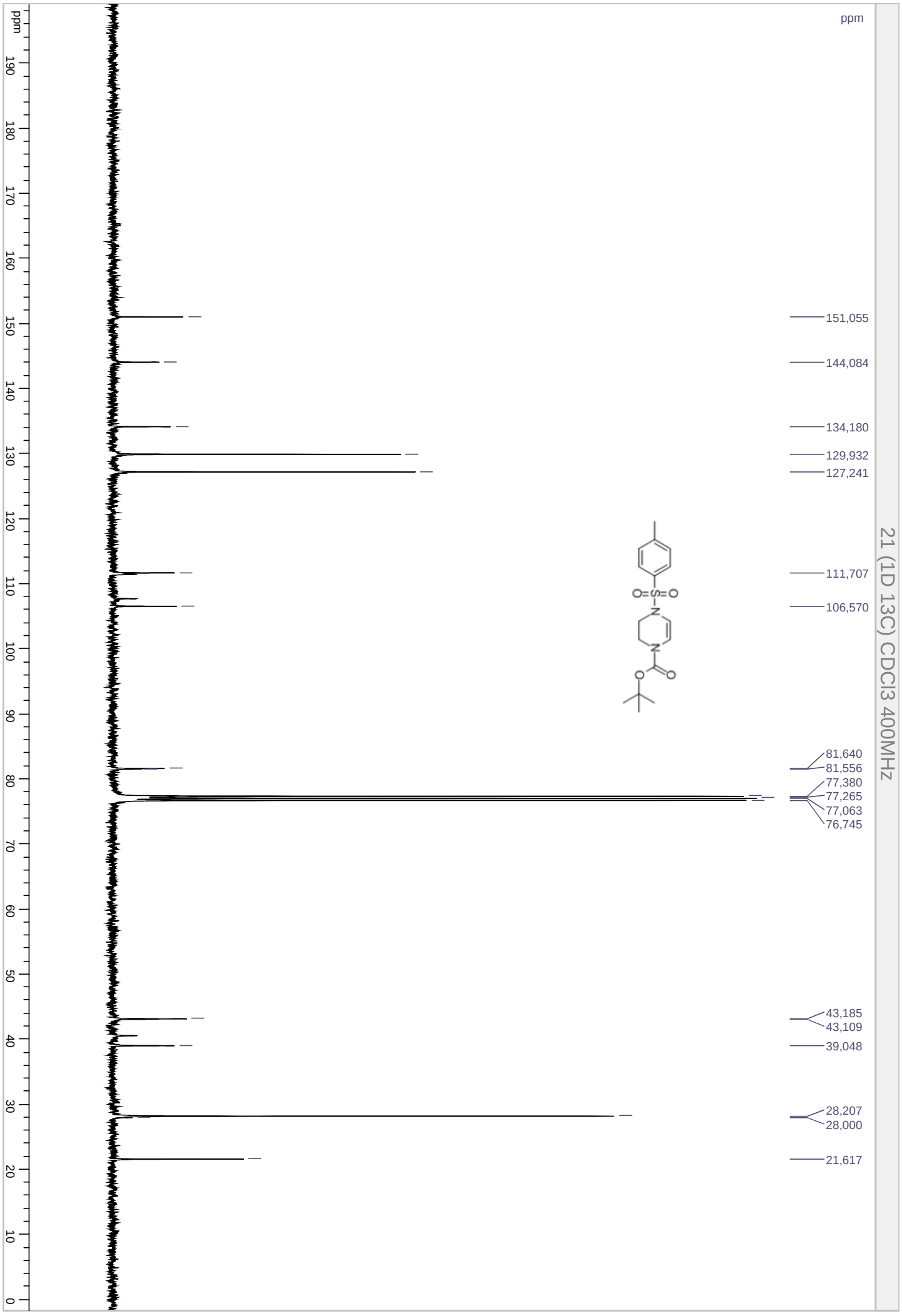


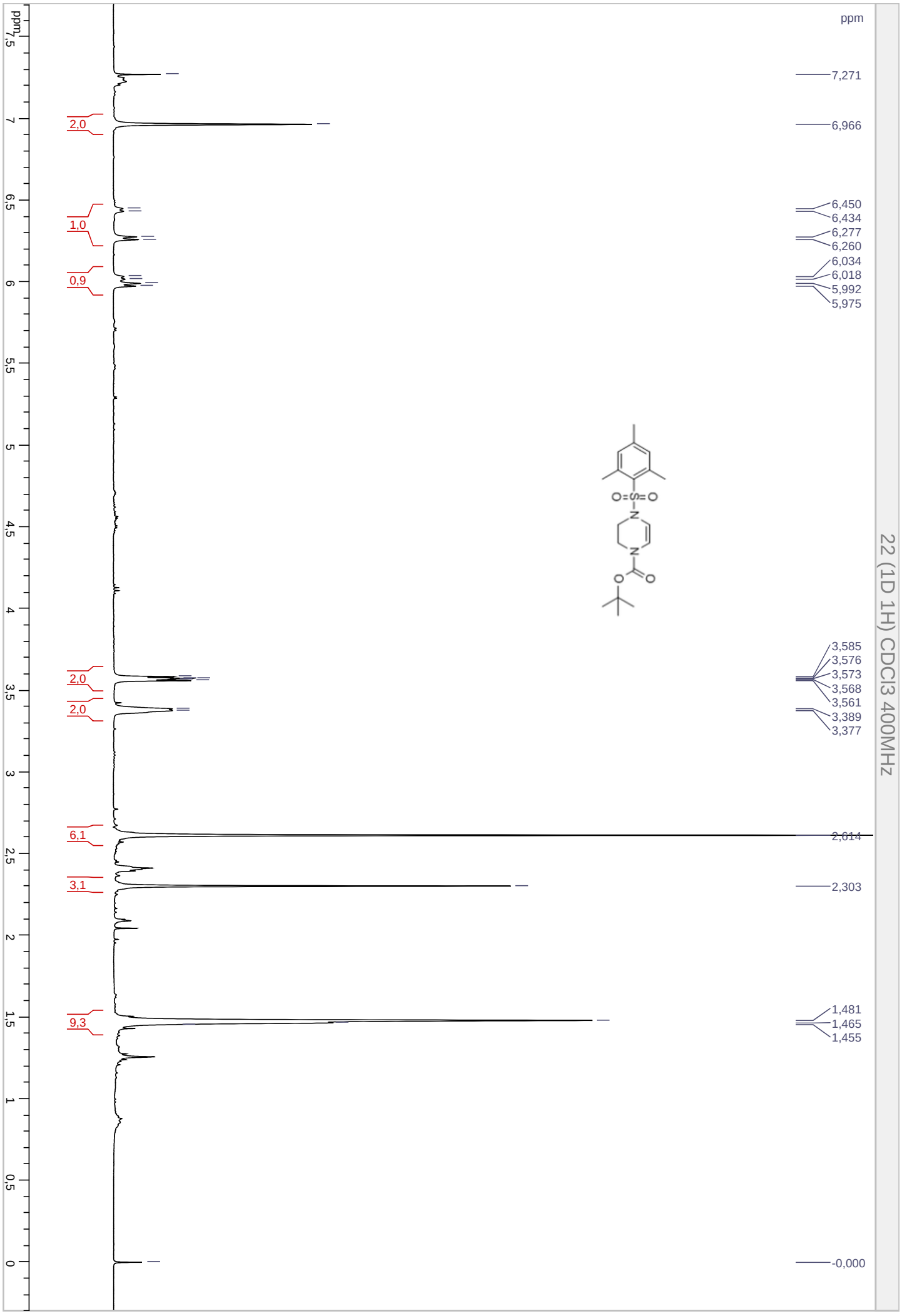


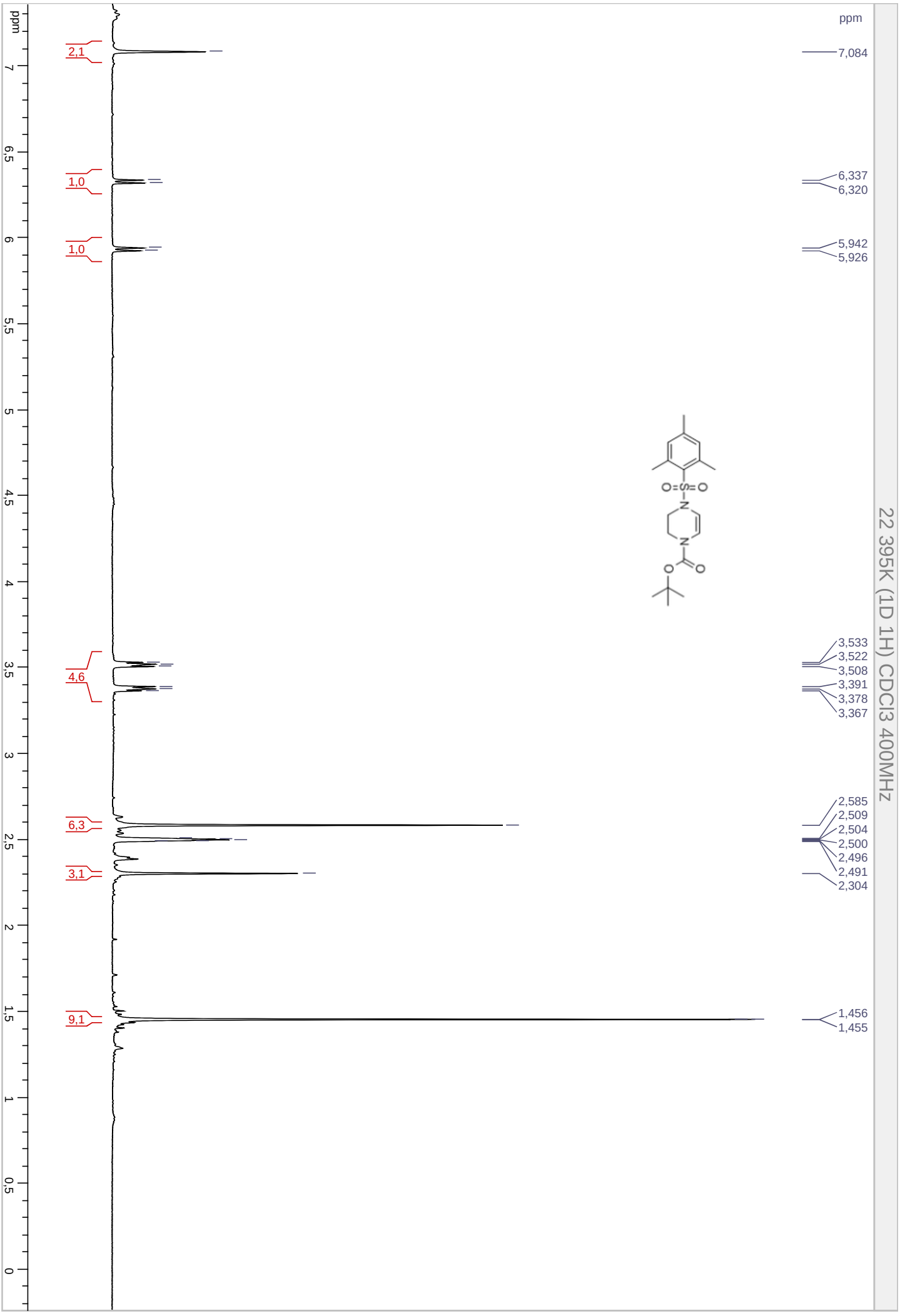


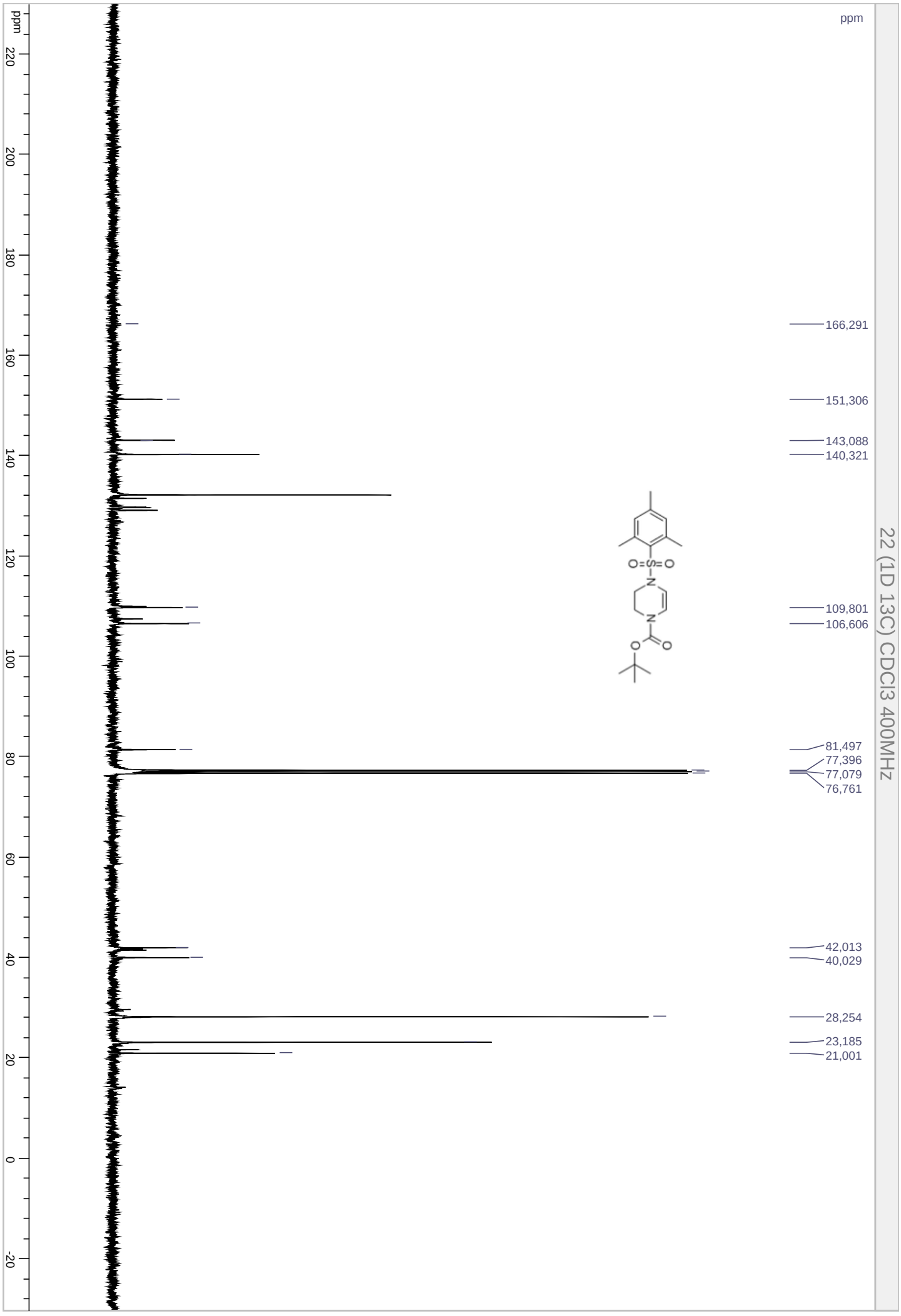


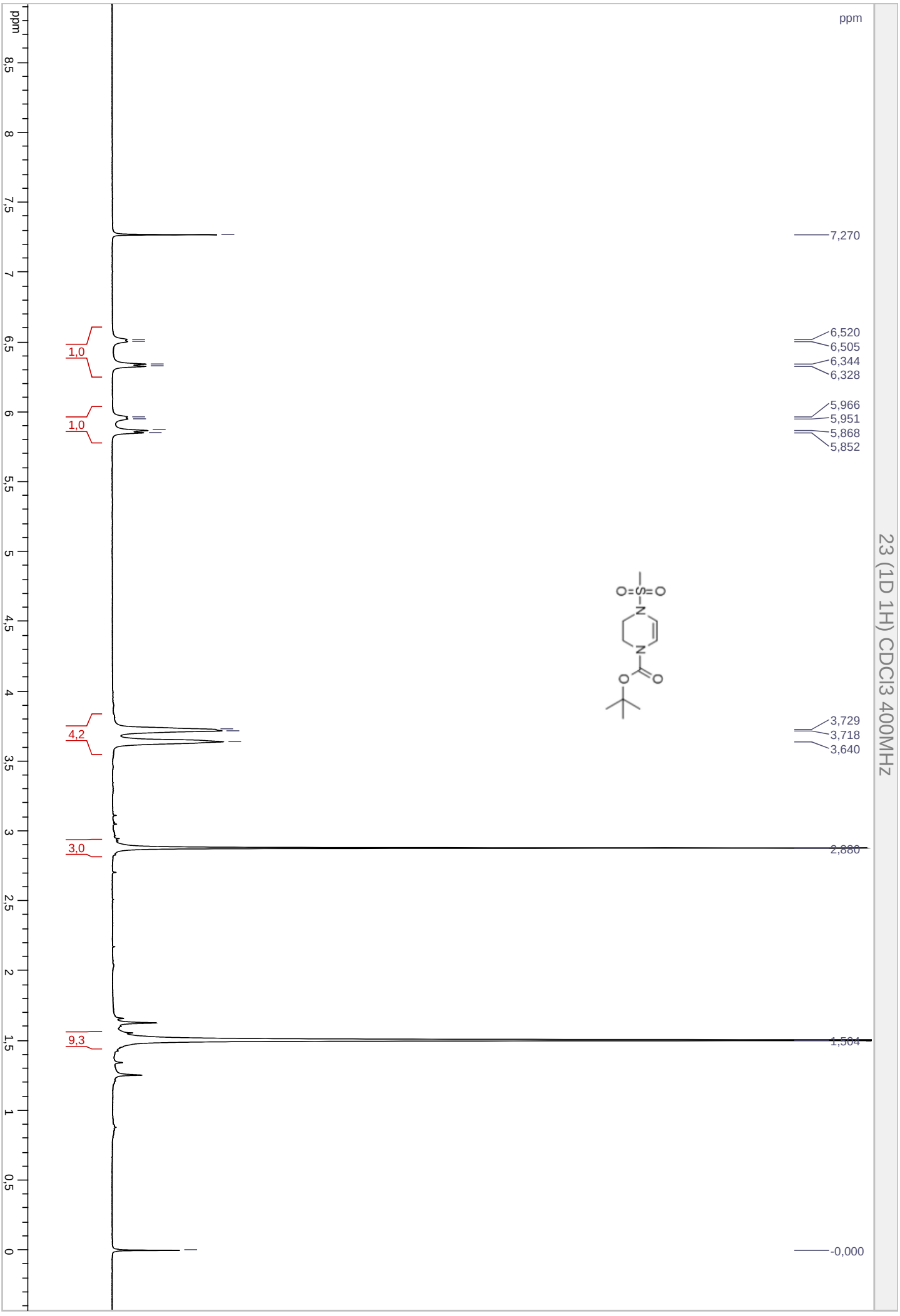


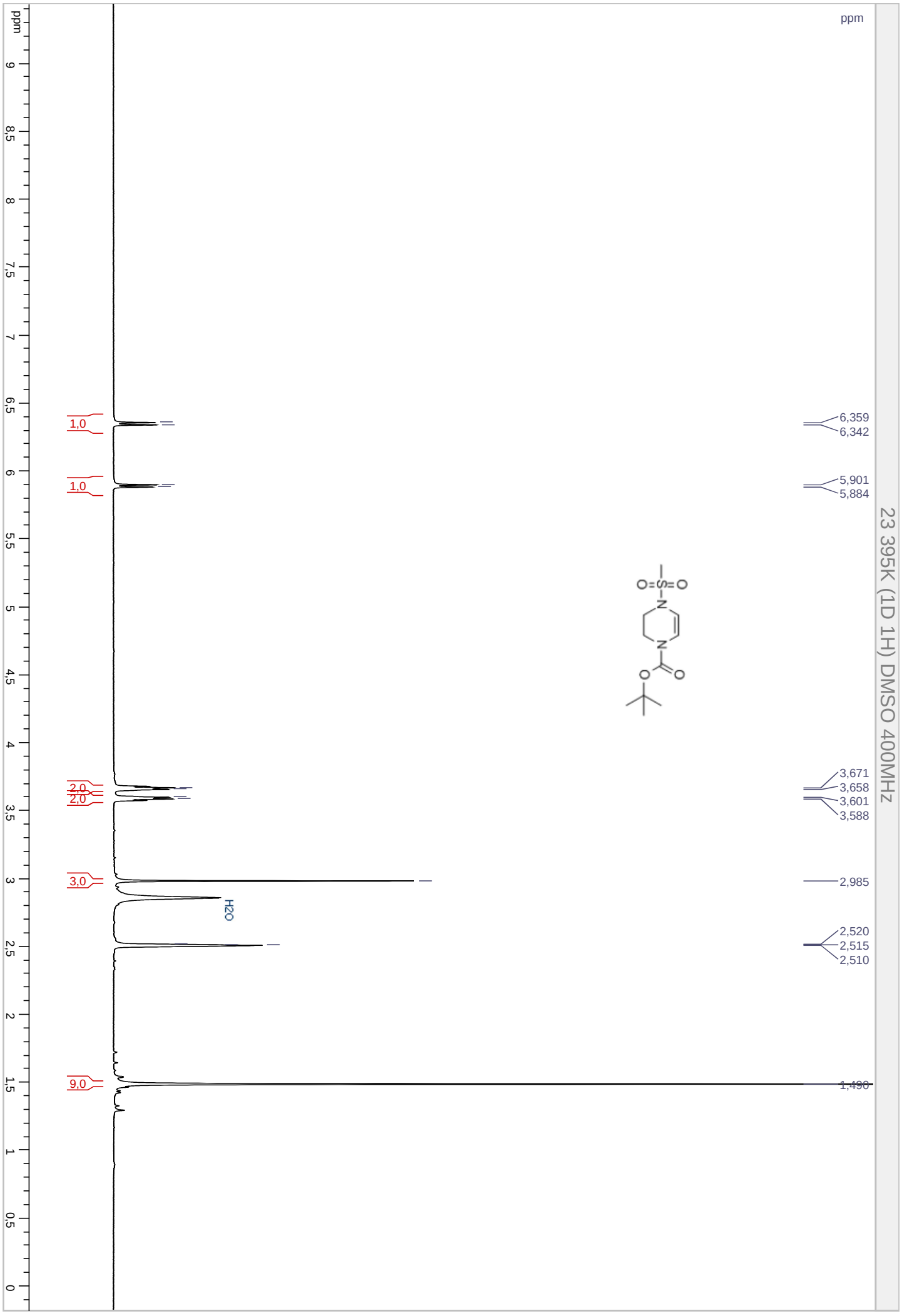


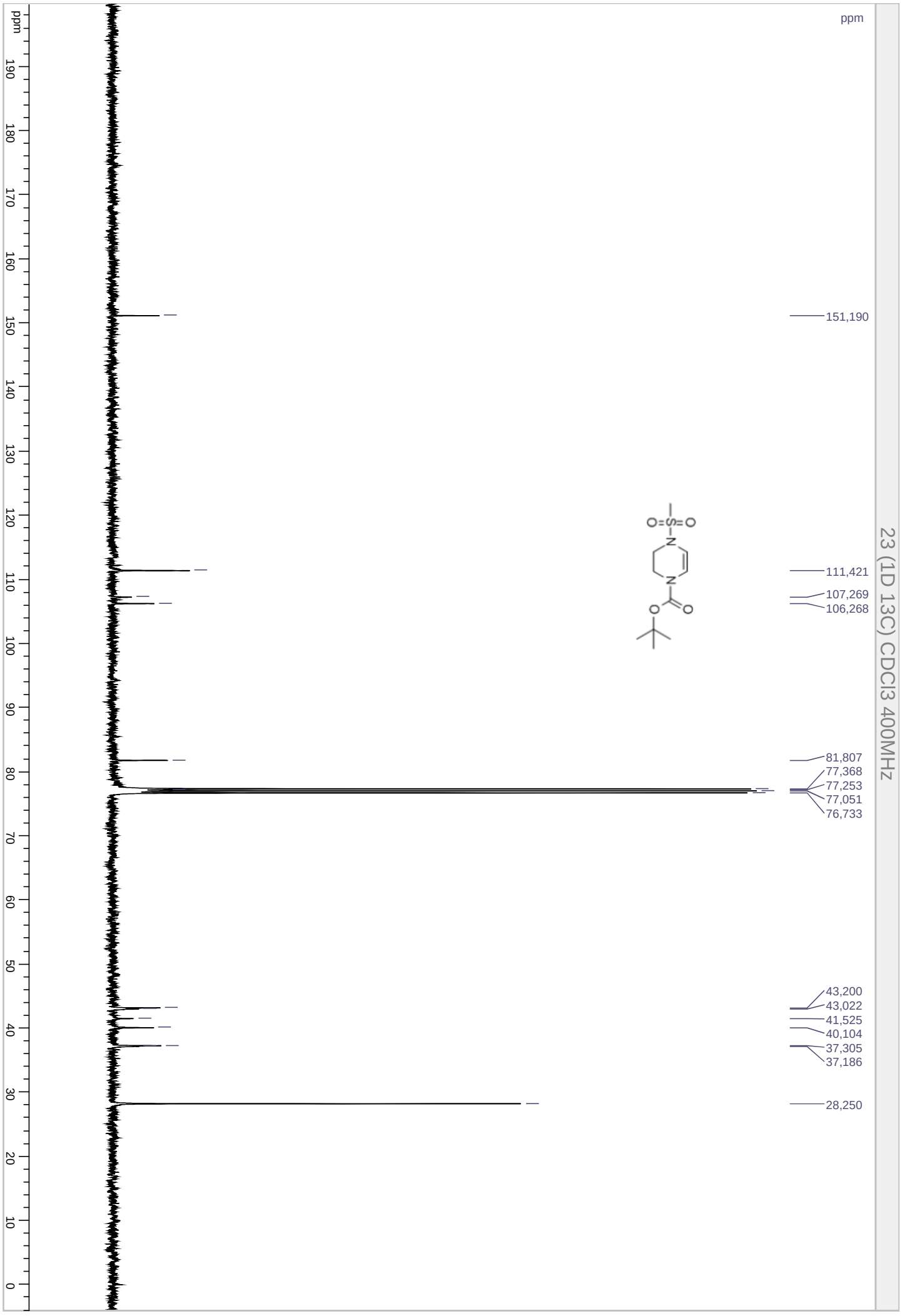


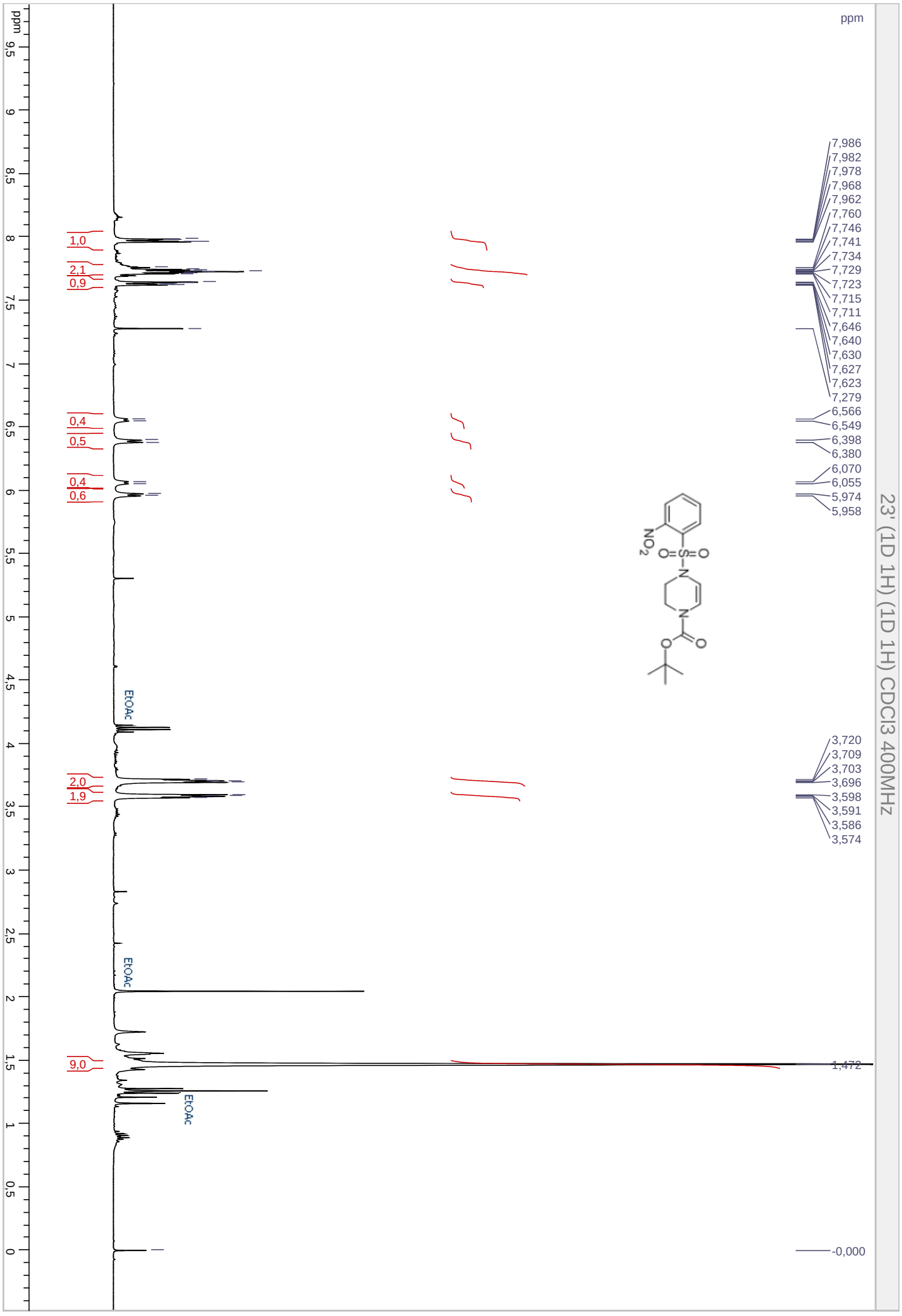

ppm
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
2,1
1,0
1,0
4,6
6,3
3,1
9,1
ppm
7,084
6,337
6,320
5,942
5,926
3,533
3,522
3,508
3,391
3,378
3,367
2,585
2,509
2,504
2,500
2,496
2,491
2,304
1,456
1,455
22 395K (1D 1H) CDCl3 400MHz

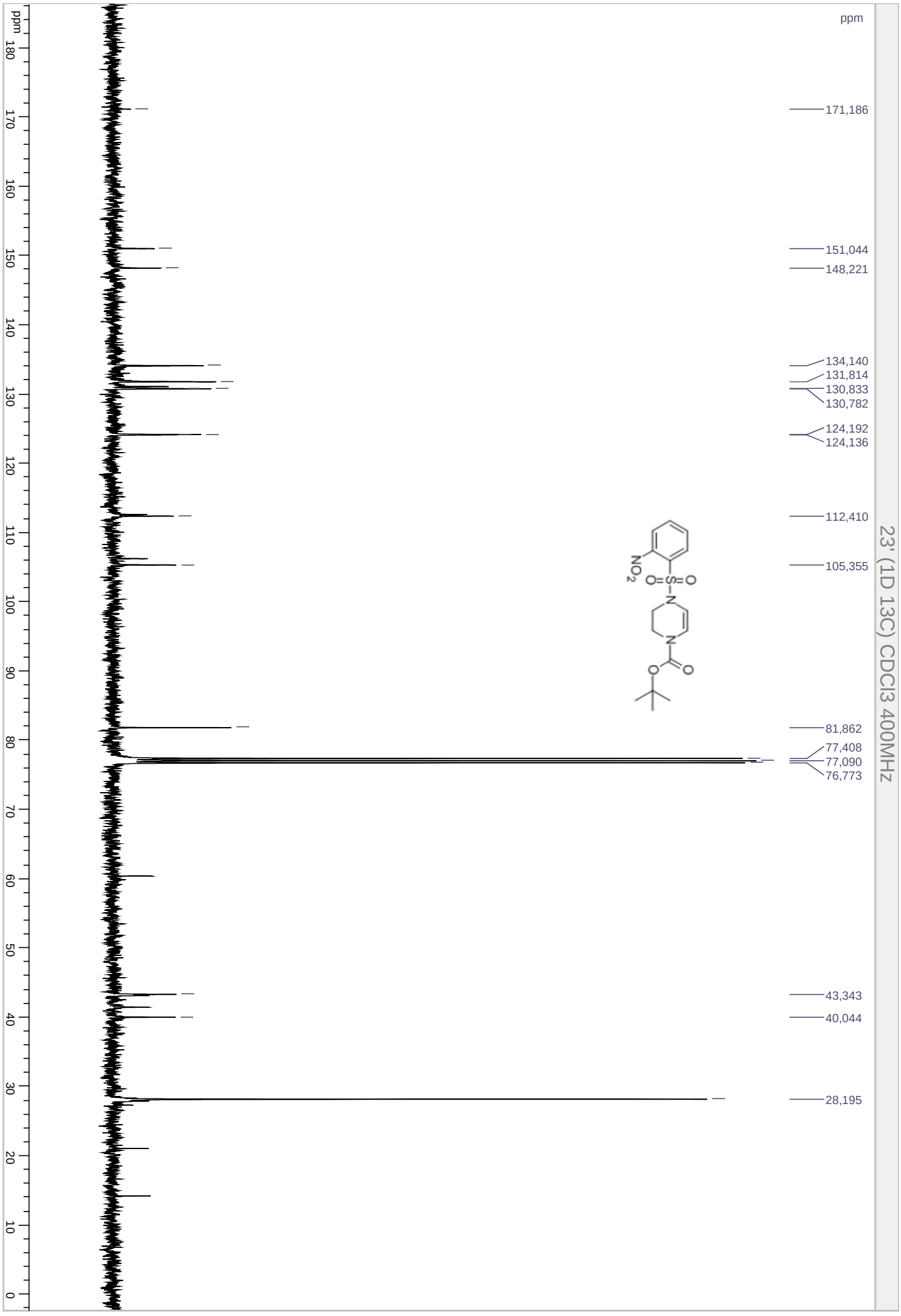


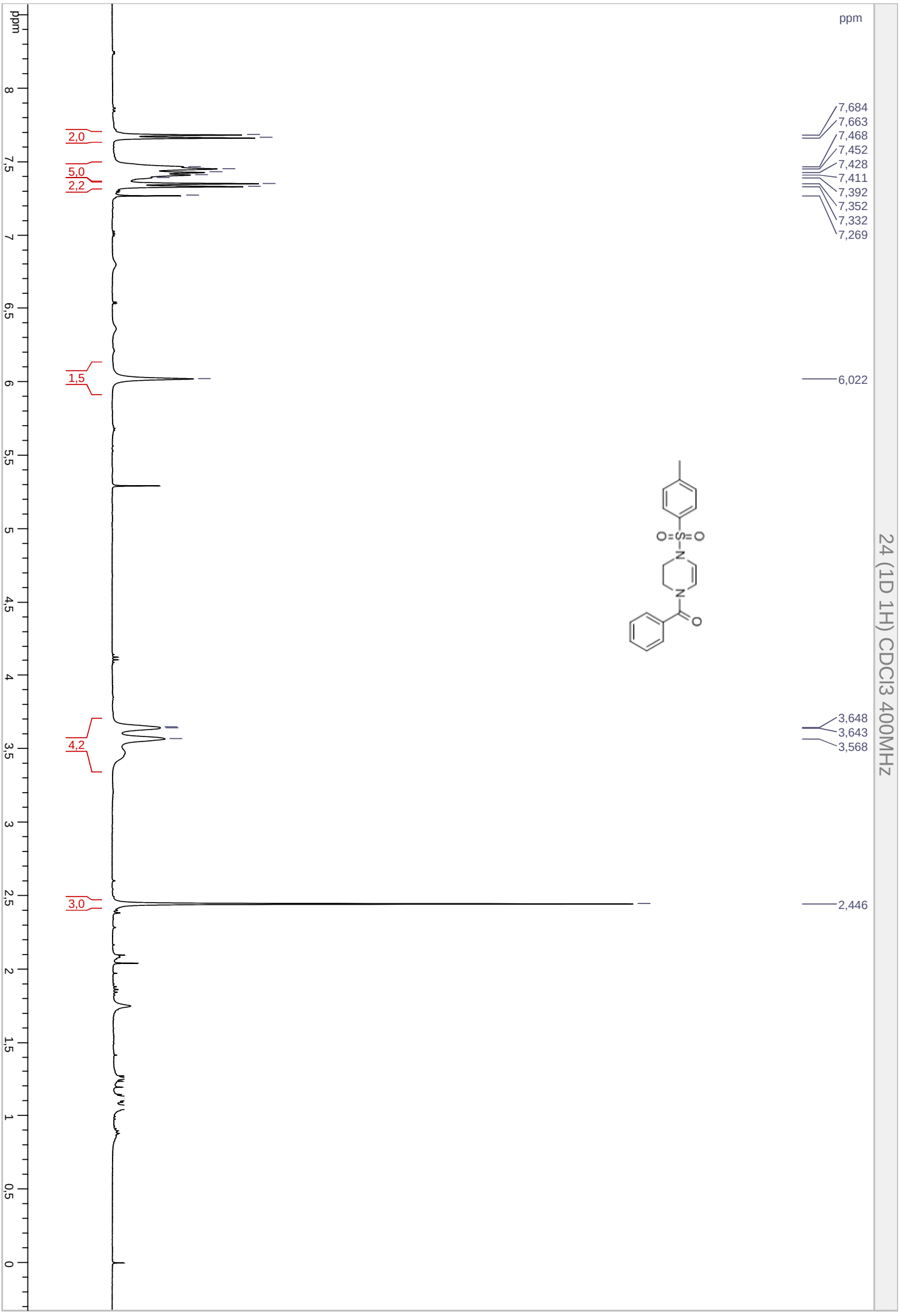


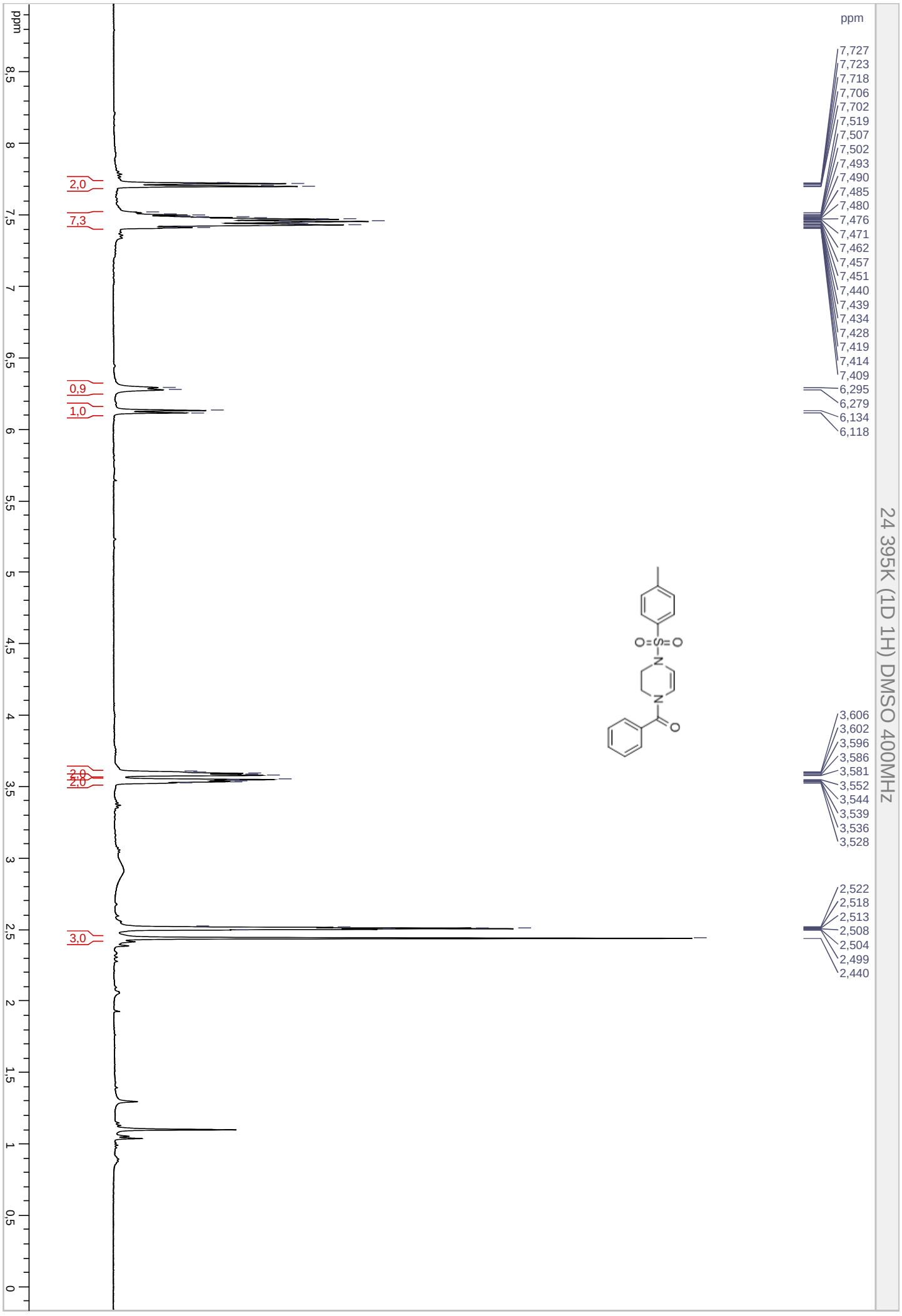


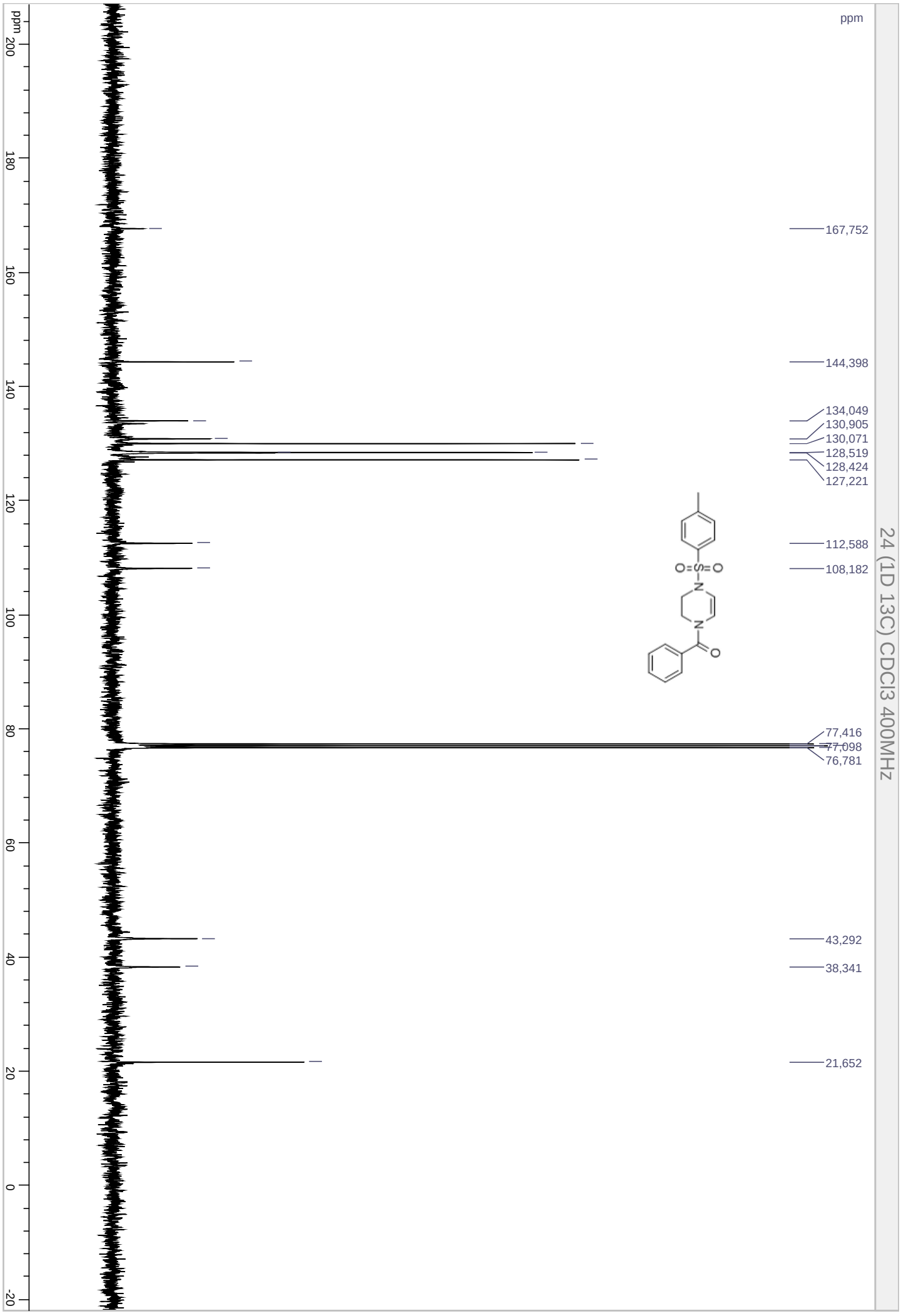


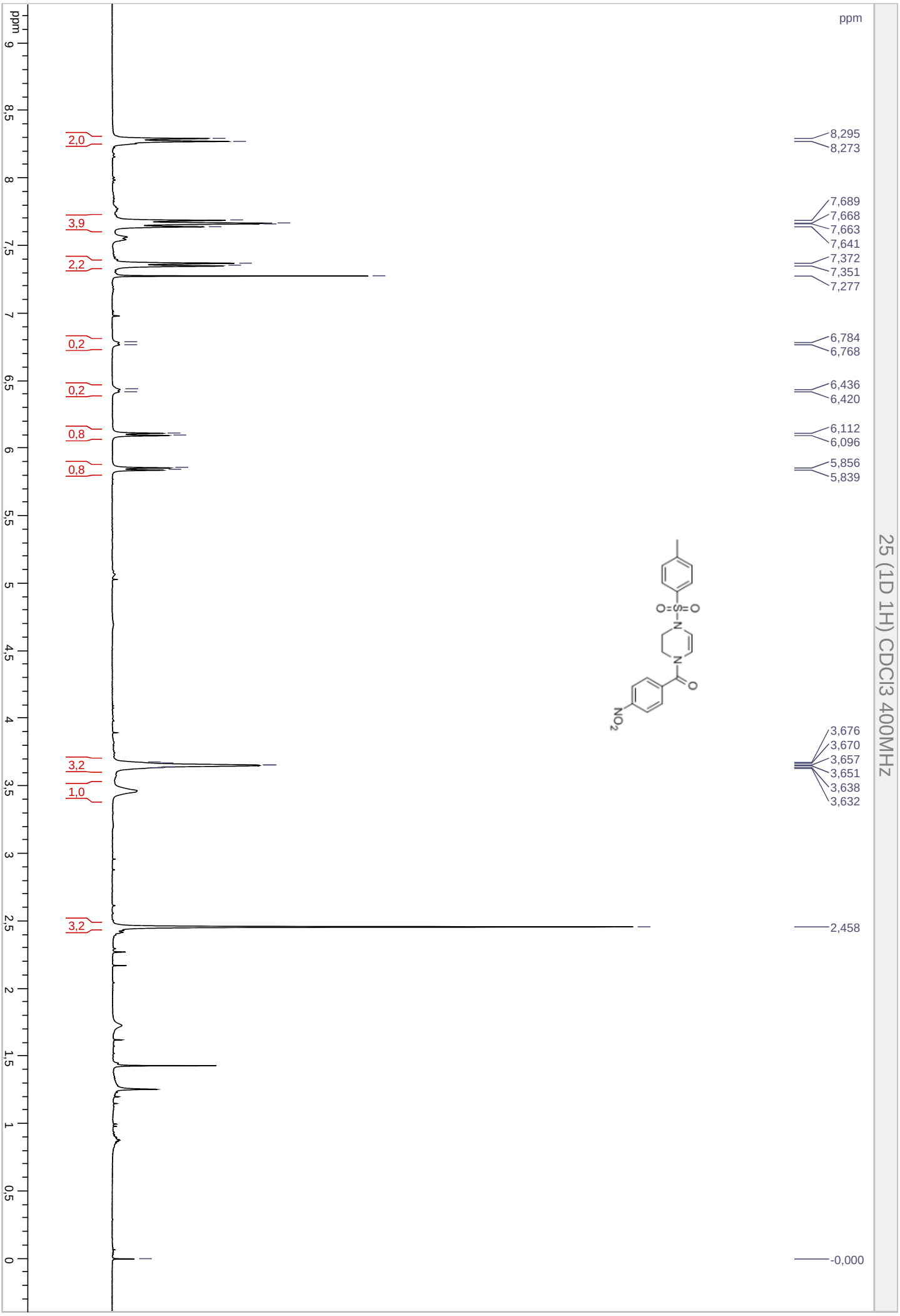







ppm
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
2,0
7,3
0,9
1,0
2,0
2,0
3,0
ppm
7,727
7,723
7,718
7,706
7,702
7,519
7,507
7,502
7,493
7,490
7,485
7,480
7,476
7,471
7,462
7,457
7,451
7,440
7,439
7,434
7,428
7,419
7,414
7,409
6,295
6,279
6,134
6,118
3,606
3,602
3,596
3,586
3,581
3,552
3,544
3,539
3,536
3,528
2,522
2,518
2,513
2,508
2,504
2,499
2,440
O=S=O
N
N
O
24 395K (1D 1H) DMSO 400MHz




ppm
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
2,0
3,9
2,2
0,2
0,2
0,8
0,8
3,2
1,0
3,2
ppm
8,295
8,273
7,689
7,668
7,663
7,641
7,372
7,351
7,277
6,784
6,768
6,436
6,420
6,112
6,096
5,856
5,839
3,676
3,670
3,657
3,651
3,638
3,632
2,458
-0,000
25 (1D 1H) CDCl3 400MHz