

Introduction of cyclopropyl and cyclobutyl ring on alkyl iodides through cobalt-catalyzed cross-coupling

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1 GENERAL INFORMATION

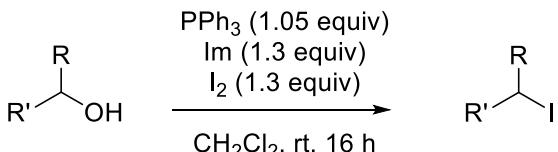
All commercially available products were used as received without any purification. All commercially available Grignard reagents (cyclopropylmagnesium bromide, isopropenylmagnesium bromide, 1-propenylmagnesium bromide, 2-methyl-1-propenylmagnesium bromide, vinylmagnesium bromide, allylmagnesium bromide, phenylmagnesium bromide, phenylmagnesium chloride, benzylmagnesium chloride, cyclopentylmagnesium bromide, isopropylmagnesium chloride) were titratedⁱ. 2-methyl-1-propenylmagnesium bromide was used after the addition of lithium chloride (1:1). The commercially available cyclopropylmagnesium bromide reagent was used on regular basis but has also been synthesized using standard magnesium insertion techniques. Non-commercially available Grignard reagents (cyclobutylmagnesium bromide) were synthesized using standard magnesium insertion techniques. All synthesized iodides were dried by azeotrope removal of H₂O utilizing toluene and stored in a round bottom flask concealed by aluminium foil at -18°C prior to use. All reactions were performed under an argon atmosphere using easy balloon techniques (tubes or round bottom flasks with rubber septum purged with Ar balloon via needles through the septum). TLC were performed on silica gel plates and visualized either with a UV lamp (254 nm) or using a staining solution (*p*-anisaldehyde or KMnO₄). Flash chromatography was performed on silica gel (Merck-Kieselgel 60, 230-400 mesh). ¹H NMR spectra were recorded on a Bruker AVANCE 400 at 400 MHz and data are reported as follows: chemical shifts in ppm with the solvent peak as internal standard (CDCl₃, δ 7.26 ppm), multiplicity (s = singulet, d = doublet, t = triplet, q = quartet, quint = quintuplet, hex = hexuplet, hept = heptuplet, m = multiplet or overlap of non-equivalent resonances, br = broad). ¹³C NMR spectra were recorded on a Bruker AVANCE 400 at 100 MHz and data are reported as follows: chemical shifts in ppm with the solvent peak as internal standard (CDCl₃ at 77.1 ppm). Coupling constants *J* were measured in Hertz. Infrared (IR) spectra were recorded on a Bruker TENSOR™ 27 (IRFT) and wave numbers are indicated in cm⁻¹. Mass spectra with electronic impact (MS-EI) were recorded with a Shimadzu GCMS-QP 2010S (70 eV). High resolution mass spectra (HRMS) were performed at the Laboratoire de Spectrométrie de Masse de l'Université Pierre et Marie Curie de Paris. Nomenclature of organic compounds was indicated following the IUPAC rules. THF, Et₂O, CH₂Cl₂ and toluene were dried using a MBraun SPS800 purifier.

PE = petroleum ether, EA = ethyl acetate, SP = side product (of elimination and dehalogenation)

2 SUBSTRATES AND REAGENTS SYNTHESIS

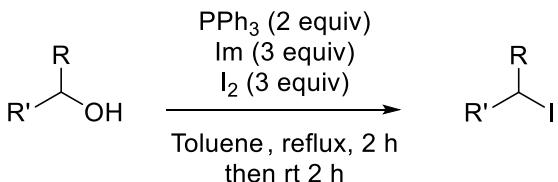
2-1 IODIDE SYNTHESIS

Procedure A:



To a solution of alcohol (1 equiv) in CH_2Cl_2 at rt were added PPh_3 (1.05 equiv) and imidazole (1.3 equiv). The mixture was cooled down to 0 °C and iodide (1.3 equiv) was added over 4 to 5 portions. The reaction was allowed to warm to rt and stirred overnight for 16 h concealed by aluminum foil. The reaction was quenched by the addition of H_2O , the aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were washed with an aqueous solution of sodium thiosulphate, dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (solid deposit) afforded the desired iodide.

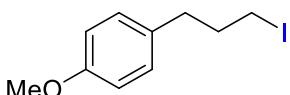
Procedure B:



To a solution of alcohol (1 equiv) in toluene at rt were added PPh_3 (2 equiv), imidazole (3 equiv) and iodide (3 equiv). The reaction was refluxed and stirred for 2 h before being cooled down to room temperature and stirred for another 2 h. The reaction was quenched by the addition of H_2O , the aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were washed with an aqueous solution of sodium thiosulphate, dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (solid deposit) afforded the desired iodide.

Primary iodides

1-(3-Iodopropyl)-4-methoxybenzene, 1.1¹



Iodine **1.1** was prepared according to Procedure **A** from 3-(4-methoxyphenyl)propan-1-ol (3.5 g, 20.64 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 9:1) yielded iodine **1.1** (5.48 g, 19.85 mmol, 96%) as a colourless oil.

Formula: $\text{C}_{10}\text{H}_{13}\text{OI}$

Mass: 276.1 g.mol⁻¹

¹ Rezazadeh, S.; Devannah, V.; Watson, D. A. *J. Am. Chem. Soc.* **2017**, *139*, 8110-8113.

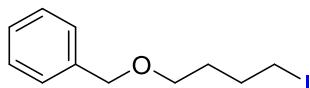
IR (neat): 1611, 1584, 1511, 1463, 1441, 1300, 1245, 1213, 1177, 1120, 1101, 1035 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.12 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.16 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.10 (quint, *J* = 7.0 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 158.1, 132.5, 129.6 (2C), 114.0 (2C), 55.3, 35.3, 35.2, 6.5

MS (EI) *m/z*: 277 (3), 276 (32), 122 (9), 121 (100), 91 (6), 78 (7), 77 (8)

((4-Iodobutoxy)methyl)benzene, **1.2**²



Iodine **1.2** was prepared according to Procedure A from 4-(benzyloxy)butan-1-ol (200.0 mg, 1.08 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 99:1 to 99:3) yielded iodine **1.2** (0.69 mmol, 200.5 mg, 64%) as a colourless oil.

Formula: C₁₁H₁₅OI

Mass: 290.1 g.mol⁻¹

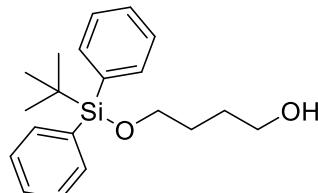
IR (neat): 1494, 1453, 1430, 1362, 1223, 1174, 1101, 1077, 1028, 908, 871 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.33 – 7.15 (m, 5H), 4.42 (s, 2H), 3.42 (*t*_{app}, *J* = 6.2 Hz, 2H), 3.14 (*t*_{app}, *J* = 7.0 Hz, 2H), 1.87 (quint_{app}, *J* = 7.2 Hz, 2H), 1.69 – 1.59 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 138.5, 128.5 (2C), 127.7 (2C), 127.7, 73.0, 69.1, 30.7, 30.5, 6.9

MS (EI) *m/z*: 183 (1, M-107, -OCH₂Ph), 163 (2, M-127, -I), 105 (1), 92 (12), 91 (100), 71 (11), 65 (7), 55 (5)

4-((tert-Butyldiphenylsilyl)oxy)butan-1-ol, **S1**³



To a solution of 1,4-butanediol (0.50 mL, 5.55 mmol, 1 equiv) and imidazole (400.6 mg, 5.83 mmol, 1.05 equiv) in DMF (2.5 mL) at 0 °C was slowly added TBDPSCI (1.54 mL, 5.83 mmol, 1.05 equiv). The reaction mixture was allowed to warm up to rt and was stirred overnight before being quenched by the addition of H₂O. The aqueous phase was extracted with cyclohexane 3 times. The combined organic phases were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 9:1 to 4:6) yielded alcohol **S1** (803 mg, 2.44 mmol, 44%) as a colourless oil.

Formula: C₂₀H₂₈O₂Si

Mass: 328.5 g.mol⁻¹

IR (neat): 3324, 1472, 1428, 1389, 1361, 1109, 1063, 1028 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.77 – 7.56 (m, 4H), 7.55 – 7.29 (m, 6H), 3.70 (t, *J* = 5.7 Hz, 2H), 3.67 (brt, *J* = 5.6 Hz, 2H), 2.07 (brs, 1H), 1.76 – 1.58 (m, 4H), 1.06 (s, 9H)

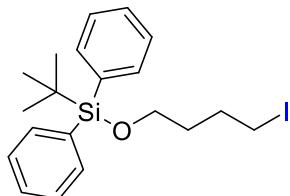
² Vu, V. H.; Louafi, F.; Girard, N.; Marion, R.; Roisnel, T.; Dorcet, V.; Hurvois, J.-P. *J. Org. Chem.* **2014**, *79*, 3358-3373.

³ Qian, P.-Z.; Yao, W. Y.; Huang, L.-B.; Meng, X.-b.; Li, Z.-J. *Tetrahedron Letters*, **2015**, *56*, 5238-5241.

¹³C NMR (100 MHz, CDCl₃) δ 135.7 (4C), 133.7 (2C), 129.7 (2C), 127.8 (4C), 64.1, 62.9, 29.9, 29.4, 26.9 (3C), 19.2

MS (EI) m/z: 271 (9, M-57, -t-Bu), 229 (19), 211 (7), 201 (5), 200 (18), 199 (100), 194 (6), 193 (34), 181 (9), 167 (5), 151 (6), 139 (20), 135 (6), 131 (6), 123 (7), 121 (7), 105 (8), 91 (13), 78 (5), 77 (18), 55 (7)

tert-Butyl(4-iodobutoxy)diphenylsilane, 1.3



Iodine **1.3** was prepared according to Procedure **A** from 4-((tert-butyldiphenylsilyl)oxy)butan-1-ol **S1** (779.3 mg, 2.37 mmol). Purification by flash chromatography on silica gel (PE/ Et₂O 9:1) yielded iodine **1.3** (2.14 mmol, 939.2 mg, 90%) as a colourless oil.

Formula: C₂₀H₂₇OSiI

Mass: 438.4 g.mol⁻¹

IR (neat): 1696, 1472, 1427, 1389, 1361, 1225, 1173, 1145, 1107, 1031, 958 cm⁻¹

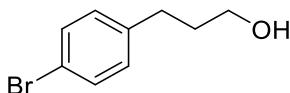
¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.63 (m, 4H), 7.47 – 7.36 (m, 6H), 3.69 (t, J = 6.1 Hz, 2H), 3.20 (t, J = 7.0 Hz, 2H), 2.00 – 1.91 (m, 2H), 1.71 – 1.61 (m, 2H), 1.06 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 135.6 (4C), 133.9 (2C), 129.7 (2C), 127.8 (4C), 62.8, 33.4, 30.2, 26.9 (3C), 19.3, 7.14

MS (EI) m/z: 382 (15), 381 (69, M-57, -t-Bu), 339 (20), 310 (19), 309 (100), 253 (14), 249 (17), 212 (13), 211 (70), 199 (34), 197 (11), 183 (14), 181 (26), 175 (10), 149 (9), 135 (14), 121 (9), 105 (26), 91 (20), 77 (25), 55 (28)

HRMS: Calculated for C₂₀H₂₇OSiIH [M+H]⁺: 439.0949, Found: 439.0949

3-(4-Bromophenyl)propan-1-ol, S2⁴



To a solution of 3-(4-bromophenyl)propanoic acid (500 mg, 2.18 mmol, 1 equiv) in THF (21.83 mL) at 0 °C was added dropwise a solution of BH₃•THF (1 M, 4.37 mL, 4.36 mmol, 2 equiv). The reaction mixture was allowed to warm up to rt and was stirred for 2 h before being quenched by a 1:1 solution of Rochelle salts/saturated aqueous solution of NaHCO₃. The aqueous phase was extracted with Et₂O. The combined organic phases were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 7:3 to 5:5) yielded alcohol **S2** (466.7 mg, 2.17 mmol, 99%) as a colourless oil.

Formula: C₉H₁₁BrO

Mass: 215.1 g.mol⁻¹

IR (neat): 3310, 1487, 1452, 1404, 1070, 1040, 1010, 913 cm⁻¹

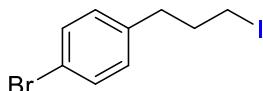
⁴ Pettit, G. R.; Quistorf, P. D.; Fry, J. A.; Herald, D. L.; Hamel, E.; Chapuis, J.-C. *J. Nat. Prod.* **2009**, 72, 876-883.

¹H NMR (400 MHz, CDCl₃) δ 7.40 (brd, *J* = 8.4 Hz, 2H), 7.07 (brd, *J* = 8.3 Hz, 2H), 3.66 (t, *J* = 6.4 Hz, 2H), 2.66 (t, *J* = 7.8 Hz, 2H), 1.90 – 1.81 (m, 2H), 1.49 (m, 1H)

¹³C NMR (100 MHz, CDCl₃) δ 140.8, 131.5 (2C), 130.3 (2C), 119.6, 62.0, 34.1, 31.5

MS (EI) *m/z*: 216 (20, M+1), 214 (20, M⁺), 205 (9), 198 (26), 196 (27), 171 (27), 169 (30), 118 (10), 117 (100), 116 (9), 115 (23), 104 (19), 103 (12), 91 (38), 90 (25), 89 (18), 78 (10), 77 (20), 63 (10), 51 (12), 50 (7)

1-Bromo-4-(3-iodopropyl)benzene, 1.4⁵



Iodine **1.4** was prepared according to Procedure A from 3-(4-bromophenyl)propan-1-ol **S2** (460 mg, 2.14 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 96:4) yielded iodine **1.4** (622.2 mg, 1.92 mmol, 90%) as a colourless oil.

Formula: C₉H₁₀BrI

Mass: 325.0 g.mol⁻¹

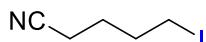
IR (neat): 1487, 1445, 1425, 1403, 1347, 1262, 1211, 1166, 1094, 1072, 1011, 958, 936 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.41 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 3.15 (t, *J* = 6.8 Hz, 2H), 2.69 (t, *J* = 7.3 Hz, 2H), 2.10 (quint_{app}, *J* = 7.1 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 139.4, 131.6 (2C), 130.4 (2C), 120.0, 35.6, 34.6, 6.0

MS (EI) *m/z*: 326 (41, M+1), 325 (4, M⁺), 324 (40), 199 (14), 197 (15), 172 (7), 171 (97), 170 (7), 169 (100), 118 (34), 117 (24), 116 (6), 115 (16), 91 (14), 90 (41), 89 (33), 77 (6), 65 (5), 64 (5), 63 (16), 58 (7), 51 (10)

5-Iodovaleronitrile, 1.5⁶



Iodine **1.5** was prepared from 5-bromovaleronitrile (700 mg, 4.32 mmol, 1 equiv) in refluxing in acetone (8.6 mL) overnight in the presence of NaI (3.2 g, 21.60 mmol, 5 equiv). The reaction mixture was filtered and concentrated under reduced pressure before being dissolved in diethyl ether. The organic phase was washed with H₂O, a saturated aqueous solution of Na₂S₂O₃, H₂O and brine successively, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 7:3) yielded iodine **1.5** (897.2 mg, 4.29 mmol, 99%) as a colourless oil.

Formula: C₅H₈IN

Mass: 209.0 g.mol⁻¹

IR (neat): 2246, 1738, 1456, 1425, 1362, 1329, 1287, 1254, 1213, 1170, 1131, 1075, 1009, 978 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 3.20 (t, *J* = 6.6 Hz, 2H), 2.39 (t, *J* = 7.0 Hz, 2H), 1.97 (quint_{app}, *J* = 7.0 Hz, 2H), 1.79 (quint_{app}, *J* = 7.1 Hz, 2H)

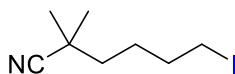
¹³C NMR (100 MHz, CDCl₃) δ 119.2, 31.8, 26.2, 16.3, 4.6

MS (EI) *m/z*: 209 (9, M⁺), 127 (4), 83 (6), 82 (100), 55 (77), 54 (19), 53 (6)

⁵ Thornton, A. R.; Martin, V. I.; Blakey, S. B. *J. Am. Chem. Soc.* **2009**, *131*, 2434-2435.

⁶ Jackman, M. M.; Im, S.; Bohman, S. R.; Lo, C. C. L.; Garrity, A. L.; Castle, S. L. *Chem. Eur. J.* **2018**, *24*, 594-598.

6-Iodo-2,2-dimethylhexanenitrile, 1.6



Iodine **1.6** was prepared from 6-bromo-2,2-dimethylhexanenitrile (1.1 g, 5.12 mmol, 1 equiv) in refluxing acetone (25 mL) overnight in the presence of NaI (3.8 g, 25.60 mmol, 5 equiv). The reaction mixture filtered and concentrated under reduced pressure before being dissolved in diethyl ether. The organic phase was washed with H₂O, a saturated aqueous solution of Na₂S₂O₃, H₂O and brine successively, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 98:2 to 91:9) yielded iodine **1.6** (1.3 g, 5.10 mmol, 100%) as a colourless oil.

Formula: C₈H₁₄NI

Mass: 251.1 g.mol⁻¹

IR (neat): 1471, 1458, 1428, 1391, 1369, 1298, 1270, 1237, 1197, 1180, 997, 971, 945, 887 cm⁻¹

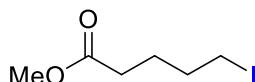
¹H NMR (400 MHz, CDCl₃) δ 3.19 (td, *J* = 6.9, 1.0 Hz, 2H), 1.86 (quint_{app}, *J* = 7.0 Hz, 2H), 1.66 – 1.47 (m, 4H), 1.34 (s, 6H)

¹³C NMR (100 MHz, CDCl₃) δ 124.9, 39.9, 33.2, 32.3, 26.7 (2C), 26.3, 6.0

MS (EI) *m/z*: 251 (1), 155 (3), 125 (7), 124 (74), 98 (3), 97 (45), 96 (2), 83 (3), 82 (13), 81 (3), 79 (3), 70 (2), 69 (24), 68 (8), 67 (3), 57 (3), 56 (8), 55 (100), 54 (6), 53 (7), 52 (2)

HRMS: Calculated for C₈H₁₄NIH [M+H]⁺: 252.0244, Found: 252.0245

Methyl 5-iodovalerate, 1.7



Iodine **1.7** was prepared from methyl-5-bromovalerate (2.0 g, 9.45 mmol, 1 equiv) by refluxing overnight in acetone (25 mL) in the presence of NaI (7.5 g, 49.70 mmol, 5 equiv). The reaction mixture was filtered and concentrated under reduced pressure before being dissolved in diethyl ether. The organic phase was washed with H₂O, a saturated aqueous solution of Na₂S₂O₃, H₂O and brine successively, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 9:1) yielded iodine **1.7** (2.2 g, 8.88 mmol, 89%) as a colourless oil.

Formula: C₆H₁₁O₂I

Mass: 242.1 g.mol⁻¹

IR (neat): 1733, 1435, 1365, 1260, 1196, 1175, 1120, 1022, 994 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 3.66 (s, 3H), 3.17 (t, *J* = 6.8 Hz, 2H), 2.33 (t, *J* = 7.3 Hz, 2H), 1.92 – 1.78 (m, 2H), 1.78 – 1.66 (m, 2H)

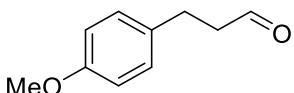
¹³C NMR (100 MHz, CDCl₃) δ 173.6, 51.7, 32.9, 32.8, 25.8, 5.9

MS (EI) *m/z*: 211 (14), 183 (8), 155 (4), 116 (5), 115 (80), 73 (53), 71 (2), 60 (1), 59 (45), 56 (7), 55 (100), 54 (3), 53 (5)

HRMS: Calculated for C₆H₁₁O₂IH [M+H]⁺: 242.9876, Found: 242.9876

Secondary iodide

3-(4-Methoxyphenyl)propanal, S3⁷



To a solution of 3-(4-methoxyphenyl)-1-propanol (2 g, 11.91 mmol, 1 equiv) in CH₂Cl₂ (59.6 mL) was added DAIB (4.70 g, 14.29 mmol, 1.2 equiv) and TEMPO (190 mg, 1.19 mmol, 0.1 equiv). The reaction mixture was stirred at rt for 24 h before being concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 87:13) yielded aldehyde **S3** (1.7 g, 10.37 mmol, 87%) as a colourless oil.

Formula: C₁₀H₁₂O₂

Mass: 164.2 g.mol⁻¹

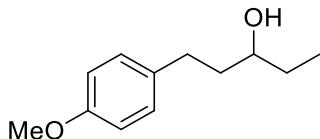
IR (neat): 1720, 1611, 1584, 1512, 1465, 1443, 1300, 1245, 1178, 1111, 1034 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 9.82 (t, J = 1.5 Hz, 1H), 7.12 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H), 2.91 (t, J = 7.5 Hz, 2H), 2.78 – 2.72 (brt_{app}, J = 7.3 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 201.8, 158.0, 132.3, 129.2 (2C), 114.0 (2C), 55.2, 45.5, 27.2

MS (EI) *m/z*: 165 (3, M+1), 164 (30, M⁺), 135 (2), 122 (10), 121 (100), 108 (25), 91 (13), 89 (3), 79 (4), 78 (9), 77 (15), 65 (7), 63 (4), 51 (5)

1-(4-Methoxyphenyl)pentan-3-ol, S4⁸



To a solution of 3-(4-methoxyphenyl)propanal **S3** (1.70 g, 10.34 mmol, 1 equiv) in THF (51.9 mL) at 0 °C was added dropwise a solution of EtMgBr in Et₂O (1.8 M, 8.61 mL, 15.51 mmol, 1.5 equiv). The reaction mixture was allowed to warm to rt and was stirred for 1 h. A saturated aqueous solution of NH₄Cl was added dropwise and the aqueous phase was extracted with Et₂O. The combined organic phases were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 82:18 to 74:26) yielded alcohol **S4** (1.48 g, 7.61 mmol, 74%) as a colourless oil.

Formula: C₁₂H₁₈O₂

Mass: 194.3 g.mol⁻¹

IR (neat): 3359, 1611, 1584, 1559, 1511, 1456, 1420, 1376, 1320, 1299, 1243, 1177, 1117, 1063, 1034, 991, 934 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 3.79 (s, 3H), 3.55 (m, 1H), 2.74 (ddd_{AB}, J = 13.9, 9.5, 6.8 Hz, 1H), 2.62 (ddd_{AB}, J = 13.9, 9.5, 6.8 Hz, 1H), 1.85 – 1.61 (m, 2H), 1.61 – 1.43 (m, 2H), 1.40 (s, 1H), 0.95 (t, J = 7.5 Hz, 3H).

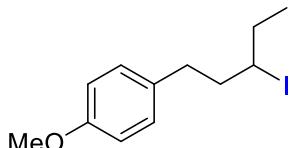
¹³C NMR (100 MHz, CDCl₃) δ 157.8, 134.3, 129.3 (2C), 113.9 (2C), 72.7, 55.3, 38.9, 31.2, 30.4, 9.9

⁷ Schaubach, S.; Gebauer, K.; Ungeheuer, F.; Hoffmeister, L.; Ilg, M. K.; Wirtz, C.; Fürstner, A. *Chem. Eur. J.* **2016**, 22, 8494–8507.

⁸ Alderson, J. M.; Schomaker, J. M. *Chem. Eur. J.* **2017**, 23, 8571–8576.

MS (EI) *m/z*: 195 (4), 194 (28), 176 (11), 148 (9), 147 (85), 134 (6), 122 (19), 121 (100), 119 (4), 108 (9), 107 (3), 105 (4), 91 (18), 79 (4), 78 (10), 77 (13), 65 (5), 59 (4), 57 (5)

1-(3-Iodopentyl)-4-methoxybenzene, 1.8



Iodine **1.8** was prepared according to Procedure **A** from 1-(4-methoxyphenyl)pentan-3-ol **S4** (329 mg, 1.70 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 97:3) yielded iodine **1.8** (357.9 mg, 1.18 mmol, 69%) as a colourless oil.

Formula: C₁₂H₁₇OI

Mass: 304.2 g.mol⁻¹

IR (neat): 1611, 1583, 1510, 1455, 1441, 1300, 1244, 1196, 1176, 1136, 1107, 1083 cm⁻¹

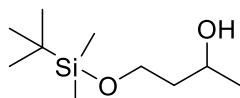
¹H NMR (400 MHz, CDCl₃) δ 7.16 – 7.10 (m, 2H), 6.87 – 6.81 (m, 2H), 4.01 (dtd, *J* = 13.9, 9.1, 4.7 Hz, 1H), 3.79 (s, 3H), 2.83 (ddd_{AB}, *J* = 13.9, 9.0, 5.0 Hz, 1H), 2.66 (ddd_{AB}, *J* = 13.9, 8.9, 7.1 Hz, 1H), 2.16 (m, 1H), 1.97 – 1.71 (m, 3H), 1.02 (t, *J* = 7.2 Hz, 3H)

¹³C NMR (100 MHz, CDCl₃) δ 158.0, 133.0, 129.5 (2C), 114.0 (2C), 55.3, 42.1, 41.6, 34.8, 33.9, 14.1

MS (EI) *m/z*: 305 (2), 304 (12), 177 (7), 176 (1), 147 (2), 122 (10), 121 (100), 115 (1), 106 (1), 105 (1), 91 (7), 90 (2), 89 (2), 79 (1), 78 (7), 77 (7), 65 (3), 63 (1), 55 (1), 52 (2), 51 (2)

HRMS: unstable compound

4-((tert-Butyldimethylsilyl)oxy)butan-2-ol, S5⁹



To a solution of 1,3-butanediol (1.5 mL, 16.48 mmol, 1 equiv) and imidazole (2.72 g, 39.57 mmol, 2.4 equiv) in CH₂Cl₂ (40 mL) at 0 °C was cannulated a solution of TBSCl (3.53 mL, 19.78 mmol, 1.2 equiv) in CH₂Cl₂ (15 mL). The reaction mixture was allowed to warm up to rt and stirred overnight. Brine was added, and the aqueous phase was extracted with Et₂O. The combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 8:2 to 7:3) yielded alcohol **S5** (2.90 g, 14.17 mmol, 86%) as a colourless liquid.

Formula: C₁₀H₂₄O₂Si

Mass: 204.4 g.mol⁻¹

IR (neat): 3355, 1472, 1463, 1410, 1388, 1362, 1254, 1085, 997, 938, 910 cm⁻¹

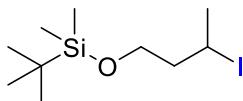
¹H NMR (400 MHz, CDCl₃) δ 4.01 (m, 1H), 3.88 (m, 1H), 3.80 (m, 1H), 3.40 (bs, 1H), 1.74 – 1.56 (m, 2H), 1.22 – 1.14 (m, 3H), 0.89 (brs, 9H), 0.07 (s, 3H), 0.06 (s, 3H)

¹³C NMR (100 MHz, CDCl₃) δ 68.3, 62.8, 40.0, 25.9 (3C), 23.4, 18.2, -5.47, -5.52

MS (EI) *m/z*: 147 (7, M-57, -t-Bu), 129 (4), 106 (7), 105 (83), 101 (5), 91 (5), 89 (6), 77 (6), 76 (7), 75 (100), 73 (12), 59 (6), 57 (4), 55 (13)

⁹ Dupuy, S.; Zhang, K.-F.; Goutierre, A.-S.; Daudoin, O. *Angew. Chem.* **2016**, 47, 15013-15017.

tert-Butyl(3-iodobutoxy)dimethylsilane, 1.10¹⁰



Iodine **1.10** was prepared according to Procedure A from 4-((*tert*-butyldimethylsilyl)oxy)butan-2-ol **S5** (2.5 g, 12.47 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 95:5) yielded iodine **1.10** (3.1 g, 9.70 mmol, 78%) as a pale yellow liquid.

Formula: C₁₀H₂₃OSi

Mass: 314.3 g.mol⁻¹

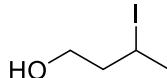
IR (neat): 1724, 1591, 1501, 1470, 1446, 1398, 1361, 1266, 1174, 1113, 1099, 1071, 1034, 1012, 987, 968, 948, 898 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.35 (m, 1H), 3.76 (ddd_{AB}, J = 10.3, 8.1, 4.8 Hz, 1H), 3.65 (ddd_{AB}, J = 10.3, 8.1, 4.8 Hz, 1H), 2.01 (m, 1H), 1.96 (d, J = 6.9 Hz, 3H), 1.79 (m, 1H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H)

¹³C NMR (100 MHz, CDCl₃) δ 62.8, 45.5, 29.2, 26.2, 26.0 (3C), 18.4, -5.19, -5.21

MS (EI) *m/z*: 258 (10, (M+1)-57, -*t*-Bu), 257 (89, (M-57, -*t*-Bu), 216 (8), 215 (100), 201 (6), 185 (60), 145 (4), 131 (5), 129 (30), 115 (9), 101 (14), 99 (6), 89 (18), 88 (4), 75 (50), 73 (41), 61 (6), 59 (19), 58 (11), 57 (12), 55 (47)

3-Iodobutan-1-ol, S6



To a solution of *tert*-butyl(3-iodobutoxy)dimethylsilane **1.10** (1.5 g, 4.77 mmol, 1 equiv) in MeOH (47.7 mL) was added *p*TsOH.H₂O (181.6 mg, 0.95 mmol, 0.2 equiv). The reaction mixture was stirred at rt overnight. A saturated aqueous solution of NaHCO₃ was added and the aqueous phase was extracted with Et₂O. The combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 8:2) yielded iodo-alcohol **S6** (736.8 mg, 3.68 mmol, 77%) as a colourless liquid.

Formula: C₄H₉IO

Mass: 200.0 g.mol⁻¹

IR (neat): 3305, 1463, 1444, 1416, 1378, 1253, 1219, 1151, 1123, 1091, 1050, 1024 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.42 – 4.28 (m, 1H), 3.83 (ddd_{AB}, J = 10.7, 5.8, 4.8 Hz, 1H), 3.74 (ddd_{AB}, J = 10.8, 8.1, 5.1 Hz, 1H), 2.04 (ddd, J = 19.7, 9.8, 5.0 Hz, 1H), 1.98 (d, J = 6.9 Hz, 3H), 1.85 (m, 1H), 1.60 (brs, 1H)

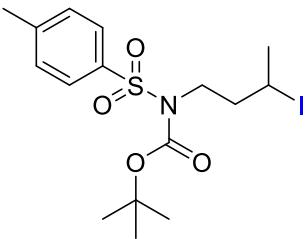
¹³C NMR (100 MHz, CDCl₃) δ 62.7, 44.9, 29.2, 26.1

MS (EI) *m/z*: 200 (4), 128 (1), 127 (2), 74 (3), 73 (52), 71 (1), 57 (3), 56 (5), 55 (100), 54 (1), 53 (2)

HRMS: calculated for C₄H₉IOH [M+H]⁺: 200.9771, Found: 200.9770

tert-Butyl (3-iodobutyl)(tosyl)carbamate, 1.9

¹⁰ Hofmayer, M. S.; Hammann, J. M.; Cahiez, G.; Knochel, P. *Synlett*, **2018**, 29, 65-70.



3-Iodobutan-1-ol (730.0 mg, 3.65 mmol, 1 equiv), PPh₃ (957.3 mg, 3.65 mmol, 1 equiv) and NH(Boc)Ts (990.3 mg, 3.65 mmol, 1 equiv) were dissolved in THF (22 mL). DIAD was added by syringe pump over 10 min (4.32 mL/h, 0.72 mL, 3.65 mmol, 1 equiv) at 0 °C. The reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was concentrated under reduced pressure and purification by flash chromatography on silica gel (PE/Et₂O 9:1) yielded iodine **1.9** (1.3 g, 2.89 mmol, 79%) as a colourless oil.

Formula: C₁₆H₂₄INO₄S

Mass: 453.3 g.mol⁻¹

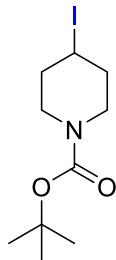
IR (neat): 1725, 1597, 1495, 1475, 1445, 1394, 1352, 1288, 1257, 1234, 1186, 1154, 1140, 1088, 1050, 1020, 991, 947, 909 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.15 (dqd, J = 8.8, 6.8, 4.8 Hz, 1H), 3.99 (ddd_{AB}, J = 14.3, 10.0, 1.3 Hz, 1H), 3.83 (ddd_{AB}, J = 14.3, 10.0, 1.3 Hz, 1H), 2.44 (s, 3H), 2.27 (m, 1H), 2.10 (m, 1H), 1.98 (d, J = 6.9 Hz, 3H), 1.35 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 150.9, 144.3, 137.2, 129.4 (2C), 127.9 (2C), 84.6, 47.7, 42.5, 29.0, 28.0 (3C), 24.3, 21.68

HRMS: Calculated for C₁₆H₂₄INO₄SH [M+H]⁺: 454.0543, Found: 454.0543

tert-Butyl-4-iodopiperidine-1-carboxylate, **1.11**¹¹



Iodine **1.11** was prepared according to Procedure A from *tert*-butyl-4-hydroxypiperidine-1-carboxylate (682.5 mg). Purification by flash chromatography on silica gel (PE/Et₂O 95:5 to 9:1) yielded iodine **1.11** (217.8 mg, 0.70 mmol, 21%) as an off-white solid.

Formula: C₁₀H₁₈NO₂I

Mass: 311.2 g.mol⁻¹

mp: 46-49 °C

IR (neat): 1687, 1476, 1464, 1446, 1415, 1365, 1331, 1274, 1233, 1153, 1100, 1008, 994, 932 cm⁻¹

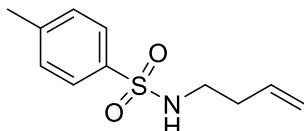
¹H NMR (400 MHz, CDCl₃) δ 4.44 (quint_{app}, J = 6.0 Hz, 1H), 3.58 (brdt, J = 13.3, 5.0 Hz, 2H), 3.27 (dt, J = 13.7, 5.9 Hz, 2H), 2.02 (brq_{app}, J = 5.8 Hz, 4H), 1.45 (s, 9H)

¹¹ Kulbitski, K.; Nisnevich, G.; Gandelman, M. *Adv. Synth. Catal.* **2011**, 353, 1438-1442.

¹³C NMR (100 MHz, CDCl₃) δ 154.8, 79.9, 44.0 (2C), 37.4 (2C), 28.5 (3C), 27.8

MS (EI) *m/z*: 311 (1, M⁺), 256 (4), 255 (2), 238 (8), 184 (21), 128 (33), 84 (29), 83 (2), 82 (3), 68 (3), 67 (4), 58 (4), 57 (100), 56 (11), 55 (10)

N-(But-3-en-1-yl)-4-methylbenzenesulfonamide, S7¹²



To a solution of TsNH₂ (455.1 mg, 2.61 mmol, 1 equiv) in acetone was added K₂CO₃ (720 mg, 5.21 mmol, 2 equiv) and 4-bromo-1-butene (0.3 mL, 2.87 mmol, 1.1 equiv). The reaction mixture was refluxed overnight. A saturated aqueous solution of NH₄Cl was added and the aqueous phase was extracted with Et₂O. The combined organic phases were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/EA 9:1 to 8:2) yielded homoallylamine S7 (279.5 mg, 1.24 mmol, 48%) as a colourless oil.

Formula: C₁₁H₁₅NO₂S

Mass: 225.3 g.mol⁻¹

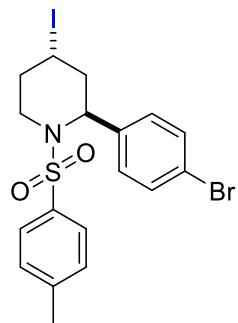
IR (neat): 3280, 1641, 1598, 1495, 1425, 1321, 1305, 1290, 1155, 1093, 1074, 1019, 990, 916 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 5.62 (m, 1H), 5.03 (m, 2H), 4.63 (brs, 1H), 3.00 (*q*_{app}, *J* = 6.5 Hz, 2H), 2.42 (s, 3H), 2.19 (*q*_{app}, *J* = 6.7 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 143.5, 137.0, 134.2, 129.8 (2C), 127.2 (2C), 118.2, 42.1, 33.7, 21.6

MS (EI) *m/z*: 225 (1, M⁺), 185 (5), 184 (57), 157 (4), 156 (7), 155 (75), 92 (9), 91 (100), 89 (5), 66 (1), 65 (23), 63 (4)

trans-2-(4-Bromophenyl)-4-iodo-1-tosylpiperidine, 1.12¹³



Hexamethyldisilane (1.3 mL, 6.15 mmol, 4.1 equiv) and I₂ (777.0 mg, 3.00 mmol, 2 equiv) were heated in a sealed vial at 120 °C for 25 min until the violet colour almost disappeared (can be quite virulent, so extra care is necessary). The mixture was then cooled to rt before adding a solution of *N*-(but-3-en-1-yl)-4-methylbenzenesulfonamide S7 (338.0 mg, 1.50 mmol, 1 equiv) and 4-bromobenzaldehyde (280.3 mg, 1.50 mmol, 1 equiv) in CH₂Cl₂ (3 mL). AlCl₃ (2 mg, 0.01 mmol, 7 mol %) was then added to the reaction mixture and the vial was sealed and the reaction mixture was stirred at rt for 23 h. H₂O was added to the mixture and the aqueous phase was extracted with Et₂O. The combined organic phases were washed

¹² Teichert, J. F.; Zhang, S.; van Zijl, A. W.; Slaa, J. W.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2010**, 12 4658-4660.

¹³ Liu, G.-Q.; Cui, B.; Xu, R.; Li, Y.-M. *J. Org. Chem.* **2016**, 12, 5144-5161.

with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$, dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 95:5 to 8:2) yielded iodine **1.12** (297.4 mg, 0.57 mmol, 38%) as a white solid (dr > 95:5).

Formula: $\text{C}_{18}\text{H}_{19}\text{BrINO}_2\text{S}$

Mass: 520.2 g.mol⁻¹

mp: 125–127 °C

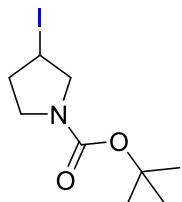
IR (neat): 1597, 1489, 1450, 1397, 1370, 1334, 1303, 1284, 1261, 1246, 1210, 1174, 1154, 1118, 1091, 1076, 1061, 998, 950, 928, 906 cm⁻¹

¹H NMR (400 MHz, CDCl_3) δ 7.74 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.3 Hz, 2H), 5.12 (brd, J = 4.3 Hz, 1H), 4.06 (tt_{app}, J = 12.4, 3.7 Hz, 1H), 3.73 (brd_{app}, J = 14.4 Hz, 1H), 2.99 (td, J = 12.4, 2.9 Hz, 1H), 2.86 (brd, J = 13.8 Hz, 1H), 2.46 (s, 3H), 2.24 (td, J = 13.4, 5.3 Hz, 1H), 2.09 (brd_{app}, J = 11.9 Hz, 1H), 1.90 (qd_{app}, J = 12.7, 4.6 Hz, 1H)

¹³C NMR (100 MHz, CDCl_3) δ 143.8, 137.8, 136.4, 132.1 (2C), 130.1 (2C), 128.5 (2C), 127.0 (2C), 121.5, 57.3, 43.5, 40.5, 37.9, 21.7, 18.4

HRMS : Unstable compound

tert-Butyl-3-iodopyrrolidine-1-carboxylate, **1.13**¹⁴



Iodine **1.13** was prepared according to Procedure **B** from *tert*-butyl 3-hydroxypyrrolidine-1-carboxylate (600 mg). Purification by flash chromatography on silica gel (PE/Et₂O 95:5 to 8:2) yielded iodine **1.13** as a mixture of rotamers in a ratio a/b = 73:27 (706 mg, 2.37 mmol, 74%) as a colourless oil.

Formula: $\text{C}_9\text{H}_{16}\text{O}_2\text{I}$

Mass: 297.1 g.mol⁻¹

IR (neat): 1689, 1477, 1454, 1394, 1365, 1346, 1295, 1257, 1222, 1156, 1108, 977, 929, 916 cm⁻¹

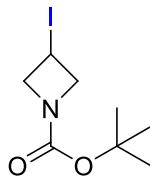
¹H NMR (400 MHz, CDCl_3) δ 4.35 (m, 1H), 3.89 – 3.72 (m, 1.46H), 3.67 (m, 0.54H), 3.57 (m, 1H), 3.42 (m, 1H), 2.32 – 2.15 (m, 2H), 1.45 (s, 9H)

¹³C NMR (100 MHz, CDCl_3) δ [154.3, 154.2], [79.82, 79.76], [57.4, 57.1], [45.1, 44.8], [38.4, 37.7], 28.5 (3C), 20.0

MS (EI) *m/z*: 297 (2), 242 (23), 240 (4), 224 (8), 197 (7), 114 (4), 70 (17), 69 (4), 68 (6), 58 (5), 57 (100), 56 (10)

tert-Butyl-3-iodoazetidine-1-carboxylate, **1.14**¹¹

¹⁴ Barré, B.; Gonnard, L.; Campagne, R. ; Reymond, S. ; Marin, J. ; Ciapetti, Brellier, Guérinot, A.; Cossy, J. *Org. Lett.* **2014**, *16*, 6160-6163.



Iodine **S20** was prepared according to Procedure **B** from *tert*-butyl 3-iodo-azetidine-1-carboxylate (1.0 g). Purification by flash chromatography on silica gel (PE/Et₂O 8:2) yielded iodine **S20** (1.6 g, 5.60 mmol, 100%) as a colourless oil.

Formula: C₈H₁₄NO₂I

Mass: 283.1 g.mol⁻¹

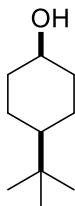
IR (neat): 1696, 1536, 1477, 1456, 1381, 1365, 1302, 1254, 1201, 1145, 1140, 1032, 969, 886 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.73 – 4.52 (m, 2H), 4.45 (m, 1H), 4.34 – 4.17 (m, 2H), 1.42 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 155.6, 80.2, 61.6 (2C), 28.4 (3C), 2.7

MS (EI) *m/z*: 283 (1), 228 (6), 183 (7), 156 (5), 82 (10), 58 (4), 57 (100), 56 (24), 55 (4), 54 (4)

cis-4-(*tert*-Butyl)cyclohexan-1-ol, **S8**¹⁶



cis/trans > 95:5

To a solution of 4-*tert*-butylcyclohexanone (600 mg, 3.89 mmol, 1 equiv) in THF (19 mL) at 0 °C was added a solution of L-selectride (1 M in THF, 4.28 mL, 4.28 mmol, 1.1 equiv). The reaction mixture was stirred at 0 °C for 30 min and then warmed to rt and stirred for another 2 h. H₂O and HCl (1 M in H₂O) were added to the reaction mixture and the aqueous phase was extracted with CH₂Cl₂. The combined organic phases were washed with a saturated aqueous solution of NaHCO₃, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 9:1 to 85:15) yielded alcohol **S8** (505.3 mg, 3.23 mmol, 83%) as a white solid as a single diastereomer (*cis/trans* > 95:5).

Formula: C₁₀H₂₀O

Mass: 156.3 g.mol⁻¹

mp: 78 °C

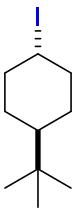
IR (neat): 3313, 3241, 1474, 1431, 1391, 1363, 1338, 1312, 1273, 1237, 1182, 1146, 1114, 1029, 1007, 958, 929, 917, 904 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.03 (m, 1H), 1.93 – 1.77 (m, 2H), 1.59 – 1.41 (m, 4H), 1.41 – 1.21 (m, 2H), 1.01 (m, 1H), 0.86 (s, 9H) -OH not visible

¹³C NMR (100 MHz, CDCl₃) δ 66.0, 48.1, 33.5 (2C), 32.6, 27.6 (3C), 21.0 (2C)

MS (EI) *m/z*: 156 (1, M⁺), 123 (11), 101 (6), 99 (24), 98 (6), 83 (28), 82 (38), 81 (38), 80 (31), 79 (8), 69 (6), 67 (47), 58 (5), 57 (100), 56 (35), 55 (20), 54 (11), 53 (5)

trans-1-(*tert*-Butyl)-4-iodocyclohexane, **1.15a**¹⁵



trans/cis = 91:9

Iodine **1.15a** was prepared according to Procedure **B** from *cis*-4-(*tert*-butyl)cyclohexan-1-ol **S8** (497.7 mg). Purification by flash chromatography on silica gel (PE 100%) yielded iodine XX as a mixture of diastereomers (*trans/cis* = 91:1) (231 mg, 0.87 mmol, 27%) as a colourless oil contaminated by 4-*tert*-butylcyclohex-1-ene (76.3 mg, 0.55 mmol, 17%). The mixture was dissolved in THF/H₂O = 1:5 and cooled to 0 °C before adding NMO (80.0 mg, 0.66 mmol, 1.2 equiv) followed by OsO₄ (0.35 mL, 0.03 mmol, 5 mol %, 0.08 M in *tert*-butanol). The reaction mixture was stirred at rt overnight concealed by aluminum foil before adding an aqueous solution of Na₂S₂O₃ and stirred again for 1 h. The mixture was extracted with Et₂O. Purification by flash chromatography on silica gel (PE 100%) yielded iodine **1.15a** as a mixture of diastereomers (*trans/cis* = 91:1) (219.4 mg, 0.82 mmol, 95%). Only the *trans* diastereomer is described below.

Formula: C₁₀H₁₉I

Mass: 266.2 g·mol⁻¹

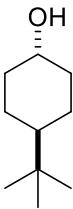
IR (neat): 1478, 1448, 1393, 1365, 1338, 1310, 1265, 1228, 1196, 1187, 1147, 1079, 1036, 1014, 995, 931 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.09 (tt, J = 12.3, 4.1 Hz, 1H), 2.53 – 2.39 (m, 2H), 2.03 – 1.86 (m, 2H), 1.71 – 1.60 (m, 2H), 1.15 – 1.02 (m, 3H), 0.82 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 46.8, 41.2 (2C), 32.7, 31.0, 30.4 (2C), 27.5 (3C)

MS (EI) m/z: 266 (1), 139 (27), 123 (6), 97 (6), 83 (47), 81 (14), 79 (4), 71 (5), 69 (19), 67 (10), 58 (5), 57 (100), 55 (24)

trans-4-(*tert*-Butyl)cyclohexan-1-ol, **S9**¹⁶



trans/cis = 92:8

To a solution of LiAlH₄ (393.7 mg, 10.37 mmol, 4 equiv) in Et₂O (6 mL) was added a solution of 4-*tert*-butylcyclohexanone (400 mg, 2.60 mmol, 1 equiv) in Et₂O (7 mL). The reaction mixture was stirred for 10 min at rt and poured into ice water. Et₂O and HCl (1 M in H₂O) were added in order to have a clear solution. The aqueous phase was extracted with Et₂O. The combined organic phases were washed with a

¹⁵ Seel, S.; Dagousset, G.; Thaler, T.; Frischmuth, A. *Chem. Eur. J.* **2013**, *19*, 4614-4622.

¹⁶ Hofmayer, M. S.; Hammann, J. M. Cahiez, G.; Knochel, P. *Synlett*, **2018**, *29*, 65-70.

saturated aqueous solution of NaHCO₃, dried over MgSO₄, filtered and concentrated under reduced pressure. The alcohol **S9** (399.9 mg, 2.56 mmol, 99%) was obtained as a white solid as a mixture of diastereomers *trans/cis* = 92:2. Only the *trans*-diastereomer is described below.

Formula: C₁₀H₂₀O

Mass: 156.3 g.mol⁻¹

mp: 79 °C

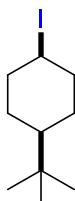
IR (neat): 3252, 1448, 1392, 1364, 1337, 1290, 1263, 1240, 1225, 1186, 1133, 1065, 1037, 1009, 981, 961, 901 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 3.51 (tt, *J* = 10.9, 4.4 Hz, 1H), 2.07 – 1.94 (m, 2H), 1.82 – 1.71 (m, 2H), 1.29 – 1.13 (m, 2H), 1.10 – 0.91 (m, 3H), 0.84 (s, 9H) -OH not visible

¹³C NMR (100 MHz, CDCl₃) δ 71.3, 47.3, 36.2 (2C), 32.4, 27.7 (3C), 25.7 (2C)

MS (EI) *m/z*: 156 (1, M⁺), 138 (9), 123 (15), 110 (4), 99 (13), 95 (8), 83 (21), 82 (23), 81 (45), 80 (15), 79 (6), 69 (6), 67 (31), 58 (5), 57 (100), 56 (39), 55 (18), 54 (7), 53 (4)

cis-1-(*tert*-Butyl)-4-iodocyclohexane, **1.15b**¹⁵



cis/trans = 87:13

Iodine **1.15b** was prepared according to Procedure B from *trans*-4-(*tert*-butyl)cyclohexan-1-ol **S9** (379.9 mg). Purification by flash chromatography on silica gel (PE 100%) yielded iodine XX as a mixture of diastereomers (*cis/trans* = 87:13) (408.8 mg, 1.54 mmol, 63%) as a colourless oil contaminated by 4-*tert*-butylcyclohex-1-ene (76.3 mg, 0.55 mmol, 17%). The mixture was dissolved in THF/H₂O = 1:5 and cooled to 0 °C before adding NMO (80.0 mg, 0.66 mmol, 1.2 equiv) followed by OsO₄ (94 µL, 0.05 mmol, 0.7 mol %, 0.08 M in *tert*-butanol). The reaction mixture was stirred at rt overnight concealed by aluminum foil before adding an aqueous solution of Na₂S₂O₃ and stirred again for 1 h. The mixture was extracted with Et₂O. Purification by flash chromatography on silica gel (PE 100%) yielded iodine **1.15b** as a mixture of diastereomers (*cis/trans* = 87:13) (367.5 mg, 1.38 mmol, 92%). Only the *cis* diastereomer is described below.

Formula: C₁₀H₁₉I

Mass: 266.2 g.mol⁻¹

mp: ~33 °C

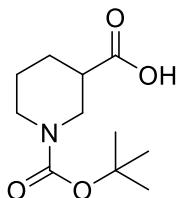
IR (neat): 1478, 1469, 1438, 1426, 1393, 1365, 1351, 1338, 1310, 1244, 1235, 1186, 1147, 1079, 1065, 1038, 1015, 996, 930, 919, 902 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.88 (brs, 1H), 2.17 – 2.04 (m, 2H), 1.69 – 1.42 (m, 6H), 1.06 (m, 1H), 0.89 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 47.9, 38.0, 36.9 (2C), 32.7, 27.5 (3C), 23.4 (2C)

MS (EI) *m/z*: 266 (1, M⁺), 139 (25), 123 (6), 97 (6), 83 (42), 81 (14), 79 (4), 71 (4), 69 (15), 67 (10), 58 (5), 57 (100), 55 (19)

1-(tert-Butoxycarbonyl)piperidine-3-carboxylic acid, S10¹⁷



To a solution of nipecotic acid (1.5 g, 11.38 mmol, 1 equiv) in MeOH (44 mL) at 0°C, were added Et₃N (1.92 mL, 13.66 mmol, 1.2 equiv) and Boc₂O (3.48 mL, 15.93 mmol, 1.4 equiv). The reaction mixture was allowed to warm up to rt and stirred overnight. A mixture of CH₂Cl₂/H₂O = 5:1 (60 mL) was added followed by HCl (1 N) to get pH = 3. The aqueous phase was extracted with CH₂Cl₂. The combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (CH₂Cl₂/MeOH 95:5 to 85:15) yielded acid **S10** (2.54 g, 11.08 mmol, 97%) as a white solid.

Formula: C₁₁H₁₉NO₄

Mass: 229.3 g.mol⁻¹

IR (neat): 1732, 1693, 1655, 1477, 1426, 1394, 1364, 1291, 1269, 1241, 1169, 1149, 1004, 935 cm⁻¹

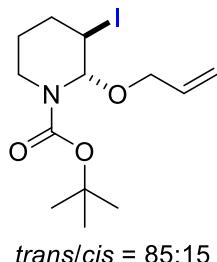
¹H NMR (400 MHz, CDCl₃) δ 9.90 (brs, 1H), 4.08 (brs, 1H), 3.87 (brd, J = 13.3 Hz, 1H), 3.04 (brs, 1H), 2.84 (brt_{app}, J = 11.0 Hz, 1H), 2.47 (m, 1H), 2.06 (brdd_{app}, J = 12.8, 3.8 Hz, 1H), 1.79 – 1.55 (m, 2H), 1.52 – 1.40 (m, 1H), 1.44 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 179.1, 154.8, 80.0, 45.6, 43.7, 41.2, 28.5 (3C), 27.2, 24.2

MS (EI) m/z: 229 (1), 174 (4), 156 (12), 129 (4), 128 (14), 100 (4), 84 (15), 58 (5), 57 (100), 56 (38), 55 (8)

mp: 158–160 °C

tert-Butyl-trans-2-(allyloxy)-3-iodopiperidine-1-carboxylate, 1.16



trans/cis = 85:15

To a solution of *N*-tert-butoxycarbonyl-piperidine-3-carboxylic acid (**S10**) (1.5 g, 6.41 mmol, 1 equiv) in CH₂Cl₂ (88 mL) were added PhI(OAc)₂ (4.2 g, 12.82 mmol, 2 equiv) and I₂ (1.4 g, 5.45 mmol, 0.85 equiv). The reaction mixture was stirred at rt for 2 h, then quenched with 2-propen-1-ol (4.4 mL, 64.12 mmol, 10 equiv). The reaction mixture was stirred at rt for another 2 h before being quenched by the addition of a saturated solution of Na₂S₂O₃ and the aqueous phase was extracted with CH₂Cl₂. The combined organic phases were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (PE/Et₂O 99:1 to 98:2) afforded the title

¹⁷ Catalano, A.; Carocci, A.; Corbo, F.; Franchini, C.; Muraglia, M.; Scilimati, A.; De Bellis, M.; De Luca, A.; Camerino, D. C.; Sinicropi, M. S.; Tortorella, V. *Eur. J. Med. Chem.* **2008**, 43, 2535–2540.

compound **1.16** (581 mg, 1.58 mmol, 25%) as a yellow oil as a mixture of diastereomers (*trans/cis* = 85:15) as a mixture of rotamers (a/b = 70:30). Only the *trans*-diastereomer is described below.

Formula: C₁₃H₂₂NO₃I

Mass: 367.2 g.mol⁻¹

IR (neat): 1698, 1475, 1455, 1410, 1391, 1379, 1365, 1348, 1303, 1281, 1255, 1239, 1200, 1172, 1146, 1108, 1093, 1043, 988, 965, 926 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 5.87 (m, 1H), 5.66 (s, 0.3H), 5.52 (s, 0.7H), 5.26 (brdd, *J* = 17.2, 1.5 Hz, 1H), 5.18 (brd, *J* = 10.3 Hz, 1H), 4.47 (brs_{app}, 1H), 4.06 – 3.80 (m, 3H), 3.10 – 2.81 (m, 1H), 2.21 – 2.07 (m, 1H), 1.95 (qt_{app}, *J* = 13.2, 4.4 Hz, 1H), 1.85 (brd_{app}, *J* = 14.6 Hz, 1H), 1.49– 1.47 (m, 1H), 1.48 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 134.1, 117.3, 84.4, 80.6, 68.0, 37.4, 30.7, 28.4 (3C), 28.3, 21.1 – CO not visible

MS (EI) *m/z*: 310 (4), 254 (41), 226 (3), 210 (9), 184 (12), 181 (4), 140 (14), 128 (5), 127 (19), 126 (14), 98 (8), 84 (5), 83 (19), 82 (11), 70 (5), 68 (5), 58 (9), 57 (100), 56 (7), 55 (13), 54 (4)

HRMS: Calculated for C₁₃H₂₂NO₃INa [M+Na]⁺: 390.0537, Found: 390.0538

2-2 GRIGNARD REAGENT SYNTHESIS

- Cyclopropylmagnesium bromide

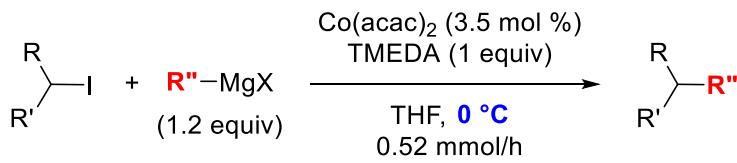
Mg turnings (1.46 g, 60.00 mmol, 2 equiv) were covered by freshly distilled MeTHF¹⁸ (3 mL) and a crystal of I₂ was added. The reaction mixture was warmed at 40 °C and a few drops of a cyclopropylbromide (2.4 mL, 30.00 mmol, 1 equiv in 17 mL MeTHF) were added without any stirring to start the reaction. When the I₂ colour disappeared, a cyclopropylbromide solution (2.4 mL, 30.00 mmol, 1 equiv in 17 mL MeTHF) was added dropwise over 10 min with stirring. The reaction mixture was stirred at reflux for 1.5. The Grignard reagent formed was titrated and measured to be 0.48 M.

- Cyclobutylmagnesium bromide

Mg turnings (371 mg, 15.25 mmol, 1.5 equiv) were covered by freshly distilled MeTHF¹⁸ (2 mL) and a crystal of I₂ was added. The reaction mixture was warmed by a H₂O bath (40 °C) and a few drops of a cyclobutylbromide solution in THF (2.4 mL, 30 mmol, 1 equiv in 8 mL MeTHF) were added without any stirring to start the reaction. When the I₂ colour disappeared, a cyclobutylbromide solution in MeTHF (1.0 mL, 10.17 mmol, 1 equiv in 8 mL MeTHF) was added dropwise over 10 min with stirring. The reaction mixture was stirred at reflux for 1.5 h. The Grignard reagent formed was titrated and measured to be 0.38 M.

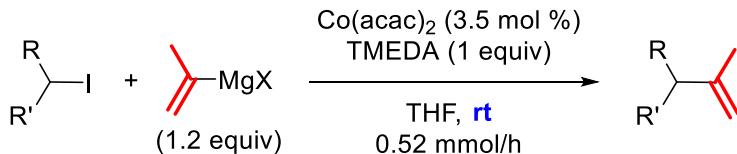
¹⁸ Distilled over Na and benzophenone.

3 CROSS-COUPLEINGS



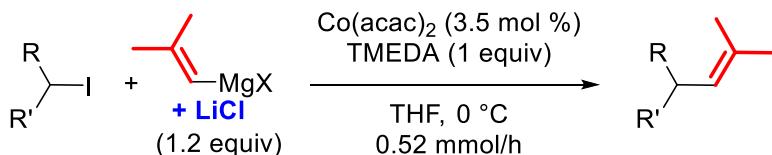
Procedure C:

To iodide (0.2173 mmol, 1 equiv) was added a solution of Co(acac)₂ (2.016 mg, 3.5 mol %) in THF (0.15 mL), followed by TMEDA (0.2173 mmol, 32.8 μL, 1 equiv) and THF (0.15 mL). The reaction mixture was cooled to 0 °C with an ice bath and stirred while the Grignard reagent (1.2 equiv) was added slowly via syringe pump (0.52 mmol/h) over 30 min. After addition of the Grignard reagent, the reaction mixture was stirred for another 30 min at 0 °C. The reaction was quenched with an aqueous saturated solution of NH₄Cl and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel afforded the desired coupling product.



Procedure D:

To iodide (0.2173 mmol, 1 equiv) was added a solution of Co(acac)₂ (2.016 mg, 3.5 mol %) in THF (0.15 mL), followed by TMEDA (0.2173 mmol, 32.8 μL, 1 equiv) and THF (0.15 mL). The Grignard reagent (1.2 equiv) was added slowly via syringe pump (0.52mmol/h) over 30 min at rt. After addition of the Grignard reagent, the reaction mixture was stirred for another 30 min at 0 °C. The reaction was quenched with an aqueous saturated solution of NH₄Cl and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel afforded the desired coupling product.



Procedure E:

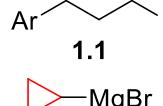
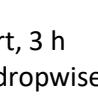
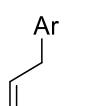
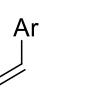
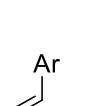
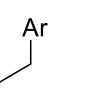
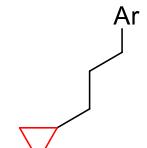
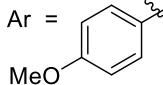
To iodide (0.2173 mmol, 1 equiv) was added a solution of Co(acac)₂ (2.016 mg, 3.5 mol %) in THF (0.15 mL), followed by TMEDA (0.2173 mmol, 32.8 μL, 1 equiv) and THF (0.15 mL). The reaction mixture was cooled to 0 °C in an ice bath and stirred while the Grignard reagent (1.2 equiv), premixed with LiCl (1.2 equiv), is added slowly by syringe pump (0.52 mmol/h) over 30 min. After addition of the Grignard reagent, the reaction mixture was stirred for another 30 min at 0 °C. The reaction was quenched with an aqueous saturated solution of NH₄Cl and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel afforded the desired coupling product

3-1 CROSS-COUPLING WITH CYCLOPROPYLMAGNESIUM BROMIDE

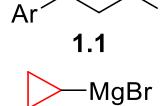
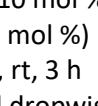
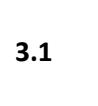
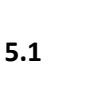
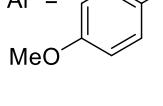
Optimization

Homo = homocoupling product of the respective iodide. Black = ratios. Blue & brackets = isolated yields.

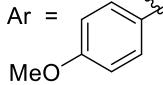
Without catalyst

	THF, rt, 3 h manual dropwise						Homo	
		13	1	0	0	13	0	0

Ligand screening

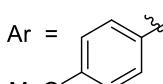
	CoCl ₂ (10 mol %) L (20 mol %) THF, rt, 3 h manual dropwise						Homo		
		TMEDA	0	0	1 (17)	0	0.5 (3)	0	3.3 (56)
		TMCD	0	0	1 (28)	0	0.5 (11)	0	1.5 (42)
		TMPDA	t	0.3	1	0	0.6	0	0.5
		Bipy	0.1	1	0.6	0	0.8	0	0.6
		IMes	2.6	1	0.1	0	0.7	0	0.6
		PPh ₃	0.2 (2)	0.1 (2)	1 (20)	0.3 (4)	0.5 (6)	0	1.1 (28)
		O=PPh ₃	0	1	0.5	T	1.2	0	0.5
		Dppe	0.6	0.1	1	0.2	0.7	0	0
		Dppp	T	0.2	1	0.3	1.5	0	0
		Dppbz	0.3	1	1.3	0.3	6.2	0	0
		Xantphos	t	t	1	0.3	2.7	0	1

Iron vs Cobalt

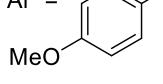
Ar 1.1 Δ-MgBr	Catalytic system							Homo	2.1
		1.1	3.1	4.1E	4.1Z	5.1			
Ar = 	THF, rt, 3 h manual dropwise	1.1	3.1	4.1E	4.1Z	5.1	0	1.7 (32)	
	FeCl ₃ (10 mol %) TMEDA (20 mol %)	0	1 (19)	0.1 (2)	0	0.8 (15)			
	(FeCl ₃) ₂ (TMEDA) ₃ (10 mol %)	1.1	1 (11)	0	0	0.7 (8)			
Ar = 	CoCl ₂ (10 mol %) TMEDA (20 mol %)	0	0	1 (17)	0	0.5 (3)	0	3.3 (56)	

Temperature

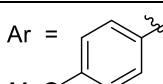
Manual dropwise

Ar 1.1 Δ-MgBr	CoCl ₂ (10 mol %) TMEDA (20 mol %) THF, T, 3 h manual dropwise							Homo	2.1
		1.1	3.1	4.1E	4.1Z	5.1			
Ar = 	rt	0	0	1 (17)	0	0.5 (3)	0	3.3 (56)	
	0 °C	0.1 (0)	1 (6)	0.7 (4)	0	0.7 (3)			
	-10 °C	0	0.2 (2)	1 (16)	0	0.5 (5)			
	-25 °C	0.7 (13)	1 (14)	0.2 (3)	0	0.4 (6)			

Syringe-pump

Ar 1.1 Δ-MgBr	CoCl ₂ (10 mol %) TMEDA (20 mol %) THF, T, 1 h 0.52 mmol/h							Homo	2.1
		1.1	3.1	4.1E	4.1Z	5.1			
Ar = 	rt	t (0)	t (1)	1 (5)	0	1.2 (6)	0	9.2 (69)	
	0 °C	0	0.5 (1)	1 (2)	0	0.8 (3)			
	-10 °C	0.2 (1)	1.1 (6)	1 (6)	0	0.7 (3)			
	-25 °C	2.5 (14)	1 (3)	0	0	0.8 (1)			

Rate

Ar 1.1 Δ-MgBr	CoCl ₂ (10 mol %) TMEDA (20 mol %) THF, 0 °C, 1 h v							Homo	2.1
		1.1	3.1	4.1E	4.1Z	5.1			
Ar = 	manual dropwise	0.1 (0)	1 (6)	0.7 (4)	0	0.7 (3)	0	12 (69)	
	0.52 mmol/h	0	0.5 (1)	1 (2)	0	0.8 (3)			
	1.04 mmol/h	0.1 (0)	0.8 (3)	1 (4)	0	0.7 (2)			

Solvent

 1.1 	CoCl ₂ (10 mol %) TMEDA (20 mol %) S, 0 °C, 1 h 0.52 mmol/h	1.1	3.1	4.1E	4.1Z	5.1	Homo	2.1
		Ar =	THF	0	0.5 (1)	1 (2)	0	0.8 (3)
 1.1 	MeTHF MTBE	MeTHF	0	0.7 (1)	1 (3)	0	0.8 (2)	0
		MTBE	t (0)	0.9 (3)	1 (4)	0	0.7 (3)	0

Catalytic charge

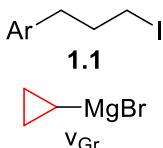
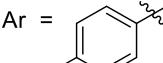
 1.1 	CoCl ₂ (X mol %) TMEDA (Y mol %) THF, 0 °C, 1 h 0.52 mmol/h (X/Y)	1.1	3.1	4.1E	4.1Z	5.1	Homo	2.1
		10/0	0.1	1	0.8	0	1.4	0
 1.1 	Ar =	10/20	0	0.5 (1)	1 (2)	0	0.8 (3)	0
		10/10	0.2 (1)	0.4 (1)	1 (4)	0	0.8 (2)	0
		5/10	0.2 (1)	1 (3)	1 (2)	0	0.8 (3)	0
		5/5	0	1 (5)	0.7 (3)	0	0.7 (2)	0
		3.5/7	t (0)	1 (6)	0.4 (3)	0	0.7 (3)	0
		3.5/3.5	0.1 (1)	1 (5)	0.5 (2)	0	0.6 (2)	0
		2.5/5	7.1 (21)	1 (1)	0	0	1.2 (1)	0
								21.0 (62)

Cobalt source

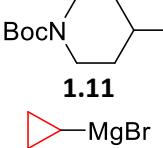
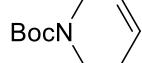
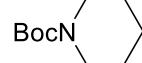
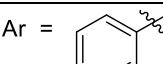
 1.1 	[Co] (3.5 mol %) TMEDA (X mol %) THF, 0 °C, 1 h 0.52 mmol/h	1.1	3.1	4.1E	4.1Z	5.1	Homo	2.1
		CoCl ₂	t (0)	1 (6)	0.4 (3)	0	0.7 (3)	0
 1.1 	X = CoCl ₂ 7 mol % CoBr ₂ Co(acac) ₂ X = CoCl ₂ 3.5 mol % Co(acac) ₃ Co(acac) ₂ X = 0 % Co(acac) ₂	CoCl ₂	0.3 (2)	1 (5)	0.4 (3)	0	0.7 (3)	0
		CoBr ₂	0.3 (2)	1 (7)	0.5 (3)	0	0.6 (3)	0
		Co(acac) ₂	0	1 (5)	0.5 (2)	0	0.6 (3)	0
		CoCl ₂	0.1 (1)	1 (5)	0.5 (2)	0	0.6 (2)	0
		Co(acac) ₃	t (2)	1 (5)	0.6 (2)	0	0.8 (3)	0
		Co(acac) ₂	0.2 (1)	1 (3)	0.2 (1)	0	1 (1)	0

CoCl₂ (99.999%), CoCl₂ (98%), CoBr₂ (99%), Co(acac)₂ (97%), Co(acac)₃ (99.99%)

Dilution factor

 1.1  v_{Gr}	Co(acac) ₂ (3.5 mol %) TMEDA (3.5 mol %) THF (V_{THF}), 0 °C, 1 h 0.52 mmol/h	1.1	3.1	4.1E	4.1Z	5.1	Homo	2.1
		v_{THF}/v_{Gr} (mL)						
-> Concentration (M)								
Ar =  MeO	0.25 / 0.54 mL -> 0.87-0.28 M	0.1 (1)	1 (7)	0.5 (3)	0	0.7 (5)	0	6.8 (64)
	2.0 / 0.41 mL -> 0.11-0.09 M	5.5 (28)	1 (4)	t (3)	0	0.8 (1)	0	12.5 (59)
	10.0 / 0.54 mL -> 0.02-0.02 M	2.0 (43)	t (0)	t (0)	0	0.2 (1)	0	1 (13)

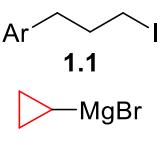
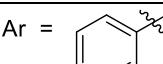
TMEDA equiv

 1.11 	Co(acac) ₂ (3.5 mol %) TMEDA (X) THF, 0 °C, 1 h 0.52 mmol/h	1.11			2.11
		3.5 mol %	0	1 (5-20)	0.3 (2-6)
 MeO	0.5 equiv 1 equiv 2 equiv	0.5 equiv	0	1 (6)	0.3 (3)
		1 equiv	0	2 (2)	1 (2)
		2 equiv	0	2 (3)	1 (4)
					75 (96)
					55 (89)

Same trend with 3-iodo-pyrrolidine

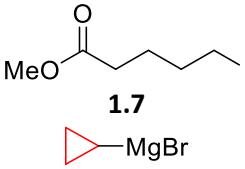
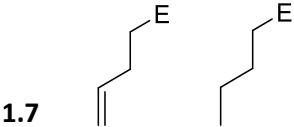
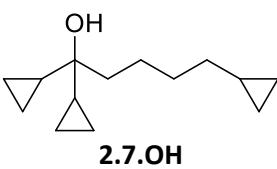
Grignard reagent

The idea was to mimic an old load of Grignard reagent (presence of a lot of salts MgBr₂) but without compromising the concentration of the Grignard reagent. Therefore, the addition of dry MgBr₂ to the mixture was done.

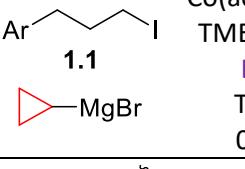
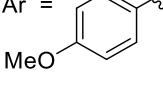
 1.1 	Co(acac) ₂ (3.5 mol %) TMEDA (1 equiv) MgBr₂ (X equiv) THF, 0 °C, 1 h 0.52 mmol/h	1.1	3.1	4.1E	4.1Z	5.1	Homo	2.1
		0	0	1 (3)	0.4 (1)	0	0.4 (1)	0
 MeO	0.1 (0)	1	0.1 (7)	0.3 (3)	0	0.4 (3)	0	5.4 (70)
								33.1 (84)

Iodoester

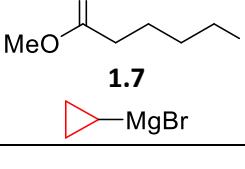
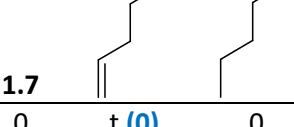
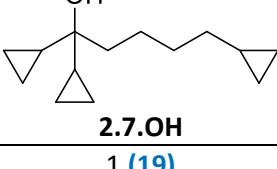
Salts

 1.7	Co(acac) ₂ (3.5 mol %) TMEDA (3.5 mol %) Salt (X) THF, 0 °C, 1 h 0.52 mmol/h	 1.7	 2.7.OH	 2.7		
					-	0 t (0) 0
E = CO ₂ Me	Lil (7 mol %)	0	0	0	1 (19)	2.2 (39)
	LiCl (7 mol %)	22.6	t	0	1	19
	LiCl (1 equiv)	0	0.5 (2)	t (1)	1 (5)	4.3 (45)
	MgI ₂ (7 mol %)	Major	-	-	t	t
	MgI ₂ (1 equiv)	0.3 (0)	t (0)	t (0)	1 (17)	2.7 (12)
	MgBr ₂ (7 mol %)	t (0)	t (0)	t (0)	1 (5)	19 (52)
	MgBr ₂ (1 equiv)	t (0)	t (0)	t (0)	1 (3)	9 (53)

No effect on a regular substrate with Lil:

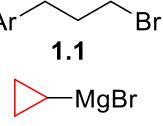
 1.1	Co(acac) ₂ (3.5 mol %) TMEDA (3.5 mol %) Lil (X mol %) THF, 0 °C, 1 h 0.52 mmol/h	 1.1	 3.1	 4.1E	 4.1Z	 5.1	Homo		 2.1
							0	19.5 (80)	
Ar = 	0	0.2 (1)	1 (3)	0.2 (1)	0	1 (1)	0	19.5 (80)	
	7	0.1 (1)	1 (6)	0.3 (2)	0	0.7 (3)	0	11.1 (73)	

Iron vs Cobalt

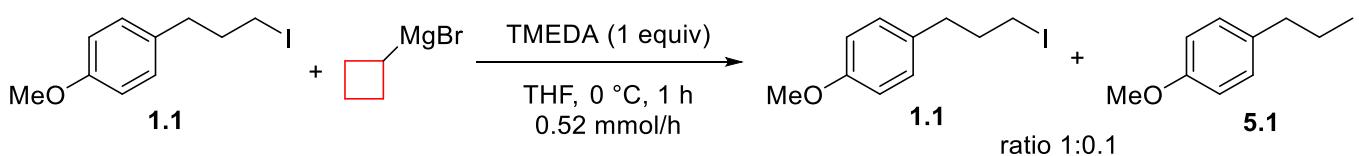
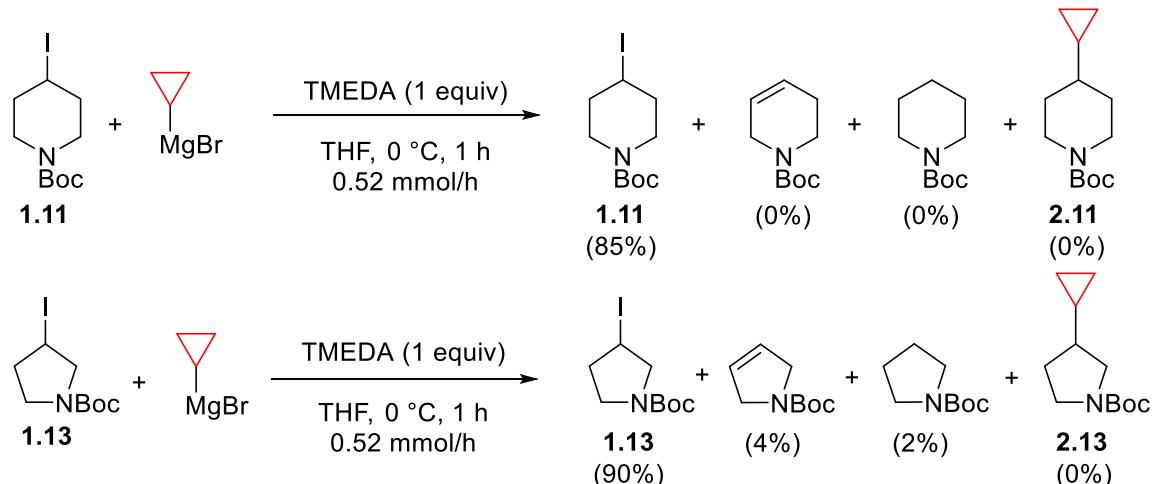
 1.7	[M] (3.5 mol %) TMEDA (3.5 mol %) THF, 0 °C, 1 h 0.52 mmol/h	 1.7	 2.7.OH	 2.7		
					Co(acac) ₂	0 t (0) 0
E = CO ₂ Me	FeCl ₃ ^[a]	0	2.2	0.7	1	1.9
	FeCl ₂	0	1	0.2	1	0.3
	Fe(acac) ₃	0	1.9	0.5	1	1.3

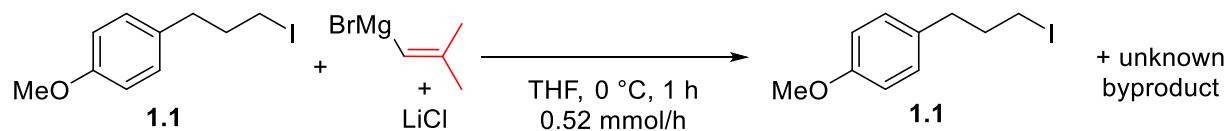
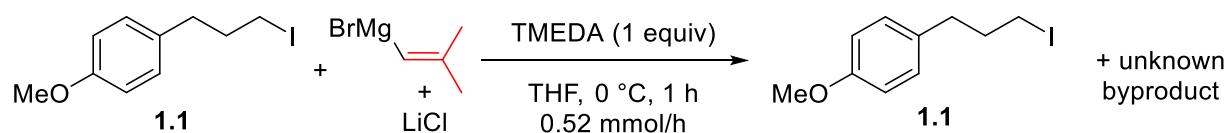
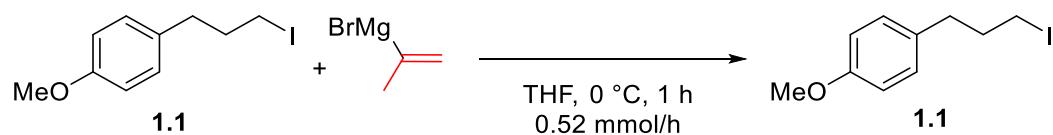
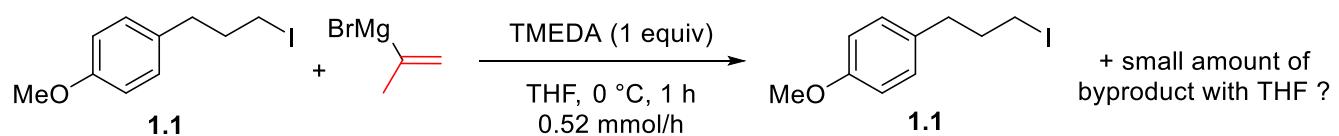
[a] = 7 mol % of TMEDA

Bromide

Ar	1.1	[Co] (X mol %)	TMEDA (Y mol %)	additive (Z mol %)	T	1.1	3.1	4.1E	4.1Z	5.1	Homo	2.1
					THF, 0 °C, 1 h 0.52 mmol/h							
Ar =		CoCl ₂ 10 TMEDA 20	0 °C	0		1 (15)	1 (15)	0	1 (14)	0	3.1 (51)	
		Co(acac) ₂ 10 TMEDA 20 NaI 10	0 °C	0.7 (5)		1 (10)	0.9 (10)	0	0.8 (8)	0	3.9 (43)	
		Co(acac) ₂ 3.5 TMEDA 3.5 LiI 7	0 °C	12.3 (46)		2 (10)	1 (5)	0	1.3 (6)	0	3.1 (18)	
		Co(acac) ₂ (3.5 mol %) TMEDA (1 équiv)	0 °C	4.8 (64)		1 (9)	0.4 (4)	0	0.3 (3)	0	1 (9)	
		Co(acac) ₂ (3.5 mol %) TMEDA (1 équiv)	rt	0.2 (3)		1 (15)	0.7 (10)	0	0.5 (7)	0	2.7 (45)	

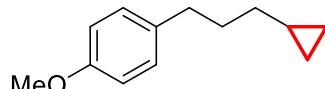
References without Cobalt salt





Primary iodides

1-(3-Cyclopropylpropyl)-4-methoxybenzene, **2.1**



Cyclopropane **2.1** was prepared according to Procedure C from 1-(3-iodopropyl)-4-methoxybenzene **1.1** (60 mg) and cyclopropylmagnesium bromide (0.54 mL, 0.48 M in MeTHF, 1.08 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.35) yielded cyclopropane **2.1** (33.2 mg, 0.17 mmol, 80%) contaminated by dehalogenated and elimination products (up to 2.5 mg, 6%) as a colourless oil.

Formula: C₁₃H₁₈O

Mass: 190.3 g.mol⁻¹

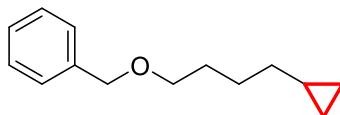
IR (neat): 1612, 1584, 1511, 1462, 1441, 1300, 1245, 1177, 1119, 1038, 1014 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.11 (brd, *J* = 8.5 Hz, 2H), 6.87-6.81 (brd, *J* = 8.7 Hz, 2H) 3.80 (s, 3H), 2.59 (*t*_{app}, *J* = 7.8 Hz, 2H), 1.71 (dddd, *J* = 7.8, 7.7, 7.3, 7.3 Hz, 2H), 1.29-1.20 (m, 2H), 0.69 (m, 1H), 0.41 (ddd, *J* = 8.1 Hz, 5.6 Hz and 4.1Hz, 2H), 0.04(-)0.02 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 157.7, 135.0, 129.3 (2C), 113.7 (2C), 55.3, 34.9, 34.4, 31.7, 10.8, 4.5 (2C)

MS (EI) *m/z*: 190 (18), 162 (11), 161 (16), 159 (7), 148 (5), 147 (29), 135 (5), 134 (24), 122 (11), 121 (100), 119 (4), 117 (4), 109 (4), 91 (15), 78 (10), 77 (14), 65 (6)

((4-Cyclopropylbutoxy)methyl)benzene, **2.2**



Cyclopropane **2.2** was prepared according to Procedure **C** from ((4-iodobutoxy)methyl)benzene **1.2** (63.1 mg) and cyclopropylmagnesium bromide (0.42 mL, 0.63 M, 0.84 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 99:1) yielded cyclopropane **2.2** (38.0 mg, 0.19 mmol, 86%) contaminated by dehalogenated and elimination products (2.7 mg, 7%) as a colourless oil.

Formula: C₁₄H₂₀O

Mass: 204.3 g.mol⁻¹

IR (neat): 1496, 1454, 1361, 1204, 1100, 1028, 1013, 956, 909 cm⁻¹

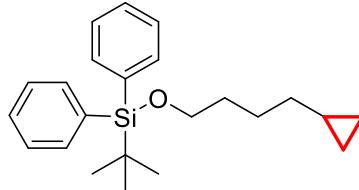
¹H NMR (400 MHz, CDCl₃) δ 7.36 (brd, *J* = 4.4 Hz, 4H), 7.29 (m, 1H), 4.52 (s, 2H), 3.48 (t, *J* = 6.6 Hz, 2H), 1.67 (quint_{app}, *J* = 7.3 Hz, 2H), 1.49 (quint_{app}, *J* = 7.3 Hz, 2H), 1.22 (q_{app}, *J* = 7.3 Hz, 2H), 0.67 (m, 1H), 0.40 (ddd, *J* = 7.8, 4.8, 4.6 Hz, 2H), 0.01 (q_{app}, *J* = 4.7 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 138.8, 128.4 (2C), 127.7 (2C), 127.5, 73.0, 70.6, 34.6, 29.7, 26.3, 10.9, 4.5 (2C, C₁₁)

MS (EI) *m/z*: 204 (1), 107 (5), 106 (2), 104 (24), 95 (6), 92 (16), 91 (100), 85 (10), 79 (5), 71 (6), 67 (8), 65 (9), 55 (11)

HRMS: Calculated for C₁₄H₂₀ONa [M+Na]⁺: 227.1406, Found: 227.1403

tert-Butyl(4-cyclopropylbutoxy)diphenylsilane, **2.3**



Cyclopropane **2.3** was prepared according to Procedure **C** from *tert*-butyl(4-iodobutoxy)diphenylsilane **1.3** (95.3 mg) and cyclopropylmagnesium bromide (0.47 mL, 0.55 M in MeTHF, 0.94 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.1) yielded cyclopropane **2.3** (68 mg, 0.19 mmol, 89%) contaminated by dehalogenated and elimination products (4.4 mg, 7%) as a colourless oil.

Formula: C₂₃H₃₂OSi

Mass: 352.6 g.mol⁻¹

IR (neat): 1472, 1461, 1427, 1389, 1361, 1106, 1012, 998, 938, 915 cm⁻¹

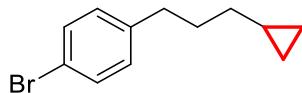
¹H NMR (400 MHz, CDCl₃) δ 7.71-7.64 (m, 4H), 7.45-7.34 (m, 6H), 3.67 (t, *J* = 6.5 Hz, 2H), 1.60 (quint_{app}, *J* = 7.3 Hz, 2H), 1.50-1.41 (m, 2H), 1.18 (q_{app}, *J* = 7.3 Hz, 2H), 1.06 (s, 9H), 0.64 (m, 1H), 0.45-0.31 (m, 2H), -0.02 (brq_{app}, *J* = 4.8 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 135.7 (4C), 134.3 (2C), 129.6 (2C), 127.7 (4C), 64.1, 34.5, 32.5, 27.0 (3C), 25.9, 19.3, 10.9, 4.5 (2C)

MS (EI) *m/z*: 296 (24, (M+1)-57, -*t*-Bu), 295 (88, M-57, -*t*-Bu), 217 (18), 200 (18), 199 (100), 197 (10), 189 (7), 183 (33), 181 (17), 177 (13), 175 (10), 163 (10), 161 (11), 137 (7), 135 (12), 123 (18), 121 (10), 105 (11), 95 (9), 91 (6), 77 (16), 55 (8)

HRMS: Calculated for C₂₃H₃₂OSiH [M+H]⁺: 353.2295, Found: 353.2294

1-Bromo-4-(3-cyclopropylpropyl)benzene, 2.4



Cyclopropane **2.4** was prepared according to Procedure **C** from 1-bromo-4-(3-iodopropyl)benzene **1.4** (70.6 mg) and cyclopropylmagnesium bromide (0.54 mL, 0.48 M in MeTHF, 1.08 mL/h). Purification by flash chromatography on silica gel (PE 100%) yielded cyclopropane **2.4** (40.6 mg, 0.17 mmol, 78%) contaminated by dehalogenated and elimination products (2.1 mg, 5%) as a colourless oil.

Formula: C₁₂H₁₅Br

Mass: 239.2 g.mol⁻¹

IR (neat): 1488, 1459, 1403, 1352, 1178, 1041, 1011 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.39 (brd, *J* = 8.3 Hz, 2H), 7.06 (brd, *J* = 8.2 Hz, 2H), 2.59 (*t_{app}*, *J* = 7.7 Hz, 2H), 1.70 (quint_{app}, *J* = 7.7 Hz, 2H), 1.23 (*q_{app}*, *J* = 7.4 Hz, 2H), 0.68 (m, 1H), 0.46-0.37 (m, 2H), 0.04-(-)0.04 (m, 2H)

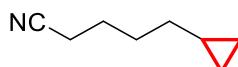
¹³C NMR (100 MHz, CDCl₃) δ 141.9, 131.3 (2C), 130.2 (2C), 119.3, 35.2, 34.3, 31.3, 10.8, 4.5 (2C)

HRMS: Unstable compound

5-Cyclopropylpentanenitrile and 1,5-dicyclopropylpentan-1-one, 2.5 and 2.5.CO

Cyclopropanes **2.5** and **2.5.CO** were obtained according to Procedure **C** from 5-iodopentanenitrile **1.5** (45.4 mg) and cyclopropylmagnesium bromide (0.47 mL, 0.55 M in MeTHF, 0.94 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 97:3 to 95:5) yielded cyclopropane **2.5** (8.2 mg, 0.07 mmol, 31%) and cyclopropane **2.5.CO** (3.6 mg, 0.02 mmol, 10%).

5-Cyclopropylpentanenitrile, 2.5



Formula: C₈H₁₃N

Mass: 123.2 g.mol⁻¹

IR (neat): 2246, 1461, 1427, 1387, 1327, 1269, 1043, 1015, 953, 938, 905 cm⁻¹

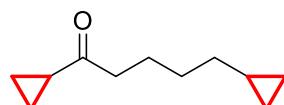
¹H NMR (400 MHz, CDCl₃) δ 2.34 (t, *J* = 7.0 Hz, 2H), 1.74-1.64 (m, 2H), 1.60-1.51 (m, 2H), 1.23 (*q_{app}*, *J* = 7.4 Hz, 2H), 0.65 (m, 1H), 0.45-0.38 (m, 2H), 0.04-(-)0.03 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 119.9, 33.9, 28.9, 25.3, 17.3, 10.6, 4.5 (2C)

HRMS: Calculated for C₈H₁₃NH [M+H]⁺: 124.1121, Found: 124.1120

1,5-Dicyclopropylpentan-1-one, 2.5.CO

Contaminated by an impurity



Formula: C₁₁H₁₈O

Mass: 166.3 g.mol⁻¹

IR (neat): 1699, 1460, 1444, 1432, 1387, 1233, 1196, 1159, 1137, 1120, 1086, 1060, 1014, 971 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 2.54 (t_{app}, J = 7.5 Hz, 2H), 1.92 (m, 1H), 1.64 (quint_{app}, J = 7.7 Hz, 2H), 1.45 - 1.36 (m, 2H), 1.20 (q_{app}, J = 7.3 Hz, 2H), 1.03-0.97 (m, 2H), 0.89 - 0.80 (m, 2H), 0.65 (m, 1H), 0.44 - 0.34 (m, 2H), 0.03(-)0.05 (m, 2H)

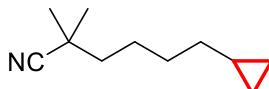
¹³C NMR (100 MHz, CDCl₃) δ 211.4, 43.7, 34.6, 29.4, 24.0, 20.4, 10.8, 10.6 (2C), 4.5 (2C)

MS (EI) m/z: 151 (2, M-15), 137 (4), 123 (4), 109 (4), 97 (45), 84 (41), 83 (13), 82 (5), 81 (4) 79 (5), 70 (5),

69 (100), 67 (6), 56 (10), 55 (36)

HRMS: Calculated for C₁₁H₁₈OH [M+H]⁺: 167.1430, Found: 167.1430

6-Cyclopropyl-2,2-dimethylhexanenitrile, 2.6



Cyclopropane **2.6** was prepared according to Procedure **C** from 6-iodo-2,2-dimethylhexanenitrile **1.6** (54.6 mg) and cyclopropylmagnesium bromide (0.46 mL, 0.57 M in MeTHF, 0.92 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.3 to 50:0.5) yielded cyclopropane **2.6** (29.1 mg, 0.18 mmol, 81%) contaminated by dehalogenated and elimination products (1 mg, 2%) as a colourless oil.

Formula: C₁₁H₁₉N

Mass: 165.3 g.mol⁻¹

IR (neat): 2360, 2341, 2234, 1692, 1471, 1462, 1389, 1369, 1321, 1279, 1170, 1045, 1014, 955 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 1.54-1.47 (m, 4H), 1.47-1.37 (m, 2H), 1.33 (s, 6H), 1.26-1.17 (m, 2H), 0.71 - 0.58 (m, 1H), 0.44-0.35 (m, 2H), 0.02(-)0.04 (m, 2H)

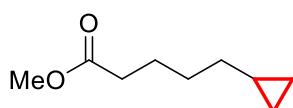
¹³C NMR (100 MHz, CDCl₃) δ 125.3, 41.2, 34.5, 32.5, 29.7, 26.8 (2C), 25.1, 10.8, 4.5 (2C)

HRMS: Calculated for C₁₁H₁₉NH [M+H]⁺: 166.1590, Found: 166.1590

Methyl-5-cyclopropylpentanoate and 1,1,5-tricyclopropylpentan-1-ol, 2.7 and 2.7.OH

Cyclopropanes **2.7** and **2.7.OH** were obtained according to Procedure **C** from methyl-5-iodopentanoate **1.7** (52.6 mg) and cyclopropylmagnesium bromide (0.46 mL, 0.57 M in MeTHF, 0.92 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 97:3 to 96:4) yielded cyclopropane **2.7** as a colourless oil (19.1 mg, 0.12 mmol, 56%) and cyclopropane **2.7.OH** as a colourless oil (2.4 mg, 0.01 mmol, 5%).

Methyl-5-cyclopropylpentanoate, 2.7



Formula: C₉H₁₆O₂

Mass: 156.2 g.mol⁻¹

IR (neat): 1738, 1459, 1436, 1362, 1308, 1238, 1195, 1169, 1119, 1074, 1014, 953, 913 cm⁻¹

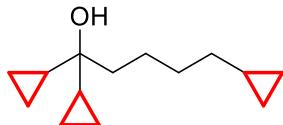
¹H NMR (400 MHz, CDCl₃) δ 3.66 (s, 3H), 2.30 (t, J = 7.5 Hz, 2H), 1.64 (quint_{app}, J = 7.6 Hz, 2H), 1.41 (quint_{app}, J = 7.7 Hz, 2H), 1.19 (q_{app}, J = 7.4 Hz, 2H), 0.64 (m, 1H), 0.38 (ddd, J = 7.9, 5.3, 5.0 Hz, 2H), -0.02 (q_{app}, J = 4.8 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 174.4, 51.5, 34.4, 34.2, 29.3, 24.9, 10.8, 4.5 (2C)

MS (EI) *m/z*: 156 (1, M⁺), 124 (13), 107 (8), 97 (8), 96 (41), 87 (39), 83 (16), 82 (31), 81 (13), 79 (8), 74 (100), 69 (9), 68 (33), 67 (17), 59 (29), 57 (6), 56 (6), 55 (68), 54 (13), 53 (8)

HRMS: Calculated for C₉H₁₆O₂Na [M+Na]⁺: 179.1043, Found: 179.1036

1,1,5-Tricyclopropylpentan-1-ol, 2.7.OH



Formula: C₁₄H₂₄O

Mass: 208.3 g.mol⁻¹

IR (neat): 3496, 1463, 1428, 1378, 1319, 1295, 1264, 1203, 1171, 1042, 1015, 985, 952, 911 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 1.65–1.45 (m, 4H), 1.45–1.34 (m, 2H), 1.35 – 1.16 (m, 2H), 0.86 – 0.76 (m, 2H), 0.66 (m, 1H), 0.47–0.32 (m, 6H), 0.32–0.22 (m, 4H), 0.04–(-)0.06 (m, 2H)

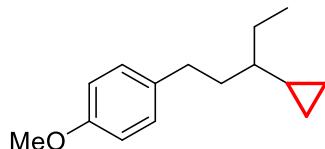
¹³C NMR (100 MHz, CDCl₃) δ 70.9, 42.8, 34.9, 30.5, 23.8, 18.6 (2C), 11.0, 4.5 (2C), 0.9 (2C), -0.6 (2C), -OH not visible

MS (EI) *m/z*: 190 (1, M-H₂O), 121 (3), 119 (3), 112 (8), 111 (100), 93 (8), 91 (7), 83 (7), 81 (5), 79 (12), 77 (5), 69 (57), 67 (9), 55 (21), 53 (4)

HRMS: Calculated for C₁₄H₂₄OH [M+H]⁺: 209.1900, Found: 209.1899

Secondary Iodide

1-(3-Cyclopropylpentyl)-4-methoxybenzene, 2.8



Cyclopropane **2.8** was prepared according to Procedure **C** from 1-(3-iodopentyl)-4-methoxybenzene **1.8** (66.1 mg) and cyclopropylmagnesium bromide (0.49 mL, 0.53 M in MeTHF, 0.98 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.6) yielded cyclopropane **2.8** (25.8 mg, 0.12 mmol, 54%) contaminated by dehalogenated and elimination products (14.7 mg, 0.08 mmol, 38%) as a colourless oil.

Formula: C₁₅H₂₂O

Mass: 218.3 g.mol⁻¹

IR (neat): 1511, 1463, 1441, 1377, 1300, 1243, 1176, 1115, 1083, 1038, 1016, 966, 944 cm⁻¹

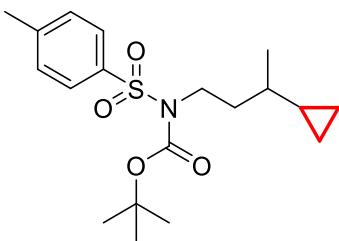
¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 2.75 – 2.56 (m, 2H), 1.76 – 1.63 (m, 2H), 1.54 – 1.45 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H), 0.63 – 0.50 (m, 2H), 0.50 – 0.37 (m, 2H), 0.14 – 0.03 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 157.6, 135.6, 129.2 (2C), 113.8 (2C), 55.3, 44.6, 36.8, 32.6, 27.4, 15.9, 11.3, 4.0, 3.9

MS (EI) *m/z*: 219 (M+1, 2), 218 (M⁺, 14), 189 (7), 162 (10), 161 (7), 148 (4), 147 (32), 135 (6), 134 (23), 122 (12), 121 (100), 109 (5), 91 (9), 78 (6), 77 (9), 55 (10)

HRMS: Calculated for C₁₅H₂₂OH [M+H]⁺: 219.1743, Found: 219.1743

tert-Butyl (3-cyclopropylbutyl)(tosyl)carbamate, 2.9



Cyclopropane **2.9** was prepared according to Procedure **C** from *tert*-butyl-(3-iodobutyl)(tosyl)carbamate **1.9** (98.5 mg) and cyclopropylmagnesium bromide (0.47 mL, 0.55 M in MeTHF, 0.94 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 94:6) yielded cyclopropane **2.9** (67.4 mg, 0.18 mmol, 84%) contaminated by the dehalogenated and elimination products (2.1 mg, 0.01 mmol, 3%) as a colourless oil.

Formula: C₁₉H₂₉NO₄S

Mass: 367.5 g.mol⁻¹

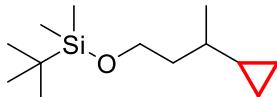
IR (neat): 1724, 1598, 1455, 1394, 1352, 1285, 1257, 1186, 1154, 1138, 1088, ,1045, 1016, 988 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 3.96 (ddd, *J*_{AB} = 14.1, 11.2, 5.5 Hz, 1H), 3.83 (ddd, *J*_{AB} = 14.2, 11.3, 4.8 Hz, 1H), 2.43 (s, 3H), 1.90 (m, 1H), 1.75 (m, 1H), 1.33 (s, 9H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.75 (m, 1H), 0.56 (m, 1H), 0.47 (m, 1H), 0.40 (m, 1H), 0.11 (m, 1H), 0.04 (m, 1H)

¹³C NMR (100 MHz, CDCl₃) δ 151.0, 144.0, 137.7, 129.3 (2C), 127.9 (2C), 84.0, 46.0, 37.9, 37.0, 28.0 (3C), 21.7, 20.0, 17.7, 4.8, 3.1

HRMS: Calculated for C₁₉H₂₉NO₄SH [M+H]⁺: 368.1890, Found: 368.1890

tert-Butyl(3-cyclopropylbutoxy)dimethylsilane, 2.10



Cyclopropane **2.10** was prepared according to Procedure **C** from *tert*-butyl(3-iodobutoxy)dimethylsilane **1.10** (68.3 mg) and cyclopropylmagnesium bromide (0.48 mL, 0.54 M in MeTHF, 0.96 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 98:2) yielded cyclopropane **2.10** (36.4 mg, 0.16 mmol, 73%) contaminated by the dehalogenated and elimination products (1 mg, 0.01 mmol, 2%) as a colourless liquid.

Formula: C₁₃H₂₈OSi

Mass: 228.5 g.mol⁻¹

IR (neat): 1472, 1462, 1406, 1388, 1361, 1255, 1091, 1044, 1016, 996, 938 cm⁻¹

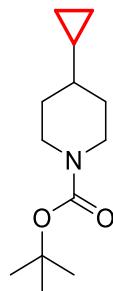
¹H NMR (400 MHz, CDCl₃) δ 3.74 – 3.63 (m, 2H), 1.68 (td, *J*_{AB} = 13.4, 6.9 Hz, 1H), 1.49 (td, *J*_{AB} = 13.6, 6.9 Hz, 1H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.79 (m, 1H), 0.48 (m, 1H), 0.43 – 0.30 (m, 2H), 0.13 - (-)0.03 (m, 2H), 0.04 (s, 6H)

¹³C NMR (100 MHz, CDCl₃) δ 61.6, 40.6, 35.4, 26.1 (3C), 20.1, 18.4, 18.1, 4.5, 3.2, -5.16, -5.19

MS (EI) *m/z*: 172 ((M+1)-57, -*t*-Bu, 7), 171 (48, M⁺-57, -*t*-Bu), 143 (11), 142 (14), 141 (100), 115 (10), 114 (6), 113 (51), 101 (36), 99 (41), 95 (7), 89 (32), 85 (10), 81 (5), 76 (7), 75 (91), 73 (35), 69 (5), 67 (5), 61 (5), 59 (23), 55 (9)

HRMS: Calculated for C₁₃H₂₈OSiH [M+H]⁺: 229.1982, Found: 229.1984

tert-Butyl-4-cyclopropylpiperidine-1-carboxylate, 2.11



Cyclopropane **2.11** was prepared according to Procedure **C** from *tert*-butyl-4-iodopiperidine-1-carboxylate **1.11** (67.6 mg) and cyclopropylmagnesium bromide (0.45 mL, 0.58 M in MeTHF, 0.90 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 93:7) yielded cyclopropane **2.11** (47.8, 0.21 mmol, 98%) as a mixture of rotamers contaminated by the dehalogenated and elimination products (1.6 mg, 0.01 mmol, 4%) as a colourless oil.

Formula: C₁₃H₂₃NO₂

Mass: 225.3 g.mol⁻¹

IR (neat): 1690, 1447, 1422, 1392, 1365, 1352, 1325, 1283, 1236, 1159, 1126, 1099, 1069, 1019, 985, 963, 945 cm⁻¹

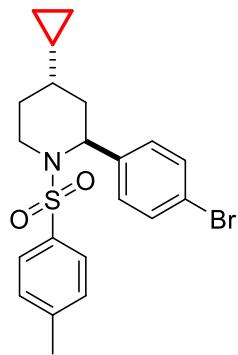
¹H NMR (400 MHz, CDCl₃) δ 4.05 (brs, 2H), 2.63 (brt, J = 12.2 Hz, 2H), 1.70 (brd_{app}, J = 12.4 Hz, 2H), 1.45 (s, 9H), 1.24 (m, 2H), 0.67-0.46 (m, 2H), 0.44-0.34 (m, 2H), 0.12-0.01 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 155.0, 79.2, 43.8 (2C), 41.5, 31.9 (2C), 28.6 (3C), 16.8, 3.2 (2C)

MS (EI) *m/z*: 225 (M⁺, 1), 170 (6), 169 (12), 168 (5), 152 (10), 141 (5), 140 (47), 126 (9), 124 (4), 113 (20), 112 (5), 96 (18), 82 (10), 81 (5), 69 (7), 58 (5), 57 (100), 56 (22), 55 (9)

HRMS: Calculated for C₁₃H₂₃NO₂H [M+H]⁺: 226.1802, Found: 226.1801

tert-Butyl-*trans*-4-cyclopropyl-2-(4-bromophenyl)piperidine-1-carboxylate, 2.12



trans/cis > 95:5

Cyclopropane **2.12** was prepared according to Procedure **C** from *trans*-2-(4-bromophenyl)-4-iodo-1-tosylpiperidine (113.0 mg) and cyclopropylmagnesium bromide (0.58 mL, 0.45 M in MeTHF, 1.16 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 85:15) yielded cyclopropane **2.12** as a colourless oil (76.4 mg, 0.18 mmol, 81%).

Formula: C₂₁H₂₄BrNO₂S

Mass: 434.4 g. mol^{-1}

IR (neat) cm^{-1} 1597, 1488, 1451, 1435, 1397, 1372, 1349, 1333, 1303, 1290, 1255, 1204, 1179, 1154, 1092, 1076, 1047, 1008, 965, 933, 906

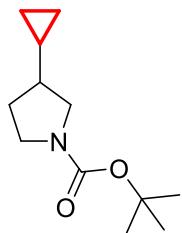
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.76 (d, $J = 8.3$ Hz, 2H), 7.42 (d, $J = 8.6$ Hz, 2H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 8.6$, 2H), 5.27 (brd, $J = 4.9$ Hz, 1H), 3.90 (brd_{app}, $J = 14.5$ Hz, 1H), 2.86 (ddd, $J = 14.4, 13.4, 2.9$ Hz, 1H), 2.44 (s, 3H), 2.27 (brd_{app}, $J = 13.9$ Hz, 1H), 1.58 – 1.36 (m, 2H), 1.06 (m, 1H), 0.55 (m, 1H), 0.39 – 0.07 (m, 3H), 0.01(-)-0.11 (m, 2H)

$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 143.3, 138.6, 138.2, 131.8 (2C), 129.8 (2C), 128.7 (2C), 127.1 (2C), 120.9, 54.9, 41.8, 35.8, 33.7, 30.7, 21.6, 17.0, 3.2, 3.1

MS (EI) m/z : 4.5 (M $^+$, 2), 434 (M+1, 2), 433 (M $^+$, 2), 406 (6), 404 (6), 281 (9), 280 (62), 279 (26), 278 (100), 277 (25), 276 (23), 264 (25), 262 (21), 251 (10), 250 (14), 236 (14), 223 (22), 210 (12), 184 (17), 183 (6), 171 (17), 169 (20), 155 (43), 91 (99), 90 (15), 89 (11), 81 (8), 77 (9), 68 (12), 67 (21), 65 (19), 55 (21), 53 (8)

HRMS: Calculated for $\text{C}_{21}\text{H}_{24}\text{BrNO}_2\text{SH}$ [M+H] $^+$: 434.0784 and 436.0763, Found: 434.0795 and 436.0773

tert-Butyl-3-cyclopropylpyrrolidine-1-carboxylate, 2.13



Cyclopropane **2.13** was prepared according to Procedure **C** from *tert*-butyl-3-iodopyrrolidine-1-carboxylate **1.13** (64.6 mg) and cyclopropylmagnesium bromide (0.45 mL, 0.58 M in MeTHF, 0.90 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 94:6 to 9:1) yielded cyclopropane **2.13** as a mixture of rotamers (40.6 mg, 0.19 mmol, 88%) contaminated by the dehalogenated and elimination products (1.4 mg, 4%) as a colourless oil.

Formula: $\text{C}_{12}\text{H}_{21}\text{NO}_2$

Mass: 211.3 g. mol^{-1}

IR (neat): 1694, 1478, 1454, 1396, 1365, 1344, 1251, 1168, 1121, 1084, 1047, 1018, 981, 948 cm^{-1}

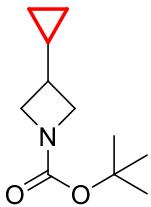
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.56-3.33 (m, 2H), 3.23 (m, 1H), 3.03 (m, 1H), 1.93 (m, 1H), 1.64 (m, 1H), 1.55-1.38 (m, 1H), 1.45 (s, 9H), 0.65 (m, 1H), 0.52-0.36 (m, 2H), 0.19-0.03 (m, 2H)

$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 154.7, 79.0, [51.3, 50.7], [45.8, 45.4], [44.2, 43.2], [31.5, 30.8], 28.6 (3C), 13.4, 3.25 (2C)

MS (EI) m/z : 211 (M $^+$, 3), 156 (12), 155 (6), 154 (11), 152 (3), 138 (7), 127 (4), 126 (8), 95 (5), 88 (18), 83 (4), 82 (16), 70 (3), 68 (6), 67 (9), 58 (5), 57 (100), 56 (8), 55 (6)

HRMS: Calculated for $\text{C}_{12}\text{H}_{21}\text{NO}_2\text{H}$ [M+H] $^+$: 212.1645 , Found: 212.1644

tert-Butyl 3-cyclopropylazetidine-1-carboxylate, 2.14



Cyclopropane **2.14** was prepared according to Procedure **C** from *tert*-butyl-3-cyclopropylazetidine-1-carboxylate **1.14** (61.5 mg) and cyclopropylmagnesium bromide (0.47 mL, 0.55 M in MeTHF, 0.94 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 85:15) yielded cyclopropane **2.14** as a colourless oil (38.86 mg, 0.20 mmol, 91%).

Formula: C₁₁H₁₉NO₂

Mass: 197.3 g·mol⁻¹

IR (neat): 1699, 1479, 1456, 1410, 1386, 1365, 1253, 1125, 1047, 1018, 932 cm⁻¹

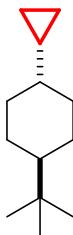
¹H NMR (400 MHz, CDCl₃) δ 3.94 (t_{app}, J = 8.5 Hz, 2H), 3.60 (dd, J = 9.0 Hz and 5.8 Hz, 2H), 2.12 (m, 1H), 1.42 (s, 9H), 0.96 (m, 1H), 0.52-0.42 (m, 2H), 0.15-0.08 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 156.5, 79.2, 53.6 (2C), 32.7, 28.5 (3C), 14.0, 2.8 (2C)

MS (EI) *m/z*: 141 (7, (M+1)-57, -t-Bu), 140 (3, M-57, -t-Bu), 126 (5), 124 (5), 96 (5), 82 (16), 81 (7) 69 (4), 68 (22), 67 (16), 58 (5), 57 (100), 56 (7), 55 (4), 53 (5)

HRMS: Calculated for C₁₁H₁₉NO₂Na [M+Na]⁺: 220.1308, Found: 220.1300

(1*r*,4*r*)-1-(*tert*-Butyl)-4-cyclopropylcyclohexane, **2.15**



trans/cis > 95:5

Cyclopropane **2.15** was prepared according to Procedure **C** from *trans*-1-(*tert*-butyl)-4-iodocyclohexane **1.15a** or *cis*-1-(*tert*-butyl)-4-iodocyclohexane **1.15b** (57.8 mg) and cyclopropylmagnesium bromide (0.52 mL, 0.50 M in MeTHF, 1.04 mL/h). Purification by flash chromatography on silica gel (PE 100%) yielded cyclopropane **2.15** as a colourless oil (32.1 mg, 0.18 mmol, 82%).

Formula: C₁₃H₂₄

Mass: 180.3 g·mol⁻¹

IR (neat): 1479, 1466, 1448, 1393, 1365, 1313, 1194, 1170, 1157, 1087, 1016, 957, 929 cm⁻¹

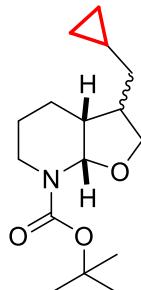
¹H NMR (400 MHz, CDCl₃) δ 1.90-1.81 (m, 2H), 1.81-1.71 (m, 2H), 1.04 (q_{app}, J = 12.0 Hz, 2H), 1.10 - 0.80 (m, 5H), 0.83 (s, 9H), 0.50-0.29 (m, 4H), -0.01 (m, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 48.3, 43.4, 33.5 (2C), 32.5, 27.7 (3C), 27.4 (2C), 17.6, 3.1 (2C)

MS (EI) *m/z*: 180 (M⁺, 1), 137 (6), 124 (14), 123 (15), 122 (13), 109 (19), 97 (5), 96 (28), 95 (12), 94 (5), 83 (19), 82 (19), 81 (51), 80 (7), 79 (11), 69 (12), 68 (7), 67 (28), 57 (100), 56 (14), 55 (21), 53 (6)

Experiment with a radical clock

tert-Butyl-(3a*R*,7a*S*)-3-(cyclopropylmethyl)hexahydrofuro[2,3-*b*]pyridine-7(4*H*)-carboxylate, 2.16



Cyclopropane **2.16** was prepared according to procedure **C** from *tert*-butyl-(2*S*,3*R*)-2-(allyloxy)-3-iodopiperidine-1-carboxylate (79.8 mg) and cyclopropylmagnesium bromide (0.58 mL, 0.45 M, 1.16 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 8:2) yielded cyclopropane **2.16** (33.0 mg, 0.12 mmol, 54%) as a mixture of diastereomers ($\alpha/\beta = 80:20$) as a colourless oil.

Formula: C₁₆H₂₇NO₃

Mass: 281.4 g.mol⁻¹

IR (neat): 1699, 1476, 1450, 1421, 1389, 1365, 1349, 1292, 1251, 1155, 1091, 1016, 976, 960, 942 cm⁻¹

¹H NMR (400 MHz, DMSO-d6) δ 5.53 (m, 0.2H), 5.47 (d, *J* = 5.0 Hz, 0.8H), 3.99 (dd, *J* = 8.5, 7.2 Hz, 0.8H), 3.79 (*t*_{app}, *J* = 8.0 Hz, 0.2H), 3.65 (brd_{app}, *J* = 12.8 Hz, 1H), 3.42 (dd, *J* = 10.5, 7.8 Hz, 0.2H), 3.30 (dd, *J* = 8.7, 4.1 Hz, 0.8H), 2.70 (brt_{app}, *J* = 11.0 Hz, 1H), 2.43 (m, *J* = 16.2 Hz, 0.2H), 1.92 (m, 0.8H), 1.80 (m, 0.8H), 1.67 – 1.51 (m, 2.2H), 1.35 (s, 9H), 1.33 – 1.08 (m, 4H), 0.65 (m, 0.8H), 0.56 (m, 0.2H), 0.40 – 0.29 (m, 2H), 0.06 - (-)0.09 (m, 2H)

¹³C NMR (100 MHz, DMSO-d6) δ 154.9, 83.0, 79.8, 69.9, 45.0 (C_α), 42.5 (C_β), 38.4, 28.4 (3C), 25.9, 22.8, 10.0 (C_β), 9.7 (C_α), 4.9 (C_α), 4.8 (C_α), 4.7 (2C, C_β) –CH₂N not visible and CH₂CHCH₂ under solvent pic

The same NMR spectra were obtained at 80 °C and 100 °C in DMSO-d6.

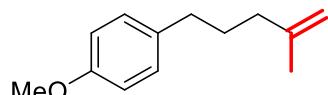
MS (EI) *m/z*: 226 (M-55, -C₄H₇, 6), 224 (43), 195 (7), 180 (38), 143 (21), 140 (28), 124 (5), 122 (5), 98 (5), 97 (6), 96 (59), 95 (5), 83 (11), 82 (12), 81 (12), 79 (7), 70 (5), 69 (10), 68 (5), 67 (9), 58 (6), 57 (100), 56 (11), 55 (21), 53 (5)

HRMS: Calculated for C₁₆H₂₇NO₃H [M+H]⁺: 282.2064, Found: 282.2064

3-2 CROSS-COUPLING WITH ISOPROPENYLMAGNESIUM BROMIDE, 1-PROPYENYLMAGNESIUM BROMIDE AND 2-METHYL-1-PROPYENYLMAGNESIUM BROMIDE

Primary iodides

1-Methoxy-4-(4-methylpent-4-en-1-yl)benzene, 6.1



Olefin **6.1** was prepared according to Procedure **D** from 1-(3-iodopropyl)-4-methoxybenzene **1.1** (60 mg) and isopropenylmagnesium bromide (0.70 mL, 0.37 M in THF, 1.40 mL/h). Purification by flash

chromatography on silica gel (PE/Et₂O 50:0.35) yielded olefin **6.1** (29.7 mg, 0.16 mmol, 72%) contaminated by the dehalogenated and elimination products (1.1 mg, 0.01 mmol, 3%) as a colourless oil.

Formula: C₁₃H₁₈O

Mass: 190.3 g.mol⁻¹

IR (neat): 1649, 1612, 1584, 1511, 1454, 1442, 1374, 1319, 1280, 1243, 1176, 1152, 1107, 1037, 965 cm⁻¹

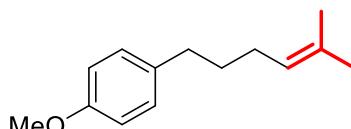
¹H NMR (400 MHz, CDCl₃) δ 7.11 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 4.73 (brs, 1H), 4.70 (brs, 1H), 3.80 (s, 3H), 2.56 (t_{app}, J = 8.0 Hz, 2H), 2.06 (t, J = 7.6 Hz, 2H), 1.80 – 1.64 (m, 5H)

¹³C NMR (100 MHz, CDCl₃) δ 157.7, 145.8, 134.7, 129.4 (2C), 113.8 (2C), 110.0, 55.3, 37.4, 34.6, 29.7, 22.5

MS (EI) *m/z*: 190 (M⁺, 2), 135 (11), 134 (100), 122 (4), 121 (41), 119 (7), 91 (8), 78 (5), 77 (7),

HRMS: Calculated for C₁₃H₁₈ONa [M+Na]⁺: 213.1250, Found: 213.1246

1-Methoxy-4-(5-methylhex-4-en-1-yl)benzene, **6.2**¹⁹



Olefin **6.2** was prepared according to Procedure **D** from 1-(3-iodopropyl)-4-methoxybenzene **1.1** (60 mg) and 2-methyl-1-propenylmagnesium bromide (0.97 mL, 0.27 M in THF, 1.96 mL/h) premixed with LiCl. Purification by flash chromatography on silica gel (PE/Et₂O 50:0.35) yielded olefin **6.2** (18.9 mg, 0.09 mmol, 43%) contaminated by the dehalogenated and elimination products (4.2 mg, 13%) as a colourless oil.

Formula: C₁₄H₂₀O

Mass: 204.3 g.mol⁻¹

IR (neat): 1671, 1647, 1612, 1584, 1511, 1463, 1454, 1441, 1376, 1300, 1244, 1176, 1111, 1038, 964 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.10 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 5.15 (brt, J = 7.1 Hz, 1H), 3.80 (s, 3H), 2.56 (t_{app}, J = 7.9 Hz, 2H), 2.01 (q_{app}, J = 7.3 Hz, 2H), 1.71 (s, 3H), 1.68–1.57 (m, 2H), 1.60 (s, 3H)

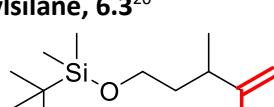
¹³C NMR (100 MHz, CDCl₃) δ 157.7, 134.9, 131.7, 129.3 (2C), 124.5, 113.7 (2C), 55.3, 34.7, 31.9, 27.7,

25.8, 17.8

MS (EI) *m/z*: 205 (M+1, 8), 204 (M⁺, 54), 161 (7), 148 (15), 147 (53), 135 (19), 134 (49), 122 (17), 121 (100), 119 (5), 105 (8), 96 (6), 91 (17), 81 (12), 79 (6), 78 (9), 77 (15), 69 (6), 65 (6), 55 (14)

Secondary iodides

tert-Butyl(3-cyclopropylbutoxy)dimethylsilane, **6.3**²⁰



Olefin **6.3** was prepared according to Procedure **C** from *tert*-butyl(3-iodobutoxy)dimethylsilane **1.10** (683 mg) and isopropenylmagnesium bromide (7.1 mL, 0.37 M in THF, 1.42 mL/h). Purification by flash

¹⁹ Nagasawa, S.; Sasano, Y.; Iwabuchi, Y.; *Chem. Eur. J.* **2017**, 23, 10276–10279.

²⁰ Speck, K.; Magauer, T. *Chem. Eur. J.* **2017**, 23, 1157–1165.

chromatography on silica gel (PE/Et₂O 99:1) yielded olefin **6.3** (443.3 mg, 1.94 mmol, 89%) as a yellowish liquid.

Formula: C₁₃H₂₈OSi

Mass: 228.5 g.mol⁻¹

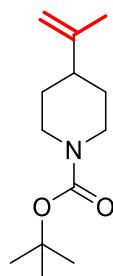
IR (neat): 1471, 1462, 1387, 1361, 1254, 1100, 1005, 981, 939, 890 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.70 – 4.65 (m, 2H), 3.56 (t, *J* = 6.9 Hz, 2H), 2.30 (sext_{app}, *J* = 7.0 Hz, 1H), 1.68 - 1.65 (m, 3H), 1.62 (m, 1H), 1.50 (quint_{app}, *J* = 6.7 Hz, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H)

¹³C NMR (100 MHz, CDCl₃) δ 149.9, 109.5, 61.6, 38.0, 37.6, 26.1 (3C), 19.8, 19.1, 18.4, -5.19, -5.21

MS (EI) *m/z*: 172 ((M+1)-57, -*t*-Bu, 12), 171 (M-57, -*t*-Bu, 75), 143 (5), 141 (29), 129 (12), 127 (5), 115 (7), 113 (12), 103 (4), 102 (6), 101 (59), 99 (35), 95 (8), 89 (23), 85 (13), 81 (5), 76 (7), 75 (100), 73 (26), 59 (17), 55 (8)

tert-Butyl 4-(prop-1-en-2-yl)piperidine-1-carboxylate, 6.4²¹



Olefin **6.4** was prepared according to Procedure **D** from *tert*-butyl-4-iodopiperidine-1-carboxylate **1.11** (67.6 mg) and isopropenylmagnesium bromide (0.70 mL, 0.37 M in THF, 1.40 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 85:15) yielded olefin **6.4** (40.7 mg, 0.18 mmol, 83%) as a mixture of rotamers contaminated by the dehalogenated and elimination products (2.0 mg, 0.01 mmol 5%) as a colourless oil.

Formula: C₁₃H₂₃NO₂

Mass: 225.3 g.mol⁻¹

IR (neat): 1692, 1645, 1477, 1446, 1419, 1392, 1365, 1334, 1313, 1291, 1276, 1245, 1229, 1163, 1123, 1084, 1043, 989, 962, 938, 887 cm⁻¹

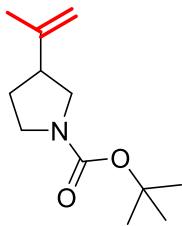
¹H NMR (400 MHz, CDCl₃) δ 4.71 (brs, 1H), 4.68 (brs, 1H), 4.26-4.03 (brs, 2H), 2.68 (brt_{app}, *J* = 11.9 Hz, 2H), 1.98 (brtt, *J* = 12.1 Hz and 3.2 Hz, 1H), 1.73-1.63 (m, 2H), 1.71 (s, 3H), 1.45 (s, 9H), 1.34 (qd_{app}, *J* = 12.4 Hz and 4.1 Hz, 2H)

¹³C NMR (100 MHz, CDCl₃) δ 154.9, 149.1, 109.1, 79.4, 44.2 (2C), 43.6, 30.8 (2C), 28.5 (3C), 20.9

MS (EI) *m/z*: 170 (M-55, -C₄H₆, 2), 169 (12), 152 (9), 126 (10), 124 (4), 113 (36), 100 (8), 83 (5), 82 (42), 69 (5), 67 (6), 58 (5), 57 (100), 56 (47), 55 (9)

tert-Butyl 3-(prop-1-en-2-yl)pyrrolidine-1-carboxylate, 6.5

²¹ Gonnard, L.; Guérinot, A.; Cossy, J. *Chem. Eur. J.* **2015**, 21, 12797-12803.



Olefin **6.5** was prepared according to Procedure **D** from *tert*-butyl-3-iodopyrrolidine-1-carboxylate **1.13** (64.6 mg) and isopropenylmagnesium bromide (0.69 mL, 0.38 M in THF, 1.38 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 9:1) yielded olefin **6.5** (37.1 mg, 0.16 mmol, 81%) as a mixture of rotamers (*a/b* = 1:1) contaminated by the elimination product (0.6 mg, 0.003 mmol, 2%) as a colourless oil.

Formula: C₁₂H₂₁NO₂

Mass: 211.3 g.mol⁻¹

IR (neat): 1693, 1649, 1478, 1453, 1399, 1365, 1339, 1292, 1253, 1167, 1121, 1091 cm⁻¹

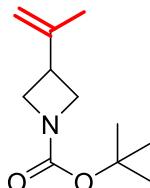
¹H NMR (400 MHz, CDCl₃) δ 4.77 (brs, 1), 4.73 (brs, 1H), 3.65–3.39 (m, 2H), 3.27 (m, 1H), 3.09 (m, 1H), 2.70 (m, 1H), 1.97 (m, 1H), 1.75 (m, 1H), 1.73 (s, 3H), 1.45 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 154.6, 144.7, [110.34, 110.29], 79.1, [50.0, 49.6], [45.9, 45.5], [45.5, 44.7], [30.4, 29.6], 28.6 (3C), [21.4, 21.3]

MS (EI) *m/z*: 156 (M-55, -C₄H₆, 5), 155 (29), 140 (5), 138 (11), 112 (7), 96 (6), 94 (5), 83 (12), 82 (5), 68 (5), 67 (8), 58 (5), 57 (100), 56 (5), 55 (5)

HRMS: Calculated for C₁₂H₂₁NO₂Na [M+Na]⁺: 234.1465, Found: 234.1465

tert-Butyl 3-cyclopropylazetidine-1-carboxylate, **6.6**



Olefin **6.6** was prepared according to Procedure **D** from *tert*-butyl-3-iodopropylazetidine-1-carboxylate **1.14** (61.5 mg) and isopropenylmagnesium bromide (0.90 mL, 0.29 M in THF, 1.80 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 85:15) yielded olefin **6.6** as a mixture of rotamers as a colourless oil (34.2 mg, 0.17 mmol, 80%).

Formula: C₁₁H₁₉NO₂

Mass: 197.3 g.mol⁻¹

IR (neat): 1700, 1650, 1602, 1479, 1455, 1392, 1375, 1365, 1298, 1249, 1162, 1128, 1031, 969 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 4.84 (m, 1H), 4.78 (m, 1H), 4.01 (t_{app}, *J* = 8.6 Hz, 2H), 3.80 (dd, *J* = 8.4 Hz and 6.5 Hz, 2H), 3.16 (quint_{app}, *J* = 7.6 Hz, 1H), 1.73 (s, 3H), 1.42 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 156.5, 144.2, 110.9, 79.4, 53.1 (2C), 35.0, 28.4 (3C), 19.6

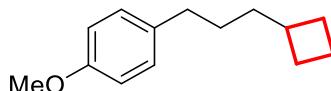
MS (EI) *m/z*: 142 (M-55, -C₄H₆, 1), 141 (6), 140 (4), 126 (6), 82 (26), 81 (7), 68 (20), 67 (9), 58 (5), 57 (100), 56 (6), 55 (5)

HRMS: Calculated for C₁₁H₁₉NO₂Na [M+Na]⁺: 220.1308, Found: 220.1316

3-3 CROSS-COUPLING WITH CYCLOBUTYLMAGNESIUM BROMIDE

Primary iodides

1-(3-Cyclobutylpropyl)-4-methoxybenzene, 8.1



Cyclobutane **8.1** was prepared according to Procedure **C** from 1-(3-iodopropyl)-4-methoxybenzene **1.1** (60 mg) and cyclobutylmagnesium bromide (0.58 mL, 0.45 M in MeTHF, 1.16 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.35) yielded cyclobutane **8.1** (354 mg, 0.17 mmol, 80%) contaminated by the dehalogenated and elimination products (1.1 mg, 3%) as a colourless oil.

Formula: C₁₄H₂₀O

Mass: 204.3 g.mol⁻¹

IR (neat): 1612, 1584, 1511, 1463, 1441, 1300, 1243, 1176, 1117, 1038, 965, 913 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.10 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 3.80 (s, 3H), 2.53 (t_{app}, J = 7.5 Hz, 2H), 2.28 (hept_{app}, J = 7.7 Hz, 1H), 2.10 – 1.96 (m, 2H), 1.92 – 1.72 (m, 2H), 1.64 – 1.55 (m, 2H), 1.55 – 1.46 (m, 2H), 1.46 – 1.37 (m, 2H)

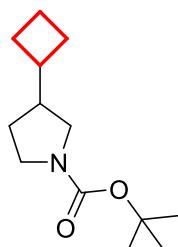
¹³C NMR (100 MHz, CDCl₃) δ 157.7, 135.1, 129.3 (2C), 113.7 (2C), 55.3, 36.7, 36.1, 35.1, 29.4, 28.4 (2C), 18.6

MS (EI) *m/z*: 204 (M⁺, 19), 161 (10), 134 (15), 122 (10), 121 (100), 91 (7), 78 (5), 77 (6)

HRMS: Calculated for C₁₄H₂₀ONa [M+Na]⁺: 227.1406, Found: 227.1408

Secondary iodides

tert-Butyl 3-cyclobutylpyrrolidine-1-carboxylate, 8.2



Cyclobutane **8.2** was prepared according to Procedure **C** from *tert*-butyl-3-iodopyrrolidine-1-carboxylate **1.13** (64.6 mg) and cyclobutylmagnesium bromide (0.69 mL, 0.38 M in MeTHF, 1.38 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 9:1) yielded cyclobutene **8.2** (31.5 mg, 0.14 mmol, 64%) as a mixture of rotamers (a/b = 1:1) contaminated by the elimination product (1.29 mg, 0.01 mmol, 4%) as a colourless oil.

Formula: C₁₃H₂₃NO₂

Mass: 225.3 g.mol⁻¹

IR (neat): 1694, 1478, 1453, 1399, 1365, 1343, 1249, 1168, 1123, 1109, 979 cm⁻¹

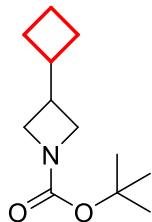
¹H NMR (400 MHz, CDCl₃) δ 3.47-3.29 (m, 2H), 3.29-3.15 (m, 1H), 2.89 (dd, *J* = 10.8 Hz and 7.2 Hz, 0.5H), 2.81 (dd, *J* = 10.8 Hz and 6.9 Hz, 0.5H), 2.27-2.06 (m, 2H), 2.06-1.94 (m, 2H), 1.92-1.72 (m, 3H), 1.72-1.58 (m, 2H), 1.50-1.36 (m, 1H), 1.44 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 154.8, 78.9, [49.5, 45.7], [49.0, 45.4], [45.2, 44.2], [38.42, 38.37], [29.2, 26.8], 28.6 (3C), 26.6 (2C), [18.3, 18.2]

MS (EI) *m/z*: 225 (M⁺, 3), 170 (16), 169 (11), 168 (13), 152 (9), 141 (6), 126 (7), 124 (5), 108 (6), 96 (5), 88 (5), 82 (14), 81 (4), 79 (5), 70 (8), 68 (6), 67 (7), 57 (100), 56 (7), 55 (8)

HRMS: Calculated for C₁₃H₂₃NO₂Na [M+Na]⁺: 248.1621, Found: 248.1622

tert-Butyl 3-cyclobutylazetidine-1-carboxylate, 8.3²²



Cyclobutane **8.3** was prepared according to Procedure **C** from *tert*-butyl-3-iodobutylazetidine-1-carboxylate **1.14** (61.5 mg) and cyclobutylmagnesium bromide (0.69 mL, 0.38 M in MeTHF, 1.38 mL/h). Purification by flash chromatography on silica gel (PE/Et₂O 92:8) yielded cyclobutane **8.3** as a colourless oil (27.2 mg, 59 mmol, 59%).

Formula: C₁₂H₂₁NO₂

Mass: 211.3 g·mol⁻¹

IR (neat): 1701, 1479, 1455, 1397, 1365, 1340, 1297, 1250, 1159, 1142 982, 931 cm⁻¹

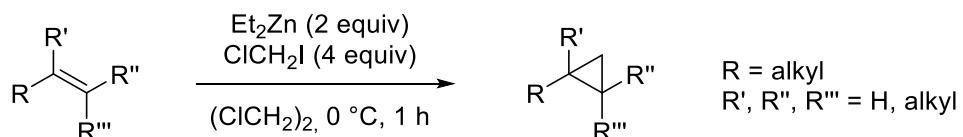
¹H NMR (400 MHz, CDCl₃) δ 3.91 (*t*_{app}, *J* = 8.0 Hz, 2H), 3.53 (dd, *J* = 8.2 Hz and 4.1 Hz, 2H), 2.59-2.46 (m, 2H, H₂), 2.08-1.93 (m, 2H), 1.96-1.74 (m, 2H), 1.71-1.56 (m, 2H), 1.42 (s, 9H)

¹³C NMR (100 MHz, CDCl₃) δ 156.5, 79.2, 52.4 (2C), 38.3, 33.1, 28.5 (3C), 24.9 (2C), 17.9

MS (EI) *m/z*: 211 (M⁺, 1), 156 (9), 138 (5), 96 (4), 94 (12), 88 (4), 83 (7), 82 (9), 79 (9), 68 (9), 67 (7), 58 (4), 57 (100), 56 (10), 55 (8), 54 (21)

4 CYCLOPROPANATION

Procedure E:

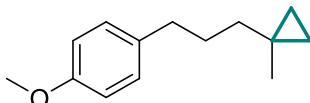


To a solution of olefin (1 equiv) in 1,2-dichloroethane at 0 °C, was added Et₂Zn (2 equiv) and then chloroiodomethane (4 equiv) was slowly added via syringe. The reaction mixture was stirred at 0 °C for 1 h

²² Vyzir, I. I.; Iminov, R. T.; Tverdokhlebov, A.; Tolmachev, A. A.; Scherbatuk, A. V.; Mykhailiuk, P. K.; Biitseva, A.; V. *Synthesis*, **2015**, 47, 3963-3971.

before the addition of a saturated aqueous solution of NH₄Cl. The organic layer was extracted with Et₂O and the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel afforded the desired cyclopropane.

1-Methoxy-4-(3-(1-methylcyclopropyl)propyl)benzene, CA484 7.1



Cyclopropane **7.1** was prepared according to Procedure **E** from 1-methoxy-4-(4-methylpent-4-en-1-yl)benzene **6.1** (50 mg, 0.27 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.35) yielded cyclopropane **7.1** as a colourless oil (45.1 mg, 0.22 mmol, 84%) contaminated by a small amount of an impurity.

Formula: C₁₄H₂₀O

Mass: 204.3 g.mol⁻¹

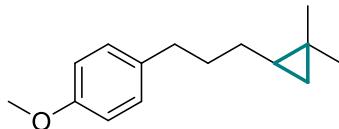
IR (neat) cm⁻¹ 1612, 1584, 1511, 1461, 1442, 1383, 1366, 1319, 1300, 1244, 1176, 1110, 1088, 1038, 1009, 935, 909

¹H NMR (400 MHz, CDCl₃) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 3.80 (s, 3H), 2.55 (*t_{app}*, *J* = 7.8 Hz, 2H), 1.73 - 1.63 (m, 2H), 1.31-1.23 (m, 2H), 1.03 (s, 3H), 0.23 (brd_{app}, *J* = 6.8 Hz, 4H)

¹³C NMR (100 MHz, CDCl₃) δ 157.7, 135.1, 129.3 (2C), 113.7 (2C), 55.3, 39.1, 35.3, 29.2, 22.8, 15.3, 13.0 (2C)

MS (EI) *m/z*: 205 (M+1, 2), 204 (16), 189 (7), 175 (8), 161 (8), 148 (6), 147 (36), 135 (9), 134 (55), 122 (11), 121 (100), 119 (5), 91 (12), 78 (7), 77 (10), 65 (4), 55 (4)

1-(3-(2,2-Dimethylcyclopropyl)propyl)-4-methoxybenzene, 7.2



Cyclopropane **7.2** was prepared according to Procedure **E** from 1-methoxy-4-(5-methylhex-4-en-1-yl)benzene **6.2** (50 mg, 0.25 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 100:0 to 50:0.35) yielded quantitatively cyclopropane **7.2** as a colourless oil (56.8 mg, 0.25 mmol, quant.).

Formula: C₁₅H₂₂O

Mass: 218.3 g.mol⁻¹

IR (neat): 1613, 1584, 1511, 1456, 1442, 1419, 1376, 1300, 1244, 1177, 1111, 1039 cm⁻¹

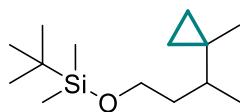
¹H NMR (400 MHz, CDCl₃) δ 7.11 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.58 (td, *J* = 7.9 Hz and 2.9 Hz, 2H), 1.72-1.61 (m, 2H), 1.42-1.24 (m, 2H), 1.02 (s, 3H), 1.01 (s, 3H), 0.48 (m, 1H), 0.36 (dd, *J* = 8.4 Hz and 4.0 Hz, 1H), (-)0.13 (*t_{app}*, *J* = 4.7 Hz, 1H)

¹³C NMR (100 MHz, CDCl₃) δ 157.7, 135.1, 129.3 (2C), 113.7 (2C), 55.3, 35.0, 32.4, 29.5, 27.7, 24.7, 20.0, 19.8, 15.4

MS (EI) *m/z*: 219 (M+1, 3), 218 (M⁺, 21), 162 (21), 161 (5), 148 (5), 147 (41), 135 (8), 134 (53), 122 (11), 121 (100), 119 (4), 91 (12), 78 (7), 77 (10), 69 (5), 55 (8)

HRMS: Calculated for C₁₅H₂₂OH [M+H]⁺: 219.1743, Found: 219.1743

tert-Butyldimethyl(3-(1-methylcyclopropyl)butoxy)silane, 7.3



Cyclopropane **7.3** was prepared according to Procedure **E** *tert*-butyl(3-cyclopropylbutoxy)dimethylsilane **1.10** (50 mg, 0.22 mmol). Purification by flash chromatography on silica gel (PE/Et₂O 50:0.1) yielded cyclopropane **7.3** as a colourless oil (43.6 mg, 0.18 mmol, 82%).

Formula: C₁₄H₃₀OSi

Mass: 242.5 g.mol⁻¹

IR (neat): 1472, 1462, 1429, 1387, 1361, 1254, 1096, 1007, 982, 93 cm⁻¹

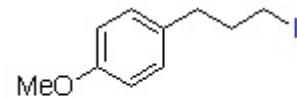
¹H NMR (400 MHz, CDCl₃) δ 3.70-3.58 (m, 2H), 1.69 (m, 1H), 1.45 (m, 1H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.91 - 0.87 (m, 3H), 0.89 (s, 9H), 0.84-0.76 (m, 1H), 0.30-0.13 (m, 4H), 0.04 (s, 6H)

¹³C NMR (100 MHz, CDCl₃) δ 61.9, 38.1, 37.9, 26.1 (3C), 19.6, 18.4, 17.8, 17.6, 14.1, 12.9, -5.2, -5.3

MS (EI) *m/z*: 186 (M+1-57, -*t*-Bu, 11), 185 (M-57, -*t*-Bu, 66), 157 (12), 155 (38), 143 (11), 129 (19), 127 (26), 115 (12), 114 (7), 113 (63), 109 (8), 102 (5), 101 (45), 99 (14), 95 (10), 89 (29), 85 (9), 82 (14), 75 (100), 73 (36), 67 (14), 59 (20), 55 (19)

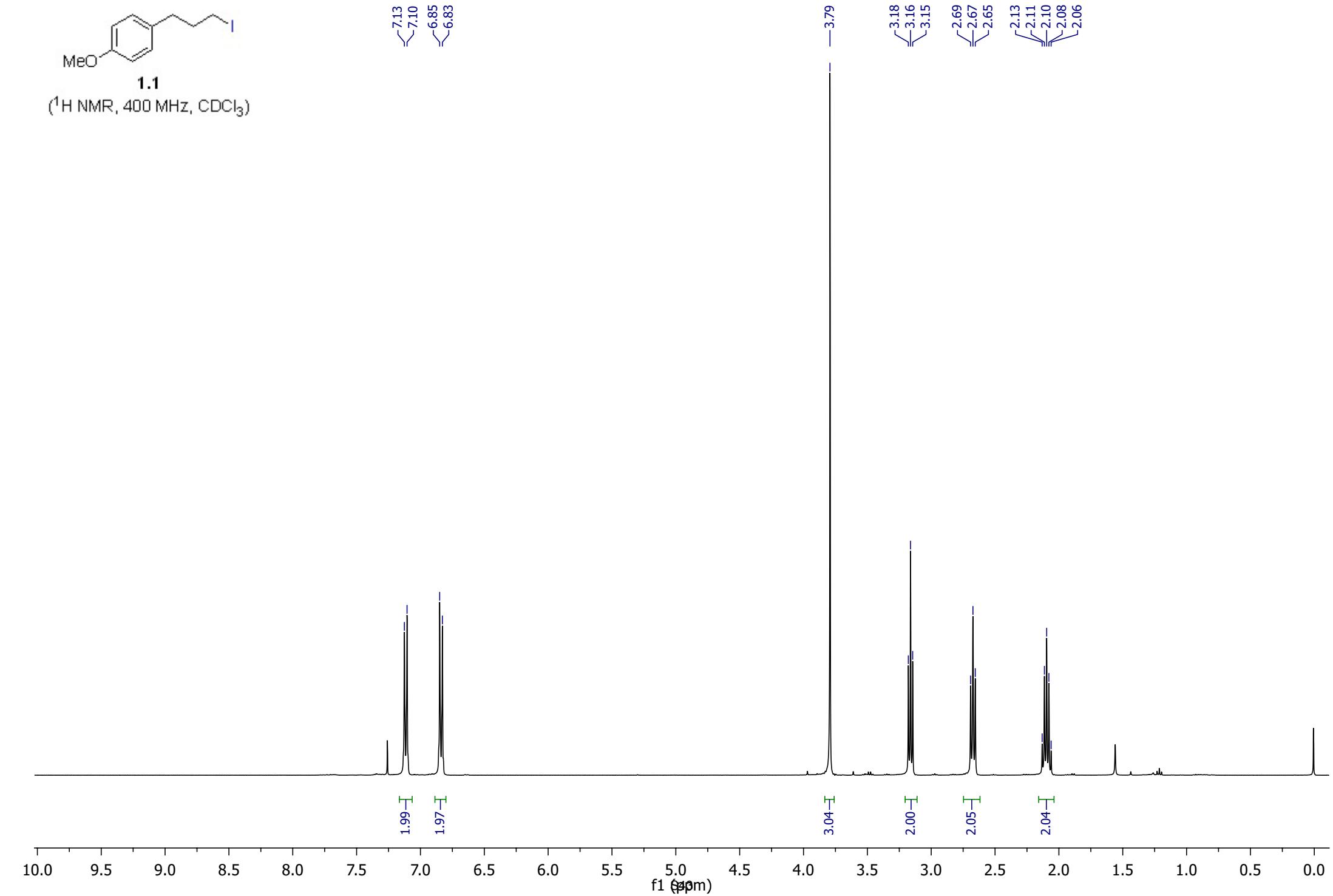
HRMS: Calculated for C₁₄H₃₀OSiH [M+H]⁺: 243.2139, Found: 243.2141

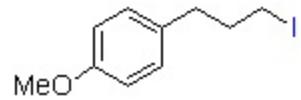
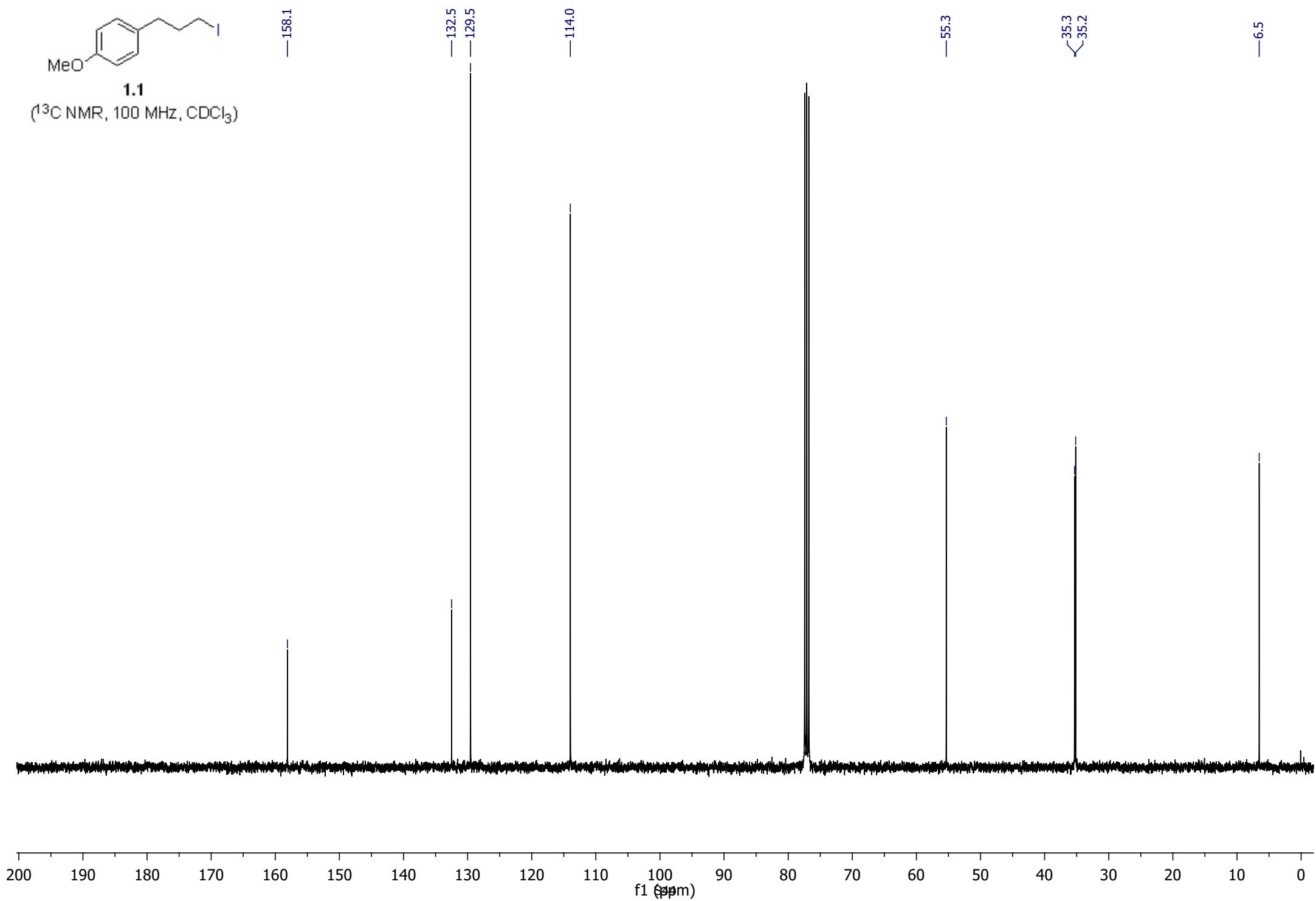
ⁱ Love, B. E.; Jones, E. G. *J. Org. Chem.*, **1999**, 64, 3755-3756

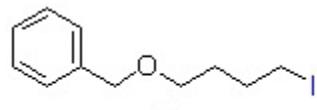


1.1

(^1H NMR, 400 MHz, CDCl_3)

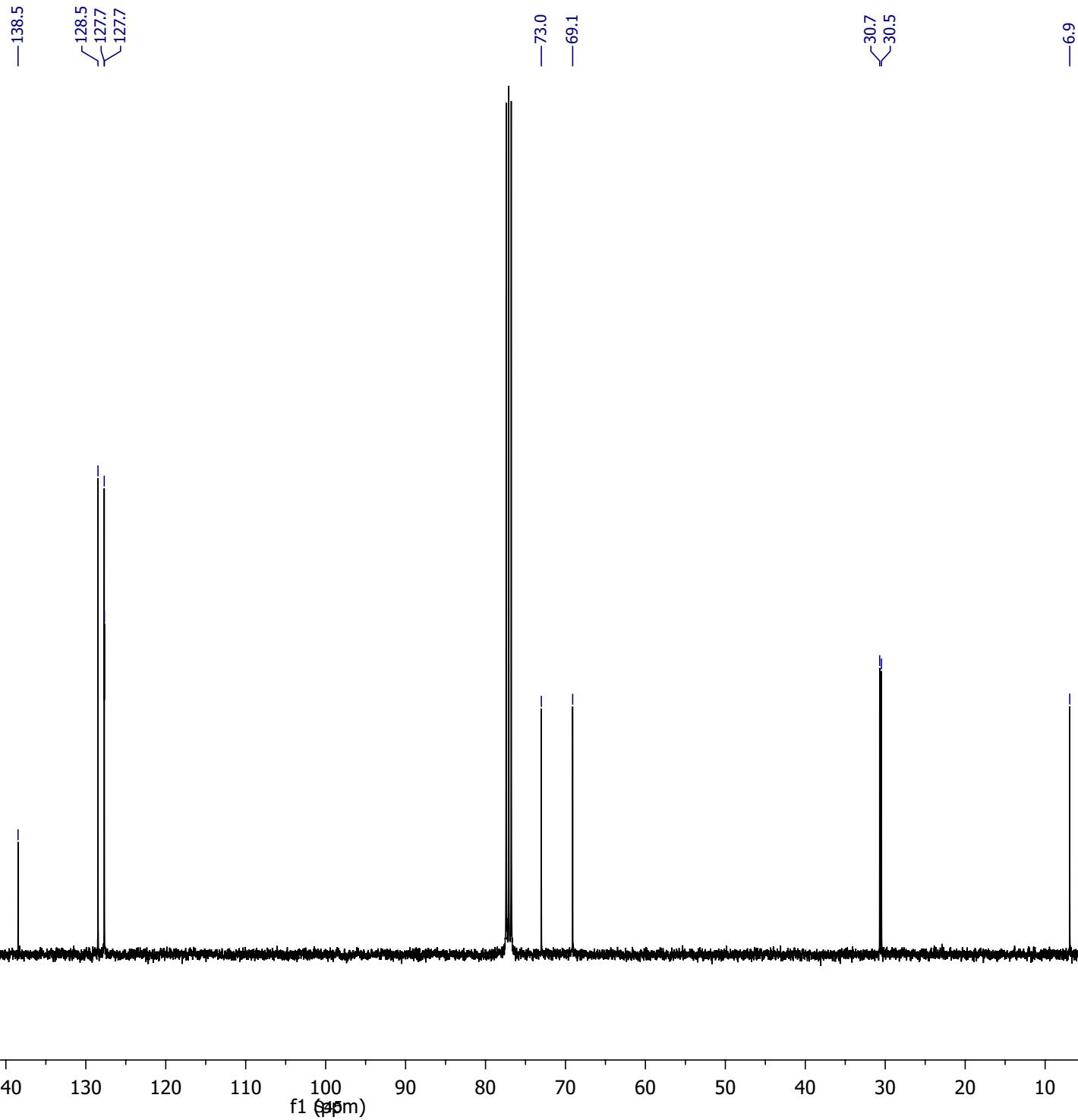


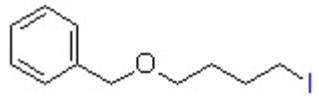
**1.1**(^{13}C NMR, 100 MHz, CDCl_3)



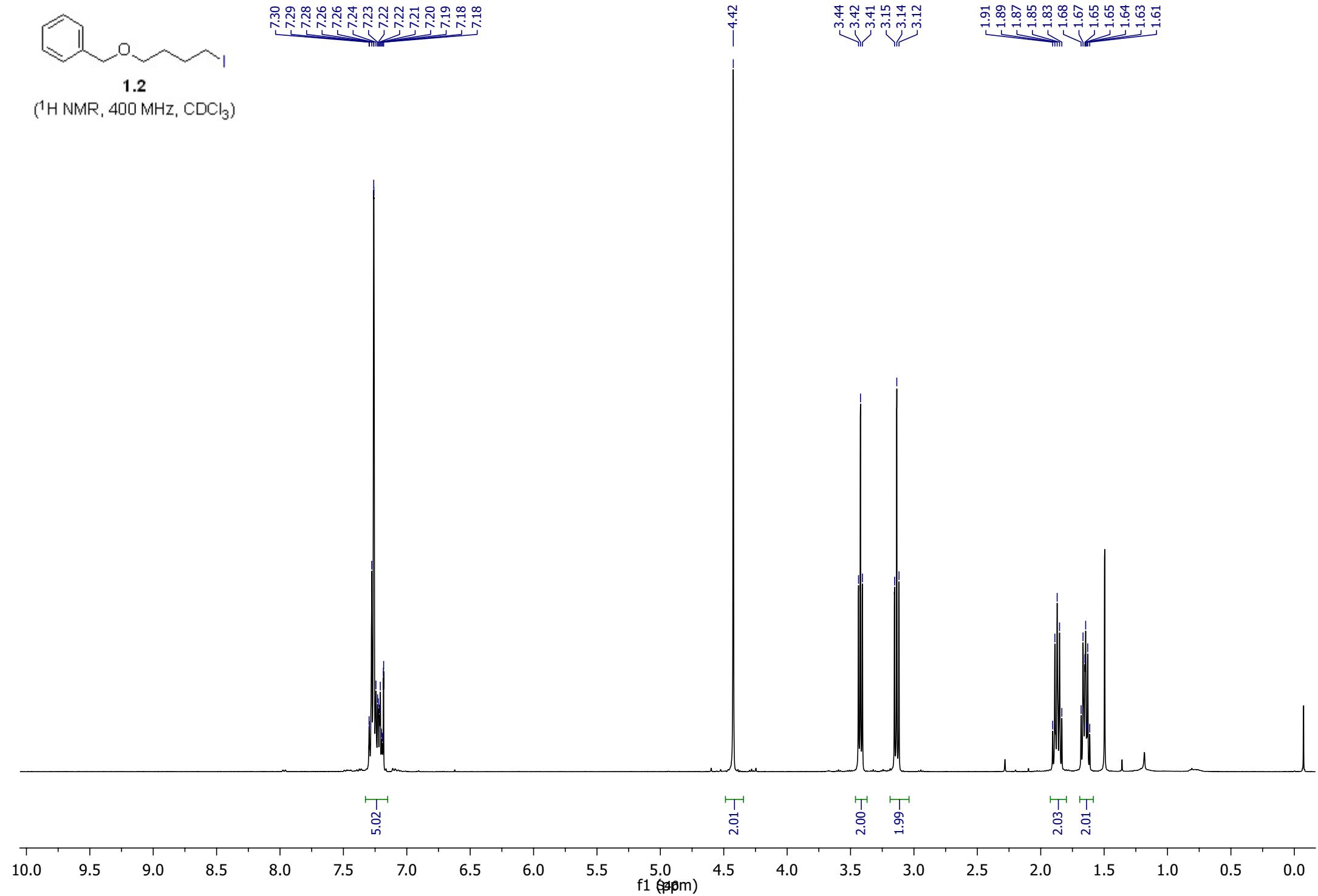
1.2

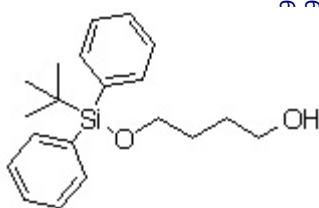
(^{13}C NMR, 100 MHz, CDCl_3)





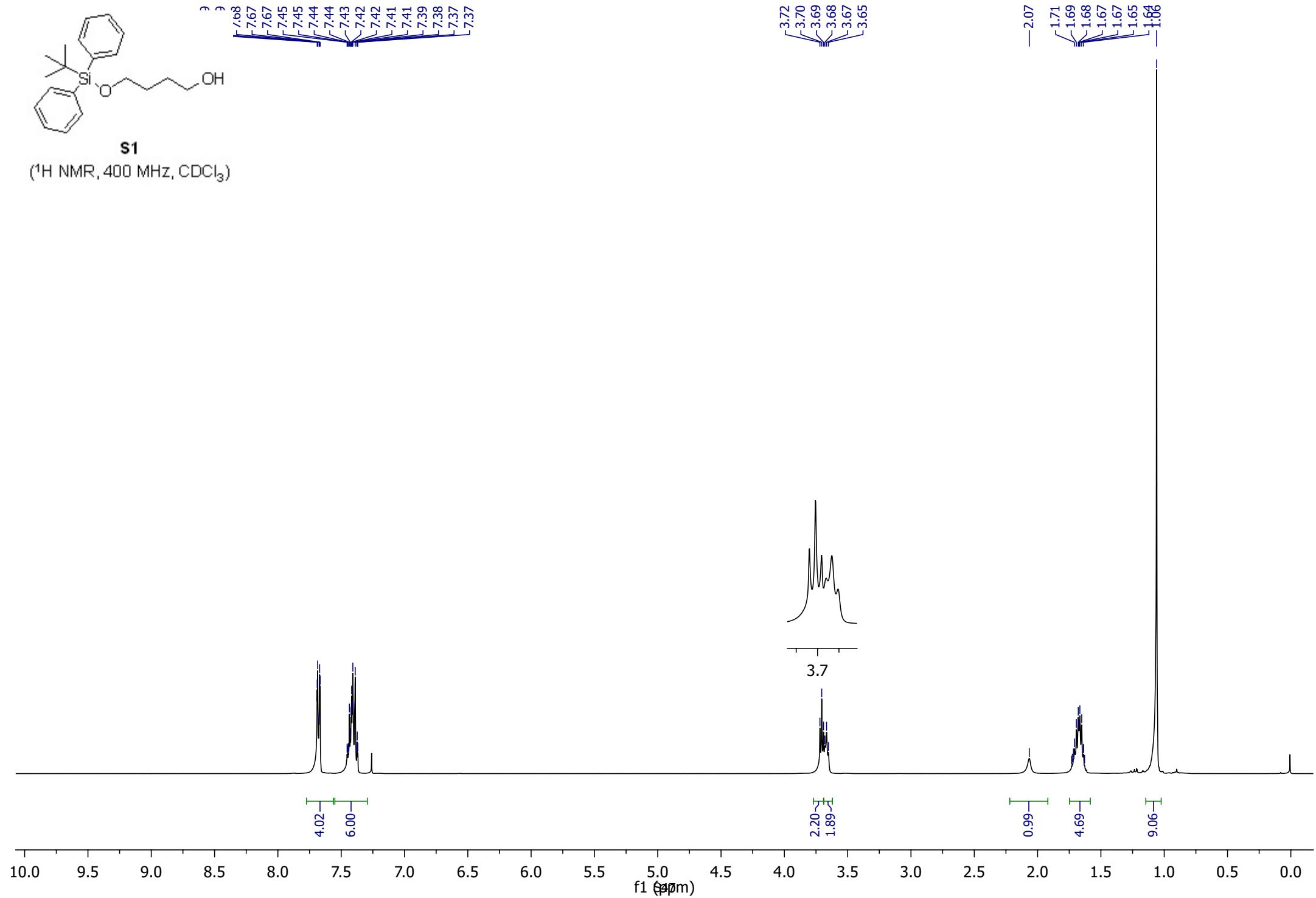
1.2
(^1H NMR, 400 MHz, CDCl_3)

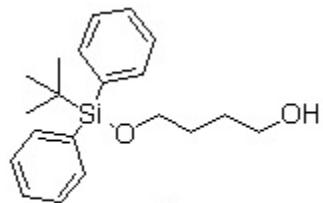




S1

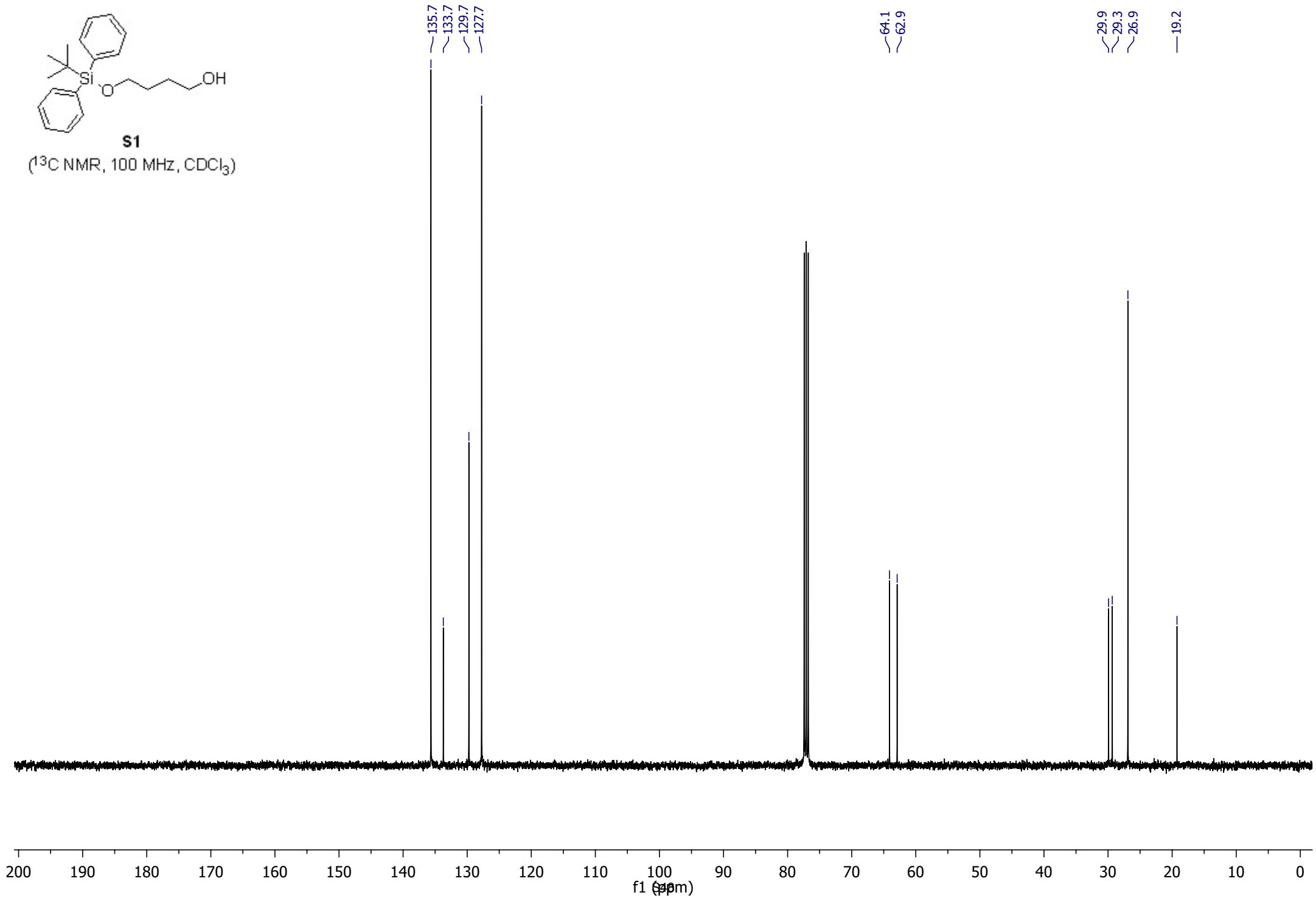
(^1H NMR, 400 MHz, CDCl_3)

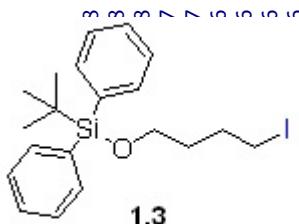




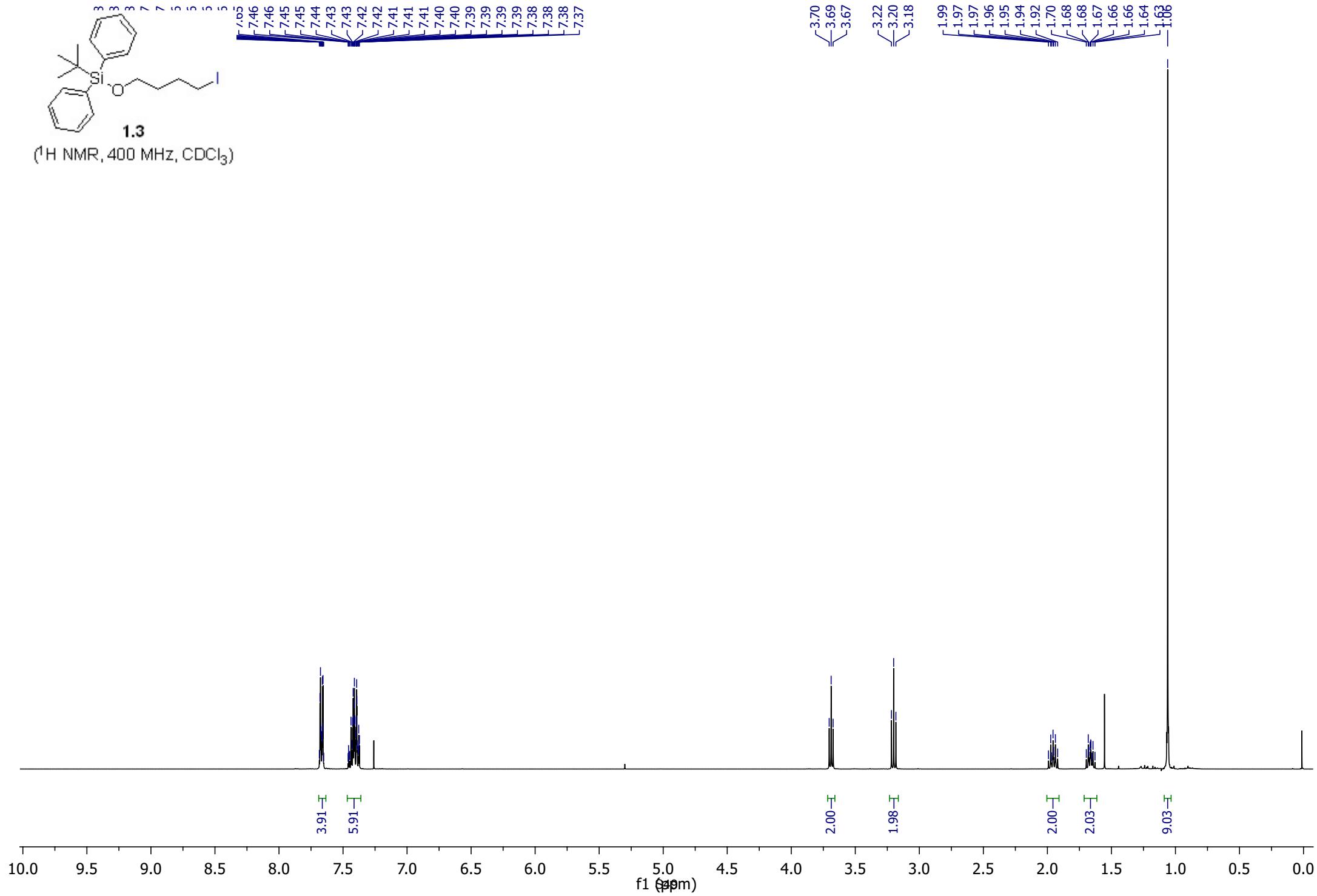
S1

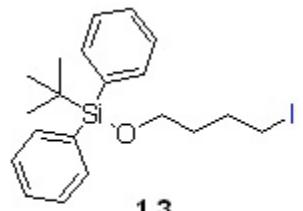
(^{13}C NMR, 100 MHz, CDCl_3)



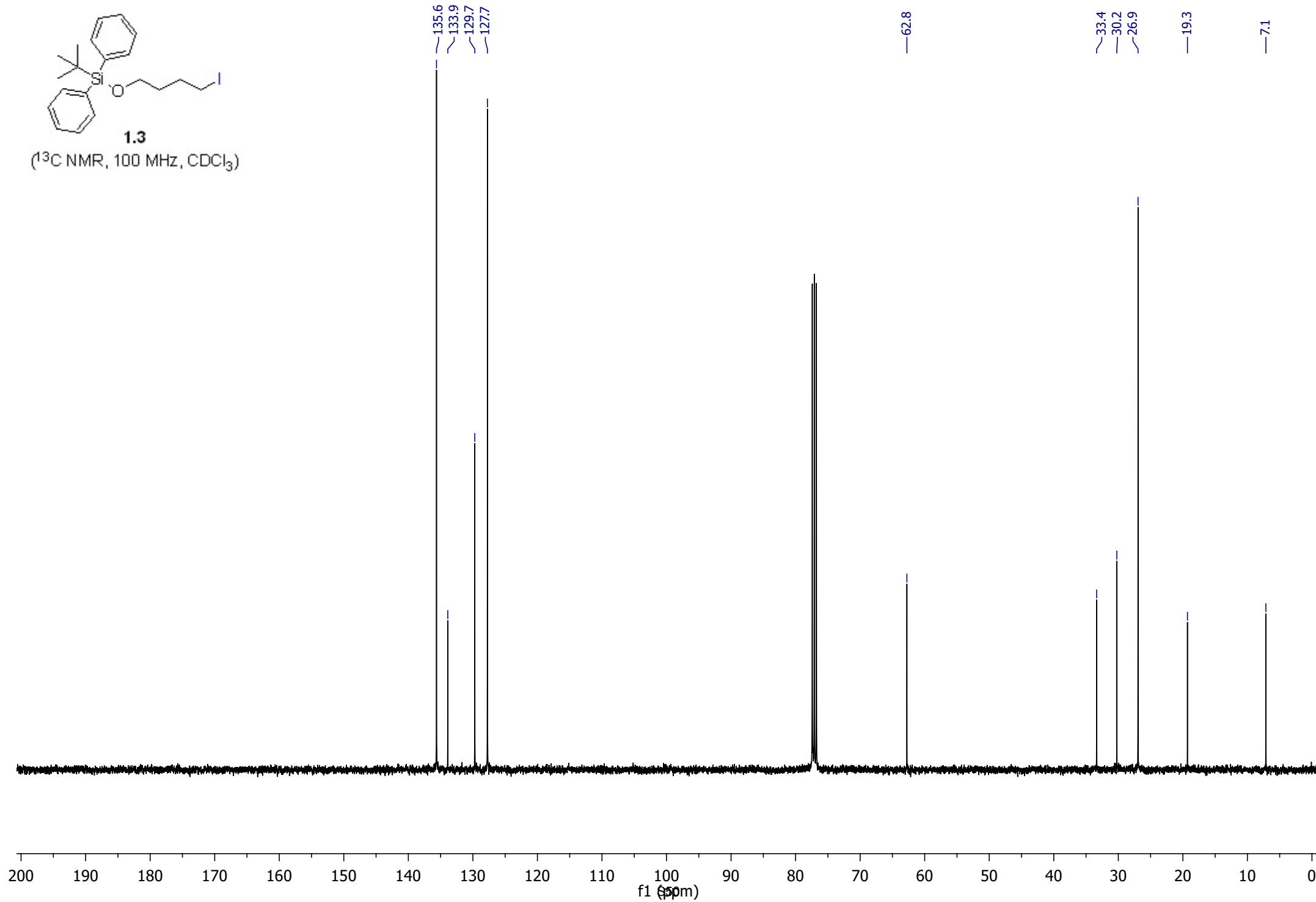


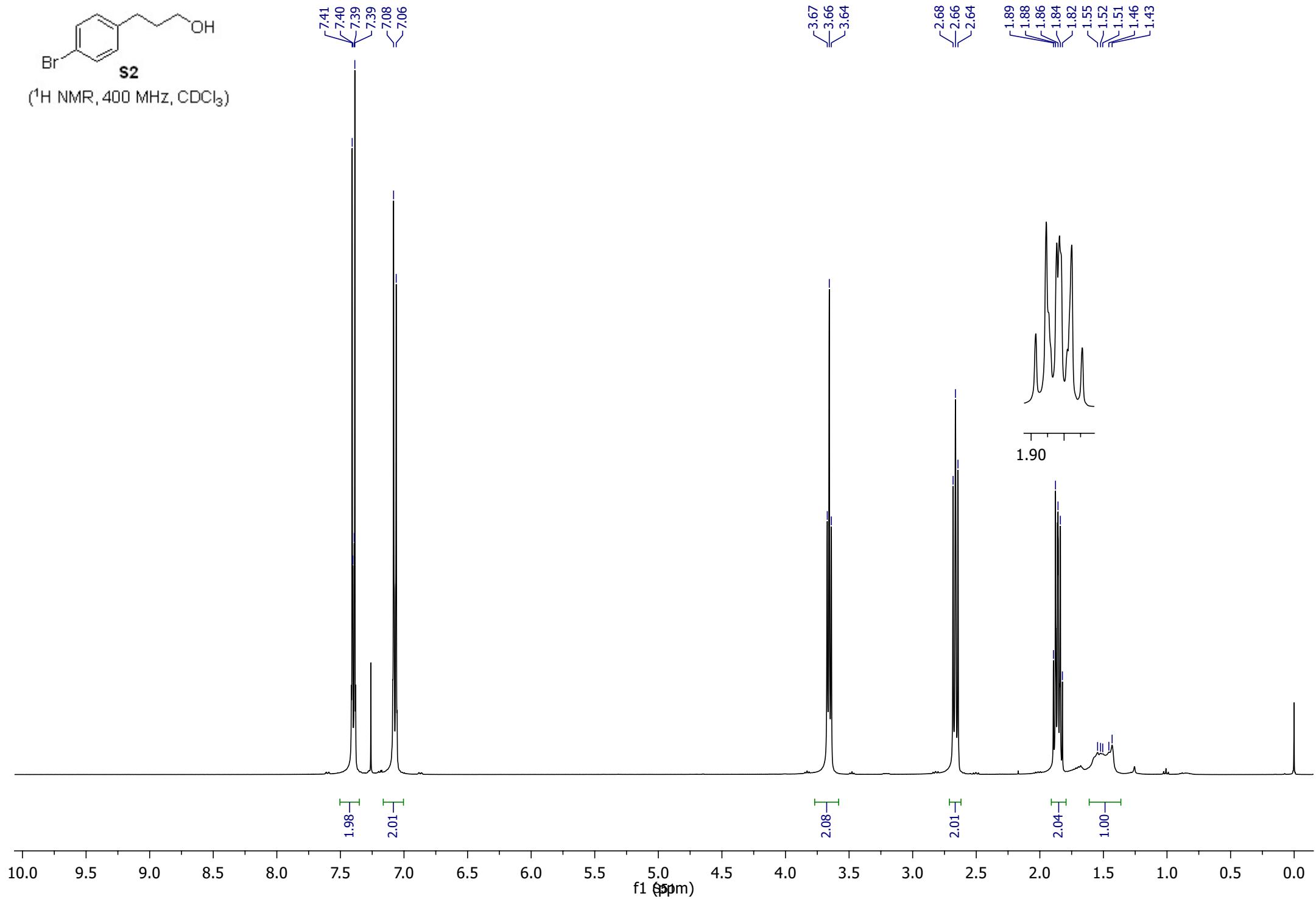
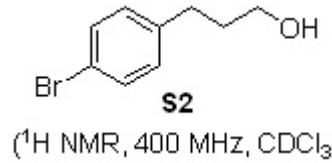
(^1H NMR, 400 MHz, CDCl_3)

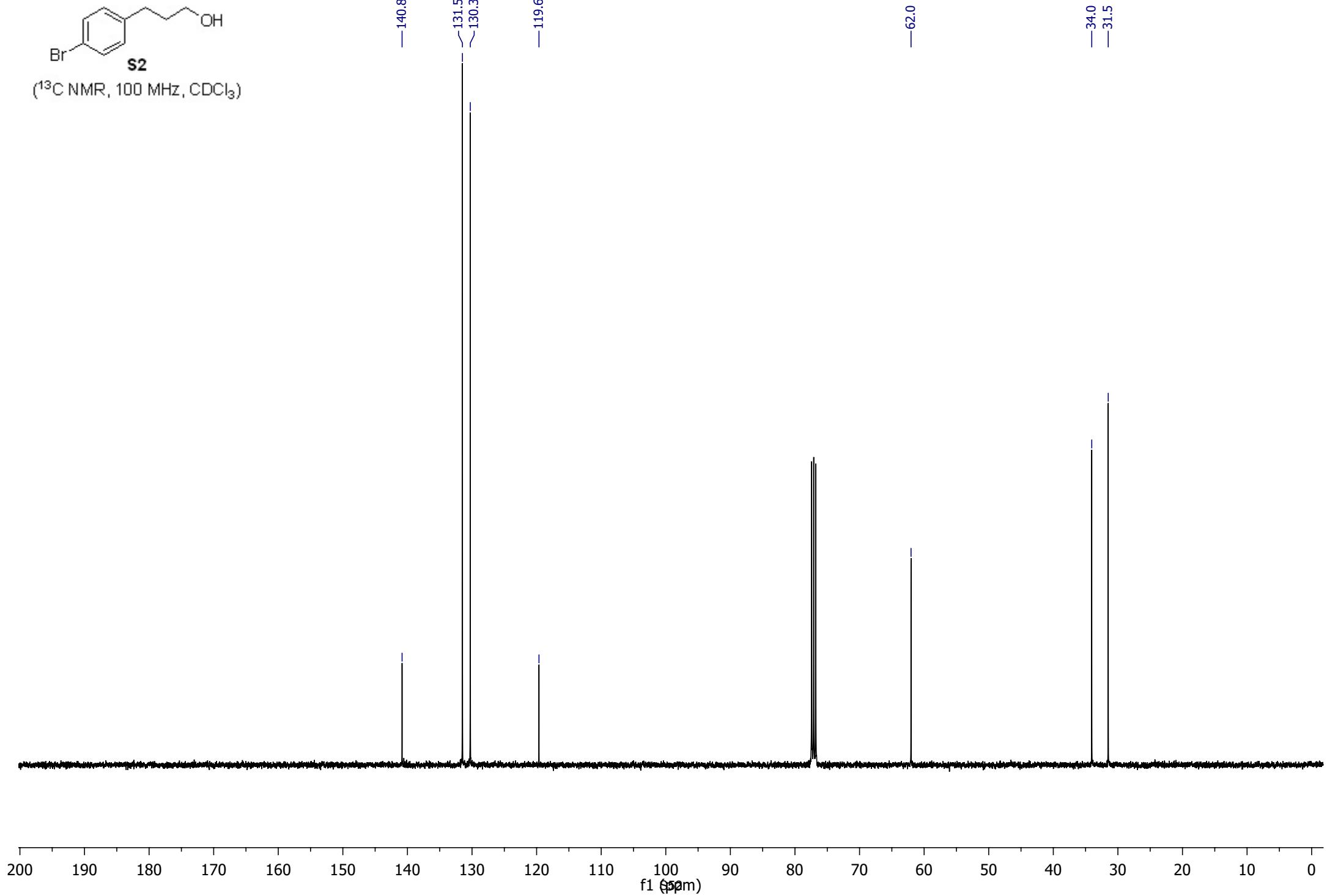
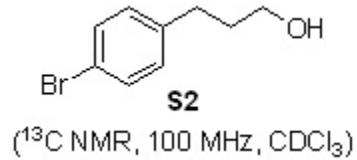


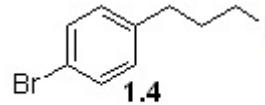


(¹³C NMR, 100 MHz, CDCl₃)

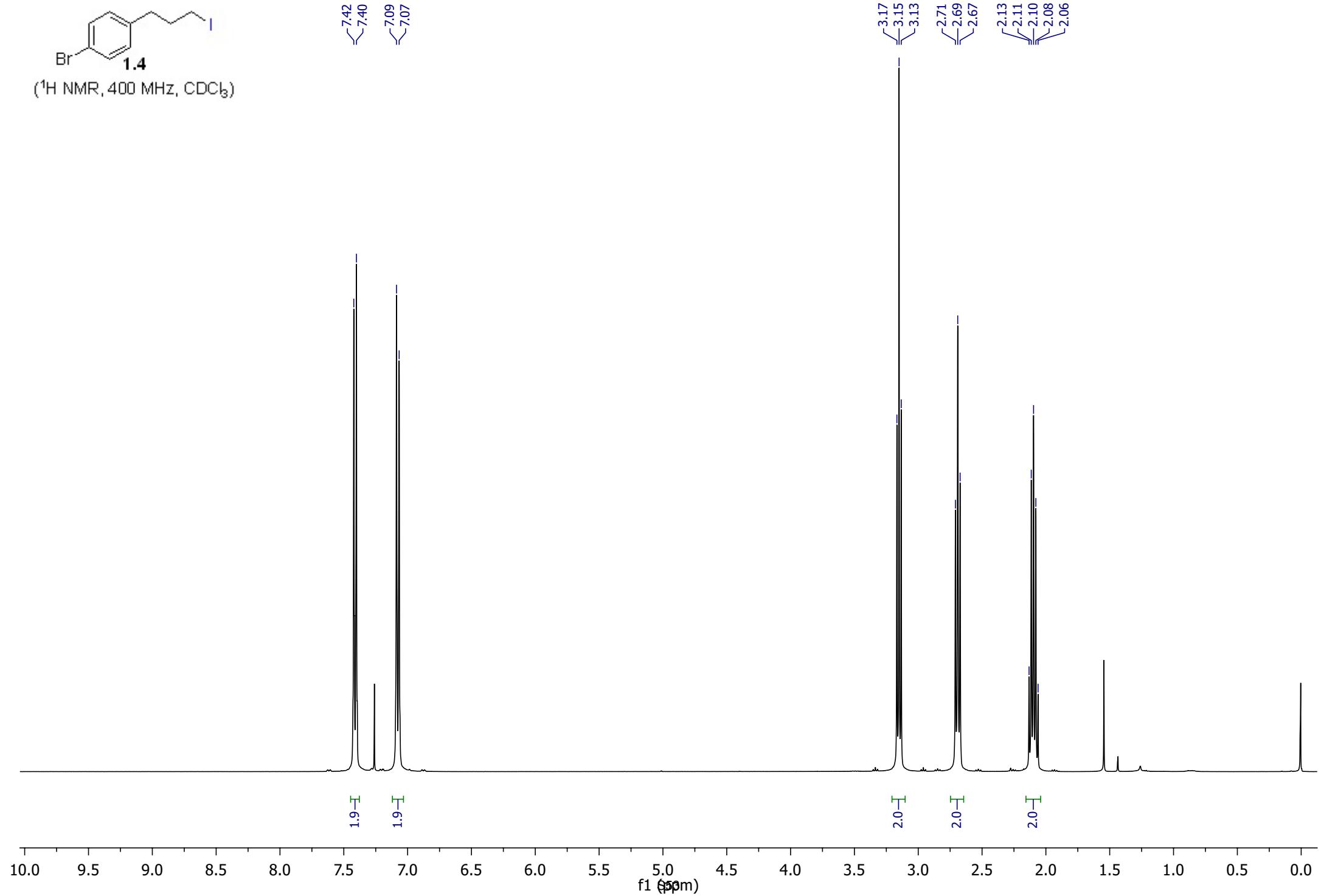


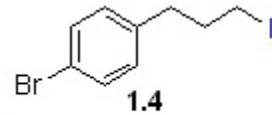




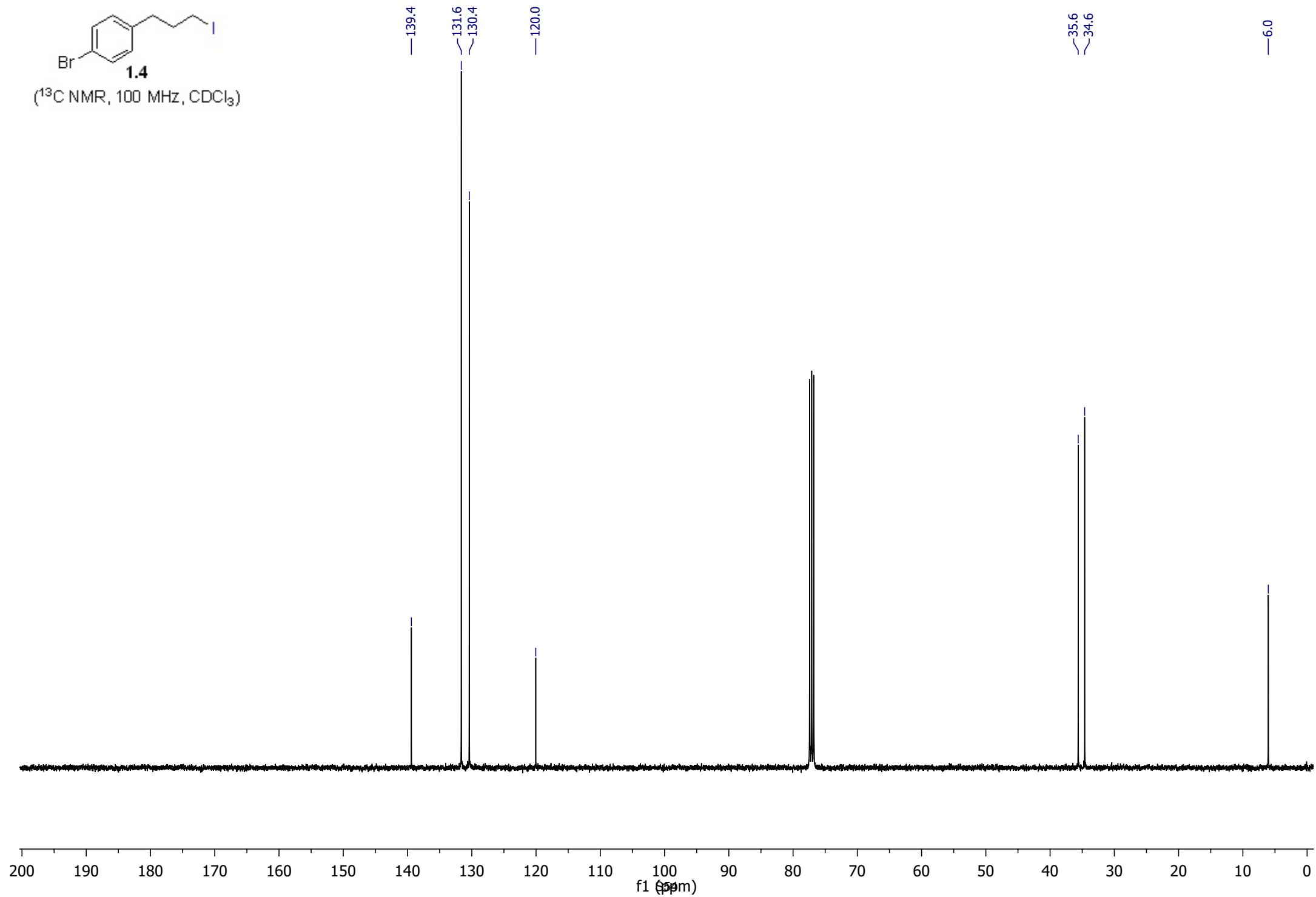


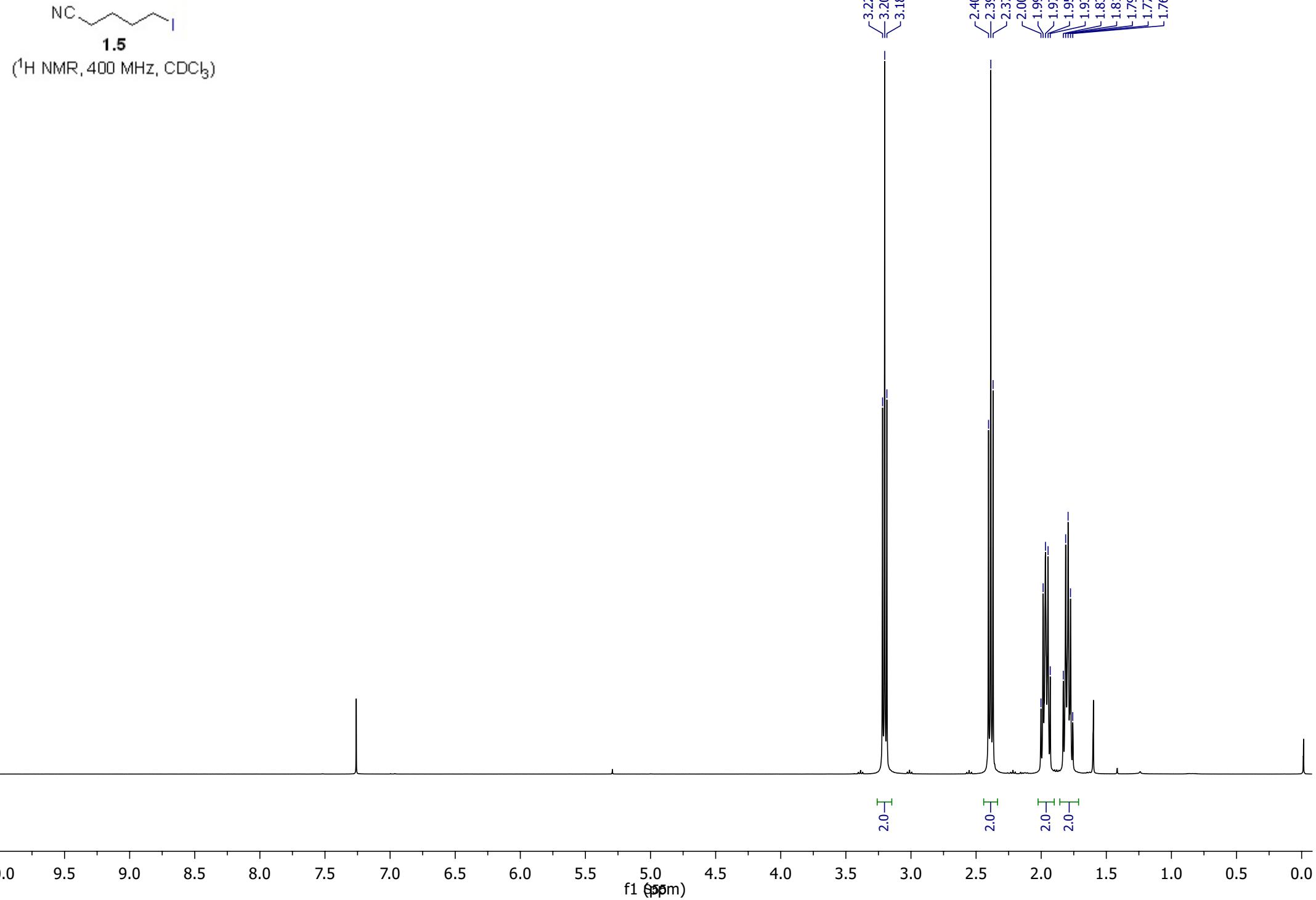
(^1H NMR, 400 MHz, CDCl_3)

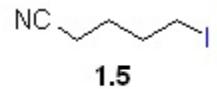




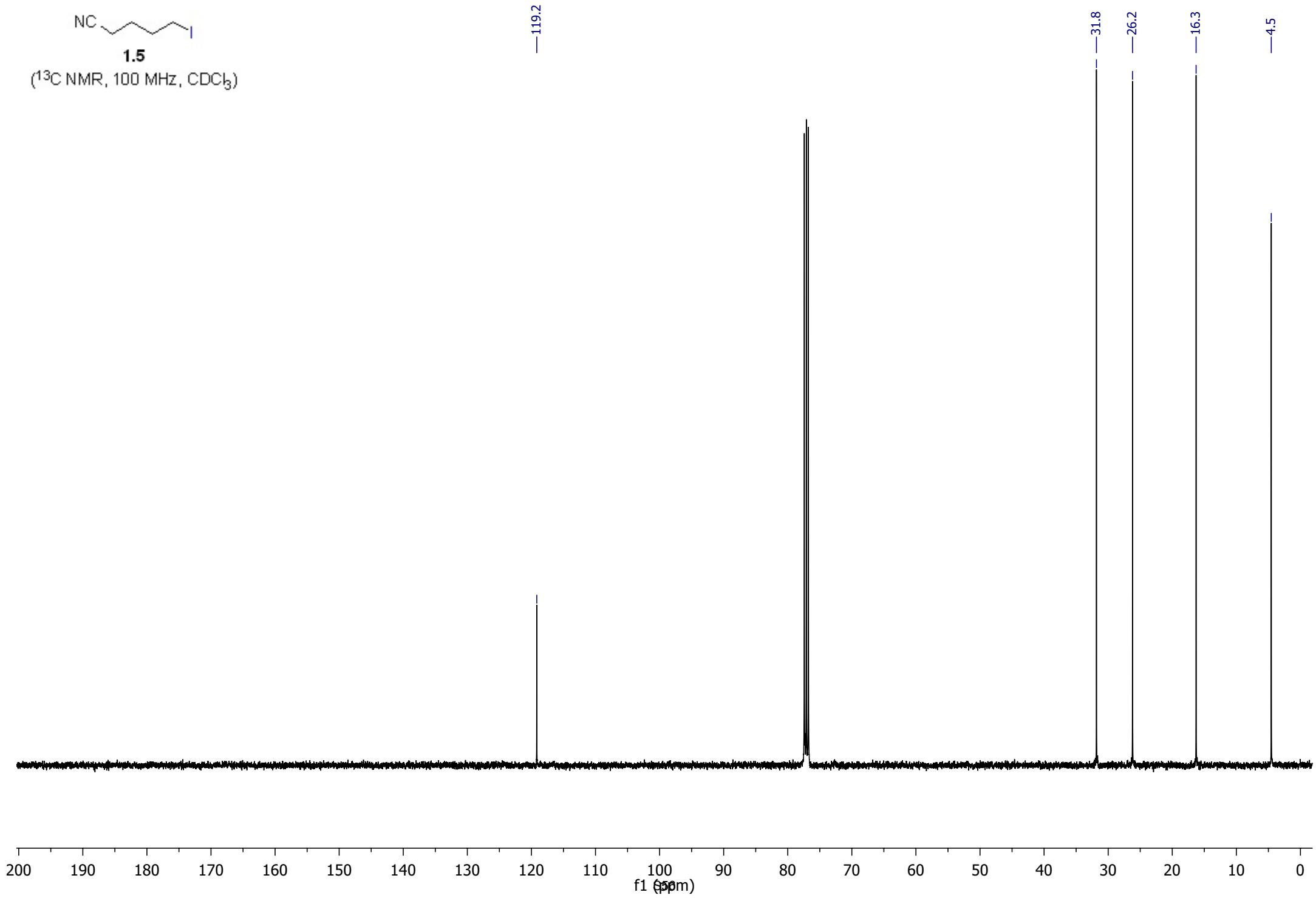
(^{13}C NMR, 100 MHz, CDCl_3)

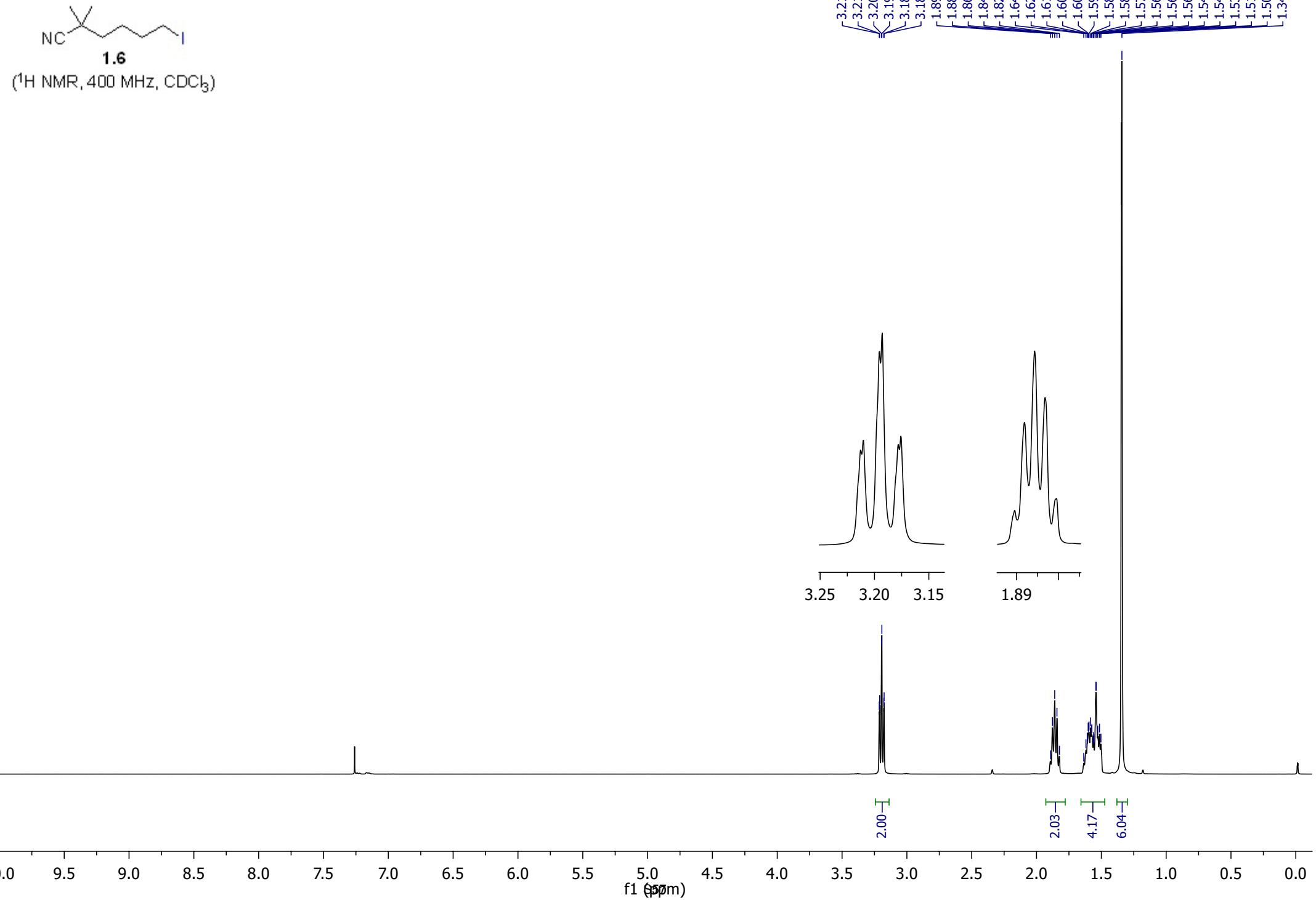


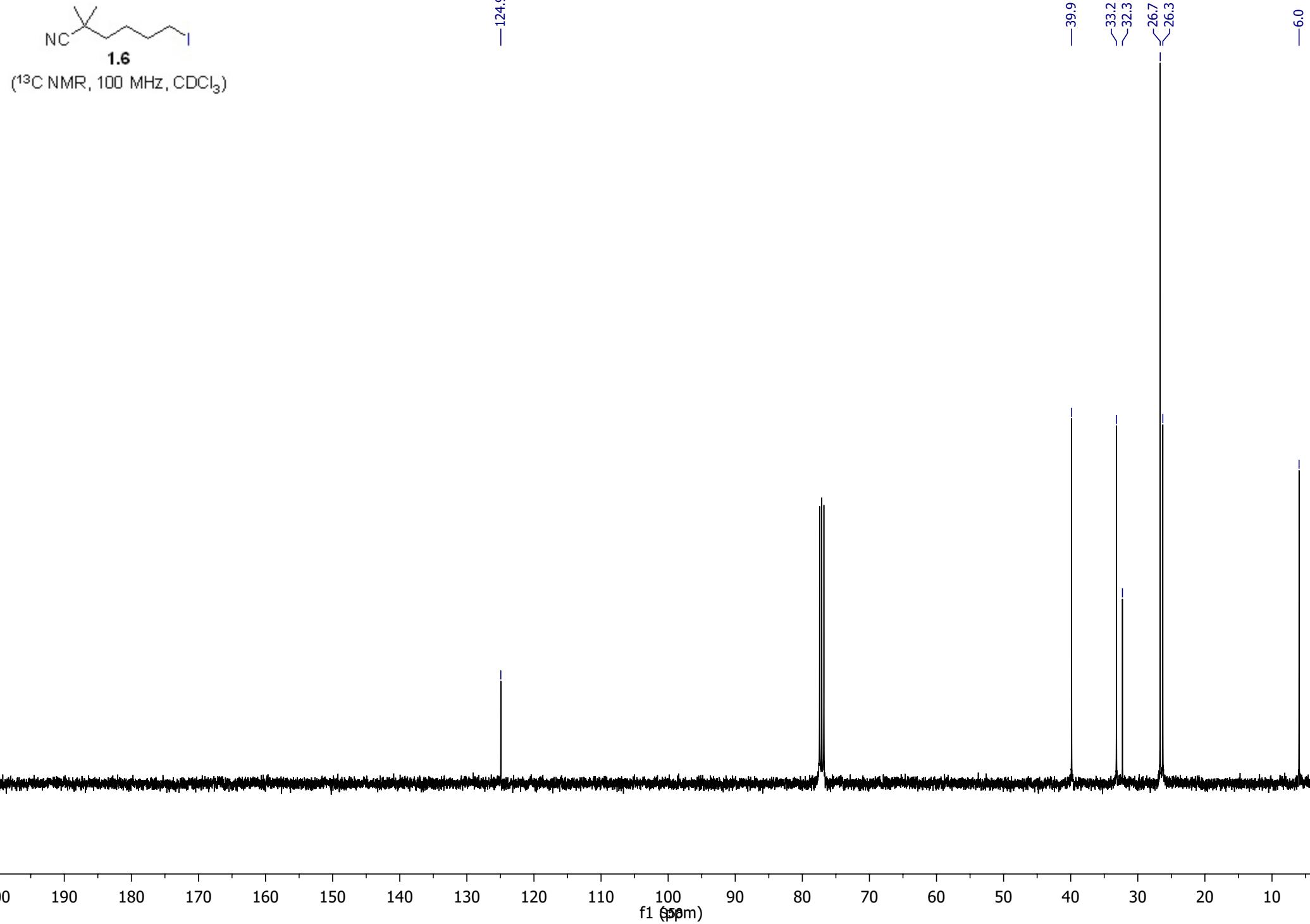


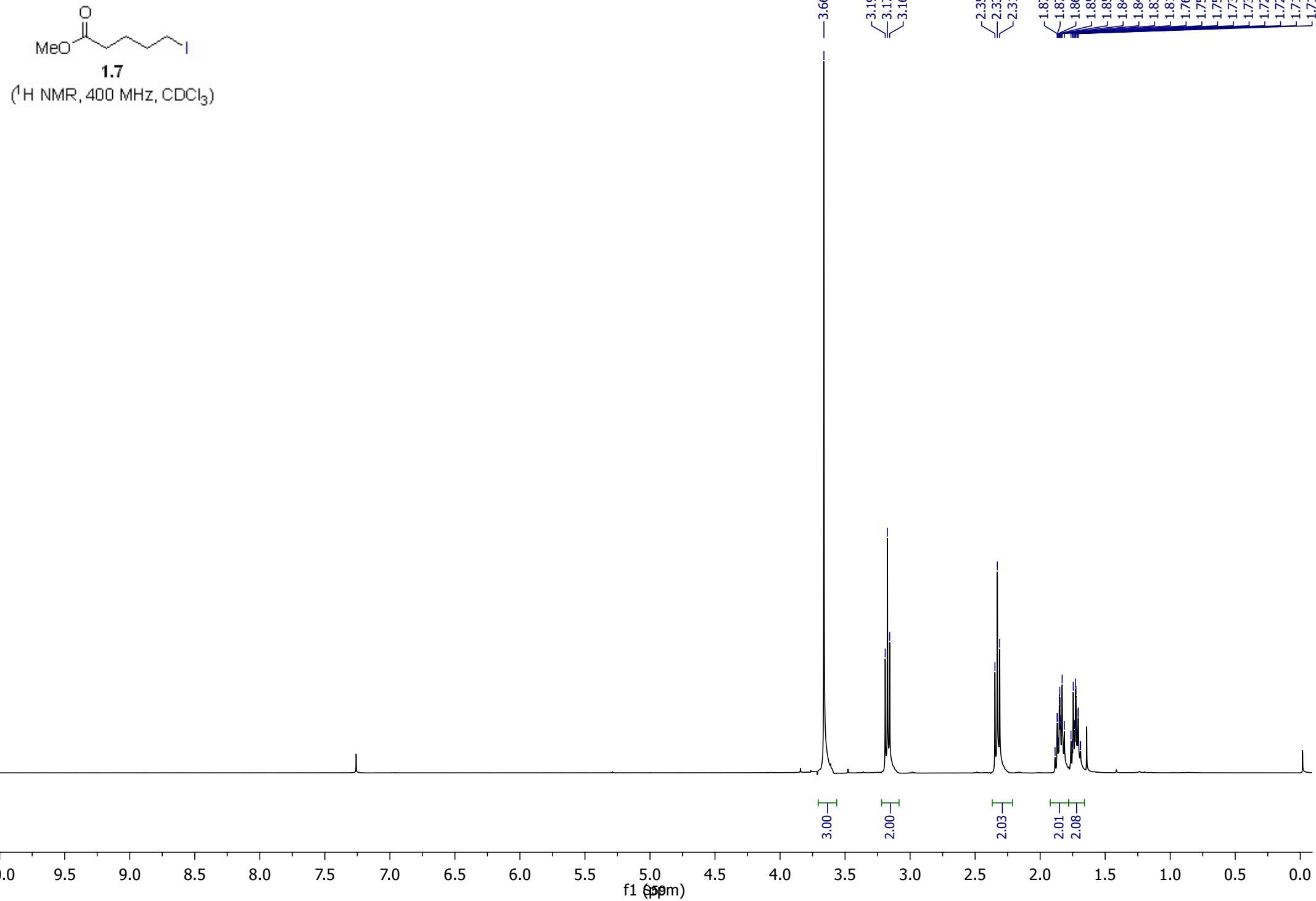


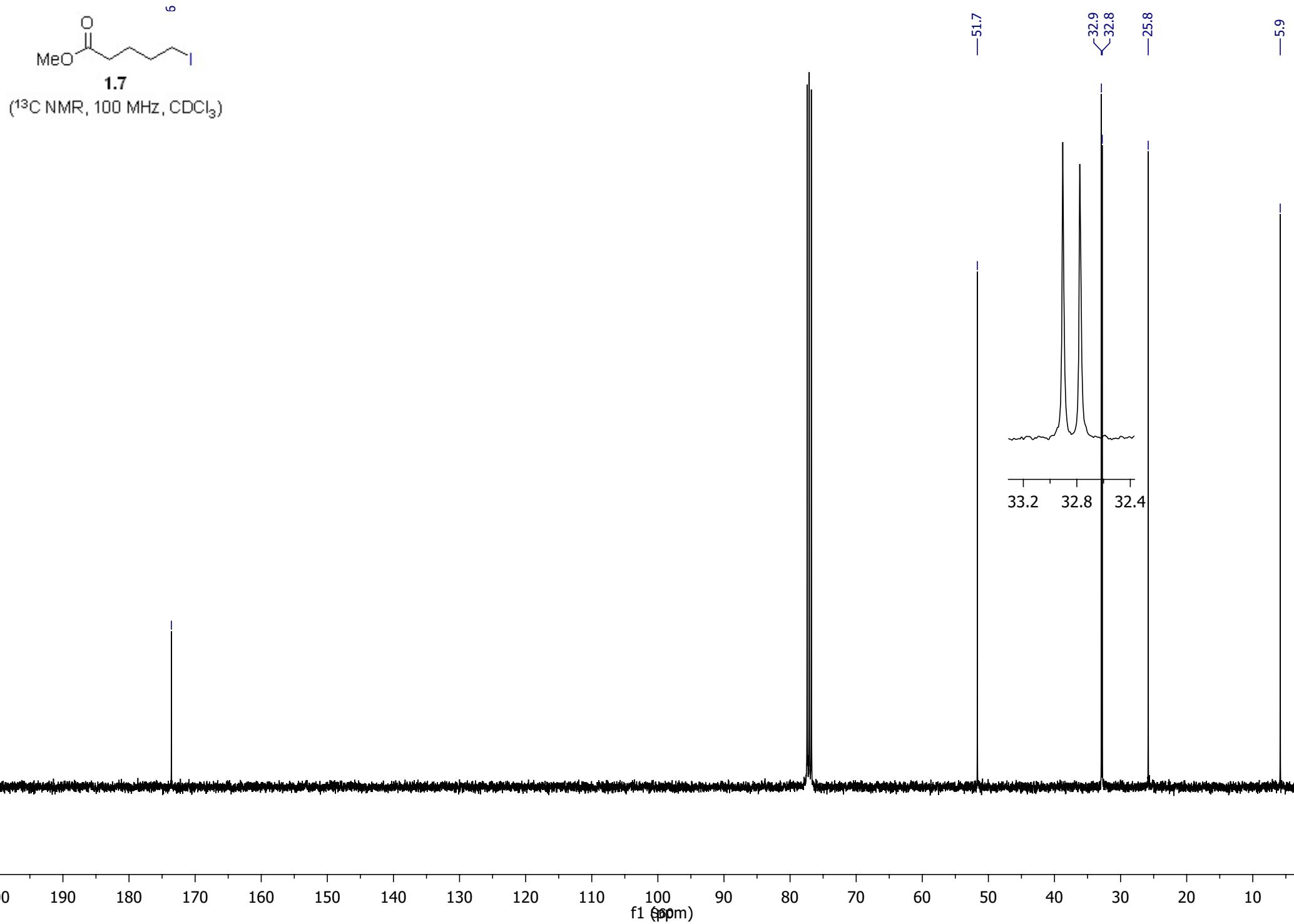
(^{13}C NMR, 100 MHz, CDCl_3)



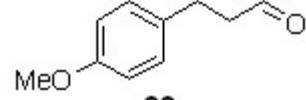








9.82
9.82
9.81



(^1H NMR, 400 MHz, CDCl_3)

7.13
7.11
6.85
6.83

3.79

2.93
2.91
2.89
2.77
2.75
2.73

1.00

2.12
2.09

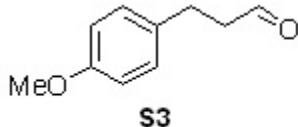
3.16

2.07
2.03

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

—201.7



(^{13}C NMR, 100 MHz, CDCl_3)

—158.0

—132.3

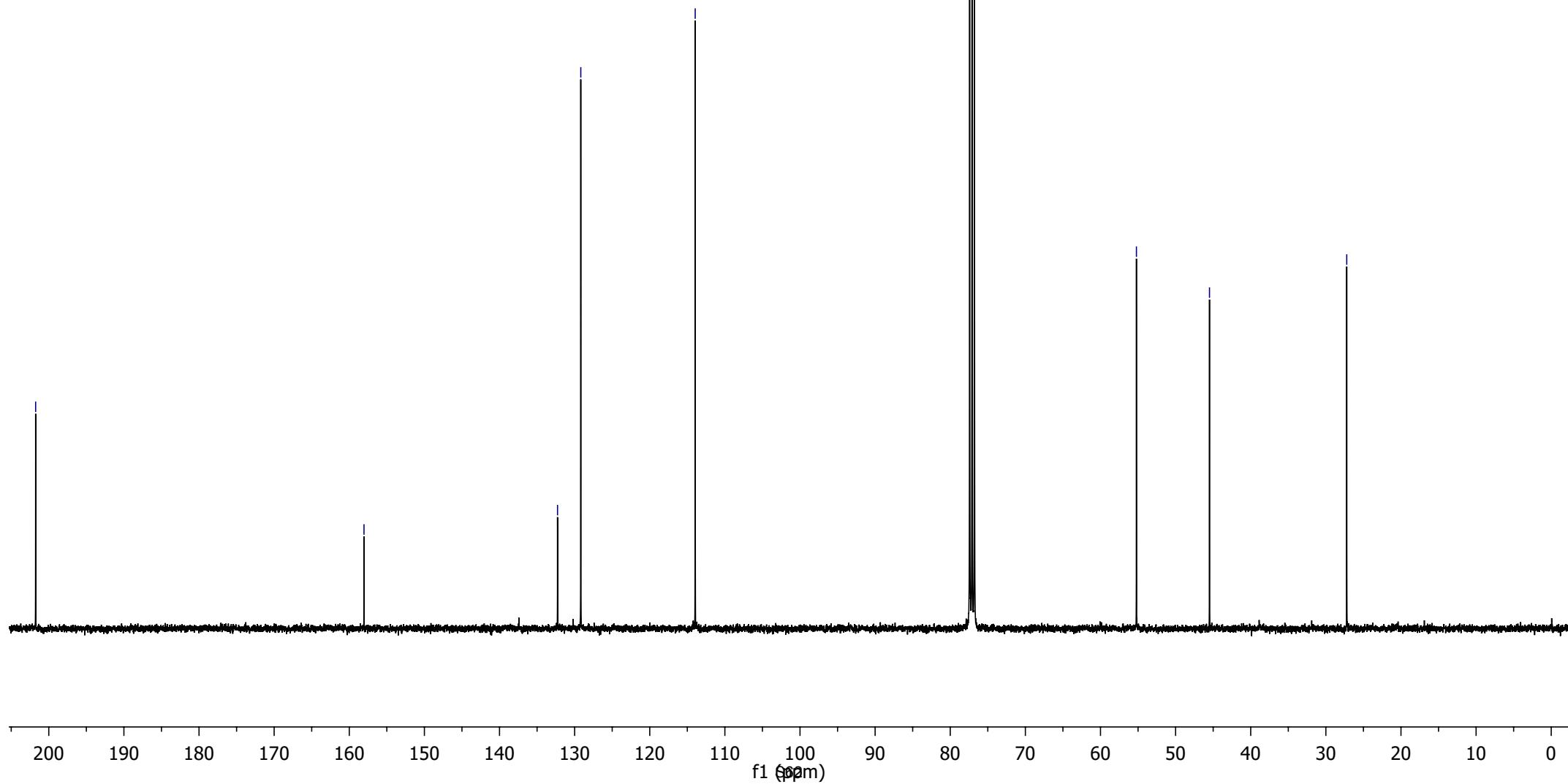
—129.2

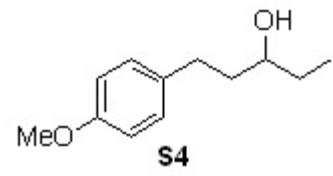
—114.0

—55.2

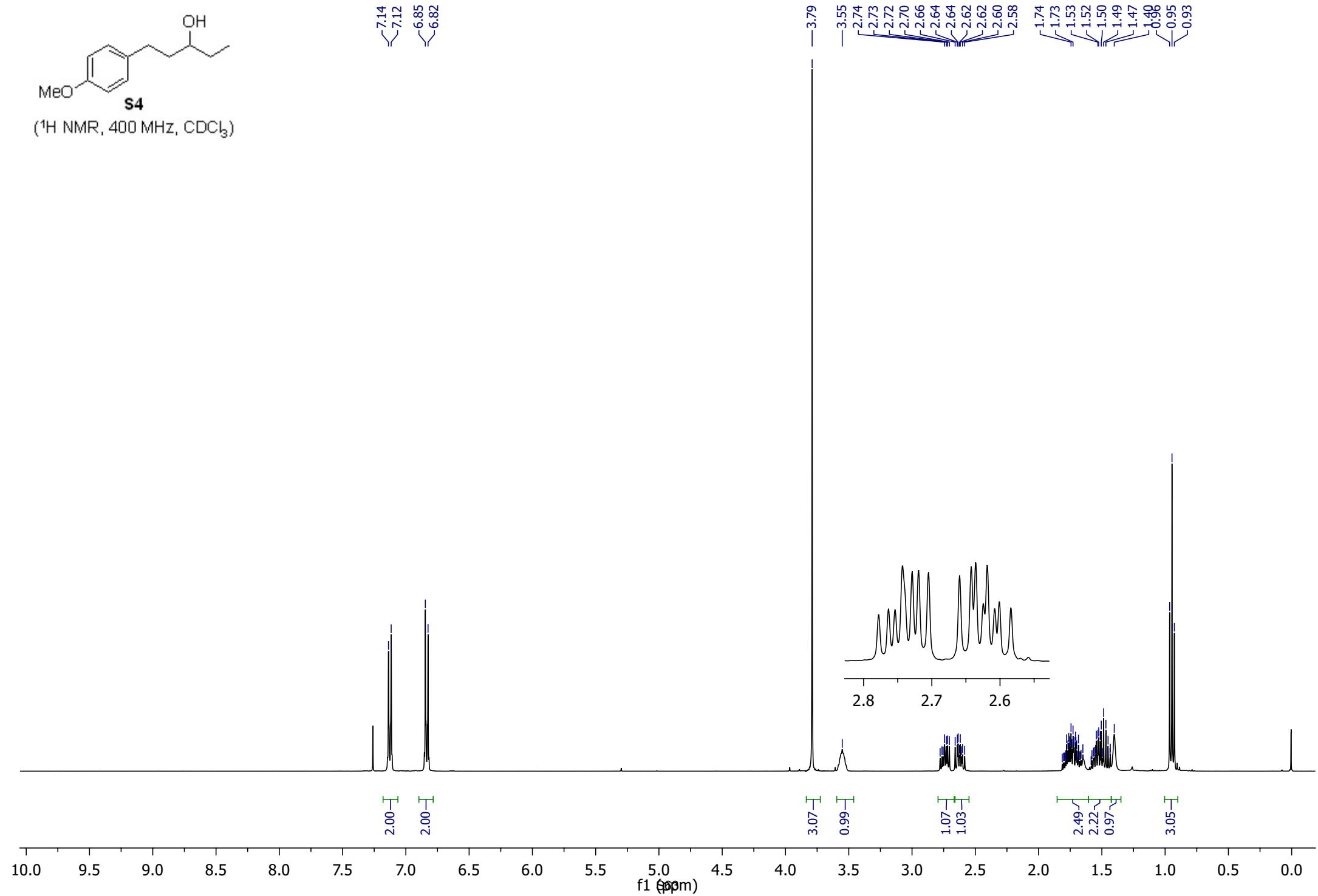
—45.5

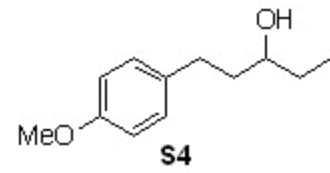
—27.2



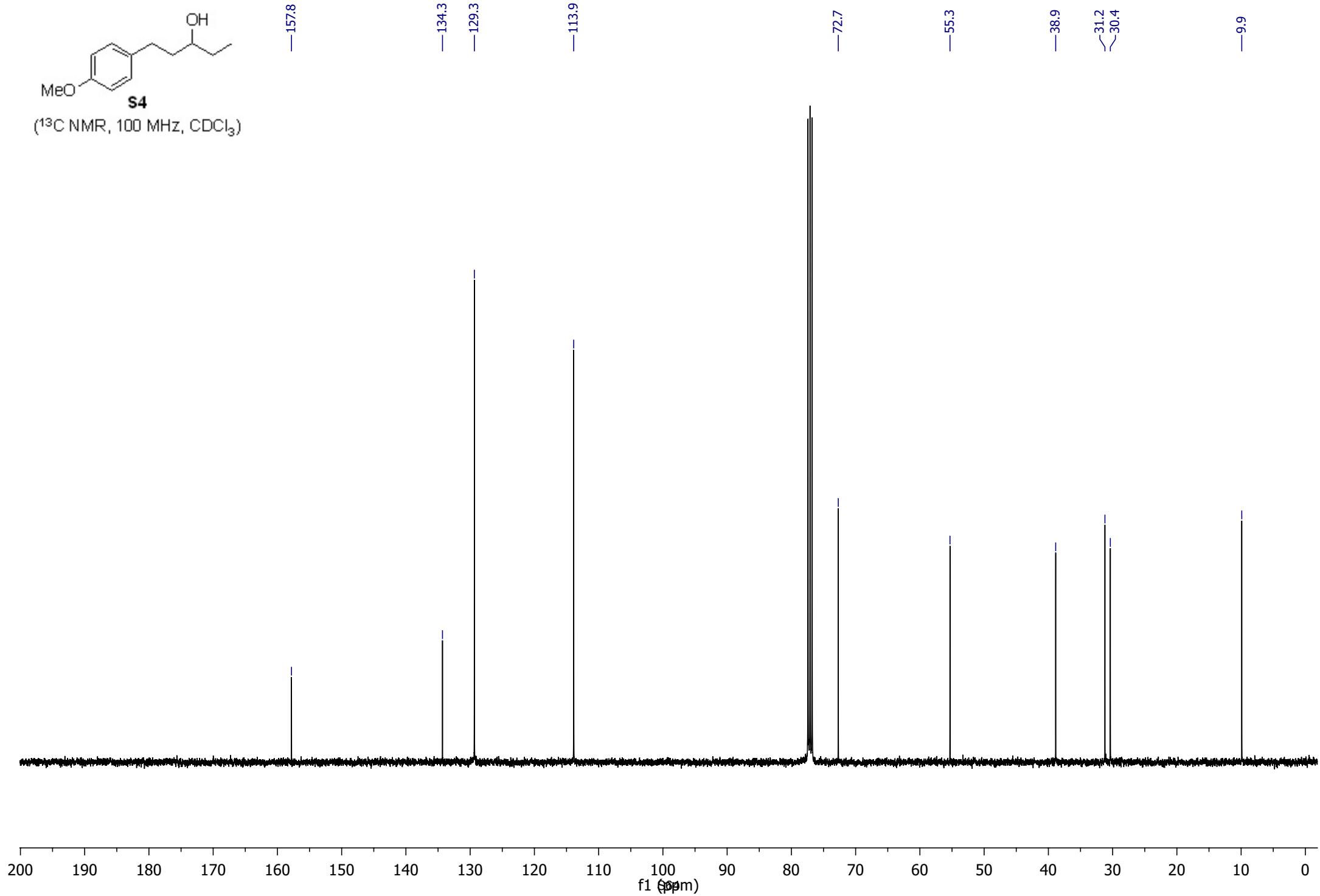


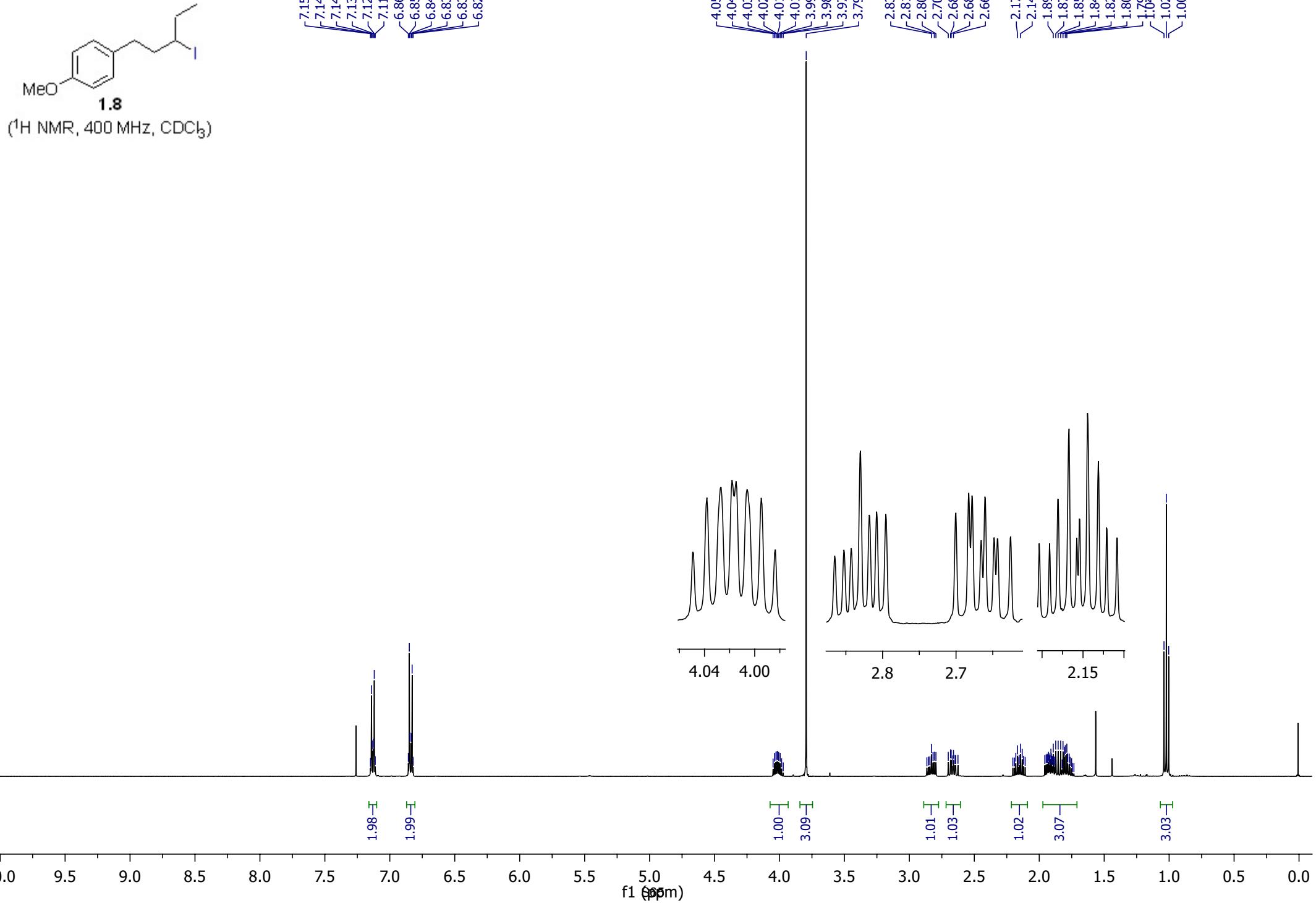
(^1H NMR, 400 MHz, CDCl_3)

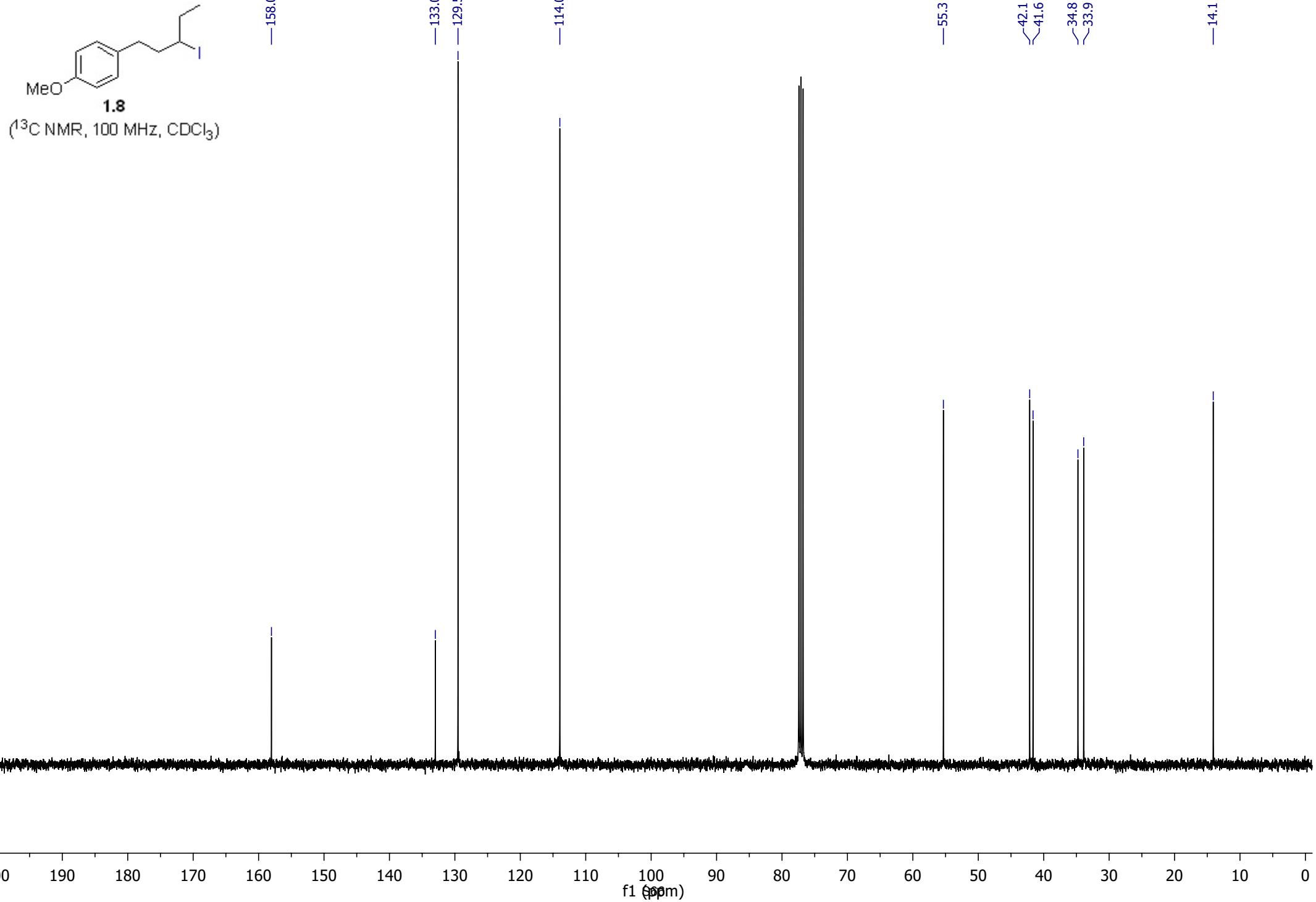


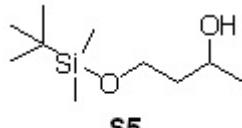


(^{13}C NMR, 100 MHz, CDCl_3)



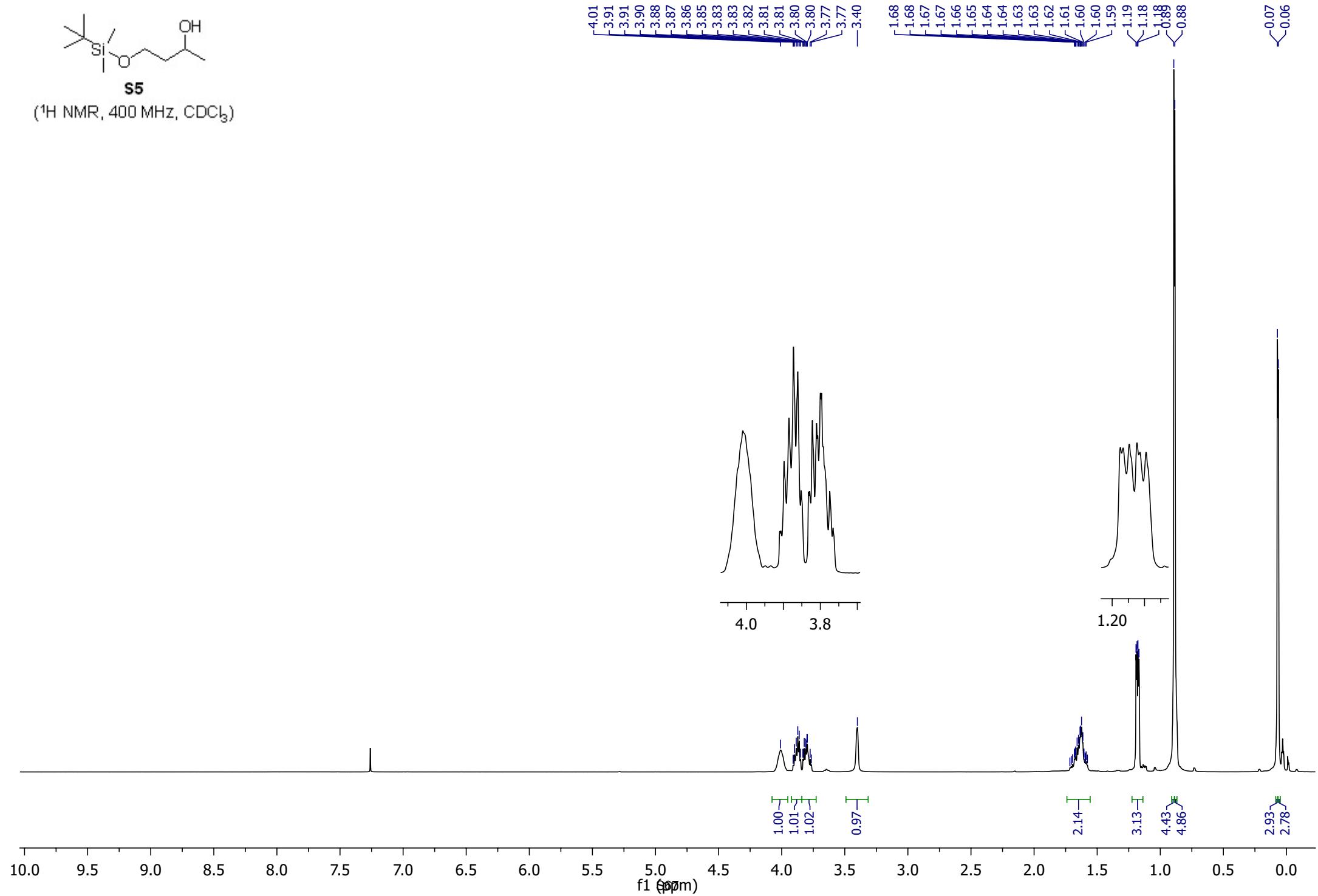


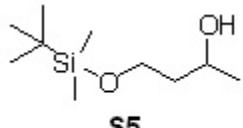




S5

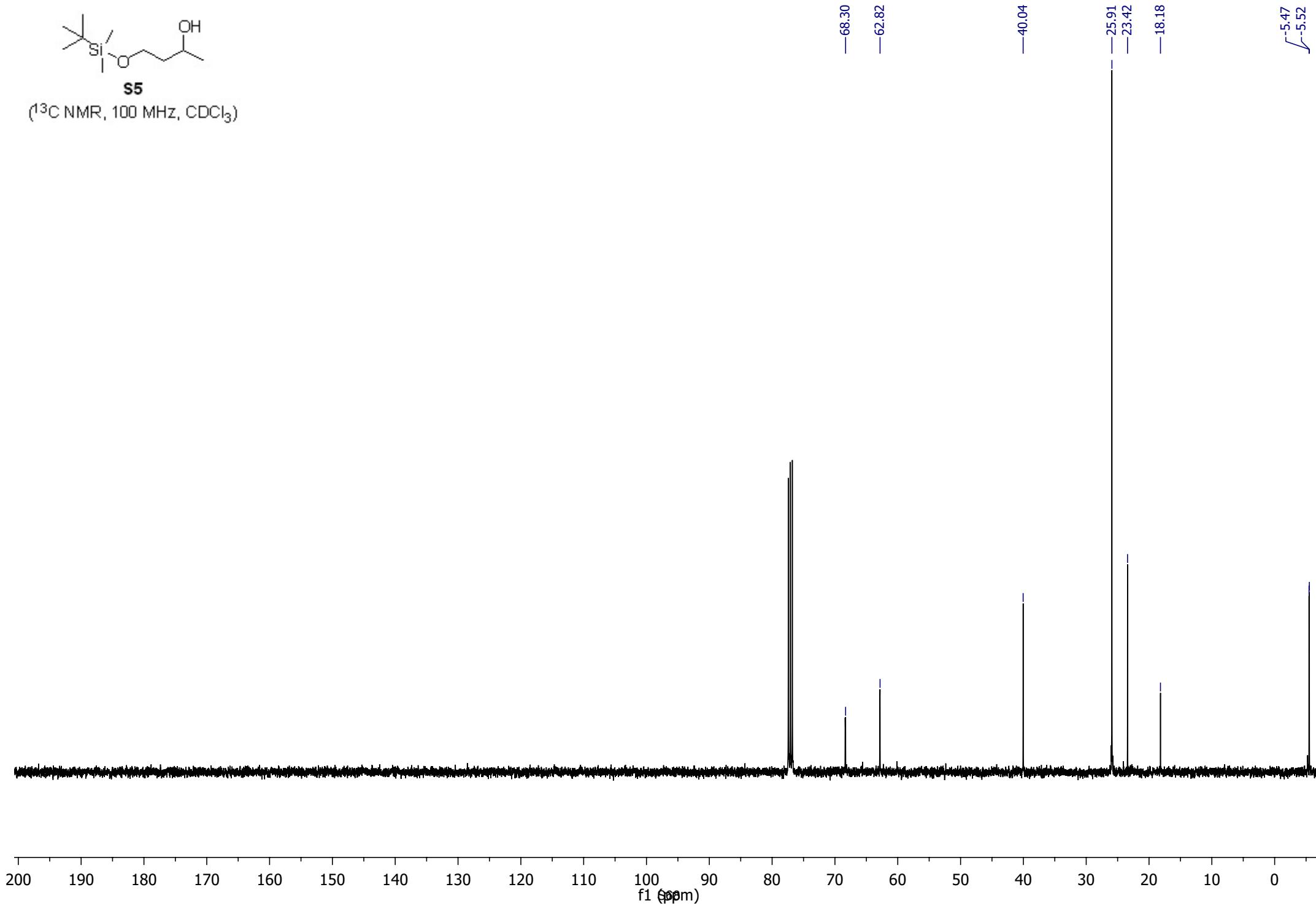
(^1H NMR, 400 MHz, CDCl_3)

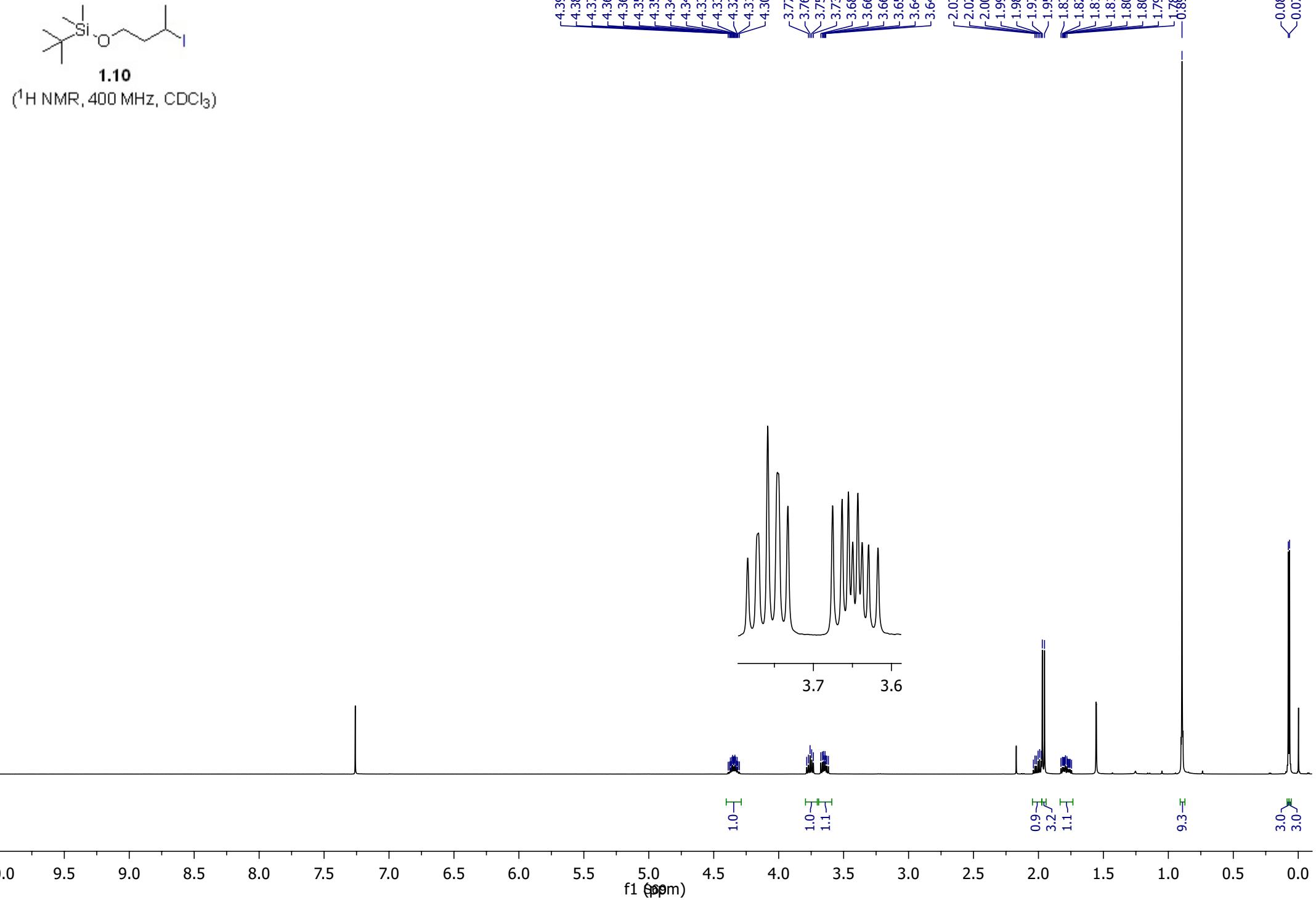


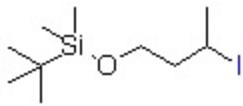


S5

(^{13}C NMR, 100 MHz, CDCl_3)

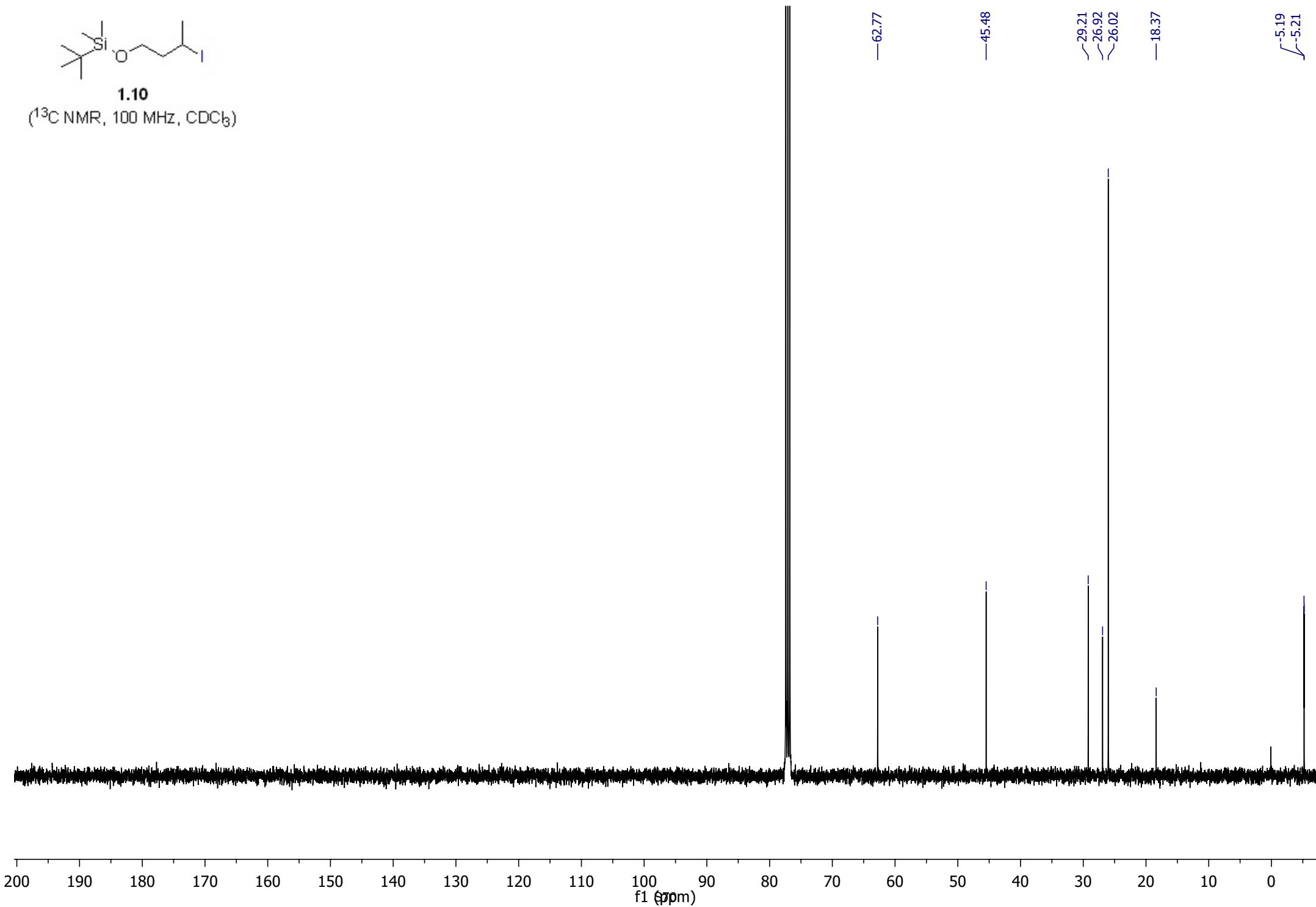






1.10

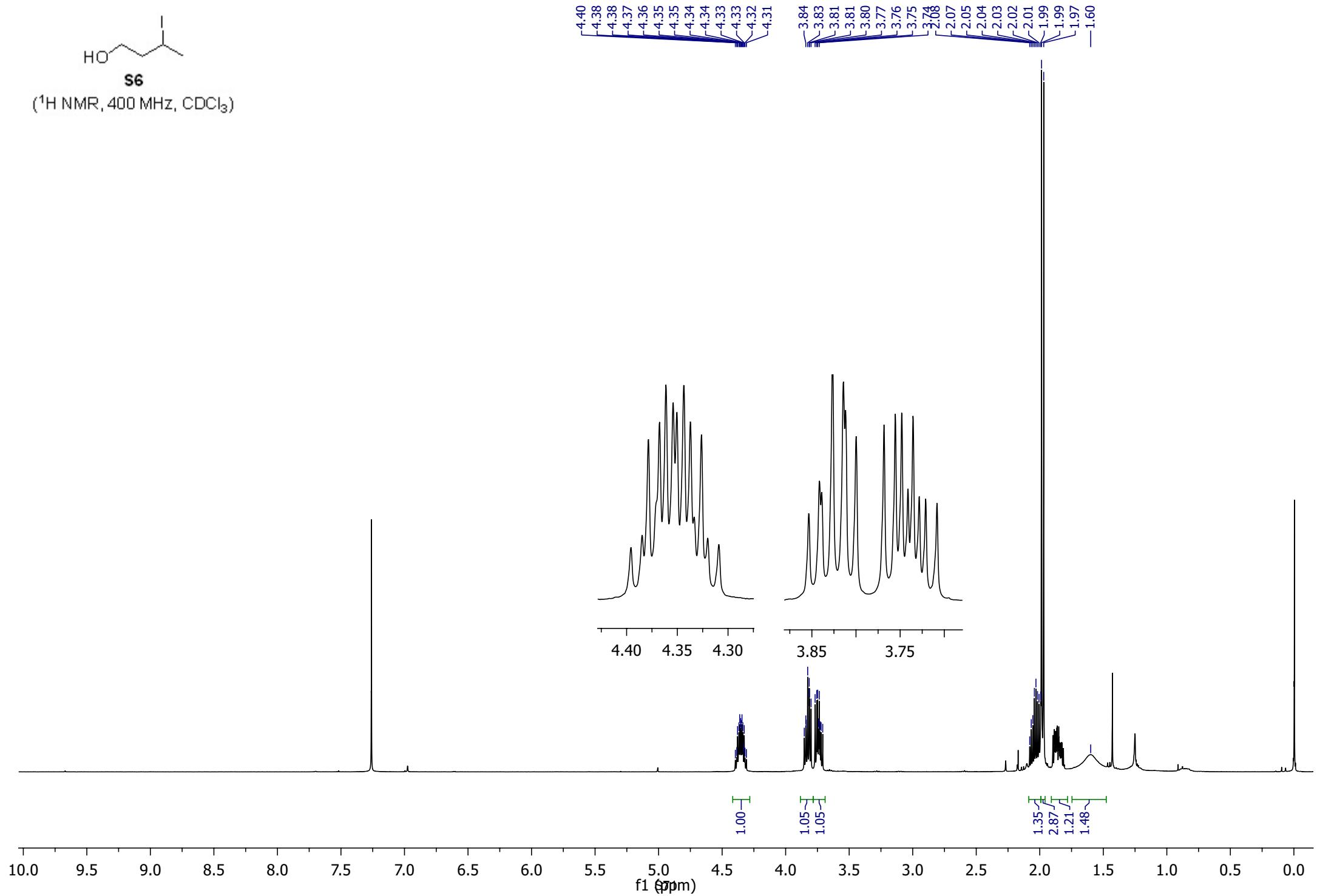
(^{13}C NMR, 100 MHz, CDCl_3)

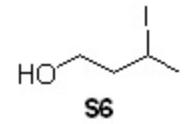




S6

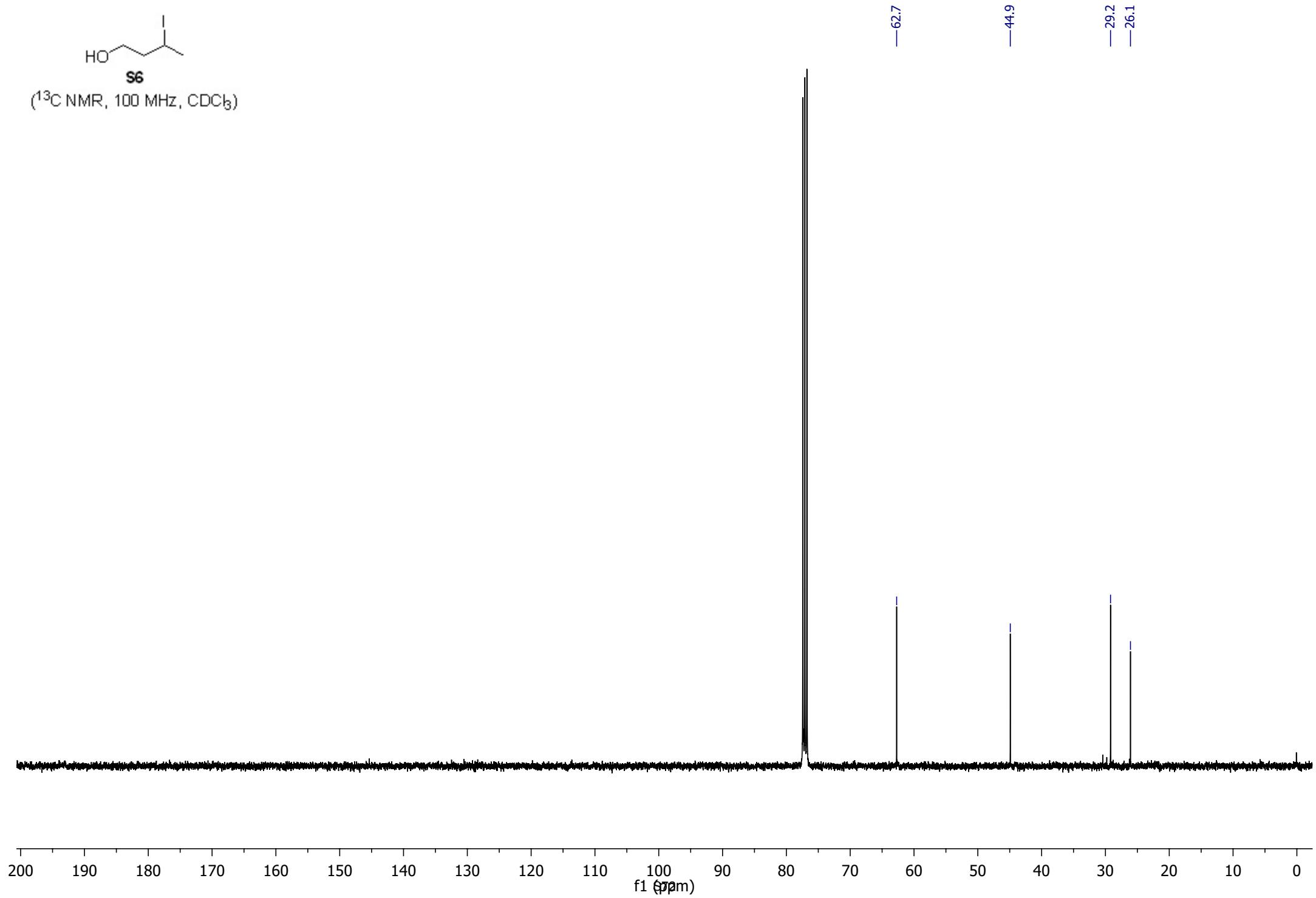
(^1H NMR, 400 MHz, CDCl_3)

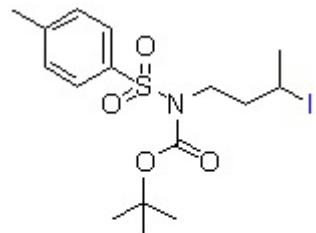




S6

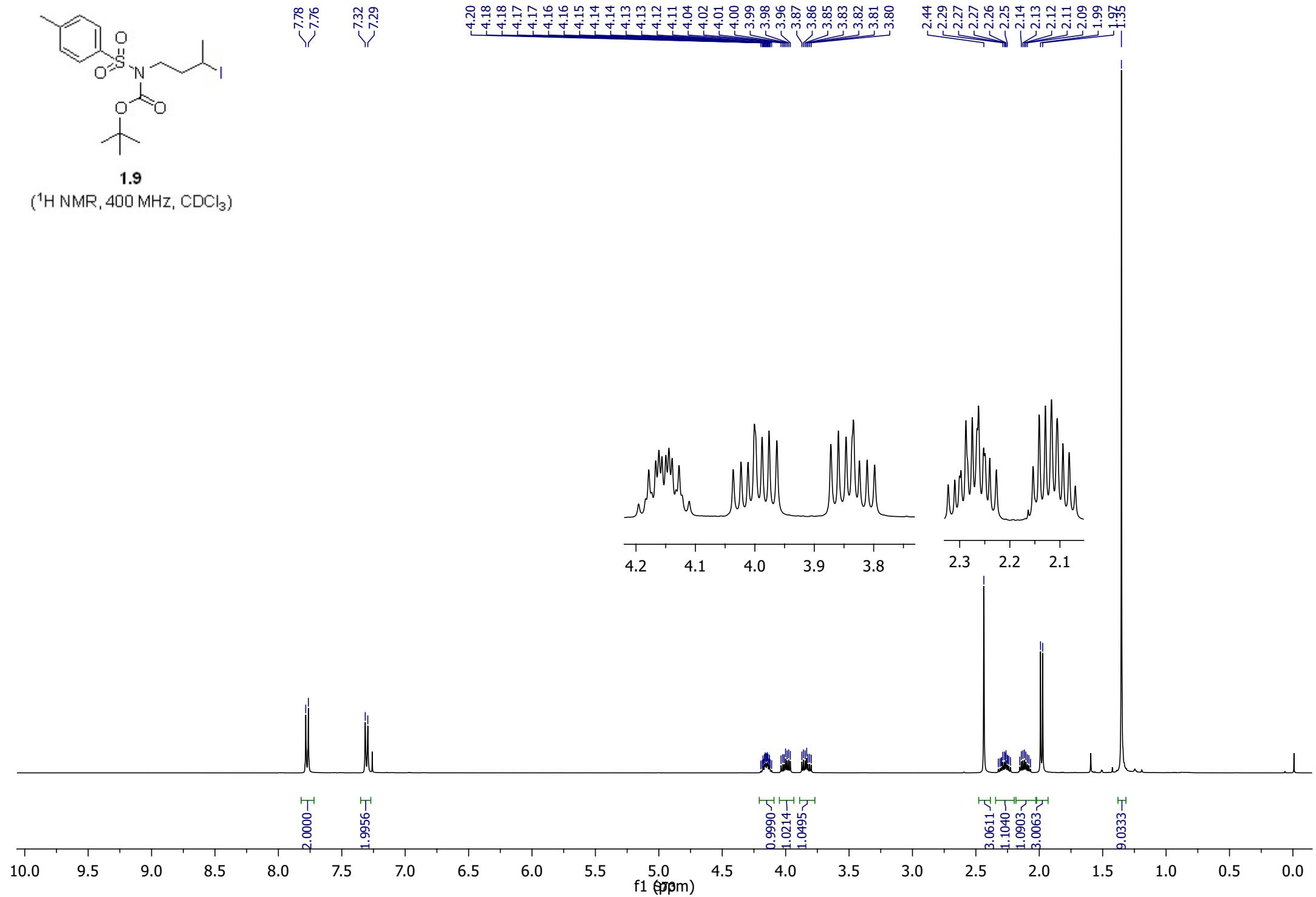
(^{13}C NMR, 100 MHz, CDCl_3)

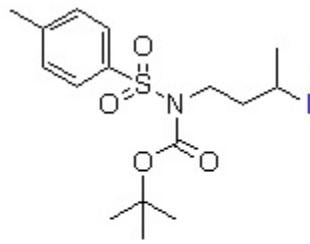




1.9

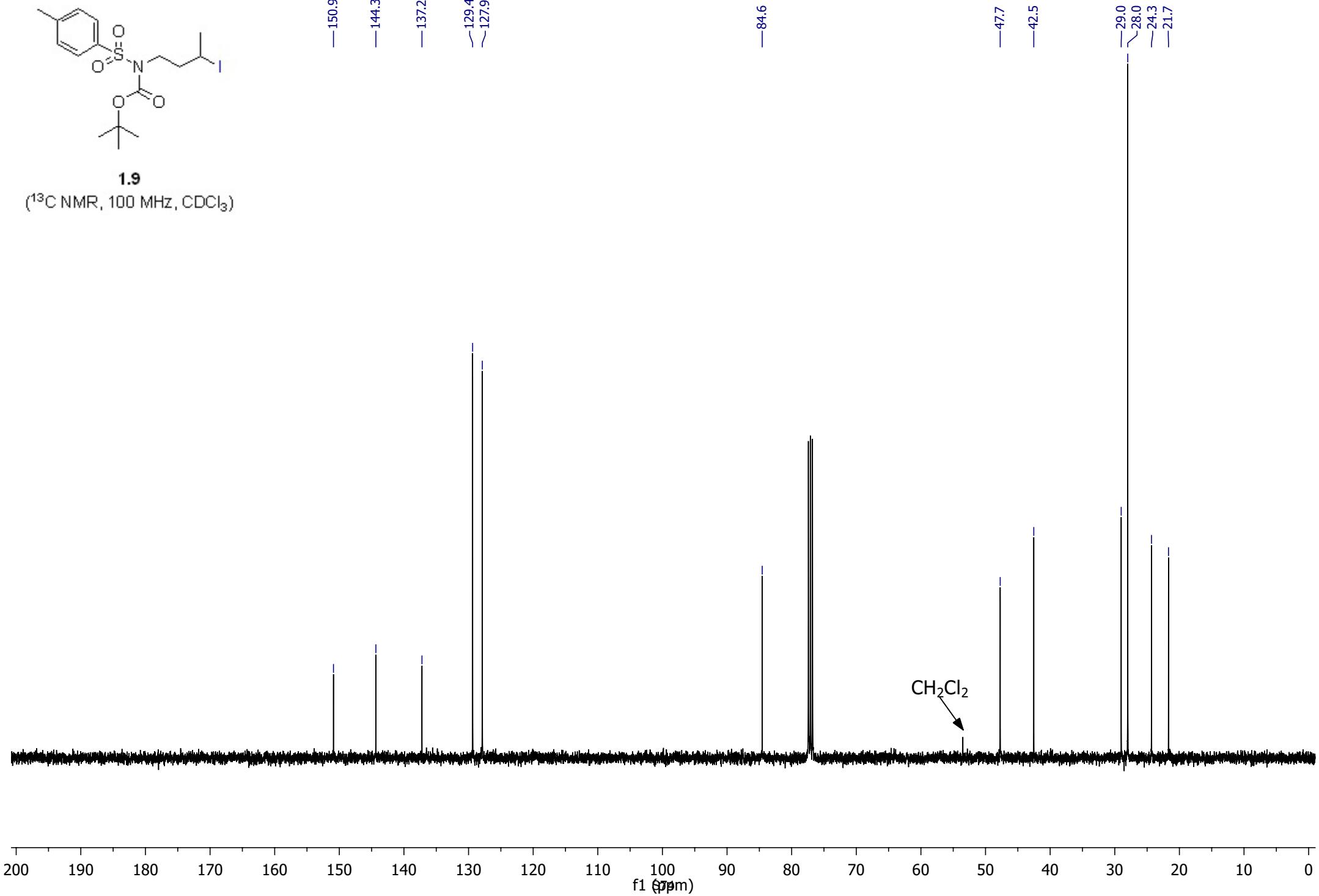
(^1H NMR, 400 MHz, CDCl_3)

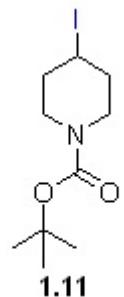




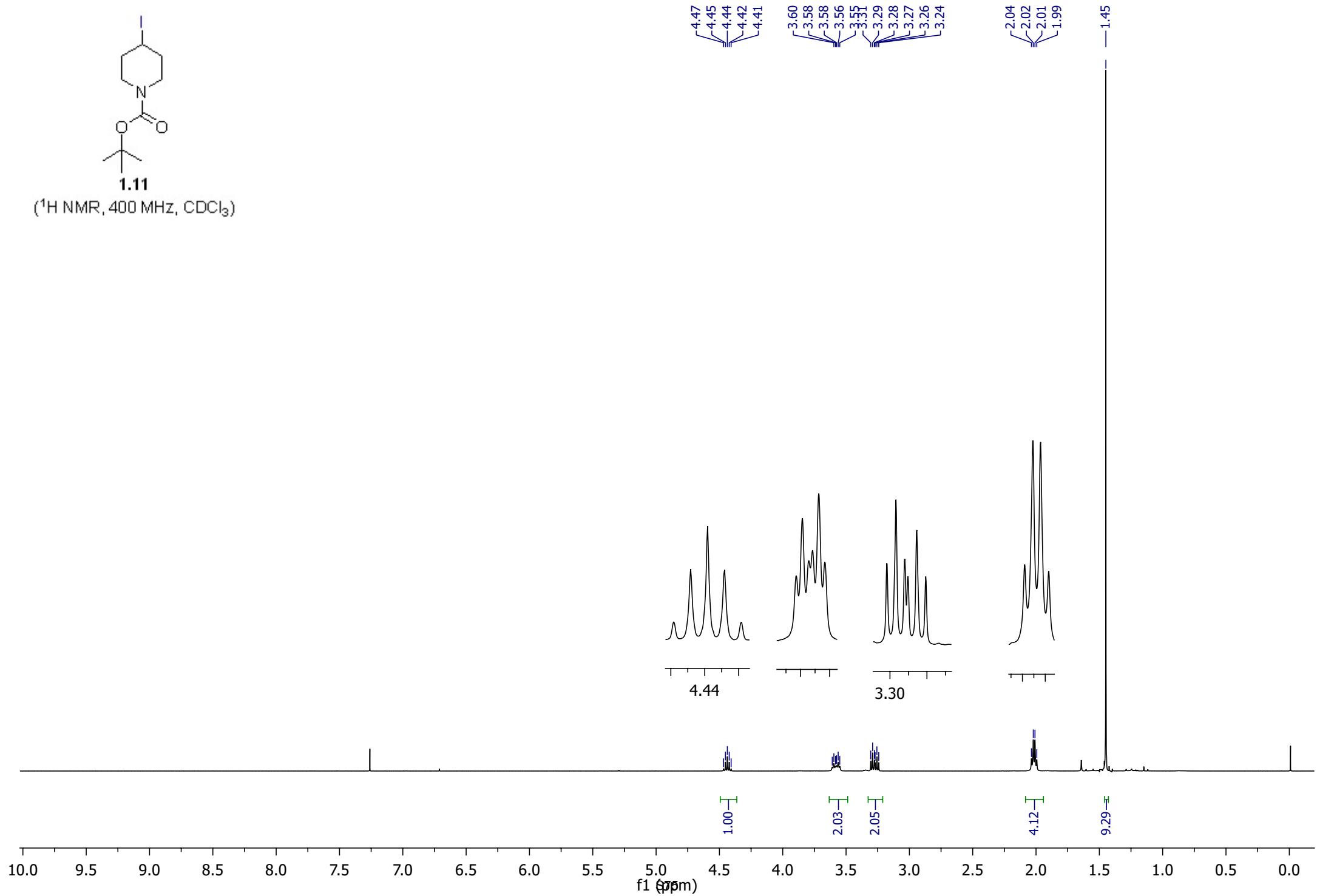
1.9

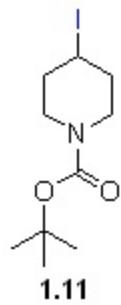
(^{13}C NMR, 100 MHz, CDCl_3)





(^1H NMR, 400 MHz, CDCl_3)





—154.8

—79.9

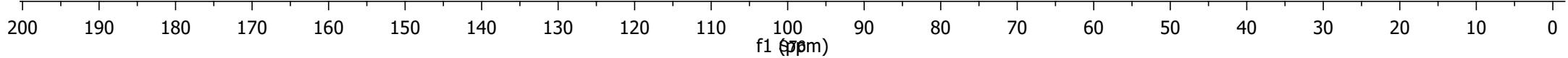
—44.0

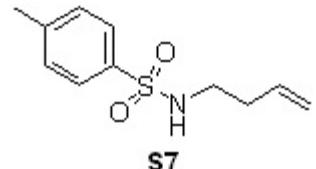
—37.4

—28.5

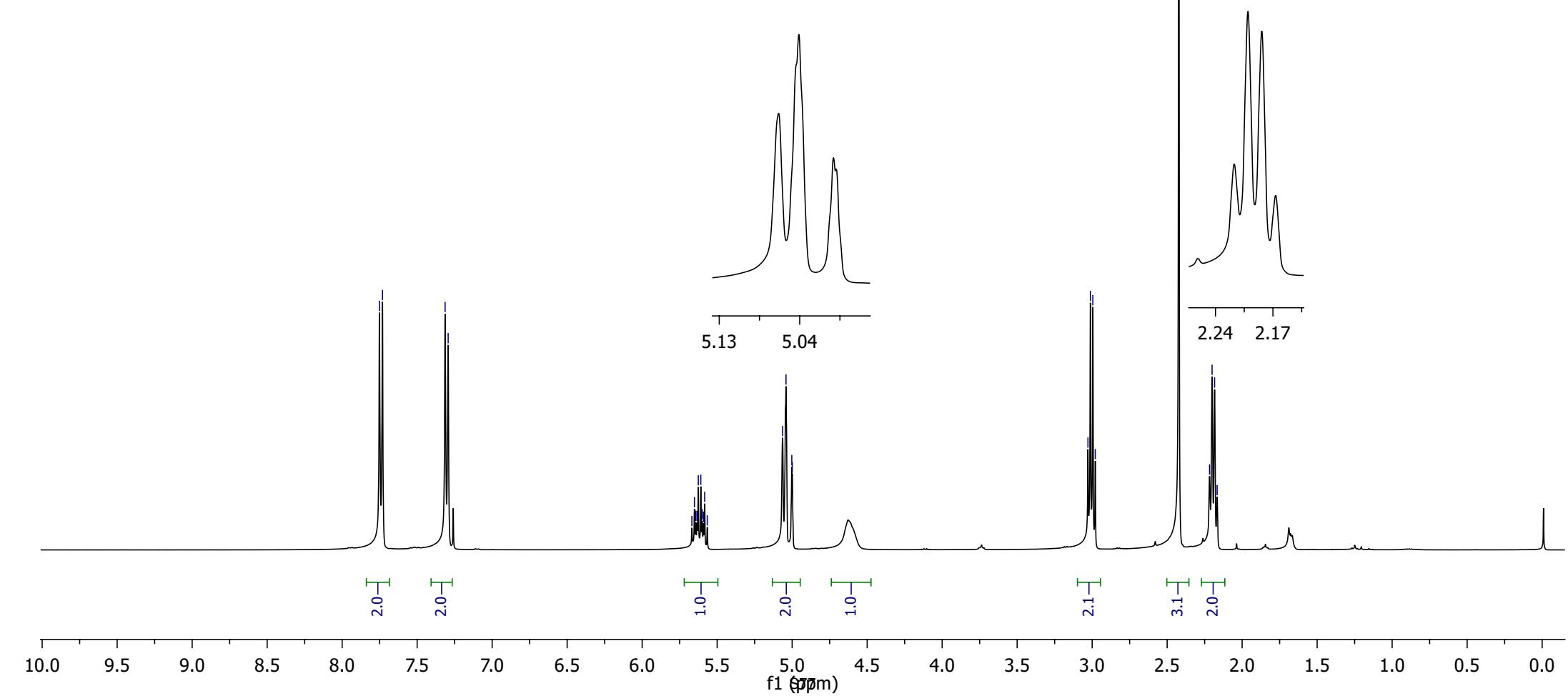
—27.8

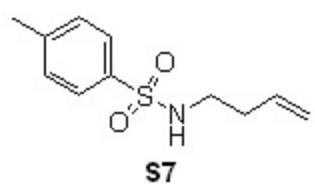
(^{13}C NMR, 100 MHz, CDCl_3)





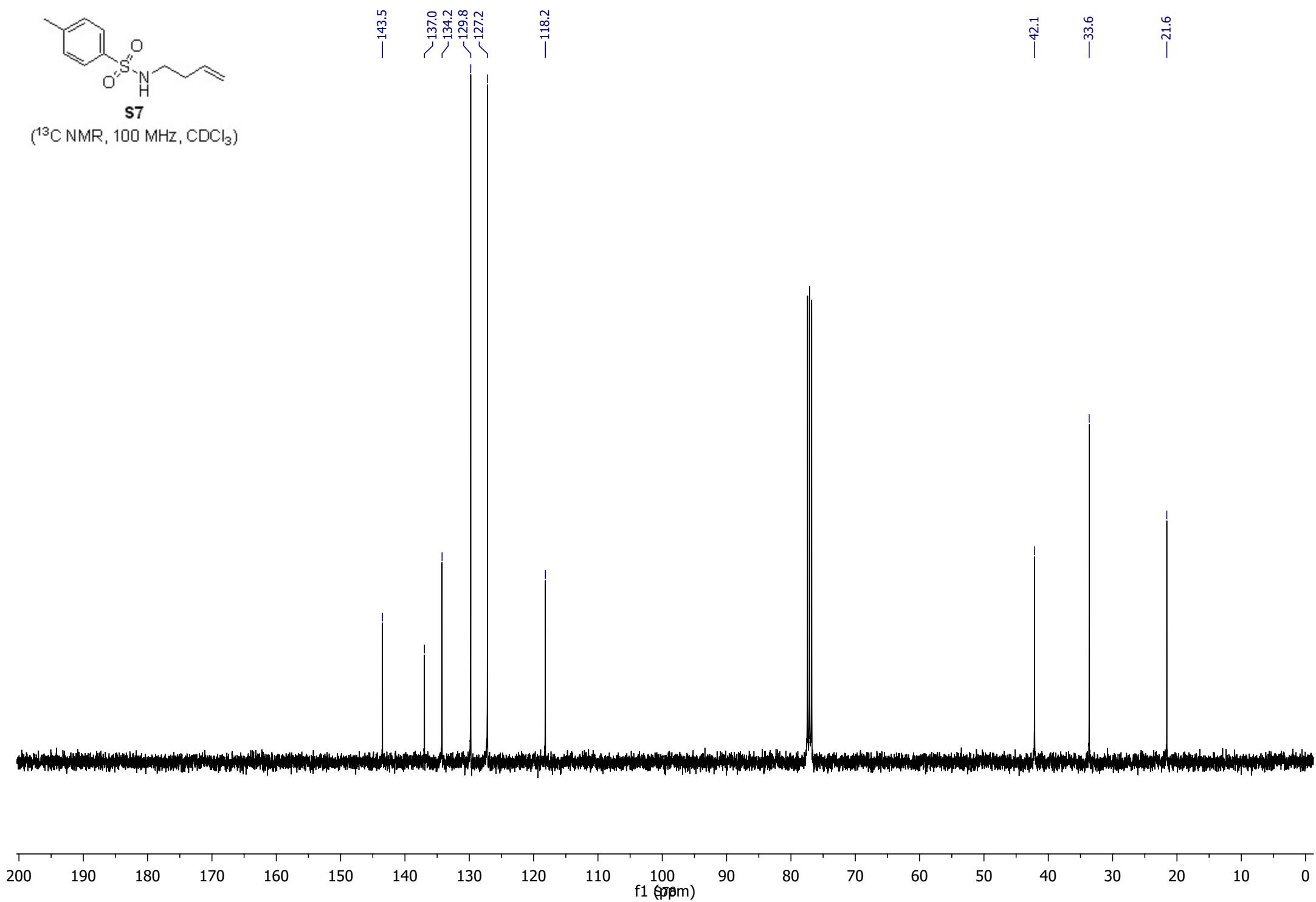
(^1H NMR, 400 MHz, CDCl_3)

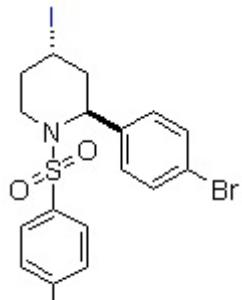




S7

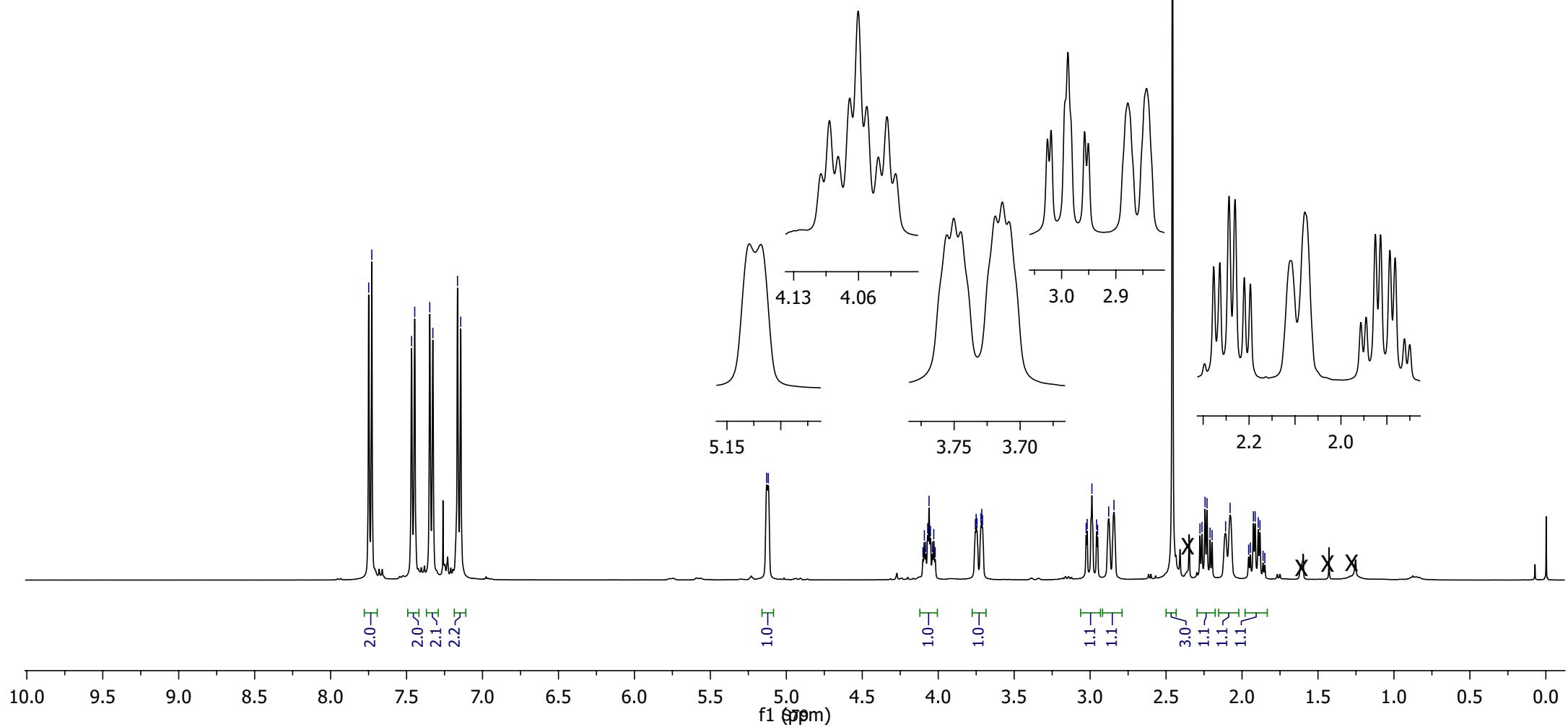
(^{13}C NMR, 100 MHz, CDCl_3)

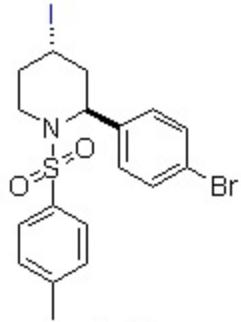




1.12

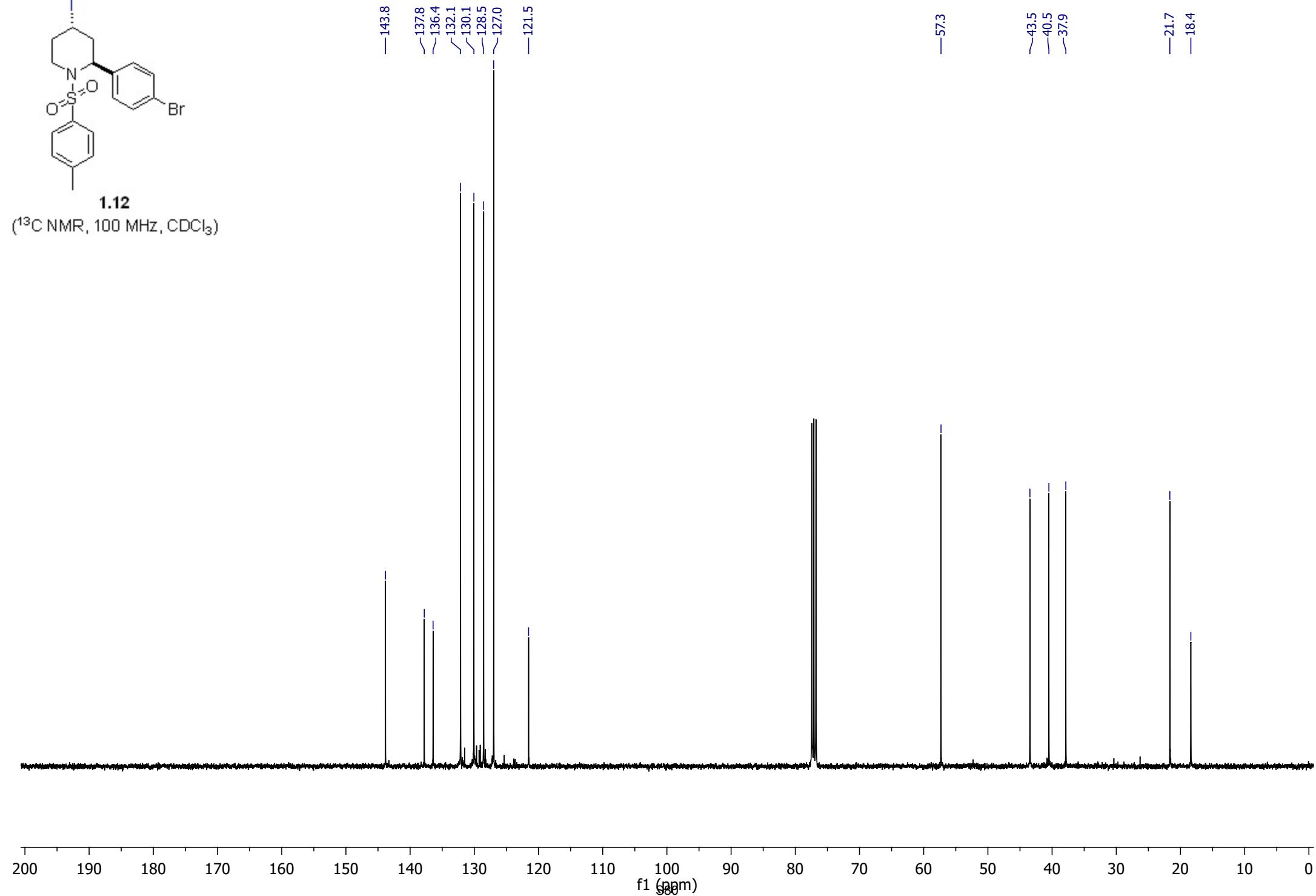
(^1H NMR, 400 MHz, CDCl_3)

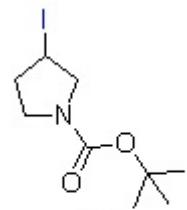




1.12

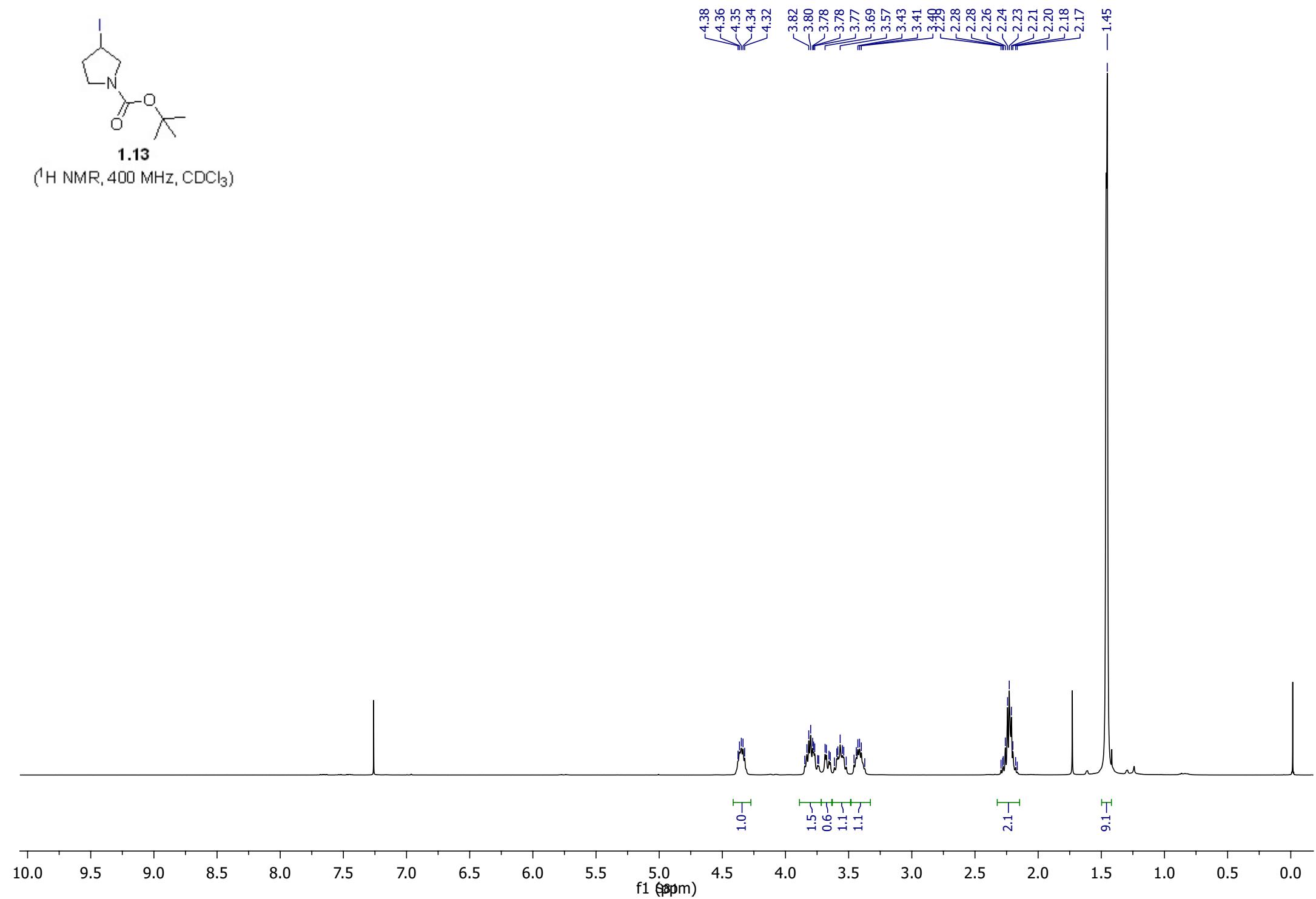
(^{13}C NMR, 100 MHz, CDCl_3)

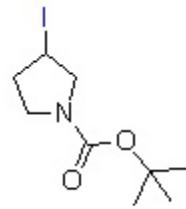




1.13

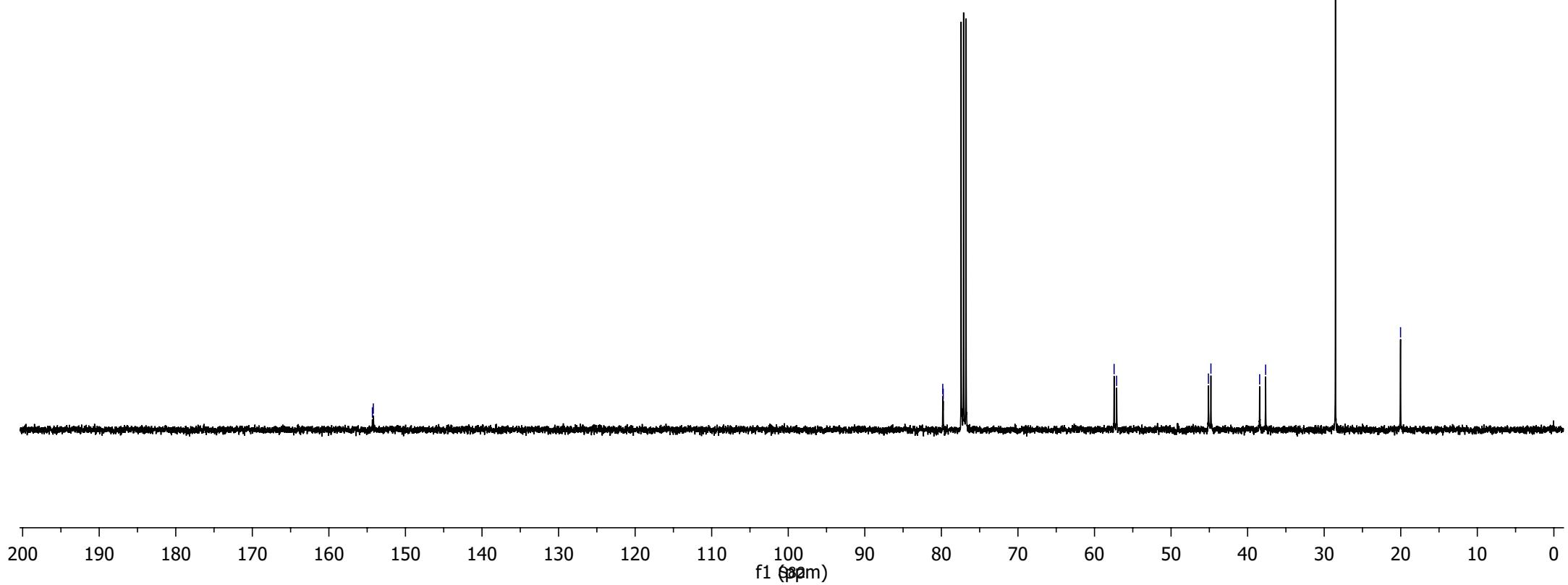
(^1H NMR, 400 MHz, CDCl_3)

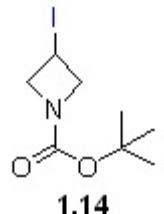




1.13

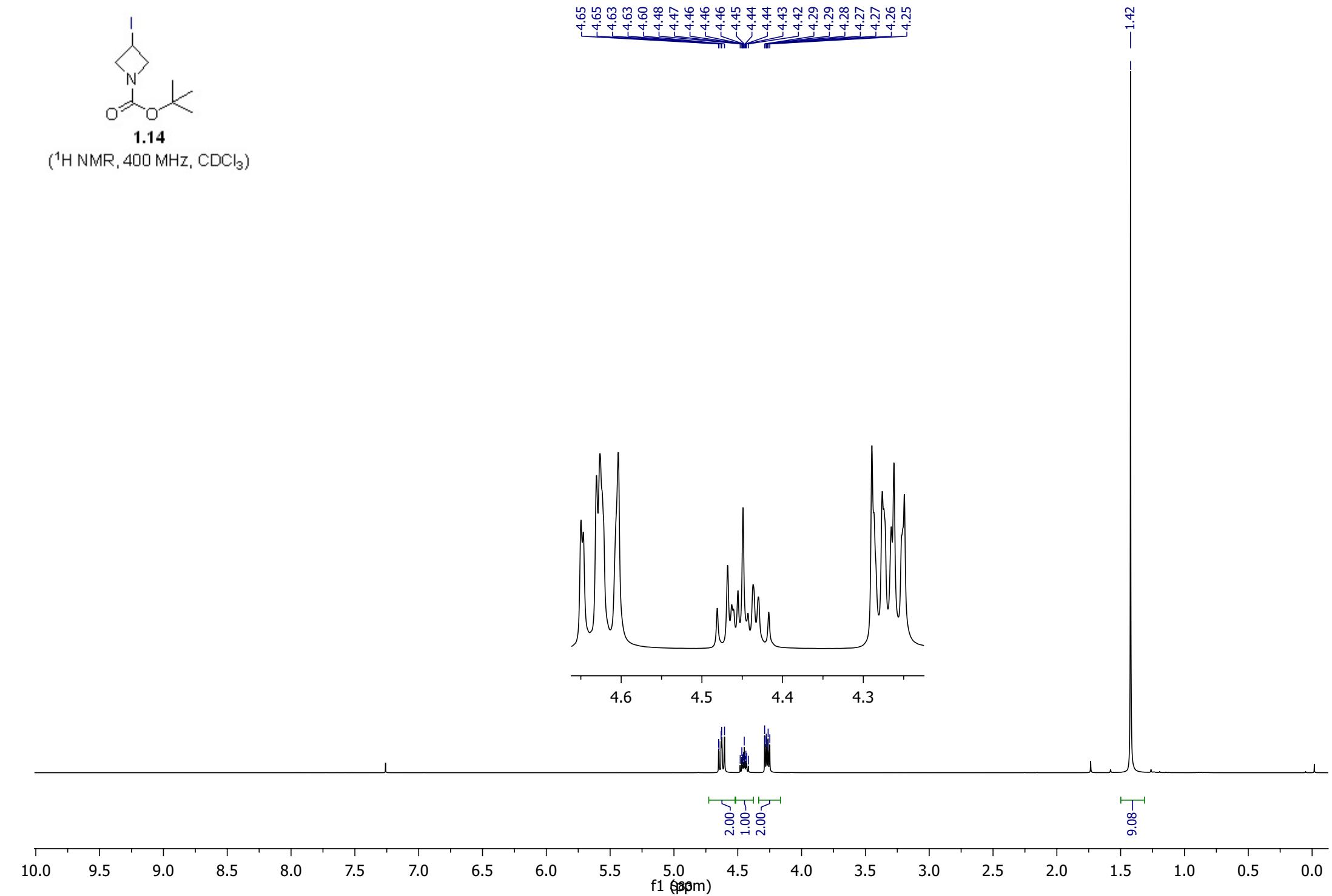
(^{13}C NMR, 100 MHz, CDCl_3)

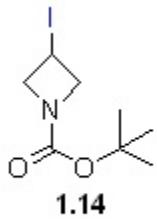




1.14

(^1H NMR, 400 MHz, CDCl_3)





1.14

(^{13}C NMR, 100 MHz, CDCl_3)

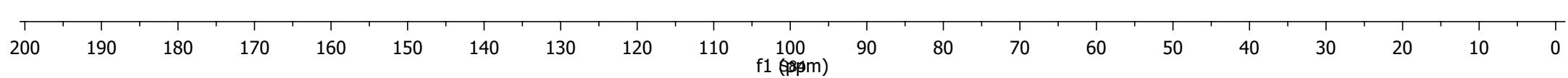
—155.6

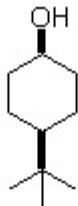
—80.2

—61.6

—28.4

—2.7

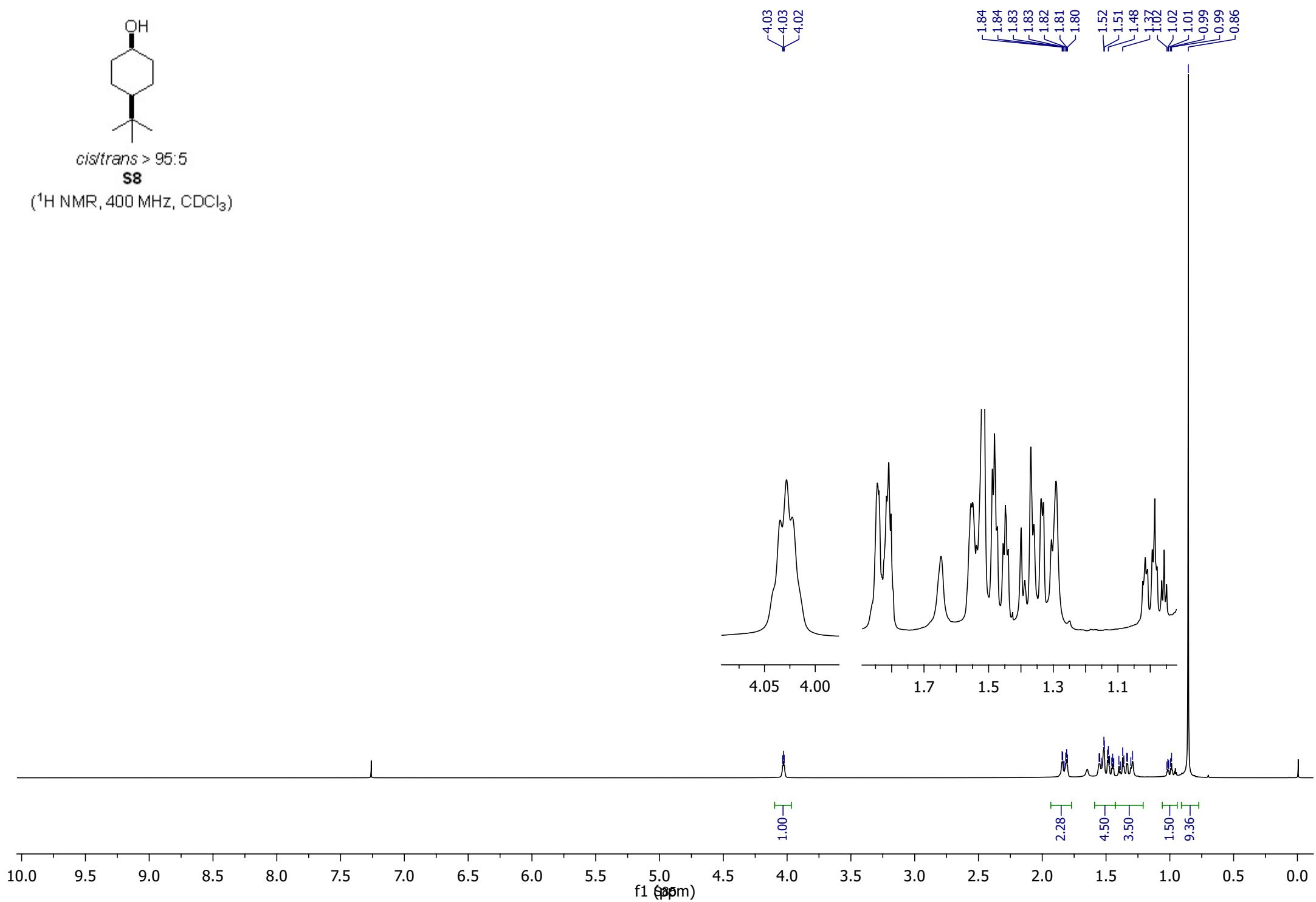


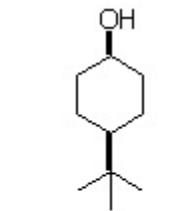


cis/trans > 95:5

S8

(^1H NMR, 400 MHz, CDCl_3)

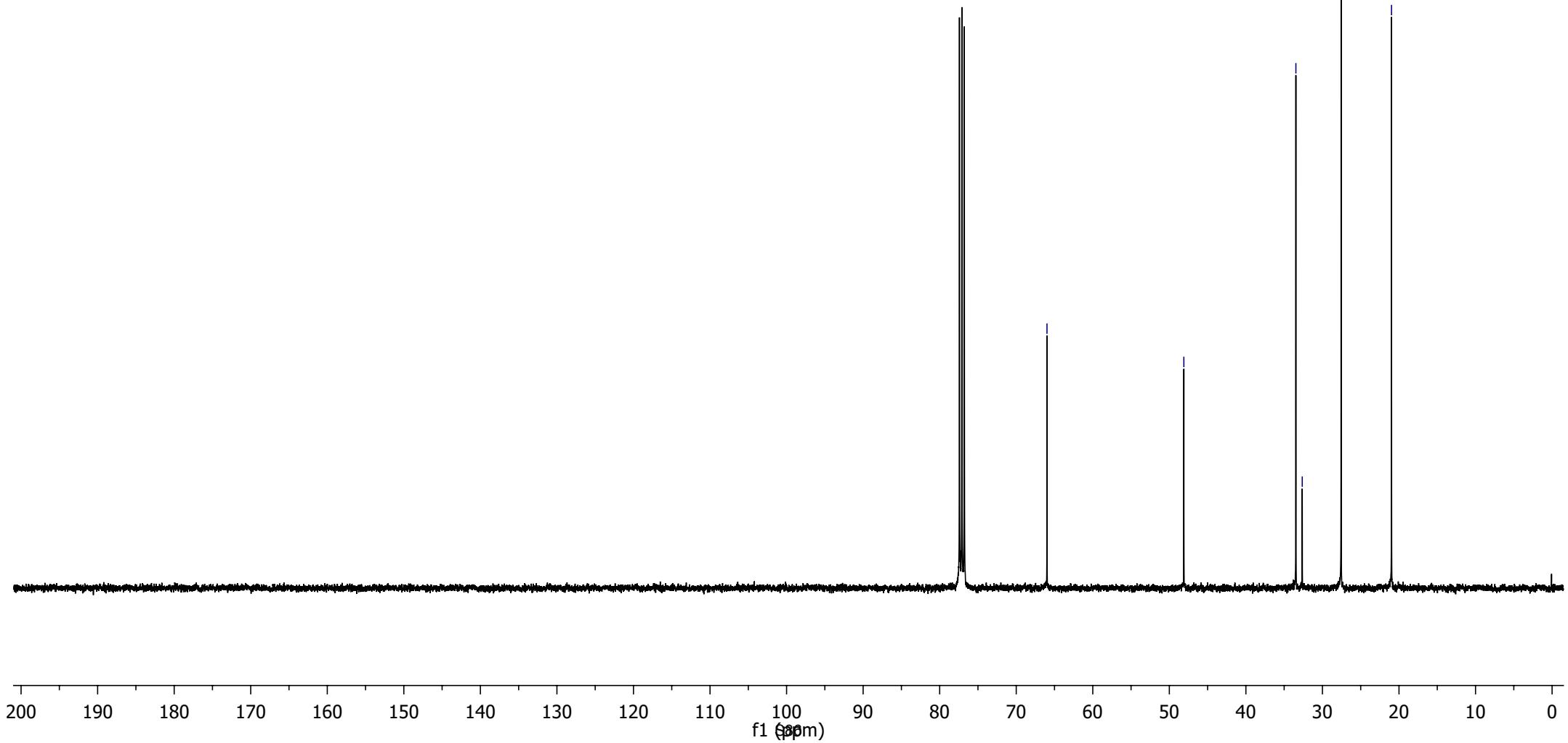


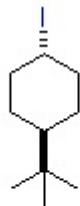


cis/trans > 95:5

S8

(^{13}C NMR, 100 MHz, CDCl_3)

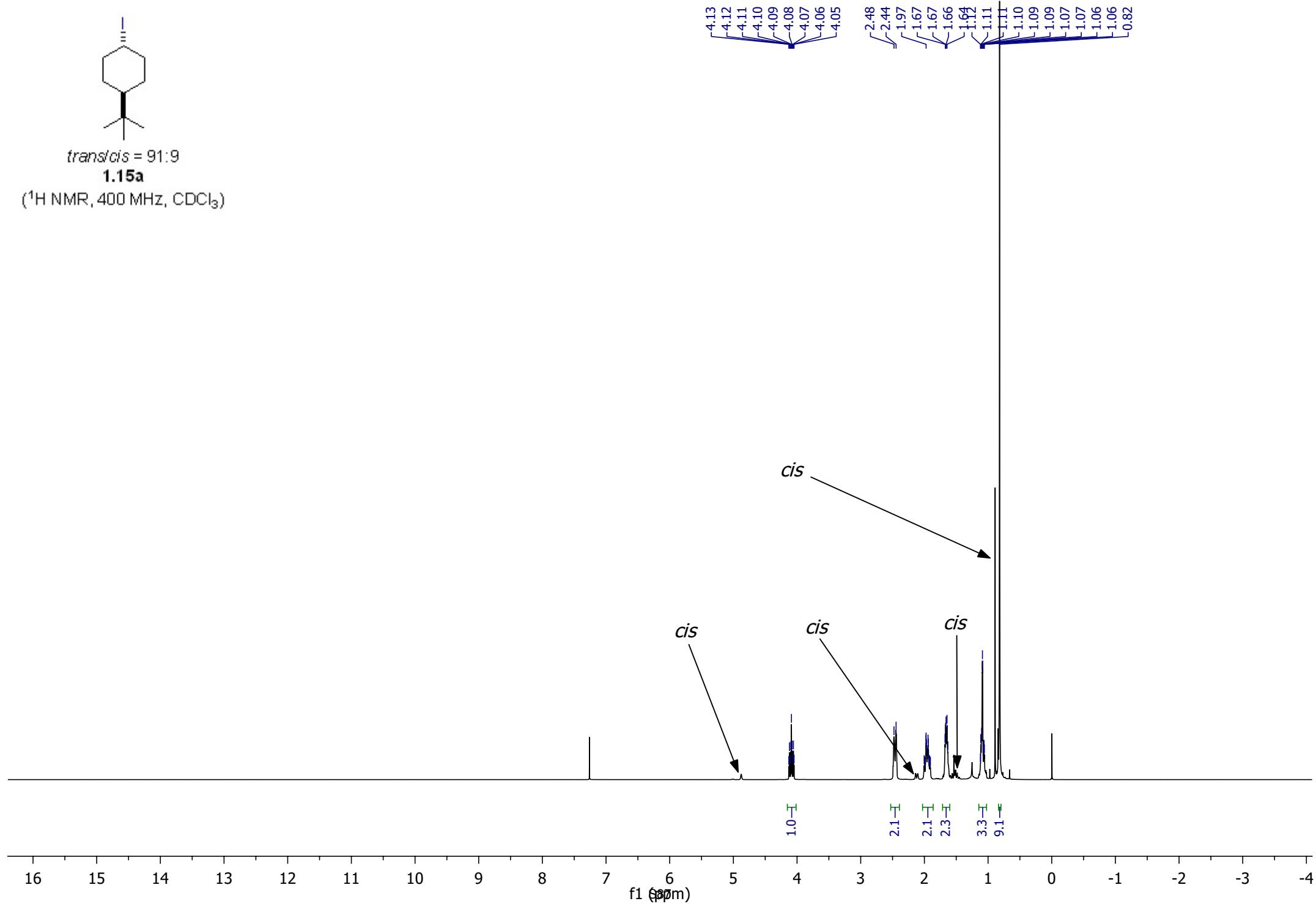




trans/cis = 91:9

1.15a

(^1H NMR, 400 MHz, CDCl_3)

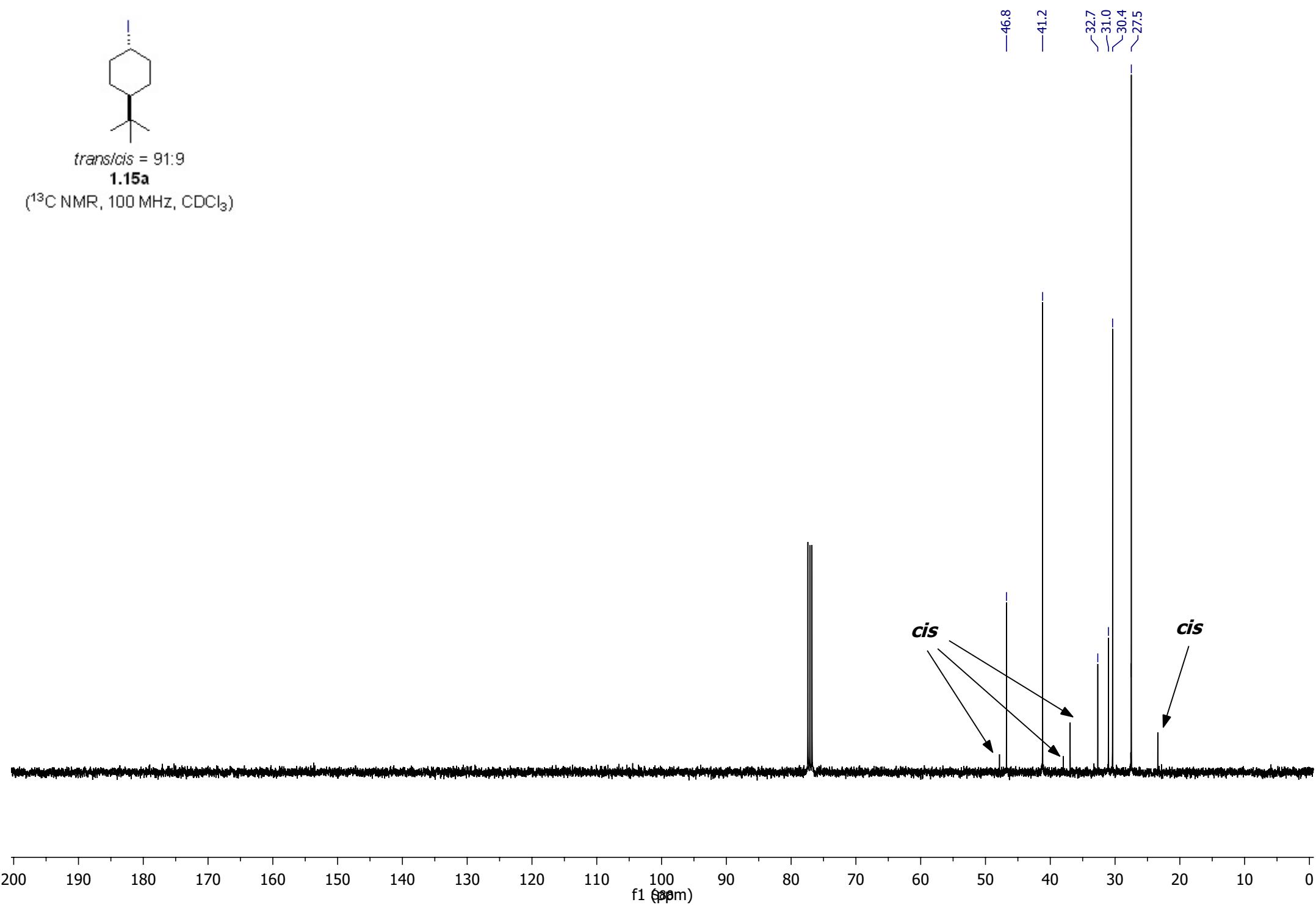


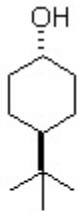


trans/cis = 91:9

1.15a

(^{13}C NMR, 100 MHz, CDCl_3)

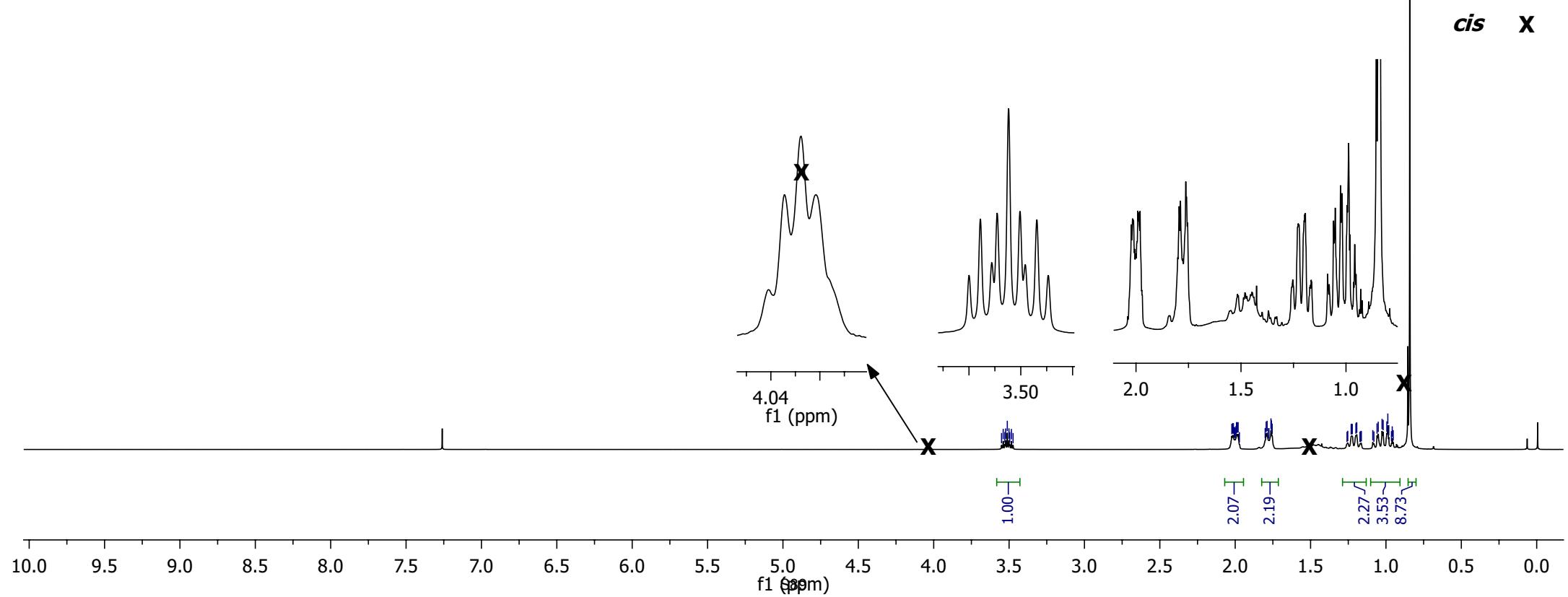


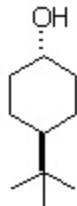


trans/cis = 92:8

S9

(^1H NMR, 400 MHz,
 CDCl_3)

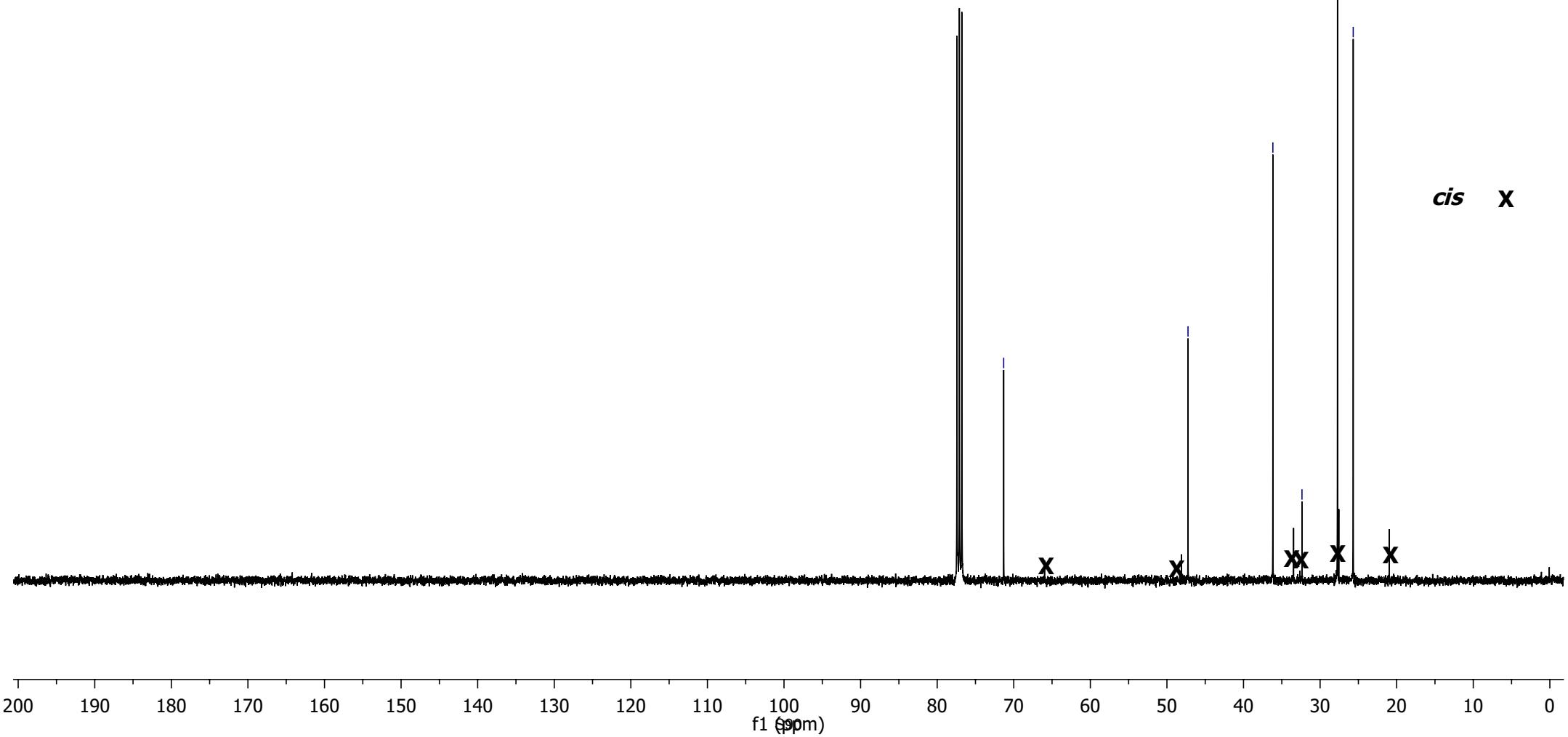


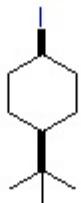


trans/cis = 92:8

s9

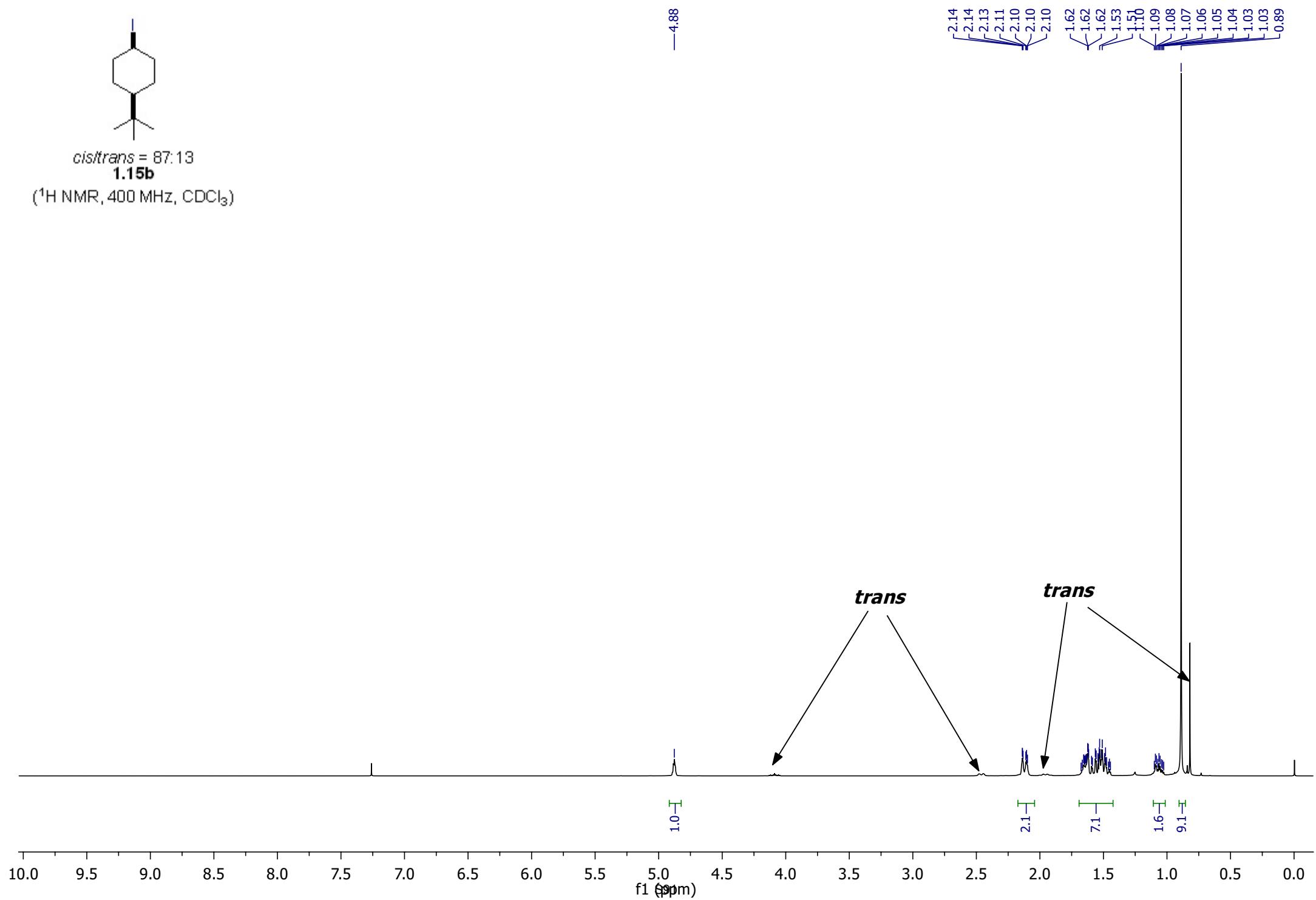
(^{13}C NMR, 100 MHz, CDCl_3)





cis/trans = 87:13
1.15b

(¹H NMR, 400 MHz, CDCl₃)

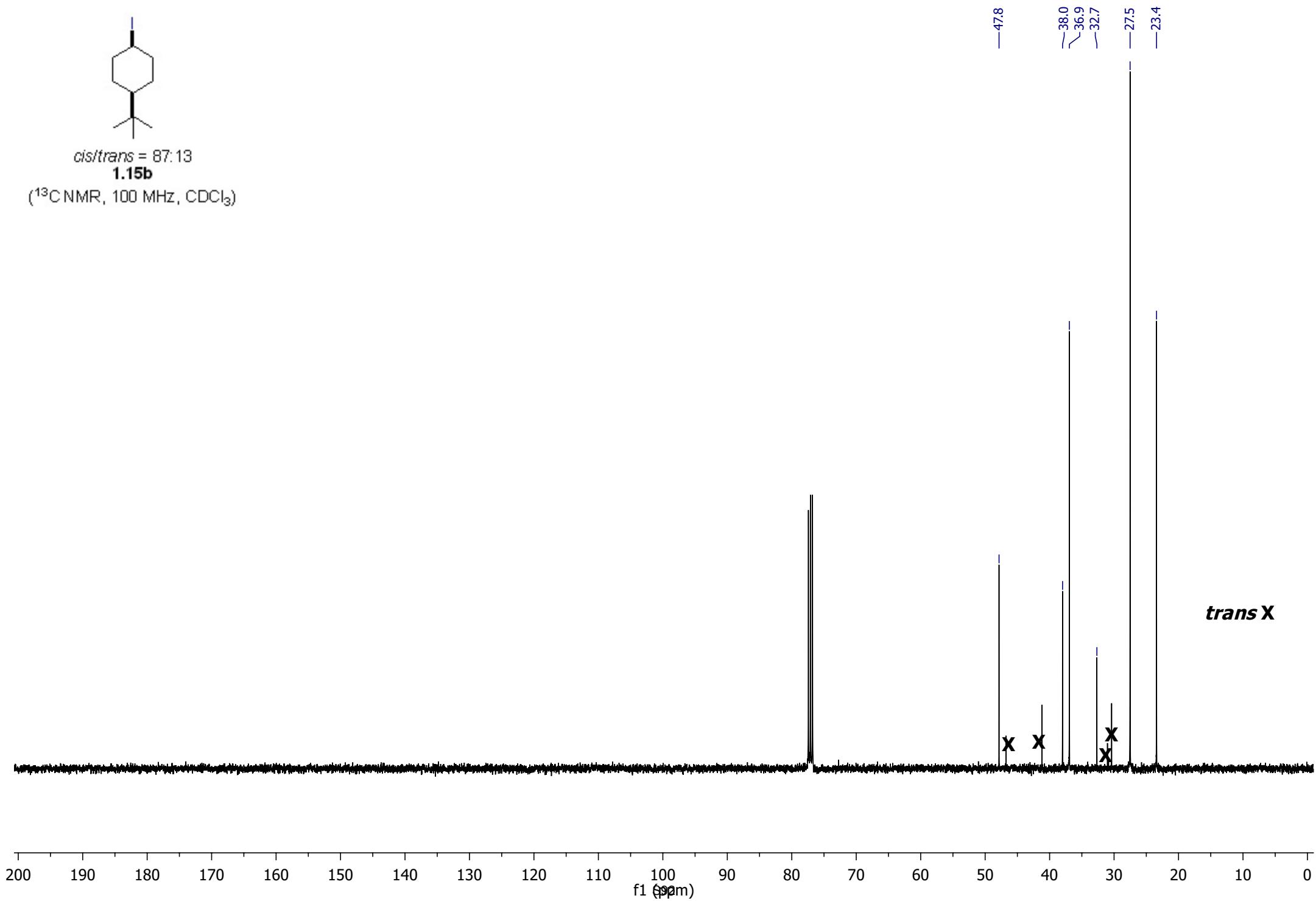


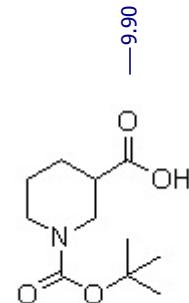


cis/trans = 87:13

1.15b

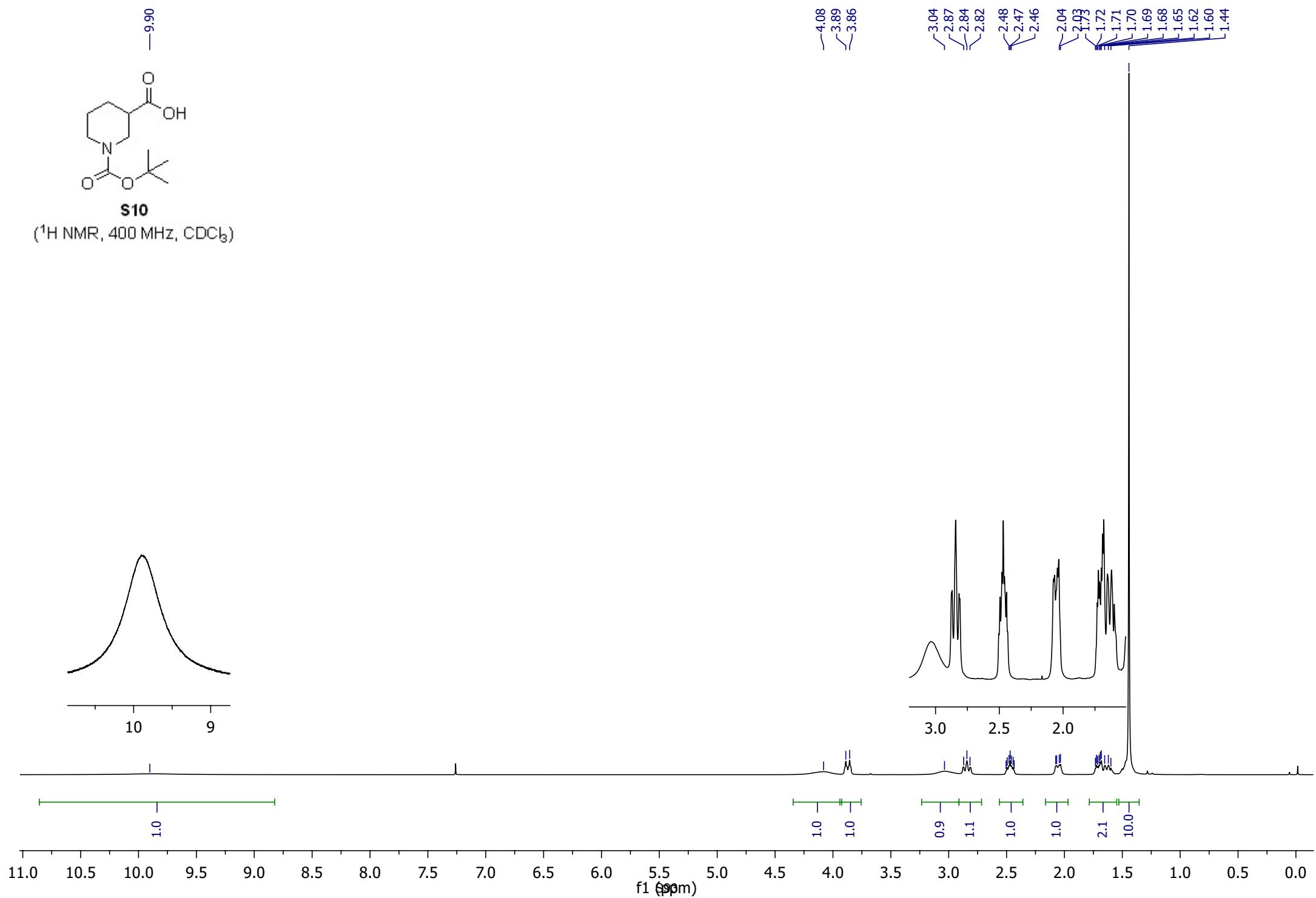
(^{13}C NMR, 100 MHz, CDCl_3)

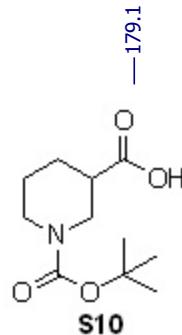




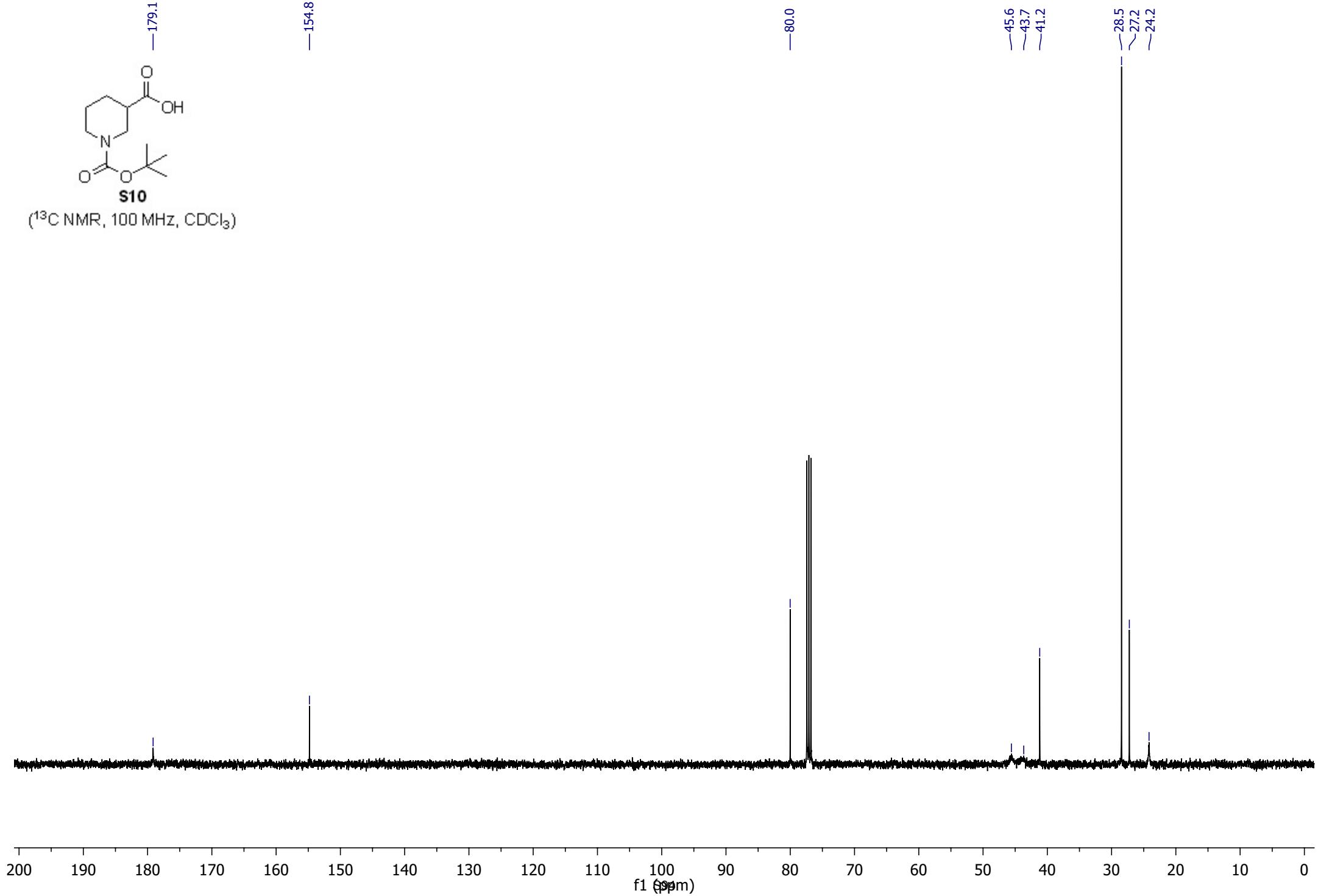
S10

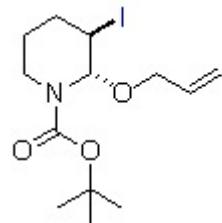
(^1H NMR, 400 MHz, CDCl_3)





(^{13}C NMR, 100 MHz, CDCl_3)

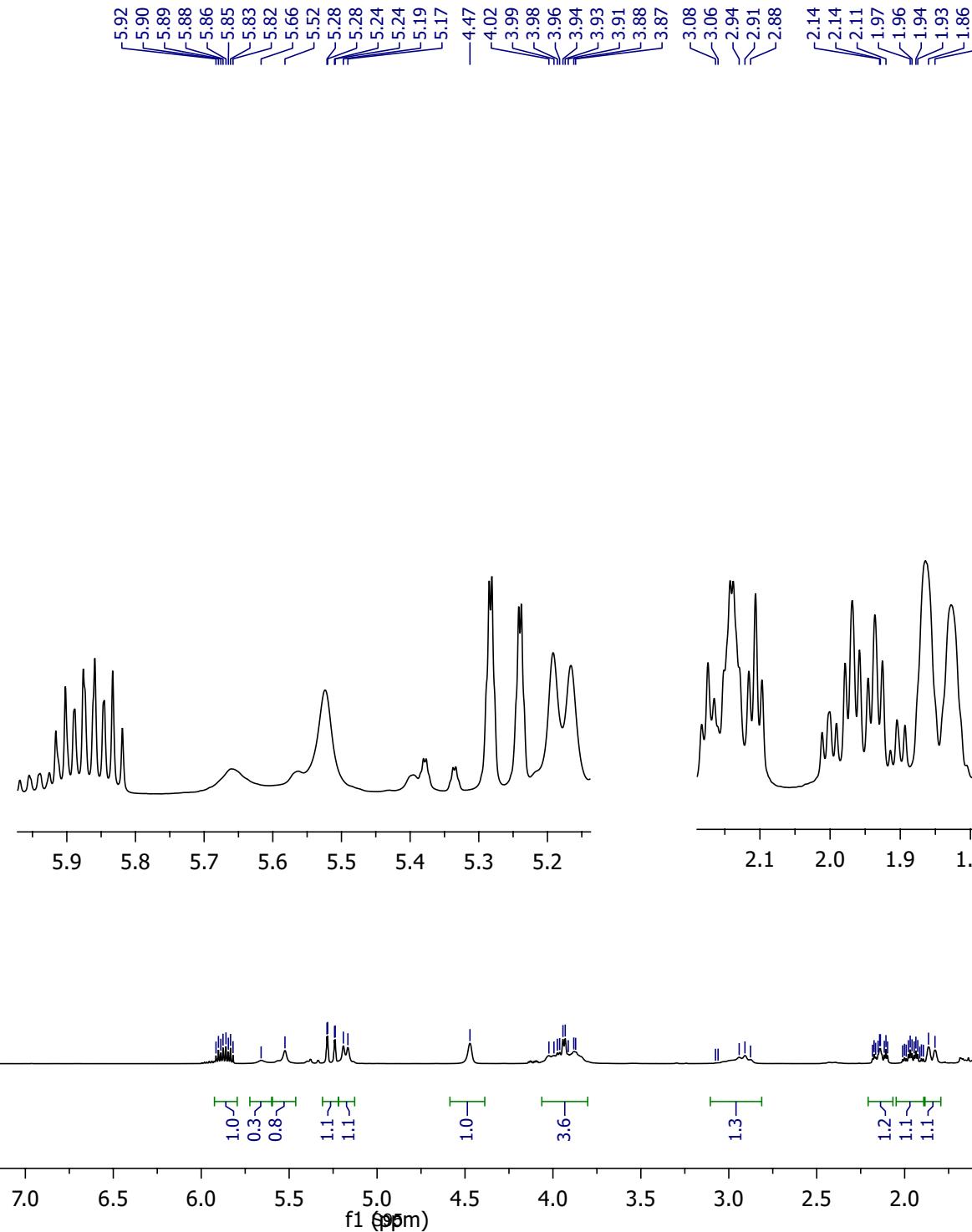


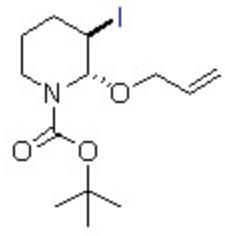


trans/cis = 86:15

1.16

(^1H NMR, 400 MHz, CDCl_3)

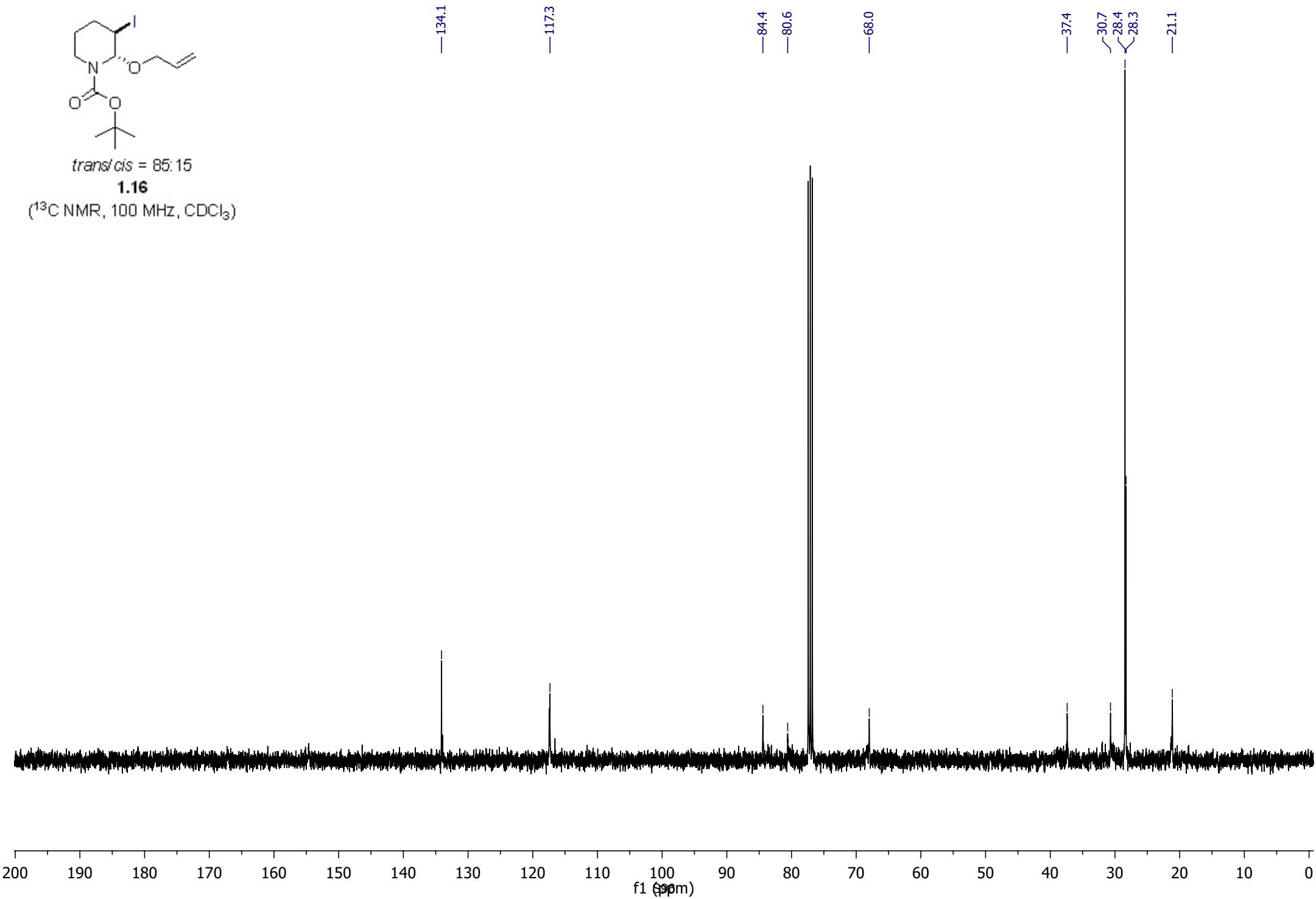


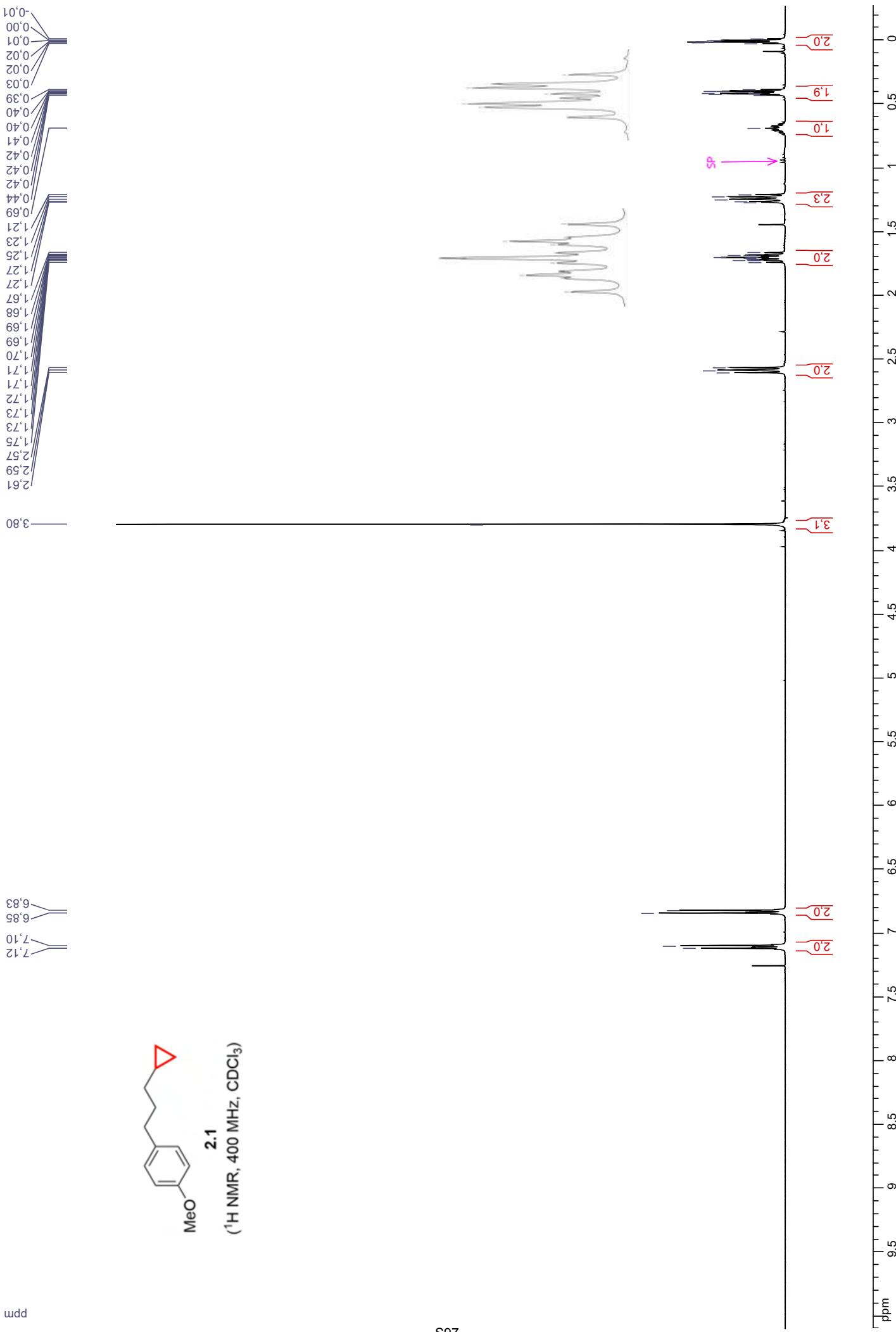


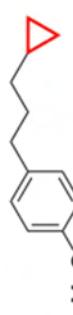
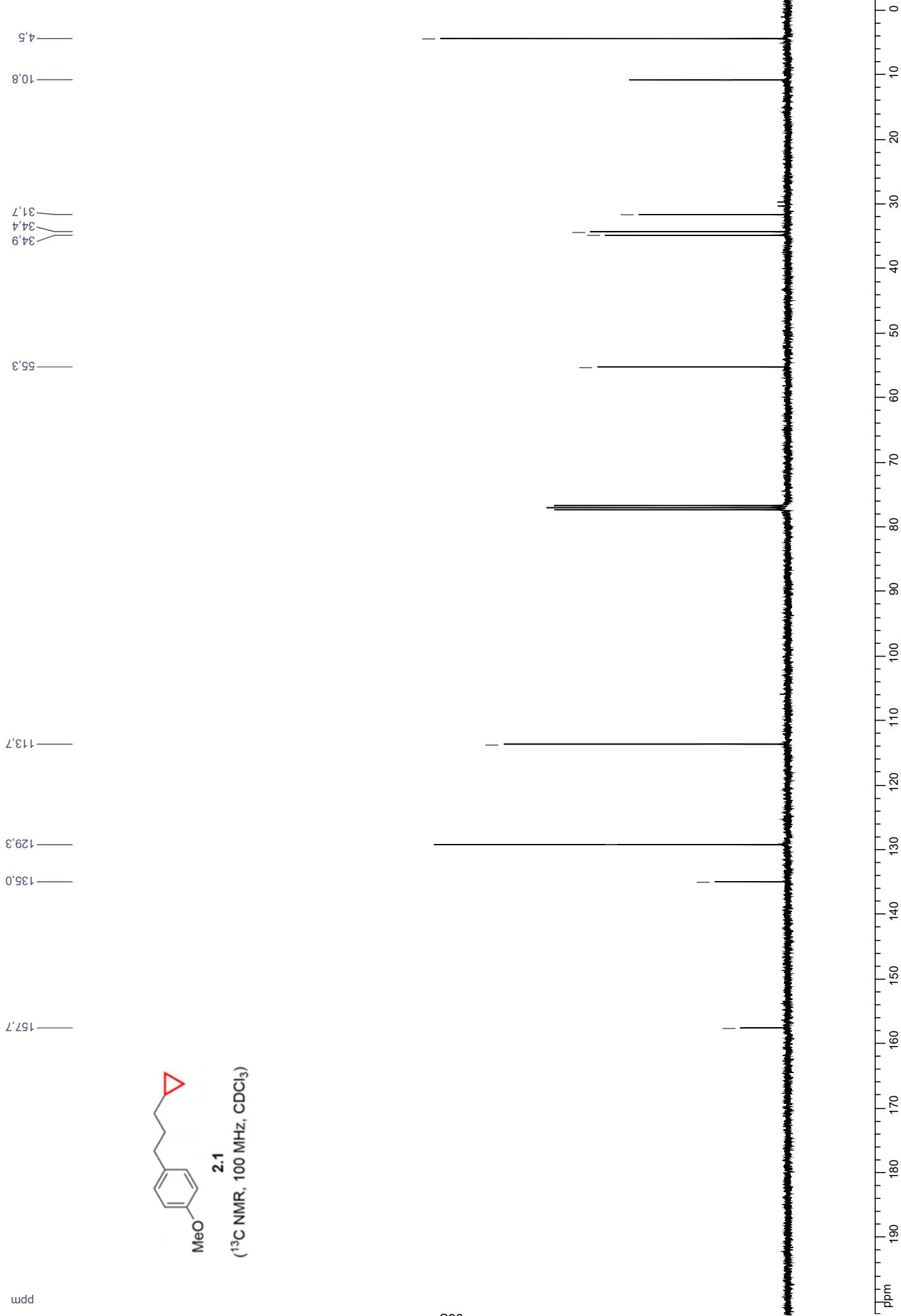
trans/cis = 85:15

1.16

(^{13}C NMR, 100 MHz, CDCl_3)

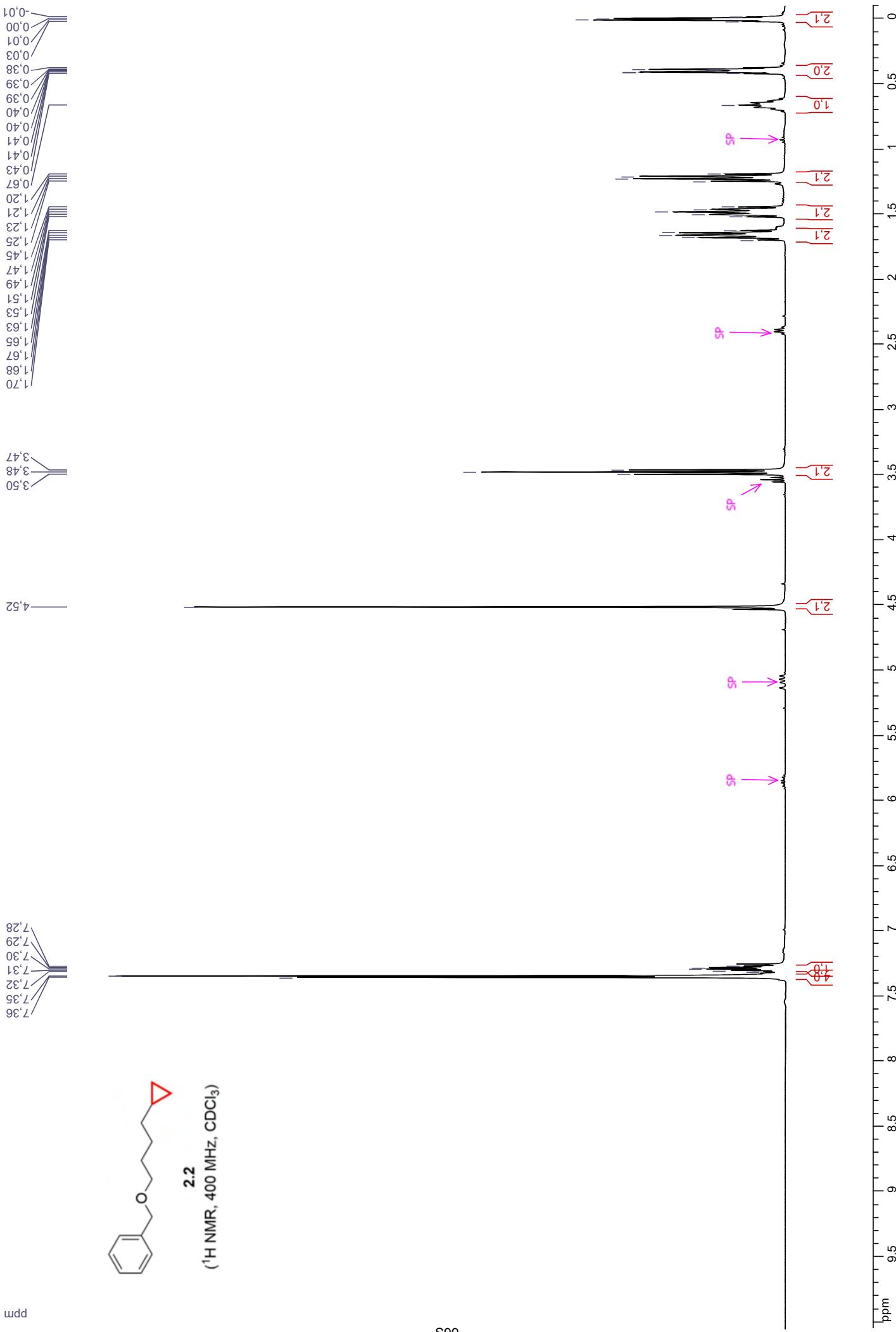


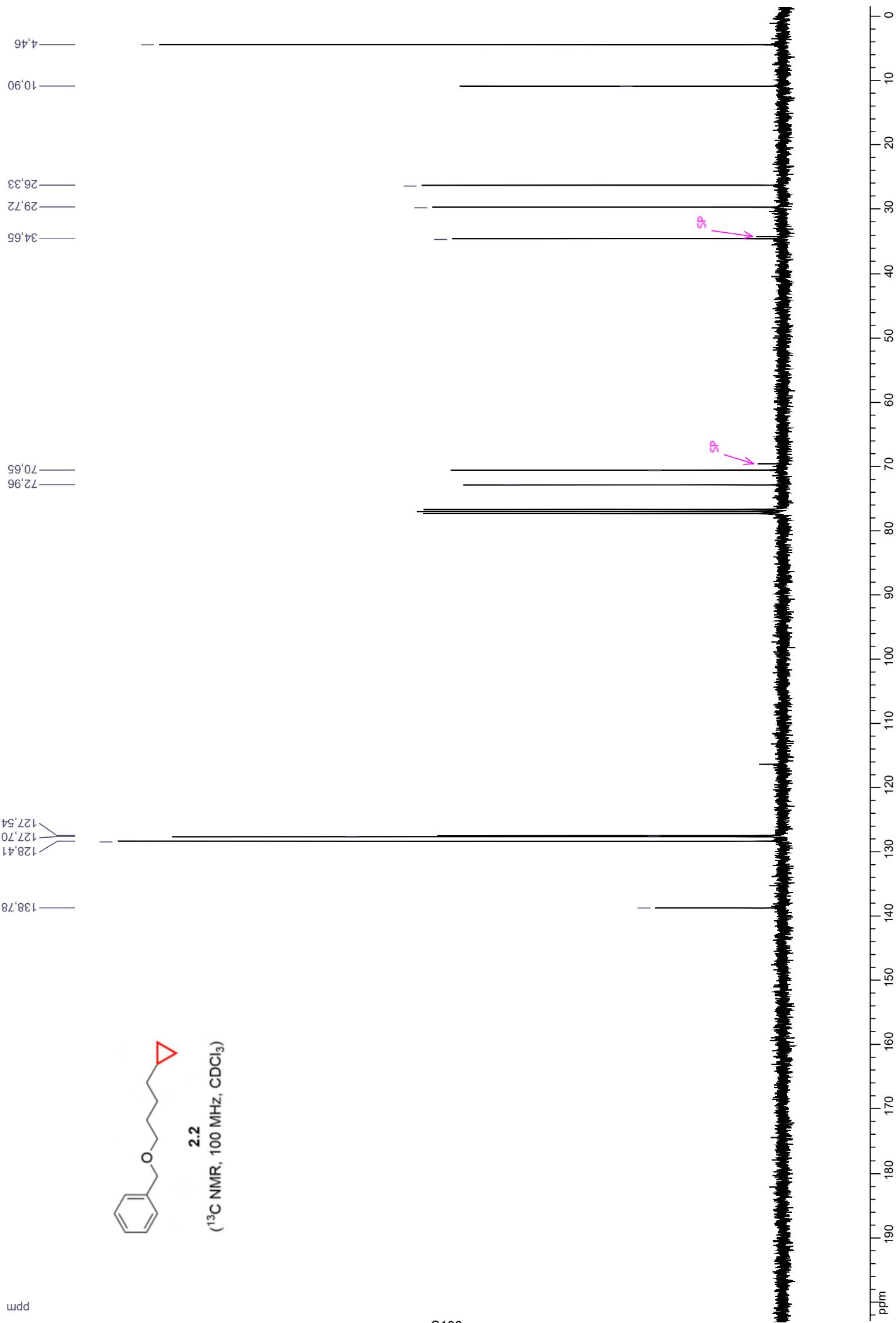




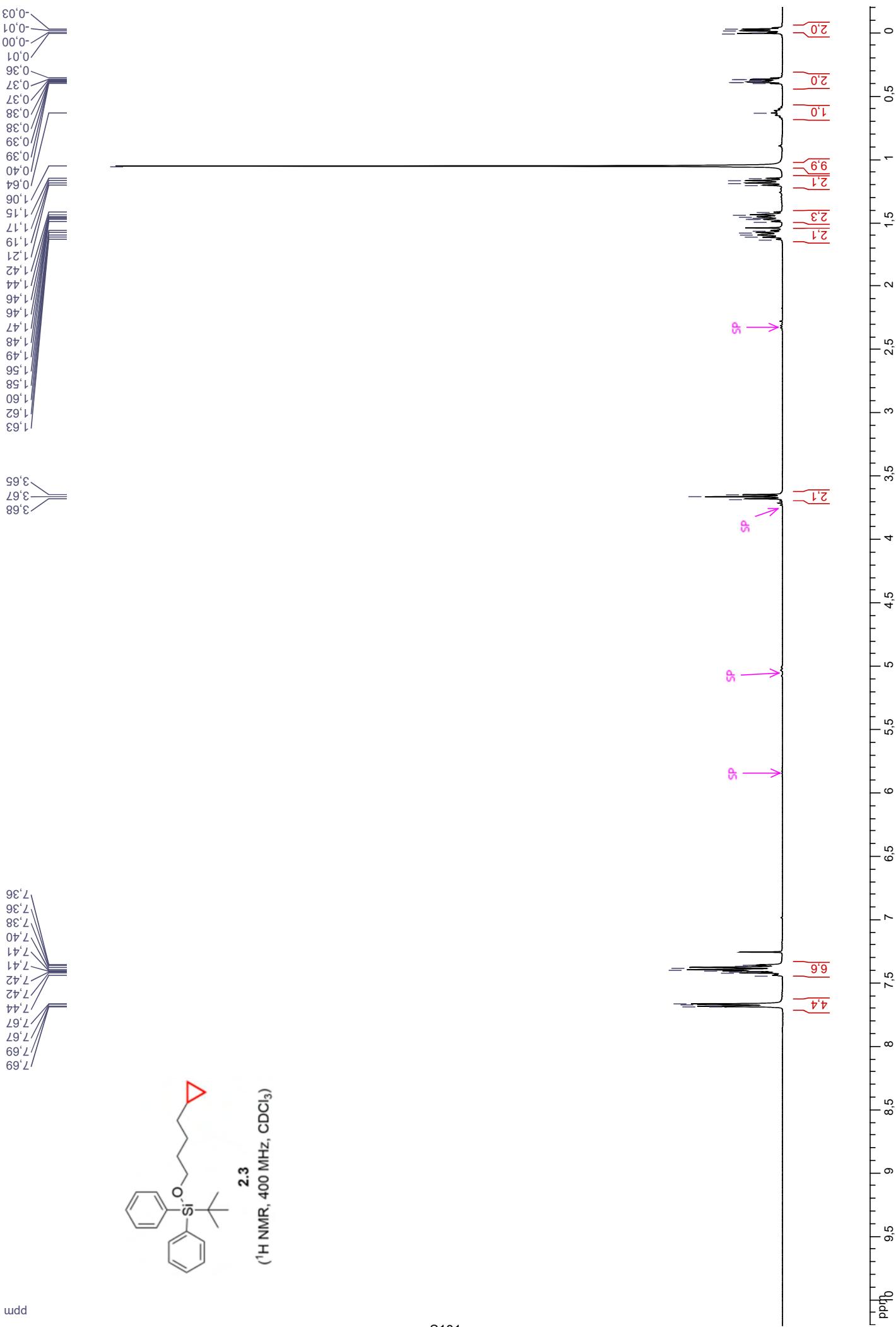
2.1

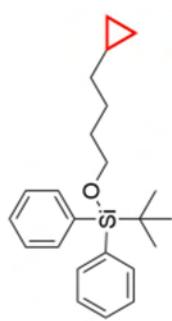
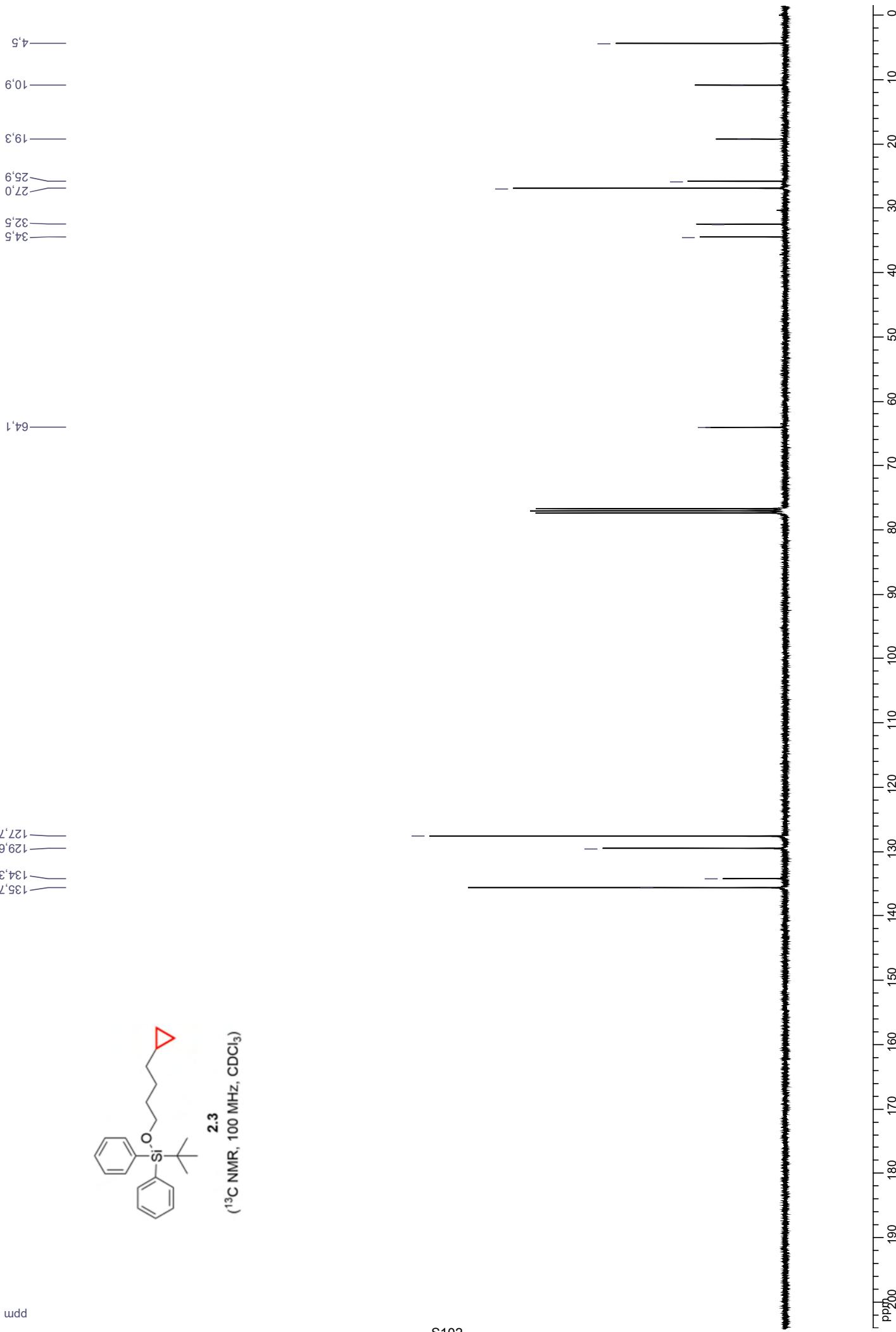
(^{13}C NMR, 100 MHz, CDCl_3)





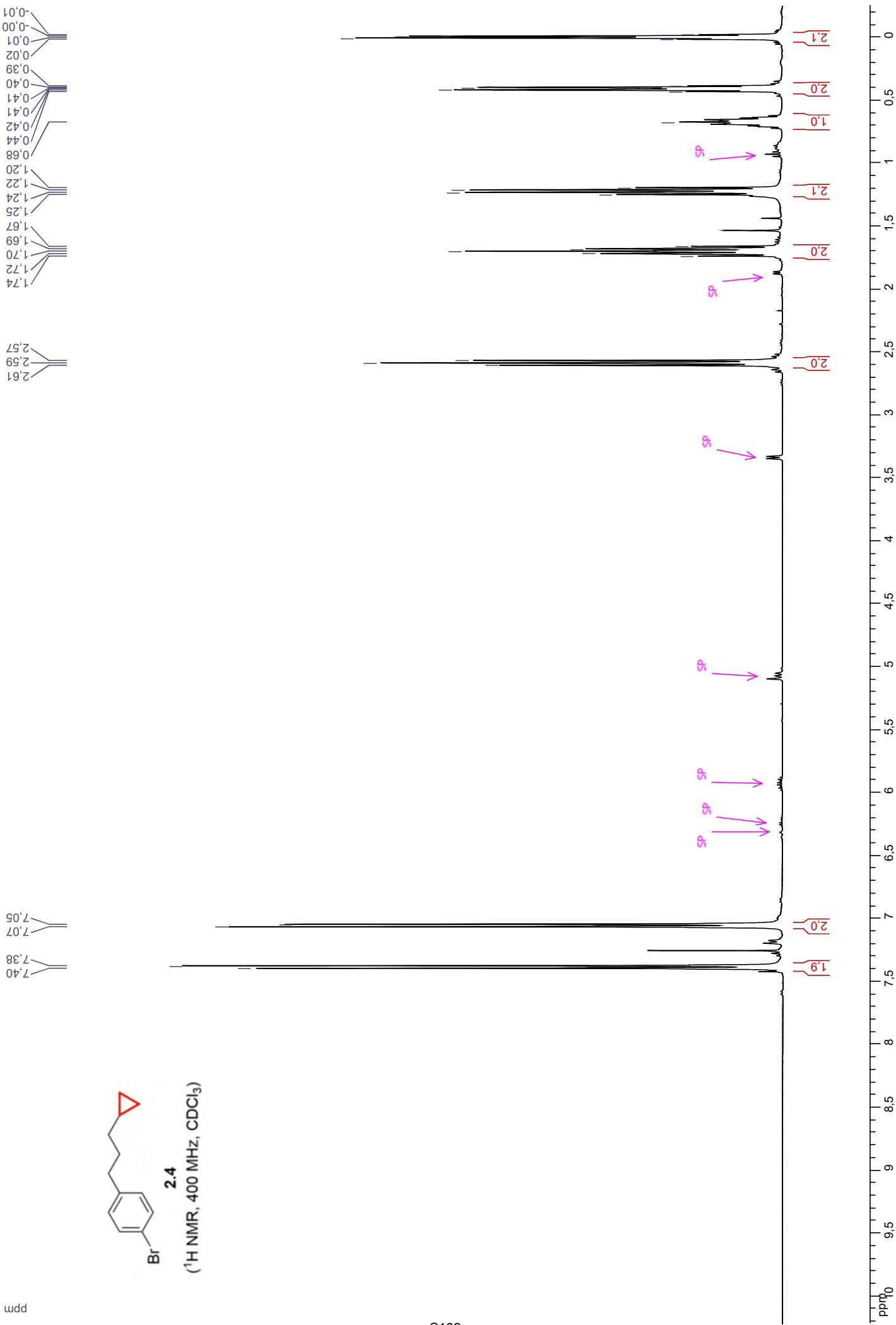
ppm

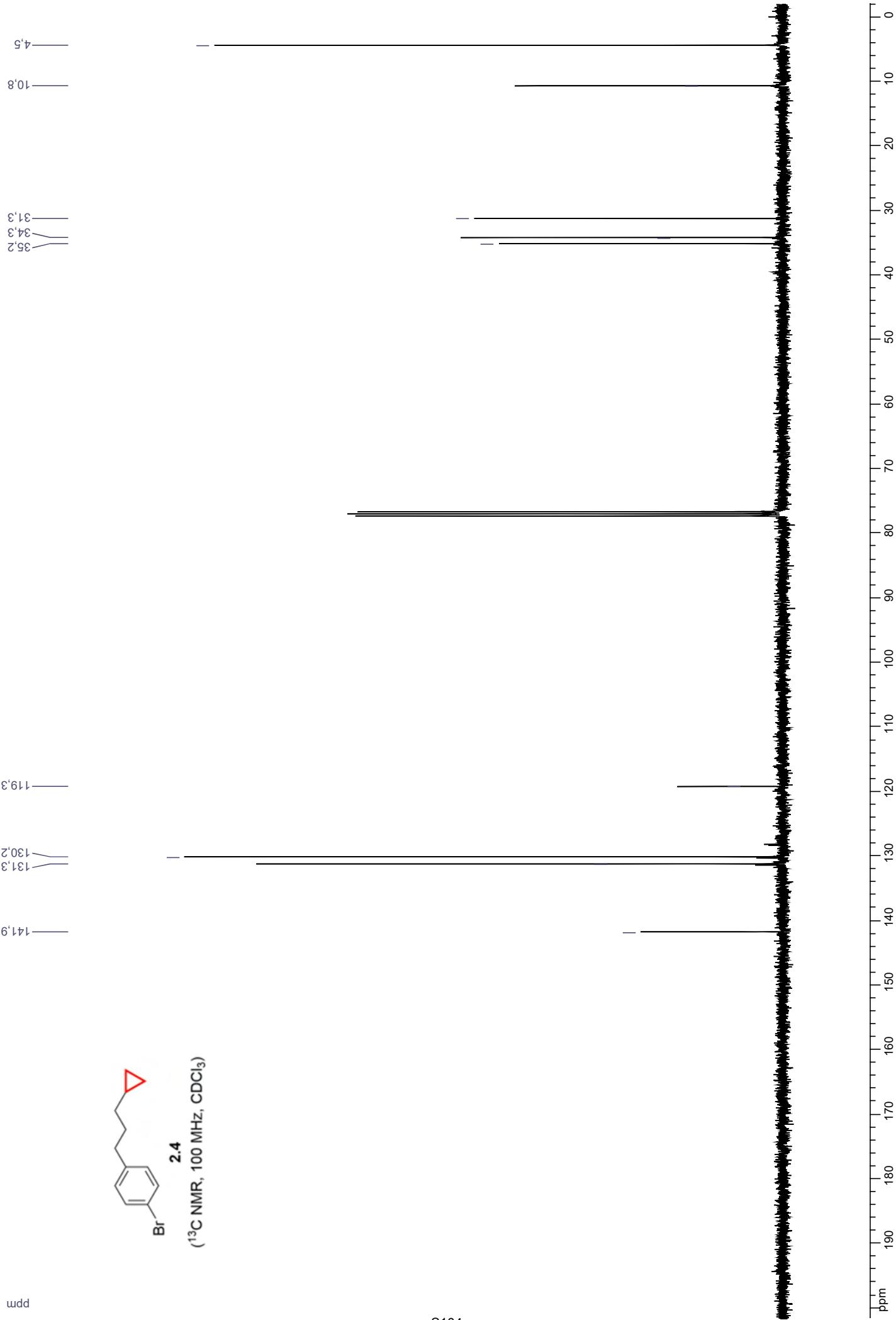


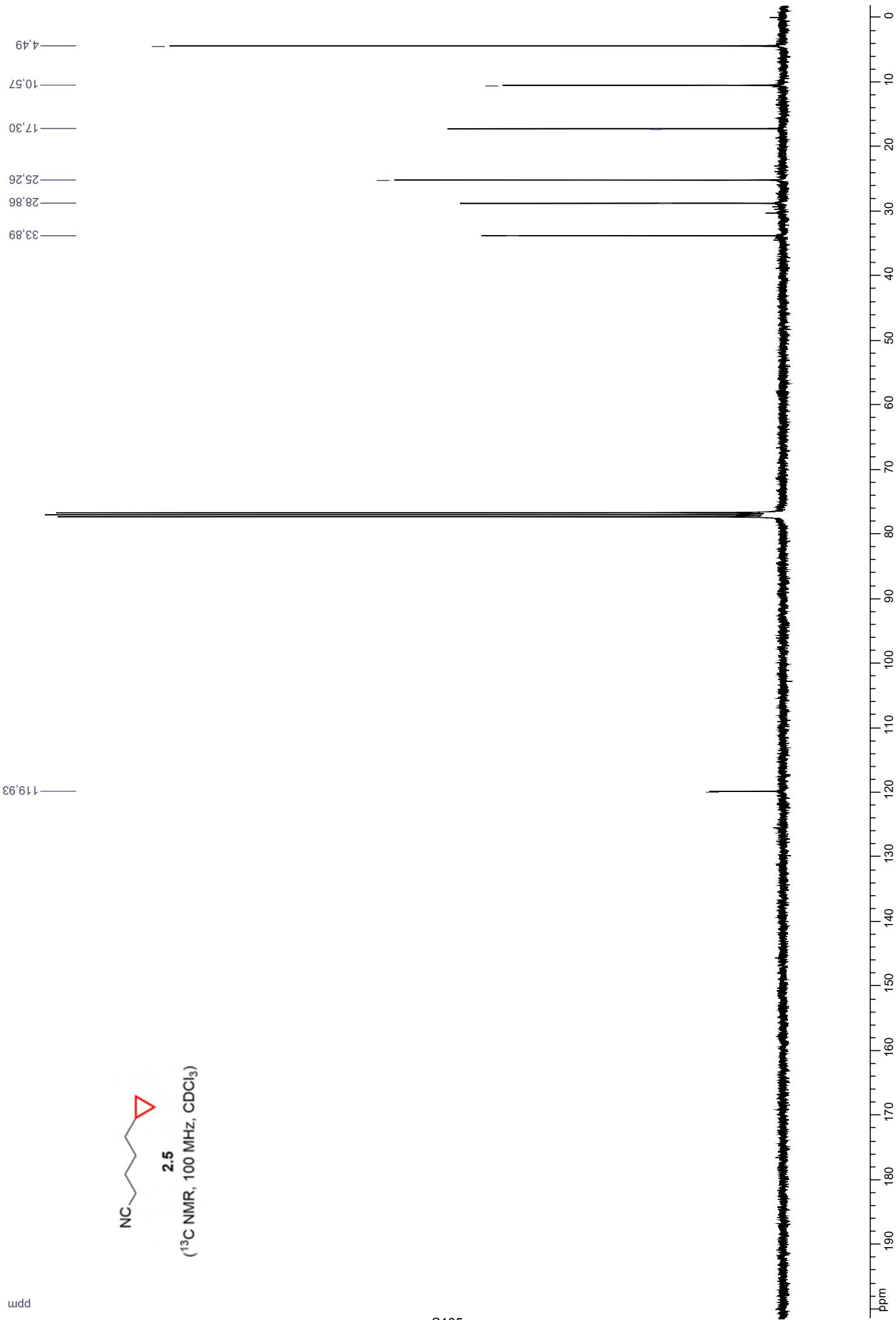


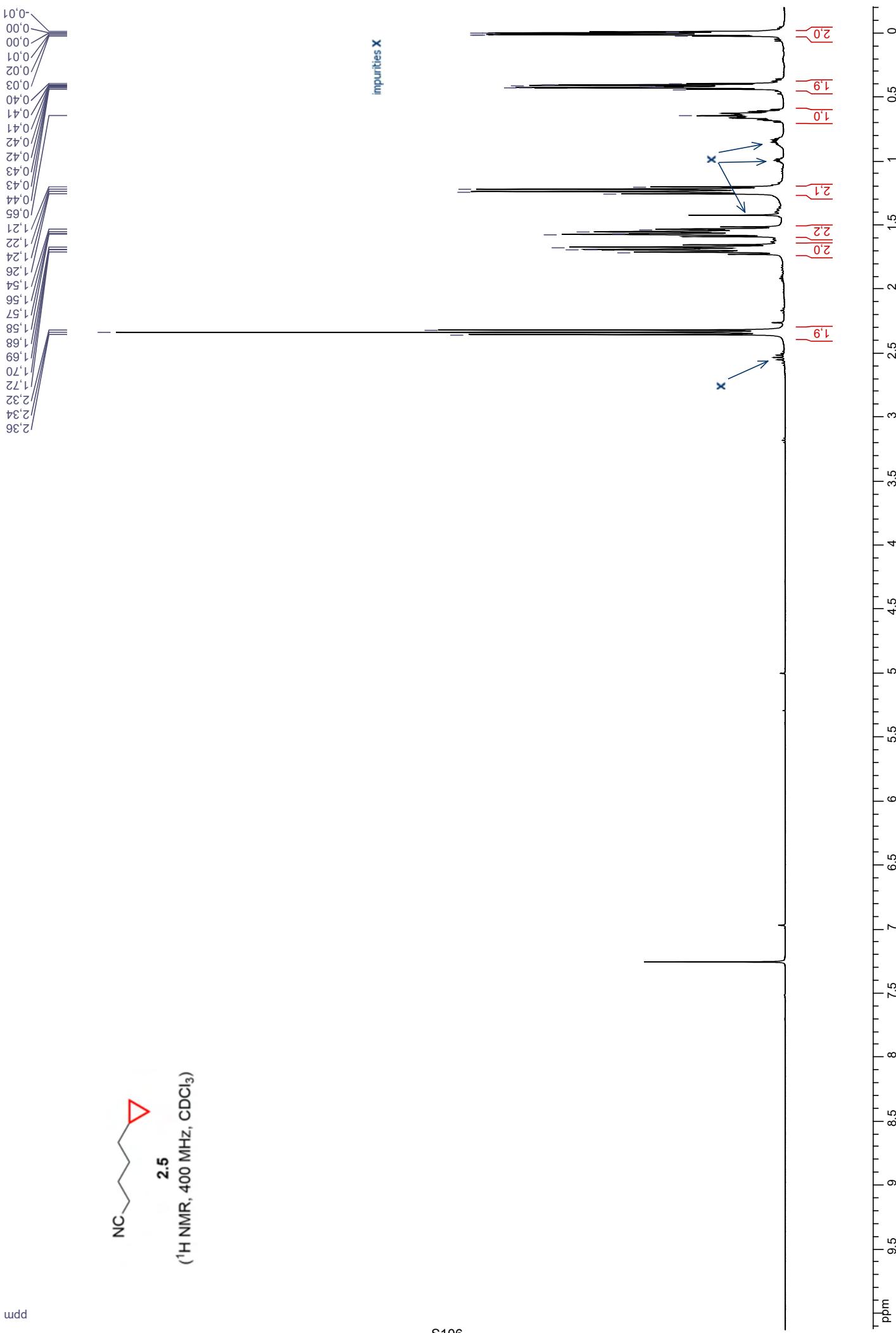
2.3
(^{13}C NMR, 100 MHz, CDCl_3)

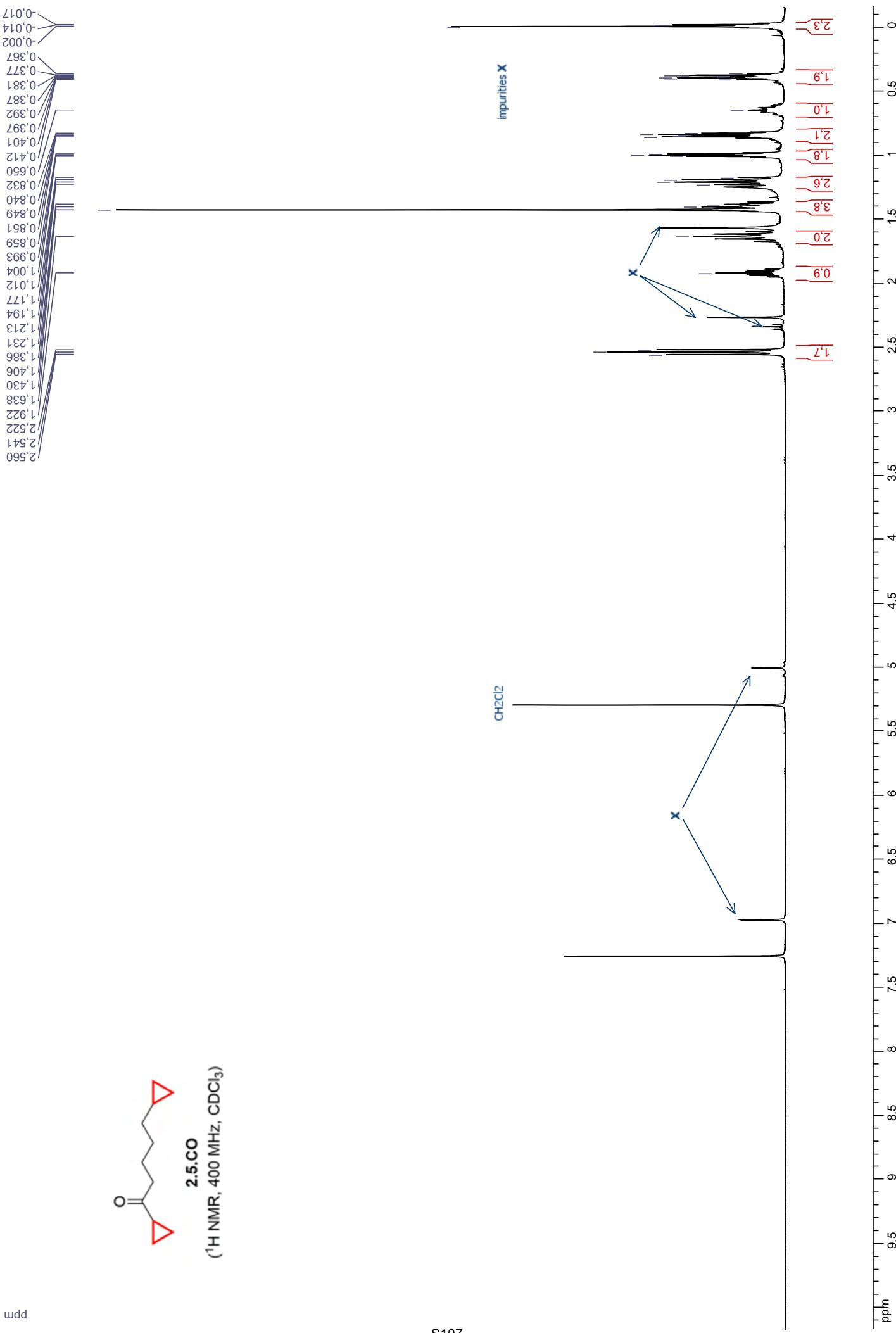
ppm

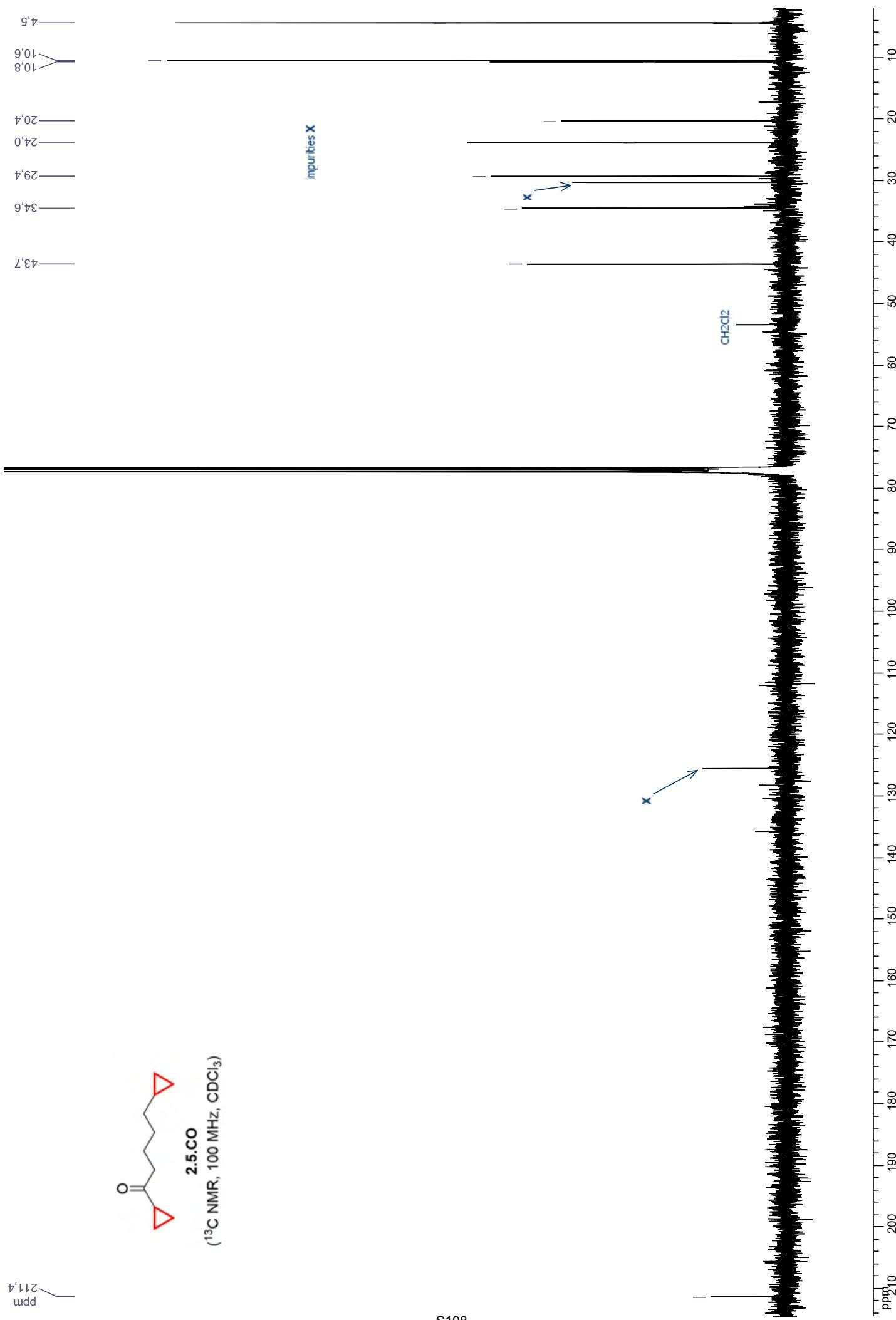


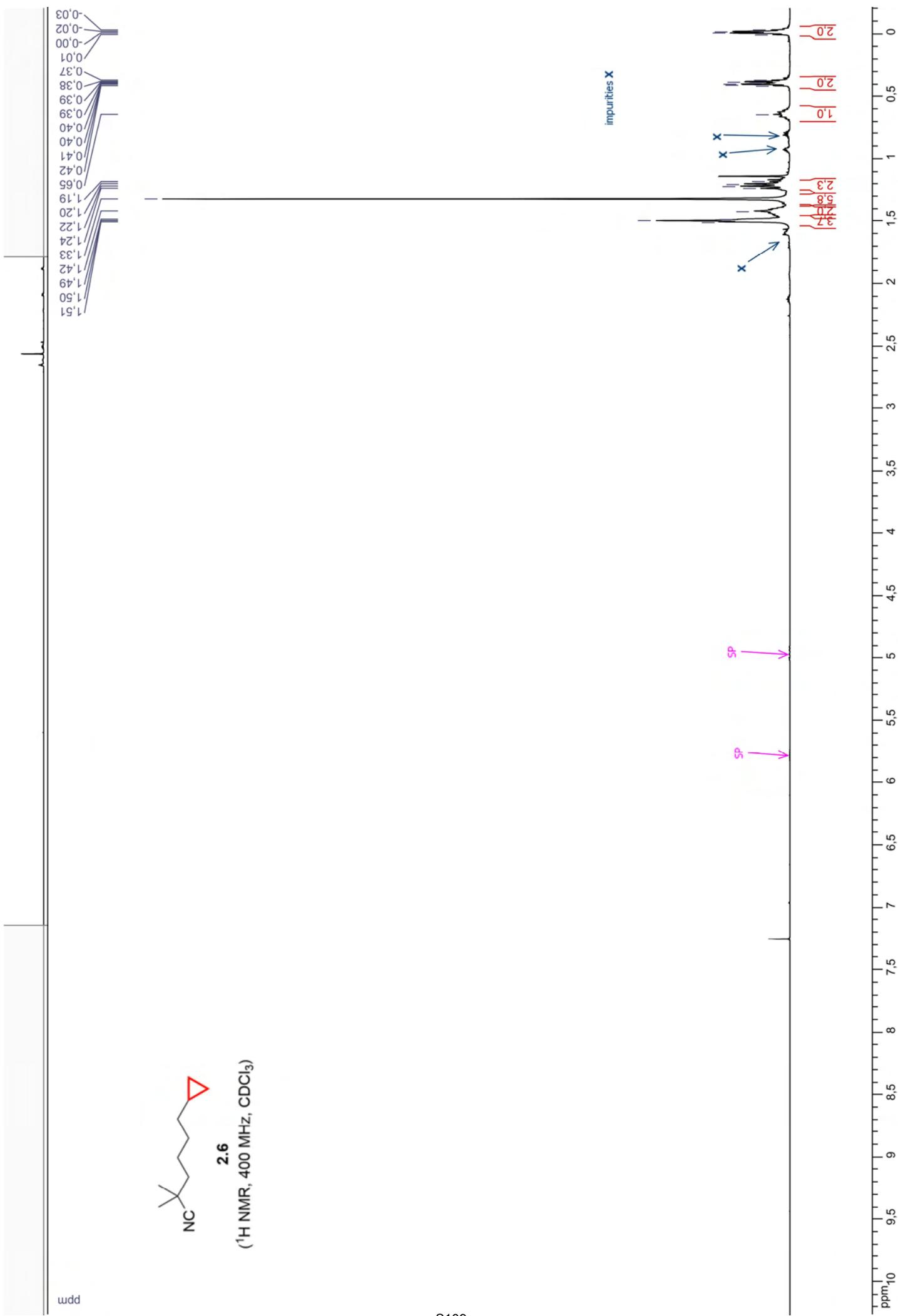




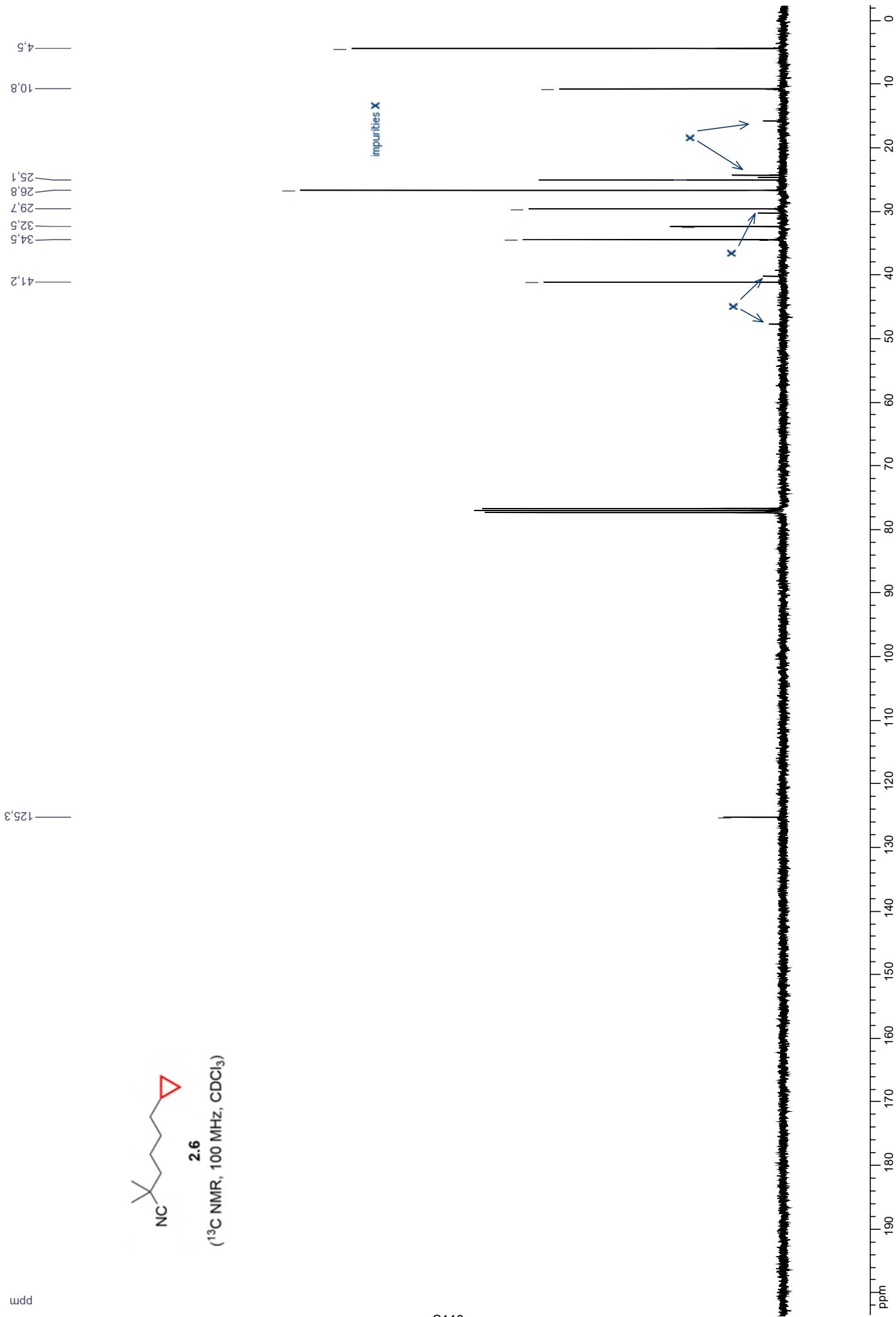




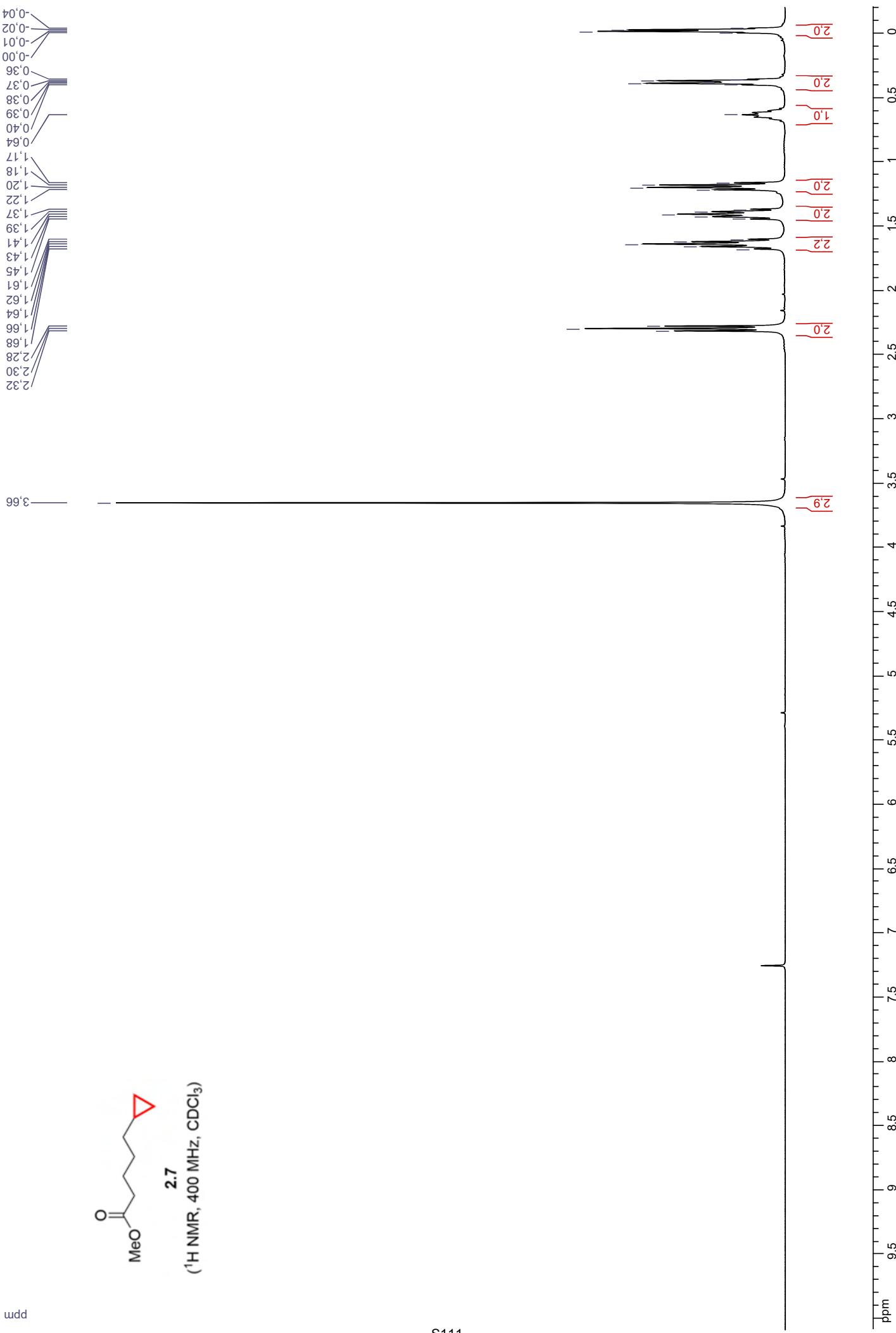




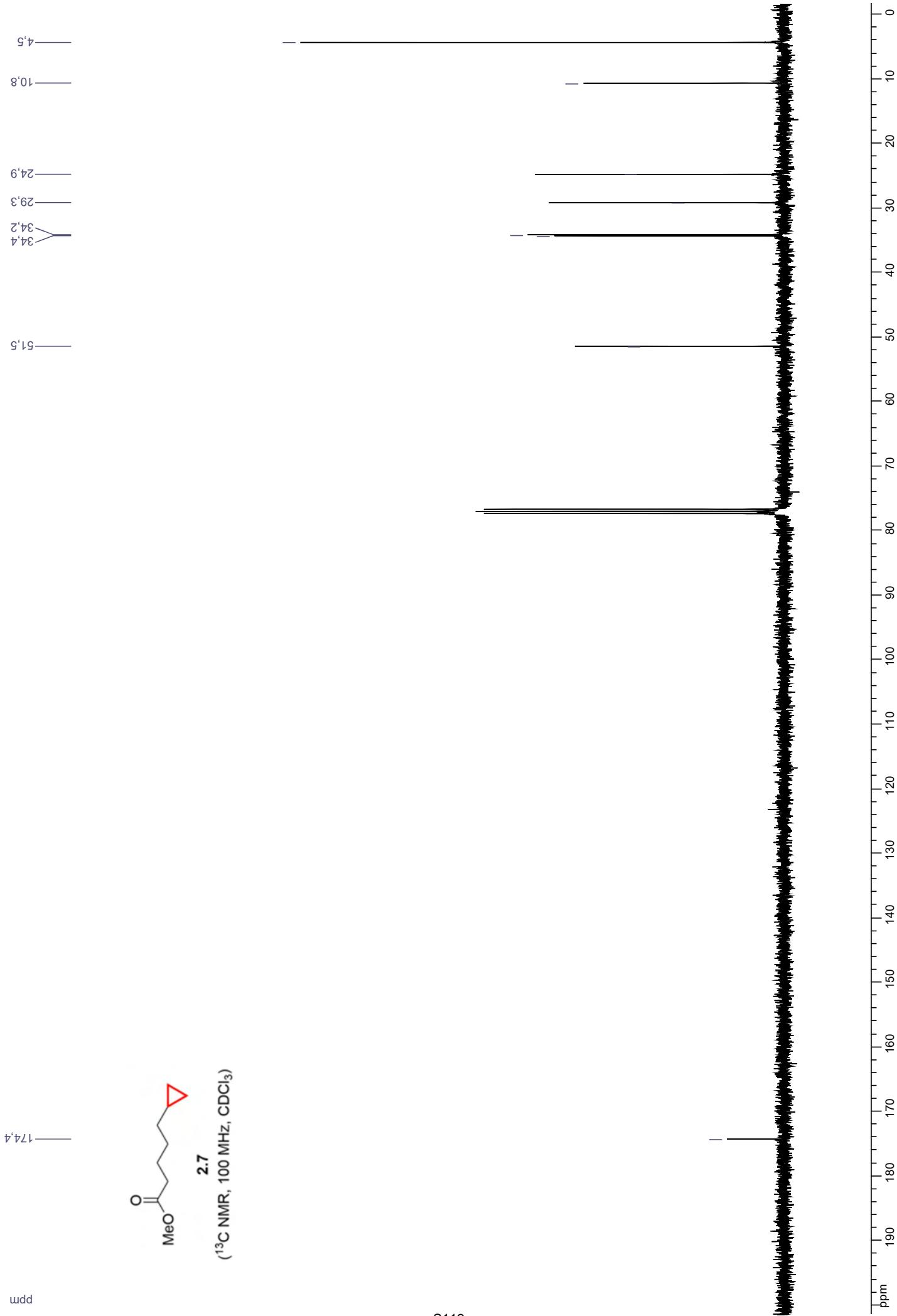
2.6
(¹H NMR, 400 MHz, CDCl₃)

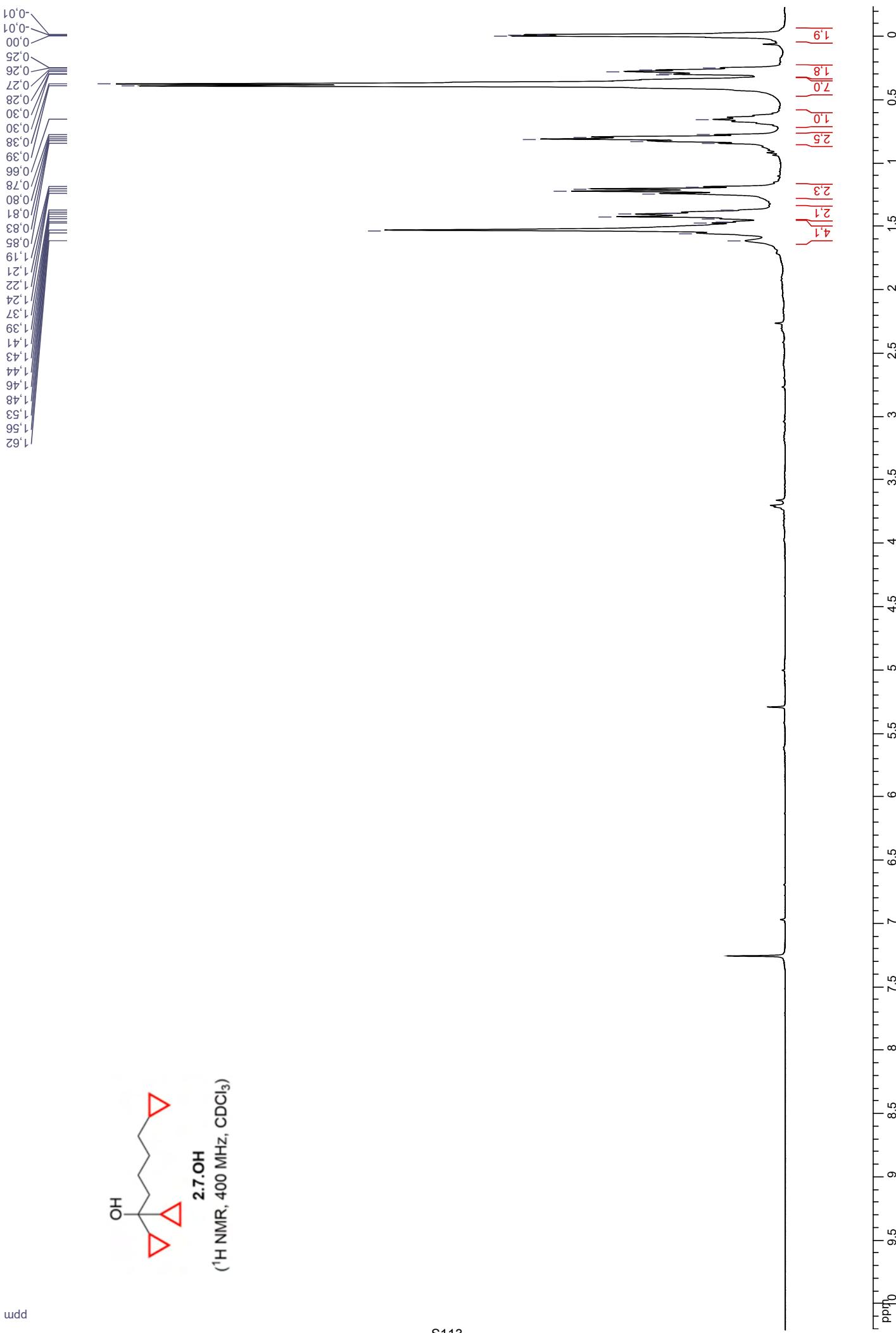


2.6
(¹³C NMR, 100 MHz, CDCl₃)

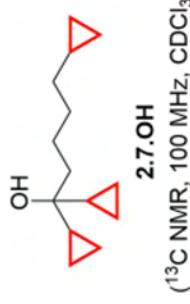
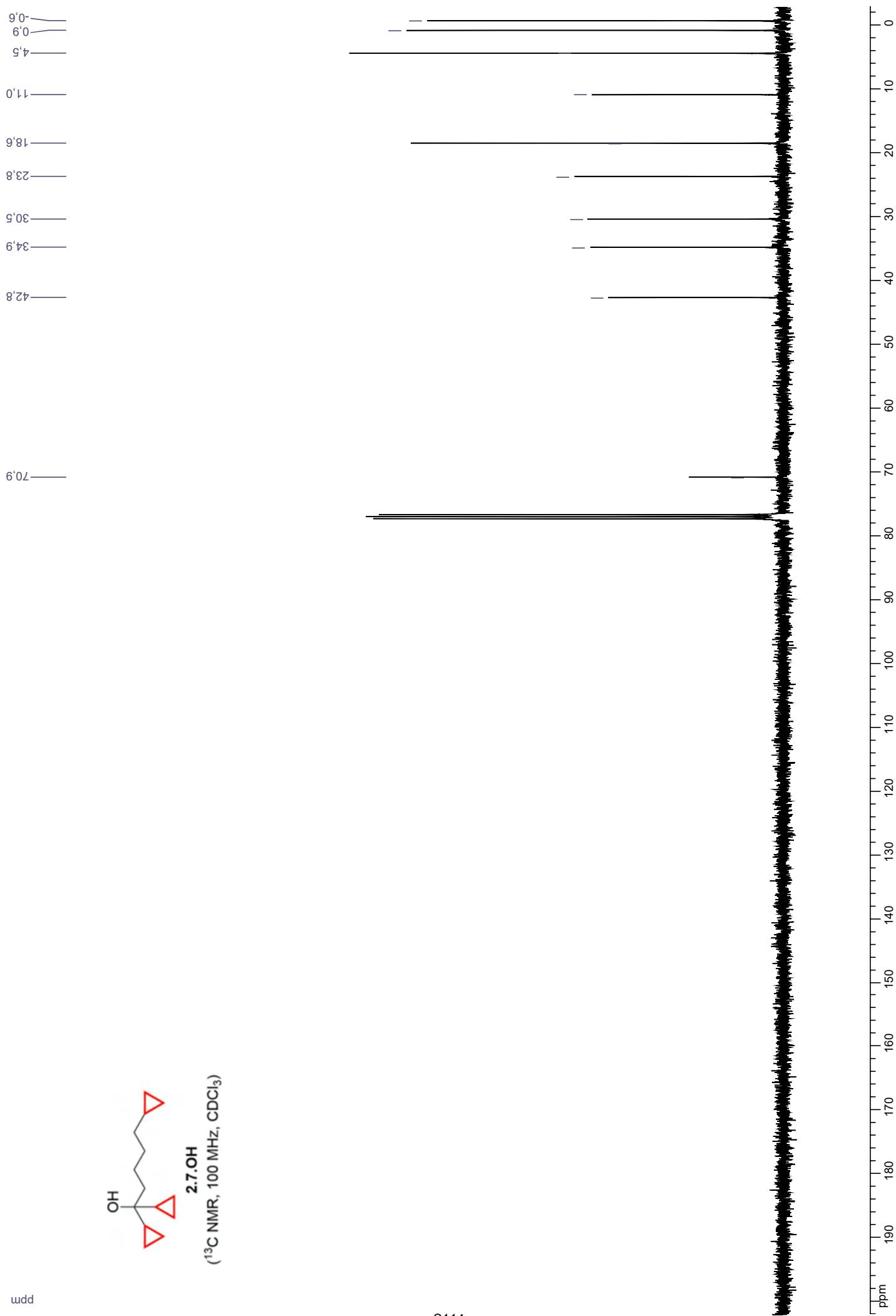


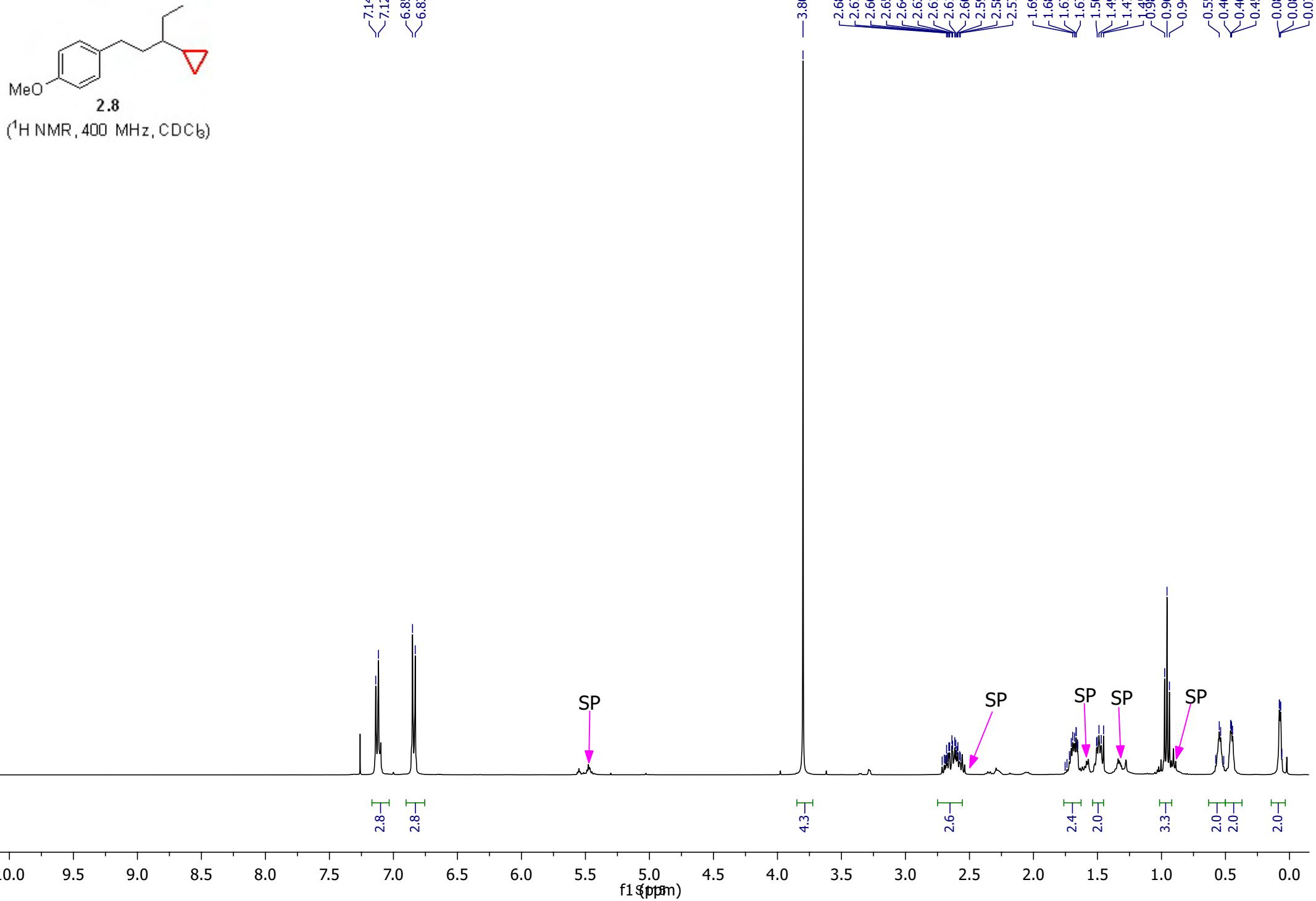
2.7
(¹H NMR, 400 MHz, CDCl₃)

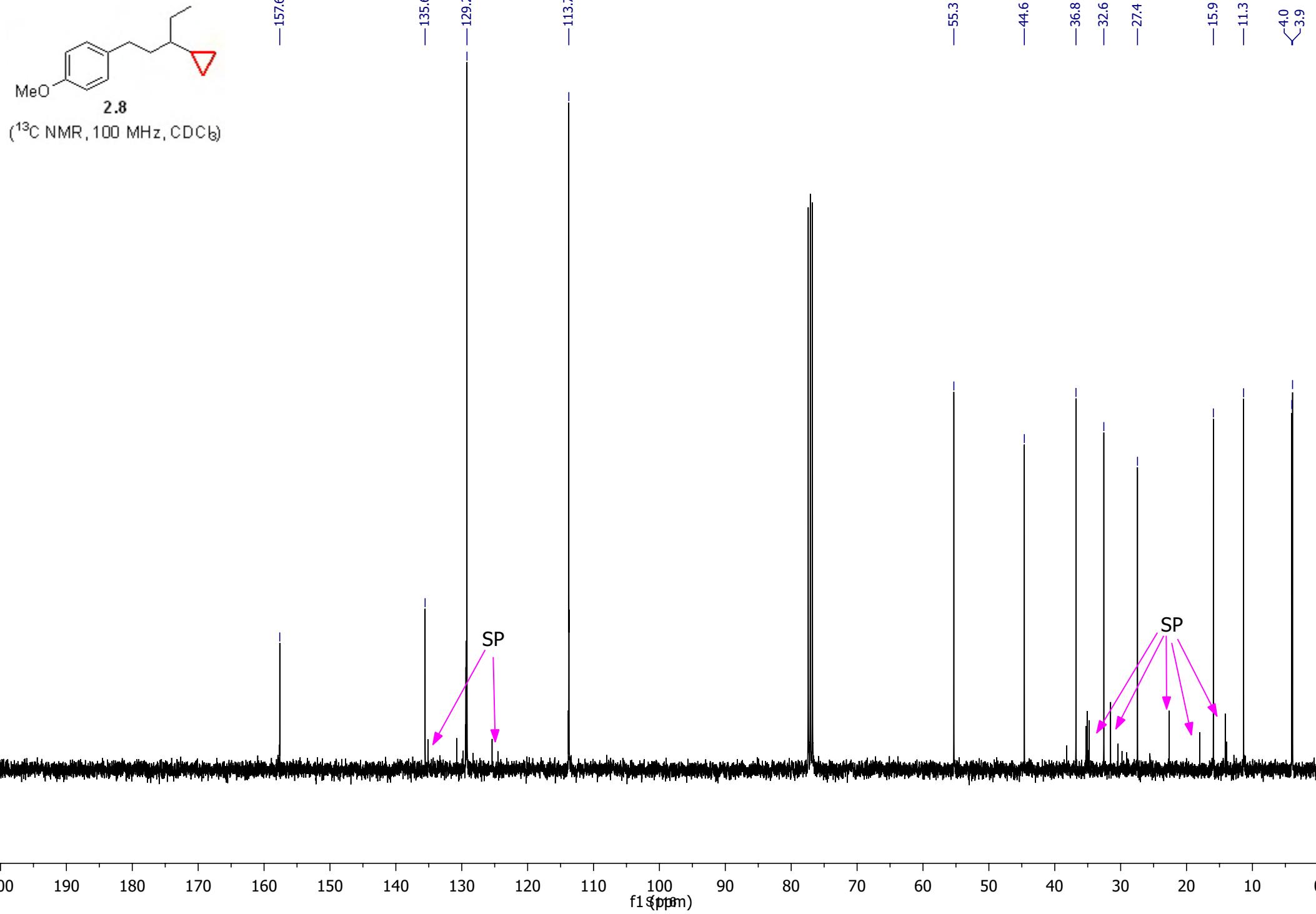


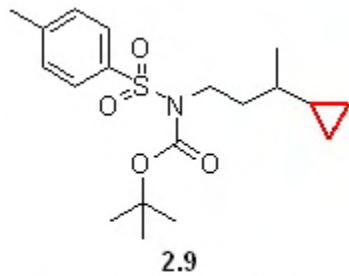


2.7.OH
(^1H NMR, 400 MHz, CDCl_3)

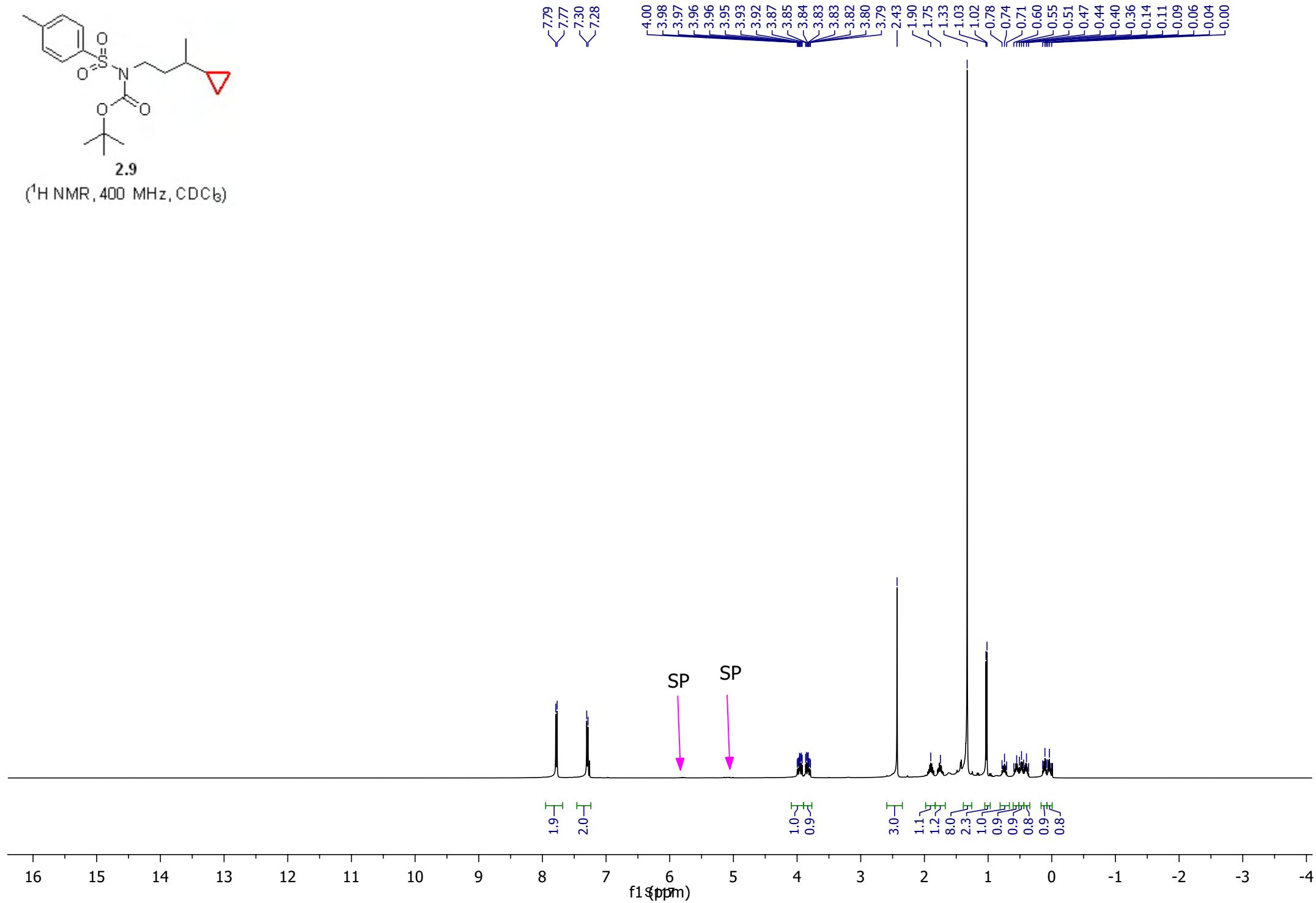


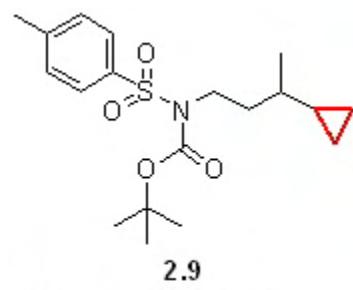




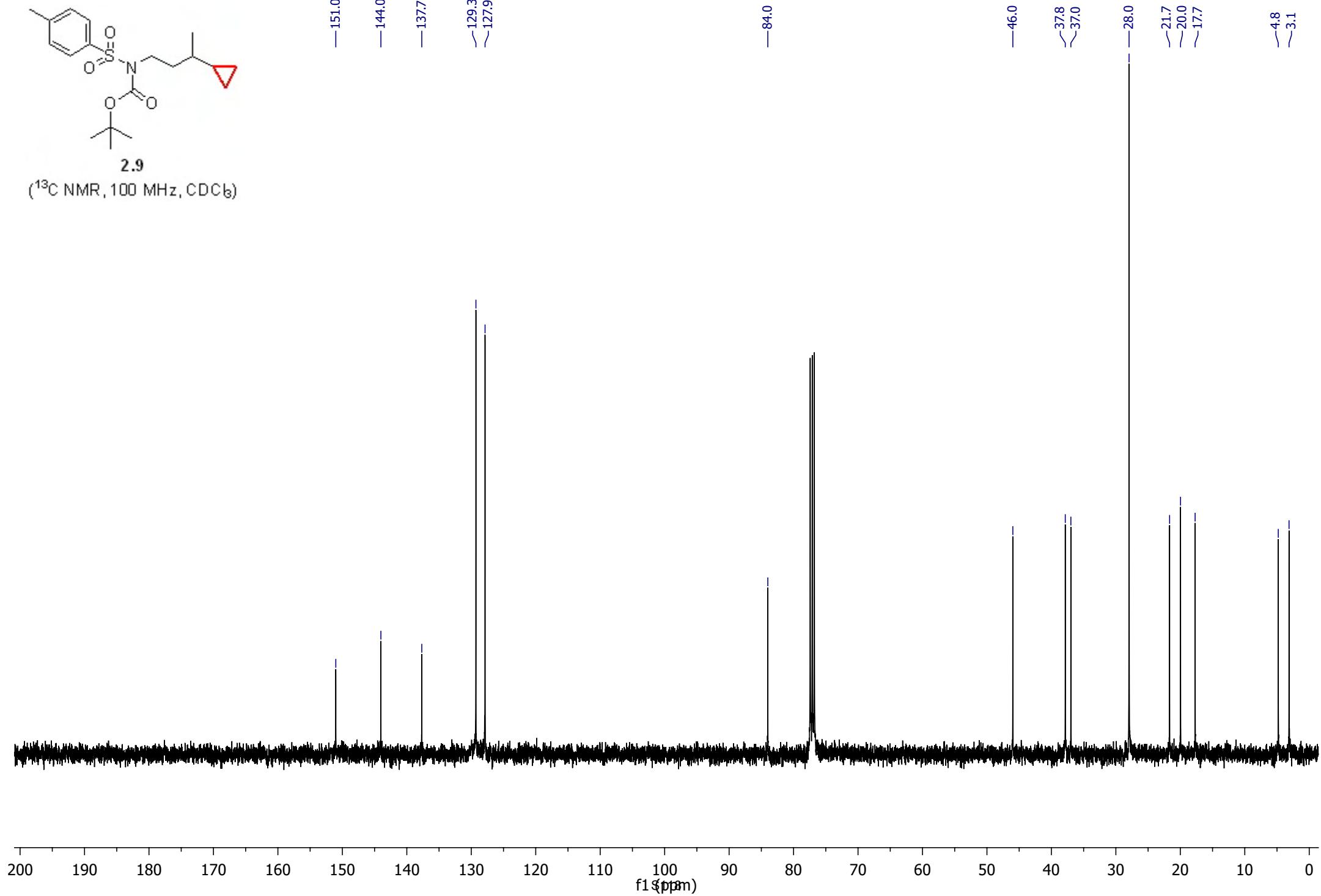


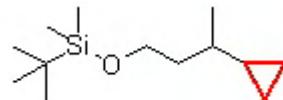
(^1H NMR, 400 MHz, CDCl_3)



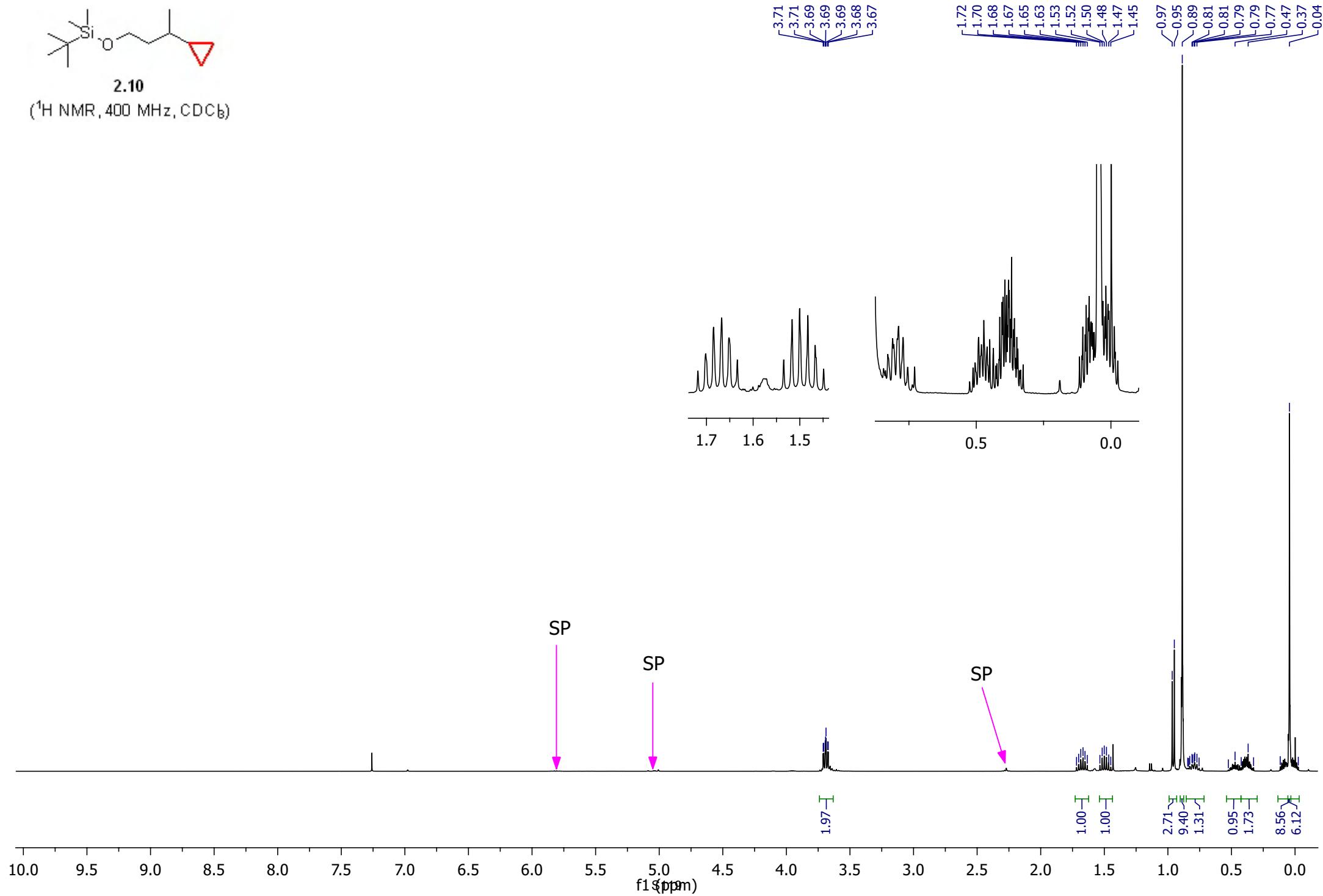


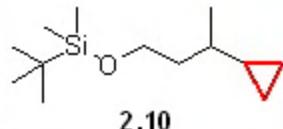
(^{13}C NMR, 100 MHz, CDCl_3)





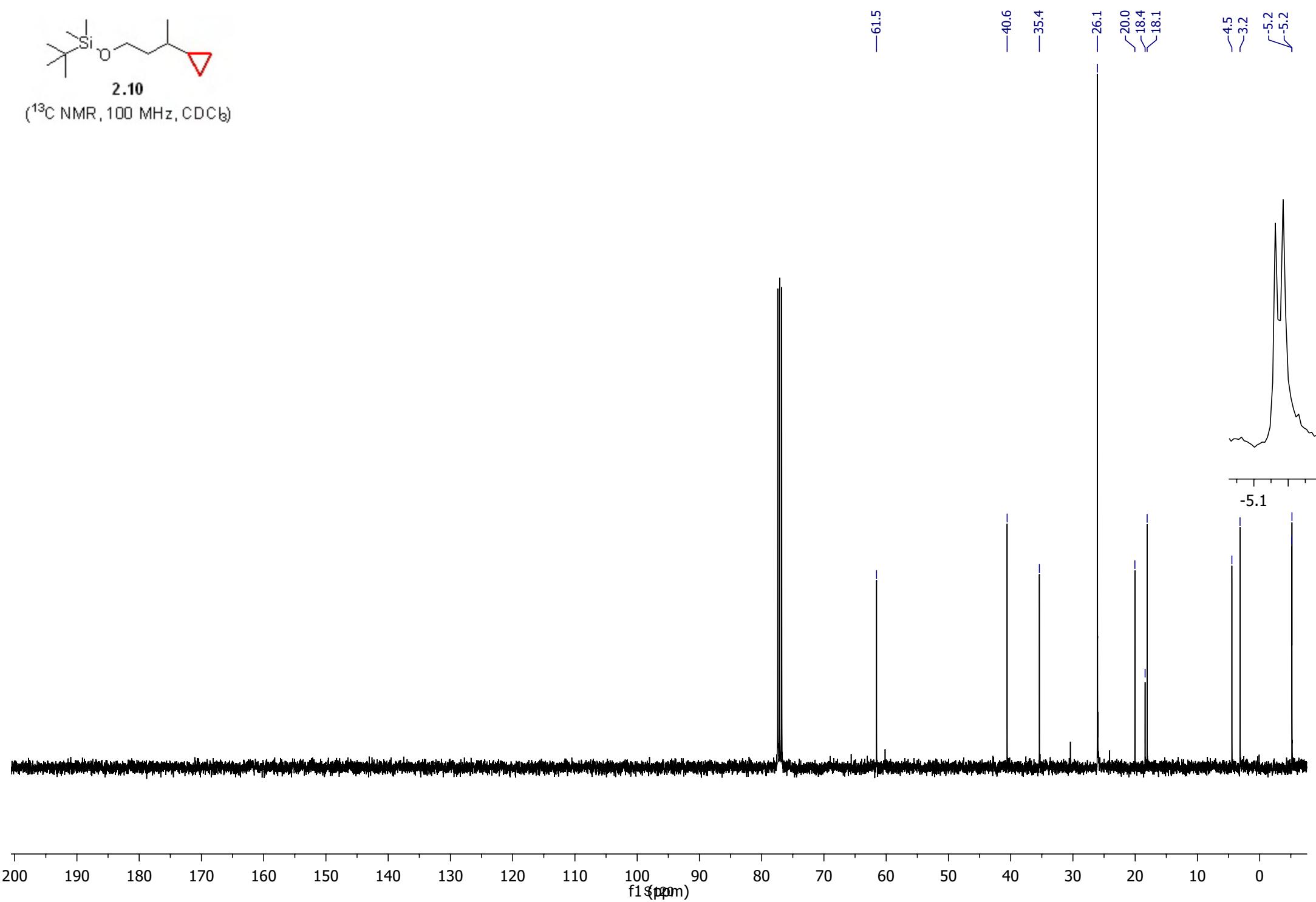
2.10

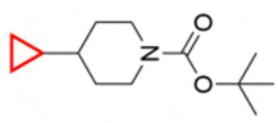
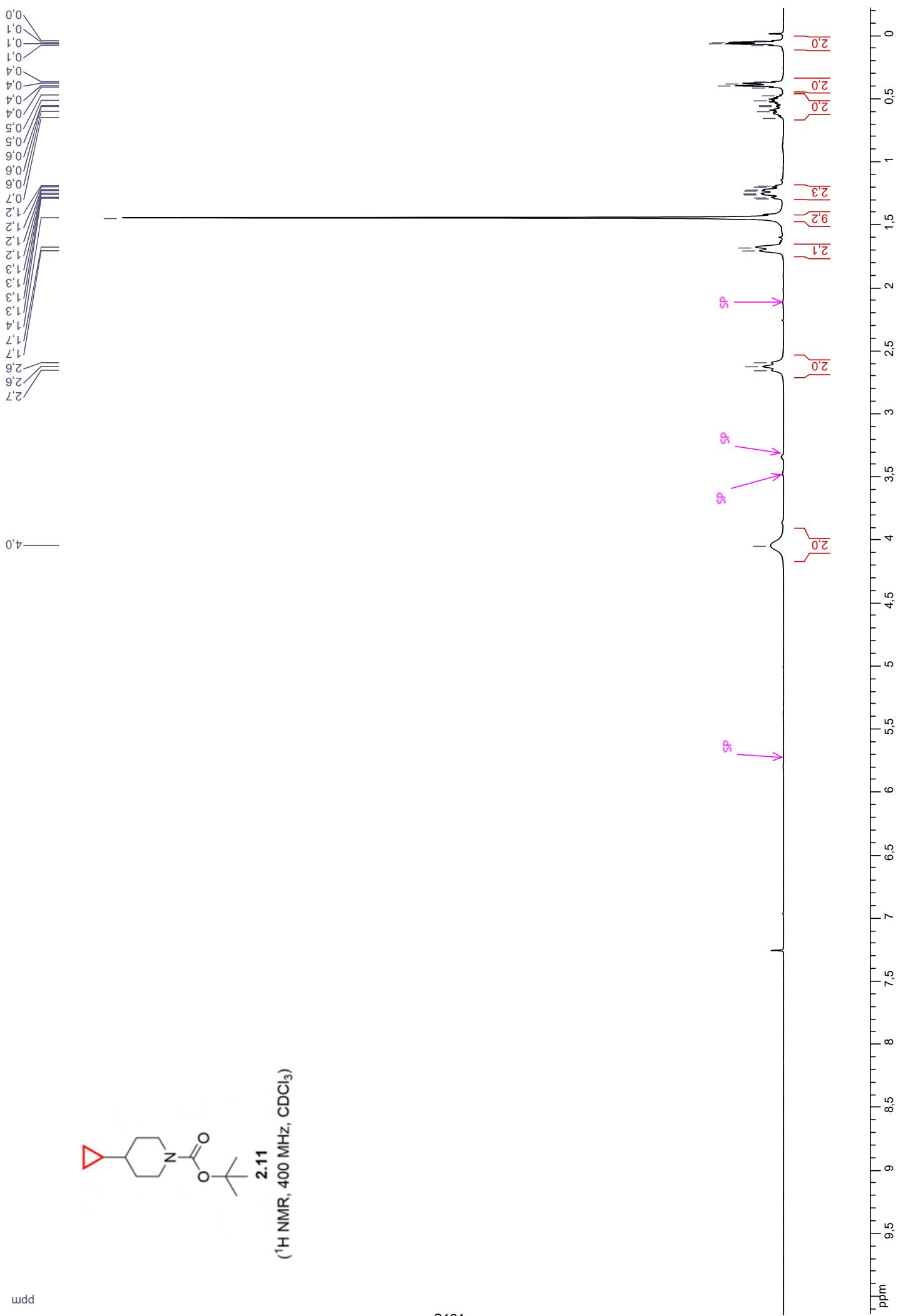
(1H NMR, 400 MHz, CDCl₃)



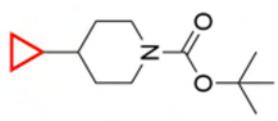
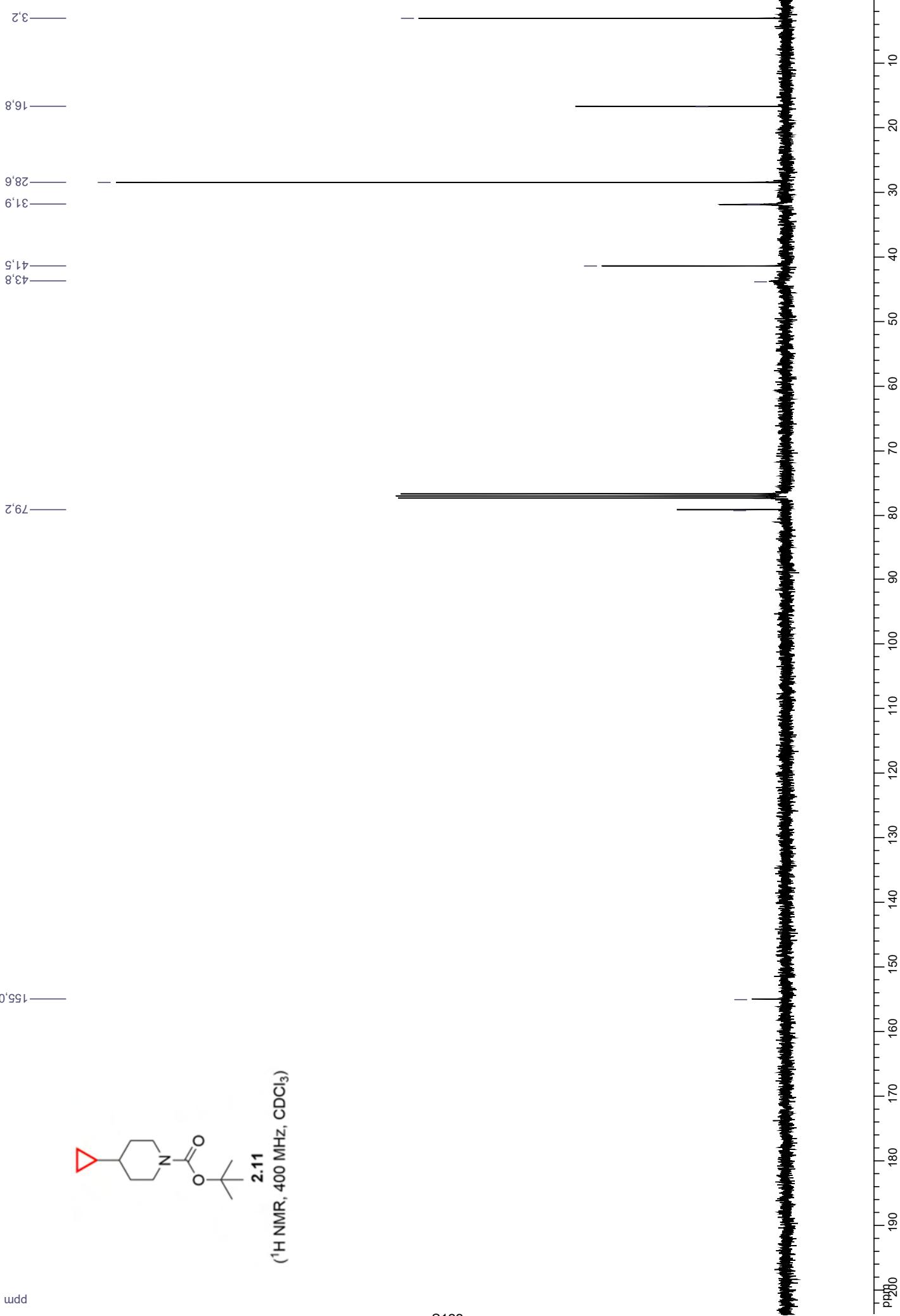
2.10

(¹³C NMR, 100 MHz, CDCl₃)

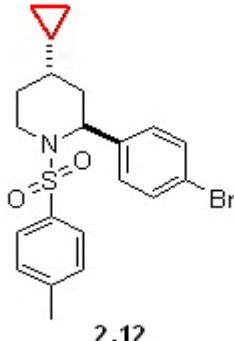




2.11 (^1H NMR, 400 MHz, CDCl_3)

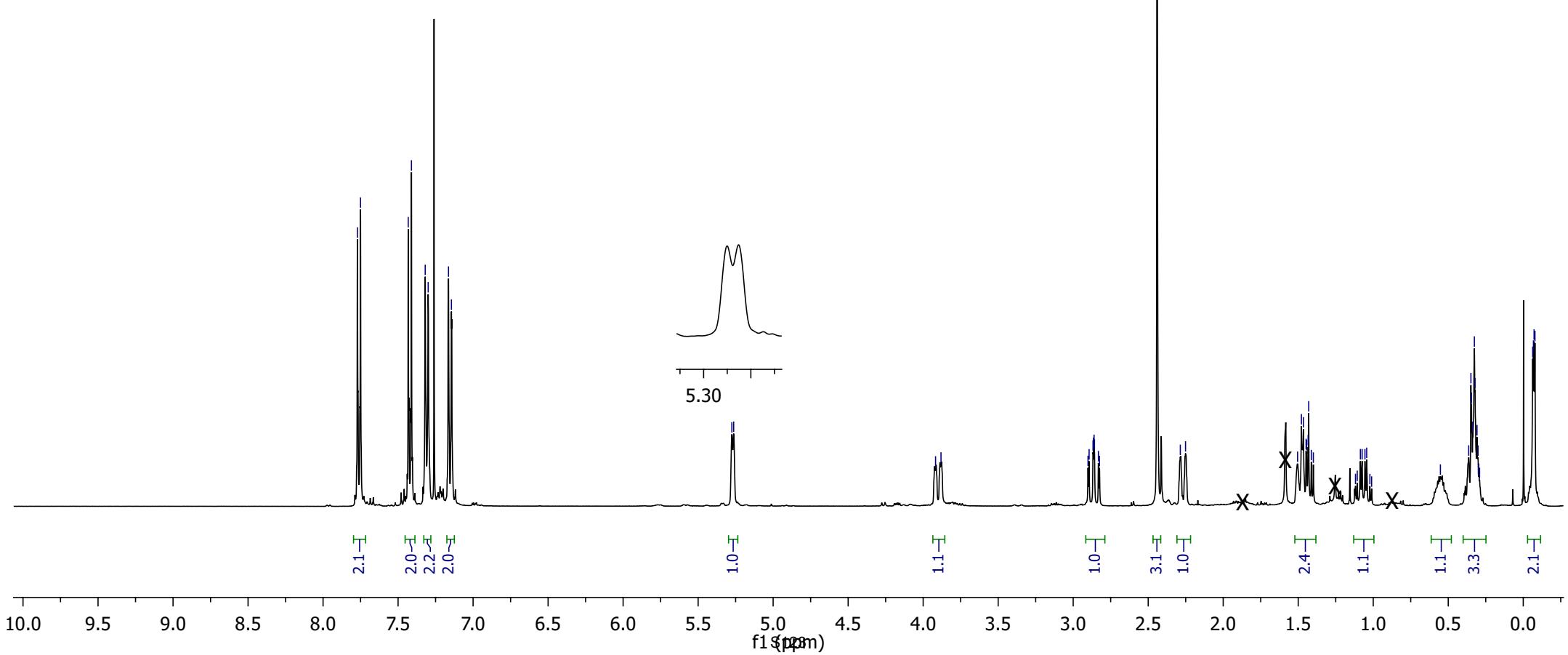


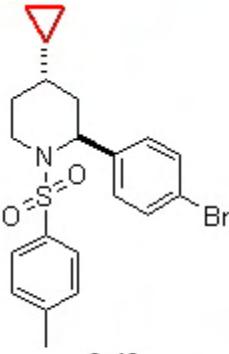
2.11
(^1H NMR, 400 MHz, CDCl_3)



trans/cis > 95:5

(^1H NMR, 400 MHz, CDCl_3)

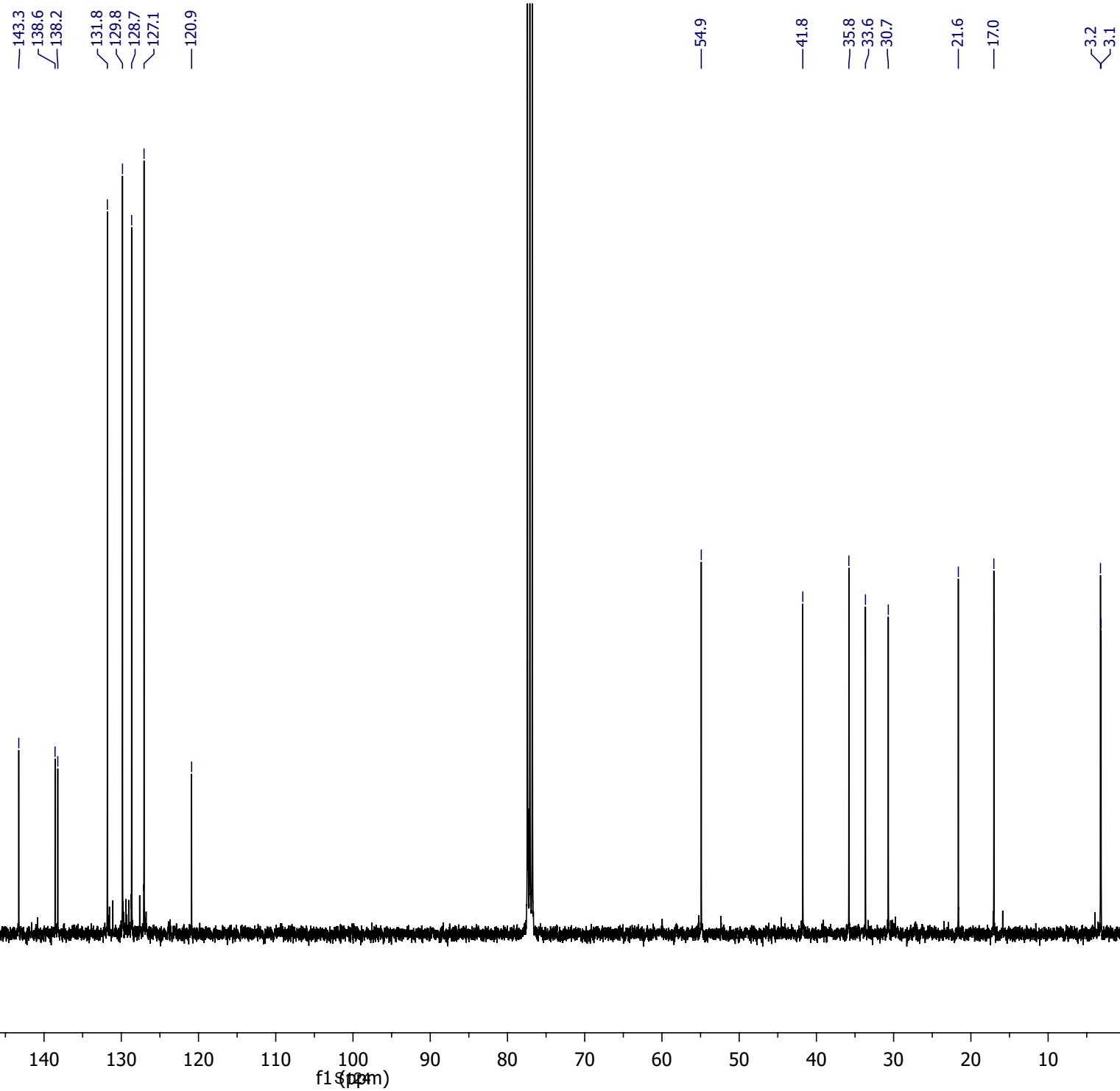


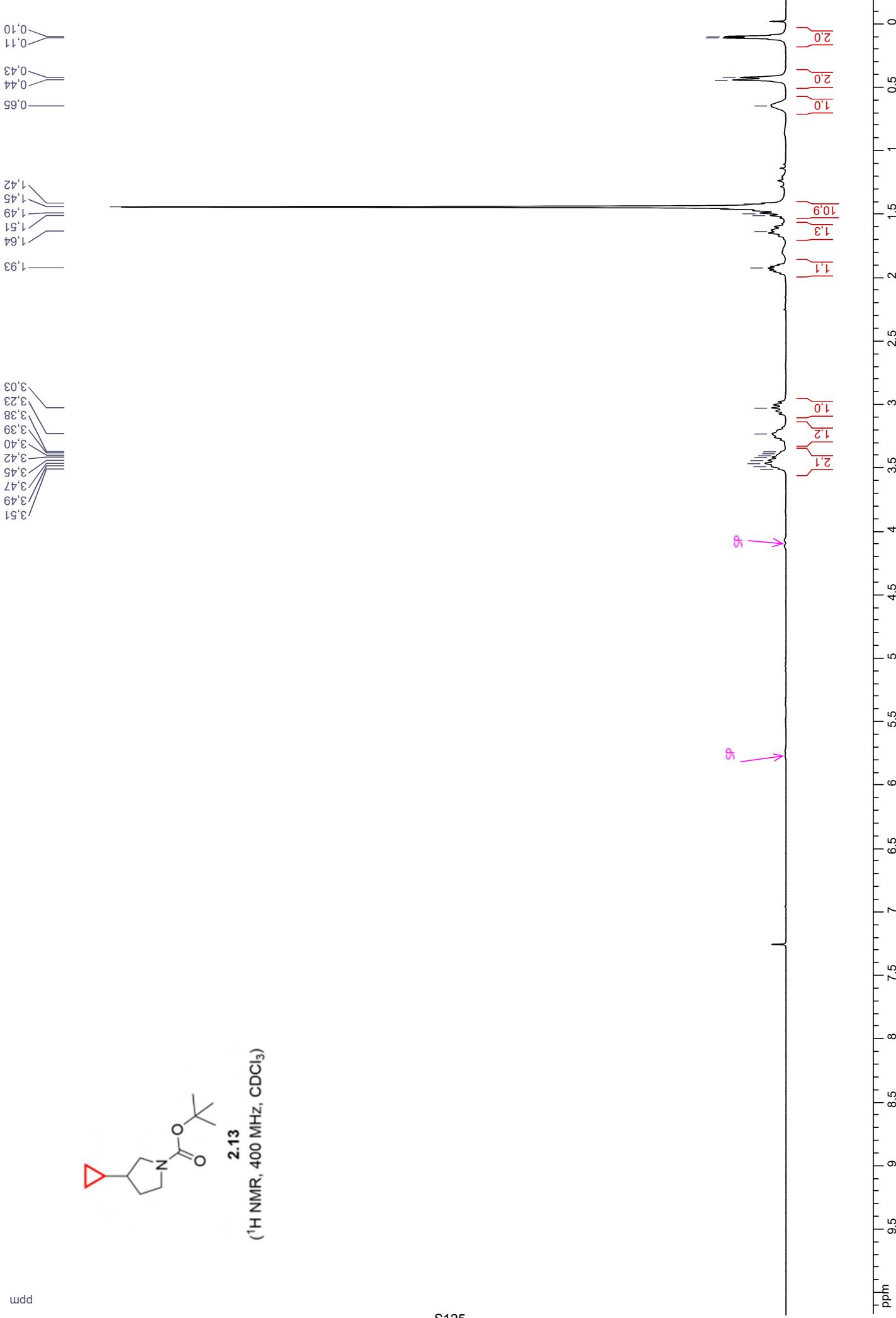


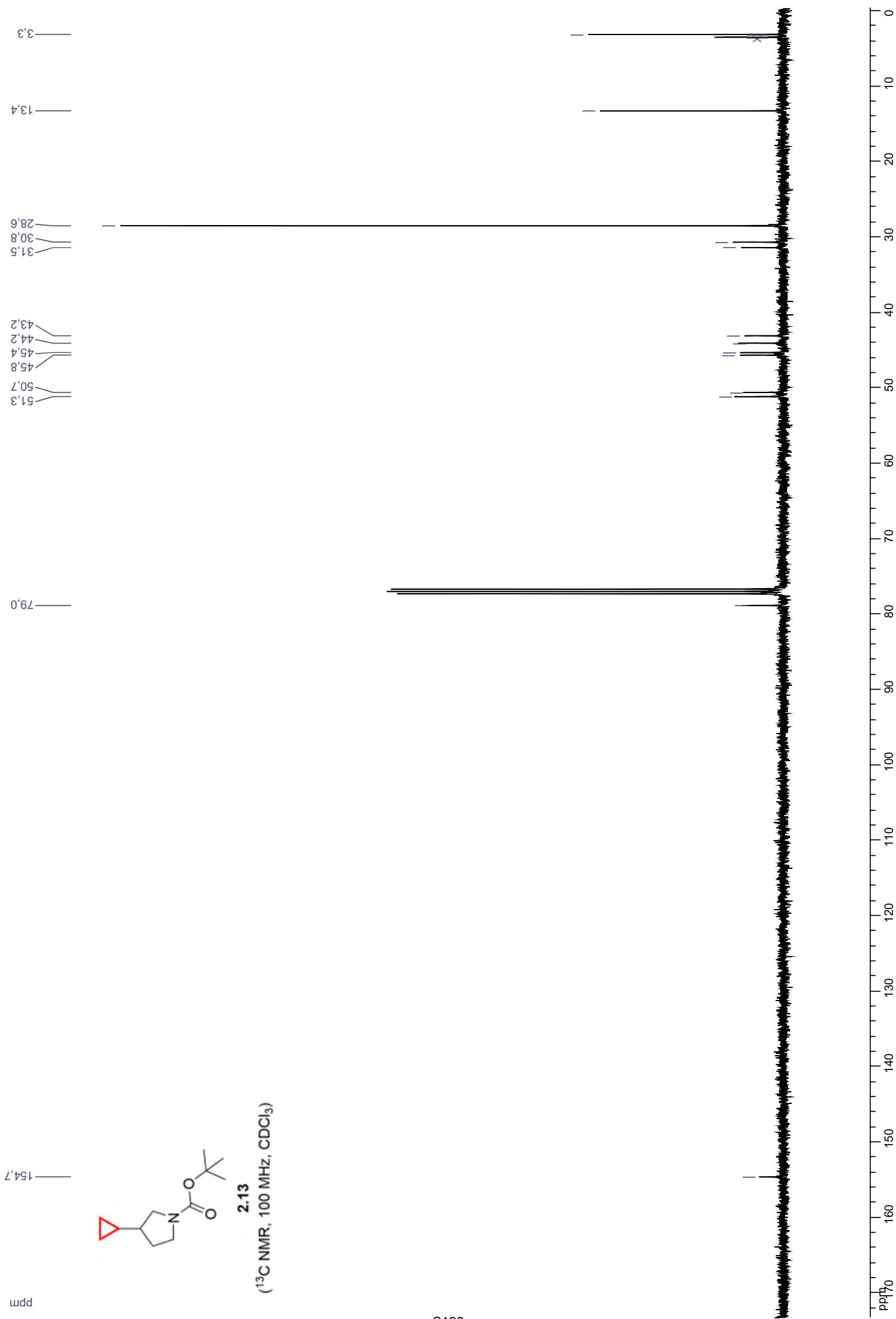
2.12

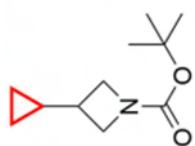
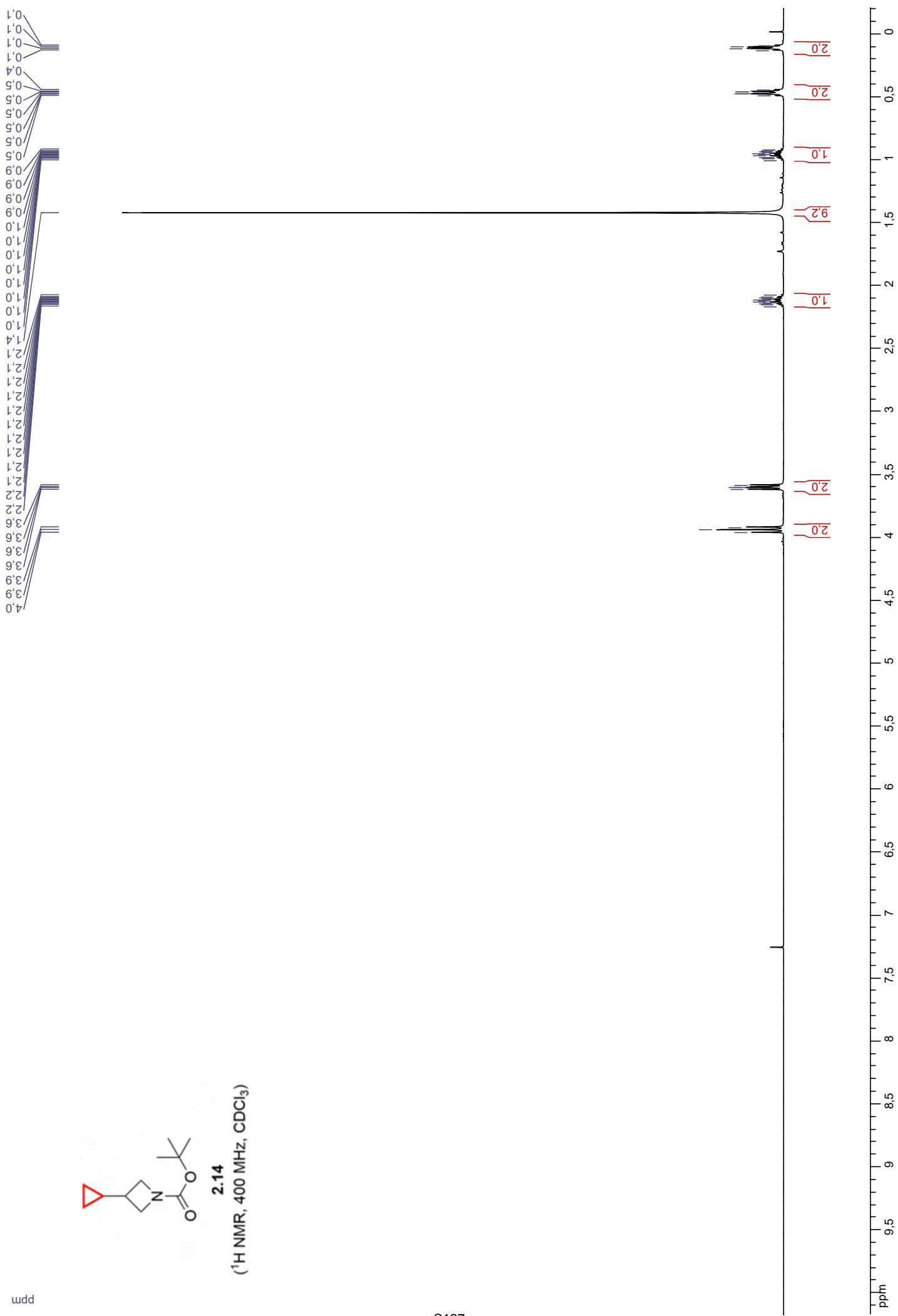
trans/cis > 95:5

(^{13}C NMR, 100 MHz, CDCl_3)

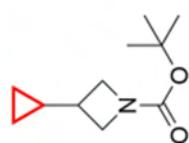
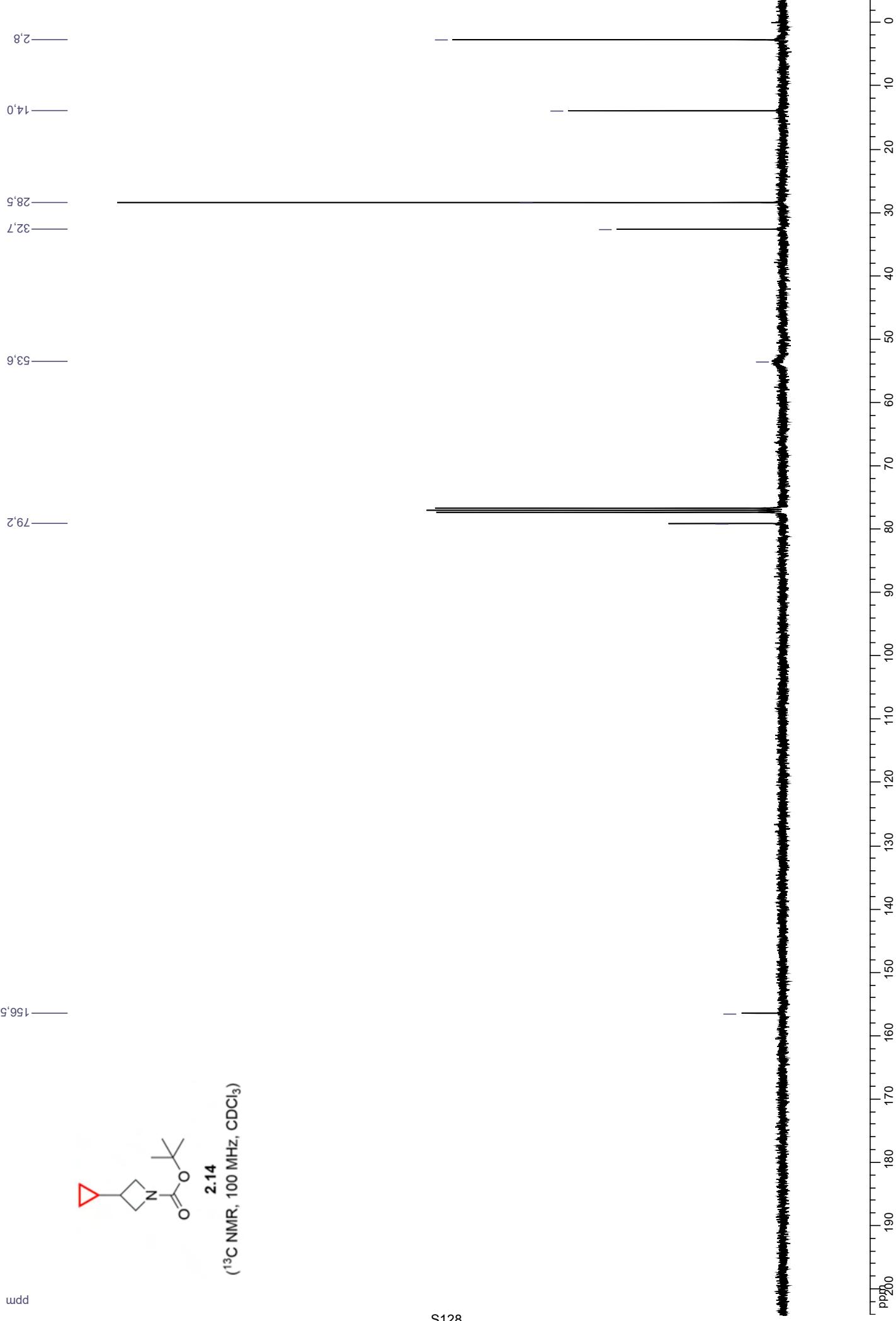




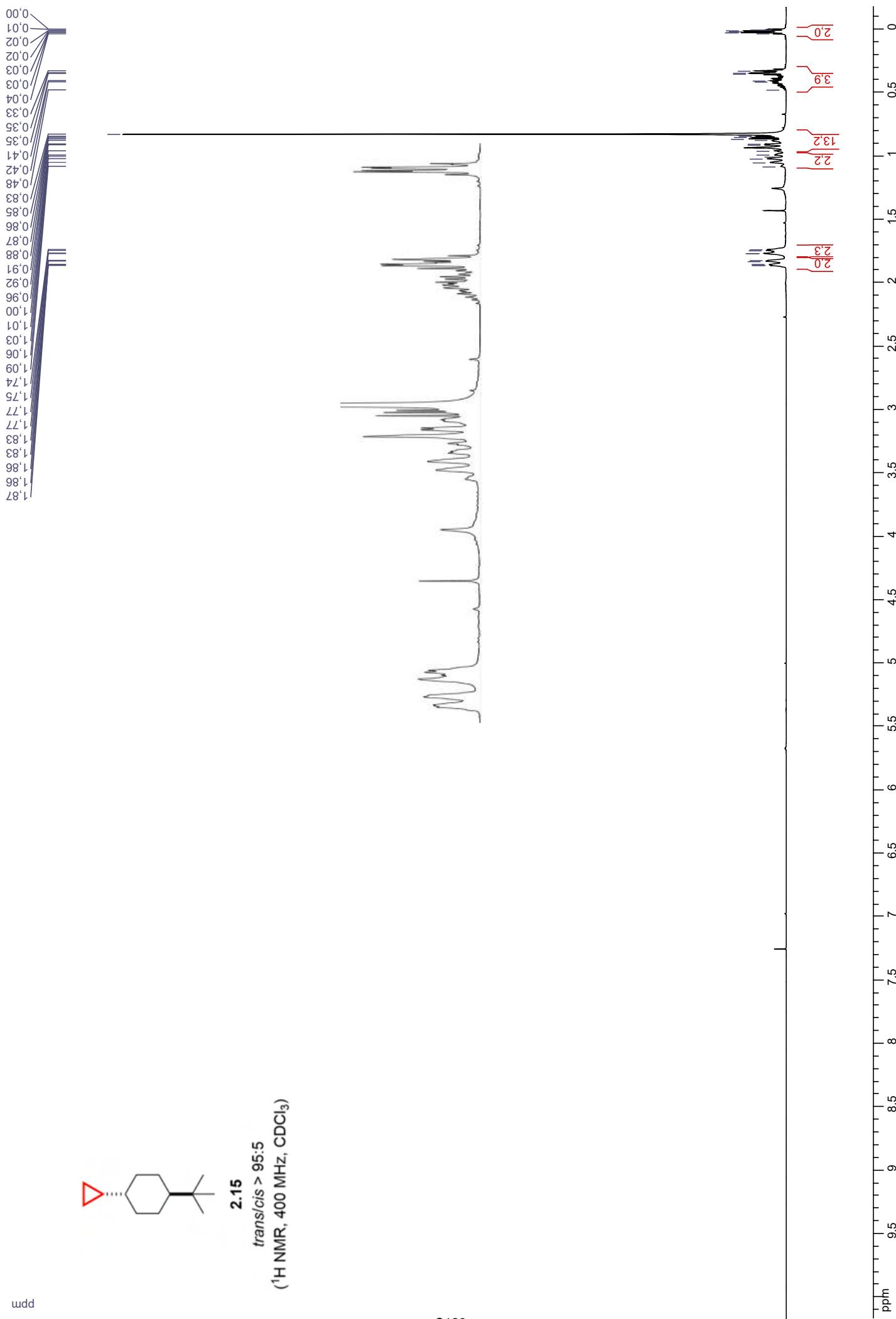




2.14 (^1H NMR, 400 MHz, CDCl₃)



2.14
(^{13}C NMR, 100 MHz, CDCl_3)



2.15

trans/cis > 95:5

(^1H NMR, 400 MHz, CDCl_3)

—3,09

—17,64

—27,44

—27,71

—32,52

—33,54

—43,36

—48,34

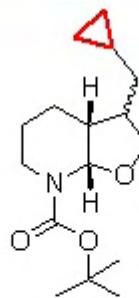


2.15

trans/cis > 95:5
(^{13}C NMR, 100 MHz, CDCl_3)

ppm

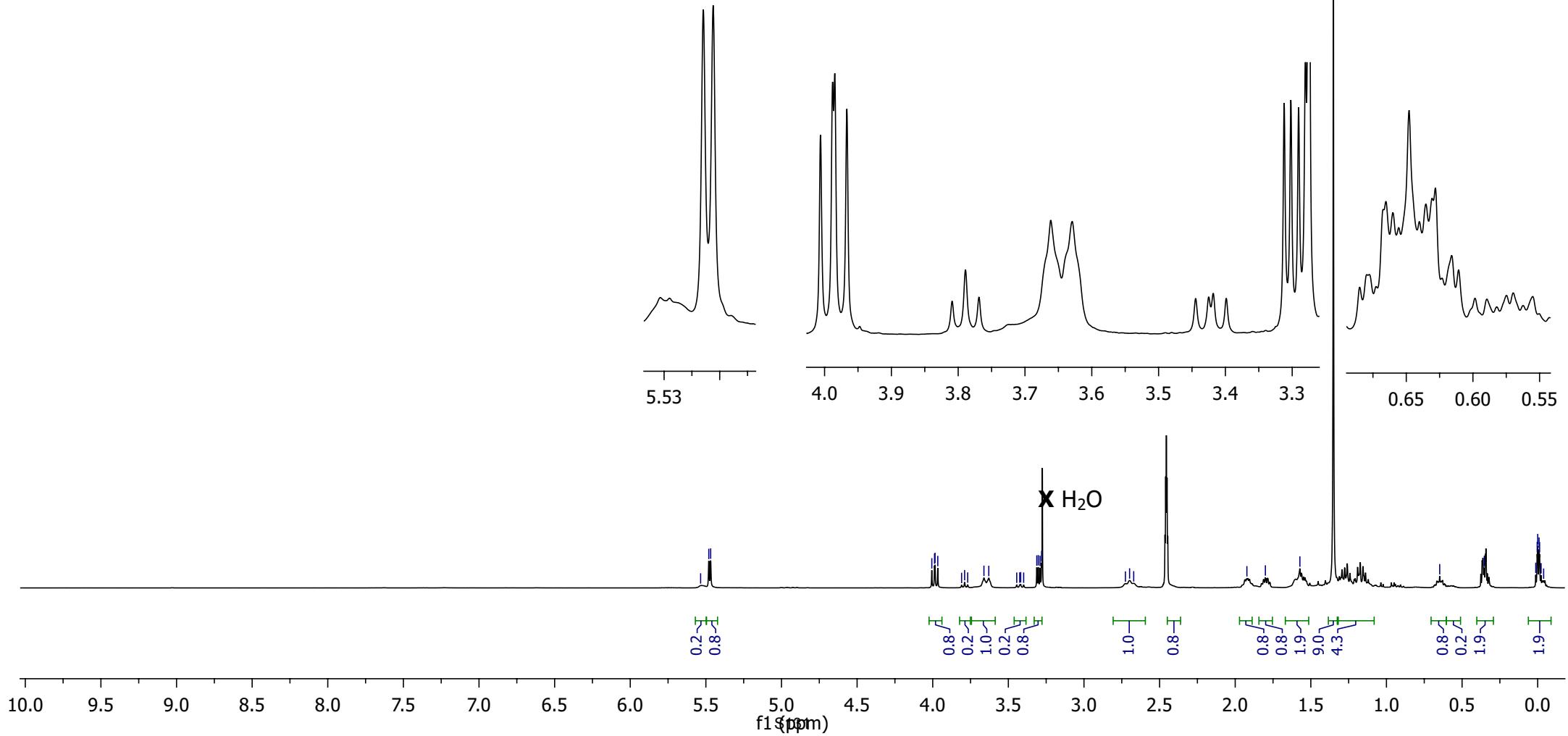


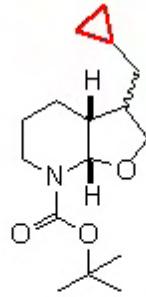


diastereomer ratio 80:20

2.16

(^1H NMR, 400 MHz, DMSO-d₆)





—154.88

—82.97

—79.80

—69.87

~44.99

~42.45

~38.40

~28.40

~25.94

~22.84

~10.00

~9.65

~4.87

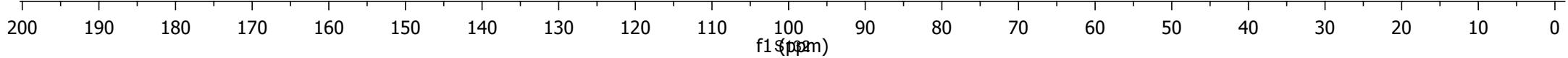
~4.83

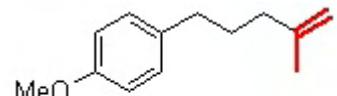
~4.68

diastereomer ratio 80:20

2.16

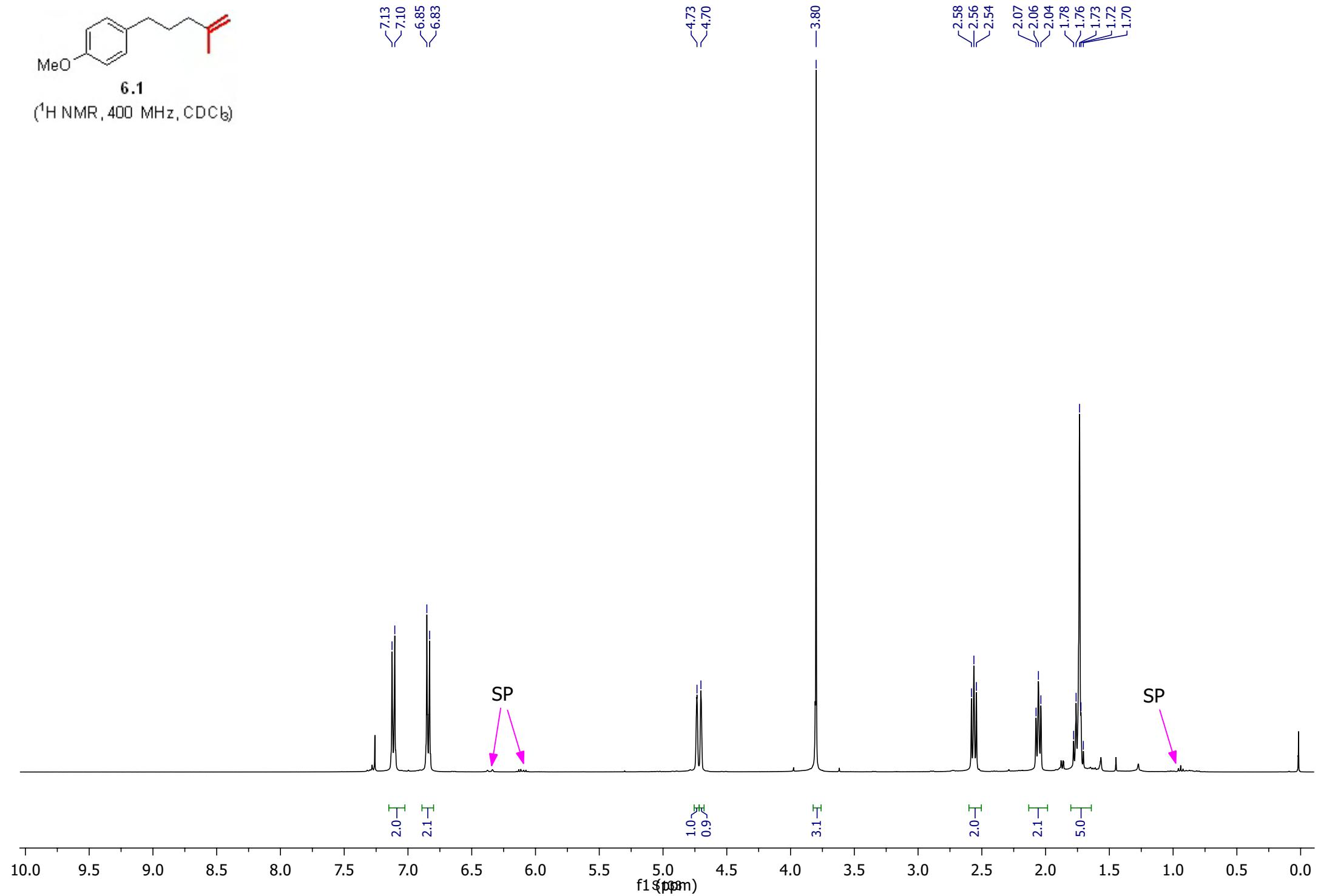
(^{13}C NMR, 100 MHz, DMSO-d6)

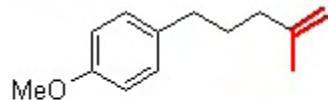




6.1

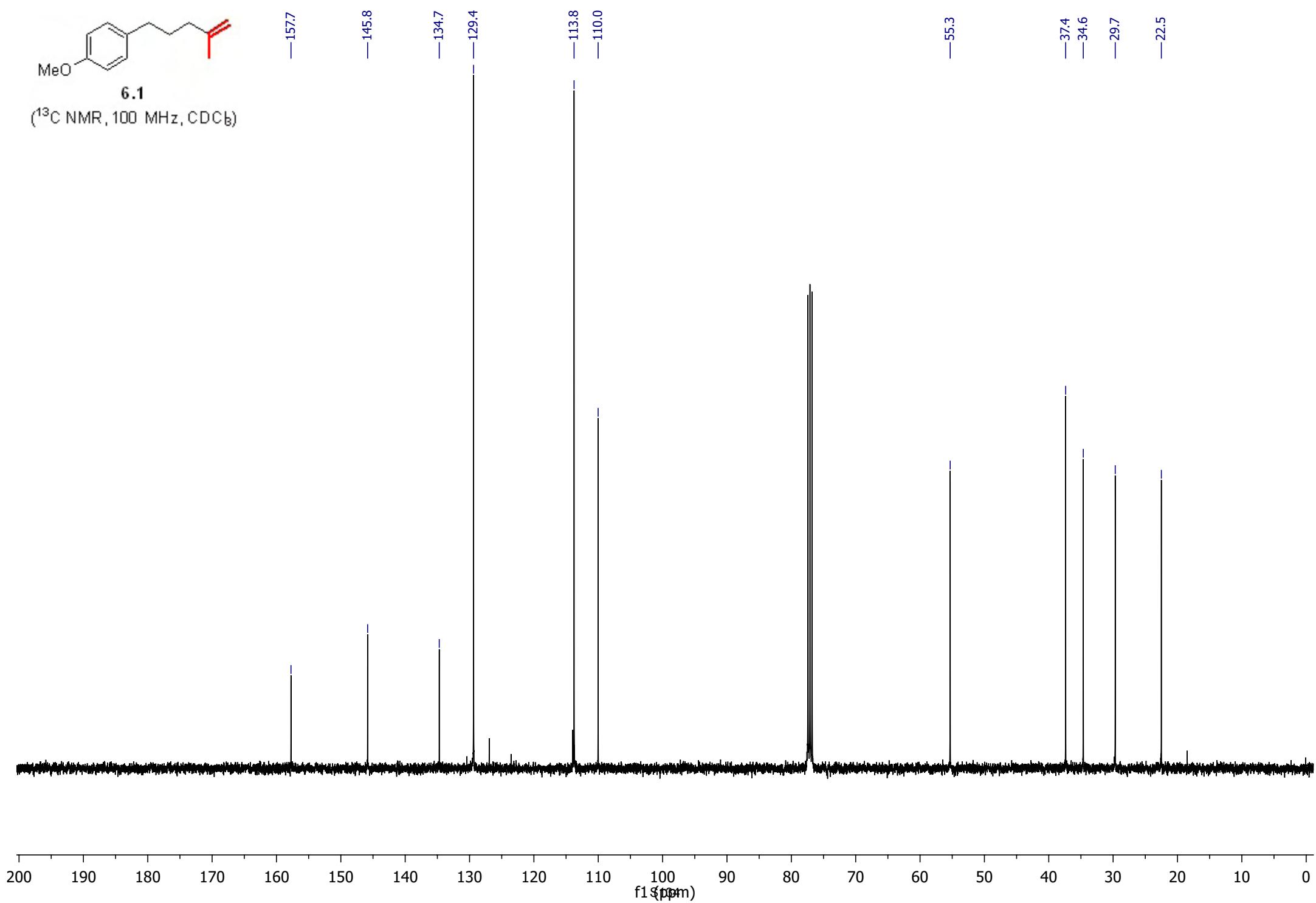
(^1H NMR, 400 MHz, CDCl_3)

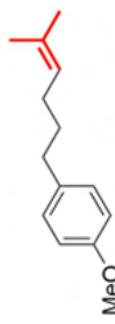




6.1

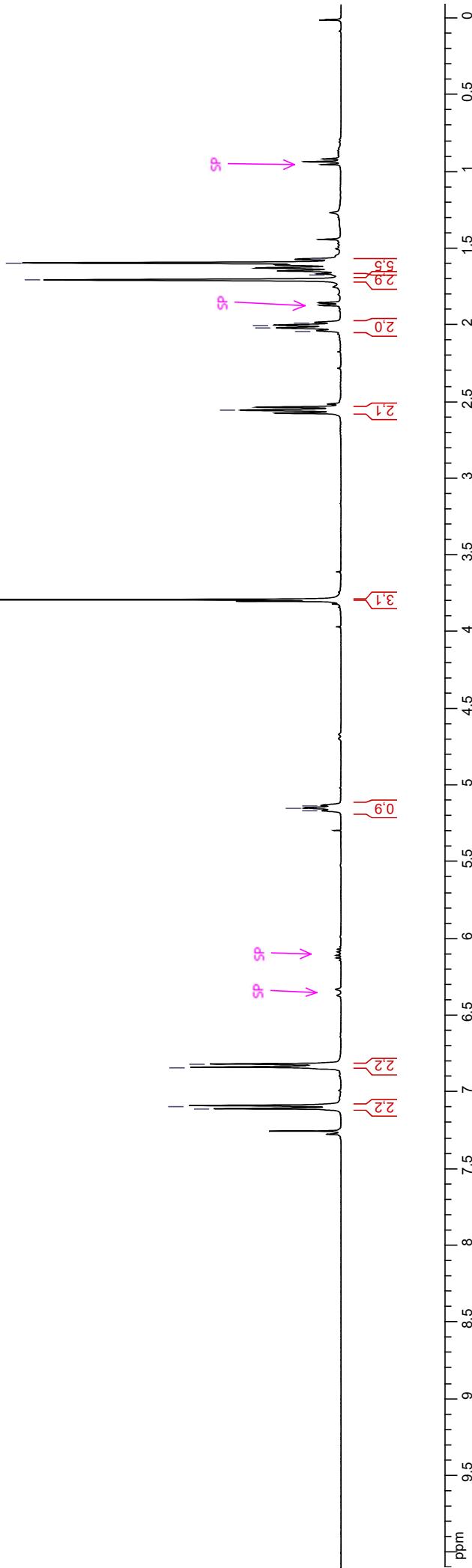
(^{13}C NMR, 100 MHz, CDCl_3)

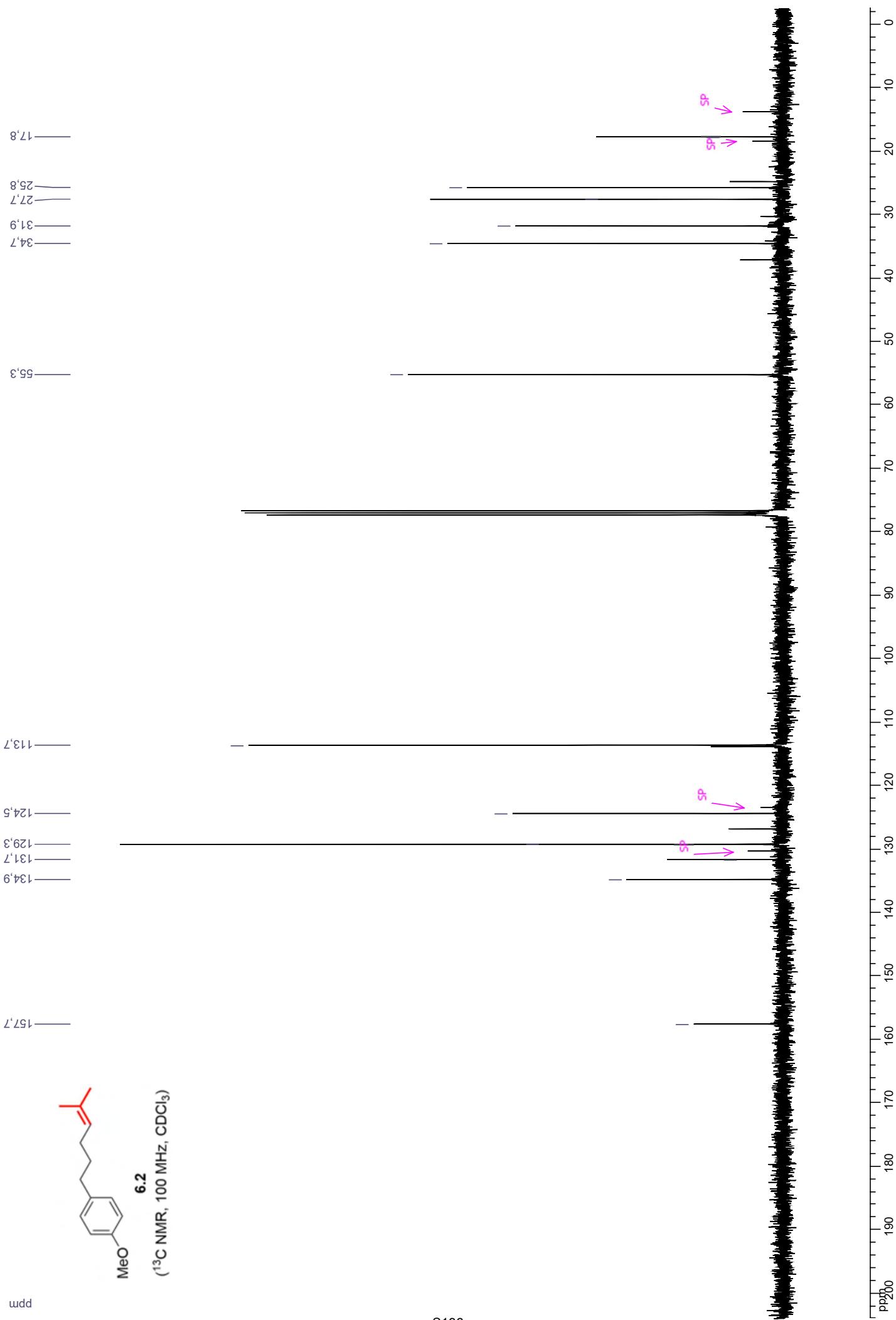




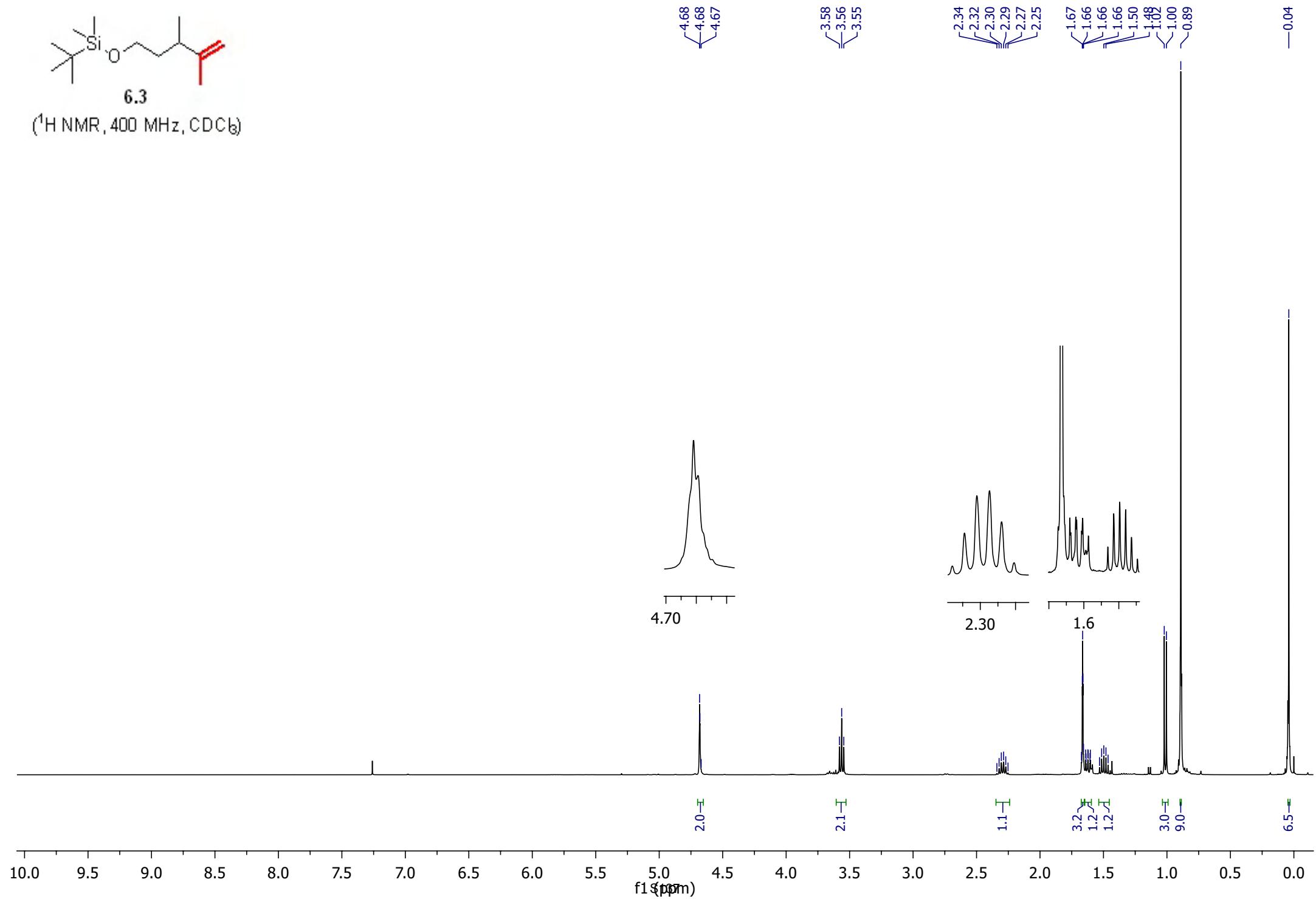
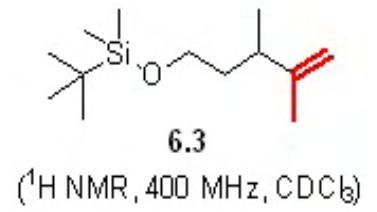
6.2
(^1H NMR, 400 MHz, CDCl_3)

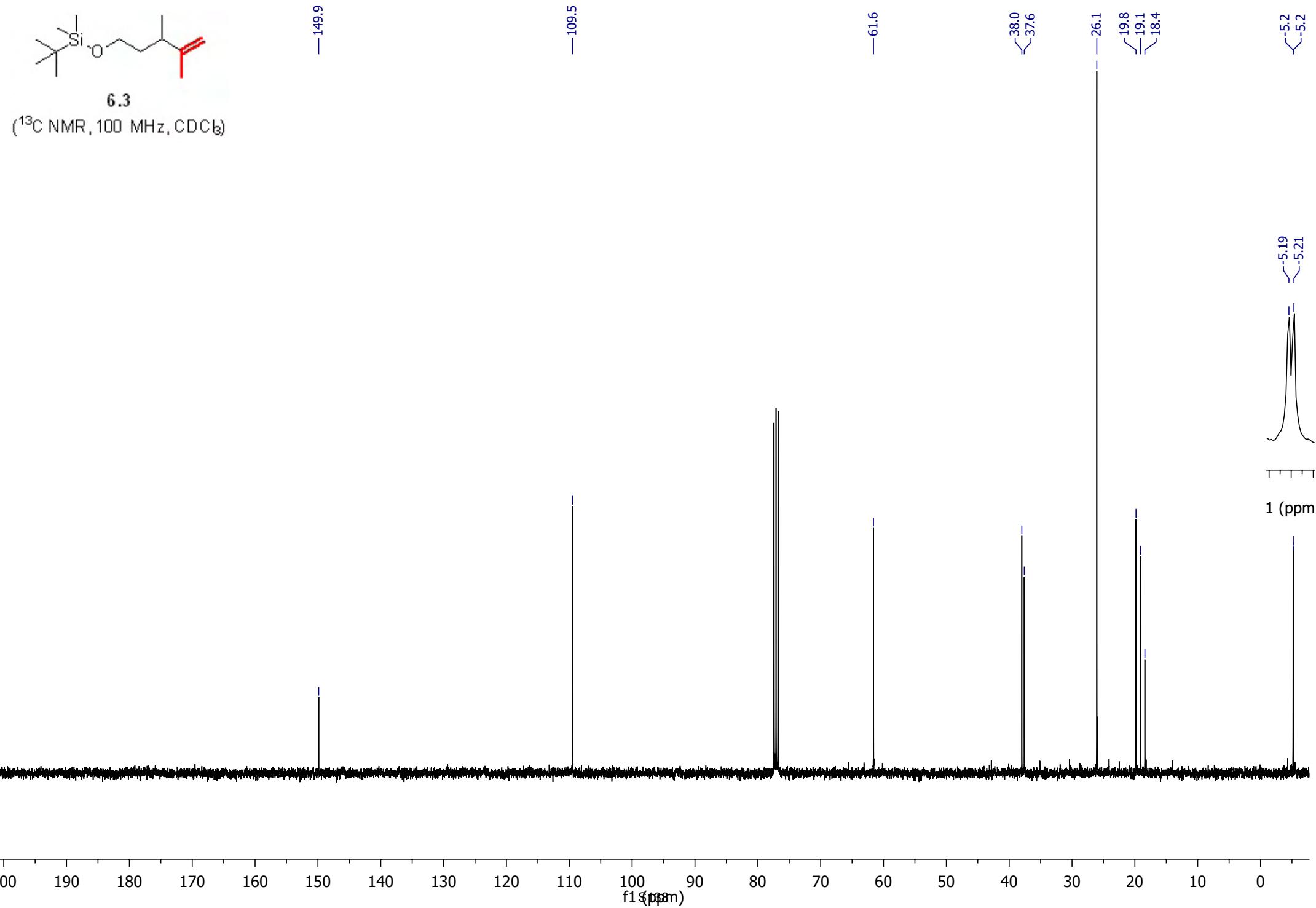
2,56
3,80
5,13
5,15
6,82
6,84
7,09
7,11
2,04
2,02
2,01
1,99
1,71
1,68
1,60
1,57

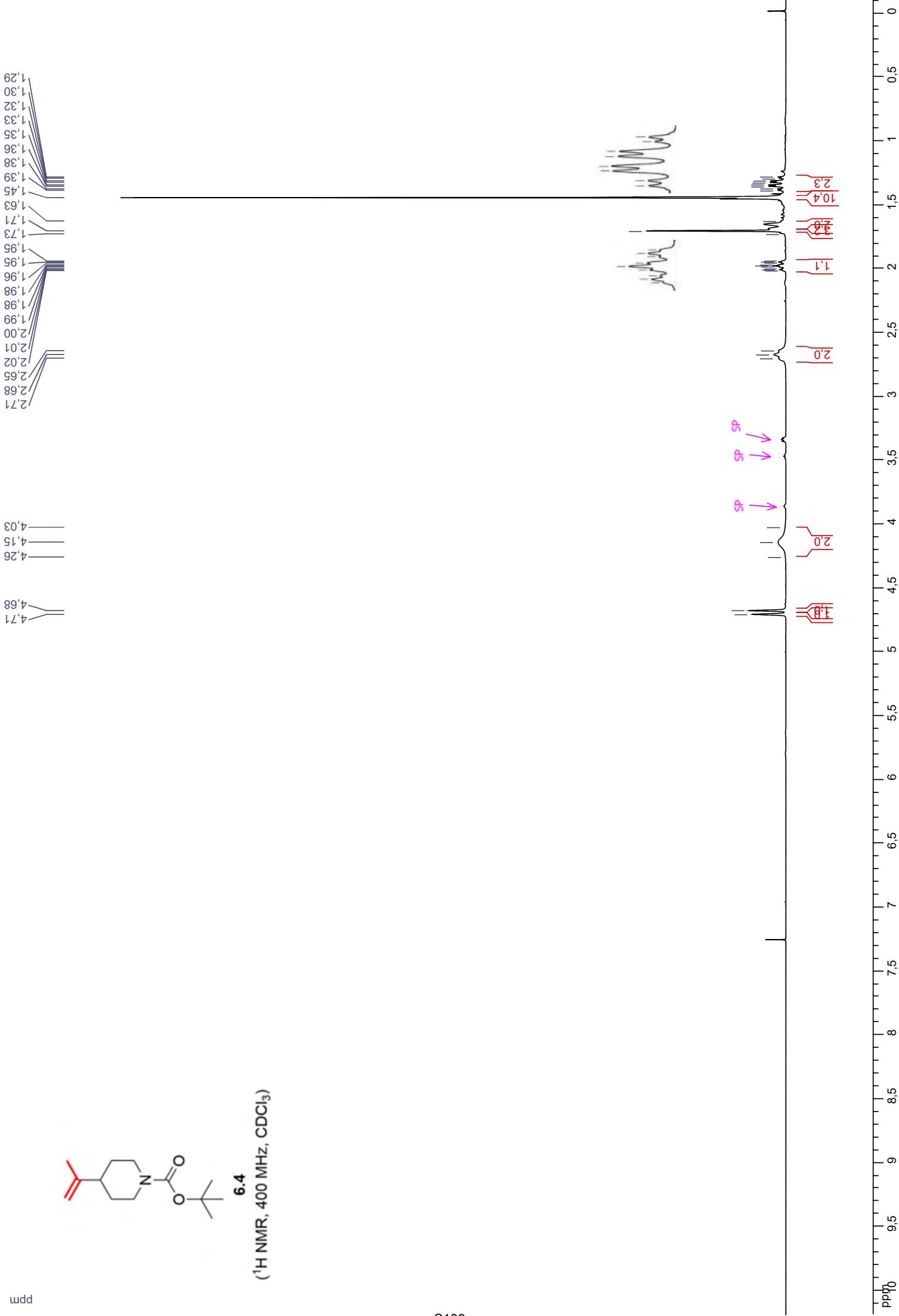


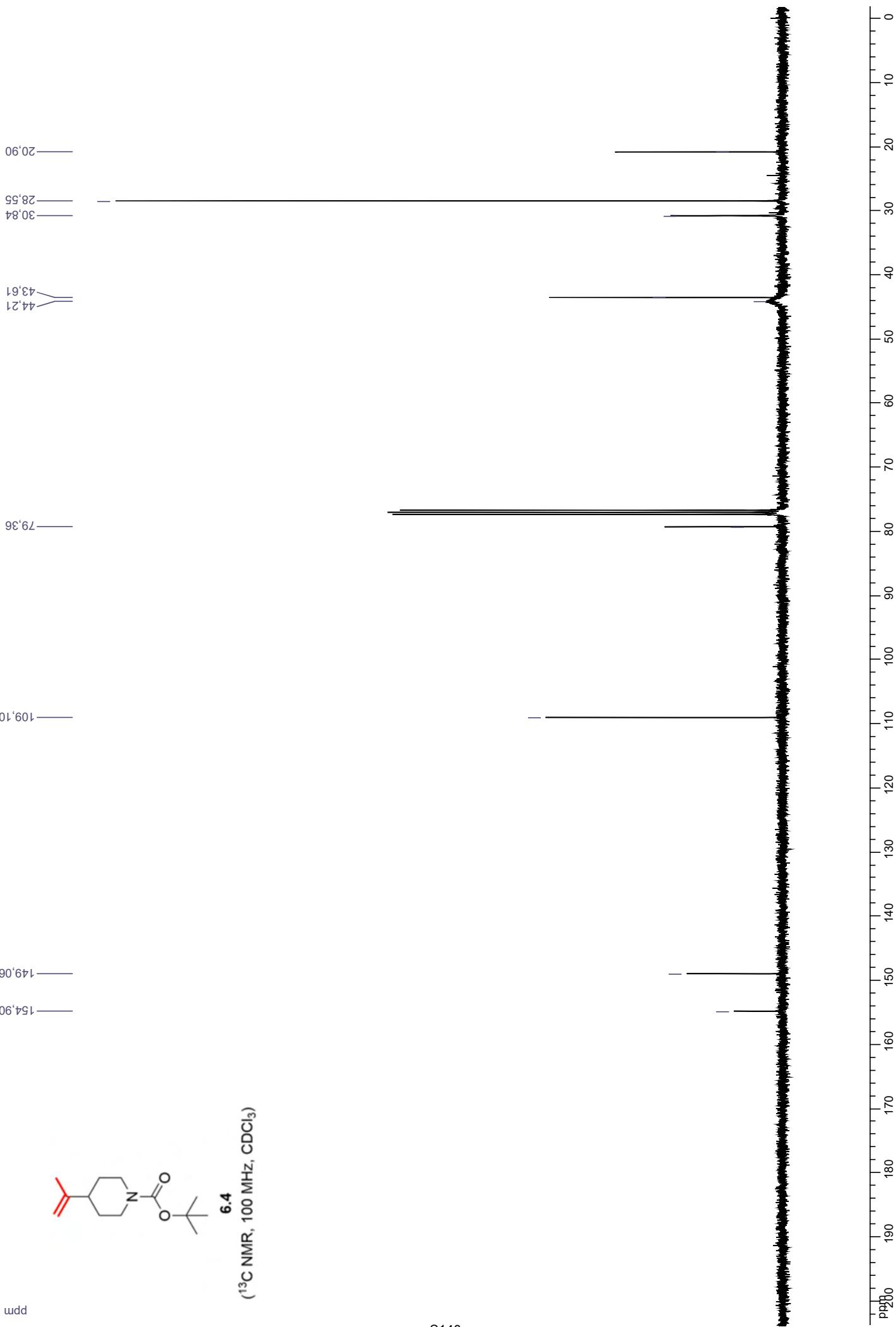


ppm

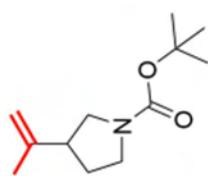








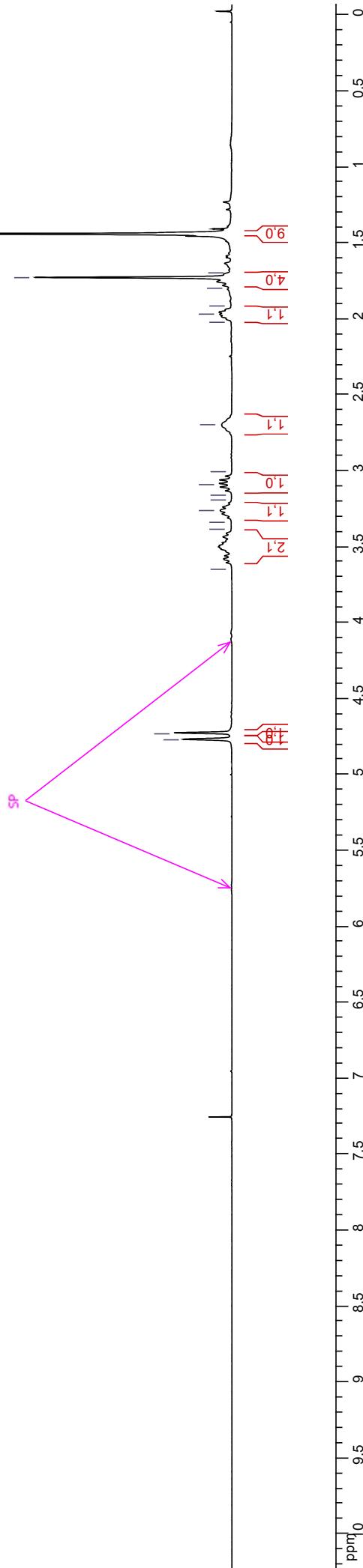
ppm

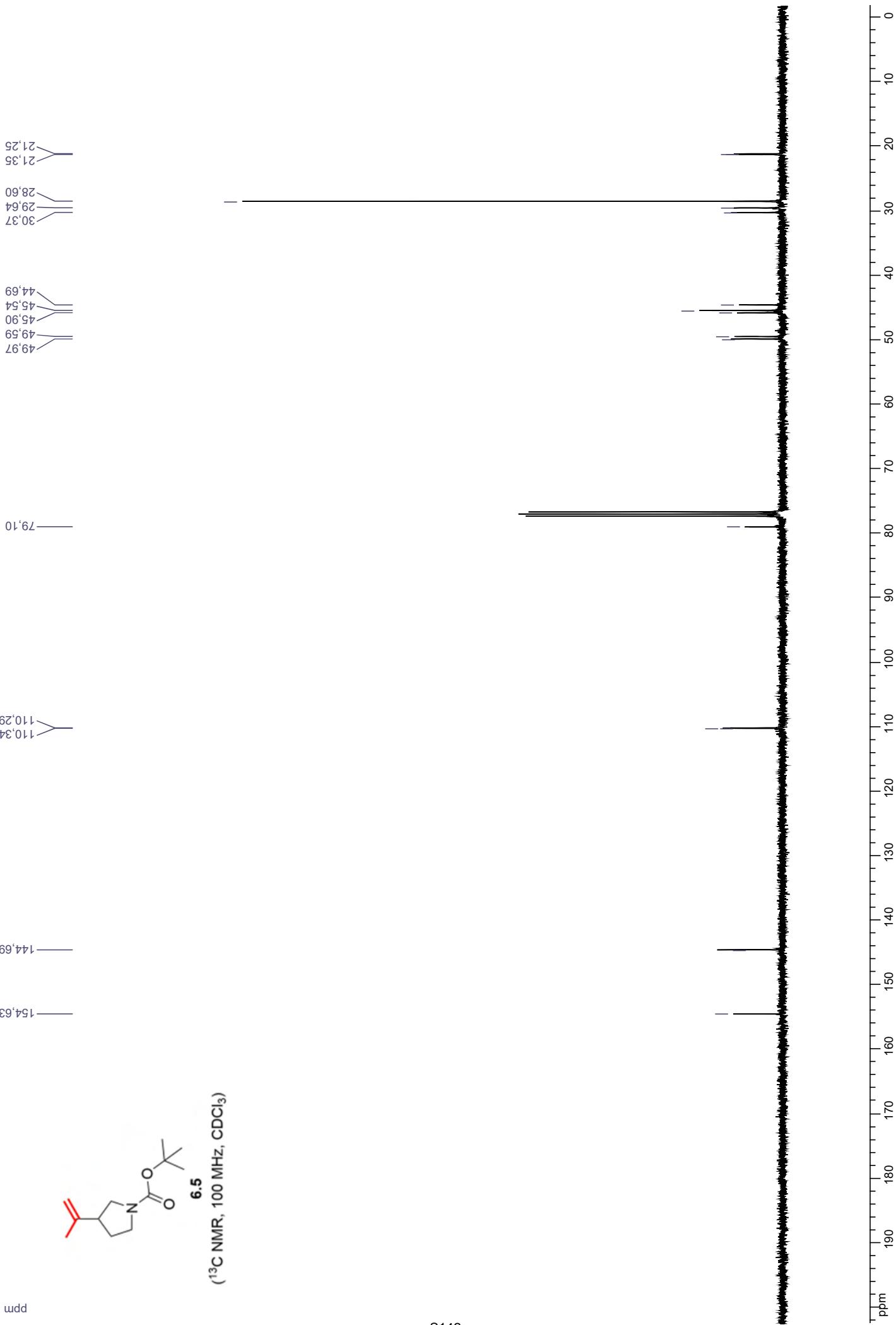


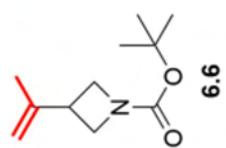
6.5
(^1H NMR, 400 MHz, CDCl_3)

ppm

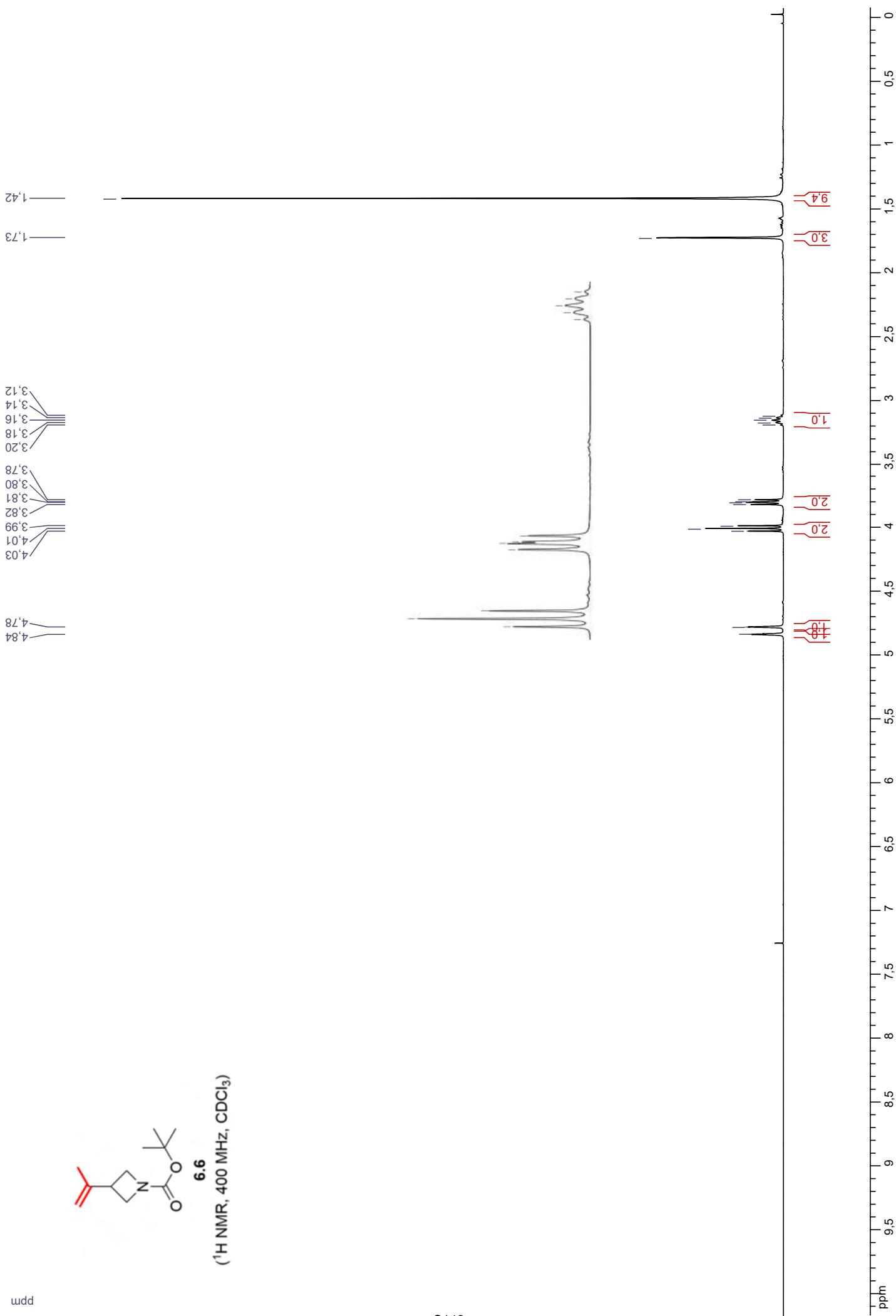
4,73
3,65
3,39
3,34
3,27
3,19
3,17
3,09
3,01
2,70
2,03
1,97
1,92
1,80
1,73
1,70
1,45

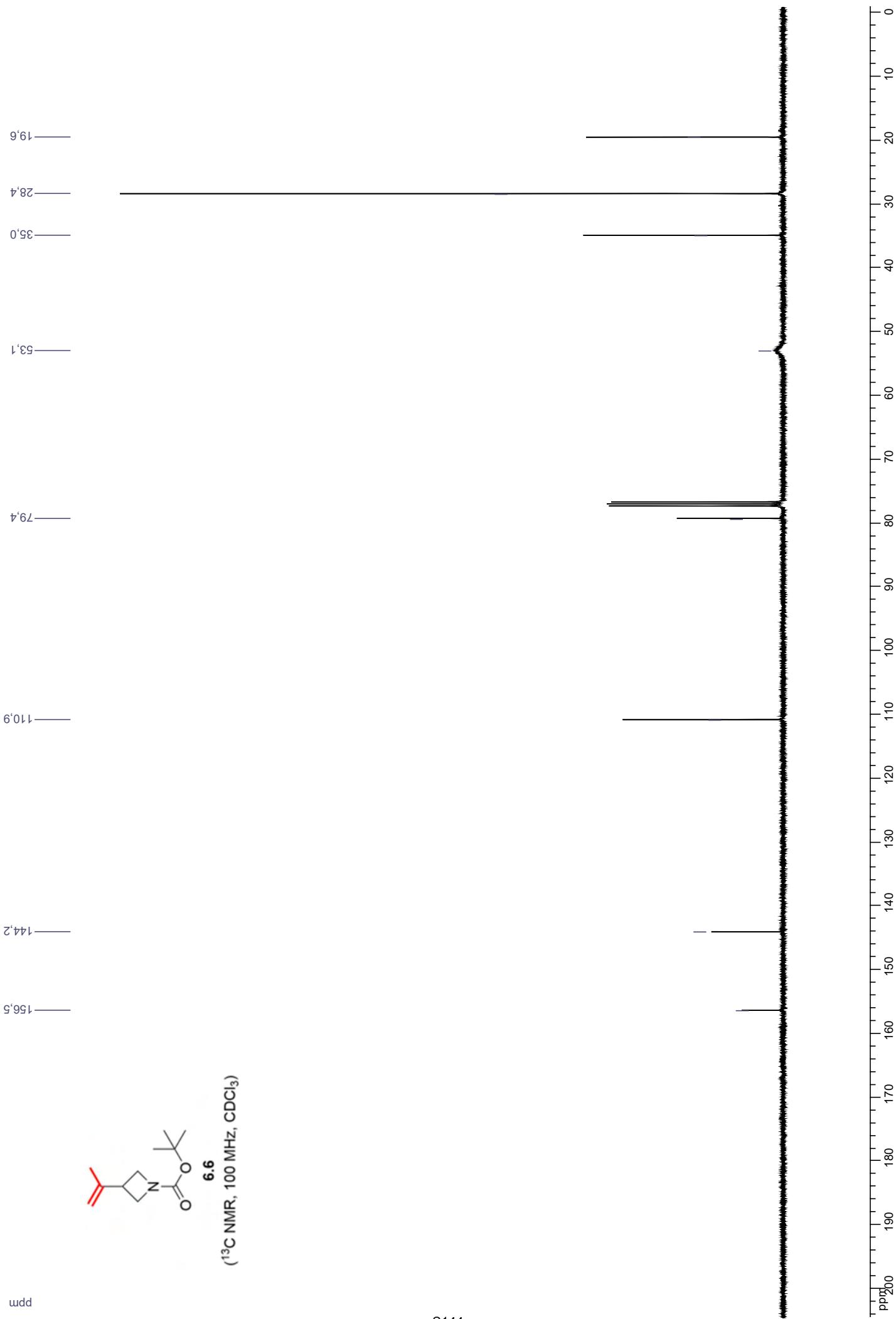


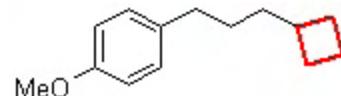




(^1H NMR, 400 MHz, CDCl_3)

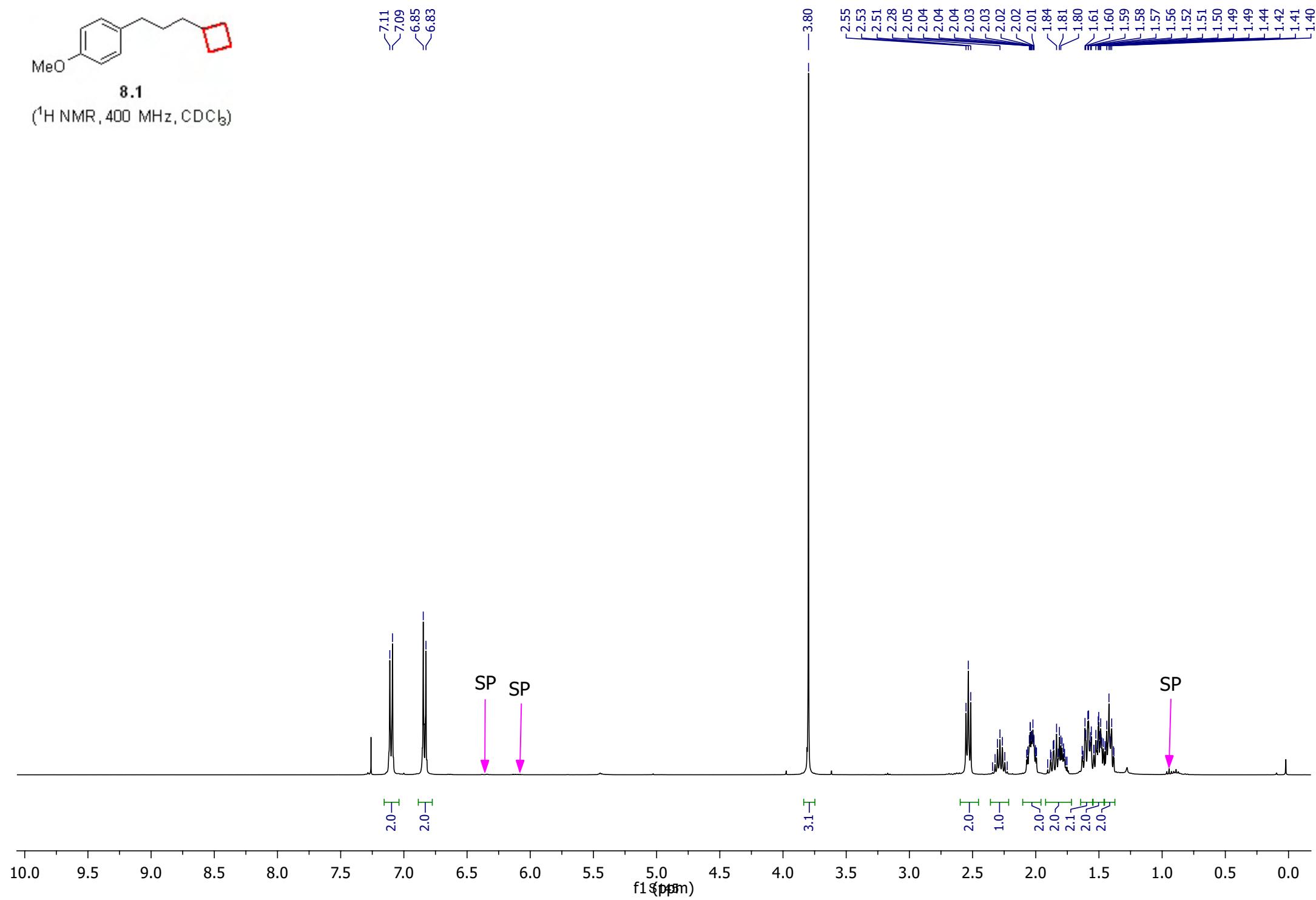


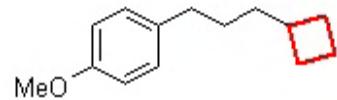




8.1

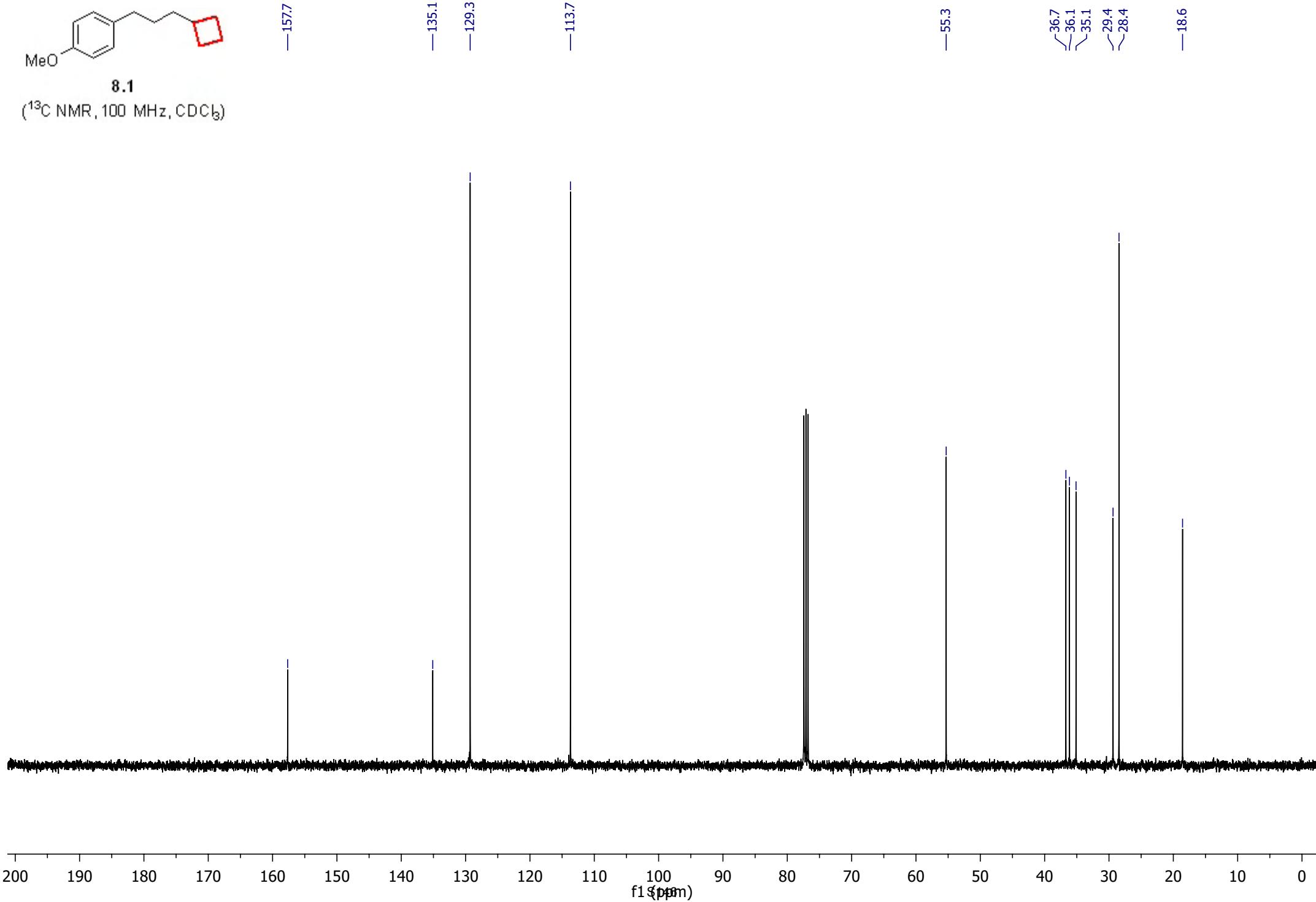
(^1H NMR, 400 MHz, CDCl_3)

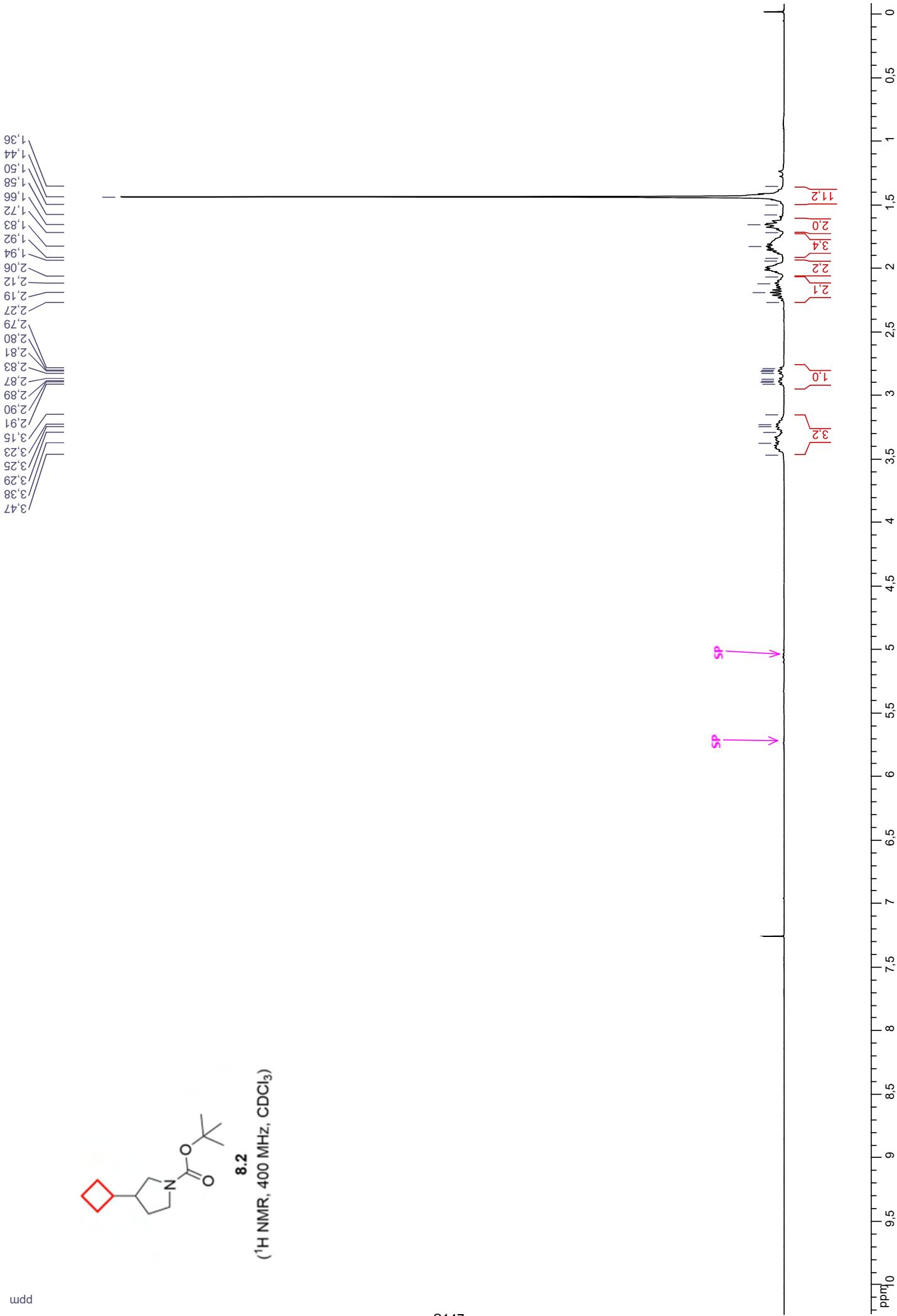




8.1

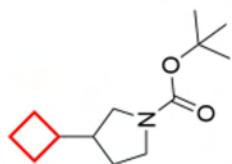
(^{13}C NMR, 100 MHz, CDCl_3)



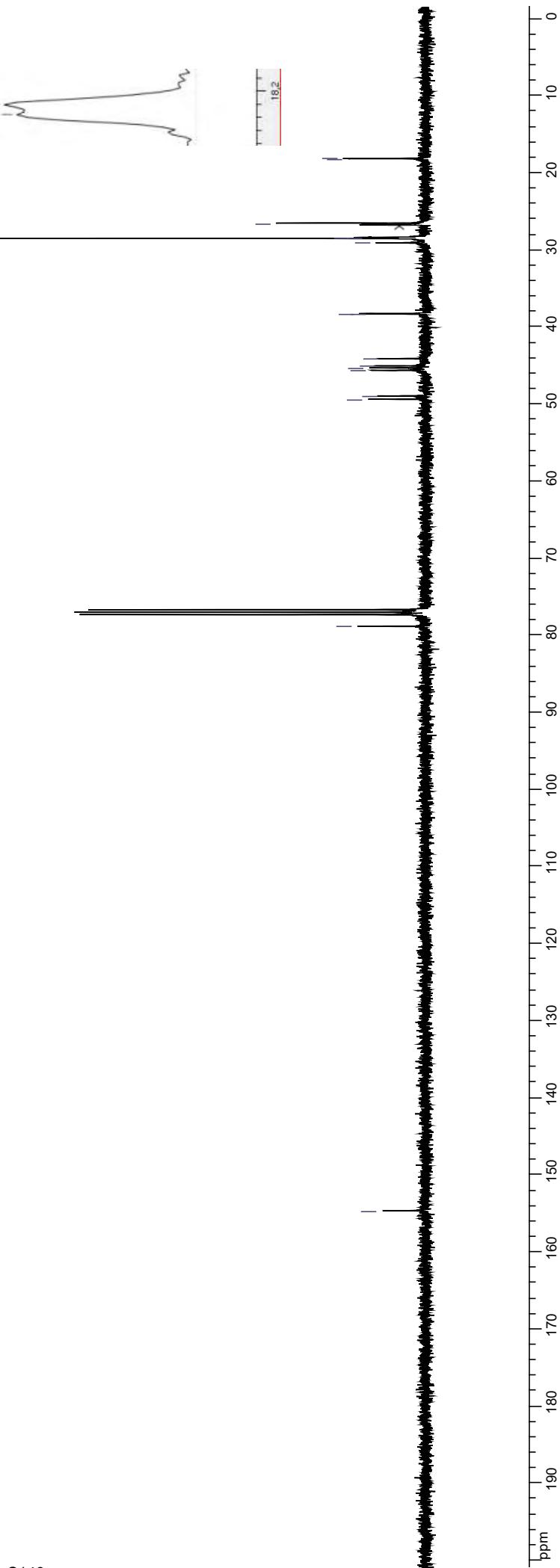


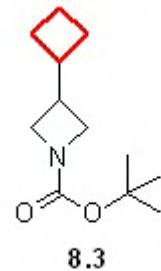
—154.8

—154.8
—78.9
—
—18.3
—18.2
—
—26.6
—28.5
—28.6
—29.2
—
—38.4
—38.4
—44.2
—45.2
—45.4
—45.7
—49.0
—49.5



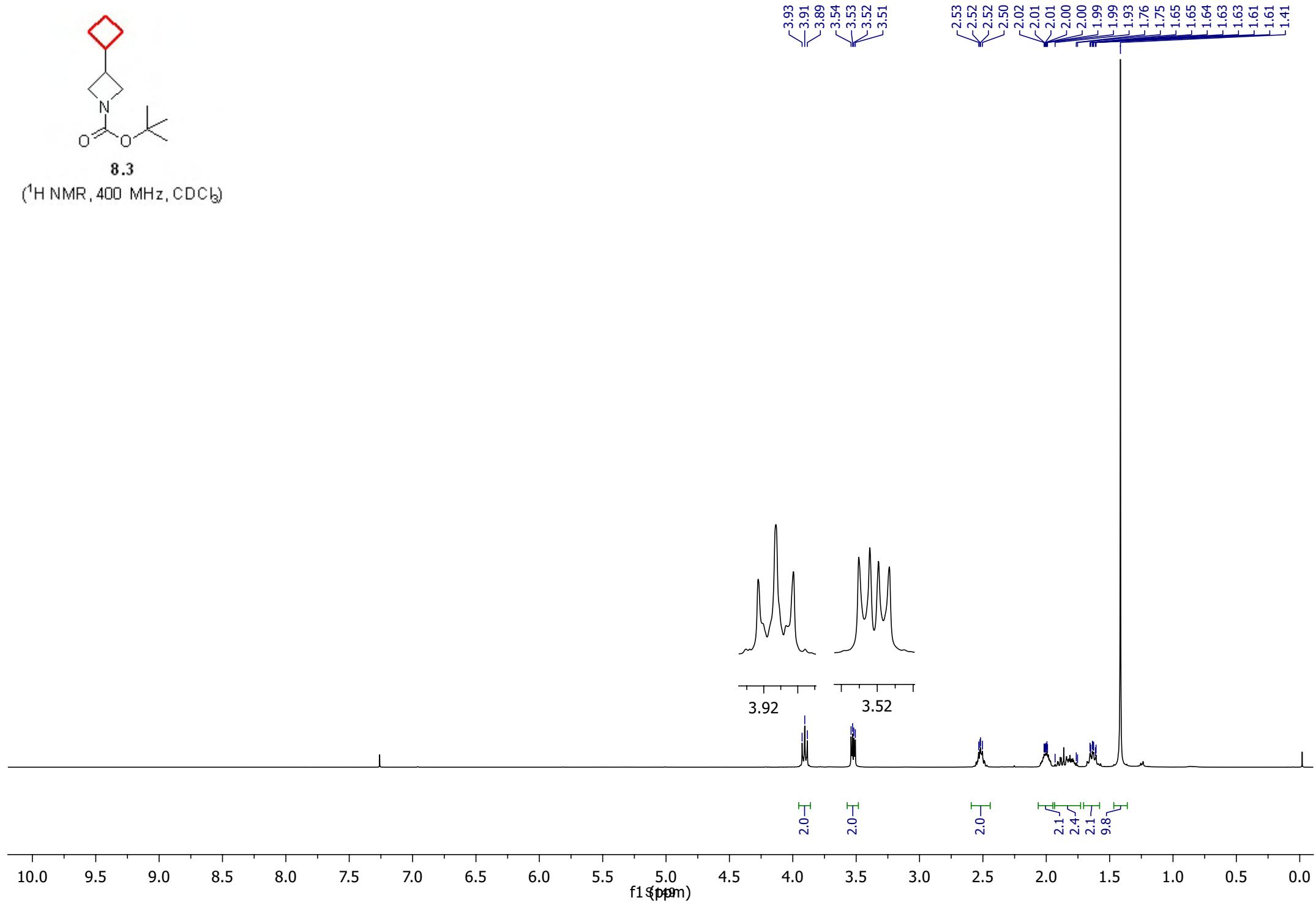
8.2
(^{13}C NMR, 100 MHz, CDCl_3)

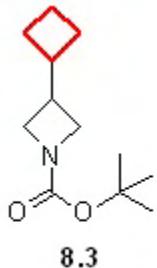




8.3

(^1H NMR, 400 MHz, CDCl_3)





—156.5

—79.1

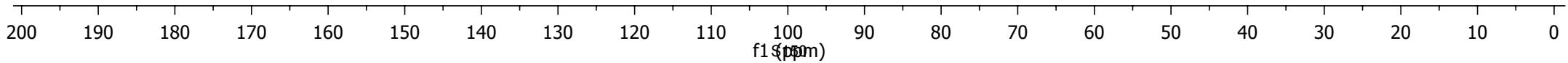
—52.4

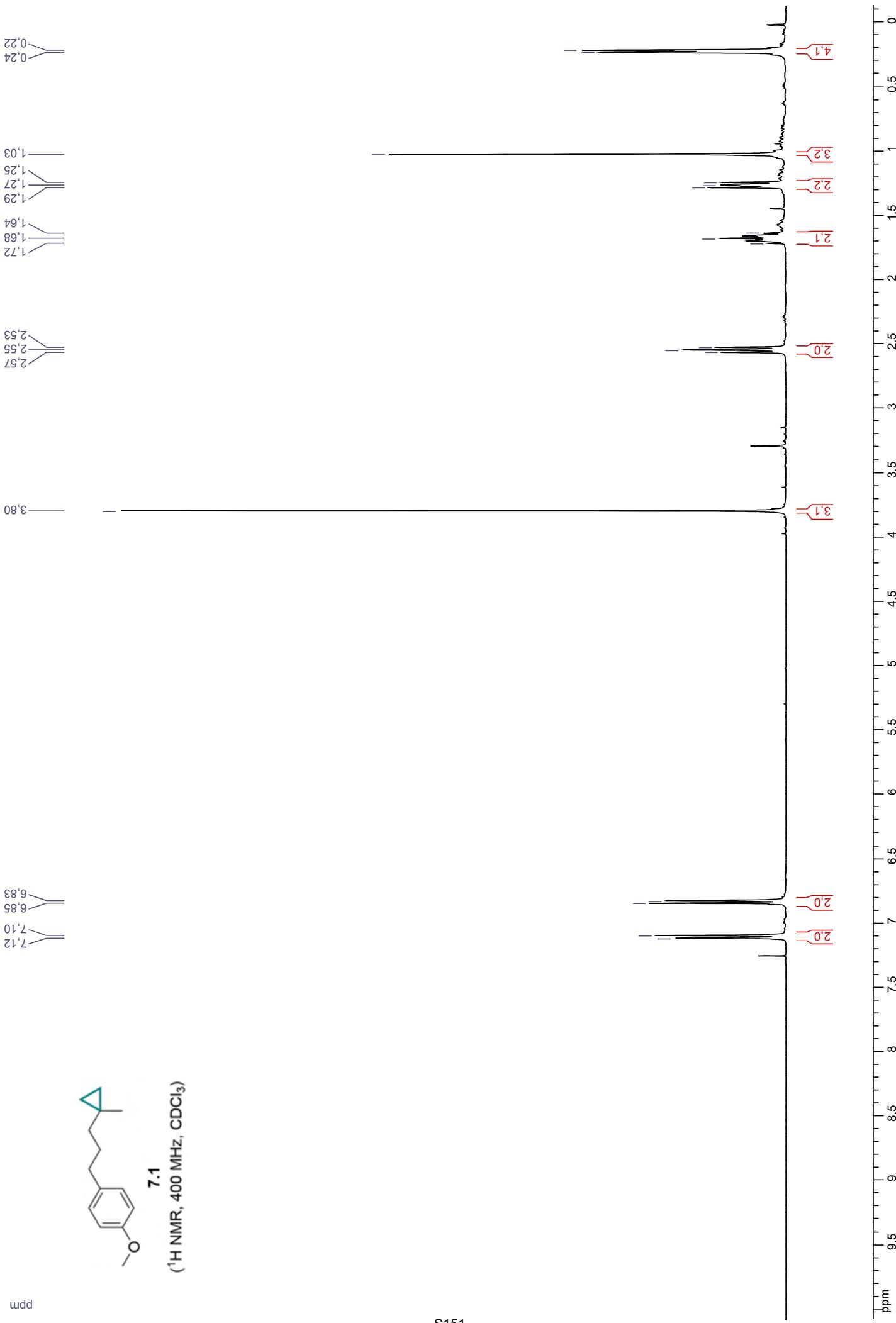
—38.3

—33.1
—28.5
—24.9

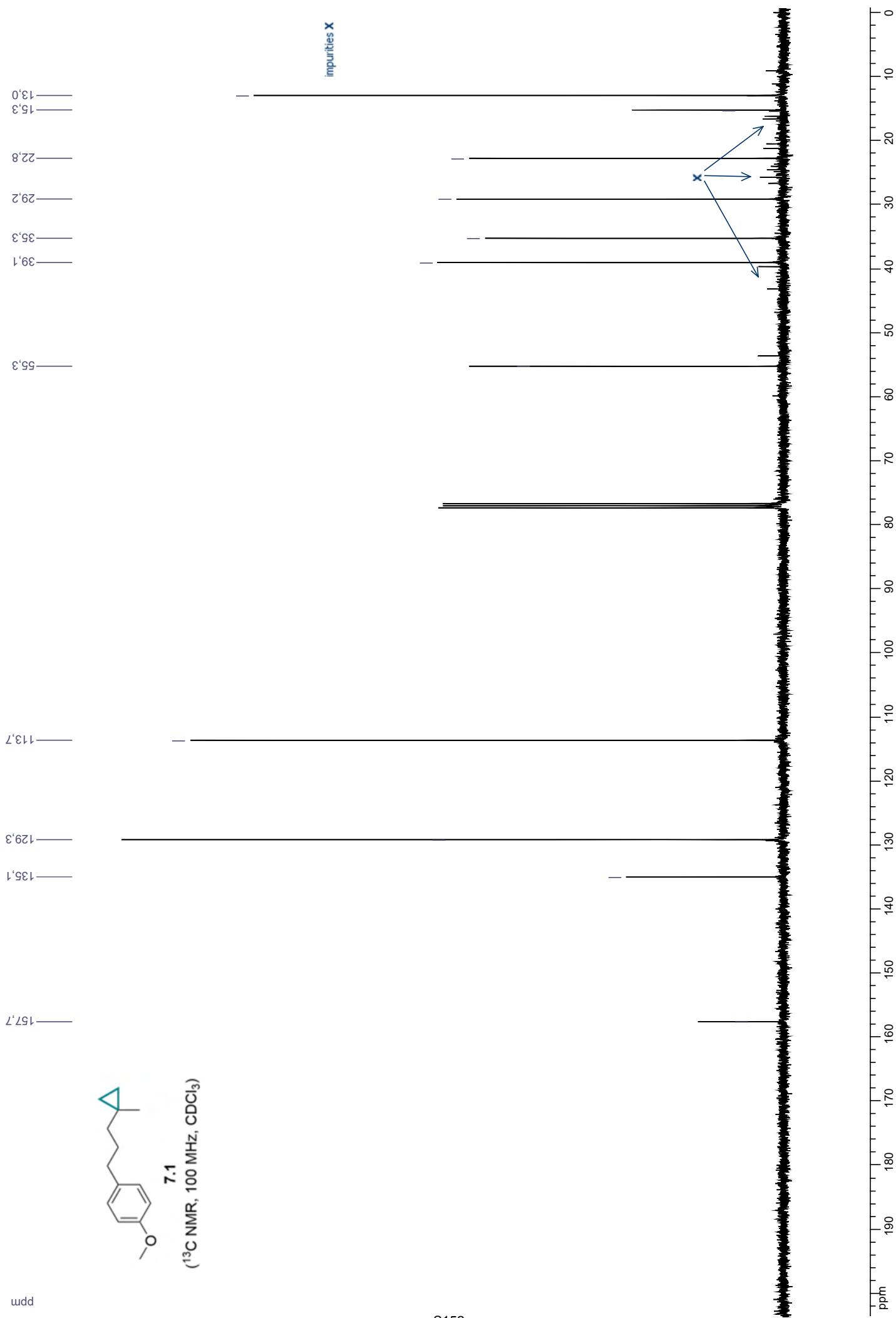
—17.9

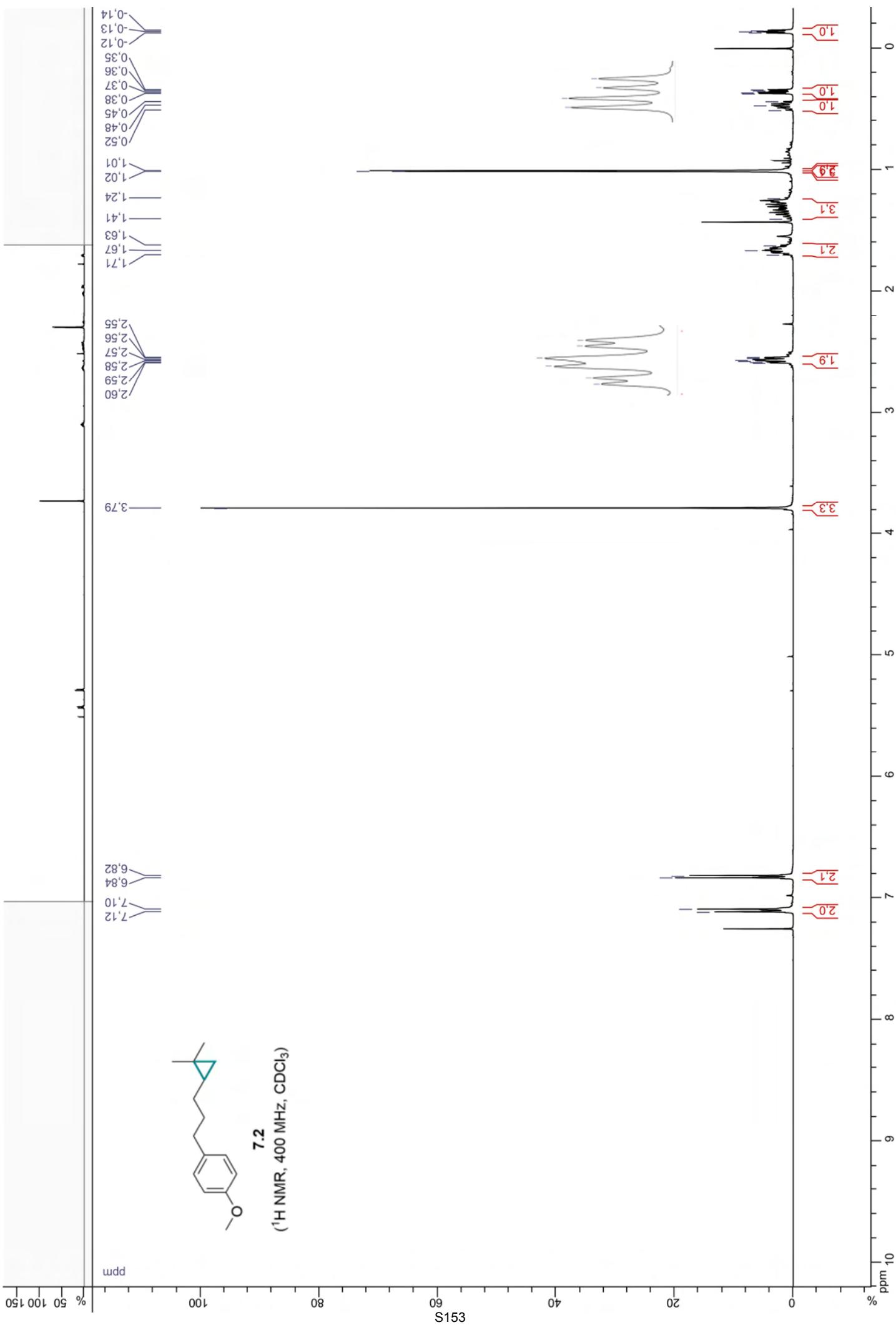
(^{13}C NMR, 100 MHz, CDCl_3)

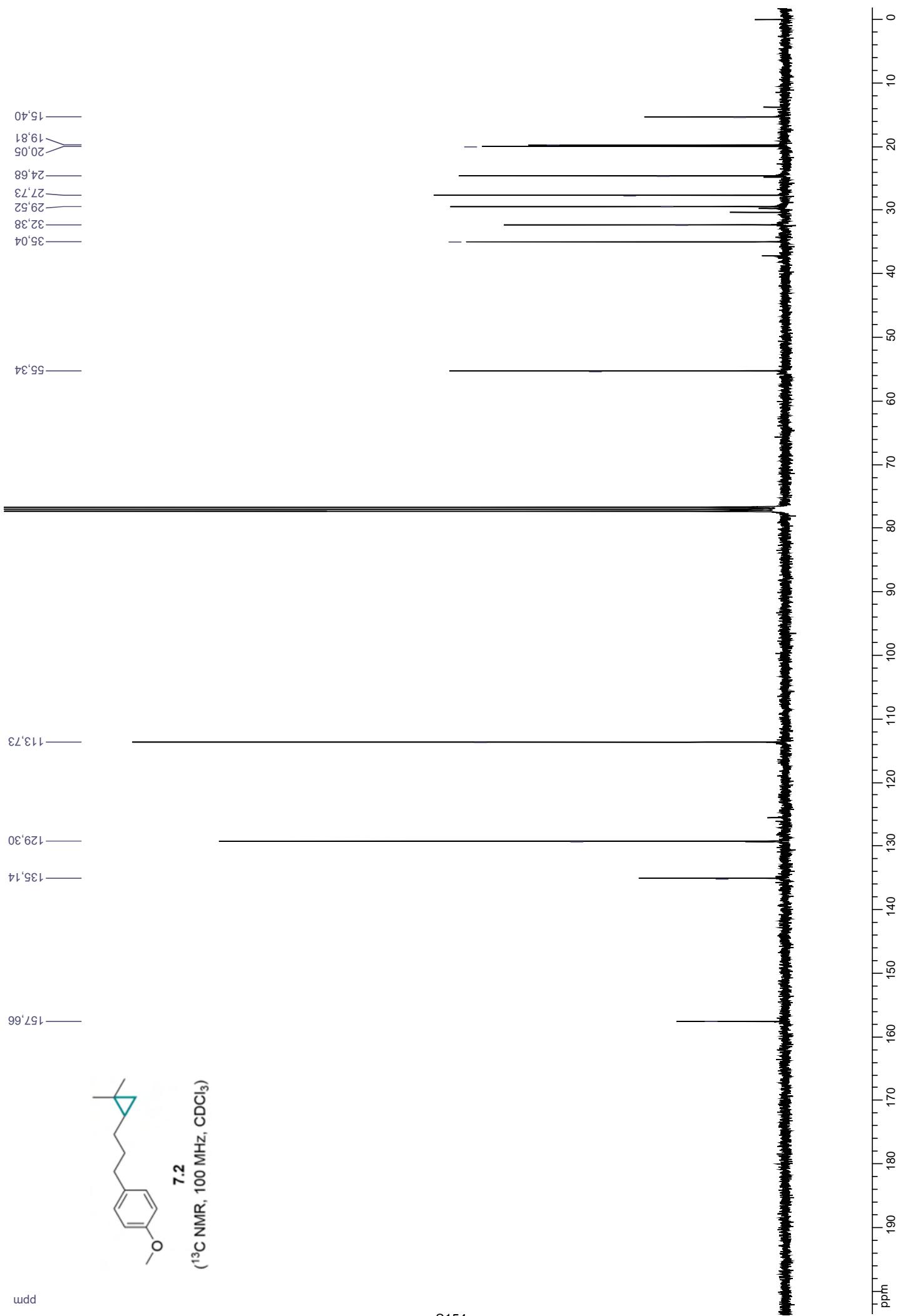


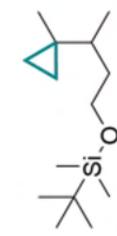


ppm







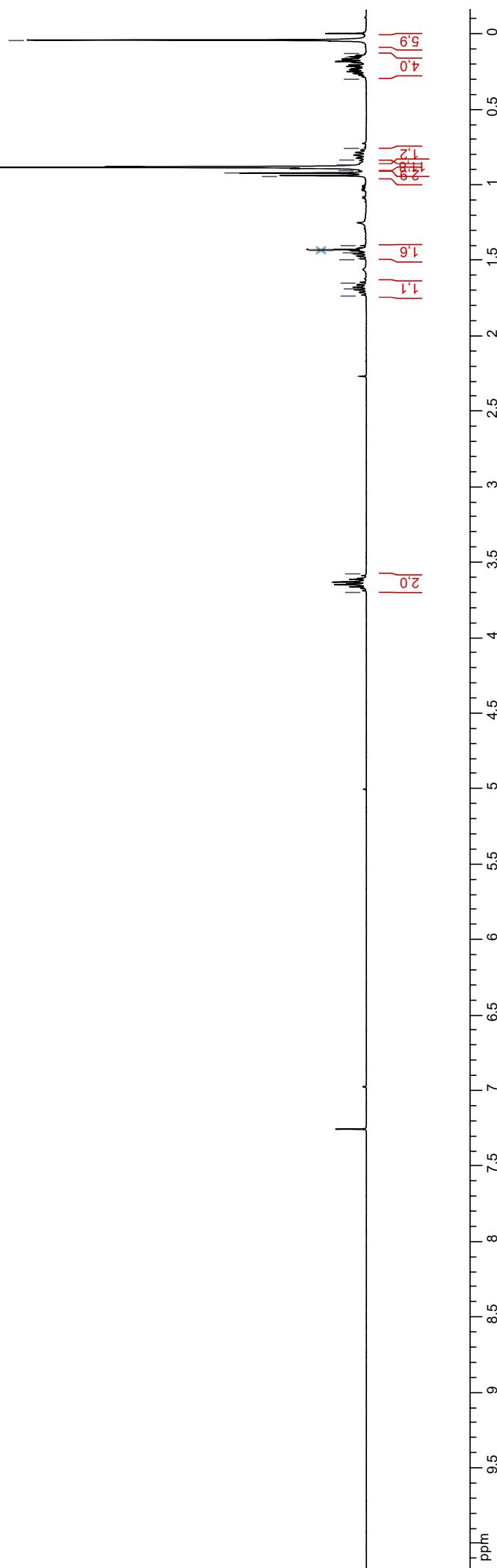


7.3

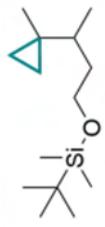
(^1H NMR, 400 MHz, CDCl_3)

3,70
3,58

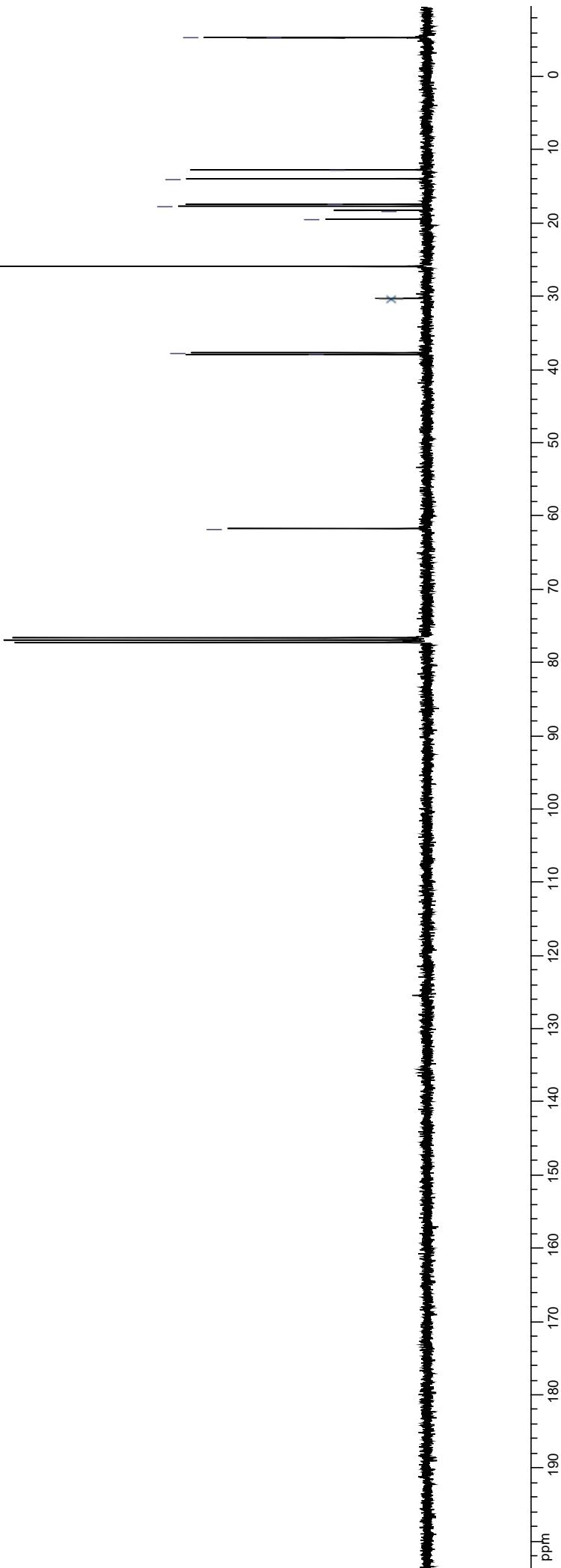
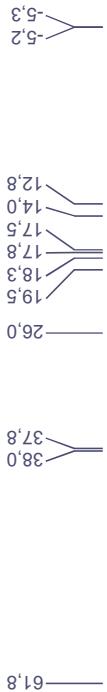
1,73
1,69
1,65
1,49
1,45
1,41
0,94
0,91
0,87
0,84
0,76
0,30
0,13
0,04



ppm



7.3
(^{13}C NMR, 100 MHz, CDCl_3)



ppm