

Supporting Information

Metathesis at an Implausible Site: A Formal Total Synthesis of Rhizoxin D

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SUPPORTING INFORMATION

Metathesis at an Implausible Site: A Formal Total Synthesis of Rhizoxin D

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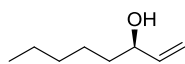
General. All reactions were carried out under Ar in glassware dried with a heat gun under vacuum (Schlenk line). The solvents were purified by distillation over the indicated drying agents and were transferred under Ar: THF, Et₂O (Mg/anthracene), acetone (B₂O₃), toluene (Na/K), CH₂Cl₂ (CaH₂), MeOH (Mg, stored over 3 Å MS); DMSO, DMF, CH₃CN, NEt₃ and pyridine were dried by an adsorption solvent purification system based on molecular sieves. Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Strem, TCI) were used as received. [(Cp**Ru*Cl)₄] was prepared according to a literature procedure and was stored under Argon.¹

Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM® SIL/UV254); Flash chromatography: Merck silica gel 60 (40–63 μm) with predistilled or HPLC grade solvents; IR: ALPHA spectrometer (Bruker), wavenumbers (ν̃) in cm⁻¹. MS (EI): Finnigan MAT 8200 (70 eV), ESIMS: ESQ 3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan); Optical rotations ($[\alpha]_D^{20}$) were measured with a Perkin-Elmer Model 343 polarimeter.

NMR: Spectra were recorded on a Bruker AV 400, AV 500 or AV 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl₃ at 7.26 and 77.16 ppm, CD₃OD at 3.31 ppm and 49.00 ppm for ¹H and ¹³C NMR spectroscopy, respectively).

Where indicated, the signal assignments in the NMR spectra are unambiguous; the numbering scheme is arbitrary as shown in the inserts.

(*R*)-Oct-1-en-3-ol (4). Novozyme (300 mg) was added to a solution of (±)-oct-1-en-3-ol (8.0 mL, 6.6 g, 52

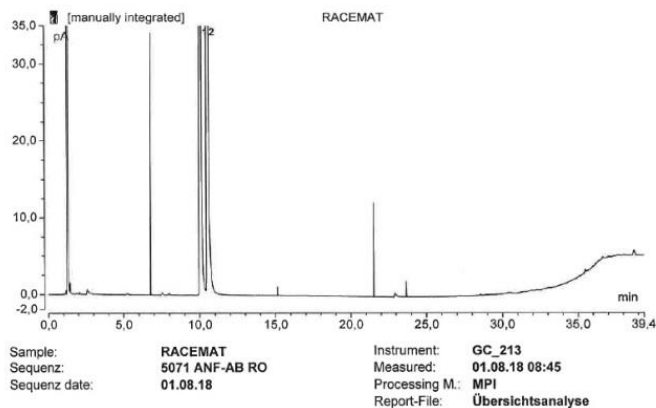


mmol) and vinyl acetate (18.0 mL, 194 mmol) in hexane (70 mL) and the resulting suspension was gently stirred (~ 50 rpm) at ambient temperature. The progress of the

reaction was monitored by GC-MS. After 42 h the immobilized enzyme was filtered off and rinsed with hexane (4 x 10 mL) and the combined filtrates were concentrated under reduced pressure. Purification of the residue by flash chromatography (hexane/*tert*-butyl methyl ether, 9:1 → 1:1) yielded the product as colorless liquid with a mushroom-like odor (2.27 g, 34%). The physical properties of the product were in full accordance with the literature;² the enantiomeric excess (> 99% ee) was determined by gas chromatography using a chiral stationary phase, cf:

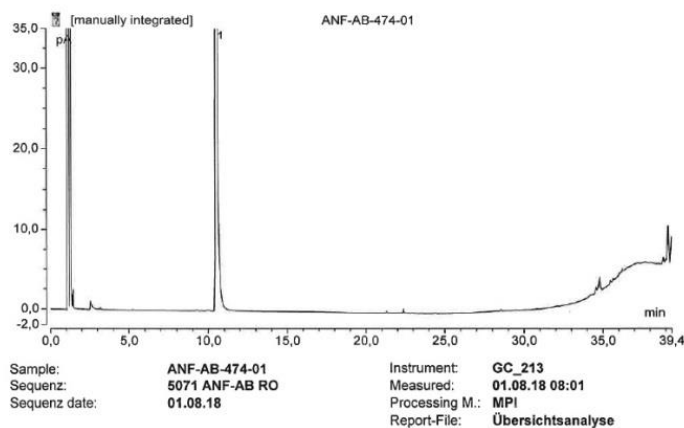
¹ P. J. Fagan, M. D. Ward, J. C. Calabrese, *J. Am. Chem. Soc.* **1989**, *111*, 1698-1719.

² E. E. Nagy, I. F. Dempsey-Hyatt, K. E. Gettys, S.T. Yeazell, S. K. Frempong, M. P. Croatt, *Org. Lett.* **2013**, *15*, 586-589.



No.	Ret. Time min	area-% %	Peak Name
1	10,08	49,55	S
2	10,50	50,45	R

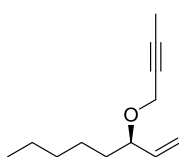
Instrument parameters:
 Column: 15,0 m LIPODEX A G 717
 Temperature: 230 85 17 MIN ISO 8/MIN 220 3 MIN ISO 350
 Gas: 0,50 bar H2
 Sample size: 1,0 µL



No.	Ret. Time min	area-% %	Peak Name
1	10,50	100,00	R

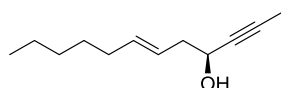
Instrument parameters:
 Column: 15,0 m LIPODEX A G 717
 Temperature: 230 85 17 MIN ISO 8/MIN 220 3 MIN ISO 350
 Gas: 0,50 bar H2
 Sample size: 1,0 µL

(R)-3-(But-2-yn-1-yloxy)oct-1-ene (5). *(R)*-Oct-1-en-3-ol (2.24 g, 17.4 mmol) was slowly added to a stirred suspension of sodium hydride (750 mg, 31.3 mmol) in THF (100 mL) at 0°C. Once the addition was complete, stirring was continued at ambient temperature for 1 h before the mixture was cooled to 0°C. 1-Bromobut-2-yne (2.7 mL, 4.0 g, 30 mmol) was added dropwise and stirring continued at ambient temperature for 16 h. The mixture was



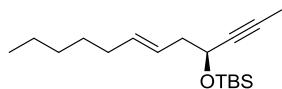
carefully poured onto saturated aqueous sodium chloride solution (150 mL) and the aqueous phase was extracted with pentane (3 x 100 mL). The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. Purification of the residue by flash chromatography (pentane/Et₂O, 100:0 → 95:5) yielded the product as pale yellow oil (2.93 g, 93%). $[\alpha]_D^{20} = +36.6$ (c = 1.61, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 5.63 (ddd, *J* = 17.7, 9.8, 7.9 Hz, 1H), 5.23 – 5.21 (m, 1H), 5.20 – 5.16 (m, 1H), 4.13 (dq, *J* = 15.0, 2.4 Hz, 1H), 3.95 (dq, *J* = 15.0, 2.3 Hz, 1H), 3.85 – 3.74 (m, 1H), 1.85 (app. t, *J* = 2.3 Hz, 3H), 1.68 – 1.55 (m, 1H), 1.52 – 1.41 (m, 1H), 1.40 – 1.22 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 117.7, 81.8, 80.3, 75.8, 56.0, 35.4, 31.9, 25.1, 22.8, 14.2, 3.8. IR (neat): 3078, 2956, 2929, 2858, 2290, 2225, 1642, 1459, 1422, 1379, 1359, 1322, 1262, 1156, 1136, 1066, 1097, 993, 925, 845, 804, 771, 726, 685, 503, 441; HRMS (ESI): *m/z* calcd for C₁₂H₂₀ONa [M+Na⁺]: 203.14063, found 203.14068.

(*S,E*)-Dodec-6-en-2-yn-4-ol (S-1). A solution of *n*-butyllithium (1.6 M in hexane, 12.2 mL, 19.5 mmol) was



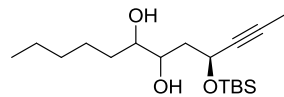
slowly added to a solution of compound **5** (2.93 g, 16.2 mmol) in THF (50 mL) at -78°C. The resulting mixture was stirred for 4 h before saturated ammonium chloride solution (100 mL) was introduced and the mixture was allowed to reach ambient temperature. The aqueous layer was extracted with Et₂O (3 x 100 mL) and the combined organic phases were dried over magnesium sulfate and concentrated under reduced pressure. The remaining pale yellow liquid was directly used in the next step without further purification.

(*S,E*)-*tert*-Butyl(dodec-6-en-2-yn-4-yloxy)dimethylsilane (6). *tert*-Butyldimethylsilyl chloride (2.90 g, 19.3



mmol) was added to a solution of compound **S-1** (2.9 g, 16.1 mmol) and imidazole (1.64 g, 24.2 mmol) in CH₂Cl₂ (200 mL) at 0°C and the resulting mixture was stirred at ambient temperature for 4 h. Water (250 mL) was added, the layers were separated and the aqueous phase was extracted with CH₂Cl₂ (3 x 150 mL). The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. Purification of the residue by flash chromatography (hexane/*tert*-butyl methyl ether, 100:0 → 98:2) yielded the product as pale yellow oil (3.77 g, 79%). $[\alpha]_D^{20} = -14.7$ (c = 0.51, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 5.59 – 5.34 (m, 2H), 4.27 (ddt, *J* = 6.6, 4.4, 2.1 Hz, 1H), 2.31 (td, *J* = 6.6, 1.5 Hz, 2H), 1.99 (dt, *J* = 8.5, 6.3 Hz, 2H), 1.82 (d, *J* = 2.1 Hz, 3H), 1.40 – 1.22 (m, 6H), 0.90 (s, 9H), 0.88 (t, *J* = 8.2, Hz, 3H), 0.11 (s, 3H), 0.09 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 133.8, 125.7, 81.0, 80.3, 63.7, 42.6, 32.8, 31.5, 29.3, 26.0, 22.7, 18.5, 14.2, 3.7, -4.4, -4.8. IR (neat): 2956, 2927, 2856, 1463, 1389, 1360, 1344, 1251, 1216, 1186, 1145, 1079, 1005, 968, 938, 833, 813, 775, 728, 666, 562, 524; HRMS (ESI): *m/z* calcd for C₁₈H₃₄OSiNa [M+Na⁺] 317.22711, found 317.22714.

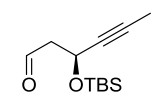
(4S)-4-((*tert*-Butyldimethylsilyl)oxy)dodec-2-yne-6,7-diol (S-2). A solution of osmium tetroxide in CH₂Cl₂



(0.22 M, 30 μ L, 6.6 μ mol) was added to a stirred suspension of **6** (882 mg, 3.0 mmol) and N-methylmorpholine-N-oxide (469 mg, 4.0 mmol) in acetone (25 mL). The yellow mixture was stirred at ambient temperature for 6 h. A

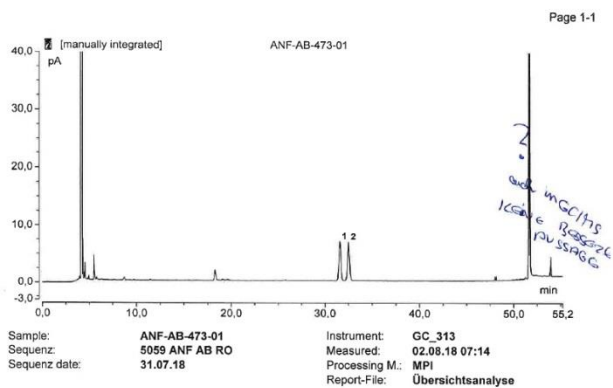
saturated aqueous solution of sodium thiosulfate (25 mL) was added to the mixture, which had turned brown. The resulting biphasic system was extracted with ethyl acetate (8 x 20 mL). The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. The residue was dissolved in hexane/ethyl acetate (3:1, 10 mL) and filtered through a plug of silica (6 x 3.5 cm), which was carefully rinsed with hexane/ethyl acetate (3:1, 250 mL). The combined filtrates were concentrated under reduced pressure to yield the diol as a mixture of two diastereomers (\approx 1:1, ¹H NMR), which was directly used in the next step.

(S)-3-((*tert*-Butyldimethylsilyl)oxy)hex-4-ynal (7). Sodium periodate (805 mg, 3.76 mmol) was added to



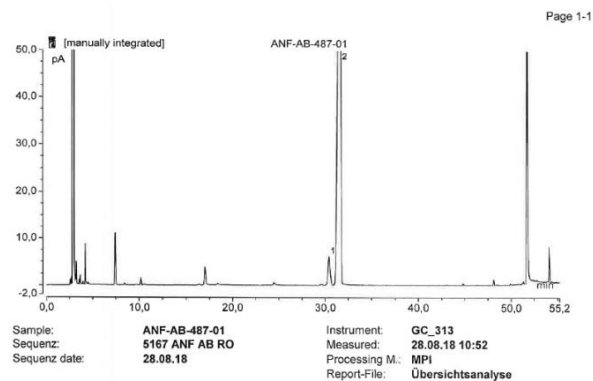
a solution of diol **S-2** (811 mg, 2.47 mmol) and pyridine (0.4 mL, 4.9 mmol) in 1,4-dioxane (15 mL) and water (5 mL). The mixture became turbid within \approx 1 min; it was stirred at

ambient temperature for further 45 min. Water (30 mL) was added and the resulting mixture was extracted with *tert*-butyl methyl ether (4 x 30 mL). The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. Purification of the residue by flash chromatography (hexane/*tert*-butyl methyl ether, 92:8) yielded the product as pale yellow liquid (467 mg, 69%). $[\alpha]_D^{20} = -64.7$ ($c = 0.9$, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 9.82 (t, $J = 2.2$ Hz, 1H), 4.94 – 4.69 (m, 1H), 2.72 (ddd, $J = 16.1, 6.6, 2.4$ Hz, 1H), 2.63 (ddd, $J = 16.1, 5.1, 2.1$ Hz, 1H), 1.83 (d, $J = 2.1$ Hz, 3H), 0.88 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 201.2, 82.1, 79.4, 58.7, 51.9, 25.8, 18.3, 3.6, -4.4, -5.0; IR (neat): 2956, 2922, 2887, 2857, 2718, 2238, 1728, 1472, 1464, 1441, 1390, 1361, 1343, 1253, 1213, 1147, 1089, 1026, 1006, 962, 940, 836, 815, 778, 684, 668, 573, 524, 465, 428, 419 cm⁻¹; HRMS (ESI): m/z calcd for C₁₂H₂₂O₂SiNa [M+Na⁺] 249.12813, found 249.12810. The enantiomeric excess (93% ee) of the product was determined by gas chromatography on a chiral stationary phase.



No.	Ret.Time min	area-% %	Peak Name
1	31,58	49,82	
2	32,50	50,18	

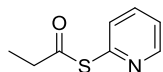
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Gas: 0,40 bar H2
Sample size: 1,0 µL



No.	Ret.Time min	area-% %	Peak Name
1	30,42	3,62	
2	31,65	96,48	

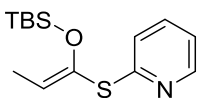
Instrument parameters:
Column: 30,0 m BGB 176/BGB 15 G 618
Temperature: 230 110 40 MIN ISO 9/MIN 220 3 MIN ISO 350
Gas: 0,40 bar H2
Sample size: 1,0 µL

S-(Pyridin-2-yl) propanethioate (S-3). Propionyl chloride (1.17 mL, 13.5 mmol) and Et₃N (2.15 mL, 15.5 mmol) were successively added to a stirred solution of 2-mercaptopyridine (1.5 g, 13.5



mmol) in THF (20 mL). The resulting thick slurry was stirred for 30 min before the precipitate was filtered off. The filtrate was washed with sat. aq. NaHCO₃ (50 mL). After phase separation, the organic solvent was removed under reduced pressure to give the title compound as a yellow oil (2.01 g, 89%), which was used in the next step without further purification. ¹H NMR (400 MHz, CDCl₃): δ 8.55 (ddd, *J* = 4.8, 1.9, 0.9 Hz, 1H), 7.67 (td, *J* = 7.7, 1.9 Hz, 1H), 7.54 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.24 – 7.19 (m, 1H), 2.66 (q, *J* = 7.5 Hz, 2H), 1.17 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃): δ = 197.4, 151.6, 150.5, 137.2, 130.3, 123.5, 37.7, 9.5; IR (film): 2980, 1703, 1572, 1562, 1449, 1420, 1082, 1011, 922, 764; HRMS (ESI): *m/z* calcd for C₈H₁₀NOS [M + H]: 168.04792, found 168.04776.

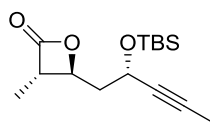
O,S-Keteneacetal 13. Pyridyl thioester **S-3** (538 mg, 3.2 mmol) was added dropwise to a stirred solution of LiHMDS (647 mg, 4.0 mmol), TBSCl (600 mg, 4.0 mmol) and DMF (0.77 mL, 9.7 mmol) in THF (10 mL) at –78°C. The mixture was stirred for 2 h at this temperature before the reaction was quenched with a sat. aq. NH₄Cl (10 mL). The aqueous layer



was extracted with Et₂O (2 x 20 mL), the combined organic phases were dried over MgSO₄ and volatiles were removed under reduced pressure. The crude material was purified by flash chromatography on silica gel (pentane/Et₂O, 9:1) to yield the title compound as a colorless liquid (826 mg, 91%). ¹H NMR (400 MHz, CDCl₃): δ 8.42 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.54 (ddd, *J* = 8.1, 7.4, 1.9 Hz, 1H), 7.32 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.00 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1H), 5.45 (q, *J* = 6.8 Hz, 1H), 1.73 (d, *J* = 6.8 Hz, 3H), 0.88 (s, 9H),

0.09 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3): δ 160.5, 149.5, 140.3, 136.6, 121.7, 119.7, 118.1, 25.8, 18.2, 12.5, -4.2; IR (film): 2930, 2858, 1635, 1574, 1450, 1418, 1308, 1254, 1137, 1116, 1069, 862, 839; HRMS (ESI): m/z calcd for $\text{C}_{14}\text{H}_{23}\text{NOSSiNa}$ [$\text{M} + \text{Na}$]: 304.11633; found 304.11618.

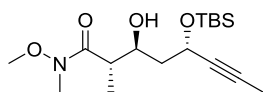
β -Lactone 8. The O,S-keteneacetal **13** (1.29 g, 4.6 mmol) was added to a stirred solution of zinc chloride



(fused under vacuum prior to use; 1.09 g, 8 mmol) in CH_2Cl_2 (50 mL). After 15 min, a solution of aldehyde **7** (906 mg, 4 mmol) in CH_2Cl_2 (2 mL) was added dropwise over a period of 1 min and the resulting mixture was stirred at ambient temperature for 3

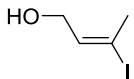
h. The reaction was quenched with pH 7 buffer (15 mL) and the aqueous layer was extracted with EtOAc (2 x 15 mL). The combined organic phases were dried over MgSO_4 and concentrated under reduced pressure. The orange residue was purified by flash chromatography on silica gel (pentane/EtOAc, 99.5:0.5 \rightarrow 97:3) to yield the title compound as a colorless oil (912 mg, 90%, dr = 6:1). ^1H NMR (400 MHz, CDCl_3) δ 4.52 (ddq, J = 8.3, 4.3, 2.2 Hz, 1H), 4.40 (ddd, J = 7.4, 5.9, 4.0 Hz, 1H), 3.37 (qd, J = 7.5, 4.0 Hz, 1H), 2.28 – 1.94 (m, 2H), 1.82 (d, J = 2.2 Hz, 3H), 1.41 (d, J = 7.6 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.2, 81.4, 79.9, 76.3, 59.5, 51.2, 43.2, 25.9, 18.3, 12.6, 3.6, -4.4, -4.9; IR (film): 2955, 2929, 2857, 1825, 1472, 1462, 1252, 1095, 1064, 1016; HRMS (ESI): m/z calcd for $\text{C}_{15}\text{H}_{26}\text{O}_3\text{SiNa}$ [$\text{M} + \text{Na}$]: 305.15434; found 305.15426.

Weinreb amide 9. AlMe_3 (2.0 M in toluene, 1.7 mL, 3.4 mmol) was added at 0°C to a stirred solution of



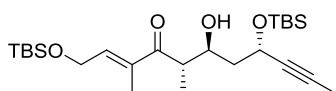
N,O-dimethylhydroxamine-HCl (332 mg, 3.4 mmol) in CH_2Cl_2 (80 mL). The resulting mixture was stirred at 0°C for 30 min and for another 30 min at ambient temperature.

A solution of β -lactone **8** (320 mg, 1.13 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the cooling bath was removed. Stirring was continued at ambient temperature for 2 h before the reaction was carefully quenched by slow addition of a sat. aq. solution of Rochelle's salt (50 mL). After phase separation, the aqueous layer was extracted with EtOAc (3 x 15 mL), and the combined organic phases were dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EtOAc 4:1 \rightarrow 2:1) to yield title compound as a colorless oil (373 mg, 96%). $[\alpha]_D^{20} = -30.4$ (c = 1.1, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 4.66 (ddt, J = 7.9, 4.3, 2.2 Hz, 1H), 3.98 (dtd, J = 10.0, 6.1, 2.4 Hz, 1H), 3.71 (s, 3H), 3.59 (d, J = 6.2 Hz, 1H), 3.20 (s, 3H), 2.92 (bs, 1H), 1.87 – 1.79 (m, 4H), 1.77 – 1.65 (m, 1H), 1.20 (d, J = 6.5 Hz, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 177.2, 80.8, 80.6, 70.6, 61.7, 60.8, 43.9, 40.5, 32.0, 26.0, 18.3, 14.7, 3.7, -4.4, -5.0; IR (film): 3437, 2957, 2928, 2856, 1599, 1472, 1418, 1388, 1283, 1082, 1063; HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{34}\text{NO}_4\text{Si}$ [$\text{M} + \text{H}$]: 344.22516; found 344.22527.

(E)-3-Iodobut-2-en-1-ol (S-4). Bis-(cyclopentadienyl)titanium-(IV)-dichloride (0.57 g, 2.30 mmol) was added in portions to a stirred solution of  (2.0 M in Et₂O, 53.0 mL, 106 mmol) in Et₂O (60 mL) at 0°C. The mixture was stirred at this temperature for 10 min before a solution of 2-butyne-1-ol (3.0 mL, 40.1 mmol) in Et₂O (12 mL) was added dropwise. The mixture was warmed to ambient temperature and stirring continued for 4 h until complete consumption of the starting material was observed (TLC). The mixture was cooled to -78°C and stirred vigorously while iodine (35.1 g, 138 mmol) was added in small portions. The solution was warmed to 0°C and stirred for 1 h prior to quenching of the reaction with sat. aq. NH₄Cl (30 mL). The mixture was diluted with Et₂O (60 mL) and water (20 mL). After phase separation, the aqueous layer was extracted with Et₂O (3 x 30 mL). The combined organic phases were washed with sat. aq. Na₂S₂O₃ (50 mL) and dried over MgSO₄. The crude material was purified by flash chromatography on silica gel (pentane/Et₂O, 95:5) to yield the title compound as a colorless oil (3.6 g, 45%). ¹H NMR (400 MHz, CDCl₃): δ = 6.36 (tq, *J* = 6.9, 1.5 Hz, 1H), 4.05 (dq, *J* = 7.0, 0.9 Hz, 2H), 2.43 (dd, *J* = 1.6, 0.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃): δ = 139.8, 98.4, 59.8, 28.1; IR (film,): 3300, 2917, 1638, 1424, 1376, 1218, 1095, 1059; HRMS (ESI): *m/z* calcd for C₄H₇OI [M + H]: 197.95434, found 197.95416.

(E)-tert-Butyl((3-iodobut-2-en-1-yl)oxy)dimethylsilane (14). TBSCl (0.87 g, 5.8 mmol) was added to a stirred solution of alcohol **S-4** (1.1 g, 5.5 mmol) and imidazole (0.74 g, 11.0 mmol) in THF (15 mL) at 0°C. The mixture was stirred for 16 h at ambient temperature before the reaction was quenched with H₂O (30 mL). The aqueous layer was extracted with Et₂O (3 x 20 mL), the combined organic phases were successively washed with sat. aq. Na₂S₂O₃ (20 mL) and H₂O (20 mL) before they were dried over MgSO₄. All volatile materials were removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (pentane/Et₂O, 95:5) to yield the title compound as a colorless oil (1.17 g, 68%). ¹H NMR (400 MHz, Chloroform-*d*) δ 6.30 (tq, *J* = 6.5, 1.5 Hz, 1H), 4.12 (dd, *J* = 6.5, 0.9 Hz, 2H), 2.41 (dt, *J* = 1.6, 0.9 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 140.8, 96.1, 60.8, 28.2, 26.0, 18.5, -5.1.

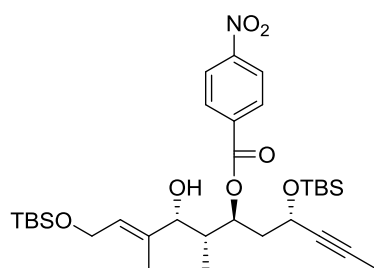
Enone 10. Compound **9** (260 mg, 0.76 mmol) and TMSCl (100 μL, 0.83 mmol) were added to a stirred solution of pyridine (150 μL, 1.5 mmol) in CH₂Cl₂ (2 mL) at 0°C. After stirring for 10 min at 0°C and for another 60 min at ambient temperature, the reaction was quenched by addition of pH 7 buffer (5 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (2 x 15 mL) and the combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. The resulting crude material **S-5** was used in the next step without further purification.



*t*BuLi (1.7 M in pentane; 2.22 ml, 3.79 mmol) was diluted with THF (13 mL) at -78°C , resulting in a yellow colored solution. Alkenyl iodide **14** (591 mg, 1.89 mmol) was added dropwise and stirring was continued for 30 min at -78°C . In parallel, a solution of $\text{CeCl}_3 \cdot 2\text{LiCl}$ (0.30 M in THF, 5 mL) was added at -78°C to a solution of the silylated Weinreb amide **S-5** (314 mg, 0.76 mmol) in THF (16 mL). After 5 min, the solution of the alkenyl lithium reagent derived from **14** was added via cannula to the mixture containing the Weinreb amide, causing a color change to deep orange. After stirring for 1 h at -78°C , the reaction was quenched by the addition of pH 7 buffer (30 mL). The mixture was allowed to warm to ambient temperature before the layers were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 5 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated under reduced pressure.

The resulting crude material was dissolved in CH_2Cl_2 (10 mL) and MeOH (2 mL) at 0°C . CSA (tip of spatula) was added and the resulting mixture was stirred at 0°C for 5 min. Excess reagent was then quenched by addition of a pH 7 buffer solution (10 mL) and *tert*-butyl methyl ether (20 mL). After phase separation, the aqueous layer was extracted with *tert*-butyl methyl ether (2 x 15 mL) and the combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EtOAc, 20:1 \rightarrow 10:1) to yield title compound as a colorless oil (310 mg, 87% over 3 steps). $[\alpha]_D^{20} = -28.1$ ($c = 0.8$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.67 (td, $J = 5.2, 1.4$ Hz, 1H), 4.66 (ddd, $J = 7.4, 3.7, 2.1$ Hz, 1H), 4.42 (d, $J = 5.1$ Hz, 2H), 4.22 – 4.07 (m, 1H), 3.38 – 3.29 (m, 2H), 1.90 – 1.76 (m, 4H), 1.74 (d, $J = 1.2$ Hz, 3H), 1.12 (d, $J = 7.1$ Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.10 (s, 6H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 206.2, 143.3, 135.7, 81.0, 80.5, 71.1, 61.3, 61.2, 44.4, 42.9, 26.1, 26.0, 18.5, 18.3, 15.4, 11.8, 3.7, -4.4 , -5.07 , -5.07 , -5.10 ; IR (film): 3500, 2955, 2929, 2886, 2857, 1667, 1472, 1463, 1361, 1257, 1106, 1063, 1006; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{49}\text{O}_4\text{Si}_2$ $[\text{M} + \text{H}]^+$ 469.31639; found 469.31675.

Compound 11. A solution of *p*-nitrobenzaldehyde (300 mg, 1.98 mmol) in degassed THF (13 mL) was

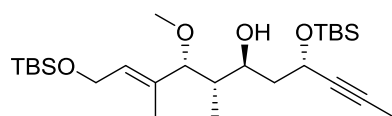


added at -25°C to a stirred solution of β -hydroxyketone **10** (310 mg, 0.66 mmol) and a freshly prepared solution of SmI_2 in THF (0.1 M, 2.9 mL, 0.29 mmol).³ The resulting deep orange mixture was stirred at -25°C for 3 h before the reaction was quenched at that temperature with sat. aq. NaHCO_3 (20 mL) and *tert*-butyl methyl ether (10 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 10 mL)

³ P. Girard, J.-L. Namy, H. B. Kagan, *J. Am. Chem. Soc.*, **1980**, *102*, 2693 – 2698.

and the combined organic fractions were dried and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EtOAc, 20:1) to yield the title compound as a yellow oil (240 mg, 62% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.34 – 8.26 (m, 2H), 8.24 – 8.16 (m, 2H), 5.66 (ddt, $J = 6.8, 5.7, 1.2$ Hz, 1H), 5.26 (ddt, $J = 6.3, 4.5, 3.6$ Hz, 1H), 4.43 – 4.34 (m, 1H), 4.24 (qd, $J = 13.1, 6.2$ Hz, 2H), 3.93 (t, $J = 4.3$ Hz, 1H), 2.24 – 2.00 (m, 4H), 1.72 (d, $J = 2.1$ Hz, 3H), 1.65 (d, $J = 1.2$ Hz, 3H), 0.97 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.85 (s, 9H), 0.07 (s, 6H), 0.05 (s, 3H), -0.06 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 164.8, 150.7, 136.3, 135.8, 130.9, 126.8, 123.8, 80.9, 80.8, 76.0, 74.8, 60.1, 59.9, 40.1, 39.5, 26.1, 25.9, 18.6, 18.2, 13.1, 9.5, 3.6, -4.3 , -5.0 (2C), -5.1 ; IR (film): 3510, 2956, 2929, 2884, 2856, 1723, 1608, 1529, 1463, 1348, 1276, 1251, 1100, 1045, 1014, 954; HRMS (ESI): m/z calcd for $\text{C}_{32}\text{H}_{53}\text{NO}_7\text{Si}_2\text{Na}$ [M + Na]: 642.32528, found 642.32536.

Compound S-6. $[\text{MeO}_3\text{-BF}_4]$ (309 mg, 2.01 mmol) was added at 0°C in one portion to a stirred suspension

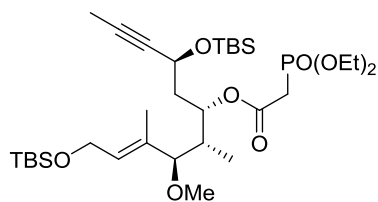


containing MS 4 Å (100 mg), proton sponge (576 mg, 2.69 mmol) and benzoate **11** (185 mg, 0.30 mmol) in CH_2Cl_2 (50 mL). The resulting mixture was allowed to reach ambient temperature and stirring was

continued for 3 h before the reaction was quenched with sat. aq. NaHCO_3 (50 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (2 x 30 mL), the combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 20:1) to yield the corresponding methyl ether as a colorless oil (170 mg, 90%).

This material was dissolved in THF/MeOH (1:1, 6 mL) and K_2CO_3 (62 mg, 0.45 mmol) was added at 0°C . The cooling bath was removed and the mixture was stirred at ambient temperature for 20 h. The reaction was then quenched with a sat. aq. NH_4Cl (20 mL) and *tert*-butyl methyl ether (30 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (2 x 20 mL), the combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure, and the residue was purified by flash chromatography (hexane/EtOAc, 20:1) to yield the title compound as colorless oil (85 mg, 63%). $[\alpha]_D^{20} = -13.4$ ($c = 0.4$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 5.50 (tt, $J = 6.1, 1.3$ Hz, 1H), 4.67 (ddq, $J = 6.2, 4.1, 1.8$ Hz, 1H), 4.36 – 4.17 (m, 2H), 3.93 (ddq, $J = 9.0, 6.2, 2.9$ Hz, 1H), 3.62 (d, $J = 4.8$ Hz, 1H), 3.43 (d, $J = 3.9$ Hz, 1H), 3.25 (s, 3H), 1.83 (d, $J = 2.1$ Hz, 3H), 1.80 – 1.65 (m, 2H), 1.56 (d, $J = 1.4$ Hz, 3H), 0.90 (s, 9H), 0.90 (s, 9H), 0.89 – 0.85 (m, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 133.7, 127.6, 86.6, 81.1, 80.6, 70.7, 62.0, 60.1, 57.0, 42.2, 41.1, 26.1, 26.0, 18.5, 18.3, 13.3, 10.8, 3.7, -4.4 , -4.92 , -4.94 , -5.1 ; IR (film): 3530, 2954, 2928, 2885, 2856, 1463, 1361, 1251, 1088, 1056; HRMS (ESI): m/z calcd for $\text{C}_{26}\text{H}_{52}\text{O}_4\text{Si}_2\text{Na}$ [M + Na]: 507.32964, found 507.32974.

Phosphonate 12. EDC·HCl (57 mg, 0.30 mmol) was added at 0°C to a stirred solution of diethyl



phosphonoacetic acid (74 μ L, 0.46 mmol) in CH_2Cl_2 (4 mL). After 15 min, a solution of compound **S-6** (80 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added, the cooling bath was removed and DMAP (6 mg, 0.05 mmol) was introduced. The resulting solution was stirred for 10 min at

ambient temperature before the reaction was quenched with sat. aq. NaHCO_3 (10 mL). The aqueous layer was extracted with Et_2O (2 x 10 mL), the combined organic fractions were dried over MgSO_4 and concentrated, and the residue was purified by flash chromatography on silica gel (hexane/ EtOAc , 4:1 \rightarrow 2:1) to yield the title compound as a colorless oil (78 mg, 72%). $[\alpha]_D^{20} = -27.0$ (c = 0.7, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 5.52 (t, $J = 6.0$ Hz, 1H), 5.02 – 4.89 (m, 1H), 4.38 – 4.25 (m, 2H), 4.24 – 4.05 (m, 5H), 3.20 (d, $J = 7.4$ Hz, 1H), 3.17 (s, 3H), 3.01 – 2.92 (m, 1H), 2.90 – 2.81 (m, 1H), 2.13 – 1.98 (m, 1H), 1.93 – 1.82 (m, 2H), 1.81 (d, $J = 2.1$ Hz, 3H), 1.60 (s, 3H), 1.34 (t, $J = 7.2$ Hz, 6H), 0.94 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.87 (s, 9H), 0.10 (s, 3H), 0.07 (s, 6H), 0.04 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 165.0 (d), 133.3, 129.5, 87.7, 81.2, 80.3, 73.5, 62.7 (apparent t), 60.0, 59.5, 56.5, 38.5 (d), 35.3, 34.0, 26.1, 26.0, 18.5, 18.2, 16.5 (d), 16.5 (d), 11.9, 10.0, 3.6, -4.4, -4.96, -5.05 (2 C); IR (film): 2956, 2929, 2886, 2857, 1734, 1472, 1463, 1388, 1362, 1256, 1203, 1085, 1045, 1006, 962; HRMS (ESI): m/z calcd for $\text{C}_{32}\text{H}_{63}\text{O}_8\text{Si}_2\text{PNa}$ [$\text{M} + \text{Na}$]: 685.3691, found 685.3691.

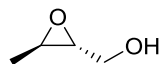
Penta-1,3-diyne (S-7).⁴ Ammonia (300 mL) was condensed at -78°C into a 1 L three-necked-cooling flask



equipped with a mechanical stirrer and an addition funnel. The solution was allowed to warm to -47°C, before a catalytic amount of $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (400 mg, 1 mmol) was introduced, followed by careful addition of sodium (20.8 g, 905 mmol) in small portions. Once the sodium had completely dissolved, 1,4-dichloro-2-butyne (29.5 mL, 302 mmol) was added over 45 min, resulting in the formation of a thick suspension. Stirring was continued for another 15 min at -47°C before methyl iodide (26.3 mL, 142 mmol) was cannulated over 20 min into the reaction vessel. After another 15 min at this temperature, the mixture was allowed to slowly warm to ambient temperature before undecane (150 mL) was added in several portions. After stirring for 30 min, the mixture was poured onto ice water (300 mL). The layers were separated and the aqueous layer was extracted with undecane (7 x 35 mL). The combined organic phases were washed with aqueous hydrochloric acid (2 M, 250 mL), dried over MgSO_4 and filtered. Distillation of the filtrate (25–50°C, 10 mbar) gave the title compound as a colorless liquid (\approx 95% in undecane, 10.3 g, 51%). ^1H NMR (400 MHz, CDCl_3): δ = 1.93–1.91 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ = 74.3, 68.6, 64.0, 4.2.

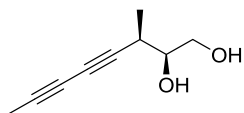
⁴ H. D. Verkruijse, L. Brandsma, *Synth. Commun.* **1991**, *21*, 141 – 144.

Epoxide 16. D-(-)-Diisopropyltartrate (702 mg, 3.0 mmol) and $\text{Ti}(\text{O}i\text{Pr})_4$ (568 mg, 2 mmol) were added successively to a gently stirred suspension of activated molecular sieves 4 Å (approx. 2 g)



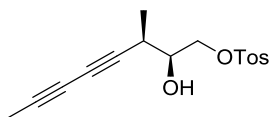
in CH_2Cl_2 (100 mL) at ambient temperature. The suspension was cooled to -20°C before crotyl alcohol (19:1 *trans/cis*; 3.6 g, 50 mmol) was added in one portion. After stirring for 30 min at this temperature, *t*BuOOH (5.5 M in decane, 13.63 mL, 75 mmol) was added in one portion and the mixture was left stirring at -20°C for 18 h. Dimethylsulfide (7.3 mL, 100 mmol) was added to quench excess reagent and the mixture was allowed to reach ambient temperature. Stirring was continued for 6 h before the mixture was filtered through a plug of Celite®. The filtrate was evaporated and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 6:1 \rightarrow 1:1) to yield the title compound as a colorless oil (3.44 g, 78%, er = 4.6:1). $[\alpha]_D^{20} = +42.3$ (CHCl_3 , $c = 1.0$); $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 3.90$ (ddd, $J = 12.6, 5.6, 2.5$ Hz, 1H), 3.61 (ddd, $J = 12.6, 7.2, 4.4$ Hz, 1H), 3.04 (qd, $J = 5.3, 2.3$ Hz, 1H), 2.89 (dt, $J = 4.7, 2.4$ Hz, 1H), 2.51 (t, $J = 5.3$, OH), 1.33 (d, $J = 5.2$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 61.8, 59.7, 52.1, 17.2; IR (film): 3397; 2984, 2929, 2874, 1451, 1383, 1241, 1102, 988; HRMS (ESI): m/z calcd for $\text{C}_4\text{H}_8\text{O}_2\text{Na}$ [$\text{M} + \text{Na}$]: 111.04165; found 111.04170.

Diol 17. A solution of *n*BuLi (1.6 M in hexanes; 44.4 mL, 71.0 mmol) was added dropwise to a stirred solution of pentadiyne (**S-7**) (95% in decane, 5.27 g, 78.1 mmol) in CH_2Cl_2 (200 mL) at -78°C . After stirring for 30 min, the mixture was allowed to warm to 0°C and diethylaluminium chloride (25% *w/w* in toluene, 35.7 mL, 71.0 mmol) was added.



After stirring for 3 h at 0°C , a solution of epoxide **16** (3.12 g, 35.5 mmol) in CH_2Cl_2 (14 mL) was introduced over 15 min. Stirring was continued overnight at 0°C before the reaction was quenched by the careful addition of aq. HCl (1 M, 150 mL) and sat. aq. potassium sodium tartrate (150 mL). The biphasic mixture was vigorously stirred for 4 h to reach phase separation, the aqueous layer was extracted with EtOAc (3 \times 100 mL), the combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 4:1 \rightarrow 1:1) to yield the title compound as a colorless oil (5.12 g, 95%, 10:1 mixture of isomers). $[\alpha]_D^{20} = +53.0$ ($c = 1.79$, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 3.84$ (ddd, $J = 11.0, 6.6, 3.1$ Hz, 1H), 3.69 (ddd, $J = 11.2, 6.9, 4.6$ Hz, 1H), 3.59 (dddd, $J = 10.4, 7.2, 5.6, 3.2$ Hz, 1H), 2.66 (qdq, $J = 7.0, 7.0, 1.1$ Hz, 1H), 2.41 (br s, 1H, -OH), 1.96 (br s, 1H, -OH), 1.91 (d, $J = 1.1$ Hz, 3H), 1.26 (d, $J = 7.0$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 74.9, 74.8$ (2C), 67.9, 64.7, 64.2, 30.3, 16.9, 4.3; IR (film): 3345, 2940, 1453, 1053; HRMS (ESI): m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_2\text{Na}$ [$\text{M} + \text{Na}$]: 175.0730, found 175.0730.

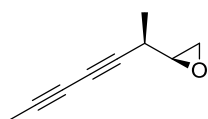
Tosylate S-8. Pyridine (6.6 mL) and *p*-toluenesulfonyl chloride (3.43 g, 18.04 mmol) were added at 0°C to



a stirred solution of diol **17** (2.49 g, 16.37 mmol) in CH₂Cl₂ (80 mL). Stirring was continued at ambient temperature for 6 h before the reaction was quenched with sat. aq. NH₄Cl (80 mL). The aqueous layer was extracted with CH₂Cl₂ (3 × 60

mL), the combined organic fractions were dried over MgSO₄, filtered and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc 4:1, →2:1) to afford the title compound as a colorless oil (4.87 g, 97%). $[\alpha]_D^{20} = +68.6$ (c = 1.05, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 7.81 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.6 Hz, 2H), 4.30 (dd, *J* = 10.5, 3.0 Hz, 1H), 4.08 (dd, *J* = 10.5, 6.5 Hz, 1H), 3.74–3.67 (m, 1H), 2.65–2.56 (m, 1H), 2.46 (s, 3H), 2.22 (br s, 1H), 1.91 (d, *J* = 1.1 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 145.3, 132.6, 130.1 (2C), 128.2 (2C), 75.7, 75.2, 72.6, 72.2, 68.3, 64.1, 29.9, 21.9, 16.8, 4.3; IR (film): 3528, 2980, 1598, 1358, 1190, 1175, 1096, 959; HRMS (ESI): *m/z* calcd for C₁₆H₁₈O₄SNa [M+Na]: 329.0818, found 329.0817.

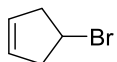
Epoxide 18. DBU (630 μL, 4.23 mmol) was added at 0°C to a stirred solution of tosylate **S-8** (720 mg, 2.11 mmol) in CH₂Cl₂ (6 mL). Stirring was continued at ambient temperature for 18 h



before the mixture was carefully concentrated under reduced pressure (Caution: the product is fairly volatile). The residue was purified by flash chromatography on silica

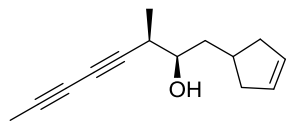
gel (hexane/EtOAc, 20:1) to afford the title compound as a colorless oil (236 mg, 83%). $[\alpha]_D^{20} = +59.7$ (c = 0.5 CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 2.91 (ddd, *J* = 6.4, 3.8, 2.6 Hz, 1H), 2.78 (dd, *J* = 4.9, 3.9 Hz, 1H), 2.67 (dd, *J* = 4.9, 2.5 Hz, 1H), 2.51 – 2.39 (m, 1H), 1.91 (d, *J* = 1.1 Hz, 3H), 1.32 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃): δ = 75.3, 74.9, 67.6, 64.1, 54.7, 46.4, 29.9, 17.7, 4.3; IR (film): 2982, 2932, 1722, 1455, 1258, 1073, 1025, 922; HRMS (ESI): *m/z* calcd for C₉H₁₀O [M+1]: 134.07333, found 134.07317.

4-Bromocyclopent-1-ene (S-9). A solution of bromine (1.60 mL, 31.2 mmol) in CH₂Cl₂ (10 mL) was added



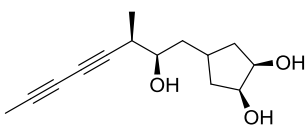
at –30°C over a period of 1 h to a stirred solution of Ph₃P (8.21 g, 31.2 mmol) in CH₂Cl₂ (30 mL). After stirring for additional 15 min, a premixed solution of 3-cyclopenten-1-ol (2.53 g, 29.7 mmol) and pyridine (2.50 mL, 29.7 mmol) in CH₂Cl₂ (7 mL) was introduced over 1 h. Once the addition was complete, the mixture was allowed to reach ambient temperature over the course of 3 h and stirring was continued for additional 5 h. Excess reagent was quenched with sat. aq. Na₂S₂O₃ (30 mL). The aqueous layer was extracted with CH₂Cl₂ (2 × 30 mL), the combined organic fractions were dried over MgSO₄, the volatiles were very carefully removed (600 mbar, 35°C) and the residue was purified by flash chromatography on silica (pentane) to yield the title compound as a colorless liquid (4.08 g, 93%). ¹H NMR (400 MHz, Chloroform-*d*) δ 5.76 (s, 2H), 4.59 (tt, *J* = 6.6, 3.1 Hz, 1H), 2.97 (ddd, *J* = 17.3, 6.4, 0.9 Hz, 2H), 2.85 – 2.71 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 128.7, 48.7, 44.9.

Compound 19. Mg powder was successively washed with aq. HCl (1 M, 10 mL), *i*PrOH (10 mL) and *tert*-butyl methyl ether (10 mL) before being dried under vacuum. To a vigorously stirred suspension of the resulting activated Mg powder (150 mg, 6.25 mmol) in Et₂O (3 mL) were added a few droplets of 1,2-dibromoethane and the mixture was briefly heated using a heat gun. 4-Bromocyclopent-1-ene (**S-9**) (415 mg, 2.8 mmol) was then added dropwise to the suspension at such a rate as to maintain gentle reflux and stirring was continued for 2 h once the addition was complete.



The resulting solution of the Grignard reagent was then transferred via cannula into a -40°C cold stirred suspension of copper(I) iodide (279 mg, 1.5 mmol) in Et₂O (2 mL). Stirring was continued for 30 min at -40°C before a solution of epoxide **18** (250 mg, 1.8 mmol) in Et₂O (0.5 mL) was added dropwise. After another 4 h at -40°C, the excess reagent was carefully quenched with sat. aq. NH₄Cl (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic fractions were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EtOAc, 10:1 → 6:1) to afford the title compound as a colorless oil (300 mg, 78%). $[\alpha]_D^{20} = +9.2$ (c = 0.4, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 5.73 – 5.63 (m, 2H), 3.59 (dd, *J* = 9.0, 4.5 Hz, 1H), 2.64 (ddt, *J* = 6.7, 5.6, 1.4 Hz, 1H), 2.58 – 2.43 (m, 3H), 2.01 (tddd, *J* = 16.8, 8.3, 3.9, 2.4 Hz, 2H), 1.92 (d, *J* = 1.1 Hz, 3H), 1.66 – 1.62 (m, 3H), 1.18 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃): δ = 130.2, 129.7, 78.0, 74.5, 73.4, 67.6, 64.3, 40.4, 39.6, 38.5, 34.3, 34.0, 15.8, 4.3; IR (film): 3393, 2931, 2842, 1451, 1070, 1038, 971; HRMS (ESI): *m/z* calcd for C₁₄H₁₈ONa [M + Na]: 225.12475, found 225.12498.

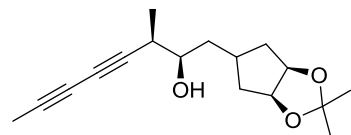
Triol S-10. N-Methylmorpholine-N-oxide (415 mg, 3.55 mmol) and OsO₄ (4 % w/w in water, 0.5 mL, 0.084 mmol) were added to a stirred solution of compound **19** (422 mg, 2.09 mmol) in acetone (8 mL) and water (6 mL). The resulting brown solution was allowed to stir for 4 h before the reaction was quenched with sat. aq.



Na₂S₂O₃ (10 mL). After stirring for 1 h, the mixture was diluted with EtOAc (30 mL). The aqueous layer was extracted with EtOAc (2 x 20 mL), the combined organic fractions were dried over MgSO₄, filtered and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, gradually changed to EtOAc containing 5% MeOH) to yield the title compound as a white solid (337 mg, 68%, dr = 8:1). $[\alpha]_D^{20} = +17.1$ (c = 0.4, CHCl₃); ¹H NMR (400 MHz, CD₃OD): δ = 4.04 (ddd, *J* = 4.7, 3.4, 1.6 Hz, 2H), 3.36 (ddd, *J* = 9.7, 7.0, 2.6 Hz, 1H), 2.59 – 2.47 (m, 1H), 2.44 (tq, *J* = 7.0, 1.1 Hz, 1H), 1.94 – 1.84 (m, 2H), 1.88 (d, *J* = 1.1 Hz, 3H), 1.61 (ddd, *J* = 13.9, 10.0, 2.6 Hz, 1H), 1.53 – 1.40 (m, 3H), 1.17 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CD₃OD) δ 79.4, 74.4, 73.8, 73.6, 73.5, 67.5, 65.0,

42.6, 39.8, 38.6, 34.6, 31.9, 16.8, 3.4; IR (film): 3302, 1933, 2914, 1343, 1134, 1111, 1078, 1040, 1026, 986, 882, 869, 716; HRMS (ESI): m/z calcd for $C_{14}H_{20}O_3Na$ [$M + Na$]: 259.13021; found 259.13046.

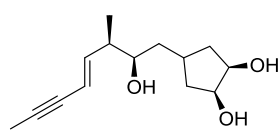
Acetonide 20. PPTS (tip of a spatula) was added to a stirred solution of **S-10** (337 mg, 1.43 mmol) in acetone (40 mL) and the resulting mixture was stirred for 5 h. The



reaction was quenched with sat. aq. $NaHCO_3$ (40 mL) and EtOAc (60 mL), the aqueous layer was extracted with EtOAc (2 x 50 mL), the combined organic fractions were dried over $MgSO_4$ and concentrated under

reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EtOAc, 2:1 \rightarrow 1:1) to yield the title compound as a sticky oil (330 mg, 83%). $[\alpha]_D^{20} = +34.8$ ($c = 0.8$, $CHCl_3$); 1H NMR (400 MHz, $CDCl_3$) δ 4.72 – 4.53 (m, 2H), 3.80 – 3.45 (m, 1H), 2.67 – 2.58 (m, 1H), 2.37 (ddq, $J = 11.7, 7.3, 5.8$ Hz, 1H), 2.14 – 1.98 (m, 2H), 1.94 (s, 3H), 1.70 (d, $J = 5.8$ Hz, 1H), 1.64 – 1.52 (m, 2H), 1.45 (s, 3H), 1.31 (s, 3H), 1.31 – 1.05 (m, 2H), 1.20 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 108.9, 80.6, 80.5, 78.0, 74.6, 73.8, 67.7, 64.3, 40.5, 39.8, 38.4, 34.1, 33.2, 26.2, 23.9, 15.9, 4.4; IR (film): 3462, 2978, 2931, 2917, 2847, 1444, 1407, 1305, 1261, 1212, 1173, 1133, 1101, 1043; HRMS (ESI): m/z calcd for $C_{17}H_{24}O_3Na$ [$M + Na$]: 299.16176; found 299.16193.

Compound 21. A solution of Red-Al[®] (3.5 M in toluene; 0.34 mL, 1.19 mmol) was added to a stirred solution of compound **20** (150 mg, 0.54 mmol) in THF (10 mL) at ambient temperature. After stirring for 4 h, the reaction was quenched with aq. sat. NH_4Cl (10 mL) and EtOAc (20 mL). The aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic fractions were dried over $MgSO_4$ and concentrated, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 2:1) to yield the desired product as a colorless oil.

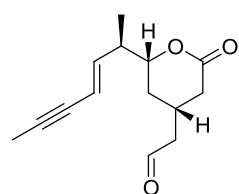


$pTSA$ (15 mg, 0.08 mmol) was added in one portion to a solution of this material in wet MeOH (10 mL) and the resulting mixture was stirred at 40°C for 4 d. The mixture was diluted with EtOAc (20 mL) and aq. sat. Na_2CO_3 (10 mL).

The aqueous layer was extracted with EtOAc (2 x 10 mL), the combined organic fractions were dried over $MgSO_4$ and concentrated, and the residue was purified by flash chromatography on silica gel (EtOAc \rightarrow EtOAc + 10% MeOH) to yield the title compound as a white solid (119 mg, 93%). $[\alpha]_D^{20} = +5.8$ ($c = 1.1$, MeOH); 1H NMR (400 MHz, CD_3OD) δ 5.91 (ddd, $J = 15.9, 8.4, 0.8$ Hz, 1H), 5.43 (ddd, $J = 15.9, 2.3, 1.1$ Hz, 1H), 4.03 (td, $J = 3.9, 2.0$ Hz, 2H), 3.38 – 3.30 (m, 1H), 2.61 – 2.36 (m, 1H), 2.17 (dtd, $J = 8.2, 5.8, 1.2$ Hz, 1H), 1.92 – 1.81 (m, 5H), 1.56 – 1.32 (m, 4H), 1.00 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 146.3,

111.3, 85.0, 79.1, 74.81, 74.79, 74.7, 45.3, 43.2, 39.4, 38.2, 32.3, 15.8, 3.7; IR (film): 3355, 2917, 1440, 1377, 1340, 1108, 1083; HRMS (ESI): m/z calcd for $C_{14}H_{22}O_3Na$ [$M + Na$]: 261.14611; found 261.14613.

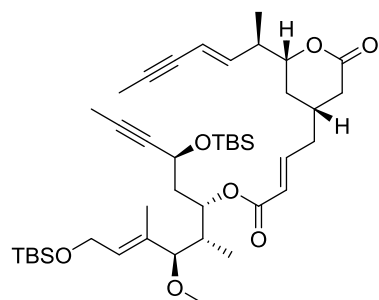
Compound 22. $NaIO_4$ (10% w/w supported on SiO_2 , 4.57 g, 2.39 mmol) was added to a vigorously stirred suspension of triol **21** (200 mg, 0.84 mmol) in CH_2Cl_2 (16 mL). The mixture was stirred at ambient temperature for 20 min before it was filtered through a short plug of SiO_2 , rinsing with *tert*-butyl methyl ether (20 mL). The combined filtrates were evaporated under reduced pressure to yield a mixture of anomers that was used directly in the next step.



PIDA (572 mg, 1.78 mmol) and TEMPO (19 mg, 0.12 mmol) were added to a stirred solution of the crude material in CH_2Cl_2 (12 mL). The yellowish solution was cooled to 0°C before $Yb(OTf)_3$ (37 mg, 0.059 mmol) was introduced. Stirring was continued at ambient temperature for 1 h before the mixture was diluted with CH_2Cl_2 (20 mL) and aq. sat. $Na_2S_2O_3$ (30 mL). The aqueous layer was extracted with EtOAc (2 x 20 mL), the

combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/EtOAc, 6:4) to yield the title compound as a white solid (112 mg, 57% over two steps). 1H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 5.93 (ddd, $J = 15.9, 8.2, 0.8$ Hz, 1H), 5.52 (ddd, $J = 15.9, 2.3, 1.1$ Hz, 1H), 4.16 (ddd, $J = 11.8, 6.3, 2.9$ Hz, 1H), 2.77 (ddd, $J = 17.6, 5.8, 1.9$ Hz, 1H), 2.60 – 2.40 (m, 4H), 2.10 (dd, $J = 17.5, 10.3$ Hz, 1H), 2.03 – 1.95 (m, 1H), 1.93 (dd, $J = 2.3, 0.6$ Hz, 3H), 1.32 – 1.14 (m, 1H), 1.11 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7, 170.2, 141.9, 112.2, 86.1, 83.0, 77.9, 49.9, 42.3, 36.0, 32.0, 26.0, 15.6, 4.3; IR (film): 2964, 2917, 2852, 2732, 170, 1678, 1441, 1382, 1234, 1078, 1005; HRMS (ESI): m/z calcd for $C_{14}H_{18}O_3Na$ [$M + Na$]: 257.11481; found 257.11492.

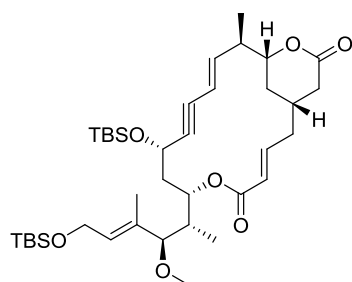
Compound 23. DBU (19 μ L, 0.13 mmol) was added to a stirred suspension of phosphonate **12** (78 mg, 0.12 mmol) and lithium chloride (13 mg, 0.29 mmol) in acetonitrile (8 mL). After stirring for 30 min, the mixture was cooled to 0°C and a solution of aldehyde **22** (55 mg, 0.24 mmol) in acetonitrile (3 mL) was slowly added. After stirring for another 30 min, the reaction was quenched by addition of pH 7 buffer (10 mL), the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 20 mL), the combined



organic fractions were dried over $MgSO_4$ and concentrated under reduced pressure, and the residue was purified by flash chromatography (hexane/EtOAc, 6:1) to afford title compound as a white foam (75 mg, 86%). $[\alpha]_D^{20} = +3.2$ ($c = 0.4, CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, $J = 15.2, 7.5$ Hz, 1H), 5.94 (dd, $J = 15.8, 8.0$ Hz, 1H), 5.85 (d, $J = 15.6$ Hz, 1H), 5.62 – 5.45 (m, 2H), 4.92 (ddd, $J = 10.6, 4.2, 2.3$ Hz, 1H), 4.42 –

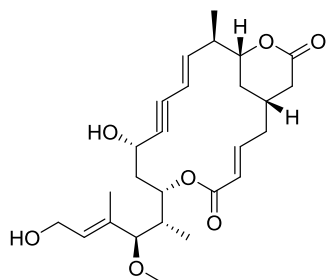
4.24 (m, 2H), 4.23 – 4.03 (m, 2H), 3.17 (s, 3H), 3.16 (d, $J = 6$ Hz, 1H), 2.68 (dd, $J = 11.7, 1.9$ Hz, 1H), 2.49 (q, $J = 7.1$ Hz, 1H), 2.21 (t, $J = 6.7$ Hz, 2H), 2.17 – 2.04 (m, 4H), 1.94 – 1.78 (m, 2H), 1.93 (d, $J = 2.1$ Hz, 3H), 1.80 (d, $J = 2.1$ Hz, 3H), 1.63 (s, 3H), 1.41 – 1.34 (m, 1H), 1.11 (d, $J = 6.8$ Hz, 3H), 0.93 (d, $J = 6.8$ Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.07 (s, 9H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.3, 165.2, 144.2, 141.8, 133.3, 129.6, 124.4, 112.1, 88.1, 82.9, 81.1, 80.1, 71.9, 59.9, 59.3, 56.3, 42.1, 38.6, 38.2, 38.1, 36.0, 31.8, 31.0, 27.0, 26.0, 25.8, 18.4, 18.1, 15.4, 14.2, 11.5, 10.0, 4.2, 3.5, -4.5 , -5.1 , -5.3 (2 C); IR (film): 2956, 2928, 2856, 1737, 1718, 1665, 1463, 1375, 1247, 1201, 1088, 1045, 1005; HRMS (ESI): m/z calcd for $\text{C}_{42}\text{H}_{70}\text{O}_7\text{Si}_2\text{Na}$ [$\text{M} + \text{Na}$]: 765.45523, found 765.45570.

Compound 24. A solution of complex **30** (4 mg, 6.25 μmol) and CH_2Cl_2 (0.1 mL, 0.4 mmol) in toluene (2



mL) was stirred for 5 min before it was added to a solution of diyne **23** (60 mg, 0.081 mmol) in degassed toluene (60 mL, water content of 4 ppm) at 80°C. Stirring was continued at this temperature for 3 h before the reaction was quenched with EtOH (5 mL). The mixture was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 4:1 \rightarrow 1:1) to yield the

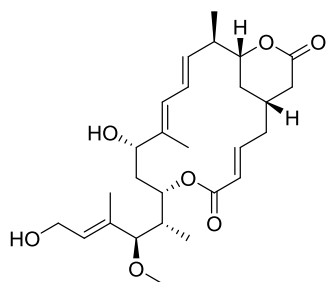
title compound as a white solid (38 mg, 67%). $[\alpha]_D^{20} = +39.4$ ($c = 0.8$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.76 (ddd, $J = 15.7, 10.7, 5.1$ Hz, 1H), 5.84 (d, $J = 16.5$ Hz, 1H), 5.73 (dd, $J = 16.1, 8.5$ Hz, 1H), 5.55 (dd, $J = 16.2, 1.7$ Hz, 1H), 5.46 (t, $J = 5.2$ Hz, 1H), 4.73 (dd, $J = 9.3, 3.6$ Hz, 1H), 4.41 – 4.29 (m, 2H), 4.21 (ddd, $J = 13.3, 5.2, 1.2$ Hz, 1H), 3.89 (ddd, $J = 11.2, 7.8, 3.6$ Hz, 1H), 3.17 (s, 3H), 3.17 (d, $J = 8.3$ Hz, 1H), 2.72 (ddd, $J = 17.3, 5.1, 1.8$ Hz, 1H), 2.55 – 2.36 (m, 2H), 2.24 – 2.03 (m, 3H), 2.01 – 1.92 (m, 2H), 1.89 – 1.77 (m, 2H), 1.67 (s, 3H), 1.15 (d, $J = 6.7$ Hz, 3H), 0.96 (d, $J = 6.8$ Hz, 3H), 0.90 (s, 9H), 0.90 (s, 9H), 0.90 – 0.81 (m, 1H), 0.12 (s, 3H), 0.12 (s, 3H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.9, 165.8, 144.5, 143.4, 134.6, 129.9, 126.3, 112.8, 90.8, 88.8, 82.4, 82.2, 73.1, 63.3, 59.9, 56.4, 43.8, 39.2, 38.3, 38.2, 36.7, 31.6, 29.3, 26.1, 25.9, 18.5, 18.3, 15.7, 11.3, 10.0, -4.2 , -4.7 , -4.98 , -5.0 ; IR (film): 2954, 2929, 2856, 1741, 1714, 1653, 1462, 1348, 1250, 1167, 1105, 1050, 1002, 961; HRMS (ESI): m/z calcd for $\text{C}_{38}\text{H}_{64}\text{O}_7\text{Si}_2\text{Na}$ [$\text{M} + \text{Na}$]: 711.40828, found 711.40842.



Compound 26. A solution of TBAF in THF (1 M, 160 μl , 0.16 mmol) was added dropwise at -50°C to a stirred solution of compound **24** (40 mg, 58 μmol) in THF (10 mL). Stirring was continued for 2 h while the mixture was allowed to reach -10°C . After stirring for another 1 h at this temperature, the reaction was quenched with water (5 mL) and the mixture was warmed

to ambient temperature. The aqueous layer was extracted with EtOAc (3 x 15 mL), the combined organic fractions were dried over MgSO₄ and concentrated, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc, 2:1 → EtOAc/MeOH, 95:5) to yield the title compound as a white solid (24 mg, 90 %). $[\alpha]_D^{20} = +76.2$ (c = 0.7, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.77 (ddd, *J* = 15.7, 10.7, 5.1 Hz, 1H), 5.85 (d, *J* = 16.5 Hz, 1H), 5.77 (dd, *J* = 16.0, 8.8 Hz, 1H), 5.64 – 5.45 (m, 2H), 4.74 (dd, *J* = 9.2, 3.6 Hz, 1H), 4.38 (ddd, *J* = 10.9, 3.6, 2.5 Hz, 1H), 4.27 (d, *J* = 6.7 Hz, 2H), 3.87 (ddd, *J* = 11.2, 7.9, 3.4 Hz, 1H), 3.18 (d, *J* = 8.9 Hz, 1H), 3.16 (s, 3H), 2.73 (ddd, *J* = 17.4, 5.2, 2.0 Hz, 1H), 2.60 – 2.32 (m, 2H), 2.26 – 1.79 (m, 9H), 1.72 (d, *J* = 1.3 Hz, 3H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H) 0.95 – 0.81 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 170.8, 165.8, 144.9, 144.6, 137.0, 128.8, 126.1, 112.3, 90.0, 89.2, 83.0, 82.2, 73.0, 62.5, 59.0, 56.4, 43.9, 39.2, 38.3, 37.3, 36.7, 31.9, 29.4, 15.8, 11.2, 10.3; IR (film): 3400, 2965, 2933, 1720, 1654, 1431, 1370, 1251, 1169, 1093, 1045, 999; HRMS (ESI): *m/z* calcd for C₂₆H₃₆O₇Na [M + Na]: 483.23532; found 483.23545.

Compound 28. A solution of [Cp**Ru*Cl]₄ (0.6 mg; 0.5 μmol) in 1,2-dichloroethane (60 μL) was added to a stirred solution of enyne **26** (19 mg, 41 μmol) in 1,2-dichloroethane (3 mL) at ambient temperature, causing an immediate color change to deep purple. After 5 min, a solution of Bu₃SnH (12 μL, 45 μmol) in 1,2-dichloroethane (1 mL) was added dropwise over a period of 20 min. Once the addition was complete, all volatile materials were evaporated under reduced pressure.

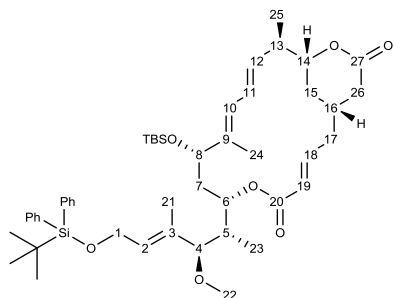


[(cod)Pd(Me)(Cl)] (33 mg, 124 μmol) was added in one portion to a solution of the crude alkenylstannane thus formed (31.7 mg, 41 μmol) in THF (5 mL) and the resulting mixture was stirred at ambient temperature for 2 h. The mixture was adsorbed on silica and put on top of a flash column filled with silica gel. Elution of the product with hexane/EtOAc (2:1 → 0/1) afforded the title compound as a white solid (11 mg, 56% over two steps).

Alternatively, a solution of [Ph₂PO₂][NBu₄] (fused under vacuum prior to use; 1.1 mg, 2.4 μmol) in DMSO was added to a stirred solution of the crude alkenylstannane (1.7 mg, 2.2 μmol) in DMSO (0.9 mL). A solution of MeI (0.4 μL, 6.6 μmol) in DMSO (20 μL) was added in one portion, followed – *within 15 seconds* – by addition of a suspension of CuTC (0.5 mg, 2.3 μmol) in DMSO (20 μL). The resulting mixture was stirred at ambient temperature for 3 h before it was diluted with *tert*-butyl methyl ether (0.5 mL). Adsorption on silica followed by purification as described above gave the title compound as a white solid (0.7 mg, 70%). ¹H NMR (400 MHz, CDCl₃) δ 6.74 (ddd, *J* = 15.7, 10.9, 4.7 Hz, 1H), 6.24 (dd, *J* = 15.2, 11.0

Hz, 1H), 5.84 (d, $J = 10.1$ Hz, 1H), 5.67 – 5.58 (m, 2H), 5.19 (dd, $J = 15.2, 9.7$ Hz, 1H), 4.60 (dd, $J = 10.5, 3.1$ Hz, 1H), 4.28 (d, $J = 3.8$ Hz, 2H), 3.97 (dd, $J = 10.9, 2.9$ Hz, 1H), 3.69 (ddd, $J = 12.1, 9.6, 2.7$ Hz, 1H), 3.20 (d, $J = 8.6$ Hz, 1H), 3.18 (s, 3H), 2.76 (ddd, $J = 18.0, 5.3, 2.3$ Hz, 1H), 2.53 (ddd, $J = 8.5, 4.9, 1.8$ Hz, 1H), 2.33 – 2.07 (m, 5H), 1.99 – 1.92 (m, 1H), 1.79 (s, 3H), 1.74 (s, 3H), 1.72 – 1.56 (m, 2H), 1.21 (d, $J = 6.4$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H), 0.68 (dt, $J = 14.3, 11.8$ Hz, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.0, 165.0, 143.8, 138.4, 136.8, 133.7, 128.8, 127.7, 126.6, 126.3, 89.1, 81.3, 78.5, 73.4, 59.1, 56.4, 39.1, 38.3, 37.9, 34.3, 32.8, 27.7, 25.1, 13.8, 11.4, 11.2, 10.4; IR (film): 3395, 2963, 2925, 2855, 1716, 1653, 1446, 1367, 1257, 1170, 1093, 1045, 999; HRMS (ESI): m/z calcd for $\text{C}_{27}\text{H}_{40}\text{O}_7\text{Na}$ [$\text{M} + \text{Na}$]: 499.26662; found 499.26685.

Compound 29. A solution of TBDPSCI (10.5 mg, 40.8 μmol) in CH_2Cl_2 (1 mL) was added at -60°C to a stirred solution of diol **28** (6.5 mg, 13.6 μmol) and imidazole (4.7 mg, 68.2 μmol) in CH_2Cl_2 (2 mL). After stirring for 5 h at this temperature, the solvent was evaporated and the residue purified by flash chromatography on silica gel (hexane/EtOAc, 3:1).



The resulting monoprotected compound was dissolved in CH_2Cl_2 (0.5 mL). Imidazole (9.3 mg, 136 μmol), DMAP (one crystal) and TBSCl (10.2 mg, 68 μmol) were successively added and the suspension was stirred overnight. After evaporation of the solvents, the residue was purified by flash chromatography on silica gel (pentane/EtOAc, 6:1 \rightarrow 4:1) to yield the title compound as a colorless oil (8 mg, 71% over two steps). $[\alpha]_D^{20} = -4.8$ ($c = 0.24$, CHCl_3), $[\alpha]_D^{20}$ (ref. 5) = -11.0 ($c = 1.3$, CHCl_3);

^1H NMR (400 MHz, CDCl_3) δ 7.87 – 7.60 (m, 4H), 7.51 – 7.32 (m, 6H), 6.72 (ddd, $J = 15.6, 11.0, 4.7$ Hz, 1H), 6.22 (dd, $J = 15.2, 11.0$ Hz, 1H), 5.68 (d, $J = 10.8$ Hz, 1H), 5.61 (t, $J = 5.9$ Hz, 1H), 5.59 (d, $J = 16.7$ Hz, 1H), 5.05 (dd, $J = 15.2, 9.6$ Hz, 1H), 4.51 (dd, $J = 10.5, 3.2$ Hz, 1H), 4.37 (dd, $J = 13.1, 7.0$ Hz, 1H), 4.26 (ddd, $J = 13.0, 5.0, 1.2$ Hz, 1H), 3.88 (dd, $J = 10.7, 3.2$ Hz, 1H), 3.68 (ddd, $J = 12.1, 9.9, 2.7$ Hz, 1H), 3.17 (d, $J = 9.1$ Hz, 1H), 3.15 (s, 3H), 2.76 (ddd, $J = 18.0, 5.2, 1.9$ Hz, 1H), 2.57 – 2.49 (m, 1H), 2.30 – 1.93 (m, 5H), 1.73 (d, $J = 1.3$ Hz, 3H), 1.86 – 1.70 (m, 2H), 1.67 – 1.60 (m, 1H), 1.54 (s, 3H), 1.20 (d, $J = 6.5$ Hz, 3H), 1.05 (s, 9H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.87 (s, 9H), 0.67 (dt, $J = 14.2, 12.3$ Hz, 1H), 0.05 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.6, 165.7, 145.9, 140.3, 135.7, 135.2, 134.0, 133.4, 130.2, 129.8, 129.4, 127.9, 127.8, 124.8, 124.6, 89.3, 83.6, 79.1, 74.4, 60.8, 56.1, 45.5, 38.4, 38.4, 37.1, 34.8, 34.3, 29.9, 27.0, 25.9, 19.4, 18.2, 16.8, 11.2, 11.1, 10.0, -4.4 , -4.7 ; HRMS (ESI): m/z calcd for $\text{C}_{49}\text{H}_{72}\text{O}_7\text{Si}_2\text{Na}$ [$\text{M} + \text{Na}$]: 851.47088; found 851.47086.

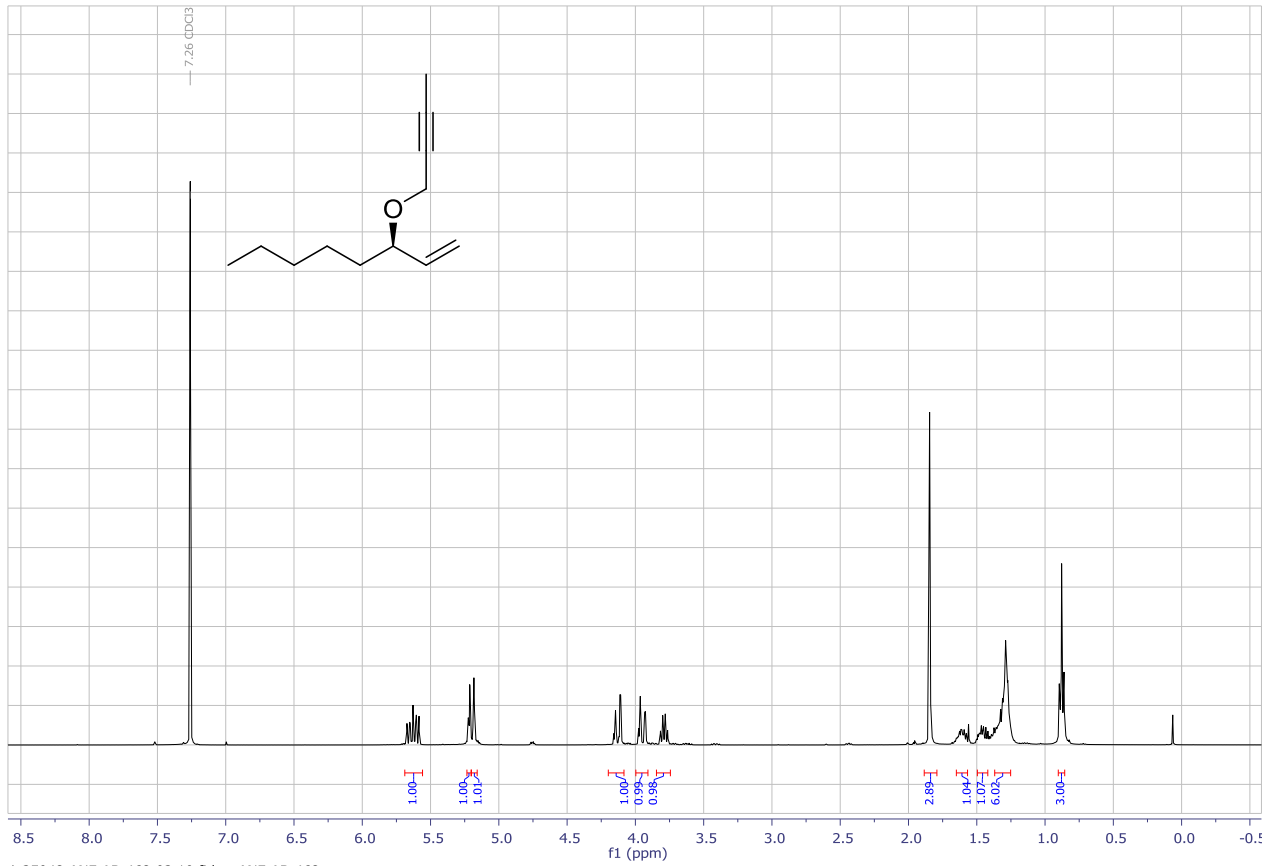
Table S1. Comparison of the ^1H NMR data of Compound **29** in CDCl_3 with those Reported in the Literature; Arbitrary Numbering Scheme as Shown in the Insert

position	δ (ppm) literature ⁵	δ (ppm) synthetic	$\Delta\delta$	J (Hz) literature ⁵	J (Hz) synthetic
1a	4.37	4.37	0.00	7.2/12.9	7.9/13.1
1b	4.27	4.26	0.01	12.9/4.8/br. s	13.0/5.0/1.2
2	5.62	5.61	0.01	5.7	5.6
3					
4	3.18	3.17	0.01	9.2	9.1
5	m	m	0.00		
6	4.52	4.51	0.00	3.0/10.5	3.2/10.5
7a	m	m	0.00		
7b	m	m	0.00		
8	3.87	3.88	-0.01	3.1/10.7	3.0/10.7
9					
10	5.69	5.68	0.01	1.0/11.0	br./10.8
11	6.23	6.22	0.01	11.0/15.2	11.0/15.2
12	5.06	5.05	0.01	9.7/15.2	9.6/15.2
13	m	m			
14	3.69	3.68	0.01	2.6/9.8/12.1 12.1/12.1/14.3	2.7/9.9/12.1 12.3/14.2
15a (ax.)	0.66	0.67	0.01	(ddd)	(app. dt)
15b (eq.)	1.98	m		2.6/14.3	
16	m	m			
17a	2.57 - 2.51	2.55 - 2.49			
17b	m	m			
18	6.73	6.72	0.01	4.7/11.0/15.7	4.7/11.0/15.6
19	5.60	5.59	0.01	15.7	16.7
20					
21	1.74	1.73	0.01	1.0	1.3
22	3.16	3.15	0.01		
23	0.96	0.95	0.01	6.7	6.8
24	1.55	1.54	0.01		
25	1.21	1.20	0.01	6.5	6.5
26a	2.77	2.76	0.01	2.0/5.2/17.8	1.9/5.2/18.0
26b	m	m			

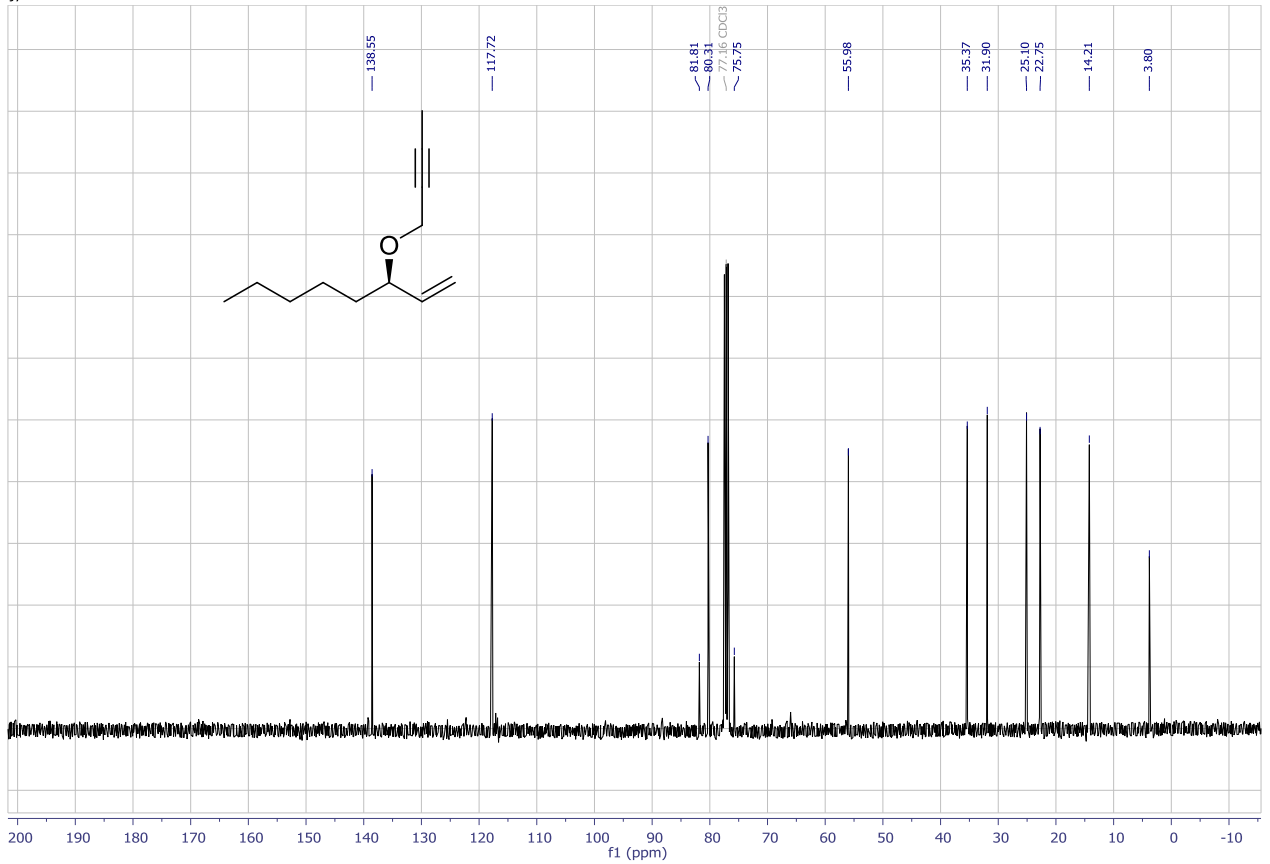
⁵ I. S. Mitchell, G. Pattenden, J. Stonehouse, *Org. Biomol. Chem.*, **2005**, *3*, 4412 - 4431

Table S2. Comparison of the ^{13}C NMR data of Compound **29** in CDCl_3 with those Reported in the Literature; Arbitrary Numbering Scheme as Shown in the Insert

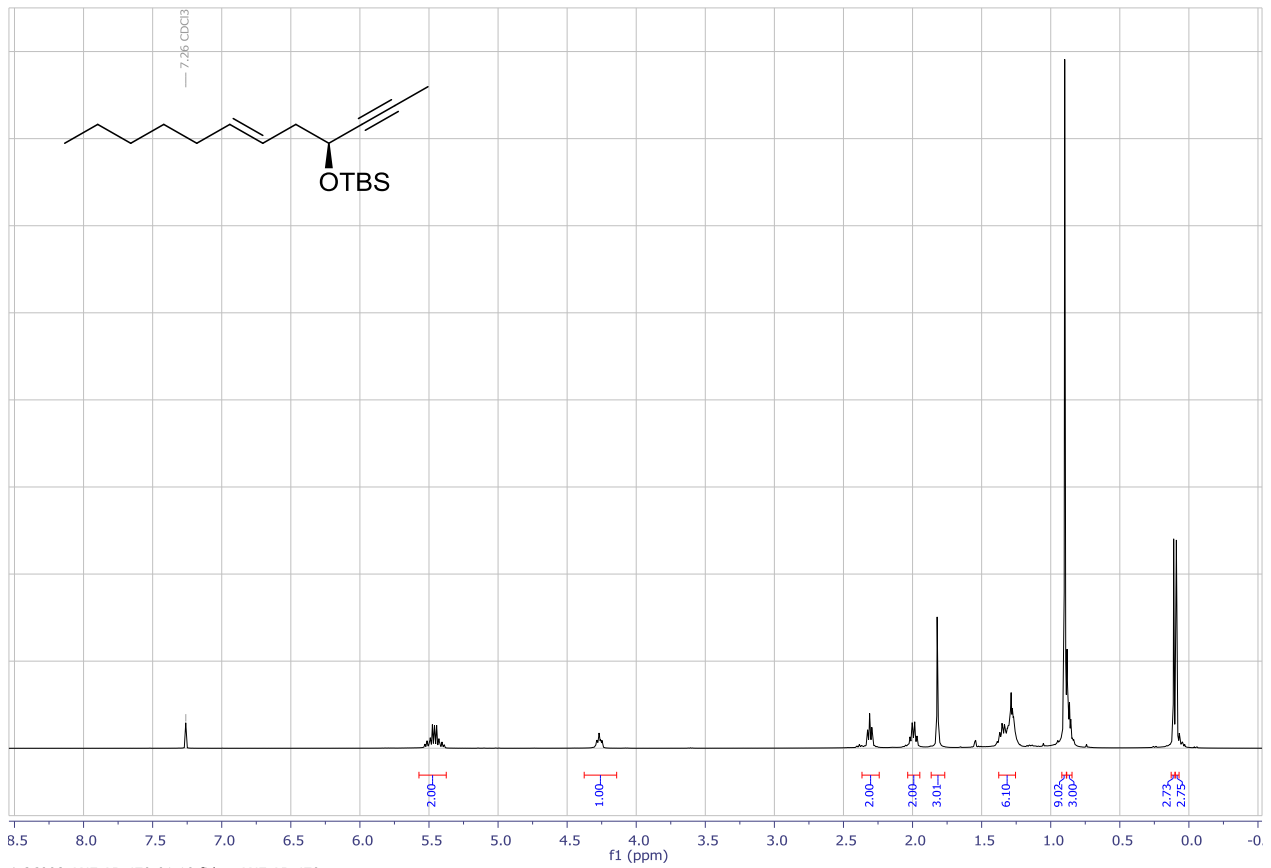
position	δ (ppm) literature⁵	δ (ppm) synthetic	$\Delta\delta$
1	-4.9	-4.7	0.2
2	-4.6	-4.4	0.2
3	9.8	10.0	0.2
4	10.9	11.1	0.2
5	11.0	11.1	0.1
6	16.6	16.8	0.2
7	18.0	18.2	0.2
8	19.2	19.4	0.2
9	25.7	25.9	0.2
10	26.8	27.0	0.2
11	29.8	30.0	0.2
12	34.1	34.3	0.2
13	34.6	34.8	0.2
14	36.9	37.1	0.2
15	38.2	38.4	0.2
16	38.2	38.4	0.2
17	45.3	45.5	0.2
18	56.0	56.1	0.1
19	60.6	60.8	0.2
20	74.2	74.4	0.2
21	78.9	79.1	0.2
22	83.4	83.6	0.2
23	89.2	89.3	0.1
24	124.4	124.6	0.2
25	124.6	124.8	0.2
26	127.6	127.8	0.2
27		127.9	
28	129.3	129.4	0.1
29	129.6	129.8	0.2
30	130.1	130.2	0.1
31	133.2	133.4	0.2
32	133.,7	133.9	0.2
33		134.0	
34	135.0	135.2	0.2
35	135.5	135.7	0.2
36		135.7	
37	140.1	140.3	0.2
38	145.7	145.9	0.2
39	165.5	165.7	0.2
40	170.4	170.6	0.2



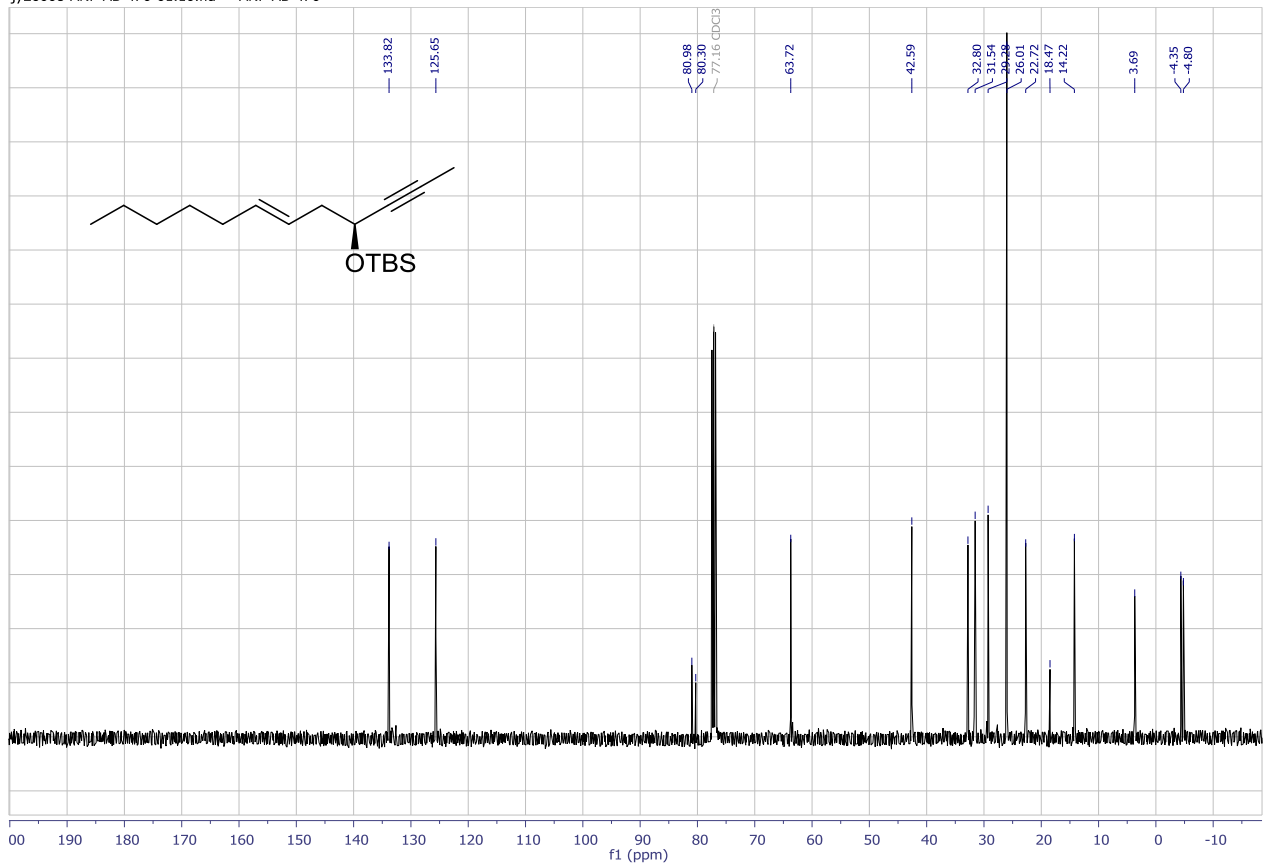
fy25048-ANF-AB-468-02.10.fid — ANF-AB-468



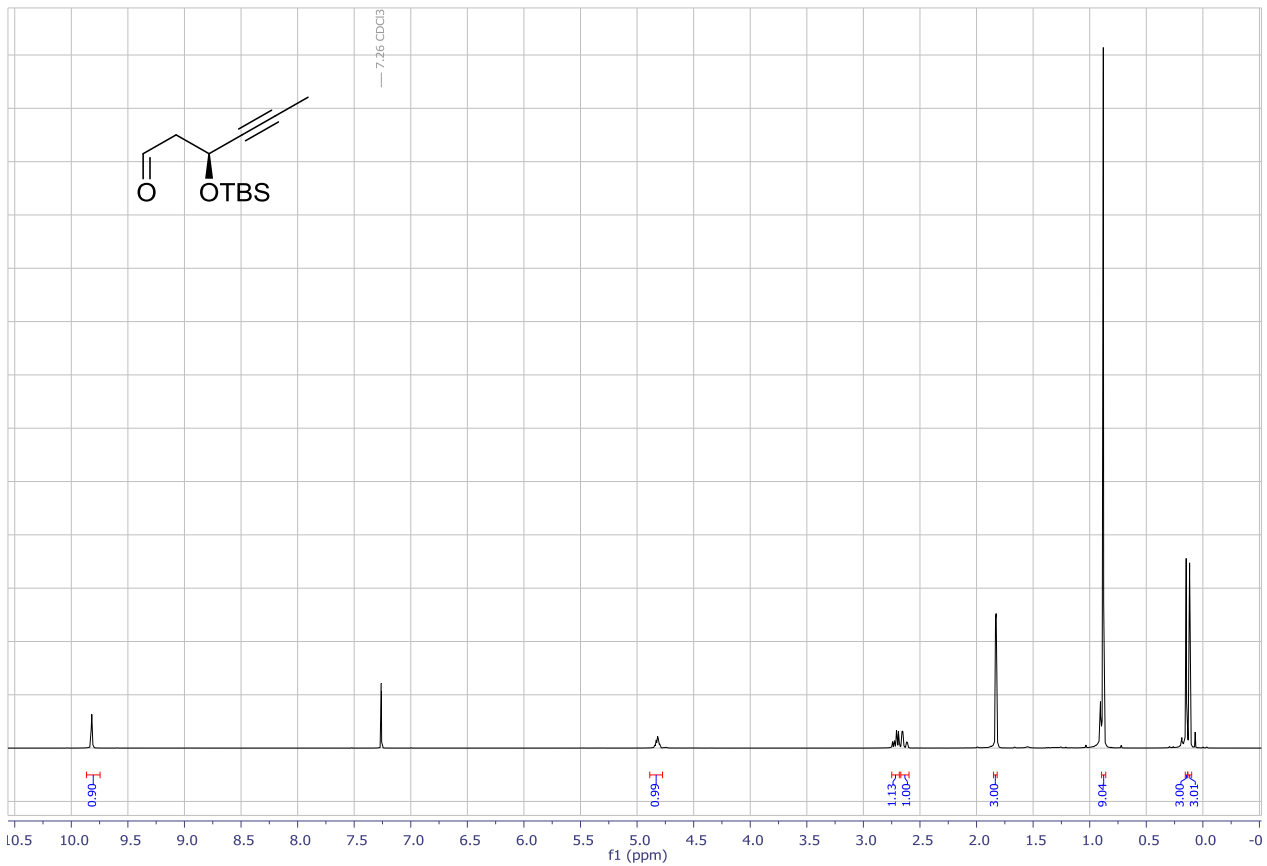
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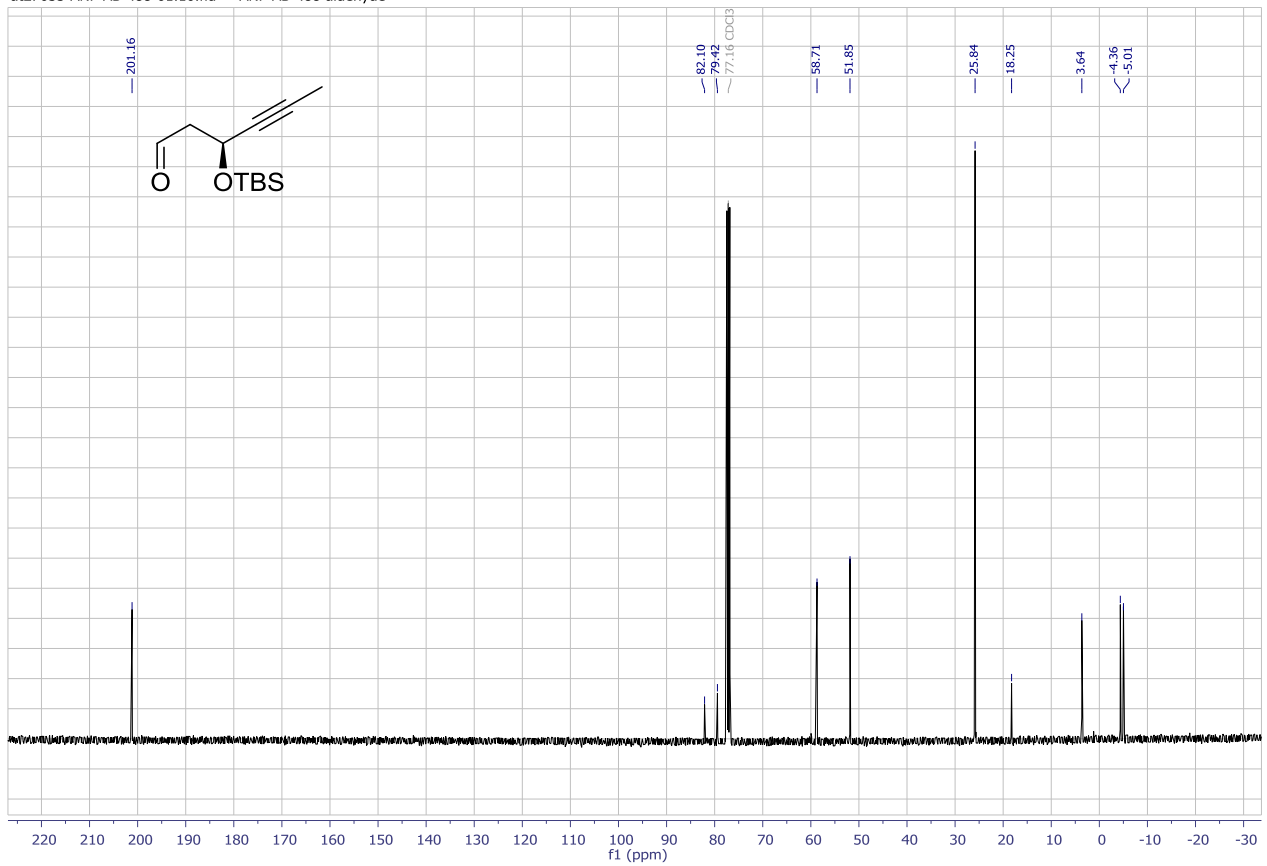
26008-ANF-AB-470-01.10.fid — ANF-AB-470



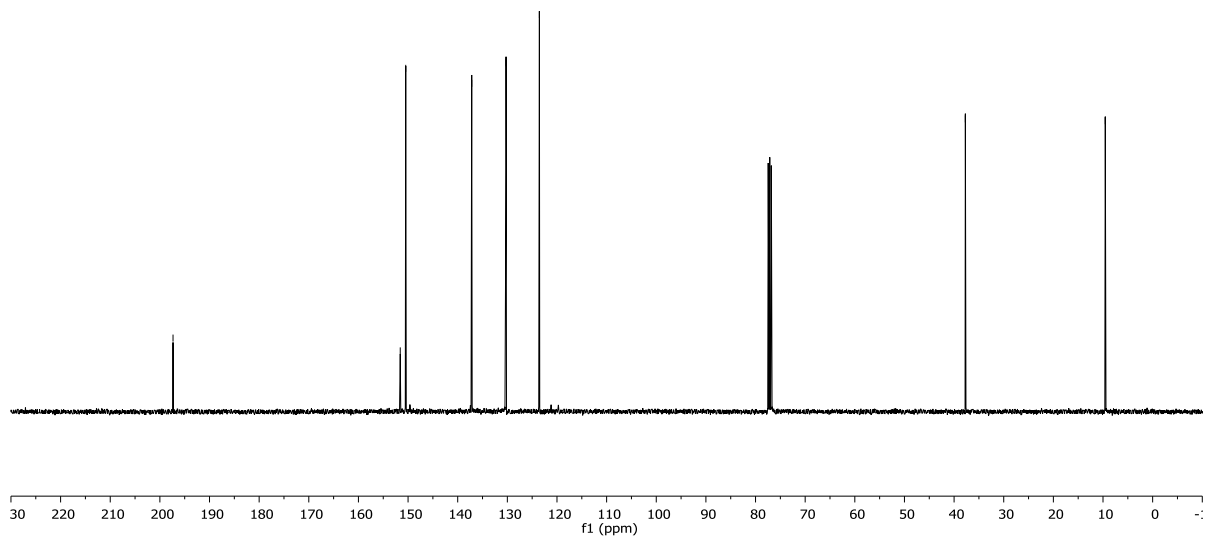
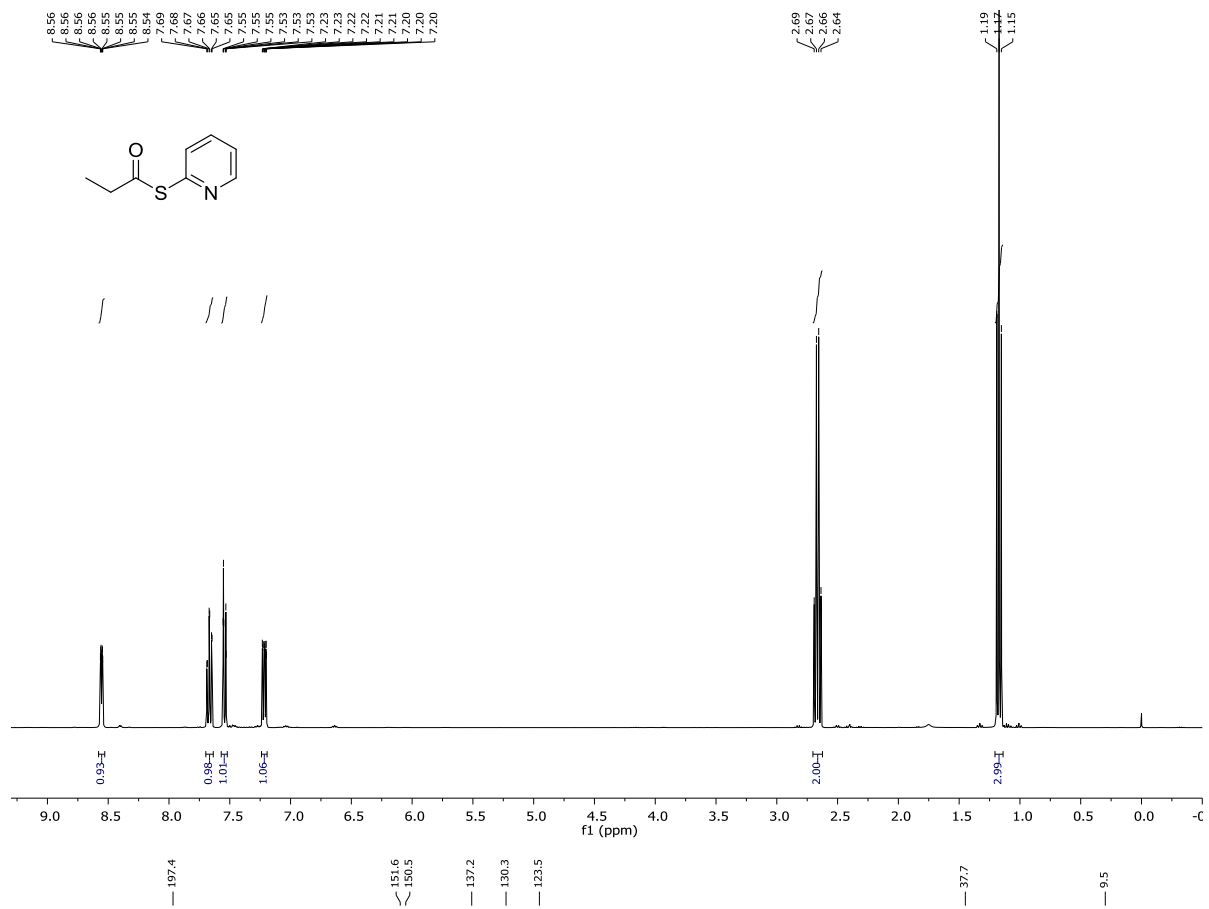
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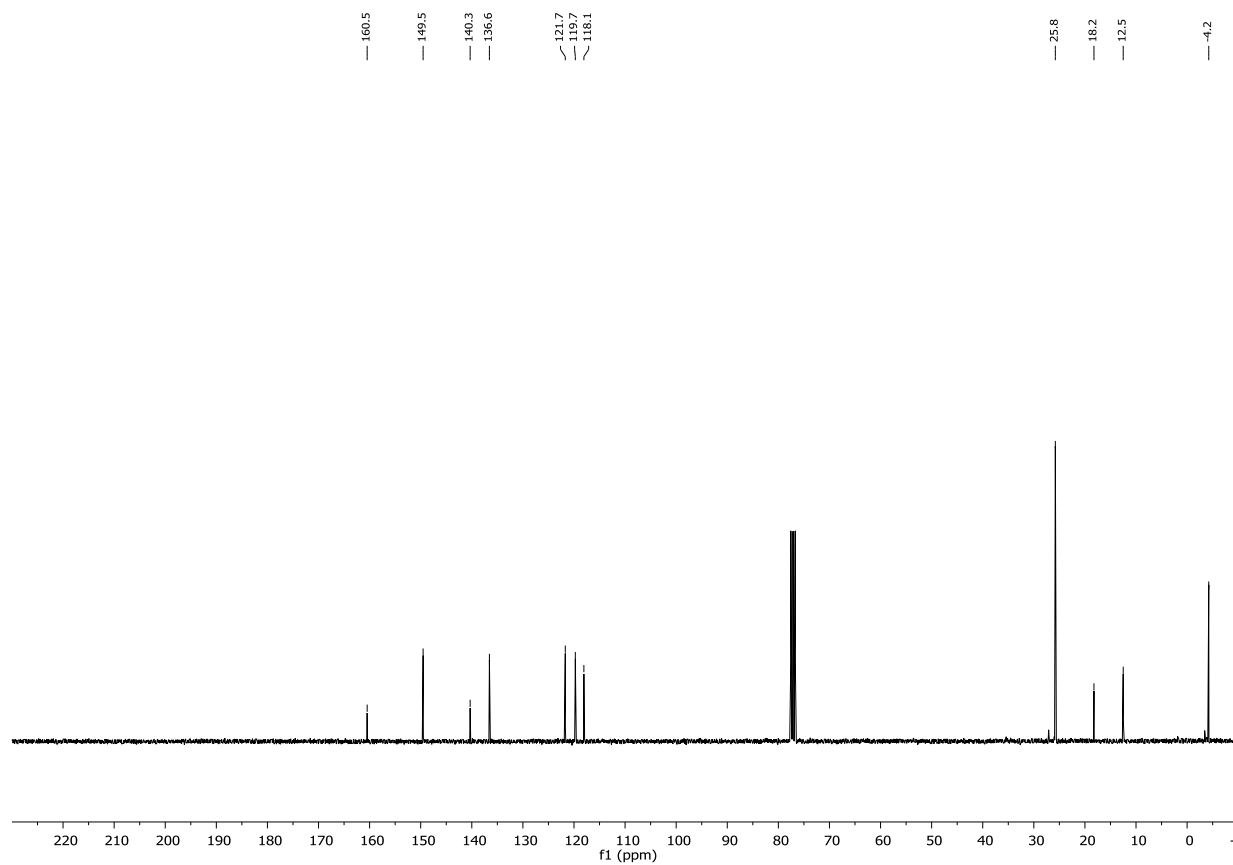
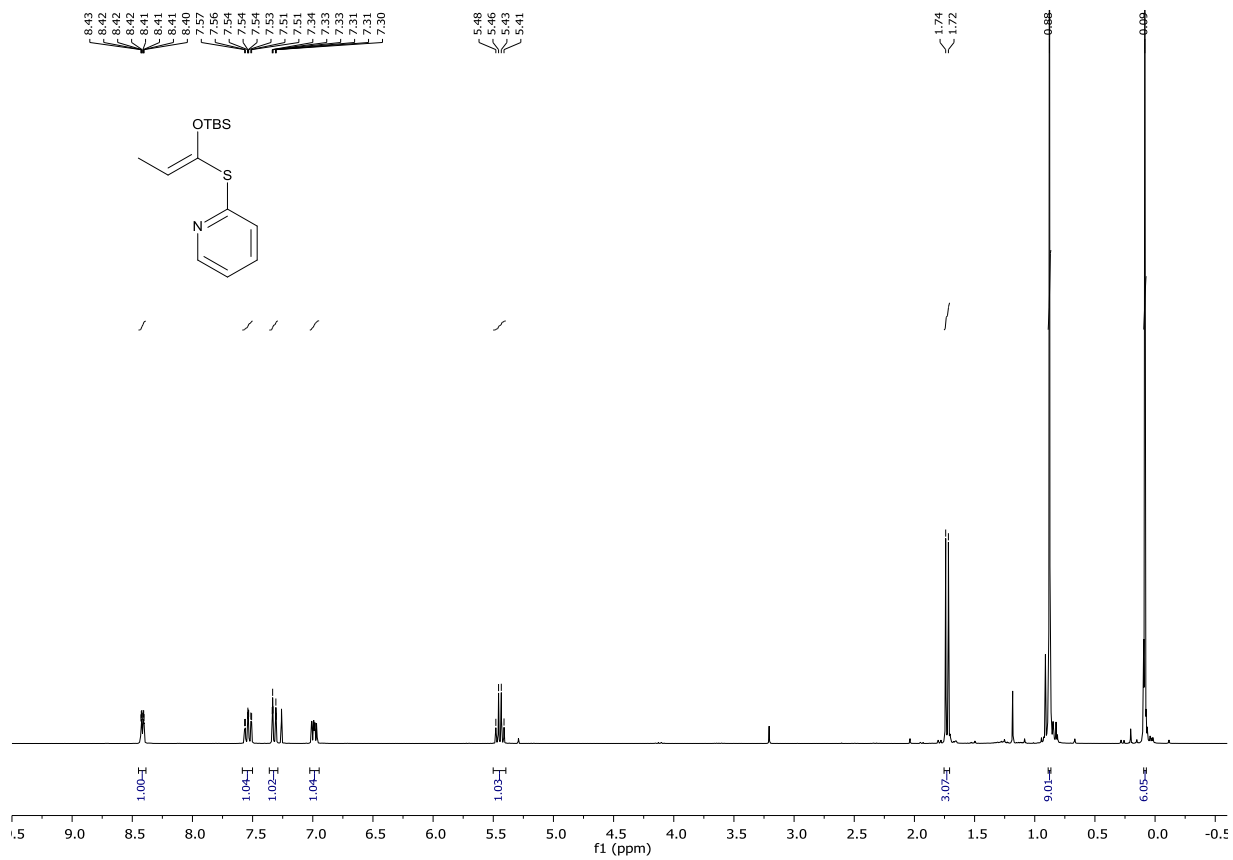


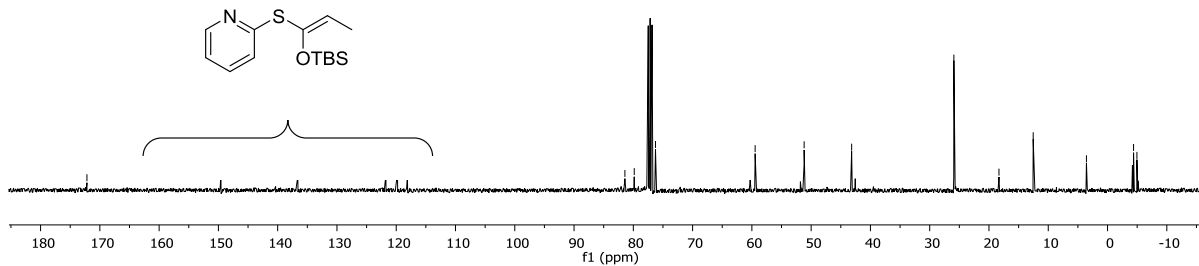
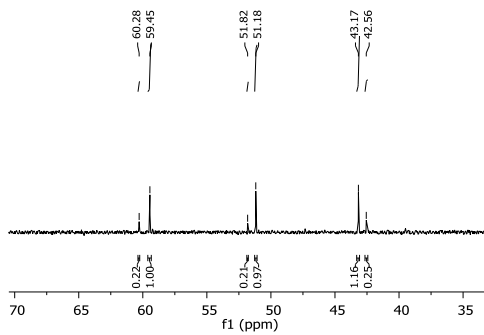
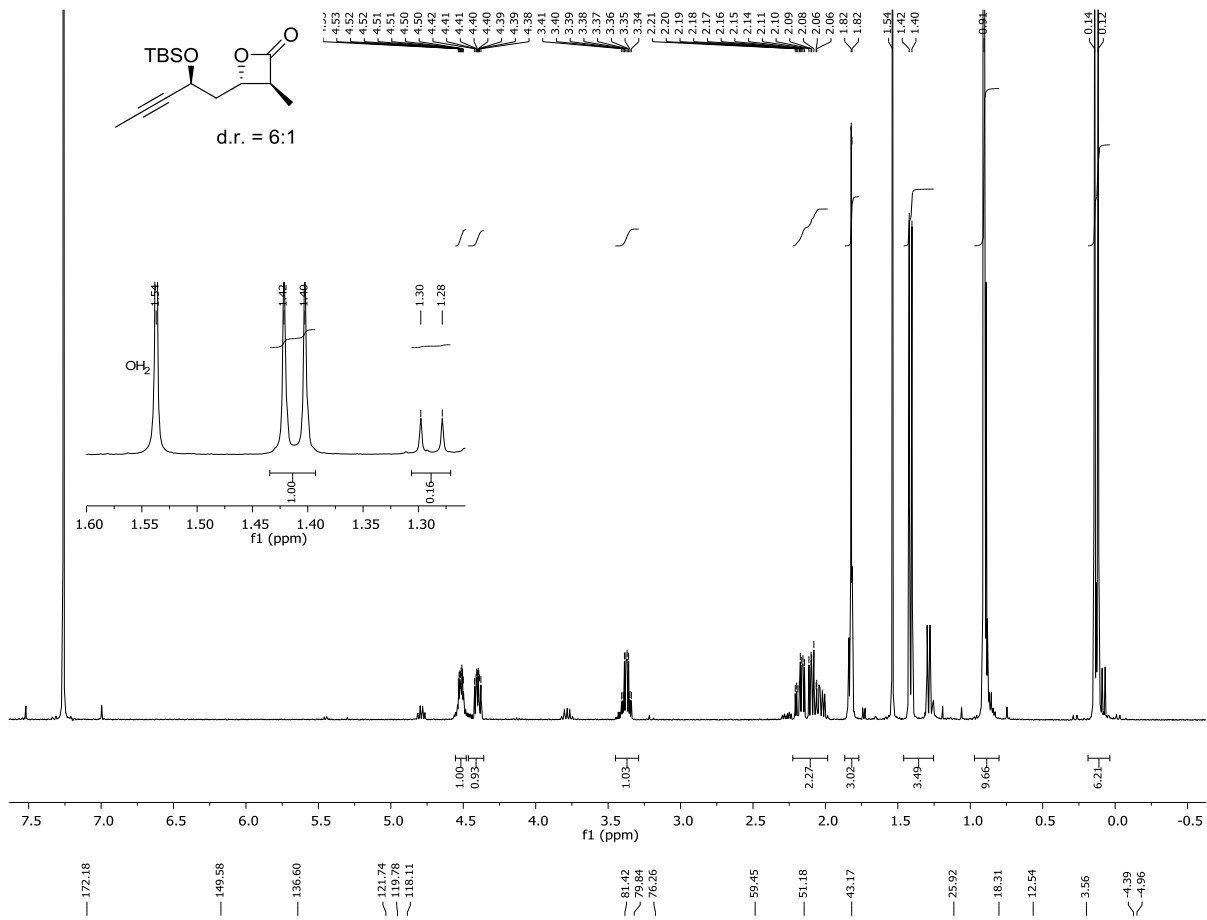
at27055-ANF-AB-488-01.10.fid — ANF-AB-488 aldehyde

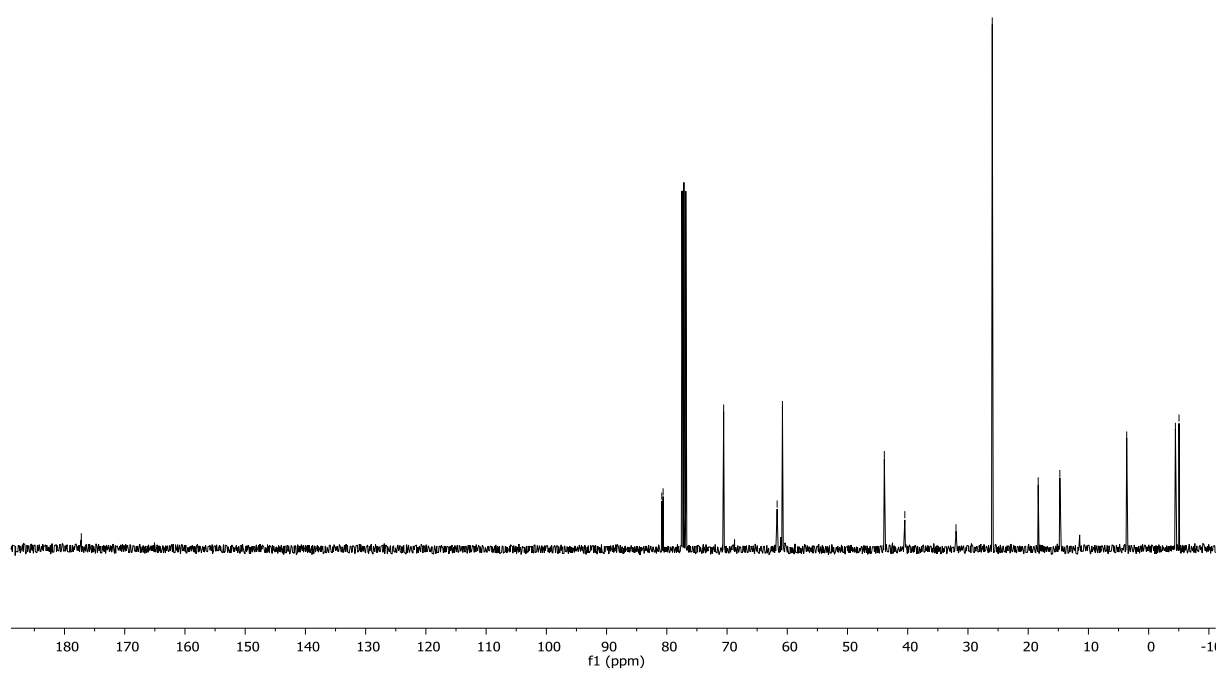
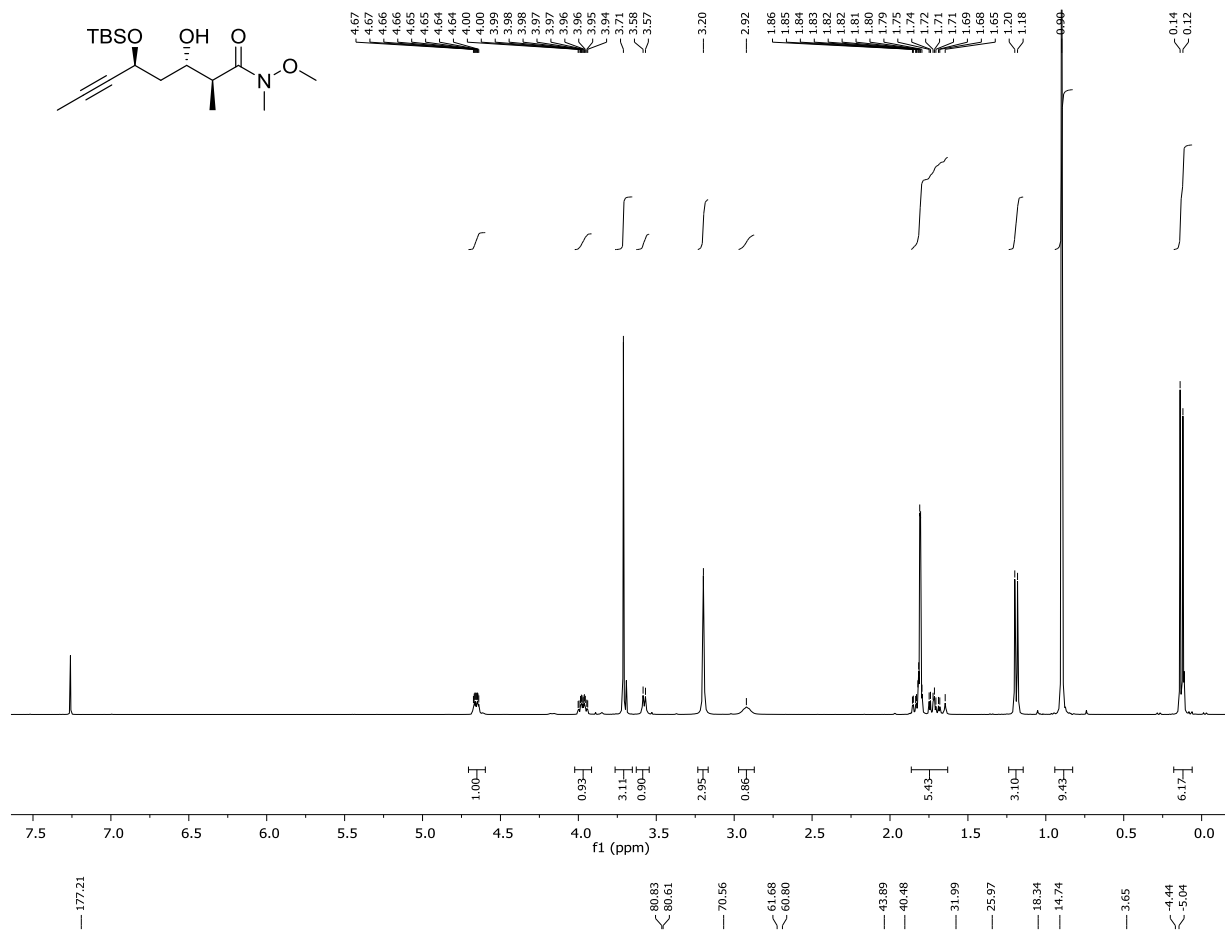


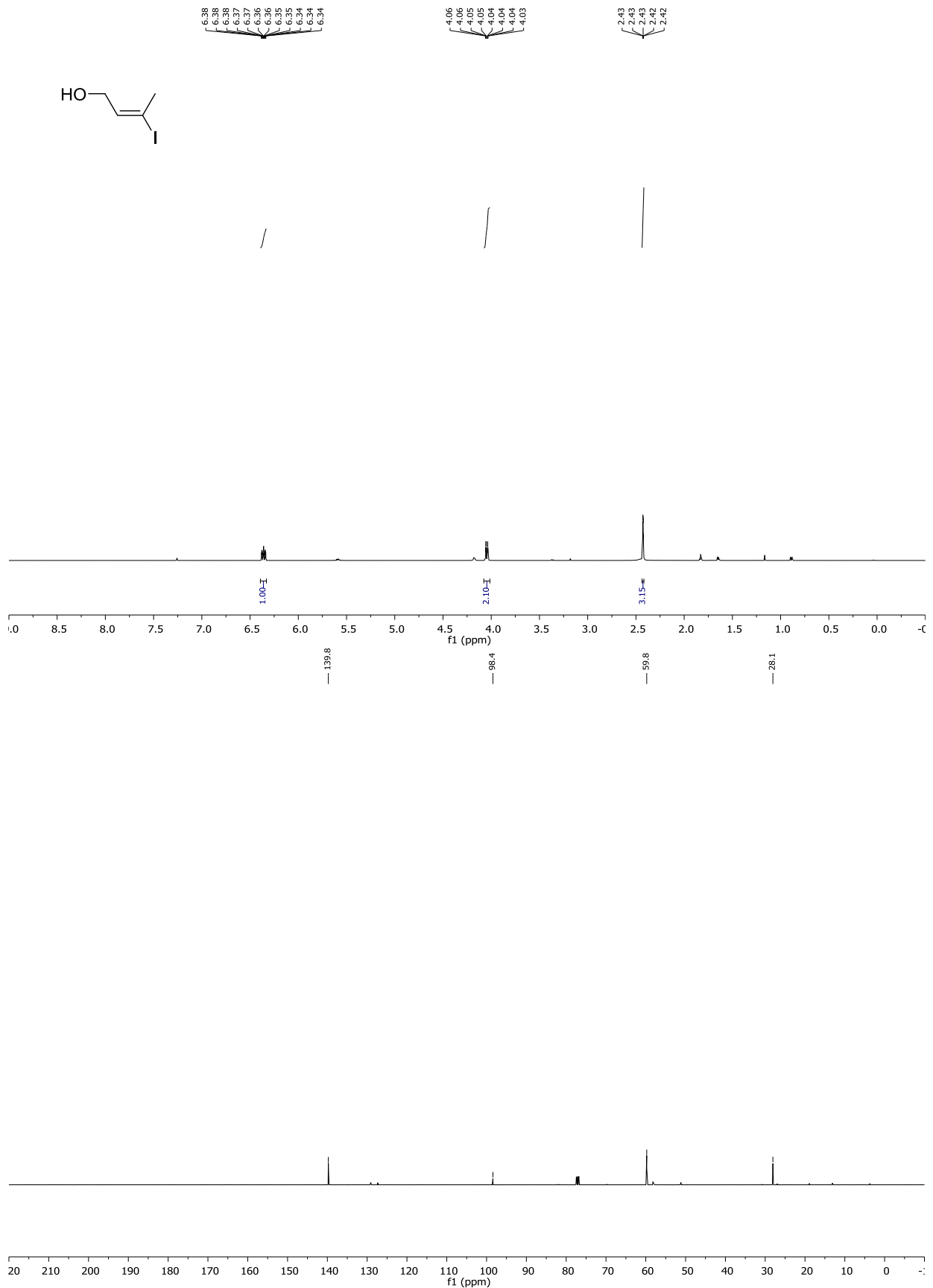
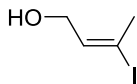
at27055-ANF-AB-488-01.12.fid — ANF-AB-488 aldehyde

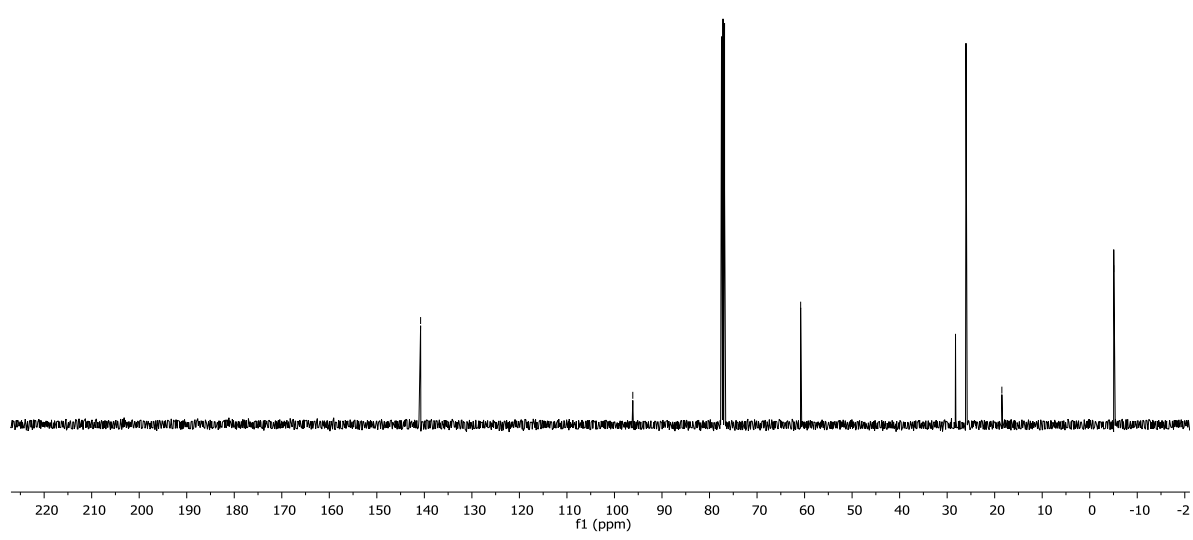
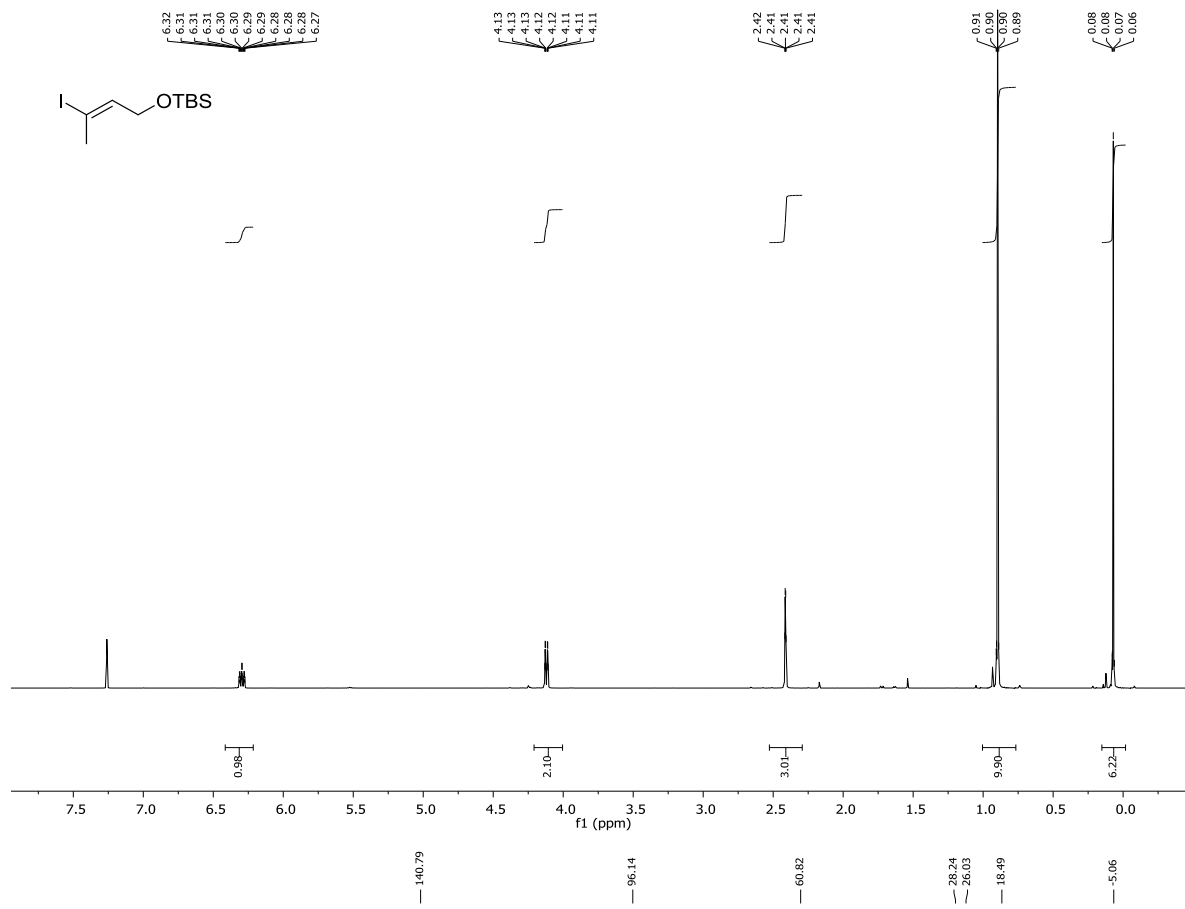


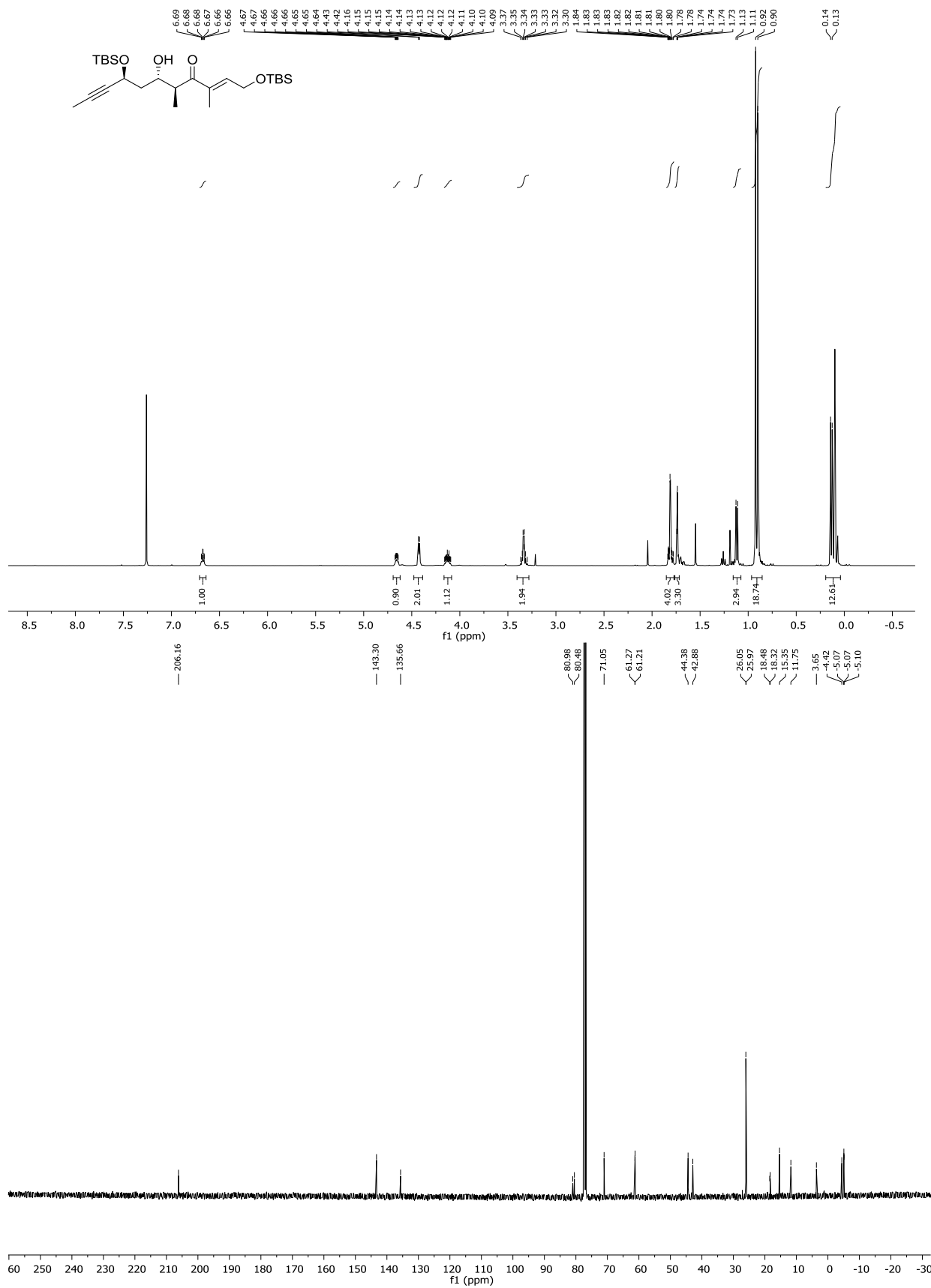


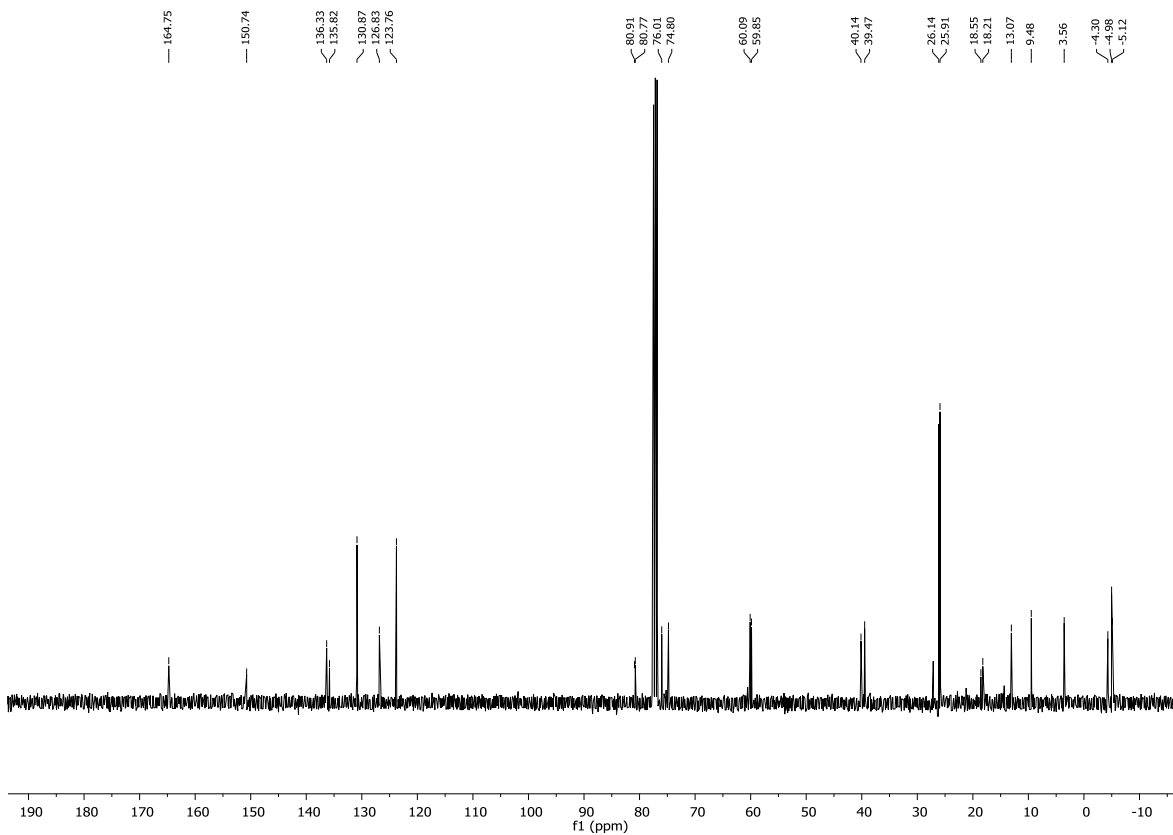
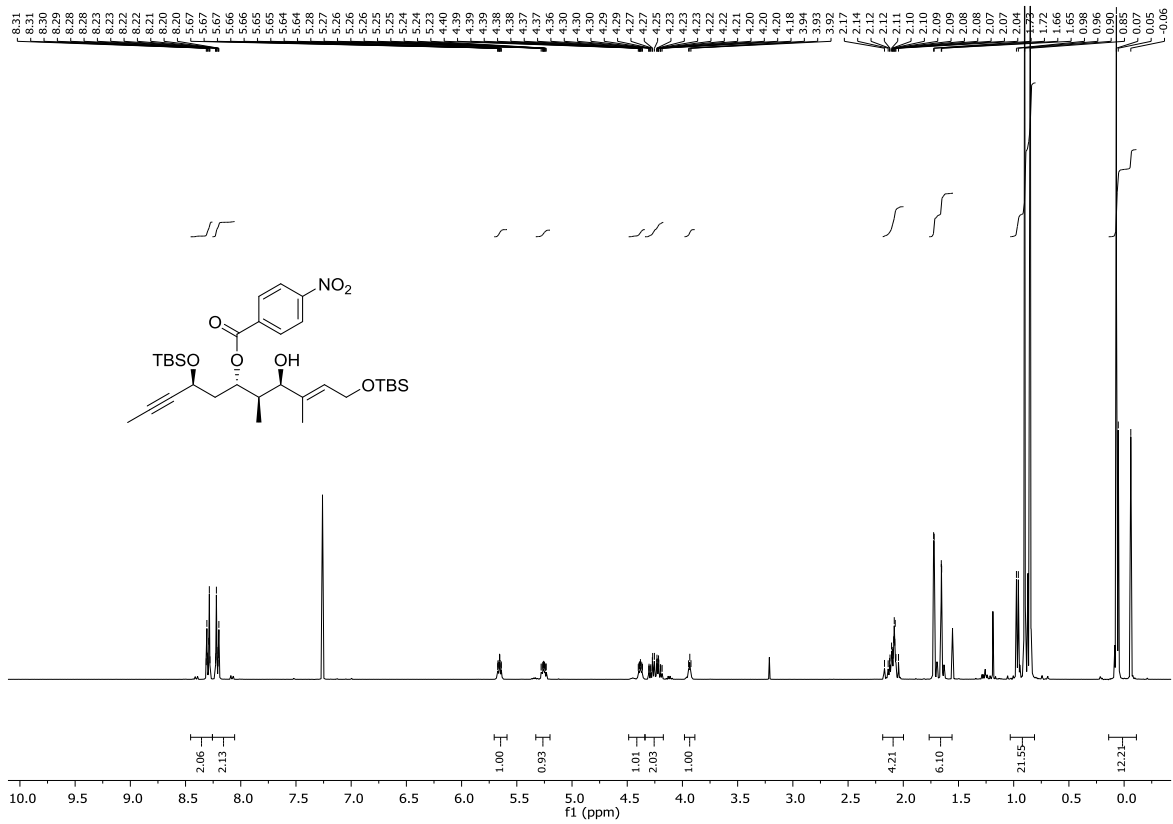


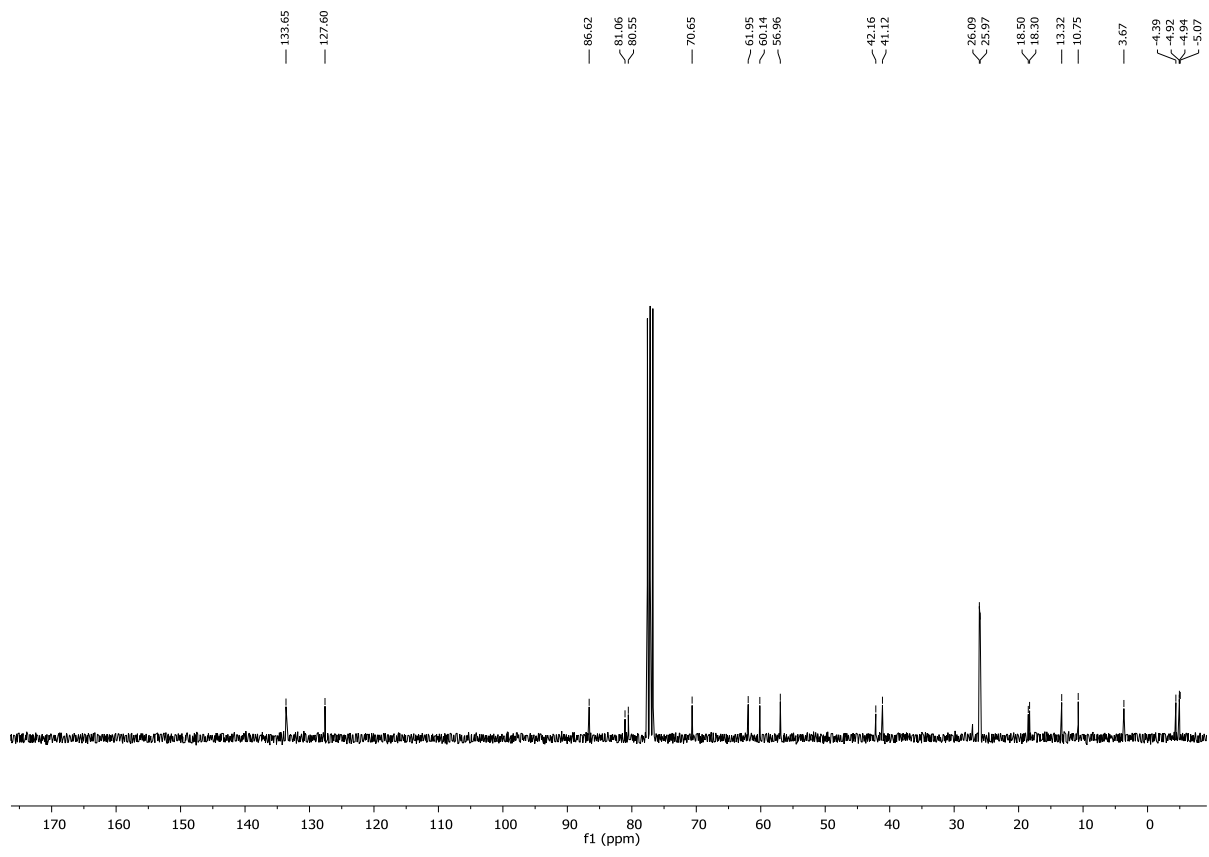
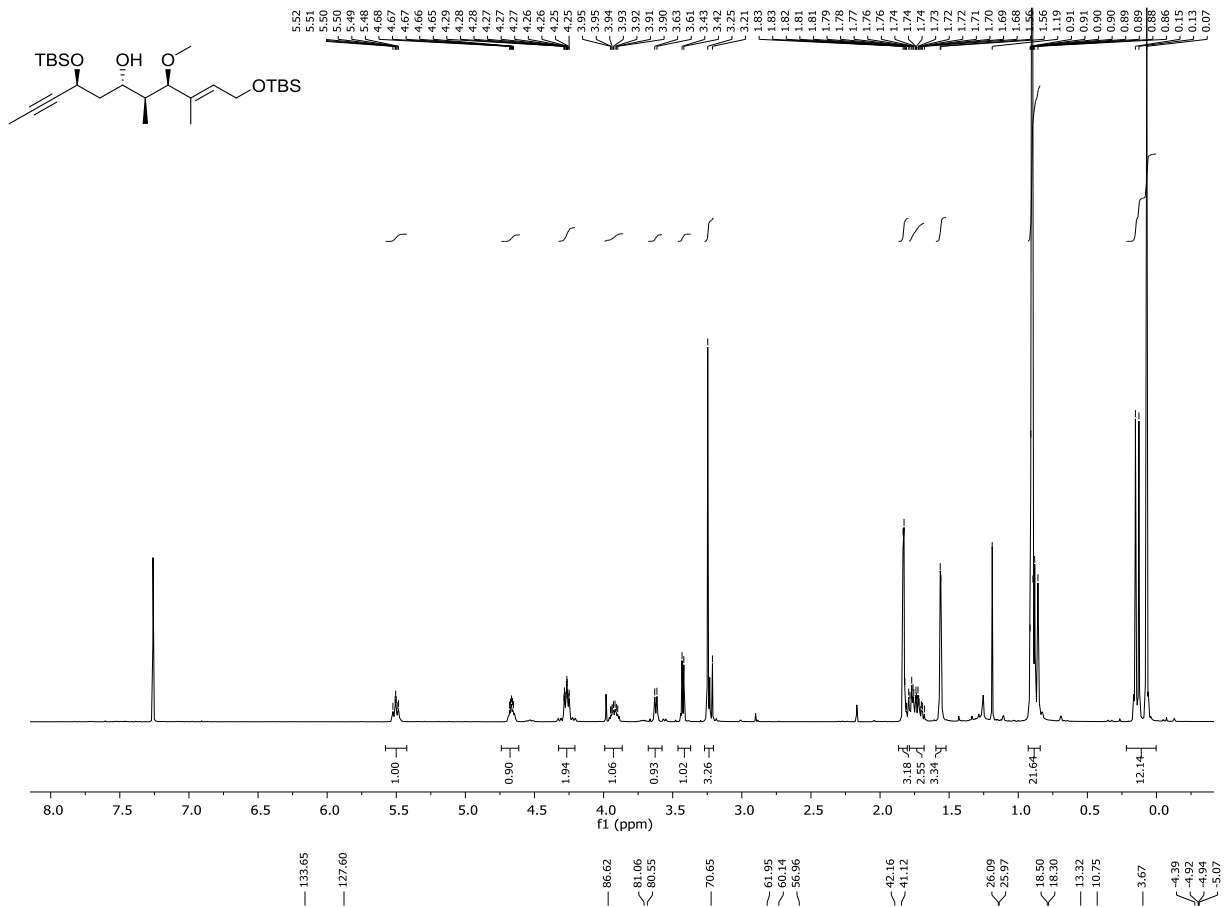


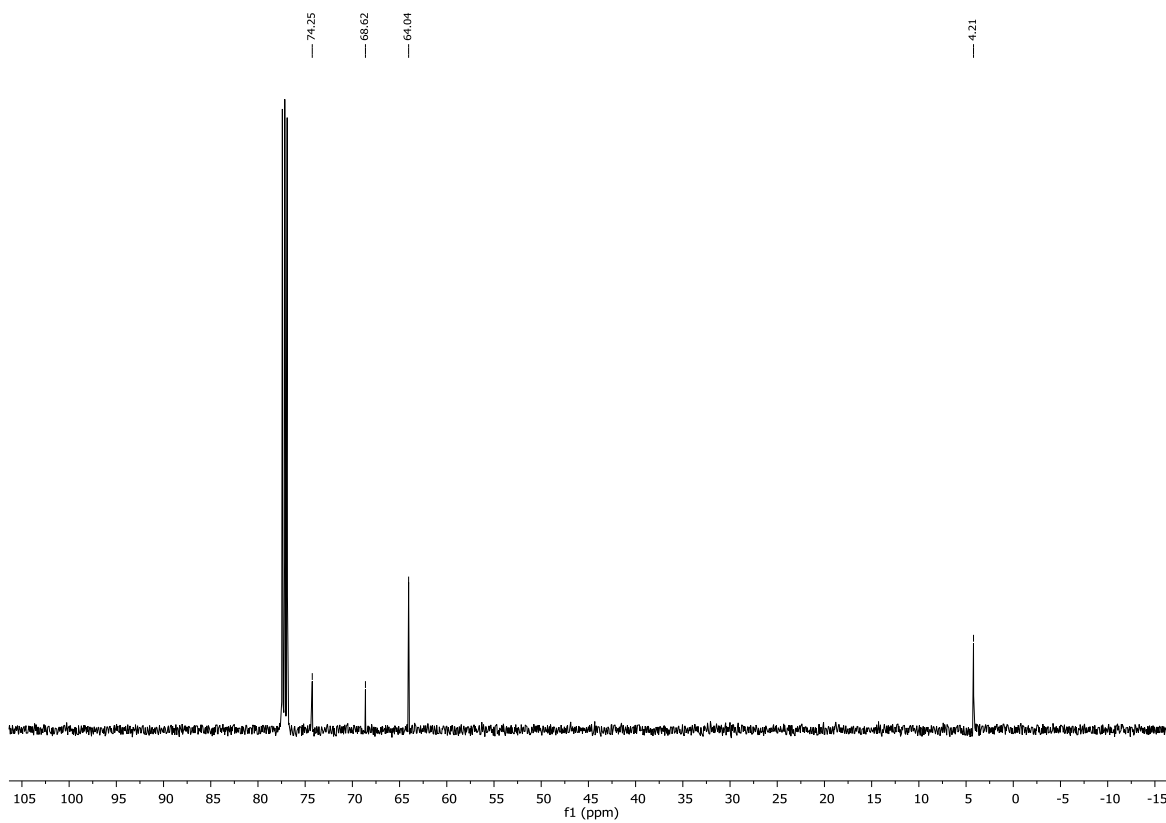
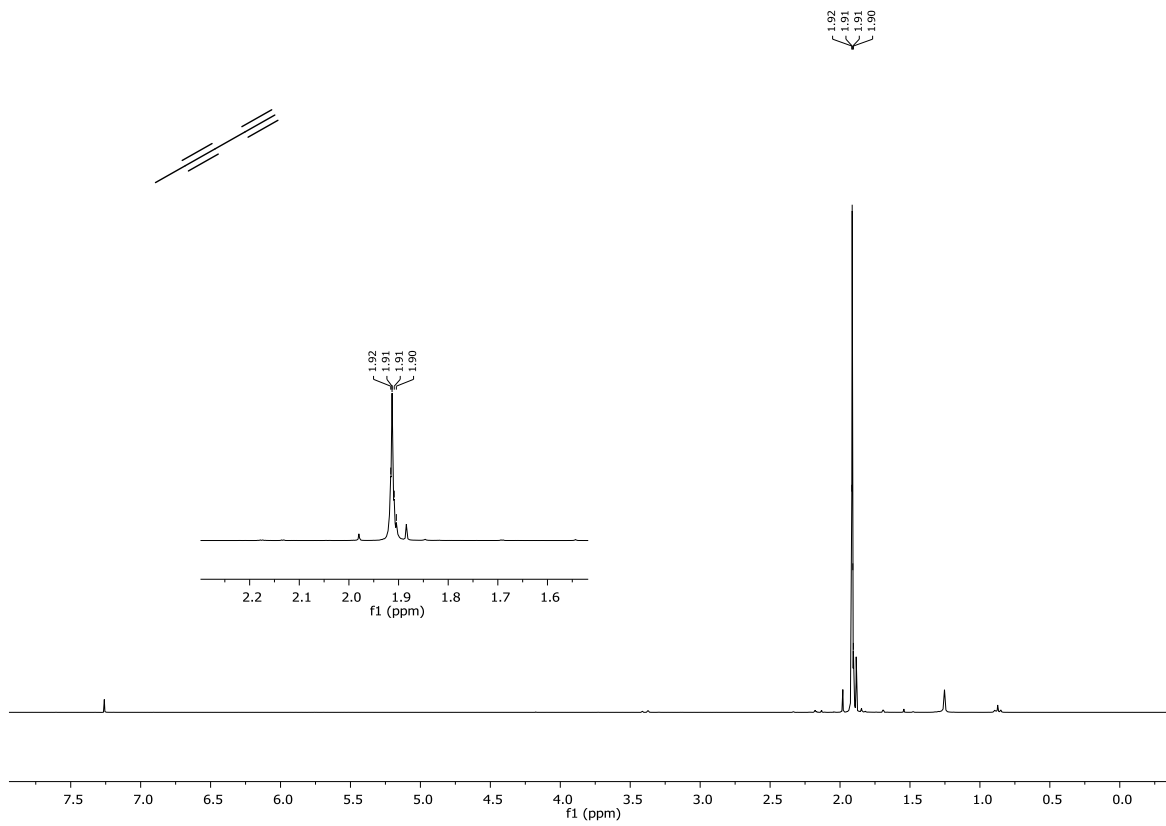


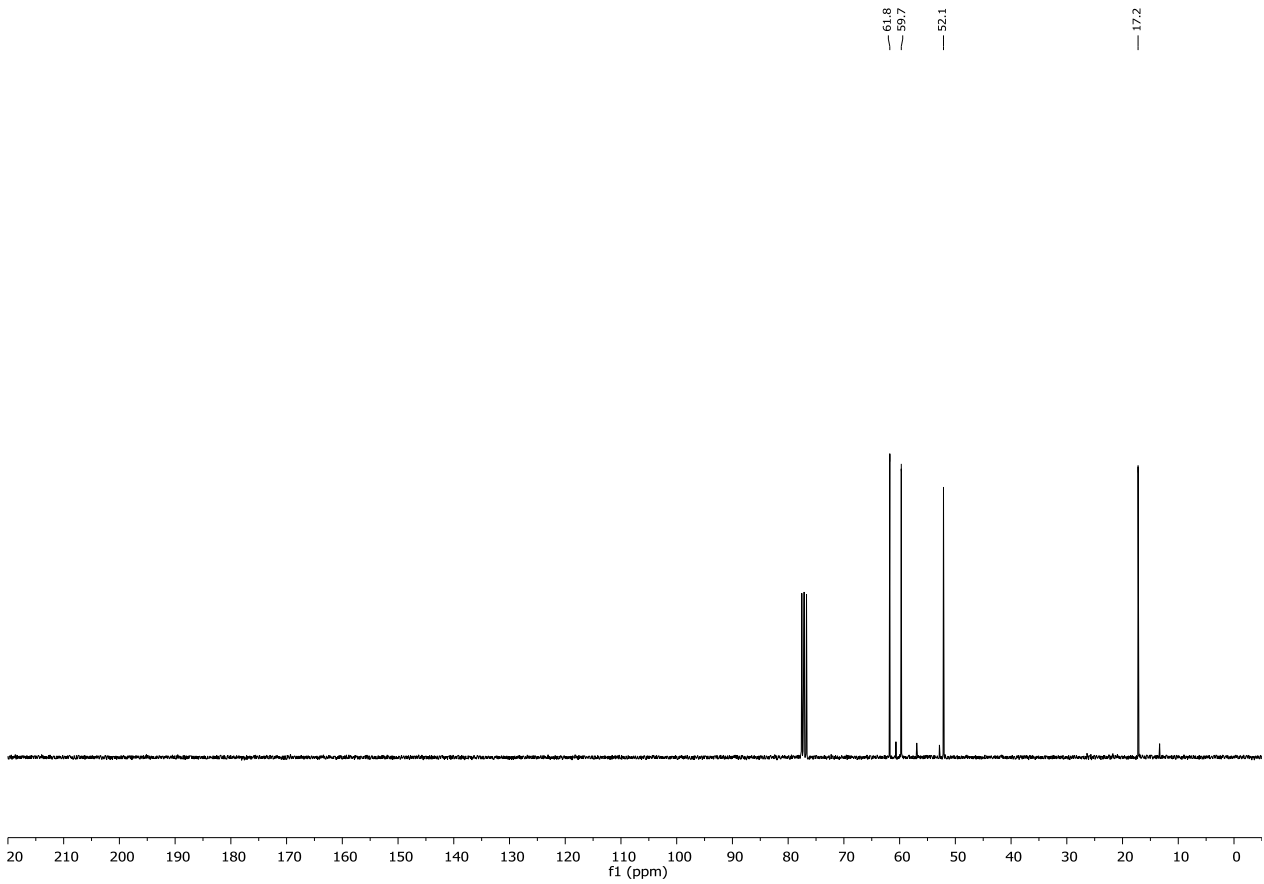
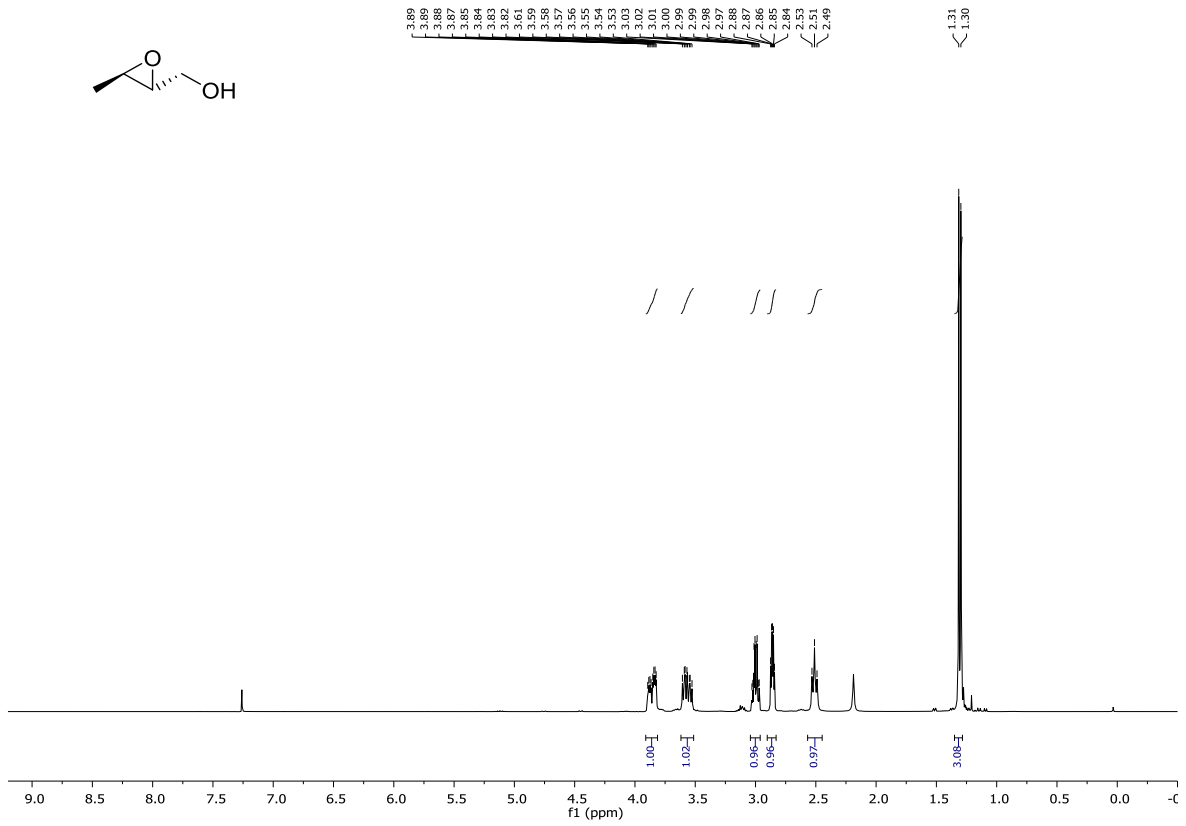
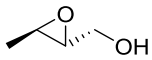


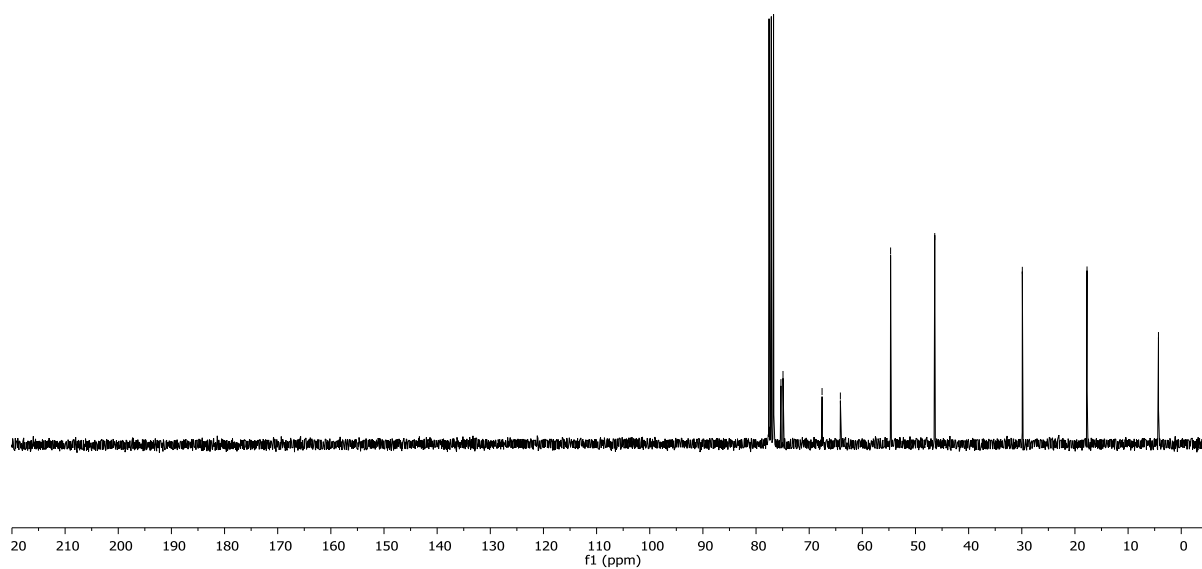
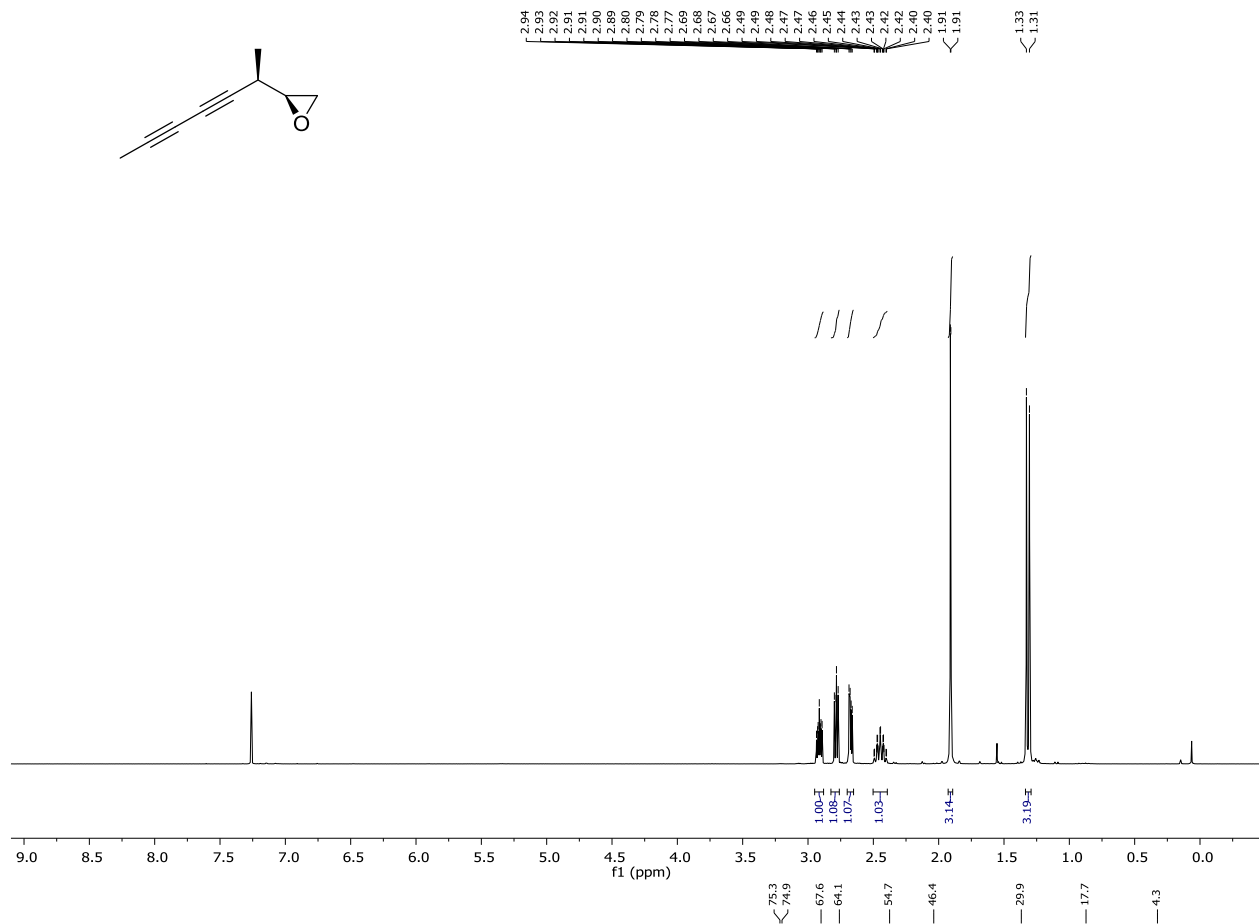
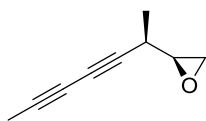


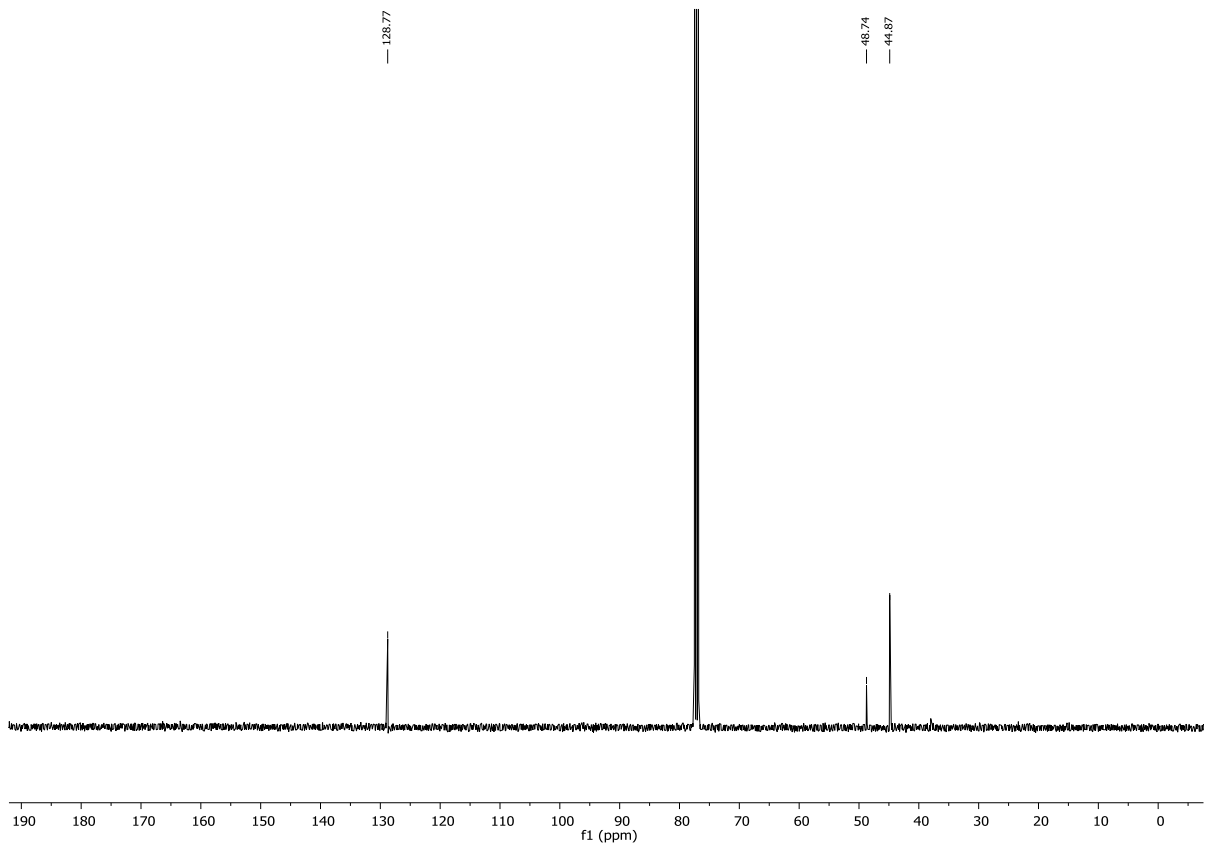
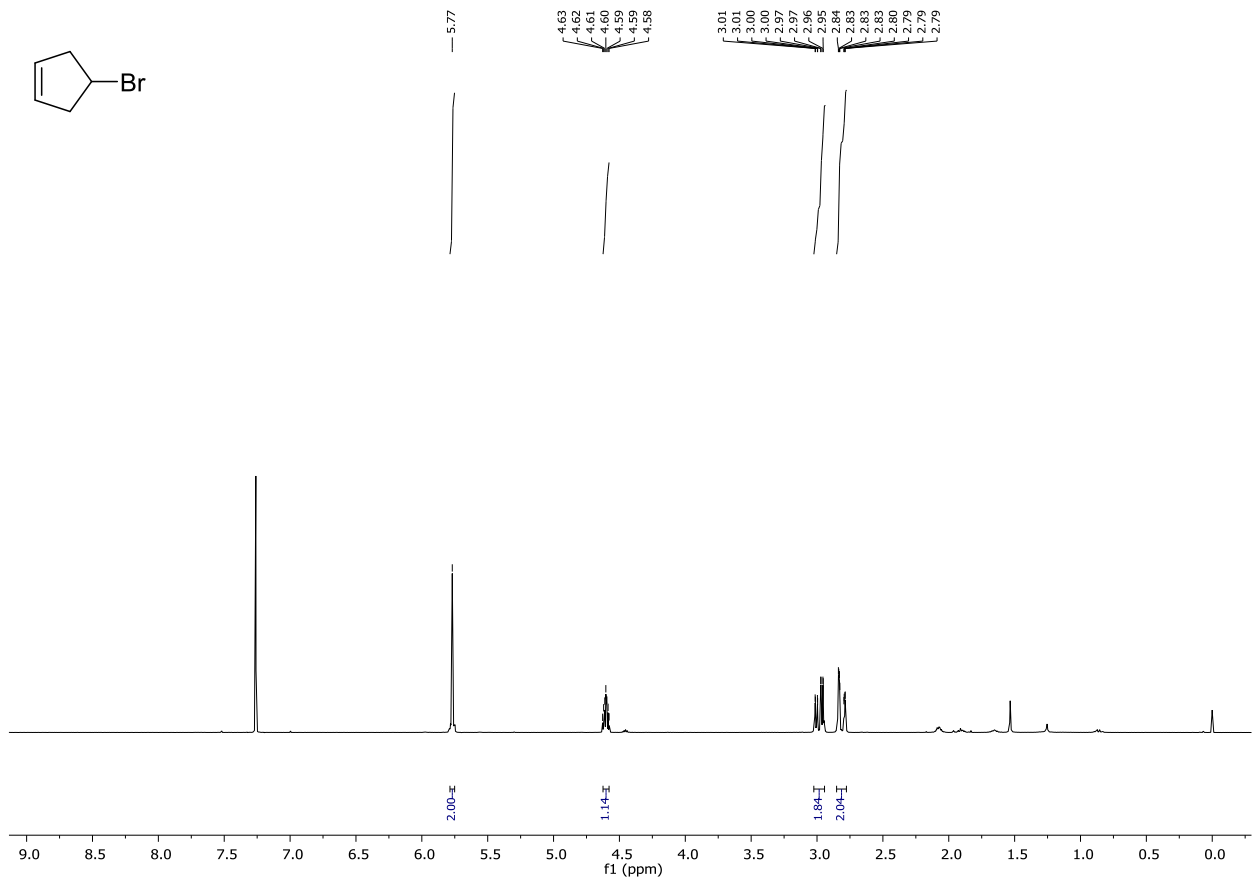
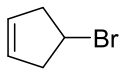


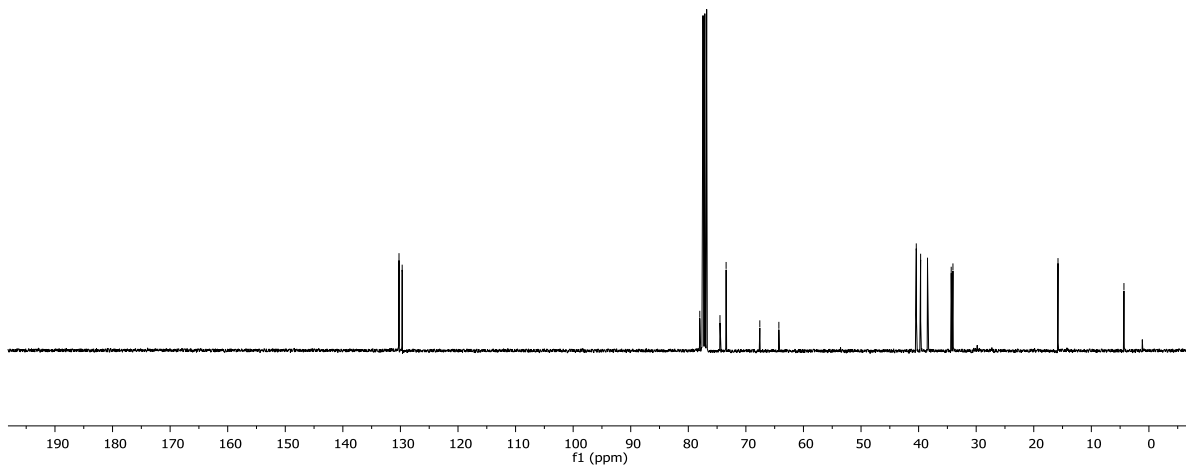
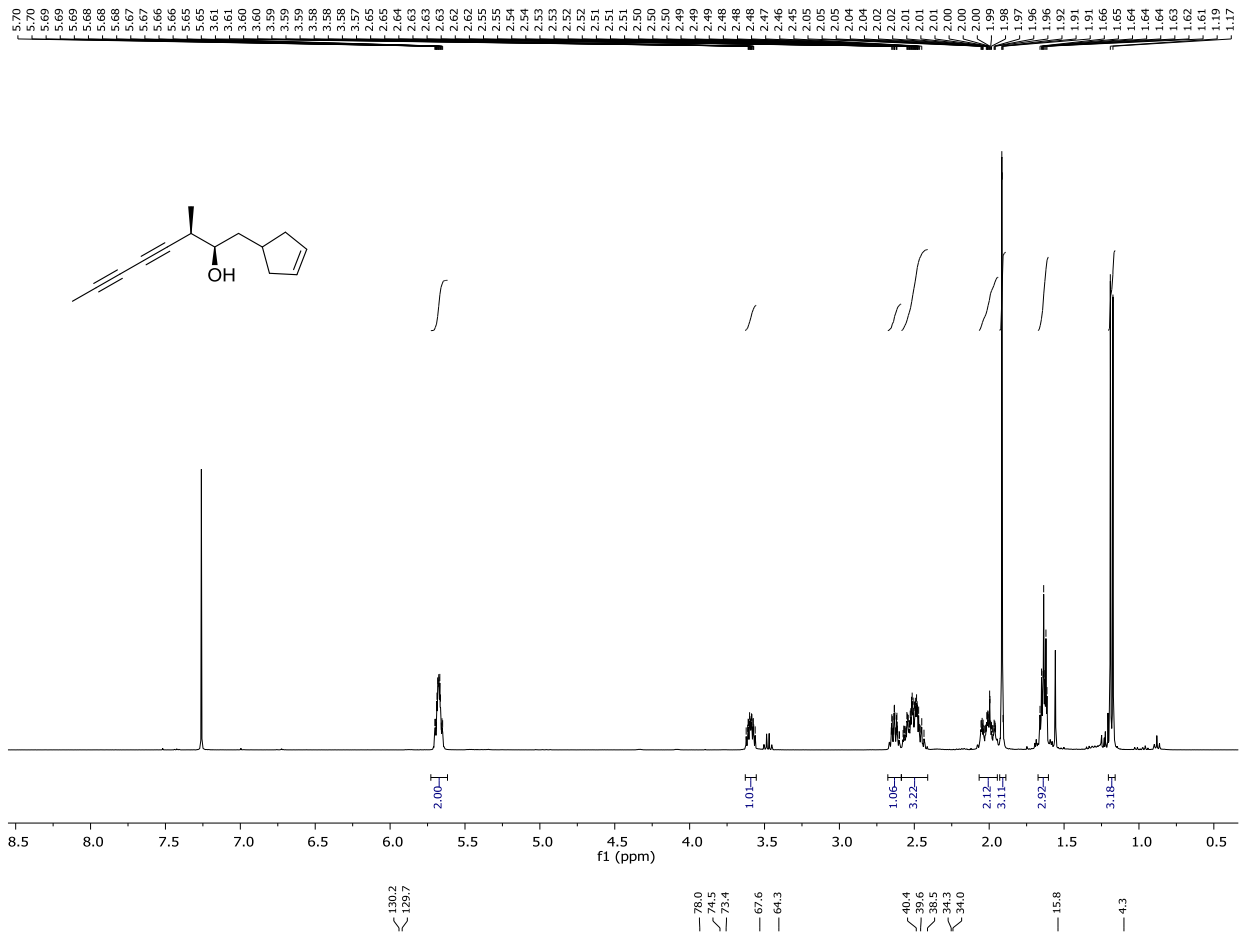


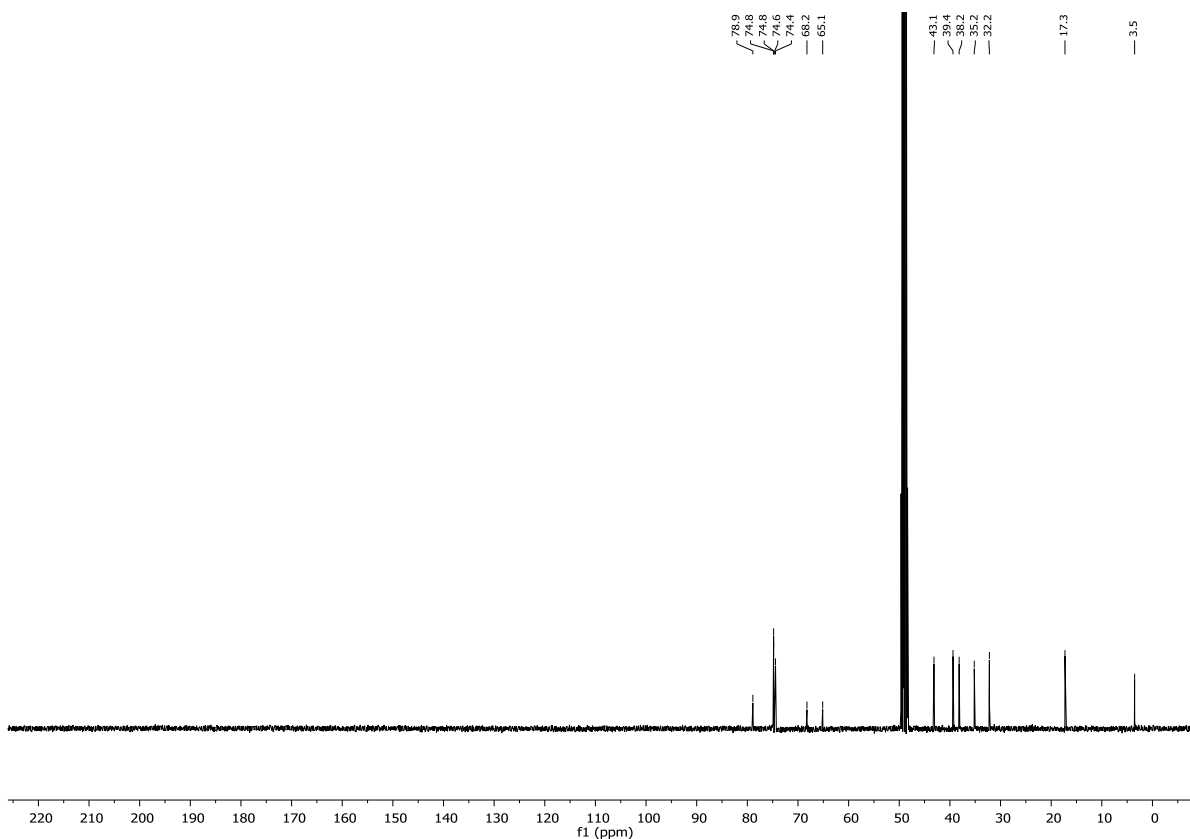
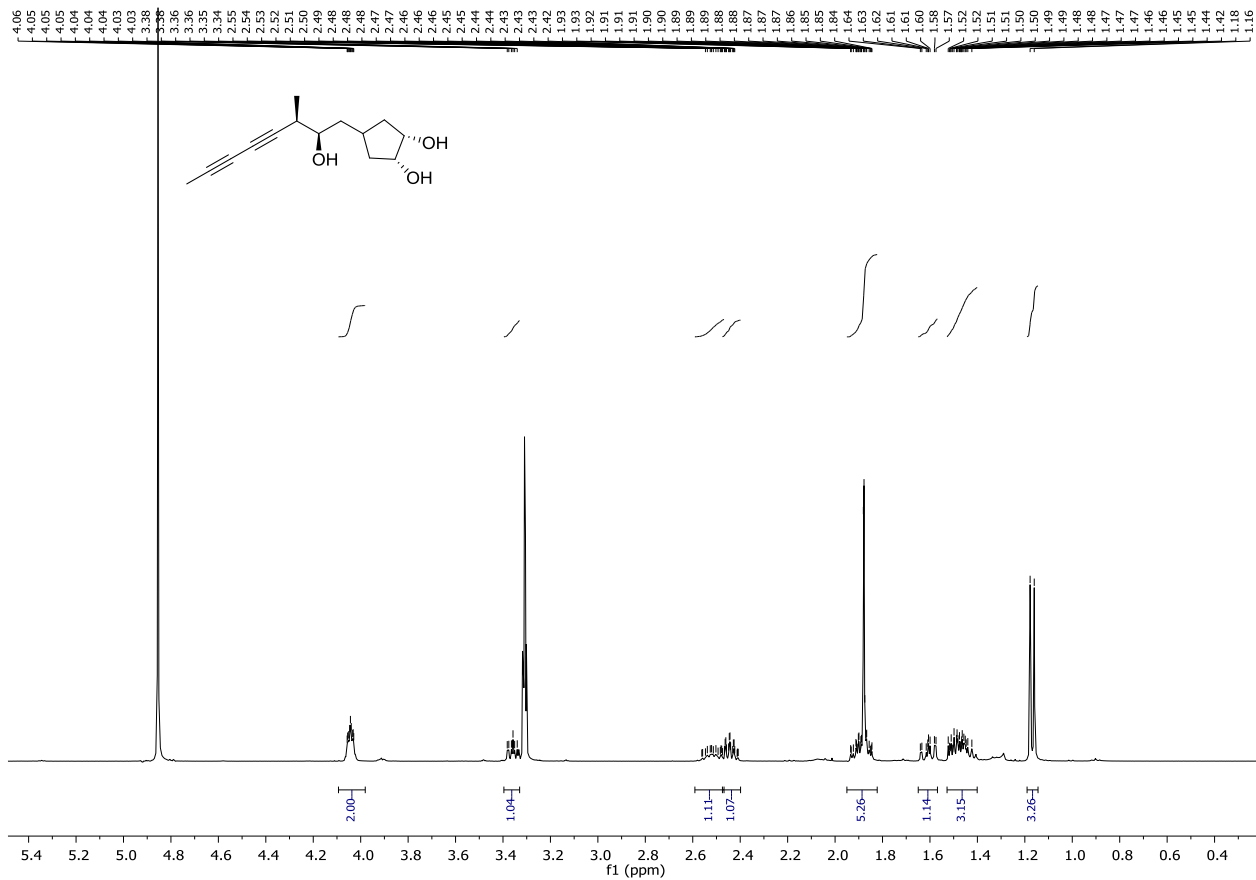


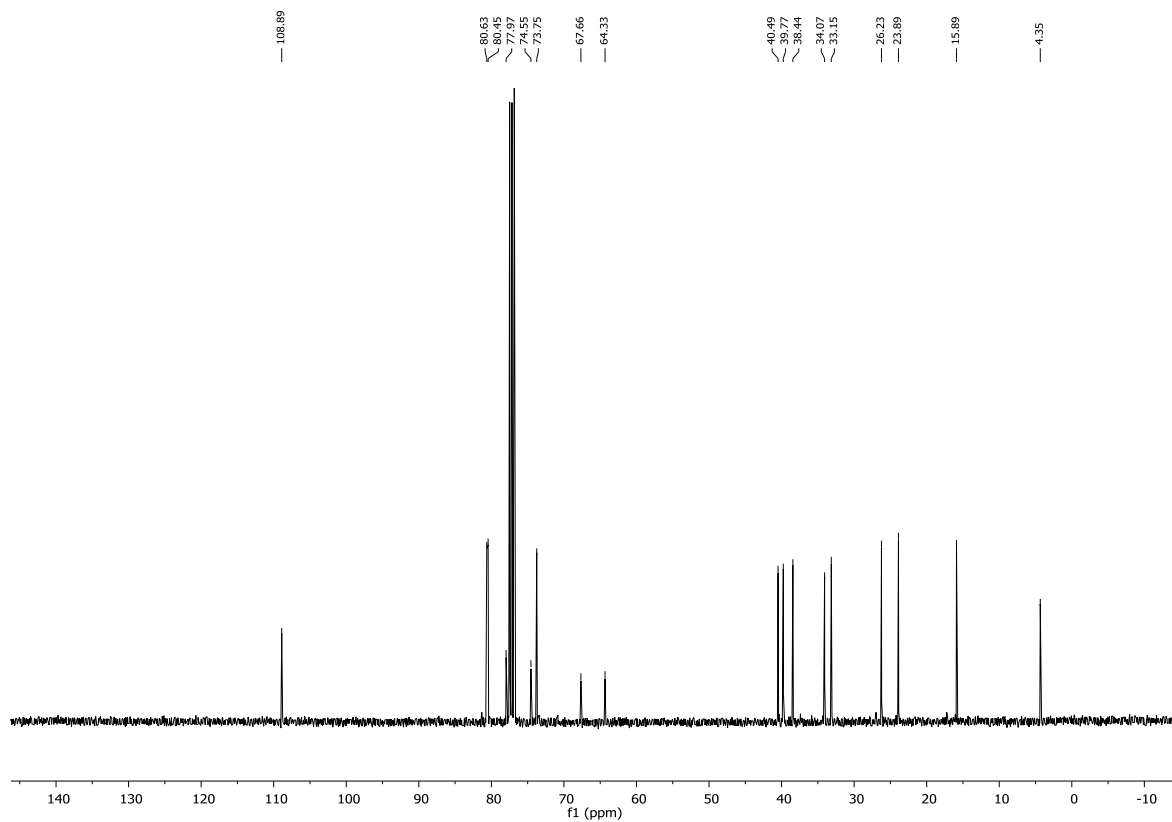
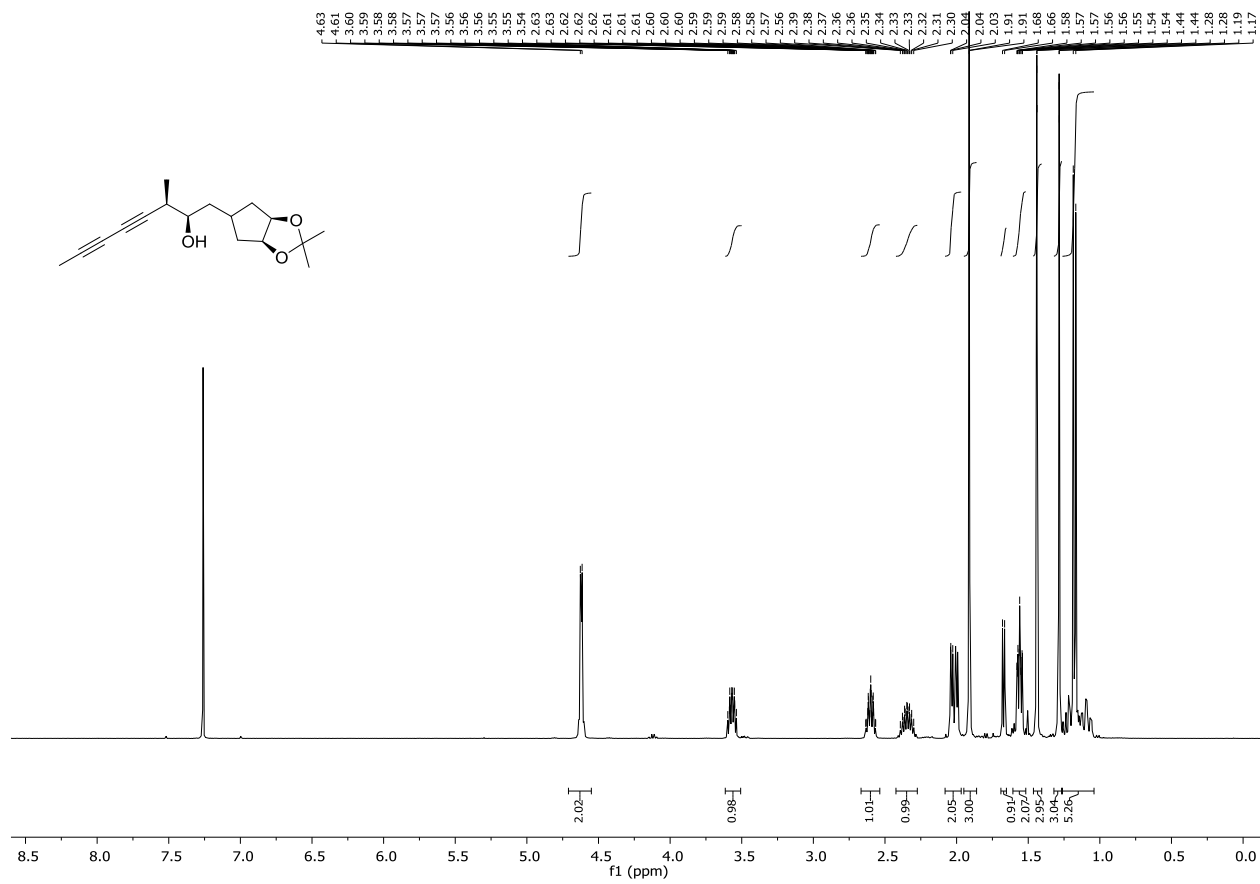


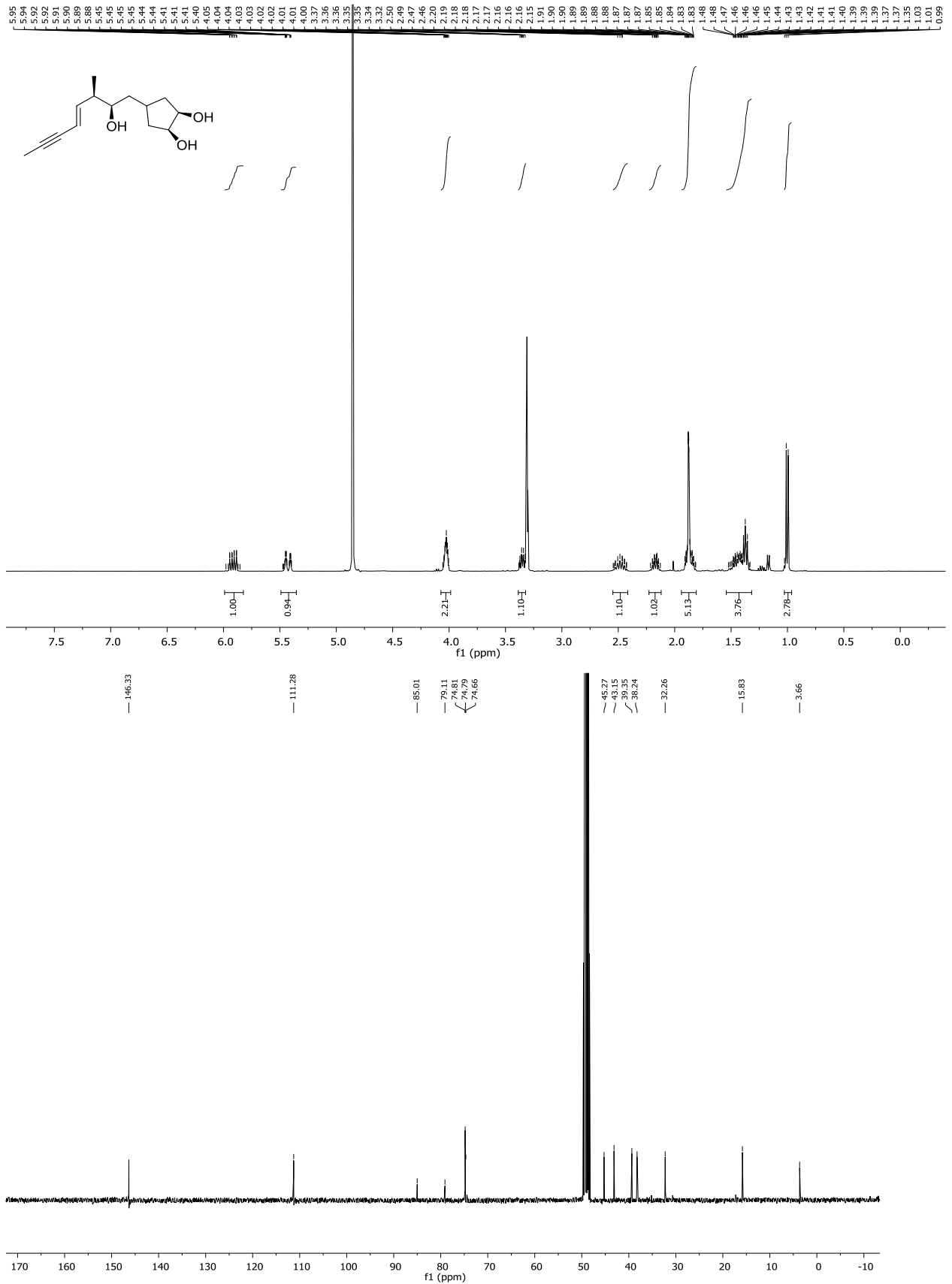


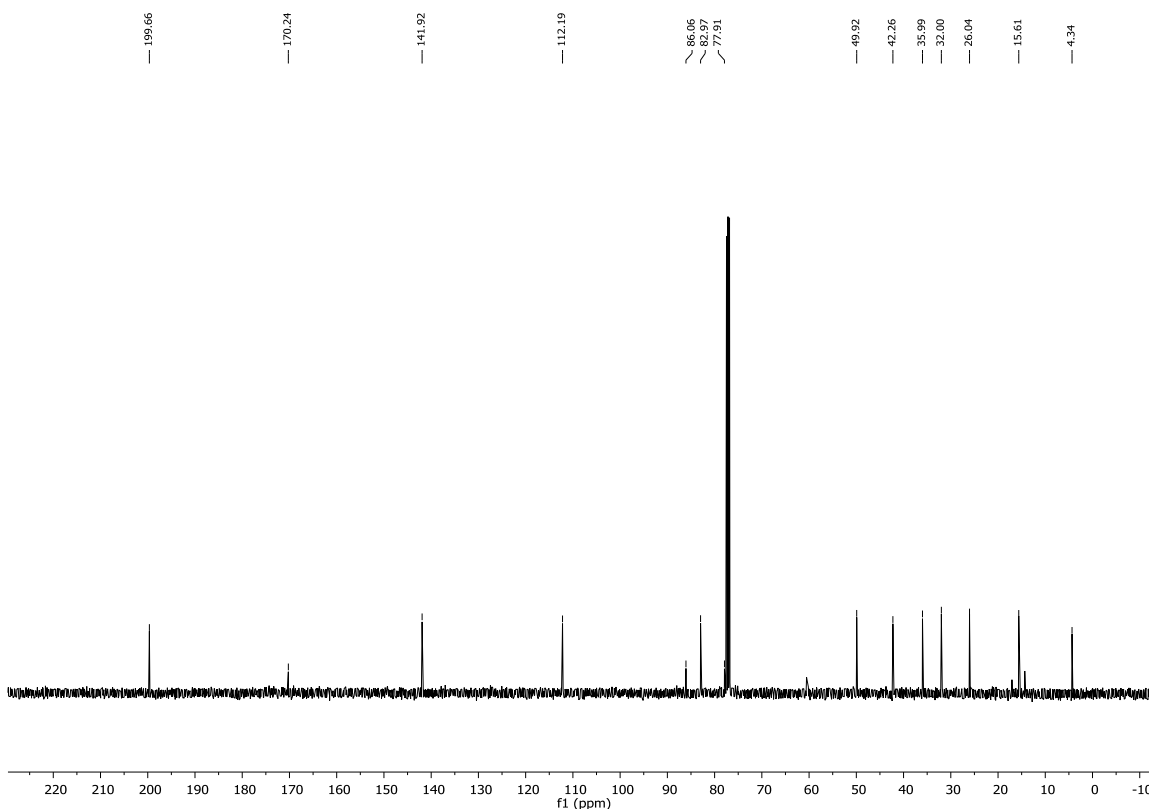
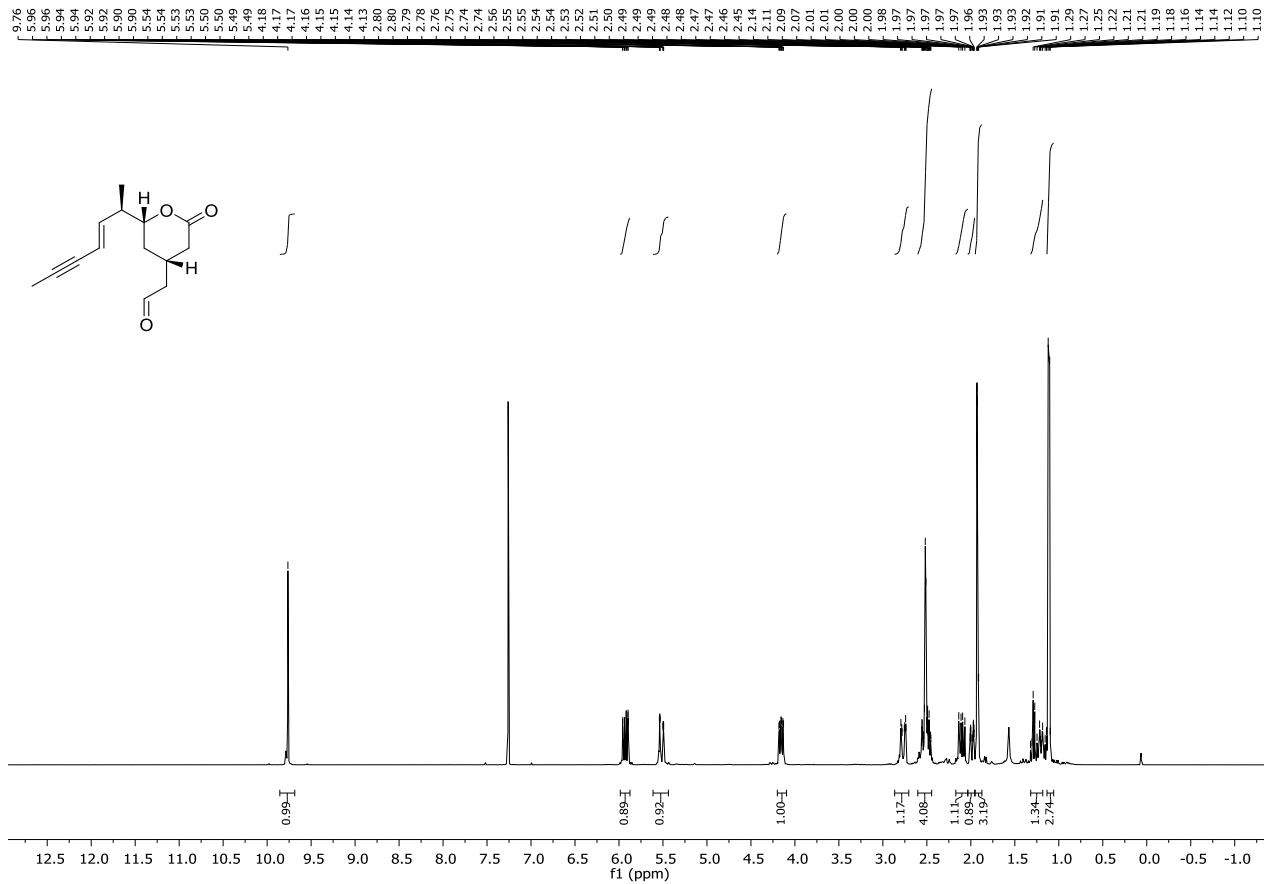


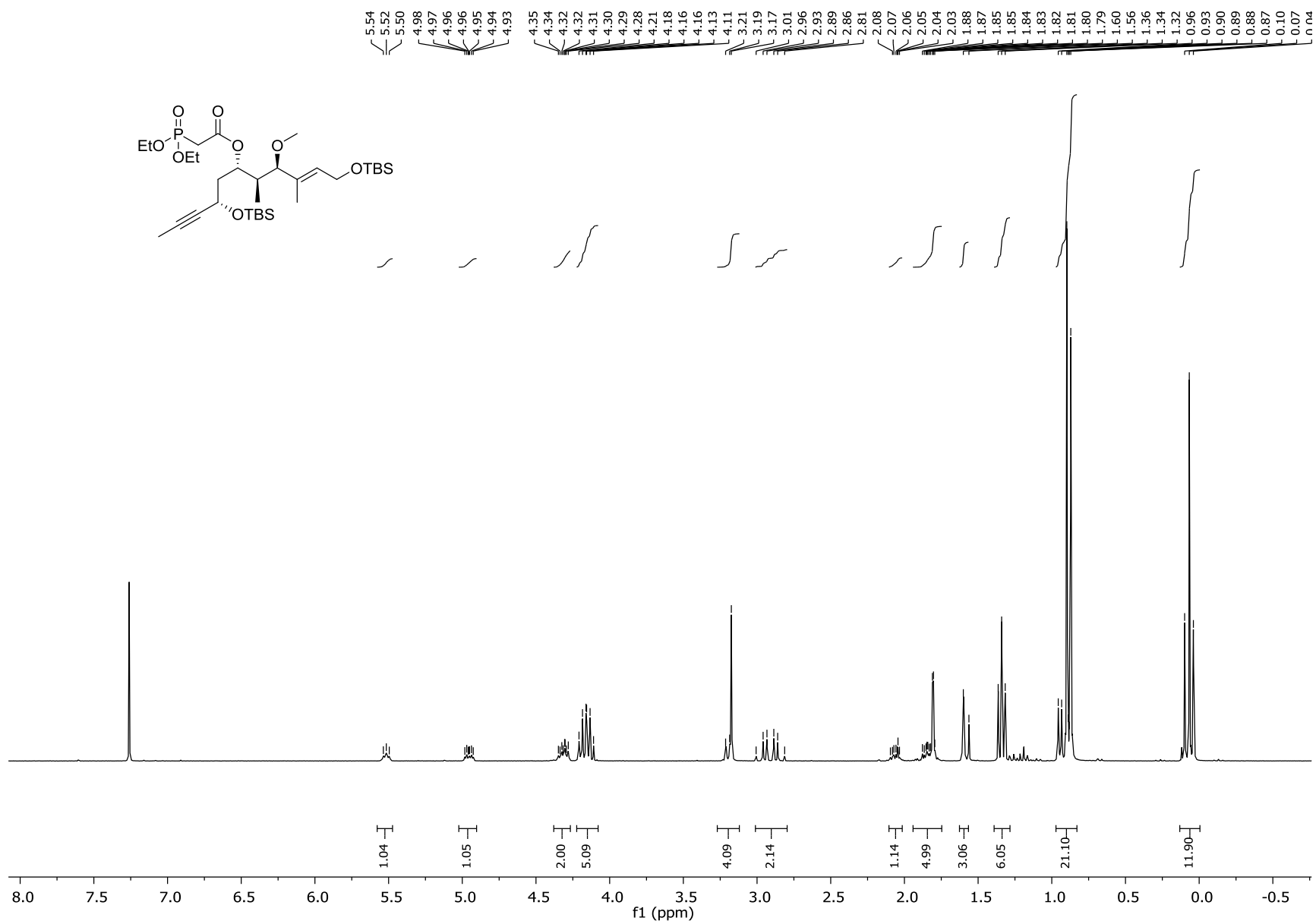


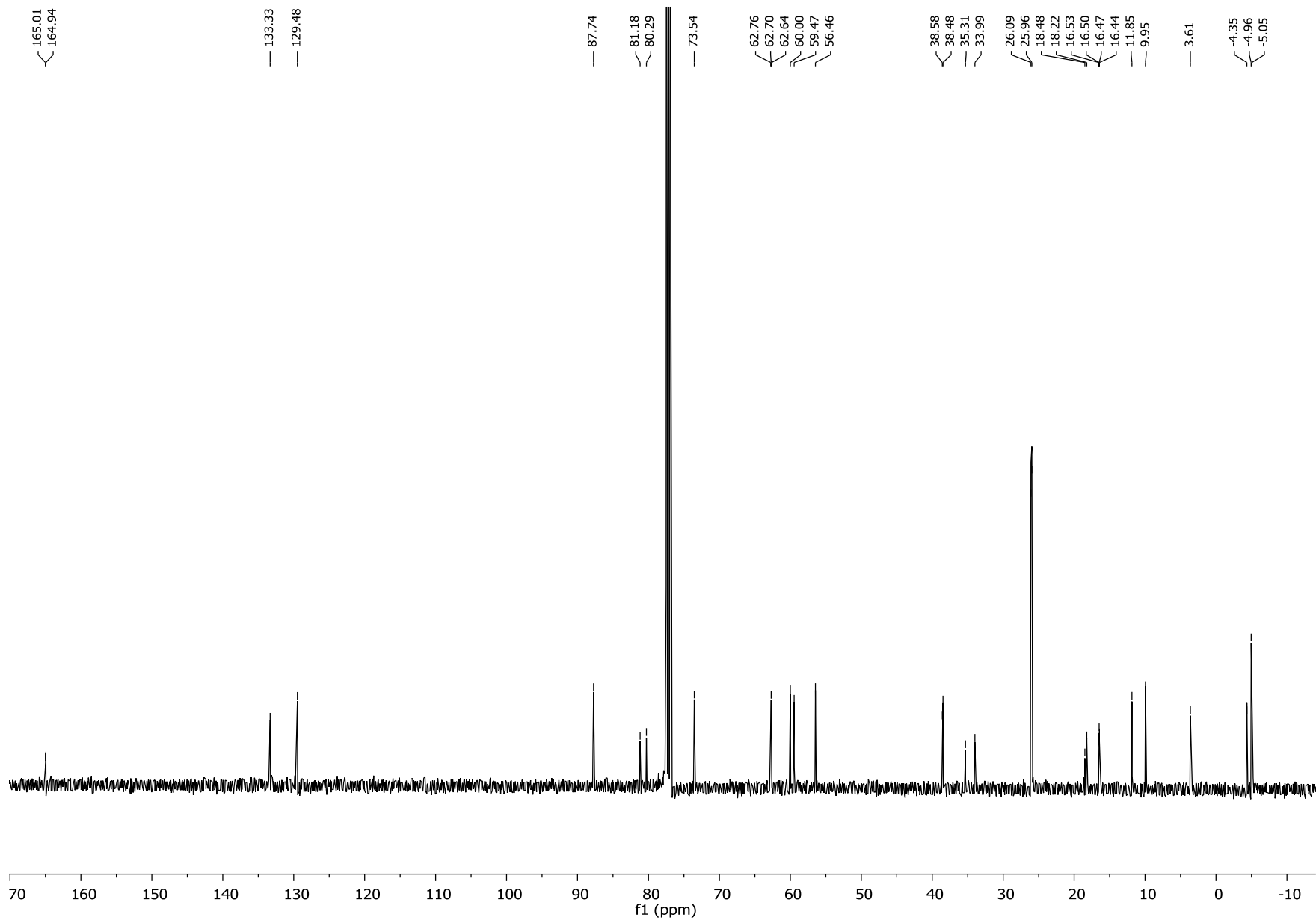




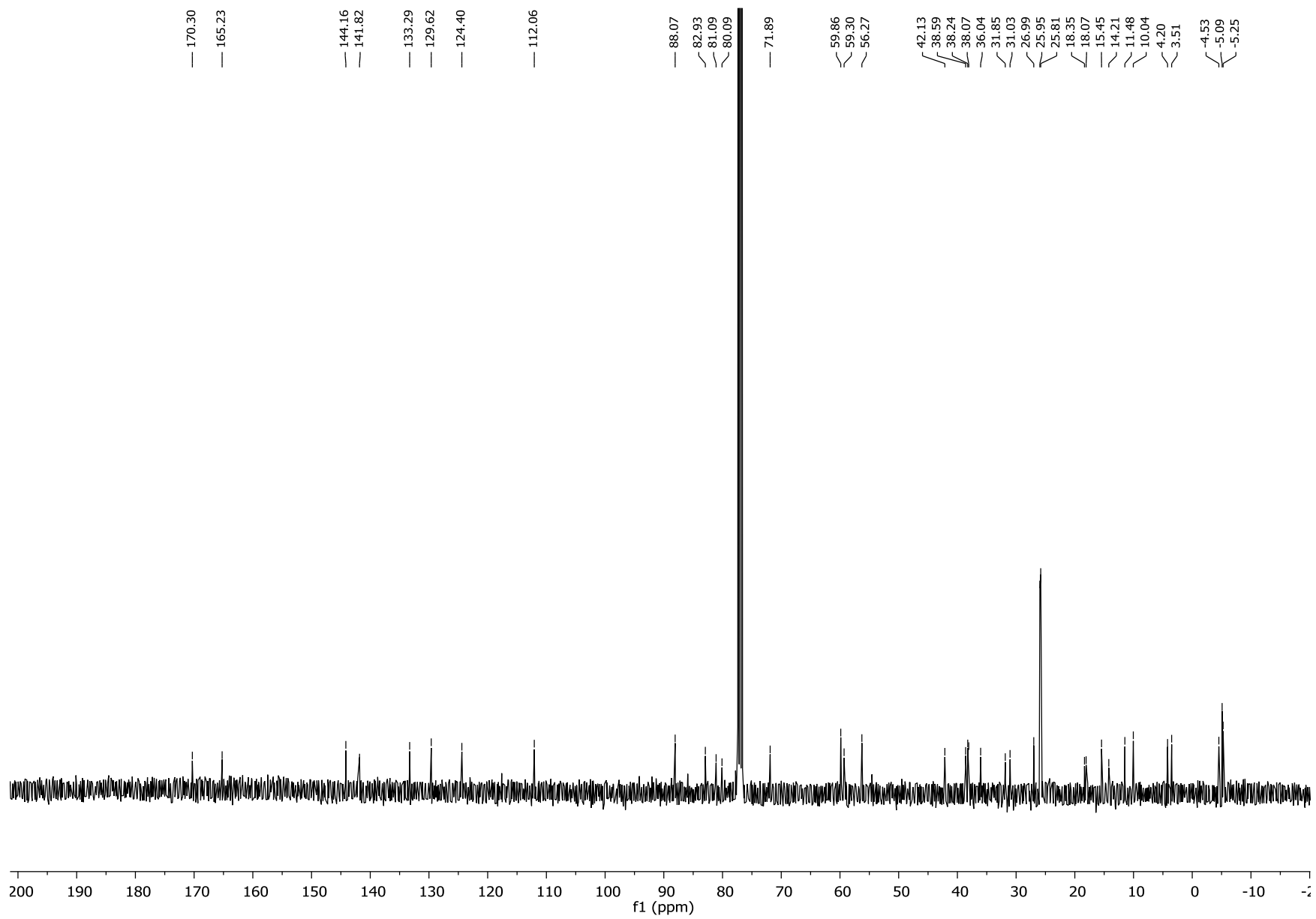


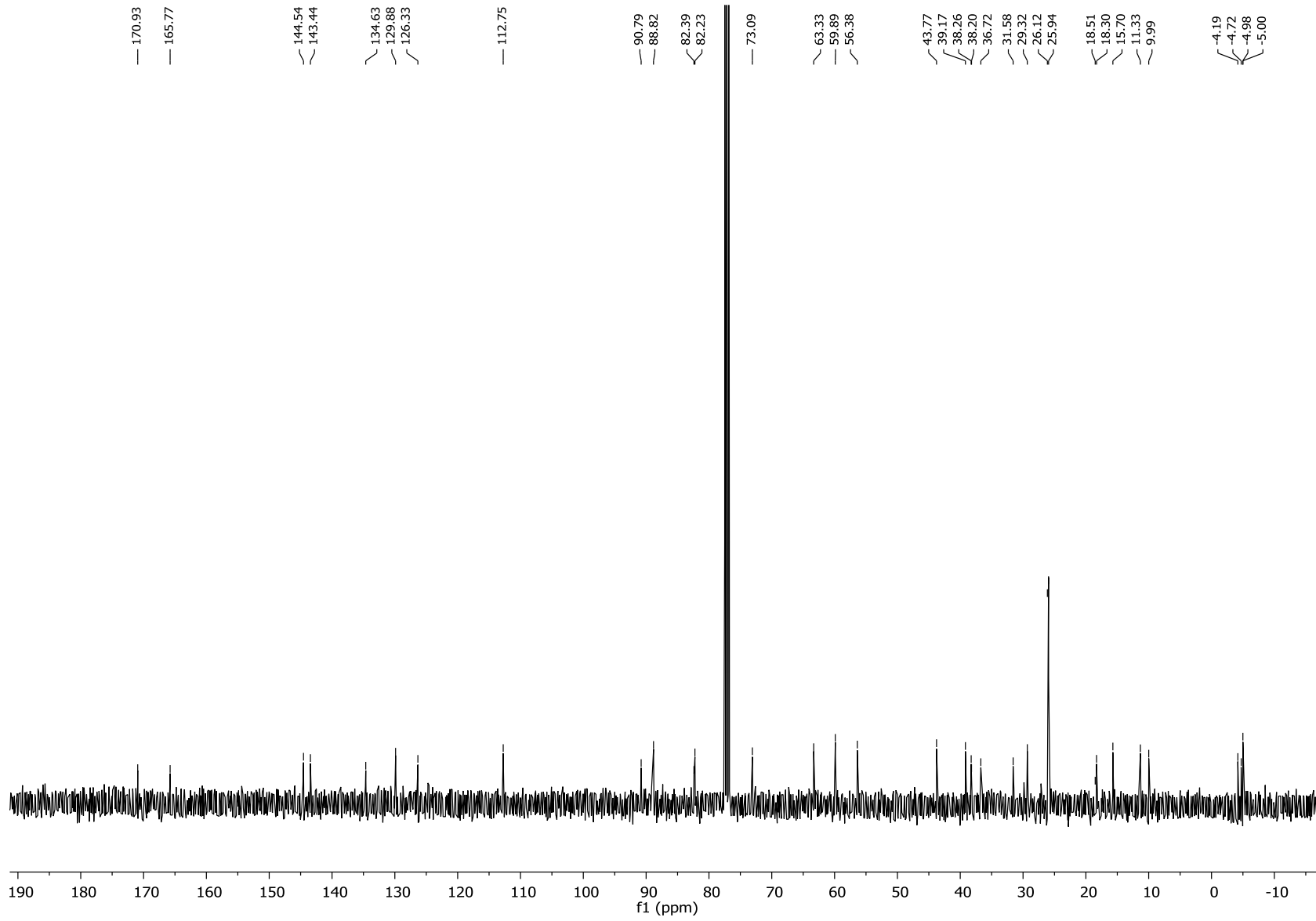


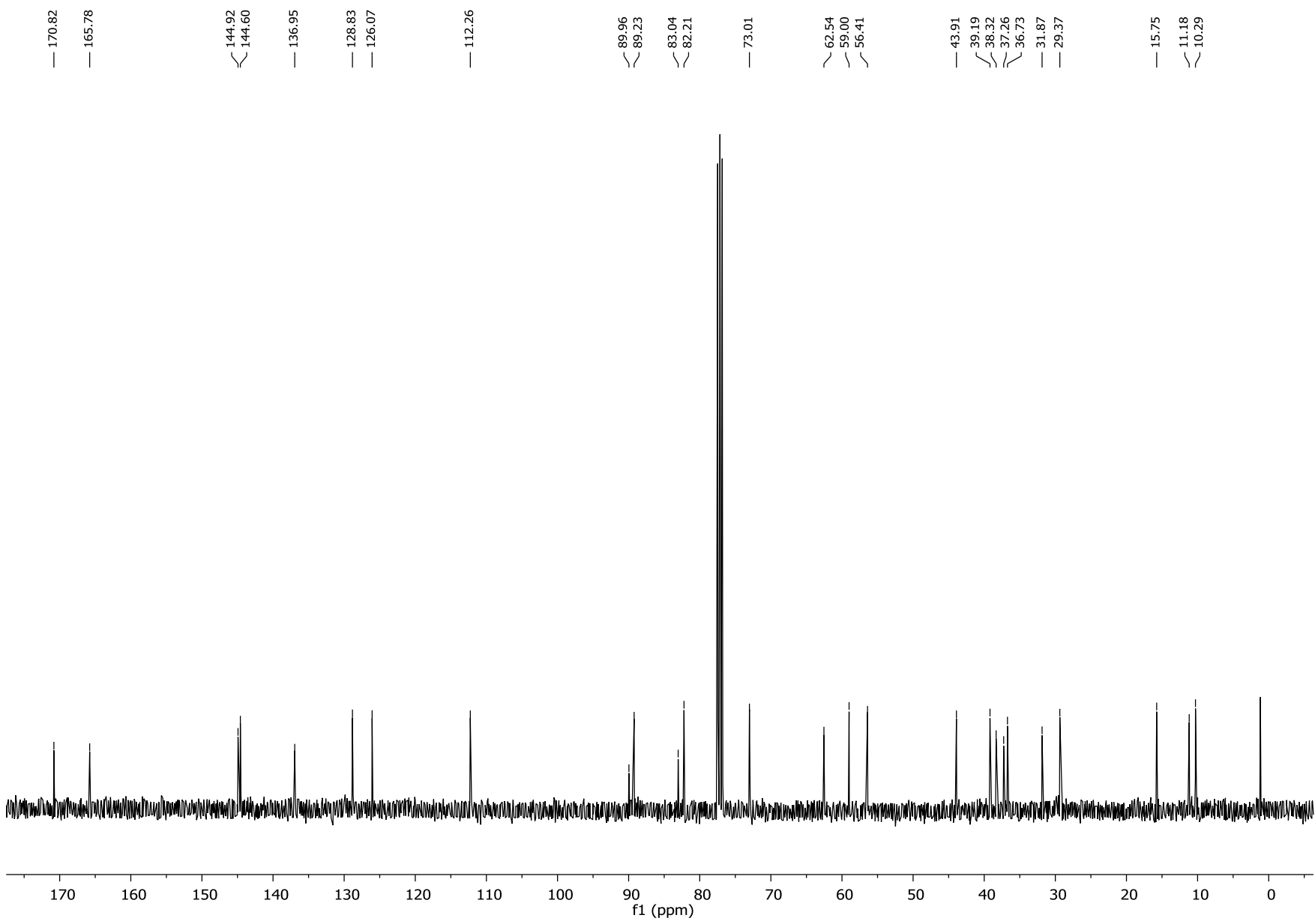


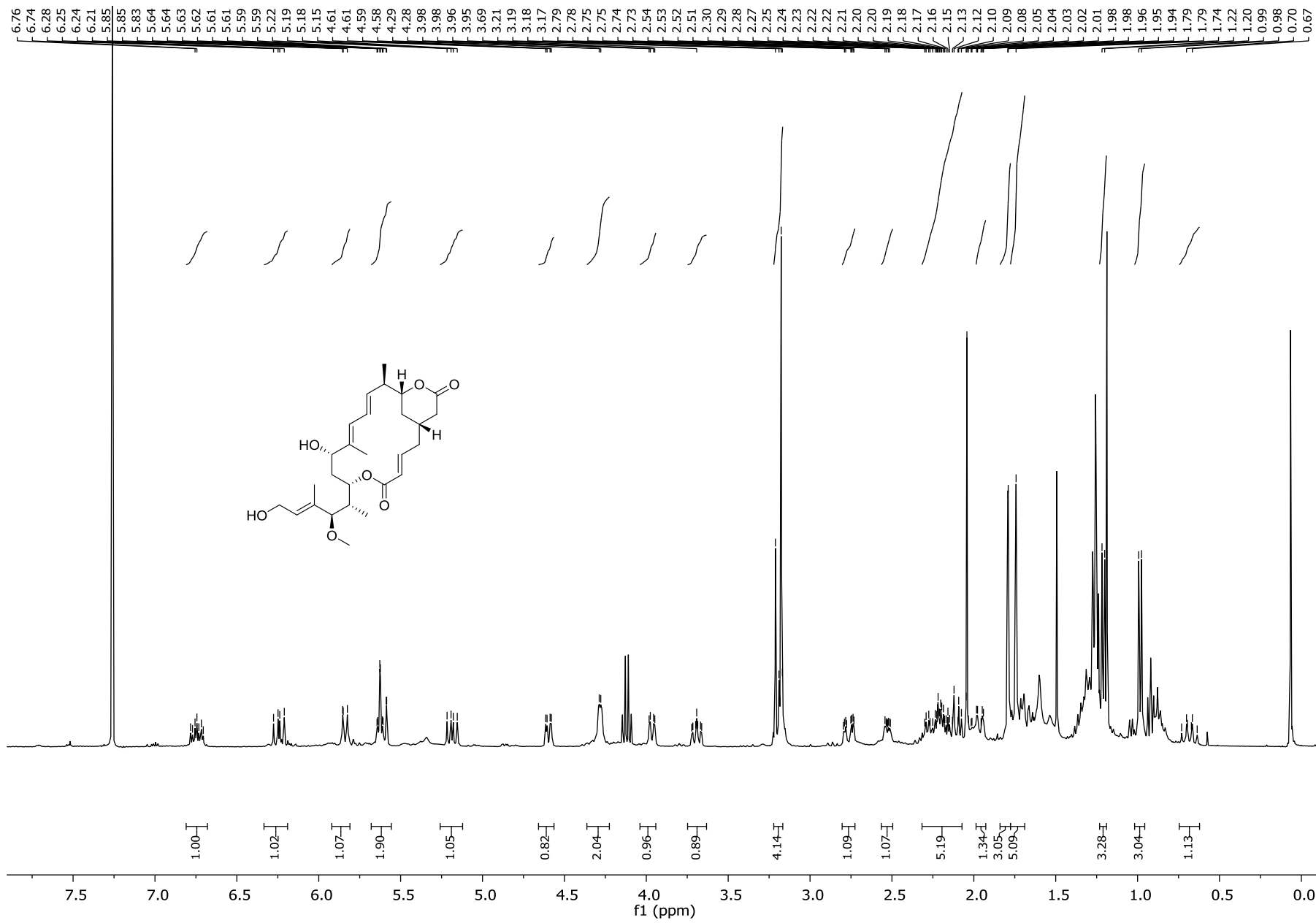


S45

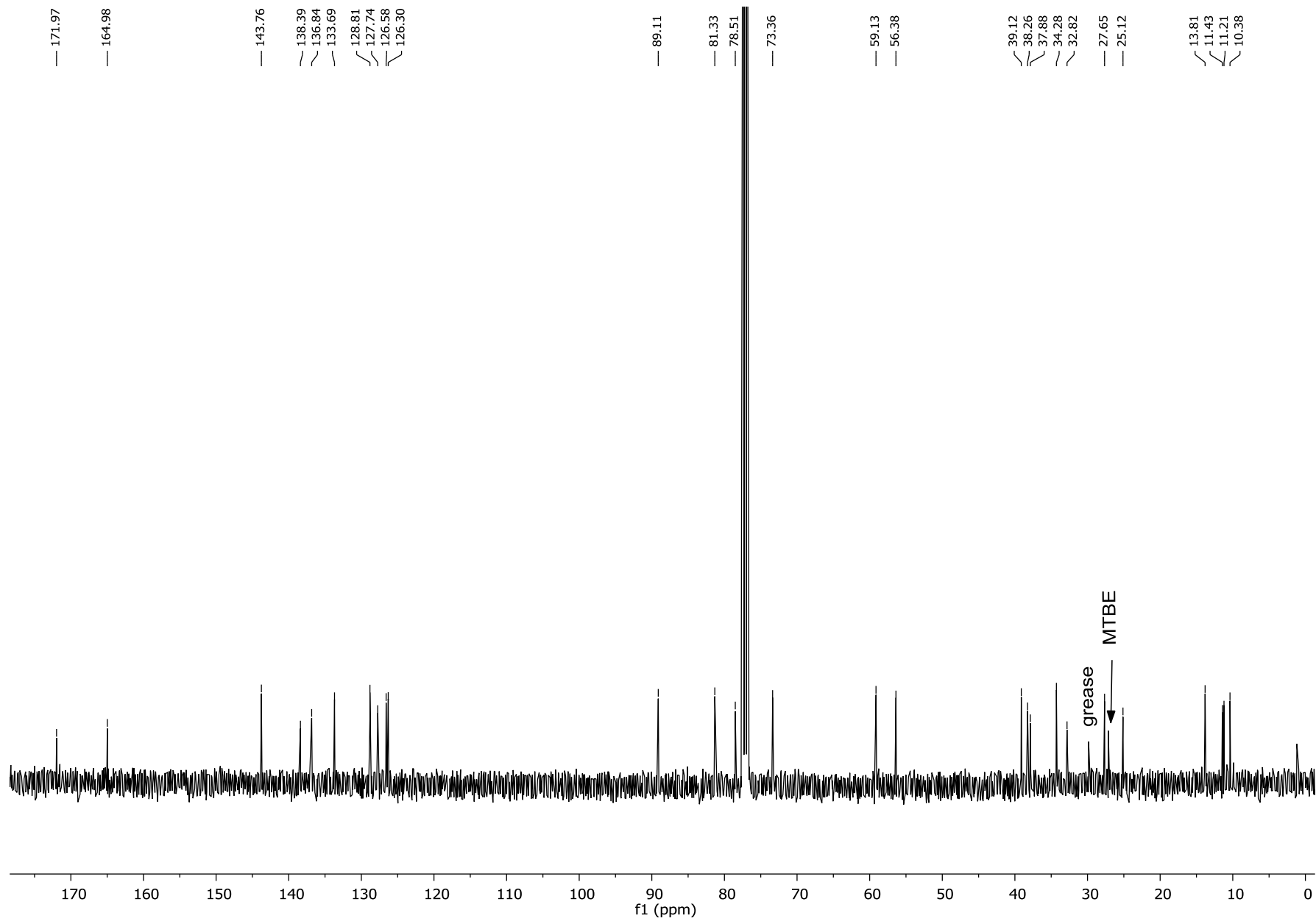




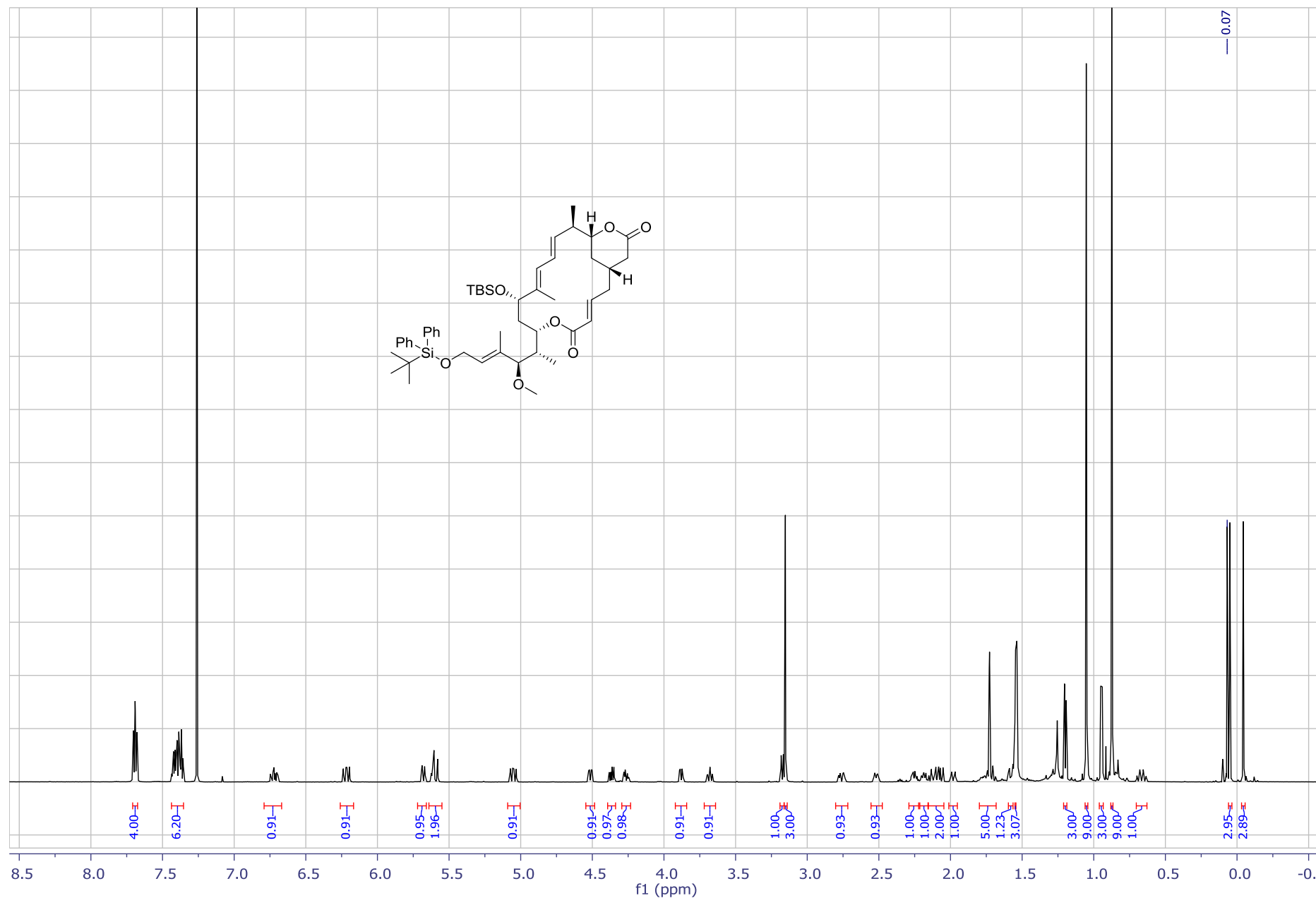




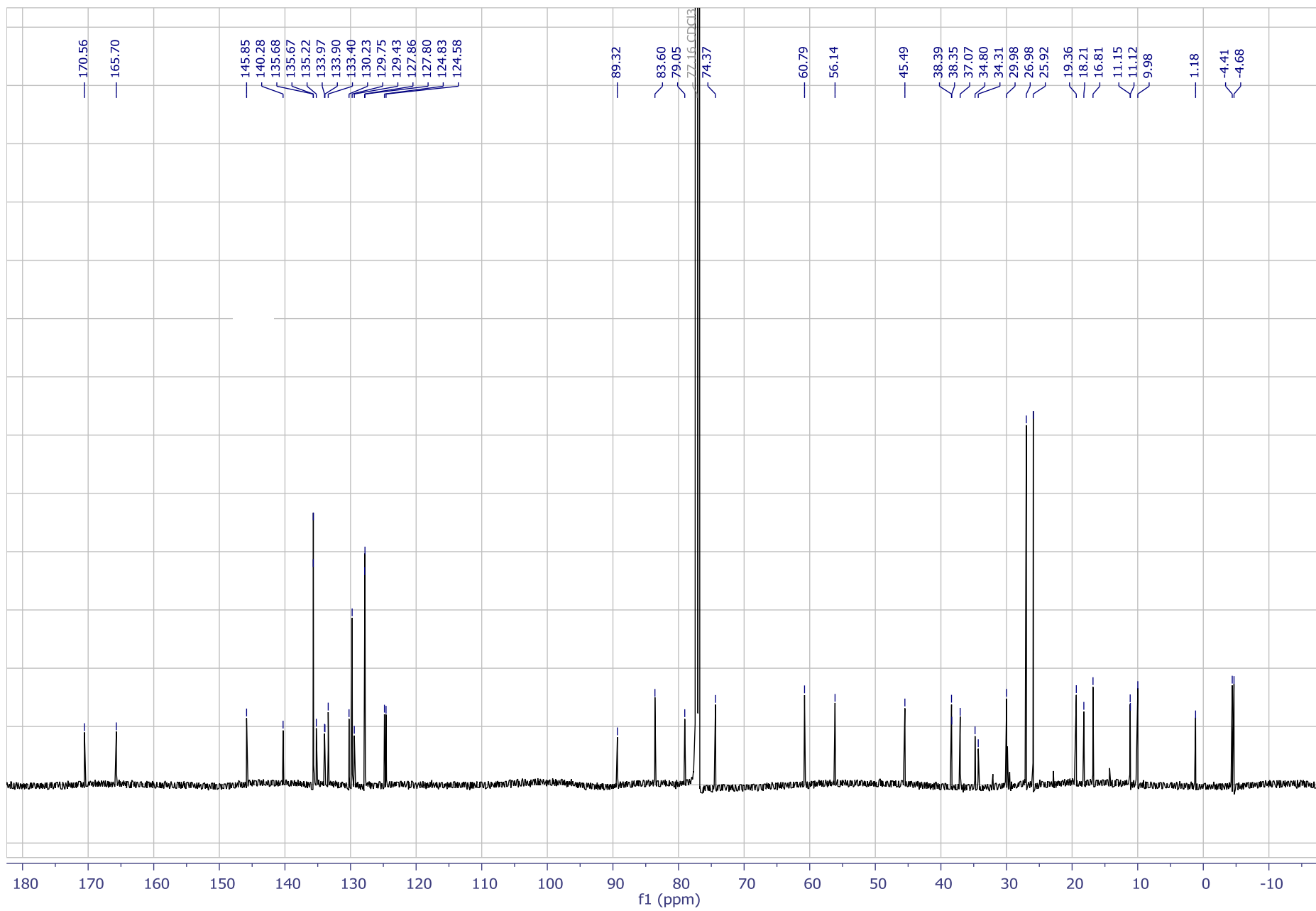
S52



S53



anfab44901.120.fid — ANF-AB-449-01 — 1H @ 298K — 0.5 mg CDCl3 — av600a, cryoTCI — 13/07/2018



anfab44901.11.fid — ANF-AB-449-01 — 13C @ 298K — 0.5 mg CDCl3 — av600a, cryoTCL — 13/07/2018

