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Supporting Information

Concise Total Synthesis of Ivorenolide B

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SUPPORTING INFORMATION

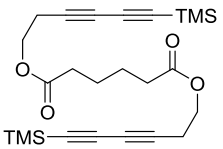
Table of Contents

General. Unless stated otherwise, all reactions were carried out in flame-dried glassware under argon. The solvents were purified by distillation over the drying agents indicated and were transferred under argon: THF (Mg-anthracene), diethyl ether (Mg-anthracene), dichloromethane, 1,2-dichloroethane (CaH_2), acetonitrile (CaH_2), triethylamine (CaH_2), toluene (Na/K); anhydrous acetone was purchased (> 99.5%, Aldrich) and used as received. Flash chromatography: Merck silica gel 60 (230-400 mesh). Optical rotations were measured on a Perkin Elmer Polarimeter 343+ at 20°C. IR: Nicolet FT-7199 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 8200, MS (CI): Finnigan MAT 95, MS (ESI) ESQ 3000, accurate mass determinations: Bruker APEX III FT-MS (7 T magnet). NMR: Spectra were recorded on a Bruker DPX 300, AV 400 or AV 600 spectrometer in the solvents indicated; ^1H and ^{13}C chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Fluka, Lancaster, Strem) were used as received.

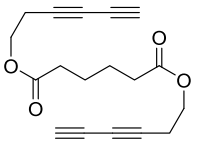
6-(Trimethylsilyl)hexa-3,5-diyn-1-ol,[1] hepta-3,5-diyne-1-ol,[2] substrate **3a**[2] and complex **7**[3] were prepared according to the cited literature procedures.

Model Studies

Bis(6-(trimethylsilyl)hexa-3,5-diyn-1-yl) adipate (3b). Adipoyl dichloride (0.22 mL, 1.5 mmol) was added dropwise to a solution of 6-(trimethylsilyl)hexa-3,5-diyn-1-ol (500 mg, 3.0 mmol) in CH_2Cl_2 (33 mL) and pyridine (1.6 mL) at 0 °C. The cooling bath was removed and the mixture stirred for 16 h. Excess base was neutralized by addition of HCl (0.1 M), the aqueous phase was extracted with Et_2O (3 x 20 mL), the combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the title compound as a colorless oil which was used without further purification in the next step (605 mg, 91%). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.16 (t, J = 6.7 Hz, 4H), 2.62 (t, J = 6.7 Hz, 4H), 2.41 – 2.28 (m, 4H), 1.74 – 1.54 (m, 4H), 0.18 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 88.0, 84.3, 75.3, 66.9, 61.6, 33.8, 24.3, 19.9, –0.3; IR (film, cm^{-1}): 1738, 1251, 1181, 845; MS: m/z calcd for $C_{24}H_{34}O_4Si_2Na$: 465.18870, found 465.18879.



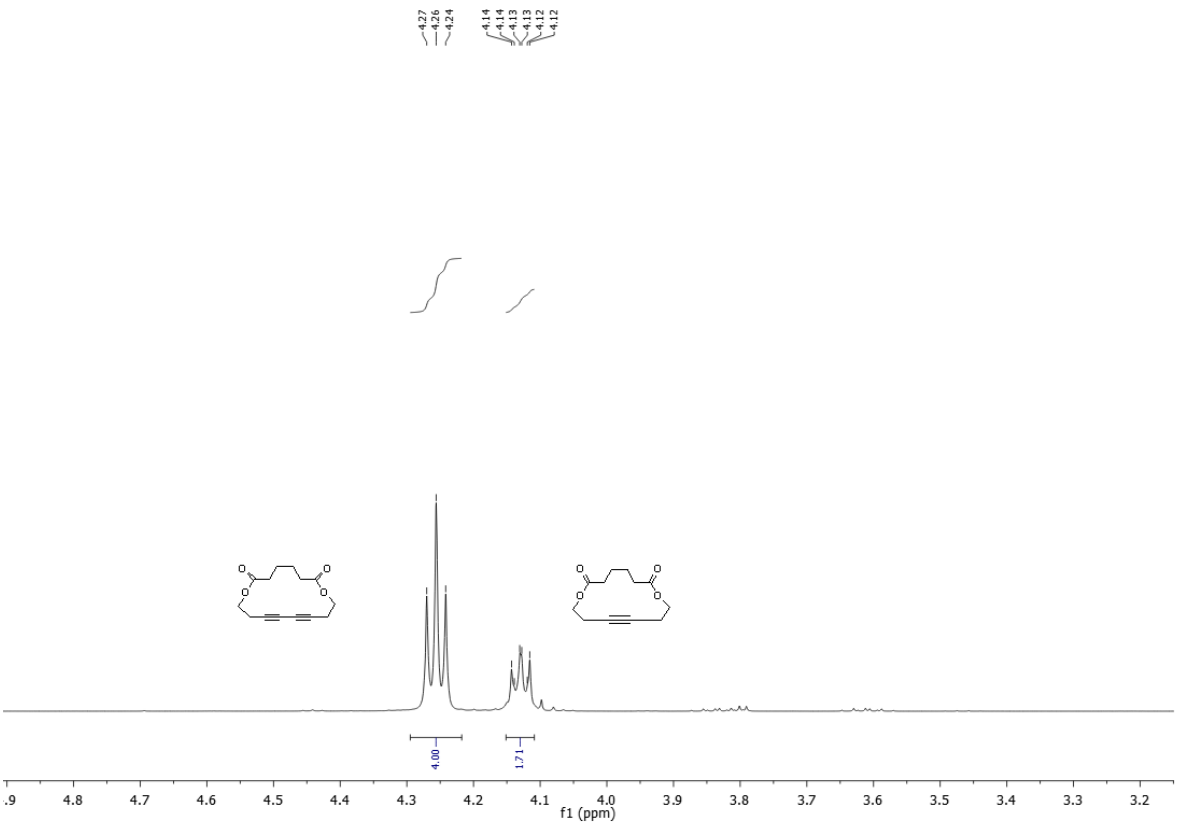
Di(hexa-3,5-diyn-1-yl) adipate (3c). TBAF (1 M in THF, 0.42 mL, 0.42 mmol) was added dropwise to a solution of compound **3b** (92.1 mg, 0.208 mmol) in THF (6 mL) at 0 °C, causing an immediate color change to dark red. Stirring was continued for 20 min at 0 °C before H_2O (5 mL) was added. The aqueous phase was extracted with Et_2O (3 x 5 mL), the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, 10% Et_2O in pentane) to yield the title compound as an orange solid which rapidly decomposes on standing (39 mg, 62%). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.18 (t, J = 6.6 Hz, 4H), 2.61 (td, J = 6.7, 1.2 Hz, 4H), 2.41 – 2.33 (m, 4H), 2.00 (t, J = 1.2 Hz, 2H), 1.77 – 1.63 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 73.9, 68.1, 66.2, 65.5, 61.5, 33.8, 24.4, 19.8; IR (film, cm^{-1}): 3263, 1731, 1370, 1259, 1177, 1146, 979; MS: m/z calcd for $C_{18}H_{18}O_4Na$: 321.10947, found 321.10973.



[1] J. Lee, J. S. Panek, *Org.Lett.* **2014**, *16*, 3320–3323.
[2] S. Lysenko, J. Volbeda, P. G. Jones, M. Tamm, *Angew. Chem. Int. Ed.* **2012**, *51,* 6757–6761.
[3] J. Heppekausen, R. Stade, A. Kondoh, G. Seidel, R. Goddard, A. Fürstner, *Chem. Eur. J.* **2012**, *18*, 10281-10299.

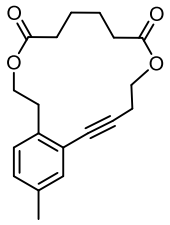
Representative Procedure for the Ring Closing Diyne Metathesis. **1,8-Dioxacyclohexadeca-11,13-diyne-2,7-dione (4).** A flame dried Schlenk flask was charged with activated 5 Å molecular sieves (300 mg). The flask was evacuated (10^{-2} mbar) and the molecular sieves were heated with a heat gun for 5 min. After cooling to room temperature, the flask was backfilled with argon before a solution of compound **3a** (50 mg, 0.15 mmol) in toluene (15 mL) was introduced. The suspension was stirred for 1 h before complex **7** (16.1 mg, 0.015 mmol, 10 mol%) was added. The resulting mixture was stirred for 16 h at ambient temperature. The insoluble materials were filtered off through a short pad of SiO_2, which was carefully rinsed with EtOAc. The combined filtrates were evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, 10% → 15% EtOAc in hexane) to yield macrocycle **4** (31.3 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.26 (t, *J* = 5.7 Hz, 4H), 2.58 (t, *J* = 5.7 Hz, 4H), 2.31- 2.43 (m, 4H), 1.67 – 1.79 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.2, 74.4, 67.6, 60.7, 35.0, 25.7, 20.3; IR (film, cm^{-1}): 2960, 1728, 1282, 1230, 1171, 1128, 1011; MS: *m/z* calcd for $C_{14}H_{16}O_4Na$: 271.09405, found 271.09408.

The exact same procedure was used for the cyclization of compound **3c** (30.0 mg) to give product **4** (22.3 mg, 88%). For the cyclization of substrate **3b** (66.1 mg) the mixture had to be heated to 60°C for 24 h; in this case, the product was an inseparable mixture of **4** and the ring contracted macrocycle **5**[4] (2.33:1, 32.1 mg, 53% calculated by NMR), cf. the following spectra:

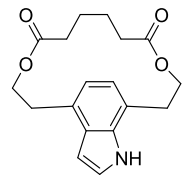


[4] Identified by comparison with an authentic sample, cf: J. Heppekausen, R. Stade, R. Goddard, A. Fürstner, *J. Am. Chem. Soc*. **2010**, *132*, 11045-11057.

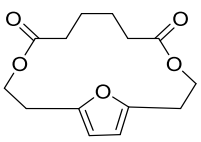
Compound 10. Compound **4** (5.0 mg, 0.021 mmol) and enyne **11** (2.71 mg, 0.042 mmol) were added to a solution of $Pd(PPh_3)_4$ (2.3 mg, 0.002 mmol, 10 mol%) in THF (0.3 mL) and the resulting mixture was stirred overnight at 65 °C until TLC analysis showed complete consumption of **4**. The mixture was filtered through a short pad of SiO_2, which was rinsed with EtOAc (5 mL). The combined filtrates were evaporated under reduced pressure and the crude product purified by flash chromatography (SiO_2, 10% EtOAc in hexane) to give the title compound as a yellow oil (5.6 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 7.8 Hz, 1H), 7.02 – 6.97 (m, 2H), 4.34 – 4.24 (m, 4H), 3.12 (t, *J* = 7.6 Hz, 2H), 2.79 (dd, *J* = 5.9, 4.9 Hz, 2H), 2.42 – 2.38 (m, 2H), 2.33 (m, 5H), 1.79 – 1.72 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.6, 173.4, 132.2, 139.4, 138.4, 129.5, 127.5, 120.8, 89.6, 80.1, 64.8, 62.8, 34.1, 33.7, 33.4, 24.4, 24.1, 21.6, 20.4; IR (cm^{-1}): 2924, 1732, 1458, 1340, 1238, 1144, 1066, 1030, 1005; MS: *m*/*z* calcd for $C_{19}H_{22}O_4Na$ 337.14083, found 337.14103.



11*H*-4,11-Dioxa-1(4,7)-indolacyclotridecaphane-5,10-dione (9). Pyrrole (13.0 mg, 0.2 mmol) and [BrettPhosAu(MeCN)SbF_6] (2.1 mg, 0.002 mmol, 10 mol%) were added to a solution of compound **4** (5 mg, 0.02 mmol) in 1,2-dichloroethane (0.2 mL) and the resulting mixture was stirred at 80 °C for 6 h. The mixture was filtered through a short pad of SiO_2 and the filtrate adsorbed on silica for purification by flash chromatography (15% EtOAc in Hexane). The resulting product was further purified by HPLC (Kromasil, C18, 5µm, 150 x 21.4 mm, MeOH/H_2O 80/20) to give the title compound as a dark green solid (1.2 mg, 21%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.93 (s, br N-H), 6.84 (td, *J* = 2.7, 1.5 Hz, 1H), 6.35 – 6.20 (m, 2H), 5.80 (t, *J* = 7.2 Hz, 1H), 4.37 (t, *J* = 5.6 Hz, 2H), 4.31 (t, *J* = 5.4 Hz, 2H), 2.78 (q, *J* = 6.1 Hz, 2H), 2.68 (t, *J* = 5.7 Hz, 2H), 2.39 – 2.33 (m, 2H), 2.30 – 2.25 (m, 2H), 1.69 – 1.62 (m, 4H); ^{13}C NMR (600 MHz, $CDCl_3$) δ = 174.1, 173.5, 131.6, 118.1, 109.6, 109.0, 62.7, 61.3, 35.2, 34.7, 32.1, 29.5, 25.6, 25.4, 22.9, 20.7, 14.3, 1.2; IR (cm^{-1}): 2925, 2854, 1730, 1460, 1283, 1243, 1175.

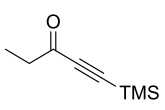


4,11-Dioxa-1(2,5)-furanacyclotridecaphane-5,10-dione (8). H_2O (72.0 mg, 4 mmol) and [SPhosAuNTf_2] (15.8 mg, 0.018 mmol, 5 mol%) were added to a solution of diyne **4** (90 mg, 0.362 mmol) in THF (4 mL). The resulting mixture was stirred at 60°C for 16 h before it was filtered through a short pad of SiO_2. The filtrate was evaporated and the crude material was purified by flash chromatography (SiO_2, 15% → 20% EtOAc in hexane) to yield the title compound as a white solid (59 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.02 (s, 2H), 4.34 – 4.30 (m, 4H), 2.96 – 2.92 (m, 4H), 2.30 – 2.24 (m, 4H), 1.55 – 1.49 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$):173.5, 151.6, 107.4, 63.2, 34.9, 27.8, 25.1; IR (cm^{-1}): 1731, 1279, 1170, 1141; MS: *m*/*z* calcd for $C_{14}H_{18}O_5Na$ 298.10454, found 289.10404.



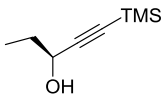
Total Synthesis of Ivorenolide B

1-(Trimethylsilyl)pent-1-yn-3-one (21). A mixture of bis[trimethylsilyl]acetylene (4.50 g, 26.5 mmol) and propionyl chloride (2.3 mL, 26.5 mmol) was added dropwise at 0 °C to a suspension of $AlCl_3$ (3.53 g, 26.5 mmol) in CH_2Cl_2 (80 mL). The mixture was stirred at this temperature for 1 h and at room temperature for an additional 1 h. After cooling to −78 °C, HCl (1 M, 20 mL) was added dropwise and the mixture was allowed to reach room temperature. The CH_2Cl_2 layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were dried ($MgSO_4$) and evaporated to yield the title compound



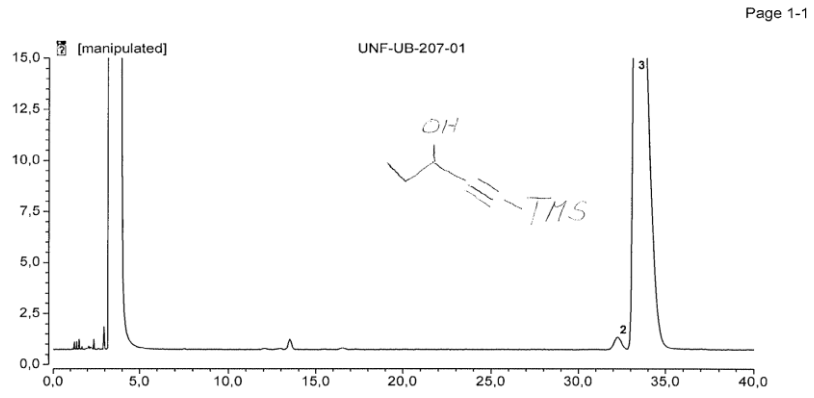
as a pale yellow liquid which was used in the next step without further purification (4.01 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.58 (q, *J* = 7.4 Hz, 2H), 1.13 (t, *J* = 7.4 Hz, 3H), 0.24 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 188.6, 102.0, 97.8, 38.8, 8.1, –0.6; IR (film, cm^{-1}): 1681, 1253, 1130, 846 MS: *m*/*z* calcd for $C_8H_{14}OSi$ 154.08125, found 154.08139.

(*S*)-1-(Trimethylsilyl)pent-1-yn-3-ol (22). Dichloro(*p*-cymene)ruthenium (II) dimer (25.1 mg, 0.041 mmol), (*1S,2S*)-(+)-*N*-*p*-tosyl-1,2-diphenylethylenediamine (30.0 mg, 0.082 mmol) and KOH (32.5 mg, 0.579 mmol) were added to a flask containing 1 mL of anhydrous CH_2Cl_2. The orange mixture was stirred for 10 min when a purple color appeared. Water (2 mL) and CH_2Cl_2 (2 mL) were added and the organic layer was separated and washed with water. The organic extract was then dried using CaH_2, filtered, and evaporated to give the activated catalyst as a purple solid (50.3 mg).



This catalyst was dissolved in anhydrous isopropanol (6 mL) to give an orange solution. A solution of ketone **21** (1.0 g, 6.5 mmol) in anhydrous isopropanol (3 mL) was added dropwise and the mixture was stirred for 30 min once the addition was complete. The solvent was carefully evaporated under reduced pressure and the residue purified by flash chromatography (SiO_2, 3% Et_2O in pentane) to yield the title compound as a pale yellow liquid (902 mg, 89%, *97% ee*). The spectral data were in good agreement with those reported in literature.[5] $[\alpha]_D^{20}$ = –4.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.31 (t, *J* = 6.5 Hz, 1H), 1.80 – 1.63 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 106.7, 89.6, 64.3, 30.9, 9.6, 0.03; IR (film, cm^{-1}): 2964, 1250, 1014, 967, 837; MS: *m*/*z* calcd for $C_8H_{16}OSiNa$: 179.08629, found 179.08626.

The enantiomeric excess (*ee*) was determined by GC/MS:



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Sequenz date: **19.01.15**
Instrument: **GC_412**
Measured: **19.01.15 10:48**
Processing M.: c17121 UNF-UB-207-01
Report-File: c17121 UNF-UB-207-01

chirale Messung, ee-Verhältnis
Probe gelöst in 100µL Toluol dest.
Zuordnung siehe GC/MS c17121 UNF-UB-207-01;15/94408/K und Racematprobe UNF-UB-266-01;3 15/94409/K
GC-Analyse ELNA Nr. 314

No.	Ret.Time min	Rel.Area %	Peak Name
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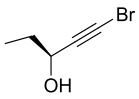
3	33,26	98,82	MG:156;2 c17121 = P4 UNF-UB-266-01

Instrument parameters:

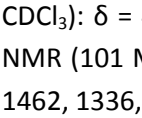
Column:	25,0 m	Hydrodex-ß-TBDAc-CD 0,25/ ?df G/625
Temperature:	220 / 65 iso / 350	
Gas:	0,50 bar	Hydrogen
Sample size:	0,2 µL	

[5] N. K. Bejjanki, A. Venkatesham, K. Balraju, K. Nagaiah, *Helv. Chim. Acta* **2013**, *96*, 1571-1578.

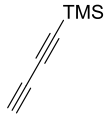
(*S*)-1-Bromopent-1-yn-3-ol (23). NBS (710.0 mg, 3.98 mmol) and $AgNO_3$ (89.0 mg, 0.52 mmol, 20 mol%) were added to a stirred solution of compound **22** (376.1 mg, 2.41 mmol) in anhydrous acetone (6 mL). The resulting mixture was stirred in the dark for 2 h. After cooling to 0 °C, the reaction was quenched by the addition of cold H_2O (10 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL), the combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, 4% → 5% Et_2O in pentane) to give the title compound as a pale yellow liquid (345 mg, 88%). $[\alpha]_D^{20} = -4.3$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.35 (t, *J* = 6.4 Hz, 1H), 2.17 (s, 1H, OH) 1.77 – 1.69 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 81.1, 64.8, 45.2, 30.9, 9.5; IR (film, cm^{-1}): 3332, 2969, 2936, 2878, 2210, 1462, 1336, 1117, 1100, 1054; MS: *m*/*z* calcd for C_5H_7BrONa 184.95732, found 184.95726.



(*S*)-Octa-4,6-diyn-3-ol (24). A round bottom flask was charged under air with aq. $BuNH_2$ (30% in water, 4 mL) and Cu(I)Cl (19.0 mg, 0.19 mmol, 10 mol%). The solution was cooled to −5 °C before liquid propyne (0.1 mL), which had been condensed into a separate flask, was added via a pre-cooled syringe. The resulting solution turned green. A few crystals of $NH_2OH{\cdot}HCl$ were added until a yellow color persisted. The solution was warmed to ambient temperature and bromoalkyne **23** (320.3 mg, 1.9 mmol) was added dropwise. During the addition, several portions of $NH_2OH{\cdot}HCl$ were added to maintain the yellow/golden color of the mixture. After complete addition, the mixture was stirred at room temperature until TLC showed complete conversion of **23**. The solution was transferred into a separation funnel and was extracted with Et_2O (4 x 10 mL). The combined extracts were successively washed with sat. aq. $CuSO_4$, brine and H_2O (10 mL each), and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2 10% → 15% Et_2O in pentane) to yield the title compound as a colorless oil (144 mg, 62%). $[\alpha]_D^{20} = -5.5$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.35 (t, *J* = 6.8 Hz, 1H), 1.94 (d, *J* = 1.0 Hz, 3H), 1.89 (s, 1H, OH) 1.78 – 1.67 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 75.8, 70.1, 66.0, 64.2, 63.8, 30.9, 9.5, 4.5; IR (film, cm^{-1}): 3362, 2970, 2936, 1460, 1333, 1379, 1335, 1280, 1238, 1097, 1047; MS: *m*/*z* calcd for $C_8H_{10}ONa$: 145.06245, found 145.06238.



Buta-1,3-diyn-1-yltrimethylsilane (15). A Schlenk flask was charged with Et_2O (40 mL) and bis-TMS-butadiyne (4.0 g, 20.0 mmol). The solution was cooled to 0 °C before MeLi (1.6 M in Et_2O, 20.6 mL, 24.0 mmol) was added over a period of 20 min. After the addition was complete, the solution was stirred at room temperature until GC/MS showed complete monodesilylation. The mixture was cooled to −78 °C and the reaction was carefully quenched by addition of sat. aq. NH_4Cl (20 mL). After warming to room temperature, the layers were separated and the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined extracts were dried over $MgSO_4$ and the solvent was carefully evaporated. The crude material was purified by distillation (bp. 55°C, 60 mbar) to yield the title compound as a colorless liquid which turns yellow upon standing (1.80 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 1H), 0.21 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 87.5, 84.9, 68.4, 66.8, −0.40; IR (film, cm^{-1}): 2960, 1250, 840, 759 MS: *m*/*z* calcd for $C_7H_{10}Si$ 122.05506, found 122.05518. The data are in accordance with those reported in the literature.[6]



[6] V. Fiandanese, D. Bottalico, G. Marchese, A. Punzi, *Tetrahedron* **2006**, *62*, 5126-5132.

(*Z*)-3-Iodopropenal (13). A 50 mL 3-neck flask equipped with a thermometer, a gas inlet and a rubber septum was charged with ethyl-(*Z*)-iodoacrylate (0.64 mL, 5.0 mmol) and CH_2Cl_2 (10 mL). The solution was cooled to −80 °C before DIBAL-H (1.0 M in CH_2Cl_2, 5.1 mL, 5.1 mmol) was very carefully added at such a rate as to maintain the internal temperature between −75 °C and −80 °C. After complete addition the reaction was stirred at −78 °C until GC/MS indicated complete consumption of the starting ester. The reaction was carefully quenched with cold anhydrous MeOH (2.5 mL). sat. aq. Rochelle salt solution (12.5 mL) was then added and the solution stirred for 30 min at room temperature before it was filtered through a pad of Celite. The filtrate was carefully evaporated under reduced pressure, keeping the temperature of the water bath at 0 °C. The crude aldehyde (810 mg, 86%) was not purified any further due to its instability. Rather, it was dissolved in toluene (8.1 mL); this solution can be stored under Ar at −20 °C for at least 3- 4 weeks without noticeable decomposition or isomerization of the double bond.

(*S,Z*)-1-Iodo-7-(trimethylsilyl)hepta-1-en-4,6-diyn-3-ol (16). A Schlenk flask equipped with a stir bar was charged with $Ph_3P{=}O$ (122.2 mg, 0.44 mmol, 20 mol%), (*R,R*)-**14** (140.0 mg, 0.22 mmol, 10 mol%) and toluene (9 mL). Diyne **15** (0.66 mL, 4.40 mmol) was added via syringe, followed by dimethylzinc (1.2 M in toluene, 3.65 mL, 4.40 mmol). The resulting alkynylzinc solution was stirred at room temperature for 30 min before it was cooled to 0 °C. A cold (0°C) solution of aldehyde **13** (400 mg, 4 mL of the previously prepared solution in toluene, 2.2 mmol) was added over the course of 1 h. The mixture was stirred at 0 °C for additional 3 h until TLC showed complete consumption of starting materials. The reaction was then quenched at −20 °C with sat. aq. NH_4Cl (10 mL) and the mixture was vigorously stirred for 10 min. The organic layer was separated and the aqueous phase extracted with Et_2O (3 x 15 mL). The combined extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 4% EtOAc in hexane) to yield the desired product as light yellow oil which darkens on standing (575 mg, 86%, 89% *ee*). $[\alpha]_D^{20}$ = +340.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.56 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.38 (t, *J* = 7.7 Hz, 1H), 5.18 (dd, *J* = 7.8, 4.2 Hz, 1H), 0.20 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.8, 89.1, 87.1, 85.3, 75.1, 71.0, 66.0, −0.4; IR (film, cm^{-1}): 2960, 1683, 1611, 1251, 1130; MS: *m/z* calcd for $C_{10}H_{13}IOSi$: 303.97812, found 303.97804. The absolute configuration was determined as (*S*) by the advanced Mosher Ester method.[7]

(*R*)-MTPA-Ester: (S)-*α*-Methoxy-*α*-trifluoromethyl phenylacetic acid chloride (10.0 mg, 0.064 mmol) was added to a solution of **16** (10.0 mg, 0.032 mmol) and pyridine (0.008 mL, 0.1 mmol) in CH_2Cl_2 (0.5 mL). After stirring for 16 h at room temperature, the reaction was quenched with water (5 mL). The aqueous phase was extracted with Et_2O (3 x 5 mL), the combined organic layers were dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The crude product was of sufficient purity for the determination of the absolute configuration.

(*S*)-MTPA-Ester. Prepared analogously, using (*R*)-*α*-methoxy-*α*-trifluoromethyl phenylacetic acid chloride as the reagent.

[7] T. Hoye, C. S. Jeffrey, F. Shao, *Nature Protocols* **2007**, *2*, 2451.

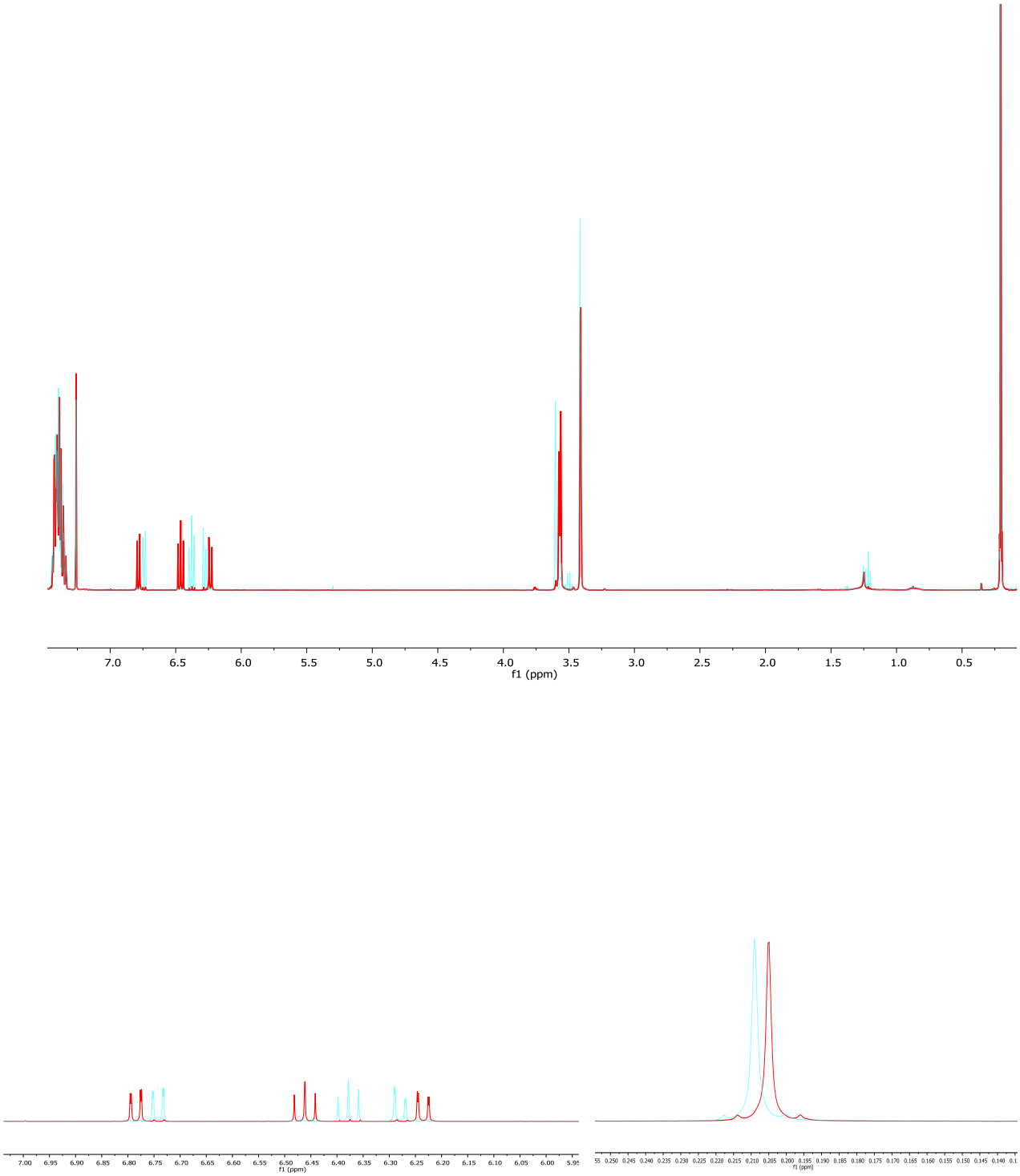
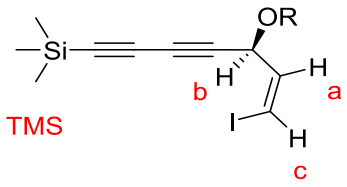


Figure S1. Superposition of the (*R*)-Mosher-ester (red) and the (*S*)-Mosher-ester (green) for the determination of the carbinol stereocenter in **16**.



Proton	(*R*)-MTPA	(*S*)-MTPA
a	6.44 – 6.48	6.36 – 6.40
b	6.22 – 6.25	6.27 – 6.29
c	6.77 – 6.80	6.73 – 6.75
TMS	0.205	0.209

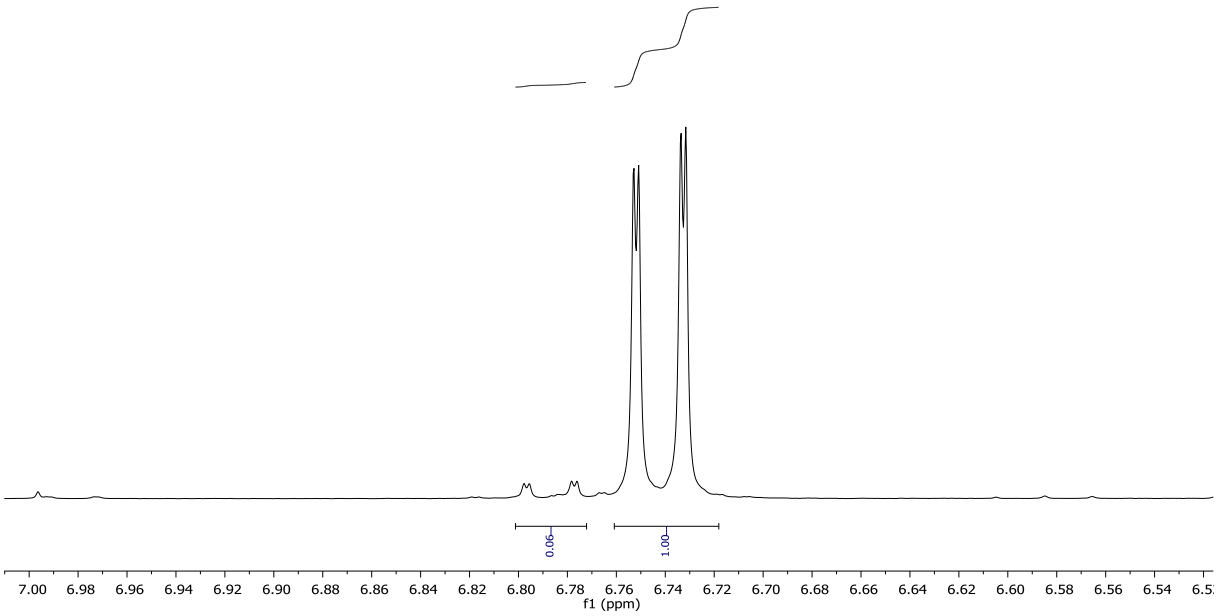
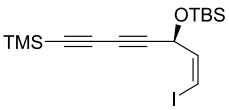


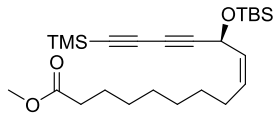
Figure S-2. Determination of the *ee* of **16** by integration of H_a in the spectra of the derived (*S*)-MTPA ester.

(*S,Z*)-*tert*-Butyl((1-iodo-7-(trimethylsilyl)hepta-1-en-4,6-diyn-3-yl)oxy)dimethylsilane (17). TBSCl (313.0 mg, 2.1 mmol), 1-methylimidazol (0.45 mL, 5.7 mmol) and I_2 (960.2 mg, 3.8 mmol) were successively added to a solution of alcohol **16** (575.0 mg, 1.9 mmol) in CH_2Cl_2 (8 mL) at 0 °C. The mixture was stirred at room temperature until TLC indicated complete consumption of starting material. The reaction was quenched with sat. aq. $Na_2S_2O_3$ (10 mL) and stirring was conintued until the orange color



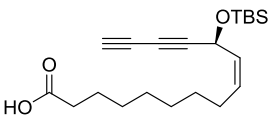
disappeared (ca. 30 min). The organic layer was separated and the aqueous layer extracted with Et_2O (3 x 10 mL). The combined extracts were washed with brine and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 1% EtOAc in hexane), yielding the product as a yellow oil (785 mg, 98%). $[\alpha]_D^{20}$ = +221.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.41 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.31 (t, *J* = 7.6 Hz, 1H), 5.14 (dd, *J* = 7.6, 0.9 Hz, 1H), 0.90 (s, 9H), 0.19 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.0, 88.1, 87.4, 83.0, 76.0, 69.8, 67.1, 25.8, −0.3, −4.4, −4.6; IR (film, cm^{-1}): 2957, 2929, 2857, 2108, 1253, 1076, 1005; MS: *m*/*z* calcd for $C_{16}H_{27}OISi_2Na$: 441.05379, found 441.05374.

Methyl (*S,Z*)-11-((tert-butyldimethylsilyl)oxy)-15-(trimethylsilyl)pentadeca-9-en-12,14-diynoate (20). A Schlenk flask was charged with Zn dust (65.4 mg, 1.0 mmol) and I_2 (12.3 mg, 0.05 mmol, 10 mol%). The flask was evacuated for ca. 30 sec before it was backfilled with Ar. DMF (0.5 mL) was added and the resulting slurry was vigorously stirred until the orange color had disappeared (2-4 min.). At this point, methyl 8-iodoocatanoate (142.2 mg, 0.5 mmol) was added via syringe and the mixture was heated to 75 °C for 4 h. After reaching ambient temperature the remaining zinc dust was allowed to settle (20 min), yielding a ca. 1 M solution of the organozinc compound **19**.



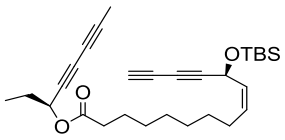
A second Schlenk flask was charged with alkenyl iodide **17** (81.1 mg, 0.2 mmol), $Pd(PPh_3)_2Cl_2$ (7.1 mg, 0.01 mmol, 5 mol%), TMEDA (0.045 mL, 0.3 mmol) and THF (0.5 mL). The mixture was stirred for 5 min before an aliquot of the freshly prepared solution of **19** (0.28 mL, 0.28 mmol) was added dropwise. Stirring was continued for 14 h before the reaction was quenched with sat. aq. NH_4Cl and EtOAc (5 mL each). The organic layer was separated and the aqueous phase extracted with EtOAc (3 x 5 mL). The combined extracts were evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, 0.5% EtOAc in hexane) to yield the title compound which contained a trace impurity that could not be removed (75.5 mg, 68% yield based on NMR purity). $[\alpha]_D^{20}$ = +43.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.50 – 5.41 (m, 2H), 5.17 – 5.14 (m, 1H), 3.66 (s, 3H), 2.30 (t, *J* = 7.6 Hz, 2H), 2.10 – 2.00 (m, 2H), 1.67 – 1.57 (m, 2H), 1.41 – 1.33 (m, 2H), 1.34 – 1.24 (m, 6H), 0.89 (s, 9H), 0.18 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 174.5, 132.0, 129.4, 87.7, 87.4, 78.3, 69.1, 59.5, 51.6, 34.3, 29.4, 29.3, 29.2, 29.1, 27.8, 25.9, 25.1, 18.3, −0.3, −4.4, −4.6; IR (film, cm^{-1}): 2952, 2930, 2857, 1742, 1252, 1075; MS: *m*/*z* calcd for $C_{25}H_{44}O_3Si_2Na$: 471.27210, found 471.27212.

(*S,Z*)-11-((*tert*-Butyldimethylsilyl)oxy)pentadeca-9-en-12,14-diynoic acid (S-1). A 10 mL flask open to air was charged with methyl ester **20** (40.1 mg, 0.089 mmol) and THF (0.6 mL). An aqueous solution of LiOH (6.5 mg in 0.3 mL water, 0.271 mmol) was added. The reaction was stirred at room temperature for 6.5 h until TLC showed complete consumption of the starting material. The pH was adjusted to 3 – 4 by dropwise addition of aqueous HCl (0.1 M). The organic phase was separated and the aqueous layer was extracted with Et_2O (4 x 5 mL), the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (SiO_2, 10% → 15% EtOAc in hexane) to give the title compound as a pale yellow oil, which had to be stored under Ar at −20°C due to its instability (25.2 mg, 78%). $[\alpha]_D^{20}$ = +62.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 – 5.43 (m, 2H), 5.17 – 5.14 (m, 1H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.18 (d, *J* = 1.0 Hz, 1H), 2.10 – 2.04 (m, 2H), 1.69 – 1.59 (m, 2H), 1.45 – 1.23 (m, 8H), 0.89 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 180.6, 132.3, 129.3, 77.4, 77.0,



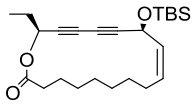
68.4, 67.9, 59.4, 33.9, 31.8, 29.3, 29.2, 29.2, 29.1, 27.9, 25.9, 24.8, –4.4, –4.6; IR (film, cm^{-1}): 2928, 2856, 1709, 1253, 1076, 838; MS: *m*/*z* calcd for $C_{21}H_{34}O_3SiNa$: 385.21693, found 385.21694.

(*S*)-Octa-4,6-diyn-3-yl (*S,Z*)-11-((*tert*-butyldimethylsilyl)oxy)pentadeca-9-en-12,14-diynoate (**25**).



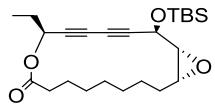
EDC·HCl (22.1 mg, 0.115 mmol) and DMAP (6.5 mg, 0.069 mmol) were added to a solution of alcohol **24** (6.5 mg, 0.053 mmol) and acid **S-1** (17.0 mg, 0.046 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The cooling bath was removed and the mixture was stirred for 16 h at room temperature The reaction was quenched with H_2O (2 mL) and excess base was neutralized with HCl (1 M). The phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 mL). The combined extracts were dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash chromatography (SiO_2, 1% EtOAc in hexane) to yield the title compound as a colorless syrup (13.2 mg, 62%). $[\alpha]_D^{20}$ = +18.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 – 5.43 (m, 2H), 5.34 (td, *J* = 6.4, 1.0 Hz, 1H), 5.17 – 5.14 (m, 1H), 2.35 – 2.29 (m, 2H), 2.18 (d, *J* = 1.0 Hz, 1H), 2.08 – 2.04 (m, 2H), 1.93 (d, *J* = 1.0 Hz, 3H), 1.78 (qd, *J* = 7.4, 6.4 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.41 – 1.35 (m, 2H), 1.30 – 1.24 (m, 6H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 132.3, 129.3, 77.0, 72.4, 70.4, 68.4, 67.9, 65.2, 63.8, 59.4, 34.4, 29.9, 29.3, 29.2, 29.2, 29.1, 28.2, 27.9, 25.9, 25.0, 18.4, 9.5, 4.4, 1.2, –4.4, –4.6; IR (film, cm^{-1}): 2929, 2856, 1739, 1252, 1073, 837, 805; MS: *m*/*z* calcd for $C_{29}H_{42}O_3SiNa$: 489.27961, found 489.27954.

(*12S,17S,Z*)-12-((*tert*-Butyldimethylsilyl)oxy)-17-ethyloxacycloheptadeca-10-en-13,15-diyn-2-one (26). A Schlenk flask was charged with pre-dried molecular sieves (4 Å and 5 Å, 100 mg each). The



flask was evaporated and the molecular sieves were dried for 5 min with a heat gun. After reaching ambient temperature, the flask was backfilled with Ar and a solution of compound **25** (20 mg, 0.042 mmol) in toluene (4.4 mL) was introduced. The mixture was stirred for 1 h before complex **7** (8.7 mg, 0.008 mmol, 20 mol%) was added. The pale orange mixture was stirred for 16 h at room temperature before a second batch of the catalyst (20 mol%) was added. Stirring was continued for 6 h until TLC showed complete conversion. The suspension was filtered through a small pad of silica which was rinsed with EtOAc (20 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 0.3% → 2% EtOAc in hexane) to give product **26** contaminated with traces of triphenylsilanol (17.8 mg, comprising 14.2 mg of product, 82%) which were best removed after the next step. $[\alpha]_D^{20}$ = –21.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 – 5.42 (m, 2H), 5.28 (td, *J* = 6.7, 1.0 Hz, 1H), 5.21 (d, *J* = 4.7 Hz, 1H), 2.39 – 2.27 (m, 2H), 2.10 – 2.01 (m, 2H), 1.83 – 1.75 (p, 2H), 1.72 – 1.60 (m, 2H), 1.44 – 1.29 (m, 8H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.5, 132.1, 130.8, 80.9, 77.7, 69.8, 68.3, 65.3, 59.9, 34.6, 30.4, 29.7, 29.3, 28.7, 27.3, 26.5, 25.9, 18.4, 9.6, 1.2, –4.5, –4.8; IR (film, cm^{-1}): 2929, 2856, 1741, 1257, 1077, 909, 836; MS: *m*/*z* calcd for $C_{24}H_{38}O_3Si$: 402.25897, found 402.25902.

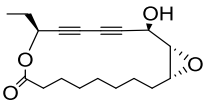
(*1R,2R,7S,17R*)-2-((*tert*-Butyldimethylsilyl)oxy)-7-ethyl-8,18-dioxabicyclo[15.1.0]octadeca-3,5-diyn-9-one (S-2). *m*-CPBA (26.0 mg, 0.12 mmol) was added in one portion to a solution of alkene **26** (15.1



mg, 0.04 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The cooling bath was removed and the solution stirred for 8 h. The reaction was quenched by addition of sat. aq. $NaHCO_3$ solution (3 mL) and the resulting mixture was stirred for 15 min before it was extracted with EtOAc (3 x 5 mL). The combined extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2 3% →

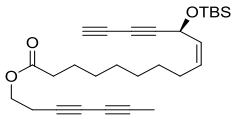
5% EtOAc in hexane) to give the title compound as a colorless oil (13.1 mg, 80%). $[\alpha]_D^{20}$ = –14.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.28 (td, *J* = 6.7, 0.9 Hz, 1H), 4.23 (dd, *J* = 7.2, 0.9 Hz, 1H), 3.15 (dd, *J* = 7.3, 4.3 Hz, 1H), 2.96 (ddd, *J* = 11.0, 4.3, 2.9 Hz, 1H), 2.47 – 2.43 (m, 1H), 2.41 – 2.37 (m, 1H), 2.04 – 1.96 (m, 2H), 1.82 (q, *J* = 7.3 Hz, 2H), 1.75 – 1.61 (m, 2H), 1.46 – 1.22 (m, 8H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.91 (s, 9H), 0.13 (d, *J* = 2.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.2, 77.9 69.8, 69.1, 65.1, 63.9, 61.5, 56.5, 34.5, 30.3, 30.0, 29.1, 28.0, 27.2, 26.4, 25.9, 25.8, 18.4, 9.6, 1.2, –4.7, –4.8; IR (film, cm^{-1}): 2932, 1731, 1279, 1170; MS: *m*/*z* calcd for $C_{24}H_{38}O_4SiNa$: 441.24348, found 441.24316.

Ivorenolide B (1). TBAF (1 M in THF, 0.043 mmol, 0.043 mL) was added dropwise via syringe to a solution of compound **S-2** (12.1 mg, 0.029 mmol) in THF (1.0 mL) at 0 °C. After stirring for 30 min at 0 °C, the reaction was quenched with sat. aq. NH_4Cl (2 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 mL). The combined extracts were dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, 10% → 15% EtOAc in hexane) to yield the title compound as a colorless oil (6.5 mg, 74%). $[\alpha]_D^{20}$ = –9.3 (*c* = 0.2, MeOH); ^{1}H NMR (600 MHz, C_5D_5N): δ = 8.42 (s, 1H, OH) 5.49 (td, *J* = 6.7, 0.9 Hz, 1H), 4.86 (d, *J* = 7.6, Hz, 1H), 3.59 (dd, *J* = 7.6, 4.3 Hz, 1H), 3.11 (ddd, *J* = 10.8, 4.3, 2.9 Hz, 1H), 2.48 – 2.37 (m, 2H), 2.00 – 1.94 (m, 1H), 1.81 – 1.76 (m, 2H), 1.71 – 1.64 (m, 1H), 1.63 – 1.56 (m, 1H), 1.55 – 1.51 (m, 1H), 1.48 – 1.41 (m, 1H) 1.36 – 1.17 (m, 7H) 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (600 MHz, C_6D_5N): δ = 173.0, 80.4, 78.8, 69.8, 69.8, 65.6, 62.7, 61.9, 56.7, 34.7, 30.6, 30.4, 29.5, 28.5, 27.5, 26.8, 26.2, 9.7; IR (film, cm^{-1}): 2928, 2857, 1741, 1462, 1236, 1085, 1041, 981; MS: *m*/*z* calcd for $C_{18}H_{24}O_4Na$: 327.15688, found 327.15668.

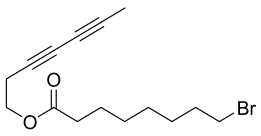


Analogue

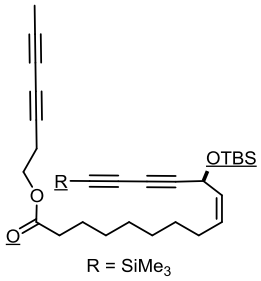
Hepta-3,5-diyn-1-yl (*S,Z*)-11-((*tert*-butyldimethylsilyl)oxy)pentadeca-9-en-12,14-diynoate (29a). 2,4,6-Trichlorobenzoyl chloride (0.005 mL, 0.035 mmol) was added to a solution of acid **S-1** (10.1 mg, 0.027 mmol) and Et_3N (0.011 mL, 0.082 mmol) in toluene (1 mL) at 0 °C. The ice bath was removed and the mixture was stirred for 90 min at room temperature. DMAP (11.7 mg, 0.096 mmol) was introduced, followed by a solution of hepta-3,5-diyne-1-ol (2.9 mg, 0.027 mmol) in toluene (0.4 mL). The mixture was stirred for 3 h before the reaction was quenched with sat. aq. $NaHCO_3$ and EtOAc (2 mL each). The organic layer was separated and the aqueous phase was extracted with EtOAc (3 x 5 mL), the combined extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by flash chromatography (SiO_2, 0.5% → 1% EtOAc in hexane) to yield the title compound as a yellow oil (9.4 mg, 74%). $[\alpha]_D^{20}$ = +53.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 – 5.43 (m, 2H), 5.17 – 5.12 (m, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 2.58 (tq, *J* = 6.6, 1.1 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.18 (d, *J* = 1.0 Hz, 1H), 2.10 – 2.03 (m, 2H), 1.90 (t, *J* = 1.2 Hz, 3H), 1.66 – 1.57 (m, 2H), 1.43 – 1.35 (m, 2H), 1.35 – 1.24 (m, 6H), 0.89 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.7, 132.3, 129.3, 77.0, 74.0, 72.2, 68.4, 67.9, 66.9, 64.3, 61.8, 59.4, 34.3, 29.3, 29.2, 29.2, 29.2, 27.9, 25.9, 25.0, 19.9, 18.4, 4.3, –4.4, –4.6; IR (film, cm^{-1}): 2927, 2855, 1737, 1463, 1252, 1168, 1074, 838; MS *m*/*z* calcd for $C_{28}H_{40}O_3SiNa$ 475.26413, found 475.26389.



Hepta-3,5-diyn-1-yl 8-bromooctanoate (28). DMAP (149.1 mg, 1.11 mmol) and DCC (1.53 g, 7.2 mmol,) were successively added to a solution of hepta-3,5-diyne-1-ol (400 mg, 3.7 mmol) and bromoctanoic acid (946 mg, 4.25 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The mixture was stirred overnight at room temperature before the reaction was quenched with sat. aq. NaCl (20 mL). The aqueous phase was extracted with EtOAc (4 x 10 mL), the combined extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by flash chromatography (SiO_2, 5% EtOAc in hexane) to give the title compound as a yellow oil (994 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.14 (t, *J* = 6.7 Hz, 2H), 3.39 (t, *J* = 6.8 Hz, 2H), 2.60 – 2.55 (m, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.90 (t, *J* = 1.2 Hz, 3H), 1.88 – 1.79 (m, 2H), 1.65 – 1.59 (m, 2H), 1.45 – 1.39 (m, 2H), 1.35 – 1.29 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.6, 74.0, 72.2, 66.9, 64.3, 61.8, 34.2, 34.1, 32.8, 29.0, 28.5, 28.1, 24.9, 19.8, 4.3; IR (film, cm^{-1}): 2932, 2856, 1734, 1234, 1164, 1121; MS *m*/*z* calcd for $C_{15}H_{21}BrO_3Na$ 335.06168, found 335.06172.

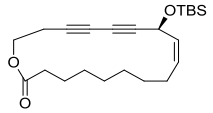


6-(Trimethylsilyl)hexa-3,5-diyn-1-yl (*S,Z*)-11-((*tert*-butyldimethylsilyl)oxy)hexadeca-9-en-12,14-diynoate (29b). A Schlenk flask was charged with Zn dust (32.6 mg, 0.5 mmol) and I_2 (3.5 mg, 0.012 mmol, 5 mol%). The flask was evacuated for 30 sec and then backfilled with Ar. DMF (0.5 mL) was added and the suspension was vigorously stirred until the orange color disappeared (2-4 min.) Alkyl bromide **28** (78.3 mg, 0.25 mmol) was added via syringe and the solution was stirred at 75 °C for 4 h. After cooling to room temperature, the remaining zinc dust was allowed to settle (20 min) yielding an orange solution of the corresponding organozinc compound (ca. 0.5 M).

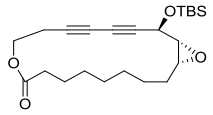


In the meantime, a second Schlenk flask was charged with alkenyl iodide **17** (41.1 mg, 0.1 mmol), $PdCl_2$ (0.8 mg, 0.005 mmol, 2 mol%), tri-*o*-tolylphosphine (4.6 mg, 0.015 mmol, 6 mol%) and THF (0.5 mL). The mixture was stirred for 5 min before the freshly prepared solution of the organozinc reagent (0.28 mL, 0.14 mmol) was added dropwise. The mixture was stirred for 4 h before the reaction was quenched with sat. aq. NH_4Cl solution and EtOAc (5 mL each). The organic layer was separated and the aqueous layer was extracted with EtOAc, the combined extracts were evaporated and the residue was purified by flash chromatography (SiO_2, 0.5% EtOAc in hexane) to yield the title compound as a colorless syrup (18.5 mg, 36%). $[\alpha]_D^{20}$ = 93.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.51 – 5.40 (m, 2H), 5.18 – 5.13 (m, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 2.58 (td, *J* = 6.7, 1.2 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.10 – 2.01 (m, 2H), 1.90 (d, *J* = 1.2 Hz, 3H), 1.66 – 1.58 (m, 2H), 1.41 – 1.22 (m, 8H), 0.88 (s, 9H), 0.18 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.7, 132.0, 129.3, 87.7, 87.4, 78.3, 74.0, 72.2, 69.0, 66.9, 64.3, 61.8, 59.5, 34.3, 29.4, 29.3, 29.2, 29.2, 27.8, 25.9, 25.0, 19.9, 18.3, 4.4, –0.3, –4.4, –4.6; IR (film, cm^{-1}): 2928, 2856, 2105, 1738, 1251, 1165, 1072, 839; MS *m*/*z* calcd. for $C_{31}H_{48}O_3Si_2Na$ 547.30372, found 547.30342.

(*S,Z*)-12-((*tert*-Butyldimethylsilyl)oxy)oxacyclooctadeca-10-en-13,15-diyn-2-one (30). A Schlenk flask was charged with activated molecular sieves (4 Å, 52 mg; 5 Å, 54 mg). The flask was evacuated and the molecular sieves were dried for 5 min with a heat gun. After reaching ambient temperature, the flask was backfilled with argon and a solution of compound **29a** (12 mg, 0.026 mmol) in toluene (2.8 mL) was introduced. The suspension was stirred for 1 h before complex **7** (2.7 mg, 0.0026 mmol, 10 mol%) was added. The resulting pale orange mixture was stirred for 16 h until TLC showed complete conversion of the starting material.

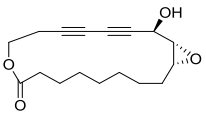


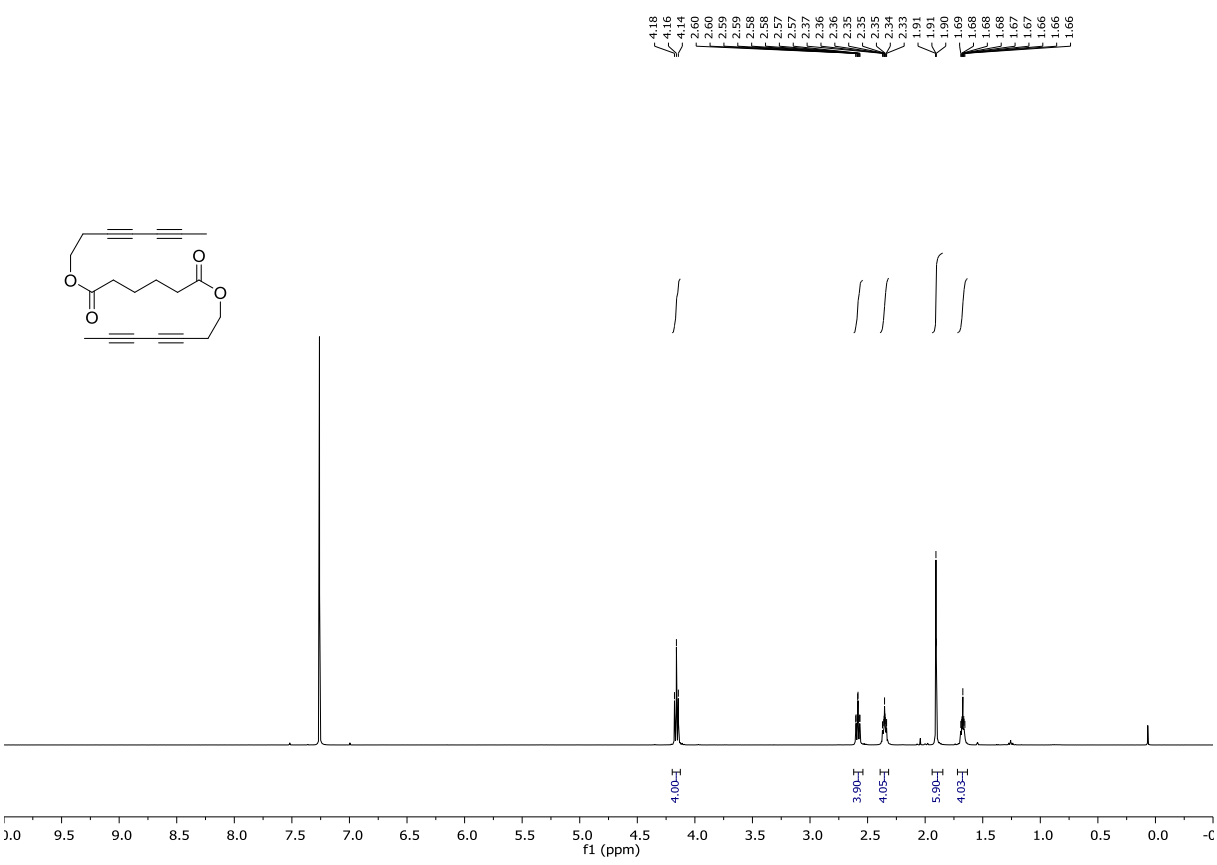
The mixture was filtered through a small pad of silica, which was rinsed with EtOAc (15 mL). The combined filtrates were evaporated under reduced pressure and the residue was purified by flash chromatography (SiO_2, 0.5% → 2% EtOAc in hexane) to give the title compound as a colorless oil (8.4 mg, 82%). The cyclization of compound **29b** was performed analogously. $[\alpha]_D^{20}$ = +39.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.53 – 5.35 (m, 2H), 5.22 – 5.18 (m, 1H), 4.24 – 4.11 (m, 2H), 2.64 (ddt, *J* = 8.1, 4.8, 1.1 Hz, 2H), 2.38 – 2.28 (m, 2H), 2.15 – 2.03 (m, 2H), 1.70 – 1.58 (m, 2H), 1.40 – 1.29 (m, 6H), 1.24 – 1.18 (m, 2H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0, 131.4, 130.8, 77.3, 76.7, 69.1, 66.4, 61.6, 59.8, 35.3, 30.1, 29.7, 29.3, 29.0, 28.3, 26.1, 25.9, 20.1, 1.2, −4.5, −4.6; IR (film, cm^{-1}): 2957, 2928, 2856, 1731, 1274, 1075; MS *m*/*z* calcd for $C_{23}H_{36}O_3SiNa$ 411.23228, found 411.23259.

(*1R,2R,18R*)-2-((*tert*-Butyldimethylsilyl)oxy)-9,19-dioxabicyclo[16.1.0]nonadeca-3,5-diyn-10-one (S-3). 

m-CPBA (10.8 mg, 0.063 mmol) was added in one portion to a solution of compound **30** (7.0 mg, 0.018 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The ice bath was removed and the solution stirred for 16 h until TLC showed complete conversion of the starting material. The reaction was quenched by addition of sat. aq. $NaHCO_3$ (3 mL) and the mixture was extracted with EtOAc (3 x 5 mL). The combined extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, 3% → 5% EtOAc in hexane) to yield the title compound as a yellow oil (5.3 mg, 74%). $[\alpha]_D^{20}$ = +5.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.26 – 4.13 (m, 3H), 3.14 (dd, *J* = 7.7, 4.2 Hz, 1H), 2.96 (ddd, *J* = 10.6, 4.3, 2.8 Hz, 1H), 2.70 – 2.64 (m, 2H), 2.39 – 2.34 (m, 2H), 2.09 – 1.97 (m, 2H), 1.71 – 1.57 (m, 2H), 1.53 – 1.36 (m, 6H), 1.18 – 1.09 (m, 2H), 0.91 (s, 9H), 0.14 (d, *J* = 2.4 Hz, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 174.0, 78.0, 73.4, 70.9, 65.7, 63.7, 61.6, 61.0, 57.0, 34.6, 30.2, 30.2, 28.9, 28.6, 27.1, 26.1, 25.9, 25.9, 20.1, −4.6, −4.7; IR (film, cm^{-1}): 2927, 2856, 1738, 1253, 1076, 1005; MS *m*/*z* calcd for $C_{23}H_{36}O_4SiNa$ 427.22797, found 427.22751.

(*1S,2R,18R*)-2-Hydroxy-9,19-dioxabicyclo[16.1.0]nonadeca-3,5-diyn-10-one (31). TBAF (1 M in THF, 0.015 mL, 0.015 mmol) was added dropwise at 0°C to a solution of compound **S-3** (5.3 mg, 0.012 mmol) in THF (0.85 mL). The resulting yellow solution was stirred at 0 °C for 10 min before the reaction was quenched with sat. aq. NH_4Cl (1 mL). The phases were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 5 mL). The combined extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (SiO_2, 15% → 20% EtOAc in hexane) to give the title compound as a colorless solid (3.0 mg, 83%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.28 – 4.23 (m, 2H), 4.16 (ddd, *J* = 10.7, 6.3, 4.3 Hz, 1H), 3.39 – 3.34 (m, 1H, OH), 3.17 (dd, *J* = 8.2, 4.2, Hz, 1H), 3.03 (ddd, *J* = 10.7, 4.2, 2.9 Hz, 1H), 2.70 – 2.66 (m, 2H), 2.40 – 2.33 (m, 2H), 2.15 – 2.06 (m, 1H), 1.69 – 1.62 (m, 2H), 1.51 – 1.45 (m, 2H), 1.43 – 1.32 (m, 5H), 1.20 – 1.13 (m, 2H); ^{13}C NMR (600 MHz, $CDCl_3$): δ = 173.7, 78.5, 72.0, 71.9, 65.4, 62.5, 61.3, 60.3, 57.5, 34.6, 30.2, 30.0, 28.9, 28.2, 25.9, 25.8, 20.0; IR (film, cm^{-1}): 2923, 2853, 1735, 1462, 1261, 1038, MS *m*/*z* calcd for $C_{17}H_{22}O_4Na$ 313.14065, found 313.14103.

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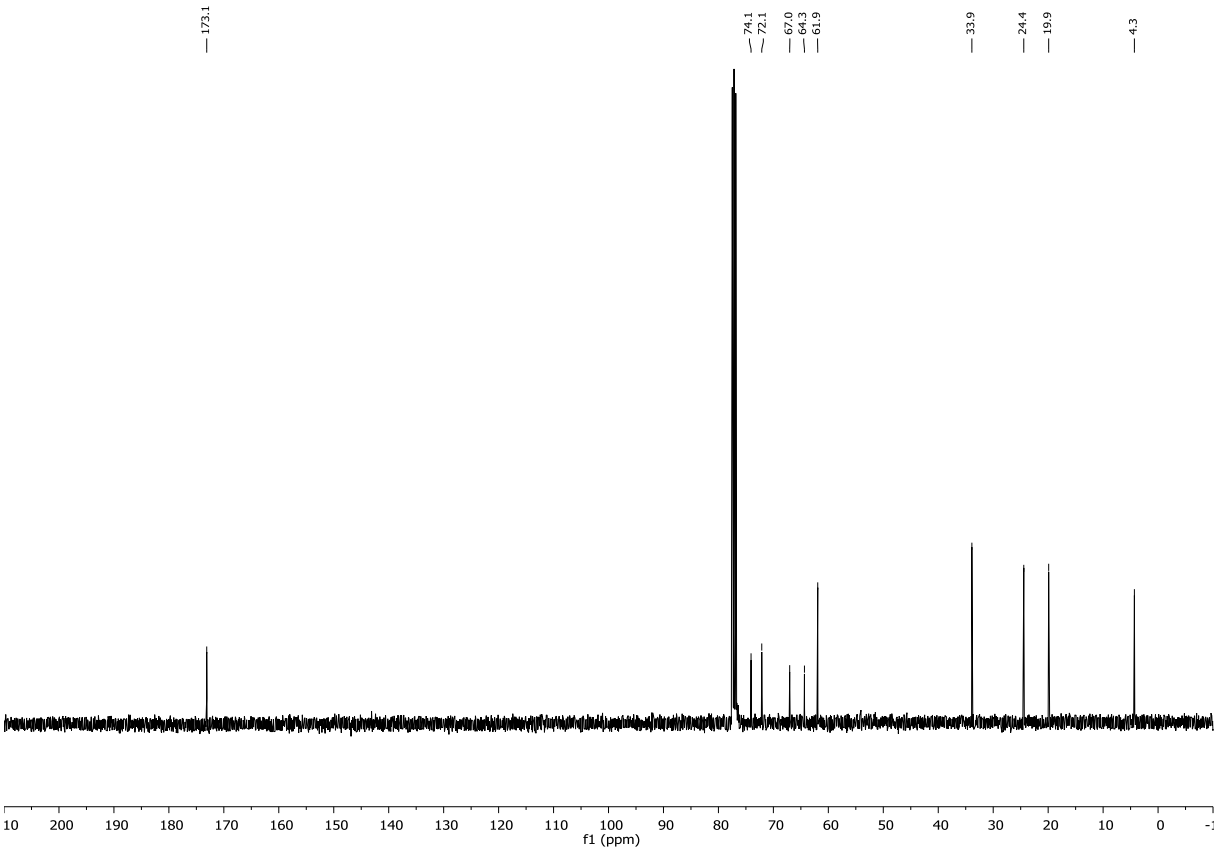
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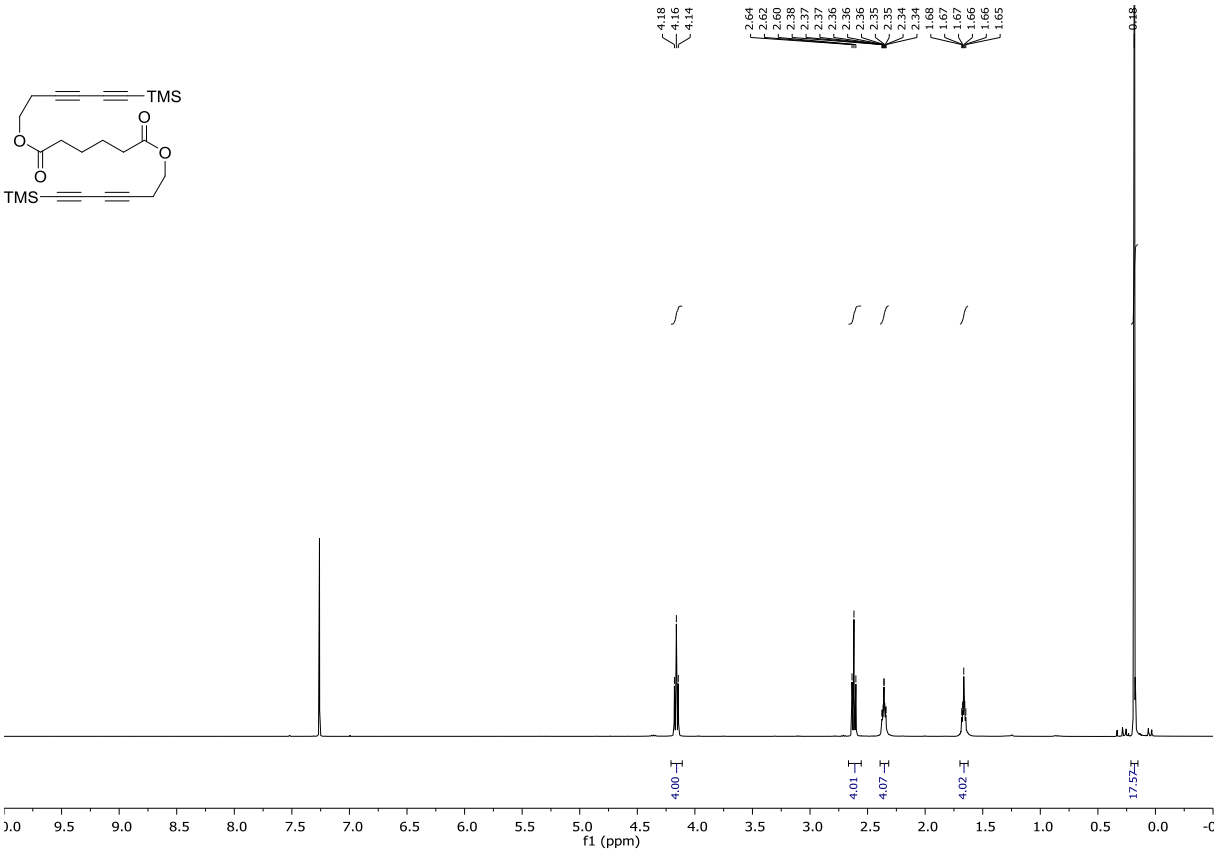
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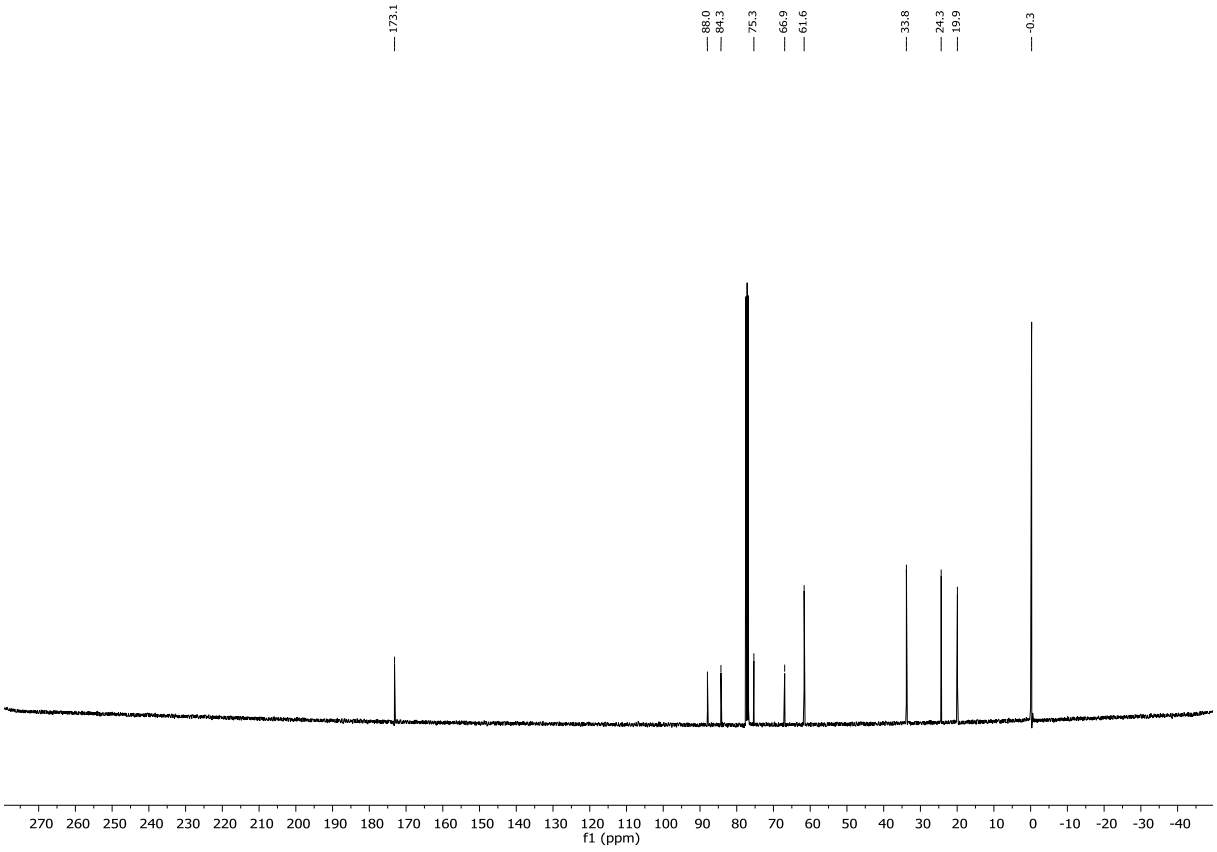
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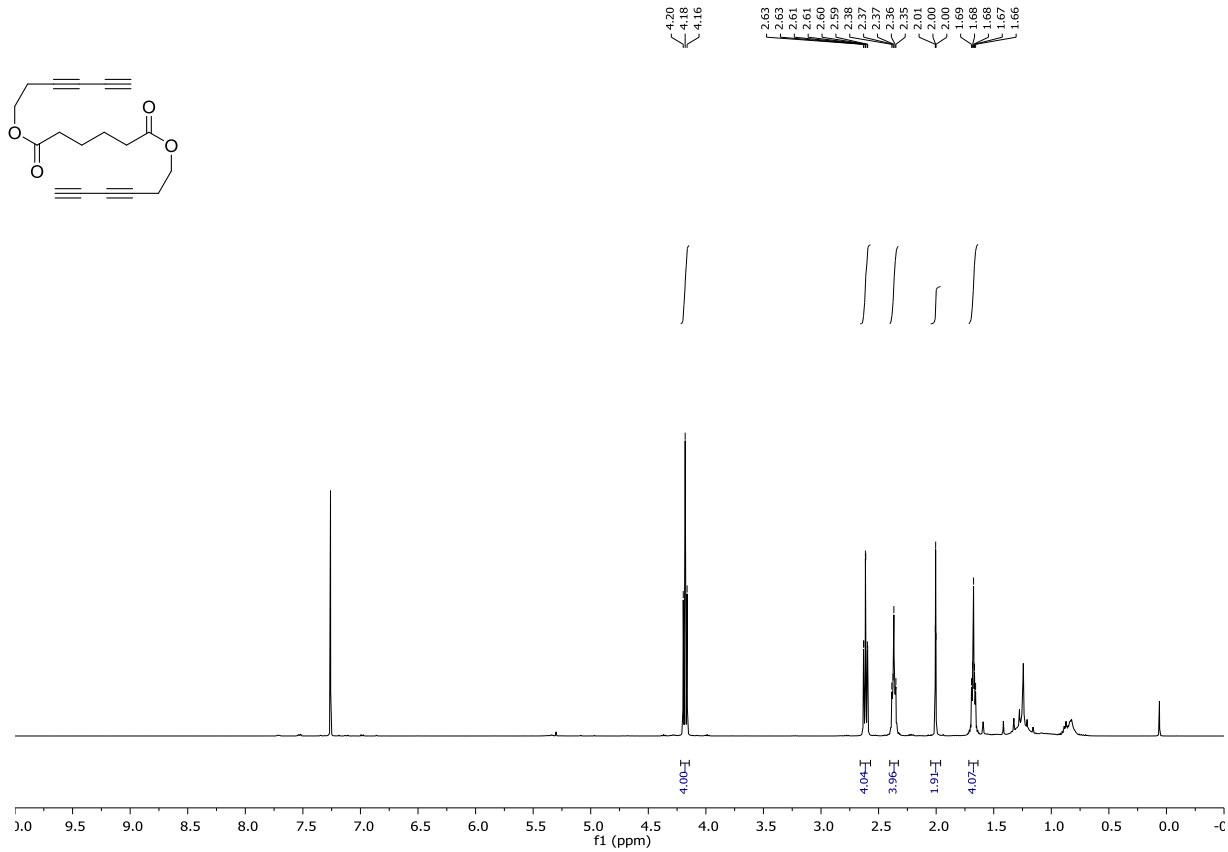
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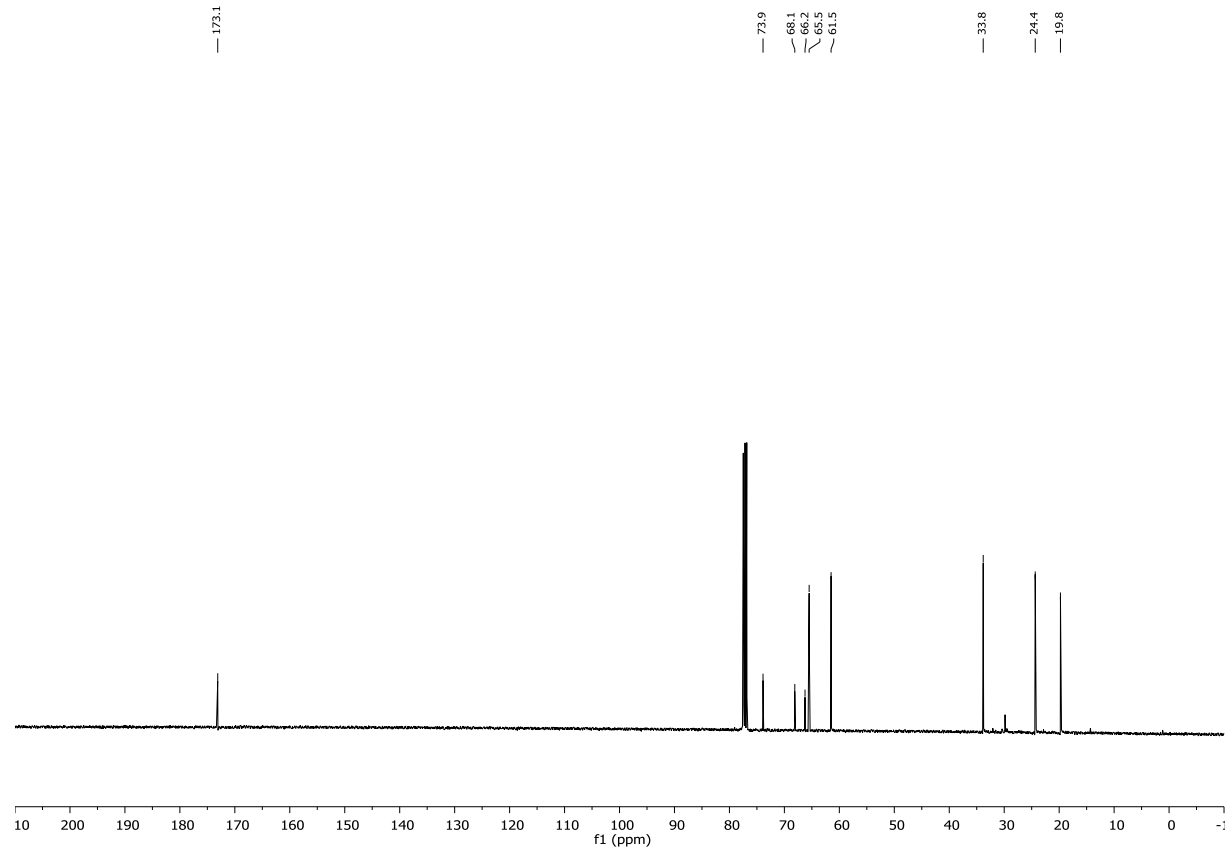
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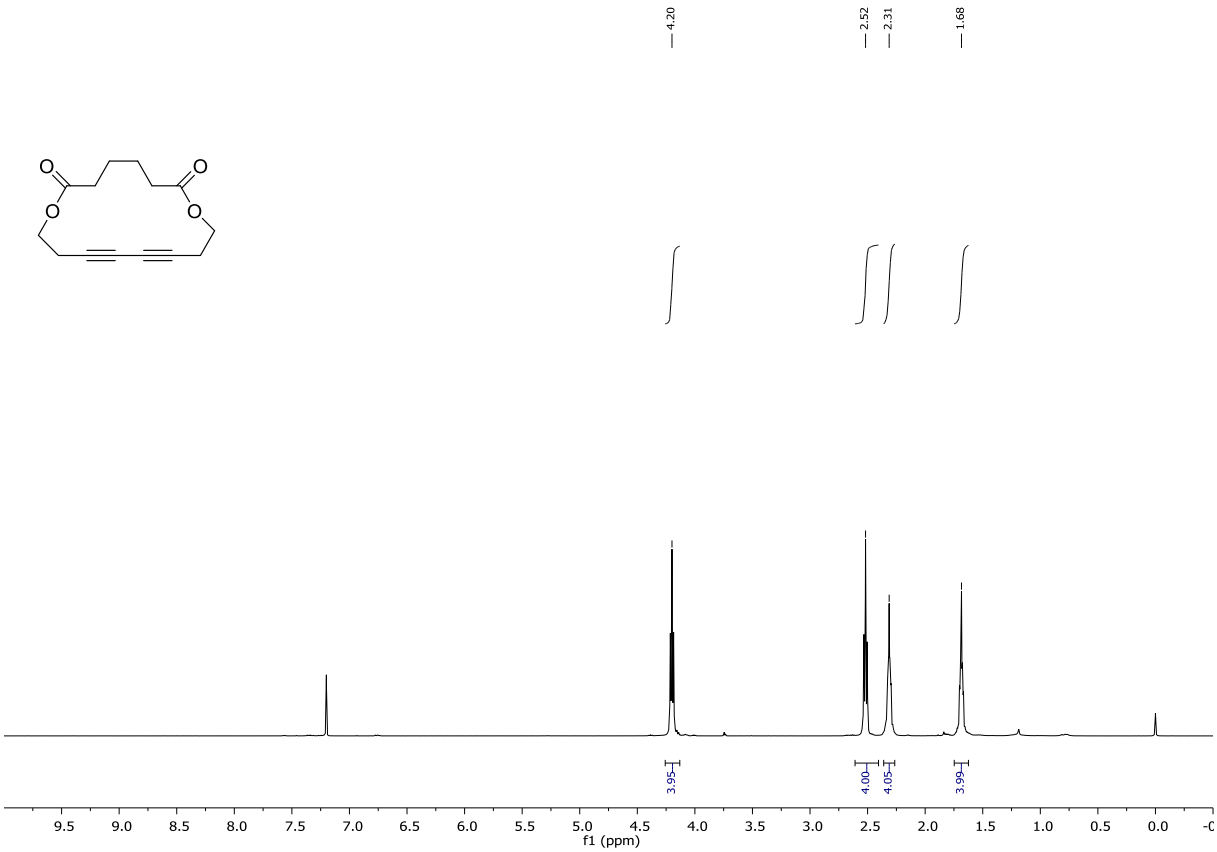
f1 (ppm)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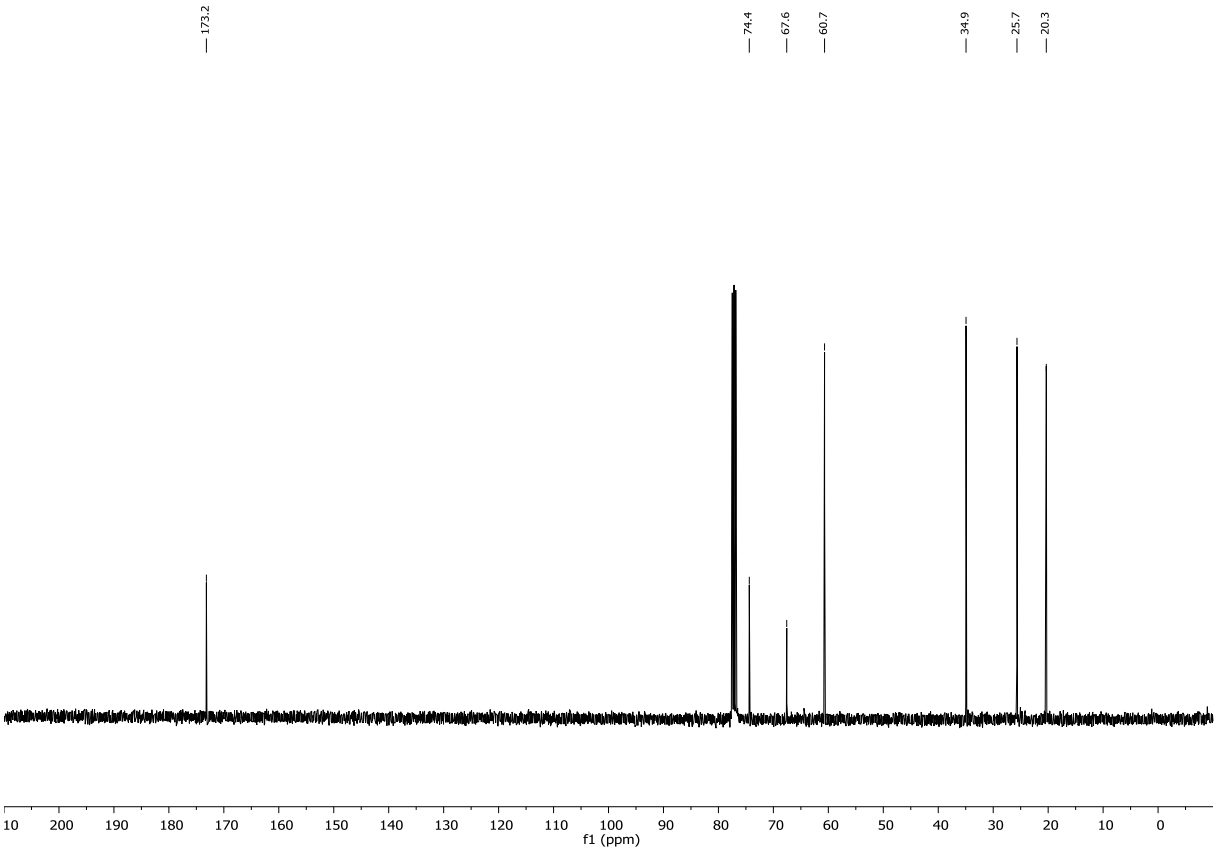
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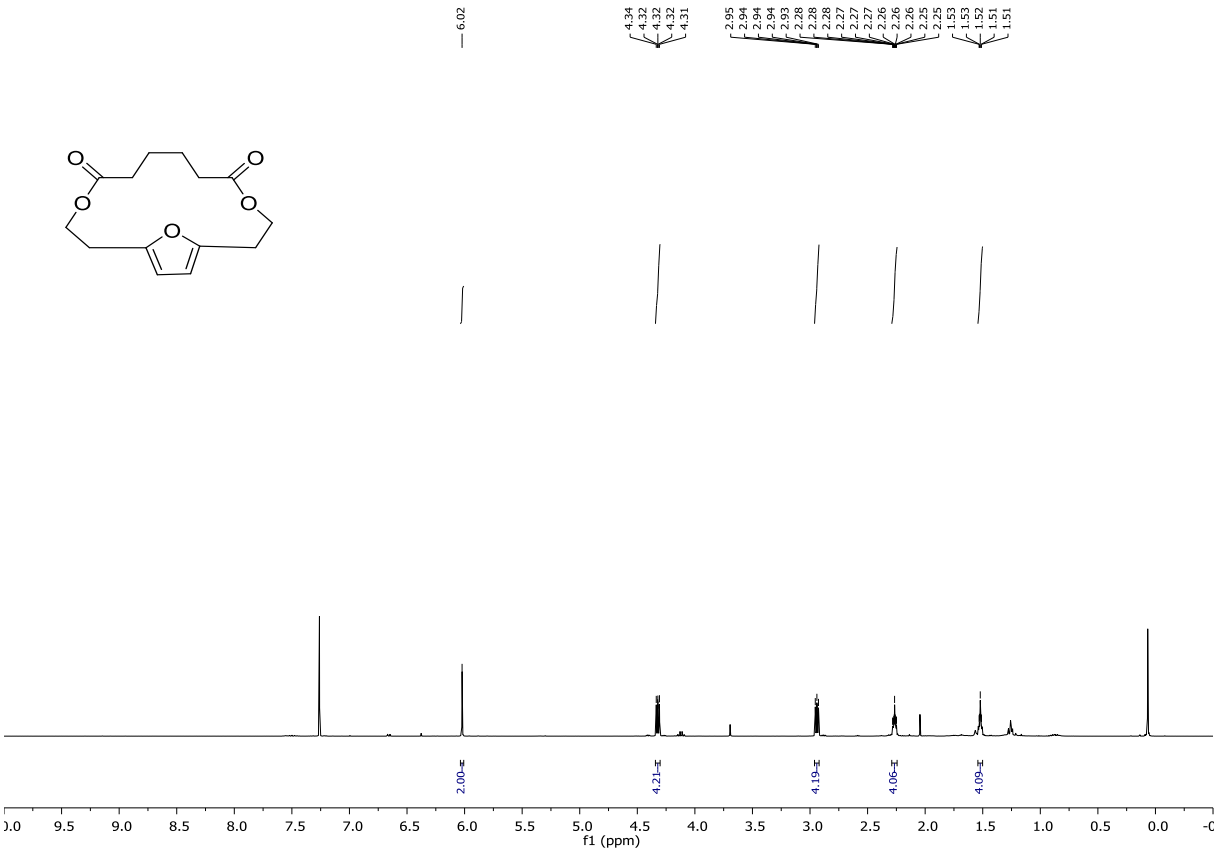
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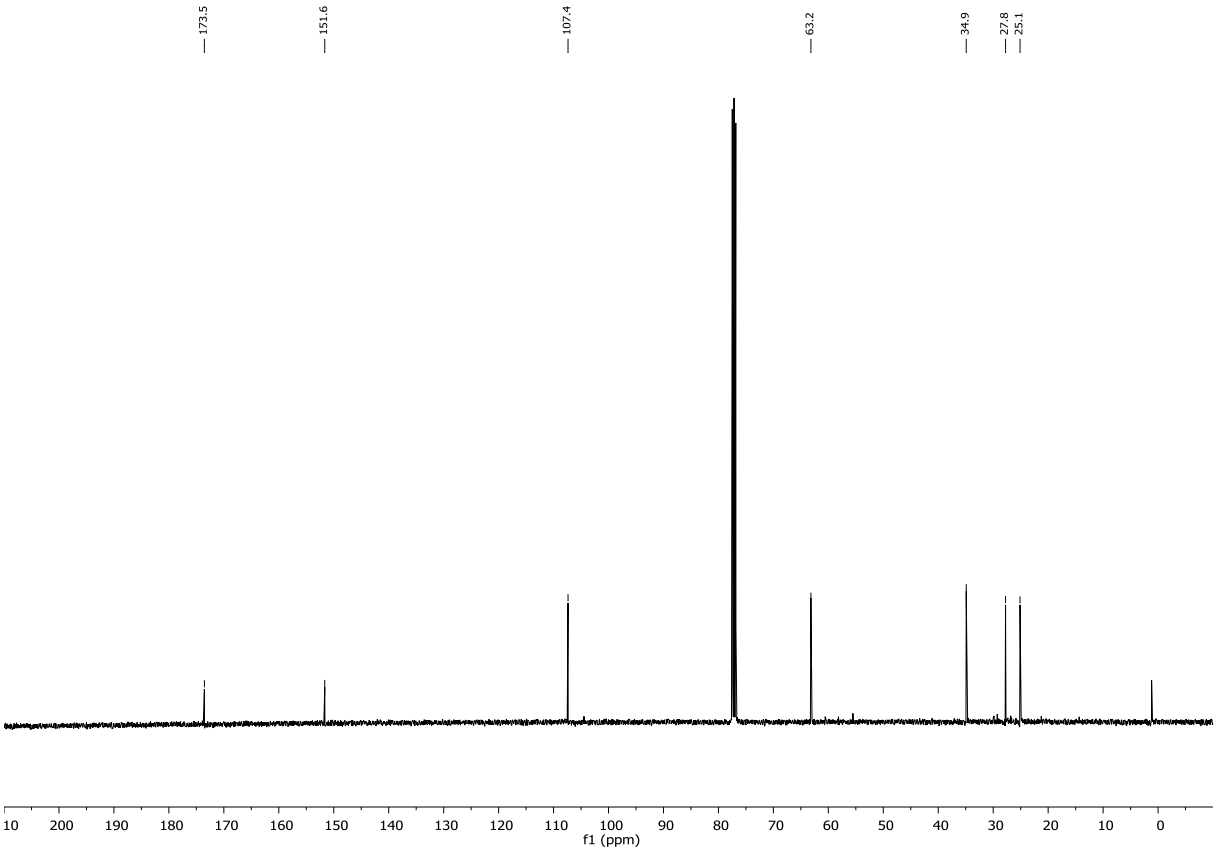
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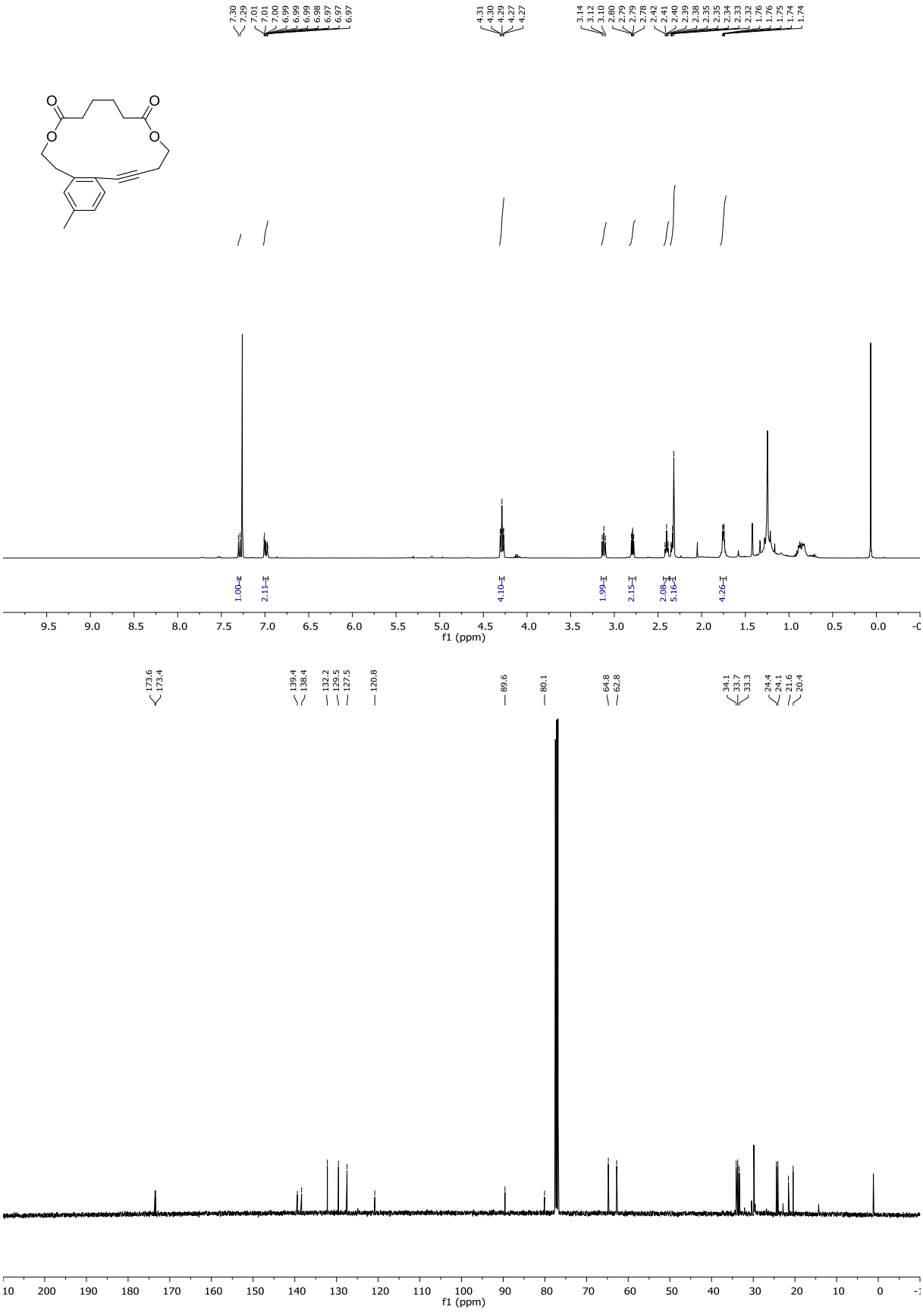
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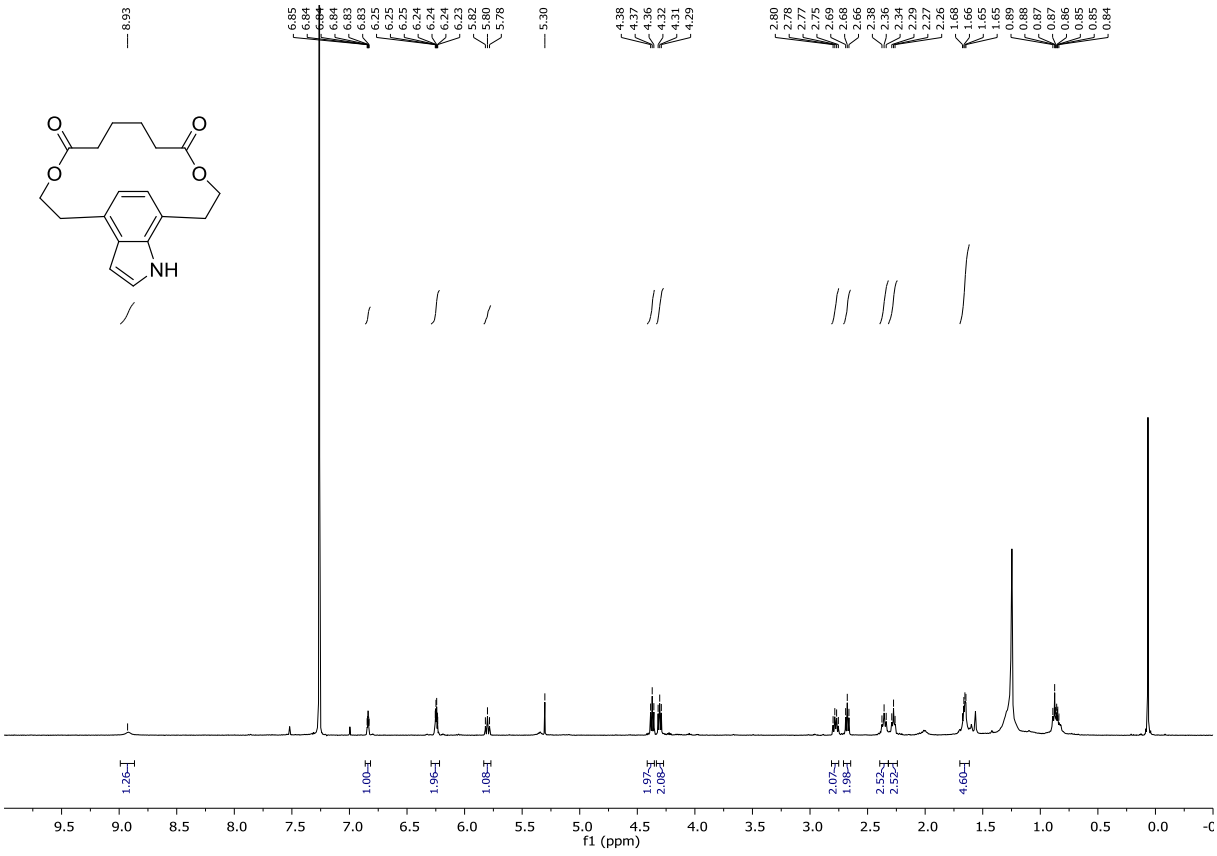
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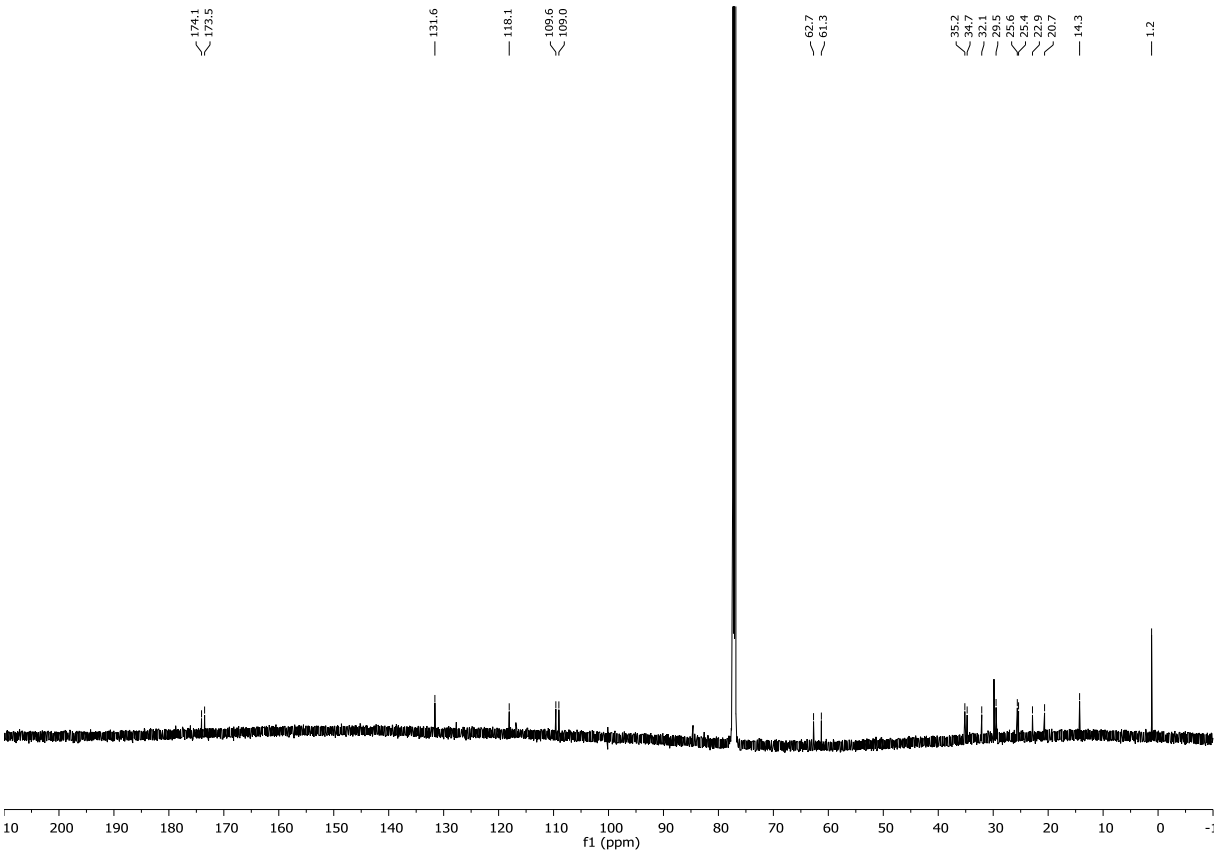
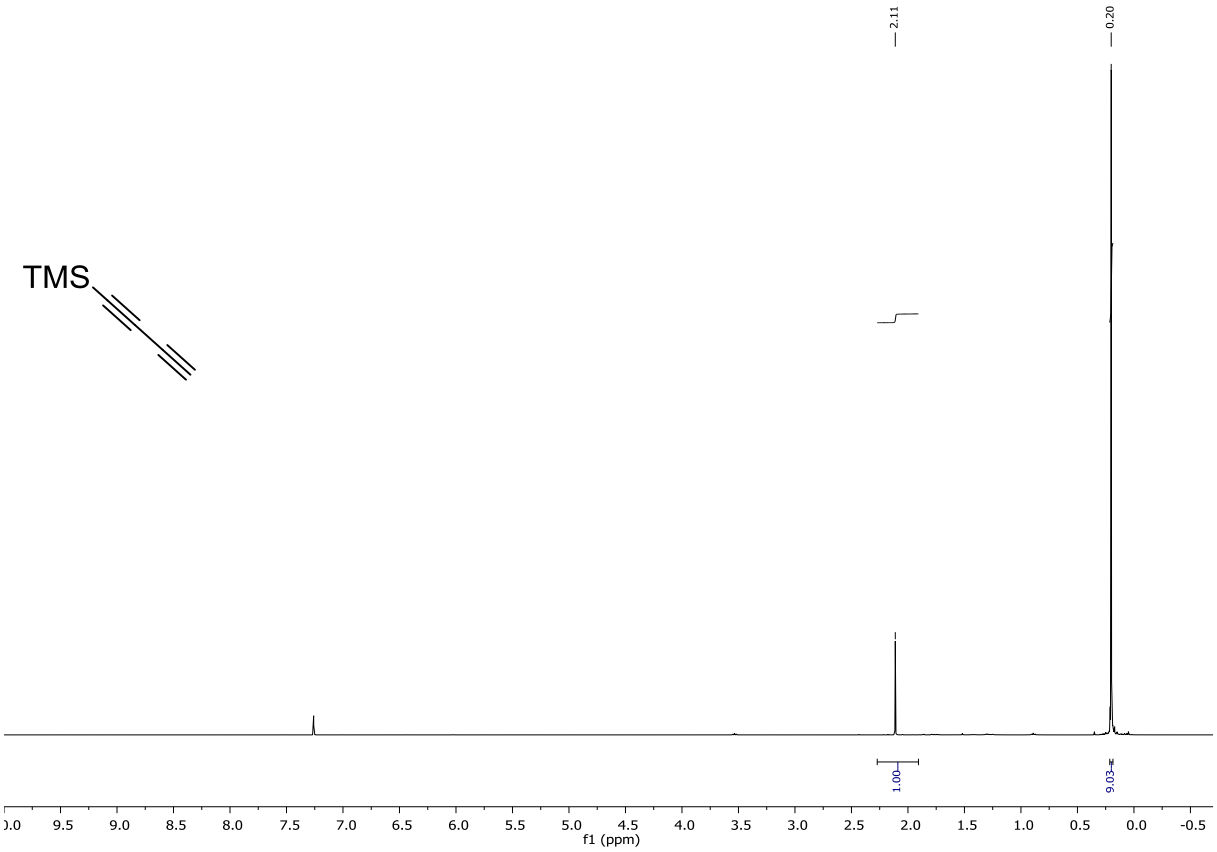
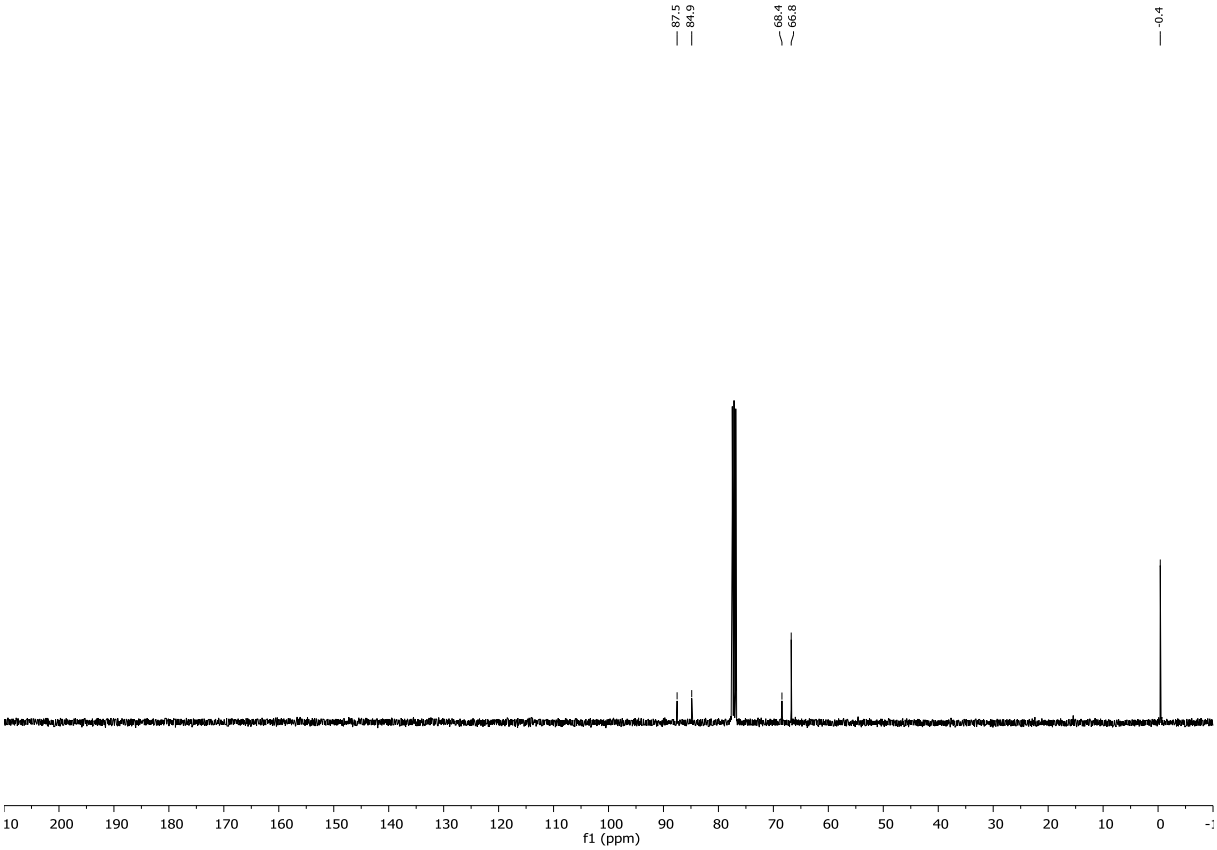
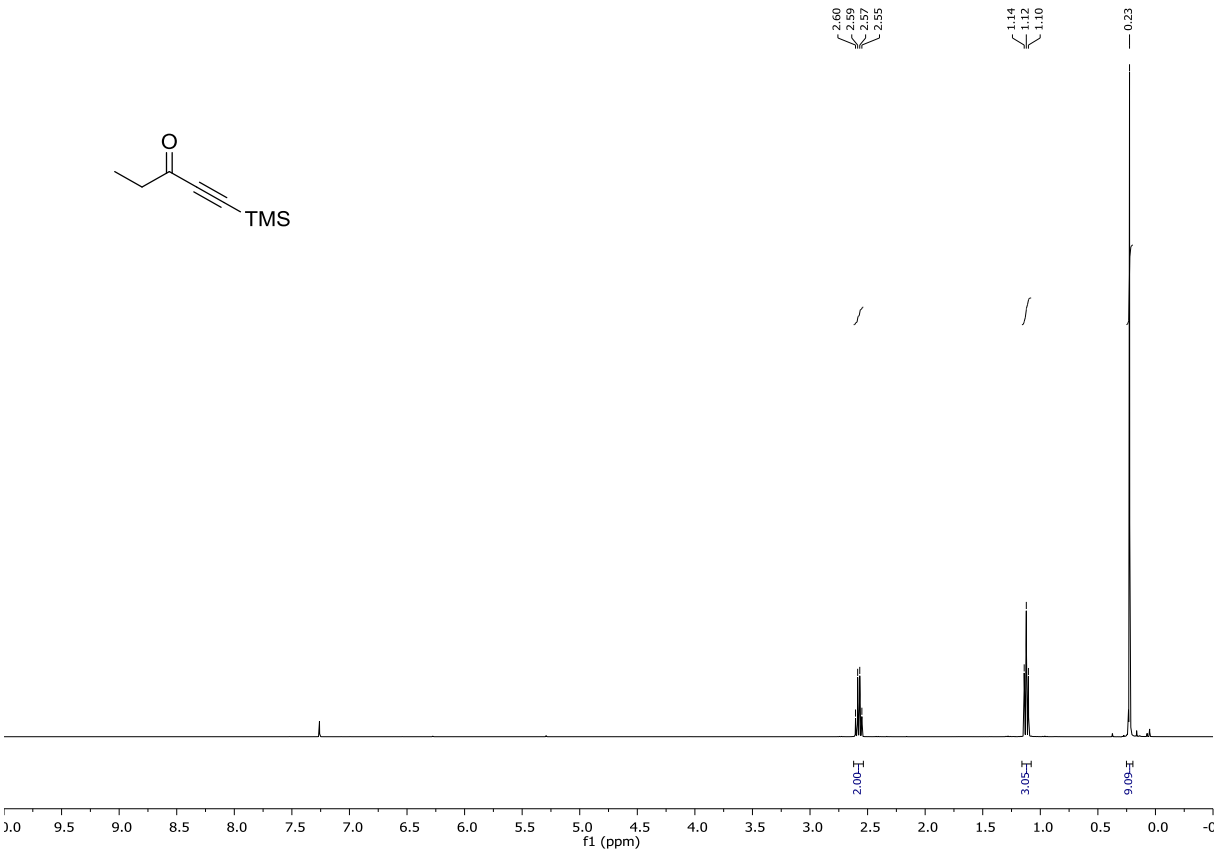
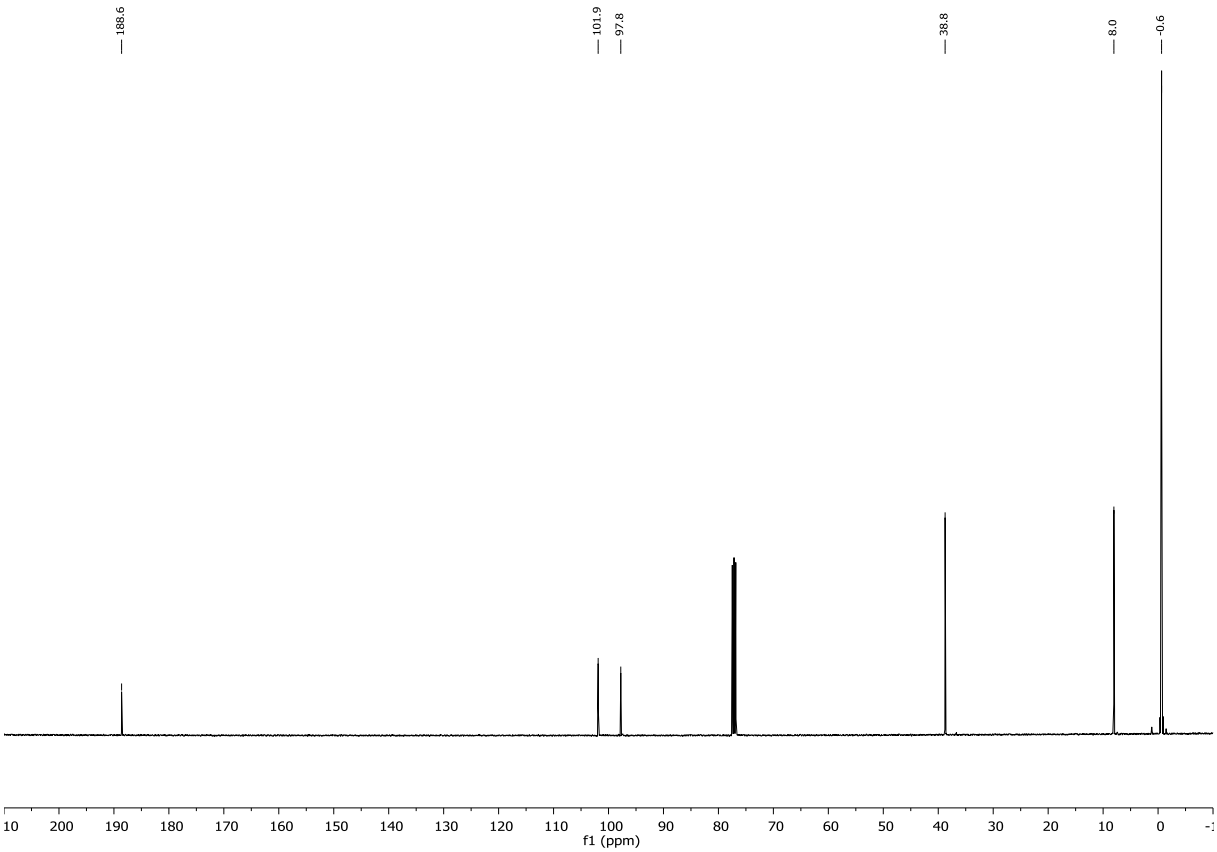
4.60
f1 (ppm)

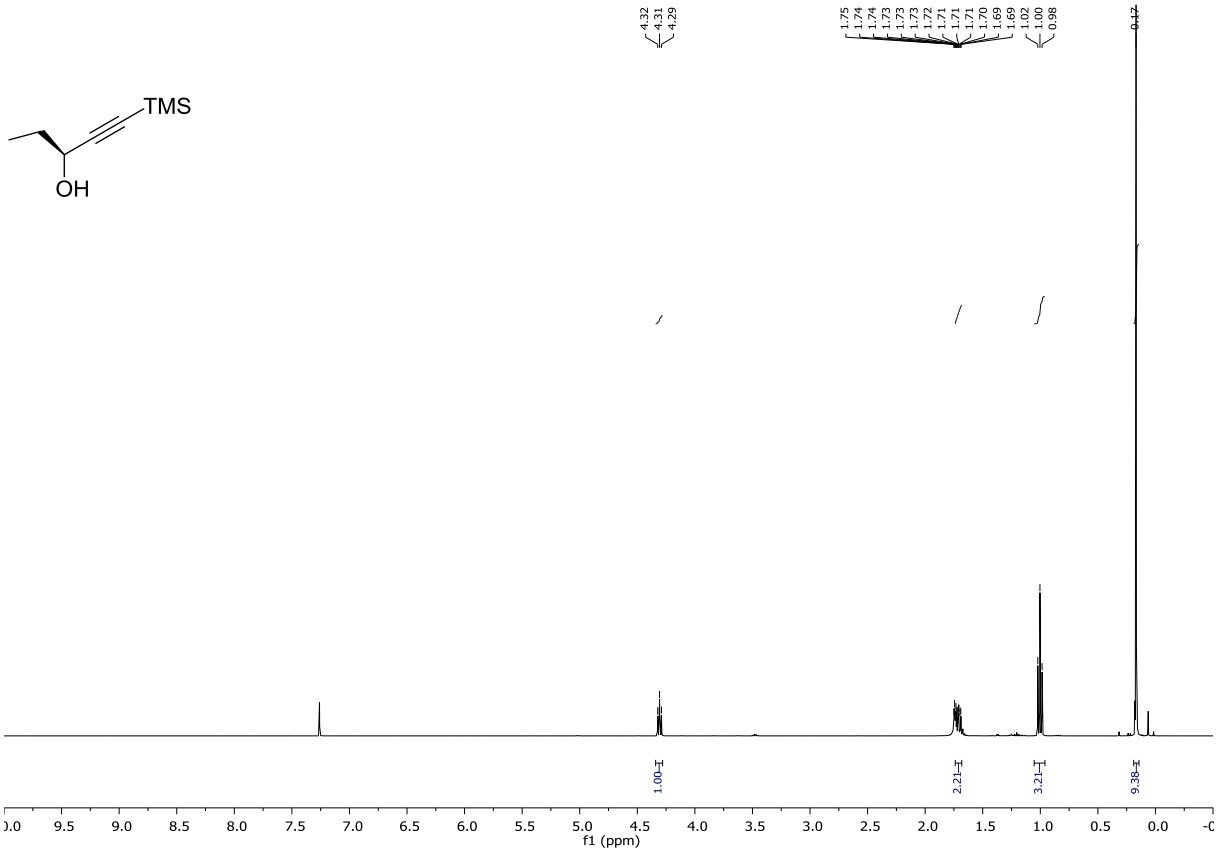

174.1
173.5
131.6
118.1
109.6
109.0
62.7
61.3
35.2
34.7
32.1
29.5
25.6
25.4
22.9
20.7
14.3
1.2
f1 (ppm)

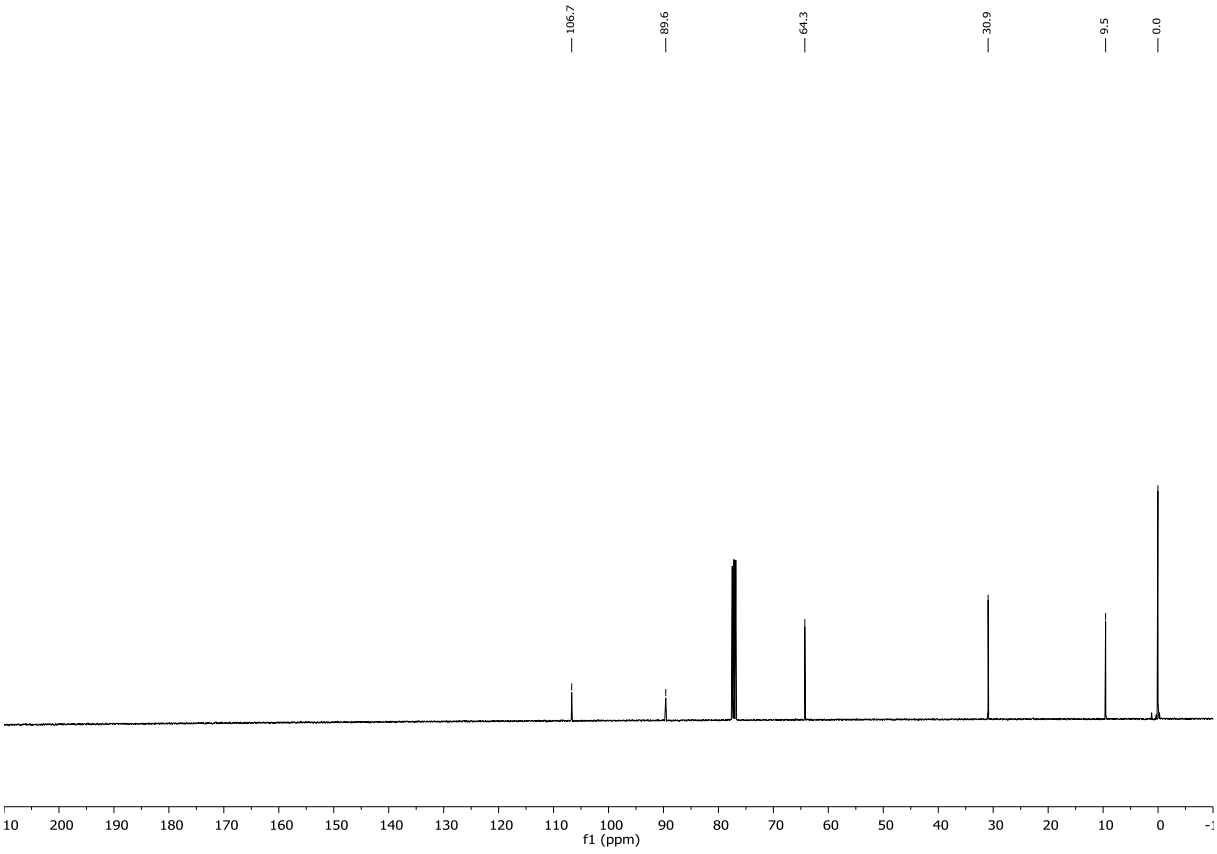

TMS
2.11
0.20
1.00
9.03
f1 (ppm)

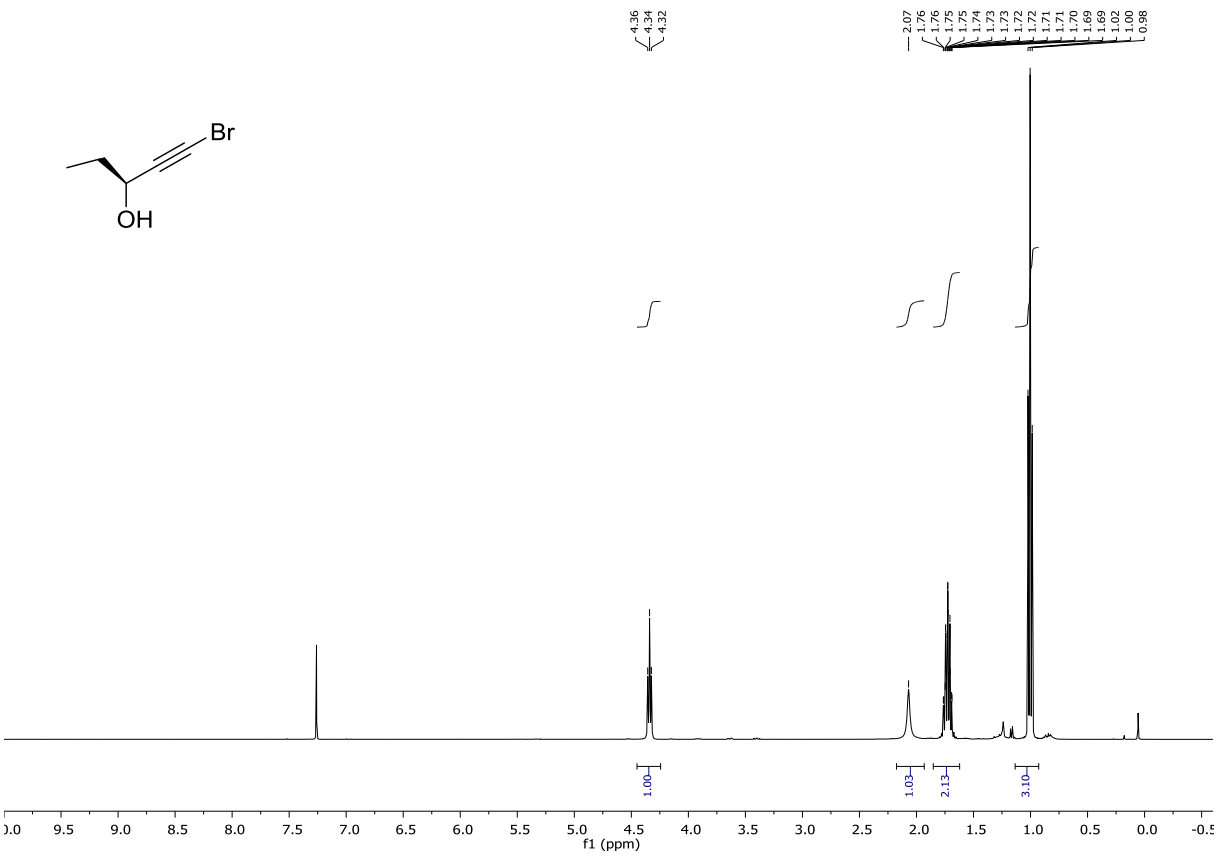

87.5
84.9
68.4
66.8
-0.4
f1 (ppm)

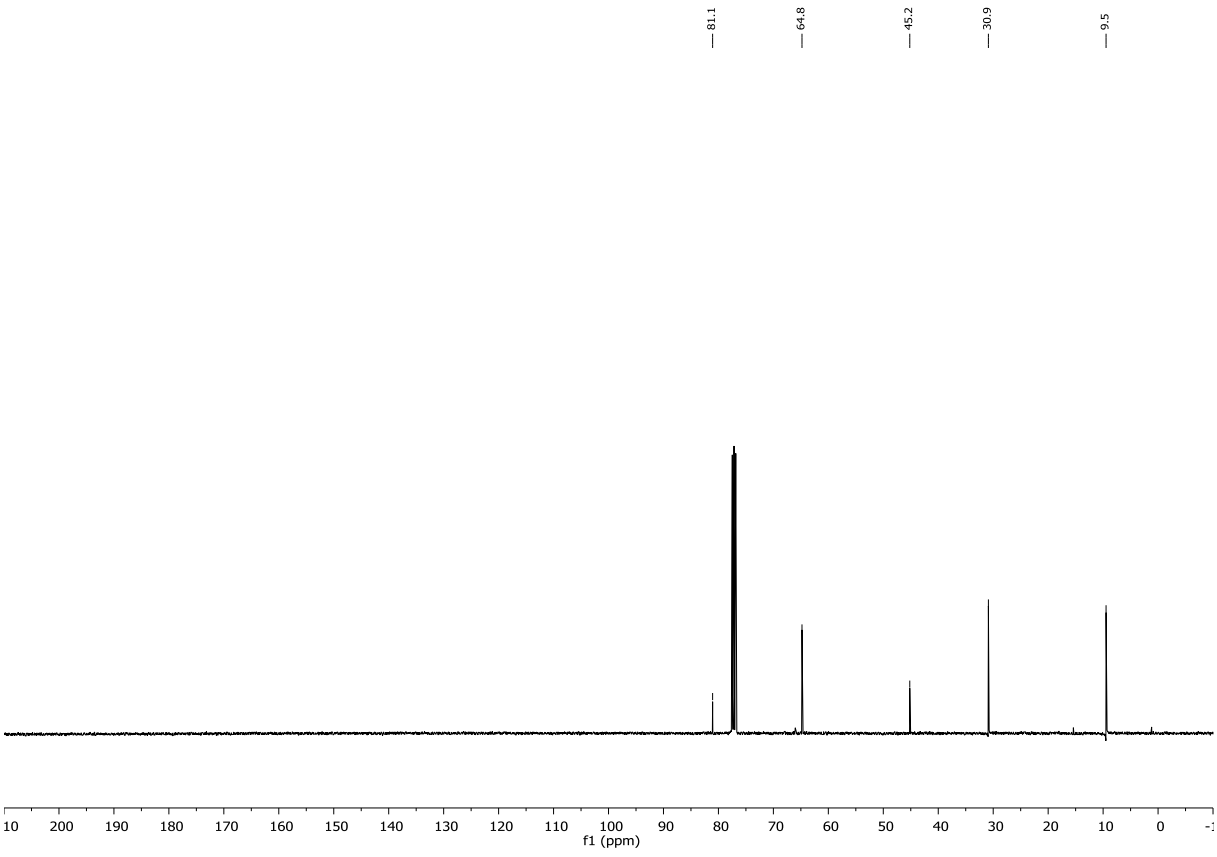

O
TMS
2.60
2.59
2.57
2.55
1.14
1.12
1.10
0.23
2.00
3.05
9.09
f1 (ppm)

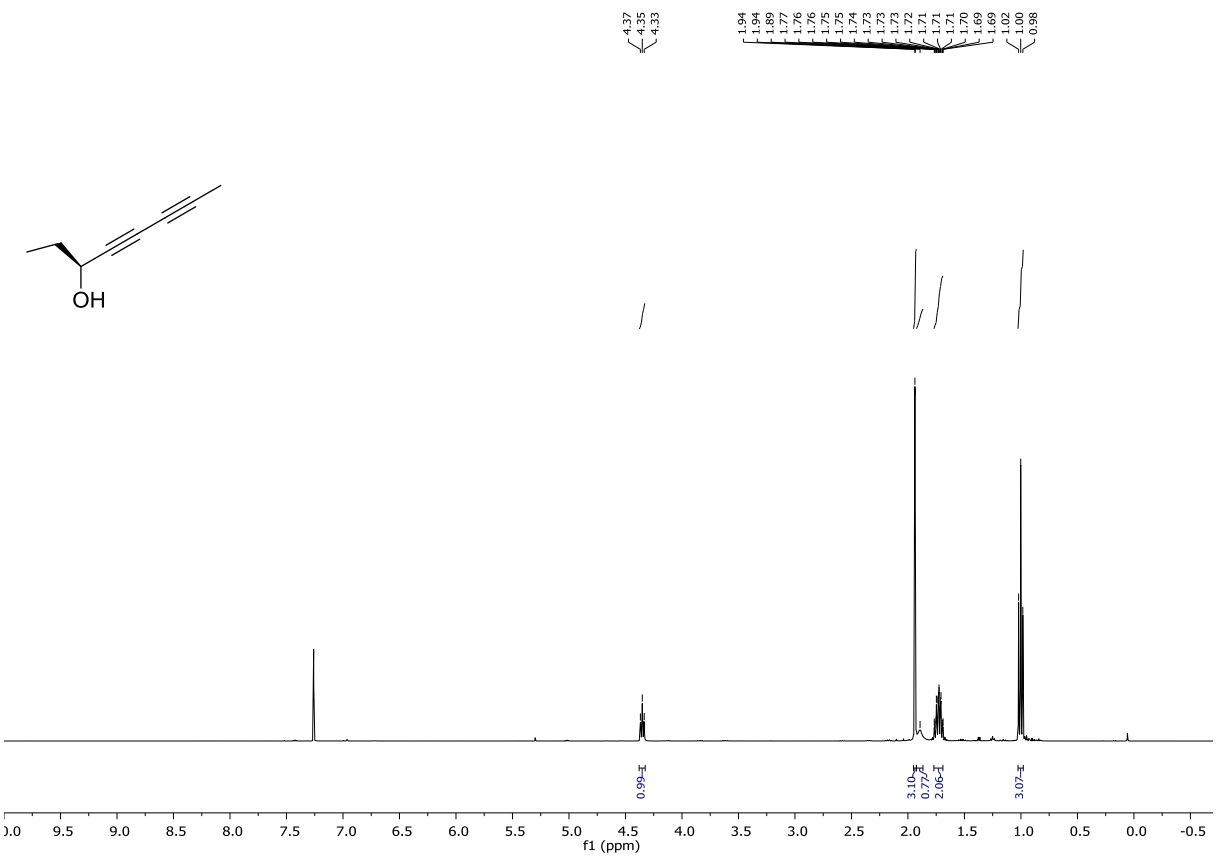

188.6
101.9
97.8
38.8
8.0
-0.6
f1 (ppm)

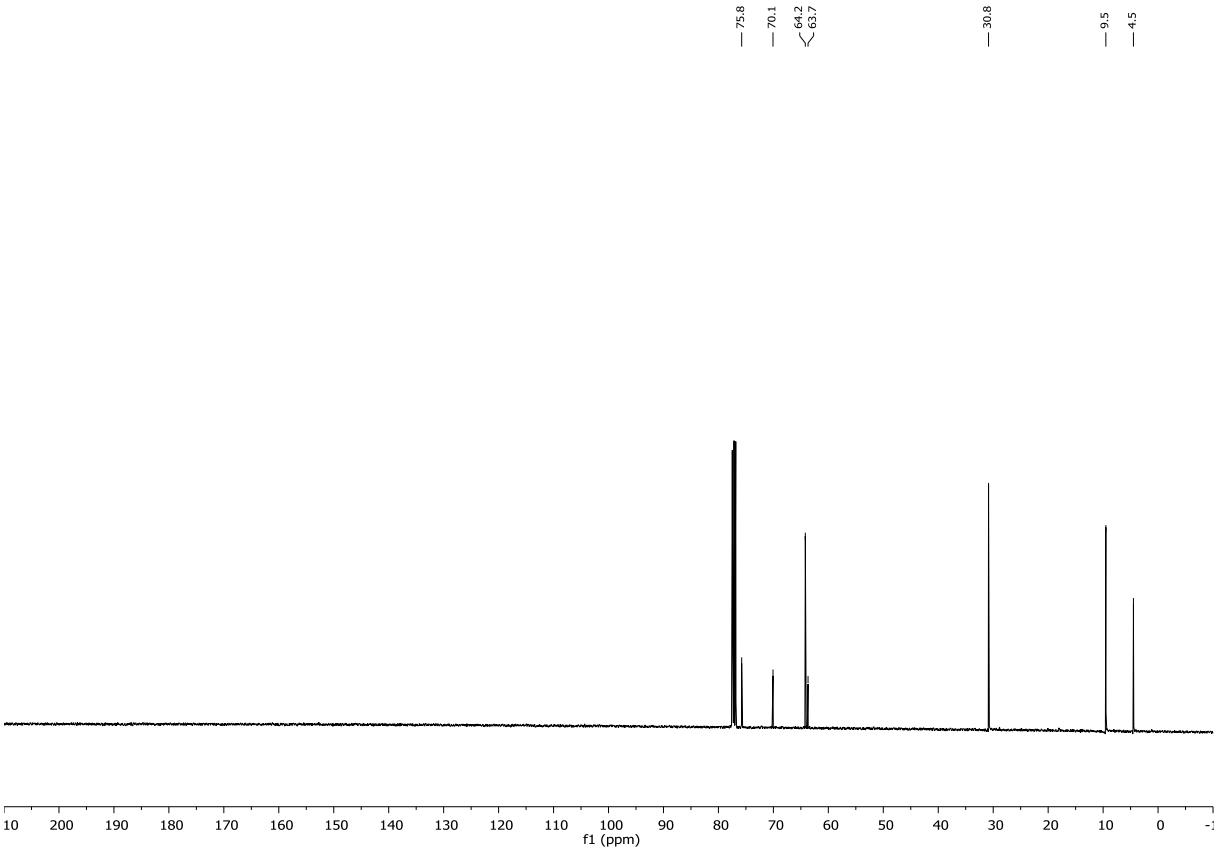

TMS
OH
4.32
4.31
4.29
1.75
1.74
1.74
1.73
1.73
1.73
1.72
1.71
1.71
1.71
1.70
1.69
1.69
1.02
1.00
0.98
0.17
1.00
2.21
3.21
9.38
f1 (ppm)

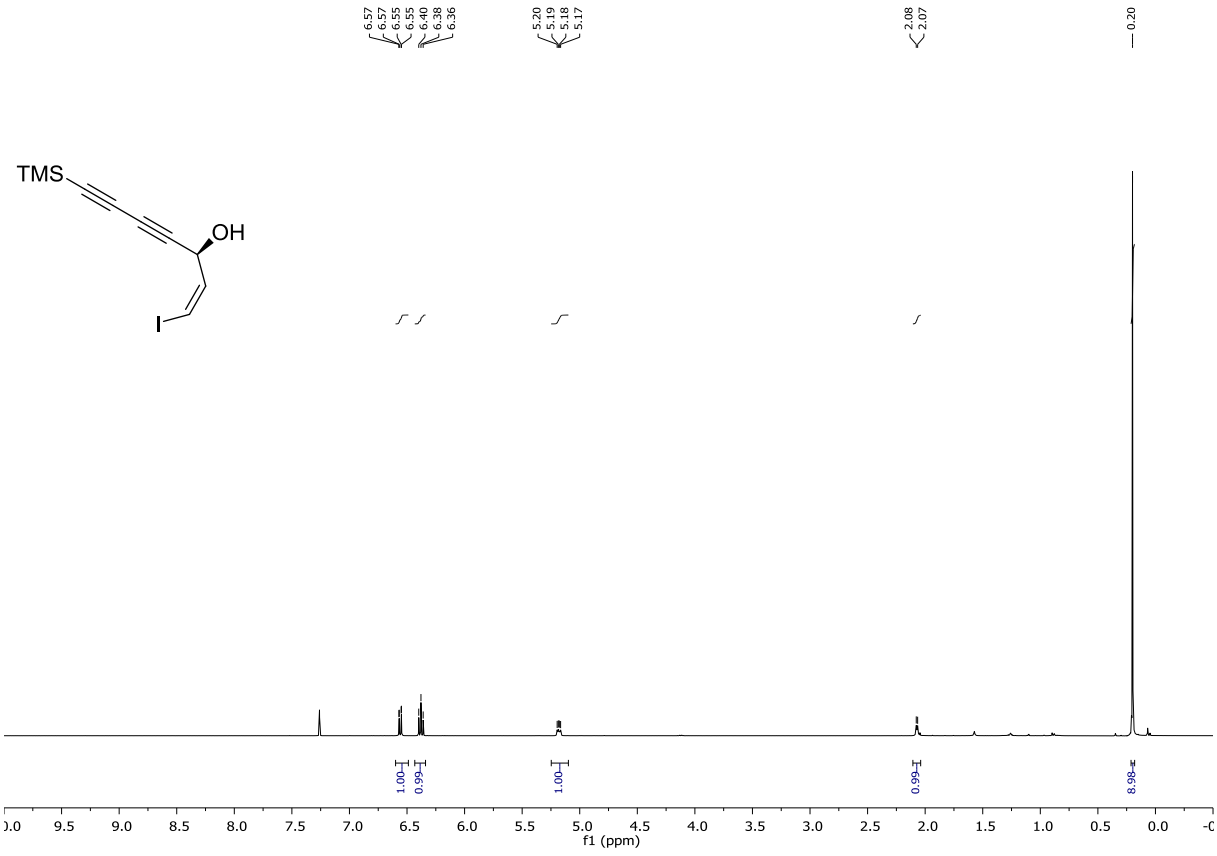

106.7
89.6
64.3
30.9
9.5
0.0
f1 (ppm)

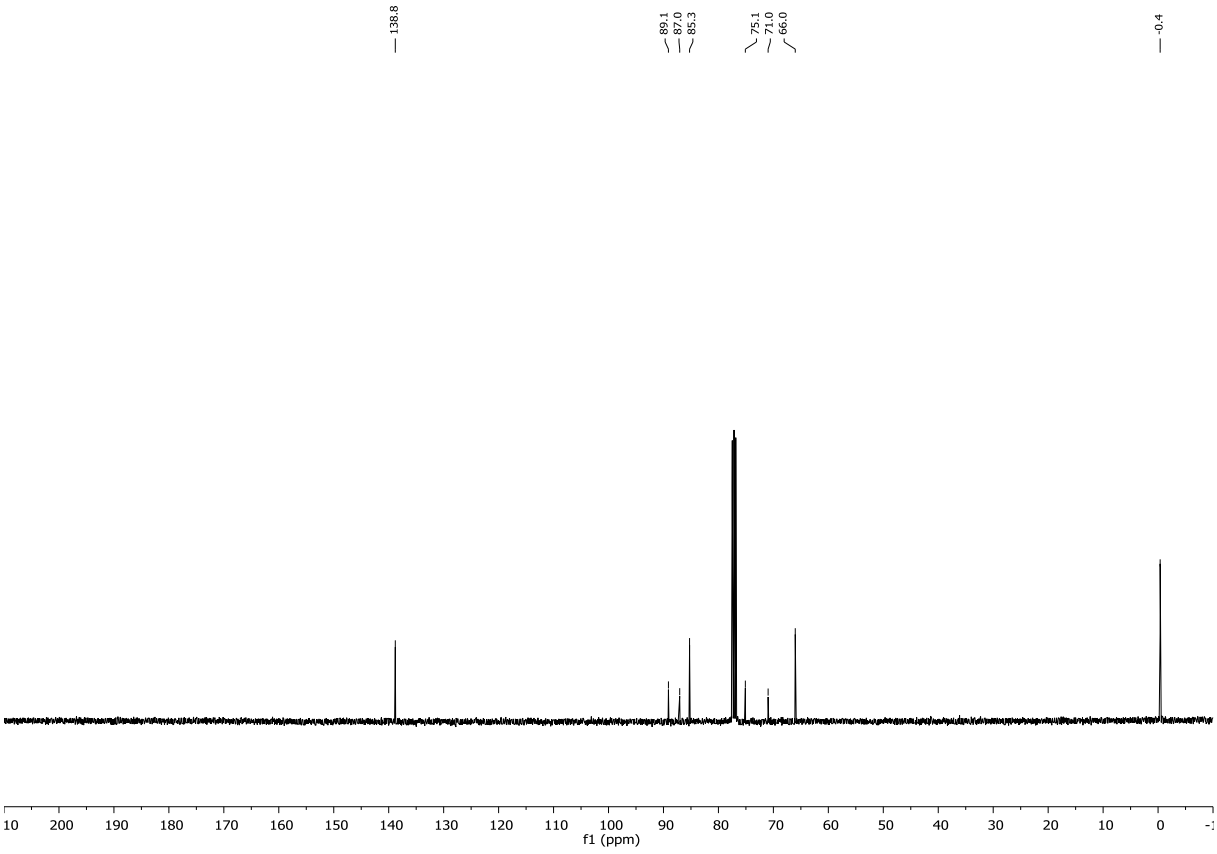

Br
OH
4.36
4.34
4.32
2.07
1.76
1.76
1.75
1.75
1.74
1.73
1.73
1.72
1.72
1.71
1.71
1.70
1.69
1.69
1.02
1.00
0.98
1.00
1.03
2.13
3.10
f1 (ppm)

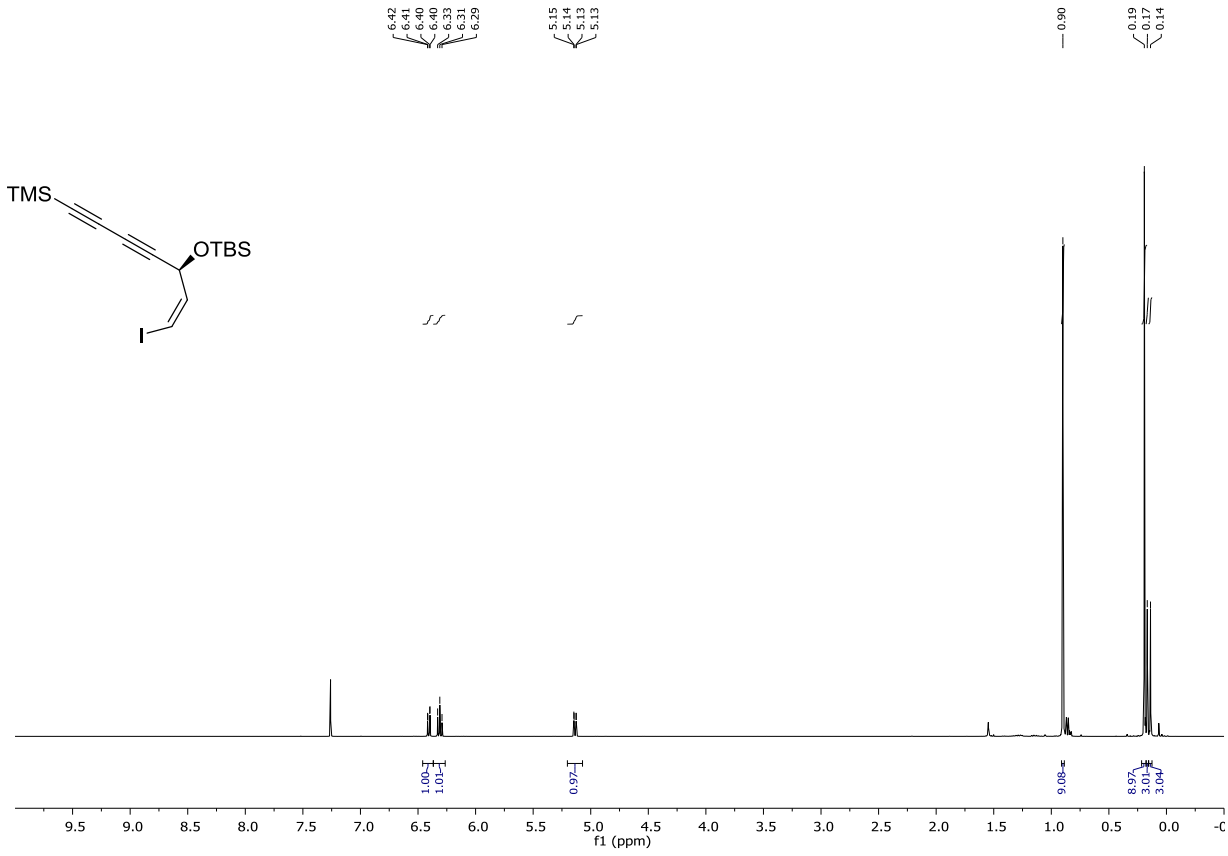

81.1
64.8
45.2
30.9
9.5
f1 (ppm)

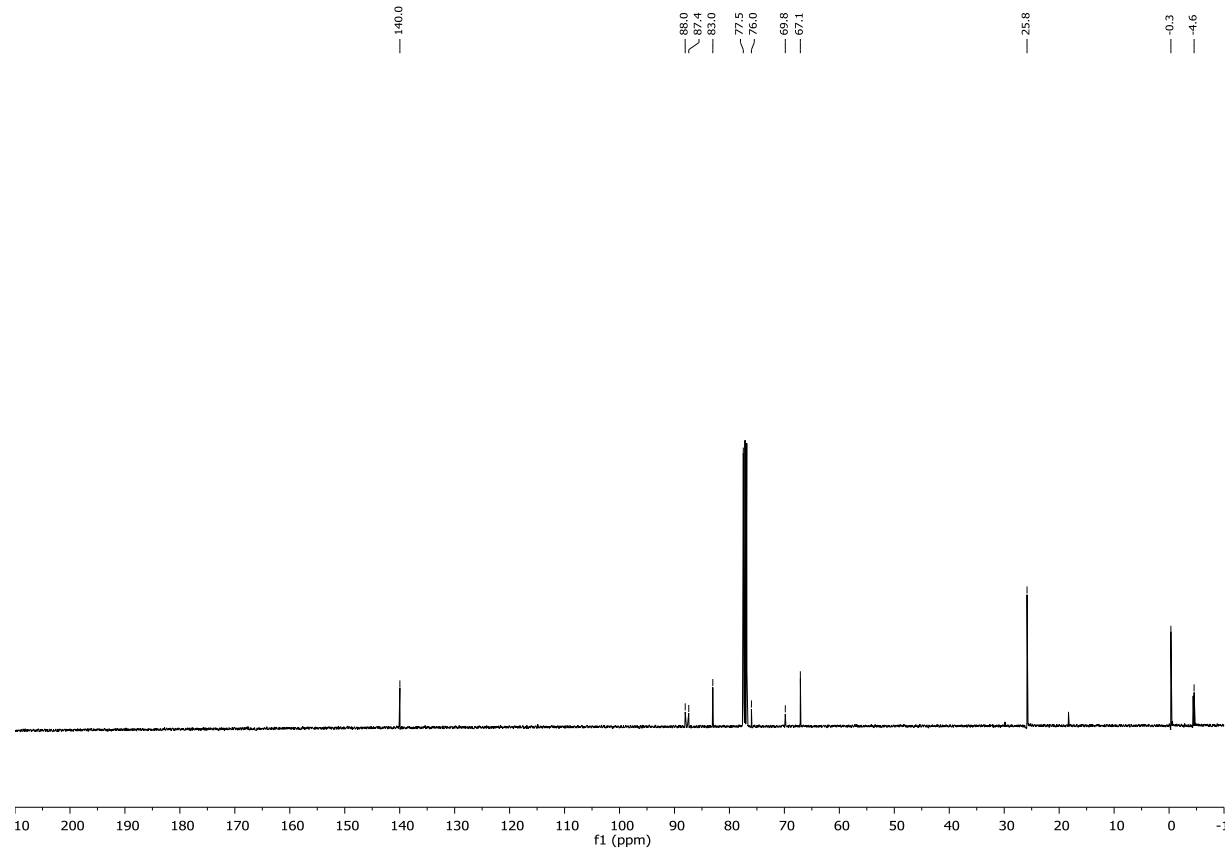

4.37
4.35
4.33
1.94
1.94
1.89
1.77
1.76
1.76
1.75
1.75
1.74
1.73
1.73
1.72
1.71
1.71
1.70
1.69
1.69
1.02
1.00
0.98
OH
0.99
3.10
0.77
2.06
3.07
f1 (ppm)

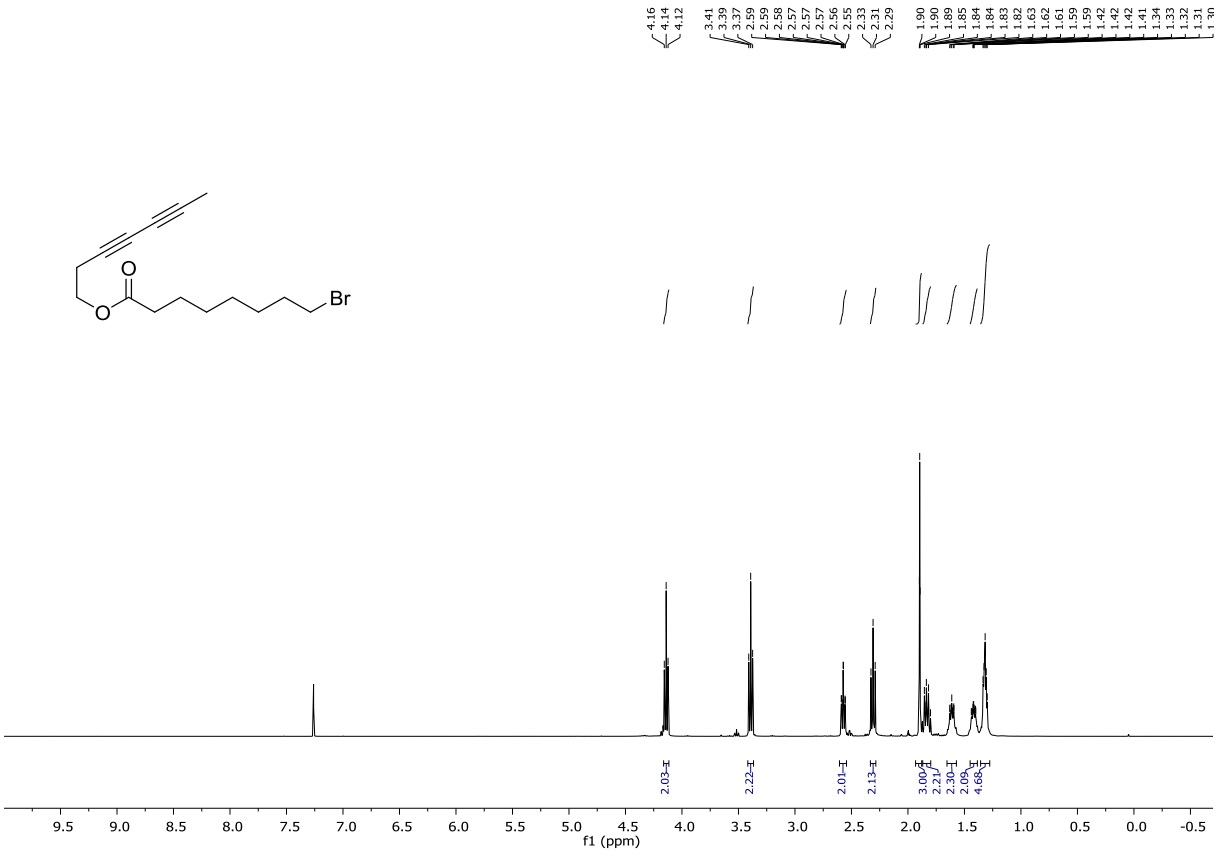

75.8
70.1
64.2
63.7
30.8
9.5
4.5
f1 (ppm)

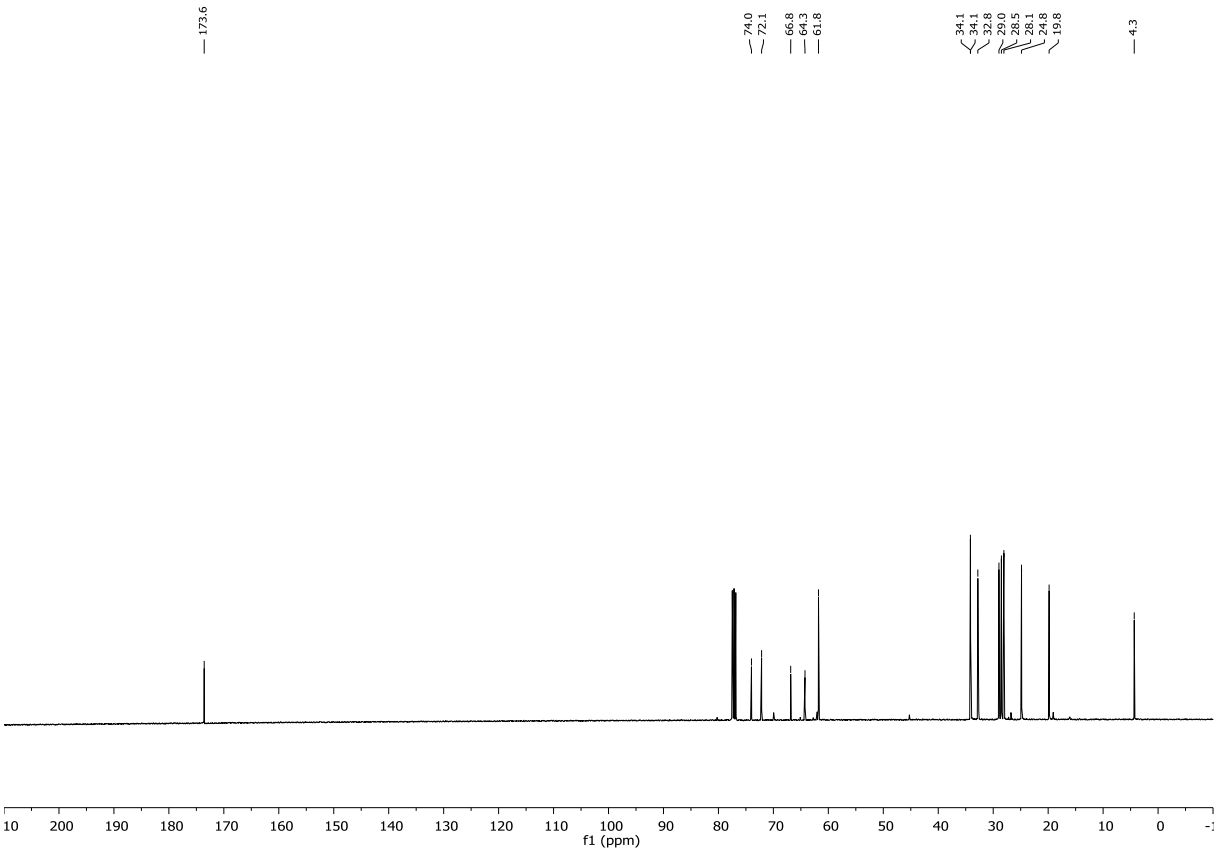

6.57
6.57
6.55
6.55
6.40
6.38
6.36
5.20
5.19
5.18
5.17
2.08
2.07
0.20
TMS
OH
I
1.00
0.99
1.00
0.99
8.98
f1 (ppm)

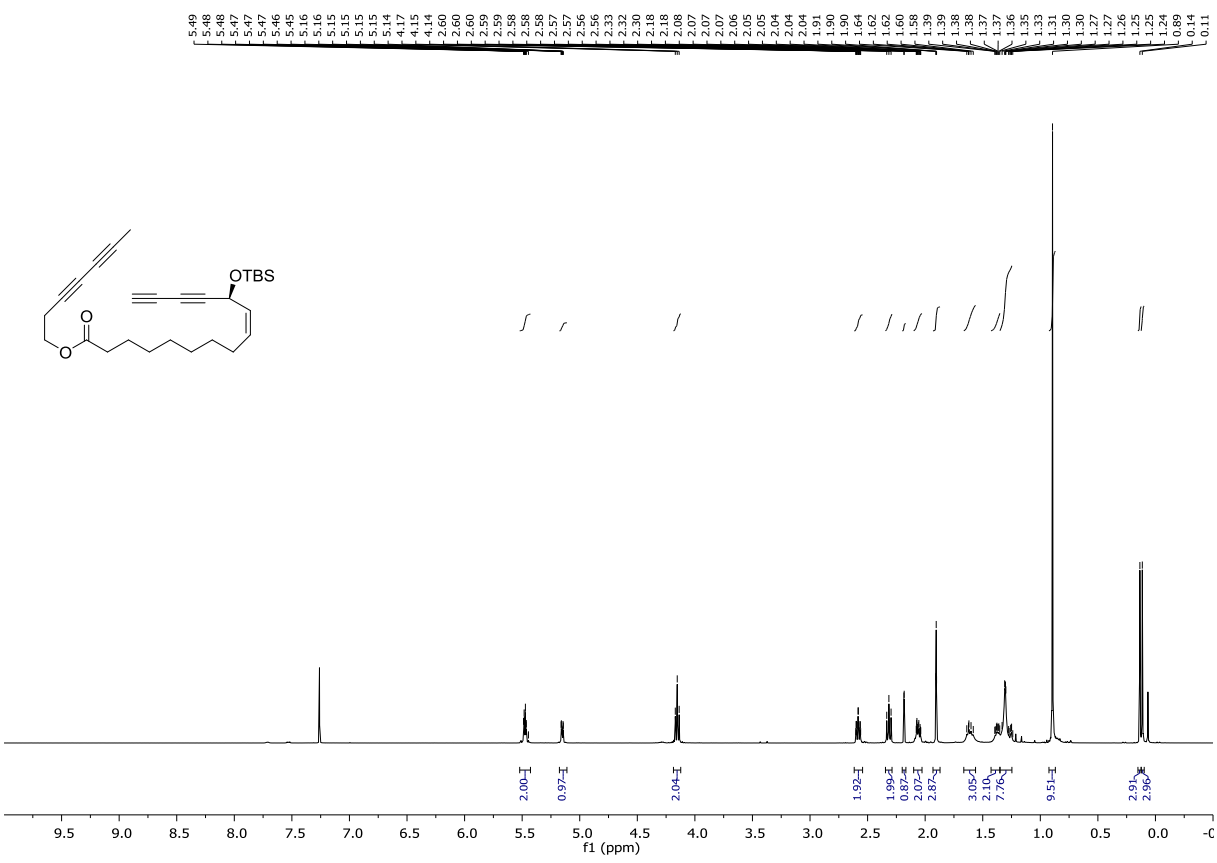

138.8
89.1
87.0
85.3
75.1
71.0
66.0
-0.4
f1 (ppm)

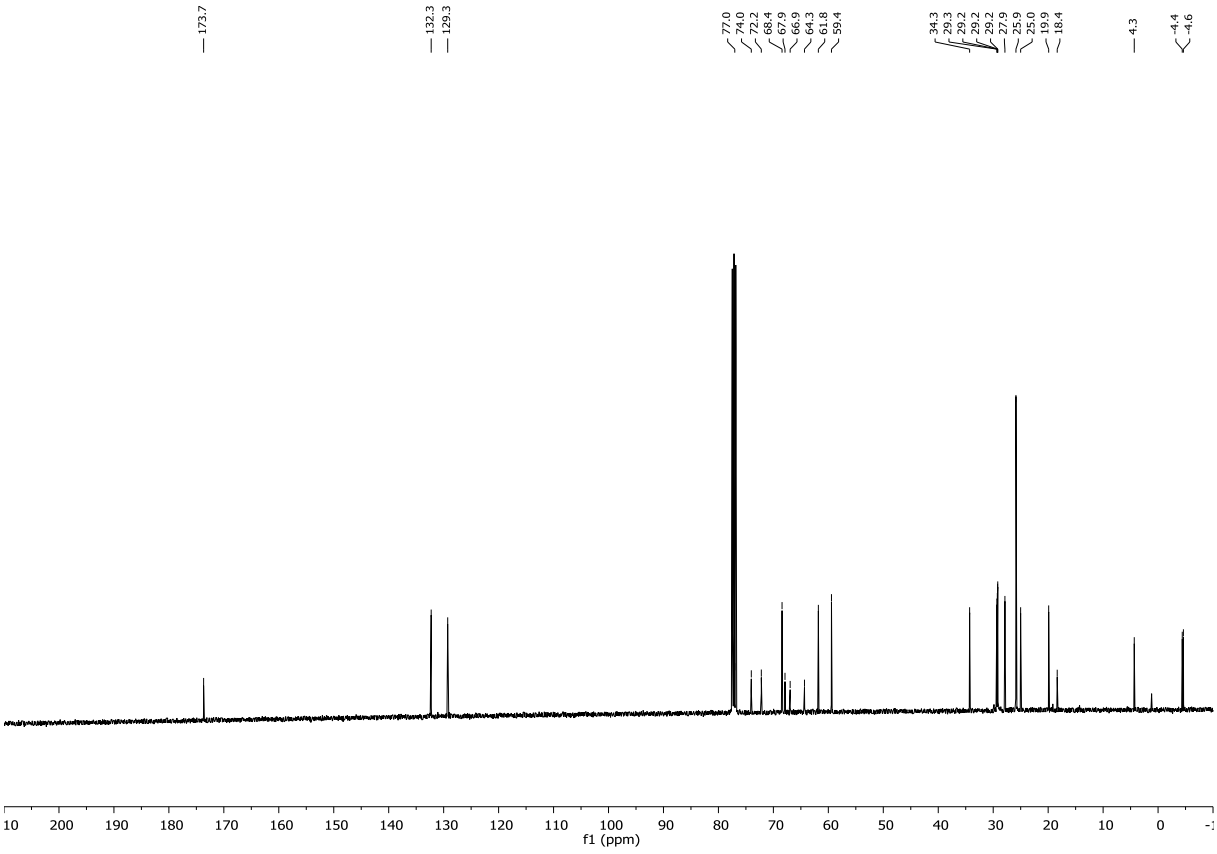

6.42
6.41
6.40
6.40
6.33
6.31
6.29
5.15
5.14
5.13
5.13
0.90
0.19
0.17
0.14
TMS
OTBS
I
1.00
1.01
0.97
9.08
8.97
3.01
3.04
f1 (ppm)

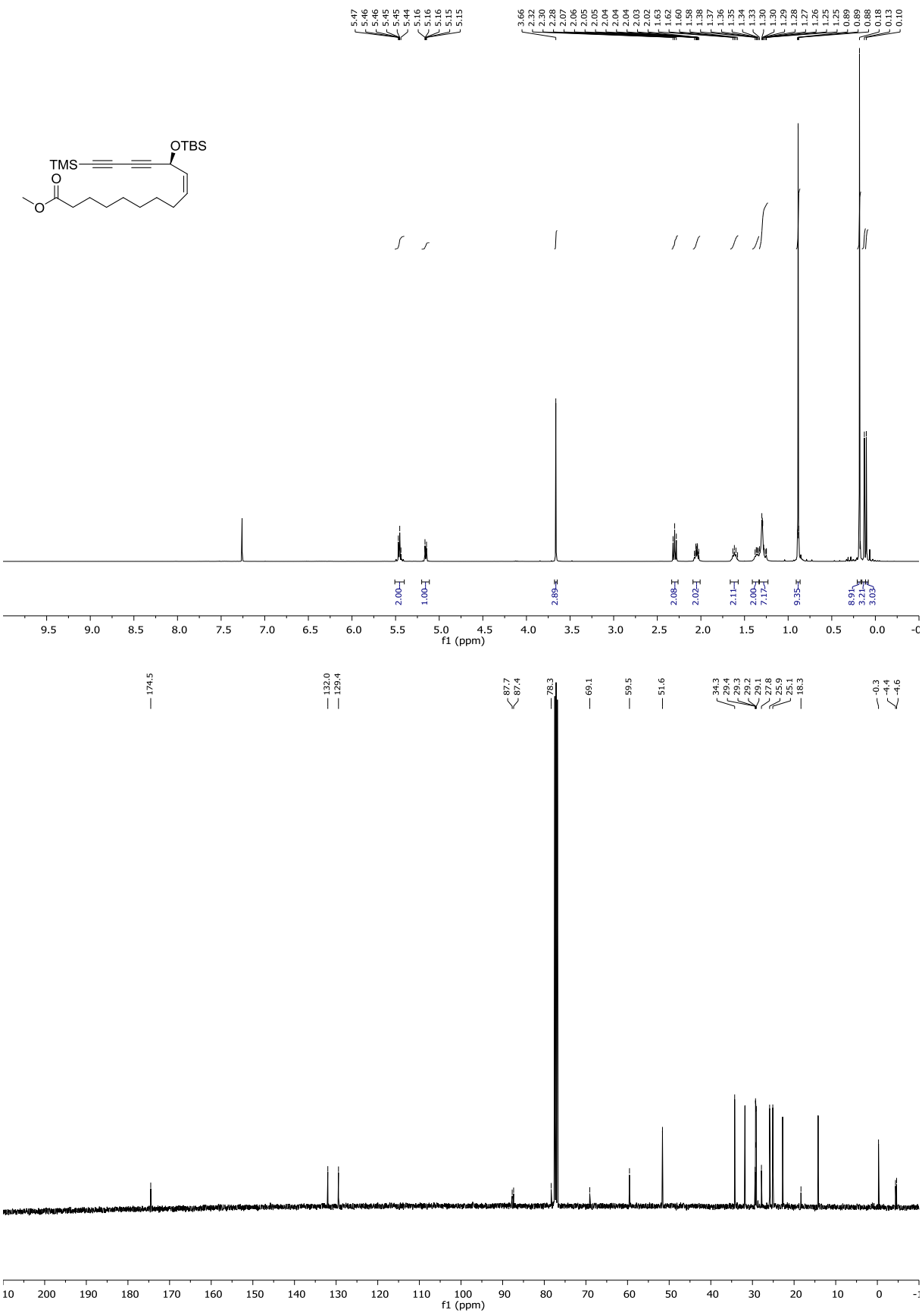

140.0
88.0
87.4
83.0
77.5
76.0
69.8
67.1
25.8
-0.3
-4.6
f1 (ppm)

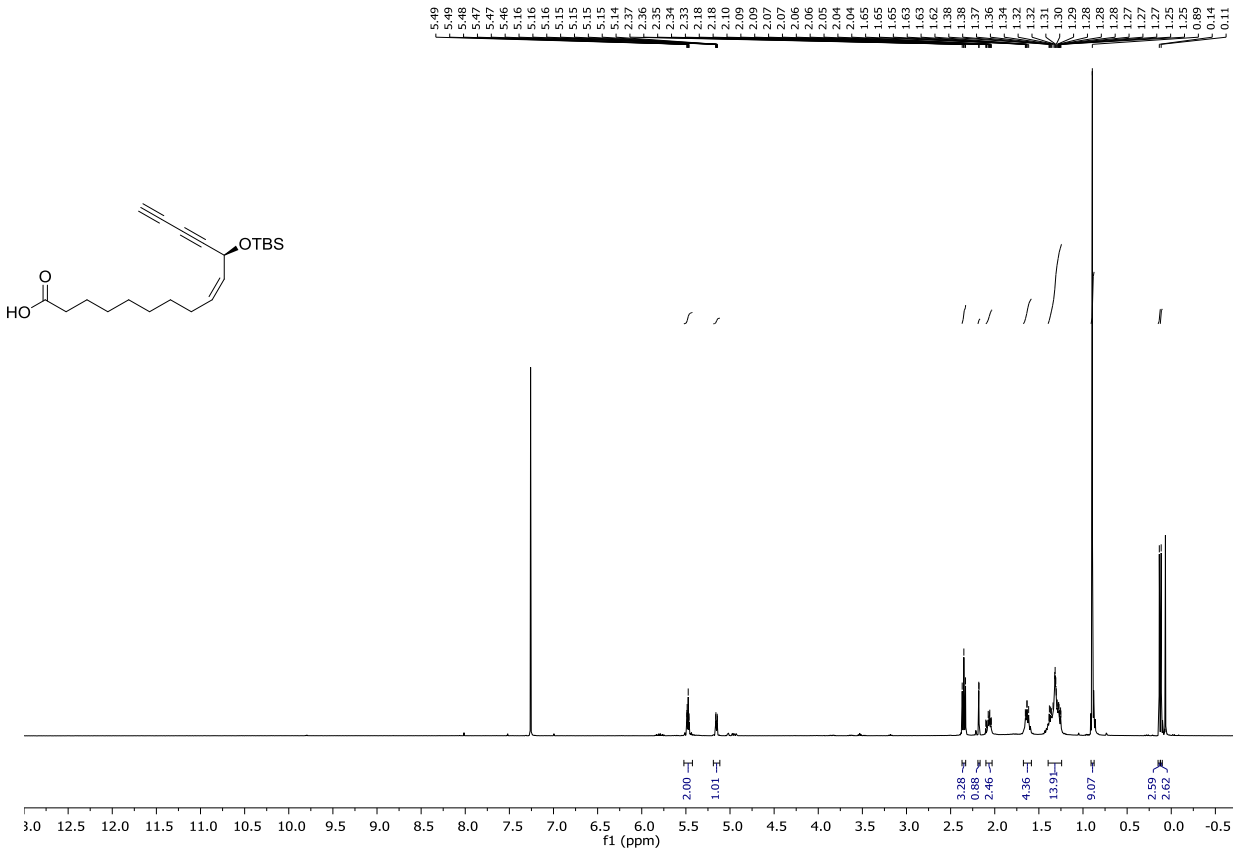

4.16
4.14
4.12
3.41
3.39
3.37
2.59
2.59
2.58
2.57
2.57
2.57
2.56
2.55
2.33
2.31
2.29
1.90
1.90
1.88
1.85
1.85
1.84
1.83
1.82
1.63
1.62
1.61
1.59
1.59
1.42
1.42
1.42
1.41
1.34
1.33
1.32
1.31
O
O
Br
2.03
2.22
2.01
2.13
3.00
2.21
2.30
2.09
4.68
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

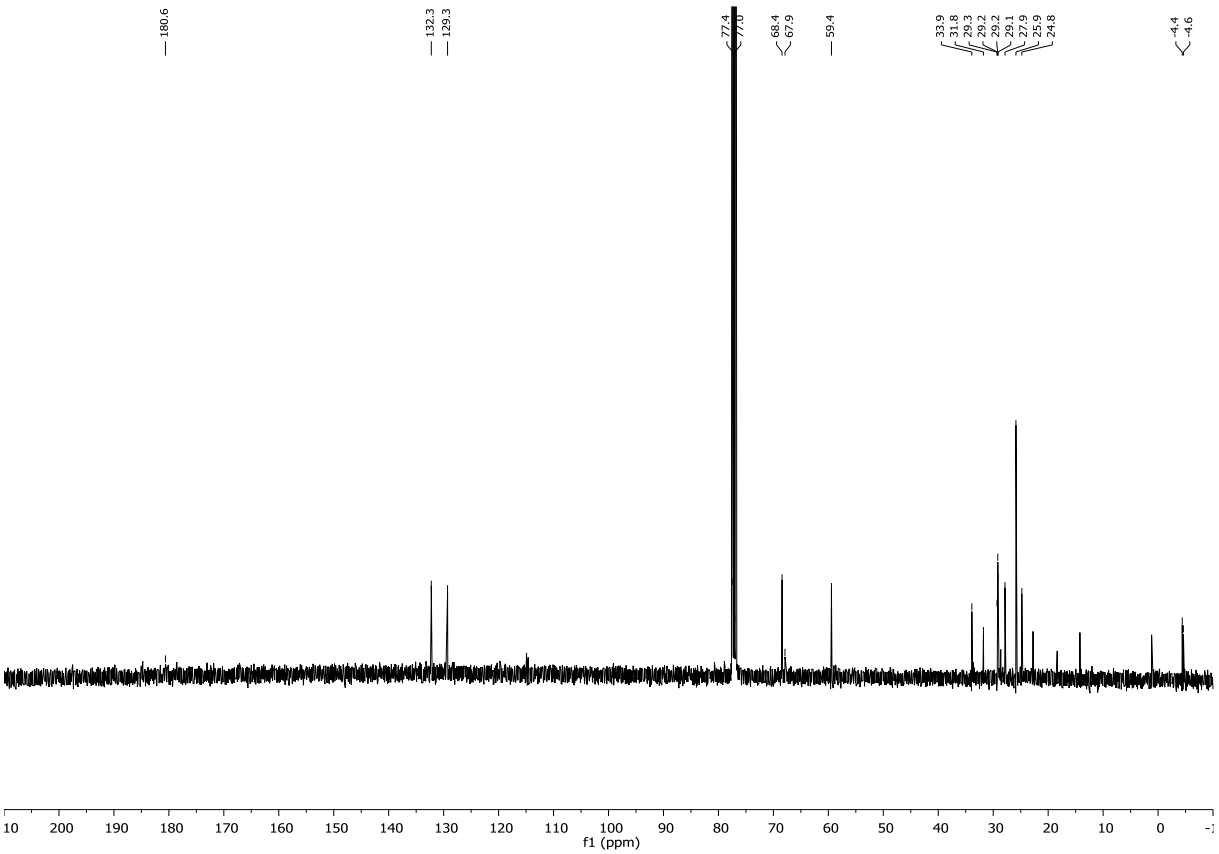

173.6
74.0
72.1
66.8
64.3
61.8
34.1
34.1
32.8
29.0
28.5
28.1
24.8
19.8
4.3
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

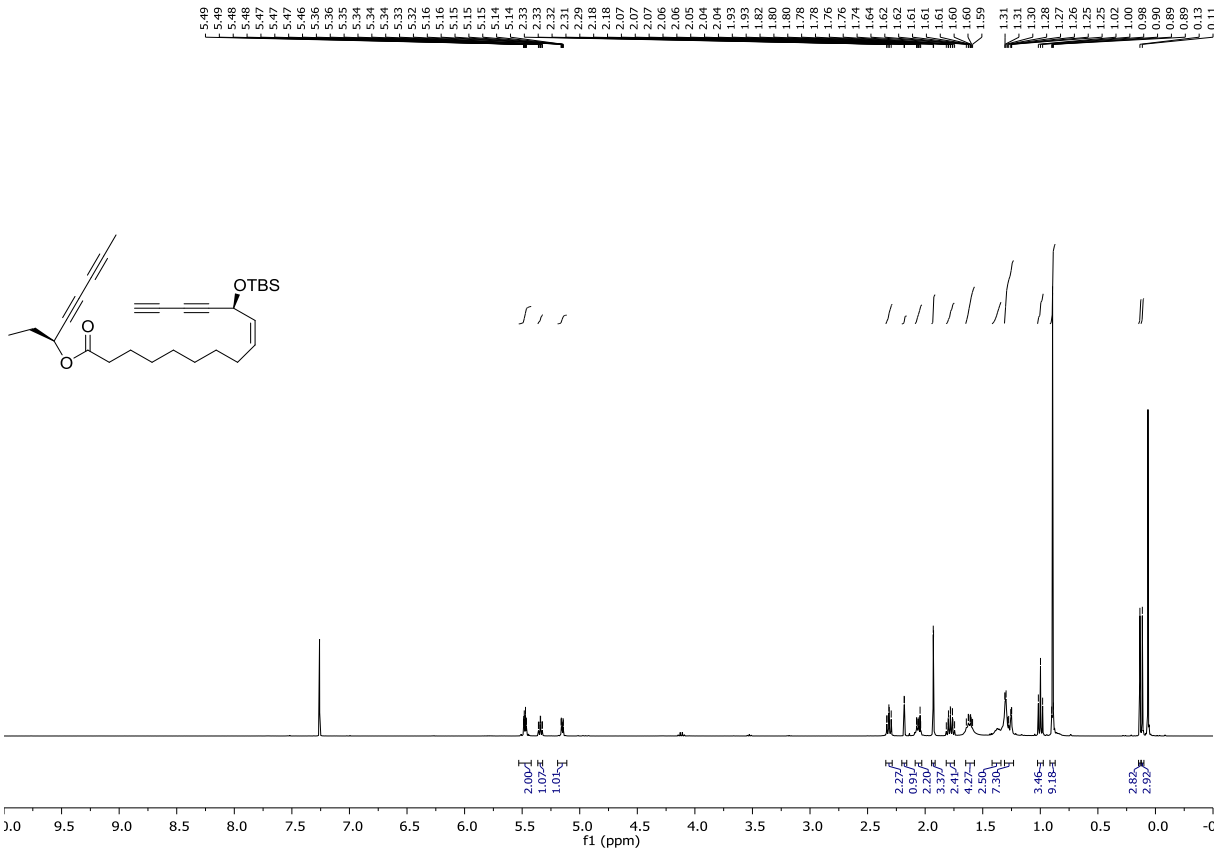

OTBS
O
O
f1 (ppm)

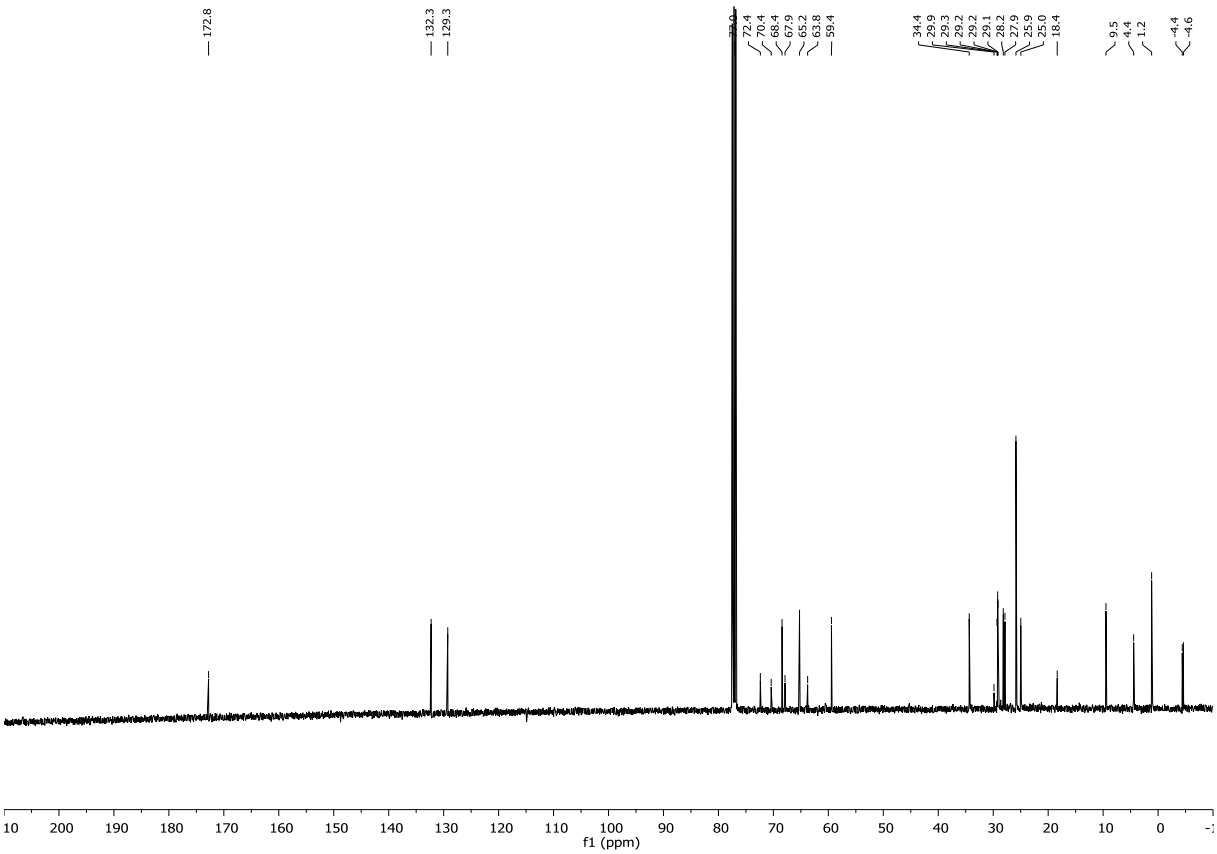

f1 (ppm)

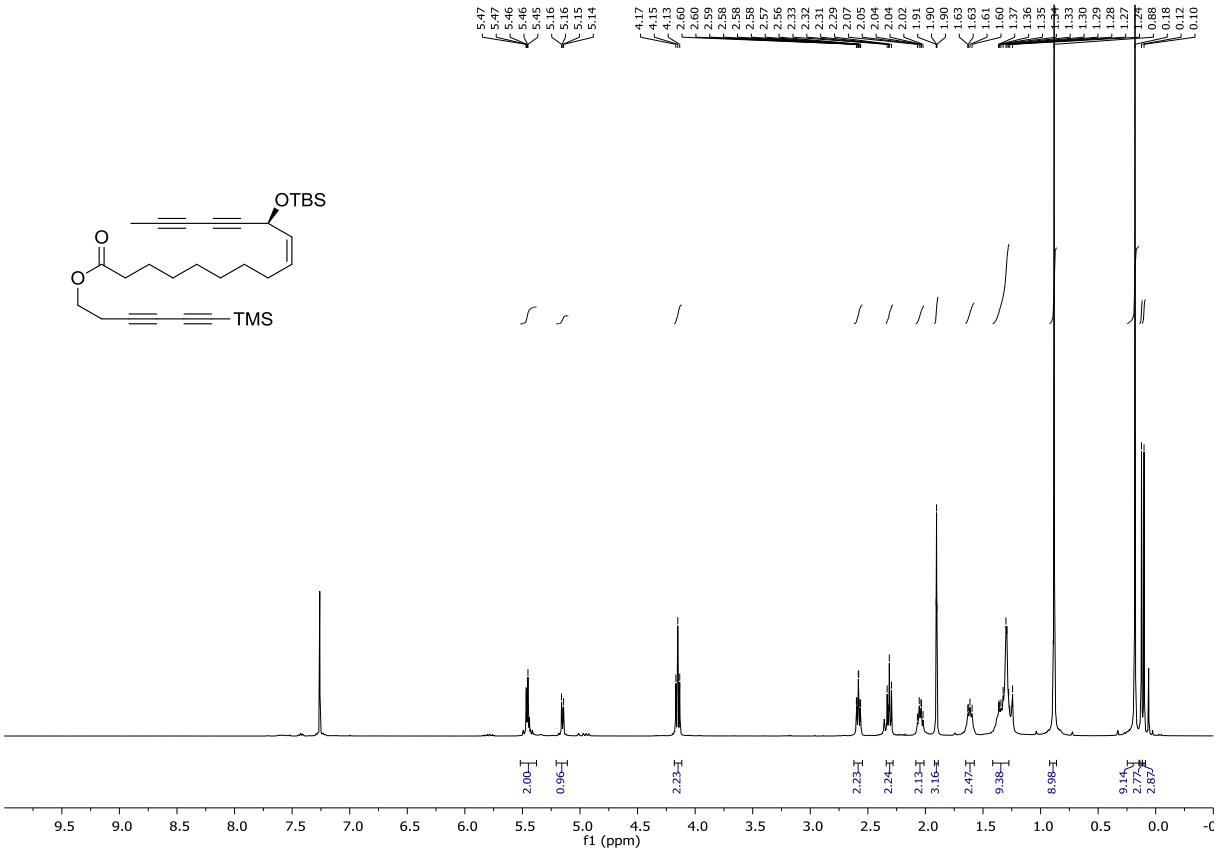

OTBS
TMS
O
O
f1 (ppm)
f1 (ppm)

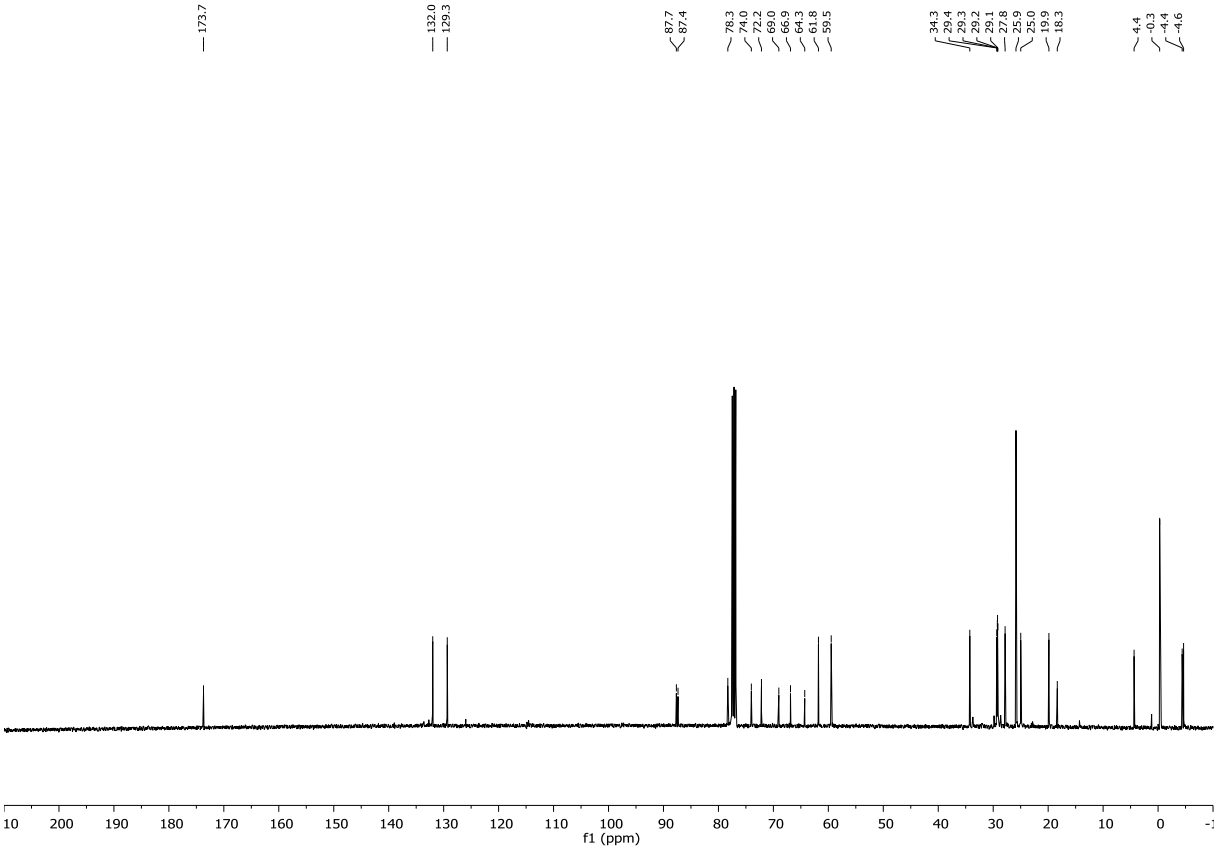

OTBS
O
HO
f1 (ppm)

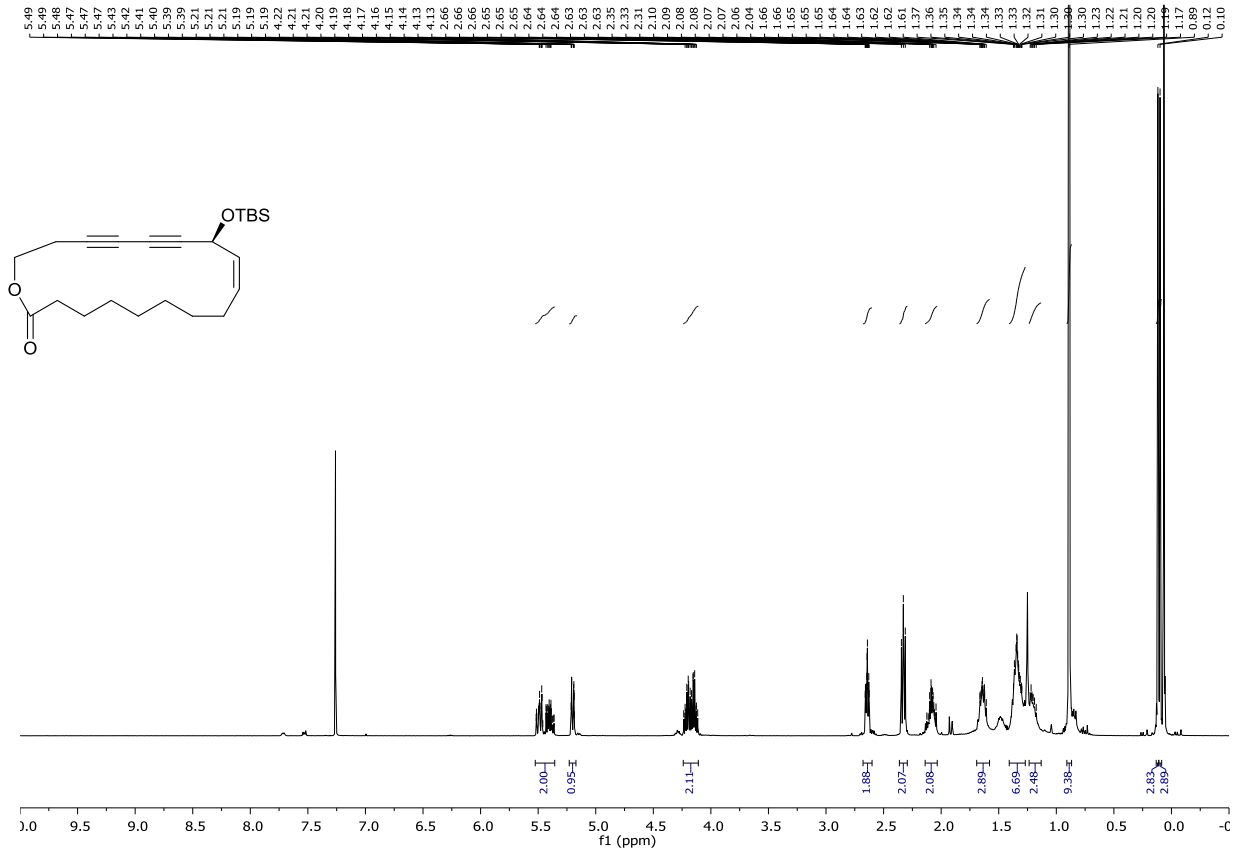

f1 (ppm)

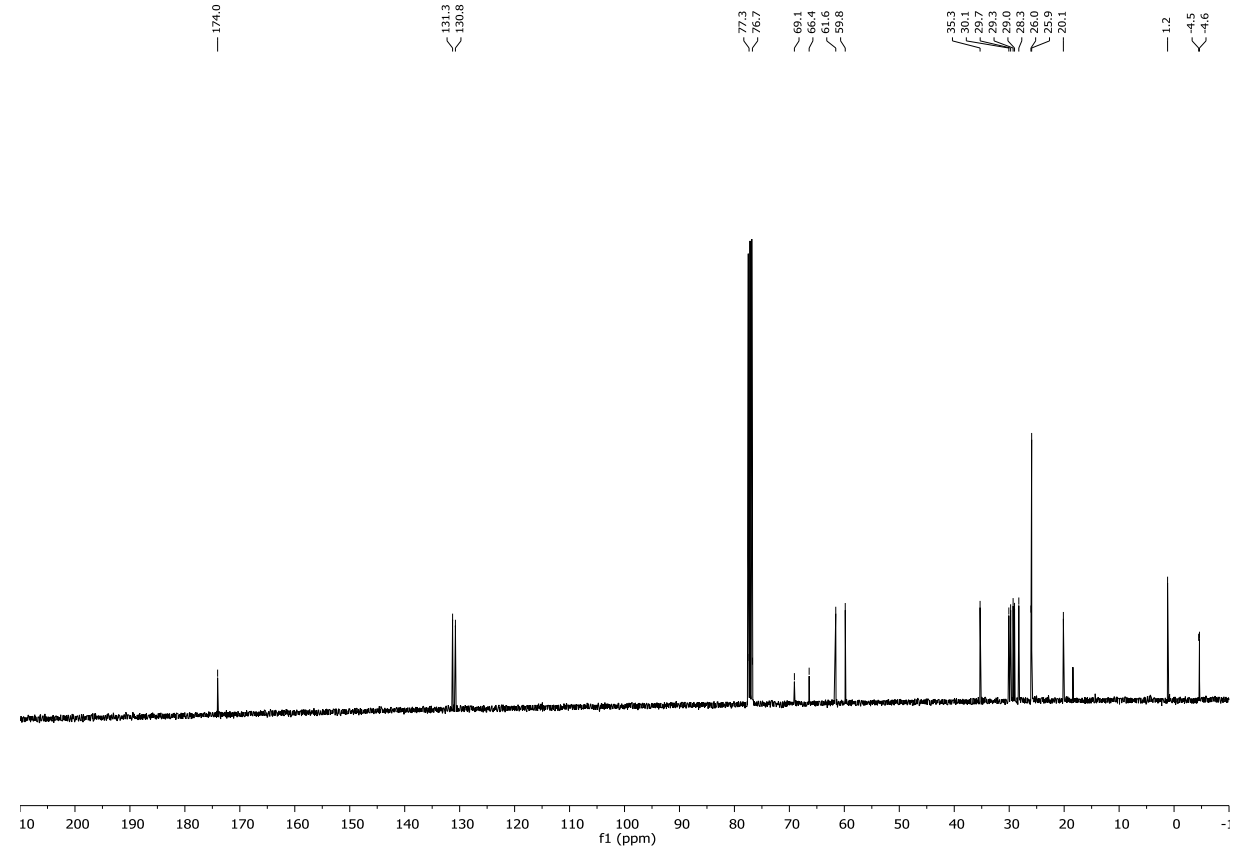

OTBS
O
O
f1 (ppm)

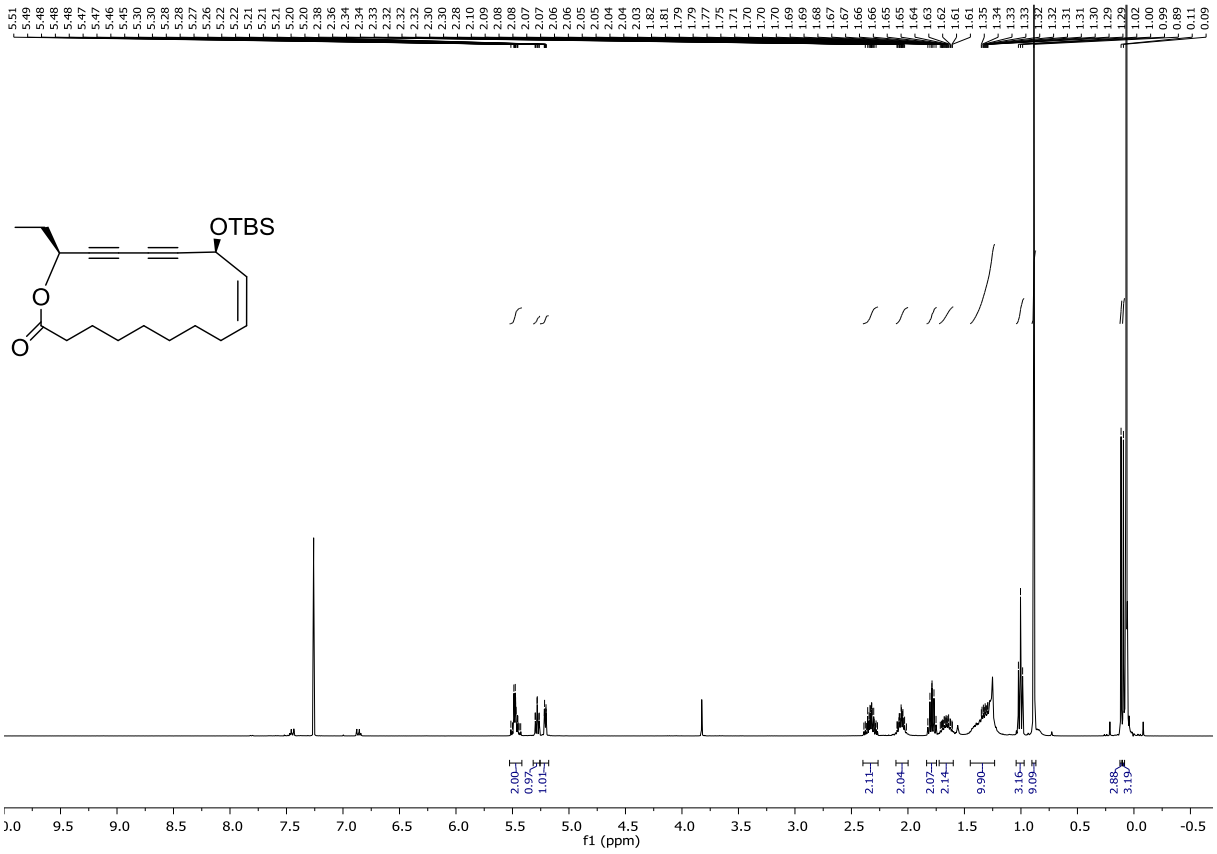

f1 (ppm)

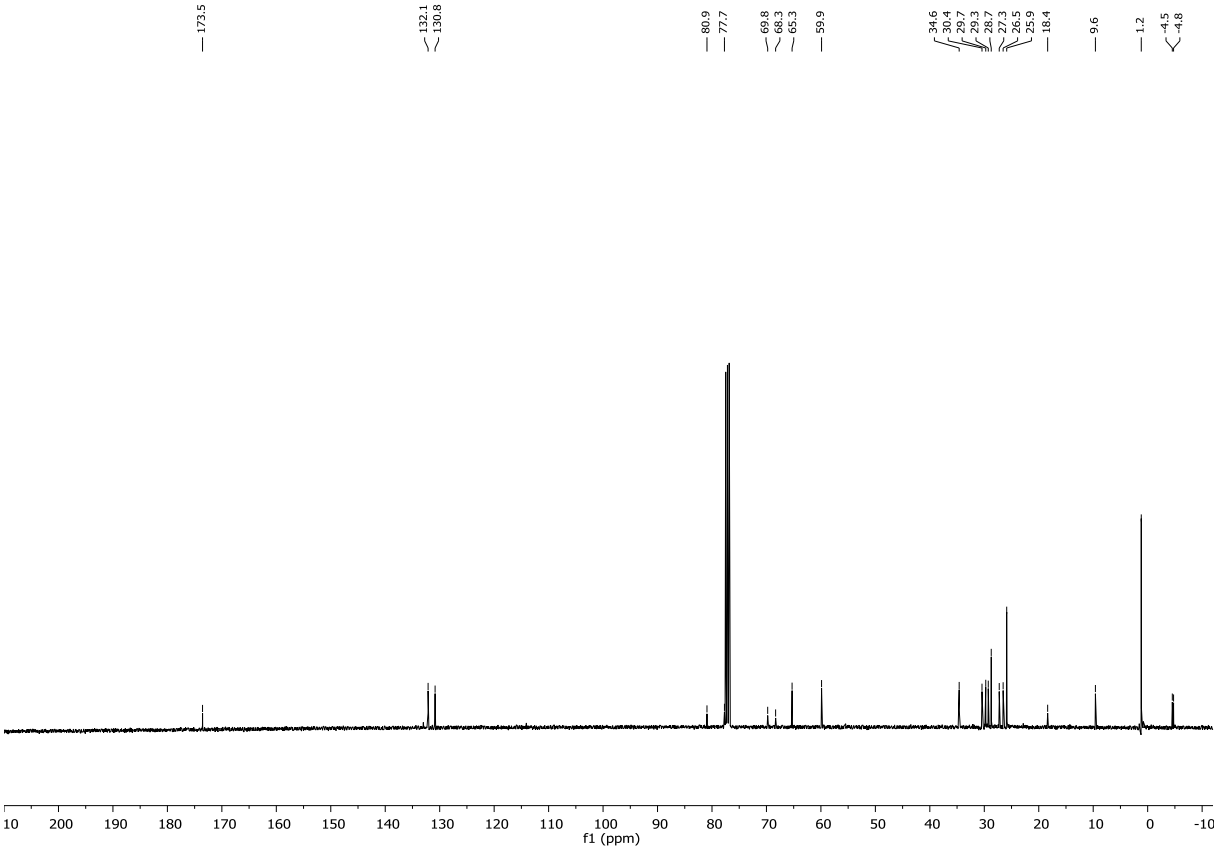

OTBS
O
O
TMS
f1 (ppm)

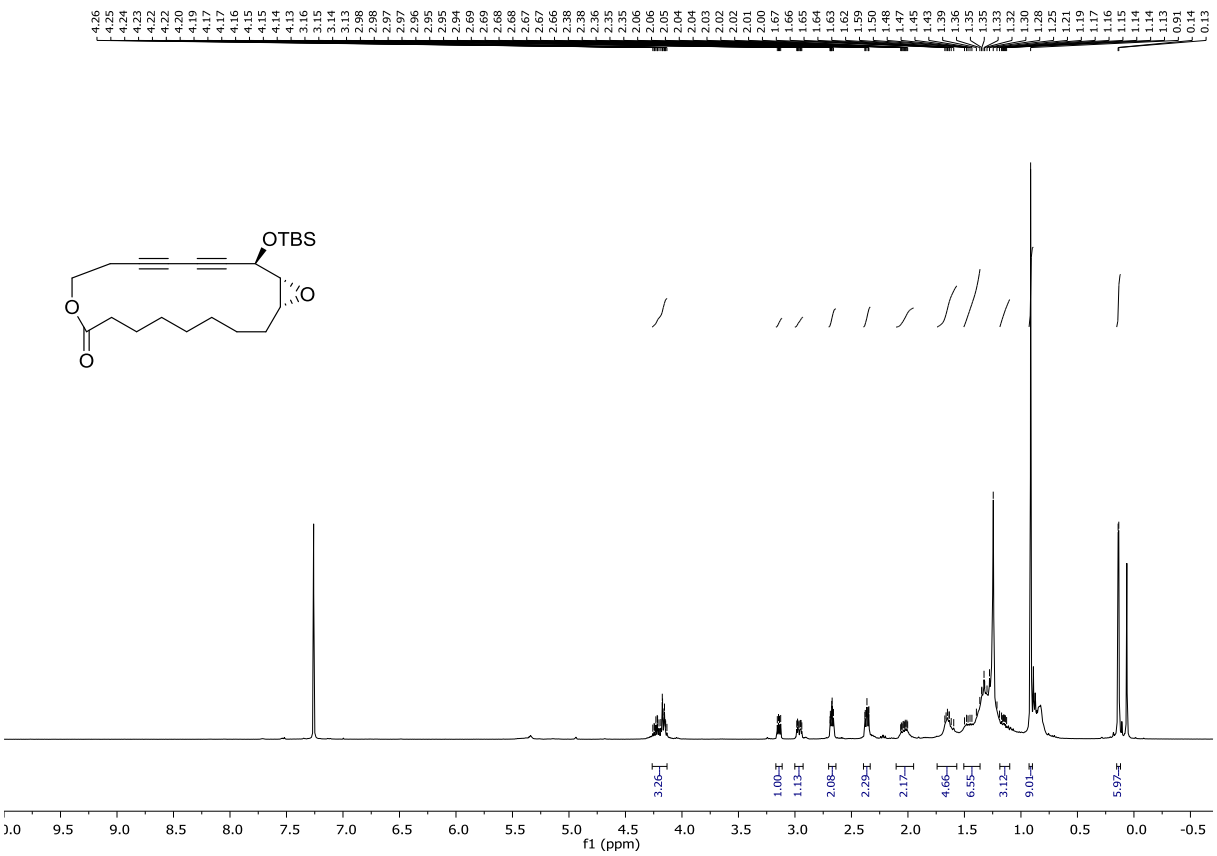

f1 (ppm)


OTBS
O
O
f1 (ppm)


f1 (ppm)


OTBS
O
O
f1 (ppm)


f1 (ppm)


OTBS
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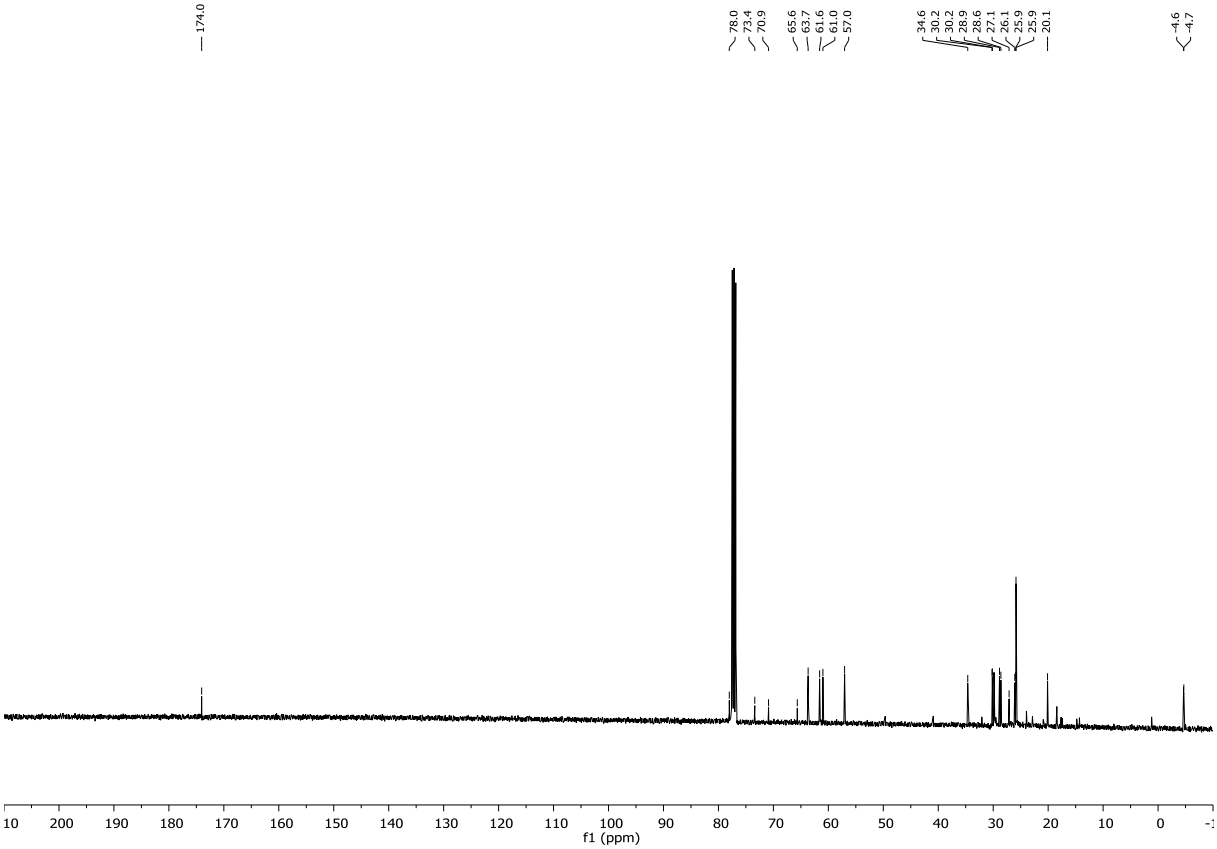
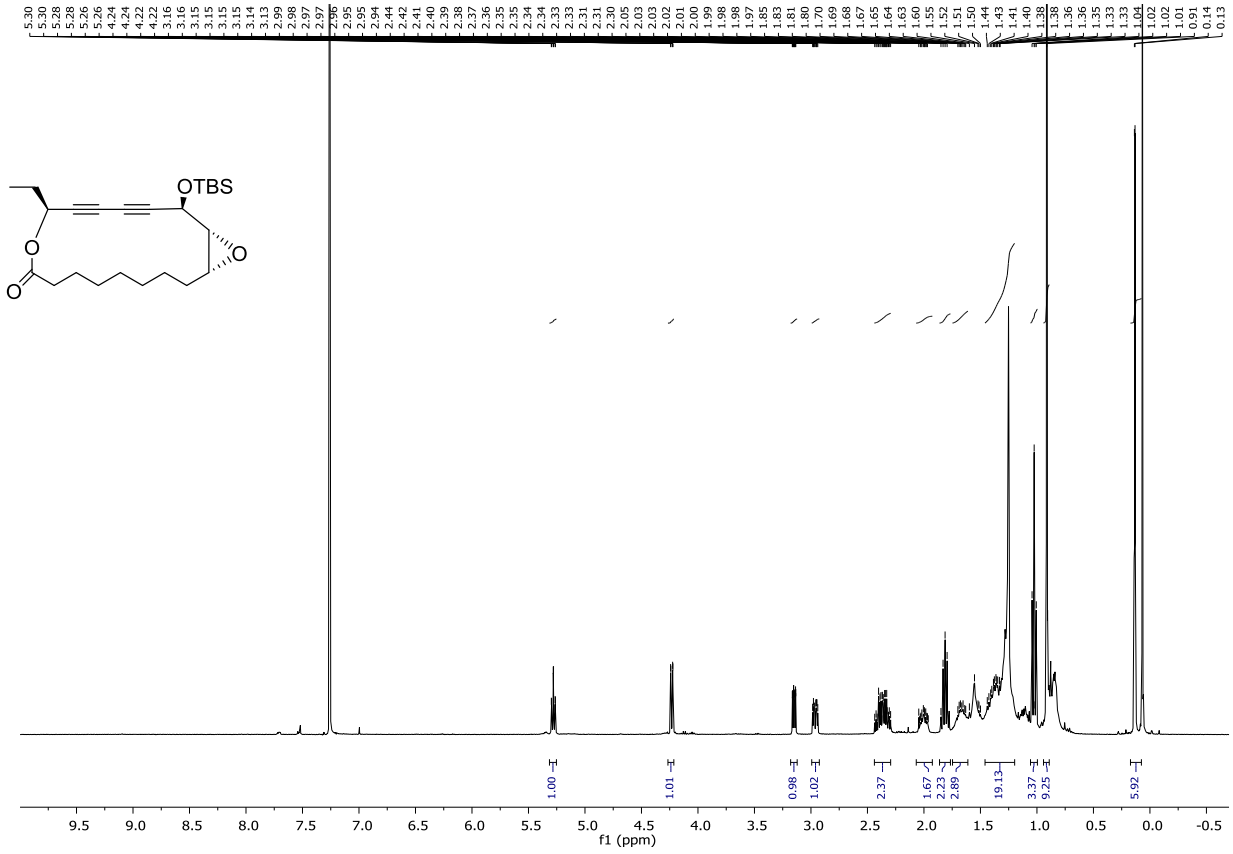
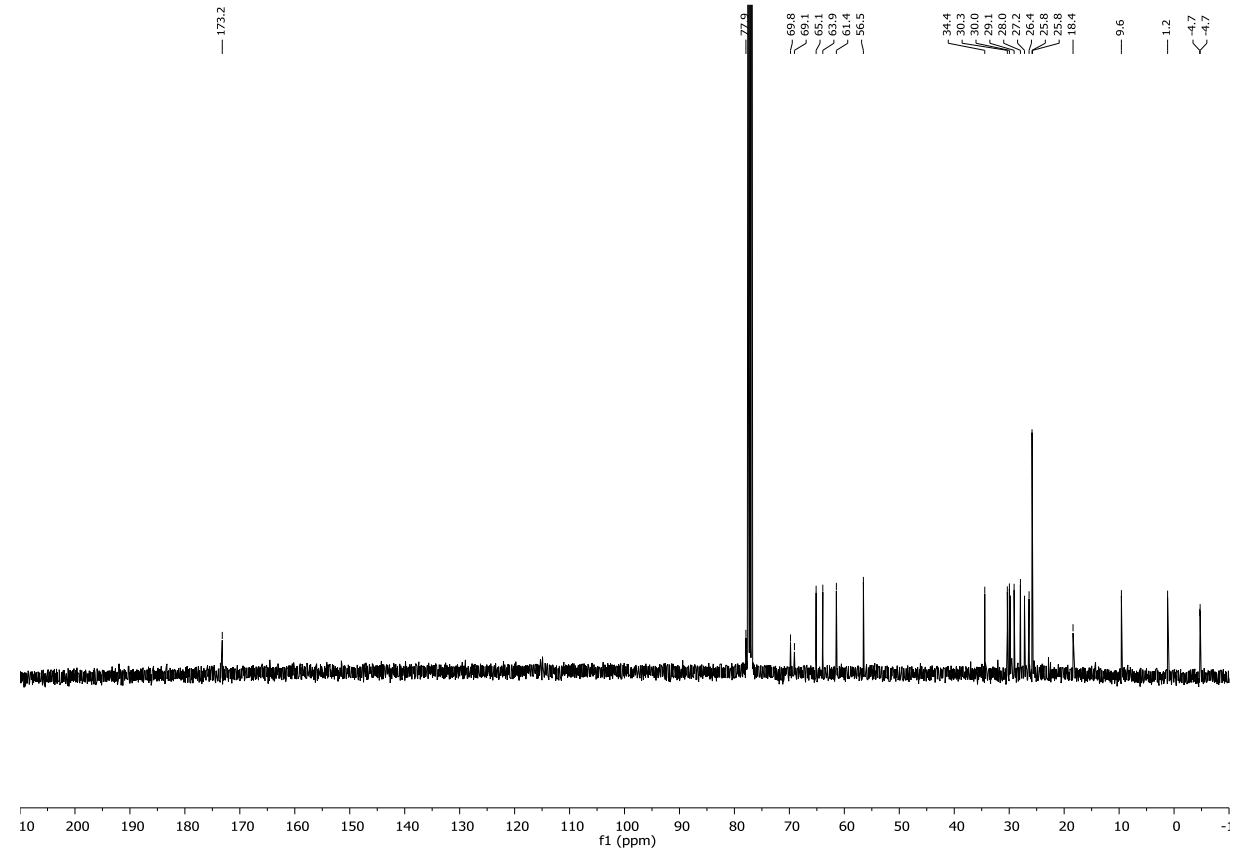
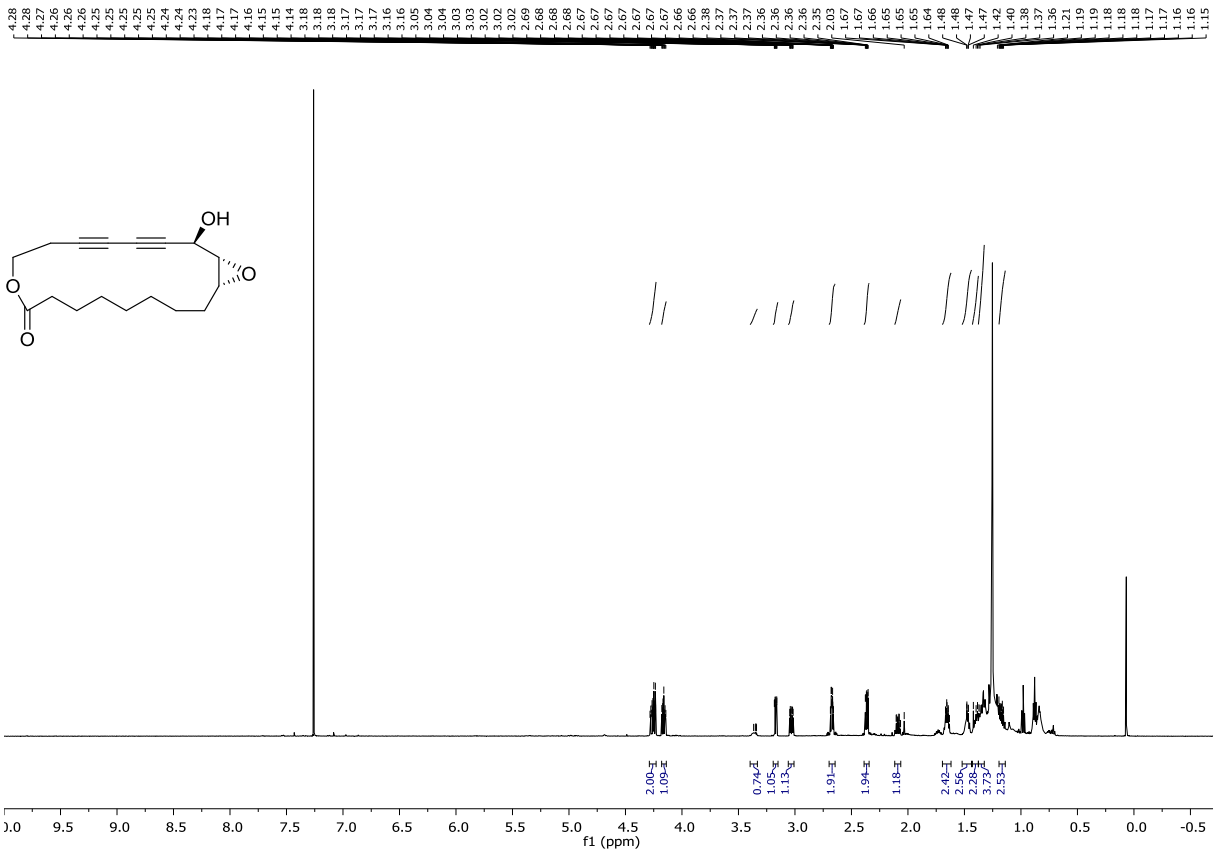
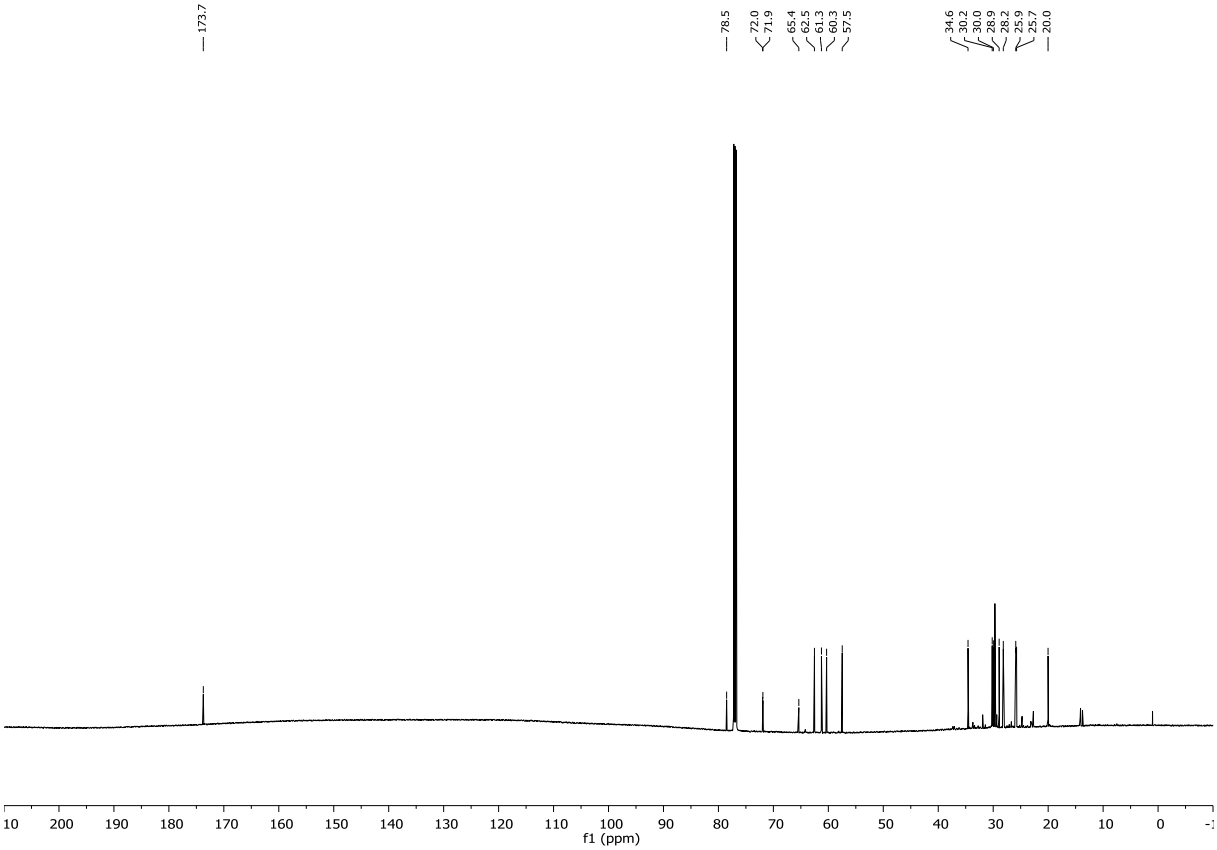
O
O
f1 (ppm)

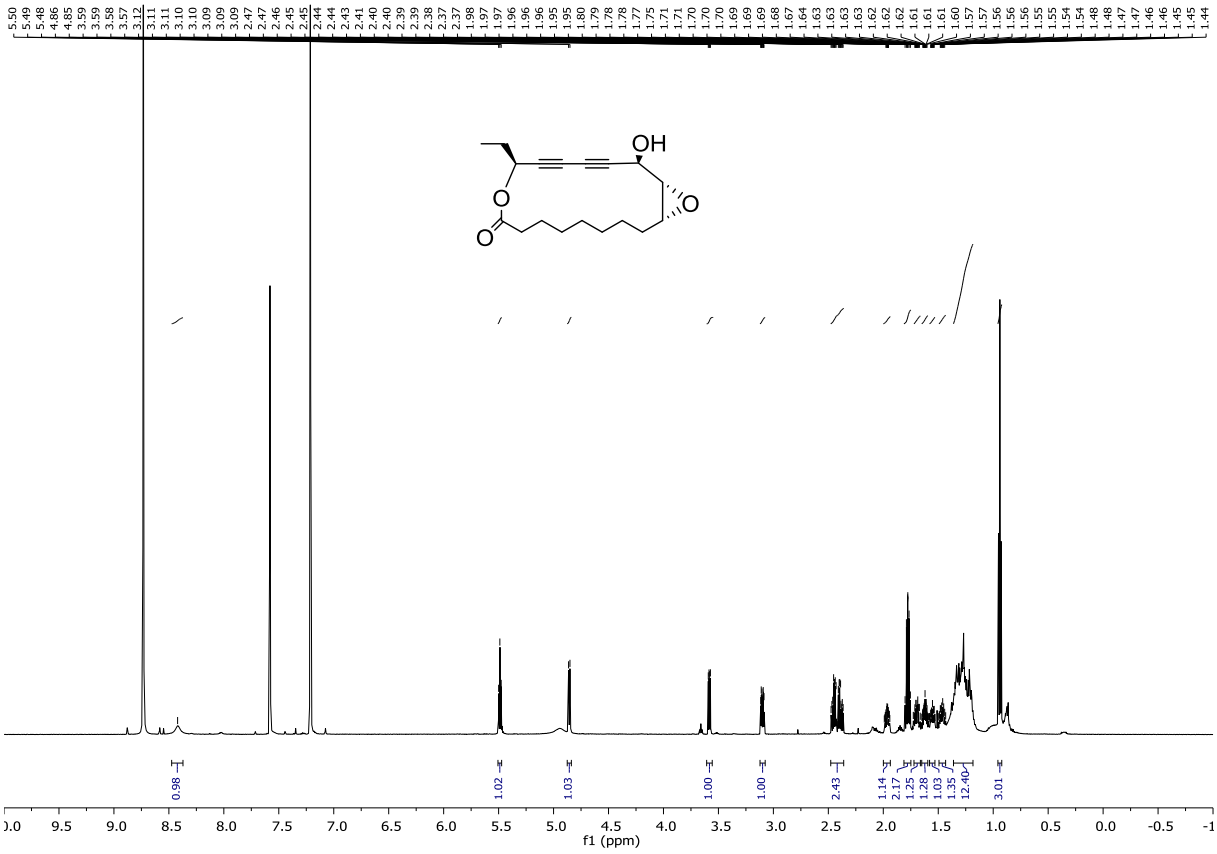

f1 (ppm)

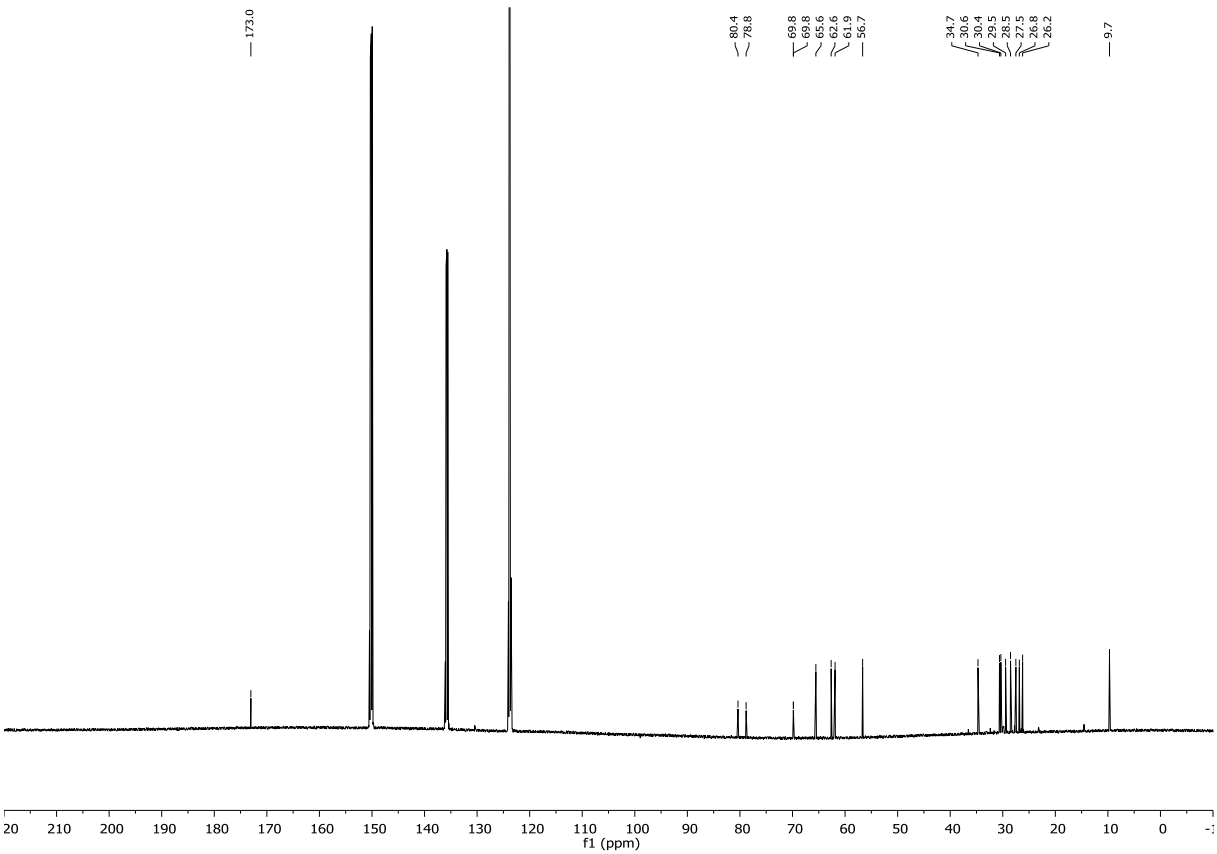

OTBS
O
O
O
f1 (ppm)

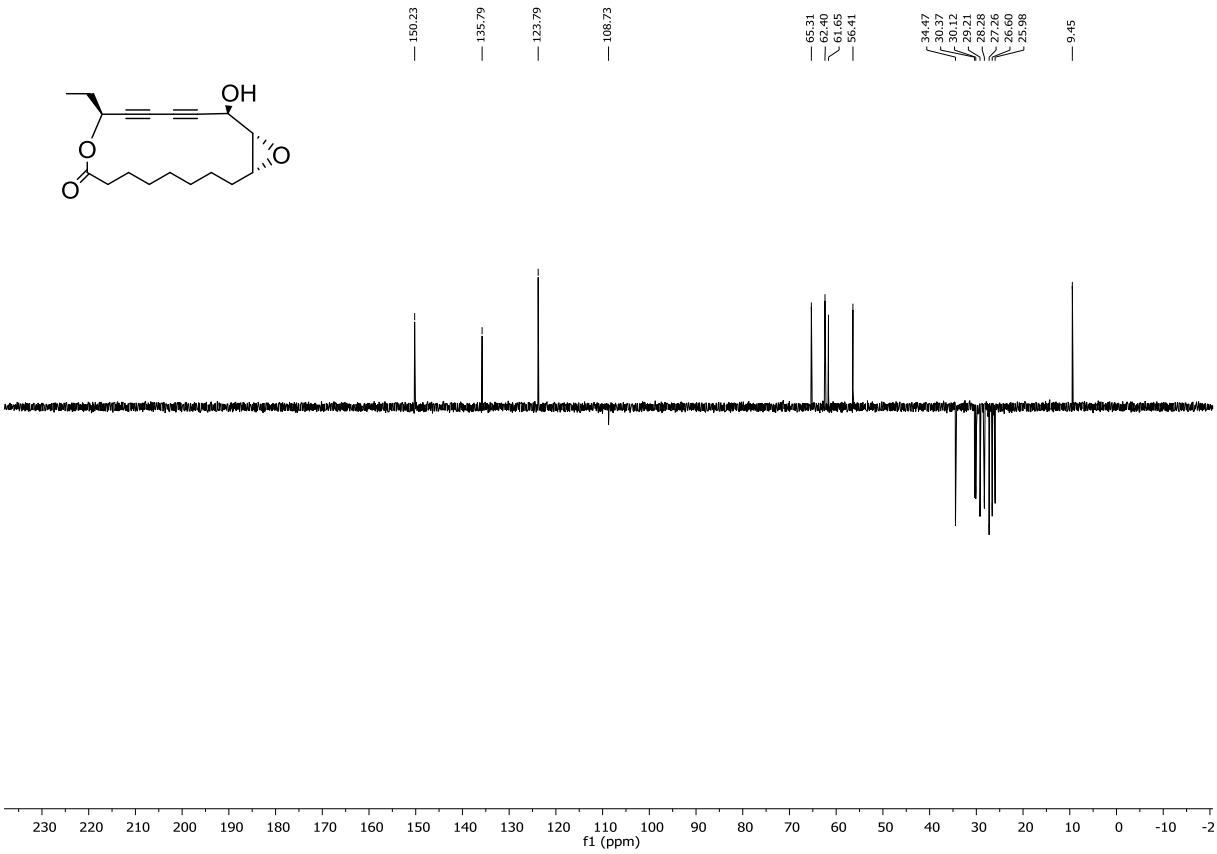

f1 (ppm)


OH
O
O
O
f1 (ppm)


f1 (ppm)


OH
O
O
O
f1 (ppm)


f1 (ppm)


150.23
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62.40
61.65
56.41
34.47
30.37
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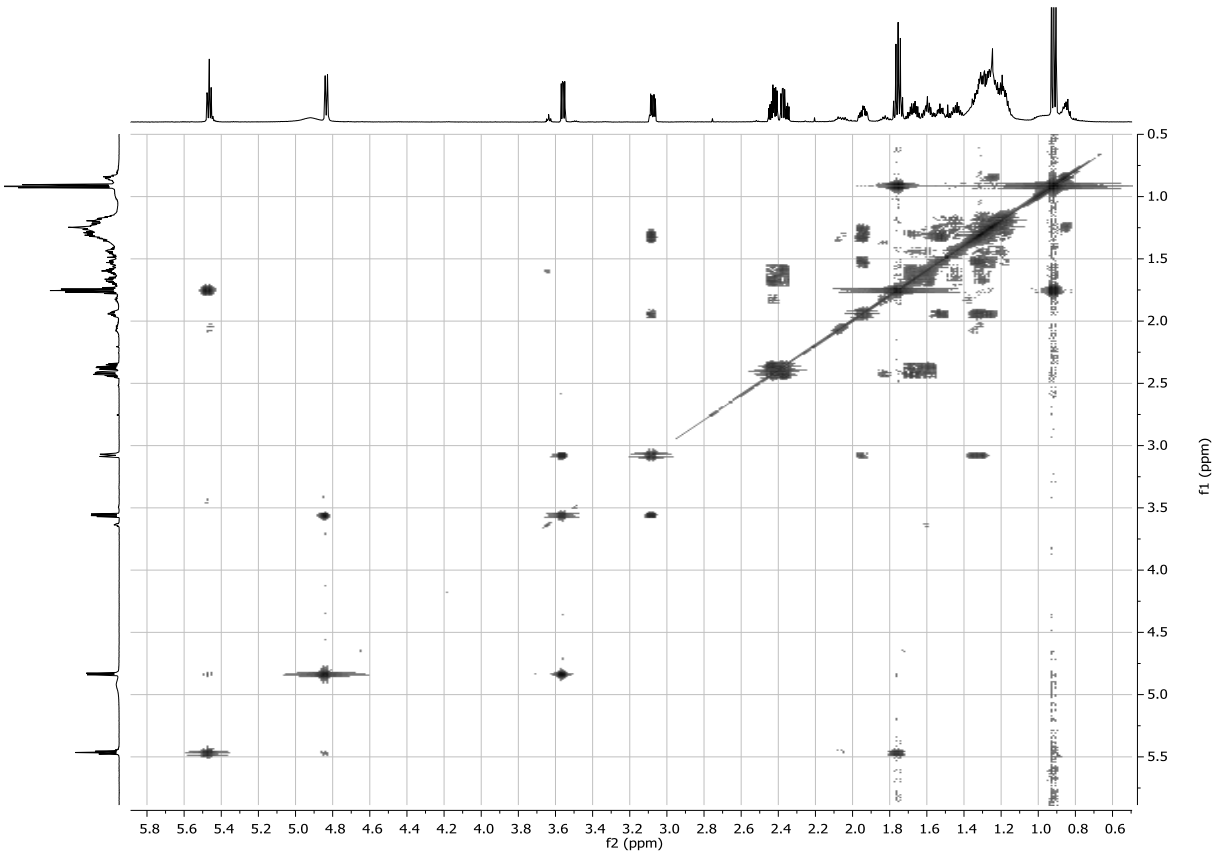
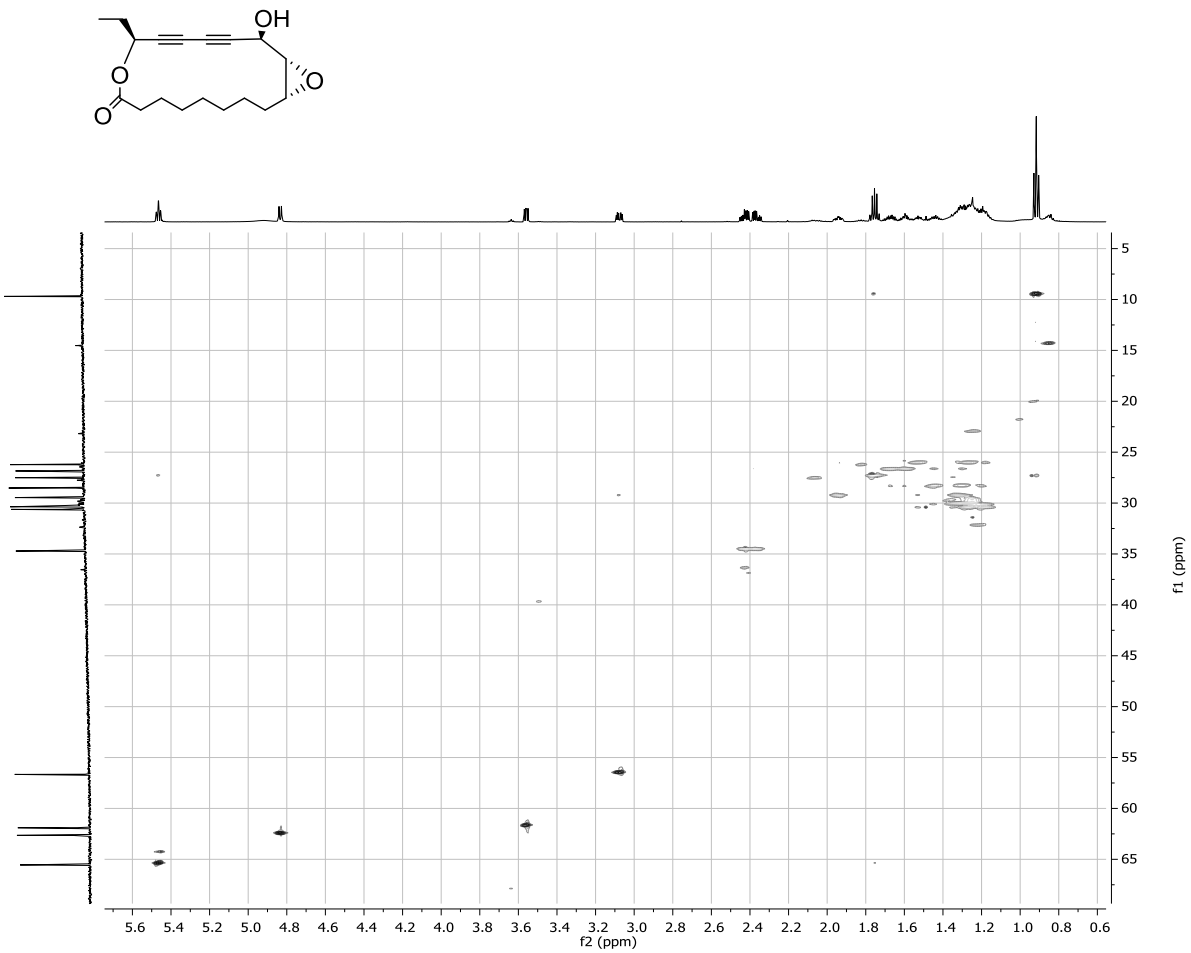
29.21
28.28
27.26
26.60
25.98
9.45
OH
O
O
O
f1 (ppm)


f2 (ppm)
f1 (ppm)


OH
O
O
O
f1 (ppm)
f2 (ppm)