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Supporting Information

Copper-Catalyzed Double Additions and Radical Cyclization Cascades in the Re-Engineering of the Antibacterial Pleuromutilin

Rebecca E. Ruscoe, Neal J. Fazakerley, Huanming Huang, Sabine Flitsch, and David J. Procter*[a]

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Supporting Information

Radical cyclization cascades in the re-engineering of the skeleton of the antibacterial pleuromutilin

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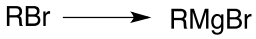
General Information

All reactions were carried out under an inert nitrogen atmosphere unless otherwise stated. Glassware for inert atmosphere reactions was oven-dried and cooled under a flow of nitrogen. Tetrahydrofuran (THF) was distilled over sodium wire and benzophenone. CH_2Cl_2, toluene, di-*iso*-propyl amine (DIPA) and triethylamine were distilled over calcium hydride, and dimethyl formamide (DMF) was dried over activated molecular sieves. All other solvents and reagents were purchased from commercial sources and used as supplied. ^{1}H NMR spectra were recorded on a 400, or 500 MHz spectrometer; ^{13}C NMR spectra were recorded at 101 or 126 MHz. ^{19}F NMR spectra were recorded at 376 MHz. All chemical shift values are reported in parts per million (ppm) relative to the solvent signal and were determined in $CDCl_3$, with coupling constant (*J*) values reported in Hz. The notation of signals is: Proton: δ *chemical shift (number of protons, multiplicity, J value(s), proton assignment)*. Carbon: δ *chemical shift (carbon assignment)*. Fluorine: δ *chemical shift (fluorine assignment)*. For multiplets and overlapping signals a range of shifts is reported. Routine TLC analysis was carried out on aluminum sheets coated with silica gel 60 Å F254, 0.2 mm thickness. Plates were viewed using 254 nm ultraviolet light and dipped in aqueous potassium permanganate, *p*-anisaldehyde or phosphomolybdic acid. Flash column chromatography was carried out on 40-63 μ, 60 Å silica gel. Low resolution and high resolution mass spectra were obtained using either positive and/or negative electrospray ionisation (ES), electron impact ionisation (EI) or chemical ionisation (CI) techniques. IR spectra were recorded on an ATR FTIR spectrometer as evaporated films (from $CHCl_3$) or neat.

General Procedures

General Procedure A: Formation of Grignard Reagents

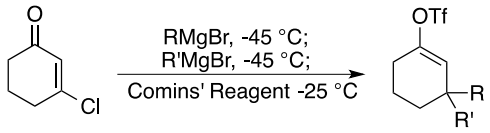


Grignard reagents were synthesised using the Schlenk method. 1,2-Dibromoethane (0.1 equiv.) was added to thermally activated magnesium turnings (3.0 equiv.) in THF (4.0 M) under an atmosphere of argon. The reaction was allowed to return to room temperature. The solution was then placed in a water bath at 40 – 50 °C and a solution of RBr (1.0 equiv.) in THF (1.3 M) was added at a rate of 1 mL/min. After the addition of the bromide the water bath was removed. Once the solution had cooled to room temperature, THF was added until the precipitate was completely dissolved. The resulting Grignard solution was titrated against iodine to determine its concentration.

General preparation of PhSLi (0.8 M in THF/hexanes)

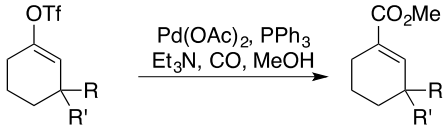
To a stirred solution of PhSH (205 µL, 2.0 mmol, 1.0 equiv.) in THF (1.3 mL) at −78 °C (acetone/CO_2) under argon, was added BuLi (1.58 M in hexanes, 1.27 mL, 2mmol, 1.0 equiv.). The resultant solution was stirred for 10 minutes before being allowed to warm to ambient temperature. The deprotonation was assumed to be quantitative and the total volume of the solution was measured. The resultant solution of PhSLi (0.8 M in THF/*n*-hexane, 2.5 mL) was used directly.

General Procedure B: 1,4-Double Addition Reactions Followed by Enolate Trapping with Comins' Reagent



The chloro-enone (1.0 equiv.) was added to a solution of PhSLi (0.1 equiv.) and CuI (0.1 equiv) at -45 °C under an atmosphere of argon. After 10 minutes, the first Grignard reagent, RMgBr (1.0 equiv.), was added dropwise and the reaction mixture was left to stir for 30 minutes. The second Grignard reagent, R'MgBr (1.5 equiv.) was then added dropwise and the reaction was left to stir for 4 hours. The solution was then allowed to warm to -25 °C and a solution of Comins' reagent (1.6 equiv.) in THF was added in one portion and the reaction mixture was allowed to warm to room temperature and stirred for 72 hours. The reaction was quenched with aqueous saturated NH_4Cl and left to stir for 1 hour, followed by extraction into Et_2O. The organic component was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by column chromatography (50:1, hexane:ethyl acetate).

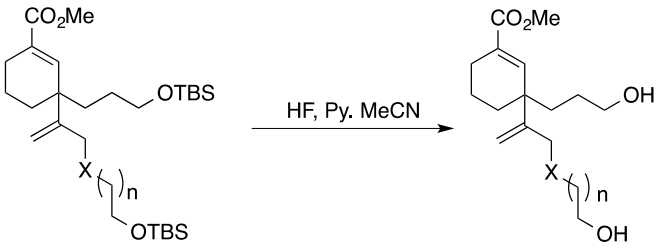
General Procedure C: Palladium-Catalysed Methoxycarbonylation



Carbon monoxide was bubbled through a solution of the triflate (1.0 equiv.), dimethylformamide (0.2 M), methanol (40 equiv.), Et_3N (2.0 equiv.), $Pd(OAc)_2$ (0.2 equiv.), and PPh_3 (0.4 equiv.) for 30 minutes. The resulting yellow solution was then heated to 40 °C under an atmosphere of carbon monoxide, to give a red solution. After 24 hours, the black solution was quenched with distilled water and extracted

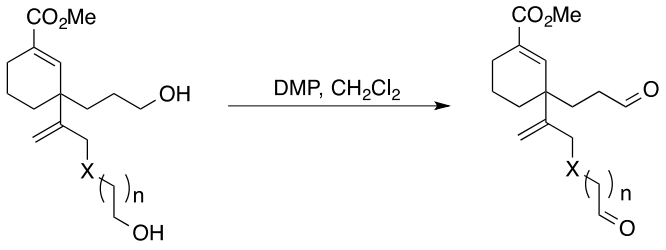
into Et_2O. The organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by column chromatography (50:1, hexane:ethyl acetate).

General Procedure D: Double-TBS Deprotection



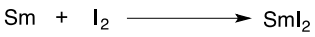
A solution of HF (60% aqueous solution, 20 equiv.) was added to a mixture of the bis-silyl ether (1.0 equiv.), pyridine (0.2 M) and acetonitrile (0.1 M) at 0 °C. After 18 hours, the reaction was quenched with aqueous saturated $NaHCO_3$ and extracted into Et_2O. The organic layer was washed successively with aqueous $CuSO_4$ and brine. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product. The compound was purified by column chromatography on silica gel (EtOAc) to give the desired diol.

General Procedure E: Double-Oxidation with Dess-Martin Periodinane



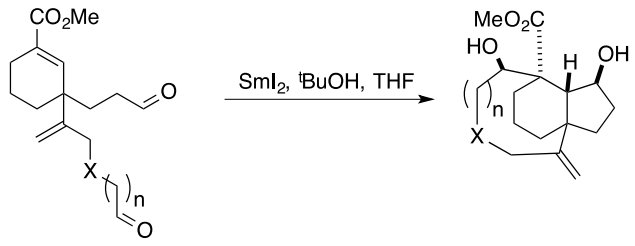
Dess-Martin Periodinane (2.2 equiv.) was added to a solution of the diol (1.0 equiv.) in CH_2Cl_2 (0.1 M) under an atmosphere of nitrogen. After 3 hours, the mixture was concentrated *in vacuo* to give the crude product, which was purified using column chromatography (30% EtOAc/hexane) to give the desired dialdehyde.

General Procedure F: Formation of SmI_2 Solution[1]



The reaction vessel was flushed with nitrogen for 30 minutes prior to the addition of Sm (1.4 equiv.) and THF (1.0 M). Nitrogen was then bubbled through the solution for a further 10 minutes. Iodine (1.0 equiv.) was added and the resulting mixture was heated to 40 °C for 12 hours to give the desired SmI_2 solution (0.1M). The concentration was determined using the method developed by Hilmersson.[2]

General Procedure G: SmI_2-Mediated Cascade Reaction



A mixture of degassed ^tBuOH (5.0 equiv.) and SmI_2 (2.5 equiv.) under a nitrogen atmosphere were stirred at room temperature for 15 minutes before being cooled to 0 °C. The dialdehyde (1.0 equiv.) was added dropwise to the solution via cannula and the reaction was stirred for 30 minutes before being quenched by exposure to air at 0 °C. After the addition of aqueous saturated NaK tartrate and Et_2O, the reaction mixture was allowed to warm to room temperature. The product was extracted into Et_2O, dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by column chromatography (60% EtOAc/hexane).

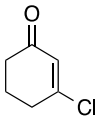
[1] M. Szostak, M. Spain, D. J. Procter, *J. Org. Chem*., **2012**, *77*, 3049.
[2] A. Dahlen, G. Hilmersson, *Eur. J. Inorg. Chem*., **2004**, *15*, 3020.

General Procedure H: TBS-Protection

Imidazole (1.6 equiv.) was added to solution of ROH (1.0 equiv.) in CH_2Cl_2 at room temperature. The resulting mixture was left to stir until homogeneous, after which, TBSCl (1.2 equiv.) was added portion wise. The reaction was then left to stir for 18-20 hours in air, before the reaction was quenched with aqueous saturated $NaHCO_3$ and extracted into Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by column chromatography on silica gel (petroleum ether (40-60) – 10% Ethyl acetate/petroleum ether (40-60)).

Synthesis of Starting Materials

3-Chlorocyclohex-2-en-1-one (4)[3]

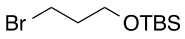


4

A mixture of 1,3-cyclohexanedione (5.61 g, 50.0 mmol, 1.0 equiv.), dichloromethane, (125 mL) and dimethylformamide (5.01 mL, 65.0 mmol, 1.3 equiv.) were cooled to 0 °C under a nitrogen atmosphere. Oxalyl chloride (5.10 mL, 60.0 mmol, 1.2 equiv.) was added to this solution dropwise. The reaction was allowed to warm to room temperature and left to stir for one hour before being quenched with distilled water (100 mL) and extracted with Et_2O (3 X 100 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product. Purification by column chromatography on silica gel (30% EtOAc/petroleum ether 40/60) gave **4** (5.76 g, 44.1 mmol, 88%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (1H, s, C*H*=Cl), 2.69 (2H, t, *J* = 6.2 Hz, CH_2C=O), 2.41 (2H, t, *J* = 6.7 Hz, CH_2C(Cl)=CH), 2.09 (2H, quin, *J* = 6.4 Hz, CH_2CH$_2$C(Cl)=CH); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0 (*C*=O), 158.7 (*C*Cl=CH), 128.5 (CCl=*C*H), 36.4 (*C*H$_2$C=O), 33.9 (*C*H$_2$CCl), 22.2 (*C*H$_2$CH$_2$CCl); v_{max} (thin film/cm^{-1}): 2953 (w), 2887 (w), 1678 (s, C=O), 1606 (m), 1426(w), 1341 (m), 1289 (m), 1187 (w), 991 (m). Data consistent with literature.

[3] R. E. Mewshaw, *Tetrahedron Lett.*, **1989**, *30*, 3753.

(3-Bromopropoxy)(*tert*-butyl)dimethylsilane (S1)[4]



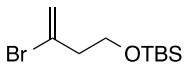
S1

General procedure H was followed: 3-bromo-propan-1-ol (25.2 g, 0.18 mol, 1.0 equiv.), imidazole (19.6 g, 0.28 mol, 1.6 equiv.), TBSCl (32.6 g, 0.22 mol, 1.2 equiv.) in CH_2Cl_2 (400 mL) gave the crude product. Purification by chromatography on silica gel (5% EtOAc/petroleum ether 40/60) gave **S1** (41.0 g, 0.17 mol, 97%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (2H, t, *J* = 5.7 Hz, C*H*$_2$OTBS), 3.53 (2H, t, *J* = 6.5 Hz, C*H*$_2$Br), 2.04 (2H, quin, *J* = 6.1 Hz, C*H*$_2$CH$_2$OTBS), 0.91 (9H, s, OSiC(C*H*$_3$)$_3$), 0.08 (6H, s, OSi(C*H*$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 60.4 (*C*H$_2$OTBS), 35.5 (*C*H$_2$CH$_2$OTBS), 30.7 (*C*H$_2$Br), 25.9 (SiC(*C*H$_3$)$_3$), -18.3 (Si*C*), -5.4 (Si(*C*H$_3$)$_2$). Data consistent with literature.

[4] Y. Maeda, K. Saito, N. Akamatsu, Y. Chiba, S. Ohno, Y. Okui, M. Yamada, T. Hasegawa, M. Kako, T. Akasaka, *J. Am. Chem. Soc*., **2012**, *134*, 18101.

Synthesis of Vinyl Bromides

((3-Bromobut-3-en-1-yl)oxy)(*tert*-butyl)dimethyllsilane (S2)[5]

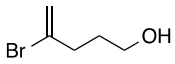


S2

Prepared according to general procedure H. TBSCl (8.32 g, 55.2 mmol, 1.2 equiv.), 3-bromo-3-buten-1-ol (7.00 g, 46 mmol, 1.0 equiv.), imidazole (5.00 g, 73.6 mmol, 1.6 equiv.) in CH_2Cl_2 (92 mL), after quenching with aqueous saturated $NaHCO_3$ (100 mL) and extraction into Et_2O (3 X 100 mL), gave the crude product, which was then purified on silica gel (10% EtOAc/petroleum ether) to give **S2** (10.1 g, 38.1 mmol, 82%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (1H, s, 1H from C=CH_2), 5.47 (1H, d, *J* = 1.2 Hz, 1H from C=CH_2), 3.79 (2H, t, *J* = 6.4 Hz, CH_2OTBS), 2.55 (2H, t, *J* = 6.4, CH_2CH$_2$OTBS), 0.90 (9H, s, SiC(CH_3)$_3$), 0.08 (6H, s, Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 130.9 (*C*=CH$_2$), 118.4 (C=*C*H$_2$), 60.9 (*C*H$_2$OTBS), 44.8 (*C*H$_2$CH$_2$OTBS), 25.9 (Si(*C*H$_3$)$_2$), 14.2 (Si*C*), -5.3 (SiC(*C*H$_3$)$_3$); ν_{max} (thin film/cm^{-1}): 2954 (w), 2928 (m), 2857 (m), 1630 (m), 1471 (w), 1388 (w), 252 (m), 1099 (s), 1006 (w), 925 (w), 886 (w), 833 (s), 774 (s). Data consistent with literature.

[5] B. V. S. Reddy, S. G. Reddy, M. R. Reddy, M. Pal Bhadra, A. V. S. Sarma, *Org. Biomol. Chem.*, **2014**, *12*, 7257.

4-Bromopent-4-en-1-ol (S3)[6]



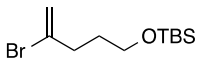
S3

*n*BuLi (47.5 mL, 75.0 mmol, 1.58 M in hexanes) was added to a solution of di*iso*propylamine (10.7 mL, 75.8 mmol, 1.0 equiv.) in THF (25 mL) at - 78 °C under a nitrogen atmosphere. The reaction mixture was allowed to warm to room temperature over 2 h. The resulting LDA solution was added to a suspension of EtOAc (7.35 mL, 75.0 mmol, 1.0 equiv.) and CuI (28.6 g, 150 mmol, 2.0 equiv.) in THF (75 mL) at -45 °C. The reaction was allowed to warm to -30 °C, before the addition of a solution of 2,3-dibromopropene[7] (3.88 mL, 37.5 mmol, 0.5 equiv.) in THF (17.5 mL). After stirring for 2.5 hours, the reaction mixture was quenched with aqueous saturated NH_4Cl (100 mL), extracted into Et_2O (3 X 50 mL) and washed with brine (100 mL). The organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to give the crude ester product.

A solution of the crude ester in THF (50 mL) was added to a mixture of $LiAlH_4$ (1.89 g, 50.0 mmol, 0.7 equiv.) in THF (150 mL) at 0 °C and stirred for 1 h. Et_2O (50 mL) was added followed by; distilled water (2 mL), 1 M aqueous NaOH (2 mL), and distilled water (3 X 2 mL). The mixture was allowed to warm to room temperature and $NaSO_4$ was added and left to stir for 15 min. Concentraction *in vacuo* then gave the crude product, which was taken onto the next step without further purification.

[6] T. Mandai, J. Nokami, T.Yano, Y. Yoshinaga, J. Otera, *J. Org. Chem.,* **1984**, *49*, 72.
[7] Prepared following procedure: R. Lespieau, M. Bourguel, *Org. Synth*., **1925**, 5, 49.

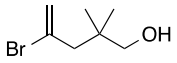
((4-Bromopent-4-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S4)[8]



S4

Prepared according to general procedure H. **S3** (75.0 mmol, 1.0 equiv.), imidazole (7.62 g, 112 mmol, 1.5 equiv.), TBSCl (11.3 g, 90.0 mmol, 1.2 equiv.) in CH_2Cl_2 (150 mL), after quenching with aqueous saturated $NaHCO_3$ (100 mL), extraction into Et_2O (3 X 100 mL) and purification by column chromatography (5-10% EtOAc/petroleum ether 40/60) gave **S4** (12.9 g, 46.1 mmol, 62%(2 steps)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (1H, d, *J* = 1.5 Hz, 1H from C=C*H*$_2$), 5.41 (1H, d, *J* = 1.5 Hz, 1H from C=C*H*$_2$), 3.64 (2H, t, *J* = 6.2 Hz, C*H*$_2$OTBS), 2.52 (2H, td, *J* = 7.4, 0.9 Hz, C*H*$_2$C=CH$_2$), 1.78 (2H, tt, *J* = 7.3, 6.2 Hz, C*H*$_2$CH$_2$OTBS), 0.90 (9H, s, SiC(C*H*$_3$)$_3$), 0.06 (6H, s, Si(C*H*$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.4 (*C*=CH$_2$), 116.6 (C=*C*H$_2$), 61.5 (*C*H$_2$OTBS), 37.9 (*C*H$_2$C=CH$_2$), 31.0 (*C*H$_2$CH$_2$OTBS), 25.9 (OSiC(*C*H$_3$)$_3$), 18.3 (OSi*C*), −5.3 (OSi(*C*H$_3$)$_2$); MS (ES$^+$) *m/z* (%): 279 (M$^+$H$^+$, 70), 301 (M$^+$Na$^+$, 50). HRMS could not be obtained. Data consistent with literature.[6]

4-Bromo-2,2-dimethylpent-4-en-1-ol (S5)



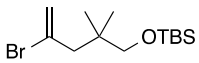
S5

*n*BuLi (35.7 mL, 50.0 mmol, 1.0 equiv.) was added dropwise to a solution of di*iso*propylamine (7.00 mL, 50.0 mmol, 1.0 equiv.) in THF (36 mL) at –78 °C under

[8] J. D. Eckelbarger, *Chem. Eur. J.*, **2008**, *14*, 4293.

an atmosphere of nitrogen and left to stir for 30 min. After warming to room temperature, the solution of LDA was added to a suspension of methyl *iso*butyrate (5.70 mL, 50.0 mmol, 1.0 equiv.), CuI (19.1 g, 100 mmol, 2.0 equiv.) in THF (50 mL) at -40 °C under an atmosphere of nitrogen. After stirring for 30 min, 2,3-dibromoprop-1-ene[7] (2.44 mL, 25.0 mmol, 0.5 equiv.) was added to the reaction mixture. After being allowed to stir for 1 h, the reaction was quenched with aqueous saturated NH_4Cl (100 mL) followed by extraction into Et_2O (3 X 50 mL). The organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting crude ester was dissolved in THF (25 mL) and was added dropwise to a suspension of $LiAlH_4$ (1.27 g, 33.5 mmol, 0.67 equiv.) in THF (152 mL) under nitrogen at 0 °C and left to stir for 4 h. The reaction was quenched at 0 °C by the addition of water (1.27 mL), NaOH (1.27 mL, 1 M) followed by another addition of water (3.81 mL). The mixture was then diluted in Et_2O (10 mL), exposed to the air and allowed to warm to room temperature. $MgSO_4$ was then added and the suspension was left to stir for 15 min. The precipitate was removed by filtration, washed with a mixture of Et_2O (40 mL) and EtOAc (40 mL) and was then concentrated *in vacuo* to give the crude product, which was taken onto the next step without further purification.

((4-Bromo-2,2-dimethylpent-4-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S6)

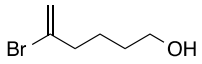


S6

Prepared according to general procedure H. Imidazole (170 mg, 2.50 mmol, 1.6 equiv.), **S5** (775 mg, 4.00 mmol, 1.0 equiv.), TBSCl (723 mg, 4.8 mmol, 1.2 equiv.) in CH_2Cl_2 (8 mL) after quenching with aqueous saturated $NaHCO_3$ (10 mL), extraction into Et_2O (3 X 10 mL) and purification by column chromatography (10%

EtOAc/hexane) gave **S6** (0.56 g, 1.82 mmol, 46% (2 steps)) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 - 5.57 (2H, m, C=CH_2), 3.31 (2H, s, CH_2OTBS), 2.49 (2H, s, CH_2C(CH_3)$_2$), 0.95 (6H, s, C(CH_3)$_2$), 0.87 (9H, s, OSiC(CH_3)$_3$), 0.02 (6H, s, OSi(CH_3)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 130.4 (*C*=CH_2), 120.1 (C=*C*H_2), 70.7 (*C*H_2OTBS), 48.9 (*C*H_2C(CH_3)$_2$), 36.5 (CH_2*C*(CH_3)$_3$), 25.9 (OSiC(*C*H_3)$_3$), 24.3 (CH_2C(*C*H_3)$_2$), 18.3 (OSi*C*), -5.50 (OSi(*C*H_3)$_2$); ν_{max} (thin film/cm^{-1}): 3002 (w), 2944 (w), 1442 (m), 1375 (m), 1038 (w), 918 (w), 749 (m); MS was uninformative.

5-Bromohex-5-en-1-ol (S7)[9]

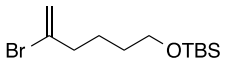


S7

A solution of bromine (11.3 mL, 0.22 mmol, 1.0 equiv.) in CH_2Cl_2 (18 mL) was added to a solution of 5-hexen-1-ol (21.8 g, 0.22 mmol, 1.0 equiv.) in CH_2Cl_2 (18 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 hour. The resulting mixture was concentrated *in vacuo* to give the crude dibromide. A solution of KO*t*Bu (22.7 g, 0.22 mol, 1.0 equiv.) in dry THF (100 mL) was added to a solution of the crude dibromide in THF (100 mL) under a nitrogen atmosphere at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 4 hours before being quenched with water (150 mL), extracted into Et_2O (3 X 100 mL) and dried ($MgSO_4$). The organic component was concentrated *in vacuo* to give crude **S7** as a brown oil, which was taken onto the next without further purification.

[9] *US Pat*., US2001071951, **2011**.

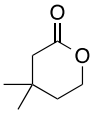
((5-Bromohex-5-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S8)



S8

Prepared according to general procedure H. Imidazole (1.84 g, 270 mmol, 1.5 equiv.), **S7** (3.20 g, 18.0 mmol, 1.0 equiv.), TBSCl (3.32 g, 22 mmol, 1.2 equiv.) in CH_2Cl_2 (80 mL), after quenching with aqueous sat. $NaHCO_3$ (80 mL), extraction into Et_2O (3 X 80 mL) and purification by column chromatography (30% EtOAc/petroleum ether 40/60) gave **S8** (5.28 g, 17.8 mmol, 99%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (1H, d, *J* = 1.5 Hz, 1H from C=C*H*$_2$), 5.40 (1H, d, *J* = 1.5 Hz, 1H from C=C*H*$_2$), 3.63 (2H, t, *J* = 6.3 Hz, C*H*$_2$OSi), 2.45 (2H, td, *J* = 7.2, 0.8 Hz, C*H*$_2$C=CH$_2$), 1.57 - 1.67 (2H, m, C*H*$_2$CH$_2$CH$_2$OSi), 1.49 - 1.56 (2H, m, C*H*$_2$CH$_2$OSi), 0.90 (9H, s, SiC(C*H*$_3$)$_3$), 0.06 (6H, s, Si(C*H*$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.7 (CH$_2$=*C*(Br)), 116.4 (*C*H$_2$=C(Br)), 62.8 (*C*H$_2$OTBS), 41.2 (*C*H$_2$(CH$_2$)$_2$OTBS), 31.5 (*C*H$_2$(CH$_2$)$_2$OTBS), 26.0 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 24.3 (*C*H$_2$CH$_2$OTBS), 18.3 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), -5.3 (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$); ν_{max} (thin film/cm^{-1}): 2930 (s), 2885 (m), 2858 (m), 1471 (m), 1387 (m) 1361 (w), 1254 (m), 1146 (w), 1101 (m). MS was uninformative.

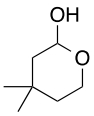
4,4-Dimethyltetrahydro-2*H*-pyran-2-one (S9)[10]



S9

A solution of 3,3-dimethylglutaric anhydride (10.0 g, 70.0 mmol, 1.0 equiv.) in THF (30 mL), was added to a suspension of sodium borohydride (2.66 g, 70.3 mmol, 1.0 equiv.) in THF (40 mL) at 0 °C under a nitrogen atmosphere. The reaction mixture was allowed to warm to room temperature and was stirred for 20 hours. The reaction was quenched with aqueous HCl (20 mL, 6 M) and extracted into Et_2O (3 X 50 mL). The organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was taken onto the next step with no further purification.

4,4-Dimethyltetrahydro-2*H*-pyran-2-ol (S10)[11]



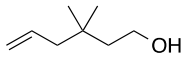
S10

A solution of DIBAL-H (1M in hexanes, 84.0 mL, 1.2 equiv.) was added to a mixture of **S9** (70.0 mmol, 1.0 equiv.), pentane (70.0 mL) and dichloromethane (70 mL) at -78 °C under a nitrogen atmosphere. After 4 hours, methanol (11.7 mL, 70 mmol, 1.0 equiv., 6 M) was added, stirred for 15 minutes and allowed to warm to room temperature for 4 hours. The reaction mixture was poured onto aqueous saturated NaK tartrate (50 mL) and extracted into Et_2O (3 X 50 mL). The organic layers were

[10] J. Picha, V. Vanek, M. Budesinsky, J. Mladkova, T. A. Garrow, *Eur. J. Med. Chem.*, **2013**, 65, 256.
[11] R. D. Little, G. W. Muller, M. G. Venegas, G. L. Carroll, A. Bukhari, L. Patton, K. Stone, *Tetrahedron*, **1981**, 37, 4371.

dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was taken onto the next step with no further purification.

3,3-Dimethylhex-5-en-1-ol (S11)[12]

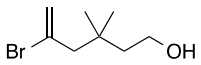


S11

*n*BuLi (87.5 mL, 140 mmol, 2.0 equiv.) was added dropwise to a stirred solution of Me_3PhPBr (55.0 g, 154 mmol, 2.2 equiv.) in THF (350 mL) at -78 °C under an atmosphere of nitrogen. The resulting yellow mixture was allowed to warm to room temperature over 2 hours. At which point a solution of **S10** (70.0 mmol, 1.0 equiv.) in THF (70 mL) was added dropwise and the reaction was refluxed for 4 hours. Once cooled the reaction was quenched with aqueous saturated NH_4Cl (200 mL), extracted into Et_2O (3 X 100 mL) and dried ($MgSO_4$). The organic layers were concentrated *in vacuo* to give the crude product. Purification by flash column chromatography (30% EtOAc/hexane) gave **S11** (3.68 g, 28.7 mmol, overall 41% (3 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 (1H, ddt, *J* = 16.8, 10.3, 7.3, 7.3 Hz, C*H*=CH_2), 4.97 - 5.08 (2H, m, CH=C*H*$_2$), 3.72 (2H, td, *J* = 7.6, 4.8 Hz, C*H*$_2$OH), 1.98 (2H, d, *J* = 7.3 Hz, C*H*$_2$CH=CH_2), 1.53 (2H, t, *J* = 7.6 Hz, C*H*$_2$$CH_2$OH), 0.92 (6H, s, C(C*H*$_3$)$_2$). Data consistent with the literature.

[12] L. V. Tinao-Wooldridge, K. D. Moeller, C. M. Hudson, *J. Org. Chem*., **1994**, 59, 2381.

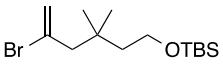
5-Bromo-3,3-dimethylhex-5-en-1-ol (S12)



S12

A solution of bromine (2.40 mL, 460 mmol, 1.0 equiv.) in CH_2Cl_2 (8.3 mL) was added to a solution of **S11** (5.90 g, 460 mmol, 1.0 equiv.) in CH_2Cl_2 (8.3 mL) at 0 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 1 hour. The resulting mixture was concentrate *in vacuo* to give the crude dibromide. A solution of KO*t*Bu (4.74 g, 460 mmol, 1.0 equiv.) in dry THF (23 mL) was added to a solution of the dibromide in THF (23 mL) under a nitrogen atmosphere at 0 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 4 hours. The reaction was quenched with water (40 mL), extracted into Et_2O (3 X 30 mL) and dried ($MgSO_4$). The organic component was concentrated *in vacuo* to give crude product as a brown oil, which was used in the next steps without further purification.

((5-Bromo-3,3-dimethylhex-5-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S13)

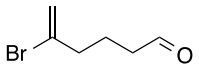


S13

Prepared according to general Procedure H. **S12** (9.16 mmol, 1.0 equiv), imidazole (1.00 g, 14.7 mmol, 1.6 equiv.), TBSCl (1.66 g, 11.0 mmol, 1.2 equiv.) in CH_2Cl_2 (18.3 mL), after quenching with aqueous saturated $NaHCO_3$ (20 mL), extracted into Et_2O (3 X 20 mL) and purification gave **S13** (2.13 g, 6.63 mmol, overall 72% (3 steps)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.56 (1H, s, 1H from C=CH_2), 5.54 (1H, s, 1H from C=CH_2), 3.71 (2H, t, J = 7.3 Hz, CH_2OTBS), 2.45 - 2.48 (2H, s, BrC(=C)CH_2),

1.58 (2H, t, *J* = 7.1 Hz, C*H*$_2$CH$_2$OTBS), 1.02 (6H, s, (C*H*$_3$)$_2$), 0.89 - 0.92 (9H, m, OSiC(C*H*$_3$)$_3$), 0.05 - 0.08 (6H, m, OSi(C*H*$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 130.2 (*C*=CH$_2$), 120.4 (C=*C*H$_2$), 59.9 (*C*H$_2$OSi), 53.1 (*C*H$_2$C=CH$_2$), 44.3 (*C*H$_2$CH$_2$OSi), 33.6 (*C*(CH$_3$)$_2$), 27.4 (C(*C*H$_3$)$_2$), 26.0 (SiC(*C*H$_3$)$_3$), 18.3 (Si*C*), −5.3 (Si(*C*H$_3$)$_2$); ν_{max} (thin film/cm^{-1}): 2955 (m), 2928 (m), 2885 (w), 2856 (m), 1622 (m), 1471 (m), 1463 (m), 1431 (w), 1388 (m), 1367 (m), 1361 (w), 1254 (s), 1171 (m), 1090 (s), 1047 (m), 999 (m), 939 (w), 887 (m), 834 (s), 810 (m). MS was uninformative.

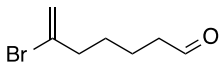
5-Bromohex-5-enal (S14)



S14

Et_3N (132 mL, 0.95 mol, 7.0 equiv.) and anhydrous DMSO (94.4 mL, 1.33 mol, 9.5 equiv.) were added to a solution of **S7** (24.3 g, 0.14 mol, 1.0 equiv.), which was then cooled to 0 °C, followed by the addition of SO_3Py. (66.8 g, 0.42 mol, 3.0 equiv.). The reaction mixture was allowed to warm to room temperature and left to stir for 16 h. The reaction was diluted with EtOAc (200 mL), washed with water (200 mL), aqueous saturated $NaHCO_3$ (200 mL) and brine (200 mL). After drying ($MgSO_4$) the organic layers were concentrated *in vacuo* to give the crude product, which was taken onto the next step without further purification.

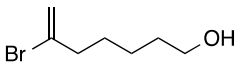
6-Bromohept-6-enal (S15)



S15

A solution of anhydrous KO*t*Bu (20.0 g, 0.18 mol, 1.3 equiv.) in THF (140 mL) was added to $ClPh_3PCHOCH_3$ (61.7 g, 0.18 mol, 1.3 equiv.) in THF (140 mL) at 0 °C. **S14** (0.14 mol, 1.0 equiv.) in THF (47 mL) was added dropwise, after which the reaction mixture was allowed to warm to room temperature over 4 h. The reaction mixture was quenched with water (140 mL), cooled to 0 °C for the addition of H_2SO_4 (30% aqueous solution)(39 mL) and was allowed to warm to room temperature. After 18 h, the reaction mixture was cooled to 0 °C, aqueous saturated $NaHCO_3$ (50 mL) was added and the reaction mixture was extracted into pentane (3 X 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was taken onto the next step without further purification.

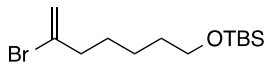
6-Bromohept-6-en-1-ol (S16)



S16

Sodium borohydride (15.9 g, 0.42 mol, 2.0 equiv.), was added portionwise to **S15** (0.14 mmol, 1.0 equiv.) in MeOH (460 mL, 0.14 mol, 0.3 M) at 0 °C. After 10 min the reaction was allowed to warm to room temperature. After 16 h, the solvent was removed *in vacuo,* washed with water (300 mL), extracted into Et_2O (3 X 200 mL) dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography (5% EtOAc/petroleum ether (40-60)) to give **S16** (12.4 g, 64.2 mmol, 46% (3 steps)).

((6-Bromohept-6-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S17)

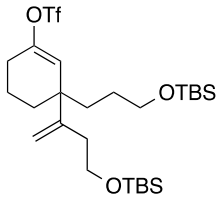


S17

Prepared according to general procedure H. TBSCl (11.6 g, 77.0 mmol, 1.2 equiv.), Imidazole (6.90 g, 102 mmol, 1.6 equiv.), **S16** (12.4 g, 64.0 mmol, 1.0 equiv.) in CH_2Cl_2 (128 mL), after quenching with aqueous saturated $NaHCO_3$ (100 mL), extraction into Et_2O (3 X 100 mL) and purification (5% EtOAc/petroleum ether(40-60)) gave **S17** (13.8 g, 44.9 mmol, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 (1H, d, *J* = 1.5 Hz, 1H from C=C*H*$_2$), 5.33 (1H, d, *J* = 1.5 Hz, 1H from C=C*H*$_2$), 3.56 (2H, t, *J* = 6.4 Hz, C*H*$_2$OTBS), 2.38 (2H, t, *J* = 7.3 Hz, CH_2=CC*H*$_2$), 1.44 - 1.56 (4H, m, 2 X C*H*$_2$), 1.26 – 1.35 (2H, m, C*H*$_2$), 0.82 - 0.86 (9H, m, C(C*H*$_3$)$_3$), -0.03 - 0.03 (6H, m, Si(C*H*$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.8 (*C*=CH_2), 116.3 (C=*C*H_2), 63.0 (*C*H_2OTBS), 41.4 (CH_2=C*C*H_2), 32.5 (*C*H_2), 27.7 (*C*H_2), 26.0 (C(*C*H_3)$_3$), 24.7 (*C*H_2), 18.4 (*C*(CH$_3$)$_3$), -5.3 (Si(*C*H$_3$)$_2$); v_{max} (thin film/cm^{-1}): 2929 (m, CH), 2896 (w), 2857 (m, CH), 1629 (w), 1471 (w), 1388 (w), 1388 (w), 1254 (m), 1099 (s), 1021 (m), 938 (w), 883 (w), 833 (s), 813 (w), 773 (s); MS was uninformative.

Synthesis of Unsaturated Esters

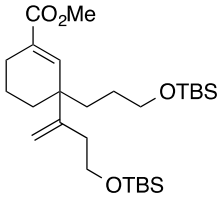
3-(4-((*tert*-Butyldimethylsilyl)oxy)but-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-en-1-yl trifluoromethanesulfonate (S18)



S18

Prepared according to general procedure B. PhSLi (0.44 mL, 0.91 M, 0.40 mmol, 0.1 equiv.), CuI (76 mg, 0.40 mmol, 0.1 equiv.), **4** (517 mg, 3.96 mmol, 1.0 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide (22 mL, 3.96 mmol, 0.18 M, 1.0 equiv.), (4-((*tert*-butyldimethylsilyl)oxy)but-1-en-2-yl)magnesium bromide (33 mL, 5.94 mmol, 0.18 M, 1.5 equiv.), Comins' reagent (2.49 g, 6.34 mmol, 1.6 equiv.), after quenching with aqueous saturated NH_4Cl (50 mL) and extraction into Et_2O (3 X 50 mL) and partial purification by column chromatography (50:1, hexane:EtOAc) to remove excess Comins' reagent gave **S18**, which was taken onto the next step.

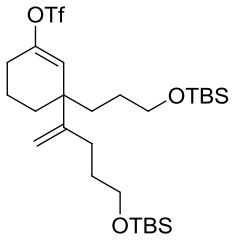
Methyl-3-(4-((*tert*-butyldimethylsilyl)oxy)but-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (6a)



6a

Prepared according to general procedure C. **S18** (3.66 mmol, 1.0 equiv.), $Pd(OAc)_2$ (177 mg, 0.79 mmol, 0.20 equiv.), PPh_3 (414 mg, 1.58 mmol, 0.4 equiv.), Et_3N (1.1 mL, 7.92 mmol, 2.0 equiv.), MeOH (6.41 mL, 158 mmol, 40 equiv.) and DMF (19.8 mL, 0.2 M), after quenching with water (10 mL), extraction into Et_2O (3 x 10 mL) and purification by column chromatography (50:1, hexane:EtOAc) gave **6a** (863 mg, 1.74 mmol, 44% (2 steps)) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (1H, s, C=C*H*), 4.87 (1H, s, 1H from C=CH_2), 4.70 (1H, s, 1H from C=CH_2), 3.70 (3H, s, CO_2CH_3), 3.63 - 3.69 (2H, m, CH_2OTBS), 3.50 - 3.58 (2H, m, CH_2OTBS), 2.25 - 2.29 (1H, m, 1H from CH_2), 2.17 – 2.22 (2H, m, CH_2), 2.05 - 2.15 (1H, m, 1H from CH_2), 1.66 - 1.73 (1H, m, 1H from CH_2), 1.55 - 1.63 (1H, m, 1H from CH_2), 1.25 - 1.52 (6H, m, 3 x CH_2) 0.85 (18H, s, 2 x SiC(CH_3)$_3$), -0.04 (12H, s, 2 x Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (CO_2CH_3), 149.2 (*C*=CH_2), 144.7 (*C*=CH), 130.0 (CCO_2CH_3), 113.5 (C=CH_2), 63.5 (CH_2OTBS), 63.1 (CH_2OTBS), 51.6 (CO_2CH_3), 45.0 (*C*C=CH_2), 34.9 (CH_2), 33.8 (CH_2), 31.6 (CH_2), 27.4 (CH_2), 26.0 (2 x Si(CH_3)$_2$), 24.8 (CH_2), 22.7 (CH_2), 18.6 (*C*Si), 18.4 (*C*Si), -5.2 (SiC(CH_3)$_3$), -5.3 (SiC(CH_3)$_3$); v_{max} (thin film/cm^{-1}): 2929 (m, CH), 2856 (m), 1719 (m, C=O), 1407 (m), 1435 (w), 1097 (s), 835 (s), 775 (m); MS (ES$^+$) m/z (%): 519 (M+Na$^+$, 100); HRMS cald. for $C_{27}H_{52}O_4NaSi_2$ (M+Na$^+$): 519.3309. Found: 519.3297.

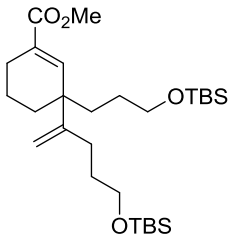
3-(5-((*tert*-Butyldimethylsilyl)oxy)pent-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-en-1-yl trifluoromethanesulfonate (S19)



S19

Prepared according to general procedure B. **4** (435 mg, 1.62 mmol, 1.0 equiv.), CuI (30.5 mg, 0.16 mmol, 0.1 equiv.), THF (1.3 mL), PhSLi (0.74 M, 0.22 mL, 0.10 mmol, 0.1 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide (0.15 M in THF, 10.8 mL, 1.62 mmol, 1.0 equiv.), (5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl)magnesium bromide (0.27 M in THF, 9.00 mL, 1.50 mmol, 1.5 equiv.) and Comins' reagent (1.02 g, 2.59 mmol, 1.6 equiv.) in THF (2.6 mL), after quenching with aqueous saturated NH_4Cl (15 mL), extraction into Et_2O (3 X 10 mL) and purification by column chromatography (50:1, hexane:EtOAc) gave **S19** (940 mg, 1.56 mmol), which was taken onto the next step.

Methyl 3-(5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (6b)

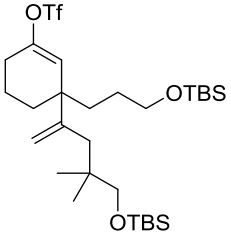


6b

Prepared according to general procedure C. **S19** (940 mg, 1.56 mmol, 1.0 equiv.), $Pd(OAc)_2$ (70 mg, 0.31 mmol, 0.2 equiv.), PPh_3 (163 mg, 0.63 mmol, 0.4 equiv.), MeOH (2.5 mL, 62.4 mmol, 40 equiv.) and Et_3N (435 µL, 3.12 mmol, 2.0 equiv.) in DMF (7.8 mL), after quenching with water (10 mL), extraction into Et_2O (3 X 10 mL) and purification by column chromatography (50:1, hexane:EtOAc), gave **6b** (591 mg, 1.20 mmol, 74% (2 steps)) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (1H, s, C=C*H*), 4.90 (1H, s, 1H from C=CH_2), 4.68 (1H, s, 1H from C=CH_2), 3.70 (3H, s, OCH_3), 3.60 (2H, t, *J* = 6.4 Hz, CH_2=C$(CH_2)_2$CH_2OSi), 3.52 (2H, td, *J* = 6.1, 1.9 Hz, C$(CH_2)_2$CH_2OSi), 2.19 - 2.31 (1H, m, 1H from CH_2), 2.06 - 2.16 (1H, m, 1H from CH_2), 1.91 - 2.05 (2H, m, CH_2=CCH_2), 1.24 - 1.76 (10H, m, 5 × CH_2), 0.86 (9H, s, SiC(C$H_3)_3$), 0.85 (9H, s, SiC(C$H_3)_3$), 0.02 (6H, s, 2 × SiCH_3), 0.00 (6H, s, 2 × SiCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (*C*=O), 152.1 (*C*=CH_2), 145.1 (C=*C*H), 129.6 (*C*=CH), 111.9 (C=*C*H_2), 63.5 (C$(CH_2)_2$CH_2OSi), 62.9 (CH_2=C$(CH_2)_2$CH_2OSi), 51.6 (O*C*H_3), 45.1 (CH_2=C*C*), 35.0 (*C*H_2), 31.9 (*C*H_2), 31.7 (*C*H_2), 27.4 (*C*H_2), 26.6 (CH_2=C*C*H_2), 26.0 (SiC(*C*$H_3)_3$), 25.9 (SiC(*C*$H_3)_3$), 24.8 (*C*H_2), 18.6 (*C*H_2), 18.3 (Si*C*), 18.3 (Si*C*), −5.3 (Si*C*H_3), −5.3 (Si*C*H_3); v_{max}(thin film/cm^{-1}): 2950 (s), 2930 (s), 2886 (m), 2857 (s), 1718 (s, C=O), 1647 (w), 1633 (w), 1472 (m), 1463 (w), 1435 (w),

1387 (w), 1361 (w), 1250 (s), 1190 (w), 1101 (s), 1006 (w), 972 (m), 939 (w), 836 (s), 813 (m), 775 (s); MS (ES^+) m/z (%): 533 ($M+Na^+$, 100); HRMS calcd. for $C_{28}H_{54}O_4NaSi_2$ ($M+Na^+$): 533.3453. Found: 533.3440.

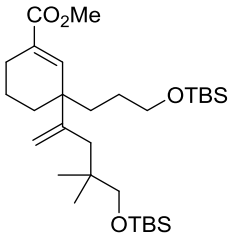
3-(5-((*tert*-Butyldimethylsilyl)oxy)-4,4-dimethylpent-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-en-1-yl trifluoromethanesulfonate (S20)



S20

Prepared according to general procedure B. CuI (55 mg, 0.29 mmol, 0.1 equiv.), THF (3 mL), PhSLi (0.83 M, 0.35 mL, 0.29 mmol, 0.1 equiv.), **4** (0.38 g, 2.90 mmol, 1.0 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide (36 mL in THF, 0.08 M, 2.90 mmol, 1.0 equiv.), (5-((*tert*-butyldimethylsilyl)oxy)-4,4-dimethylpent-1-en-2-yl)magnesium bromide (36 mL in THF, 0.12 M, 4.36 mmol, 1.5 equiv.), Comins' reagent (1.83 g, 4.65 mmol, 1.6 equiv.), quenching with aqueous saturated NH_4Cl (50 mL) and extraction into Et_2O (3 X 50 mL) gave **S20** (1.88 mg) as a pale yellow oil. Partial purification by column chromatography (50:1, hexane:EtOAc) was carried out to remove the Comins' reagent before the next step.

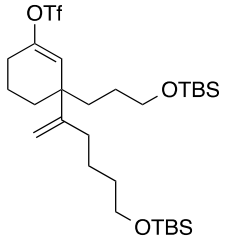
Methyl 3-(5-((*tert*-butyldimethylsilyl)oxy)-4,4-dimethylpent-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (6c)



6c

Prepared according to general procedure C. **S20** (1.88 g mg, 3 mmol, 1.0 equiv.), $Pd(OAc)_2$ (135 mg, 0.60 mmol, 0.2 equiv.), PPh_3 (315 mg, 1.2 mmol, 0.4 equiv.), MeOH (5 mL, 120 mmol, 40 equiv.) and Et_3N (0.84 mL, 6.0 mmol, 2.0 equiv.) in DMF (15 mL), quenching with water (15 mL), extraction into Et_2O (3 X 20 mL) and purification by column chromatography (50:1, hexane:EtOAc) gave **6c** (0.99g, 61% (2 steps)) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (1H, s, C=C*H*), 5.06 (1H, s, 1H from C=CH_2), 4.83 (1H, s, 1H from C=CH_2), 3.70 (3H, s, CO_2CH_3), 3.49 - 3.58 (2H, m, CH_2CH_2OTBS), 3.22 (2H, s, CCH_2OTBS), 2.05 - 2.46 (3H, m, 2H from CH_2 and 1H from CH_2), 1.21 - 1.78 (9H, m, 8H from 4 X CH_2 and 1H from CH_2), 0.83 - 0.88 (24H, m, 6H from 2 X CH_3, 9H from SiC(CH_3)$_3$ and 9H from SiC(CH_3)$_3$), -0.02 - 0.02 (12H, m, 2 X Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (CO_2CH_3), 149.5 (CH_2=*C*), 145.8 (C=*C*H), 129.5 (*C*CO_2CH_3), 114.6 (C=*C*H_2), 71.9 (*C*H_2OTBS), 63.6 (*C*H_2OTBS), 51.6 (CO_2CH_3), 45.7 (*C*C=CH_2), 37.3 (*C*H_2), 36.4 (*C*$(CH_3)_2$), 35.2 (*C*H_2), 32.9 (*C*H_2), 31.4 (*C*H_2), 27.5 (*C*H_2), 26.0 (SiC(*C*H_3)$_3$), 25.9 (*C*H_3), 25.6 (*C*H_3), 24.8 (2 X Si*C*), 18.7 (*C*H_2), -5.27 (Si(*C*H_3)$_2$), -5.46 (Si(*C*H_3)$_2$); ν_{max} (thin film/cm^{-1}): 2949 (w, C-H), 2856 (w), 1716 (s, C=O), 1645 (w), 1434 (w), 1246 (s), 1097 (s), 833 (s), 773 (w); MS (ES$^+$) *m/z* (%): 539 (M+H$^+$, 100); HRMS calcd. for $C_{30}H_{58}O_4Si_2$ (M+H$^+$): 539.3952. Found: 539.3955.

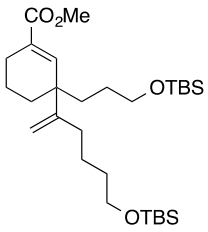
3-(6-((*tert*-Butyldimethylsilyl)oxy)hex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-en-1-yl-trifluoromethanesulfonate (S21)



S21

Prepared according to general procedure B. CuI (38.1 mg, 0.20 mmol, 0.1 equiv.), PhSLi (0.24 mL, 0.83 M, 0.2 mmol, 0.1 equiv.), **4** (261 mg, 2.0 mmol, 1.0 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide (12.2 mL, 2.0 mmol, 1.0 equiv.), (6-((*tert*-butyldimethylsilyl)oxy)hex-1-en-2-yl)magnesium bromide (20 mL, 3.0 mmol, 1.5 equiv.), quenching with aqueous saturated NH_4Cl (40 mL), extraction into Et_2O (3 X 40 mL) and partial purification by column chromatography (50:1, hexane:EtOAc) gave **S21** (1.01 g, 1.64 mmol), which was taken onto the next step with no further purification.

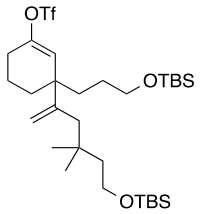
Methyl 3-(6-((*tert*-Butyldimethylsilyl)oxy)hex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (6e)



6e

Prepared according to general procedure C. **S21** (1.01 g, 1.61 mmol, 1.0 equiv.), $Pd(OAc)_2$ (71.8 mg, 0.32 mmol, 0.2 equiv.), PPh_3 (170.5 mg, 0.65 mmol, 0.4 equiv.), Et_3N (326 mg, 3.22 mmol, 2.0 equiv.), MeOH (2.6 mL, 64.4 mmol, 40 equiv.), in DMF (8.1 mL), after quenching with water (10 mL), extraction into Et_2O (3 X 10 mL) and purification by column chromatography (50:1, hexane:EtOAc) gave **6e** (0.49 g, 0.93 mmol, 60% (2 steps)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (1H, s, C=C*H*), 4.95 (1H, s, 1H from CH_2=C), 4.72 (1H, m, 1H from CH_2=C), 3.72 - 3.76 (3H, m, CO_2CH_3), 3.59 - 3.65 (4H, m, 2 X CH_2OTBS), 2.11 - 2.22 (2H, m, C$H_2CCO_2CH_3$), 1.95 - 2.01 (2H, m, CH_2=CCH_2), 1.72 - 1.78 (1H, m, 1H from CH_2), 1.56 - 1.65 (3H, m, CH_2, 1H from CH_2), 1.46 - 1.56 (8H, m, 4 X CH_2), 0.90 (18H, br. s, 2 X OSiC(CH_3)$_3$), 0.05 (12 H, br. s, 2 X (OSi(CH_3)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4 (CO_2CH_3), 152.6 (CH_2=*C*), 145.5 (*C*H=C), 129.9 (CCO_2CH_3), 112.2 (CH_2=C), 63.7 ($CCH_2CH_2CH_2CH_2$OTBS), 63.4 ($CH_2CH_2CH_2$OTBS), 51.2 (CO_2CH_3), 45.2 (*C*(CH_2)$_3$OTBS), 35.2 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 30.4 (CH_2), 27.9 (CH_2), 26.2 (OSiC(CH_3)$_3$), 25.0 (CH_2), 22.9 (CH_2), 18.8 (CH_2), 18.61 (OSi*C*), -5.02 (OSi(CH_3)$_2$; ν_{max} (thin film/cm^{-1}): 2950 (w), 2929 (m), 2856 (w), 1717 (m, C=O), 1645 (w), 1471 (w), 1435 (w), 1387 (w), 1251 (s), 1099 (s), 1006 (w); MS (ES$^+$) m/z (%): 525 (M^+H^+, 5), 547 (M^+Na^+, 100); HRMS calcd. for $C_{29}H_{56}O_4NaSi_2$ (M^+Na^+): 547.3609. Found: 547.3622.

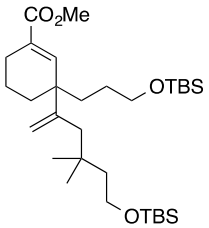
3-(6-((*tert*-Butyldimethylsilyl)oxy)-4,4-dimethylhex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-en-1-yl trifluoromethanesulfonate (S22)



S22

Prepared according to general procedure B. CuI (45,7 mg, 0.24 mmol, 0.1 equiv.), PhSLi (0.29 mL, 0.83 M, 0.24 mmol, 0.1 equiv.), **4** (313 mg, 2.40 mmol, 1.0 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide (24.0 mL, 2.40 mmol, 1.0 equiv.) and (6-((*tert*-butyldimethylsilyl)oxy)-4,4-dimethylhex-1-en-2-yl)magnesium bromide (28.0 mL, 3.60 mmol, 1.5 equiv.), after quenching with aqueous saturated NH_4Cl (50 mL), extraction into Et_2O (3 X 50 mL) and partial purification by column chromatography (50:1, hexane:EtOAc) gave **S22** (0.81 g, 1.26 mmol), which was used in the next step.

Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)-4,4-dimethylhex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (6d)

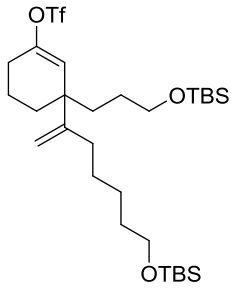


6d

Prepared according to general procedure C. **S22** (0.81 g, 1.30 mmol, 1.0 equiv.), $Pd(OAc)_2$ (58.4 mg, 0.26 mmol, 0.2 equiv.), PPh_3 (136 mg, 0.52 mmol, 0.4 equiv.), Et_3N (0.36 mL, 2.6 mmol, 2.0 equiv.), MeOH (2.1 mL, 52 mmol, 40 equiv.) in DMF

(8.0 mL), after quenching with water (10 mL), extraction into Et_2O (3 X 10 mL) and purification gave **6d** (0.46 g, 0.83 mmol, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (1H, s, C=C*H*), 5.13 (1H, s, 1H from C=CH_2), 4.87 (1H, s, 1H from C=CH_2), 3.73 - 3.77 (3H, s, CO_2CH_3), 3.65 - 3.72 (2H, m, CCH_2CH_2OTBS), 3.58 - 3.63 (2H, m, $CH_2CH_2CH_2$OTBS), 2.24 - 2.48 (2H, m, CH_2), 2.11 - 2.17 (1H, m, 1H from CH_2=CCH_2), 1.93 - 1.97 (1H, m, CH_2=CCH_2), 1.72 - 1.78 (1H, m, 1H from CH_2), 1.59 - 1.64 (2H, m, CH_2), 1.56 - 1.36 (1H, m, 1H from CH_2), 1.50 - 1.55 (4H, m, 2 X CH_2), 1.38 - 1.47 (2H, m, CCH_2CH_2OTBS), 0.96 - 1.00 (6H, m, 2 X CCH_3), 0.90 (18H, s, 2 X OSiC$(CH_3)_3$), 0.02 - 0.08 (12H, br. s, 2 X OSi$(CH_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3 (CO_2CH_3), 149.7 (CH_2=*C*), 145.9 (C=*C*H), 129.9 (CH=*C*(CO_2CH_3)), 114.5 (CH_2=C), 63.7 ($CH_2CH_2CH_2$OTBS), 60.4 (CCH_2CH_2OTBS), 51.8 (CO_2CH_3), 46.0 ($C(CH_2)_2$OTBS), 45.5 (CCH_2CH_2OTBS), 41.6 (CH_2=CCH_2), 35.5 (CH_2), 33.5 ($C(CH_3)_2$), 31.9 (CH_2), 28.9 (($CH_3)_2$), 27.7 (CH_2), 26.3 (OSiC$(CH_3)_3$), 25.0 (CH_2), 18.0 (CH_2), 18.6 (OSi*C*), -5.0 (OSi$(CH_3)_2$); ν_{max} (thin film/cm^{-1}): 2952 (m), 2929 (m), 2857 (m), 1716 (m, C=O), 1471 (w), 1252(s), 1094 (s). 1005 (w); MS (ES$^+$) m/z (%): 575 (M+Na$^+$, 100); HRMS calcd. for $C_{31}H_{60}O_4NaSi_2$ (M+Na$^+$): 575.3922. Found: 575.3920.

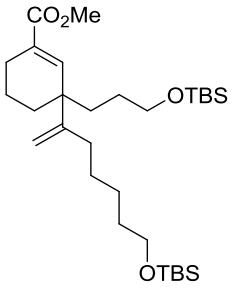
3-(6-((*tert*-Butyldimethylsilyl)oxy)hexyl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-en-1-yl trifluoromethanesulfonate (S23)



S23

Prepared according to general procedure B. CuI (59 mg, 0.31 mmol, 0.1 equiv.), THF (3 mL), PhSLi (0.37 mL, 0.83 M, 0.31 mmol, 0.1 equiv.), **4** (403 mg, 3.09 mmol, 1.0 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide in THF (20.6 mL, 3.09 mmol, 0.15 M), (7-((tert-butyldimethylsilyl)oxy)hept-1-en-2-yl)magnesium bromide (29 mL, 4.64 mmol, 0.16 M), Comins' reagent (1.94 g, 4.94 mmol, 1.6 equiv.), after quenching with aqueous saturated $NH_4Cl_{(aq)}$ (50 mL) and extraction into Et_2O (3 x 50 mL) gave the crude product. Partial purification by column chromatography (50:1, hexane:EtOAc) removed the Comins' reagent and allowed the product to be taken onto the next step.

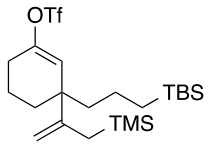
Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)hexyl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (6f)



6f

Prepared according to general procedure C. **S23** (3.09 mmol), DMF (13.0 mL, 2.59 mmol, 0.2 M), MeOH (4.20 mL, 103.6 mmol, 40 equiv.), Et_3N (0.72 mL, 5.18 mmol, 2.0 equiv.), $Pd(OAc)_2$ (117 mg, 0.52 mmol, 0.2 equiv.), PPh_3 (273 mg, 1.04 mmol, 0.4 equiv.), after quenching with water (15 mL), extraction with Et_2O (3 x 15 mL) and purification by column chromatography (50:1, hexane:EtOAc) gave **6f** (0.78 g, 1.45 mmol, 56% (2 steps)) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (1H, s, C=C*H*), 4.93 (1H, s, 1H from CH_2=C), 4.70 (1H, s, CH_2=C), 3.74 (3H, s, CO_2CH_3) 3.56 - 3.64 (4H, m, 2 x CH_2OTBS) 1.93 - 2.36 (6H, m, 3 X CH_2) 1.23 - 1.58 (12H, m, 6 x CH_2) 0.90 (18H, s, 2 x SiC(CH_3)$_3$), -0.05 (12H, s, 2 X Si(CH_2)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (*C*O_2Me), 152.4 (CH_2=*C*), 145.3 (*C*H=CCO_2Me), 129.6 (*C*CO_2Me), 111.9 (*C*H_2=C), 63.5 (*C*H_2OTBS), 63.2 (*C*H_2OTBS), 51.6 (CO_2CH_3), 45.0 (*C*CCH_2), 35.0 (*C*H_2), 32.9 (*C*H_2), 31.6 (*C*H_2), 30.4 (*C*H_2), 28.3 (*C*H_2), 27.4 (*C*H_2), 26.0 (SiC(*C*H_3)$_3$), 24.8 (*C*H_2), 22.7 (*C*H_2), 18.3 (Si*C*), 14.2 (CH_2), -5.3 (Si(*C*H_3)$_2$); v_{max} (thin film/cm^{-1}): 2930 (m, C-H), 2895 (w), 2857 (m), 1718 (m, C=O), 1471 (m), 1254 (m), 1100 (s), 1005 (w), 908 (w), 835 (s), 774 (m); MS (ES$^+$) *m/z* (%): 539 (M+H$^+$, 75), 561 (M+Na$^+$, 100); HRMS cald for $C_{30}H_{58}O_4NaSi_2$ (M+Na$^+$): 561.3771. Found: 561.3762.

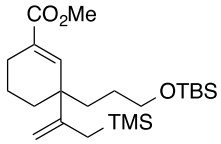
3-(3-(*tert*-Butyldimethylsilyl)propyl)-3-(3-(trimethylsilyl)prop-1-en-2-yl)cyclohex-1-en-1-yl trifluoromethanesulfonate (S24)



S24

Prepared according to general procedure B. CuI (74 mg, 0.39 mmol, 0.1 equiv.), THF (4 mL), PhSLi, **4** (505 mg, 3.87 mmol, 1.0 equiv.), (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide (35 mL, 3.87 mmol, 0.11 M in THF), (3-(trimethylsilyl)prop-1-en-2-yl)magnesium bromide (37 mL, 5.81 mmol, 0.14 M in THF), Comins' reagent (2.43 g, 6.19 mmol, 1.6 equiv.) in THF (3 mL), after quenching with aqueous saturated NH_4Cl (60 mL), extraction with Et_2O (3 x 50 mL) and partial purification by column chromatography (1:80, ethyl acetate: hexane) gave **S24**, which was taken onto the next step without further purification.

Methyl 3-(3-((tert-butyldimethylsilyl)oxy)propyl)-3-(3-(trimethylsilyl)prop-1-en-2-yl)cyclohex-1-ene-1-carboxylate (6g)



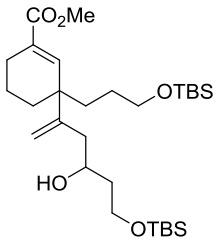
6g

Prepared according to general procedure C. **S24** (3.87 mmol), DMF (19.4 mL, 3.87 mmol, 0.2 M), MeOH (6.27 mL, 155 mmol, 40 equiv.) and Et_3N (1.08 mL, 7.74 mmol, 2.0 equiv.), $Pd(OAc)_2$ (174 mg, 0.77 mmol, 0.2 equiv.), PPh_3 (406 mg, 1.54 mmol, 0.4 equiv.), after quenching with water (5 mL), extraction with Et_2O (3 x 5 mL) and

purification by column chromatography (50:1, hexane/EtOAc) gave **6g** (1.04 g, 2.45 mmol, 63% (2 steps)) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (1H, s, C*H*=CCO_2Me), 4.81 (1H, s, 1H from C=CH_2), 4.63 (1H, s, 1H from C=CH_2), 3.74 (3H, s, CO_2CH_3), 3.57 (2H, m, CH_2OTBS), 2.22 - 2.36 (1H, m, 1H from CH_2CCO_2Me), 2.07 - 2.19 (1H, m, 1H from CH_2CCO_2Me), 1.59 - 1.76 (4H, m, 2H from C$H_2CH_2CCO_2Me$ and 2H C$H_2CH_2CH_2CCO2Me$), 1.25 - 1.52 (6H, m, 2H from CH_2CH_2OTBS, 2H from CH_2OTBS and 2H from CH_2TMS), 0.89 (9H, s, SiC(CH_3)$_3$), 0.09 (6H, s, OSi(CH_3)$_2$), 0.05 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8 (*C*=O), 149.6 (*C*=CH_2), 145.1 (*C*H=CCO_2Me), 129.3 (*C*CO_2Me), 111.8 (*C*H_2=C), 63.1 (*C*H_2OTBS), 51.3 (O*C*H_3), 45.2 (*C*C=CH_2), 34.6 (*C*H_2TMS), 30.8 (*C*H_2), 27.1 (*C*H_2), 25.6 (*C*H_2), 24.5 (*C*HCCO_2Me), 19.8 (*C*H_2), 18.4 (Si*C*(CH_3)$_3$), 18.0 (OSiC(*C*H_3)$_3$),-0.9 (Si(*C*H_3)$_3$), -5.7 (OSi(*C*H_3)$_2$); v_{max} (thin film/cm^{-1}): 2952 (w), 2858 (w), 1418 (m), 1246 (m), 1209 (v.s), 1143 (m), 1099 (w), 1000 (w), 908 (w), 835 (s); MS (ES$^+$) *m/z* (%): 425 (M+H$^+$, 50), 447 (M+Na$^+$, 100); HRMS cald for $C_{23}H_{44}O_3NaSi_2$ (M+Na$^+$): 447.2727. Found: 447.2741.

Sakurai Cross-Coupling Substrate

Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyhex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (8)

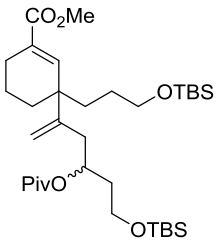


8

A solution of **6g** (200 mg, 0.47 mmol, 1.0 equiv.) and 3-((*tert*-butyldimethylsilyl)oxy)propanal[13] (134 mg, 0.71 mmol, 1.5 equiv.) in CH_2Cl_2 (0.62 mL) was added to TBAT (25.4 mg, 0.05 mmol, 0.1 equiv.), activated 4Å MS (200 mg) in CH_2Cl_2 (0.21 mL) at -78 °C under nitrogen. After 1 hour BF_3•OEt_2 (0.09 mL, 0.75 mmol, 1.6 equiv.) was added and the reaction was left to stir at -78 °C. After 18 hours, the reaction was allowed to warm to -35 °C and was then quenched with aqueous saturated NH_4Cl (5 mL), extracted into CH_2Cl_2 (3 X 5 mL) and dried ($MgSO_4$). Partial purification by column chromatography (5% EtOAc/hexane) gave **8** (247.6mg), which was taken onto the next step impure.

[13] Prepared following procedure in: P. A. Allegretti, E. M. Ferreira, *Org. Lett*., **2011**, 13, 5924.

Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)-4-(pivaloyloxy)hex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (S25)

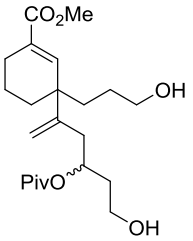


S25

PivCl (0.25 mL, 2.05 mmol, 5.0 equiv.) was added to a mixture of **8** (0.41 mmol, 1.0 equiv.), DMAP (5.00 mg, 0.04 mmol, 0.1 equiv.) and pyridine (1.23 mL, 0.41 mmol, 0.33 M) in CH_2Cl_2 (1.23 mL). After 18 hours the reaction was quenched with aqueous saturated $NaHCO_3$ (4 mL), extracted into Et_2O (3 X 5 mL) and was washed successively with aqueous saturated $CuSO_4$ (3 X 5 mL) and brine (2 X 5 mL). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was taken onto the next step with no further purification.

Synthesis of Pre-Cascade Intermediates

Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)-4-(pivaloyloxy)hex-1-en-2-yl)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)cyclohex-1-ene-1-carboxylate (S26)

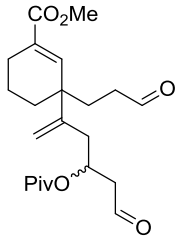


S26

Prepared according to general procedure D. HF (60% aqueous solution)(0.27 mL, 8.20 mmol, 20 equiv.), **S25** (0.41 mmol, 1.0 equiv.), pyridine (2.05 mL, 0.2 M, 1.0 equiv.), in MeCN (4.1 mL) after quenching with aqueous saturated $NaHCO_3$ (2 mL), extraction into Et_2O (3 X 4 mL) and successive washing with $CuSO_4$ (3 X 2mL) and brine (3 X 2 mL) gave the crude product. Purification by column chromatography (20% EtOAc/hexane) gave **S26** (76.5 mg, 0.19 mmol, 46% (3 steps) (dr:1:1)) as a pale yellow oil. ^{1}H NMR (500 MHz,$CDCl_3$) δ 6.89 (1H, d, *J* = 9.77 Hz, C=C*H* (both diastereoisomers)), 5.24 - 5.28 (1H, m, C*H*(OPiv) (both diastereoisomers)), 4.96 (1H, d, *J* = 4.41 Hz, 1H from C=CH_2 (both diastereoisomers)), 4.82 (1H, d, *J* = 11.35 Hz, 1H from C=CH_2 (both diastereoisomers)), 3.74 (3H, s, CO_2CH_3 (both diastereoisomers)), 3.57 - 3.67 (3H, m, 1H from CH_2OH, 2H CH_2OH (both diastereoisomers)), 3.45 - 3.52 (1H, m, 1H from CH_2OH (both diastereoisomers)), 2.61 - 2.78 (1H, br. s., O*H*), 2.36 - 2.43 (1H, m, 1H from CH_2 (both diastereoisomers)), 2.11 - 2.32 (3H, m, 1H from CH_2, CH_2 (both diastereoisomers)), 1.87 - 1.97 (1H, m, 1H from CH_2 (both diastereoisomers)) 1.35 - 1.78 (10H, m, 5 X CH_2 (both diastereoisomers)) 1.19 (9H, d, *J* = 3.78 Hz, C(O)C(CH_3)$_3$ (both diastereoisomers)); ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.7 (*C*(O)C(CH_3)$_3$ (one

diastereoisomer)), 179.6 (*C*(O)C(CH_3)$_3$ (one diastereoisomer)), 167.9 (*C*$O_2$$CH_3$ (both diastereoisomers)), 147.5 (*C*=CH (both diastereoisomers)), 144.0 (C=*C*H (both diastereoisomers)), 130.4 (*C*=CH_2 (one diastereoisomer)), 130.3 (*C*=CH_2 (one diastereoisomer)), 114.7 (C=*C*H_2 (one diastereoisomer)), 114.3 (C=*C*H_2 (one diastereoisomer)), 69.2 (*C*H(OPiv) (one diastereoisomer)), 69.1 (*C*H(OPiv) (one diastereoisomer)), 63.1 (*C*H_2OH (one diastereoisomer)), 63.0 (*C*H_2OH (one diastereoisomer)), 58.3 (*C*H_2OH (one diastereoisomer)), 58.2 (*C*H_2OH (one diastereoisomer)), 51.7 (CO_2*C*H_3 (both diastereoisomers)), 44.8 (*C*C=CH_2 (both diastereoisomers)), 38.9 (*C*(CH_3)$_3$ (both diastereoisomers)), 38.0 (*C*H_2 (one diastereoisomer)), 37.8 (*C*H_2 (one diastereoisomer)), 36.1 (*C*H_2 (both diastereoisomers)), 34.9 (*C*H_2 (both diastereoisomers)), 32.1 (*C*H_2 (both diastereoisomers)), 31.7 (*C*H_2 (both diastereoisomers)), 27.2 (C(*C*H_3)$_3$ (both diastereoisomers)), 24.7 (*C*H_2 (both diastereoisomers)), 18.5 (*C*H_2 (one diastereoisomer)), 18.4 (*C*H_2 (one diastereoisomer)); ν_{max} (thin film/cm^{-1}): 3433 (w, OH), 2938 (m), 2870 (w), 1716 (C=O), 1645 (w), 1480 (w), 1435 (w), 1280 (m), 1160 (s), 1105 (w), 1053 (m), 957 (w), 903 (w); MS (ES$^+$) m/z (%): 397 (M+H$^+$, 5), 419 (M+Na$^+$, 100); HRMS calcd. for $C_{22}H_{36}O_6Na$ (M+Na$^+$): 419.2410. Found: 419.2405.

Methyl 3-(6-oxo-4-(pivaloyloxy)hex-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (9)

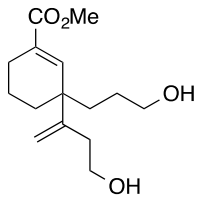


9

Prepared according the general procedure E. DMP (178 mg, 0.42 mmol, 2.2 equiv.), **S26** (76.5 mg, 0.19 mmol, 1.0 equiv.), CH_2Cl_2 (1.9 mL), after concentrated in vacuo and purification by column chromatography (30% EtOAc/hexane) gave **9** (54.3 mg, 0.14 mmol, 73%, (dr:1:1) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.8 (1H, s, C*H*O) 9.71 - 9.74 (1H, s, C*H*O (both diastereoisomers)), 6.79 (1H, d, *J* = 11.0 Hz, C=C*H* (both diastereoisomers)), 5.44 - 5.51 (1H, m, C*H*(OPiv) (both diastereoisomers)), 5.04 (1H, s, 1H from C=CH_2 (both diastereoisomers)), 4.90 (1H, d, *J* = 2.5 Hz, 1H from C=CH_2 (both diastereoisomers)), 3.75 (3H, s, CO_2CH_3 (both diastereoisomers), 2.63 - 2.75 (2H, m, CH_2 (both diastereoisomers)), 2.14 - 2.54 (8H, m, 4 X CH_2 (both diastereoisomers)), 1.71 - 1.92 (4H, m, 2 X CH_2 (both diastereoisomers)), 1.15 (9H, d, *J* = 3.8 Hz, C(O)C(CH_3)$_3$ (both diastereoisomers)); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.5 (*C*HO (both diastereoisomers)), 199.0 (*C*HO (both diastereoisomers)), 177.8 (O*C*(O)C$(CH_3)_3$ (both diastereoisomers)), 167.6 (*C*O_2CH_3 (both diastereoisomers)), 146.6 (*C*=CH_2 (both diastereoisomers)), 142.5 (C=*C*H (one diastereoisomer)), 142.4 (one diastereoisomer)), 131.5 (*C*=CH, one diastereoisomer), 131.4 (*C*=CH, one diastereoisomer), 115.5 (C=*C*H_2 (one diastereoisomer)), 115.4 (C=*C*H_2 (one diastereoisomer)), 67.3 (*C*HOPiv (one diastereoisomer)), 67.2 (*C*HOPiv (one diastereoisomer)), 51.8 (CO_2CH_3 both diastereoisomers)), 48.2 (*C*C=CH_2 (both diastereoisomers)), 44.4 (*C*H_2 (one diastereoisomer)), 44.3 (*C*H_2 (one diastereoisomer)), 39.0 ((*C*H_2 (both

diastereoisomers)), 38.7 (*C*(CH_3)$_3$ both diastereoisomers)), 35.5 (*C*H_2 (one diastereoisomer)), 35.2 (*C*H_2 (one diastereoisomer)), 31.6 (*C*H_2 (both diastereoisomers)), 31.1 (*C*H_2 (one diastereoisomer)), 31.0 (*C*H_2 (one diastereoisomer)), 27.0 (C(*C*H_3)$_3$ (both diastereoisomers)), 24.6 (*C*H_2 (both diastereoisomers)), 18.4 (*C*H_2 (both diastereoisomers)); ν_{max} (thin film/cm^{-1}): 2934 (m), 2870 (w), 2849 (w), 2724 (w), 1721 (s, C=O), 1648 (w), 1480 (w), 1460 (w), 1436 (w), 1396 (w), 1366 (w), 1279 (m), 1251 (m), 1156 (m), 1108 (w), 1036 (w), 968 (w), 921 (w), 823 (w). Complete characterisation was not possible due to instability.

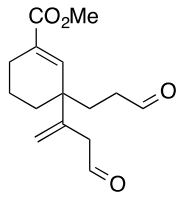
Methyl 3-(4-hydroxybut-1-en-2-yl)-3-(3-hydroxypropyl)cyclohex-1-ene-1-carboxylate (S27)



S27

Prepared according to general procedure D. Hydrofluoric acid (60%, w/v H_2O) (1.2 mL, 34.6 mmol, 20 equiv.), **6a** (863 mg, 1.73 mmol, 1.0 equiv.), pyridine (8.65 mL, 0.2 M), MeCN (17.3 mL), after quenching with aqueous saturated $NaHCO_3$ (2 mL) and extraction into Et_2O (3 X 2 mL) and washing with $CuSO_4$ (3 X 2 mL) and brine (3 X 2 mL), and purification gave **S26** (360 mg, 1.34 mmol, 78%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (1H, s, C=C*H*), 4.97 (1H, s, 1H from C=CH_2), 4.80 (1H, s, 1H from C=CH_2), 3.76 (2H, t, *J* = 6.3 Hz, CH_2=CCH_2CH_2OH), 3.73 (3H, s, CO_2CH_3), 3.52 - 3.64 (2H, m, $CH_2CH_2CH_2$OH), 2.53 – 2.67 (2H, m, 2 x OH), 2.24 - 2.35 (3H, m, CH_2 and 1H from CH_2), 2.08 – 2.19 (1H, m, 1H from CH_2), 1.74 (1H, dd, *J = 12.6, 5.3 Hz*, 1H from CH_2), 1.30 – 1.68 (7H, m, 3 X CH_2 and 1H from CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (CO_2CH_3), 148.7 (CCO_2CH_3), 144.3 (C=*C*H), 130.1 (*C*=CH_2), 113.4 (C=*C*H_2), 62.8 ($CH_2CH_2CH_2$OH), 61.4 (CH_2=CCH_2CH_2OH), 51.7 (CO_2CH_3), 44.8 (*C*C=CH_2), 34.7 (*C*H_2), 33.3 (*C*H_2), 31.8 (*C*H_2), 27.1 (*C*H_2), 24.7 (*C*H_2), 18.4 (*C*H_2); v_{max} (thin film/ cm^{-1}): 3349 (m, OH), 2939 (s, CH), 2867 (w), 1714 (s), 1698 (m), 1643 (w), 1435 (w), 1338 (w), 1248 (s), 1190 (w), 1057 (s), 900 (w). MS was uninformative.

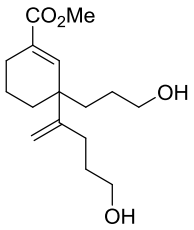
Methyl 3-(4-oxobut-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (7a)



7a

Prepared according to general procedure E: DMP (292 mg, 0.69 mmol, 2.2 equiv.), **S26** (84.2 mg, 0.31 mmol, 1.0 equiv.), CH_2Cl_2 (3.1 mL, 0.1 M), evaporation of the solvent and purification gave **7a** (69 mg, 0.26 mmol, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (1H, s, C*H*O), 9.52 (1 H, t, *J* = 2.5 Hz, C*H*O), 6.72 (1H, s, C=C*H*), 5.03 (1H, s, 1H from C=CH_2), 5.00 (1H, s, 1H from C=CH_2), 3.69 (3H, s, CO_2CH_3), 3.02 (2H, d, *J* = 2.4 Hz, CH_2CHO), 2.41 - 2.51 (1H, m, 1H from CH_2), 2.23 - 2.37 (2H, m, CH_2), 2.06 - 2.16 (1H, m, 1H from CH_2), 1.69 - 1.84 (2H, m, CH_2), 1.50 - 1.65 (4H, m, 2 X CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3 (*C*HO), 199.5 (*C*HO), 167.5 (CO_2CH_3), 142.9 (C=*C*H), 141.6 (*C*=CH_2), 131.9 (*C*CO_2CH_3), 118.8 (C=*C*H_2), 51.9 (CH_2CHO), 46.4 (CH_2CHO), 44.2 (*C*C=CH_2), 38.9 (CO_2CH_3), 31.1 (CH_2), 29.7 (CH_2), 24.6 (CH_2), 18.2 (CH_2); v_{max} (thin film/cm^{-1}): 2918 (m), 2850 (w), 1727 (m, C=O), 1463 (w), 1378 (w), 1262 (m), 1122 (w), 1072 (m), 1018 (m), 908 (w). Complete characterisation was not possible due to instability.

Methyl 3-(5-hydroxypent-1-en-2-yl)-3-(3-hydroxypropyl)cyclohex-1-ene-1-carboxylate (S28)

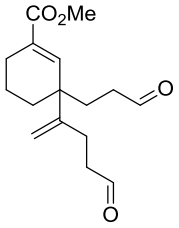


S28

Prepared according to general procedure D. **6b** (591 mg, 1.2 mmol, 1.0 equiv.), MeCN (11.5 mL), pyridine (5.8 mL), HF (60% aqueous solution, 770 µL, 23 mmol, 20 equiv.), quenching with aqueous saturated $NaHCO_3$ (1 mL), extraction into diethyl ether (3 X 2 mL) and purification by column chromatography (EtOAc) gave **S28** (320 mg, 1.1 mmol, 98%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (1H, d, *J* = 1.3 Hz, C*H*CC(O)OMe), 4.97 (1H, s, 1H from C=CH_2), 4.78 (1H, d, *J* = 0.6 Hz, 1H from C=CH_2), 3.75 (3H, s, OCH_3), 3.70 (2H, td, *J* = 6.2, 1.4 Hz, CH_2=C$CH_2CH_2CH_2$OH), 3.56 - 3.67 (2H, m, $CCH_2CH_2CH_2$OH), 2.30 (1H, dt, *J* = 18.0, 4.4 Hz, 1H from $CCH_2CH_2CH_2OH$), 2.12 - 2.22 (1H, m, 1H from $CCH_2CH_2CH_2OH$), 2.10 (2H, td, *J* = 7.7, 3.2 Hz, CH_2=C$CH_2CH_2CH_2$OH), 1.72 -1.83 (3H, m, 1H from CH_2=CCH_2, CH_2), 1.32 - 1.71 (7H, m, CC$H_2CH_2CH_2OH$, 1H from CH_2=CCH_2 , 2 × CH_2); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1 (CO_2CH_3), 151.6 (C=CH_2), 144.6 (C=CH), 130.0 (CCO_2CH_3), 112.2 (C=CH_2), 63.2 ($CCH_2CH_2CH_2OH$), 62.4 (CH_2=C$CH_2CH_2CH_2$OH), 51.6 (OCH_3), 45.1 (CC=CH_2), 34.9 ($CCH_2CH_2CH_2OH$), 32.0 (CH_2=CCH_2), 31.4 (CH_2), 27.3 (CH_2), 26.3 (CH_2=CCH_2CH_2), 24.8 ($CCH_2CH_2CH_2OH$), 18.5 (CH_2); v_{max} (thin film/cm^{-1}): 3339 (br, OH), 3088 (w), 2941 (s), 2867 (m), 1714 (s, C=O), 1699 (s), 1644 (w), 1632 (w), 1435 (m), 1378 (w), 1338 (w), 1249 (s), 1204 (w), 1190 (w), 1164 (w), 1106 (m),

1057 (s), 974 (w), 946 (w), 900 (m); MS (ES^+) *m/z* (%): 283 ($M+H^+$, 100), 305 ($M+Na^+$, 80); HRMS calcd. for $C_{16}H_{30}O_4N$ ($M+NH_4^+$): 300.2169. Found: 300.2168.

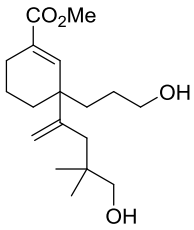
Methyl 3-(5-oxopent-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (7b)



7b

Prepared according to general procedure E. Dess-Martin periodinane (187 mg, 0.44 mmol, 2.2 equiv.), **S28** (56.5 mg, 0.20 mmol, 1.0 equiv.), CH_2Cl_2 (2 mL), after purification by column chromatography (30% EtOAc/hexane) gave **7b** (54.3 mg, 0.20 mmol, 98%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (1H, t, *J* = 1.3 Hz, C(O)*H*), 9.77 (1H, t, *J* = 1.3 Hz, C(O)*H*), 6.83 (1H, d, *J* = 1.3 Hz, C*H*=CC(O)OCH_3), 4.89 (1H, t, *J* = 1.4 Hz, 1H from C=CH_2), 4.82 (1H, s, 1H from C=CH_2), 3.74 (3H, s, OCH_3), 1.06 - 2.77 (14H, m, 7 × CH_2); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.6 (*C*HO), 201.5 (*C*HO), 167.7 (*C*O_2CH_3), 149.9 (*C*=CH_2), 142.9 (*C*H=C), 131.1 (CH=*C*), 113.1 (C=*C*H_2), 51.8 (O*C*H_3), 44.5 (CH_2=C*C*), 42.1 (*C*H_2), 39.1 (*C*H_2), 31.8 (*C*H_2), 30.2 (*C*H_2), 24.6 (*C*H_2), 22.7 (*C*H_2), 18.4 (*C*H_2); ν_{max} (thin film/cm^{-1}): 2945 (m), 2863 (w), 2842 (w), 2725 (w), 2359 (w), 2343 (w), 1842 (w), 1716 (s, C=O), 1647 (w), 1634 (w), 1435 (m), 1414 (w), 1389 (w), 1250 (s), 1164 (w), 1107 (m), 1079 (s), 1062 (w), 1017 (w), 906 (m).

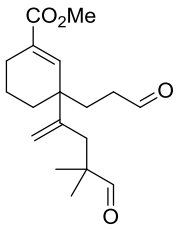
Methyl 3-(5-hydroxy-4,4-dimethylpent-1-en-2-yl)-3-(3-hydroxypropyl)cyclohex-1-ene-1-carboxylate (S29)



S29

Prepared according to general procedure D. **6c** (871 mg, 1.62 mmol, 1.0 equiv.), MeCN (16.2 mL, 0.1 M), pyridine (8.1 mL, 0.2 M), HF (60% aqueous solution, 1.80 mL, 36.4 mmol, 20 equiv.), quenching with aqueous saturated $NaHCO_3$ (2 mL), extraction into Et_2O (3 X 5 mL) and purification by column chromatography (EtOAc) gave **S29** (239 mg, 0.77 mmol, 48%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 6.95 (1H, d, *J* = 1.3 Hz, C=C*H*), 5.13 (1H, s, 1H from C=CH_2), 4.93 (1H, s, 1H from C=CH_2), 3.75 (3H, s, CO_2CH_3), 3.56 - 3.65 (2H, m, CCH_2OH), 3.33 - 3.40 (2H, m, CH_2CH_2OH), 2.24 - 2.31 (1H, m, 1H from CH_2), 2.14 - 2.21 (1H, m, 1H from CH_2), 2.08 - 2.12 (1H, m, 1H from CH_2), 1.98 - 2.03 (1H, m, 1H from CH_2), 1.81 (1H, m, 1H from CH_2), 1.61 - 1.68 (1H, m, 1H from CH_2), 1.51 - 1.60 (3H, m, 3 X 1H from CH_2), 1.42 - 1.51 (2H, m, 2 X 1H from CH_2), 1.35 (1H, ddd, *J* = 13.6, 11.0, 2.8 Hz, 1H from CH_2), 0.96 (6H, d, *J* = 1.9 Hz, 2 X CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) 168.2 (CO_2CH_3), 149.2 (C=CH_2), 145.3 (C=CH), 129.9 ($C$$CO_2CH_3$), 114.7 (C=$CH_2$), 71.8 ($CH_2CH_2$OH), 63.2 (C$C$$H_2$OH), 51.7 ($CO_2CH_3$), 45.7 ($C$C=$CH_2$), 37.5 ($CH_2$), 36.2 ($C(CH_3)_2$), 35.2 ($CH_2$), 31.5 ($CH_2$), 27.3 ($CH_2$), 25.3 ($CH_3$), 25.0 ($CH_3$), 24.8 ($CH_2$), 18.7 ($CH_2$); v_{max} (thin film/cm^{-1}): 3345 (br, OH), 3080 (w), 2939 (w), 2863 (m), 1716 (s, C=O), 1701 (s), 1649 (w), 1628 (w), 1374 (w), 1243 (m), 1180 (w), 1164 (w), 1090 (m), 1045 (s), 945; HRMS calcd. for $C_{30}H_{58}O_4Sa$ (M+Na$^+$): 333.2042. Found: 333.2049.

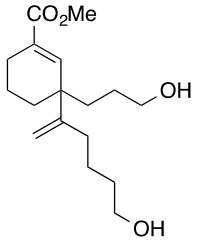
Methyl 3-(4,4-dimethyl-5-oxopent-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (7c)



7c

Prepared according to general procedure E. Dess-Martin periodinane (250 mg, 0.58 mmol, 2.2 equiv.), **S29** (80 mg, 0.26 mmol, 1.0 equiv.), CH_2Cl_2 (3 mL), after purification by column chromatography (30% EtOAc/hexane) gave **7c** (65.8 mg, 0.22 mmol, 83%), as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (1H, t, *J* = 1.1 Hz, C*H*O), 9.48 (1H, s, C*H*O), 6.72 (1H, d, *J* = 1.3 Hz, C=C*H*), 4.79 (1H, s, 1H from C=CH_2), 4.67 (1H, s, 1H from C=CH_2), 3.68 (3H, s, CO_2CH_3), 2.40 - 2.49 (1H, m, 1H from CH_2), 2.28 - 2.35 (1H, m, 1H from CH_2), 1.67 – 2.12 (6H, m, 2 X CH_2), 1.57 - 1.65 (2H, m, CH_2), 1.37 - 1.48 (2H, m, CH_2), 1.02 - 1.07 (6H, m, 2 X (CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.9 (*C*HO), 201.6 (*C*HO), 167.6 (*C*O_2CH_3), 147.2 (C=*C*H), 142.8 (*C*=CH_2), 131.2 (*C*O_2CH_3), 115.2 (C=*C*H_2), 51.7 (CO_2CH_3), 45.9 (*C*C=CH_2), 44.6 (*C*(CH_3)$_2$), 39.0 (CH_2), 38.0 (CH_2), 31.4 (CH_2), 29.9 (CH_2), 24.6 (CH_2), 22.7 (C(*C*H_3)$_2$), 22.0 (C(*C*H_3)$_2$), 18.32 (*C*H_2); v_{max} (thin film/cm^{-1}): 2931 (m, C-H), 2715 (w), 1713 (s, C=O), 1646 (w), 1434 (m), 1394 (w), 1248 (s), 1104 (w), 1045 (w), 904 (w), 812 (w), 777 (w). Complete characterisation was not possible due to instability.

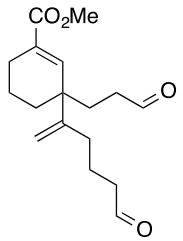
Methyl 3-(6-hydroxyhex-1-en-2-yl)-3-(3-hydroxypropyl)cyclohex-1-ene-1-carboxylate (S30)



S30

Prepared according to general procedure D. **6e** (490 mg, 0.94 mmol, 1.0 equiv.), Pyridine (4.70 mL, 0.20 M), HF (60% aqueous solution) (0.637 mL, 18.8 mmol, 20 equiv.) in acetonitrile (9.4 mL), after quenching with aqueous sat. $NaHCO_3$ (2 mL), extraction into diethyl ether (3 X 2 mL) and purification gave **S30** (195 mg, 0.66 mmol, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (1H, d, *J* = 1.0 Hz, C=C*H*), 4.97 (1H, s, 1H from C=CH_2), 4.75 (1H, d, *J* = 0.5 Hz, 1H from C=CH_2), 3.75 (3H, s, OCH_3), 3.66 - 3.71 (2H, m, CH_2OH), 3.63 (2H, d, *J* = 4.8 Hz, CH_2OH), 2.30 (1H, dt, *J* = 18.1, 4.5 Hz, 1H from CH_2CCO$_2$Me), 2.10 - 2.22 (1H, m, 1H from CH_2CCO$_2$Me), 2.01 (2H, t, *J* = 8.0 Hz, CH_2C=CH$_2$), 1.76 (1H, dd, *J* = 12.5, 5.3 Hz, 1H from CH_2), 1.30 - 1.70 (11H, m, 1H from CH_2, 5 X CH_2); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1 (*C*O$_2$CH$_3$), 152.0 (*C*=CH$_2$), 144.7 (*C*H=C), 129.9 (*C*CO$_2$CH$_3$), 112.2 (*C*H$_2$=C), 63.3 (*C*H$_2$OH), 62.7 (*C*H$_2$OH), 50.4 (CO$_2$*C*H$_3$), 44.9 (*C*(CH$_2$)$_3$OH), 35.0 (*C*H$_2$), 32.6 (*C*H$_2$), 32.0 (*C*H$_2$), 30.1 (*C*H$_2$(CH$_2$)$_3$OH), 27.4 (*C*H$_2$), 24.8 (*C*H$_2$C(CO$_2$CH$_3$), 21.1 (*C*H$_2$), 18.5 (*C*H$_2$); v_{max} (thin film/cm^{-1}): 3349 (br., s, OH), 2938.3 (s), 2866 (m), 1713 (s, C=O), 1644 (w), 1435 (m), 1252 (s), 1057 (m); MS (ES+) m/z (%): 319 (M+Na$^+$, 100). HRMS calcd. For $C_{17}H_{28}O_4Na$ (M+Na$^+$): 319.1885. Found: 319.1887.

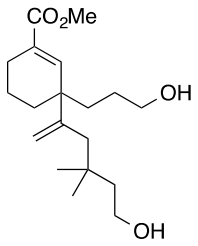
Methyl 3-(6-oxohex-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (7e)



7e

Prepared according to general procedure E. **S30** (195 mg, 0.66 mmol, 1.0 equiv.), DMP (614 mg, 1.45 mmol, 2.2 equiv.), in CH_2Cl_2 (6.6mL), after purification by column chromatography gave **7e** (0.14 g, 0.48 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 - 9.81 (1 H, m, C*H*O), 9.77 - 9.78 (1 H, m, C*H*O), 6.83 (1 br. s, C=C*H*), 5.02 (1 H, br. s, 1H from CH_2=C), 4.83 (1 H, br. s, 1H from CH_2=C), 3.76 (3 H, s, CO_2CH_3), 1.60 - 2.27 – 2.55 (6H, m, 3 X CH_2), 1.96 – 2.05 (2H, m, CH_2), 1.62 – 1.92 (8H, m, 4 X CH_2); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.1 (*C*HO), 201.8 (*C*HO), 167.8 (CO_2CH_3), 150.8 ($C(CH_2)_3CHO$), 143.2 (*C*=CH), 130.9 (CCO_2CH_3), 113.22 (CH_2=C), 51.8 (CO_2CH_3), 44.5 ($C(CH_2)_2CHO$), 43.6 (CH_2), 39.1 (CH_2), 31.7 (CH_2), 30.2 (CH_2), 29.6 (CH_2), 24.7 (CH_2), 20.8 (CH_2), 18.5 (CH_2); Complete characterisation was not possible due to instability.

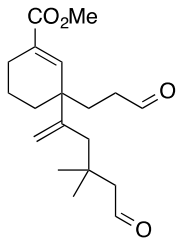
Methyl 3-(6-hydroxy-4,4-dimethylhex-1-en-2-yl)-3-(3-hydroxypropyl)cyclohex-1-ene-1-carboxylate (S31)



S31

Prepared according to general procedure D. **6d** (340 mg, 0.61 mmol, 1.0 equiv.), pyridine (3.05 mL, 1.0 equiv.), HF (0.41 mL, 12.2 mmol, 20.0 equiv.) in MeCN (6.1 mL), quenching with aqueous sat. $NaHCO_3$ (2 mL), extraction into diethyl ether (3 X 2 mL) and purification gave **S31** (63.4 mg, 0.20 mmol, 32%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (1H, s, C=C*H*), 5.14 (1H, s, 1H from C=CH_2), 4.92 (1H, s, 1H from C=CH_2), 3.75 (3H, s, CO_2CH_3), 3.70 - 3.73 (2H, m, CCH_2CH_2OH), 3.60 - 3.63 (2H, m, $CH_2CH_2CH_2OH$), 2.24 - 2.28 (1H, m, 1H from CH_2C=CH), 2.16 - 2.20 (1H, m, 1H from CH_2C=CH), 1.92 - 2.05 (2H, m, CH_2C=CH_2), 1.75 - 1.81 (1H, m, 1H from CH_2), 1.40 - 1.67 (8H, m, CCH_2CH_2OH 1H from 6 x CH_2), 1.35 (1H, ddd, *J* = 13.5, 11.0, 3.0 Hz, 1H from CH_2), 1.00 (3H, s, CH_3), 0.95 (3H, s, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0 (*C*=O), 149.3 (*C*=CH_2), 145.2 (C=*C*H), 129.9 (*C*=CH), 114.5 (C=*C*H_2), 63.3 ($CH_2CH_2CH_2OH$), 59.9 (CCH_2CH_2OH), 51.6 (OCH_3), 45.7 (*C*C=CH_2), 45.2 (CCH_2CH_2OH), 41.5 (CH_2C=CH_2), 35.2 (CH_2), 33.3 ($C(CH_3)_2$), 31.7 (CH_2), 28.7 (CCH_3), 28.6 (CCH_3), 27.4 (CH_2), 24.7 (CH_2C=CH), 18.7 (CH_2); v_{max} (thin film/cm^{-1}): 3339 (br, OH), 2942 (s), 2869 (m), 1714 (s, C=O), 1698 (s), 1644 (m), 1435 (m), 1384 (w), 1384 (w), 1365 (w), 1339 (w), 1246 (s), 1190 (w), 1103 (m), 1056 (s), 1025 (s), 976 (w), 903 (m), 814 (w); MS (ES$^+$) m/z (%): 325 (M+H$^+$, 10), 347 (M+Na$^+$, 100). HRMS calcd. for $C_{19}H_{33}O_4$ (M+H$^+$): 325.2373. Found: 325.2382.

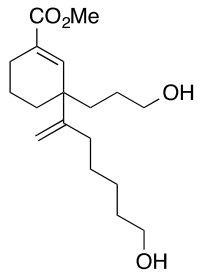
Methyl 3-(4,4-dimethyl-6-oxohex-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (7d)



7d

Prepared according to general procedure E. **S31** (63.4 mg, 0.20 mmol, 1,0 equiv.), DMP (187 mg, 0.44 mmol, 2.2 equiv.) in CH_2Cl_2 (2 mL), after purification by column chromatography gave **7d** (32 mg, 0.1 mmol, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (1H, t, *J* = 2.9 Hz, C*H*O), 9.77 (1H, t, *J* = 1.6 Hz, C*H*O), 6.81 (1H, d, *J* = 1.0 Hz, C=C*H*), 5.17 (1H, s, 1H from C=CH_2), 4.98 (1H, s, 1H from C=CH_2), 3.75 (3H, s, CO_2CH_3), 2.42 – 2.52 (1H, m, 1H from CH_2), 2.39 (2H, d, *J* = 2.8 Hz, CH_2CHO), 2.16 - 2.28 (3H, m, 1H from CH_2, CH_2), 2.08 (2H, s, CH_2), 1.73 - 1.83 (3H, m, 1H from CH_2, CH_2), 1.61 - 1.68 (1H, m, 1H from CH_2), 1.62 – 1.67 (1H, m, 1H from CH_2), 1.47 – 1.56 (1H, m, 1H from CH_2), 1.14 (9H, d, *J* = 3.3 Hz, C(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.2 (*C*HO), 201.8 (*C*HO), 167.7 (*C*O_2CH_3), 148.0 (*C*=CH_2), 143.6 (C=*C*H), 130.9 (*C*=CH), 115.6 (C=*C*H_2), 55.2 (*C*H_2), 51.8 (O*C*H_3), 45.1 (*C*C=CH_2), 41.7 (*C*H_2), 39.1 (*C*H_2), 34.3 (*C*(CH_3)$_2$), 31.3 (*C*H_2), 30.4 (*C*H_2), 28.6 (2 X C*C*H_3), 24.6 (*C*H_2), 18.5 (*C*H_2). Incomplete data due to instability of compound.

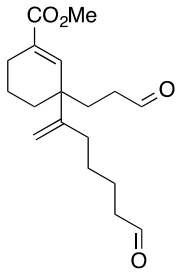
Methyl 3-(7-hydroxyhept-1-en-2-yl)-3-(3-hydroxypropyl)cyclohex-1-ene-1-carboxylate (S32)



S32

Prepared according to general procedure D. HF (60% aqueous solution)(0.96 mL, 28.9 mmol, 20 equiv.), **6f** (781 mg, 1.45 mmol, 1.0 equiv.), Pyridine (7.25 mL, 1.45 mmol, 0.2 M) in MeCN (14.5 mL, 1.45 mmol, 0.1 M), after quenching with aqueous saturated $NaHCO_3$ (5 mL), extraction into Et_2O (3 X 5 mL) and purification by column chromatography (EtOAc) gave **S32** (286 mg, 0.92 mmol, 63%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (1H, s, C=C*H*), 4.92 - 4.96 (1H, m, 1H from C=CH_2), 4.71 - 4.76 (1H, m. 1H from C=CH_2), 3.75 (3H, s, CO_2CH_3), 3.57 - 3.70 (4H, m, 2 X CH_2OH), 2.23 – 2.33 (1H, m,1H from CH_2), 1.95 - 2.18 (6H, m, 3 X CH_2), 1.74 (1H, dd, *J* = 13.2, 4.6 Hz, 1H from CH_2), 1.23 - 1.55 (10H, m, 5 X CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2 (CO_2CH_3), 152.0 (C=CH_2), 145.0 (C=CH), 129.7 ($C$$CO_2CH_3$), 112.0 (C=$CH_2$), 63.1 ($CH_2$OH), 62.7 ($CH_2$OH), 51.7 ($C$C=CH2), 44.9 ($CO_2CH_3$), 34.8 ($CH_2$), 32.5 ($CH_2$), 31.9 ($CH_2$), 30.1 ($CH_2$), 28.0 ($CH_2$), 27.3 ($CH_2$), 25.6 ($CH_2$), 24.7 ($CH_2$), 18.4 ($CH_2$); v_{max} (thin film/cm^{-1}): 3342 (br., m, O-H), 2933 (s, C-H), 2859 (m), 1713 (s, C=O), 1700 (s, C=O), 1435 (m), 1378 (w), 1250 (s), 1106 (w), 1054 (s), 906 (m), 752 (m), 731 (s); MS (ES$^+$) *m/z* (%): 311 (M+H$^+$,75), 333 (M+Na$^+$, 100); HRMS cald for $C_{18}H_{30}O_4$ (M+H$^+$): 310.2144. Found: 310.2137.

Methyl 3-(7-oxohept-1-en-2-yl)-3-(3-oxopropyl)cyclohex-1-ene-1-carboxylate (7f)

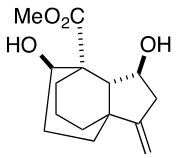


7f

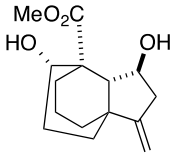
Prepared according to general procedure E. DMP (636 mg, 1.5 mmol, 2.2 equiv.), **S32** (212 mg, 0.68 mmol, 1.0 equiv.) in CH_2Cl_2 (6.8 mL), after partial purification by column chromatography (30% EtOAc/hexane) gave impure **7f** (182 mg, 0.59 mmol, 87%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_2$) δ 9.69 - 9.72 (2H, m, 2 x C*H*O), 6.76 (1H, s, C=C*H*), 4.90 (1H, s, 1H from C=CH_2), 4.69 - 4.73 (1H, s, 1H from C=CH_2), 3.68 (3H, s, CO_2CH_3), 1.37 - 2.57 (18H, m, 9 x CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.5 (*C*HO), 201.9 (*C*HO), 167.8 (CO_2CH_3), 150.9 (*C*=CH_2), 143.4 (C=*C*H), 130.6 (CCO_2CH_3), 112.8 (C=*C*H_2), 60.4 (*C*H_2), 51.7 (*C*C=CH_2), 44.0 (CO_2CH_3), 43.7 (*C*H_2), 39.1 (*C*H_2), 31.7 (*C*H_2), 30.2 (*C*H_2), 27.9 (*C*H_2), 24.6 (*C*H_2), 21.9 (*C*H_2), 18.4 (*C*H_2); v_{max} (thin film/cm^{-1}): 2934 (m, C-H), 2859 (w), 2721 (w), 1720 (s, C=O), 1645 (w), 1435 (w), 1410 (w), 1249 (m), 1103 (w), 1017 (w), 972 (w), 909 (w), 836 (w), 774 (w), 732 (w). No MS data due to instability of compound.

Synthesis of Cores

Methyl (1*S*,6*S*,7*S*,7a*R*)-1,6-dihydroxy-3-methylenehexahydro-3a,7-propanoindene-7(4*H*)-carboxylate (10a), methyl (1*S*,3a*S*,7*S*,8*S*,8a*R*)-1,7-dihydroxy-3-methyleneoctahydro-8*H*-3a,8-propanoazulene-8-carboxylate (10a')



10a



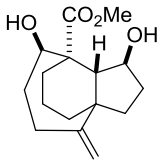
10a'

Prepared according to general procedure G. *t*BuOH (0.13 mL, 1.35 mmol, 5.0 equiv.), SmI_2 (6.7 mL, 0.67 mmol, 0.1 M, 2.4 equiv.), **7a** (70.7 mg, 0.27 mmol, 1.0 equiv.), after quenching with air and aqueous saturated Na/K tartrate (10 mL), extraction into Et_2O (3 X 6 mL) and purification by column silica chromatograpy (30% ethyl acetate/hexane) gave **10a** (29 mg, 0.10 mmol, 40%) as a white solid and **10a'** (13 mg, 0.045 mmol, 18%) as a white solid. Data for **10a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (1H, s, O*H*), 4.59 - 4.65 (2H, m, C=C*H*$_2$), 4.48 (1H, td, *J* = 8.7, 5.8 Hz, CHC*H*OH), 4.14 (1H, d, *J* = 2.8 Hz, CC*H*OH), 3.69 (3H, s, CO_2CH_3), 2.96 - 3.06 (1H, m, 1H from CH_2=CC*H*$_2$), 2.18 - 2.33 (2H, m, 1H from CH_2=CC*H*$_2$, 1H from CH_2), 2.12 (1H, d, *J* = 9.0 Hz, C*H*CHOH), 1.98 (1H, br. s., O*H*), 1.68 - 1.87 (5H, m, 1H from C*H*$_2$, 2 x C*H*$_2$), 1.47 - 1.65 (2H, m, C*H*$_2$), 1.29 - 1.38 (2H, m., C*H*$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.1 (*C*O_2CH_3), 157.1 (*C*=CH_2), 102.7 (C=*C*H_2), 72.6 (C*C*HOH), 69.2 (CH*C*HOH), 52.6 (CO_2*C*H_3), 52.3 (*C*CO_2CH_3), 49.1 (*C*HCHOH), 45.5 (CH_2=C*C*), 39.2 (*C*H_2), 31.5 (*C*H_2), 31.5 (*C*H_2), 30.8 (*C*H_2), 25.5 (*C*H_2), 20.7 (*C*H_2); ν_{max} (thin film/cm^{-1}): 3385 (br, OH), 2983 (w), 2935 (w), 2915 (m), 1709 (s, C=O), 1655 (w), 1534 (w), 1435 (m), 1346 (w), 1273 (m), 1210 (w), 1182 (w), 1027 (m), 995

(m), 878 (m); MS (ES^+) m/z (%): 267 ($M+H^+$, 100), 289 ($M+Na^+$, 75); HRMS cald. for $C_{15}H_{22}O_4Na$ ($M+Na^+$): 289.1416. Found: 298.1410; Melting point = 110 – 112 °C (recrystallized from hexane).

Data for **10a'**: ^1H NMR (400 MHz, $CDCl_3$) δ 4.64 (1H, t, *J* = 4.0 Hz, 1H from C=CH_2), 4.61 (1H, t, *J* = 2.4 Hz, 1H from C=CH_2), 4.50 (1H, m, CHC*H*OH), 4.18 (1H, m, CC*H*OH), 3.69 (3H, s, CO_2CH_3), 2.97-3.04 (1H, m, 1H from $CH_2C=CH_2$), 2.48 (1H, d, *J* = 4.0 Hz, 1H from $CH_2C=CH_2$), 2.24 - 2.30 (2H, m, CH_2CH_2CHOH), 1.93 – 2.22 (5H, m, 2 X CH_2, 1H from C*H*CHOH), 1.83 - 1.89 (2H, m, CH_2), 1.32 - 1.39 (2H, m, CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.9 (CO_2CH_3), 155.9 ($C=CH_2$), 103.6 ($C=CH_2$), 74.1 (C*C*HOH), 69.1 (CH*C*HOH), 55.5 (*C*HCHOH), 52.5 (CO_2CH_3), 49.5 (CCO_2CH_3), 44.3 ($CH_2=CC$), 40.0 (CH_2), 33.9 (CH_2), 31.5 (CH_2), 31.0 (CH_2), 21.4 (CH_2), 20.72 (CH_2); v_{max} (thin film/cm^{-1}): 3430 (br, OH), 2946(m), 2870(w), 1715(s), 1632(w), 1451(m), 1246(m), 1203(m), 1057(m), 924(w), 890(w); MS (ES^+) m/z (%): 267 ($M+H^+$, 50), 289 ($M+Na^+$, 100); HRMS cald for $C_{15}H_{22}O_4Na$ (M+Na): 289.1416. Found: 289.1418; Melting point = 114 – 118 °C (recrystallized from hexane).

Methyl (1*S*,3a*R*,7*R*,8*S*,8a*R*)-1,7-dihydroxy-4-methyleneoctahydro-8*H*-3a,8-propanoazulene-8-carboxylate (10b)

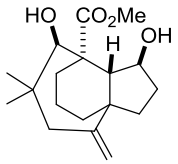


10b

Prepared according to general procedure G. SmI_2 (0.1 M in THF, 7.25 mL, 0.73 mmol, 2.5 equiv.), *t*BuOH (70 µL, 0.73 mmol, 2.5 equiv.), **7b** (74 mg, 0.26 mmol, 1.0 equiv.) in THF (2 mL), quenching with air, followed by Na/K tartrate (1 mL),

extraction into Et_2O (3 X 1 mL) and purification by column chromatography (60% EtOAc/hexane) gave **10b** (46 mg, 0.16 mmol, 63%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.92 (1H, t, *J* = 1.4 Hz, 1H from C=C*H*$_2$), 4.76 (1H, s, 1H from C=C*H*$_2$), 4.27 (1H, td, *J* = 8.5, 3.5 Hz, CHC*H*OH), 3.98 (1H, d, *J* = 3.8 Hz, CH_2C*H*OH), 3.74 (3H, s, OC*H*$_3$), 2.94 (1H, br. s., O*H*), 2.71 (1H, t, *J* = 9.0 Hz, 1H from CH_2=CC*H*$_2$), 2.55 (1H, br. s., O*H*), 2.45 (1H, d, *J* = 7.6 Hz, C*H*CHOH), 2.15 - 2.33 (3H, m, 1H from CH_2=CC*H*$_2$, 1H from CHCH(OH)C*H*$_2$, 1H from CCH(OH)C*H*$_2$), 1.80 - 1.98 (4H, m, 1H from CCH(OH)C*H*$_2$, 3H from 3 × C*H*$_2$), 1.75 (1H, dd, *J* = 14.2, 2.8 Hz, 1H from C*H*$_2$), 1.48 - 1.68 (4H, m, 1H from 2 × C*H*$_2$, C*H*$_2$), 1.35 (1H, td, *J* = 13.4, 3.8 Hz, 1H from C*H*$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.9 (*C*(O)OCH$_3$), 154.8 (*C*=CH$_2$), 110.4 (C=*C*H$_2$), 73.9 (CH*C*HOH), 72.8 (C*C*HOH), 52.3 (*C*C(O)OCH$_3$), 52.3 (O*C*H$_3$), 52.1 (*C*HCHOH), 49.7 (*C*C=CH$_2$), 39.0 (*C*H$_2$), 32.7 (CCH(OH)*C*H$_2$), 32.1 (CHCH(OH)*C*H$_2$), 32.1 (*C*H$_2$) 29.4 (*C*H$_2$C=CH$_2$), 26.3 (*C*H$_2$), 19.2 (*C*H$_2$); v_{max} (thin film/cm^{-1}): 3420 (br, OH), 3075 (w), 2946 (s), 2871 (m), 1716 (s), 1633 (m), 1452 (m), 1434 (m), 1403 (w), 1339 (w), 1246, (s), 1204 (s), 1159 (w), 1058 (m), 1070 (m), 1025 (w), 1007 (w), 992 (w), 975 (w), 962 (w), 924 (m), 890 (m); MS (ES$^+$) *m/z* (%): 281 (M+H$^+$, 100), 303 (M+Na$^+$, 50); MS (ES$^-$) *m/z* (%): 279 (M−H$^+$, 95); HRMS calcd. for $C_{16}H_{25}O_4$ (M+H$^+$): 281.1747. Found: 281.1746; Melting point = 116-117 °C. Recrystallized from hexane.

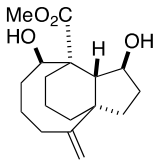
Methyl (1*S*,7*R*,8*S*,8a*R*)-1,7-dihydroxy-6,6-dimethyl-4-methyleneoctahydro-8*H*-3a,8-propanoazulene-8-carboxylate (10c)



10c

Prepared according to general procedure G. SmI_2 (0.1 M in THF, 4.90 mL, 0.49 mmol, 2.5 equiv.), *t*BuOH (94 µL, 0.98 mmol, 5.0 equiv.), **7c** (60 mg, 0.20 mmol, 1.0 equiv.) in THF (1.3 mL), after quenching with air, followed by aqueous saturated Na/K tartrate (5 mL), extraction into Et_2O (3 X 5 mL) and purification by column chromatography (60% EtOAc/hexane) gave **10c** (29 mg, 0.09 mmol, 50%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85 (1H, s, 1H from C=C*H*$_2$), 4.80 (1H, s, 1H from C=C*H*$_2$), 4.30 (1H, td, *J* = 8.8, 4.0 Hz, CH_2CH(OH)), 3.64 (3H, s, CO_2CH_3), 3.56 (1H, s, CC*H*OH), 2.46 (1H, d, *J* = 13.6 Hz, 1H from C*H*$_2$C=CH$_2$), 2.40 (1H, d, *J* = 8.3 Hz, CC*H*), 2.04 - 2.28 (5H, m, C*H*$_2$, 2 x O*H*, 1H from C*H*$_2$C=CH$_2$), 1.14 - 1.86 (8H, m, 4 X C*H*$_2$), 1.13 (3 H, s, C*H*$_3$), 1.06 (3 H, s, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3 (*C*O_2CH_3), 148.8 (CH_2=*C*), 110.1 (*C*H_2=C), 77.2 (C*C*H(OH)), 72.5 (CH_2*C*H(OH)), 53.3 (C*C*H), 52.7 (*C*CO_2CH_3), 51.8 (CO_2*C*H_3), 48.5 (CH_2=C*C*), 46.5 (*C*H_2C=CH$_2$), 39.2 (*C*$(CH_3)_2$, 37.5 (*C*H_2), 32.3 (*C*H_2), 31.5 (*C*H_3), 27.8 (*C*H_2), 26.4 (*C*H_2), 23.1 (*C*H_3), 17.9 (*C*H_2); ν_{max} (thin film/cm^{-1}) 3466 (br., m, O-H), 2950 (s), 2873 (m), 1711 (s, C=O), 1635 (w), 1469 (m), 1256 (m), 1077 (w), 1049 (m), 993 (w), 892 (w), 755 (s); MS (ES$^+$) m/z (%) 309 (M+H$^+$, 100), 331 (M+Na$^+$, 100); HRMS calcd. for $C_{18}H_{29}O_4$ (M+H$^+$): 309.2066. Found: 309.2071. Melting point = 122 – 127 °C. Recrystallized from hexanes.

Methyl (1*S*,3a*R*,8*R*,9*S*,9a*R*)-1,8-dihydroxy-4-methyleneoctahydro-3a,9-propanocyclopenta[8]annulene-9(4*H*)-carboxylate (10e)

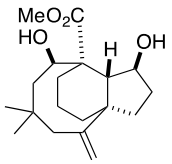


10e

Prepared according to general procedure G. SmI_2 (0.1 M in THF, 2.5 mL, 0.25 mmol, 2.5 equiv.), *t*BuOH (24 µL, 0.25 mmol, 2.5 equiv.) and **7e** (0.15 M in THF, 670 µL, 0.1 mmol, 1.0 equiv.) were stirred for 45 minutes, the reaction was quenched with air, followed by a saturated solution of K/Na tartrate (aq) (5 mL), extracted with Et_2O (4 × 7 mL) then dried (Na_2SO_4). Column chromatography (60% EtOAc/*n*-hexane) gave **10e** (12.4 mg, 0.042 mmol, 42%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (1H, s, 1H from C=CH_2), 4.90 (1H, s, 1H from C=CH_2), 4.42 (1H, ddt, *J* = 8.3, 7.8, 4.0 Hz, CHC*H*OH), 3.97 (1H, td, *J* = 6.9, 2.5 Hz, CC*H*OH), 3.71 (3H, s, OCH_3), 2.71 (1H, dddd, *J* = 15.6, 13.6, 7.9, 2.5 Hz, CCH(OH)CH_2), 2.42 (1H, d, *J* = 7.8 Hz, C*H*CHOH), 2.21 - 2.37 (2H, m, 1H from CH_2C=CH_2, 1H from CHCH(OH)CH_2), 1.99 - 2.13 (2H, m, 1H from CH_2C=CH_2, 1H from CH_2), 1.89 - 1.97 (2H, m, CH_2), 1.42 - 1.86 (7H, m, 1H from CCH(OH)CH_2, 1H from CHCH(OH)CH_2, 3H from 3 X CH_2, CH_2), 1.08 - 1.30 (2H, m, 2H from 2 X CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6 (*C*(O)OCH_3), 153.5 (*C*=CH_2), 110.5 (C=*C*H_2), 74.1 (CH*C*HOH), 72.7 (C*C*HOH), 52.2 (*C*HCHOH), 52.2 (*C*C(O)OCH_3), 51.8 (O*C*H_3), 48.6 (*C*C=CH_2), 37.9 (*C*H_2), 35.3 (CCH(OH)*C*H_2), 33.2 (*C*H_2), 32.0 (CHCH(OH)*C*H_2), 32.0 (*C*H_2C=CH_2), 27.5 (*C*H_2), 25.8 (*C*H_2), 17.3 (*C*H_2); ν_{max} (thin film/cm^{-1}): 3436 (br., s, OH), 3082 (w), 2945 (s), 2872 (m), 1710 (s, C=O), 1628 (m), 1459 (m), 1434 (m), 1348 (m), 1332 (w), 1289 (m), 1226 (s), 1206 (s), 1163 (m), 1127 (w), 1087 (m), 1068 (m), 1058 (m), 1023 (w), 1005 (m), 976 (w), 952 (w), 932 (w), 914 (m), 894 (m), 864 (w); MS (ES$^+$) m/z (%):

317 (M^+Na^+, 100); HRMS calcd. for $C_{17}H_{26}O_4Na$ (M^+Na^+): 317.1723. Found: 317.1718. Melting point = 101-102 °C.

Methyl (1*S*,3a*R*,8*R*,9*S*,9a*R*)-1,8-dihydroxy-6,6-dimethyl-4-methyleneoctahydro-3a,9-propanocyclopenta[8]annulene-9(4*H*)-carboxylate (10d)

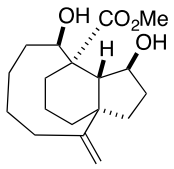


10d

Prepared according to general procedure G. SmI_2 (0.1 M in THF, 2.5 mL, 0.25 mmol, 2.5 equiv.), *t*BuOH (50 µL, 0.50 mmol, 5.0 equiv.) and **7d** (0.15 M in THF, 667 µL, 0.1mmol, 1.0 equiv.) were stirred for 30 minutes, the reaction was quenched with air, followed by a saturated solution of K/Na tartrate (aq) (5 mL), extracted with Et_2O (5 × 5 mL) then dried (Na_2SO_4). Column chromatography (60% EtOAc/n-hexane) gave **10d** (26 mg, 0.081 mmol, 81%) as a colourless foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.99 (1H, s, 1H from C=CH_2), 4.83 (1H, s, 1H from C=CH_2), 4.45 (1H, ddd, *J* = 10.8, 7.5, 3.3 Hz, CHC*H*OH), 3.86 - 3.96 (1H, m, CC*H*OH), 3.71 (3H, s, OCH_3), 2.65 (1H, dd, *J* = 15.4, 7.2 Hz, 1H from CCH(OH)CH_2), 2.38 (1H, d, *J* = 3.3 Hz, CHCHO*H*), 2.32 (1H, d, *J* = 7.5 Hz, C*H*CHOH), 2.21 - 2.32 (1H, m, 1H from CHCH(OH)CH_2), 2.14 (1H, d, *J* = 13.6 Hz, 1H from CH_2), 1.74 - 2.03 (6H, m, 2 × CH_2, 2H from 2 × CH_2), 1.55 - 1.73 (3H, m, CCHO*H*, 1H from CHCH(OH)CH_2, 1H from CH_2), 1.44 - 1.54 (1H, m, 1H from CH_2), 1.22 - 1.31 (1H, m, 1H from CH_2), 1.10 - 1.16 (1H, m, 1H from CH_2), 1.09 (3H, s, CCH_3), 1.03 (3H, s, CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8 (*C*=O), 148.2 (*C*=CH_2), 112.0 (C=*C*H_2), 73.8 (CH*C*HOH), 67.8 (C*C*HOH), 52.5 (*C*HCHOH), 51.9 (O*C*H_3), 51.7 (*C*C(O)OCH_3), 49.1 (*C*C=CH_2), 48.2 (CCH(OH)*C*H_2), 44.5 (*C*H_2), 38.5 (*C*H_2), 34.1 (*C*(CH_3)$_2$), 33.7 (C*C*H_3), 31.7 (CHCH(OH)*C*H_2), 27.4 (*C*H_2), 25.7 (*C*H_2), 25.5 (C*C*H_3), 17.3 (*C*H_2); v_{max} (thin film/cm^{-1}): 3457 (br, s, OH),

3085 (w), 2949 (s), 2870 (m), 2237 (w), 1710 (s, C=O), 1624 (m), 1462 (m), 1434 (m), 1387 (m), 1364 (m), 1346 (m), 1329 (m), 1271 (s), 1229 (s), 1197 (s), 1169 (m), 1095 (w), 1066 (m), 1058 (m), 1033 (w), 1020 (w), 966 (w), 947 (m), 896 (m), 878 (s), 854 (w), 815 (w); MS (ES^+) m/z (%): 345 ($M+Na^+$, 100); HRMS calcd. for $C_{19}H_{30}O_4Na$ ($M+Na^+$): 345.2036. Found: 345.2035.

Methyl (1*S*,3a*R*,9*R*,10*S*,10a*R*)-1,9-dihydroxy-4-methylenedecahydro-10*H*-3a,10-propanocyclopenta[9]annulene-10-carboxylate (10g)

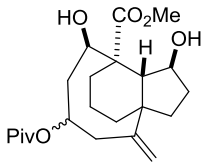


10g

Prepared according to general procedure G. SmI_2 (2.6 mL, 0.1 M, 0.26 mmol, 2.5 equiv.), *t*BuOH (0.05 mL, 0.55 mmol, 5.0 equiv.), **6g** (32.2 mg, 0.11 mmol, 1.0 equiv.) in THF (0.75 mL), after quenching with air and saturated aqueous Na/K tartrate (2 mL), extraction into Et_2O (3 x 2 mL) and purification by column chromatography (60% EtOAc/hexane) gave **10g** (8.8 mg, 0.03 mmol, 26%) as a colourless foam. ^{1}H NMR (400 MHz, $CDCl_3$) 4.84 (2H, d, *J* = 8.8 Hz, C=C*H*$_2$), 4.35 (1H, td, *J* = 8.3, 4.0 Hz, CHC*H*(OH)), 3.90 (1H, d, *J* = 7.8 Hz, CC*H*(OH)), 3.62 - 3.65 (3H, m, CO_2CH_3), 2.58 - 2.70 (1H, m, 1H from C*H*$_2$), 2.35 (1H, d, *J* = 7.5 Hz, C*H*CH(OH)), 2.13 - 2.29 (3H, m, C*H*$_2$, 1H from CH_2), 1.93 - 2.03 (2H, m, C*H*$_2$), 1.86 (2H, dd, *J* = 10.2, 3.9 Hz, *C*H$_2$), 1.50 - 1.78 (3H, m, C*H*$_2$, 1H from C*H*$_2$, 2 X C*H*$_2$), 1.12 - 1.45 (4H, m, C*H*$_2$, C*H*$_2$), 1.07 (1H, ddd, *J* = 12.9, 9.1, 2.1 Hz, 1H from C*H*$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6 (*C*O_2CH_3), 153.5 (*C*=CH_2), 110.6 (C=*C*H_2), 74.1 (CH*C*H(OH)), 72.7 (C*C*H(OH)), 52.2 (*C*HCH(OH)), 52.2 (*C*CO_2CH_3), 51.8 (CO_2*C*H_3),

48.6 (*C*C=CH_2), 37.9 (*C*H_2), 35.2 (*C*H_2), 33.2 (*C*H_2), 32.0 (*C*H_2), 32.0 (*C*H_2), 27.5 (*C*H_2), 25.8 (*C*H_2), 22.6 (*C*H_2), 17.3 (*C*H_2); v_{max} (thin film/cm^{-1}): 3434 (m, OH), 2945 (s, CH), 2871 (m), 1714 (s, C=O), 1629 (w), 1460 (m), 1434 (w), 1258 (w), 1227 (m), 1086 (m), 1056 (m), 895 (m), 799 (w), 755 (s); MS was inconclusive.

Methyl (1*S*,8*R*,9*S*,9a*R*)-1,8-dihydroxy-4-methylene-6-(pivaloyloxy)octahydro-3a,9-propanocyclopenta[8]annulene-9(4*H*)-carboxylate (10f)



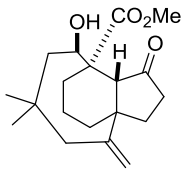
10g

Prepared according to general procedure G. **9** (22.3 mg, 0.06 mmol, 1.0 equiv.), SmI_2 (1.5 mL, 0.1 M, 0.15 mmol, 2.5 equiv.), *t*BuOH (22 mg, 0.30 mmol, 5.0 equiv.), in THF (0.4 mL), quenched with air, followed by aqueous saturated NaK tartrate (3 mL). After extraction with Et_2O (3 X 3 mL) and purification by column chromatography (60 % EtOAc/hexane) gave **10f** (10.2 mg, 25.8 µmol, 43% (dr:1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 - 5.13 (1H, m, C*H*OPiv (both diastereoisomers)), 5.02 (1H, s, 1H from C=C*H*$_2$ (both diastereoisomers)), 4.86 (1H, s, 1H from C=C*H*$_2$ (both diastereoisomers)), 4.36 - 4.45 (1H, m, C*H*(OH) (both diastereoisomer)), 4.23 (1H, s, C*H*(OH) (both diastereoisomers)), 3.66 (3H, s, CO_2CH_3 (both diastereoisomers)), 2.85 - 2.94 (1H, m, 1H from C*H*$_2$ (both diastereoisomers)), 2.55 - 2.67 (1H, m, C*H*CH(OH) (both diastereoisomers)), 2.21 – 2.30 (2H, m, 2 X 1H from C*H*$_2$ (both diastereoisomers)), 2.15 (1H, d, *J* = 7.9 Hz, 1H from C*H*$_2$ (both diastereoisomers)), 1.91 – 1.95 (2H, m, 2 X 1H from C*H*$_2$ (both diastereoisomers)), 1.81 - 1.86 (1H, m, 1H from C*H*$_2$ (both diastereoisomers)), 1.70 - 1.78 (1H, m, 1H

from C*H*$_2$ (both diastereoisomers)), 1.43 - 1.65 (6H, m, 3 X CH_2 (both diastereoisomers)), 1.18 - 1.21 (9H, m, C(C*H*$_3$)$_3$ (both diastereoisomers)); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.4 (*C*(O)C(CH_3)$_3$ (both diastereoisomers), 176.3 (*C*O_2CH_3 (both diastereoisomers)), 151.4 (*C*=CH_2, (both diastereoisomers)), 110.7 (C=*C*H_2 (both diastereoisomers)), 78.5 (*C*H(OPiv) (both diastereoisomers)), 77.3 (*C*H(OH) (both diastereoisomers)), 51.8 (*C*H(OH) (both diastereoisomers)), 50.8 (*C*HCH(OH) (one diastereoisomer), 50.8 (*C*HCH(OH), (one diastereoisomer)), 49.3 (*C*CO_2CH_3 (both diastereoisomer)), 42.6 (CO_2*C*H_3, (both diastereoisomer)), 32.4 (*C*C=CH_2, (one diastereoisomer)), 32.4 (*C*C=CH_2, (one diastereoisomer)), 32.2 (*C*H_2 (both diastereoisomer)), 31.8 (*C*H_2 (both diastereoisomer)), 31.6 (*C*H_2 (both diastereoisomer)), 29.4 (*C*H_2 (both diastereoisomer)), 27.2 (C(*C*H_3)$_3$ (both diastereoisomer)), 26.3 (*C*H_2 (both diastereoisomer)), 22.7 (*C*H_2 (both diastereoisomer)), 20.2 ((*C*H_3)$_3$ (both diastereoisomer)), 14.2 (*C*H_2 (both diastereoisomer)); v_{max} (thin film/cm^{-1}):3457 (br, OH), 2953 (s), 2933 (s), 2873 (m), 1725 (s, C=O), 1632 (w), 1479 (m), 1459 (m), 1435 (m), 1397 (w), 1366 (w), 1283 (s), 1262 (m), 1227 (m), 1163 (s), 1091 (w), 1060 (m), 1028 (m), 974 (w), 933 (w), 905 (w); MS (ES+) m/z (%): 417 (M+Na+, 100); HRMS calcd. for $C_{22}H_{34}O_6Na$ (M+Na$^+$): 417.2253. Found: 417.2266.

Synthesis of Pleuromutilin Analogue

Methyl (8*R*,9*S*,9a*R*)-8-hydroxy-6,6-dimethyl-4-methylene-1-oxooctahydro-3a,9-propanocyclopenta[8]annulene-9(4*H*)-carboxylate (11b)

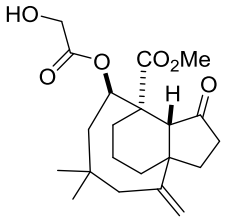


11

DMP (132, 0.31 mmol) was added to a solution of **10d** (101 mg, 0.31 mmol) in CH_2Cl_2 (3.00 mL, 0.1 M) under nitrogen and after 1 hour the reaction was quenched with 5% NaOH (w/v water) (3 mL). Extraction into Et_2O (3 X 5 mL) and purification by column chromatography (30% ethyl acetate/hexane) gave **11** (48.3 mg, 0.15 mmol, 49%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (1H, s, 1H from C=C*H*$_2$), 4.87 (1H, s, 1H from C=C*H*$_2$), 3.86 (1H, d, *J* = 7.6 Hz, CH_2CH(OH))), 3.66 (3H, s, CO_2CH_3), 3.01 (1H, s, C*H*C=O), 2.47 (1H, dd, *J* = 15.6, 7.6 Hz, 1H from C*H*$_2$CH(OH)), 2.08 - 2.33 (4H, m, 2 X C*H*$_2$), 1.78 - 1.96 (4H, m, 2 X C*H*$_2$), 1.34 - 1.62 (4H, m 2 X C*H*$_2$), 1.14 (1H, dd, *J* = 15.8, 1.7 Hz, C*H*$_2$CH(OH)), 1.03 (3H, s, C*H*$_3$), 0.97 (3H, s, C*H*$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.9 (CH_2C=O), 174.8 (CO_2CH_3), 147.4 (*C*=CH_2), 113.3 (C=*C*H$_2$), 67.5 (CH_2CH(OH)), 56.5 (C*C*H), 51.7 (CO_2CH_3), 48.8 (CCO_2CH_3), 46.7 (CH_2CH(OH)), 46.5 (CH_2CC), 44.7 (CH_2), 34.0 ($C(CH_3)_2$), 33.9 (($CH_3)_2$), 33.4 (*C*H$_2$), 33.4 (*C*H$_2$), 27.8 (*C*H$_2$), 25.4 (*C*H$_2$), 25.6 (*C*H$_2$), 17.2 (*C*H$_2$); v_{max} (thin film/cm^{-1}): 3473 (br, OH), 3087 (w), 2950 (s), 2873 (m), 1744 (s, C=O), 1723 (s, C=O), 1626 (w), 1460 (m), 1433 (w), 1388 (w), 1364 (w), 1342 (w), 1295 (w), 1268 (w), 1225 (s), 1205 (m), 1168 (w), 1142 (w), 1105 (w), 1080 (w), 1036 (w), 1011 (w), 985 (w), 897 (w), 859 (w), 813 (w); MS (ES+) m/z (%): 321 (M+H$^+$, 50), 338 (M+NH_4^+, 40) , 343 (M+Na$^+$, 40); HRMS calcd. for $C_{19}H_{32}O_4N$ (M+NH_4^+):

338.2326. Found: 338.2329.

Methyl (8*R*,9*S*,9a*R*)-8-(2-hydroxyacetoxy)-6,6-dimethyl-4-methylene-1-oxooctahydro-3a,9-propanocyclopenta[8]annulene-9(4*H*)-carboxylate (12)



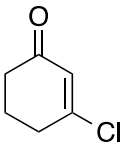
12

DCC (124 mg, 0.60 mmol, 4.0 equiv.) and DMAP (73 mg, 0.60 mmol, 4.0 equiv.) were added to a solution of **11** (48.3 mg, 0.15 mmol, 1.0 equiv.) and Ph_3COCH_2COOH[14] (191 mg, 0.60 mmol, 4.0 equiv.) in CH_2Cl_2 (14 mL). After 2 hours, the reaction mixture was quenched with water (15 mL), extracted into CH_2Cl_2 (3 X 15 mL) and dried ($MgSO_4$). Concentration *in vacuo* and partial purification by column chromatography (10 % EtOAc/hexane) gave the trityl protected product, which was taken onto the next step. HCl (0.15 mL, 1 M) was added to a solution of the protected product in MeOH (10 mL). After 18 hours, $NaHCO_3$ (150 mg) was added to the reaction and it was left to stir for 15 minutes before being filtered through a pad of celite. Concentration *in vacuo* and purification by column chromatography (15% EtOAc/hexane) gave **12** (33.3 mg, 88.0 µmol, 59%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (1H, d, *J* = 8.0 Hz, C*H*OC(O)CH_2), 5.24 (1H, s, 1H from C=C*H*$_2$), 5.06 (1H, s, 1H from C=C*H*$_2$), 4.08 (AB system, 1H, d, *J* = 2.8 Hz, 1H from C*H*$_2$OH), 4.07 (AB system, 1H, d, *J* = 2.8 Hz, 1H from C*H*$_2$OH), 3.74 (3H, s, OC*H*$_3$), 3.13 (1H, br. s., C*H*C=O), 2.68 (1H, dd, *J* = 16.1, 8.0 Hz, 1H from C*H*$_2$CHOC=O), 2.28 (1H, t, *J* = 5.5 Hz, O*H*), 2.21 - 2.41 (1H, m, 1H from CH_2), 2.21

[14] B. L. Murr, C. Santiago, S. Wang, *J. Am. Chem. Soc.*, **1969**, 91, 3827.

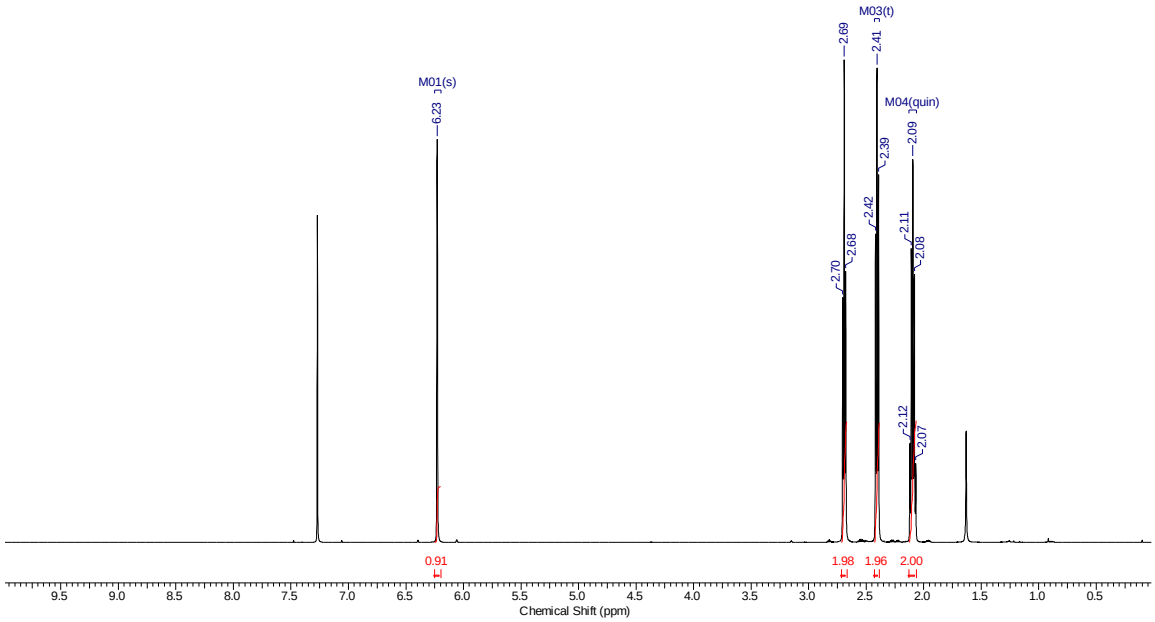
(1H, d, *J* = 14.6 Hz, 1H from $CH_2C=CH_2$), 2.19 - 2.40 (4H, m, 1H from 4 X C*H*$_2$), 1.87 – 2.16 (4H, m, 1H from 4 X CH_2), 1.68 - 1.80 (1H, m, 1H from C*H*$_2$), 1.43 - 1.56 (4H, m, 2 X C*H*$_2$), 1.18 (1H, dd, *J* = 16.1, 1.3 Hz, 1H from C*H*$_2$), 1.14 (3H, s, CC*H*$_3$), 1.05 (3H, s, CC*H*$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.4 (*C*(O)), 171.9 (*C*(O)OCH_3), 171.9 (CHO*C*(O)CH_2), 146.4 (*C*=CH_2),114.5 (C=*C*H_2), 71.0 (*C*HOC(O)CH_2), 60.6 (*C*H_2OH), 56.2 (*C*HC=O), 51.8 (O*C*H_3), 47.6 (*C*C(O)OCH_3), 46.5 (*C*C=CH_2), 44.4 (*C*$H_2C=CH_2$), 44.2 (*C*H_2CHOC=O), 34.1 (*C*$(CH_3)_2$), 33.8 (C*C*H_3), 33.5 (*C*H_2), 32.3 (*C*H_2), 27.8 (*C*H_2), 26.0 (C*C*H_3), 25.6 (*C*H_2), 17.1 (*C*H_2); v_{max} (thin film/cm^{-1}): 3468 (br, OH), 2951 (m), 2877 (m), 1742 (s, C=O), 1728 (s, C=O), 1462 (m), 1433 (w), 1390 (w), 1366 (w), 1314 (w), 1289 (w), 1267 (m), 1225 (s), 1205 (s), 1196 (s), 1169 (m), 1144 (w), 1097 (m), 1055 (w), 1002 (w), 984 (w), 962 (w), 948 (w), 918 (w), 903 (w), 890 (w); MS (ES^+) m/z (%): 401 ($M+Na^+$, 80); HRMS calcd. for $C_{21}H_{30}O_6Na$ ($M+Na^+$): 401.1940. Found: 401.1932.

^{1}H and ^{13}C NMR Spectra of Compounds

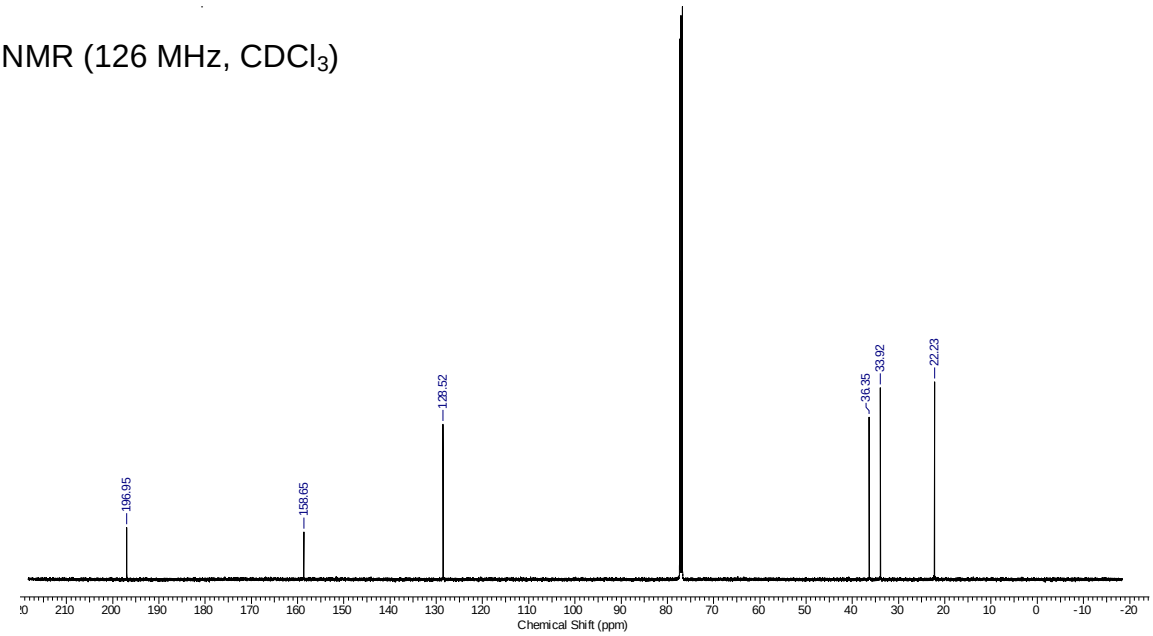


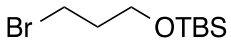
4

^{1}H NMR (500 MHz, $CDCl_3$)



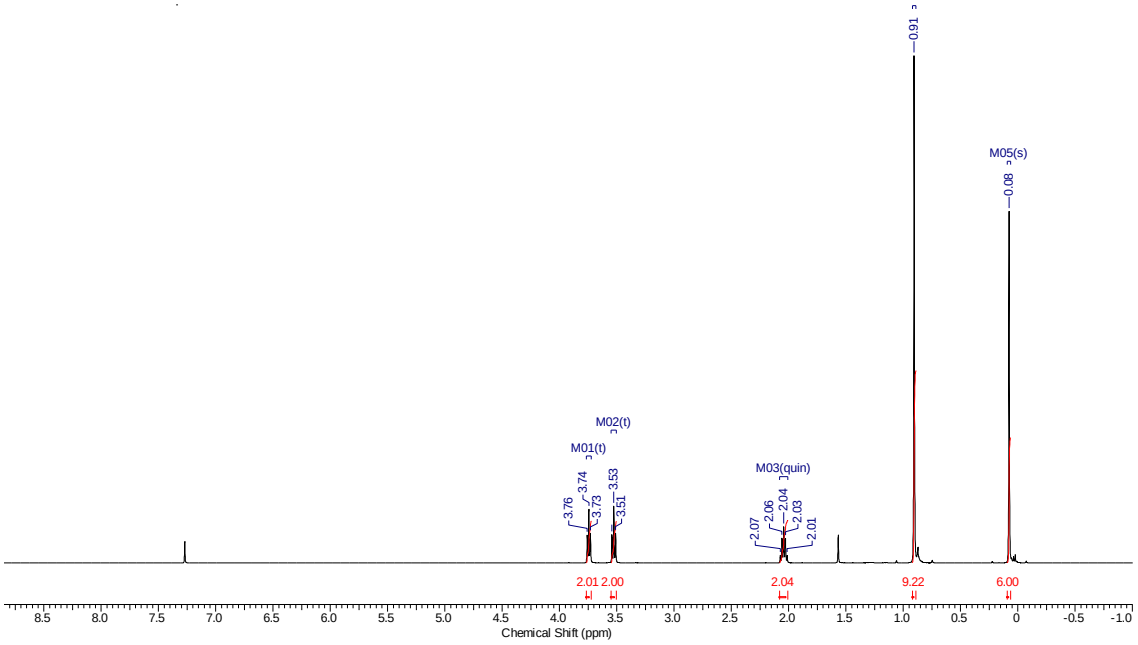
^{13}C NMR (126 MHz, $CDCl_3$)



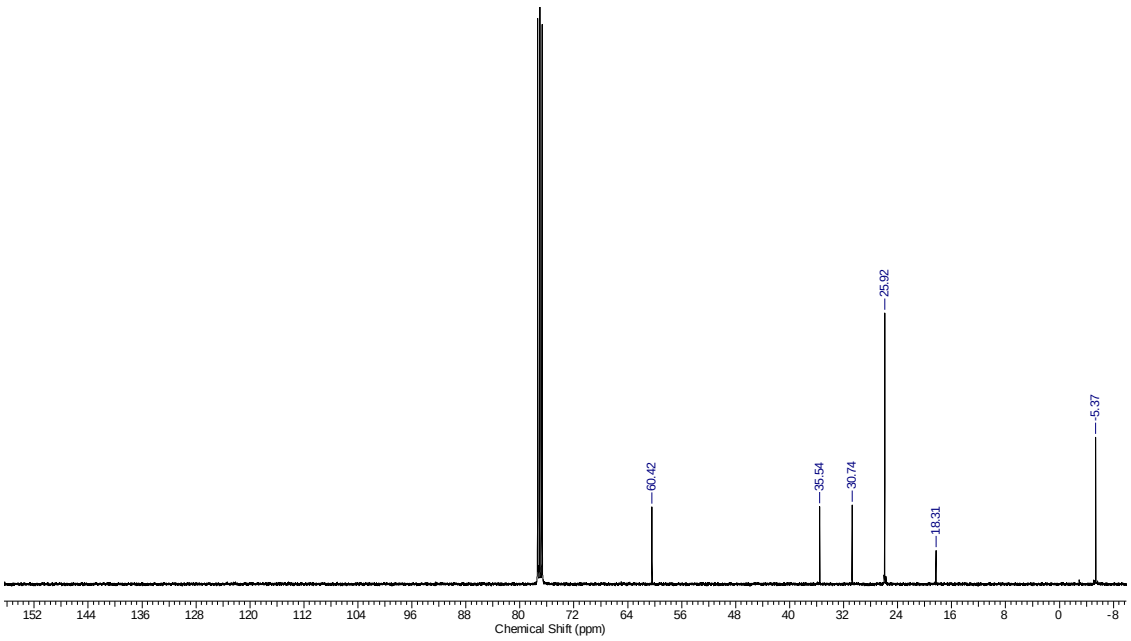


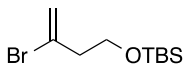
S1

^{1}H NMR (500 MHz, $CDCl_3$)



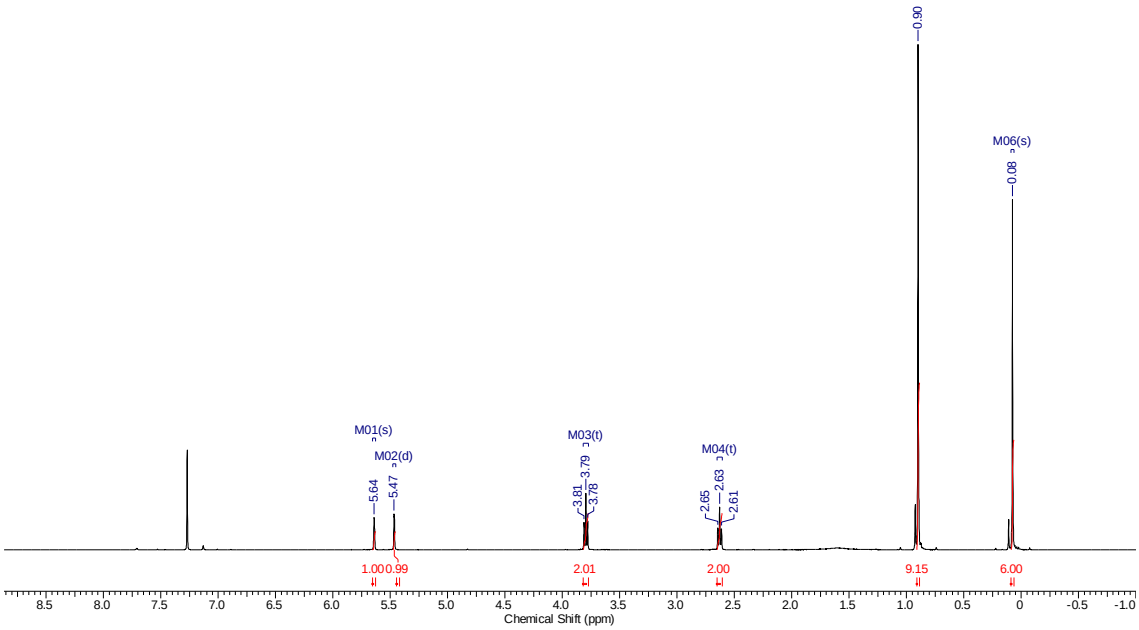
^{13}C NMR (126 MHz, $CDCl_3$)



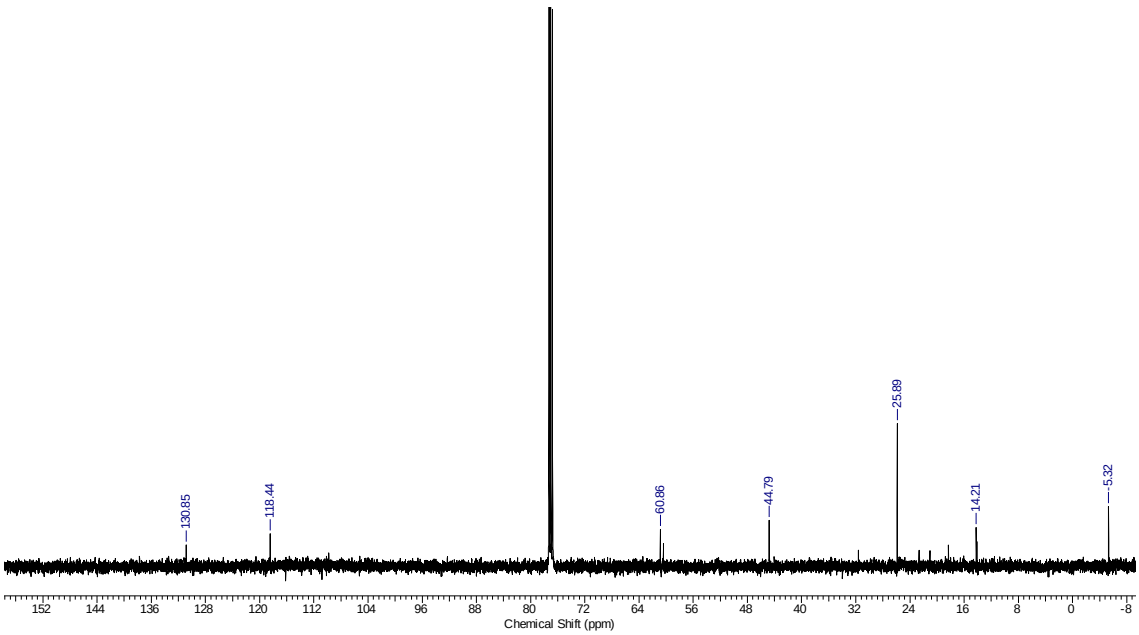


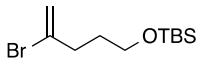
S2

^{1}H NMR (400 MHz, $CDCl_3$)



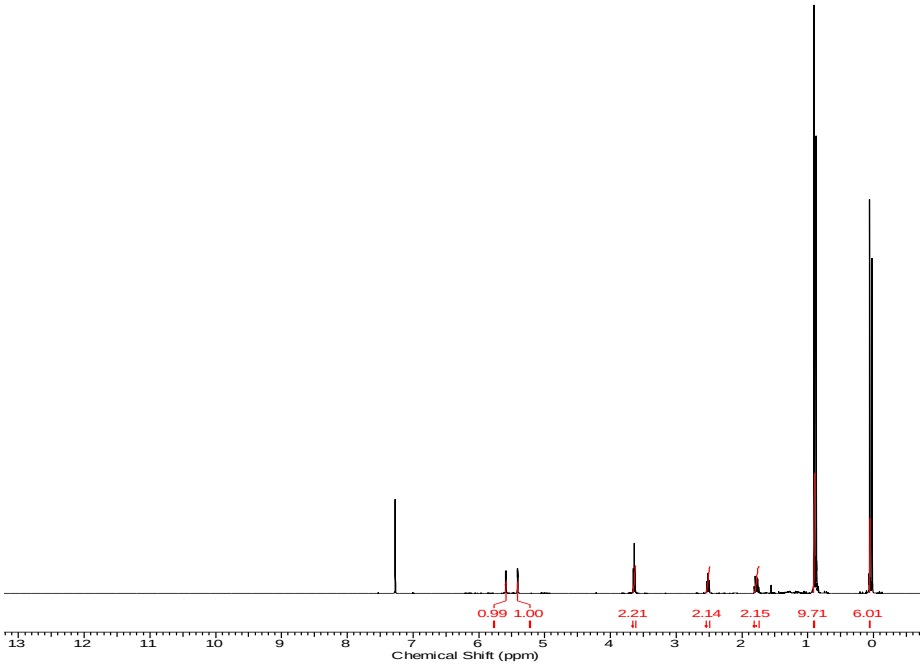
^{13}C NMR (101 MHz, $CDCl_3$)



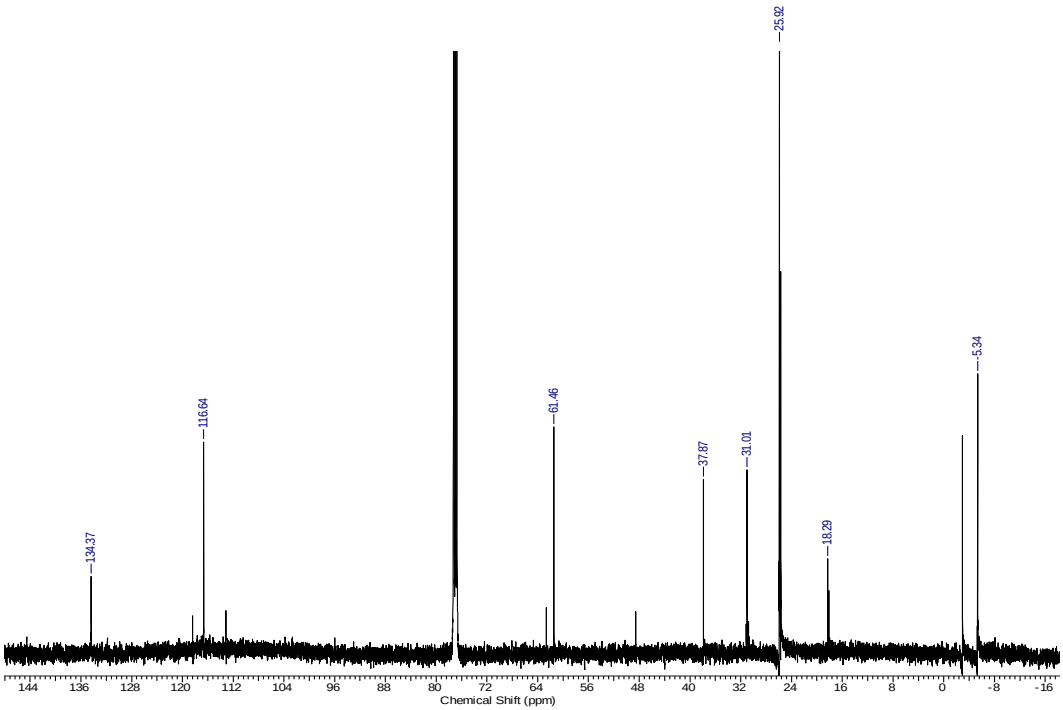


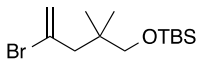
S3

^{1}H NMR (500 MHz, $CDCl_3$)



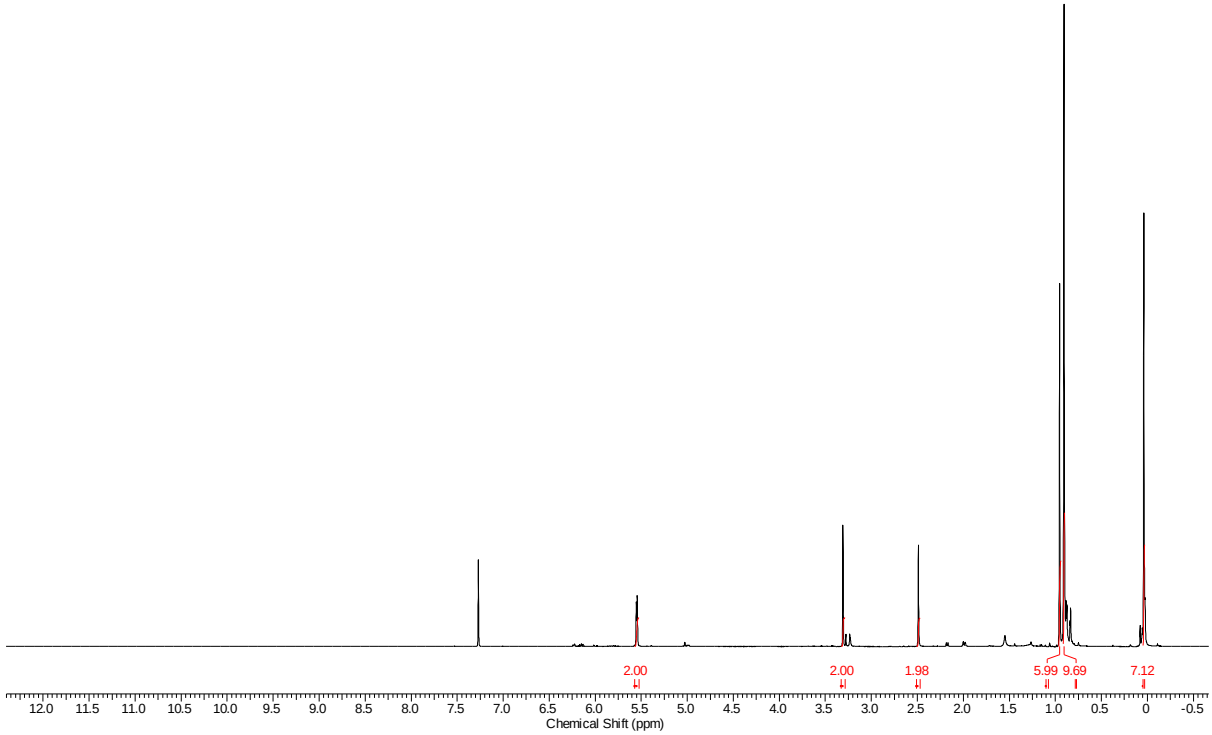
^{13}C NMR (126 MHz, $CDCl_3$)



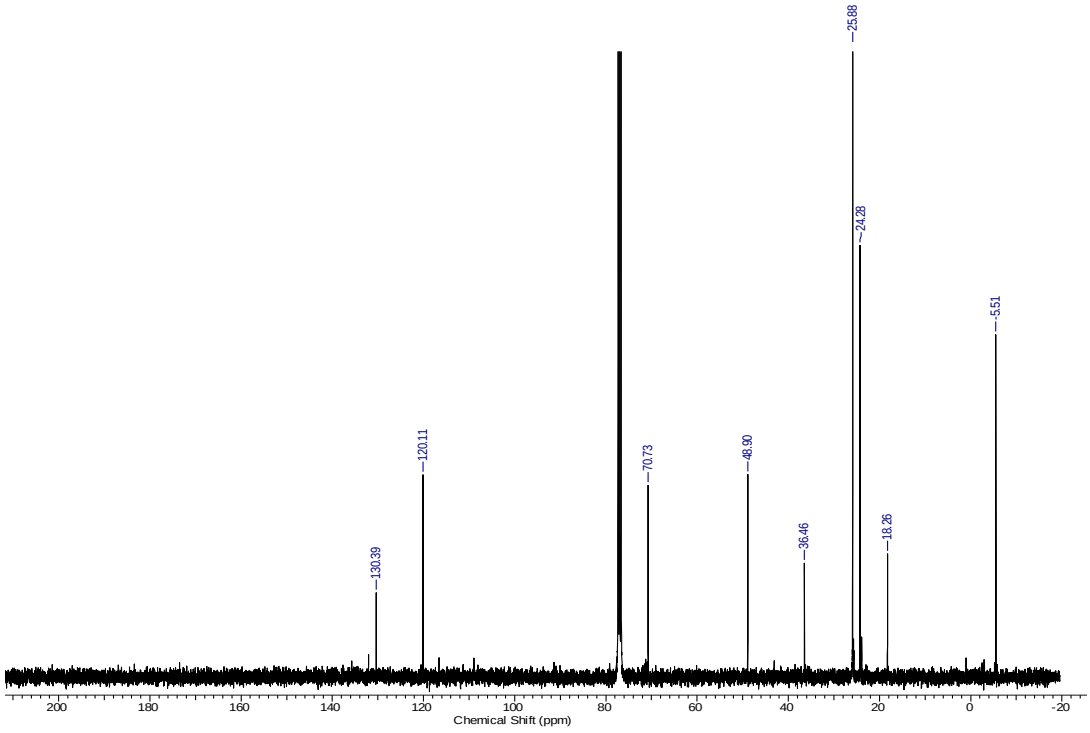


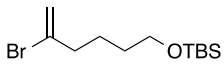
S4

^{1}H NMR (500 MHz, $CDCl_3$)



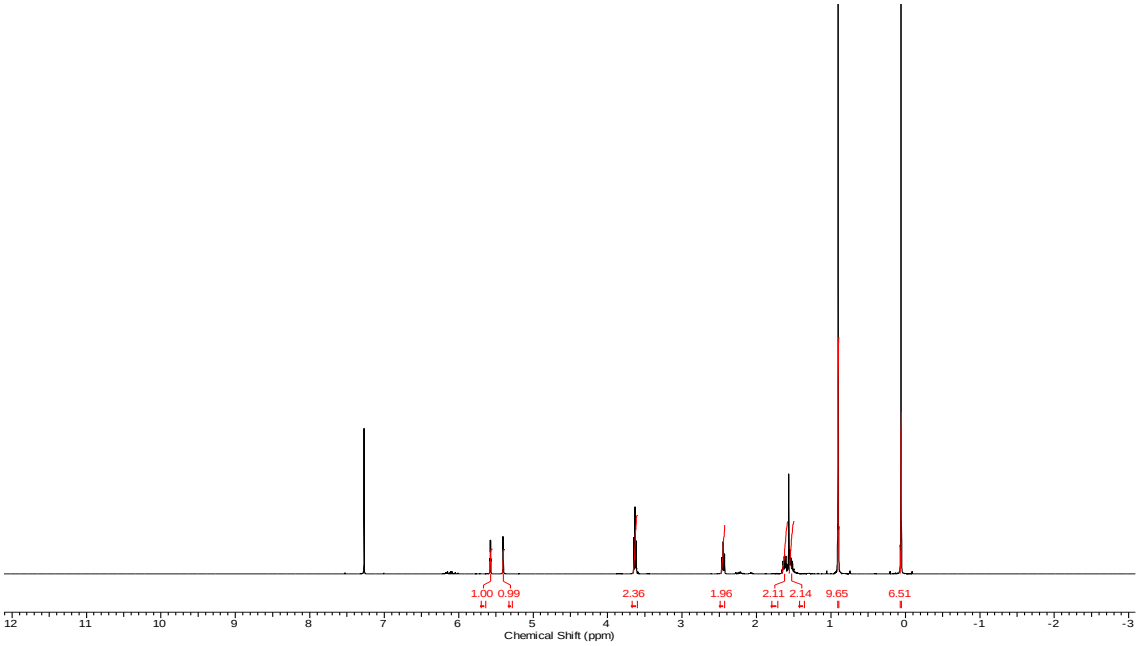
^{13}C NMR (126 MHz, $CDCl_3$)



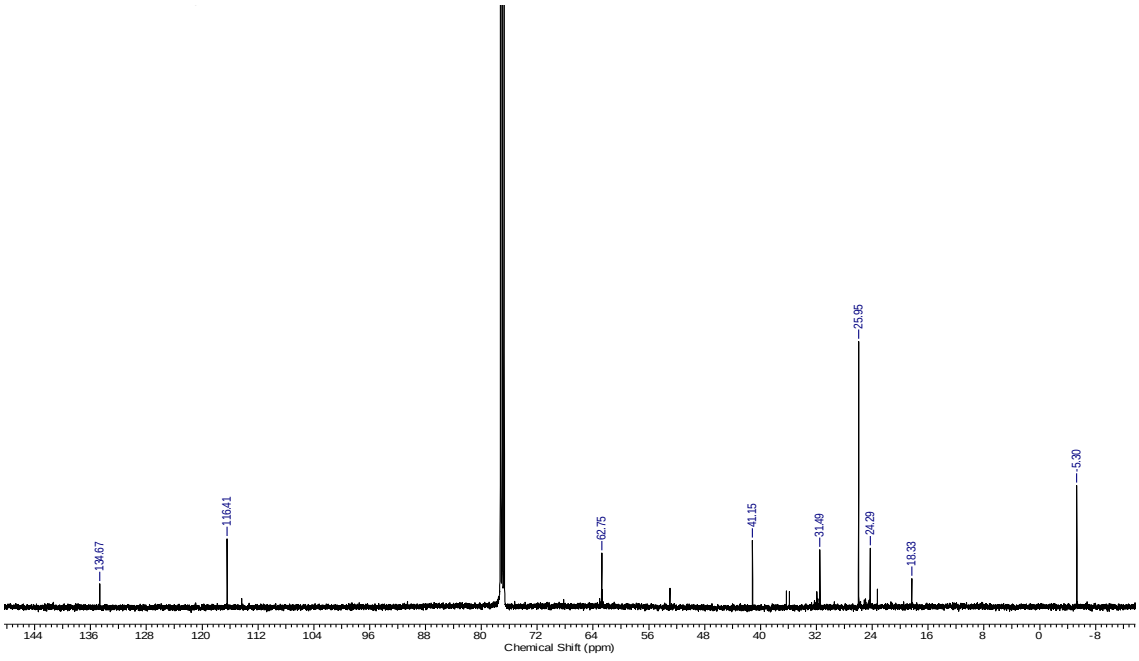


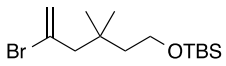
S5

^{1}H NMR (400 MHz, $CDCl_3$)



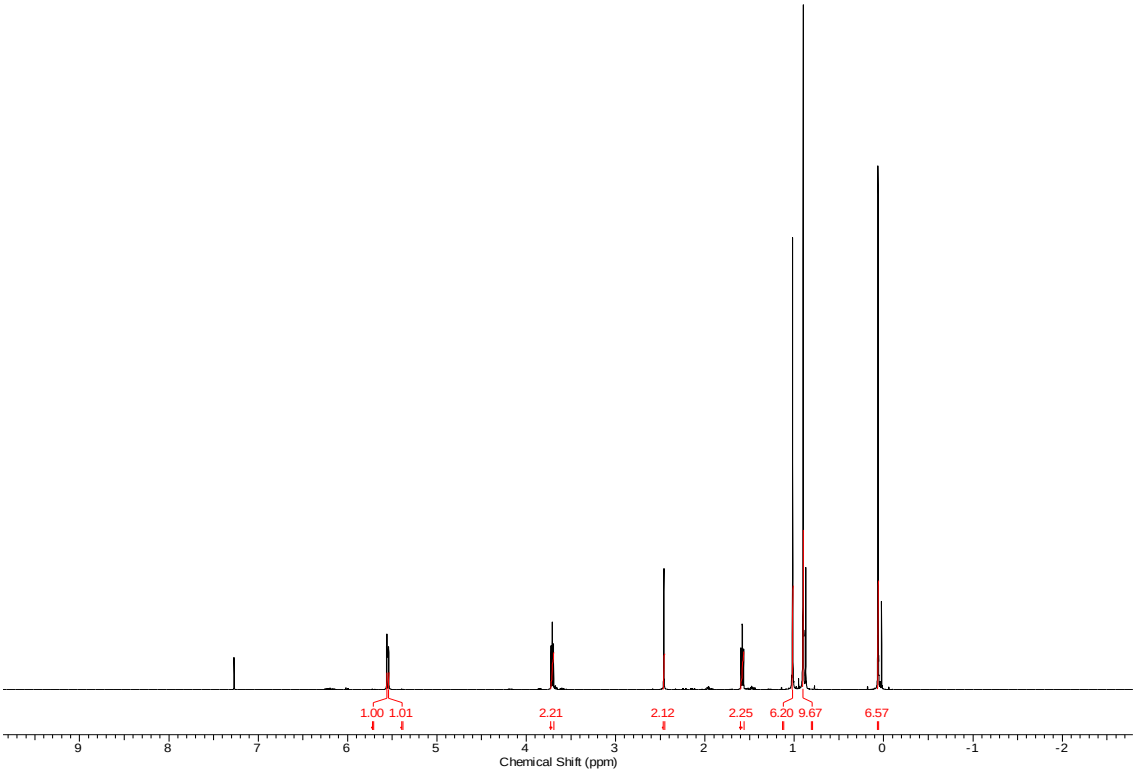
^{13}C NMR (126 MHz, $CDCl_3$)



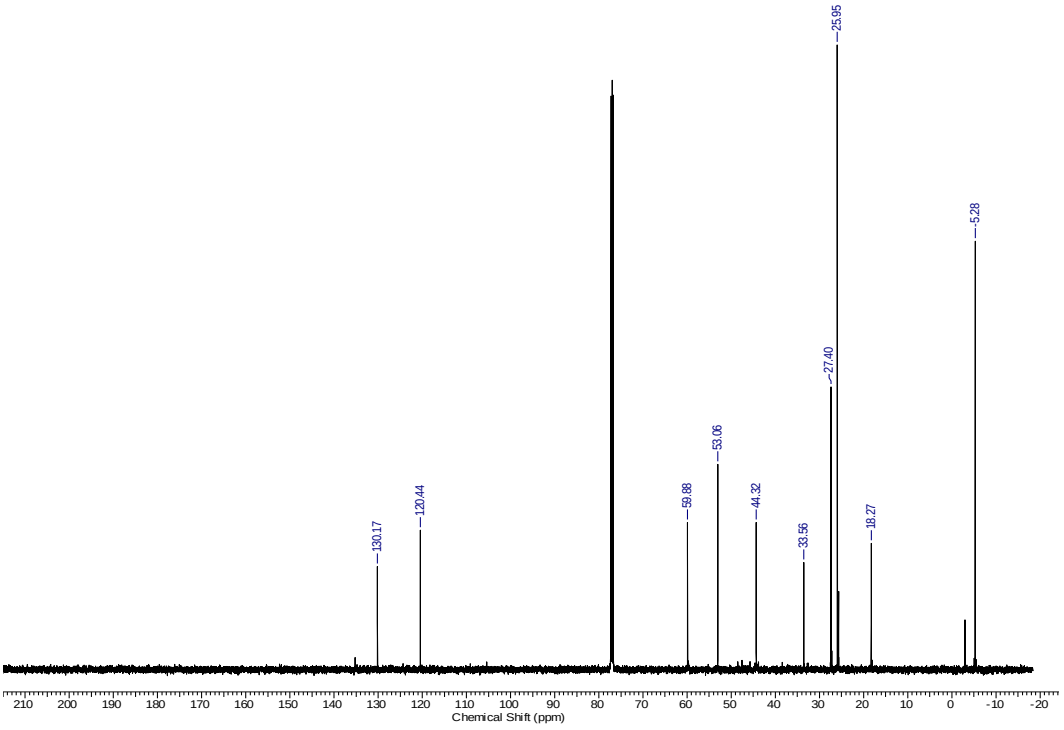


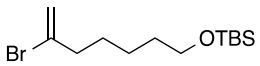
S6

^{1}H NMR (400 MHz, $CDCl_3$)



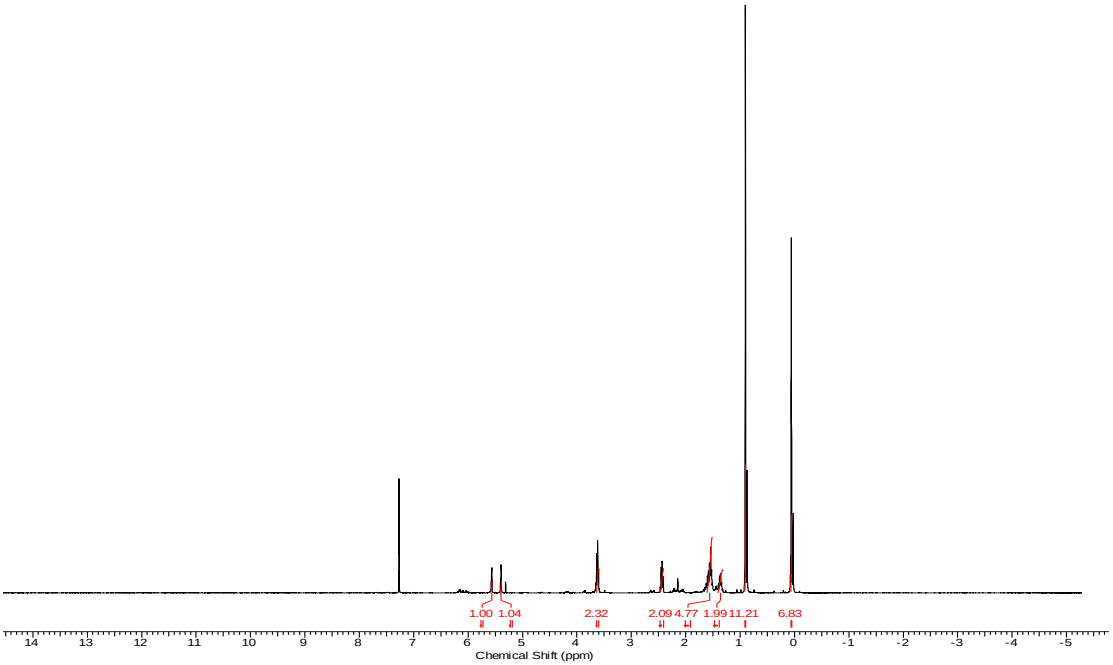
^{13}C NMR (126 MHz, $CDCl_3$)



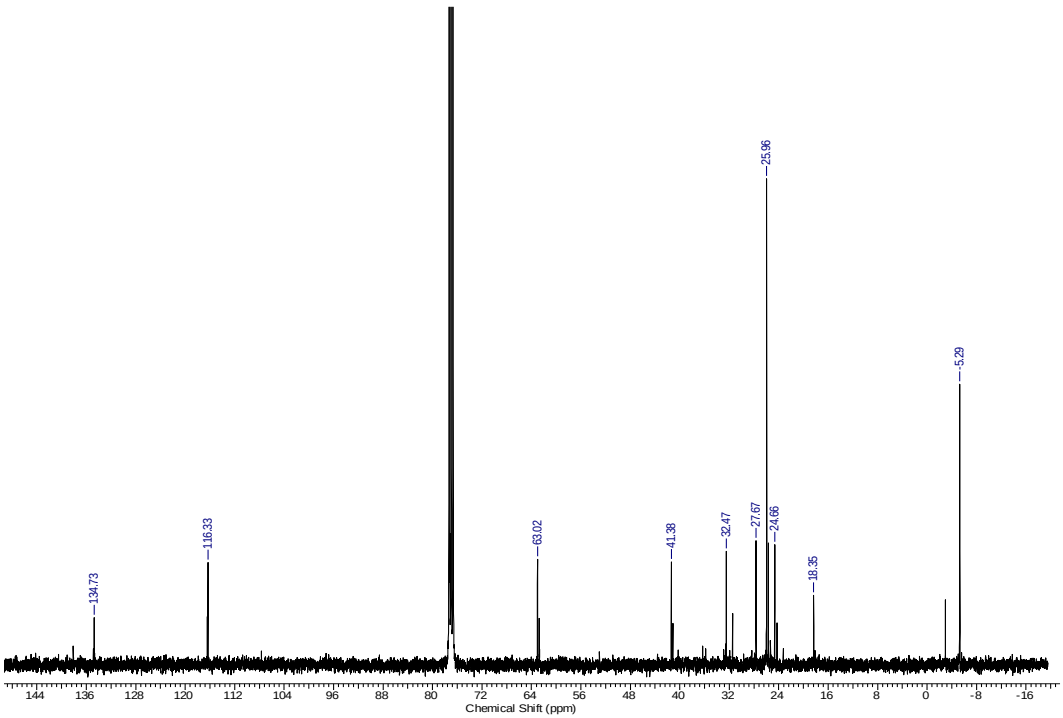


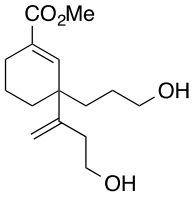
S7

^{1}H NMR (500 MHz, $CDCl_3$)



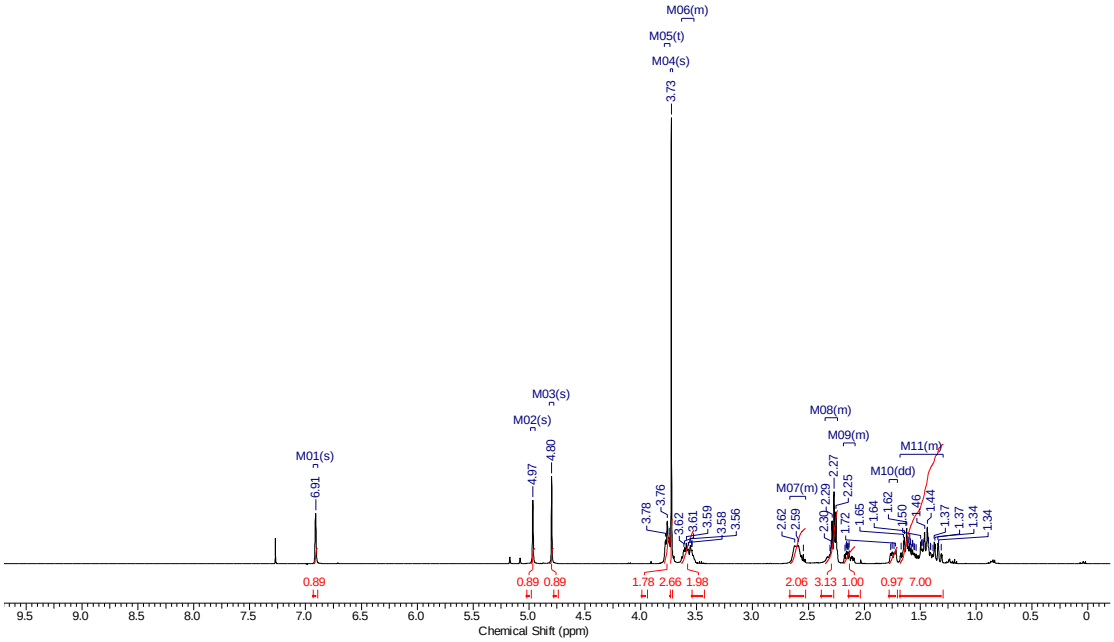
^{13}C NMR (126 MHz, $CDCl_3$)



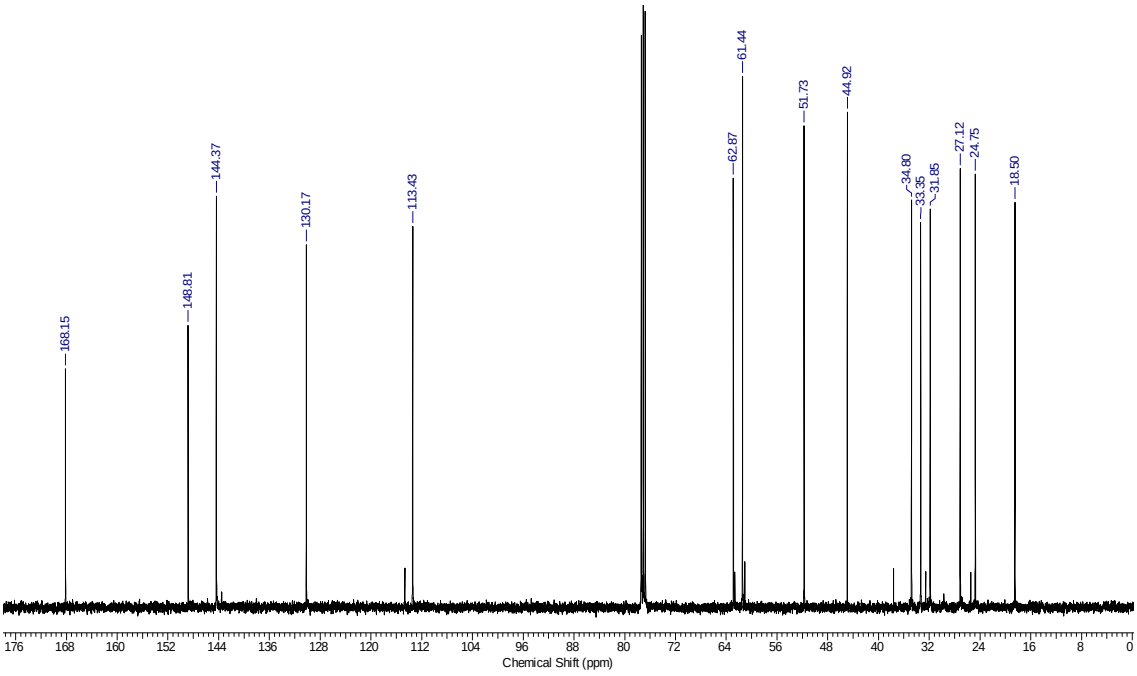


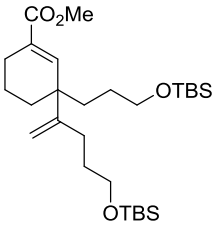
6a

^{1}H NMR (500 MHz, $CDCl_3$)



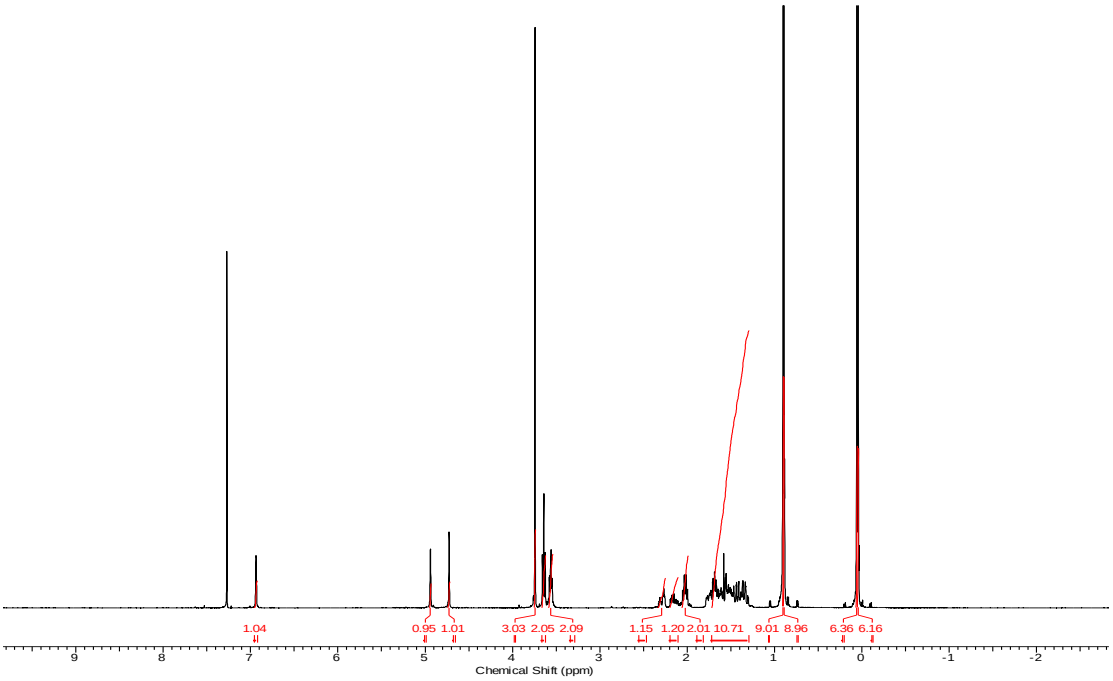
^{13}C NMR (126 MHz, $CDCl_3$)



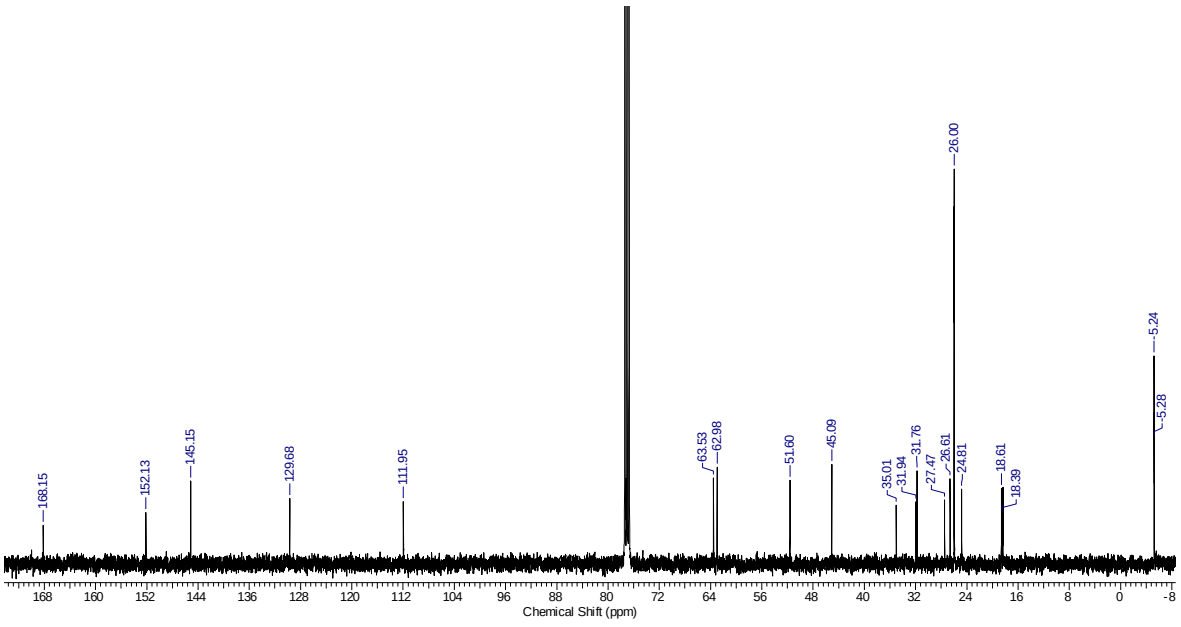


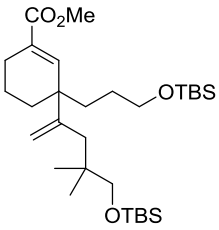
6b

^{1}H NMR (400 MHz, $CDCl_3$)



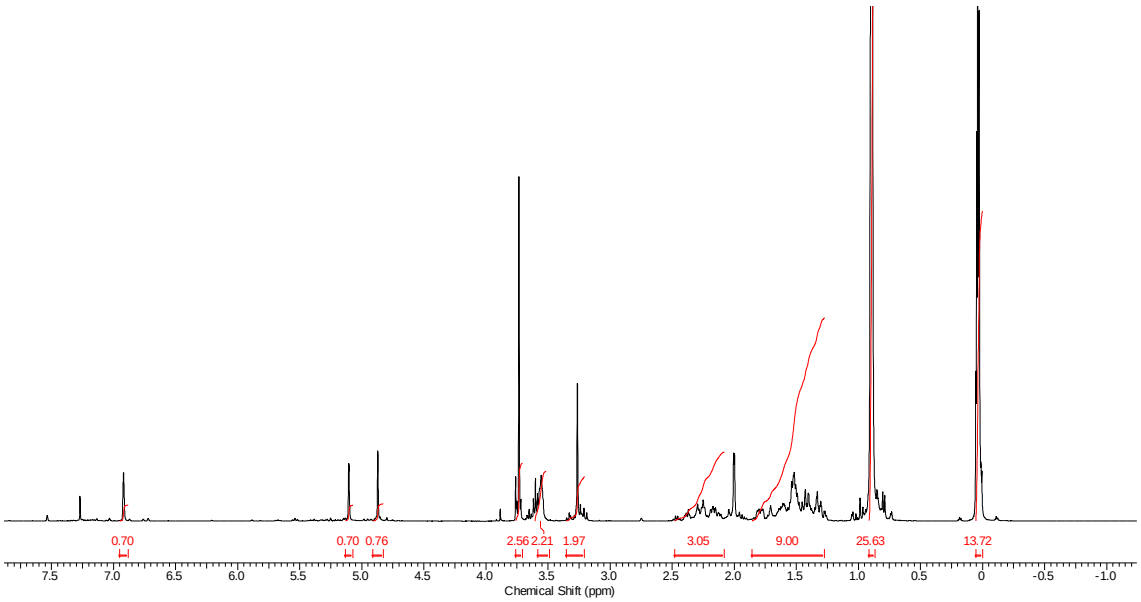
^{13}C NMR (126 MHz, $CDCl_3$)



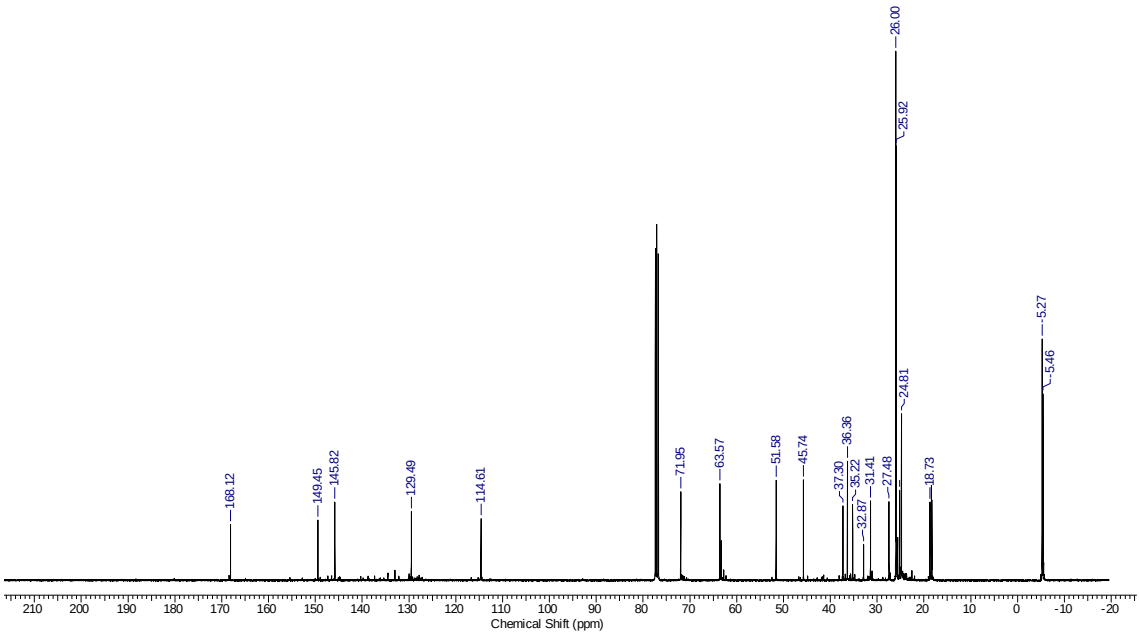


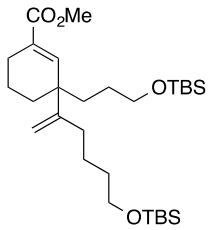
6c

^{1}H NMR (400 MHz, $CDCl_3$)



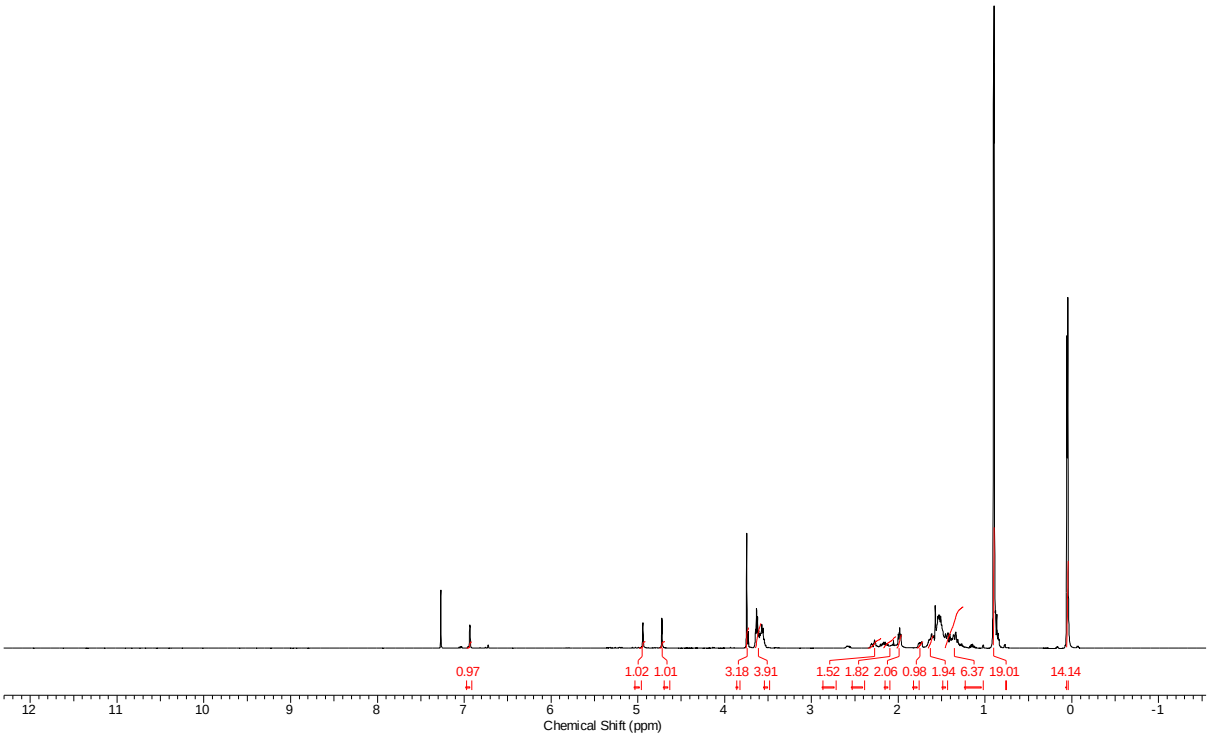
^{13}C NMR (126 MHz, $CDCl_3$)



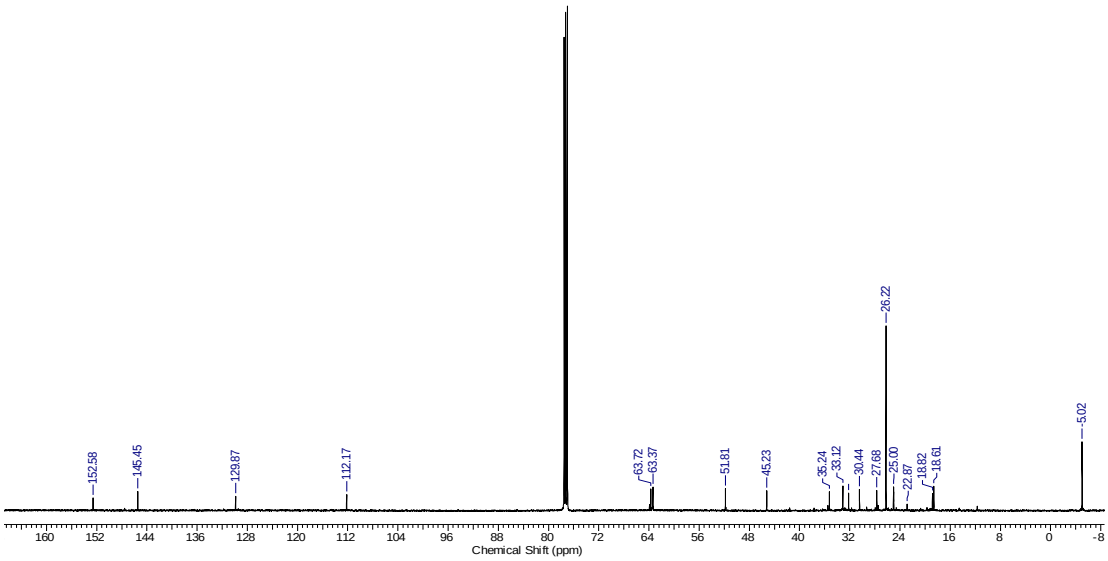


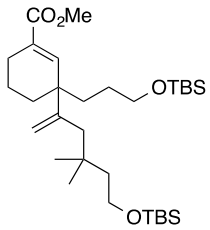
6e

^{1}H NMR (500 MHz, $CDCl_3$)



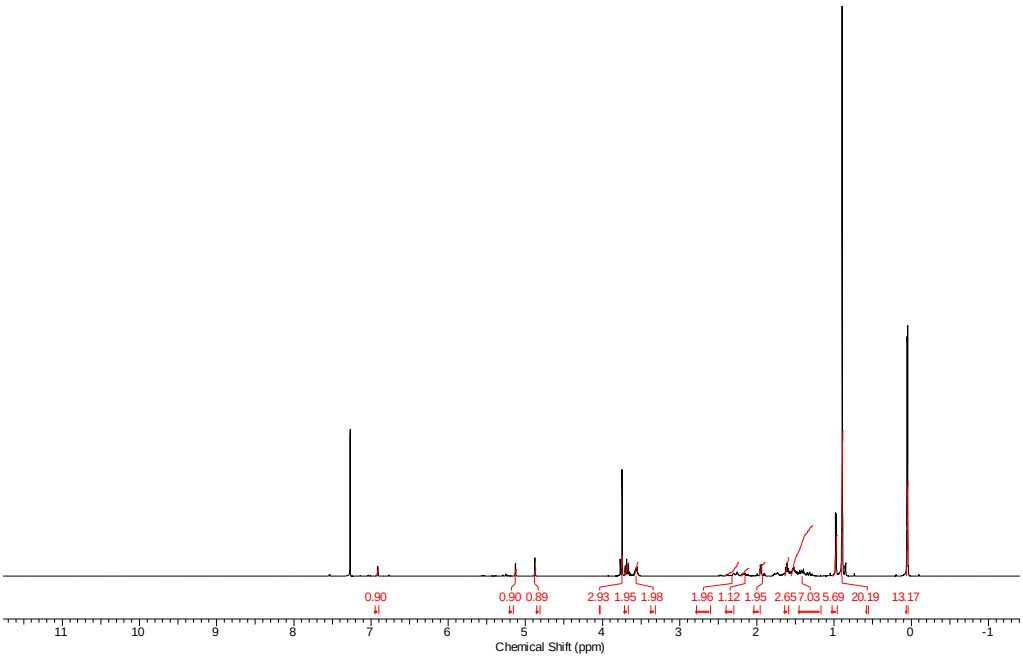
^{13}C NMR (126 MHz, $CDCl_3$)



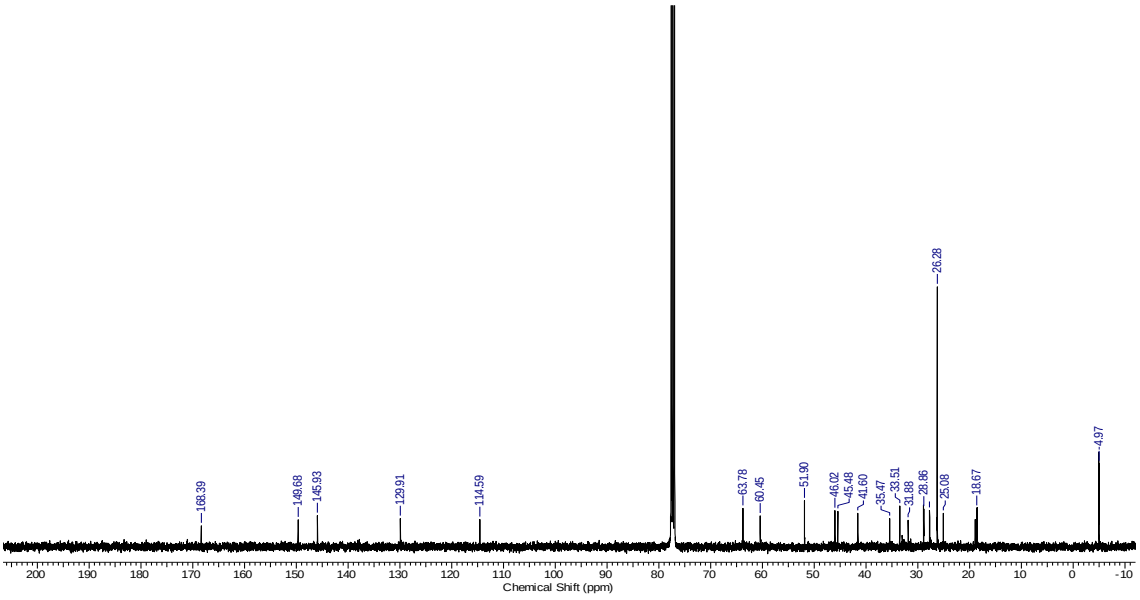


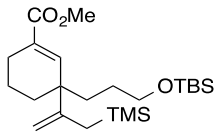
6d

^{1}H NMR (400 MHz, $CDCl_3$)



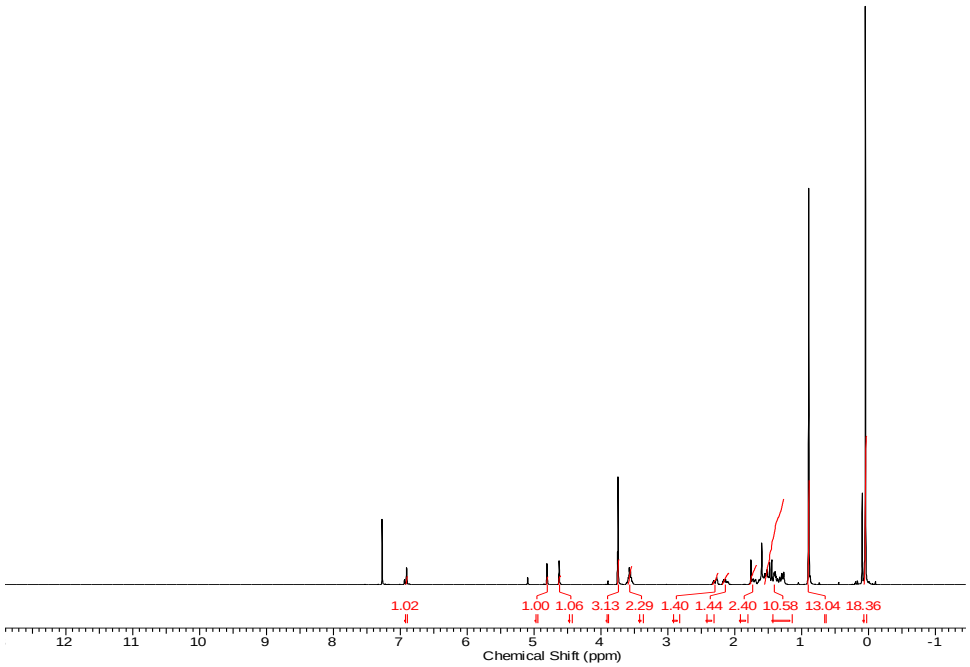
^{13}C NMR (101 MHz, $CDCl_3$)



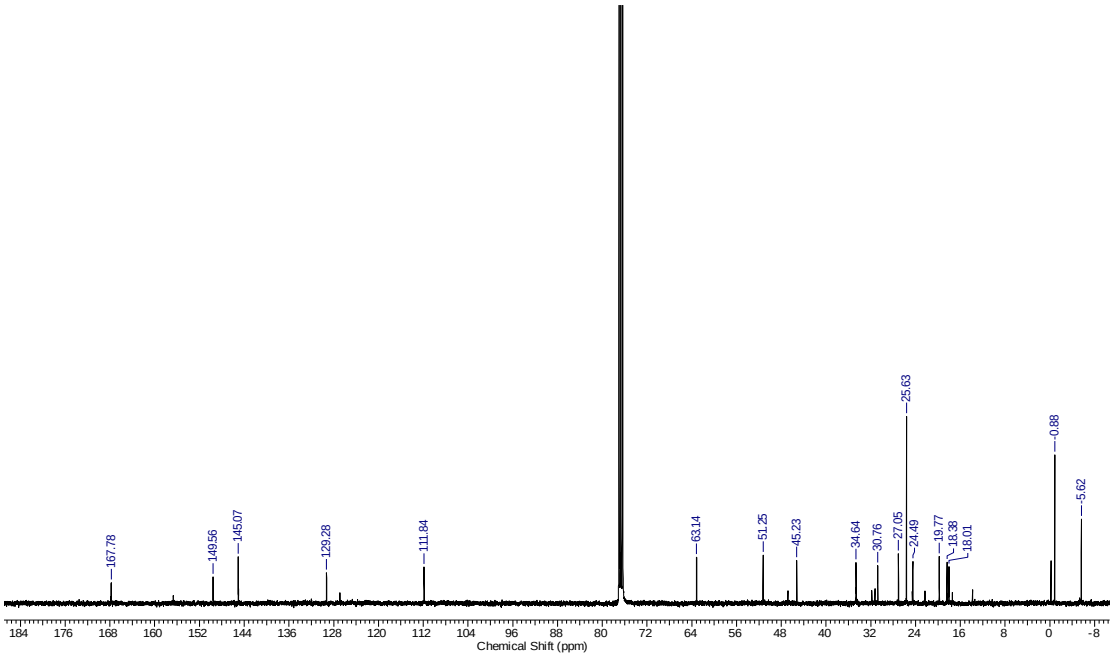


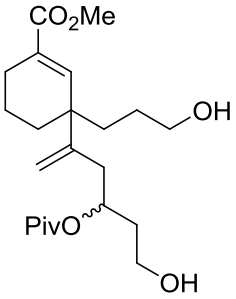
6g

^{1}H NMR (400 MHz, $CDCl_3$)



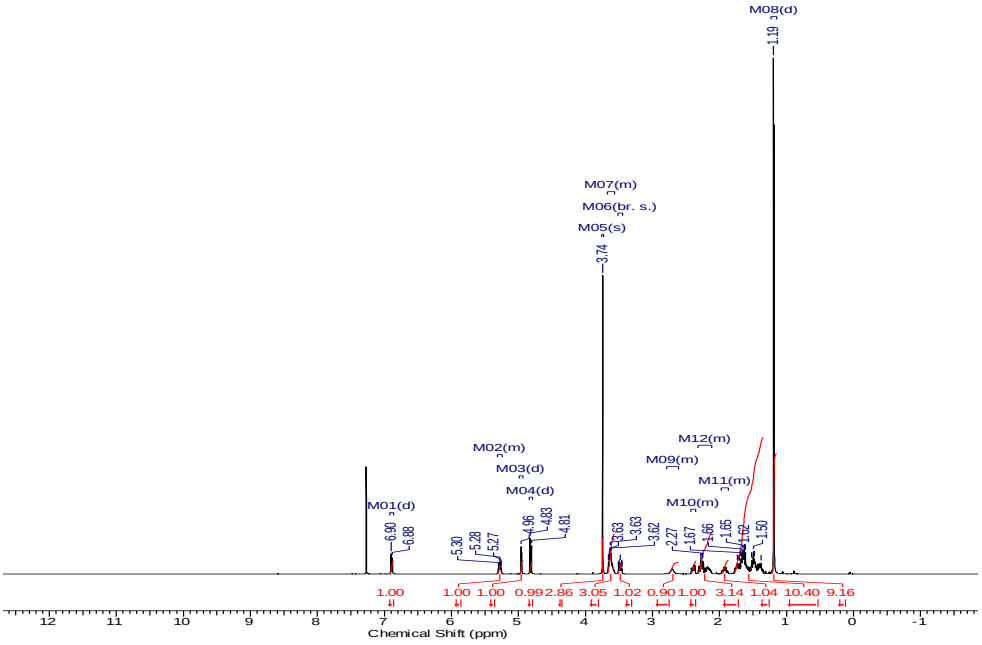
^{13}C NMR (101 MHz, $CDCl_3$)



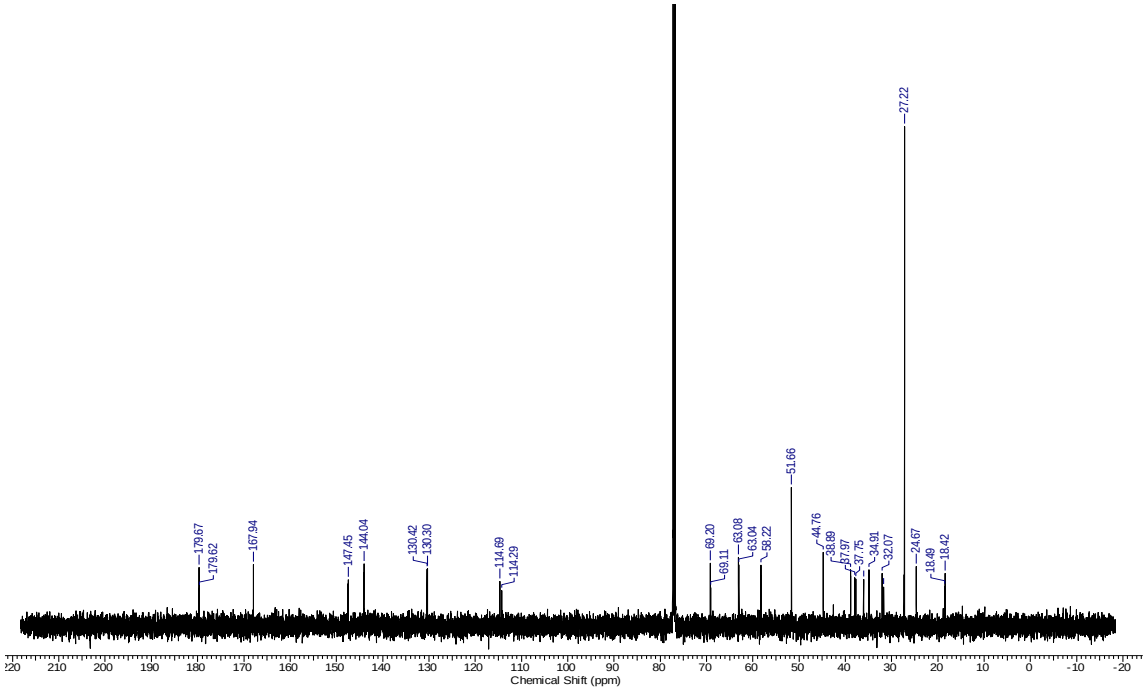


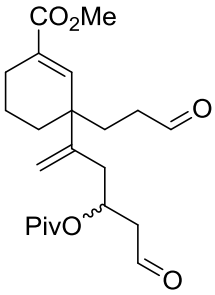
S25

^{1}H NMR (400 MHz, $CDCl_3$)



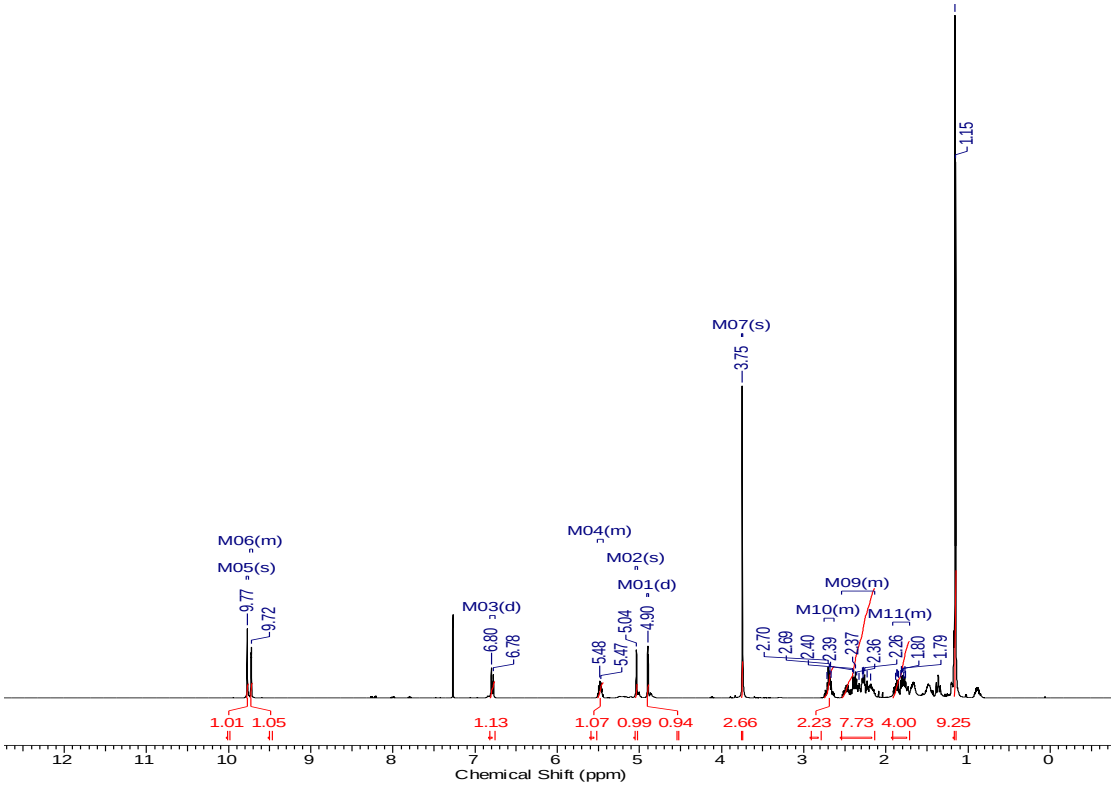
^{13}C NMR (101 MHz, $CDCl_3$)



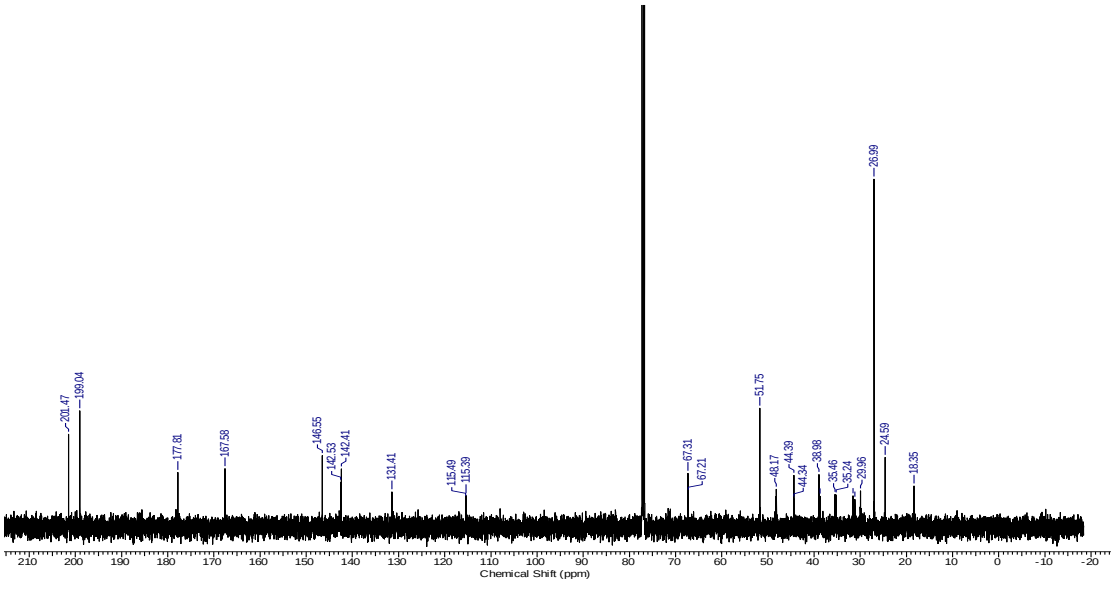


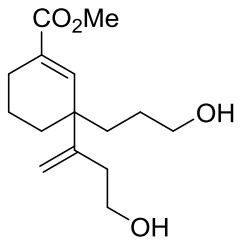
9

^{1}H NMR (400 MHz, $CDCl_3$)



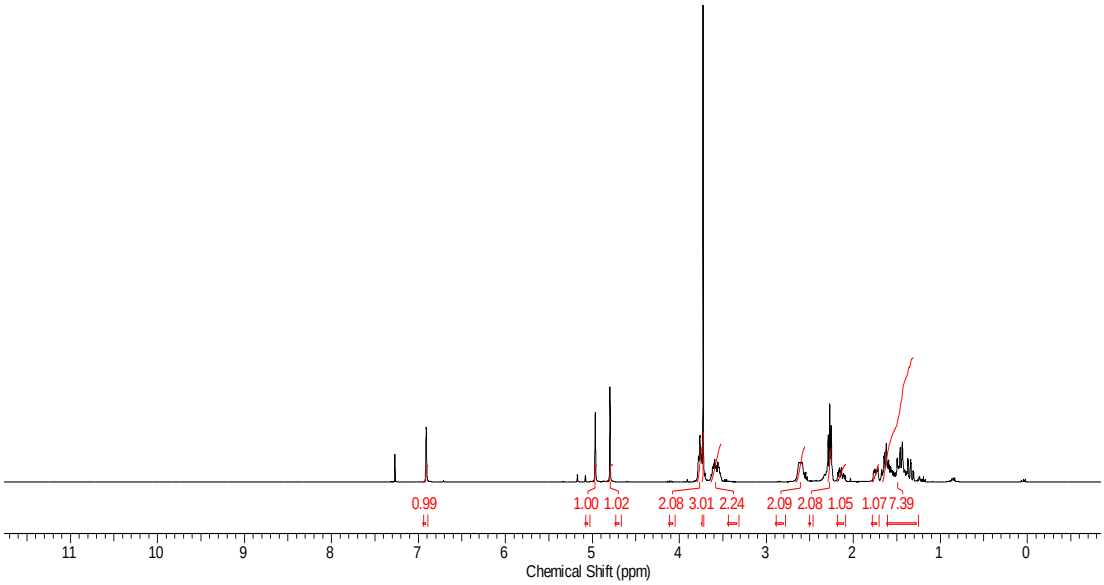
^{13}C NMR (101 MHz, $CDCl_3$)



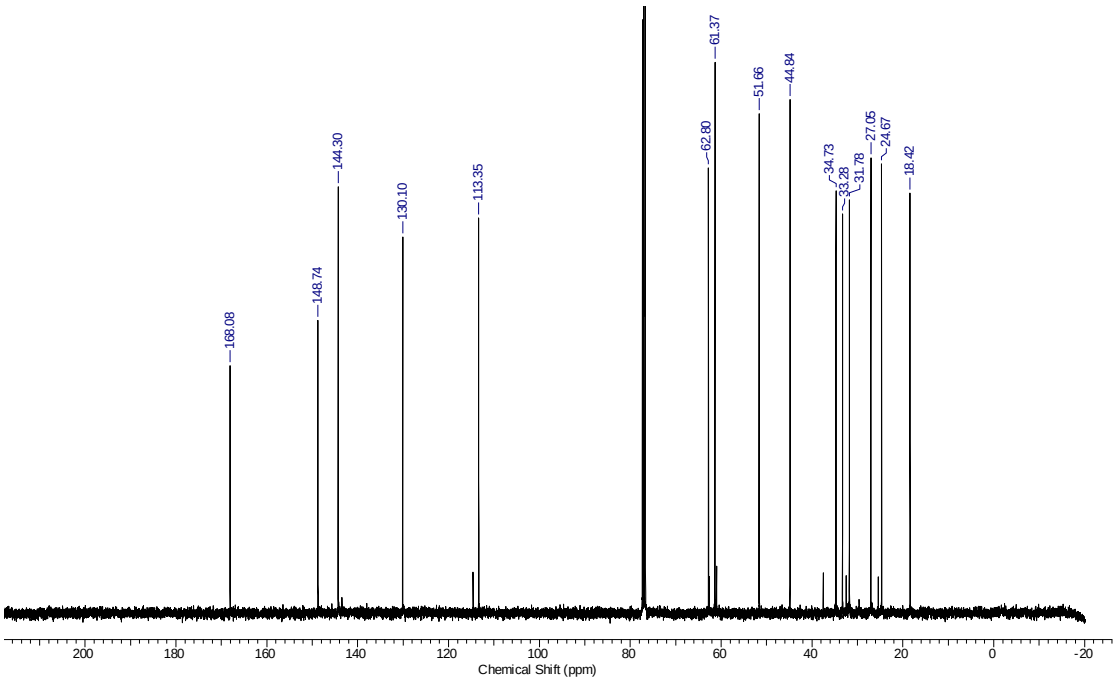


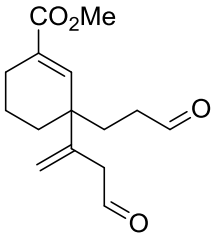
S26

^{1}H NMR (400 MHz, $CDCl_3$)



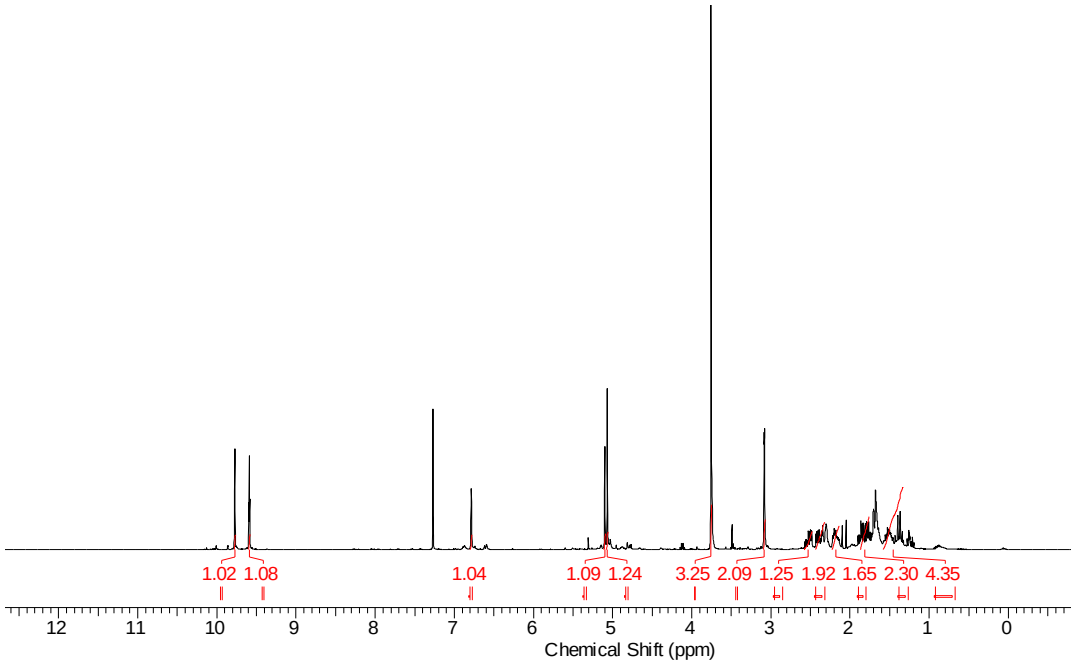
^{13}C NMR (101 MHz, $CDCl_3$)



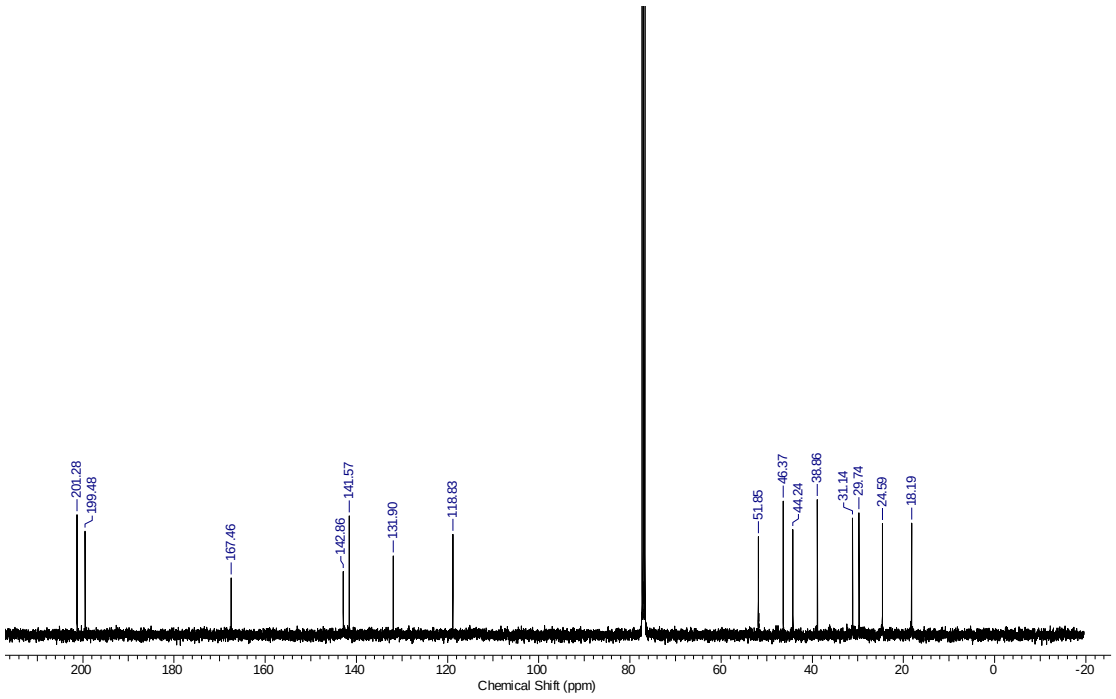


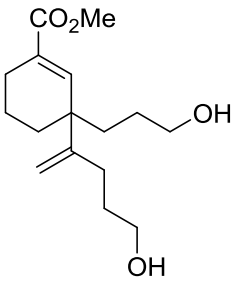
7a

^{1}H NMR (400 MHz, $CDCl_3$)



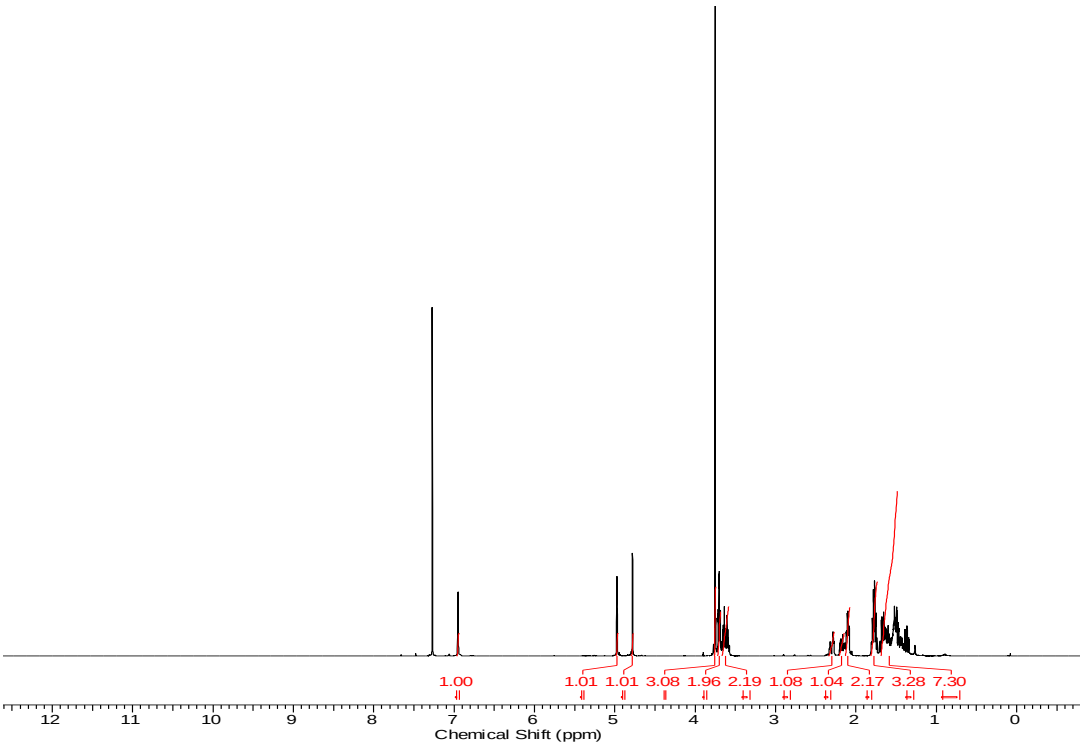
^{13}C NMR (101 MHz, $CDCl_3$)



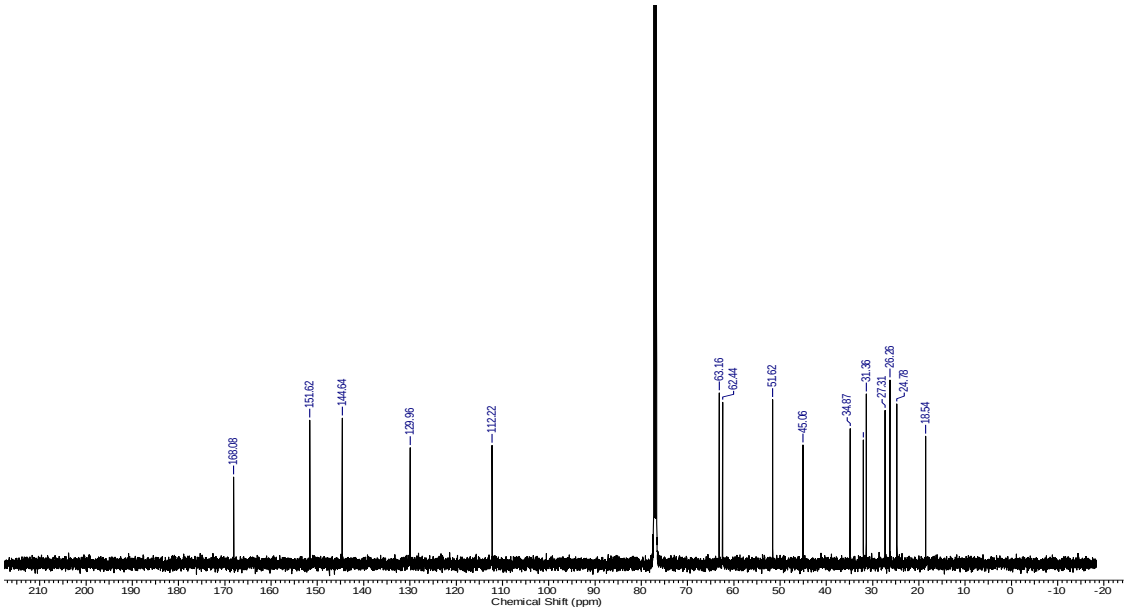


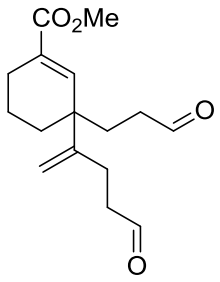
S27

^{1}H NMR (400 MHz, $CDCl_3$)



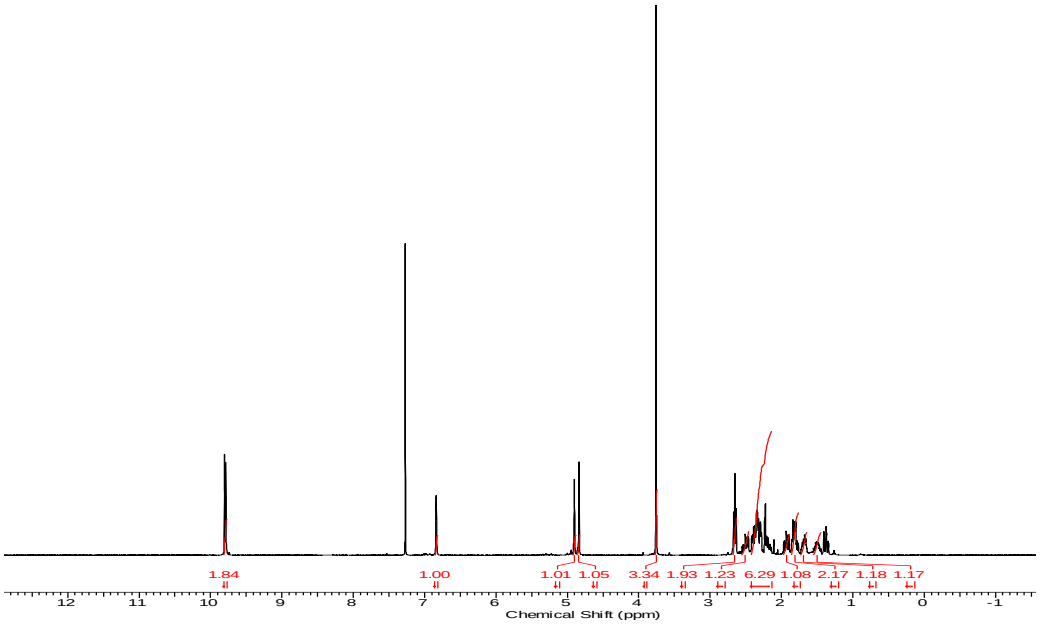
^{13}C NMR (101 MHz, $CDCl_3$)



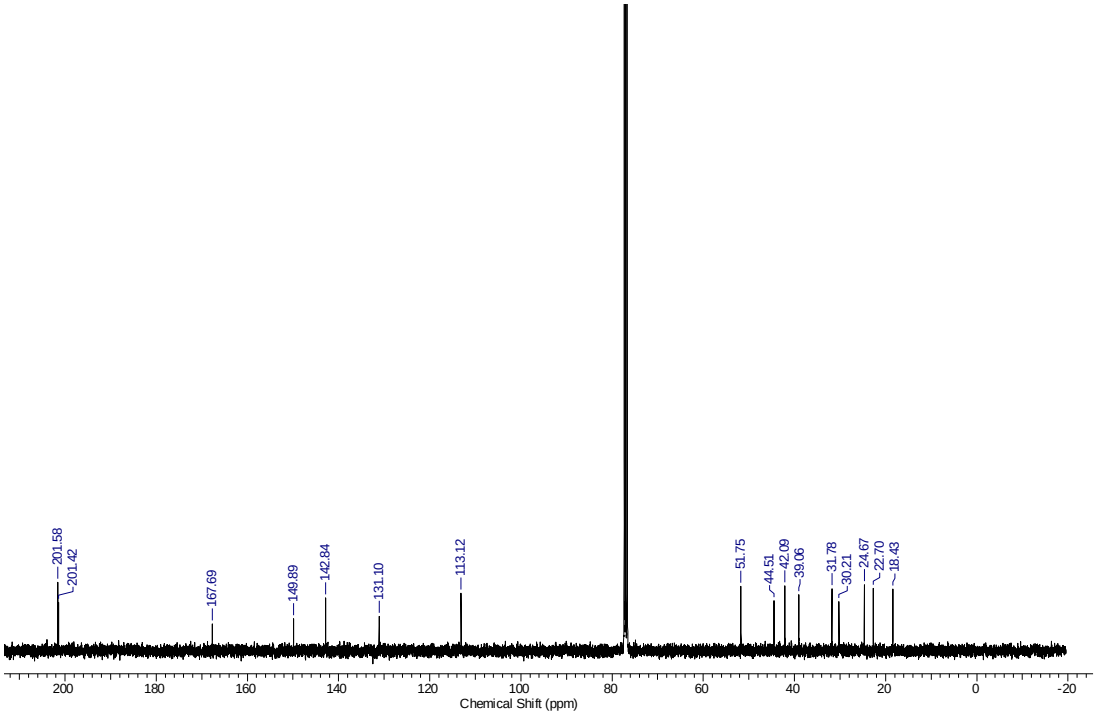


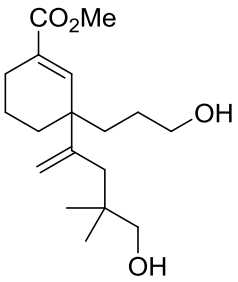
7b

^{1}H NMR (400 MHz, $CDCl_3$)



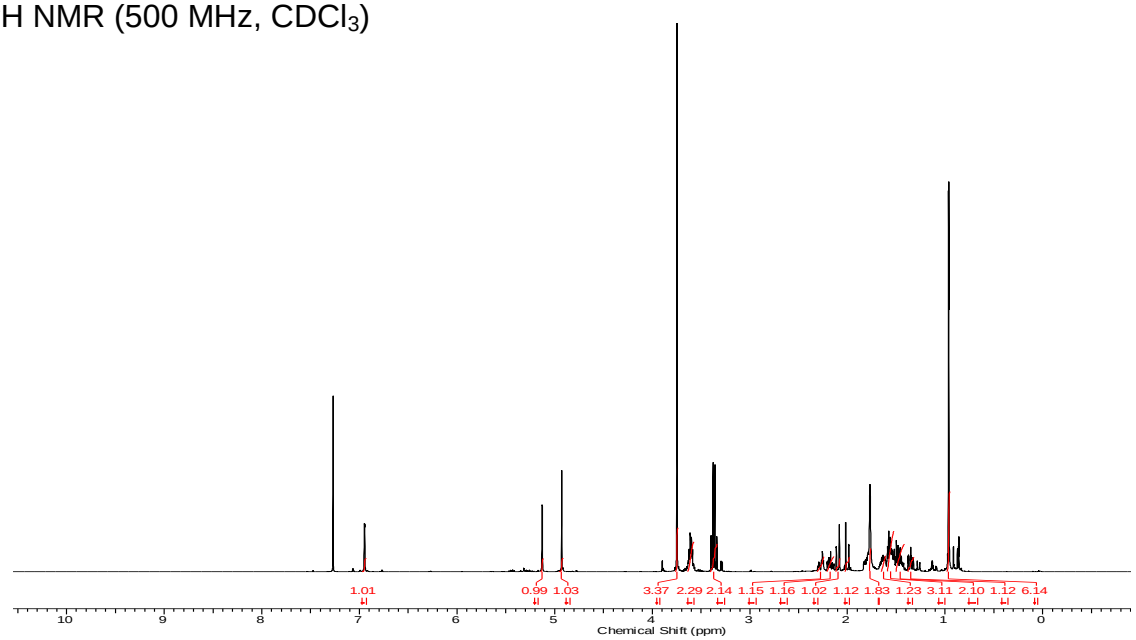
^{13}C NMR (101 MHz, $CDCl_3$)



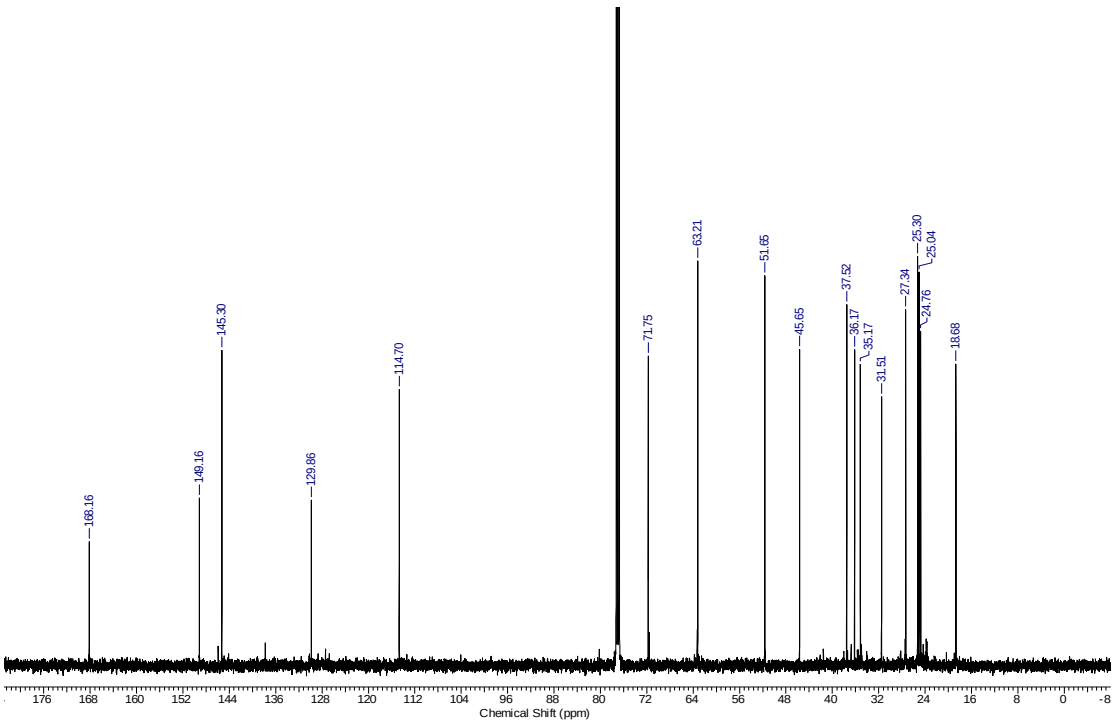


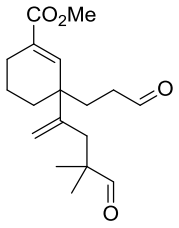
S28

^{1}H NMR (500 MHz, $CDCl_3$)



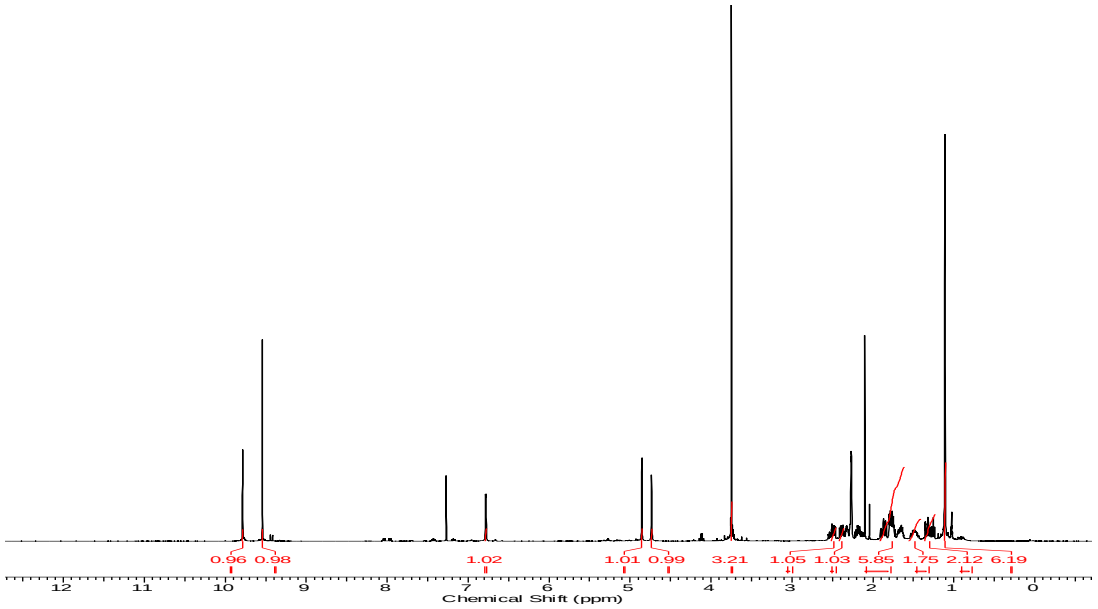
^{13}C NMR (126 MHz, $CDCl_3$)



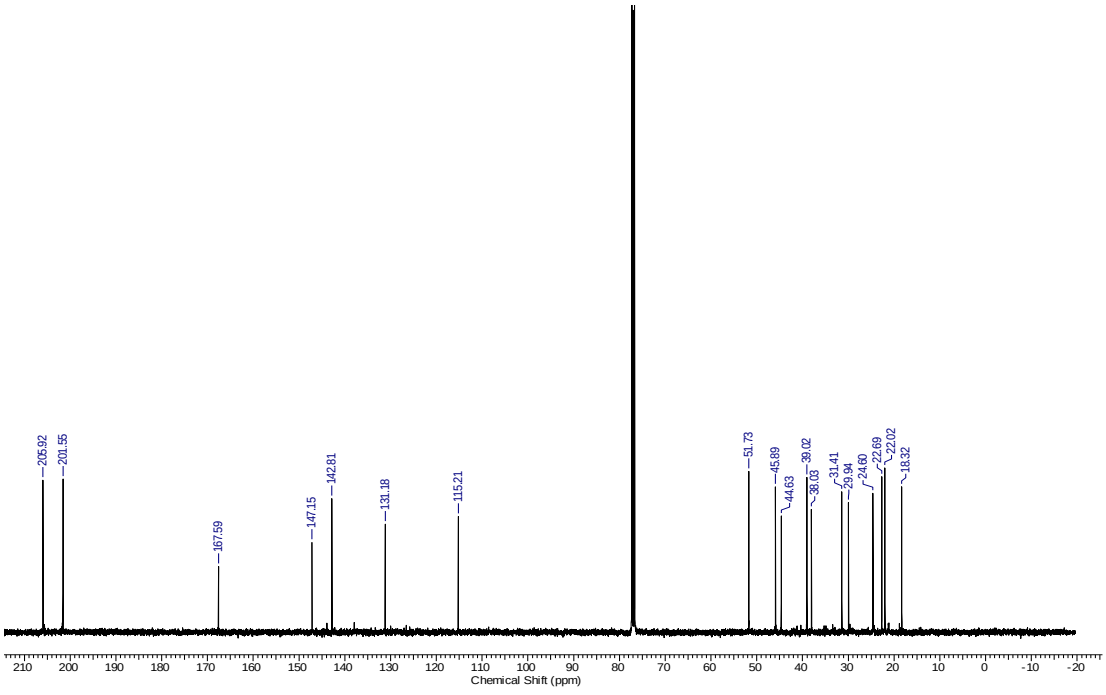


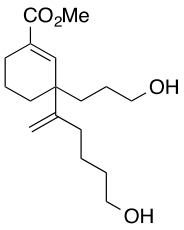
7c

^{1}H NMR (400 MHz, $CDCl_3$)



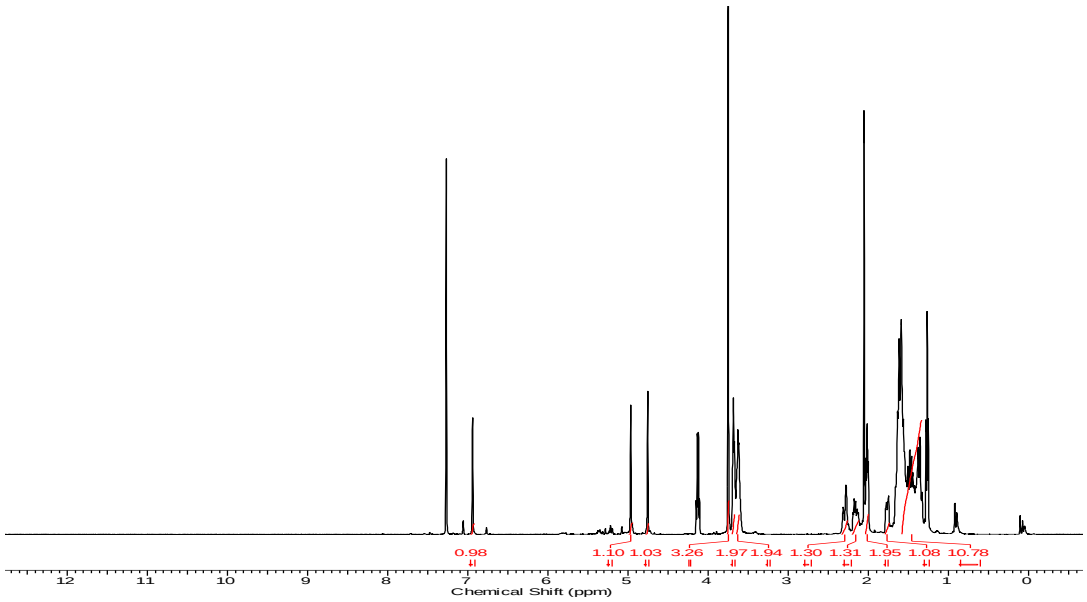
^{13}C NMR (101 MHz, $CDCl_3$)



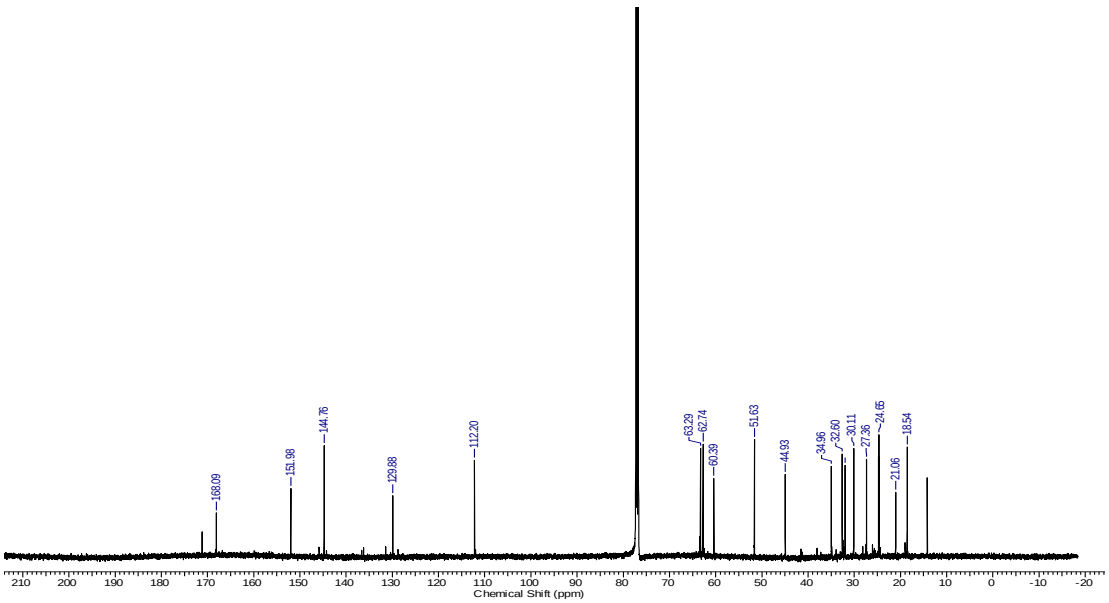


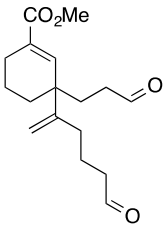
S29

^{1}H NMR (400 MHz, $CDCl_3$)



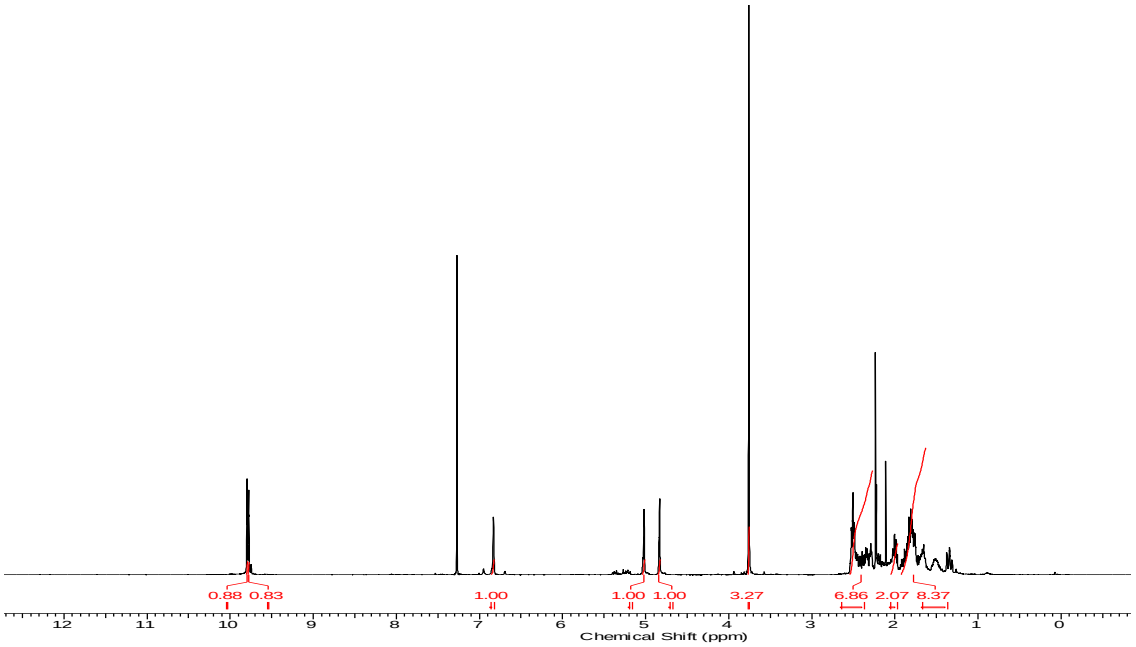
^{13}C NMR (101 MHz, $CDCl_3$)



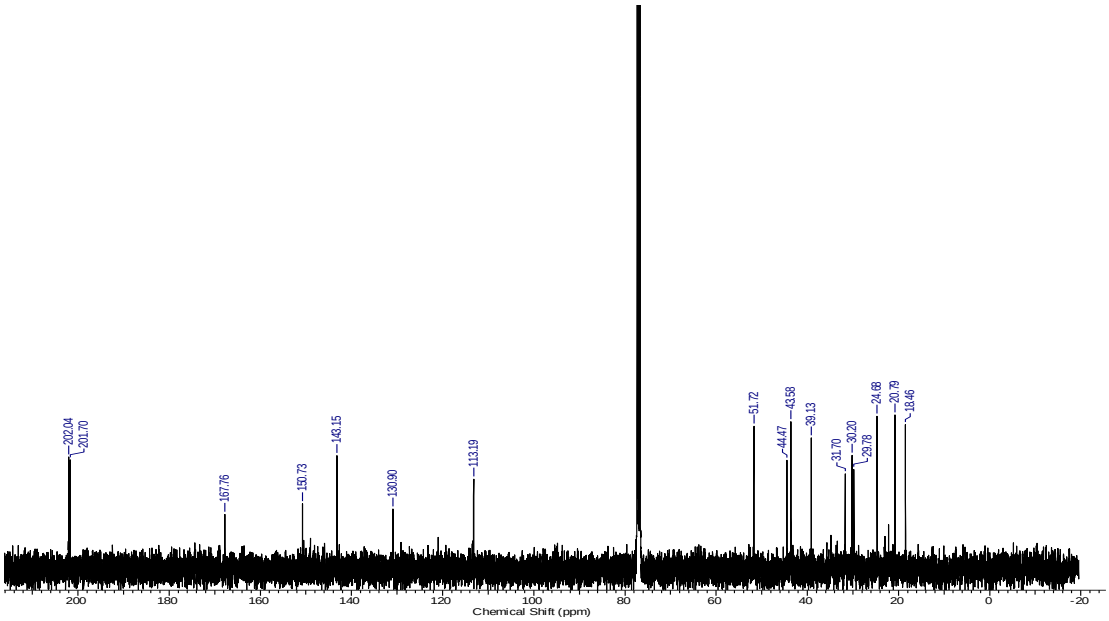


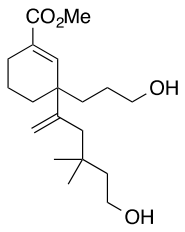
7e

^{1}H NMR (400 MHz, $CDCl_3$)



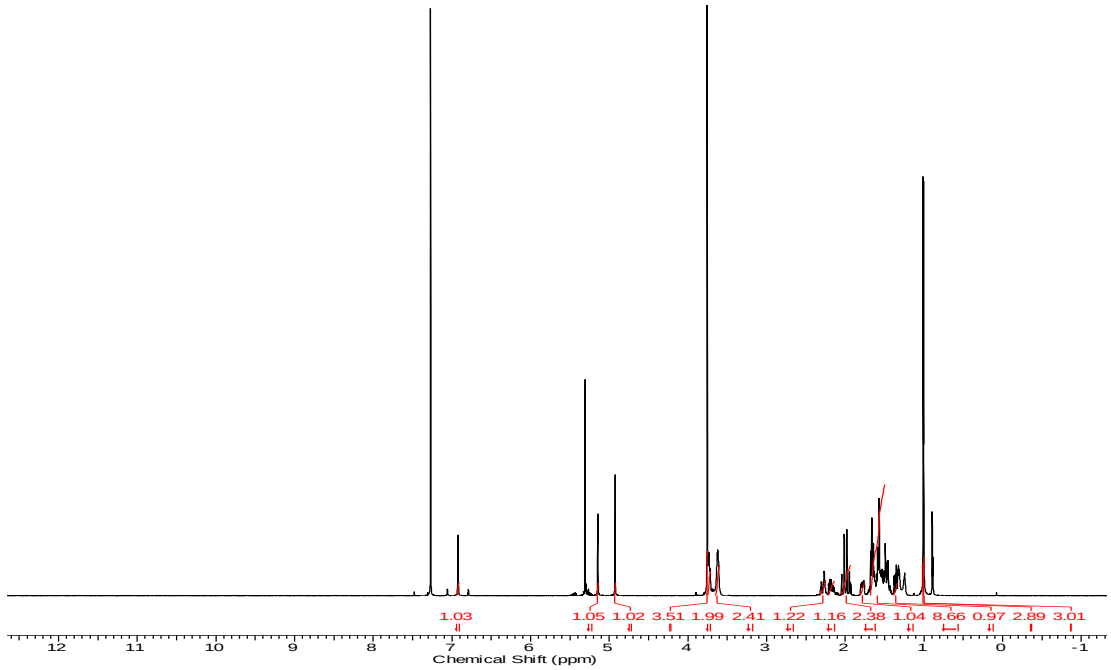
^{13}C NMR (101 MHz, $CDCl_3$)



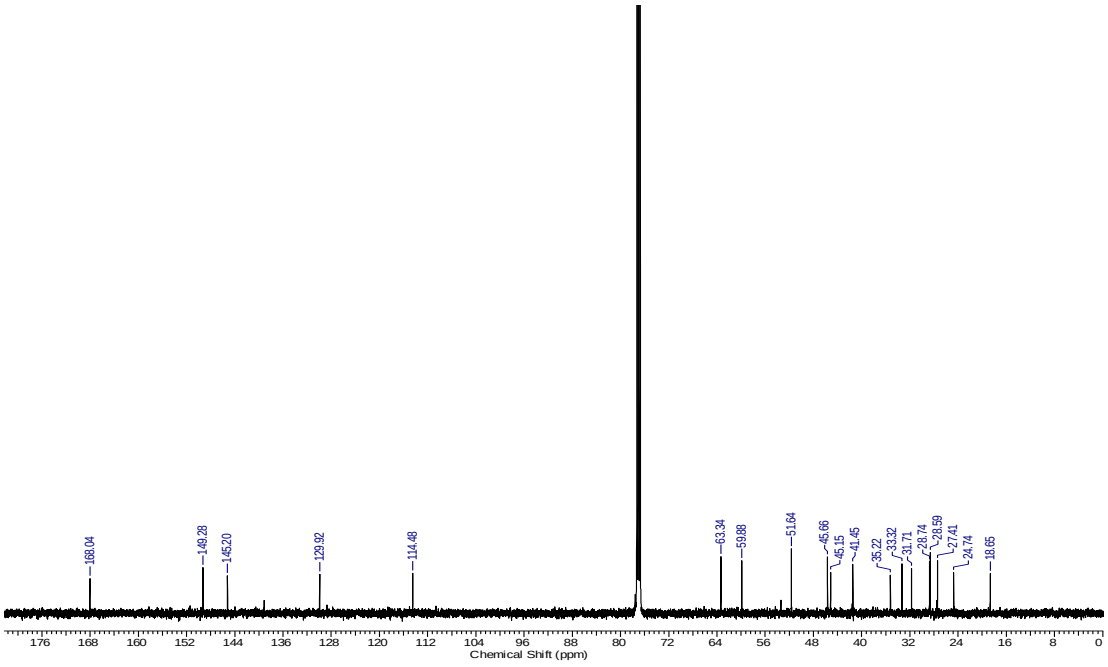


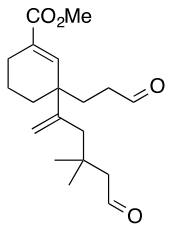
S30

^{1}H NMR (400 MHz, $CDCl_3$)



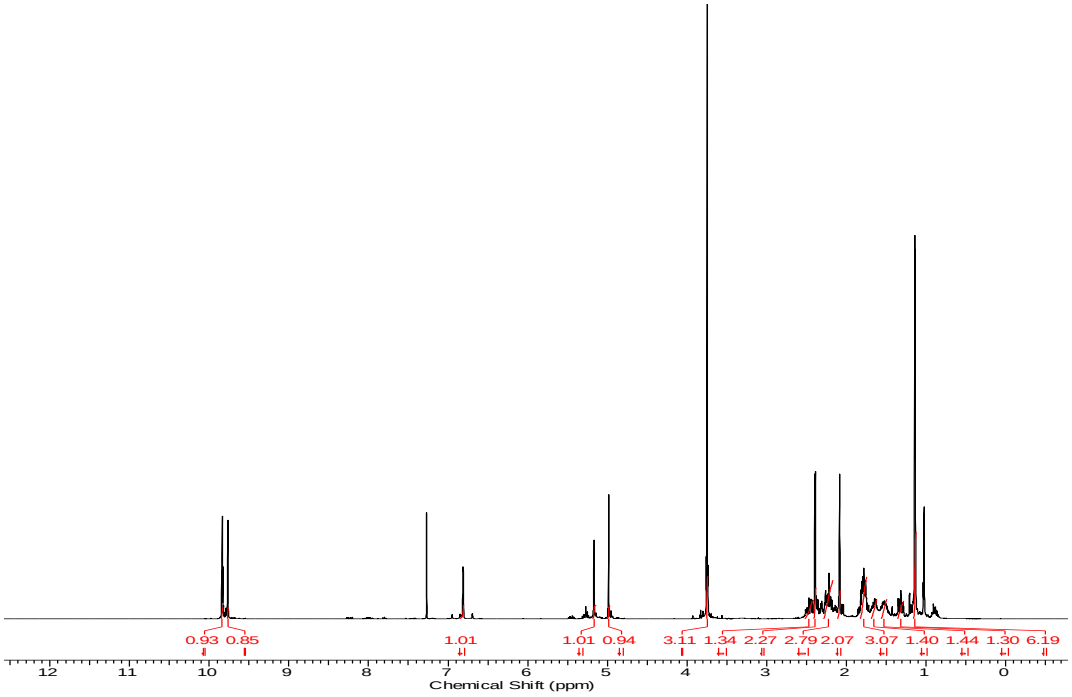
^{13}C NMR (101 MHz, $CDCl_3$)



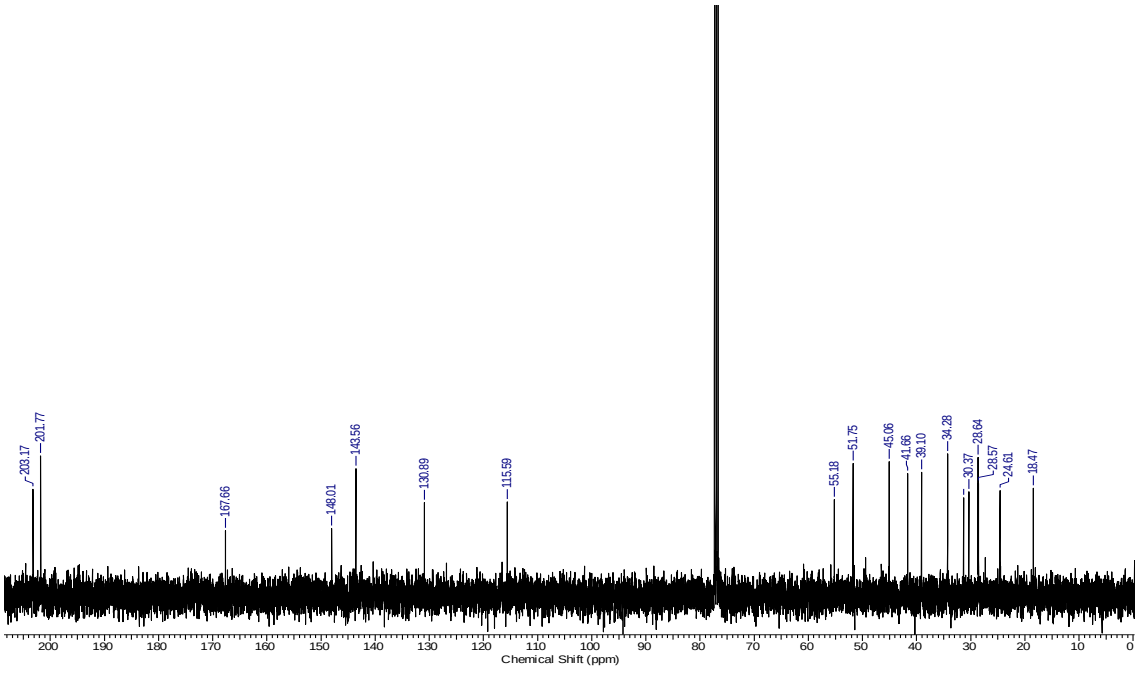


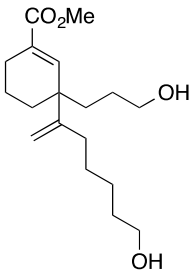
7d

^{1}H NMR (400 MHz, $CDCl_3$)



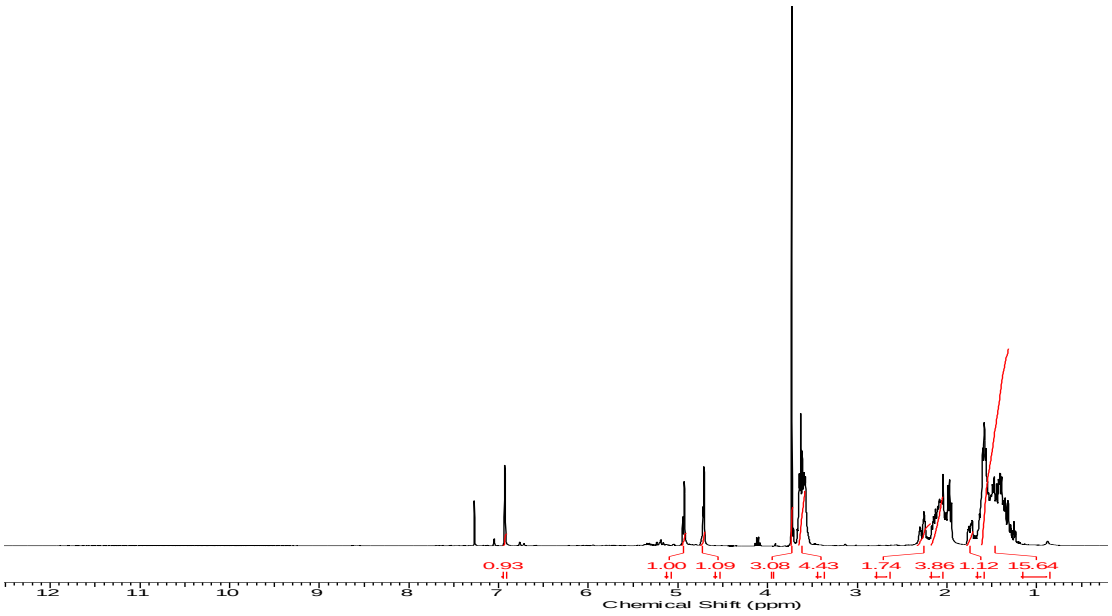
^{13}C NMR (101 MHz, $CDCl_3$)



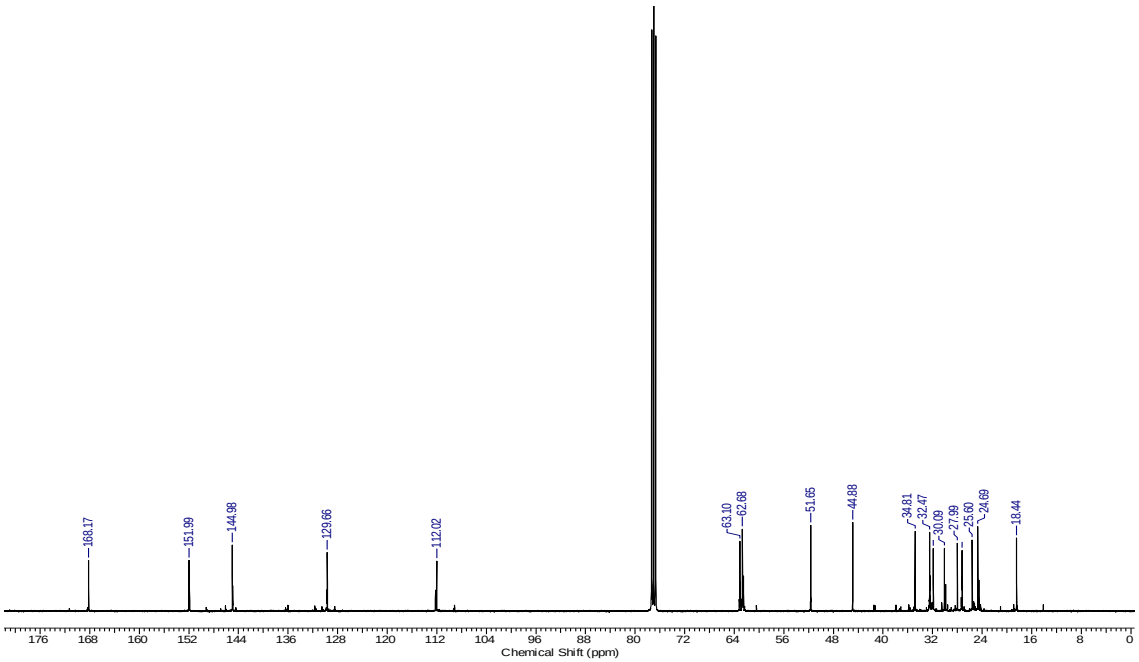


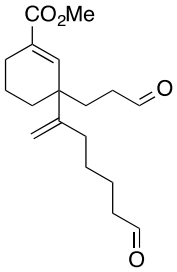
S31

^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

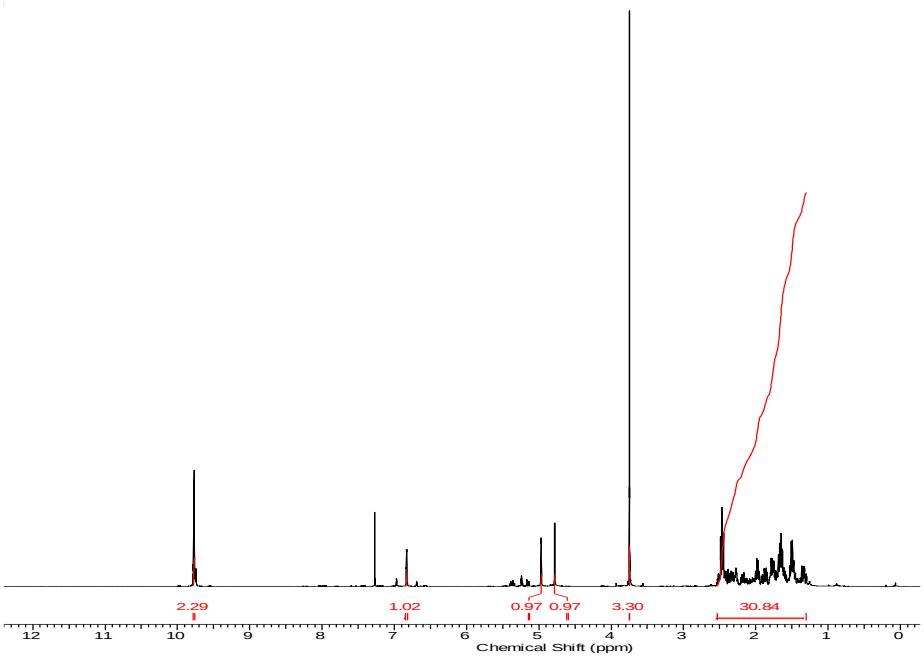




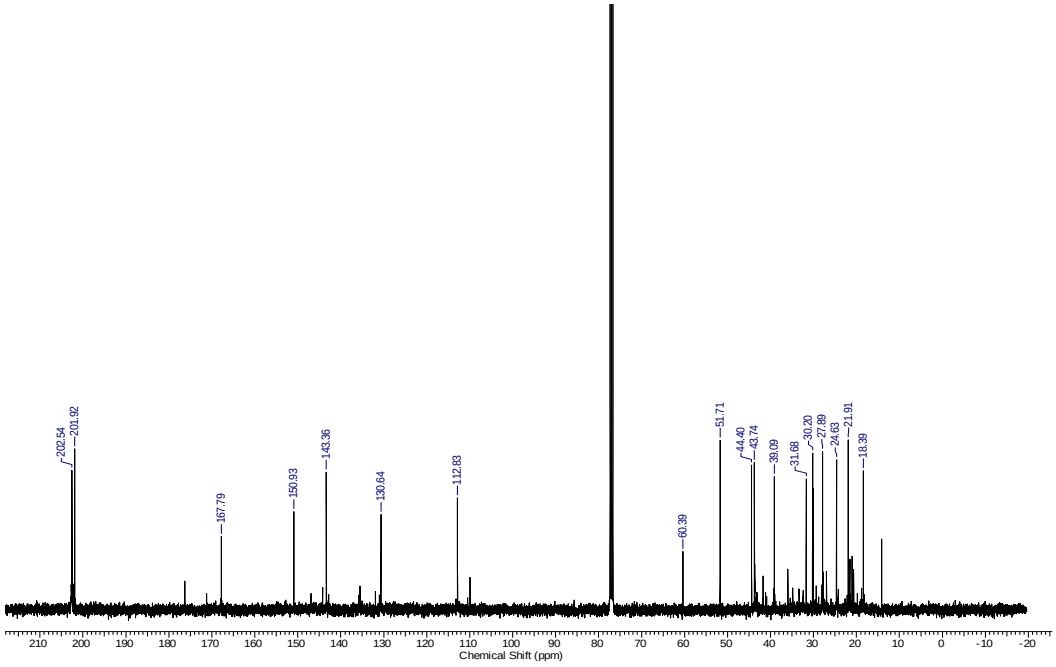
7f

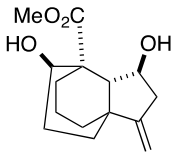
^{1}H NMR (400 MHz, $CDCl_3$)

(After partial purification)



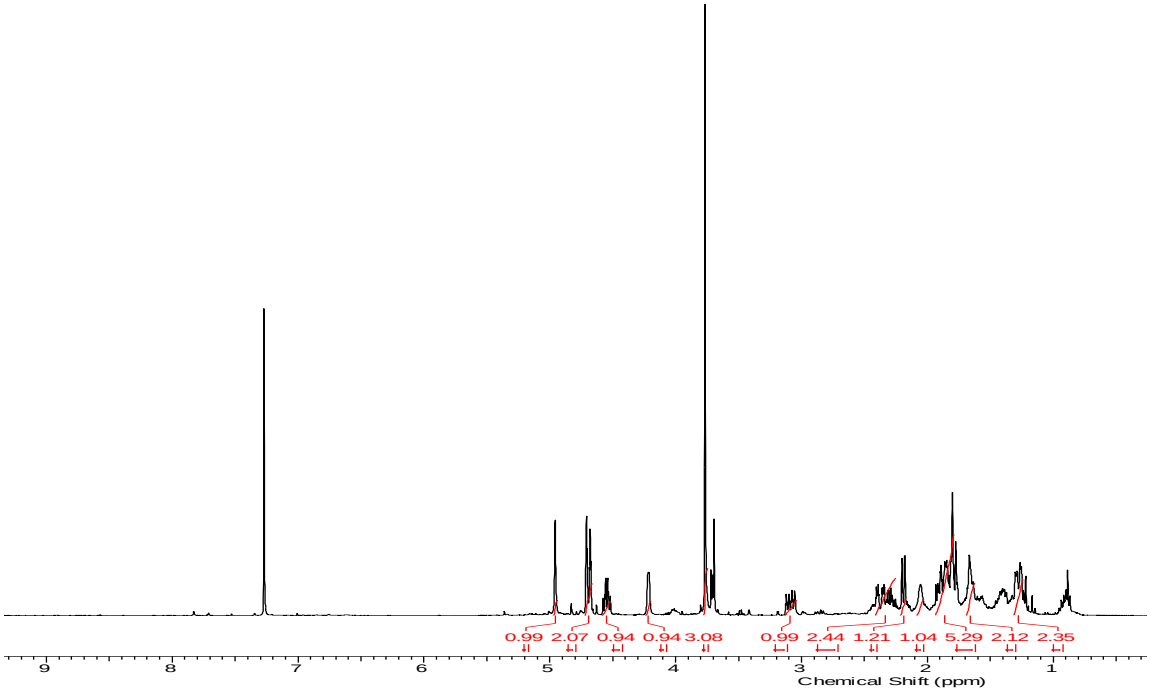
^{13}C NMR (101 MHz, $CDCl_3$)



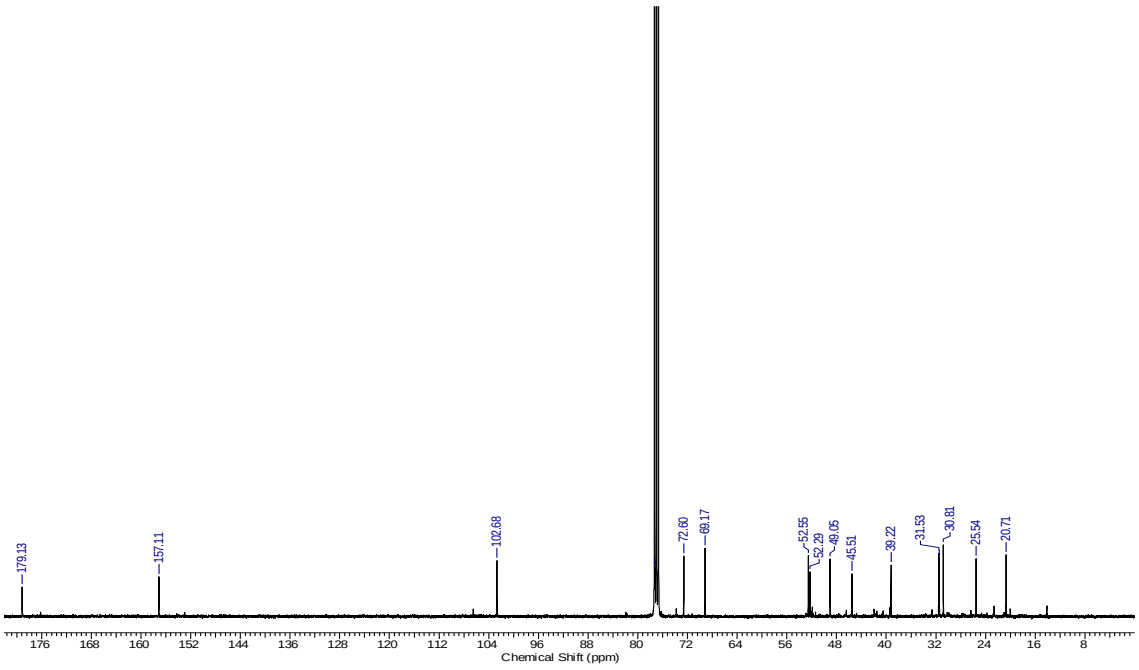


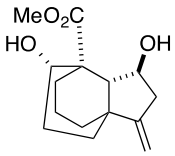
10a

^{1}H NMR (400 MHz, $CDCl_3$)



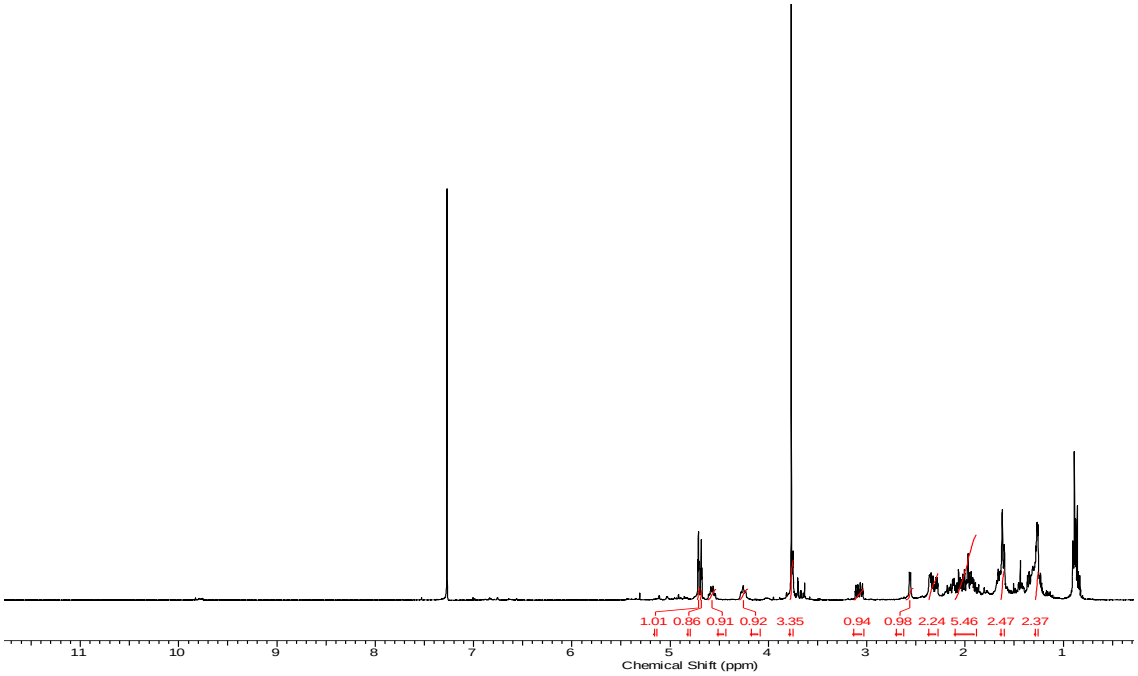
^{13}C NMR (101 MHz, $CDCl_3$)



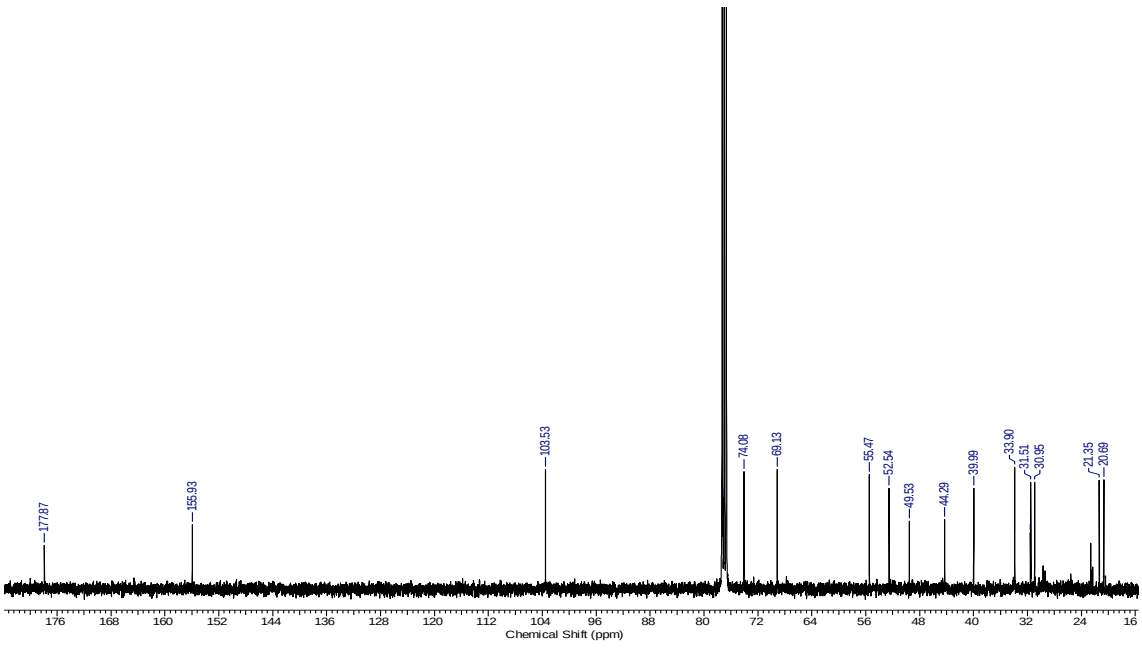


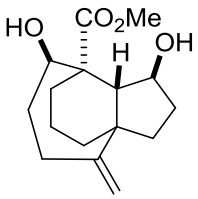
10a'

^{1}H NMR (400 MHz, $CDCl_3$)



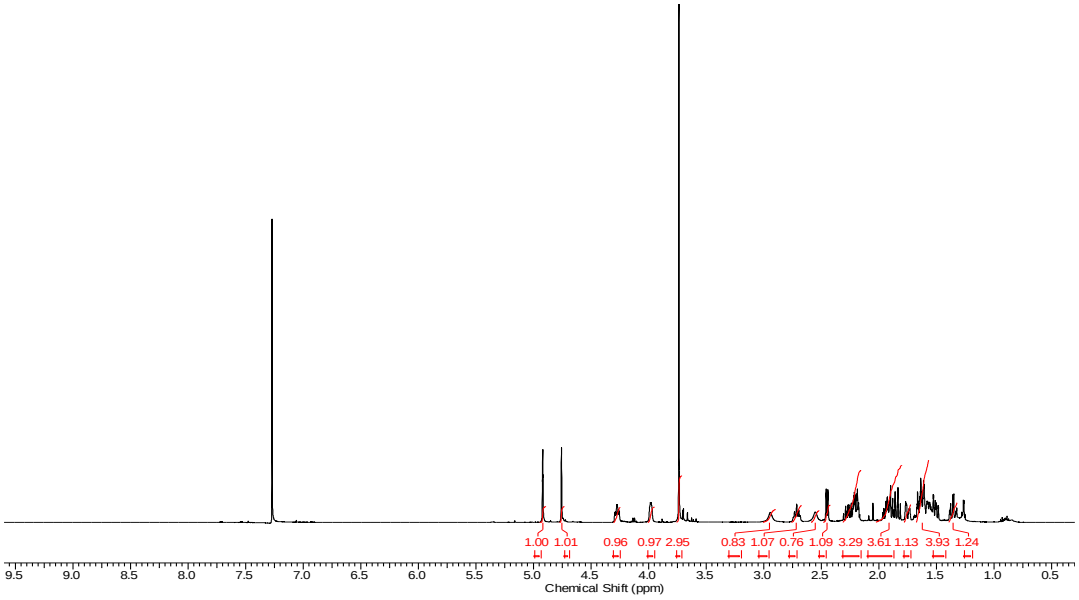
^{13}C NMR (101 MHz, $CDCl_3$)



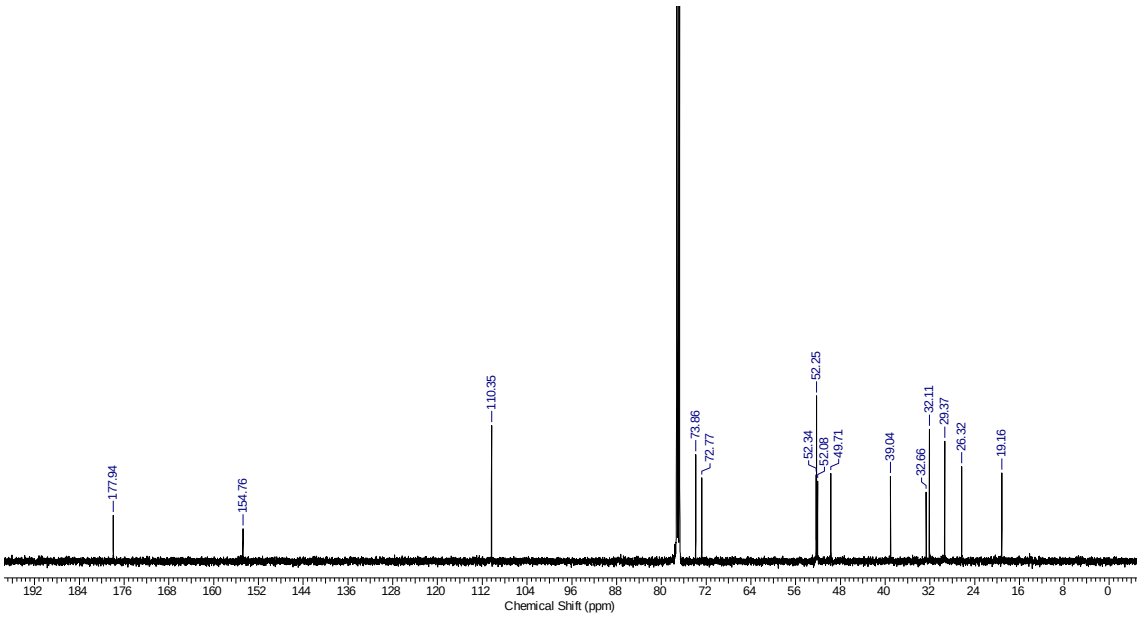


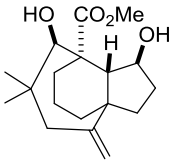
10b

^{1}H NMR (500 MHz, $CDCl_3$)



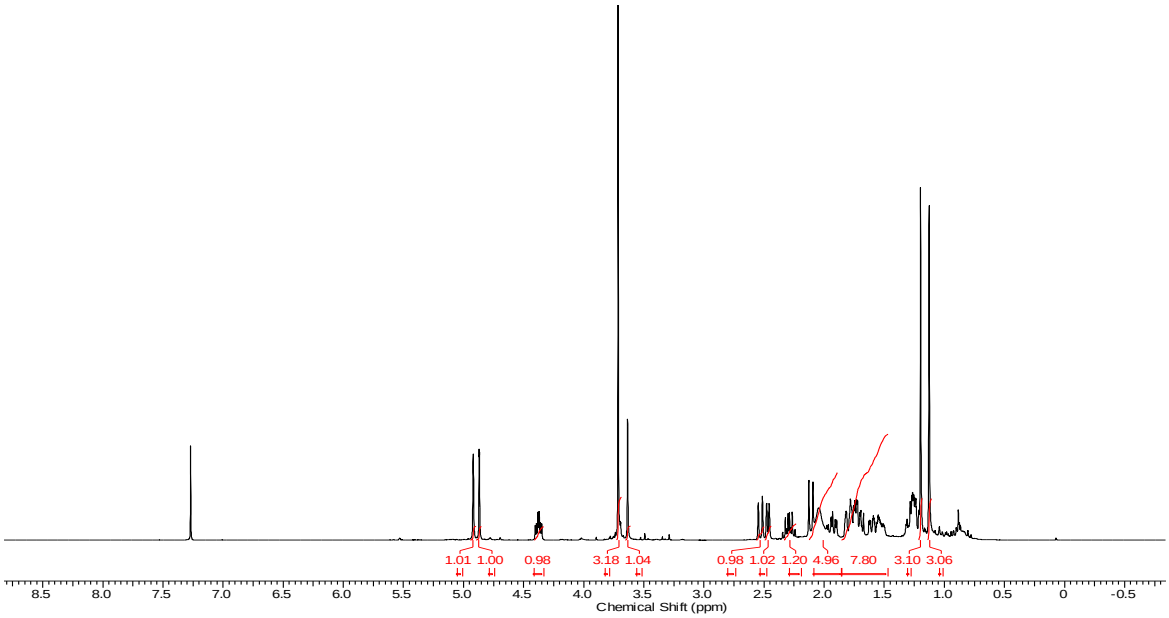
^{13}C NMR (101 MHz, $CDCl_3$)



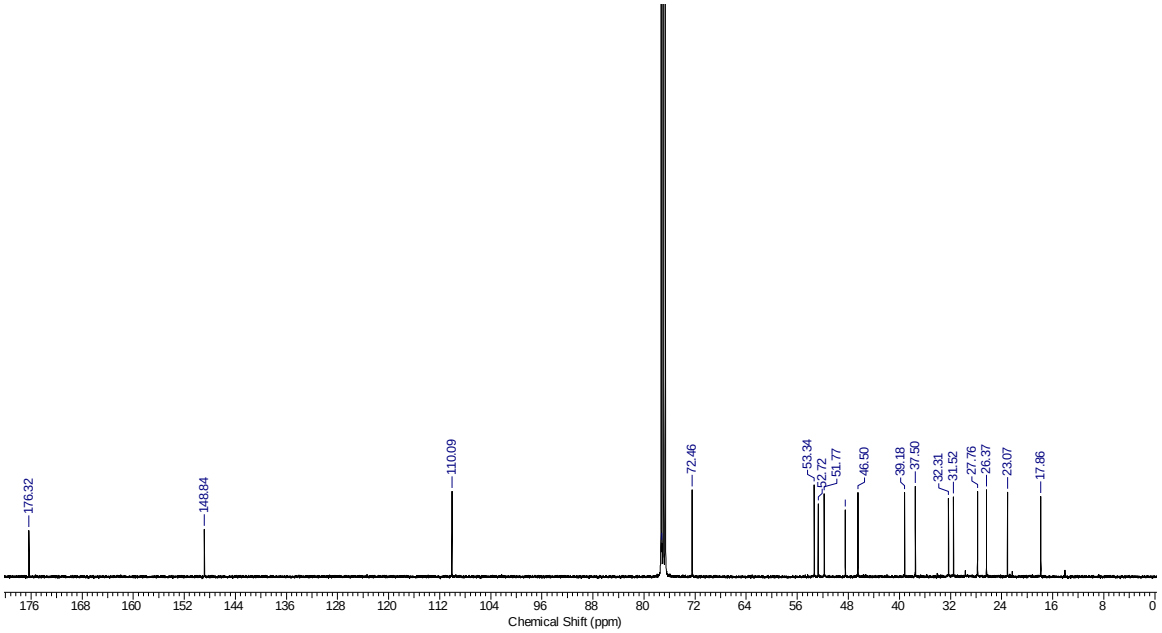


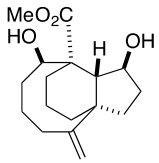
10c

^{1}H NMR (400 MHz, $CDCl_3$)



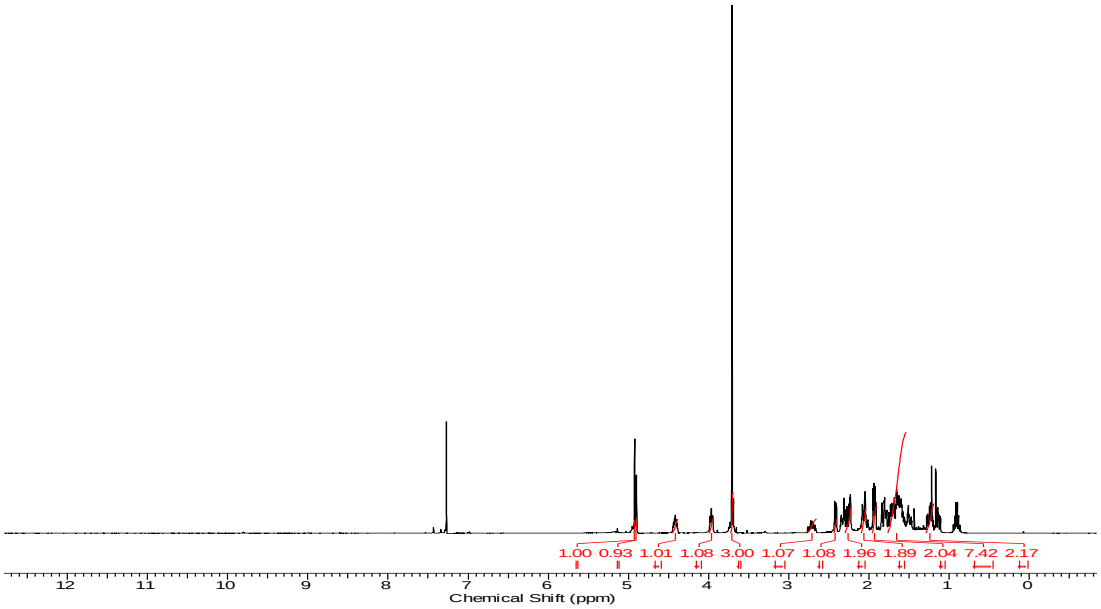
^{13}C NMR (101 MHz, $CDCl_3$)



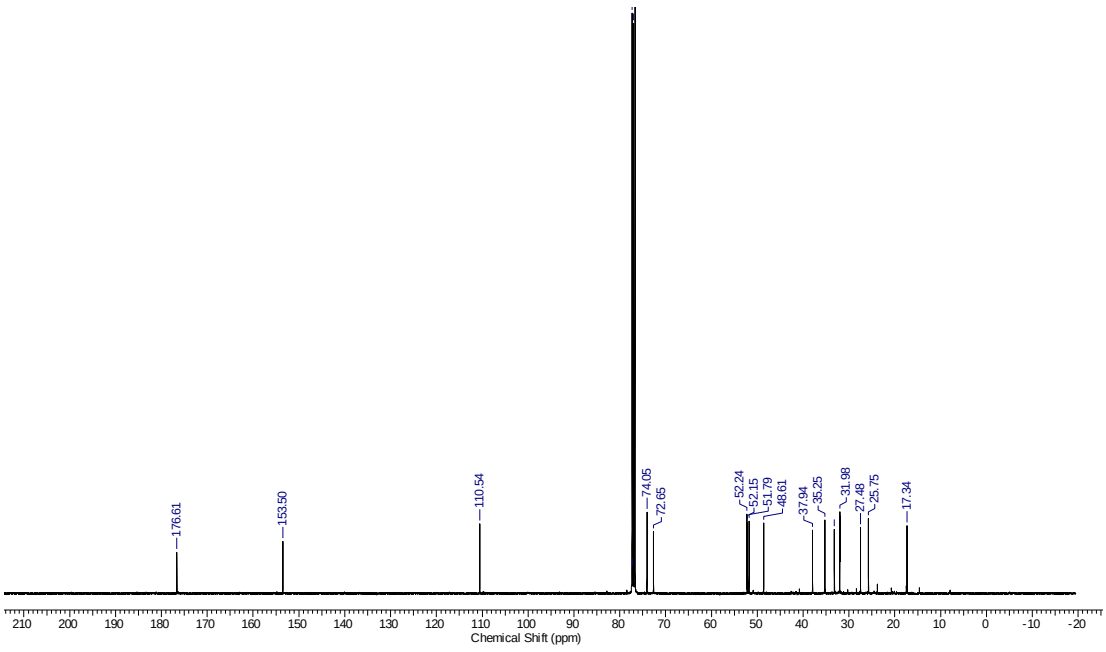


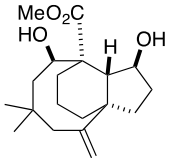
10e

^{1}H NMR (400 MHz, $CDCl_3$)



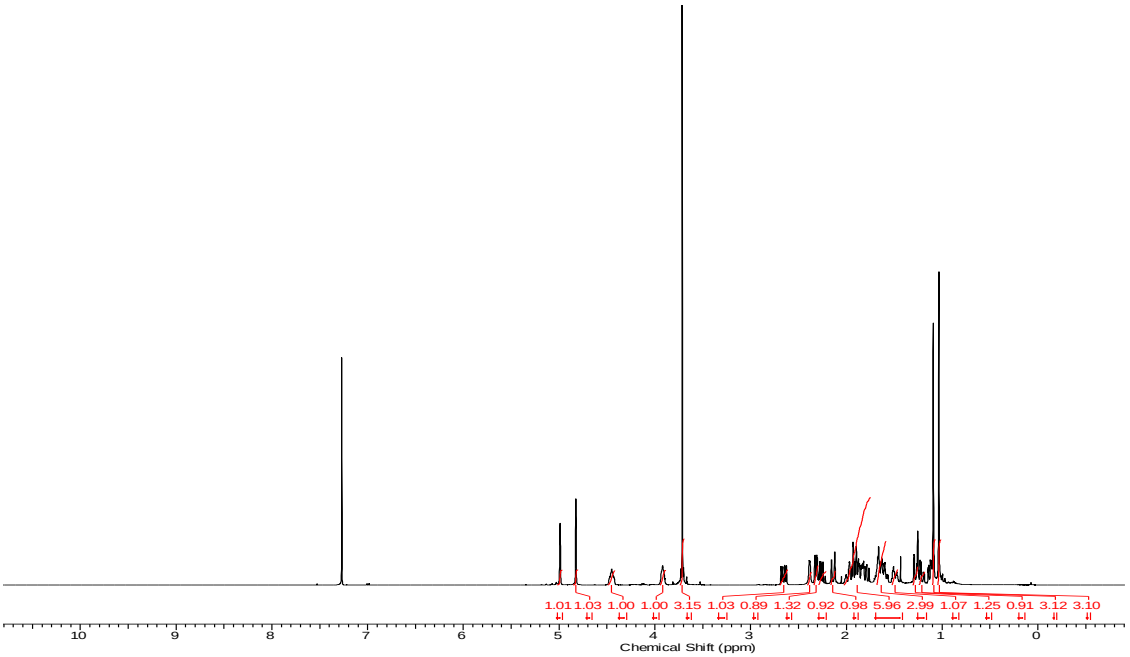
^{13}C NMR (101 MHz, $CDCl_3$)



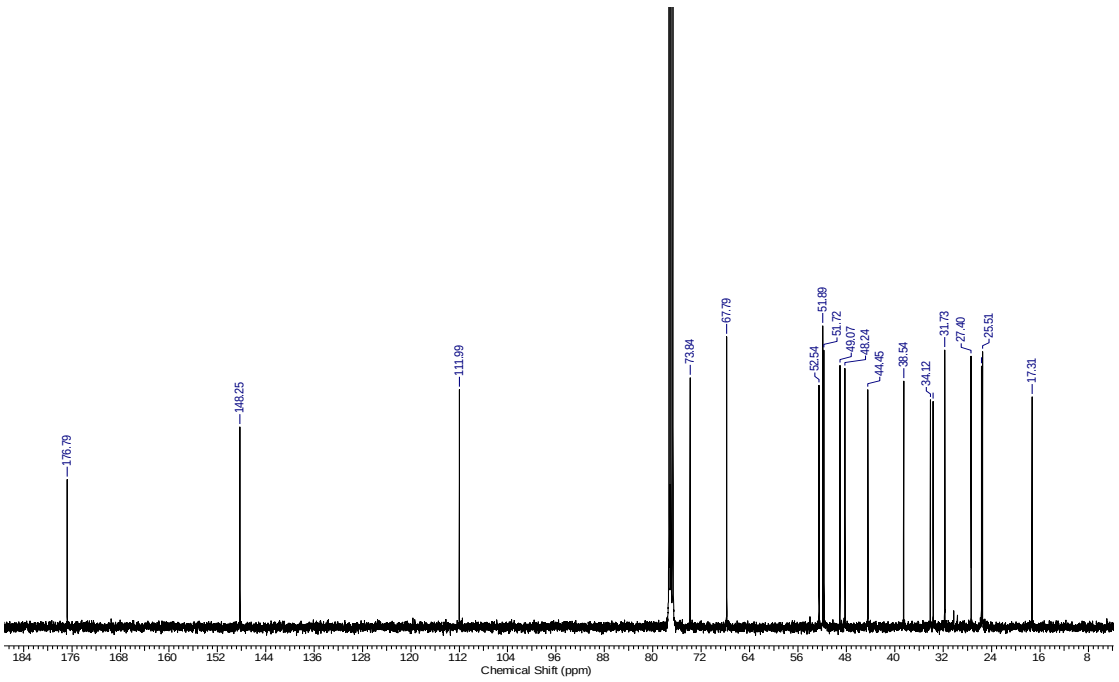


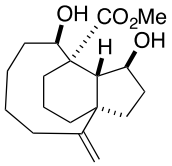
10d

^{1}H NMR (400 MHz, $CDCl_3$)



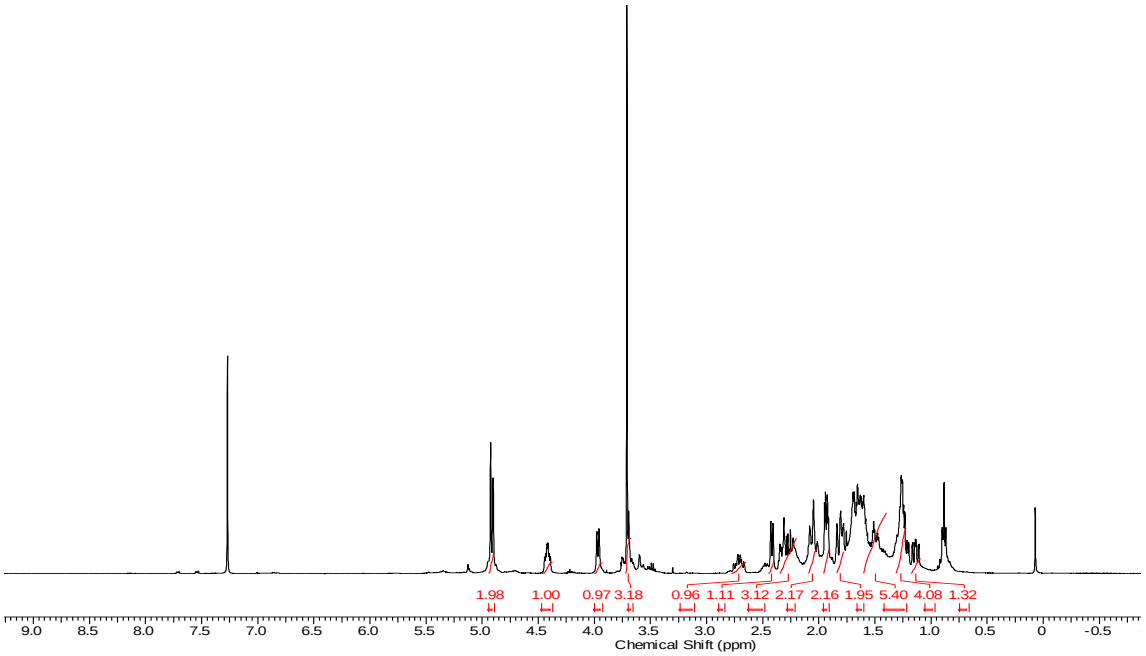
^{13}C NMR (101 MHz, $CDCl_3$)



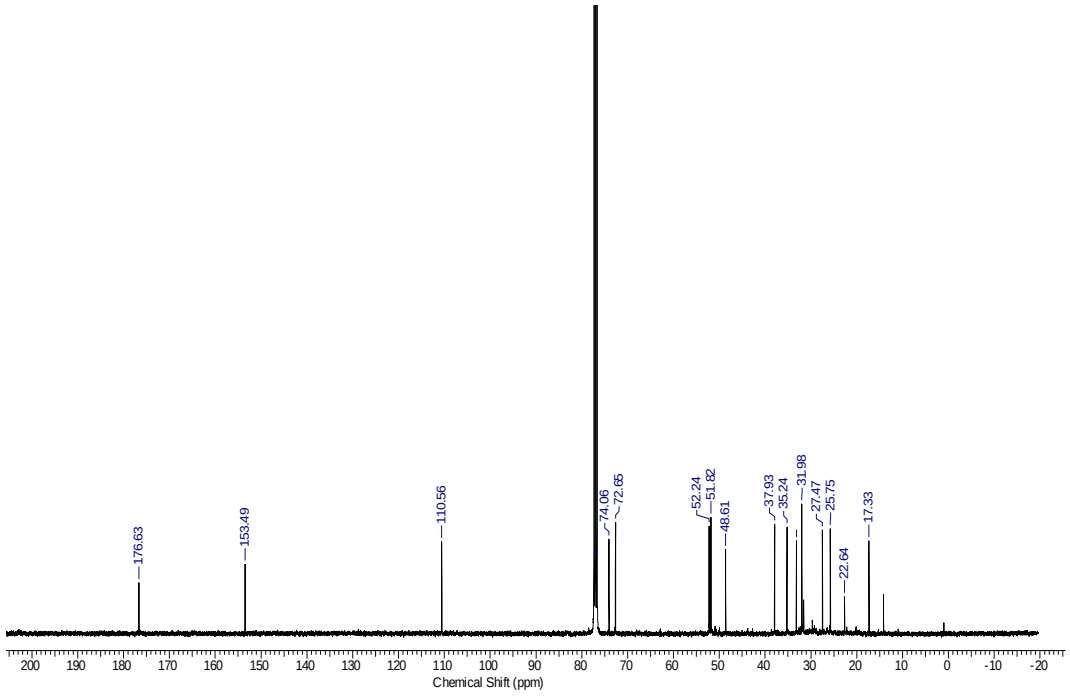


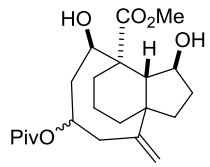
10g

^{1}H NMR (400 MHz, $CDCl_3$)



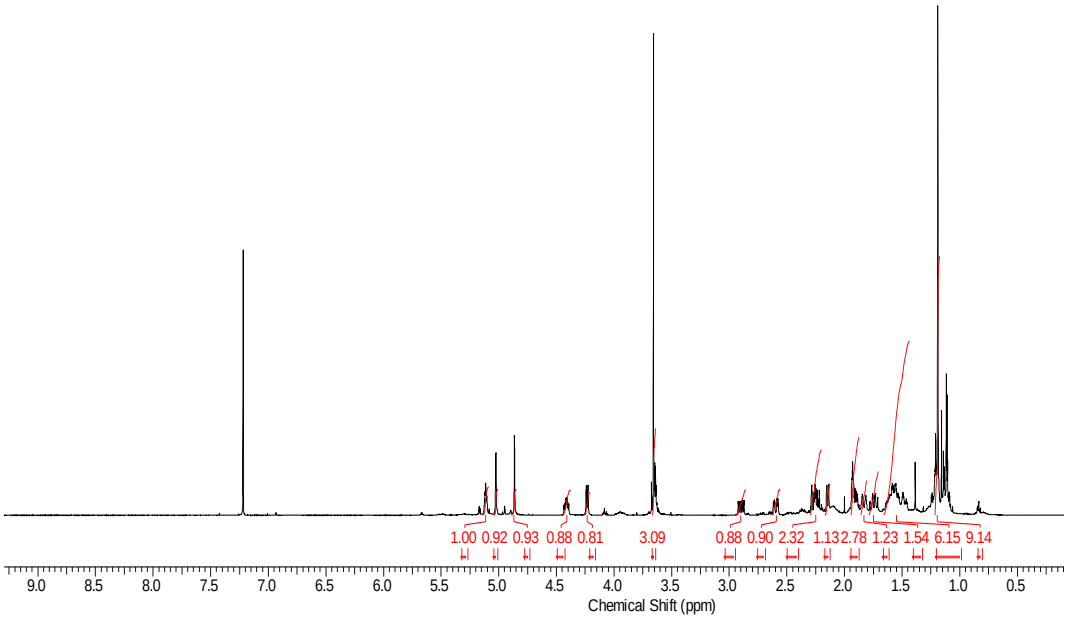
^{13}C NMR (101 MHz, $CDCl_3$)



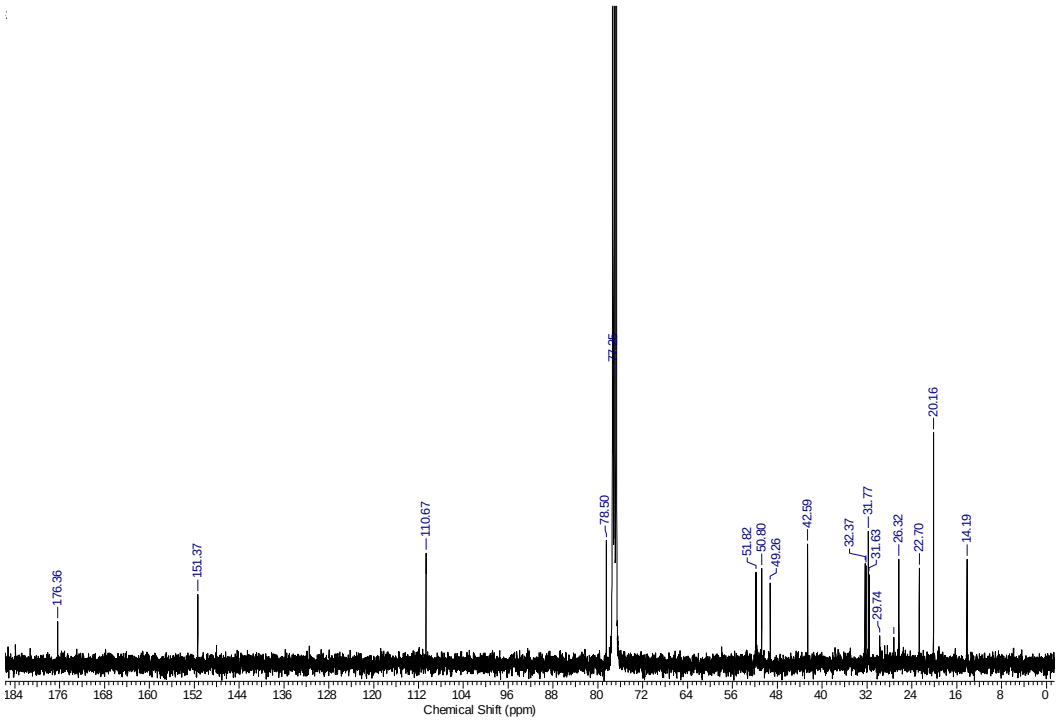


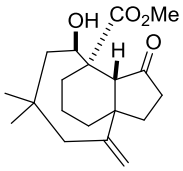
10f

^{1}H NMR (500 MHz, $CDCl_3$)



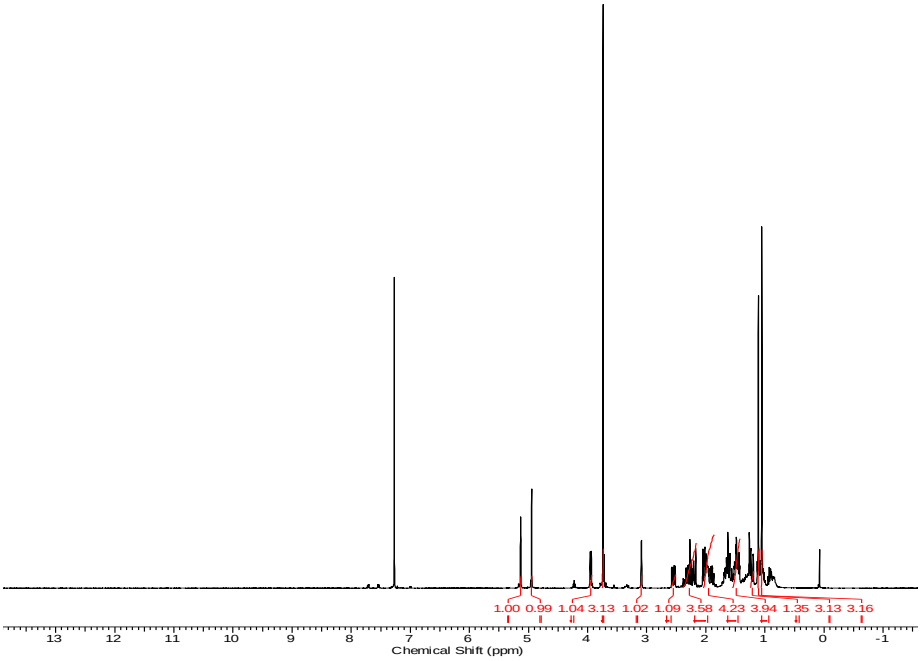
^{13}C NMR (101 MHz, $CDCl_3$)



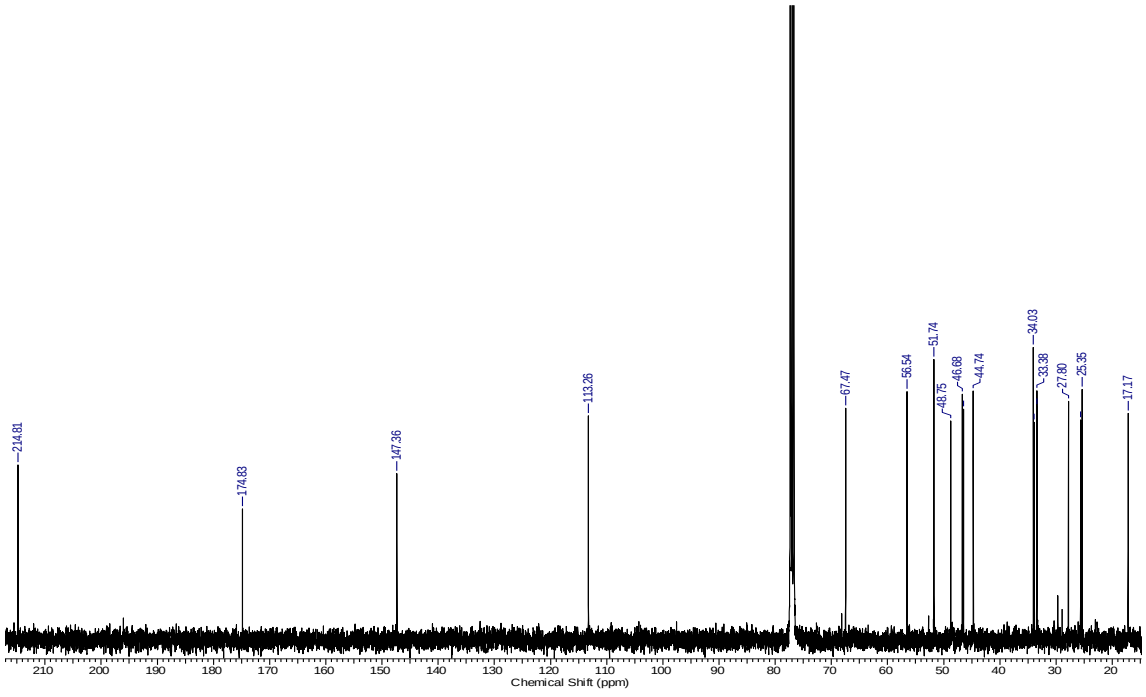


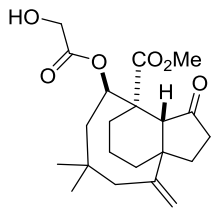
11

^{1}H NMR (400 MHz, $CDCl_3$)



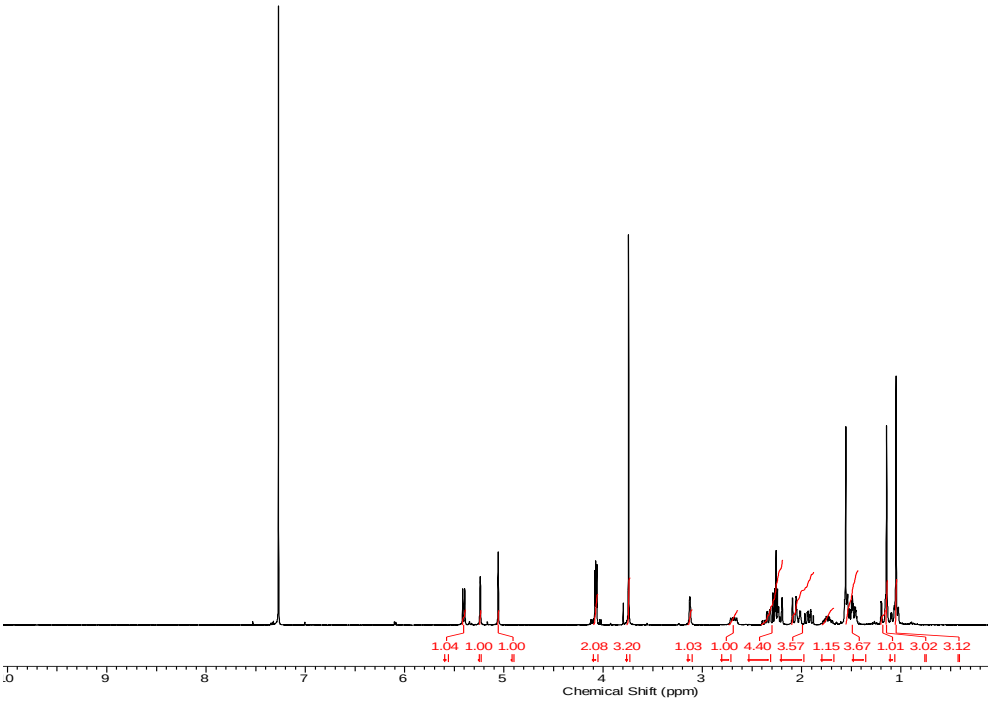
^{13}C NMR (101 MHz, $CDCl_3$)



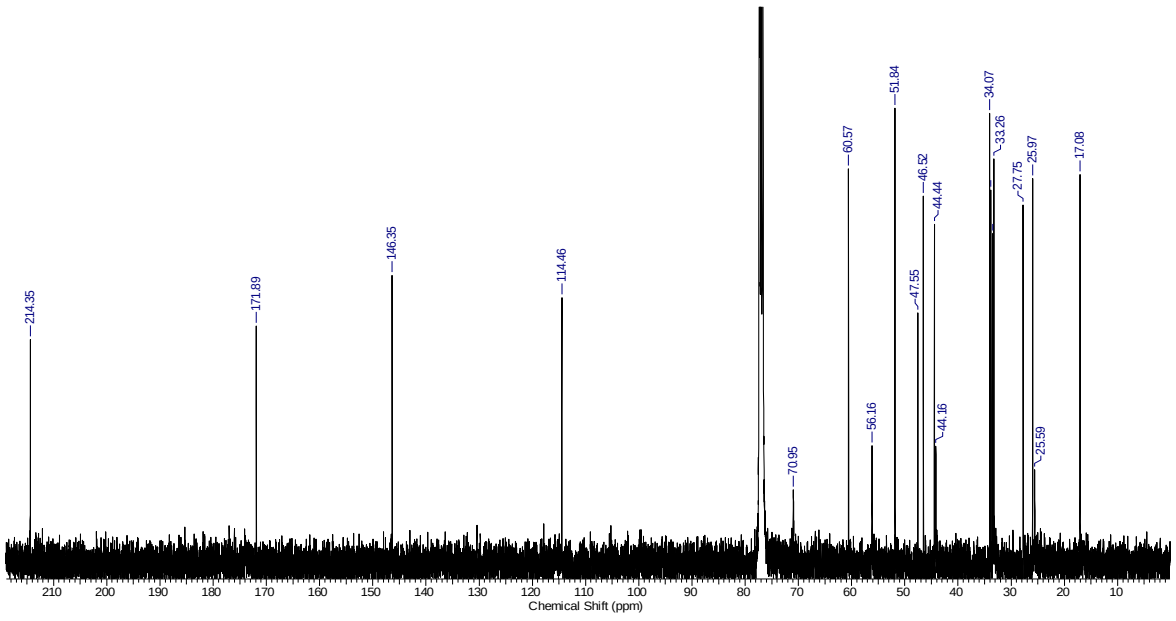


12

^{1}H NMR (400 MHz, $CDCl_3$)

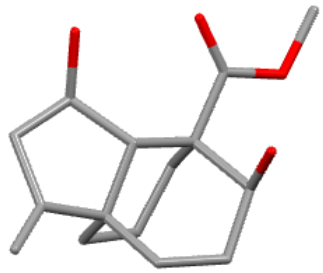


^{13}C NMR (101 MHz, $CDCl_3$)

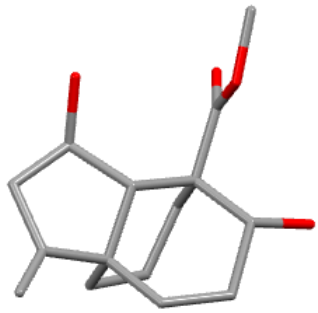


X-Ray Crystal Strucres and CCDC Numbers

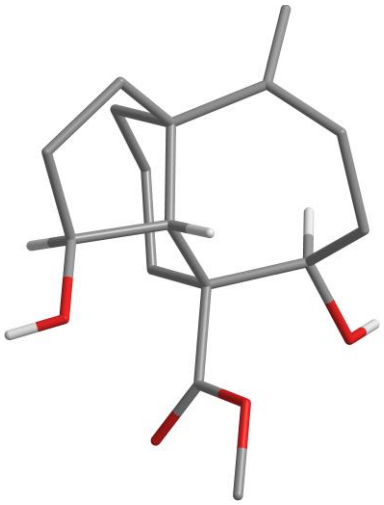
Compound **10a** (CCDC 1429468)



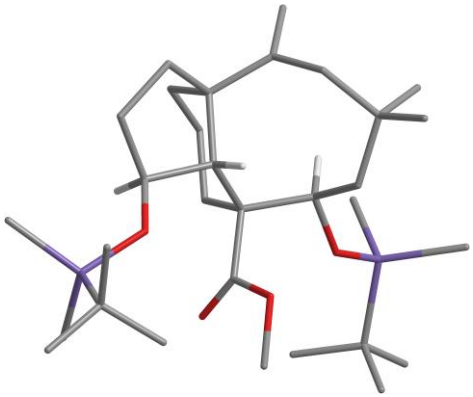
Compound **10a'** (CCDC 1429467)



Compound **10b** (CCDC 1429469)



Compound **10d** (*bis* TBS) (CCDC 1429470)



Compound **10e** (CCDC 1429471)