# A modular, enantioselective synthesis of resolvins D3, E1 and hybrids

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## Supporting Information

## 1. General Experimental

**Solvents and Reagents.** Dichloromethane, tetrahydrofuran, toluene and methanol were dried by passing through an activated alumina column under argon in a solvent dispenser. Dimethyl sulfoxide, 1,2-dimethoxyethane (DME) and propane-1,3-diol were distilled over calcium hydride under reduced pressure prior to use. Diethylamine was distilled under nitrogen over 3 Å molecular sieves. Benzaldehyde was washed with saturated $NaHCO_3$ solution and dried ($MgSO_4$) prior to use. All other reagents were used as received. Tetrabutylammonium fluoride (TBAF) solution was obtained by dissolving tetrabutylammonium fluoride trihydrate in anhydrous THF. TBAF•$3H_2O$, and potassium trimethylsilanolate were weighed out in a glove box under nitrogen. Potassium trimethylsilanolate was purchased from CombiBlocks. Petrol refers to the fraction of petroleum ether which boils in the range 40-60 °C. Brine refers to a saturated aqueous solution of NaCl. $NaHCO_3$, $K_2CO_3$, $NH_4Cl$ and $Na_2S_2O_3$ solutions refer to saturated aqueous solutions. HCl was also used as an aqueous solution. Isolated Noyori catalyst was prepared according a literature procedure (*J. Am. Chem. Soc.* **1997**, *119*, 8738-8739) and the stereochemistry of the resulting propargylic alcohols assigned by analogy to literature reports.

**Reactions.** All reactions were carried out under argon or nitrogen unless otherwise stated. Oven-dried glassware was used for reactions requiring anhydrous conditions.

**Chromatography.** Thin-layer chromatography was performed on Merck aluminium-backed DC 60 F254 0.2 mm precoated plates, which were visualised with UV fluorescence and staining with potassium(VII) manganate or vanillin. Flash column chromatography was performed on MN Kieselgel 60M (particle size 40-63 μm), with the solvent system used in parentheses.

**Infrared Spectroscopy.** Infrared spectra were recorder on a Bruker Tensor 27 Fourier transform spectrometer, as a thin film on a diamond ATR module.

**NMR Spectroscopy.** $^1$H NMR spectra were recorded at 200, 250, 400 or 500 MHz on Bruker DPX 200, DPX 250, DPX 400, DQX400, AVN 400, DRX500 and AVII 500 spectrometers. 13C NMR spectra were recorded at 101 MHz or 125 MHz on Bruker DQX 400, AVN 400, DRX500 or ACII 500 (with $^{13}$C cryoprobe) spectrometers. Chemical shifts (δH and δC) are expressed in parts per million (ppm), referenced to the residual solvent peak of $CDCl_3$ or $C_6D_6$. Coupling constants (*J*) are reported to the nearest 0.1 Hz. Spectra are assigned based on chemical shift, coupling constants, COSY, HSQC and HMBC data and / or comparison with similar compounds. Splitting patterns are described using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), quin. (quintet), sept. (septet).

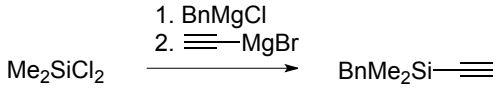
**Mass spectromety.** Low-resolution mass spectra (m/z) were performed on a Micromass LCT Premier Open Access. High resolution mass spectra were recorded under ESI or EI conditions on a Bruker MicroTOF.

**Heating.** For reactions that require heating, an oil bath was employed. The temperature was monitored via a temperature probe plugged into the stirrer plate.

## 2. Experimental Procedures and Characterization Data

## 2a. Synthesis of the right hand side 5-membered cyclic siloxanes

**Benzyl(ethynyl)dimethylsilane, S1**



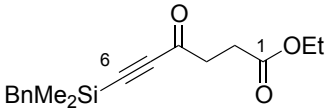

A solution of benzylmagnesium chloride was prepared via slow addition of benzyl chloride (35.5 mL, 308 mmol, 1.0 equiv.) and ether (250 mL) to an excess of magnesium turnings (10.5 g, 431 mmol. 1.4 equiv.) in ether (50 mL). The reaction mixture was stirred at room temperature for 2 h, then the etheral layer was decanted into a dropping funnel and added dropwise over 10 min to dimethyldichlorosilane (52.0 mL, 400 mmol, 1.4 equiv.) at 0 °C under argon. After 15 min the ice bath was removed and stirring was continued for 1 h at room temperature, during which period a white salt precipitated. The suspension was allowed to settle, and the supernatant decanted into a flask under argon. The solvent and excess dimethyldichlorosilane were removed by concentration *in vacuo* to afford crude benzyldimethylchlorosilane (BDMSCl) as a pale yellow oil.

To a solution of crude BDMSCl in THF (250 mL) at 0 °C was added dropwise a solution of ethynyl magnesium bromide (800 mL, 0.5 M in THF, 400 mmol, 1.3 equiv.) over 45 min. The reaction mixture was warmed to room temperature, stirred overnight, then quenched at 0 °C with saturated $NH_4Cl$ (aq., 100 mL) and diluted with water (100 mL). The organic layer was separated and the aqueous layer was extracted with ether (2 x 100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (petrol eluent) gave ethynylbenzyldimethylsilane (42.0 g, 241 mmol, 79%) as a colourless oil. The physical data were found to be in agreement with previous reported (*JACS* **2005**, 127, 3666).

**$^{1}$H** NMR (400 MHz, $CDCl_3$) $\delta_H$ 7.28-7.20 (2H, m, ArH), 7.16-7.06 (3H, m, ArH), 2.44 (1H, s, CCH), 2.25 (2H s, $SiCH_2$), 0.18 (6H, s, SiMe).

**$^{13}$C** NMR $\delta_C$ (101 MHz, $CDCl_3$) 138.7, 128.5, 128.4, 124.6, 94.5, 88.7, 26.0, -2.2.

**Ethyl 6-(benzyldimethylsilyl)-4-oxohex-5-ynoate, 13**




A solution of methylmagnesium bromide (5.70 mL of a 3 M solution in $Et_2O$, 17.2 mmol, 1.5 equiv.) was added dropwise to a stirred solution of ethynylbenzyldimethylsilane (2.00 g, 11.5 mmol, 1.0 equiv.) in THF (20 mL) at 0 °C under $N_2$. The solution was warmed to room temperature over 20 min. Then, it was added dropwise to a solution of glutaric acid monoethyl ester chloride (3.3 mL, 22.9 mmol, 2.0 equiv.) in THF (50 mL) at 0 °C. After 2 h the ice bath was removed and stirring continued for 1 h at room temperature before the reaction was quenched by addition of saturated $NH_4Cl$ (10 mL) and diluted with water (20 mL). The aqueous layer was extracted with $Et_2O$ (3 x 20 mL), and the combined organic phases were washed with brine (20 mL), dried

($MgSO_4$), and concentrated. Purification by flash column chromatography on silica gel (7:1→4:1 petrol / $Et_2O$) gave **13** (1.98 g, 6.54 mmol, 57%) as a colourless oil.

$R_f$ 0.18 (9:1 petrol / $Et_2O$).

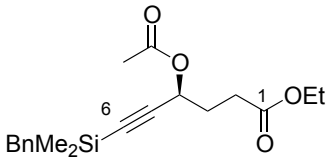
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2981, 1734, 1680, 1206, 1111, 838, 700.

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 7.29-7.21 (2H, m, 2H, ArH), 7.17-7.09 (1H, m, ArH), 7.09 – 7.04 (m, 2H, ArH), 4.15 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.88 (2H, t, *J* = 6.8 Hz, H3), 2.62 (2H, t, *J* = 6.7 Hz, H2), 2.26 (2H, s, $CH_2Ph$), 1.26 (3H, t, *J* = 7.2 Hz, $OCH_2C\underline{H}_3$), 0.20 (6H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 185.3, 172.1, 137.9, 128.5, 128.5, 124.9, 102.6, 97.2, 61.0, 40.0, 28.0, 25.4, 14.3, -2.6.

**HRMS** ($ES^-$) calc. for $C_{17}H_{22}O_3Si$ $[M-H]^-$ 301.1250, found 301.1263.

**Ethyl (*S*)-4-acetoxy-6-(benzyldimethylsilyl)hex-5-ynoate, 15**




This procedure was adapted from the literature (*J. Am. Chem. Soc.* **1997**, *119*, 8738-8739). A solution of ynone **13** (1.94 g, 6.43 mmol, 1.0 equiv.) in isopropyl alcohol (78 mL) was degassed (vacuum / $N_2$ purge, x 4), then a solution of (1*S*,2*S*)-(+)-*N*-Tosyl-1,2-diphenylethane-1,2-diamine[$\eta^6$-1-isopropyl-4-methylbenzene)-ruthenium(II) (Noyori catalyst, 78.7 mg, 0.13 mmol, 0.02 equiv.) in $CH_2Cl_2$ (1 mL) was added, and the mixture further degassed twice. The mixture was stirred for 1.5 h, before being concentrated to give the crude intermediate propargylic alcohol. The alcohol was redissolved in $CH_2Cl_2$ (30 mL), then acetic anhydride (1.22 mL, 12.9 mmol, 2.0 equiv.), DMAP (crystals) and $Et_3N$ (2.68 mL, 19.3 mmol, 3.0 equiv.) were added. The mixture was stirred for 1 h, then quenched by addition of 1N HCl (10 mL) and diluted with $H_2O$ (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL), and the combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Purification *via* flash column chromatography on silica gel (6:1→4:1 petrol / $Et_2O$) gave **15** (1.94 g, 5.60 mmol, 88% over two steps) as a colourless oil.

Data for the intermediate propargylic alcohol (purified for the purposes of characterization):

$R_f$ 0.34 (2:1 petrol / $Et_2O$).

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 7.22 (2H, dd, *J* = 8.2, 6.9 Hz, ArH), 7.14-7.02 (3H, m, ArH) 4.45 (1H, app q, *J* = 5.9 Hz, H4), 4.16 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.67-2.32 (2H, m, H2), 2.25 (1H, d, *J* = 5.6 Hz, OH), 2.20 (2H, s, $CH_2Ph$), 2.08-1.90 (2H, m, H3), 1.28 (3H, t, *J* = 7.2 Hz, $OCH_2C\underline{H}_3$), 0.14 (3H, s, SiMe), 0.14 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 173.8, 138.9, 128.5, 128.3, 124.6, 107.2, 88.7, 62.1, 60.8, 32.4, 30.1, 26.2, 14.3, -2.0.

Data for acetate **15**:

$R_f$ 0.28 (6:1 petrol / $Et_2O$).

**$[\alpha]_D^{25}$** -67.3 (*c* 1.0, $CHCl_3$).

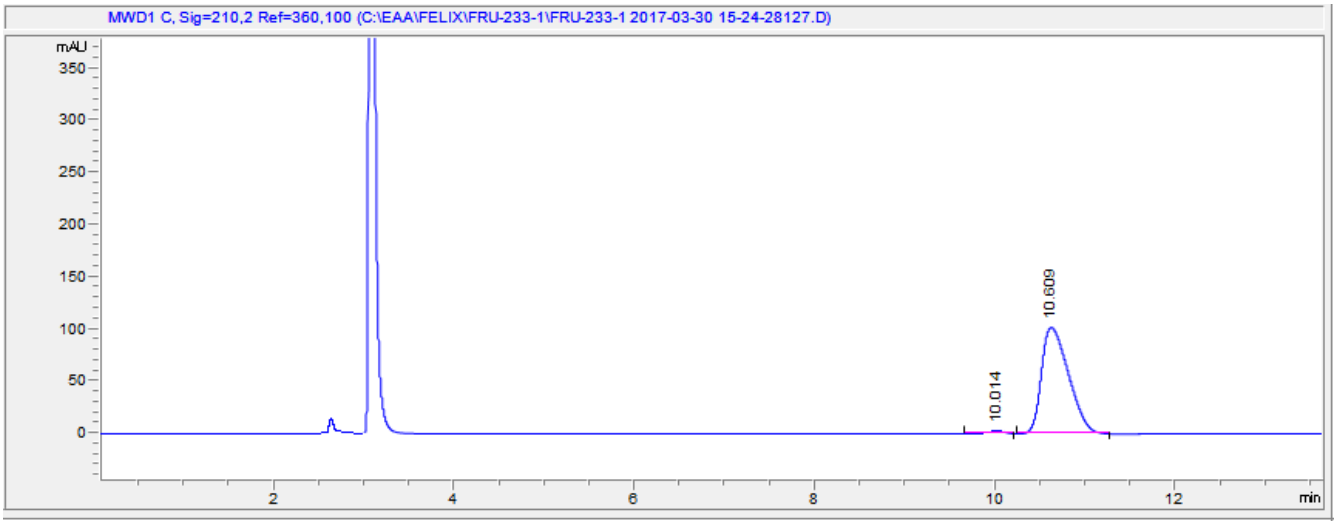
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2962, 1735, 1372, 1227, 1163, 1025, 837, 700.

**$^{1}$H** NMR (400 MHz, $CDCl_3$) δ 7.25-7.18 (3H, m, ArH), 7.14-7.00 (3H, m, ArH), 5.43 (1H, t, *J* = 6.2 Hz, H4), 4.15 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.44 (m, H2), 2.19 (2H, s, $CH_2Ph$), 2.12-2.04 (2H, m, H3), 2.08 (3H, s, COMe), 1.28 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.13 (3H, SiMe), 0.13 (3H, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 172.7, 169.8, 138.8, 128.5, 128.3, 124.6, 103.1, 89.6, 63.3, 60.8, 29.9, 26.1, 21.1, 14.4, -2.1.

**HRMS** ($ES^+$) calc. for $C_{19}H_{26}O_4Si$ $[M+Na]^+$ 369.1493, found 369.1492.

**HPLC** 96.9% *ee*. Chiralpak IB, 0.2% IPA/*n*-Hexane, 1.3 mL/min. *S*: 9.9 min; *R*: 10.5 min.

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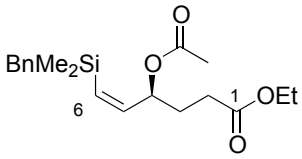
| 2 | 10.609 | BB | 0.3324 | 2151.78076 | 102.70937 | 98.4168 |

**Ethyl (*S*,*Z*)-4-acetoxy-6-(benzyldimethylsilyl)hex-5-enoate, 17**




A suspension of $Pd/CaCO_3$ (590 mg, 5 wt% Pd, 0.28 mmol, 0.05 equiv.) in toluene (15 mL) was evacuated / flushed with hydrogen three times, and then stirred for 15 min. A solution of alkynylsilane (1.92 g, 5.54 mmol, 1.0 equiv.) and quinoline (0.12 mL, 1.11 mmol, 0.2 equiv.) in toluene (15 mL) and cyclohexene (3 mL) was added. After stirring for 30 min, the mixture was filtered through celite, and the filtrate was washed with 1N HCl (2 x 10 mL) and brine (20 mL), then dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by flash column chromatography (6:1→4:1 petrol / $Et_2O$) to give **17** (1.60 g, 4.58 mmol, 83%, Z:E >20:1) as a pale yellow oil.

***R*$_f$** 0.32 (4:1 petrol / $Et_2O$).

**$[\alpha]_D^{25}$** -4.8 (*c* 1.0, $CHCl_3$).

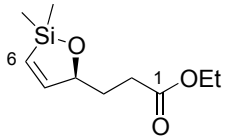
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3024, 2936, 1736, 1370, 1236, 1027, 834, 700.

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 7.24-7.17 (2H, m, 2H, ArH), 7.12-7.04 (1H, m, ArH), 7.04-6.98 (2H, m, ArH), 6.17 (1H, dd, *J* = 14.4, 9.2 Hz, H5), 5.71 (1H, dd, *J* = 14.4, 0.8 Hz, H6), 5.35 (1H, dddd, *J* = 8.8, 7.8, 5.4, 0.8 Hz, H4), 4.13 (2H, qd, *J* = 7.2, 1.1 Hz, $OC\underline{H}_2CH_3$), 2.41-2.25 (2H, m, H2), 2.20 (2H, ABq, *J* = 14.5 Hz, $CH_2Ph$), 2.04 (3H, s, COMe), 1.99-1.73 (2H, m,H3), 1.26 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.16 (3H, SiMe), 0.16 (3H, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 172.9, 170.2, 145.3, 139.8, 132.3, 128.4, 128.3, 124.3, 73.6, 60.7, 30.1, 30.1, 26.5, 21.4, 14.4, -1.7, -1.7.

**HRMS** ($ES^+$) calc. for $C_{19}H_{28}O_4Si$ $[M+Na]^+$ 371.1649, found 371.1648.

**Ethyl (*S*)-3-(2,2-dimethyl-2,5-dihydro-1,2-oxasilol-5-yl)propanoate, 5**




To a solution of **17** (100 mg, 0.29 mmol, 1.0 equiv.) in THF (1 mL) at room temperature was added a 1.0 M solution of TBAF•$3H_2O$ in THF (0.30 mL, 0.30 mmol, 1.05 equiv.), and the reaction was stirred for 30 min. $K_2CO_3$ (60 mg, 0.43 mmol, 1.5 equiv.) was added to the reaction mixture, followed by water (50 µL, 5 vol.%, 14.6 equiv.). After stirring for 2 h, water (1 mL) and $Et_2O$ (1 mL) were added, the aqueous layer was extracted with $Et_2O$ (3 x 1mL) and the combined organic phases were dried ($MgSO_4$) and concentrated. The alkenylsiloxane **5** (62 mg, 0.29 mmol, quantitative), which was unstable to purification on silica gel, was obtained as a pale yellow oil which was used without further purification.

**$[\alpha]_D^{20}$** +78.6 (*c* 1.0, $CHCl_3$).

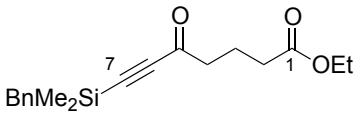
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2958, 2855, 1734, 1251, 1162, 1035, 852, 788.

**$^1$H** NMR (400 MHz, $CDCl_3$) 6.78 (1H, dd, *J* = 10.5, 1.5 Hz, H6), 6.06 (1H, dd, *J* = 10.5, 2.2 Hz, H5), 4.74 (1H, td, *J* = 6.6, 4.0 Hz, H4), 4.12 (2H, qd, *J* = 7.1, 1.5 Hz, $OC\underline{H}_2CH_3$), 2.47 – 2.30 (2H, m, H2), 2.09 – 1.96 (1H, m, H3), 1.78 – 1.67 (1H, m, H3), 1.24 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.26 (3H, s, SiMe), 0.23 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) 173.9, 152.7, 127.9, 81.8, 60.4, 31.9, 30.0, 14.4, 1.4, 0.7.

**HRMS** ($ES^+$) calc. for $C_{10}H_{18}O_3Si$ $[M+Na]^+$ 237.0917, found 237.0920.

**Ethyl 7-(benzyldimethylsilyl)-5-oxohept-6-ynoate, 14**




Butyllithium (0.50 mL of a 2.1 M solution in $Et_2O$, 1.05 mmol, 1.15 equiv.) was added dropwise to a solution of ethynylbenzyldimethylsilane (177 mg, 1.02 mmol, 1.1 equiv.) in THF (1 mL) at -78 °C. The solution immediately turned pale yellow and was stirred for 10 min at -78 °C. Then, a solution of $ZnCl_2$ (1.20 mL of a 0.86 M solution

in THF, 1.02 mmol, 1.1 equiv.) was added, which caused the yellow colour to disappear. The solution was stirred for a further 10 min at this temperature, then warmed to 0 °C and stirred for 30 min, before glutaric acid monoethyl ester chloride (0.14 ml, 0.9 mmol, 1.0 eq.) was added. After stirring for 1 h at 0 °C, the solution was warmed to room temperature, stirred for another 1 h, and then quenched by addition of $NH_4Cl$ (5 mL). The aqueous layer was extracted with $Et_2O$ (3 x 20 mL) and the combined organic phases were dried ($Na_2SO_4$) and concentrated. Purification by flash column chromatography on silica gel (7:1 petrol / $Et_2O$) gave ynone **14** (146 mg, 0.46 mmol, 52%) as a colourless oil.

***R*$_f$** 0.15 (9:1 petrol / $Et_2O$).

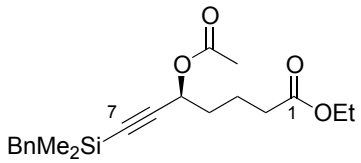
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2963, 1732, 1676, 1112, 842.

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 7.29-7.19 (2H, m, ArH), 7.16-7.02 (3H, m, ArH), 4.14 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.63 (2H, t, *J* = 7.2 Hz, H4), 2.35 (2H, t, *J* = 7.3 Hz, H2), 2.26 (2H, s, $CH_2Ph$), 1.97 (2H, p, J = 7.2 Hz, H3), 1.26 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.20 (6H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 186.7, 173.0, 138.0, 128.5, 128.5, 124.9, 103.0, 96.7, 60.6, 44.4, 33.2, 25.5, 19.5, 14.4, -2.6.

**HRMS** ($ESI^+$) calc. for $C_{18}H_{24}O_3Si$ $[M+H]^+$ 317.1574, found 317.1573.

**Ethyl (*S*)-5-acetoxy-7-(benzyldimethylsilyl)hept-6-ynoate, 16**




A solution of **14** (100 mg, 0.32 mmol, 1.0 equiv.) in isopropyl alcohol (4 mL) was degassed (evacuation / argon backfill x 4). A solution of (1*S*,2*S*)-(+)-*N*-Tosyl-1,2-diphenylethane-1,2-diamine[$\eta^6$-1-isopropyl-4-methylbenzene)-ruthenium(II) (Noyori catalyst, 4.6 mg, 0.006 mmol, 0.02 equiv.) in $CH_2Cl_2$ (0.1 mL)was added and, the solution degassed twice further. The mixture was stirred for 1 h, before being concentrated to give the crude propargylic alcohol. The alcohol was redissolved in $CH_2Cl_2$ (2 mL), and acetic anhydride (0.07 mL, 0.64 mmol, 2.0 equiv.), DMAP (crystals) and $Et_3N$ (0.14 mL, 0.96 mmol, 3.0 equiv.) were added. The mixture was stirred for 1 h, then quenched by addition of saturated $NH_4Cl$ (5 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 x 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (6:1→4:1 petrol / $Et_2O$) gave propargylic acetate **16** (107 mg, 0.30 mmol, 93% over two steps) as a colourless oil.

***R*$_f$** 0.40 (2:1 petrol / $Et_2O$).

**$[\alpha]_D^{25}$** -5.8 (*c* 0.1, $CHCl_3$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2962, 1736, 1372, 1231, 1159, 1022, 840, 700.

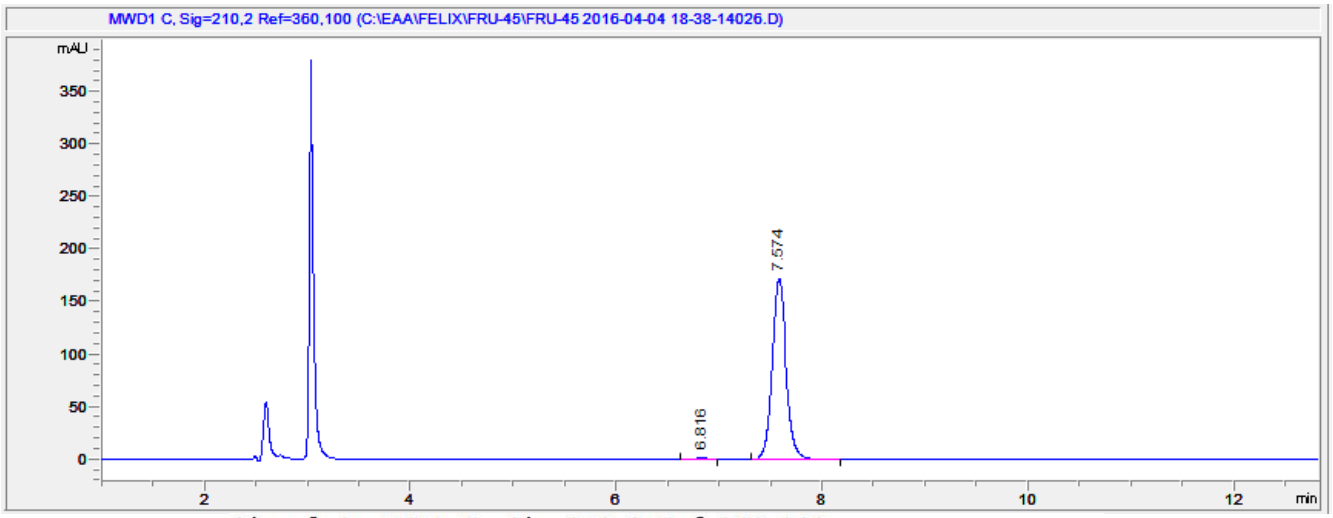
**$^1$H** NMR (400 MHz, $CDCl_3$) δ 7.21 (2H, dd, *J* = 8.3, 6.7 Hz, ArH), 7.13-7.01 (3H, m, ArH), 5.42-5.34 (1H, m, H5), 4.14 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.38-2.30 (2H, m, H2), 2.20 (2H, s, $CH_2Ph$), 2.09 (3H, s, COMe), 1.71-1.55 (4H, m, H5, H3), 1.26 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.13 (3H, s, SiMe), 0.13 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 173.2, 169.9, 138.8, 128.5, 128.5, 128.3, 128.3, 124.5, 103.7, 89.2, 64.0, 60.5, 34.1,

33.8, 26.1, 21.2, 20.6, 14.4, -2.1.

**HRMS** ($ESI^+$) calc. for $C_{20}H_{28}O_4Si$ $[M+Na]^+$ 383.1649, found 383.1653.

**HPLC** 99.2% *ee*. Chiralpak IB, 0.5 IPA/*n*-Hexane, 1.3 mL/min. *R*: 6.8 min; *S*: 7.6 min.

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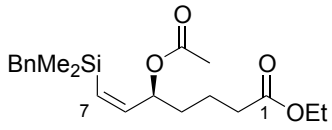
| 2 | 7.574 | BV | 0.1354 | 1606.04712 | 172.04387 | 99.6162 |

**Ethyl (*S*,*Z*)-5-acetoxy-7-(benzyldimethylsilyl)hept-6-enoate, 18**




A suspension of $Pd/CaCO_3$ (30.3 mg, 5 wt% Pd, 0.014 mmol, 0.05 equiv.) in toluene (1 mL) was evacuated / flushed with hydrogen three times, and then stirred for 15 min. A solution of **16** (103 mg, 0.284 mmol, 1.0 equiv.) and quinoline (7.0 µL, 0.060 mmol, 0.2 equiv.) in toluene (0.4 mL) and cyclohexene (0.14 mL) was added to the reation mixture. After stirring for 2 h, the reaction mixture was directly subjected to purification by flash column chromatography (6:1 petrol / $Et_2O$) to give alkene **18** (77 mg, 0.21 mmol, 75%) as a pale yellow oil.

$R_f$ 0.45 (2:1 petrol / $Et_2O$)

$[\alpha]_D^{25}$ -7.2 (*c* 1.0, $CHCl_3$).

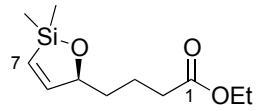
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2957, 1734, 1494, 1370, 1239, 1025, 833, 700.

$^1$**H** NMR (400 MHz, $CDCl_3$) δ 7.25-7.15 (2H, m, ArH), 7.11-7.02 (1H, m, ArH), 7.04-6.91 (2H, m, ArH), 6.19 (1H, dd, *J* = 14.4, 9.2 Hz, H6), 5.69 (1H, dd, *J* = 14.4, 0.8 Hz, H7), 5.38-5.28 (1H, m, H5), 4.12 (2H, q, *J* = 7.1 Hz, $OCH_2CH_3$), 2.35-2.22 (2H, m, H2), 2.19 (2H, ABq, *J* = 14.5 Hz, $CH_2Ph$), 2.04 (3H, s, 3H, COMe), 1.71-1.55 (3H, m, H3 and 2 x H4), 1.54-1.40 (1H, m, H3), 1.25 (3H, t, *J* = 7.1 Hz, $OCH_2CH_3$), 0.16 (3H, s, SiMe), 0.15 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 173.3, 170.3, 145.9, 139.8, 131.7, 128.4, 128.3, 124.2, 74.2, 60.5, 34.4, 34.1, 26.5, 21.4, 20.7, 14.4, -1.7, -1.7.

**HRMS** ($ESI^+$) calc. for $C_{20}H_{30}O_4Si$ $[M+NH_4]^+$ 380.2251, found 380.2261.

**Ethyl (*S*)-4-(2,2-dimethyl-2,5-dihydro-1,2-oxasilol-5-yl)butanoate, 6**




To a stirred solution of silane **18** (339 mg, 0.934 mmol, 1.0 equiv.) in THF (3.0 mL) at room temperature was added a 1.0 M solution of TBAF•$3H_2O$ in THF (0.98 mL, 0.98 mmol, 1.05 equiv.). The mixture was stirred for 30 min, then $K_2CO_3$ (193 mg, 1.40 mmol, 1.5 equiv.) was added to the reaction mixture, followed by water (150 µL, 5 vol%). After 30 min reaction was judged complete by TLC. Water (20 ml) and $Et_2O$ (20 ml) were added and the aqueous layer was extract with $Et_2O$ (3 x 20 ml) and the combined organic phases were dried ($MgSO_4$) and concentrated. The resultant alkenylsiloxane **6** (185 mg, 0.809 mmol, 87%), which was unstable to silica gel, was obtained as pale yellow oil that was used without further purification.

***$R_f$*** not measured due to instability towards silica gel.

**$[\alpha]_D^{25}$** +48.9° (*c* 1.0, $CHCl_3$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2959, 1734, 1250, 1158, 1030, 853, 788.

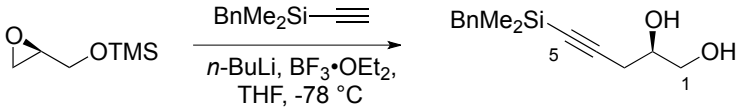
**$^1$H** NMR (400 MHz, $CDCl_3$) δ 6.81 (1H, dd, *J* = 10.5, 1.5 Hz, H6), 6.04 (1H, dd, *J* = 10.5, 2.2 Hz, H7), 4.71 (1H, ddt, *J* = 6.6, 4.0, 1.9 Hz, H5), 4.10 (2H, q, *J* = 7.2 Hz, $OC\underline{H}_2CH_3$), 2.36 (2H, t, *J* = 6.8 Hz, H2), 1.84-1.59 (m, 3H, H3 and 2 x H4), 1.53 – 1.30 (m, 1H, H3), 1.24 (3H, t, *J* = 6.9 Hz, $OCH_2C\underline{H}_3$), 0.25 (3H, s, SiMe), 0.23 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 173.7, 153.2, 127.3, 82.6, 60.4, 36.6, 34.5, 20.9, 14.4, 1.5, 0.7.

**HRMS** ($ESI^+$) calc. for $C_{11}H_{20}O_3Si$ $[M+H]^+$ 229.1255, found 229.1256.

## 2b. Synthesis of the central 6-membered cyclic siloxanes

**(*R*)-5-(Benzyldimethylsilyl)pent-4-yne-1,2-diol, 19.**




*n*-Butyllithium (4.82 mL of a 2.2 M solution in hexane, 10.6 mmol, 1.4 equiv.) was added to a solution of benzyl(ethynyl)dimethylsilane (1.98 g, 11.4 mmol, 1.5 equiv.) in THF (60 mL) at -78 °C. The mixture was stirred at -78 °C for 30 min, then $BF_3{\cdot}OEt_2$ (1.40 mL, 11.4 mmol, 1.5 equiv.) was added. The mixture was stirred for a further 10 min, then TMS-glycidol (1.13 g, 7.63 mmol, 1.0 equiv.) was added. The mixture was stirred for 1 h at -78 °C before being quenched by addition of 1N HCl (10 mL). The mixture was warmed to room temperature, and the aqueous phase was extracted with $Et_2O$ (3 x 15 ml). The combined organic phases were washed with brine (15 ml), dried ($Na_2SO_4$) and concentrated. The product was purified *via* flash column chromatography (2%→6% MeOH / $CH_2Cl_2$) to give the homopropargylic alcohol **19** (1.84 g, 7.38 mmol, 97%) as a colourless oil.

$R_f$ 0.20 (2% MeOH / $CH_2Cl_2$).

$[\alpha]_D^{25}$ -10.8 (*c* 1.0, $CHCl_3$).

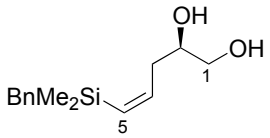
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3367 (br), 2958, 2177, 1600, 1493, 1250, 1030, 833.

**$^1$H** NMR (400 MHz, $CDCl_3$) This compound displayed unusual peak doubling in the proton NMR spectrum. δ 7.28-7.18 (2H, m, ArH), 7.15-7.02 (3H, m, ArH), 4.09 (1H, br s, OH), 3.91 (br s, 0.5H, H2), 3.82 (dq, *J* = 8.8, 3.2, 2.5 Hz, 0.5H, H2), 3.69 (dt, *J* = 9.5, 4.5 Hz, 0.5H, H3), 3.54 (dt, *J* = 10.8, 5.3 Hz, 0.5H, H3), 2.58-2.48 (1H, m, H3), 2.46 (1H, dd, *J* = 6.3, 2.7 Hz, H3), 2.26 (d, *J* = 4.8 Hz, 0.5H, H1), 2.21-2.14 (2H, m, $SiCH_2$), 1.92 (d, *J* = 5.9 Hz, 0.5H, H3), 0.14 (3H, s, SiMe), 0.11 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 141.0, 130.2, 130.1, 126.3, 105.7, 88.1, 71.9, 67.4, 28.2, 26.9, -0.0, -0.1.

**HRMS** ($ES^+$) calc. for $C_{14}H_{20}O_2Si$ $[M+NH_4]^+$ 266.1571, found 266.1590.

**(*R*,*Z*)-5-(Benzyldimethylsilyl)pent-4-ene-1,2-diol, S2**




A suspension of 5% $Pd/CaCO_3$ (128 mg, 0.060 mmol, 0.05 equiv.) in 5 mL toluene was evacuated three times and back-filled with hydrogen, and stirred for 15 min under a hydrogen atmosphere (1 atm, balloon). A solution of homopropargylic alcohol **19** (300 mg, 1.20 mmol, 1.0 equiv.) in toluene (1.5 mL), quinoline (0.07 mL, 0.60 mmol, 0.50 equiv.) and cyclohexene (0.6 mL) was added to the active palladium catalyst. The reaction was closely monitored by TLC and immediatedly flushed with nitrogen upon complete consumption of the starting material (1.5 h, varies with catalyst activity). Then, the reaction was filtered through celite and concentrated *in vacuo.* The product was purified *via* flash column chromatography (5% MeOH / $CH_2Cl_2$) to give (*R*,*Z*)-5-(benzyldimethylsilyl)pent-4-ene-1,2-diol as a colourless oil (243 mg, 0.94 mmol, 79%).

$R_f$ 0.20 (MeOH/ $CH_2Cl_2$ 2%).

**$[\alpha]_D^{25}$** -9.7 (*c* 1.0, $CHCl_3$).

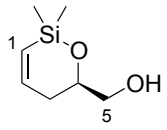
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3361 (br), 2361, 2341, 1601, 1493, 1248, 1207, 832

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 7.24-7.16 (2H, m, 2H, ArH), 7.12-7.03 (1H, m, ArH), 7.07-6.95 (2H, m, ArH), 6.35 (1H, dt, *J* = 14.2, 7.4 Hz, H5), 5.66 (1H, dt, *J* = 14.1, 1.4 Hz, H6), 3.75-3.64 (1H, m, H2), 3.61 (1H, ddd, *J* = 11.0, 5.6, 3.4 Hz, H1), 3.41 (1H, ddd, *J* = 11.2, 6.9, 4.1 Hz, H1), 2.22-2.15 (2H, m, H3), 2.17 (2H, s, $SiCH_2$), 2.03 (1H, d, *J* = 3.7 Hz, OH), 1.92 (1H, m, 1H, OH), 0.13 (6H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 144.6, 140.0, 131.0, 128.4, 128.3, 124.2, 71.7, 66.4, 37.4, 26.8, -1.4.

**HRMS** ($ES^+$) calc. for $C_{14}H_{22}O_2Si$ $[M+NH_4]^+$ 268.1727, found 268.1726.

**(*R*)-(2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasilin-6-yl)methanol, 20.**




The following hydrogenation was carried out in two batches (2 x 2.70 g) for scale purposes, to maxmise exposure of the solution to $H_2$. A suspension of $Pd/CaCO_3$ (462 mg, 0.22 mmol, 0.01 equiv.) in toluene (48 mL) was evacuated / backfilled with hydrogen three times, and stirred for 15 min under a hydrogen atmosphere (1 atm, balloon). Homopropargylic alcohol **19** (2.70 g, 10.8 mmol, 1.0 equiv.) in toluene (12 mL), quinoline (0.63 mL, 5.4 mmol, 0.50 equiv.) and cyclohexene (6 mL) were added to the active palladium catalyst. The reaction was closely monitored by TLC and immediately flushed with nitrogen upon complete consumption of the starting material (45 min, varies with catalyst activity). The material of the two runs was combined, filtered through celite ($Et_2O$ eluent), and the filtrate washed with 1N HCl (30 mL), and brine (30 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated *in vacuo.*

A 1.0 M solution of tetrabutylammonium fluoride in THF (26 mL, 26 mmol, 1.2 equiv., freshly prepared from TBAF•$3H_2O$ (8.22 g) and THF (26 mL) was added to a solution of the crude homoallylic alcohol in THF (120 mL), which was stirred for 1.5 h. The reaction mixture was then diluted with water (60 mL), the organic layer was separated, and the aqueous phase was extracted with $Et_2O$ (3x 30 mL). The combined organic phase was washed with brine (50 mL), dried ($Na_2SO_4$) and concentrated. The crude product was filtered rapidly through a short plug of silica gel ($Et_2O$ eluent) to give the cyclic alkenylsiloxane **20** as a colourless oil (2.79 g, 17.6 mmol, 81%).

$R_f$ 0.50 ($Et_2O$).

**$[\alpha]_D^{25}$** +24.6 (*c* 0.95, $CHCl_3$).

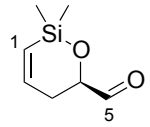
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3376 (br), 2955, 2919, 2851, 2362, 1589, 1252, 1040, 841, 790.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.77 (1H, ddd, *J* = 14.2, 6.0, 2.3 Hz, H2), 5.76 (1H, ddd, *J* = 14.1, 2.9, 1.0 Hz, H1), 4.03 (1H, app ddt, *J* = 10.4, 6.3, 3.0 Hz, H4), 3.60 (1H, ddd, *J* = 11.1, 7.6, 3.4 Hz, H5), 3.49 (1H, ddd, *J* = 11.2, 6.6, 4.7 Hz, 1H, H5), 2.34-2.14 (2H, m, H3, OH), 2.06 (1H, dddd, *J* = 17.7, 6.0, 2.7, 0.9 Hz, H3), 0.20 (3H, s, SiMe), 0.19 (3H, s, SiMe).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 146.7, 127.1, 71.8, 67.0, 32.2, -0.2, -0.5.

**HRMS** ($ES^+$) calc. for $C_7H_{14}O_2Si$ $[M+H]^+$ 159.0841, found 159.0841.

**(*R*)-2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasiline-6-carbaldehyde, S3**




Dimethylsulfoxide (1.56 mL, 22.0 mmol, 13.6 equiv.) was added to a solution of $SO_3$•py (834 mg, 5.24 mmol, 3.5 equiv.) in $CH_2Cl_2$ (4 mL) and stirred for 30 min, then a solution of diisopropylethylamine (1.56 mL, 8.96 mmol, 5.5 equiv.) and alcohol **20** (257 mg, 1.62 mmol, 1.0 equiv.) in $CH_2Cl_2$ (5.5 mL) was added *via* cannula. After 90 min the reaction was quenched by addition of 0.1 N HCl solution, extracted with $CH_2Cl_2$, dried ($Na_2SO_4$) and concentrated to give the aldehyde as a yellow oil which was used in the next step without further purification (226 mg, 1.37 mmol, 85%. sample contained in addition ~5% by mass DMSO).

$R_f$ 0.20 (9:1 petrol / $Et_2O$).

$[\alpha]_D^{25}$ +59.9 (*c* 1.0, $CHCl_3$).

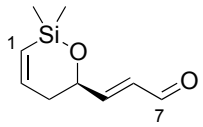
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3427, 2959, 2924, 2361, 1589, 1252, 1085, 1045, 842, 790.

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 9.68 (1H, s, H5), 6.77 (1H, ddd, *J* = 14.8, 6.5, 3.1 Hz, H2), 5.81 (1H, ddd, *J* = 14.1, 2.6, 1.1 Hz, H1), 4.33 (1H, dd, *J* = 10.0, 3.7 Hz, H4), 2.42 (1H, dddd, *J* = 17.8, 5.2, 3.7, 1.1 Hz, H3), 2.31 (1H, app ddt, *J* = 17.7, 10.0, 2.7 Hz, H3), 0.26 (3H, s, SiMe), 0.23 (3H, s, SiMe).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 203.1, 145.2, 128.1, 76.1, 30.6, -0.1, -0.4.

**HRMS** ($ES^+$) calc. for $C_7H_{12}O_2Si$ $[M+H]^+$ 157.0685, found 157.0649.

**(*R*,*E*)-3-(2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasilin-6-yl)acrylaldehyde, 21**




(Triphenylphosphoranylidene)acetaldehyde (402 mg, 1.32 mmol, 1.2 equiv.) was added to a solution of (*R*)-2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasiline-6-carbaldehyde **S3** (238 mg, 1.10 mmol) in toluene (11 mL), and the mixture was stirred overnight in the dark. The $^1$H NMR of an aliquot showed remaining starting material (12%), and additional triphenylphosphoranylidene)acetaldehyde (40.2 mg, 0.13 mmol, 0.12 equiv.) was added, and the reaction was stirred for 24 h until complete as judged by $^1$H NMR spectroscopy. The reaction mixture was directly purified by flash column chromatography (9:1→6:1 Petrol / $Et_2O$) to give aldehyde **21** (101 mg, 0.553 mmol, 50%) as a colourless oil.

$R_f$ 0.25 (5:1 petrol / $Et_2O$).

$[\alpha]_D^{25}$ +96.9 (*c* 1.0, $CHCl_3$).

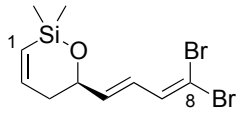
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2992, 2958, 2361, 1691, 1588, 1252, 1101, 971, 958, 844, 790.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.59 (1H, d, *J* = 8.0 Hz, H7), 6.81 (1H, dd, *J* = 15.6, 3.9 Hz, H5), 6.81-6.71 (1H, m, H2), 6.37 (1H, ddd, *J* = 15.5, 8.0, 1.7 Hz, H6), 5.83 (1H, ddd, *J* = 14.1, 2.6, 1.2 Hz, H1), 4.77-4.66 (1H, m, H4), 2.46-2.11 (2H, m, H3), 0.22 (3H, s, SiMe), 0.22 (3H, s, SiMe).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.8, 158.2, 145.8, 130.9, 127.9, 70.3, 35.4, -0.1, -0.5.

**HRMS** ($EI^+$) calc. for $C_9H_{14}O_2Si$ $[M+H]^+$ 183.0841, found 183.0808.

**(*R*,*E*)-6-(4,4-Dibromobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 22**




An oven dried flask containing $PPh_3CHBr_2Br$•MeCN (252 mg, 0.45 mmol, 2.2 equiv.) was evacuated and backfilled with nitrogen. Potassium *t*-butoxide (1 M in THF, 0.41 mL, 0.41 mmol, 2.0 equiv.) was added, and the resulting suspension was stirred for 1 h. A solution of aldehyde **21** (40.3 mg, 0.206 mmol, 1.0 equiv.) in 0.2 mL THF was added (rinse with 0.2 mL THF). The reaction was stirred for 2 h, and then directly purified by flash column chromatography on silica gel (9:1 petrol / $Et_2O$) to give the dibromide **22** as a colourless oil (59.3 mg, 0.175 mmol, 86%).

$R_f$ 1.00 (9:1 petrol / $Et_2O$).

**$[\alpha]_D^{20}$** +25.8 (*c* 1.0, $CHCl_3$).

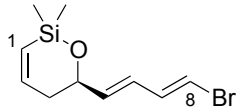
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2981, 2889, 2358, 2341, 1588, 1251, 958.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.93 (1H, dd, *J* = 10.3, 0.7 Hz, H7), 6.85-6.65 (1H, m, H2), 6.33 (1H, ddd, *J* = 15.3, 10.3, 1.5 Hz, H6), 5.95 (1H, ddd, *J* = 15.3, 5.5, 0.8 Hz, H5), 5.85-5.69 (1H, m, H1), 4.48 (1H, dtd, *J* = 9.0, 5.3, 1.5 Hz, 1H, H4), 2.54-2.02 (2H, m, H3), 0.21 (3H, s, H1), 0.21 (3H, s, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 146.3, 139.6, 136.6, 127.7, 126.5, 91.2, 71.3, 36.2, 0.0, -0.4.

**HRMS** ($ES^+$) calc. for $C_{14}H_{24}O_4$ $[M+2H]^{2+}$ not found.

**(*R*)-6-((1*E*,3*E*)-4-Bromobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 8**




**22** (562 mg, 1.66 mmol, 1.00 equiv.) was dissolved in diethyl phosphite (3.40 mL, 41.5 mmol, 25 equiv.) and triethylamine (1.20 mL, 8.30 mmol, 5.0 equiv.) was added. The reaction was stirred at room temperature for 24 h, during which time its colour changed to orange. The mixture was diluted with water (10 mL) and 1 N NaOH (30 mL), and extracted with pentane (3 x 20 mL). The combined organic phases were washed with 1 N NaOH (3 x 20 mL), dried ($MgSO_4$) and concentrated. Purification by flash column chromatography (19:1 petrol / $Et_2O$) afforded the dienyl bromide **8** as a 2:1 *E*:*Z* mixture (358 mg, 1.38 mmol, 84%).

This *E*/*Z* mixture (0.89 g, 3.40 mmol) was dissolved in ethanol (10 mL), and NaOMe (25% w/w, 3.5 mL, 1.7 mmol, 0.5 equiv.) was added. The mixture was heated to reflux for 6 h. After cooling to room temperature, the

mixture was diluted with water (20 mL), and extracted with ether (3 x 20 mL). The organic layers were dried ($MgSO_4$) and concentrated, affording a mixture of the *E*,*E*-dienyl bromide **8** and the terminal alkyne. This mixture was directly carried on to the following reaction.

To a solution of CuI (65 mg, 0.34 mmol, 0.10 equiv.), $Pd(PPh_3)_4$ (198 mg, 0.17 mmol, 0.05 equiv.) in triethylamine (34 mL) and DMF (17 mL) was added the *E*-dienyl bromide / alkyne mixture from the previous step. The reaction mixture was stirred overnight, then diluted with water (10 mL) and petrol / $Et_2O$ (1:1, 150 mL). The organic layer was washed with half-saturated $NH_4Cl$ solution (3 x 50 mL), brine (20 mL), dried ($MgSO_4$) and concentrated. Purification by flash column chromatography (19:1 petrol / $Et_2O$) afforded the product as the pure (*E*) isomer (477 mg, 1.6 mmol, 46% over 2 steps, 87% pure with $PPh_3$). Additional $PPh_3$ was removed by stirring with CuCl in acetone for 1 h and subsequent filtration.

***R*$_f$** 1.00 (9:1 petrol / ether).

**[α]$_D^{20}$** +51.1 (*c* 1.0, $CHCl_3$).

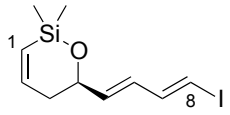
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$). 2988, 2957, 2361, 1587, 1251, 976, 789.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.81-6.66 (2H, m, H2, H7), 6.31 (1H, dq, *J* = 13.5, 0.7 Hz, H8), 6.22 (1H, dddd, *J* = 15.2, 10.9, 1.5, 0.6 Hz, H6), 5.89-5.67 (2H, m, H1, H5), 4.62-4.29 (1H, m, H4), 2.25-2.15 (2H, m, H3), 0.20 (3H, s, H1), 0.20 (3H, s, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 146.6, 137.1, 136.8, 127.6, 127.0, 108.8, 71.1, 36.4, -0.1, -0.4.

**HRMS** ($ES^+$) calc. for $C_{10}H_{15}BrOSi$ $[M+MeOH+H]^+$ 293.0396, found 293.0385.

**(*R*)-6-((1*E*,3*E*)-4-Iodobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 7**




Anhydrous $CrCl_2$ (515 mg, 4.19 mmol, 8.0 equiv.) was weighed into a dry Schlenk tube under an $N_2$ atmosphere. It was gently heated under vacuum until the greenish colour turned grey, and the solid became free-flowing. The flask was cooled to room temperature and anhydrous THF (5.5 mL) was added. After stirring this suspension for 10 min, iodoform (413 mg, 1.05 mmol, 2.0 equiv.) in THF (2.6 mL) was introduced which caused the solution to immediately turn red. A solution of aldehyde **21** (96.4 mg, 0.52 mmol, 1.0 equiv.) in THF (5.5 mL) was added, and the mixture was stirred for 1 h in the dark. The reaction was quenched by addition of aqueous $Na_2S_2O_3$ solution, and the aqueous layer extracted with $Et_2O$ (3 x 30 mL). The combined organic layers were washed with brine, dried ($Na_2SO_4$) and concentrated. Purification by flash column chromatography (1:0→50:1 petrol / $Et_2O$) gave an inseparable mixture of *E*/*Z* isomers (5:1) of the iodidiene **7** (95.7 mg, 0.312 mmol, 60%).

***R*$_f$** 0.20 (petrol).

**[α]$_D^{25}$** +46.0 (*c* 1.0, $CHCl_3$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2956, 2922, 2854, 2360, 2341, 1681, 1259, 1030, 798.

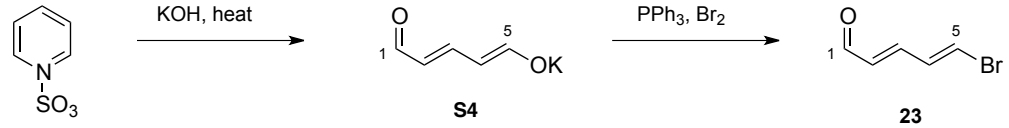
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.02 (1H, ddd, *J* = 14.4, 10.7, 0.7 Hz, H7), 6.86-6.65 (1H, m, H2), 6.32 (1H, dd, *J* =

14.4, 0.8 Hz, H8), 6.22 (1H, dddd, *J* = 15.2, 10.8, 1.6, 0.6 Hz, H6), 5.85-5.66 (2H, m, H1, H5), 4.44 (1H, dtd, *J* = 10.0, 5.1, 1.4 Hz, H4), 2.36-2.02 (2H, m, H3), 0.21 (3H, s, SiMe), 0.20 (3H, s, SiMe).

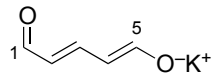
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 146.54, 144.82, 136.51, 129.49, 127.55, 79.18, 70.99, 36.39, -0.04, -0.41.

**HRMS** ($EI^+$) calc. for $C_{10}H_{15}IO_2Si$ $[M+H]^+$ 307.0015, found 306.9994.

Bromide **23** was prepared according to the following Scheme:




**Potassium (1*E*,3*E*)-5-oxopenta-1,3-dien-1-olate, S4**

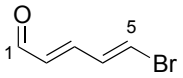



Pyridine sulfur trioxide complex (21.6 g, 98% purity, 136 mmol, 1.0 equiv.) was added portionwise over 5 min to a 500 mL flask containing a solution of KOH (31.0 g, 4.1 equiv.) in 75 mL of $H_2O$ at -20 °C. The reaction was stirred vigorously at -20°C for 1.5 h, then the ice bath was removed. The mixture was stirred for a further 1.5 h, then heated to 40 °C for 30 min, and then cooled and maintained at 5 °C overnight. During this time, a solid precipitated which was isolated by filtration. The solid was washed with acetone (2 x 30 mL) and dried in air. In a 1 L flask, 500 mL methanol and 1 g activated carbon were added to the solid, and the resulting mixture was heated to reflux for 30 min. The activated carbon was then removed by hot filtration. the filtrate was concentrated to 30 mL and cooled to 5 °C for 2 h. The resulting precipitate was washed with acetone until the filtrate was colourless, then dried. The title compound **S4** (10.0 g, 73.5 mmol, 54%) was isolated as a yellow solid. The analytical data was in agreement with that reported in the literature (*Org. Synth.* **1979**, *59*, 79).

**$^1$H NMR** (400 MHz, DMSO-d6) δ 8.64 (2H, d, *J* = 9.2 Hz, H1, H5), 7.02 (1H, t, *J* = 13.1 Hz, H3), 5.08 (2H, dd, *J* = 13.1, 9.2 Hz, H2, H4).

**$^{13}$C NMR** (101 MHz, DMSO-d6) δ 184.4, 159.9, 106.3

**(2*E*,4*E*)-5-Bromopenta-2,4-dienal, 23**




Potassium (1*E*,3*E*)-5-oxopenta-1,3-dien-1-olate **S4** (3.72 g, 27.3 mmol, 1.0 equiv.) was added to a solution of $PPh_3$ (7.16 g, 27.3 mmol, 1.0 equiv.) and $Br_2$ (1.54 mL, 30.0 mmol, 1.1 equiv.) in dry $CH_2Cl_2$ (150 mL) at 0 °C in the dark. The reaction mixture was stirred for 4 h. 30 g of silica was added, and the solvent was removed *in vacuo*. The dry-loaded crude product was purified by flash column chromatography (eluent 7:3 petrol:$Et_2O$). The solvent was removed from the eluate to form a white solid (mixture of *E*,*E* and *E*,*Z* isomers). This solid was melted by heating it to 60 °C in a water bath, and heptane (20 mL) was added under vigorous stirring. A solid precipitated immediatedly upon addition of heptane. The heptane was removed by filtration, the solid washed

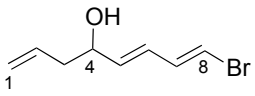
with 5 mL of heptane and dried under low vacuum to afford **23** (2.00 g, 12.4 mmol, 46%). The analytical data was in good agreement with that reported in the literature (*J. Chem. Soc. Perkin Trans. 1*, **1997**, 1639-1645).

$R_f$ 0.60 (2:1 petrol / $Et_2O$).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.59 (1H, d, J = 7.8 Hz), 7.05-6.92 (3H, m), 6.24-6.13 (1H, m).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.2, 147.8, 135.7, 132.1, 119.9.

**(5*E*,7*E*)-8-Bromoocta-1,5,7-trien-4-ol, (±)-24**




Allylmagnesium chloride (1.7 M in THF, 8.7 mL, 14.8 mmol, 1.2 equiv.) was added dropwise over 5 min to a solution of (2*E*,4*E*)-5-bromopenta-2,4-dienal (1.99 g, 12.4 mmol, 1.0 equiv.) in dry THF (24 mL) at 0 °C. The reaction was stirred for 1 h, then quenched by addition of 1 N HCl (20 mL) and extracted with $Et_2O$ (3 x 30 mL). The combined organic layers were extracted with brine (30 mL), then dried ($MgSO_4$) and concentrated to yield a yellow-brown oil. Purification by flash column chromatography (4:1 petrol / $Et_2O$) to afford (±)-**24** (2.34 g, 11.5 mmol, 93%) as a yellow oil.

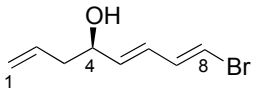
$R_f$ 0.32 (3:1 petrol / $Et_2O$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3360, 3072, 2926, 1641, 1584, 978, 919, 741.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.71 (1H, ddd, *J* = 13.5, 10.8, 0.8 Hz, H7), 6.33 (1H, dd, *J* = 13.4, 0.6 Hz, H8), 6.19 (1H, dddd, *J* = 15.3, 10.8, 1.4, 0.6 Hz, H6), 5.86-5.72 (2H, m, H2, H5), 5.22-5.12 (2H, m, H1), 4.21 (1H, app q, *J* = 5.7 Hz, H4), 2.43-2.23 (2H, m, H3), 1.71 (1H, s (br), OH).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 136.9, 136.4, 133.8, 127.7, 119.0, 109.2, 70.9, 41.9.

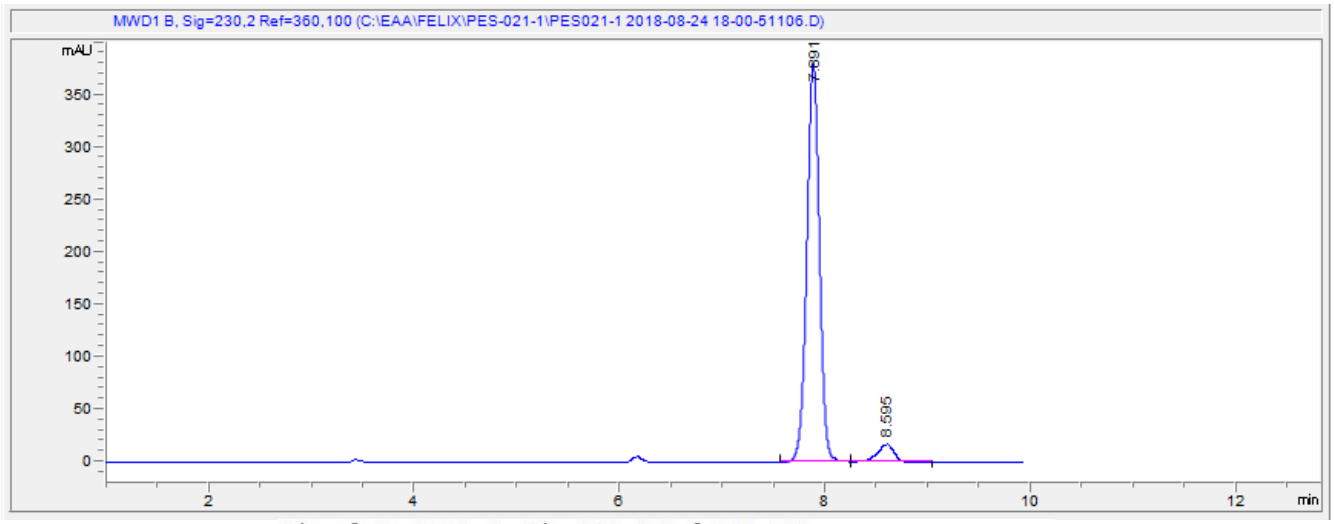
**(*R*,5*E*,7*E*)-8-Bromoocta-1,5,7-trien-4-ol, 24**




(5*E*,7*E*)-8-bromoocta-1,5,7-trien-4-ol (500 mg, 2.46 mmol, 1.0 equiv.) was added dropwise to a solution of Ti(O*i*-Pr)$_4$ (0.73 mL, 2.46 mmol, 1.0 equiv.) and (+)-diisopropyl-L-tartrate (0.62 mL, 2.95 mmol, 1.2 equiv.) in $CH_2Cl_2$ (25 mL) at -20 °C, and the mixture was stirred for 40 min. *Tert*-butylhydroperoxide (0.27 mL, 1.48 mmol, 0.6 equiv.) was added dropwise over 5 min, and the resultant solution was stored in the freezer (-20 °C) for 24 h. NaOH (200 mg) and brine (10 mL) were then added, the reaction was stirred for 1 h at room temperature, then citric acid (3 g) was added and the solution formed was extracted with $Et_2O$ (3 x 30 mL). The organic phase was dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by flash column chromatography (5:1 petrol:$Et_2O$) afforded **24** (198 mg, 0.975 mmol, 40%, 97.5% *ee*) as a yellow oil. The spectroscopic analytical data were identical to that of (5*E*,7*E*)-8-bromoocta-1,5,7-trien-4-ol, **(±)-24**.

**$[\alpha]_D^{20}$** +6.9 (*c* 1.0, $CHCl_3$).

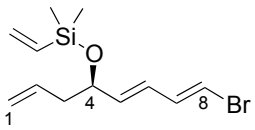
**HPLC:** 97.3% *ee.* Chiralpak IC, 2.5% IPA/*n*-Hexane, 1.0 mL/min. *R*: 7.9 min; *S*: 8.6 min.




Signal 2: MWD1 B, Sig=230,2 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.891 | BV | 0.1315 | 3254.82471 | 381.45050 | 98.6510 |
| 2 | 8.595 | MM | 0.0503 | 44.50709 | 14.74728 | 1.3490 |

**(((*R*,5*E*,7*E*)-8-Bromoocta-1,5,7-trien-4-yl)oxy)dimethyl(vinyl)silane, S5**




Chlorodimethylvinylsilane (0.75 mL 5.41 mmol, 1.5 equiv.) was added dropwise to a solution of **24** (733 mg, 3.61 mmol, 1.0 equiv.) and $Et_3N$ (1.0 mL, 7.22 mmol, 2.0 equiv.) in $CH_2Cl_2$ (4.0 mL) at 0 °C. The mixture was stirred for 15 min, then quenched by addition of $NH_4Cl$ (1 mL) and $H_2O$ (1 mL), and extracted with $Et_2O$ (1 x 2 mL then 2 x 1 mL). The organic layer was dried ($MgSO_4$) and concentrated to leave a yellow oil. Purification by flash column chromatography (19:1 pentane / $Et_2O$) afforded the title compound **S5** (916 mg, 3.19 mmol, 89%) as a yellow oil.

***R*$_f$** 0.91 (19:1 petrol / $Et_2O$)**.**

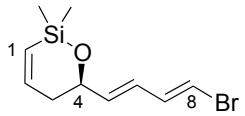
**[α]$_D^{20}$** +12.6 (*c* 1.0, $CHCl_3$).

**IR** (thin film, vmax / cm-1) 3065, 2960, 1642, 1585, 1407, 1361, 1253, 1076, 978, 916, 836, 786.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.69 (1H, ddd, J = 13.4, 10.8, 0.7 Hz, H7), 6.29 (1H, d, J = 13.5 Hz, H8), 6.17-5.97 (m, 3H, H2/H5/H6/SiCH=$CH_2$), 5.81-5.67 (m, 3H, H2/H5/H6/SiCH=$CH_2$), 5.08-5.01 (2H, m, H1), 4.17 (1H, m, H4), 2.34-2.20 (2H, m, H3), 0.18 (3H, s, SiMe), 0.18 (3H, s, SiMe).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.8, 137.3, 137.1, 134.5, 133.4, 127.0, 117.5, 108.6, 72.6, 42.6, -1.3, -1.4.

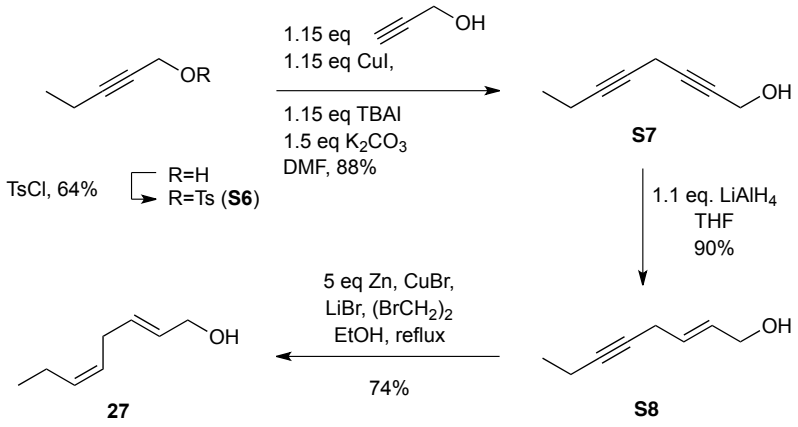
**(*R*)-6-((1*E*,3E)-4-Bromobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 8.**



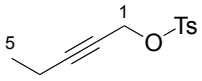

(((*R*,5*E*,7*E*)-8-bromoocta-1,5,7-trien-4-yl)oxy)dimethyl(vinyl)silane **S5** (897 mg, 3.12 mmol, 1.0 equiv.) was added to a solution of Schrock's catalyst (100 mg, 0.13 mmol, 0.04 equiv.) in degassed benzene (31 mL, freeze-pump-thaw x 3) under argon, which formed a brown solution. The reaction mixture was stirred for 17 h at room temperature, during which time the colour turned from brown to dark green. The solvent was removed *in* vacuo, and the residue purified by flash column chromatography (19:1 petrol / $Et_2O$) to afford **8** (783 mg, 3.02 mmol, 97%) as a pale orange oil. The analytical data was in agreement with above **8** prepared as outlined above.

## 2c. Synthesis of the left hand side vinyl iodides

Alcohol **27** was prepared according to the following sequence. References are given in the subsequent synthetic procedures.




**Pent-2-yn-1-yl 4-methylbenzenesulfonate, S6**



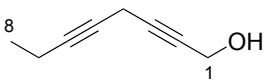

*p*-Toluenesulfonyl chloride (13.6 g, 71.3 mmol, 1.2 equiv.) was added portionwise over 10 min to a solution of pent-2-yn-1-ol (5.5 mL, 59.4 mmol, 1.0 equiv.) in $Et_2O$ (120 mL) at 0 °C. The ice bath was removed, and the mixture gradually warmed to room temperature over 30 min. The reaction was then diluted with $H_2O$ (50 mL), the aqueous layer was extracted with $Et_2O$ (3 x 50 mL), and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Purification of the residue by flash column chromatography on silica gel (9:1 → 4:1 petrol / $Et_2O$) gave the title compound **S6** (9.00 g, 37.8 mmol, 64%) as colourless oil, along with 1-chloropent-2-yne (1.60 g, 15.7 mmol, 27%). The analytical data matched that reported in the literature (*Synth. Commun.* **2017**, *47*, 1848-1853).

***R*$_f$** 0.23 (9:1 petrol / $Et_2O$).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.03-7.63 (2H, m, ArH), 7.40-7.30 (2H, m, ArH), 4.69 (2H, t, *J* = 2.2 Hz, H1), 2.44 (3H, s, ArMe), 2.28-1.89 (2H, m, H4), 1.01 (3H, t, *J* = 7.5 Hz, H5).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.0, 133.5, 129.8, 128.3, 91.9, 71.3, 58.9, 21.8, 13.3, 12.5.

**Octa-2,5-diyn-1-ol, S7**




To a solution of copper iodide (15.6 g, 82.1 mmol, 1.15 equiv., weighed in the glovebox), $Me_4NI$ (30.3 g, 82.1 mmol, 1.15 equiv.) and $K_2CO_3$ (14.8 g, 107 mmol, 1.50 equiv.) in dry DMF (142 mL) at 0 °C was added propargyl alcohol (4.8 mL, 82.1 mmol, 1.15 equiv.), which caused the formation of a solid. After stirring for 30 min, a solution of pent-2-yn-1-yl 4-methylbenzenesulfonate **S6** (17.0 g, 71.4 mmol, 1.00 equiv.) in DMF (10 mL) was

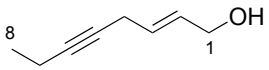
added. The reaction was stirred for 1 day at room temperature before being quenched by addition of 100 mL $NH_4Cl/NH_4OH/H_2O$ (1:1:1 v:v:v), and then being stirred for a further day. The blue solution was further diluted with $H_2O$ (100 mL), and extracted with EtOAc (150 mL, then 3 x 50 mL). The combined organic phases were washed with 5% $NaCl/H_2O$ (3 x 120 mL), brine (50 mL), dried ($MgSO_4$) and concentrated. Purification of the residue by flash column chromatography on silica gel ($Et_2O$) gave the title compound **S7** (7.73 g, 62.3 mmol, 88%) as a colourless oil. The analytical data matched that reported in the literature (*Tetrahedron Lett.* **1992**, *33*, 5757).

$R_f$ 0.3 (3:1 petrol / $Et_2O$).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.26 (2H, t, *J* = 2.2 Hz, H1), 3.18 (2H, p, *J* = 2.3 Hz, H4), 2.17 (2H, qt, *J* = 7.5, 2.4 Hz, H7), 1.11 (3H, t, *J* = 7.5 Hz, H8).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 82.6, 81.0, 78.5, 72.8, 51.4, 14.0, 12.5, 10.0.

**(*E*)-Oct-2-en-5-yn-1-ol, S8**

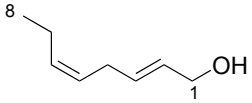



To a suspension of $LiAlH_4$ (3.93 g, 104 mmol, 1.10 equiv.) in $Et_2O$ (150 mL) under $N_2$ at 0 °C was added octa-2,5-diyn-1-ol **S7** (11.5 g, 94.1 mmol, 1.0 equiv.) in $Et_2O$ (20 mL) dropwise over 20 min (plus 10 mL $Et_2O$ rinse). The mixture was warmed to room temperature overnight while stirring and then quenched by slow addition of a solution of Na K tartrate (50 g) in water (200 mL). The resulting suspension was stirred vigorously for 6 h, then the phases were separated, and the aqueous layer was extracted with $Et_2O$ (3 x 100 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$) and concentrated before being filtered through a silica plug (petrol ether/ether 1:1) to give the title compound **S8** (10.5 g, 84.3 mmol, 90%) as a colourless oil. The analytical data matched that reported in the literature (*Synth. Commun.* **2017**, *47*, 1848-1853).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.08-5.82 (1H, m, H3), 5.80-5.58 (1H, m, H2), 4.14 (2H, app td, *J* = 5.7, 1.4 Hz, H1), 3.02-2.75 (2H, m, H4), 2.19 (2H, qt, *J* = 7.5, 2.4 Hz, H7), 1.38 (1H, t, *J* = 5.5 Hz, H0), 1.13 (3H, t, *J* = 7.5 Hz, H8).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 130.4, 127.5, 84.3, 76.1, 63.4, 21.9, 14.4, 12.6.

**(2*E*,5*Z*)-Octa-2,5-dien-1-ol, 27**



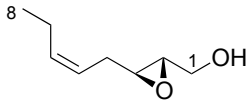

To a suspension of zinc (1.47 g, 22.3 mmol, 5.00 equiv.) in dry ethanol (2.5 mL) under argon was added dibromoethane (0.10 mL, 1.12 mmol, 0.25 equiv.). The mixture was heated to reflux and a further portion of dibromoethane (0.10 mL, 1.12 mmol, 0.25 equiv.) was added cautiously through the reflux condenser, causing vigorous gas evolution. The reaction was cooled to 50 °C and a solution of LiBr (196 mg, 2.25 mmol, 0.50 equiv.) and CuBr (323 mg, 2.25 mmol, 0.50 equiv.) in THF (3 mL) was added. The reaction was stirred for 10 min at that temperature, then (*E*)-oct-2-en-5-yn-1-ol **S8** (560 mg, 4.51 mmol, 1.0 eq) in ethanol (1 mL / rinse with 0.5 mL) was added. The reaction mixture was heated to reflux and stirred at that temperature overnight. The mixture

was then cooled to room temperature, and the resultant suspension was filtered, and rinsed with $Et_2O$ (30 mL). 30 mL half-saturated $NH_4Cl$ solution was added to the filtrate, then the aqueous layer was extracted with $Et_2O$ (3 x 10 mL). The combined organic phases were washed with brine (20 mL) and dried ($MgSO_4$) to give the alcohol **27** (403 mg, 3.19 mmol, 71%) as colourless oil. The analytical data matched that reported in the literature (*Tetrahedron* **2015**, *71*, 5589).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.83-5.51 (2H, m, H2, H3), 5.44 (1H, m, H6), 5.36-5.17 (1H, m, H5), 4.09 (2H, t, *J* = 3.4 Hz, H1), 2.78 (2H, dd, *J* = 7.3, 4.4 Hz, H4), 2.11-1.84 (2H, m, H7), 1.63-1.44 (1H, br s, OH), 0.97 (3H, t, *J* = 7.5 Hz, H8).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 133.0, 131.5, 129.3, 126.1, 63.8, 30.0, 20.6, 14.4.

**((2*S*,3*S*)-3-((*Z*)-pent-2-en-1-yl)oxiran-2-yl)methanol, S9**



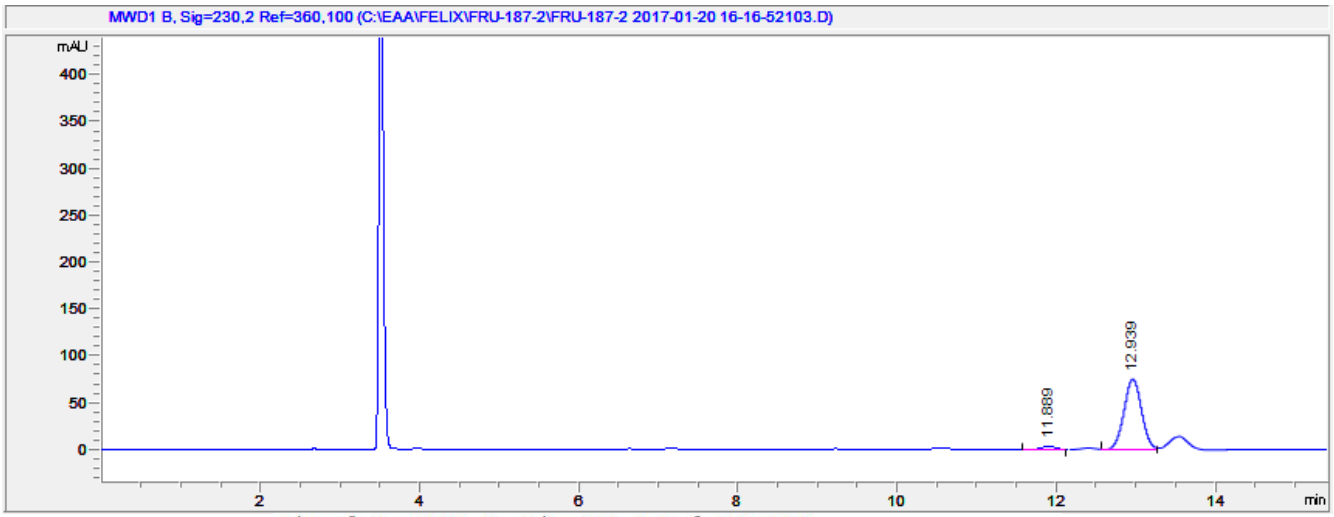

Prepared following a procedure reported in the literature (*Synth. Commun.* **2013**, *43*, 1145). To a cooled (-78 °C) suspension of activated 3 Å MS (0.4 g) in $CH_2Cl_2$ (20 mL) was added Ti(O*i*-Pr)$_4$ (0.19 mL, 0.62 mmol, 0.1 equiv.) and L-(+)-diisopropyltartrate (0.15 mL, 0.68 mmol, 0.11 equiv.). After 5 min, a solution of **27** (779 mg, 6.17 mmol) in $CH_2Cl_2$ (16 mL) was added, followed by TBHP (2.24 mL, ~5.5 M in decane, 12.3 mmol) dropwise over 5 min. The resulting mixture was maintained at -20 °C for 20 h (freezer), then quenched by addition of a cooled solution of $FeSO_4 \bullet 7H_2O$ (300 mg) and tartaric acid (100 mg) in water (5 mL). The mixture was warmed to room temperature and stirred vigorously for 2 h, then extracted with ether (2 x 30 mL). The combined organic phases were treated with a pre-cooled (0 °C) solution of 30% (w/v) NaOH in brine (10 mL) and stirred for 1 h at rt. The layers were separated, and the aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were dried ($Na_2SO_4$), filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (1:1→1:3 petrol / $Et_2O$) to give the title compound **S9** (750 mg, 5.28 mmol, 86%) as a colourless oil. The analytical data matched that reported in the literature (*Synth. Commun.* **2013**, *43*, 1145).

***R*$_f$** 0.2 (1:1 petrol / $Et_2O$).

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 5.54 (1H, dtt, *J* = 10.4, 7.2, 1.5 Hz, H6), 5.35 (1H, dtt, *J* = 10.7, 7.4, 1.6 Hz, 1H, H5), 3.91 (1H, ddd, *J* = 12.6, 5.2, 2.5 Hz, H1), 3.62 (1H, ddd, *J* = 12.5, 6.9, 4.3 Hz, H1), 3.00 – 2.84 (1H, m, 2H, H6/H7), 2.41 – 2.30 (1H, m, H4), 2.36-2.25 (1H, m, H4), 2.12-1.98 (2H, m, H7), 1.86-1.80 (1H, m, H0), 0.97 (3H, t, *J* = 7.5 Hz, H8).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 135.1, 122.4, 61.7, 58.1, 55.4, 29.3, 20.8, 14.3.

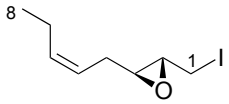
**HPLC:** 92.3% *ee.* Chiralpak IC, 1% IPA/*n*-Hexane, 1.3 mL/min. (*S*,*S*): 11.9 min; (*R*,*R*): 13.0 min, benzoate derivative of the alcohol.




Signal 2: MWD1 B, Sig=230,2 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 11.891 | VB | 0.1556 | 46.03008 | 3.47274 | 3.8319 |
| 2 | 12.938 | BV | 0.2149 | 1155.18945 | 75.34106 | 96.1681 |

**(2*R*,3*S*)-2-(Iodomethyl)-3-((*Z*)-pent-2-en-1-yl)oxirane, 25**




To a cooled (0 °C) suspension of triphenylphosphine (1.35 g, 5.20 mmol, 1.02 equiv.), imidazole (351 mg, 5.20 mmol, 1.02 equiv.) and ((2*S*,3*S*)-3-((*Z*)-pent-2-en-1-yl)oxiran-2-yl)methanol (718 mg, 5.05 mmol, 1.0 equiv.) in $CH_2Cl_2$ (10 mL) was added a solution of iodine (1.31 g, 5.15 mmol, 1.02 equiv.) in $CH_2Cl_2$ (15 mL). After stirring for 10 min, the ice bath was removed and stirring was continued at room temperature for 1 h, then water (10 mL) was added. The aqueous phase was extracted with $Et_2O$ (3 x 10 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. Purification by flash column chromatography on silica gel (1:0→15:1 petrol / $Et_2O$) gave **25** (1.10 g, 4.48 mmol, 87%) as a pale yellow oil.

$R_f$ 0.90 (4:1 petrol / $Et_2O$).

$[\alpha]_D^{25}$ +16.2 (c = 1.0 in $CHCl_3$)

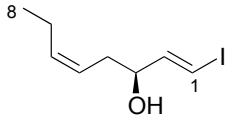
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2963, 1458, 1172, 893.

$^1$**H** NMR (400 MHz, $CDCl_3$) δ 5.55 (1H, dtt, *J* = 10.4, 7.3, 1.5 Hz, H6), 5.34 (1H, dtt, *J* = 10.7, 7.3, 1.6 Hz, H5), 3.36 – 3.16 (1H, m, H1), 3.10 – 2.99 (2H, m, H1, H2), 2.84 (1H, td, *J* = 5.4, 1.7 Hz, H3), 2.43 (1H, dddd, *J* = 14.5, 7.1, 5.3, 1.4 Hz, H4'), 2.33 – 2.20 (1H, m, H4), 2.14 – 1.95 (2H, m, H7), 0.98 (3H, t, *J* = 7.5 Hz, H8).

$^{13}$**C** NMR (101 MHz, $CDCl_3$) δ 135.3, 122.0, 61.9, 58.0, 29.4, 20.8, 14.3, 5.0.

**HRMS** ($ES^+$) calc. for $C_8H_{13}IO$ $[M+H]^+$ 253.0089, found 253.0077.

**(*S*,1*E*,5*Z*)-1-Iodoocta-1,5-dien-3-ol, 9**




NaHMDS (0.15 mL of a 1.0 M solution in THF, 0.295 mmol, 1.5 equiv.) was added dropwise to a solution of **25** (50.0 mg, 0.196 mmol, 1.0 equiv.) in DMF (0.16 mL) at -60 °C. After stirring the yellow solution for 15 min, the reaction was warmed to -10 °C over the course of 30 min. The reaction was quenched by addition of $NH_4Cl$ (1 mL), the aqueous layer was extracted with $Et_2O$ (3 x 1 mL), and the combined organic phases were dried ($MgSO_4$). Purification by flash column chromatography on silica gel (9:1→4:1 petrol / $Et_2O$) gave **9** (26.4 mg, 0.105 mmol, 53%) as pale yellow oil.

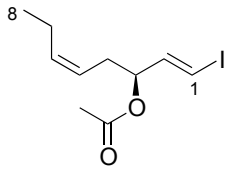
The analytical data matched that reported in the literature (*Tetrahedron Lett.* **2012**, *53*, 6990).

***R*$_f$** 0.40 (4:1 petrol / $Et_2O$).

**$^1$H** NMR (400 MHz, $CDCl_3$) δ 6.60 (1H, dd, *J* = 14.4, 5.8 Hz, H2), 6.37 (1H, dd, *J* = 14.5, 1.3 Hz, H1), 5.61 (1H, dtt, *J* = 10.4, 8.8, 5.1, 1.5 Hz, H6), 5.33 (1H, dtt, *J* = 10.8, 7.5, 1.6 Hz, H5), 4.25-3.93 (1H, m, H3), 2.40-2.25 (2H, m, H4), 2.14-2.00 (2H, m, H7), 1.73 (1H, d, *J* = 4.3 Hz, OH), 0.98 (3H, t, *J* = 7.5 Hz, H8).

**$^{13}$C** NMR (101 MHz, $CDCl_3$) δ 147.9, 136.3, 122.8, 77.4, 74.0, 34.7, 20.9, 14.4.

**(*S*,1*E*,5*Z*)-1-Iodoocta-1,5-dien-3-yl acetate, 35**




Acetic anhydride (0.080 mL, 0.80 mmol, 2.0 equiv.) was added to a solution of **9** (100 mg, 0.40 mmol, 1.0 equiv.), DMAP (few crystals) and $Et_3N$ (0.17 mL, 1.20 mmol, 3.0 equiv.) in $CH_2Cl_2$ (1 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 2 h, then the reaction was quenched by addition of $H_2O$ (2 mL). The aqueous layer was extracted with diethyl ether (4 x 1 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (19:1 petrol / $Et_2O$) gave **35** (111 mg, 0.37 mmol, 93%) as a colourless oil.

***R*$_f$** 0.9 (7:1 petrol / $Et_2O$).

**$[\alpha]_D^{20}$** -30.2 (*c* 1.0, $CHCl_3$).

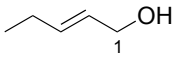
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 1741, 1433, 1231, 1021.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.50 (1H, dd, *J* = 14.6, 6.5 Hz, H2), 6.41 (1H, dd, *J* = 14.6, 0.8 Hz, H1), 5.68-5.45 (1H, m, H6), 5.34-5.22 (1H, m, H5), 5.19 (1H, app q, *J* = 6.6 Hz, H3), 2.50-2.27 (2H, m, H4), 2.05 (3H, s, COMe), 2.12-1.95 (2H, m, H7), 0.97 (3H, t, *J* = 7.5 Hz, H8).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.1, 143.6, 135.6, 122.1, 80.0, 75.3, 31.7, 21.2, 20.9, 14.3.

**HRMS** ($ES^+$) calc. for $C_{11}H_{19}IO_3$ $[M+MeOH+H]^+$ 327.0457, found 327.0461.

**(*E*)-Pent-2-en-1-ol, 28**

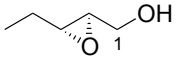



To a suspension of $LiAlH_4$ (6.93 g, 182 mmol, 1.50 equiv.) in ether (150 mL) at 0 °C was added 2-pentynol (11.2 mL 121 mmol, 1.0 equiv.) dropwise over 20 min (10 mL $Et_2O$ rinse). The reaction was stirred overnight, then cooled to 0 °C and quenched by slow addition of 10% $H_2SO_4$ (250 mL). The layers were separated, and the aqueous layer extracted with $Et_2O$ (2 x 70 mL). The combined organic phases were washed with brine (50 mL) and dried ($MgSO_4$) to give **28** (10.1 g, 97.2 mmol, 80%) as colourless oil, which was used directly without further purification. The analytical data matched that reported in the literature (*J. Org. Chem.* **1973**, *38*, 4263).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.82-5.70 (1H, m, H2 or H3), 5.68-5.58 (1H, m, H2 or H3), 4.08 (2H, d, *J* = 5.8 Hz, H1), 2.20-1.95 (2H, m, H4), 1.00 (3H, t, *J* = 7.4 Hz, H5).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 135.2, 128.0, 64.0, 25.4, 13.5.

**(2*R*,3*R*)-3-(Ethyloxiran-2-yl)methanol, S10**



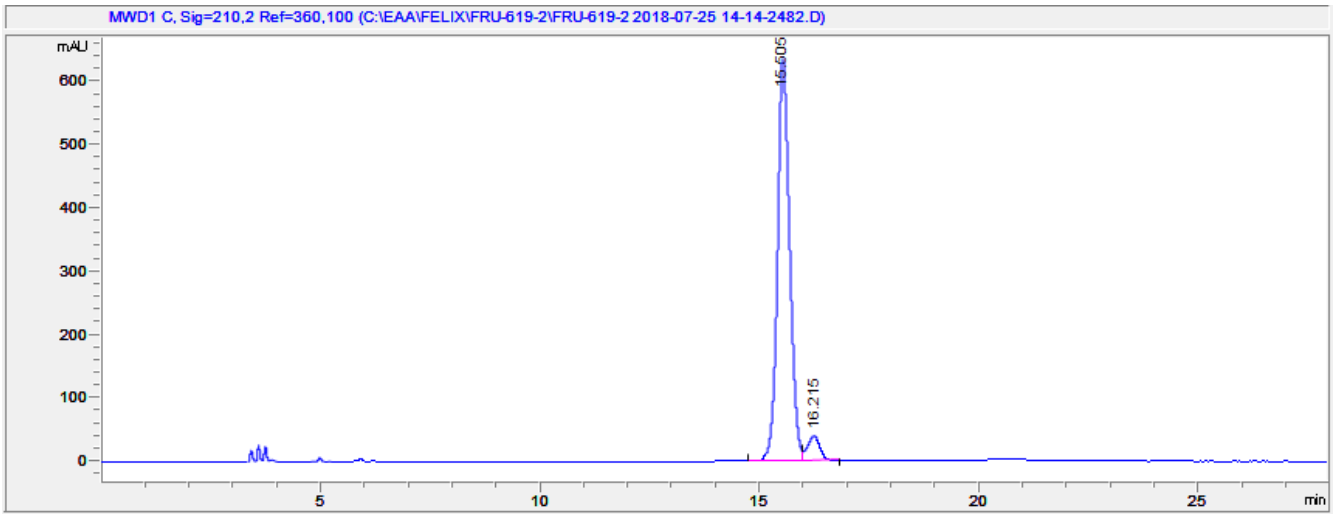

To a cooled (-78 °C) suspension of activated 3 Å MS (4.0 g) in $CH_2Cl_2$ (200 mL) was added Ti(O*i*-Pr)$_4$ (0.59 mL, 2.0 mmol, 0.1 equiv.) and D-(-)-diisopropyltartrate (0.50 mL, 2.4 mmol, 0.12 equiv.). After 5 min, a solution of (*E*)-pent-2-en-1-ol (2.5 mL, 20.0 mmol) was added and the solution stirred for 30 min. *Tert*-butyl hydroperoxide (7.3 mL, ~5.5 M in decane, 40.0 mmol) was added dropwise over 5 min. The resulting mixture was kept at -20 °C for 20 h, then quenched by addition of a cooled solution of $FeSO_4 \bullet 7H_2O$ (12.0 g) and tartaric acid (5.0 g) in water (100 mL). The mixture was stirred vigorously for 2 h, then the phases were separated and the aqueous layer extracted with $CH_2Cl_2$ (3 x 30 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (1:1→1:3 petrol / $Et_2O$) gave the title compound **S10** (1.08 g, 10.0 mmol, 50%) as a colourless oil. The analytical data matched that reported in the literature (*J. Am. Chem. Soc.* **1987**, *109*, 5765).

***R*$_f$** 0.20 (1:1 petrol / $Et_2O$).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 3.91 (1H, ddd, *J* = 12.5, 5.5, 2.3 Hz, H1), 3.63 (1H, ddd, *J* = 12.5, 7.1, 4.1 Hz, H1), 3.04-2.83 (2H, m, H2 and H3), 1.79-1.67 (1H, m, OH), 1.67-1.49 (2H, m, H4), 1.00 (3H, t, *J* = 7.5 Hz, H5).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 61.9, 58.2, 57.2, 24.8, 10.0.

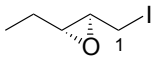
**HPLC:** 88% *ee.* Chiralpak IC, 2.5% IPA/*n*-Hexane, 1.0 mL/min. (*R,R*): 15.4 min; (*S,S*): 16.2 min, benzoate derivative of the alcohol.




Signal 3: MWD1 C, Sig=210,2 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.505 | BV | 0.2893 | 1.22655e4 | 635.15692 | 94.0581 |
| 2 | 16.215 | VB | 0.2659 | 774.84778 | 39.32748 | 5.9419 |

**(2*R*,3*S*)-2-Ethyl-3-(iodomethyl)oxirane, 26**




To a cooled (0 °C) suspension of triphenylphosphine (2.66 g, 10.1 mmol, 1.02 equiv.), imidazole (0.69 g, 10.1 mmol, 1.02 equiv.) and ((2*R*,3*R*)-3-ethyloxiran-2-yl)methanol (1.08 g, 9.91 mmol, 1.00 equiv.) in $CH_2Cl_2$ (50 mL) was added iodine (2.57 g, 10.1 mmol, 1.02 equiv.). After 10 min, the ice bath was removed and stirring was continued at room temperature for 1 h, before being quenched by addition of saturated $NaS_2O_3$ (20 mL). The layers were separated and the aqueous phase was extracted with $CH_2Cl_2$ (2 x 20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Purification by flash column chromatography on silica gel (19:1 petrol / $Et_2O$) gave **26** (1.55 g, 7.3 mmol, 74%) as pale yellow oil.

$R_f$ 0.70 (6:1 petrol / $Et_2O$).

$[\alpha]_D^{25}$ -14.0 (*c* 1.0, $CHCl_3$).

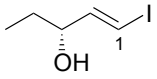
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2967, 1458, 1423, 1172, 886.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 3.35-3.18 (1H, m, H1), 3.09-2.95 (2H, m, H1 and H2), 2.79 (1H, td, *J* = 5.6, 1.8 Hz, H3), 1.76-1.48 (2H, m, H4), 1.02 (3H, t, *J* = 7.5 Hz, H5).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 63.8, 58.3, 24.9, 9.9, 5.2.

**HRMS** ($EI^+$) not found.

**(*R*,*E*)-1-Iodopent-1-en-3-ol, 10**




NaHMDS (5.4 mL of a 2.0 M solution in THF, 10.8 mmol, 1.5 equiv.) was added dropwise to a solution of **26** (1.52 g, 7.2 mmol, 1.0 equiv.) in DMF (72 mL) at -60 °C. After stirring the yellow solution for 15 min, the reaction was warmed to -20 °C over the course of 1.5 h. The reaction was quenched by addition of saturated $NH_4Cl$ (10 mL), and the reaction was diluted with water / brine (450 mL, 2:1 ratio). The aqueous layer was extracted with petrol / $Et_2O$ (1:1, 3 x 50 mL), and the combined organic phases were washed with brine (30 mL), dried ($MgSO_4$) and concentrated. Purification by flash column chromatography on silica gel (7:1 petrol / $Et_2O$) gave **10** (0.84 g, 4.0 mmol, 56%) as a pale yellow oil.

The spectroscopic data matched that reported in the literature (*Tetrahedron Lett.*, **2011**, 52, 2623):

$R_f$ 0.2 (4:1 petrol / $Et_2O$).

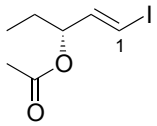
$[\alpha]_D^{25}$ +2.0 (*c* 1.0, $CHCl_3$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3331, 2964, 2930, 1607, 1460, 1177, 946.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.58 (1H, dd, *J* = 14.5, 6.3 Hz, H2), 6.35 (1H, dd, *J* = 14.5, 1.2 Hz, H1), 4.03 (1H, tdd, *J* = 6.4, 4.4, 1.2 Hz, H3), 1.72-1.49 (3H, m, H4 and OH), 0.94 (3H, t, *J* = 7.4 Hz, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 148.6, 77.4, 76.1, 29.7, 9.6. **HRMS** ($EI^+$) not found.

**(*R*,*E*)-1-Iodopent-1-en-3-yl acetate, 45**




Acetic anhydride (0.76 mL, 8.0 mmol, 2.0 equiv.) was added to a solution of **10** (837 mg, 3.95 mmol, 1.0 equiv.), DMAP (crystals) and $Et_3N$ (1.60 mL, 12.0 mmol, 3.0 equiv.) in $CH_2Cl_2$ (8 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 2 h, then quenched by addition of 1N HCl (10 mL). The layers were separated, the aqueous layer was extracted with $CH_2Cl_2$ (2 x 10 mL), the combined organic phases were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (19:1 petrol / $Et_2O$) gave **45** (709 mg, 2.74 mmol, 70%) as a colourless oil.

$R_f$ 0.6 (petrol / $Et_2O$ (19:1)).

$[\alpha]_D^{25}$ +90.2 (*c* 1.0, $CHCl_3$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 1739, 1611, 1232.

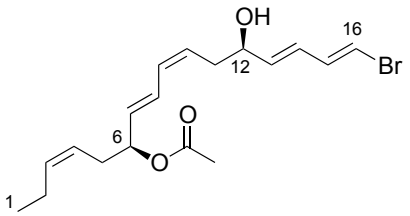
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.48 (1H, dd, *J* = 14.6, 6.5 Hz, H2), 6.41 (1H, dd, *J* = 14.5, 0.5 Hz, H1), 5.12 (1H, app q, *J* = 6.5 Hz, H3), 2.06 (3H, s, COMe), 1.78 – 1.59 (2H, m, H4), 0.90 (3H, t, *J* = 7.4 Hz, H5).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.3, 143.9, 80.0, 76.9, 26.9, 21.2, 9.4.

**HRMS** ($ES^+$) not found.

## 2d. Synthesis and cross-coupling of model substrates

**(3Z,6S,7E,9Z,12R,13E,15E)-16-bromo-12-hydroxyhexadeca-3,7,9,13,15-pentaen-6-yl acetate, 36**




To a mixture of $Pd(dba)_2$ (5.0 mg, 0.009 mmol, 0.05 equiv.), iodide **35** (51.7 mg, 0.175 mmol, 1.00 equiv.) and bromide **8** (50.0 mg, 0.193 mmol, 1.10 equiv.) under argon was added TBAF (1M in THF, 0.58 mL, 0.58 mmol, 3.3 equiv.). The reaction mixture was stirred overnight, and then directly purified by flash column chromatography on silica gel (9:1→1:1 petrol / ether) to yield the alcohol **36** (40.4 mg, 0.109 mmol, 63%) as a colourless oil.

***R*$_f$** 0.2 (2:1 petrol / ether).

**[α]$_D^{20}$** **+**4.0 (*c* 0.1, $CHCl_3$)

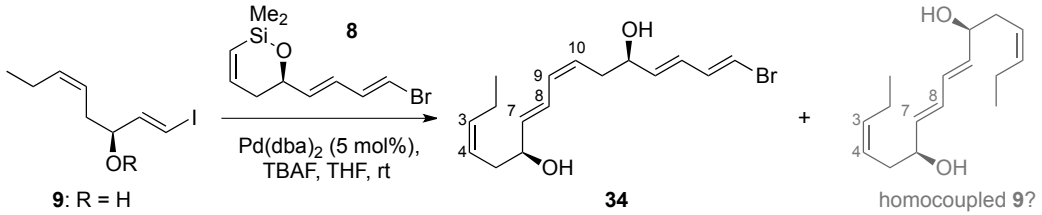
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3434, 2963, 1734, 1372, 1238.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.71 (1H, ddd, *J* = 13.5, 10.8, 0.7 Hz, H15), 6.48 (1H, ddt, *J* = 15.2, 11.1, 1.1 Hz, H14), 6.34 (1H, d, *J* = 13.5 Hz, H16), 6.19 (1H, ddd, *J* = 15.2, 10.8, 1.3 Hz, H8), 6.12 (1H, ddt, *J* = 12.7, 11.1, 1.3 Hz, H9), 5.76 (1H, ddt, *J* = 15.3, 6.0, 0.8 Hz, H13), 5.66 (1H, dd, *J* = 15.2, 7.2 Hz, H7), 5.58-5.40 (2H, m, H3 and H10), 5.36-5.14 (2H, m, H4 and H6), 4.35-4.13 (1H, m, H12), 2.56-2.18 (4H, m, H5 and H11), 2.13-1.95 (2H, m, H2), 2.05 (3H, s, COMe), 0.96 (3H, t, *J* = 7.5 Hz, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.4, 136.8, 136.3, 135.0, 132.3, 131.0, 128.0, 127.6, 127.5, 123.0, 109.4, 74.1, 71.6, 35.7, 32.5, 21.5, 20.9, 14.3.

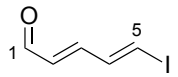
**HRMS** ($ES^+$) calc. for $C_{18}H_{25}BrO_3K$ $[M+K]^+$ 407.0624, found 407.0609.

*Attempted coupling of alcohol **9***




Coupling of **9** with **8** gave desired coupled product **34** as a mixture with a byproduct tentatively assigned as homocoupling of the alkenyl iodide **9**. This byproduct had a very similar $R_f$ to the desired product **34**. Evidence for homocoupling could be found by comparing superimposed $^1$H NMR spectra for the crude reaction mixture and purified **34**, which are included at the end of the Supporting Information (p75).

**(2*E*,4*E*)-5-Iodopenta-2,4-dienal and (2*E*,4*Z*)-5-Iodopenta-2,4-dienal, S11**

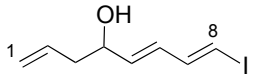



To a solution of triphenylphosphine (10.6 g, 40.4 mmol, 1.1 equiv.) in $CH_2Cl_2$ (200 mL) at 0 °C was added iodine (10.3 g, 41.7 mmol, 1.1 equiv.), followed by glutaconaldehyde potassium salt (5.00 g, 36.7 mmol, 1.0 equiv.)[*J. Chem. Soc. Perkin Trans I*, **1997**, *11*, 1639]. After stirring in the dark at room temperature for 72 h, the resulting mixture was quenched by addition of $NaHCO_3$ (100 mL, 5% w/v). The organic layer was separated and the aqueous layer further extracted with $Et_2O$ (3 × 150 mL). The combined organic layers were washed with brine (100 mL), dried ($MgSO_4$) and concentrated. Purification by column chromatography (3:2 petrol / $Et_2O$; 2$^{nd}$ column 49:1 petrol / $Et_2O$) gave (2*E*,4*Z*)-5-iodopenta-2,4-dienal (1.92 g, 9.18 mmol, 25%), and (2*E*,4*E*)-5-iodopenta-2,4-dienal **S11** (2.18 g, 10.3 mmol 28%) as orange solids. The spectroscopic data matched that reported in the literature (*J. Chem. Soc. Perkin Trans. 1*, **1997**, 1639).

**$^1$H** NMR (400 MHz, Toluene-$d_8$) δ 9.16 (1H, d, *J* = 7.6 Hz, H1), 6.48 (1H, ddd, *J* = 14.5, 11.0, 0.7 Hz, H4), 6.13 (1H, dd, *J* = 14.4, 0.7 Hz, H5), 5.86 (1H, ddd, *J* = 15.4, 10.9, 0.6 Hz, H3), 5.52 (1H, dd, *J* = 15.4, 7.7 Hz, H2).

**$^{13}$C** NMR (101 MHz, Toluene-$d_8$) δ 192.0, 148.5, 143.6, 131.8, 91.0.

**(5*E*,7*E*)-8-Iodoocta-5,7-dien-1-yn-4-ol, 37**




To a solution of (2*E*,4*E*)-5-iodopenta-2,4-dienal **S11** (300 mg, 1.44 mmol, 1.0 equiv.) in THF (3 mL) at -78 °C under argon was added dropwise a solution of allylmagnesium bromide (1.73 mL, 1M in $Et_2O$, 1.73 mmol, 1.2 equiv.). After stirring for 1 h the reaction was quenched by addition (at -78 °C) of $NH_4Cl$ (5 mL) and water (1 mL), and the mixture was warmed to room temperature. The aqueous layer was extracted with $Et_2O$ (3 x 2 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated. Purification by flash column chromatography on silica gel (5:1 petrol / $Et_2O$) gave alcohol **37** (247 mg, 0.987 mmol, 69%) as pale yellow oil.

***R*$_f$** 0.2 (5:1 petrol / $Et_2O$).

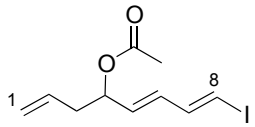
**IR** (thin film, $\nu_{max}$ / cm$^{-1}$) 345, 3073, 2923, 1681, 1599, 983.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.03 (1H, ddd, *J* = 14.4, 10.7, 0.7 Hz, H7), 6.35 (1H, dd, *J* = 14.4, 0.7 Hz, H8), 6.19 (1H, dddd, *J* = 15.3, 10.7, 1.4, 0.6 Hz, H6), 5.95-5.69 (2H, m, H5 and H2), 5.26 – 5.16 (1H, m, H1), 5.16-5.11 (1H, m, H1), 4.34-4.02 (1H, m, H4), 2.60-1.99 (2H, m, H3), 1.74 (1H, d, *J* = 4.1 Hz, OH).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.6, 136.2, 133.8, 130.1, 119.0, 79.8, 70.8, 41.8.

**HRMS** ($ES^-$) calc. for $C_8H_{10}IO$ $[M-H]^-$ 248.9771, found 248.9771.

**(5*E*,7*E*)-8-Iodoocta-1,5,7-trien-4-yl acetate, 38**




Acetic anhydride (0.08 mL, 0.80 mmol, 2.0 equiv.) was added to a solution of **37** (98 mg, 0.39 mmol, 1.0 equiv.), DMAP (crystals) and $Et_3N$ (0.17 mL, 1.20 mmol, 3.0 equiv.) in $CH_2Cl_2$ (1 mL). The reaction mixture was stirred for 1 h, the quenched by addition of 1N HCl (10 mL) and diluted with $H_2O$ (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL), and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Purification *via* flash column chromatography on silica gel (9:1 petrol / $Et_2O$) to gave allylic acetate **38** (101 mg, 0.347 mmol, 89%) as a colourless oil.

***R*$_f$** 0.6 (9:1 petrol / $Et_2O$).

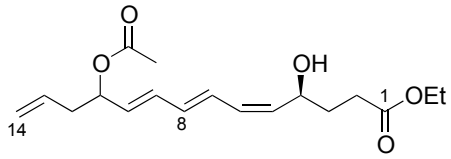
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3077, 2935, 1736, 1371, 1235.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.99 (1H, ddd, *J* = 14.4, 10.7, 0.8 Hz, H7), 6.47-6.32 (1H, d, *J* = 14.5 Hz, 1H, H8), 6.16 (1H, dddd, *J* = 15.3, 10.7, 1.1, 0.6 Hz, H6), 5.81-5.68 (1H, m, H2), 5.64 (1H, ddt, *J* = 15.3, 6.9, 0.8 Hz, 1H, H6), 5.29 (1H, app qd, *J* = 6.5, 1.1 Hz, H4), 5.14-5.09 (1H, m, H1), 5.09-5.05 (1H, m, H1), 2.47-2.33 (2H, m, H3), 2.05 (3H, s, COMe).

**$^{13}$C NMR (**101 MHz, $CDCl_3$) δ 170.3, 144.3, 132.9, 132.3, 131.6, 118.5, 81.0, 72.9, 38.9, 21.3.

**HRMS** ($ES^+$) calc. for $C_{18}H_{26}O_5Na$ $[M+Na]^+$ 345.1673, found 345.1673.

**Ethyl (4*S*,5*Z*,7*E*,9*E*)-11-acetoxy-4-hydroxytetradeca-5,7,9,13-tetraenoate, 40**




To a mixture of $Pd(dba)_2$ (2.3 mg, 4.0 μmol, 0.05 equiv.), iodide **38** (23.4 mg, 0.080 mmol, 1.00 equiv.) and silane **5** (20.6 mg, 0.096 mmol, 1.20 equiv.) under argon was added TBAF (1 M in THF, 0.29 mL, 0.29 mmol, 3.6 equiv.). The reaction was stirred overnight, then the solvent was removed *in vacuo*, and the residue was purified by flash column chromatography on silica gel (7:1 petrol / EtOAc) to yield alcohol **40** (16.8 mg, 0.053 mmol, 55%) as a colourless oil.

***R*$_f$** 0.1 (7:1 petrol / EtOAc).

**$[\alpha]_D^{20}$** not recorded as mixture of diastereomers at C11.

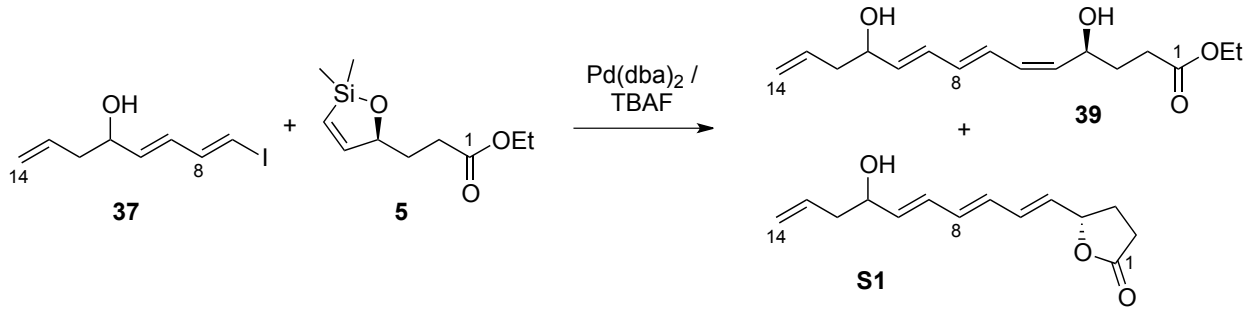
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3469, 2982, 1731, 1372, 1235, 998.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.50 (1H, dd, *J* = 14.4, 11.6 Hz, H7), 6.35-6.13 (2H, m, H8 and H9), 6.07 (1H, t, *J* = 11.2 Hz, H6), 5.83-5.55 (2H, m, H10 and H13), 5.46-5.40 (1H, m, H5), 5.34 (1H, app q, *J* = 6.6 Hz, H11), 5.16-5.04 (2H, m, H14), 4.64 (1H, app q, *J* = 7.9 Hz, H4), 4.13 (2H, qd, *J* = 7.1, 0.7 Hz, $OC\underline{H}_2CH_3$), 2.46-2.35 (4H, m, 4H, H2 and H12), 2.10-2.02 (3H, s, COMe), 1.95-1.81 (2H, m, H3), 1.25 (3H, td, *J* = 7.1, 0.6 Hz, $OCH_2C\underline{H}_3$).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 173.9, 170.4, 133.9, 133.7, 133.1, 132.5, 132.0, 130.2, 128.5, 118.3, 73.4, 67.4, 60.7, 39.1, 32.3, 30.4, 21.4, 14.4.

**HRMS** ($ES^+$) calc. for $C_{15}H_{21}BrO_3Na$ $[M+Na]^+$ 351.0566, found 351.0568.

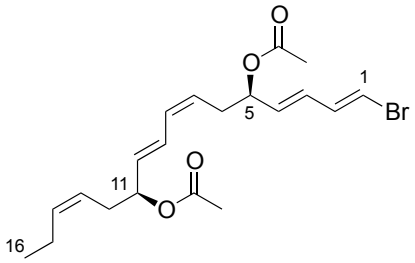
*Attempted coupling of alcohol **37***




Coupling of **37** with **5** gave desired coupled product **39** along with a significant amount of the γ-lactone **S1** (2:1 ratio of **39**:**S1**). The formation of **S1** was evidenced by the downfield shift of the allylic alcohol proton H4 to 5.00 ppm, compared to 4.65 for H4 in **39**. The isomerization of the C5–C6 double bond was evidenced by a coupling constant of 15.0 Hz for H5 (5.70 ppm, dd, J = 15.0, 6.7 Hz). Additional support for the formation of **S1** was gained from partial lactone formation in later coupling experiments. Copies of the $^1$H NMR spectra for the mixture of **39** and **S1**, and purified **39**, are shown on p76.

## 2e. Synthesis of resolvins and analogues

**(1*E*,3*E*,5*R*,7*Z*,9*E*,11*S*,13*Z*)-1-Bromohexadeca-1,3,7,9,13-pentaene-5,11-diyl diacetate, 41**




Acetic anhydride (0.04 mL, 0.33 mmol, 2.0 equiv.) was added to a solution of (3Z,6S,7E,9Z,12R,13E,15E)-16-bromo-12-hydroxyhexadeca-3,7,9,13,15-pentaen-6-yl acetate (61 mg, 0.16 mmol, 1.0 equiv., **36**, see above), DMAP (crystals) and $Et_3N$ (0.09 mL, 0.50 mmol, 3.0 equiv.) in $CH_2Cl_2$ (1 mL). The mixture was stirred for 1 h, then quenched by addition of $NH_4Cl$ (5 mL). The aqueous layer was extracted with $CH_2Cl_2$ (4 x 5 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated. The residue was purified *via* flash column chromatography on silica gel (9:1→4:1 petrol / $Et_2O$) to give **41** (60 mg, 0.14 mmol, 88%) as a colourless oil.

$R_f$ 0.5 (3:1 petrol / ether).

$[\alpha]_D^{20}$ +3.3 (*c* 0.1, $CHCl_3$).

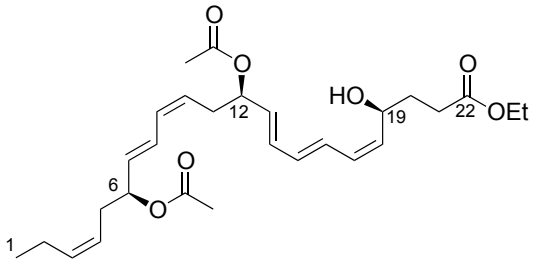
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2931, 1738, 1372, 1235.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.67 (1H, ddd, *J* = 13.5, 10.8, 0.8 Hz, H2), 6.45 (1H, ddt, *J* = 15.2, 11.1, 1.2 Hz, H3), 6.36 (1H, d, *J* = 13.5 Hz, H1), 6.16 (1H, ddd, *J* = 15.4, 10.5, 0.9 Hz, H9), 6.06 (1H, dd, *J* = 11.9, 10.3 Hz, H8), 5.74-5.59 (2H, m, H4 and H10), 5.56-5.45 (1H, m, 1H, H7 or H14), 5.39 (1H, dt, *J* = 10.9, 7.7 Hz, H7 or H14), 5.34-5.22 (3H, m, H5, H11 and H13), 2.83-2.26 (4H, m, H6 and H12), 2.09-2.01 (8H, m, H15 and 2 x COMe), 0.96 (3H, t, *J* = 7.5 Hz, H16).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.4, 170.3, 136.5, 135.0, 132.3, 131.7, 130.7, 130.0, 127.6, 126.6, 123.0, 110.4, 74.1, 73.1, 32.8, 32.5, 21.4, 21.3, 20.9, 14.3.

**HRMS** ($ES^+$) calc. for $C_{20}H_{27}BrO_4K$ $[M+K]^+$ 451.0712, found 451.0758

**(1*E*,3*E*,5*R*,7*Z*,9*E*,11*S*,13*Z*)-1-Bromohexadeca-1,3,7,9,13-pentaene-5,11-diyl diacetate, S12**




To a mixture of $Pd(dba)_2$ (4.1 mg, 0.008 mmol, 0.05 equiv.), **41** (59.6 mg, 0.142 mmol, 1.00 equiv.) and **6** (52.2 mg, 0.171 mmol, 1.20 equiv.) under argon was added TBAF (1M in THF, 0.43 mL, 0.43 mmol, 3.0 equiv.). The reaction mixture was stirred overnight, then directly purified by flash column chromatography on silica gel

(4:1→1:1 petrol / ether) to give the title compound **S12** (24.9 mg, 0.051 mmol, 36%) as a colourless oil.

$R_f$ 0.1 (2:1 petrol / ether).

$[\alpha]_D^{20}$ +2.3 (*c* 0.19, $CHCl_3$).

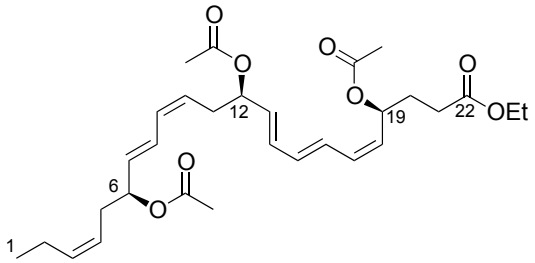
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3449, 2928, 1734, 1374, 1238, 1025.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.55 – 6.30 (2H, m,H15, H16), 6.32-6.07 (2H, m, H8 and H14), 6.07-5.85 (2H, m, H9 and H17), 5.75 – 5.50 (2H, m, H7 and H13), 5.49-5.14 (6H, m, H3, H4, H6, H10, H12 and H18), 4.58 (1H, q, *J* = 7.4 Hz, H19), 4.07 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.63-2.23 (6H, m, H2, H5 and H11), 2.20 (1H, s, OH), 2.05 – 1.91 (8H, m, H21 and 2 x COMe), 1.90-1.70 (2H, m, H20), 1.19 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.89 (3H, t, *J* = 7.5 Hz, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 173.9, 170.4, 170.3, 135.0, 134.0, 133.7, 132.6, 132.1, 131.8, 130.6, 130.2, 128.6, 127.5, 126.8, 123.0, 74.1, 73.4, 67.4, 60.6, 33.0, 32.5, 32.4, 30.5, 21.4, 21.3, 20.8, 14.4, 14.3.

**HRMS** ($ES^+$) calc. for $C_{28}H_{40}O_7Na$ $[M+Na]^+$ 511.2672, found 511.2674.

**(4*S*,5*Z*,7*E*,9*E*,11*R*,13*Z*,15*E*,17*S*,19*Z*)-1-Ethoxy-1-oxodocosa-5,7,9,13,15,19-hexaene-4,11,17-triyl triacetate, 42**




Acetic anhydride (0.01 mL) was added to a solution of (1*E*,3*E*,5*R*,7*Z*,9*E*,11*S*,13*Z*)-1-bromohexadeca-1,3,7,9,13-pentaene-5,11-diyl diacetate **S12** (7.1 mg, 14.5 µmol, 1.0 equiv.), DMAP (crystals) and $Et_3N$ (0.02 mL, excess) in $CH_2Cl_2$ (0.5 mL). The mixture was stirred for 1 h, then the reaction was quenched by addiiton of $NH_4Cl$ (1 mL). The aqueous layer was extracted with diethyl ether (3 x 1 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (2:1→1:1 petrol / $Et_2O$) gave **42** as a colourless oil (7.0 mg, 13.2 µmol, 91%).

$R_f$ 0.7 (1:1 petrol / ether).

$[\alpha]_D^{20}$ +49.2 (*c* 0.61, $CHCl_3$)

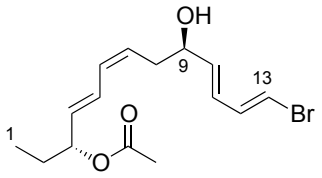
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.59 (1H, dd, *J* = 14.6, 11.5 Hz, H14), 6.46 (1H, ddt, *J* = 15.2, 11.1, 1.1 Hz, H15), 6.33 (1H, ddd, *J* = 15.1, 10.9, 1.1 Hz, H16), 6.21 (1H, dd, *J* = 14.7, 10.7 Hz, H8), 6.12 (1H, t, *J* = 11.5 Hz, H17), 6.05 (1H, t, *J* = 10.9 Hz, H9), 5.76-5.58 (3H, m, H7, H13 and H18), 5.55-5.45 (1H, m, H10), 5.45-5.23 (5H, m, H3, H4, H6, H12 and H19), 4.13 (2H, q, *J* = 7.2 Hz, $OC\underline{H}_2CH_3$), 2.61-2.36 (4H, m, H5 and H11), 2.33 (2H, t, *J* = 7.6 Hz, H21), 2.12-1.86 (13H, m, H2, H20 and 3 x COMe), 1.25 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.96 (3H, t, *J* = 7.5 Hz, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.9, 170.4, 170.4, 170.3, 135.0, 134.5, 132.3, 132.2, 132.1, 131.9, 130.6, 128.9, 128.4, 127.5, 126.8, 123.0, 74.1, 73.2, 69.6, 60.7, 33.0, 32.5, 30.2, 30.0, 21.4, 21.3, 21.3, 20.9, 14.4, 14.3.

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2961, 2934 1736, 1372, 1236, 1021.

**HRMS** ($ES^+$) calc. for $C_{30}H_{42}O_8Na$ $[M+Na]^+$ 553.2772, found 553.2770.

**(3*Z*,6*S*,7*E*,9*Z*,12*R*,13*E*,15*E*)-16-bromo-12-hydroxyhexadeca-3,7,9,13,15-pentaen-6-yl acetate, S13**




To a mixture of $Pd(dba)_2$ (20.2 mg, 0.035 mmol, 0.05 equiv.), **5** (182 mg, 0.70 mmol, 1.00 equiv.), **8** (200 mg, 0.77 mmol, 1.10 equiv.) under argon was added TBAF (1M solution in THF, 2.30 mL, 2.30 mmol, 3.3 equiv.). The reaction was stirred overnight, and then concentrated. Purification by flash column chromatography on silica gel (4:1→1:1 petrol / ether) gave the title compound **S13** (144 mg, 0.44 mmol, 63%) as a colourless oil.

$R_f$ 0.2 (2:1 petrol / ether).

$[\alpha]_D^{20}$ +27.3 (*c* 1.0, $CHCl_3$).

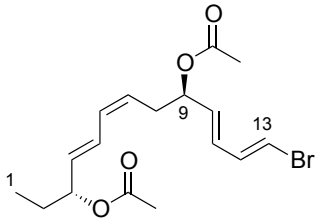
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3416, 2969, 1729, 1372, 1241, 980.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.70 (1H, ddd, *J* = 13.5, 10.8, 0.8 Hz, H12), 6.48 (1H, ddt, *J* = 15.2, 11.1, 1.1 Hz, H11), 6.33 (1H, dq, *J* = 13.6, 0.6 Hz, H13), 6.24-6.08 (2H, m, H5 and H6), 5.76 (1H, ddt, *J* = 15.3, 6.1, 0.8 Hz, H4), 5.62 (1H, dd, *J* = 15.1, 7.4 Hz, H10), 5.47 (1H, dt, *J* = 10.9, 7.8 Hz, H7), 5.22 (1H, app q, *J* = 6.4 Hz, H3), 4.33 – 4.07 (1H, m, H9), 2.55-2.39 (2H, m, H8), 2.06 (3H, s, COMe), 1.81-1.52 (3H, m, H2 and OH), 0.90 (3H, t, *J* = 7.4 Hz, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.6, 136.8, 136.3, 132.5, 131.0, 128.0, 127.7, 127.4, 109.4, 75.9, 71.6, 35.7, 27.6, 21.5, 9.7.

**HRMS** ($ES^+$) calc. for $C_{15}H_{21}BrO_3Na$ $[M+Na]^+$ 351.0566, found 351.0568.

**(3*R*,4*E*,6*Z*,9*R*,10*E*,12*E*)-13-bromotrideca-4,6,10,12-tetraene-3,9-diyl diacetate, 46**




Acetic anhydride (0.080 mL, 0.82 mmol, 2.0 equiv.) was added to a solution of (3*Z*,6*S*,7*E*,9*Z*,12*R*,13*E*,15*E*)-16-bromo-12-hydroxyhexadeca-3,7,9,13,15-pentaen-6-yl acetate **S13** (135 mg, 0.41 mmol, 1.0 equiv.), DMAP (crystals) and $Et_3N$ (0.170 mL, 1.23 mmol, 3.0 equiv.) in $CH_2Cl_2$ (1 mL). The mixture was stirred for 1 h, then quenched by addition of with $NH_4Cl$ (2 mL). The aqueous layer was extracted with diethyl ether (3 x 1 mL), and the combined organic layers dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (9:1→4:1 petrol / $Et_2O$) gave **46** as a colourless oil (137 mg, 0.37 mmol, 91%).

$R_f$ 0.5 (3:1 petrol / ether).

$[\alpha]_D^{20}$ 29.3 (*c* 1.0, $CHCl_3$).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2970, 1738, 1372, 1235.

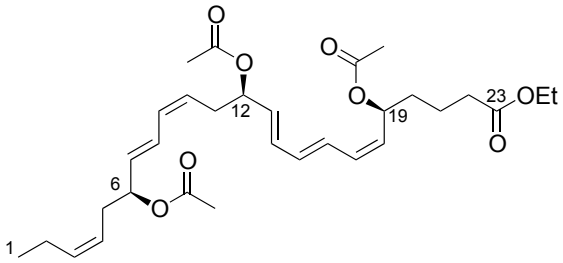
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.67 (1H, ddd, *J* = 13.6, 10.8, 0.8 Hz, H12), 6.46 (1H, ddt, *J* = 15.2, 11.1, 1.1 Hz, H10),

6.36 (1H, d, *J* = 13.5 Hz, H13), 6.16 (1H, ddt, *J* = 15.3, 10.8, 0.7 Hz, H11), 6.07 (1H, t, *J* = 11.0 Hz, H6), 5.71-5.57 (2H, m, H4 and H5), 5.38 (1H, dt, *J* = 10.8, 7.7 Hz, H7), 5.29 (1H, app qd, *J* = 6.6, 1.1 Hz, H9), 5.22 (1H, app q, *J* = 6.4 Hz, H3), 2.63-2.42 (2H, m, H8), 2.06 (3H, s, COMe), 2.04 (3H, s, COMe), 1.76-1.57 (2H, m, H2), 0.90 (3H, t, *J* = 7.4 Hz, H1).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.5, 170.3, 136.5, 132.5, 131.7, 130.8, 130.1, 127.6, 126.4, 110.4, 75.8, 73.2, 32.8, 27.7, 21.5, 21.3, 9.7.

**HRMS** ($ES^+$) calc. for $C_{17}H_{23}BrO_4Na$ $[M+Na]^+$ 393.0672, found 393. 0672.

**(5*S*,6*Z*,8*E*,10*E*,12*R*,14*Z*,16*E*,18*S*,20*Z*)-1-Ethoxy-1-oxotricosa-6,8,10,14,16,20-hexaene-5,12,18-triyl triacetate, 43**




To a mixture of $Pd(dba)_2$ (8.4 mg, 0.015 mmol, 0.10 equiv.), **41** (60.4 mg, 0.146 mmol, 1.00 equiv.), and **9** (42.5 mg, 0.175 mmol, 1.20 equiv.) under argon was added TBAF (1M in THF, 0.44 mL, 0.44 mmol, 3.0 equiv.). The reaction was stirred overnight, and then directly purified by flash column chromatography on silica gel (2:1→1:2 petrol / ether) to give the intermediate cross-coupled product (33.6 mg, 0.067 mmol, 46%) as a colourless oil. This product was redissolved in $CH_2Cl_2$ (0.5 mL), then acetic anhydride (0.020 mL, 0.20 mmol, 2.0 equiv.), DMAP (crystals) and $Et_3N$ (0.04 mL, 0.30 mmol, 3.0 equiv.) were added. The mixture was stirred for 1 h, then it was quenched by addition of $NH_4Cl$ (1 mL). The aqueous layer was extracted with diethyl ether (3 x 1 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (3:2 petrol / $Et_2O$) gave **43** (31.2 mg, 0.057 mmol, 40% over 2 steps) as a colourless oil.

***R*$_f$** 0.3 (3:2 petrol / ether).

**$[\alpha]_D^{20}$** +15.6 (*c* 0.38, $CHCl_3$)

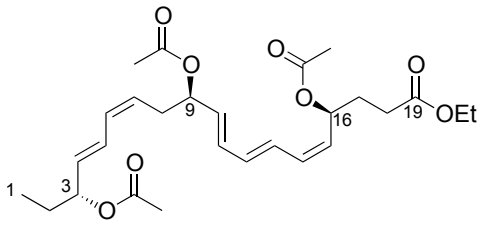
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2963, 1735, 1372, 1236, 1021.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.60 (1H, dd, *J* = 14.8, 11.4 Hz, H14), 6.46 (1H, ddt, *J* = 15.2, 11.2, 1.2 Hz, H15), 6.33 (1H, dd, *J* = 14.5, 10.7 Hz, H16), 6.20 (1H, dd, *J* = 14.8, 10.8 Hz, H8), 6.15-6.08 (1H, m, H17), 6.06 (1H, t, *J* = 11.0 Hz, H9), 5.75-5.60 (3H, m, H7, H13 and H18), 5.55-5.46 (1H, m, H10), 5.41 (1H, dt, *J* = 11.2, 7.7 Hz, H3 or H4), 5.38-5.24 (4H, m, H3 or H4, H6, H12 and H19), 4.12 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.67-2.47 (2H, m, H11), 2.47-2.34 (2H, m, H5), 2.31 (2H, t, *J* = 7.2 Hz, H22), 2.11-1.98 (13H, m, H2, H21 and 3 x COMe), 1.72 (1H, ddt, *J* = 11.5, 6.9, 3.1 Hz, H21), 1.68-1.60 (1H, m, H21), 1.25 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.96 (3H, t, *J* = 7.5 Hz, H1).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 173.4, 170.5, 170.4, 170.4, 135.0, 134.3, 132.3, 132.1, 132.0, 131.6, 130.6, 129.5, 128.5, 127.5, 126.9, 123.0, 74.1, 73.3, 70.0, 60.5, 34.3, 34.1, 33.0, 32.5, 21.4, 21.4, 21.3, 20.9, 20.7, 14.4, 14.3.

**HRMS** ($ES^+$) calc. for $C_{31}H_{44}O_8Na$ $[M+Na]^+$ 567.2934, found 567.2927.

**(3*R*,4*E*,6*Z*,9*R*,10*E*,12*E*,14*Z*,16*S*)-19-Ethoxy-19-oxononadeca-4,6,10,12,14-pentaene-3,9,16-triyl triacetate, 48**



To a mixture of $Pd(dba)_2$ (10.5 mg, 0.018 mmol, 0.10 equiv.), **46** (68.2 mg, 0.183 mmol, 1.00 equiv.) and **6** (47.1 mg, 0.220 mmol, 1.20 equiv.) under argon was added TBAF (1M in THF, 0.55 mL, 0.55 mmol, 3.0 equiv.). The reaction was stirred overnight, and then directly purified by flash column chromatography on silica gel (1:1→1:2 petrol / ether) to give a mixture of the cross-coupled lactone and alcohol as a colourless oil (36.6 mg, 0.082 mmol, 45%). This mixture was redissolved in $CH_2Cl_2$ (0.5 mL), and acetic anhydride (0.020 mL, 0.20 mmol, 2.0 equiv.) DMAP (crystals) and $Et_3N$ (0.04 mL, 0.30 mmol, 3.0 equiv.) were added. The mixture was stirred for 1 h, then it was quenched by addition of $NH_4Cl$ (1 mL). The aqueous layer was extracted with diethyl ether (3 x 1 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel 3:2 (petrol / $Et_2O$) gave **48** (29.3 mg, 0.060 mmol, 34% over 2 steps) as a colourless oil.

$R_f$ 0.3 (3:2 petrol / ether).

$[\alpha]_D^{20}$ +28.5 (*c* 0.37, $CHCl_3$).

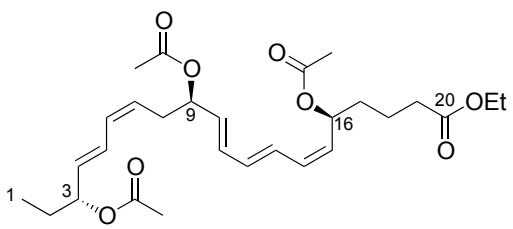
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2971, 1734, 1372, 1236, 1021.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.58 (1H, dd, *J* = 14.7, 11.5 Hz, H11), 6.46 (1H, ddt, *J* = 15.3, 11.2, 1.1 Hz, H12), 6.32 (1H, dd, *J* = 14.8, 10.5 Hz, H13), 6.21 (1H, dd, *J* = 14.7, 10.8 Hz, H5), 6.12 (1H, t, *J* = 11.1 Hz, H6), 6.07 (1H, dd, *J* = 12.0, 10.2 Hz, H14), 5.75-5.65 (2H, m, H9 and H15), 5.61 (1H, dd, *J* = 15.2, 7.3 Hz, H4), 5.48-5.27 (3H, m, H7, H9 and H16), 5.23 (1H, app q, *J* = 6.6 Hz, H3), 4.13 (2H, q, *J* = 7.1 Hz, C$\underline{H}_2$CH$_3$), 2.58 (1H, dddd, *J* = 14.7, 8.2, 6.7, 1.5 Hz, H8), 2.48 (1H, dddd, *J* = 14.8, 7.6, 6.1, 1.5 Hz, H8), 2.33 (2H, t, *J* = 7.6 Hz, H18), 2.13-1.96 (10H, m, H17 and 3 x COMe), 1.95-1.86 (1H, m, H17), 1.75-1.60 (2H, m, H2), 1.25 (3H, t, *J* = 7.2 Hz, CH$_2$C$\underline{H}_3$), 0.90 (3H, t, *J* = 7.4 Hz, H1).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 173.0, 170.6, 170.4, 170.3, 134.5, 132.4, 132.4, 132.2, 131.9, 130.7, 128.9, 128.4, 127.6, 126.7, 75.8, 73.3, 69.6, 60.7, 33.0, 30.2, 30.0, 27.7, 21.5, 21.3, 21.3, 14.4, 9.7.

**HRMS** ($ES^+$) calc. for $C_{27}H_{38}O_8Na$ $[M+Na]^+$ 513.2465, found 513.2464.

**(3*R*,4*E*,6*Z*,9*R*,10*E*,12*E*,14*Z*,16*S*)-20-Ethoxy-20-oxoicosa-4,6,10,12,14-pentaene-3,9,16-triyl triacetate, 47**



To a mixture of $Pd(dba)_2$ (10.6 mg, 0.019 mmol, 0.10 equiv.), **46** (68.7 mg, 0.185 mmol, 1.00 equiv.) and **9** (50.7

mg, 0.222 mmol, 1.20 equiv.) under argon was added TBAF (1M in THF, 0.56 mL, 0.56 mmol, 3.0 equiv.). The reaction was stirred overnight and then directly purified by flash column chromatography on silica gel (1:1→1:2 petrol / ether) to give the cross-coupled product alcohol as a colourless oil (41.7 mg, 0.090 mmol, 49%). This product was redissolved in $CH_2Cl_2$ (0.5 mL), and acetic anhydride (0.020 mL, 0.20 mmol, 2.0 equiv.), DMAP (crystals) and $Et_3N$ (0.040 mL, 0.30 mmol, 3.0 equiv.) were added. The mixture was stirred for 1 h, then it was quenched by addition of $NH_4Cl$ (1 mL). The aqueous layer was extracted with diethyl ether (3 x 1 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Purification *via* flash column chromatography on silica gel (3:2 petrol / $Et_2O$) gave **47** (36.0 mg, 0.071 mmol, 39% over 2 steps) as a colourless oil.

***R*$_f$** 0.3 (3:2 petrol / ether).

**[α]$_D^{20}$** +13.0 (*c* 0.37, $CHCl_3$).

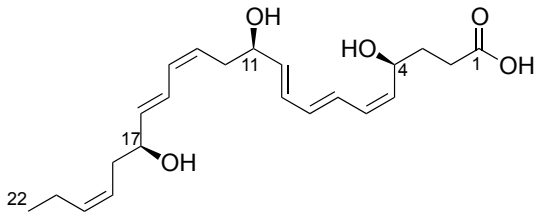
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 2971, 1734, 1372, 1237, 1023.

**$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.59 (1H, dd, *J* = 14.7, 11.5 Hz, H11), 6.46 (1H, ddt, *J* = 15.2, 11.1, 1.1 Hz, H12), 6.33 (1H, dd, *J* = 15.4, 11.0 Hz, H13), 6.20 (1H, dd, *J* = 14.7, 10.8 Hz, H5), 6.15-6.03 (2H, m, H6 and H14), 5.72-5.64 (2H, m, H4 and H10), 5.61 (1H, dd, *J* = 15.2, 7.2 Hz, H15), 5.45-5.31 (3H, m, H7, H9 and H16), 5.23 (1H, app q, *J* = 6.8 Hz, H3), 4.12 (2H, q, *J* = 7.1 Hz, C<u>H</u>$_2$CH$_3$), 2.58 (1H, dddd, *J* = 14.6, 8.1, 6.7, 1.6 Hz, H8), 2.53-2.43 (1H, m, H8), 2.31 (2H, t, *J* = 7.2 Hz, H19), 2.10-2.00 (9H, m, 3 x COMe), 1.82-1.56 (4H, m, H2 and H17), 1.25 (3H, t, *J* = 7.1 Hz, CH$_2$C<u>H</u>$_3$), 0.90 (3H, t, *J* = 7.4 Hz, H1).

**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 173.3, 170.5, 170.5, 170.3, 134.3, 132.4, 132.4, 132.0, 131.6, 130.7, 129.5, 128.5, 127.6, 126.7, 75.8, 73.3, 70.0, 60.5, 34.3, 34.1, 33.0, 27.7, 21.5, 21.4, 21.4, 20.7, 14.4, 9.7.

**HRMS** ($ES^+$) calc. for $C_{27}H_{38}O_8Na$ $[M+Na]^+$ 527.2621, found 527.2638.

**(4*S*,5*Z*,7*E*,9*E*,11*R*,13*Z*,15*E*,17*S*,19*Z*)-4,11,17-trihydroxydocosa-5,7,9,13,15,19-hexaenoic acid (1, RvD3)**




To a solution of HPLC-purified **42** (3.9 mg, 7.3 µmol, 1.0 equiv.) in THF (0.3 mL) was added LiOH (1M, 0.30 mL, 0.30 mmol, ~ 50 equiv.) and the reaction was stirred overnight. The reaction was quenched by addition of pH 6 phosphate buffer (1 M, 1 mL) and the aqueous phase extracted with ethyl acetate (3 x 1 mL). The combined organic layers extracts were dried ($Na_2SO_4$), filtered and concentrated to afford **1** (2.7 mg, 7.2 µmol, 99%).

***R*$_f$** not measured.

**[α]$_D^{20}$** +7.9 (*c* 0.34, MeOH).

**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3378, 2925, 1706, 1418, 1051, 996.

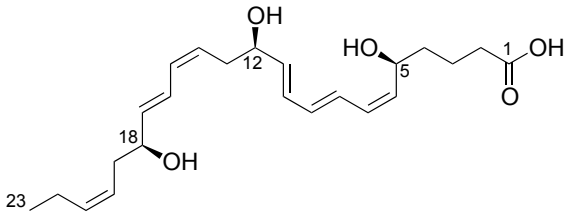
**$^1$H NMR** (500 MHz, Methanol-*d*$_4$) δ 6.60-6.44 (2H, m), 6.36-6.20 (2H, m), 6.08 (2H, app q, *J* = 11.3 Hz), 5.76 (1H, dd, *J* = 14.4, 6.5 Hz), 5.68 (1H, dd, *J* = 15.2, 6.5 Hz), 5.46 (2H, ddt, *J* = 10.6, 8.7, 7.3 Hz), 5.41-5.30 (2H, m), 4.69-

4.52 (1H, m), 4.26-4.06 (2H, m), 2.59-2.16 (6H, m), 2.13-1.99 (2H, m), 1.84 (1H, dq, *J* = 14.6, 7.5 Hz), 1.76-1.67 (1H, m), 0.96 (3H, t, *J* = 7.5 Hz).

**$^{13}$C NMR** (126 MHz, Methanol-$d_4$) δ 177.4, 137.9, 137.5, 135.2, 134.8, 134.6, 131.5, 131.1, 130.8, 128.7, 128.1, 126.6, 125.5, 73.2, 73.0, 67.7, 36.7, 36.2, 33.7, 30.9, 21.7, 14.6.

**HRMS** ($ES^-$) calc. for $C_{22}H_{31}O_5$ $[M-H]^-$ 375.2177, found 375.2175.

**(5*S*,6*Z*,8*E*,10*E*,12*R*,14*Z*,16*E*,18*S*,20*Z*)-5,12,18-trihydroxytricosa-6,8,10,14,16,20-hexaenoic acid, 44**




To a solution of **43** (4.6 mg, 8.4 µmol, 1.0 equiv.) in THF (0.3 mL) was added LiOH (1 M, 0.30 mL, 0.30 mmol, ~ 50 equiv.) and the reaction was stirred overnight. The reaction was quenched by addition of pH 6 phosphate buffer (1 M, 1 mL) and the aqueous phase extracted with ethyl acetate (3 x 1 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated to afford **44** (2.7 mg, 6.9 µmol, 83%).

***R*$_f$** not measured.

**$[\alpha]_D^{20}$** +4.7 (*c* 0.27, MeOH)

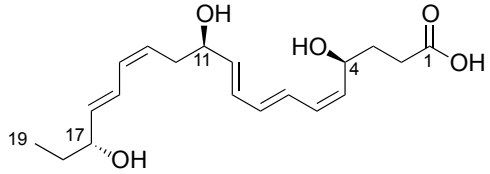
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3368, 2930, 1714, 1417, 996.

**$^1$H NMR** (500 MHz, Methanol-$d_4$) δ 6.60 – 6.44 (2H, m), 6.37-6.20 (2H, m), 6.08 (2H, td, *J* = 11.1, 5.4 Hz), 5.76 (1H, dd, *J* = 14.7, 6.5 Hz), 5.68 (1H, dd, *J* = 15.2, 6.5 Hz), 5.52-5.41 (2H, m), 5.42-5.31 (2H, m), 4.57 (1H, dt, *J* = 9.0, 6.2 Hz), 4.16 (1H, app q, *J* = 6.5 Hz), 4.12 (1H, app q, *J* = 6.5 Hz), 2.57-2.37 (2H, m), 2.37-2.19 (4H, m), 2.12-1.97 (2H, m), 1.65 (4H, m), 0.96 (3H, t, *J* = 7.5 Hz).

**$^{13}$C NMR** (126 MHz, Methanol-$d_4$) δ 177.5, 137.8, 137.5, 135.2, 135.1, 134.6, 131.5, 131.1, 130.5, 128.8, 128.1, 126.6, 125.5, 73.2, 73.0, 68.2, 38.0, 36.7, 36.2, 34.8, 22.1, 21.7, 14.6.

**HRMS** ($ES^-$) calc. for $C_{23}H_{33}O_5$ $[M-H]^-$ 389.2334, found 389.2333.

**(4*S*,5*Z*,7*E*,9*E*,11*R*,13*Z*,15*E*,17*R*)-4,11,17-trihydroxynonadeca-5,7,9,13,15-pentaenoic acid, 49**




To a solution of **48** (4.5 mg, 9.2 µmol, 1.0 equiv.) in THF (0.3 mL) was added LiOH (1 M, 0.3 mL, 0.3 mmol, ~ 50 equiv.) and the reaction was stirred overnight. The reaction was quenched by addition of pH 6 phosphate buffer (1 M, 1mL), and extracted with ethyl acetate (3 x 1 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated to afford **49** (2.8 mg, 8.3 µmol, 91%).

$R_f$ not measured.

**$[\alpha]_D^{20}$** +2.0 (*c* 0.28, MeOH)

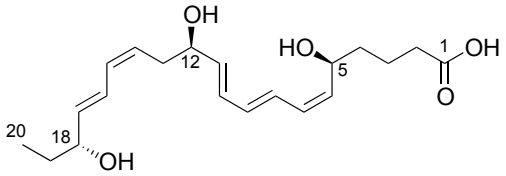
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3336, 2924, 1708, 1412, 1055, 996.

**$^1$H NMR** (500 MHz, Methanol-$d_4$) δ 6.61-6.42 (2H, m), 6.41-6.18 (2H, m), 6.10 (1H, t, *J* = 11.1 Hz), 6.09 (1H, t, *J* = 11.1 Hz), 5.77 (1H, dd, *J* = 14.5, 6.5 Hz), 5.66 (1H, dd, *J* = 15.2, 6.7 Hz), 5.45 (1H, dt, *J* = 11.0, 7.5 Hz), 5.40-5.34 (1H, m), 4.72-4.46 (1H, m), 4.24-4.08 (1H, m), 4.08-3.92 (1H, m), 2.57-2.41 (2H, m), 2.37 (2H, t, *J* = 7.5 Hz), 1.84 (1H, app dq, *J* = 14.6, 7.3 Hz), 1.80 – 1.67 (1H, m), 1.62-1.45 (2H, m), 0.92 (3H, t, *J* = 7.5 Hz).

**$^{13}$C NMR** (126 MHz, MeOD) δ 177.4, 137.9, 137.8, 135.2, 134.8, 131.5, 131.1, 130.8, 128.8, 128.0, 126.6, 74.7, 73.0, 67.8, 36.7, 33.7, 31.2, 30.9, 10.2.

**HRMS** ($ES^-$) calc. for $C_{19}H_{27}O_5$ $[M-H]^-$ 335.1864, found 335.1863.

**(5*S*,6*Z*,8*E*,10*E*,12*R*,14*Z*,16*E*,18*R*)-5,12,18-trihydroxyicosa-6,8,10,14,16-pentaenoic acid (2, RvE1)**




To a solution of **47** (3.2 mg, 6.3 µmol, 1.0 equiv.) in THF (0.3 mL) was added LiOH (1 M, 0.30 mL, 0.30 mmol, ~ 50 equiv.) and the reaction was stirred overnight. The reaction was quenched by addition of pH 6 phosphate buffer (1 M, 1 mL) and the aqueous phase extracted with ethyl acetate (3 x 1 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated to afford **2** (2.0 mg, 5.7 µmol, 91%).

$R_f$ not measured.

**$[\alpha]_D^{20}$** +1.1 (*c* 0.20, MeOH)

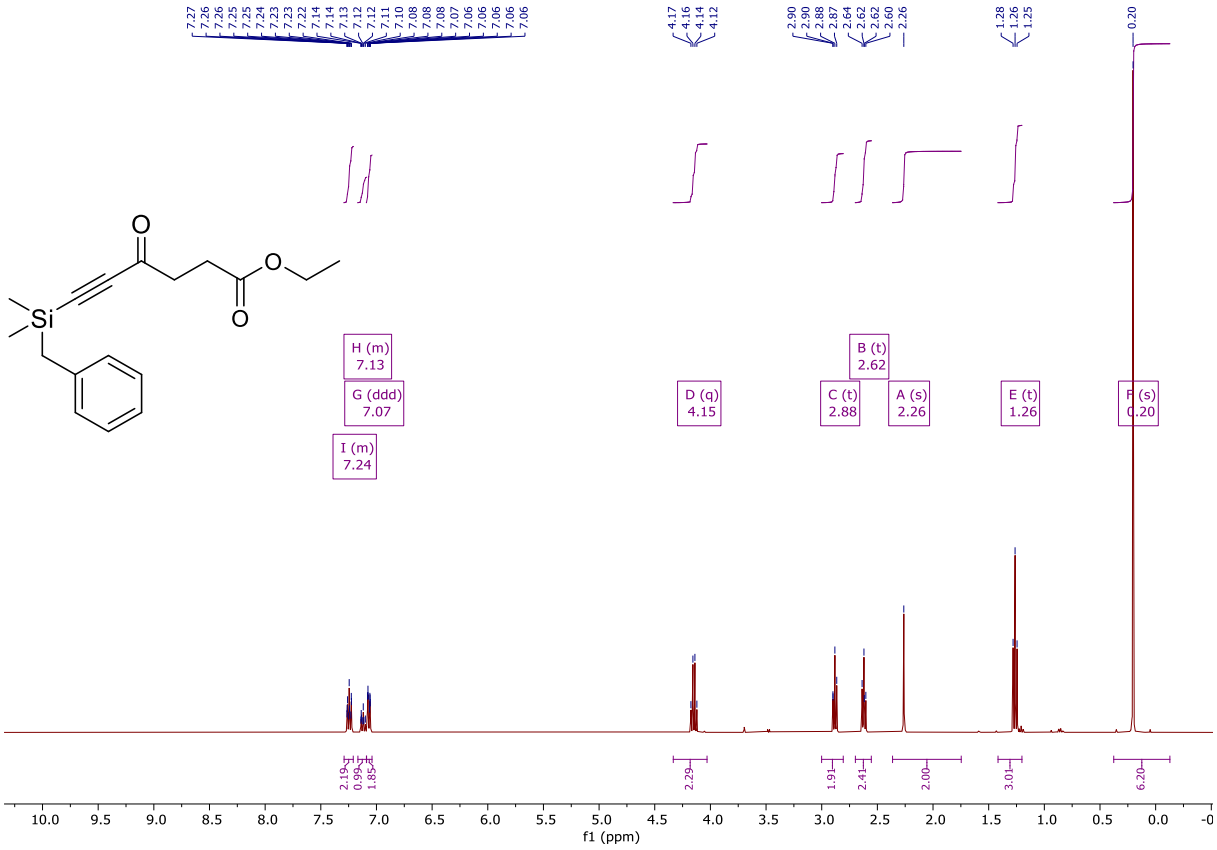
**IR** (thin film, $\nu_{max}$ / $cm^{-1}$) 3350, 2925, 1709, 1412, 1246, 996.

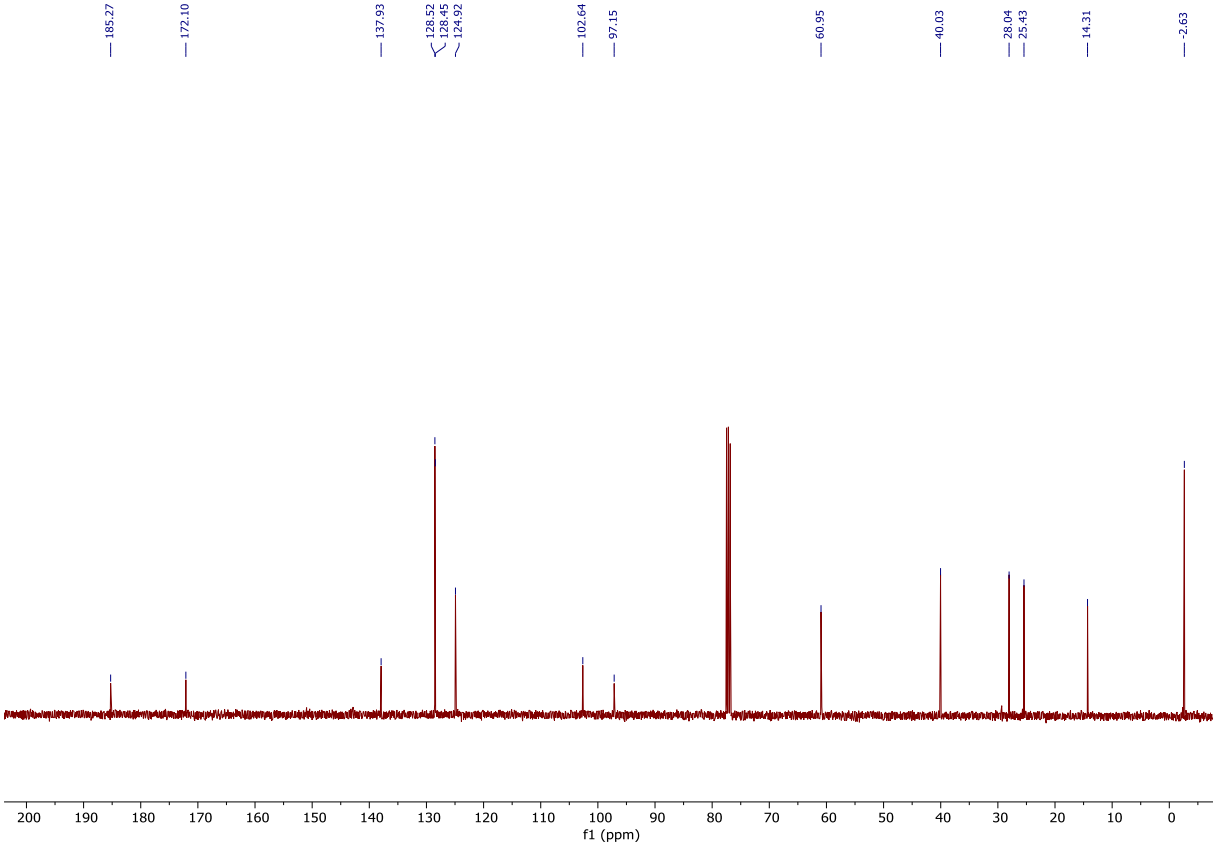
**$^1$H NMR** (500 MHz, Methanol-$d_4$) δ 6.60-6.43 (2H, m), 6.40-6.18 (2H, m), 6.09 (1H, t, *J* = 11.2 Hz), 6.09 (1H, t, *J* = 11.2 Hz), 5.76 (1H, dd, *J* = 14.8, 6.5 Hz), 5.66 (1H, dd, *J* = 15.2, 6.6 Hz), 5.46 (1H, dt, *J* = 11.0, 7.5 Hz), 5.37 (1H, dd, *J* = 10.9, 9.1 Hz), 4.57 (1H, dt, *J* = 9.0, 6.1 Hz), 4.17 (1H, app q, *J* = 6.5 Hz), 4.02 (1H, app q, *J* = 6.5 Hz), 2.57-2.37 (2H, m), 2.32 (2H, t, *J* = 7.0 Hz), 1.81-1.44 (6H, m), 0.92 (3H, t, *J* = 7.4 Hz).

**$^{13}$C NMR** (126 MHz, Methanol-$d_4$) δ 177.5, 137.8, 137.8, 135.2, 135.1, 131.5, 131.1, 130.5, 128.8, 128.0, 126.6, 74.7, 73.0, 68.2, 38.0, 36.7, 34.8, 31.2, 22.1, 10.2.

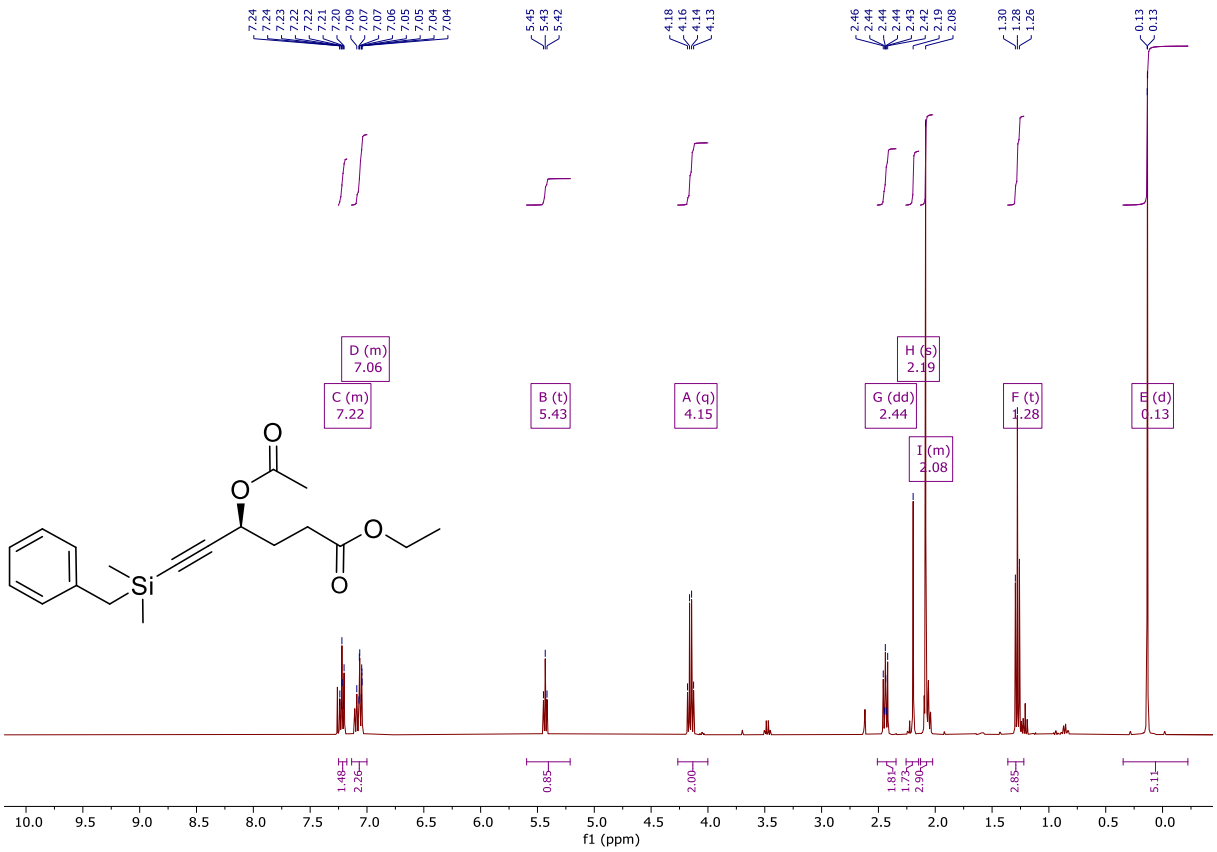
**HRMS** ($ES^-$) calc. for $C_{20}H_{29}O_5$ $[M-H]^-$ 349.2021, found 349.2020.

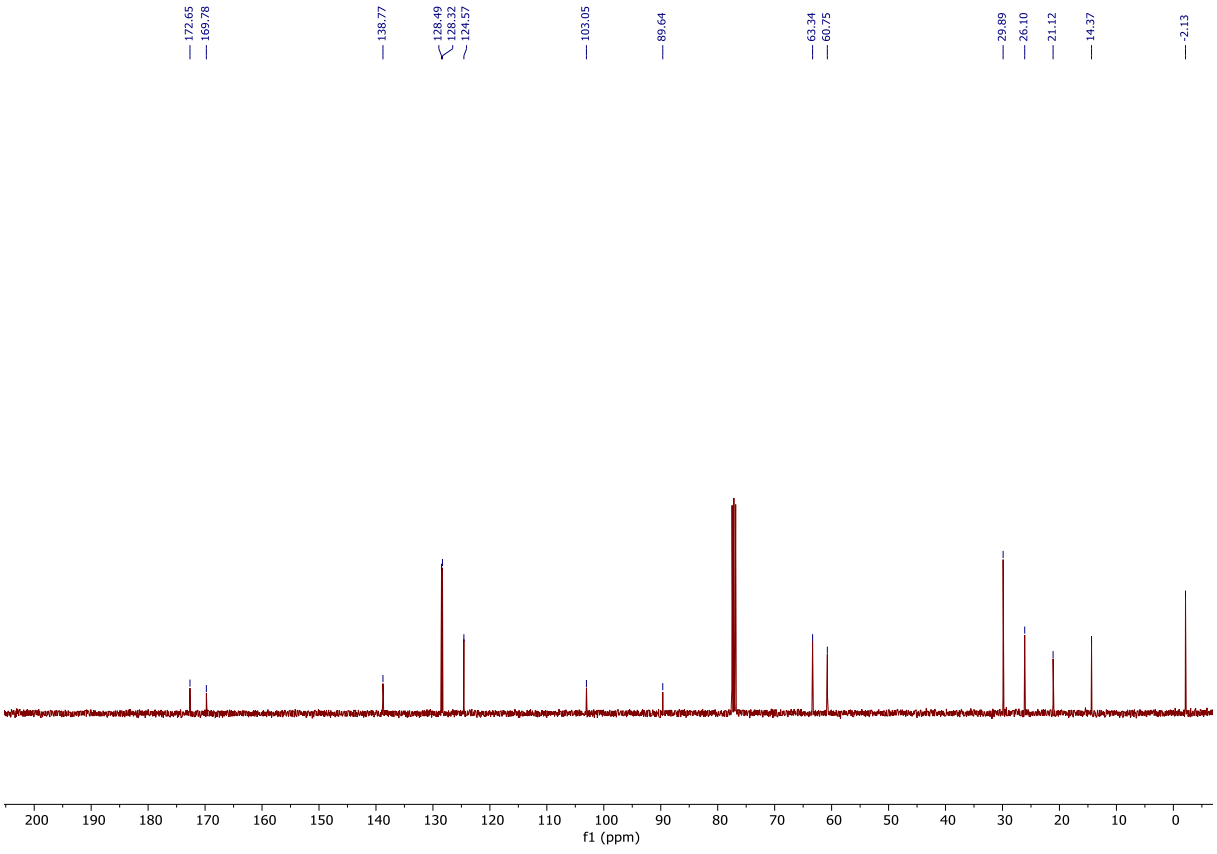
**Ethyl 6-(benzyldimethylsilyl)-4-oxohex-5-ynoate, 13**



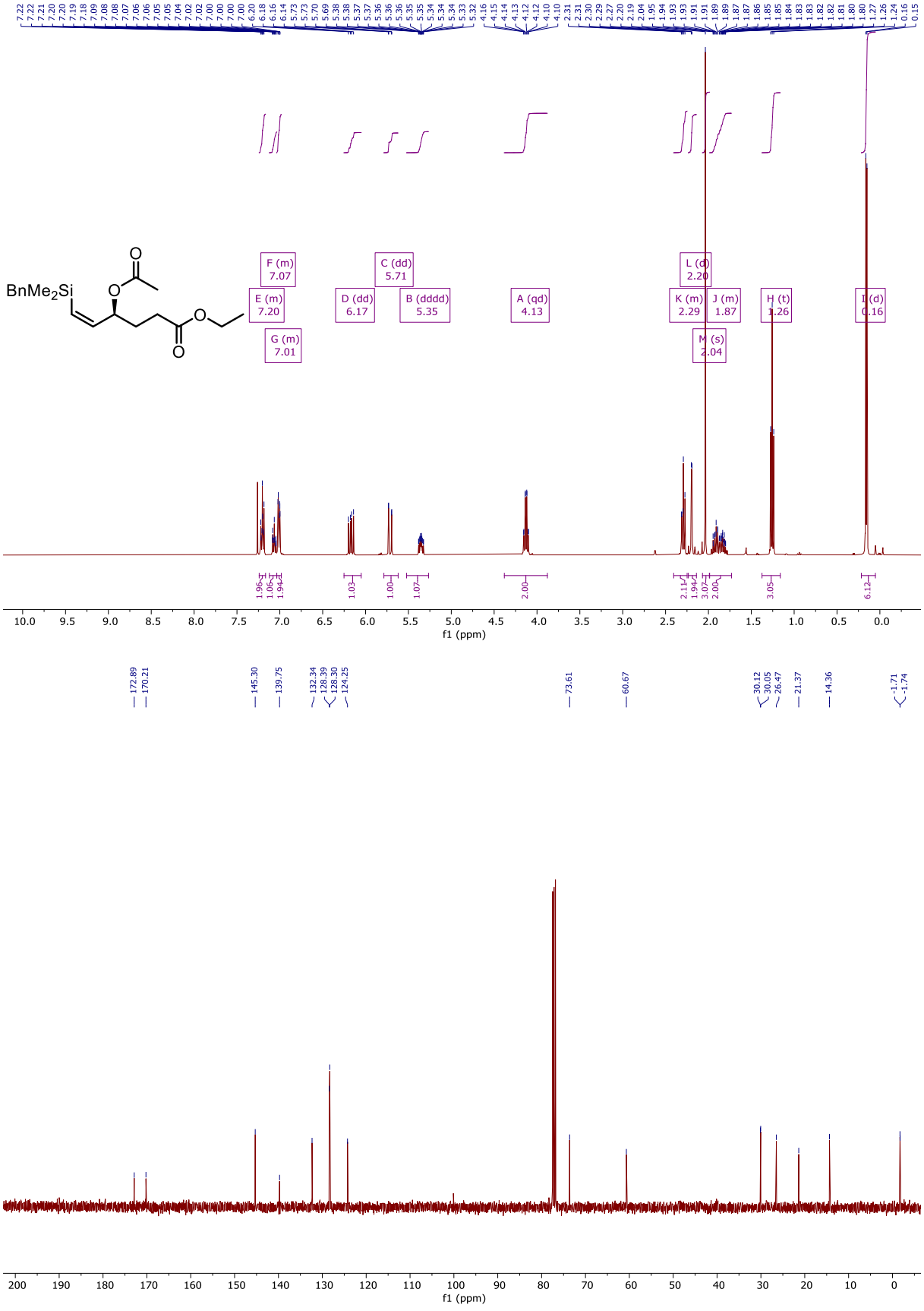



**Ethyl (*S*)-4-acetoxy-6-(benzyldimethylsilyl)hex-5-ynoate, 15**

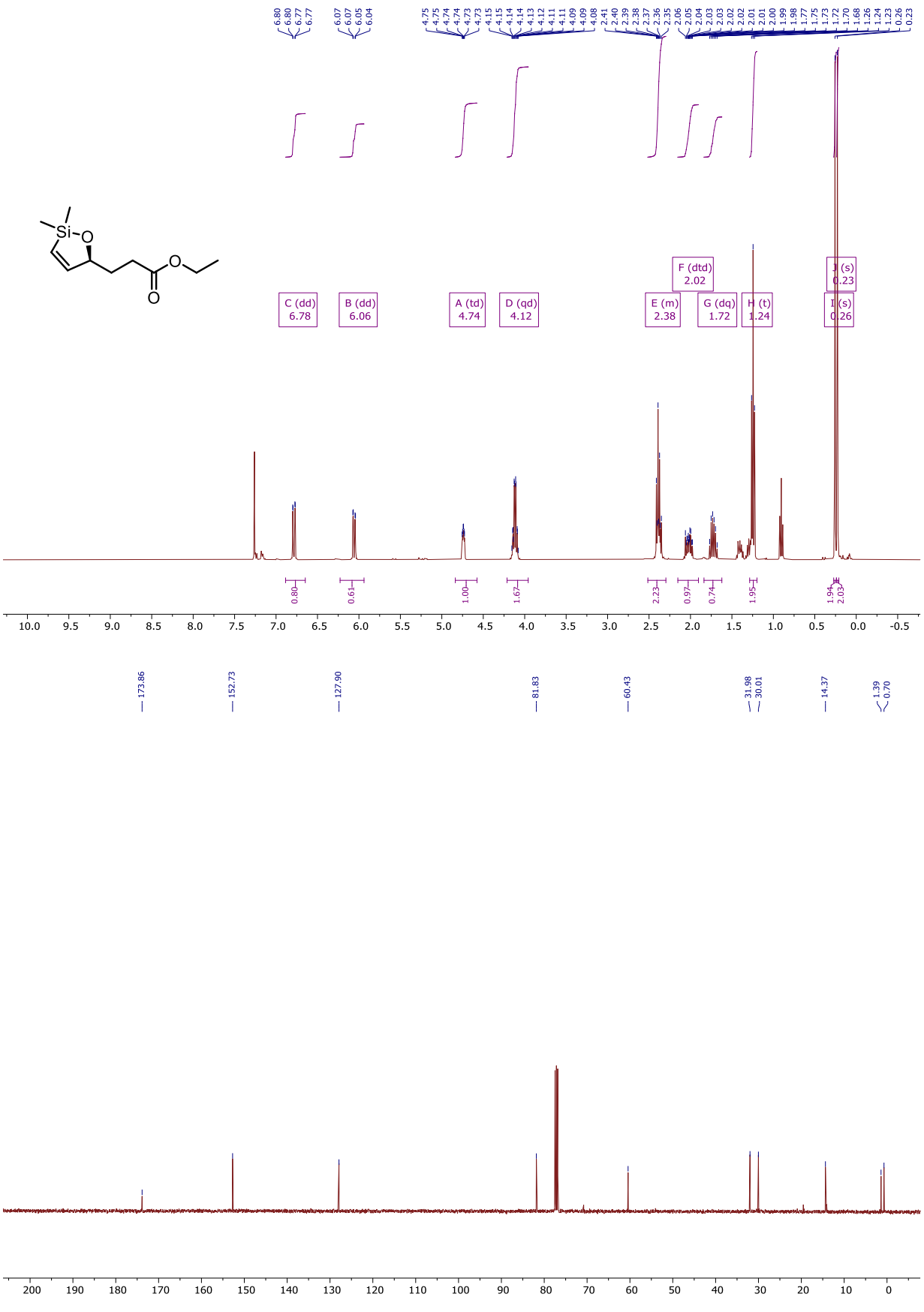


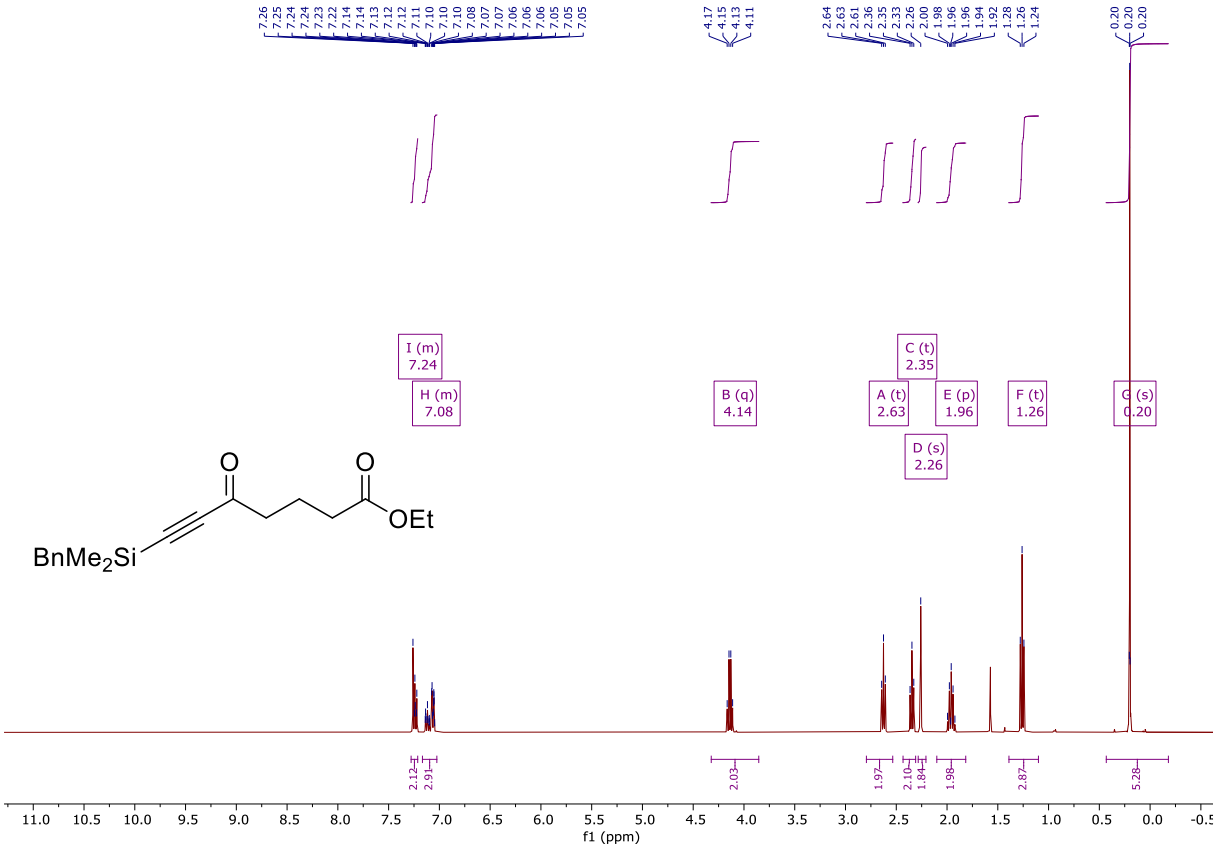
**Ethyl (*S*,*Z*)-4-acetoxy-6-(benzyldimethylsilyl)hex-5-enoate, 17**

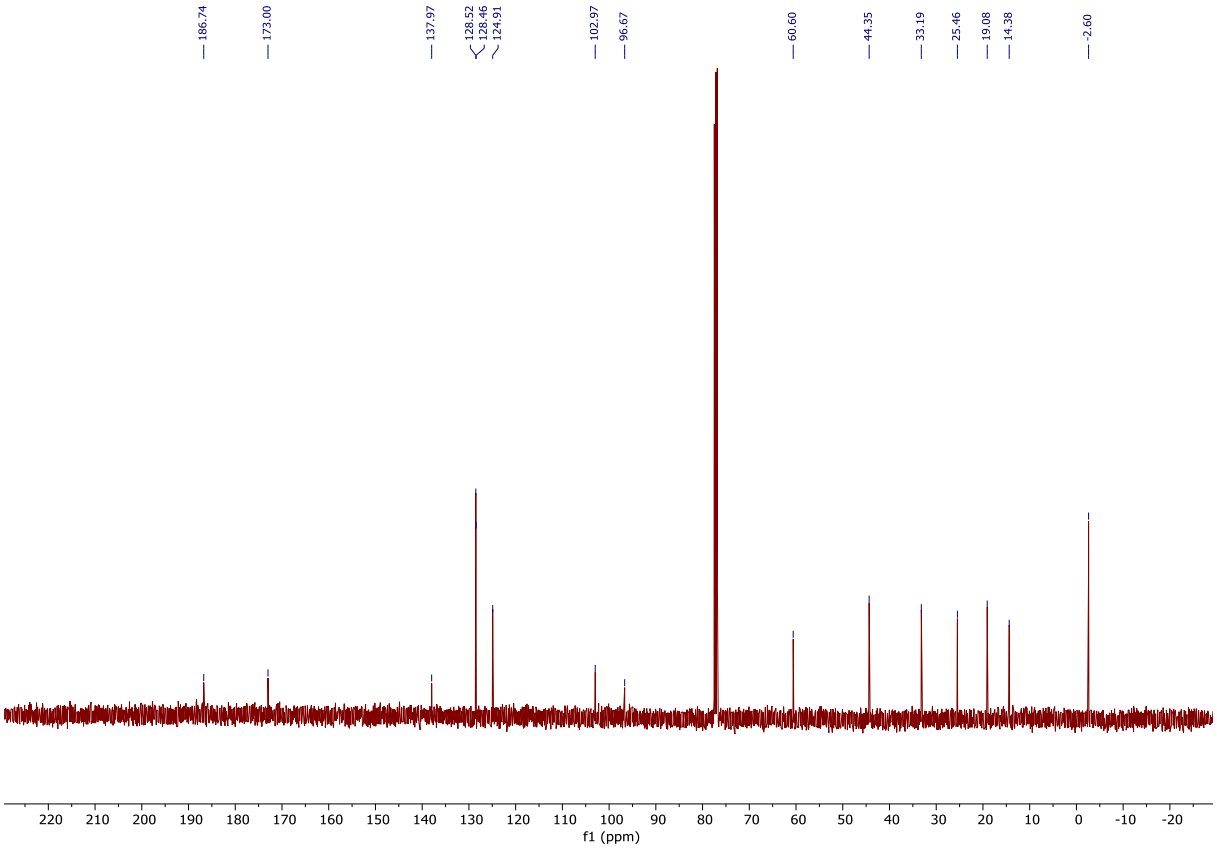


**Ethyl (*S*)-3-(2,2-dimethyl-2,5-dihydro-1,2-oxasilol-5-yl)propanoate, 5**

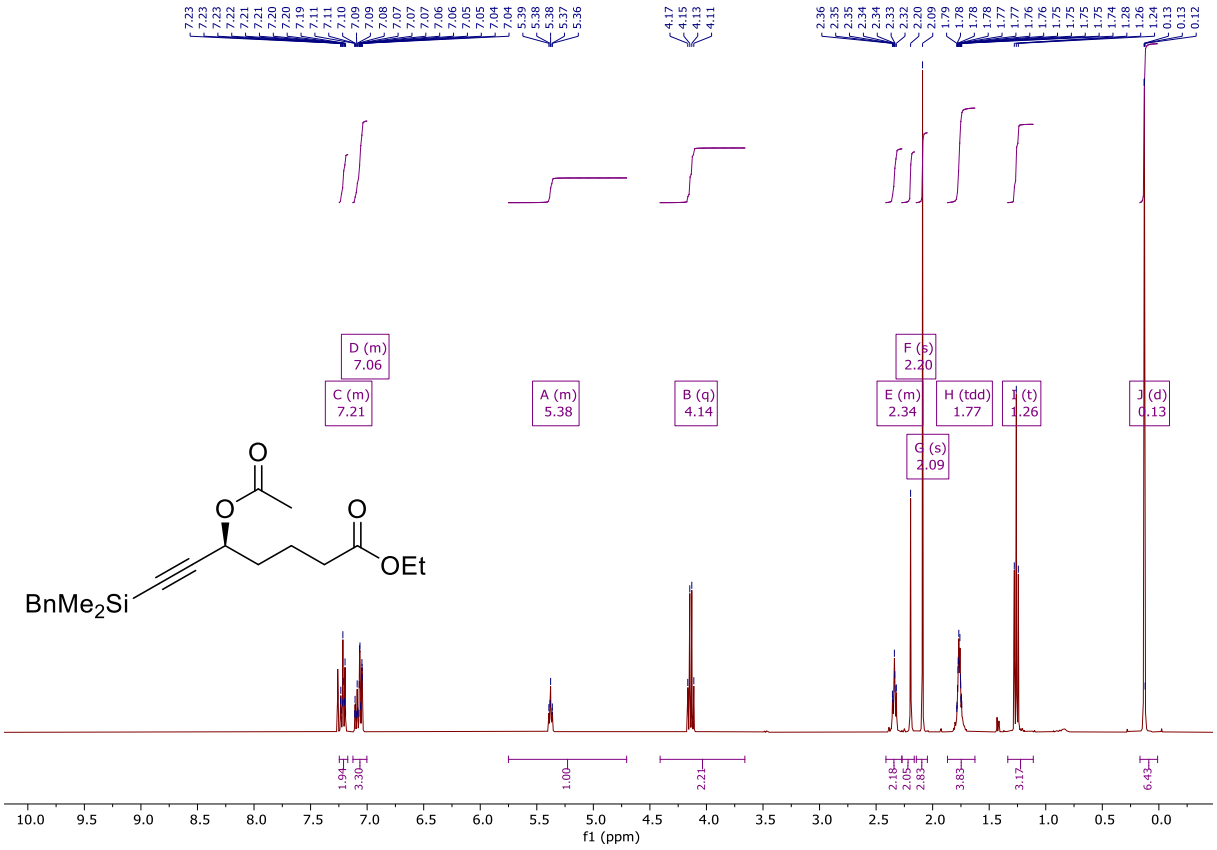


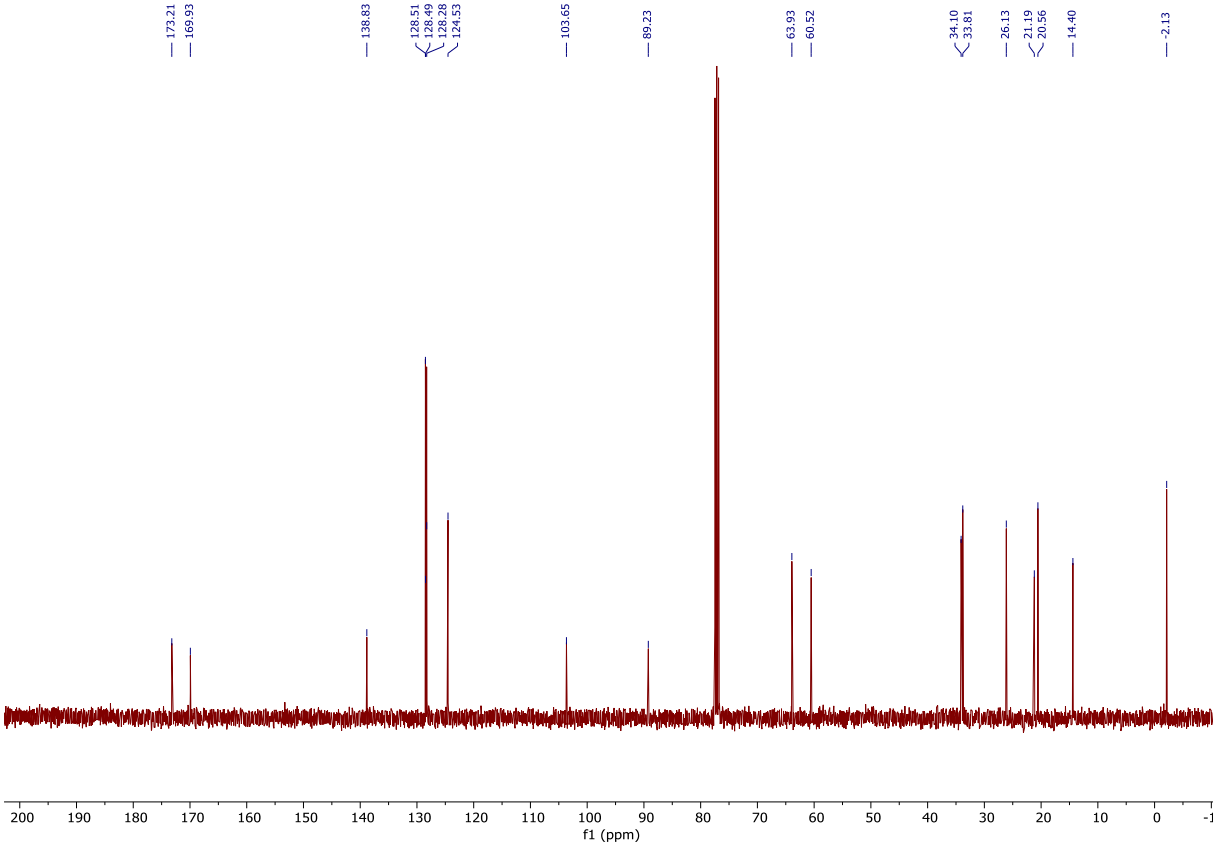
**Ethyl 7-(benzyldimethylsilyl)-5-oxohept-6-ynoate, 14**



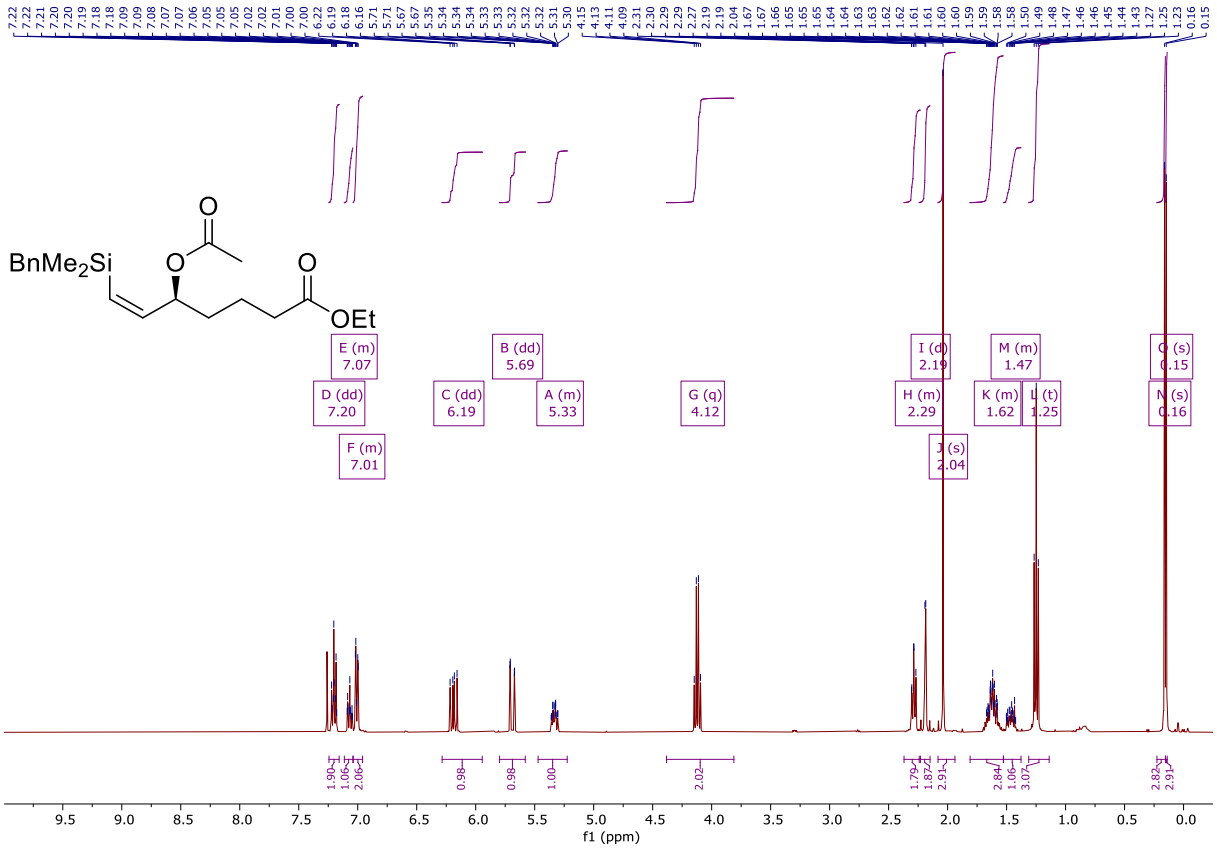



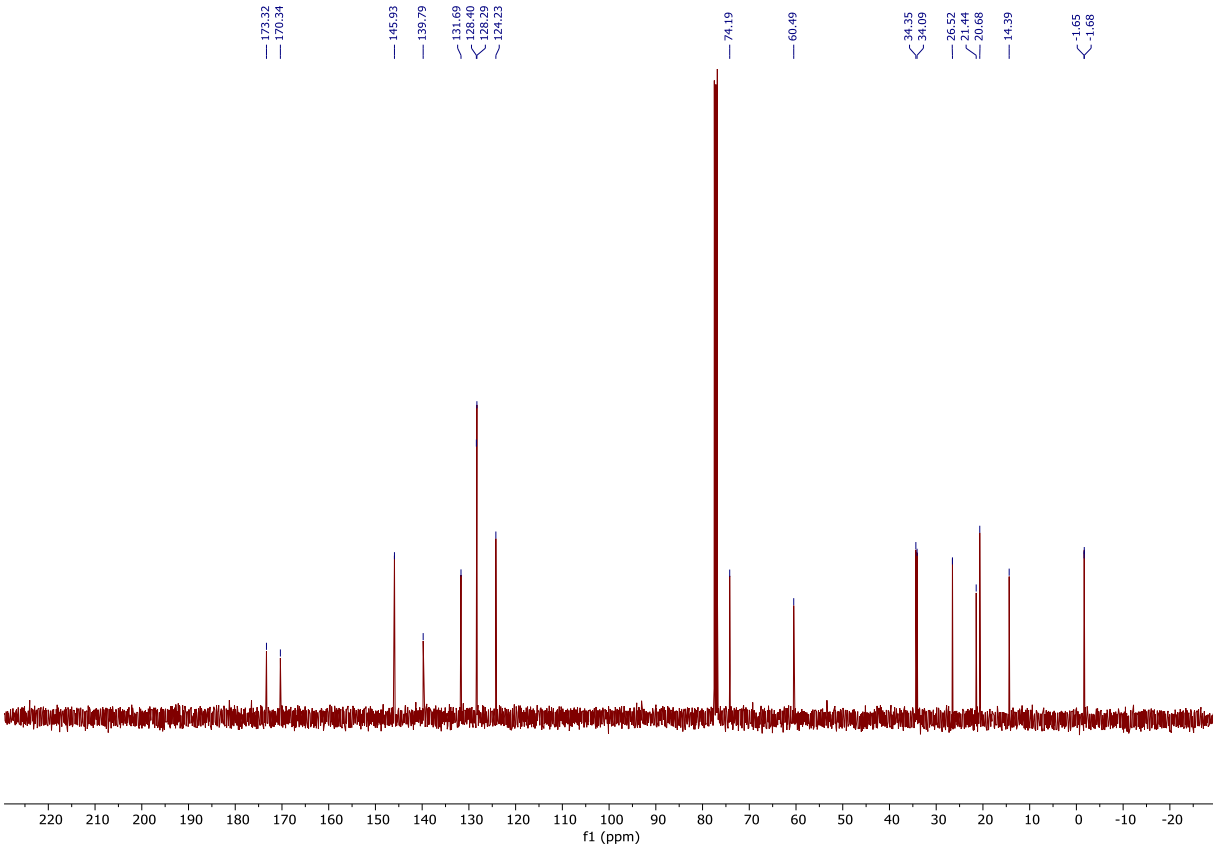
**Ethyl (*S*)-5-acetoxy-7-(benzyldimethylsilyl)hept-6-ynoate, 16**



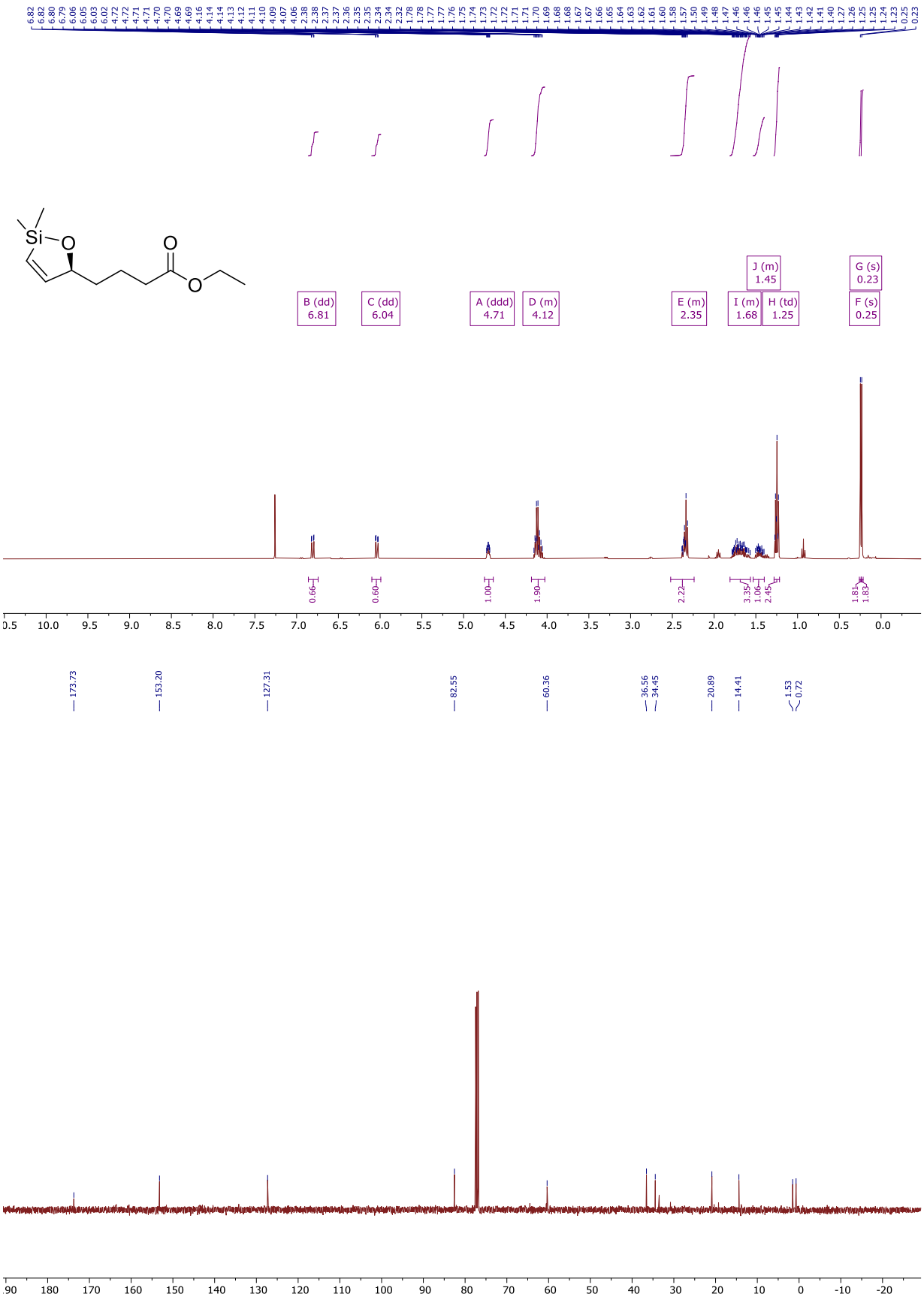



**Ethyl (*S*,*Z*)-5-acetoxy-7-(benzyldimethylsilyl)hept-6-enoate, 18**

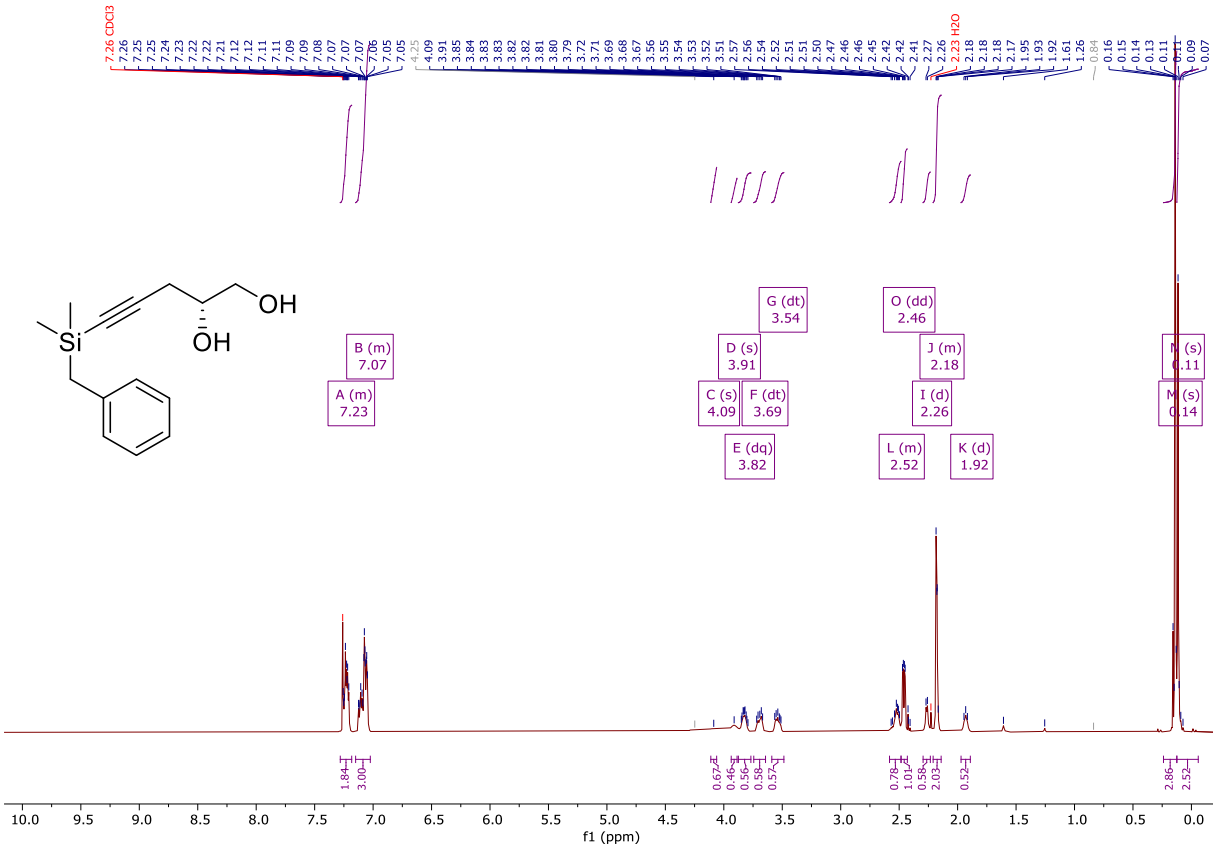


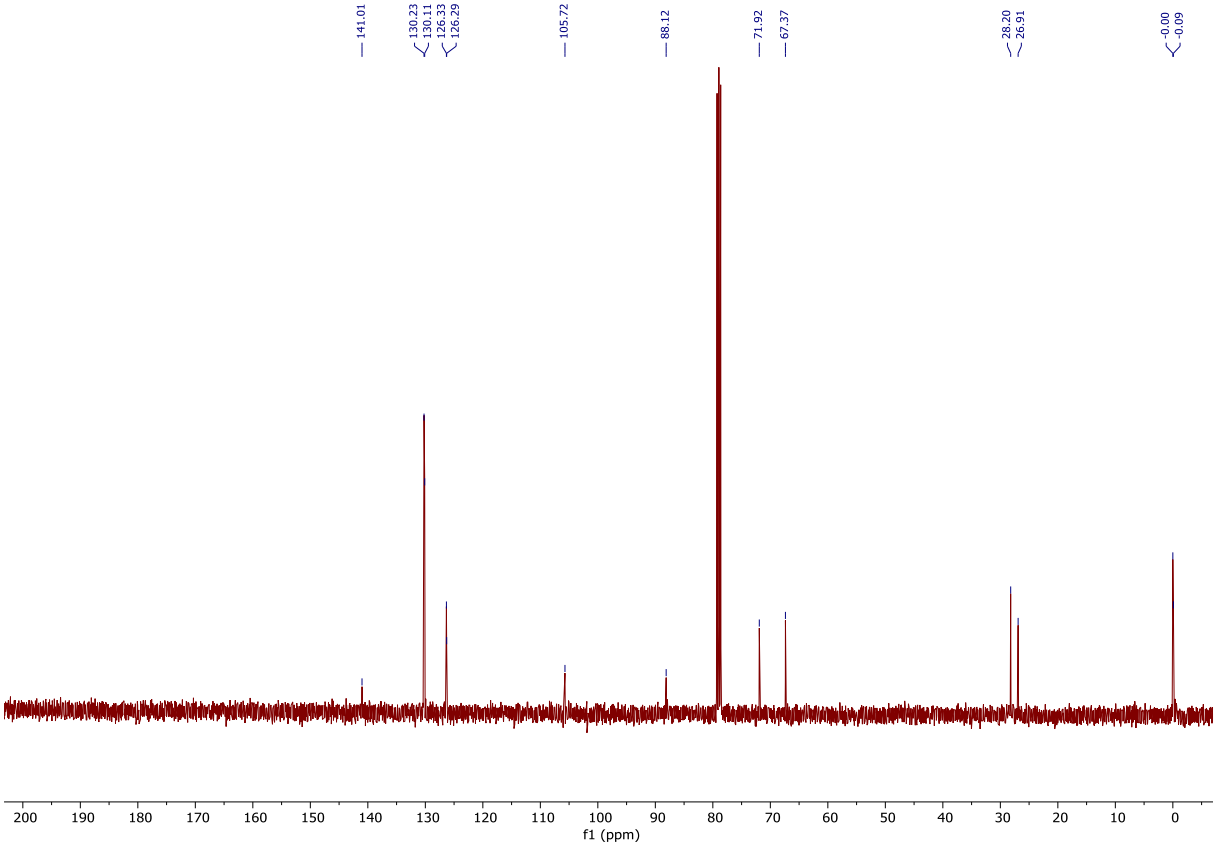



**Ethyl (*S*)-4-(2,2-dimethyl-2,5-dihydro-1,2-oxasilol-5-yl)butanoate, 6**

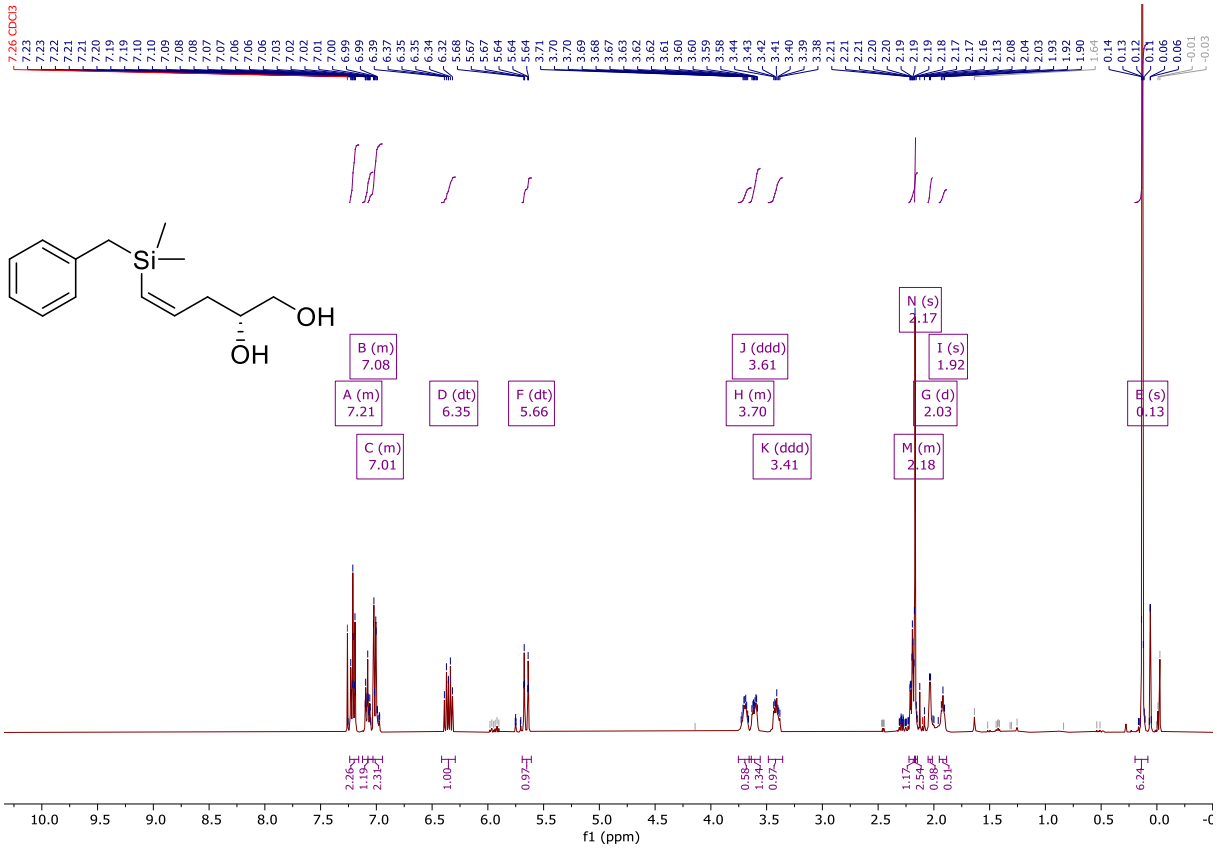


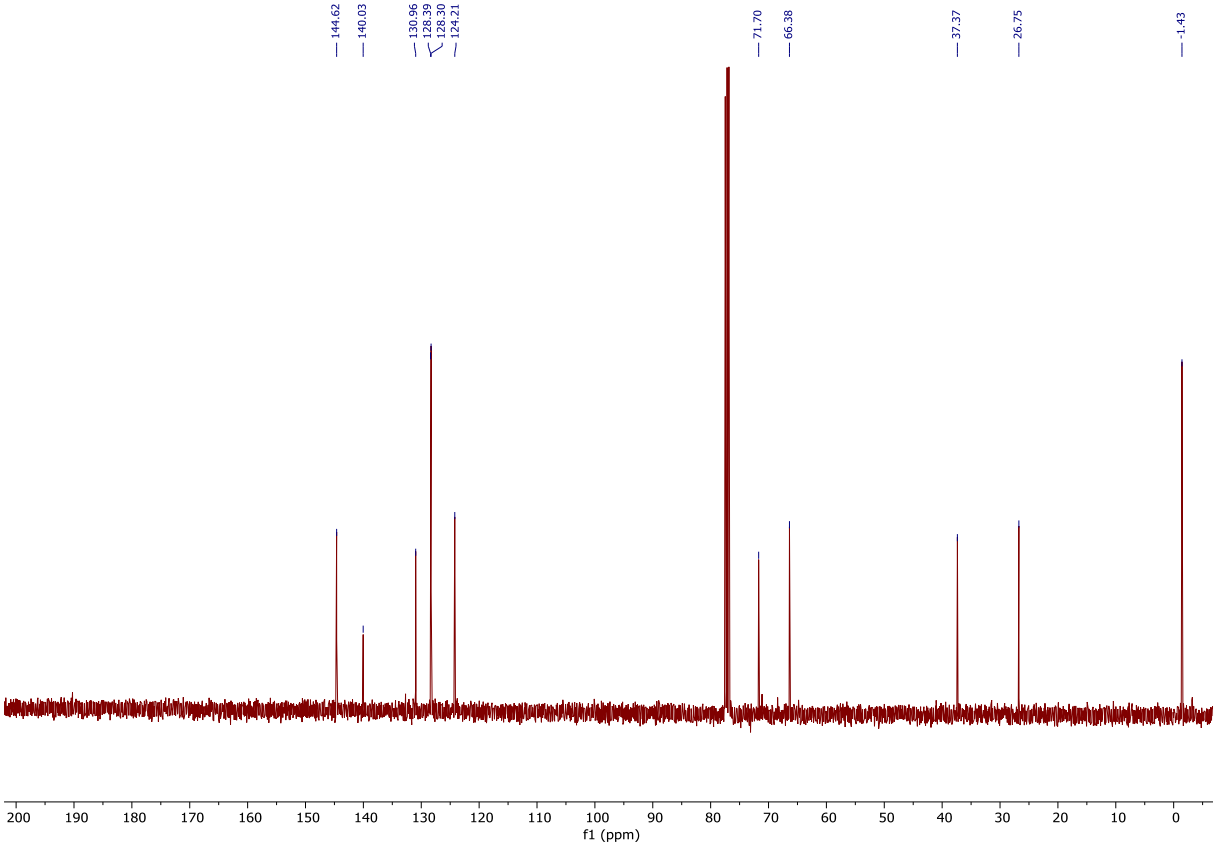
**(*R*)-5-(Benzyldimethylsilyl)pent-4-yne-1,2-diol, 19**



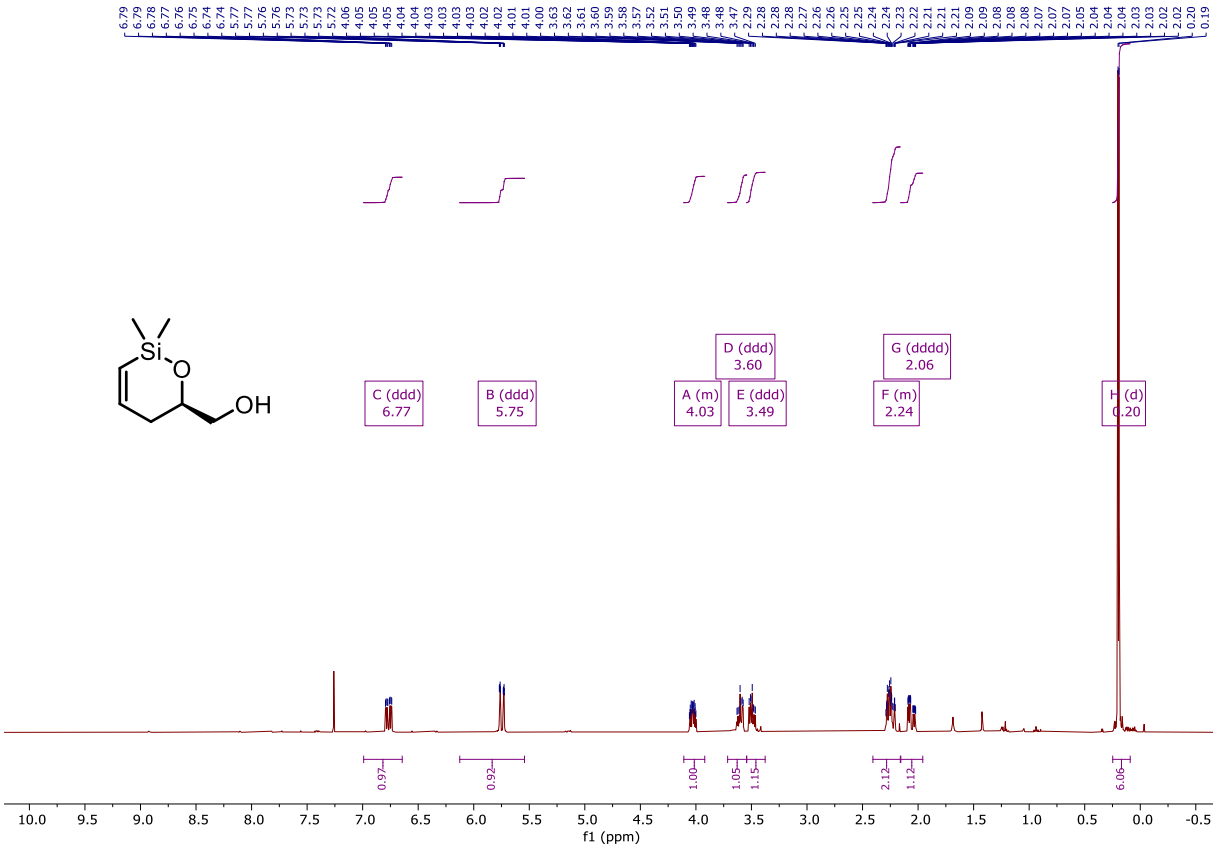



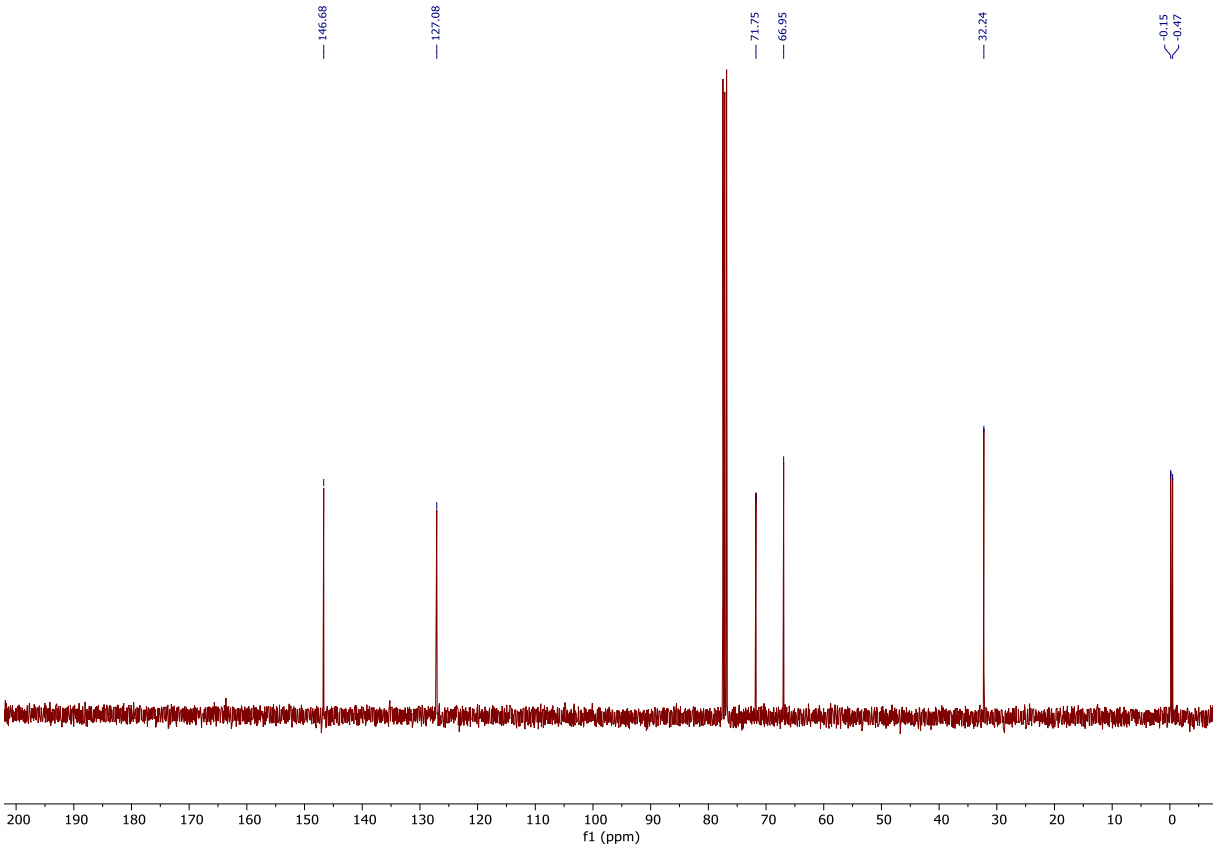
**(*R*,*Z*)-5-(Benzyldimethylsilyl)pent-4-ene-1,2-diol, S2**



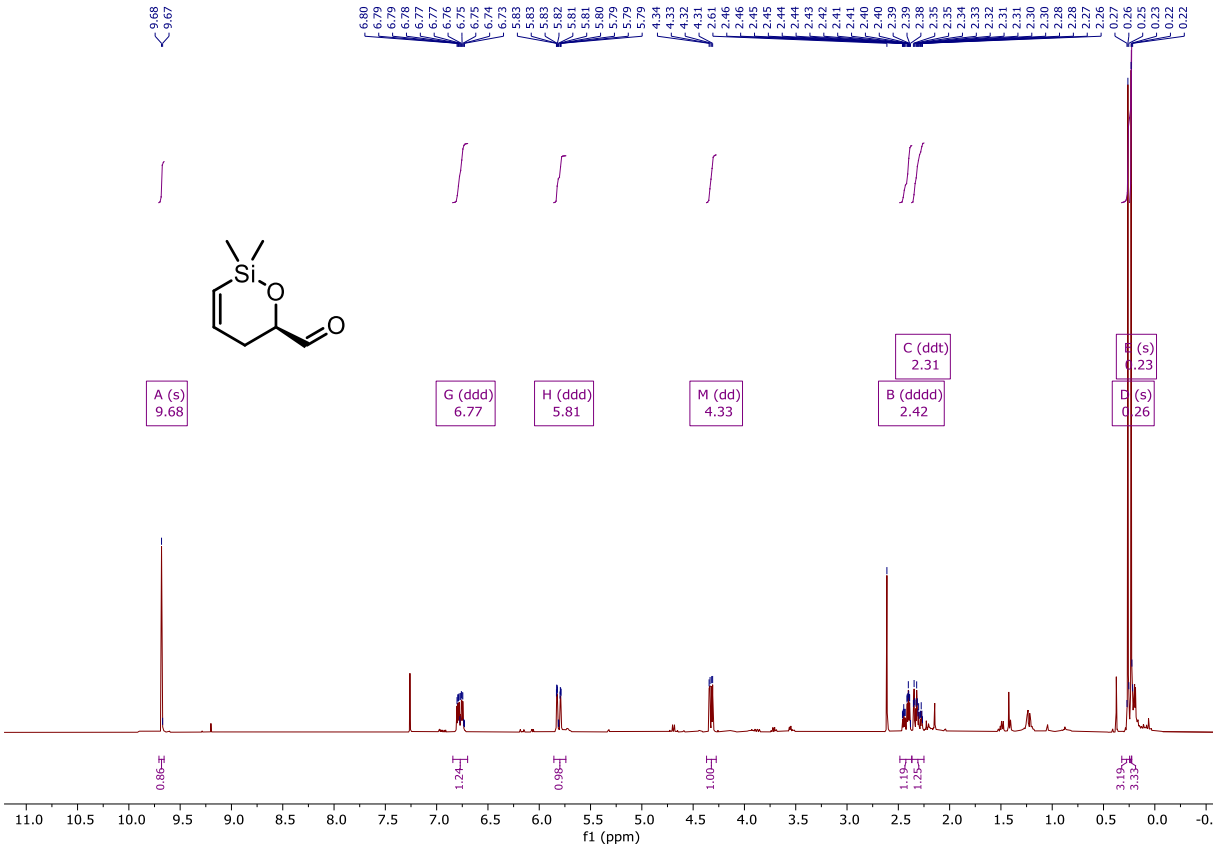



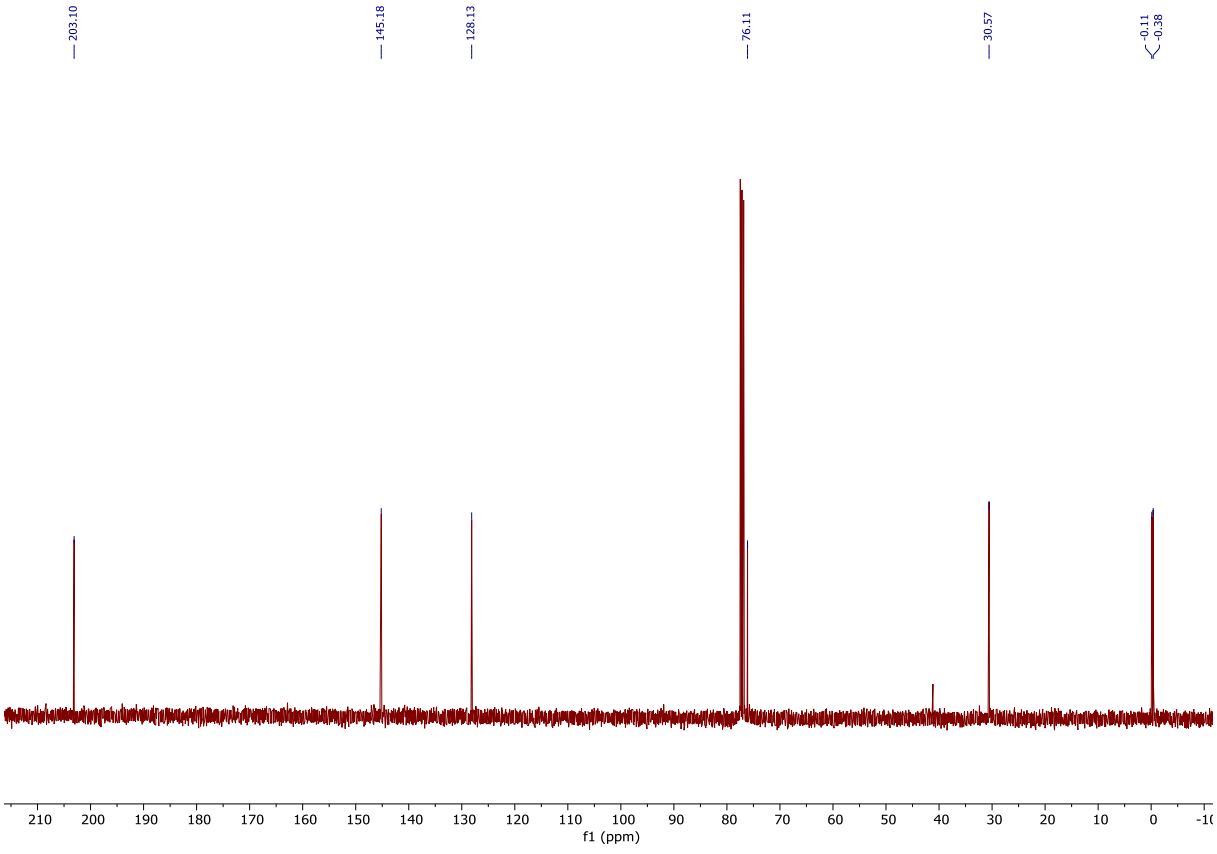
**(*R*)-(2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasilin-6-yl)methanol, 20**



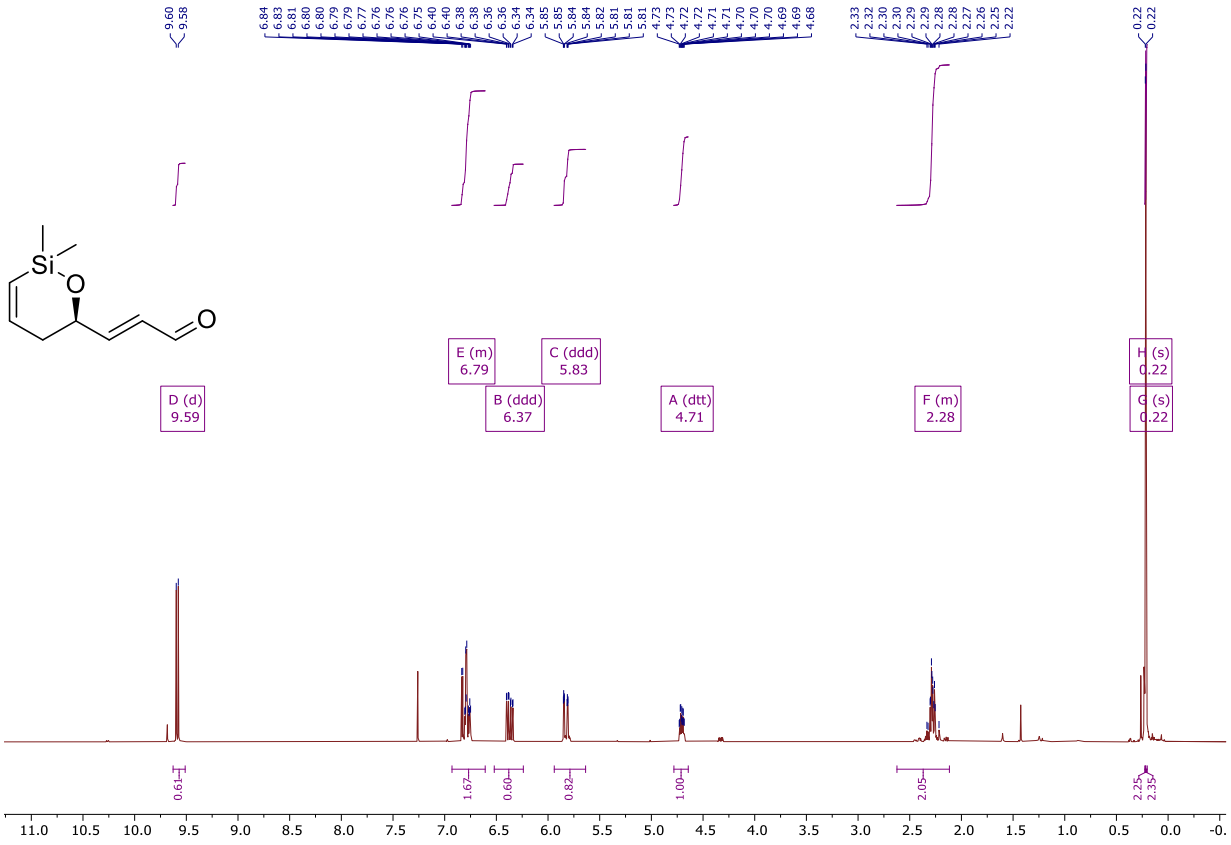



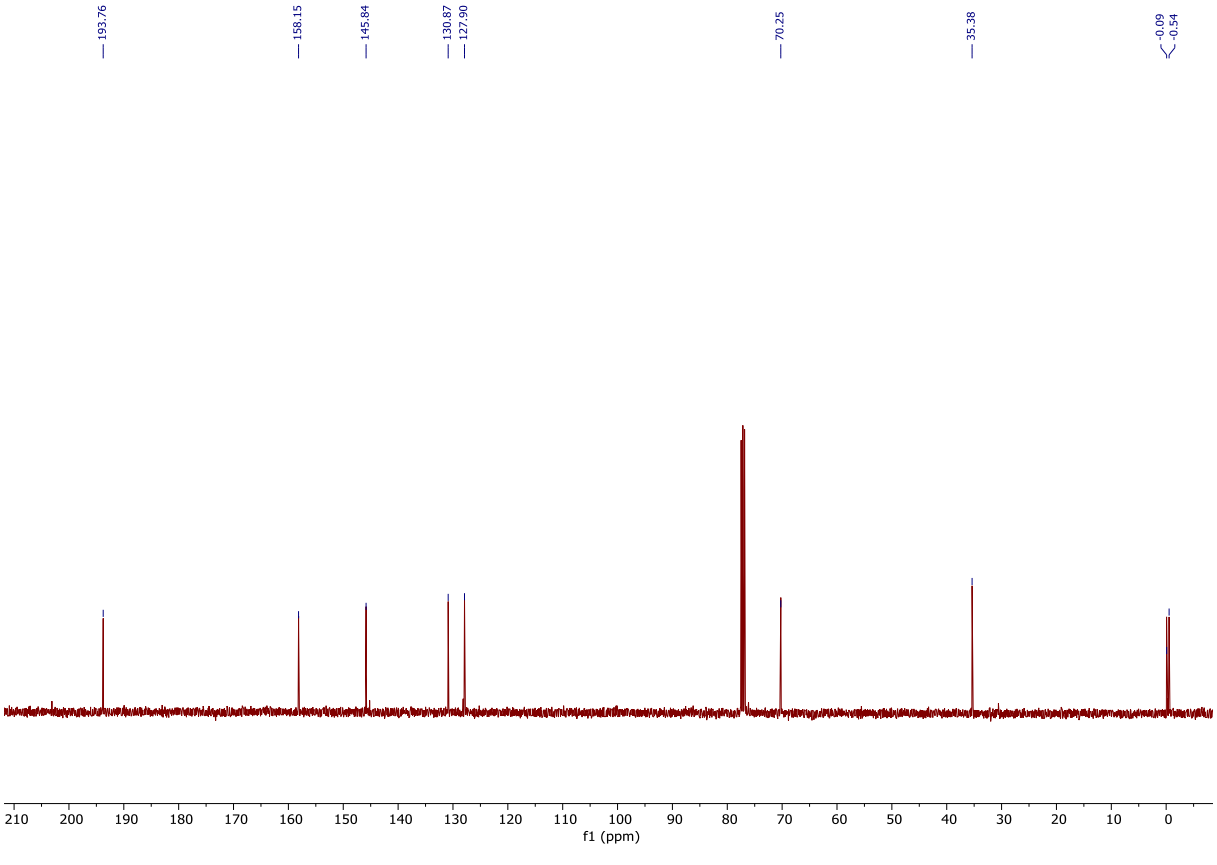
**(*R*)-2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasiline-6-carbaldehyde, S3**



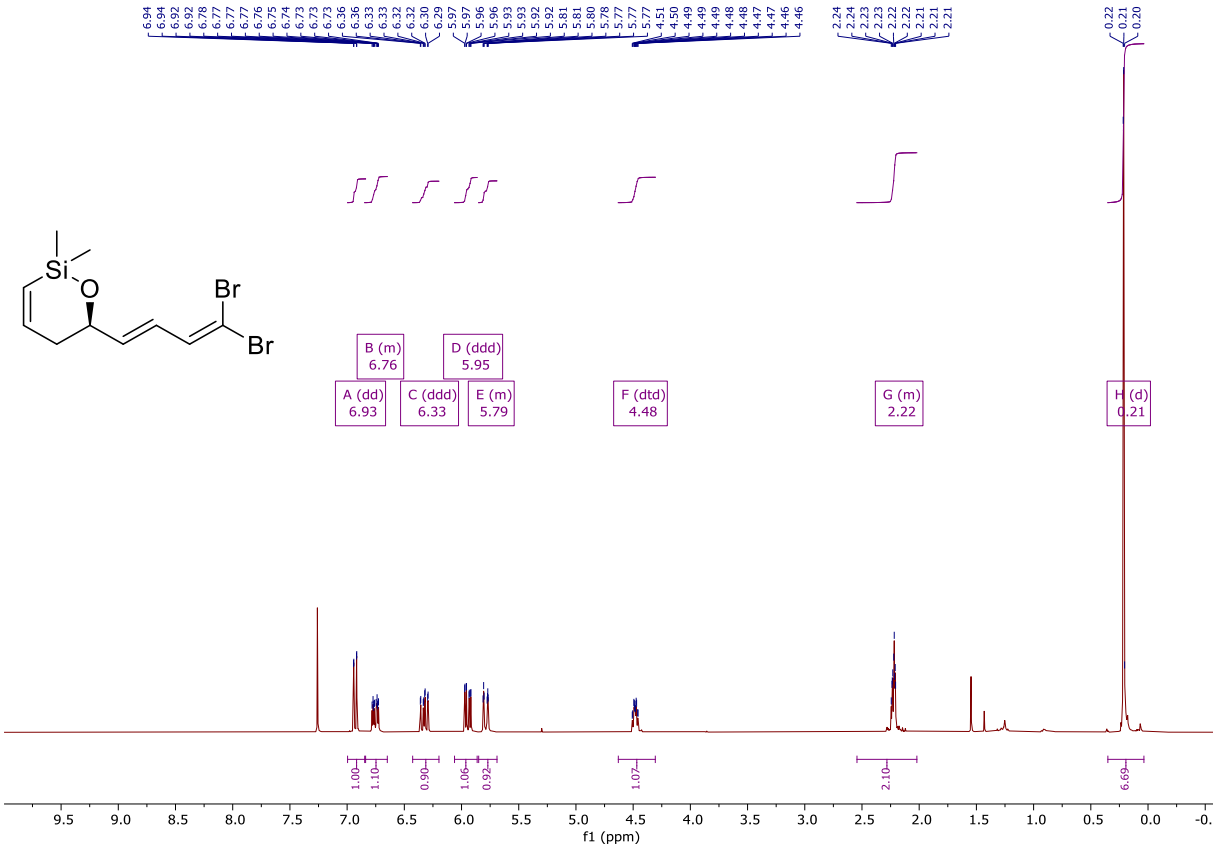



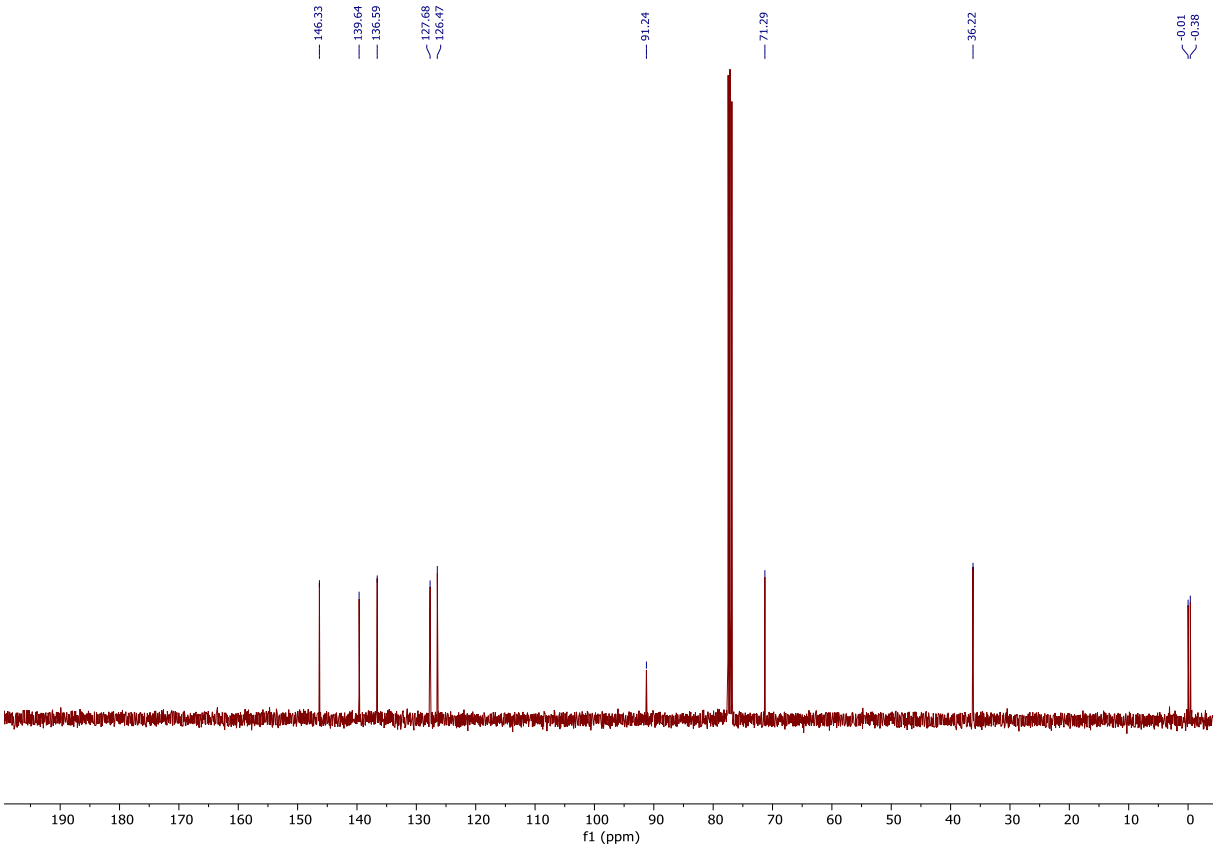
**(*R*,*E*)-3-(2,2-Dimethyl-5,6-dihydro-2H-1,2-oxasilin-6-yl)acrylaldehyde, 21**



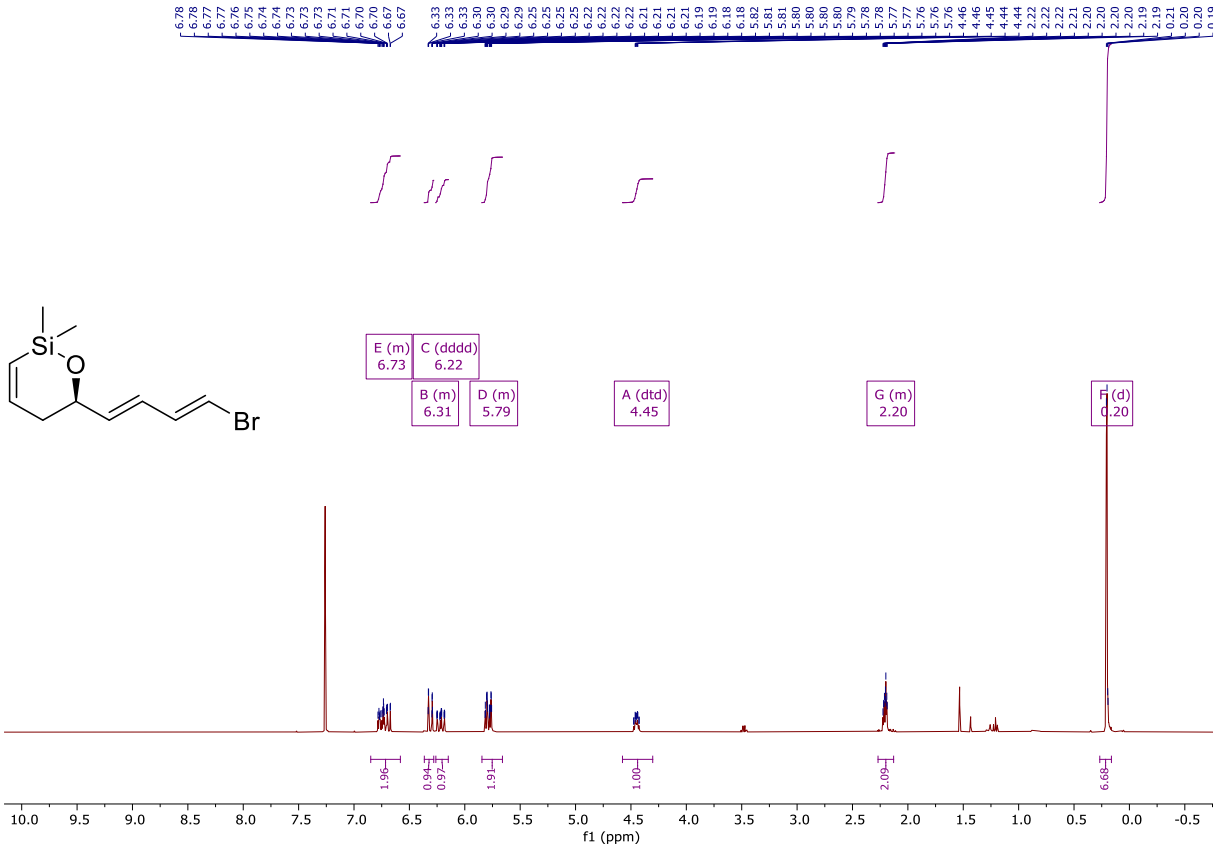



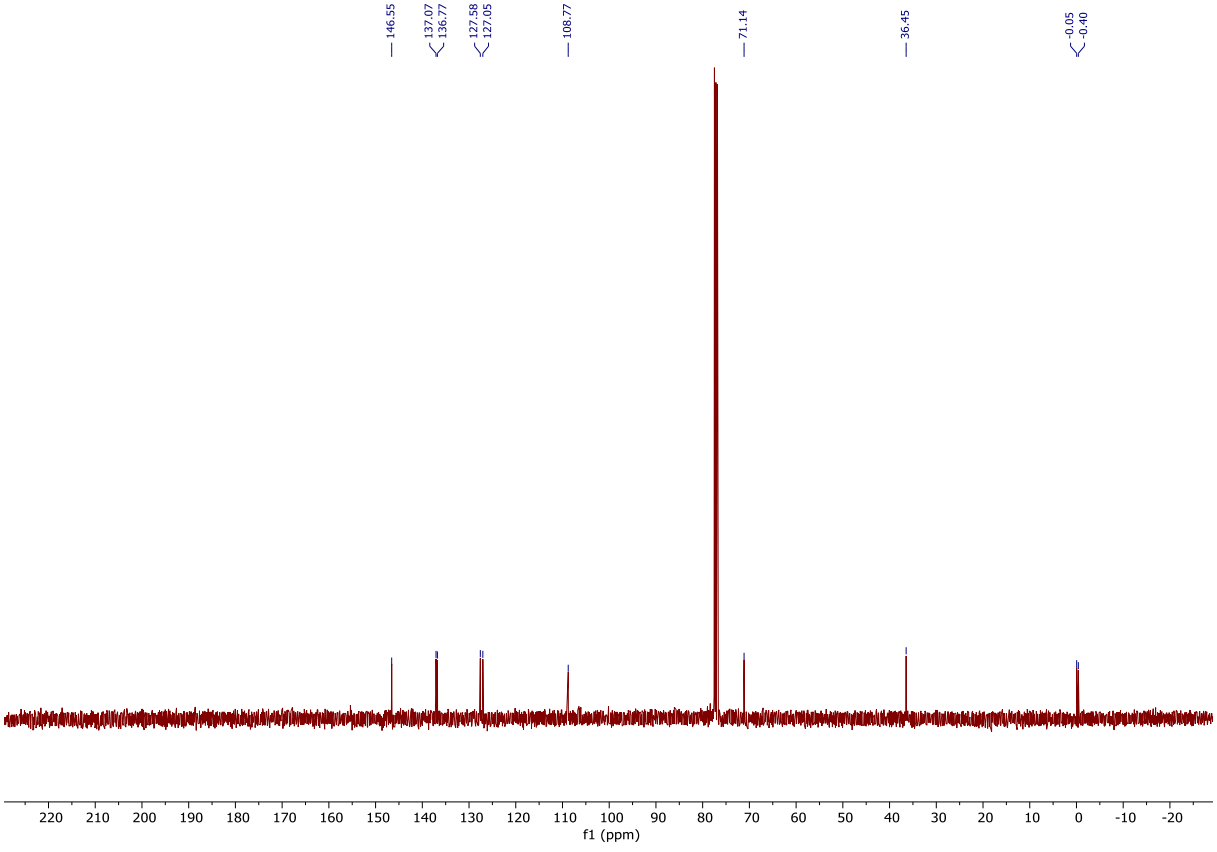
**(*R*,*E*)-6-(4,4-Dibromobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 22**



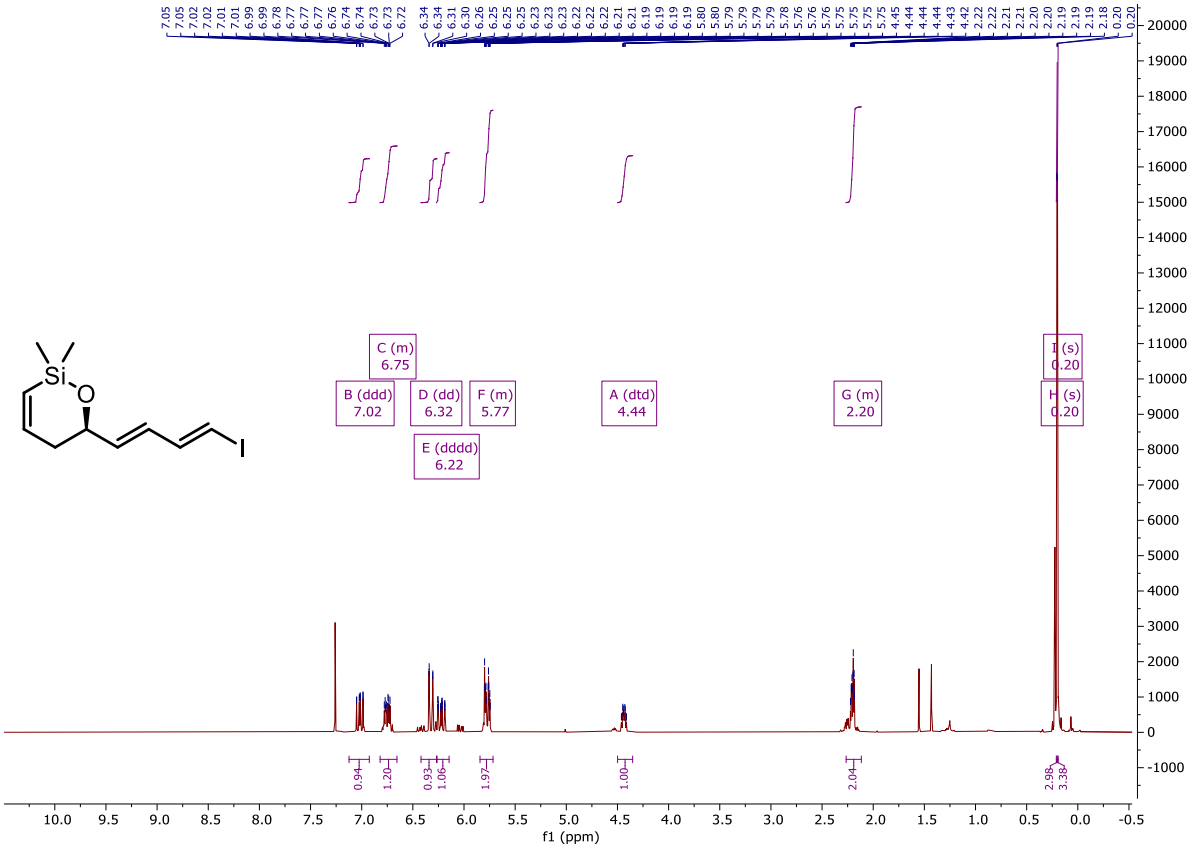



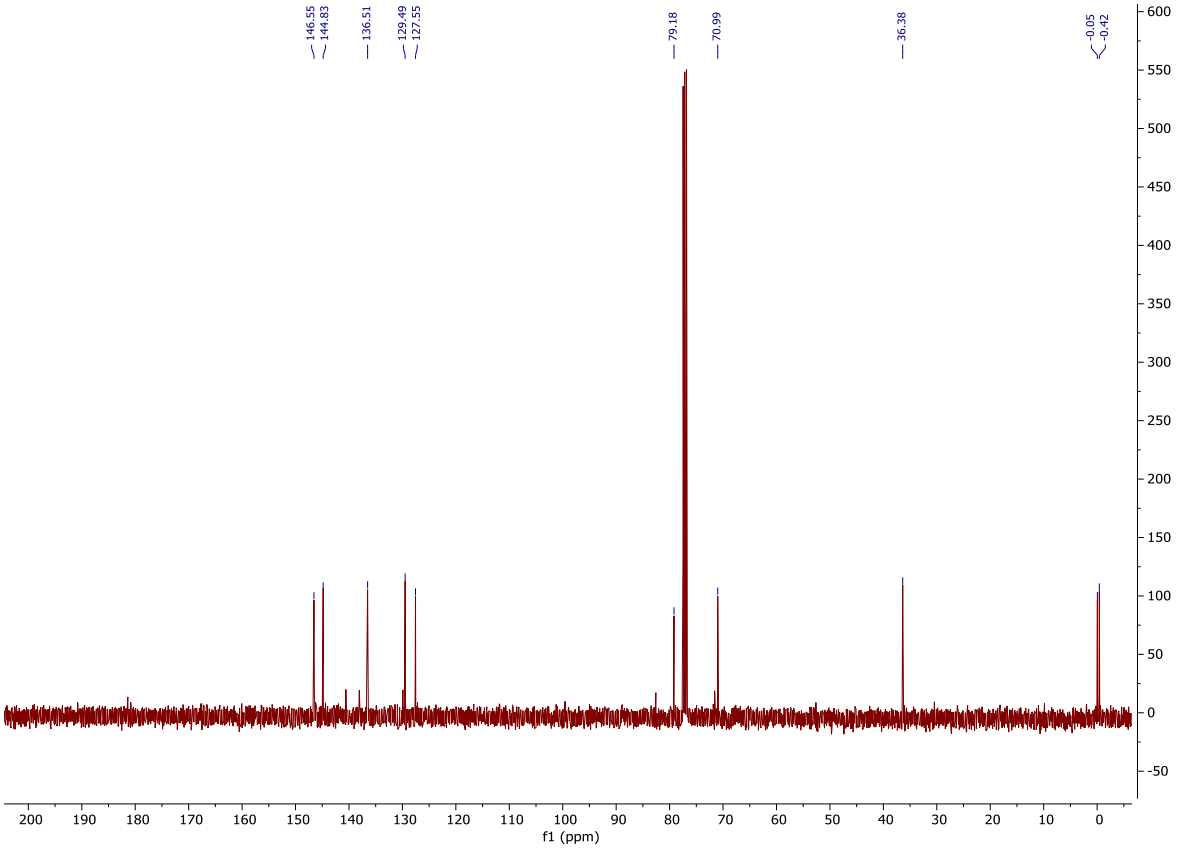
**(*R*)-6-((1*E*,3*E*)-4-Bromobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 8**



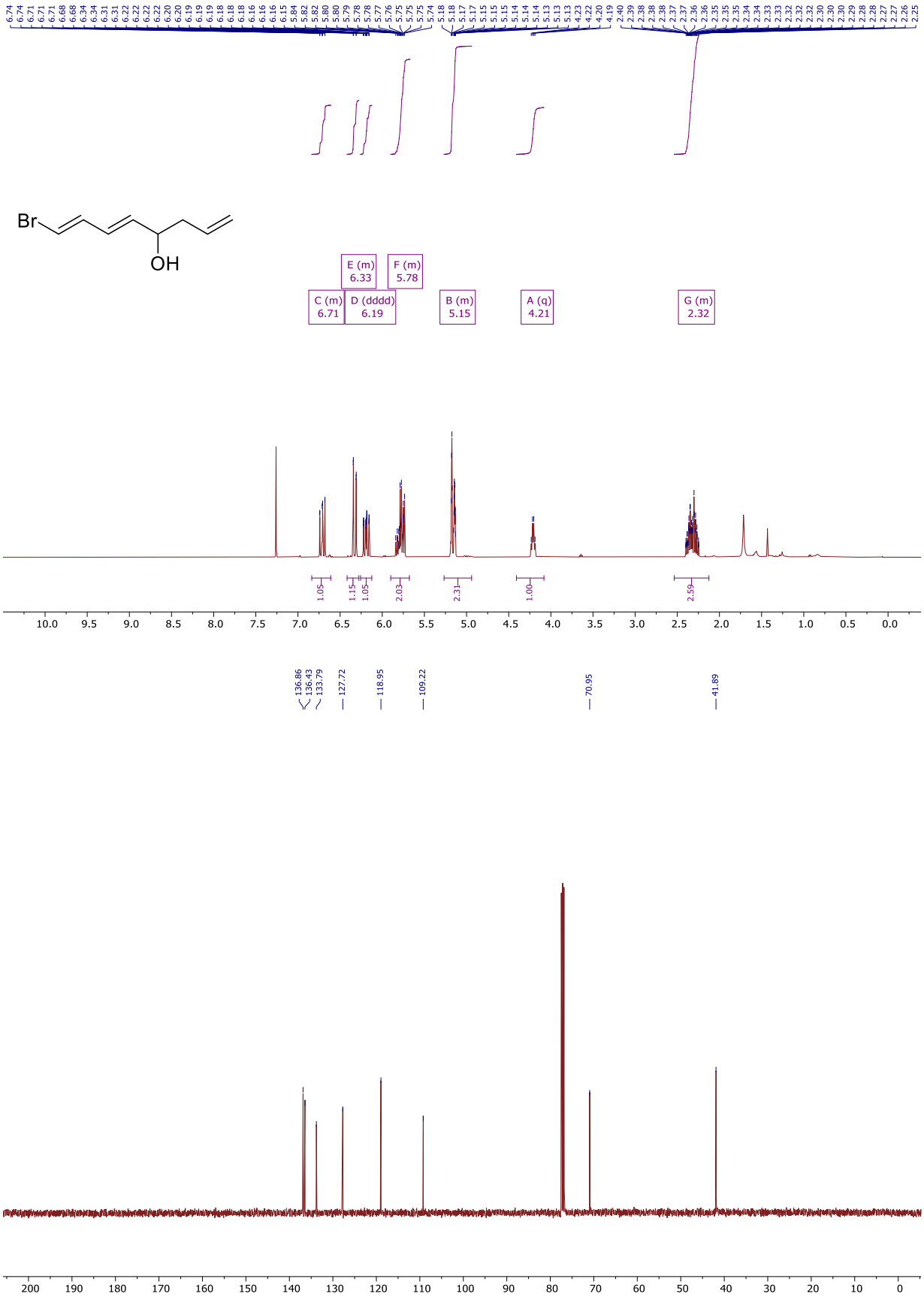



**(*R*)-6-((1*E*,3*E*)-4-Iodobuta-1,3-dien-1-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline, 7**

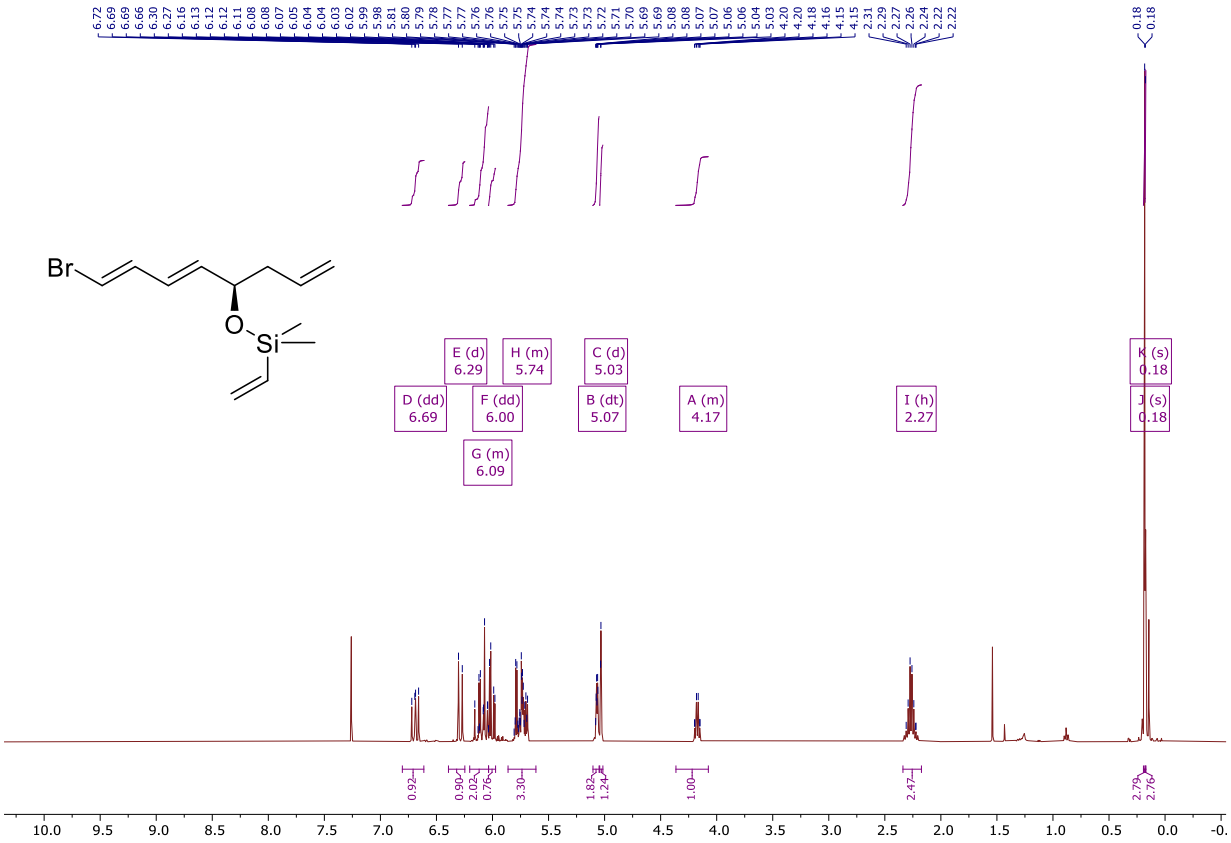


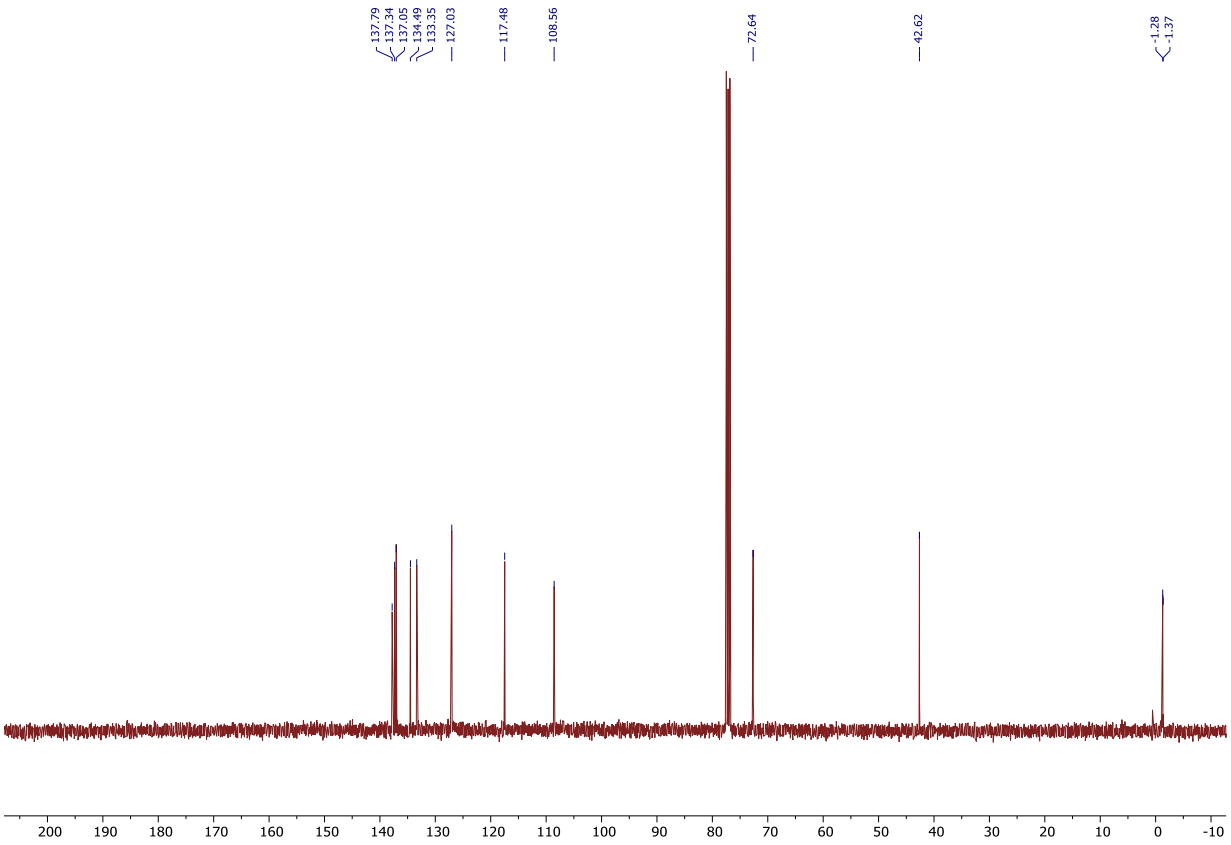



**(5*E*,7*E*)-8-Bromoocta-1,5,7-trien-4-ol, (±)-24**

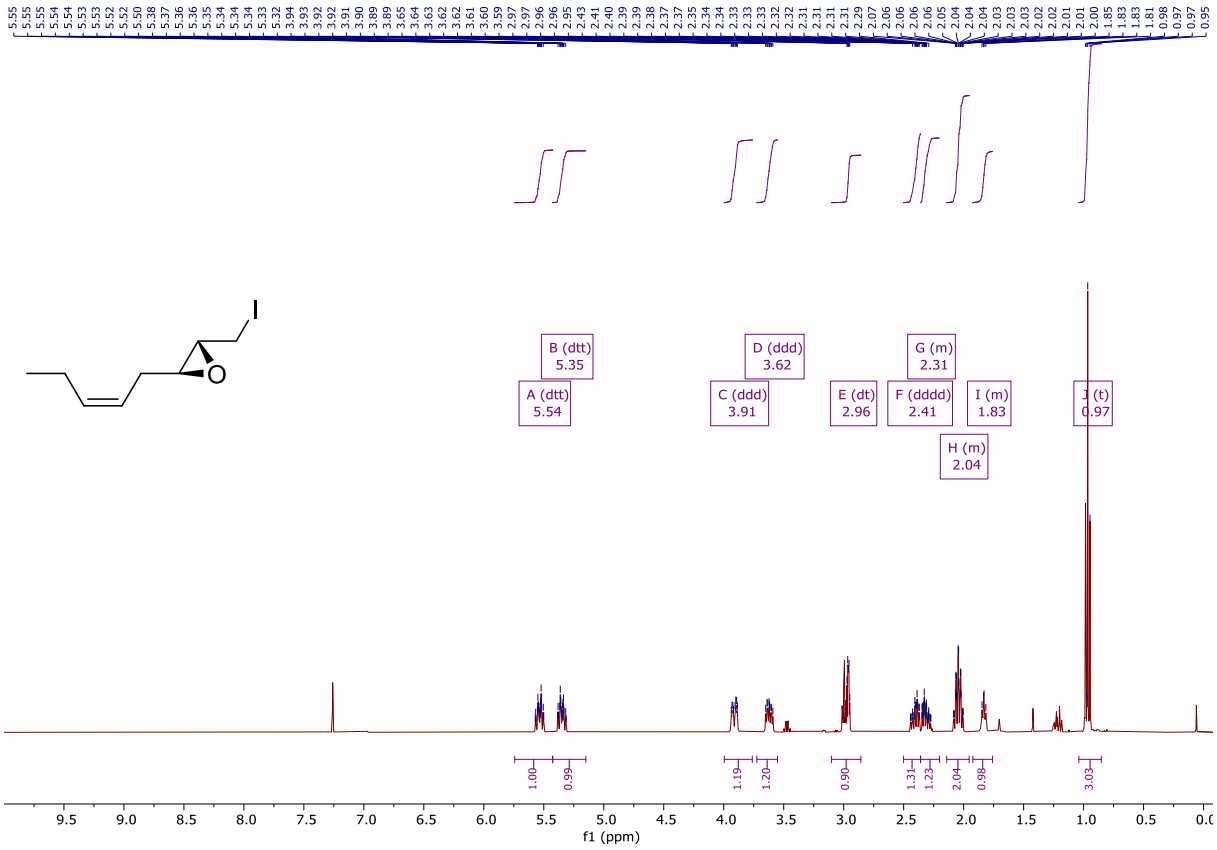


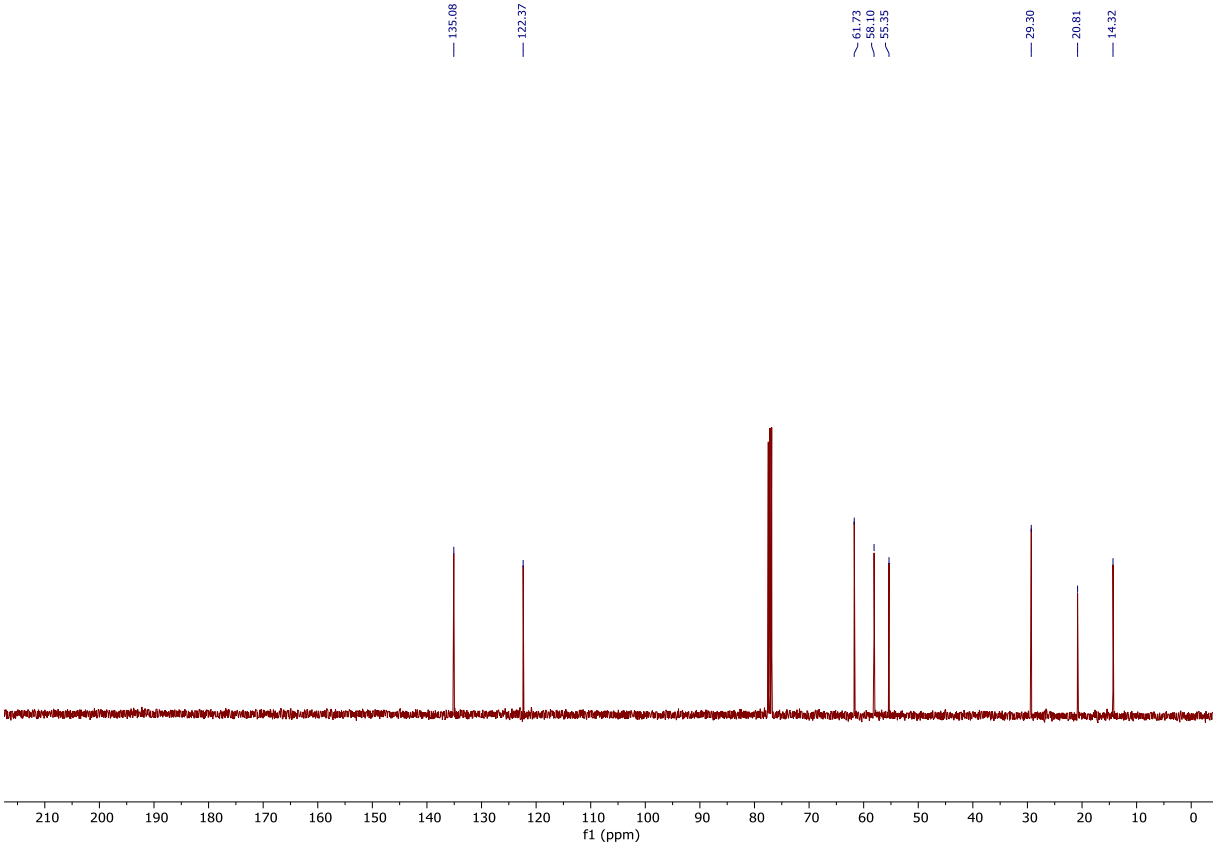
**(((*R*,5*E*,7*E*)-8-Bromoocta-1,5,7-trien-4-yl)oxy)dimethyl(vinyl)silane, S5**



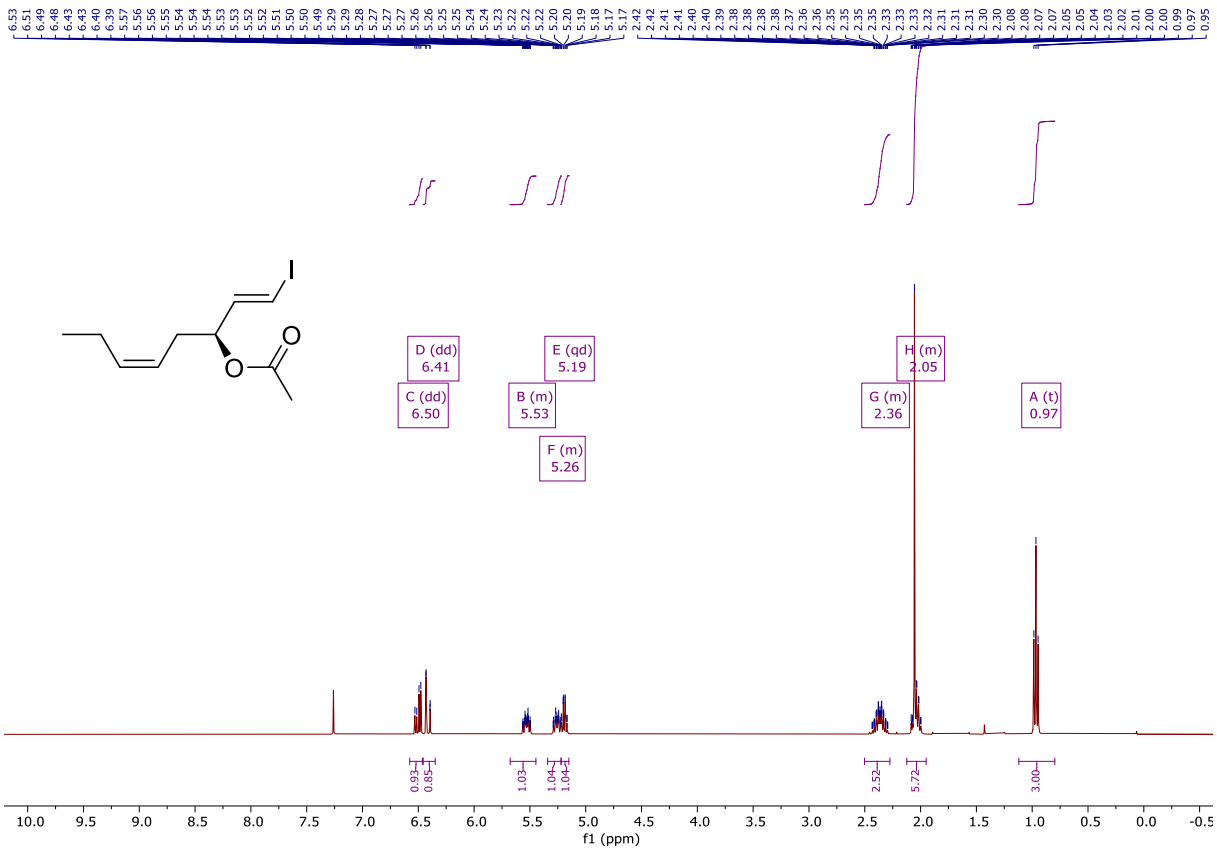



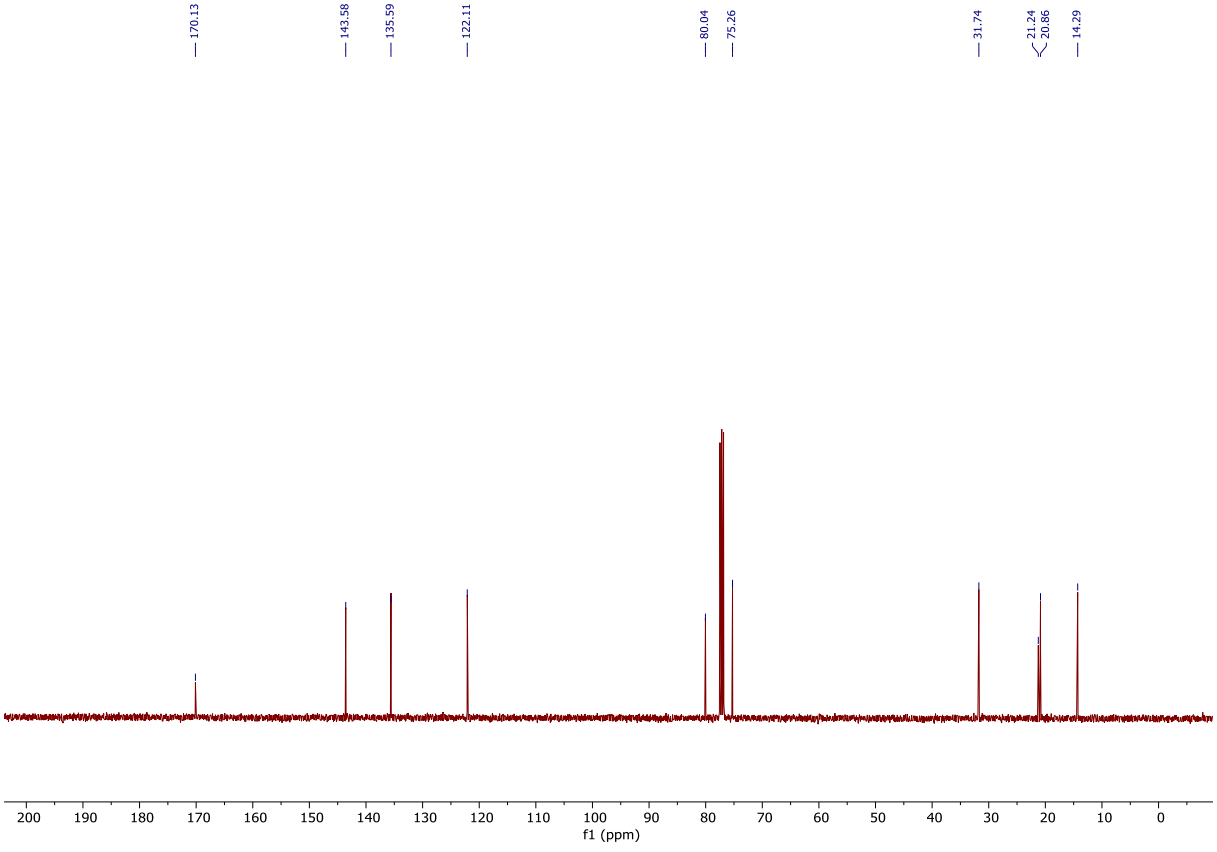
**(2*R*,3*S*)-2-(Iodomethyl)-3-((*Z*)-pent-2-en-1-yl)oxirane, 25**



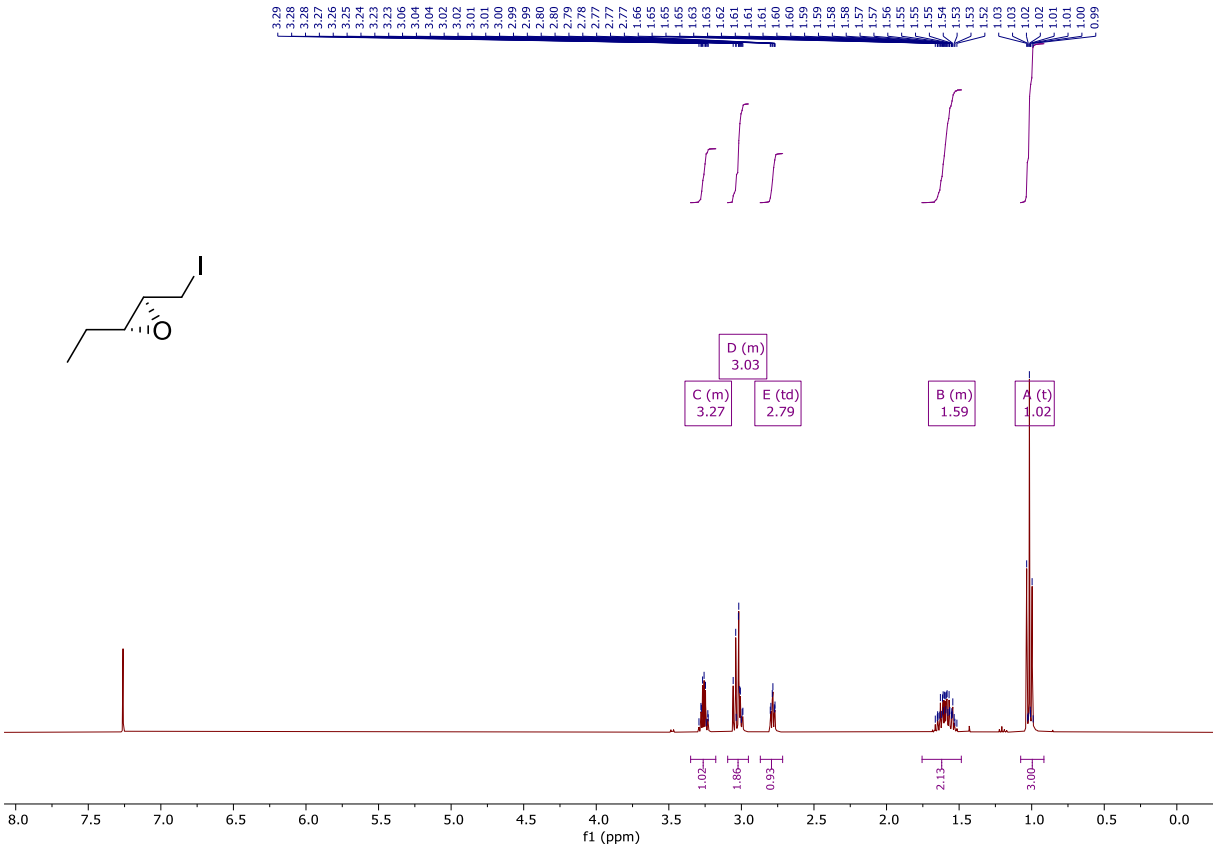



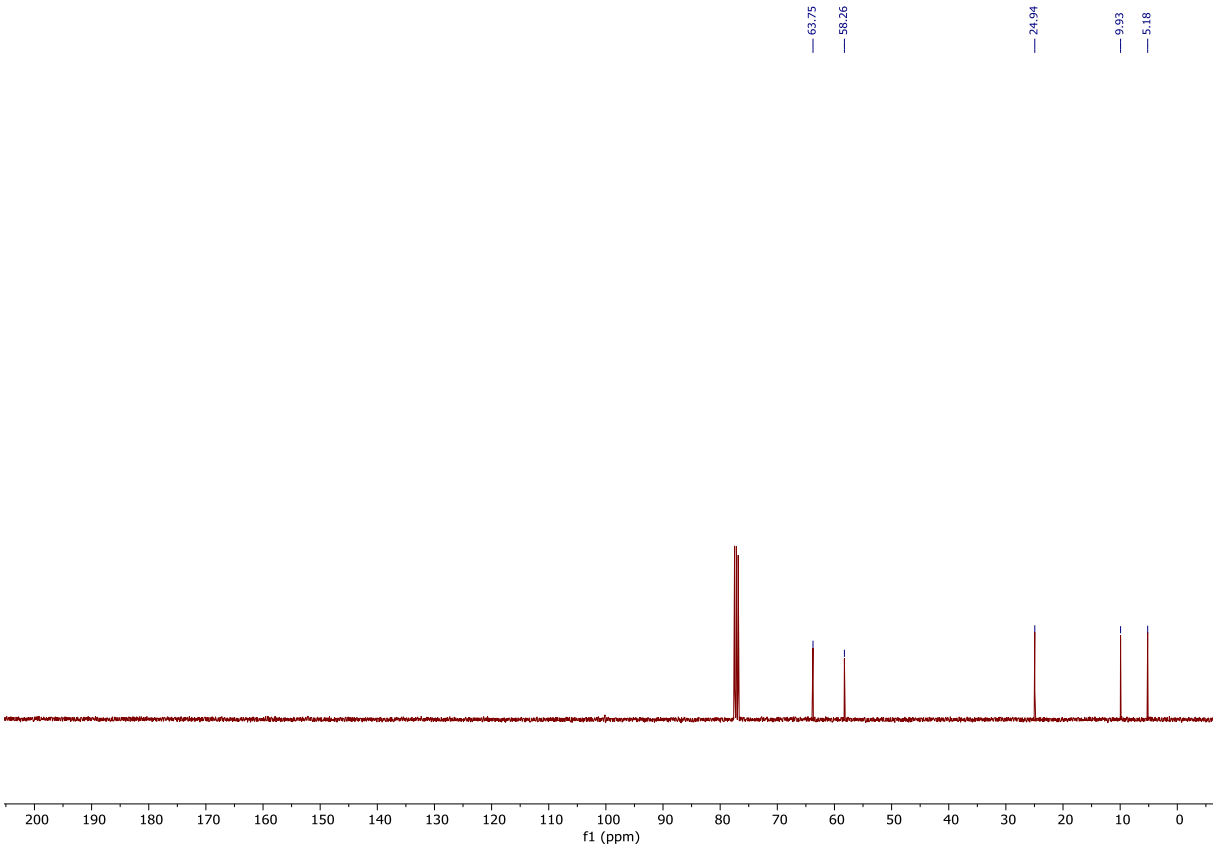
**(*S*,1*E*,5*Z*)-1-Iodoocta-1,5-dien-3-yl acetate, 35**



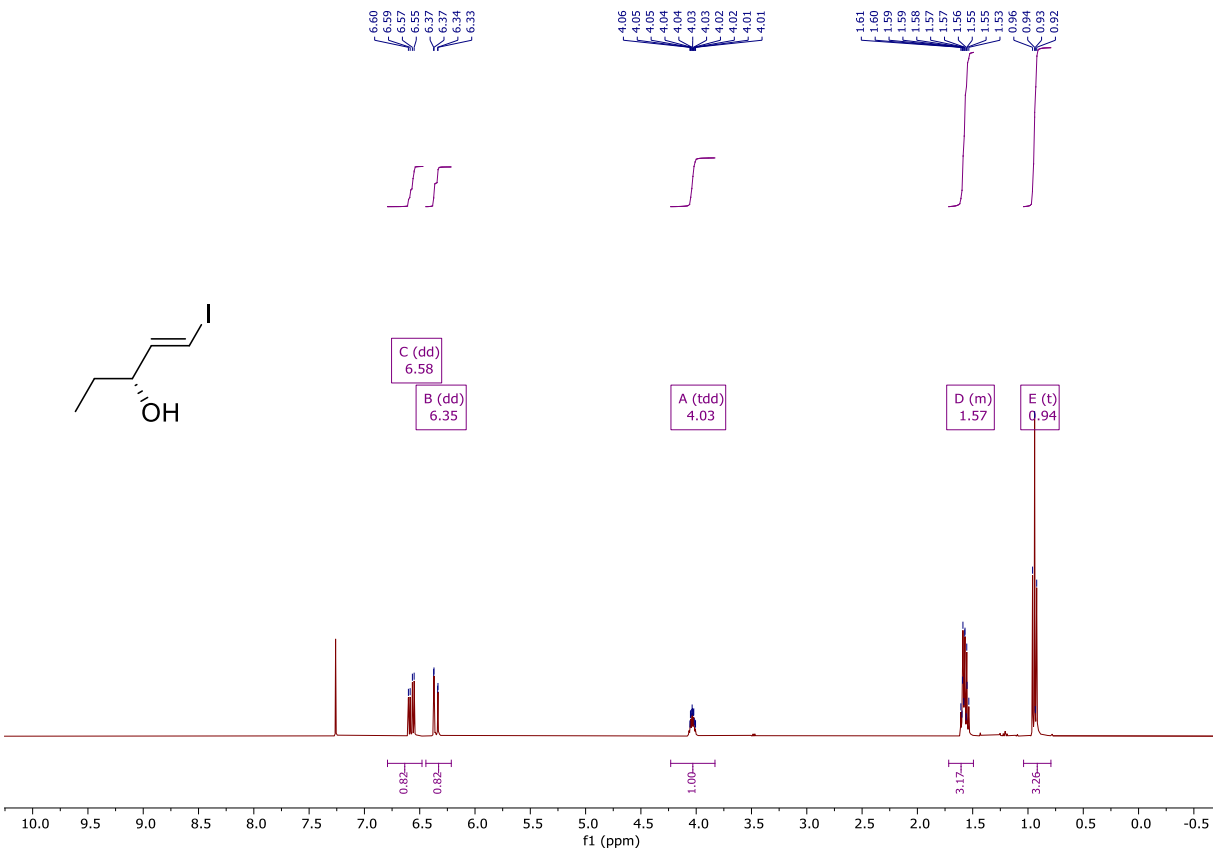



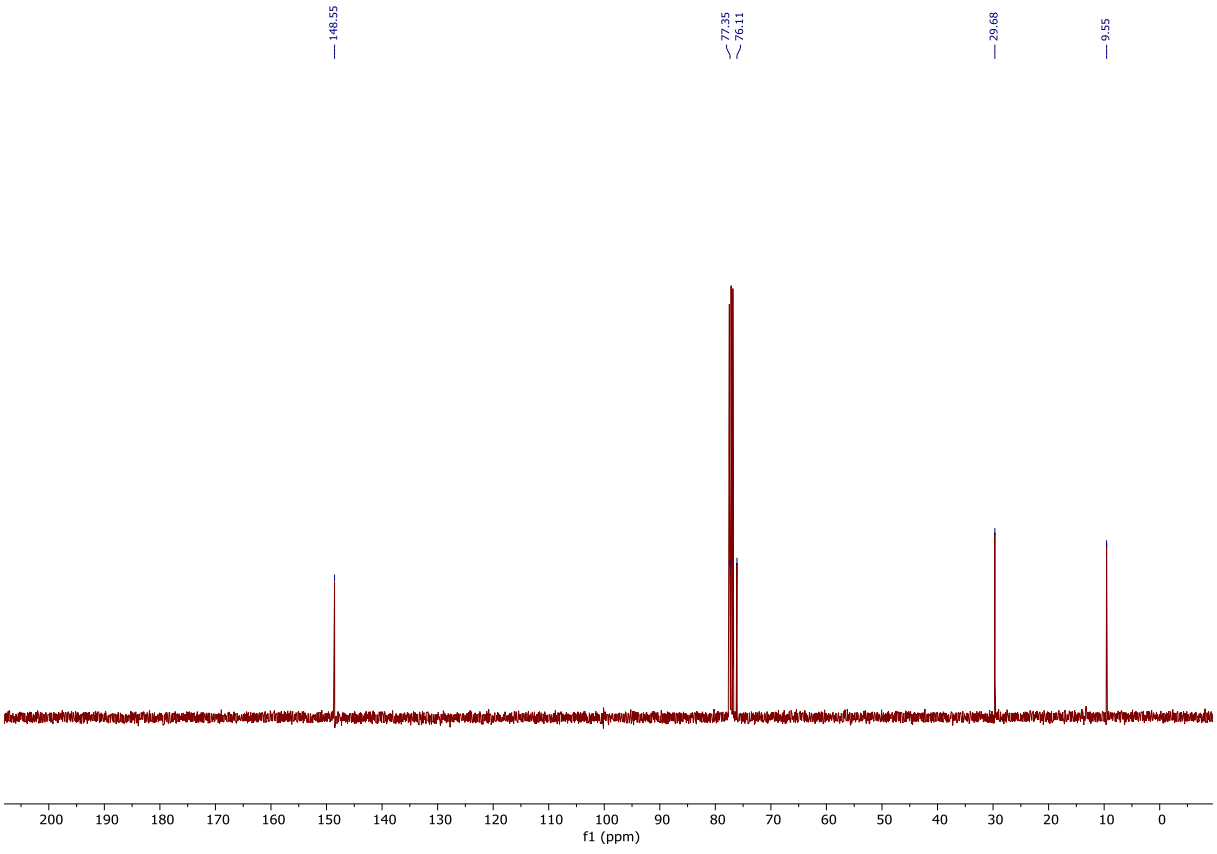
**(2*R*,3*S*)-2-Ethyl-3-(iodomethyl)oxirane, 26**



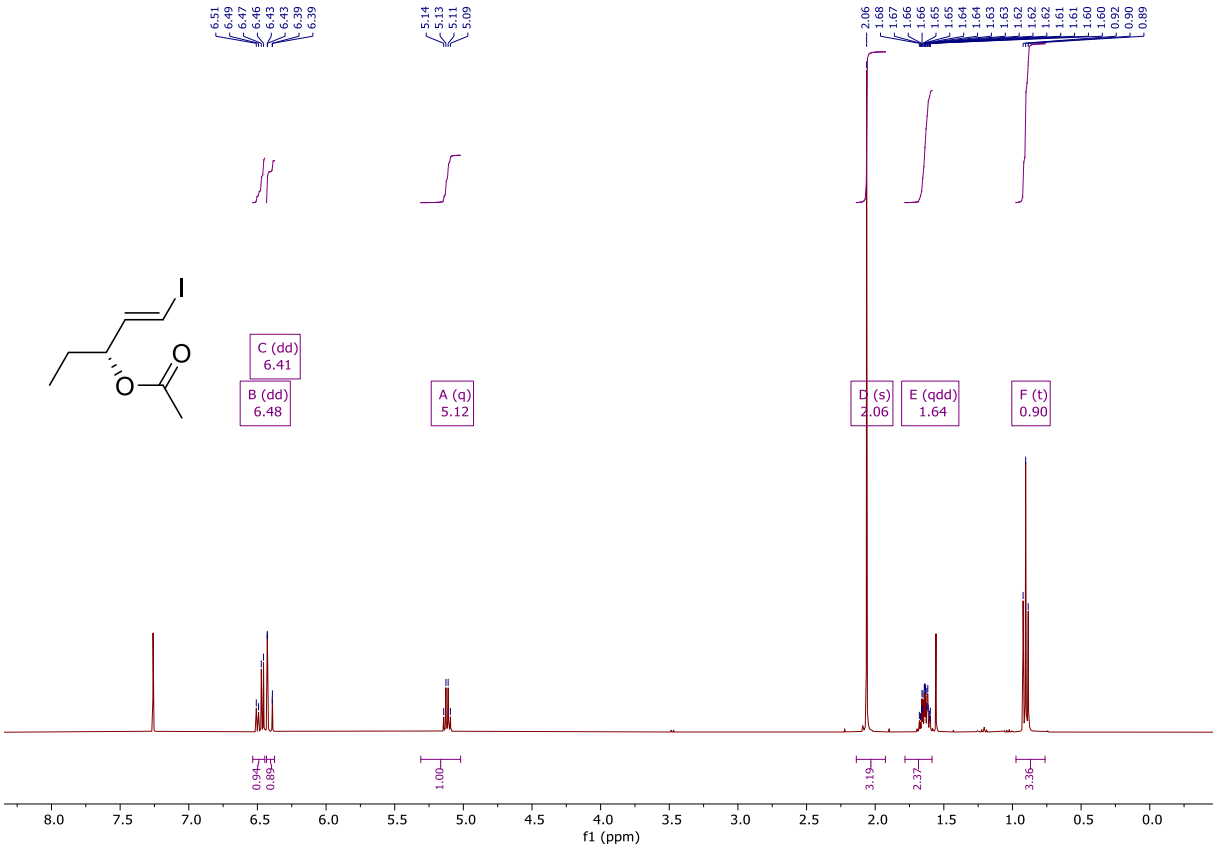



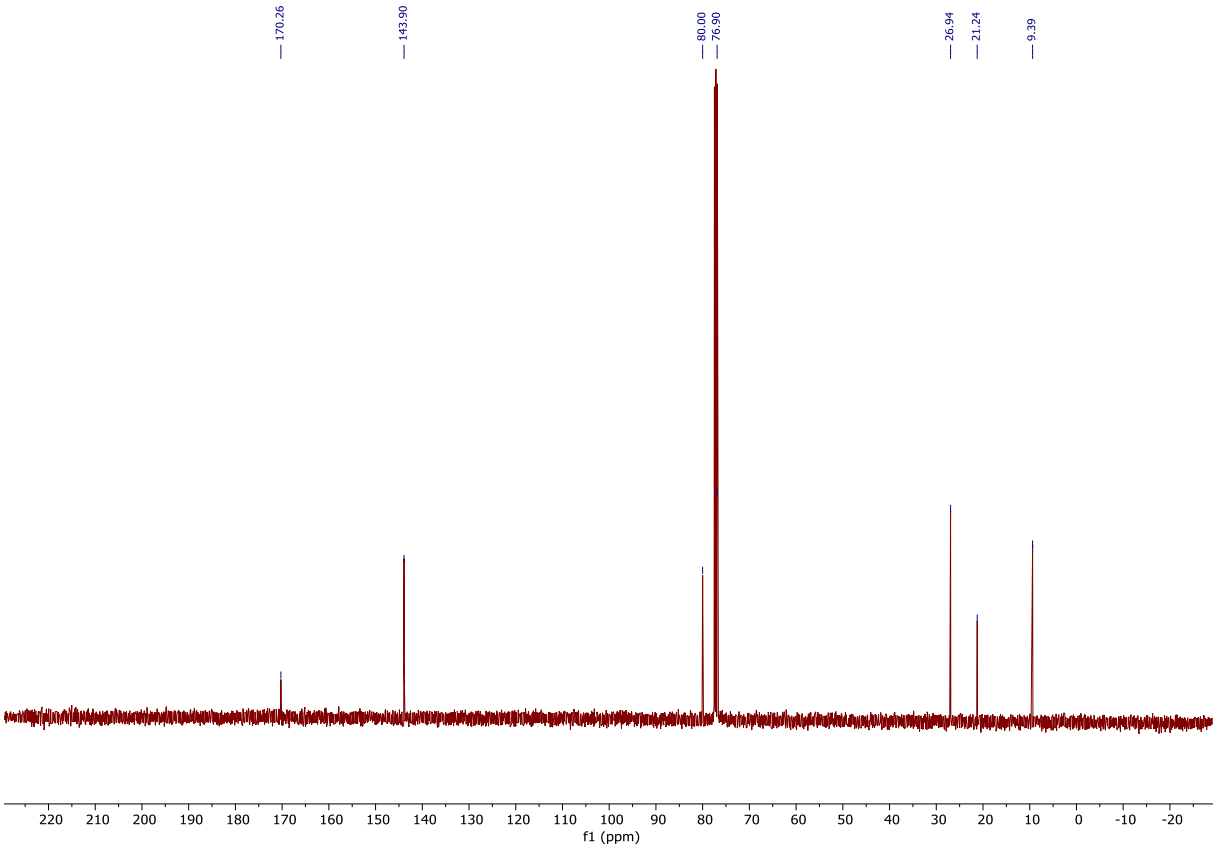
**(*R*,*E*)-1-Iodopent-1-en-3-ol, 10**



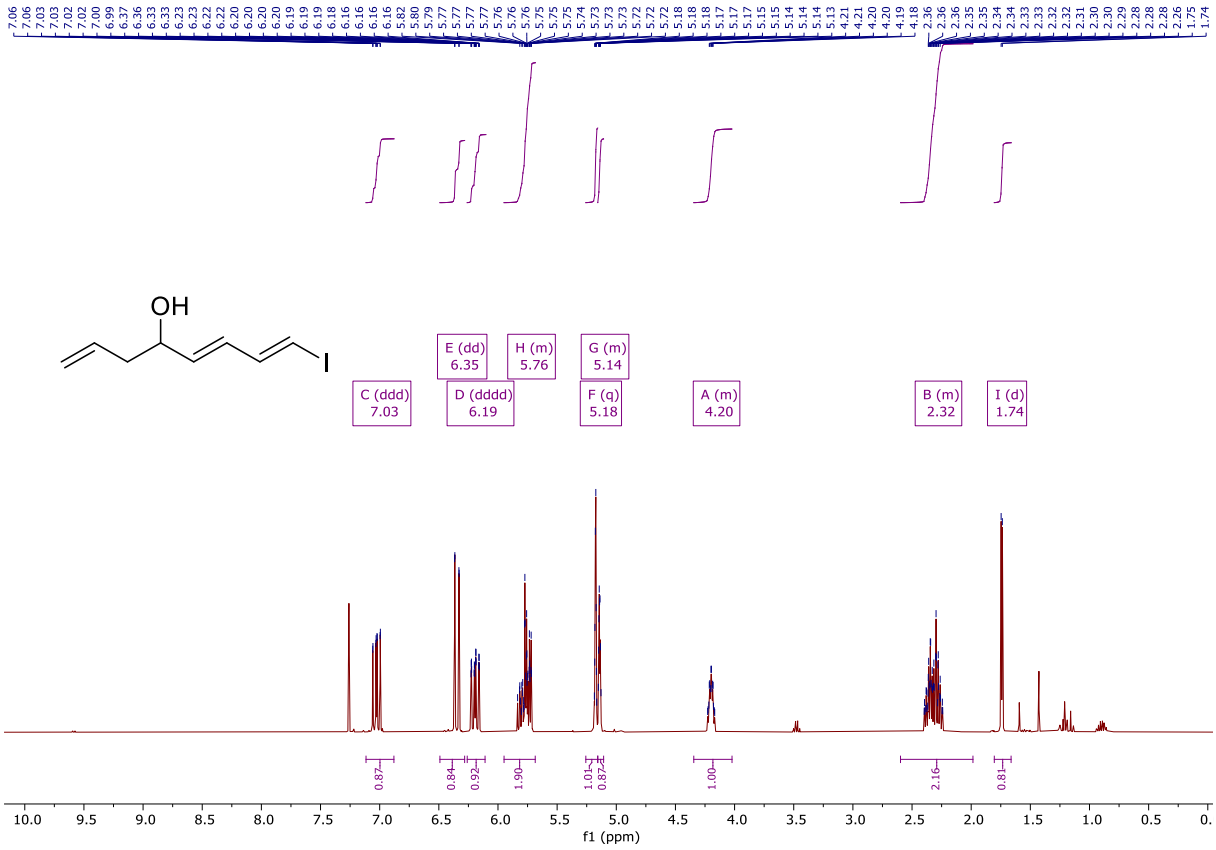



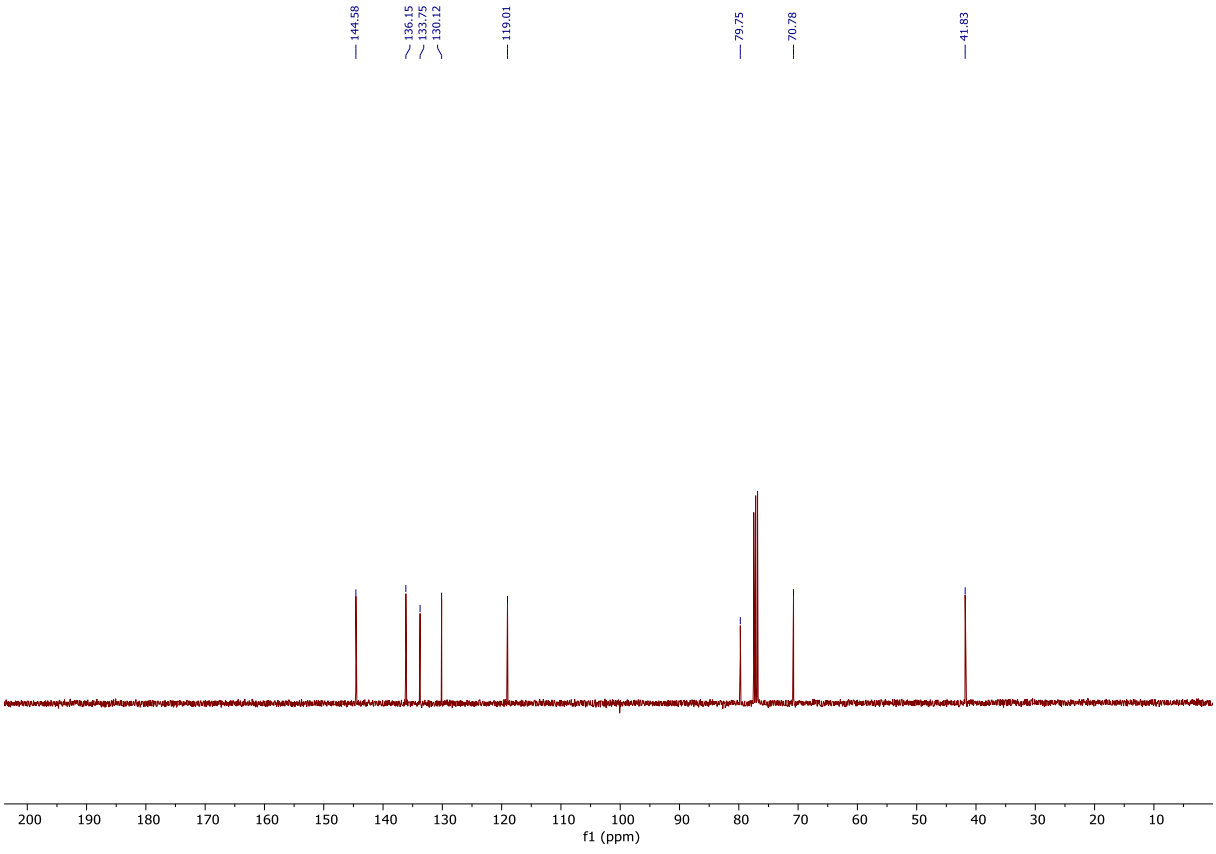
**(*R*,*E*)-1-Iodopent-1-en-3-yl acetate, 45**



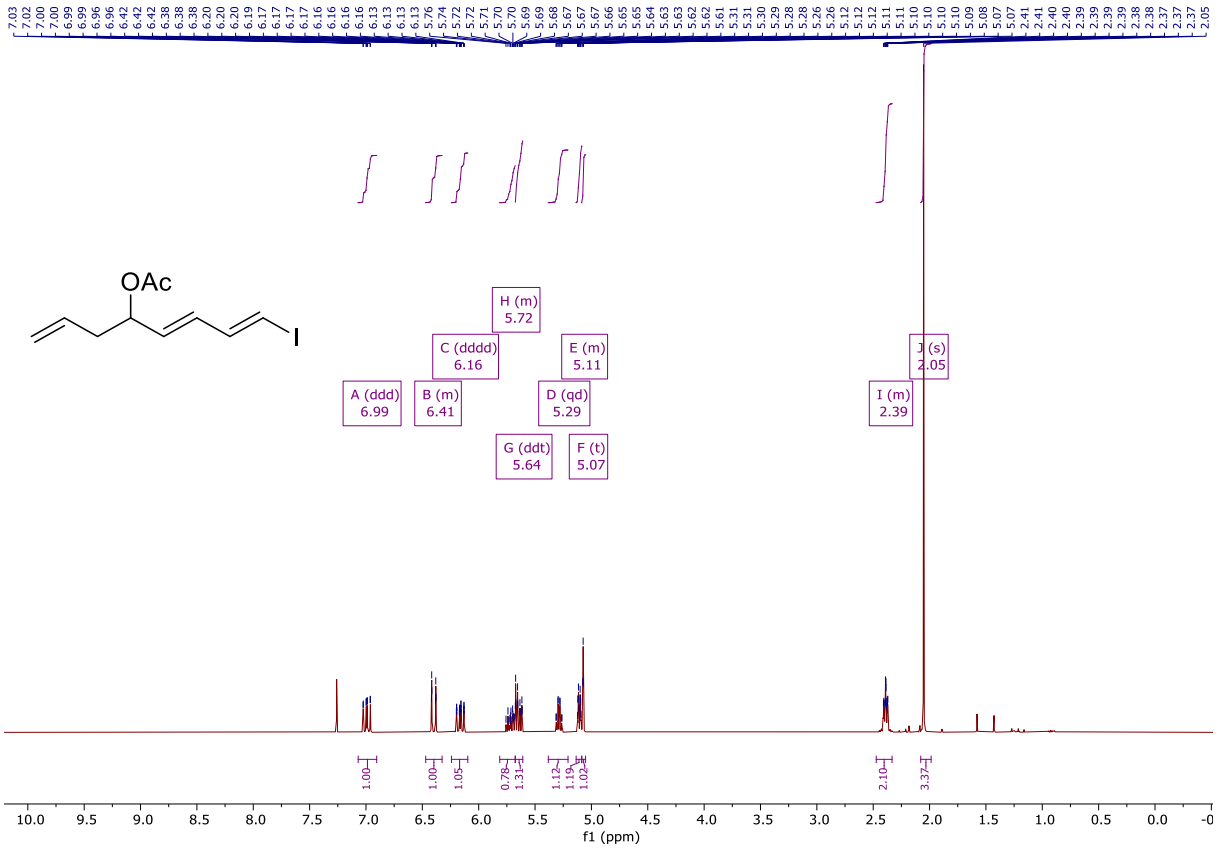



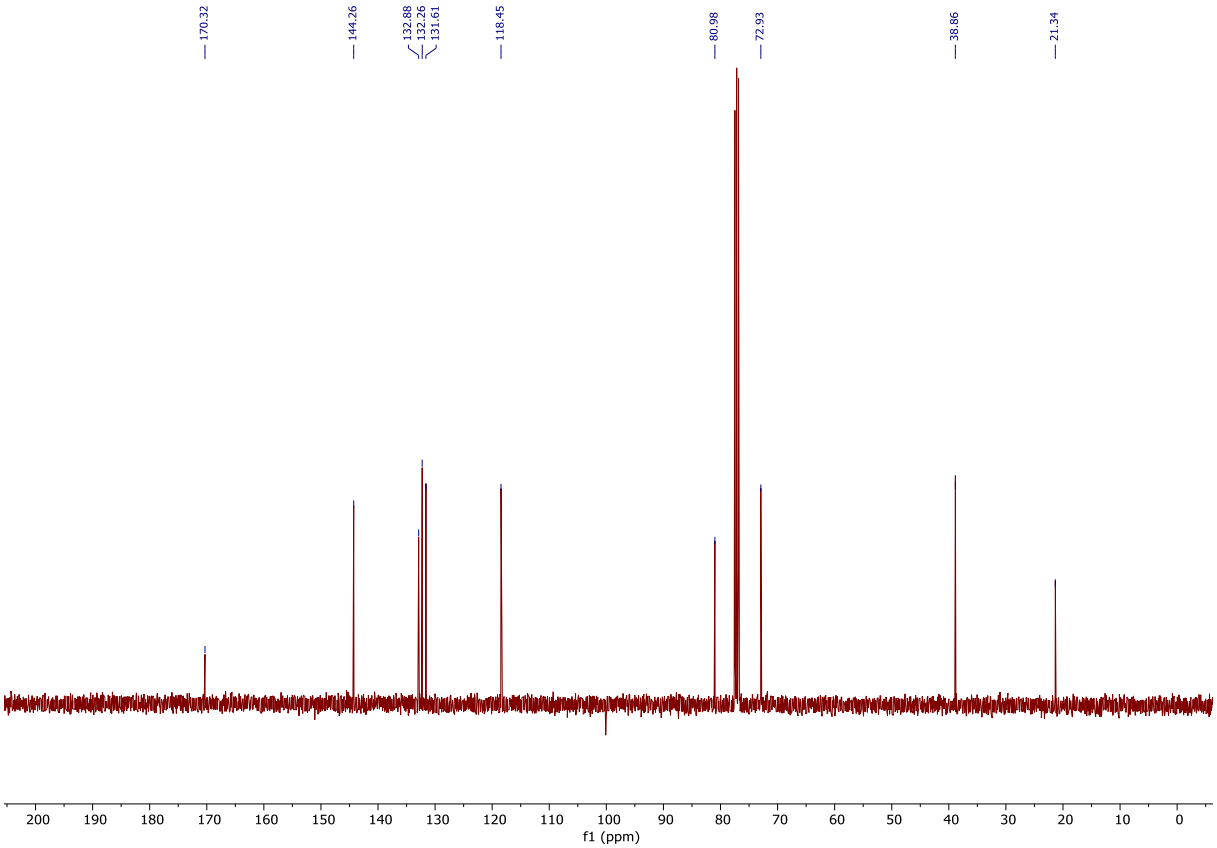
**(5*E*,7*E*)-8-Iodoocta-5,7-dien-1-yn-4-ol, 37**



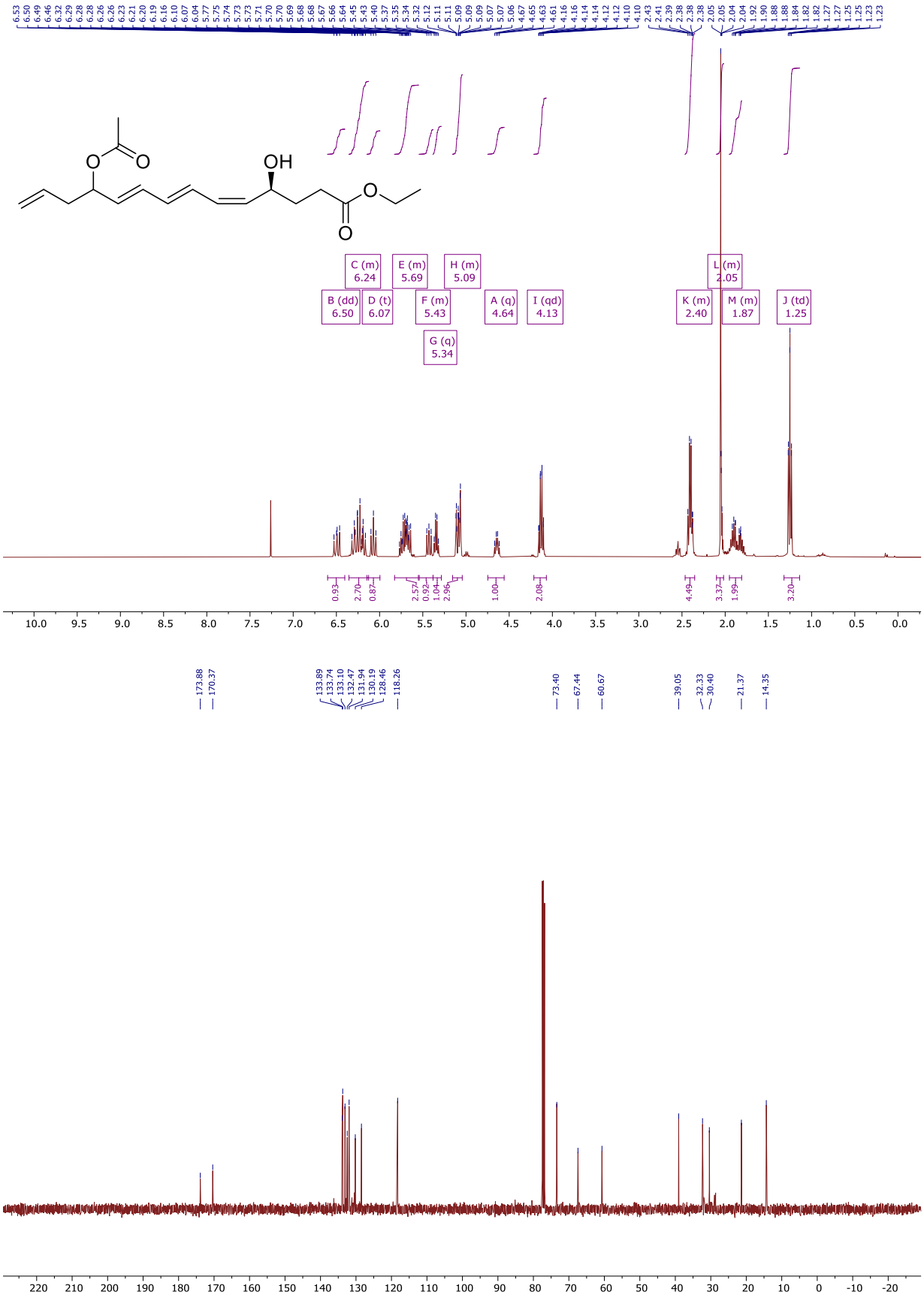



**(5*E*,7*E*)-8-Iodoocta-1,5,7-trien-4-yl acetate, 38**

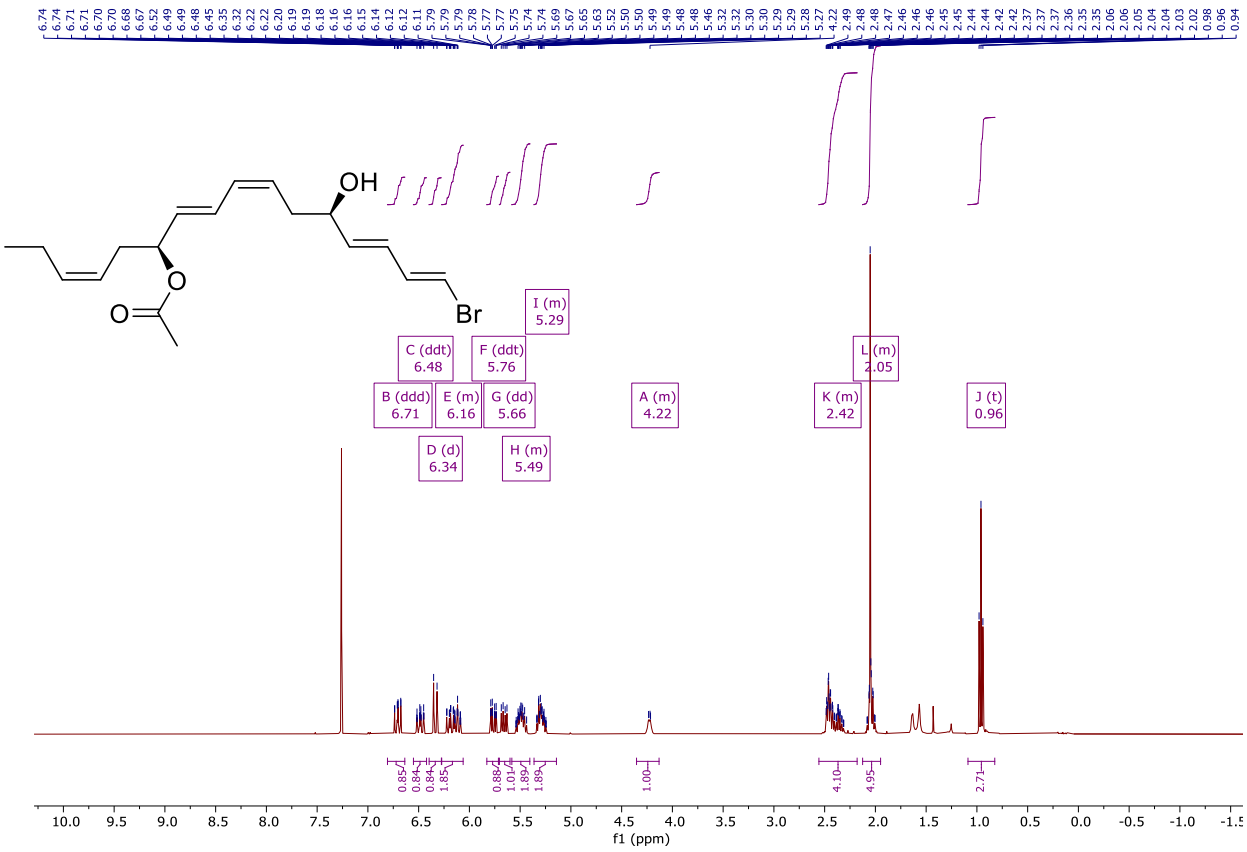


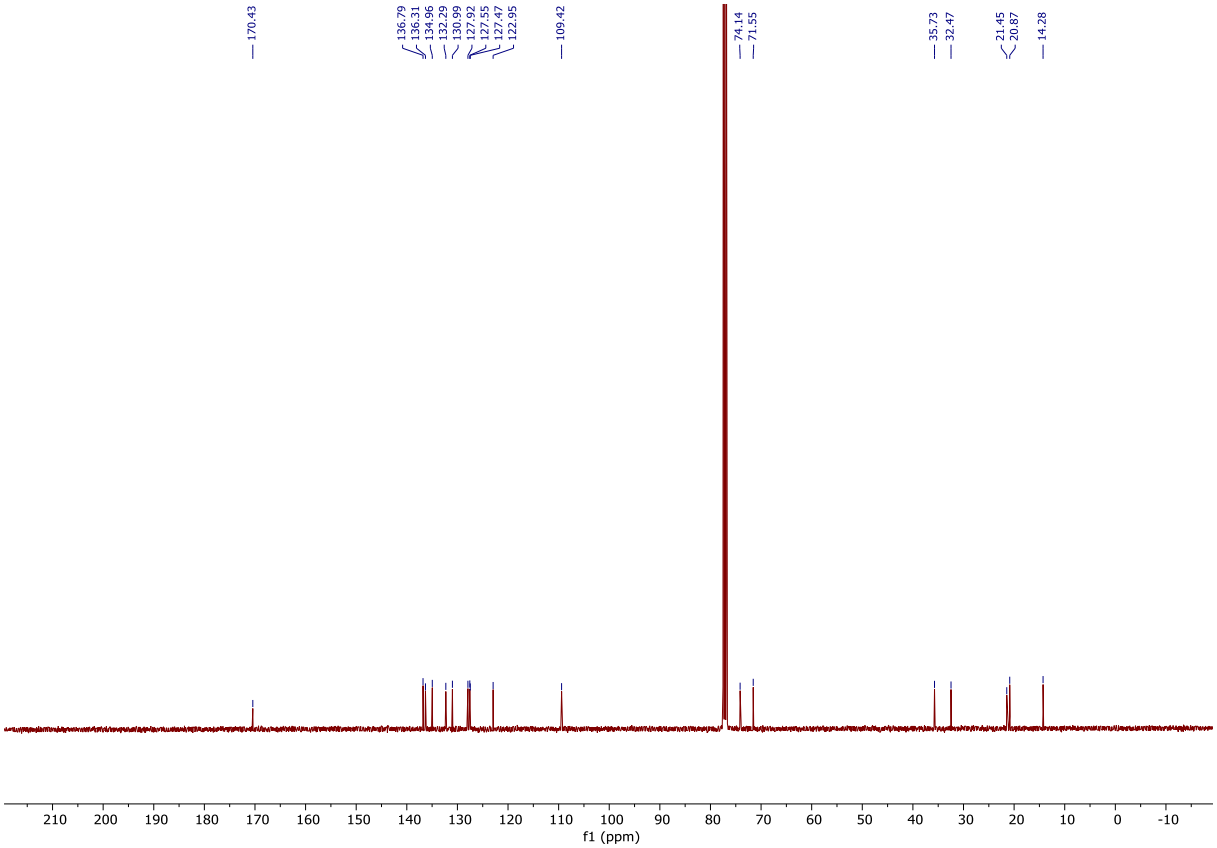



**Ethyl (4*S*,5*Z*,7*E*,9*E*)-11-acetoxy-4-hydroxytetradeca-5,7,9,13-tetraenoate, 40**

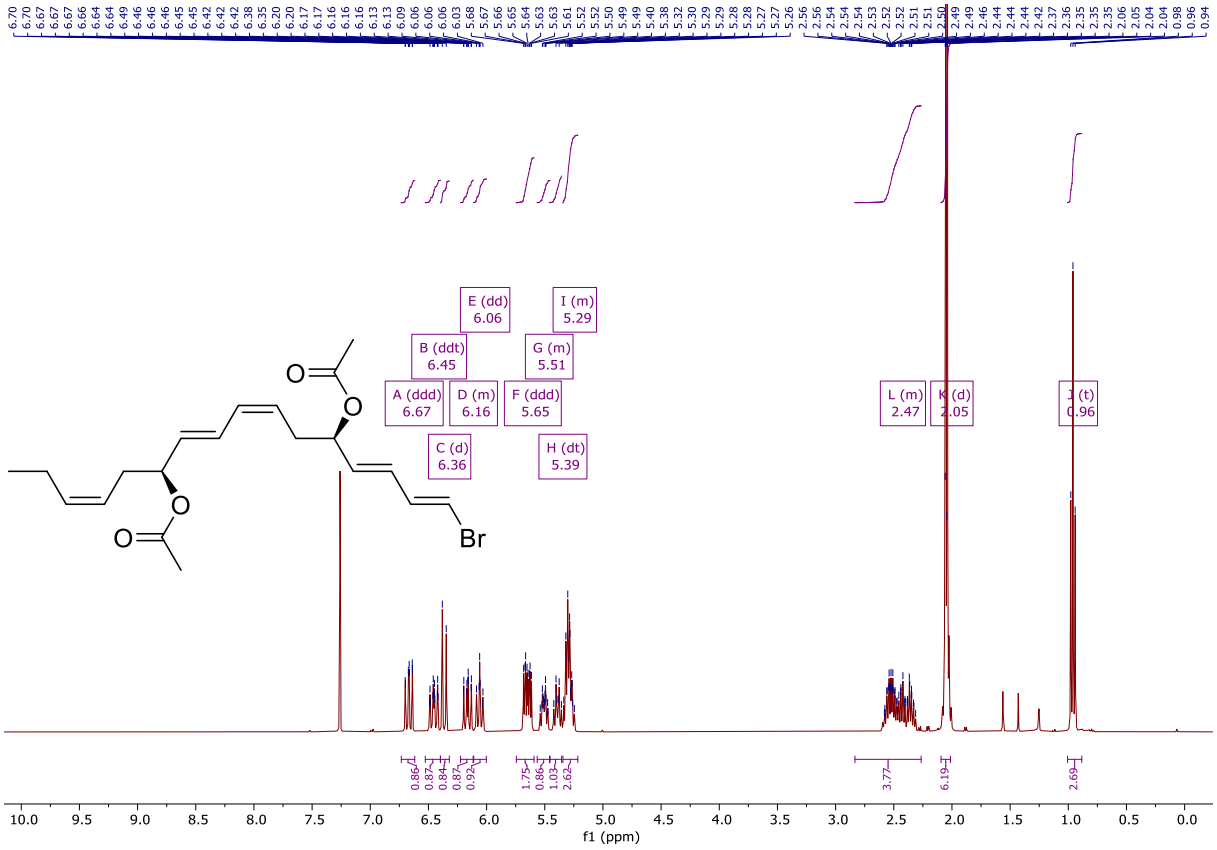


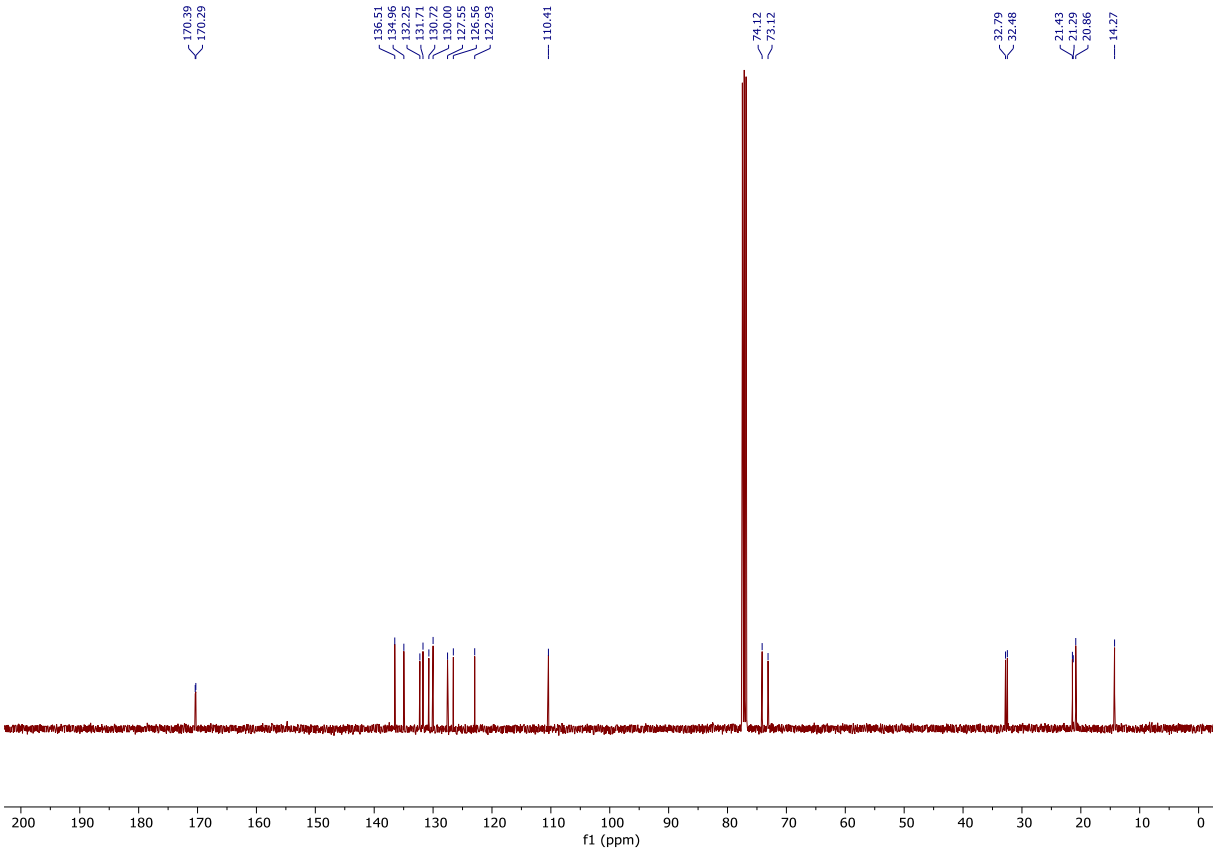
**(3Z,6S,7E,9Z,12R,13E,15E)-16-bromo-12-hydroxyhexadeca-3,7,9,13,15-pentaen-6-yl acetate, 36**



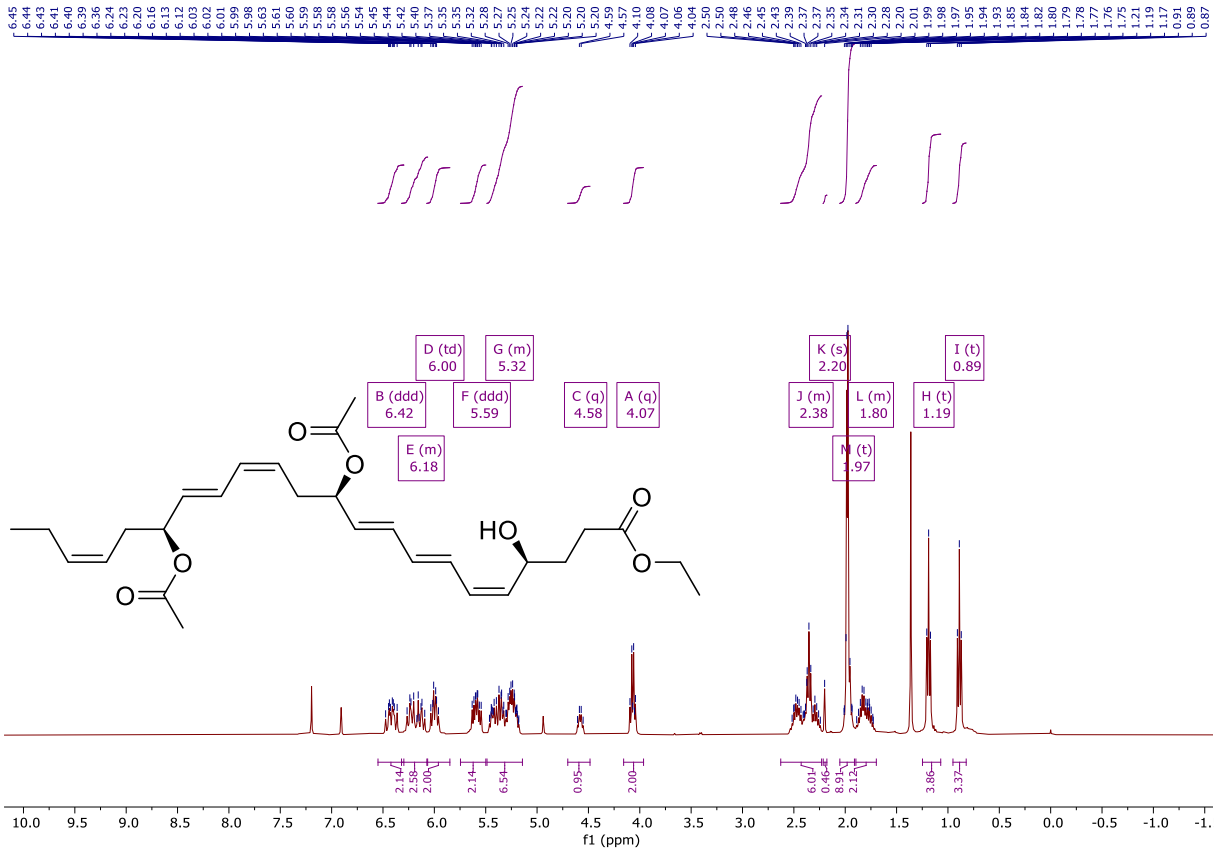



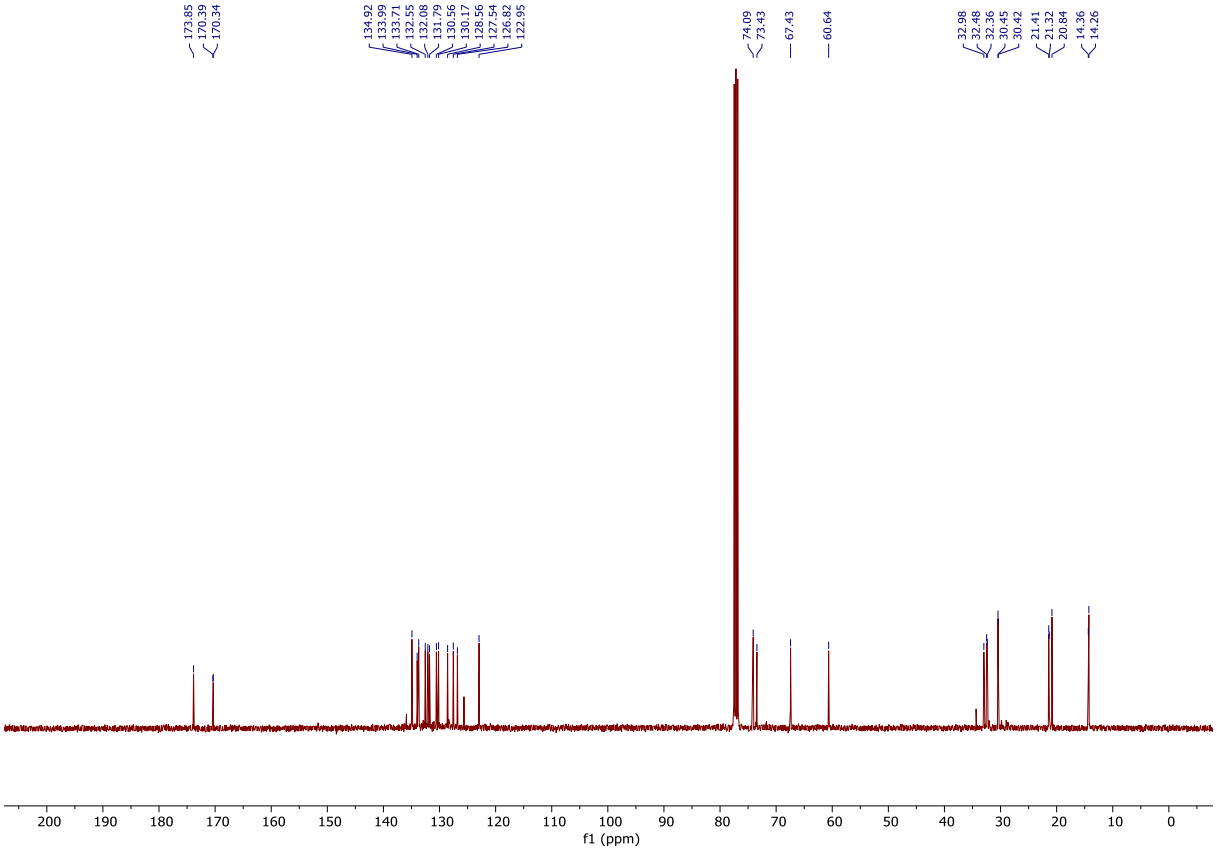
**(1*E*,3*E*,5*R*,7*Z*,9*E*,11*S*,13*Z*)-1-Bromohexadeca-1,3,7,9,13-pentaene-5,11-diyl diacetate, 41**



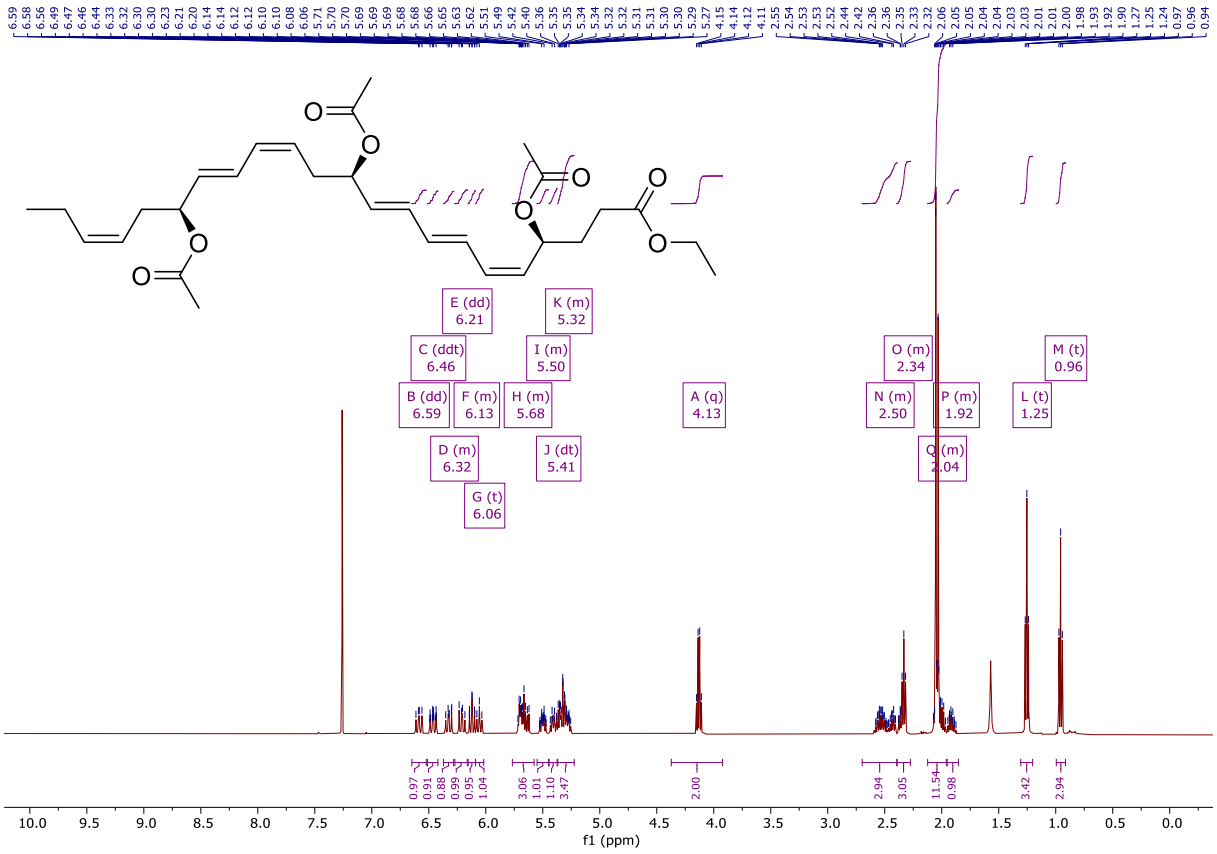



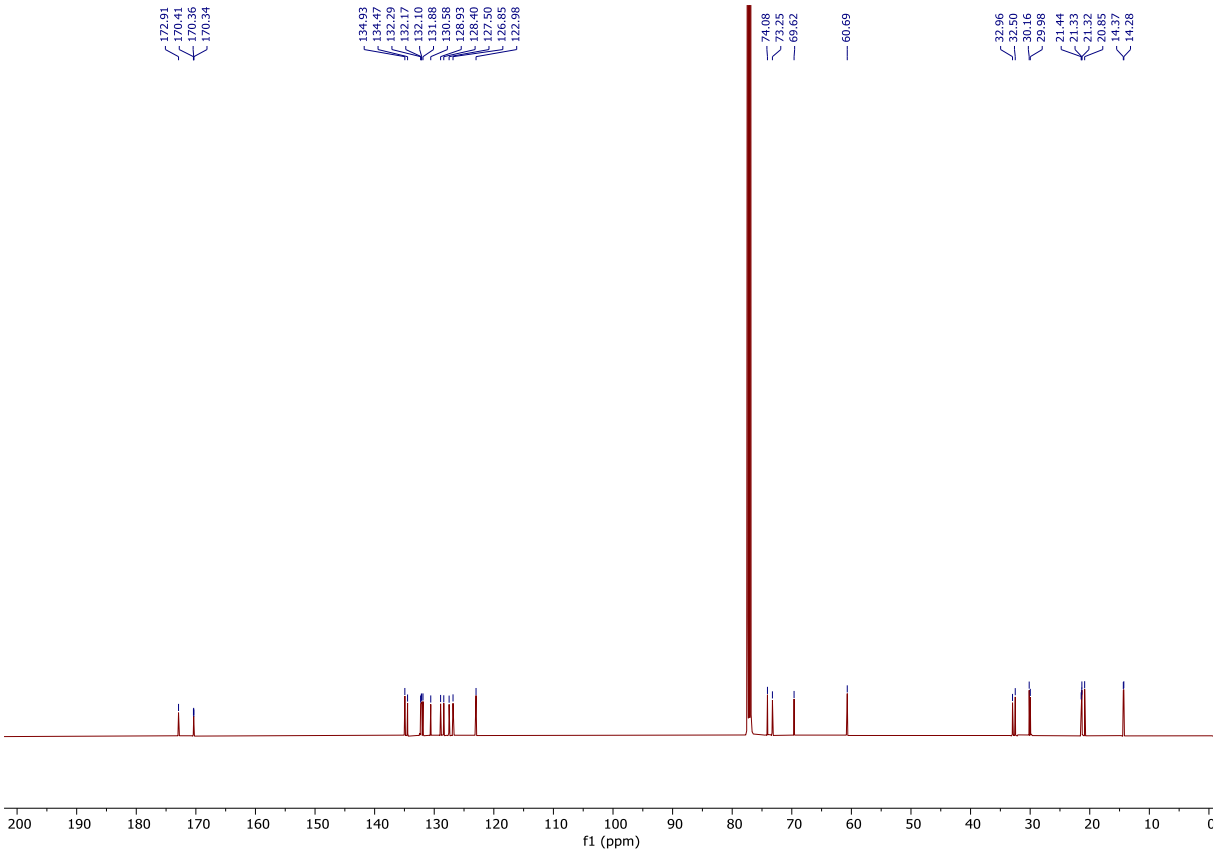
**(1*E*,3*E*,5*R*,7*Z*,9*E*,11*S*,13*Z*)-1-Bromohexadeca-1,3,7,9,13-pentaene-5,11-diyl diacetate, S12**



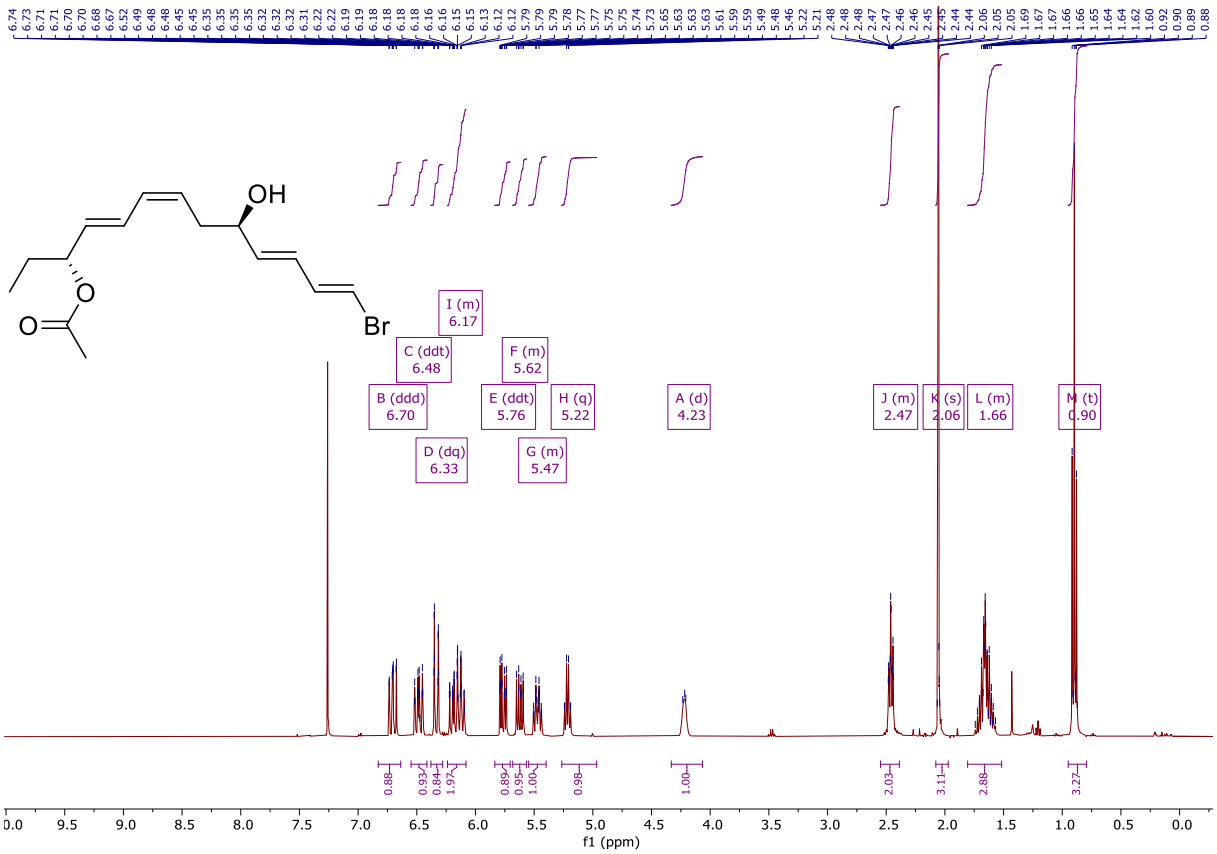



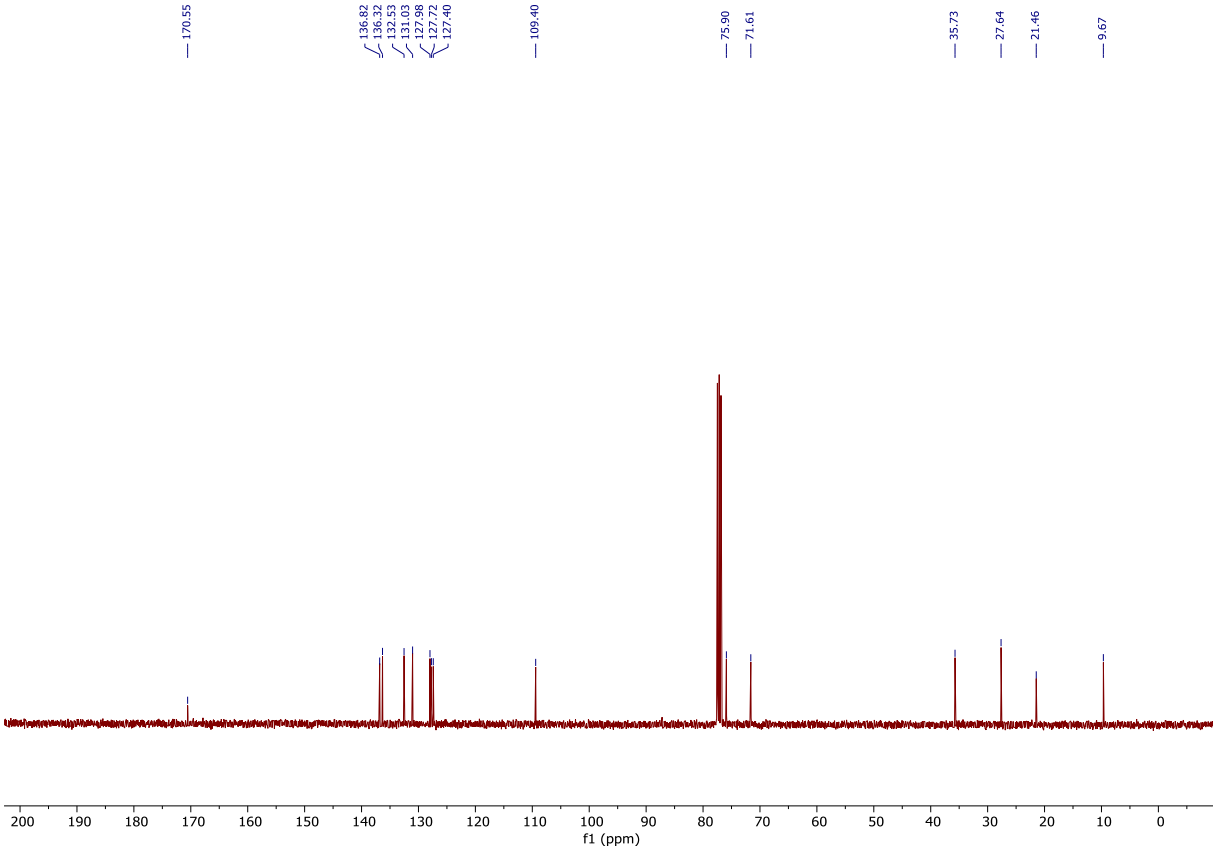
**(4*S*,5*Z*,7*E*,9*E*,11*R*,13*Z*,15*E*,17*S*,19*Z*)-1-Ethoxy-1-oxodocosa-5,7,9,13,15,19-hexaene-4,11,17-triyl triacetate, 42**



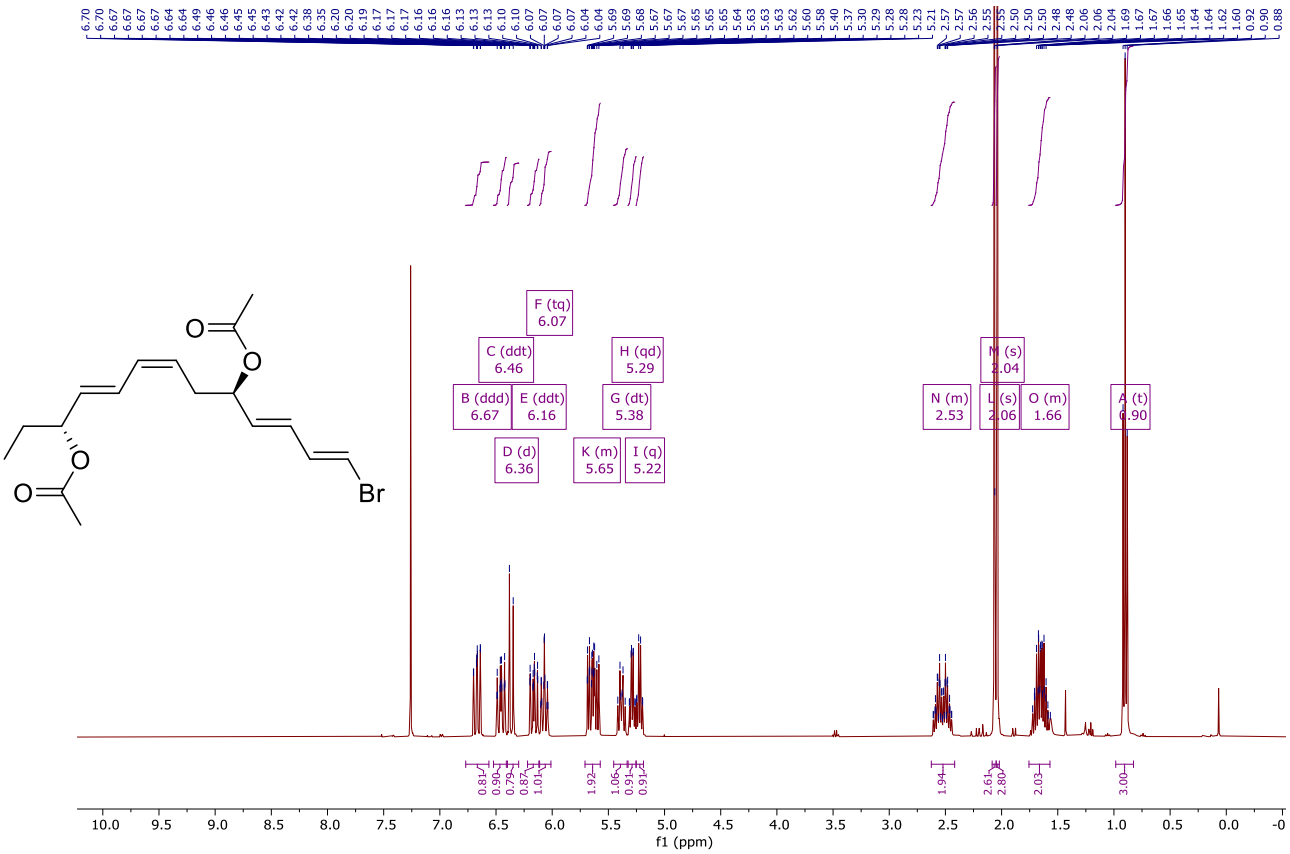



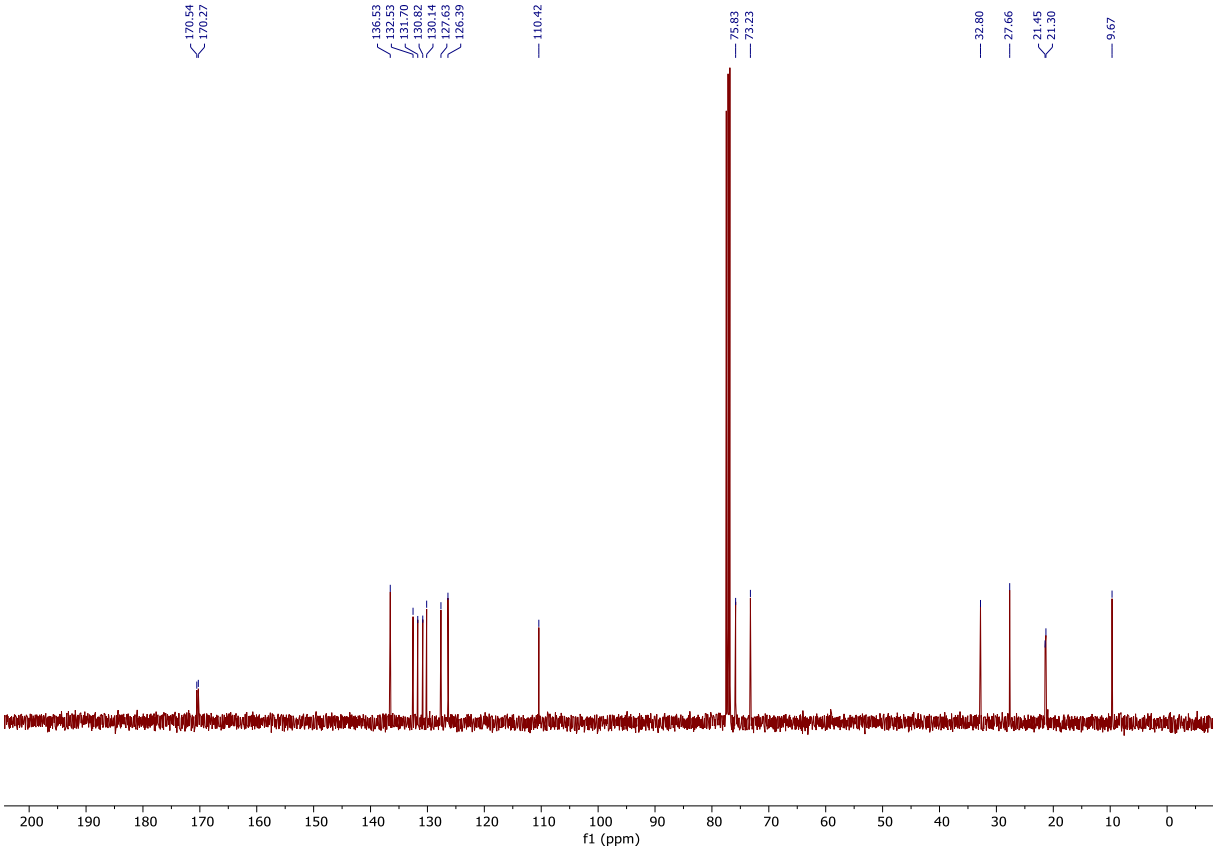
**(3*Z*,6*S*,7*E*,9*Z*,12*R*,13*E*,15*E*)-16-bromo-12-hydroxyhexadeca-3,7,9,13,15-pentaen-6-yl acetate, S13**



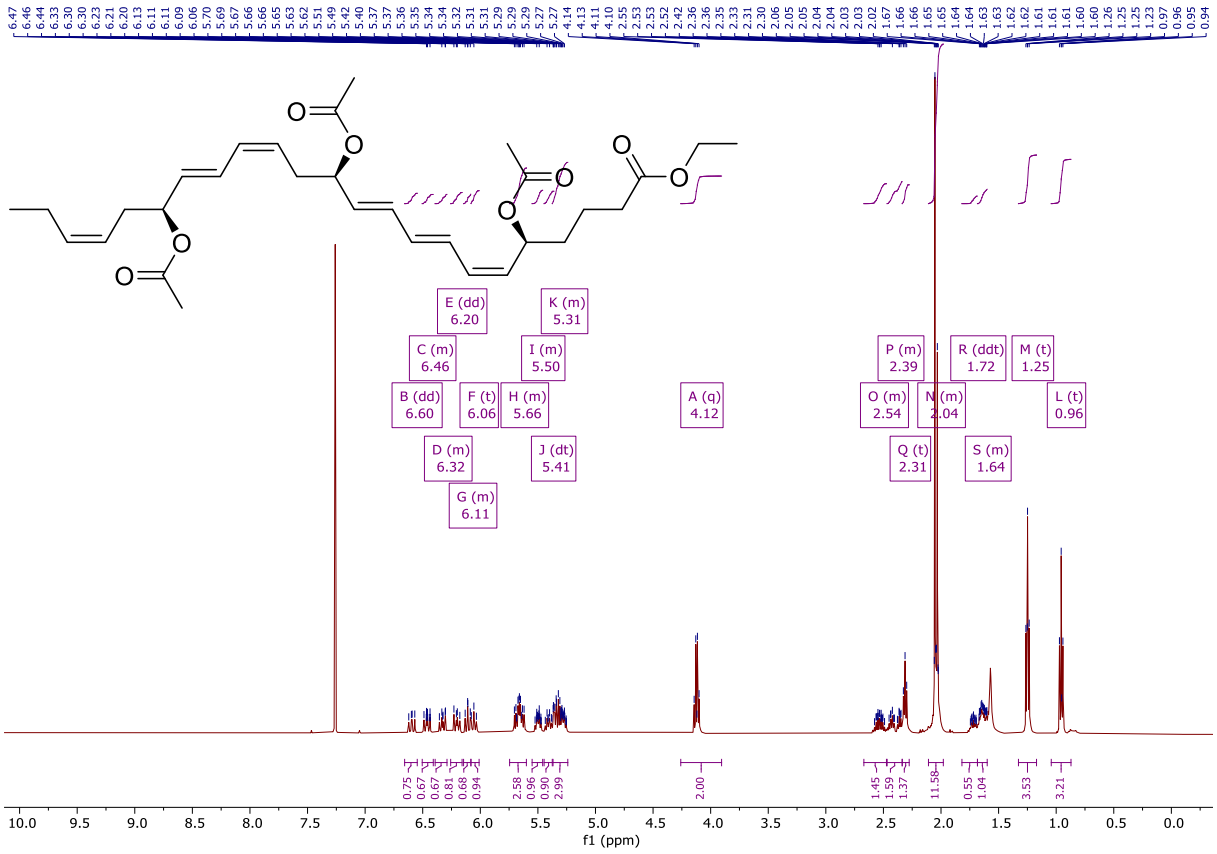



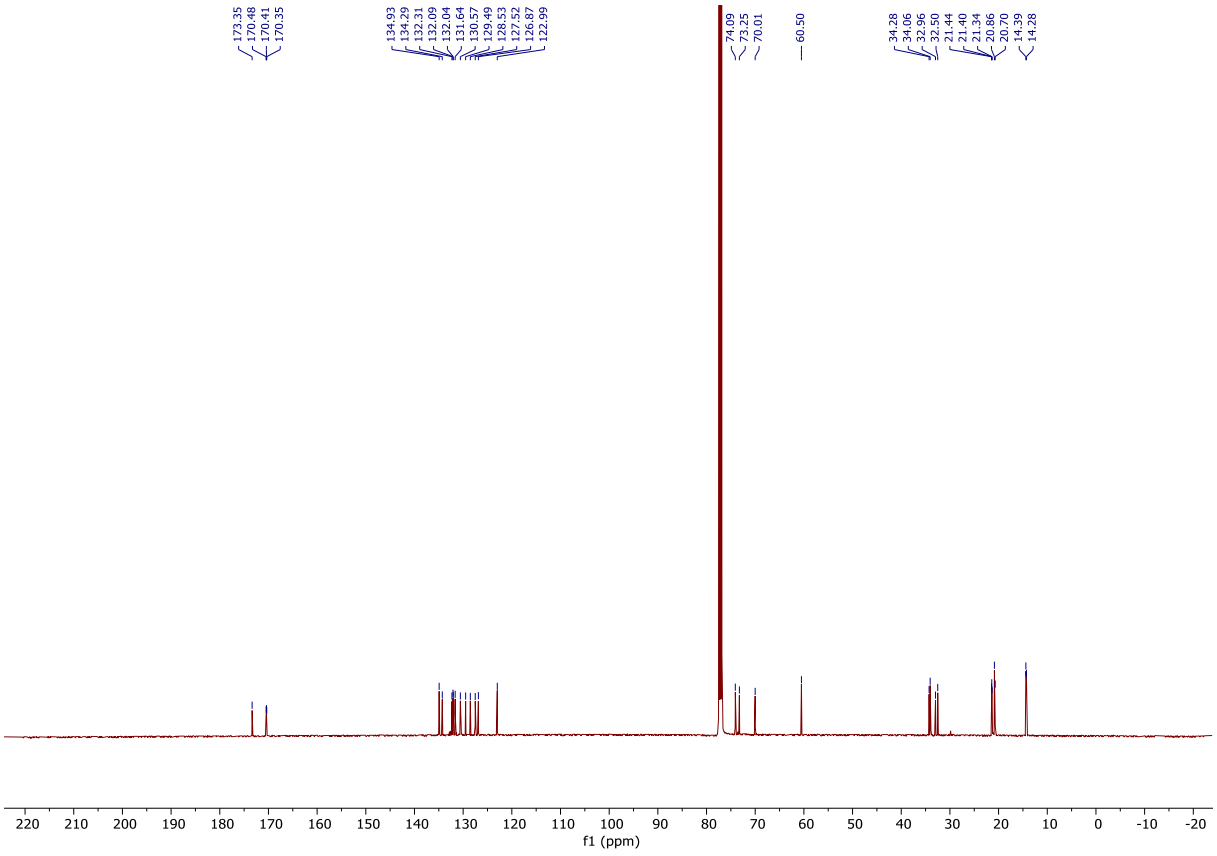
**(3*R*,4*E*,6*Z*,9*R*,10*E*,12*E*)-13-bromotrideca-4,6,10,12-tetraene-3,9-diyl diacetate, 46**



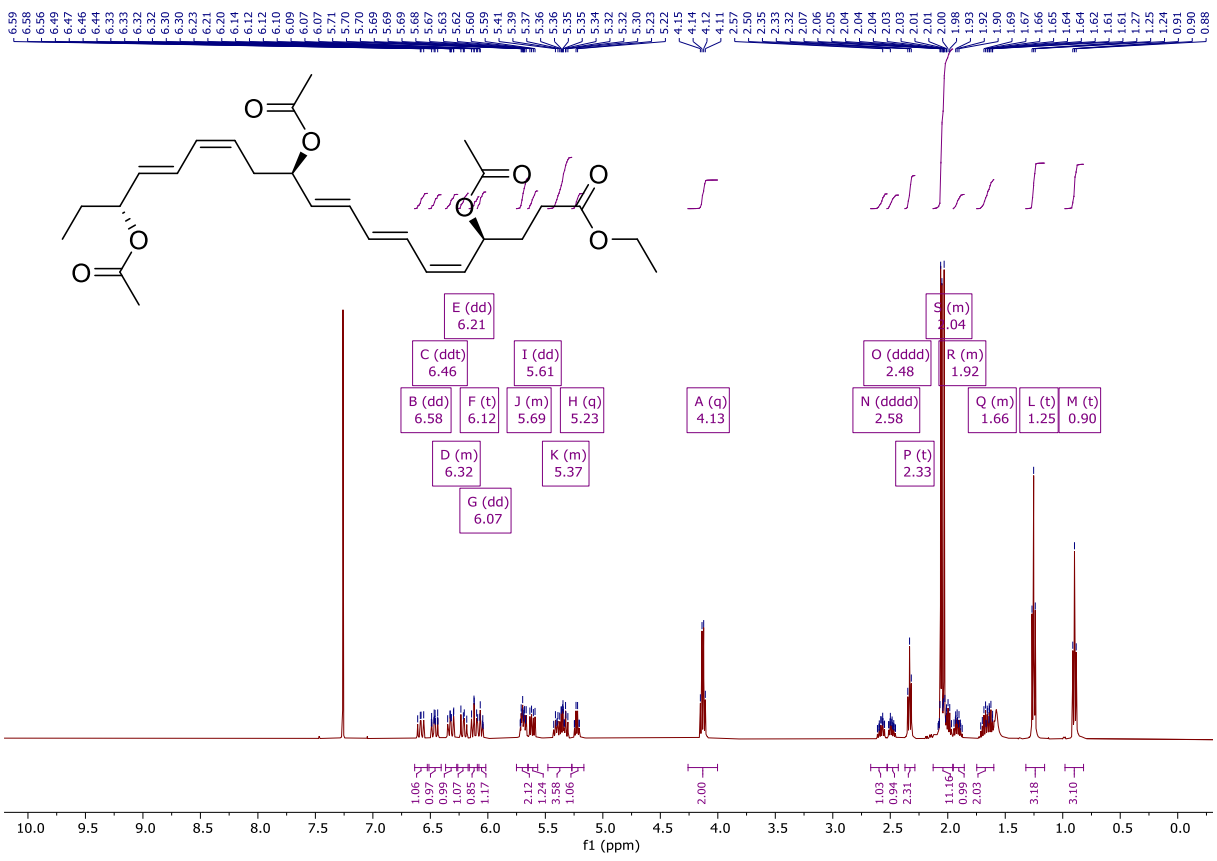



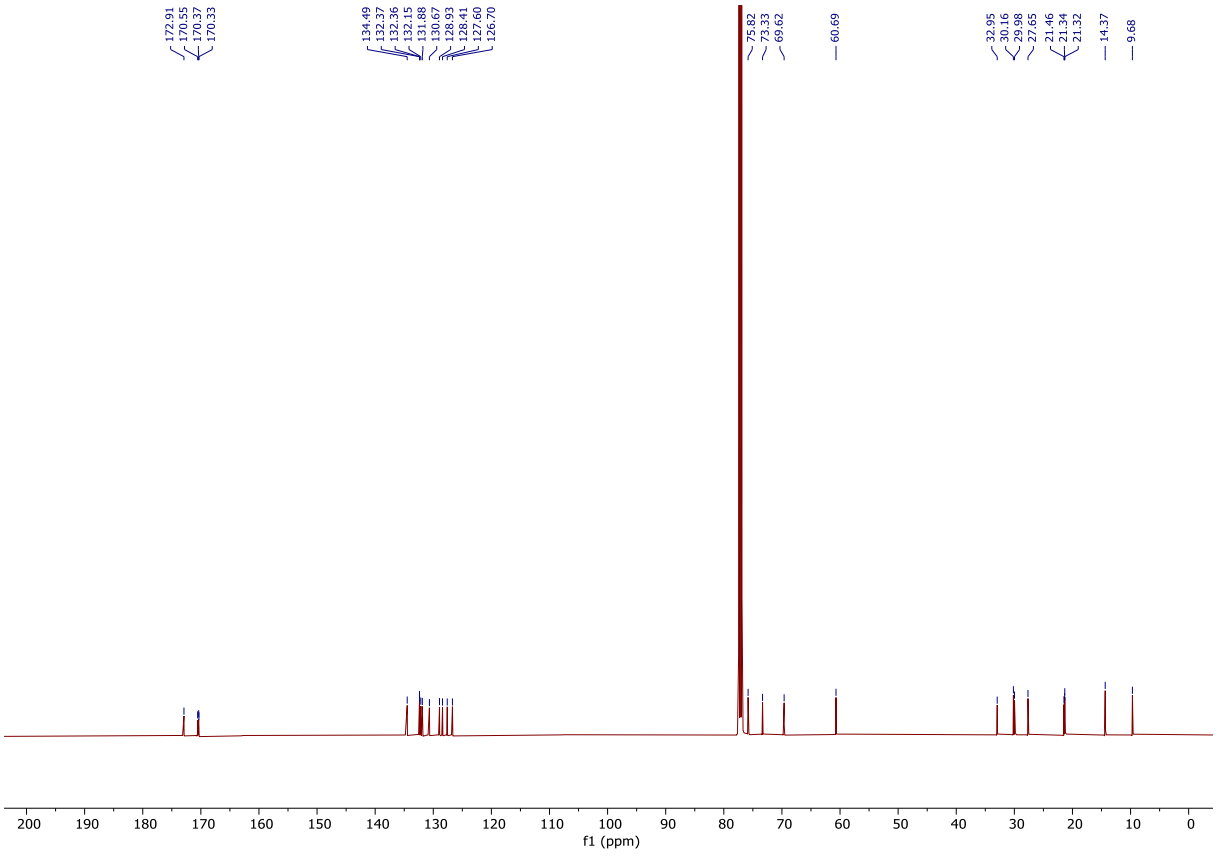
**(5*S*,6*Z*,8*E*,10*E*,12*R*,14*Z*,16*E*,18*S*,20*Z*)-1-Ethoxy-1-oxotricosa-6,8,10,14,16,20-hexaene-5,12,18-triyl triacetate, 43**



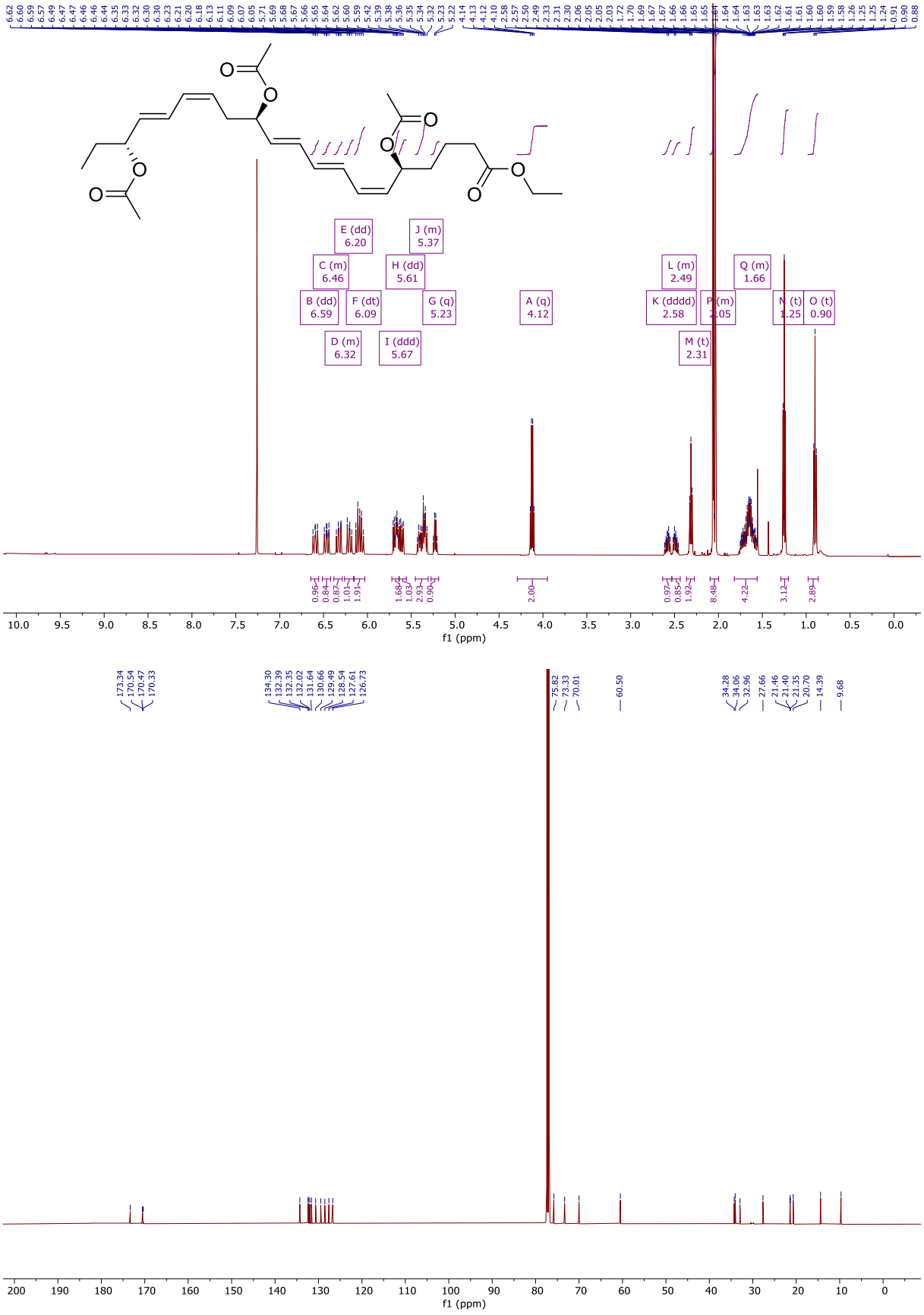



**(3*R*,4*E*,6*Z*,9*R*,10*E*,12*E*,14*Z*,16*S*)-19-Ethoxy-19-oxononadeca-4,6,10,12,14-pentaene-3,9,16-triyl triacetate, 48**

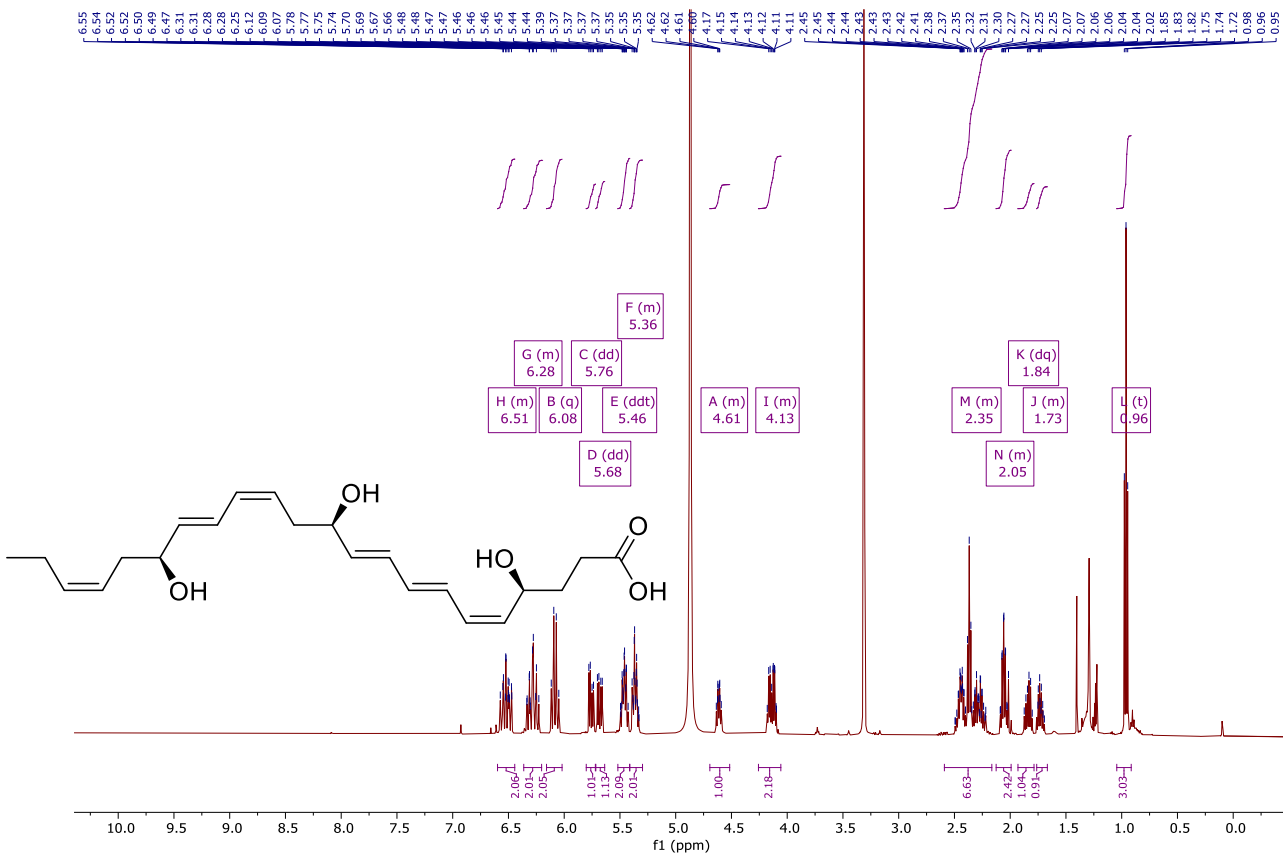


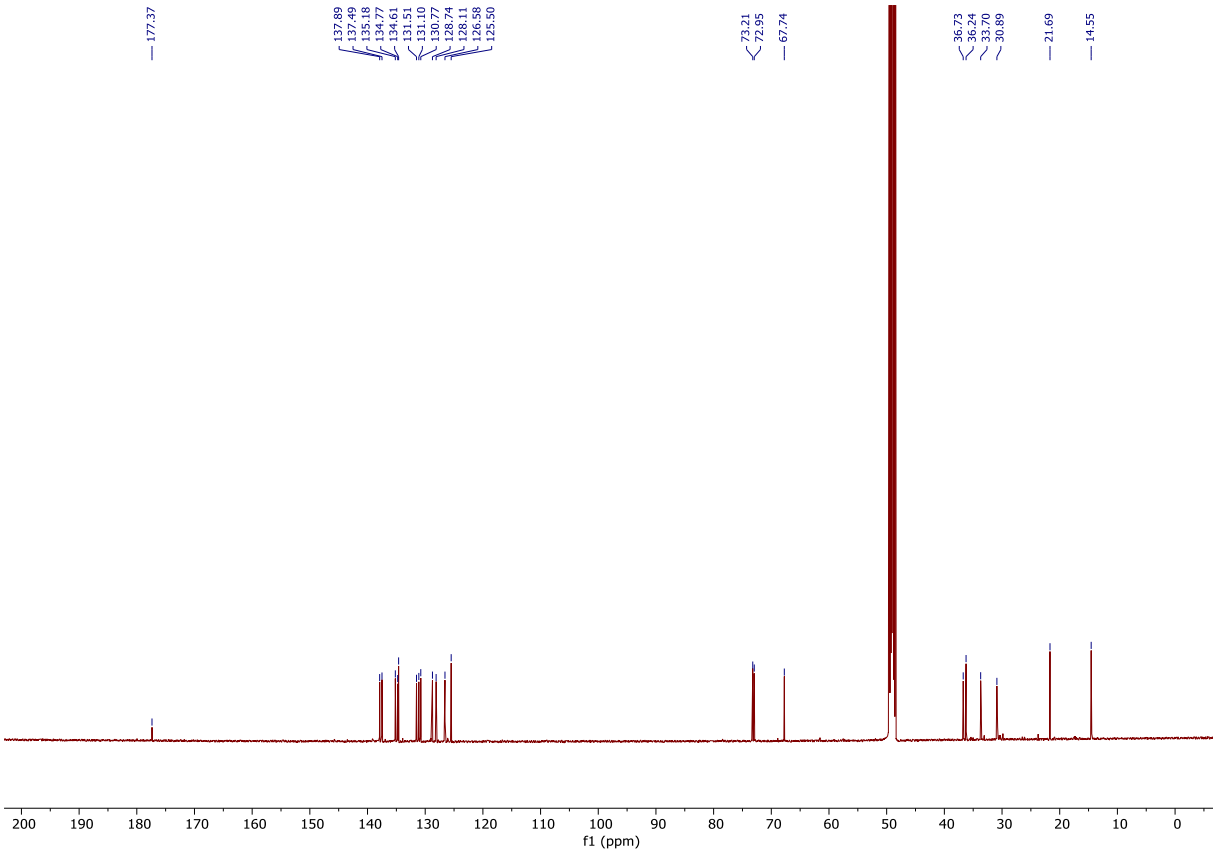



**(3*R*,4*E*,6*Z*,9*R*,10*E*,12*E*,14*Z*,16*S*)-20-Ethoxy-20-oxoicosa-4,6,10,12,14-pentaene-3,9,16-triyl triacetate, 47**

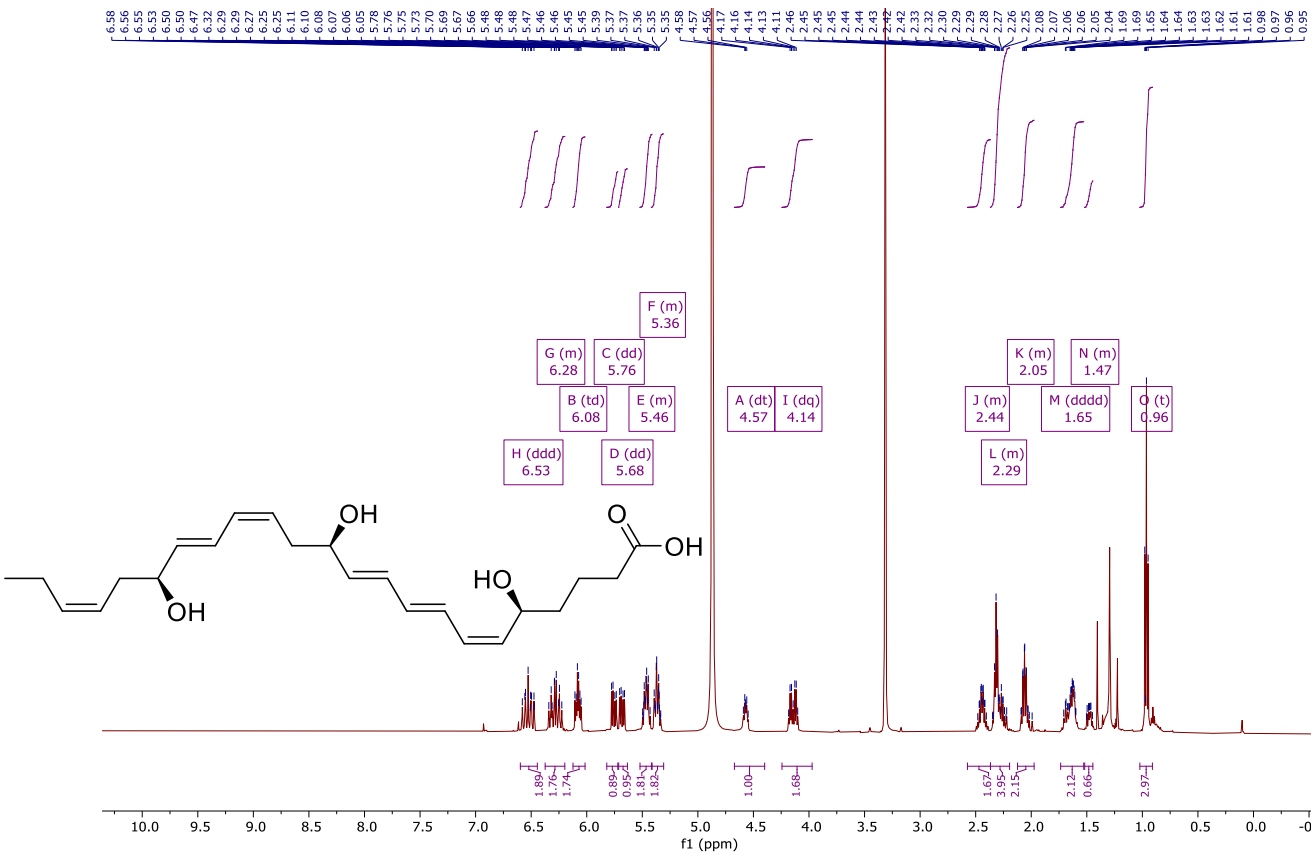


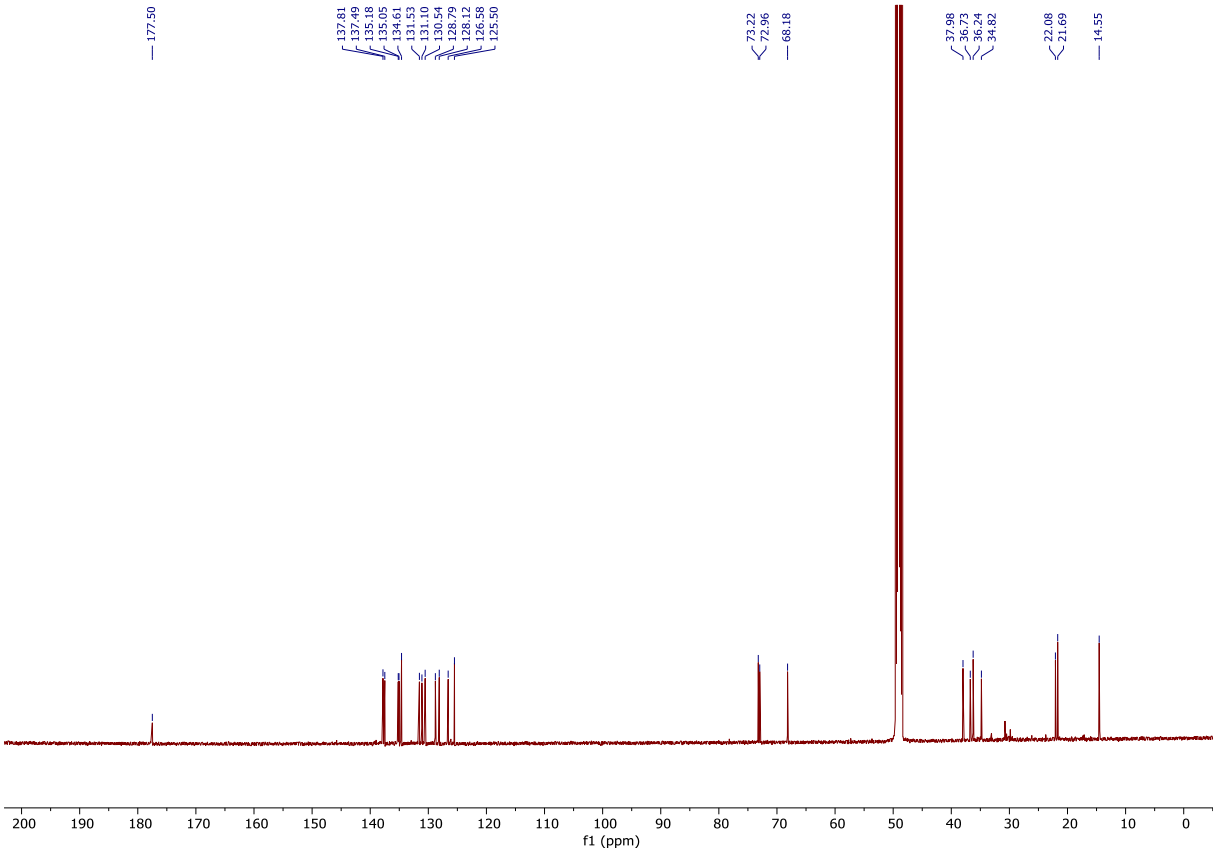
**(4*S*,5*Z*,7*E*,9*E*,11*R*,13*Z*,15*E*,17*S*,19*Z*)-4,11,17-trihydroxydocosa-5,7,9,13,15,19-hexaenoic acid (1, RvD3)**



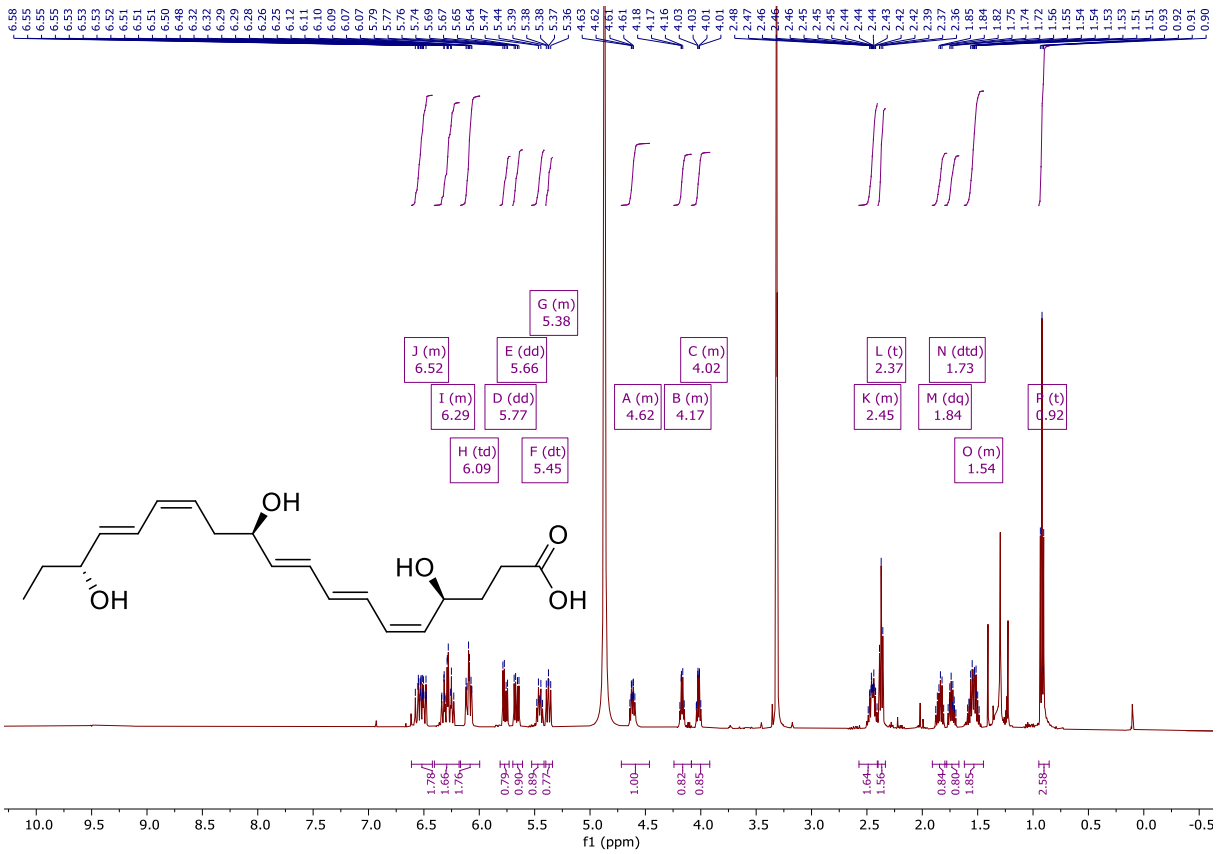



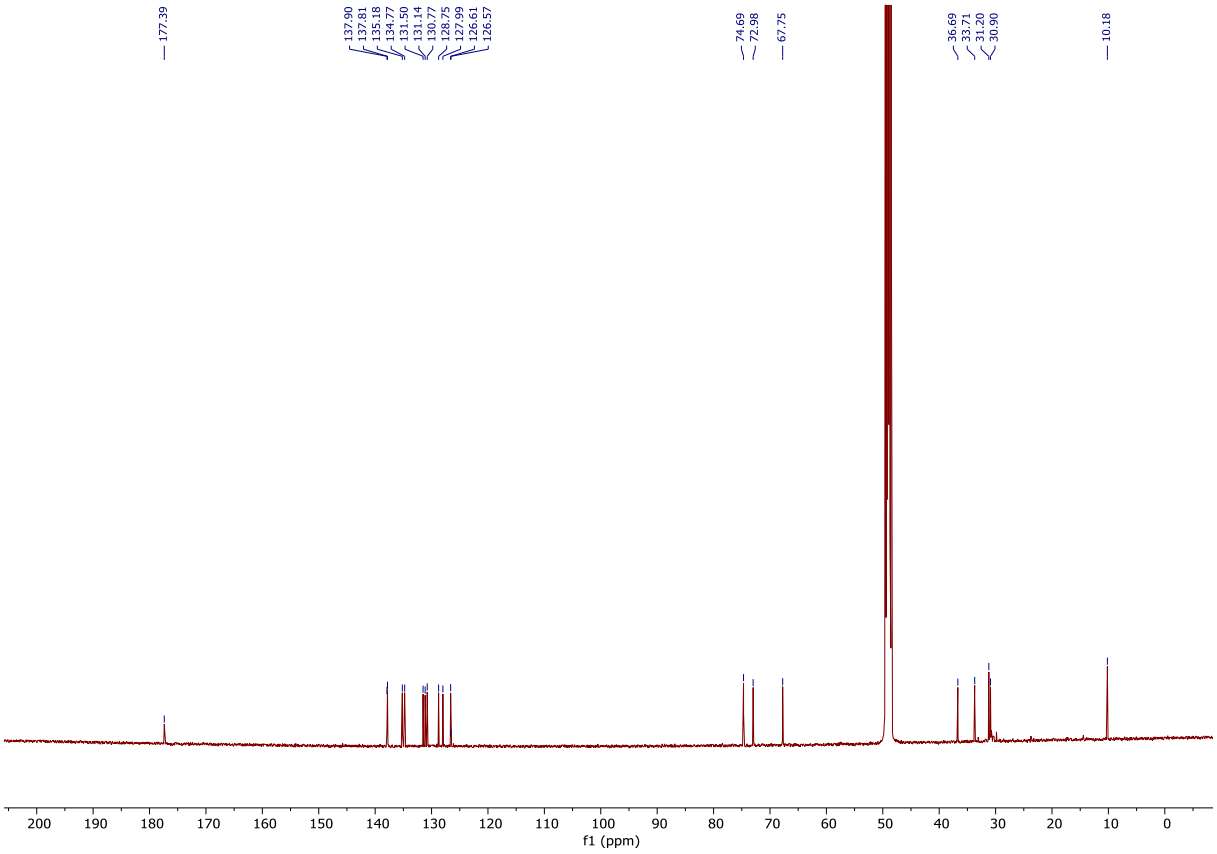
**(5*S*,6*Z*,8*E*,10*E*,12*R*,14*Z*,16*E*,18*S*,20*Z*)-5,12,18-trihydroxytricosa-6,8,10,14,16,20-hexaenoic acid, 44**



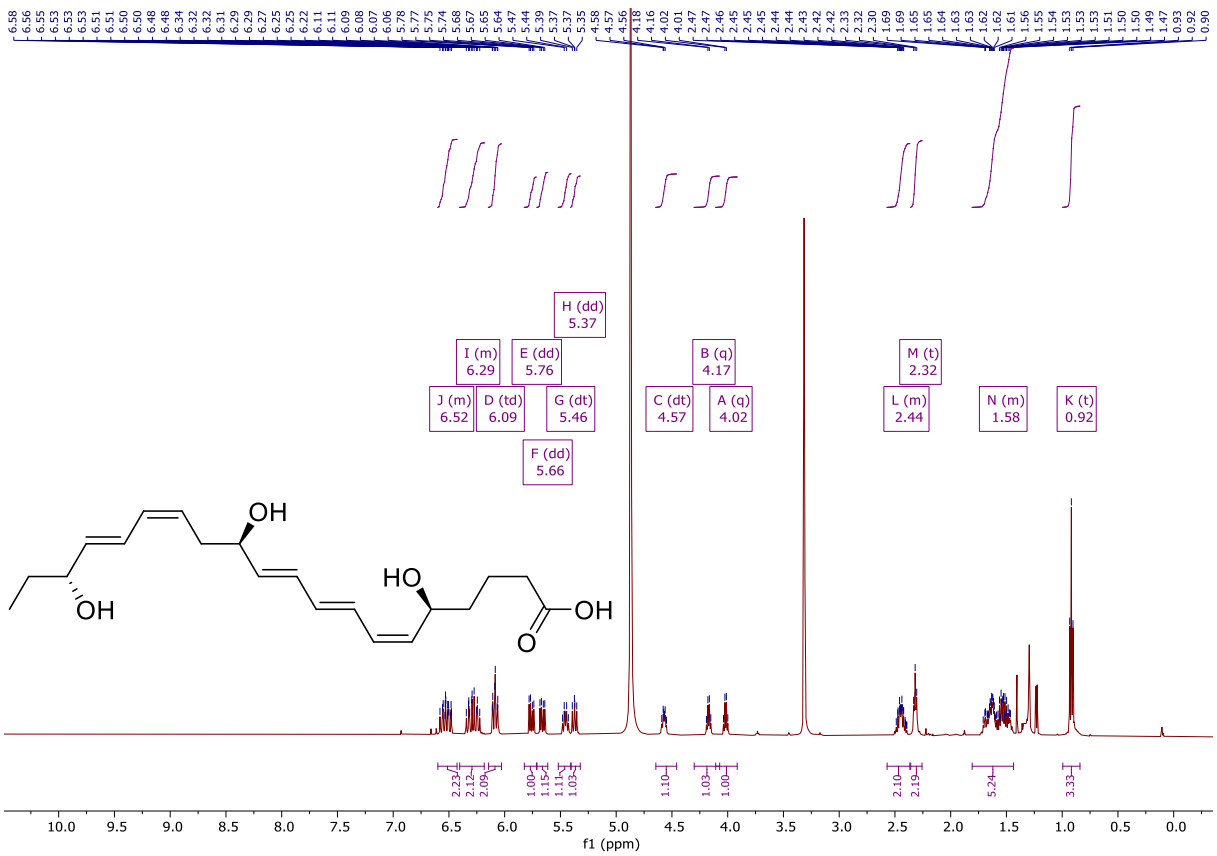



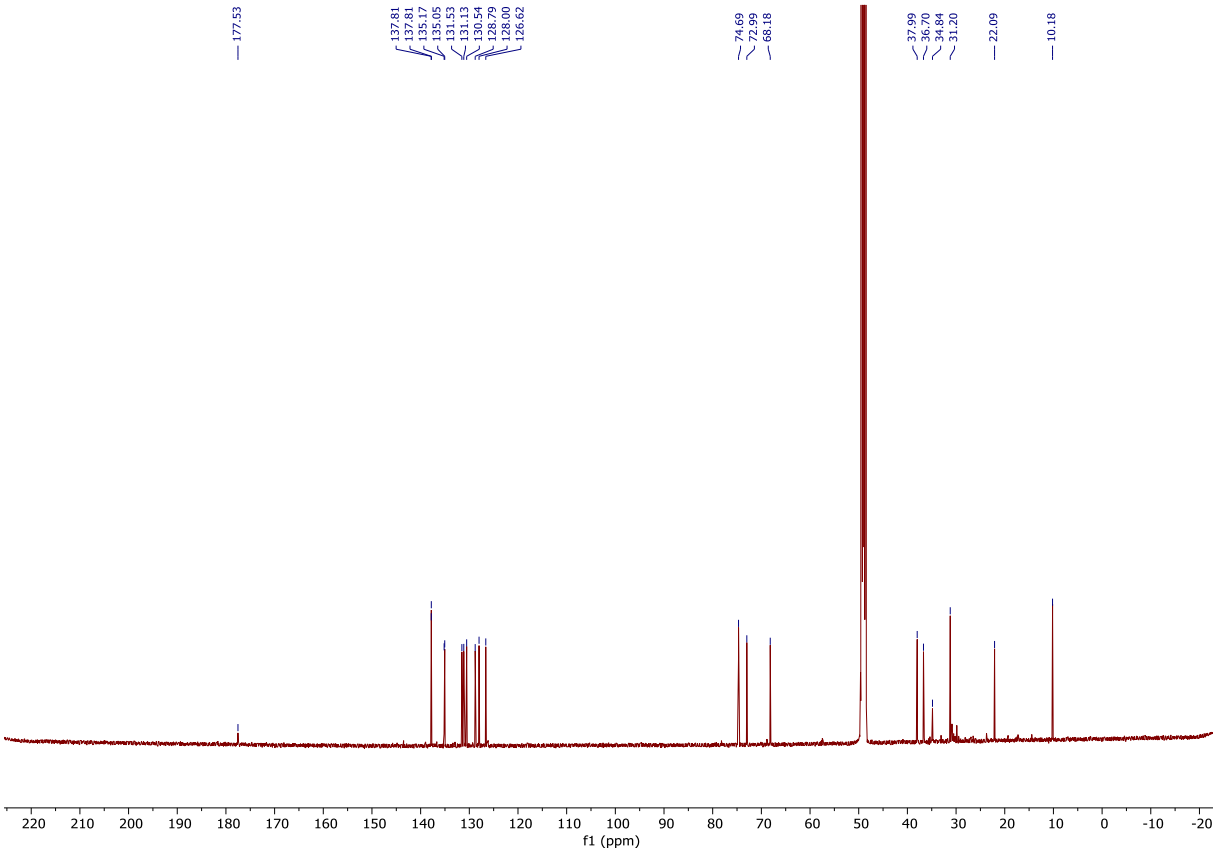
**(4*S*,5*Z*,7*E*,9*E*,11*R*,13*Z*,15*E*,17*R*)-4,11,17-trihydroxynonadeca-5,7,9,13,15-pentaenoic acid, 49**



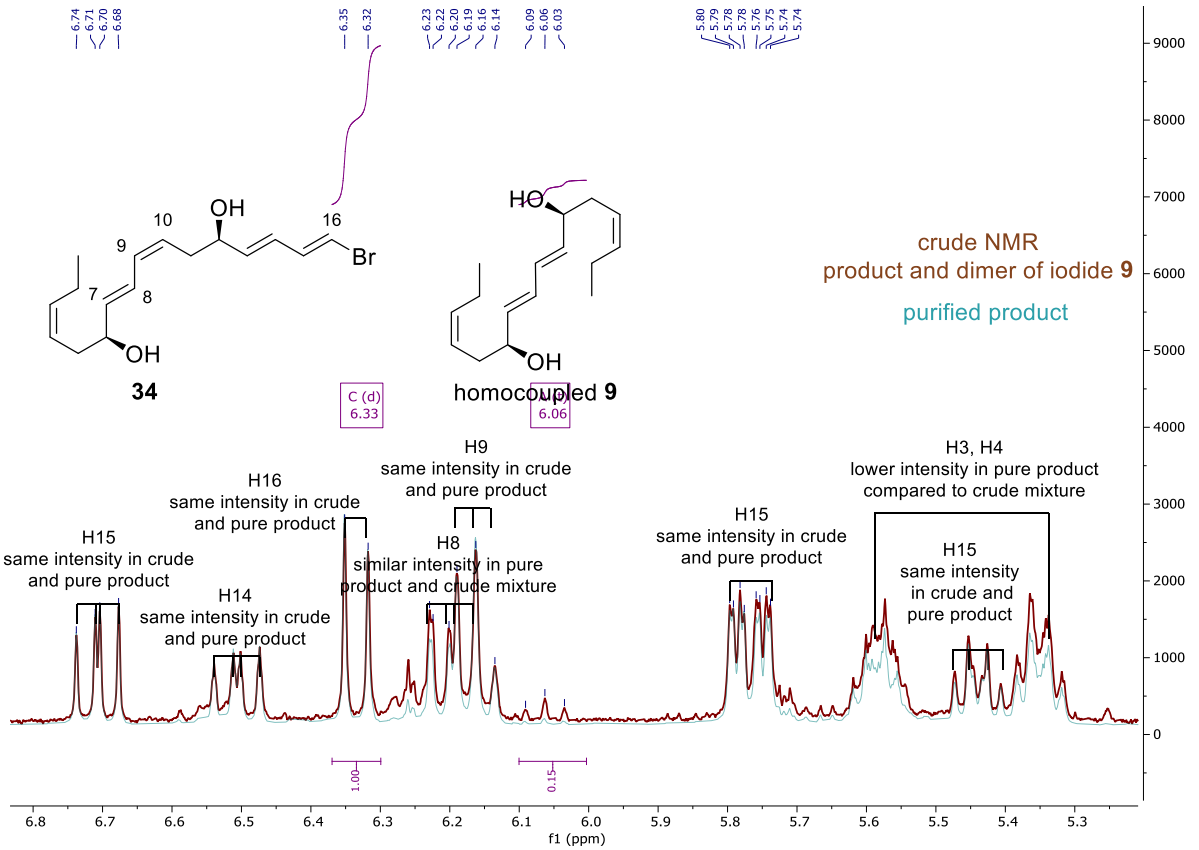



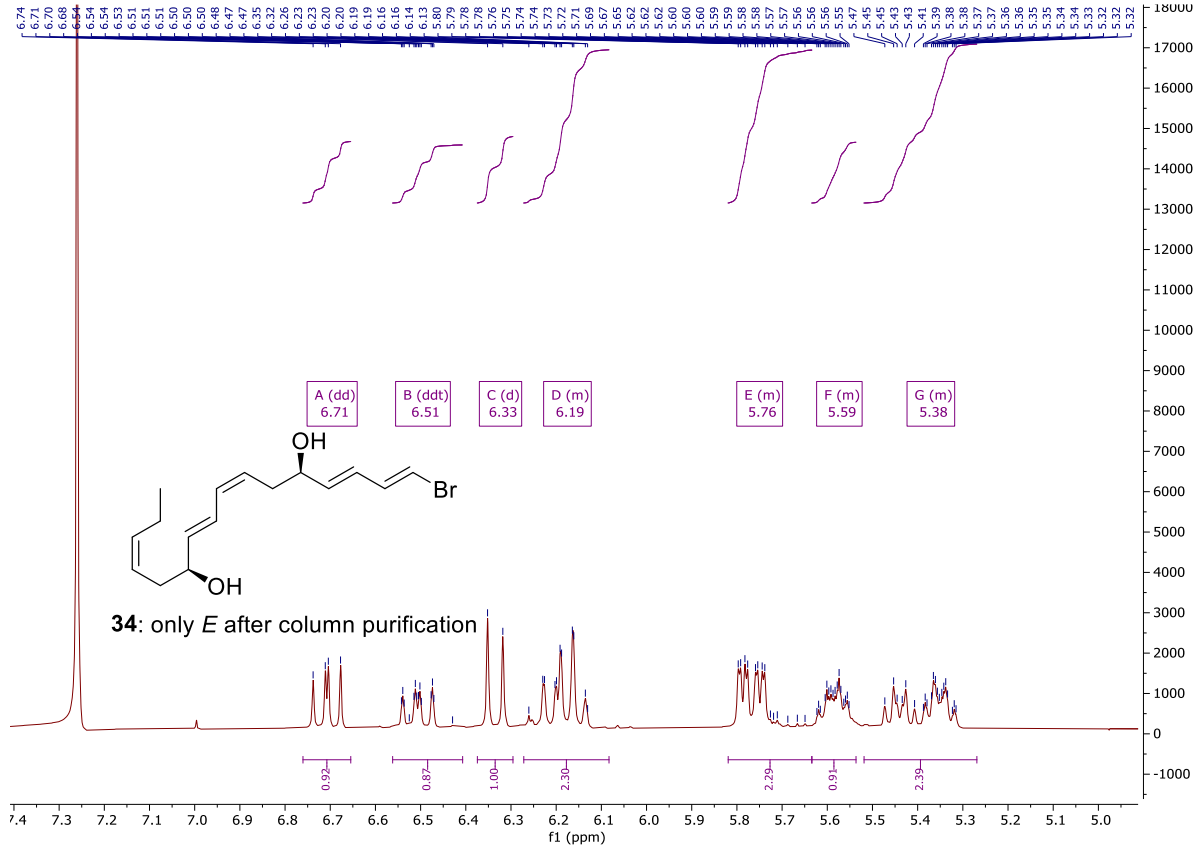
**(5*S*,6*Z*,8*E*,10*E*,12*R*,14*Z*,16*E*,18*R*)-5,12,18-trihydroxyicosa-6,8,10,14,16-pentaenoic acid (2, RvE1)**



## Attempted coupling of alcohol 9



## Attempted coupling of alcohol 37