SUPPORTING INFORMATION

Relay Cross Metathesis for the Iterative Construction of Terpenoids and Synthesis of a Diterpene Benzoate Macrolide of Biogenetic Relevance to the Bromophycolides

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General Experimental

Experimental Techniques: All reactions were carried out in oven-dried glassware. Air-sensitive reactions were performed under a positive pressure of nitrogen unless stated otherwise. Reaction temperatures other than room temperature were achieved using an oil bath, ice/water bath or a dry ice/acetone bath. 'Concentrated' refers to concentrating of the solution *in vacuo* until all (or most) of the solvent and/or volatile components have been removed. 'Chromatographed' refers to flash column chromatography on silica gel, particle size 33−70 μm or 40−63 μm, unless otherwise stated. Analytical TLC was performed on silica gel 60 F254 pre-coated aluminium-backed plates and visualized with either irradiation with UV light (254 nm) or potassium permanganate, vanillin or phosphomolybdic acid staining. Brine refers to a saturated aqueous NaCl solution.

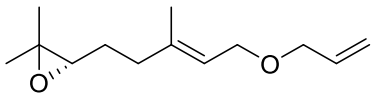
Characterization: Melting points were recorded on a Stanford Research Systems 'OptiMelt' automated melting point system. Fourier transform infra-red (IR) spectra were recorded neat using an ATR-IR spectrometer and absorptions are reported to the nearest wavenumber. ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker DRX-400 or Bruker AV-400. Chemical shifts (δ) are expressed in parts per million (ppm) relative to the residual solvent peak. ^{1}H NMR spectra were recorded at 400 MHz. ^{13}C NMR spectra were recorded at 101 MHz. NMR acquisitions were performed at 298 K unless stated otherwise. Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; qu., quintet, m, multiplet. High resolution MS was recorded by the Imperial College Department of Chemistry Mass Spectrometry Service.

Reagents: Triethylamine was distilled under nitrogen before use. The molarity of ^{i}PrMgCl was determined by titration with menthol and 2,2'-bipyridine in THF directly before use. All other reagents were obtained from commercial suppliers and used as received.

Solvents: All reactions were carried out in anhydrous solvents, unless used in combination with H_2O. HPLC grade CH_2Cl_2, THF and toluene were dried by passing through a column of alumina beads. Extraction solvents and chromatography eluents (*n*-hexane, pentanes, CH_2Cl_2, Et_2O and EtOAc) were used as received. Et_2O and pentanes were GPR (VWR) grade. EtOAc, *n*-hexane, and CH_2Cl_2 were HiPerSolv (VWR) grade.

Experimental details and characterizing data for compounds.

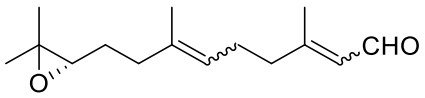
*(S,E)-3-(5-(Allyloxy)-3-methylpent-3-en-1-yl)-2,2-dimethyloxirane (**2**)*



2

Following a modified procedure of Corey,[1] to a solution of (*R*,*E*)-8-(allyloxy)-2,6-dimethyloct-6-ene-2,3-diol (**1**)[2] (1.13 g, 5.00 mmol, 1.00 equiv.) in CH_2Cl_2 (10 mL) at 0 ˚C was added pyridine (0.81 mL, 10 mmol, 2.0 equiv.) followed by MsCl (0.50 mL, 6.5 mmol, 1.3 equiv.) dropwise. The reaction was allowed to gradually warm to room temperature and the mixture was stirred for 18 h. Additional pyridine (2.4 mL, 30 mmol, 6.0 equiv.) was added and stirring was continued for an additional 5 hours. The mixture was poured into a suspension of K_2CO_3 (11.4 g, 82.5 mmol) in MeOH (50 mL) and the resulting suspension was stirred for a further 17 h. The reaction mixture was concentrated, diluted with H_2O (100 mL) and extracted with EtOAc (3 × 40 mL). The combined organic phase was washed with a saturated aqueous $CuSO_4$ solution (3 × 50 mL), then brine (2 × 50 mL), dried over Na_2SO_4 and concentrated. The residue was chromatographed (5-10% EtOAc in *n*-hexane), to give epoxide **2** (891 mg, 4.23 mmol, 85%) as a colorless oil. 10.14469/hpc/5771. R_f 0.57 (30% EtOAc in pentanes); $[\alpha]_D^{20}$ - 4.9 (*c* 1.0, $CHCl_3$); IR (ATR, neat) 3075, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.92 (ddt, *J* = 17.5, 10.5, 5.7 Hz, 1H), 5.43 – 5.36 (m, 1H), 5.26 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.17 (dq, *J* = 10.5, 1.5 Hz, 1H), 3.99 (d, *J* = 6.8 Hz, 2H), 3.97 – 3.94 (m, 2H), 2.70 (t, *J* = 6.2 Hz, 1H), 2.26 – 2.07 (m, 2H), 1.68 (s, 3H), 1.67 – 1.62 (m, 2H), 1.29 (s, 3H), 1.25 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.4, 135.1, 121.5, 117.2, 71.3, 66.7, 64.2, 58.5, 36.4, 27.3, 25.0, 18.9, 16.7; HRMS (CI^+) calcd for $C_{13}H_{21}O_2$ $[M - H]^+$ 209.1536, found 209.1535.

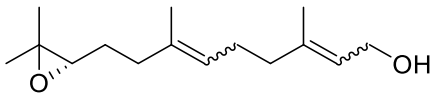
*(S)-9-(3,3-Dimethyloxiran-2-yl)-3,7-dimethylnona-2,6-dienal (**4**)*[3]



4

To a mixture of epoxide **2** (53 mg, 0.25 mmol, 1.0 equiv.), citral **3** (0.210 mL, 1.25 mmol, 5.00 equiv.), AcOH (5.7 µL, 0.1 mmol, 40 mol%) and CuI (14 mg, 0.075 mmol, 30 mol%) was added ruthenium benzylidene **5** (42 mg, 0.050 mmol, 20 mol%). The mixture was heated to 50 °C using an oil bath for 1 h under a strong positive pressure of N_2 (g) *via* a needle in/out to aid the removal of volatiles. The resulting mixture was loaded directly onto a column of silica gel and chromatographed (10-20% EtOAc in *n*-hexane), to give epoxy enal sesquiterpene **4** (51 mg, 0.22 mmol, 88%) as a light brown oil and as a mixture of *E*/*Z* geometrical isomers; *E*/*Z* = 73:27) at the newly formed olefin and *E*/*Z* = 76:24 at the α,β-unsaturated aldehyde. 10.14469/hpc/5772. R_f 0.37 (20% EtOAc in *n*-hexane); IR (ATR, neat), 1671, 1632, 1611 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.98 (d, *J* = 8.0 Hz, 0.76H), 9.89 (d, *J* = 8.2 Hz, 0.24H), 5.86 (d, *J* = 8.1 Hz, 1H), 5.19 – 5.08 (m, 1H), 2.72 – 2.65 (m, 1H), 2.59 (t, 0.50H), 2.29 – 2.03 (m, 8.5H), 1.72 – 1.56 (m, 5H), 1.29 (s, 0.81H), 1.28 (s, 2.19H), 1.26 (s, 0.81H), 1.24 (s, 2.19H). The *E*:*Z* ratio at the newly formed olefin was determined by integration of the resonances at δ 1.24 (major) and 1.26 (minor) ppm, and at the α,β-unsaturated aldehyde by integration of the resonances at δ 9.98 (major) and 9.89 (minor) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 191.4, 190.8, 163.7, 136.6, 135.8, 135.8, 128.8, 127.6, 127.5, 124.0, 123.2, 122.8, 64.2, 64.0, 58.5, 58.4, 40.8, 40.6, 36.4, 32.6, 28.7, 27.5, 27.5, 27.4, 27.1, 25.7, 25.6, 25.2, 25.0, 25.0, 23.4, 18.9, 18.9, 17.7, 17.7, 16.2, 16.2. The major geometry of the newly formed trisubstituted olefin was assigned as the *E* on the basis of a characteristic shielded methyl resonance[4] at 16.2 vs 23.4 ppm for the minor *Z*-isomer; HRMS (ES^+) calcd for $C_{15}H_{25}O_2$ $[M + H]^+$ 237.1855, found 237.1854.

(S)-9-(3,3-Dimethyloxiran-2-yl)-3,7-dimethylnona-2,6-dien-1-ol (7)

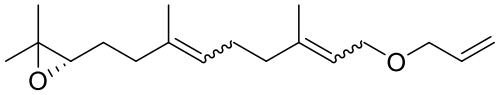


7

Using a modified procedure of Zeynizadeh and Shirini,[5] to a solution of epoxy enal **4** (709 mg, 3.00 mmol, 1.00 equiv.) in THF (15 mL) was added DOWEX® 50WX8 (0.60 mg, 0.20 g mol^{-1}), then $NaBH_4$ (125 mg, 3.30 mmol, 1.1 equiv.) at 0 ˚C and the mixture was stirred for 30 min. The reaction was quenched by the addition of a saturated aqueous NH_4Cl solution (150 mL) and extracted with EtOAc (4 × 50 mL). The combined organic phase was washed with brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was chromatographed (30% EtOAc in *n*-hexane), to give allylic alcohol **7** (542 mg, 2.27 mmol, 76%) as a colorless oil and mixture of *E*/*Z* geometrical isomers ($\Delta^{2,3}$ *E*/*Z* = 69:31, $\Delta^{6,7}$ *E*/*Z* = 73:27). 10.14469/hpc/5774. R_f 0.28 (20% EtOAc in *n*-hexane); IR (ATR, neat) 3600-3100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 – 5.33 (m, 1H), 5.20 – 5.09 (m, 1H), 4.18 – 4.11 (m, 1.38H), 4.11 – 4.06 (m, 0.62H), 2.70 (t, *J* = 6.1 Hz, 0.27H), 2.68 (t, *J* = 6.2 Hz, 0.73H), 2.23 – 1.98 (m, 6H), 1.75 – 1.73 (m, 1H), 1.71 – 1.68 (m, 1H), 1.67 (s, 2H), 1.64 – 1.57 (m, 4H), 1.42 (br s, 1H), 1.30 (s, 0.81H), 1.29 (s, 2.19H), 1.26 (s, 0.81H), 1.25 (s, 2.19H). The *E*:*Z* ratio at $\Delta^{2,3}$ was determined by integration of the resonances at δ 4.18 – 4.11 (major) and 4.11 – 4.06 (minor) ppm, and at $\Delta^{6,7}$ by integration of the resonances at δ 1.25 (major) and 1.26 (minor) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 139.3, 134.9, 134.5, 134.3, 125.3, 124.7, 124.6, 124.5, 124.3, 123.6, 123.6, 64.2, 64.1, 64.1, 59.3, 59.0, 58.9, 58.5, 58.4, 39.7, 39.4, 36.3, 36.3, 32.1, 31.8, 28.5, 27.4, 27.3, 27.2, 26.5, 26.4, 26.2, 24.9, 24.9, 23.6, 23.3, 23.3, 23.2, 18.8, 18.7, 16.3, 16.2, 16.0. The major geometry of the $\Delta^{6,7}$ trisubstituted olefin was assigned as the *E*-isomer on the basis of characteristic shielded methyl resonances[4] at 16.2 and 16.0 vs 23.2

and 23.3 ppm for the minor *Z*-isomer; HRMS (CI^+) calcd for $C_{15}H_{25}O$ $[M - OH]^+$ 221.1900, found 221.1892.

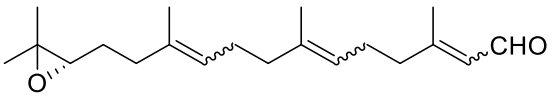
*(S)-3-(9-(Allyloxy)-3,7-dimethylnona-3,7-dien-1-yl)-2,2-dimethyloxirane (**8**)*



8

Using a modified procedure of Rao and Senthilkumar,[6] to a mixture of allylic alcohol **7** (474 mg, 2.00 mmol, 1.00 equiv.), allyl bromide (0.52 mL, 6.0 mmol, 3.0 equiv.) and TBAI (37 mg, 0.10 mmol, 5 mol%) was added crushed KOH pellets (224 g, 4.00 mmol, 2.00 equiv.) at room temperature. The resultant mixture was stirred for 7 h. The crude reaction mixture was loaded directly onto a column of silica gel and chromatographed (5-10% EtOAc in *n*-hexane), to give allyl ether **8** (541 mg, 1.94 mmol, 98%) as a colourless oil. 10.14469/hpc/5779. R_f 0.81 (20% EtOAc in *n*-hexane); IR (ATR, neat) 3080, 1668, 1648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.00 – 5.84 (m, 1H), 5.40 – 5.33 (m, 1H), 5.31 – 5.23 (m, 1H), 5.22 – 5.12 (m, 2H), 4.02 – 3.92 (m, 4H), 2.74 – 2.66 (m, 1H), 2.22 – 1.99 (m, 6H), 1.77 – 1.73 (m, 1H), 1.71 – 1.65 (m, 3H), 1.63 – 1.58 (m, 4H), 1.32 – 1.28 (m, 3H), 1.28 – 1.24 (m, 3H). *E:Z* ratios could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 140.0, 139.9, 135.1, 134.7, 134.4, 125.3, 125.2, 124.5, 124.3, 122.0, 121.9, 121.0, 120.9, 116.9, 116.9, 71.8, 71.1, 71.0, 68.7, 66.6, 66.3, 64.2, 64.1, 64.1, 58.3, 39.8, 39.5, 36.7, 36.3, 32.4, 32.2, 29.6, 28.5, 27.4, 26.6, 26.4, 26.3, 26.1, 24.9, 23.5, 23.3, 18.8, 18.7, 16.5, 16.0; HRMS (ES^+) calcd for $C_{18}H_{31}O_2$ $[M + H]^+$ 279.2324, found 279.2323.

*(S)-13-(3,3-Dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trienal (**9**)*[7]

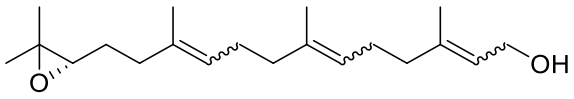


9

To a mixture of allyl ether **8** (144 mg, 0.520 mmol, 1.00 equiv.), citral **3** (0.44 mL, 2.6 mmol, 5.0 equiv.), AcOH (12 µL, 0.21 mmol, 40 mol%) and CuI (31 mg, 0.16 mmol, 30 mol%) was added ruthenium benzylidene **5** (85 mg, 0.10 mmol, 20 mol%) and heated to 50 °C using an oil bath for 30 min. under a strong positive pressure of N_2 (g) via a needle in/out to aid the removal of volatiles. The resulting mixture was loaded directly onto a column of silica gel and chromatographed (10-20% EtOAc in *n*-hexane) to give diterpene epoxy enal **9** (98 mg, 0.32 mmol, 62%) as a light brown oil and a mixture of *E*/*Z* geometrical isomers (*E*/*Z* = 66:34 at the α,β-unsaturated aldehyde). 10.14469/hpc/5780. R_f 0.51 (20% EtOAc in *n*-hexane); IR (ATR, neat) 1673, 1631 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.99 (d, *J* = 8.1 Hz, 0.66H), 9.93 – 9.88 (m, 0.34H), 5.93 – 5.84 (m, 1H), 5.18 – 5.05 (m, 2H), 2.73 – 2.67 (m, 1H), 2.62 – 2.55 (m, 1H), 2.27 – 2.20 (m, 3H), 2.18 – 2.16 (m, 2H), 2.12 – 2.02 (m, 4H), 2.00 – 1.96 (m, 2H), 1.72 – 1.67 (m, 2H), 1.64 – 1.54 (m, 8H), 1.32 – 1.28 (m, 3H), 1.27 – 1.25 (m, 3H). The *E*:*Z* ratio at the α,β-unsaturated aldehyde was determined by integration of the resonances at δ 9.99 (major) and 9.93 – 9.88 (minor) ppm, *E*:*Z* ratios at the remaining olefins could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 163.8, 136.6, 136.5, 134.5, 134.2, 128.6, 127.4, 125.4, 124.6, 124.5, 123.3, 122.6, 122.5, 64.2, 64.1, 58.3, 40.8, 40.6, 39.8, 39.6, 36.3, 31.9, 30.9, 28.6, 27.5, 27.4, 27.1, 26.6,

26.4, 26.4, 25.7, 25.5, 24.9, 23.4, 18.8, 17.6, 16.1, 16.0; HRMS (CI^+) calcd for $C_{20}H_{33}O_2$ $[M + H]^+$ 305.2475, found 305.2464.

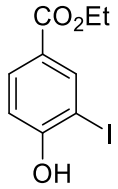
*(S)-13-(3,3-Dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trien-1-ol (**10**)*[8]



10

Using a modified procedure of Zeynizadeh and Shirini,[5] to a solution of epoxy enal **9** (163 mg, 0.540 mmol, 1.0 equiv.) in THF (2.7 mL) was added DOWEX® 50WX8 (0.11 mg, 0.20 g mol^{-1}), then $NaBH_4$ (22 mg, 0.59 mmol, 1.1 equiv.) at 0 ˚C and the mixture was stirred for 30 min. The reaction was quenched by the addition of a saturated aqueous NH_4Cl solution (30 mL) and extracted with EtOAc (3 × 25 mL). The combined organic phase was washed with brine (50 mL), dried over Na_2SO_4 and concentrated. The residue was chromatographed (15% EtOAc in toluene) to give allylic alcohol **10** (117 mg, 0.380 mmol, 71%) as a colorless oil. 10.14469/hpc/5781. R_f 0.37 (20% EtOAc in toluene); IR (ATR, neat) 3600-3050, 1667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.48 – 5.33 (m, 1H), 5.21 – 5.03 (m, 2H), 4.13 (d, *J* = 6.9 Hz, 1.45H), 4.11 – 4.03 (m, 0.55H), 2.74 – 2.66 (m, 1H), 2.21 – 1.92 (m, 10H), 1.75 – 1.53 (m, 11H), 1.29 (s, 0.87H), 1.29 (s, 2.13H), 1.26 (s, 0.87H), 1.24 (s, 2.13H). *E:Z* ratios could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 139.5, 139.4, 134.0, 135.74, 135.4, 135.2, 135.1, 134.3, 134.3, 134.1, 134.1, 134.0, 125.7, 125.6, 124.8, 124.7, 124.7, 124.6, 124.5, 124.5, 124.0, 123.9, 123.7, 123.6, 123.5, 64.22, 64.2, 59.3, 59.0, 58.5, 58.4, 39.9, 39.9, 39.8, 39.8, 39.6, 39.5, 39.5, 36.3, 32.3, 32.2, 32.0, 32.0, 31.9, 31.8, 28.5, 28.5, 27.5, 27.4, 26.6, 26.5, 26.4, 26.3, 26.2, 25.3, 24.9, 23.5, 23.4, 23.4, 23.3, 19.5, 18.7, 18.7, 16.3, 16.3, 16.0, 16.0; HRMS (ES^+) calcd for $C_{20}H_{34}O_2Na$ $[M + Na]^+$ 329.2457, found 329.2468.

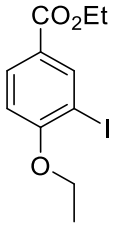
*Ethyl 4-hydroxy-3-iodobenzoate (**12**)*[9]



12

Using the procedure of Carroll,[9] to a solution of ethyl 4-hydroxybenzoate (**11**) (25.6 g, 152 mmol, 1.00 equiv.) in AcOH (125 mL) at 65 ˚C, was added dropwise a solution of ICl (25.0 g, 152 mmol, 1.00 equiv.) in AcOH (50 mL). The reaction mixture was stirred at 65 ˚C using a heating mantle for 5 h., before pouring onto ice/H_2O. The resulting precipitate was collected by filtration and successively washed with a saturated aqueous Na_2SO_3 solution (100 mL) and H_2O (100 mL). The cream solid was dissolved in EtOAc, dried over Na_2SO_4 and concentrated. The crude reaction mixture was purified by recrystallization (*n*-hexane) to give iodophenol **12** (46.0 g, 137 mmol, 90 %) as colourless crystals. 10.14469/hpc/5784. m.p. 117-118 °C; R_f 0.38 (CH_2Cl_2); IR (ATR, neat) 3450 – 3050, 1679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 2.0 Hz, 1H), 7.95 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 5.76 (br s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 159.1, 140.5, 131.9, 124.4, 114.7, 84.8, 61.3, 14.3; MS (ES^-) *m/z* 291 $[M - H]^-$; HRMS (ES^-) *m/z* calcd for $C_9H_8O_3{}^{127}I$ $[M - H]^-$ 290.9518, found 290.9515.

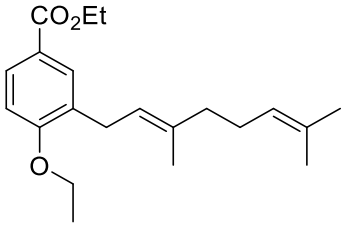
*Ethyl 4-ethoxy-3-iodobenzoate (**13**)*



13

To a solution of iodophenol **12** (2.92 g, 10.0 mmol, 1.00 equiv.) in DMF (100 mL) at 0 ˚C, was added K_2CO_3 (1.15 g, 30.0 mmol, 3.00 equiv.) and the mixture was stirred at 0 ˚C for 10 min. Ethyl iodide (1.61 mL, 20.0 mmol, 2.00 equiv.) was added dropwise and the mixture was allowed to warm to room temperature at which the mixture was stirred for 17 h. The reaction mixture was then concentrated. H_2O (150 mL) was added to the residue and this was extracted with EtOAc (4 × 50 mL). The combined organic phase was washed with a 10% LiCl aqueous solution (5 × 20 mL), brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was dissolved in *n*-hexane (200 mL), and the product was precipitated by cooling in a liquid N_2 bath. Collection by filtration gave ethyl ether **13** (2.97 g, 9.28 mmol, 93%) as a cream solid. Recrystallization (*n*-hexane) provided **13** as colorless crystals. 10.14469/hpc/5785. m.p. 47-49 °C; IR (ATR, neat) 1699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 2.1 Hz, 1H), 7.98 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.78 (d, *J* = 8.6 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 1.50 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 161.0, 140.9, 131.5, 124.5, 110.7, 85.9, 65.1, 60.9, 14.6, 14.4; HRMS (EI^+) calcd for $C_{11}H_{13}O_3I$ $[M]^{\bullet+}$ 319.9909, found 319.9894.

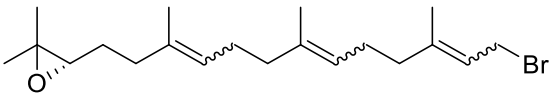
*Ethyl (E)-3-(3,7-dimethylocta-2,6-dien-1-yl)-4-ethoxybenzoate (**14**)*



14

Using a modified procedure of Lang and Steglich,[10] to a solution of iodo ether **13** (5.72 g, 17.9 mmol, 1.00 equiv.) in THF (90 mL) at -30 °C was added a solution of ^{i}PrMgCl in THF (2 M, 10.1 mL, 20.1 mmol, 1.125 equiv.) over 10 min. at -30 ˚C. A solution of Li_2CuCl_4 in THF (0.1 M, 5.4 mL, 0.54 mmol, 3.0 mol%) was added and stirring was continued for 5 min. at -30 °C before geranyl bromide (3.55 mL, 17.9 mmol, 1.00 eq.) was added using a syringe-pump over 35 min. The reaction mixture was stirred at -30 °C for 2 h and allowed to warm to room temperature at which it was stirred for 18 h. A saturated aqueous NH_4Cl solution (150 mL) was added and the mixture was extracted with EtOAc (3 × 100 mL). The combined organic phase was washed with a 2 M aqueous NH_4OH solution (2 × 100 mL) and brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was chromatographed (80-100% toluene in *n*-hexane), to give geranyl benzoate **14** (5.68 g, 17.2 mmol, 96%) as a colourless oil. 10.14469/hpc/5786. R_f 0.60 (20% EtOAc in *n*-hexane); IR (ATR, neat) 1712, 1604 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.77 (m, 2H), 6.82 (d, *J* = 8.5 Hz, 1H), 5.37 – 5.24 (m, 1H), 5.16 – 5.05 (m, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.09 (q, *J* = 7.0 Hz, 2H), 3.34 (d, *J* = 7.3 Hz, 2H), 2.17 – 1.96 (m, 4H), 1.72 (s, 3H), 1.66 (s, 3H), 1.59 (s, 3H), 1.44 (t, *J* = 7.0 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 160.5, 136.3, 131.4, 130.9, 130.1, 129.3, 124.3, 122.3, 122.0, 110.2, 63.7, 60.5, 39.8, 28.5, 26.8, 25.7, 17.7, 16.2, 14.8, 14.4; HRMS (ES^+) calcd for $C_{21}H_{31}O_3$ $[M + H]^+$ 331.2273, found 331.2273.

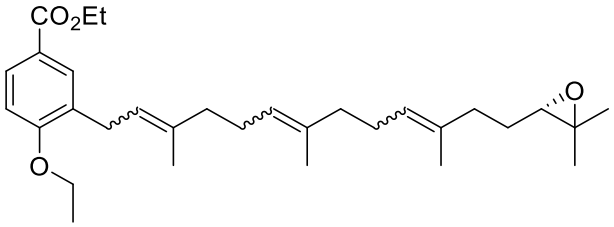
*(S)-3-(13-Bromo-3,7,11-trimethyltrideca-3,7,11-trien-1-yl)-2,2-dimethyloxirane (**15**).*[8]



15

To a solution of diterpene alcohol **10** (113 mg, 0.37 mmol, 1.0 equiv.) in CH_2Cl_2 (1.9 mL) was added NEt_3 (61 µL, 0.44 mmol, 1.2 equiv.), then MsCl (34 µL, 0.44 mmol, 1.2 equiv.) at 0 ˚C and the mixture was stirred for 40 min. LiBr (38 mg, 0.44 mmol, 1.2 equiv.) in THF (1 mL) was added and the mixture was stirred for an additional 4 h at 0 ˚C. The mixture was chromatographed (CH_2Cl_2) to give crude bromide **15** (111 mg, 0.27 mmol, 74%) which was used directly in the next step. 10.14469/hpc/5783. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 – 5.44 (m, 1H), 5.22 – 5.08 (m, 2H), 4.13 (d, *J* = 8.0 Hz, 1H), 4.05 (d, *J* = 8.4 Hz, 1H), 2.77 – 2.70 (m, 1H), 2.23 – 1.94 (m, 10H), 1.81 – 1.53 (m, 11H), 1.35 – 1.32 (m, 3H), 1.30 – 1.28 (m, 3H) *E:Z* ratios could not be determined due to overlapping ^{1}H NMR resonances.

*Ethyl (S)-3-(13-(3,3-dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trien-1-yl)-4-ethoxybenzoate (**16**)*

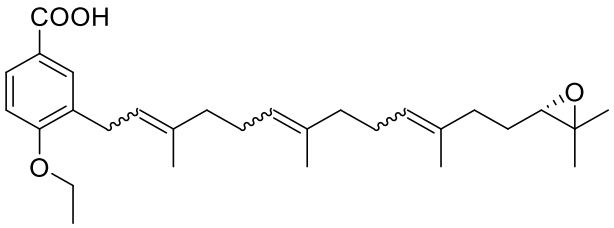


16

Using a modified procedure of Lang and Steglich,[10] to a solution of iodo ether **13** (106 mg, 0.330 mmol, 1.22 equiv.) in THF (1.5 mL) at -30 °C was added dropwise a solution of ^{i}PrMgCl in THF (2 M, 0.19 mL, 0.37 mmol, 1.4 equiv.) over 10 min. at -30 ˚C. A solution of Li_2CuCl_4 in THF (0.1 M, 0.1 mL, 0.01 mmol, 3 mol%) was added and stirring was continued for 5 min. at -30 °C. A

solution of crude bromide **15** (111 mg, 0.27 mmol, 1.0 equiv.) in THF (1 mL) was added using a syringe-pump over 35 min. The reaction mixture was stirred at -30 °C for 2 h and allowed to warm to room temperature at which it was stirred for 19 h. A saturated aqueous NH_4Cl solution (30 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic phase was washed with a 2 M aqueous NH_4OH solution (2 × 30 mL) and brine (30 mL), dried over Na_2SO_4 and concentrated. The residue was chromatographed (10-15% EtOAc in *n*-hexane), to give diterpene benzoate **16** (80 mg, 0.17 mmol, 63%) as a colourless oil. Alternatively, diterpene benzoate **16** could be prepared by the following procedure: to a mixture of allyl ether **8** (70 mg, 0.25 mmol, 1.0 equiv.), geranyl benzoate **14** (413 mg, 1.25 mmol, 5.0 equiv.), AcOH (5.7 µL, 0.10 mmol, 40 mol%) and CuI (14 mg, 0.075 mmol, 30 mol%) was added ruthenium benzylidene **5** (42 mg, 0.05 mmol, 20 mol%) and heated to 50 °C using an oil bath for 1 h under a strong positive pressure of N_2 (g) via a needle in/out to aid the removal of volatiles. The resulting mixture was loaded directly onto a column of silica gel and chromatographed (toluene to 5% Et_2O in toluene) to give diterpene benzoate **16** (63 mg, 0.13 mmol, 52%) as a light brown oil. 10.14469/hpc/5792. R_f 0.33 (20% EtOAc in *n*-hexane); IR (ATR, neat) 1712, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.77 (m, 2H), 6.81 (d, *J* = 8.5 Hz, 1H), 5.34 – 5.24 (m, 1H), 5.23 – 5.08 (m, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.08 (q, *J* = 7.0 Hz, 2H), 3.34 (d, *J* = 7.3 Hz, 2H), 2.76 – 2.64 (m, 1H), 2.19 – 1.92 (m, 10H), 1.74 – 1.56 (m, 11H), 1.44 (t, *J* = 7.0 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.31 – 1.27 (m, 3H), 1.27 – 1.23 (m, 3H) *E:Z* ratios could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 160.5, 136.4, 136.3, 136.2, 135.0, 134.9, 134.8, 134.2, 134.0, 130.9, 130.1, 129.2, 125.7, 125.2, 125.0, 124.9, 124.8, 124.4, 124.3, 122.6, 122.3, 122.1, 121.9, 110.2, 110.0, 64.2, 64.1, 63.7, 60.5, 58.4, 58.3, 40.1, 39.8, 39.6, 36.3, 32.1, 31.9, 28.5, 28.2, 27.5, 27.4, 26.7, 26.6, 26.6, 26.5, 26.5, 26.3, 24.9, 23.6, 23.4, 23.3, 18.8, 18.7, 18.3, 16.2, 16.0, 16.0, 14.8, 14.4; HRMS (ES^+) calcd for $C_{31}H_{47}O_4$ $[M + H]^+$ 483.3474, found 483.3479.

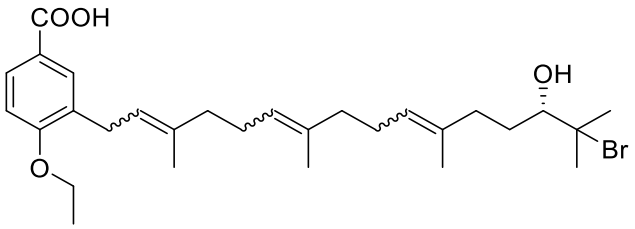
*(S)-3-(13-(3,3-Dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trien-1-yl)-4-ethoxybenzoic acid (**17**)*



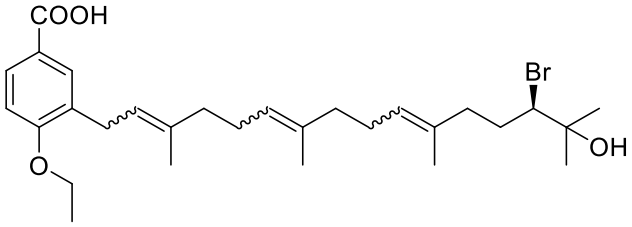
17

Using a modified procedure of Lang and Steglich,[10] to a stirred solution of ester **16** (73 mg, 0.15 mmol, 1.0 equiv.) in EtOH (0.75 mL) and H_2O (0.25 mL) was added LiOH•H_2O (13 mg, 0.30 mmol, 2.0 equiv.) and the mixture was heated to 50 ˚C using an oil bath for 7 h. The mixture was cooled to room temperature and quenched by the addition of a 2.5% aqueous AcOH solution (25 mL). The aqueous mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic phase was dried over Na_2SO_4 and concentrated. The residue was chromatographed (15% MeCN in toluene with 1% AcOH), to give carboxylic acid **17** (66 mg, 0.146 mmol, 97%) as a white solid. 10.14469/hpc/5788. R_f 0.33 (20% EtOAc in *n*-hexane with 1% AcOH); IR (ATR, neat) 1673, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (br d, *J* = 8.5 Hz, 1H), 7.92 (br s, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 5.34 (br t, *J* = 7.3 Hz, 1H), 5.27 – 5.08 (m, 2H), 4.14 (q, *J* = 6.9 Hz, 2H), 3.38 (d, *J* = 7.3 Hz, 2H), 2.82 – 2.69 (m, 1H), 2.25 – 1.94 (m, 10H), 1.80 – 1.57 (m, 11H), 1.48 (t, *J* = 7.0 Hz, 3H), 1.33 (br s, 3H), 1.31 – 1.26 (m, 3H). *E:Z* ratios could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 161.2, 136.5, 135.1, 135.0, 134.8, 134.2, 133.9, 131.5, 130.3, 130.2, 125.8, 125.0, 124.9, 124.3, 124.2, 121.8, 121.8, 110.3, 64.3, 64.2, 63.8, 58.6, 40.1, 39.9, 39.8, 39.6, 36.3, 31.9, 28.5, 28.4, 27.4, 26.7, 26.6, 26.5, 26.5, 24.9, 24.9, 23.3, 18.8, 18.7, 16.2, 16.0, 16.0, 14.8; HRMS (ES^+) calcd for $C_{29}H_{43}O_4$ $[M + H]^+$ 455.3161, found 455.3166.

*(S)-3-(15-Bromo-14-hydroxy-3,7,11,15-tetramethylhexadeca-2,6,10-trien-1-yl)-4-ethoxybenzoic acid (**18**) and (R)-3-(14-bromo-15-hydroxy-3,7,11,15-tetramethylhexadeca-2,6,10-trien-1-yl)-4-ethoxybenzoic acid (**18a**)*



18

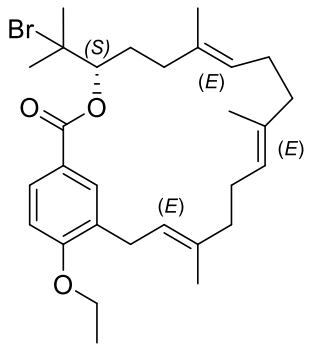


18a

Using a modified procedure of Krauss,[11] to a solution of epoxide **17** (41 mg, 0.09 mmol, 1.0 equiv.) in CH_2Cl_2 (0.9 mL) at -78 ˚C, was added *n*-Bu_4NBr (174 mg, 0.54, 6.0 equiv.), then $MgBr_2$•OEt_2 (139 mg, 0.54 mmol, 6.0 equiv.). The reaction mixture was allowed to gradually warm to -40 ˚C and was maintained at -40 ˚C, with stirring, for 5 h. Silica gel was added and the mixture was concentrated and chromatographed (5-15% Et_2O in *n*-hexane with 1% AcOH), to give first 3˚ bromide **18** (39 mg, 0.073 mmol, 81%) as a white solid and second 2˚ bromide **18a** (5 mg, 0.009 mmol, 10%) as a white solid. **18**: 10.14469/hpc/5789. R_f 0.46 (20% MeCN in toluene with 1% AcOH); IR (ATR, neat) 1675, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.93 (m, 1H), 7.91 – 7.87 (m, 1H), 6.85 (d, *J* = 8.6 Hz, 1H), 5.36 – 5.27 (m, 1H), 5.24 – 5.10 (m, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 3.46 – 3.37 (m, 1H), 3.35 (d, J = 7.4 Hz, 2H), 2.34 – 1.92 (m, 10H), 1.87 – 1.54 (m, 16H), 1.50 – 1.42 (m, 4H). *E:Z* ratios could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 161.2, 136.4, 134.9, 134.5, 134.2, 131.5, 130.3, 130.1,

126.2, 125.3, 125.2, 125.1, 124.4, 124.2, 121.9, 121.8, 121.1, 110.3, 79.3, 79.1, 75.1, 63.8, 40.1, 40.0, 39.8, 39.6, 36.4, 31.9, 31.0, 30.2, 30.1, 29.0, 28.8, 28.6, 28.4, 26.6, 26.6, 26.5, 23.3, 16.2, 16.2, 16.0, 15.9, 15.9, 14.8; HRMS (ES^+) calcd for $C_{29}H_{44}O_4{}^{79}Br$ $[M + H]^+$ 535.2423, found 535.2419. **18a**: 10.14469/hpc/5790. R_f 0.43 (20% MeCN in toluene with 1% AcOH); IR (ATR, neat) 1680, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 1H), 7.91 – 7.85 (m, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 5.37 – 5.26 (m, 1H), 5.26 – 5.08 (m, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 4.03 – 3.92 (m, 1H), 3.35 (d, *J* = 7.3 Hz, 2H), 2.38 – 1.90 (m, 11H), 1.85 – 1.69 (m, 4H), 1.71 – 1.63 (m, 2H), 1.64 – 1.55 (m, 4H), 1.51 – 1.41 (m, 4H), 1.36 – 1.31 (m, 6H). *E:Z* ratios could not be determined due to overlapping ^1H NMR resonances; ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 161.2, 161.2, 136.7, 136.5, 136.4, 135.0, 134.9, 134.9, 134.8, 133.4, 133.2, 133.1, 132.8, 130.9, 130.3, 130.1, 128.8, 126.9, 126.9, 126.1, 125.8, 125.1, 124.4, 124.2, 122.4, 121.8, 121.7, 121.0, 111.1, 110.3, 72.6, 72.6, 70.9, 70.9, 70.7, 70.6, 68.2, 63.8, 40.0, 40.0, 39.7, 39.6, 38.7, 38.2, 38.0, 32.4, 32.2, 32.1, 31.9, 31.9, 30.5, 30.4, 30.3, 29.7, 28.9, 28.4, 28.3, 28.3, 28.1, 26.7, 26.6, 26.6, 26.5, 26.4, 25.9, 25.8, 23.7, 23.5, 23.4, 23.2, 23.0, 16.2, 16.2, 16.0, 15.8, 14.8; HRMS (ES^+) calcd for $C_{29}H_{44}O_4{}^{79}Br$ $[M + H]^+$ 535.2423, found 535.2418.

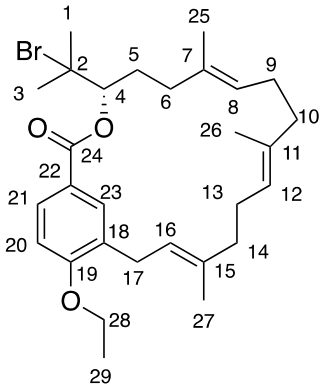
*(S,7E,11E,15E)-4-(2-Bromopropan-2-yl)-1^4-ethoxy-7,11,15-trimethyl-3-oxa-1(1,3)-benzenacycloheptadecaphane-7,11,15-trien-2-one (E,E,E-**19**)*



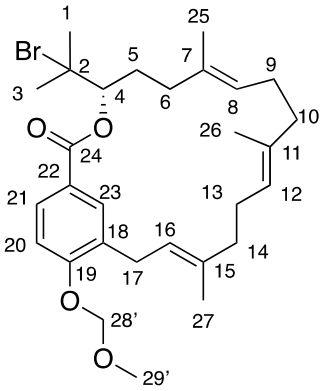
E,E,E-**19**

Using a modified procedure of Shiina *et al.*,[12] a solution of 2-methyl-6-nitrobenzoic anhydride (MNBA) (15.5 mg, 0.045 mmol, 1.30 equiv.) and DMAP (15.4 mg, 0.126 mmol, 3.6 equiv.) in toluene (50 mL) was heated to 50 °C using a heating mantle and seco acid **18** (18.5 mg, 0.035 mmol, 1.0 equiv.)) in toluene (4 mL) was added over 2 days *via* syringe pump. Additional MNBA (15.5mg, 0.045 mmol, 1.3 equiv.) and DMAP (15.4 mg, 0.126 mmol, 3.6 equiv.) were added after 10 h. After complete addition, the mixture was stirred for 3 h at 50 °C, then cooled to 0 °C and quenched with a saturated aqueous $NaHCO_3$ solution (25 mL). The mixture was concentrated and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extract was dried over Na_2SO_4 and concentrated. The residue was chromatographed (5% Et_2O in *n*-hexane) to obtain the non-polar components. Further purification by preparative thin-layer chromatography on silica gel (5% EtOAc in *n*-hexane), gave macrolide 7*E*,11*E*,15*E*-**19** (5.0 mg, 0.010 mmol, 29%) as a colourless oil. 10.14469/hpc/5791. The olefin geometry was established as *E,E,E*- by the presence of characteristic (shielded) ^{13}C NMR resonances at δ 16.5, 15.9, 15.0 ppm (for *E*-olefins) and the absence of ^{13}C NMR resonances between 22-24 ppm (for *Z*-olefins).[4] R*f* 0.43 (10% EtOAc in *n*-hexane); $[\alpha]_D^{33}$ - 48.1 (*c* 0.2, $CHCl_3$); IR (ATR, neat) 1714, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.77 (m, 2H), 6.81 (d, *J* = 8.5 Hz, 1H), 5.27 (br t, *J* = 7.3 Hz, 1H), 5.07 – 4.96 (m, 3H), 4.15 – 4.06 (m, 2H), 3.58 (dd, *J* = 15.5, 6.8 Hz, 1H), 3.15 (dd, *J* = 15.5, 8.1 Hz, 1H), 2.27 – 1.96 (m, 9H), 1.97 – 1.80 (m, 2H), 1.77 (s, 3H), 1.74 (s, 3H), 1.68 (br s, 3H), 1.50 (br s, 3H), 1.46 (t, *J* = 7.0 Hz, 3H), 1.48 – 1.43 (m, 1H), 1.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 160.3, 135.3, 135.0, 132.4, 131.7, 130.8, 128.9, 127.4, 123.5, 123.0, 122.1, 110.1, 79.5, 68.2, 63.9, 39.2, 39.0, 38.4, 31.5, 30.2, 28.6, 27.5, 26.7, 24.4, 16.5, 15.9, 15.0, 14.9; HRMS (ES^+) calcd for $C_{29}H_{42}O_3{}^{79}Br$ $[M + H]^+$ 517.2317, found 517.2330.

Comparison of ^{1}H and ^{13}C NMR shifts of *E,E,E*-19 (P = Et; this work) vs *E,E,E*-19 (P = MOM).[11]



E,E,E-**19** (P = Et)



E,E,E-**19** (P = MOM)[11]

Table 1. ^{1}H NMR data comparison between macrolide *E,E,E*-**19** (P = Et) and Krauss' macrolide **19** (P = MOM).[11]

19 (P = MOM)[11] ∂ / ppm	*E,E,E*-**19** (P = Et) ∂ / ppm	Assignment	^{1}H Δ∂ / ppm
7.87-7.78	7.86 – 7.77	21, 23	0.01[a]
7.06	6.81	20	0.25
5.28	5.27	16	0.01
5.08-4.95	5.07 – 4.96	4, 8, 12	0.00[a]
-	4.15 – 4.06	28	-
3.58	3.58	17α	0.00
3.50	-	29'	-
3.18	3.15	17β	0.03
2.32-1.90	2.27 – 1.96	CH_2 (multiple)	-0.01[a]
1.90-1.70	1.97 – 1.80	CH_2	-0.09[a]
1.76	1.77	1/3	-0.01
1.73	1.74	1/3	-0.01
1.68	1.68	27	0.00
1.50	1.50	25/26	0.00
1.52-1.43	1.48-1.43	CH_2/29	0.02[a]
1.40	1.40	25/26	0.00
		Average Δ∂:	0.02 ppm
		Root-mean-square deviation:	0.1 ppm

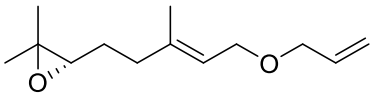
[a] Based on the centre of the multiplet range.

Table 2. ^{13}C NMR data comparison between macrolide *E,E,E*-**19** (P = Et) and Krauss' macrolide **19** (P = MOM).[11]

19 (P = MOM)[11] ∂ / ppm	*E,E,E*-**19** (P = Et) ∂ / ppm	Assignment	^{13}C $\Delta\partial$ / ppm
165.3	165.5	24	0.2
158.5	160.3	19	1.8
135.4	135.3	22	-0.1
135.2	135.0	15	-0.3
132.4	132.4	7/11	0.0
131.9	131.7	23	-0.2
131.3	130.8	7/11	-0.5
128.8	128.9	21	0.1
127.3	127.4	8/12	0.1
123.4	123.5	16	0.1
123.3	123.0	8/12	-0.3
122.9	122.1	18	-0.8
112.8	110.1	20	-2.7
94.2	-	28'	-
79.6	79.5	4	-0.1
68.0	68.2	2	0.2
-	63.9	28	-
56.5	-	29'	-
39.2	39.2	*C*H_2	0.0
39.0	39.0	*C*H_2	0.0
38.4	38.4	*C*H_2	0.0
31.4	31.5	1/3	0.1
30.1	30.2	1/3	0.1
28.5	28.6	*C*H_2	0.1
27.6	27.5	*C*H_2	-0.1
26.6	26.7	*C*H_2	0.0
24.4	24.4	*C*H_2	0.0
16.5	16.5	25/26/27	0.0
15.8	15.9	25/26/27	0.0
-	15.0	29	-
14.9	14.9	25/26/27	0.0
		Average $\Delta\partial$:	-0.1 ppm
		Root-mean-square deviation:	0.7 ppm

Copies of ^{1}H and ^{13}C NMR spectra

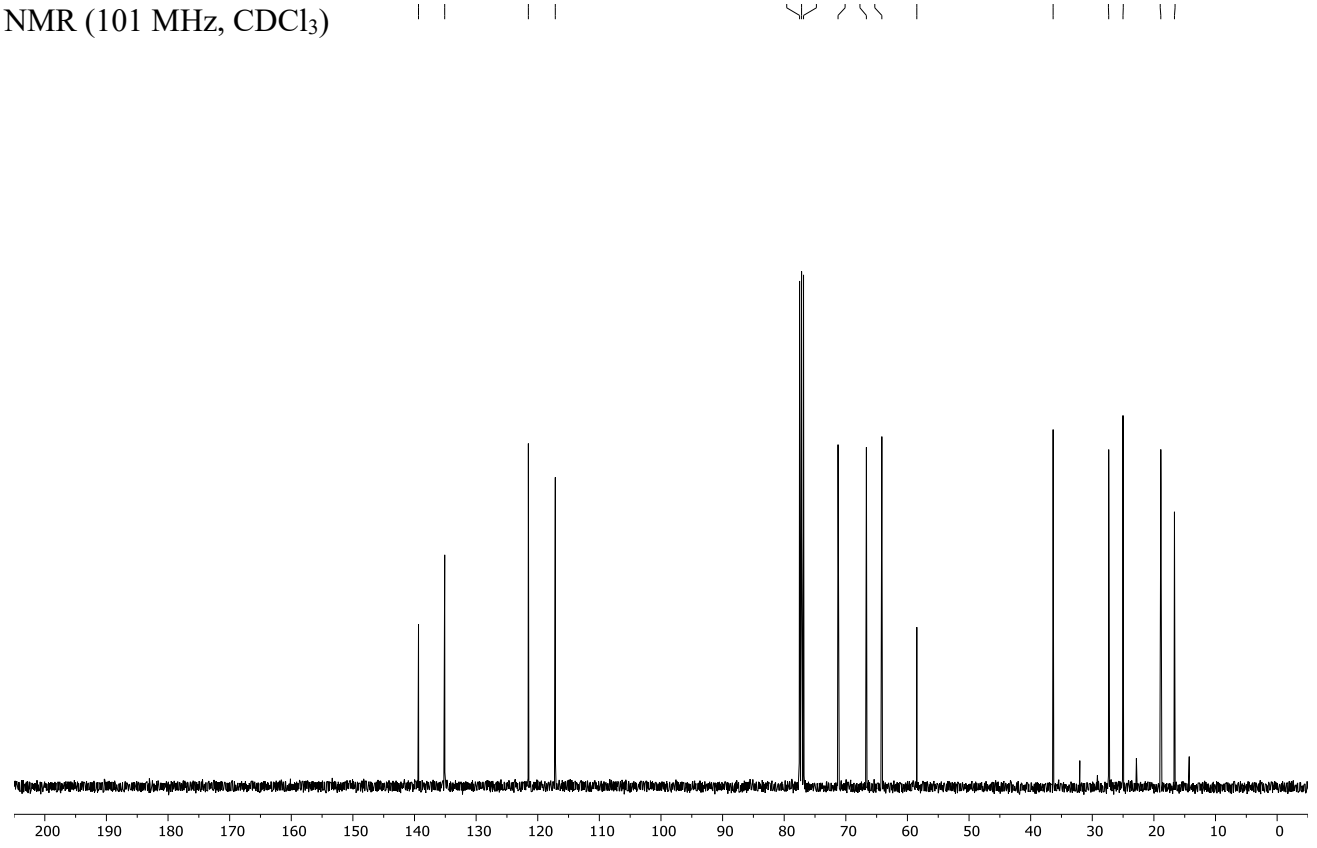
*(S,E)-3-(5-(Allyloxy)-3-methylpent-3-en-1-yl)-2,2-dimethyloxirane (**2**)*



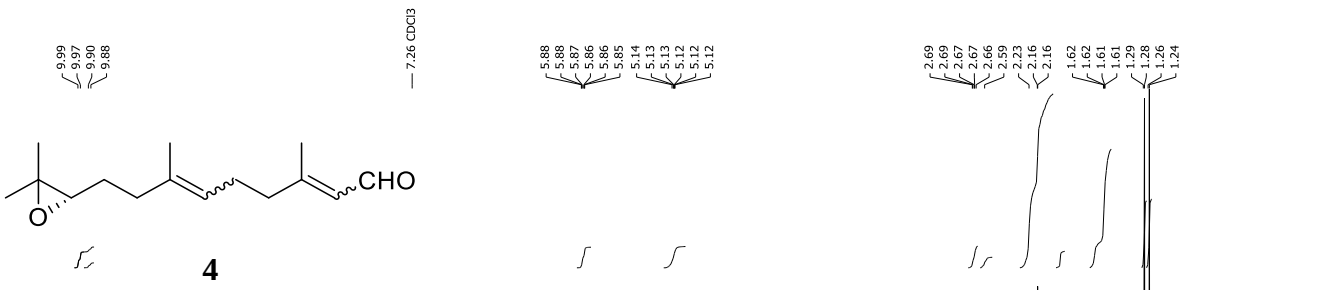
2

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

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



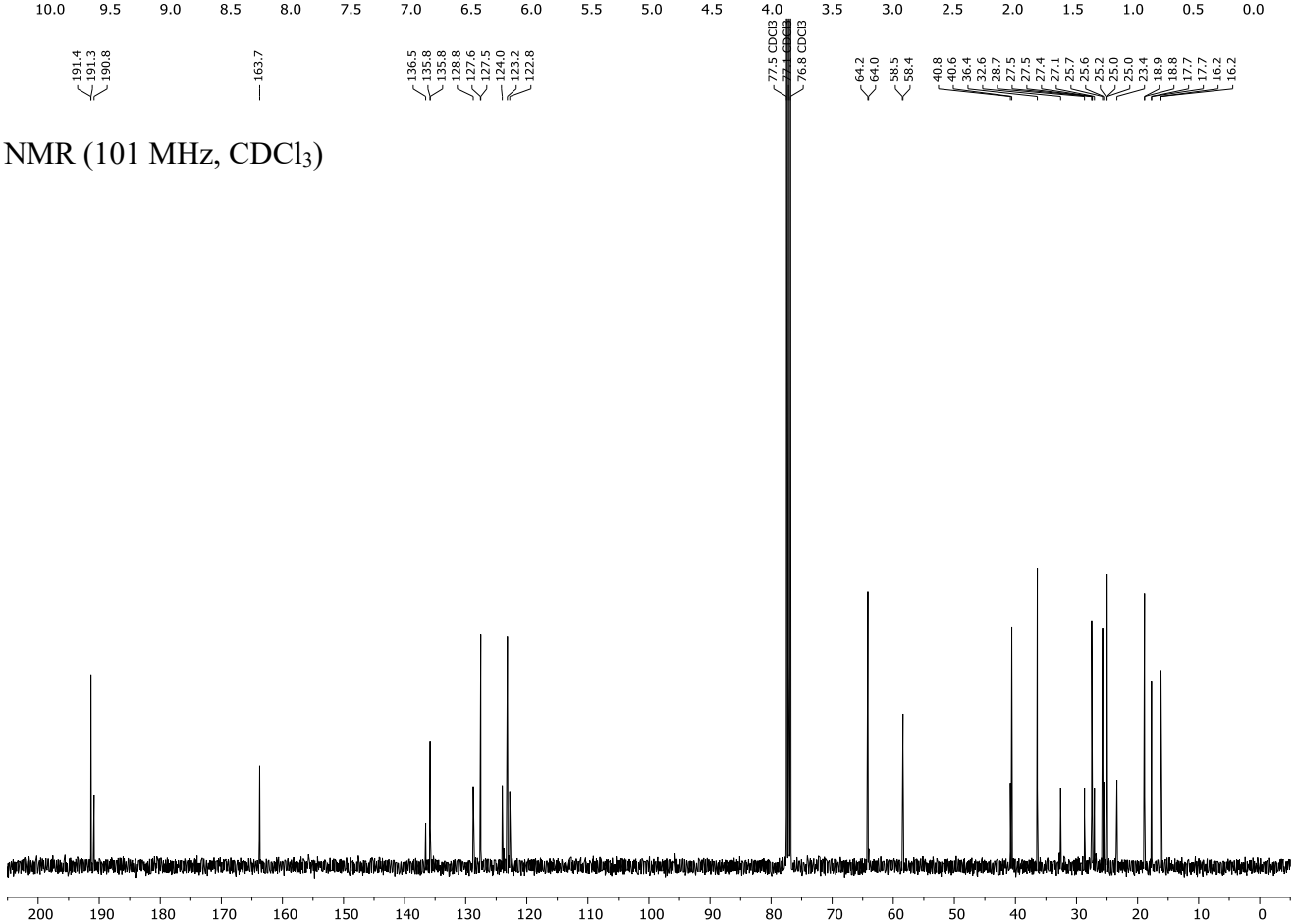
*(S)-9-(3,3-Dimethyloxiran-2-yl)-3,7-dimethylnona-2,6-dienal (**4**)*[3]



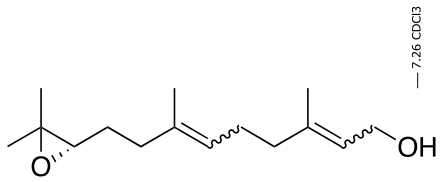
4

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

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



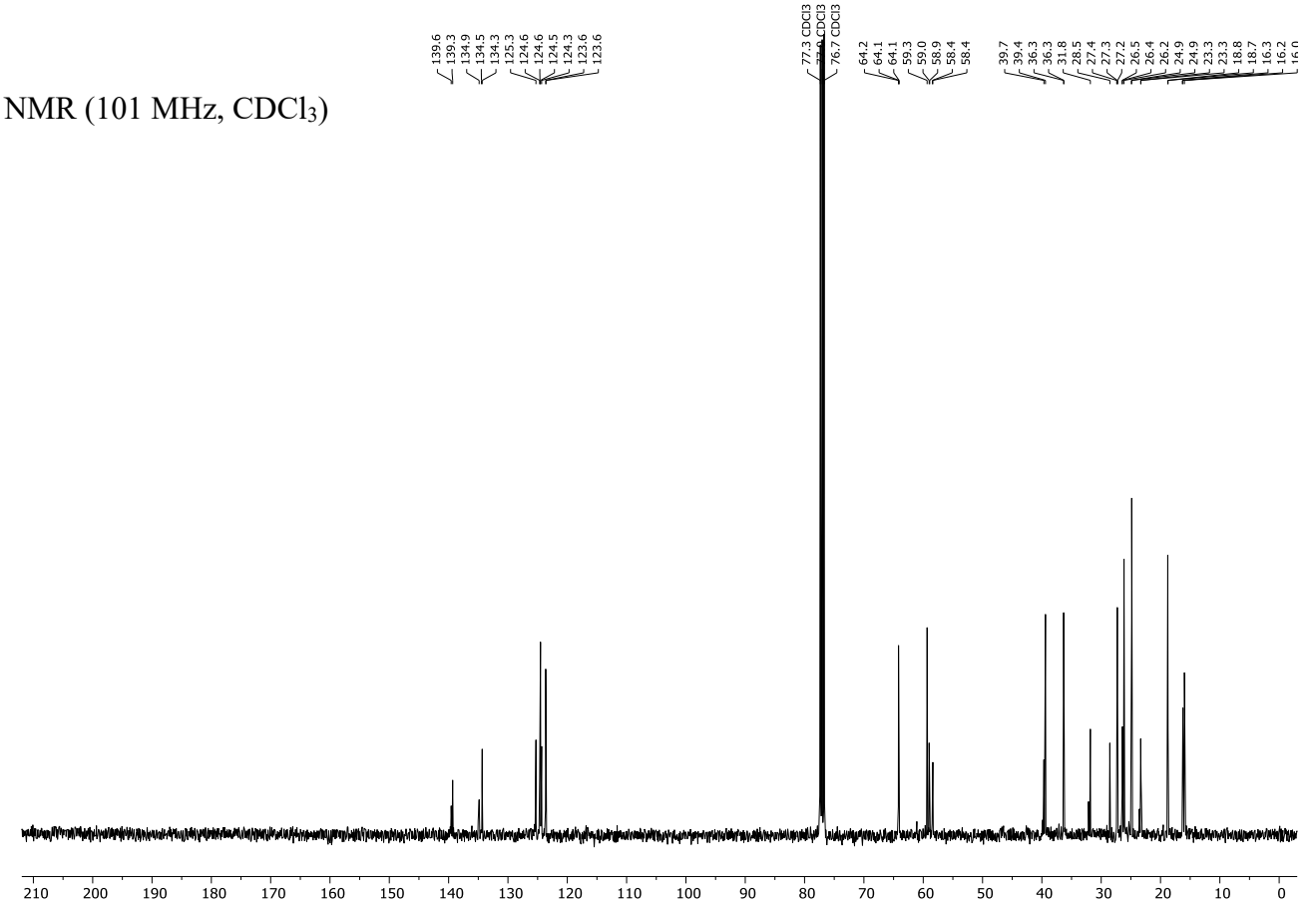
(S)-9-(3,3-Dimethyloxiran-2-yl)-3,7-dimethylnona-2,6-dien-1-ol (7)



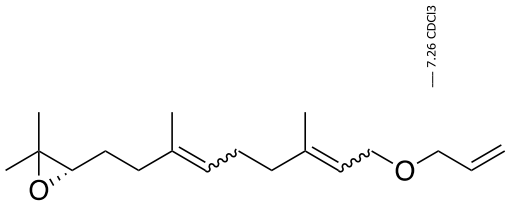
7

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

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



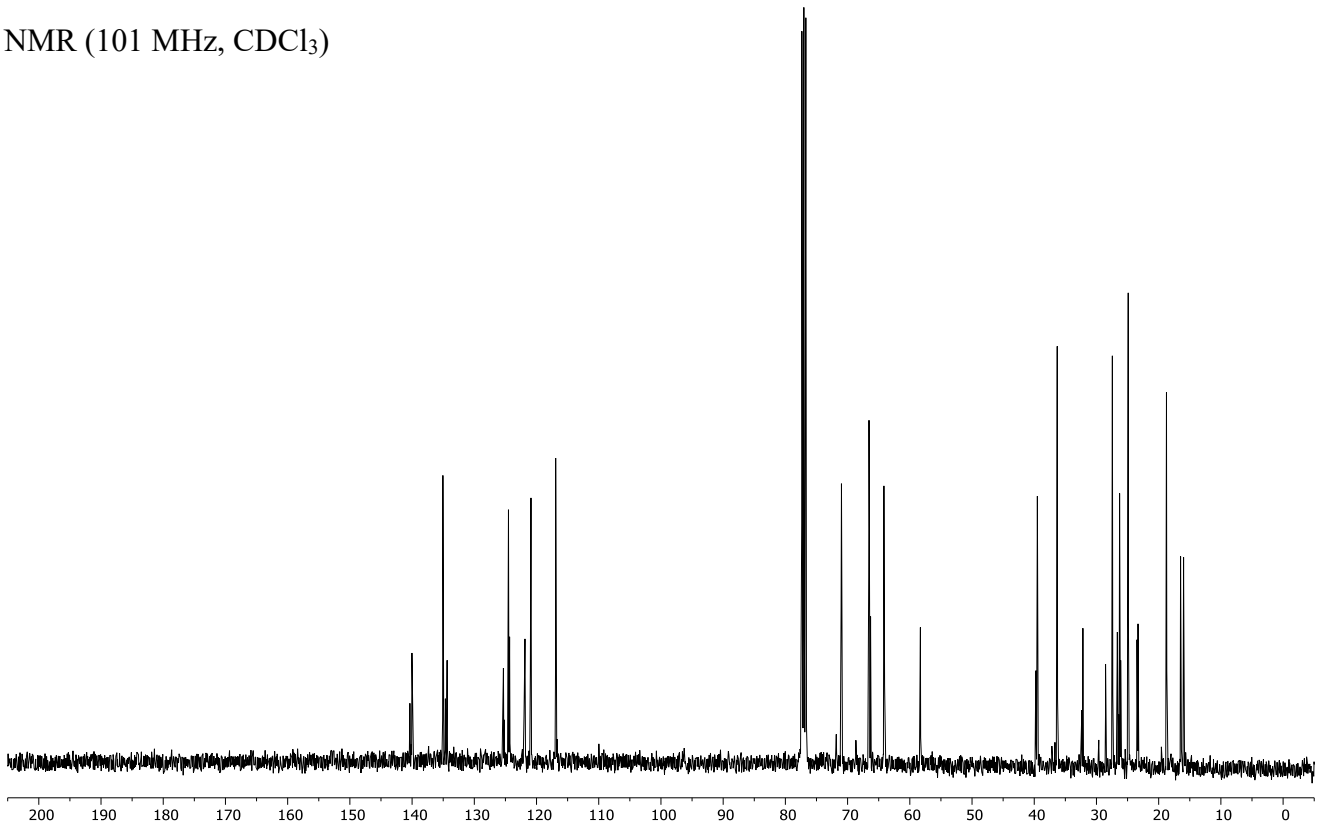
*(S)-3-(9-(Allyloxy)-3,7-dimethylnona-3,7-dien-1-yl)-2,2-dimethyloxirane (**8**)*



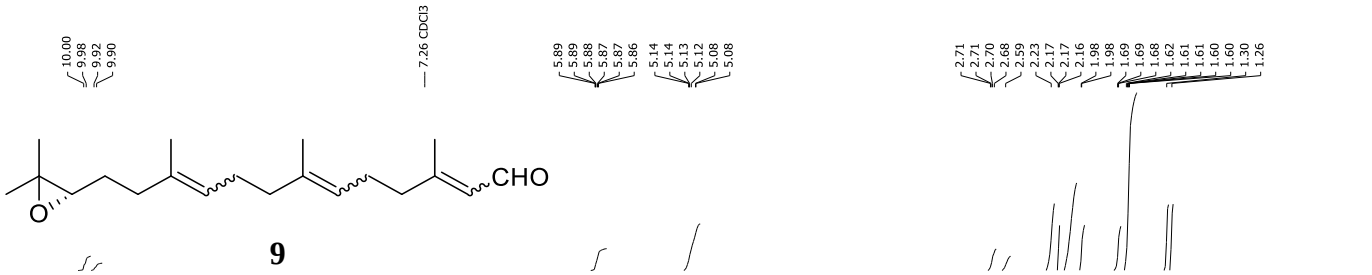
8

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

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

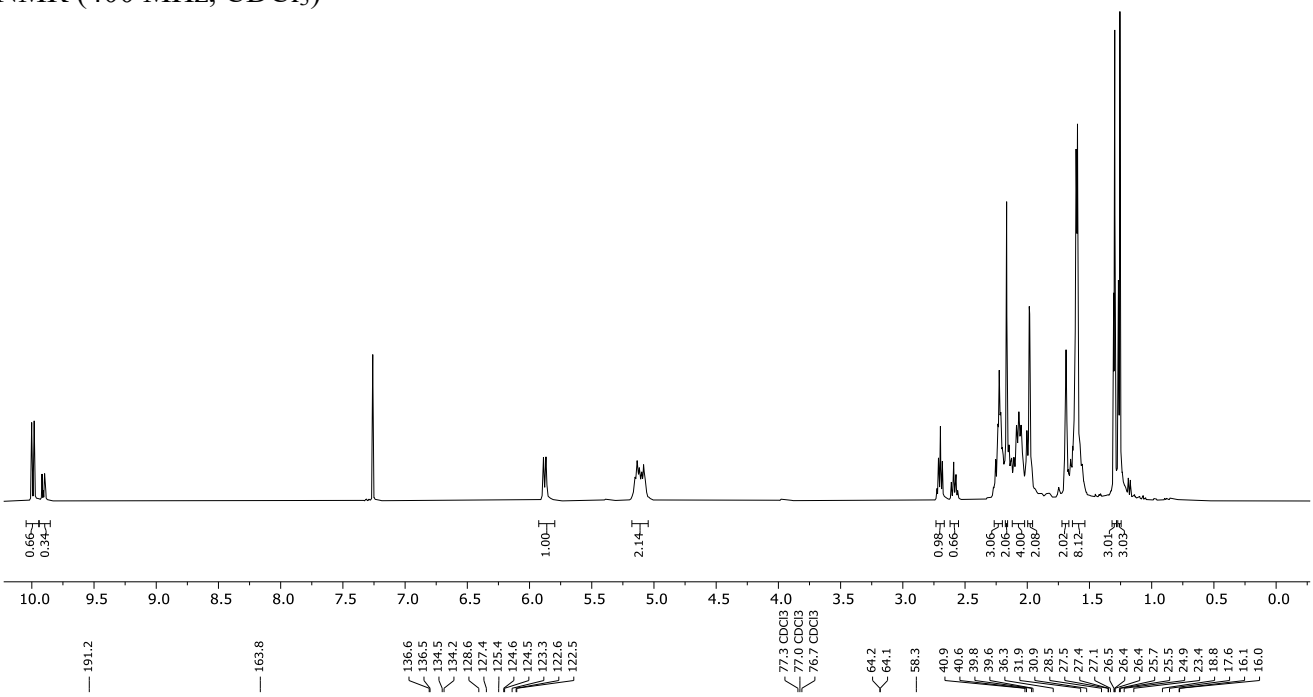


*(S)-13-(3,3-Dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trienal (**9**)*[7]

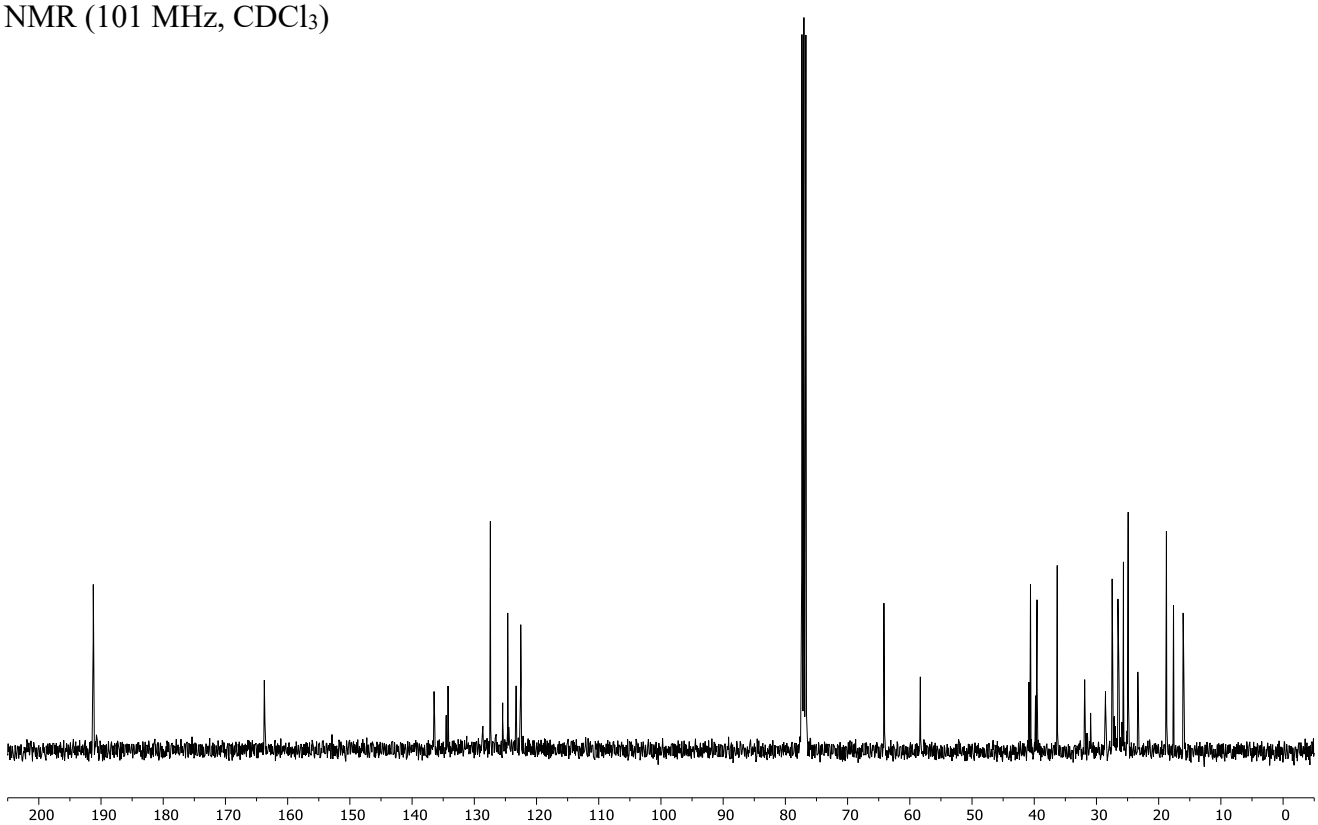


9

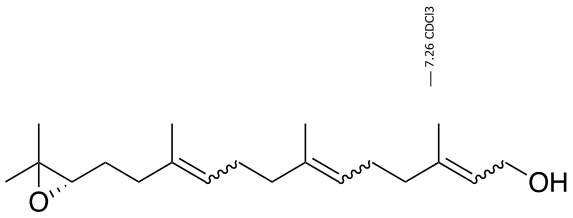
^{1}H NMR (400 MHz, $CDCl_3$)



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



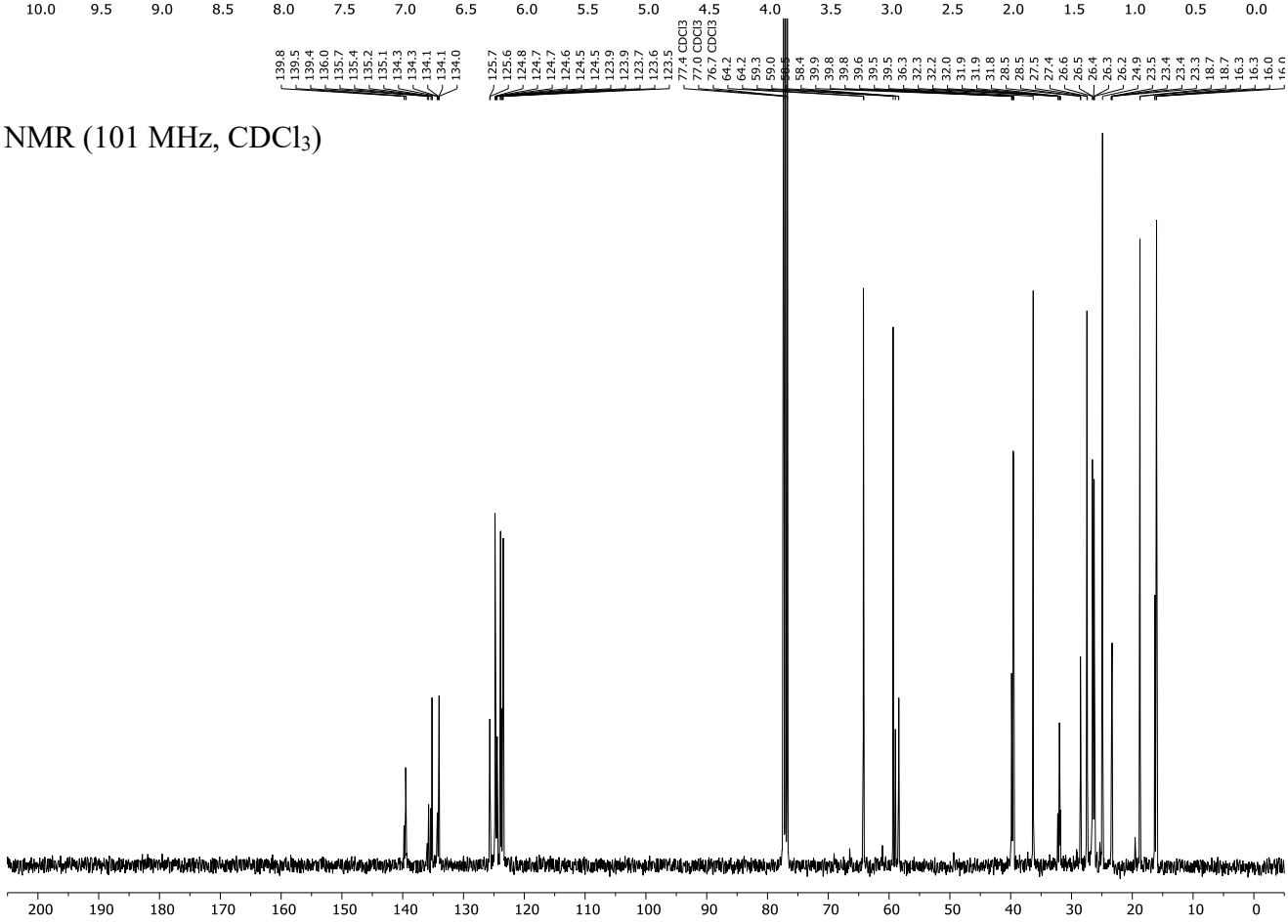
*(S)-13-(3,3-Dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trien-1-ol (**10**)*[8]



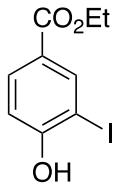
10

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

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



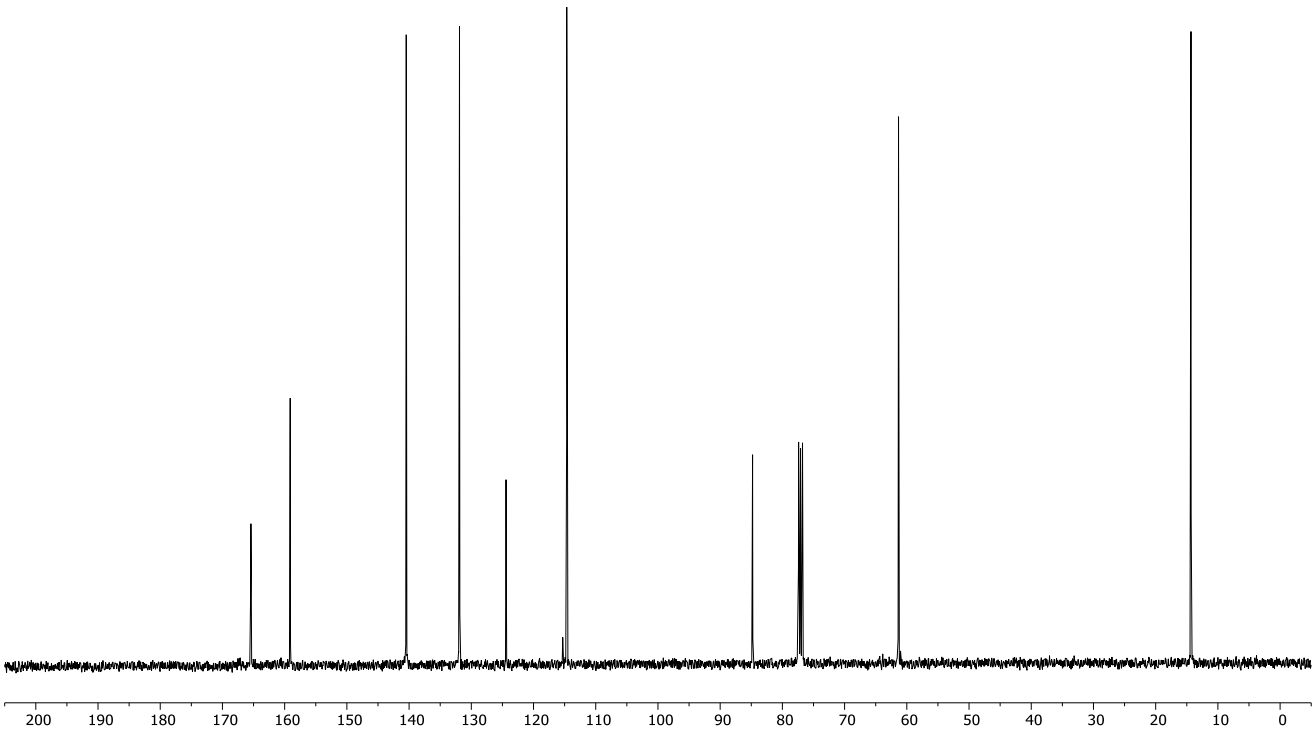
*Ethyl 4-hydroxy-3-iodobenzoate (**12**)*[9]



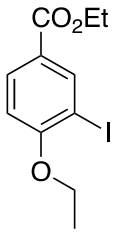
12

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

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



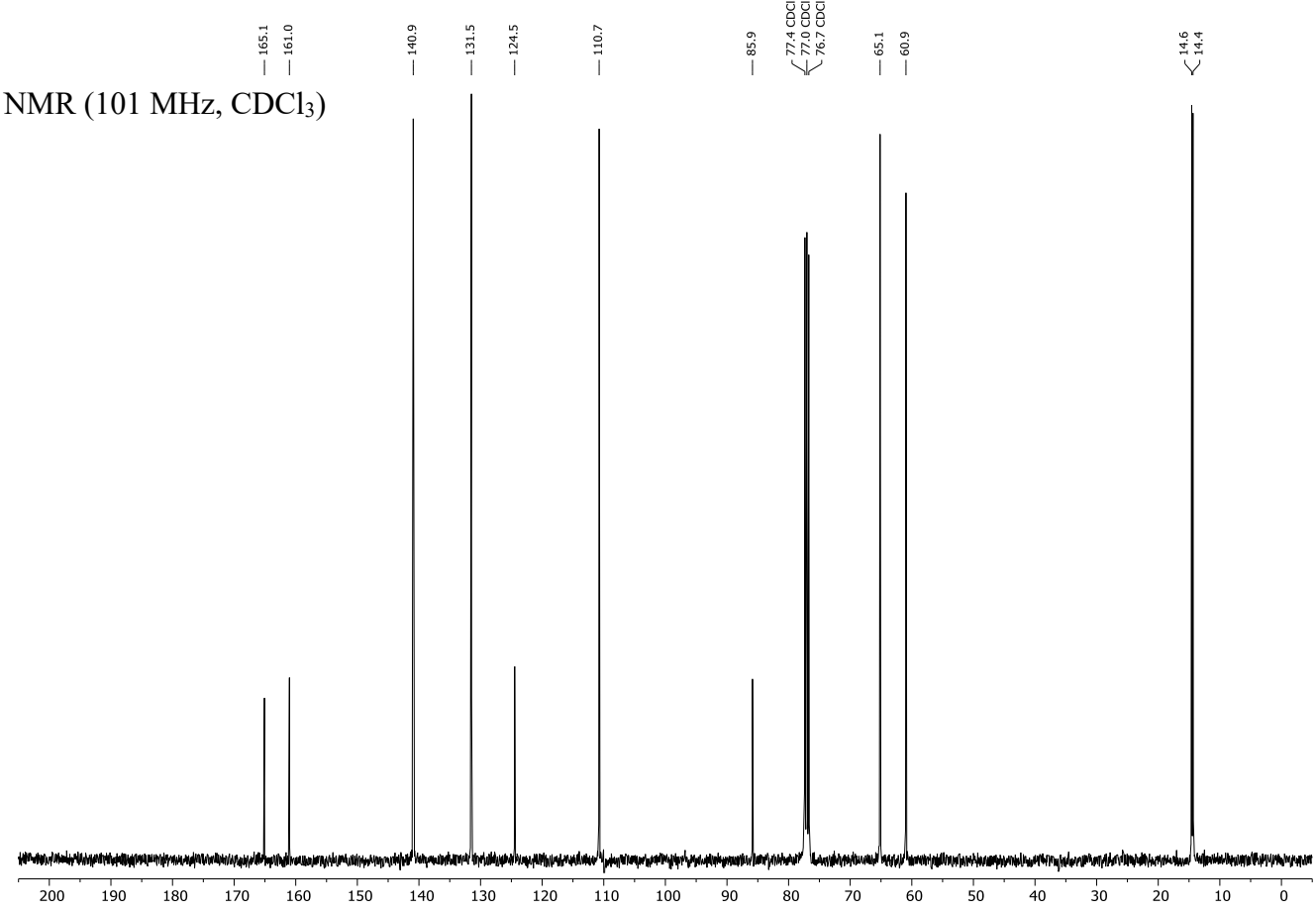
Ethyl 4-ethoxy-3-iodobenzoate ***(13)***



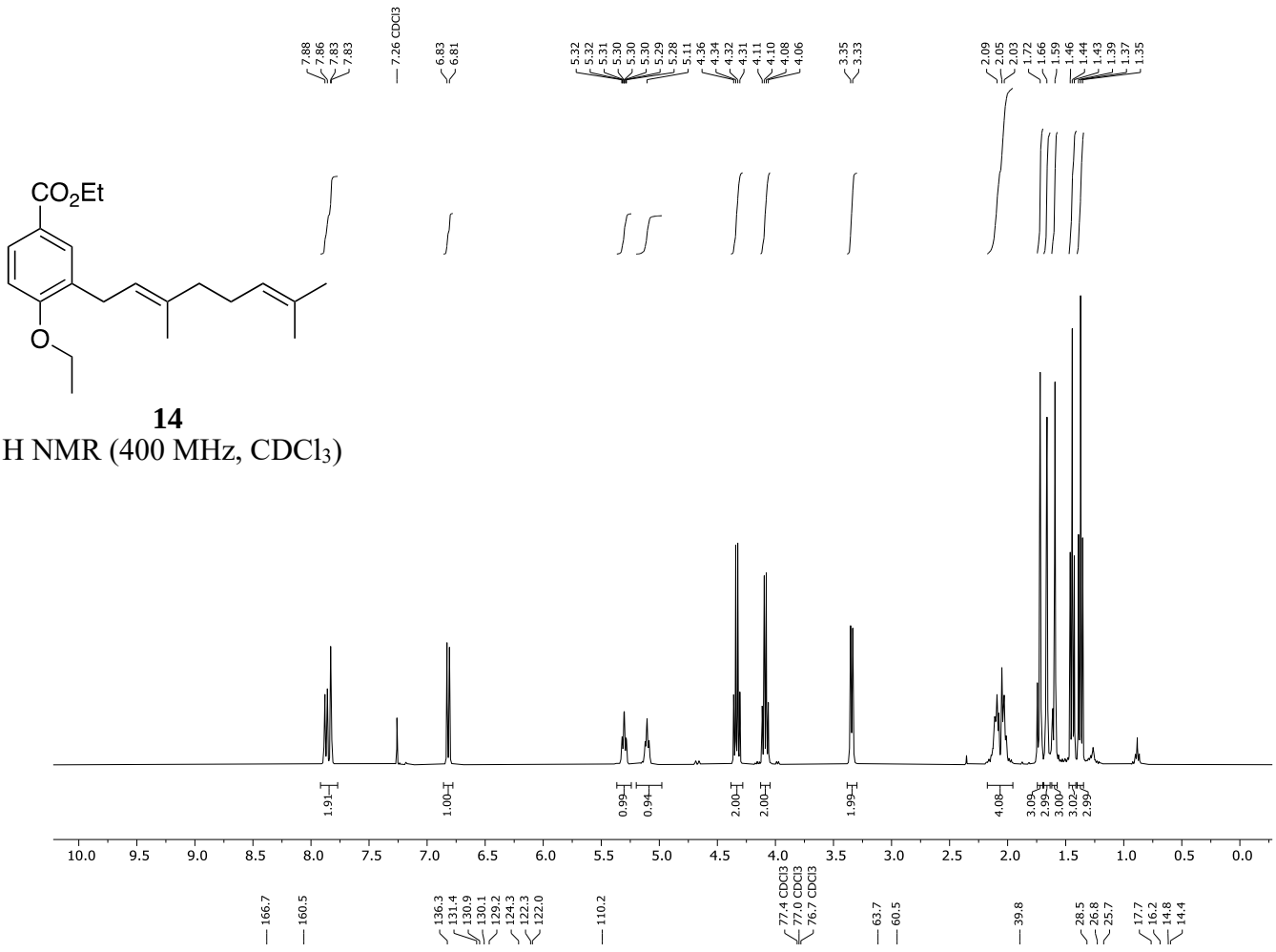
13

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

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



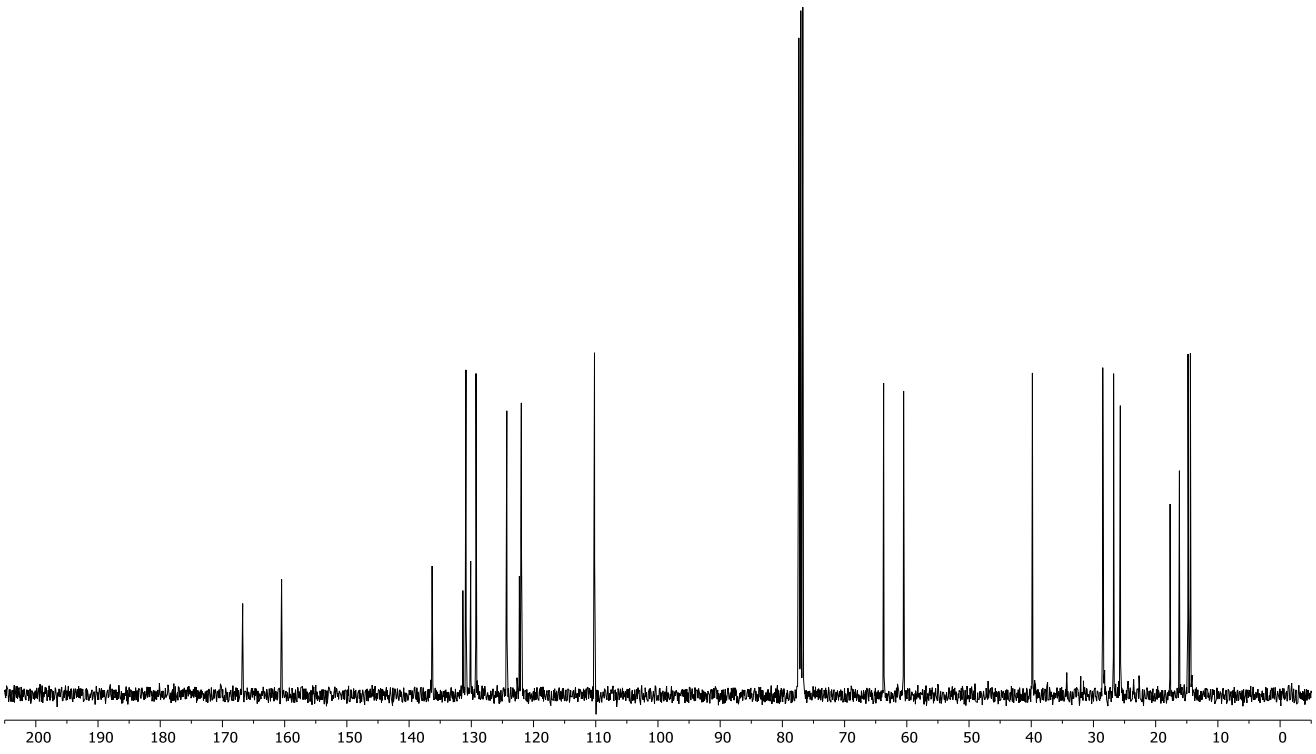
*Ethyl (E)-3-(3,7-dimethylocta-2,6-dien-1-yl)-4-ethoxybenzoate (**14**)*



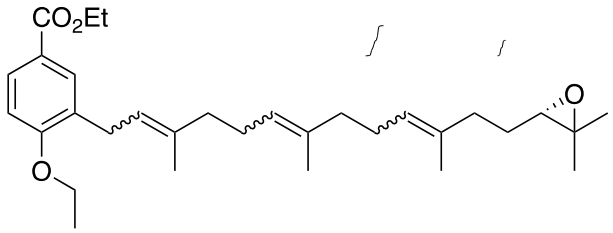
14

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

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



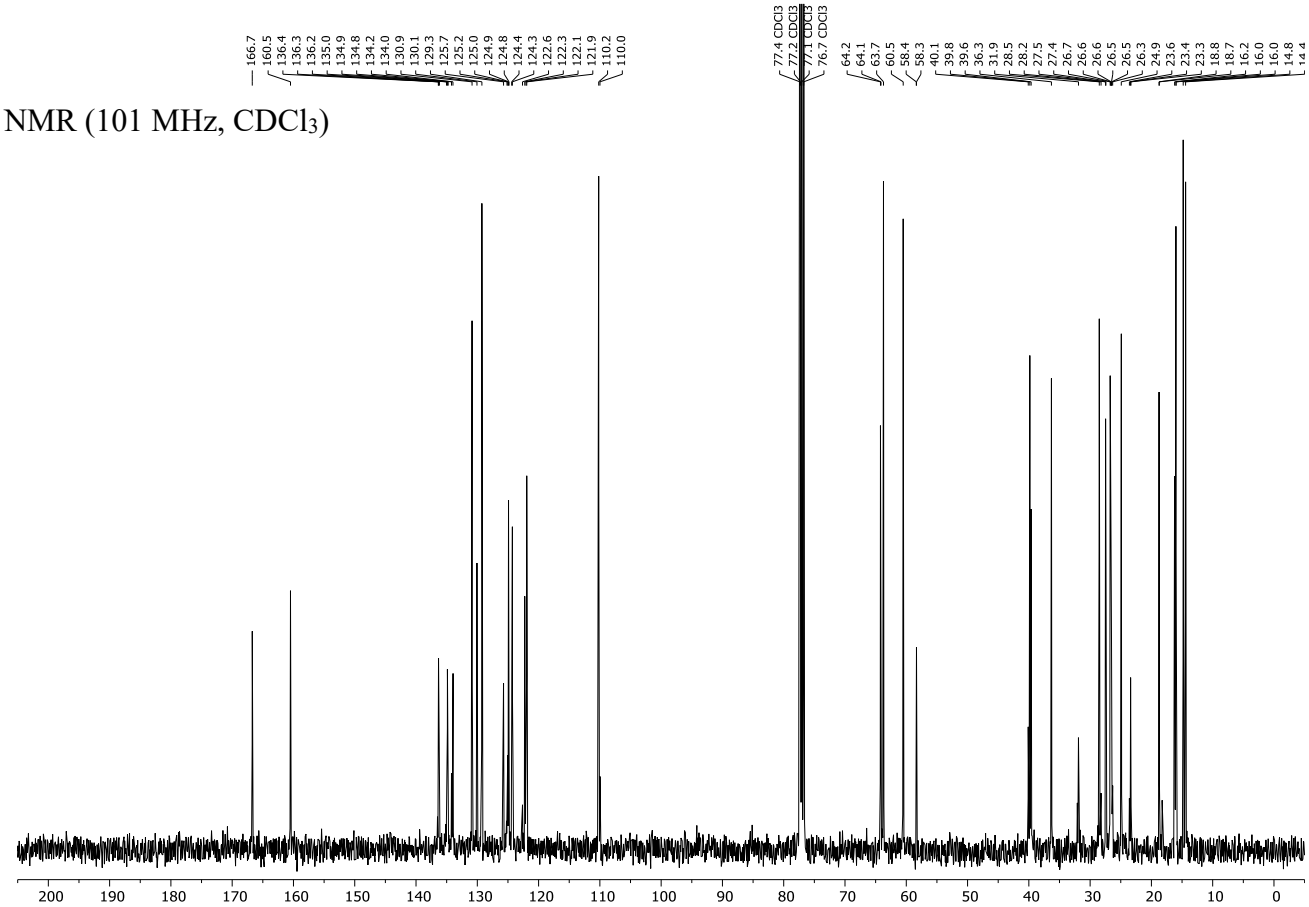
*Ethyl (S)-3-(13-(3,3-dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trien-1-yl)-4-ethoxybenzoate (**16**)*



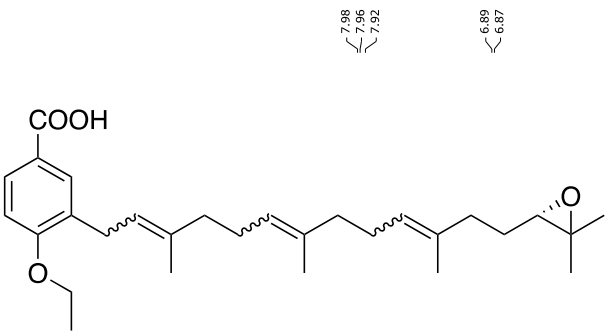
16

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

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



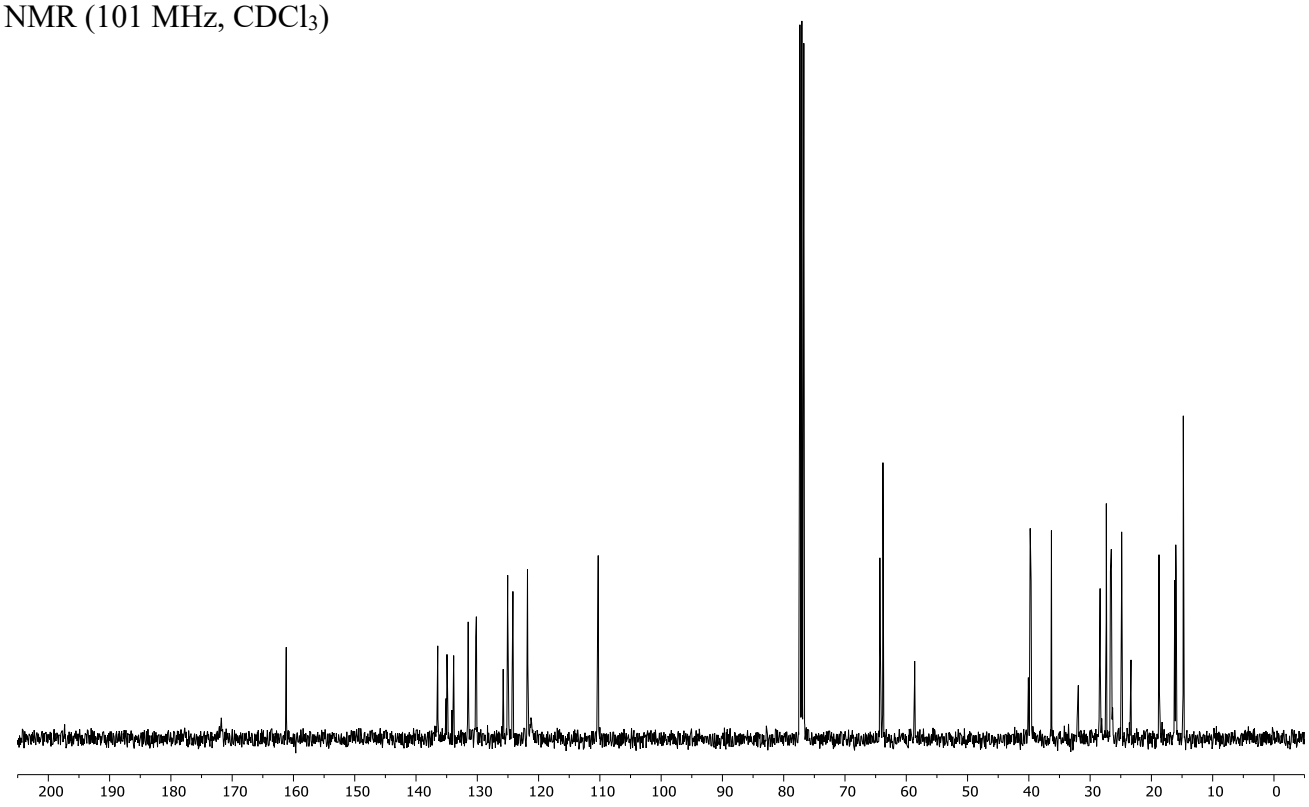
*(S)-3-(13-(3,3-Dimethyloxiran-2-yl)-3,7,11-trimethyltrideca-2,6,10-trien-1-yl)-4-ethoxybenzoic acid (**17**)*



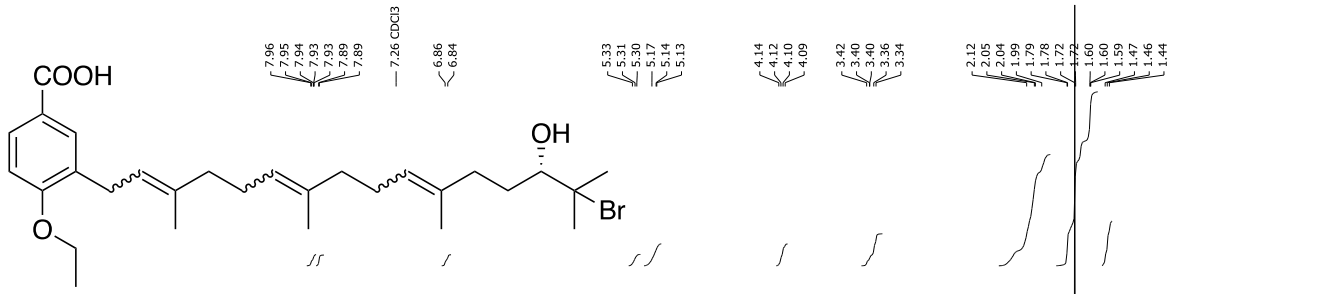
17

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

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



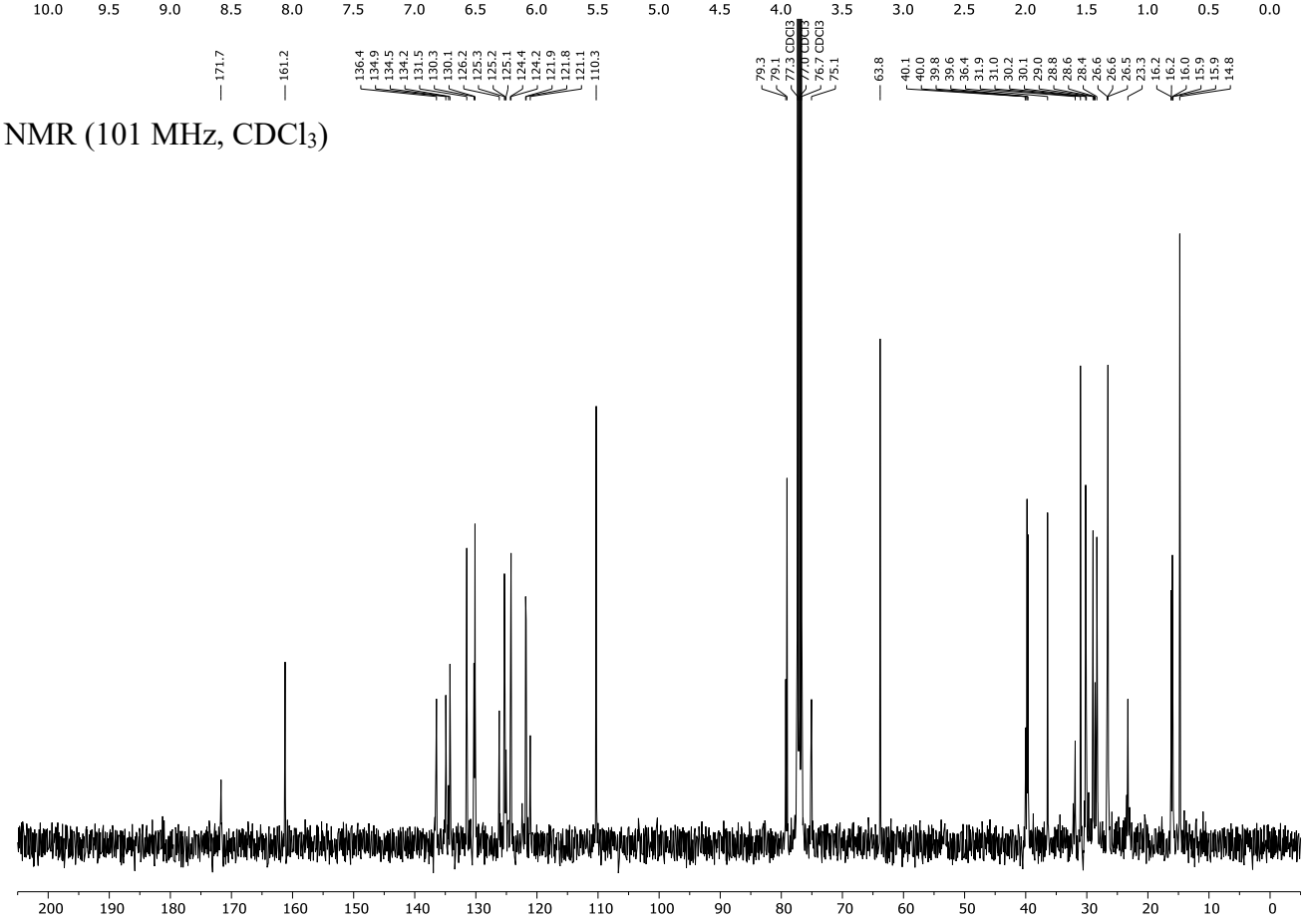
*(S)-3-(15-Bromo-14-hydroxy-3,7,11,15-tetramethylhexadeca-2,6,10-trien-1-yl)-4-ethoxybenzoic acid (**18**)*



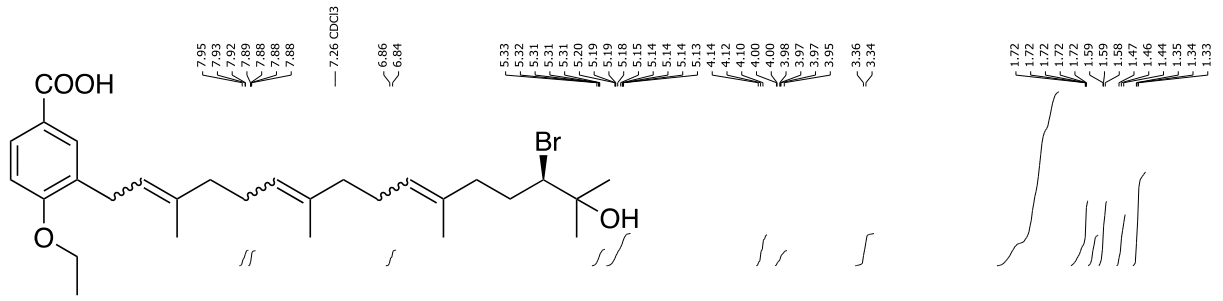
18

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

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

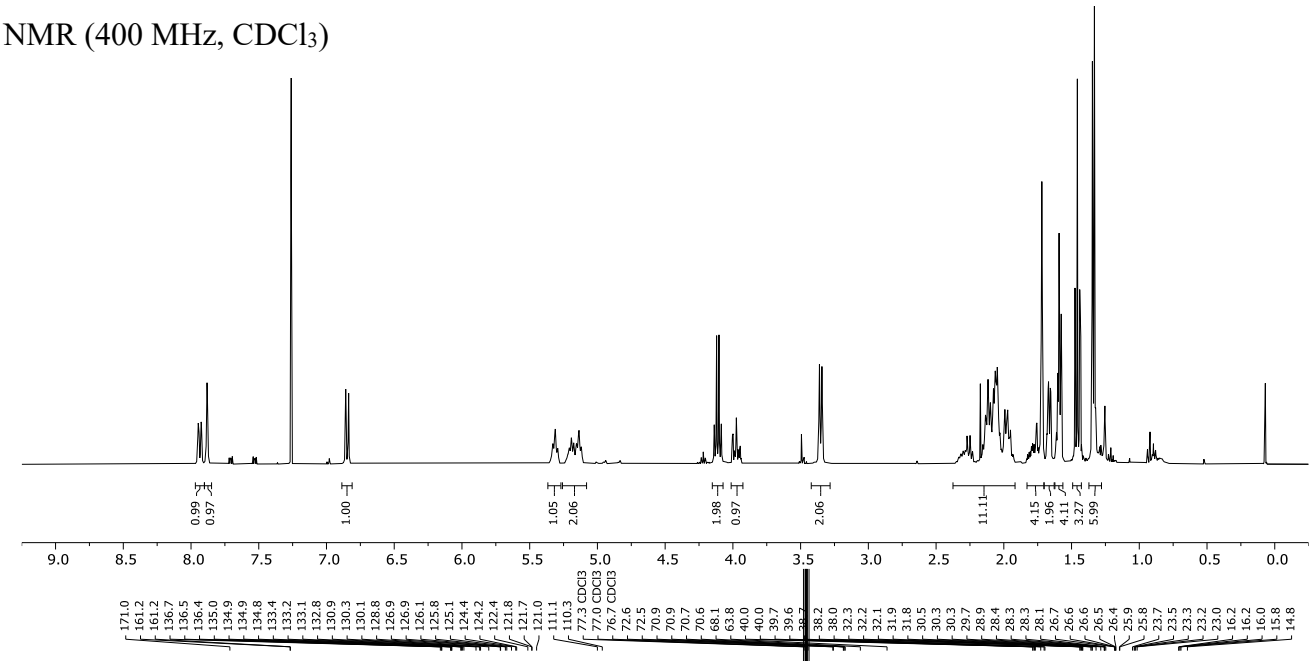


*(R)-3-(14-bromo-15-hydroxy-3,7,11,15-tetramethylhexadeca-2,6,10-trien-1-yl)-4-ethoxybenzoic acid (**18a**)*

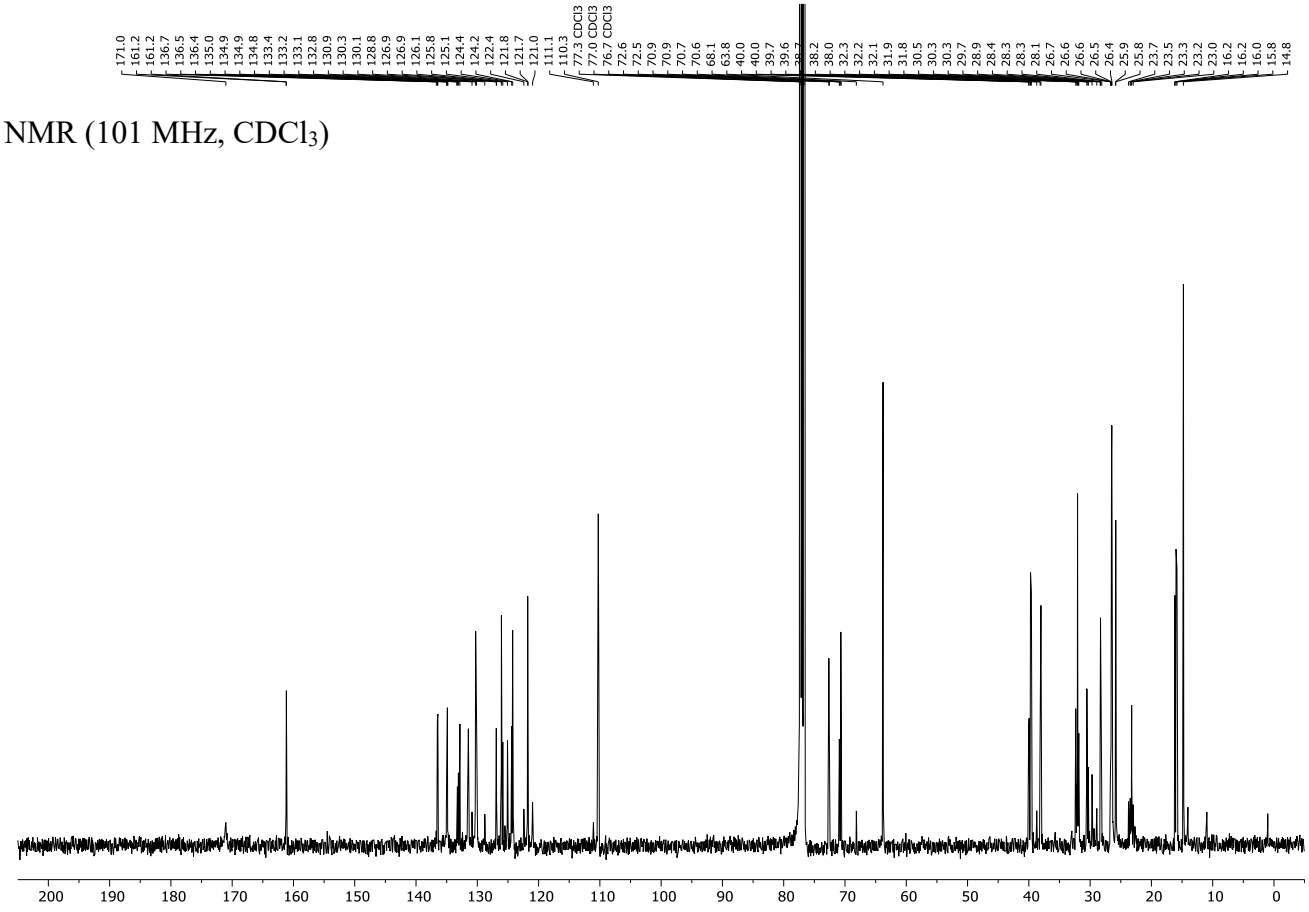


18a

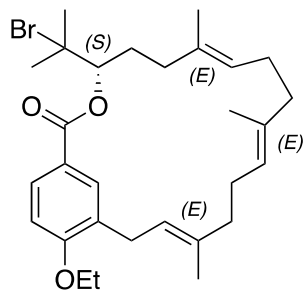
^{1}H NMR (400 MHz, $CDCl_3$)



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



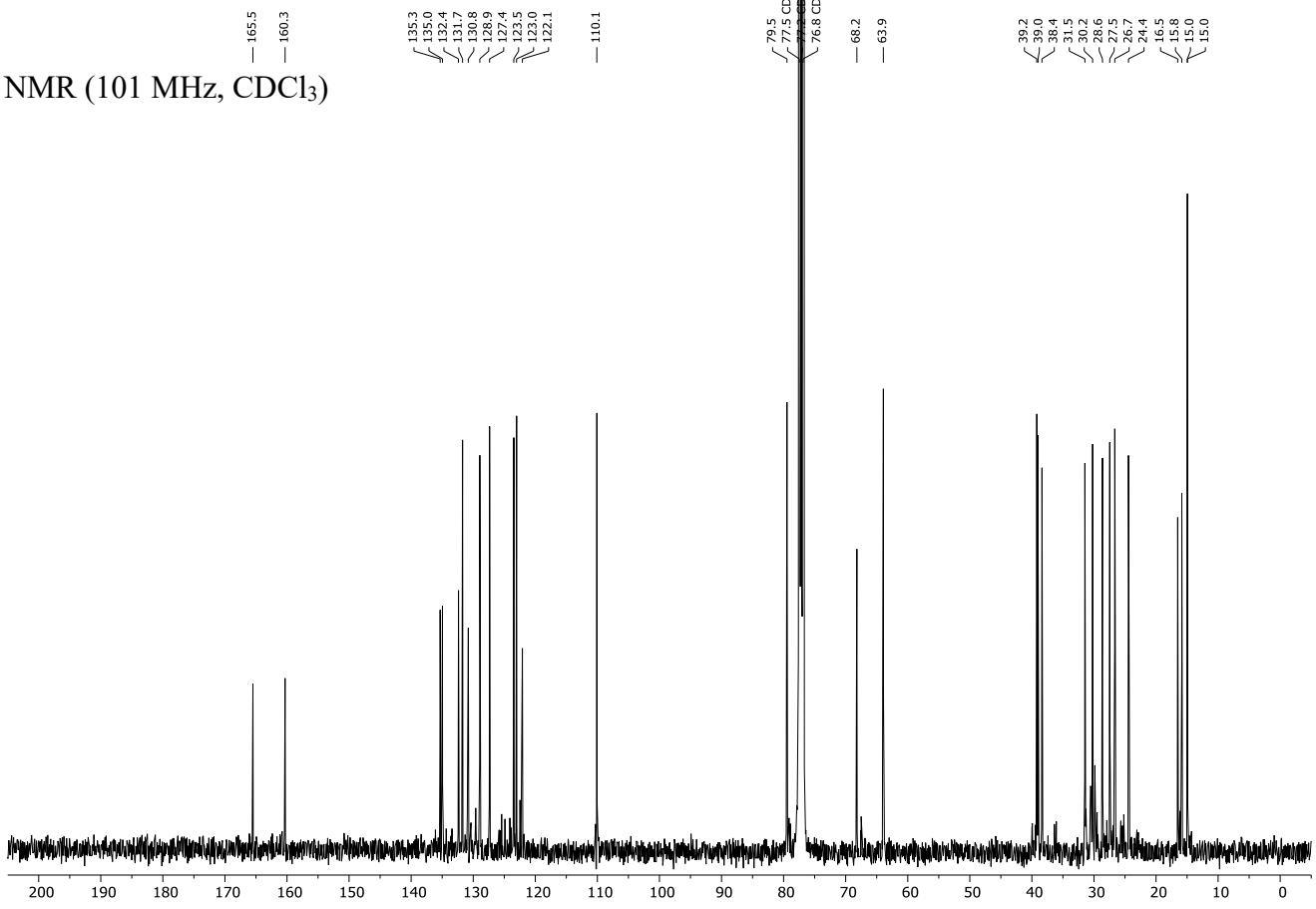
*(S,7E,11E,15E)-4-(2-Bromopropan-2-yl)-1⁴-ethoxy-7,11,15-trimethyl-3-oxa-1(1,3)-benzenacycloheptadecaphane-7,11,15-trien-2-one (E,E,E-**19**)*



E,E,E-**19**

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

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



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