Supporting Information

A Pot-Economical Approach to the Total synthesis of Sch-725674

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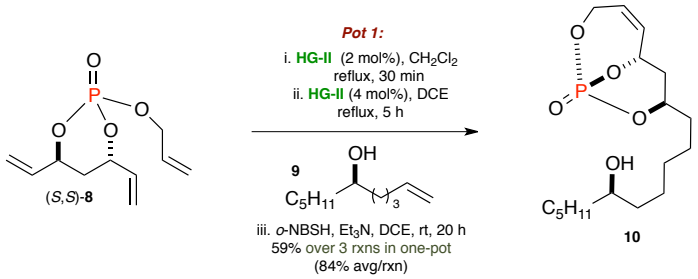
General Experimental Methods

Unless otherwise stated, all the reagents were purchased from commercial sources and were used without additional purification. All reactions were performed under an inert atmosphere unless noted otherwise. Stirring was achieved with oven-dried magnetic stir bars. THF and CH_2Cl_2 were purified by passage through the Solv-Tek purification system employing activated Al_2O_3 (Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification *Organometallics* **1996**, *15*, 1518–1520). $CHCl_3$ was passed through basic alumina and dried over molecular sieves. Et_3N was purified by passage through basic alumina or distilled over CaH_2 and stored over KOH. All the solvents for routine isolation of products and chromatography were reagent grade. Flash chromatography was performed using silica gel (300−400 mesh) with the indicated solvents. Melting points were recorded on an Electrothermal digital melting point apparatus and were uncorrected. IR spectra were recorded on a spectrophotometer using either neat or KBr optics. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 or 500 MHz (1H NMR) and 100 or 126 MHz (^{13}C NMR) spectrometers using $CDCl_3$ or Methanol-d_4 as the solvents and TMS as the internal standard. The ^{1}H NMR data are reported as the chemical shift in parts per million, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet), coupling constant in hertz, and number of protons. High-resolution mass spectra were obtained using a high-resolution ESI-TOF mass spectrometer.

Experimental Procedures and Characterization Data:

One-pot RCM, CM, chemoselective hydrogenation sequential protocol to **(6*S*,8*R*)-8-((*R*)-6-hydroxyundecyl)-2,9,10-trioxa-1-phosphabicyclo[4.3.1]dec-4-ene-1-oxide (10):**



To a stirred solution of (*S*,*S*)-triene **8**[1] (2.0 g, 8.69 mmoL) in a freshly distilled, freeze-degas-thawed CH_2Cl_2 (1.08 L, 0.008 M) was added Hoveyda-Grubbs 2nd Gen. catalyst (HG-**II**) (108 mg, 0.17 mmol, 2 mmol%) and the reaction was heated to reflux for 30 min. After completion of RCM, CH_2Cl_2 was completely removed under reduced pressure. Next, freshly distilled, freeze-degas-thawed 1,2-dichloroethane (DCE) (174 mL, 0.05 M) was added to the crude RCM product. The cross partner **9**[2] (1.77 g, 10.4 mmol) and HG-**II** (216 mg, 0.34 mmol, 4 mmol%) were introduced under argon atmosphere. The reaction was refluxed for an additional 5 h until completion of the CM reaction (monitored by TLC). The reflux was stopped, and *o*-nitrobenzenesulfonyl hydrazine (*o*-NBSH) (18.86 g, 86.9 mmol) and Et_3N (37.7 mL, at 2 mL/g of *o*-NBSH) were added at room temperature and the reaction was stirred for about 12 h. Next, excess *o*-NBSH (9.43 g, 43.45 mmol) and Et_3N (18.8 mL, at 2 mL/g of *o*-NBSH) were added. The reaction was stirred for an additional 8 h at the same temperature until the crude NMR showed the absence of starting material (CM product). A saturated solution of $NaHCO_3$ (50 mL) was added to the reaction mixture and diluted with excess EtOAc (400 mL). The organic layer was separated and aqueous phase was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with brine (80 mL), dried (Na_2SO_4), concentrated under reduced pressure, and subjected to flash chromatography (25% EtOAc/CH_2Cl_2) to provide phosphate **10** as a brownish semi solid (1.77 g, 59% over 3 rxns in one-pot, 84% avg/rxn).

Optical Rotation: $[\alpha]_D^{23}$ +58.0 (*c* 0.25, $CHCl_3$);

FTIR (neat)**:** 3405, 2929, 2856, 1463, 1292, 1101, 1070, 975, 877 cm^{-1};

^{1}H NMR (400 MHz, Chloroform-*d*)**:** δ 6.07–5.99 [m, 1H, -C<u>H</u>=CHCH$_2$OP(O)-], 5.59 [dt, *J* = 11.9, 3.5 Hz, 1H, -CH=C<u>H</u>CH$_2$OP(O)-], 5.18 [d, *J* = 24.0 Hz, 1H, -CH$_2$C<u>H</u>P(O)CH=CH-], 5.00 [ddd, *J* = 15.0, 6.1, 3.1 Hz, 1H, -CH$_2$CH$_2$C<u>H</u>OP(O)CH$_2$], 4.61–5.51 [m, 1H, -CH=CHC<u>H$_a$</u>H$_b$OP(O)-], 4.36 [ddd, *J* = 27.6, 14.9, 6.7 Hz, 1H, 1H, -CH=CHCH$_a$<u>H$_b$</u>OP(O)-], 3.62–3.53 [m, 1H, -CH$_2$C<u>H</u>(OH)CH$_2$], 2.17 [ddd, *J* = 18.1, 11.9, 6.0 Hz, 1H, -CHOP(O)C<u>H$_a$</u>H$_b$CHOP(O)-], 1.82–1.65 [m, 2H, -C<u>H$_a$</u>H$_b$CHOP(O)CH$_a$<u>H$_b$</u>CHOP(O)-], 1.64–1.19 [m, 17H, aliphatic protons and -CH$_a$<u>H$_b$</u>CHOP(O)CH$_a$H$_b$CHOP(O)-], 0.89 [t, *J* = 6.8 Hz, 3H, C<u>H$_3$</u>];

^{13}C NMR (126 MHz, Chloroform-*d*)**:** δ 129.9, 127.9, 76.7, 71.9, 62.94, 62.89, 37.5, 37.2, 35.6, 34.8, 31.9, 29.2, 25.4, 25.3, 24.5, 22.6, 14.0;

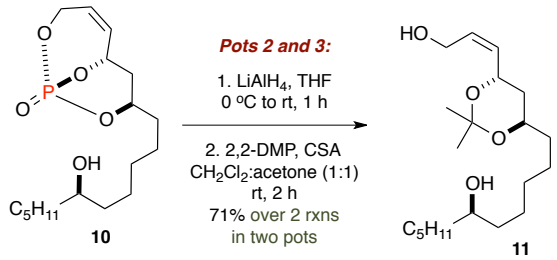
^{31}P NMR (162 MHz, Chloroform-*d*)**:** δ -3.72;

HRMS: calculated for $C_{17}H_{31}NaO_5P$ $(M+Na)^+$ 369.1807; found 369.1825 (TOF MS ES+).

(1) For the preparation of (*S,S*)-**8**, see: (a) Whitehead, A.; McReynolds, M. D.; Moore, J. D.; Hanson, P. R. *Org. Lett.* **2005**, *7*, 3375−3378. (b) Thomas, C. D.; McParland, J. M.; Hanson, P. R. *Eur. J. Org. Chem.* **2009**, 5487−5500. (c) Venukadasula, P. K. M.; Chegondi, R.; Maitra, S.; Hanson, P. R. *Org. Lett.* **2010**, *12*, 1556−1559.

(2) For the preparation of **9**, see: Kubizna, P.; Špánik, I.; Kožíšek, J.; Szolcsányi, P. *Tetrahedron* **2010**, *66*, 2351–2355.

(*R*)-1-((4*R*,6*S*)-6-((*Z*)-3-Hydroxyprop-1-en-1-yl)-2,2-dimethyl-1,3-dioxan-4-yl)un- decan-6-ol (11):



To a stirring solution of phosphate **10** (1.5 g, 4.33 mmol) in anhydrous THF (45 mL) was added $LiAlH_4$ (0.494 g, 13.0 mmol) in portions at 0 °C under argon atmosphere. The reaction was stirred at the same temperature for 1 h. After reaction completion (monitored by TLC), it was quenched with the slow sequential addition of H_2O (1.5 mL), followed by 10% NaOH (1.5 mL) and H_2O (4.5 mL) [Fieser workup].[3] The mixture was warmed to room temperature and stirred for another 30 min and added 10% HCl (pH ~ 4). The aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (40 mL), dried over Na_2SO_4 and concentrated under reduced pressure to give the crude tetrol (1.35 g) as a white solid. Without chromatographic purification, the crude tetrol was directly subjected to the next step.

To a stirring solution of the above crude tetrol (1.35 g) in a 1:1 mixture of CH_2Cl_2 and acetone (25 mL) was added 2,2-dimethoxy propane (6 mL) and followed by a catalytic amount of CSA (50 mg, 0.216 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. Next, it was treated with aqueous saturated $NaHCO_3$ solution (15 mL) and diluted with CH_2Cl_2 (120 mL). The organic layer was separated and the aqueous layer was back extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with brine (40 mL), dried (Na_2SO_4), filtered and concentrated in *vacuo*. The crude material was purified using silica gel column chromatography (25% EtOAc/Hexanes) to afford 1,3-acetonide **11** (1.05 g, 71% over 2 rxns in 2 pots) as a colorless liquid.

Optical Rotation: $[\alpha]_D^{23}$ –41.6 (*c* 0.25, $CHCl_3$);

FTIR (neat)**:** 3415, 3384, 2929, 2856, 1629, 1458, 1379, 1222, 1033, 1010 cm^{-1};

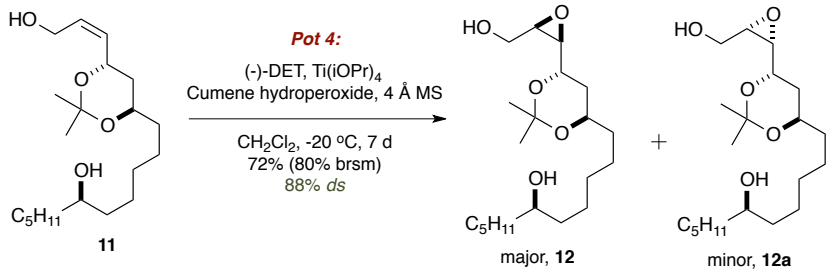
^{1}H NMR (400 MHz, Chloroform-*d*)**:** δ 5.76 (dt, J = 12.4, 6.5 Hz, 1H), 5.58 (dd, J = 11.3, 7.1 Hz, 1H), 4.65 (dd, J = 15.3, 7.3 Hz, 1H), 4.26 (dd, J = 13.3, 6.7 Hz, 1H), 4.15 (dd, J = 13.3, 6.6 Hz, 1H), 3.87–3.77 (m, 1H), 3.62–3.53 (m, 1H), 1.98 (bs, 1H), 1.79–1.60 (m, 2H), 1.59–1.49 (m, 1H), 1.49–1.20 (m, 23H), 0.89 (t, J = 6.4 Hz, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*)**:** δ 132.6, 131.1, 100.4, 71.9, 66.4, 63.5, 58.9, 38.7, 37.4, 37.3, 35.8, 31.9, 29.5, 25.5, 25.3 (2C), 25.3, 24.6, 22.6, 14.0;

HRMS: calculated for $C_{20}H_{38}NaO_4$ $(M+Na)^+$ 365.2668; found 365.2564 (TOF MS ES+).

(3) (a) Fieser, L. F.; Fieser, M. Reagents for Organic Synthesis, Vol. 1; Wiley: New York, 1967; pp 581−595. (b) Mićović, V. M.; Mihailović, M. L.The reduction of acid amides with lithium aluminum hydride. *J. Org. Chem.* **1953**, *18*, 1190–1200.

(*R*)-1-((4*R*,6*S*)-6-((2*S*,3*R*)-3-(hydroxymethyl)oxiran-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)undecan-6-ol (12):



To a stirred suspension of (–)-diethyl tartrate (72 mg, 0.35 mmol) and 4Å MS in anhydrous CH_2Cl_2 (3.0 mL) at -20 °C was added titanium isopropoxide (85 µL, 0.292 mmol) under argon atmosphere. The suspension was stirred for 20 min at the same temperature. Next, cumene hydroperoxide (115 µL, 0.605 mmol, 80%) was added slowly to the reaction mixture and allowed to stir for 20 min. A solution of allyl alcohol **11** (100 mg, 0.292 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise and allowed to stir at -20 °C for 7 days until TLC indicated most of the starting material was consumed (stirring during day, freezer at night). The reaction mixture was quenched with NaOH in aq. saturated Na_2SO_4 solution (100 mg in 1.5 mL) and stirred for 2 h at the room temperature. The quenched mixture was filtered through celite and EtOAc (3x10 mL) was used to wash the filter cake. The filtrate (EtOAc soln) was washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude material was subjected to column chromatography (28-30% EtOAc/Hexanes) to afford a major diastereomer **12** (67 mg, 64%, 88% *ds*) and minor diastereomer **12a** (9.0 mg, 8.6%) as colorless liquids, along with recovered starting material **11** (10.0 mg).

Optical Rotation: $[\alpha]_D^{23}$ –8.4 (*c* 0.25, $CHCl_3$);

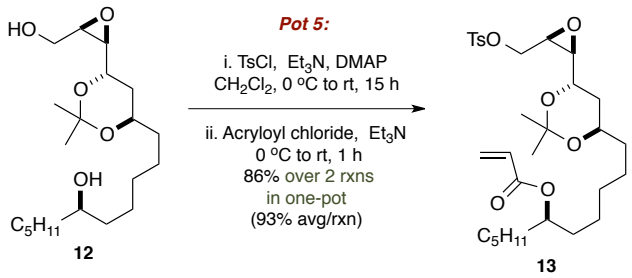
FTIR (neat)**:** 3398, 3379, 2985, 2856, 1456, 1379, 1225, 1027, 895 cm^{-1};

^{1}H NMR (400 MHz, Chloroform-*d*)**:** δ 3.91–3.82 (m, 2H), 3.77 (dd, *J* = 14.6, 7.4 Hz, 1H), 3.69 (dd, *J* = 12.2, 6.3 Hz, 1H), 3.63–3.54 (m, 1H), 3.35 (s, 1H), 3.25 (dd, *J* = 10.7, 5.8 Hz, 1H), 3.04 (dd, *J* = 7.3, 4.3 Hz, 1H), 1.95 (ddd, *J* = 14.3, 8.5, 6.2 Hz, 1H), 1.83 (ddd, *J* = 15.1, 8.2, 6.3 Hz, 1H), 1.63–1.18 (m, 24H), 0.90 (t, *J* = 6.6 Hz, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*)**:** δ 100.4, 71.9, 66.3, 66.1, 61.1, 58.3, 55.9, 37.4, 37.3, 36.2, 35.8, 31.9, 29.5, 25.5, 25.54, 25.3, 25.2, 24.7, 22.6, 14.0;

HRMS: calculated for $C_{20}H_{38}NaO_5$ $(M+Na)^+$ 381.2617; found 381.2074 (TOF MS ES+).

One-pot tosylation, acryloylation sequential protocol to **(*R*)-1-((4*R*,6*S*)-2,2-dimethyl-6-((2*S*,3*R*)-3-((tosyloxy)methyl)oxiran-2-yl)-1,3-dioxan-4-yl)undecan-6-yl acrylate (13):**



To a stirred solution of epoxy diol **12** (500 mg, 1.39 mmol) in CH_2Cl_2 (25 mL) was added Et_3N (0.4 mL, 2.78 mmol), followed by the addition of DMAP (34 mg, 0.278 mmol) at 0 °C under argon atmosphere. After being stirred for 15 min at the same temperature, it was treated with toluene-*p*-sulfonyl choride (0.53 g, 2.78 mmol). The reaction mixture was stirred at room temperature for 15 h. Upon consumption of starting material (monitored by TLC), the mixture was cooled to 0 °C and more Et_3N (1.0 mL, 6.95 mmol) was added, followed by the slow addition of acryloyl chloride (282 µL, 3.47 mmol). The resulting mixture was stirred at room temperature for 1 h (reaction progress was monitored by TLC, and was subsequently quenched with saturated NH_4Cl solution (10 mL). The organic layer was separated and aqueous phase was extracted with CH_2Cl_2 (2 x 15 mL). The combined organic layers were washed with brine (10 mL), then dried (Na_2SO_4), filtered and concentrated in *vacuo*. The resulting crude oil was chromatographed over silica gel (12% EtOAc/Hexanes) to afford the desired product **13** (0.68 g, 86% over 2 rxns in one-pot, 93% avg/rxn) as a pale yellow gummy liquid.

Optical Rotation: $[\alpha]_D^{23}$ +8.8 (*c* 0.25, $CHCl_3$);

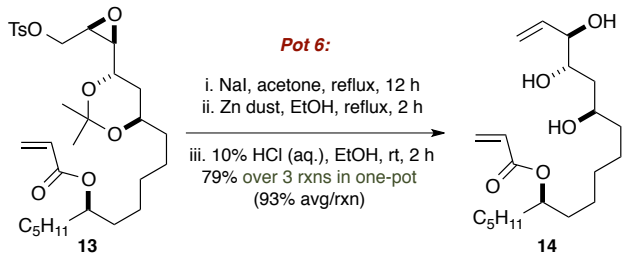
FTIR (neat)**:** 2931, 2858, 1720, 1579, 1460, 1369, 1190, 979, 812 cm^{-1};

^{1}H NMR (500 MHz, Chloroform-*d*)**:** δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 6.39 (dd, *J* = 17.2, 1.5 Hz, 1H), 6.11 (dd, *J* = 17.2, 10.3 Hz, 1H), 5.81 (dd, *J* = 10.4, 1.5 Hz, 1H), 4.95 (tt, *J* = 7.1, 5.3 Hz, 1H), 4.42 (dd, *J* = 11.6, 3.1 Hz, 1H), 4.05 (dd, *J* = 11.6, 7.4 Hz, 1H), 3.80–3.74 (m, 1H), 3.63 (dt, *J* = 8.8, 6.4 Hz, 1H), 3.23 (ddd, *J* = 7.4, 4.2, 3.2 Hz, 1H), 3.02 (dd, *J* = 6.7, 4.3 Hz, 1H), 2.46 (s, 3H), 1.84 (ddd, *J* = 14.7, 8.9, 5.8 Hz, 1H), 1.69 (ddd, *J* = 15.4, 9.3, 6.2 Hz, 1H), 1.60–1.45 (m, 8H), 1.44–1.19 (m, 16H), 0.87 (t, *J* = 6.5, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*)**:** δ 166.1, 145.1, 132.7, 130.2, 129.9 (2), 128.9, 128.0 (2), 100.3, 74.5, 68.5, 66.2, 65.0, 57.9, 53.7, 36.0, 35.7, 34.1, 31.7, 29.7, 29.4, 25.2, 25.1 (2C), 24.9, 24.4, 22.5, 21.7, 14.0;

HRMS: calculated for $C_{30}H_{46}NaO_8S$ $(M+Na)^+$ 589.2811; found 589.2831 (TOF MS ES+).

One-pot Finkelstein substitution, Boord olefination, acetonide deprotection sequential protocol to **(6*R*,12*R*,14*S*,15*R*)-12,14,15-Trihydroxyheptadec-16-en-6-yl acrylate (14):**



To a stirring solution of tosylate **13** (100 mg, 0.176 mmol) in acetone (3 mL) was added sodium iodide (526 mg, 3.52 mmol) and the reaction mixture was heated to reflux for 12 h. After consumption of the starting material (indicated by TLC), acetone was removed under reduced pressure, and EtOH (5 mL) was added to the resulting mixture at room temperature, followed by the addition of activated Zn powder (344 mg, 5.33 mmol). The reaction was heated to reflux for 2 h until TLC indicated the absence of the iodo-derivative. The reaction mixture was cooled to room temperature and subsequently treated with slow addition of 10% aq. HCl (2.0 mL). Stirring was continued for 2 h and the mixture was quenched with saturated aq. $NaHCO_3$ solution (8.0 mL, until pH = 5). EtOH was completely removed under *vacuo* and to the resulting residue was added EtOAc (20 mL), followed by and H_2O (5 mL). The organic layer was removed and aqueous layer was again extracted with EtOAc (2x10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated under *vacuo*. The crude material was subjected to silica gel column chromatography (50% EtOAc/Hexanes) to provide triol **14** (49 mg, 79% over 3 rxns in one-pot, 93% avg/rxn) as a colorless gummy oil. Compound **14** matched the reported material in all respects.[4]

Optical Rotation: $[\alpha]_D^{23}$ –2.91 (*c* 0.3, $CHCl_3$);

FTIR (neat)**:** 3398, 3361, 2939, 1720, 1404, 1271, 1195, 1045, 983, 808 cm^{-1};

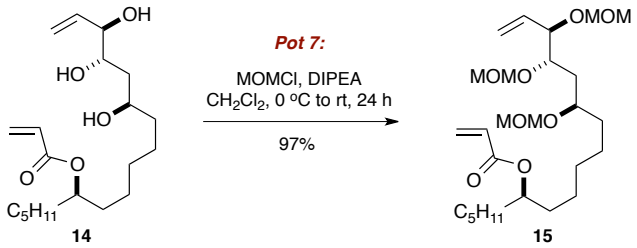
^{1}H NMR (400 MHz, Chloroform-*d*)**:** δ 6.38 (dd, *J* = 17.3, 1.2 Hz, 1H), 6.11 (dd, *J* = 17.2, 10.4 Hz, 1H), 5.91 (ddd, *J* = 17.2, 10.4, 6.1 Hz, 1H), 5.81 (d, *J* = 10.4 Hz, 1H), 5.35 (d, *J* = 17.2 Hz, 1H), 5.27 (d, *J* = 10.5 Hz, 1H), 4.95 (p, *J* = 6.4 Hz, 1H), 4.14 (t, *J* = 5.4 Hz, 1H), 4.02–3.90 (m, 2H), 2.72 (s, 1H), 2.26–2.02 (m, 2H), 1.70 (ddd, *J* = 14.3, 9.5, 2.8 Hz, 1H), 1.56–1.49 (m, 6H), 1.48–1.41 (m, 1H), 1.38–1.21 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*)**:** δ 166.2, 136.4, 130.4, 128.9, 117.6, 76.1, 74.5, 71.2, 69.3, 37.4, 37.2, 34.1, 34.0, 31.7, 29.2, 25.6, 25.1, 24.9, 22.5, 14.0;

HRMS: calculated for $C_{20}H_{36}NaO_5$ $(M+Na)^+$ 379.2460; found 379.2400 (TOF MS ES+).

(4) Bali, A. K.; Sunnam, S. K.; Prasad, K. R. *Org. Lett.* **2014**, *16*, 4001–4008.

(6*R*,12*R*,14*S*,15*R*)-12,14,15-tris(Methoxymethoxy)heptadec-16-en-6-yl acrylate (15):



To a stirring solution of triol **14** (30 mg, 0.084 mmol) in anhydrous CH_2Cl_2 (1.5 mL) under argon atmosphere was added *N*,*N*-disopropylethylamine (110 µL, 0.63 mmol). After being stirred for 15 min, chloro(methoxy)methane (34 µL, 0.42 mmol) was added slowly at 0 °C. The reaction mixture was stirred at room temperature for 15 h; then excess *N*,*N*-disopropylethylamine (110 µL, 0.63 mmol) and chloro(methoxy)methane (34 µL, 0.42 mmol) were added at 0 °C. The stirring was continued for another 9 h at room temperature (until TLC showed the absence of starting material). Upon reaction completion, saturated $NaHCO_3$ (5.0 mL) was added followed by CH_2Cl_2 (15 mL). The organic layer was separated and the aqueous layer was back extracted with CH_2Cl_2 (2x5 mL). The combined CH_2Cl_2 extracts were washed with brine (5.0 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The obtained crude material was subjected to silica gel column chromatography (15% EtOAc/Hexanes) to furnish the tri-MOM protected diene **15** (40 mg, 97%) as a colorless liquid.

Optical Rotation: $[\alpha]_D^{23}$ –30.1 (*c* 0.25, $CHCl_3$);

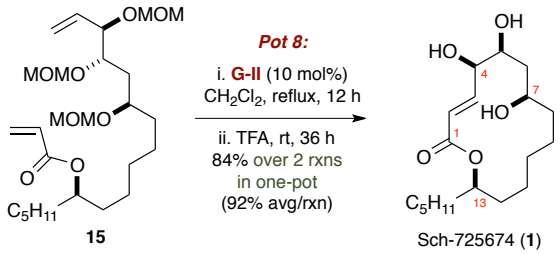
FTIR (neat)**:** 3033, 2821, 1720, 1465, 1404, 1296, 1271, 1195, 1149, 1099, 1035, 918 cm^{-1};

^{1}H NMR (400 MHz, Chloroform-*d*)**:** δ 6.38 (d, *J* = 17.2, 1H), 6.11 (dd, *J* = 17.2, 10.4 Hz, 1H), 5.84–5.71 (m, 2H), 5.33-5.25 (m, 2H), 4.94 (p, *J* = 6.2 Hz, 1H), 4.83 (d, *J* = 6.8 Hz, 1H), 4.73–4.65 (m, 4H), 4.62 (d, *J* = 6.7 Hz, 1H), 4.16 (d, *J* = 7.3 Hz, 1H), 3.87–3.81 (m, 1H), 3.73–3.65 (m, 1H), 3.42 (s, 3H), 3.38 (s, 6H), 1.65–1.46 (m, 8H), 1.38–1.16 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H);

^{13}C NMR (126 MHz, Chloroform-*d*)**:** δ 166.1, 134.5, 130.2, 129.0, 119.0, 96.9, 96.1, 94.1, 79.6, 77.1, 75.3, 74.5, 55.9, 55.6, 55.4, 36.3, 35.3, 34.1 (2C), 31.7, 29.8, 25.3, 24.9, 24.8, 22.5, 14.0;

HRMS: calculated for $C_{26}H_{48}NaO_8$ $(M+Na)^+$ 511.3247; found 511.3239 (TOF MS ES+).

One-pot RCM, MOM deprotection sequential protocol to **(5*R*,6*S*,8*R*,14*R*,*E*)-5,6,8-Trihydroxy-14-pentyloxacyclotetradec-3-en-2-one (1):**



To a stirred solution of tri-MOM protected diene **15** (10 mg, 0.02 mmol) in a freshly distilled, freeze-degas-thawed CH_2Cl_2 (14 mL, 0.0015 M) was added the Grubbs 2nd generation catalyst (**G-II**) (1.0 mg, 6 mol%). The reaction was heated to reflux for 6 h and cooled down to room temperature to add a second batch of **G-II** (0.7 mg, 4 mol%). The reflux was resumed for 6 h (until the RCM completed by TLC). The solvent was reduced to a final volume of approximately 1.0 mL by removing the reflux condenser from the reaction flask. The reaction mixture was then cooled to room temperature and treated with TFA (1.5 mL) under argon atmosphere. The reaction was allowed to stir for 36 h (reaction progress was monitored by TLC) and the volatiles were removed under *vacuo*. The crude residue was chromatographed over silica gel (75% EtOAc/Hexanes) to furnish the target natural product, Sch-725674 (**1**) (5.6 mg, 84% over 2 rxns in one-pot, 92% avg/rxn) as a colorless solid. Characterization data noted below was compared and matched to those reported by Prasad[4] and Curran.[5]

M.P. Range: 181–183 ºC;

Optical Rotation: $[\alpha]_D^{23}$ +4.97 (*c* 0.15, CH_3OH), {Reported: $[\alpha]_D$ +5.15 (*c* 0.27, CH_3OH)};

FTIR (neat)**:** 3451, 2931, 1708, 1279, 1068, 983, 896, 805 cm^{-1};

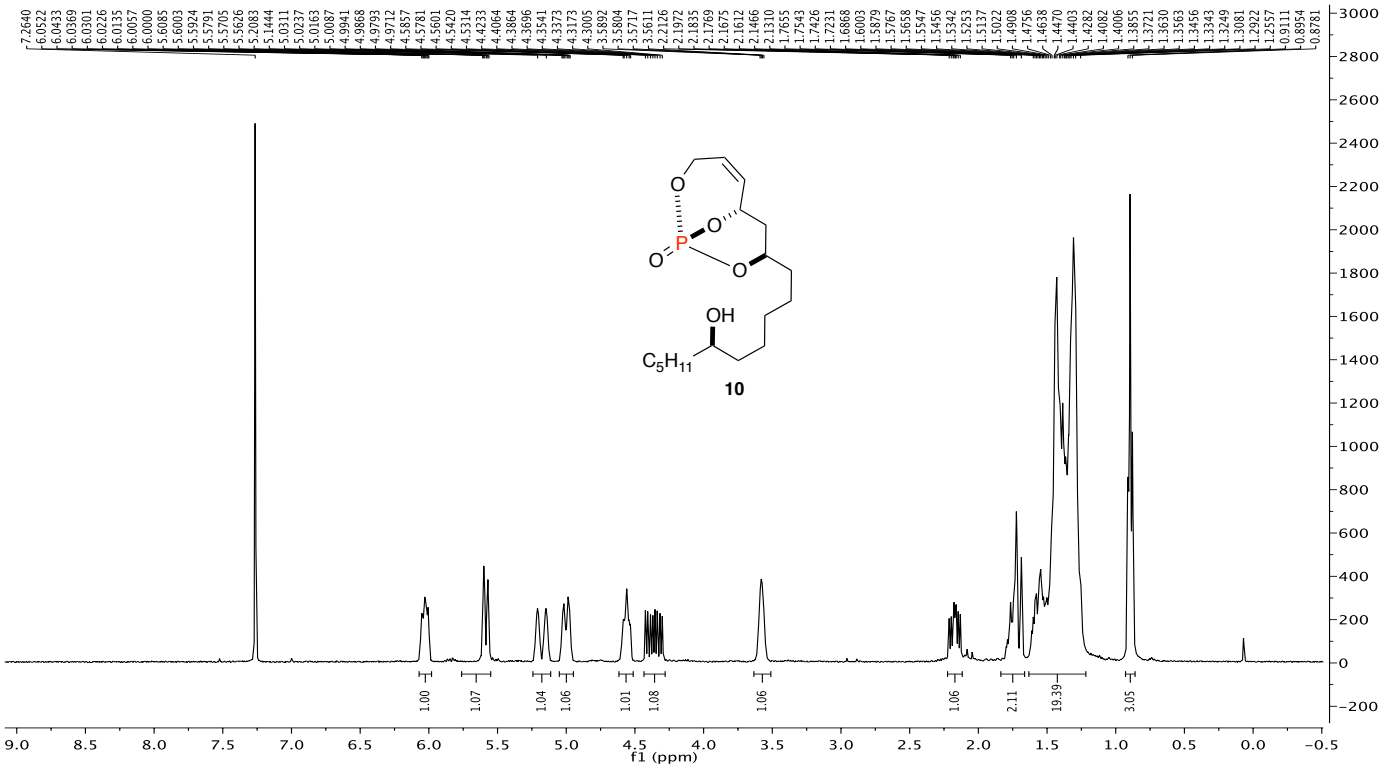
^{1}H NMR (400 MHz, Methanol-d_4)**:** δ 6.87 [dd, J = 15.8, 6.1 Hz, 1H, -C<u>H</u>=CH(C=O)O-], 6.08 [dd, J = 15.8, 1.5 Hz, 1H, -CH=C<u>H</u>(C=O)O-], 4.98–4.93 [m, 1H, $CH_2C\underline{H}(OC{=}O)CH_2CH_3$], 4.51–4.46 [m, 1H, -CH=CHC<u>H</u>-(OH)], 3.99 [p, J = 6.1 Hz, 1H, $-CH_2C\underline{H}(OH)CH_2$-], 3.85 [dd, J = 6.3, 4.4 Hz, 1H, $-CH_2C\underline{H}(OH)CH(OH)$-], 1.83 [dt, J = 14.7, 6.0 Hz, 1H, -CH(OH)C<u>H_aH_b</u>CH(OH)-], 1.73–1.51 (m, 5H, aliphatic protons), 1.40–1.25 (m, 11H, aliphatic protons), 1.23–1.12 (m, 3H, aliphatic protons), 0.90 (t, J = 6.8 Hz, 3H, $C\underline{H_3}$);

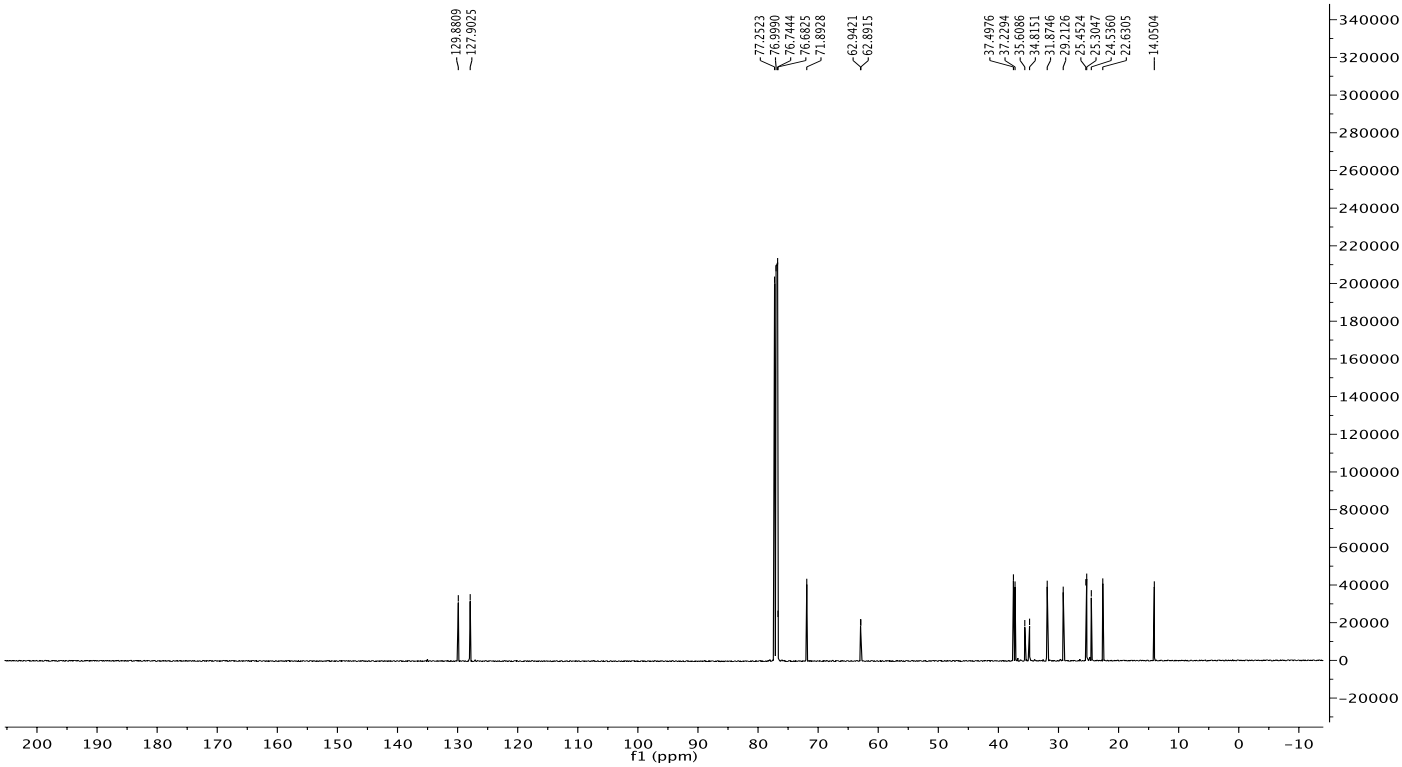
^{13}C NMR (126 MHz, Methanol-d_4)**:** δ 168.4, 149.3, 123.1, 77.6, 76.0, 72.9, 69.5, 38.3, 36.8, 36.5, 34.1, 32.9, 29.5, 27.0, 26.4, 25.8, 23.8, 14.5;

HRMS: calculated for $C_{18}H_{32}NaO_5$ $(M+Na)^+$ 351.2147; found 351.2135 (TOF MS ES+).

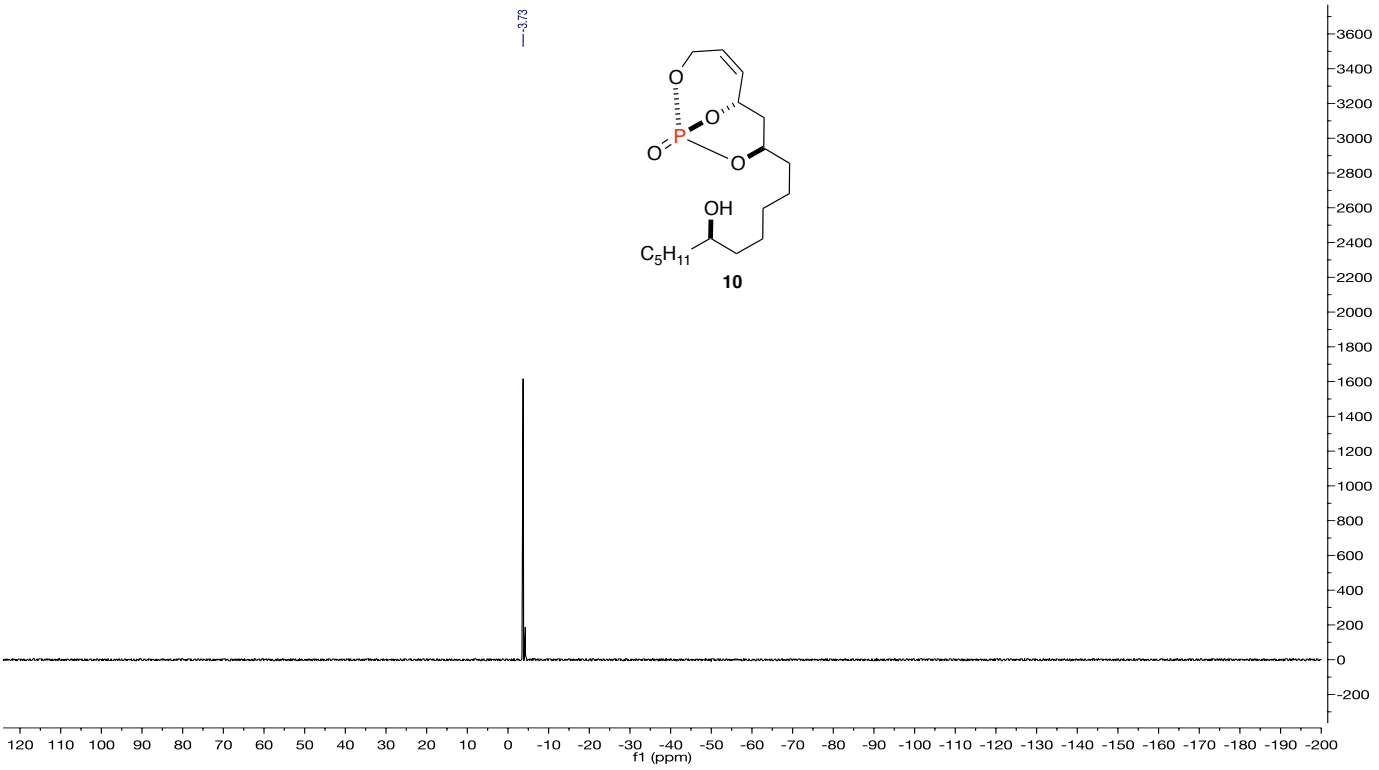
(5) Moretti, J. D.; Wang, X.; Curran, D. P. *J. Am. Chem. Soc.* **2012**, *134*, 7963–7970.

(6*S*,8*R*)-8-((*R*)-6-hydroxyundecyl)-2,9,10-trioxa-1-phosphabicyclo[4.3.1]dec-4-ene-1-oxide (10):

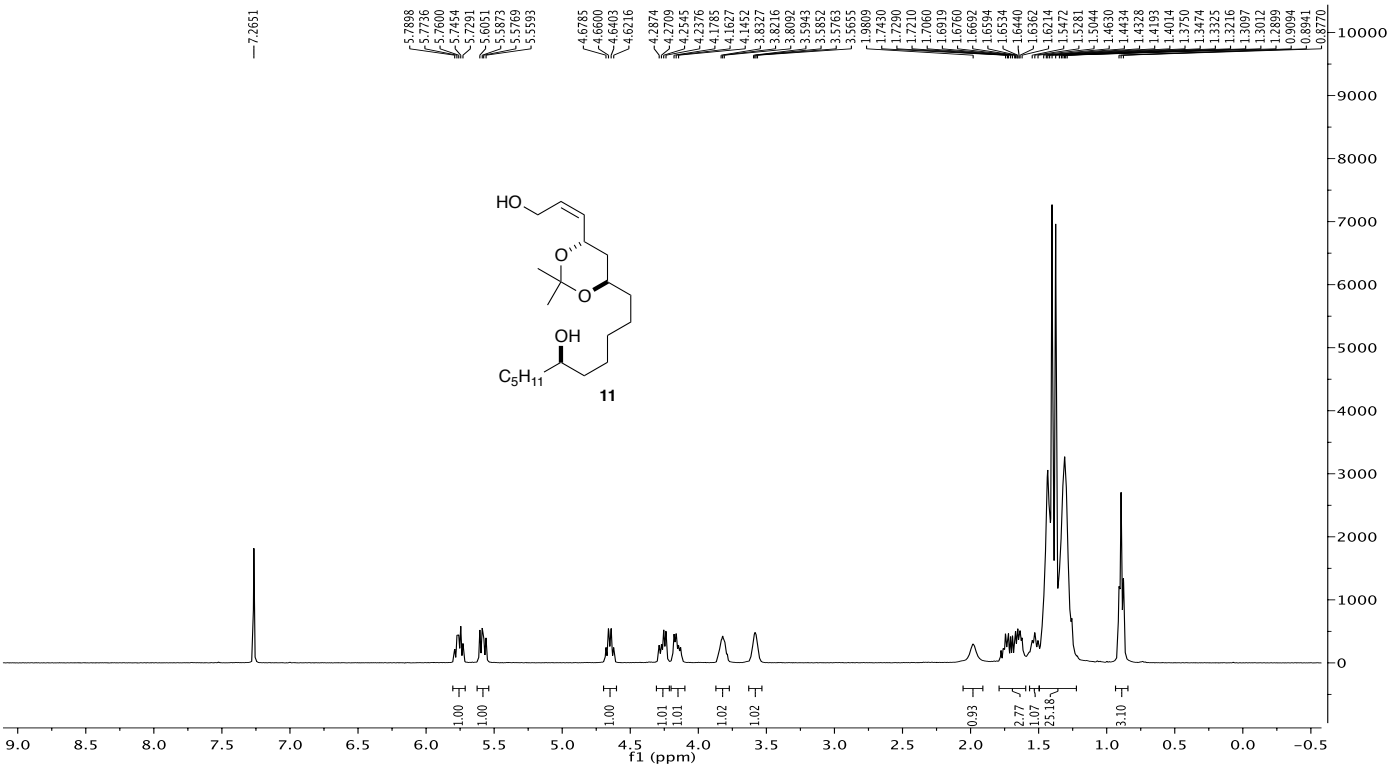


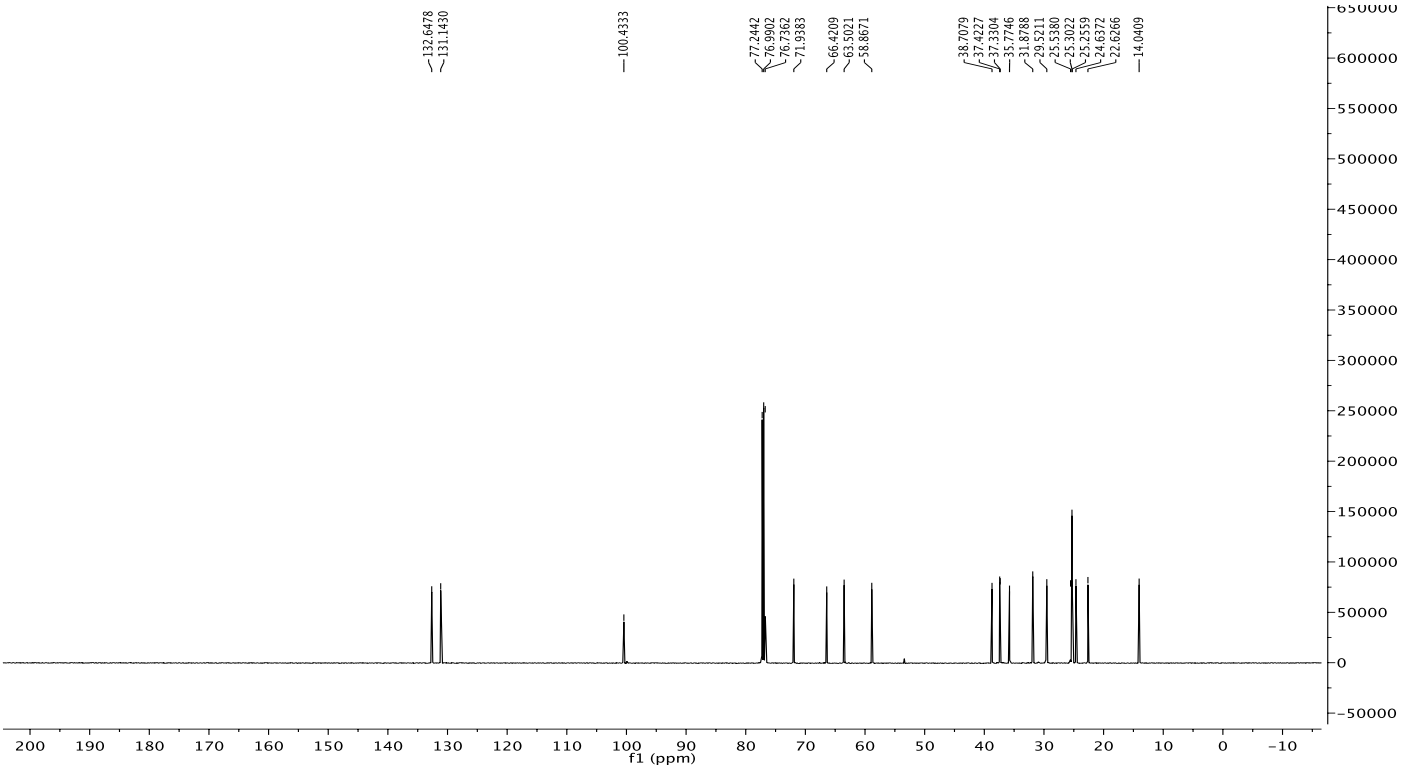


(6*S*,8*R*)-8-((*R*)-6-hydroxyundecyl)-2,9,10-trioxa-1-phosphabicyclo[4.3.1]dec-4-ene-1-oxide (10):

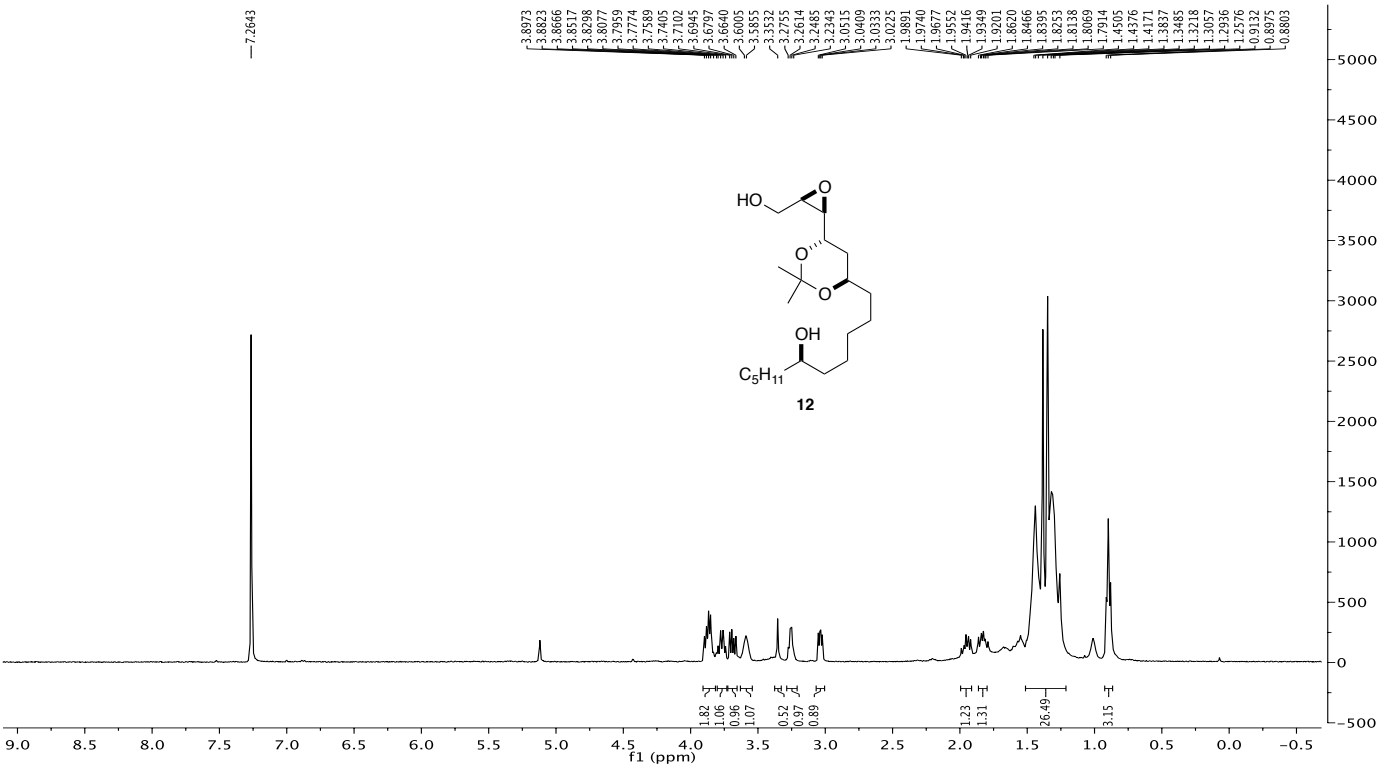


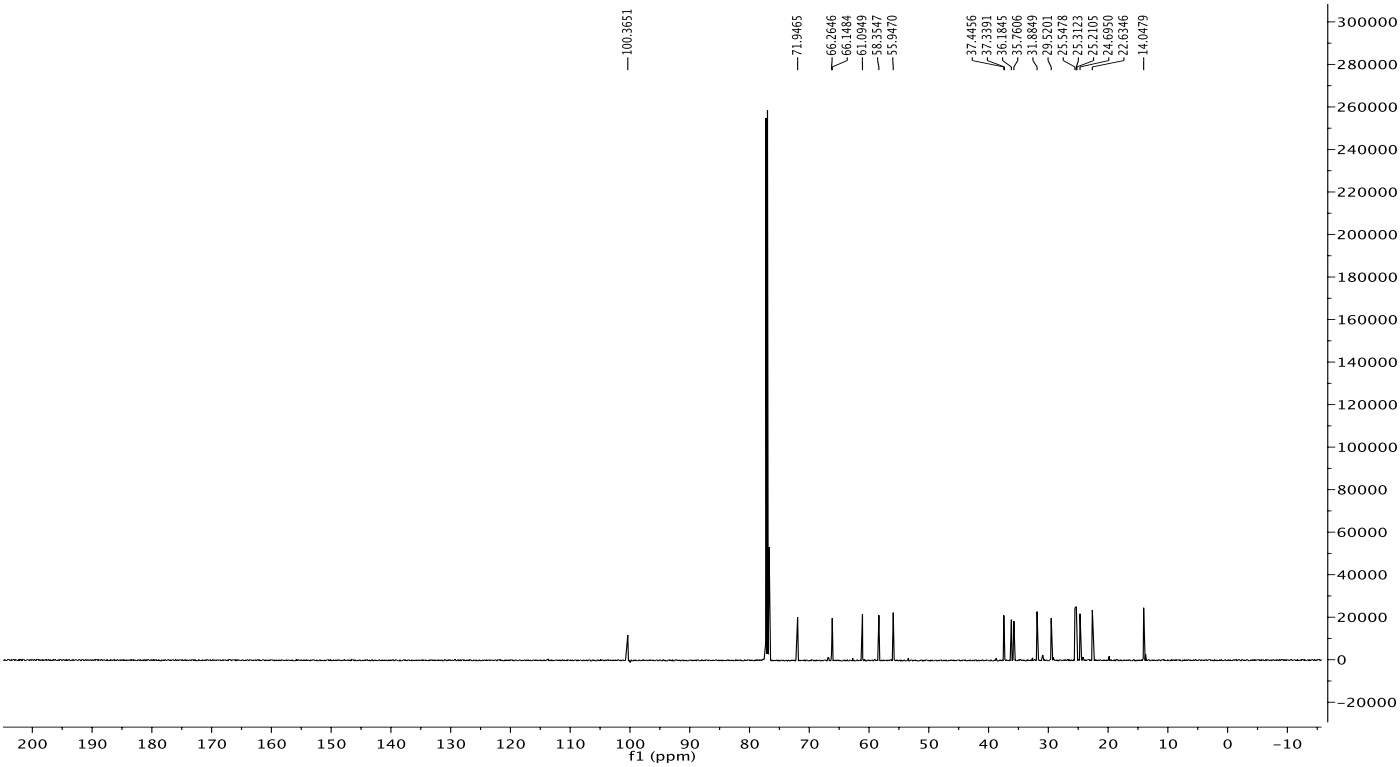
(*R*)-1-((4*R*,6*S*)-6-((*Z*)-3-Hydroxyprop-1-en-1-yl)-2,2-dimethyl-1,3-dioxan-4-yl)un- decan-6-ol (11):



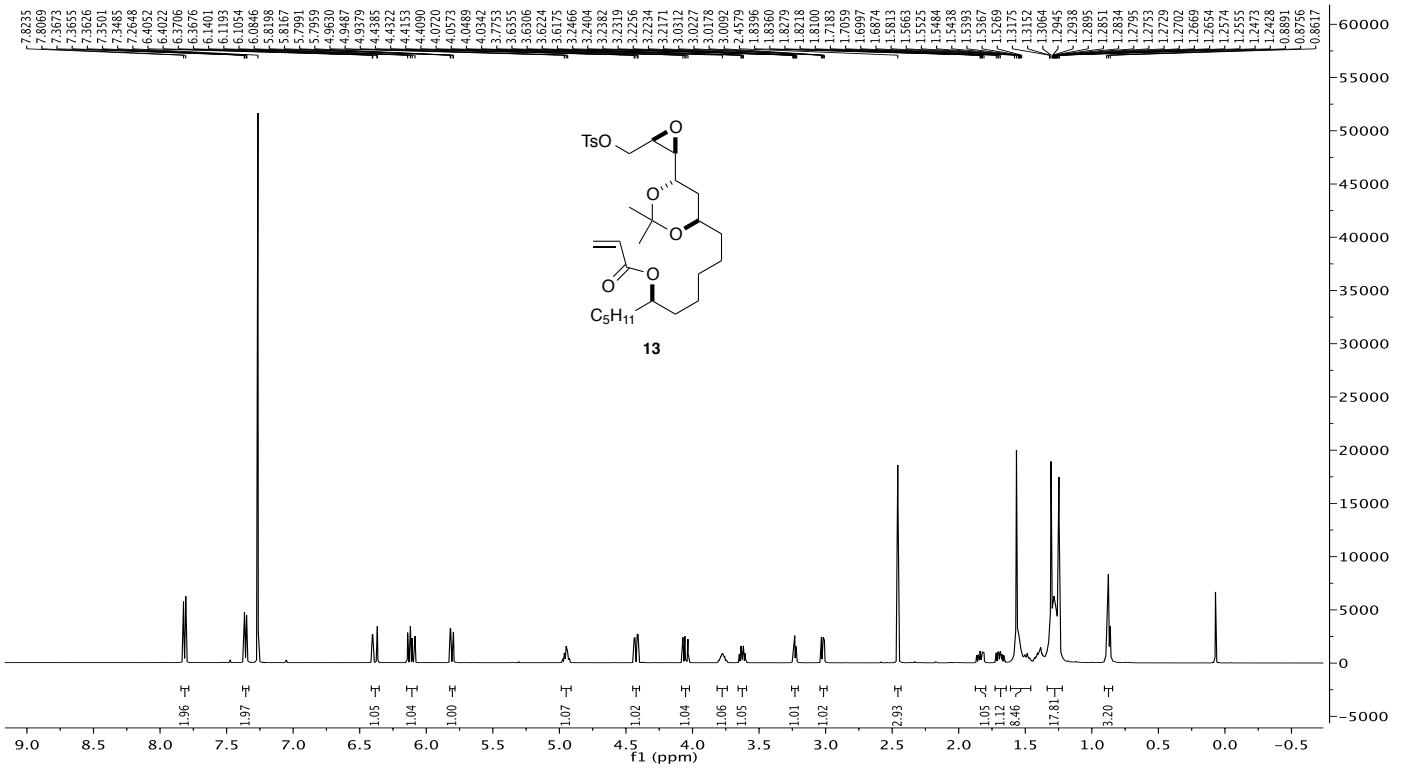


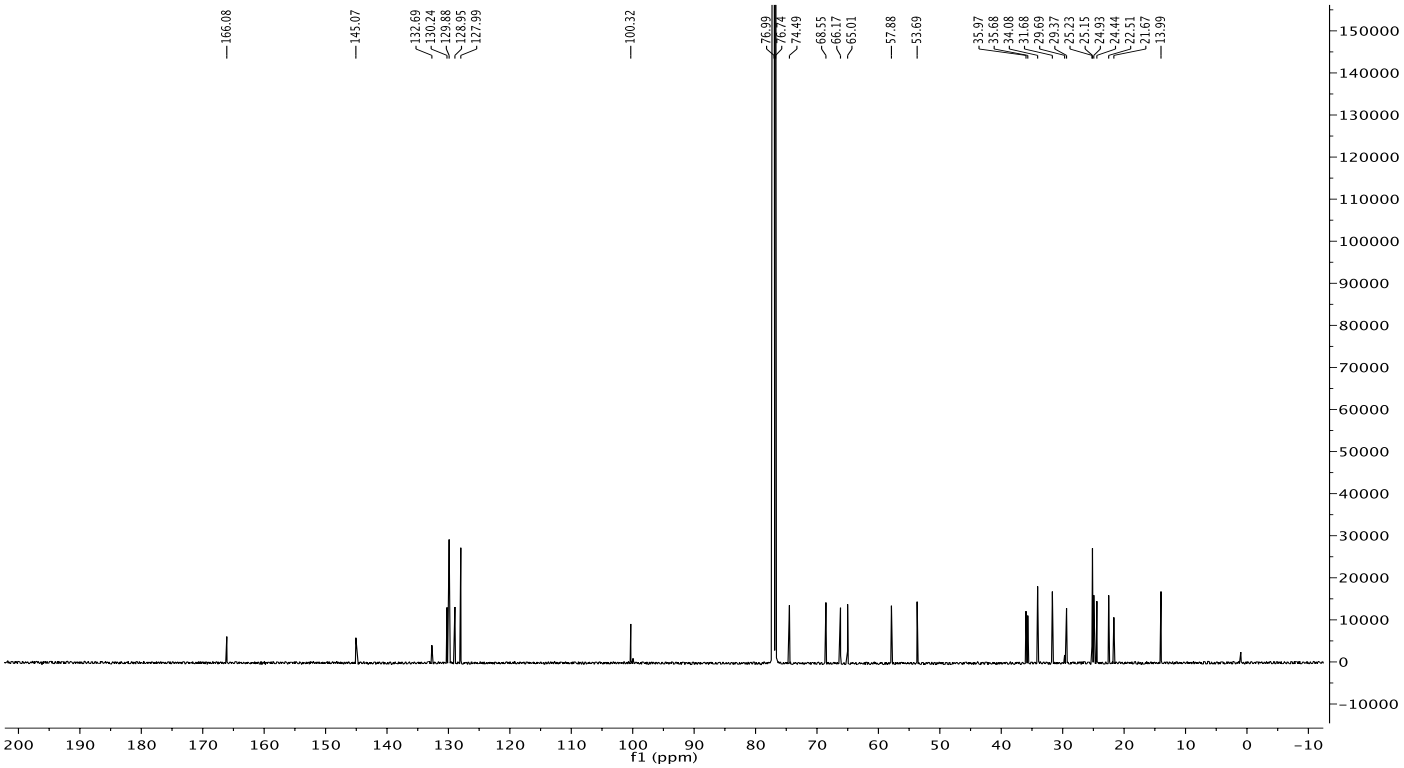
(*R*)-1-((4*R*,6*S*)-6-((2*S*,3*R*)-3-(hydroxymethyl)oxiran-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)undecan-6-ol (12):



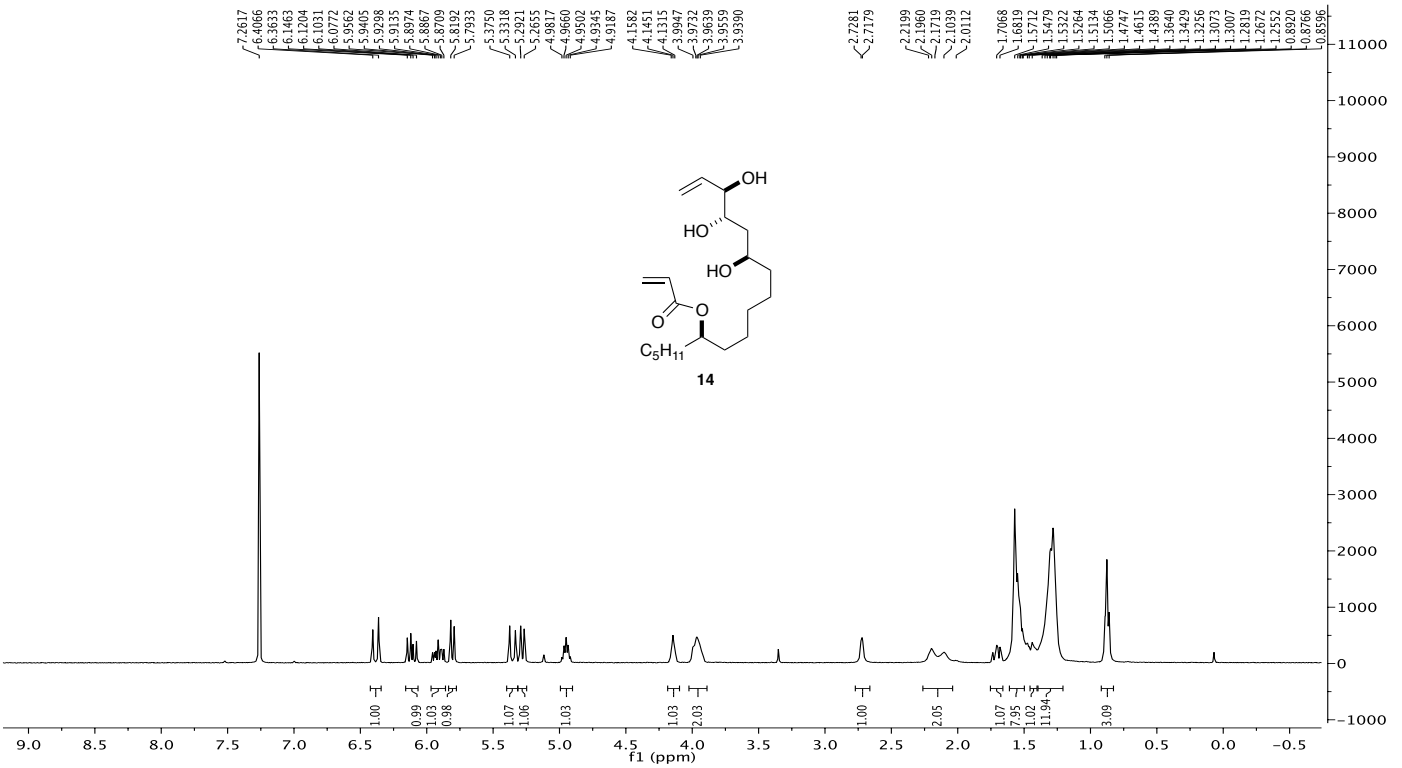


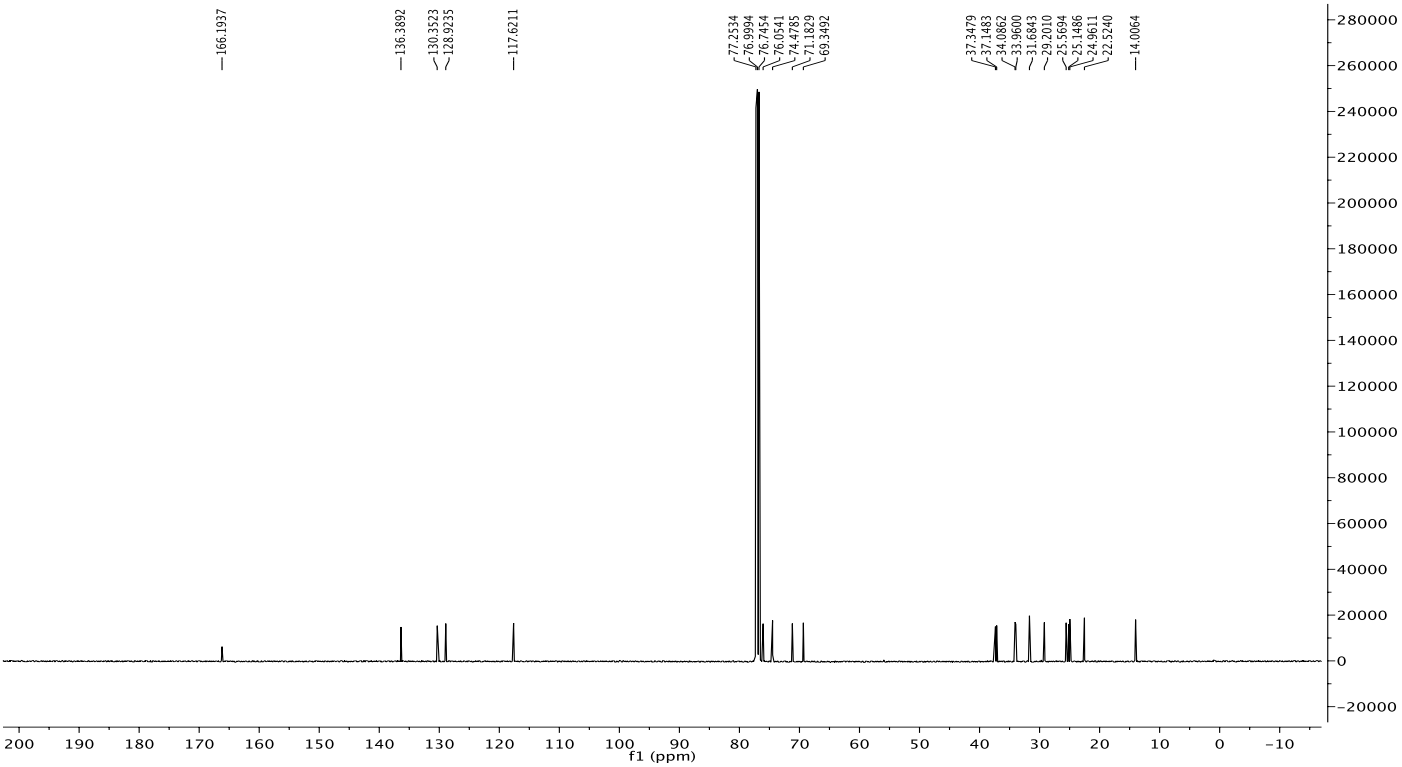
(*R*)-1-((4*R*,6*S*)-2,2-dimethyl-6-((2*S*,3*R*)-3-((tosyloxy)methyl)oxiran-2-yl)-1,3-dioxan-4-yl)undecan-6-yl acrylate (13):



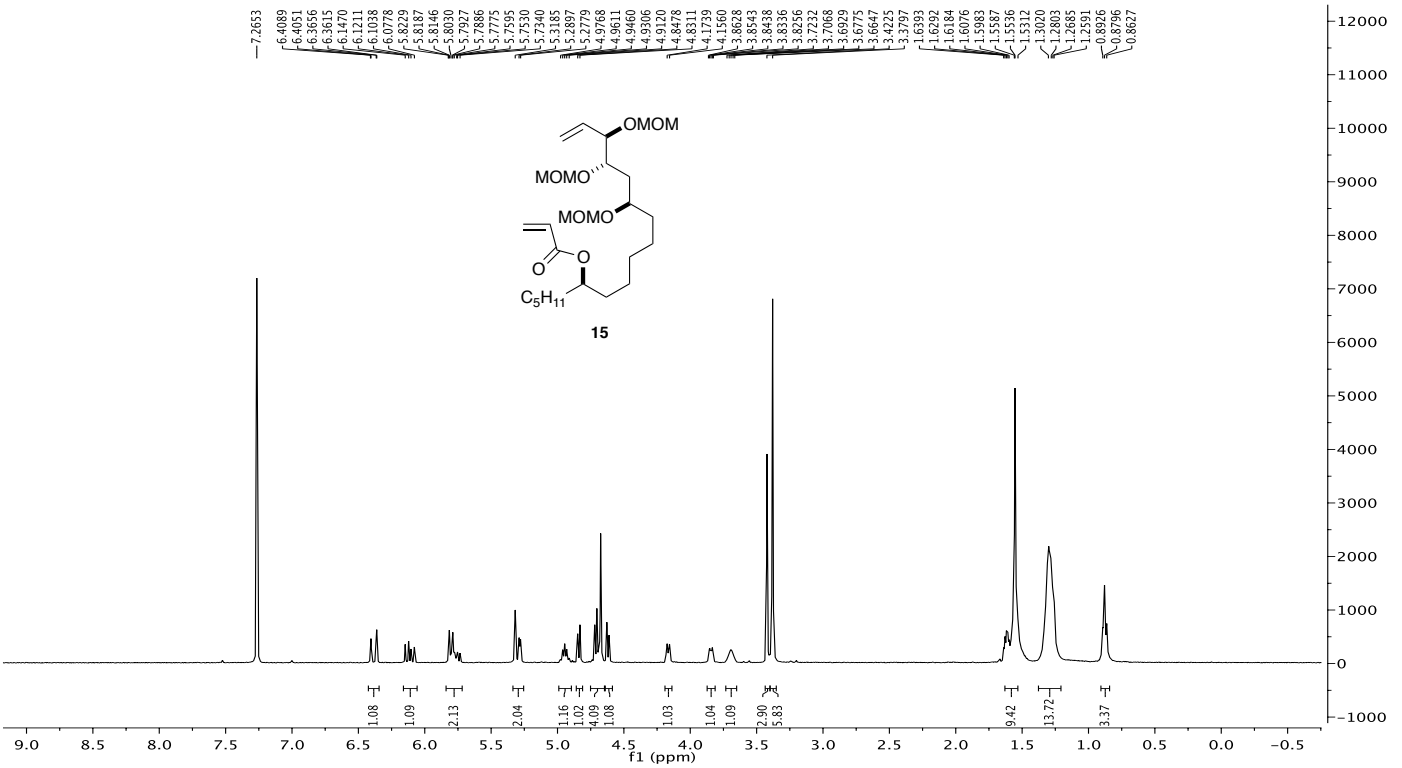


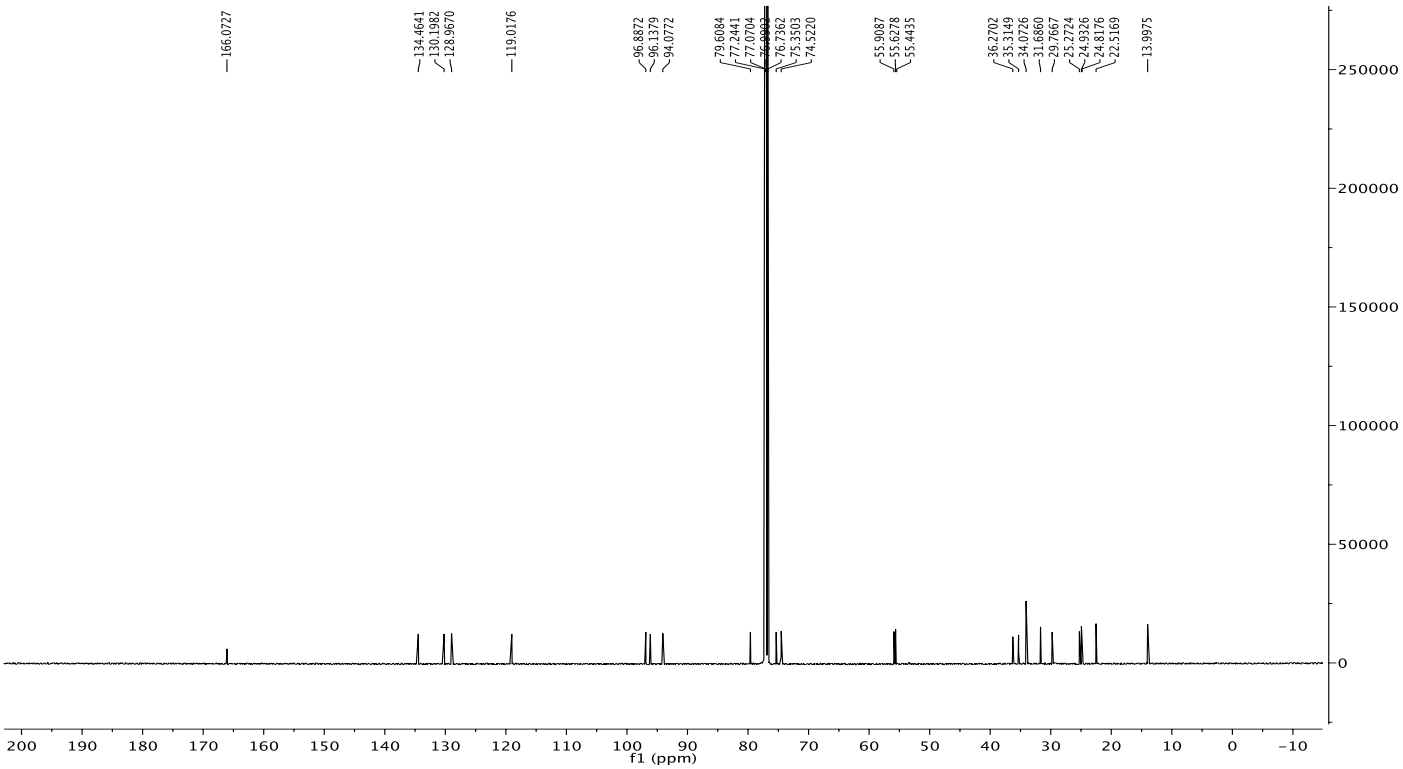
(6*R*,12*R*,14*S*,15*R*)-12,14,15-Trihydroxyheptadec-16-en-6-yl acrylate (14):





(6*R*,12*R*,14*S*,15*R*)-12,14,15-tris(Methoxymethoxy)heptadec-16-en-6-yl acrylate (15):





(5*R*,6*S*,8*R*,14*R*,*E*)-5,6,8-Trihydroxy-14-pentyloxacyclotetradec-3-en-2-one (1):