Supporting Information

New Strategy for the Construction of Monotetrahydrofuran Ring in *Annonaceous* Acetogenin based on a Ruthenium Ring Closing Metathesis: Application to the Synthesis of Solamin

Guillaume Prestat, Christophe Baylon, Marie-Pierre Heck,* Gabriela A. Grasa,

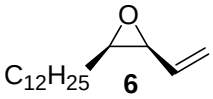
Steven P. Nolan, and Charles Mioskowski*

E-mail: heck@dsvidf.cea.fr, mioskow@bioorga.u-strasbg.fr;

Table of Contents:

General Methods: All reagents are commercial grade and were used as received. 2,6-Diisopropylphenylimidoneophylidenemolybdenum (VI) bis (hexafluoro-t-butoxide) **A** (Schrock's catalyst) was purchased from Strem Chemical INC. Bis(tricyclohexylphosphine)benzylidene ruthenium (IV) dichloride **B** (Grubbs catalyst) was purchased from Strem Chemical INC. 1,3-Dimesitylimidazol-2-ylidene ruthenium benzylidene **B** (Grubbs catalyst 2nd generation) was prepared according to the literature procedure.[39] All reactions were performed under inert atmosphere using anhydrous solvents which were dried and distilled before use. Thin-layer chromatograms (TLC) and flash chromatography separations were respectively performed on precoated silica gel 60 F254 plates (Merck, 0.25 mm) and on Merck silica gel 60 (230-400 mesh). ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$; ^{13}C NMR spectra were obtained at 75 MHz with $CDCl_3$ as internal reference. Mass spectra were recorded at 70 eV using chemical ionization mode (CI-NH_3) or electrospray mode. IR spectra were recorded as casts on a FT instrument.

(3S,4R)-3,4-epoxy-hexadecan-1-ol (6)

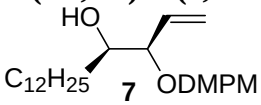


6

To a stirred solution of epoxy allylic alcohol **5** (13.2 g, 54.5 mmol) in CH_2Cl_2 (180 mL) at 0°C was added DMSO (45 mL, 600 mmol) and NEt_3 (38 mL, 272.5 mmol), then SO_3.pyridine (6.9 g, 218 mmol) was added in six portions at 0°C. After 1 hour of stirring at 0°C, the solution was diluted with ether (150 mL), washed with a saturated aqueous NH_4Cl solution (2x150 mL) and with HCl 1M (2x100 mL). The organic layer was separated, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude aldehyde which were immediately used in the next step. Sodium bis(trimethylsilyl)amide (1.0 M in THF, 65.5 mL, 65.5 mmol) was added dropwise to a suspension of methyltriphenylphosphonium bromide (29.2 g, 81.7 mmol) in THF (15 mL) at 0°C. After 45 min of stirring, a solution of crude aldehyde in THF (50 mL) was added at 0°C. Stirring was continuted for 90 min at 0°C and then acetone (20 mL) and ether (150 mL) were added. The organic layer was washed with a saturated aqueous NH_4Cl solution (3x150 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 98/2) to provide epoxide **6** (10 g, 77%). ^{1}H NMR ($CDCl_3$) δ = 5.72 (ddd, *J* = 17.1, 10.4, 7.3 Hz, 1H), 5.47 (dd, *J* = 17.1, 1.8 Hz, 1H), 5.35 (dd, *J* = 10.4, 1.8 Hz, 1H), 3.40 (dd, *J* = 6.1, 4.3 Hz, 1H), 3.39 (dd, *J* = 5.5, 2.0 Hz, 1H), 3.08-3.05 (m, 1H), 1.62-1.25 (m, 2H),

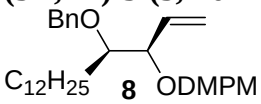
0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ = 132.7, 120.2, 58.8, 57.2, 31.9, 29.6, 29.5, 29.4, 27.7, 26.3, 22.7, 14.1; IR (NaCl, cm^{-1}) 2924, 2854, 1466, 985, 921, 816 cm^{-1}; SM (CI NH_3) *m/z* : 256 ($M+NH_4^+$); Anal. Calcd for $C_{16}H_{30}O$: C, 80.6; H, 12.68. Found: C, 80.35; H, 12.38.

(3R,4R)-3-(3,4-dimethoxy-benzyloxy)-hexadec-1-en-4-ol (7)



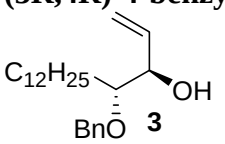
To a solution of epoxide **6** (2 g, 8.47 mmol) and 3,4-dimethoxybenzyl alcohol (6.2 mL, 42 mmol) in CH_2Cl_2 (15 mL) was added $BF_3.Et_2O$ (107 μL, 0.85 mmol) and the solution was stirred at RT for 10 min. After addition of a saturated aqueous $NaHCO_3$ solution (20 mL), the mixture was extracted with CH_2Cl_2 (2x20 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure. The crude product was purified by flash column chromatography (pentane/ether 7/3) to provide alcohol **7** (2.34 g , 75%). ^{1}H NMR ($CDCl_3$) δ = 6.87-6.80 (m, 3H), 5.72 (ddd, *J* = 17.1, 9.8, 8.5 Hz, 1H), 5.36 (dd, *J* = 9.8, 1.8 Hz, 1H), 5.32 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.27 (d, *J* = 11.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.65-3.49 (m, 2H), 2.68 (d, *J* = 2.5 Hz, 1H), 1.55-1.24 (m, 22H), 0.87 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ = 149.0, 148.6, 135.4, 130.6, 120.4, 119.8, 111.3, 111.0, 84.1, 73.3, 70.2, 55.81, 55.74, 32.5, 31.8, 29.6, 29.2, 25.4, 22.6, 14.0; IR (NaCl) 3561, 2924, 2854, 1515, 1264, 157, 1032 cm^{-1}; SM (CI NH_3) *m/z* : 424 ($M+NH_4^+$); Anal. Calcd for $C_{25}H_{42}O_4$: C, 73.85; H, 10,41. Found: C, 73.81; H, 10.42.

(3R,4R)-3-(3,4-dimethoxy-benzyloxy)-4-benzyloxy-hexadec-1-ene (8)



To a suspension of NaH (340 mg, 8.59 mmol) in DMF (10 mL) at 0°C, was added a solution of alcohol **7** (2.33 g, 5.73 mmol) in DMF (15 mL) and the mixture was stirred for 15 min. Then was added benzyl bromide (2.04 mL, 17.19 mmol) and the solution was stirred overnight at RT. After addition of a saturated aqueous NH_4Cl solution (20 mL), the mixture was extracted with CH_2Cl_2 (3x30 mL). The organic layers were separated, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by flash column chromatography (pentane/Et_2O 9/1) to provide ether **8** (2.7 g, 95%) ^{1}H NMR ($CDCl_3$) δ = 7.34-7.22 (m, 5H), 6.90-6.79 (m, 3H), 5.82 (ddd, *J* = 14.7, 12.6, 8.1 Hz, 1H), 5.30 (dd, *J* = 14.7, 1.8 Hz, 1H), 5.26 (dd, *J* = 12,6, 1.8 Hz, 1H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.56 (dd, *J* = 11.6 Hz, 2H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.34 (d, *J* = 11.6 Hz, 1H), 3.87 (s, 3H), 3.78 (s, 3H), 3.47-3-40 (m, 1H), 1.65-1.20 (m, 22H), 0.88 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ =149.9, 148.4, 139.0, 135.7, 131.1, 128.1; 127.8, 127.4, 120.1, 118.4, 111.2, 110.8, 82.3, 81.3, 73.1, 70.4, 55.8, 55.6, 31.9, 30.8, 29.6, 29.3, 25.6, 22.6, 14.0; SM (CI NH_3) *m/z* : 514 ($M+NH_4^+$); IR (NaCl) 2925, 2854, 1516, 1265, 1139, 736, 698 cm^{-1}.

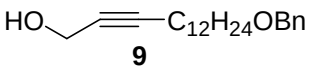
(3R,4R)-4-benzyloxy-hexadec-1-en-3-ol (3)



3

To a solution of alkene **8** (2.70 g, 5.44 mmol) in CH_2Cl_2/H_2O (60 mL, 18/1) was added DDQ (1.32 g, 5.84 mmol) and the solution was stirred at RT for 15 min. The mixture was filtered through a pad of celite washed with CH_2Cl_2. The combined extracts were dried ($MgSO_4$), concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 8/2) to provide allyl alcohol **3** (1.8 g, 95%). ^{1}H NMR ($CDCl_3$) δ = 7.39-7.30 (m, 5H), 5.91 (ddd, *J* = 17.7, 10.4, 5.5 Hz, 1H), 5.38 (dd, *J* = 17.7, 1.2 Hz, 1H), 5.24 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.63 (q, *J* = 11.6 Hz, 2H), 4.14-4.08 (dd, *J* = 10.4, 6.1 Hz, 1H), 3.36 (dd, *J* = 11.3, 5.8 Hz, 1H), 2.61 (d, *J* = 4.3 Hz, 1H), 1.71-1.28 (m, 22H), 0.92 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ = 138.3, 137.7, 128.3, 127.8, 127.7, 116.5, 82.3, 74.3, 72.5, 31.9, 30.3, 29.8, 29.6, 29.3, 25.0, 22.6, 14.0; IR (NaCl) 3452, 2925, 2854, 1456, 1069, 734, 697 cm^{-1}; SM (CI NH_3) *m/z* : 364 ($M+NH_4^+$); Anal. Calcd for $C_{23}H_{38}O_2$: C, 79.71; H, 11.05. Found: C, 79.71; H, 11.01. HRMS cald for $C_{23}H_{39}O_2$ ($M+H^+$) = 347.2950, found 347.2954.

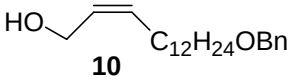
15-benzyloxy-pentadec-2-yn-1-ol (9)



9

To a solution of $LiNH_2$, prepared from Li (3.1 g, 0.44 mol) and liquid NH_3 (450 mL), was added dropwise a solution of 2-propyn-1-ol (12.9 mL, 0.22 mol) in THF (25 mL). After stirring for 90 min at –45°C, a solution of benzyl-12-bromododecylether[30] (26.3 g, 0.074 mol) in THF (50 mL) was added dropwise to the reaction mixture. After 1 hour of stirring at –45°C, ether (300 mL) was aded, and the ammonia was allowed to evaporate overnight. After addition of a saturated aqueous NH_4Cl solution (300 mL), the aqueous layer was extracted with ether (2x200 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 8/2) to provide propargyl alcohol **9** (20.61 g, 85%). ^{1}H NMR ($CDCl_3$) δ = 7.37-7.25 (m, 5H), 4.50 (s, 2H), 4.22 (br s, 2H), 3.46 (t, *J* = 6.6 Hz, 2H), 2.23-2.16 (m, 2H), 1.90 (br s, 1H), 1.63-1.55 (m, 2H), 1.51-1.44 (m, 2H), 1.36-1.25 (m, 20H); ^{13}C NMR ($CDCl_3$) δ = 138.8, 128.4, 127.7, 127.6, 86.6, 78.5, 72.9, 70.6, 51.2, 29.8, 29.7, 29.6, 29.2, 29.0, 28.7, 26.3, 18.8; SM (CI NH_3) *m/z* : 331 ($M+H^+$), 348 ($M+NH_4^+$); IR (NaCl) 3415, 2927, 2854, 735, 698 cm^{-1}; Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10,37. Found: C, 80.17; H, 10.24.

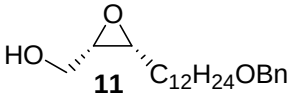
15-benzyloxy-pentadec-2-yn-1-ol (10)



10

To a solution of nickel acetate tetrahydrate (3.76 g, 15.11 mmol) in methanol (75 mL) was added at 0°C sodium borohydride (0.57g, 15.11 mmol). The mixture was stirred at RT for 15 min and then ethylene diamine (2 mL, 30.2 mmol) and alkyne **9** (20 g, 60.4 mmol) in solution in methanol (50 mL) were added. The mixture was stirred under H_2 atmosphere for 5 hours, and filtered through a pad of celite. Solvent were removed under reduced pressure and the residue was purified by flash column chromatography (pentane/Et_2O 8/2) to provide allyl alcohol **10** (19.48 g, 82%). ^{1}H NMR ($CDCl_3$) δ = 7.34-7.24 (m, 5H), 5.60-5.49 (m, 2H), 4.49 (s, 2H), 4.16 (d, *J* = 5.8 Hz, 2H), 3.41 (t, *J* = 5.9 Hz, 2H), 2.09-2.01 (m, 2H), 1.74 (br s, 1H), 1.66-1.52 (m, 2H), 1.35-1.25 (m, 18H); ^{13}C NMR ($CDCl_3$) δ = 138.8, 133.0, 128.5, 127.7, 127.5, 72.9, 70.6, 58.6, 29.8, 29.7, 29.6, 29.3, 27.5, 26.3 ; SM (CI NH_3) *m/z* : 350 ($M+NH_4^+$); IR (NaCl) 3372, 2925, 2853, 734, 697cm^{-1}; Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 80.63; H, 10.77.

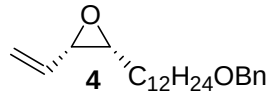
(2S, 3R)-15-benzyloxy-2,3-epoxy-hexadecan-1-ol (11)



11

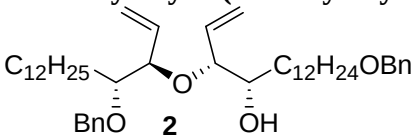
Titanium (IV) isopropoxide (0.45 mL, 1.5 mmol) was added dropwise to a mixture of (+)-DET (0.31 mL, 1.8 mmol) in CH_2Cl_2 (75 mL) and molecular sieves (4Å, 4 g) cooled to -25°C. After stirring for 30 min, a solution of *tert*-butyl hydroperoxide (5M, 25 mL, 75 mmol) in CH_2Cl_2 was added slowly. The mixture was kept at –25°C and stirred for 30 min before a solution of alcohol **10** (10 g, 30 mmol) in CH_2Cl_2 (25 mL) was added over a period of 45 min. The solution was kept at -25°C and stirred for 14 days. The reaction mixture was warmed to 0°C, and quenched with a solution of tartaric acid (1.6 g) and iron (II) sulfate heptahydrate (5 g) in water (50 mL). After 30 min of stirring the mixture was filtered, the organic layer was separated and the aqueous phase was extracted with ether (3x50 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 7/3) to provide epoxy alcohol **11** (10.91 g, 82%).^{1}H NMR ($CDCl_3$) δ = 7.34-7.25 (m, 5H), 4.49 (s, 2H), 3.83 (dd, *J* = 12.2, 4.3 Hz, 1H), 3.64 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.45 (t, *J* = 6.7 Hz, 2H), 3.14 (dt, *J* = 7.3, 4.3 Hz, 1H), 3.04-2.98 (m, 1H), 1.68-1.14 (m, 20H); ^{13}C NMR ($CDCl_3$) δ = 138.8, 128.4, 127.7, 127.5, 72.9, 70.6, 60.9, 58.8, 57.2, 29.9, 29.7, 28.1, 26.7, 26.3; IR (NaCl) 3416, 2924, 2853, 1102, 735, 698 cm^{-1}; SM (CI NH_3) *m/z* : 366 ($M+NH_4^+$). $[\alpha]^{20}_D$ = -1.2 (*c* = 1.05, CH_2Cl_2); Anal. Calcd for $C_{22}H_{36}O_3$: C, 75.72; H, 10.41. Found: C, 75.82; H, 10.38.

(3S, 4R)-16-benzyloxy-3,4-epoxy-pentadecan-1-ol (4)



A solution of allyl alcohol **11** (1.05 g, 3.0 mmol) in CH_2Cl_2 (10 mL) at 0°C was treated with DMSO (2.5 mL, 35.2 mmol) and NEt_3 (2.1 mL, 15.0 mmol). To this solution, kept at 0°C was added SO_3.pyridine complex (1.92 g, 12.0 mmol) in four portions. After 1 hour of stirring at 0°C the solution was diluted with ether (20 mL) and washed with a saturated aqueous NH_4Cl solution (2x15 mL) and with HCl 1M (2x15 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford the crude aldehyde (1.1 g). Sodium bis(trimethylsilyl)amide (1.0M in THF, 3.6 mL, 3.6 mmol) was added dropwise to a suspension of methyltriphenylphosphonium bromide (1.61 g, 4.5 mmol) in THF (15 mL) at 0°C. After 45 min of stirring, the crude aldehyde (1.1 g) in THF (5 mL) was added at 0°C. Stirring was continued for 90 min at 0°C before acetone (2 mL) and ether (15 mL) were added. The organic layer was separated, washed with a saturated aqueous NH_4Cl solution (3x15 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 98/2) to provide epoxide **4** (745 mg, 71%). ^{1}H NMR ($CDCl_3$) δ = 7.34-7.25 (m, 5H), 5.73-5.65 (m, 1H), 5.39 (dd, *J* = 1.8, 18.9 Hz, 1H), 5.34 (dd, *J* = 1.8, 10.4 Hz, 1H), 4.50 (s, 2H), 3.46 (t, *J* = 6.7 Hz, 2H), 3.39 (dd, *J* = 5.5, 2.0 Hz, 1H), 3.08-3.05 (m, 1H), 1.62-1.22 (m, 22H); ^{13}C NMR ($CDCl_3$) δ = 138.8, 132.8, 128.3, 127.6, 127.5, 120.3, 72.9, 70.6, 58.8, 57.2, 29.9, 29.7, 27.8, 26.4, 26.3; IR (NaCl) 2926, 2854, 1455, 1103, 739, 697 cm^{-1}; SM (CI NH_3) *m/z* : 345 ($M+H^+$), 362 ($M+NH_4^+$); Anal. Calcd for $C_{23}H_{36}O_2$: C, 80.18; H, 10.53. Found: C, 80.08; H, 10.51. $[\alpha]^{20}_D$ = +13.7 (*c* = 1.05, CH_2Cl_2).

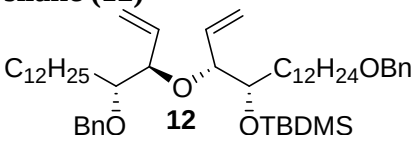
16-benzyloxy-3-(2-benzyloxy-1-vinyl-pentadecyloxy)-hexadec-1-en-4-ol (2)



A solution of allyl alcohol **3** (175 mg, 0.5 mmol) and vinyl epoxide **4** (185 mg, 0.5 mmol) in CH_2Cl_2 (2 mL) was treated with $Cu(OTf)_2$ (2 mg, 5 μmol) and stirred at RT for 1 hour. The mixture was then concentrated under reduced pressure. The crude was purified by flash column chromatography (pentane/Et_2O 9/1) to provide diene **2** (121 mg, 35%) and alcohol **3** (80 mg, 46%). ^{1}H NMR ($CDCl_3$) δ = 7.36-7.27 (m, 10H), 5.68 (ddd, *J* = 17.6, 10.4, 8.1 Hz, 1H), 5.67 (ddd, *J* = 17.1, 14.1, 7.9 Hz, 1H), 5.33-5.19 (m, 4H), 4.70 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.51 (s, 2H), 3.96 (dd, *J* = 7.9, 5.5 Hz, 1H), 3.64 (t, *J* = 7.9 Hz, 1H), 3.49-3.41 (m, 3H), 3.47 (t, *J* = 6.7 Hz, 2H), 1.70-1.20 (m, 44H), 0.89 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ = 138.9, 135.7, 135.5, 128.4, 128.1, 127.7, 127.6, 120.2, 119.4, 81.7, 81.4, 79.8, 73.5, 73.3, 73.0, 70.7, 32.7, 32.1,

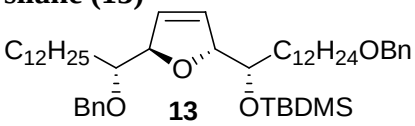
30.9, 29.8, 29.5, 26.3, 25.8, 25.7, 25.2, 22.8, 14.3; IR (NaCl) 3463, 2924, 2853, 1455, 1102, 733, 696 cm^{-1}; SM (CI NH_3) *m/z* : 708 ($M+NH_4^+$). HRMS cald for $C_{46}H_{75}O_4$ $(M + H)^+$ = 691.5665, found: 651.5671.

(13-benzyloxy-1-[1-(2-benzyloxy-1-vinyl-tetradecyloxy)-allyl] tridecyloxy)-*tert*-butyl-dimethyl-silane (12)



A solution of diene alcohol **2** (90 mg, 0.13 mmol) in CH_2Cl_2 (2 mL) was treated with 2,6-lutidine (75 μL, 0.65 mmol) and then cooled to –40°C. TBDMSOTf (90 μL, 0.39 mmol) was added and the mixture was stirred for 1 hour. After addition of a saturated aqueous $NaHCO_3$ solution (2 mL), the mixture was extracted with CH_2Cl_2 (2x10 mL). The combined extracts were dried ($MgSO_4$), concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 98/2) to provide **12** (100 mg, 95%). ^{1}H NMR ($CDCl_3$) δ = 7.37-7.27 (m, 10H), 5.83-5.66 (m, 2H), 5.30-5.20 (m, 4H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.53 (s, 2H), 3.93 (t, *J* = 7.0 Hz, 1H), 3.82 (t, *J* = 6.1 Hz, 1H), 3.70-3.60 (m, 1H), 3.47 (t, *J* = 6.7 Hz, 2H), 3.47-3.40 (m, 1H), 1.70-1.20 (m, 44H), 0.80 (br s , 12H), 0.08 (s, 6H); ^{13}C NMR ($CDCl_3$) δ = 139.3, 138.9, 136.0, 135.6, 128.5, 128.4, 128.2, 127.8, 127.6, 118.7, 118.2, 81.3, 80.8, 80.7, 74.5, 73.5, 73.0, 70.7, 32.6, 32.1, 31.1, 30.1, 30.0, 29.8, 29.5, 26.4, 26.1, 25.9, 25.8, 22.9, 18.3, 14.3, -3.9, -4.4; IR (NaCl) 2926, 2854, 1459, 1106, 731, 696 cm^{-1}; SM (CI NH_3) *m/z* : 822 ($M+NH_4^+$); HRMS calcd for $C_{52}H_{89}O_4Si$ ($M+H^+$) = 805.6530, found: 805.6536; $[\alpha]^{20}_D$ = +25.8 (*c* = 1.1, CH_2Cl_2).

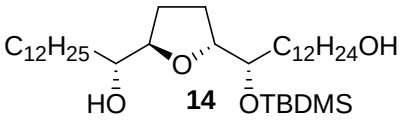
(13-benzyloxy-1-[5-(1-benzyl-tridecyl)-2,5dihydrofuran-2-yl]tridecyloxy)-*tert*-butyl-dimethyl-silane (13)



A solution of diene **12** (100 mg, 124 μmol) in CH_2Cl_2 (6 mL) was treated and stirred with $IMesRuCl_2PCy_3$=CHPh (5 mg, 5 μmol). The mixture was refluxed for 24 hours and then concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 98/2) to provide cyclic ether **13** (77 mg, 80%). ^{1}H NMR ($CDCl_3$) δ = 7.37-7.27 (m, 10H), 5.90 (br s, 2H), 4.95 (t, *J* = 5.2 Hz, 1H), 4.82 (t, *J* = 5.2 Hz, 1H), 4.73 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.52 (s, 2H), 3.69 (br s, 1H), 3.48 (t, *J* = 6.7 Hz, 1H), 3.41 (br s, 1H), 1.68-1.27 (m, 44H), 0.92-0.88 (m, 12H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ = 139.1, 138.9, 129.0, 128.4, 128.1, 127.8, 127.6, 89.4, 88.2, 81.4, 74.6, 73.0, 70.7, 32.5, 32.1, 30.9, 30.0,

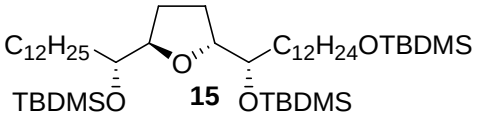
29.8, 29.7, 29.5, 26.4, 26.1, 22.9, 18.3, 14.3, -4.1, -4.5; IR (NaCl) 2925, 2854, 1461, 1251, 1102, 1076, 835, 775 cm^{-1}; SM (CI NH_3) *m/z* : 794 ($M+NH_4^+$); HRMS calcd for $C_{50}H_{84}O_4Si$ ($M+H^+$) = 777.6207, found : 777.6217; $[\alpha]^{20}_D$ = +110.2 (*c* = 1.3, CH_2Cl_2).

1-{5-[1-(*tert*-butyl-dimethyl-silanyloxy)-13-hydroxy-tridecyl)-tetrahydrofuran-2-yl] tridecan-1-ol (14)



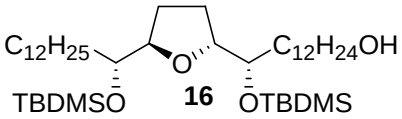
A solution of dihydrofuran **13** (100 mg, 128 μmol) in ethanol (2 mL) was treated with a catalytic quantity of Pd/C 10% and stirred overnight under an hydrogen atmosphere. The mixture was filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 7/3) to provide tetrahydrofuran **14** (76 mg, 100%). ^1H NMR ($CDCl_3$) δ = 3.90-3.73 (m, 2H), 3.64 (t, *J* = 6.7 Hz, 2H), 3.58-3.53 (m, 1H), 3.44-3.33 (m, 1H), 2.00-1.90 (m, 2H), 1.70-1.20 (m, 48H), 0.91-0.80 (m, 12H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 82.6, 82.4, 75.4, 74.3, 63.2, 33.7, 33.4, 33.0, 32.1, 30.0, 29.8, 29.6, 29.5, 29.0, 28.8, 28.6, 25.9, 25.8, 25.6, 22.9, 18.5, 14.3, -3.9,-4.4; IR (NaCl) 3364, 2924, 2853, 1463, 1251, 1070, 834, 775 cm^{-1}; SM (CI NH_3) *m/z* : 616 ($M+NH_4^+$); HRMS calcd for $C_{36}H_{75}O_4Si$ ($M+H^+$) = 599.5435, found: 599.5447; $[\alpha]^{20}_D$ = +9.1 (*c* = 1.2, CH_2Cl_2).

2-[1,13-bis-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-5-[1-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydrofuran (15)



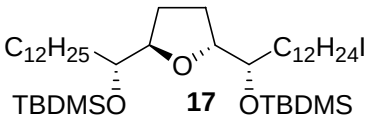
A solution of diol **14** (80 mg, 0.134 mmol) in CH_2Cl_2 (5 mL) was treated with 2,6-lutidine (155 μL, 1.34 mmol) and then cooled to –40°C. TBDMSOTf (184 μL, 0.80 mmol) was added and the mixture was stirred for 1 h. After addition of a saturated aqueous $NaHCO_3$ solution (5 mL), the mixture was extracted with CH_2Cl_2 (2x10 mL). The combined extracts were dried ($MgSO_4$), concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 98/2) to provide **15** (105 mg, 95%). ^1H NMR ($CDCl_3$) δ = 3.94-3.88 (m, 2H), 3.62-3.56 (m, 4H), 1.85-1.25 (m, 48H), 0.90 (br s, 12H), 0.89 (s, 9H), 0.87 (s, 9H), 0.07 (s, 6H), 0.06 (s, 6H) 0.02 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 82.0, 75.0, 63.5, 33.1, 32.8, 32.1, 30.1, 29.8, 29.7, 29.5, 27.5, 26.1, 25.9, 22.9, 18.6, 18.4, 14.3, -4.1, -4.4, -5.1; IR (NaCl) 2927, 2855, 1099, 835, 774 cm^{-1}; SM (CI NH_3) *m/z* : 844 ($M+NH_4^+$); HRMS calcd for $C_{44}H_{93}O_4Si_3$ ($M-tBu^+$) = 769.6382, found : 769.6387; $[\alpha]^{20}_D$ = +15.5 (*c* = 0.9, CH_2Cl_2).

13-(*tert*-butyl-dimethyl-silanyloxy)-13-{5-[1-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydrofuran-2-yl}-tridecan-1-ol (16)



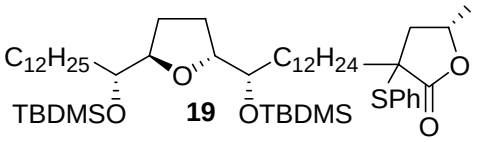
A solution of furan **15** (100 mg, 0.12 mmol) in CH_2Cl_2/MeOH (4 mL, 1/1), cooled to –30°C was treated with CSA (3 mg, 0.012 mmol) and stirred for 4 hours. After addition of a saturated aqueous $NaHCO_3$ solution (4 mL), the mixture was extracted with CH_2Cl_2 (2x5 mL). The combined extracts were dried ($MgSO_4$), concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 8/2) to provide alcohol **16** (81 mg, 95%). ^{1}H NMR ($CDCl_3$) δ = 3.94-3.88 (m, 2H), 3.65 (t, *J* = 6.4 Hz, 2H), 3.62-3.56 (m, 2H), 1.85-1.25 (m, 49H), 0.89 (br s, 21H), 0.07 (s, 6H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 82.0, 75.0, 63.3, 33.0, 32.8, 32.1, 30.0, 29.8, 29.6, 29.5, 27.5, 26.2, 26.1, 25.9, 22.9, 18.4, 14.3, -4.1, -4.3; IR (NaCl) 3423, 2926, 2854, 835, 774 cm^{-1}; SM (CI NH_3) *m/z* : 730 ($M+NH_4^+$); HRMS calcd for $C_{32}H_{63}O_3Si$ (M-*t*Bu-OTBDMS-H^+) = 523.4546, found : 523.4539; $[\alpha]^{20}_D$ = +17 (*c* = 0.785, CH_2Cl_2).

2-[1-(*tert*-Butyl-dimethyl-silanyloxy)-13-iodo-tridecyl]-5-[1-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydrofuran (17)



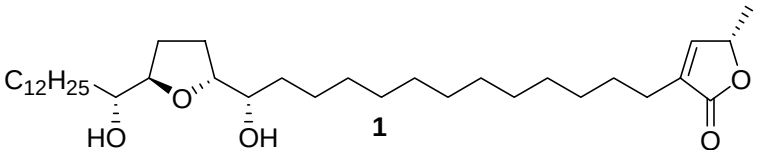
To a solution of **16** (80mg, 0.11 mmol) in CH_2Cl_2 (5 mL) at 0°C was added PPh_3 (40 mg, 0.154 mmol), imidazole (22 mg, 0.33 mmol) and I_2 (35 mg, 0.14 mmol). The mixture was stirred for 1 hour and poured into 10% aqueous Na_2SO_3 solution and diluted with Et_2O. The organic layer was separated and washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash column chromatography (pentane/Et_2O 98/2) to provide iodide **17** (65 mg, 73%). ^{1}H NMR ($CDCl_3$) δ = 3.94-3.88 (m, 2H), 3.64-3.54 (m, 2H), 3.20 (t, *J* = 7.0 Hz, 2H), 1.90-1.20 (m, 48H), 0.89 (br s, 21H), 0.06 (s, 6H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 81.0, 75.0, 63.3, 33.8, 32.8, 32.1, 30.7, 30.1, 29.8, 29.7, 29.6, 28.8, 27.5, 26.1, 22.9, 18.5, 14.3, 7.5, -4.1, -4.3; IR (NaCl) 2922, 2854, 1251, 835, 774 cm^{-1}; SM (CI NH_3) *m/z* : 840 ($M+NH_4^+$); HRMS calcd for $C_{38}H_{78}O_3Si_2$ (M-*t*Bu^+) = 765.4534, found : 765.4526.

3-(13-(*tert*-Butyl-dimethyl-silanyloxy)-13-{5-[1-*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydro-furan-2-yl}-tridecyl)-5-methyl-3-phenylsulfanyl-dihydro-furan-2-one (19)



To a solution of 4-(*S*)-methyl-2-phenylthio-γ-butyrolactone **18** (33 mg, 0.16 mmol) in THF (1.5 mL) at 0°C was added sodium bis(trimethylsilyl)amide (158 μL, 1.0 M solution in THF). After 1 hour of stirring, the mixture was treated with a solution of iodide **17** (65 mg, 0.08 mmol) in HMPA (1.5 mL). The mixture was stirred for 2 hours and then poured into a saturated aqueous NH_4Cl solution and extracted with ether. The combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash column chromatography (pentane/Et_2O 9/1) to provide **19** (54 mg, 75%); ^1H NMR ($CDCl_3$) δ = 7.60-7.32 (m, 5H) , 4.50-4.44 (m, 1H), 3.92-3.86 (m, 2H), 3.58-3.55 (m, 2H), 2.52 (dd, *J* = 14.0, 7.9 Hz, 1H), 1.97 (dd, *J* = 14.0, 6.7 Hz, 1H), 1.80-1.20 (m, 48H), 0.89 (br s, 25H), 0.04 (s, 6H) 0.03 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 177.1, 136.8, 129.7, 129.0, 81.8, 74.8, 73.5, 73.1 56.2, 36.5, 32.6, 31.9, 30.3, 29.9, 29.6, 29.4, 27.3, 26.0, 25.9, 24.7, 22.7, 21.5, 18.2, 14.1, -4.3, -4.5; IR (NaCl) 2926, 2854, 1770, 1463, 1251, 1183, 835, 774 cm^{-1}; SM (CI NH_3) *m/z* : 920 ($M+NH_4^+$); HRMS calcd for $C_{53}H_{99}O_5S_1Si_2$ ($M+ H^+$) = 903.6751, found : 903.6758.

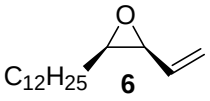
Solamin (1)



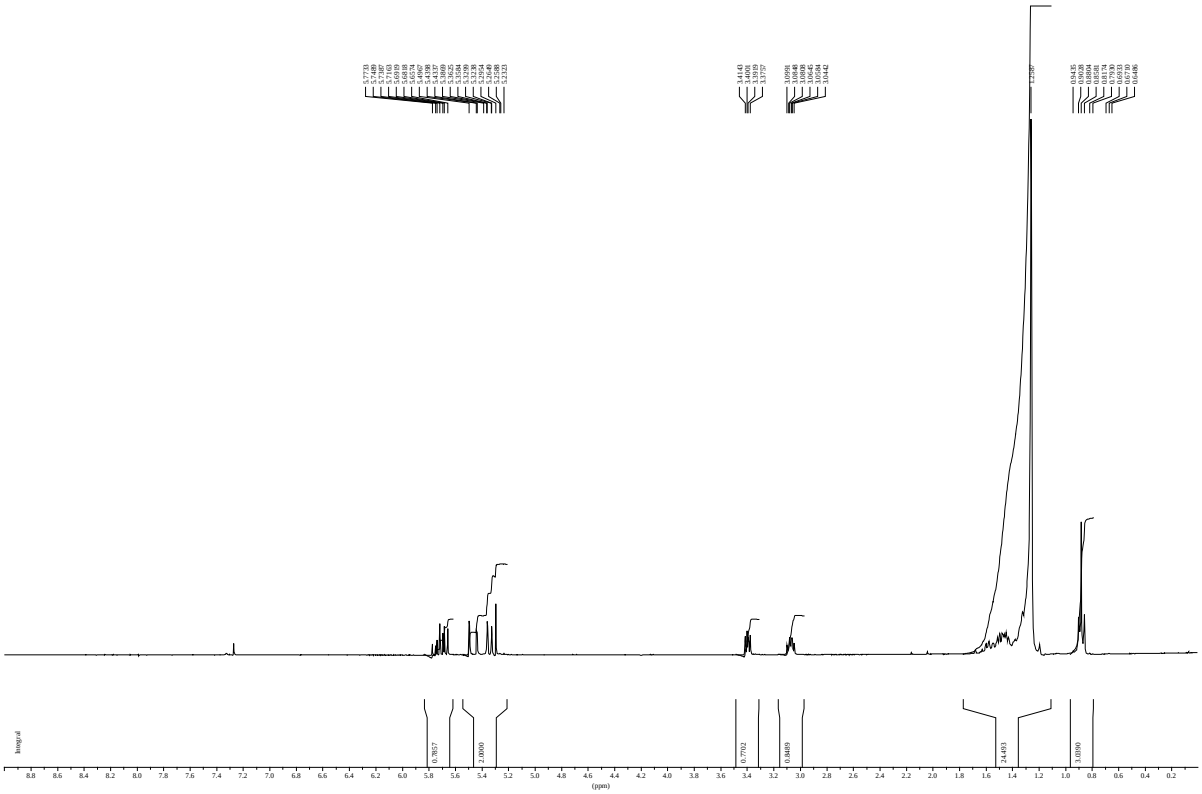
To a solution of lactone **19** (30 mg, 33.2 μmol) in CH_2Cl_2 (1 mL) at 0°C was added *m*CPBA (12 mg, 39.8 μmol). The reaction mixture was stirred for 30 min. and then diluted with CH_2Cl_2 (5 mL) and washed with saturated aqueous $NaHSO_3$ solution (5 mL), followed by a saturated aqueous $NaHCO_3$ solution (5 mL) and brine (5 mL). The organic layers were separated, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dissolved in toluene (1.5 mL) and refluxed for 1 hour, and then the solvent was removed under reduced pressure. The residue was diluted (pentane/Et_2O: 9/1) and filtered through a short plug of silicagel. The filtrate was concentrated, dissolved in methanol (1 mL) and treated with a 5% (v/v) solution of acetyl chloride in methanol (1 mL). The reaction mixture was stirred for 1 hour and then diluted with CH_2Cl_2 (5 mL) and neutralized by the addition of solid $NaHCO_3$. The mixture was filtered through celite, washed with EtOAc and concentrated under reduced pressure. The crude product was purified by flash column

chromatography (pentane/Et_2O 1/1) to provide pure Solamin **1** (16 mg, 85 %) as colourless needles. ^{1}H NMR ($CDCl_3$) δ = 6.99 (d, *J* = 1.5 Hz, 1H), 5.05-4.96 (m, 1H), 3.85-3.75 (m, 2H), 3.45-3.37 (m, 2H), 2.29-2.24 (m, 2H), 2.00-1.97 (m, 2H), 1.72-1.64 (m, 2H), 1.60-1.20 (m, 47H), 0.88 (t, *J* = 6.5 Hz 3H); ^{13}C NMR ($CDCl_3$) δ 173.9, 148.8, 134.4, 82.6, 77.4, 74.0, 33.5, 31.9, 30.3, 29.6, 29.3, 29.2, 28.7, 27.4, 25.6, 25.2, 22.7, 19.2, 14.1; IR (NaCl) 3460, 2919, 2850, 1737, 1469, 1082, 720 cm^{-1}; SM (CI NH_3) *m/z* : 582 ($M+NH_4^+$); HRMS calcd for $C_{35}H_{65}O_5$ ($M+H^+$) = 565.4832, found : 565.4833; Anal. Calcd for $C_{35}H_{64}O_5$: C, 74.42; H, 11.42, Found: C, 74.44; H, 11.40; m.p.= 66-68°C (lit. [25a-b] m.p = 64-68°C); $[\alpha]^{20}_D$ = +21 (*c* = 0.16, MeOH), (lit. [25a-b] $[\alpha]^{20}_D$ = +21 (*c* = 0.16, MeOH)).

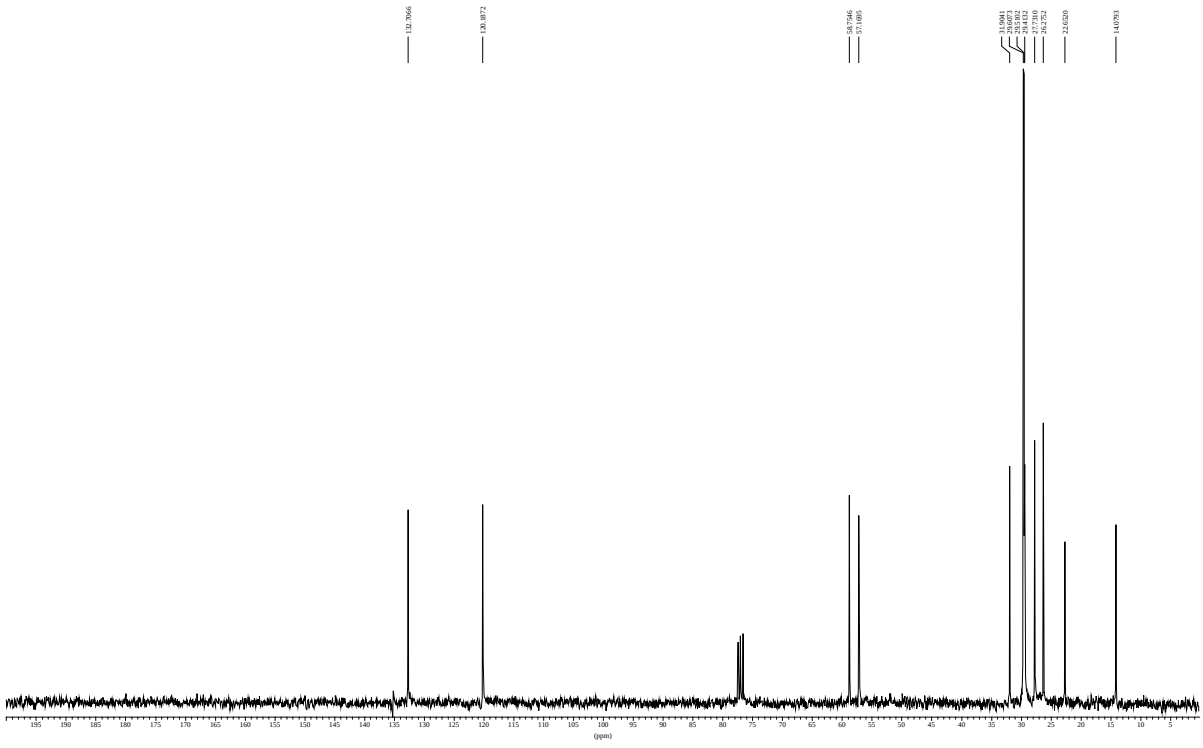
(3S,4R)-3,4-epoxy-hexadecan-1-ol (6)



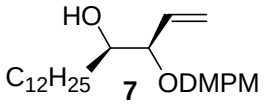
epox 6



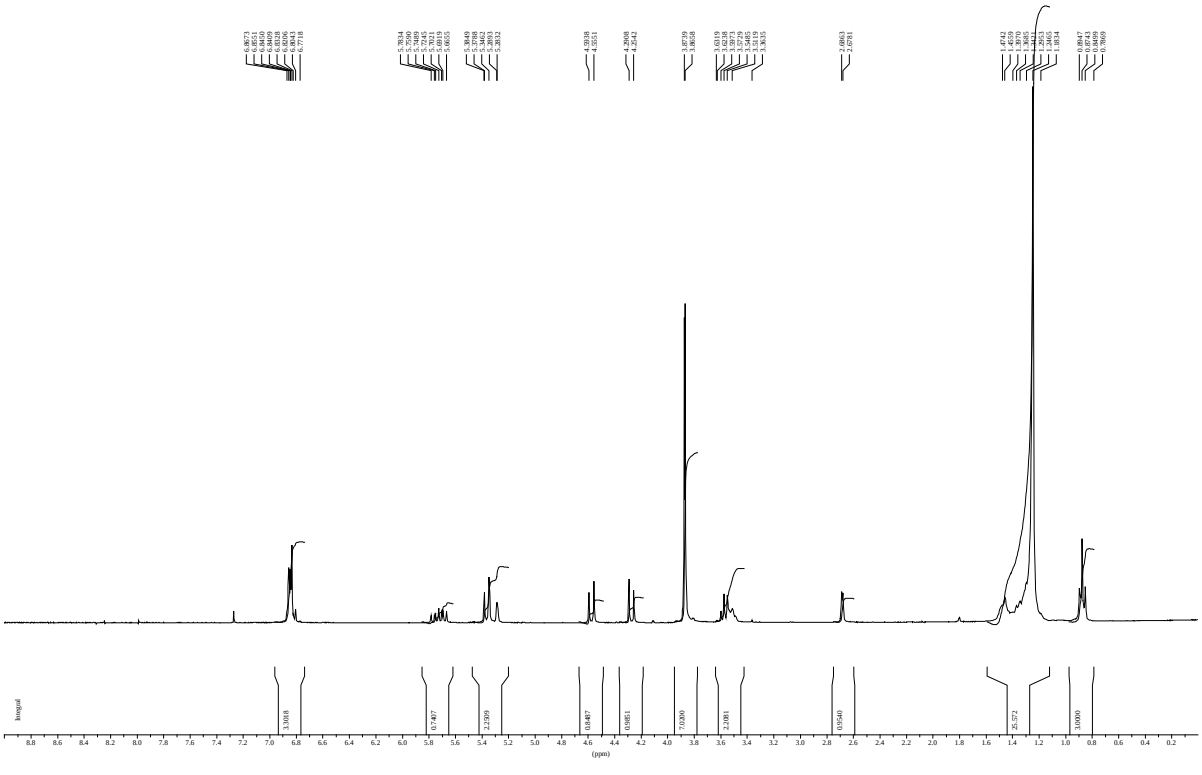
CB 424A



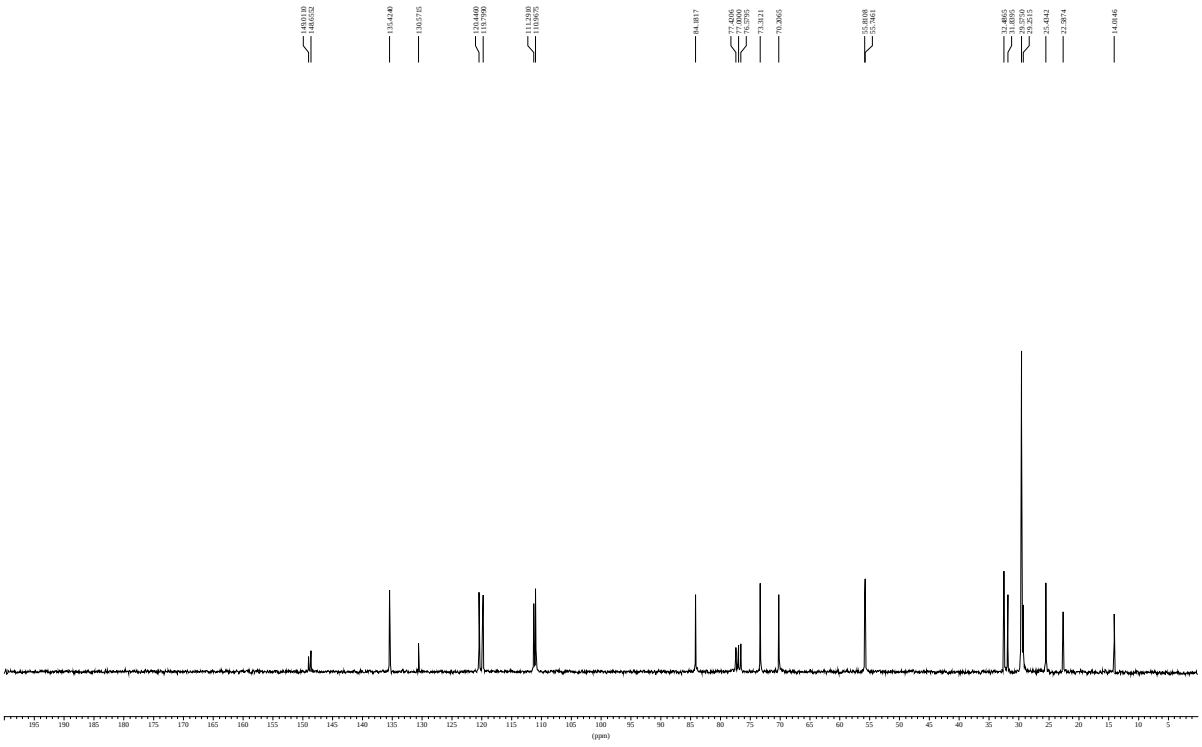
(3R,4R)-3-(3,4-dimethoxy-benzyloxy)-hexadec-1-en-4-ol (7)



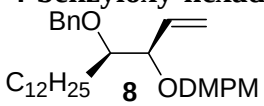
CB 424A



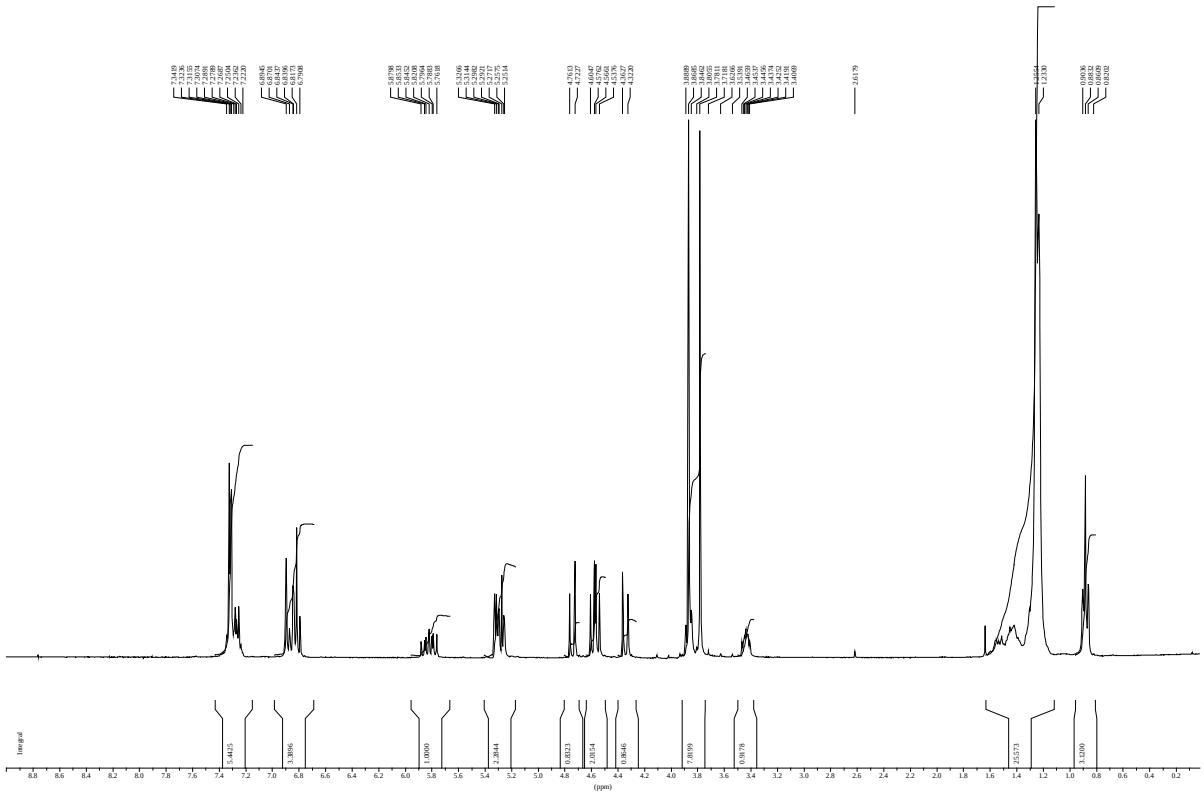
CB 424A



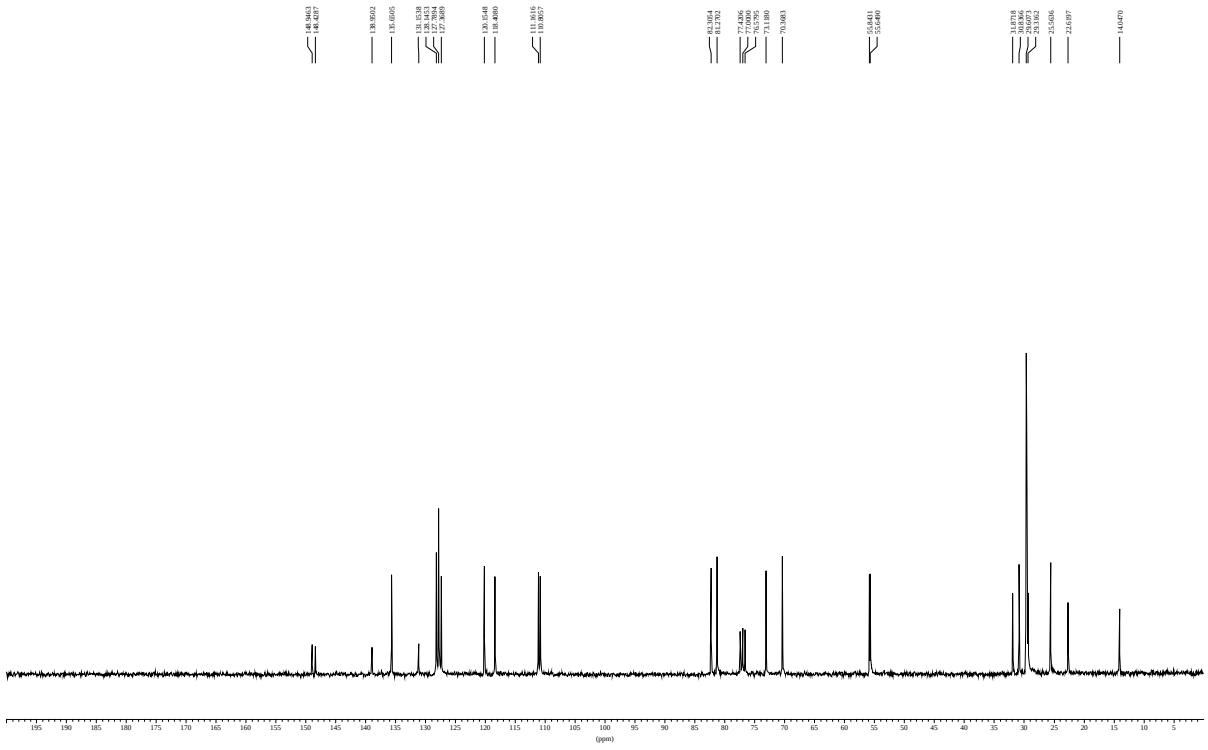
(3R,4R)-3-(3,4-dimethoxy-benzyloxy)-4-benzyloxy-hexadec-1-ene (8)



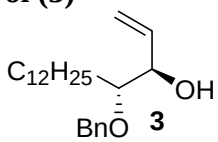
CB 424A



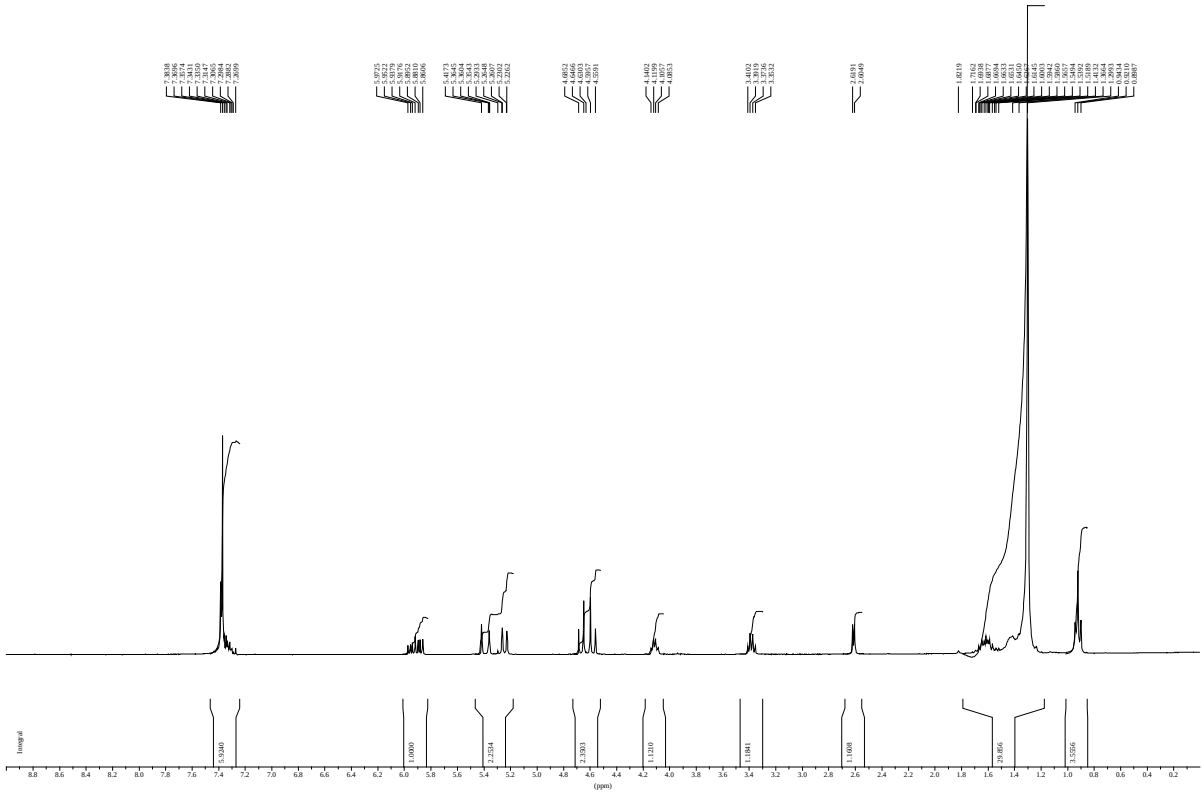
CB 424A



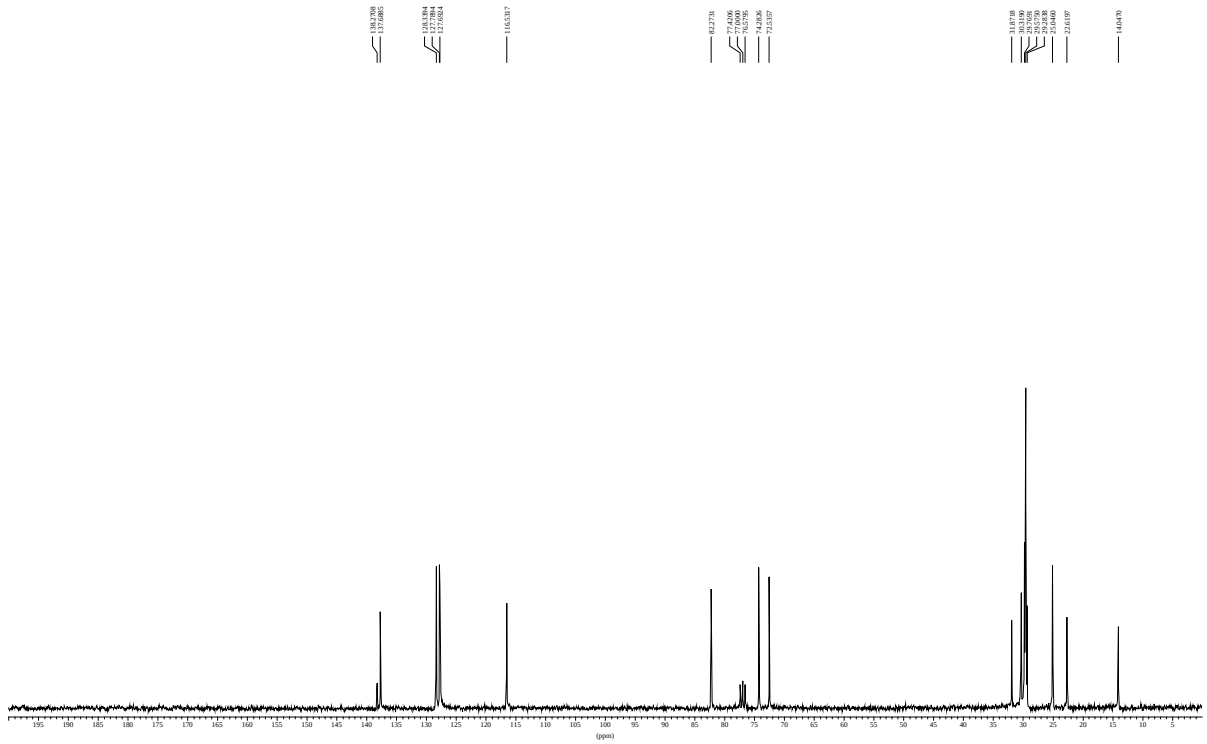
(3R,4R)-4-benzyloxy-hexadec-1-en-3-ol (3)



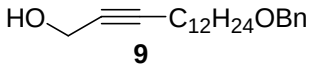
CB 424A



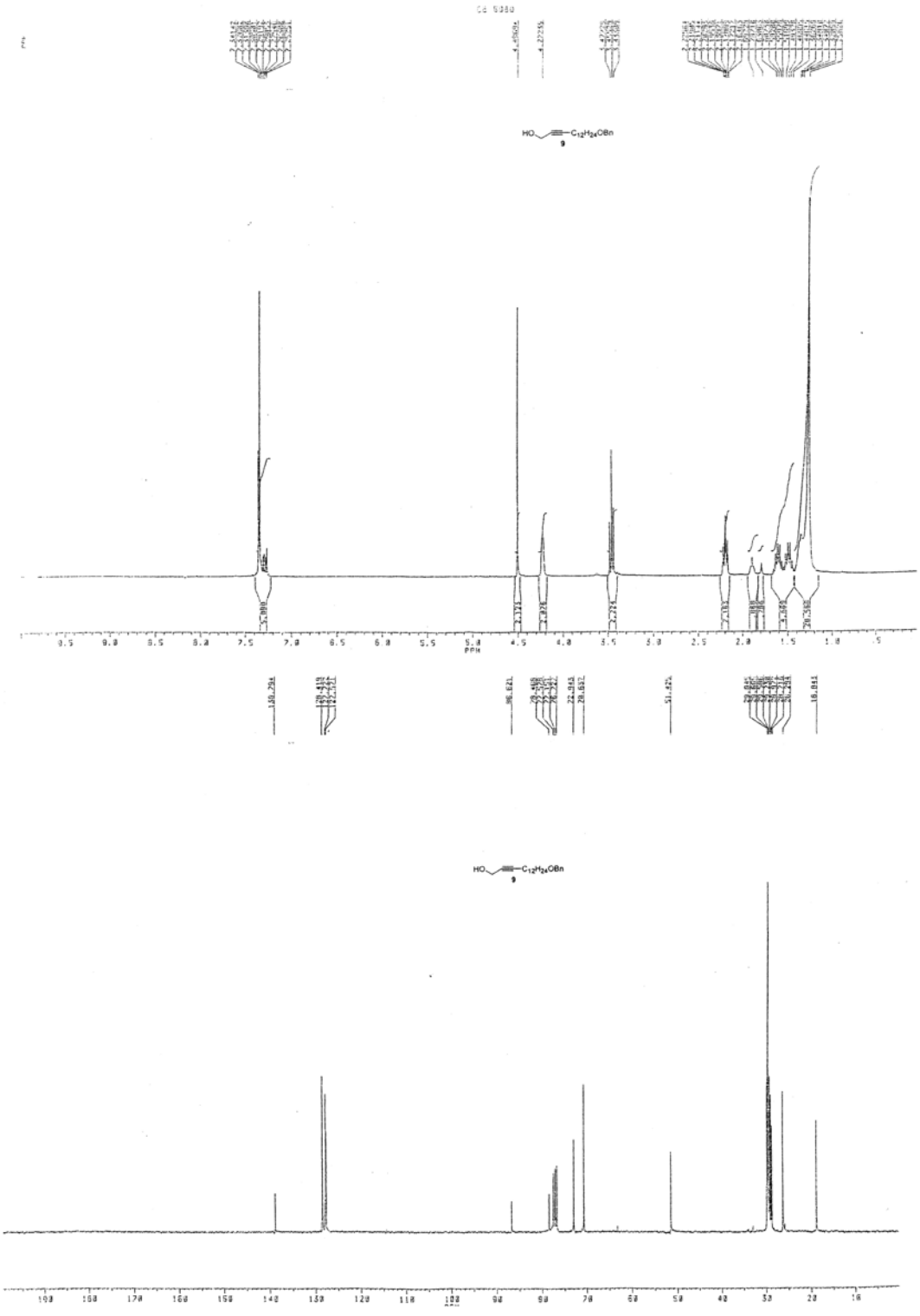
CB 424A



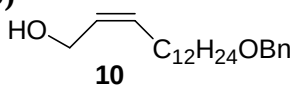
15-benzyloxy-pentadec-2-yn-1-ol (9)



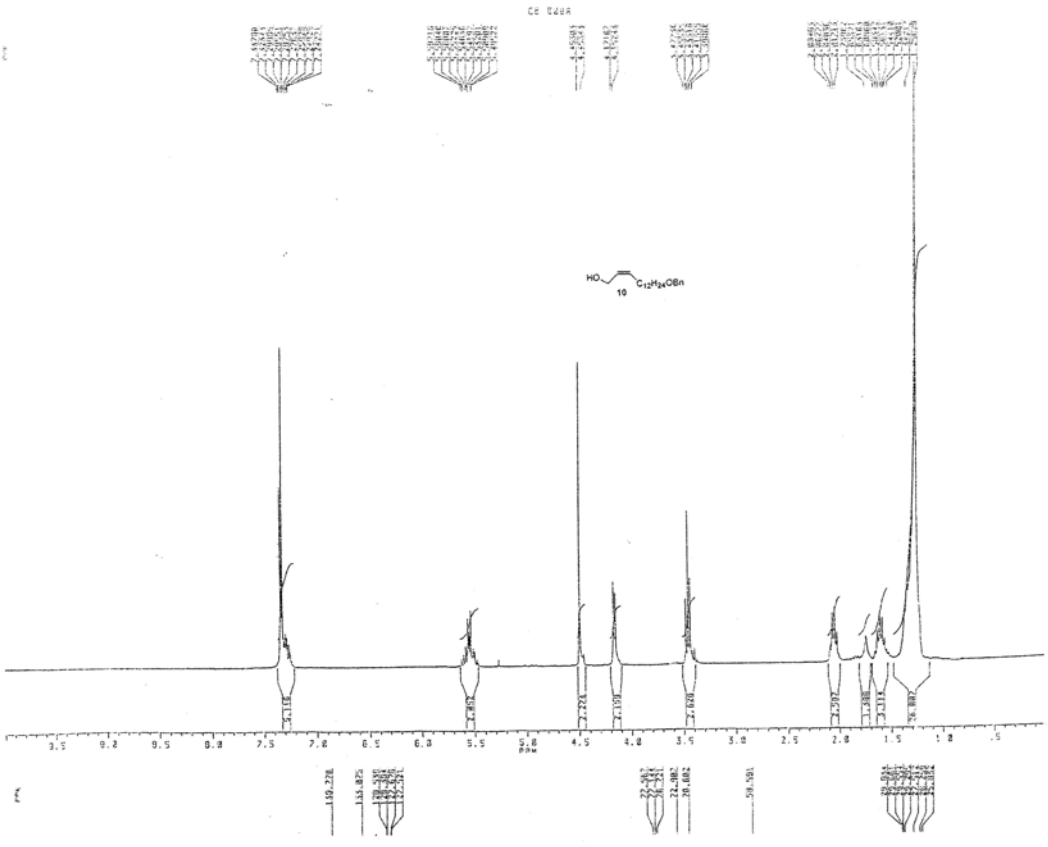
9

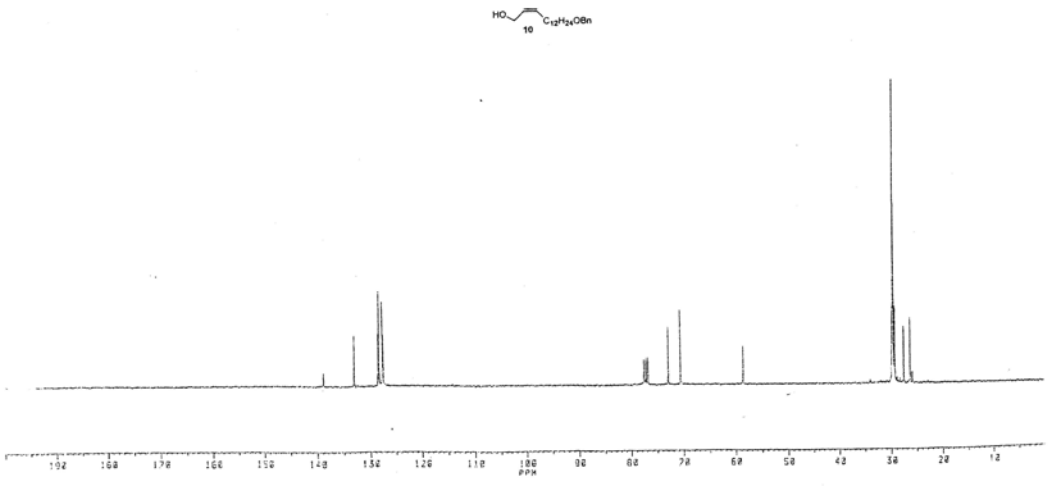


15-benzyloxy-pentadec-2-yn-1-ol (10)

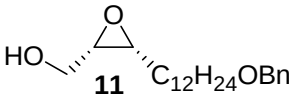


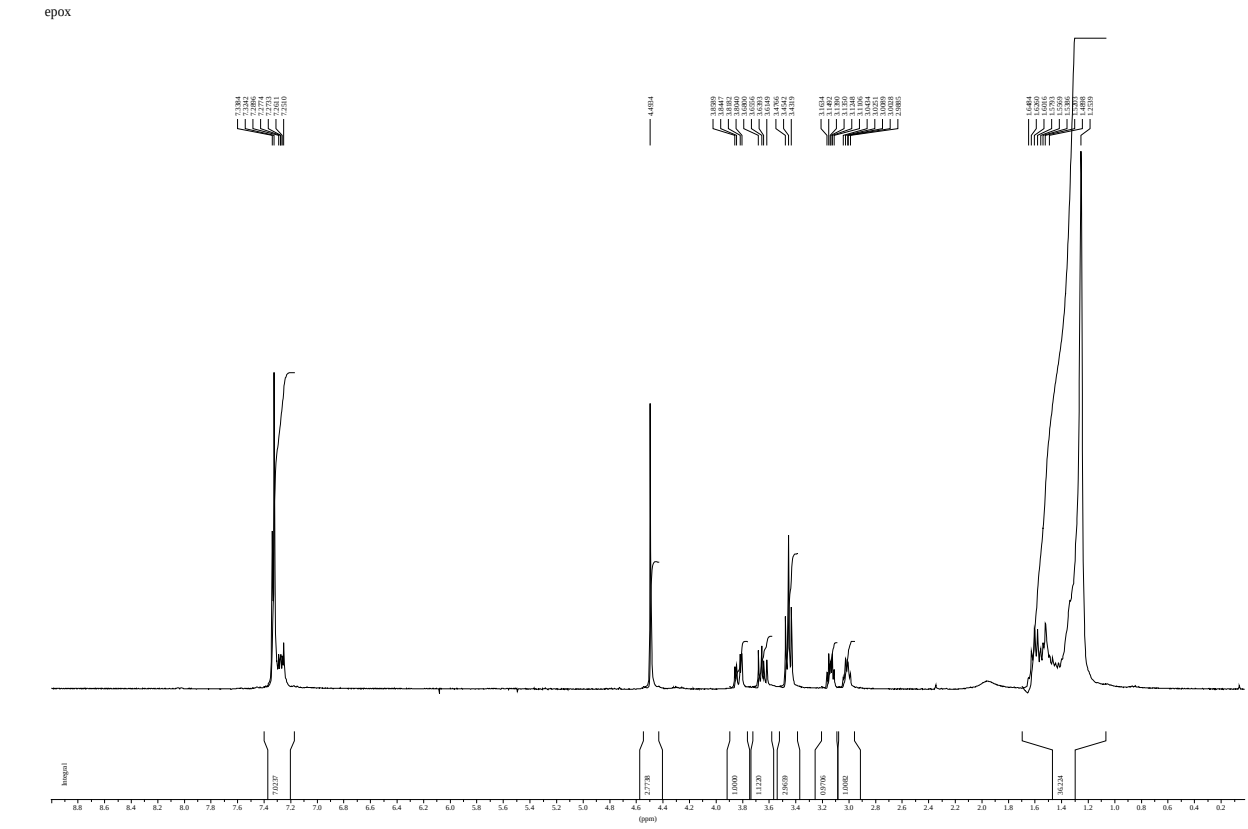
10

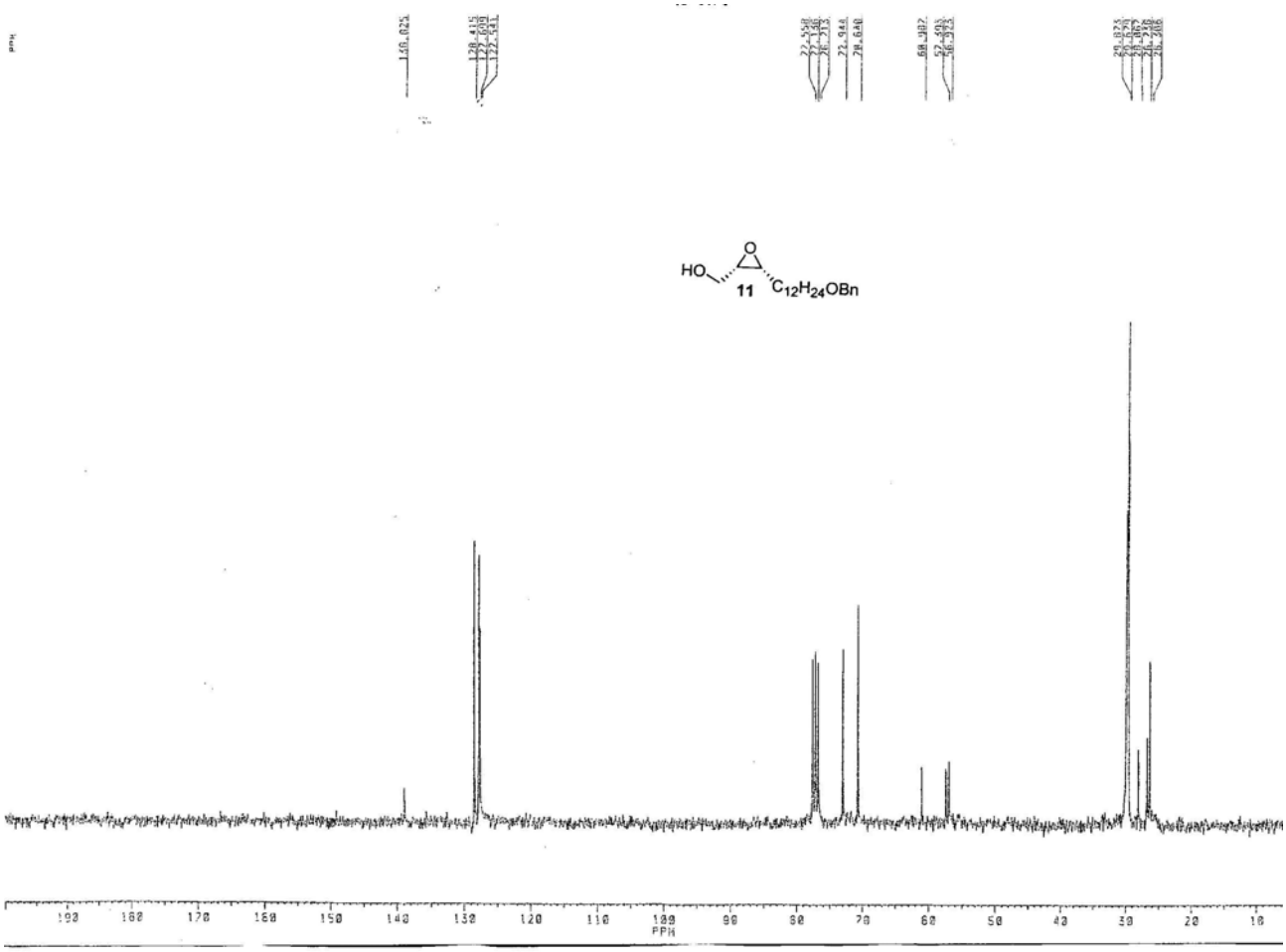




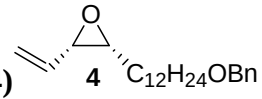
(2S,3R)-15-benzyloxy-2,3-epoxy-hexadecan-1-ol (11)

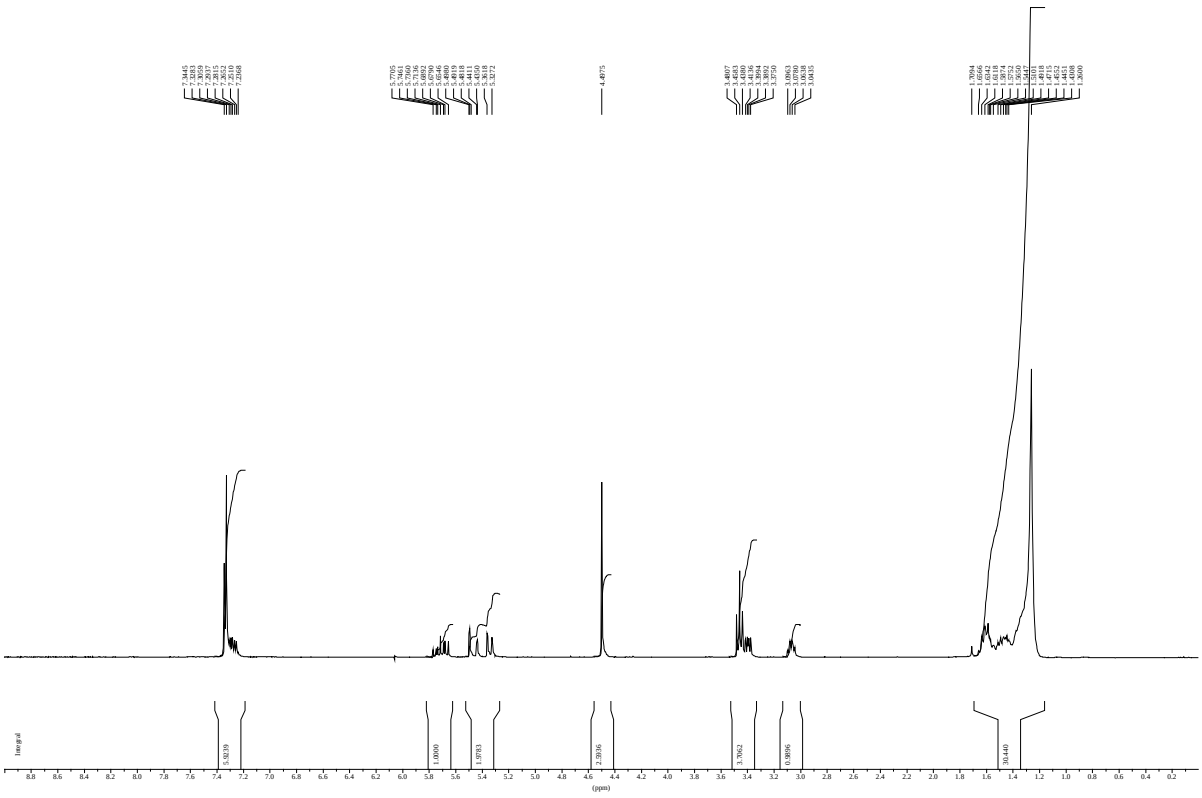


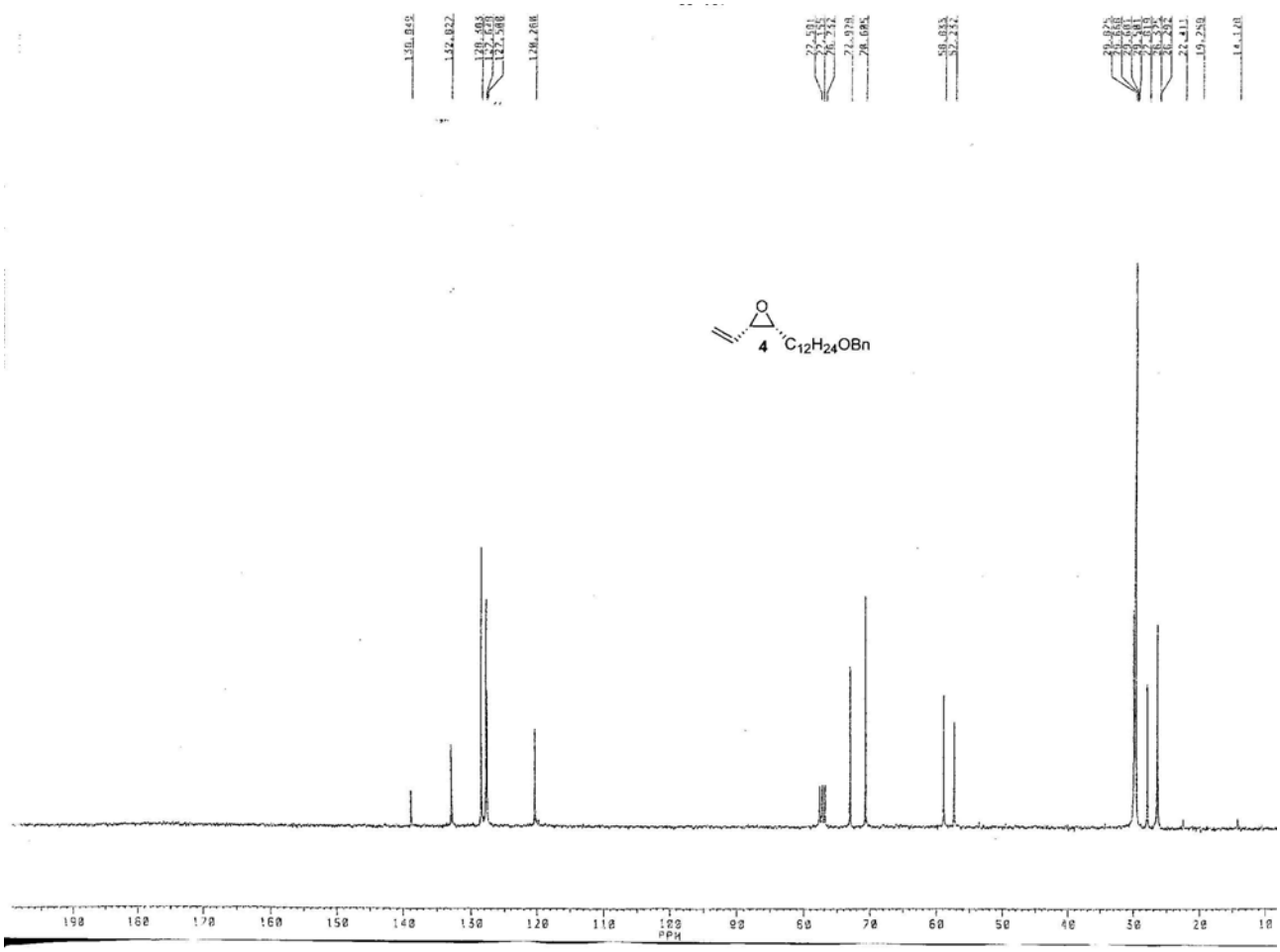




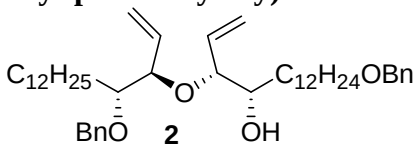
(3S,4R)-16-benzyloxy-3,4-epoxy-pentadecan-1-ol (4)



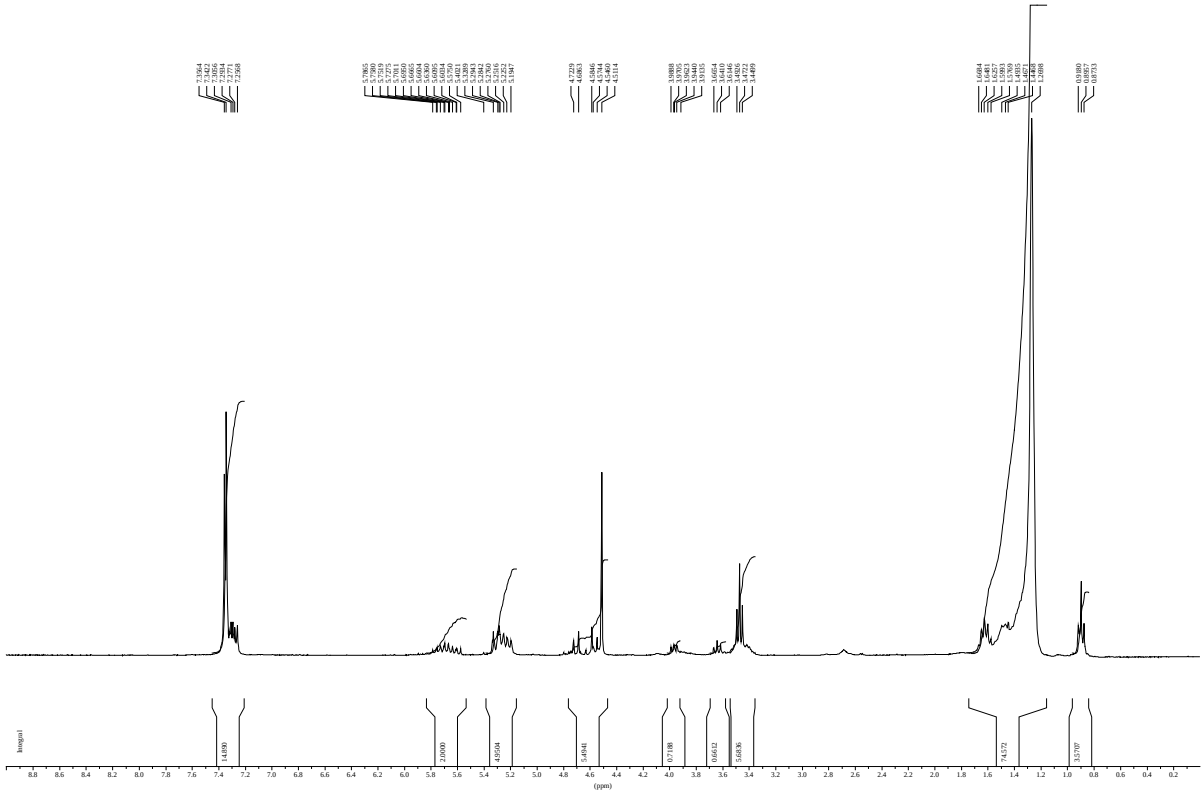




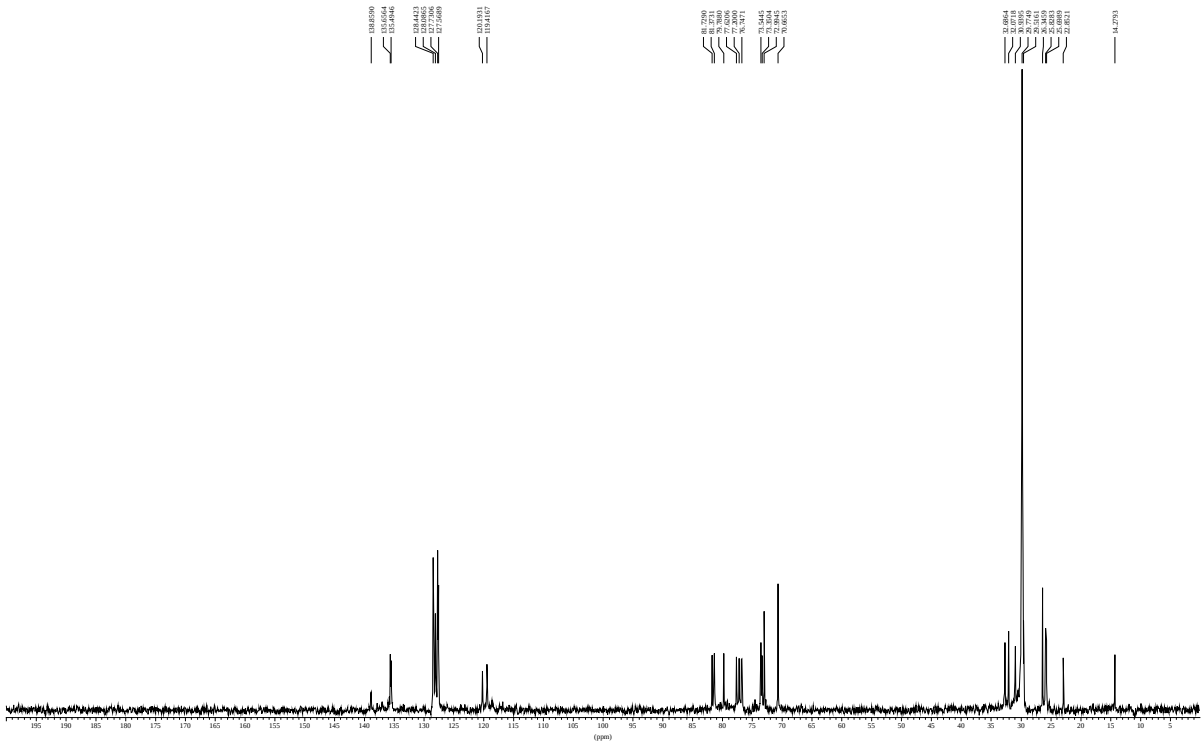
16-benzyloxy-3-(2-benzyloxy-1-vinyl-pentadecyloxy)-hexadec-1-en-4-ol (2)



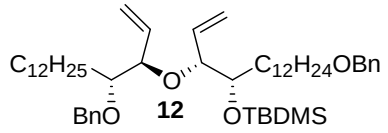
CB 424A



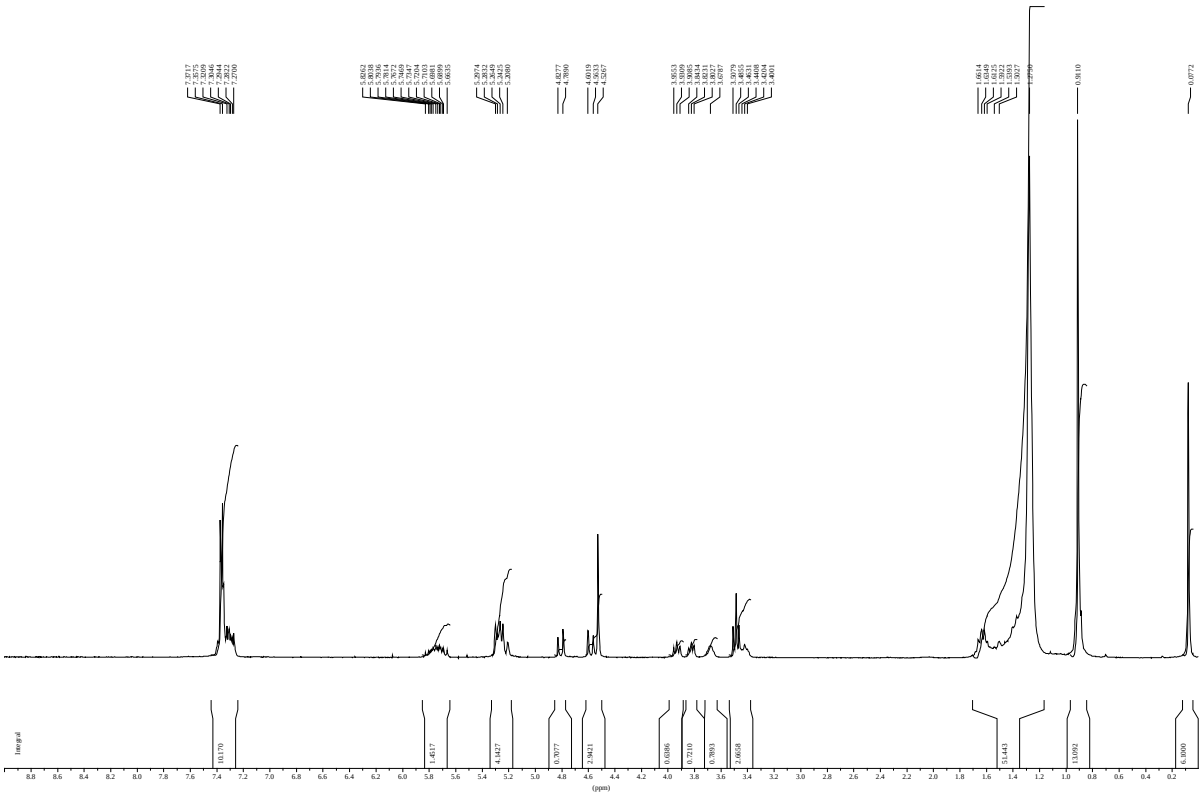
CB 424A



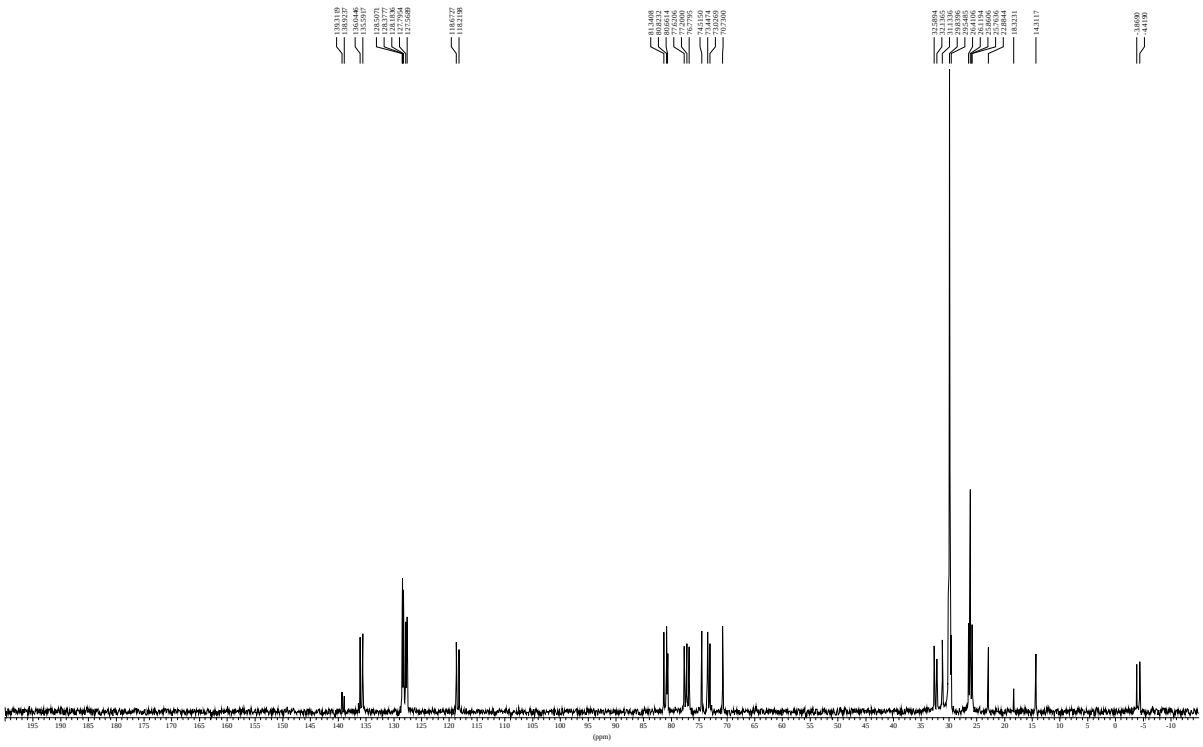
(13-benzyloxy-1-[1-(2-benzyloxy-1-vinyl-tetradecyloxy)-allyl] tridecyloxy)-*tert*-butyl-dimethyl-silane (12)



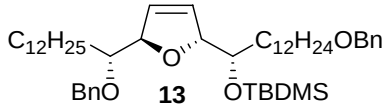
CB 424A



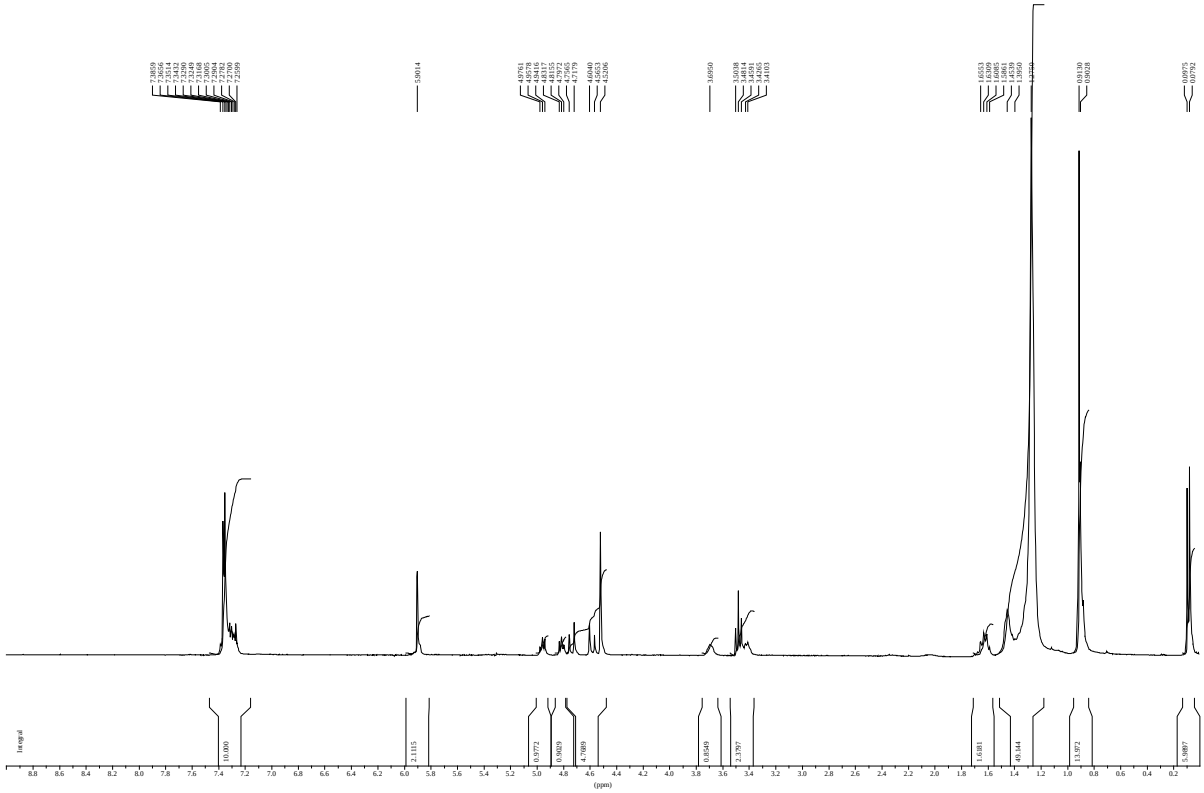
CB 424A



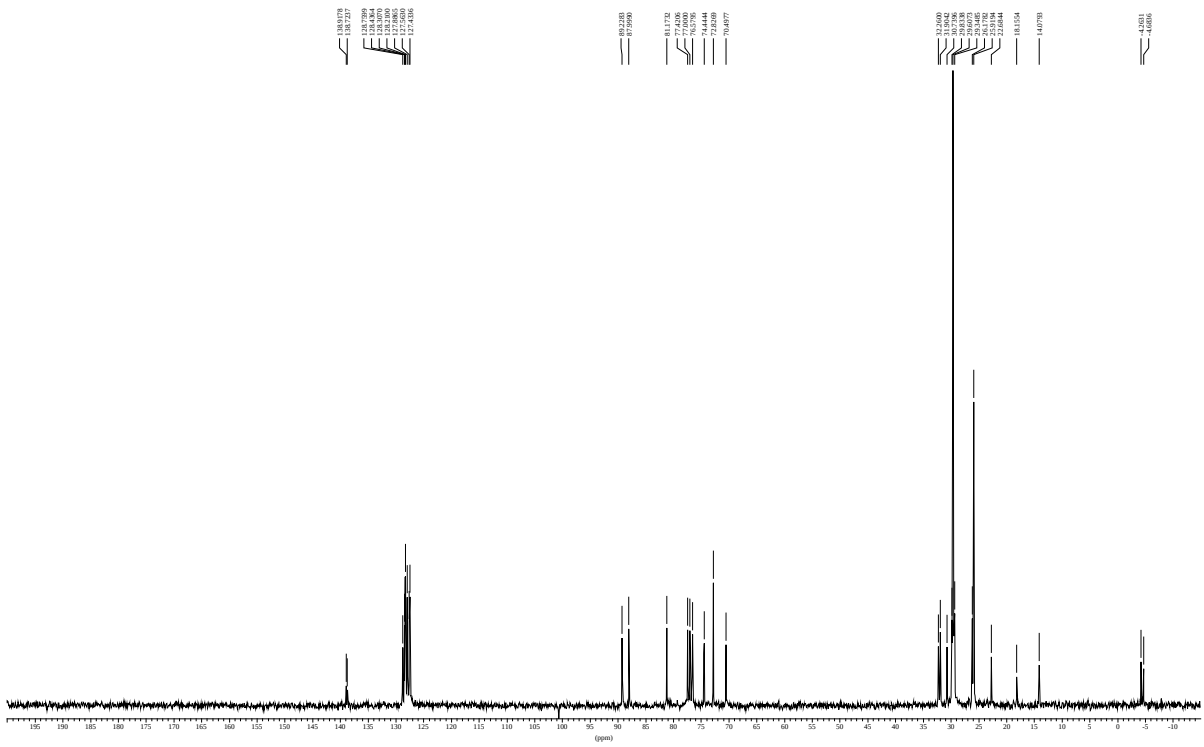
(13-benzyloxy-1-[5-(1-benzyl-tridecyl)-2,5dihydrofuran-2-yl]tridecyloxy)-*tert*-butyl-dimethyl-silane (13)



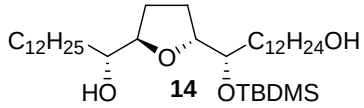
CB 424A



gp 128b

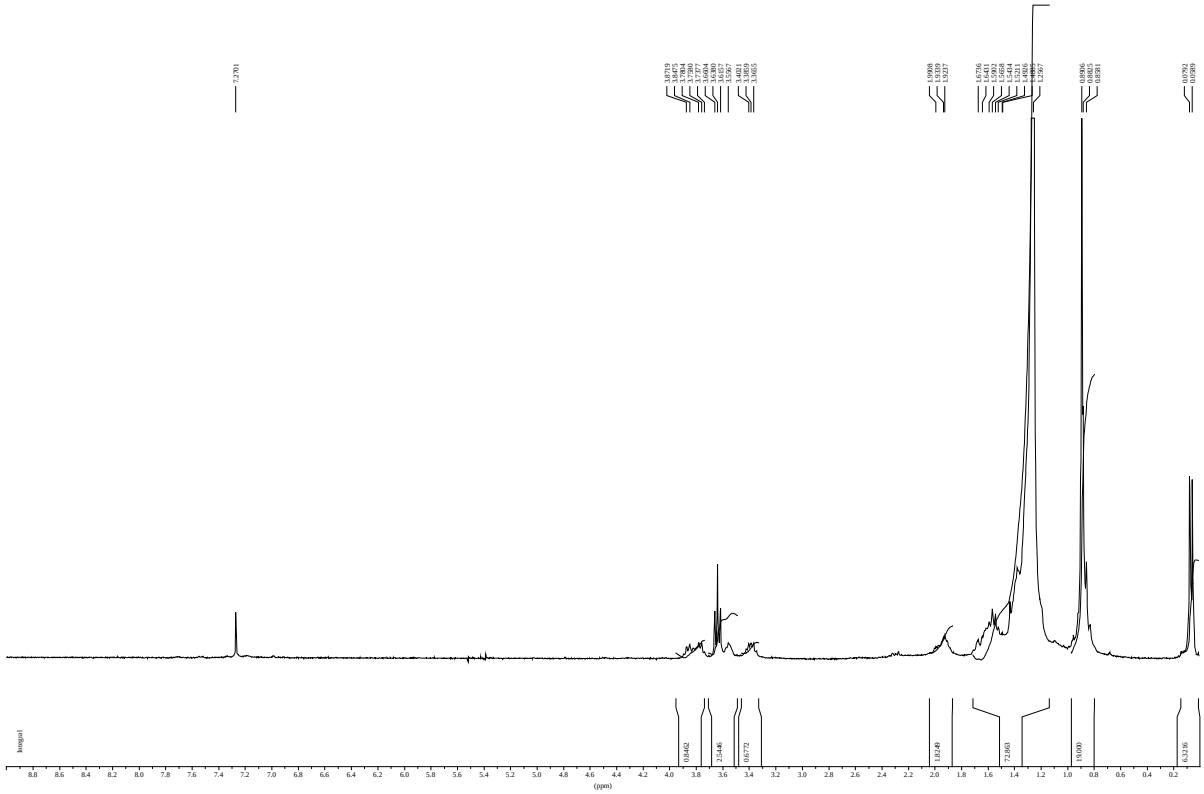


1-{5-[1-(*tert*-butyl-dimethyl-silanyloxy)-13-hydroxy-tridecyl)-tetrahydrofuran-2-yl] tridecan-1-ol (14)

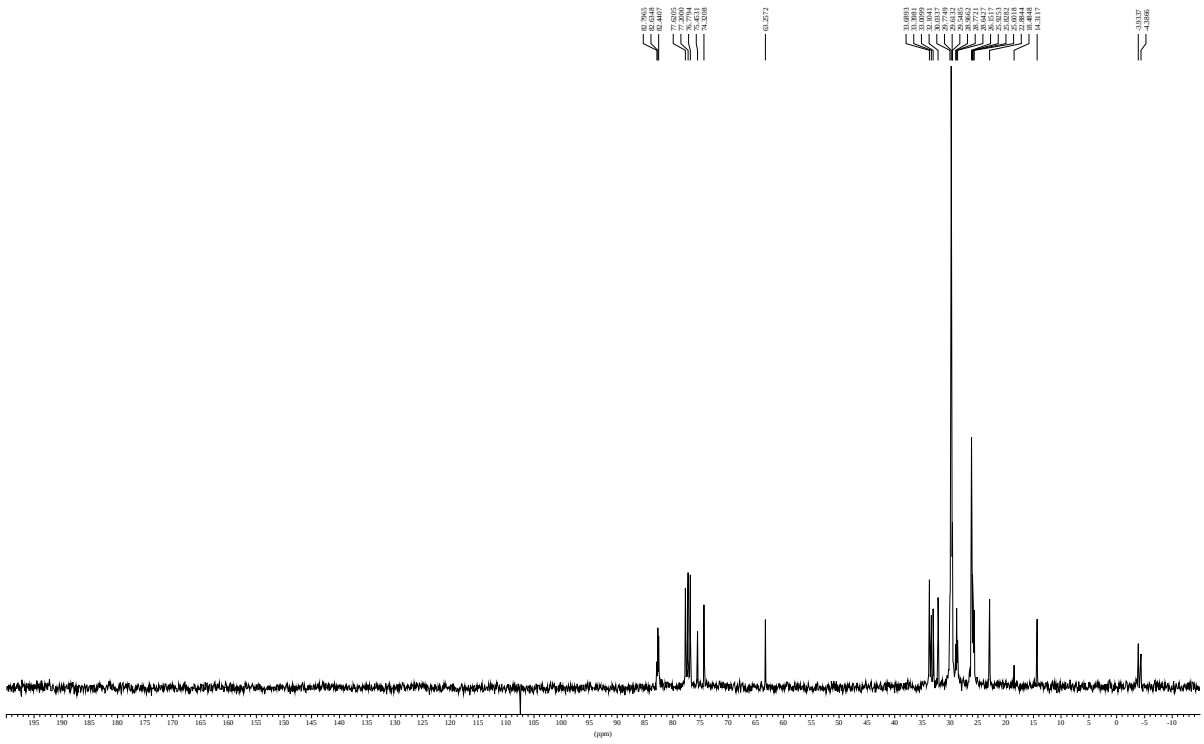


14

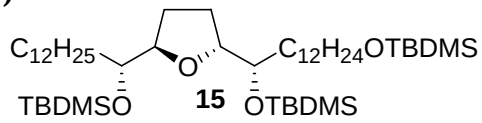
CB 424A



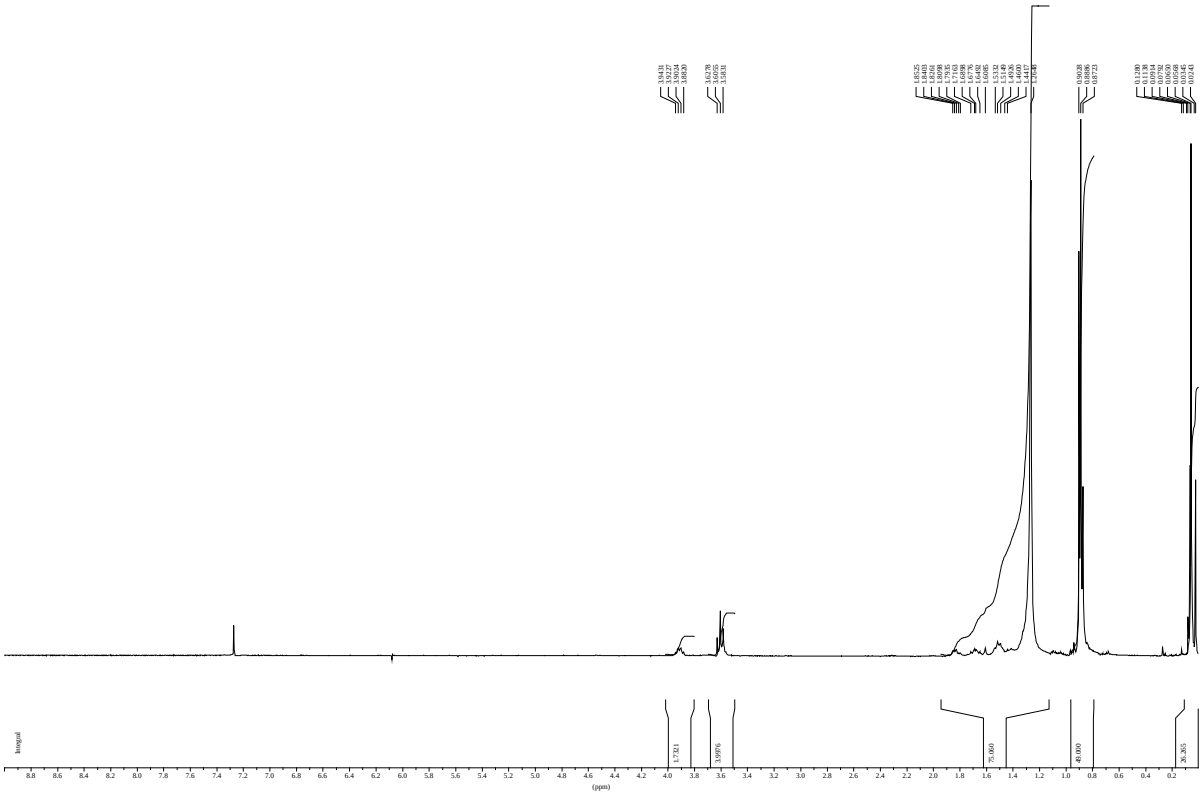
CB 424A



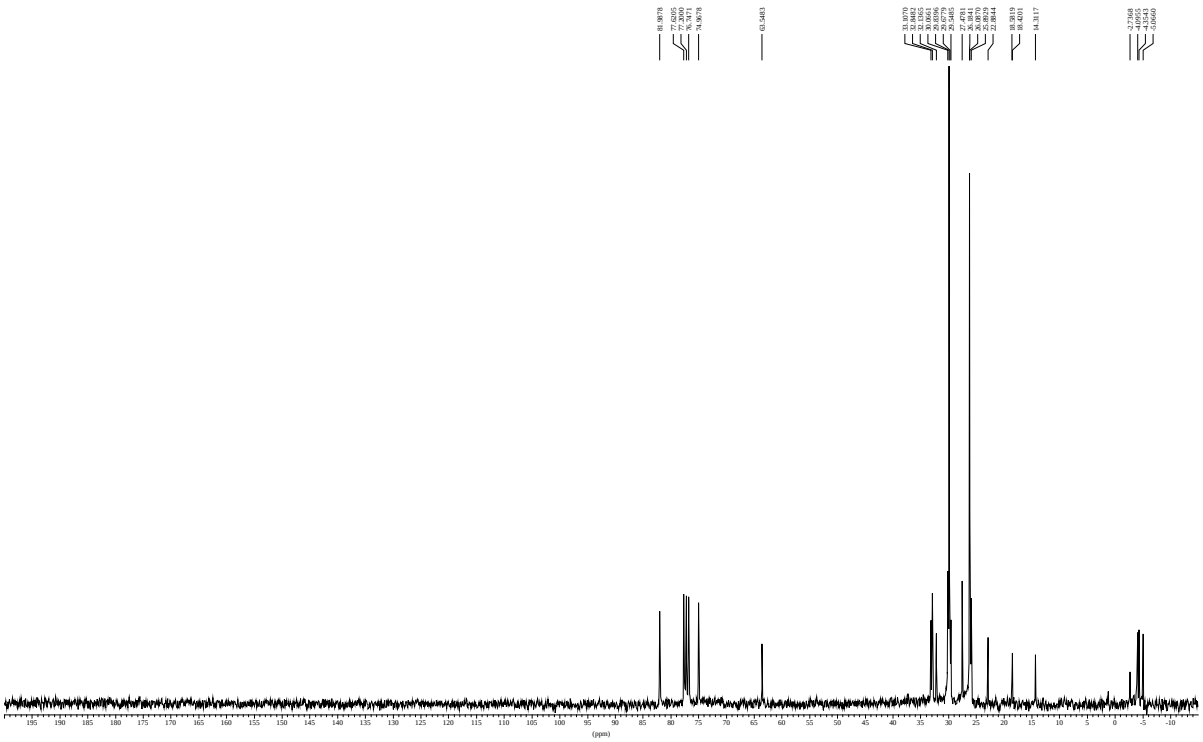
2-[1,13-bis-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-5-[1-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydrofuran (15)



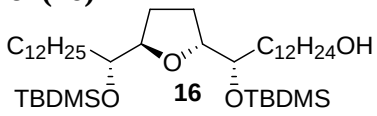
CB 424A



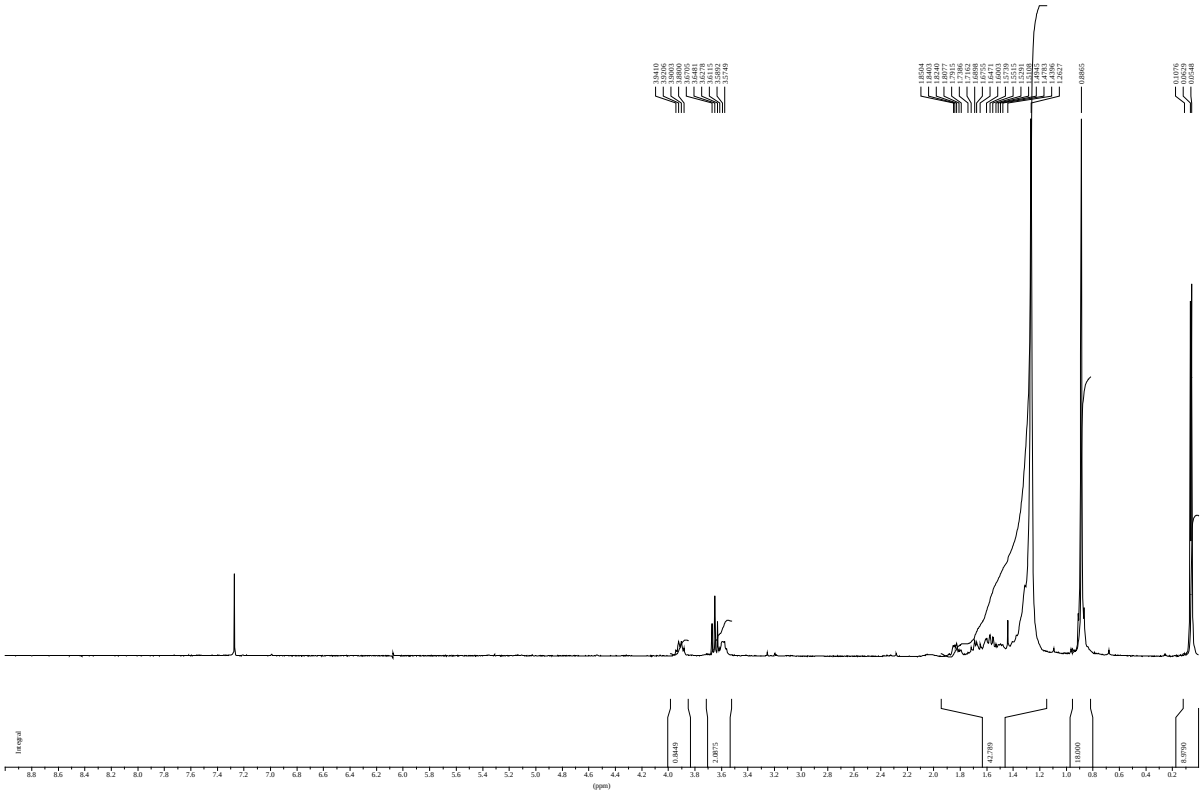
CB 424A



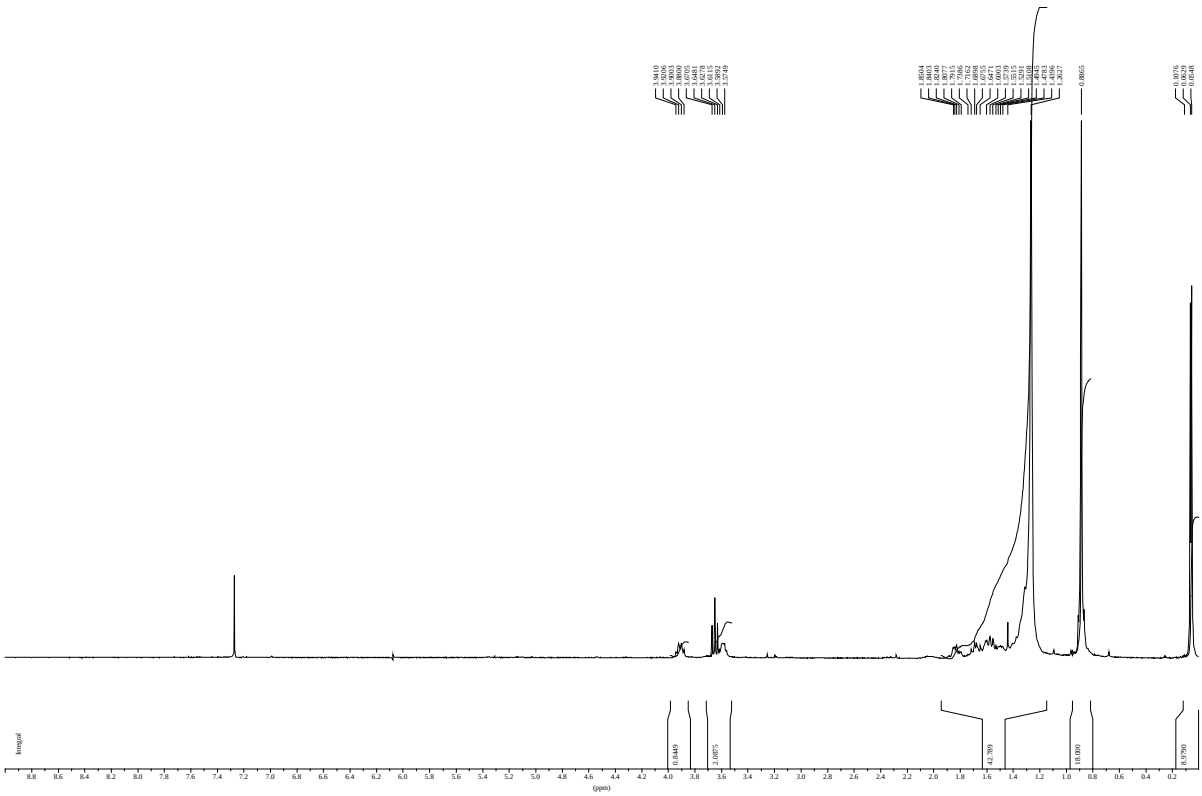
13-(*tert*-butyl-dimethyl-silanyloxy)-13-{5-[1-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydrofuran-2-yl}-tridecan-1-ol (16)



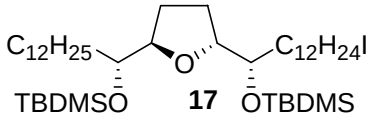
CB 424A



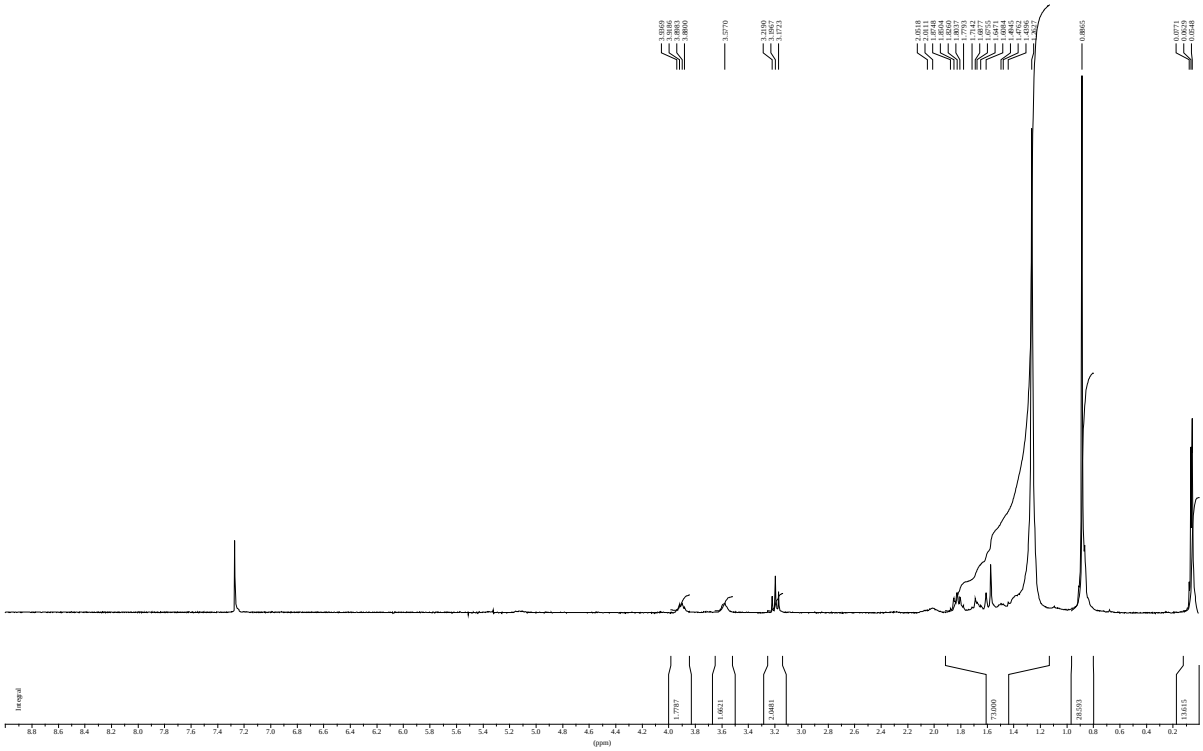
CB 424A



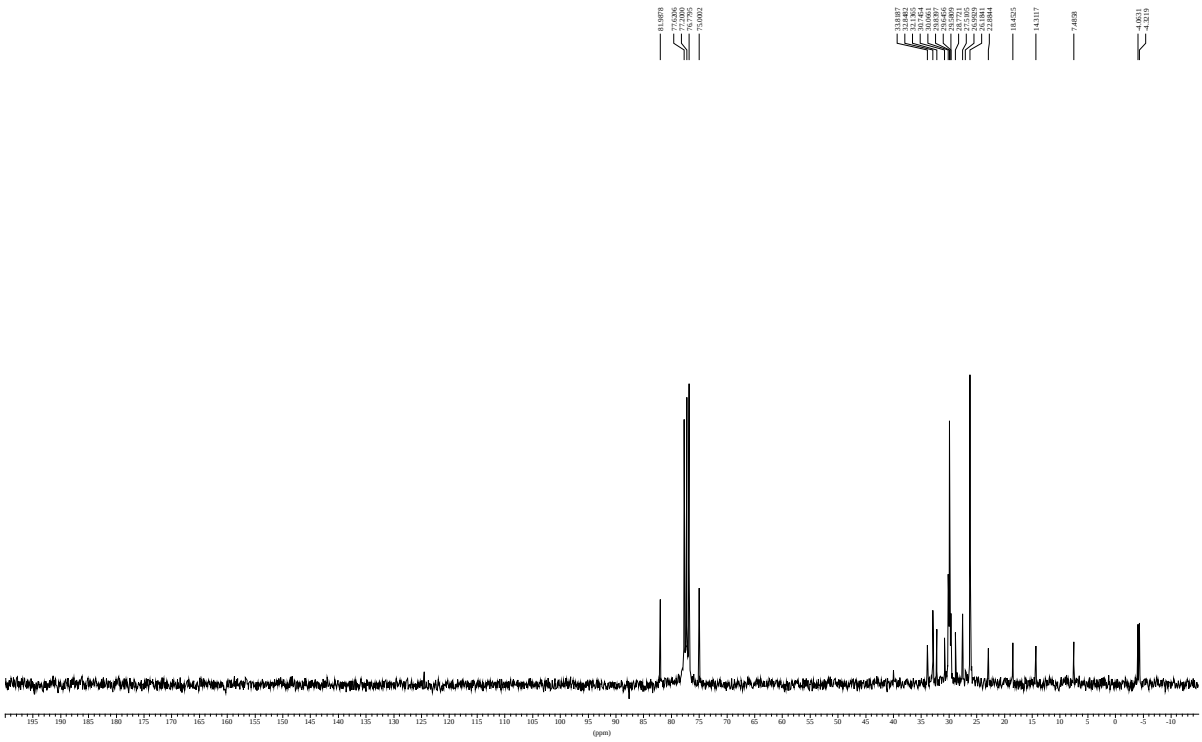
2-[1-(*tert*-Butyl-dimethyl-silanyloxy)-13-iodo-tridecyl]-5-[1-(*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydrofuran (17)



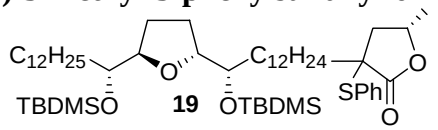
CB 424A



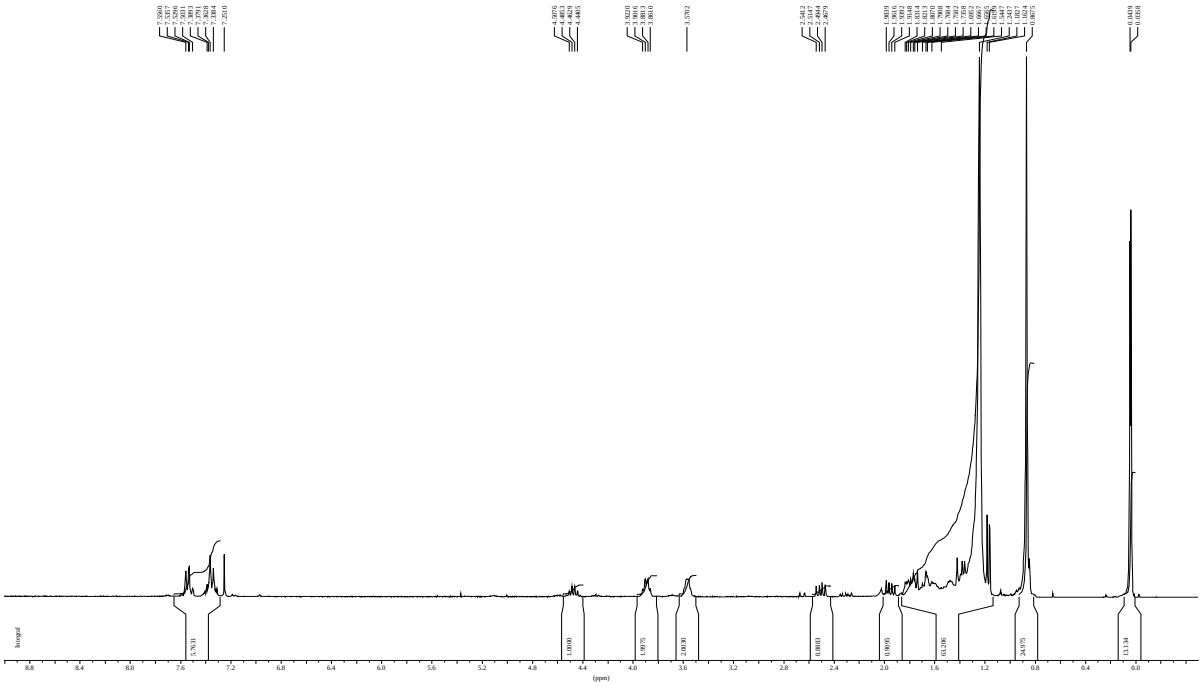
CB 424A



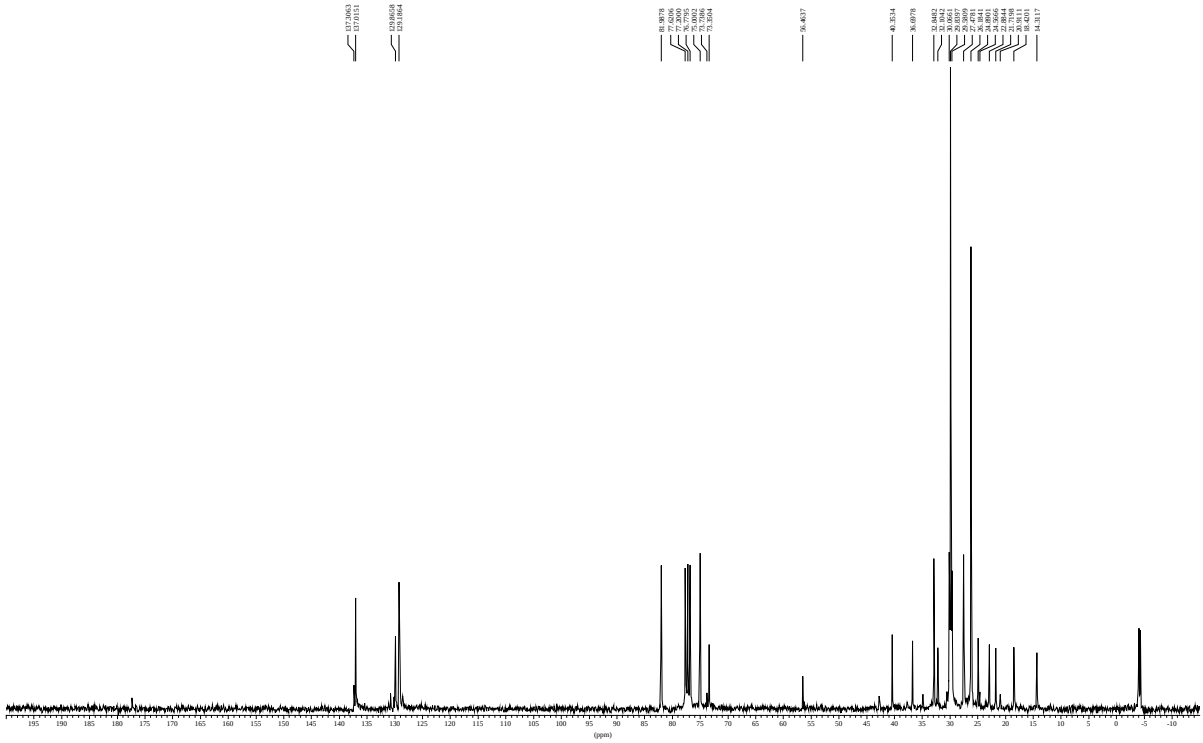
3-(13-(*tert*-Butyl-dimethyl-silanyloxy)-13-{5-[1-*tert*-butyl-dimethyl-silanyloxy)-tridecyl]-tetrahydro-furan-2-yl}-tridecyl)-5-methyl-3-phenylsulfanyl-dihydro-furan-2-one (19)



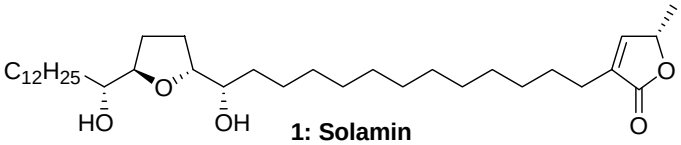
CB 424A



CB 424A



Solamin (1)



1: Solamin

CB 424A