Supplementary Information for

Total Synthesis of Resolvin D3

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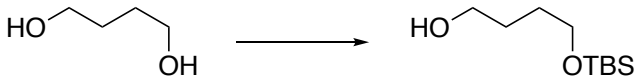
Experimental Procedures

General Information

Infrared (IR) spectra are reported in wave number (cm^{-1}). The ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ or CD_3OD with Me_4Si (δ = 0 ppm), the centerline of $CDCl_3$ triplet (δ = 77.1 ppm) or tesidual protonated solvent as an internal standard. Signal patterns are indicated as br s, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in hertz (Hz). High-resolution mass spectroscopy (HRMS) was obtained by ionizing samples *via* field desorption (FD). After the reactions were finished, the organic extracts were concentrated by using an evaporator and then the residues were purified by chromatography on silica gel (Kanto, spherical silica gel 60 N).

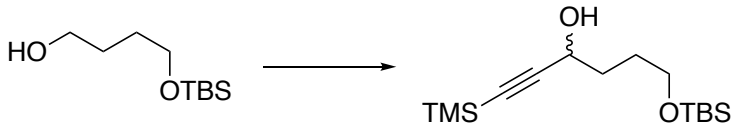
4-[(*tert*-Butyldimethylsilyl)oxy]butan-1-ol (11)



10 **11**

To an ice-cold solution of 1,4-butanediol (**10**) (5.30 mL, 60.0 mmol) in THF (200 mL) was added NaH (55% dispersion in mineral oil, 2.62 g, 60.0 mmol). After being stirred at room temperature for 1 h, TBSCl (9.04 g, 60.0 mmol) was added at 0 ºC. The mixture was stirred at room temperature for 3 h, and diluted with H_2O. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give silyl ether **11** (11.7 g, 96%) as a colorless liquid: R_f = 0.26 (hexane/EtOAc = 3:1); ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 6 H), 0.90 (s, 9 H), 1.59–1.71 (m, 4 H), 2.71 (br s, 1 H), 3.61–3.68 (m, 2 H), 3.67 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.3, 18.4, 26.0, 30.0, 30.3, 62.8, 63.4. The spectroscopic data were consistent with the literature values.[S1]

6-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)hex-1-yn-3-ol (*rac*-12)



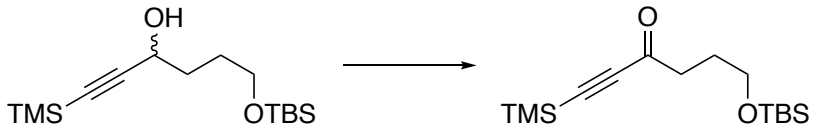
11 ***rac*-12**

To an ice-cold solution of silyl ether **11** (4.10 g, 20.1 mmol) in CH_2Cl_2 (50 mL) were added DMSO (7.10 mL, 100 mmol), Et_3N (11.2 mL, 80.4 mmol), and SO_3·pyridine (6.39 g, 40.1 mmol). The mixture was stirred at room temperature for 2 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over

$MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude aldehyde, which was used for the next reaction without further purification.

To an ice-cold solution of trimethylsilylacetylene (4.15 mL, 30.0 mmol) in THF (50 mL) was added *n*-BuLi (1.59 M in hexane, 16.4 mL, 26.1 mmol). The mixture was cooled to –78 ºC for 1 h, and a solution of the above aldehyde in THF (15 mL) was added to the mixture. The solution was stirred at –78 ºC for 2 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give alcohol *rac*-**12** (4.92 g, 82%) as a pale yellow liquid: R_f = 0.41 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 3 H), 0.09 (s, 3 H), 0.17 (s, 9 H), 0.91 (s, 9 H), 1.62–1.74 (m, 1 H), 1.76–1.89 (m, 3 H), 3.34 (d, J = 6.4 Hz, 1 H), 3.62–3.75 (m, 2 H), 4.43 (dt, J = 6.4, 4.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.32, –5.28, 0.00, 18.4, 26.0, 28.6, 35.5, 62.5, 63.3, 89.0, 106.9. The spectroscopic data were consistent with the literature values.[S2]

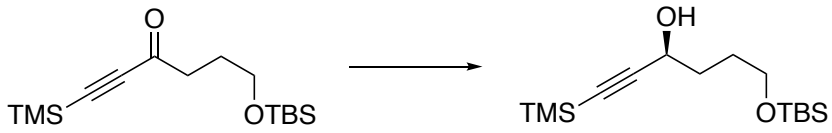
6-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)hex-1-yn-3-one (13)



rac-**12** **13**

To a solution of alcohol *rac*-**12** (4.37 g, 14.6 mmol) in CH_2Cl_2 (50 mL) were added Celite (7.06 g) and PCC (4.70 g, 21.8 mmol). After being stirred at room temperature for 14 h, the mixture was diluted with hexane and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography on silica gel (hexane/EtOAc) to give ketone **13** (3.87 g, 89%) as a colorless liquid: R_f = 0.64 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6 H), 0.24 (s, 9 H), 0.89 (s, 9 H), 1.89 (tt, J = 7.2, 6.4 Hz, 2 H), 2.64 (t, J = 7.2 Hz, 2 H), 3.63 (t, J = 6.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.3, –0.7, 18.4, 26.0, 27.1, 42.0, 61.9, 97.7, 102.1, 187.9. The spectroscopic data were consistent with the literature values.[S3]

(*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)hex-1-yn-3-ol [(*S*)-12]

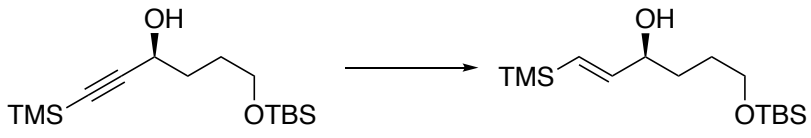


13 (*S*)-**12**

A mixture of RuCl[(*S*,*S*)-TsDPEN](*p*-cymene) (293 mg, 0.468 mmol) and KOH (310 mg, 5.52 mmol) in CH_2Cl_2 (2 mL) was stirred at room temperature for 12 min and washed with H_2O several

times. The CH_2Cl_2 layer was transferred to another flask with CH_2Cl_2, dried over CaH_2, and concentrated to afford purple solids, to which were added *i*-PrOH (8 mL) and a solution of ketone **13** (2.75 g, 9.21 mmol) in *i*-PrOH (5 mL). The mixture was stirred at room temperature for 1 h and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give alcohol (*S*)-**12** (2.63 g, 95%): 98% ee by HPLC analysis (Chiralcel OD-H, hexane, 1.0 mL/min, 35 ºC, t_R/min 13.4 (*R*-isomer, minor) and 14.0 (*S*-isomer, major); The ^1H and ^{13}C NMR spectroscopic data were consistent with those of the racemate.

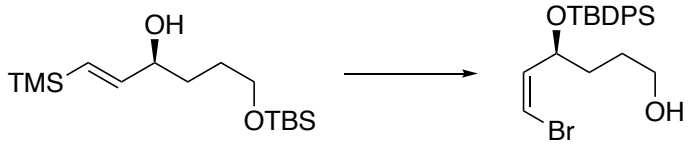
(*S*,*E*)-6-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)hex-1-en-3-ol (6)



(*S*)-**12** **6**

To an ice-cold solution of alcohol (*S*)-**12** (2.63 g, 8.75 mmol) in Et_2O (20 mL) was added Red-Al (3.6 M in toluene, 6.00 mL, 21.6 mmol) dropwise. After being stirred at room temperature for 1.5 h, the mixture was poured into saturated Rochelle salt. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give allyl alcohol **6** (2.03 g, 77%) as a colorless liquid: R_f = 0.41 (hexane/EtOAc = 5:1); $[\alpha]_D^{21}$ –1.1 (*c* 1.03, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.066 (s, 9 H), 0.073 (s, 6 H), 0.91 (s, 9 H), 1.53–1.74 (m, 4 H), 2.79 (d, *J* = 4.4 Hz, 1H), 3.67 (t, *J* = 5.6 Hz, 2 H), 4.08–4.16 (m, 1 H), 5.87 (dd, *J* = 18.8, 1.2 Hz, 1 H), 6.05 (dd, *J* = 18.8, 5.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.3, –1.2, 18.4, 26.0, 28.9, 34.5, 63.6, 74.2, 129.0, 148.6. The spectroscopic data were consistent with the literature values.[S4]

(*S*,*Z*)-6-Bromo-4-[(*tert*-butyldiphenylsilyl)oxy]hex-5-en-1-ol (15)



6 **15**

To a solution of allyl alcohol **6** (1.90 g, 6.28 mmol) in CH_2Cl_2 (20 mL) at –78 ºC was added Br_2 (0.35 mL, 6.8 mmol) in CH_2Cl_2 (3 mL) dropwise. After stirring at –78 ºC for 15 min, excess bromine was quenched with aqueous $Na_2S_2O_3$. The resulting mixture was extracted with hexane three times. The combined extracts were dried over $MgSO_4$ and concentrated to give the crude dibromide, which was used for the next reaction without further purification.

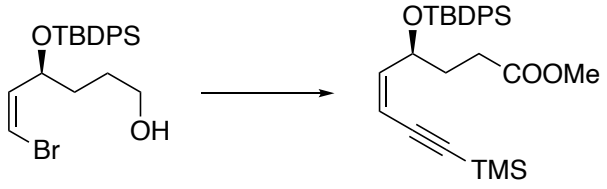
To a solution of the above dibromide in THF (20 mL) at –78 ºC was added TBAF (1.0 M in THF, 6.91 ml, 6.91 mmol) dropwise. After stirring at –78 ºC for 13 min the mixture and poured

into brine. The resulting mixture was extracted with Et_2O three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude (*Z*)-bromide **14**, which was used for the next reaction without further purification.

To an ice-cold solution of the above (*Z*)-bromide **14** in CH_2Cl_2 (10 mL) were added imidazole (641 mg, 9.42 mmol) and TBDPSCl (2.10 mL, 8.10 mmol). After being stirred at room temperature for 19 h, the mixture was diluted with saturated $NaHCO_3$. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude silyl ether, which was used for the next reaction without further purification.

To an ice-cold solution of the above silyl ether in MeOH (10 mL) was added PPTS (947 mg, 3.77 mmol). The solution was stirred at room temperature for 19 h and concentrated. The resulting mixture was diluted with saturated $NaHCO_3$ and extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel to afford alcohol **15** (1.33 g, 49%) as a colorless liquid: R_f = 0.17 (hexane/EtOAc = 5:1); $[\alpha]_D^{21}$ +61 (*c* 1.02, $CHCl_3$); IR (neat) 3333, 1428, 1110, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 9 H), 1.47 (br s, 1 H), 1.52–1.70 (m, 4 H), 3.50 (dd, *J* = 10.0, 6.4 Hz, 1 H), 3.56 (dd, *J* = 10.0, 6.0 Hz, 1 H), 4.63–4.71 (m, 1 H), 6.01 (dd, *J* = 7.2 Hz, 1.2 Hz, 1 H), 6.18 (t, *J* = 7.2 Hz, 1 H), 7.33–7.47 (m, 6 H), 7.64 (dd, *J* = 7.6, 1.2 Hz, 2 H), 7.68 (dd, *J* = 7.6, 1.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 27.0, 27.8, 33.3, 62.9, 71.5, 106.8, 127.6, 127.7, 129.7, 129.8, 133.76, 133.82, 135.9, 136.0, 137.6; HRMS (FD) calcd for $C_{22}H_{30}BrO_2Si$ $[M+H]^+$ 433.11984, found 433.12089.

Methyl (*S*,*Z*)-4-[(*tert*-butyldiphenylsilyl)oxy]-8-(trimethylsilyl)oct-5-en-7-ynoate (17)



15 **17**

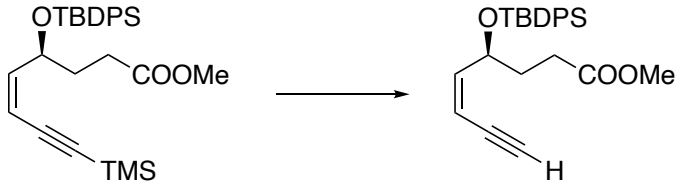
To a mixture of bromoolefin **15** (1.05 g, 2.42 mmol), $Pd(PPh_3)_4$ (419 mg, 0.363 mmol), and trimethylsilylacetylene (1.00 mL, 7.23 mmol) in *t*-$BuNH_2$ (15 mL) was added CuI (92.0 mg, 0.483 mmol). The mixture was stirred at room temperature for 5 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude alcohol **16**, which was used for the next reaction without further purification.

To an ice-cold solution of the above alcohol **16** in CH_2Cl_2 (16 mL) and DMSO (4 mL) were added Et_3N (1.67 mL, 12.0 mmol) and SO_3·pyridine (1.13 g, 7.23 mmol). The mixture was stirred at room temperature for 2 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude aldehyde, which was used for the next reaction without further purification.

To an ice-cold solution of the above aldehyde in *t*-BuOH (5 mL) and H_2O (10 mL) were added 2-methyl-2-butene (1.30 mL, 12.2 mmol), $NaH_2PO_4·2H_2O$ (604 mg, 3.87 mmol), and $NaClO_2$ (70% purity, 1.10 g, 8.51 mmol). The mixture was stirred at room temperature for 1 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude carboxylic acid, which was used for the next reaction without further purification.

To an ice-cold solution of the above carboxylic acid in MeOH (5 mL) and Et_2O (5 mL) was added $TMSCHN_2$ (0.60 M in hexane, 6.00 mL, 3.60 mmol) dropwise. The mixture was stirred at room temperature for 2 h and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give ester **17** (963 mg, 83%): R_f = 0.59 (hexane/EtOAc = 5:1); $[\alpha]_D^{28}$ +108 (*c* 0.85, $CHCl_3$); IR (neat) 2150, 1742, 1428, 1251 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 9 H), 1.06 (s, 9 H), 1.79–1.98 (m, 2 H), 2.31 (t, *J* = 8.0 Hz, 2 H), 3.62 (s, 3 H), 4.80 (dt, *J* = 8.0, 6.0 Hz, 1 H), 5.34 (dd, *J* = 11.2, 0.8 Hz, 1 H), 5.90 (dd, *J* = 11.2, 8.0 Hz, 1 H), 7.32–7.45 (m, 6 H), 7.61–7.68 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –0.2, 19.4, 27.1, 29.5, 32.7, 51.6, 71.0, 100.4, 100.8, 109.3, 127.5, 127.6, 129.6, 129.7, 133.99, 134.04, 135.9, 136.0, 146.1, 174.0; HRMS (FD) calcd for $C_{28}H_{38}O_3Si_2$ $[M]^+$ 478.23595, found 478.23479.

Methyl (*S*,*Z*)-4-[(*tert*-butyldiphenylsilyl)oxy]oct-5-en-7-ynoate (18)

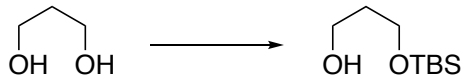


17 **18**

To an ice-cold solution of ester **17** (890 mg, 1.86 mmol) in MeOH (15 mL) was added K_2CO_3 (360 mg, 2.60 mmol). The mixture was stirred at room temperature for 3 h and concentrated. The resulting mixture was diluted with saturated NH_4Cl and extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give acetylene **18** (696 mg, 92%) as a colorless oil: R_f = 0.38 (hexane/EtOAc = 5:1); $[\alpha]_D^{25}$ +105 (*c* 0.69, $CHCl_3$); IR (neat) 3294, 1740, 1428,

1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9 H), 1.80–2.00 (m, 2 H), 2.34 (t, *J* = 8.0 Hz, 2 H), 2.86 (dd, *J* = 2.4, 0.8 Hz, 1 H), 3.61 (s, 3 H), 4.78 (dtd, *J* = 8.8, 6.8, 0.8 Hz, 1 H), 5.29 (ddd, *J* = 11.2, 2.4, 0.8 Hz, 1 H), 5.95 (ddd, *J* = 11.2, 8.8, 0.8 Hz, 1 H), 7.32–7.45 (m, 6 H), 7.61–7.69 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 27.0, 29.5, 32.6, 51.6, 70.9, 79.2, 83.0, 108.2, 127.5, 127.6, 129.6, 129.7, 133.88, 133.94, 135.9, 136.0, 146.9, 173.9; HRMS (FD) calcd for $C_{25}H_{30}O_3Si$ $[M]^+$ 406.19642, found 406.19609.

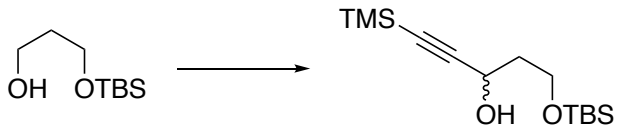
3-[(*tert*-Butyldimethylsilyl)oxy]propan-1-ol (20)



19 **20**

To an ice-cold solution of 1,3-propanediol (**19**) (4.35 mL, 60.0 mmol) in THF (150 mL) was added NaH (55% dispersion in mineral oil, 2.62 g, 60.0 mmol). After being stirred at room temperature for 30 min, TBSCl (9.04 g, 60.0 mmol) was added. The mixture was stirred at room temperature for 2.5 h, and diluted with H_2O. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give silyl ether **20** (10.9 g, 95%) as a colorless liquid: R_f = 0.26 (hexane/EtOAc = 5:1); ^1H NMR (400 MHz, $CDCl_3$) δ 0.15 (s, 6 H), 0.97 (s, 9 H), 1.85 (quint, *J* = 5.2 Hz, 2 H), 2.75 (t, *J* = 5.2 Hz, 1 H), 3.88 (q, *J* = 5.2 Hz, 2 H), 3.91 (t, *J* = 5.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.4, 18.2, 25.9, 34.2, 62.5, 63.0. The spectroscopic data were consistent with the literature values.[S5]

5-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)pent-1-yn-3-ol (*rac*-21)



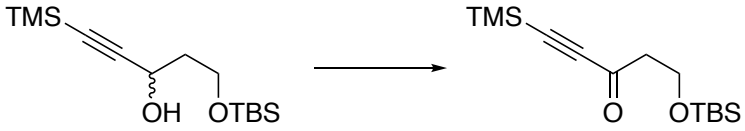
20 ***rac*-21**

To an ice-cold solution of silyl ether **20** (10.9 g, 57.3 mmol) in CH_2Cl_2 (120 mL) were added DMSO (20.2 mL, 284 mmol), Et_3N (31.8 mL, 228 mmol), and SO_3·pyridine (18.2 g, 114 mmol). The mixture was stirred at room temperature for 1 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude aldehyde, which was used for the next reaction without further purification.

To a solution of trimethylsilylacetylene (9.50 mL, 68.7 mmol) in THF (60 mL) was added *n*-

BuLi (1.64 M in hexane, 34.7 mL, 56.9 mmol) at –78 ºC. After being stirred at –78 ºC for 1 h, a solution of the above aldehyde in THF (6 mL) was added. The solution was stirred at –78 ºC for 10 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give alcohol *rac*-**21** (12.1 g, 74%) as a pale yellow liquid: R_f = 0.36 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 3 H), 0.10 (s, 3 H), 0.17 (s, 9 H), 0.91 (s, 9 H), 1.81–1.91 (m, 1 H), 1.96–2.06 (m, 1 H), 3.48 (d, *J* = 6.4 Hz, 1 H), 3.81 (ddd, *J* = 10.4, 6.0, 4.4 Hz, 1 H), 4.03 (ddd, *J* = 10.4, 8.2, 4.0 Hz, 1 H), 4.60 (dt, *J* = 6.4, 4.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.50, –5.54, –0.02, 18.3, 25.9, 38.3, 61.3, 62.5, 89.4, 106.2. The spectroscopic data were consistent with the literature values.[S6]

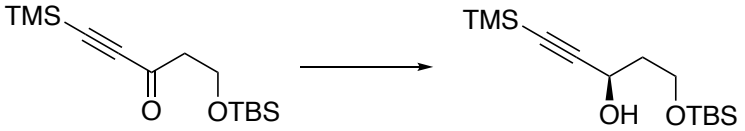
5-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)pent-1-yn-3-one (22)



rac-**21** **22**

To a solution of alcohol *rac*-**21** (3.36 g, 11.7 mmol) in CH_2Cl_2 (30 mL) were added Celite (5.68 g) and PCC (3.79 g, 17.6 mmol). After being stirred at room temperature for 18.5 h, the mixture was diluted with hexane and filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by chromatography on silica gel (hexane/EtOAc) to give ketone **22** (2.77 g, 83%) as a colorless liquid: R_f = 0.65 (hexane/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.24 (s, 9 H), 0.88 (s, 9 H), 2.75 (t, *J* = 6.2 Hz, 2 H), 3.98 (t, *J* = 6.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.4, –0.7, 18.3, 25.9, 48.4, 58.6, 98.2, 102.0, 186.4. The spectroscopic data were consistent with the literature values.[S6]

(*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)pent-1-yn-3-ol [(*R*)-21]

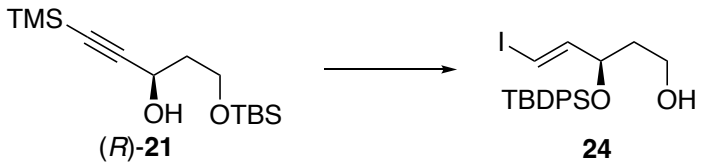


22 (*R*)-**21**

A mixture of RuCl[(*R*,*R*)-TsDPEN](*p*-cymene) (173 mg, 0.272 mmol) and KOH (183 mg, 3.26 mmol) in CH_2Cl_2 (2.0 mL) was stirred at room temperature for 10 min and washed with H_2O several times. The CH_2Cl_2 layer was transferred to another flask with CH_2Cl_2, dried over CaH_2, and concentrated to afford purple solids, to which were added *i*-PrOH (8 mL) and a solution of ketone **22** (1.55 g, 5.45 mmol) in *i*-PrOH (7 mL). The mixture was stirred at room temperature for 2 h and concentrated. The residue was purified by chromatography on silica gel

(hexane/EtOAc) to give alcohol (*R*)-**21** (1.47 g, 94%): 98% ee by HPLC analysis (Chiralcel OD-H, hexane, 1.0 mL/min, 35 ºC, t_R/min 8.9 (*R*-isomer, major) and 10.0 (*S*-isomer, minor)); The ^{1}H and ^{13}C NMR spectroscopic data were consistent with those of the racemate.

(*R*,*E*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-5-iodopent-4-en-1-ol (24)



To an ice-cold solution of alcohol (*R*)-**21** (1.47 g, 5.13 mmol) in CH_2Cl_2 (30 mL) were added imidazole (1.05 g, 15.4 mmol) and TBDPSCl (2.00 mL, 7.69 mmol). After being stirred at room temperature for 5 h, the mixture was diluted with saturated $NaHCO_3$. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude silyl ether, which was used for the next reaction without further purification.

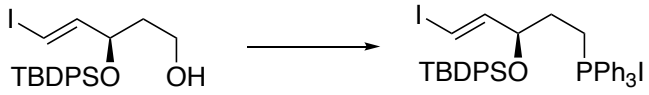
To a solution of the above silyl ether in MeOH (15 mL) was added K_2CO_3 (1.07 g, 7.74 mmol). The mixture was stirred at room temperature for 3 h and concentrated. The resulting mixture was diluted with saturated NH_4Cl and extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude acetylene **23**, which was used for the next reaction without further purification.

To an ice-cold mixture of Cp_2ZrCl_2 (3.00 g, 10.3 mmol) in THF (10 mL) was added DIBAL (1.02 M in hexane, 9.07 mL, 9.25 mmol). The mixture was stirred at 0 ºC for 1 h and a solution of the above acetylene **23** in THF (5.0 mL) was added. The mixture was warmed to room temperature over 3 h and then cooled to –78 ºC. The solution of I_2 (2.61 g, 10.3 mmol) in THF (3.0 mL) was added. The solution was stirred at room temperature for 1 h and diluted with saturated $Na_2S_2O_3$ and saturated Rochelle salt. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude olefin, which was used for the next reaction without further purification.

To an ice-cold solution of the above olefin in MeOH (13 mL) was added PPTS (1.29 g, 5.13 mmol). The mixture was stirred at room temperature for 31 h and concentrated. The resulting mixture was diluted with saturated $NaHCO_3$ and extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give iodoolefin **24** (1.93 g, 81%) as a liquid: R_f = 0.20 (hexane/EtOAc = 5:1); $[\alpha]_D^{20}$ +114 (*c* 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 9 H),

1.63–1.82 (m, 3 H), 3.64 (sext, J = 5.6 Hz, 1 H), 3.69–3.78 (m, 1 H), 4.33 (qd, J = 6.0, 0.8 Hz, 1 H), 5.96 (dd, J = 14.8, 0.8 Hz, 1 H), 6.49 (dd, J = 14.8, 6.0 Hz, 1 H), 7.37–7.48 (m, 6 H), 7.61–7.70 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 27.1, 39.1, 59.2, 74.5, 77.7, 127.7, 127.8, 130.0, 130.1, 133.1, 133.3, 135.9, 136.0, 147.4. The spectroscopic data were consistent with the literature values.[S7]

(*R*,*E*)-[3-[(*tert*-Butyldiphenylsilyl)oxy]-5-iodopent-4-en-1-yl]iodotriphenyl-λ^5-phosphane (8)

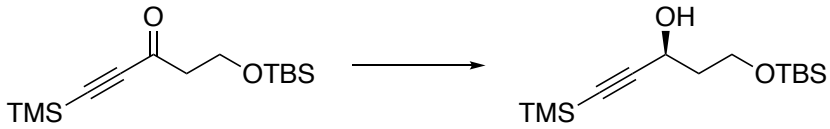


24 **8**

To an ice-cold solution of iodoolefin **24** (1.75 g, 3.75 mmol) in CH_2Cl_2 (13 mL) were added PPh_3 (1.18 g, 4.50 mmol) and imidazole (306 mg, 4.49 mmol). After being stirred at 0 ºC for 15 min, iodine (1.14 g, 4.49 mmol) in CH_2Cl_2 (4 mL) was added. The mixture was stirred at room temperature for 1 h, and diluted with saturated $Na_2S_2O_3$. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude iodide, which was used for the next reaction without further purification.

To a solution of the above iodide in MeCN (25 mL) was added PPh_3 (1.52 g, 5.80 mmol). The solution was stirred at 80 ºC for 48 h and concentrated. The residue was purified by chromatography on silica gel (CH_2Cl_2 then 5% MeOH) to give the phosphonium salt **8** (3.15 g, quant.) as a yellow solids: R_f = 0.64 (CH_2Cl_2/MeOH = 10:1); mp 79–80 °C; $[\alpha]_D^{23}$ +31 (*c* 1.00, $CHCl_3$); IR (neat) 1438, 1112, 941 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.0 (s, 9 H), 1.65–1.91 (m, 2 H), 3.15–3.27 (m, 1 H), 3.53–3.66 (m, 1 H), 4.77 (dt, J = 6.4, 4.4 Hz, 1 H), 6.33 (d, J = 14.4 Hz, 1 H), 6.50 (dd, J = 14.4, 6.4 Hz, 1 H), 7.31–7.49 (m, 5 H), 7.54–7.71 (m, 17 H), 7.77–7.85 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.7 (d, J = 53 Hz), 19.5, 27.1, 30.1 (d, J = 4 Hz), 74.8 (d, J = 16 Hz), 80.3, 117.7 (d, J = 86 Hz), 128.0, 128.1, 130.11, 130.15, 130.7 (d, J = 13 Hz), 132.9, 133.5, 133.6 (d, J = 10 Hz), 135.3 (d, J = 3 Hz), 135.6, 135.9, 146.1; HRMS signals were not detected by FD-MS.

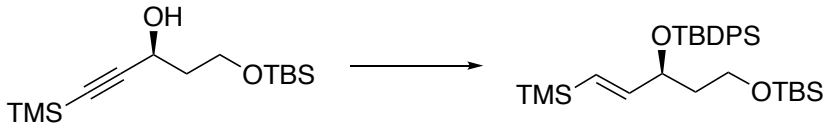
(*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]-1-(trimethylsilyl)pent-1-yn-3-ol [(*S*)-21]



22 (*S*)-**21**

A mixture of RuCl[(*S*,*S*)-TsDPEN](*p*-cymene) (223 mg, 0.351 mmol) and KOH (236 mg, 4.21 mmol) in CH_2Cl_2 (2 mL) was stirred at room temperature for 15 min and washed with H_2O several times. The CH_2Cl_2 layer was transferred to another flask with CH_2Cl_2, dried over CaH_2, and concentrated to afford purple solids, to which were added *i*-PrOH (8 mL) and a solution of ketone **22** (1.99 g, 6.99 mmol) in *i*-PrOH (7 mL). The mixture was stirred at room temperature for 1 h and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give alcohol (*S*)-**21** (1.87 g, 93%): 99% ee by HPLC analysis (Chiralcel OD-H, hexane, 1.0 mL/min, 35 ºC, t_R/min 9.1 (*R*-isomer, minor) and 9.7 (*S*-isomer, major)). The spectroscopic data were consistent with the literature values.[S6]

(*S*,*E*)-2,2,9,9,10,10-Hexamethyl-3,3-diphenyl-5-[2-(trimethylsilyl)vinyl]-4,8-dioxa-3,9-disilaundecane (26)



(*S*)-**21** **26**

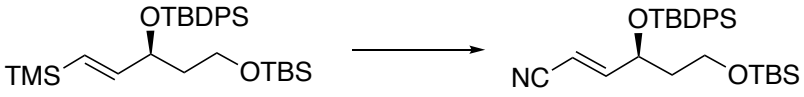
To an ice-cold solution of alcohol (*S*)-**21** (1.87 g, 6.53 mmol) in Et_2O (25 mL) was added Red-Al (3.6 M in toluene, 5.40 mL, 19.4 mmol) dropwise. After being stirred at room temperature for 2 h, the mixture was poured into saturated Rochelle salt at 0 ºC. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude diol **25**, which was used for the next reaction without further purification.

To an ice-cold solution of the above diol **25** in CH_2Cl_2 (30 mL) were added imidazole (420 mg, 6.17 mmol) and TBSCl (787 mg, 5.22 mmol). After being stirred at 0 ºC for 1 h, the mixture was diluted with saturated $NaHCO_3$ and H_2O at 0 ºC and was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$, and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude allyl alcohol, which was used for the next reaction without further purification.

To an ice-cold solution of the above allyl alcohol in CH_2Cl_2 (20 mL) were added imidazole (970 mg, 14.2 mmol) and TBDPSCl (1.85 mL, 7.13 mmol). After being stirred at room temperature for 6 h, the solution was diluted with saturated $NaHCO_3$, and the mixture was

extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel to give silyl ether **26** (2.23 g, 65%) as a colorless liquid: R_f = 0.68 (hexane/EtOAc = 5:1); $[\alpha]_D^{24}$ –23 (*c* 0.98, $CHCl_3$); IR (neat) 1249, 1111, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 9 H), 0.126 (s, 3 H), 0.129 (s, 3 H), 0.99 (s, 9 H), 1.20 (s, 9H), 1.82 (sext, *J* = 6.4 Hz, 1H), 1.99 (sext, *J* = 6.4 Hz, 1H), 3.68–3.81 (m, 2 H), 4.40 (qd, *J* = 6.4, 0.8 Hz 1 H), 5.61 (dd, *J* = 18.8 Hz, 0.8 Hz, 1 H), 6.05 (dd, *J* = 18.8 Hz, 6.4 Hz, 1 H), 7.45–7.59 (m, 6 H), 7.76–7.84 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.3, –5.2, –1.4, 18.3, 19.4, 26.0, 27.1, 40.7, 59.7, 74.3, 127.3, 127.5, 129.4, 129.6, 129.8, 134.3, 134.5, 136.0, 136.1, 148.1; HRMS (FD) calcd for $C_{30}H_{50}O_2Si_3$ $[M]^+$ 526.31186, found 526.31041.

(*S*,*E*)-6-[(*tert*-Butyldimethylsilyl)oxy]-4-[(*tert*-butyldiphenylsilyl)oxy]hex-2-enenitrile (27)

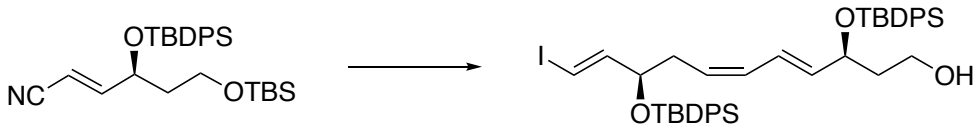


26 **27**

To an ice-cold solution of silyl ether **26** (2.10 g, 3.98 mmol) in CH_2Cl_2 (30 mL) was added *m*-CPBA (65% purity, 2.11 g, 7.94 mmol) portionwise. The mixture was stirred at room temperature for 24 h, and Me_2S (0.50 mL, 6.8 mmol) was added slowly at 0 ºC. The mixture was stirred at room temperature for 15 min, diluted with saturated $NaHCO_3$, and extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$, and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude epoxide, which was used for the next reaction without further purification.

To an ice-cold solution of the above epoxide in toluene (15 mL) was added Et_2AlCN (0.71 M in toluene, 11.2 mL, 7.95 mmol) dropwise. After being stirred at room temperature for 2 h, the solution was poured into saturated Rochelle salt at 0 ºC. The resulting mixture was stirred at room temperature for 15 h, and extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel to give cyanoolefin **27** (1.47 g, 77%) as a colorless liquid: R_f = 0.40 (hexane/EtOAc = 10:1); $[\alpha]_D^{20}$ –26 (*c* 1.01, $CHCl_3$); IR (neat) 2224, 1112, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ –0.04 (s, 3 H), –0.03 (s, 3 H), 0.82 (s, 9 H), 1.08 (s, 9 H), 1.58–1.68 (m, 1 H), 1.73–1.83 (m, 1 H), 3.56 (t, *J* = 6.0 Hz, 2 H), 4.45–4.52 (m, 1 H), 5.46 (dd, *J* = 16.4 Hz, 1.6 Hz, 1 H), 6.72 (dd, *J* = 16.4 Hz, 5,2 Hz, 1 H), 7.35–7.48 (m, 6 H), 7.57–7.66 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.4, 18.2, 19.4, 25.9, 27.0, 39.9, 58.6, 70.8, 98.3, 117.5, 127.85, 127.89, 130.0, 130.2, 133.0, 133.2, 135.7, 135.9, 156.8; HRMS (FD) calcd for $C_{28}H_{42}NO_2Si_2$ $[M+H]^+$ 480.27541, found 480.27584.

(3*S*,4*E*,6*Z*,9*R*,10*E*)-3,9-Bis[(*tert*-butyldiphenylsilyl)oxy]-11-iodoundeca-4,6,10-trien-1-ol (33)



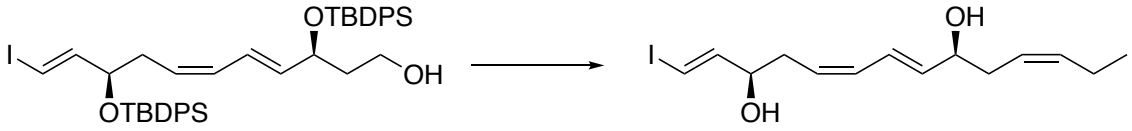
27 **33**

To a solution of cyanoolefin **27** (1.02 g, 2.13 mmol) in toluene (18 mL) at –78 ºC was added DIBAL (1.02 M in hexane, 2.49 mL, 2.54 mmol) dropwise. After being stirred at –78 °C for 3 h, the mixture was poured into saturated Rochelle salt at 0 ºC. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude aldehyde **9**, which was used for the next reaction without further purification.

To an ice-cold mixture of phosophonium salt **8** (2.85 g, 3.40 mmol) in THF (15 mL) was added NaHMDS (1.0 M in THF, 3.0 mL, 3.0 mmol). The resulting reddish-orange mixture was stirred at 0 ºC for 1 h and cooled to −78 ºC. A solution of the above aldehyde **9** in THF (6 mL) was added to the mixture dropwise. After 1 h, the mixture was warmed to 0 ºC over 1 h and added saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude olefin **32**, which was used for the next reaction without further purification.

To an ice-cold solution of the above olefin **32** in CH_2Cl_2 (2 mL) and MeOH (8 mL) was added PPTS (532 mg, 2.12 mmol). The solution was stirred at room temperature for 15 h and concentrated. The resulting mixture was diluted with saturated $NaHCO_3$ and extracted with Et_2O three times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel to afford alcohol **33** (1.41 g, 83%) as a colorless liquid: R_f = 0.20 (hexane/EtOAc = 10:1); $[\alpha]_D^{22}$ –2.3 (*c* 0.76, $CHCl_3$); IR (neat) 3385, 1428, 1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9 H), 1.06 (s, 9 H), 1.66–1.76 (m, 1 H), 1.78–1.88 (m, 1 H), 1.96 (br s, 1 H), 2.09–2.22 (m, 2 H), 3.60–3.70 (m, 1 H), 3.71–3.82 (m, 1 H), 4.07 (q, *J* = 6.8 Hz, 1 H), 4.41 (q, *J* = 6.4 Hz, 1 H), 5.22 (dt, *J* = 9.6, 7.2 Hz, 1 H), 5.58 (dd, *J* = 14.4, 7.2 Hz, 1 H), 5.79–5.90 (m, 2 H), 5.95 (dd, *J* = 14.4, 0.8 Hz, 1 H), 6.39 (dd, *J* = 14.4, 6.4 Hz, 1 H), 7.28–7.45 (m, 12 H), 7.57–7.71 (m, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 19.4, 27.0, 27.1, 35.5, 39.8, 59.8, 73.2, 75.4, 77.2, 125.6, 126.1, 127.5, 127.7, 129.8, 129.86, 129.89, 130.0, 133.4, 133.6, 133.7, 133.8, 135.7, 135.91, 135.95, 136.1, 147.6; HRMS (FD) calcd for $C_{43}H_{53}IO_3Si_2$ $[M]^+$ 800.25779, found 800.25558.

(1*E*,3*R*,5*Z*,7*E*,9*S*,11*Z*)-1-Iodotetradeca-1,5,7,11-tetraene-3,9-diol (7)



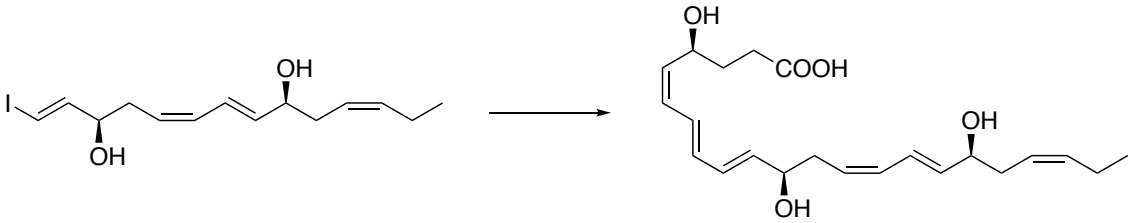
33 **7**

To an ice-cold solution of alcohol **33** (1.07 g, 1.34 mmol) in CH_2Cl_2 (7 mL) and DMSO (7 mL) were added Et_3N (0.93 mL, 6.7 mmol), and SO_3·pyridine (638 mg, 4.01 mmol). The mixture was stirred at room temperature for 2.5 h and diluted with saturated $NaHCO_3$. The resulting mixture was extracted with CH_2Cl_2 three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude aldehyde, which was used for the next reaction without further purification.

To an ice-cold solution of *n*-propyltriphenylphosphonium bromide (922 mg, 2.39 mmol) in THF (6.7 mL) and HMPA (1.3 mL) was added NaHMDS (1.0 M in THF, 2.0 mL, 2.0 mmol). The resulting mixture was stirred at 0 ºC for 40 min and cooled to –90 ºC. After being stirred at –90 ºC for 20 min, a solution of the above aldehyde in THF (3.3 mL) and HMPA (0.7 mL) was added to the mixture dropwise. After being stirred at –90 ºC for 45 min, the mixture was warmed to 0 ºC over 1 h and diluted saturated with NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude disilyl ether, which was used for the next reaction without further purification.

To an ice-cold solution of the above disilyl ether in THF (5 mL) was added TBAF (1.0 M in THF, 8.0 mL, 8.0 mmol). The solution was stirred at 35 ºC for 22 h and diluted with saturated NH_4Cl. The resulting mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc) to give diol **7** (383 mg, 82%) as a pale yellow liquid: R_f = 0.11 (hexane/EtOAc = 3:1); $[\alpha]_D^{20}$ +39 (*c* 0.60, $CHCl_3$); IR (neat) 3354, 1414, 949 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.2 Hz, 3 H), 1.76 (s, 1 H), 1.83 (d, *J* = 3.6 Hz, 1 H), 2.07 (d of quint, *J* = 7.2, 1.2 Hz, 2 H), 2.27–2.42 (m, 2 H), 2.41–2.2.53 (m, 2 H), 4.13–4.21 (m, 1 H), 4.23 (q, *J* = 6.4 Hz, 1 H), 5.31–5.40 (m, 1 H), 5.44 (dt, *J* = 10.8, 8.0 Hz, 1 H), 5.54–5.63 (m, 1 H), 5.78 (dd, *J* = 14.8, 6.0 Hz, 1 H), 6.18 (t, *J* = 10.8 Hz, 1 H), 6.40 (dd, *J* = 14.8, 1.6 Hz, 1 H), 6.50 (ddt, *J* = 15.2, 10.8, 1.2 Hz, 1 H), 6.60 (dd, *J* = 14.8, 6.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 20.9, 35.1, 35.3, 72.0, 73.9, 77.8, 123.6, 125.1, 125.8, 131.7, 135.6, 137.1, 147.6; HRMS (FD) calcd for $C_{14}H_{21}IO_2$ $[M]^+$ 348.05862, found 348.05876.

Resolvin D3 (1)



7 Resolvin D3 (**1**)

To an ice-cold solution of acetylene **18** (79.3 mg, 0.195 mmol) in THF (3 mL) was added dropwise freshly prepared Sia_2BH (1.2 mL, 0.50 M in THF, 0.60 mmol). After being stirred at 0 ºC for 50 min, and aqueous 2 N LiOH (5.25 mL, 10.5 mmol) and a solution of iodoolefin **7** (52.2 mg, 0.150 mmol) in THF (2 mL) were added. Argon was bubbled into the reaction mixture for 10 min and $Pd(PPh_3)_4$ (34.7 mg, 0.0300 mmol) was added. After being stirred at 35 ºC for 21 h, the mixture was diluted with saturated NH_4Cl at 0 ºC. The resulting mixture was extracted with Et_2O three times. The combined extracts were dried over $MgSO_4$ and concentrated. The residue was passed through a short column of silica gel (hexane/EtOAc) to give the crude triene, which was used for the next reaction without further purification.

To an ice-cold solution of the above triene in THF (1.5 mL) was added TBAF (1.5 mL, 1.5 mmol). After being stirred at 35 ºC for 7 h, the mixture was diluted with McIlvaine's phosphate buffer (pH 5.0) and extracted with a mixture of CH_2Cl_2 and THF (small volume) five times. The combined extracts were dried over $MgSO_4$ and concentrated to give a residue, which was purified by chromatography on silica gel to afford resolvin D3 (**1**) (27.1 mg, 48%) as a colorless liquid: R_f = 0.46 ($CHCl_3$/MeOH = 5:1); $[\alpha]_D^{22}$ +9 (*c* 0.40, MeOH), [lit.[S8] +7.9 (*c* 0.34, MeOH)]; UV (MeOH) λ_{max} 237, 262, 271, 282 nm; IR (neat) 3382, 1726, 1470 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 0.96 (t, *J* = 7.5 Hz, 3 H), 1.67–1.79 (m, 1 H), 1.79–1.90 (m, 1 H), 2.06 (quint, *J* = 7.5 Hz, 2 H), 2.21–2.37 (m, 2 H), 2.35 (t, *J* = 7.2 Hz, 2 H), 2.41 (dt, *J* = 14.0, 6.8 Hz, 1 H), 2.46 (dt, *J* = 14.0, 6.8 Hz, 1 H), 4.12 (q, *J* = 6.8 Hz, 1 H), 4.16 (q, *J* = 6.8 Hz, 1 H), 4.61 (dt, *J* = 10.8, 7.2 Hz, 1 H), 5.31–5.52 (m, 4 H), 5.68 (dd, *J* = 15.2, 6.8 Hz, 1 H), 5.75 (dd, *J* = 14.4, 6.8 Hz, 1 H), 6.07 (t, *J* = 10.8 Hz, 1 H), 6.09 (t, *J* = 10.8 Hz, 1 H), 6.25 (dd, *J* = 14.4, 11.2 Hz, 1 H), 6.31 (dd, *J* = 14.4, 10.8 Hz, 1 H), 6.50 (dd, *J* = 15.2, 11.2 Hz, 1 H), 6.55 (dd, *J* = 14.4, 10.8 Hz, 1 H); ^{13}C NMR (100 MHz, CD_3OD) δ 14.6, 21.7, 31.0, 33.7, 36.2, 36.7, 67.8, 73.0, 73.2, 125.5, 126.6, 128.1, 128.8, 130.8, 131.1, 131.5, 134.6, 134.8, 135.2, 137.5, 137.9, 177.5; HRMS (FD) calcd for $C_{22}H_{32}O_5$ $[M]^+$ 376.22497 found 376.22592.

Table S1 Comparison of ^{1}H NMR data between our synthetic reoslvin D3 and the reported data

NO.	synthetic Resolvin D3 (**1**) (400 MHz, CD_3OD)	Petasis's Resolvin D3 (**1**) (600 MHz, CD_3OD)[S8]	Anderson's Resolvin D3 (**1**) (500 MHz, CD_3OD)[S9]
1	0.96, t (7.5 Hz)	0.98, t (7.5 Hz)	0.96, t (7.5 Hz)
2	1.67–1.79, m	1.71–1.82, m	1.67–1.76, m
3	1.79–1.90, m	1.88, dd (14.1, 7.2 Hz)	1.84, dq (14.6, 7.5 Hz)
4	2.06, quint (7.5 Hz)	2.07, q (7.3 Hz)	1.99–2.13, m
5	2.21–2.37, m	2.22–2.38, m	2.16–2.59, m
6	2.35, t (7.2 Hz)		
7	2.41, dt (14.0, 6.8 Hz)	2.45, q (7.9 Hz)	
8	2.46, dt (14.0, 6.8 Hz)		
9	4.12, q (6.8 Hz)	4.08–4.23, m	4.06–4.26, m
10	4.16, q (6.8 Hz)		
11	4.61, dt (10.8, 7.2 Hz)	4.60, m	4.52–4.69, m
12	5.31–5.52, m	5.31–5.55, m	5.30–5.41, m 5.46, ddt (10.6, 8.7, 7.3 Hz)
13	5.68, dd (15.2, 6.8 Hz)	5.70, dd (15.4, 6.5 Hz)	5.68, dd (15.2, 6.5 Hz)
14	5.75, dd (14.4, 6.8 Hz)	5.75, dd (15.2, 6.7 Hz)	5.76, dd (14.4, 6.5 Hz)
15	6.07, t (10.8 Hz)	6.02–6.13, m	6.08, q (11.3 Hz)
16	6.09, t (10.8 Hz)		
17	6.25, dd (14.4, 11.2 Hz)	6.24, dd (14.6, 10.7 Hz)	6.20–6.36, m
18	6.31, dd (14.4, 10.8 Hz)	6.34, dd (14.9, 10.8 Hz)	
19	6.50, dd (15.2, 11.2 Hz)	6.52, dd (15.4, 11.1 Hz)	6.60–6.44, m
20	6.55, dd (14.4, 10.8 Hz)	6.60, dd (14.6, 11.5 Hz)	

Table S2 Comparison of ^{13}C NMR data between our synthetic reoslvin D3 and the reported data

NO.	synthetic Resolvin D3 (**1**) (100 MHz, CD_3OD)	Petasis's Resolvin D3 (**1**) (150 MHz, CD_3OD)[S8]	Anderson's Resolvin D3 (**1**) (126 MHz, CD_3OD)[S9]
1	14.6	14.5	14.6
2	21.7	21.7	21.7
3	31.0	35.3	30.9
4	33.7	35.4	33.7
5	36.2	36.2	36.2
6	36.7	36.7	36.7
7	67.8	68.9	67.7
8	73.0	73.1	73.0
9	73.2	73.2	73.2
10	125.5	125.5	125.5
11	126.6	126.6	126.6
12	128.1	128.2	128.1
13	128.8	129.1	128.7
14	130.8	130.3	130.8
15	131.1	131.0	131.1
16	131.5	131.8	131.5
17	134.6	134.6	134.6
18	134.8	134.8	134.8
19	135.2	135.5	135.2
20	137.5	137.5	137.5
21	137.9	137.5	137.9
22	177.5	182.5	177.4

References

S1) B. M.Trost and M. J. Bartlett, *Org. Lett.*, 2012, **14**, 1322.

S2) E. E. Kwan, J. R. Scheerer and D. A. Evans, *J. Org. Chem.*, 2013, **78**, 175.

S3) E. C. McLaughlin and M. P. Doyle, *J. Org. Chem.*, 2008, **73**, 4317.

S4) M. Morita, S. Tanabe and Y. Kobayashi, *Synlett*, 2019, **30**, 1351.

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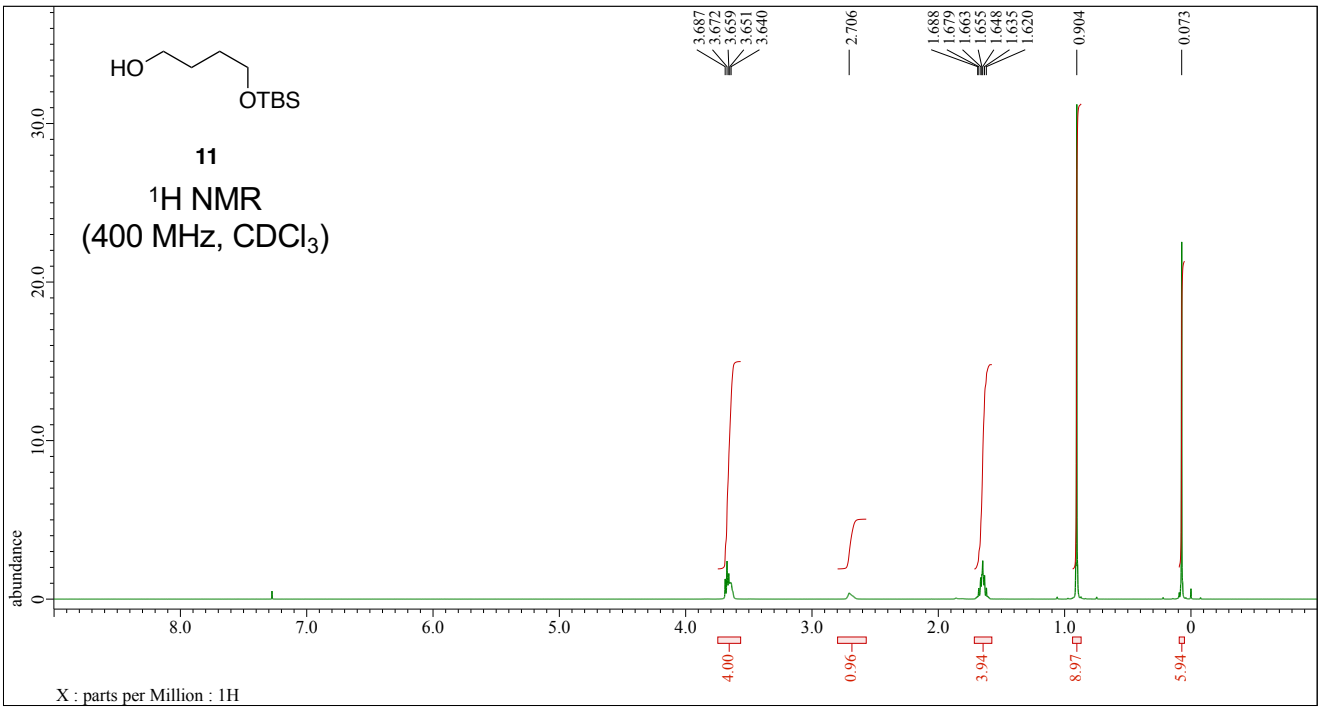
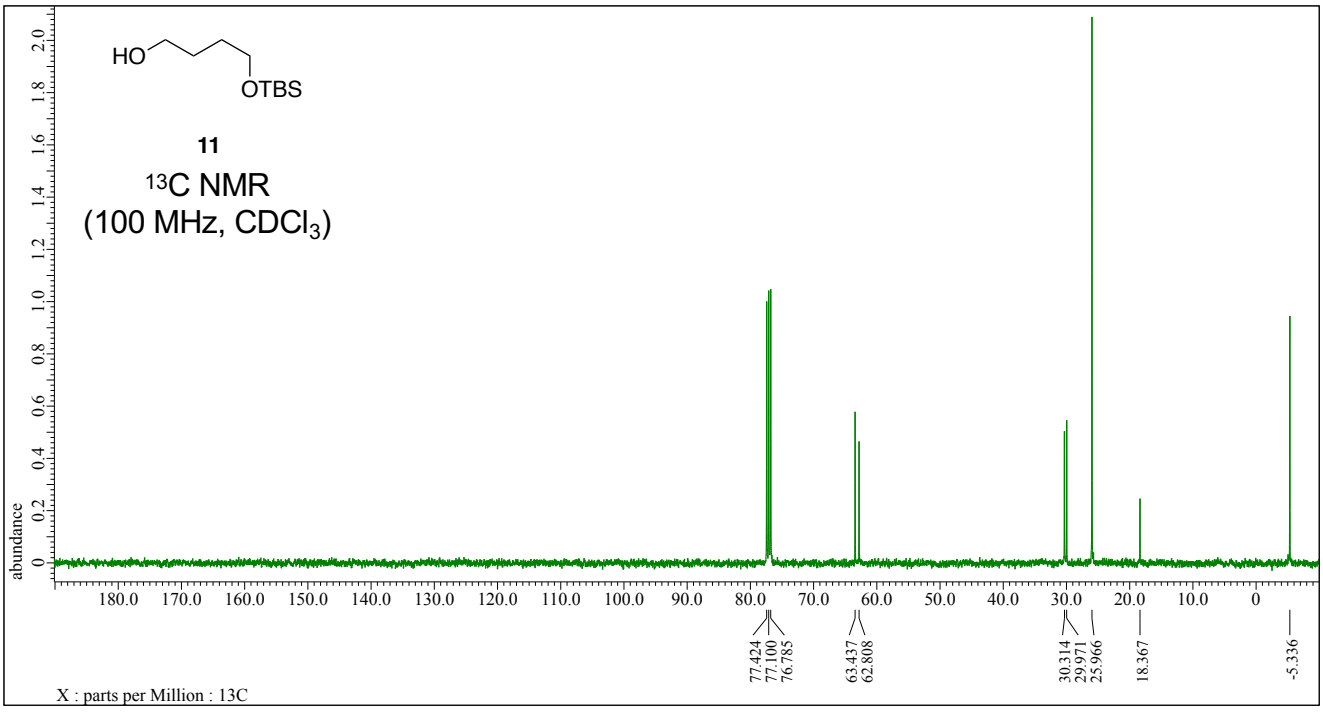
S6) O. Hartmann and M. Kalesse, *Org. Lett.*, 2012, **14**, 3064.

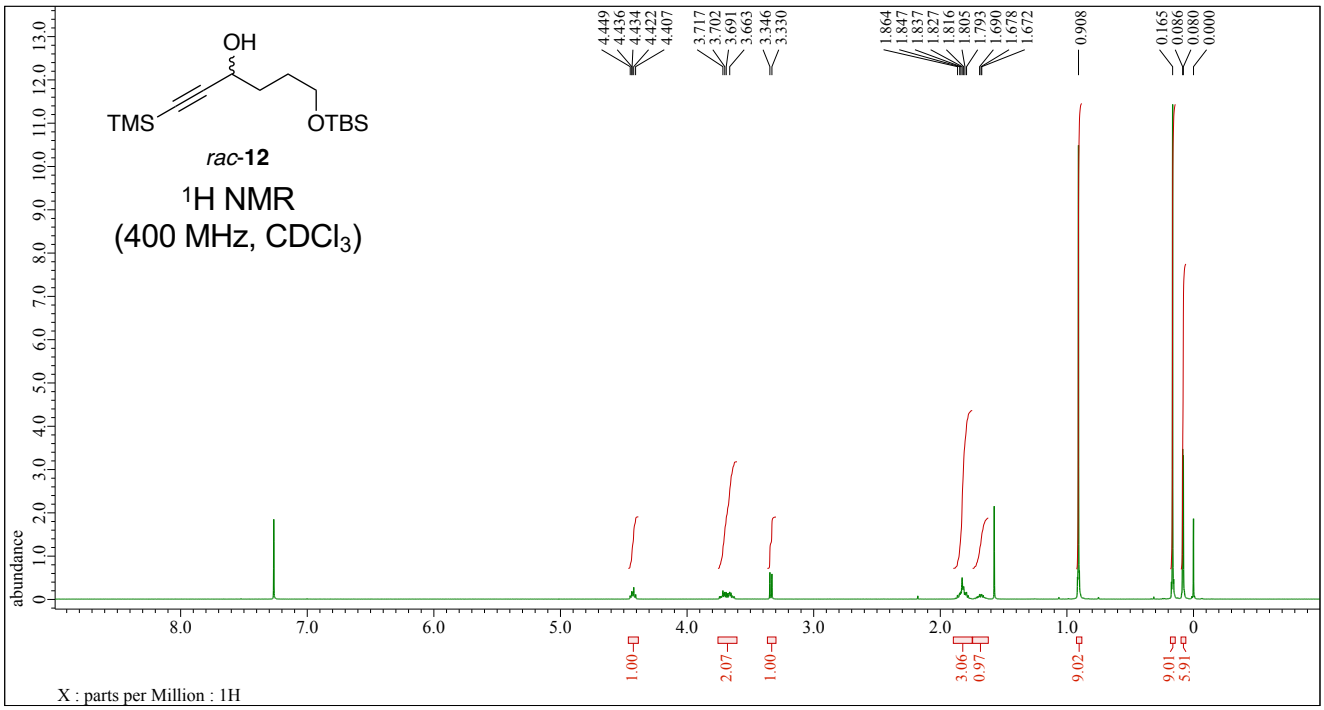
S7) N. Ogawa, S. Sone, S. Hong, Y. Lu and Y. Kobayashi, *Synlett*, 2020, **31**, 1735.

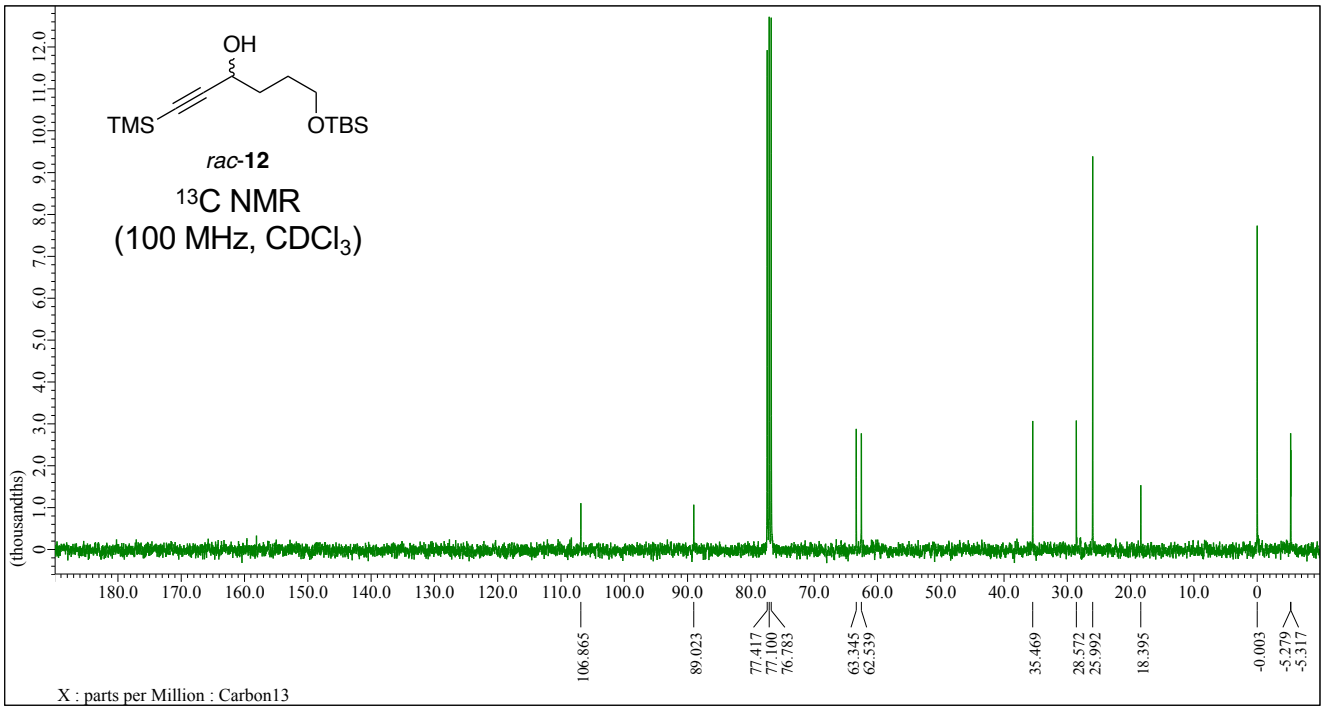
S8) J. W. Winkler, J. Uddin, C. N. Serhan and N. A. Petasis, *Org. Lett.*, 2013, **15**, 1424.

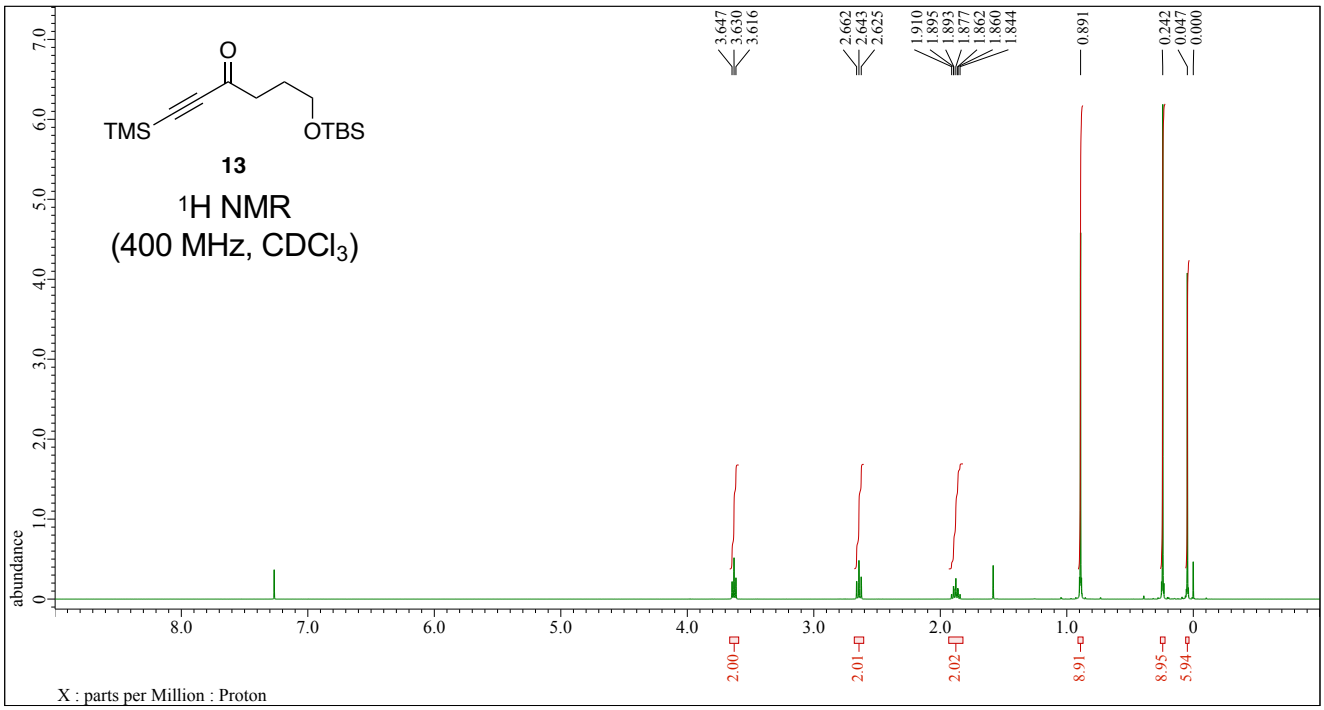
S9) F. Urbitsch, B. L. Elbert, J. Llaveria, P. E. Streatfeild and E. A. Anderson, *Org. Lett.*, 2020, **22**, 1510.

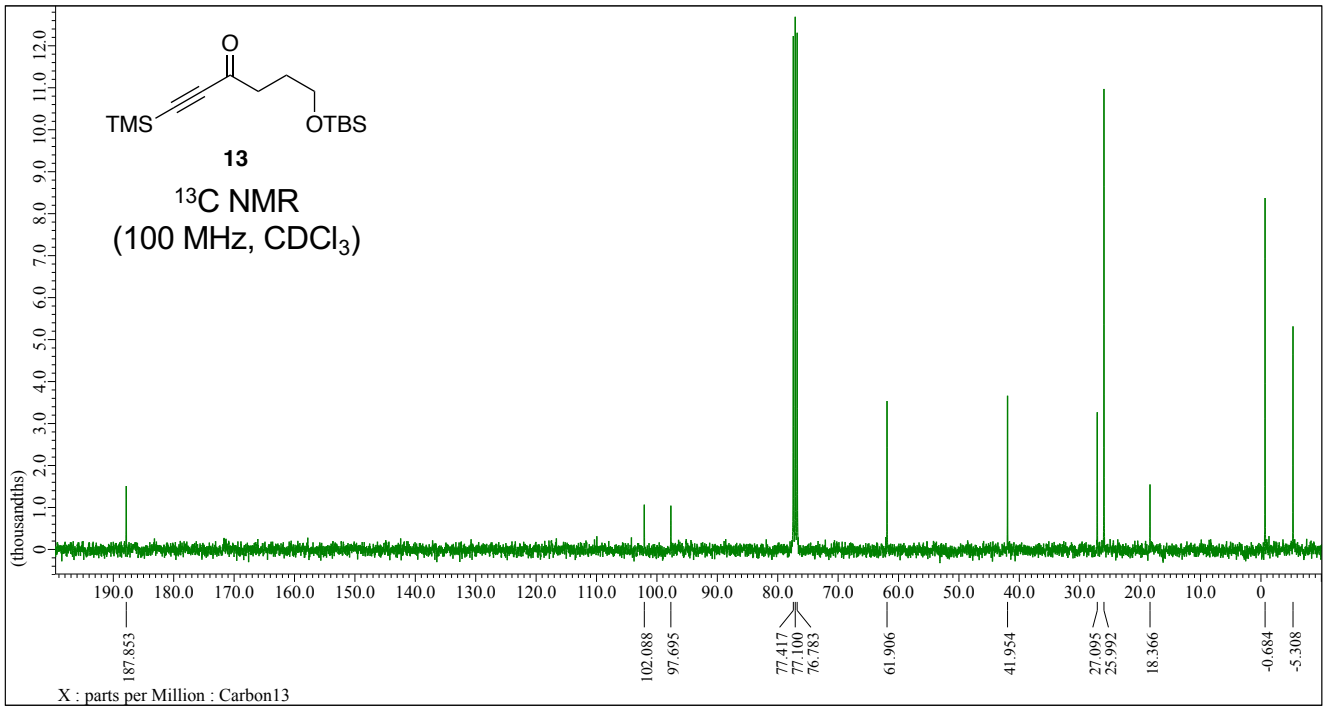

HO
OTBS
11
1H NMR
(400 MHz, CDCl3)
3.687
3.672
3.659
3.651
3.640
2.706
1.688
1.679
1.663
1.655
1.648
1.635
1.620
0.904
0.073
abundance
X : parts per Million : 1H
4.00
0.96
3.94
8.97
5.94


HO
OTBS
11
13C NMR
(100 MHz, CDCl3)
77.424
77.100
76.785
63.437
62.808
30.314
29.971
25.966
18.367
-5.336
abundance
X : parts per Million : 13C


OH
TMS
OTBS
rac-12
1H NMR
(400 MHz, CDCl3)
4.449
4.436
4.434
4.422
4.407
3.717
3.702
3.691
3.663
3.346
3.330
1.864
1.847
1.837
1.827
1.816
1.805
1.793
1.690
1.678
1.672
0.908
0.165
0.086
0.080
0.000
abundance
1.00
2.07
1.00
3.06
0.97
9.02
9.01
5.91
X : parts per Million : 1H


OH
TMS
OTBS
rac-12
13C NMR
(100 MHz, CDCl3)
(thousandths)
106.865
89.023
77.417
77.100
76.783
63.345
62.539
35.469
28.572
25.992
18.395
-0.003
-5.279
-5.317
X : parts per Million : Carbon13


TMS
O
OTBS
13
1H NMR
(400 MHz, CDCl3)
3.647
3.630
3.616
2.662
2.643
2.625
1.910
1.895
1.893
1.877
1.862
1.860
1.844
0.891
0.242
0.047
0.000
abundance
2.00
2.01
2.02
8.91
8.95
5.94
X : parts per Million : Proton


TMS
O
OTBS
13
13C NMR
(100 MHz, CDCl3)
(thousandths)
187.853
102.088
97.695
77.417
77.100
76.783
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27.095
25.992
18.366
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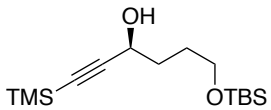
-5.308
X : parts per Million : Carbon13

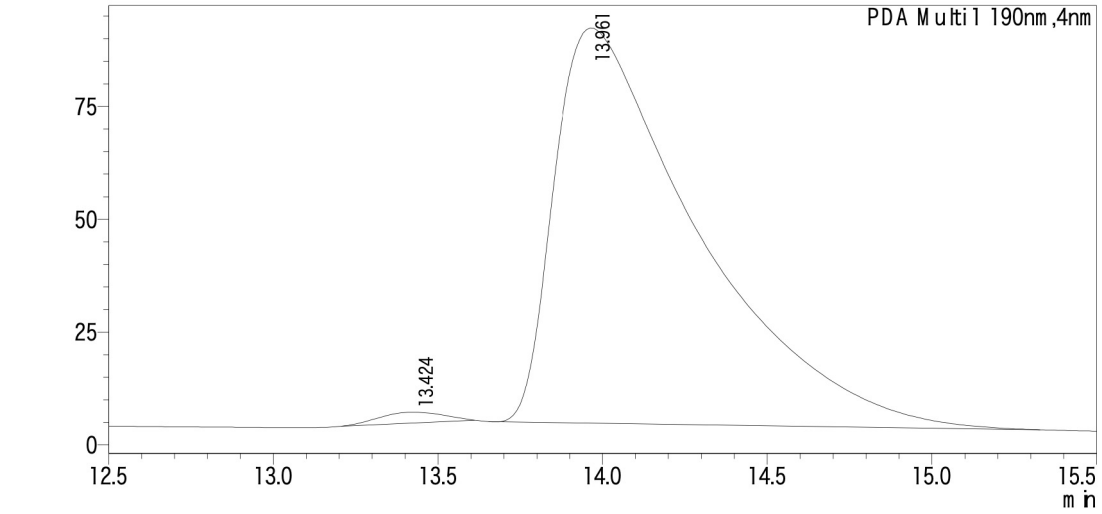
HPLC analysis



(*S*)-**12**

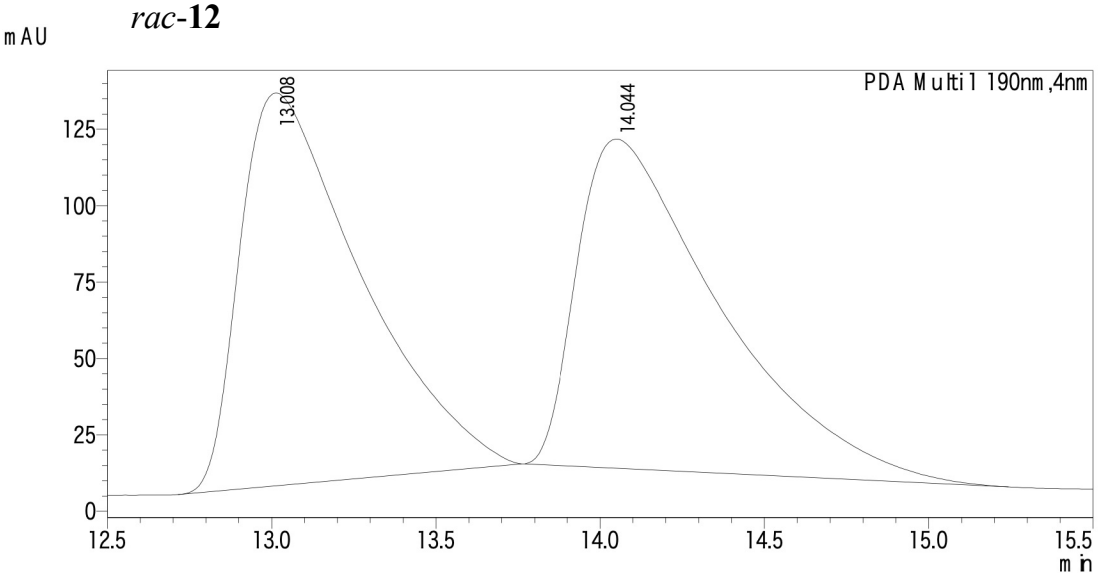
ee = (98.763–1.237)×100/(98.763+1.237)
= 97.526
≈ 98%

(*S*)-**12**

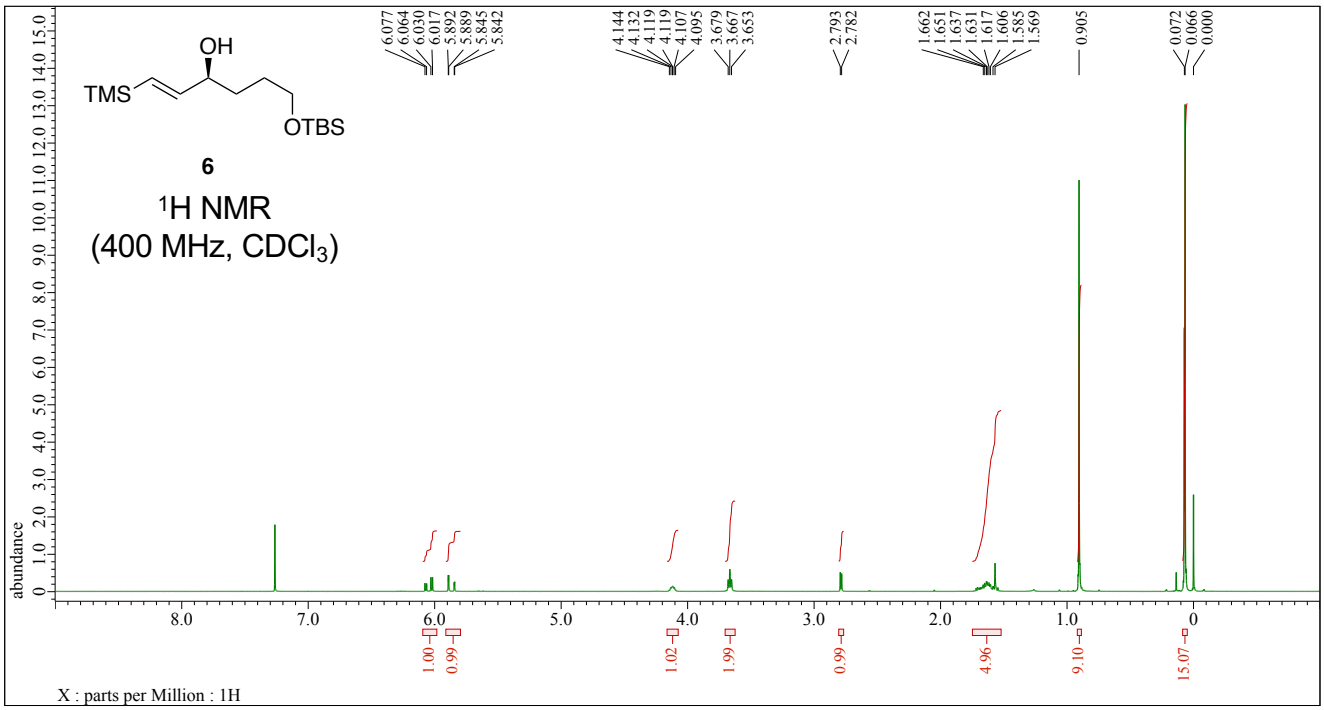


1	13.424	33253	1.237	2400	2.669
2	13.961	2654178	98.763	87533	97.331

rac-**12**



Conditions: Chiralcel OD-H, hexane, 1.0 mL/min, 35 ºC


OH
TMS
OTBS
6
1H NMR
(400 MHz, CDCl3)
6.077
6.064
6.030
6.017
5.892
5.889
5.845
5.842
4.144
4.132
4.119
4.119
4.107
4.095
3.679
3.667
3.653
2.793
2.782
1.662
1.651
1.637
1.631
1.617
1.606
1.585
1.569
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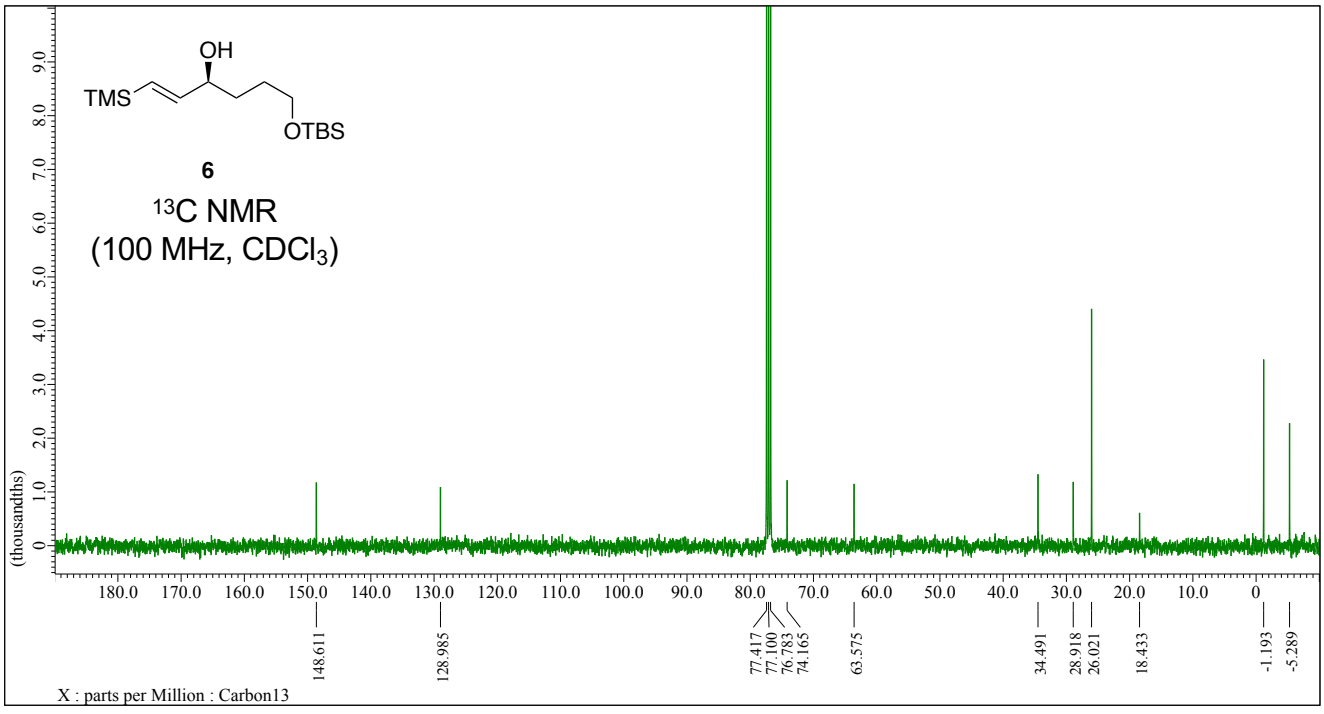
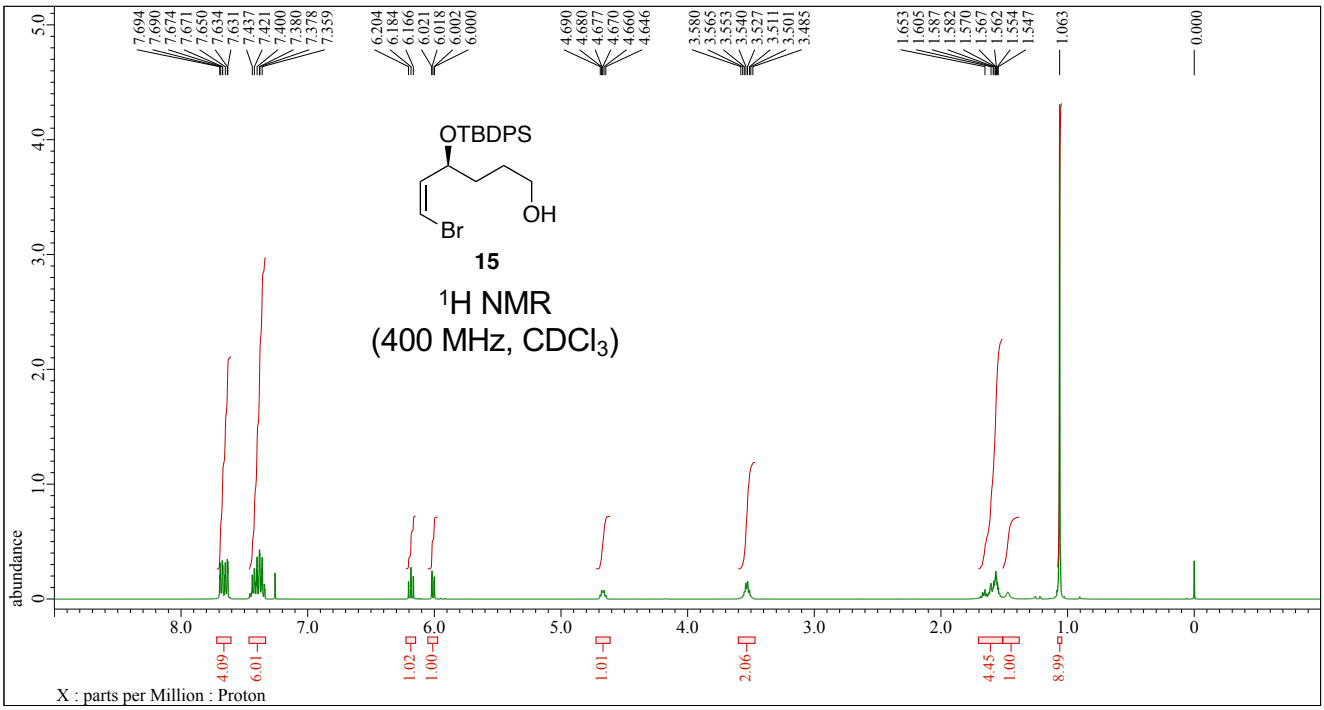
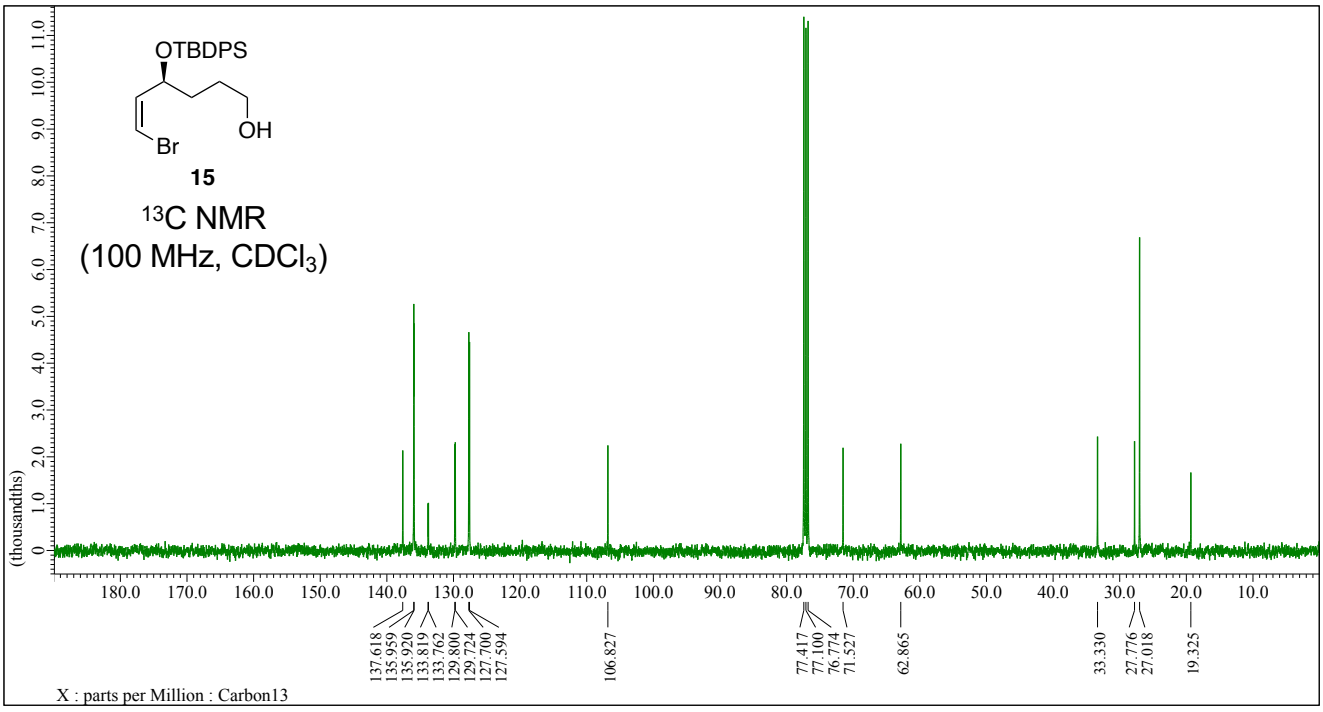
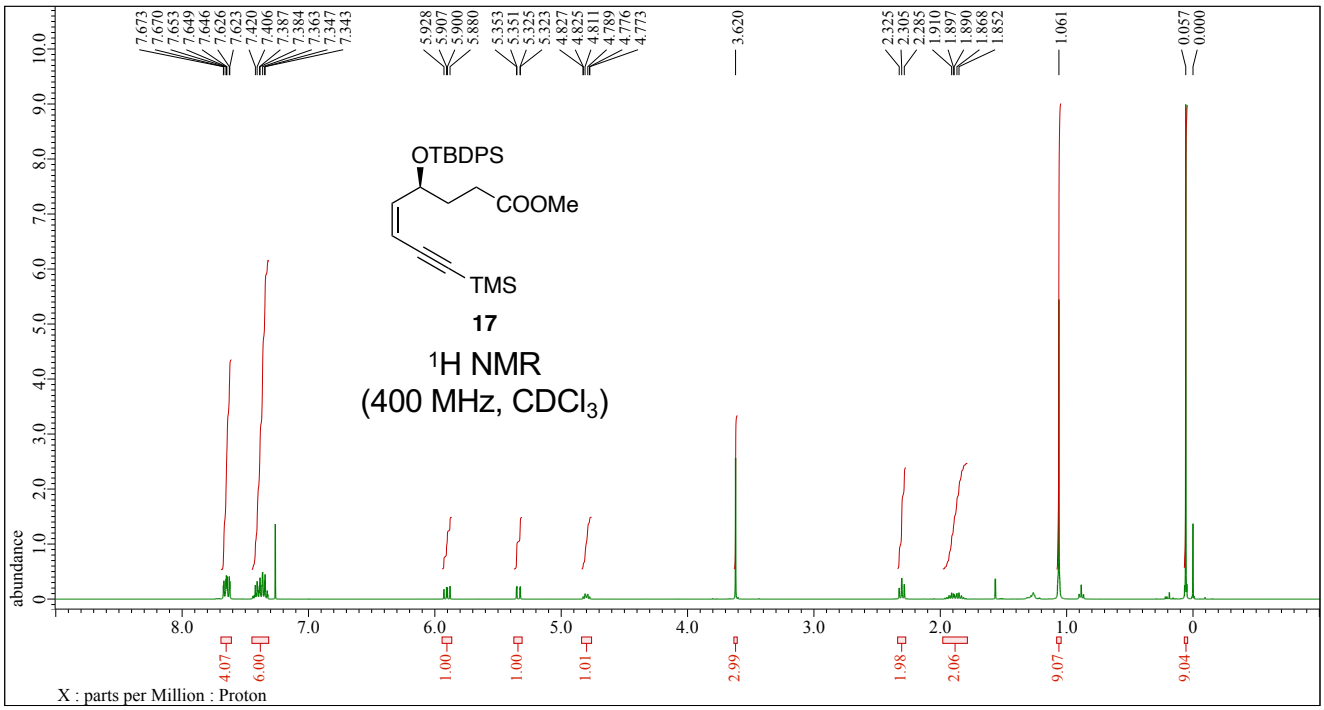
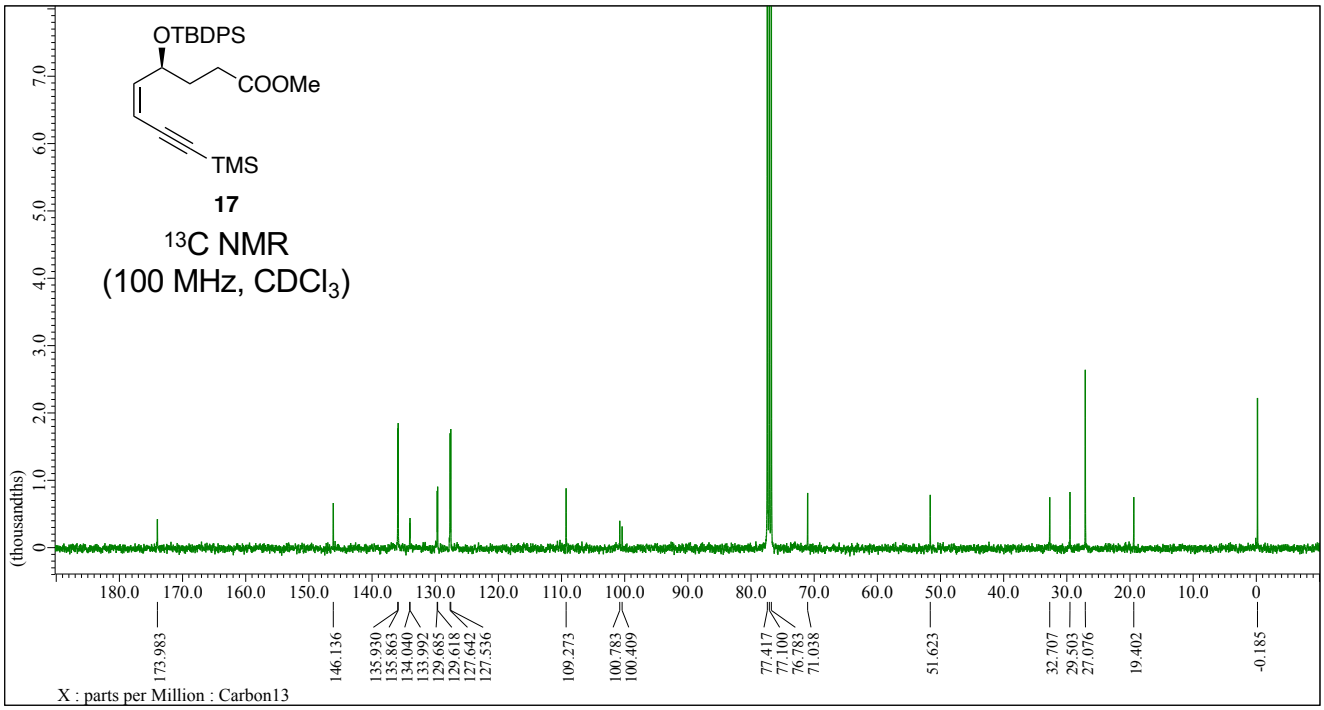
0.072
0.066
0.000
abundance
X : parts per Million : 1H


OH
TMS
OTBS
6
13C NMR
(100 MHz, CDCl3)
(thousandths)
148.611
128.985
77.417
77.100
76.783
74.165
63.575
34.491
28.918
26.021
18.433
-1.193
-5.289
X : parts per Million : Carbon13


OTBDPS
Br
OH
15
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton


OTBDPS
Br
OH
15
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13


OTBDPS
COOMe
TMS
17
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton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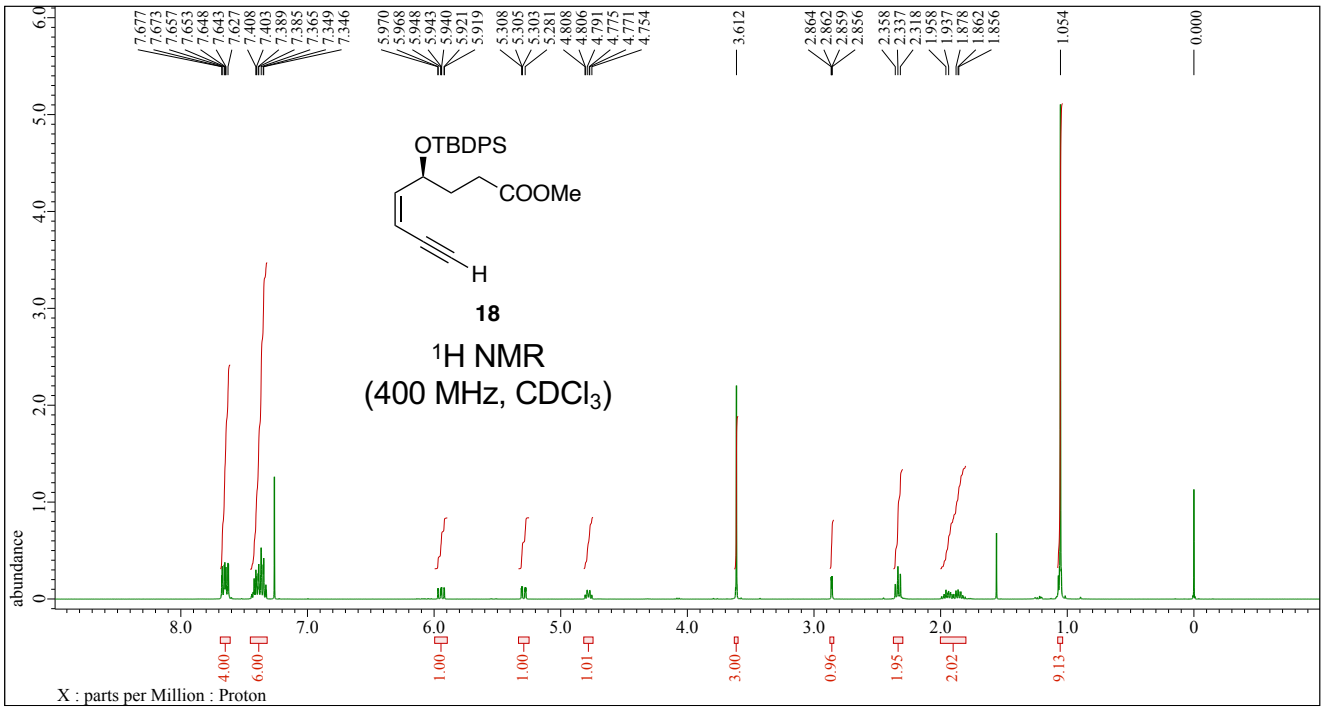
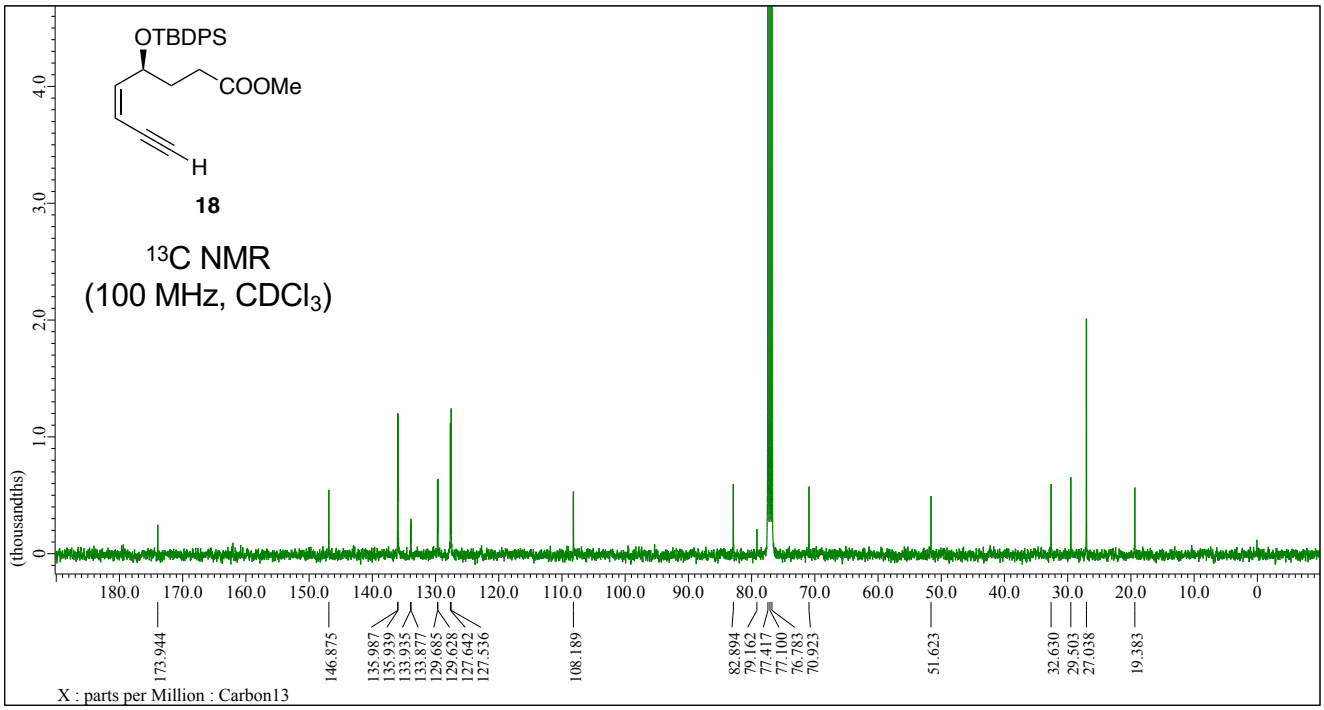
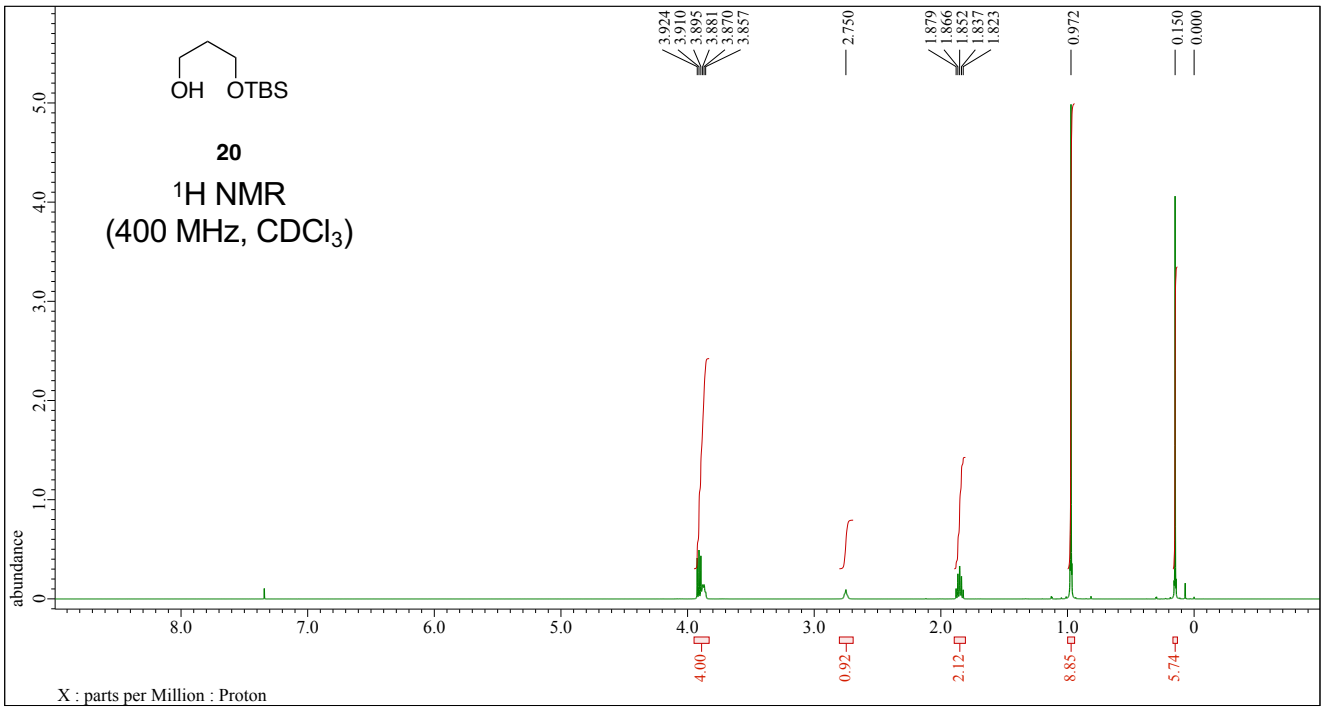
COOMe
TMS
17
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13


OTBDPS
COOMe
H
18
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton


OTBDPS
COOMe
H
18
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13


OH OTBS
20
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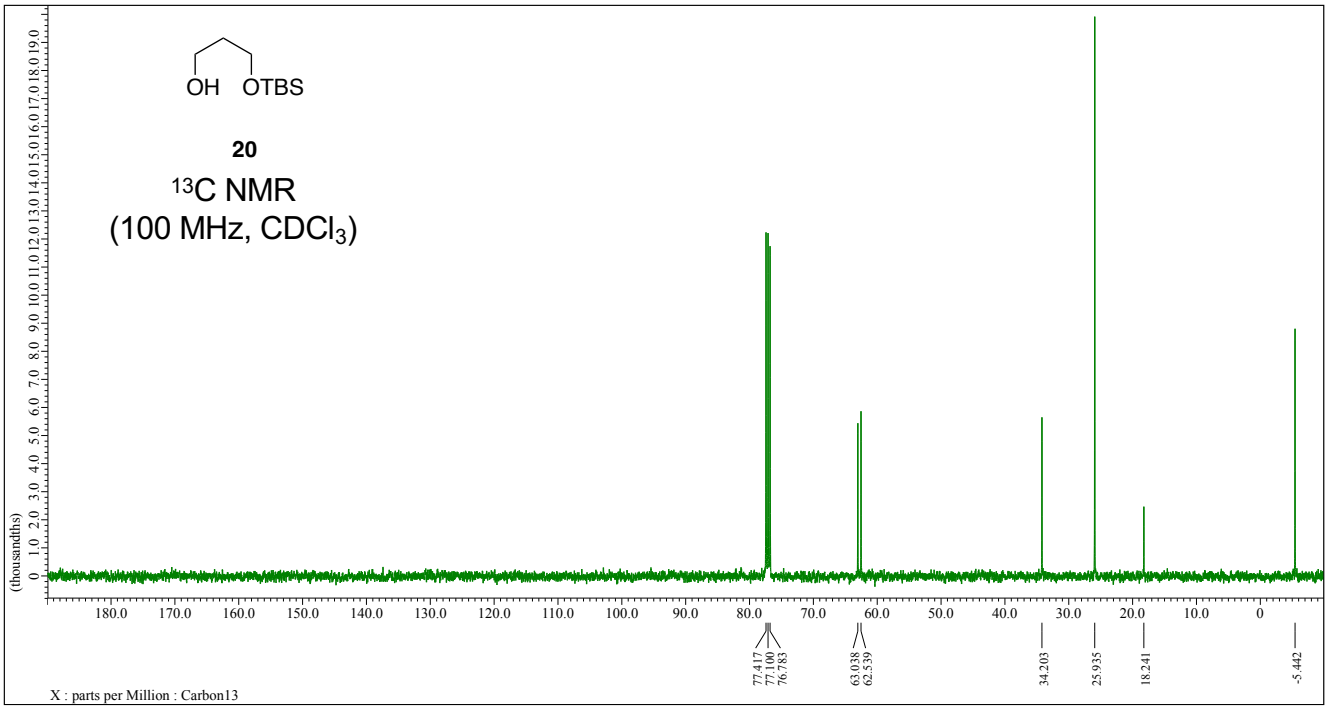
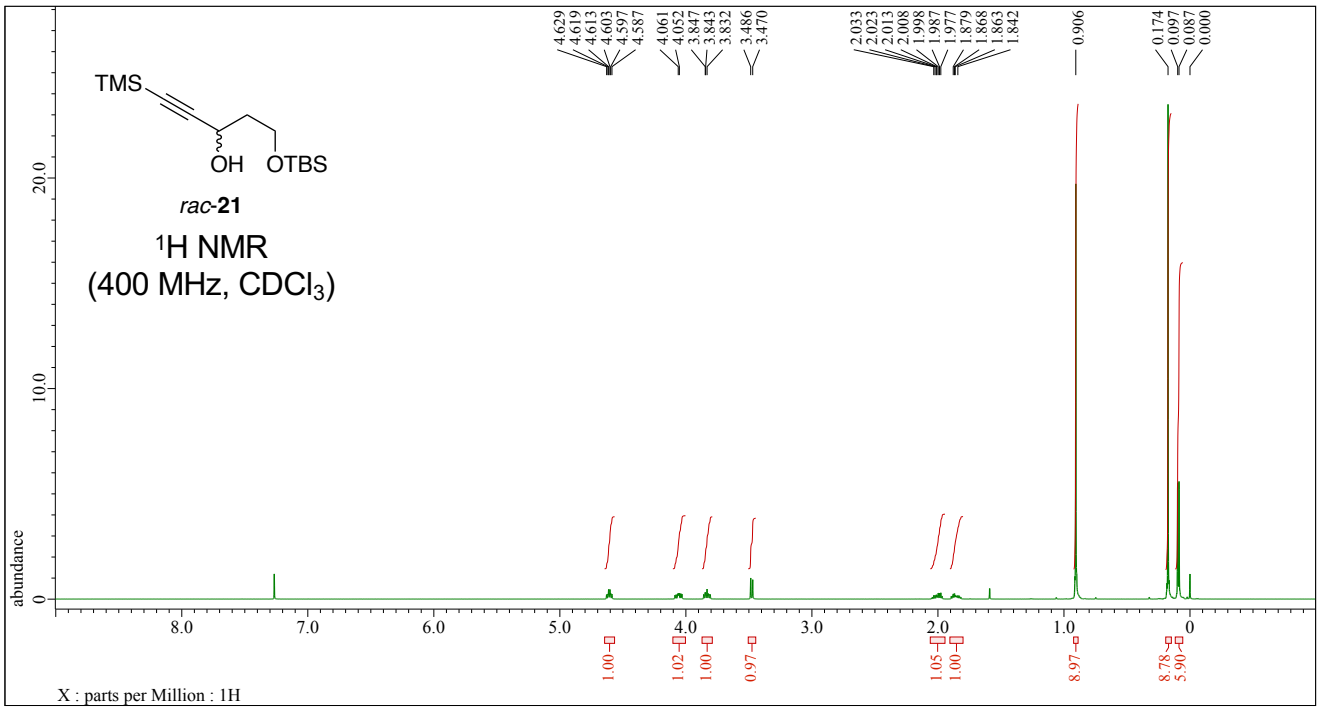
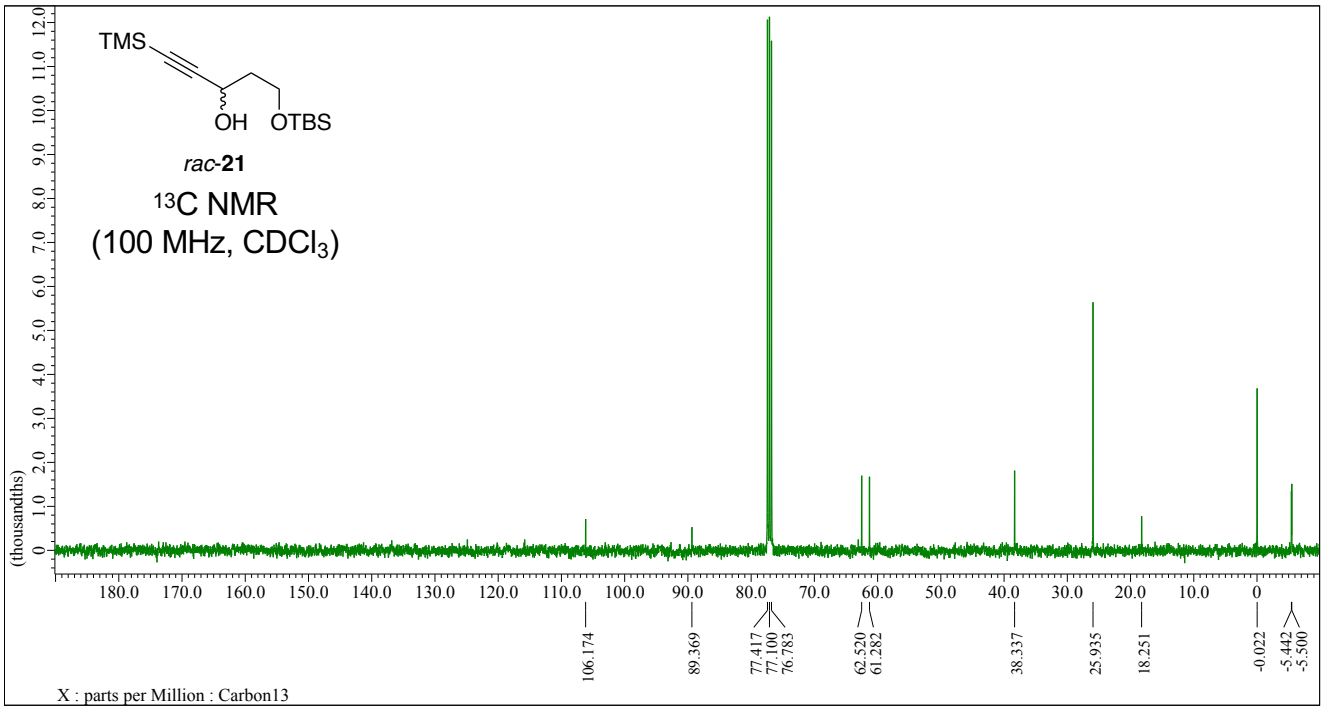
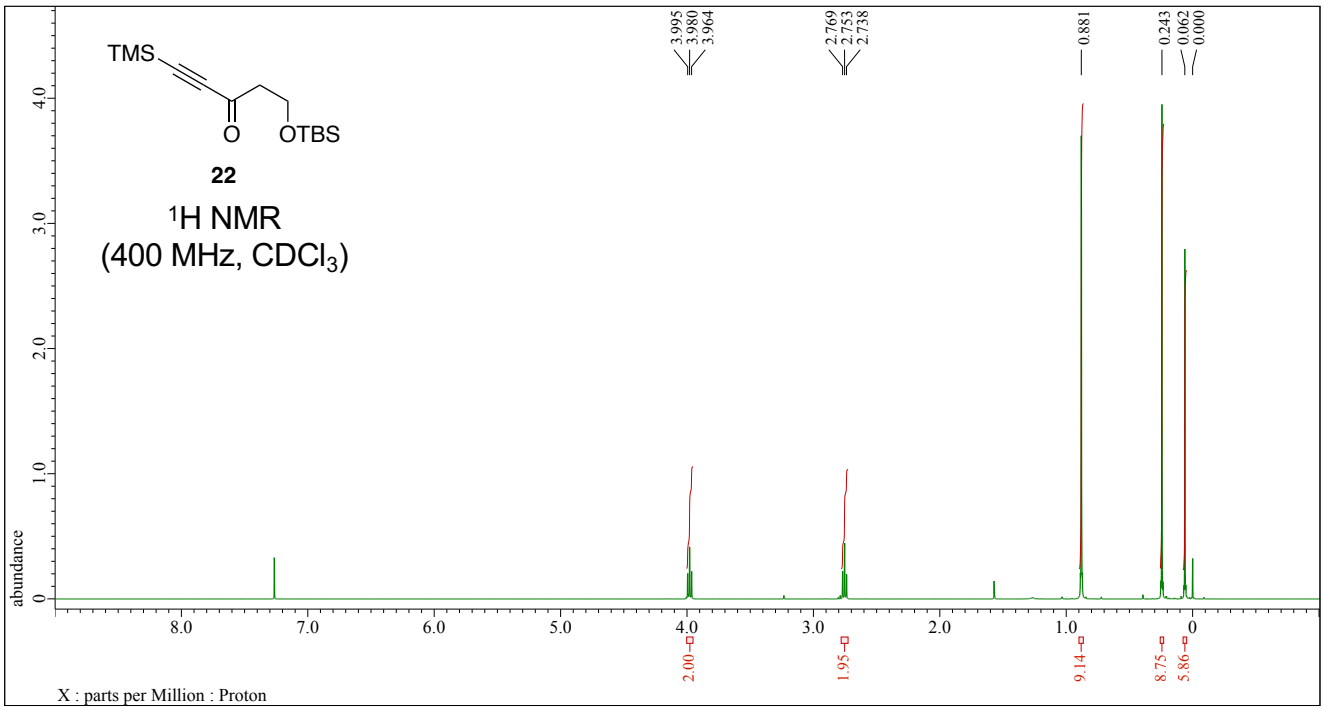
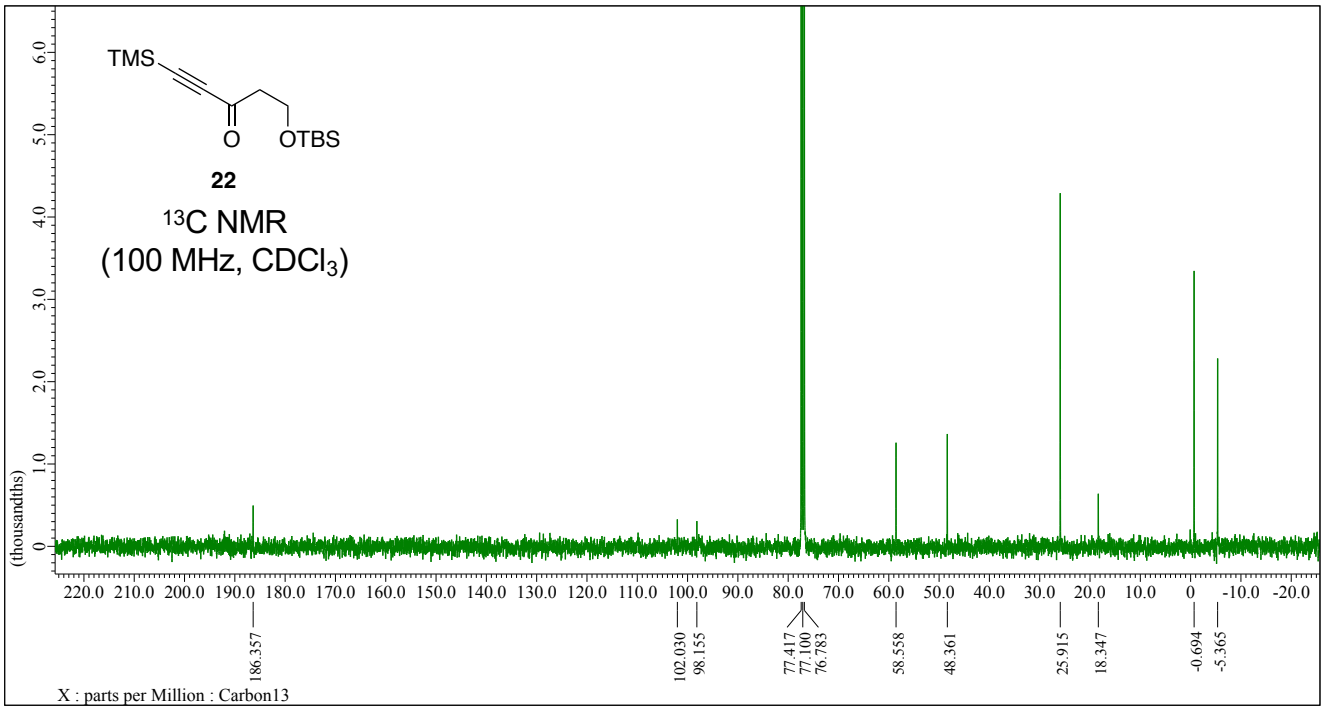
(400 MHz, CDCl3)
3.924
3.910
3.895
3.881
3.870
3.857
2.750
1.879
1.866
1.852
1.837
1.823
0.972
0.150
0.000
abundance
4.00
0.92
2.12
8.85
5.74
X : parts per Million : Proton


OH OTBS
20
13C NMR
(100 MHz, CDCl3)
(thousandths)
77.417
77.100
76.783
63.038
62.539
34.203
25.935
18.241
-5.442
X : parts per Million : Carbon13

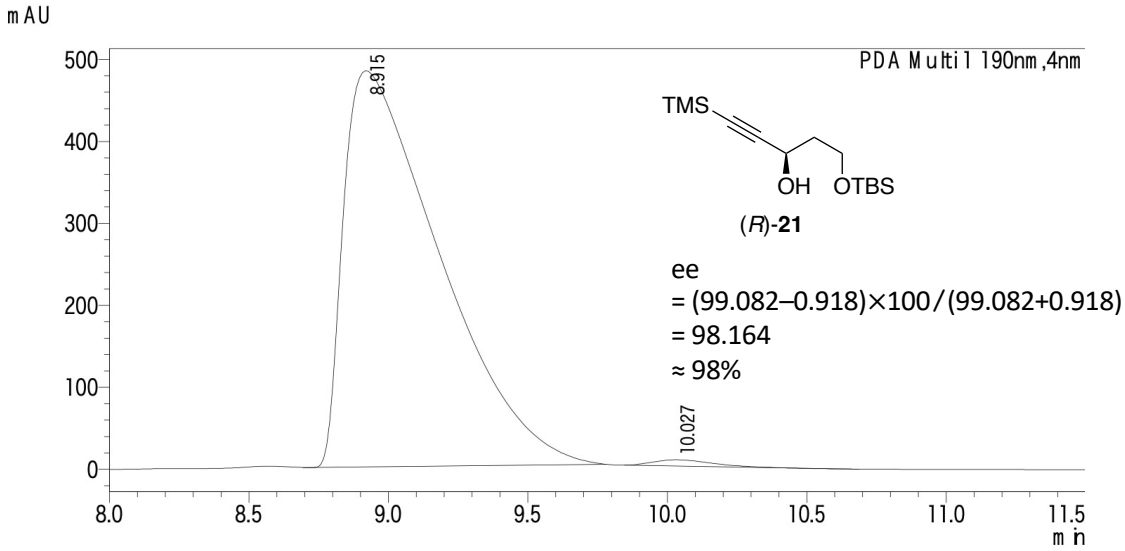

TMS
OH
OTBS
rac-21
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : 1H


TMS
OH
OTBS
rac-21
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13

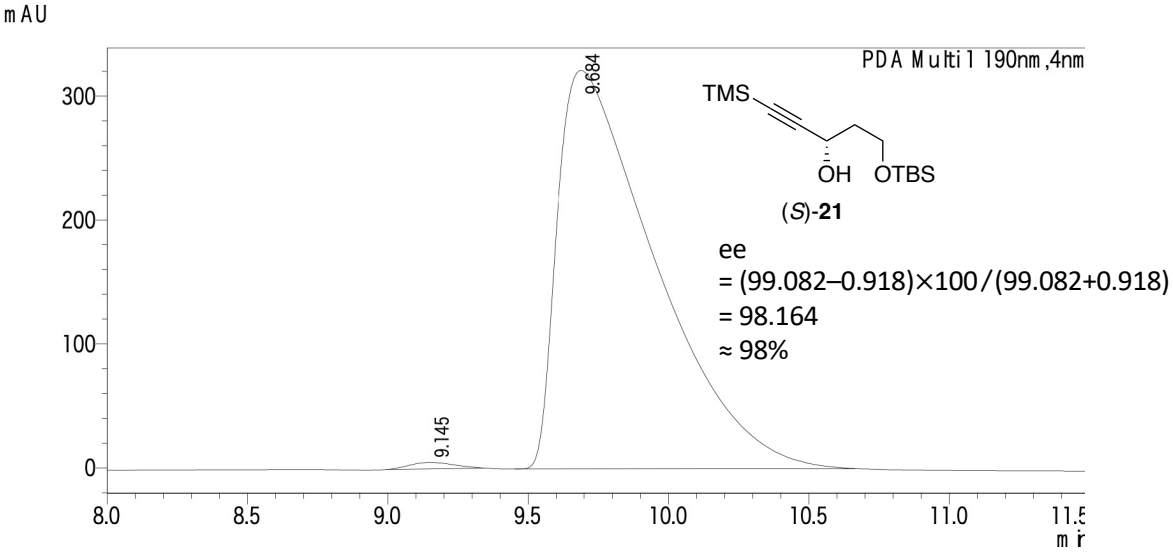

TMS
O
OTBS
22
1H NMR
(400 MHz, CDCl3)
3.995
3.980
3.964
2.769
2.753
2.738
0.881
0.243
0.062
0.000
abundance
2.00
1.95
9.14
8.75
5.86
X : parts per Million : Proton


TMS
O
OTBS
22
13C NMR
(100 MHz, CDCl3)
(thousandths)
186.357
102.030
98.155
77.417
77.100
76.783
58.558
48.361
25.915
18.347
-0.694
-5.365
X : parts per Million : Carbon13

HPLC analysis

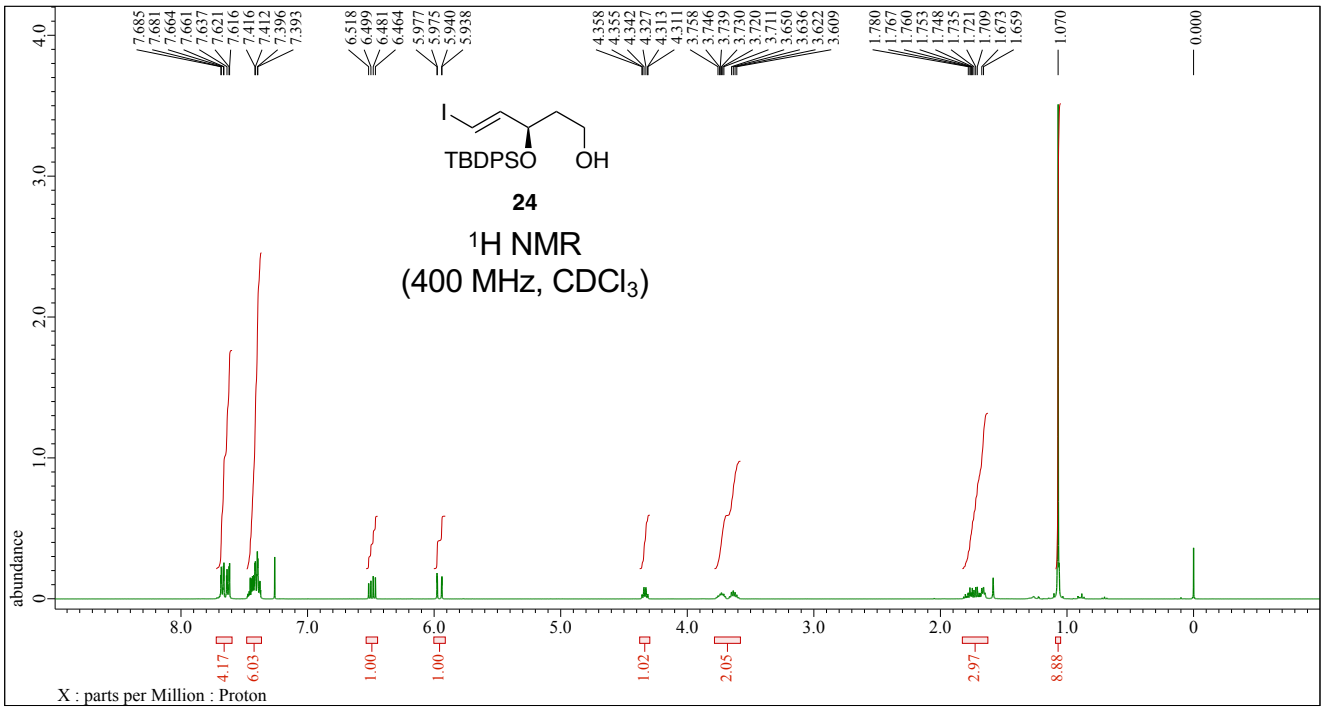


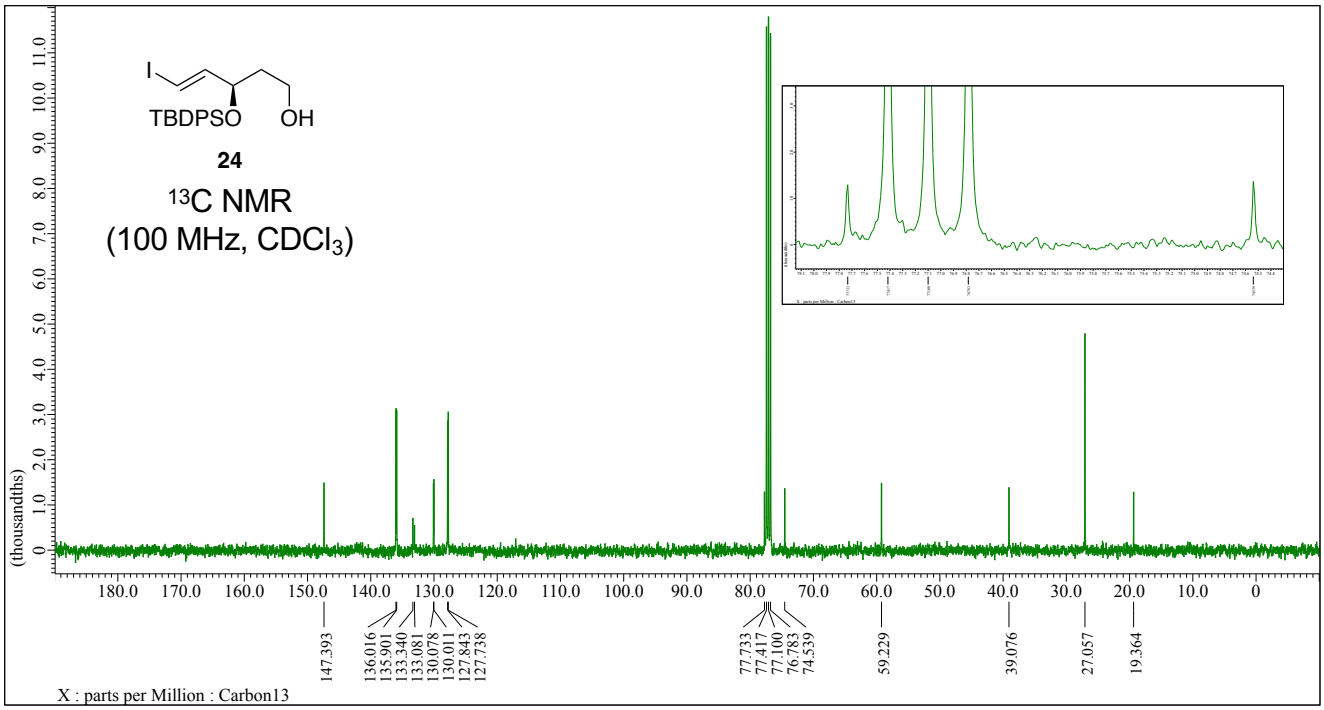
peak#	t_R	area	area%	height	height%
1	8.915	11568443	99.082	483300	98.462
2	10.027	107221	0.918	7550	1.538

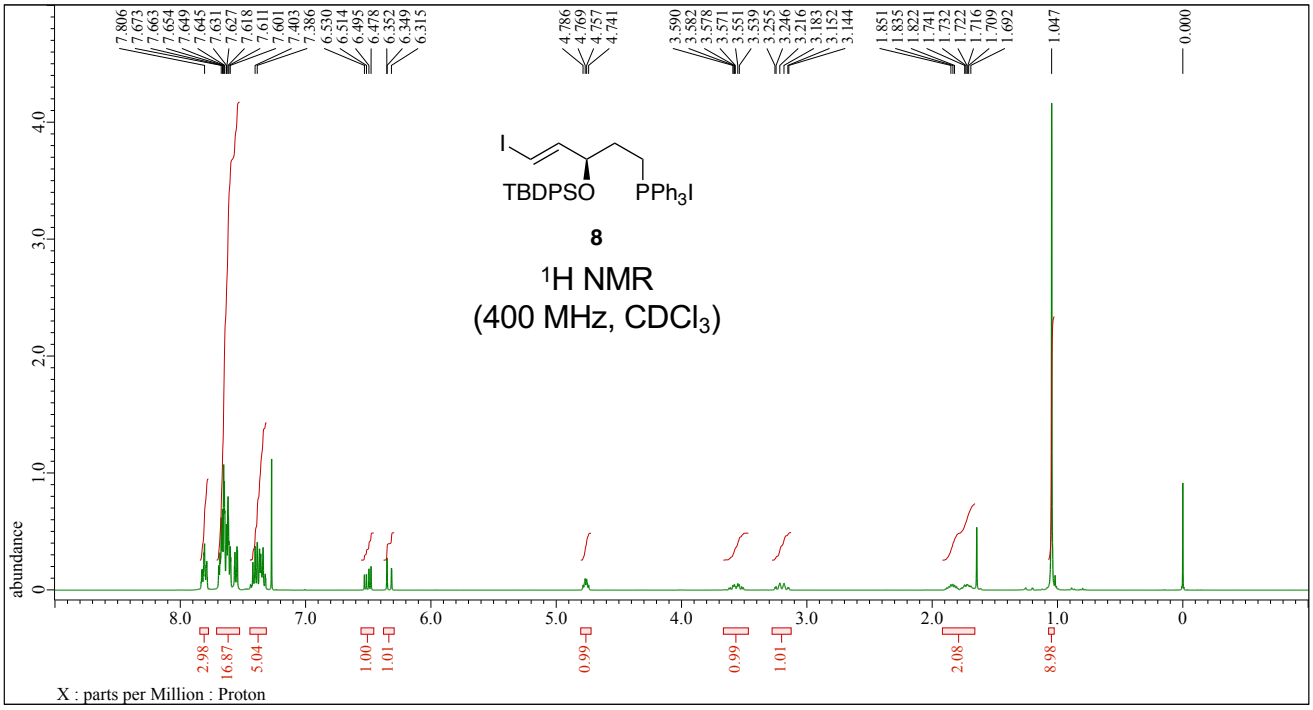


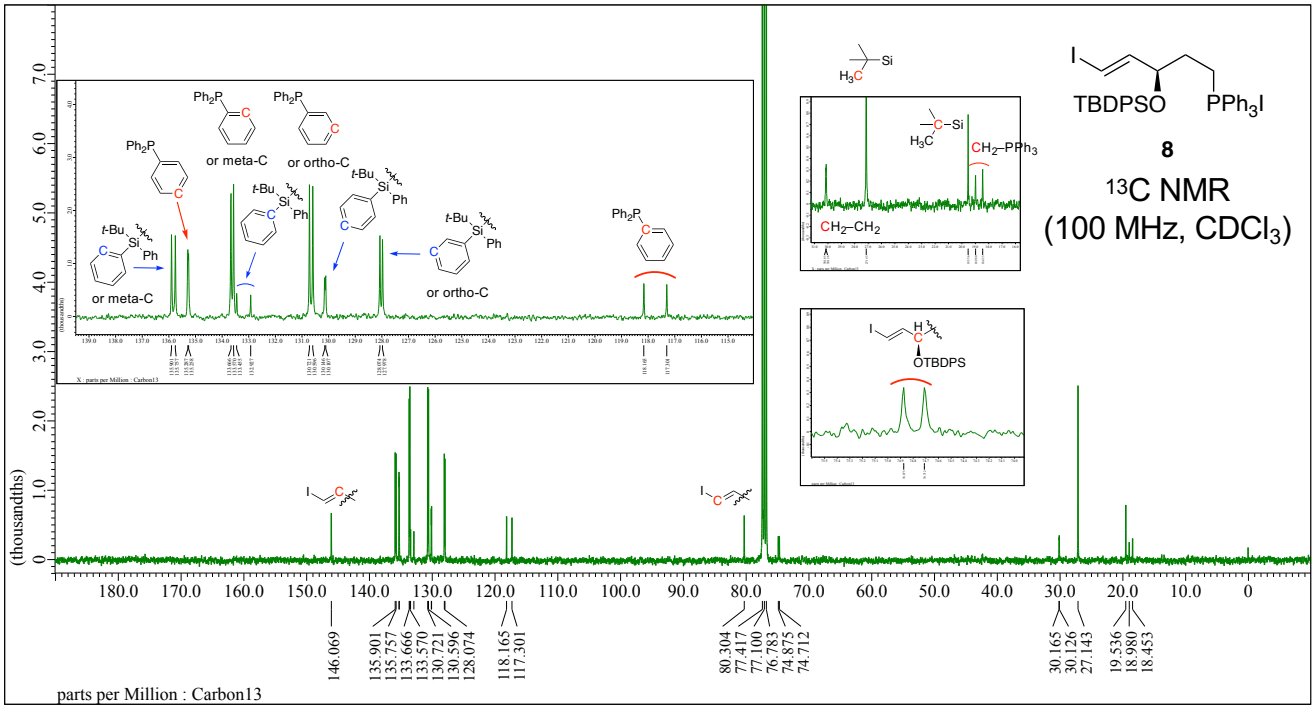
peak#	t_R	area	area%	height	height%
1	9.145	58276	0.742	5318	1.625
2	9.684	7800049	99.258	321845	98.375

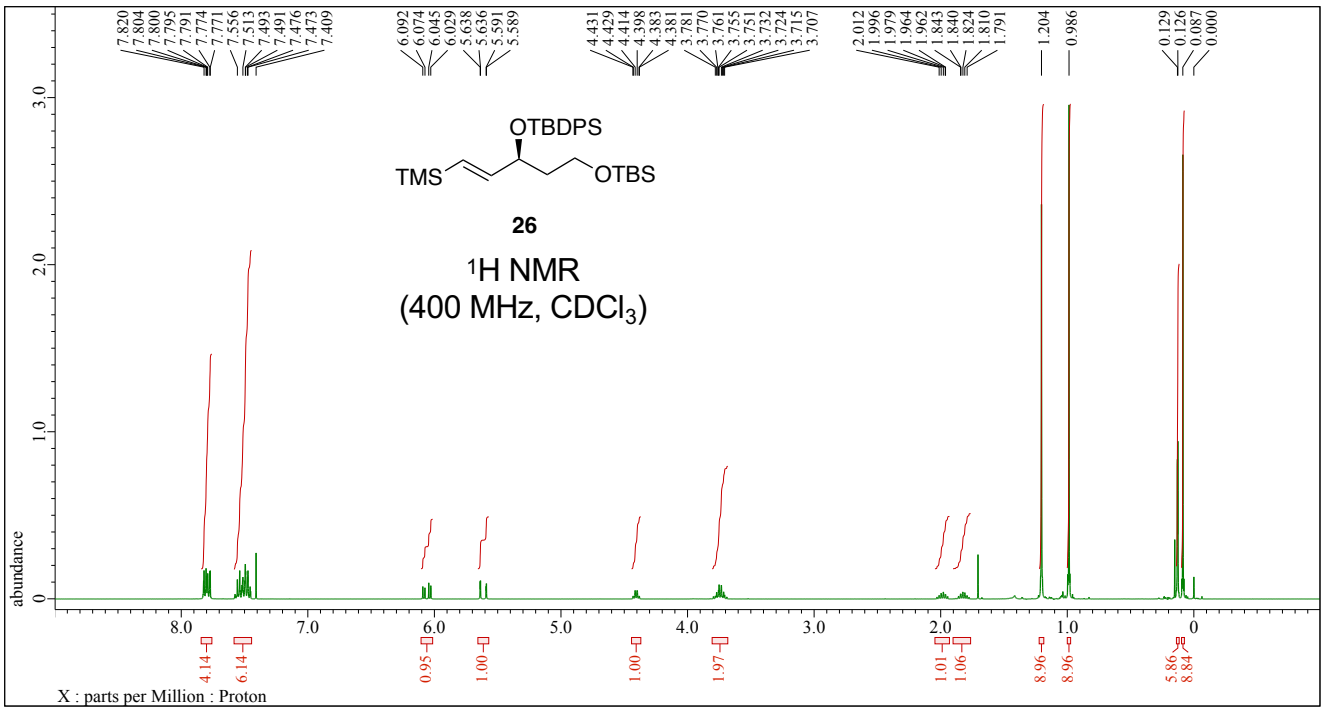
Conditions: Chiralcel OD-H, hexane, 1.0 mL/min, 35 ºC

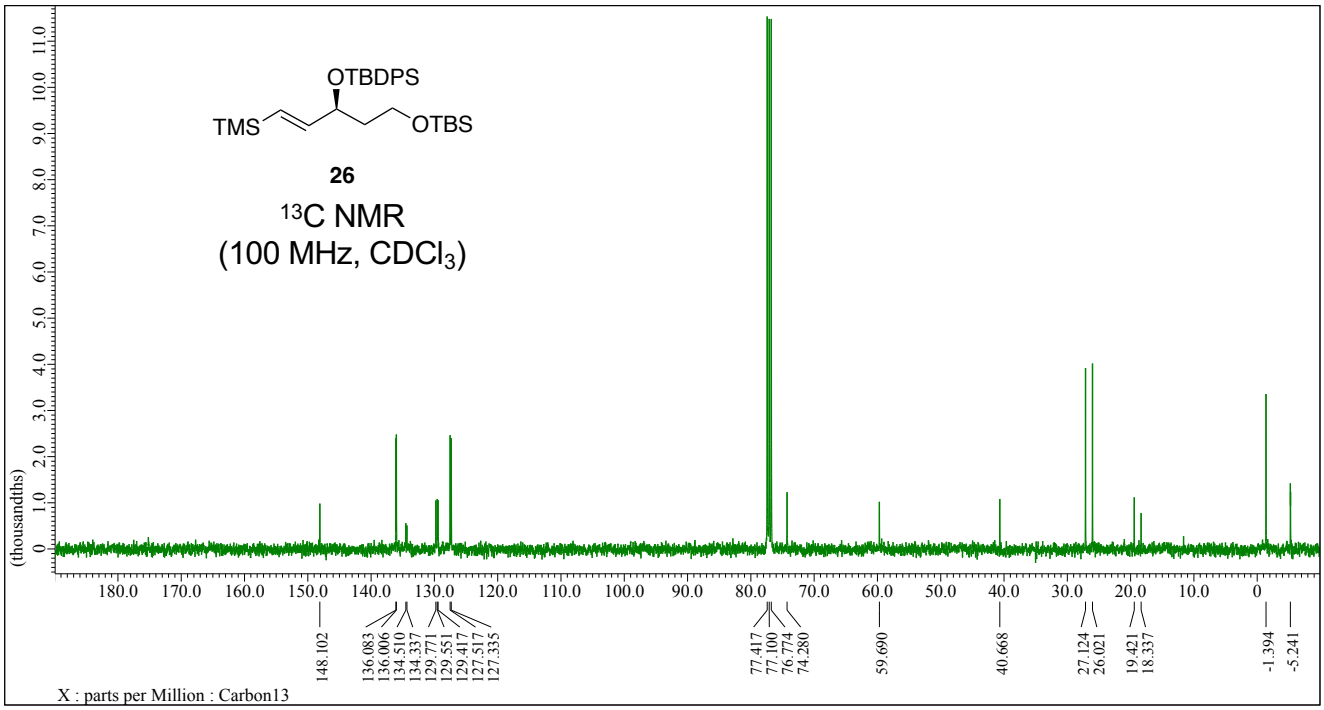

7.685
7.681
7.664
7.661
7.637
7.621
7.616
7.416
7.412
7.396
7.393
6.518
6.499
6.481
6.464
5.977
5.975
5.940
5.938
4.358
4.355
4.342
4.327
4.313
4.311
3.758
3.746
3.739
3.730
3.720
3.711
3.650
3.636
3.622
3.609
1.780
1.767
1.760
1.753
1.748
1.735
1.721
1.709
1.673
1.659
1.070
0.000
I
TBDPSO
OH
24
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton
4.17
6.03
1.00
1.00
1.02
2.05
2.97
8.88

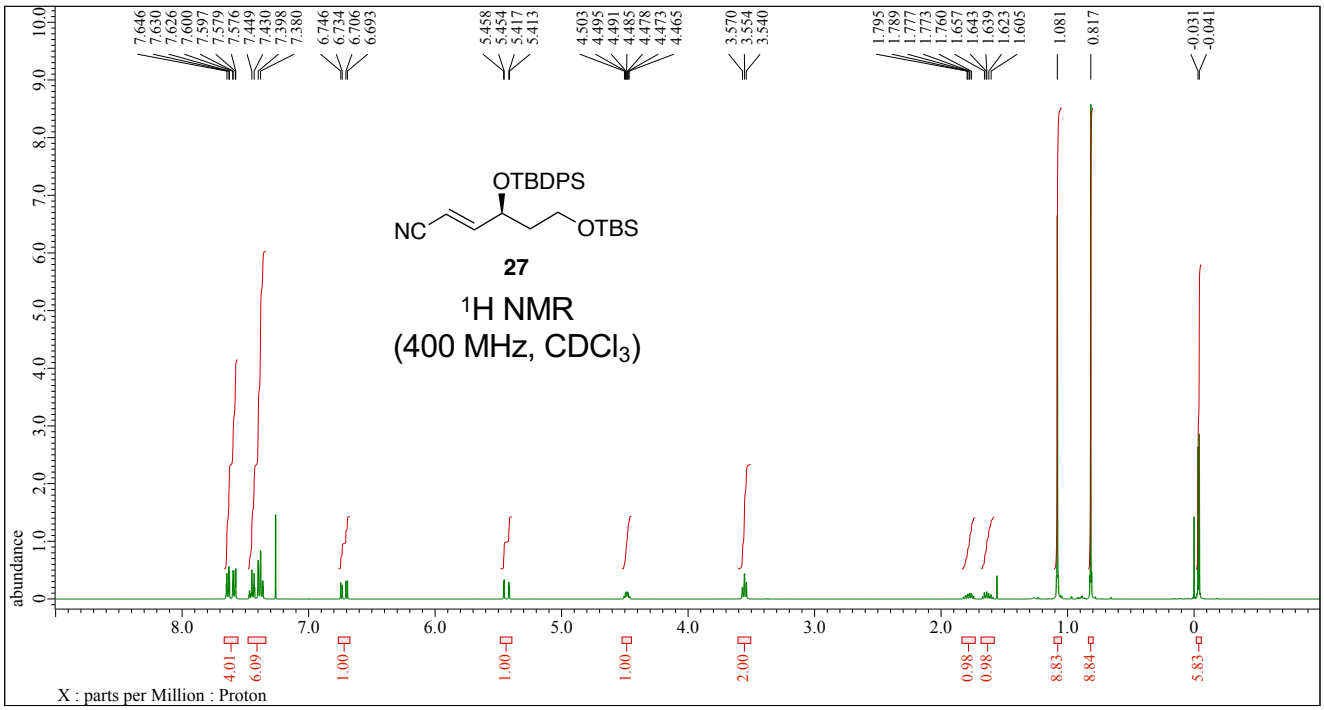

I
TBDPSO
OH
24
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13
147.393
136.016
135.901
133.340
133.081
130.078
130.011
127.843
127.738
77.733
77.417
77.100
76.783
74.539
59.229
39.076
27.057
19.364

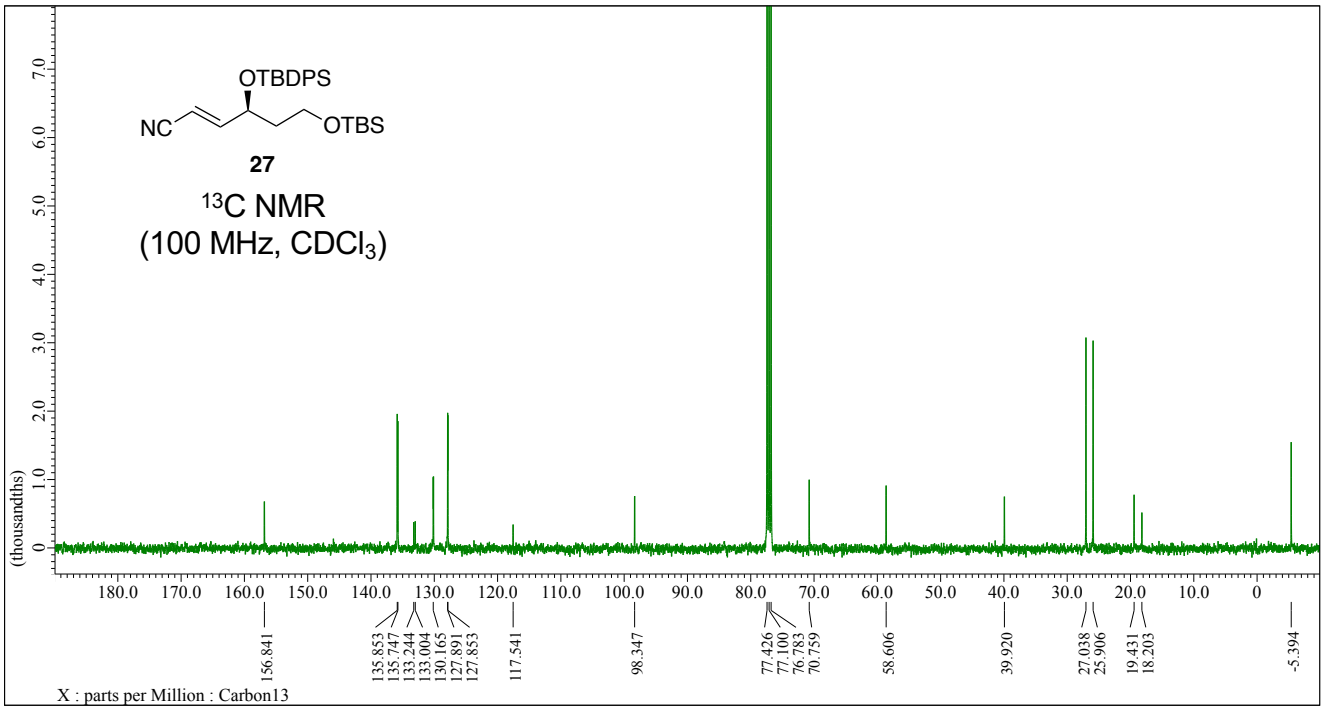

7.806
7.673
7.663
7.654
7.649
7.645
7.631
7.627
7.618
7.611
7.601
7.403
7.386
6.530
6.514
6.495
6.478
6.352
6.349
6.315
4.786
4.769
4.757
4.741
3.590
3.582
3.578
3.571
3.551
3.539
3.255
3.246
3.216
3.183
3.152
3.144
1.851
1.835
1.822
1.741
1.732
1.722
1.716
1.709
1.692
1.047
0.000
I
TBDPSO
PPh3I
8
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton

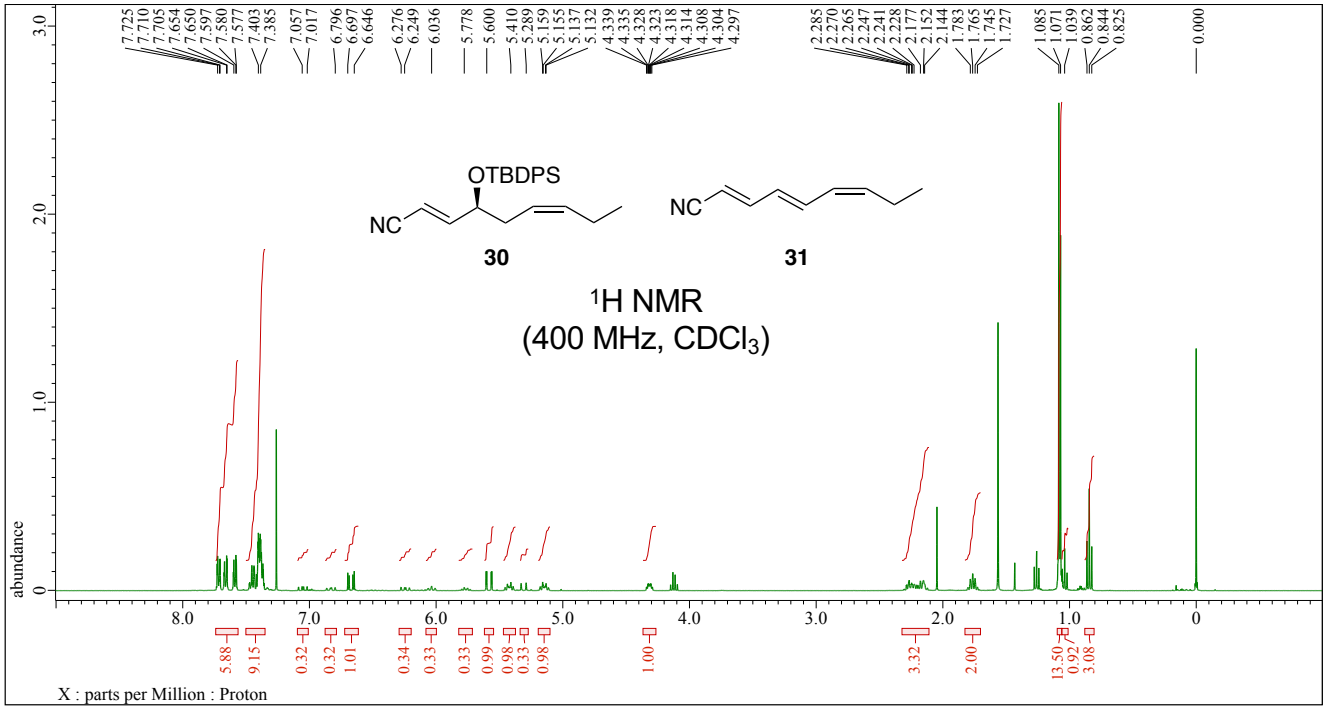

Ph2P
or meta-C
or ortho-C
t-Bu
Si
Ph
H3C
CH2–PPh3
CH2–CH2
OTBDPS
I
TBDPSO
PPh3I
8
13C NMR
(100 MHz, CDCl3)
(thousandths)
146.069
135.901
135.757
133.666
133.570
130.721
130.596
128.074
118.165
117.301
80.304
77.417
77.100
76.783
74.875
74.712
30.165
30.126
27.143
19.536
18.980
18.453
parts per Million : Carbon13


OTBDPS
TMS
OTBS
26
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton

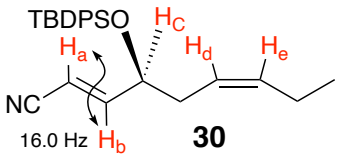

OTBDPS
TMS
OTBS
26
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13

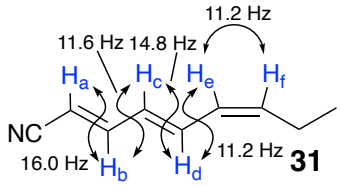

OTBDPS
NC
OTBS
27
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton

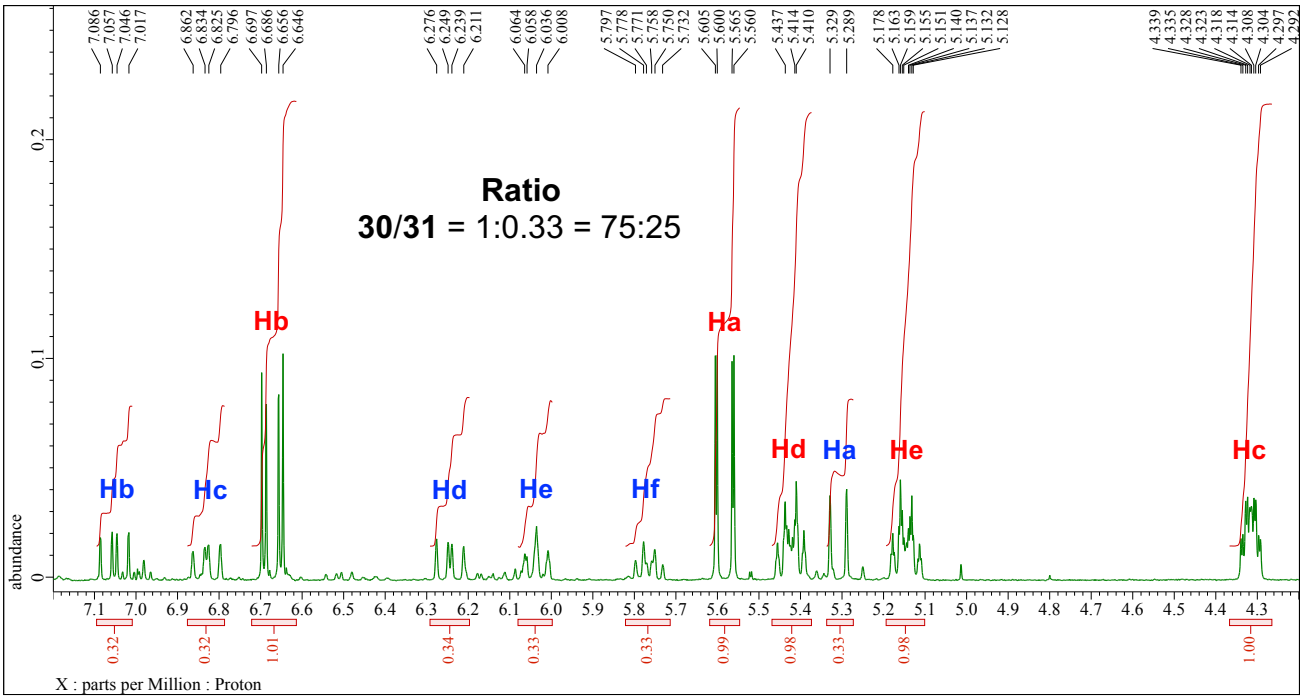

OTBDPS
NC
OTBS
27
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13

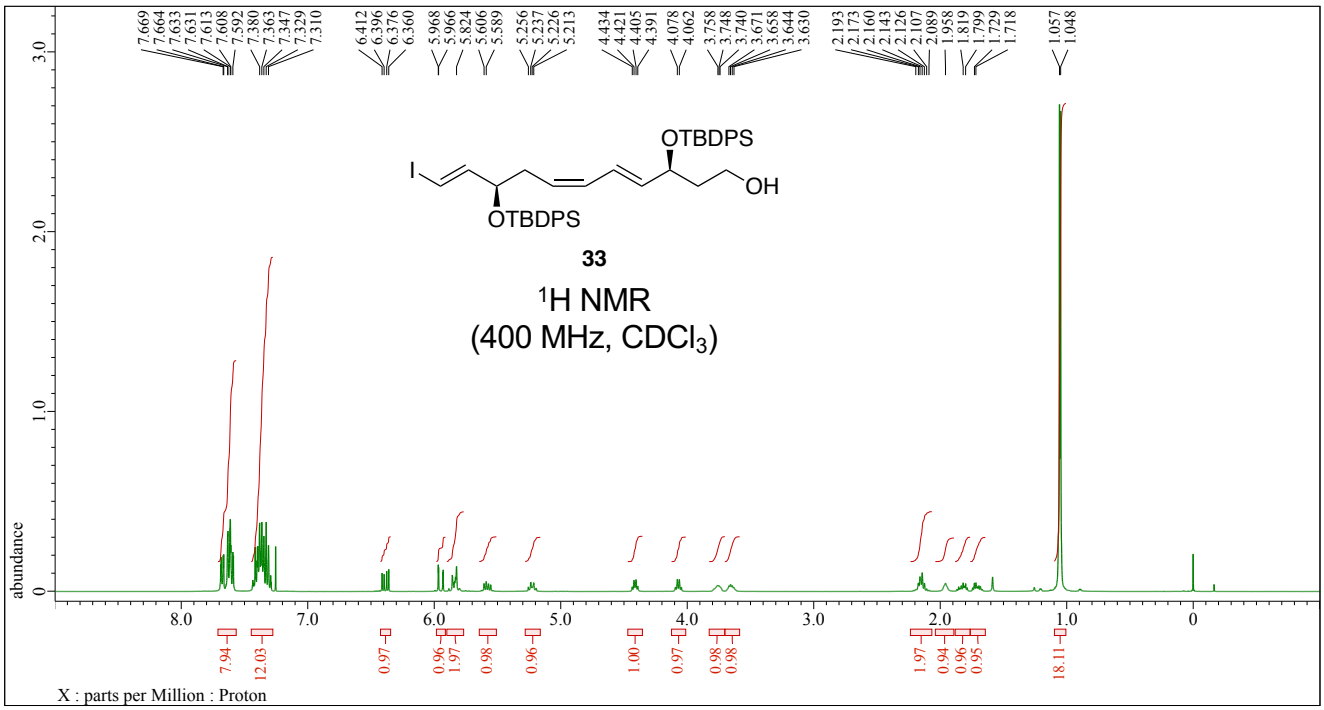


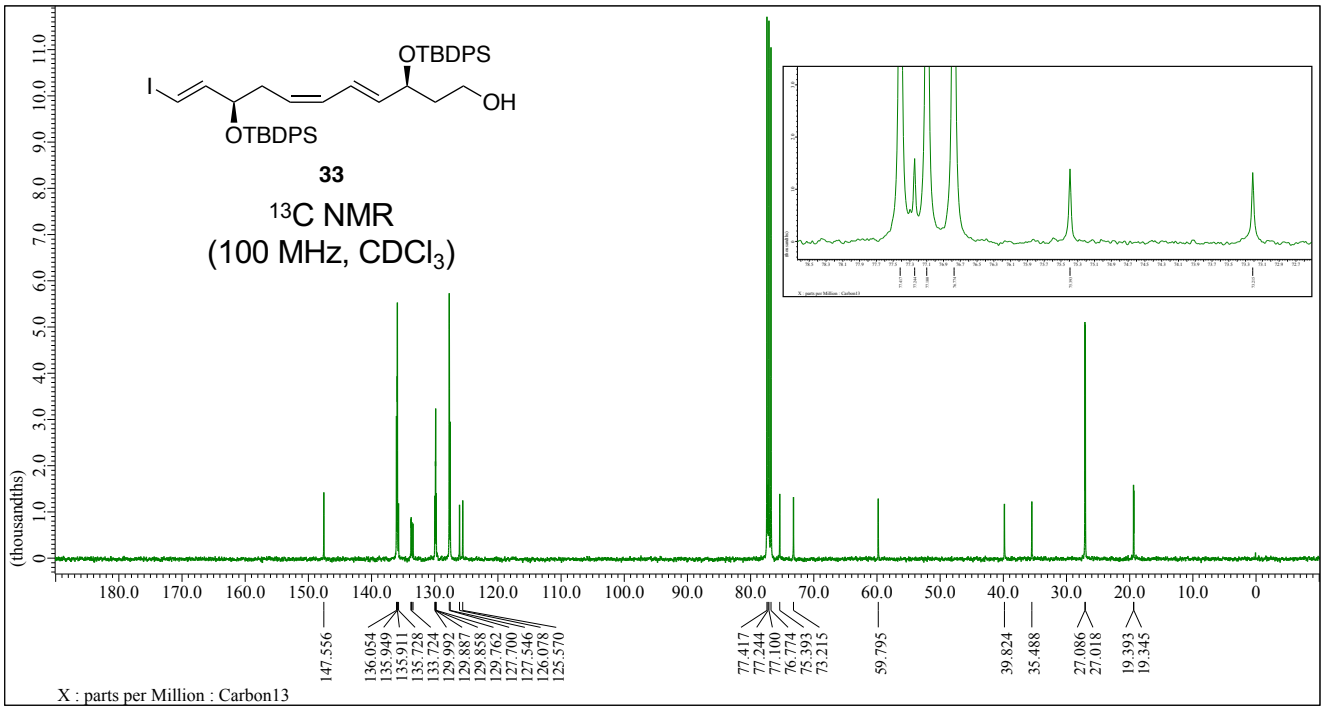
expansion of 4.2–7.2ppm

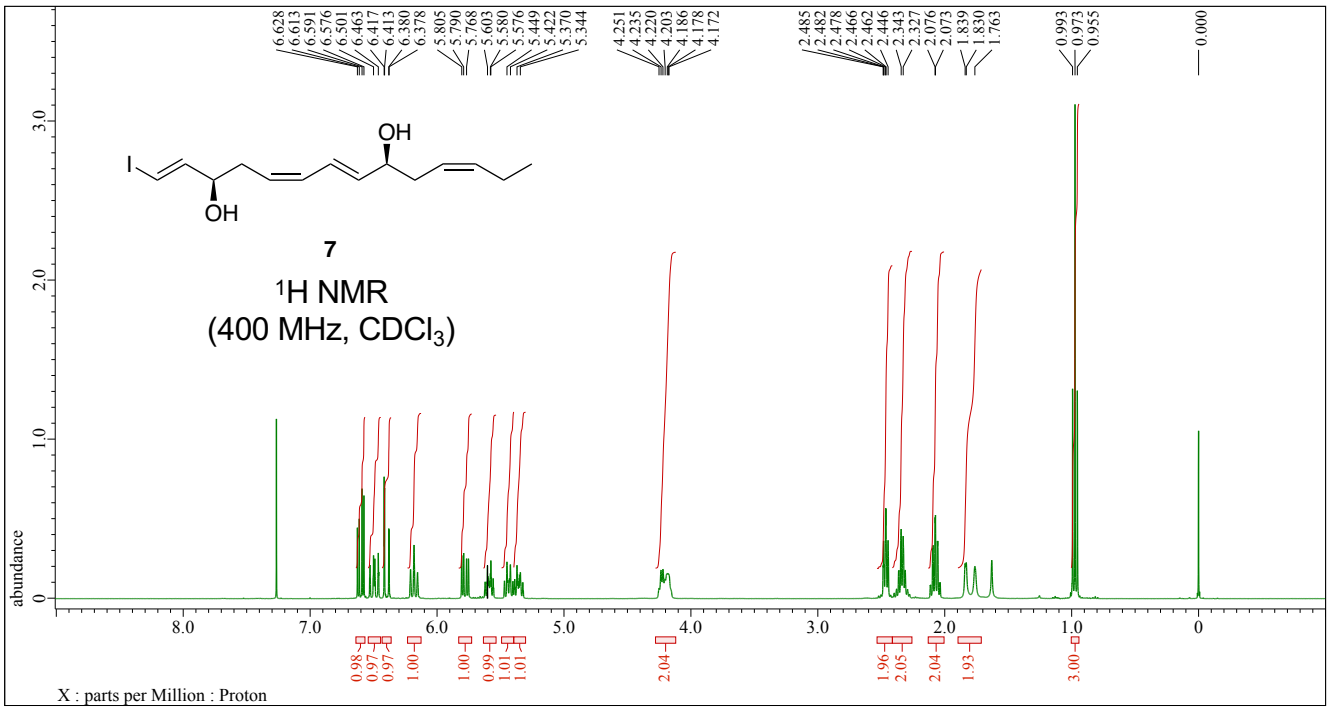


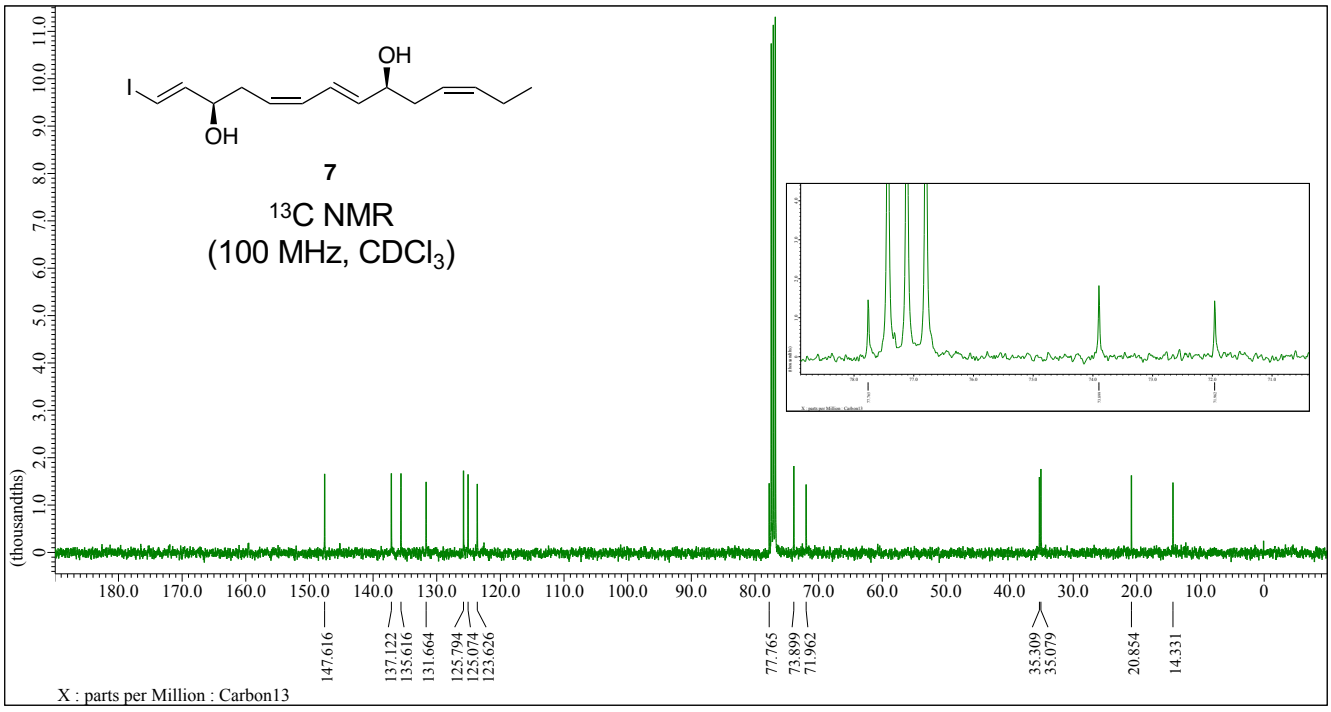


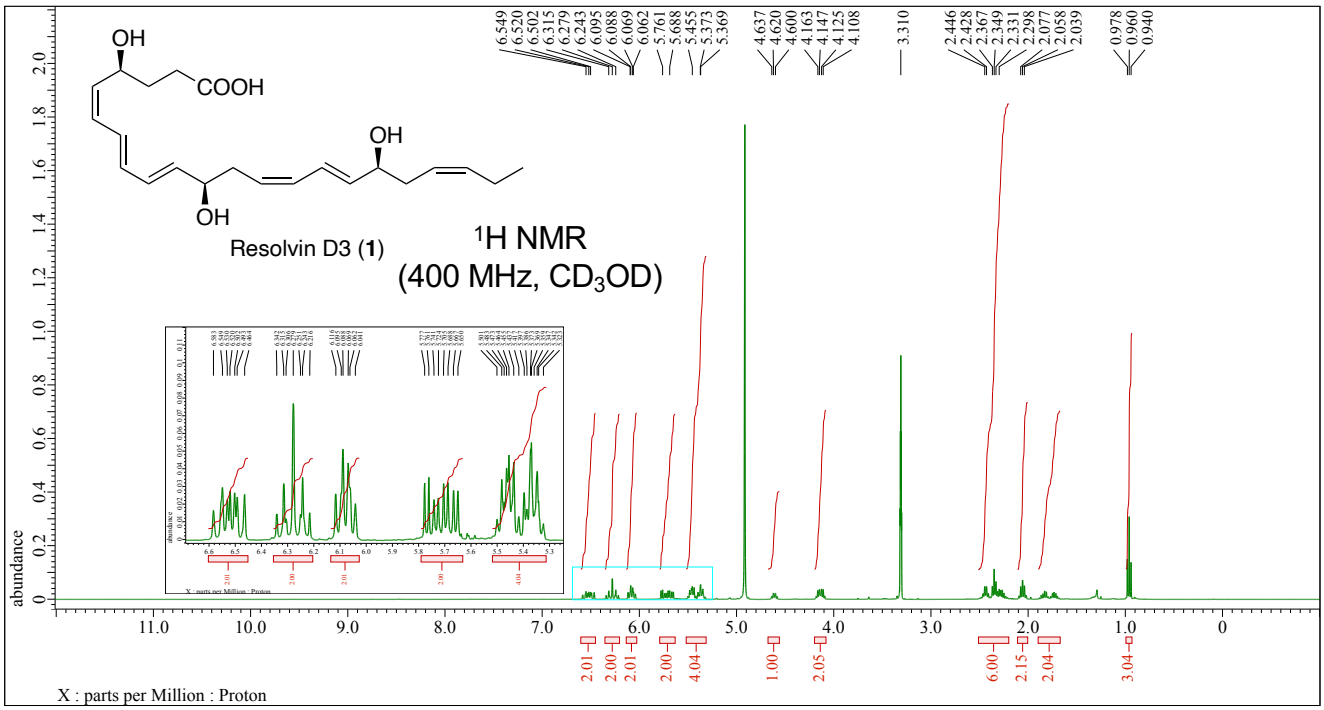


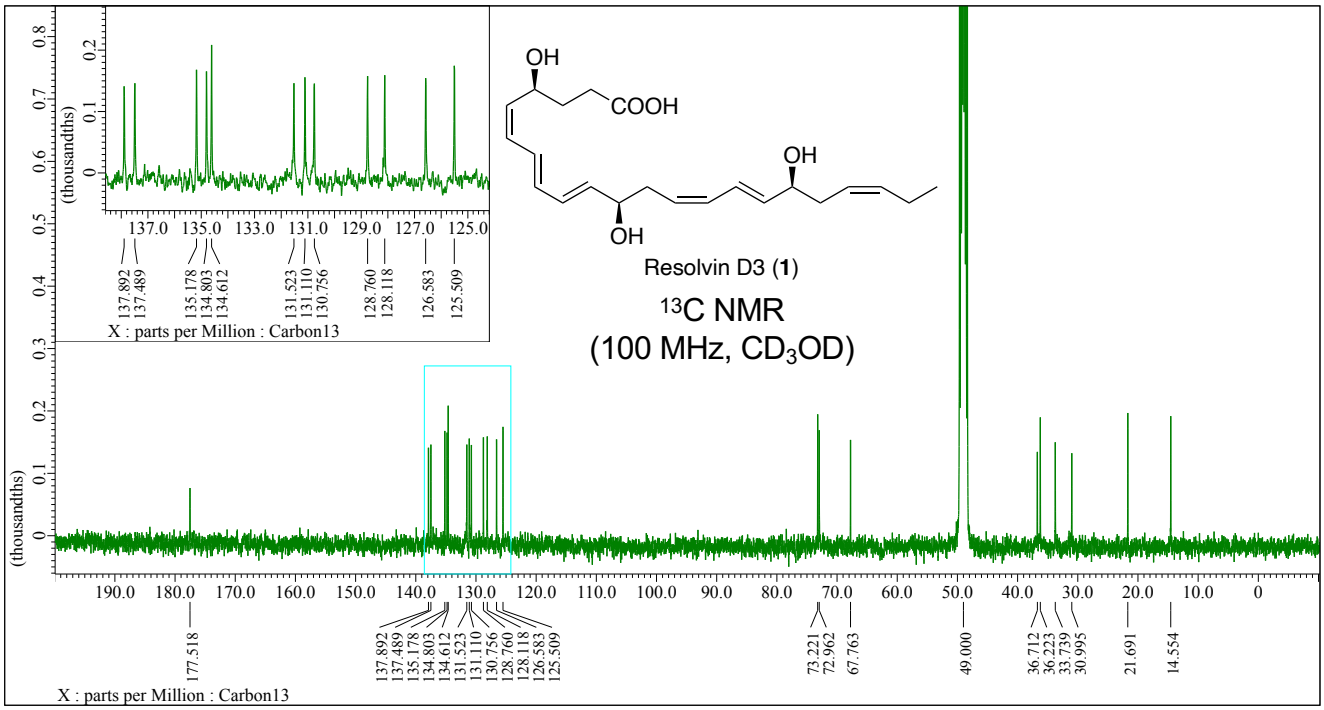

OTBDPS
I
OH
OTBDPS
33
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton

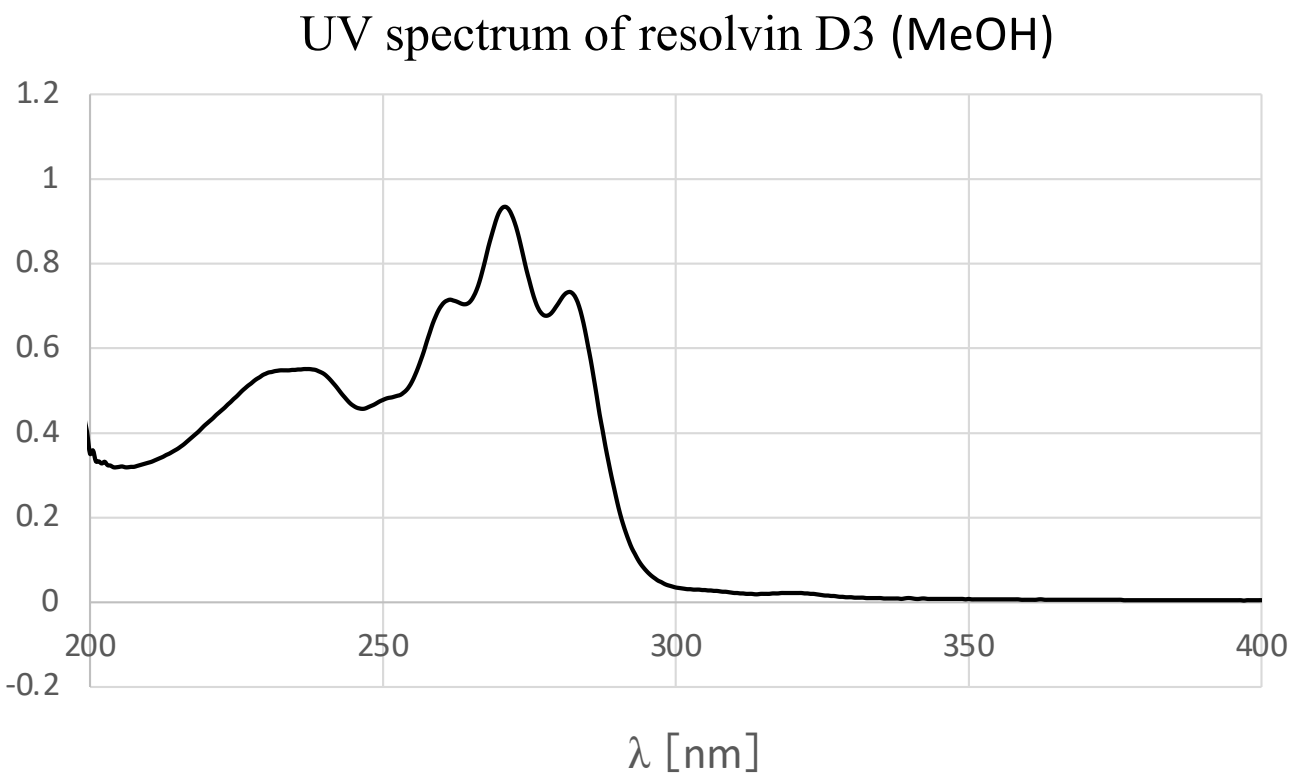

OTBDPS
I
OH
OTBDPS
33
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13


OH
I
OH
7
1H NMR
(400 MHz, CDCl3)
abundance
X : parts per Million : Proton


OH
I
OH
7
13C NMR
(100 MHz, CDCl3)
(thousandths)
X : parts per Million : Carbon13


OH
COOH
OH
OH
Resolvin D3 (1)
1H NMR
(400 MHz, CD3OD)
abundance
X : parts per Million : Proton


OH
COOH
OH
OH
Resolvin D3 (1)
13C NMR
(100 MHz, CD3OD)
(thousandths)
X : parts per Million : Carbon13


UV spectrum of resolvin D3 (MeOH)
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
200
250
300
350
400
λ [nm]