Supporting Information

Photochemistry of Mycolactone A/B, the Causative Toxin of Buruli Ulcer

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Supporting Information

1. General Procedures and Methods

NMR spectra were recorded on a Varian Inova 500 MHz or 600 MHz spectrometer. Chemical shifts are reported in parts per million (ppm). For ^{1}H NMR spectra ($CDCl_3$, CD_3COCD_3, or C_6D_6), the residual solvent peak was used as the internal reference (7.26 ppm in $CDCl_3$; 2.05 ppm in CD_3COCD_3; 7.16 ppm in C_6D_6), while the central solvent peak as the reference (77.0 ppm in $CDCl_3$; 29.8 ppm in CD_3COCD_3; 128.0 ppm in C_6D_6) for ^{13}C NMR spectra. In reporting spectral data, the following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, td = triplet doublet, qd = quartet doublet. High resolution mass spectra (HRMS) were obtained on an Agilent 6210 Time-of-Flight LC/MC Machine and were reported in units of m/e. The Ms/Ms experiments were performed on AB Sciex QSTAR Elite Hybride Quadrupole- TOF mass spectrometer. Analytical thin layer chromatography (TLC) was performed with E. Merck pre-coated TLC plates, silica gel 60 F254, layer thickness 0.25 mm and Wako precoated NH_2-TLC plates, silica gel 60 F254, layer thickness 0.25 mm. TLC plates were visualized by staining with potassium permanganate or *p*-anisaldehyde. Flash chromatography separations were performed on E. Merck Kieselgel 60 (230-400) mesh silica gel. All reactions were conducted under an inert atmosphere. Reaction vessels were either overnight oven-dried or flame-dried. Reagents and solvents were commercial grade and were used as supplied.

2. Photochemistry

2a. Photolysis through a 365 nm filter

Figure 1 illustrates the photo-reactor assembled from a carton box (45 cm x 32 cm x 30 cm), equipped with two UV lamps (UVP Inc., Model UVL-28, 8 W) with a 365 nm filter, a thermometer, and a temperature controlling system. Figure 2 shows the filter specification. A sample in a NMR tube or 20 ml test tube was placed at ca. 2 cm from the light source. The temperature of reactor was controlled by circulating chilled aq ethylene glycol provided from a Neslab chiller (Model RTE-110).

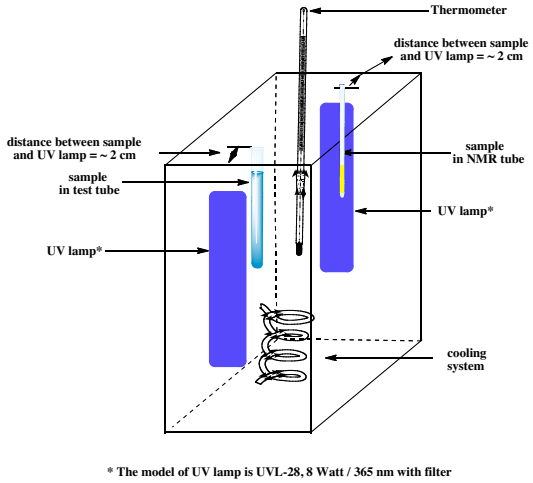


Figure 1. Photo-reactor

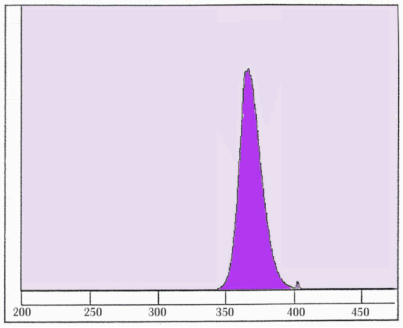
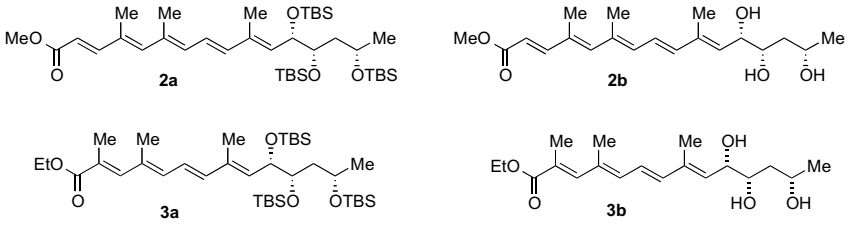


Figure 2. Specification of a 365 nm UV filter

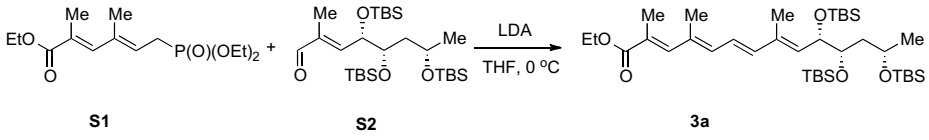
2b. Photolysis with sunlight

An acetone solution of a substrate (0.7 ~ 0.8 mmol) in a 500 mL round-bottle flask (Chemglass) was directly irradiated with sunlight at the roof of Naito Laboratories, without stirring. Photolysis was performed in the winter through spring of 2012, when the daytime out-door temperature varied from 0 °C to 25 °C.

3. Synthesis of substrates 2a, 2b, 3a and 3b

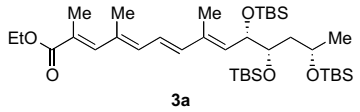


Substrates **2a** were prepared according to the reported methods.[1] The TBS groups of **2a** and **3a** were deprotected to give **2b** and **3b** under the conditions reported for deprotection of the protected mycolactone A/B to mycolatone A/B.[1]



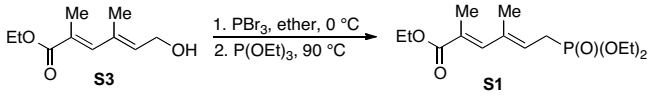
Phosphonate ester **S1** (4.04 g, 13.27 mmol) and aldehyde **S2**[1] (3.52 g, 6.64 mmol) were dissolved in dry THF (66 mL) and cooled to 0 °C. The freshly prepared LDA (24.4 mL, 0.49 M) was added slowly. The reaction was stirred at 0 °C for 30 min and then stirred at rt for 5 min. The reaction was quenched with sat. NH_4Cl solution, extracted with EtOAc, washed with sat. NaCl solution and dried over Na_2SO_4. Solvent was removed *in vacuo*,

and the residue was purified by a flash column chromatography to give tetraenoate **3a** (4.09 g, 90%)



3a

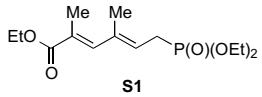
Tetraenoate **3a**: $[\alpha]_D^{20}$ = -20 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 7.20 (s, 1H), 6.66 (dd, *J* = 15.0, 10.5 Hz, 1H), 6.52 (d, *J* = 15.0 Hz, 1H), 6.42 (d, *J* = 11.0 Hz, 1H), 5.68 (d, *J* = 9.0 Hz, 1H), 4.58 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.17 (q, *J* = 7.0, Hz, 2H), 4.00 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.87 (m, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 1.94 (s, 3H), 1.89 (ddd, *J* = 12.5, 7.5, 6.0 Hz, 1H), 1.66 (ddd, *J* = 12.5, 6.0, 6.0 Hz, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.17 (d, *J* = 6.5 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 9H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 169.2, 143.2, 141.1, 137.3, 135.8, 135.4, 134.7, 126.9, 125.1, 74.5, 72.2, 66.9, 61.2, 41.1, 26.5(3C), 26.4 (6C), 24.4, 18.5, 18.7(2C), 17.0, 14.8, 14.7, 14.0, -3.7, -3.8, -3.9, -4.0, -4.2, -4.3; HRMS (ESI) m/z 703.4606 [$(M+Na)^+$, calcd 703.4580 for $C_{37}H_{72}NaO_5Si_3$].



S3 **S1**

To a cooled solution of alcohol **S3**[2] (4.78 g, 25.93 mmol) in CH_2Cl_2 (50 mL) was added PBr_3 (0.97 mL, 10.37 mmol) and stirred at 0 °C for 1 h. The reaction was quenched by addition of sat. aq KBr solution and extracted (ether). The combined organic layers were dried over Na_2SO_4. Evaporation of the solvent gave crude allyl bromide which was subjected to the next step without purification.

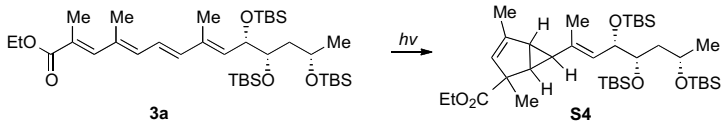
The above crude allyl bromide was dissolved in triethyl phosphite (12 mL) and the resulting mixture was stirred at 90 °C overnight. The excess of triethyl phosphite was removed under vacuum and the residue was purified by column chromatography on silica gel eluted with 70% EtOAc in hexanes to give product **S1** as a colorless oil (7.81 g, 99% in two steps).



S1

Dienoate **S1**: ^{1}H NMR (500MHz, $CDCl_3$) δ 7.09 (br s, 1H), 5.56 (dd, J = 8.0, 7.5 Hz, 1H), 4.19 (q, J = 6.5 Hz, 2H), 4.09 (m, 4 H), 2.71 (d, J = 8.0 Hz, 1H), 2.66 (d, J = 8.5 Hz, 1H), 1.98 (s, 3H), 1.84 (d, J = 4.0 Hz, 3H), 1.29 (m, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 141.6, 136.1, 126.9, 122.9, 61.9, 61.9, 60.7, 27.5, 26.4, 16.4, 16.3, 14.2, 13.9. HRMS (ESI) m/z 327.1333 [$(M+Na)^+$, calcd 327.1332 for $C_{14}H_{25}NaO_5P$].

4. Photochemistry of ethyl tetraenoate 3a



3a S4

4a. Photolysis in NMR tubes: With use of the photo-reactor shown in Figure 1, photolysis of **3a** (1.5 mg in 0.8 mL CD_3COCD_3) was done in a NMR tube at 30 °C. The progress of photolysis was monitored by ^{1}H NMR: at t = 2.5 h, a mixture of geometric isomers was detected; at t = 5 h, photo-cyclized products were observed (~5% completion); at t = 2 days, the photolysis completed.

4b. Temperature-dependency study: This study was performed at 10, 20, 30 and 40 °C under the condition given for photolysis in NMR tubes. The photolysis was monitored by ^{1}H NMR, showing that the cyclization completed for 105 h, 48 h, 33 h and 35 h for 10, 20, 30 and 40 °C, respectively.

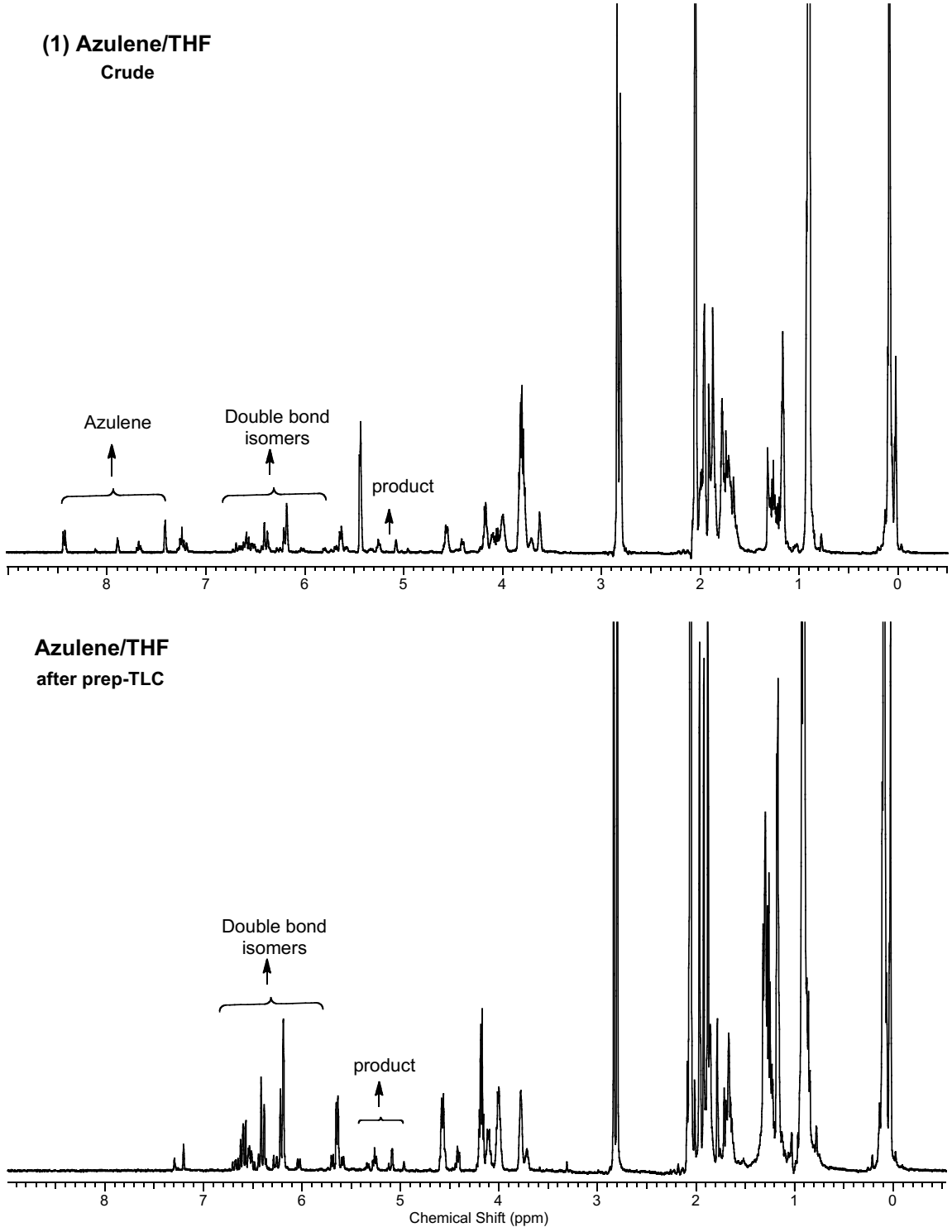
4c. Photolysis in test tubes: With use of the photo-reactor shown in Figure 1, photolysis of **3a** was done in a 160 mg scale. Thus, an acetone solution of **3a** (160 mg, 0.23 mmol, 160 ml acetone) was divided into 8 test tubes, capped with serum caps, and photolyzed at 30 °C for 5 days. Solvent was then removed *in vacuo*, the residue was purified by passing through a short silica pad to afford the mixture of four photo-products **S4** (80 mg, 50%).

4d. Preparative photolysis with sunlight: To a 1 L round bottom flask (Chemglass), an acetone solution of **3a** (500 mg, 0.74 mmol, 500 mL acetone) was irradiated with sunlight at the roof of the Naito Laboratories (the daytime outdoor temperature was ~ 25 °C). An NMR analysis showed that photolysis was completed for 1 week. After the solvent was removed *in vacuo*, the residue was passed through a short silica pad, to give a mixture of four photo-products **S4** (255 mg, 51%).

5d. Triplet quenching/sensitization experiments: With use of the photo-reactor shown in supporting information Figure 1, photolysis of **3a** was done in a 3 mg scale. Thus, a solution of 3a (3 mg, 2 mL solvent) and quencher/sensitizer in test tube was capped with serum caps, and photolyzed at 30 °C for about 35 hr. All the triplet quenchers did not affect the product formation, the triplet sensitizer benzophenone give no phtoto-products. For all the quenching experiments, crude ^{1}H NMR spectra and ^{1}H NMR spectra obtained after prep-TLC (quenchers were removed) were attached.

	Solvent	sensitizer	quencher	equivalent
1	THF		Azulene	0.5
2	THF		Ferrocene	0.5
3	CH_3CN		Azulene	0.5
4	CH_3CN		Ferrocene	0.5
5	THF		Rubrene	0.5
6	CH_3CN		Rubrene	0.5
7	Acetone		Rubrene	0.5
8	CH_3CN	Benzophenone		0.5

Table 1. Triplet quenching/sensitization experiments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Crude
Azulene
Double bond
isomers
product
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7
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5
4
3
2
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after prep-TLC
Double bond
isomers
product
8
7
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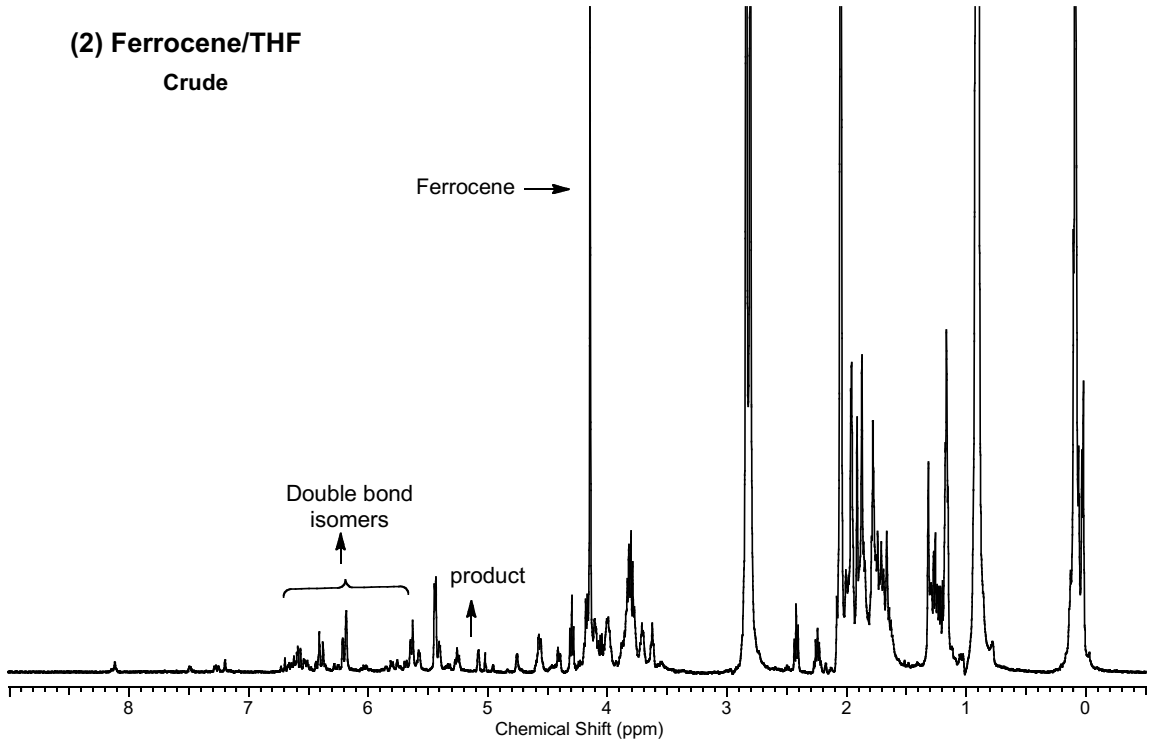
5
4
3
2
1
0
Chemical Shift (ppm)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Crude
Ferrocene
Double bond
isomers
product
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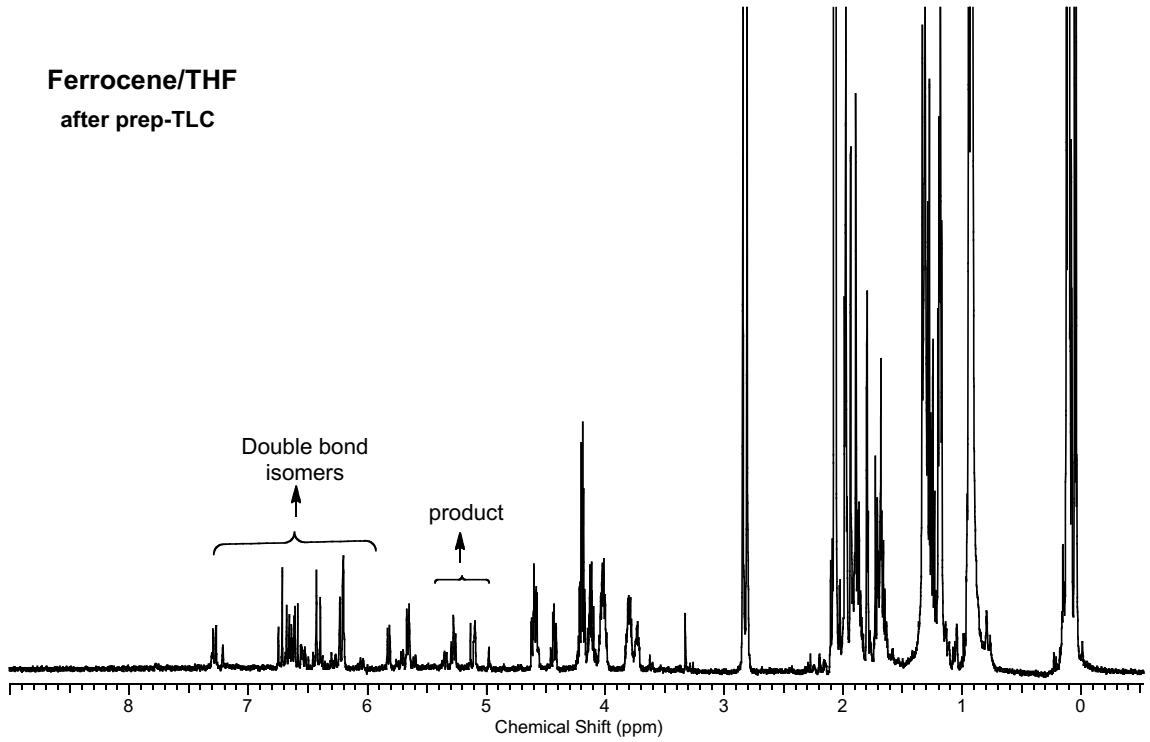
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Ferrocene/THF
after prep-TLC
Double bond
isomers
product
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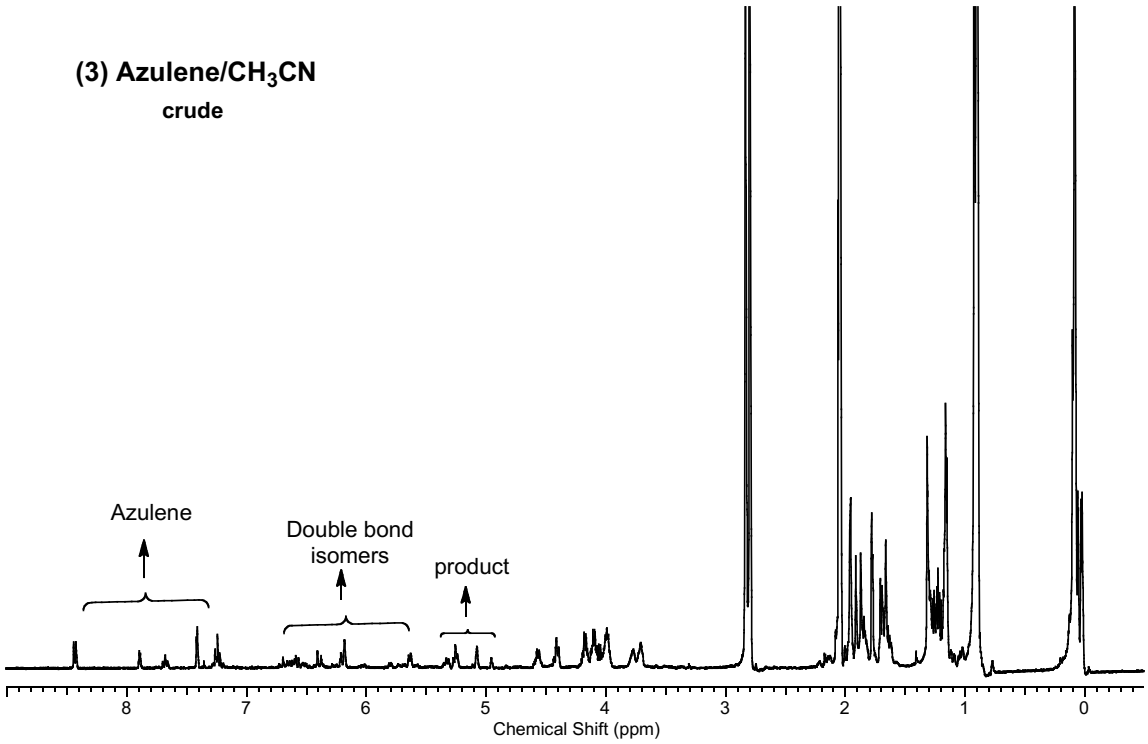
Chemical Shift (ppm)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isomers
product
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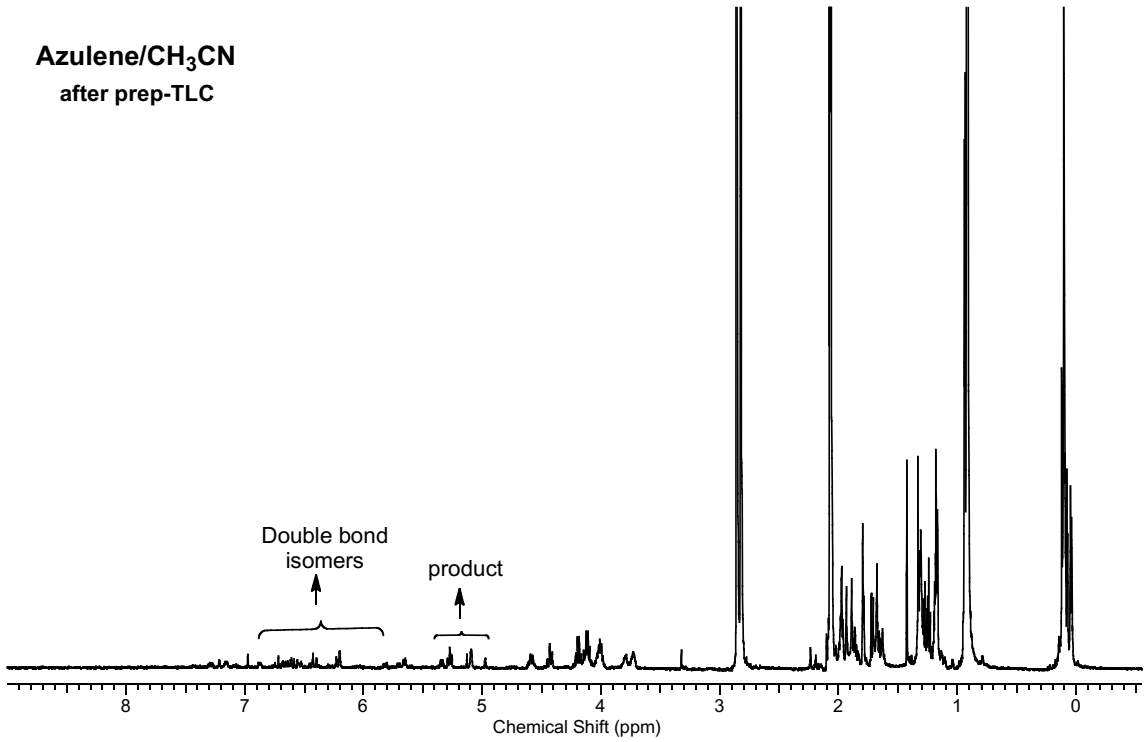
Azulene/CH3CN
after prep-TLC
Double bond
isomers
product
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7
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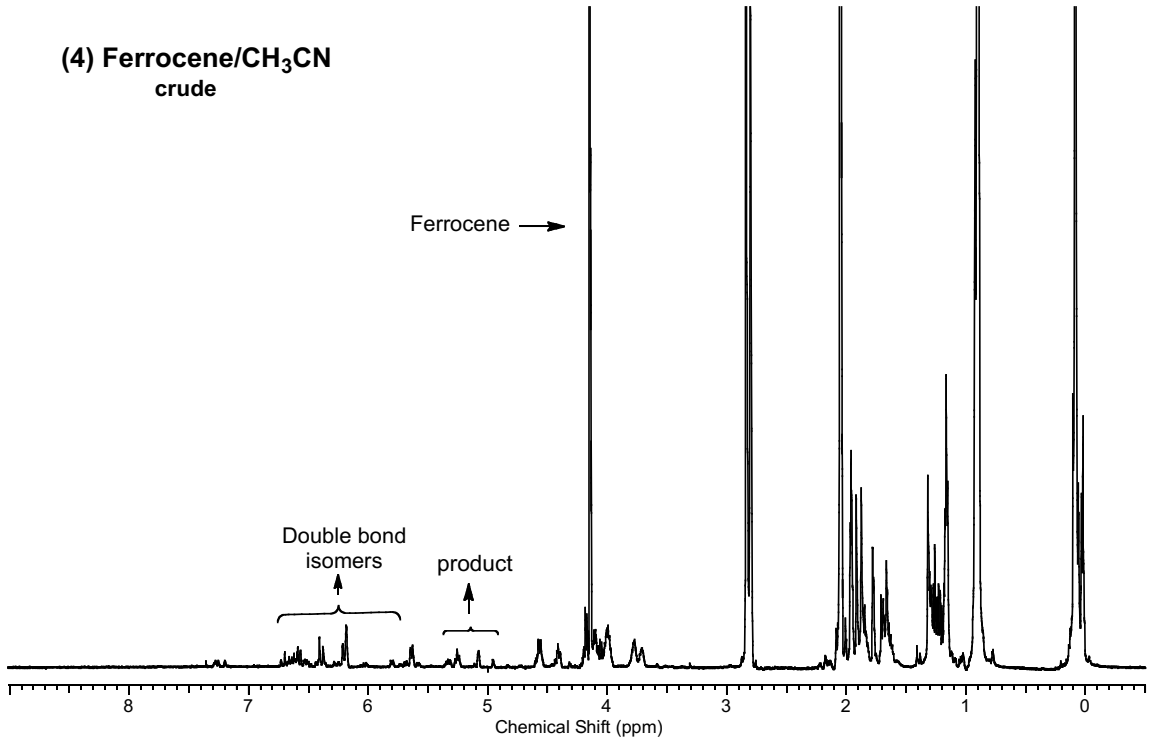
5
4
3
2
1
0
Chemical Shift (ppm)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Ferrocene
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isomers
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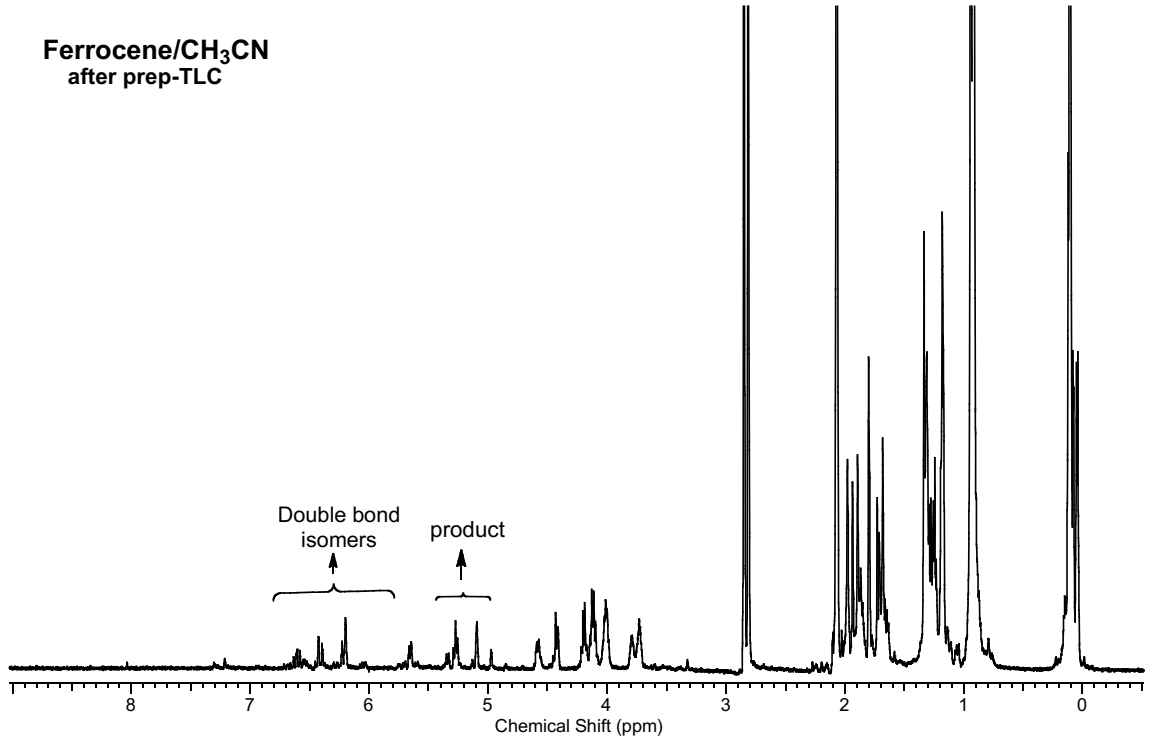
Chemical Shift (ppm)


Ferrocene/CH3CN
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Double bond
isomers
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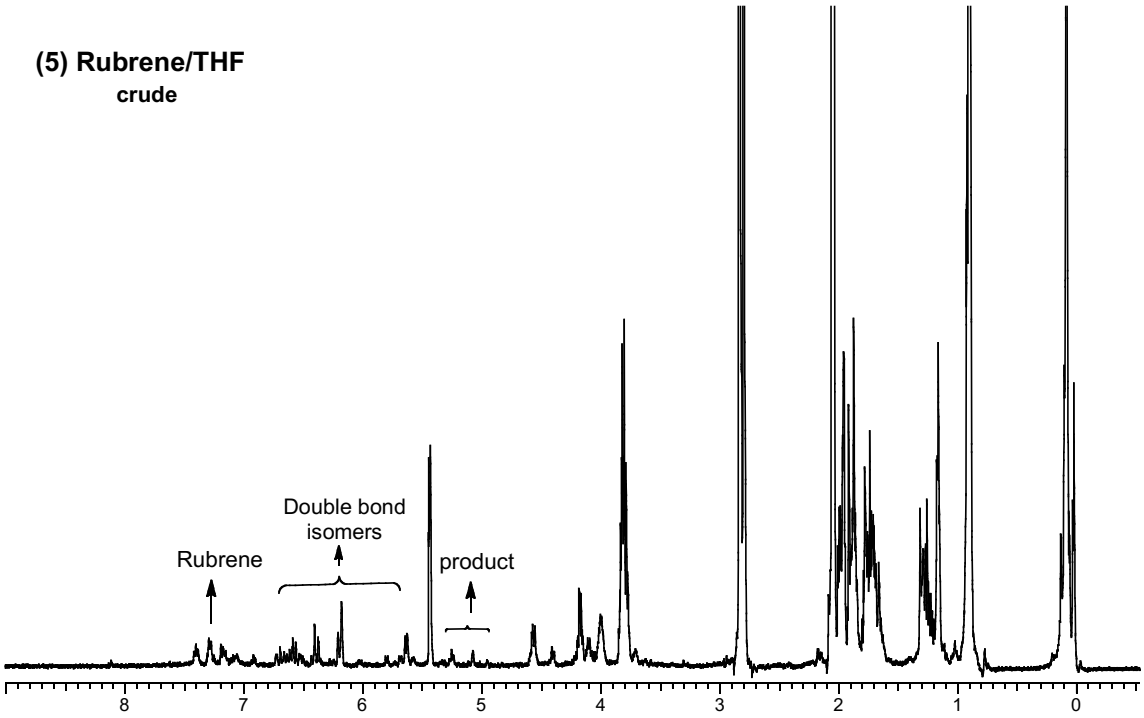
Chemical Shift (ppm)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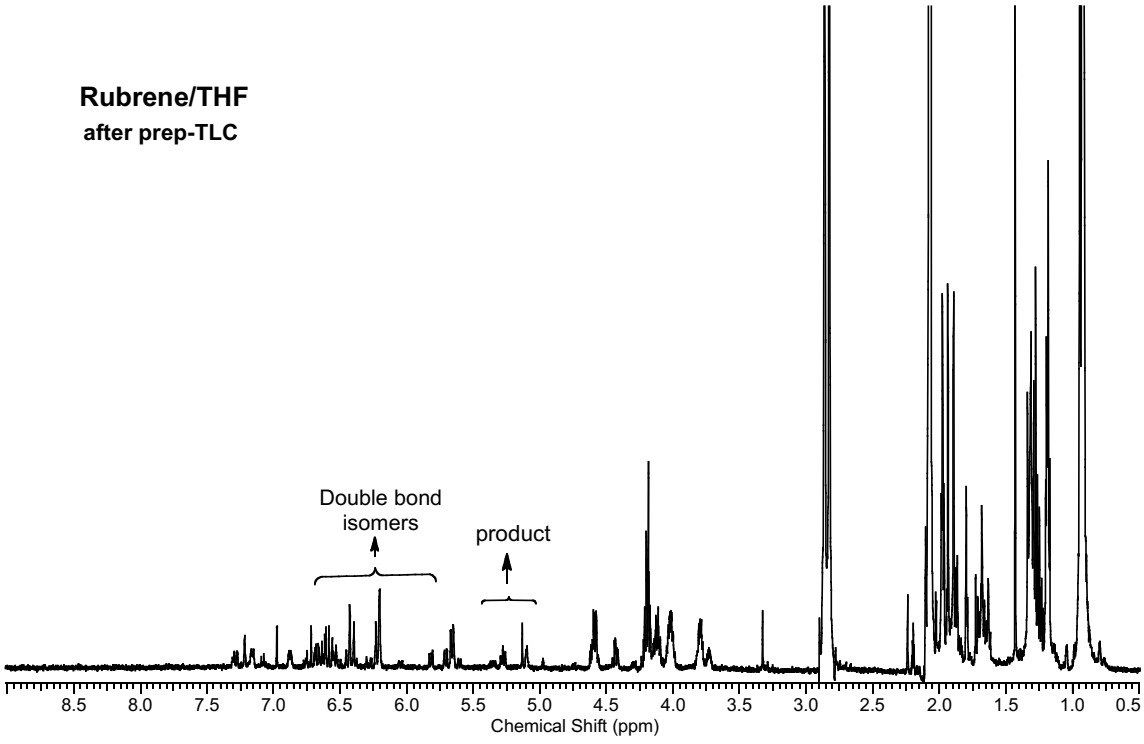
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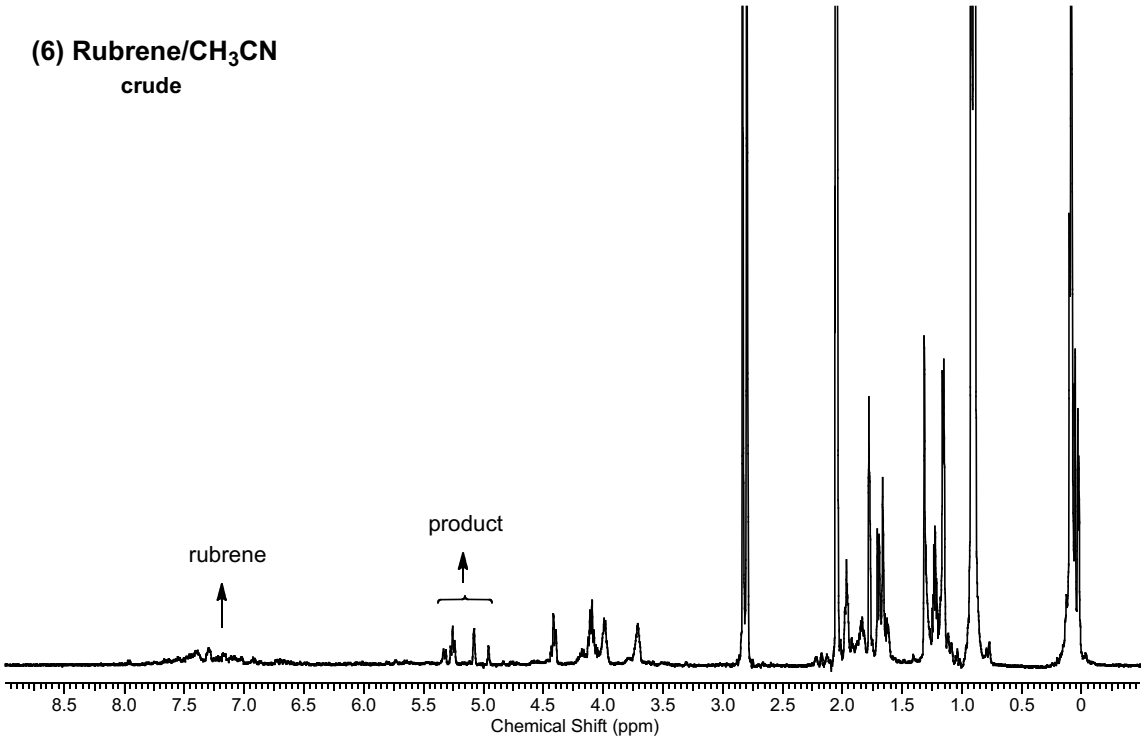
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)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rubrene
product
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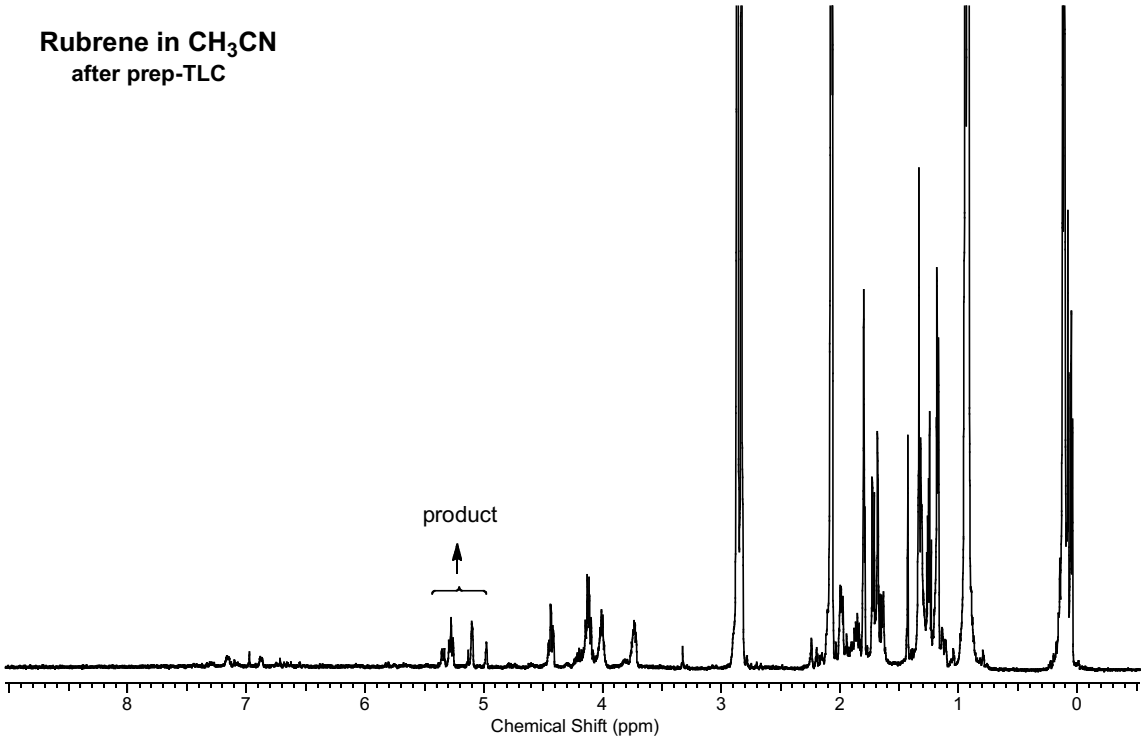
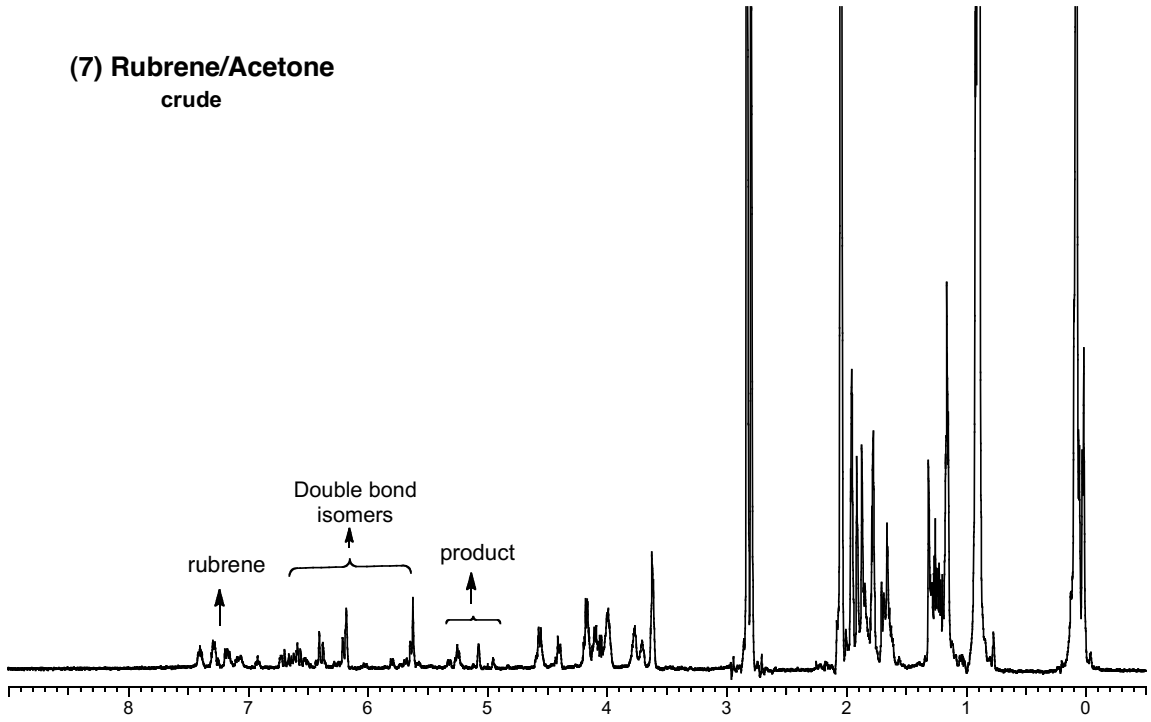
Chemical Shift (ppm)


Rubrene in CH3CN
after prep-TLC
product
8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)


(7) Rubrene/Acetone
crude
Double bond
isomers
rubrene
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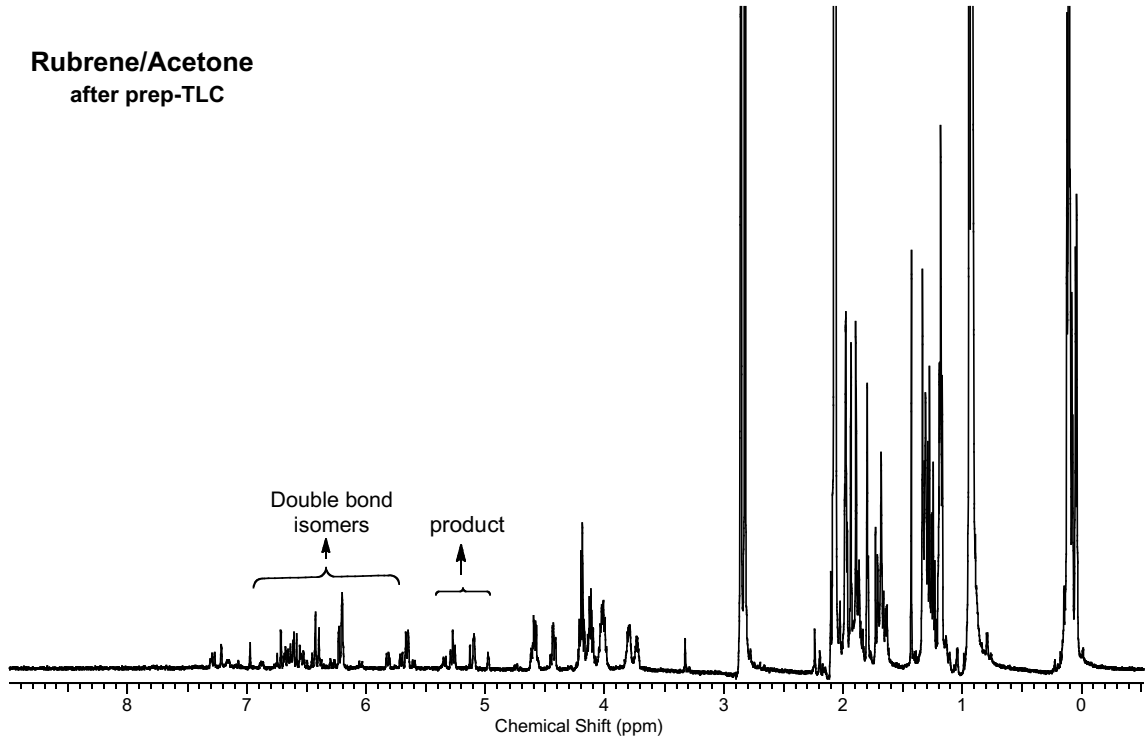
Rubrene/Acetone
after prep-TLC
Double bond
isomers
product
8
7
6
5
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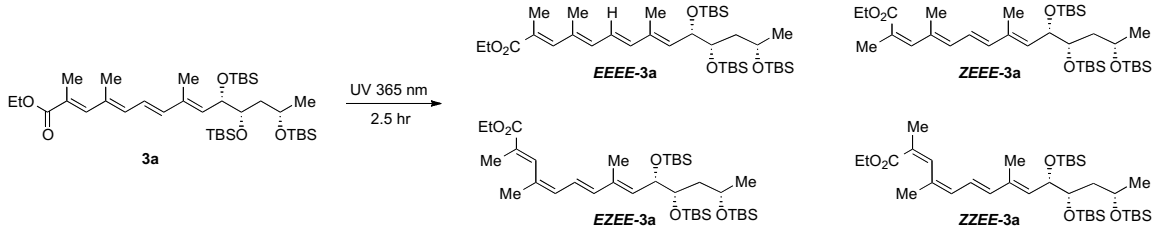
3
2
1
0
Chemical Shift (ppm)

5. Separation, isolation, and characterization of four geometrical isomers of 3a.



5a. Ratio and separation of four geometrical isomers

With use of the photo-reactor shown in Figure 1, photolysis of **3a** (1.5 mg in 0.8 mL CD_3COCD_3) was done in a NMR tube for 2.5 h at 30 °C. A ^{1}H NMR analysis showed formation of the four geometrical isomers (*EEEE, ZEEE, EZEE, ZZEE*) but no photo-cyclization products detected. The ratio of four isomers was estimated from ^{1}H NMR and HPLC analysis (see below). Similarly, the ratio of the four geometrical isomers was estimated at ~40% (15 h at 30 °C) and ~70% (23 h at 30 °C) completion of the photo-cyclization (Table 2).

photo-cyclization	ratio estimated by	*EEEE*	*ZEEE*	*EZEE*	*ZZEE*
0% products	^{1}H NMR*	1.7	7.2	0.9	1.0
	HPLC**	1.5	7.4	1.1	1.0
~40% products	^{1}H NMR*	1.6	7.1	1.0	1.5
	HPLC**	1.3	6.2	1.0	1.1
~70% products	^{1}H NMR*	1.6	7.0	1.0	1.4
	HPLC**	1.5	6.5	1.0	1.3

* ^{1}H NMR ratio was estimated from the peak intensity of 5'- and 11'-Hs resonances (see below).
** HPLC ratio was estimated from the corrected peak-intensity at 310 nm (see below).

Table 2. Estimated Ratios of Four Geometrical Isomers

NMR method: The 5'- and 11'-proton resonances were used to estimate the ratio of the four geometrical isomers (Figure 3). Indicate 5'- and 11'-Hs.

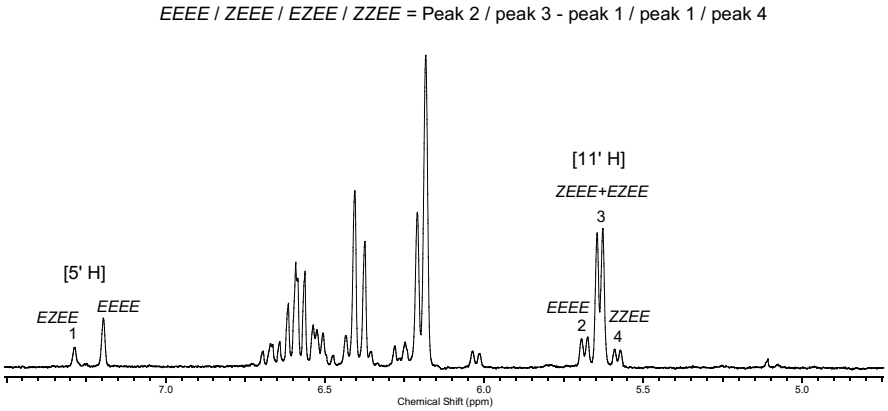


Figure 3. ^{1}H NMR of mixture of four geometrical isomers

HPLC method: The four geometrical isomers were separated/isolated by HPLC (ZORBA silica column, 25 cm ~ 21.2 mm, 6% ether/hexanes, 5 mL/min) and characterized, thereby making the peak assignment possible. A UV detector at 310 nm was used to trace the four peaks (Figure 4), and the observed peak intensity was corrected by dividing the molar absorption coefficient of four isomers, to give the HPLC ratio (Table 1).

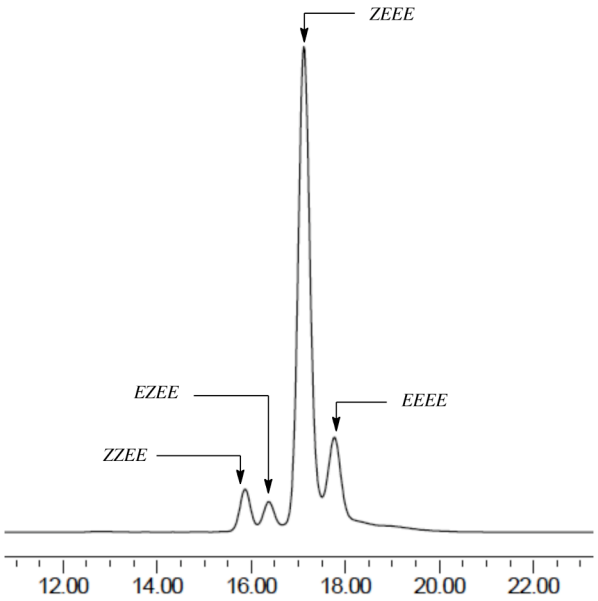
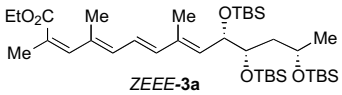


Figure 4. HPLC chart of four isomers at 310 nm

5b. Characterization of *EEEE, ZEEE, EZEE,* and *ZZEE* geometrical isomers of 3a

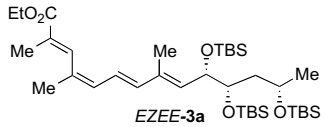
For the characterization of *EEEE* isomer, see page S4.



ZEEE-**3a**

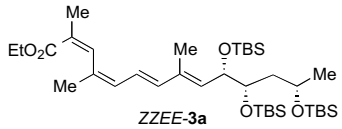
ZEEE-**3a** isomer:

^{1}H NMR (600 MHz, CD_3COCD_3) δ 6.59 (dd, *J* = 15.0, 11.0 Hz, 1H), 6.39 (d, *J* = 15.0, 1H), 6.20 (d, *J* = 11.0 Hz, 1H), 6.18 (s, 1H), 5.64 (d, *J* = 9.0 Hz, 1H), 4.56 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.17 (q, *J* = 7.2, Hz, 2H), 4.00 (qt, *J* = 6.0, 5.4 Hz, 1H), 3.77 (m, 1H), 1.96 (s, 3H), 1.91 (s, 3H), 1.90 (m, 1H), 1.87 (s, 3H), 1.66 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 6.0 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 18H), 0.09 (s, 3H), 0.08 (s, 9H), 0.07(s, 3H), 0.01 (s, 3H); HRMS (ESI) m/z 719.4291 [(M+K)$^+$, calcd 719.4319 for $C_{37}H_{72}KO_5Si_3$].



EZEE-**3a**

EZEE-**3a** isomer:
^{1}H NMR (600 MHz, CD_3COCD_3) δ 7.28 (s, 1H), 6.37 (d, *J* = 15.0 Hz, 1H), 6.23 (dd, *J* = 15.0, 11.0 Hz, 1H), 6.20 (d, *J* = 11.0 Hz, 1H), 5.63 (d, *J* = 9.0 Hz, 1H), 4.55 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.19 (q, *J* = 7.2, Hz, 2H), 4.00 (qt, *J* = 6.0, 5.4 Hz, 1H), 3.77 (m, 1H), 1.96 (s, 3H), 1.87 (m, 1H), 1.84 (s, 6H), 1.65 (m, 1H), 1.29 (t, *J* = 6.6 Hz, 3H), 1.17 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 18H), 0.09 (s, 3H), 0.08 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H); HRMS (ESI) m/z 719.4283 [(M+K)$^+$, calcd 719.4319 for $C_{37}H_{72}KO_5Si_3$].

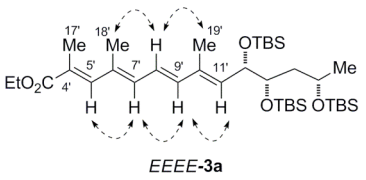


ZZEE-**3a**

ZZEE-**3a** isomer:
^{1}H NMR (600 MHz, CD_3COCD_3) δ 6.52 (s, 1H), 6.49 (dd, *J* = 15.0, 11.0 Hz Hz, 1H), 6.26 (d, *J* = 15.0 Hz, 1H), 6.02 (d, *J* = 11.0 Hz, 1H), 5.58 (d, *J* = 9.0 Hz, 1H), 4.55 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.10 (q, *J* = 7.2, Hz, 2H), 4.00 (qt, *J* = 6.0, 5.4 Hz, 1H), 3.75 (m, 1H), 2.01 (s, 3H), 1.87 (s, 3H), 1.86 (m, 1H), 1.85 (s, 3H), 1.65 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 3H), 1.16 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 18H), 0.09 (s, 3H), 0.08 (s, 9H), 0.07(s, 3H), 0.01 (s, 3H); HRMS (ESI) m/z 703.4550 [(M+Na)$^+$, calcd 703.4580 for $C_{37}H_{72}NaO_5Si_3$].

5c. Assignment of the stereochemistry of four geometrical isomers with NMR spectroscopy

The stereochemistry of the four geometrical isomers was assigned by NMR spectroscopy, including 2D NOESY and proton chemical shifts/vicinal proton spin-spin coupling constants data shown below. The UV spectra of four isomers were also attached in the following figures.



EEEE-**3a**

C no.	^{1}H shift (ppm)	*J* Hz
5'	7.20	s
7'	6.42	d, *J* = 11.0
8'	6.67	dd, *J* = 15.0, 11.0
9'	6.52	d, *J* = 15.0
11'	5.68	d, *J* = 8.5

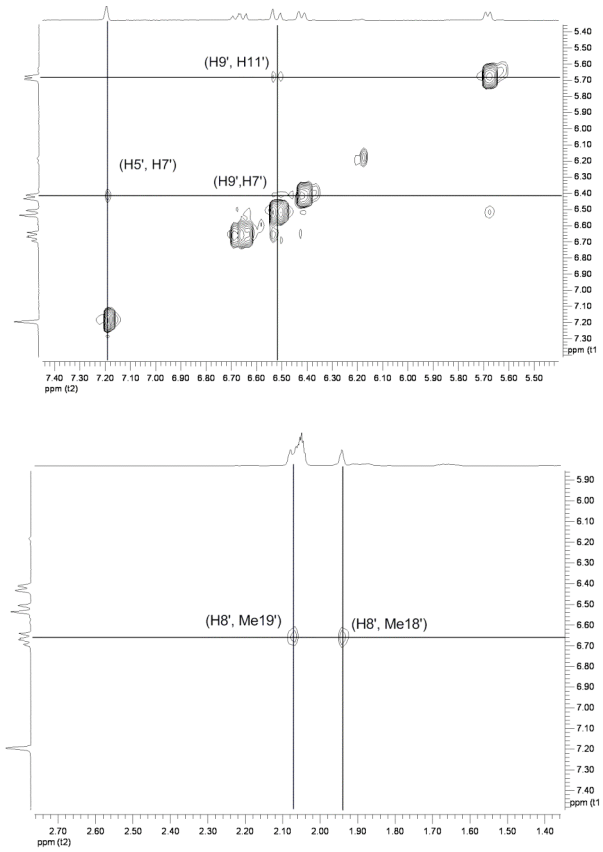
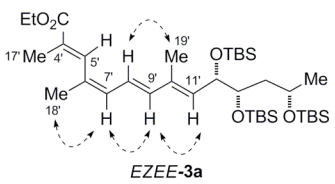


Figure 5. NMR spectroscopy of *EEEE*-**3a** isomer



EZEE-**3a**

C no.	^{1}H shift (ppm)	*J* (Hz)
5'	7.29	s
7'	6.20	d, *J* = 11.0
8'	6.23	dd, *J* = 15.0, 11.0
9'	6.37	d, *J* = 15.0
11'	5.63	d, *J* = 8.5

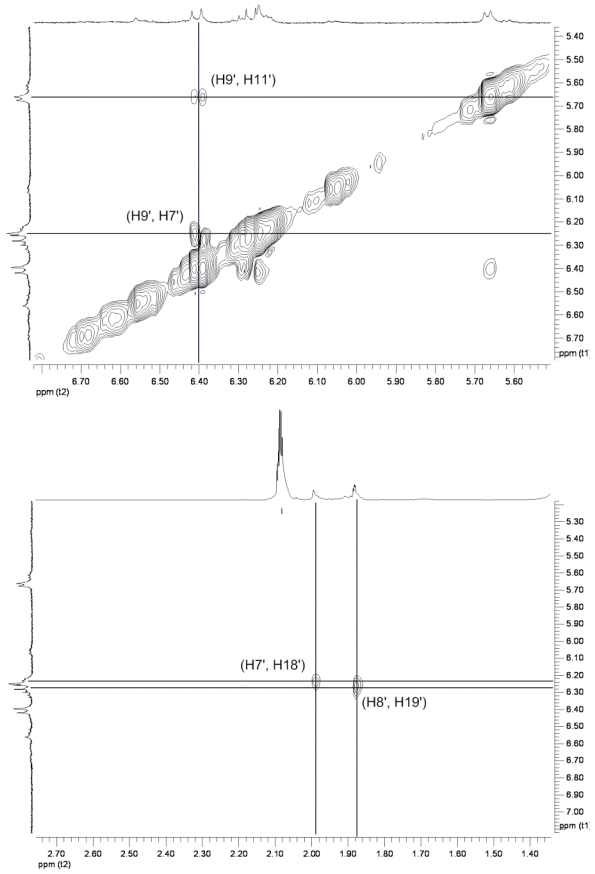
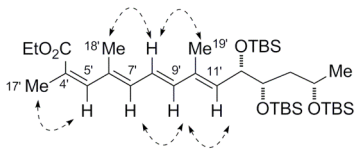


Figure 6. NMR spectroscopy of *EZEE*-**3a** isomer



ZEEE-**3a**

C no.	^{1}H shift (ppm)	*J* (Hz)
5'	6.18	s
7'	6.20	d, *J* = 11.0
8'	6.59	dd, *J* = 15.0, 11.0
9'	6.39	d, *J* = 15.0
11'	5.64	d, *J* = 8.5

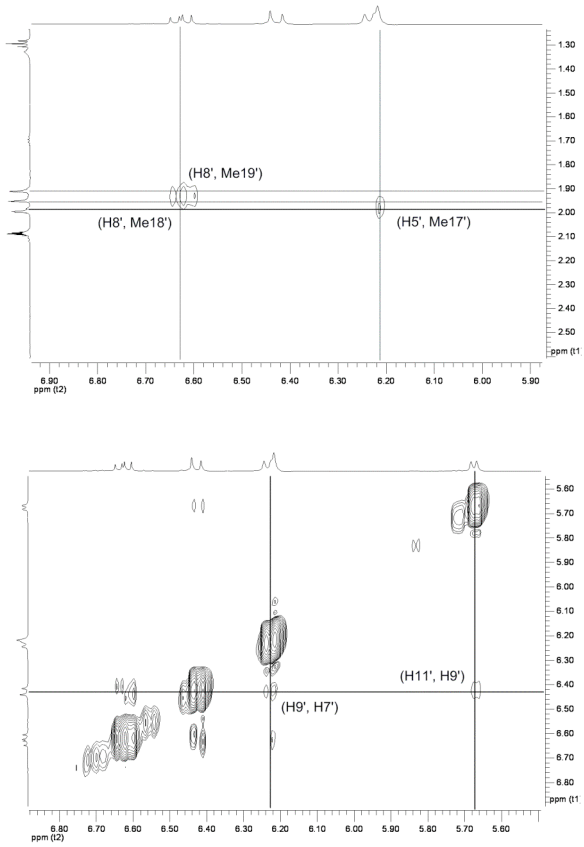
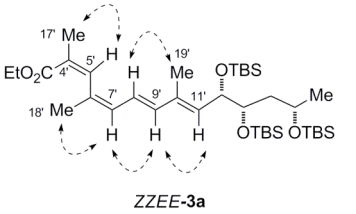


Figure 7. NMR spectroscopy of *ZEEE*-**3a** isomer



ZZEE-**3a**

C no.	^{1}H shift (ppm)	*J* (Hz)
5'	6.52	s
7'	6.02	d, *J* = 11.0
8'	6.49	dd, *J* = 15.0, 11.0
9'	6.26	d, *J* = 15.0
11'	5.58	d, *J* = 8.5

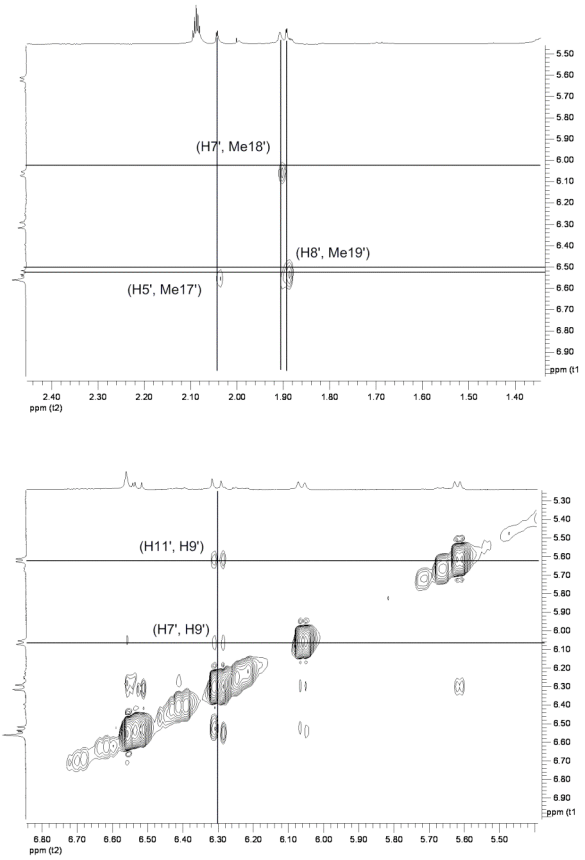


Figure 8. NMR spectroscopy of *ZZEE*-**3a** isomer

5d. UV spectra of four geometrical isomers

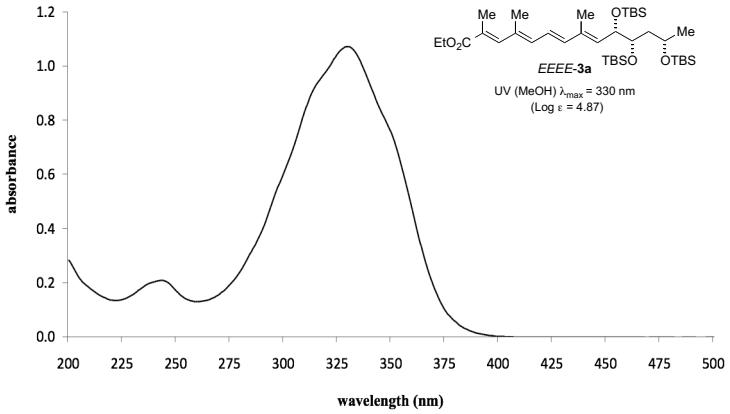


Figure 9. UV spectroscopy of *EEEE*-**3a** isomer

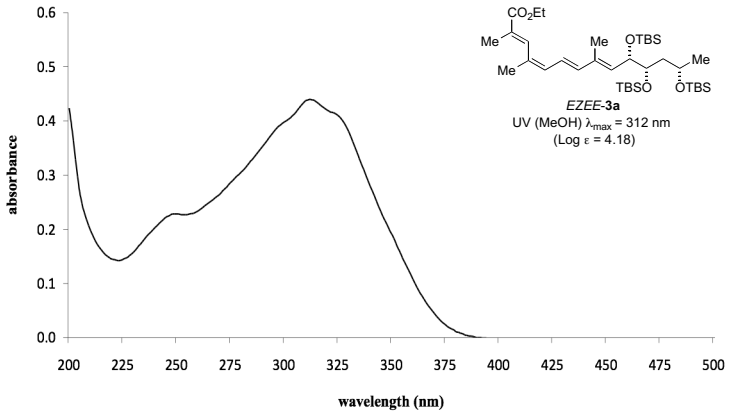


Figure 10. UV spectroscopy of *EZEE*-**3a** isomer

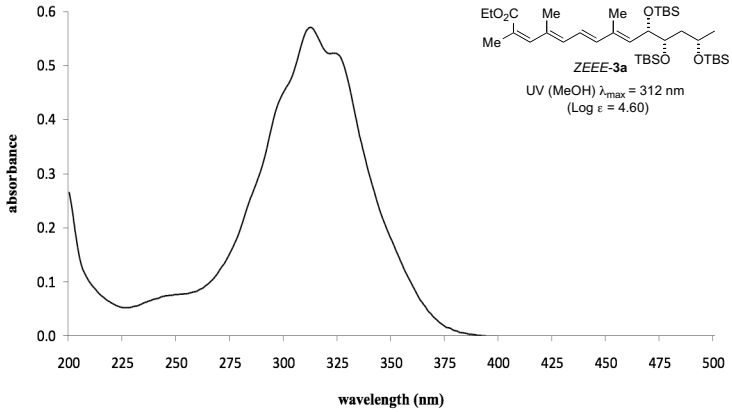


Figure 11. UV spectroscopy of *ZEEE*-**3a** isomer

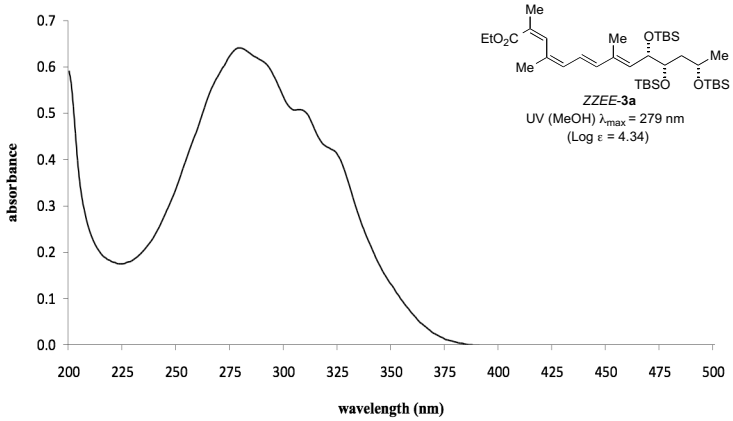
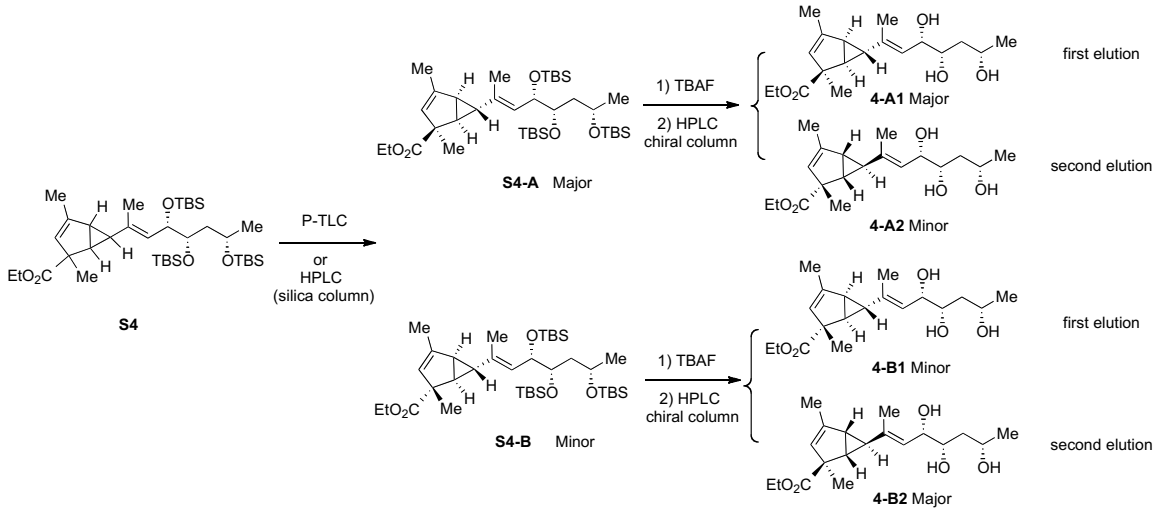


Figure 12. UV spectroscopy of *ZZEE*-**3a** isomer

6. Photo-products in the tetraenoate series

6a. Separation and isolation of four photo-products



After photolysis completed, the mixture of four cyclized isomers **S4** was first separated by Prep-TLC (5% ether/hexanes) or HPLC (ZORBA silica column, 25 cm ~ 21.2 mm, 5% ether/hexanes, 6 mL/min, UV detection at $\lambda = 250$ nm) to give the major isomer **S4-A** and minor isomer **S4-B**, in 3:1 ratio, respectively.

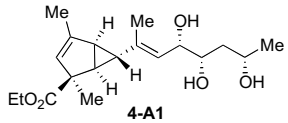
i. TBS-deprotection and HPLC separation of **S4-A**

To a 0.1 M THF solution of mixture of tri-TBS **S4-A** (1 eq), TBAF (1 M/THF, 6 eq) was added. The reaction was allowed to stir for 12 h, then washed with sat. NaCl, extracted with EtOAc and dried over Na_2SO_4. Solvent was removed *in vacuo*, and the residue was purified by a flash column chromatography to give the mixture of triol **4-A1** and **4-A2** (90%). The mixture of triol **4-A1** and **4-A2** was separated by HPLC using a chiral column, to furnish optically pure major triol **4-A1** as the first elution and minor compound **4-A2** as second elution (A1 : A2 = 3 : 2). HPLC condition for separating **4-A1** and **4-A2**: Regiscell, 25 cm ~ 21.1 mm, 10% i-PrOH/hexanes, 4 mL/min, detection at $\lambda = 250$ nm.

ii. TBS-deprotection and HPLC separation of **S4-B**

The mixture of tri-TBS **S4-B** was deprotected under the same condition, to give a mixture triol **4-B1** and **4-B2** (90%). The mixture triol **4-B1** and **4-B2** was separated by HPLC using chiral column, to furnish optically pure major triol as the second elution and minor isomer as first elution (major : minor = 3 : 2). HPLC condition for separating **4-B1** and **4-B2**: Chiralpak AD, ADOOCG-FE007, 12% i-PrOH/hexanes, 2 mL/min, detection at $\lambda = 250$ nm.

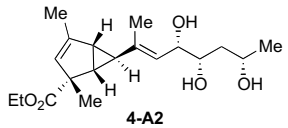
6b. Characterization of four photo-products



4-A1

Triol **4-A1**

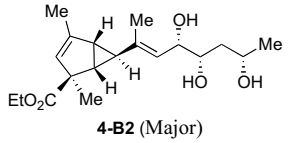
$[\alpha]_D^{20}$ = -144 (acetone, *c* 1.0); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 5.14 (d, *J* = 8.5 Hz, 1H), 5.07 (s, 1H), 4.12-4.06 (m, 3H), 3.96 (m, 1H), 3.56 (m, 1H), 1.99 (dd, *J* = 6.0, 3.0 Hz, 1H), 1.77 (s, 3H), 1.66 (s, 3H), 1.59 (ddd, *J* = 5.5, 3.0, 1.0 Hz, 1H), 1.49 (dd, *J* = 3.5, 3.0 Hz, 1H), 1.52-1.43 (m, 2H), 1.31 (s, 3H), 1.22 (t, *J* = 7.5 Hz, 3H), 1.10 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 175.5, 143.9, 138.2, 127.7, 124.4, 75.6, 72.0, 67.4, 60.5, 57.5, 41.7, 37.6, 33.2, 33.1, 26.3, 23.9, 16.2, 15.8, 14.5; HRMS (ESI) m/z 361.1987 [$(M+Na)^+$, calcd 361.1985 for $C_{19}H_{30}NaO_5$].



4-A2

Triol **4-A2**

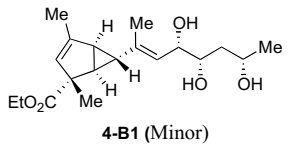
$[\alpha]_D^{20}$ = + 90 (acetone, *c* 1.0); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 5.14 (d, *J* = 8.5 Hz, 1H), 5.07 (s, 1H), 4.13-4.06 (m, 3H), 3.96 (m, 1H), 3.57 (m, 1H), 1.99 (dd, *J* = 6.0, 3.0 Hz, 1H), 1.77 (s, 3H), 1.63 (s, 3H), 1.62 (m, 1H), 1.50 (m, 1H), 1.53-1.40 (m, 2H), 1.31 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 175.8, 144.3, 138.6, 128.1, 124.8, 76.1, 72.3, 67.8, 60.8, 57.8, 42.0, 38.0, 33.6, 33.3, 26.6, 24.3, 16.2, 16.1, 14.9; HRMS (ESI) m/z 361.1989 [$(M+Na)^+$, calcd 361.1985 for $C_{19}H_{30}NaO_5$].



4-B2 (Major)

Triol **4-B2** (Major)

$[\alpha]_D^{20}$ = +148 (acetone, *c* 0.75); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 5.19 (d, *J* = 8.5 Hz, 1H), 4.95 (s, 1H), 4.14-4.07 (m, 3H), 3.96 (m, 1H), 3.59 (m, 1H), 2.12 (ddd, *J* = 5.5, 3.5, 1.5 Hz, 1H), 1.92 (dd, *J* = 6.0, 2.5 Hz, 1H), 1.76 (s, 3H), 1.67 (s, 3H), 1.51 (dd, *J* = 4.0, 3.0 Hz, 1H), 1.54-1.43 (m, 2H), 1.30 (s, 3H), 1.22 (t, *J* = 7.5 Hz, 3H), 1.12 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 176.5, 146.3, 138.7, 128.0, 124.8, 76.0, 72.4, 67.8, 61.1, 57.4, 42.1, 37.1, 34.7, 31.4, 24.3, 22.2, 16.6, 16.3, 14.7; HRMS (ESI) m/z 361.1980 [$(M+Na)^+$, calcd 361.1985 for $C_{19}H_{30}NaO_5$].

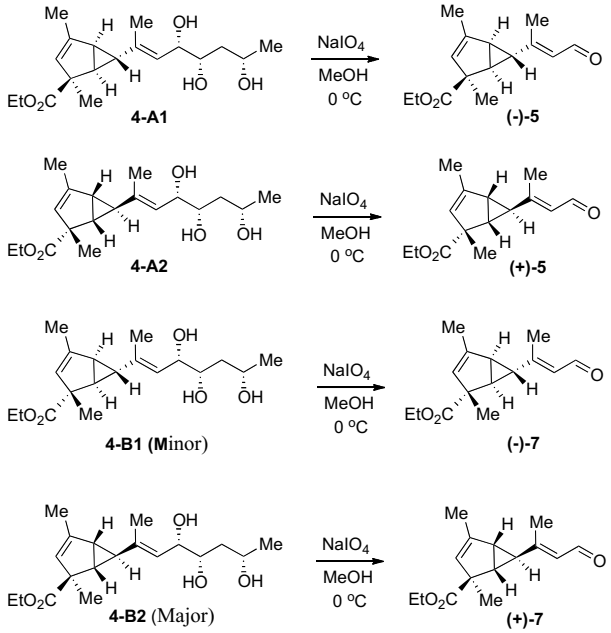


4-B1 (Minor)

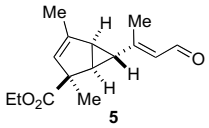
Triol **4-B1 (**Minor)

$[\alpha]_D^{20}$ = -213 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 5.20 (d, *J* = 8.5 Hz, 1H), 4.94 (s, 1H), 4.15-4.06 (m, 3H), 3.97 (m, 1H), 3.58 (m, 1H), 2.10 (m, 1H), 1.93 (dd, *J* = 6.0, 3.0 Hz, 1H), 1.76 (s, 3H), 1.66 (s, 3H), 1.51 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.54-1.45 (m, 2H), 1.30 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 176.5, 146.2, 138.6, 127.9, 124.9, 76.0, 72.3, 67.8, 61.0, 57.4, 42.1, 37.2, 34.4, 31.4, 24.3, 22.1, 16.4, 16.3, 14.6; HRMS (ESI) m/z 361.1988 [$(M+Na)^+$, calcd 361.1985 for $C_{19}H_{30}NaO_5$].

6c. Periodate cleavage to form unsaturated aldehydes

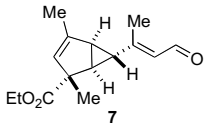


To a MeOH (0.1 mL) solution of triol **4-A1** (4.0 mg, 0.01 mmol, after HPLC chiral column separation), $NaIO_4$ (12.6 mg, 5 equiv) was added at 0 °C The reaction solution was warmed up to rt and stirred for 5 h. EtOAc was added to dilute the solution, sat. NaCl was used to wash the organic layers 3 times, solvent was removed *in vacuo*, the residue was purified by a flash column chromatography to give aldehyde (-)-**5** (2.5 mg, 85%). Optical pure aldehyde (+)-**5**, (-)-**7** and **(+)-7** were prepared by the same procedure from **4-A2**, **4-B1** and **4-B2**, respectively.



Aldehyde (-)-**5**: $[\alpha]_D^{20}$ = -115 (CH_2Cl_2, *c* 0.24); ^{1}H NMR (600 MHz, C_6D_6) δ 9.85 (d, *J* = 7.8 Hz, 1H), 5.71 (d, *J* = 7.8 Hz, 1H), 5.20 (s, 1H), 3.94 (m, 1H), 1.66 (dd, *J* = 6.0, 2.4 Hz, 1H), 1.56 (m, 1H), 1.52 (s, 3H), 1.49 (s, 3H), 1.33 (s, 3H), 1.17 (dd, *J* = 3.0, 3.0 Hz, 1H), 0.93 (t, *J* = 7.2 Hz, 3H); HRMS (ESI) m/z 271.1313 [$(M+Na)^+$, calcd 271.1305 for $C_{15}H_{20}NaO_3$].

Aldehyde (+)-**5**: $[\alpha]_D^{20}$ =+113 (CH_2Cl_2, *c* 0.08).



7

Aldehyde (-)-**7**: $[\alpha]_D^{20}$ = -449 (CH_2Cl_2, *c* 0.09); ^{1}H NMR (600 MHz, C_6D_6) δ 9.82 (d, *J* = 7.8 Hz, 1H), 5.79 (d, *J* = 7.8 Hz, 1H), 5.00 (s, 1H), 3.97 (m, 1H), 2.43 (m, 1H), 1.73 (dd, *J* = 6.0, 2.4 Hz, 1H), 1.50 (s, 3H), 1.34 (s, 3H), 1.26 (s, 3H), 0.96 (t, *J* = 7.2 Hz, 3H), 0.86 (dd, *J* = 3.6, 3.0 Hz, 1H),; HRMS (ESI) m/z 271.1312 [$(M+Na)^+$, calcd 271.1305 for $C_{15}H_{20}NaO_3$].
Aldehyde (+)-**7**: $[\alpha]_D^{20}$ = +413 (CH_2Cl_2, *c* 0.24).

6d. NOESY spectra of two unsaturated aldehydes

NOSEY experiments were performed on the two unsaturated aldehydes **5** and **7**, to assign the relative stereochemistry.

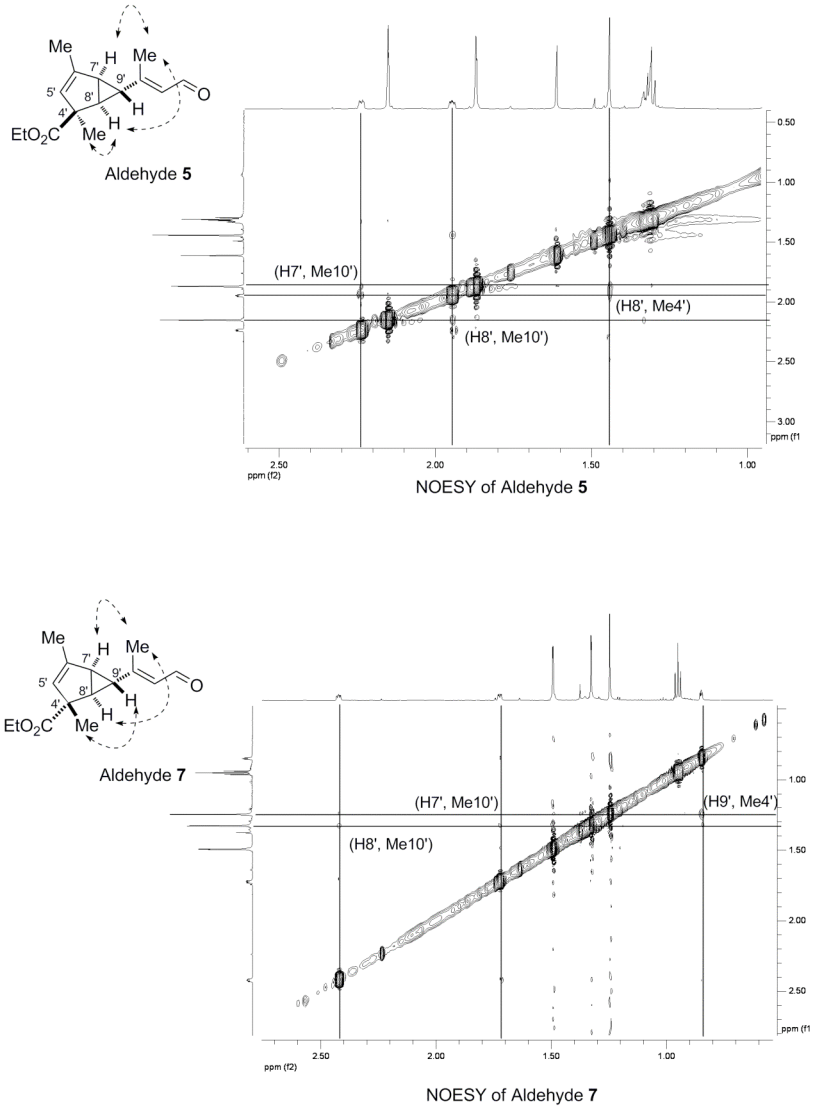
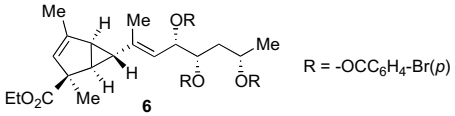


Figure 13. NOESY spectra of Aldehydes **5** and **7**

6e. X-Ray structure of triol 4-A1

Preparation of tri-*p*-bromobenzoate **6** in triol **4-A1**:



To a solution of triol **4-A1** (4.0 mg, 0.0012 mmol) in CH_2Cl_2 (1 mL) were successively added DMAP (0.3 mg, 0.0002 mmol), EDCI (13.6 mg, 0.0071 mmol) and *p*-bromobenzoic acid (14.2 mg, 0.0071 mmol). The solution was stirred at rt for overnight. The reaction was quenched by addition of sat. aq $NaHCO_3$ solution and extracted (CH_2Cl_2). The combined organic layers were dried over Na_2SO_4. Evaporation of the solvent and purification of the residue by preparative TLC with 20% EtOAc in hexanes gave **6** (9.8 mg, 91%). ^{1}H NMR (600MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 5.92 (dd, *J* = 9.6, 7.2 Hz, 1H), 5.52 (m, 1H), 5.29 (sextate, *J* = 6.6 Hz, 1H), 5.11 (d, *J* = 9.0 Hz, 1H), 5.09 (s, 1H), 4.11 (dq, *J* = 10.2, 7.2 Hz, 1H), 4.04 (dq, *J* = 10.8, 7.2 Hz, 1H), 2.20 (ddd, *J* = 15.0, 9.0, 7.2 Hz, 1H), 1.98 (ddd, *J* = 15.0, 6.0, 3.6 Hz, 1H), 1.90 (dd, *J* = 6.0, 3.0 Hz, 1H), 1.78 (d, *J* = 1.0 Hz, 3H), 1.75 (d, *J* = 1.5 Hz, 3H), 1.57 (m, 1H), 1.39 (d, *J* = 6.0 Hz, 3H), 1.33 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 1H), 1.16 (t, *J* = 7.2 Hz, 3H). HRMS (ESI) m/z 902.0518 $[(M+NH_4)^+$, calcd 902.0533 for $C_{40}H_{43}Br_3NO_8$].

Single crystal of the **4-A1** was prepared using vapor diffusion technique. A minimum amount of mixed solvent (EtOAc/hexanes; 1:9) was added to dissolve the above tribenzoate **6** (8 mg) at rt. This solution in a small vial was placed in closed hexanes chamber and kept at rt to effect crystallization. A single crystal thus obtained was subjected to the X-ray analysis.

X-ray analysis was done by Dr. Shao-Liang Zheng, Chemistry and Chemical Biology, Harvard University.

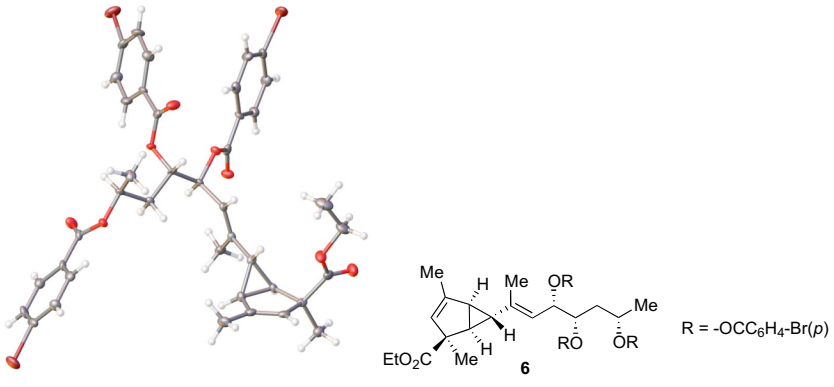
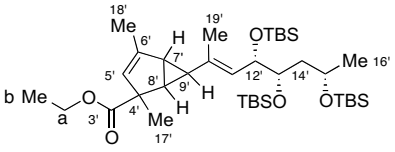
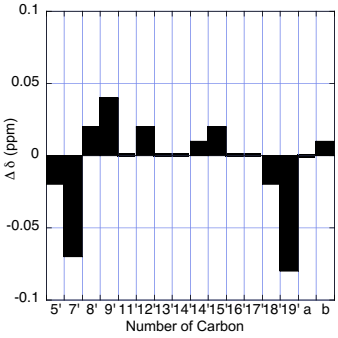


Figure 14. X-Ray structure of **4-A1**

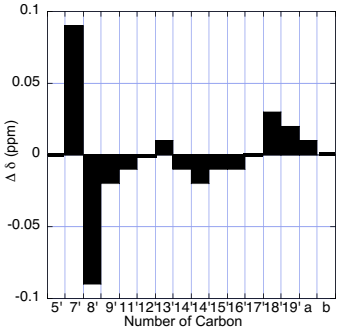
6f. Δδ NMR profile of TBS-protected triols S6-A1, S6-A2, S6-B1, and S6-B2

As discussed in the text, we could conclude that the major remote diastereomer corresponds either to **B1** or **B2** and the minor remote diastereomer to the other. We have compared the Δδ ^{1}H NMR and ^{13}C NMR profiles, which might suggest that **A1** and **minor remote diastereomer in B series** share the same absolute stereochemistry (numbering of mycolactone A/B used).

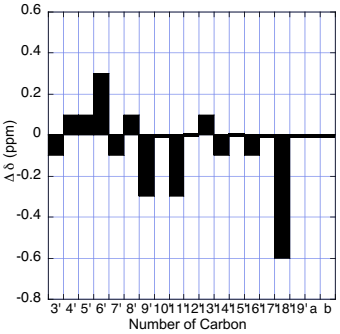




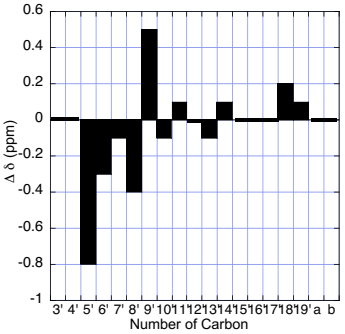
Difference in ^{1}H chemical shift between **S6-A1** and **S6-A2**



Difference in ^{1}H chemical shift between major and minor remote diastereomer in B series



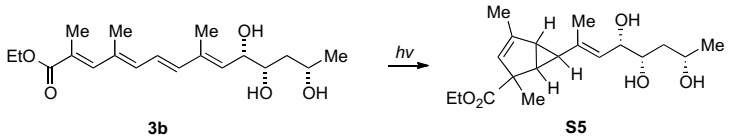
Difference in ^{13}C chemical shift between **S6-A1** and **S6-A2**



Difference in ^{13}C chemical shift between major and minor remote diastereomer in B series

Figure 15. Δδ NMR profile of TBS-protected triols

6g. Photolysis of tetraenoate triol 3b



Photolysis of **3b** was done in test tubes at 30 °C, with use of the photo-reactor shown in Figure 1. In comparison with the authentic samples described in the preceding sections, the photo-product was shown to compose of the four photo-products, with the 3:1 and 3:2 mixture of the *anti/syn* and remote diastereomers, respectively, and with the major product in the tetraenoate triol A- and B-subgroups corresponding to those in the tetraenoate tri-TBS A- and B-subgroups.

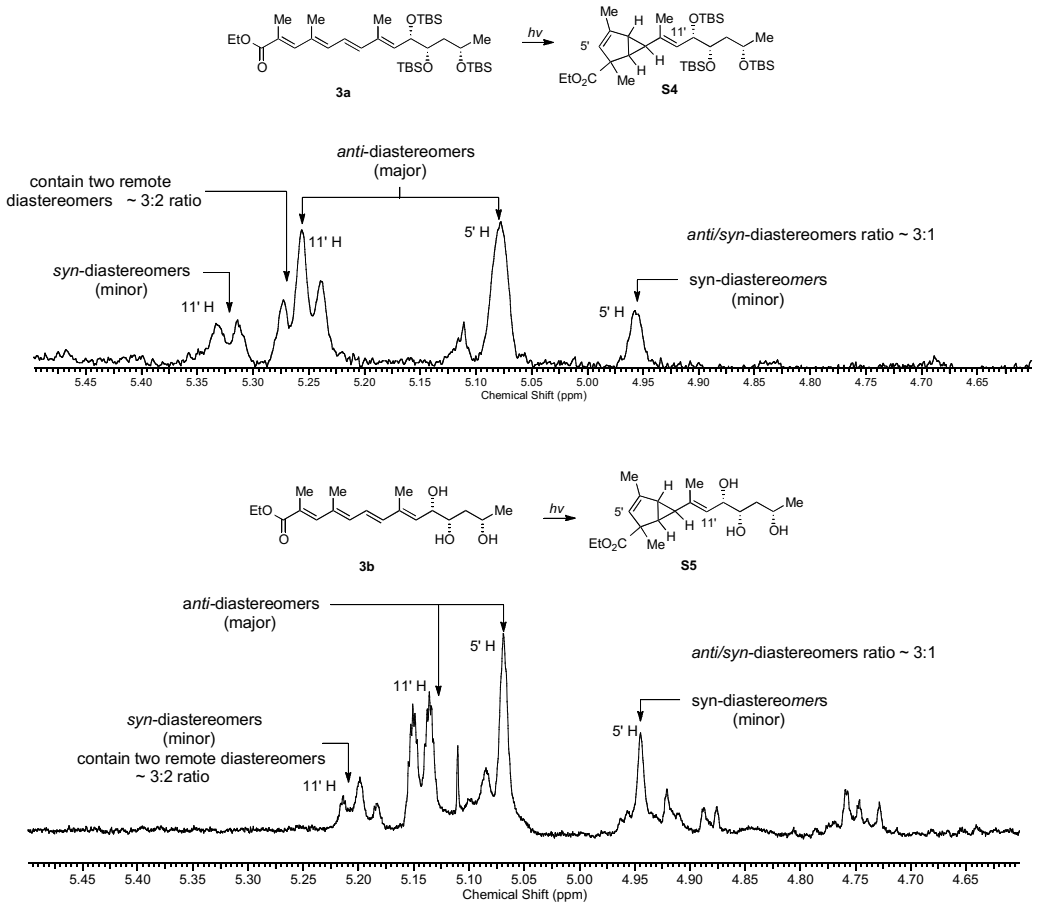
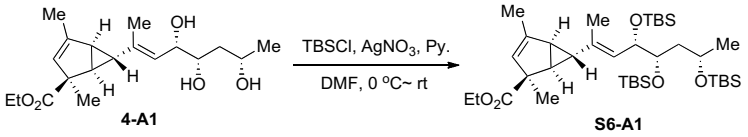


Figure 16. Photolysis of tetraenoate triol

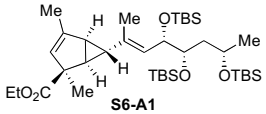
7. Transformation of the tetraenoate photo-products to the pentaenoate photo-products

7a. Chemical transformation

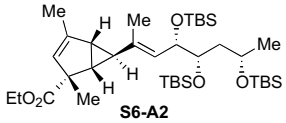
i. TBS-protection of triols



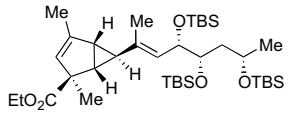
To a DMF solution (0.5 mL) of triol **4-A1** (19 mg, 0.056 mmol) at 0 °C, Pyridine (45 μL, 0.56 mmol), TBSCl (50.8 mg, 0.34 mmol) and $AgNO_3$ (76 mg, 0.45 mmol) were added. The reaction was warmed up to rt and stirred for 2 h. EtOAc was added to dilute the reaction mixture. The reaction mixture was quenched with sat. $NaHCO_3$ followed by sat. NaCl, extracted with EtOAc and dried over Na_2SO_4. Solvent was removed *in vacuo*, the residue was purified by a flash column chromatography to give **S6-A1** (34 mg, 94%). Compound **S6-A2**, **S6-B1**, **S6-B2** were prepared by the same procedure.



Ester **S6-A1**:
$[\alpha]_D^{20}$ = -66 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.49 (d, *J* = 9.0 Hz, 1H), 5.26 (s, 1H), 4.53 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.12 (qt, *J* = 6.0, 6.0 Hz, 1H), 4.04 (q, *J* = 7.0 Hz, 2H), 3.86 (m, 1H), 2.15 (ddd, *J* = 12.5, 7.5, 6.0 Hz, 1H), 1.94 (m, 2H), 1.79 (m, 1H), 1.71 (s, 3H), 1.64 (s, 3H), 1.46 (s, 3H), 1.42 (dd, *J* = 3.5, 3.0 Hz, 1H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.06 (t, *J* = 7.0 Hz, 3H), 1.04 (s, 9H), 1.02 (s, 9H), 1.01 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H), 0.15 (s, 9H), 0.14 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 175.1, 143.6, 135.9, 128.5, 124.7, 74.0, 71.8, 66.5, 60.3, 57.5, 43.7, 37.7, 33.3, 32.8, 26.6, 26.3 (3C), 26.2 (6C), 24.1, 18.5, 18.4, 18.3, 16.6, 16.0, 14.6, -3.6, -3.8, -3.9, -4.1, -4.2, -4.3; HRMS (ESI) m/z 703.4568 [$(M+Na)^+$, calcd 703.4580 for $C_{37}H_{72}NaO_5Si_3$].

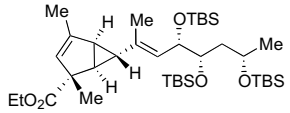


Ester **S6-A2**:
$[\alpha]_D^{20}$ = +35 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.49 (d, *J* = 9.0 Hz, 1H), 5.28 (s, 1H), 4.51 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.0, 6.0 Hz, 1H), 4.04 (m, 2H), 3.86 (m, 1H), 2.15 (ddd, *J* = 12.5, 6.0, 5.5 Hz, 1H), 2.00 (dd, *J* = 6.0, 3.0 Hz,, 1H), 1.93 (ddd, *J* = 12.5, 6.0, 5.5 Hz, 1H), 1.79 (s, 3H), 1.76 (m, 1H), 1.66 (s, 3H), 1.46 (s, 3H), 1.38 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.05 (t, *J* = 7.0 Hz, 3H), 1.04 (s, 9H), 1.03 (s, 9H), 1.00 (s, 9H), 0.19 (s, 3H), 0.16 (s, 6H), 0.15 (s, 3H), 0.12 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 175.2, 143.6, 135.6, 128.4, 125.0, 74.0, 71.7, 66.5, 60.3, 57.6, 43.8, 37.8, 33.2, 33.1, 26.6, 26.3 (3C), 26.2 (6C), 24.2, 18.5, 18.4 (2C), 17.2, 16.0, 14.6, -3.5, -3.9, -3.9, -4.1, -4.3 (2C); HRMS (ESI) m/z 703.4552 [$(M+Na)^+$, calcd 703.4580 for $C_{37}H_{72}NaO_5Si_3$].



S6-B2 (Major)

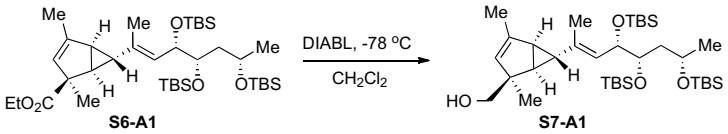
S6-B2 (Major)
$[\alpha]_D^{20}$ = +72 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.55 (d, *J* = 9.0 Hz, 1H), 5.07 (s, 1H), 4.51 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.10 (qt, *J* = 6.0, 6.0 Hz, 1H), 4.00 (q, *J* = 7.0 Hz, 2H), 3.87 (m 1H), 2.48 (m, 1H), 2.13 (ddd, *J* = 12.5, 6.0, 5.5 Hz), 2.01 (m, 1H), 1.93 (ddd, *J* = 12.5, 6.0, 5.5), 1.64 (s, 6H), 1.43 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.12 (m, 1H), 0.98 (t, *J* = 7.0 Hz, 3H), 1.04 (s, 9H), 1.02 (s, 9H), 1.00 (s, 9H), 0.18 (s, 3H), 0.16 (s, 6H), 0.14(s, 3H), 0.12 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 175.8, 145.6, 135.1, 127.6, 125.7, 74.0, 71.7, 66.5, 60.5, 57.0, 44.0, 37.1, 33.6, 30.9, 26.3 (3C), 26.2 (6C), 24.3, 22.0, 18.5, 18.4, 18.3, 16.3, 16.1, 14.3, -2.7, -3.5, -3.8, -3.9, -4.1, -4.3; HRMS (ESI) m/z 703.4604 [$(M+Na)^+$, calcd 703.4580 for $C_{37}H_{72}NaO_5Si_3$].



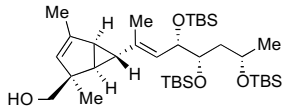
S6-B1 (Minor)

S6-B1 (Minor)
$[\alpha]_D^{20}$ = -105 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.56 (d, *J* = 9.0 Hz, 1H), 5.07 (s, 1H), 4.51 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.11 (qt, *J* = 6.0, 6.0 Hz, 1H), 3.99 (m, 2H), 3.86 (m, 1H), 2.57 (m, 1H), 2.14 (ddd, *J* = 12.5, 6.5, 6.0 Hz,, 1H), 1.95 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.92 (m, 1H), 1.62 (s, 3H), 1.61 (s, 3H), 1.43 (s, 3H), 1.27 (d, *J* = 5.5 Hz, 3H), 1.14 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.04 (s, 9H), 1.01 (s, 9H), 1.00 (s, 9H), 0.98 (t, *J* = 6.5 Hz, 3H), 0.18 (s, 3H), 0.15 (s, 6H), 0.14 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 175.8, 145.7, 135.4, 128.4, 125.6, 74.0, 71.8, 66.5, 60.5, 57.0, 43.9, 37.2, 34.0, 30.4, 26.3 (3C), 26.2 (6C), 24.3, 22.0, 18.5, 18.4, 18.3, 16.1, 16.0, 14.3, -3.5, -3.9, -3.9, -4.1, -4.2, -4.3; HRMS (ESI) m/z 703.4592 [$(M+Na)^+$, calcd 703.4580 for $C_{37}H_{72}NaO_5Si_3$].

ii. DIBAL-H reduction



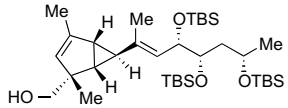
To a CH_2Cl_2 solution (0.5 mL) of **S6-A1** (38 mg, 0.056 mmol) at -78 °C, DIBAL solution (1M in hexanes, 0.28 mL) was added. The reaction was stirred at -78 °C for 2 h. Sat. sodium potassium tartrate solution was added to quench the reaction. The reaction mixture was warmed up to rt and stirred for 1 h. Then the reaction mixture was extracted with CH_2Cl_2 and dried over Na_2SO_4. Solvent was removed *in vacuo*, the residue was purified by a flash column chromatography to give the alcohol **S7-A1** (32 mg, 90%). The alcohols **S7-A2**, **S7-B1**, **S7-B2** were prepared by the same procedure.



S7-A1

Alcohol **S7-A1**

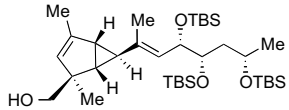
$[\alpha]_D^{20}$ = -65 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.48 (d, *J* = 9.0 Hz, 1H), 4.84 (s, 1H), 4.52 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.12 (qt, *J* = 6.0, 6.5 Hz, 1H), 3.86 (ddd, *J* = 7.5, 5.5, 3.5 Hz, 1H), 3.46 (d, *J* = 11.0 Hz, 1H), 3.29 (d, *J* = 11.0 Hz, 1H), 2.15 (ddd, *J* = 13.0, 6.5, 6.0 Hz, 1H), 1.95 (ddd, *J* = 13.0, 6.5, 6.0 Hz, 1H), 1.91 (dd, *J* = 6.0, 3.0 Hz, 1H), 1.65 (s, 3H), 1.64 (s, 3H), 1.51 (dd, *J* = 5.5, 3.5 Hz, 1H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.24 (s, 3H), 1.19 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.03 (s, 9H), 1.02 (s, 9H), 1.01 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.1, 136.1, 129.4, 124.6, 74.0, 71.9, 69.0, 66.5, 52.4, 43.8, 36.0, 33.3, 32.2, 26.3 (3C), 26.2 (6C), 25.4, 24.2, 18.5, 18.4 (2C), 16.4, 16.2, -3.5, -3.8, -3.9, -4.1, -4.2, -4.3; HRMS (ESI) m/z 661.4460 [$(M+Na)^+$, calcd 661.4474 for $C_{35}H_{70}NaO_4Si_3$].



S7-A2

Alcohol **S7-A2**

$[\alpha]_D^{20}$ = +58 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.49 (d, *J* = 9.0 Hz, 1H), 4.83 (s, 1H), 4.51 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.86 (ddd, *J* = 6.0, 5.5, 3.0 Hz, 1H), 3.44 (d, *J* = 10.5 Hz, 1H), 3.28 (d, *J* = 10.5 Hz, 1H), 2.13 (ddd, *J* = 12.5, 6.0, 5.5 Hz, 1H), 1.98 (dd, *J* = 6.0, 2.5 Hz, 1H), 1.93 (ddd, *J* = 12.5, 6.0, 5.5 Hz, 1H), 1.68 (s, 3H), 1.67 (s, 3H), 1.45 (m, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.23 (s, 3H), 1.17 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.04 (s, 9H), 1.02 (s, 9H), 1.00 (s, 9H), 0.19 (s, 3H), 0.16 (s, 6H), 0.14 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.1, 135.7, 129.4, 125.0, 74.0, 71.7, 69.0, 66.5, 52.4, 43.9, 36.0, 33.0, 32.4, 26.3 (3C), 26.2 (6C), 25.3, 24.3, 18.5, 18.4 (2C), 16.7, 16.3, -3.5, -3.8, -3.9, -4.1, -4.3, -4.3; HRMS (ESI) m/z 661.4484 [$(M+Na)^+$, calcd 661.4474 for $C_{35}H_{70}NaO_4Si_3$].

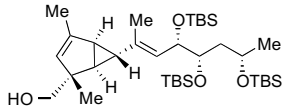


S7-B2 (Major)

Alcohol **S7-B2** (major)

$[\alpha]_D^{20}$ = +70 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.51 (d, *J* = 9.5 Hz, 1H), 4.55 (s, 1H), 4.51 (dd, *J* = 9.5, 4.0 Hz, 1H), 4.11 (qt, *J* = 6.0, 6.0 Hz, 1H), 3.86 (ddd, *J* = 5.5, 5.5, 3.5 Hz, 1H), 3.39 (d, *J* = 10.0 Hz, 1H), 3.34 (d, *J* = 10.0 Hz, 1H), 2.14 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.94 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.91 (dd, *J* = 6.0, 2.0 Hz, 1H), 1.66 (m, 1H), 1.65 (s, 3H), 1.63 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.09 (dd, *J* = 4.0, 2.5 Hz, 1H), 1.03 (s, 3H), 1.04 (s, 9H), 1.02 (s, 9H), 1.00 (s, 9H), 0.19 (s, 3H), 0.16 (s, 6H), 0.14 (s, 3H), 0.12 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 145.8, 135.7, 128.9, 125.2, 74.0,

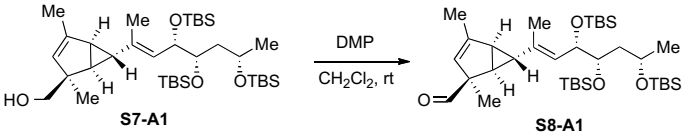
71.8, 71.3, 66.5, 52.5, 44.0, 36.3, 33.6, 31.1, 26.3 (3C), 26.2 (6C), 24.3, 19.7, 18.5, 18.4 (2C), 16.3 (2C), -3.5, -3.8, -3.9, -4.1, -4.2, -4.3; HRMS (ESI) m/z 661.4493 [$(M+Na)^+$, calcd 661.4474 for $C_{35}H_{70}NaO_4Si_3$].



S7-B1 (Minor)

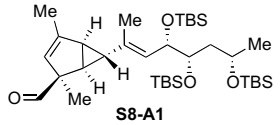
Alcohol **S7-B1** (minor)
$[\alpha]_D^{20}$ = -76 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 5.51 (d, *J* = 9.5 Hz, 1H), 4.54 (s, 1H), 4.52 (dd, *J* = 7.5, 3.5 Hz, 1H), 4.11 (qt, *J* = 6.0, 6.0 Hz, 1H), 3.86 (ddd, *J* = 6.0, 5.5, 3.0 Hz, 1H), 3.39 (d, *J* = 10.5 Hz, 1H), 3.34 (d, *J* = 10.5 Hz, 1H), 2.14 (ddd, *J* = 12.0, 6.5, 6.0 Hz, 1H), 1.94 (ddd, *J* = 12.0, 6.5, 6.0 Hz, 1H), 1.81 (dd, *J* = 6.0, 3.0 Hz, 1H), 1.73 (m, 1H), 1.64 (s, 3H), 1.61 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.09 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.04 (s, 9H), 1.04 (s, 3H), 1.01 (s, 9H), 1.00 (s, 9H), 0.18 (s, 3H), 0.16 (s, 6H), 0.14 (s, 3H), 0.13 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 145.8, 135.9, 128.8, 125.02, 74.0, 72.0, 71.3, 66.5, 52.5, 43.9, 36.3, 34.0, 30.7, 26.3 (3C), 26.2 (6C), 24.2, 19.7, 18.5, 18.4 (2C), 16.2 (2C), -3.5, -3.9, -3.9, -4.1, -4.2, -4.3; HRMS (ESI) m/z 661.4461 [$(M+Na)^+$, calcd 661.4474 for $C_{35}H_{70}NaO_4Si_3$].

iii. Oxidation of alcohol.



S7-A1 **S8-A1**

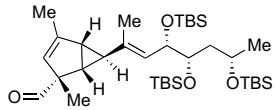
To a CH_2Cl_2 solution (0.5 mL) of alcohol **S7-A1** (32 mg, 0.05 mmol) at rt, Dess–Martin periodinane (32 mg, 0.075 mmol) and $NaHCO_3$ (8.4 mg, 0.1 mmol) were added. The reaction was stirred at rt for 2 h. The reaction mixture was quenched by sat. $NaHCO_3$ followed by sat. NaCl, extracted with EtOAc and dried over Na_2SO_4. Solvent was removed *in vacuo*, and the residue was purified by small silica pad to give the aldehyde **S8-A1** (26 mg, 84%). The aldehydes **S8-A2**, **S8-B1**, **S8-B2** were prepared by the same procedure.



S8-A1

Aldehyde **S8-A1**
^{1}H NMR (500 MHz, C_6D_6) δ 9.54 (s, 1H), 5.45 (d, *J* = 8.5 Hz, 1H), 4.67 (s, 1H), 4.49 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.11 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 2.14 (ddd, *J* = 13.0, 6.5, 6.0 Hz, 1H), 1.92 (m, 2H), 1.61 (s, 3H), 1.57 (s, 3H), 1.54 (m, 1H), 1.32 (m, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.17 (s, 3H), 1.02 (s, 9H), 1.01 (s, 9H), 1.00 (s, 9H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 6H), 0.12 (s, 3H), 0.11 (s, 3H); HRMS (ESI) m/z 659.4304

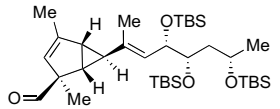
[(M+Na)$^+$, calcd 659.4318 for $C_{35}H_{68}NaO_4Si_3$].



S8-A2

Aldehyde **S8-A2**

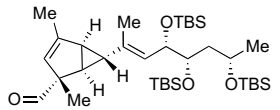
^{1}H NMR (500 MHz, C_6D_6) δ 9.53 (s, 1H), 5.45 (d, *J* = 9.0 Hz, 1H), 4.67 (s, 1H), 4.47 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.09 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.84 (m, 1H), 2.13 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.99 (dd, *J* = 5.5, 2.5 Hz, 1H), 1.92 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.61 (s, 3H), 1.59 (s, 3H), 1.45 (m, 1H), 1.30 (dd, *J* = 2.5, 2.5 Hz, 1H), 1.25 (d, *J* = 5.5 Hz, 3H), 1.16 (s, 3H), 1.03 (s, 9H), 1.02 (s, 9H), 0.99 (s, 9H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 6H), 0.10 (s, 3H), 0.08 (s, 3H); HRMS (ESI) m/z 659.4313 [(M+Na)$^+$, calcd 659.4318 for $C_{35}H_{68}NaO_4Si_3$].



S8-B2 (Major)

Aldehyde **S8-B2** (major)

^{1}H NMR (500 MHz, C_6D_6) δ 9.40 (s, 1H), 5.49 (d, *J* = 8.5 Hz, 1H), 4.49 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.12 (s, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (ddd, *J* = 7.0, 7.0, 3.5 Hz, 1H), 2.14 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.94 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.88 (m, 1H), 1.83 (m, 1H), 1.65 (s, 3H), 1.57 (s, 3H), 1.26 (d, *J* = 5.5, Hz, 3H), 1.12 (s, 3H), 1.06 (m, 1H), 1.03 (s, 9H), 1.02 (s, 9H), 1.00 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.11 (s, 3H) , 0.09 (s, 3H); HRMS (ESI) m/z 659.4318 [(M+Na)$^+$, calcd 659.4318 for $C_{35}H_{68}NaO_4Si_3$].

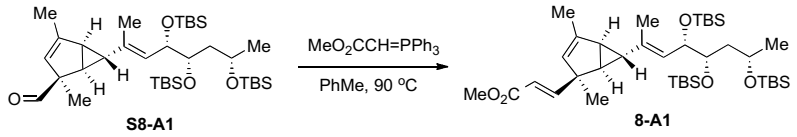


S8-B1 (Minor)

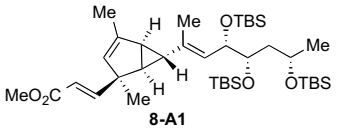
Aldehyde **S8-B1** (minor)

^{1}H NMR (500 MHz, C_6D_6) δ 9.40 (s, 1H), 5.49 (d, *J* = 9.0 Hz, 1H), 4.50 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.12 (s, 1H), 4.11 (qt, *J* = 6.0, 5.5 Hz, 1H), 3.85 (m, 1H), 2.14 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.93 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.90 (m, 1H), 1.78 (dd, *J* = 6.0, 2.5 Hz, 1H), 1.55 (s, 6H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.12 (s, 3H), 1.07 (dd, *J* = 3.0, 3.0 Hz, 1H), 1.02 (s, 9H), 1.01 (s, 9H), 1.00 (s, 9H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 6H), 0.12 (s, 3H), 0.11 (s, 3H); HRMS (ESI) m/z 659.4317 [(M+Na)$^+$, calcd 659.4318 for $C_{35}H_{68}NaO_4Si_3$].

iv. Wittig olefination

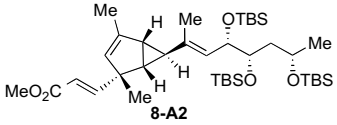


To a toluene solution (1.5 mL) of aldehyde **S8-A1** (26 mg, 0.04 mmol) at rt, $MeO_2CCH{=}PPh_3$ (86 mg, 0.25 mmol) was added. The reaction was heated up to 90 °C and stirred for 12 h. Solvent was removed *in vacuo*, and the residue was purified by flash column chromatography to give the ester **8-A1** (26 mg, 87%). The esters **8-A2**, **8-B1**, **8-B2** were prepared by the same procedure.



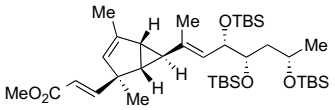
Unsaturated ester **8-A1**

$[\alpha]_D^{20}$ = -36 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 7.22 (d, *J* = 16.0 Hz, 1H), 5.92 (d, *J* = 16.0 Hz, 1H), 5.46 (d, *J* = 9.0 Hz, 1H), 4.64 (s, 1H), 4.50 (dd, *J* = 9.5, 3.0 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (ddd, *J* = 7.5, 5.5, 3.5 Hz, 1H), 3.47 (s, 3H), 2.12 (ddd, *J* = 13.5, 6.0, 5.5 Hz, 1H), 1.92 (ddd, *J* = 13.5, 6.0, 5.5 Hz, 1H), 1.86 (dd, *J* = 6.0, 2.5 Hz, 1H), 1.60 (s, 3H), 1.59 (s, 3H), 1.57 (m, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.13 (s, 3H), 1.10 (dd, *J* = 3.0, 3.0 Hz 1H), 1.04 (s, 9H), 1.01 (s, 18H), 0.18 (s, 3H), 0.15 (s, 6H), 0.14 (s, 6H), 0.13 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 166.9, 154.0, 144.0, 135.2, 129.0, 125.3, 118.9, 74.0, 71.8, 66.5, 52.7, 51.0, 43.9, 37.4, 34.0, 33.3, 27.8, 26.3 (3C), 26.2 (6C), 24.2, 18.5, 18.4 (2C), 16.3, 16.0, -3.5, -3.8, -3.9, -4.1, -4.2, -4.3; HRMS (ESI) m/z 715.4552 [$(M+Na)^+$, calcd 715.4580 for $C_{38}H_{72}NaO_5Si_3$].



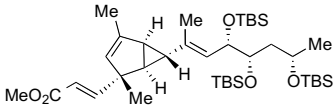
Unsaturated ester **8-A2**

$[\alpha]_D^{20}$ = +25 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 7.22 (d, *J* = 15.5 Hz, 1H), 5.91 (d, *J* = 15.5 Hz, 1H), 5.46 (d, *J* = 9.0 Hz, 1H), 4.64 (s, 1H), 4.48 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 3.47 (s, 3H), 2.13 (ddd, *J* = 12.5, 6.0, 6.0 Hz, 1H), 1.94 (m, 1H), 1.92 (ddd, *J* = 12.5, 6.0, 6.0 Hz, 1H), 1.62 (s, 3H), 1.61 (s, 3H), 1.50 (m, 1H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.12 (s, 3H), 1.08 (dd, *J* = 3.0, 3.0 Hz 1H), 1.04 (s, 9H), 1.01 (s, 9H), 1.00 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 166.9, 154.1, 143.9, 135.0, 128.9, 125.4, 118.9, 73.9, 71.6, 66.5, 52.6, 51.0, 44.0, 37.2, 33.7, 33.6, 27.7, 26.3 (3C), 26.2 (6C), 24.3, 18.5, 18.4 (2C), 16.5, 16.1, -3.5, -3.8, -3.9, -4.1, -4.3, -4.3; HRMS (ESI) m/z 715.4576 [$(M+Na)^+$, calcd 715.4580 for $C_{38}H_{72}NaO_5Si_3$].



8-B2 (Major)

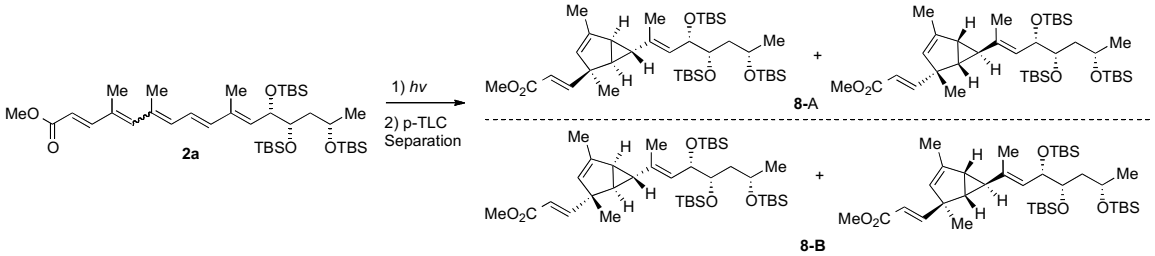
Unsaturated ester **8-B2** (major)
$[\alpha]_D^{20}$ = +118 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 7.26 (d, *J* = 16.0 Hz, 1H), 6.01 (d, *J* = 16.0 Hz, 1H), 5.47 (d, *J* = 9.0 Hz, 1H), 4.52 (s, 1H), 4.48 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (ddd, *J* = 7.0, 6.0, 3.5 Hz, 1H), 3.45 (s, 3H), 2.13 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.92 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.88 (dd, *J* = 6.5, 2.5 Hz, 1H), 1.60 (s, 3H), 1.57 (s, 3H), 1.55 (m, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.11 (dd, *J* = 3.0, 3.0 Hz 1H), 1.07 (s, 3H), 1.03 (s, 9H), 1.02 (s, 9H), 0.99 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 167.1, 156.2, 145.0, 135.0, 128.8, 125.6, 118.1, 74.0, 71.7, 66.5, 51.9, 51.0, 43.9, 36.9, 33.5, 32.8, 26.3 (3C), 26.2 (6C), 24.2, 21.7, 18.5, 18.4 (2C), 16.2, 16.1, -3.6, -3.8, -3.9, -4.1, -4.3 (2C); HRMS (ESI) m/z 715.4600 [$(M+Na)^+$, calcd 715.4580 for $C_{38}H_{72}NaO_5Si_3$].



8-B1 (Minor)

Unsaturated ester **8-B1** (minor)
$[\alpha]_D^{20}$ = -113 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 7.26 (d, *J* = 16.0 Hz, 1H), 6.01 (d, *J* = 16.0 Hz, 1H), 5.46 (d, *J* = 9.5 Hz, 1H), 4.52 (s, 1H), 4.50 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 3.45 (s, 3H), 2.13 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.92 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.80 (dd, *J* = 6.0, 2.0 Hz, 1H), 1.62 (m, 1H), 1.57 (s, 3H), 1.56 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.12 (dd, *J* = 3.5, 2.5 Hz, 1H), 1.08 (s, 3H), 1.01 (s, 9H), 1.00 (s, 18H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 6H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 167.1, 156.2, 145.0, 135.4, 128.8, 125.2, 118.1, 74.0, 71.8, 66.5, 51.9, 51.0, 43.7, 36.9, 33.9, 32.6, 26.3 (3C), 26.2 (6C), 24.2, 21.7, 18.5, 18.4, 18.3, 16.1, 16.0, -3.6, -3.8, -3.9, -4.1, -4.3 (2C); HRMS (ESI) m/z 715.4576 [$(M+Na)^+$, calcd 715.4571 for $C_{38}H_{72}NaO_5Si_3$].

7b. Photolysis of methyl pentaenoate 2a and the comparison with 8-A1, 8-A2, 8-B1 and 8-B2 (derived from photolysis products of tetraenoate)



Photolysis of **2a** was done in test tubes at 30 °C, with use of the photo-reactor shown in

Figure 1. In comparison with the authentic samples described in the preceding sections, the photo-product was shown to be composed of the four isomers, with the 3:1 and 3:2 mixture of the A/B-subgroups and remote diastereomers, respectively, and with the major product in the pentaenoate A- and B-subgroups corresponding to those in the tetraenoate A- and B-subgroups.

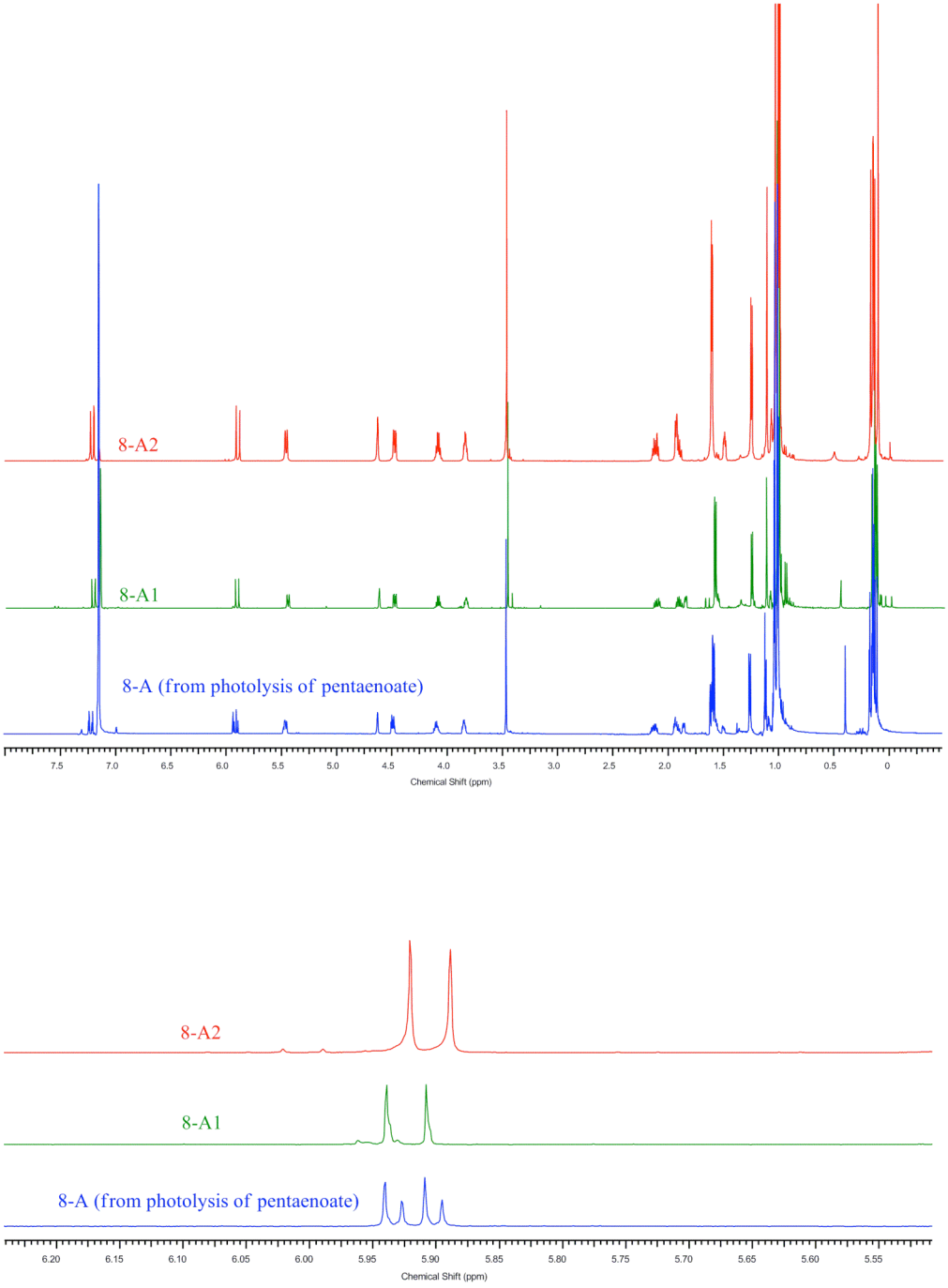


Figure 17. NMR correlation of pentaenoate product **8-A** and tetraenoate product **8-A1** and **8-A2**

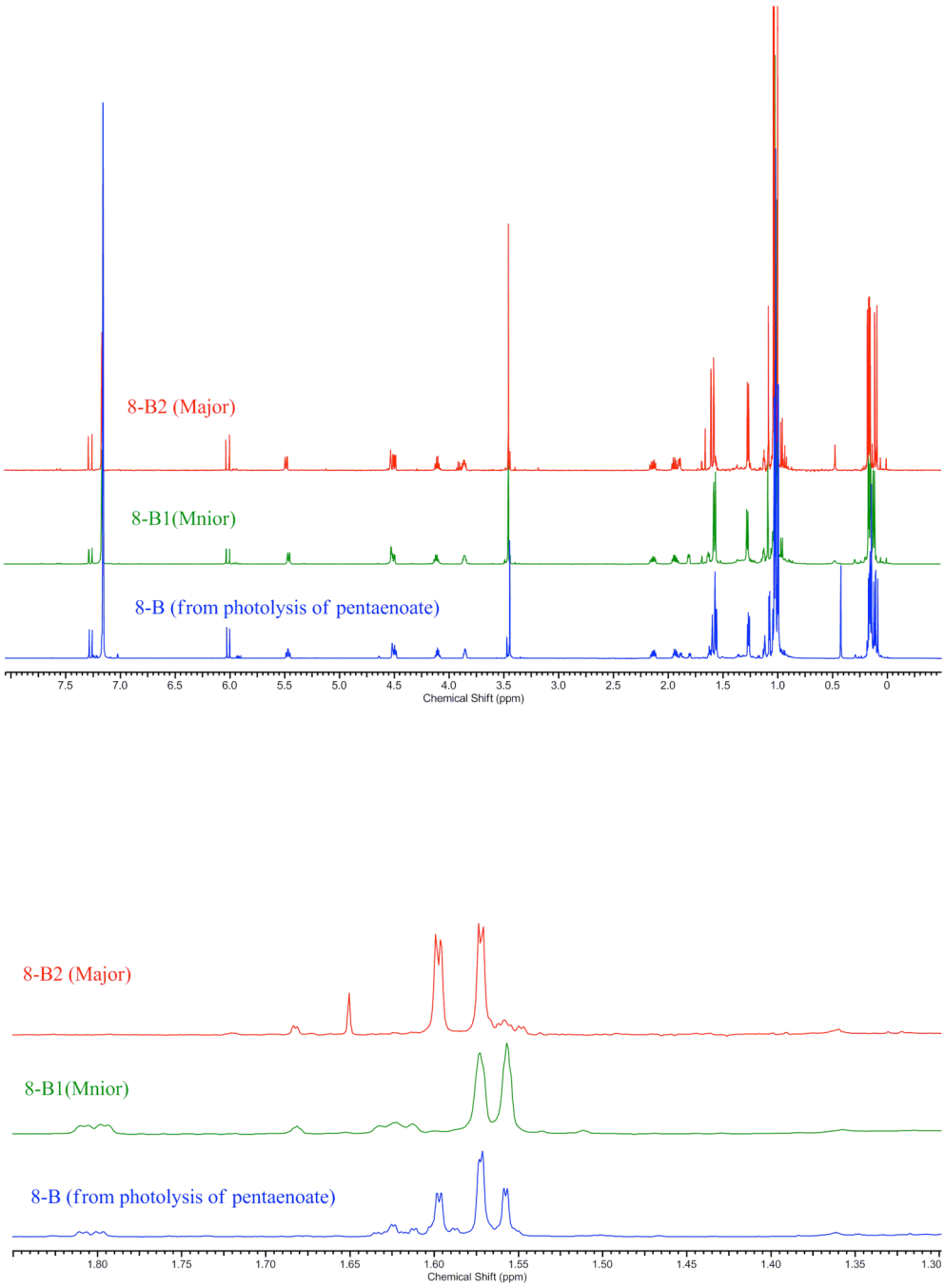
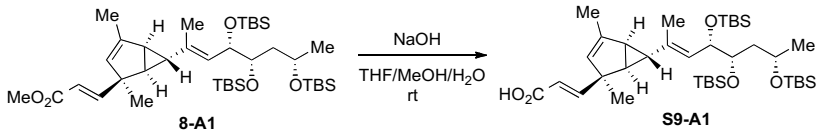


Figure 18. NMR correlation of pentaenoate product **8-B** and tetraenoate product **8-B1** and **8-B2**

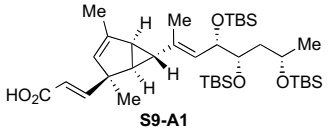
8. Transformation of the pentaenoate photo-products to the mycolactone photo-products

8a. Chemical transformation

i. Hydrolysis of ester

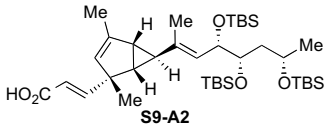


To a THF/MeOH/H_2O solution (4:1:1, 0.36 mL) of ester **8-A1** (26 mg, 0.036 mmol) at rt, NaOH (2M/MeOH, 0.54 mL) was added. The reaction was stirred for 12 h. EtOAc was added to dilute the solution, 1M HCl was added to quench the excess NaOH until the pH of the solution became about 7. The organic layer was extracted with EtOAc, washed with sat. NaCl and dried over $NaSO_4$. Solvent was removed *in vacuo*, and the residue was purified by flash column chromatography to give the acid **S9-A1** (22 mg, 90%). The acids **S9-A2**, **S9-B1**, **S9-B2** were prepared by the same procedure.



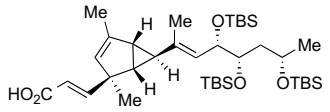
Acid **S9-A1**

^{1}H NMR (500 MHz, C_6D_6) δ 7.26 (d, *J* = 16.0 Hz, 1H), 5.86 (d, *J* = 16.0 Hz, 1H), 5.45 (d, *J* = 7.5 Hz, 1H), 4.57 (s, 1H), 4.50 (dd, *J* = 7.5, 3.5 Hz, 1H), 4.11 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 2.13 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.94 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.86 (dd, *J* = 6.0, 2.5 Hz, 1H), 1.61 (s, 3H), 1.57 (s, 3H), 1.54 (dd, *J* = 6.0, 6.0 Hz, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.07 (m, 1H), 1.08 (s, 3H), 1.05 (s, 9H), 1.03 (s, 18H), 0.19 (s, 3H), 0.17 (s, 3H), 0.16 (s, 6H), 0.15 (s, 3H), 0.14 (s, 3H); HRMS (ESI) m/z 701.4390 [$(M+Na)^+$, calcd 701.4423 for $C_{37}H_{70}NaO_5Si_3$].



Acid **S9-A2**

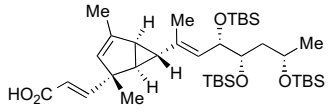
^{1}H NMR (500 MHz, C_6D_6) δ 7.27 (d, *J* = 16.0 Hz, 1H), 5.87 (d, *J* = 16.0 Hz, 1H), 5.48 (d, *J* = 9.5 Hz, 1H), 4.58 (s, 1H), 4.49 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.86 (m, 1H), 2.13 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.93 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.95 (m, 1H), 1.61 (s, 3H), 1.60 (s, 3H), 1.47 (m, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.08 (s, 3H), 1.06 (s, 9H), 1.05 (m, 1H), 1.03 (s, 9H), 1.01 (s, 9H), 0.20 (s, 3H), 0.17 (s, 6H), 0.16 (s, 3H), 0.12 (s, 6H); HRMS (ESI) m/z 701.4400 [$(M+Na)^+$, calcd 701.4423 for $C_{37}H_{70}NaO_5Si_3$].



S9-B2 (Major)

Acid **S9-B2** (major)

^{1}H NMR (500 MHz, C_6D_6) δ 7.28 (d, *J* = 15.5 Hz, 1H), 5.96 (d, *J* = 15.5 Hz, 1H), 5.47 (d, *J* = 9.0 Hz, 1H), 4.49 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.46 (s, 1H), 4.11 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.86 (ddd, *J* = 7.0, 6.0, 3.5 Hz, 1H), 2.14 (ddd, *J* = 13.0, 6.5, 6.0 Hz, 1H), 1.93 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.86 (dd, *J* = 5.5, 2.5 Hz, 1H), 1.59 (s, 3H), 1.57 (s, 3H), 1.53 (dd, *J* = 4.5, 3.5 Hz, 1H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.10 (dd, *J* = 3.0, 3.0 Hz 1H), 1.03 (s, 18H), 1.00 (s, 9H), 1.00 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (s, 6H), 0.11 (s, 3H), 0.09 (s, 3H); HRMS (ESI) m/z 701.4457 [(M+Na)$^+$, calcd 701.4423 for $C_{37}H_{70}NaO_5Si_3$].

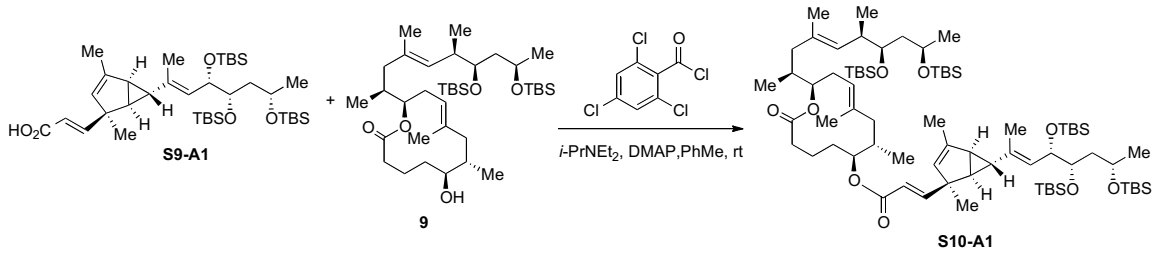


S9-B1 (Minor)

Acid **S9-B1** (minor)

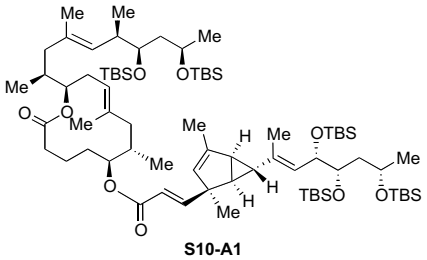
^{1}H NMR (500 MHz, C_6D_6) δ 7.29 (d, *J* = 15.5 Hz, 1H), 5.96 (d, *J* = 15.5 Hz, 1H), 5.45 (d, *J* = 9.0 Hz, 1H), 4.50 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.46 (s, 1H), 4.11 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 2.13 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.93 (ddd, *J* = 12.5, 6.5, 6.0 Hz, 1H), 1.78 (dd, *J* = 5.5, 2.5 Hz, 1H), 1.59 (m, 1H), 1.56 (s, 6H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.10 (dd, *J* = 3.5, 2.5 Hz 1H), 1.03 (s, 3H), 1.02 (s, 18H), 1.00 (s, 9H), 0.16 (s, 6H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H); HRMS (ESI) m/z 701.4403 [(M+Na)$^+$, calcd 701.4423 for $C_{37}H_{70}NaO_5Si_3$].

ii. Yamaguchi esterification



To a toluene solution (0.5 mL) of acid **S9-A1** (22 mg, 0.032 mmol) at rt, 2,4,6-trichlorobenzyl chloride (19 μL, 0.11 mmol), diisopropylethyl amine (41 μL, 0.16 mmol) and DMAP (14 mg, 0.11 mmol) were added.[3] The reaction was stirred for 1.5 h. Then core alcohol **9**[1] (22 mg, 0.034 mmol) solution in PhMe (0.9 mL) was added to the reaction. The reaction solution was stirred for 12 h. Sat. $NaHCO_3$ was added to quench the reaction. The organic layer was extracted with EtOAc, washed with sat. NaCl and dried over $NaSO_4$. Solvent was removed *in vacuo*, and the residue was purified by flash column chromatography to give the coupling product **S10-A1** (39 mg, 91%). The protected photo-mycolactones **S10-A2**, **S10-B1**, **S10-B2** were prepared by the same

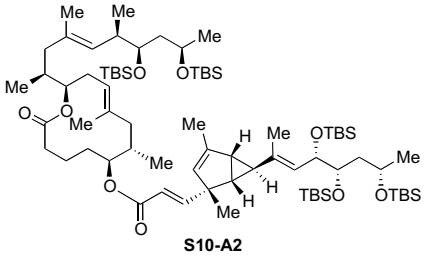
procedure.



S10-A1

Protected photo-mycolactone **S10-A1**

$[\alpha]_D^{20}$ = -19 (CH_2Cl_2, *c* 0.80); ^{1}H NMR (500 MHz, C_6D_6) δ 7.34 (d, *J* = 15.5 Hz, 1H), 6.02 (d, *J* = 15.5 Hz, 1H), 5.45 (d, *J* = 9.5 Hz, 1H), 5.35 (d, *J* = 10.0 Hz, 1H), 5.10 (m, 3H), 4.71 (s, 1H), 4.51 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.11 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.97 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 3.78 (m, 1H), 2.62 (m, 1H), 2.43 (m, 1H), 2.25 (m, 2H), 2.11 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 2.01-1.71 (m, 16 H), 1.64 (s, 3H), 1.63 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.18 (d, *J* = 6.0 Hz, 3H), 1.17 (d, *J* = 6.0 Hz, 3H), 1.14 (dd, *J* = 3.5, 2.5 Hz, 1H), 1.06 (d, *J* = 6.0 Hz, 3H), 1.04 (s, 3H), 1.05 (s, 18H), 1.04 (s, 18H), 1.03 (s, 9H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.19 (s, 3H), 0.17 (s, 3H), 0.16 (s, 15H), 0.15 (s, 3H), 0.14 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.4, 170.0, 166.0, 154.0, 143.9, 136.5, 135.5, 132.2, 131.0, 124.9, 123.4, 119.4, 78.9, 76.0, 74.0, 73.6, 71.8, 66.5, 66.3, 52.8, 46.0, 45.8, 43.8, 43.7, 37.8, 37.1, 35.6, 35.4, 34.0, 33.7, 32.4, 31.1, 30.2, 27.9, 26.3 (15C), 24.5, 24.2, 20.7, 20.6, 18.4 (5C), 16.5, 16.2, 16.0, 15.9, 15.8, 14.8, -3.4, -3.7, -3.8, -3.9 (2C), -4.1 (2C), -4.3 (3C); HRMS (ESI) m/z 1335.9189 [$(M+Na)^+$, calcd 1335.9236 for $C_{74}H_{140}NaO_9Si_5$].

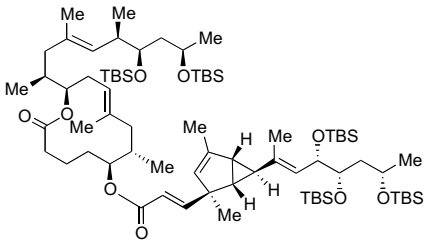


S10-A2

Protected photo-mycolactone **S10-A2**

$[\alpha]_D^{20}$ = -10 (CH_2Cl_2, *c* 1.0); ^{1}H NMR (500 MHz, C_6D_6) δ 7.33 (d, *J* = 16.0 Hz, 1H), 6.01 (d, *J* = 16.0 Hz, 1H), 5.45 (d, *J* = 7.5 Hz, 1H), 5.35 (d, *J* = 9.5 Hz, 1H), 5.06 (m, 3H), 4.71 (s, 1H), 4.49 (dd, *J* = 9.5, 3.5 Hz, 1H), 4.09 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.99 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.85 (m, 1H), 3.78 (m, 1H), 2.61 (m, 1H), 2.41 (m, 1H), 2.23 (m, 2H), 2.12 (ddd, *J* = 13.5, 6.5, 6.0 Hz, 1H), 1.99-1.79 (m, 15 H), 1.69 (s, 3H), 1.63 (s, 6H), 1.57 (s, 3H), 1.54 (m, 1H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.17 (s, 3H), 1.16 (d, *J* = 6.5 Hz, 3H), 1.10 (dd, *J* = 3.5, 2.5 Hz, 1H), 1.05 (s, 9H), 1.04 (s, 9H), 1.03 (s, 9H), 1.02 (s, 9H), 1.01 (s, 9H), 1.01 (d, *J* = 6.0 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.19 (s, 3H), 0.16 (s, 12H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.3, 166.0, 154.1, 144.0, 136.5, 135.2, 132.2, 131.0, 129.0, 125.1, 123.4, 119.4, 78.9, 76.0, 74.0, 73.6, 71.7, 66.5, 66.3, 52.6, 45.9, 45.8, 44.0, 43.7, 37.8,

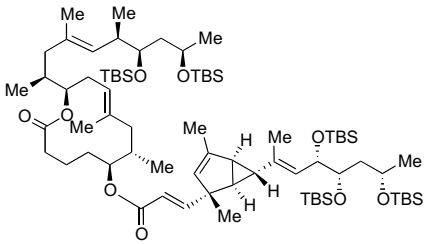
37.0, 35.6, 35.4, 34.3, 33.8, 32.3, 31.0, 30.2, 27.6, 26.3 (5C), 26.2 (10C), 24.5, 24.3, 20.7, 20.6, 18.5 (2C), 18.4 (3C), 17.2, 16.3, 16.1, 15.8, 15.7, 14.8, -3.4, -3.7, -3.8, -3.9 (2C), -4.0, -4.1, -4.2, -4.3 (2C); HRMS (ESI) m/z 1335.9236 [$(M+Na)^+$, calcd 1335.9236 for $C_{74}H_{140}NaO_9Si_5$].



S10-B2 (Major)

Protected photo-mycolactone **S10-B2** (major)

$[\alpha]_D^{20}$ = +52 (CH_2Cl_2, *c* 0.42); ^{1}H NMR (600 MHz, C_6D_6) δ 7.42 (d, *J* = 16.2 Hz, 1H), 6.16 (d, *J* = 16.2 Hz, 1H), 5.49 (d, *J* = 9.6 Hz, 1H), 5.36 (d, *J* = 9.0 Hz, 1H), 5.10 (m, 3H), 4.60 (s, 1H), 4.48 (dd, *J* = 9.6, 3.6 Hz, 1H), 4.10 (qt, *J* = 6.6, 6.0 Hz, 1H), 4.00 (qt, *J* = 6.6, 6.0 Hz, 1H), 3.86 (m, 1H), 3.78 (m, 1H), 2.62 (m, 1H), 2.40 (m, 1H), 2.24 (dd, *J* = 12.5, 4.0 Hz, 1H), 2.15 (m, 2H), 2.00-1.84 (m, 14 H), 1.72 (m, 2H), 1.64 (s, 3H), 1.61 (s, 3H), 1.57 (s, 3H), 1.55 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.17 (d, *J* = 6.6 Hz, 3H), 1.14 (s, 3H), 1.05 (s, 9H), 1.04 (s, 9H), 1.03 (s, 18H), 0.99 (s, 9H), 0.96 (d, *J* = 6.0 Hz, 3H), 0.95 (d, *J* = 6.0 Hz, 3H), 0.92 (m, 1H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.17 (s, 6H), 0.16 (s, 12H), 0.15 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.4, 166.2, 156.2, 145.1, 136.5, 135.0, 132.2, 131.0, 128.9, 125.7, 123.3 118.7, 79.0, 76.0, 74.0, 73.6, 71.7, 66.5, 66.3, 52.0, 45.9, 45.8, 43.9, 43.7, 37.8, 37.0, 35.5, 35.4, 33.6, 32.9, 32.3, 32.0, 31.1, 30.2, 26.3 (15C), 24.5, 24.3, 20.6, 20.5, 18.4 (5C), 16.3, 16.2, 16.1, 15.9, 15.7, 14.8, -3.6, -3.7, -3.8, -3.9, -4.0, -4.1 (2C), -4.3 (3C); HRMS (ESI) m/z 1335.9223 [$(M+Na)^+$, calcd 1335.9236 for $C_{74}H_{140}NaO_9Si_5$].



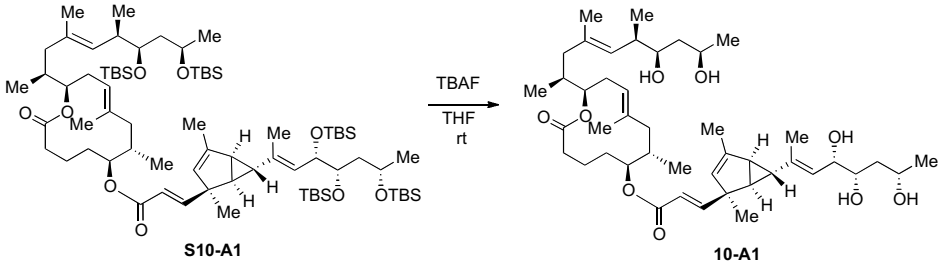
S10-B1 (Minor)

Protected photo-mycolactone **S10-B1** (minor)

$[\alpha]_D^{20}$ = -82 (CH_2Cl_2, *c* 1.0);); ^{1}H NMR (500 MHz, C_6D_6) δ 7.39 (d, *J* = 15.5 Hz, 1H), 6.15 (d, *J* = 15.5 Hz, 1H), 5.46 (d, *J* = 9.0 Hz, 1H), 5.35 (d, *J* = 9.5 Hz, 1H), 5.10 (m, 3H), 4.58 (s, 1H), 4.49 (dd, *J* = 9.0, 3.5 Hz, 1H), 4.10 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.96 (qt, *J* = 6.5, 6.0 Hz, 1H), 3.84 (m, 1H), 3.77 (m, 1H), 2.61 (m, 1H), 2.39 (m, 1H), 2.23 (dd, *J* = 13.0, 4.5 Hz, 1H), 2.13 (m, 2H), 1.99-1.75 (m, 16 H), 1.74 (m, 1H), 1.63 (s, 3H), 1.58 (s, 3H), 1.55 (s, 6H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.16 (s, 3H), 1.13 (s, 3H), 1.04 (s, 18H), 1.02 (s, 18H), 0.99 (s, 9H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.0 Hz, 3H), 0.88 (d, *J* = 7.0

Hz, 3H), 0.16 (s, 12H), 0.15 (s, 6H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.4, 166.2, 156.2, 145.0, 136.5, 135.5, 132.2, 131.0, 128.9, 125.1, 123.3, 118.5, 79.0, 76.0, 74.0, 73.5, 71.8, 66.5, 66.3, 52.0, 45.9, 45.8, 43.7, 37.8, 36.9, 35.5, 35.4, 34.0, 32.7, 32.3, 31.1, 30.2, 26.3 (15C), 26.1, 24.5, 24.2, 21.9, 20.7, 20.5, 18.4 (5C), 16.2, 16.1 (2C), 15.9, 15.7, 14.8, -3.6, -3.7, -3.9, -4.0, -4.1 (3C), -4.3 (3C); HRMS (ESI) m/z 1335.9301 [(M+Na)$^+$, calcd 1335.9236 for $C_{74}H_{140}NaO_9Si_5$].

iii. TBS-deprotection



To a THF solution (1.8 mL) of protected photo-mycolactone **S10-A1** (24 mg, 0.018 mmol) at rt, TBAF imidazole-HCl buffer solution (1M, 0.9 mL) was added. The reaction was stirred for 6 days. Then the solvent was removed *in vacuo*, the residue was purified by eluting with EtOAc from a silica pad to give the final product **10-A1** (13 mg, 96%). Photo-mycolactones **10-A2**, **10-B1**, **10-B2** were prepared by the same procedure.

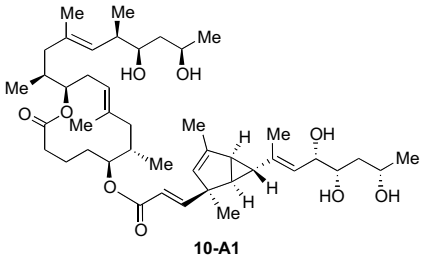
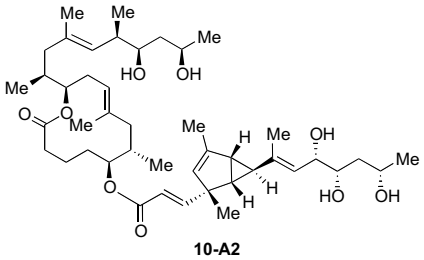


Photo-mycolactone **10-A1**

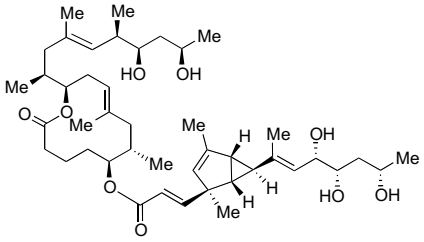
$[\alpha]_D^{20}$ = -39 (CH_2Cl_2, *c* 0.23); ^{1}H NMR (600 MHz, CD_3COCD_3) δ 7.01 (d, *J* = 16.2 Hz, 1H), 5.72 (d, *J* = 16.2 Hz, 1H), 5.16 (d, *J* = 9.0 Hz, 1H), 5.11 (d, *J* = 10.8 Hz, 1H), 5.03 (d, *J* = 9.6 Hz, 1H), 4.93 (s, 1H), 4.89 (ddd, *J* =12.0, 4.8, 2.4 Hz, 1H), 4.68 (dt, *J* = 9.0, 4.2 Hz, 1H), 4.21 (m, 1H), 4.08 (m, 1H), 3.96 (m, 1H), 3.65 (m, 1H), 3.50 (m, 1H), 2.50 (m, 1H), 2.41 (m, 2H), 2.16-2.09 (m, 3H), 2.12-1.94 (m, 4H), 1.83 (dd, *J* = 13.2, 8.4 Hz, 1H), 1.79 (s, 3H), 1.70 (s, 3H), 1.64 (s, 3H), 1.62 (s, 3H), 1.61-1.56 (m, 3H), 1.53-1.50 (m, 2H), 1.47-1.35 (m, 2H), 1.45-1.35 (m, 3H), 1.26 (s, 3H), 1.13 (d, *J* = 6.0 Hz, 3H), 1.10 (d, *J* = 6.0 Hz, 3H), 1.01 (dd, *J* = 2.4, 2.4 Hz, 1H), 0.97 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 173.4, 166.5, 154.7, 145.0, 138.6, 137.4, 133.6, 131.3, 129.5, 124.8, 124.0, 119.7, 79.5, 77.1, 76.5, 76.0, 72.3, 69.1, 67.8, 53.2, 46.5, 44.5, 44.0, 42.1, 40.6, 37.7, 36.1, 35.5, 34.5(2C), 33.0, 31.2, 30.4, 30.2, 27.9, 24.7, 24.3, 20.9, 20.6, 17.3, 16.3, 16.2, 16.0, 15.1; HRMS (ESI) m/z 765.4947 [(M+Na)$^+$, calcd 765.4912 for $C_{44}H_{70}NaO_9$].



10-A2

Photo-mycolactone **10-A2**

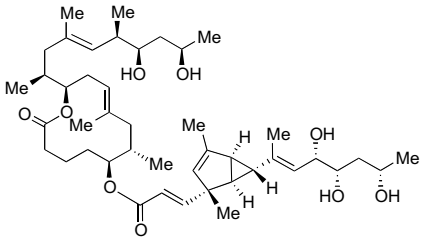
$[\alpha]_D^{20}$ = +3.7 (CH_2Cl_2, *c* 0.75); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 6.99 (d, *J* = 15.5 Hz, 1H), 5.71 (d, *J* = 15.5 Hz, 1H), 5.15 (d, *J* = 9.0 Hz, 1H), 5.12 (d, *J* = 9.5 Hz, 1H), 5.04 (d, *J* = 9.5 Hz, 1H), 4.93 (s, 1H), 4.89 (ddd, *J* =12.0, 4.5, 3.0 Hz, 1H), 4.67 (dt, *J* = 9.0, 4.0 Hz, 1H), 4.20 (m, 1H), 4.09 (m, 1H), 3.96 (m, 1H), 3.56 (m, 1H), 3.51 (m, 1H), 2.49 (m, 1H), 2.40 (m, 2H), 2.15-2.09 (m, 2H), 2.02-1.94 (m, 5H), 1.83 (dd, *J* = 13.0, 8.5 Hz, 1H), 1.79 (s, 3H), 1.70 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.58-1.49 (m, 6H), 1.47-1.35 (m, 4H), 1.26 (s, 3H), 1.13 (d, *J* = 6.5 Hz, 3H), 1.12 (d, *J* = 6.5 Hz, 3H), 1.03 (dd, *J* = 3.0, 2.5 Hz, 1H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 173.4, 166.6, 154.7, 145.0, 138.7, 137.4, 133.6, 131.4, 129.5, 124.8, 124.1, 119.6, 79.5, 77.1, 76.4, 76.1, 72.4, 69.1, 67.9, 53.4, 46.5, 44.5, 44.0, 42.1, 40.6, 37.8, 36.1, 35.5, 34.6, 34.1, 32.9, 31.4, 30.5, 30.2, 28.1, 24.8, 24.4, 20.9, 20.6, 17.3, 16.3, 16.2, 16.0, 15.1; HRMS (ESI) m/z 743.5060 [$(M+Na)^+$, calcd 765.4912 for $C_{44}H_{70}NaO_9$].



10-B2 (Major)

Photo-mycolactone **10-B2** (major)

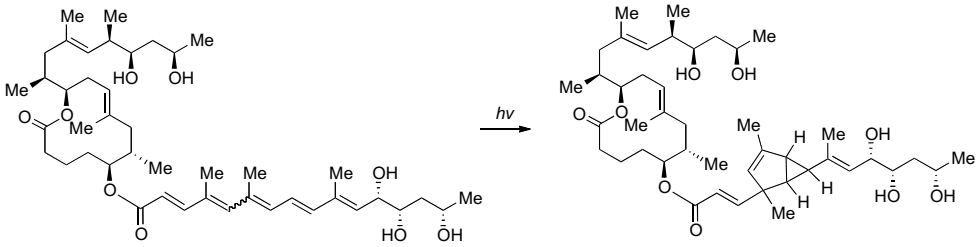
$[\alpha]_D^{20}$ = +83 (CH_2Cl_2, *c* 0.50); ^{1}H NMR (600 MHz, CD_3COCD_3) δ 7.01 (d, *J* = 16.2 Hz, 1H), 5.79 (d, *J* = 16.2 Hz, 1H), 5.19 (d, *J* = 8.4 Hz, 1H), 5.11 (d, *J* = 10.8 Hz, 1H), 5.03 (d, *J* = 9.6 Hz, 1H), 4.89 (ddd, *J* =12.0, 5.4, 3.0 Hz, 1H), 4.81 (s, 1H), 4.69 (dt, *J* = 8.4, 3.6 Hz, 1H), 4.21 (m, 1H), 4.09 (m, 1H), 3.96 (m, 1H), 3.58 (m, 1H), 3.50 (m, 1H), 2.50 (m, 1H), 2.40 (m, 2H), 2.14-2.08 (m, 2H), 2.02 (m, 1H), 1.99-1.94 (m, 4H), 1.82 (dd, *J* = 13.2, 8.4 Hz, 1H), 1.79 (s, 3H), 1.71 (s, 3H), 1.67 (s, 3H), 1.64 (s, 3H), 1.62-1.51 (m, 6H), 1.48-1.36 (m, 4H), 1.23 (s, 3H), 1.15 (dd, *J* = 3.0, 2.4 Hz, 1H), 1.12 (d, *J* = 6.0 Hz, 3H), 1.10 (d, *J* = 6.0 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 173.4, 166.8, 156.8, 145.8, 138.7, 137.4, 133.5, 131.3, 129.4, 124.7, 124.0, 118.7, 79.5, 77.1, 76.4, 76.0, 72.3, 69.1, 67.8, 52.5, 46.5, 44.5, 43.9, 42.1, 40.6, 37.1, 36.1, 35.5, 34.8, 33.6, 32.9, 31.5, 30.5, 30.2, 24.7, 24.3, 22.3, 20.8, 20.7, 17.3, 16.4, 16.3, 16.0, 15.1; HRMS (ESI) m/z 765.4947 [$(M+Na)^+$, calcd 765.4912 for $C_{44}H_{70}NaO_9$].



10-B1 (Minor)

Photo-mycolactone **10-B1** (minor)
$[\alpha]_D^{20}$ = -103 (CH_2Cl_2, *c* 0.50); ^{1}H NMR (500 MHz, CD_3COCD_3) δ 7.00 (d, *J* = 15.5 Hz, 1H), 5.79 (d, *J* = 15.5 Hz, 1H), 5.20 (d, *J* = 8.5 Hz, 1H), 5.12 (d, *J* = 9.5 Hz, 1H), 5.04 (d, *J* = 9.5 Hz, 1H), 4.89 (ddd, *J* =12.0, 4.5, 3.0 Hz, 1H), 4.81 (s, 1H), 4.69 (dt, *J* = 9.0, 4.0 Hz, 1H), 4.20 (m, 1H), 4.01 (m, 1H), 3.96 (m, 1H), 3.59 (m, 1H), 3.51 (m, 1H), 2.48 (m, 1H), 2.40 (m, 2H), 2.14-2.10 (m, 2H), 2.00-1.93 (m, 5H), 1.83 (dd, *J* = 12.5, 8.0 Hz, 1H), 1.79 (s, 3H), 1.71 (s, 3H), 1.66 (s, 3H), 1.64 (s, 3H), 1.58-1.49 (m, 6H), 1.47-1.40 (m, 4H), 1.23 (s, 3H), 1.16 (dd, *J* = 3.0, 2.5 Hz, 1H), 1.13 (d, *J* = 6.5 Hz, 3H), 1.11 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 173.4, 166.8, 156.8, 145.8, 138.7, 137.4, 133.6, 131.3, 129.5, 124.7, 124.0, 118.7, 79.5, 77.1, 76.4, 76.0, 72.3, 69.1, 67.8, 52.5, 46.5, 44.5, 43.9, 42.1, 40.6, 37.2, 36.1, 35.5, 34.6, 33.7, 32.9, 31.5, 30.5, 30.2, 24.7, 24.3, 22.3, 20.9, 20.7, 17.3, 16.4, 16.3, 16.0, 15.1; HRMS (ESI) m/z 765.4884 [$(M+Na)^+$, calcd 765.4912 for $C_{44}H_{70}NaO_9$].

8b. Photolysis of synthetic mycolactone A/B



1: Mycolactone A/B **10 : photo-MycoA/B mixture**

Photolysis of **1** was done in test tubes at 30 °C, with use of the photo-reactor shown in Figure 1. In comparison with the authentic samples described in the preceding sections, the photo-product was shown to be composed of the four photo-products, with the 3:1 and 3:2 mixture of the *anti/syn* and remote diastereomers, respectively, and with the major product in the mycolactone A- and B-subgroups corresponding to those in the tetraenoate and pentaenoate A- and B-subgroups.

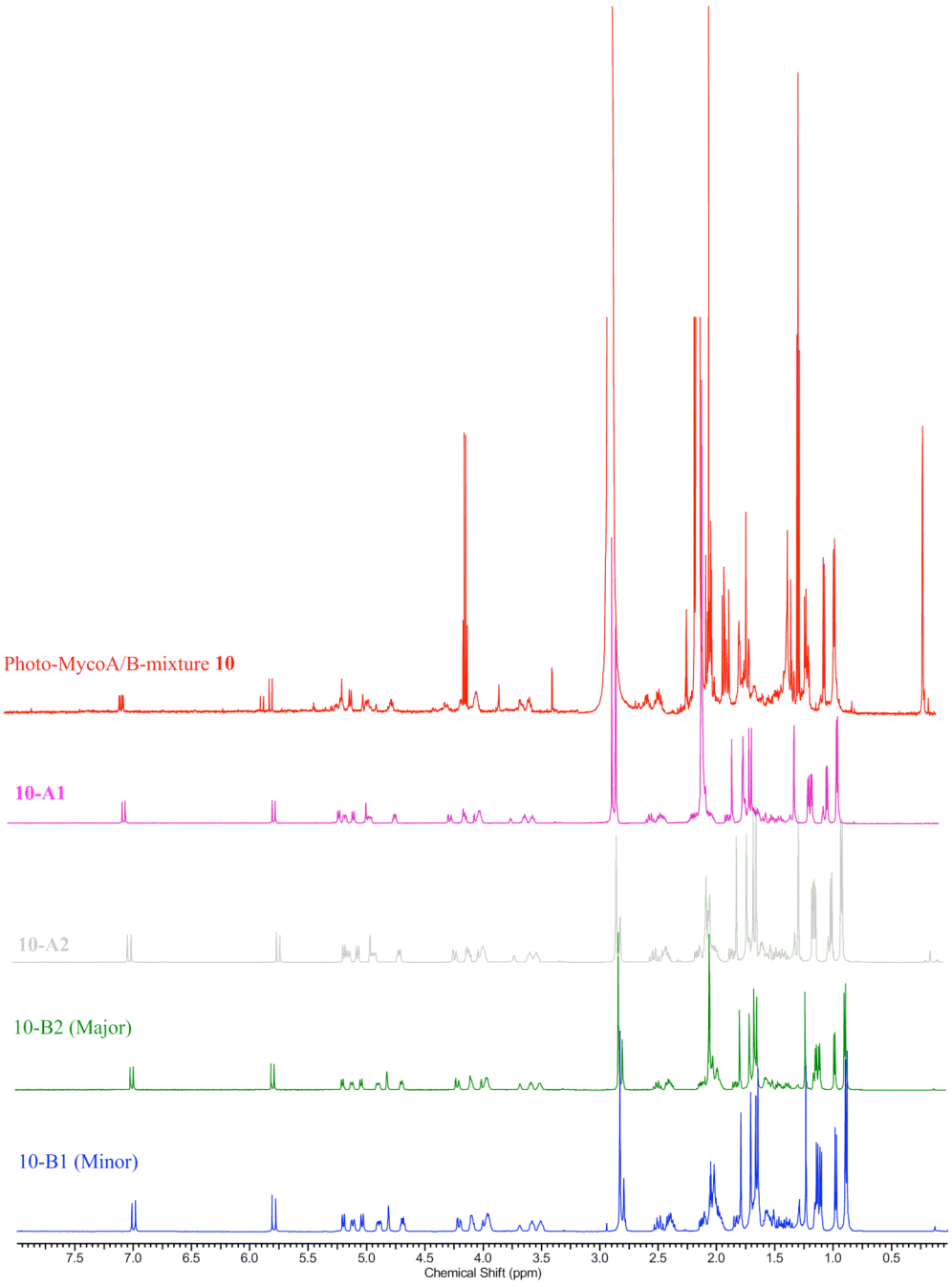


Photo-MycoA/B-mixture 10
10-A1
10-A2
10-B2 (Major)
10-B1 (Minor)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

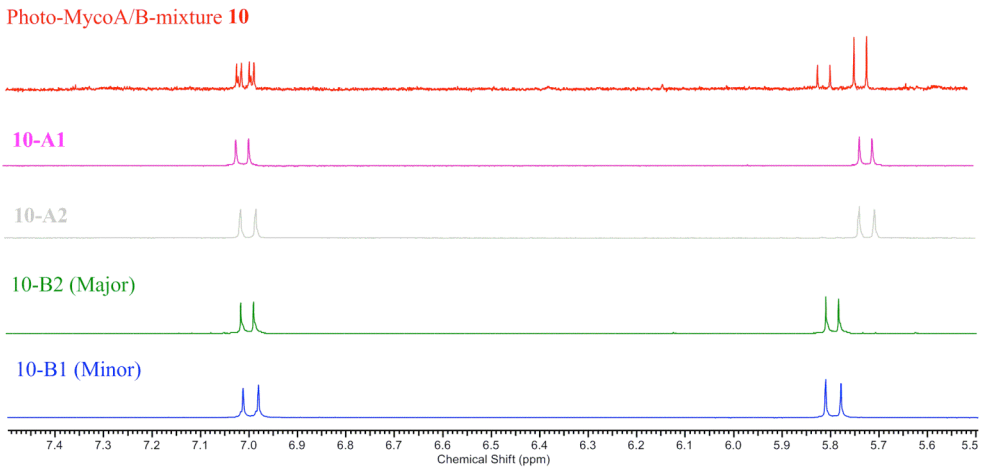


Figure 19. NMR correlation of photo-mycoA/B mixture **10** and photo product **10-A1, 10-A2, 10-B1** and **10-B2**

9. Unique NMR Spectroscopic and HPLC characteristics to differentiate photo-mycolactones from each other and also from mycolactone A/B

9a. Unique signature in 1H NMR spectra

i. Differentiation of mycolactone A/B from photo-mycolactones

The H2' and H3' ^{1}H NMR signal could differentiate mycolactone A/B from photo-mycolactones; the broken red lines in figure 20 indicate the difference.

ii. Differentiation of photo-mycolactones from each other

The H2' ^{1}H NMR signal could differentiate photo-mycolactones from each other; the broken blue lines in figure 20 indicate the difference. The H2' ^{1}H NMR signals of A1 and A2 are more up-field than that of B1 and B2.

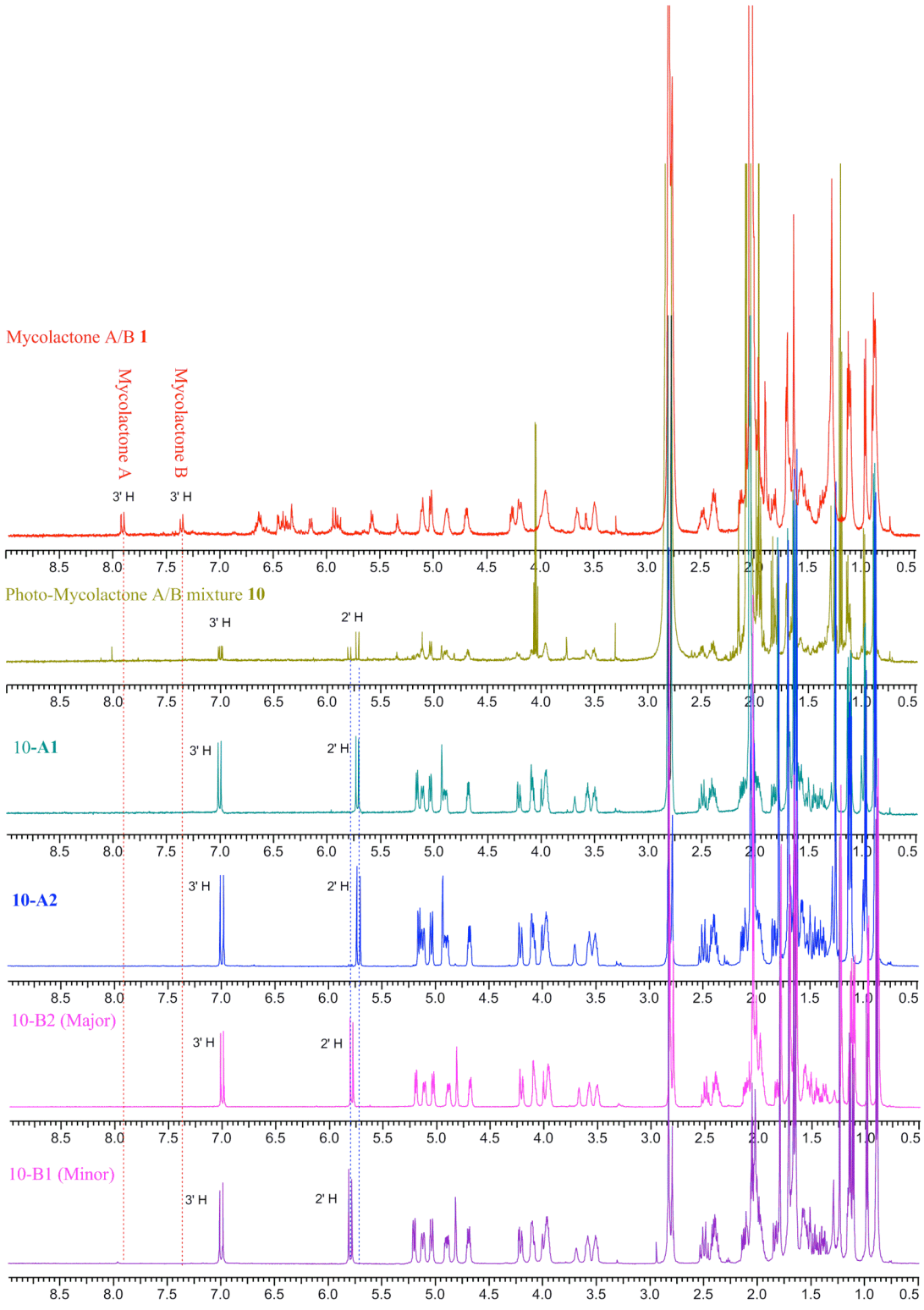


Figure 20. NMR correlation of Mycolactone A/B, photo-mycoA/B mixture **10** and photo product **10-A1, 10-A2, 10-B1** and **10-B2**

9b. Difference in the retention time in HPLC

i. Differentiation of mycolactone A/B from photo-mycolactone
HPLC retention time of Mycolactone A/B and photo-mycolactones **10-A1**, **10-A2**, **10-B1** and **10-B2** are different (shown in Figure 21).

HPLC differentiation of mycolactone A/B and the photo-mycolactones

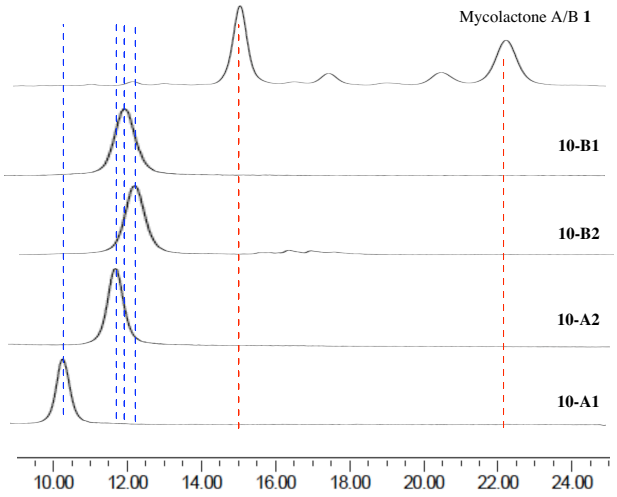


Figure 21. HPLC profile of Mycolactone A/B and photo-mycolactones

Detection: For mycolactone A/B - UV detection at 350 nm. For photo-mycolactones **10-A1**, **10-A2**, **10-B1** and **10-B2**: Waters 2424 ELS detector; Column: Regis Tech, (s,s)-whelk-01, 250mm x 4.6 mm; Solvent (isocratic): hexanes/CH_2Cl_2/EtOH/Et_3N = 65/27.5/7/0.5; flow rate: 0.6 mL/min.

ii. Differentiation of photo-mycolactones from each other
Photo-mycolactones **10-A1**, **10-A2**, **10-B1** and **10-B2** can be differentiated by HPLC retention time (Figure 22)

HPLC differentiation of the photo-mycolactones

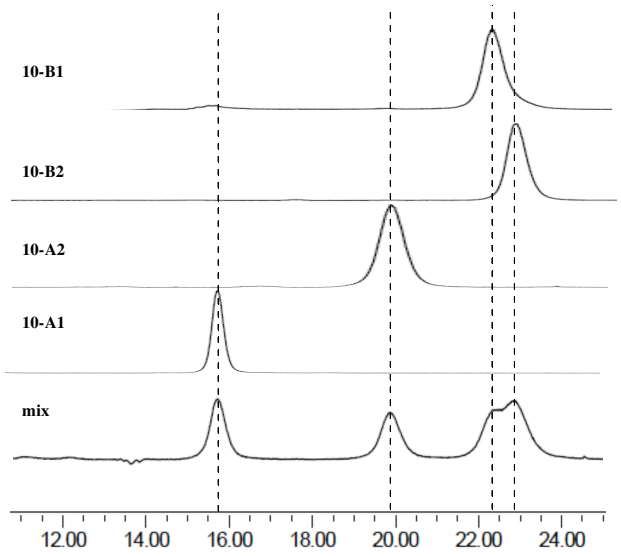


Figure 22. HPLC profile of photo-mycolactones

Detection: Photo-mycolactones **10-A1**, **10-A2**, **10-B1** and **10-B2**: Waters 2424 ELS detector; Column: Regis Tech, (s,s)-whelk-01, 250mm x 4.6 mm; Solvent (isocratic): hexanes/CH_2Cl_2/EtOH/Et_3N = 69/27.5/3/0.5; flow rate: 0.8 mL/min.

9c. MS/MS spectra

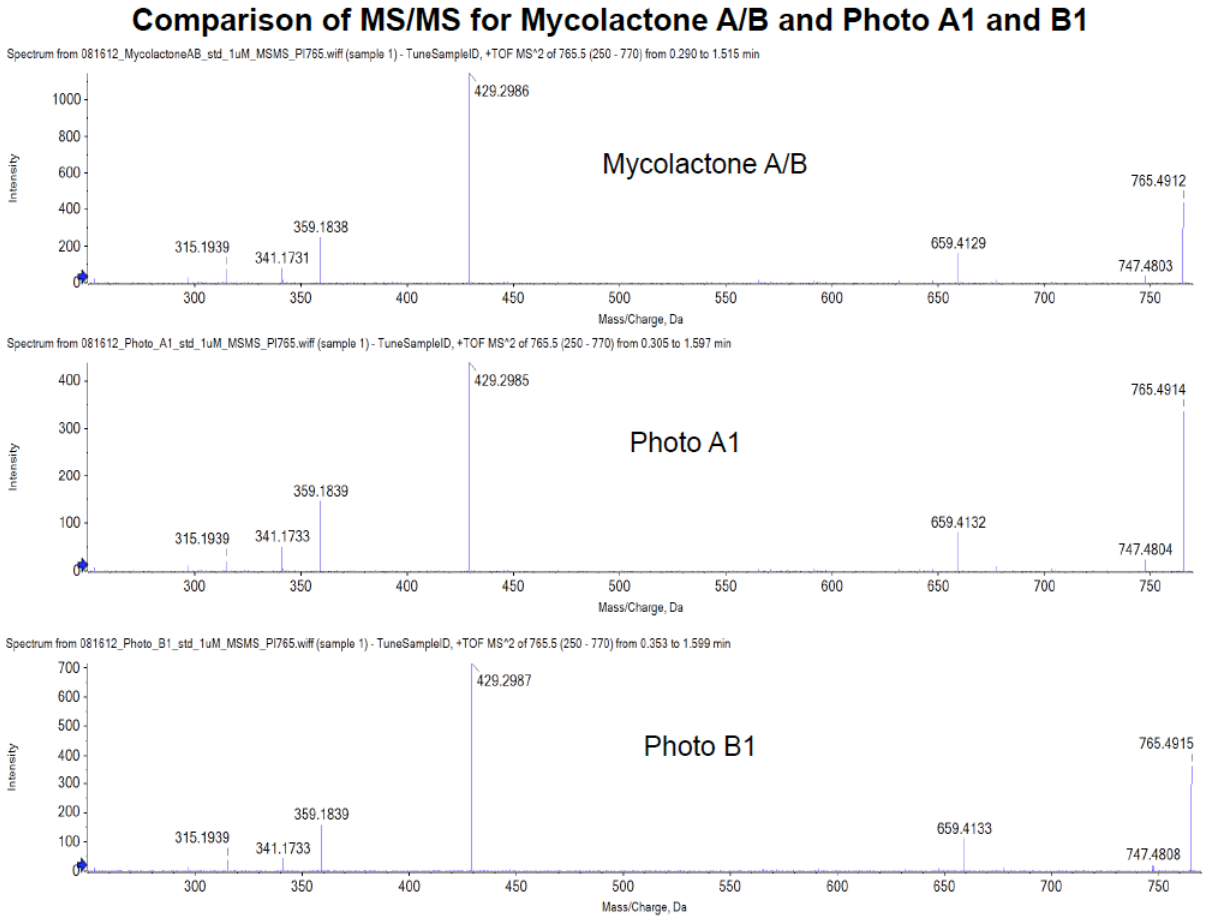


Figure 23. MS/MS spectra of mycolactone A/B, Photo A1 and Photo B1 at 70 eV

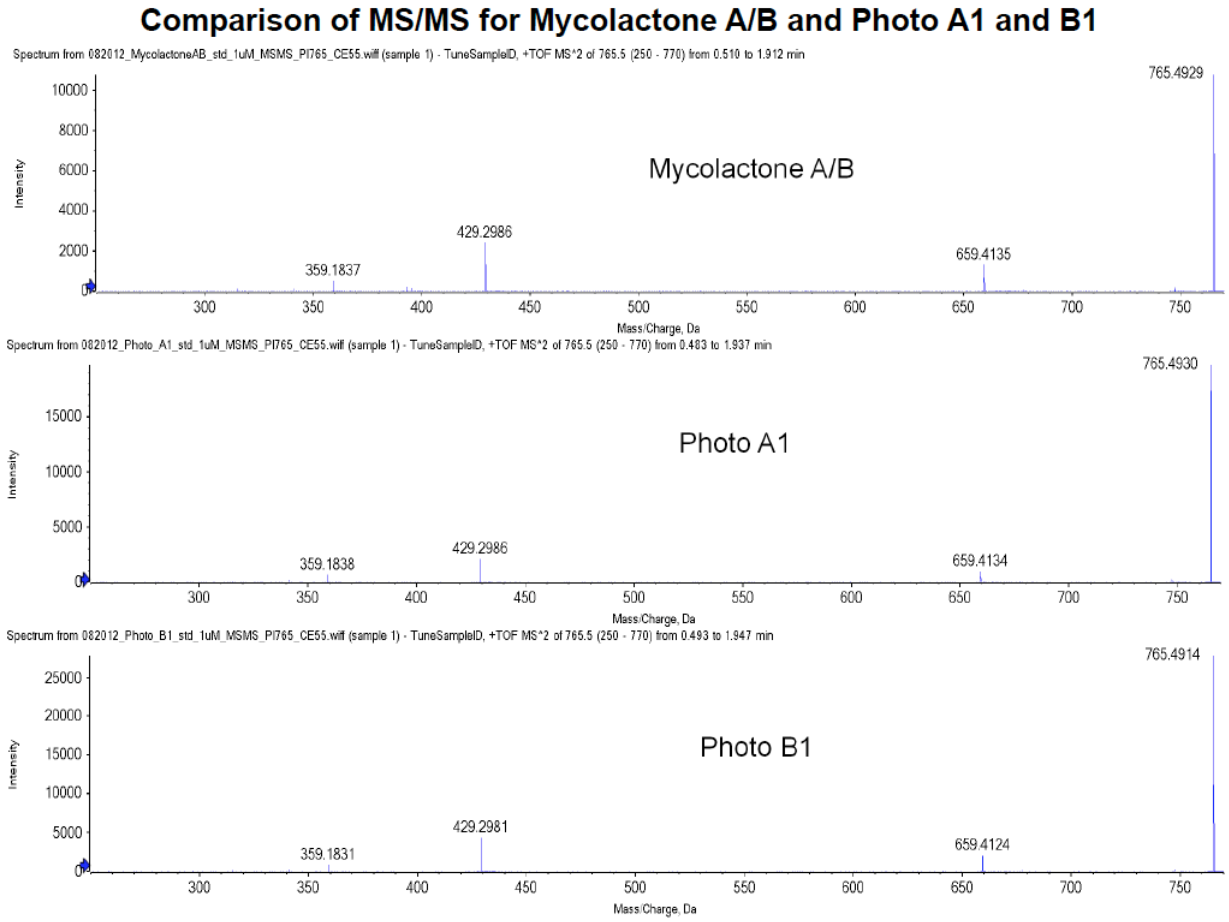
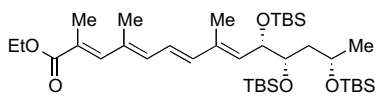


Figure 24. MS/MS spectra of mycolactone A/B, Photo A1 and Photo B1 at 55 eV

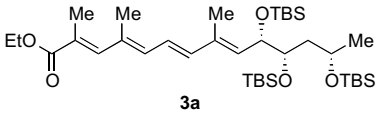
[1] (a) Song, F,; Fidanze, S,; Benowitz, A,; Kishi, Y. *Org. Lett*, **2002**, *4*, 647-650. (b) Song, F,; Fidanze, S,; Benowitz, A,; Kishi, Y. *Tetrohedron*, **2007**, *63*, 5739-5753.
[2] Wang, G., Huang, Z., Negishi, E.; *Tetrahedron Lett.* **2009**, *50*, 3220-3223.
[3] Inanaga, J., Hirata, K., Saeki, H., Katsuki, T., Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989-1993.

10. ^{1}H and ^{13}C NMR spectra



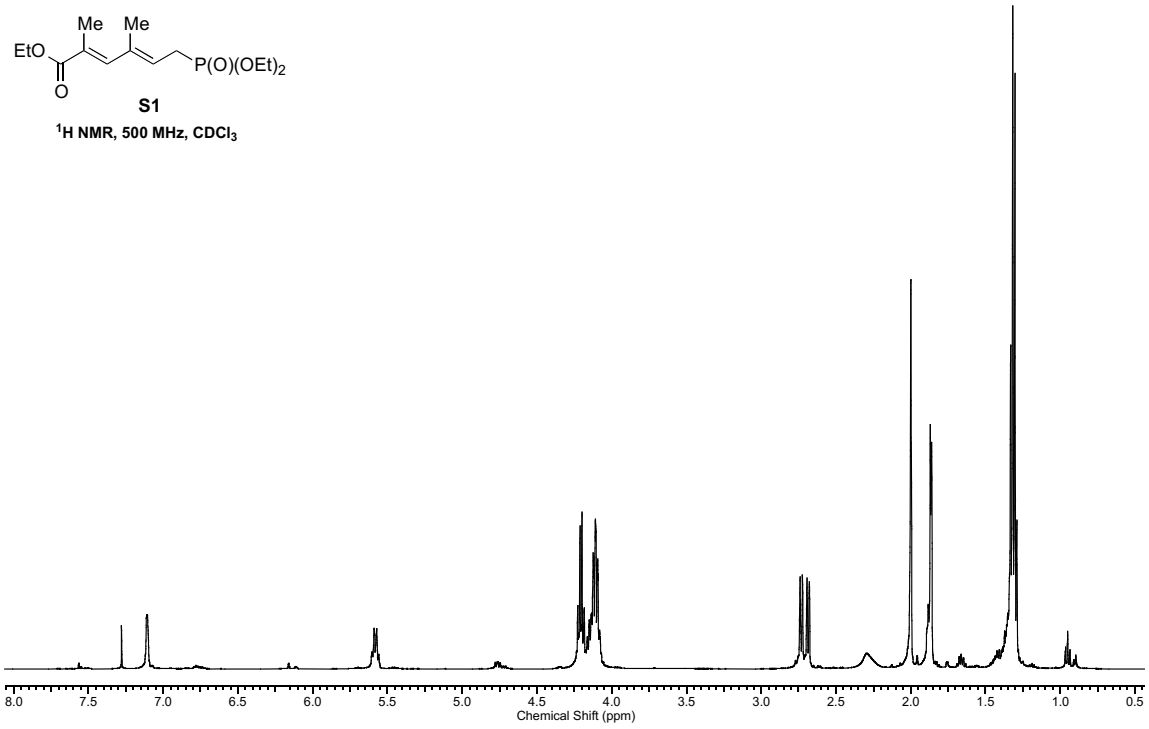
3a

^{1}H NMR, 500 MHz, CD_3COCD_3



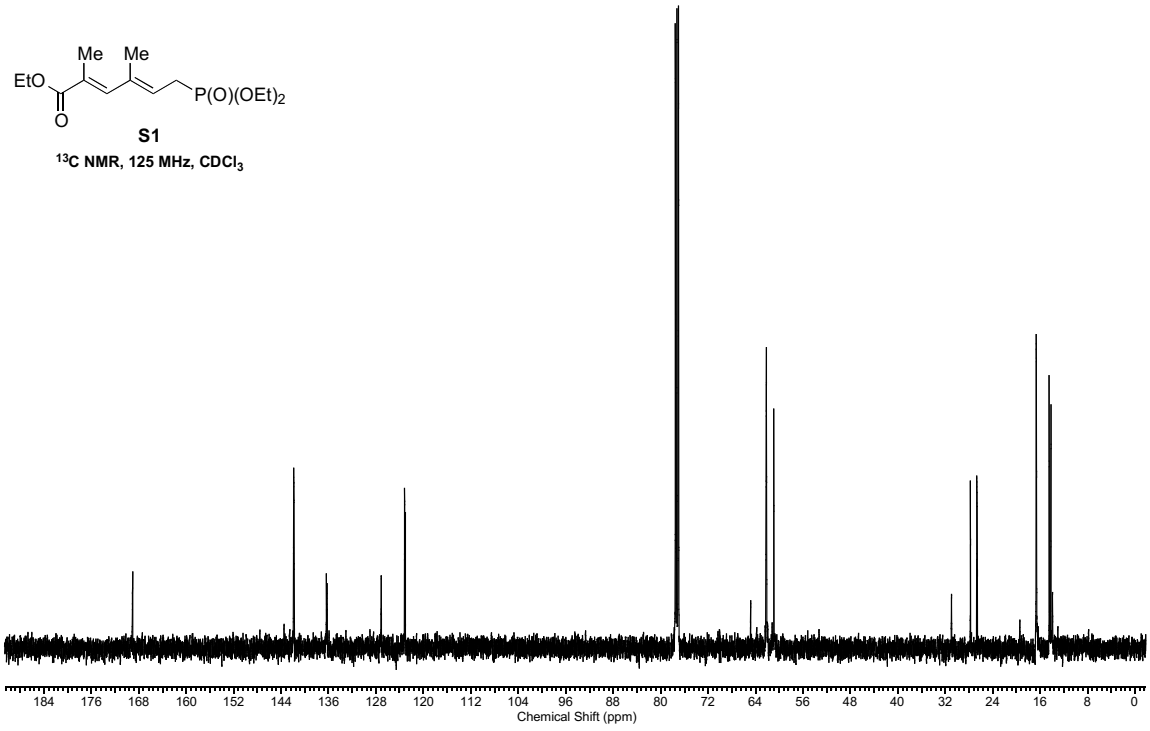
3a

^{13}C NMR, 125 MHz, CD_3COCD_3



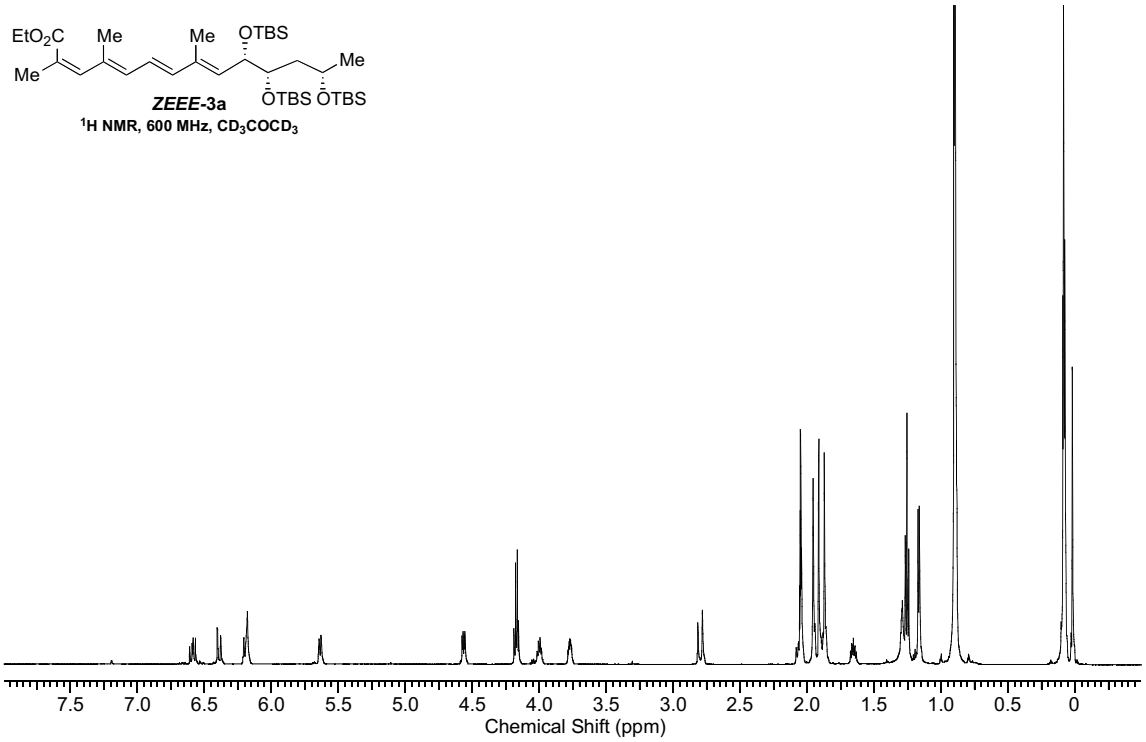
S1

^{1}H NMR, 500 MHz, $CDCl_3$



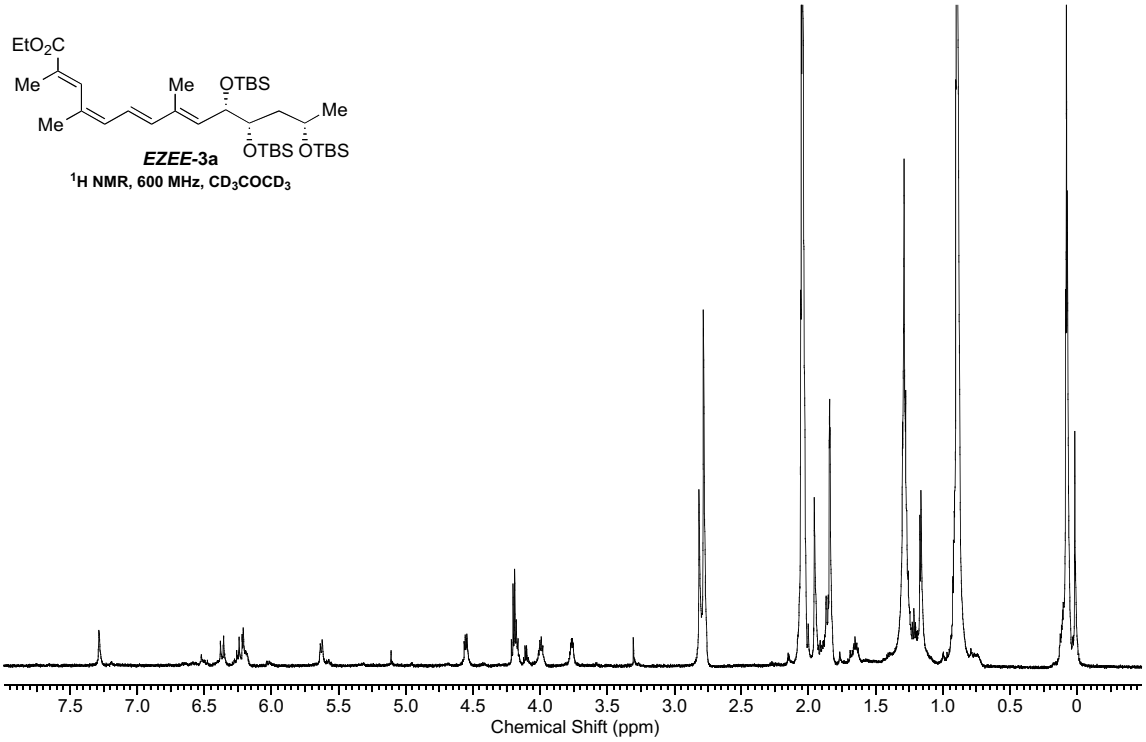
S1

^{13}C NMR, 125 MHz, $CDCl_3$



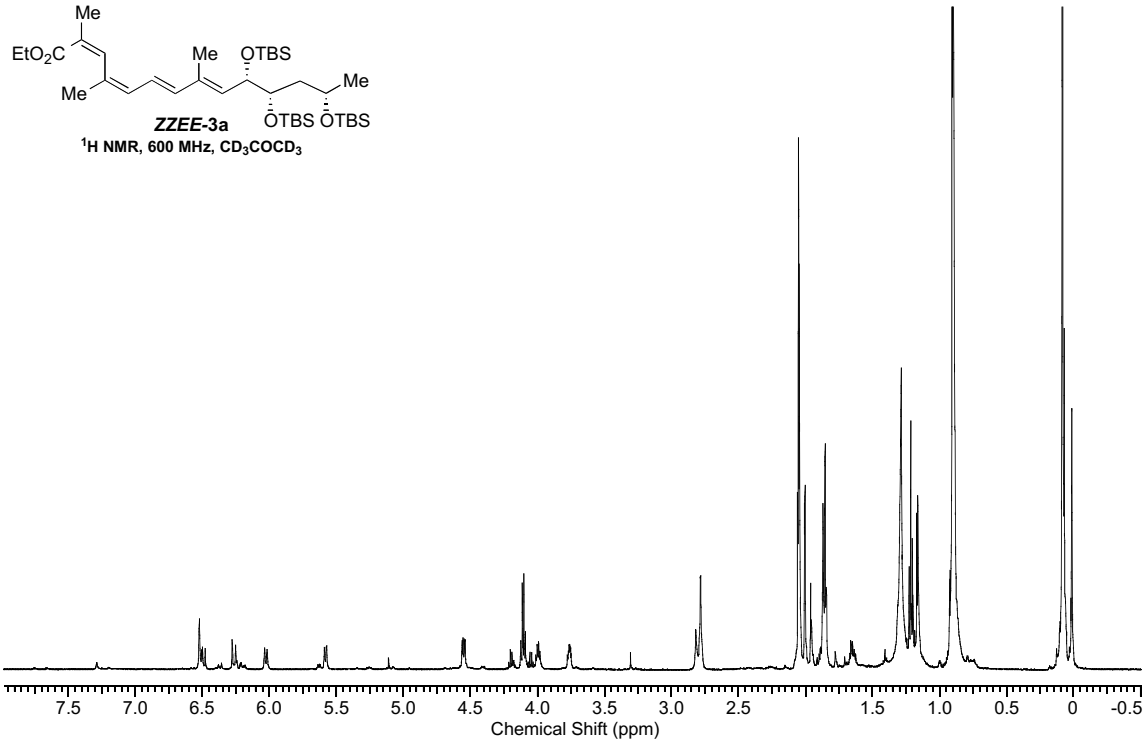
***ZEEE*-3a**

^{1}H NMR, 600 MHz, CD_3COCD_3



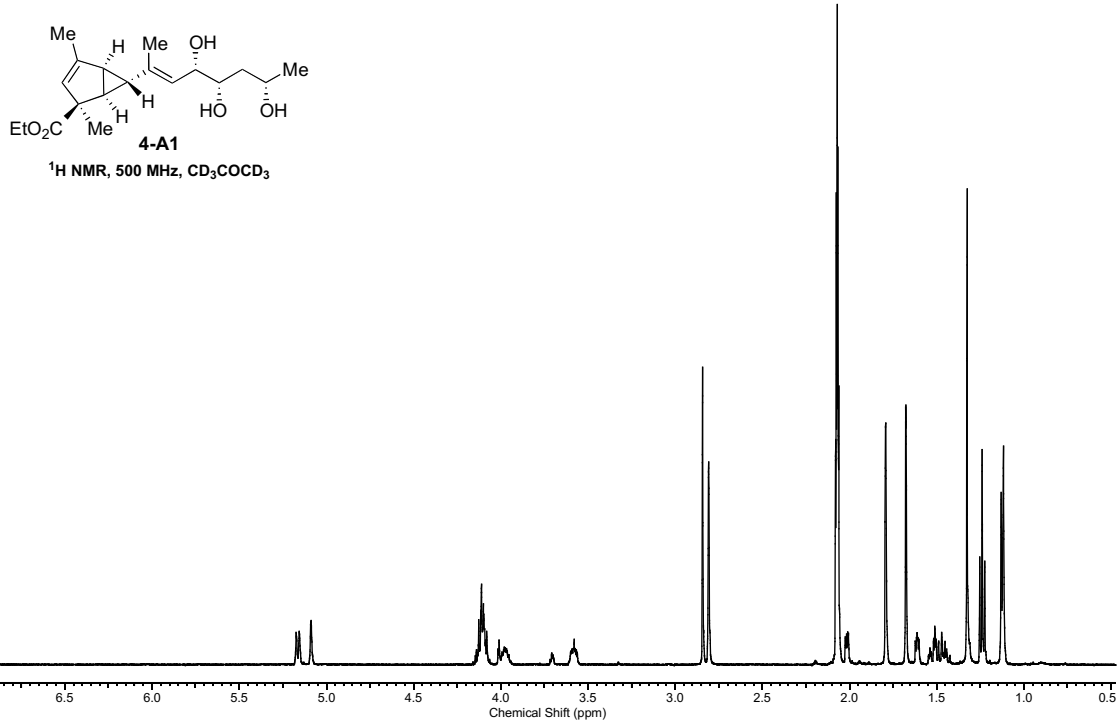
***EZEE*-3a**

^{1}H NMR, 600 MHz, CD_3COCD_3



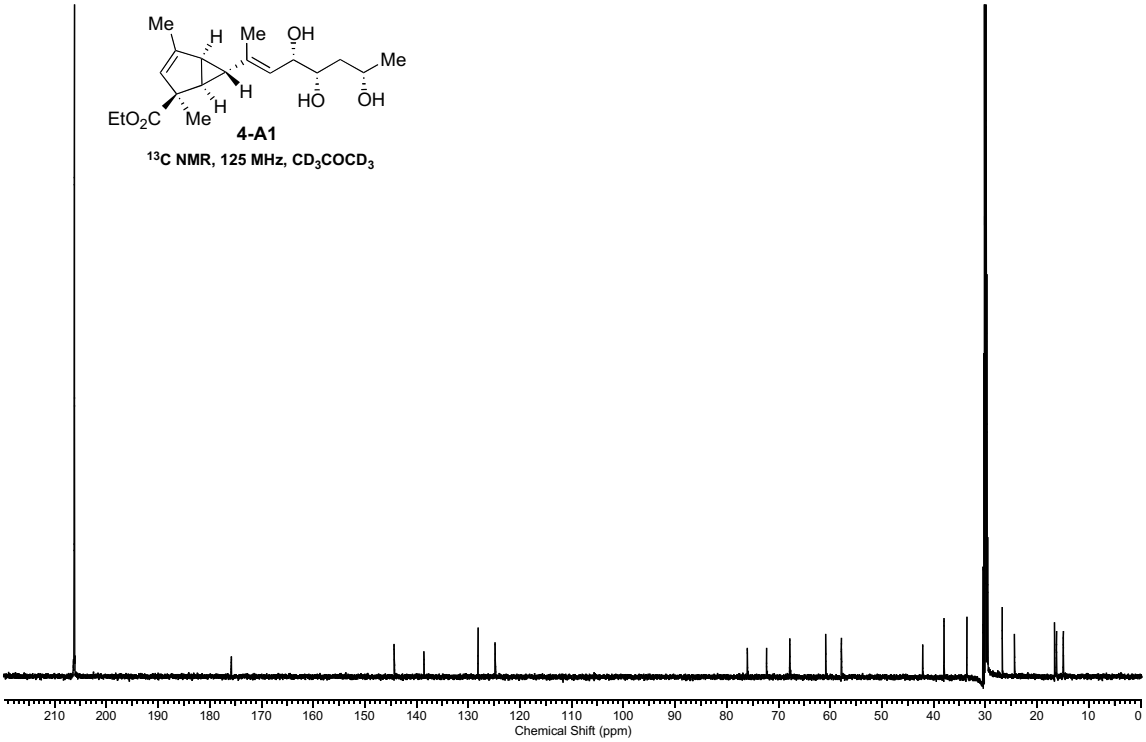
***ZZEE*-3a**

^{1}H NMR, 600 MHz, CD_3COCD_3



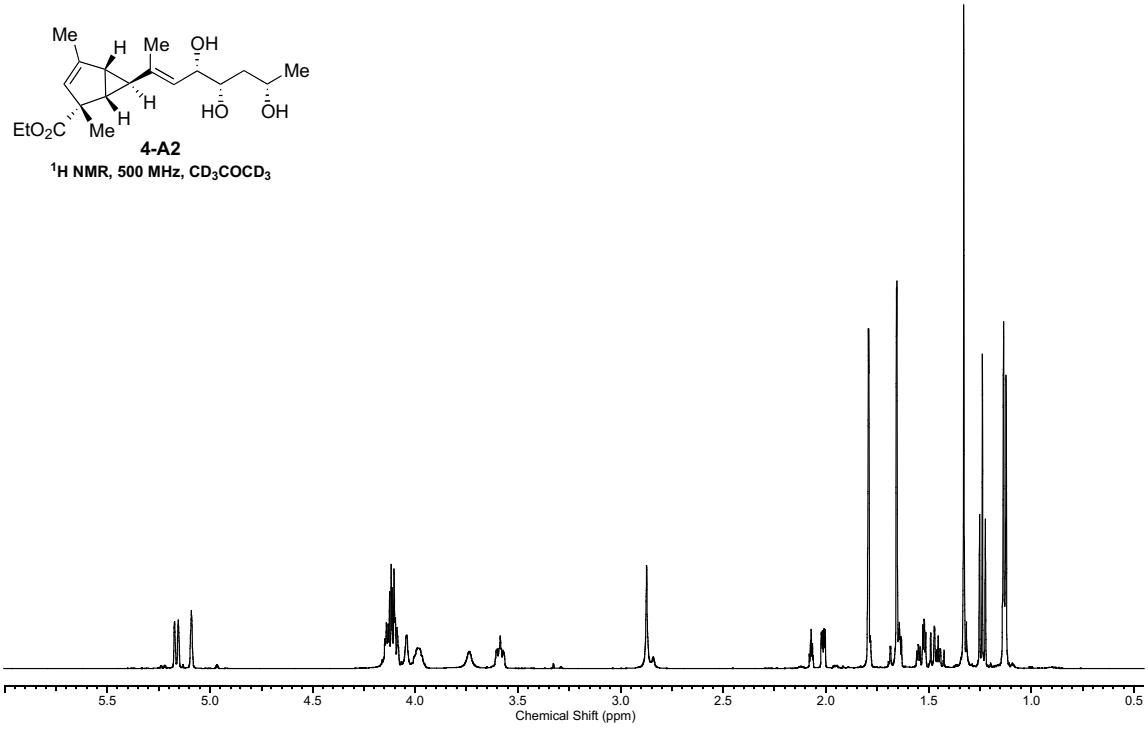
4-A1

^{1}H NMR, 500 MHz, CD_3COCD_3



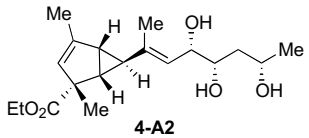
4-A1

^{13}C NMR, 125 MHz, CD_3COCD_3



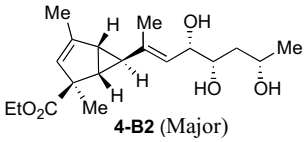
4-A2

^{1}H NMR, 500 MHz, CD_3COCD_3



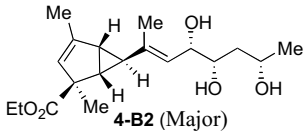
4-A2

^{13}C NMR, 125 MHz, CD_3COCD_3



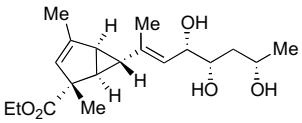
4-B2 (Major)

^{1}H NMR, 500 MHz, CD_3COCD_3



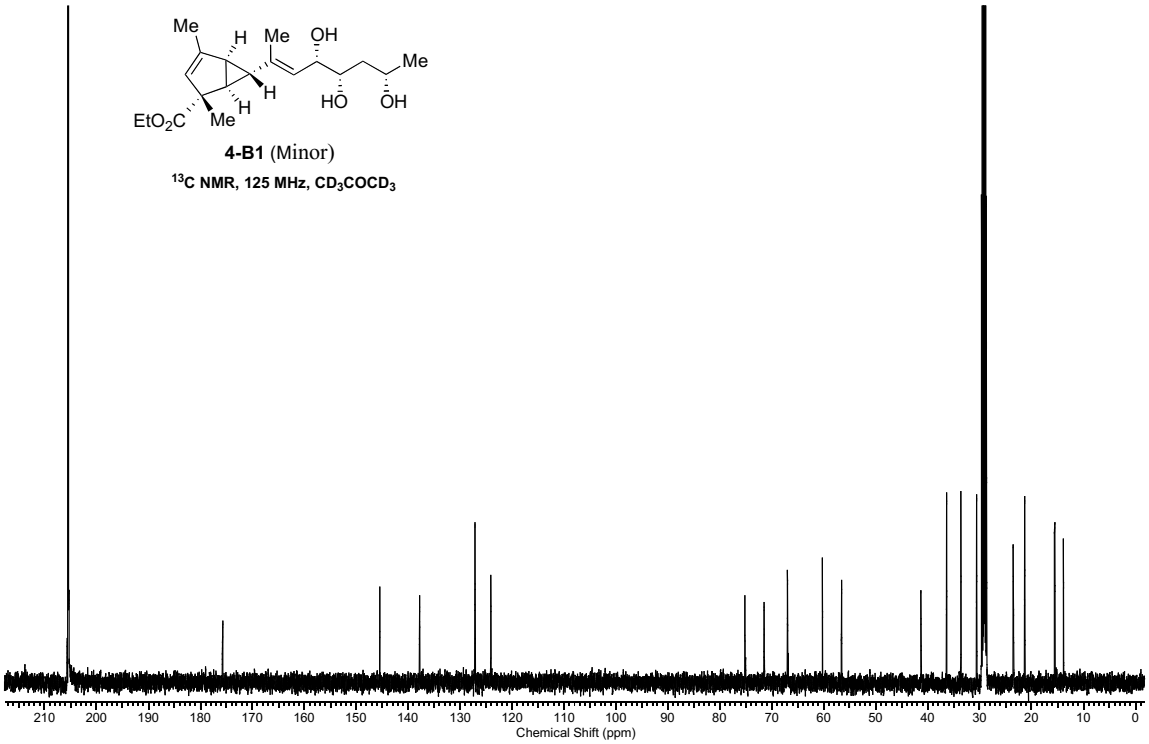
4-B2 (Major)

^{13}C NMR, 125 MHz, CD_3COCD_3



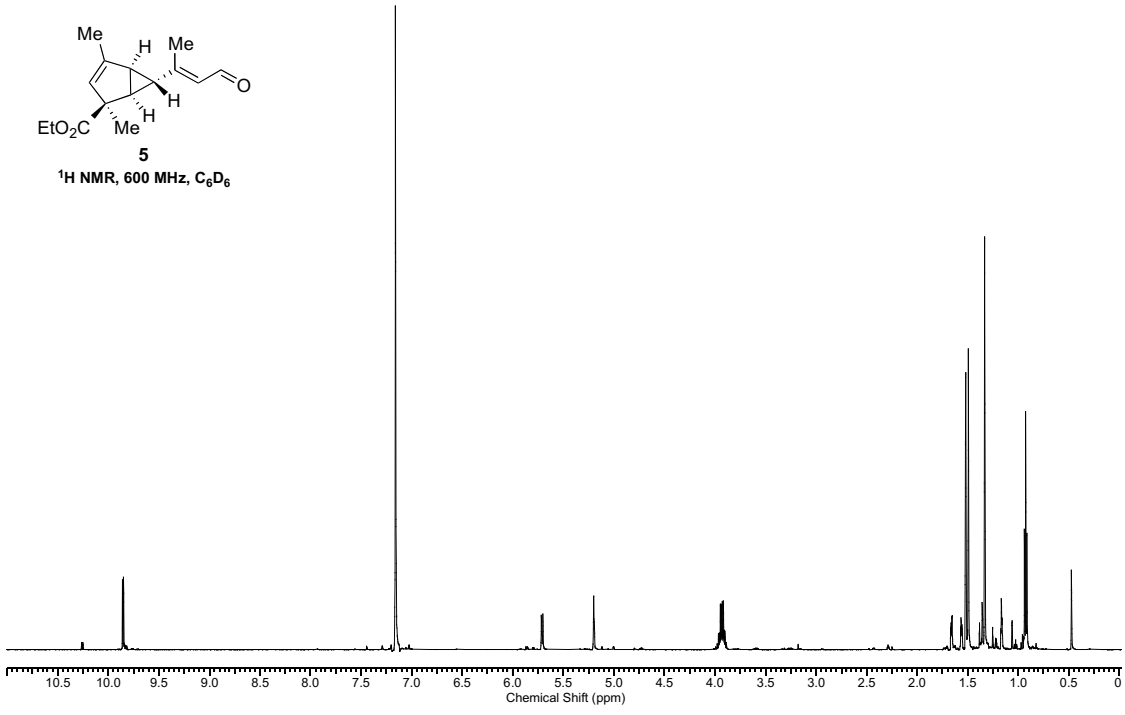
4-B1 (Minor)

^{1}H NMR, 500 MHz, CD_3COCD_3



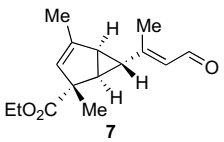
4-B1 (Minor)

^{13}C NMR, 125 MHz, CD_3COCD_3



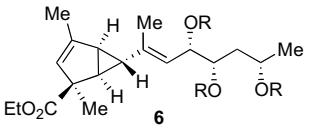
5

^{1}H NMR, 600 MHz, C_6D_6



7

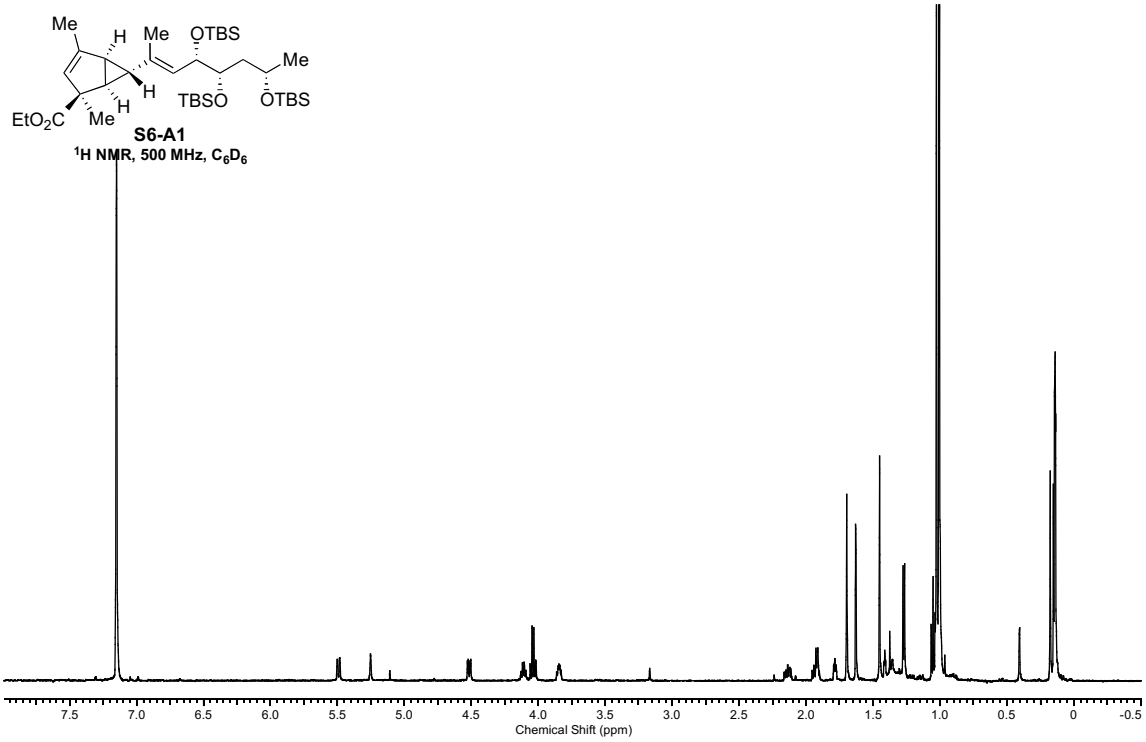
^{1}H NMR, 600 MHz, C_6D_6



6

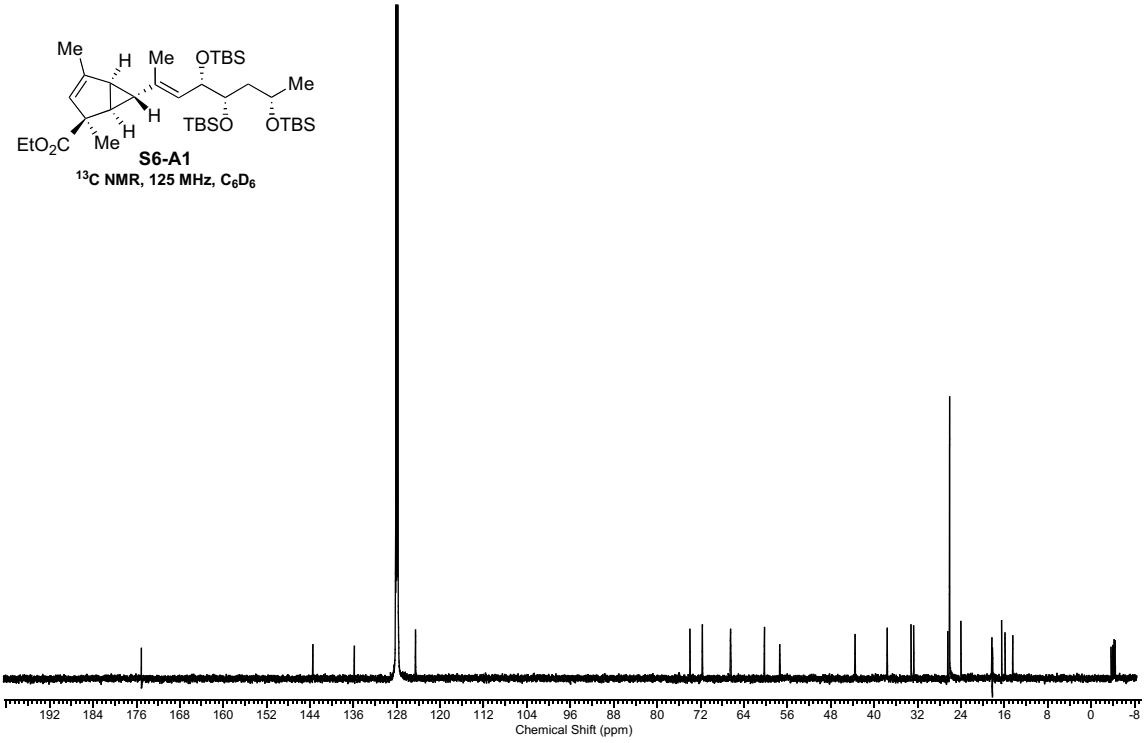
R = -OCC$_6$H$_4$-Br(*p*)

^{1}H NMR, 600 MHz, $CDCl_3$



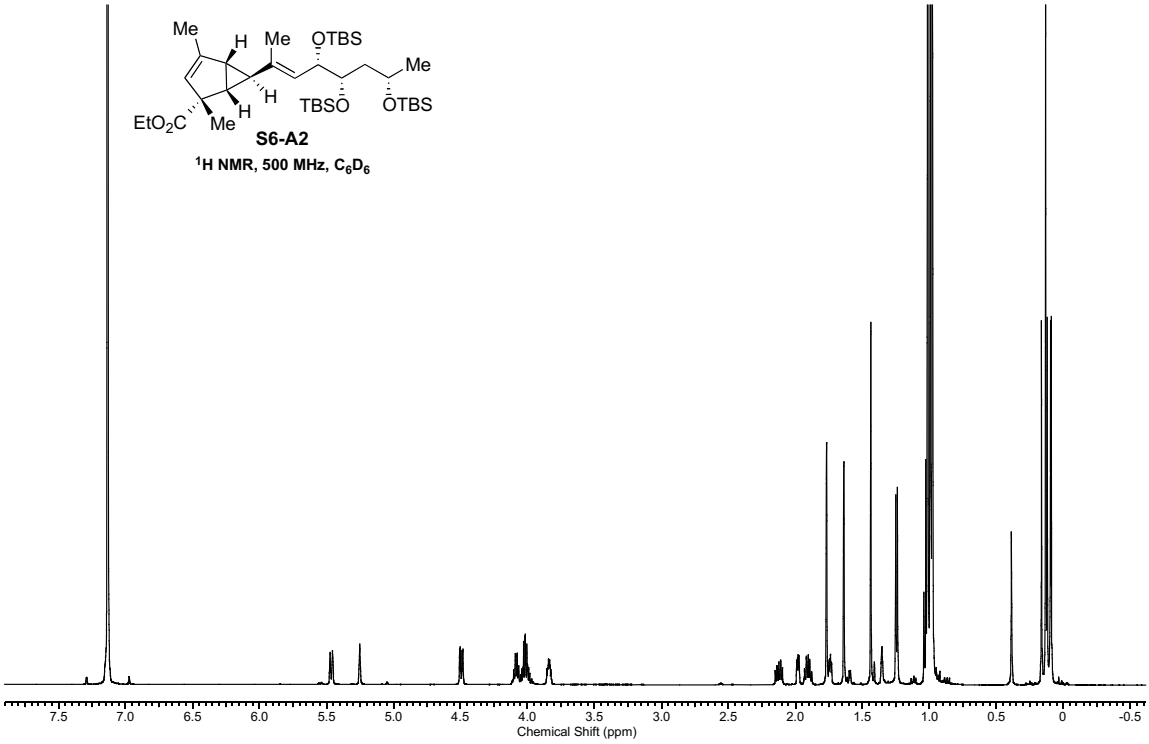
S6-A1

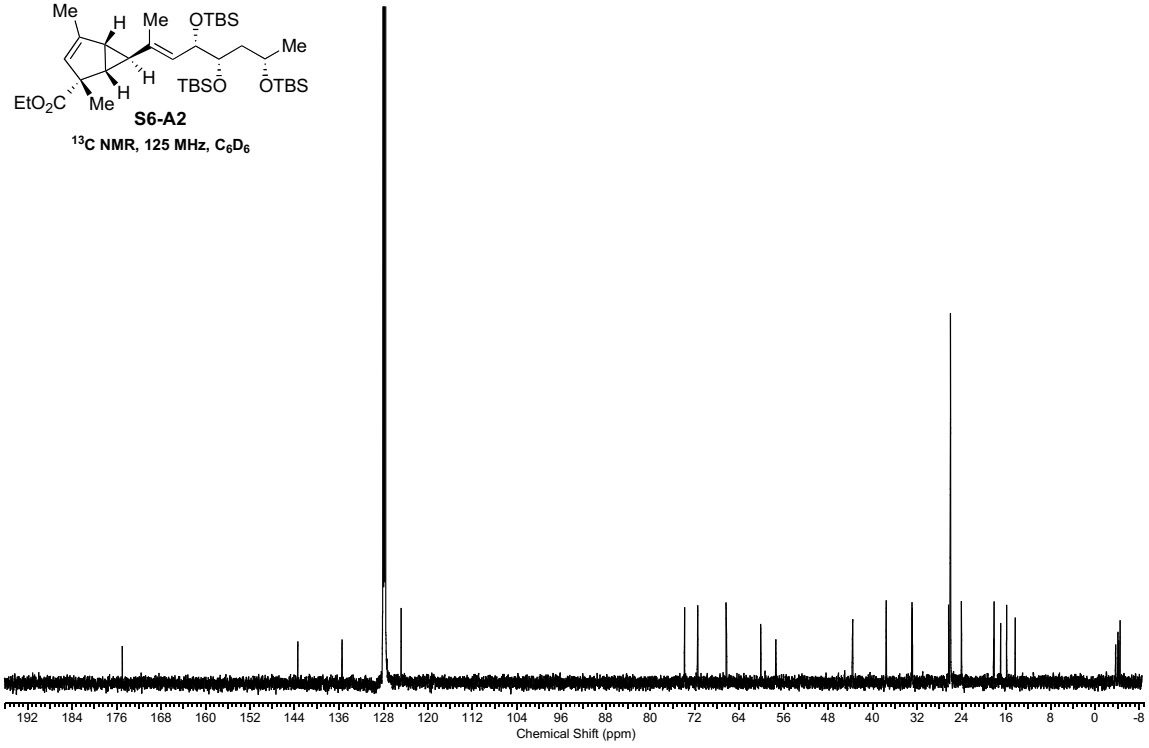
^{1}H NMR, 500 MHz, C_6D_6

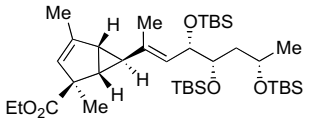


S6-A1

^{13}C NMR, 125 MHz, C_6D_6

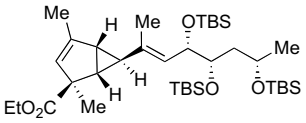

Me
H
Me
OTBS
Me
H
H
TBSO
OTBS
EtO2C
Me
S6-A2
1H NMR, 500 MHz, C6D6
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)


Me
H
Me
OTBS
Me
H
H
TBSO
OTBS
EtO2C
Me
S6-A2
13C NMR, 125 MHz, C6D6
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)



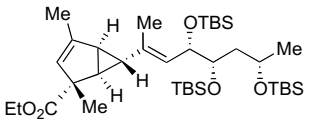
S6-B2 (Major)

^{1}H NMR, 500 MHz, C_6D_6



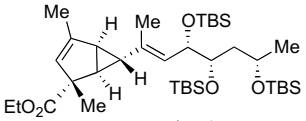
S6-B2 (Major)

^{13}C NMR, 125 MHz, C_6D_6



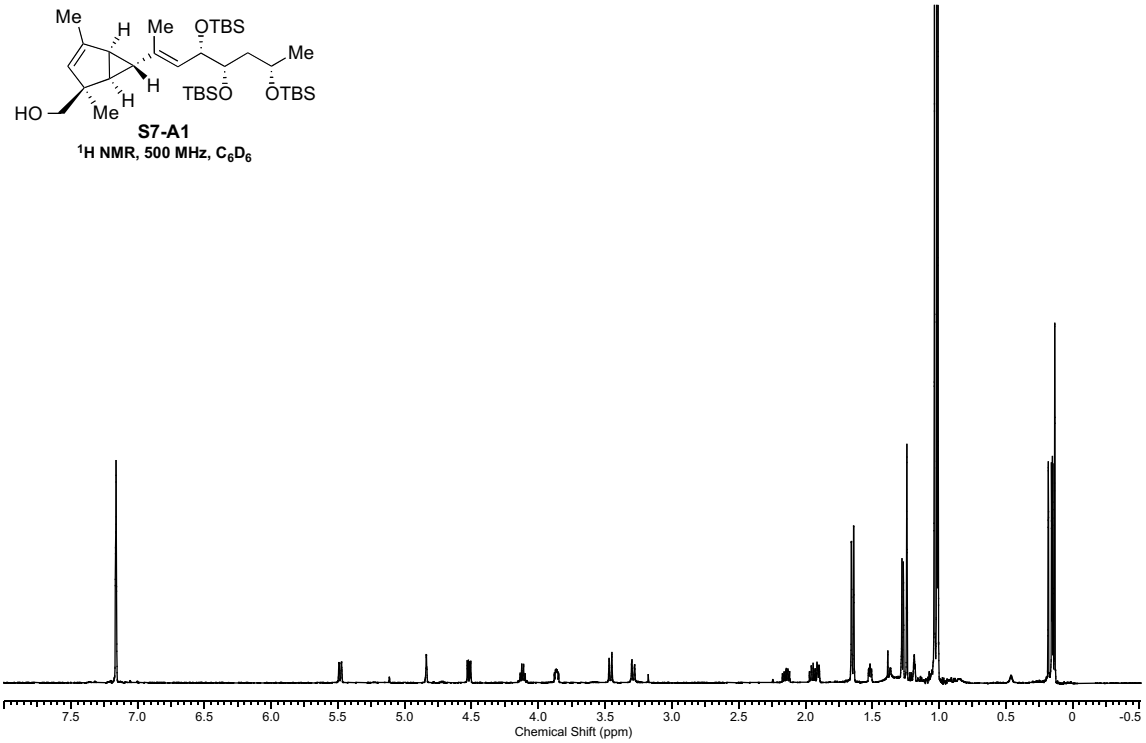
S6-B1 (Minor)

^{1}H NMR, 500 MHz, C_6D_6



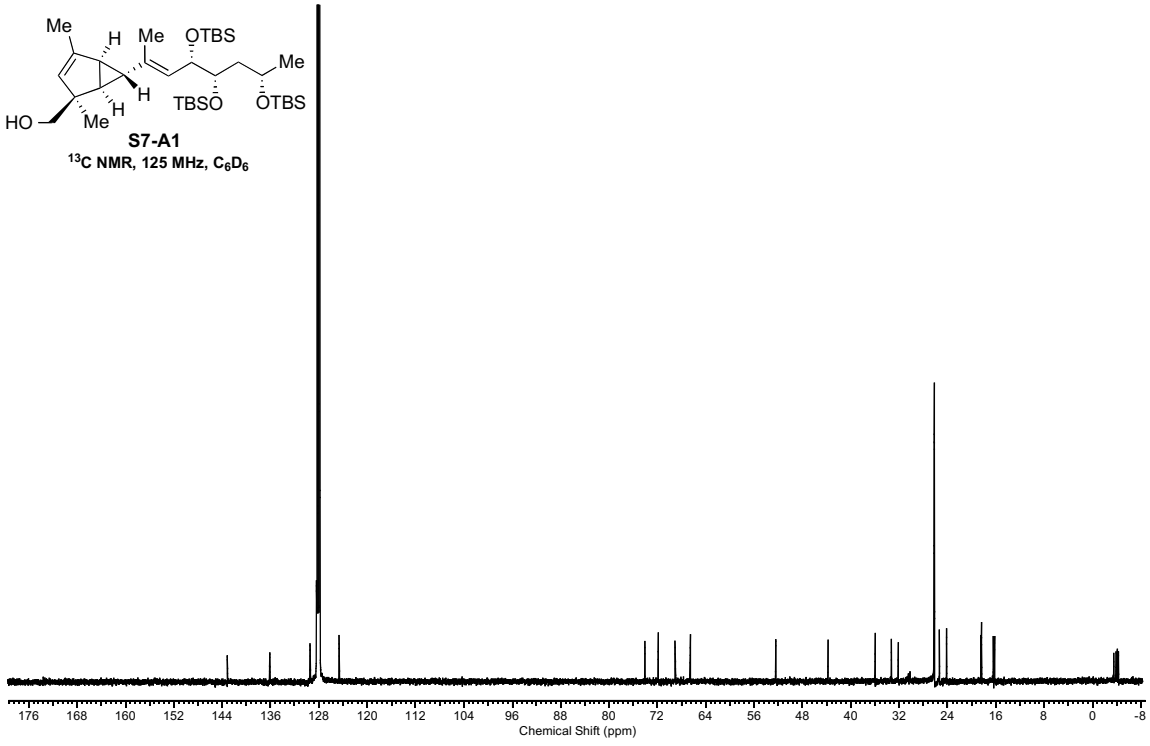
S6-B1 (Minor)

^{13}C NMR, 125 MHz, C_6D_6



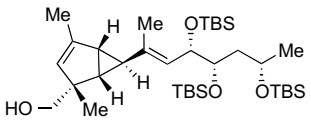
S7-A1

^{1}H NMR, 500 MHz, C_6D_6

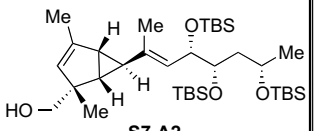


S7-A1

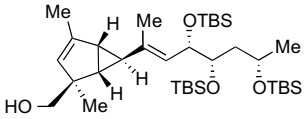
^{13}C NMR, 125 MHz, C_6D_6



S7-A2
^{1}H NMR, 500 MHz, C_6D_6

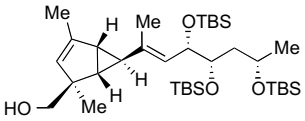


S7-A2
^{13}C NMR, 125 MHz, C_6D_6



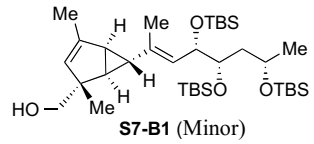
S7-B2 (Major)

^{1}H NMR, 500 MHz, C_6D_6



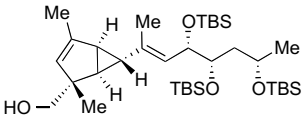
S7-B2 (Major)

^{13}C NMR, 125 MHz, C_6D_6



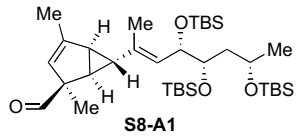
S7-B1 (Minor)

^{1}H NMR, 500 MHz, C_6D_6



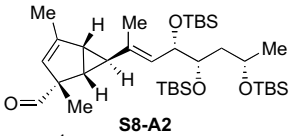
S7-B1 (Minor)

^{13}C NMR, 125 MHz, C_6D_6



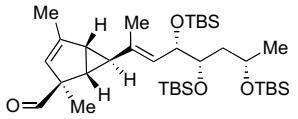
S8-A1

^{1}H NMR, 500 MHz, C_6D_6



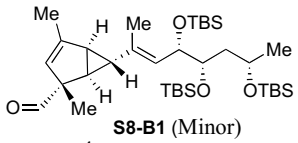
S8-A2

^{1}H NMR, 500 MHz, C_6D_6



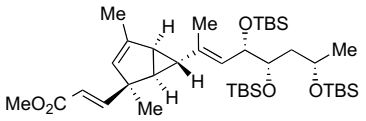
S8-B2 (Major)

^{1}H NMR, 500 MHz, C_6D_6



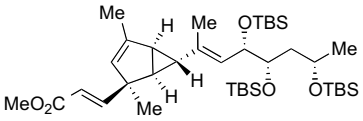
S8-B1 (Minor)

^{1}H NMR, 500 MHz, C_6D_6



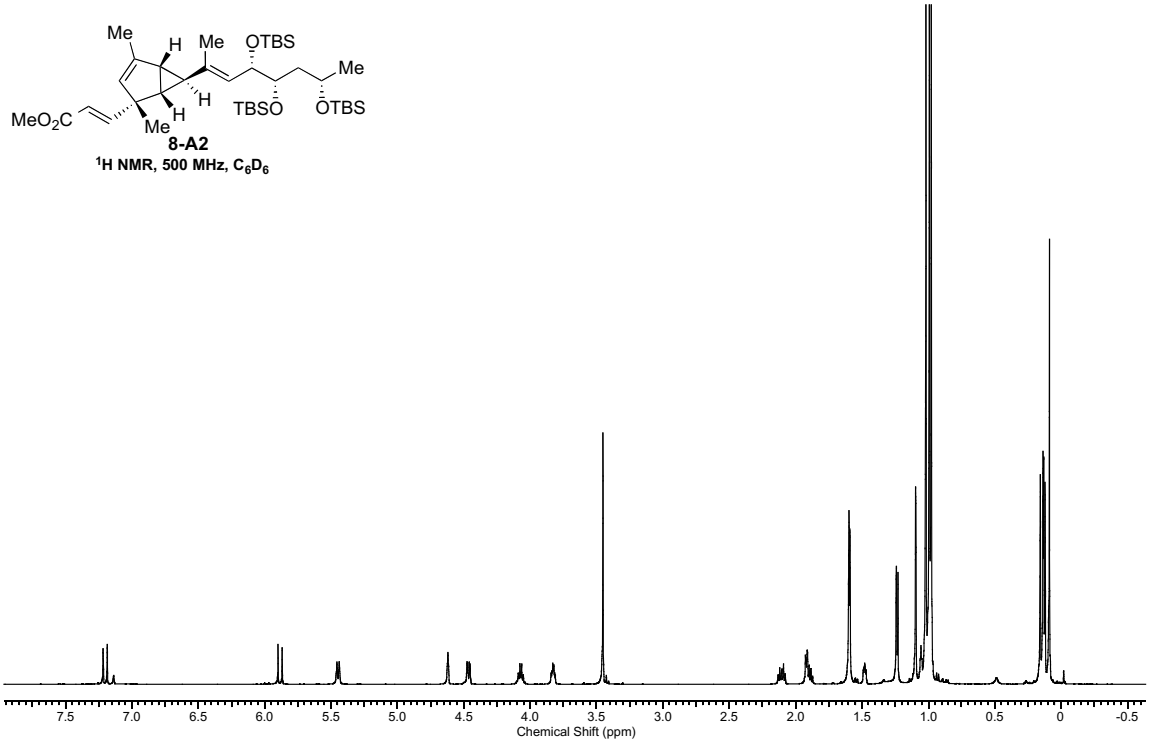
8-A1

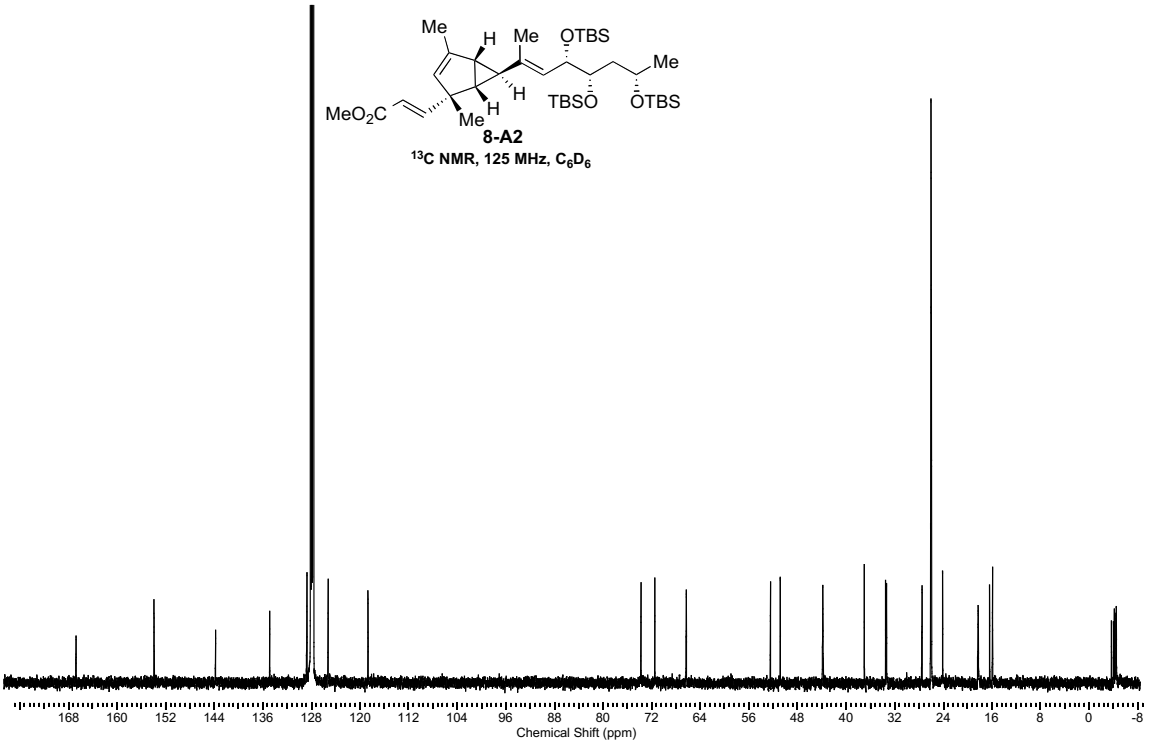
^{1}H NMR, 500 MHz, C_6D_6

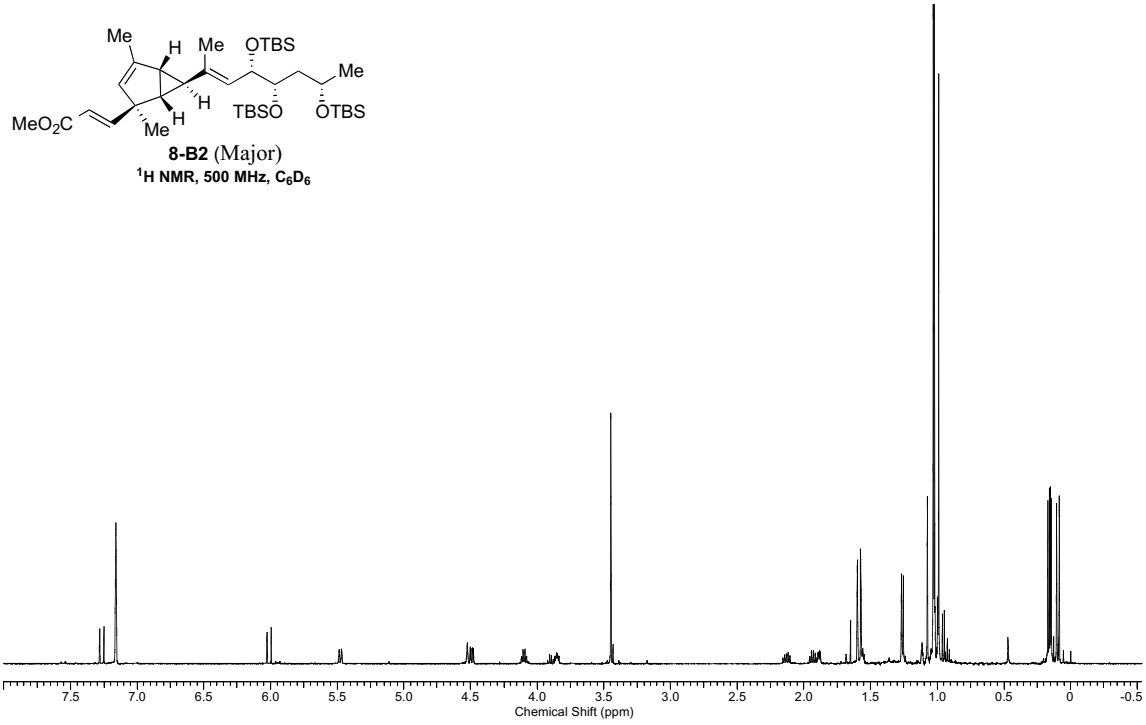


8-A1

^{13}C NMR, 125 MHz, C_6D_6

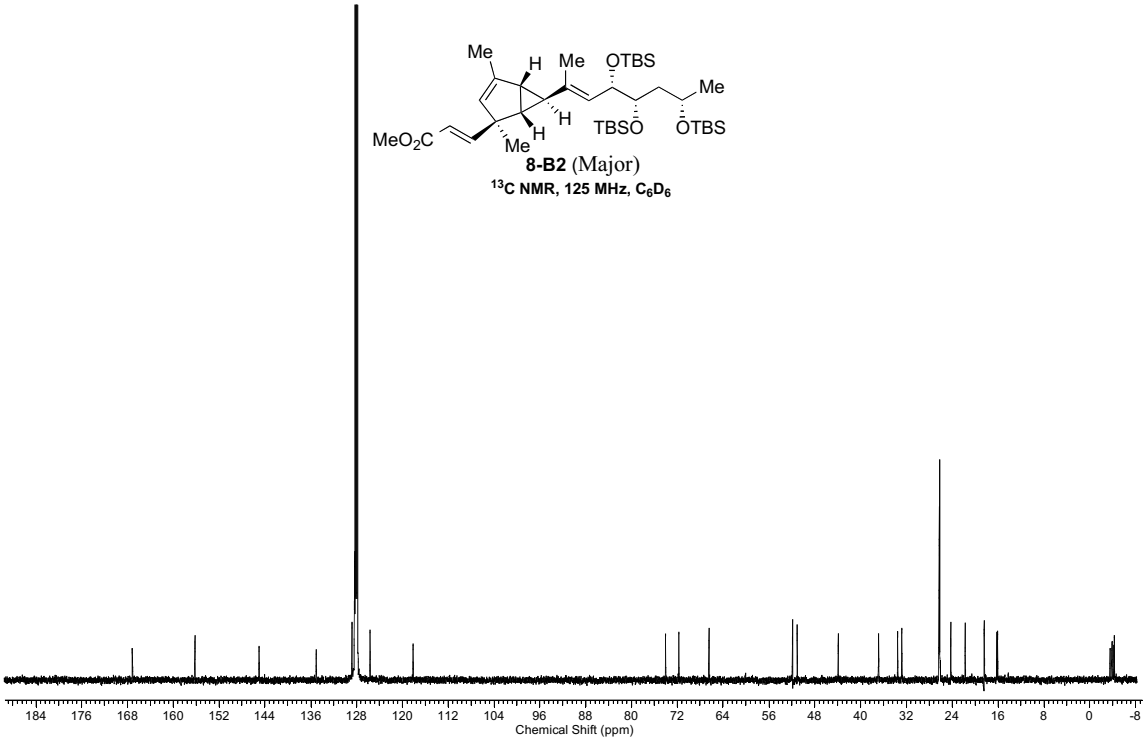

Me
H
Me
OTBS
Me
H
TBSO
OTBS
MeO2C
Me
H
8-A2
1H NMR, 500 MHz, C6D6
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)


Me
H
Me
OTBS
Me
H
TBSO
OTBS
MeO2C
H
Me
8-A2
13C NMR, 125 MHz, C6D6
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)



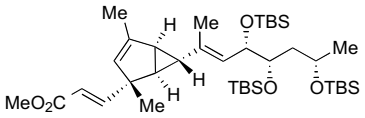
8-B2 (Major)

^{1}H NMR, 500 MHz, C_6D_6



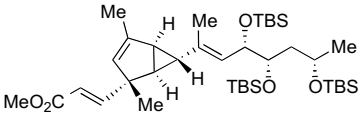
8-B2 (Major)

^{13}C NMR, 125 MHz, C_6D_6



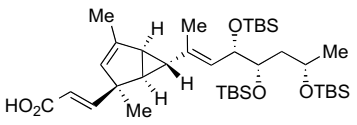
8-B1 (Minor)

^{1}H NMR, 500 MHz, C_6D_6



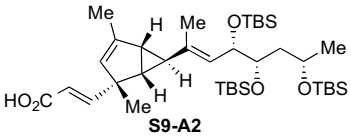
8-B1 (Minor)

^{13}C NMR, 125 MHz, C_6D_6



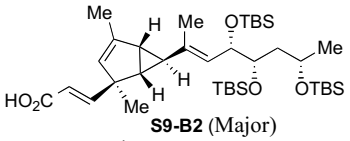
S9-A1

^{1}H NMR, 500 MHz, C_6D_6



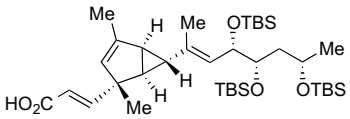
S9-A2

^{1}H NMR, 500 MHz, C_6D_6



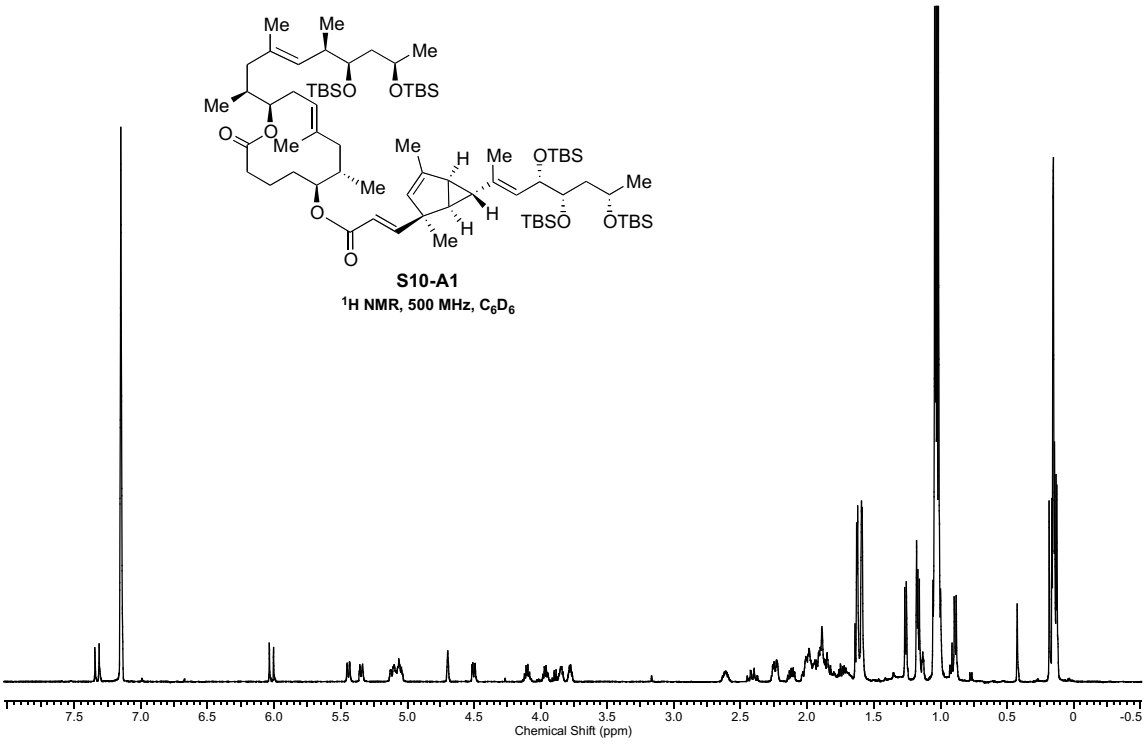
S9-B2 (Major)

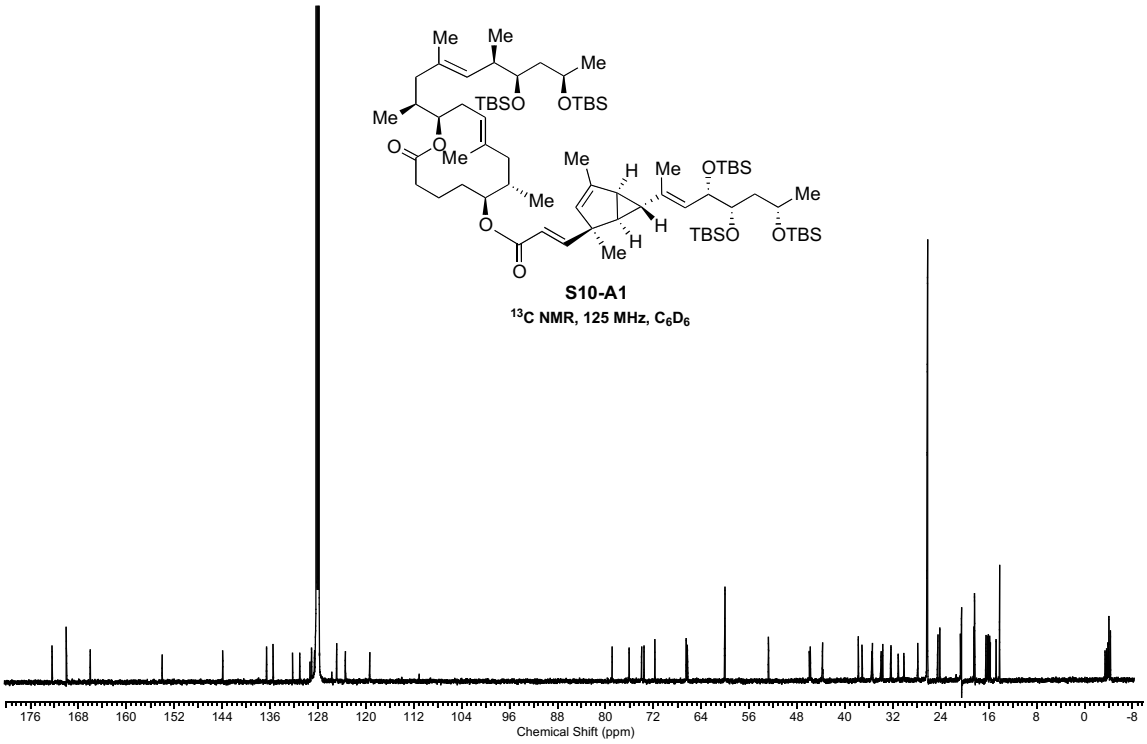
^{1}H NMR, 500 MHz, C_6D_6

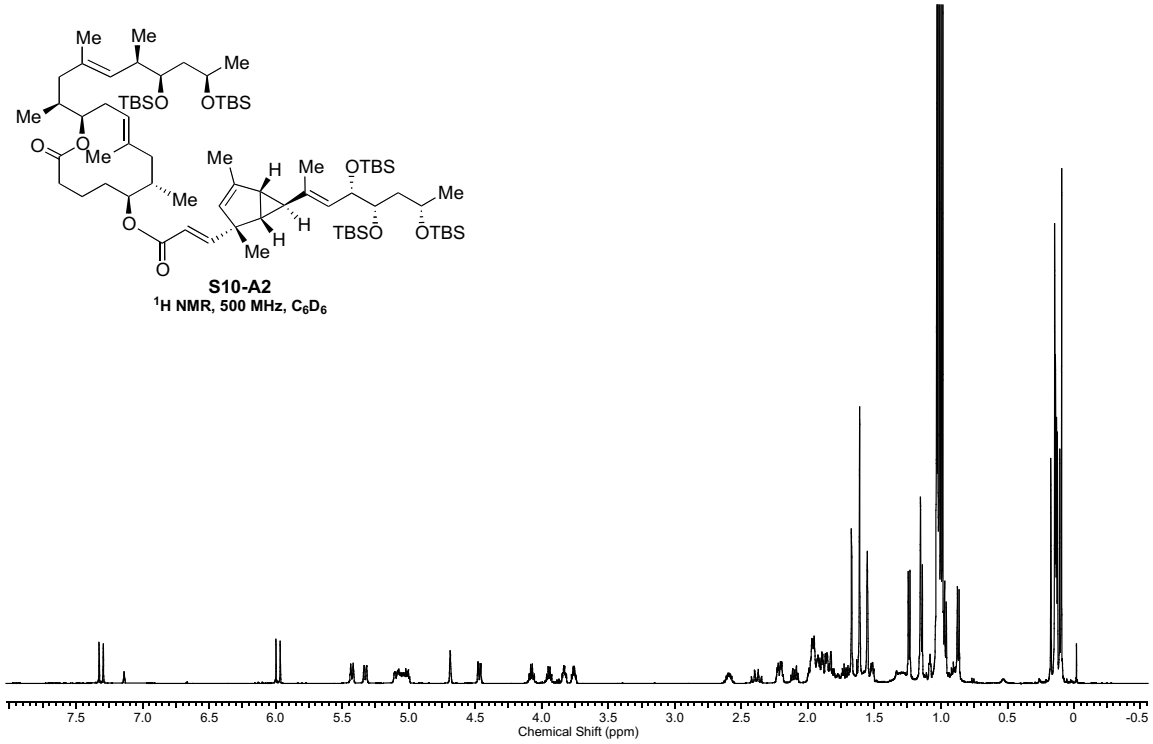


S9-B1 (Minor)

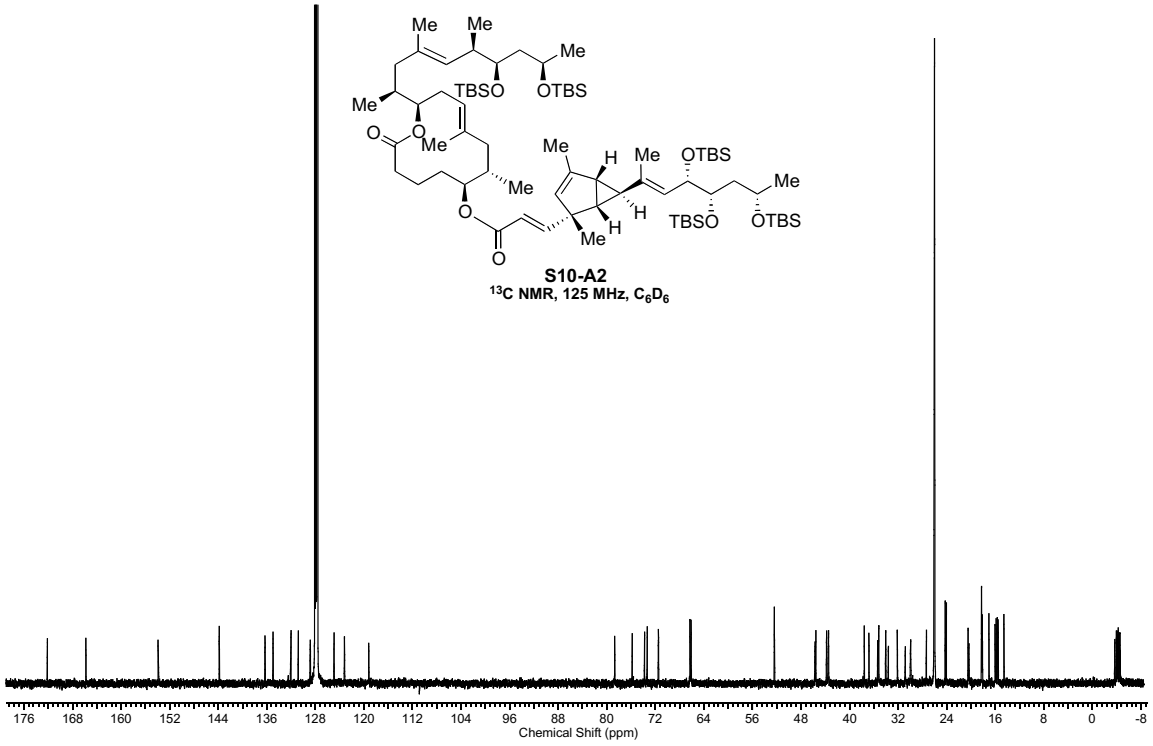
^{1}H NMR, 500 MHz, C_6D_6


Me
Me
Me
TBSO
OTBS
Me
O
O
Me
Me
Me
H
Me
OTBS
Me
O
H
TBSO
OTBS
H
Me
O
S10-A1
^{1}H NMR, 500 MHz, C_6D_6
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)

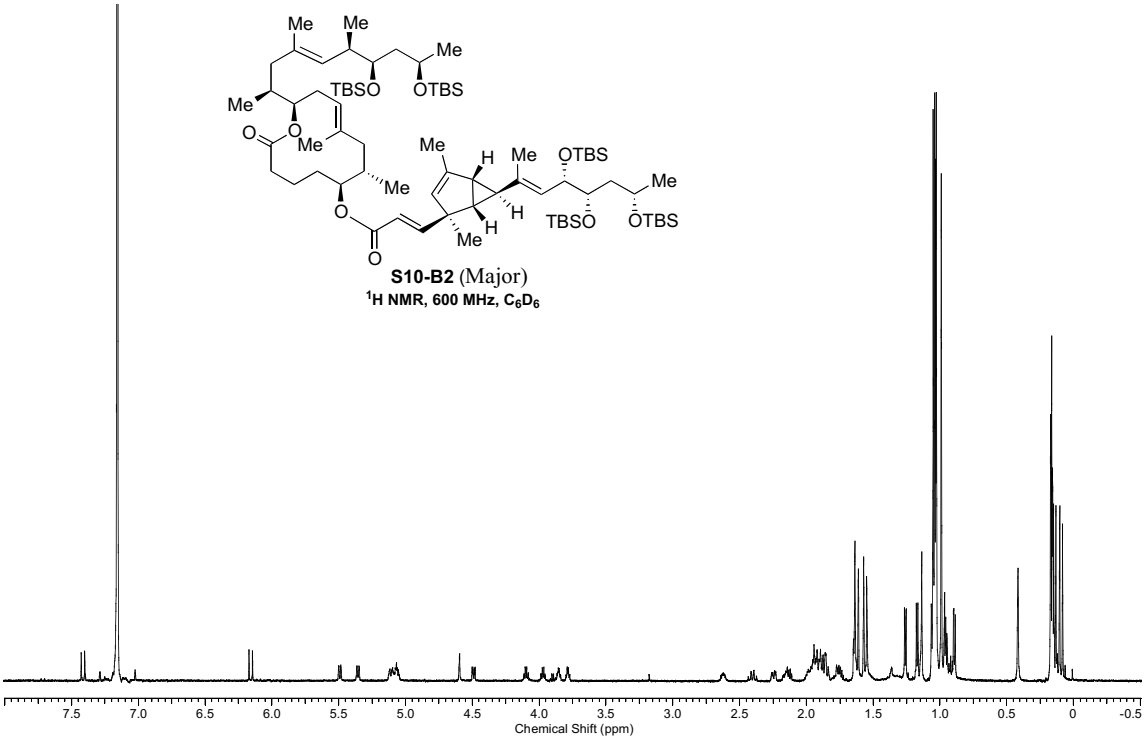

Me
Me
Me
TBSO
OTBS
Me
O
O
Me
Me
Me
H
Me
OTBS
Me
O
H
TBSO
OTBS
H
Me
O
S10-A1
^{13}C NMR, 125 MHz, C_6D_6
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)



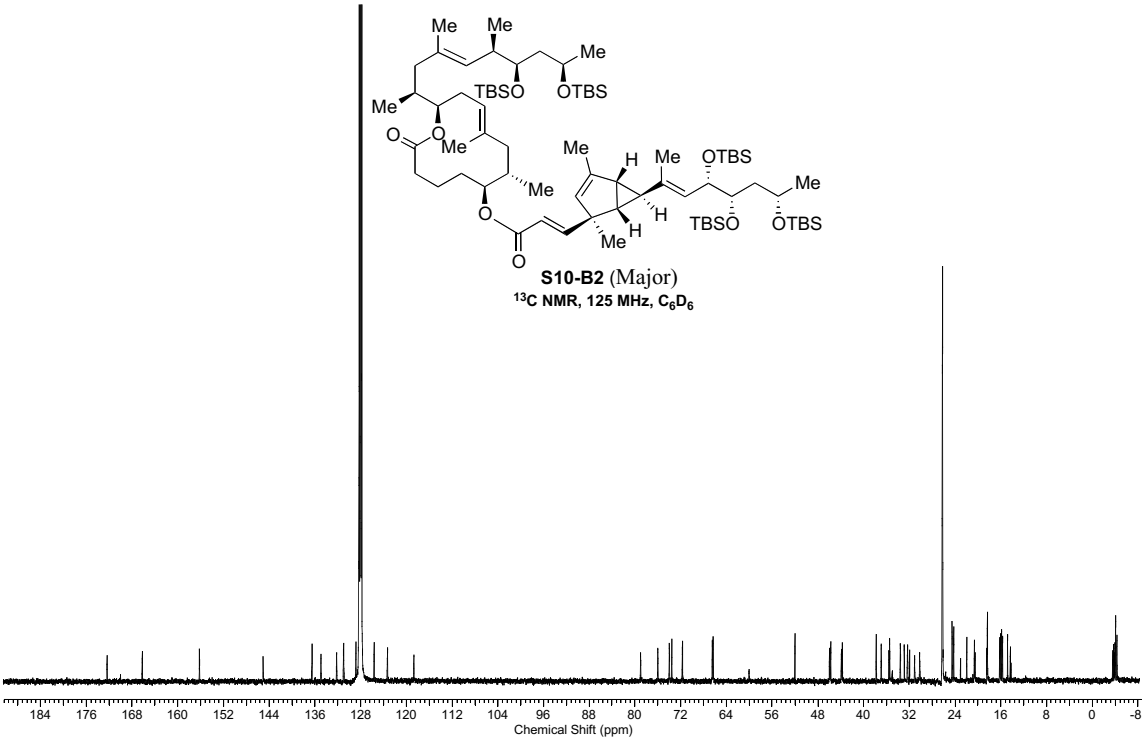
S10-A2
^{1}H NMR, 500 MHz, C_6D_6



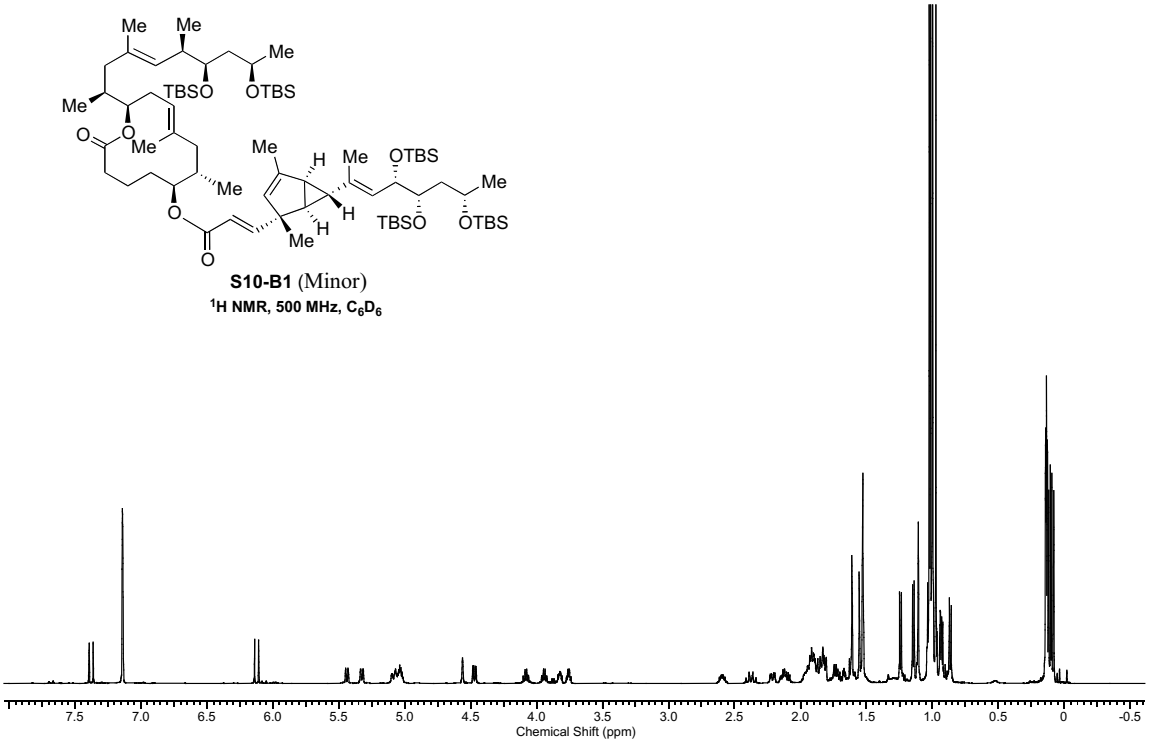
S10-A2
^{13}C NMR, 125 MHz, C_6D_6



S10-B2 (Major)
^{1}H NMR, 600 MHz, C_6D_6

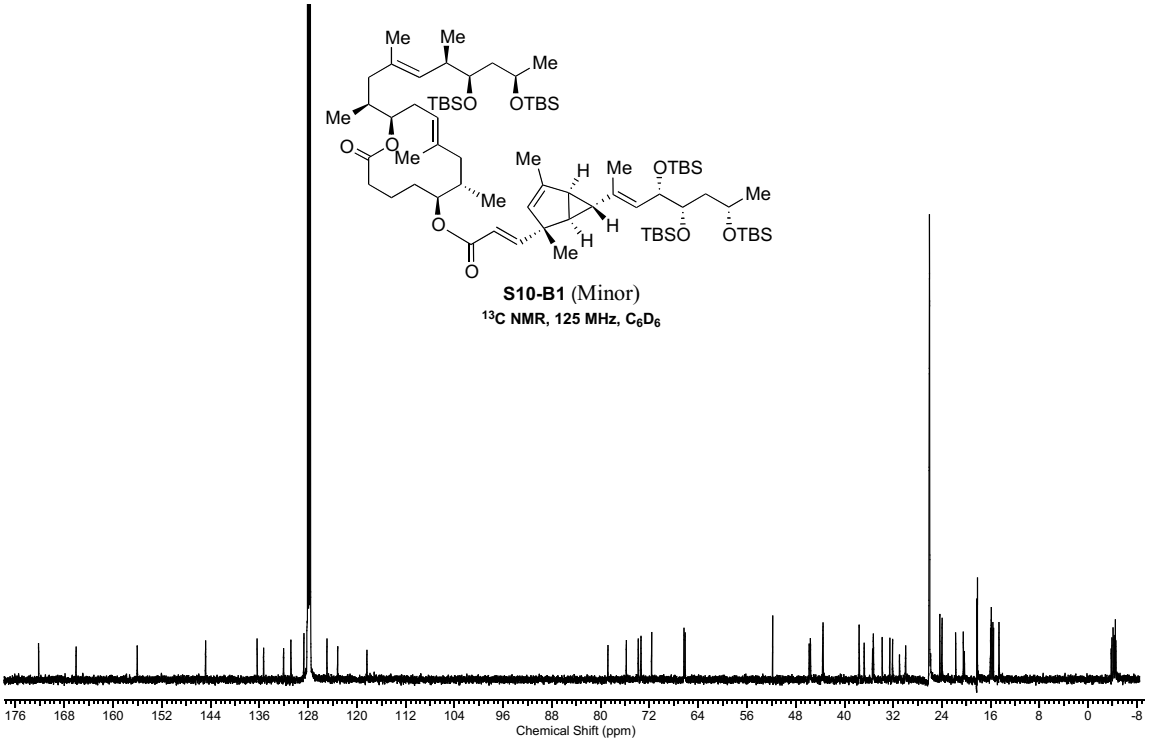


S10-B2 (Major)
^{13}C NMR, 125 MHz, C_6D_6



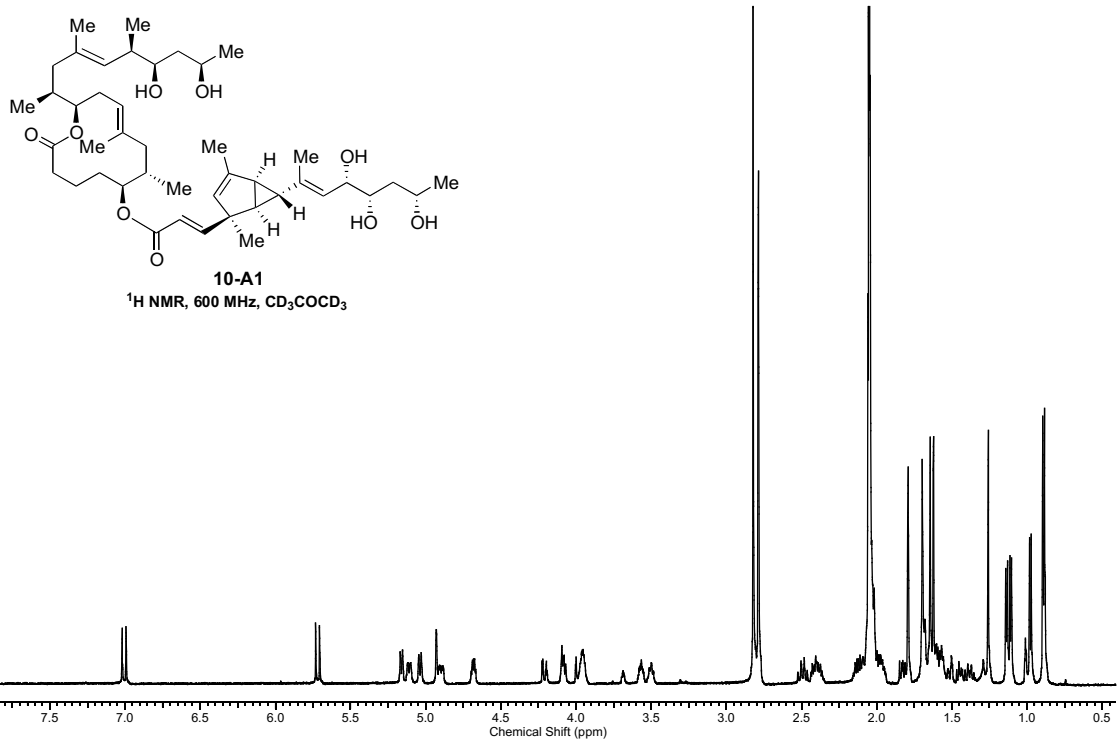
S10-B1 (Minor)

^{1}H NMR, 500 MHz, C_6D_6



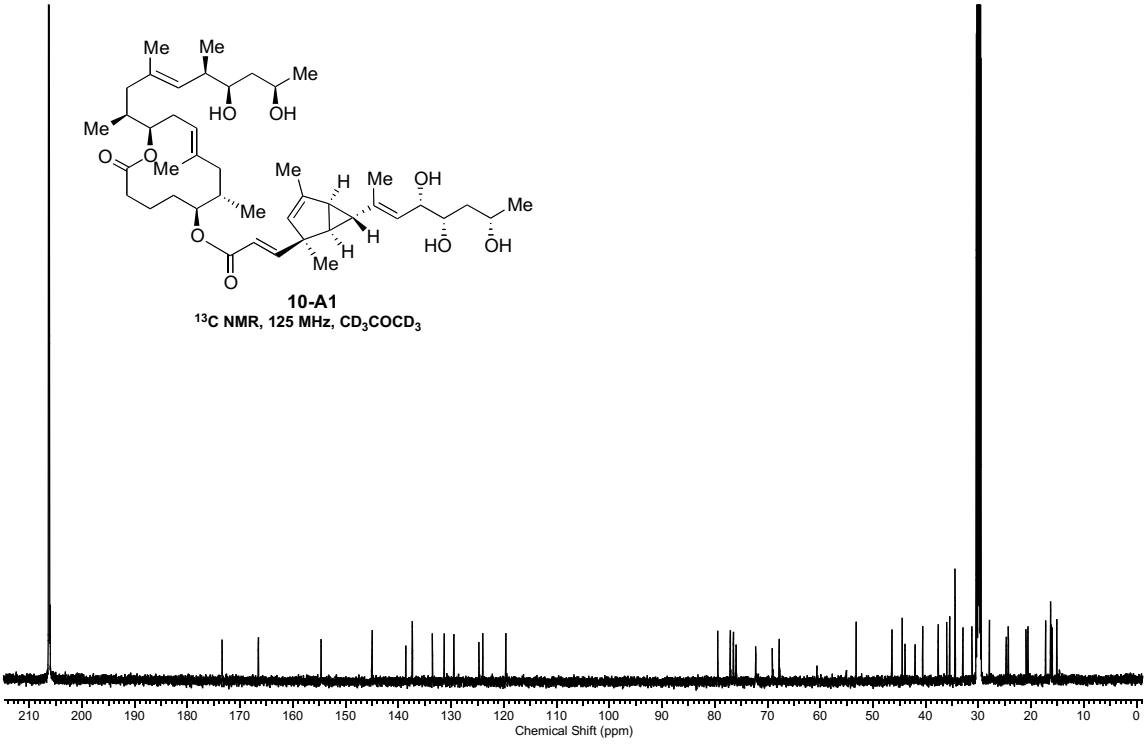
S10-B1 (Minor)

^{13}C NMR, 125 MHz, C_6D_6



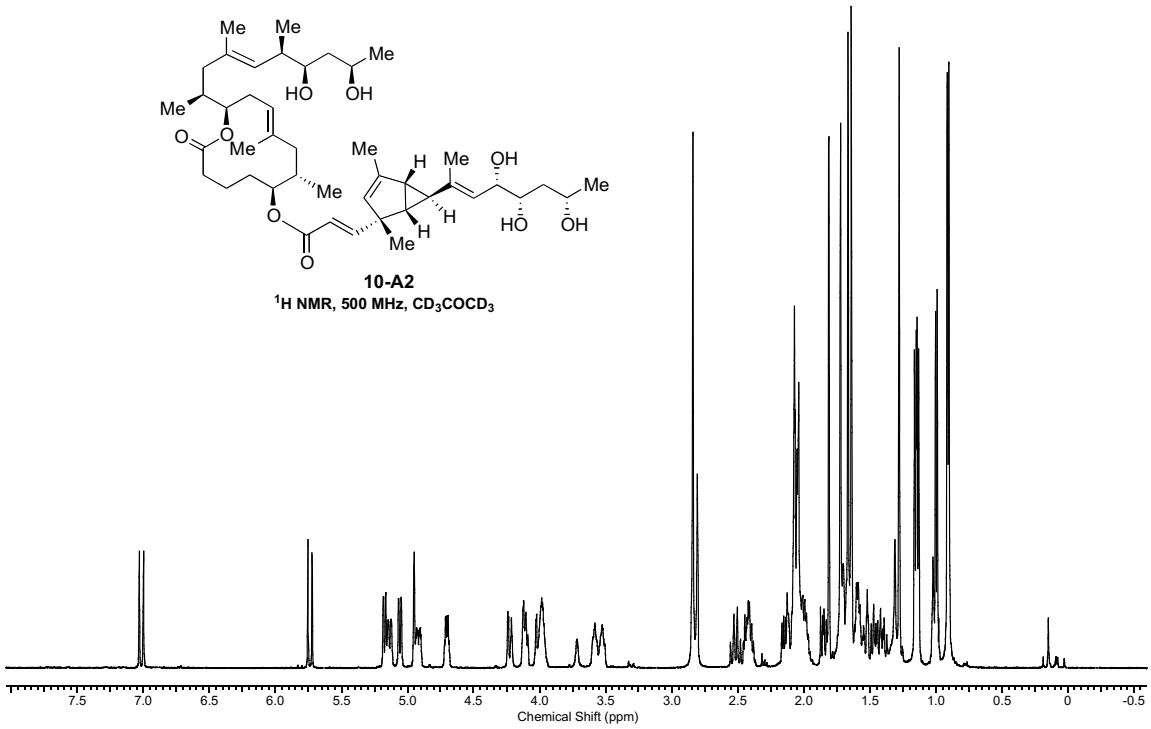
10-A1

^{1}H NMR, 600 MHz, CD_3COCD_3



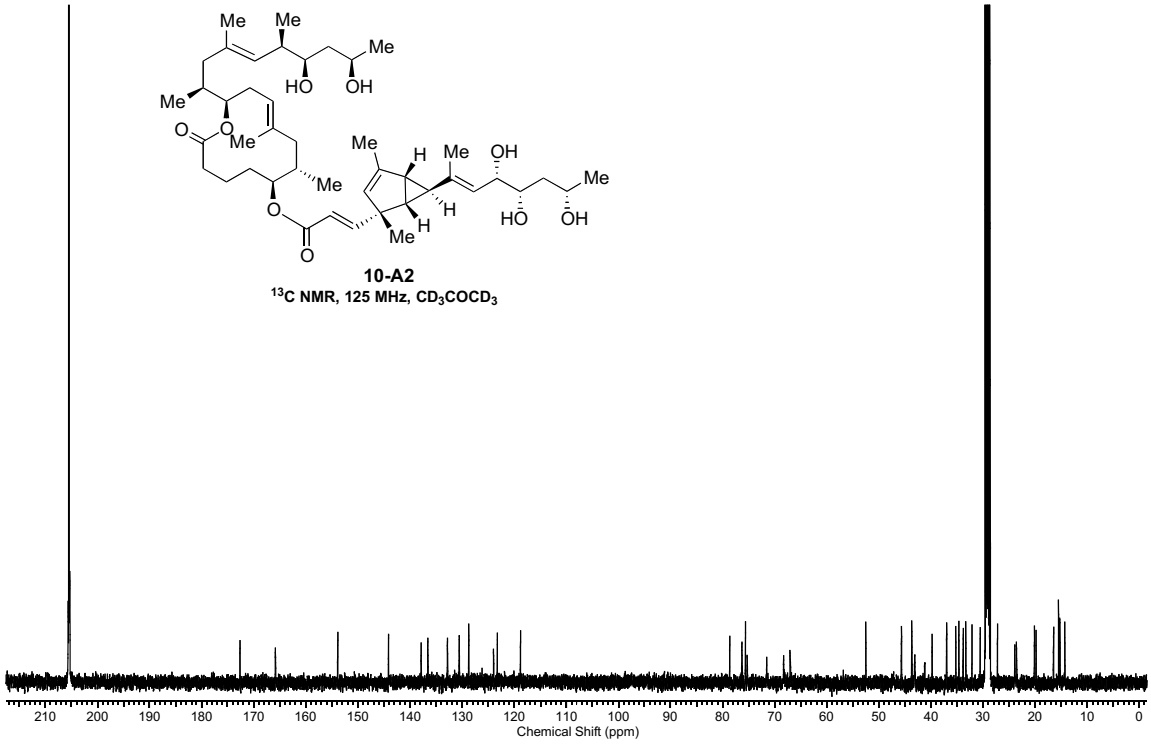
10-A1

^{13}C NMR, 125 MHz, CD_3COCD_3



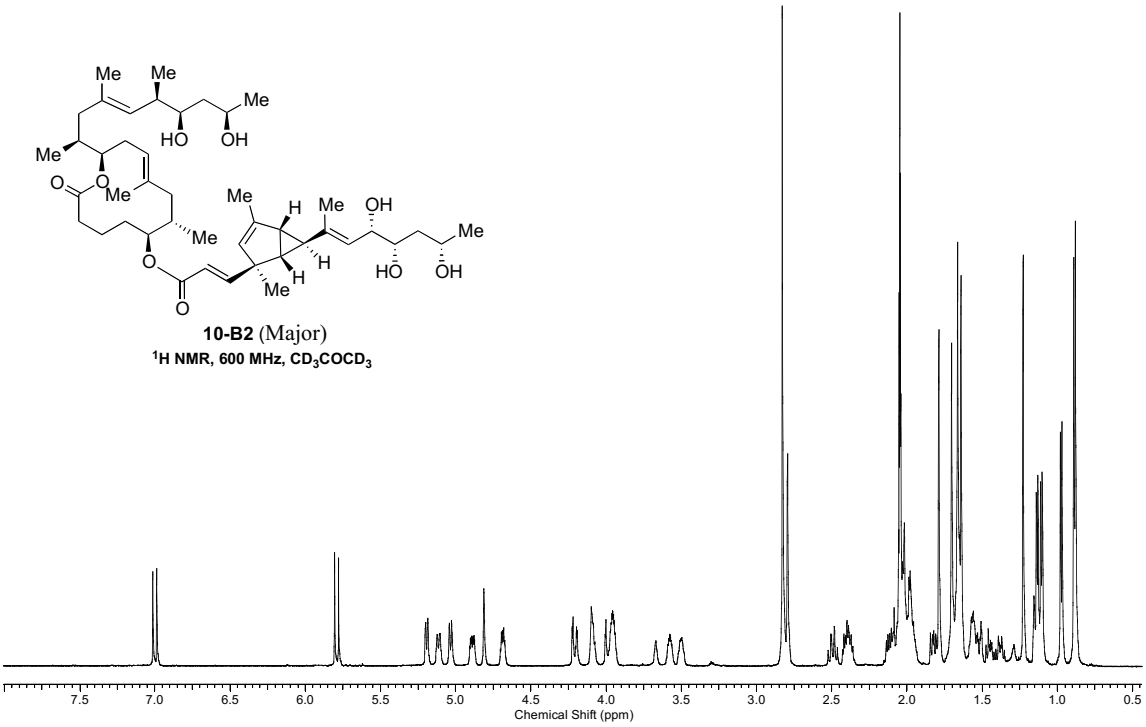
10-A2

^{1}H NMR, 500 MHz, CD_3COCD_3



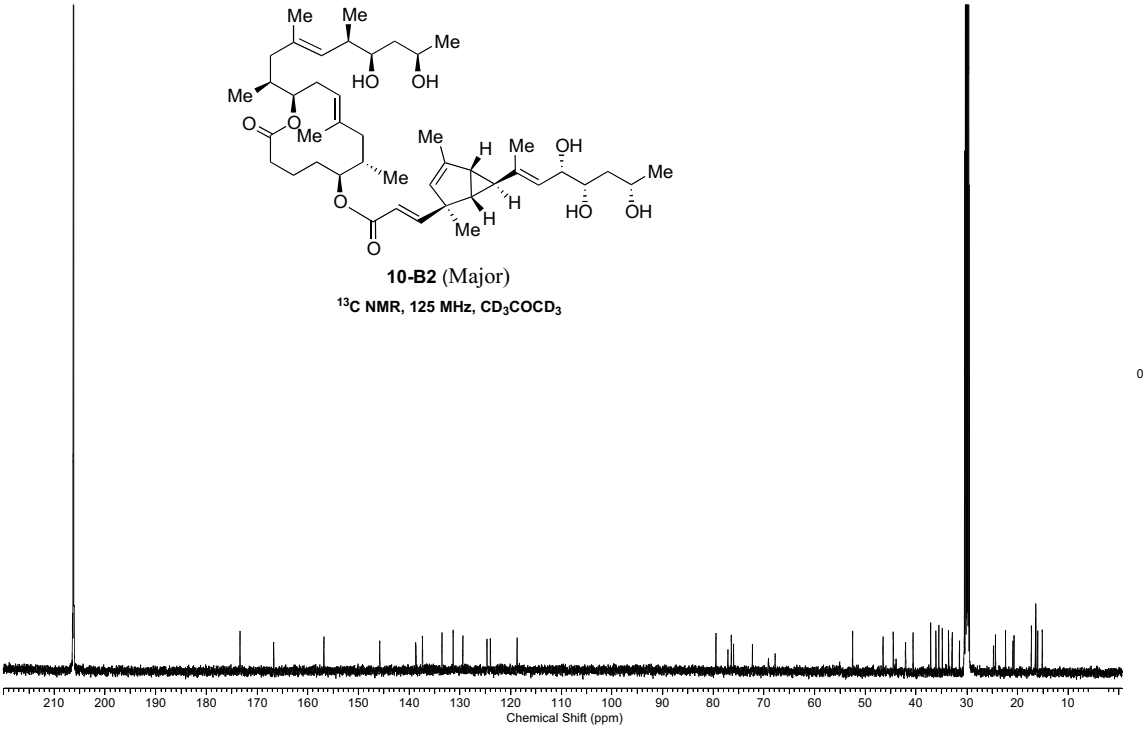
10-A2

^{13}C NMR, 125 MHz, CD_3COCD_3



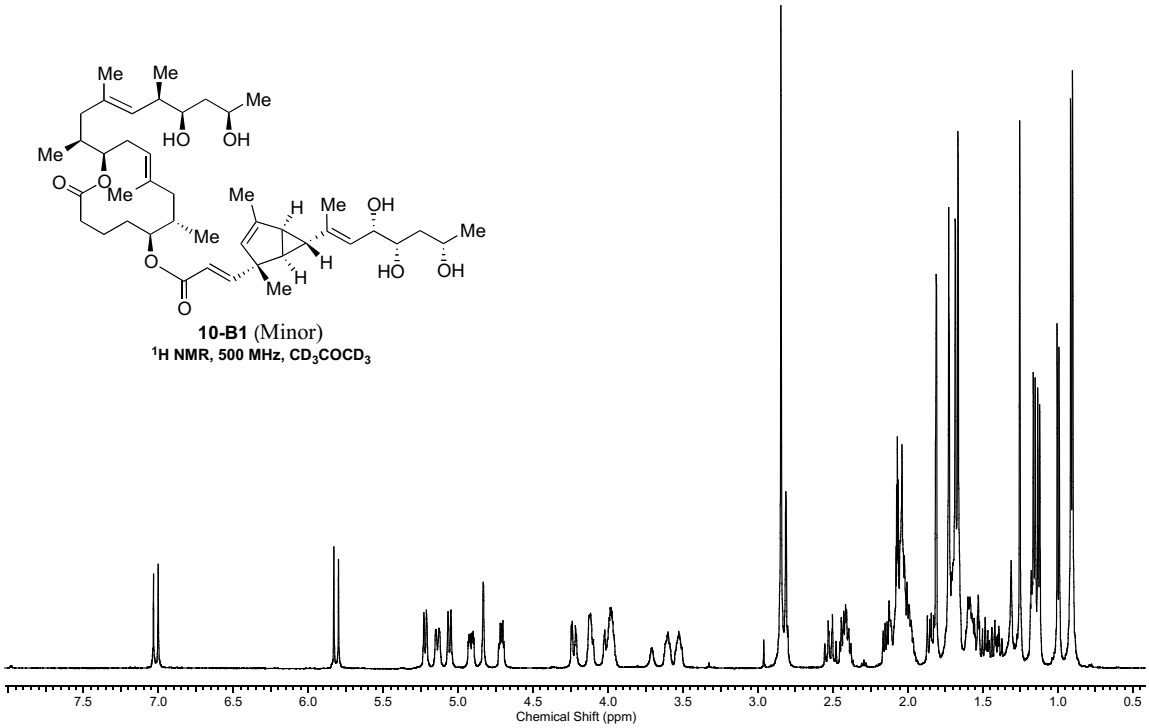
10-B2 (Major)

^{1}H NMR, 600 MHz, CD_3COCD_3



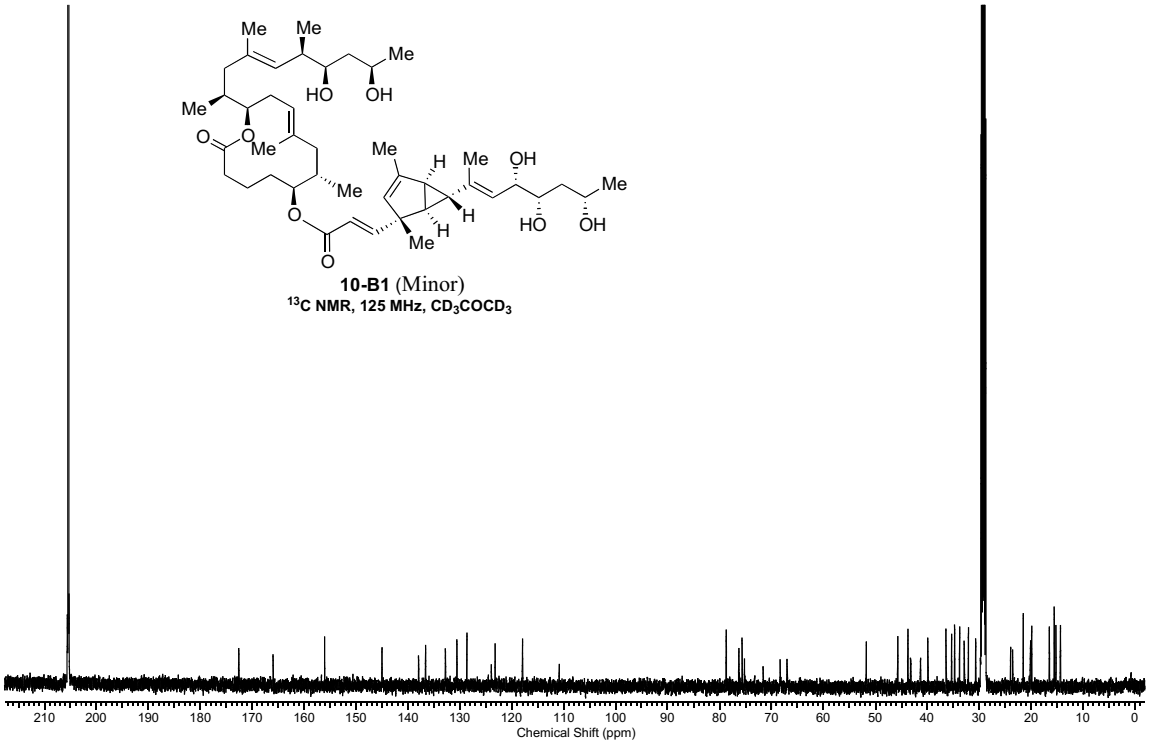
10-B2 (Major)

^{13}C NMR, 125 MHz, CD_3COCD_3



10-B1 (Minor)

^{1}H NMR, 500 MHz, CD_3COCD_3



10-B1 (Minor)

^{13}C NMR, 125 MHz, CD_3COCD_3