

## Electronic supplementary information for

### Stereoselective synthesis of (all-*Z*)-hentriaconta-3,6,9,12,15,19,22,25,28-nonaene

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### General information

All reactions were performed under a nitrogen atmosphere protected from light exposure. All reagents and solvents were commercial grade and used without further purification unless when necessary. EPA ethyl ester was obtained as a gift from Pronova Biofarma, BASF, Sandefjord, Norway. Acetone was dried under anhydrous CaSO<sub>4</sub> and distilled. Thin layer chromatography (TLC) was performed using aluminum-backed silica gel 60 F<sub>254</sub> plates and flash chromatography with silica gel 60 (40-63 μm) from Merck. <sup>1</sup>H NMR (400 MHz) and <sup>13</sup>C NMR (100 MHz) were recorded on a Bruker Ascend™ 400 instrument using CDCl<sub>3</sub> as a solvent. Chemical shifts are measured in ppm relative to residual solvent peak as internal standart set to δ 7.26 and 77.0. Mass spectra were recorded at 70 eV on a Waters Prospec Q spectrometer using EI and CI as the ionization method. The GC analyses were performed on an Agilent GC system using an Agilent J1W HP-5 GC column (20 m, i.d. = 0.18 mm) with FID detector. IR spectra (4000 – 600 cm<sup>-1</sup>) were recorded on a Perkin-Elmer Spectrum BX series FT-IR spectrophotometer using a reflectance cell (HATR).

### (3*Z*,6*Z*,9*Z*,12*Z*,19*Z*,22*Z*,25*Z*,28*Z*)-hentriaconta-3,6,9,12,19,22,25,28-octaen-15-yn-14-ol (**7a**)

*n*-BuLi (6.5 mL, 10.4 mmol, 1.6 M in hexane) was added to a solution of **5** (2.14 g, 10.4 mmol) in THF (100 mL) under nitrogen at -78 °C and stirred at this temperature for 10 min. A solution of aldehyde **4** (2.27 g, 10.4 mmol) in THF (60 mL) was added dropwise over 15 min. The mixture was stirred at -78 °C for 1 h before the solution was left to reach ambient temperature over 2 h. The reaction was quenched by the addition of aqueous NH<sub>4</sub>Cl (pH = 8), and the mixture extracted with diethyl ether (3×25 mL). The combined organic layers were washed with brine (2×25 mL), dried (MgSO<sub>4</sub>) and the solvent removed in vacuo. The crude product was purified by flash chromatography (SiO<sub>2</sub>, hexane/EtOAc 95:5) to yield 1.75 g (39%) alcohol **7a** as pale yellow oil. TLC (hexane: EtOAc 95:5, KMnO<sub>4</sub> stain): R<sub>f</sub> = 0.28. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.91 (t, J=8Hz, 6H), 1.73 (m, 1H), 2.01 (t, J=8 Hz, 4H), 2.41-2.43 (m, 2H), 2.74-2.77 (m, 12H), 2.93 (m, 2H), 4.32 (m, 1H), 5.30-5.50 (m, 16H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 14.1, 14.3, 17.2, 20.6, 25.6, 25.7, 25.9, 26.4, 35.9, 62.1, 80.6, 83.7,

124.2, 124.4, 127.0, 127.4, 127.7, 127.8, 127.9, 128.5, 128.6, 128.7, 129.8, 131.7, 132.0, 132.1. HMRS: Exact mass calculated for C<sub>31</sub>H<sub>46</sub>O [M<sup>+</sup>]: 432.3392, found 432.3376.

**(3Z,6Z,9Z,12Z,19Z,22Z,25Z,28Z)-hentriaconta-3,6,9,12,19,22,25,28-octaen-15-yn-14-yl methanesulfonate (7b)**

Mesyl chloride (36  $\mu$ l, 0.462 mmol) was added to an ice cooled solution of the propargylic alcohol **7a** (100 mg, 0.231 mmol) and Et<sub>3</sub>N (65  $\mu$ L, 0.462 mmol) in dry dichloromethane (2.5 mL). The reaction mixture was left stirring at room temperature for 2 h. Brine was added and the volatiles were removed under reduced pressure. The residue was extracted with ether (3 $\times$ 5mL), washed with saturated NaHCO<sub>3</sub> (2 $\times$ 5mL) and brine (3 $\times$ 5mL) and evaporated to obtain yellow oil. The crude oil was purified on silica gel column eluting with hexane: EtOAc 9:1 to afford 107 mg of mesylate **7b** (85% yield). TLC (hexane: EtOAc 95:5, KMnO<sub>4</sub> stain): R<sub>f</sub> = 0.26. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.91 (t, J=8 Hz, 6H), 2.01 (m, 4H), 2.58-2.59 (m, 2H), 2.75-2.76 (m, 12H), 2.96-3.02 (m, 5H), 5.09 (s, 1H), 5.30-5.54 (m, 16H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.3, 17.2, 20.6, 25.6, 25.9, 34.0, 39.2, 71.7, 75.6, 88.0, 122.3, 123.2, 126.9, 127.1, 127.5, 127.6, 127.7, 128.7, 28.8, 128.9, 130.6, 132.1, 132.4.

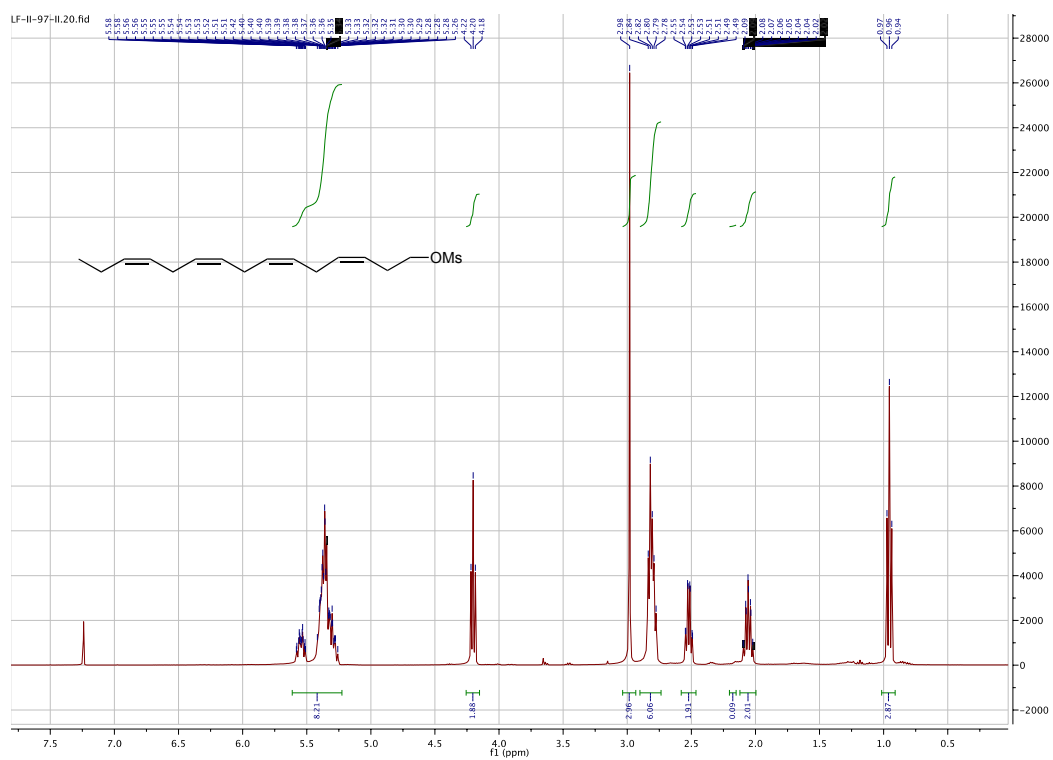
**(3Z,6Z,9Z,12Z,19Z,22Z,25Z,28Z)-14-iodohentriaconta-3,6,9,12,19,22,25,28-octaen-15-yne (8)**

A solution of mesylate **7b** (85 mg, 0.166 mmol) and NaI (75 mg, 0.5 mmol) in dry acetone was heated under reflux for 3 h. Water was added to the reaction mixture and hexane after cooling down to room temperature. The organic layer was separated; the aqueous layer was extracted with hexane (3 $\times$ 5 mL). The combined organic extracts were washed with water, brine and dried (MgSO<sub>4</sub>). Evaporation followed by silica gel column chromatography eluting with hexane: EtOAc 9:1 gave 57 mg of iodide **8** (63% yield) as pale yellow oil. TLC (hexane: EtOAc 9:1, KMnO<sub>4</sub> stain): R<sub>f</sub> = 0.70. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.91 (t, J=8 Hz, 6H), 1.99-2.03 (m, 4H), 2.76-2.94 (m, 16H), 4.46 (m, 1H), 5.16-5.55 (m, 16H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  10.9, 14.1, 14.3, 17.6, 20.6, 25.6, 25.7, 26.1, 38.0, 81.3, 85.6, 123.8, 126.8, 127.0, 127.4, 127.6, 127.7, 127.8, 128.6, 128.7, 130.0, 131.1, 132.1.

**(3Z,6Z,9Z,12Z,19Z,22Z,25Z,28Z)-hentriaconta-3,6,9,12,15,16,19,22,25,28-decaene (3)**

Propargylic iodide **8** (20 mg, 0.037 mmol) was dissolved in dry ether and cooled down to -78  $^{\circ}$ C under nitrogen and added *n*-BuLi (7.1  $\mu$ L, 0.074 mmol, 1.6 M in hexane). After stirring at -78  $^{\circ}$ C for 1 h the reaction mixture was allowed to warm up to room temperature. Water was added and the reaction mixture was extracted with diethyl ether (3 $\times$ 10 mL), washed with brine (2 $\times$ 10 mL), dried (MgSO<sub>4</sub>) and evaporated to obtain 14 mg of allene **3** (91% yield) as yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.91 (t, J=8 Hz, 6H), 2.01 (m, 6H), 2.74-2.76 (m, 14H), 5.06-5.31 (m, 18H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  13.3, 19.5, 24.5, 24.6, 24.7, 24.9, 25.9, 28.7, 89.5, 126.0, 126.6,

126.7, 127.1, 127.2, 127.5, 127.6, 131.0, 203.2. HMRS: Exact mass calculated for  $C_{31}H_{46}$   $[M^+]$ : 416.3443, found 416.3434.



**Figure S-1**  $^1H$  MNR spectrum of **11b**

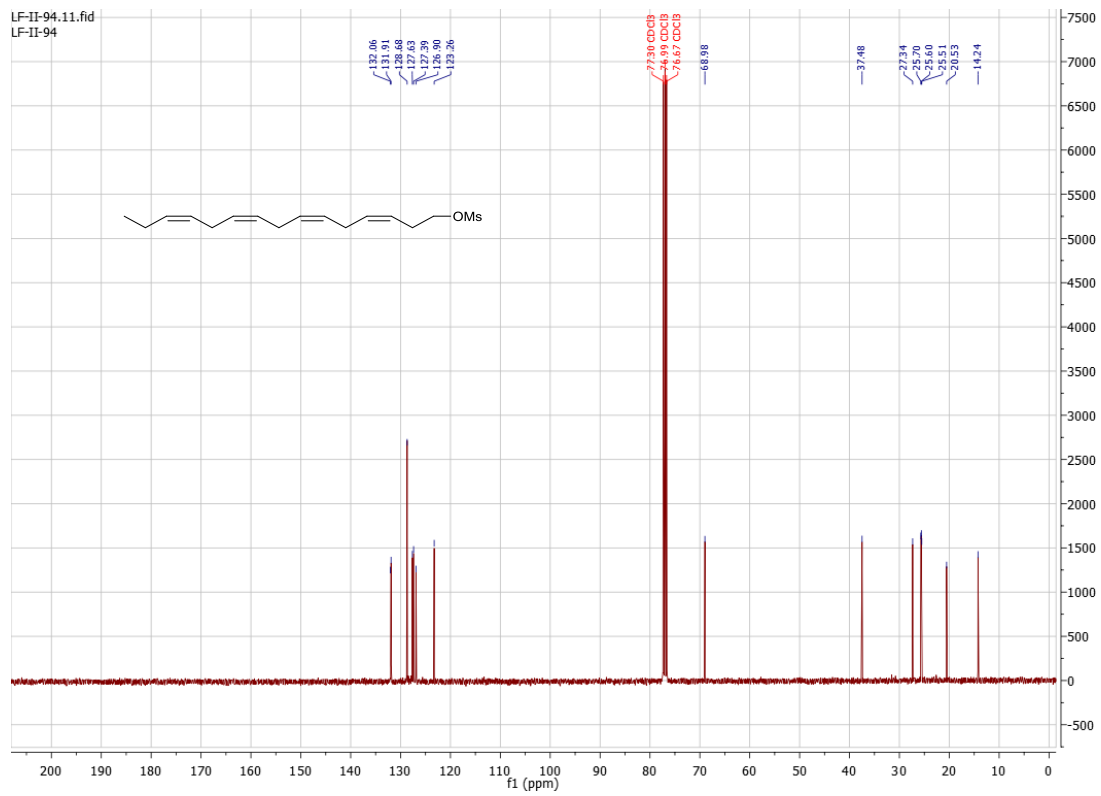


Figure S-2 <sup>13</sup>C NMR spectrum of **11b**

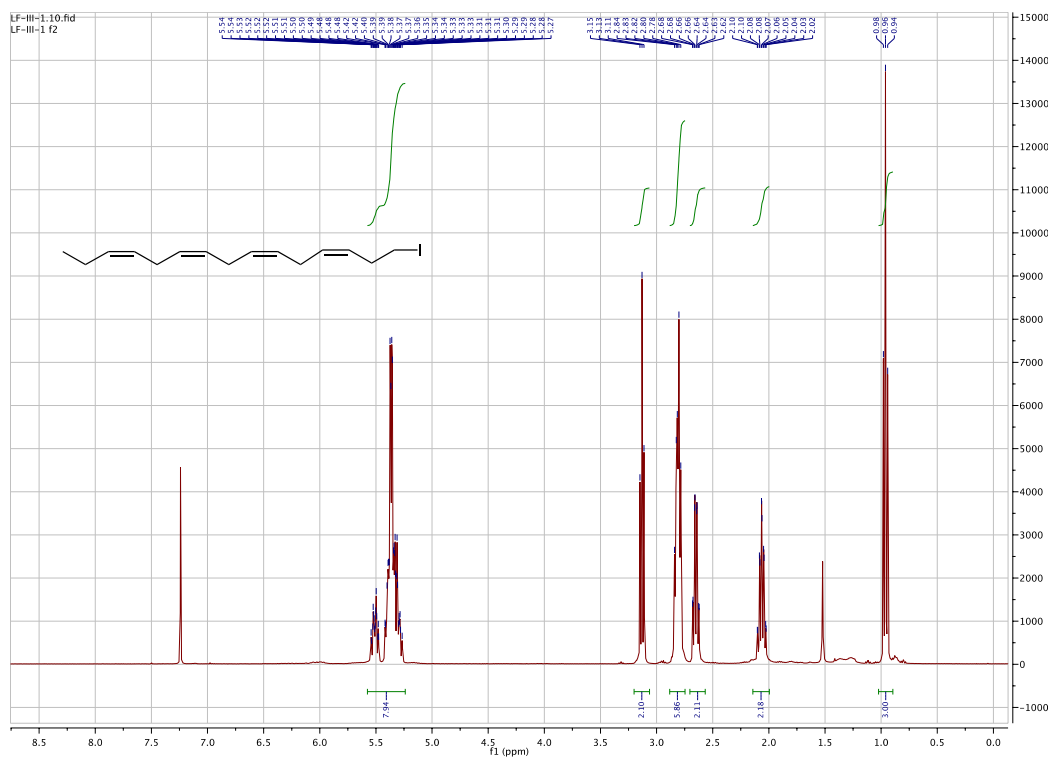


Figure S-3 <sup>1</sup>H NMR spectrum of **12**

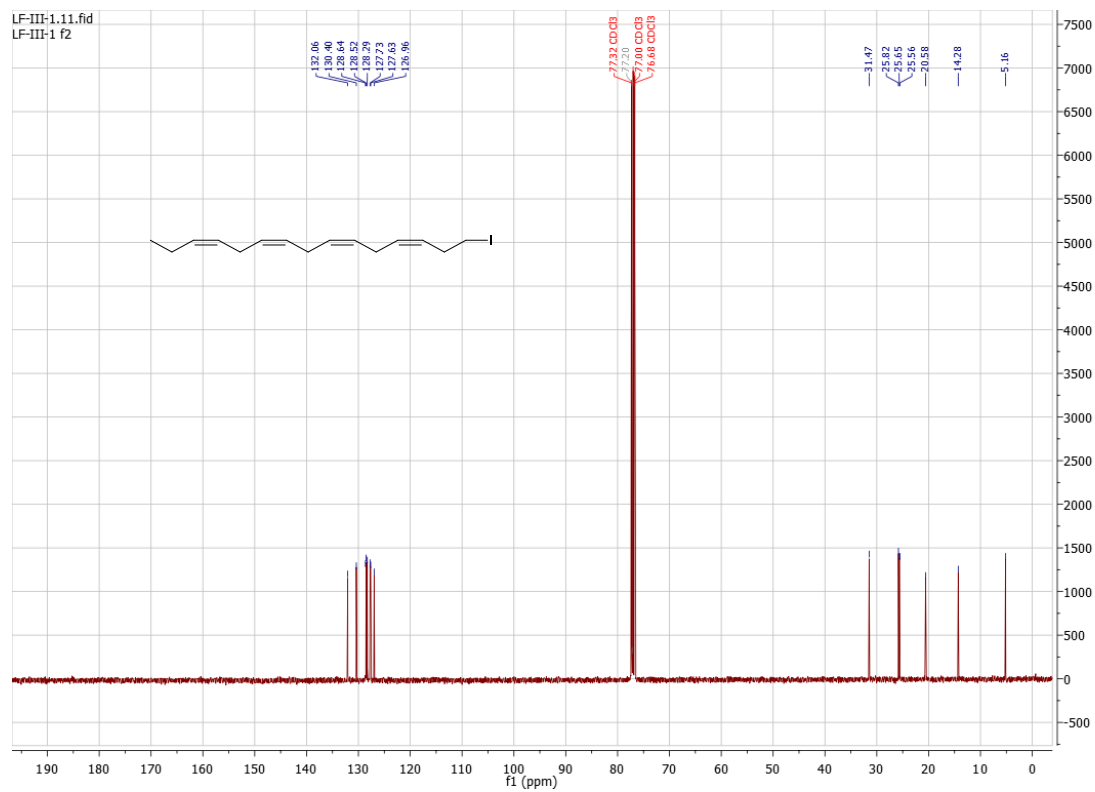


Figure S-4 <sup>13</sup>C NMR spectrum of 12

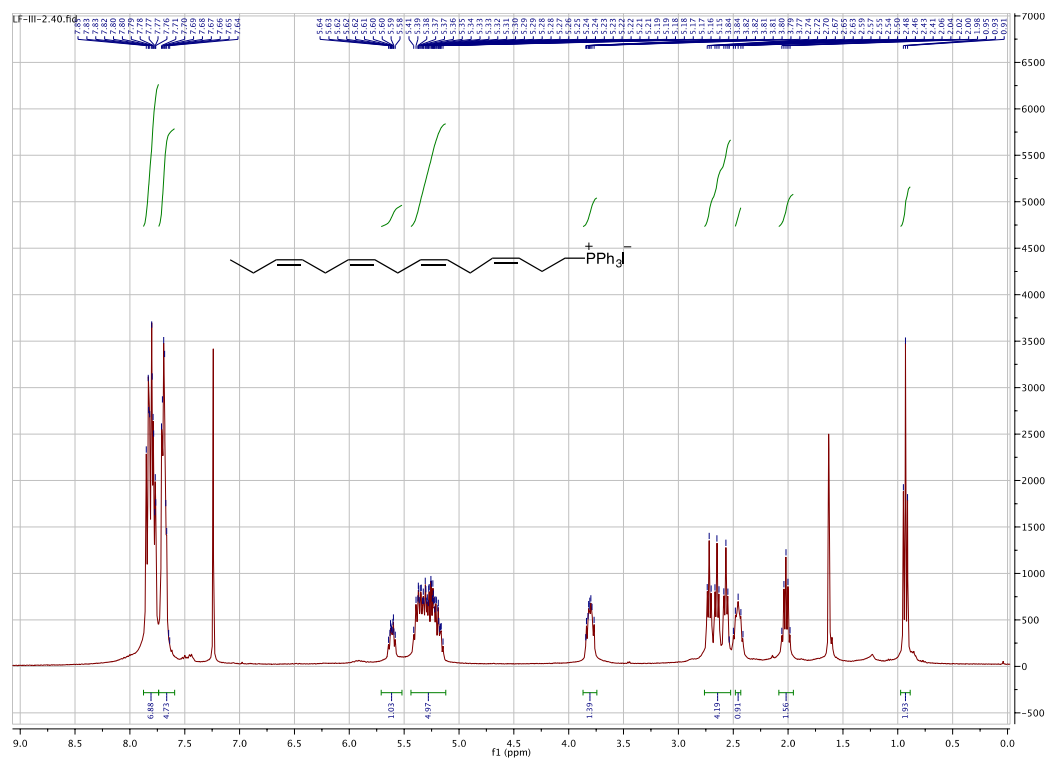


Figure S-5 <sup>1</sup>H NMR spectrum of 13

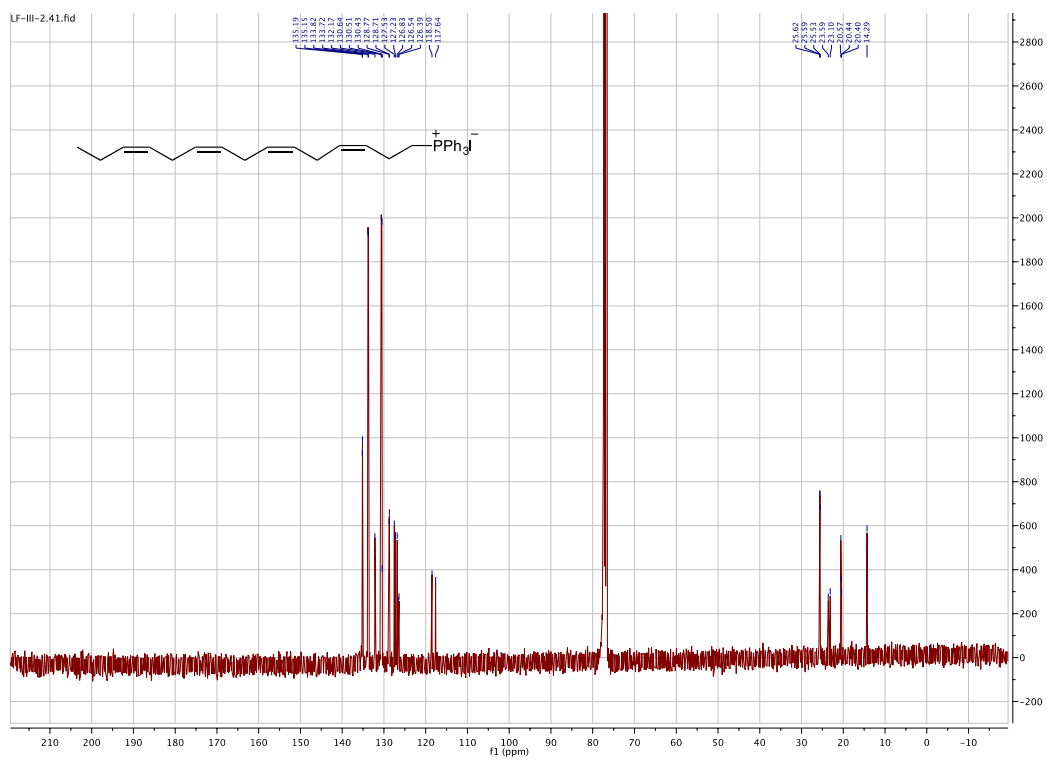


Figure S-6  $^{13}\text{C}$  NMR spectrum of 13

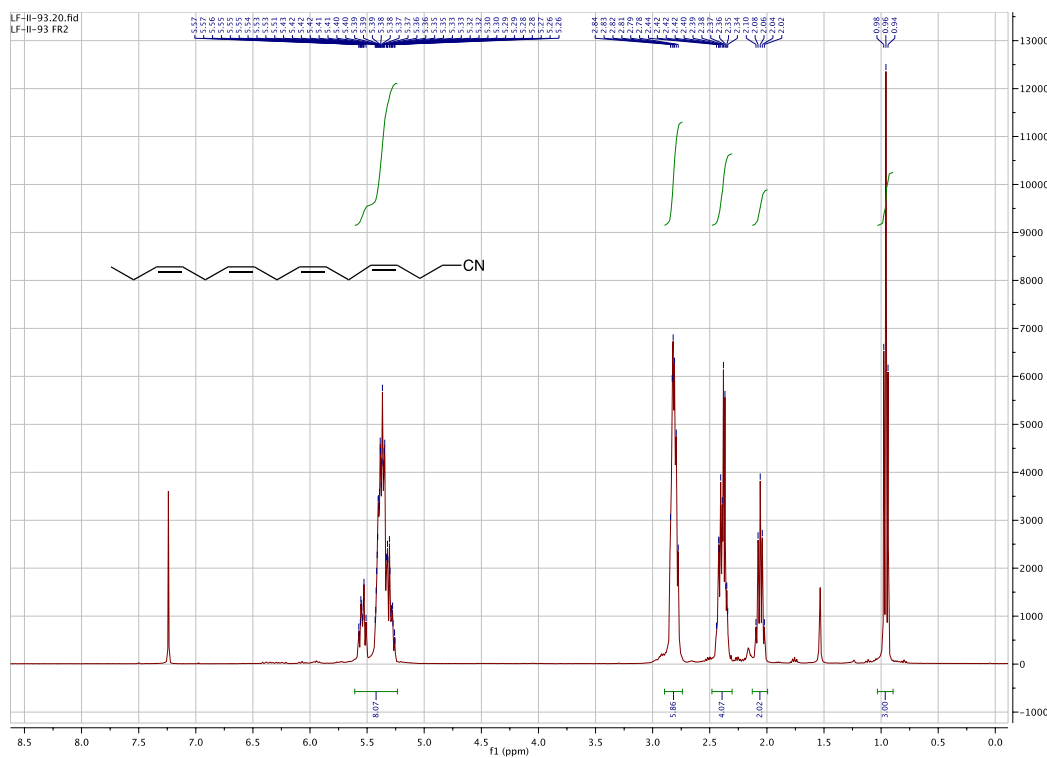


Figure S-7  $^1\text{H}$  NMR spectrum of 14

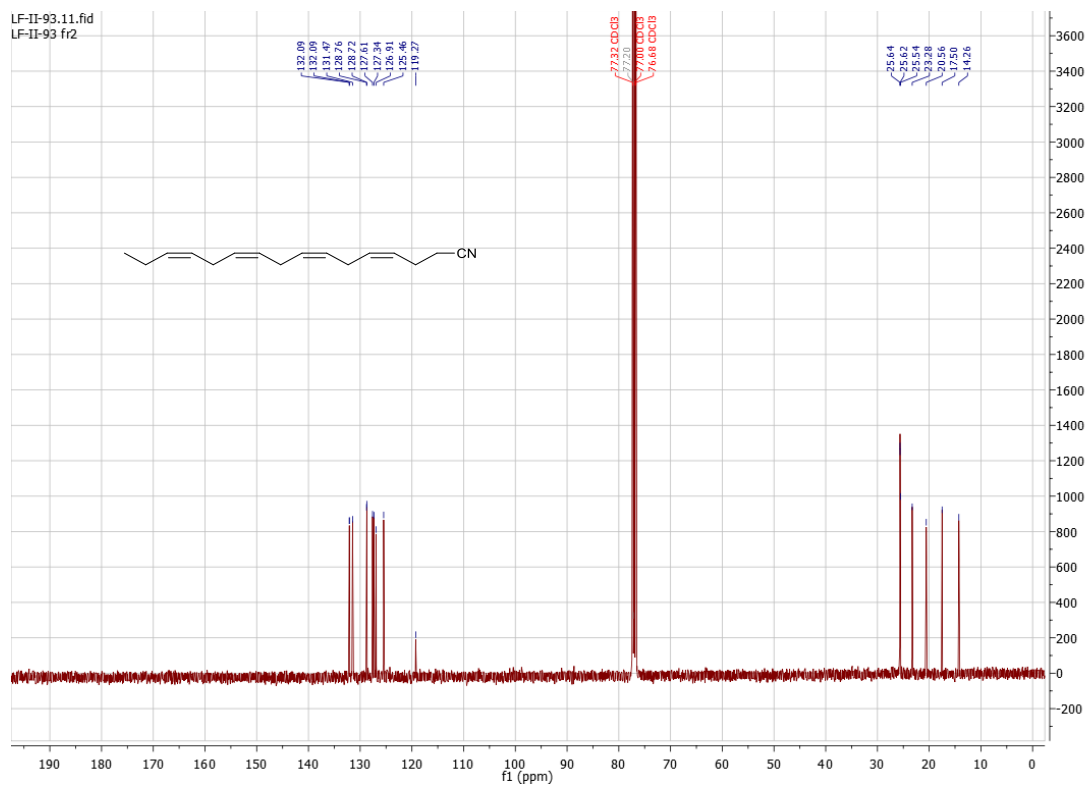


Figure S-6  $^{13}\text{C}$  NMR spectrum of 14

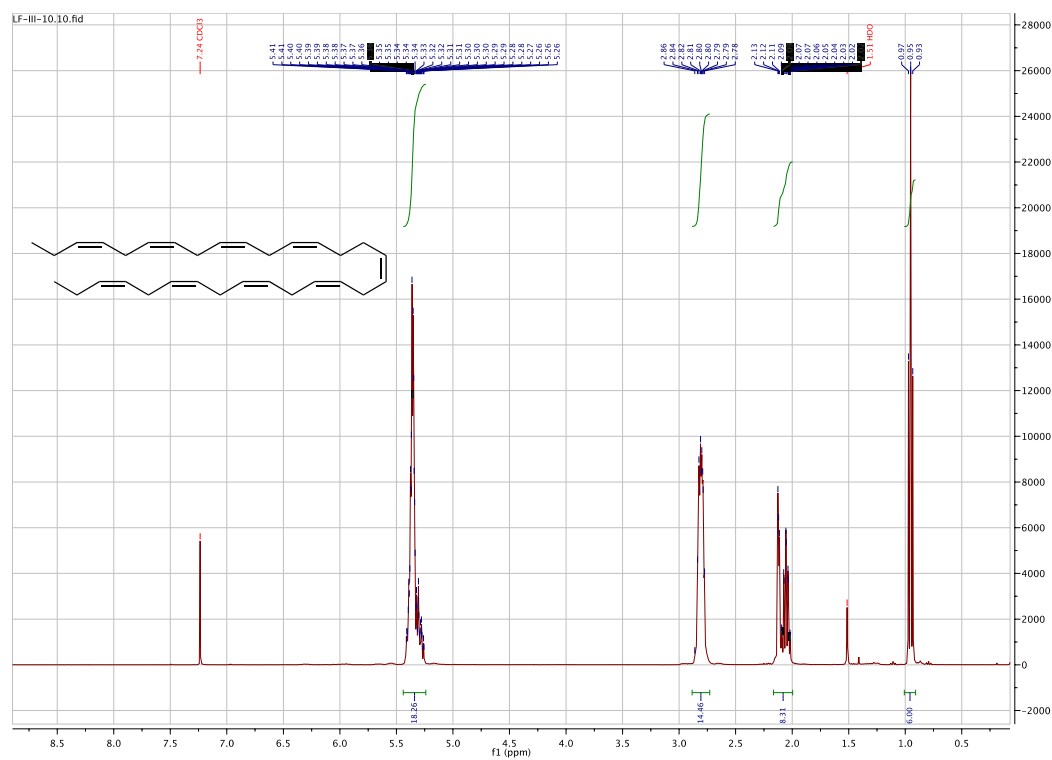
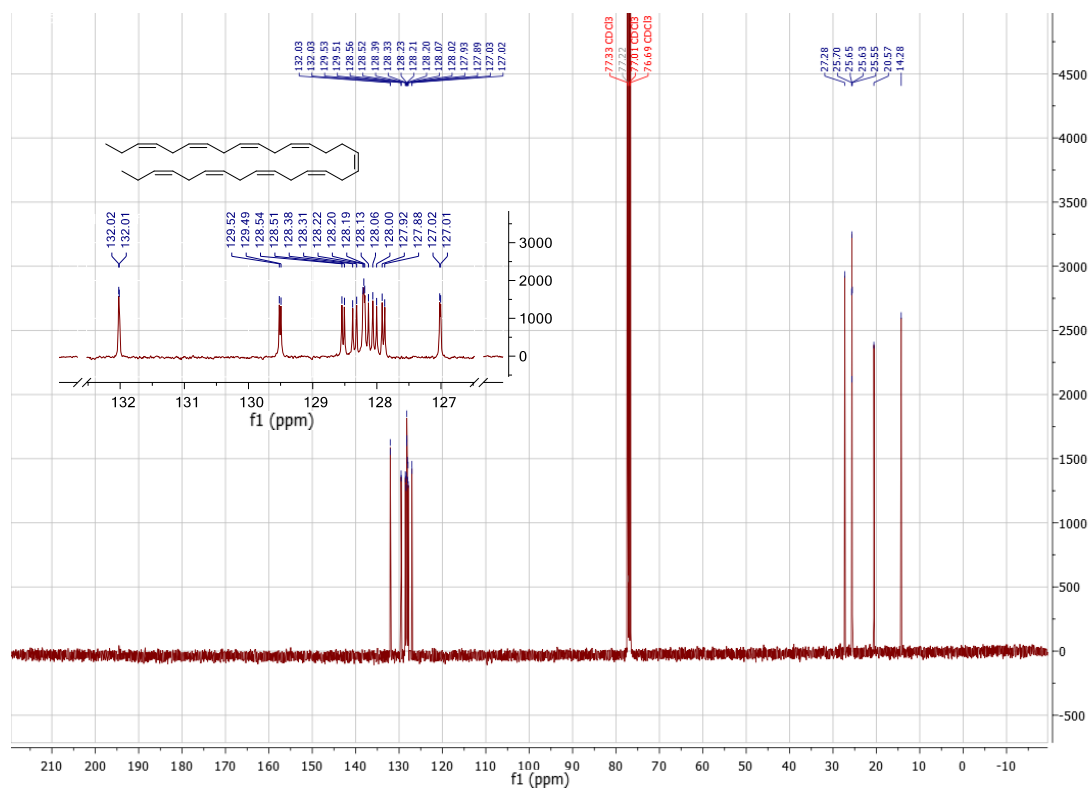
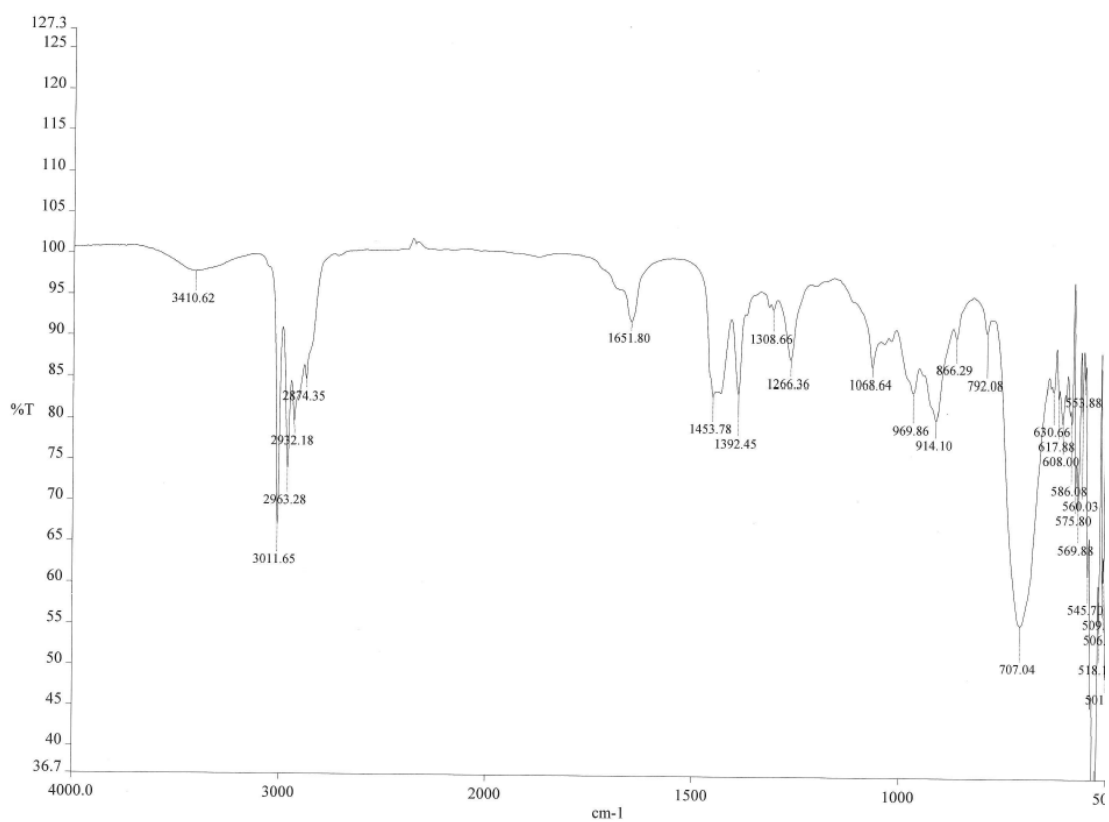


Figure S-9  $^1\text{H}$  NMR spectrum of 1



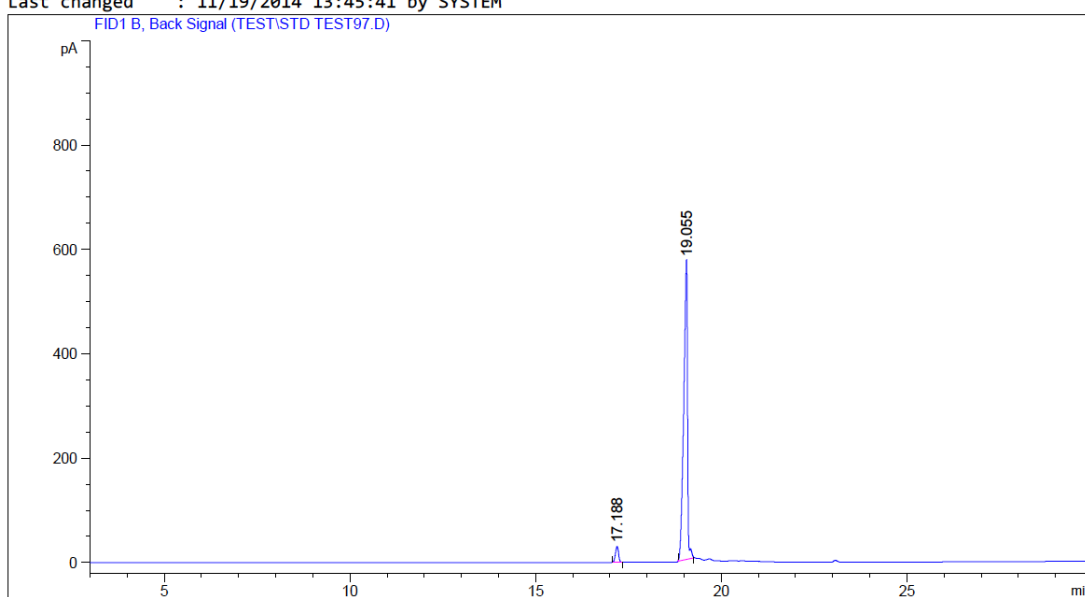
**Figure S-10** <sup>13</sup>C NMR spectrum of **1**



**Figure S-11** IR spectrum of **1**

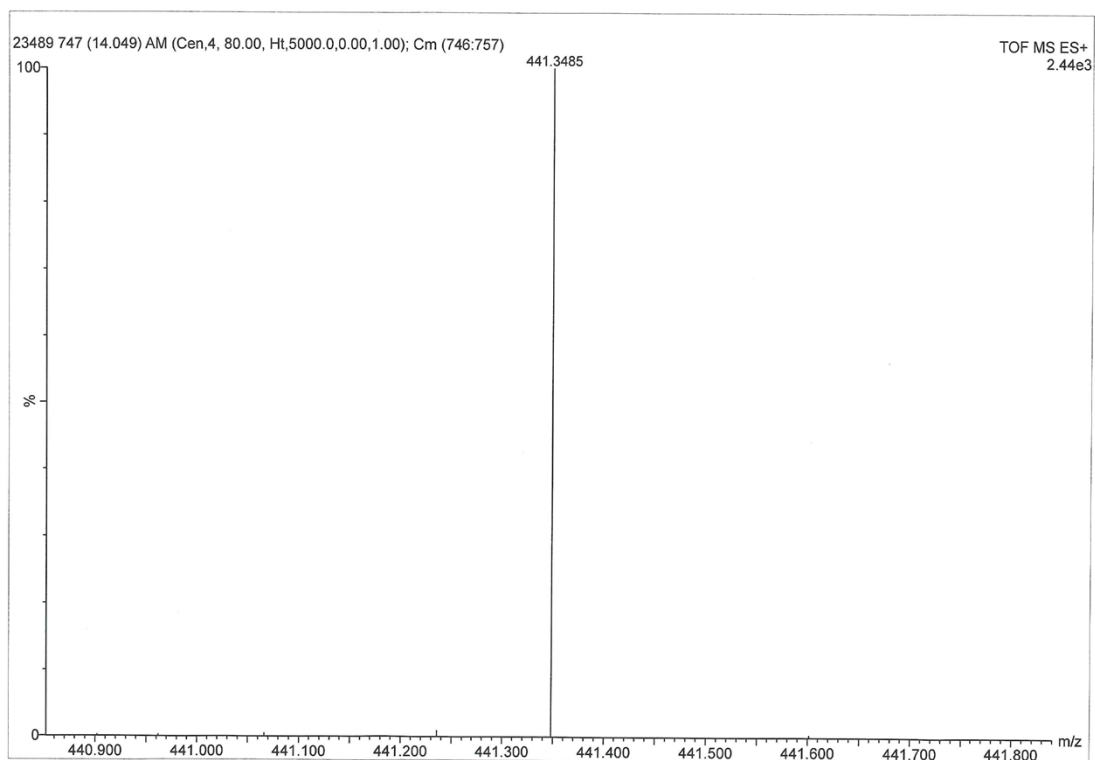


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 Last changed : 11/19/2014 13:45:41 by SYSTEM



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2	19.055	BB	0.0997	4116.70557	573.95050	95.90780
Totals :				4292.35738	604.26830	

**Figure S-12** GC chromatogram of **1**



**Figure S-13** CI-HRMS spectrum of **1**

Elemental Composition Analysis from Mass Spectrometric Data

Date: 2.2.2015

**Input**

Measured mass: 441.3485, Tolerance: 100 ppm

Element Mass min max

C	12.0000	20	40
H	1.0078	25	65
Na	22.9897	0	1

**RESULTS**

	C	H	Na	Mass	diff(amu)	diff(ppm)
1:	31	46	1	441.3497	-0.0012	-2.76
2:	33	45	0	441.3521	-0.0036	-8.21

Number of hits: 2