

Synthesis and Glycosidase Inhibition of Broussonetine M and Its Analogues

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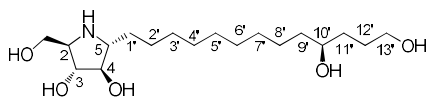
Supporting Information

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1. Comparison of NMR data of the synthetic broussonetine M (3) with natural product and the synthetic broussonetine M in literature

Table S1. Comparison of ¹H NMR of the synthetic broussonetine M (3) with natural product and the synthetic broussonetine M of J. Alberto Marco



		Natural Product ^b	Synthetic Broussonetine M (lit.) ^c	Compound 3
		(500 MHz, C ₅ D ₅ N)	(500 MHz, C ₅ D ₅ N)	(500 MHz, C ₅ D ₅ N)
Pyrrolidine Ring	CH ₂ OH	4.15 (dd, <i>J</i> = 11.0, 5.9 Hz), 4.22 (dd, <i>J</i> = 11.0, 5.9 Hz)	4.45 (dd, <i>J</i> = 22.5, 5.5 Hz), 4.41 (dd, <i>J</i> = 11.5, 5 Hz)	4.49–4.42 (m, 2H)
	2	3.75 (m)	4.26 (m)	4.31–4.28 (m, 1H)
	3	4.62 (t, <i>J</i> = 6.4 Hz)	4.90 (t, <i>J</i> = 7 Hz)	4.92 (t, <i>J</i> = 6.7 Hz)
	4	4.36 (t, <i>J</i> = 6.4 Hz)	4.65 (t, <i>J</i> = 7 Hz)	4.67 (t, <i>J</i> = 7.1 Hz)
	5	3.45 (m)	4.05 (br, q, <i>J</i> = 7.5 Hz)	4.09–4.05 (m, 1H)
Side Chain	1'	1.70 (m) ^a , 2.00 (m) ^a	2.15–2.10 (m, 1H), 2.05–2.00 (m, 1H)	2.15–2.09 (m, 1H), 2.03–1.97 (m, 1H)
	2'	1.66–1.16	1.90–1.50 (m)	1.90–1.79 (m) ^a , 1.74–1.56 (m) ^a
	3'	1.66–1.16	1.40–1.15 (m) ^a	1.33–1.07 (m)
	4'	1.66–1.16	1.40–1.15 (m) ^a	1.33–1.07 (m)
	5'	1.66–1.16	1.40–1.15 (m) ^a	1.33–1.07 (m)
	6'	1.66–1.16	1.40–1.15 (m) ^a	1.33–1.07 (m)
	7'	1.66–1.16	1.40–1.15 (m) ^a	1.33–1.07 (m)
	8'	1.66–1.16	1.90–1.50 (m) ^a	1.74–1.56 (m) ^a , 1.48–1.45 (m, 1H)
	9'	1.63 (m) ^a , 1.70 (m) ^a	1.90–1.50 (m) ^a	1.74–1.56 (m) ^a
	10'	3.90 (m)	3.90 (m)	3.92–3.87 (m 1H)
	11'	1.86 (m)	1.90–1.50 (m) ^a	1.90–1.79 (m) ^a
	12'	2.00 (m) ^a , 2.12 (m)	2.30–2.25 (br, m)	2.34–2.29 (m, 2H)
	13'	3.95 (t, <i>J</i> = 6.4 Hz)	3.96 (t, <i>J</i> = 6.5 Hz)	3.96 (t, <i>J</i> = 6.4 Hz)

a) Overlapped signals; b) Shibano, M.; Tsukamoto, D.; Fujimoto, R.; Masui, Y.; Sugimoto, H.; Kusano, G. Studies on the Constituents of Broussonetia Species. VII. Four New Pyrrolidine Alkaloids, Broussonetines M, O, P, and Q, as Inhibitors of Glycosidase, from Broussonetia kazinoki SIEB. *Chem. Pharm. Bull.* **2000**, *48*, 1281–1285; c) Ribes, C.; Falomir, E.; Murga, J.; Carda, M.; Alberto Marco, J. Convergent, stereoselective syntheses of the glycosidase inhibitors broussonetines D and M. *Org. Biomol. Chem.* **2009**, *7*, 1355–1360.

Table S2. Comparison of ^{13}C NMR of the synthetic broussonetine M (**3**) with natural product and the synthetic broussonetine M of J. Alberto Marco

		Natural Product ^b	Synthetic Broussonetine M (lit.) ^c	Compound 3
		(500 MHz, C ₅ D ₅ N)	(500 MHz, C ₅ D ₅ N)	(500 MHz, C ₅ D ₅ N)
Pyrrolidine Ring	CH ₂ OH	63.45	59.2	59.7
	2	64.17	65.0	65.2
	3	80.23	76.2	76.7
	4	84.01	80.3	80.7
	5	62.01	62.7	63.0
Side Chain	1'	35.44	30.2	30.3
	2'–8'	30.10	29.9	29.9
		30.07	29.7	29.8
		29.94	29.5	29.6
		29.88	29.4	29.5
		29.83	29.3	29.4
		27.22	26.6	26.7
	26.29	26.1	26.3	
	9'	38.27	38.3	38.5
	10'	70.94	70.8	70.9
	11'	34.93	35.1	35.2
12'	30.17	31.5	31.9	
13'	62.34	62.3	62.4	

a) Shibano, M.; Tsukamoto, D.; Fujimoto, R.; Masui, Y.; Sugimoto, H.; Kusano, G. Studies on the Constituents of Broussonetia Species. VII. Four New Pyrrolidine Alkaloids, Broussonetines M, O, P, and Q, as Inhibitors of Glycosidase, from Broussonetia kazinoki SIEB. *Chem. Pharm. Bull.* **2000**, *48*, 1281-1285; b) Ribes, C.; Falomir, E.; Murga, J.; Carda, M.; Alberto Marco, J. Convergent, stereoselective syntheses of the glycosidase inhibitors broussonetines D and M. *Org. Biomol. Chem.* **2009**, *7*, 1355-1360.

Copies of NMR spectra for all new compounds

Compound 21

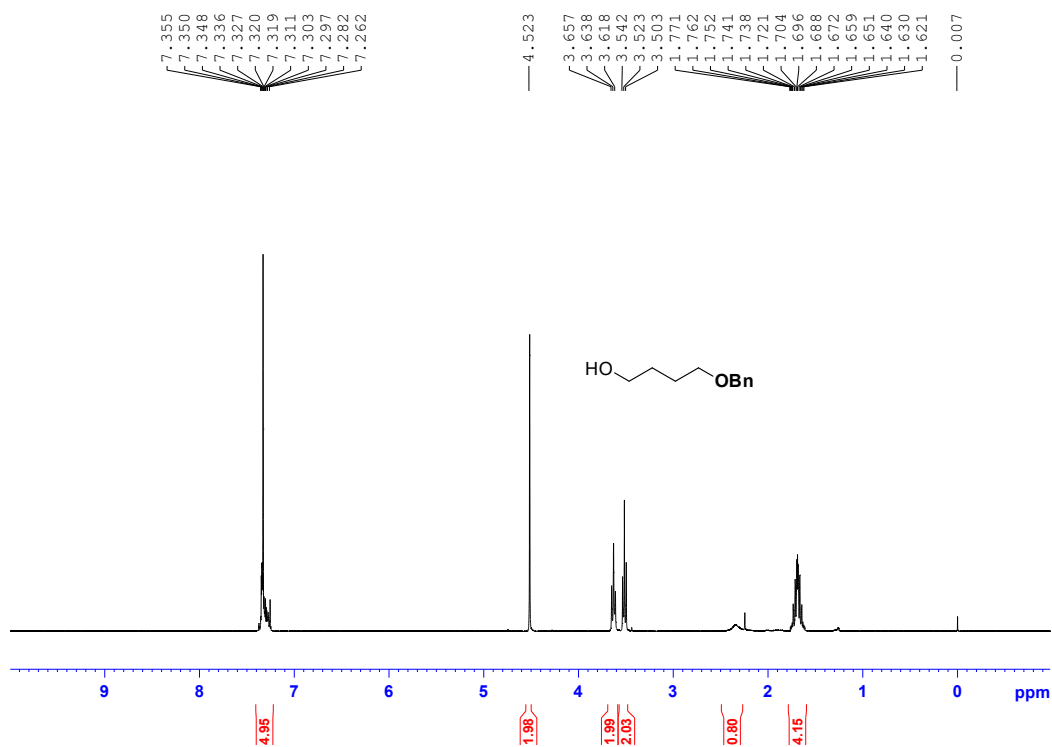


Figure S1

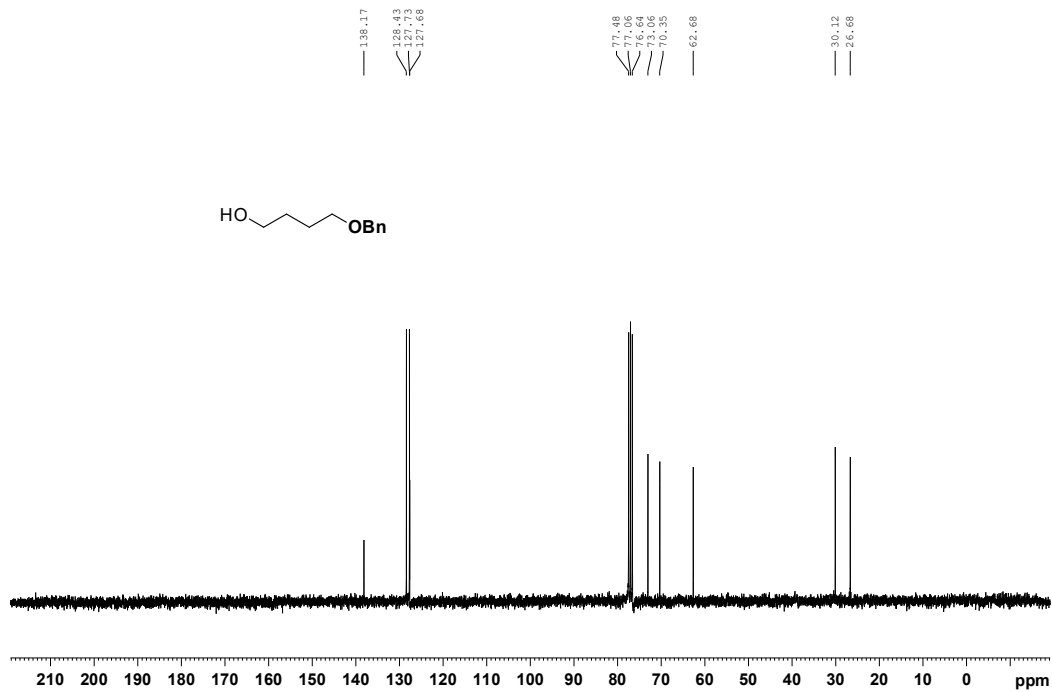


Figure S2

Compound 16

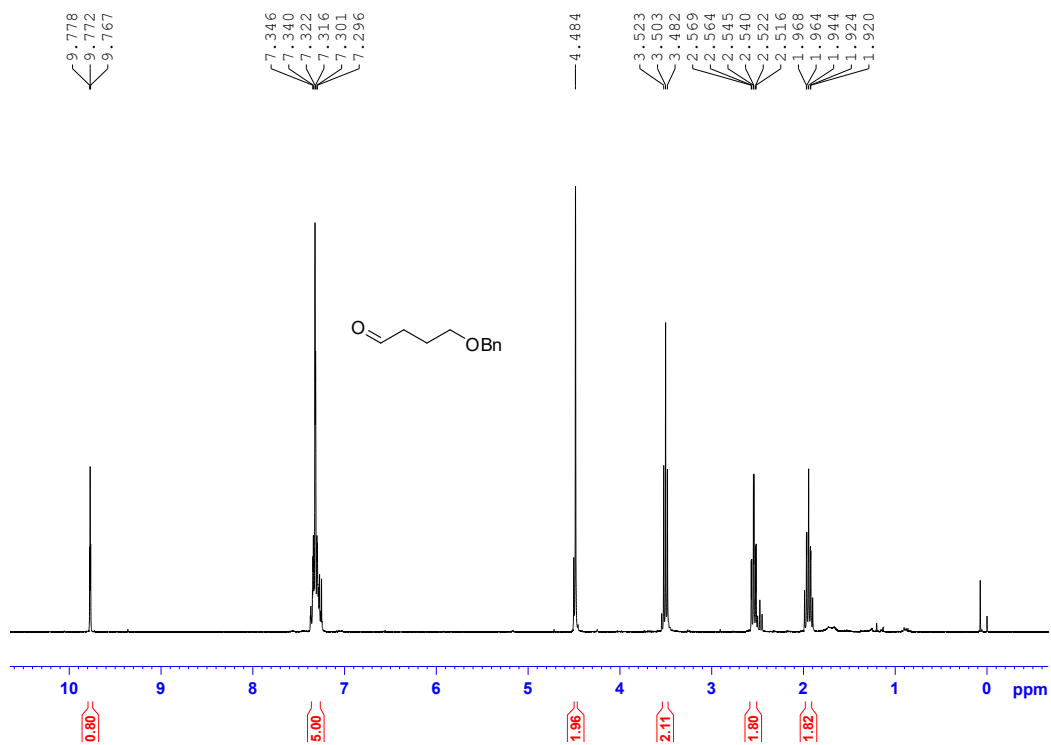


Figure S3

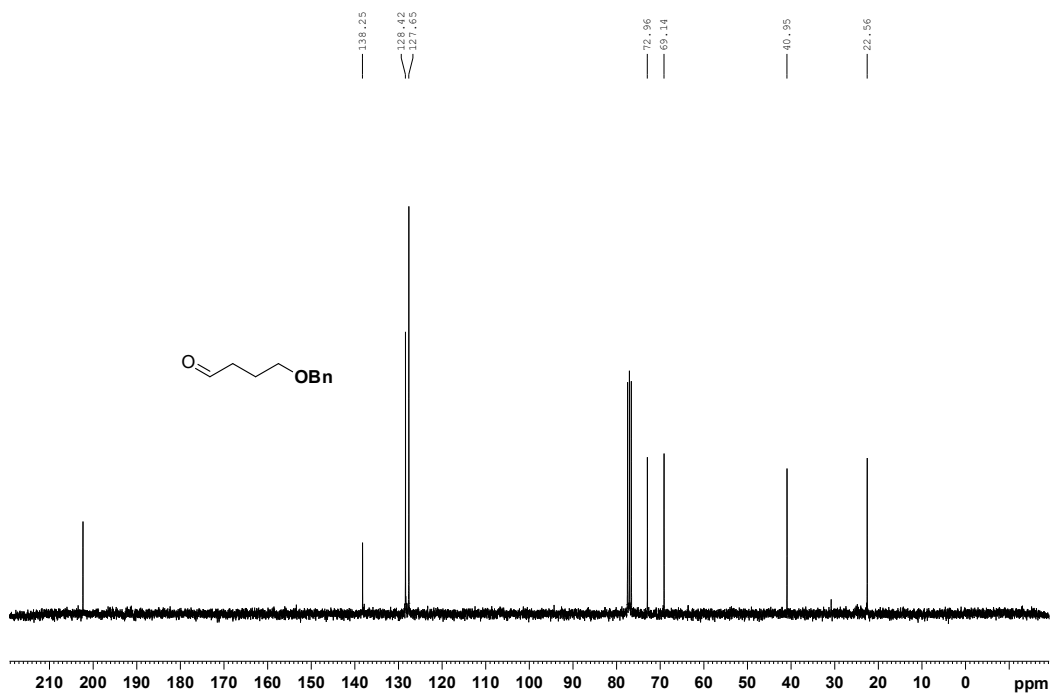


Figure S4

Compound 15

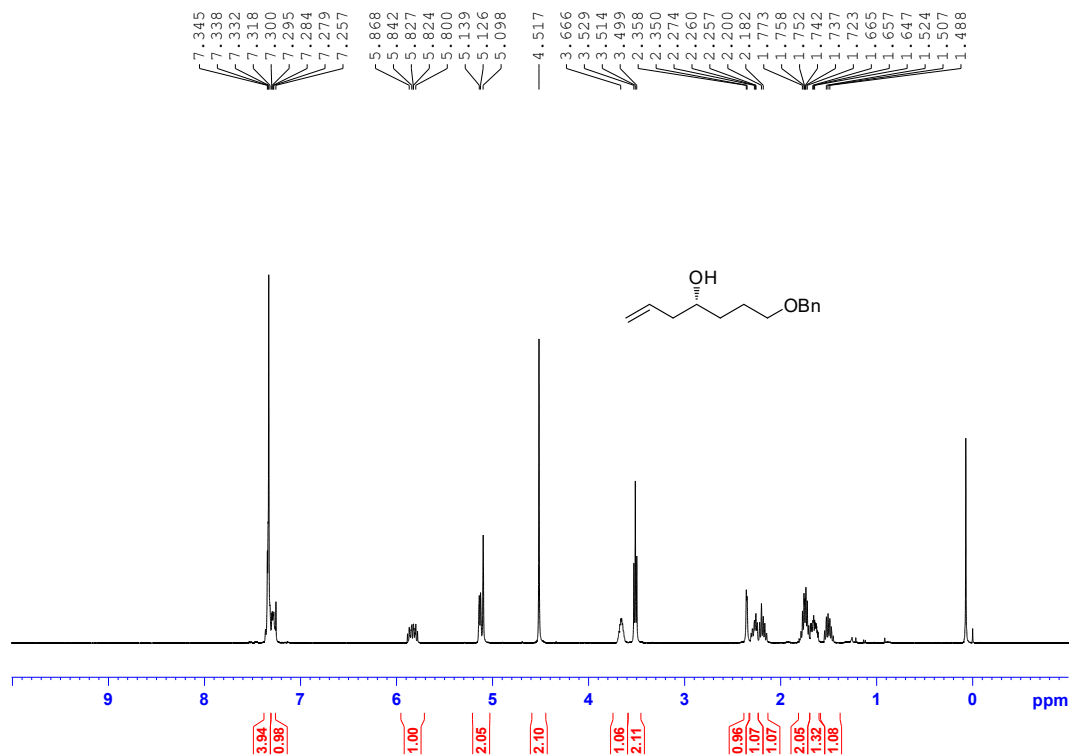


Figure S7

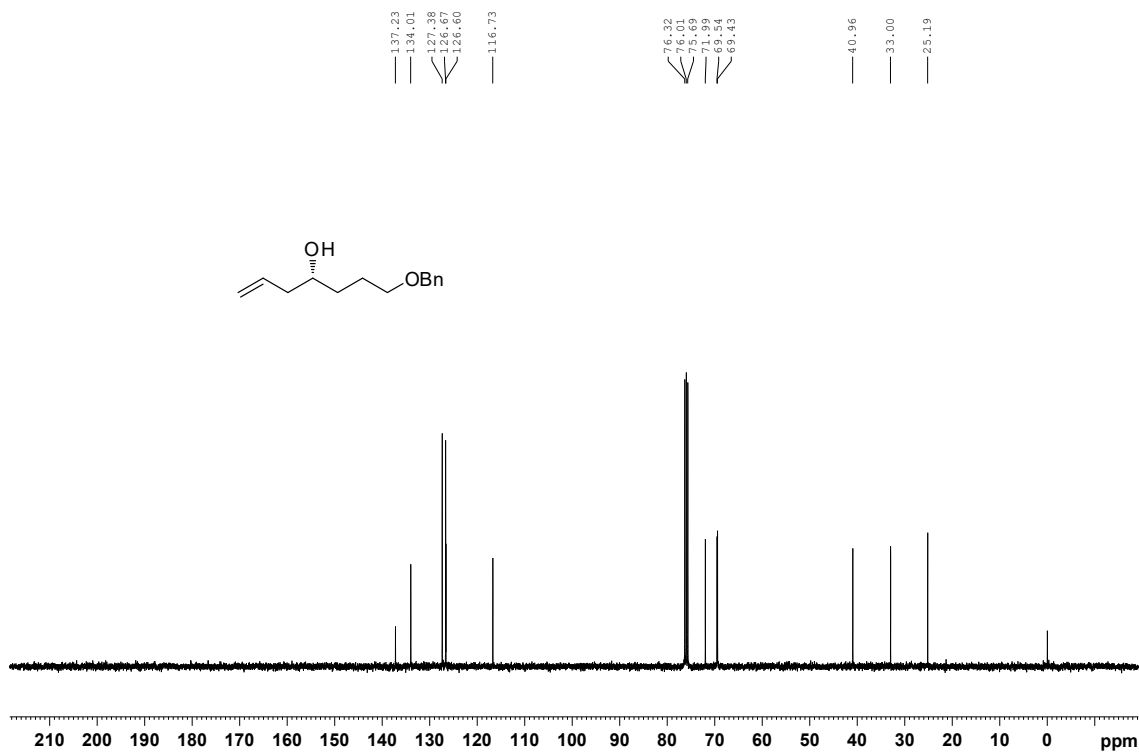


Figure S8

Compound 19

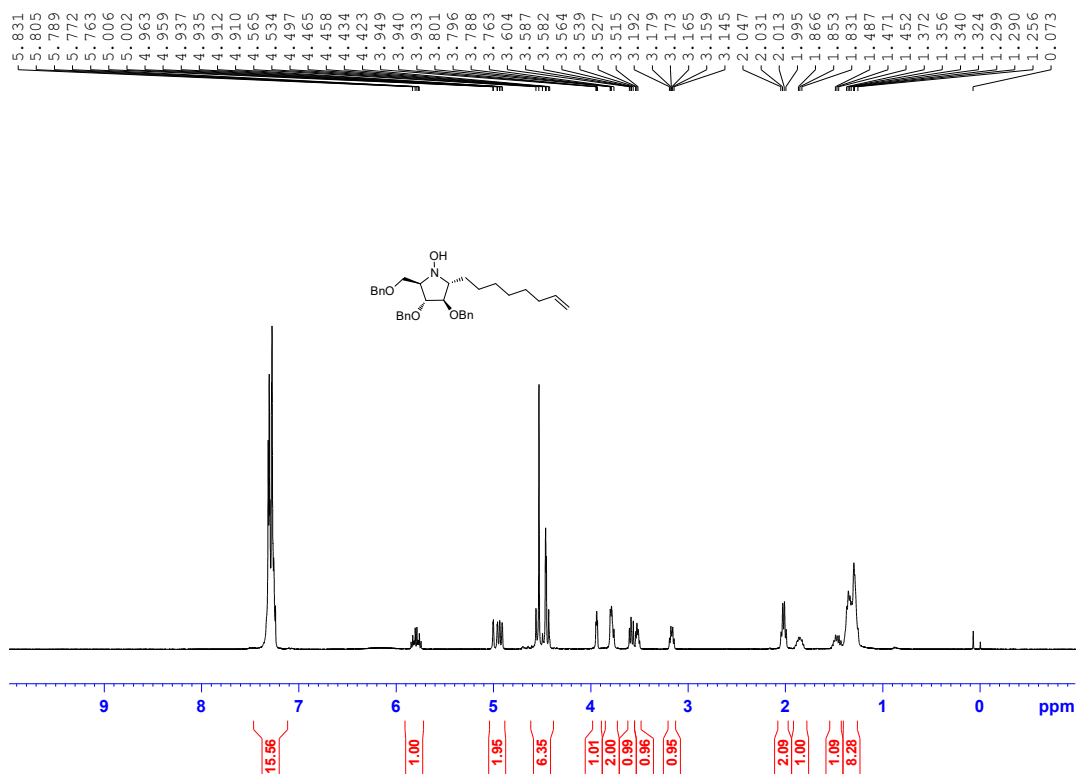


Figure S9

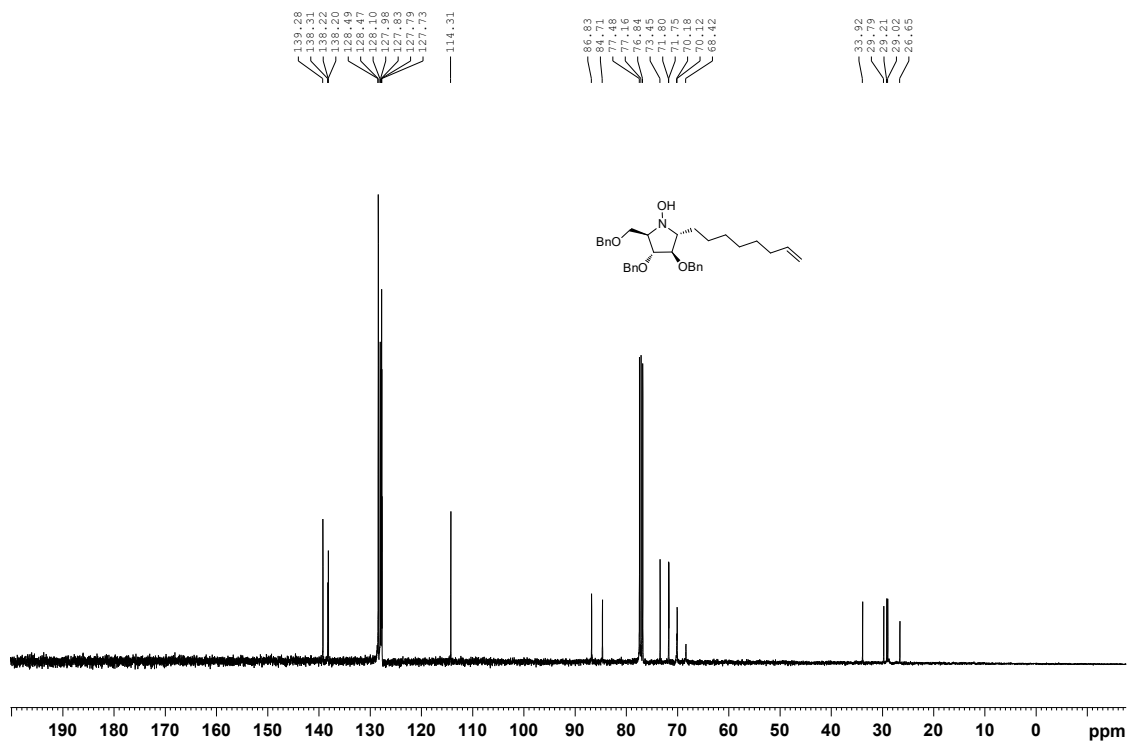


Figure S10

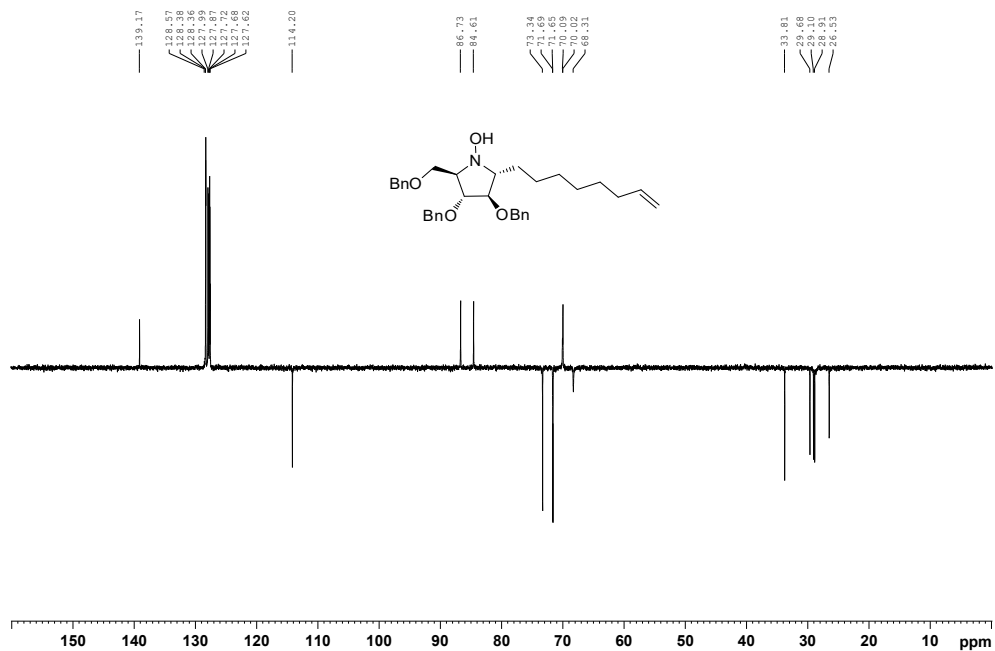


Figure S11

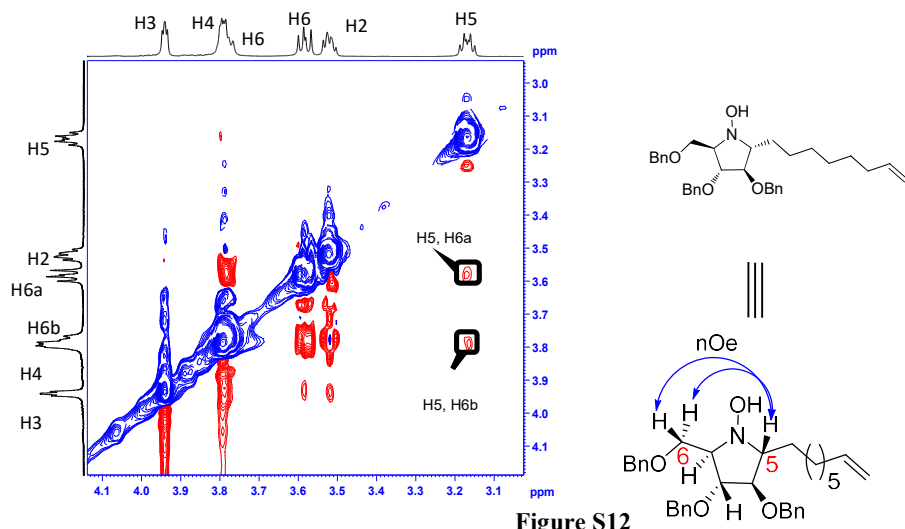
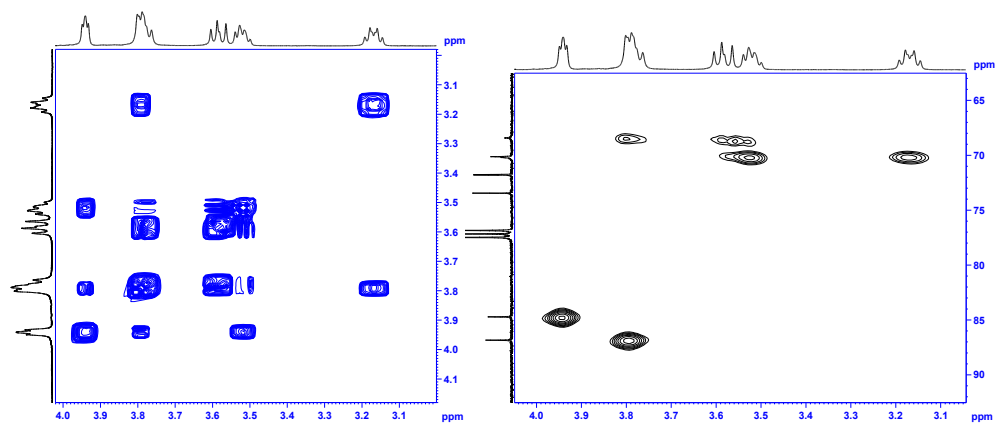


Figure S12

Compound *ent*-19

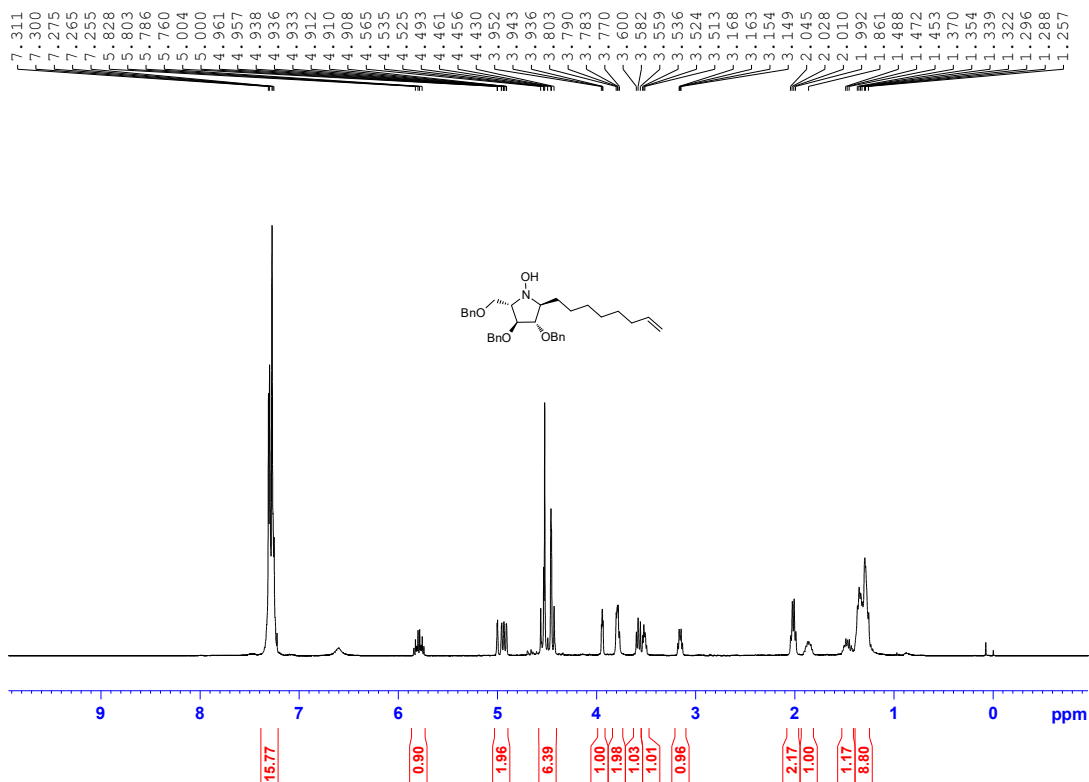


Figure S13

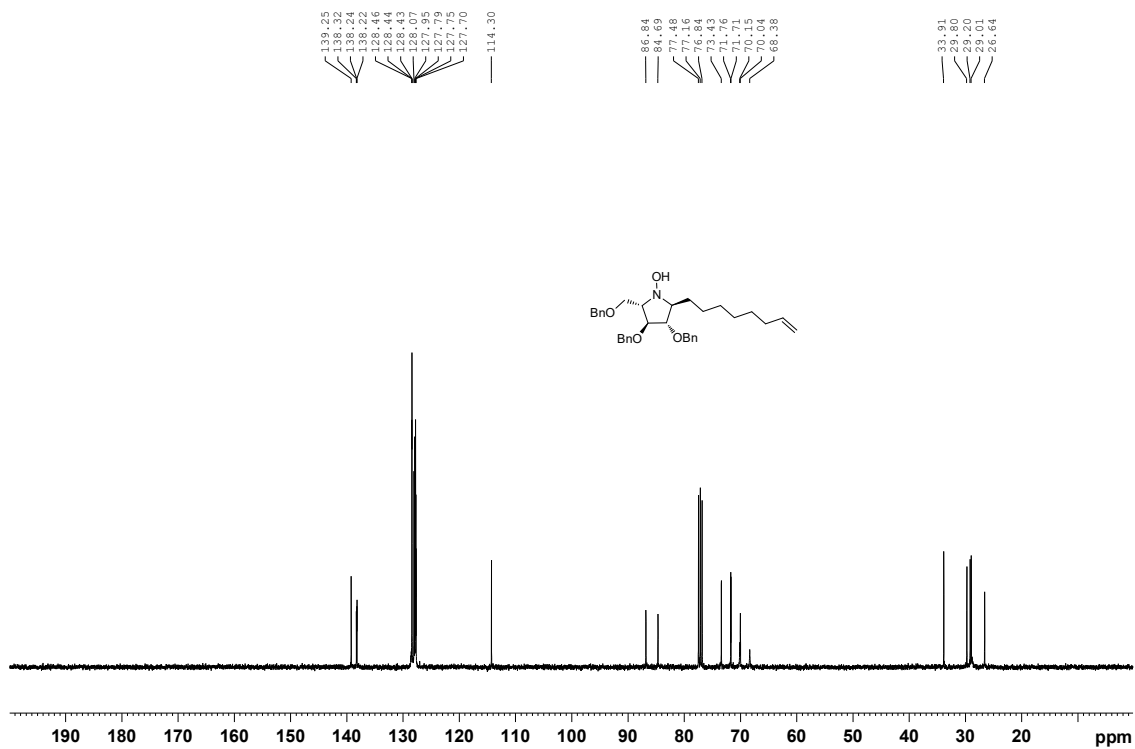


Figure S14

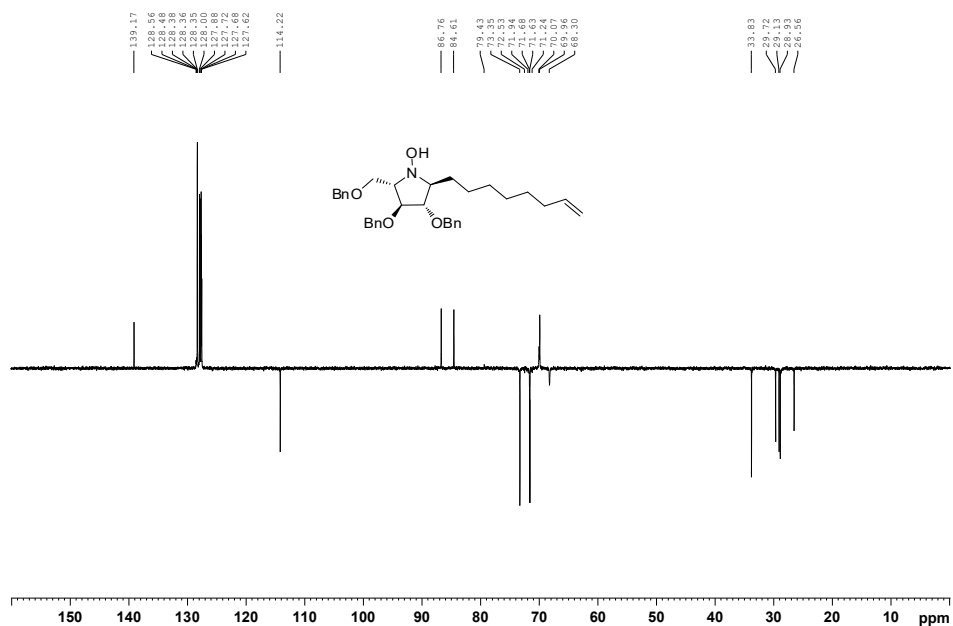


Figure S15

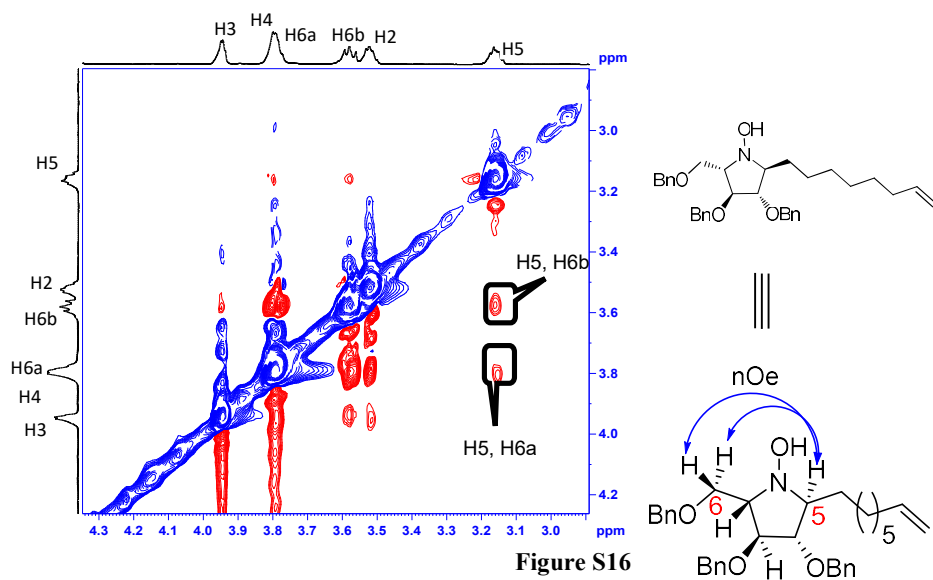
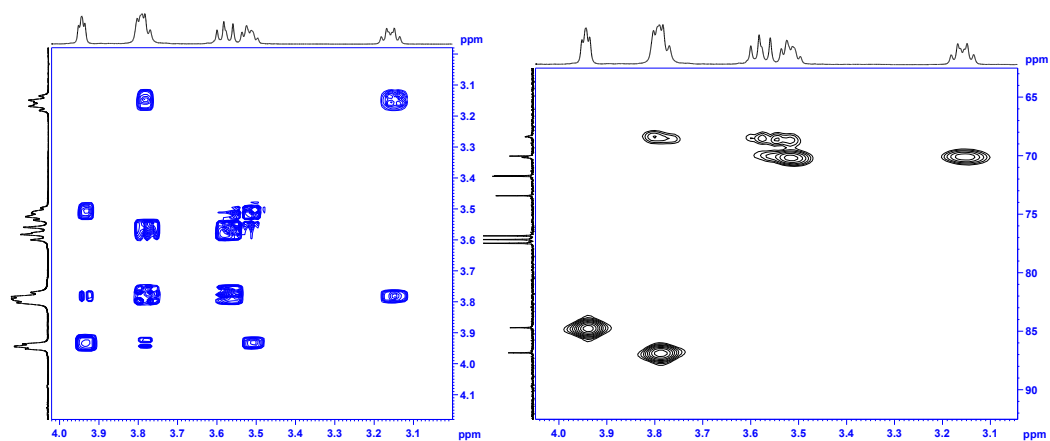


Figure S16

Compound *ent*-3-*epi*-19

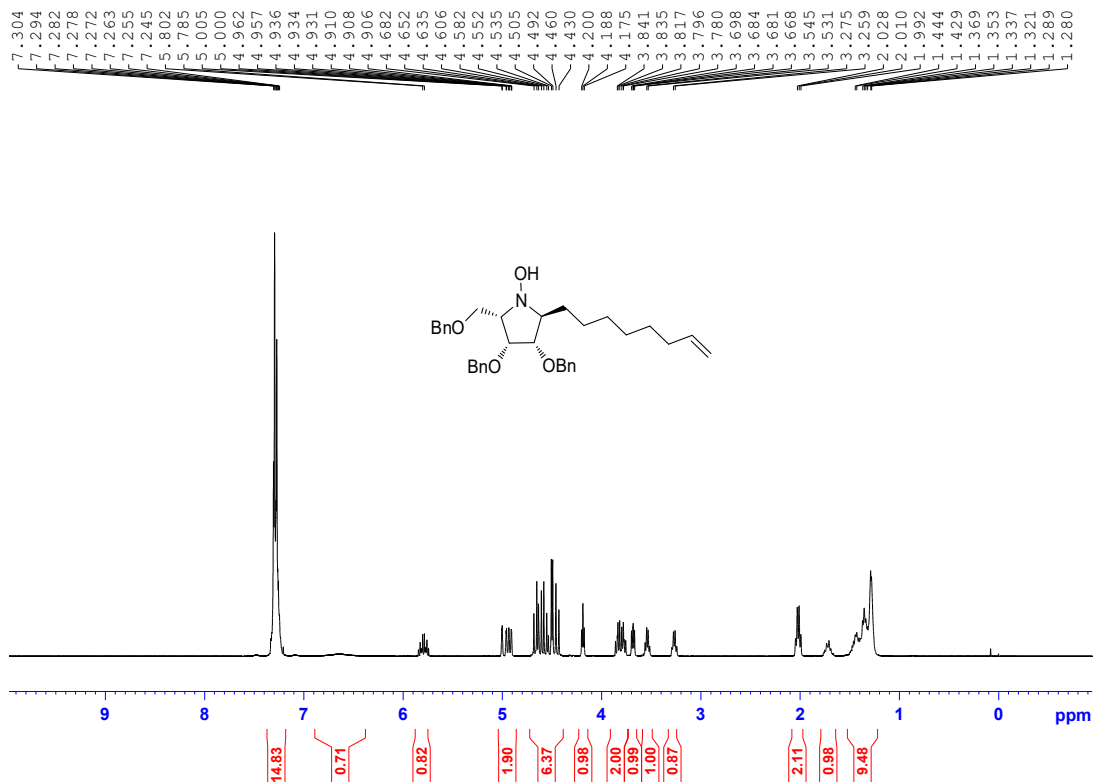


Figure S17

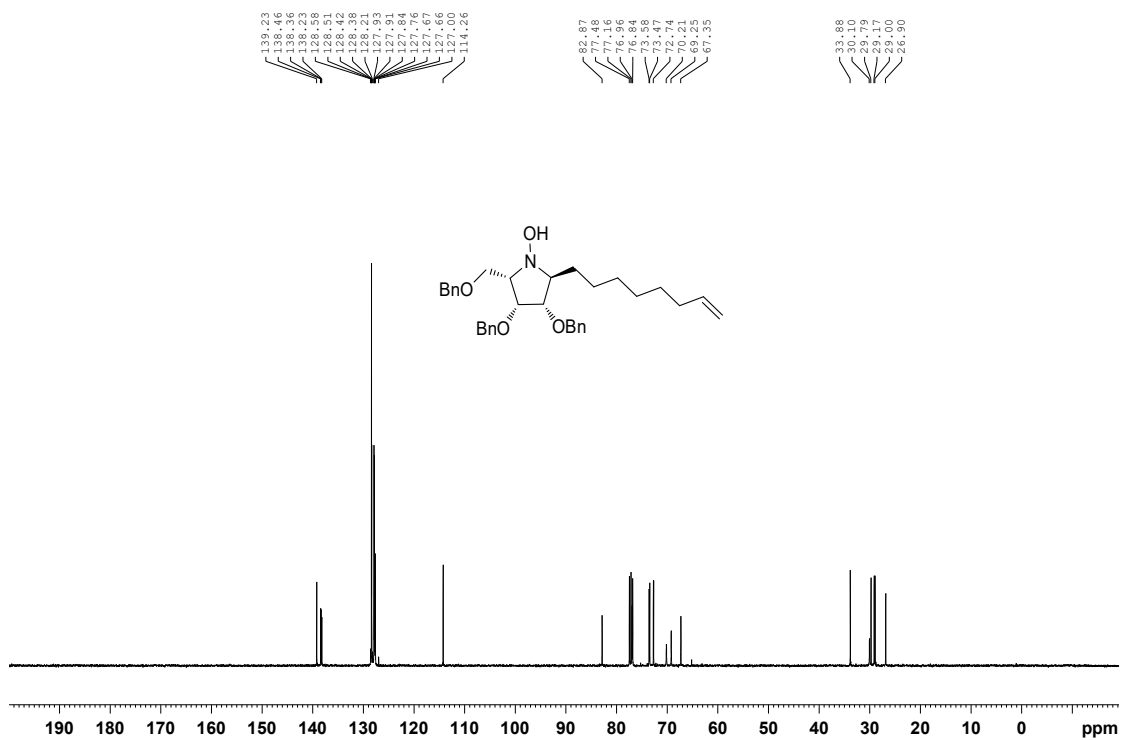


Figure S18

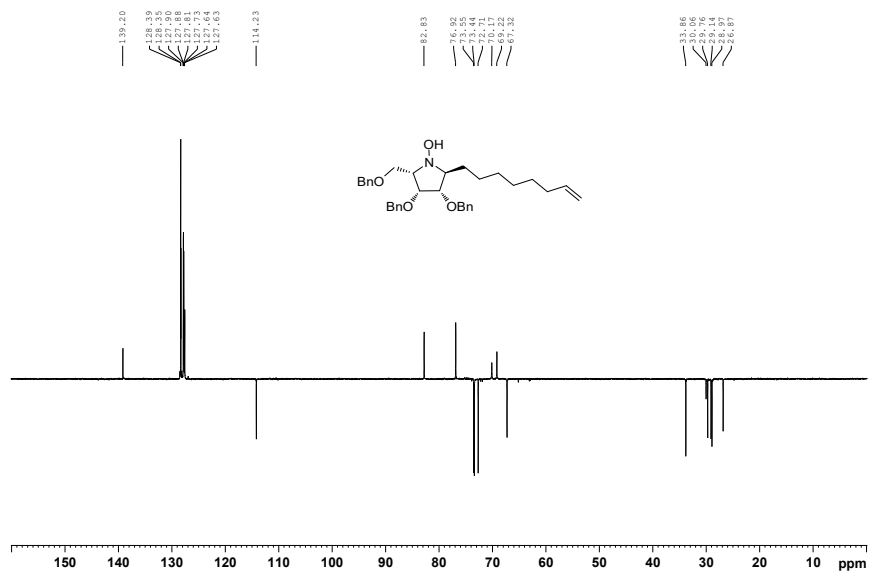


Figure S19

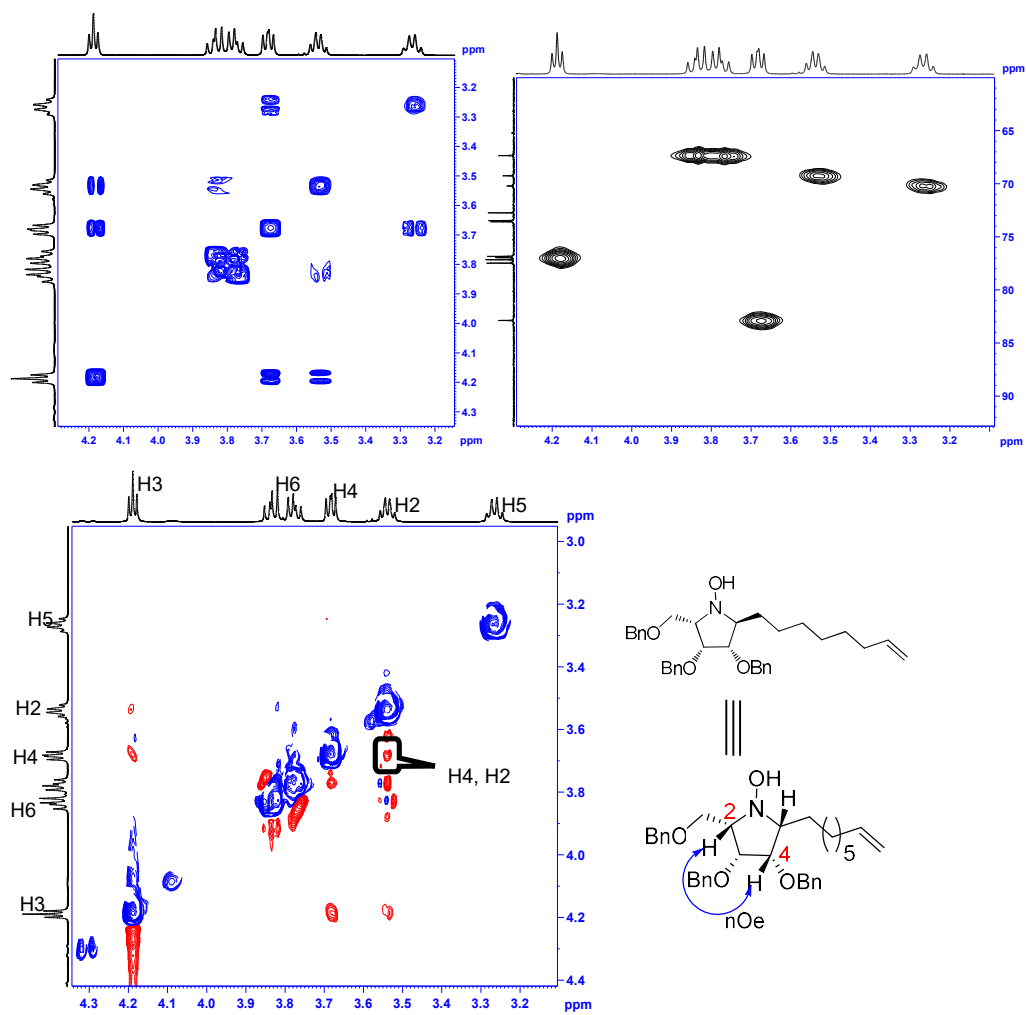


Figure S20

Compound 2-*epi*-19

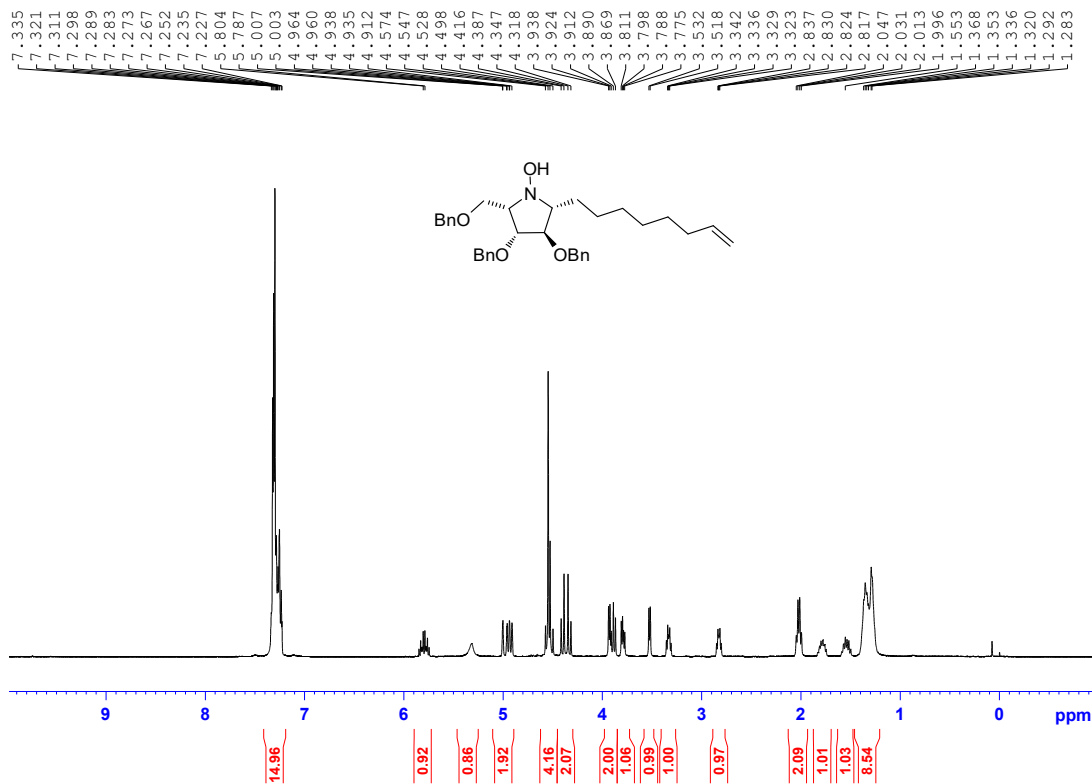


Figure S21

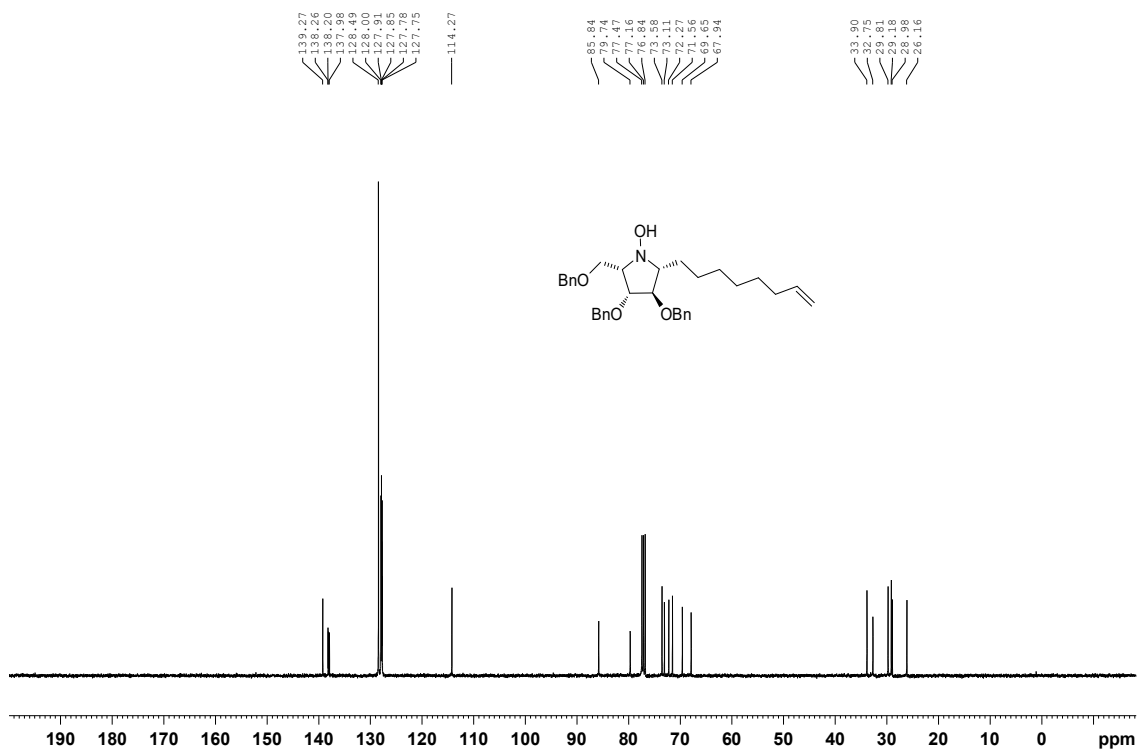


Figure S22

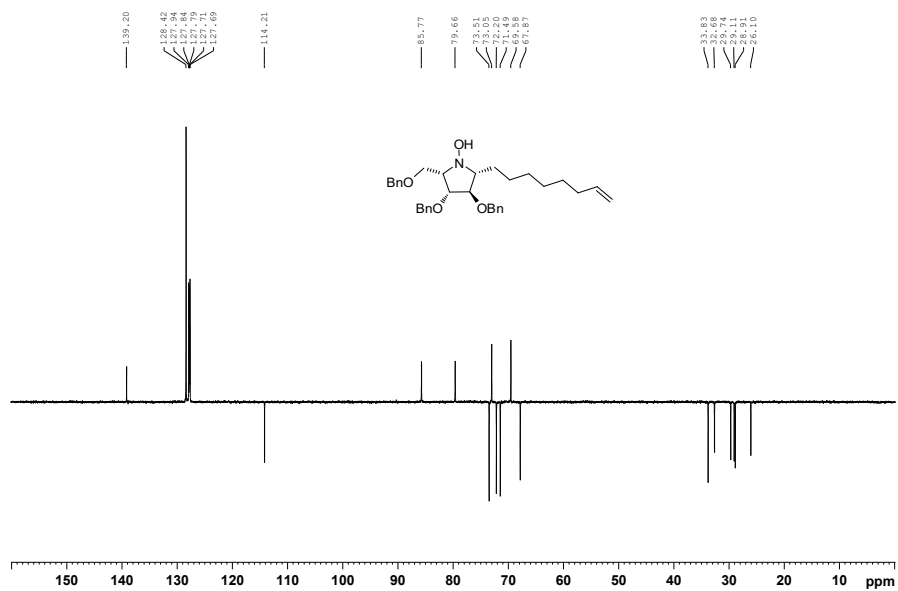


Figure S23

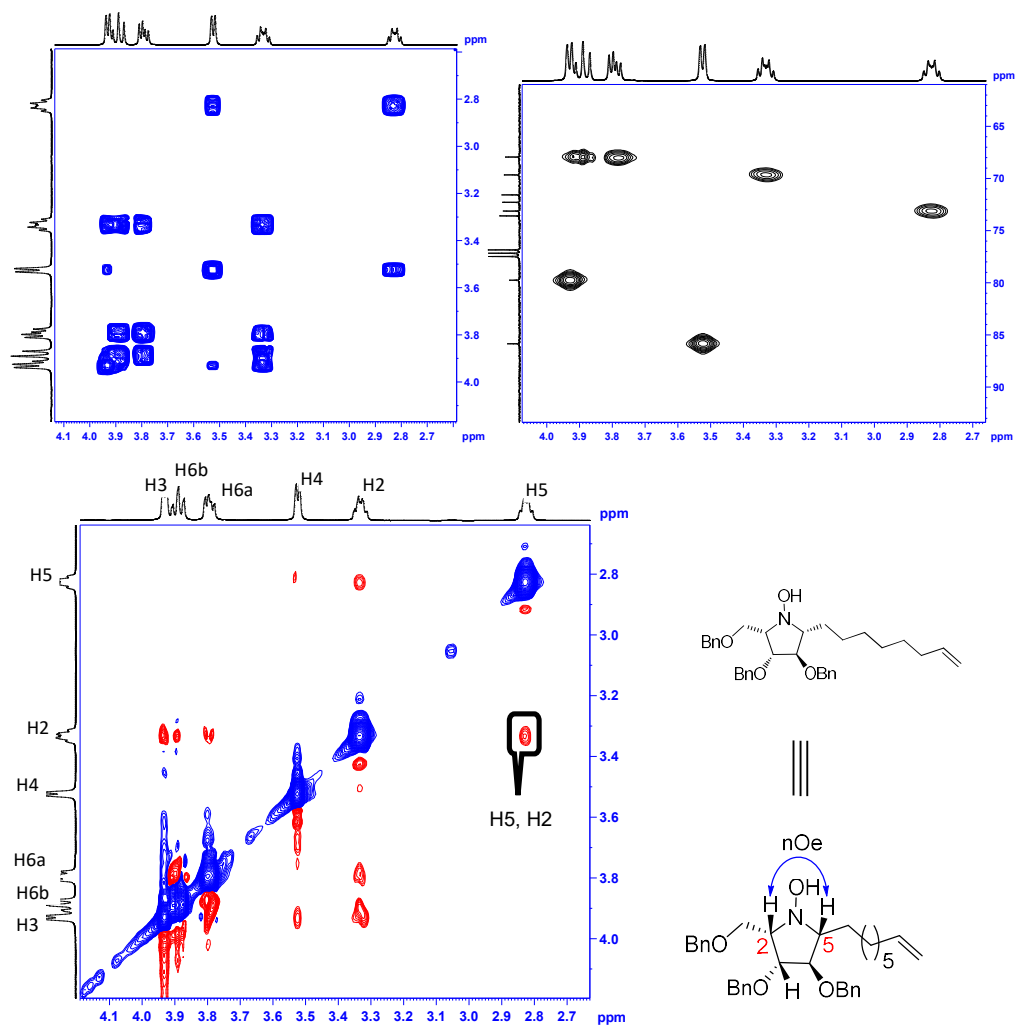


Figure S24

Compound 13

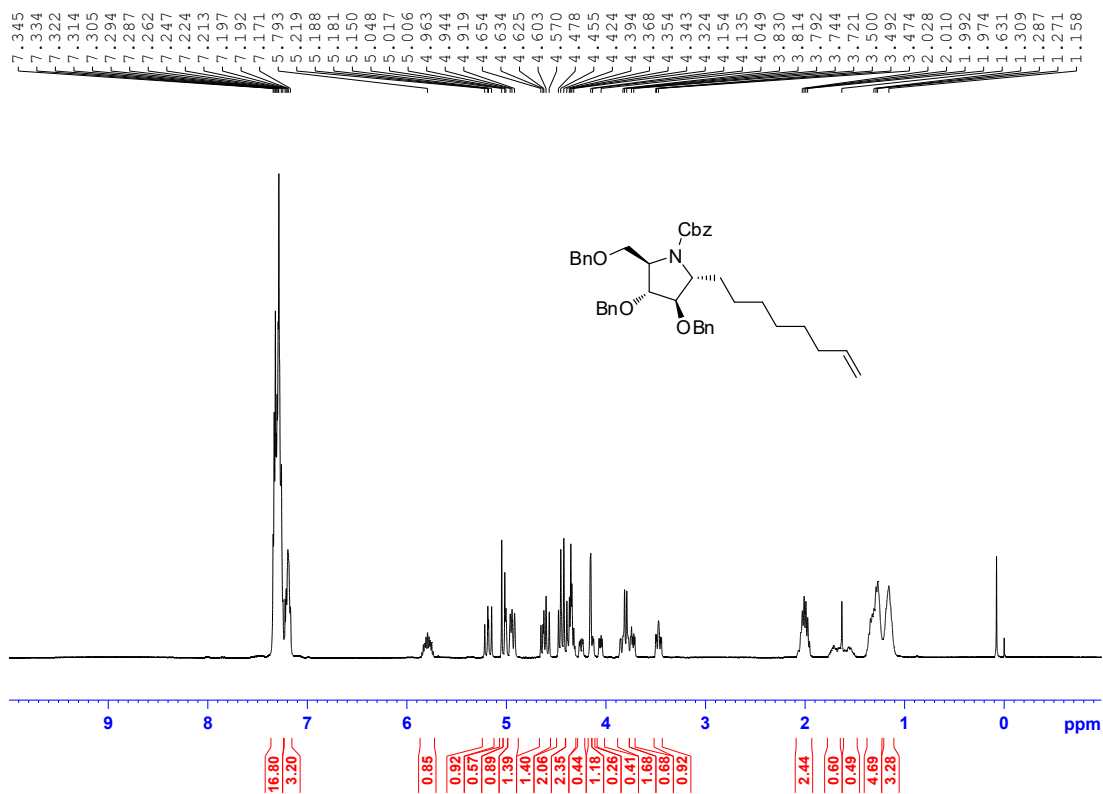


Figure S25

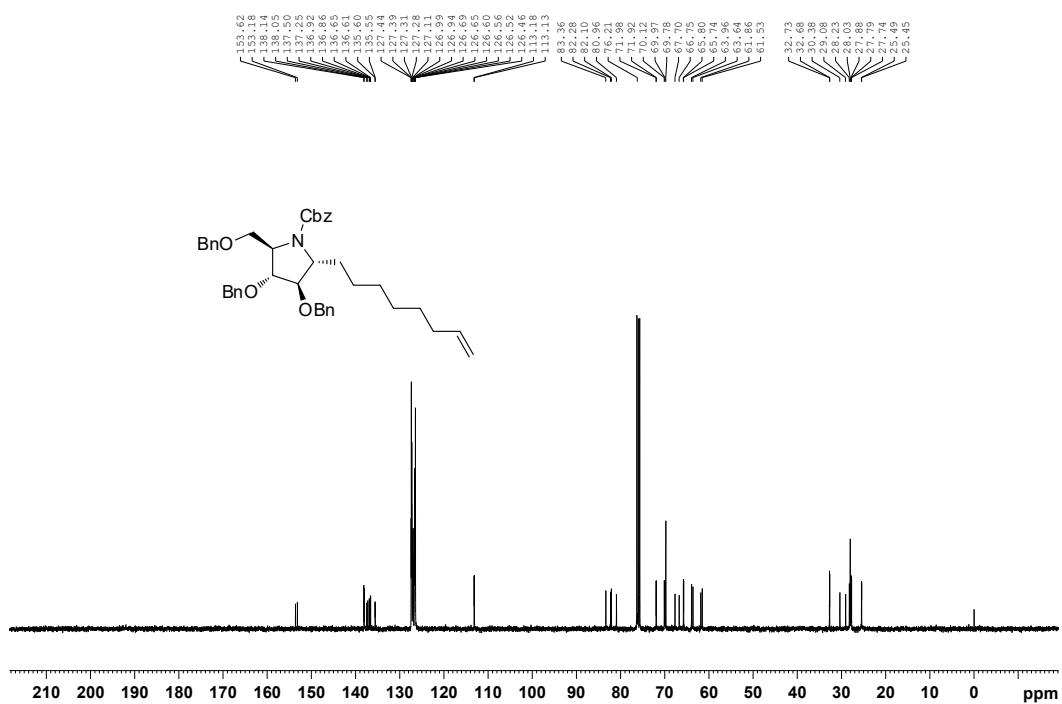


Figure S26

Compound *ent*-13

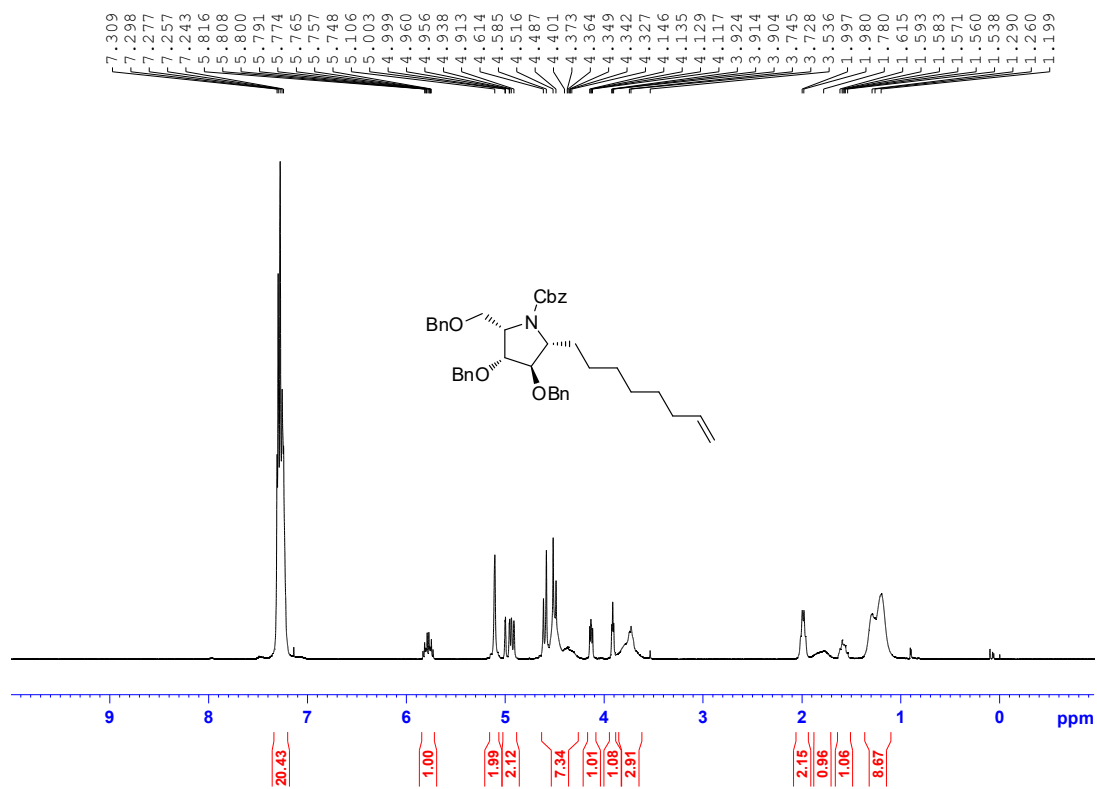


Figure S27

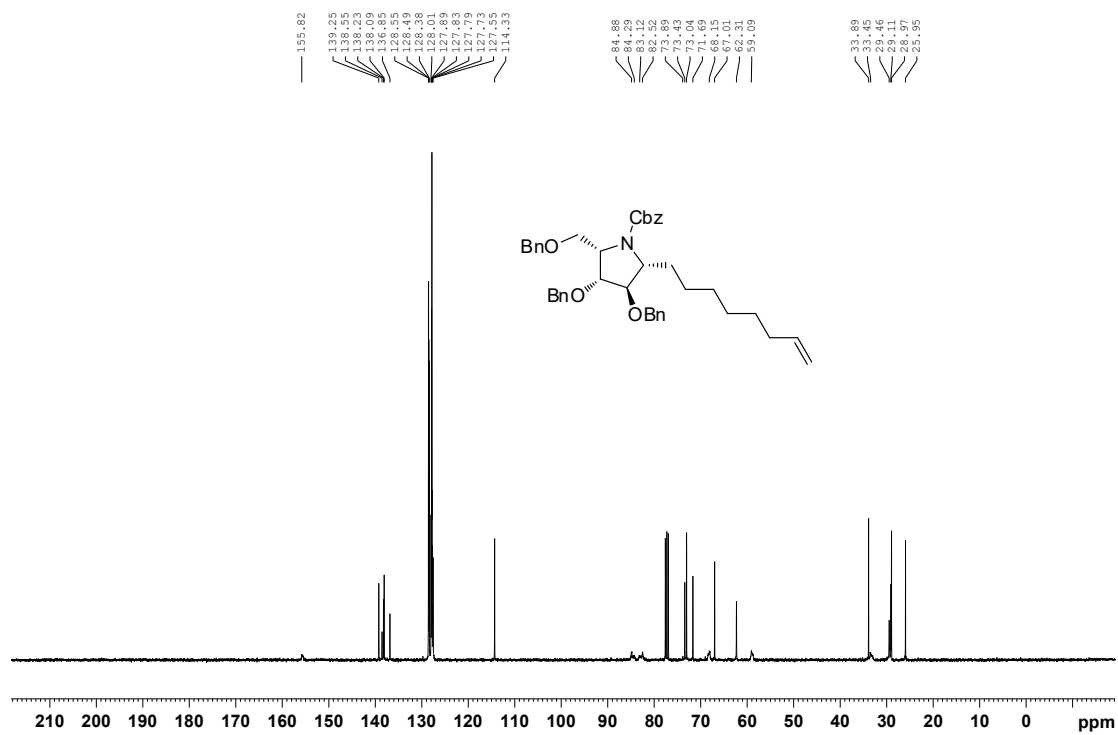


Figure S28

Compound *ent-3-epi-13*

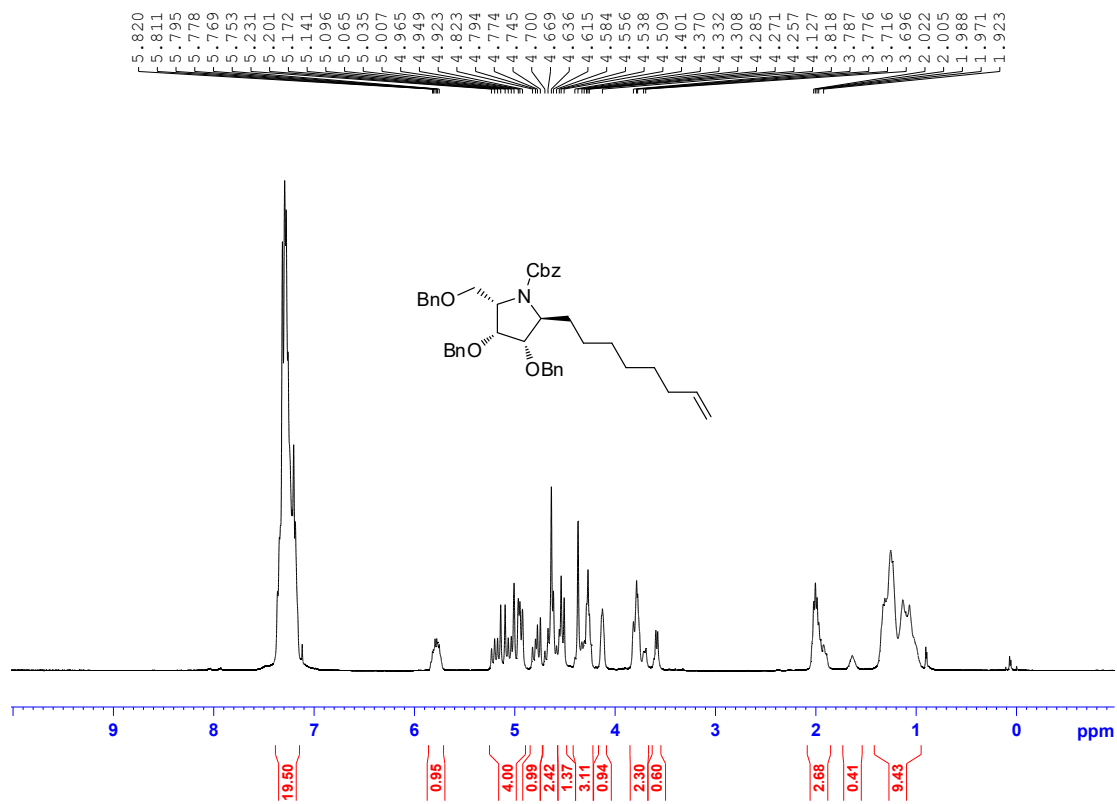


Figure S29

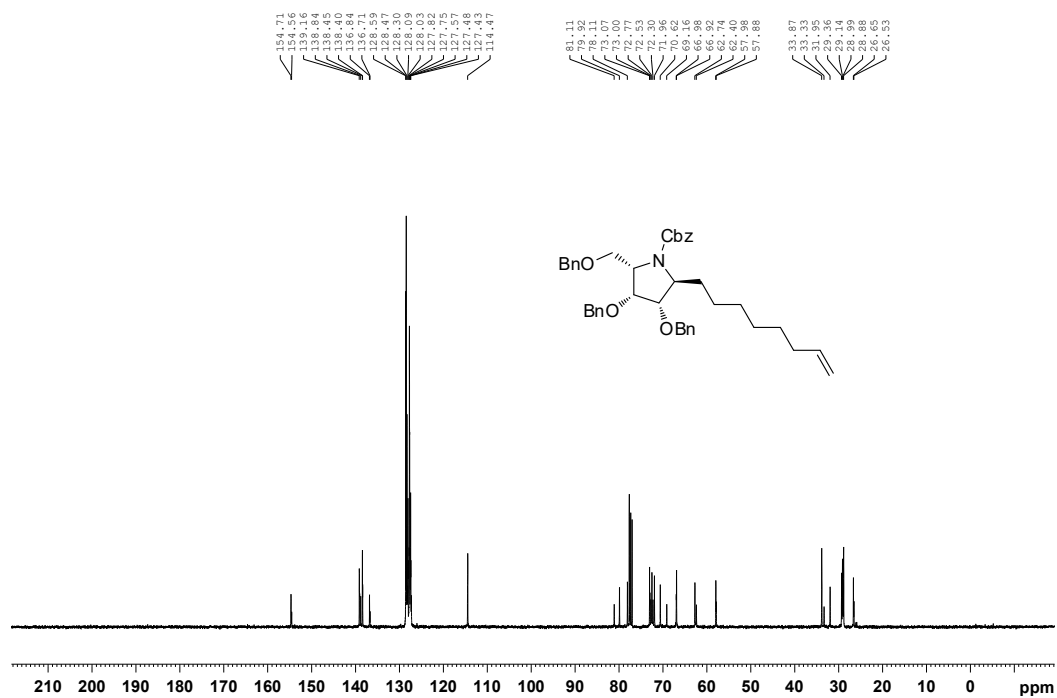


Figure S30

Compound 2-*epi*-13

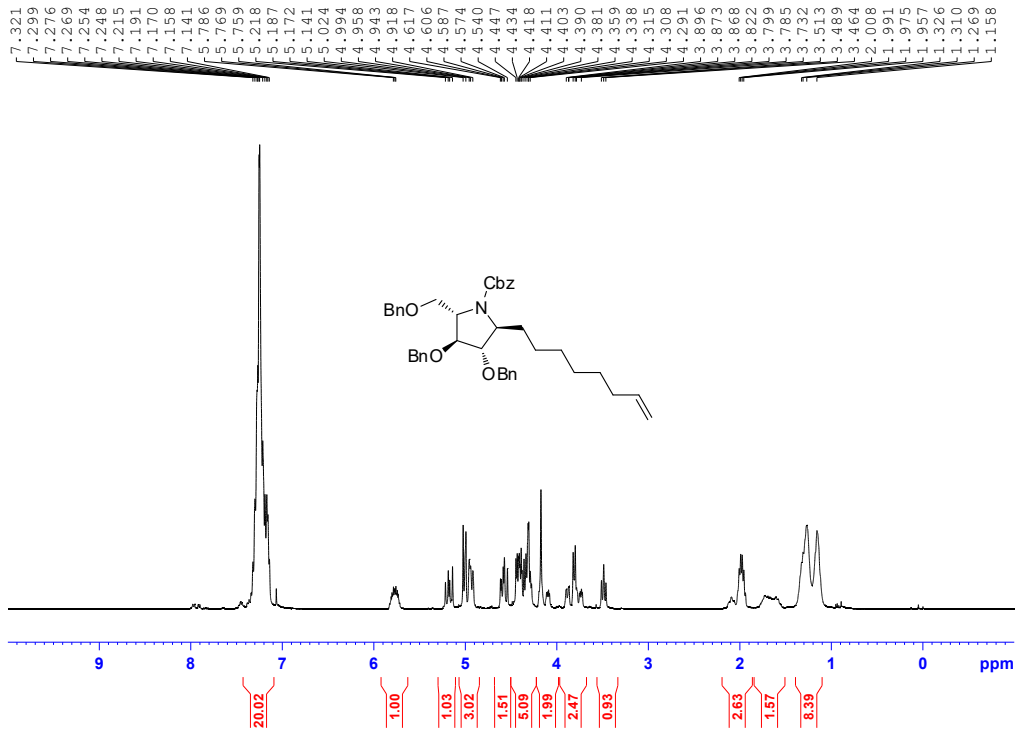


Figure S31

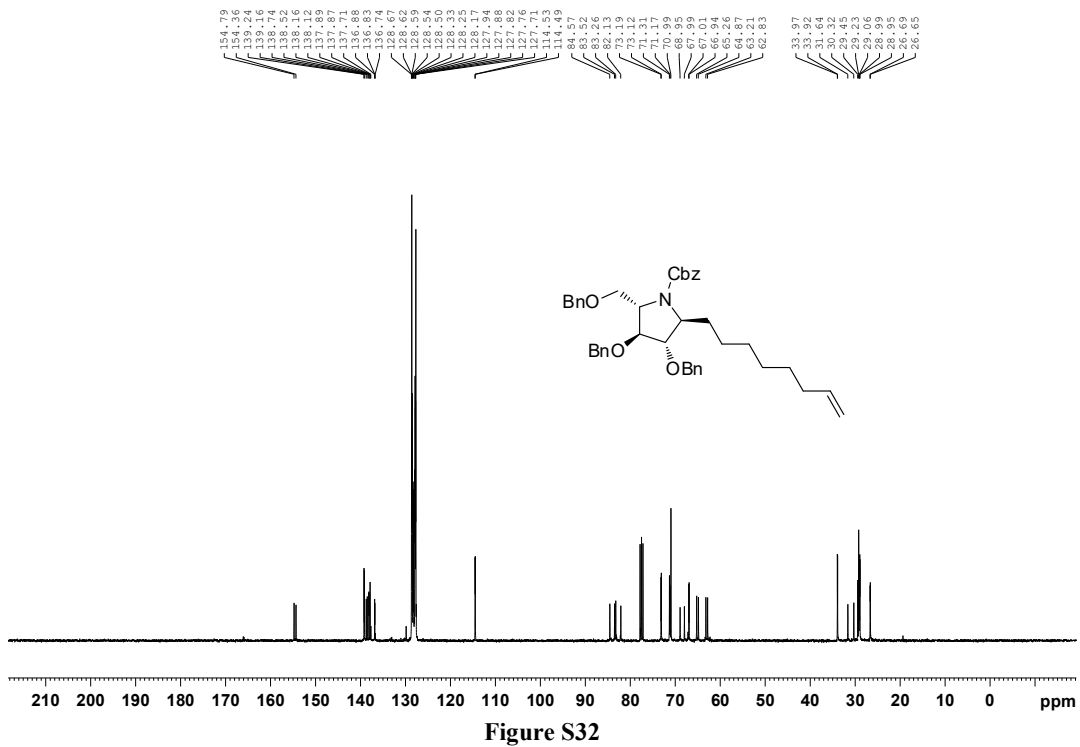


Figure S32

Compound 12

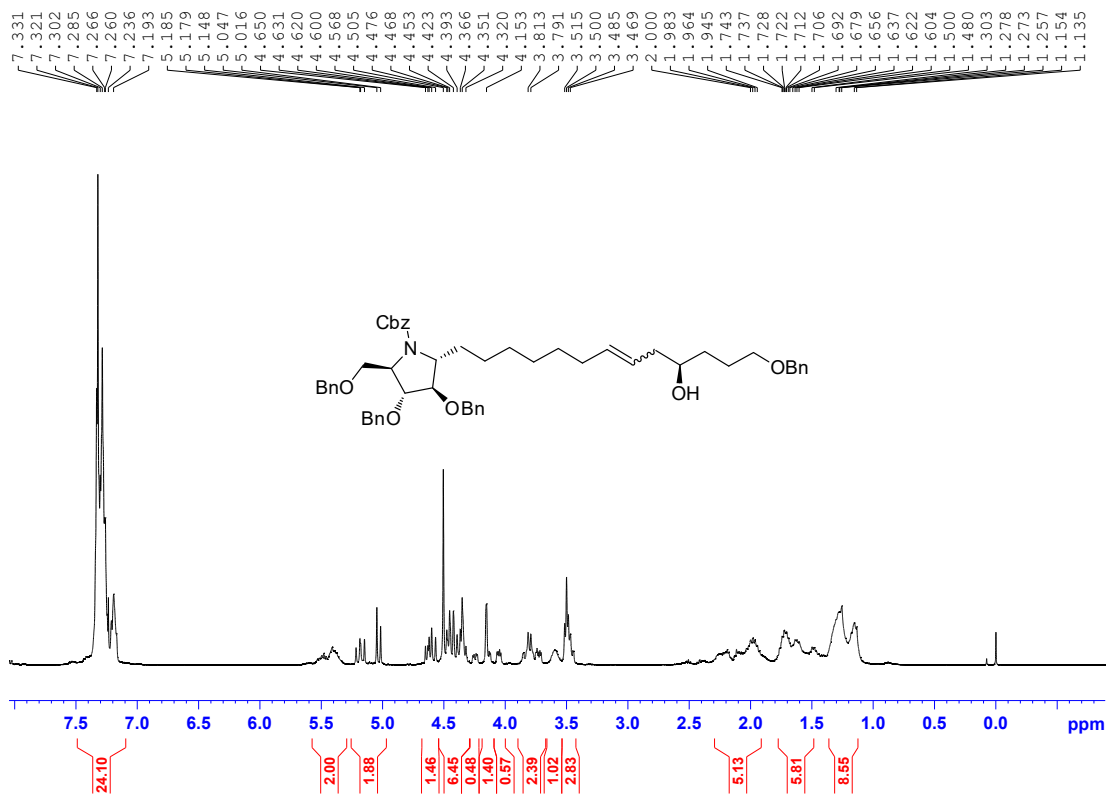


Figure S33

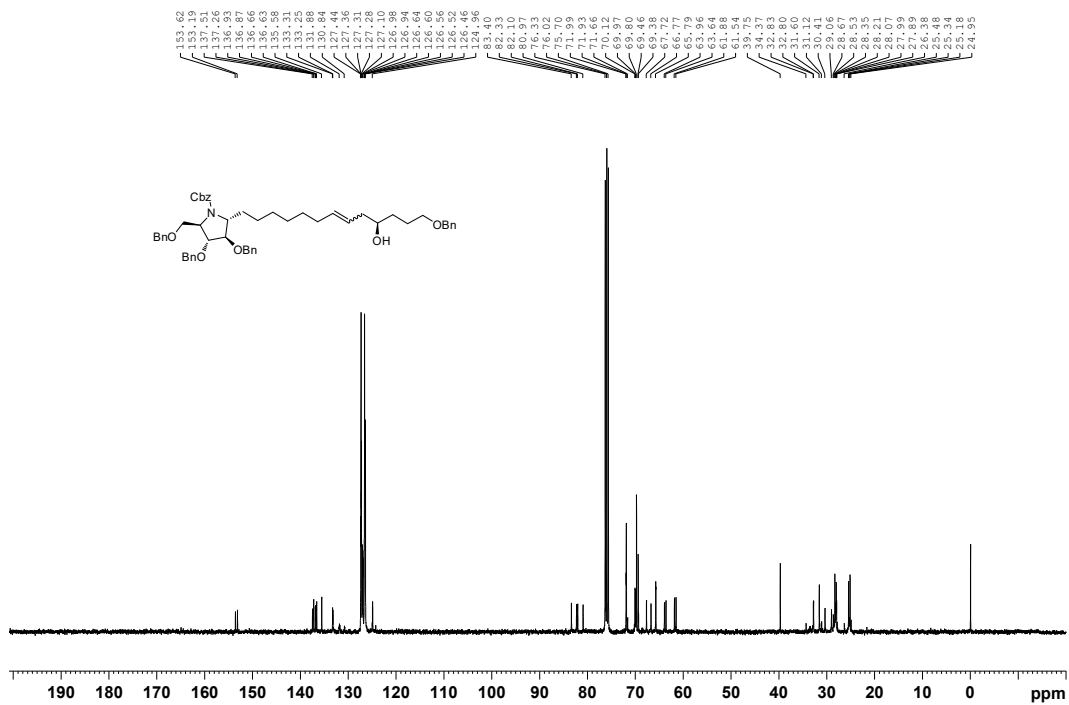


Figure S34

Compound *ent-10'-epi-12*

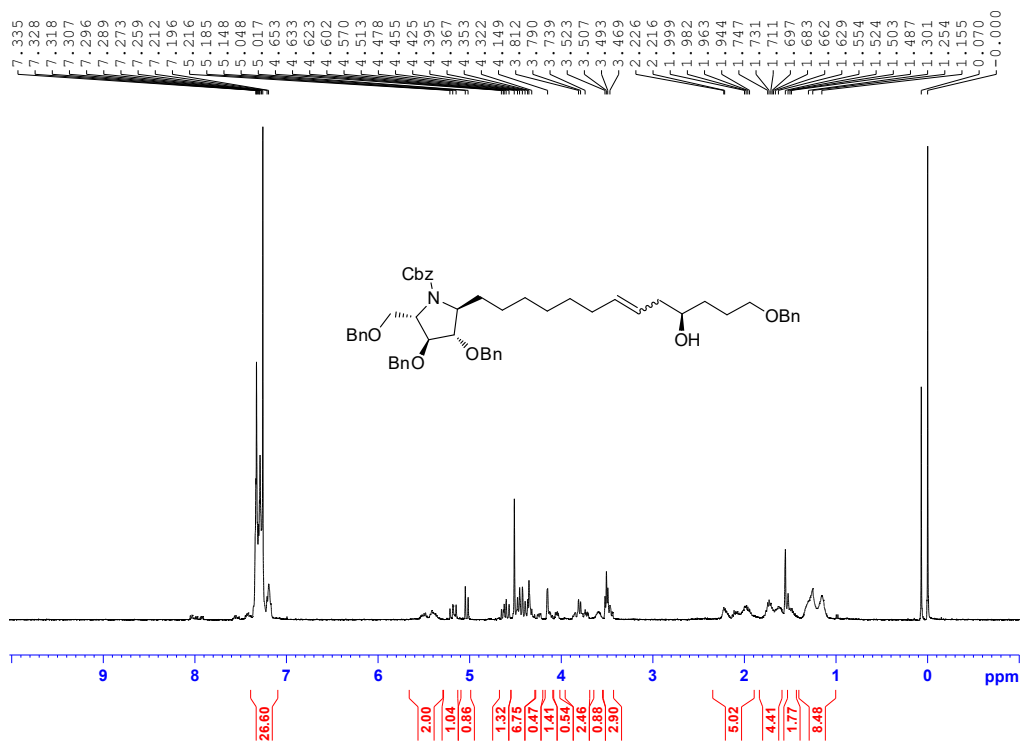


Figure S37

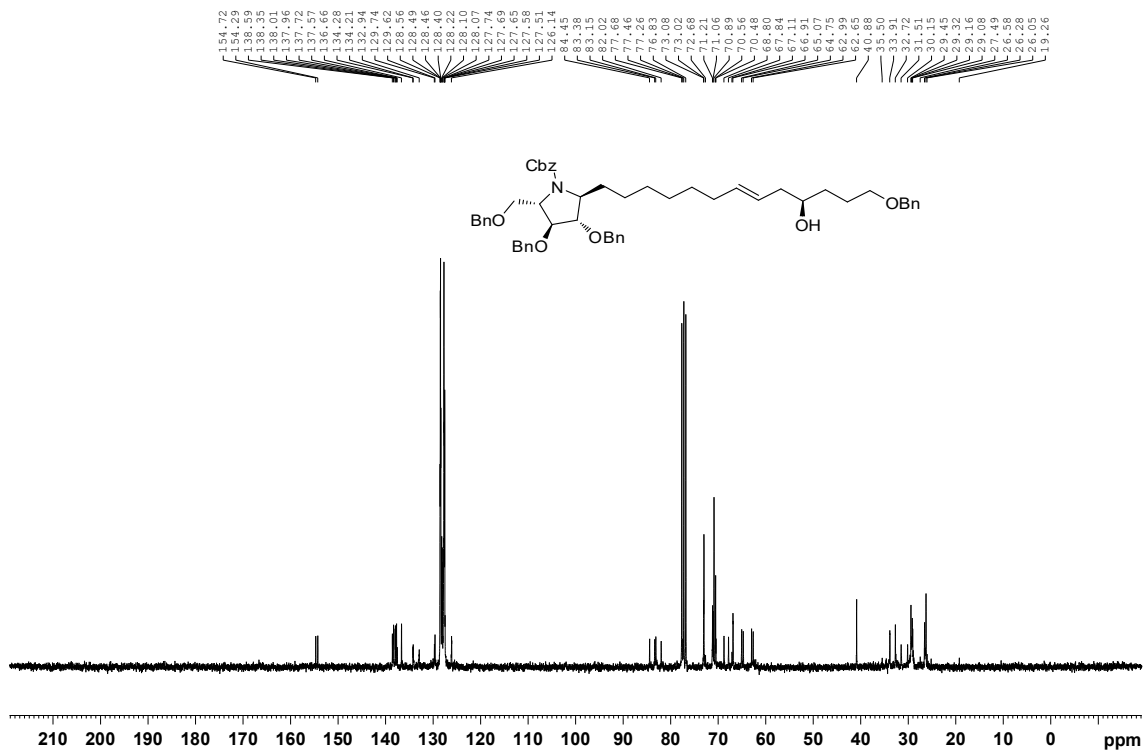


Figure S38

Compound *ent-12*

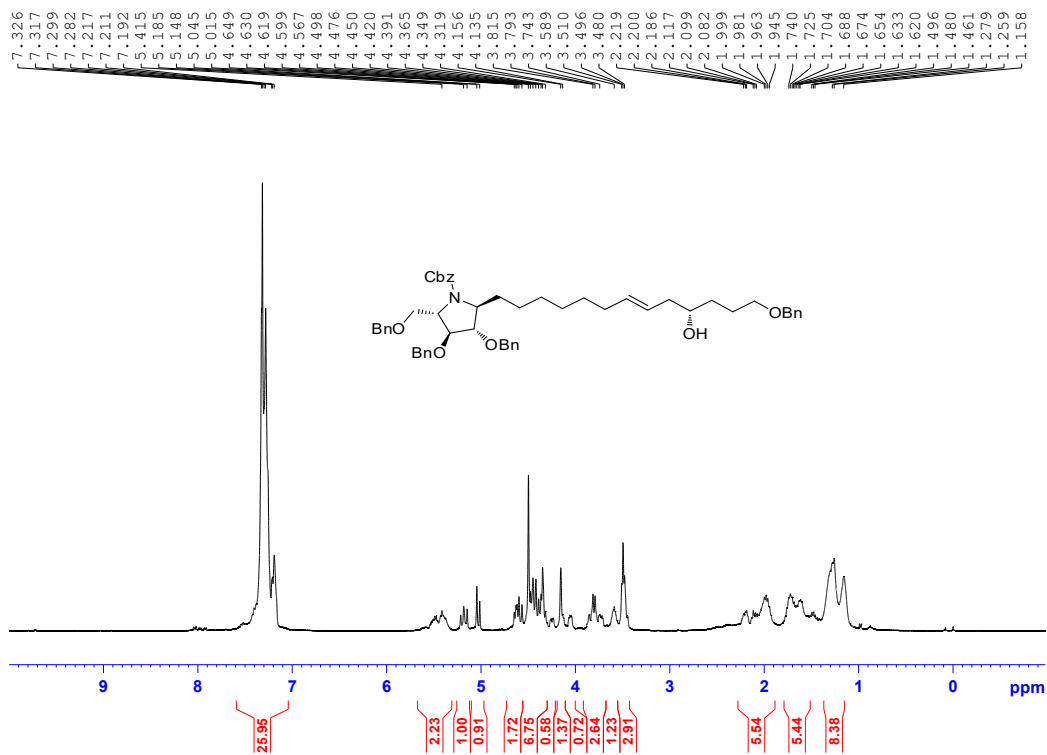


Figure S39

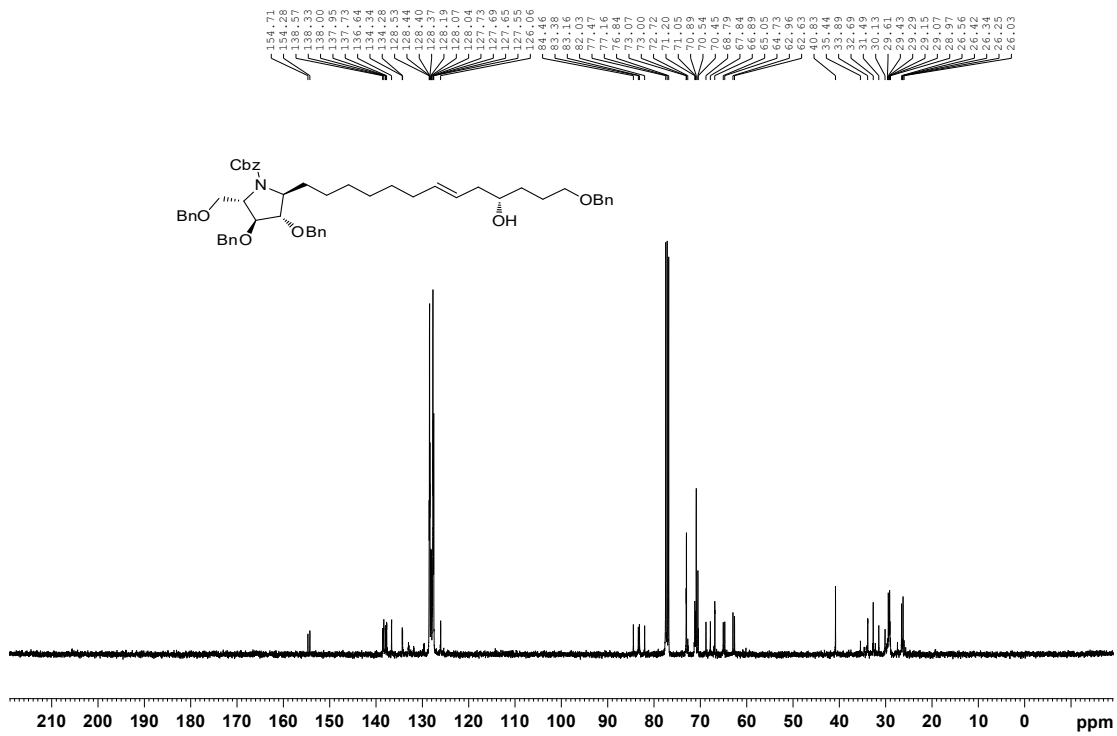


Figure S40

Compound *ent-3-epi-12*

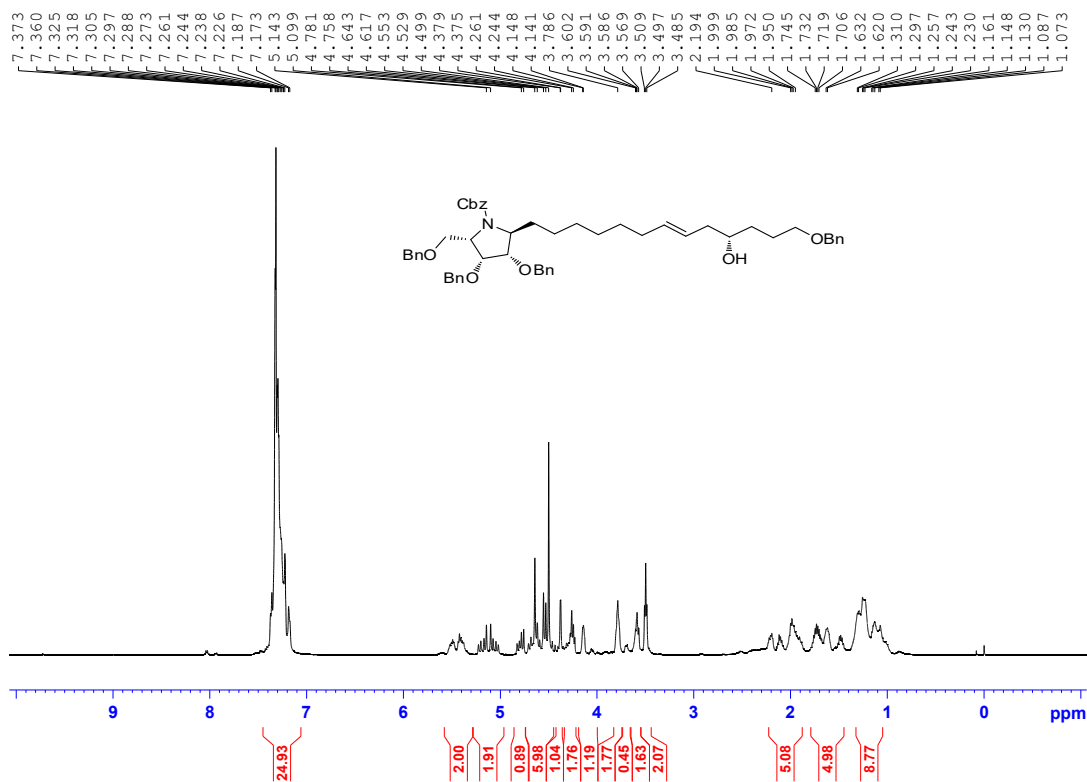


Figure S43

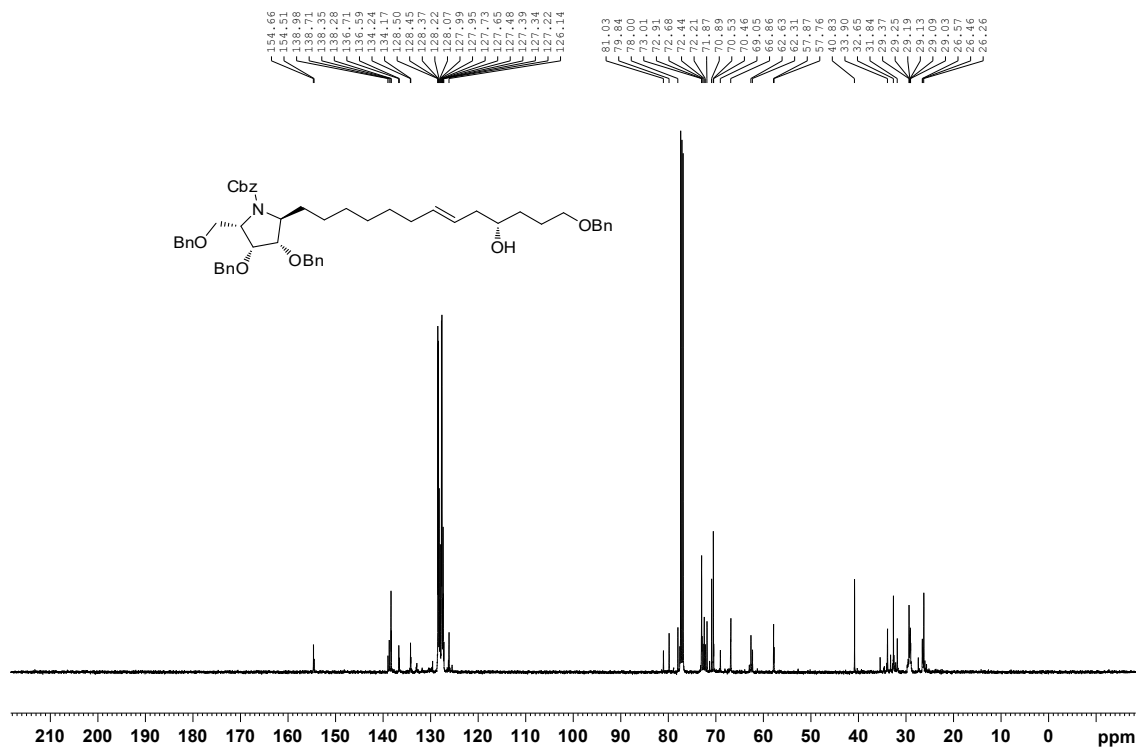


Figure S44

Compound 2-*epi*-12

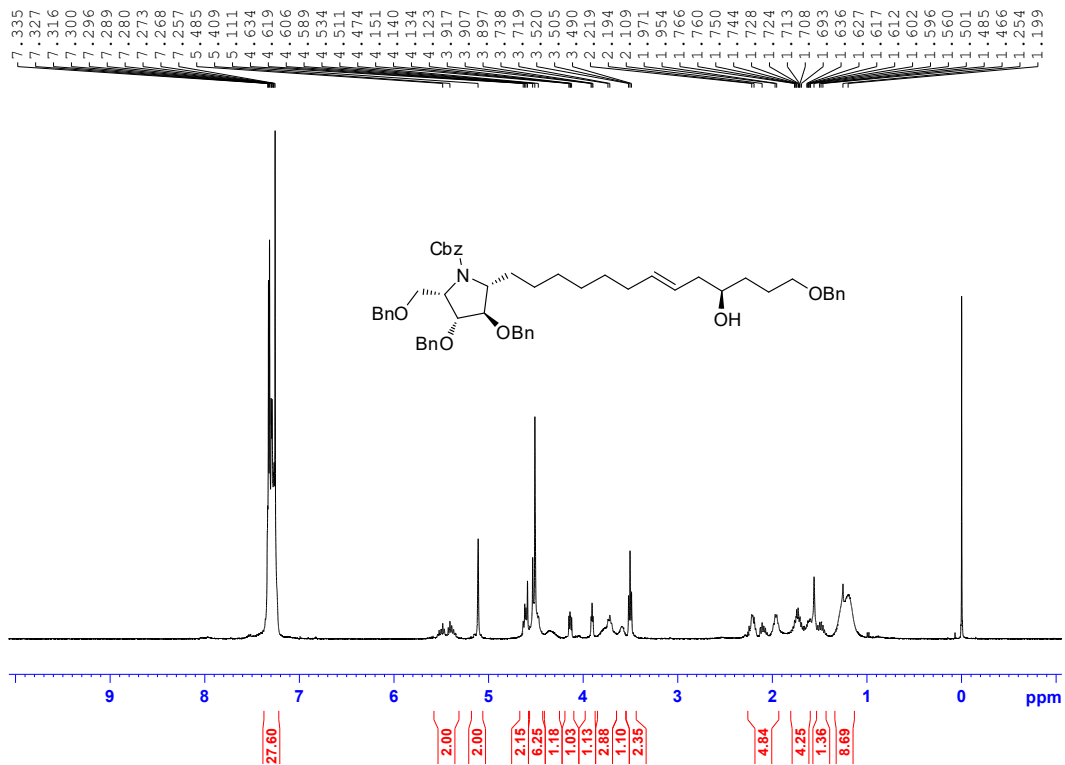


Figure S45

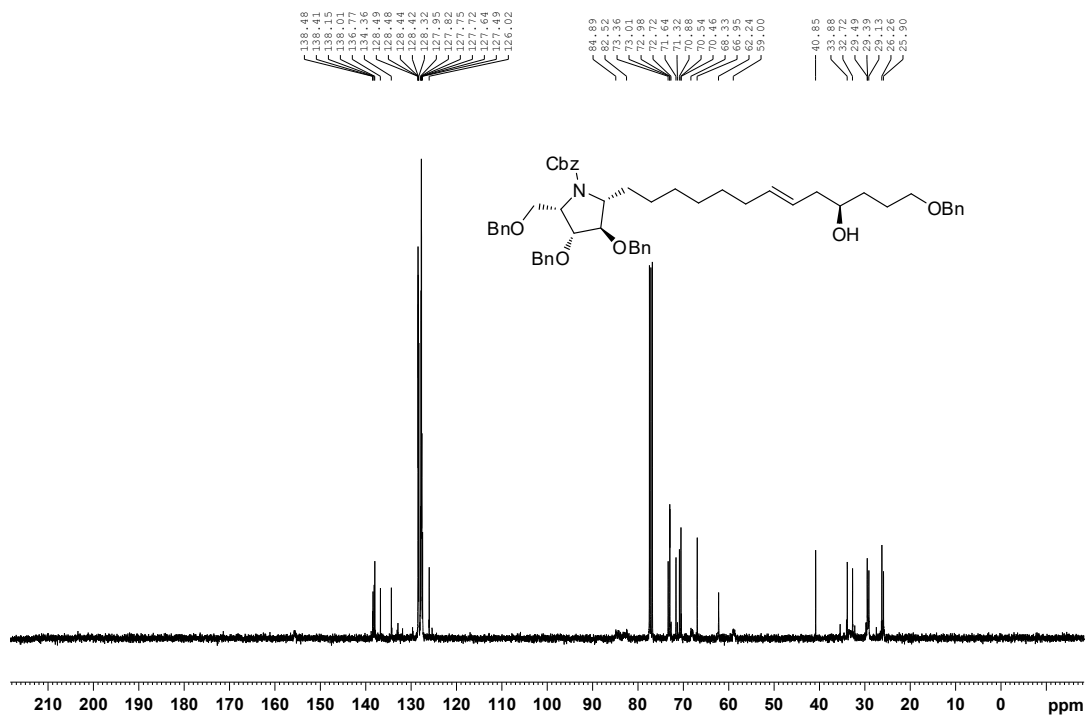


Figure S46

Compound 3 (CD₃OD)

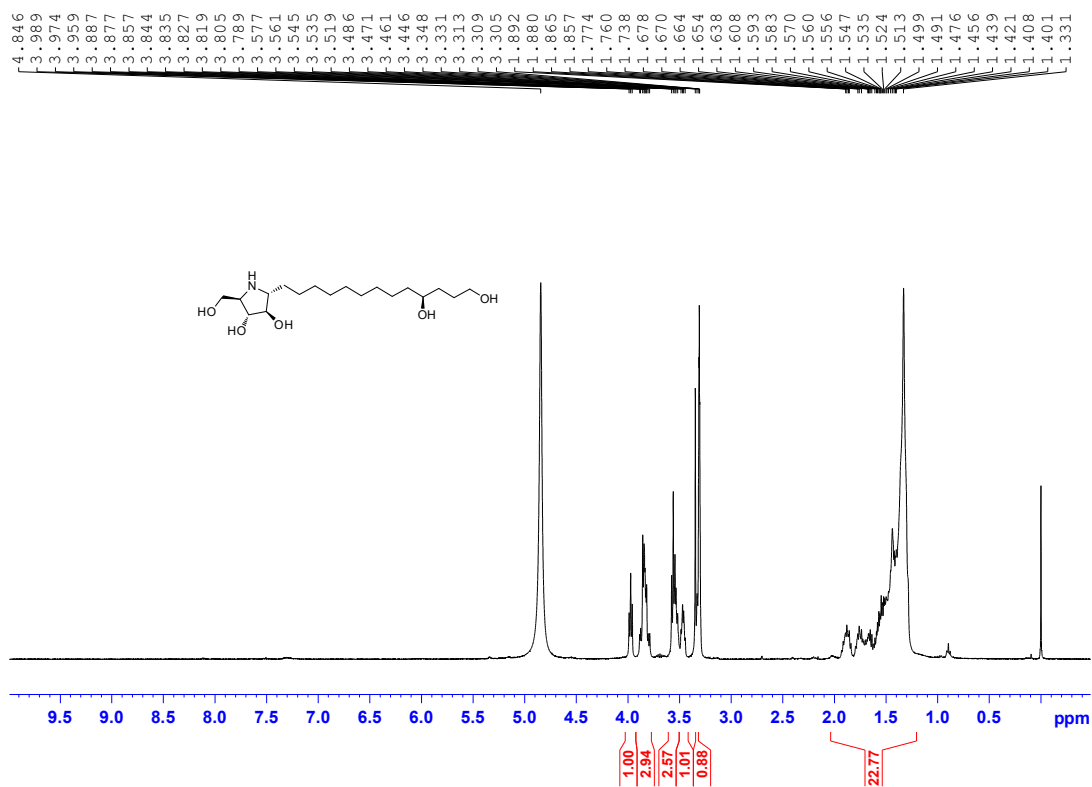


Figure S49

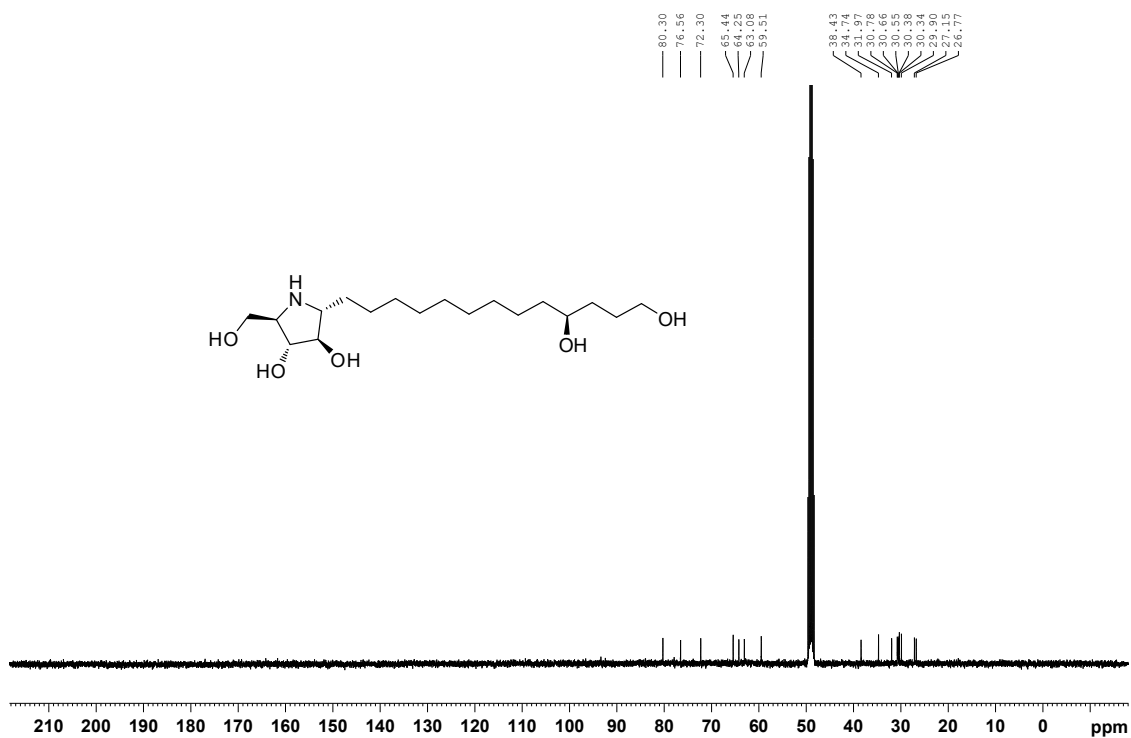


Figure S50

Compound 3 (C₅D₅N)

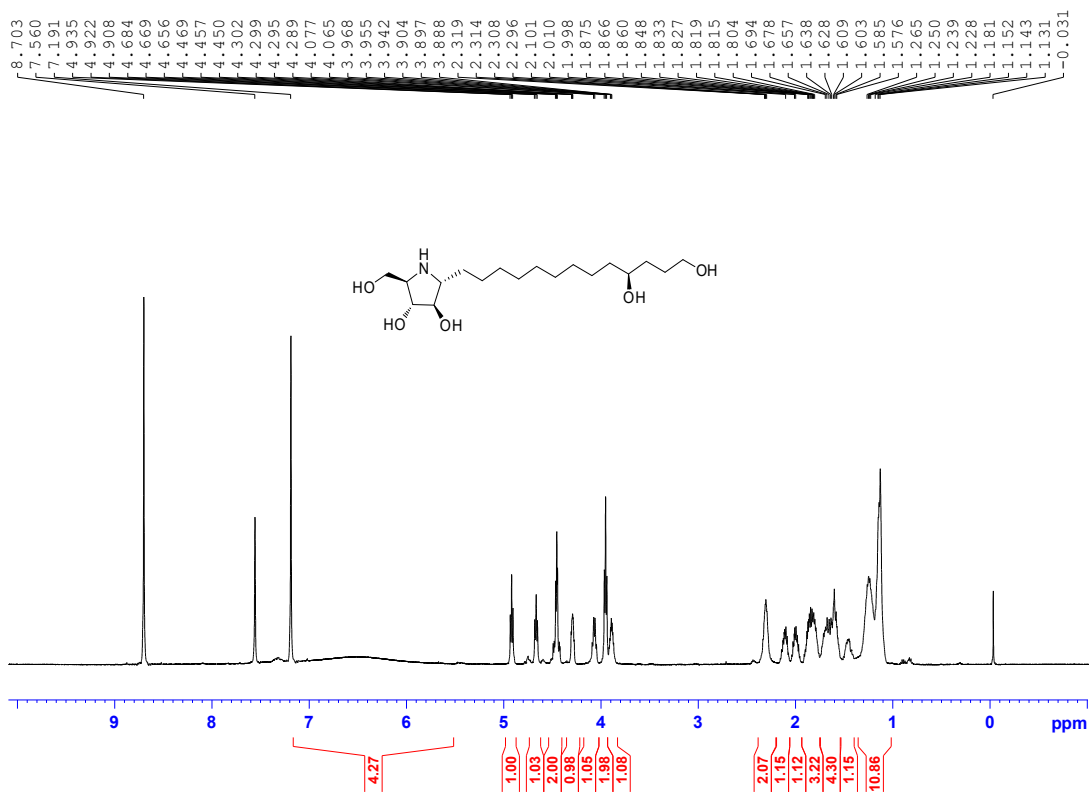


Figure S51

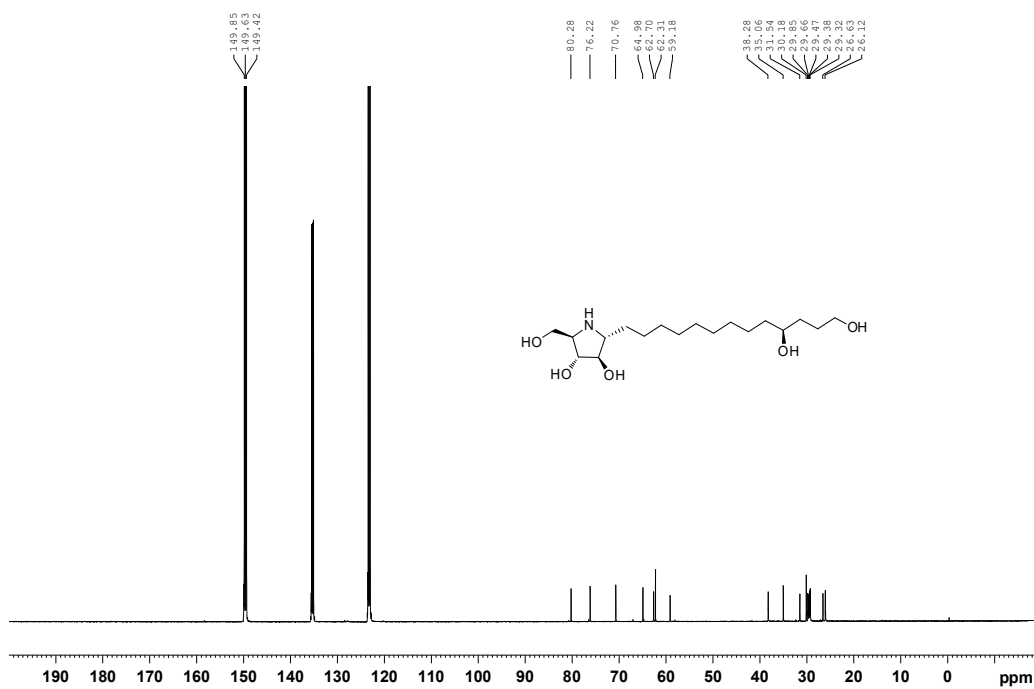


Figure S52

Compound 10'-*epi*-3

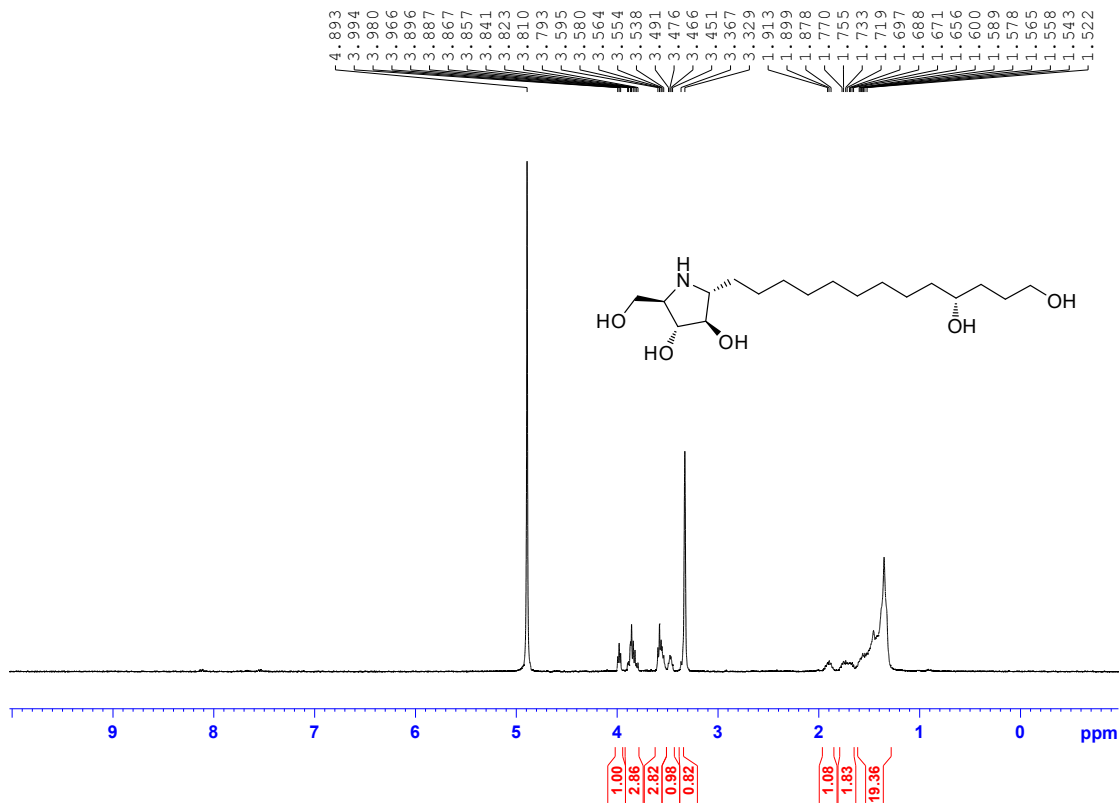


Figure S53

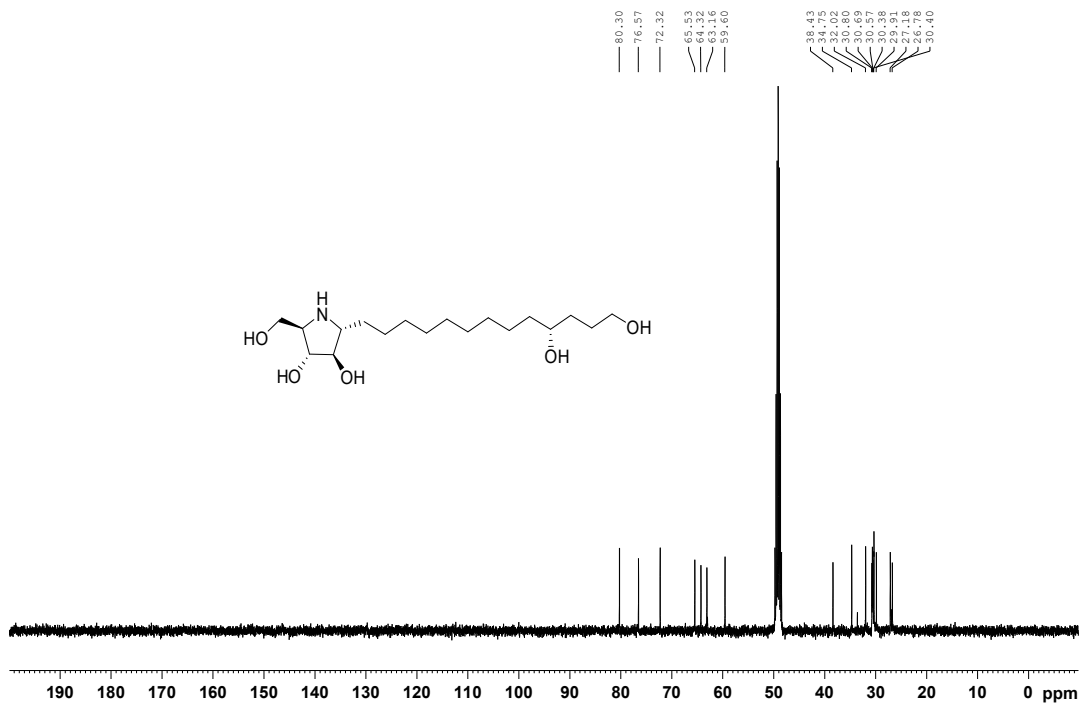


Figure S54

Compound *ent-10'-epi-3*

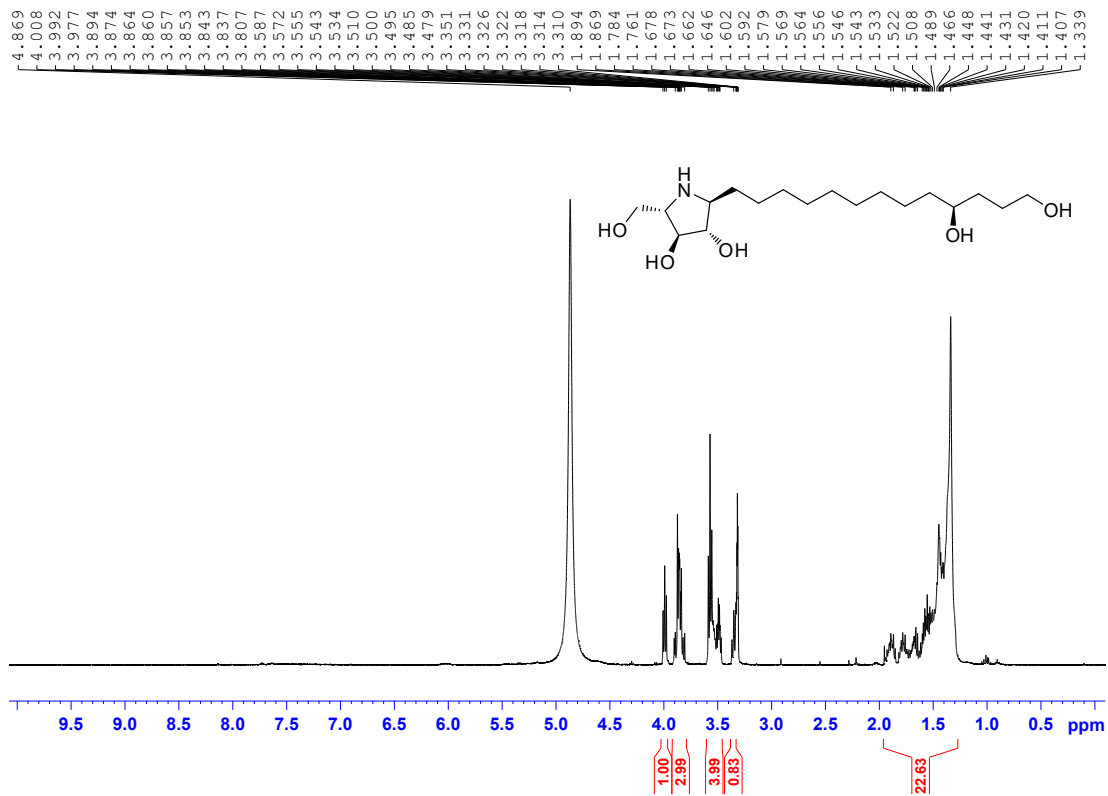


Figure S55

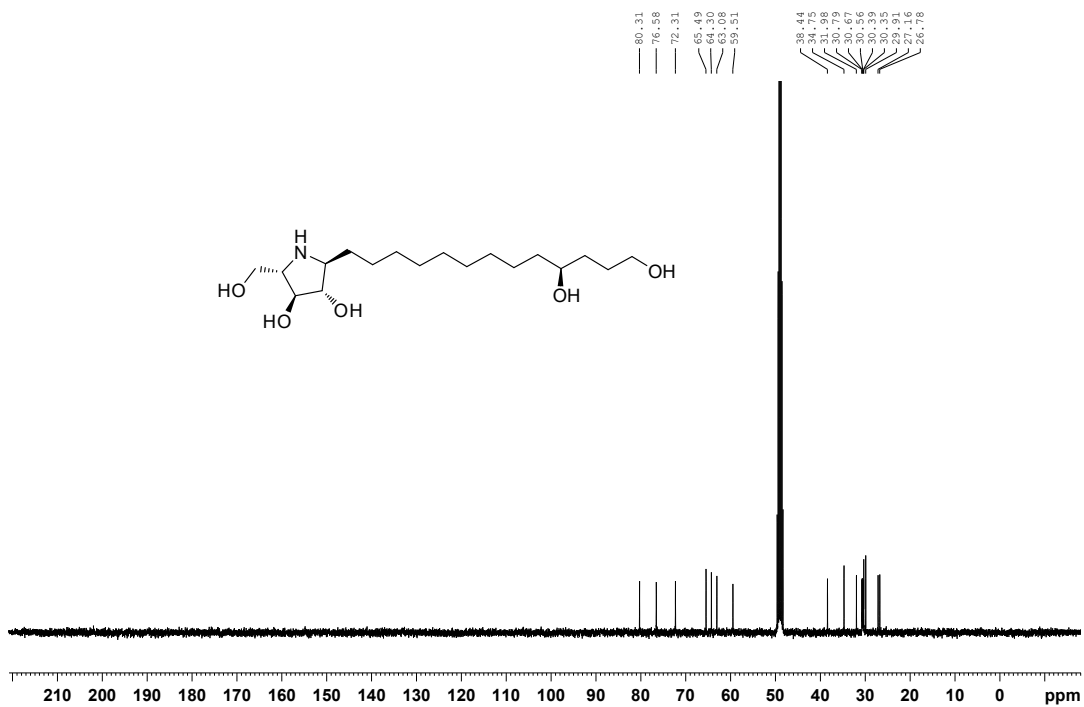


Figure S56

Compound *ent-3*

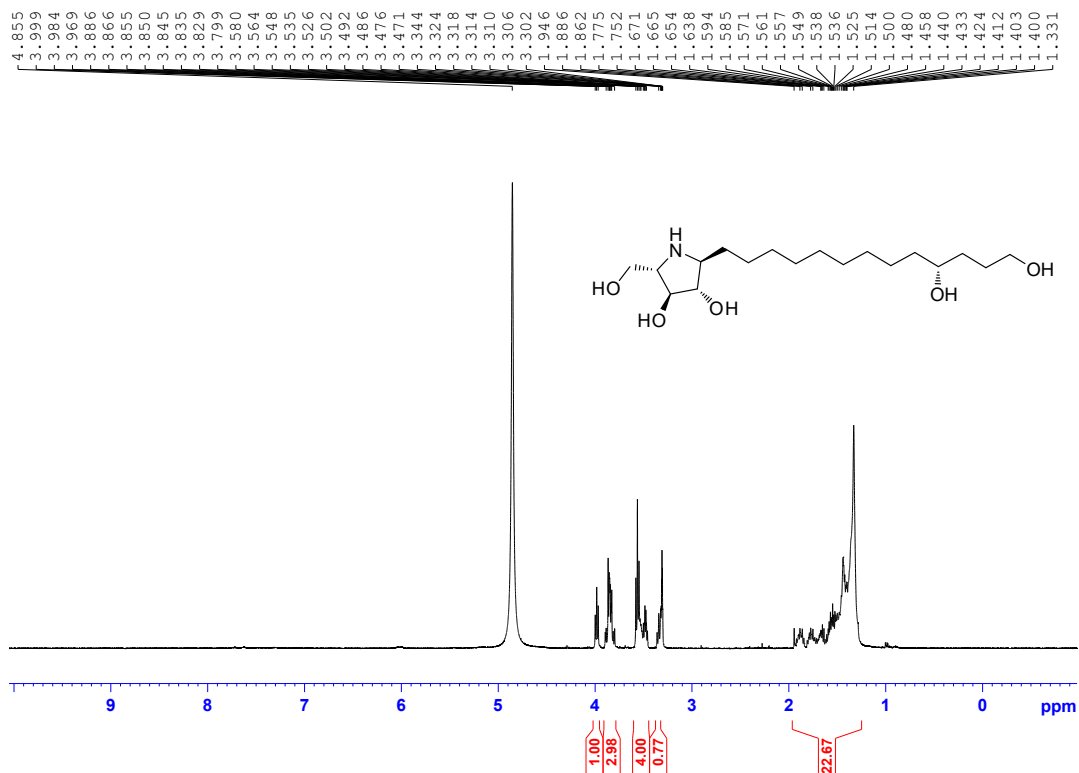


Figure S57

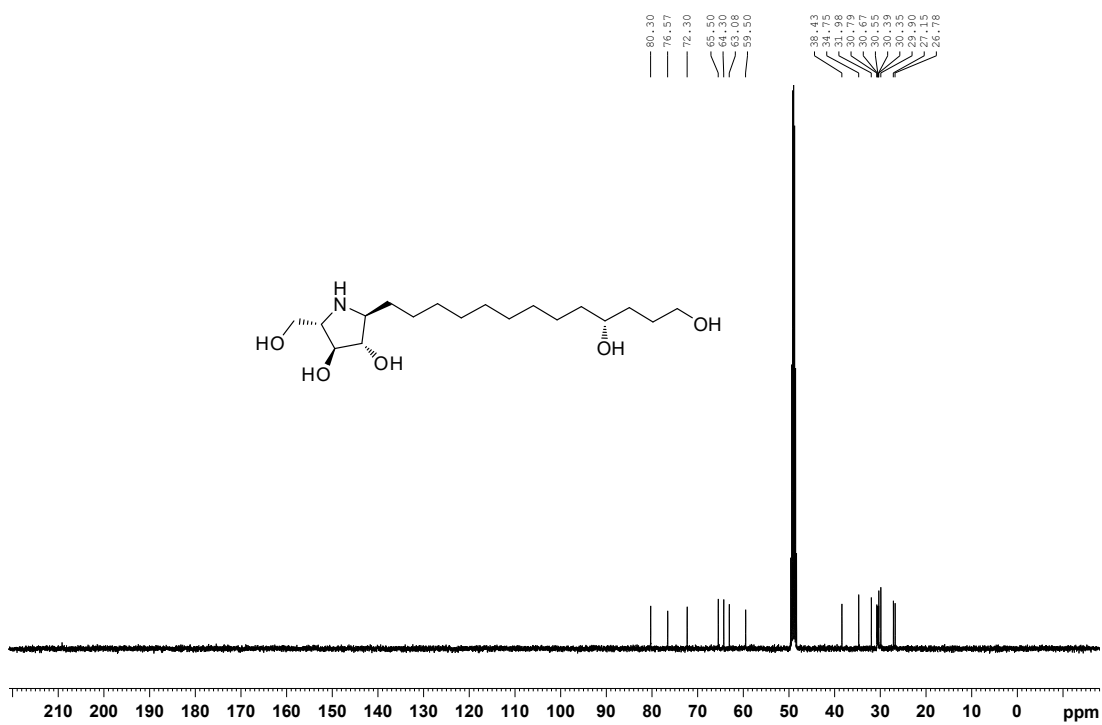


Figure S58

Compound *ent*-3,10'-di-*epi*-3

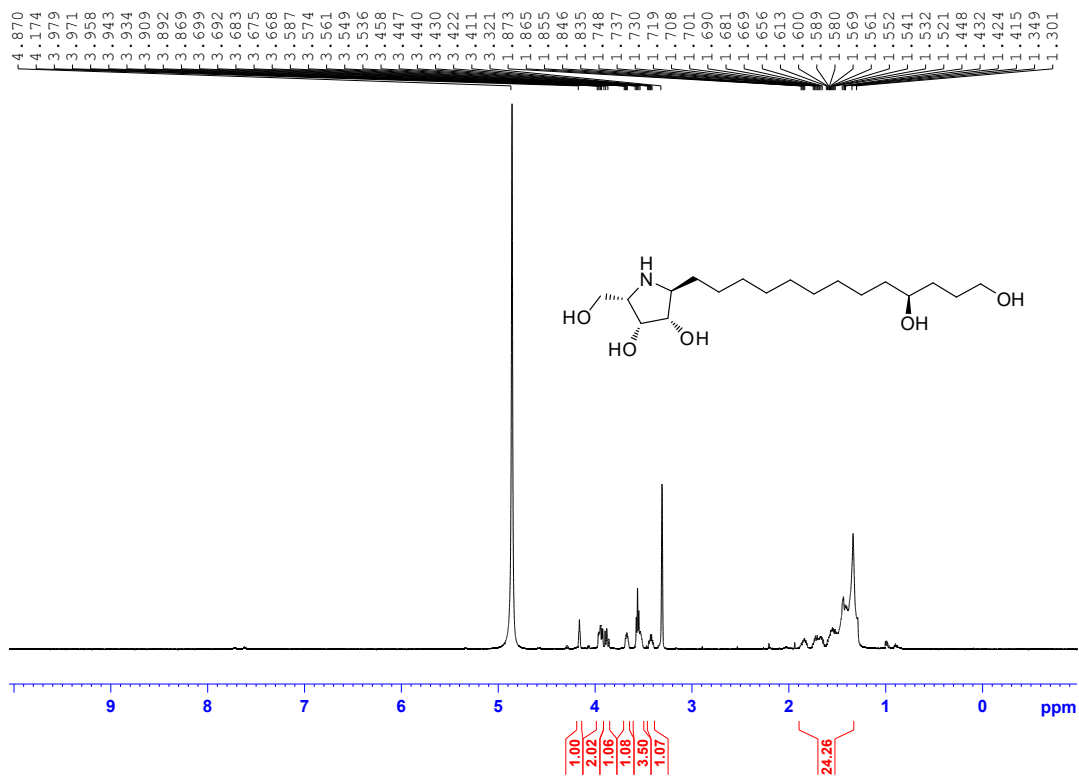


Figure S59

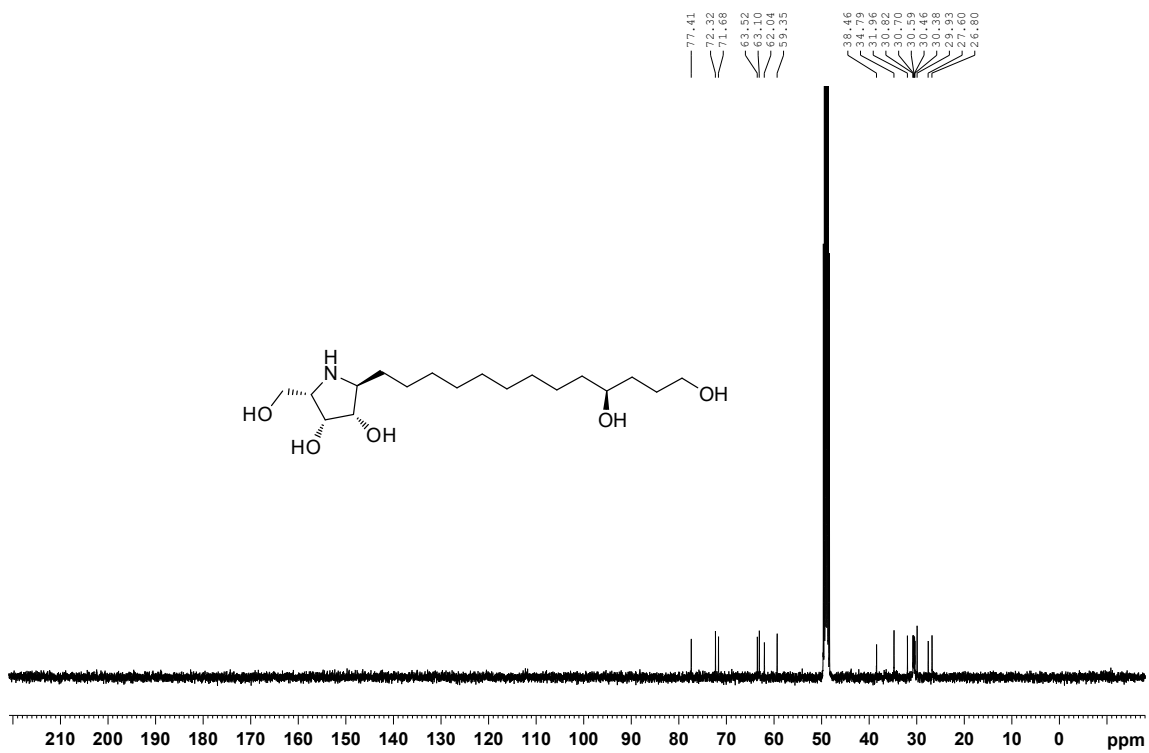


Figure S60

Compound *ent-3-epi-3*

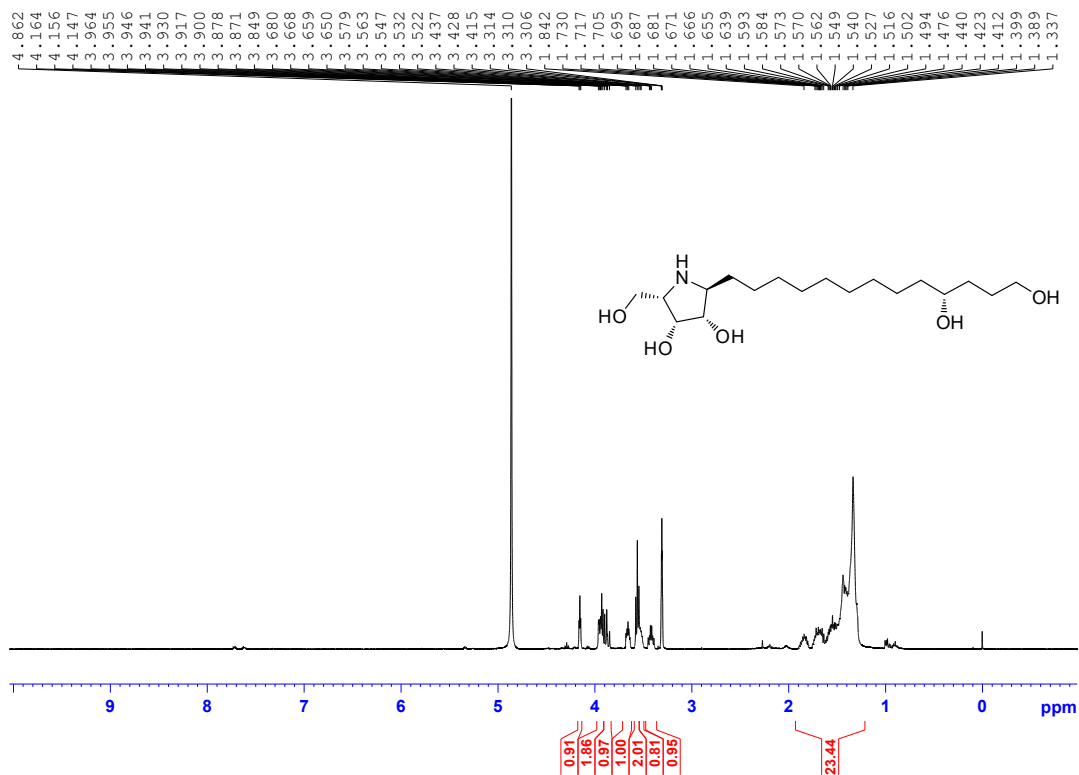


Figure S61

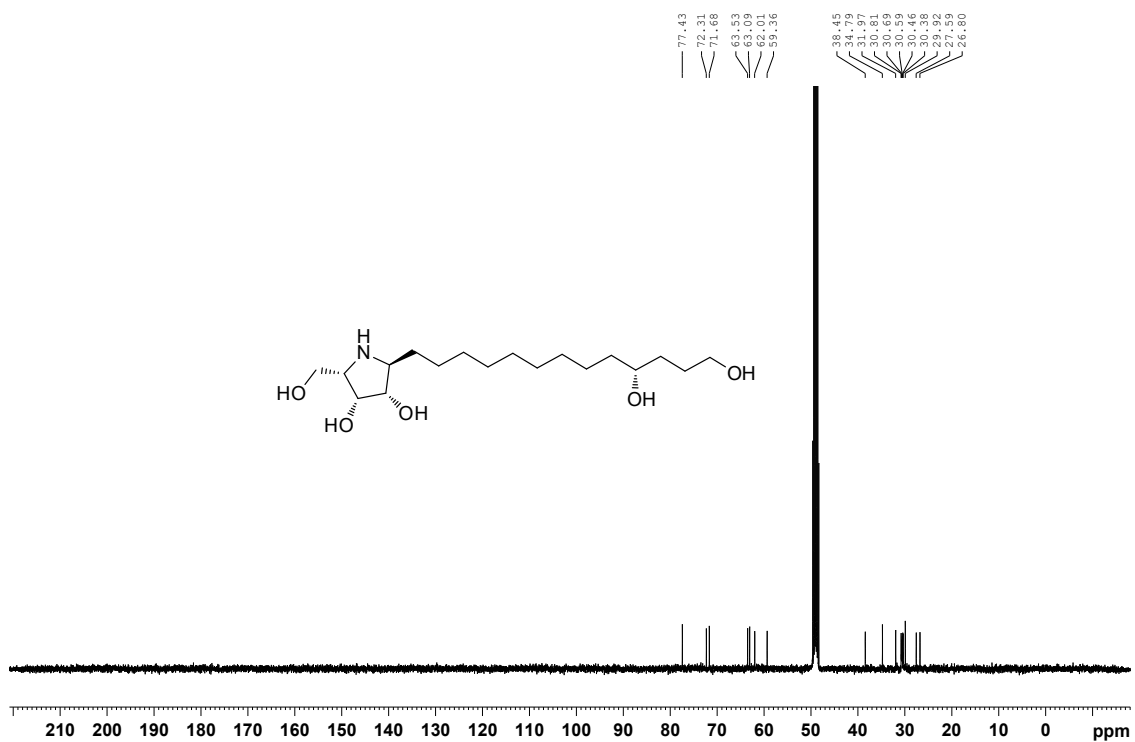


Figure S62

Compound 2-*epi*-3

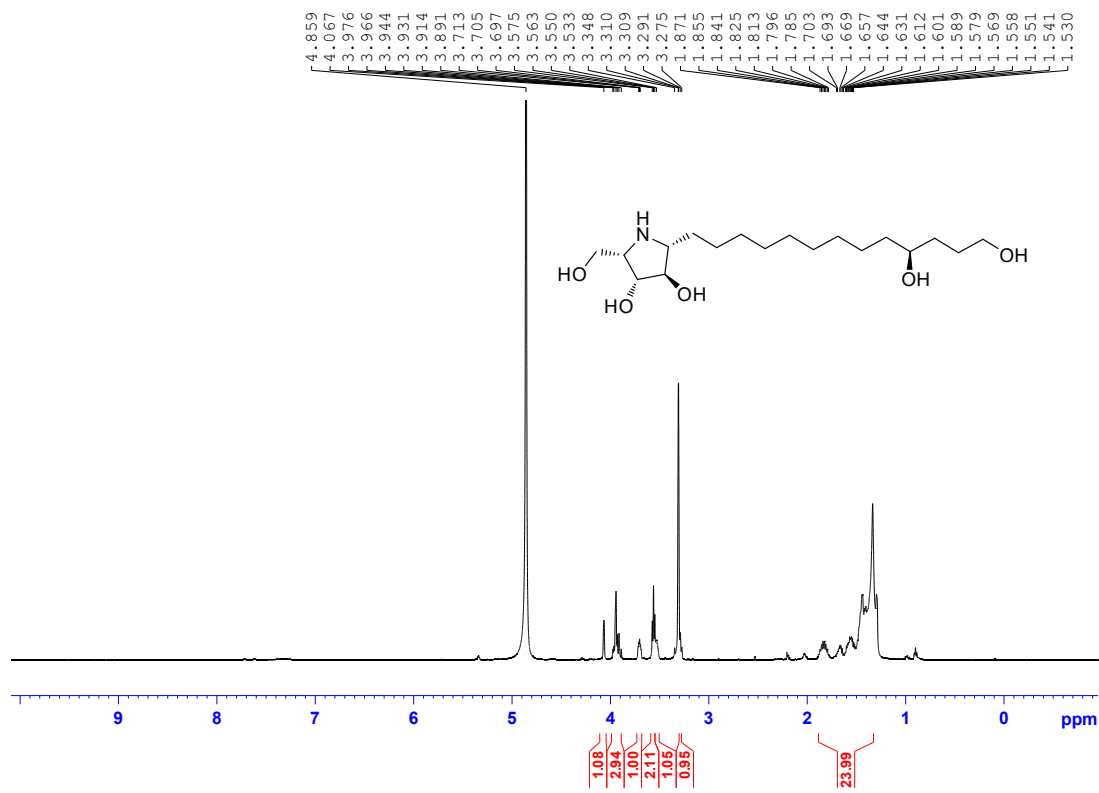


Figure S63

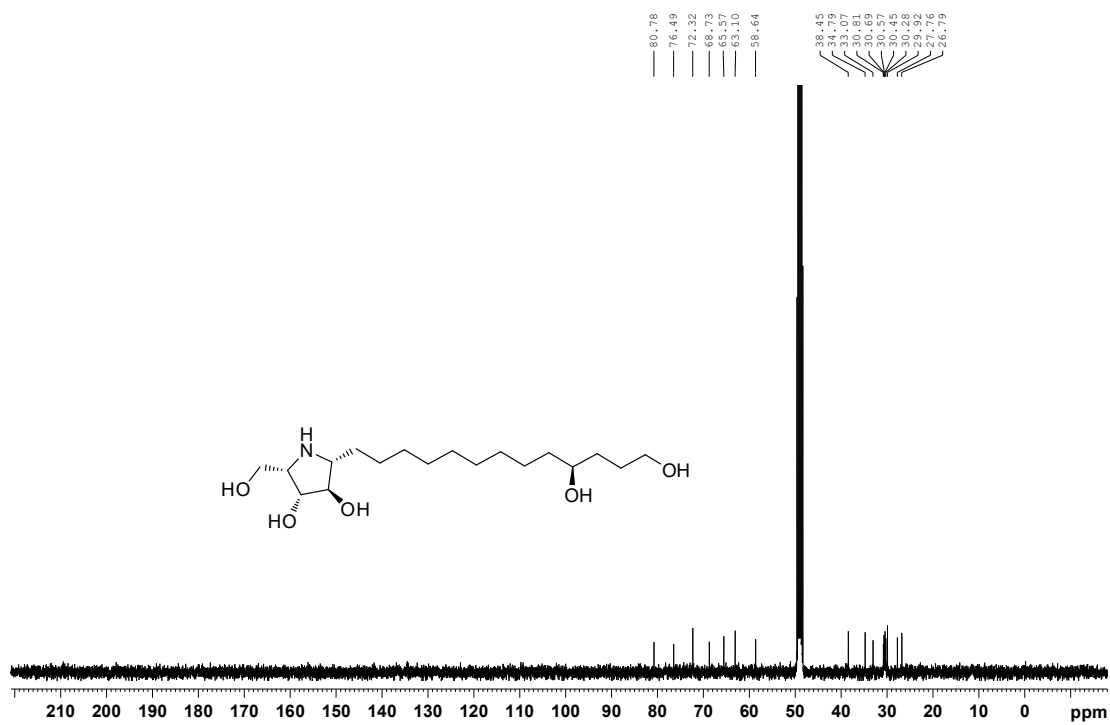


Figure S64

Compound 2,10'-di-*epi*-3

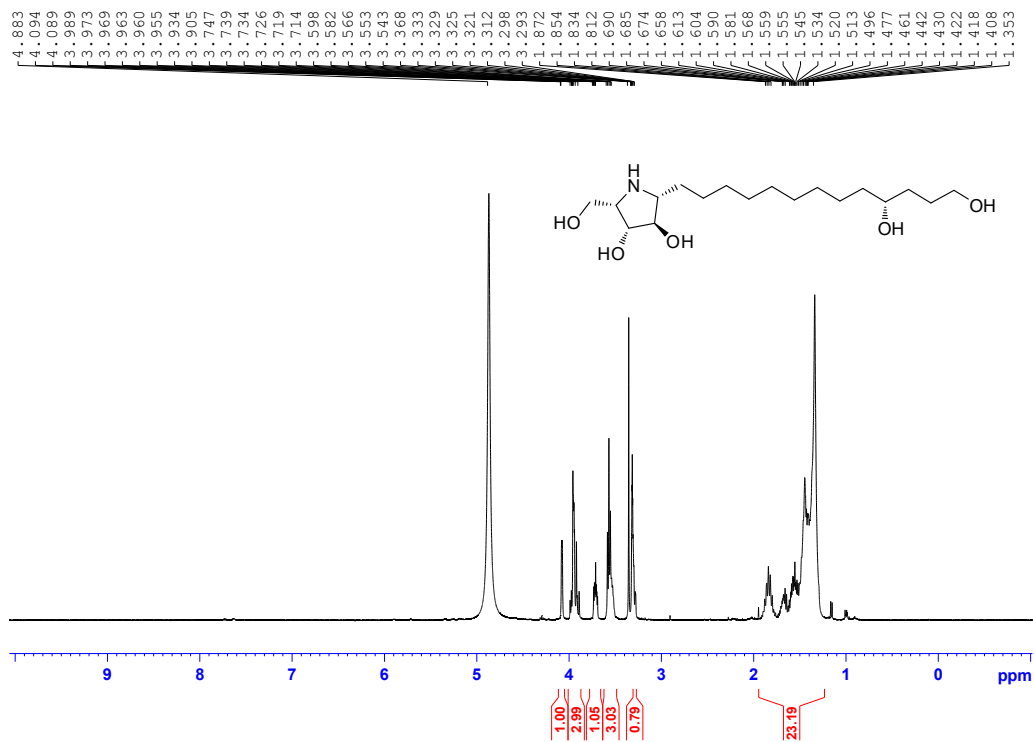


Figure S65

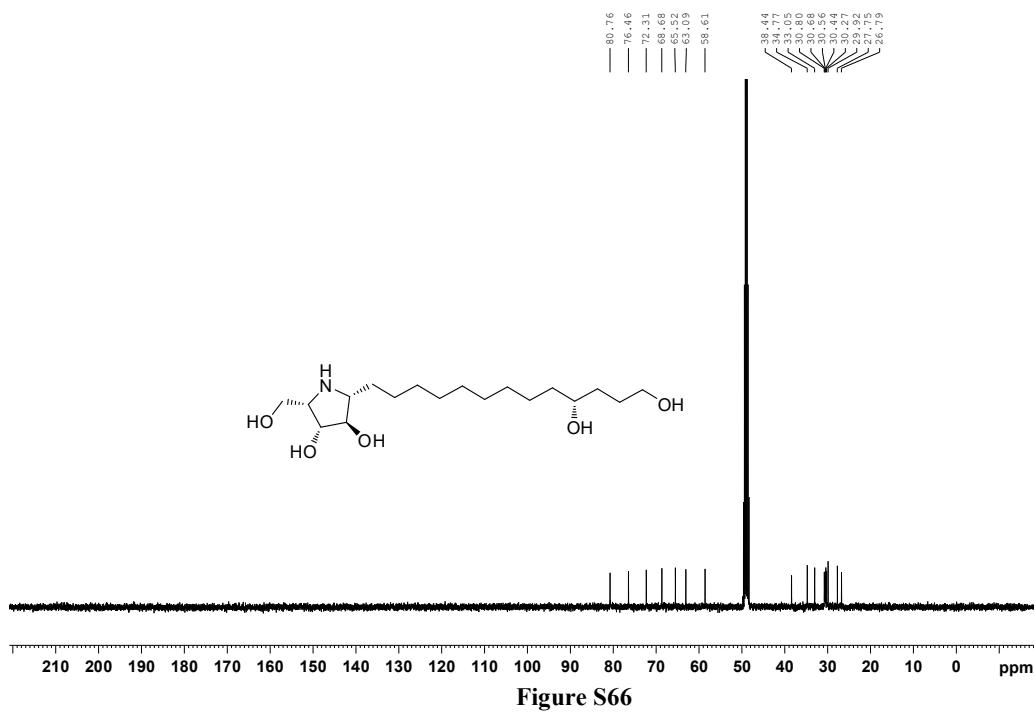


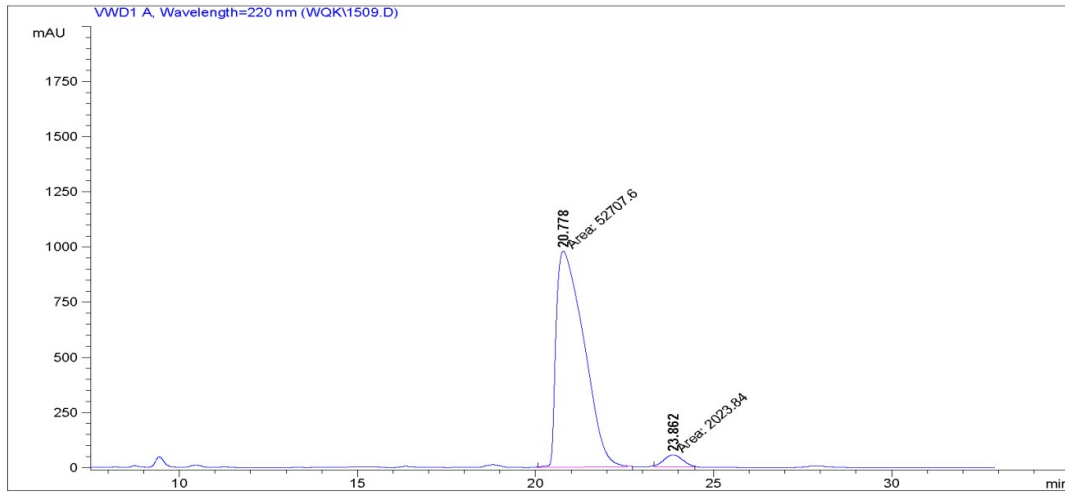
Figure S66

HPLC Analysis of Compounds 15 and *ent*-15

Compound 15

Data File C:\CHEM32\1\DATA\WQK\1509.D
Sample Name: 150901

```
=====
Acq. Operator   : WQK
Acq. Instrument : Instrument 1           Location : Vial 1
Injection Date  : 2016-9-28 9:04:04
Acq. Method     : C:\CHEM32\1\METHODS\JWQ20121205.M
Last changed    : 2016-9-28 9:02:24 by WQK
                 (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\JWQ20121205.M
Last changed    : 2016-9-28 10:26:48 by WQK
                 (modified after loading)
Sample Info     : OD-H H/I=95:5  1 ml/min, 220nm
=====
```



Area Percent Report

```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Sample Amount  : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	20.778	MM	0.8965	5.27076e4	979.92041	96.3022
2	23.862	MM	0.6126	2023.84094	55.06227	3.6978
Totals :				5.47315e4	1034.98268	

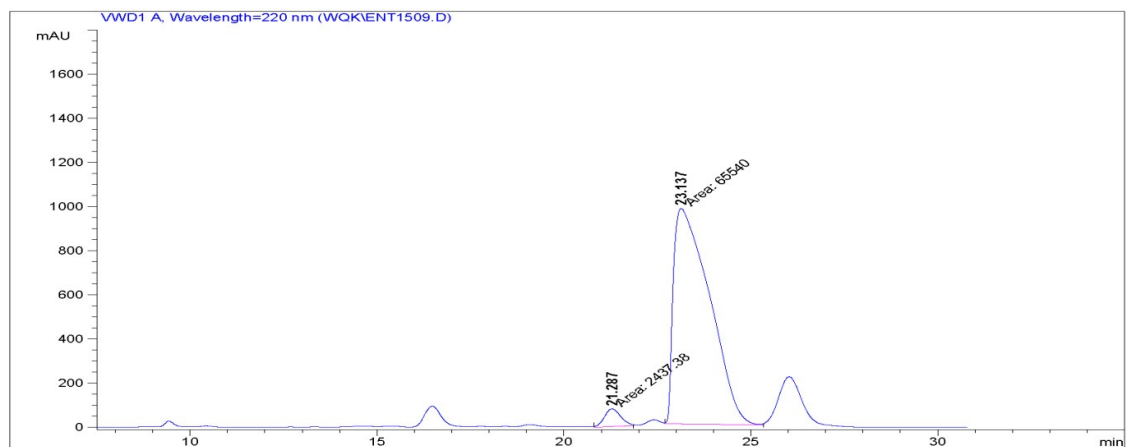
*** End of Report ***

Figure S67

Compound *ent-15*

Data File C:\CHEM32\1\DATA\WQK\ENT1509.D
Sample Name: ent150901

```
=====
Acq. Operator   : WQK
Acq. Instrument : Instrument 1                      Location : Vial 1
Injection Date  : 2016-9-28 9:38:39
Acq. Method     : C:\CHEM32\1\METHODS\JWQ20121205.M
Last changed    : 2016-9-28 9:02:24 by WQK
                 (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\JWQ20121205.M
Last changed    : 2016-9-28 10:31:20 by WQK
                 (modified after loading)
Sample Info     : OD-H H/I=95:5 1 ml/min, 220nm
=====
```



Area Percent Report

```
=====
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Sample Amount  : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
=====
```

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	21.287	MM	0.5060	2437.37939		80.27544	3.5856
2	23.137	MM	1.1179	6.55400e4		977.14410	96.4144

Totals : 6.79774e4 1057.41954

*** End of Report ***

Figure S68