Supporting Information

_N_-Benzyl-linoleamide, a Constituent of _Lepidium meyenii_ (Maca), is an Orally Bioavailable Soluble Epoxide Hydrolase Inhibitor that Alleviates Inflammatory Pain

Nalin Singh,[†,‡] Bogdan Barnych,[†,‡] Christophe Morisseau,[†] Karen M. Wagner,[†] Debin Wan,[†] Ashley Takeshita,[†] Hoang Pham,[†] Ting Xu,[§] Abhaya Dandekar,[⊥] Jun-Yan Liu,[∥] and Bruce D. Hammock[*,†]

[†]Department of Entomology and Nematology and UC Davis Comprehensive Cancer Center, University of California Davis, Davis, CA, 95616, United States

[§]Beijing Advanced Innovation Center for Food Nutrition and Human Health, College of Resources and Environmental Sciences, China Agricultural University, Beijing, 100193, People's Republic of China

[⊥]Department of Plant Sciences, University of California Davis, Davis, CA, 95616, United States

[∥]Institute of Life Sciences, Chongqing Medical University, Chongqing, 400016, People's Republic of China

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Table S1. Descriptions of thirteen commercial *L. meyenii* (maca) products

L. meyenii product	Description
Product 1	Purple maca root slices from Lijiang, China
Product 2	Yellow maca root from Lijiang, China
Product 3	Black maca root from Shaotong City, China
Product 4	Black maca root from Lijiang, China
Product 5	Black maca root from Peru
Product 6	Yellow maca root from Peru
Product 7	Black maca root from Qujing, China
Product 8	Yellow maca root powder from Zhaotong, China
Product 9	Yellow maca root powder from Qujing, China
Product 10	Black maca root powder from The Maca Team LLC
Product 11	Yellow maca root powder from The Maca Team LLC
Product 12	Red maca root powder from The Maca Team LLC
Product 13	Red maca root extract from The Maca Team LLC

Table S2. HPLC-MS/MS method Limits of Quantitation

ID	LOQ (ng/ml)
2	0.4
3	0.002
4	0.002
5	0.002
6	0.01
7	0.1
8	0.002
9	1
10	0.002
11	0.01
12	0.01
13	0.1
14	0.1
15	0.1

16	1
17	0.1
18	0.1
19	0.1

Table S3. Sum of abundance/IC_{50} ratios of individual macamides in *L. meyenii* extracts

L. meyenii extract	Σ Abundance/hsEH IC_{50} (μg/nM)	Σ Abundance/msEH IC_{50} (μg/nM)
E1	0.100	0.339
E2	18.0	62.3
E3	6.72	22.2
E4	7.75	24.8
E5	0.866	2.41
E6	0.597	1.58
E7	0.282	0.978
E8	9.72	31.5
E9	14.1	46.8
E10	1.28	4.04
E11	6.43	20.3
E12	3.37	11.2
E13	0.050	0.179

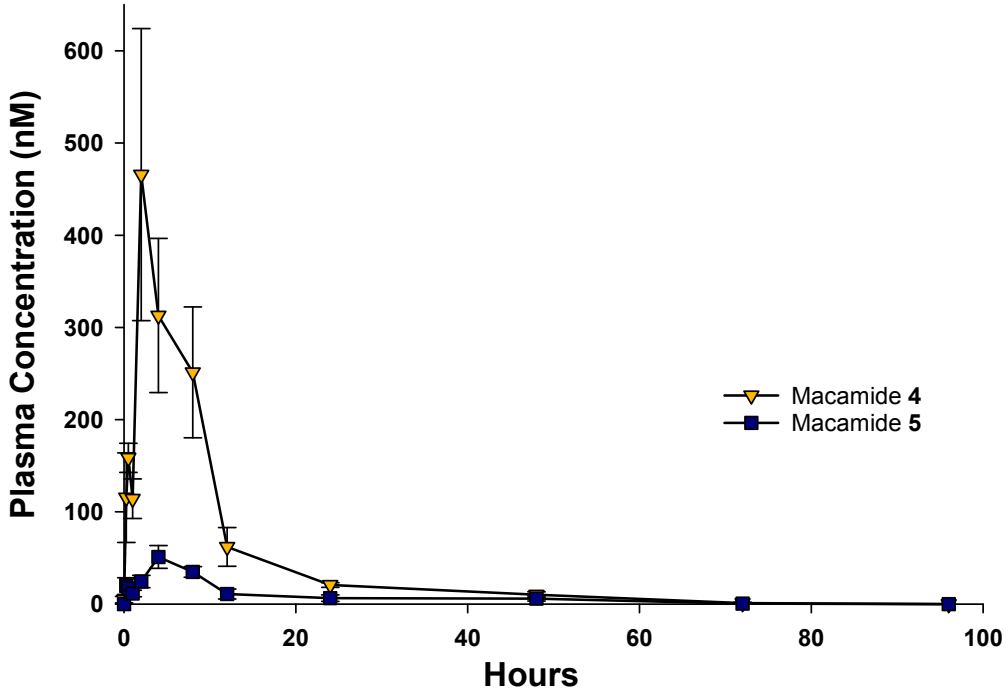


Figure S1. Pharmacokinetic study in rat: 96-hr time course for plasma concentrations of macamides **4** and **5**

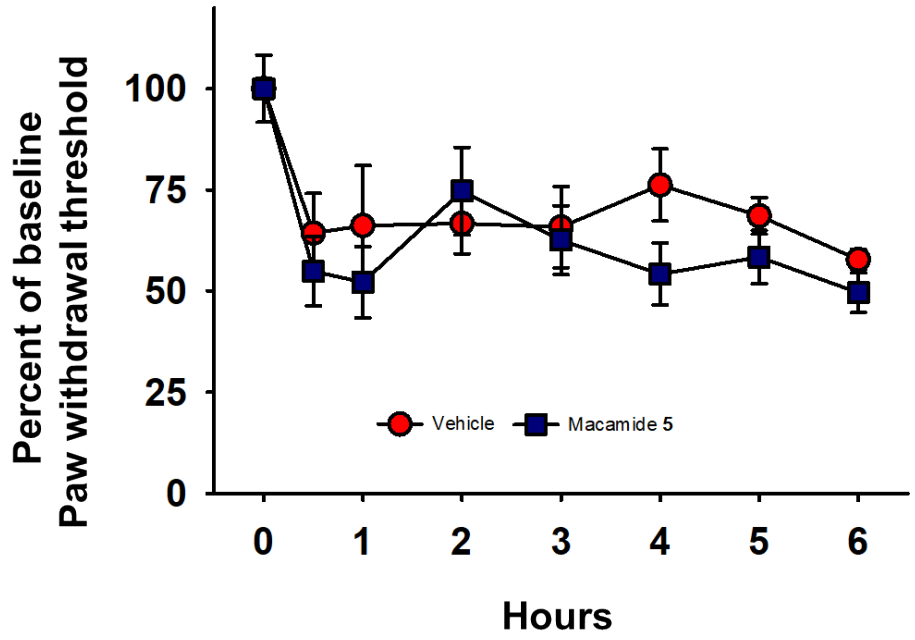


Figure S2. Analgesic efficacy of macamide **5** (100 mg/kg) against LPS induced inflammatory pain in rat was not statistically significant compared to the vehicle control. Scores are the mean ± SEM reported as percent of baseline (normalized to 100%) calculated as the score × 100/baseline score (Kruskal-Wallis One Way Analysis of Variance on Ranks, α=0.05, p=0.407, n=4/group)

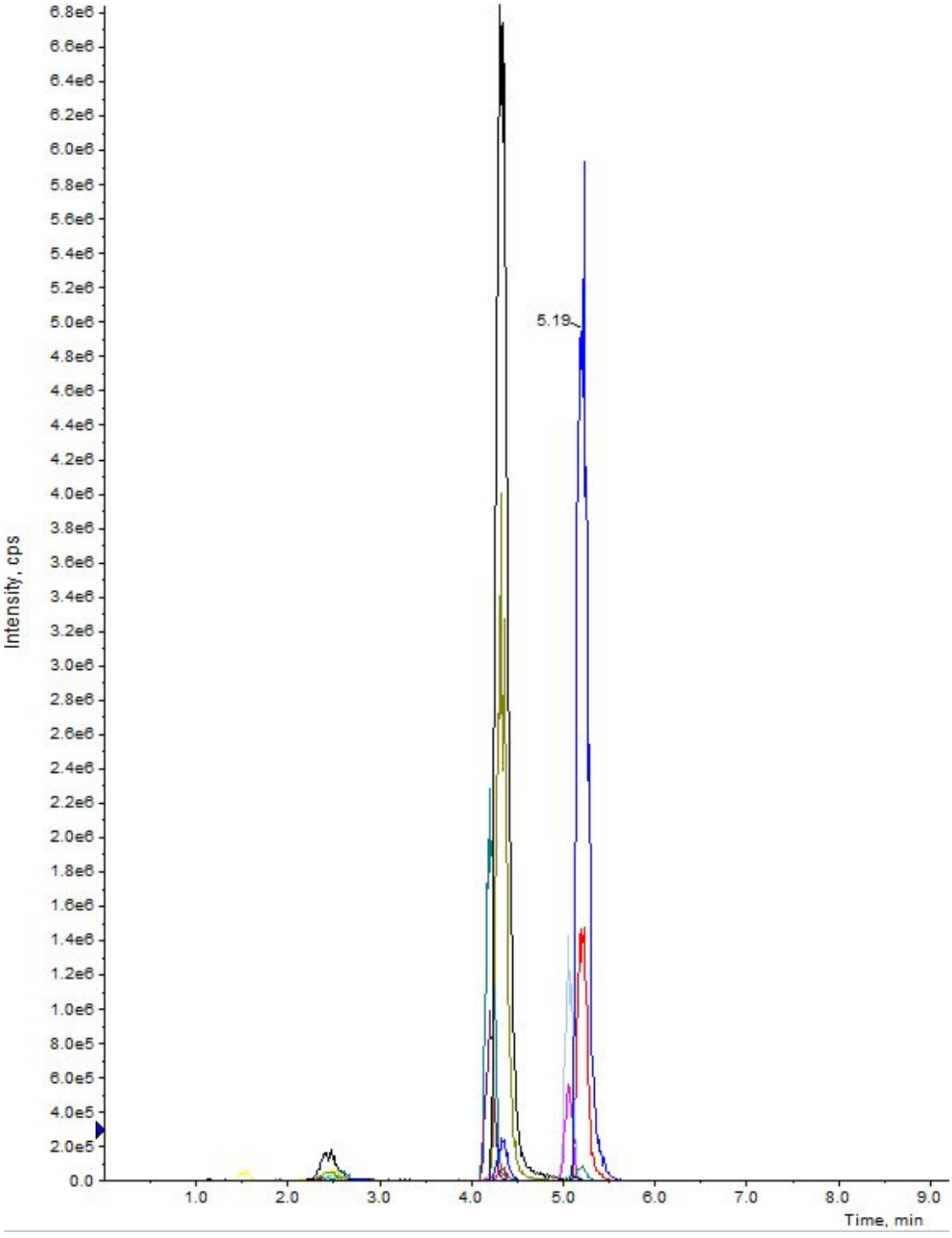
Table S4. Experimental and Literature IC_{50} values of positive control, *t*-TUCB

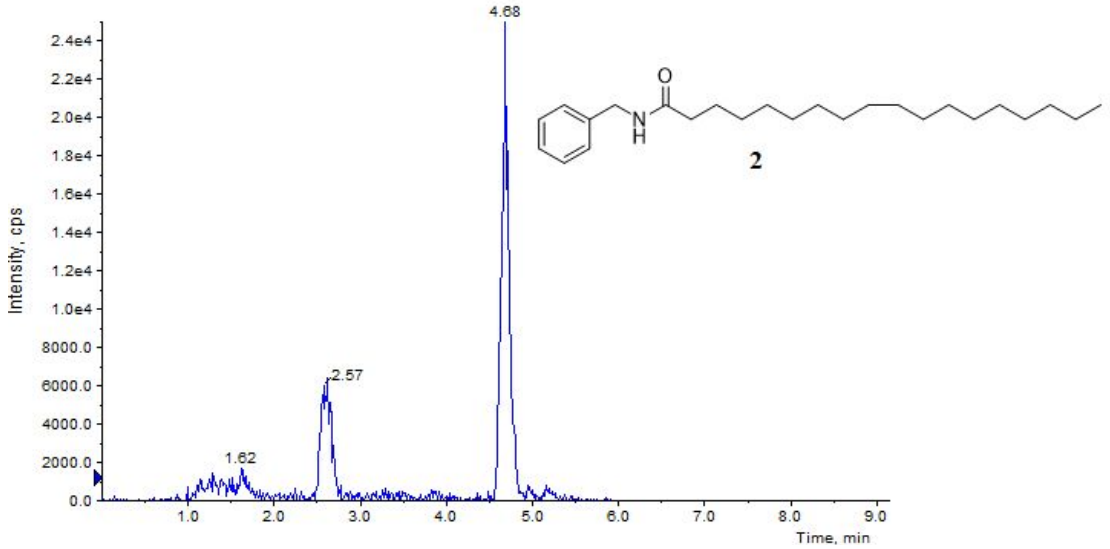
	hsEH IC_{50} (nM)	rsEH IC_{50} (nM)	msEH IC_{50} (nM)
Experimental	0.4	11	2.5
Literature	0.9	16	1.3

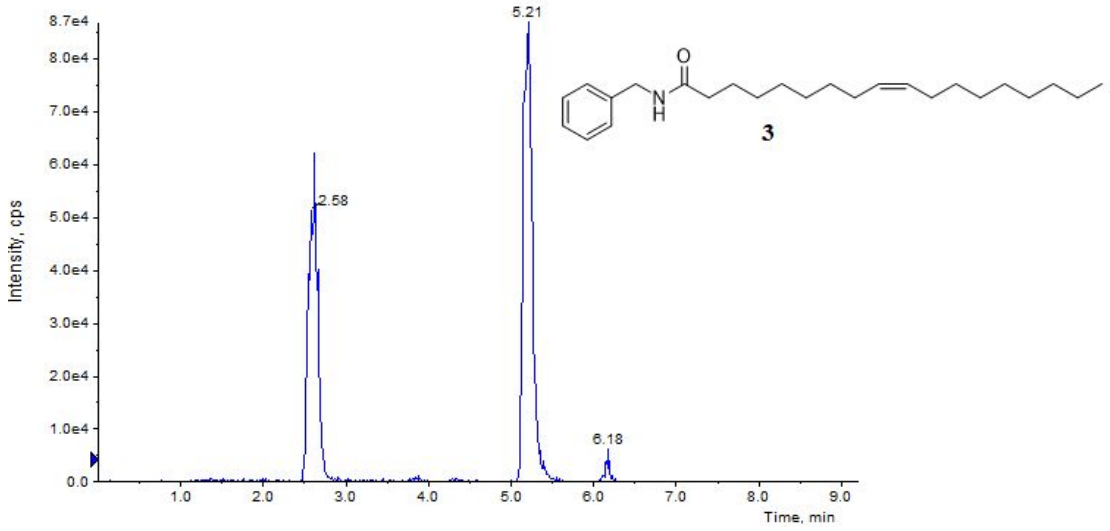
Table S5. Normalized efficiencies of macamide extraction procedures

ID	Hexanes: EtOH (7:1)/Ultrasonication (%)	Hexanes/Ultrasonication (%)	Hexanes/Soxhlet (%)
2	100	90.0	93.1
3	100	98.7	86.4
4	100	95.0	62.8

5	100	78.1	75.2
8	100	96.9	96.4
9	100	146	87.7
10	100	113	97.1
11	100	89.8	81.5
12	100	98.9	83.9




4.68
2.57
1.62
Intensity, cps
Time, min
2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2.58
6.18
Intensity, cps
Time, min
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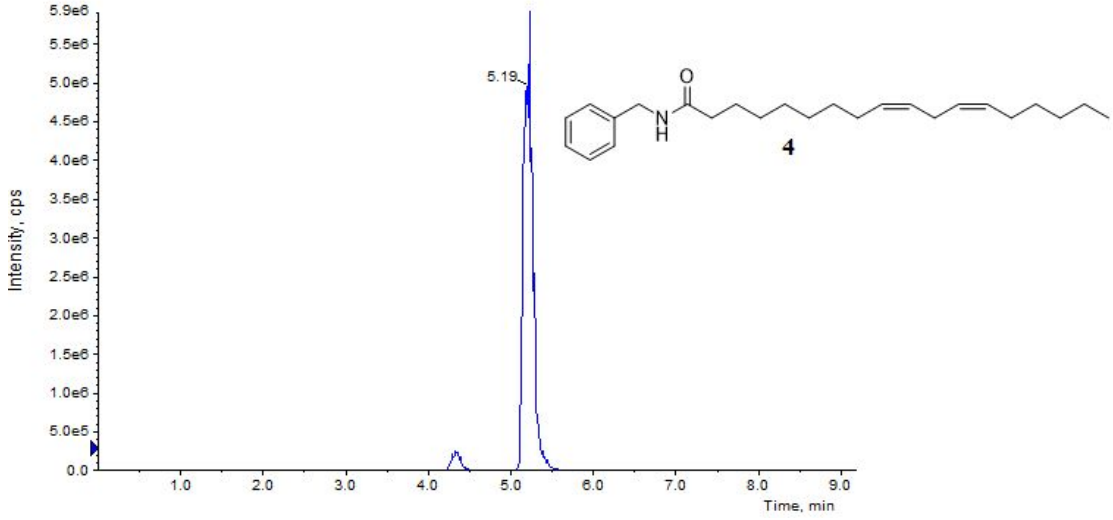
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Intensity, cps
Time, min
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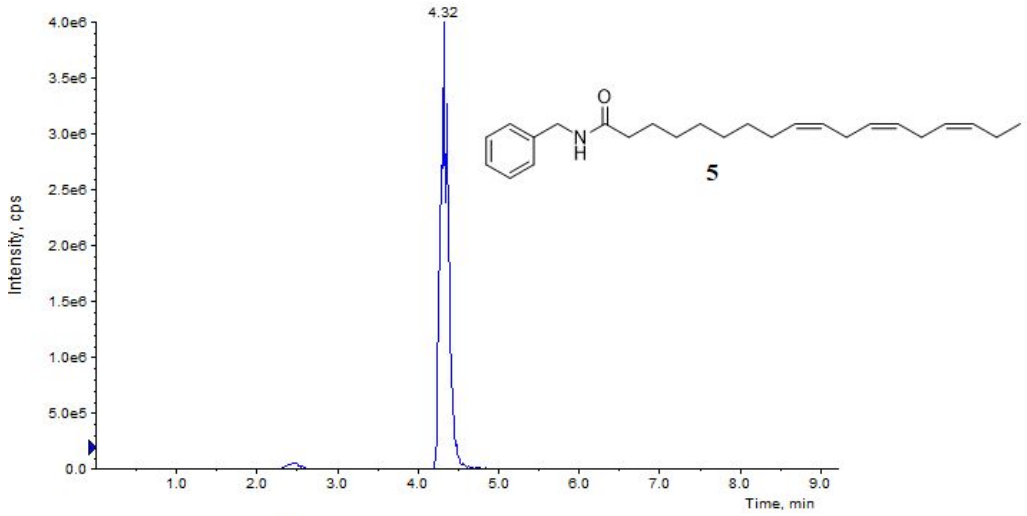
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Time, min
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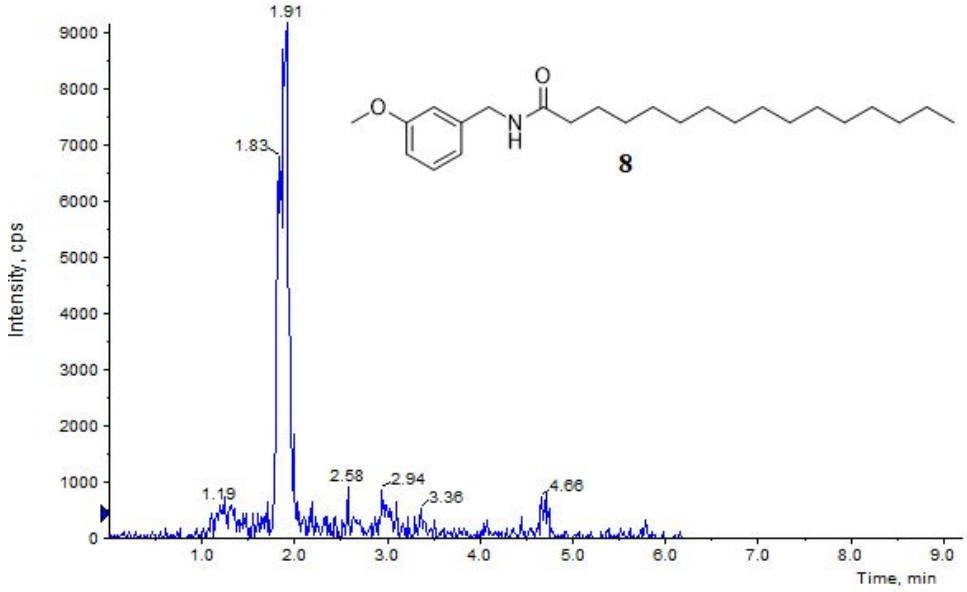
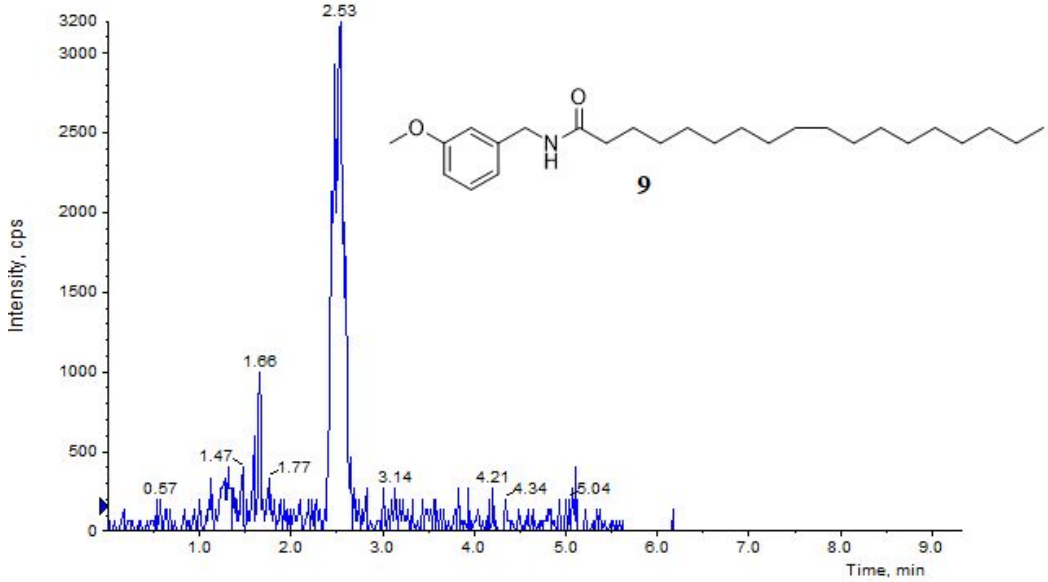

1.91
1.83
1.19
2.58
2.94
3.36
4.66
Intensity, cps
Time, min
8


2.53
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1.47
1.77
0.57
3.14
4.21
4.34
5.04
Intensity, cps
Time, min
9

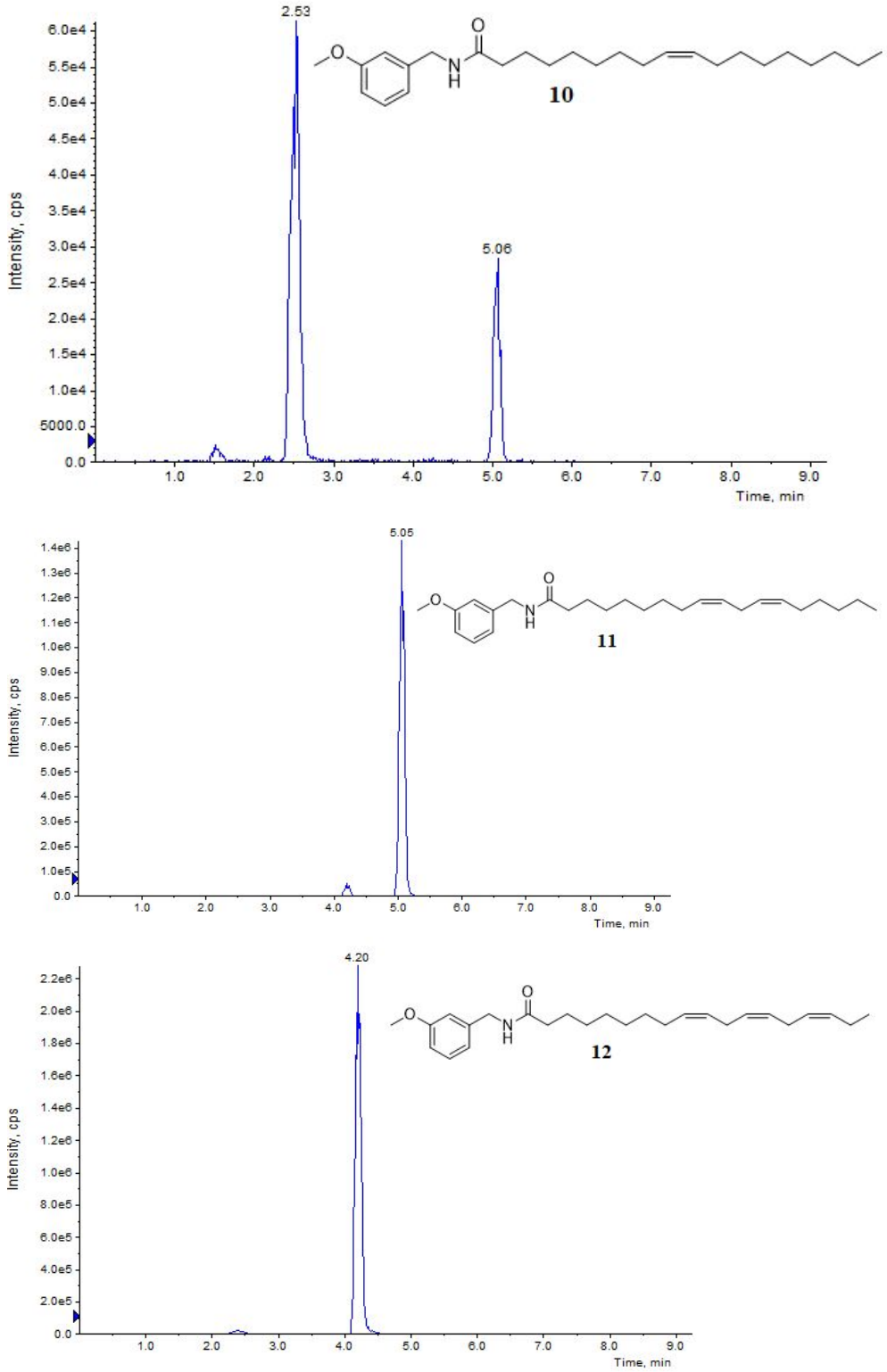
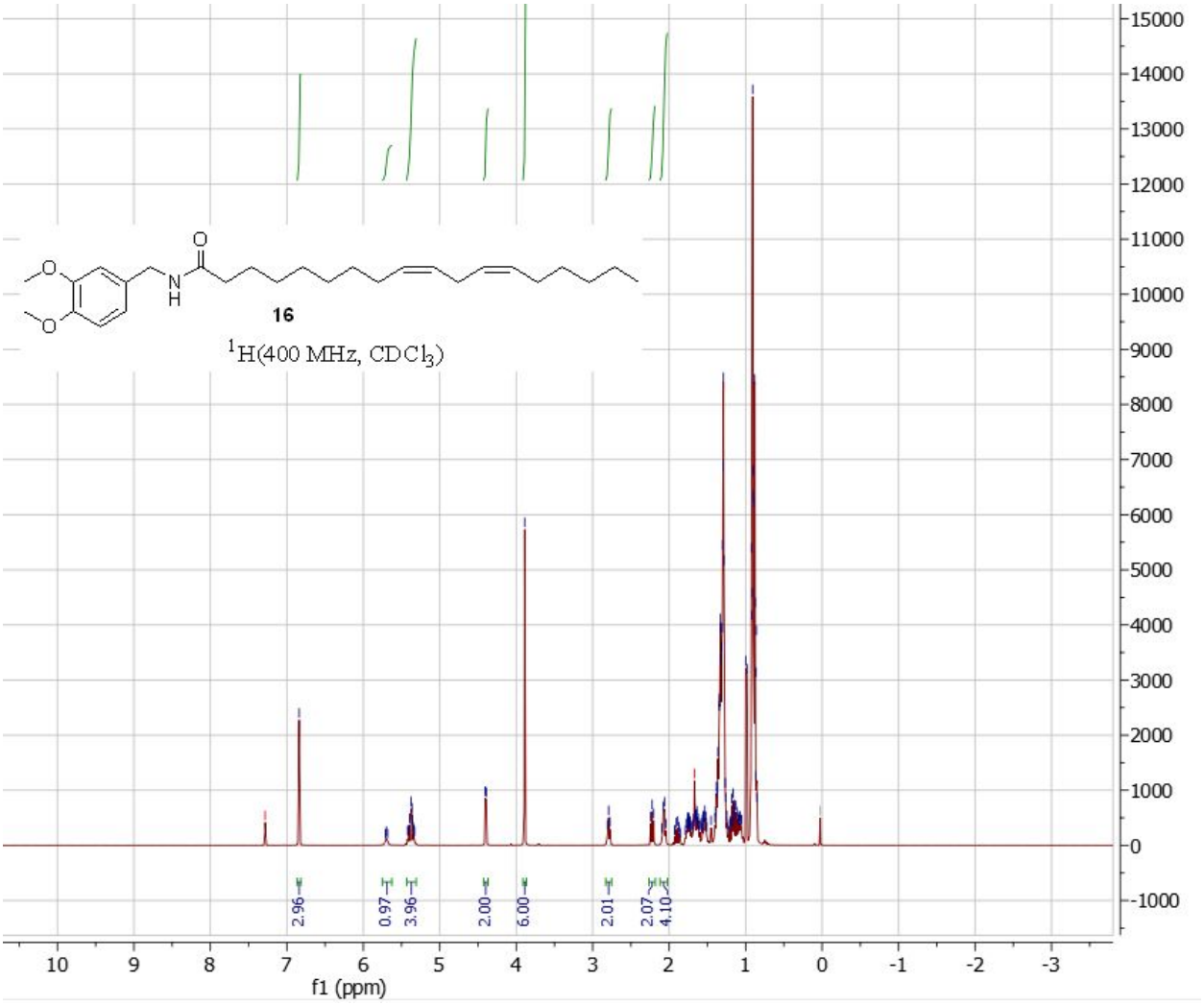
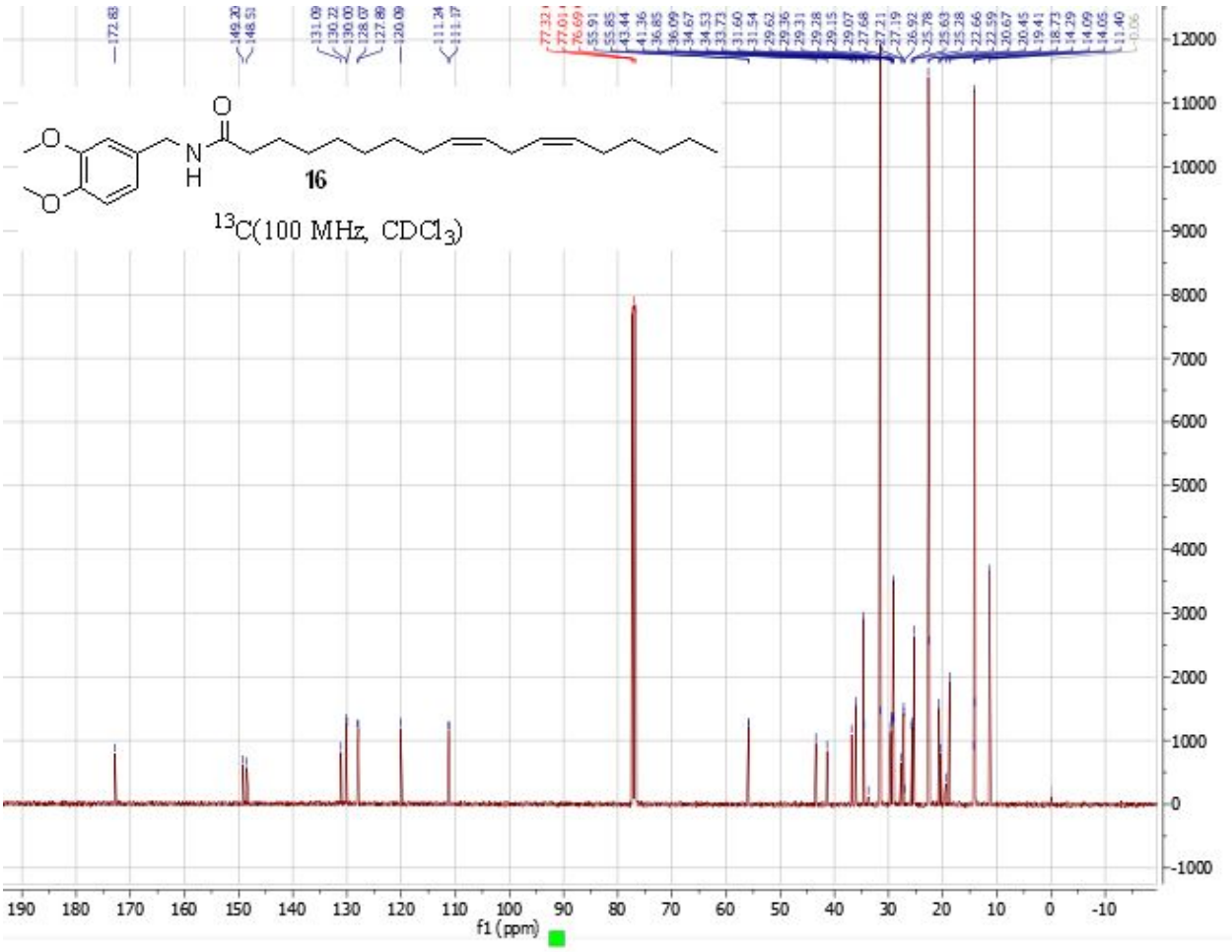
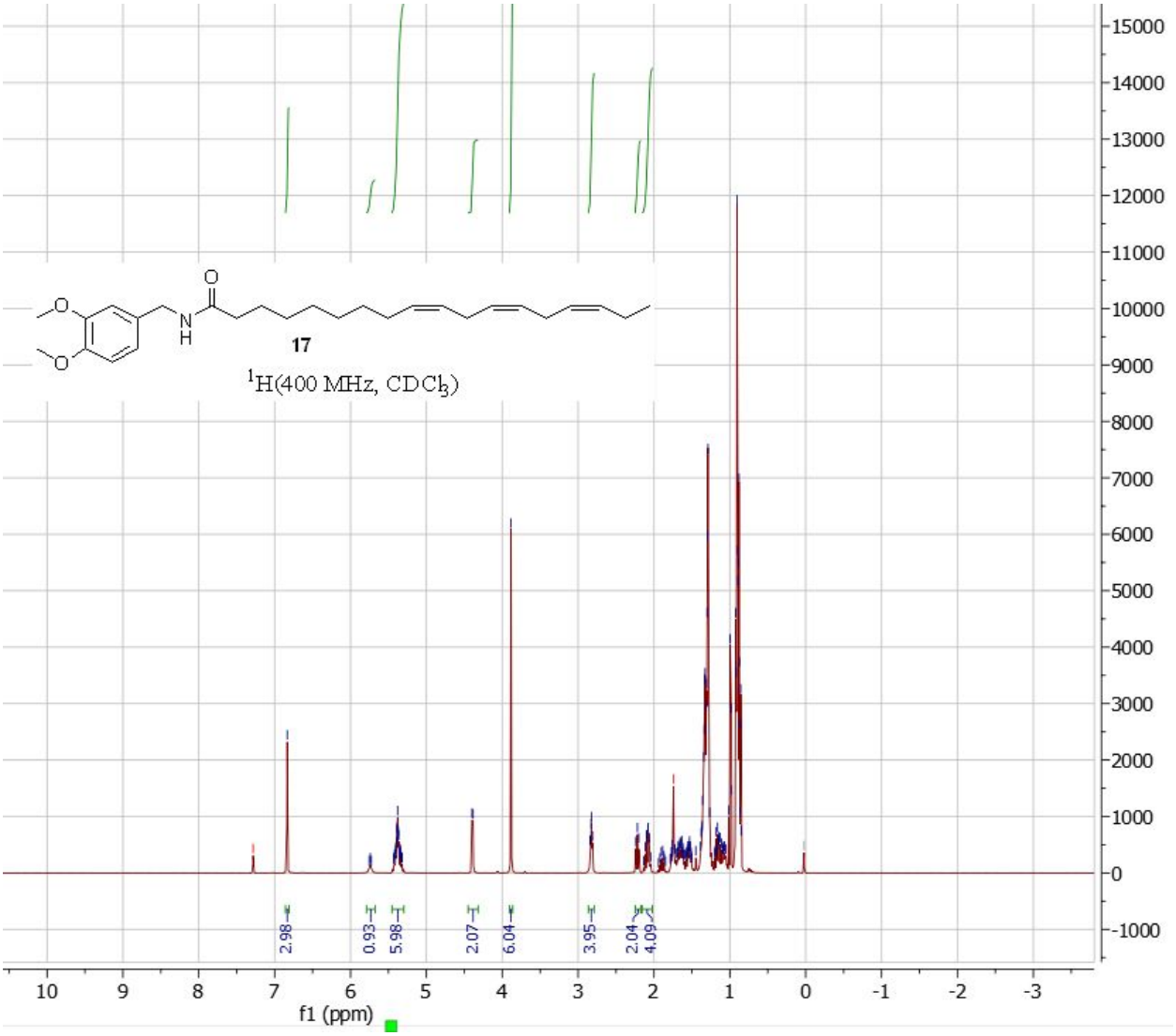


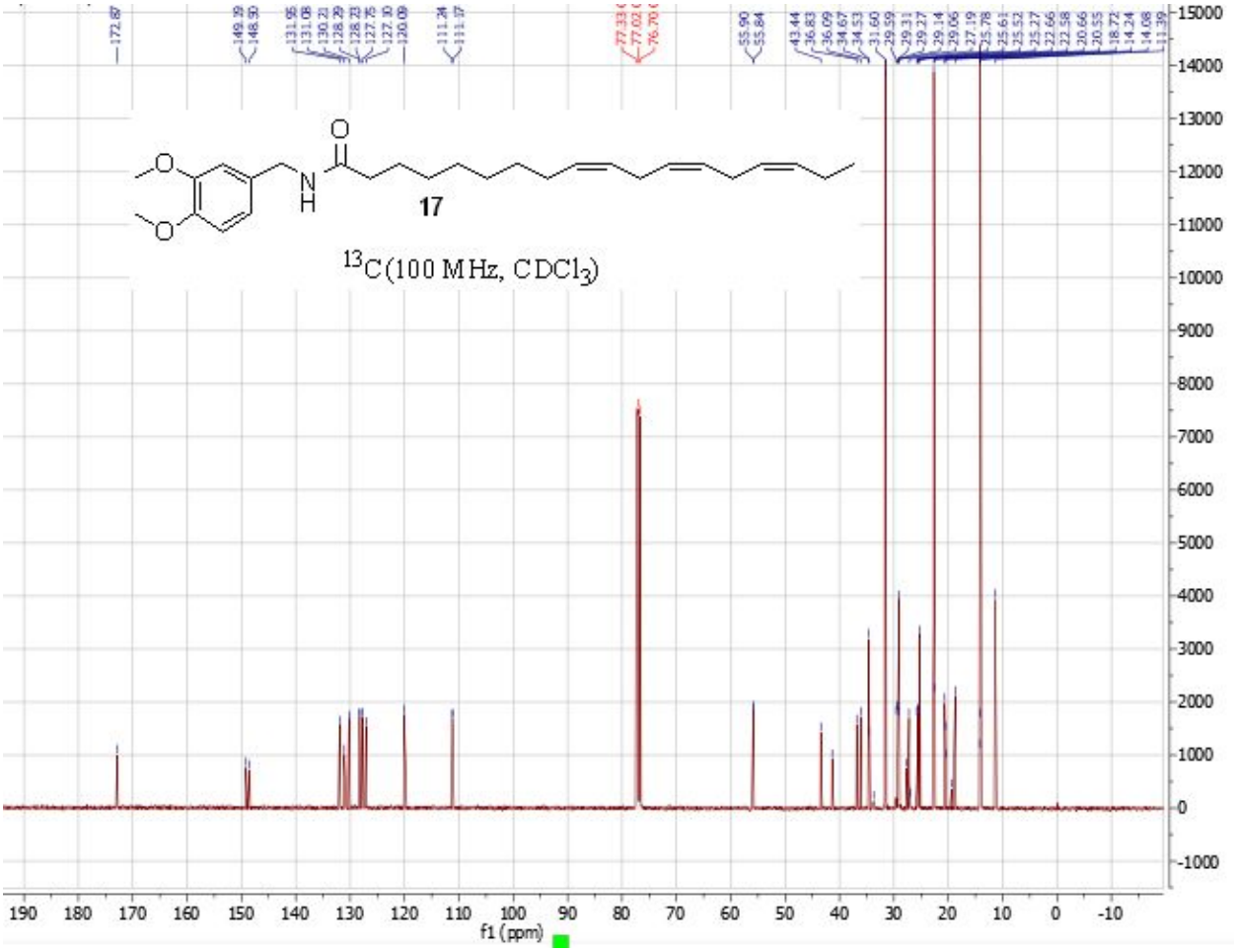
Figure S3. HPLC Trace of the extract of commercial *L. meyenii* product 2 and the known natural product macamides detected (**2-5**, **8-12**).

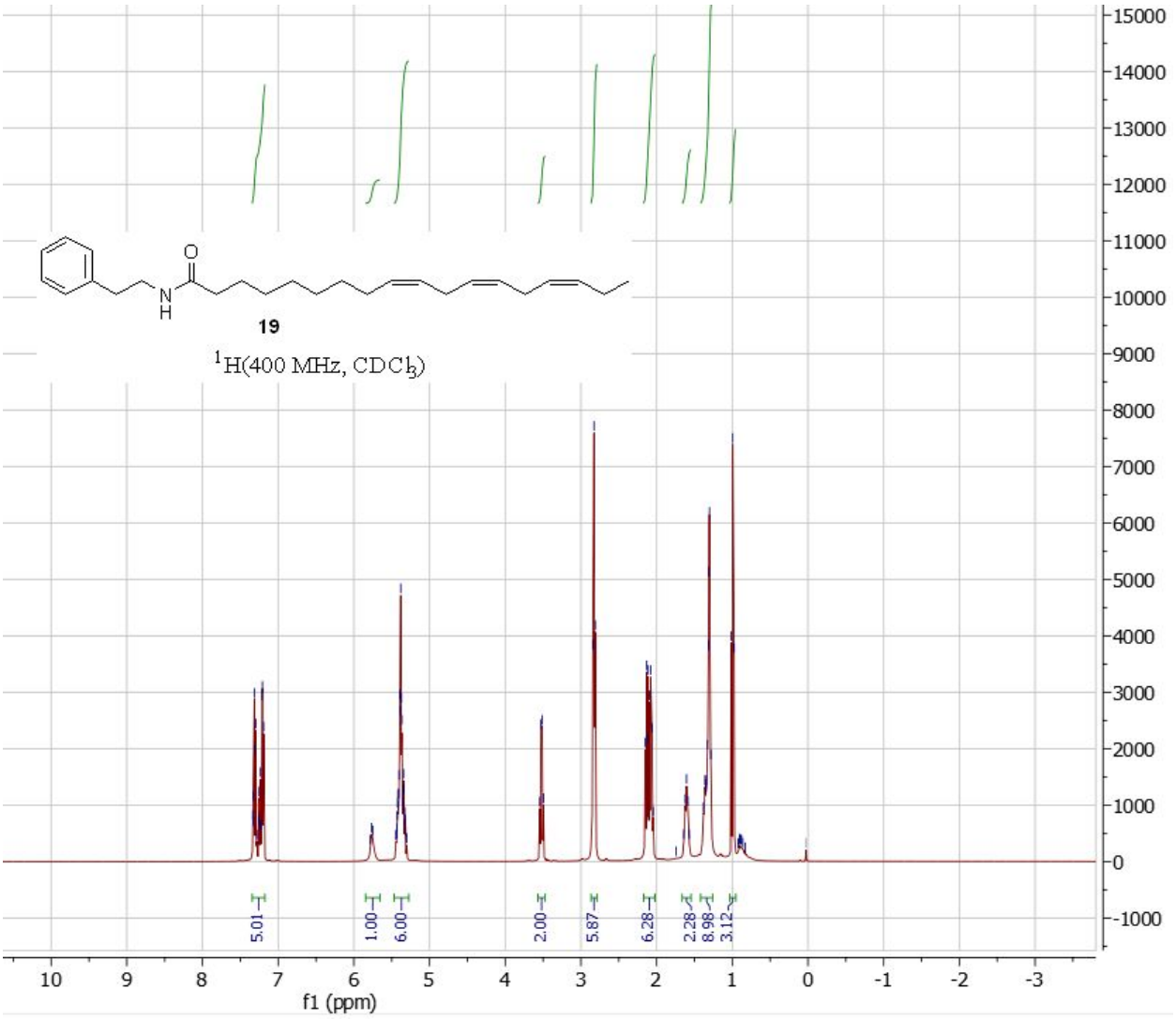
^{1}H and ^{13}C NMR Spectra of new compounds (**16**, **17** and **19)**

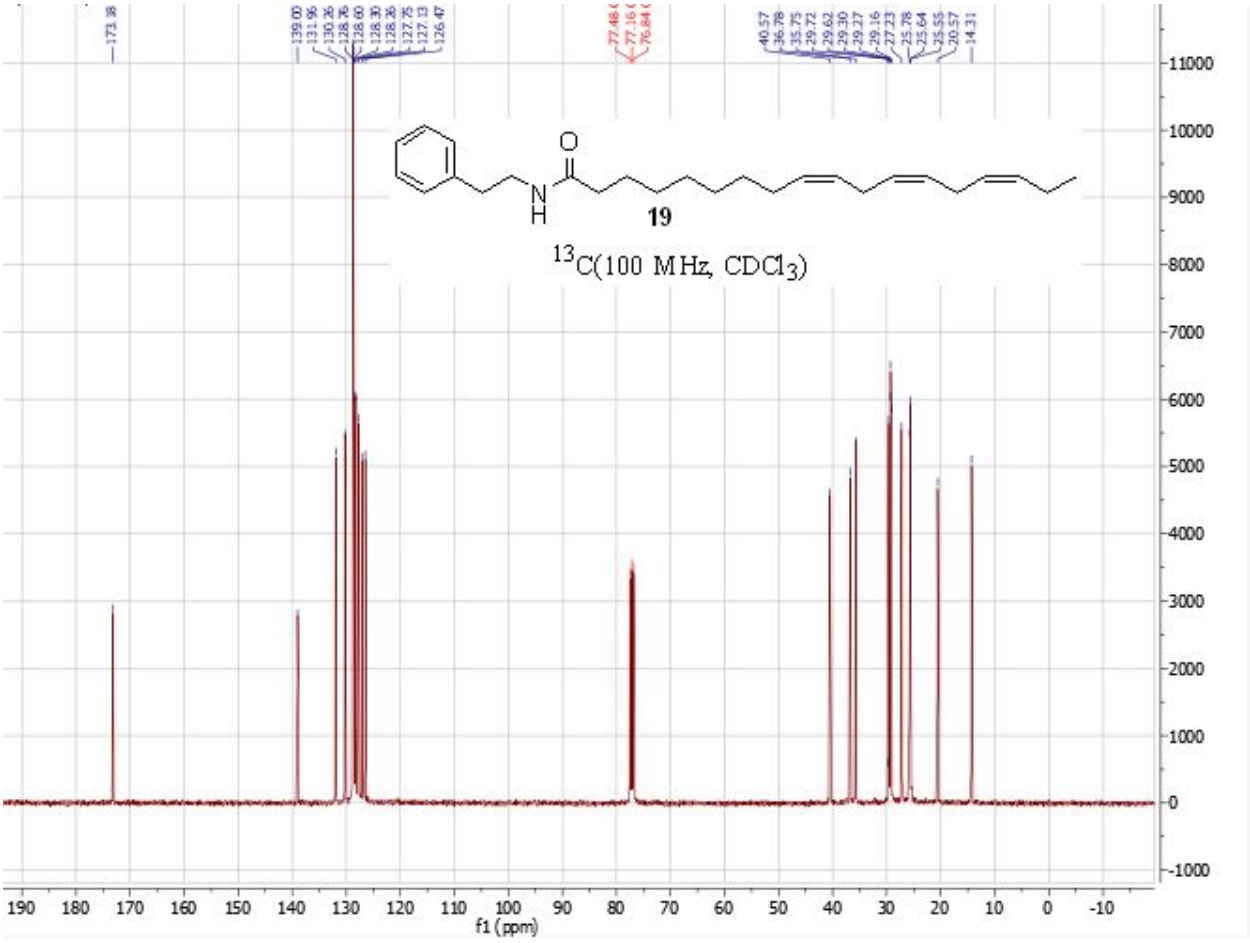



16
^{13}C(100 MHz, $CDCl_3$)
f1 (ppm)


17
^{1}H(400 MHz, CDCl$_3$)
2.98
0.93
5.98
2.07
6.04
3.95
2.04
4.09
f1 (ppm)


17
^{13}C(100 MHz, $CDCl_3$)
f1 (ppm)


19
^{1}H(400 MHz, CDCl$_3$)
5.01
1.00
6.00
2.00
5.87
6.28
2.28
8.98
3.12
f1 (ppm)


19
$^{13}C(100\ MHz, CDCl_3)$
f1 (ppm)