

## Electronic Supplementary Information

# Continuous Flow Photooxygenation of Monoterpinene

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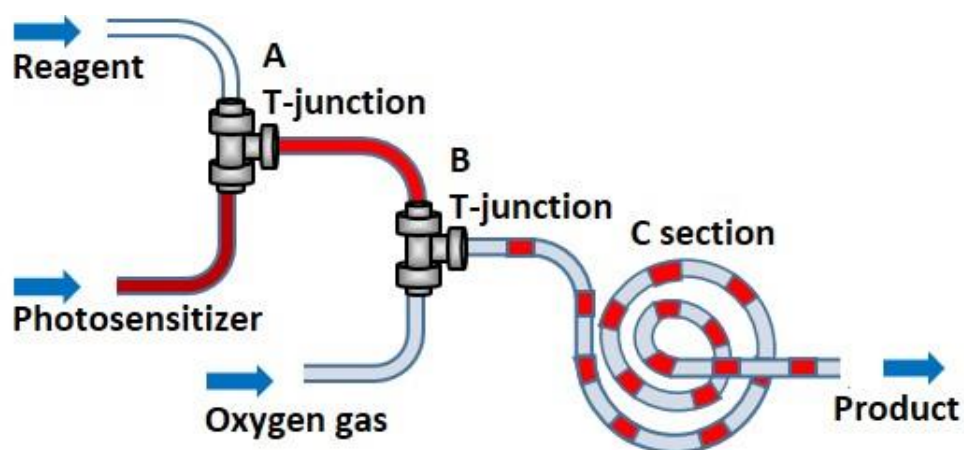
**1. General information:** All chemicals purchased from Sigma-Aldrich were used without further any purification. Thin-layer chromatography(TLC) was performed using 60 mesh silica gel plates visualized with  $\text{KMnO}_4$ . Silica gel 60 (230~400 mesh) was used for column chromatography.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a JNM-AL400 and a Bruker AC-250. Proton chemical shifts were reported in ppm ( $\delta$ ) relative to TMS with the solvent resonance employed as the internal standard ( $\text{CDCl}_3$ ,  $\delta = 7.28$  ppm). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet and doublet dt = doublet and triplet, m = multiplet), coupling constants (Hz) and integration. Carbon chemical shifts were reported in ppm from TMS with the solvent resonance as the internal standard ( $\text{CDCl}_3$   $\delta = 77.0$  ppm). GC spectra were recorded on an Agilent 5975C GC/MSD System (Agilent Tech., USA/Germany). PTFE tubing and static mixing tees were purchased from UPCHURCH, USA. Legato 210 (KD Scientific, USA) and PHD 2000 (HARVARD APPARATUS, USA) syringe pumps were used in the microchemical systems.

## 2. General procedures

### Fabrication of the microreactors

#### 1) Mono channel microreactor

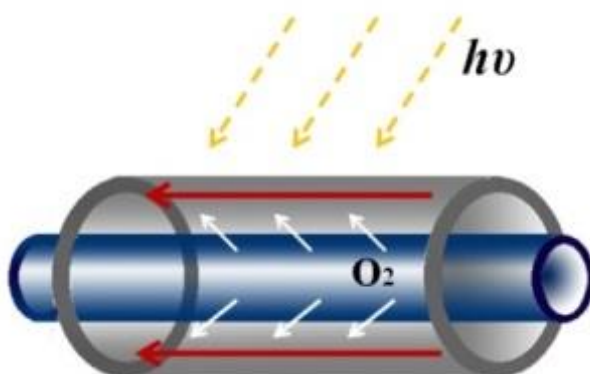
A mono channel microreactor (MC-MR) was composed of A T-junction and B T-Junction. A liquid injected from inlets for reagent and photosensitizer flew into B T-junction connected with O<sub>2</sub> inlet, O<sub>2</sub> and the liquid made slugs in the B T-junction as shown in S-1. B T-junction (UPCHURCH. USA. PEEK Cross for 1/16" OD tubing, Thru-hole 0.020"), A T-junction (UPCHURCH. USA. PEEK Cross for 1/16" OD tubing, Thru-hole 0.040"), and tube (UPCHURCH. USA. 1512 FEP Nat. 1/16 x 0.020 x 10ft) were used for reactions. Two liquids were injected by syringe pump (HARVARD APPARATUS, USA).



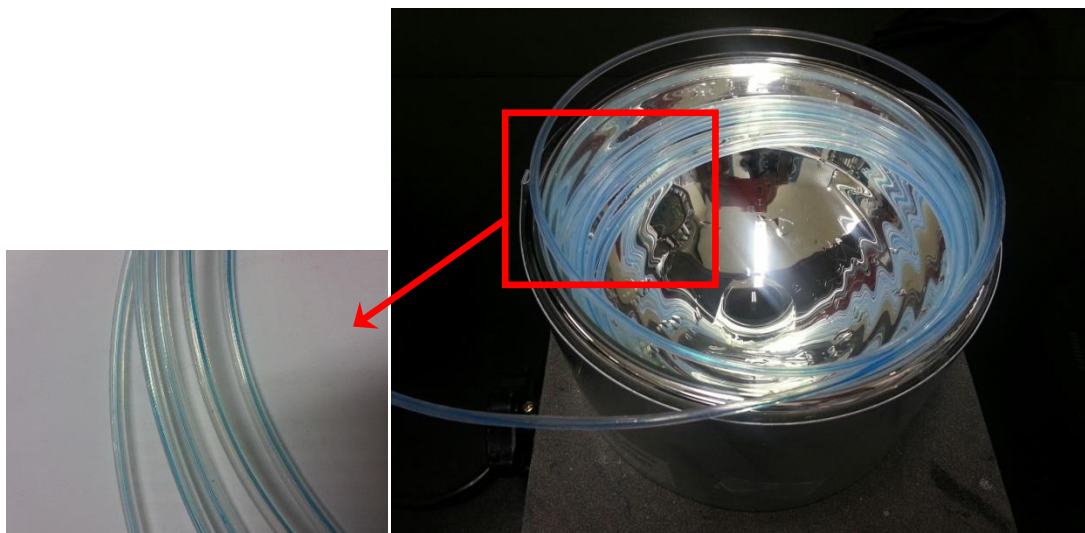
[S-1. Mono channel microreactor]

## 2) Tube in tube reactor

The reactor was made up of inner permeable tube (Advanced fiber technology, Biogeneral, TEFLON Tubing, 0.8 mm OD  $\times$  0.6 mm ID  $\times$  3 mm, Nominal, AF-2400) and transparent outer tube (UPCHURCH, USA, 1540 PEA 1.5875 mm OD  $\times$  1.016 mm ID  $\times$  2.54 mm). The inner tube could release  $O_2$  into outer tube. The whole scheme was similar to mono channel microreactor.



[S-2. Photooxygenation in the tube in tube reactor]



[F-1. Tube in tube reactor]

**General procedures for the methylene blue–catalyzed photooxygenation of (-)-Citronellol,  $\alpha$ -terpinene in the batch system:** (-)-Citronellol 7 mmol and 0.7 mmol methylene blue were dissolved in 20 mL MeOH with 50mL round-bottom flask. Firstly they were bubbled with pure oxygen gas for 1 min with the stirring. And simply the photooxygenations were taken stirring at 5 °C for 3 h under LED lamp condition.  $\alpha$ -Terpinene 2.5 mmol and 0.25 mmol methylene blue were dissolved in 20 mL MeOH. with 50mL round-bottom flask. Firstly they were bubbled with pure oxygen gas for 1 min with the stirring. the photooxygenations were taken at 5 °C for 3 h under LED lamp condition. And equally the vacuum mirror bath offered two functions of temperature controlling and enhanced light irradiation additionally. In the artificial light source, white 16 W LED lamp (FAWOO-Tech. Korea, LH16-AFE39S-White) was used.

**General procedures for the methylene blue –catalyzed photooxygenation of  $\delta$  -limonene,  $\alpha$ -pinene, and  $\beta$ -pinene in the batch system:**

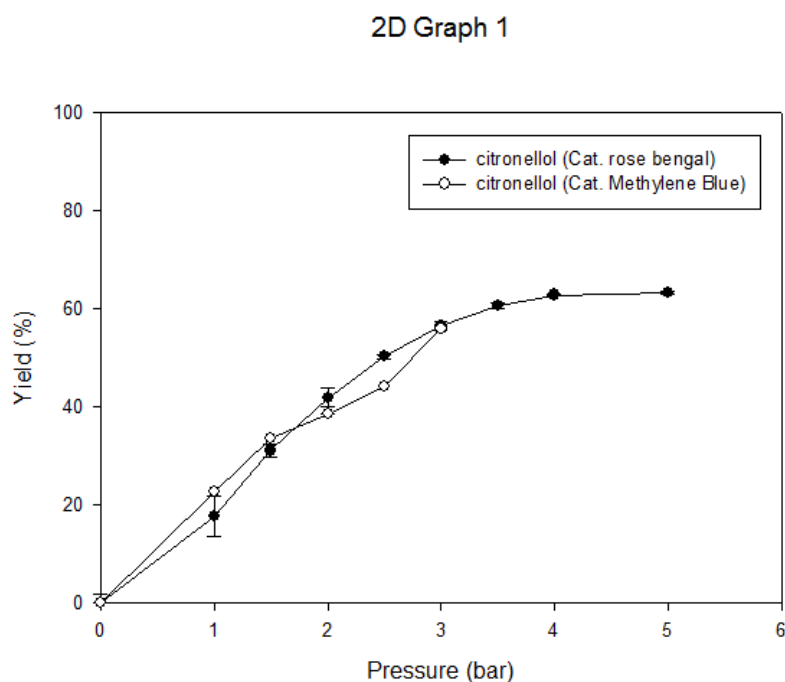
The 5 mmol reagents with 5 wt% methylene blue dissolved in 10 mL MeOH with 50mL round-bottom flask. Firstly they were bubbled with pure oxygen gas for 1 min with the stirring. And simply the photooxygenations were taken stirring at 5 °C for 3 h under LED lamp condition. And equally the vacuum mirror bath offered two functions of temperature controlling and enhanced light irradiation additionally. In the artificial light source, white 16 W LED lamp (FAWOO-Tech. Korea, LH16-AFE39S-White) was used.

**General procedures for the methylene blue –catalyzed photooxygenation of  $\delta$  -limonene,  $\alpha$ -pinene, and  $\beta$ -pinene in the mono channel microreactor:** the mono channel microreactor had two type T-junctions: A T-junction (UPCHURCH. USA. PEEK Cross for Thru-hole 0.040”), B T-junction (UPCHURCH. USA. PEEK Cross for Thru-hole 0.020”). One type of tube was used (UPCHURCH. USA. 1512 FEP. Nat.1/16”  $\times$  .020  $\times$  10 ft). The 5 mmol reagents dissolved in 5 mL MeOH was met with 5 wt% methylene blue dissolved in 5 mL MeOH through A T-junction. And then, oxygen gas and the liquid made slugs in the B T-junction. All of slugs in tubes were controlled with syringe pump. And the vacuum mirror bath offered two functions of temperature controlling and enhanced light irradiation additionally. In the artificial light source, white 16 W LED lamp(FAWOO-Tech. Korea, LH16-AFE39S-White) was used.

| Reagent            | Residence time (min) |       |       |
|--------------------|----------------------|-------|-------|
|                    | Batch                | MC-MR | TIT-R |
| $\delta$ -limonene | 1080                 | 20    | 20    |
| $\alpha$ -pinene   | 1440                 | 15    | 20    |
| $\beta$ -pinene    | 1440                 | 60    | 58    |

**General procedures for the methylene blue-catalyzed photooxygenation of (-)-Citronellol,  $\alpha$ -terpinene in the tube in tube microreactor:** (-)-Citronellol 7 mmol was dissolved in 20 mL MeOH and 0.7 mmol methylene blue was dissolved in 10 mL MeOH, the photooxygenations were taken at 5 °C for 2 min.  $\alpha$ -Terpinene 2.5 mmol was dissolved in 10 mL MeOH and 0.25 mmol methylene blue was dissolved in 10 mL MeOH, the photooxygenations were taken at 5 °C for 4 min.

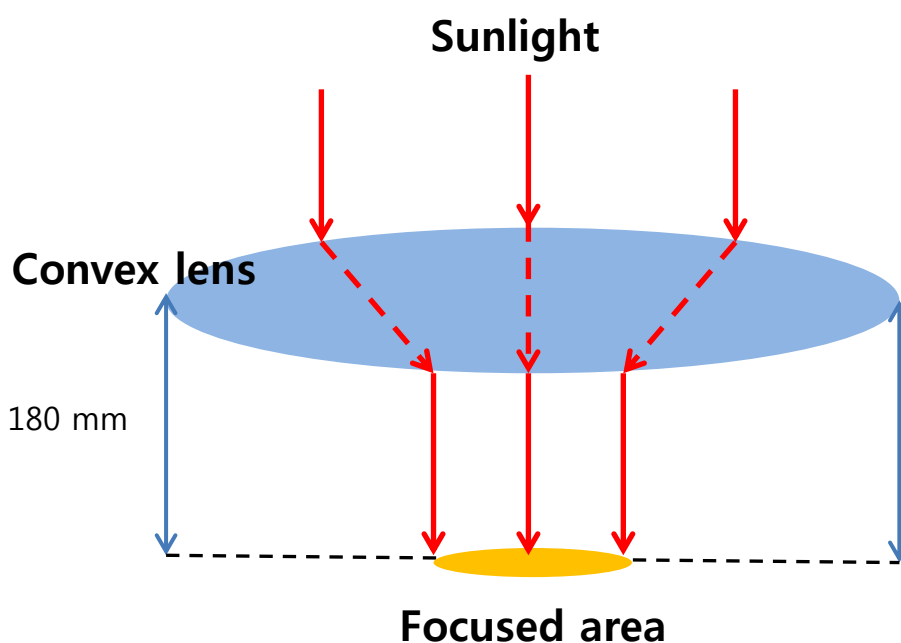
**The photooxygenation of (-)-citronellol with methylene blue and rose bengal:**



(-)-Citronellol (3.5 mmol) and methylene blue (0.7 mmol) were dissolved in 10 mL MeOH respectively, while (-)-citronellol (3.5 mmol) and rose bengal (0.7 mmol) were dissolved in 10 mL ACN respectively.

### The detail condition for sunlight experiment

In the natural light experiments, we used the convex lens (Kenis japan No. 115-552. 5RT1-114, magnification x 2.2, focal distance 200 mm, diameter 270 mm) for focusing the light. The lens was kept at a 180 mm distance from reactor to avoid undesirable high temperature. Reagent ( $\beta$ -pinene) 2.5 mmol and methylene blue 10 wt % dissolved in 5 mL MeOH were exposed to the natural sunlight for 30 min at average 28.5 °C. All experiments were conducted from 11:00 AM to 01:30 PM ( $>22.5^\circ$  solar elevation angle) to obtain similar reaction conditions.



[S-3. Photooxygenation under the natural sunlight ]



[F-2. the real sunlight experiment]

## The calculation of Daily Output (Table 2)

Reagent (mmol/1mL) x volume x 24 h x (60/retention time) x yield

### 1) Batch system (reaction volume: 10 mL)

### 2) Mono channel microreactor (reaction volume: 0.026 mL)

Tube ID : 0.5mm

Total channel length: 3000 mm

Drop length (average): 0.5 mm

Initial gas phase length (average): 21 mm

Drop volume (average): 0.000098 mL

Total drops in microreactor = 261

Total volume of solution phase =  $261 \times 0.000098 \text{ mL} \approx 0.026 \text{ mL}$

### 3) Tube in tube system (reaction volume: 7.92 mL)

Outer tube ID: 2.0 mm

Inner tube OD: 0.8 mm

Total channel length : 3000 mm

$= ((1/10^3)^2 - (0.4/10^3)^2) \pi \times 3 \approx 7.92 \text{ mL}$

### a) (-)-Citronellol (flow rate = injection rate of reagent + injection rate of methylene blue)

| a) (-)-Citronellol | Time (min)                 | Yield (%) | DOP   |
|--------------------|----------------------------|-----------|---|
| Batch              | 180                        | 92        | 25.8  |
| MC-MR              | 2 (flow rate: 0.013ml/min) | 99.9      | 6.49 (0.35 mmol/1 mL x 0.026 mL x 24 h x (60/2) x 0.999)  |
| TIT-R              | 2 (flow rate: 3.96ml/min)  | 87.8      | 1752.3 (0.35 mmol/1 mL x 7.92 mL x 24 h x (60/2) x 0.878) |

### b) $\alpha$ -Terpinene (flow rate = injection rate of reagent + injection rate of methylene blue)

| b) $\alpha$ -terpinene | Time (min)                  | Yield (%) | DOP  |
|------------------------|-----------------------------|-----------|--|
| Batch                  | 180                         | 92        | 18.4   |
| MC-MR                  | 4 (flow rate: 0.0065ml/min) | 90.1      | 2.11 (0.25 mmol/1 mL x 0.026 mL x 24 h x (60/4) x 0.901) |
| TIT-R                  | 4 (flow rate: 1.98ml/min)   | 87.4      | 623.0 (0.25 mmol/1 mL x 7.92 mL x 24 h x (60/4) x 0.874) |



**c)  $\beta$ -Pinene** (flow rate = injection rate of reagent + injection rate of methylene blue)

| c) $\beta$ -pinene | Time (min)                   | Yield (%) | DOP  |
|--------------------|------------------------------|-----------|--|
| <b>Batch</b>       | 1440                         | 98.9      | 9.9  |
| <b>MC-MR</b>       | 60 (flow rate: 0.0004ml/min) | 99.9      | 0.6 (1.0 mmol/1 mL x 0.026 mL x 24 h x (60/60) x 0.999)  |
| <b>TIT-R</b>       | 58 (flow rate: 0.136ml/min)  | 87.5      | 172.1 (1.0 mmol/1 mL x 7.92 mL x 24 h x (60/58) x 0.875) |

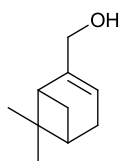
**d)  $\alpha$ -Pinene** (flow rate = injection rate of reagent + injection rate of methylene blue)

| d) $\alpha$ -pinene | Time (min)                   | Yield (%) | DOP   |
|---------------------|------------------------------|-----------|---|
| <b>Batch</b>        | 1440                         | 99.9      | 2.5   |
| <b>MC-MR</b>        | 15 (flow rate: 0.0017ml/min) | 82.7      | 0.52 (0.25 mmol/1 mL x 0.026 mL x 24 h x (60/15) x 0.827) |
| <b>TIT-R</b>        | 20 (flow rate: 0.396ml/min)  | 99.9      | 142.4 (0.25 mmol/1 mL x 7.92 mL x 24 h x (60/20) x 0.999) |

**e)  $\delta$ -Limonene** (flow rate = injection rate of reagent + injection rate of methylene blue)

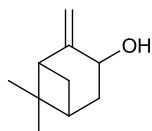
| e) $\delta$ -Limonene | Time (min)                   | Yield (%) | DOP  |
|-----------------------|------------------------------|-----------|--|
| <b>Batch</b>          | 1080                         | 96.9      | 6.46   |
| <b>MC-MR</b>          | 20 (flow rate: 0.0013ml/min) | 46.9      | 0.44 (0.5 mmol/1 mL x 0.026 mL x 24 h x (60/20) x 0.469) |
| <b>TIT-R</b>          | 20 (flow rate: 0.396ml/min)  | 46.1      | 131.4 (0.5 mmol/1 mL x 7.92 mL x 24 h x (60/20) x 0.461) |

### 3. NMR Data



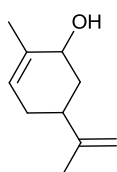
#### *(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methanol*

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.17 (s, 1H, OH), δ 5.64 (s, 1H, CH), δ 4.33-4.43 (m, 2H, CH<sub>2</sub>), δ 2.40-2.46 (m, 1H, CH), δ 2.27-2.32 (m, 2H, CH<sub>2</sub>), δ 2.23-2.25 (m, 2H, CH<sub>2</sub>), δ 1.31 (s, 3H, CH<sub>3</sub>), δ 1.17 (m, 2H, CH<sub>2</sub>), δ 0.86 (m, 3H, CH<sub>3</sub>) <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 143.30, 123.85, 80.22, 43.70, 40.71, 37.99, 31.60, 31.43, 26.09, 21.11.



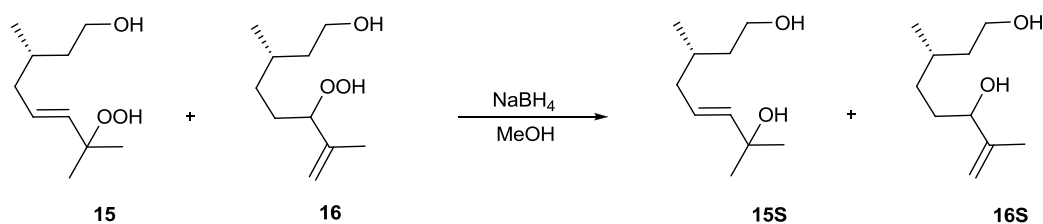
#### *6,6-dimethyl-2-methylenebicyclo[3.1.1]heptan-3-ol*

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 5.02 (s, 1H, CH<sub>2</sub>), δ 4.84 (s, 1H, CH<sub>2</sub>), δ 4.43 (d, *J* = 7.6 Hz, 1H, CHOH), δ 2.52 (t, *J* = 5.2 Hz, 1H, CH), δ 2.38-2.45 (m, 1H, CH), δ 2.29-1.99 (m, 2H, CH<sub>2</sub>), δ 1.89-1.72 (m, 2H, CH<sub>2</sub>), δ 1.30 (s, 3H, CH<sub>3</sub>), δ 0.66 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 156.16, 111.41, 67.05, 50.57, 40.43, 39.85, 34.47, 27.92, 25.93, 21.94.



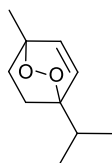
#### *2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enol*

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 5.62 (s, 1H, CH), δ 5.52 (s, 1H, CH<sub>2</sub>), δ 4.75 (s, 1H, OH), δ 4.21 (d, 2H, CH<sub>2</sub>), δ 2.26- 2.37 (m, 2H, CH), δ 2.13-2.15 (m, 1H, CH), δ 1.93-1.98 (m, 1H, CH), δ 1.82 (s, 3H, CH<sub>3</sub>), δ 1.76 (s, 3H, CH<sub>3</sub>), δ 1.58-1.67 (m, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 149.17, 134.32, 125.36, 123.87, 70.91, 68.56, 40.46, 38.02, 31.01, 20.82.



***(S,E)-7-hydroperoxy-3,7-dimethyloct-5-en-1-ol + (3S)-6-hydroperoxy-3,7-dimethyloct-7-en-1-ol***

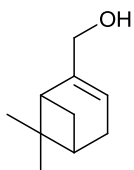
$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  5.68-5.61(m, 2H, 15S), 4.95 (s, 1H, 16S), 4.85 (s, 1H, 16S), 4.06 (s, 1H, 16S), 3.70 (br, 4H), 2.11 (t,  $J = 7.23$  Hz, 1H), 1.97-1.89 (m, 1H), 1.73 (s, 3H, 16S), 1.66-1.59 (m, 6H), 1.53 (br s, 4H), 1.46-1.38 (m, 4H), 1.31 (s, 6H, 15S).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  144.12, 143.93, 135.13, 129.81, 114.13, 113.83, 89.85, 89.42, 81.96, 60.85, 38.82, 38.94, 38.00, 32.83, 38.94, 32.83, 32.56, 32.56, 29.60, 28.05, 19.79, 19.53, 19.48 17.10, 17.00.



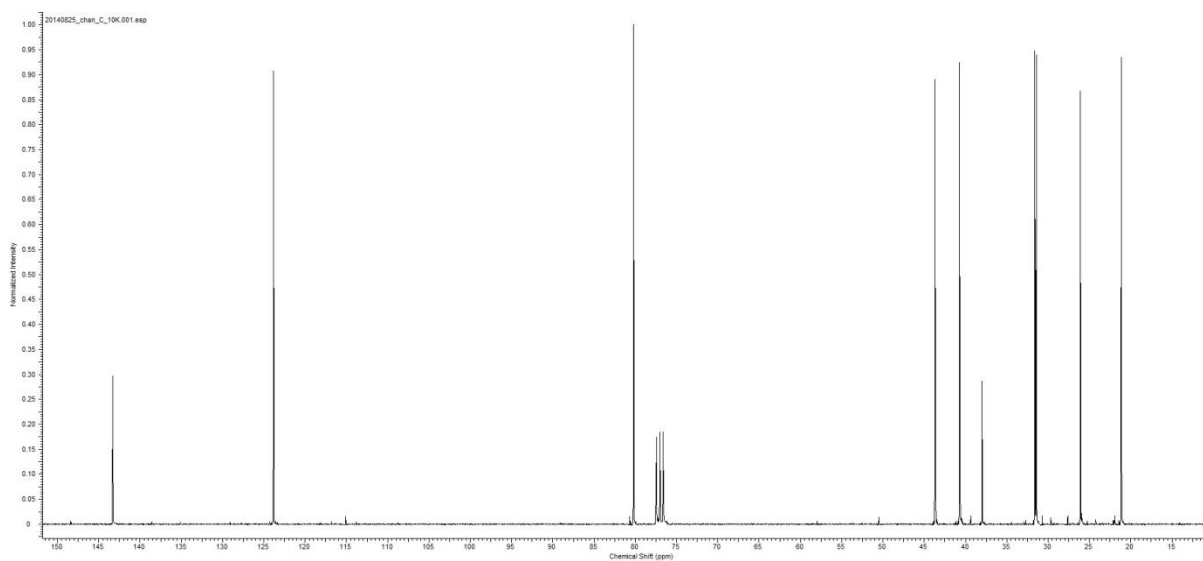
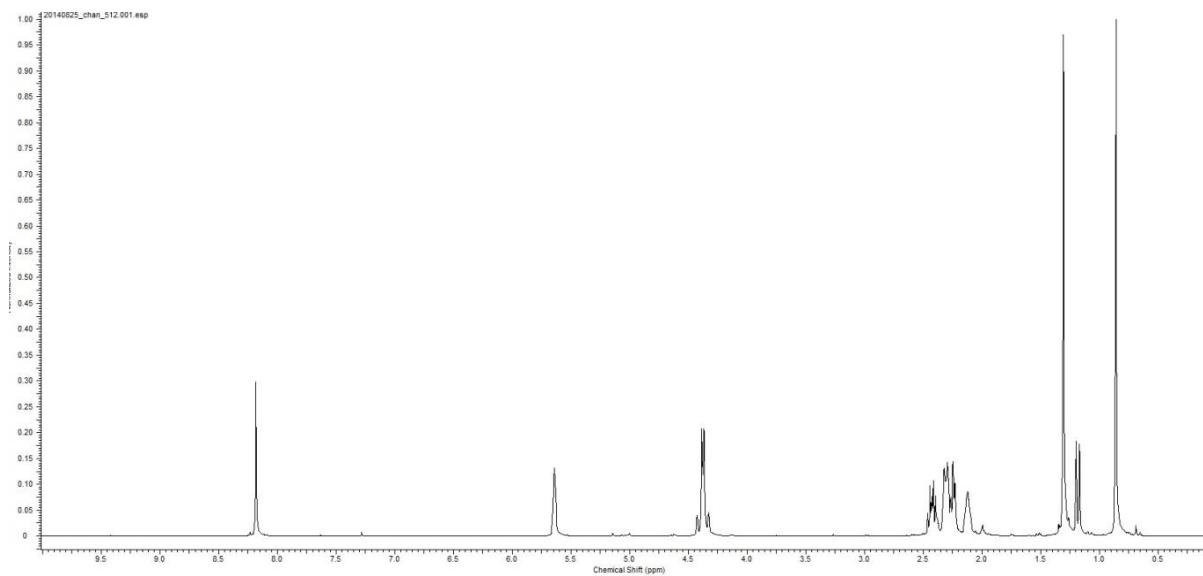
***1-isopropyl-4-methyl-2,3-dioxabicyclo[2.2.2]oct-7-ene***

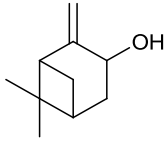
$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.49 (d,  $J = 8.5$  Hz, 1H, CH), 6.40 (d,  $J = 8.5$  Hz, 1H, CH), 2.01–2.05 (m, 2H,  $\text{CH}_2\text{CH}_2$ ), 1.93 (hept,  $J = 6.7$  Hz, 1H,  $\text{CH}(\text{CH}_3)_2$ ), 1.48–1.59 (m, 2H,  $\text{CH}_2\text{CH}_2$ ), 1.38 (s, 3H,  $\text{CH}_3$ ), 0.99 (d,  $J = 6.7$  Hz, 6H,  $\text{CH}(\text{CH}_3)_2$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  136.39, 133.05, 79.76, 74.32, 32.12, 29.53, 25.59, 21.37, 17.20.

## 4. NMR Spectra

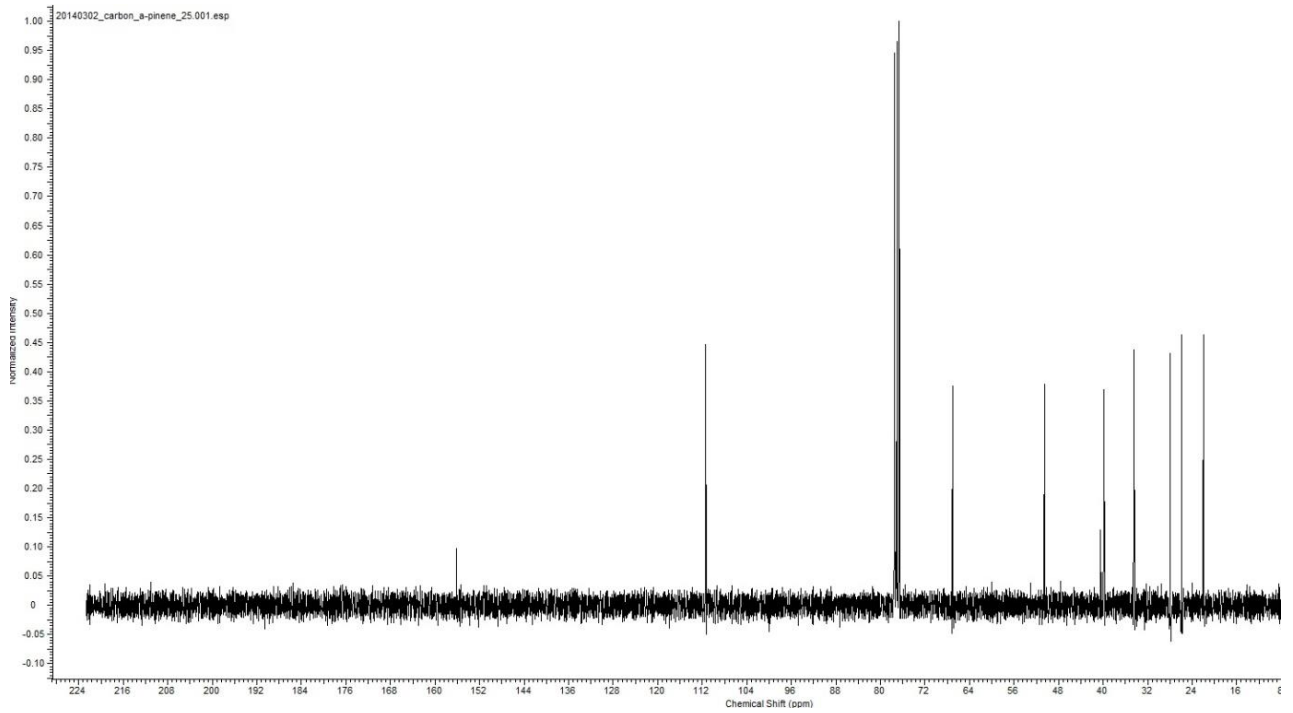
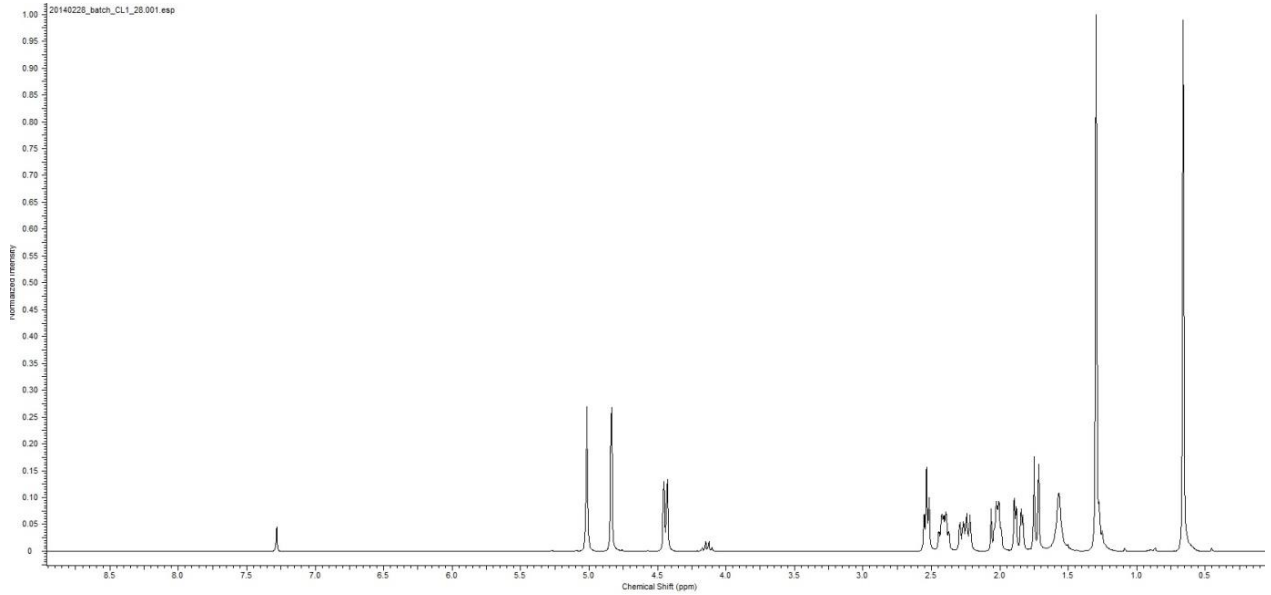


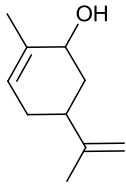
*(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methanol*



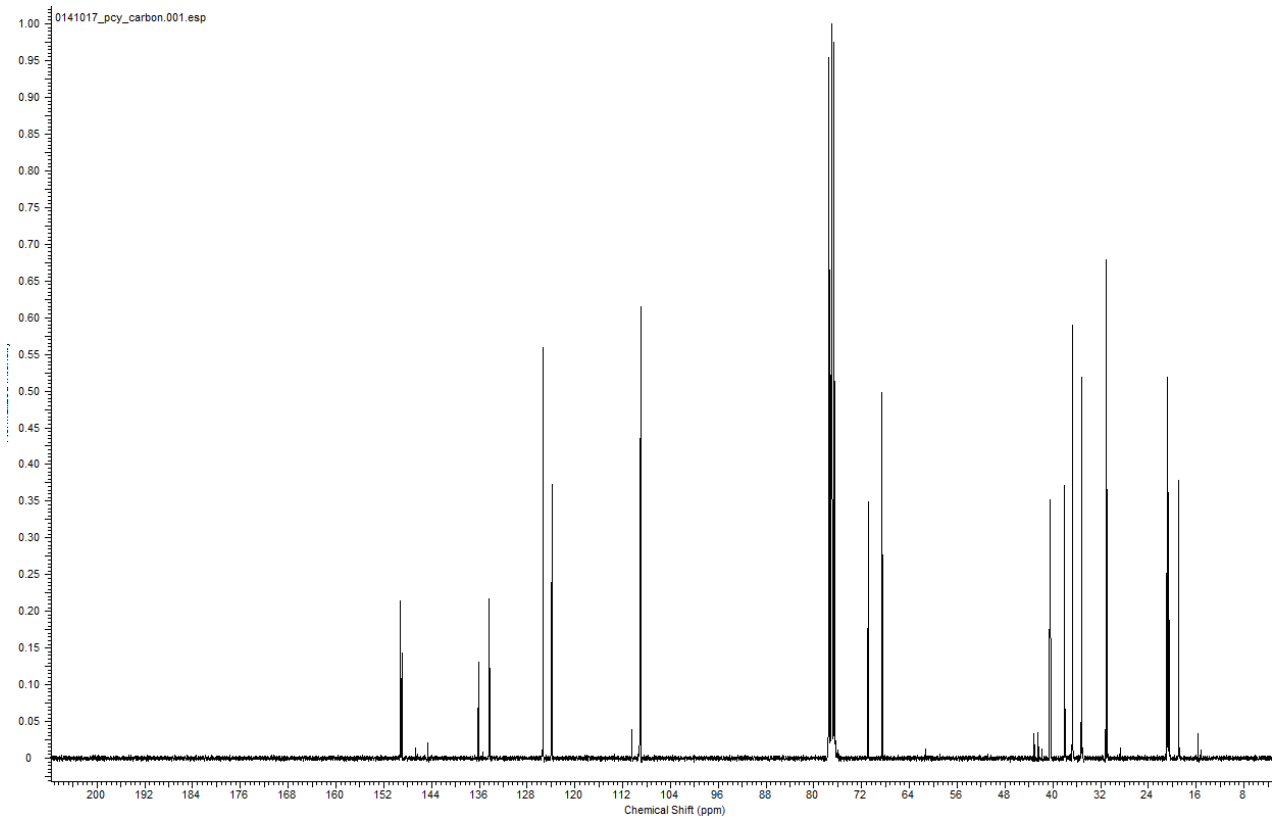
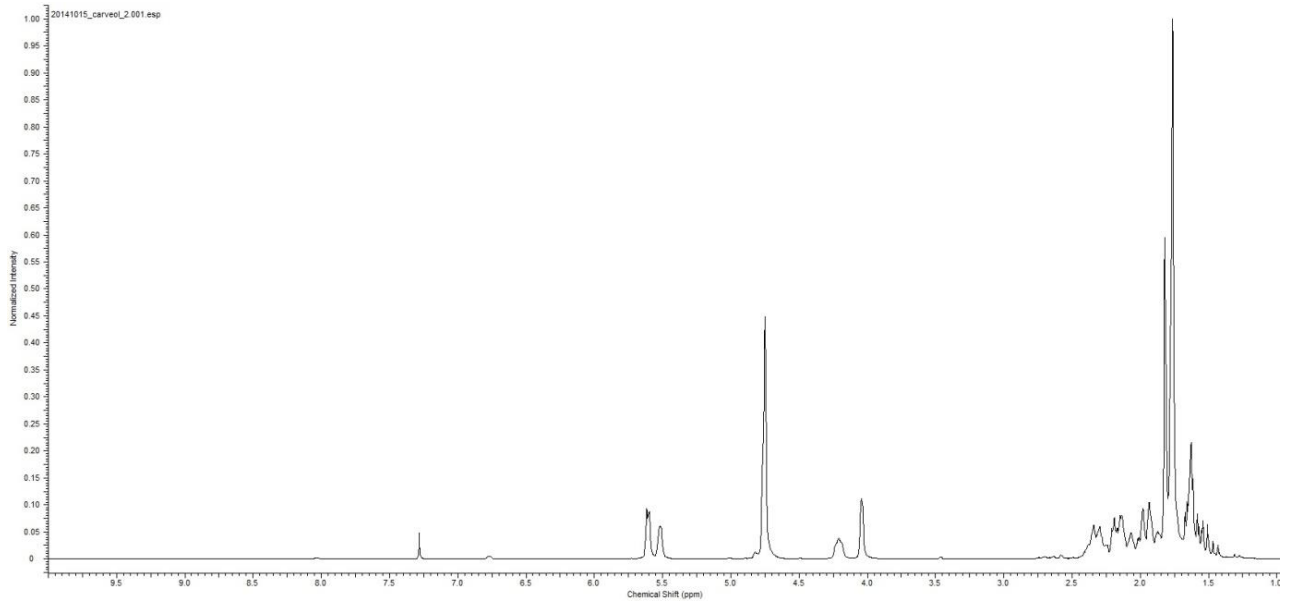


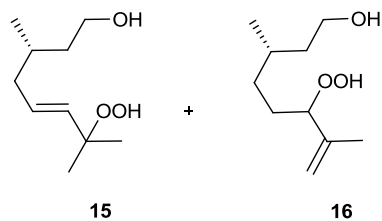
**6,6-dimethyl-2-methylenebicyclo[3.1.1]heptan-3-ol**



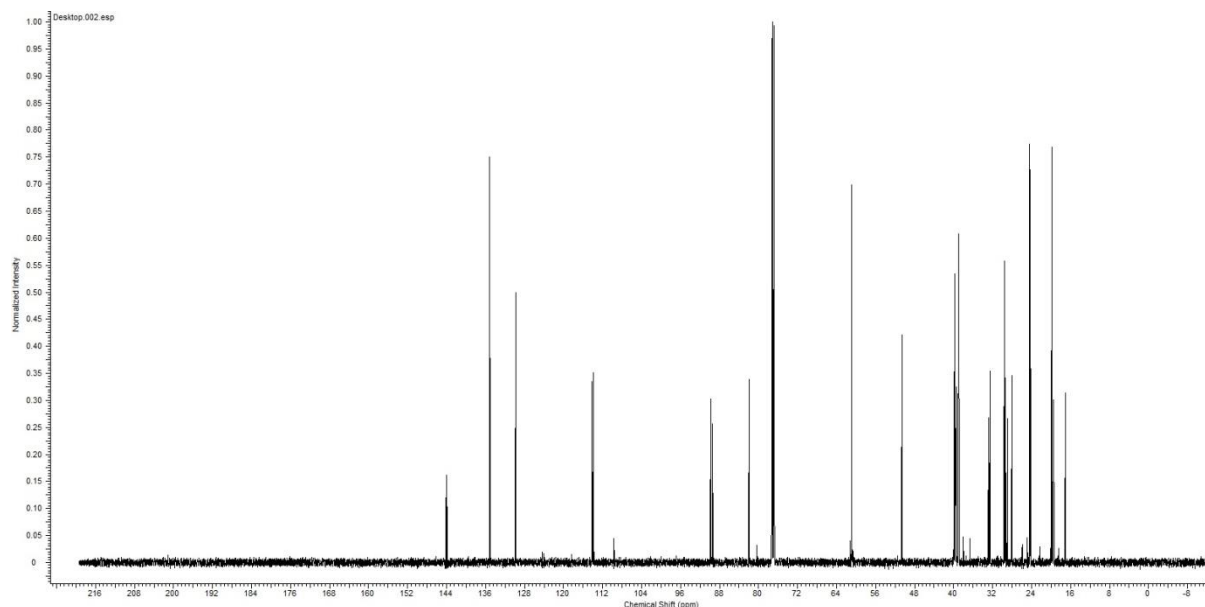
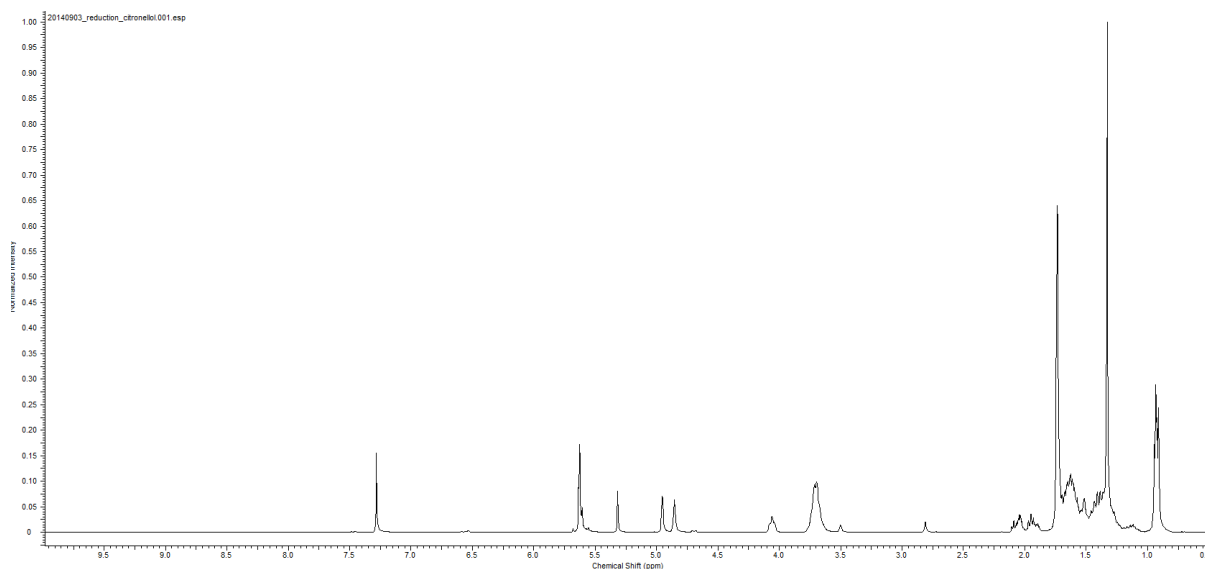


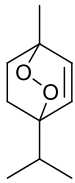
***2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enol***





***(S,E)*-7-hydroperoxy-3,7-dimethyloct-5-en-1-ol + *(3S)*-6-hydroperoxy-3,7-dimethyloct-7-en-1-ol**





***1-isopropyl-4-methyl-2,3-dioxabicyclo[2.2.2]oct-7-ene***

