

# Novel bio-based multifunctional emollients for cosmetic applications: toward the ingredients-list reduction

Floriane Rischard<sup>1,2</sup>, Amandine Flourat<sup>2\*</sup>, Léa Broche<sup>1</sup>, Abdouramane Dosso<sup>2</sup>, Blandine Godon<sup>2</sup>,  
Florent Allais<sup>2</sup>, Ecaterina Gore<sup>1\*</sup>, Géraldine Savary<sup>1</sup>

<sup>1</sup>Université Le Havre Normandie, Normandie Univ, URCOM UR 3221, F-76600 Le Havre, France

<sup>2</sup>URD Agro-Biotechnologies (ABI), CEBB, AgroParisTech, 51110 Pomacle, France

\*Corresponding authors

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## Abstract

The use of several ingredients in cosmetic formulations can often result in long ingredient lists, which can be daunting for consumers. While each of these particular ingredients serves a purpose, some are petroleum-based and may have adverse effects on the environment or human health. Ferulic acid, a *para*-hydroxycinnamic acid present in numerous agro-industrial by-products, exhibits anti-microbial, antioxidant and UV-filtering properties. In this work, ferulic acid was functionalized through chemo-enzymatic reaction steps (80 to 93% isolated yields) applying green chemistry principles, by using various natural fatty alcohols. The resulting compounds have demonstrated good emollient properties through physico-chemical and spreading evaluations. Two green metrics (Mass Intensity and Ecoscale) were used to assess the synthesis of these novel emollients, which were found to have a very low environmental impact. The findings of this study could provide a novel solution for multifunctional, bio-based ingredients in cosmetic formulations while reducing the environmental impact of the products.

## Materials

Deuterated chloroform ( $\text{CDCl}_3$ ) was purchased from Euriso-top (Cambridge Isotop Laboratories, Inc., Tewksbury, MA, USA). Ethanol (EtOH), anhydrous magnesium sulfate ( $\text{MgSO}_4$ ), Celite, ethyl acetate (AcOEt), sulfuric acid ( $\text{H}_2\text{SO}_4$ , 98%), sodium bicarbonate ( $\text{NaHCO}_3$ ) and acetone were purchased from VWR (Radnor, PA, USA). Ferulic acid was purchased from Biosynth-Carbosynth (Biosynth International Inc., Naperville, IL, USA). Palladium (10%) on activated charcoal (Pd/C) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) were purchased from Fisher Scientific (Waltham, MA, USA). Farnesol, geraniol, citronellol, oleic acid, 3,7-dimethyl-1-octanol (hydrogenated geraniol), 2,6-di-tert-butyl-4-methylphenol (BHT), L-ascorbic acid,  $\alpha$ -tocopherol, avobenzene and octinoxate were purchased from Sigma-Aldrich (Saint-Louis, MO, USA) or TCI Chemicals (TCI Europe N.V., Zwijndrecht, Belgium). Solid supported *Candida Antarctica* Lipase B (CAL B, Novozyme 435) was purchased from Novozymes (Bagsværd, Denmark) *Escherichia coli* (LMG 2092) and *Bacillus subtilis* (LMG 7135) were purchased from BCCM (Brussels, Belgium). Ampicillin was purchased from Laboratoire Humeau (La Chapelle-sur-Erdre, France). Antibiotic cellulose discs were purchased from Grosseron (Couëron, France). Vitro-skin® plates were purchased from IMS (Milford, CT, USA). Pentaerythrityl tetraethylhexanoate (DUB PTO) was provided by Stéarinerie Dubois (Boulogne-Billancourt, France) and castor oil was provided by Phileol (Reuil, France). All chemicals were used as received, without further purification.

## NMR Analysis

All synthetic compounds were characterized through NMR on a Bruker Fourier 300.  $^1\text{H}$  NMR spectra were recorded in  $\text{CDCl}_3$  (residual peak at  $\delta = 7.26$  ppm) at 300 MHz. Chemical shifts were reported in parts per million relative to the solvent residual peak. Data are reported as follows: chemical shift ( $\delta$ ppm), multiplicity (s = singlet, d = doublet, t = triplet, p = quintet, m = multiplet), coupling constant (Hz), integration and assignment.  $^{13}\text{C}$  NMR spectra were recorded in  $\text{CDCl}_3$  (residual peak at  $\delta = 77.1$  ppm) at 75 MHz. Chemical shifts were reported in parts per million. Data are reported as follows: chemical shifts (ppm) and assignment.

## LC-HRMS Analysis

High-resolution mass spectrometry experiments (HRMS) were performed on a 6545 Q-TOF hybrid quadrupole time-of-flight instrument (Wilmington, DE, USA) equipped with electrospray source ionization, coupled to an Agilent Technologies 1290 UHPLC chromatography system (Santa Clara, CA, USA). The ESI source was operated in the negative ionization mode with following parameters:

capillary voltage, 3500 V; nozzle voltage, 1500 V; gas temperature, 325°C; gas flow, 11 L/min; nebulizer, 35 psi; fragmentor, 120 V; sheath gas flow, 12 L/min; sheath gas temperature, 350°C. Nitrogen N<sub>2</sub> (99.999%) was used as the desolvation gas. The lock mass correction was applied using Agilent reference solution (m/z 966.0007) for accurate mass measurements. The scan range was m/z 100 – 1500 at 2 spectra/sec. All spectra were recorded in continuum mode. Data acquisition was performed using Agilent MassHunter Workstation Data Acquisition B.08.00 software.

UHPLC conditions: samples were prepared in EtOH at a concentration of 1 mg/ml and 1 µL was injected. A Zorbax Eclipse plus C18 (1.8 µm, 50 × 2.1 mm; Agilent Technologies, USA) column maintained at 40 °C was used to separate compounds. The elution was performed using 0.4 ml/min mobile phase of 0.1% formic acid with water (A) and 0.1% formic with ACN (B) according to the following gradient (A/B) : 95/5 (t = 0 min), 95/5 (t = 1 min), 90/10 (t = 1.5 min), 85/15 (t = 2.5 min), 75/25 (t = 4 min), 50/50 (t = 5.5 min), 50/50 (t = 7 min), 20/80 (t = 8.5 min), 20/80 (t = 11.5 min), 0/100 (t = 12 min), 0/100 (t = 14 min), 95/5 (t = 15 min).

## Synthesis description

### Synthesis of Ethylferulate (EtFe)

Ferulic acid was dissolved in ethanol (C=0.36 M) in a stirred round-bottomed flask. A few drops of concentrated H<sub>2</sub>SO<sub>4</sub> were added to the mixture which was then heated at reflux for 24 h. Ethanol was evaporated under vacuum and the product was dissolved in ethyl acetate (EtOAc). It was then washed three times with a NaHCO<sub>3</sub> solution to remove traces of acid. The organic phase was dried over anhydrous MgSO<sub>4</sub> and the final product slowly crystallized under vacuum evaporation of the solvent (orange to pink powder, 98% yield).

### Synthesis of Ethyldihydroferulate (EtHFe)

EtFe was solubilized in EtOAc and put under argon before adding 10% w/w of palladium on activated charcoal (Pd/C). The mixture was stirred at room temperature (rt) under H<sub>2</sub> flow for 16h, before being filtered over a pad of Celite. The final product crystallized under vacuum evaporation of the solvent (colorless crystal, 94% yield).

### Hydrogenation of Farnesol

Farnesol was solubilized in EtOAc (C=0.5M) and put under argon before adding 1% w/w of Pd/C. The reaction mixture was stirred at rt under H<sub>2</sub> flow for 24 h, before being filtered over a pad of Celite. The final product was dried under vacuum evaporation of the solvent (colorless oil, 97% yield). It will be further referred to as Hydrogenated Farnesol (H-Farnesol).

### Enzymatic Transesterification

Equimolar concentration of **EtHFe** and one of 6 different alcohols (**ROH**) were stirred together at 80°C and 50 mbar in a round-bottomed flask until melted. Novozym 435 (aka, CAL-B) was added to the mixture (10% w/w of the total weight), which was gently stirred for 24 h to 48 h. The reaction mixture was then dissolved in acetone and filtered over a pad of Celite to remove the CAL-B beads. The solvent was evaporated under vacuum and no more purification was necessary.

Those reactions were also undergone in the same conditions, using **EtFe** instead of **EtHFe** and more CAL-B (20% w/w of the total weight).

**GMF**: Yellow viscous oil. Isolated yield: 80%. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 7.55 (d, J = 15.9 Hz, 1H, H3), 7.04 – 6.93 (m, 2H, H5 and H9), 6.89 – 6.80 (m, 1H, H8), 6.23 (d, J = 15.9 Hz, 1H and H2), 5.77 (s,

1H, H11), 5.41 – 5.30 (m, 1H, H13), 5.06 – 4.98 (m, 1H, H17), 4.65 (d,  $J = 7.1$  Hz, 2H, H12), 3.85 (s, 3H, H10), 2.13 – 1.95 (m, 4H, H15 and H16), 1.73 – 1.44 (m, 9H, H19, H20 and H21).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 167.3 (C1), 147.9 (C6), 146.7 (C7), 144.7 (C3), 142.4 (C14), 131.9 (C18), 127.1 (C4), 123.8 (C17), 123.1 (C9), 118.4 (C13), 115.7 (C2), 114.7 (C8), 109.3 (C5), 61.3 (C12), 55.9 (C10), 39.6 (C15), 26.3 (C16), 25.7 (C19), 17.7 (C20), 16.5 (C21). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{20}\text{H}_{26}\text{O}_4$ :  $m/z$  329.1758; found  $m/z$  329.1754.

**GMF-HF**: Yellow oil. Isolated yield: 85%.  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.86 – 6.79 (m, 1H, H8), 6.73 – 6.65 (m, 2H, H5 and H9), 5.51 (s, 1H, H11), 5.38 – 5.25 (m, 1H, H13), 5.15 – 5.02 (m, 1H, H17), 4.59 (d,  $J = 7.1$  Hz, 2H, H12), 3.86 (s, 3H, H10), 2.93 – 2.83 (m, 2H, H3), 2.67 – 2.53 (m, 2H, H2), 2.17 – 1.95 (m, 4H, H15 and H16), 1.69 (s, 6H, H20 and H21), 1.60 (s, 3H, H19).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.1 (C1), 146.5 (C6), 144.6 (C7), 142.4 (C14), 132.7 (C4), 132.0 (C18), 123.9 (C17), 121.0 (C9), 118.4 (C13), 114.4 (C8), 111.1 (C5), 61.5 (C12), 56.0 (C10), 39.7 (C15), 36.5 (C2), 30.9 (C3), 26.4 (C16), 25.8 (C19), 17.8 (C20), 16.6 (C21). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{20}\text{H}_{28}\text{O}_4$ :  $m/z$  331.1915; found  $m/z$  331.1904.

**CMF**: Yellow viscous oil. Isolated yield: 80%.  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.55 (d,  $J = 15.9$  Hz, 1H, H3), 7.04 – 6.93 (m, 2H, H5 and H9), 6.89 – 6.80 (m, 1H, H8), 6.23 (d,  $J = 15.9$  Hz, 1H and H2), 5.77 (s, 1H, H11), 5.41 – 5.30 (m, 1H, H13), 5.06 – 4.98 (m, 1H, H17), 4.65 (d,  $J = 7.1$  Hz, 2H, H12), 3.85 (s, 3H, H10), 2.13 – 1.95 (m, 4H, H15 and H16), 1.73 – 1.44 (m, 9H, H19, H20 and H21).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 167.3 (C1), 147.9 (C6), 146.7 (C7), 144.7 (C3), 142.4 (C14), 131.9 (C18), 127.1 (C4), 123.8 (C17), 123.1 (C9), 118.4 (C13), 115.7 (C2), 114.7 (C8), 109.3 (C5), 61.3 (C12), 55.9 (C10), 39.6 (C15), 26.3 (C16), 25.7 (C19), 17.7 (C20), 16.5 (C21). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{20}\text{H}_{28}\text{O}_4$ :  $m/z$  331.1915; found  $m/z$  331.1910.

**CMF-HF**: Colorless oil. Isolated yield: 91%.  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.86 – 6.79 (m, 1H, H8), 6.72 – 6.64 (m, 2H, H5 and H9), 5.48 (s, 1H, H11), 5.12 – 5.03 (m, 1H, H17), 4.17 – 4.02 (m, 2H, H12), 3.87 (s, 3H, H10), 2.92 – 2.80 (m, 2H, H3), 2.64 – 2.51 (m, 2H, H2), 2.06 – 1.85 (m, 2H, H16), 1.68 (s, 3H, H20), 1.60 (s, 3H, H19), 1.55 – 1.10 (m, 5H, H13, H14 and H15), 0.93 – 0.80 (m, 3H, H21).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.2 (C1), 147.1 (C6), 146.5 (C7), 144.1 (C7), 132.7 (C4), 131.5 (C18), 124.7 (C17), 121.0 (C9), 114.4 (C8), 111.0 (C5), 63.2 (C12), 56.0 (C10), 37.1 (C15), 36.5 (C2), 35.6 (C13), 30.9 (C3), 29.6 (C14), 25.9 (C20), 25.5 (C16), 19.5 (C21), 17.8 (C19). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{20}\text{H}_{30}\text{O}_4$ :  $m/z$  333.2071; found  $m/z$  333.2066.

**FMF**: Orange viscous oil. Isolated yield: 87%.  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.61 (d,  $J = 15.9$  Hz, 1H, H3), 7.10 – 7.00 (m, 2H, H5 and H9), 6.95 – 6.86 (m, 1H, H8), 6.30 (d,  $J = 15.9$  Hz, 1H, H2), 5.87 (s, 1H, H11), 5.49 – 5.33 (m, 1H, H13), 5.19 – 5.02 (m, 2H, H17 and H21), 4.80 – 4.61 (m, 2H, H12), 3.91 (s, 3H, H10), 2.26 – 1.91 (m, 8H, H15, H16, H19 and H20), 1.86 – 1.50 (m, 12H, H23, H24, H25 and H26).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 167.4 (C1), 148.0 (C6), 146.9 (C7), 144.9 (C3), 142.5 (C14), 135.6 (C18), 131.5 (C22), 127.2 (C4), 124.5 (C17), 123.8 (C21), 123.2 (C9), 118.6 (C13), 115.8 (C2), 114.8 (C8), 109.4 (C5), 61.5 (C12), 56.0 (C10), 39.8 (C15), 39.7 (C19), 26.9 (C16), 25.8 (C20), 23.5 (C23), 17.8 (C24), 16.7 (C25), 16.2 (C26). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{25}\text{H}_{34}\text{O}_4$ :  $m/z$  397.2384; found  $m/z$  397.2387.

**FMF-HF**: Yellow oil. Isolated yield: 91%.  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.87 – 6.78 (m, 1H, H8), 6.75 – 6.62 (m, 2H, H5 and H9), 5.48 (s, 1H, H11), 5.39 – 5.25 (m, 1H, H13), 5.17 – 5.01 (m, 2H, H17 and H21), 4.59 (d,  $J = 7.0$  Hz, 2H, H12), 3.87 (s, 3H, H10), 2.95 – 2.81 (m, 2H, H3), 2.66 – 2.52 (m, 2H, H2), 2.18 – 1.92 (m, 8H, H15, H16, H19 and H20), 1.78 – 1.50 (m, 12H, H23, H24, H25 and H26).  **$^{13}\text{C}$  NMR** (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.1 (C1), 146.5 (C6), 144.1 (C7), 142.5 (C14), 135.6 (C18), 132.7 (C4), 131.5 (C22), 124.4 (C17), 123.7 (C21), 121.0 (C9), 118.4 (C13), 114.4 (C8), 111.1 (C5), 61.5 (C12), 56.0 (C10), 39.8 (C19), 39.7 (C15), 36.5 (C2), 30.9 (C3), 26.9 (C16), 26.3 (C20), 25.8 (C23), 17.8 (C24), 16.6 (C25), 16.2 (C26). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{25}\text{H}_{36}\text{O}_4$ :  $m/z$  399.2541; found  $m/z$  399.2535.

**HGMF:** Dark yellow viscous oil. Isolated yield: 86%.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.60 (d,  $J = 15.9$  Hz, 1H, 3), 7.10 – 6.99 (m, 2H, 5, 9), 6.94 – 6.88 (m, 1H, 8), 6.29 (d,  $J = 15.9$  Hz, 1H, 2), 5.87 (s, 1H, 11), 4.29 – 4.16 (m, 2H, 12"), 3.92 (s, 3H, 10), 1.63 (d,  $J = 57.4$  Hz, 4H, 13', 14, 18), 1.35 – 1.06 (m, 6H, 15', 16", 17'), 0.93 (d,  $J = 6.4$  Hz, 3H, 21), 0.90 – 0.80 (m, 6H, 19, 20).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 167.5 (1), 148.0 (6), 146.9 (7), 144.8 (3), 127.2 (4), 123.2 (9), 115.9 (2), 114.8 (8), 109.4 (5), 63.2 (12), 56.1 (10), 39.4 (17), 37.3 (15), 35.8 (13), 30.0 (14), 28.1 (18), 24.8 (16), 22.7 (19, 20), 19.7 (21). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{20}\text{H}_{30}\text{O}_4$ :  $m/z$  333.2071; found  $m/z$  333.2070.

**HGMF-HF:** Colorless oil. Isolated yield: 90%.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.87 – 6.79 (m, 1H, H8), 6.73 – 6.65 (m, 2H, H5 and H9), 5.50 (s, 1H, H11), 4.18 – 4.02 (m, 2H, H12), 3.87 (s, 3H, H10), 2.92 – 2.82 (m, 2H, H3), 2.63 – 2.54 (m, 2H, H2), 1.70 – 1.34 (m, 4H, H13, H14 and H18), 1.32 – 1.00 (m, 6H, H15, H16 and H17), 0.93 – 0.77 (m, 9H, H19, H20 and H21).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.2 (C1), 146.5 (C6), 144.1 (C7), 132.7 (C4), 121.0 (C9), 114.5 (C8), 111.0 (C5), 63.2 (C12), 56.1 (C10), 39.3 (C17), 37.2 (C15), 36.5 (C2), 35.7 (C13), 30.9 (C3), 30.0 (C14), 28.1 (C18), 24.7 (C16), 22.8 (C19 and C20), 19.6 (C21). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{20}\text{H}_{32}\text{O}_4$ :  $m/z$  335.2228; found  $m/z$  335.2229.

**HFMF:** Dark yellow viscous oil. Isolated yield: 93%.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.60 (d,  $J = 15.9$  Hz, 1H, H3), 7.11 – 7.00 (m, 2H, H5 and H9), 6.95 – 6.88 (m, 1H, H8), 6.29 (d,  $J = 15.9$  Hz, 1H, H2), 5.85 (s, 1H, H11), 4.29 – 4.18 (m, 2H, H12), 3.93 (s, 3H, H10), 1.83 – 1.43 (m, 4H, H13, H14 and H22), 1.21 (d,  $J = 41.6$  Hz, 13H, H15, H16, H17, H18, H19, H20 and H21), 0.99 – 0.75 (m, 12H, H23, H24, H25 and H26).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 167.5 (C1), 148.0 (C6), 146.9 (C7), 144.8 (C3), 127.2 (C4), 123.2 (C9), 115.9 (C2), 114.8 (C8), 109.4 (C5), 63.2 (C12), 56.0 (C10), 39.5 (C21), 37.4 (C15, C17 and C19), 35.8 (C13), 32.9 (C18), 30.1 (C14), 28.1 (C22), 24.9 (C16), 24.5 (C20), 22.8 (C23 and C24), 19.8 (C25 and C26). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{25}\text{H}_{40}\text{O}_4$ :  $m/z$  403.2854; found  $m/z$  403.2858.

**HFMF-HF:** Yellow oil. Isolated yield: 87%.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.89 – 6.75 (m, 1H, H8), 6.75 – 6.60 (m, 2H, H5 and H9), 5.48 (s, 1H, H11), 4.21 – 3.97 (m, 2H, H12), 3.87 (s, 3H, H10), 2.93 – 2.77 (m, 2H, H3), 2.67 – 2.47 (m, 2H, H2), 1.75 – 1.35 (m, 5H, H13, H14, H18 and H22), 1.34 – 0.98 (m, 12H, H15, H16, H17, H19, H20 and H21), 0.92 – 0.74 (m, 12H, H23, H24, H25 and H26).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.2 (C1), 146.5 (C6), 144.2 (C7), 132.7 (C4), 121.0 (C9), 114.5 (C8), 111.1 (C5), 63.2 (C12), 56.1 (C10), 39.5 (C21), 37.4 (C15, C17 and C19), 36.5 (C2), 35.7 (C13), 32.9 (C18), 30.9 (C3), 30.0 (C14), 28.1 (C22), 24.9 (C16), 24.4 (C20), 22.8 (C23 and C24), 19.8 (C25), 19.6 (C26). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{25}\text{H}_{42}\text{O}_4$ :  $m/z$  405.3010; found  $m/z$  405.3008.

**OIMF:** Yellow viscous oil. Isolated yield: 80%.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.61 (d,  $J = 15.9$  Hz, 1H, H3), 7.11 – 6.97 (m, 2H, H5 and H9), 6.95 – 6.83 (m, 1H, H8), 6.29 (d,  $J = 15.8$  Hz, 1H, H2), 5.86 (s, 1H, H11), 5.42 – 5.23 (m, 2H, H20 and H21), 4.18 (t,  $J = 6.7$  Hz, 2H, H12), 3.92 (s, 3H, H10), 2.08 – 1.90 (m, 4H, H19 and H22), 1.76 – 1.61 (m, 2H, H13), 1.45 – 1.13 (m, 22H, H14, H15, H16, H17, H18, H23, H24, H25, H26, H27 and H28), 0.94 – 0.79 (m, 3H, H29).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 167.5 (C1), 148.0 (C6), 146.9 (C7), 144.8 (C3), 130.1 (C20), 129.9 (C21), 127.2 (C4), 123.2 (C9), 115.8 (C2), 114.8 (C8), 109.4 (C5), 64.7 (C12), 56.1 (C10), 32.0 (C27), 29.9 (C18 and 23), 29.5 (C16, C17, C24 and C25), 28.9 (C13, C15 and C26), 27.4 (C19 and C22), 26.1 (C14), 22.8 (C28), 14.3 (C29). **TOF MS ESI-**: [M-H]<sup>-</sup> for  $\text{C}_{28}\text{H}_{44}\text{O}_4$ :  $m/z$  443.3167; found  $m/z$  443.3167.

**OIMF-HF:** Yellow viscous oil. Isolated yield: 93%.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.88 – 6.79 (m, 1H, H8), 6.74 – 6.64 (m, 2H, H5 and H9), 5.49 (s, 1H, H11), 5.41 – 5.27 (m, 2H, H20 and H21), 4.05 (t,  $J = 6.7$  Hz, 2H, H12), 3.87 (s, 3H, H10), 2.94 – 2.81 (m, 2H, H3), 2.66 – 2.50 (m, 2H, H2), 2.11 – 1.91 (m, 4H, H19 and H22), 1.67 – 1.49 (m, 2H, H13), 1.44 – 1.15 (m, 22H, H14, H15, H16, H17, H18, H23, H24, H25, H26, H27 and H28), 0.95 – 0.78 (m, 3H, H29).  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 173.2 (C1), 146.5 (C6), 144.1 (C7), 132.7 (C4), 130.1 (C20), 129.9 (C21), 121.0 (C9), 114.4 (C8), 111.0 (C5), 64.8 (C12), 56.0

(C10), 36.5 (C2), 32.0 (C27), 30.9 (C3), 29.9 (C18 and C23), 29.7 (C17 and C24), 29.5 (C16 and C25), 29.4 (C15 and C26), 28.8 (C13), 27.3 (C19 and C22), 26.0 (C14), 22.8 (C28), 14.3 (C29). **TOF MS ESI-**: [M-H]<sup>-</sup> for C<sub>20</sub>H<sub>30</sub>O<sub>4</sub>: *m/z* 333.2071; found *m/z* 333.2066. **TOF MS ESI-**: [M-H]<sup>-</sup> for C<sub>28</sub>H<sub>46</sub>O<sub>4</sub>: *m/z* 445.3323; found *m/z* 445.3319.

## Calculation method and results for green metrics

### Calculation method for the Ecoscale

For every synthesis, penalties were calculated for each parameter. For the yield, penalties were calculated using the following equation: (100-isolated yield)/2. For the price category, prices of reaction components (to obtain 10 mmol of end product) given by suppliers were considered, and penalties were given according to the following rule: no penalty if inexpensive (< \$10), a 3-point penalty if expensive (> \$10 and < \$50), and a 5-point penalty if very expensive (> \$50). Every reaction component needed to obtain 10 mmol of end product were considered and the quantity needed were given between brackets. For the safety parameter, penalties were accorded depending on the severity: 5 points if dangerous for the environment (N), toxic (T) and highly flammable (F), 10 points if explosive (E), extremely flammable (F+) and extremely toxic (T+). For the technical setup, no penalty was accorded if the setup was common, 1 point was given for the use of a H<sub>2</sub> atmosphere, and 1 point for the reduced pressure setup (50 mbar vacuum). For the time and temperature parameter, a 1-point penalty was given if the reaction was done at room temperature for less than 24 hours and a 3-point penalty was given if the reaction was heated for more than 1 hour. For the work-up and purification parameter, no penalties were given for cooling to room temperature, adding solvent, simple filtration, removal of solvent with boiling point inferior than 150°C, and a 3-point penalty was given for a liquid-liquid extraction. Ecoscales were calculated as follows: 100 points minus the sum of individual penalties for each category.

### Calculation method for the Mass Intensity (MI)

Mass of all matter necessary to synthesize 10 mmol of product were calculated. The sum of the mass of all matter was then calculated, considering solvents or not. MI were calculated as follows: mass of 10 mmol of product divided by the mass of all matter.

Results for both green metrics for each reaction step

**Table S1:** Green metrics results for EtFe

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>					
98	1	Ferulic acid	2,2	24,5	4,4
<b>2. Price</b>		Ethanol	1,9		
Ferulic acid (1,95 g)	0	H <sub>2</sub> SO <sub>4</sub>	21,3		
Ethanol (27 mL)	0	EtOAc	0,01		
H <sub>2</sub> SO <sub>4</sub> (2 drops)	0	NaHCO <sub>3</sub>	24,4		
<b>3. Safety</b>		MgSO <sub>4</sub>	7,0		
Ethanol (F, T)	10	<b>Total</b>	1,0		
<b>4. Technical setup</b>		With solvents	55,7		
Common setup	0	Without solvents	10,0		
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Removal of EtOH	0				
Addition of AcOEt	0				
Washing with aq. NaHCO <sub>3</sub>	3				
Removal of AcOEt	0				
<b>Total penalty points</b>	17				
<b>Ecoscale</b>	83				



**Table S2:** Green metrics results for EtHfE

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>			2,2		
94	3	FeEt	2,2	13,3	3,1
<b>2. Price</b>		H <sub>2</sub>	0,0		
Ethyl Ferulate (2,22 g)	0	Pd/C	0,22		
H <sub>2</sub> (flux)	0	EtOAc	24,4		
Pd/C (10%)	3	Celite	5,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	31,8	
EtOAc (F)	5		Without solvents	7,4	
Pd/C (F, N, T)	15				
<b>4. Technical setup</b>					
Common setup	0				
H <sub>2</sub> atmosphere	1				
<b>5. Time/temperature</b>					
Room temperature, < 24 h	1				
<b>6. Workup/purification</b>					
Simple filtration	0				
Removal of AcOEt	0				
<b>Total penalty points</b>	<b>28</b>				
<b>Ecoscale</b>	<b>72</b>				

**Table S3:** Green metrics results for H-Farnesol

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>			2,3		
97	2	Farnesol	2,2	10,7	3,1
<b>2. Price</b>		H <sub>2</sub>	0,0		
Farnesol (2,22 g)	0	Pd/C	0,02		
H <sub>2</sub> (flux)	0	EtOAc	18,0		
Pd/C (1%)	0	Celite	5,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	25,3	
EtOAc (F)	5		Without solvents	7,2	
Pd/C (F, N, T)	15				
<b>4. Technical setup</b>					
Common setup	0				
H <sub>2</sub> atmosphere	1				
<b>5. Time/temperature</b>					
Room temperature, < 24 h	1				
<b>6. Workup/purification</b>					
Simple filtration	0				
Removal of AcOEt	0				
<b>Total penalty points</b>	<b>23,5</b>				
<b>Ecoscale</b>	<b>76,5</b>				

**Table S4:** Green metrics results for GMF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	3,3		
80	10	Geraniol	1,5	10,9	2,8
<b>2. Price</b>		EtFe	2,2		
Geraniol (1,54 g)	0	CAL B	0,8		
EtFe (2,22 g)	0	Acetone	21,2		
CAL B (20%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	28,7	
Acetone (F)	5		Without solvents	7,5	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>19</b>				
<b>Ecoscale</b>	<b>81</b>				

**Table S5:** Green metrics results for GMF-HF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	3,3		
85	7,5	Geraniol	1,5	10,0	2,5
<b>2. Price</b>		EtFe	2,2		
Geraniol (1,54 g)	0	CAL B	0,4		
EtHFe (2,22 g)	0	Acetone	21,2		
CAL B (10%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	28,3	
Acetone (F)	5		Without solvents	7,2	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>16,5</b>				
<b>Ecoscale</b>	<b>83,5</b>				

**Table S6:** Green metrics results for CMF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>			3,3		
80	10	Geraniol	1,6	10,8	2,8
<b>2. Price</b>		EtFe	2,2		
Citronellol (1,56 g)	0	CAL B	0,8		
EtFe (2,22 g)	0	Acetone	21,2		
CAL B (20%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	28,7	
Acetone (F)	5		Without solvents	7,5	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>19</b>				
<b>Ecoscale</b>	<b>81</b>				

**Table S7:** Green metrics results for CMF-HF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>			3,3		
91	4,5	Geraniol	1,6	9,3	2,4
<b>2. Price</b>		EtFe	2,2		
Citronellol (1,56 g)	0	CAL B	0,4		
EtHFe (2,22 g)	0	Acetone	21,2		
CAL B (10%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	28,4	
Acetone (F)	5		Without solvents	7,2	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>13,5</b>				
<b>Ecoscale</b>	<b>86,5</b>				

**Table S8:** Green metrics results for FMF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	4,0		
87	6,5	Geraniol	2,2	8,5	2,4
<b>2. Price</b>		EtFe	2,2		
Farnesol (2,22 g)	0	CAL B	0,9		
EtFe (2,22 g)	0	Acetone	21,2		
CAL B (20%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	29,5	
Acetone (F)	5		Without solvents	8,3	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>15,5</b>				
<b>Ecoscale</b>	<b>84,5</b>				

**Table S9:** Green metrics results for FMF-HF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	4,0		
91	4,5	Geraniol	2,2	8,0	2,2
<b>2. Price</b>		EtFe	2,2		
Citronellol (1,56 g)	0	CAL B	0,4		
EtHFe (2,22 g)	0	Acetone	21,2		
CAL B (10%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	29,1	
Acetone (F)	5		Without solvents	7,9	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>13,5</b>				
<b>Ecoscale</b>	<b>86,5</b>				

**Table S10:** Green metrics results for HGMF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>			3,3		
87	6,5	H-geraniol	1,6	9,9	2,6
<b>2. Price</b>		EtFe	2,2		
H-geraniol (1,58 g)	0	CAL B	0,8		
EtFe (2,22 g)	0	Acetone	21,2		
CAL B (20%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	28,7	
Acetone (F)	5		Without solvents	7,6	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>15,5</b>				
<b>Ecoscale</b>	<b>84,5</b>				

**Table S11:** Green metrics results for HGMF-HF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>			3,4		
87	6,5	H-geraniol	1,6	9,7	2,5
<b>2. Price</b>		EtFe	2,2		
H-geraniol (1,58 g)	0	CAL B	0,4		
EtHFe (2,22 g)	0	Acetone	21,2		
CAL B (10%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	28,4	
Acetone (F)	5		Without solvents	7,2	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>15,5</b>				
<b>Ecoscale</b>	<b>84,5</b>				

**Table S12:** Green metrics results for HFMF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	4,0		
93	3,5	H-farnesol	2,3	7,9	2,2
<b>2. Price</b>		EtFe	2,2		
H-farnesol (2,28 g)	0	CAL B	0,9		
EtFe (2,22 g)	0	Acetone	21,2		
CAL B (20%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	29,6	
Acetone (F)	5		Without solvents	8,4	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>12,5</b>				
<b>Ecoscale</b>	<b>87,5</b>				

**Table S13:** Green metrics results for HFMF-HF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	4,1		
88	6	H-farnesol	2,3	8,1	2,2
<b>2. Price</b>		EtFe	2,2		
H-farnesol (2,28 g)	0	CAL B	0,5		
EtHFe (2,22 g)	0	Acetone	21,2		
CAL B (10%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	29,1	
Acetone (F)	5		Without solvents	8,0	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>15</b>				
<b>Ecoscale</b>	<b>85</b>				

**Table S14:** Green metrics results for OIMF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	4,4		
80	10	Oleyl Alcohol	2,7	8,4	2,5
<b>2. Price</b>		EtFe	2,2		
Oleyl Alcohol (2,68 g)	0	CAL B	1,0		
EtFe (2,22 g)	0	Acetone	21,2		
CAL B (20%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	30,1	
Acetone (F)	5		Without solvents	8,9	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>19</b>				
<b>Ecoscale</b>	<b>81</b>				

**Table S15:** Green metrics results for OIMF-HF

Category	Penalty	Mass of all matter (g)		MI	
		10 mmol of product		With solvents	Without solvents
<b>1. Yield (%) :</b>		10 mmol of product	4,5		
93	3,5	Oleyl Alcohol	2,7	7,1	2,0
<b>2. Price</b>		EtFe	2,2		
Oleyl Alcohol (2,68 g)	0	CAL B	0,5		
EtHFe (2,22 g)	0	Acetone	21,2		
CAL B (10%)	0	Celite	3,0		
<b>3. Safety</b>		<b>Total</b>	With solvents	29,6	
Acetone (F)	5		Without solvents	8,4	
<b>4. Technical setup</b>					
Reduced pressure (50 mbar vacuum)	1				
<b>5. Time/temperature</b>					
Heating, > 1 h	3				
<b>6. Workup/purification</b>					
Cooling to room temperature	0				
Adding acetone	0				
Simple filtration	0				
Removal of acetone	0				
<b>Total penalty points</b>	<b>12,5</b>				
<b>Ecoscale</b>	<b>87,5</b>				

## Protocols followed for the assessment of the properties of synthesized monophenols

UV-filtering properties and photostability

UV-Vis measurements of each sample were taken in a 10 mm wide quartz cuvette at a concentration of 10  $\mu$ M in EtOH. The samples absorbance was measured from 800 to 200 nm, using a Cary 60 Spectrometer (Agilent Technologies, Santa Clara, CA USA), both before and after a 1-hour irradiation in a Rayonet RPR-200 ( $\lambda$  = 300 nm, P = 8.32 W/m<sup>2</sup>, stirring, T = 35°C) from the Southern New England

Ultraviolet Company (Branford, CT, USA) using 14 RPR-3000Å lamps. The loss of absorbance (LoA) was the difference between the absorbances at  $\lambda_{\max}$  before ( $t_0$ ) and after irradiation ( $t_1$ ). Avobenzone and octinoxate (purchased from TCI Chemicals) were used as reference for anti-UVA and anti-UVB respectively. Experimental values for the maximum of absorbance at the corresponding wavelength before and after irradiation are available in supporting information for every monophenol.

#### Antiradical properties

To assess the radical scavenging properties of synthesized monophenols, the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay was used.<sup>26</sup> The absorbance evolution of the samples at different concentrations in ethanol (from 12.5  $\mu\text{M}$  to 400  $\mu\text{M}$ ) in presence of a DPPH solution was followed. Their absorbance was measured at 515 nm every 5 minutes for 7.5 h. Using the average of the last six absorbance points, the percentage of DPPH and the percentage of reduced DPPH was plotted as a function of the initial monophenol quantity. Using the Regressi<sup>®</sup> software, version 3.99, the  $\text{EC}_{50}$  of each sample was determined, as the crossing point of the two curves. This value represents the minimal quantity of the assessed molecule necessary to reduced 50% of the initial DPPH quantity. The same technique was used to measure the  $\text{EC}_{50}$  of three commercially available references (purchased from Sigma-Aldrich): the butylated hydroxytoluene (BHT), a synthetic antioxidant and the  $\alpha$ -tocopherol ( $\alpha\text{T}$ ) which is a naturally occurring antioxidant.

#### Antimicrobial properties

Agar plates were inoculated with 100  $\mu\text{L}$  of a standardized suspension of two microorganisms: *Escherichia coli* (E. coli) and *Bacillus subtilis* (B. subtilis), with an optical density of 1. Each monophenol was solubilized in a lysogeny broth (LB) with 2% of Tween 80 at different concentrations (from 5% to 0.039% w/v). Ethyl paraben, EtFe, EtHFe and Ferulic acid were dissolved in a 40:60 % v/v EtOH:H<sub>2</sub>O mixture at the same concentrations. Cellulose discs were placed on the agar plates and 30  $\mu\text{L}$  of the samples solutions were deposited on top of it. Ampicillin was used as positive reference. Negative controls were also performed with the LB solution with 2% of Tween 80, and the ethanolic mixture. The plates were then incubated at 30°C until growth of the microorganisms (16 to 24 h). A growth inhibition circle around a cellulose disc is an indicator of a sensitivity of the microorganism toward the corresponding sample. The results will be presented as follows: a “+” means that an inhibition was observed for 5% w/v of sample, a “++” means that an inhibition was observed for at least 2.5% w/v of sample, a “+++” means that an inhibition was observed for less than 2.5% w/v of sample, “-” means that no inhibition was observed for this sample and “N/D” (non-determined) means that no inhibition was determined due to the lack of solubility of the monophenol in the LB solution.

#### Physico-chemical properties

Sensory properties of synthesized monophenols were benchmarked against two commonly used emollients: pentaerythrityl tetraethylhexanoate (DUB PTO) provided by Stéarinerie Dubois and castor oil provided by Phileol.

#### Flow sweep experiments

Rheological properties of 2 mL of each sample were evaluated by flow sweep measurements, using a 60 mm 2.019° aluminum cone and a Peltier steel plate on a Discovery Hybrid Rheometer (DHR) from TA Instrument (New Castle, DE, USA). After a 5-minute conditioning of the sample at 25°C, a flow sweep measure was done during 5 minutes, at a shear rate from 1.0 to 100.0  $\text{s}^{-1}$  (20 points per decade) at 25°C. A Newtonian behavior was observed for all samples (viscosity independent from the shear rate), and the viscosity was determined by taking the average viscosity value at the Newtonian



plateau. Presented viscosity values represented the mean value of three experiments as well as the corresponding standard deviations.

#### Density and surface tension

Monophenols and references densities were measured by weighing 3 times 1 mL of each sample using a precision scale. Surface tension of the monophenols were calculated by the pendant drop method using a camera linked to the Windrop+ software (GBX Scientific Ltd, Dublin, Ireland). A video of the syringe was taken until falling of a drop. Surface tension was calculated on the last five images before the falling of the drop. This experiment was done in triplicate. The results of density and surface tension measurements for all monophenols and the two chosen references are available in supporting information.

#### Spontaneous spreading

Vitro-skin® (IMS, Milford, CT, USA) is an artificial skin substitute which was used to assess the spreading properties of the monophenols and references. Vitro-skin® was hydrated following the standardized protocol developed by IMS: Vitro-skin® pieces were placed for 16h on the shelf of a hydration chamber containing 350g of a 14.85% w/w glycerin/water mixture at its bottom. Spontaneous spreading values were then determined following the protocol described by Douguet *et al.*<sup>20</sup> Using a micropipette, 10 µL of each sample were deposited at the center of a 6.5 cm side square of a hydrated Vitro-skin®. This square piece of Vitro-skin® was then kept in the hydration chamber for 10 minutes to allow the spreading of the sample. After this spreading time, talcum powder was sprinkled on top of the Vitro-skin® square piece and the surplus was removed by blowing it off. The outline of spreading zone was drawn using a black marker before taking a picture of all the Vitro-skin® pieces with a ruler next to them as a scale for the following image processing. Using the ImageJ software, spreading areas of each samples were then evaluated. This experiment was done in duplicate for each sample.

#### Melting points

To measure the melting points of the starting materials, Differential Scanning Calorimetry (DSC) assays were set up (DSC Q20, TA Instruments, New Castle, DE, USA). Samples were precisely weighed in metallic trays and an empty reference was used for the evaluations. Two thermic cycles were applied to all samples, with heating and cooling ramps of 5 °C.min<sup>-1</sup> between -50 and 150 °C. Melting temperatures were determined using the first cycle.

#### Statistical analyses

All means and standard deviation were calculated using Excel. Statistical analyses were performed using XLSTAT® software (2016.02.27444 version, Addinsoft, Paris, France). Analysis of variance (ANOVA) with Tukey post hoc test was used to determine significant differences between the monophenols and corresponding references for every tested property. Differences were considered significant if p-value < 0.05.

A principal component analysis (PCA) was carried on every tested property to obtain a mapping of the monophenols. For the UV properties, absorbance values before irradiation were used. For anti-microbial properties, a score between 0 and 5 was attributed to each monophenol, depending on its inhibition toward both bacteria. An antiradical activity score was given to each monophenol by dividing the quantity of DPPH that was used (20 nmol) by the corresponding EC<sub>50</sub> values. For the other tested properties (viscosity, density, surface tension and spontaneous spreading), mean values were used.

# NMR spectrum

Figure S1. <sup>1</sup>H-NMR spectrum of GMF

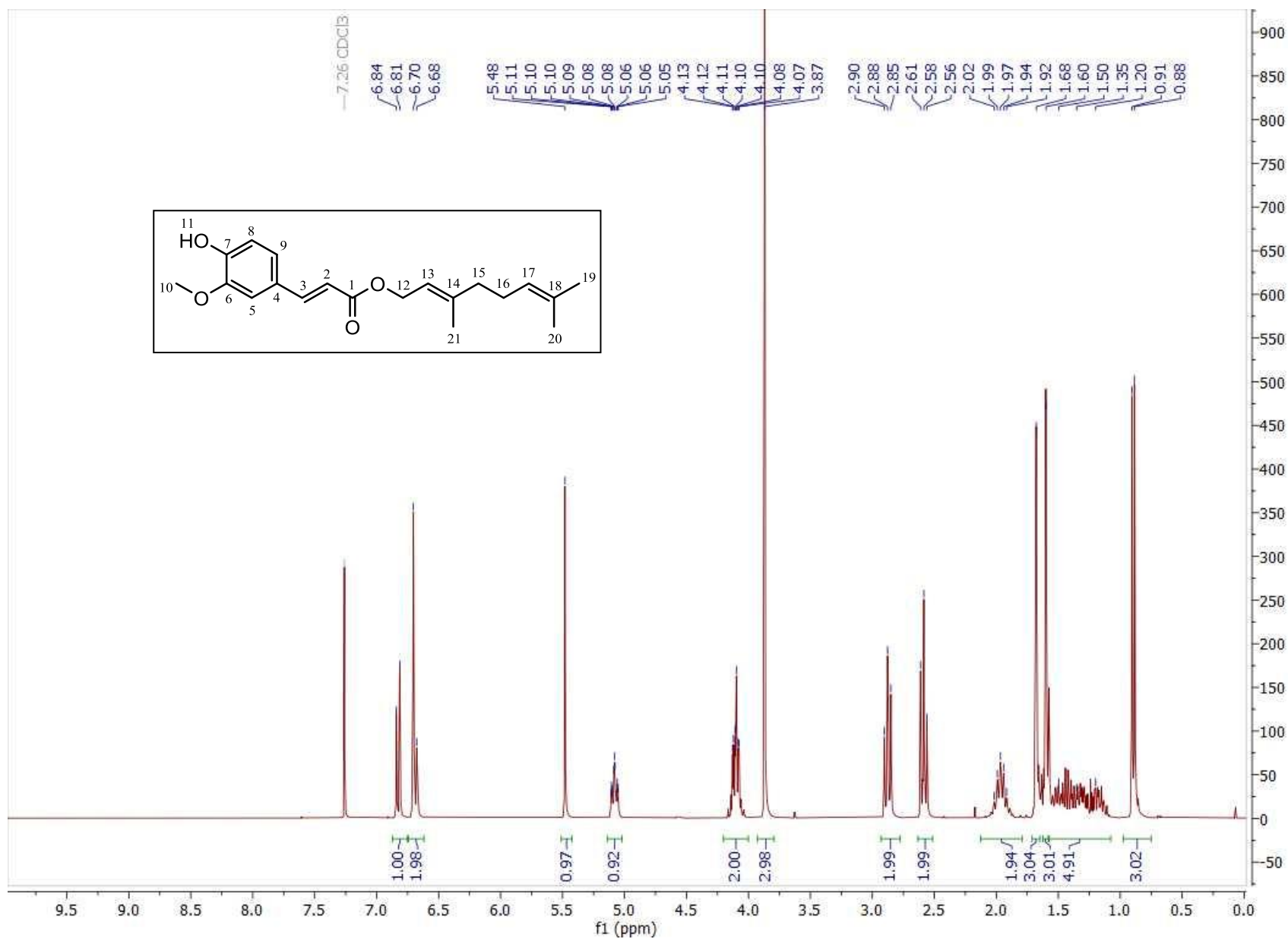


Figure S2.  $^{13}\text{C}$ -NMR spectrum of GMF

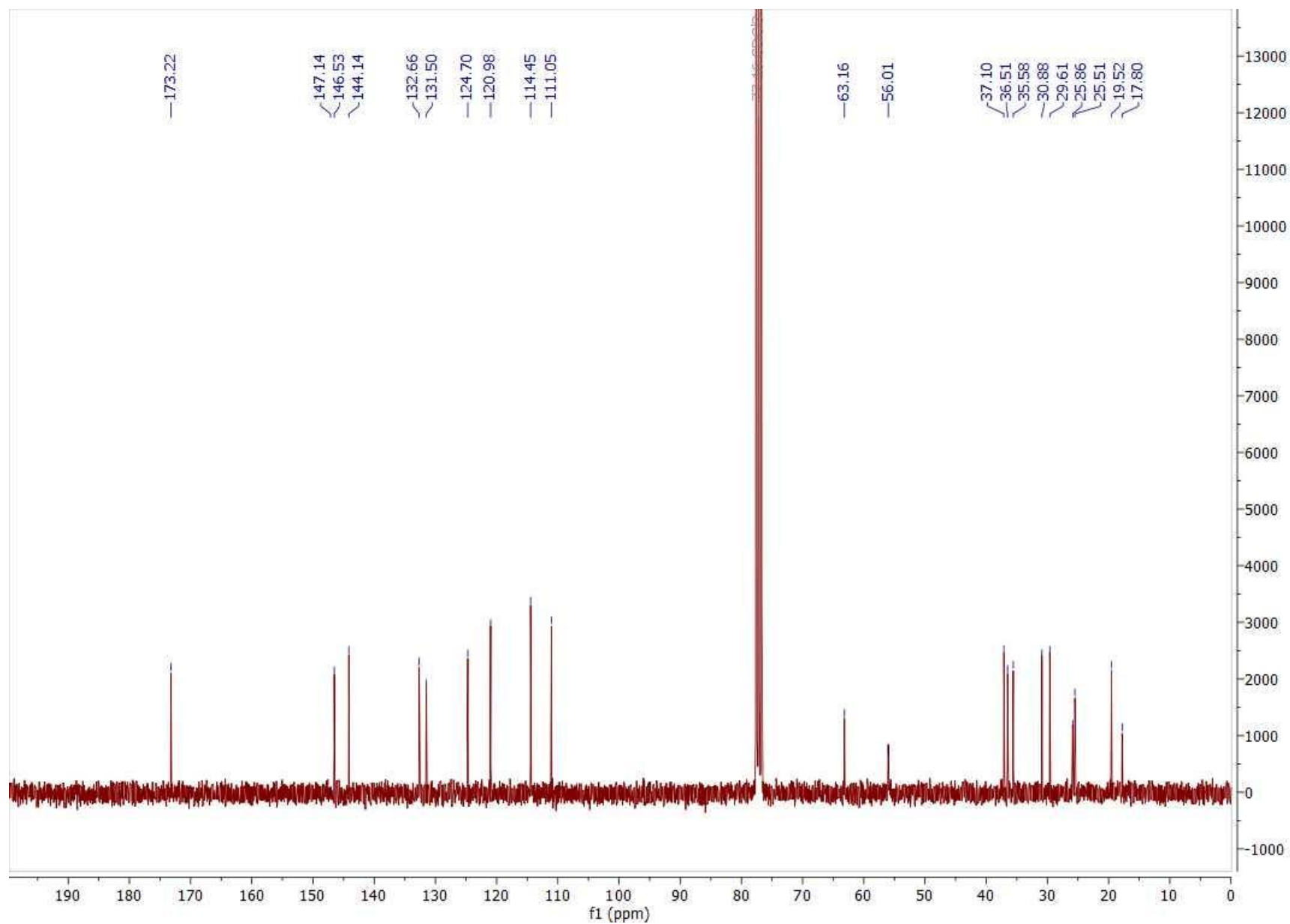


Figure S3. <sup>1</sup>H-NMR spectrum of GMF-HF

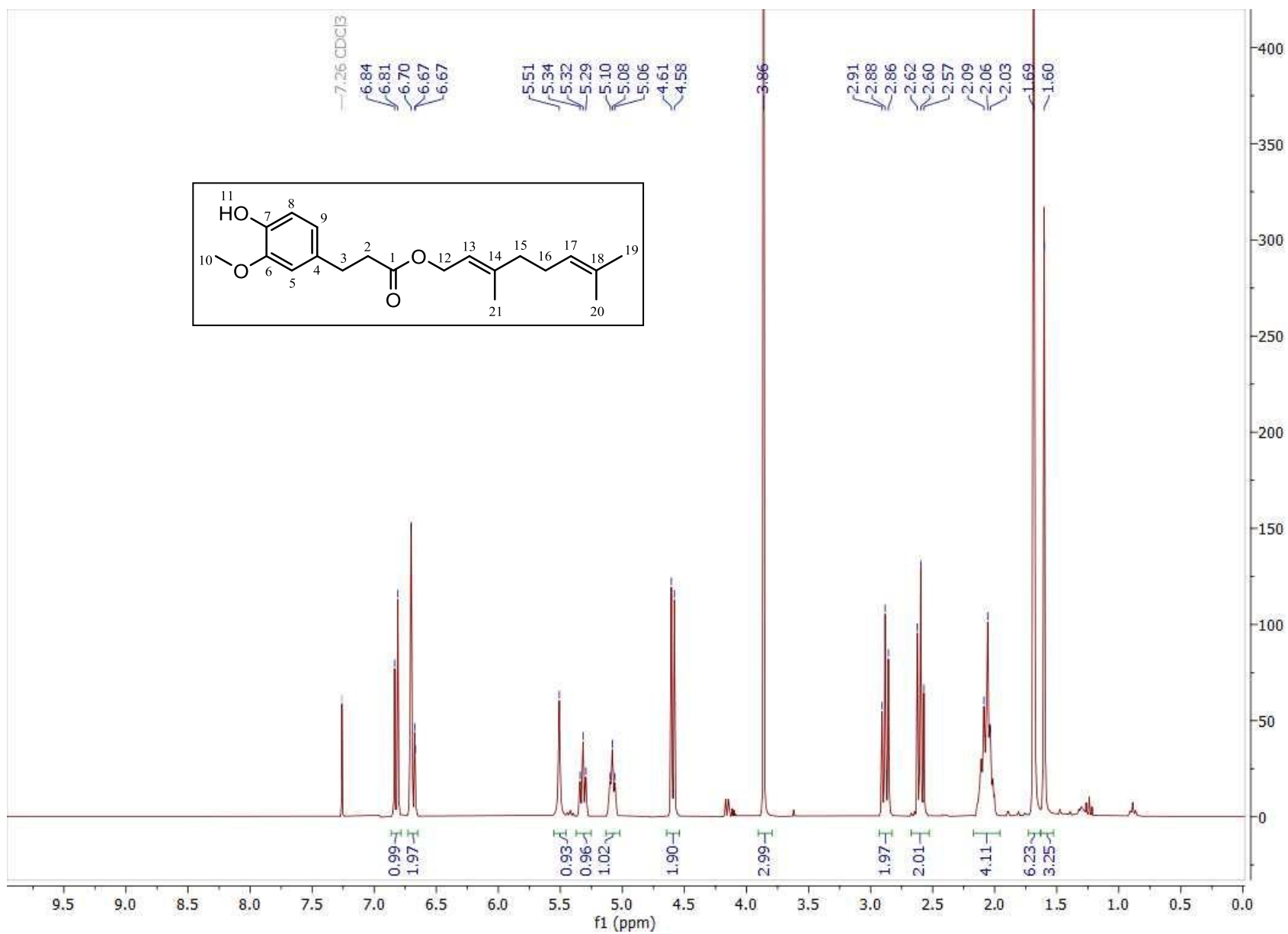


Figure S4.  $^{13}\text{C}$ -NMR spectrum of GMF-HF

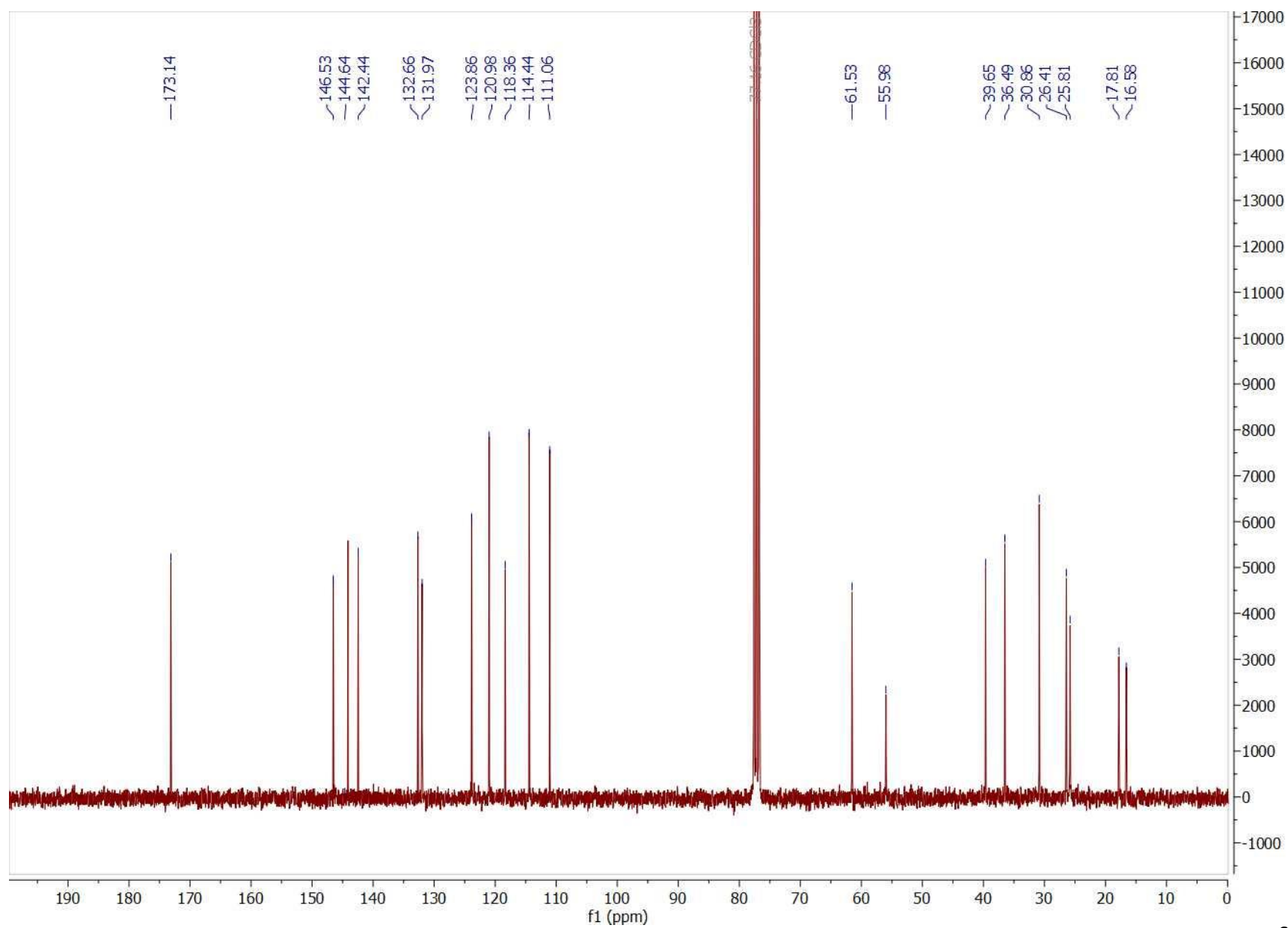


Figure S5.  $^1\text{H-NMR}$  spectrum of CMF

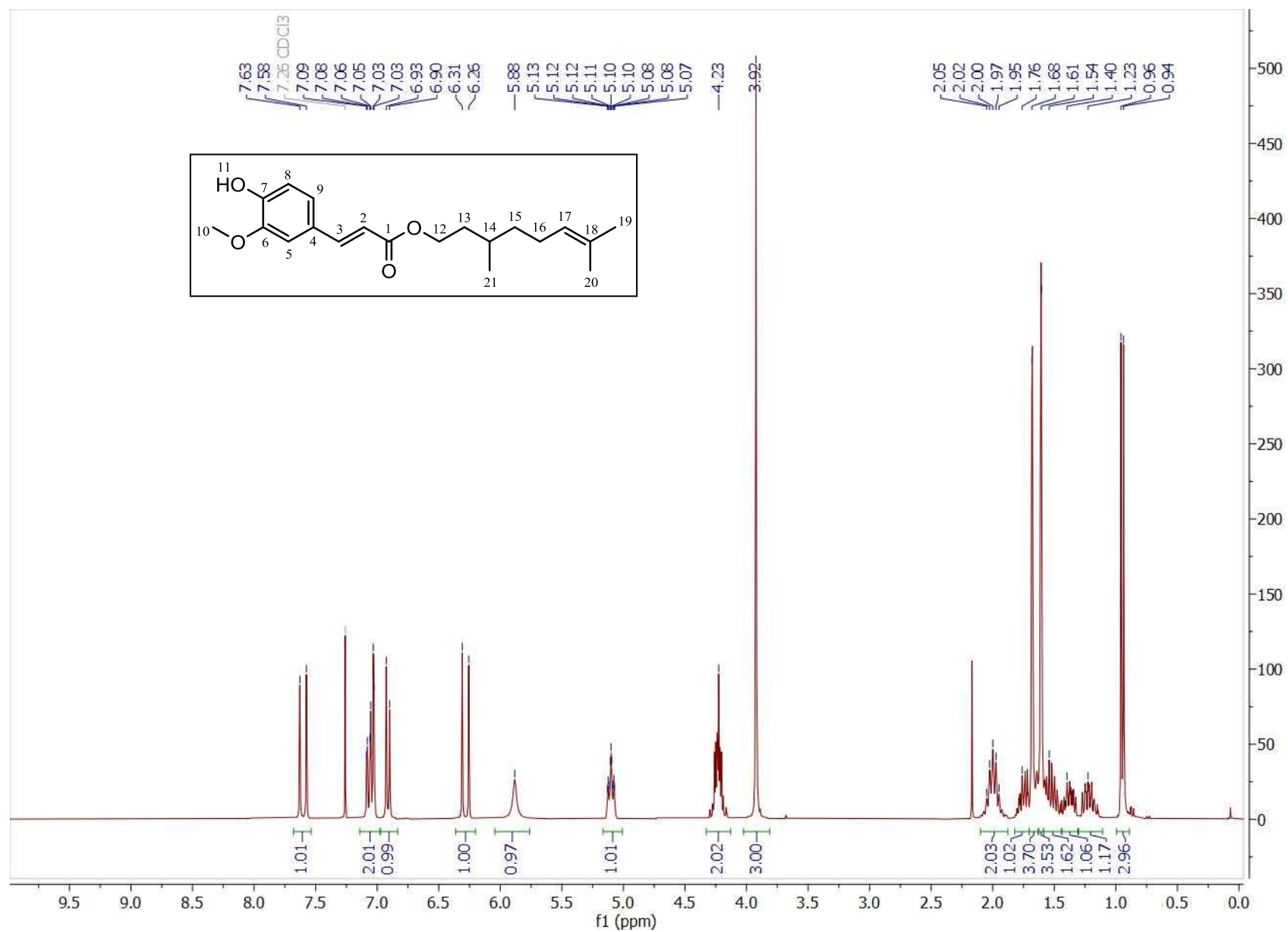


Figure S6.  $^{13}\text{C}$ -NMR spectrum of CMF

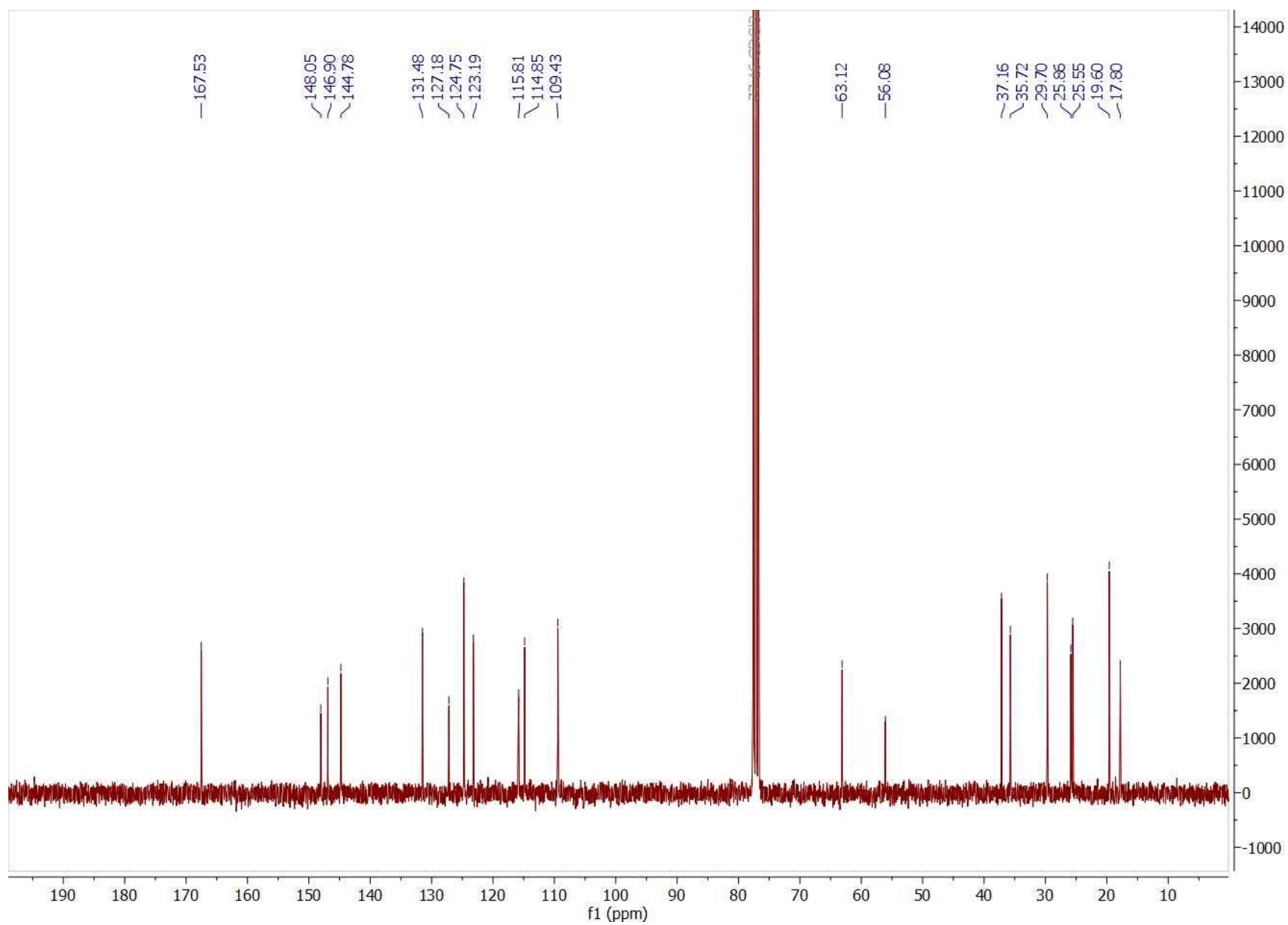


Figure S7. <sup>1</sup>H-NMR spectrum of CMF-HF

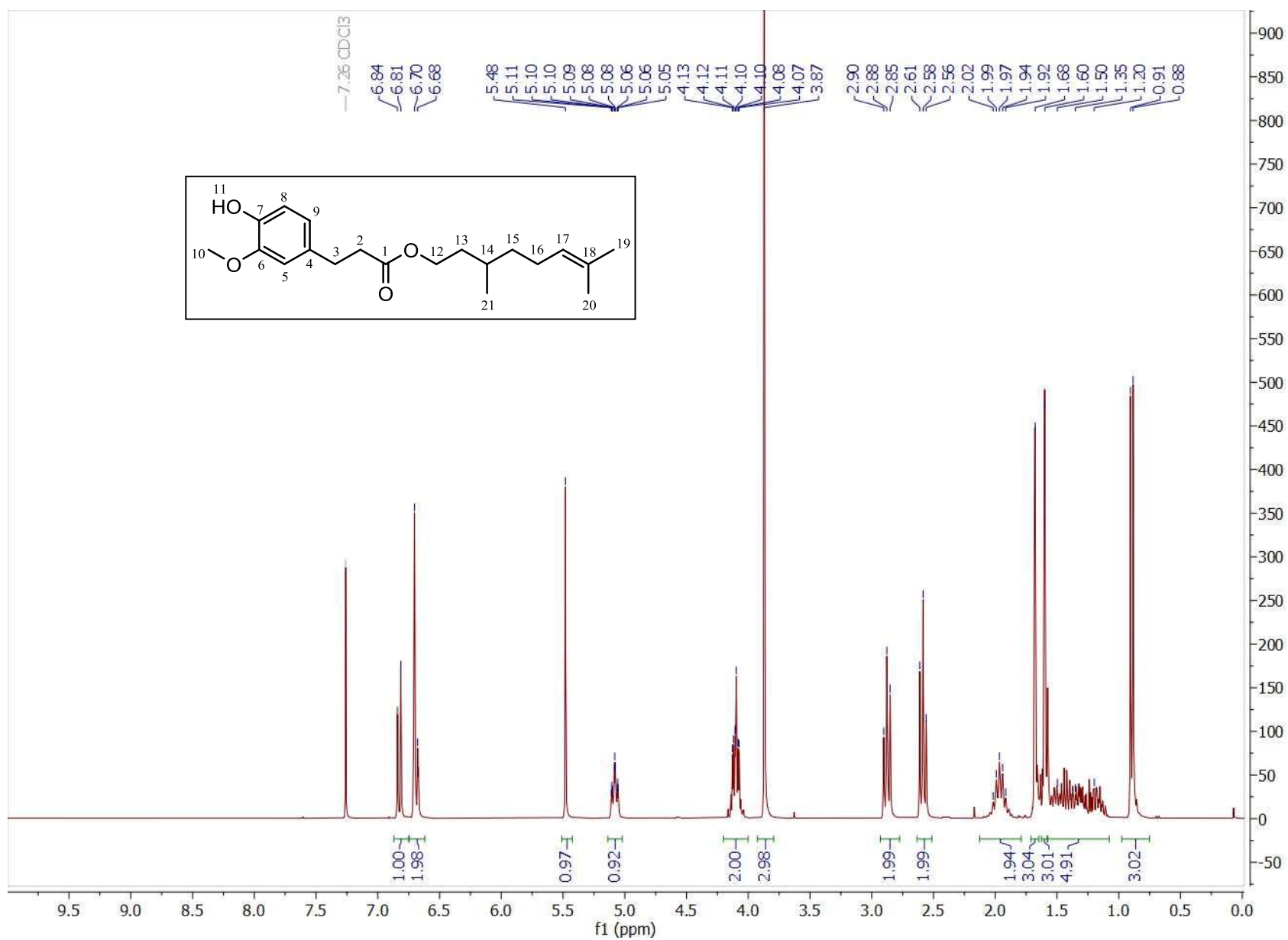




Figure S8.  $^{13}\text{C}$ -NMR spectrum of CMF-HF

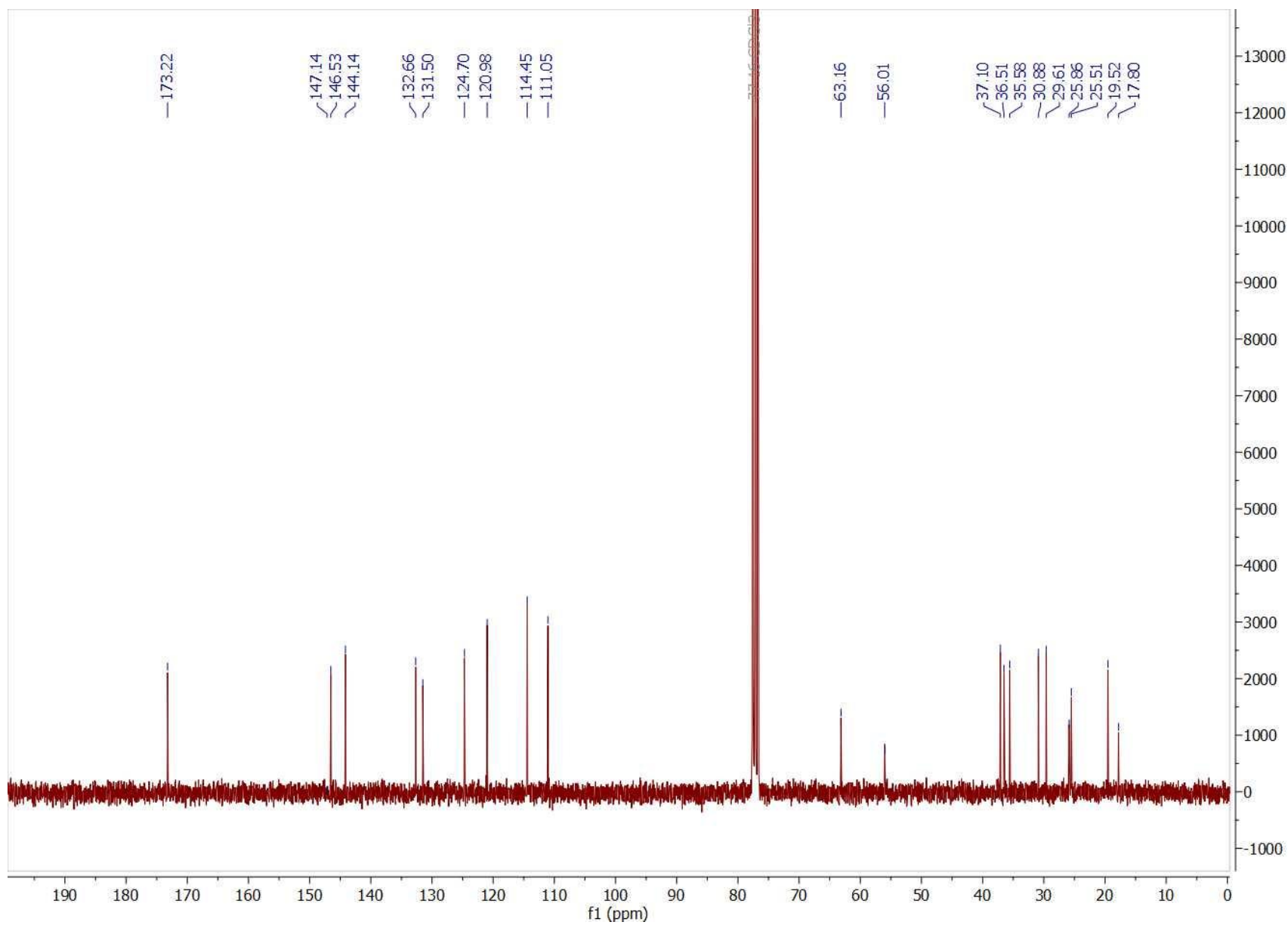


Figure S9. <sup>1</sup>H-NMR spectrum of FMF

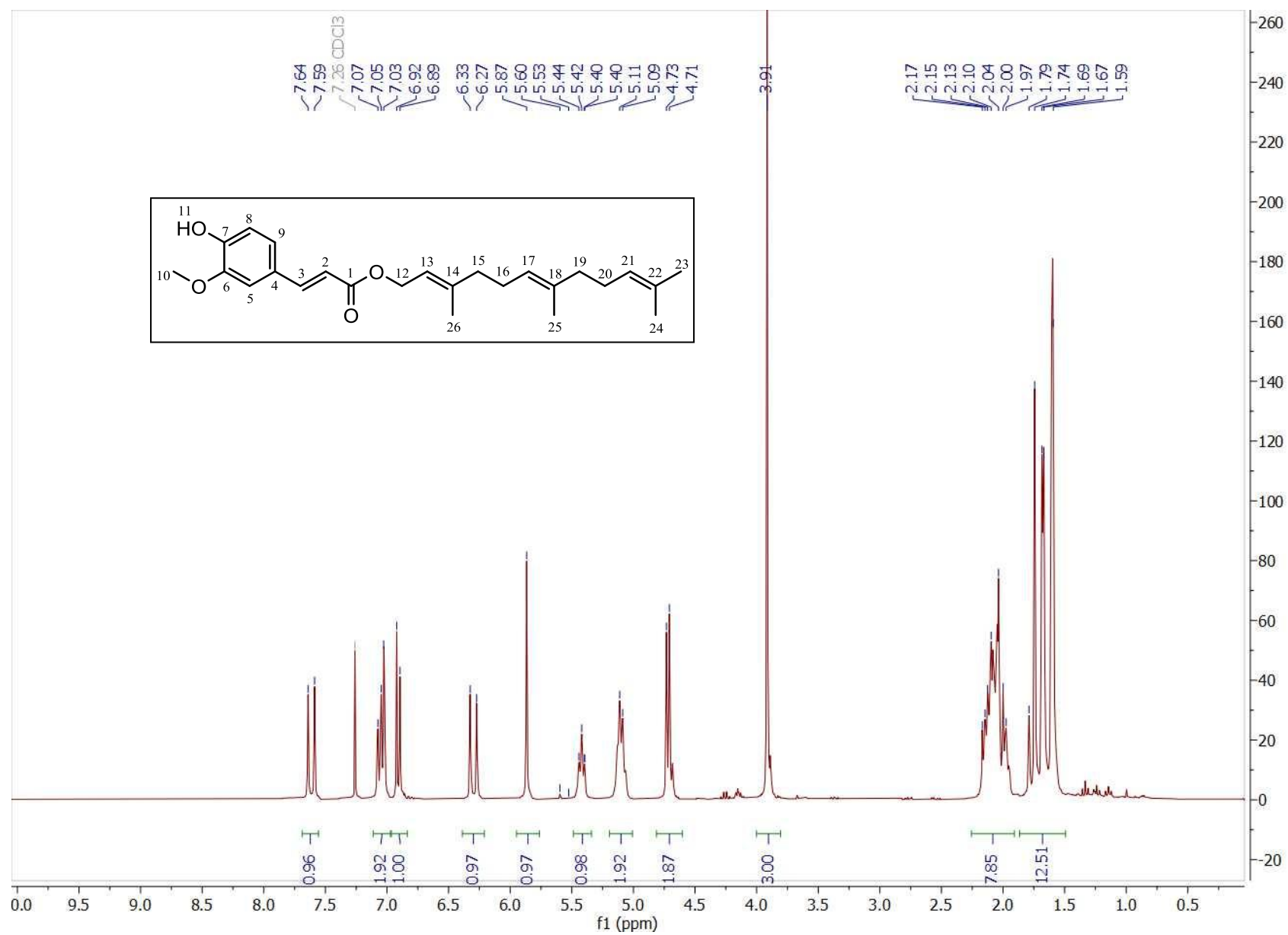


Figure S10.  $^{13}\text{C}$ -NMR spectrum of FMF

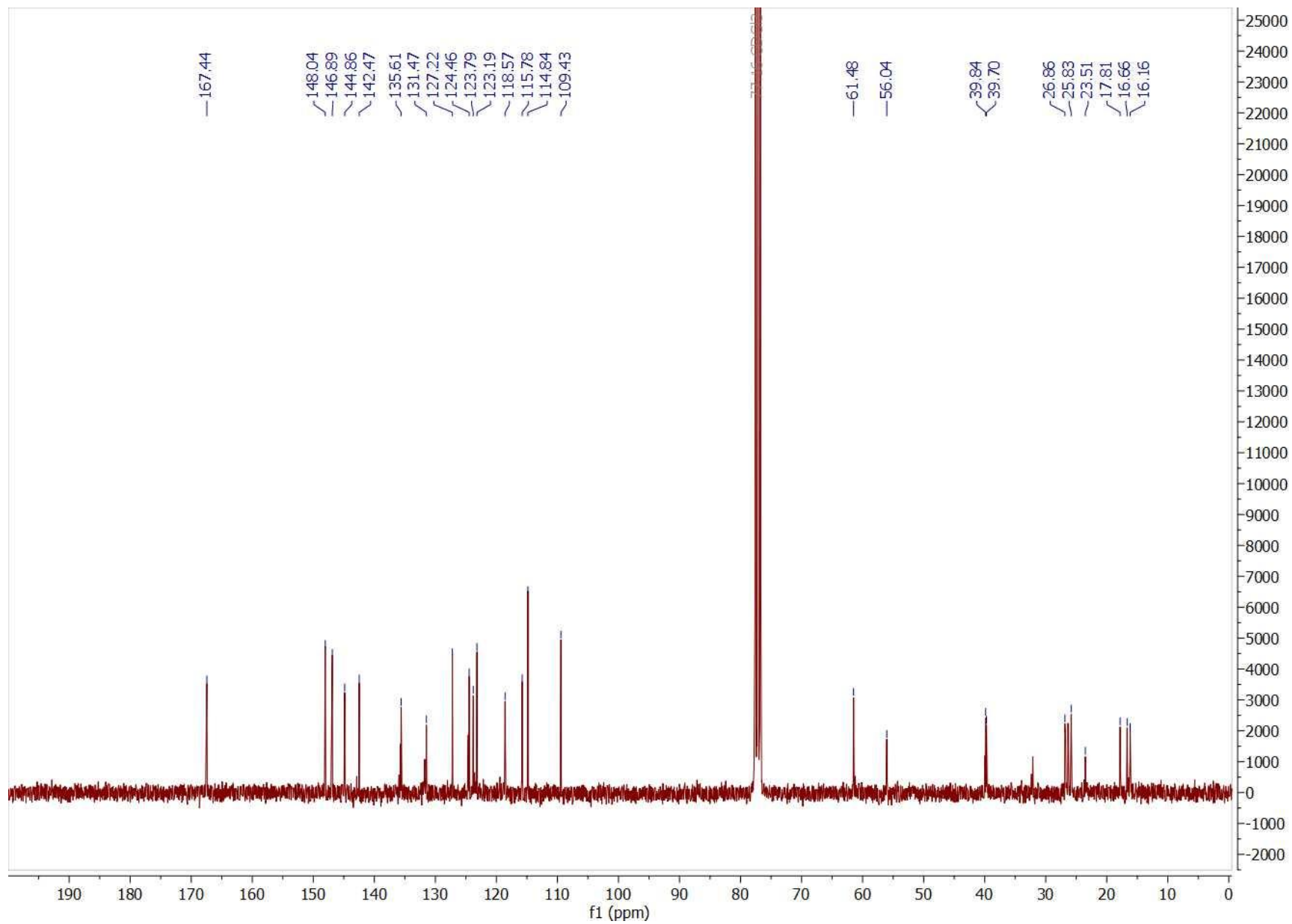


Figure S11. <sup>1</sup>H-NMR spectrum of FMF-HF

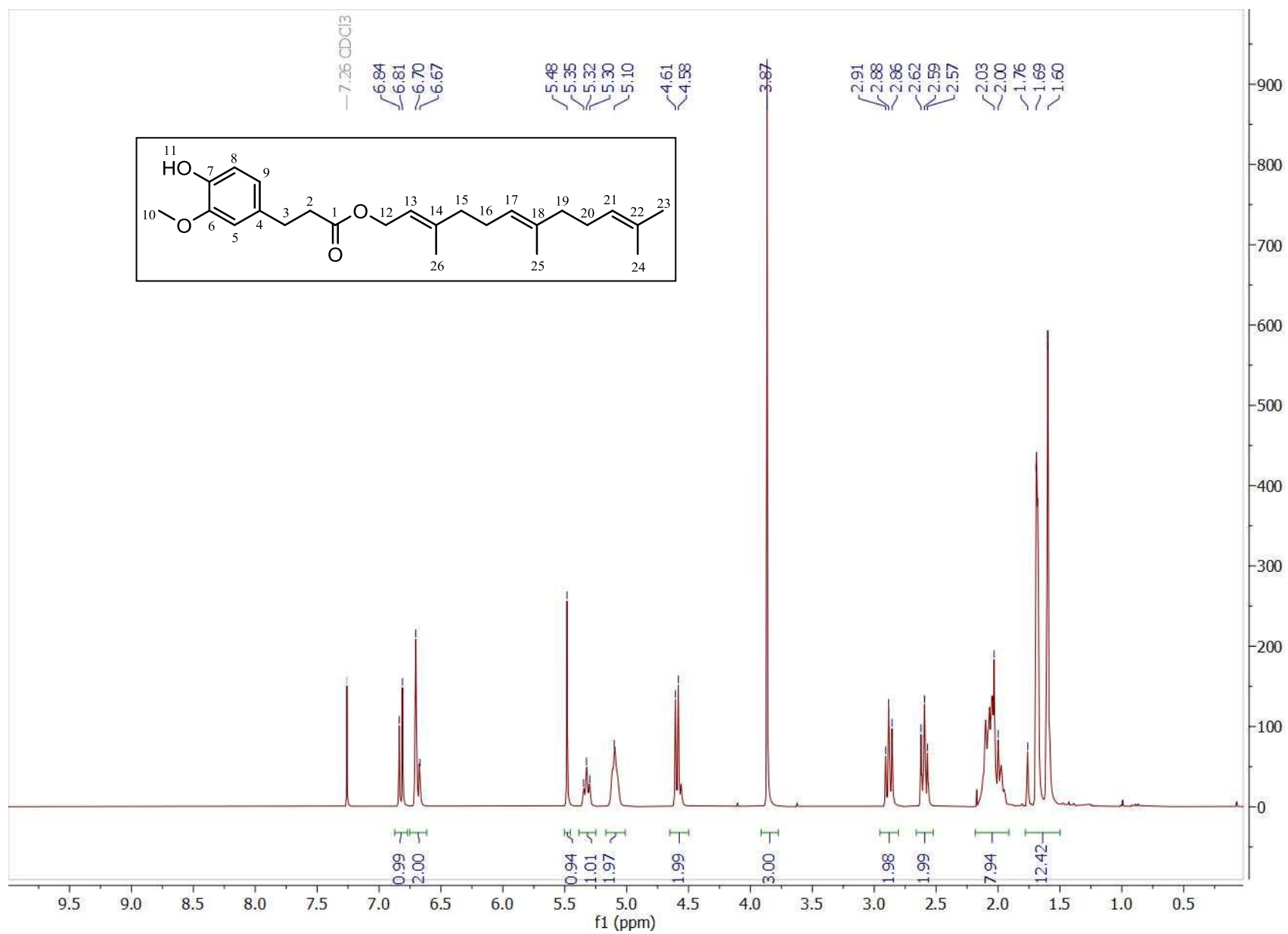


Figure S12.  $^{13}\text{C}$ -NMR spectrum of FMF-HF

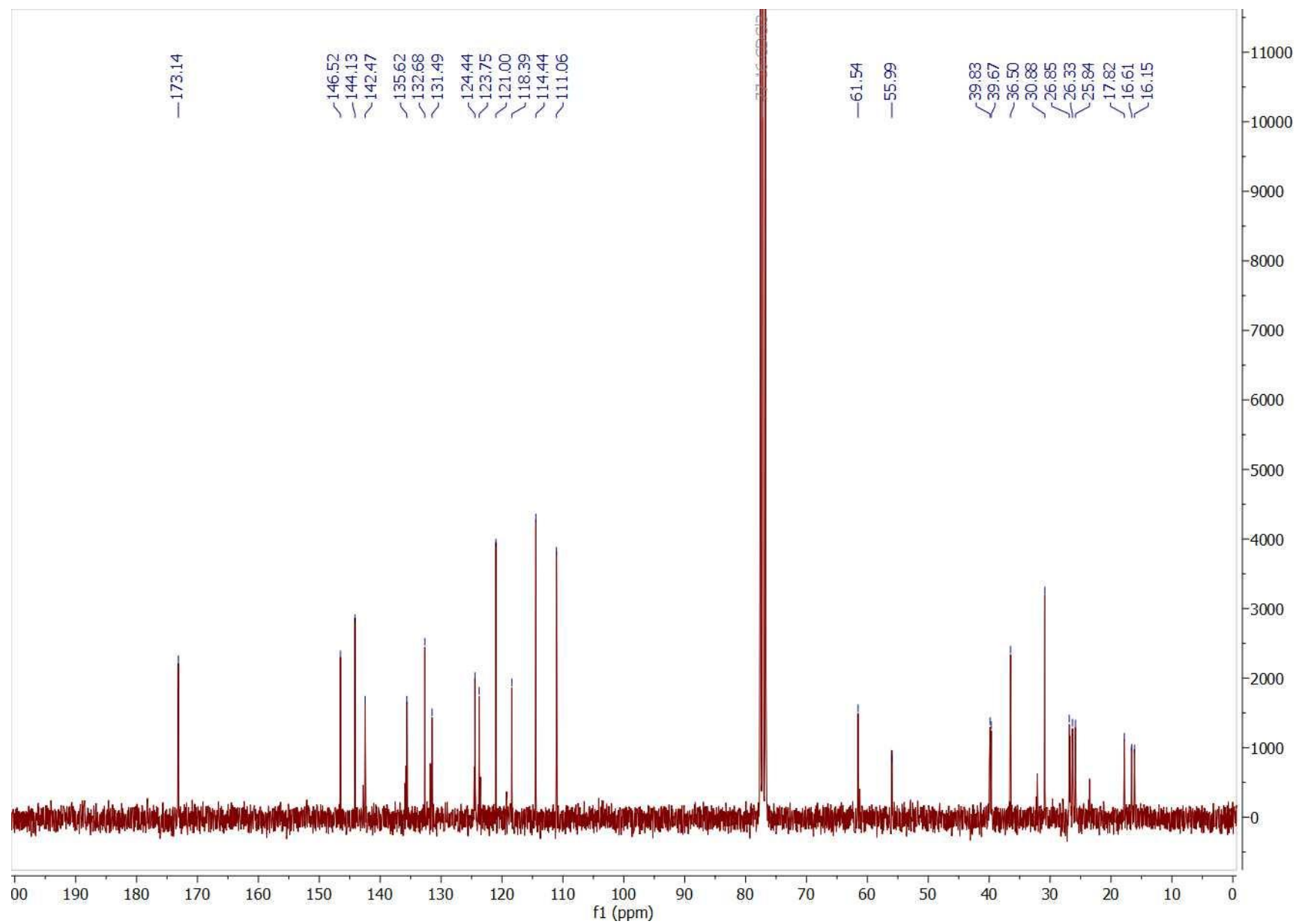


Figure S13. <sup>1</sup>H-NMR spectrum of HGMF

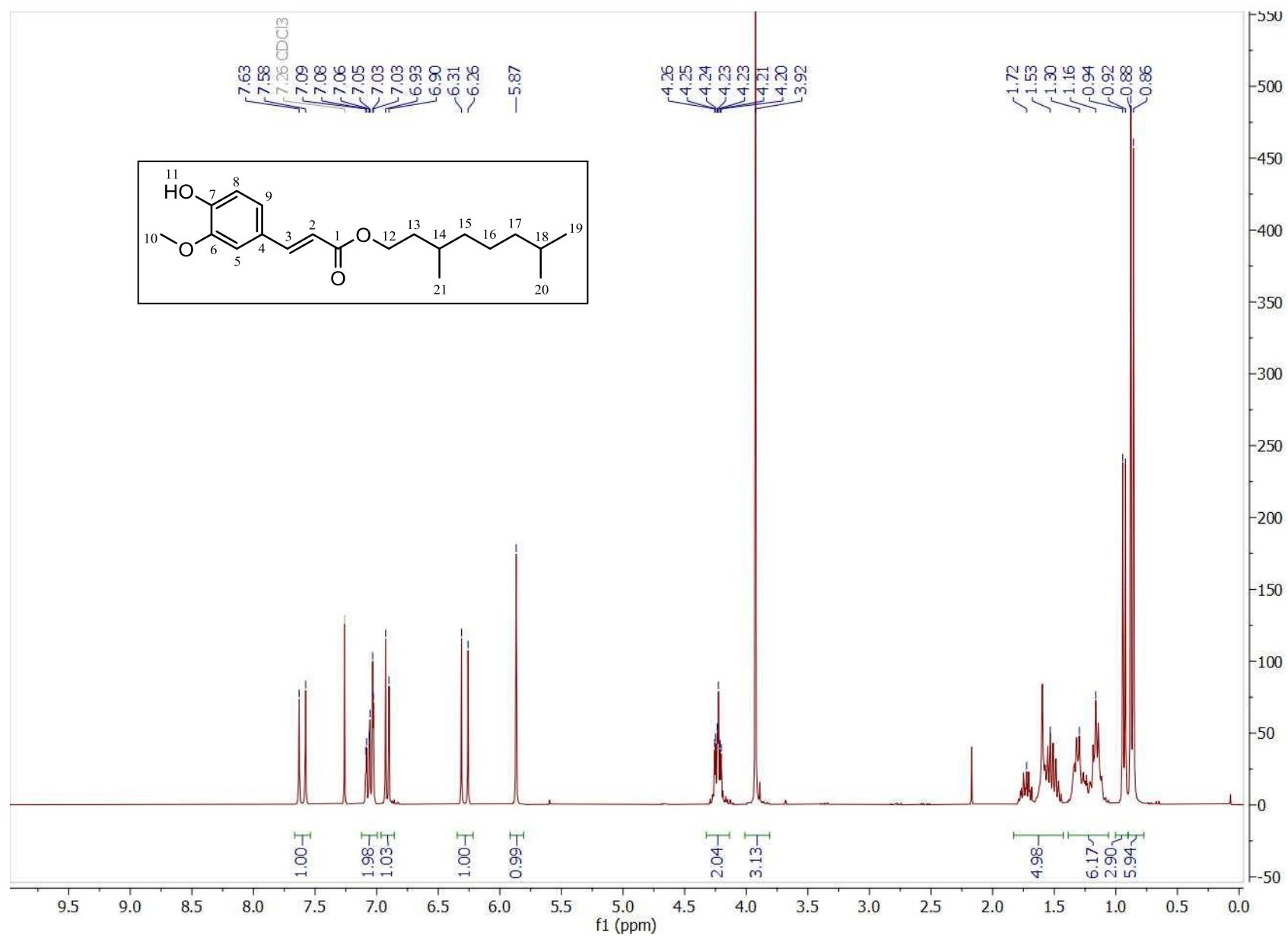


Figure S14.  $^{13}\text{C}$ -NMR spectrum of HGMF

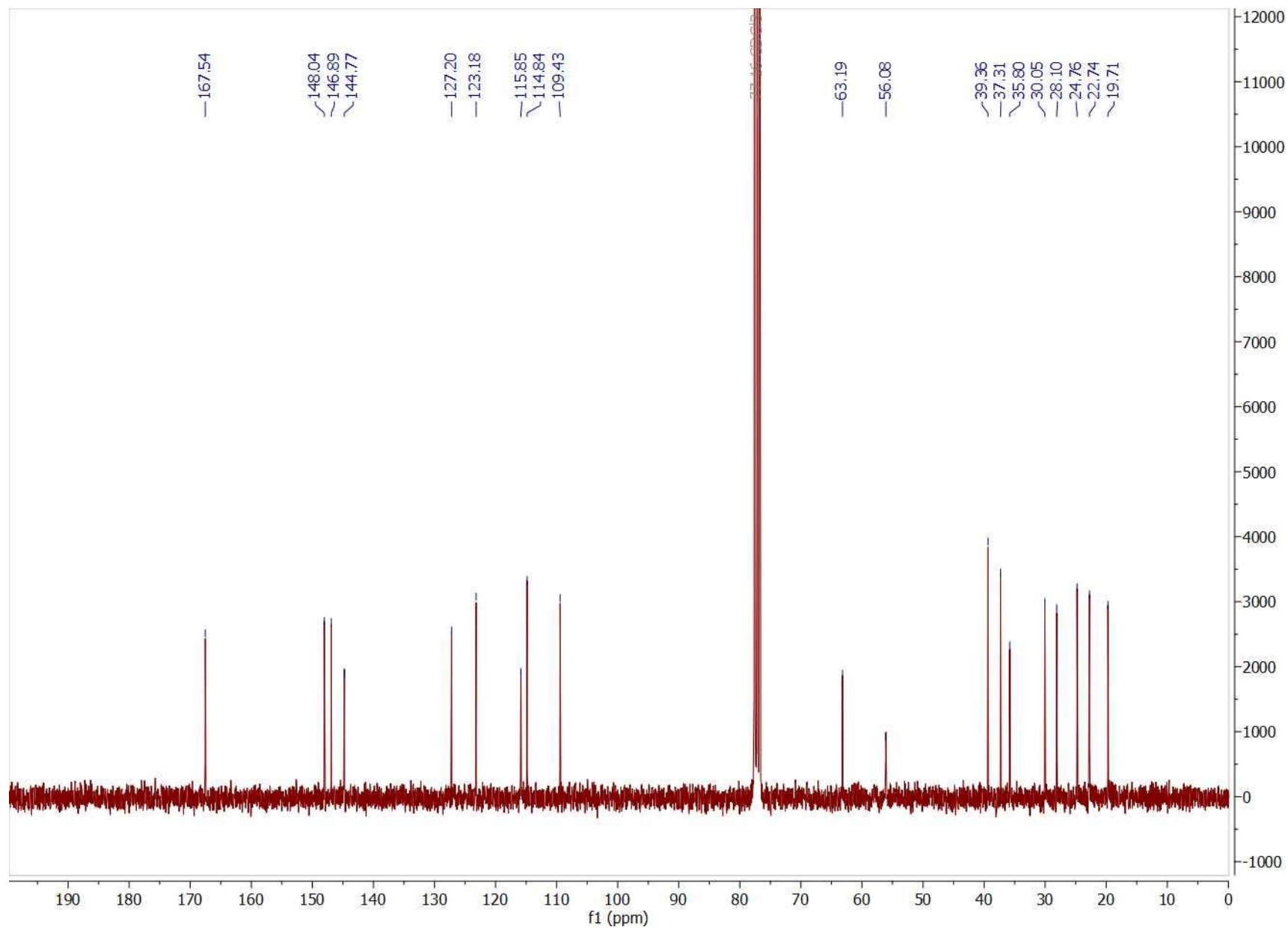


Figure S15. <sup>1</sup>H-NMR spectrum of HGMF-HF

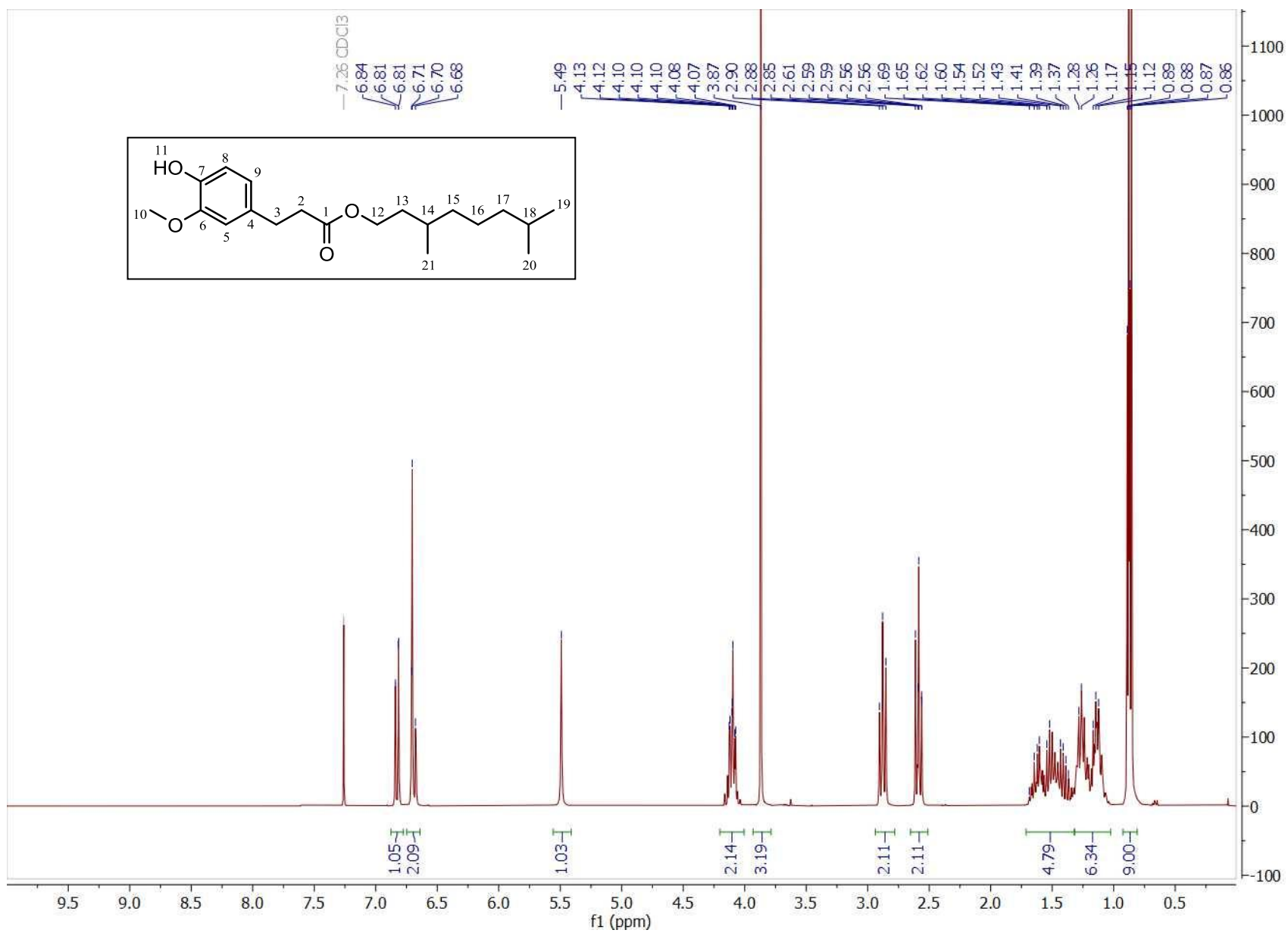




Figure S16.  $^{13}\text{C}$ -NMR spectrum of HGMF-HF

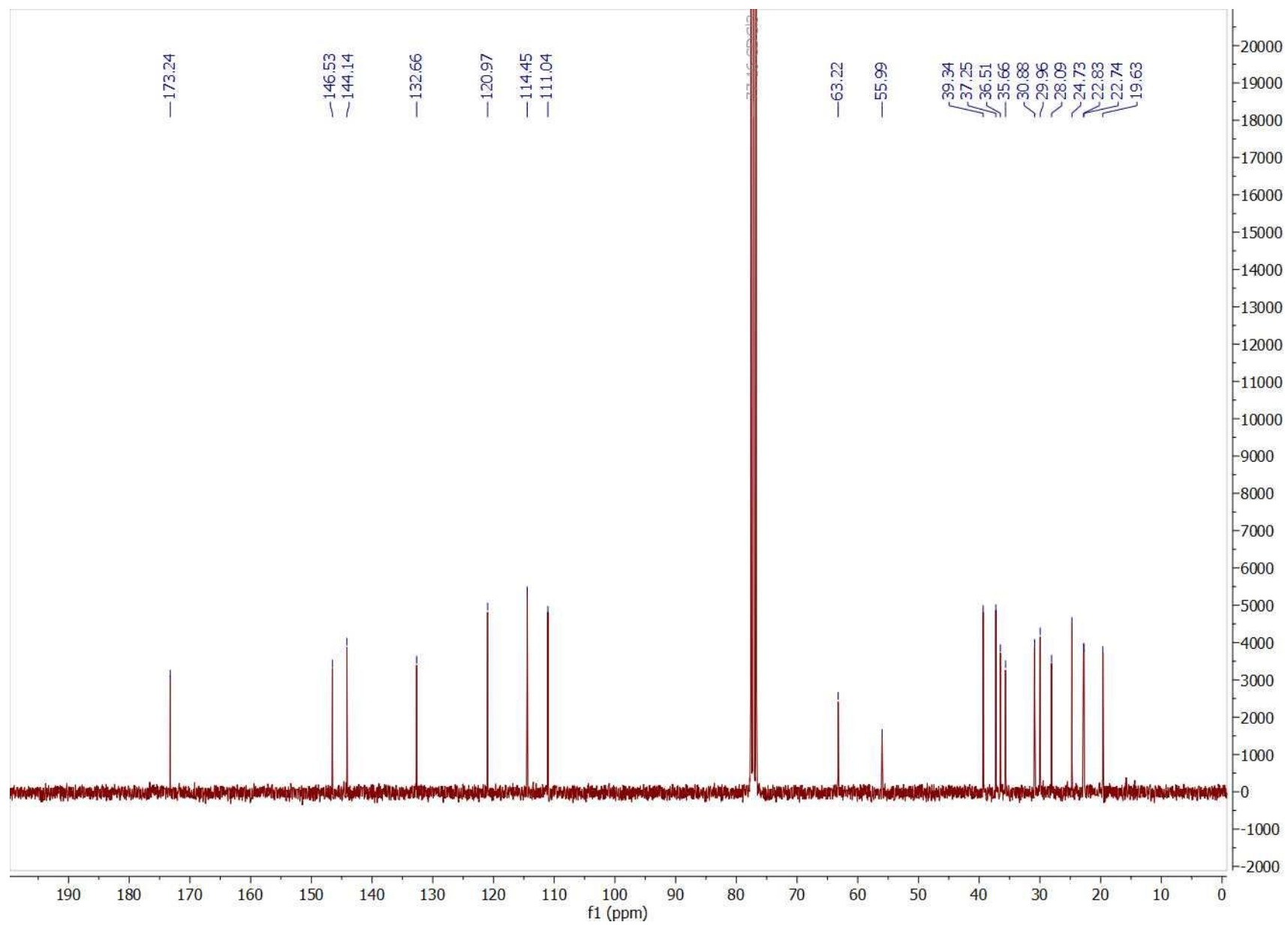


Figure S17. <sup>1</sup>H-NMR spectrum of HFMF

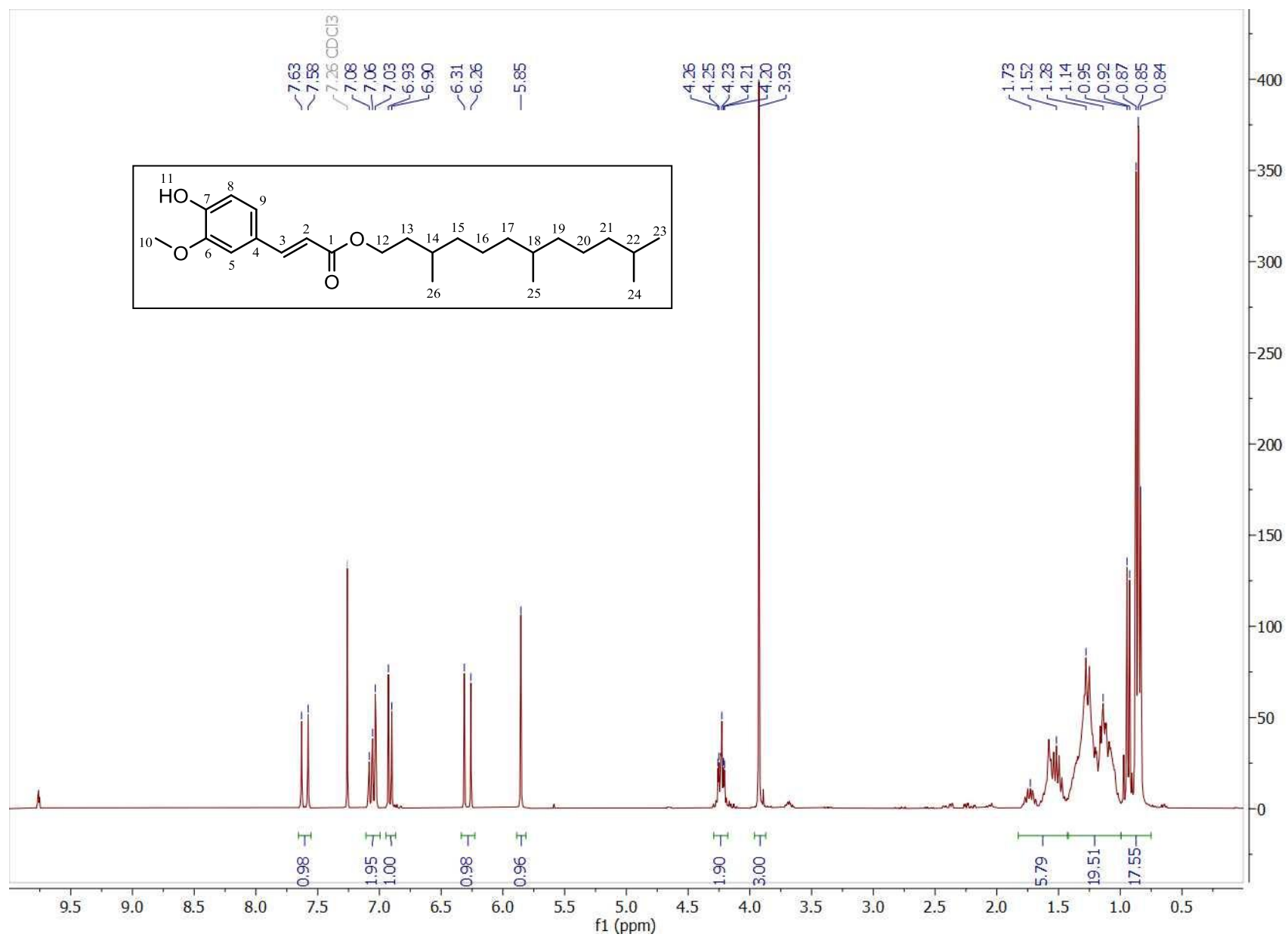


Figure S18.  $^{13}\text{C}$ -NMR spectrum of HFMF

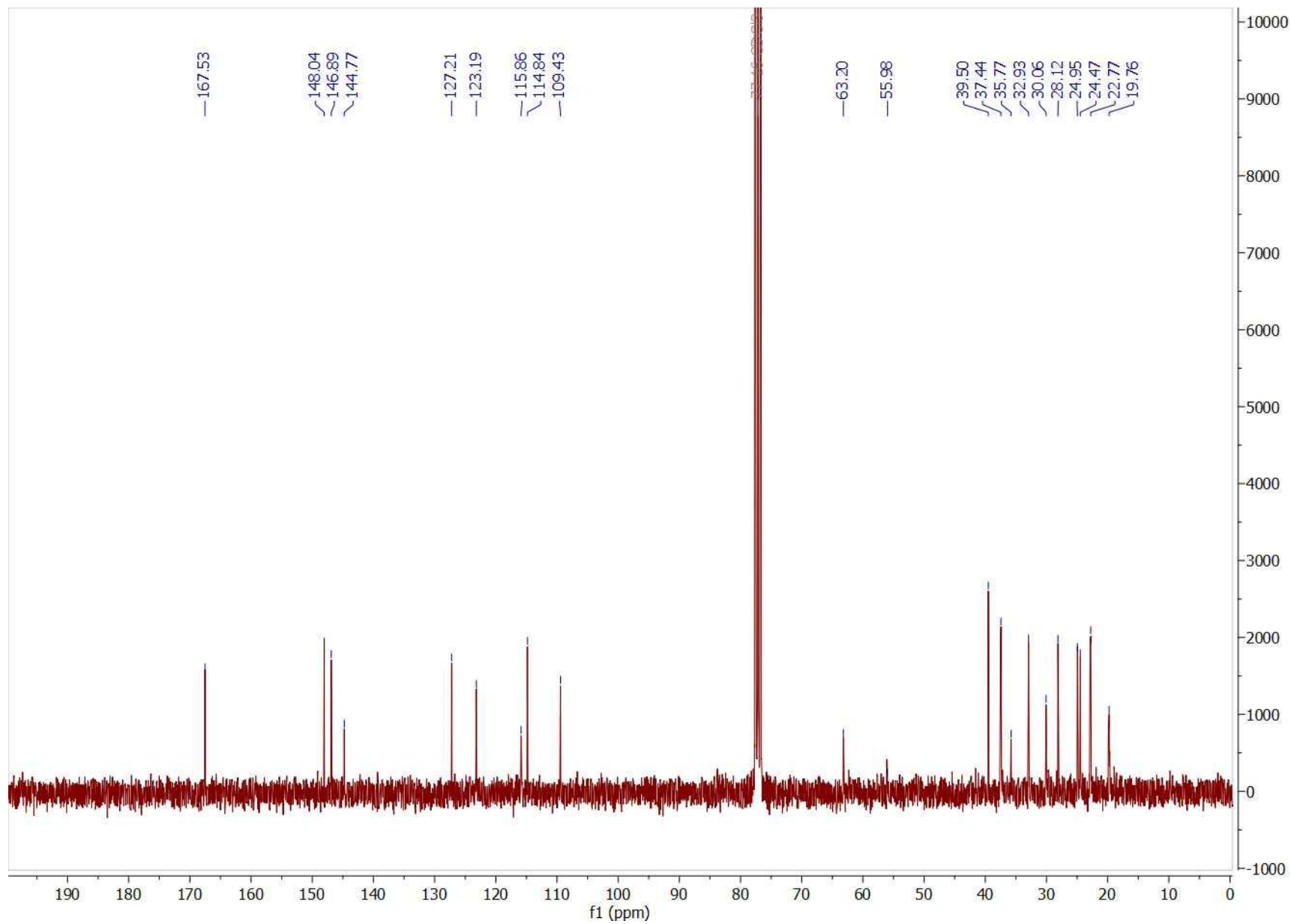


Figure S19. <sup>1</sup>H-NMR spectrum of HFMF-HF

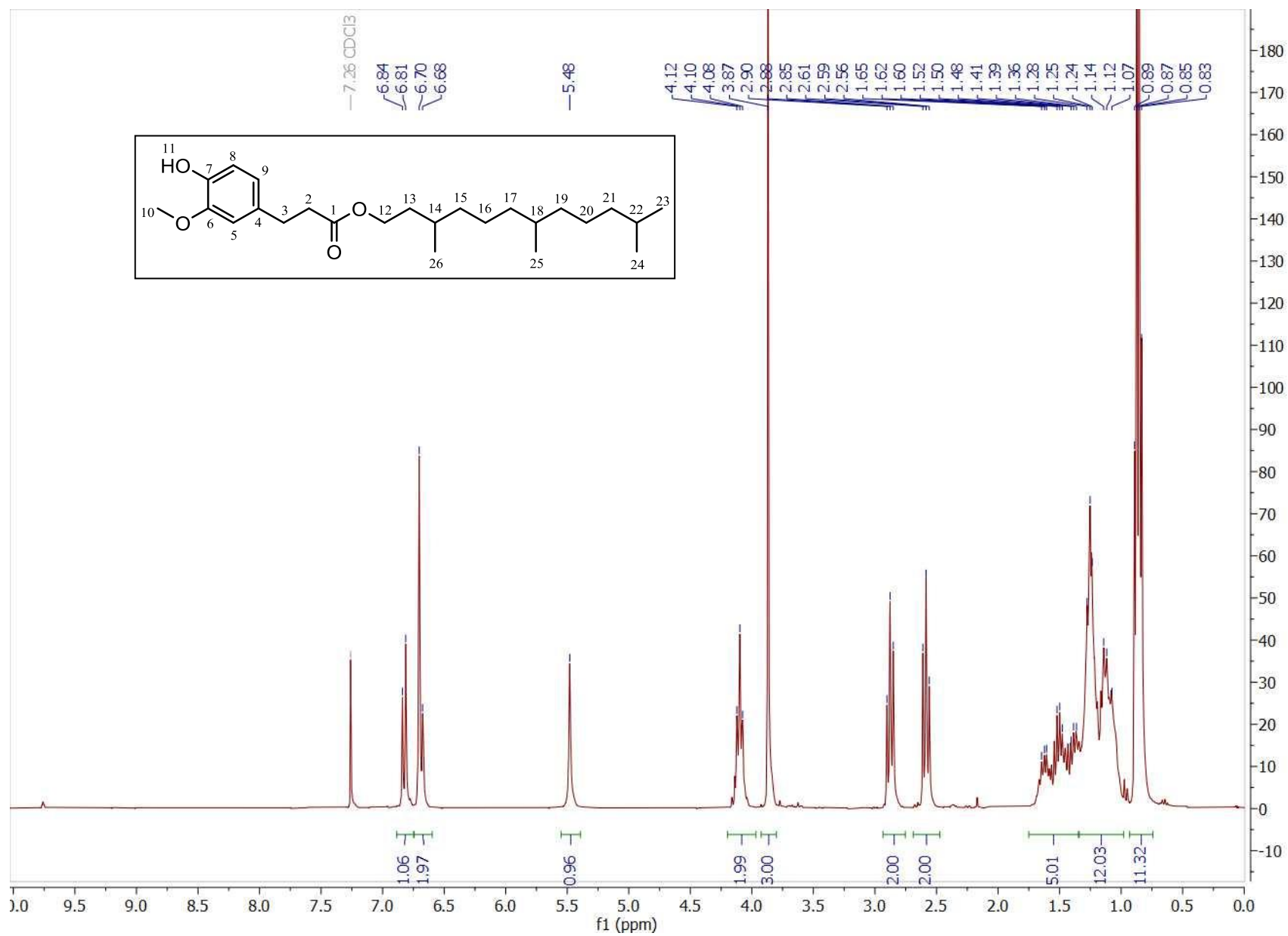


Figure S20.  $^{13}\text{C}$ -NMR spectrum of HFMF-HF

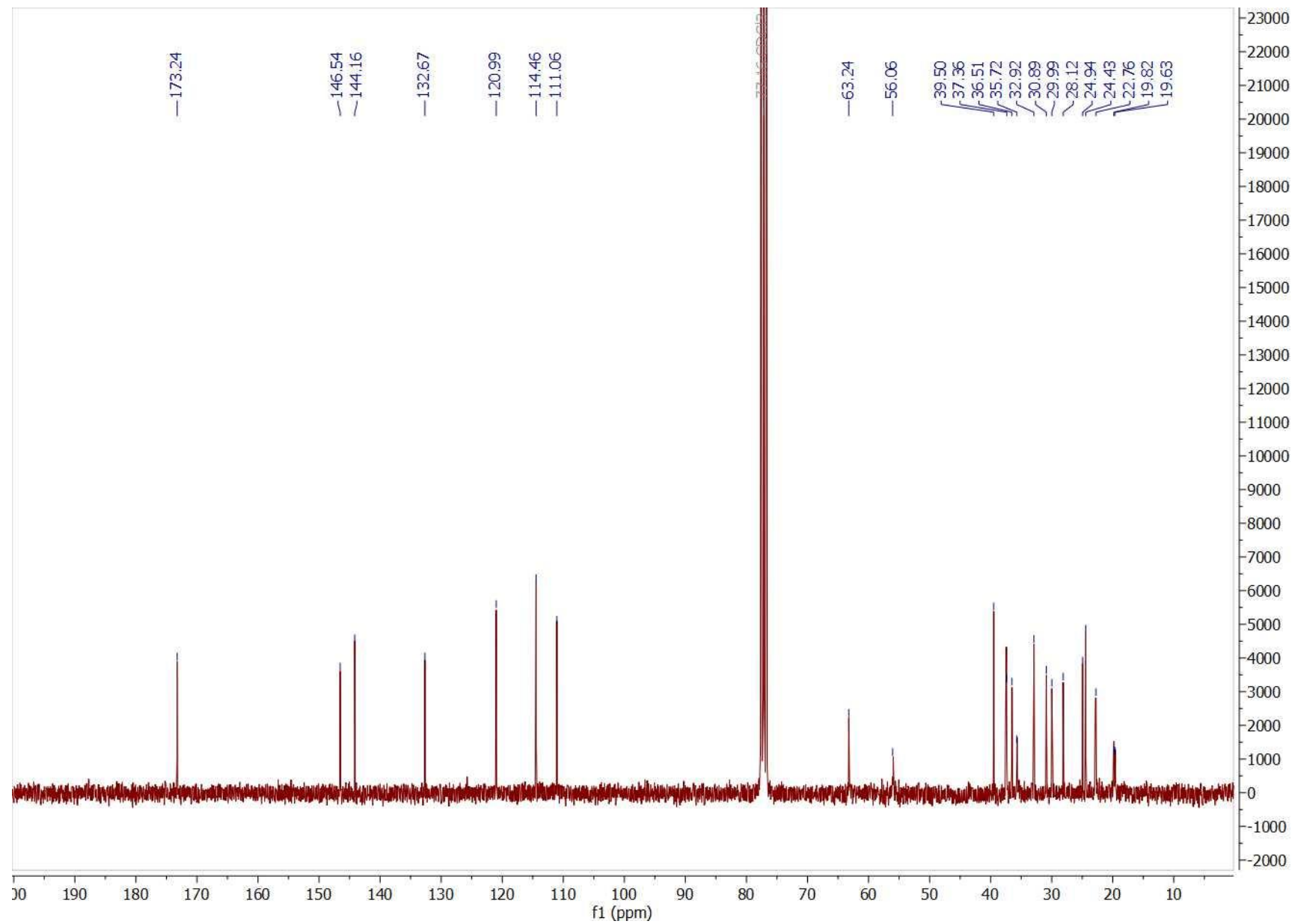


Figure S21. <sup>1</sup>H-NMR spectrum of OIMF

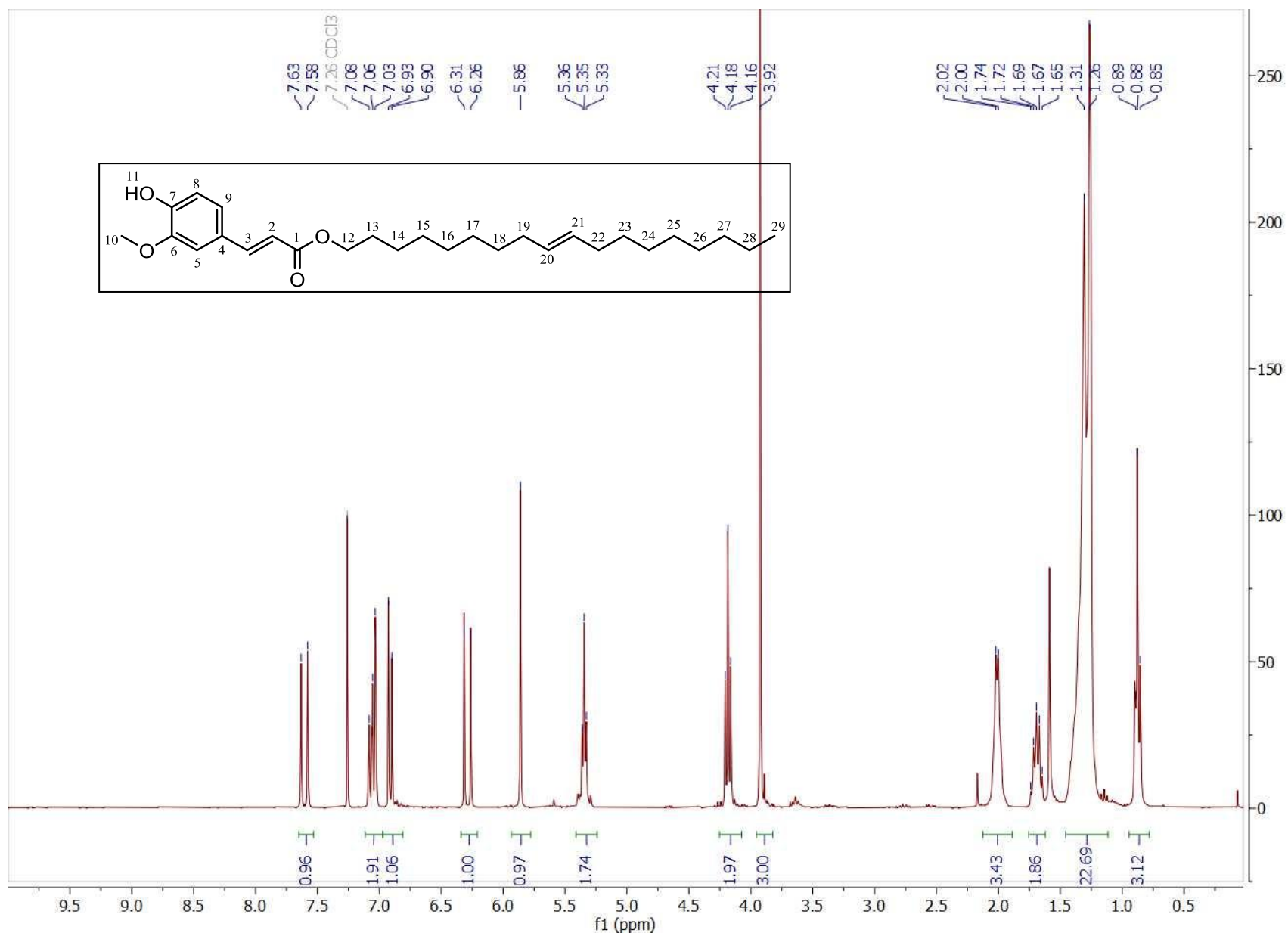


Figure S22.  $^{13}\text{C}$ -NMR spectrum of OIMF

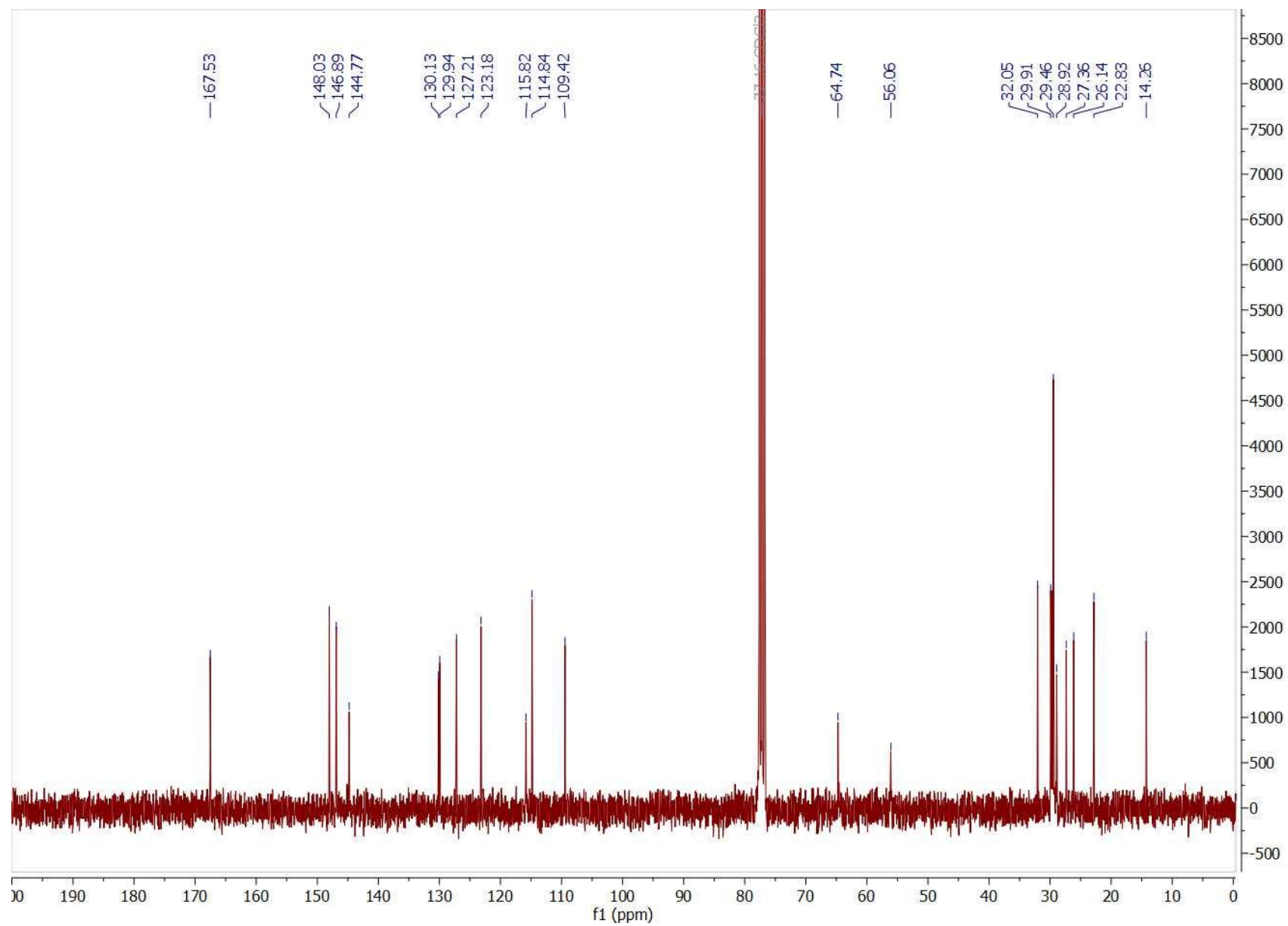


Figure S23. <sup>1</sup>H-NMR spectrum of OIMF-HF

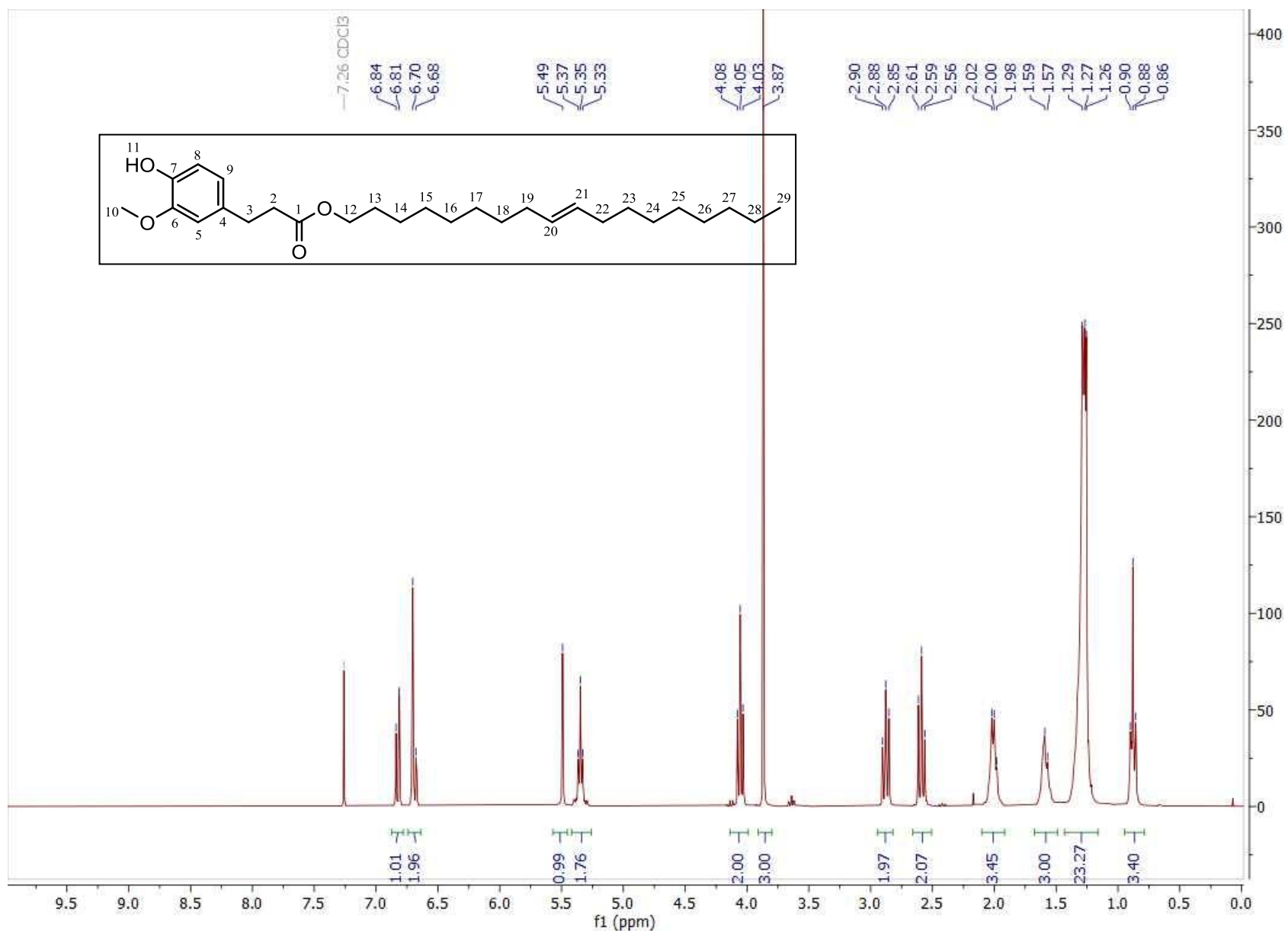
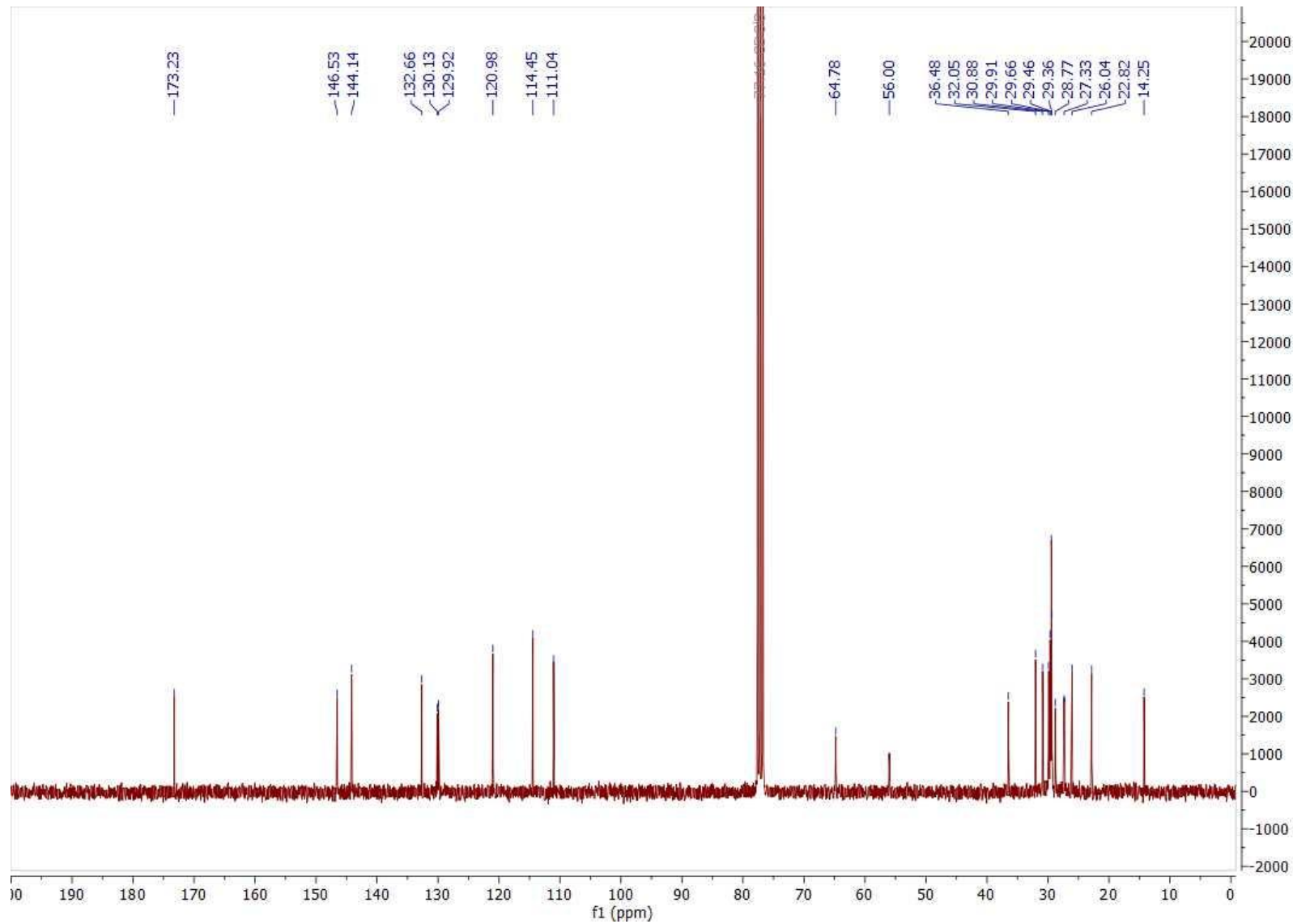
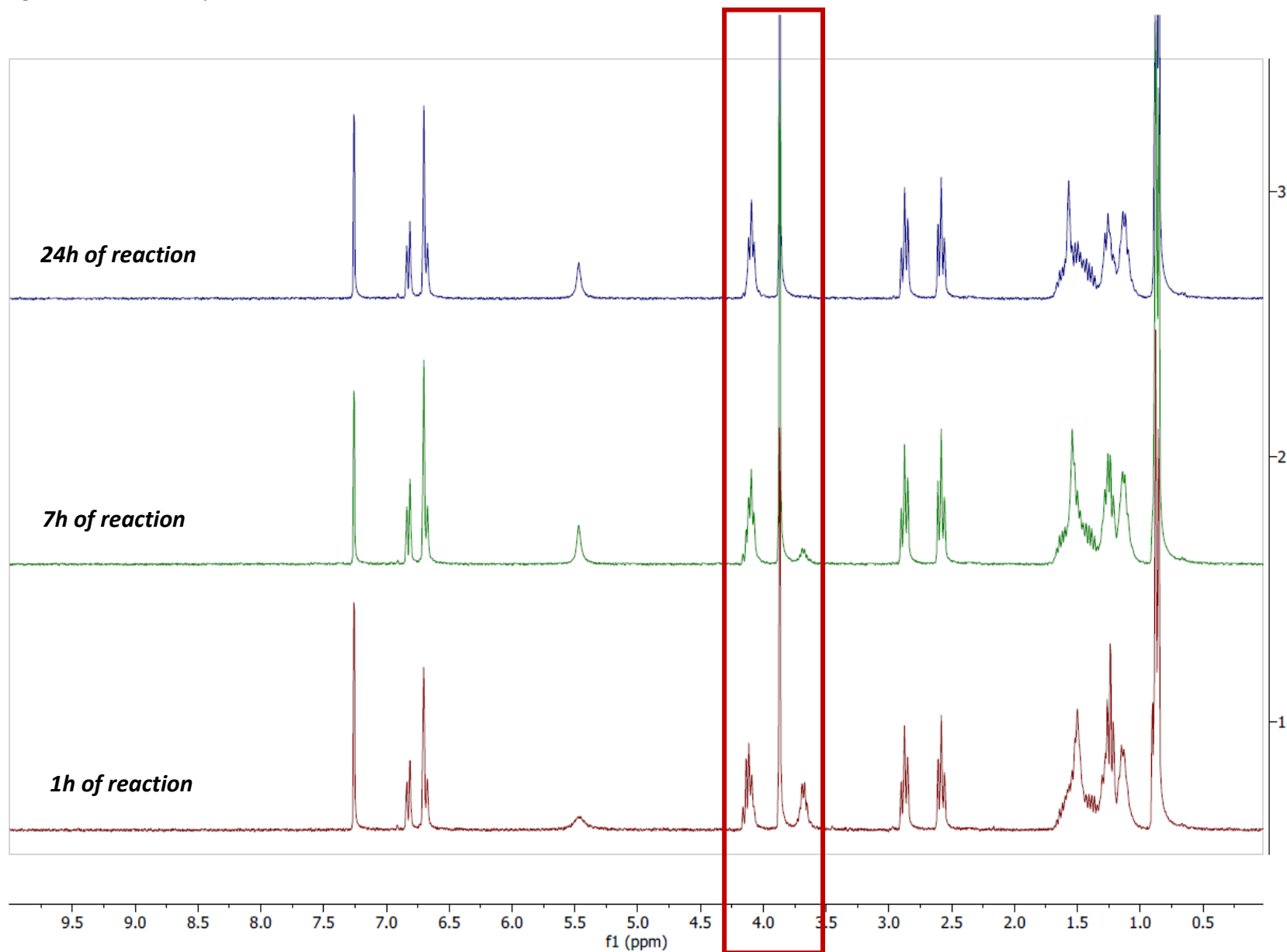




Figure S24.  $^{13}\text{C}$ -NMR spectrum of OIMF-HF

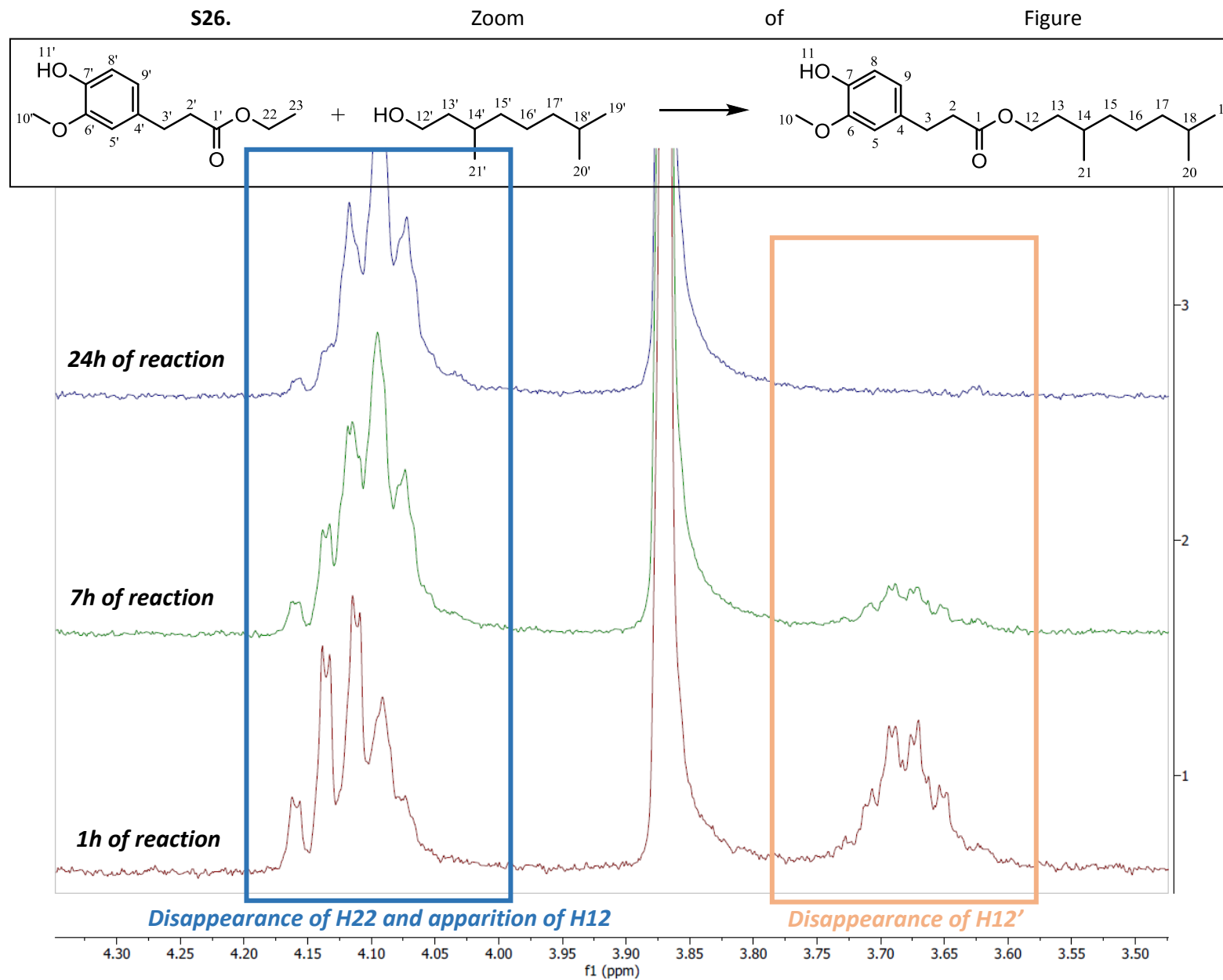


**Figure S25.**  $^1\text{H}$ -NMR spectra of the conversion of H-Geraniol and EtHFe into HGMF-HF



**Zoom for Figure S26**

Figure



S25

## Experimental values

**Table S16.** EC<sub>50</sub> of conjugated monophenols (in red) and their non-conjugated analogues (in purple), compared to starting materials and two references (in grey)

Name	EC <sub>50</sub> (nmol)
GMF	4.9±0.04
CMF	4.9±0.03
FMF	5.5±0.3
HGMF	5.1±0.3
HFMF	4.7±0.3
OIMF	4.8±0.1
GMF-HF	10.2±0.8
CMF-HF	12.0±0.5
FMF-HF	10.8±0.3
HGMF-HF	11.1±0.00
HFMF-HF	13.6±0.5
OIMF-HF	11.2±0.2
EtFe	80.4±1.9
EtHFe	41.5±2.3
Ferulic acid	60.8±8.4
BHT	7.5±0.6
α-tocopherol	9.8±0.5

**Table S17.** UV-filtering and photostability properties of conjugated (in red) and non-conjugated (in purple) monophenols, of starting materials and two references

Name	λ <sub>max</sub> (nm)	Abs <sub>max</sub> at t <sub>0</sub>	Abs <sub>max</sub> at t <sub>1</sub>	LoA (%)
GMF	327	0.27	0.22	17
CMF	327	0.26	0.22	17
FMF	328	0.25	0.23	8
HGMF	327	0.24	0.21	11
HFMF	327	0.20	0.15	24
OIMF	328	0.23	0.17	27
GMF-HF	282	0.05	0.04	13
CMF-HF	283	0.05	0.04	20
FMF-HF	281	0.04	0.03	30
HGMF-HF	281	0.05	0.03	33
HFMF-HF	283	0.07	0.06	21
OIMF-HF	283	0.04	0.03	31
EtFe	326	0.14	0.01	94
EtHFe	282	0.06	0	100
Ferulic acid	287	0.15	0	100
	313	0.15	0.02	89
Octinoxate	310	0.31	0.25	19
Avobenzone	358	0.46	0.42	10

λ<sub>max</sub>: wavelength at which the Abs<sub>max</sub> is observed;  
Abs<sub>max</sub>: maximum of absorbance between 400 and 260 nm; t<sub>0</sub>: before irradiation; t<sub>1</sub>: after 1h of irradiation; LoA: Loss of absorbance between t<sub>0</sub> and t<sub>1</sub>

**Table S18.** Density and surface tension values of conjugated (in red) and non-conjugated (in purple) monophenols and of two references

Name	Density (-)	Surface tension (mN/m)
GMF	1.08 ± 0.003	31.3 ± 0.9
CMF	1.06 ± 0.002	28.2 ± 1.0
FMF	1.04 ± 0.001	31.3 ± 1.1
HGMF	1.04 ± 0.003	28.4 ± 1.0
HFMF	1.00 ± 0.001	25.7 ± 0.5
OIMF	0.99 ± 0.003	27.3 ± 0.5
GMF-HF	1.04 ± 0.003	34.0 ± 0.7
CMF-HF	1.03 ± 0.001	31.8 ± 0.6
FMF-HF	1.01 ± 0.001	33.1 ± 1.0
HGMF-HF	1.02 ± 0.003	29.5 ± 0.9
HFMF-HF	0.98 ± 0.001	28.3 ± 0.6
OIMF-HF	0.98 ± 0.002	32 ± 1.5
DUB PTO	0.96 ± 0.001	27.8 ± 1.0
Castor Oil	0.96 ± 0.002	29.0 ± 1.3