

## *SUPPORTING INFORMATIONS*

Combining laccase-mediated dimerization of  
resveratrol and Centrifugal Partition

Chromatography: Optimisation of *E*-Labruscol  
production and identification of new resveratrol  
dimers.

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ABSTRACT Resveratrol dimers are of great interest for pharmaceutical and cosmetic applications. Nevertheless, the yield of their bio-production is limited by both the competition between the possible radical-radical coupling pathways and complex isolation procedures. Alternative organic synthesis methods do not afford higher yields. Although enzymatic routes can provide dimers in one step from resveratrol, bio-catalysis optimisation is required to improve yields and orient radical-radical coupling selectivity toward a specific resveratrol dimer, *E*-labruscol herein. After a rapid study of the relative importance of the bio-catalysis parameters, a design of experiments was implemented to produce *E*-labruscol in high yield by laccase-mediated dimerization of resveratrol. *E*-labruscol and  $\delta$ -viniferin were identified and isolated by flash chromatography as major products in 21% and 52% yields, respectively. As an alternative to purification on silica gel, an efficient separation of the aforementioned compounds was achieved by centrifugal partition chromatography (CPC). This technology provided  $\delta$ -viniferin in 63.1% yield (90% purity) and labruscol isomers in 20.4% yield with a purity of 95% after a CPC polishing step, but it also revealed the presence of *E*-labruscol diastereomers, leachianol F and leachianol G, as major reaction products, as well as less abundant products: pallidol, *Z*-labruscol,  $\epsilon$ -viniferin and two new resveratrol dimers named iso- $\delta$ -viniferin and iso- $\epsilon$ -viniferin.

## MATERIAL AND METHODS

### Material

Resveratrol and ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) were purchased from TCI (Zwijndrecht, Belgium). *Trametes versicolor* laccase and acetone (GC-MS grade) were purchased from Sigma-Aldrich (Saint Quentin Fallavier, France). Cyclohexane, ethyl acetate and methanol were purchased from VWR (Rosny-sous-bois, France). Methanol-*d*<sub>4</sub> was purchased from Eurisotop (Saclay, France). Acetonitrile HPLC grade was purchased from Fisher Scientific (Illkirch-Graffenstaden, France). The evaporations were carried out under reduced pressure. The separations on silica gel were performed on flash chromatography (PuriFlash 450XS, Interchim) using pre-packed INTERCHIM PF-30SI-HP columns (30 μm silica gel). In reverse phase the pre-packed column was a PF-30C18HP (30 μm C18). NMR spectra were recorded on an Avance III 600 spectrometer (Wissembourg, France) fitted with a 5 mm TCI cryoprobe (D, <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N). The <sup>1</sup>H-NMR spectra of the samples were recorded in MeOH-*d*<sub>4</sub> at 600 MHz, the chemical shifts are reported in parts per million (ppm) relative to the residual solvent peak (δ = 3.31 ppm). The <sup>13</sup>C-NMR spectra of the samples were recorded at 151 MHz (residual solvent peak δ = 49.00 ppm). 2D-NMR experiments were performed using standard Bruker microprograms (TopSpin 4.0 software). High-resolution mass spectrometry was performed on an Agilent 1290 system, equipped with a 6545 Q-TOF mass spectrometer and a PDA UV detector. The source was equipped with a JetStream ESI probe operating at atmospheric pressure. HPLC Chromatograms were recorded at 315, 254 and 210 nm on an Ultimate 3000 (ThermoFisher) equipped with a DAD detector using an Accucore C18 AQ column (2.6 μm x 3 mm x 100 mm). Preparative liquid chromatography (PLC) was performed on a Gilson PLC 2050 equipped with Gilson Glider software, Armen pump and Ecom UV detector, using a RP-C<sub>18</sub> column (Interchim uptisphere strategy C18-HQ, 5 μm, 250x21.2 mm). The mobile phase was

composed of H<sub>2</sub>O with TFA (0.025%)/CH<sub>3</sub>CN with a flow rate 10 mL/min. The chromatograms were monitored at 205, 286, 310 and 360 nm. Analytical HPLC experiments were performed using a Thermofisher Ultimate 3000 (Thermo Fischer Scientific, Villebon sur Yvette, France), equipped with a 4 ways pump LPG 3400 SD, an automatic injector WPS 3000 SL, an UV/visible diode array detector 3000 and the Chromeleon<sup>®</sup> software version 6.8. TLC was performed on pre-coated silicagel 60 F<sub>254</sub> Merck and compounds were visualized by spraying the dried plates with 50% H<sub>2</sub>SO<sub>4</sub>, followed by heating.

## **Methods**

### **Laccase activity assay**

In a 12-well microplate, 1300  $\mu$ L of tartaric buffer (pH 4.0) and 150  $\mu$ L of laccase solution in water (0.5 mg.L<sup>-1</sup>) or 150  $\mu$ L of water (for blank) were incubated at 30 °C, then 50  $\mu$ L of ABTS solution in water (5 mmol.L<sup>-1</sup>) were introduced. Absorbance at 405 nm was recorded every 8 seconds for 5 min using an EPOCH2 microplate reader (Biotek). All measurements were performed in triplicate. Laccase activity (a) was determined following the subsequent equation and determined as 3.8 U.mg<sup>-1</sup> ( $\mu$ mol.min<sup>-1</sup>.mg<sup>-1</sup>).<sup>1</sup>

### **General reaction procedure**

Resveratrol (114 to 456 mg) was dissolved in the organic solvent (EtOAc or acetone) then the additional volume of distilled water was added to reach 25 mL. The reaction medium was stirred at 700 rpm and brought to the targetted temperature. Using a syringe pump, 7 mL of laccase solution at the desired concentration (0.43 to 17.1 U.mL<sup>-1</sup>) was added at the predetermined rate (7 to 50 mL.h<sup>-1</sup>). The reaction was stopped by adding 1 M HCl solution (1 mL). The layers were separated when the reaction mixture was biphasic and when it was homogeneous, acetone was evaporated under reduced pressure. The aqueous layer was

extracted twice with ethyl acetate (2x10 mL). The organic layers were combined, washed with brine (10 mL), dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated.

### **HPLC method**

Samples were prepared by diluting 100  $\mu\text{L}$  of reaction medium into 900  $\mu\text{L}$  of acetonitrile, then the solution was filtered over regenerated cellulose syringe filter (0.2  $\mu\text{m}$  pore size). 1  $\mu\text{L}$  was injected on the column at 48  $^\circ\text{C}$ . The chromatograms are recorded at 210, 254 and 315 nm for the following elution gradient: 30% of formic acid solution 0.1% was maintained all along the run, acetonitrile proportion was varied from 20% at 0 min to 40% at 3.0 min, then 45% at 4.5 min, then 50% then 55% at 6.5 min, then 60% at 7 min, maintained at 60% during 0.5 min, decreased to 20% from 7.5 to 8 min and finally maintained at 20% during 1 min (total run time 9 min) and complement was brought by MilliQ water. Flow rate was set at 0.8  $\text{mL}\cdot\text{min}^{-1}$ . Calibration curves for quantification were established from commercial resveratrol and the two diastereomers of *E*-labruscol.<sup>1</sup>

### **Optimized reaction procedure**

Resveratrol (114 mg, 0.5 mmol) was dissolved in acetone (17.5 mL) then distilled water (7.5 mL) was added. The reaction medium was stirred at 700 rpm and heated at 45  $^\circ\text{C}$ . Using a syringe pump, 7 mL of laccase solution (4.3  $\text{U}\cdot\text{mL}^{-1}$ , 60  $\text{U}\cdot\text{mmol}^{-1}$ , 7.9 mg) was added over 1 hour. 0.5 h after the end of the addition, an aliquot (100  $\mu\text{L}$ ) was taken and the reaction was stopped by adding 1 M HCl solution (1 mL).

### **Scaled-up reaction procedure**

Resveratrol (2.0 g, 8.76 mmol) was dissolved in acetone (305 mL) then distilled water (130 mL) was added. The reaction medium was vigorously stirred and heated at 45  $^\circ\text{C}$ . Using a syringe pump, 28 mL of laccase solution (18.8  $\text{U}\cdot\text{mL}^{-1}$ , 60  $\text{U}\cdot\text{mmol}^{-1}$ ) was added over 4 hours. Two hours after the end of the addition, only a small amount of residual resveratrol was detected by TLC, the reaction was stopped by adding 1 M HCl solution (5 mL). Acetone

was distilled under reduced pressure. The aqueous layer was extracted twice with ethyl acetate (2x100 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated.

### **Purification on silica gel and C-18 stationary phases**

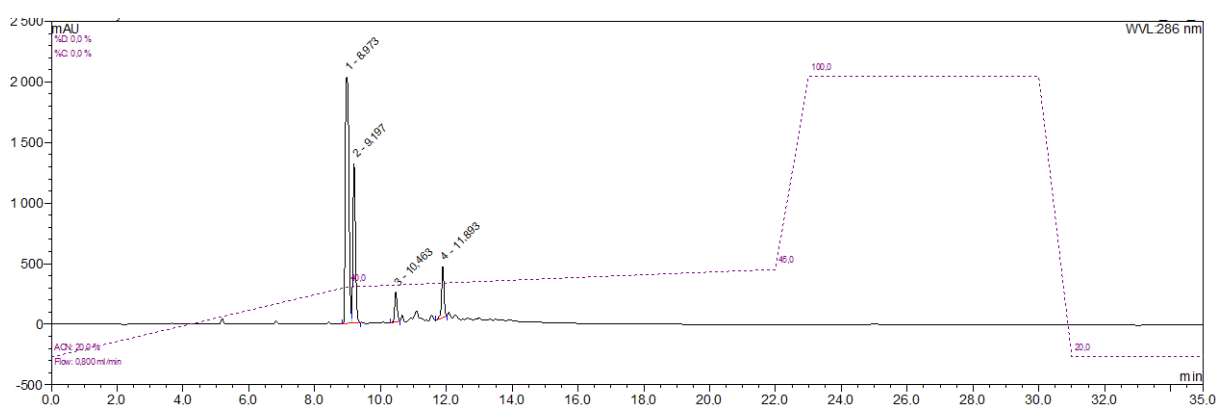
Column was conditioned in 1:1 cyclohexane:EtOAc, then the dry load of crude product was placed at the top of the column. Isocratic 1:1 was maintained during 16 column volume (cv) to afford residual resveratrol as first fraction then  $\delta$ -viniferin as second fraction. Eluant was reach at 1:4 cyclohexane:EtOAc between 16 and 22 cv then maintained at 1:4 until 26 cv to allow recovering of labruscol and sub-products in a third fraction then push to 9:1 EtOAc:MeOH from 26 to 27 cv and maintained until 33 cv to recover highly polar compounds.<sup>1</sup> The third fraction was concentrated and purified again over C-18. Starting at 87:13 water:MeOH gradient reach 63/37 at 10.2 CV and was maintained at 60:40 until 13.2 CV, labruscol was recovered. A novel polarity increase to 90% of methanol was performed to recover sub-products and clean the column.<sup>1</sup>

### **CPC fractionation**

Centrifugal partition chromatography (CPC) was carried out on a lab-scale FCPC<sup>®</sup> A200+PF 5125 column of 270 mL capacity (Rousselet Robatel Kromaton, Annonay, France) containing twenty-one circular partition disks, engraved with a total of 840 oval partition twin-cells (~10 mL per twin-cell) and connected to an integrated and automated peripheral PF 5125K including the injection valve, the gradient pump, the UV/Vis detector, the fraction collector and the control unit.

The crude mixture (2 g) (see Figure S1 for its HPLC profile) obtained from the enzyme catalysis was fractionated using a gradient elution method in the descending mode in a single run of 150 min. Three biphasic solvent systems were prepared independently by mixing *n*-

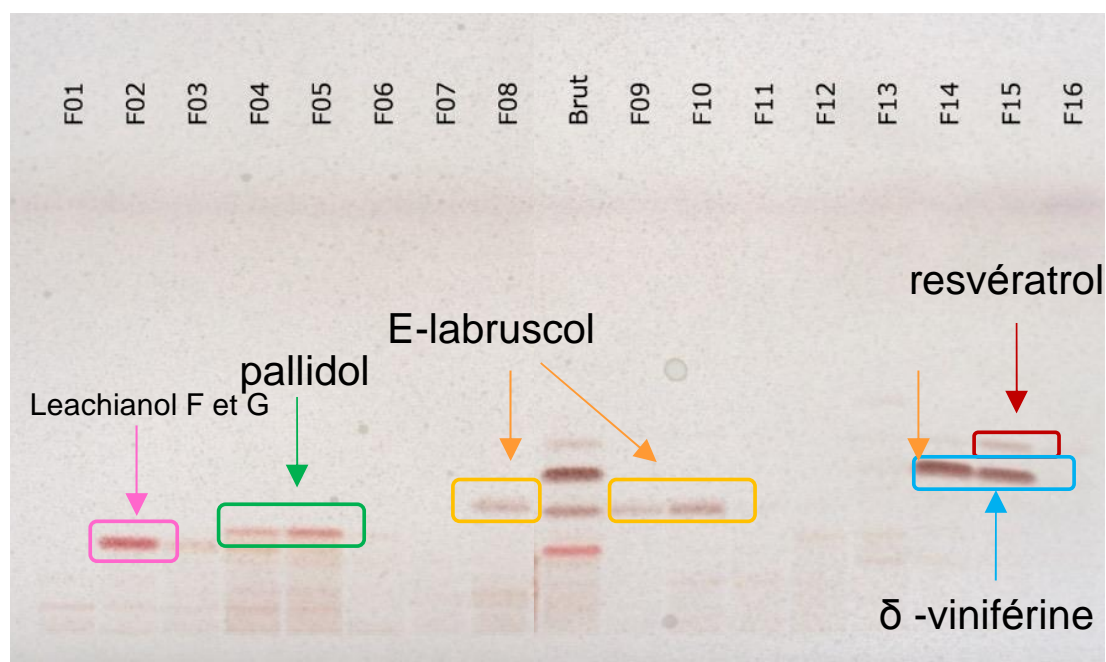
heptane, EtOAc, MeOH and water in the proportions 2/3/2/3 (v/v) for system L, 2/5/2/5 (v/v) for system J and 1/4/1/4 (v/v) for system G. The L, J and G letters for naming the biphasic solvent systems correspond to the notations used to describe the systems of the HemWat solvent scale. These three systems were selected to gradually decrease the polarity of the phase mobile from system G to system L while ensuring the biphasic character of the global system with MeOH and water as major constituents in the lower phase. The sample solution was prepared by directly dissolving the crude stilbene mixture (2 g) in 12 mL of a mixture of System J upper and System G lower phases (75/25, v/v). The CPC column was filled with the upper organic phase of System J at 600 rpm. After loading the sample solution into the column through a 20 mL sample loop, the rotation speed was adjusted to 1400 rpm and the flow rate was set at 8 mL.min<sup>-1</sup>.



**Figure S1.** HPLC chromatogram of the crude extract.

The elution was carried out, as shown in figure X, in descending mode by pumping 100% of the lower phase of system G for 20 min (first isocratic section), then this phase was reduced from 100% to 0% in 60 min (gradient section). The lower phase of system L was held at 100% for 70 min (second isocratic section). Finally, the column was extruded by switching from descending mode to ascending mode, while continuing to pump 100% of the lower phase of system L at 30 mL.min<sup>-1</sup>. The experiments were carried out at room temperature. 8

mL fractions were collected every minute and spotted onto Merck TLC plates coated with silica gel 60 F254 and developed with chloroform/methanol/acetic acid (83:17:3, v/v/v). After detection at UV254 and UV366, the plates were sprayed with vanillin-sulfuric acid and heated at 100 °C for 5 min. Fractions were then pooled based on their TLC profile similarities and solvents evaporated under vacuum (Figure S2). A total of 16 fractions were obtained.



**Figure S2.** TLC plate of CPC fractions.

Labruscol-containing fractions (517 mg) were pooled and submitted to an additional CPC purification step again in a gradient elution mode using the same three biphasic solvent systems G, J and L, but in the ascending mode. The latter was chosen as there was no issue related to the presence of residual resveratrol. The organic phase of the less polar system (system L) was used as the initial mobile phase, the organic phase of the more polar system (system G) was used as the final mobile phase, while the aqueous phase of the intermediary system (system J) was used as stationary phase. This CPC purification step (see Figure SX for the HPTLC fractogram) allowed the recovery of 408 mg of *E*-labruscol isomers



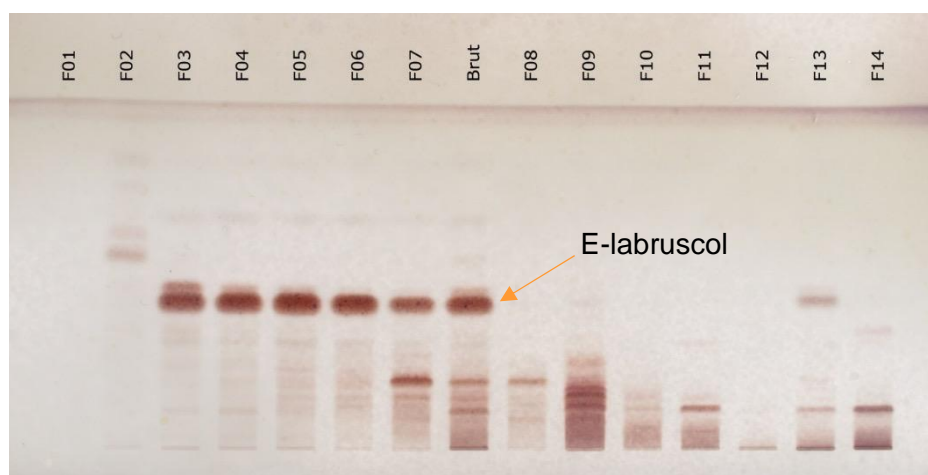


Figure S3: HPTLC fractogram of the second CPC on labruscol-containing fractions.

### Chemical profiling of CPC fractions

Identification of compounds was performed in collected fractions using a dereplication procedure based on  $^{13}\text{C}$  nuclear magnetic resonance (NMR)<sup>2,3</sup>

About 15 mg of each fraction were dissolved in 600  $\mu\text{L}$  DMSO-*d*<sub>6</sub> and analyzed by nuclear magnetic resonance (NMR) spectroscopy at 298 K on a Bruker Avance AVIII-600 spectrometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were acquired at 600.15 MHz and 150.91 MHz, respectively. Additional heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond correlation (HMBC), and homonuclear correlation spectroscopy (COSY) 2D-NMR experiments were performed on fractions containing putatively identified compounds using standard Bruker microprograms. After spectra processing using the TOPSPIN 4.0.5 software (Bruker), the absolute intensities of all  $^{13}\text{C}$  NMR signals detected in all spectra were collected by automatic peak picking. Then the  $^{13}\text{C}$  NMR spectral width (from 0 to 240 ppm) was divided into chemical shift buckets of 0.2 ppm and the absolute intensity of the NMR peaks detected in all spectra was associated to the corresponding bucket. Hierarchical Clustering Analysis (HCA) was performed on the rows for data visualization of signals corresponding to major compounds. The resulting clusters of  $^{13}\text{C}$  NMR chemical shifts were

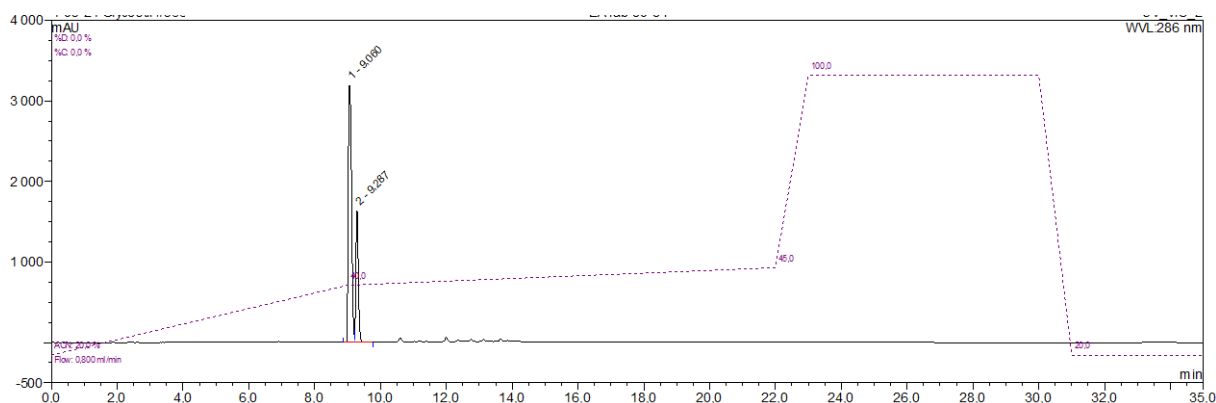
visualized as dendrograms on a heat map (Figure 4). The  $^{13}\text{C}$  NMR chemical shifts regrouped with the HCA were submitted as search keys to a local database containing the structures and predicted NMR chemical shifts (ACD/NMR Workbook Suite 2012 software, ACD/Labs, Ontario, Canada) to identify the corresponding chemical structures. Finally, each proposal given by the database search was confirmed by interpretation of 1D and 2D NMR data ( $^1\text{H}$  NMR, HSQC, HMBC, COSY).

### **Purification of CPC fractions**

The fractions obtained between 17 and 33 min were purified by Preparative Liquid Chromatography (PLC) with an elution gradient composed of a mixture of water with TFA 0.025%/CH<sub>3</sub>CN: (80/20 v/v) for 10 min, (80/20 v/v at 60/40 v/v) for 30 min and (0/100 v/v) for 10 min to identify leachianol F and G (86 mg).

Pallidol ( $t_r = 7.330$  min, 17 mg) was obtained after purification by semi-prep HPLC (elution gradient: TFA 0.025%/CH<sub>3</sub>CN (80/20 to 60/40 v/v for 20 min), Phenomenex Jupiter C18 300 column, 250 x 10 mm, 10  $\mu\text{m}$  of the fractions eluted between 50 and 57 min).

Fractions eluted from 70 to 88 min were purified by PLC with an elution gradient composed of a mixture of water with TFA 0.025%/CH<sub>3</sub>CN: (60/40 v/v) for 10 min, (60/40 v/v at 55/45 v/v) for 30 min and (0/100 v/v) for 10 min to identify the diastereoisomers of *E*-labruscol (520 mg), *Z*-labruscol (3 mg), iso- $\delta$ -viniferin and iso- $\epsilon$ -viniferin (7 mg). Under analytical HPLC conditions (InfinityLab Proshell 120 EC-C18 column, 4.6 x 150 mm, 2.7 Micron, eluent A: water + 0.025% TFA, eluent B: Acetonitrile, gradient: 20 to 40% B for 9 min, 40-45% B for 13 min, 100% B for 8 min) and TLC (CHCl<sub>3</sub>/MeOH/AcOH: 83/17/3 v/v) used, these compounds (iso- $\delta$ -viniferin and iso- $\epsilon$ -viniferin) have a retention time of 12.153 min and appear as a brick red stain with a front ratio of 0.30.

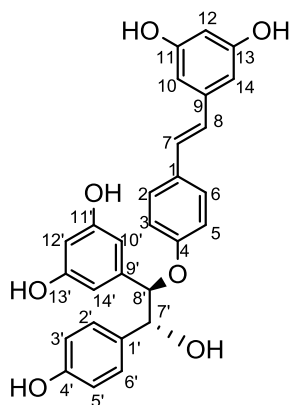


**Figure S4.** HPLC chromatogram of *E*-Labruscol fraction after CPC fractionation.

$\delta$ -viniferin (1.2 g) and  $\epsilon$ -viniferin (5 mg) were also detected in the fractions eluted from 100 to 127 min. These fractions were purified by PLC with an elution gradient composed of a water mixture with 0.025% TFA/CH<sub>3</sub>CN: (60/40 v/v) for 10 min, (60/40 v/v to 55/45 v/v) for 30 min and (0/100 v/v) for 10 min.

### Molecular modelling

The 2D structures drawn in ChemDraw were exported as isomeric SMILES chains and embedded 100 times each in 3D structures from randomly chosen starting points using the ETKDG protocol.<sup>4</sup> The 3D geometry of each conformer was then optimized using the MMFF94 force field.<sup>5</sup> Calculations were performed using the RDKit cheminformatics software library.<sup>1,6</sup>



*trans-E-Labruscol*

Carbon #	$\delta_C$ (ppm)	$\delta_H$ (ppm)	$J_{HH}$ Coupling Constant (Hz)	HMBC correlations
1	131.5	-		7, 8
2	128.4	7.33	(d) 8.3	7
3	117.3	6.88	(d) 8.3	2, 6
4	159.3	-		3, 5, 2, 6
5	117.3	6.88	(d) 8.3	2, 6
6	128.4	7.33	(d) 8.3	2, 8, 7
7	129.0	6.92	(d) 16.2	2, 6, 8
8	127.7	6.80	(d) 16.2	7, 10, 14
9	141.1	-		7, 8
10	105.7	6.43	(d) 2.2	8, 12
11	159.6	-		12, 10, 14
12	102.7	6.15	(t) 2.2	10, 14
13	159.6	-		12, 10, 14
14	105.7	6.43	(d) 2.2	8, 12
1'	132.4	-		3', 5', 7', 8'
2'	129.7	7.03	(d) 8.1	7', 8'
3'	115.6	6.66	(d) 8.1	2', 6'
4'	157.9	-		3', 5', 2', 6'
5'	115.6	6.66	(d) 8.1	2', 6'
6'	129.7	7.02	(d) 8.1	7', 8'
7'	79.0	4.79	(d) 7.4	2', 6', 8'
8'	86.2	4.99	(d) 7.4	7', 10', 14'
9'	141.9	-		7', 8'
10'	107.1	6.09	(d) 2.2	12', 8'
11'	159.2	-		8', 10', 14'
12'	102.8	6.06	(t) 2.2	10', 14'
13'	159.2	-		12', 10', 14'
14'	107.1	6.09	(d) 2.2	12', 8'

**Table 1.** NMR analysis of isolated *Trans-E*-Labruscol

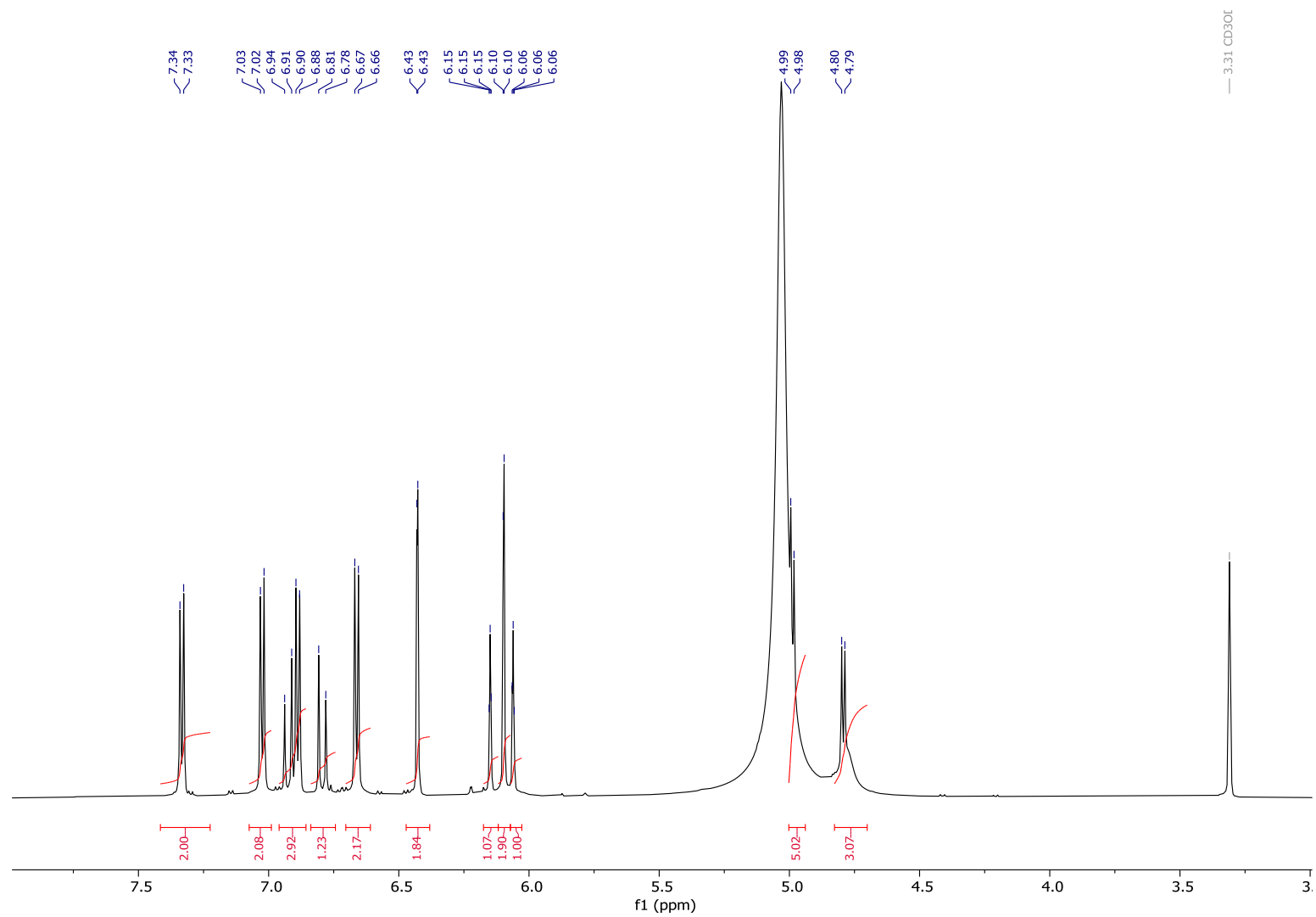


Figure S5. <sup>1</sup>H NMR spectrum of *Trans-E-Labruscol*

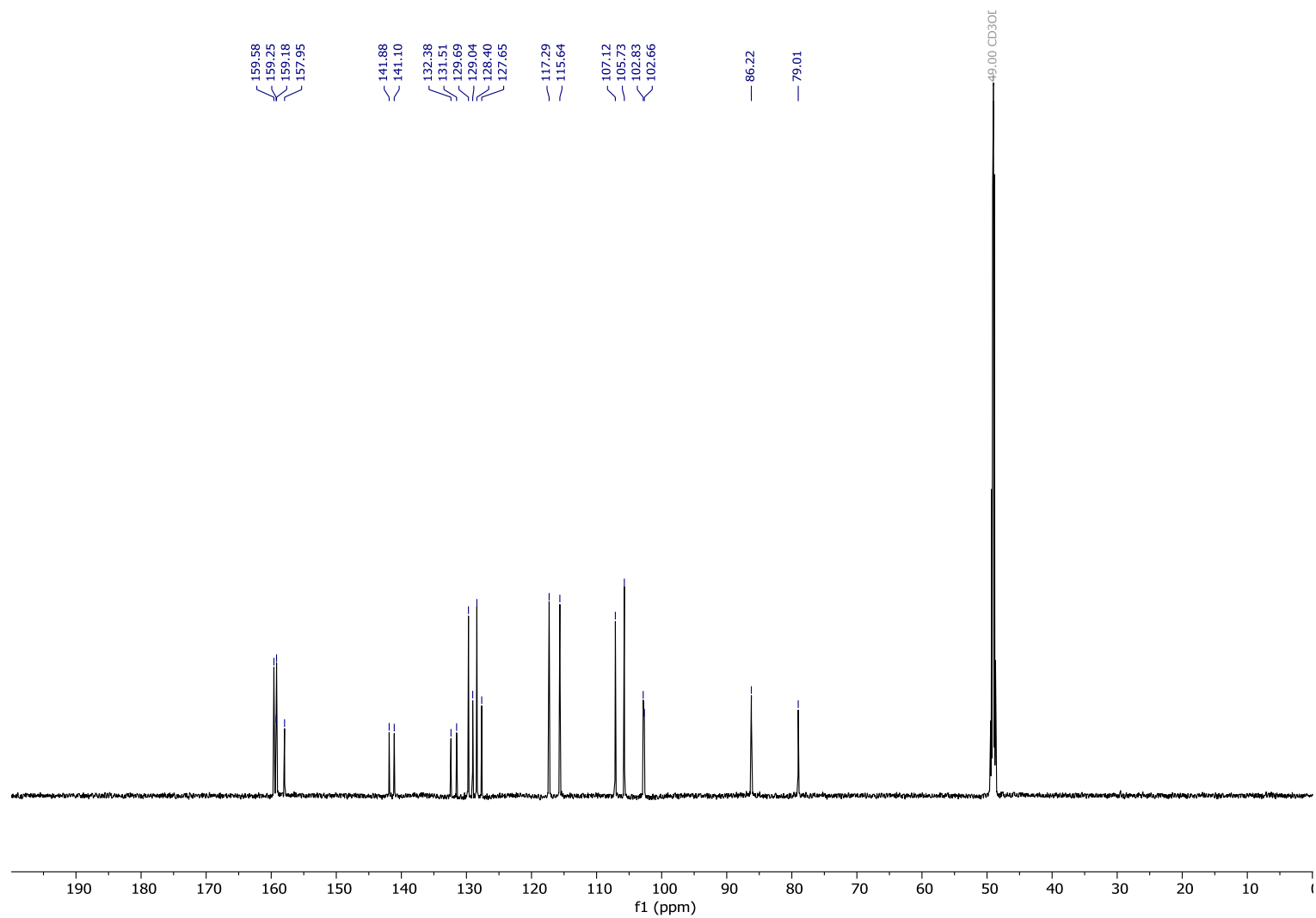
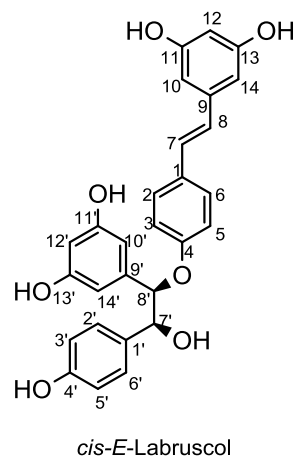


Figure S6.  $^{13}\text{C}$  NMR spectrum of *Trans-E*-Labruscol

**Table 2.** NMR analysis of *Cis-E-Labruscol*

Carbon n°	$\delta C$ (ppm)	$\delta H$ (ppm)	$J_{HH}$ Coupling Constant (Hz)	HMBC correlations
1	131.5	-	-	7, 8
2	128.4	7.31	(d) 8.7	7
3	117.1	6.77	(m)	2,6
4	159.2	-	-	3, 5, 2, 6
5	117.1	6.77	(m)	2,6
6	128.4	7.31	(d) 8.7	2, 8, 7
7	129.0	6.91	(d) 16.2	2,6, 8
8	127.6	6.78	(m)	7, 10, 14
9	141.1	-	-	7, 8
10	105.7	6.42	(d) 2.2	8, 12
11	159.6	-	-	12, 10, 14
12	102.7	6.14	(t) 2.3	10, 14
13	159.6	-	-	12, 10, 14
14	105.7	6.42	(d) 2.2	8, 12
1'	132.9	-	-	3', 5', 7', 8'
2'	129.9	7.14	(d) 8.6	7'
3'	115.4	6.71	(d) 8.5	-
4'	157.8	-	-	3', 5', 2', 6'
5'	115.4	6.71	(d) 8.5	-
6'	129.9	7.14	(d) 8.6	7'
7'	78.2	4.82	(d) 5.4	2', 6', 8'
8'	84.9	5.11	(d) 5.4	7', 10', 14'
9'	142.1	-	-	7', 8'
10'	107.2	6.22	(d) 2.2	12', 8'
11'	159.2	-	-	8', 12', 10', 14'
12'	102.9	6.14	(t) 2.3	10', 14'
13'	159.2	-	-	8', 12', 10', 14'
14'	107.2	6.22	(d) 2.2	12', 8'





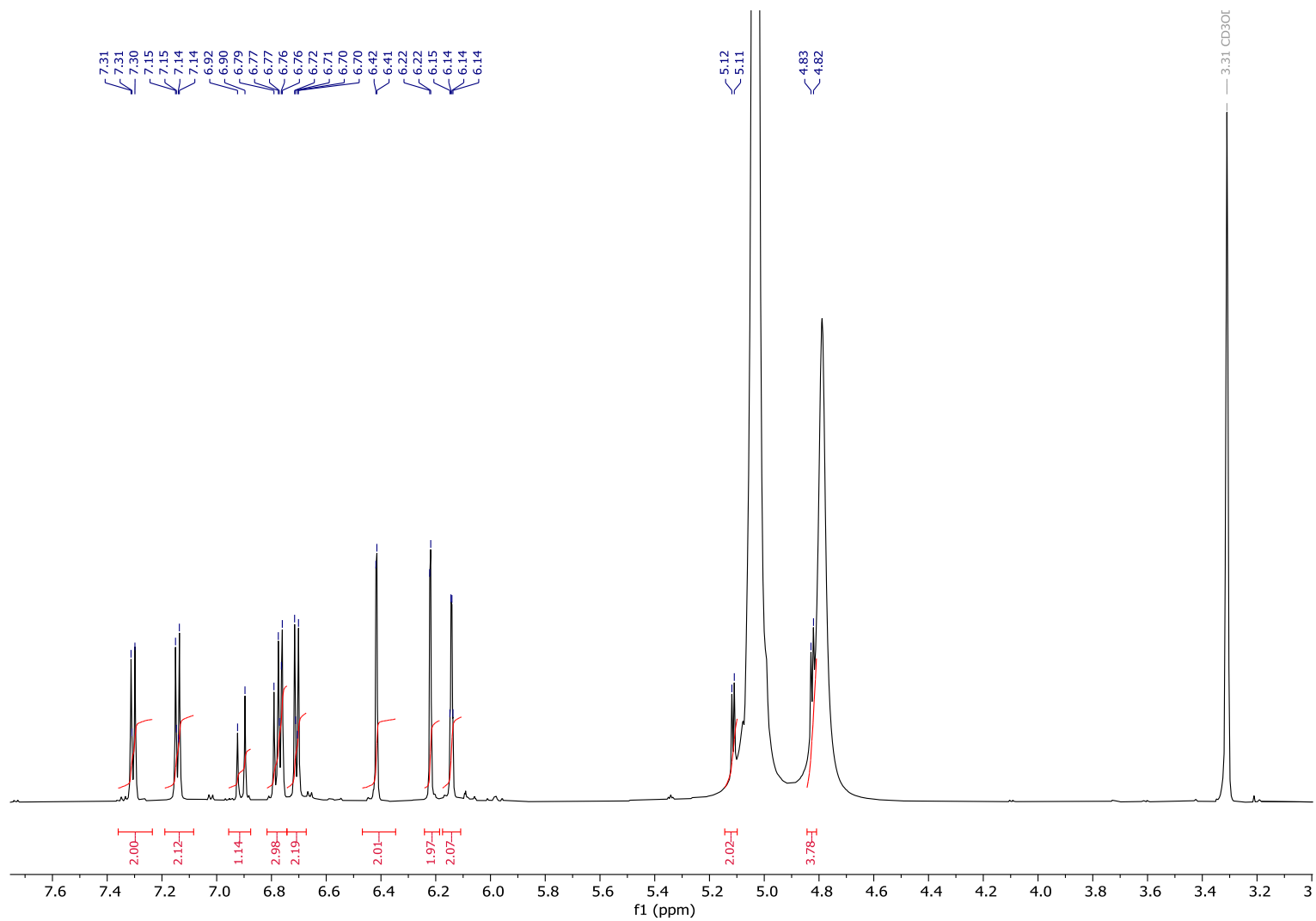


Figure S7.  $^1\text{H}$  NMR spectrum of *Cis-E-Labruscol*

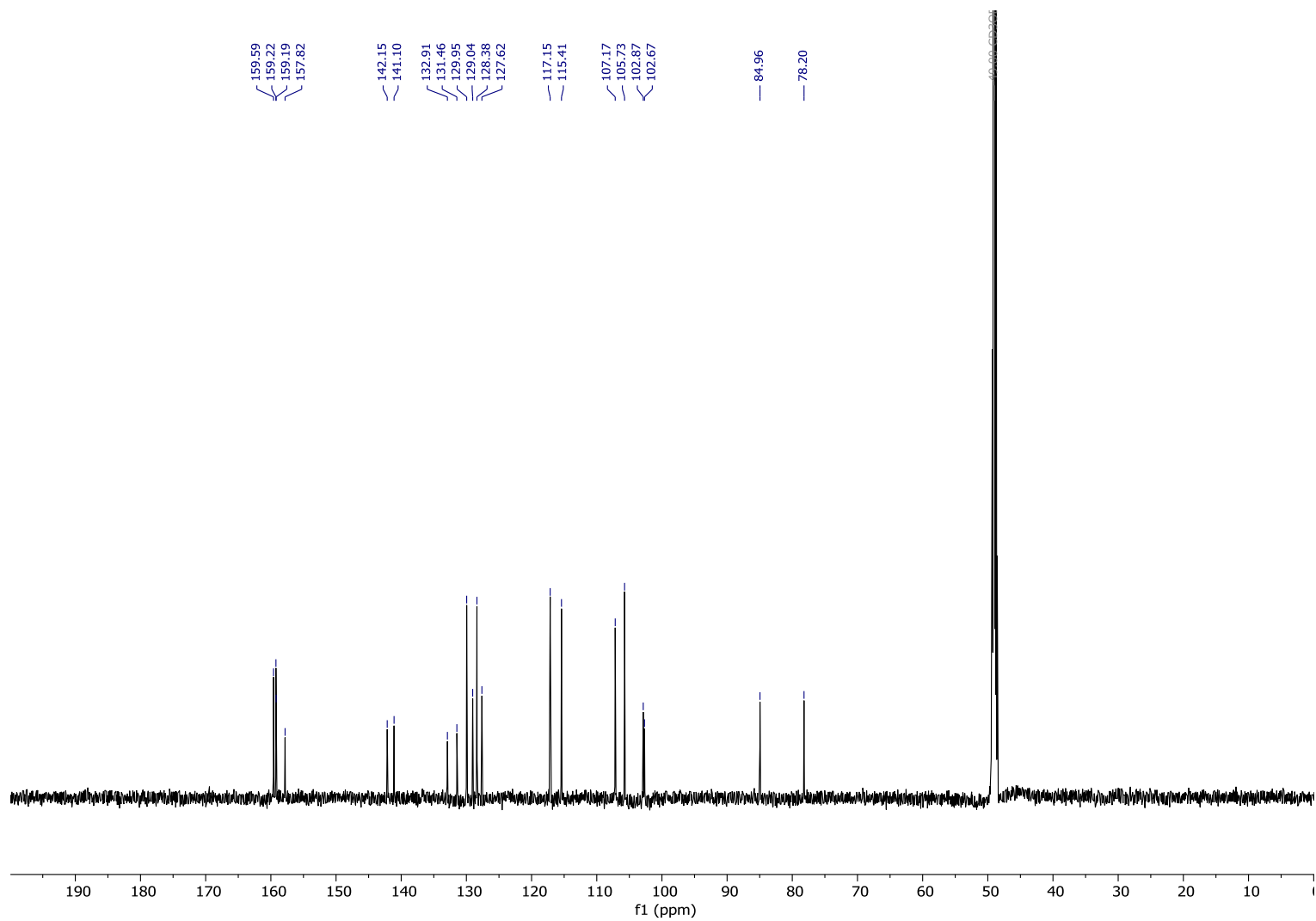
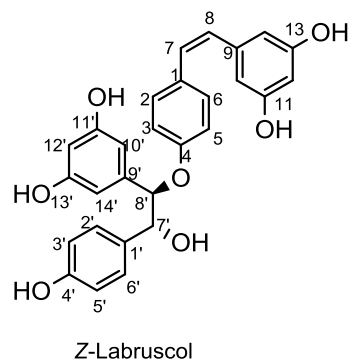


Figure S8.  $^{13}\text{C}$  NMR spectrum of *Cis-E*-Labruscol



Carbon #	$\delta_C$ (ppm)	$\delta_H$ (ppm)	$J_{HH}$ Coupling Constant (Hz)	HMBC correlations
1	141.1	-		7, 8
2	131.1	7.09	(d) 8.7	7
3	116.0	6.76	(d) 8.7	2,6
4	158.7	-		3, 5, 2, 6
5	116.0	6.76	(d) 8.7	2, 6
6	131.1	7.09	(d) 8.7	2, 8, 7
7	130.6	6.38	(d) 12.2	2, 6, 8
8	129.9	6.32	(d) 12.2	7, 10, 14
9	129.9	-		7, 8
10	106.7	6.18	(m)	8, 12
11	159.4	-		12, 10, 14
12	100.9	6.11	(m)	10, 14
13	159.4	-		12, 10, 14
14	106.7	6.18	(m)	8, 12
1'	132.5	-		3', 5', 7', 8'
2'	129.7	7.01	(d) 8.5	7'
3'	115.2	6.65	(d) 8.5	
4'	158.0	-		3', 5', 2', 6'
5'	115.2	6.65	(d) 8.5	
6'	129.7	7.01	(d) 8.5	7'
7'	77.6	4.76	(d) 7.4	2', 6', 8'
8'	84.8	4.94	(d) 7.4	7', 10', 14'
9'	142.0	-		7', 8'
10'	105.8	6.08	(m)	12', 8'
11'	159.2	-		8', 12', 10', 14'
12'	101.5	6.06	(m)	10', 14'
13'	159.2	-		8', 12', 10', 14'
14'	105.8	6.08	(m)	12', 8'

**Table 3.** NMR analysis of isolated Z-Labruscol

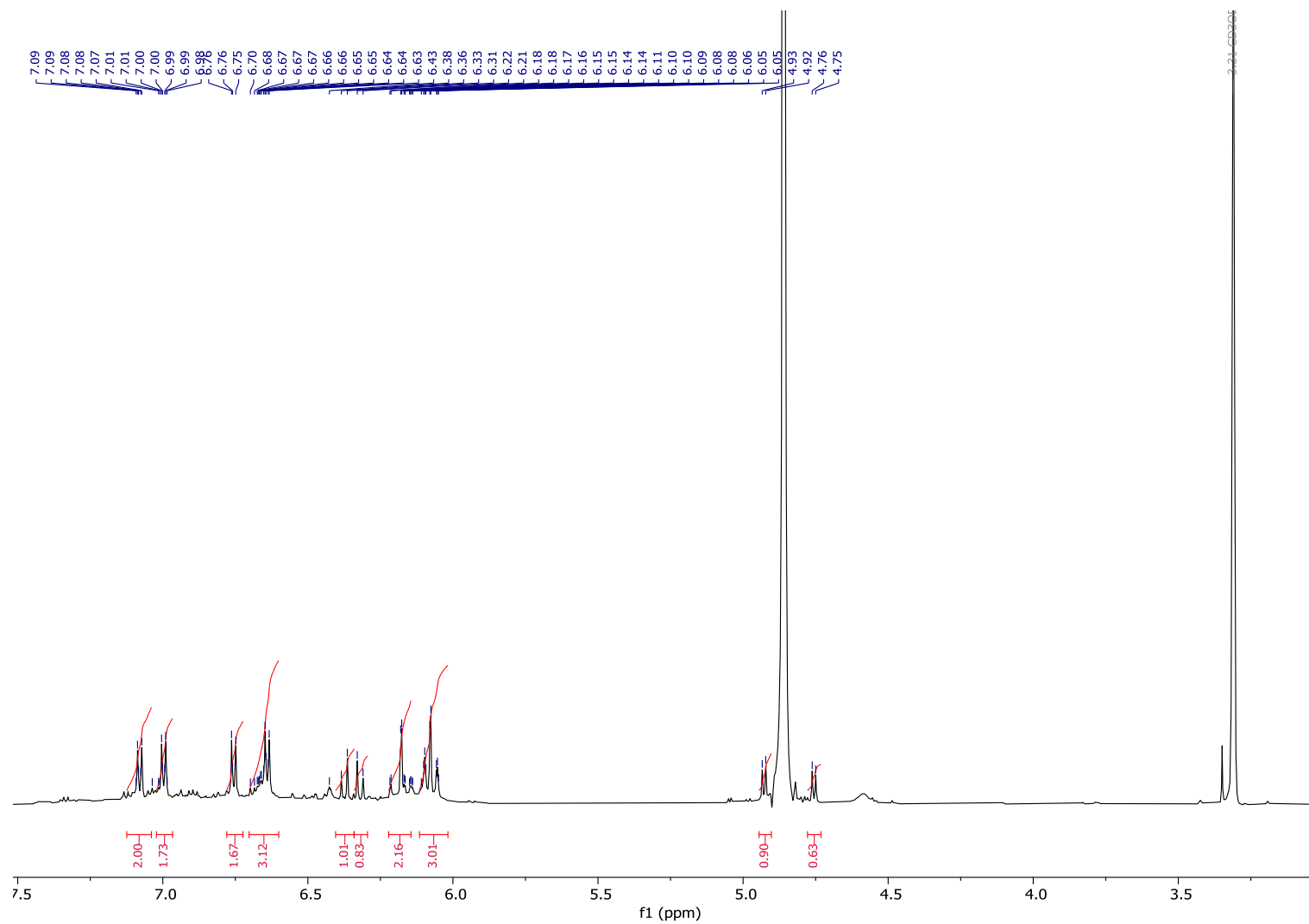


Figure S9.  $^1\text{H}$  NMR spectrum of Z-Labruscol

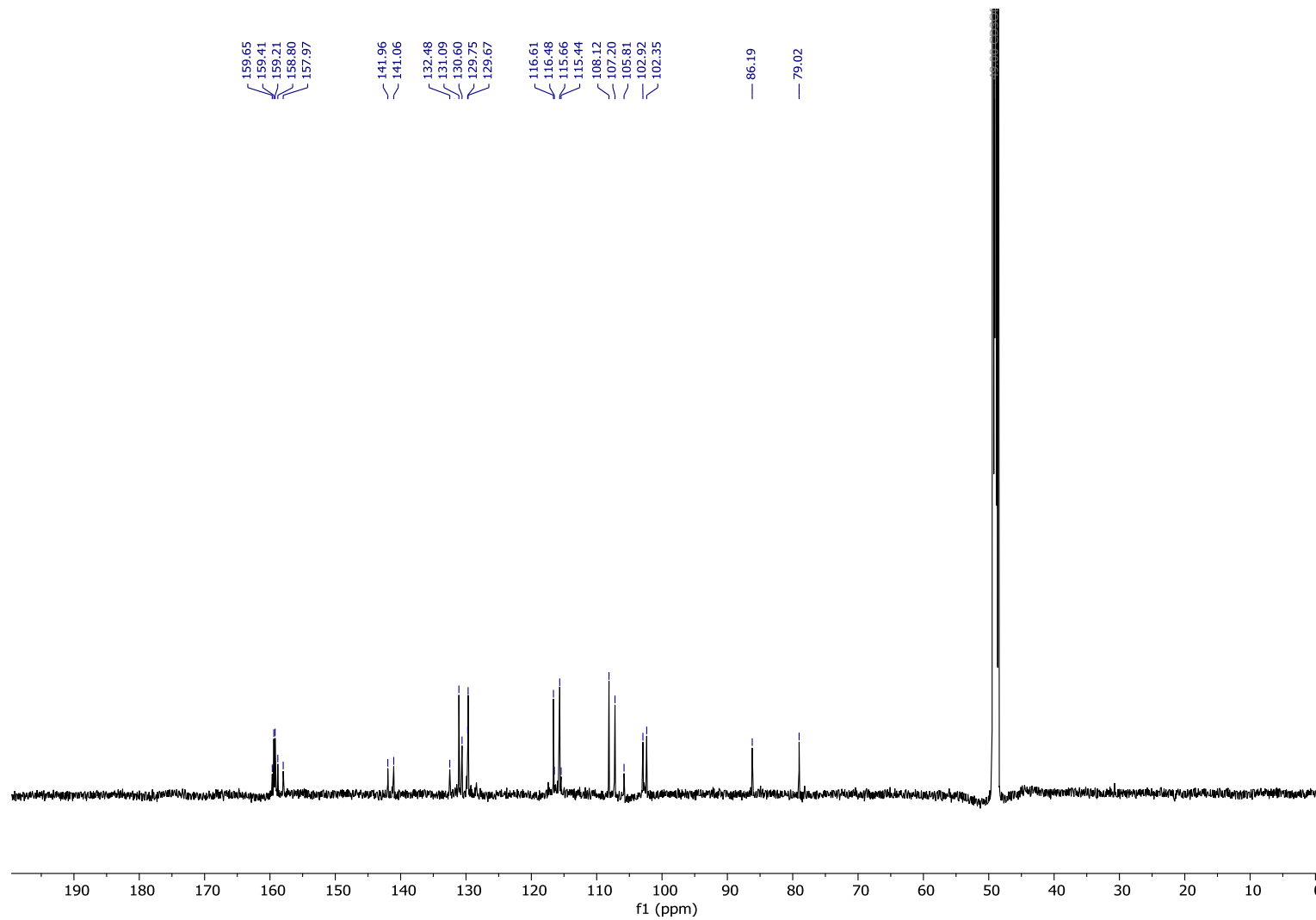
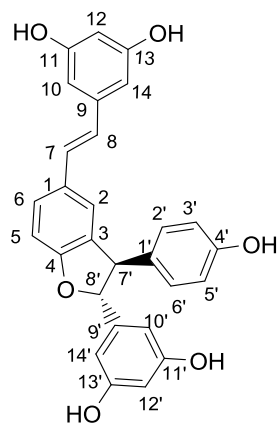


Figure S10.  $^{13}\text{C}$  NMR spectrum of Z-Labruscol

**Table 4.** NMR analysis of iso- $\delta$ -viniferin

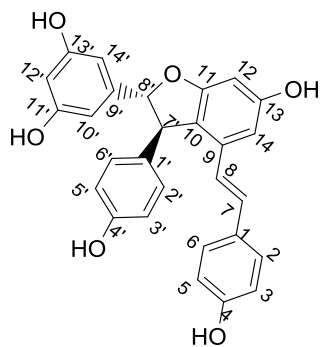


iso- $\delta$ -viniferin

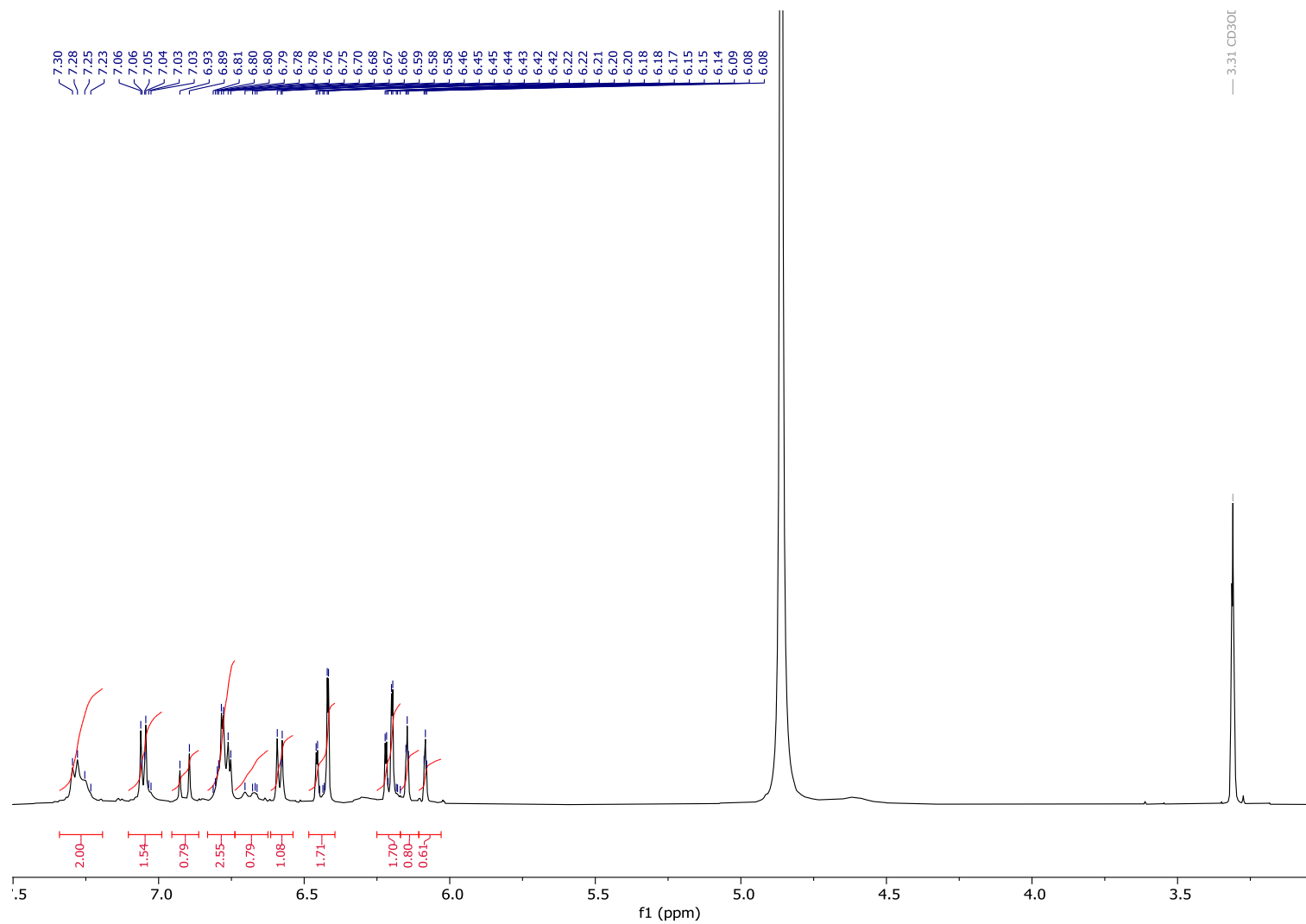
Carbon #	$\delta_C$ (ppm)	$\delta_H$ (ppm)	$J_{HH}$ Coupling Constant (Hz)	HMBC correlations
1	131.3	-		2, 6
2	128.8	6.77	(m)	3, 6
3	130.9	-		2, 5, 6
4	158.2	-		2, 6
5	105.9	6.44	(m)	3, 4, 1
6	128.3	6.81	(m)	2, 4, 7
7	129.2	6.92	(d) 16.1	2, 6, 8
8	127.5	6.78	(d) 16.1	7
9	141.2	-		8, 10, 14
10	105.8	6.44	(d) 2.2	
11	159.6	-		10, 12, 14
12	102.7	6.16	(t) 2.2	10, 13
13	159.6	-		10, 12, 14
14	105.8	6.44	(d) 2.2	12
1'	131.3	-		3', 5'
2'	128.3	7.3	(d) 7.9	
3'	117.4	6.8	(d) 7.9	
4'	159.5	-		3', 5', 2', 6'
5'	117.4	6.8	(d) 7.9	
6'	128.3	7.3	(d) 7.9	
7'	54.0	4.65	(m)	2', 6'
8'	83.4	6.31	(m)	10', 14'
9'	145.3	-		10', 14'
10'	107.2	6.21	(d) 2.2	12'
11'	159.2	-		12', 10', 14'
12'	102.9	6.10	(t) 2.2	10', 14'
13'	159.2	-		12', 10', 14'
14'	107.2	6.21	(d) 2.2	12'

**Table 5.** NMR analysis of iso- $\epsilon$ -viniferin

	Carbon #	$\delta_C$ (ppm)	$\delta_H$ (ppm)	JHH Coupling Constant (Hz)	HMBC correlations
	1	131.6	-		7
	2	128.8	7.27	m	7
	3	116.3	6.78	m	
	4	159.6	-		2, 6
	5	116.3	6.78	m	
	6	128.8	7.27	m	7
	7	129.2	6.92	(d) 16.1	2, 6, 8
	8	127.5	6.78	(d) 16.1	7
	9	142.1	-		7
	10	119.4	-		12, 14
	11	158.0	-		12
	12	103.8	6.24	(d) 2.5	14
	13	157.2	-		12, 14
	14	106.2	6.48	(d) 2.5	12
	1'	133.9	-		3', 5'
	2'	131.1	7.07	(d) 8.7	
	3'	115.5	6.61	(d) 8.7	
	4'	156.5	-		3', 5', 2', 6'
	5'	115.5	6.61	(d) 8.7	
	6'	131.1	7.07	(d) 8.7	
	7'	54.0	4.65	(m)	2', 6'
	8'	83.4	6.31	(m)	10', 14'
	9'	145.3	-		10', 14'
	10'	107.2	6.21	(d) 2.2	12'
	11'	159.2	-		12', 10', 14'
	12'	102.9	6.10	(t) 2.2	10', 14'
	13'	159.2	-		12', 10', 14'
	14'	107.2	6.21	(d) 2.2	12'



iso- $\epsilon$ -viniferin



**Figure S11.**  $^1\text{H}$  NMR spectrum of iso- $\delta$ - and iso- $\epsilon$ -viniferin



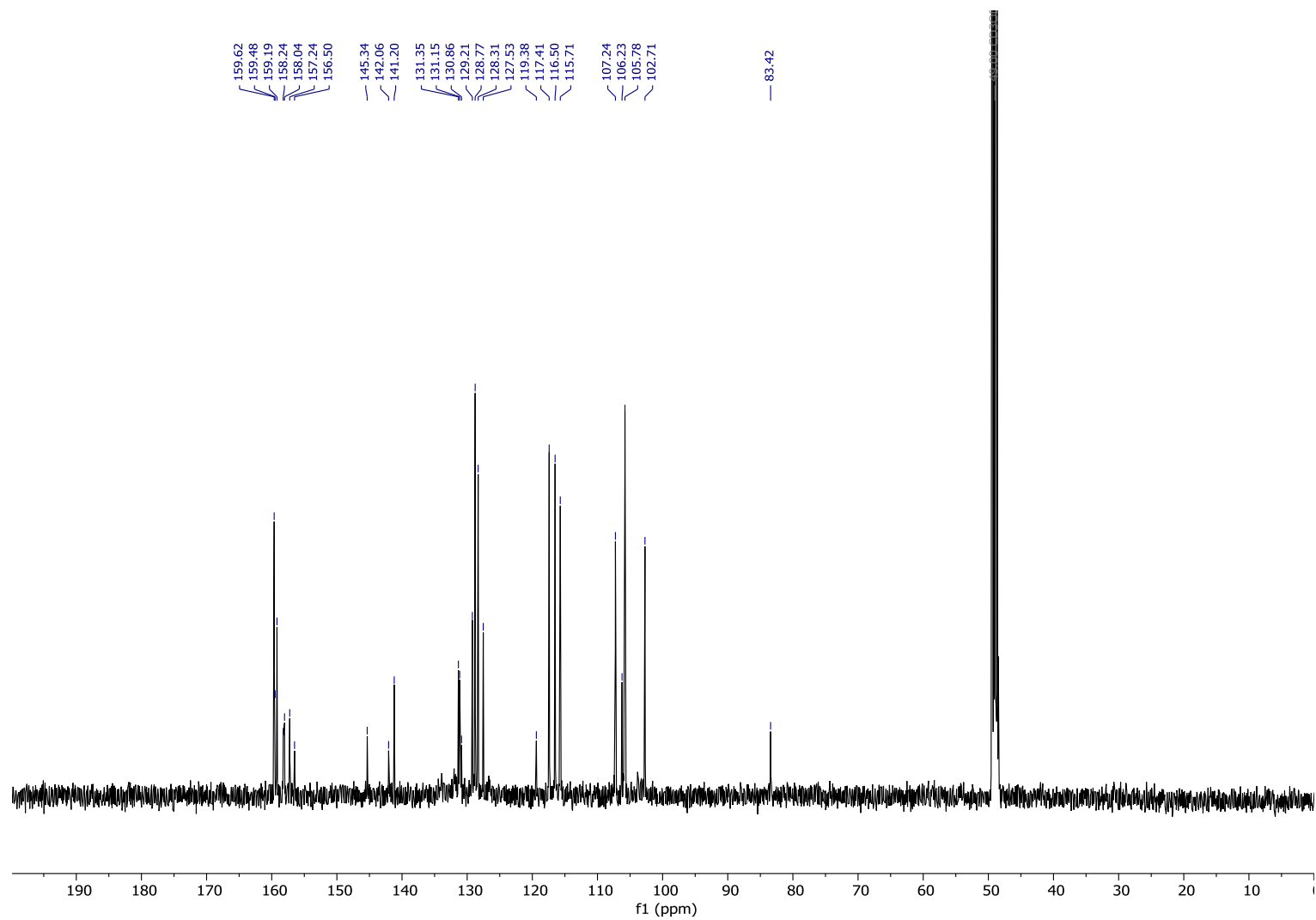


Figure S12.  $^{13}\text{C}$  NMR spectrum of iso- $\delta$ - and iso- $\epsilon$ -viniferin

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