

## 8-O-4'-Neolignans from Flower Buds of *Magnolia fargesii* and their Biological Activities

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Três novos derivados de 8-O-4'-neolignanas, fargesifenols A-C, juntamente com seis neolignanas conhecidas, foram isoladas de botões de flores de *Magnolia fargesii*. As estruturas foram elucidadas por métodos espectroscópicos, incluindo técnicas de RMN 1D e 2D. Os compostos foram também testados quanto à sua atividade anti-HIV-1 e quanto às citotoxicidades.

Three new 8-O-4'-neolignans, fargesiphenols A-C, together with six known neolignans, were isolated from the flower buds of *Magnolia fargesii*. The structures were elucidated by spectroscopic methods, including extensive 1D and 2D-NMR techniques. Compounds were also tested for their anti-HIV-1 activities and cytotoxicities.

**Keywords:** *Magnolia fargesii*, 8-O-4'-neolignans, anti-HIV-1 activity, cytotoxicity

### Introduction

The genus of *Magnolia* (Magnoliaceae) has traditionally been used as herb medicine in China for a long time. Especially, Xinyi (dried flower buds of *Magnolia fargesii*), has been used for the treatment of inflammatory-related diseases such as nasal congestion, empyema, sinusitis, and allergic rhinitis.<sup>1,2</sup> Previous phytochemical investigations have reported that this species contains several secondary metabolites such as lignans,<sup>3-5</sup> neolignans,<sup>6,7</sup> sesquiterpenes,<sup>2,8</sup> and essential oils,<sup>9</sup> which show various biological activities.

To search for more new bioactive compounds from this plant, we reexamined the flower buds of *M. fargesii*, which led to the isolation of three new 8-O-4'-neolignans, named fargesiphenols A-C (**1-3**), along with six known compounds (**4-9**). In addition, the anti-HIV-1 activities and their cytotoxicities were evaluated. Their structure elucidation and biological activities are described in this paper.

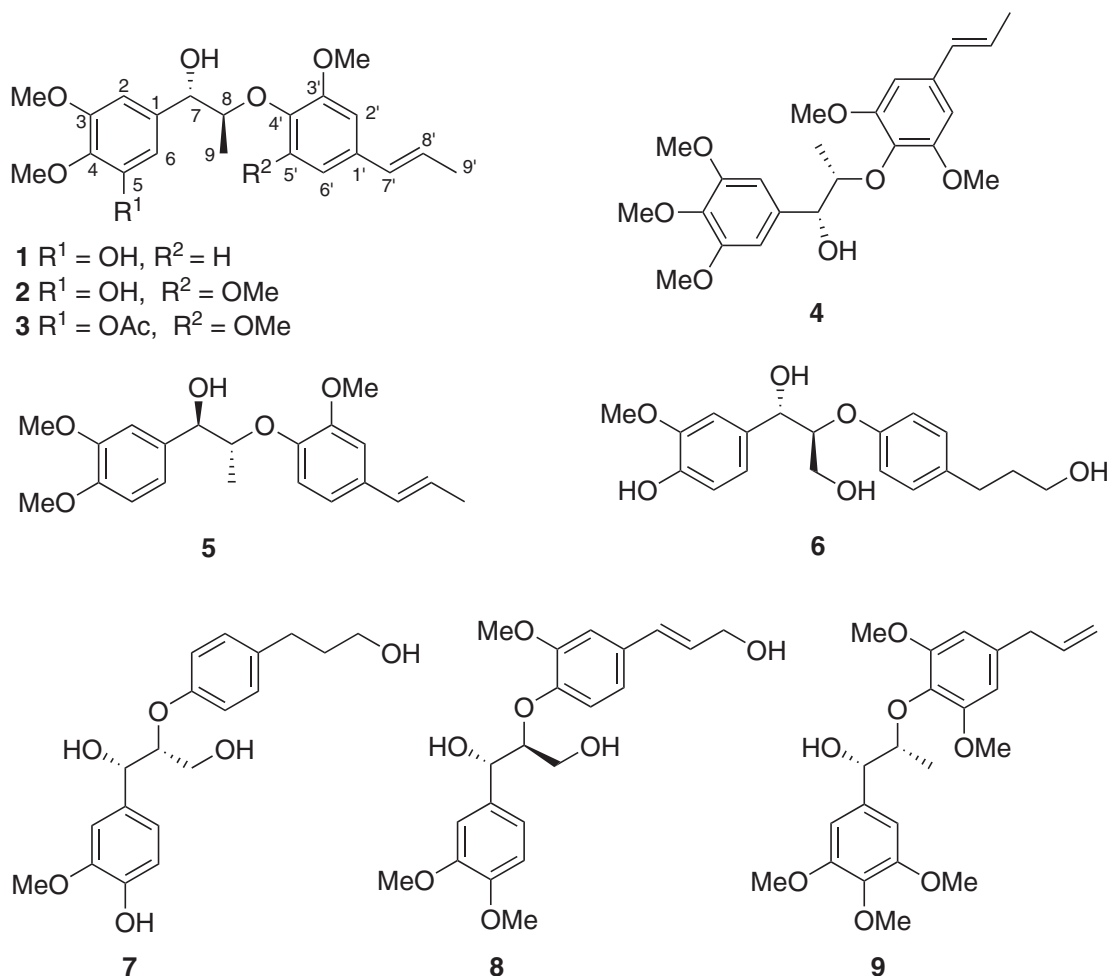
### Results and Discussion

A 70% aq. acetone extract prepared from the flower buds of *M. fargesii* was partitioned between EtOAc and

H<sub>2</sub>O. The EtOAc layer was subjected repeatedly to column chromatography on Si gel, Sephadex LH-20, RP-18 and preparative HPLC to afford compounds **1-9**, including three new 8-O-4'-neolignans named fargesiphenols A-C (**1-3**), together with six known neolignans, polysyphorin (**4**),<sup>10</sup> virolin (**5**),<sup>11</sup> 7*S*,8*S*-*threo*-4,7,9,9'-tetrahydroxy-3,3'-dimethoxy-8-O-4'-neolignan (**6**),<sup>12</sup> 7*S*,8*R*-*erythro*-4,7,9,9'-tetrahydroxy-3,3'-dimethoxy-8-O-4'-neolignan (**7**),<sup>12</sup> (7*R*,8*S*)-1-(3,4-dimethoxyphenyl)-2-[4-(3-hydroxy-1-propenyl)-methoxy-phenoxy]-propane-1,3-diol (**8**),<sup>13</sup> and raphidecursinol A (**9**).<sup>10</sup> The structures of compounds **1-9** are shown in Figure 1, and the <sup>1</sup>H and <sup>13</sup>C NMR data of compounds **1-3** are listed in Table 1.

Compound **1** was obtained as pale yellow gum. Its molecular formula was determined as C<sub>21</sub>H<sub>26</sub>O<sub>6</sub> from the HRESIMS quasi-molecular ion peak [M+Na]<sup>+</sup> at *m/z* 397.1622 (calc. 397.1627). Its <sup>1</sup>H and <sup>13</sup>C NMR spectra showed signals of 26 hydrogens and 21 carbons, respectively, corresponding to two aromatic rings with five aromatic protons ( $\delta_{\text{H}}$  6.99, 7.34, 7.09, 7.15, 6.98), two methyl groups ( $\delta_{\text{C}}$  14.5, 18.4), three methoxyl groups ( $\delta_{\text{C}}$  55.9, 55.9, 60.4), two oxidated methine groups ( $\delta_{\text{C}}$  75.1, 80.9), one allyl group ( $\delta_{\text{C}}$  131.4, 124.1, 18.4;  $\delta_{\text{H}}$  6.38 d *J* 15.8, 6.10-6.17 m, 1.75 d *J* 6.5), and a phenolic hydroxyl group ( $\delta_{\text{H}}$  11.25). Strong absorption bands accounting for hydroxyl (3498 cm<sup>-1</sup>) and aromatic groups

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**Figure 1.** The structures of 8-*O*-4'-neolignans from *Magnolia fargesii*.

(1608, 1520, 1478  $\text{cm}^{-1}$ ) could also be observed in its IR spectrum. The UV spectrum of **1** showed absorption maxima at 285 and 210 nm, which confirmed the existence of the aromatic functions. The  $^1\text{H}$ - $^1\text{H}$  COSY correlations H-7/H-8/H-9, H-7'/H-8'/H-9', together with HMBC correlations (Figure 2) of H-7 ( $\delta_{\text{H}}$  5.38) with C-8 ( $\delta_{\text{C}}$  80.9), C-9 ( $\delta_{\text{C}}$  14.5), C-1 ( $\delta_{\text{C}}$  139.5), C-2 ( $\delta_{\text{C}}$  102.9) and C-6 ( $\delta_{\text{C}}$  109.0), of H-7' ( $\delta_{\text{H}}$  6.38) with C-2' ( $\delta_{\text{C}}$  110.7), C-1' ( $\delta_{\text{C}}$  132.6) and C-6' ( $\delta_{\text{C}}$  119.3), and H-8 ( $\delta_{\text{C}}$  4.88) with C-1 ( $\delta_{\text{C}}$  139.5) and C-4' ( $\delta_{\text{C}}$  147.4), suggested that **1** is a 8-*O*-4'-neolignan possessing three methoxyl groups and a phenolic hydroxyl group.<sup>14</sup>

Three methoxyl groups located at C-3, C-4, C-3' were assigned from the HMBC correlations of the methoxyl proton signals ( $\delta_{\text{H}}$  3.77, 3.88, 3.74) with C-3 ( $\delta_{\text{C}}$  153.9), C-4 ( $\delta_{\text{C}}$  136.7), and C-3' ( $\delta_{\text{C}}$  151.9), respectively. The presence of a phenolic hydroxyl group at C-5 was supported by the HMBC correlations of the phenolic hydroxyl proton signal ( $\delta_{\text{H}}$  11.25) with C-4 ( $\delta_{\text{C}}$  136.7), C-5 ( $\delta_{\text{C}}$  151.9), and C-6 ( $\delta_{\text{C}}$  109.0), respectively. Thus, the plain structure of **1** was established.

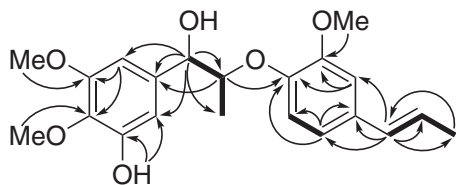
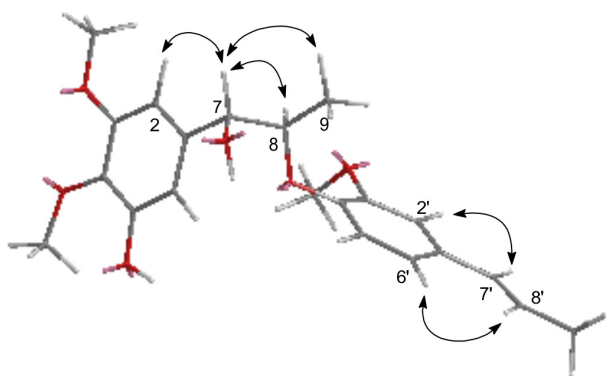
The configuration of the two chiral carbons (C-7 and C-8) was considered to be *threo* according to the coupling constant ( $J_{7,2}$  Hz) between H-7 and H-8,<sup>15</sup> which is distinct from that of the *erythro* diastereoisomers.<sup>16,17</sup> The absolute configurations at C-7 and C-8 of **1** could be established on the basis of ROESY and CD spectroscopic evidence.<sup>18</sup> The CD spectrum of **1** gave a positive cotton effect at 237 nm, and clear ROESY correlations observed between H-7 and H-8, H-7 and H-2, H-7 and H<sub>3</sub>-9 (Figure 3) indicated the 7*S*, 8*S*-configuration of **1**, which was named fargesiphenol A.

Compounds **2** and **3** (fargesiphenols B and C) were all obtained as yellow gums. HRESIMS analysis of **2** demonstrated that it has the molecular formula  $\text{C}_{22}\text{H}_{28}\text{O}_7$  ( $m/z$  427.1730, for  $[\text{M}+\text{Na}]^+$ , calc. 427.1733). The NMR spectra of **2**, when compared to those of **1**, displayed an additional methoxy group ( $\delta_{\text{H}}$  3.85;  $\delta_{\text{C}}$  55.6), which was located at C-5' from the HMBC cross-peak between this carbon ( $\delta_{\text{C}}$  152.3) and the methoxyl protons ( $\delta_{\text{C}}$  3.85).

The NMR spectra of **3**, when compared to those of **2**, displayed the characteristic signals of an acetoxy group ( $\delta_{\text{H}}$  2.19,  $\delta_{\text{C}}$  21.1 and  $\delta_{\text{C}}$  169.9). Its  $^{13}\text{C}$  NMR spectrum

**Table 1.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR Data (in  $\text{C}_5\text{D}_3\text{N}$ ) of compounds **1-3**

position	<b>1</b>		<b>2</b>		<b>3</b>	
	$\delta_{\text{C}}$ (m)	$\delta_{\text{H}}$ (m, <i>J</i> /Hz)	$\delta_{\text{C}}$ (m)	$\delta_{\text{H}}$ (m, <i>J</i> /Hz)	$\delta_{\text{C}}$ (m)	$\delta_{\text{H}}$ (m, <i>J</i> /Hz)
1	139.5 (s)		139.4 (s)		138.5 (s)	
2	102.9 (d)	6.99 (s)	102.8 (d)	6.91 (s)	107.2 (d)	7.03 (s)
3	153.9 (s)		153.5 (s)		152.7 (s)	
4	136.7 (s)		137.0 (s)		142.1 (s)	
5	151.9 (s)		151.2 (s)		144.8 (s)	
6	109.0 (d)	7.34 (s)	108.9 (d)	7.34 (s)	111.4 (d)	7.49 (s)
7	75.1 (d)	5.38 (d, <i>J</i> 7.2)	75.0 (d)	5.35 (d, <i>J</i> 7.2)	75.8 (d)	5.51 (d, <i>J</i> 7.2)
8	80.9 (d)	4.88 (m)	80.9 (d)	4.90 (m)	80.4 (d)	4.97 (m)
9	14.5 (q)	1.55 (d, <i>J</i> 5.9)	14.5 (q)	1.54 (d, <i>J</i> 5.9)	14.8 (q)	1.55 (d, <i>J</i> 5.8)
1'	132.6 (s)		133.3 (s)		133.8 (s)	
2'	110.7 (d)	7.09 (s)	104.2 (d)	6.59 (s)	103.4 (d)	6.56 (s)
3'	151.9 (s)		152.3 (s)		151.2 (s)	
4'	147.4 (s)		136.5 (s)		136.9 (s)	
5'	117.8 (d)	6.98 (d, <i>J</i> 8.2)	152.3 (s)		151.2 (s)	
6'	119.3 (d)	7.15 (d, <i>J</i> 8.2)	104.2 (d)	6.59 (s)	103.4 (d)	6.56 (s)
7'	131.4 (d)	6.38 (d, <i>J</i> 15.8)	131.6 (d)	6.34 (d, <i>J</i> 15.9)	133.1 (d)	6.41 (d, <i>J</i> 16.2)
8'	124.1 (d)	6.10-6.17 (m)	124.2 (d)	6.13-6.16 (m)	124.8 (d)	6.02-6.05 (m)
9'	18.4 (q)	1.75 (d, <i>J</i> 6.5)	18.5 (q)	1.74 (d, <i>J</i> 6.5)	18.7 (q)	1.80 (d, <i>J</i> 6.6)
OMe-3	55.9 (q)	3.77 (s)	55.9 (q)	3.80 (s)	55.9 (q)	3.82 (s)
OMe-4	60.4 (q)	3.88 (s)	60.8 (q)	3.81 (s)	60.9 (q)	3.85 (s)
OMe-2'	55.9 (q)	3.74 (s)	55.6 (q)	3.85 (s)	55.8 (q)	3.95 (s)
OMe-6'			55.6 (q)	3.85 (s)	55.8 (q)	3.95 (s)
-OAc					21.1 (q) 169.9 (s)	2.19 (s)

**Figure 2.** Selected HMBC ( $\text{H} \rightarrow \text{C}$ ) and  $^1\text{H}$ - $^1\text{H}$  COSY ( $\leftrightarrow$ ) correlations of **1**.**Figure 3.** Key ROESY ( $\leftrightarrow$ ) correlations of **1**.

showed downfield-shifted signals for C-4 ( $\delta_{\text{C}}$  142.1) and C-6 ( $\delta_{\text{C}}$  111.4), and an upfield-shifted signal for C-5 ( $\delta_{\text{C}}$  144.8), thus corroborating the placement of the acetoxy group at C-5. According to the observed ROESY

correlations and comparison of  $^1\text{H}$  and  $^{13}\text{C}$  NMR data with those of **1** (Table 1), the relative configurations of **2** and **3** were established as being the same as that of **1**. The configuration of the two chiral carbons (C-7 and C-8) for **2** and **3** was considered to be *threo* according to the coupling constant (*J* 7.2 Hz) between H-7 and H-8, and a positive cotton effect at 237 nm for **2**, and 238 nm for **3** in their CD spectrum indicated a *7S,8S*-configuration.<sup>15</sup>

Since some neolignans are reported to possess anti-HIV activities,<sup>19,20</sup> these have been tested for compounds **1-9**. The cytotoxicity assay against C8166 cells ( $\text{CC}_{50}$ ), and anti-HIV-1 activity were evaluated by the inhibition assay for the cytopathic effects of HIV-1 ( $\text{EC}_{50}$ ), using azidothymidine (AZT) as a positive control ( $\text{EC}_{50} = 0.034 \mu\text{g mL}^{-1}$  and  $\text{CC}_{50} = 200 \mu\text{g mL}^{-1}$ ).<sup>21</sup> The results (Table 2) revealed significant activity for compounds **2**, **6**, **7**, and **8**, with therapeutic index (TI) values above 30. Compounds **1**, **4**, and **9** showed moderate activity with TI values above 10.

Some neolignans are also reported to possess cytotoxic activities,<sup>22,23</sup> which led us to evaluate compounds **1-9** for their cytotoxicities. The cytotoxicity tests were performed in triplicate using a previously reported procedure.<sup>24</sup> In the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, the  $\text{IC}_{50}$  was defined as the concentration of the tested compound resulting in a 50%

**Table 2.** Anti-HIV activities of the compounds **1-9**

Compound	CC <sub>50</sub> /( $\mu\text{g mL}^{-1}$ )	EC <sub>50</sub> /( $\mu\text{g mL}^{-1}$ )	TI <sup>a</sup>
<b>1</b>	63.5	3.62	17.5
<b>2</b>	$\geq 200$	4.86	$\geq 41.2$
<b>3</b>	28.6	3.11	9.20
<b>4</b>	22.6	2.16	10.5
<b>5</b>	61.5	6.87	8.95
<b>6</b>	135.6	3.87	35.0
<b>7</b>	185.4	5.54	33.5
<b>8</b>	$\geq 200$	2.08	$\geq 96.2$
<b>9</b>	87.9	3.09	28.4

<sup>a</sup>TI = EC<sub>50</sub>/CC<sub>50</sub>.

reduction of absorbance compared with untreated cells. The cytotoxic activities against HL-60, Hep-G2, KB, and MDA-MB-231 tumor cell lines by MTT-assay (with camptothecin as the positive control) are shown in Table 3. Compound **2** revealed high cytotoxic activity to HL-60 and MDA-MB-231 cells, whereas compound **8** showed high cytotoxic activity to KB cells, both with IC<sub>50</sub> values close to those of positive control. The other compounds displayed moderate or weak cytotoxic activity.

**Table 3.** Cytotoxicities of compounds **1-9**

Compounds	Cell lines			
	HL-60	HepG2	KB	MDA-MB-231
	IC <sub>50</sub> /( $\mu\text{mol L}^{-1}$ )			
<b>1</b>	12.0	6.08	9.21	6.48
<b>2</b>	1.69	3.50	2.05	2.19
<b>3</b>	10.3	6.50	8.55	7.19
<b>4</b>	5.28	11.4	14.4	6.25
<b>5</b>	7.01	6.42	15.7	6.15
<b>6</b>	11.0	8.58	9.59	8.23
<b>7</b>	8.17	6.29	7.51	10.3
<b>8</b>	16.2	7.50	1.76	4.02
<b>9</b>	12.3	9.23	6.08	18.1
Camptothecin	1.95	0.98	1.69	2.27

For a compound to be deemed effective, an IC<sub>50</sub> value < 100  $\mu\text{mol L}^{-1}$  is required. Camptothecin was used as positive control. HL-60, human acute promyelocytic leukemia; Hep-G2, human hepatocellular carcinoma; KB, human oropharyngeal epidermoid carcinoma; MDA-MB-231, human breast cancer cells.

## Experimental

### General experimental procedures

Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tenor 27

spectrophotometer was used for scanning IR spectra with KBr pellets. CD spectra were measured on a JASCO J-810 spectropolarimeter. 1D and 2D NMR spectra were recorded on DRX-500 spectrometers with TMS as internal standard. HRESIMS was performed on an API QSTAR time-of-flight spectrometer and a VG Autospec-3000 spectrometer, respectively. Preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with a ZORBAX PrepHT GF (21.2 mm  $\times$  25 cm, 7  $\mu\text{m}$ ) column or a Venusil MP C<sub>18</sub> (20 mm  $\times$  25 cm, 5  $\mu\text{m}$ ) column. Column chromatography was performed with Si gel (200-300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40-63  $\mu\text{m}$ , Merck, Darmstadt, Germany) and MCI gel (75-150  $\mu\text{m}$ , Mitsubishi Chemical Corporation, Tokyo, Japan). The fractions were monitored by TLC, and spots were visualized by heating Si gel plates sprayed with 5% H<sub>2</sub>SO<sub>4</sub> in EtOH.

### Plant material

The flower buds of *M. fargesii*, indigenous to Nanzhao country, Henang province, were purchased from Kunming Herb Medicine Market in September 2010. A voucher specimen (YNNI-10-9-28) has been deposited in our laboratory.

### Extraction and isolation

The air-dried and powdered flower buds of *Magnolia fargesii* (4.5 kg) were extracted four times with 70% aqueous acetone (4  $\times$  3 L) at room temperature, filtered, and the filtrate evaporated under reduced pressure and partitioned with EtOAc (4  $\times$  3 L). The EtOAc phase (212 g) was applied to silica gel (200-300 mesh) column chromatography, eluting with a CHCl<sub>3</sub>-MeOH gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give six fractions A-F. Further separation of fraction B (35.8 g) by silica gel column chromatography, eluted with CHCl<sub>3</sub>-acetone (9:1-2:1), yielded mixtures B1-B6. Fraction B2 (8:2, 4.8 g) was subjected to silica gel column chromatography using petroleum ether-acetone, and semi-preparative HPLC (55% MeOH-H<sub>2</sub>O, flow rate 12 mL min<sup>-1</sup>) to give **3** (22.6 mg), **4** (18.9 mg), **5** (22.7 mg) and **9** (28.5 mg). Fraction B3 (7:3, 5.47 g) was subjected to silica gel column chromatography using CHCl<sub>3</sub>-acetone, and semi-preparative HPLC (48% MeOH-H<sub>2</sub>O, flow rate 12 mL min<sup>-1</sup>) to give **1** (11.6 mg) and **2** (28.9 mg). Fraction B4 (7:3, 3.28 g) was subjected to silica gel column chromatography using CHCl<sub>3</sub>-acetone, and semi-preparative HPLC (40% MeOH-H<sub>2</sub>O, flow rate 12 mL min<sup>-1</sup>) to give **3** (14.2 mg), **6** (22.5 mg), and **7** (18.2 mg).

### Anti-HIV-1 assay

The cytotoxicity assay against C8166 cells (CC<sub>50</sub>) was assessed using the MTT method, and anti-HIV-1 activity was evaluated by the inhibition assay for the cytopathic effects of HIV-1 (EC<sub>50</sub>).<sup>21</sup>

### Cytotoxicity assay

The cytotoxicity tests for these compounds were performed against HL-60, Hep-G2, KB, and MDA-MB-231 tumor cell lines by the MTT-assay using camptothecin as positive control.<sup>24</sup>

### Fargesiphenol A (1)

Pale yellow gum;  $[\alpha]_D^{24.2} +38.5$  (*c* 0.20, MeOH); CD (*c* 0.05, MeOH):  $\Delta\epsilon_{220\text{ nm}} +0.36$ ,  $\Delta\epsilon_{237\text{ nm}} +7.18$ ,  $\Delta\epsilon_{280\text{ nm}} -0.97$ ,  $\Delta\epsilon_{320\text{ nm}} -0.21$ ; UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 320 (2.82), 285 (3.78), 210 (4.27) nm; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3498, 2957, 2874, 1608, 1520, 1478, 1440, 1265, 958; <sup>1</sup>H NMR (500 MHz) and <sup>13</sup>C NMR (125 MHz) data, Table 1; positive ESIMS *m/z* 397 [M+Na]<sup>+</sup>; HRESIMS *m/z* 397.1622 [M+Na]<sup>+</sup> (calc. C<sub>21</sub>H<sub>26</sub>NaO<sub>6</sub> for 397.1627).

### Fargesiphenol B (2)

Yellow gum;  $[\alpha]_D^{24.0} +41.2$  (*c* 0.22, MeOH); CD (*c* 0.05, MeOH):  $\Delta\epsilon_{220\text{ nm}} +1.28$ ,  $\Delta\epsilon_{237\text{ nm}} +14.6$ ,  $\Delta\epsilon_{280\text{ nm}} -2.18$ ,  $\Delta\epsilon_{320\text{ nm}} -0.96$ ; UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 320 (2.88), 282 (3.82), 210 (4.23) nm; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3495, 2959, 2873, 1608, 1524, 1486, 1437, 1263, 954; <sup>1</sup>H NMR (500 MHz) and <sup>13</sup>C NMR (125 MHz) data, Table 1; positive ESIMS *m/z* 427 [M+Na]<sup>+</sup>; HRESIMS *m/z* 427.1730 [M+Na]<sup>+</sup> (calc. C<sub>22</sub>H<sub>28</sub>NaO<sub>7</sub> for 427.1733).

### Fargesiphenol C (3)

Yellow gum;  $[\alpha]_D^{24.5} +42.5$  (*c* 0.22, MeOH); CD (*c* 0.05, MeOH):  $\Delta\epsilon_{220\text{ nm}} +0.47$ ,  $\Delta\epsilon_{238\text{ nm}} +6.52$ ,  $\Delta\epsilon_{280\text{ nm}} -0.83$ ,  $\Delta\epsilon_{320\text{ nm}} -0.49$ ; UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 318 (2.89), 280 (3.86), 210 (4.20) nm; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3493, 2950, 2876, 1614, 1529, 1482, 1442, 1260, 959; <sup>1</sup>H NMR (500 MHz) and <sup>13</sup>C NMR (125 MHz) data, Table 1; positive ESIMS *m/z* 469 [M+Na]<sup>+</sup>; HRESIMS *m/z* 469.1833 [M+Na]<sup>+</sup> (calc. C<sub>24</sub>H<sub>30</sub>NaO<sub>8</sub> for 469.1838).

## Supplementary Information

<sup>13</sup>C NMR, DEPT, <sup>1</sup>H NMR, HSQC, HMBC, <sup>1</sup>H-<sup>1</sup>H COSY, ROESY, CD, and HRESIMS spectra of fargesiphenol A; <sup>13</sup>C NMR, DEPT, <sup>1</sup>H NMR, HSQC, HMBC, and CD spectra of fargesiphenol B and C, are available free of charge at <http://jbcs.sbq.org.br> as PDF file.

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# Supplementary Information

## 8-O-4'-Neolignans from Flower Buds of *Magnolia fargesii* and their Biological Activities

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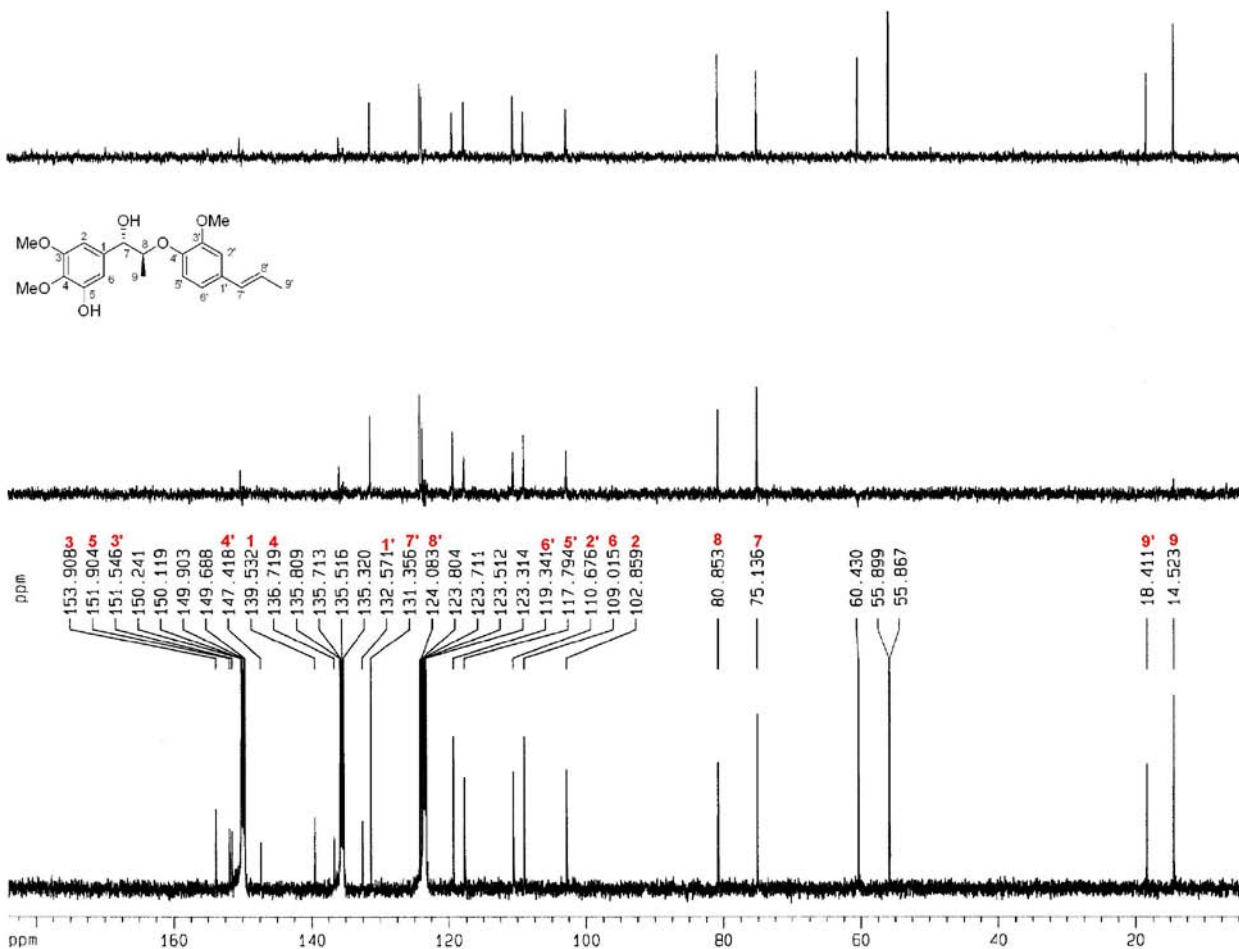


Figure S1. <sup>13</sup>C NMR and DEPT spectra of fargesiphenol A (1).

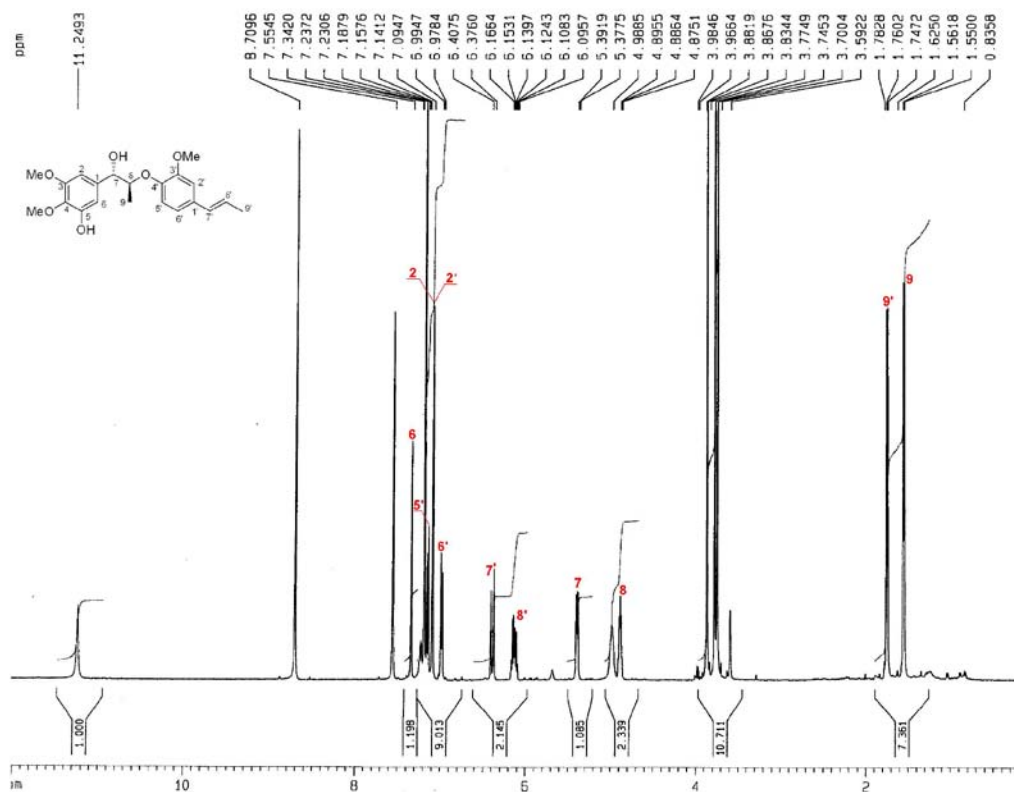
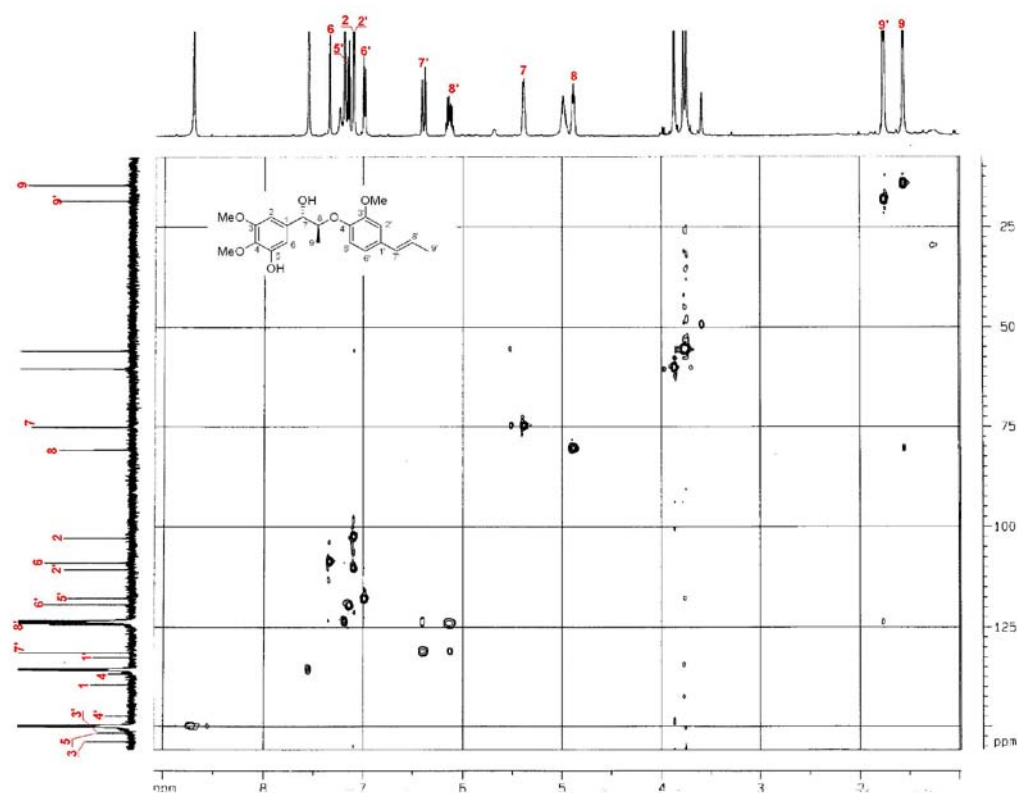
Figure S2.  $^1\text{H}$  NMR spectra of fargesiphenol A (1).

Figure S3. HSQC spectra of fargesiphenol A (1).



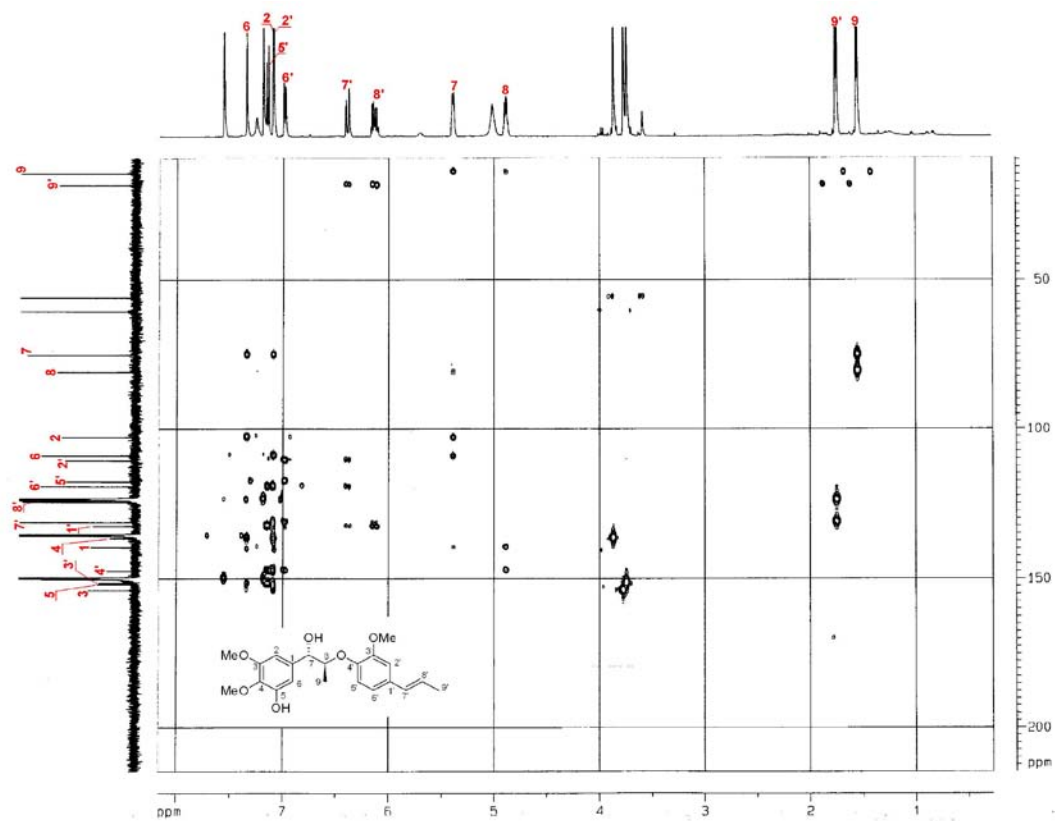


Figure S4. HMBC spectra of fargesiphenol A (1).

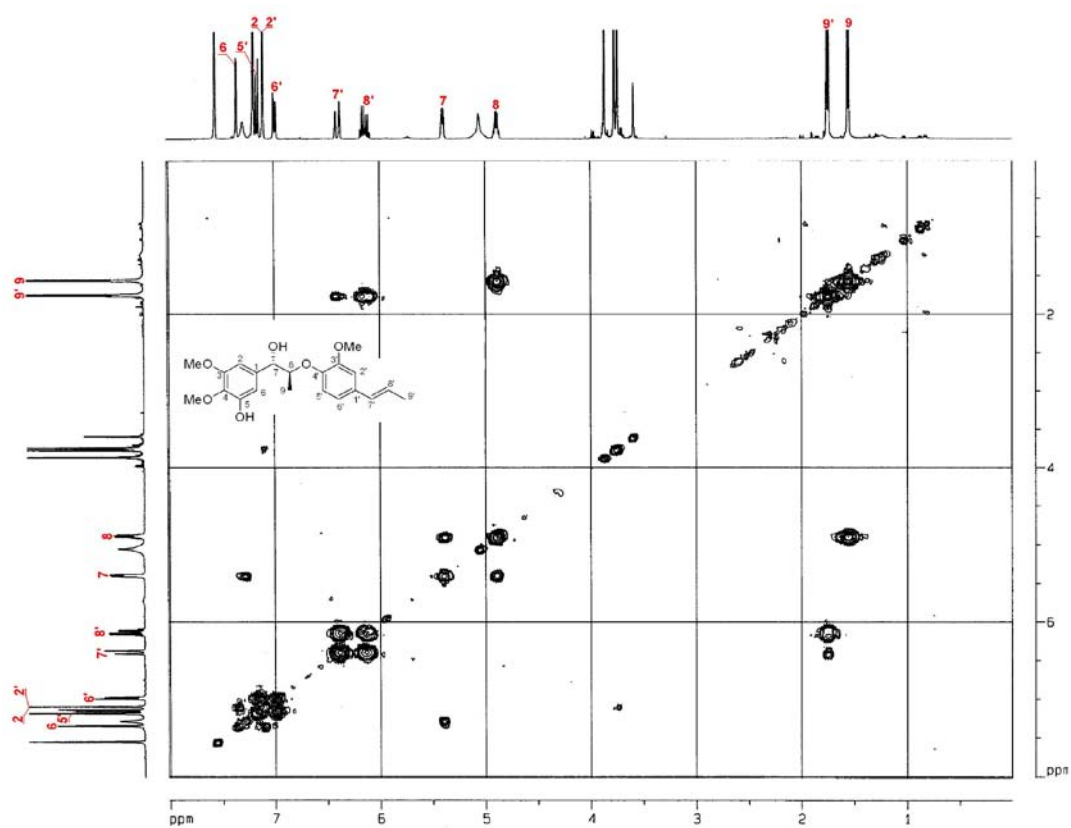


Figure S5.  $^1\text{H}$ - $^1\text{H}$  COSY spectra of fargesiphenol A (1).

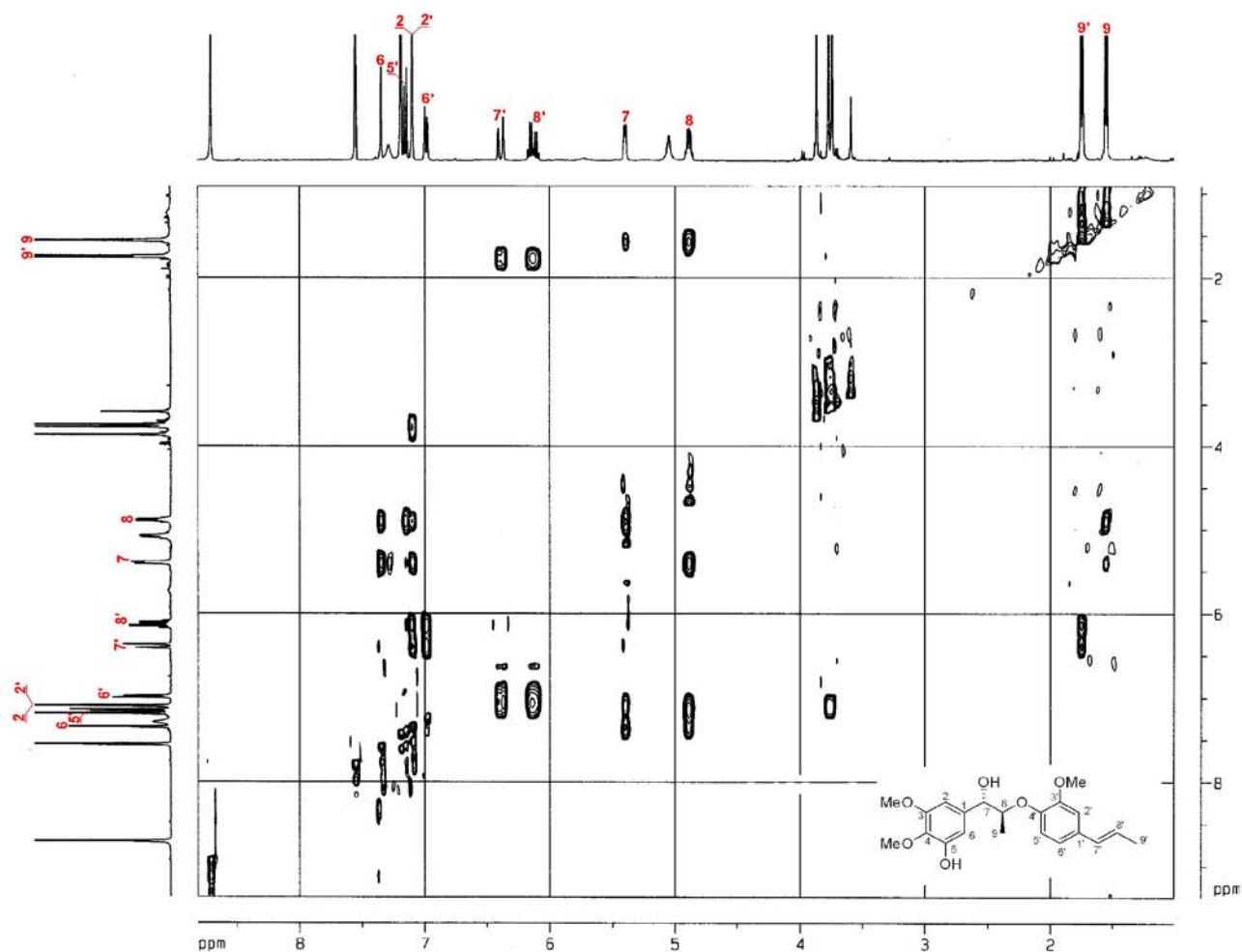


Figure S6. ROESY spectra of fargesiphenol A (1).

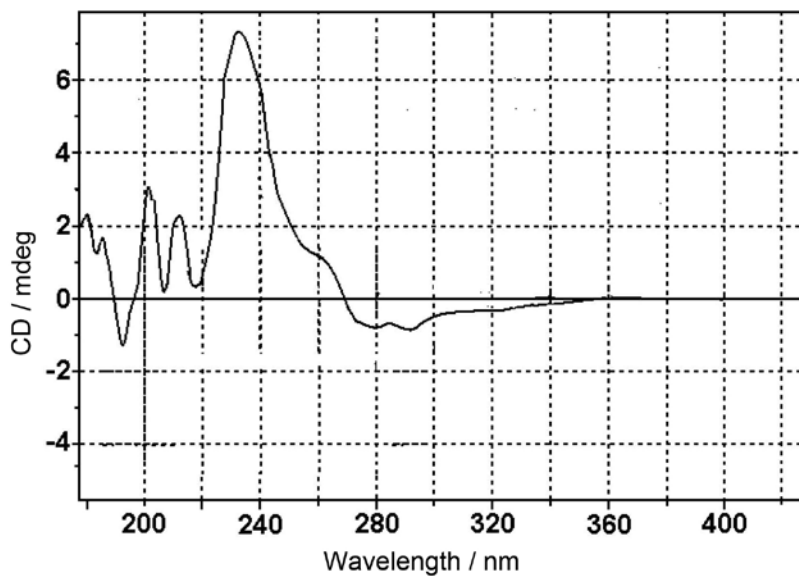


Figure S7. CD spectra of fargesiphenol A (1).

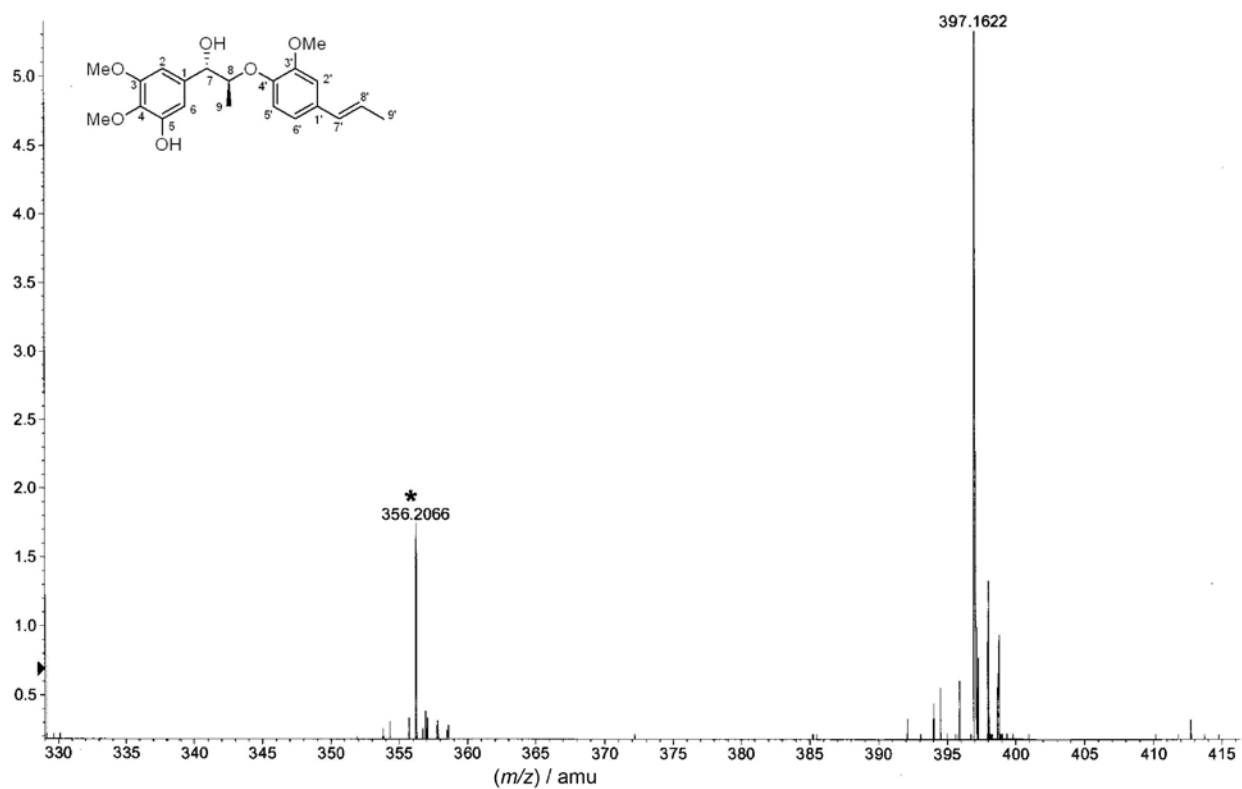
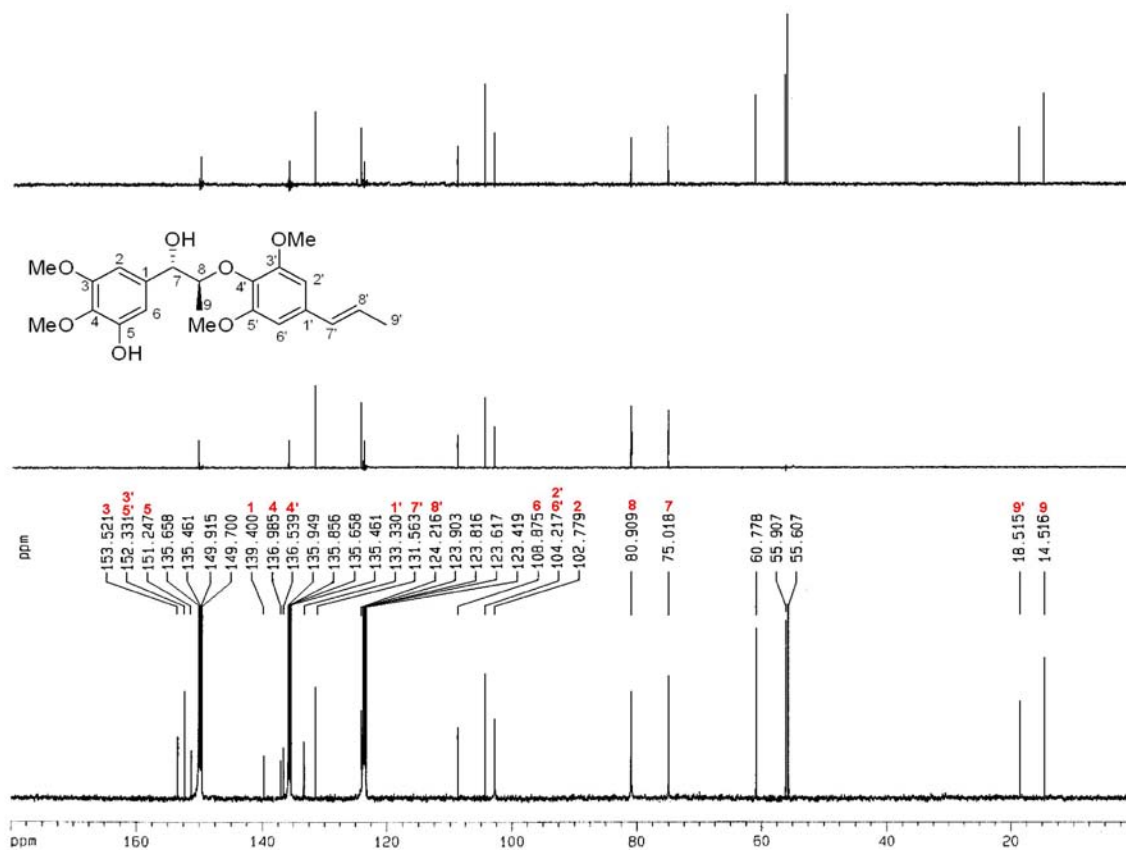


Figure S8. HRESIMS spectra of fargesiphenol A (1).

Figure S9.  $^{13}\text{C}$  NMR and DEPT spectra of fargesiphenol B (2).

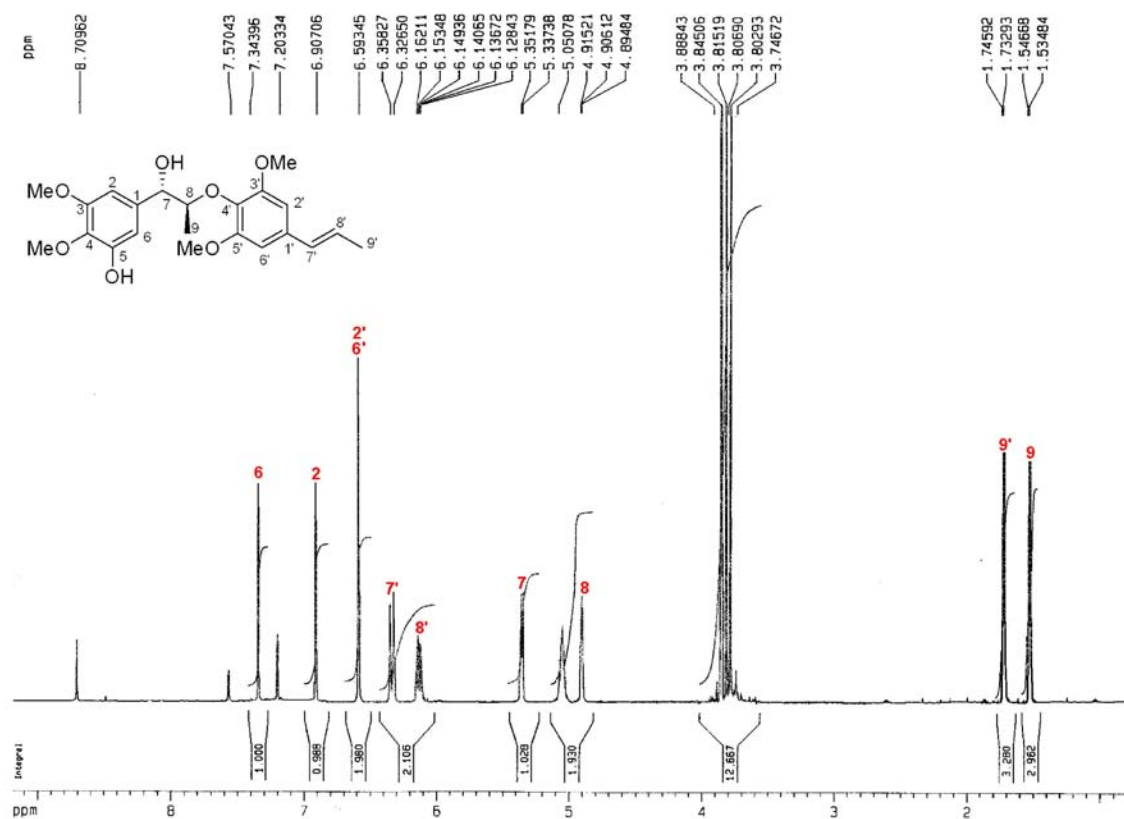
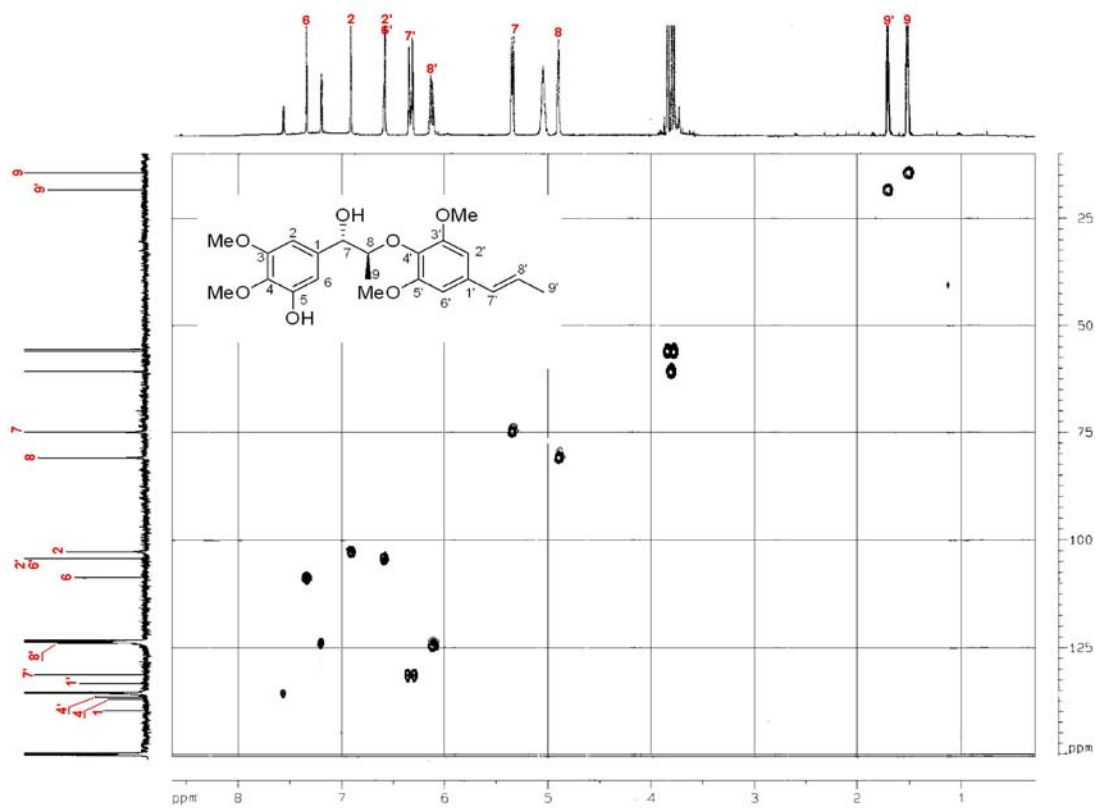
Figure S10.  $^1\text{H NMR}$  spectra of fargesiphenol B (2).

Figure S11. HSQC spectra of fargesiphenol B (2).

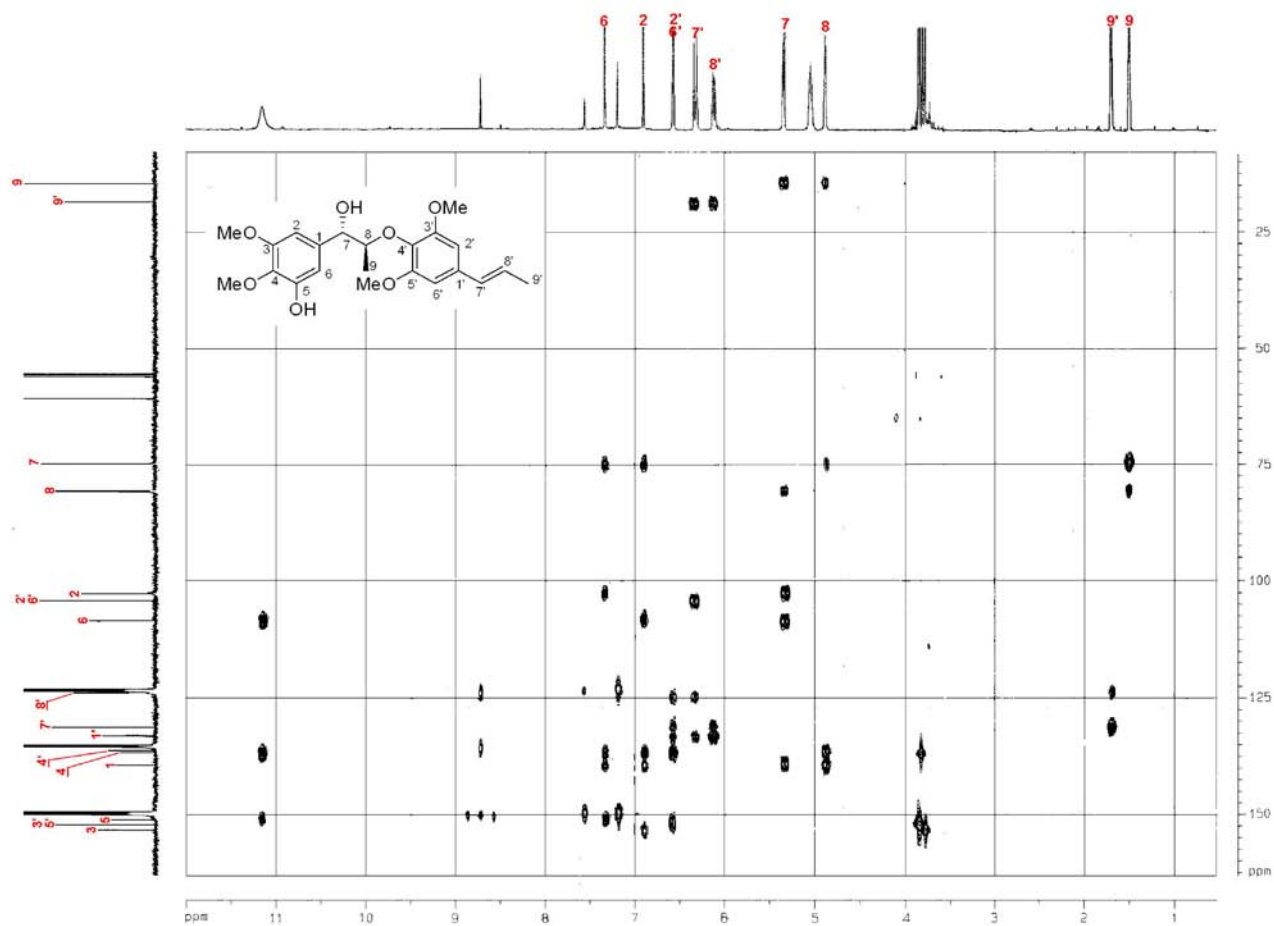


Figure S12. HMBC spectra of fargesiphenol B (2).

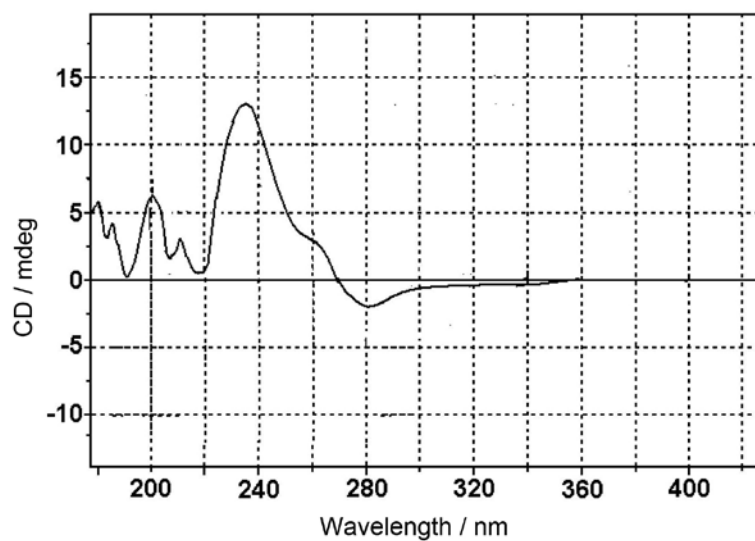


Figure S13. CD spectra of fargesiphenol B (2).

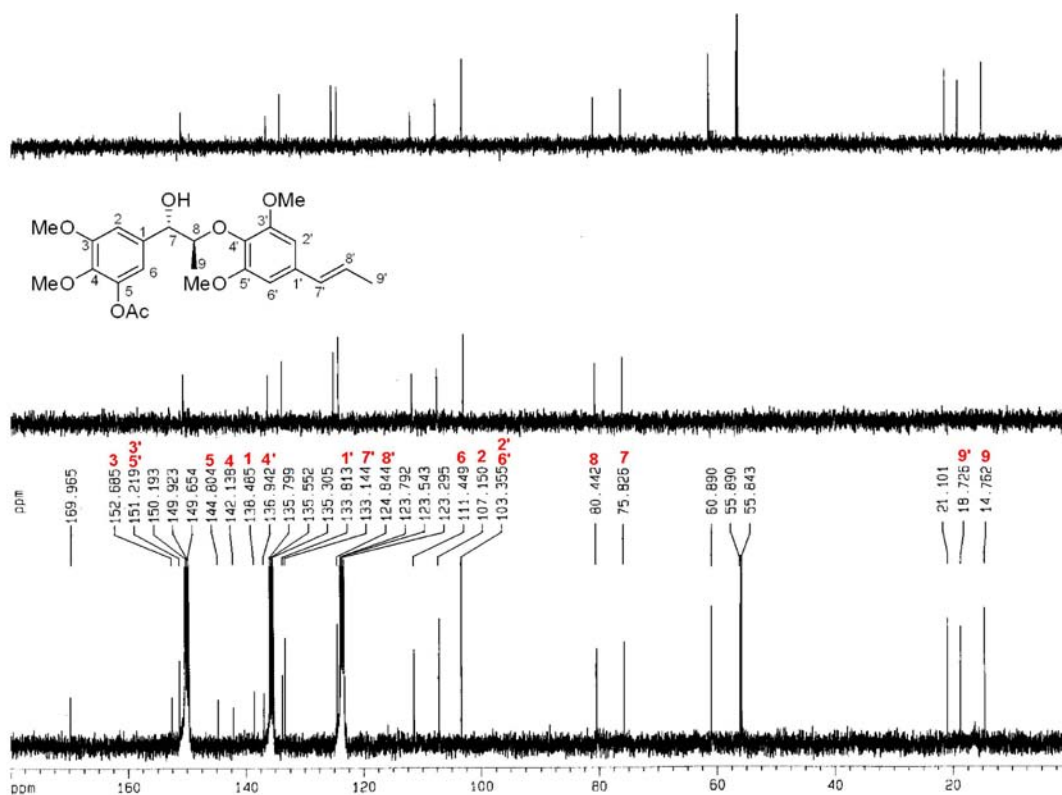


Figure S14.  $^{13}\text{C}$  NMR and DEPT spectra of fargesiphenol C (3).

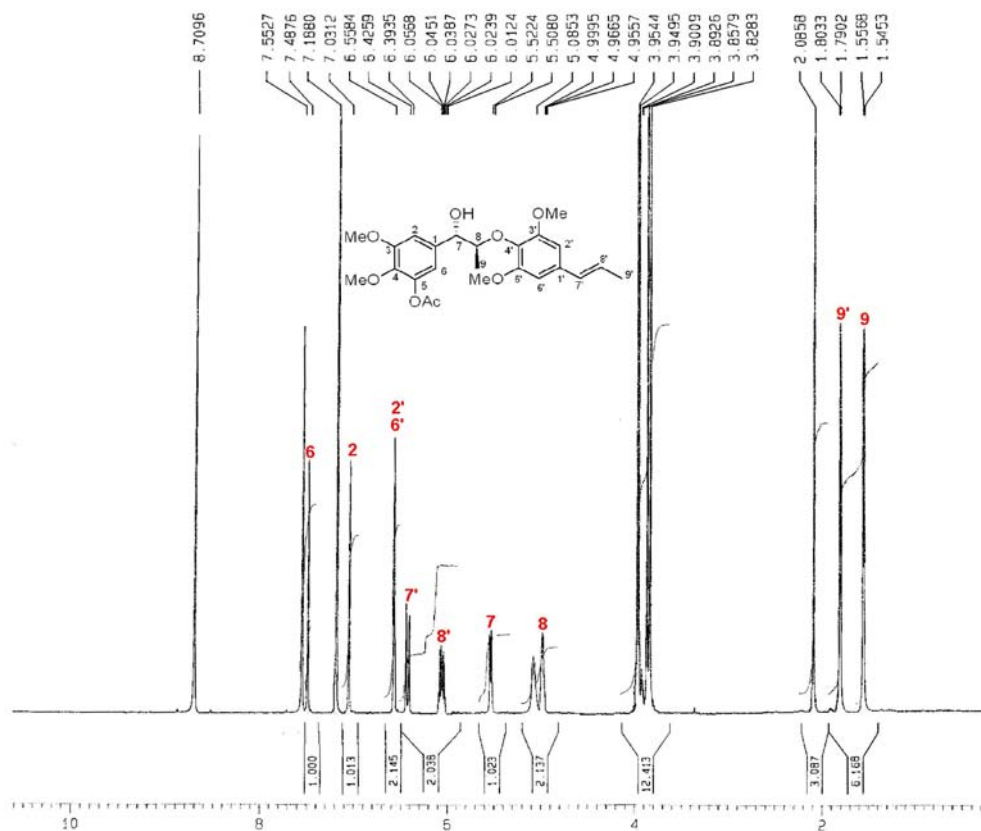


Figure S15.  $^1\text{H}$  NMR spectra of fargesiphenol C (3).

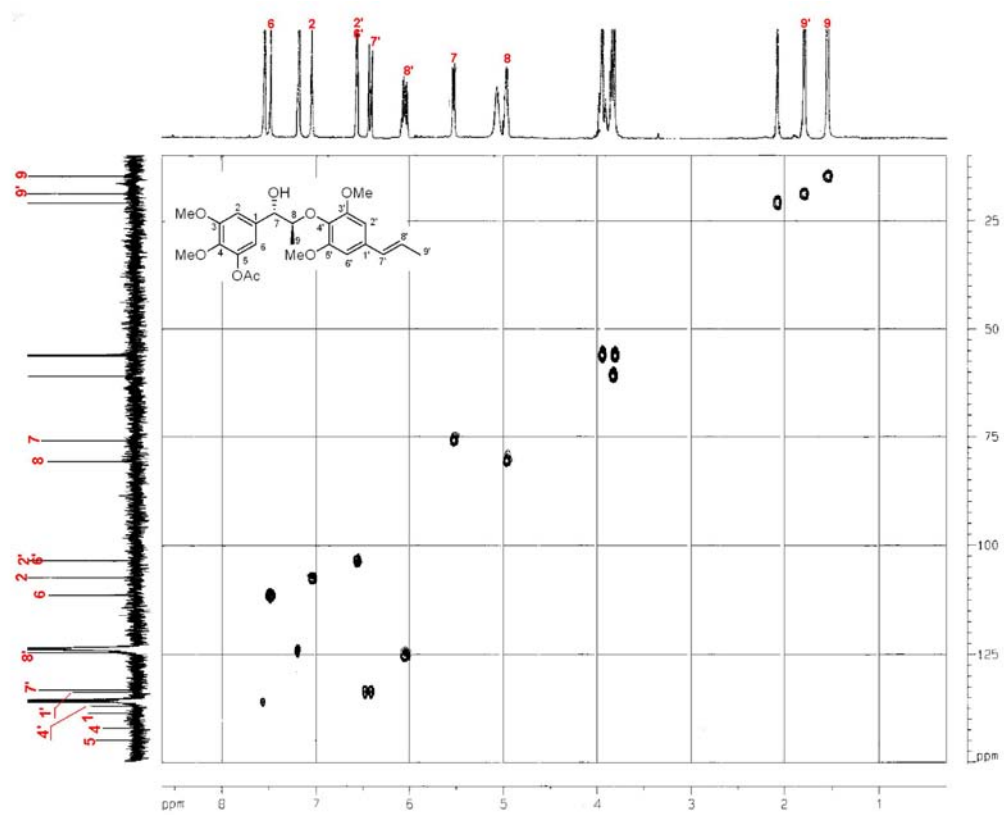


Figure S16. HSQC spectra of fargesiphenol C (3).

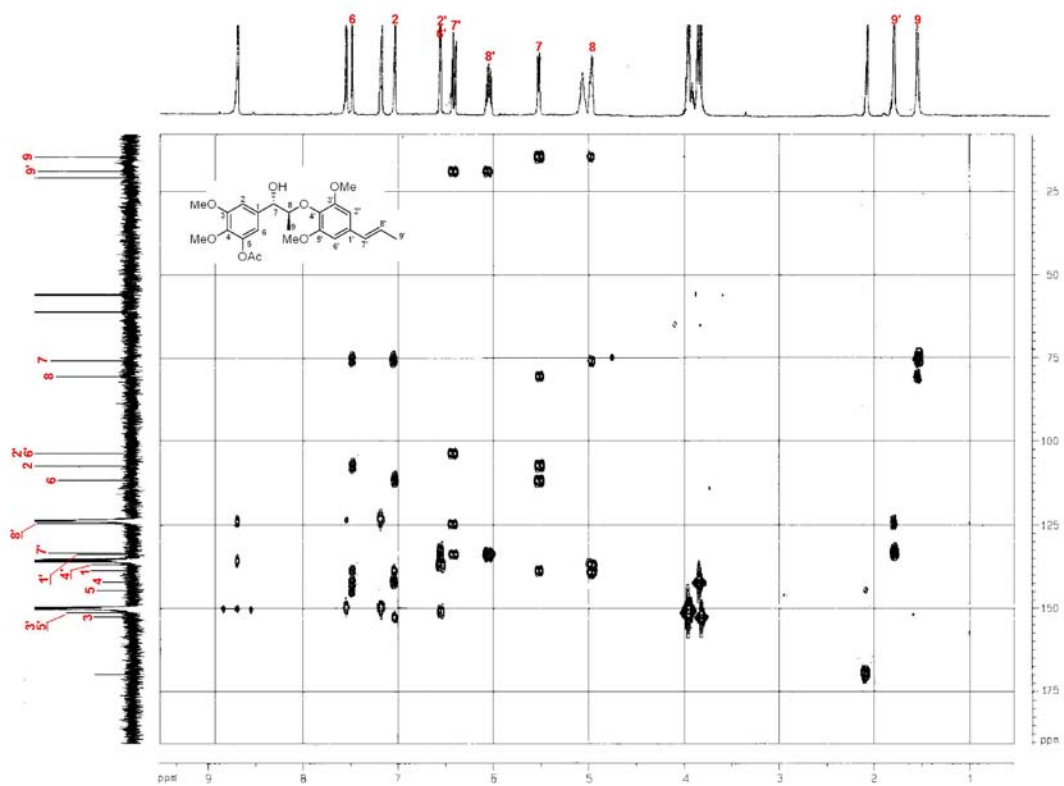
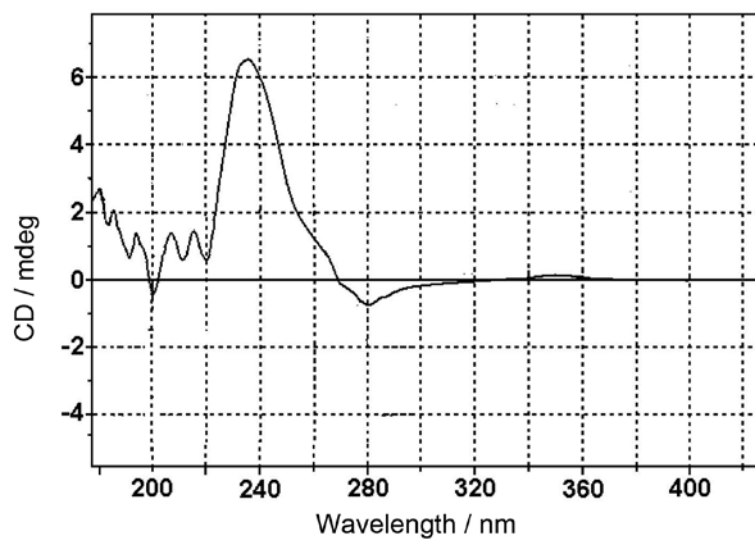


Figure S17. HMBC spectra of fargesiphenol C (3).



**Figure S18.** CD spectra of fargesiphenol C (3).