

## **Supplementary Materials**

# **An Arylbenzofuan, Stilbene Dimers and Prenylated Diels-Alder Adducts as Potent Diabetic Inhibitors from *Morus bombycis* Leaves**

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**Table S1.** Inhibitory activities of subfractions of EtOAc fraction from *Morus bombycina* leaves against peroxynitrite,  $\alpha$ -glucosidase, PTP1B and AGE formation

| Subfractions                 | Peroxynitrite<br><b>IC<sub>50</sub> (μg/mL)<sup>a</sup></b> | $\alpha$ -Glucosidase<br><b>IC<sub>50</sub> (μg/mL)<sup>a</sup></b> | PTP1B<br><b>IC<sub>50</sub> (μg/mL)<sup>a</sup></b> | BSA-AGES<br><b>IC<sub>50</sub> (μg/mL)<sup>a</sup></b> |
|------------------------------|---|---|---|--|
| E2                           | 1.23 ± 0.01   | 249.58 ± 18.53  | 56.93 ± 4.46  | 6.12 ± 0.29  |
| E3                           | < 0.032   | 10.22 ± 2.29  | 25.11 ± 4.46  | 14.65 ± 1.50   |
| E4                           | 0.13 ± 0.02   | 5.11 ± 1.87   | 14.28 ± 5.46  | 4.19 ± 0.37  |
| E6                           | 0.34 ± 0.01   | 1.30 ± 0.08   | 4.65 ± 0.56   | 3.58 ± 0.24  |
| E8                           | 1.04 ± 0.09   | 0.77 ± 0.03   | 4.86 ± 1.40   | 4.60 ± 0.05  |
| L-Penicillamine <sup>b</sup> | 0.67 ± 0.01   |   | 5.60 ± 0.77   |  |
| Acarbose <sup>b</sup>        |   | 224.27 ± 4.82   |   |  |
| Ursolic acid <sup>b</sup>    |   |   | 6.39 ± 0.42   |  |
| Aminoguanidine <sup>b</sup>  |   |   |   | 36.73 ± 1.64   |

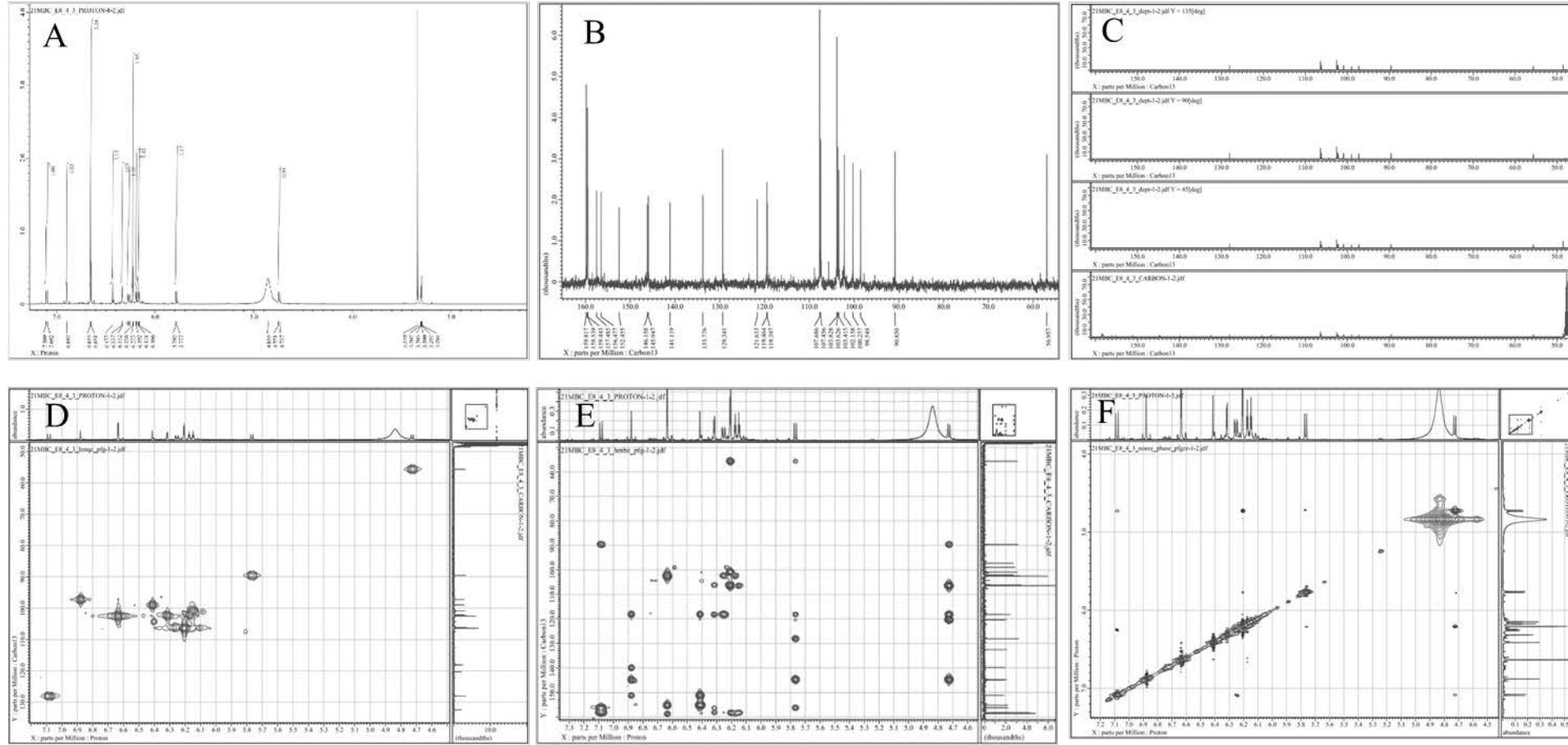
<sup>a</sup>The values are expressed as the mean ± SD of triplicate experiments. <sup>b</sup>Positive control was used in each assay

**Table S2. The 1D NMR data of compounds **4** and **6****

| Position | Macrourin B ( <b>4</b> )                   |       | Position | Austrafuran C ( <b>6</b> )                   |       |
|----------|--|-------|----------|--|-------|
|          | H  | C     |          | H  | C     |
| 2        |  | 156.5 | 2        |  | 157.3 |
| 3        | 6.43 (br s, $J=0.15\text{Hz}$ )            | 100.3 | 3        | 6.90 (1H, s)                                 | 102.1 |
| 3a       |  | 119.4 | 3a       |  | 124.1 |
| 4        |  | 121.6 | 4        | 7.07 (1H, s)                                 | 107.8 |
| 5        |  | 133.8 | 5        |  | 142.9 |
| 6        |  | 141.1 | 6        |  | 143.9 |
| 7        | 6.90 (s)                                   | 98.5  | 7        | 7.09 (1H, s)                                 | 99.8  |
| 7a       |  | 152.5 | 7a       |  | 151.2 |
| 8        |  | 146.2 | 1'       |  | 133.7 |
| 9        | 6.65 (d, $J=2\text{Hz}$ )                  | 103.8 | 2'       | 6.77 (d, $J=2.5\text{ Hz}$ )                 | 104   |
| 10       |  | 159.8 | 3'       |  | 160   |
| 11       | 6.19 (t, $J=3.2\text{Hz}$ )                | 103.4 | 4'       | 6.25 (t, $J=2.3\text{ Hz}$ )                 | 103.7 |
| 12       |  | 159.8 | 5'       |  | 160   |
| 13       | 6.65 (d, $J=2\text{Hz}$ )                  | 103.8 | 6'       | 6.78 (d, $J=2.5\text{ Hz}$ )                 | 104   |
| 1'       |  | 119.5 | 1"       |  | 116   |
| 2'       |  | 157.5 | 2"       |  | 157.7 |
| 3'       | 6.33 (d, $J=2.5\text{Hz}$ )                | 103.6 | 3"       | 6.18 (d, $J=2.3\text{ Hz}$ )                 | 103.4 |
| 4'       |  | 159.4 | 4"       |  | 159.7 |
| 5'       | 6.27 (dd, $J=8.4\text{Hz}, 2.3\text{Hz}$ ) | 107.5 | 5"       | 6.27 (dd, $J=8.4\text{ Hz}, 2.3\text{ Hz}$ ) | 108   |
| 6'       | 7.10 (d, $J=8.5\text{Hz}$ )                | 129.3 | 6"       | 7.04 (d, $J=8.5\text{ Hz}$ )                 | 131   |
| 7'       | 5.78 (d, $J=7.5\text{Hz}$ )                | 90.9  | 7"       | 5.23 (d, $J=8\text{Hz}$ )                    | 76.3  |
| 8'       | 4.74 (d, $J=7\text{Hz}$ )                  | 57    | 8"       | 5.07 (d, $J=7.6\text{Hz}$ )                  | 81    |
| 9'       |  | 145.9 | 9"       |  | 140.5 |
| 10'      | 6.23 (d, $J=2.5\text{Hz}$ )                | 107.7 | 10"      | 6.22 (d, $J=2.3\text{Hz}$ )                  | 107.5 |
| 11'      |  | 159.5 | 11"      |  | 159   |
| 12'      | 6.17 (t, $J=4.6\text{Hz}$ )                | 102.2 | 12"      | 6.13 (t, $J=2.3\text{ Hz}$ )                 | 103.4 |
| 13'      |  | 159.5 | 13"      |  | 159   |
| 14'      | 6.23 (d, $J=2.5\text{Hz}$ )                | 107.7 | 14"      | 6.22 (d, $J=2.3\text{Hz}$ )                  | 107.5 |

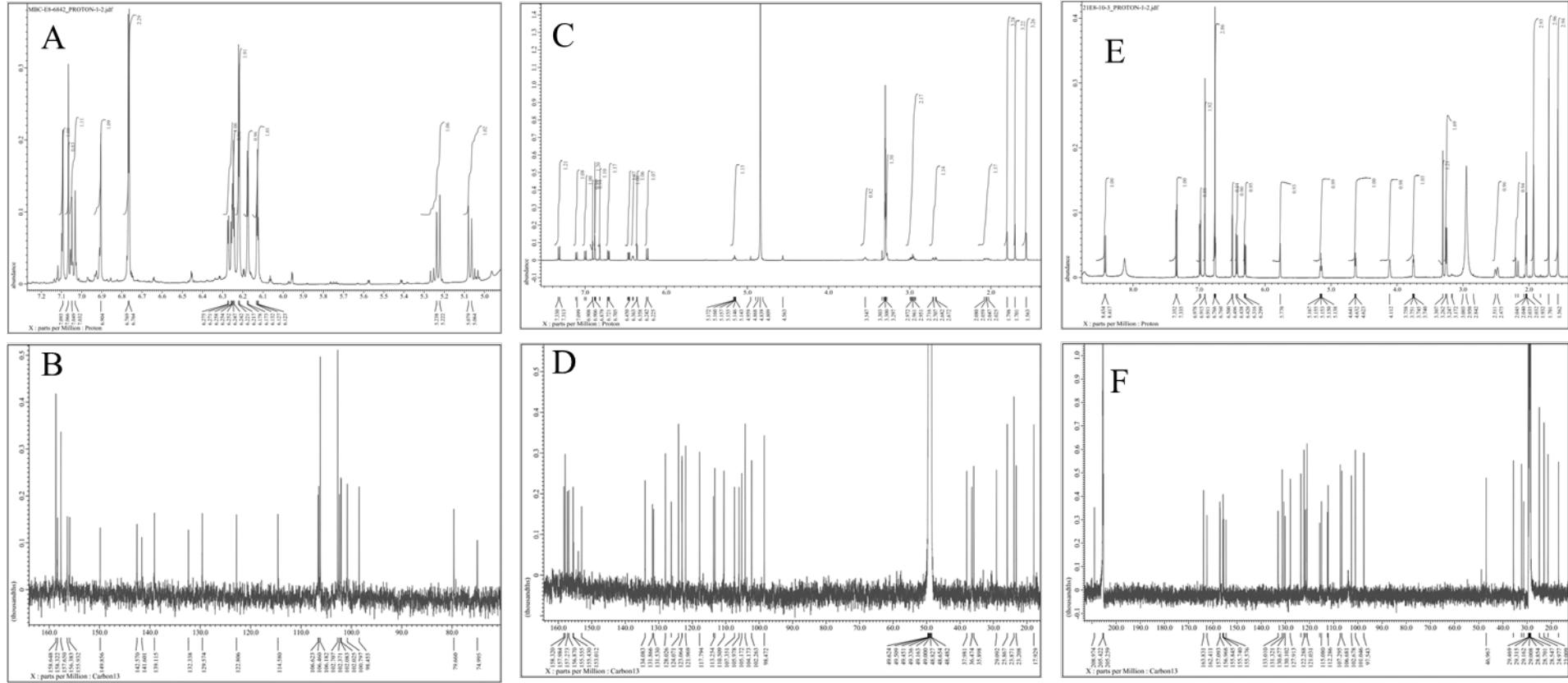
**Table S3. The 1D NMR data of compounds 7 and 8**

| Position | Mulberrofuran F (7)           |       | Position | Chalcomoracin (8)                     |       |
|----------|-------------------------------|-------|----------|---------------------------------------|-------|
|          | H                             | C     |          | H                                     | C     |
| 2        |                               | 155.4 | 2        |                                       | 156.4 |
| 3        | 6.91 (d, <i>J</i> =1Hz)       | 102.3 | 3        | 6.91 (d, <i>J</i> = 2Hz, overlapping) | 101.8 |
| 3a       |                               | 123.1 | 3a       |                                       | 122.6 |
| 4        | 7.32 (d, <i>J</i> =8.5Hz)     | 122   | 4        | 7.34 (d, <i>J</i> =8.5Hz)             | 121.8 |
| 5        | 6.71 (dd, <i>J</i> =8Hz)      | 113.7 | 5        | 6.76 (m, overlapping)                 | 113.1 |
| 6        |                               | 156.9 | 6        |                                       | 157.8 |
| 7        | 6.88 (d, <i>J</i> =1.7Hz)     | 98.5  | 7        | 6.91 (d, <i>J</i> = 2Hz, overlapping) | 98.3  |
| 7a       |                               | 156.9 | 7a       |                                       | 155.4 |
| 1'       |                               | 131.5 | 1'       |                                       | 130.9 |
| 2'       | 6.87 (d, <i>J</i> =3.4Hz)     | 106   | 2'       | 6.76 (m, overlapping)                 | 104.8 |
| 3'       |                               | 154   | 3'       |                                       | 156.5 |
| 4'       |                               | 113.3 | 4'       |                                       | 115.9 |
| 5'       |                               | 158.3 | 5'       |                                       | 156.5 |
| 6'       | (m, solvent overlapping)      | 105.2 | 6'       | 6.76 (m, overlapping)                 | 104.9 |
| 1"       |                               | 134.1 | 1"       |                                       | 133.8 |
| 2"       | 6.41 (br d, <i>J</i> =5.5Hz)  | 123   | 2"       | 5.77 (br s)                           | 124.3 |
| 3"       | (m, solvent overlapping)      | 35.9  | 3"       | 4.11 (br s)                           | 33.1  |
| 4"       | (m, solvent overlapping)      | 38    | 4"       | 4.63 (t, <i>J</i> =4.20 Hz)           | 47.8  |
| 5"       | (m, solvent overlapping)      | 29.1  | 5"       | 3.75 (t, <i>J</i> =5.7 Hz)            | 36.5  |
| 6"       | 2.69 (dd, <i>J</i> =15Hz)     | 36.5  | 6"       | 2.18 (d, <i>J</i> =18.5Hz)            | 32.2  |
| 6b"      | 2.06 (dd, <i>J</i> =15Hz)     |       | 6b"      | 2.50 (d, <i>J</i> =18Hz)              | 32.2  |
| 7"       | 1.73 (s)                      | 23.9  | 7"       | 1.93 (br s)                           | 23.8  |
| 8"       |                               | 104.2 | 8"       |                                       | 209.8 |
| 9"       |                               | ND    | 9"       |                                       | 113.4 |
| 10"      |                               | 155.6 | 10"      |                                       | 164.6 |
| 11"      |                               | 117.8 | 11"      |                                       | 116.6 |
| 12"      |                               | 157.3 | 12"      |                                       | 164.2 |
| 13"      | 6.23 (d, <i>J</i> =8.5Hz)     | 107.4 | 13"      | 6.43 (d, <i>J</i> =9Hz)               | 108.1 |
| 14"      | 7.11 (d, <i>J</i> =8.5Hz)     | 128   | 14"      | 8.43 (d, <i>J</i> =8.5Hz)             | 132.1 |
| 15"      |                               | 117.8 | 15"      |                                       | 121.9 |
| 16"      |                               | 157.3 | 16"      |                                       | 156.6 |
| 17"      | 6.36 (1H, d, <i>J</i> =2.5Hz) | 104.2 | 17"      | 6.50 (d, <i>J</i> =2Hz)               | 103.5 |
| 18"      |                               | 157   | 18"      |                                       | 157.9 |
| 19"      | 6.46 (dd, <i>J</i> =8.5Hz)    | 110.5 | 19"      | 6.30 (dd, <i>J</i> =8.4Hz, 2.3Hz)     | 107.5 |
| 20"      | 7.00 (d, <i>J</i> =9Hz)       | 126.3 | 20"      | 7.00 (d, <i>J</i> =8Hz)               | 128.7 |
| 21"      | 2.99-2.95 (m)                 | 23.2  | 21"      | 3.25 (d, <i>J</i> =7.5Hz)             | 22.2  |
| 22"      | 5.16 (m)                      | 124.1 | 22"      | 5.14 (t, <i>J</i> =7.25Hz)            | 123.1 |
| 23"      |                               | 131.9 | 23"      |                                       | 131.5 |
| 24"      | 1.80 (s)                      | 25.9  | 24"      | 1.70 (s)                              | 25.8  |
| 25"      | 1.56 (s)                      | 17.9  | 25"      | 1.56 (s)                              | 17.8  |



**Figure S1. The NMR chromatograms of compounds 4**

A:  $^1\text{H}$  NMR; B:  $^{13}\text{C}$  NMR; C: DEPT; D: HMQC; E: HMBC; F: NOESY (dissolved in  $\text{MeOH}-d_4$ )



**Figure S2. The NMR chromatograms of compounds 6, 7, and 8**

A:  $^1\text{H}$  NMR of compound 6; B:  $^{13}\text{C}$  NMR of compound 6; C:  $^1\text{H}$  NMR of compound 7; D:  $^{13}\text{C}$  NMR of compound 7; E:  $^1\text{H}$  NMR of compound 8; F:  $^{13}\text{C}$  NMR of compound 8; (dissolved in MeOH-*d*<sub>4</sub> and Acetone-*d*<sub>6</sub>)

**Table S4. The 1D NMR data of compounds 1- 3**

|  |
|--|
| <i>p</i> -Coumaric acid ( <b>1</b> )   |
| <sup>1</sup> H NMR: (500 MHz, MeOH- <i>d</i> <sub>4</sub> ) δ <sub>H</sub> 7.52 (d, <i>J</i> = 16Hz, 1H, H-7), 7.41 (d, <i>J</i> = 8.5Hz, 2H, H-2, 6), 6.77 (d, <i>J</i> = 8.5Hz, 2H, H-3, 5), 6.29 (d, <i>J</i> = 16Hz, 1H, H-8); <sup>13</sup> C NMR: (125 MHz, MeOH- <i>d</i> <sub>4</sub> ) δ <sub>C</sub> 172.5 (C-9), 160.7 (C-4), 145.2 (C-7), 130.8 (C-2, 6), 127.2 (C-1), 117.6 (C-8), 116.7 (C-3, 5).  |
| Chlorogenic acid methyl ester ( <b>2</b> )   |
| <sup>1</sup> H NMR: (500 MHz, MeOH- <i>d</i> <sub>4</sub> ) δ <sub>H</sub> 7.51 (d, <i>J</i> = 15.5Hz, 1H, H-7'), 7.03 (d, <i>J</i> =1.9Hz, 1H, H-2'), 6.94 (dd, <i>J</i> = 10.3Hz, 1H, H-6'), 6.77 (d, <i>J</i> = 8Hz, 1H, H-5'), 6.21 (d, <i>J</i> = 16Hz, 1H, H-8'), 5.27 (dd, <i>J</i> = 11.3Hz, 1H, H-3), 4.12 (br d, 1H, H-5), 3.72 (dd, <i>J</i> = 7.6Hz, 1H, H-4), 3.68 (s, 3H, COOCH <sub>3</sub> ), 2.20 (dd, <i>J</i> = 13.5Hz, 1H, H-2a), 2.16 (m, 2H, H-2b, 6a), 2.00 (br d, <i>J</i> = 13.5Hz, 1H, H-6b); <sup>13</sup> C NMR: (125 MHz, MeOH- <i>d</i> <sub>4</sub> ) δ <sub>C</sub> 174.1 (C-7), 167 (C-9'), 148.4 (C-4'), 145.9 (C-7'), 145.5 (C-3'), 126.3 (C-1'), 121.6 (C-6'), 115.2 (C-5'), 113.8 (C-2'), 113.7 (C-8'), 74.5 (C-1), 71.2 (C-4), 70.8 (C-3), 69 (C-5), 51.6 (OCH <sub>3</sub> ), 36.7 (C-6a, 6b), 36.4 (C-2a, 2b). |
| Oxyresveratrol ( <b>3</b> )  |
| <sup>1</sup> H NMR (500 MHz, MeOH- <i>d</i> <sub>4</sub> ) δ <sub>H</sub> 7.32 (d, <i>J</i> = 9Hz, 1H, H-6), 7.26 (d, <i>J</i> = 16Hz, 1H, H-β), 6.80 (d, <i>J</i> = 16.5Hz, 1H, H-α), 6.44 (d, <i>J</i> = 2Hz, 2H, H-2', 6'), 6.31-6.29 (m, 2H, H-3, 5), 6.13 (t, <i>J</i> = 2Hz, 1H, H-4'); <sup>13</sup> C NMR: (125 MHz, MeOH- <i>d</i> <sub>4</sub> ) δ <sub>C</sub> 158.2 (C-5', 3'), 157.9 (C-4), 156 (C-2), 140.9 (C-1') 127.1 (C-6), 125.3 (C-β), 123.6 (C-α), 116.5 (C-1), 107.1 (C-5), 104.3 (C-2', 6'), 102.2 (C-3), 101 (C-4').   |