

## Identification of Three New Flavonoids from the Peels of *Citrus unshiu*

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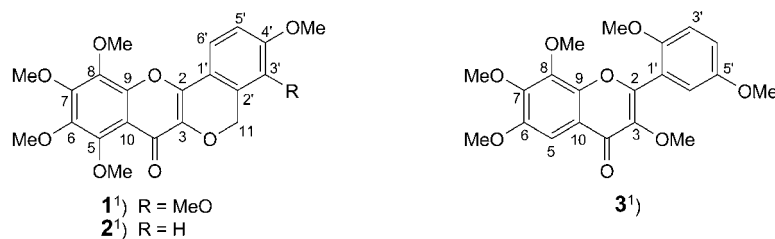
Three new flavonoids, 5,6,7,8,3',4'-hexamethoxyhomoflavone (**1**), 5,6,7,8,4'-pentamethoxyhomoflavone (**2**) and 3,6,7,8,2',5'-hexamethoxyflavone (**3**) were isolated from the peels of mature fruits of *Citrus unshiu* MARCOW (Rutaceae), together with the three known compounds 6,7,8,4'-tetramethoxyflavone (=6,7,8-trimethoxy-2-(4-methoxyphenyl)-4*H*-1-benzopyran-4-one), 3,5,7,8,2',5'-hexamethoxyflavone (=2-(2,5-dimethoxyphenyl)-3,5,7,8-tetramethoxy-4*H*-1-benzopyran-4-one), and scopoletin (=7-hydroxy-6-methoxy-2*H*-1-benzopyran-2-one) of which the former two have never been isolated from natural resources, although they have been reported as synthetic compounds. The structures of **1–3** were elucidated on the basis of spectroscopic evidence, including 1D- and 2D-NMR analysis.

**Introduction.** – *Citrus unshiu* MARCOW belongs to the family Rutaceae, which is cultivated throughout Korea, Japan, and China [1]. The peels of mature fruits of *C. unshiu* have been used in traditional Chinese medicine for treating the common cold and cancer, and relieving exhaustion [2]. Many natural products such as flavonoids and limonoids have been isolated from *C. unshiu* [3]. Some of these isolates have been reported to exhibit anti-allergic [4], anti-obesity [5], and antioxidant [6] effects.

As a part of our research program to find new bioactive compounds from medicinal plants in the Rutaceae family [7], the dried peels of mature fruits of *C. unshiu* were chosen for more detailed investigation of their chemical constituents. Repeated chromatography of the AcOEt-soluble part of a MeOH extract of *C. unshiu* led to the isolation of three new flavonoids, 5,6,7,8,3',4'-hexamethoxyhomoflavone (**1**)<sup>1</sup>, 5,6,7,8,4'-pentamethoxyhomoflavone (**2**)<sup>1</sup>, and 3,6,7,8,2',5'-hexamethoxyflavone (**3**)<sup>1</sup>, together with two new natural compounds, 6,7,8,4'-tetramethoxyflavone (=6,7,8-trimethoxy-2-(4-methoxyphenyl)-4*H*-1-benzopyran-4-one) and 3,5,7,8,2',5'-hexamethoxyflavone (=2-(2,5-dimethoxyphenyl)-3,5,7,8-tetramethoxy-4-*H*-1-benzopyran-4-one). A known compound, scopoletin (=7-hydroxy-6-methoxy-2*H*-1-benzopyran-2-one), was also identified in this plant for the first time. In this article, we describe the structural elucidation of the new compounds **1–3** (Fig. 1).

**Results and Discussion.** – Compound **1** was obtained as a yellow amorphous powder. The molecular formula of **1** was deduced to be C<sub>22</sub>H<sub>22</sub>O<sub>9</sub> by HR-ESI-MS, which exhibited a molecular-ion peak at *m/z* 430.1269 (*M*<sup>+</sup>). The IR spectrum of **1** showed a conjugated C=O group (1650 cm<sup>-1</sup>) and aromatic groups (1558 and

<sup>1</sup>) Trivial atom numbering; for systematic names, see *Exper. Part*.

Fig. 1. Compounds **1–3**, isolated from *Citrus unshiu*

1507  $\text{cm}^{-1}$ ) [8]. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **1** revealed signals for a 1,2,3,4-tetrasubstituted benzene moiety ( $\delta(\text{H})$  7.55 (*d*,  $J = 8.4$  Hz, 1 H) and  $\delta(\text{C})$  118.0 (C(6')), and  $\delta(\text{H})$  6.98 (*d*,  $J = 8.4$  Hz, 1 H) and  $\delta(\text{C})$  111.7 (C(5')). The presence of another benzene moiety, which was fully substituted, appeared at  $\delta(\text{C})$  151.0 (C(5)), 143.8 (C(6)), 148.6 (C(7)), 137.8 (C(8)), 150.3 (C(9)), and 115.4 (C(10)) in the  $^{13}\text{C}$ -NMR spectrum. The  $^{13}\text{C}$ -NMR exhibited a C=O signal at  $\delta(\text{C})$  170.3 and conjugated quaternary C-atom signals at  $\delta(\text{C})$  145.8 (C(2)) and 136.1 (C(3)). In addition, an O-bearing  $\text{CH}_2$  group appeared at  $\delta(\text{H})$  5.33 (*s*, 2 H) and  $\delta(\text{C})$  63.7 (C(11)). These NMR data indicated that compound **1** had a homoflavone skeleton [9][10]. Six MeO groups attached to benzene moieties appeared at  $\delta(\text{H})$  4.10, 4.03, 3.95, 3.95, 3.94, and 3.88 and  $\delta(\text{C})$  61.7, 62.0, 62.3, 61.9, 56.0, and 61.0. To each MeO group was assigned a position by means of NOESY and HMBC experiments. The positions of the two MeO groups at  $\delta(\text{H})$  3.94 and 3.88 were assigned to C(4') and C(3'), respectively, by the HMBCs H–C(6')/C(2'), C(2), and C(4'), and H–C(5')/C(6'), C(3'), and C(4'). The other MeO groups at  $\delta(\text{H})$  4.10, 4.03, 3.95, and 3.95 showed three-bond HMBCs with C-atoms at  $\delta(\text{C})$  151.0 (C(5)), 137.8 (C(8)), 143.8 (C(6)), and 148.6 (C(7)), respectively. Additionally, the NOESY correlations MeO–C(7)/MeO–C(6) and MeO–C(8)/H–C(6') and MeO–C(7) clearly confirmed the locations of these MeO groups at ring A. The HMBC cross-peaks  $\text{CH}_2(11)/\text{C}(2')$ , C(3'), and C(3) and the NOESY correlation  $\text{CH}_2(11)/\text{MeO–C}(3')$  suggested that the O-bearing  $\text{CH}_2$  group was linked to C(2') and C(3), forming an additional ring to the flavonoid skeleton (Fig. 2). As a result, the structure of **1** was elucidated as a new compound, 5,6,7,8,3',4'-hexamethylhomoflavone (= 3,4,8,9,10,11-hexamethoxy[2]benzopyrano[4,3-*b*][1]benzopyran-7(5*H*)-one).

Compound **2** was obtained as a yellow amorphous powder and gave a molecular-ion peak at  $m/z$  400.1161 ( $M^+$ ) in the HR-ESI-MS, corresponding to a molecular formula  $\text{C}_{21}\text{H}_{20}\text{O}_8$ . The IR spectrum of **2** exhibited strong absorption bands of a conjugated C=O group (1648  $\text{cm}^{-1}$ ) and aromatic groups (1556 and 1505  $\text{cm}^{-1}$ ) [8]. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR data were similar to those of **1**, except for some signals arising from ring B. Compound **2** showed *ABX* signals for a benzene moiety at  $\delta(\text{H})$  7.77 (*d*,  $J = 8.5$  Hz;  $\delta(\text{C})$  123.5 (C(6')), 6.98 (*dd*,  $J = 8.5, 2.0$  Hz;  $\delta(\text{C})$  114.1 (C(5'))), and 6.73 (*d*,  $J = 2.0$  Hz;  $\delta(\text{C})$  110.3 (C(3'))), instead of two *ortho*-coupled H-atom of a benzene moiety as observed for **1**. The HMBCs H–C(5')/C(4'), H–C(6')/C(4'), and H–C(3')/C(4') and the NOESY correlations  $\text{CH}_2(11)/\text{H–C}(3')$  and MeO–C(4')/H–C(5') and H–C(3') provided evidence that only one MeO group was located at ring B of compound **2**

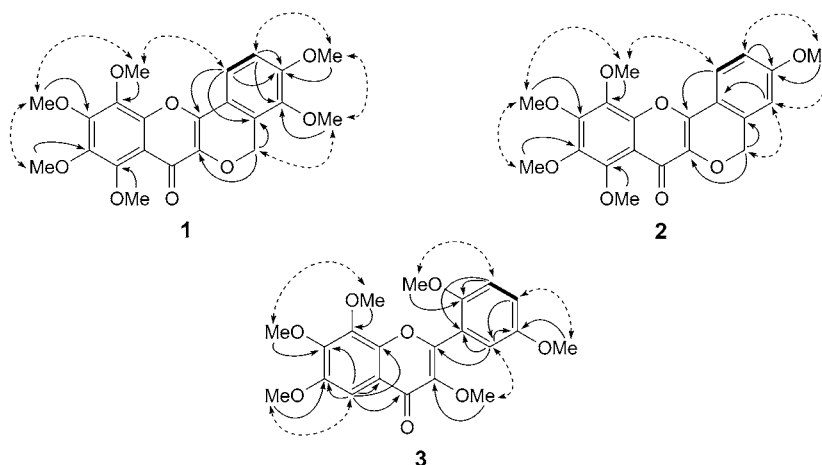


Fig. 2. Important  $^1\text{H},^1\text{H}$ -COSY (—), NOESY ( $\text{H} \leftrightarrow \text{H}$ ), and HMBC ( $\text{H} \rightarrow \text{C}$ ) features of **1–3**

(Fig. 2). Therefore, the structure of **2** was determined as a new compound, 5,6,7,8,4'-pentamethoxyhomoflavone (= 3,8,9,10,11-pentamethoxy[2]benzopyrano[4,3-*b*][1]-benzopyran-7(5*H*)-one).

Compound **3** was isolated as a pale yellow powder and possessed a molecular formula  $\text{C}_{21}\text{H}_{22}\text{O}_8$ , as determined by HR-ESI-MS ( $m/z$  402.1317 ( $M^+$ )). In the IR spectrum of **3**, characteristic absorption bands for a conjugated  $\text{C}=\text{O}$  group ( $1642\text{ cm}^{-1}$ ) and aromatic groups ( $1606, 1512, 1462\text{ cm}^{-1}$ ) appeared [8]. In the  $^1\text{H}$ -NMR spectra of **3**, *ABX* signals of benzene moiety were present at  $\delta(\text{H})$  7.71 (*dd*,  $J = 9.2, 2.0\text{ Hz}$ , 1 H), 7.70 (*d*,  $J = 2.0\text{ Hz}$ , 1 H), and 6.99 (*d*,  $J = 9.2\text{ Hz}$ , 1 H), corresponding to the  $\delta(\text{C})$  121.7 ( $\text{C}(4')$ ), 110.9 ( $\text{C}(3')$ ), and 111.4 ( $\text{C}(6')$ ). Four quaternary aromatic C-atoms appeared at  $\delta(\text{C})$  140.8 ( $\text{C}(3)$ ), 157.7 ( $\text{C}(6)$ ), 140.2 ( $\text{C}(7)$ ), and 152.4 ( $\text{C}(8)$ ), evidence for the existence of another benzene moiety. Additional observations of a conjugated  $\text{C}=\text{O}$  group at  $\delta(\text{C})$  173.7 ( $\text{C}(4)$ ) together with quaternary C-atom signals at  $\delta(\text{C})$  153.3 ( $\text{C}(2)$ ), 153.6 ( $\text{C}(9)$ ), and 113.1 ( $\text{C}(10)$ ) suggested that the molecule had a flavonoid structure. Another aromatic H-atom appeared at  $\delta(\text{H})$  6.75 (*s*, 1 H) in the  $^1\text{H}$ -NMR spectrum and was positioned at  $\text{C}(5)$  by the HMBCs  $\text{H}-\text{C}(5)/\text{C}(6), \text{C}(7), \text{C}(9), \text{C}(10)$ , and  $\text{C}(4)$ . In addition, this H-atom did not show any NOE with  $\text{MeO}-\text{C}(2')$ . A total of six MeO groups at benzene moieties appeared at  $\delta(\text{H})$  4.02 (*s*, 3 H), 3.98 (*s*, 3 H), 3.97 (*s*, 6 H), 3.92 (*s*, 3 H), and 3.87 (*s*, 3 H) and  $\delta(\text{C})$  62.2, 56.3, 56.1, 56.0, 61.6, and 60.0. The NOESY and HMBC data were employed to decide the assignment of these MeO groups. One of the two MeO groups at  $\delta(\text{H})$  3.97 (*s*, 6 H) showed connectivities to  $\delta(\text{C})$  148.7 ( $\text{C}(5')$ ), and the other to 151.0 ( $\text{C}(2')$ ) in the HMBC spectrum. Further HMBC analysis revealed the correlations ( $\text{H}-\text{C}(3')/\text{C}(5'), \text{C}(1'),$  and  $\text{C}(2')$ ),  $\text{H}-\text{C}(4')/\text{C}(6')$ , and  $\text{H}-\text{C}(6')/\text{C}(2'), \text{C}(1'), \text{C}(2), \text{C}(4'),$  and  $\text{C}(5')$ , and the NOESY  $\text{MeO}-\text{C}(2')/\text{H}-\text{C}(3')$ , and  $\text{MeO}-\text{C}(5')/\text{H}-\text{C}(4')$  and  $\text{H}-\text{C}(6')$ ), confirmed the presence of the 2',5'-dimethoxybenzene moiety (ring *B*) of flavones. Other MeO signals at  $\delta(\text{H})$  4.01 (*s*, 3 H), 3.98 (*s*, 3 H), and 3.92 (*s*, 3 H), exhibited three-bond HMBCs with C-atom signals at  $\delta(\text{C})$  157.7 ( $\text{C}(6)$ ), 140.2 ( $\text{C}(7)$ ), and 152.4 ( $\text{C}(8)$ ), respectively. Their positions were confirmed as

being attached to ring *A* of flavones, as evidenced by the HMBC cross-peaks H–C(5)/C(6), C(7), C(9), C(10), and C(4), as well as by the NOESY correlations MeO–C(6)/H–C(5) and MeO–C(7)/MeO–C(8). The remaining unassigned MeO group was placed at C(3) of ring *C*, supported by a three-bond HMBC cross-peak at  $\delta(\text{H})$  3.87 (s, 3 H)/ $\delta(\text{C})$  140.8 (C(3)) and the NOESY correlations MeO–C(3)/H–C(6'). Comparison of the spectral data with 3,5,6,7,8,3',4'-heptamethoxyflavone indicated that these compounds shared similar flavone structures, with the exception of different locations and numbers of MeO groups in their structure (Fig. 2) [11]. A detailed analysis of the NMR spectra revealed the structure of **3** as a new compound, *i.e.*, 3,6,7,8,2',5'-hexamethoxyflavone (=2-(2,5-dimethoxyphenyl)-3,6,7,8-tetramethoxy-4*H*-1-benzopyran-4-one).

The three known compounds were identified as 6,7,8,4'-tetramethoxyflavone (=6,7,8-trimethoxy-2-(4-methoxyphenyl)-4*H*-1-benzopyran-4-one) [12], 3,5,7,8,2',5'-hexamethoxyflavone (=2-(2,5-dimethoxyphenyl)-3,5,7,8-tetramethoxy-4*H*-1-benzopyran-4-one) [13], and scopoletin (=7-hydroxy-6-methoxy-2*H*-1-benzopyran-2-one) [14], respectively. The structures of the former two were deduced by analysis of their <sup>1</sup>H- and <sup>13</sup>C-NMR, <sup>1</sup>H,<sup>1</sup>H-COSY, NOESY, HSQC, and HMBC data; they have never been isolated from natural sources, but have previously been reported as synthetic compounds. Scopoletin was isolated from *C. unshiu* for the first time. The structures of the three known compounds were confirmed by comparison of their physical and spectroscopic data with those reported previously [12–14].

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### Experimental Part

*General.* Column chromatography (CC): silica gel (SiO<sub>2</sub>, 230–400 mesh; Merck, Germany) and Sephadex LH-20 (Amersham Pharmacia Biotech, UK). TLC: silica gel 60 F<sub>254</sub> and RP-18 F<sub>254s</sub> silica gel plates (Merck, Germany); detection under UV light and by spraying with 10% aq. H<sub>2</sub>SO<sub>4</sub> soln., followed by heating at 120° for 5 min. HPLC: prep. HPLC Acme 9000 (Young Lin, Republic of Korea) equipped with a 5-ODS-H column (S-5 μm, 250 mm × 20 mm; Chemco, Japan); *t<sub>R</sub>* in min. UV Spectra: Hitachi U3000 spectrophotometer;  $\lambda_{\text{max}}$  (log  $\epsilon$ ) in nm. IR Spectra: Bio-Rad-FTS-135-FT-IR spectrometer; KBr pellets;  $\tilde{\nu}$  in cm<sup>-1</sup>. NMR Spectra: Varian-Unity-Inova-400 FT-NMR instrument;  $\delta$  in ppm rel. to Me<sub>4</sub>Si as internal standard, *J* in Hz. HR-EI-MS: Agilent-6220 accurate-mass TOF LC/MS system; in *m/z*.

*Plant Material.* The peels of mature fruits of *Citrus unshiu* MARCOW (Rutaceae) were purchased in May 2009 from the *Insan Oriental Herbal Market* in Seoul, South Korea. The sample was identified by Dr. Je-Hyun Lee (College of Oriental Medicine, Dongguk University, Korea). A voucher specimen (No. EA293) was deposited with the Natural Product Chemistry Laboratory, College of Pharmacy, Ewha Womans University, Korea.

*Extraction and Isolation.* The dried peels of mature fruits of *C. unshiu* (10 kg) were extracted with MeOH at r.t. (6 × 24 l, overnight). The extract was concentrated at 40° to afford a MeOH-soluble residue (5640.05 g). The aq. soln. was defatted with hexane (3 × 44 l) and subsequently partitioned with AcOEt (3 × 44 l) and BuOH (3 × 30 l). The AcOEt extract (200.53 g) was subjected to CC (SiO<sub>2</sub> (2 kg), 0.1 → 50% MeOH/CHCl<sub>3</sub>): Fractions 1–33. Fr. 19 (10.06 g) was subjected to CC (SiO<sub>2</sub> (200 g), 0.1 → 50%

acetone/hexane  $\rightarrow$  0.1–50% MeOH/CHCl<sub>3</sub>): *Frs. 19-1–19-40. Frs. 19-19* (0.893 g) was subjected again to CC (*Sephadex LH-20* (100 g), 100% MeOH): *scopoletin* (1.32 mg) and *Frs. 19-19-1–19-19-3. Frs. 19-19-3* (0.174 g) was purified by prep. HPLC (*RP-C<sub>18</sub>*, MeOH/H<sub>2</sub>O 70:30; 2 ml/min): **1** (*t<sub>R</sub>* 90; 0.60 mg), **2** (*t<sub>R</sub>* 100; 0.26 mg), and **3** (*t<sub>R</sub>* 63; 6.19 mg). The mixture of *Fr. 19-12* and *Fr. 19-13* (1.183 g) was subjected to CC (SiO<sub>2</sub> (150 g), 0.1  $\rightarrow$  50% acetone/hexane): *Frs. 19-12-1–19-12-5. Fr. 19-12-3* (0.682 g) was subjected to CC (SiO<sub>2</sub> (150 g), 0.1  $\rightarrow$  50% MeOH/CHCl<sub>3</sub>): *Frs. 19-12-3-1–19-12-3-4. Fr. 19-12-3-2* (0.50 g) was purified by prep. HPLC (*RP-C<sub>18</sub>*, MeOH/H<sub>2</sub>O 75:35; 2 ml/min): 6,7,8,4-tetramethoxyflavone (*t<sub>R</sub>* 110; 1.18 mg). *Fr. 19-21* (0.203 g) was subjected to CC (SiO<sub>2</sub> (100 g), 0.1  $\rightarrow$  50% MeOH/CHCl<sub>3</sub>): *Frs. 19-21-1–19-21-10. Frs. 19-21-5* (46.64 mg) was again subjected to CC (*ODS-A* (80 g), MeOH/H<sub>2</sub>O 7:3–9:1): 3,5,7,8,2',5'-hexamethoxyflavone (1.18 mg).

*5,6,7,8,3',4'-Hexamethoxyhomoflavone* (=3,4,8,9,10,11-Hexamethoxy[2]benzopyrano[4,3-b][1]benzopyran-7(5H)-one; **1**): Pale yellow amorphous powder. UV (MeOH): 364 (3.97), 256 (4.03), 205 (4.31). IR (KBr): 2920, 1650, 1558, 1508, 1209. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): 7.55 (*d*, *J* = 8.4, H–C(6')); 6.98 (*d*, *J* = 8.4, H–C(5')); 5.33 (*s*, CH<sub>2</sub>(11)); 4.10 (*s*, MeO–C(5)); 4.03 (*s*, MeO–C(8)); 3.95 (*s*, MeO–C(6)); 3.95 (*s*, MeO–C(7)); 3.94 (*s*, MeO–C(4')); 3.88 (*s*, MeO–C(3')). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): 170.3 (C(4)); 155.3 (C(4')); 151.0 (C(5)); 150.3 (C(9)); 148.6 (C(7)); 145.8 (C(2)); 144.3 (C(3')); 143.8 (C(6)); 137.8 (C(8)); 136.1 (C(3)); 126.1 (C(2')); 118.3 (*s*, C(1')); 118.0 (*s*, C(6')); 115.4 (C(10)); 111.7 (C(5')); 63.7 (C(11)); 62.3 (MeO–C(7)); 62.0 (MeO–C(8)); 61.9 (MeO–C(6)); 61.7 (MeO–C(5)); 61.0 (MeO–C(3')); 56.0 (MeO–C(4')). HR-ESI-MS: 430.1269 (*M*<sup>+</sup>, C<sub>22</sub>H<sub>22</sub>O<sub>8</sub><sup>+</sup>; calc. 430.1264).

*5,6,7,8,4'-Pentamethoxyhomoflavone* (=3,8,9,10,11-Pentamethoxy[2]benzopyrano[4,3-b][1]benzopyran-7(5H)-one; **2**): Yellow amorphous powder. UV (MeOH): 367 (4.30), 273 (4.34). IR (KBr): 2919, 1648, 1556, 1506. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 600 MHz): 7.77 (*d*, *J* = 8.5, H–C(6')); 6.98 (*dd*, *J* = 8.5, 2.0, H–C(5')); 6.73 (*d*, *J* = 2.0, H–C(3')); 5.22 (*s*, CH<sub>2</sub>(11)); 4.10 (*s*, MeO–C(7)); 4.04 (*s*, MeO–C(8)); 3.95 (*s*, MeO–C(6)); 3.95 (*s*, MeO–C(5)); 3.88 (*s*, MeO–C(4')). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 150 MHz): 170.3 (C(4)); 162.2 (C(4')); 151.0 (C(7)); 148.6 (C(5)); 147.1 (C(9)); 146.2 (C(2)); 143.8 (C(6)); 137.8 (C(8)); 136.0 (C(3)); 134.2 (C(2')); 123.5 (C(6')); 117.8 (C(1')); 115.4 (C(10)); 114.1 (C(5')); 110.3 (C(3')); 68.3 (C(11)); 62.4 (MeO–C(6)); 62.0 (MeO–C(8)); 61.9 (MeO–C(5)); 61.7 (MeO–C(6)); 55.6 (MeO–C(4')). HR-ESI-MS: 400.1161 (*M*<sup>+</sup>, C<sub>21</sub>H<sub>20</sub>O<sub>8</sub><sup>+</sup>; calc. 400.1158).

*3,6,7,8,2',5'-Hexamethoxyflavone* (=2-(2,5-Dimethoxyphenyl)-3,6,7,8-tetramethoxy-4H-1-benzopyran-4-one; **3**): Pale yellow powder. UV (MeOH): 334 (4.18), 241 (4.12), 210 (4.42). IR (KBr): 2920, 1633, 1604, 1516, 1469, 1269, 995. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): 7.71 (*dd*, *J* = 9.2, 2.0, H–C(4')); 7.70 (*d*, *J* = 2.0, H–C(6')); 6.99 (*d*, *J* = 9.2, H–C(3')); 6.75 (*s*, H–C(5)); 4.02 (*s*, MeO–C(8)); 3.98 (*s*, MeO–C(6)); 3.97 (*s*, MeO–C(2')), MeO–C(5')); 3.92 (*s*, MeO–C(7)); 3.87 (*s*, MeO–C(3')). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): 173.7 (C(4)); 157.7 (C(6)); 153.6 (C(9)); 153.3 (C(2)); 152.4 (C(8)); 151.0 (C(2')); 148.7 (C(5')); 140.8 (C(3)); 140.2 (C(7)); 123.4 (C(1')); 121.7 (C(4')); 113.1 (C(10)); 111.4 (C(6')); 110.9 (C(3')); 96.0 (C(5)); 62.2 (MeO–C(8)); 61.6 (MeO–C(7)); 60.0 (MeO–C(3)); 56.3 (MeO–C(6)); 56.1 (MeO–C(2')); 56.0 (MeO–C(5')). HR-ESI-MS: 402.1317 (*M*<sup>+</sup>, C<sub>21</sub>H<sub>22</sub>O<sub>8</sub><sup>+</sup>; calc. 402.1315).

*6,7,8,4'-Tetramethoxyflavone* (=6,7,8-Trimethoxy-2-(4-methoxyphenyl)-4H-1-benzopyran-4-one): Yellow powder. UV (MeOH): 320 (4.27), 267 (3.93), 214 (4.49). IR (KBr): 2919, 1637, 1603, 1513, 1118. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): 7.83 (*dd*, *J* = 9.2, H–C(2')), H–C(6')); 7.01 (*dd*, *J* = 9.2, H–C(3')), H–C(5')); 6.80 (*s*, H–C(5)); 6.59 (*s*, H–C(3)); 3.99 (*s*, MeO–C(8)); 3.98 (*s*, MeO–C(6)); 3.92 (*s*, MeO–C(7)); 3.89 (*s*, MeO–C(4')). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): 177.2 (C(4)); 162.1 (C(4')); 161.2 (C(2)); 157.6 (C(6)); 154.5 (C(9)); 152.6 (C(8)); 140.3 (C(7)); 127.7 (C(2'), C(6')); 123.9 (C(1')); 114.4 (C(3'), C(5')); 112.9 (C(10)); 107.1 (C(3)); 96.2 (C(5)); 62.2 (MeO–C(8)); 61.6 (MeO–C(7)); 56.3 (MeO–C(6)); 55.5 (MeO–C(4')). HR-ESI-MS: 342.1111 (*M*<sup>+</sup>, C<sub>19</sub>H<sub>18</sub>O<sub>6</sub><sup>+</sup>; calc. 342.1103).

*3,5,7,8,2',5'-Hexamethoxyflavone* (=2-(2,5-Dimethoxyphenyl)-3,5,7,8-tetramethoxy-4H-1-benzopyran-4-one): Pale yellow powder. UV (MeOH): 351 (4.17), 271 (4.21), 252 (4.24). IR (KBr): 2919, 1697, 1599, 1574, 1516, 1215. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz): 7.85 (*dd*, *J* = 8.4, 2.0, H–C(4')); 7.84 (*d*, *J* = 2.0, H–C(6')); 7.01 (*d*, *J* = 8.4, H–C(3)); 6.42 (*s*, H–C(5)); 4.01 (*s*, MeO–C(7)); 4.00 (*s*, MeO–C(5)); 3.97 (*s*, MeO–C(2')), MeO–C(5')); 3.94 (*s*, MeO–C(8)); 3.90 (*s*, MeO–C(3)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz): 174.3 (C(4)); 156.4 (C(7)); 156.3 (C(6)); 152.3 (C(2)); 151.0 (C(9)); 150.9 (C(2')); 148.7 (C(5')); 140.9 (C(3)); 130.5 (C(6)); 123.6 (C(1)); 121.8 (C(4)); 111.0 (C(6)); 111.0 (C(3)); 109.4 (C(10)); 92.3 (C(5)); 61.5

(MeO–C(8)); 59.9 (MeO–C(3)); 56.6 (MeO–C(7)); 56.4 (MeO–C(6)); 56.0 (MeO–C(2')); 55.9 (MeO–C(5')). HR-ESI-MS: 402.1317 ( $M^+$ ,  $C_{21}H_{22}O_8^+$ ; calc. 402.1315).

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