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## Synthesis of Pyranoisoflavones by the Oxidative Rearrangement of Dihydropyranochalcones with Thallium(III) Nitrate: Synthesis of Elongatin, Its Angular Isomer, Toxicarol Isoflavone, and Related Compounds<sup>1)</sup>

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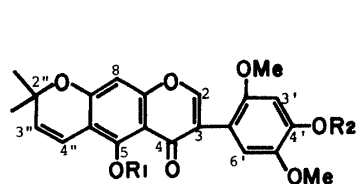
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Elongatin, 4',5-dihydroxy-2',5'-dimethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone (**1**), was prepared by the oxidative rearrangement of 6'-acetoxy-2',4-bis(benzyloxy)-2,5-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (**15**) with thallium(III) nitrate and by dehydrogenation of the resultant linear 4',5-dihydroxy-2',5'-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]isoflavone (**19**) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. Its angular isomer, 4',5-dihydroxy-2',5'-dimethoxy-2'',2''-dimethylpyrano[6'',5''-h]isoflavone (**2**), was also synthesized from the corresponding chalcone (**28**) in a similar manner and then converted into toxicarol isoflavone (**3**).

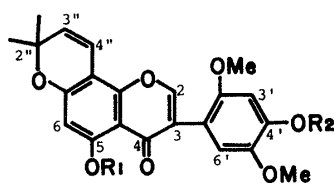
**Keywords**—pyranoisoflavone; elongatin; dihydropyranoisoflavone; dihydropyranochalcone; oxidative rearrangement; thallium(III) nitrate; dehydrogenation; 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

The linear and angular pyranoisoflavones which possess a prenyl unit as a trioxxygenated benzopyran of the phloroglucinol type in the A ring are well known to occur in nature.<sup>3)</sup> Recently, it has been reported that 6-prenylated isoflavones (luteone<sup>4)</sup> and wighteone<sup>5)</sup>) and a pyranoisoflavone (parvisoflavone B<sup>6)</sup>) exhibit considerable antifungal activity. This fact has aroused a renewed interest in the synthesis and biochemical properties of pyranoisoflavones. The structures of pyranoisoflavones having no hydroxyl group in the B ring (robustone,<sup>7)</sup> ichthyone,<sup>8)</sup> and toxicarol isoflavone<sup>9)</sup>) have been confirmed by total syntheses. Although most of the linear pyranoisoflavones having hydroxyl groups in the B ring (elongatin,<sup>10)</sup> alpinumisoflavone,<sup>11)</sup> parvisoflavone B,<sup>12)</sup> and 3',5-dihydroxy-4'-dimethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone<sup>13)</sup>) have not been synthesized, their structures have been confirmed by syntheses of their derivatives<sup>14,15)</sup> and by spectroscopic and chemical studies. The total syntheses of pyranoisoflavones are useful for the determination of their structures and for the development of biological studies.

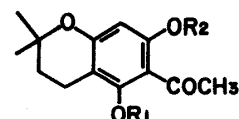
We have been studying the synthesis of isoflavones having a prenyl unit by applying the oxidative rearrangement of chalcones with thallium(III) nitrate.<sup>16)</sup> In the continuation of these studies, elongatin and its angular isomer were chosen as models of pyranoisoflavones having a hydroxyl group in the B ring. The structure of elongatin isolated from *Tephrosia elongata* E. MEY. has been shown to be 4',5-dihydroxy-2',5'-dimethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone (**1**) on the basis of chemical and spectroscopic evidence.<sup>10)</sup> The present paper describes the unambiguous syntheses and properties of natural linear pyranoisoflavone (elongatin) (**1**) and its angular isomer, 4',5-dihydroxy-2',5'-dimethoxy-



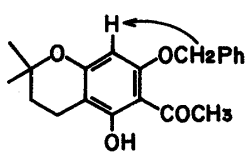
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 20 :  $R_1=R_2=Me$   
 21 :  $R_1=R_2=CH_3CO$   
 35 :  $R_1=H, R_2=Me$   
 36 :  $R_1=CH_3CO, R_2=Me$



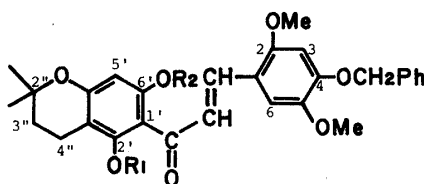
- 2 :  $R_1=R_2=H$   
 3 :  $R_1=H, R_2=Me$   
 33 :  $R_1=R_2=Me$   
 34 :  $R_1=R_2=CH_3CO$   
 37 :  $R_1=CH_3CO, R_2=Me$



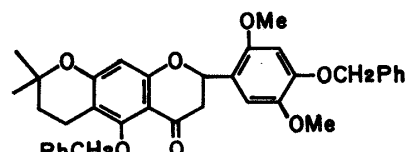
- 10 :  $R_1=R_2=H$   
 11 :  $R_1=PhCH_2, R_2=H$   
 13 :  $R_1=H, R_2=Ts$   
 14 :  $R_1=PhCH_2, R_2=Ts$   
 22 :  $R_1=Me, R_2=H$



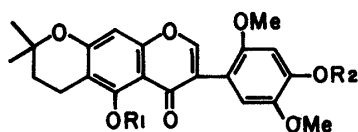
12



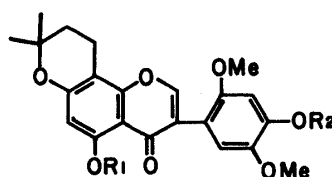
- 15 :  $R_1=PhCH_2, R_2=H$   
 17 :  $R_1=PhCH_2, R_2=CH_3CO$   
 23 :  $R_1=Me, R_2=H$   
 24 :  $R_1=Me, R_2=CH_3CO$   
 28 :  $R_1=H, R_2=PhCH_2$   
 29 :  $R_1=CH_3CO, R_2=PhCH_2$



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- 18 :  $R_1=H, R_2=PhCH_2$   
 19 :  $R_1=R_2=H$   
 25 :  $R_1=Me, R_2=PhCH_2$   
 26 :  $R_1=Me, R_2=H$   
 27 :  $R_1=R_2=Me$



- 30 :  $R_1=R_2=PhCH_2$   
 31 :  $R_1=H, R_2=PhCH_2$   
 32 :  $R_1=R_2=H$

2'',2''-dimethylpyrano[6'',5''-*h*]isoflavone (2), toxicarol isoflavone (3),<sup>17)</sup> and related compounds.

The Baeyer–Villiger oxidation of the dimethyl ether **5**<sup>18)</sup> of 2,5-dihydroxyacetophenone (**4**),<sup>19)</sup> followed by hydrolysis of the resulting acetate **6**<sup>18)</sup> afforded 2,5-dimethoxyphenol (**7**).<sup>18)</sup> The benzyl ether **8**<sup>20)</sup> of **7** was converted into 4-benzyloxy-2,5-dimethoxybenzaldehyde (**9**)<sup>21)</sup> by means of the Vilsmeier reaction. Condensation of 2,4,6-trihydroxyacetophenone with isoprene in the presence of phosphoric acid in anhydrous xylene at 30–35 °C afforded 6-acetyl-5,7-dihydroxy-2,2-dimethylchroman (**10**). The partial benzylation of **10** afforded two chroman derivatives, **11** as a minor product and **12** as a major product. The distinction between the two isomeric chromans **11** and **12** was achieved by nuclear Overhauser effect (NOE) experiments at the C<sub>8</sub>-proton: the integrated intensity of the signal at  $\delta$  5.88 for **12** increased up to 30%, when the benzyl methylene protons were saturated by double irradiation, but the intensity of the signal at  $\delta$  6.17 for **11** did not increase. The direct benzylation of **10** is not suitable for the preparation of the starting material of elongatin because of a poor yield of **11**. Therefore, the 7-tosyloxychroman **13**, which was predominantly obtained from **10**, was benzylated to give the 5-benzyloxychroman **14** and subsequently hydrolyzed with alkali to give the desired 5-benzyloxy-7-hydroxychroman **11** in a good yield. Condensation of **11** with **9** in the presence of piperidine afforded the chalcone **15** as a major product and the flavanone derivative **16** as a minor product. The mixture of **15** and **16** was converted into the acetate **17**. The oxidative rearrangement of **17** with thallium(III) nitrate

trihydrate (TTN) in methanol, followed by the cyclization of the resultant compound with diluted hydrochloric acid afforded the linear 5-hydroxydihydropyranoisoflavone **18**. The  $^1\text{H}$ -nuclear magnetic resonance ( $^1\text{H}$ -NMR) spectrum of **18** showed the presence of one methylene group as a singlet at  $\delta$  5.18, the  $\text{C}_2$ -proton as a singlet at  $\delta$  7.77, and one hydroxyl group as a singlet at  $\delta$  13.17. Hydrogenolysis of **18** with palladium on charcoal afforded the 4',5-dihydroxydihydropyranoisoflavone **19**.<sup>10)</sup> Dehydrogenation of **19** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in anhydrous *o*-dichlorobenzene under reflux afforded the desired linear pyranoisoflavone (elongatin) (**1**) (mp 182—184 °C; lit.,<sup>10)</sup> mp 181—182 °C), which was converted into the diacetate **21**. Compound **1** was also converted into the dimethyl ether **20**, which was identical with a sample synthesized by condensation of **9** with 6-acetyl-7-hydroxy-5-methoxy-2,2-dimethylchroman (**22**) *via* six steps by a method similar to that described above. The melting point of the synthetic linear pyranoisoflavone **1** was not depressed by admixture with natural elongatin. The physical data for the synthetic pyranoisoflavones **1**, **20**, and **21** were shown to be identical with those for natural elongatin and its derivatives, respectively. On the basis of these results, the structure of elongatin was confirmed to be 4',5-dihydroxy-2',5'-dimethoxy-2'',2''-dimethylpyrano[5'',6''-*g*]isoflavone (**1**).

Condensation of the 7-benzyloxy-5-hydroxychroman **12** with **9** afforded the chalcone derivative **28**, which was subsequently converted into the acetate **29**. The oxidative rearrangement of **29** with TTN, followed by the cyclization of the resultant compound with diluted hydrochloric acid afforded the angular dihydropyranoisoflavone **30** as a main product and a small amount of 5-hydroxydihydropyranoisoflavone **31**. The  $^1\text{H}$ -NMR spectrum of **30** showed the presence of two methylene groups as a singlet (4H) at  $\delta$  5.17 and the  $\text{C}_2$ -proton as a singlet at  $\delta$  7.78. Hydrogenolysis of **30** with palladium on charcoal afforded the 4',5-dihydroxydihydropyranoisoflavone **32**. Dehydrogenation of **32** with DDQ in anhydrous chlorobenzene under reflux to give the desired angular pyranoisoflavone **2**, which was converted into the diacetate **34**. Compound **2** was also converted into the 5-hydroxy-4'-methoxypyranoisoflavone (toxicarol isoflavone) (**3**) (mp 219—220 °C)<sup>9,17)</sup> by partial methylation with iodomethane and into the dimethyl ether **33** by exhaustive methylation with dimethyl sulfate. The properties of the synthetic angular pyranoisoflavone derivatives **3** and **33** were identical with those of natural toxicarol isoflavone and its methyl ether, respectively.

In the  $^1\text{H}$ -NMR spectra, the methylation or acetylation of the  $\text{C}_5$ -OH in the linear pyranoisoflavones **1** and **35**<sup>10)</sup> causes a marked downfield shift ( $\Delta\delta = 0.25$ —0.4) of the  $\text{C}_8$ -H signal (**20**, **36**,<sup>10)</sup> and **21**), while that of the  $\text{C}_5$ -OH in the angular isomers **2** and **3** causes a slight downfield shift ( $\Delta\delta = 0.02$ —0.25) of the  $\text{C}_6$ -H signal (**33**, **37**,<sup>22)</sup> and **34**), as shown in Table I. In Table II, acetylation of the linear pyranoisoflavone **1** causes a shift ( $\Delta\delta = 0.27$ —0.28) to higher field of the  $\text{C}_{4''}$ -H signal and a slight downfield shift ( $\Delta\delta = 0.14$ ) of the  $\text{C}_{3''}$ -H signal. The effect of acetylation has been observed in the  $^1\text{H}$ -NMR spectra of 5-hydroxy-2,2-dimethylchromenes.<sup>23)</sup> However, acetylation of the angular isomer **2** causes no such shift of the  $\text{C}_{4''}$ -H and  $\text{C}_{3''}$ -H signals.

In general, the ultraviolet (UV) spectra of isoflavones having a  $\text{C}_5$ -OH show a band II (240—285 nm) bathochromic shift of 10—14 nm on addition of aluminum chloride.<sup>24)</sup> On addition of aluminum chloride, the UV spectra of the angular pyrano- and dihydropyranoisoflavones **2**, **3**, **32**, and **31** show a band II bathochromic shift of 5—12 nm and a new absorption maximum at a much longer wavelength (373—408 nm), as shown in Table III. In the UV spectra of the linear isomers **1**, **19**, and **18**, on the contrary, no such characteristic shift is observed. The UV spectra (in ethanol) of the linear pyranoisoflavones **1** and **35**<sup>10)</sup> show an intense absorption maximum at a longer wavelength (277—281 nm) than those (at 268 nm) of the angular pyranoisoflavones **2** and **3**, while in the UV spectra of the linear and angular dihydropyranoisoflavones **19**, **18**, **32**, and **31**, no such property is observed and the spectra are

TABLE I. Comparison of Chemical Shifts ( $\delta$ ) of C<sub>8</sub>-H, C-H, and C<sub>3</sub>-H in Linear and Angular Pyranoisoflavones

| Linear form              |                   |                   | Angular form             |                   |                   |
|--------------------------|-------------------|-------------------|--------------------------|-------------------|-------------------|
| Compd.                   | C <sub>8</sub> -H | C <sub>3</sub> -H | Compd.                   | C <sub>6</sub> -H | C <sub>3</sub> -H |
| <b>1</b>                 | 6.32              | 6.66              | <b>2</b>                 | 6.27              | 6.63              |
| <b>35</b> <sup>10)</sup> | 6.30              | 6.59              | <b>3</b>                 | 6.24              | 6.57              |
| <b>20</b>                | 6.57              | 6.57              | <b>33</b>                | 6.29              | 6.57              |
| <b>36</b> <sup>10)</sup> | 6.70              | 6.58              | <b>37</b> <sup>22)</sup> | 6.49              | 6.57              |
| <b>21</b>                | 6.69              | 6.69              | <b>34</b>                | 6.46              | 6.67              |

TABLE II. Comparison of Chemical Shifts ( $\delta$ ) of C<sub>3</sub>-H and C<sub>4</sub>-H in Linear and Angular 5-Hydroxy (**1** and **2**)- and 5-Acetoxypyranoisoflavones (**21**, **34**, **36**, and **37**)

| Linear form              |                   |                   | Angular form             |                   |                   |
|--------------------------|-------------------|-------------------|--------------------------|-------------------|-------------------|
| Compd.                   | C <sub>3</sub> -H | C <sub>4</sub> -H | Compd.                   | C <sub>3</sub> -H | C <sub>4</sub> -H |
| <b>1</b>                 | 5.59              | 6.74              | <b>2</b>                 | 5.56              | 6.67              |
| <b>21</b>                | 5.73              | 6.47              | <b>34</b>                | 5.63              | 6.71              |
|                          | 5.59              | 6.74              |                          | 5.56              | 6.67              |
|                          | $\Delta 0.14$     | $-\Delta 0.27$    |                          | $\Delta 0.07$     | $\Delta 0.04$     |
| <b>36</b> <sup>10)</sup> | 5.73              | 6.46              | <b>37</b> <sup>22)</sup> | 5.68              | 6.78              |
|                          | 5.59              | 6.74              |                          | 5.56              | 6.67              |
|                          | $\Delta 0.14$     | $-\Delta 0.28$    |                          | $\Delta 0.12$     | $\Delta 0.11$     |

TABLE III. UV Data for Linear and Angular 5-Hydroxypyrano- and Dihydroxypyranoisoflavones

| Linear form              |                                       |            | Angular form         |                                       |                                      |
|--------------------------|---------------------------------------|------------|----------------------|---------------------------------------|--------------------------------------|
| Compd.                   | $\lambda_{\max}$ nm (log $\epsilon$ ) |            | Compd.               | $\lambda_{\max}$ nm (log $\epsilon$ ) |                                      |
| <b>1</b>                 | 281 (4.57)                            |            | <b>2</b>             | 268 (4.62)                            | 302i <sup>a)</sup> (4.11) 350 (3.56) |
| (AlCl <sub>3</sub> )     | 281 (4.54)                            |            | (AlCl <sub>3</sub> ) | 278 (4.62)                            | 408 (3.53)                           |
| <b>35</b> <sup>10)</sup> | 277 (4.52)                            |            | <b>3</b>             | 268 (4.63)                            | 305i <sup>a)</sup> (4.07) 347 (3.57) |
|                          |                                       |            | (AlCl <sub>3</sub> ) | 278 (4.63)                            | 407 (3.56)                           |
| <b>19</b>                | 263 (4.44)                            | 298 (4.24) | <b>32</b>            | 265 (4.47)                            | 296 (4.17)                           |
| (AlCl <sub>3</sub> )     | 263 (4.43)                            | 298 (4.24) | (AlCl <sub>3</sub> ) | 270 (4.39)                            | 296 (4.24) 373 (3.41)                |
| <b>18</b>                | 264 (4.47)                            | 298 (4.27) | <b>31</b>            | 265 (4.52)                            | 296 (4.22)                           |
| (AlCl <sub>3</sub> )     | 264 (4.47)                            | 298 (4.27) | (AlCl <sub>3</sub> ) | 277 (4.45)                            | 296 (4.32) 380 (3.58)                |

a) i: inflection.

similar to each other. Thus, in the UV spectra of linear pyrano- and dihydroxypyranoisoflavones having a C<sub>5</sub>-OH, the new finding that a characteristic bathochromic shift of band II is not caused by addition of aluminum chloride can be used to distinguish clearly between linear and angular structural isomers.

### Experimental

Melting points are uncorrected. The UV spectra were taken in ethanol on a Hitachi 124 spectrophotometer. The <sup>1</sup>H-NMR spectra were measured with a Hitachi R-20 spectrometer (60 MHz), using tetramethylsilane as an internal standard ( $\delta$ , ppm). Column chromatography and thin-layer chromatography (TLC) were carried out on Kieselgel 60 (70—230 mesh) and with Kiesel 60 F-254 (Merck).

**2-Benzyl-1,4-dimethoxybenzene (8)**—Benzylation of 2,5-dimethoxyphenol (**7**)<sup>19)</sup> (7.11 g) with benzyl chloride (9.92 g), and K<sub>2</sub>CO<sub>3</sub> (19.2 g) in *N,N*-dimethylformamide (DMF) (20 ml) at 140 °C for 1 h gave **8** (10.16 g, 90%), bp 171–172 °C/6 mmHg; mp 32–34 °C (lit.,<sup>20)</sup> mp 38–39 °C).

**4-Benzyl-2,5-dimethoxybenzaldehyde (9)**—After a cold solution of **8** (11.76 g) in ClCH<sub>2</sub>CH<sub>2</sub>Cl (40 ml) was added to the reagent prepared from DMF (4.8 ml)–POCl<sub>3</sub> (5.67 ml) at 10 °C, the reaction mixture was stirred at room temperature for 30 min, and then heated with stirring at 80 °C for a further 2 h. The resulting compound was recrystallized from acetone–water to give **9**<sup>21)</sup> (11.15 g, 85%) as colorless needles, mp 137–139 °C.

**6-Acetyl-5,7-dihydroxy-2,2-dimethylchroman (10)**—A solution of isoprene (8 ml) in anhydrous xylene (20 ml) was gradually added to a mixture of 2,4,6-trihydroxyacetophenone (10 g) and H<sub>3</sub>PO<sub>4</sub> (10 ml) with stirring at 30–35 °C over a period of 2 h, and then the mixture was further stirred at the same temperature for 16–18 h. The reaction mixture was extracted with ether, washed with NaHCO<sub>3</sub> solution and brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed and the residue was chromatographed over a short silica gel column with CHCl<sub>3</sub>–acetone (20:1) to give two fractions (the fraction containing the major product showed a *R*<sub>f</sub> value of 0.57). The main fraction was concentrated under reduced pressure, and the residue was recrystallized from petroleum ether to give **10** (6.3 g, 45%) as colorless needles, mp 218–220 °C. <sup>1</sup>H-NMR (DMSO) δ: 1.26 (6H, s, CH<sub>3</sub> × 2), 1.72 and 2.46 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.58 (3H, s, COCH<sub>3</sub>), 5.81 (1H, s, C<sub>8</sub>-H), 10.48 and 13.90 (each 1H, s, OH). *Anal.* Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>4</sub>: C, 66.08; H, 6.83. Found: C, 65.97; H, 6.79.

**6-Acetyl-5-benzyl-7-hydroxy-2,2-dimethylchroman (11) and 6-Acetyl-7-benzyl-5-hydroxy-2,2-dimethylchroman (12)**—A mixture of **10** (3.55 g), benzyl chloride (1.75 ml), and K<sub>2</sub>CO<sub>3</sub> (5 g) in hexamethylphosphoramide (HMPA) (30 ml) was heated with stirring in a nitrogen atmosphere at 105 °C for 40 min. Potassium carbonate was filtered off and the filtrate was poured into water, acidified with 10% HCl, extracted with EtOAc, washed with water, and dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the residue was crystallized from petroleum ether to give **12** (1.82 g) as colorless needles, mp 120–121 °C. The mother liquor was chromatographed over a silica gel column with ClCH<sub>2</sub>CH<sub>2</sub>Cl–petroleum ether (4:5) to give **12** (0.15 g; *R*<sub>f</sub> = 0.53) and **11** (0.45 g, 10%; *R*<sub>f</sub> = 0.35) as colorless needles, mp 99–100 °C. <sup>1</sup>H-NMR of **11** (CDCl<sub>3</sub>) δ: 1.33 (6H, s, CH<sub>3</sub> × 2), 1.74 and 2.65 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.64 (3H, s, COCH<sub>3</sub>), 4.84 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.17 (1H, s, C<sub>8</sub>-H), 7.31 (5H, m, C<sub>6</sub>H<sub>5</sub>), 12.70 (1H, s, OH). *Anal.* Calcd for C<sub>20</sub>H<sub>22</sub>O<sub>4</sub>: C, 73.60; H, 6.79. Found: C, 73.40; H, 6.85.

Compound **12** was crystallized from MeOH to give colorless needles, mp 120–121 °C, in a total yield of 1.97 g (40%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.31 (6H, s, CH<sub>3</sub> × 2), 1.76 and 2.58 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.50 (3H, s, COCH<sub>3</sub>), 4.98 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 5.88 (1H, s, C<sub>8</sub>-H), 7.32 (5H, s, C<sub>6</sub>H<sub>5</sub>), 14.45 (1H, s, OH). *Anal.* Calcd for C<sub>20</sub>H<sub>22</sub>O<sub>4</sub>: C, 73.60; H, 6.79. Found: C, 73.52; H, 6.55.

**6-Acetyl-5-hydroxy-2,2-dimethyl-7-tosyloxylchroman (13)**—A mixture of **10** (10 g), *p*-toluenesulfonyl chloride (4.25 g), and K<sub>2</sub>CO<sub>3</sub> (11.3 g) was heated with stirring in acetone (100 ml) at 56 °C for 1 h. After the removal of K<sub>2</sub>CO<sub>3</sub> and the solvent, the residue was extracted with EtOAc, washed with NaHCO<sub>3</sub> solution and water, and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the residue was recrystallized from MeOH to give **13** (5.9 g, 75%) as colorless needles, mp 139–140 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.29 (6H, s, CH<sub>3</sub> × 2), 1.76 and 2.58 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.44 (3H, s, COCH<sub>3</sub>), 2.56 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 5.99 (1H, s, C<sub>8</sub>-H), 7.27 and 7.71 (each 2H, d, *J* = 9 Hz, arom-H), 13.57 (1H, s, OH). *Anal.* Calcd for C<sub>20</sub>H<sub>22</sub>O<sub>6</sub>S: C, 61.53; H, 5.68. Found: C, 61.56; H, 5.52.

**6-Acetyl-5-benzyl-2,2-dimethyl-7-tosyloxylchroman (14)**—A mixture of **13** (4.6 g), benzyl chloride (1.63 ml), and KI (2 g) in acetone (100 ml) was refluxed in the presence of K<sub>2</sub>CO<sub>3</sub> (8.3 g) with stirring for 15 h. After the removal of K<sub>2</sub>CO<sub>3</sub> and acetone, the residue was recrystallized from MeOH to give **14** (4.82 g, 85%) as colorless needles, mp 112–113 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.27 (6H, s, CH<sub>3</sub> × 2), 1.69 and 2.59 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.37 (3H, s, COCH<sub>3</sub>), 2.43 (3H, s, C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>), 4.77 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.45 (1H, s, C<sub>8</sub>-H), 7.26 and 7.73 (each 2H, d, *J* = 9 Hz, arom-H), 7.25 (5H, s, C<sub>6</sub>H<sub>5</sub>). *Anal.* Calcd for C<sub>27</sub>H<sub>28</sub>O<sub>6</sub>S: C, 67.48; H, 5.87. Found: C, 67.54; H, 5.81.

**6-Acetyl-5-benzyl-7-hydroxy-2,2-dimethylchroman (11)**—Compound **14** (4.60 g) was hydrolyzed with 10% KOH solution (50 ml) in EtOH (150 ml) under reflux for 3 h. The reaction mixture was concentrated to about 50 ml, poured into ice-cold water, acidified with diluted HCl, and extracted with EtOAc. The EtOAc solution was washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the residue was recrystallized from MeOH to give **11** (2.66 g, 85%) as colorless needles, mp 99–100 °C (no depression in a mixed melting-point determination with a sample prepared by the direct benzylation of **10**).

**2',4-Bis(benzyl-2,5-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (15) and 4',5-Bis(benzyl-2,5-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]flavanone (16)**—A mixture of **11** (2 g) and **9** (1.40 g) was refluxed in the presence of piperidine (1.5 ml) in EtOH (100 ml) for 6 h. The reaction mixture was concentrated to about 50 ml and poured into ice-cold water, and acidified with diluted HCl. The mixture was allowed to stand overnight in a refrigerator to give yellow precipitates, which were extracted with EtOAc, washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure, and the residue was chromatographed over a silica gel column with ClCH<sub>2</sub>CH<sub>2</sub>Cl to give the chalcone **15** (*R*<sub>f</sub> = 0.60) and the flavanone **16** (*R*<sub>f</sub> = 0.44). The chalcone **15** was recrystallized from MeOH to give yellow needles (1.30 g, 44%), mp 128–130 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.35 (6H, s, CH<sub>3</sub> × 2), 1.78 and 2.70 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.55 and 3.67 (each 3H, s, OCH<sub>3</sub>), 4.75 and 5.17 (each 2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.20 (1H, s, C<sub>5</sub>-H), 6.45 (1H, s, C<sub>3</sub>-H), 6.85 (1H, s, C<sub>6</sub>-H), 7.25 and 7.35 (each 5H, brs,

C<sub>6</sub>H<sub>5</sub>), 7.82 and 8.26 (each 1H, d, *J* = 16 Hz, CH =), 13.10 (1H, s, OH). *Anal.* Calcd for C<sub>36</sub>H<sub>36</sub>O<sub>7</sub>: C, 74.46; H, 6.25. Found: C, 74.22; H, 6.06.

The flavanone **16** was recrystallized from MeOH to give pale yellow needles (0.70 g, 24%), mp 176–177 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.28 (6H, s, CH<sub>3</sub> × 2), 1.66 and 2.50 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.70–3.00 (2H, m, C<sub>3</sub>-H), 3.67 and 3.84 (each 3H, s, OCH<sub>3</sub>), 5.12 (4H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> × 2), 5.50–5.90 (1H, m, C<sub>2</sub>-H), 6.21 (1H, s, C<sub>8</sub>-H), 6.50 (1H, s, C<sub>3</sub>-H), 7.08 (1H, s, C<sub>6</sub>-H), 7.20–7.60 (10H, br s, C<sub>6</sub>H<sub>5</sub> × 2). *Anal.* Calcd for C<sub>36</sub>H<sub>36</sub>O<sub>7</sub>: C, 74.46; H, 6.25. Found: C, 74.42; H, 6.23.

**6'-Acetoxy-2',4-bis(benzyloxy)-2,5-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (17)**—A mixture (1.92 g) of **15** and **16** was converted into the acetate **17** by an acetic anhydride–sodium acetate method. Compound **17** was recrystallized from MeOH–EtOAc to give pale yellow needles (1.96 g, 95%), mp 164–165 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.28 (6H, s, CH<sub>3</sub> × 2), 1.72 and 2.63 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.15 (3H, s, COCH<sub>3</sub>), 3.68 and 3.76 (each 3H, s, OCH<sub>3</sub>), 4.80 and 5.13 (each 2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.34 (1H, s, C<sub>5</sub>-H), 6.43 (1H, s, C<sub>3</sub>-H), 6.95 (1H, s, C<sub>6</sub>-H), 7.03 and 7.78 (each 1H, d, *J* = 16 Hz, CH =), 7.20 and 7.30 (each 5H, s, C<sub>6</sub>H<sub>5</sub>). *Anal.* Calcd for C<sub>38</sub>H<sub>38</sub>O<sub>8</sub>: C, 73.29; H, 6.15. Found: C, 73.24; H, 6.18.

**4'-Benzyloxy-5-hydroxy-2',5'-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]isoflavone (18)**—A mixture of **17** (3.90 g) and thallium (III) nitrate trihydrate (3.64 g) was stirred in MeOH (3 l) at 35–36 °C for 8 h, and then 10% HCl (150 ml) was added, and the mixture was further refluxed for 3 h. The precipitates were filtered off, and the filtrate was concentrated to 2 l and poured into a large amount of ice-cold water. The mixture was allowed to stand overnight at room temperature to give precipitates. The precipitates were recrystallized from MeOH–EtOAc to give the linear 5-hydroxydihydropyranoisoflavone **18** (2.30 g, 75%) as pale yellow needles, mp 150–151 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.37 (6H, s, CH<sub>3</sub> × 2), 1.83 and 2.73 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.65 and 3.85 (each 3H, s, OCH<sub>3</sub>), 5.18 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.32 (1H, s, C<sub>8</sub>-H), 6.61 (1H, s, C<sub>3</sub>-H), 6.90 (1H, s, C<sub>6</sub>-H), 7.20–7.50 (5H, m, C<sub>6</sub>H<sub>5</sub>), 7.77 (1H, s, C<sub>2</sub>-H), 13.17 (1H, s, OH). *Anal.* Calcd for C<sub>29</sub>H<sub>28</sub>O<sub>7</sub>: C, 71.30; H, 5.78. Found: C, 71.24; H, 5.74.

**4',5-Dihydroxy-2',5'-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]isoflavone (Dihydroelongatin) (19)**—Compound **18** (1.65 g) was hydrogenolyzed over 10% palladium on charcoal (0.46 g) in a mixture of MeOH (300 ml) and EtOAc (100 ml) until the uptake of hydrogen ceased. The catalyst was filtered off and the solvent was removed under reduced pressure. The residue was recrystallized from acetone–hexane to give the dihydropyranoisoflavone **19** (1.19 g, 88%) as colorless needles, mp 181–183 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.37 (6H, s, CH<sub>3</sub> × 2), 1.83 and 2.72 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.70 and 3.83 (each 3H, s, OCH<sub>3</sub>), 5.80 (1H, s, C<sub>4</sub>-OH), 6.30 (1H, s, C<sub>8</sub>-H), 6.62 (1H, s, C<sub>3</sub>-H), 6.85 (1H, s, C<sub>6</sub>-H), 7.78 (1H, s, C<sub>2</sub>-H), 13.17 (1H, s, C<sub>5</sub>-OH). *Anal.* Calcd for C<sub>22</sub>H<sub>22</sub>O<sub>7</sub>: C, 66.32; H, 5.57. Found: C, 66.29; H, 5.55.

**4',5-Dihydroxy-2',5'-dimethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone (Elongatin) (1)**—A mixture of **19** (406 mg) and DDQ (304 mg) in anhydrous *o*-dichlorobenzene (25 ml) was heated with stirring at 180 °C for 5 h, and then the solvent was removed under reduced pressure. The residue was chromatographed over a silica gel column with 1,2-dichloroethane–acetone (40:1) to give the desired linear pyranoisoflavone **1**, which was further purified by preparative TLC on silica gel with CCl<sub>4</sub>–EtOAc (6:1) and recrystallized from MeOH to give colorless needles (155 mg, 38%), mp 182–184 °C; lit.,<sup>10</sup> mp 181–182 °C (no depression in a mixed melting-point determination with natural elongatin). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.48 (6H, s, CH<sub>3</sub> × 2), 3.73 and 3.87 (each 3H, s, OCH<sub>3</sub>), 5.59 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.74 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 5.76 (1H, s, C<sub>4</sub>-OH), 6.32 (1H, s, C<sub>8</sub>-H), 6.66 (1H, s, C<sub>3</sub>-H), 6.88 (1H, s, C<sub>6</sub>-H), 7.83 (1H, s, C<sub>2</sub>-H), 13.20 (1H, s, C<sub>5</sub>-OH). *Anal.* Calcd for C<sub>22</sub>H<sub>20</sub>O<sub>7</sub>: C, 66.66; H, 5.09. Found: C, 66.69; H, 5.00.

**4',5-Diacetoxy-2',5'-dimethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone (21)**—Acetylation of **1** (62 mg) by an acetic anhydride–pyridine method afforded the diacetate **21**, which was recrystallized from MeOH to give colorless needles (59 mg, 78%), mp 227–228 °C (lit.,<sup>10</sup> mp 226–227 °C). UV λ<sub>max</sub> nm (log ε): 263 (4.57), 292 (4.22), 334 (3.94). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.48 (6H, s, CH<sub>3</sub> × 2), 2.30 and 2.41 (each 3H, s, COCH<sub>3</sub>), 3.68 and 3.77 (each 3H, s, OCH<sub>3</sub>), 5.73 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.47 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 6.69 (1H, s, C<sub>8</sub>-H), 6.69 (1H, s, C<sub>3</sub>-H), 6.92 (1H, s, C<sub>6</sub>-H), 7.73 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>26</sub>H<sub>24</sub>O<sub>9</sub>: C, 64.99; H, 5.04. Found: C, 64.95; H, 5.14.

**2',4',5,5'-Tetramethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone (20)**—A mixture of **1** (74 mg), dimethyl sulfate (2 ml), and K<sub>2</sub>CO<sub>3</sub> (3 g) was refluxed with stirring in acetone (30 ml) for 6 h. The resulting compound was chromatographed over a silica gel column with CHCl<sub>3</sub>–acetone (20:1) and crystallized from MeOH to give **20** (59 mg, 75%) as colorless needles, mp 132–134 °C. UV λ<sub>max</sub> nm (log ε): 266 (4.55), 292i (4.29), 335i (3.85). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.46 (6H, s, CH<sub>3</sub> × 2), 3.73, 3.82, 3.86, and 3.88 (each 3H, s, OCH<sub>3</sub>), 5.66 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.71 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 6.57 (1H, s, C<sub>8</sub>-H), 6.57 (1H, s, C<sub>3</sub>-H), 6.86 (1H, s, C<sub>6</sub>-H), 7.72 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>24</sub>H<sub>24</sub>O<sub>7</sub>: C, 67.91; H, 5.70. Found: C, 67.81; H, 5.71.

**4-Benzyloxy-6'-hydroxy-2,2',5-trimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (23)**—A mixture of 6-acetyl-7-hydroxy-5-methoxy-2,2-dimethylchroman (**22**) (2 g) and **9** (2.2 g) was refluxed in the presence of piperidine (1.4 ml) in EtOH (50 ml) for 10 h. The reaction mixture was poured into ice-cold water, acidified with diluted HCl, and extracted with EtOAc. The EtOAc solution was washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed, and the residue was chromatographed over a silica gel column with ClCH<sub>2</sub>CH<sub>2</sub>Cl–EtOAc (40:1). The resulting compound was crystallized from petroleum ether to give the chalcone **23** (2.62 g, 65%) as yellow needles, mp

85–86 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.35 (6H, s, CH<sub>3</sub> × 2), 1.80 and 2.71 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.69, 3.77, and 3.87 (each 3H, s, OCH<sub>3</sub>), 5.18 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.17 (1H, s, C<sub>5</sub>-H), 6.50 (1H, s, C<sub>3</sub>-H), 7.13 (1H, s, C<sub>6</sub>-H), 7.30 (5H, s, C<sub>6</sub>H<sub>5</sub>), 7.80 and 8.20 (each 1H, d, *J* = 16 Hz, CH =), 13.18 (1H, s, OH). *Anal.* Calcd for C<sub>30</sub>H<sub>32</sub>O<sub>7</sub>: C, 71.41; H, 6.39. Found: C, 71.13; H, 6.56.

**6'-Acetoxy-4-benzyloxy-2,2',5-trimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (24)**—Compound **23** (1.5 g) was converted into the acetate **24** by an acetic anhydride–sodium acetate method. Compound **24** was recrystallized from MeOH to give pale yellow needles (1.31 g, 83%), mp 137–138 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.33 (6H, s, CH<sub>3</sub> × 2), 1.77 and 2.71 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.11 (3H, s, COCH<sub>3</sub>), 3.68 (6H, s, OCH<sub>3</sub> × 2), 3.81 (3H, s, OCH<sub>3</sub>), 5.12 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.32 (1H, s, C<sub>5</sub>-H), 6.45 (1H, s, C<sub>3</sub>-H), 7.00 (1H, s, C<sub>6</sub>-H), 6.97 and 7.72 (each 1H, d, *J* = 16 Hz, CH =), 7.31 (5H, s, C<sub>6</sub>H<sub>5</sub>). *Anal.* Calcd for C<sub>32</sub>H<sub>34</sub>O<sub>7</sub>: C, 72.43; H, 6.46. Found: C, 72.33; H, 6.33.

**4'-Benzyloxy-2',5,5'-trimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]isoflavone (25)**—A mixture of **24** (1.06 g) and TTN (1.03 g) was stirred in MeOH (80 ml) at 35–36 °C for 8 h, and then 10% HCl (5 ml) was added, and the mixture was further refluxed for 3 h. The reaction mixture was worked up by a method similar to that used for the preparation of **18**. The resulting precipitates were chromatographed over a silica gel column with CHCl<sub>3</sub>–acetone (50:1) and crystallized from CH<sub>2</sub>Cl<sub>2</sub>–petroleum ether to give **25** (605 mg, 62%) as colorless needles, mp 151–152 °C. UV λ<sub>max</sub> nm (log ε): 254 (4.42), 298 (4.32). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.35 (6H, s, CH<sub>3</sub> × 2), 1.81 and 2.82 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.60, 3.81, and 3.85 (each 3H, s, OCH<sub>3</sub>), 5.12 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.53 (1H, s, C<sub>8</sub>-H), 6.53 (1H, s, C<sub>3</sub>-H), 6.88 (1H, s, C<sub>6</sub>-H), 7.15–7.45 (5H, m, C<sub>6</sub>H<sub>5</sub>), 7.68 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>30</sub>H<sub>30</sub>O<sub>7</sub>: C, 71.70; H, 6.02. Found: C, 71.71; H, 6.04.

**4'-Hydroxy-2',5,5'-trimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]isoflavone (26)**—Compound **25** (1.50 g) was hydrogenolyzed over 10% palladium on charcoal (380 mg) in MeOH (150 ml) until the uptake of hydrogen ceased. The resulting compound was chromatographed over a silica gel column with ClCH<sub>2</sub>CH<sub>2</sub>Cl–EtOAc (5:1) to give the 4'-hydroxyisoflavone **26**, which was crystallized from ether to give colorless needles (920 mg, 75%), mp 188–189 °C. UV λ<sub>max</sub> nm (log ε): 253 (4.35), 297 (4.28). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.37 (6H, s, CH<sub>3</sub> × 2), 1.83 and 2.85 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.68, 3.83, and 3.88 (each 3H, s, OCH<sub>3</sub>), 5.83 (1H, s, C<sub>4</sub>-OH), 6.60 (1H, s, C<sub>8</sub>-H), 6.60 (1H, s, C<sub>3</sub>-H), 6.87 (1H, s, C<sub>6</sub>-H), 7.74 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>23</sub>H<sub>24</sub>O<sub>7</sub>: C, 66.98; H, 5.87. Found: C, 66.95; H, 5.90.

**2',4',5,5'-Tetramethoxy-2'',2''-dimethyldihydropyrano[5'',6''-g]isoflavone (27)**—A mixture of **26** (560 mg), dimethyl sulfate (0.8 ml), and K<sub>2</sub>CO<sub>3</sub> (2.5 g) was refluxed with stirring in anhydrous acetone (50 ml) for 5 h. The resulting compound was recrystallized from MeOH–H<sub>2</sub>O to give **27** (500 mg, 86%) as colorless needles, mp 160–161 °C. UV λ<sub>max</sub> nm (log ε): 254 (4.34), 297 (4.28). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.35 (6H, s, CH<sub>3</sub> × 2), 1.82 and 2.83 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.71 and 3.80 (each 3H, s, OCH<sub>3</sub>), 3.87 (6H, s, OCH<sub>3</sub> × 2), 6.54 (1H, s, C<sub>8</sub>-H), 6.54 (1H, s, C<sub>3</sub>-H), 6.83 (1H, s, C<sub>6</sub>-H), 7.67 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>24</sub>H<sub>26</sub>O<sub>7</sub>: C, 67.59; H, 6.15. Found: C, 67.61; H, 6.26.

**2',4',5,5'-Tetramethoxy-2'',2''-dimethylpyrano[5'',6''-g]isoflavone (20)**—A mixture of **27** (213 mg) and DDQ (136 mg) in anhydrous *o*-dichlorobenzene (30 ml) was heated with stirring at 185 °C for 6 h. The resulting compound was chromatographed over a silica gel column with CHCl<sub>3</sub>–acetone–petroleum ether (10:1:2) to give the pyranisoflavone **20**, which was crystallized from petroleum ether to give colorless needles (85 mg, 40%), mp 131–133 °C (no depression in a mixed melting-point determination with a sample prepared by the methylation of **1**). *Anal.* Calcd for C<sub>24</sub>H<sub>24</sub>O<sub>7</sub>: C, 67.91; H, 5.70. Found: C, 67.90; H, 5.62.

**4,6'-Bis(benzyloxy)-2'-hydroxy-2,5-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (28)**—A mixture of **12** (2.91 g) and **9** (2.74 g) was refluxed in the presence of piperidine (1.4 ml) in EtOH (130 ml) for 6 h. The reaction mixture was worked up by a method similar to that used for the preparation of **15**. The precipitates were recrystallized from CHCl<sub>3</sub> to give the chalcone **28** (2.50 g, 48%) as yellow needles, mp 180–182 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.35 (6H, s, CH<sub>3</sub> × 2), 1.80 and 2.65 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.47 and 3.64 (each 3H, s, OCH<sub>3</sub>), 5.06 and 5.15 (each 2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 5.95 (1H, s, C<sub>5</sub>-H), 6.43 (1H, s, C<sub>3</sub>-H), 6.76 (1H, s, C<sub>6</sub>-H), 7.10–7.50 (10H, m, C<sub>6</sub>H<sub>5</sub> × 2), 7.76 and 8.13 (each 1H, d, *J* = 16 Hz, CH =), 14.70 (1H, s, OH). *Anal.* Calcd for C<sub>36</sub>H<sub>36</sub>O<sub>7</sub>: C, 74.46; H, 6.25. Found: C, 74.32; H, 6.18.

**2'-Acetoxy-4,6'-bis(benzyloxy)-2,5-dimethoxy-2'',2''-dimethyldihydropyrano[5'',6''-c]chalcone (29)**—Compound **28** (2 g) was converted into the acetate **29** by an acetic anhydride–pyridine method. The resulting precipitates were crystallized from ether to give **29** (1.80 g, 84%) as pale yellow needles, mp 111–113 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.33 (6H, s, CH<sub>3</sub> × 2), 1.77 and 2.53 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 2.20 (3H, s, COCH<sub>3</sub>), 3.68 and 3.73 (each 3H, s, OCH<sub>3</sub>), 5.00 and 5.18 (each 2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.38 (1H, s, C<sub>5</sub>-H), 6.47 (1H, s, C<sub>3</sub>-H), 6.97 (1H, s, C<sub>6</sub>-H), 7.03 and 7.78 (each 1H, d, *J* = 16 Hz, CH =), 7.10–7.50 (10H, m, C<sub>6</sub>H<sub>5</sub> × 2). *Anal.* Calcd for C<sub>38</sub>H<sub>38</sub>O<sub>8</sub>: C, 73.29; H, 6.15. Found: C, 73.16; H, 5.98.

**4',5-Bis(benzyloxy)-2',5'-dimethoxy-2'',2''-dimethyldihydropyrano[6'',5''-h]isoflavone (30) and 4'-Benzyloxy-5-hydroxy-2',5'-dimethoxy-2'',2''-dimethyldihydropyrano[6'',5''-h]isoflavone (31)**—A mixture of **29** (1.51 g) and TTN (1.28 g) was stirred in MeOH (300 ml) at 35–36 °C for 7 h, and then 10% HCl (15 ml) was added, and the mixture was further refluxed for 3 h. The reaction mixture was worked up by a method similar to that used for the preparation of **18**. The resulting precipitates were recrystallized from acetone–water to give the angular dihydropyranoisoflavone **30** [750 mg, 53%; *R*<sub>f</sub> = 0.56 (CHCl<sub>3</sub>–acetone = 40:1)] as colorless needles, mp 192–193 °C. UV λ<sub>max</sub> nm (log ε): 254i (4.44), 259 (4.52), 295 (4.22). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.36 (6H, s, CH<sub>3</sub> × 2), 1.83 and 2.78 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>),

3.63 and 3.85 (each 3H, s, OCH<sub>3</sub>), 5.17 (4H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> × 2), 6.35 (1H, s, C<sub>6</sub>-H), 6.61 (1H, s, C<sub>3</sub>-H), 7.00 (1H, s, C<sub>6</sub>-H), 7.20–7.70 (10H, m, C<sub>6</sub>H<sub>5</sub> × 2), 7.78 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>36</sub>H<sub>34</sub>O<sub>7</sub>: C, 74.73; H, 5.92. Found: C, 74.61; H, 5.82.

The mother liquor was chromatographed over a silica gel column with CHCl<sub>3</sub>–acetone (40:1). The resulting compound was crystallized from MeOH to give the 5-hydroxydihydropyranoisoflavone **31** (80 mg; *R*<sub>f</sub> = 0.72) as colorless needles, mp 196–197 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.36 (6H, s, CH<sub>3</sub> × 2), 1.84 and 2.77 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.66 and 3.85 (each 3H, s, OCH<sub>3</sub>), 5.18 (2H, s, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 6.26 (1H, s, C<sub>6</sub>-H), 6.63 (1H, s, C<sub>3</sub>-H), 6.92 (1H, s, C<sub>6</sub>-H), 7.25–7.55 (5H, m, C<sub>6</sub>H<sub>5</sub>), 7.90 (1H, s, C<sub>2</sub>-H), 12.60 (1H, s, C<sub>5</sub>-OH). *Anal.* Calcd for C<sub>29</sub>H<sub>28</sub>O<sub>7</sub>: C, 71.30; H, 5.78. Found: C, 71.58; H, 5.50.

**4',5-Dihydroxy-2'',2''-dimethoxy-2'',2''-dimethyldihydropyrano[6'',5''-h]isoflavone (32)**—Compound **30** (583 mg) was hydrogenolyzed over 10% palladium on charcoal (150 mg) in a mixture of MeOH (200 ml) and EtOAc (30 ml) until the uptake of hydrogen ceased. The reaction mixture was worked up by a method similar to that used for the preparation of **19** and recrystallized from acetone–water to give **32** (357 mg, 89%) as colorless needles, mp 212–213 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.38 (6H, s, CH<sub>3</sub> × 2), 1.85 and 2.78 (each 2H, t, *J* = 7 Hz, CH<sub>2</sub>), 3.73 and 3.86 (each 3H, s, OCH<sub>3</sub>), 5.78 (1H, s, C<sub>4</sub>-OH), 6.26 (1H, s, C<sub>6</sub>-H), 6.65 (1H, s, C<sub>3</sub>-H), 6.88 (1H, s, C<sub>6</sub>-H), 7.91 (1H, s, C<sub>2</sub>-H), 12.60 (1H, s, C<sub>5</sub>-OH). *Anal.* Calcd for C<sub>22</sub>H<sub>22</sub>O<sub>7</sub>: C, 66.33; H, 5.56. Found: C, 66.27; H, 5.61.

**4',5-Dihydroxy-2'',5'-dimethoxy-2'',2''-dimethylpyrano[6'',5''-h]isoflavone (2)**—A mixture of **32** (100 mg) and DDQ (85 mg) in anhydrous chlorobenzene (15 ml) was heated with stirring at 140 °C for 2 h. The resulting compound was chromatographed over a silica gel column with ClCH<sub>2</sub>CH<sub>2</sub>Cl–EtOAc–petroleum ether (50:3:1) and crystallized from petroleum ether to give the desired angular pyranoisoflavone **2** (51 mg, 51%) as pale yellow needles, mp 173–175 °C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.48 (6H, s, CH<sub>3</sub> × 2), 3.72 and 3.86 (each 3H, s, OCH<sub>3</sub>), 5.56 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.67 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 5.76 (1H, s, C<sub>4</sub>-OH), 6.29 (1H, s, C<sub>6</sub>-H), 6.63 (1H, s, C<sub>3</sub>-H), 6.88 (1H, s, C<sub>6</sub>-H), 7.86 (1H, s, C<sub>2</sub>-H), 12.92 (1H, s, C<sub>5</sub>-OH). *Anal.* Calcd for C<sub>22</sub>H<sub>20</sub>O<sub>7</sub>: C, 66.66; H, 5.09. Found: C, 66.65; H, 4.95.

**4',5-Diacetoxy-2'',5'-dimethoxy-2'',2''-dimethylpyrano[6'',5''-h]isoflavone (34)**—Compound **2** (250 mg) was converted into the diacetate **34** by an acetic anhydride–pyridine method. The resulting compound was recrystallized from MeOH to give **34** (220 mg, 82%) as colorless needles, mp 224–226 °C. UV λ<sub>max</sub> nm (log ε): 263 (4.53), 299 (4.06). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.47 (6H, s, CH<sub>3</sub> × 2), 2.29 and 2.35 (each 3H, s, COCH<sub>3</sub>), 3.67 and 3.76 (each 3H, s, OCH<sub>3</sub>), 5.63 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.71 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 6.46 (1H, s, C<sub>6</sub>-H), 6.67 (1H, s, C<sub>3</sub>-H), 6.92 (1H, s, C<sub>6</sub>-H), 7.78 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>26</sub>H<sub>24</sub>O<sub>9</sub>: C, 64.99; H, 5.04. Found: C, 64.95; H, 4.81.

**5-Hydroxy-2'',4',5'-trimethoxy-2'',2''-dimethylpyrano[6'',5''-h]isoflavone (Toxicarol Isoflavone) (3)**—A mixture of **2** (200 mg), CH<sub>3</sub>I (0.1 ml), and K<sub>2</sub>CO<sub>3</sub> (2.07 g) was heated with stirring in anhydrous acetone (30 ml) at 55–57 °C for 7 h. The resulting compound was recrystallized from EtOAc to give **3** (178 mg, 86%) as pale yellow needles, mp 219–220 °C; lit., mp 220–220.5 °C,<sup>9)</sup> mp 219 °C.<sup>16)</sup> <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.46 (6H, s, CH<sub>3</sub> × 2), 3.75, 3.81, and 3.89 (each 3H, s, OCH<sub>3</sub>), 5.52 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.64 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 6.24 (1H, s, C<sub>6</sub>-H), 6.57 (1H, s, C<sub>3</sub>-H), 6.84 (1H, s, C<sub>6</sub>-H), 7.84 (1H, s, C<sub>2</sub>-H), 12.85 (1H, s, C<sub>5</sub>-OH). *Anal.* Calcd for C<sub>23</sub>H<sub>22</sub>O<sub>7</sub>: C, 67.31; H, 5.40. Found: C, 67.13; H, 5.38.

**2',4',5,5'-Tetramethoxy-2'',2''-dimethylpyrano[6'',5''-h]isoflavone (33)**—A mixture of **2** (60 mg), dimethyl sulfate (1.5 ml), and K<sub>2</sub>CO<sub>3</sub> (2.5 g) was refluxed with stirring in anhydrous acetone (30 ml) for 8 h. The resulting compound was recrystallized from MeOH–H<sub>2</sub>O to give the dimethyl ether **33** (51 mg, 80%) as colorless needles, mp 179–180 °C; lit.,<sup>16)</sup> mp 178 °C. UV λ<sub>max</sub> nm (log ε): 265 (4.63), 296i (4.11). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 1.47 (6H, s, CH<sub>3</sub> × 2), 3.72 and 3.82 (each 3H, s, OCH<sub>3</sub>), 3.88 (6H, s, OCH<sub>3</sub> × 2), 5.57 (1H, d, *J* = 10 Hz, C<sub>3</sub>-H), 6.70 (1H, d, *J* = 10 Hz, C<sub>4</sub>-H), 6.29 (1H, s, C<sub>6</sub>-H), 6.57 (1H, s, C<sub>3</sub>-H), 6.93 (1H, s, C<sub>6</sub>-H), 7.78 (1H, s, C<sub>2</sub>-H). *Anal.* Calcd for C<sub>24</sub>H<sub>24</sub>O<sub>7</sub>: C, 67.91; H, 5.70. Found: C, 67.83; H, 5.72.

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