Regioselective Synthesis of 6-Alkyl- and 6-Prenylpolyhydroxyisoflavones and 6-Alkylcoumaronochromone Derivatives

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The palladium-catalyzed coupling reaction of 6-iodoisoflavone, prepared from 3′-iodoacetophenone derivative, with 2-methyl-3-buten-2-ol gave 6-alkynylisoflavone derivative, which was hydrogenated to give 6-alkylhydroxyisoflavone (luteone hydrate) (2). Dehydration of 2 gave 2′,4′,5,7-tetrahydroxy-6-prenylisoflavone (luteone) (1). Wighteone hydrate (3) was also synthesized from 6-iodotris(benzyloxy)isoflavone in a similar manner. 6-Alkyl-4′,5,7-trihydroxy-coumaronochromone (4) was synthesized by oxidative cyclization of 2 with o-chloranil.

Key words isoflavone; prenylisoavone; luteone; regioselective prenylation; coumaronochromone; o-chloranil

Prenyl (=3-methyl-2-butenyl)isoflavones and (3-hydroxy-3-methylbutyl)isoflavones, which contain an alkyl or alkenyl group in the A- and/or B-ring, are widely distributed in nature and have antifungal activity. Luteone, known as a phytoalexin, was first isolated in 1973 from immature fruits of Lupinus luteus (Leguminosae). The structure was assigned as 2′,4′,5,7-tetrahydroxy-6-(3-methyl-2-butenyl)isoflavone (1) by spectroscopic and chemical studies. The same isoflavone 1 was also isolated from healthy leaves or roots of white lupin (Lupinus albus L., cv. Kievskij Mutant) and the roots of yellow lupin (Lupinus luteus L., cv. Barpin) together with luteone hydrate, the structure of which was assigned to be 2′,4′,5,7-tetrahydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (2) by spectroscopic analysis. Luteone hydrate (2) was isolated as a fungal metabolite of luteone (1) with cultures of Aspergillus flavus and Botrytis cinerea. Wighteone hydrate [4′,5,7-trihydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone] (3) was also isolated as a fungal metabolite of wighteone [4′,5,7-trihydroxy-6-(3-methyl-2-butenyl)isoflavone] as a by-product during the isolation of 1 and 2 from the same natural source, it is considered that 2 is a precursor of 1 and dehydration of 2 would lead to 1. The total syntheses of isoflavones 1, 2, and 3 have not been achieved yet, although the dimethyl ether of luteone (1) has been synthesized. The reason seems to be due to the difficulty in introducing an alkyl or alkenyl group regioselectively into the isoflavone nucleus and the selectivity of protection and consequent deprotection. Furthermore, 6-alkylpolyhydroxyisoflavones are isomerized to the corresponding isomers, 8-alkylpolyhydroxyisoflavones, by bases. We need to solve these problems for the regioselective synthesis of alkylpolyhydroxyisoflavones. As a continuation of our studies on the regioselective synthesis of alkyl- and prenylisoavones, we wish to report here the first syntheses of 1, 2, and 3 using the palladium (0)-catalyzed coupling reaction of the corresponding iodoisoflavone with 2-methyl-3-buten-2-ol. Recently, the new coumaronochromones (=benzofuro[2,3-b][1]benzopyran-1-ones) lupulin (8-alkylcoumaronochromone from the root of yellow lupin) and lupalbin B (6-prenylcoumaronochromone from the root of white lupin) have also been isolated. However, 6-alkylcoumaronochromone (4), which is considered to be a precursor of lupalin B, has yet to be isolated from natural sources. We have examined the simple and general applicability of DDQ or o-chloranil to the synthesis of alkylpolyhydroxycoumaronochromones from the corresponding 2′-hydroxyisoflavones. We wish to report here the synthesis of compound 4 by oxidative cyclization of compound 2 with o-chloranil.

Results and Discussion

The catalytic hydrogenation of 2′,4′-bis(benzyloxy)-6′-methoxymethoxyacetophenone over Pd/C, followed by iodination of the resulting 2′,4′-dihydroxyacetophenone 5 with I₂ and H₂O₂ gave the 3′-iodoacetophenone 6 in 92% yield. Compound 6 was converted into bis(benzyloxy)acetophenone 7, the structure of which was determined by direct comparison with a sample of the isomer [2′,4′-bis(benzyloxy)-5′-iodo-6′-methoxymethoxyacetophenone (mp 99—100°C)] and 1H-NMR-NOE analysis. The mixture of 7 with the isomer showed a marked decrease in the melting point relative to that of each compound. Compound 7 was not obtainable with the phenyl group of 5, which was oxidatively rearranged by treatment with dilute HCl to give 3′-iodo-6′-hydroxychalcone 9 in 86% yield. Oxidative rearrangement of acetate 10, prepared from 9, with thallium(III) nitrate trihydrate (TTN), followed by hydrolysis of the resulting mixture 11 with aqueous sodium hydroxide gave the desired 6-iodoisoflavone 12 in 40% yield and the chalcone 9, the structures of which were identified by 1H-NMR spectral analysis. On the basis of the results, it was shown that decacylation of 10 with TTN took place more easily than the oxidative rearrangement of the phenyl group of 10 to give the chalcone 9. Therefore 9 was converted into benzoate 13, which was oxidatively rearranged with TTN to give the corresponding acetal 14 easily. The crude acetal 14 was hydrolyzed with aqueous sodium hydroxide to give the 6-iodoisoflavone 12 in 70% yield via two steps from 13. The coupling reaction of 12 with 2-methyl-3-buten-2-ol in the presence of Pd(0) in triethylamine gave 6-(3-hydroxy-3-methylbutyl)isoflavone 15 in 71% yield. The catalytic hydrogenation of 15 gave 2′,4′,5,7-
tetrahydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (2) in 96% yield. The 1H-NMR spectrum of 2 was identical to that of a natural sample of luteone hydrate7) (Table 1) and other physical properties (see Experimental). On the basis of these results, the structure of luteone hydrate was confirmed by the first synthesis of 2/H11032,4/H11032,5,7-tetrahydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (2).

Exhaustive benzoylation (7 h) of 2 afforded partly the isomer [2/H11032,4/H11032,7-tris(benzoyloxy)-5-hydroxy-8-(3-hydroxy-3-methylbutyl)isoflavone]. To prevent the isomerization, the partial benzoylation of compound 2 gave 2/H11032,4/H11032,7-tris(benzoyl-oxy)isoflavone 16 for 30 min in 85% yield, and subsequently compound 16 was tosylated for 20 min to give 5-tosyloxyisoflavone 17 in 91% yield. Compound 17 was dehydrated with BF3 · OEt2 at room temperature to give 6-prenyl-5-tosyloxyisoflavone (20%), 5-hydroxy-6-prenylisoflavone (25%), and dihydropyran derivative 20 (45%), respectively. In this reaction, it was shown that part of 18 was initially detosylated, and the resulting compound 19 was subsequently cyclized to give 20. The formation of 20 strongly supported the structure of 2 and decreased the yield of 19. The tosylate 17 was dehydrated with TsOH · H2O to give a mixture of 6-prenylisoflavone 18 and the regioisomer 6-(3-methyl-3-butenyl)isoflavone 21. The 1H-NMR spectrum of the tosylate mixture (18 and 21) showed the ratio of 18 to 21 to be 85 : 15 [peaks due to CH2CH2C(CH3)2 at δ = 3.36 (2H, d) and CH2CH2C(CH3)2 at δ = 4.57 (2H, s)]. The mixture (18 and 21) reacted quantitatively with benzohydroxymoyl chloride14) in dry CH2Cl2 at room temperature to give a mixture of the unchanged 6-prenylisoflavone 18 and the terminal alkene-cyclic adduct, and then 18 was purified by silica gel column chromatography. The detosylation of 18 with BCl3, followed by hydrolysis of the resultant compound 19 with 10% NaOH in a mixture of methanol and dioxane at room temperature, gave 2/H11032,4/H11032,5,7-tetrahydroxy-6-(3-methyl-2-butenyl)isoflavone (1) in 66% yield (1H-NMR in Table 1), which was converted into the tetraacetate derivative 22. The 1H-NMR, IR, and UV spectral data for 1 were completely identical to those of a natural sample of luteone.5,6) On the basis of these results, the structure of luteone was confirmed for the first time by the synthesis of 2/H11032,4/H11032,5,7-tetrahydroxy-6-(3-methyl-2-butenyl)isoflavone (1).

Table 1. 1H-NMR (400 MHz, CD3COCD3) Data for Prenyl- and Alkylisoflavones 1, 2, Luteone, and Luteone Hydratea)

<table>
<thead>
<tr>
<th>Compound</th>
<th>2-H</th>
<th>8-H</th>
<th>3'-H</th>
<th>5'-H</th>
<th>6'-H</th>
<th>2'-H</th>
<th>Me</th>
<th>CH2</th>
<th>CH=C</th>
<th>OH</th>
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<tr>
<td>1</td>
<td>8.14 s</td>
<td>6.53 s</td>
<td>6.48 d</td>
<td>6.44 dd</td>
<td>7.12 d</td>
<td>1.65 s</td>
<td>3.37 d</td>
<td>5.28 t</td>
<td>(J = 2.4)</td>
<td>(J = 2.4, 8.3)</td>
</tr>
<tr>
<td>Natural product7)</td>
<td>8.14 s</td>
<td>6.53 s</td>
<td>6.48 d</td>
<td>(Incomplete)</td>
<td>7.12 d</td>
<td>1.65 s</td>
<td>3.37 br d</td>
<td>5.28 br t</td>
<td>(J = 2.4, 8.9)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>8.15 s</td>
<td>6.52 s</td>
<td>6.49 d</td>
<td>6.44 dd</td>
<td>7.12 d</td>
<td>1.26 s</td>
<td>1.71 m</td>
<td>2.79 m</td>
<td>(J = 2.4, 8.3)</td>
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</tr>
<tr>
<td>Natural product7)</td>
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<td>6.52 s</td>
<td>6.48 d</td>
<td>(Incomplete)</td>
<td>7.12 d</td>
<td>1.25 s</td>
<td>1.71 m</td>
<td>2.81 m</td>
<td>(J = 2.4, 8.8)</td>
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</tr>
<tr>
<td>3</td>
<td>8.15 s</td>
<td>6.47 s</td>
<td>6.90 d</td>
<td>6.90 d</td>
<td>7.45 d</td>
<td>1.26 s</td>
<td>1.71 m</td>
<td>2.78 m</td>
<td>(J = 8.8)</td>
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<tr>
<td>Natural product7)</td>
<td>8.15 s</td>
<td>6.47 s</td>
<td>6.90 d</td>
<td>6.90 d</td>
<td>7.45 d</td>
<td>1.26 s</td>
<td>1.71 m</td>
<td>2.78 m</td>
<td>(J = 8.8)</td>
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</tr>
</tbody>
</table>

a) s, singlet; d, doublet; dd, double doublet; t, triplet; br, broad; m, multiplet.
Condensation of 7 with 4-benzylxybenzaldehyde and the subsequent hydrolysis of the resultant chalcone 24, which was converted into the corresponding benzoxo 25. The oxidative rearrangement of 25 with TTN for 20 h, followed by the hydrolysis of the resultant acetal 26, gave the corresponding 4'-benzylxy-6-iodoisoflavone 27 in 30% yield via three steps from 24. The yield of compound 27 was lower than that of the 2',4'-bis(benzyloxy)-6-iodoisoflavone 12. The reason depends on the number of the electron-releasing substituents in the B-ring.12,21 The coupling reaction of 27 with 2-methyl-3-buty-2-ol in the presence of Pd(0) gave 6-(3-hydroxy-3-methyl-1-butylnyl)isoflavone 28 in 57% yield. The catalytic hydrogenation of 28 over Pd/C gave 4',5,7,3'-tetrahydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (3) in 92% yield. The 4H-NMR spectrum and other physical properties were identical to those of a natural sample of wighteone hydrate10 (Table 1). On the basis of these results, the structure of wighteone hydrate was confirmed by the synthesis of 4',5,7,3'-tetrahydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (3).

The oxidative cyclization of the 2'-hydroxyisoflavone 2 with o-chloranil (2.2 eq) [the reduction potential (0.83 V) is lower than that (1.0 V) of DDQ]22,23 in dioxane gave the desired coumaronochrome 4 at 80 °C for 2 h in good yield. Compound 4 was easily converted into diacetate 29 at 0 °C using the acetic anhydride-pyridine method.

The present regioselective synthesis of isoidoisoflavones and the palladium (0)-catalyzed coupling reaction of isoidoisoflavones with 2-methyl-3-buty-2-ol have been shown to be efficient and useful procedures for the syntheses of prenyl- and alklypolyhydroxyisoflavones and O-alkylated prenylisoflavones.

Experimental

All the melting points were measured on a Yanaco MP-39 micro melting-point apparatus and are uncorrected. The 4H-NMR spectra were measured with a JEOL EX400 spectrometer (400 MHz), using tetramethylsilane as internal standard (δ, ppm). The IR spectra were recorded on a Hitachi 215 spectrophotometer, and the UV spectra were recorded on a Hitachi 124 spectrophotometer. Elemental analyses were performed with a Yanaco CHN corder model MT-5. Column chromatography and thin-layer chromatography (TLC) were carried out on Kieselgel 60 (70—230 mesh) and Kieselgel 60 F-254 (Merek).

2',4'-Dihydroxy-6'-methoxymethoxyacetophenone (5) 2',4'-Bis(benzylxy)-6'-methoxymethoxyacetophenone (4.5 g, 11.46 mmol) was hydrogenolyzed over Pd/C (5%) (450 mg) in MeOH (100 ml) and AcOEt (100 ml) at 18—23 °C until uptake of hydrogen ceased. After removal of the solvent under reduced pressure, the resulting compound was purified by silica gel column chromatography (AcOEt: hexane = 2:1 as a solvent) and recrystallized from a mixture of AcOEt and hexane to give dihydroxyacetophenone 5 (2.28 g, 94%) as colorless needles, mp 118—120 °C; 5'H-NMR (CDCl3) δ = 2.65 (3H, s, COCH3), 3.52 (3H, s, OCH3), 5.25 (2H, s, OCH2O), 5.25 (1H, s, C-OH), 6.04 (1H, d, J = 2.4 Hz, Ar-H), 6.14 (1H, d, J = 2.4 Hz, Ar-H), 13.79 (1H, s, C-OH). Anal. Calcd for C10H12O5: C, 66.67; H, 6.26. Found: C, 66.53; H, 6.07.

2',4'-Dihydroxy-3'-iodo-6'-methoxymethoxyacetophenone (6) The acetophenone 5 (3.16 g, 14.8 mmol) was dissolved in EtOH (30 ml), and iodine (1.88 g, 7.4 mmol) and periodic acid (3.16 g, 14.8 mmol) in water (10 ml) were added to the solution; the mixture was then stirred for 30 min at 40 °C. The mixture was cooled and diluted with water to give compound 6 as colorless needles (4.63 g, 92%), mp 160—161 °C; H-NMR (CDCl3) δ = 2.69 (3H, s, COCH3), 3.52 (3H, s, OCH3), 5.28 (2H, s, OCH2O), 5.98 (1H, s, C-OH), 6.44 (1H, s, C-H), 14.97 (1H, s, C-OH). Anal. Calcd for C10H12IO5: C, 55.61; H, 4.48. Found: C, 55.66; H, 4.48.

2',4'-Dihydroxy-3'-iodochalcone (10) and 2',4'-Dihydroxy-6'-methoxymethoxyacetophenone (8) To a mixture of 6 (1.0 g, 2.95 mmol), KOH (2.03 g, 35 mmol), and DMF (8 ml), a solution of benzyl chloride (0.75 ml, 6.5 mmol) in DMF (1 ml) was added dropwise with stirring under nitrogen at 70 °C for 30 min. The reaction mixture was extracted with CHCl3, washed with diluted HCl and water, and dried (Na2SO4). The resulting compound was recrystallized from a mixture of MeOH and AcOEt to yield 7 (623 mg, 80%) as colorless needles, mp 96—98 °C; 5'H-NMR (CDCl3) δ = 2.47 (3H, s, COCH3), 3.46 (3H, s, OCH3), 4.97 (2H, s, ArCH2), 5.15 (2H, s, OCH2O), 5.18 (2H, s, ArCH2), 6.65 (1H, s, C=H), 7.32—7.60 (10H, m, Ar-H×10). Anal. Calcd for C10H12O5: C, 66.74; H, 6.47. Found: C, 66.56; H, 6.48.

2',4'-Tetrahydroxy-3'-iodochalcone (9) A mixture of the acetophenone 7 (1.84 g, 5.34 mmol) and 2,4-bis(benzylxy)-benzaldehyde (1.70 g, 5.3 mmol) was stirred in the presence of KOH (2.0 g, 35 mmol) in EtOH (120 ml) at 80 °C for 45 min. Ice-water and 10% HCl were added to the reaction mixture to give 6'-methoxyacetophenone 8 as yellow precipitates. The collected crude solid 8 was dissolved in a mixture of CHCl3 (60 ml) and MeOH (60 ml). Concentrated HCl (3 ml) was added to the solution, and then the mixture was stirred at 40 °C for 1 h. The whole solution was extracted with CHCl3, and the chloroform extract was washed with water and dried (Na2SO4). After removal of the solvent, the resulting compound was recrystallized from a mixture of CHCl3 and MeOH to give 6'-hydroxychalcone 9 (2.35 g, 86% from 7) as yellow needles, mp 158—160 °C; H-NMR (CDCl3) δ = 4.82, 5.00, 5.07, and 5.20 (each 2H, s, PhCH2), 6.38 (1H, dd, J = 2.4 and 8.8 Hz, C=H), 6.41 (1H, s, C=H), 6.54 (1H, d, J = 2.4 Hz, C=H), 7.1—7.53 (21H, m, Ar-H×20), 7.90, and 8.29 (each 1H, d, J = 15.6 Hz, CH=), 13.77 (1H, s, C=OH). Anal. Calcd for C29H21O5C, 66.67; H, 6.45. Found: C, 66.43; H, 6.42.

6'-Acetoxy-2',4',2',4'-tetrahydroxy-3'-iodochalcone (10) and 2',4',5,7-Tetrahydroxy-6'-methoxyacetophenone (11) The chalcone 9 (540 mg, 0.70 mmol) was converted into acetate 10 at 70 °C for 30 min using an acetic anhydride (20 ml)-pyridine (2 ml) method. After the addition of water to the reaction mixture, the whole solution was extracted with CHCl3, and the extract was washed with water and dried (Na2SO4). After removing the acetate 10 (530 mg) and TTN (420 mg, 0.9 mmol) were stirred in a solution of MeOH (25 ml) and CHCl3 (10 ml) at 30 °C for 4 h, 10% HCl (15 ml) was added to the reaction mixture, and the whole solution was stirred at room temperature for 1 h to give white precipitates. After removal of the precipi-
tates by filtration, the filtrate was extracted with CHCl₃, and the extract was washed with water and dried (Na₂SO₄). The resulting crude acetal 11 in dioxane (10 ml) and MeOH (10 ml) was stirred with 10% aqueous NaOH (8 ml) at room temperature for 2 h, and then water and 10% HCl were added to the reaction mixture to give precipitates. The collected precipitates were extracted with CHCl₃, washed with water, and dried (Na₂SO₄). The resulting compound was purified by column chromatography on a silica gel flash column (4:1 as a solvent) to give the isoflavone 12 (218 mg, 40% from 9), and recrystallized from a solution of MeOH and CHCl₃ as pale yellow needles, mp 174-176 °C.

2,4,7-Tetra(tosyl benzoxyl)-6'-benzoxyl-3'-iodochalcone (13) A mixture of the chalcone 9 (3.0 g, 3.87 mmol), benzoyl chloride (0.68 ml, 5.59 mmol), and K₂CO₃ (2.68 g, 19 mmol) in DMF (35 ml) was stirred under nitrogen at 60 °C for 30 min. After removal of K₂CO₃ and the solvent under reduced pressure, the residue was extracted with CHCl₃, washed with 10% HCl and water, and dried (Na₂SO₄). The resulting compound was purified by silica gel column chromatography (CHCl₃: hexane = 1:1 as a solvent) and further recrystallized from a mixture of MeOH and AcOEt to give 13 (260 mg, 85%) as pale yellow needles, mp 154-155 °C; [α]D 179° (C 3.0 g, CH₂Cl₂). 7.87 (1H, s, C-4-H), 7.9-8.2 (8H, m, Ar-H), 7.81 (1H, s, C-2-H), 8.0-8.2 (2H, m, Ar-H)2). Anal. Calcd for C₄₈H₄₀O₁₁S: C, 71.91; H, 4.78.

2,4,7-Tris(benzoxyl)-6-(3-hydroxy-3-methylbutyl)iso flavone (14) A mixture of 16 (820 mg, 1.19 mmol), TsCl (342 mg, 1.8 mmol), and K₂CO₃ (1.66 g, 12 mmol) in MeOH (35 ml) was refluxed with stirring under nitrogen for 20 min. After removal of K₂CO₃ and the solvent, the residue was extracted with AcOEt, washed with 5% HCl and water, and dried (Na₂SO₄). The resulting compound was purified by column chromatography from a mixture of CHCl₃ and MeOH to give 14 (906 mg, 91%) as colorless needles, mp 116-119 °C; [α]D 179° (C 3.0 g, CH₂Cl₂), 1.39 (1H, s, OH), 4.28 (2H, d, J= 6.8 Hz, 2H), 7.26-7.70 (15H, m, Ar-H), 7.81 (1H, s, C-2-H), 8.2-8.7 (8H, m, Ar-H)2). Anal. Calcd for C₅₀H₃₉O₁₁S: C, 69.74; H, 4.76.

2,4,7-Tris(benzoxyl)-6-(3-hydroxy-3-methylbutyl)-5-tosyl iso flavone (17) With Boron Trifluoride Diethyl Etherate To a solution of 17 (50 mg, 0.06 mmol) in dry CH₂Cl₂ (2 ml) was added a solution of BF₃·OEt (0.05 mmol) in CH₂Cl₂ (0.4 ml); the mixture was stirred under nitrogen at room temperature for 2 h. To the reaction mixture was added aqueous NaHCO₃ and the whole solution was extracted with chloroform, washed with water, and dried (Na₂SO₄). The resulting compound was chromatographed over a silica gel column (CHCl₃) as a solvent to give 5-tosylisoflavone 18 (10 mg 20% as colorless needles, mp 188-189 °C), 5-hydroxisoflavone 19 (10 mg 25% as pale yellow needles, mp 177-179 °C), and dihydropyranoisoflavone 20 (18 mg 45% as colorless prisms), mp 187-190 °C; [α]D 179° (C 3.0 g, CH₂Cl₂), 1.81 and 2.68 (each 2H, t, J= 6.8 Hz, 2H), 6.81 (1H, s, C-2-H), 7.2-7.7 (12H, m, Ar-H), 7.81 (1H, s, C-2-H), 8.09-8.25 (8H, m, Ar-H)2). Anal. Calcd for C₅₀H₃ₙO₁₁S: C, 73.87; H, 4.54. Found: C, 73.65; H, 4.80.

2,4,7-Tris(benzoxyl)-6-(3-methyl-2-butenyl)-5-tosylisoflavone (18) To a solution of 17 (1.0 g, 1.19 mmol) in dry toluene (6 ml) was added TsOH·H₂O (1.81 ml of a 5.25×10⁻² mol dm⁻³ in acetic acid); the mixture was stirred under nitrogen at 110 °C for 45 min. The reaction mixture was extracted with ether, washed with 5% aqueous NaHCO₃, 2% HCl, and water, and dried (Na₂SO₄). The resulting compound was chromatographed over a silica gel column (CHCl₃: hexane = 1:1 as a solvent) to give 5-(alkenyl)isoflavones (745 mg) as colorless needles. The [α]D spectrum of the mixture was shown to be an 85:15 mixture of the 6-(3-methyl-2-butenyl)isoflavone 18 and the isomer 6-(3-methyl-3-butenyl)isoflavone 21. The mixture (18 and 21) in CH₂Cl₂ (0.5 ml) was added to a solution of benzoyldioxymethyl chloride (63 mg, 0.4 mmol) in CH₂Cl₂ (2 ml) in an ice-bath, and then the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was quenched with saturated aqueous NH₄Cl and extracted with CH₂Cl₂, washed with water, and dried (Na₂SO₄). The resulting compound was chromatographed over a silica gel column (CHCl₃: MeCO=15:1 as a solvent) to give the 6-phenylisoflavone 22, which was recrystallized from a mixture of CHCl₃ and hexane as colorless needles (500 mg, 68% from 17), mp 188-189 °C; [α]D 179° (C 3.0 g, CH₂Cl₂), 1.38 and 1.45 (each 3H, s, CH₃), 2.44 (3H, s, Ar-CH₃), 3.36 (2H, d, J= 6.4 Hz, CH₂), 4.92 (1H, brt, J= 6.4 Hz, CH₂), 7.2-7.7 (15H, m, Ar-H), 7.81 (1H, s, C-2-H), 8.09-8.25 (8H, m, Ar-H)2). Anal. Calcd for C₅₀H₃ₙO₁₁S: C, 72.70; H, 4.42. Found: C, 72.19; H, 4.59.

2,4,7-Tris(benzoxyl)-6-(3-hydroxy-3-methylbutyl)-2-tosylisoflavone (19) A mixture of 18 (160 mg, 0.19 mmol) and BCl₃ (0.14 ml; 1 mol solution: Aldrich) on dry CH₂Cl₂ (2 ml) was stirred under argon at 15 °C. The reaction mixture was quenched with saturated NH₄Cl and extracted with CH₂Cl₂, washed with water, and dried (Na₂SO₄). The resulting compound was purified by silica gel column chromatography (CHCl₃: MeCO=10:1 as a solvent) and recrystallized from CHCl₃-hexane to give 19 (123 mg, 95%) as pale yellow needles, mp 177-179 °C; [α]D 179° (C 3.0 g, CH₂Cl₂), 1.55 and 1.59 (each 3H, s, CH₃), 3.24 (2H, d, J= 7.3 Hz, CH₂), 5.12 (1H, t, J= 7.3 Hz, =CH), 6.80 (1H, s, C-2-H), 7.3-7.5 (15H, m, Ar-H), 7.97 (1H, s, C₂-
H). 8.1—8.2 (6H, m, Ar-H×6), 12.90 (1H, s, C-H). Anal. Calcd for C31H22O7C: 73.87; H: 5.44. Found: C: 73.73; H: 4.76.

2',4',5',7-Tetrahydroxy-6-(3-methyl-2-butenyl)isoflavone (Lutone) (1) Compound 19 (150 mg, 0.22 mmol) in MeOH (2 ml) and dioxane (2 ml) was hydrolyzed with 10% aqueous NaOH (2 ml) under argon at room temperature for 1 h. To the reaction mixture water and diluted HCl were added; the organic solvent was then evaporated under reduced pressure. The residue was extracted with ether, washed with water, and dried (Na2SO4). The compound was chromatographed over a silica gel column (CHCl3: AcOEt=2:1 as a solvent) to give 6'-glycosylisoflavone 4 (52 mg, 66%), which was crystallized from CH2Cl2–hexane as pale yellow prisms, mp 223—225°C; IR (KBr) ν 3432, 3300, 3100 br, 1650, 1615, 1590, 1215, 1060, 815 cm−1; UV λmax nm (log ε) (MeOH) 266 (4.56), 280 (4.33), 340 (3.63), (1αCl) 271 (4.41), (1αNaOAc) 269 (4.55), 340 (3.83). Anal. Calcd for C20H16O7C: 67.79; H: 5.12. Found: C: 67.75; H: 5.11.

2',4',5',7-Tetraacetoxy-6-(3-methyl-2-butenyl)isoflavone (22) Compound 1 (159 mg, 0.05 mmol) was converted into tetraacetate 22 by treatment with acetic anhydride (2 ml)-pyridine (0.3 ml) at 110°C for 2 h. The resulting compound was purified by silica gel column chromatography (AcOEt: hexane=2:1 as a solvent) to give 22 as colorless pastes (188 mg, 80%); 1H-NMR (CDCl3) δ=1.68 and 1.75 (each 3H, s, CH3), 2.16, 2.30, 2.36, and 2.40 (each 3H, s, COCH3), 2.32 (2H, brd, C3-H), 5.00 (1H, brt, =CH), 7.04—7.29 (4H, m, Ar-H), 7.80 (1H, s, C-H2).

4',2'-Tris(benzoyl)-6'-hydroxy-3'-iodochalcone (24) A mixture of the compound 19 (150 mg, 0.26 mmol), benzoyl chloride (0.08 ml, 0.7 mmol), and K2CO3 (433 mg, 3.07 mmol) in MeOH (50 ml) was stirred in the presence of KOH (350 mg, 6 mmol) at 0°C for 1 h. The resulting 6'-methoxymethoxychalcone 23 was used for the same manner as in the case of the 6'-hydroxychalcone 8 to 6'-hydroxy-benzoylchalcone 24, which was recrystallized from a mixture of CHCl3 and MeOH as yellow needles (334 mg, 87%) via two steps from 8 (as colorless needles, mp 271—274°C; 1H-NMR (CDCl3) δ=1.31 (6H, s, CH2×2), 1.55 (1H, s, OH), 1.71 and 2.73 (each 2H, m, C3-H), 3.26 and 2.39 (each 3H, s, COCH3), 6.87 (1H, s, C-H2), 7.20 (1H, dd, J=1.9 and 8.3 Hz, C5-H), 7.39 (1H, d, J=1.9 Hz, C7-H), 8.08 (1H, d, J=8.3 Hz, C7- H), 13.16 (1H, s, C-H). Anal. Calcd for C30H24O6C: 63.43; H: 4.88. Found: C: 63.53; H: 4.85.

4',5',7-Trihydroxy-6-(3-hydroxy-3-methylbutyl)coumaronochromone (29) To a dioxane solution (12 ml) of the 2'-hydroxyisoflavone 2 (350 mg; 0.93 mmol), o- chloranil (303 mg, 1.2 mmol) was added and stirred at 80°C for 10 min, and subsequently o-chloranil (305 mg, 1.2 mmol) was again added to the mixture, and the whole was stirred at 80°C for 2 h. After removal of the solvent, unreacted o-chloranil was removed by silica gel column chromatography (AcOEt: CHCl3=2:1 as a solvent) and the obtained coumaronochromone 4 was converted into the diacetate 29 by treatment with acetic anhydride (20 ml)-pyridine (1.5 ml) at 0°C for 30 min. The resulting compound was purified by silica gel column chromatography (AcOEt: CHCl3: MeOH=3:1 as a solvent) to give 29 (205 mg, 61% via two steps from 2) as colorless needles, mp 271—274°C; 1H-NMR (CDCl3) δ=1.31 (6H, s, CH2×2), 1.55 (1H, s, OH), 1.71 and 2.73 (each 2H, m, C3-H), 3.26 and 2.39 (each 3H, s, COCH3), 6.87 (1H, s, C-H2), 7.20 (1H, dd, J=1.9 and 8.3 Hz, C5-H), 7.39 (1H, d, J=1.9 Hz, C7-H), 8.08 (1H, d, J=8.3 Hz, C7-H), 13.16 (1H, s, C-H). Anal. Calcd for C36H29IO5: 61.83; H: 4.82.

References and Notes