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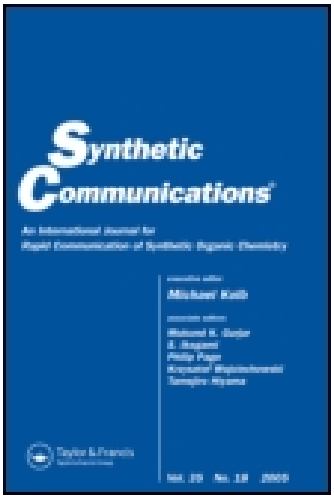

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# Regioselective Synthesis of 6-Prenylpolyhydroxyisoflavone (Wighteone) and Wighteone Hydrate with Hypervalent Iodine

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# Regioselective Synthesis of 6-Prenylpolyhydroxyisoflavone (Wighteone) and Wighteone Hydrate with Hypervalent Iodine

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**Abstract:** The oxidative rearrangement of 3′-iodotetraalkoxychalcone with [hydroxyl(tosyloxy)iodo]benzene, followed by cyclization of the resultant acetal gave 6-iodotrialkoxyisoflavone. The coupling reaction of the isoflavone with 2-methyl-3-butyn-2-ol gave 6-alkynylisoflavone, whose hydrogenation gave wighteone hydrate. Wighteone was synthesized by dehydration of wighteone hydrate.

**Keywords:** Synthesis, wighteone, 6-prenylisoflavone, 3′-iodochalcone, hypervalent iodine

Isoflavone derivatives are widely distributed in nature and are very important as precursors of prenylisoflavones and pterocarpans.[1,2] In addition, isoflavone derivatives exhibit phytoalexin, antifungal, antiinflammatory, and anticancer properties.[3–5] Hence, isoflavones have attracted considerable attention in recent years. Wighteone **1**, a prenylated isoflavone, was first isolated from healthy leaves of *Lupinus albus* together with luteone in 1976, but its structure was not fully identified at that time.[6] In 1977, wighteone **1**

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was isolated from fungus-inoculated stems of *Glycine wightii* as a phytoalexin, and the structure was assigned to be 4′,5,7-trihydroxy-6-(3-methyl-2-butenyl)isoflavone **1** on the basis of spectroscopic data.[3] Wighteone **1** was also isolated as erythrinin B from the barks of *Erythrina vareigata*[7] and from the roots of *white lupin* together with luteone.[8,9] Wighteone **1** was also metabolized in a culture of *Aspergillus flavus* and transformed into wighteone hydrate **2** as a major metabolite, whose structure was determined as 4′,5,7-trihydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone **2** by spectroscopic analysis.[10]

The total synthesis of wighteone **1** has yet to be achieved even though it is an important compound because it shows unique biological activity.[10] However, the isomer [lupiwighteone = 4′,5,7-trihydroxy-8-(3-methyl-2-butenyl)isoflavone] of wighteone **1** has already been synthesized.[11,12] The regioselective and direct introduction of alkenyl or alkyl group at the 6-position of isoflavone skeleton is relatively difficult, because it consists of many protections and consequent deprotections, and the easy isomerization of 6-alkylpolyhydroxyisoflavones into 8-alkylpolyhydroxyisoflavones by bases.[13,14] Generally, isoflavones are synthesized by oxidative rearrangement of chalcones with $Tl(III)(NO_3)_3 \cdot 3H_2O$, thallium(III) nitrate trihydrate (TTN).[15,16]

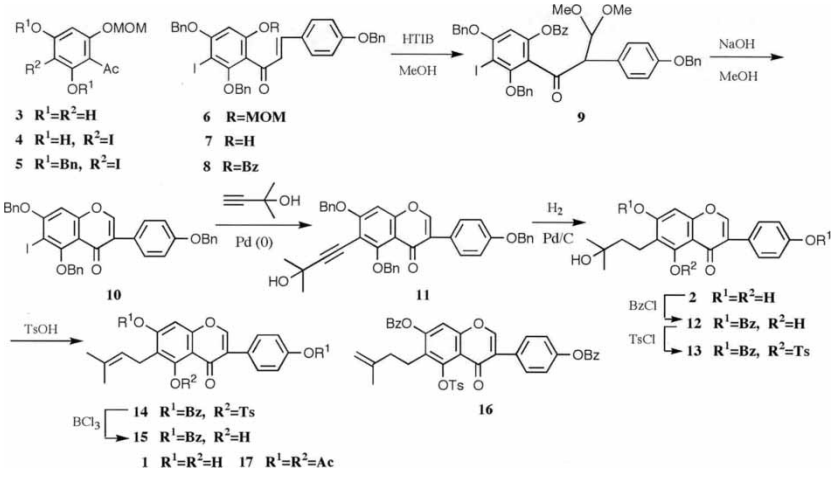
Wighteone hydrate **2** was synthesized by oxidative rearrangement of the corresponding 3′-iodochalcone with TTN in low yield.[17] 5,7-Bis(benzyloxy)-6-iodo-3′,4′-methylenedioxyisoflavone was also obtained by the oxidative rearrangement of the corresponding chalcone with TTN in low yield (17%). These results show a limit and scope of TTN as an oxidative reagent of chalcone. Moreover, TTN is toxic and has adverse effects on the environment. Recently, it has been reported that hypervalent iodine reagents such as [hydroxy(tosyloxy)iodo]benzene (HTIB)[18] and [bis(trifluoroacetoxy) iodo]benzene (BTIB)[19] have become more useful for the oxidative rearrangement of chalcones. We have achieved better results by using hypervalent iodine as oxidizing agents for the conversions of chalcones to acetals and isoflavones.[20] Moreover, unlike TTN, hypervalent iodine reagents are environmentally friendly and easy to prepare and handle.[21] In continuation of our studies on the synthesis of prenylisoflavones, we report here the first total synthesis of wighteone **1** and wighteone hydrate **2** from the corresponding 3′-iodochalcone using [hydroxy(tosyloxy)iodo]benzene.[21]

## RESULTS AND DISCUSSION

The introduction of iodine at the 3′-position of 6′-methoxymethoxyacetophenone **3**, obtained by the catalytic hydrogenation (5% Pd/C) of 2′,4′-bis(benzyloxy)-6′-methoxymethoxyacetophenone,[14] was carried out with iodine and periodic acid[17,22] to give the desired 3′-iodoacetophenone **4** in 94% yield.

The benzylation of compound **4** with benzyl chloride in the presence of $K_2CO_3$ in dimethyl formamide (DMF) gave 2′,4′-bis(benzyloxy)-3′-iodo-acetophenone **5** in 82% yield. Condensation of **5** with 4-benzyloxy-benzaldehyde in the presence of alcoholic KOH solution gave 6′-methoxymethoxychalcone **6** (Scheme 1).

6′-Hydroxychalcone **7** was obtained in 85% yield from the crude compound **6** by conc. HCl-mediated hydrolysis in a mixture of methanol and chloroform (via two steps from **5**). A crucial oxidative rearrangement of 6′-benzoyloxychalcone **8**, prepared by benzoylation of **7**, with HTIB in a mixture of methanol and chloroform gave the crude acetal **9**. The structure of acetal **9** was confirmed by $^1$H NMR [$\delta$: 3.05 and 3.23, $CH(OCH_3)_2$]. The subsequent hydrolysis of the crude **9** with 20% NaOH and in situ ring closure afforded the desired 6-iodoisoflavone **10** in 67% yield (via two steps from **8**). The oxidative rearrangement and cyclization methodology is much easier than the case of that with TTN. The coupling reaction of **10** with 2-methyl-3-butyn-2-ol in the presence of Pd(0)[23] in a mixture of triethyl-amine and DMF gave 6-(3-hydroxy-3-methylbutynyl)isoflavone **11** in 91% yield. The quantitative catalytic hydrogenation of **11** with 5% Pd/C in a mixture of methanol and dioxane afforded 4′,5,7-trihydroxy-6-(3-hydroxy-3-methylbuyl)isoflavone **2** in 88% yield. The spectral data and other physical properties of **2** were identical with those of the natural sample of wighteone hydrate[10] (Table 1 and Experimental section). The exhaustive bezoylation of **2** by bases in prolonged reaction time causes the isomerization of 6-alkyl-polyhydroxyisoflavone to 8-alkylpolyhydroxyisoflavone.[13,14] Therefore, the partial benzoylation of **2** was achieved in acetone at 45°C for 20 min to give the 5-hydroxyisoflavone **12** in 85% yield. The tosylation of **12** with *p*-TsCl




***Scheme 1.***

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***Table 1.*** $^{1}$H-NMR (400 MHz, $CD_3COCD_3$) data for 6-prenyl- and alkylisoflavones **1**, **2**, wighteone, and wighteone hydrate[a]

| Compound | 2-H | 8-H | 2′-H | 3′-H | Me 6′-H | $CH_2$ 5′-H | CH═C | OH |
|---|---|---|---|---|---|---|---|---|
| **1** | 8.14s ($J = 8.7$) | 6.49s ($J = 8.7$) | 7.46d 1.78s | 6.90d ($J = 7.1$) | 1.65s ($J = 7.1$) | 3.37d | 5.28t | 13.32s |
| Natural Product[10] (**1**) | 8.15s ($J = 8.8$) | 6.49s ($J = 8.8$) | 7.45br.d 1.78s | 6.90br.d ($J = 7.1$) | 1.65s ($J = 7.1$) | 3.37br.d | 5.28br.t | 13.32s |
| **2** | 8.15s ($J = 8.7$) | 6.47s ($J = 8.7$) | 7.46d (6H) | 6.91d 2.78m | 1.26s 13.32s | 1.71m | 8.43s | |
| Natural Product[10] (**2**) | 8.14s ($J = 8.8$) | 6.47s ($J = 8.8$) | 7.46br.d (6H) | 6.91br.d 2.78m | 1.26s 13.31s | 1.71m | | |

[a]s: singlet; d: doublet; t: triplet; br: broad; m: multiplet.

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under reflux in acetone for 2 h gave 5-tosylated isoflavone **13** in 84% yield. Compound **13** was dehydrated with $TsOH \cdot H_2O$ in a solution of acetic acid and toluene under reflux for 1.5 h to give a mixture of the desired 6-prenylisoflavone **14** and the regioisomer, 6-(3-methyl-3-butenyl)isoflavone **16**. The $^1H$ NMR spectrum of the alkenyl mixture (**14** and **16**) showed the ratio of **14** to **16** to be 74 : 26 [peaks due to $\underline{CH_2}CH{=}C(CH_3)_2$ at $\delta$: 3.37 (2H, d) and $CH_2CH_2$-$C(CH_3){=}\underline{CH_2}$ at $\delta$: 4.51 and 4.62 (each 1H, s)]. The treatment of the mixture (**14** and **16**) with benzohydroximoyl chloride[17] in dry dichloromethane at room temperature gave a mixture of the unchanged 6-pryenylisoflavone **14** and the terminal alkene-cyclic adduct, and then **14** was separated by silica-gel column chromatography in 57% yield (via two steps from **13**). The detosylation of **14** with 1 M $BCl_3$ solution in dichloromethane at room temperature gave 5-hydroxyisoflavone **15** in 91% yield. The hydrolysis of **15** with 10% NaOH in a mixture of methanol and dioxane at room temperature gave 4′,5,7-trihydroxy-6-(3-methyl-2-butenyl)isoflavone **1** in 72% yield. The spectral data and other physical properties of **1** were identical with those of the natural sample of wighteone[10] (Table 1 and Experimental section). On the basis of these results, the structure of wighteone was confirmed for the first time by the synthesis of 4′,5,7-trihydroxy-6-(3-methyl-2-butenyl)isoflavone **1**. Synthetic wighteone **1** was converted into 6-prenyltriacetoxyisoflavone **17**.

## EXPERIMENTAL

All the melting points were taken on a Yanaco MP-J3 micro-melting-point apparatus and are uncorrected. The $^1H$ NMR spectra were recorded with a JEOL EX-400 spectrophotometer (400 MHz) using tetramethylsilane (TMS) as internal standard. The IR spectra were obtained on Hitachi 260-10 spectrophotometer using KBr pellets. The UV spectra were obtained on Hitachi U-2000 spectrophotometer. Elemental analyses were obtained on Yanaco CHN corder model MT-5. Column chromatography and thin-layer chromatography (TLC) were carried out with Kieselgel 60 (70–230 mesh) and Kieselgel 60 F-254 (Merck).

**2′,4′-Dihydroxy-6′-methoxymethoxyacetophenone (3)**: The palladium-carbon-catalyzed hydrogenolysis of 2′,4′-bis(benzyloxy)-6′-methoxymethoxyacetophenone[14] (4.8 g, 12.24 mmol) in a mixture of MeOH (100 ml) and AcOEt (100 ml) was carried out at 20°C until the uptake of hydrogen ceased. The solvent was removed under reduced pressure, and the resulting compound was recrystallized from a mixture of AcOEt and hexane to give **3** (2.48 g, 95%) as colorless crystals, mp 117–119°C. $^1H$ NMR ($CDCl_3$) $\delta$: 2.65 (3H, s, $COCH_3$), 3.52 (3H, s, $OCH_3$), 5.25 (2H, s, $OCH_2O$), 6.04 (1H, d, $J = 2.4$ Hz, Ar-H), 6.14 (1H, d, $J = 2.4$ Hz, Ar-H), 13.79 (1H, s, $C_{2'}$-OH); anal. calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70; found: C, 56.61; H, 5.60.

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**2′,4′-Dihydroxy-3′-iodo-6′-methoxymethoxyacetophenone (4)**: Compound **3** (3.75 g, 17.61 mmol) was dissolved in ethanol (80 ml), followed by the successive addition of iodine (2.22 g, 8.74 mmol) and periodic acid (806 mg, 3.53 mmol in water, 9 ml). The reaction mixture was stirred for 1 h at 40°C. Cooling and diluting the reaction mixture with water gave a crystalline solid, which was recrystallized from the mixture of AcOEt and hexane to give **4** (5.59 g, 94%) as pale yellow needles, mp 162–164°C. $^1$H NMR ($CDCl_3$) $\delta$: 2.69 (3H, s, $COCH_3$), 3.52 (3H, s, $OCH_3$), 5.28 (2H, s, $OCH_2O$), 5.98 (1H, s, $C_{4'}$-OH), 6.44 (1H, s, $C_{5'}$-H), 14.97 (1H, s, $C_{2'}$-OH); anal. calcd. for $C_{10}H_{11}IO_5$: C, 35.52; H, 3.28; found: C, 35.32; H, 3.17.

**2′,4′-Bis(benzyloxy)-3′-iodo-6′-methoxymethoxyacetophenone (5)**: A solution of benzyl chloride (4.1 g, 32.41 mmol) in DMF (5 ml) was added slowly to a mixture of **4** (5.0 g, 14.79 mmol) and $K_2CO_3$ (10 g, 72.46 mmol) in DMF (50 ml) under nitrogen. The reaction mixture was heated at 70°C for 1 h, then cooled to rt, and extracted with $CHCl_3$. The extract was washed with 5% HCl and water and dried ($Na_2SO_4$), and the solvent was removed. The residue was recrystallized from a mixture of AcOEt and MeOH to give **5** (6.3 g, 82%) as colorless needles, mp 98–99°C. $^1$H NMR ($CDCl_3$) $\delta$: 2.47 (3H, s, $COCH_3$), 3.46 (3H, s, $OCH_3$), 4.97 (2H, s, $PhCH_2$), 5.15 (2H, s, $OCH_2O$), 5.18 (2H, s, $PhCH_2$), 6.65 (1H, s, $C_{5'}$-H), 7.32–7.6 (10H, m, Ar-H); anal. calcd. for $C_{24}H_{23}IO_5$: C, 55.61; H, 4.47; found: C, 55.66; H, 4.48.

**4,2′,4′-Tris(benzyloxy)-6′-methoxymethoxy-3′-iodochalcone (6) and 4,2′,4′-tris(benzyloxy)-6′-hydroxy-3′-iodochalcone (7)**: A mixture of **5** (5.0 g, 9.64 mmol) and 4-benzyloxybenzaldehyde (2.66 g, 12.53 mmol) was dissolved in alc · KOH (5.40 g, 96.2 mmol in 150 ml of EtOH). The reaction mixture was refluxed for 1 h and monitored by TLC to establish completion. The reaction mixture was neutralized with 10% HCl and extracted with $CHCl_3$, and solvent was removed under reduced pressure to give a yellow semisolid mass of 6′-methoxymethoxychalcone **6**, which was hydrolyzed with conc. HCl in a mixture of MeOH (100 ml) and $CHCl_3$ (100 ml) at 40°C for 1 h. The hydrolyzed mixture was allowed to cool to rt, extracted with $CHCl_3$, washed with water, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure to give a solid mass, which was recrystallized from $CHCl_3$ and AcOEt to afford 6′-hydroxychalcone **7** (5.48 g, 85% two steps yield from **5**) as yellow needles, mp 138–140°C. $^1$H NMR ($CDCl_3$) $\delta$: 4.85, 5.10, and 5.21 (each 2H, s, $PhCH_2$), 6.42 (1H, s, $C_{5'}$-H), 6.82 (2H, d, $J = 8.7$ Hz, $C_3$- and $C_5$-H), 7.18–7.52 (17H, m, Ar-H), 7.85 (2H, d, $J = 15.4$ Hz, CH═CH), 13.77 (1H, s, $C_{6'}$-OH); anal. calcd. for $C_{36}H_{29}IO_5$: C, 64.68; H, 4.37; found: C, 64.53; H, 4.54.

**4,2′,4′-Tris(benzyloxy)-6′-benzoyloxy-3′-iodochalcone (8)**: Benzoyl chloride (1.27 g, 9.0 mmol) was slowly added to a mixture of chalcone **7** (6.0 g, 8.98 mmol) and $K_2CO_3$ (8.6 g, 62.3 mmol) in DMF (30 ml). The

reaction mixture was heated at 60–70°C under nitrogen for 30 min and filtered of $K_2CO_3$. Then the filtrate was neutralized with 5% HCl, extracted with $CHCl_3$, washed with water, and dried ($Na_2SO_4$). After removal of the solvent a pale yellow crude mass was obtained. The crude was purified on silica-gel column chromatography ($CHCl_3$:hexane 3 : 2) and gave fluffy crystalline solid of **8** (6.1 g, 88%), mp 47–48°C. $^1$H NMR ($CDCl_3$) $\delta$: 4.99, 5.07, and 5.21 (each 2H, s, $PhCH_2$), 6.76 (1H, s, $C_{5'}$-H), 6.88 (2H, d, $J = 15.8$ Hz, CH═CH), 6.89 (2H, d, $J = 8.7$ Hz, $C_2$- and $C_6$-H), 7.27–7.63 (20H, m, Ar-H), 8.03 (2H, d, $J = 8.7$ Hz, $C_3$- and $C_5$-H); anal. calcd for $C_{43}H_{33}IO_6$: C, 66.85; H, 4.31; found: C, 66.68; H, 4.45.

**1-[6-Benzoyloxy-2,4-bis(benzyloxy)-3-iodophenyl]-2-[4-benzyloxyphenyl]-3,3-dimethoxypropan-1-one (9) and 4′,5,7-tris(benzyloxy)-6-iodoisoflavone (10):** Compound **8** (6.65 g, 8.61 mmol) was dissolved in a mixture of MeOH (80 ml) and $CHCl_3$ (25 ml) followed by the addition of HTIB (4.56 g, 11.63 mmol). The reaction mixture was stirred at rt under nitrogen for 24 h. The excess HTIB was decomposed with 5% $Na_2SO_3$ solution (2 ml), and then the reaction mixture was extracted with $CHCl_3$, washed with water, and dried ($Na_2SO_4$). Removal of the solvent under reduced pressure gave crude acetal **9** (8.5 g) as a semisolid mass. This crude mass was dissolved in a mixture of MeOH (60 ml) and $CHCl_3$ (20 ml) followed by the addition of 20% NaOH (35 ml) and stirred at 25°C for 5 h. The reaction mixture was neutralized with 10% HCl, extracted with $CHCl_3$, washed with water, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure to give yellow solid. The crude solid was purified by column chromatography ($CH_2Cl_2$:hexane 3 : 1) and further recrystallized from a mixture of AcOEt and MeOH (1 : 1) to give 6-iodoisoflavone **10** (3.82 g, 67%, two steps yield from **8**), mp 154–156°C. $^1$H NMR ($CDCl_3$) $\delta$: 5.07, 5.10, and 5.26 (each 2H, s, $PhCH_2$), 6.74 (1H, s, $C_8$-H), 7.03 (2H, d, $J = 8.3$ Hz, $C_{3'}$- and $C_{5'}$-H), 7.31–7.53 (15H, m, Ar-H), 7.77 (2H, d, $J = 8.5$ Hz, $C_{2'}$- and $C_{6'}$-H), 7.81 (1H, s, $C_2$-H); anal. calcd for $C_{36}H_{27}IO_5$: C, 64.87; H, 4.08; found: C, 64.65; H, 4.22.

**Acetal 9:** $^1$H NMR ($CDCl_3$) $\delta$: 3.05 and 3.23 (each 3H, s, $OCH_3$), 4.92, 4.98, and 5.11 (each 2H, s, $PhCH_2$), 4.78 and 4.95 (each 1H, d, $J = 10.2$ Hz, CH), 6.59 (1H, s, $C_8$-H), 7.05 (2H, d, $J = 8.7$ Hz, $C_{3'}$- and $C_{5'}$-H), 7.11 (2H, d, $J = 8.6$ Hz, $C_{2'}$- and $C_{6'}$-H), 7.15–7.71 (24H, m, Ar-H).

**4′,5,7-Tris(benzyloxy)-6-(3-hydroxy-3-methyl-1-butynyl)isoflavone (11)**: Compound **10** (3.0 g, 4.49 mmol) was dissolved in DMF (15 ml) followed by the successive addition of $Et_3N$ (70 ml), $PdCl_2$ (41 mg, 0.23 mmol), $PPh_3$ (120 mg, 0.45 mmol), CuI (44 mg, 0.23 mmol), and finally 2-methyl-3-butyn-2-ol (1.3 ml, 13.5 mmol). The reaction mixture was heated at 80°C under nitrogen for 2 h and then cooled to rt. The cool mixture was filtered through sintered glass using celite, and the filtrate was extracted with

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AcOEt, washed with 5% HCl and water, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure, and the resulting solid was chromatographed on silica-gel column ($CH_2Cl_2$:AcOEt 9 : 1) and further recrystallized from AcOEt and $Me_2CO$ (2 : 1) to give **11** as a colorless crystalline solid (2.54 g, 91%), mp 170–171°C. $^1$H NMR ($CDCl_3$) $\delta$: 1.50 and 1.54 (each 3H, s, $CH_3$), 5.10 (2H, s, $PhCH_2$), 5.20 (4H, s, $PhCH_2 \times 2$), 6.71 (1H, s, $C_8$-H), 7.04 (2H, d, $J = 8.7$ Hz, $C_{3'}$- and $C_{5'}$-H), 7.68 (2H, d, $J = 8.3$ Hz, $C_{2'}$- and $C_{6'}$-H), 7.29–7.52 (15H, m, Ar-H), 7.79 (1H, s, $C_2$-H); anal. calcd. for $C_{41}H_{34}O_6$: C, 79.08; H, 5.50; found: C, 79.11; H, 5.68.

**4′,5,7-Trihydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (wighteone hydrate) (2):** Compound **11** (1.0 g, 1.6 mmol) was hydrogenolyzed over 5% Pd/C (120 mg) in a mixture of methanol (35 ml) and dioxane (35 ml) until the uptake of hydrogen ceased. The resulting compound was recrystallized from MeOH and $Me_2CO$ to give **2** (504 mg, 88%) as colorless solid, mp 230–232°C (lit.[10] 225–228°C). $^1$H NMR (Table 1); IR (KBr) $\nu$ 3340, 3300, 2920, 1620, 1500, 1450, 1220, 1058 $cm^{-1}$; UV $\lambda_{max}$ nm (log $\varepsilon$) (MeOH): 265sh (4.41), 214 (4.29), (+$AlCl_3$) 269 (4.37), (+NaOAc) 335.5 (4.1), 274.5sh (4.39), 231sh (4.45); anal. calcd. for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66; found: C, 67.36; H, 5.80.

**4′,7-Bis(benzoyloxy)-5-hydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (12):** A mixture of **2** (650 mg, 1.82 mmol), benzoyl chloride (0.48 ml, 4.13 mmol), and $K_2CO_3$ (1.4 g, 10.14 mmol) in acetone (25 ml) was heated at 45°C under nitrogen for 25 min. Filtering off $K_2CO_3$ and removing the solvent under reduced pressure gave a residue, which was extracted with AcOEt, washed with 5% HCl and water, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure, and the resulting compound was recrystallized from a mixture of $CH_2Cl_2$ and $Me_2CO$ to give **12** (880 mg, 85%) as colorless needles, mp 160–161°C. $^1$H NMR ($CDCl_3$) $\delta$: 1.20 (6H, s, $CH_3 \times 2$), 1.74 and 2.77 (each 2H, m, $CH_2$), 6.90 (1H, s, $C_8$-H), 7.34 (2H, d, $J = 8.5$ Hz, $C_{3'}$- and $C_{5'}$-H), 7.25–7.68 (10H, m, Ar-H), 8.01 (1H, s, $C_2$-H), 8.24 (2H, d, $J = 8.5$ Hz, $C_{2'}$- and $C_{6'}$-H, Ar-H); 13.13 (1H, s, $C_{5'}$-OH); anal. calcd. for $C_{34}H_{28}O_8$: C, 72.33; H, 5.00; found: C, 72.45; H, 5.10.

**4′,7-Bis(benzoyloxy)-6-(3-hydroxy-3-methylbutyl)-5-tosyloxyisoflavone (13):** A mixture of **12** (860 mg, 1.52 mmol), tosyl chloride (498 mg, 2.61 mmol), and $K_2CO_3$ (2.1 g, 15.2 mmol) in acetone (40 ml) was refluxed under nitrogen for 2 h. The reaction mixture was cooled to rt, neutralized with 5% HCl, extracted with AcOEt, washed with water, and dried ($Na_2SO_4$). After removal of the solvent, the obtained crude solid was recrystallized from a mixture of $CHCl_3$ and $Me_2CO$ (10 : 3) to give **13** (925 mg, 84%) as colorless needles, mp 178–181°C. $^1$H NMR ($CDCl_3$) $\delta$: 1.14 (6H, s, $CH_3 \times 2$), 1.33 (1H, br.s, OH), 1.74 and 2.82 (each 2H, m, $CH_2$), 2.42 (3H, s, Ar-$CH_3$), 7.25–7.74 (15H, m, Ar-H), 7.90 (1H, s, $C_2$-H),

7.96 (2H, d, $J = 8.5$ Hz, $C_{3'}$- and $C_{5'}$-H), 8.23 (2H, d, $J = 8.5$ Hz, $C_{2'}$- and $C_{6'}$-H, Ar-H); anal. calcd. for $C_{41}H_{34}O_{10}S$; C, 68.51; H, 4.77; found: C, 68.75; H, 4.81.

**4′,7-Bis(benzoyloxy)-6-(3-methyl-2-butenyl)-5-tosyloxyisoflavone (14):** To a solution of **13** (1.0 g, 1.4 mmol) in dry toluene (10 ml) was added *p*-TsOH · $H_2O$ (2.4 ml of a $5.24 \times 10^{-1}$ M solution in acetic acid). The reaction mixture was refluxed under nitrogen for 90 min. After cooling, the reaction mixture was extracted with ether, washed with 5% $NaHCO_3$ and water, and dried ($Na_2SO_4$). After removal of the solvent, the obtained crude was chromatographed on a silica-gel column ($CHCl_3$ as a solvent) to give 6-alkenylisoflavone (748 mg) as crystalline solid. The $^1$H NMR spectrum showed that it was a mixture of 6-(3-methyl-2-butenyl)isoflavone **14** and the regioisomer, 6-(3-methyl-3-butenyl)isoflavone **16** (**14 : 16** = 74 : 26). The mixture was dissolved in $CH_2Cl_2$ (4 ml) followed by the careful addition of benzohydroximoyl chloride (133 mg, 0.86 mmol) and $Et_3N$ (0.2 ml, 1.42 mmol) in an ice bath. The reaction mixture was then stirred at 25°C under nitrogen for 8 h. The mixture was quenched with aqueous $NH_4Cl$ and extracted with $CH_2Cl_2$, washed with water, and dried ($Na_2SO_4$). The resulting compound was chromatographed on a silica-gel column ($CHCl_3$:$Me_2CO$ 15 : 1) to give the 6-prenylisoflavone **14**, which was recrystallized from a mixture of $CHCl_3$ and $Me_2CO$ (5 : 1) to give **14** (554 mg, 57% from **13**) as a crystalline solid, mp 202–204°C. $^1$H NMR ($CDCl_3$) $\delta$: 1.41 and 1.46 (each 3H, s, $CH_3$), 2.40 (3H, s, Ar-$CH_3$), 3.36 (2H, d, $J = 6.5$ Hz, $CH_2$), 4.96 (1H, t, $J = 6.5$ Hz,=CH), 7.25–7.70 (13H, m, Ar-H), 7.89 (1H, s, $C_2$-H), 7.92–8.25 (6H, m, Ar-H); anal. calcd. for $C_{41}H_{32}O_9S$; C, 70.27; H, 4.60; found: C, 70.05; H, 4.72.

**4′,7-Bis(benzoyloxy)-5-hydroxy-6-(3-methyl-2-butenyl)isoflavone (15):** Compound **14** (400 mg, 0.57 mmol) was dissolved in dry $CH_2Cl_2$ (10 ml), followed by the addition of $BCl_3$ (0.58 ml, 1 M solution in $CH_2Cl_2$) in an ice bath. The reaction mixture was stirred at 20–25°C under nitrogen for 2.5 h. The resulting mixture was quenched with saturated $NH_4Cl$ solution, extracted with $CH_2Cl_2$, washed with water, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure, and the obtained compound was purified on a silica-gel column ($CHCl_3$ as a solvent) and further recrystallized from AcOEt to give **15** (285 mg, 91%) as colorless crystalline solid, mp 192–194°C. $^1$H NMR ($CDCl_3$) $\delta$: 1.58 and 1.60 (each 3H, s, $CH_3$), 3.39 (2H, d, $J = 6.8$ Hz, $CH_2$), 5.17 (1H, t, $J = 6.8$ Hz, =CH), 6.87 (1H, s, $C_8$-H), 7.32–7.67 (10H, m, Ar-H), 8.00 (1H, s, $C_2$-H), 8.20–8.24 (4H, m, Ar-H), 13.10 (1H, s, $C_5$-OH); anal. calcd. for $C_{34}H_{26}O_7$; C, 74.71; H, 4.79; found: C, 74.57; H, 4.91.

**4′,5,7-Trihydroxy-6-(3-methyl-2-butenyl)isoflavone (wighteone) (1):** Compound **15** (180 mg, 0.32 mmol) was dissolved in a mixture of methanol

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(3 ml) and dioxane (3 ml) followed by the addition of 10% NaOH (2.0 ml, 5.0 mmol). The reaction mixture was stirred at 25°C for 20 min. The resulting mixture was neutralized with 2% HCl, and the organic layer was evaporated under reduced pressure. The obtained residue was extracted with AcOEt, washed with water, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure to give a solid mass, which was chromatographed on a silica-gel column (AcOEt : $CHCl_3$; 1 : 6), and the resulting compound was recrystallized from a mixture of $CHCl_3$ and EtOAc to give the targeted 6-prenylisoflavone **1** (80 mg, 72%) as a pale yellow crystalline solid, mp 205–207°C (lit.[10] 206–208°C). $^1$H NMR (Table 1); IR (KBr) $\nu$ 3365, 3240br., 2930, 1650, 1615, 1510, 1215, 1065, 818 $cm^{-1}$; UV $\lambda_{max}$ nm (log $\varepsilon$) (MeOH): 266sh (4.45), 214 (4.38), (+$AlCl_3$) 268.5sh (4.41), (+NaOAc) 341 (3.93), 275.5 (4.43), 229sh (4.70); anal. calcd. for $C_{20}H_{18}O_5$; C, 70.99; H, 5.36; found: C, 70.88; H, 5.52.

**4′,5,7-Triacetoxy-6-(3-methyl-2-butenyl)isoflavone (17):** Acetylation of **1** (40 mg, 0.11 mmol) was achieved by the acetic anhydride–pyridine method at 110°C for 2 h. The obtained gummy mass was chromatographed on a silica-gel column ($CHCl_3$:hexane 5 : 1) to give **17** in 71% yield. $^1$H NMR ($CDCl_3$) $\delta$: 1.67 and 1.75 (each 3H, s, $CH_3$), 2.31, 2.35, and 2.43 (each 3H, s, $COCH_3$), 3.32 (2H, br.d, $CH_2$), 5.01 (1H, br.t, =CH), 7.12–7.26 (5H, m, Ar-H), 7.86 (1H, s, $C_2$-H).

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