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Microwave-assisted regioselective synthesis of natural 6-prenylpolyhydroxyisoflavones and their hydrates with hypervalent iodine reagents

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Abstract—Microwave-assisted oxidative rearrangement of 3′-iodotetraalkoxychalcones with hypervalent iodine such as [hydroxy(tosyloxy)-iodo]benzene or [bis(trifluoroacetoxy)iodo]benzene, followed by microwave-mediated hydrolysis and in situ cyclization of the resultant acetals gave 6-iodotrialkoxyisoflavones. Pd(0)-catalyzed coupling reaction of the 6-iodoisoflavones with 2-methyl-3-butyn-2-ol under microwave irradiation gave 6-alkynylisoflavones, whose hydrogenation gave the respective hydrates of wighteone, lupisoflavone and derrubone. Wighteone (**1a**), lupisoflavone (**1b**) and derrubone (**1c**) were obtained by dehydration of their respective hydrates under microwave irradiation.

1. Introduction

In the 10 years since the appearance of the first paper on organic synthesis under microwave dielectric heating, the field has expanded dramatically.[1–4] Chemistry in the 21st century is increasingly being called upon to develop green chemistry methods as it attempts to deal with the scientific challenges of protecting the human health and the environment from the hazards posed by chemical processes. Considerable research efforts to use microwave for organic synthesis have been expended over the last two decades. This is because microwave minimizes the formation of unwanted by-products, and it reduces the need for organic solvents to a minimum or can even be used under solvent-free conditions.[5,6] Our present study will report on the total synthesis of some physiologically important prenylisoflavones under microwave dielectric heating with environmentally-friendly hypervalent iodine reagents and minimal use of solvents. Isoflavone derivatives are widely distributed in nature and are very important as precursors of prenylisoflavones and pterocarpans.[7,8] In addition, they exhibit phytoalexin, antifungal, anti-inflammatory and anticancer properties.[9–11] Recent studies have shown that some isoflavones have excellent health-promoting effects.[12] Hence, isoflavones and their derivatives have been receiving considerable attention in the fields of preventive medicine, food supplements, agrochemicals and cosmetics in recent years. Soy isoflavones show oxidative metabolism properties in humans in vitro and in vivo.[13] However, very recent studies[14] have also indicated that some soy isoflavones such as genistein and/or daidzein induced cancers of reproductive organs of female rodents. Despite these findings, there is growing research interest in isoflavonoids due to their health-related properties.

Wighteone, which has a strong antifungal property, was first isolated from healthy leaves of *Lupinus albus* together with luteone in 1976, but its structure was not fully identified at the time.[15] The following year (1977), wighteone was isolated from fungus-inoculated stems of *Glycine wightii* as a phytoalexin and the structure was assigned to be 5,7,4′-trihydroxy-6-(3-methyl-2-butenyl)isoflavone (**1a**) on the basis of spectroscopic method.[9] Wighteone was also isolated as erythrinin B from the bark of *Erythrina variegata*[16] and, together with luteone, from the roots of white lupin.[17,18] Moreover, wighteone was metabolized in a culture of *Aspergillus flavus* to be transformed into wighteone hydrate as a major metabolite, whose structure was determined as 5,7,4′-trihydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (**2a**) by spectroscopic analysis.[19] Synthesis of **1a** and **2a** by classical heating method has been reported earlier.[20] The isomer [lupiwighteone=5,7,4′-trihydroxy-8-(3-methyl-2-butenyl)-isoflavone] of wighteone has also been synthesized by conventional method.[21,22] But, we report here the first total synthesis of wighteone (**1a**) and wighteone hydrate (**2a**) under microwave irradiation (MWI). Lupisoflavone, a new

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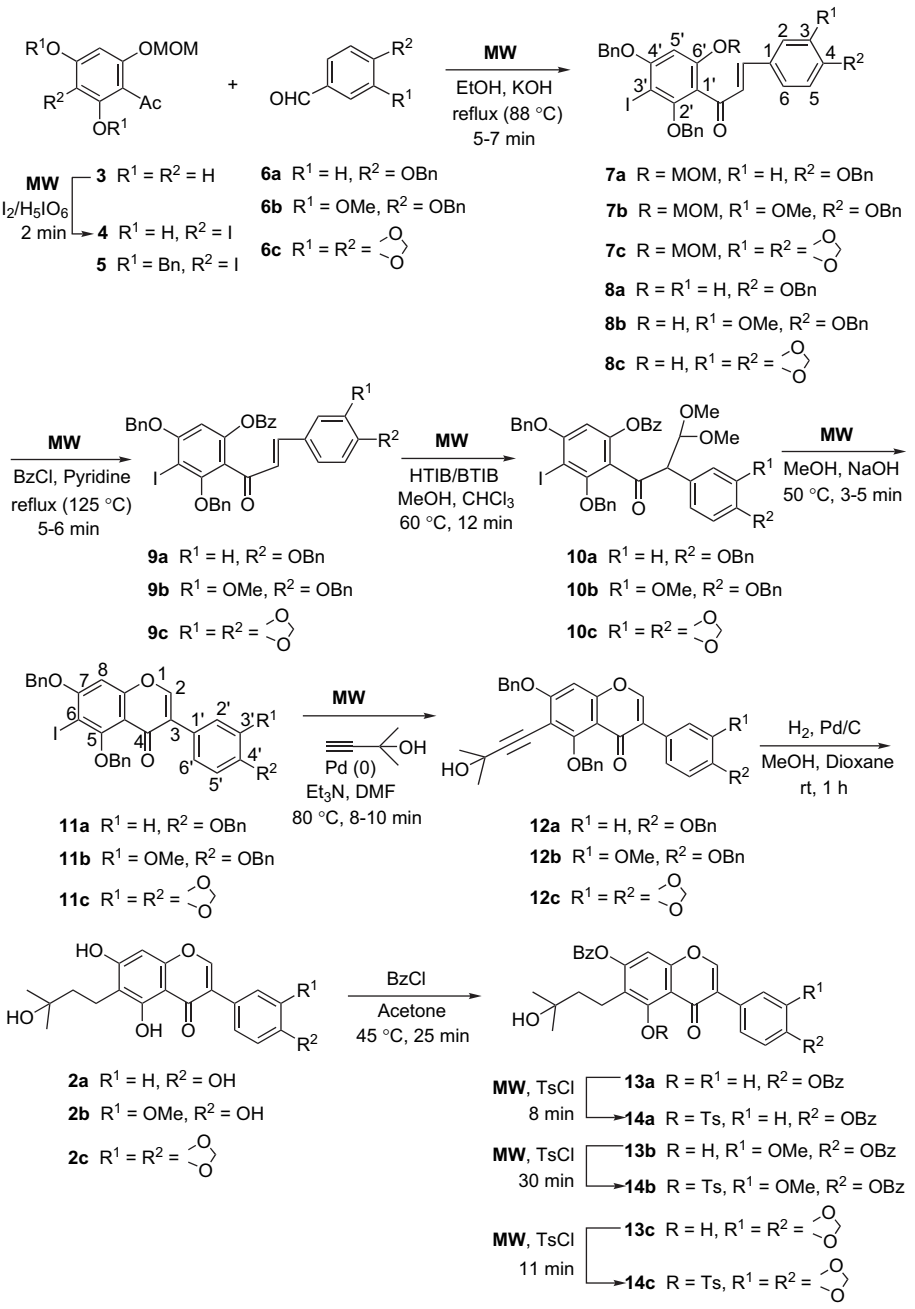


Scheme 1.

prenylated isoflavone, was isolated as a minor constituent from the leaf extract of white lupin (*L. albus* L.) and the structure was deduced as 5,7,4′-trihydroxy-6-(3-methyl-2-butenyl)-3′-methoxyisoflavone (**1b**) with the help of spectroscopic analyses.[17,18] Lupisoflavone shows moderate antifungal activity.[17] Furthermore, lupisoflavone induces the conversion of both the C_1 and C_2 cell wall isoperoxidases to the C_5 isoperoxidases, which possess scopoletin-peroxidase activity.[23] This is a unique characteristic of lupisoflavone to bring about the conformational change of these cell wall enzymes. Neither partial nor total synthesis of lupisoflavone has yet been reported by either conventional or MWI methods. Derrubone was isolated from the root of the Indian tree *Derris Robosta*.[24] Structural investigation of derrubone and its analogues (especially robustic acid, robustone and derrustone) was carried out by chemical and spectroscopic methods.[24–27] From degradative and spectroscopic analyses, the structure of derrubone was found to be 5,7-dihydroxy-6-(3-methyl-2-butenyl)-3′,4′-methylenedioxyisoflavone (**1c**). Synthesis of derrubone has been reported, however, the yield obtained was very low.[28] Moreover, the report lacked spectroscopic data to establish the structure of derrubone except for the melting point. Therefore, we report here the first total synthesis of **1b** and **1c** under MWI.

The regioselective and direct introduction of an alkenyl or alkyl group at the 6-position of the isoflavone skeleton is relatively difficult, as it consists of many protections and consequent deprotections, and the easy isomerization of 6-alkylpolyhydroxyisoflavones into 8-alkylpolyhydroxyisoflavones

by bases.[29,30] Generally, isoflavones are synthesized by oxidative rearrangement of chalcones with thallium(III) nitrate trihydrate, Tl(III)$(NO_3)_3\cdot 3H_2O$ (TTN).[31,32] Compound **2a** was also synthesized by oxidative rearrangement of the corresponding 3′-iodochalcone with TTN under conventional heating in low yield.[33] These results show the limit and scope of TTN as an oxidizing reagent of chalcones. Moreover, TTN is toxic, expensive and adversely affects the environment. Recently, it has been reported that hypervalent iodine reagents such as [hydroxy(tosyloxy)iodo]benzene (HTIB)[34] and [bis(trifluoroacetoxy)iodo]benzene (BTIB)[35] have become more useful for the oxidative rearrangement of chalcones. We were able to achieve far better results by using hypervalent iodine reagents as oxidizing agents for the conversions of chalcones to acetals and isoflavones.[20,36] Unlike TTN, hypervalent iodine reagents are environmentally-friendly and have the added benefits of being easier to prepare and handle.[37] The use of MW-technique with hypervalent iodine reagents was not only accelerated reaction pathways but also very advantageous from both the economical and the environmental standpoints. We do report here on the first total syntheses of **1a**, **2a**, **1b**, 5,7,4′-trihydroxy-6-(3-hydroxy-3-methylbutyl)-3′-methoxyisoflavone (**2b**), **1c** and 5,7-dihydroxy-6-(3-hydroxy-3-methylbutyl)-3′,4′-methylenedioxyisoflavone (**2c**) from their corresponding 3′-iodochalcones using hypervalent iodine reagents under MWI, a better synthetic route considering green chemistry (Scheme 1).

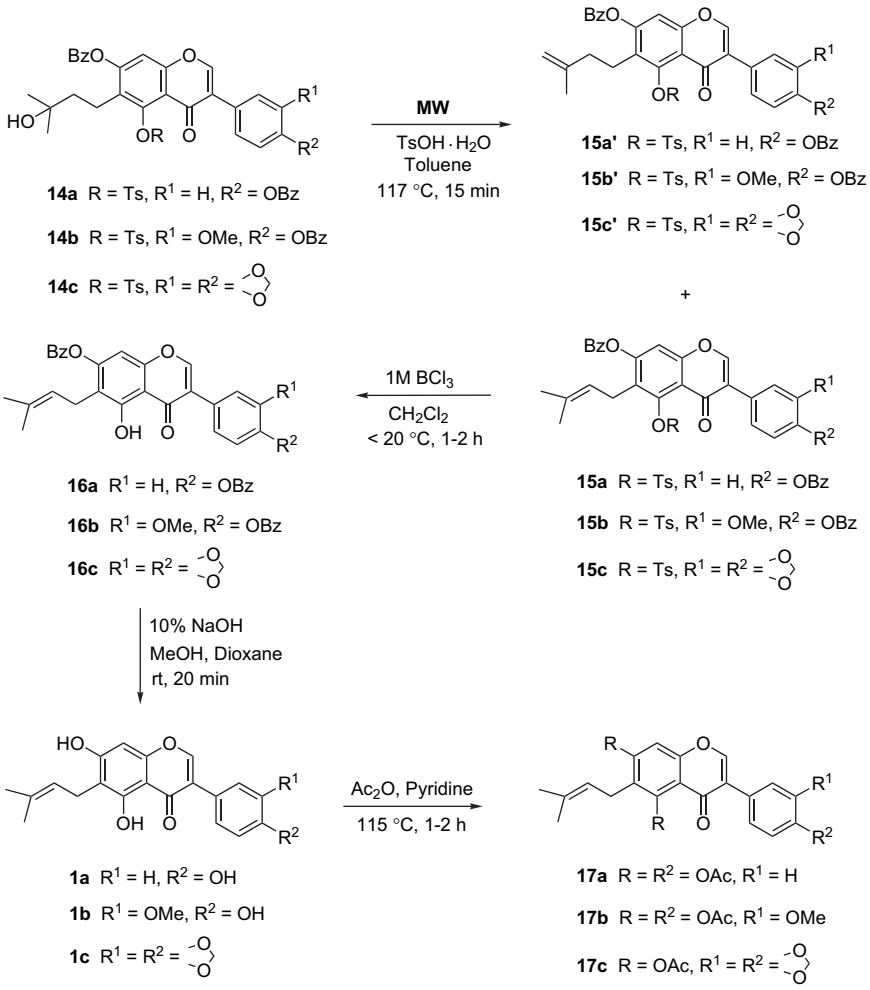
2. Results and discussion

Microwave-assisted regioselective introduction of iodine at the 3′-position of 6′-methoxymethoxyacetophenone **3**, obtained by the catalytic hydrogenolysis (5% Pd/C) of 2′,4′-bis(benzyloxy)-6′-methoxymethoxyacetophenone, was carried out with iodine and periodic acid[33,38] under temperature controlled MWI for 2 min to give the desired 3′-iodoacetophenone **4** in 96% yield. The benzylation of compound **4** with benzyl chloride in the presence of K_2CO_3 in dimethylformamide (DMF) gave 2′,4′-bis(benzyloxy)-3′-iodoacetophenone **5** in 82% yield. Microwave-mediated cross aldol condensations of **5** with different aromatic aldehydes such as 4-benzyloxybenzaldehyde (**6a**), 4-benzyloxy-3-methoxybenzaldehyde (**6b**) and 3,4-methylenedioxybenzaldehyde (**6c**) in the presence of alcoholic KOH solution from 5 to 7 min gave the 6′-methoxymethoxychalcones **7a–c** as crude semisolids, respectively. 6′-Hydroxychalcones **8a–c** were obtained from their respective crude compounds **7a–c** by concd HCl-mediated hydrolysis in a mixture of methanol and chloroform in more than 85% yields (via two steps from **5**). The separate treatment of **8a–c** with benzoyl chloride in pyridine under MWI from 5 to 6 min afforded 6′-benzoyloxychalcones **9a–c** in 91, 98 and 89% yields, respectively. The separate oxidative rearrangement of **9a–c** with HTIB in methanol under MWI for 12 min gave the respective crude acetals **10a–c**, which were liable to be unstable through silica gel column chromatography (decomposition takes place). The structures of **10a–c** were confirmed by ^{1}H NMR [δ: 3.0 and 3.22, CH(OCH_3)$_2$]. The subsequent hydrolysis of **10a–c** with 20% NaOH and in situ ring closure under MWI from 3 to 5 min afforded the desired 6-iodoisoflavones **11a–c** in 74, 59 and 46% yields (via two steps from their corresponding 6′-benzoyloxychalcones **9a–c**),

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

Compound	2-H	8-H	2′-H	6′-H	3′-H	5′-H	Me	CH_2	=CH	OCH_3/OCH_2O	OH
1a	8.14s	6.49s	7.46d, J=8.7 [1H]	7.46d, J=8.7 [1H]	6.90d, J=8.7 [1H]	6.90d, J=8.7 [1H]	1.65s, 1.78s	3.37d, J=7.1	5.28t, J=7.1		13.32s
Natural product[19] (**1a**)	8.15s	6.49s	7.45d, J=8.8 [1H]	7.45d, J=8.8 [1H]	6.90d, J=8.8 [1H]	6.90d, J=8.8 [1H]	1.65s, 1.78s	3.37br d, J=7.1	5.28br t, J=7.1		13.32s
2a	8.15s	6.47s	7.46d, J=8.7 [1H]	7.46d, J=8.7 [1H]	6.91d, J=8.7 [1H]	6.91d, J=8.7 [1H]	1.26s [6H]	1.71m, 2.78m			8.43s, 13.32s
Natural product[19] (**2a**)	8.14s	6.47s	7.45d, J=8.8 [1H]	7.45d, J=8.8 [1H]	6.91d, J=8.8 [1H]	6.91d, J=8.8 [1H]	1.26s [6H]	1.71m, 2.78m			13.31s
1b	8.19s	6.50s	7.25d, J=2.0 [1H]	7.05dd, J=8.3, 2.0 [1H]		6.89d, J=8.3 [1H]	1.65s, 1.78s	3.36d, J=7.1	5.27br t	3.88s, OCH_3 [3H]	9.70s, 13.35s
Natural product[17] (**1b**)	8.19s	6.52s	7.25d, J=2.4 [1H]	7.06dd, J=8.3, 2.4 [1H]		6.89d, J=8.3 [1H]	1.65s, 1.78s	3.36d, J=7.1	5.27br t	3.89s, OCH_3 [3H]	13.35s
2b	8.18s	6.47s	7.25d, J=2.0 [1H]	7.05dd, J=8.3, 2.0 [1H]		6.89d, J=8.3 [1H]	1.26s [6H]	1.71m, 2.78m		3.88s, OCH_3 [3H]	13.34s
1c[b]	8.19s	6.50s	7.15d, J=1.7 [1H]	7.06dd, J=8.1, 1.7 [1H]		6.90d, J=8.1 [1H]	1.65s, 1.78s	3.35d, J=7.1	5.27br t	6.04s, OCH_2O [2H]	9.75s, 13.25s
2c	8.18s	6.47s	7.15d, J=1.7 [1H]	7.06dd, J=8.1, 1.7 [1H]		6.90d, J=8.1 [1H]	1.26s [6H]	1.71m, 2.77m		6.04s, OCH_2O [2H]	13.24s

[a] s: Singlet; d: doublet; t: triplet; dd: double doublet; m: multiplet; br: broad.
[b] The NMR of the natural derrubone (**1c**) is not available in the literature. So, comparison could not be made with the natural sample.



Scheme 2.

respectively. In a similar manner, the oxidative rearrangement of **9a–c** was also carried out with BTIB under MWI for 12 min and the resultant acetals **10a–c** were cyclized with 20% NaOH to give **11a–c** in 69, 25 and 32% yields, respectively. Microwave-assisted coupling reaction of **11a–c** with 2-methyl-3-butyn-2-ol in the presence of Pd(0)[39,40] in a mixture of triethylamine and DMF from 8 to 10 min gave 6-(3-hydroxy-3-methylbutynyl)isoflavones **12a–c** in 78, 64 and 68% yields, respectively. The quantitative catalytic hydrogenation and hydrogenolysis of **12a–c** with 5% Pd/C in a mixture of methanol and 1,4-dioxane at room temperature afforded 6-(3-hydroxy-3-methylbuyl)isoflavones **2a–c** in 88, 93 and 87% yields, respectively. It has been mentioned earlier that compound **2a** (wighteone hydrate) is a natural product although the other two compounds **2b** and **2c** are not yet obtained as natural products. The spectral data and other physical properties of **2a** were identical with those of the natural sample of wighteone hydrate[19] (see Table 1, Section 4). Exhaustive benzoylation of **2a** with benzoyl chloride under MWI gave a mixture (about 1:1) of 4′,7-bis(benzoyloxy)isoflavone **13a** and 4′,5,7-tris(benzoyloxy)-6-(3-hydroxy-3-methylbutyl)isoflavone. On the other hand, the exhaustive benzoylation of 6-alkylpolyhydroxyisoflavones with bases in prolonged reaction time causes their isomerization to 8-alkylpolyhydroxyisoflavones by conventional heating method.[29,30,33] Therefore, the partial benzoylation of **2a–c** was achieved in acetone at 45 °C for 25 min to give the 5-hydroxyisoflavones **13a–c** in 85, 86 and 91% yields, respectively. The failure of exhaustive benzoylation of compounds **2a–c** is presumably due to the non-bonding interaction of 5-OH with C-4 carbonyl oxygen. Tosylation of the 5-hydroxyisoflavones **13a–c** with TsCl under MWI from 8 to 30 min in acetone gave 5-tosyloxyisoflavones **14a–c** in 89, 93 and 94% yields, respectively Scheme 2.

Compound **14a** was dehydrated with $TsOH \cdot H_2O$ in a solution of acetic acid and dry toluene under MWI for 15 min[†] to give a mixture of the desired 6-prenylisoflavone **15a** and the regioisomer, 6-(3-methyl-3-butenyl)isoflavone **15a′**. The dehydration of the other compounds **14b** and **14c** was also carried out in a similar manner to give the respective 6-prenylisoflavones **15b** and **15c** with a slight amount of their corresponding regioisomers **15b′** and **15c′**. The ^1H NMR spectra of each of the isomeric alkenyl mixtures (**15a** and **15a′**, **15b** and **15b′**, **15c** and **15c′**) showed that the unwanted regioisomers (**15a′–c′**) were less than 5% in

[†] The total reaction time was observed to be 30 min. But, it took 15 min for the reaction mixture to get reflux.

every case. The formation of the 6-alkenylisoflavones **15a–c** as major products can easily be understood by their ^{1}H NMR spectra [peaks due to $CH_2CH{=}C(CH_3)_2$ at δ: 3.37 (2H, d) and $CH_2CH_2C(CH_3){=}CH_2$ at δ: 4.51 and 4.62 (each 1H, s)]. The same dehydration under classical heating conditions, which was reported in our previous papers,[20,33] led to the formation of the unwanted regioisomer in about 28% yield. It is difficult to remove the regioisomer from the mixture by the usual physical methods. But, in the case of the microwave method, the unwanted regioisomer, which is less than 5%, is very easy to remove by usual physical methods such as recrystallization. It is clear from our data that microwave heating has advantages over the classical heating in that it reduces reaction time and solvent quantity and also on account of its very high regioselectivity, which is explained below.

2.1. High regioselectivity of MW dehydration—formation of 6-prenylisoflavone as major product

It has been reported that microwave dielectric heating and non-thermal effects play an important role in the regio-, chemo- and stereoselectivity, however, it is worth noting that there is no concrete clarification of these observations.[4] Without exception, we were able to achieve very high regioselectivity of the MW dehydration of compounds **14a–c**. Each of the dehydrations led to the formation of the required 6-prenylisoflavones **15a–c** as major products (in some cases, one product exclusively) and far less or almost no regioisomers **15a′–c′**. This increased selectivity is the most important factor in MW-synthesis, because the desired product was obtained, rather than the unwanted regioisomer. The possible explanation for the formation of 6-prenylisoflavones as major products lies in the fact that, due to its powers, MW provides elevated heating rates and accelerated reaction times. We used toluene as solvent for the dehydration and the reflux temperature was observed to be 117 °C, which was higher than its conventional boiling point (110 °C). Under such elevated heating conditions, the thermodynamically-controlled products, 6-prenylisoflavones, predominated over the kinetically-controlled regioisomers. The unwanted regioisomer, thermally labile, is converted into the more stable 6-prenylisoflavone due to such elevated heating rates.

The detosylation of **15a–c** with 1 M BCl_3 solution in dichloromethane at room temperature gave the respective 5-hydroxyisoflavones **16a–c** in 91, 94 and 79% yields, respectively. The hydrolysis of **16a–c** with 10% NaOH in a mixture of methanol and 1,4-dioxane at room temperature gave 5,7,4′-trihydroxy-6-(3-methyl-2-butenyl)isoflavone (wighteone) (**1a**) in 72%, 5,7,4′-trihydroxy-6-(3-methyl-2-butenyl)-3′-methoxyisoflavone (lupisoflavone) (**1b**) in 62% and 5,7-dihydroxy-6-(3-methyl-2-butenyl)-3′,4′-methylenedioxyisoflavone (derrubone) (**1c**) in 79% yields, respectively. The spectral data and other physical properties of **1a**, **1b** and **1c** were identical with those of the natural samples of wighteone,[19] lupisoflavone[17] and derrubone,[24] respectively (see Table 1, Section 4). On the basis of these results, the structures of wighteone, lupisoflavone and derrubone were confirmed for the first time by the MW-synthesis of **1a**, **1b** and **1c**, respectively. 6-Prenylisoflavones **1a–c** were converted into their respective acetate derivatives **17a–c**.

3. Conclusion

For the total synthesis of biologically important 6-prenylisoflavones **1a–c**, MWI technique was employed successfully. MW-synthesis was much more advantageous over the conventional method with regard to reaction time, solvent quantity and product yield. By using the MWI method in our synthesis, moreover, we were able to achieve very high regioselectivity compared to the results obtained under conventional heating. And though wighteone was obtained in a slight mixture with its regioisomer (5%), the other two compounds (lupisoflavone and derrubone) were obtained with a very small amount of regioisomers under microwave dehydration. This high regioselective synthesis of prenylisoflavones under microwave conditions is very important as it gave clean product and avoided the need for arduous regioisomeric separation.

4. Experimental

4.1. General

All the melting points were taken on a Yanaco MP-J3 micro melting-point apparatus and were uncorrected. The ^{1}H NMR spectra were recorded with a JEOL EX-400 spectrophotometer (400 MHz) using tetramethylsilane (TMS) as the internal standard. The IR spectra were obtained on an FT/IR-460 Plus (JASCO) spectrophotometer using KBr pellets. The UV spectra were obtained on a Hitachi U-2000 spectrophotometer. Elemental analyses were obtained on a Yanaco CHN corder model MT-5. A microwave oven (650 W and 2.45 GHz, modified properly by fitting a condenser and a thermo-sensor through the holes made in the roof; Shikoku Instrumentation Co., Ltd, Japan) was used as a reaction apparatus. Column chromatography and thin-layer chromatography (TLC) were carried out with Kieselgel 60 (70–230 mesh) and Kieselgel 60 F_{254} (Merck).

4.1.1. 2′,4′-Dihydroxy-6′-methoxymethoxyacetophenone (3). The palladium/carbon catalyzed hydrogenolysis of 2′,4′-bis(benzyloxy)-6′-methoxymethoxyacetophenone[30] (4.80 g, 12.2 mmol), which was synthesized by methoxymethylation of 2′,4′-bis(benzyloxy)-6′-hydroxyacetophenone, 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 colourless crystals, mp 117–119 °C. ^{1}H NMR ($CDCl_3$) δ: 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.

4.1.2. MW-synthesis of 2′,4′-dihydroxy-3′-iodo-6′-methoxymethoxyacetophenone (4). Compound **3** (2.50 g, 11.8 mmol) was dissolved in ethanol (40 ml), followed by the successive addition of iodine (1.49 g, 5.87 mmol) and periodic acid (542 mg, 2.37 mmol in water, 5 ml). The reaction mixture was irradiated under MW for 2 min at 45 °C. Cooling and diluting the reaction mixture with water gave a crystalline solid, which was recrystallized from a mixture

of AcOEt and hexane to give **4** (3.85 g, 96%) as a pale yellow solid, mp 162–164 °C. ^{1}H NMR ($CDCl_3$) δ: 2.68 (3H, s, $COCH_3$), 3.51 (3H, s, OCH_3), 5.27 (2H, s, OCH_2O), 6.0 (1H, s, $C_{4'}$–OH), 6.43 (1H, s, $C_{5'}$–H), 14.95 (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.

4.1.3. 2′,4′-Bis(benzyloxy)-3′-iodo-6′-methoxymethoxyacetophenone (5). A solution of benzyl chloride (4.10 g, 32.4 mmol) in DMF (5 ml) was added slowly to a mixture of **4** (5.0 g, 14 mmol) and K_2CO_3 (10.0 g, 72.3 mmol) in DMF (50 ml) under nitrogen. The reaction mixture was heated at 70 °C for 1 h, and then cooled to room temperature, and extracted with $CHCl_3$. The extract was washed with 5% HCl and water and dried (Na_2SO_4) after which the solvent was removed. The residue was recrystallized from a mixture of AcOEt and MeOH to give **5** (6.30 g, 82%) as colourless needles, mp 98–99 °C. ^{1}H NMR ($CDCl_3$) δ: 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), 7.32–7.61 (10H, m, Ar–H×10); Anal. Calcd for $C_{24}H_{23}IO_5$: C, 55.61; H, 4.47. Found: C, 55.66; H, 4.48.

4.1.4. MW-synthesis of 4,2′,4′-tris(benzyloxy)-3′-iodo-6′-methoxymethoxychalcone (7a) and 4,2′,4′-tris(benzyloxy)-6′-hydroxy-3′-iodochalcone (8a). A mixture of **5** (5.0 g, 9.6 mmol) and **6a** (2.66 g, 12.5 mmol) was dissolved in alc. KOH (5.40 g, 96.2 mmol in 100 ml EtOH). The reaction mixture was irradiated under MW for 6 min (1 min×6 times irradiation, 1–2 min interval/irradiation), and monitored by TLC to establish completion. The reaction mixture was neutralized with 10% HCl and extracted with $CHCl_3$, and then the solvent was removed under reduced pressure to give a yellow semisolid mass of **7a**, which was hydrolyzed with concd HCl in a mixture of MeOH (60 ml) and $CHCl_3$ (60 ml) at 40 °C for 1 h. The hydrolyzed mixture was allowed to cool to room temperature, 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 a mixture of $CHCl_3$ and AcOEt to afford **8a** (5.99 g, 93%, two steps yield from **5**) as a yellow solid, mp 138–140 °C. ^{1}H NMR ($CDCl_3$) δ: 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×17), 7.83 and 7.88 (each 1H, d, J=15.4 Hz, =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, 64.81; H, 4.53.

4.1.5. MW-synthesis of 4,2′,4′-tris(benzyloxy)-6′-benzoyloxy-3′-iodochalcone (9a). Benzoyl chloride (1.73 g, 12.3 mmol) was slowly added to a mixture of **8a** (5.50 g, 8.23 mmol) in pyridine (45 ml). The reaction mixture was irradiated incessantly under MW at 125 °C for 5 min. After cooling, it was extracted with $CHCl_3$, washed with 5% HCl and 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) to give **9a** as a fluffy crystalline solid (5.75 g, 91%), mp 47–48 °C. ^{1}H NMR ($CDCl_3$) δ: 4.99, 5.07 and 5.21 (each 2H, s, $PhCH_2$), 6.76 (1H, s, $C_{5'}$–H), 6.88 (1H, d, J=15.8 Hz, =CH), 6.89 (2H, d, J=8.7 Hz, C_2– and C_6–H), 7.27–7.63 (20H, m, Ar–H×20), 8.04 (2H, d, J=8.7 Hz, C_3– and C_5–H), 8.08 (1H, d, J=15.8 Hz, =CH); Anal. Calcd for $C_{43}H_{33}IO_6$: C, 66.85; H, 4.31. Found: C, 66.68; H, 4.45.

4.1.6. MW-synthesis of 1-[6-benzoyloxy-2,4-bis(benzyloxy)-3-iodophenyl]-2-(4-benzyloxyphenyl)-3,3-dimethoxypropan-1-one (10a) and 5,7,4′-tris(benzyloxy)-6-iodoisoflavone (11a). Compound **9a** (5.50 g, 7.12 mmol) was dissolved in a mixture of MeOH (50 ml) and $CHCl_3$ (20 ml), followed by the addition of HTIB (4.12 g, 10.5 mmol). The reaction mixture was irradiated under MW for 12 min (2 min×6 times irradiation, 1–2 min interval/irradiation) at 60 °C. The excess HTIB was decomposed with 5% Na_2SO_3 solution (1.5 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 **10a** (6.50 g) as a semisolid mass. This crude mass was dissolved in a mixture of MeOH (40 ml) and $CHCl_3$ (10 ml), followed by the addition of 20% NaOH (32 ml) and irradiated under MW at 50 °C for 5 min. 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 a 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 **11a** (3.51 g, 74%, two steps yield from **8a**), mp 154–156 °C. ^{1}H NMR ($CDCl_3$) δ: 5.07, 5.10 and 5.26 (each 2H, s, $PhCH_2$), 6.74 (1H, s, C_8–H), 7.02 (2H, d, J=8.3 Hz, $C_{3'}$– and $C_{5'}$–H), 7.31–7.49 (15H, m, Ar–H×15), 7.76 (2H, d, J=8.3 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 **10a**: ^{1}H NMR ($CDCl_3$) δ: 3.0 and 3.22 (each 3H, s, OCH_3), 4.92, 5.02 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, Ar–H), 7.05 (2H, d, J=8.7 Hz, Ar–H×2), 7.11 (2H, d, J=8.6 Hz, Ar–H×2), 7.13–7.71 (24H, m, Ar–H×24).

The similar treatment of compound **9a** (2.11 g, 2.97 mmol) with BTIB (1.91 g, 4.44 mmol) under MWI for 12 min (2 min×6 times irradiation, 1–2 min interval/irradiation) at 60 °C gave crude acetal **10a**, which was cyclized with 20% NaOH under MWI for 5 min to give **11a** (1.25 g, 69%).

4.1.7. MW-synthesis of 5,7,4′-tris(benzyloxy)-6-(3-hydroxy-3-methyl-1-butynyl)isoflavone (12a). Compound **11a** (3.50 g, 5.25 mmol) was dissolved in DMF (15 ml), followed by the successive addition of Et_3N (60 ml), $PdCl_2$ (46 mg, 0.25 mmol), PPh_3 (120 mg, 0.457 mmol) and CuI (44 mg, 0.23 mmol) and finally 2-methyl-3-butyn-2-ol (1.53 ml, 15.7 mmol). The reaction mixture was irradiated under MW at 80 °C under nitrogen for 8 min (1 min×8 times irradiation, 1–2 min interval/irradiation), and then cooled to room temperature. The cool mixture was filtered through a sintered glass using Celite and the filtrate was extracted with AcOEt. The AcOEt extract was 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 a mixture of AcOEt and Me_2CO (2:1) to give **12a** as a colourless crystalline solid (2.55 g, 78%), mp 170–171 °C. ^{1}H NMR ($CDCl_3$) δ: 1.50

(6H, s, $CH_3\times2$), 5.10 (2H, s, $PhCH_2$), 5.20 (4H, s, $PhCH_2\times2$), 6.71 (1H, s, C_8–H), 7.02 (2H, d, J=8.7 Hz, $C_{3'}$– and $C_{5'}$–H), 7.66 (2H, d, J=8.7 Hz, $C_{2'}$– and $C_{6'}$–H), 7.29–7.52 (15H, m, Ar–H×15), 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.

4.1.8. 5,7,4′-Trihydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (wighteone hydrate) (2a). Compound **12a** (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 a mixture of MeOH and Me_2CO to give **2a** (504 mg, 88%) as a colourless solid, mp 230–232 °C (lit.[19] 225–228 °C). ^{1}H NMR (see Table 1); IR (KBr) ν_{max} 3340, 3300, 2920, 1620, 1500, 1450, 1220, 1058 cm^{-1}; UV λ_{max} nm (log ε) (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, 67.61; H, 5.80.

4.1.9. 7,4′-Bis(benzoyloxy)-5-hydroxy-6-(3-hydroxy-3-methylbutyl)isoflavone (13a). A mixture of **2a** (650 mg, 1.82 mmol), benzoyl chloride (0.48 ml, 4.1 mmol) and K_2CO_3 (1.40 g, 10.1 mmol) in acetone (25 ml) was heated at 45 °C under nitrogen for 25 min. Filtered off K_2CO_3, and removal of 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 **13a** (880 mg, 85%) as a colourless solid, mp 160–161 °C. ^{1}H NMR ($CDCl_3$) δ: 1.20 (6H, s, $CH_3\times2$), 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×10), 8.01 (1H, s, C_2–H), 8.24 (2H, d, J=8.5 Hz, $C_{2'}$– and $C_{6'}$–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.

4.1.10. MW-synthesis of 7,4′-bis(benzoyloxy)-6-(3-hydroxy-3-methylbutyl)-5-tosyloxyisoflavone (14a). A mixture of **13a** (500 mg, 0.885 mmol), tosyl chloride (290 mg, 1.52 mmol) and K_2CO_3 (1.29 g, 9.33 mmol) in acetone (35 ml) was irradiated under MW for 8 min (2 min×4 times irradiation, 1–2 min interval/irradiation). The reaction mixture was cooled to room temperature, and neutralized with 5% HCl and then 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 **14a** (566 mg, 89%) as colourless needles, mp 178–181 °C. ^{1}H NMR ($CDCl_3$) δ: 1.14 (6H, s, $CH_3\times2$), 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×15), 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); Anal. Calcd for $C_{41}H_{34}O_{10}S$: C, 68.51; H, 4.77. Found: C, 68.75; H, 4.81.

4.1.11. MW-synthesis of 7,4′-bis(benzoyloxy)-6-(3-methyl-2-butenyl)-5-tosyloxyisoflavone (15a). To a solution of **14a** (1.0 g, 1.4 mmol) in dry toluene (15 ml) was added $TsOH\cdot H_2O$ (2.38 ml of a 5.24×10^{-1} M solution in acetic acid). The reaction mixture was refluxed under MWI at 117 °C for 15 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 mass was chromatographed on silica gel column ($CHCl_3$ as a solvent) to give 6-alkenylisoflavone as a crystalline solid. The ^{1}H NMR spectrum showed that it was a mixture of 6-(3-methyl-2-butenyl)isoflavone **15a** and the regioisomer, 6-(3-methyl-3-butenyl)isoflavone **15a′** (**15/15a′**=95:5). The isomeric mixture was recrystallized twice from a mixture of $CHCl_3$ and Me_2CO (5:1) to give **15a** (720 mg, 74% from **14a**) as a crystalline solid, mp 202–204 °C. ^{1}H NMR ($CDCl_3$) δ: 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×13), 7.89 (1H, s, C_2–H), 7.92–8.25 (6H, m, Ar–H×6); Anal. Calcd for $C_{41}H_{32}O_9S$: C, 70.27; H, 4.60. Found: C, 70.05; H, 4.72.

4.1.12. 7,4′-Bis(benzoyloxy)-5-hydroxy-6-(3-methyl-2-butenyl)isoflavone (16a). Compound **15a** (400 mg, 0.571 mmol) was dissolved in dry CH_2Cl_2 (10 ml), followed by the addition of BCl_3 (0.60 ml, 1 M solution in CH_2Cl_2) in an ice bath. The reaction mixture was stirred below 20 °C under nitrogen for 2.5 h. The resulting mixture was quenched with saturated NH_4Cl solution and 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 silica gel column chromatography ($CHCl_3$ as a solvent) and further recrystallized from AcOEt to give **16a** (285 mg, 91%) as a colourless crystalline solid, mp 192–194 °C. ^{1}H NMR ($CDCl_3$) δ: 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×10), 8.00 (1H, s, C_2–H), 8.20–8.24 (4H, m, Ar–H×4), 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.

4.1.13. 5,7,4′-Trihydroxy-6-(3-methyl-2-butenyl)isoflavone (wighteone) (1a). Compound **16a** (180 mg, 0.329 mmol) was dissolved in a mixture of methanol (3 ml) and dioxane (3 ml), followed by the addition of 10% NaOH (2 ml). 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 silica gel column (AcOEt/$CHCl_3$; 1:6) and the resulting compound was recrystallized from a mixture of $CHCl_3$ and AcOEt to give the 6-prenylisoflavone **1a** (80 mg, 72%) as a pale yellow crystalline solid, mp 205–207 °C (lit.[19] 206–208 °C). ^{1}H NMR (see Table 1); IR (KBr) ν_{max} 3365, 3240, 2930, 1650, 1615, 1510, 1215, 1065, 818 cm^{-1}; UV λ_{max} nm (log ε) (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.

4.1.14. 5,7,4′-Triacetoxy-6-(3-methyl-2-butenyl)isoflavone (17a). Acetylation of **1a** (40 mg, 0.11 mmol) was achieved by acetic anhydride/pyridine method at 115 °C for 2 h. The obtained gummy mass was chromatographed on silica gel column ($CHCl_3$/hexane; 5:1) and further

recrystallized from a mixture of $CHCl_3$ and hexane to give **17a** (38 mg, 71%) as a colourless crystalline solid, mp 173–175 °C. ^{1}H NMR ($CDCl_3$) δ: 1.67 and 1.75 (each 3H, s, CH_3), 2.31, 2.35 and 2.43 (each 3H, s, $COCH_3$), 3.25 (2H, br d, CH_2), 5.01 (1H, br t, =CH), 7.13 (2H, d, J=8.6 Hz, $C_{3'}$– and $C_{5'}$–H), 7.21 (1H, s, C_8–H), 7.49 (2H, d, J=8.6 Hz, $C_{2'}$– and $C_{6'}$–H), 7.86 (1H, s, C_2–H). Anal. Calcd for $C_{26}H_{24}O_8$: C, 67.23; H, 5.21. Found: C, 67.35; H, 5.32.

4.1.15. MW-synthesis of 4,2′,4′-tris(benzyloxy)-3′-iodo-3-methoxy-6′-methoxymethoxychalcone (7b) and 4,2′,4′-tris(benzyloxy)-6′-hydroxy-3′-iodo-3-methoxychalcone (8b). A mixture of **5** (4.40 g, 8.48 mmol) and **6b** (2.46 g, 10.2 mmol) was dissolved in alc. KOH (3.30 g, 58.8 mmol in 60 ml EtOH). The reaction mixture was irradiated under MW for 7 min (1 min×7 times irradiation, 1–2 min interval/irradiation), and monitored by TLC to establish completion. A similar treatment of the reaction mixture (as in the case of compound **8a**) gave **8b** (5.65 g, 95%, two steps yield from **5**) as a yellow solid, mp 133–134 °C. ^{1}H NMR ($CDCl_3$) δ: 3.66 (3H, s, OCH_3), 4.82 (2H, s, $PhCH_2$), 5.20 (4H, s, $PhCH_2$×2), 6.42 (1H, s, $C_{5'}$–H), 6.76 (1H, d, J=8.3 Hz, C_5–H), 6.82 (1H, d, J=1.7 Hz, C_2–H), 6.91 (1H, dd, J=8.3 and 1.7 Hz, C_6–H), 7.15–7.52 (15H, m, Ar–H×15), 7.81 and 7.86 (each 1H, d, J=15.3 Hz, =CH), 13.77 (1H, s, $C_{6'}$–OH); Anal. Calcd for $C_{37}H_{31}IO_6$: C, 63.62; H, 4.47. Found: C, 63.47; H, 4.63.

4.1.16. MW-synthesis of 4,2′,4′-tris(benzyloxy)-6′-benzoyloxy-3′-iodo-3-methoxychalcone (9b). Benzoyl chloride (1.56 g, 11.2 mmol) was slowly added to a mixture of **8b** (6.0 g, 8.6 mmol) in pyridine (55 ml). The reaction mixture was irradiated incessantly under MW at 125 °C for 5 min. The reaction mixture was worked up in a similar manner (as in the case of compound **9a**) to give **9b** (6.79 g, 98%) as a fluffy crystalline solid, mp 65–68 °C. ^{1}H NMR ($CDCl_3$) δ: 3.83 (3H, s, OCH_3), 4.98, 5.17 and 5.20 (each 2H, s, $PhCH_2$), 6.76 (1H, s, $C_{5'}$–H), 6.79 (1H, d, J=8.3 Hz, C_5–H), 6.91 (1H, dd, J=8.3 and 1.7 Hz, C_6–H), 6.89 (1H, d, J=15.8 Hz, =CH), 6.94 (1H, d, J=1.7 Hz, C_2–H), 6.96 (1H, d, J=15.8 Hz, =CH), 7.25–7.59 (20H, m, Ar–H×20); Anal. Calcd for $C_{44}H_{35}IO_7$: C, 65.84; H, 4.58. Found: C, 65.84; H, 4.43.

4.1.17. MW-synthesis of 1-[6-benzoyloxy-2,4-bis(benzyloxy)-3-iodophenyl]-2-(4-benzyloxy-3-methoxyphenyl)-3,3-dimethoxypropan-1-one (10b) and 5,7,4′-tris(benzyloxy)-6-iodo-3′-methoxyisoflavone (11b). Compound **9b** (7.0 g, 8.7 mmol) was dissolved in a mixture of MeOH (50 ml) and $CHCl_3$ (10 ml), followed by the addition of HTIB (5.46 g, 13.9 mmol). The reaction mixture was irradiated under MW for 12 min (2 min×6 times irradiation, 1–2 min interval/irradiation) at 60 °C. The reaction mixture was worked up in a similar manner (as in the case of compound **10a**) to give crude acetal **10b**. This crude mass was hydrolyzed and cyclized in a similar manner (as in the case of compound **11a**) to give isoflavone **11b** (3.53 g, 59%, two steps yield from **8b**), mp 198–200 °C. ^{1}H NMR ($CDCl_3$) δ: 3.92 (3H, s, OCH_3), 5.06, 5.20 and 5.26 (each 2H, s, $PhCH_2$), 6.75 (1H, s, C_8–H), 6.92 (1H, d, J=7.8 Hz, $C_{5'}$–H), 6.94 (1H, dd, J=7.8 and 1.9 Hz, $C_{6'}$–H), 7.16 (1H, d, J=1.9 Hz, $C_{2'}$–H), 7.26–7.53 (15H, m, Ar–H×15), 7.81 (1H, s, C_2–H); Anal. Calcd for $C_{37}H_{29}IO_6$: C, 63.80; H, 4.22. Found: C, 63.63; H, 4.26.

Acetal **10b**: ^{1}H NMR ($CDCl_3$) δ: 3.0 and 3.22 (each 3H, s, OCH_3), 4.68 and 4.78 (each 1H, d, J=10.2 Hz, CH), 5.10 (2H, s, $PhCH_2$), 5.16 and 5.20 (each 2H, s, $PhCH_2$), 6.56 (1H, d, J=8.3 Hz, Ar–H), 6.60 (1H, dd, J=8.3 and 1.7 Hz, Ar–H), 6.65 (1H, d, J=1.7 Hz, Ar–H), 6.71–7.70 (21H, m, Ar–H×21).

The similar treatment of compound **9b** (180 mg, 0.224 mmol) with BTIB (145 mg, 0.337 mmol) under MWI for 12 min (2 min×6 times irradiation, 1–2 min interval/irradiation) at 60 °C gave crude acetal **10b**, which was cyclized with 20% NaOH under MWI for 5 min to give **11b** (39 mg, 25%).

4.1.18. MW-synthesis of 5,7,4′-tris(benzyloxy)-6-(3-hydroxy-3-methyl-1-butynyl)-3′-methoxyisoflavone (12b). Compound **11b** (1.50 g, 2.15 mmol) was dissolved in DMF (12 ml), followed by the successive addition of Et_3N (40 ml), $PdCl_2$ (30 mg, 0.16 mmol), PPh_3 (70 mg, 0.26 mmol) and CuI (44 mg, 0.23 mmol) and finally 2-methyl-3-butyn-2-ol (0.85 ml, 8.7 mmol). The similar treatment of the reaction mixture under MWI for 10 min (2 min×5 times irradiation, 1–2 min interval/irradiation) (as in the case of compound **12a**) gave **12b** as a colourless crystalline solid (0.89 g, 64%), mp 151–153 °C. ^{1}H NMR ($CDCl_3$) δ: 1.51 (6H, s, CH_3×2), 3.92 (3H, s, OCH_3), 5.20 (6H, s, $PhCH_2$×3), 6.72 (1H, s, C_8–H), 6.90 (1H, d, J=8.3 Hz, $C_{5'}$–H), 6.94 (1H, dd, J=8.3 and 1.7 Hz, $C_{6'}$–H), 7.16 (H, d, J=1.9 Hz, $C_{2'}$–H), 7.26–7.52 (15H, m, Ar–H×15), 7.79 (1H, s, C_2–H); Anal. Calcd for $C_{42}H_{36}O_7$: C, 77.28; H, 5.56. Found: C, 77.13; H, 5.49.

4.1.19. 5,7,4′-Trihydroxy-6-(3-hydroxy-3-methylbutyl)-3′-methoxyisoflavone (lupisoflavone hydrate) (2b). Compound **12b** (1.0 g, 1.5 mmol) was hydrogenolyzed over 5% Pd/C (150 mg) in a mixture of methanol (45 ml) and dioxane (45 ml) until the uptake of hydrogen ceased. The resulting compound was recrystallized from a mixture of MeOH and Me_2CO to give **2b** (550 mg, 93%) as a colourless solid, mp 220–223 °C. ^{1}H NMR (see Table 1); IR (KBr) ν_{max} 3443, 3083, 2966, 1665, 1519, 1464, 1208, 1057 cm^{-1}; UV λ_{max} nm (log ε) (MeOH): 269 (4.34), 219 (4.3), (+$AlCl_3$) 267sh (4.36), 219 (4.31), (+NaOAc) 334 (3.93), 277 (4.36), 234sh (4.24); Anal. Calcd for $C_{21}H_{22}O_7$: C, 65.28; H, 5.74. Found: C, 65.22; H, 5.61.

4.1.20. 7,4′-Bis(benzoyloxy)-5-hydroxy-6-(3-hydroxy-3-methylbutyl)-3′-methoxyisoflavone (13b). A mixture of **2b** (480 mg, 1.24 mmol), benzoyl chloride (0.52 ml, 4.5 mmol) and K_2CO_3 (1.71 g, 12.4 mmol) in acetone (30 ml) was heated at 45 °C under nitrogen for 25 min. The reaction mixture was worked up in a similar manner (as in the case of compound **13a**) to give **13b** (642 mg, 86%) as colourless needles, mp 182–183 °C. ^{1}H NMR ($CDCl_3$) δ: 1.21 (6H, s, CH_3×2), 1.74 and 2.77 (each 2H, m, CH_2), 3.86 (3H, s, OCH_3), 6.90 (1H, s, C_8–H), 7.10–7.71 (13H, m, Ar–H×13), 8.03 (1H, s, C_2–H), 13.16 (1H, s, C_5–OH); Anal. Calcd for $C_{35}H_{30}O_9$: C, 70.70; H, 5.09. Found: C, 70.57; H, 5.17.

4.1.21. MW-synthesis of 7,4′-bis(benzoyloxy)-6-(3-hydroxy-3-methylbutyl)-3′-methoxy-5-tosyloxyisoflavone (14b). A mixture of **13b** (500 mg, 0.840 mmol), tosyl chloride (257 mg, 1.34 mmol) and K_2CO_3 (1.16 g, 8.32 mmol) in acetone (20 ml) was irradiated under MW for 30 min (3 min×10 times irradiation, 1–2 min interval/irradiation). The reaction mixture was worked up in a similar manner (as in the case of compound **14a**) to give compound **14b** as a colourless crystalline solid (585 mg, 93%), mp 170–171 °C. ^{1}H NMR ($CDCl_3$) δ: 1.13 (6H, s, CH_3×2), 1.71 and 2.79 (each 2H, m, CH_2), 2.42 (3H, s, CH_3–Ar), 3.86 (3H, s, OCH_3), 7.02–7.82 (18H, m, Ar–H×18), 7.92 (1H, s, C_2–H); Anal. Calcd for $C_{42}H_{36}O_{11}S$: C, 67.37; H, 4.85. Found: C, 67.19; H, 4.96.

4.1.22. MW-synthesis of 7,4′-bis(benzoyloxy)-6-(3-methyl-2-butenyl)-3′-methoxy-5-tosyloxyisoflavone (15b). To a solution of **14b** (430 mg, 0.574 mmol) in dry toluene (20 ml) was added $TsOH\cdot H_2O$ (1.40 ml of a 5.24×10^{-1} M solution in acetic acid). The reaction mixture was irradiated incessantly under MW at 117 °C for 15–20 min. The similar work up of the reaction mixture (as in the case of compound **15a**) gave the 6-alkenylisoflavone. The ^{1}H NMR spectrum showed that it was a mixture of 6-(3-methyl-2-butenyl)isoflavone **15b** and the regioisomer, 6-(3-methyl-3-butenyl)isoflavone **15b′** (**15b**/**15b′**=99:1). The isomeric mixture was recrystallized from a mixture of $CHCl_3$ and AcOEt to give **15b** (359 mg, 86% from **14b**) as a crystalline solid, mp 170–172 °C. ^{1}H NMR ($CDCl_3$) δ: 1.39 and 1.46 (each 3H, s, CH_3), 2.39 (3H, s, CH_3–Ar), 3.35 (2H, d, J=6.3 Hz, CH_2), 3.86 (3H, s, OCH_3), 4.95 (1H, br t, =CH), 7.02–7.70 (18H, m, Ar–H×18), 7.91 (1H, s, C_2–H); Anal. Calcd for $C_{42}H_{34}O_{10}S$: C, 69.03; H, 4.69. Found: C, 68.80; H, 4.77.

4.1.23. Synthesis of 7,4′-bis(benzoyloxy)-5-hydroxy-6-(3-methyl-2-butenyl)-3′-methoxyisoflavone (16b). Compound **15b** (200 mg, 0.273 mmol) was dissolved in dry CH_2Cl_2 (10 ml), followed by the addition of BCl_3 (0.25 ml, 1 M solution in CH_2Cl_2) in an ice bath. The similar treatment and work up of the reaction mixture (as in the case of compound **16a**) gave the 6-alkenylisoflavone **16b** (148 mg, 94%) as a colourless crystalline solid, mp 153–155 °C. ^{1}H NMR ($CDCl_3$) δ: 1.58 and 1.60 (each 3H, s, CH_3), 3.39 (2H, d, J=6.6 Hz, CH_2), 3.88 (3H, s, OCH_3), 5.16 (1H, br t, =CH), 6.87 (1H, s, C_8–H), 7.10–7.70 (13H, m, Ar–H×13), 8.02 (1H, s, C_2–H), 13.13 (1H, s, C_5–OH); Anal. Calcd for $C_{35}H_{28}O_8$: C, 72.91; H, 4.89. Found: C, 72.97; H, 5.12.

4.1.24. Synthesis of 5,7,4′-trihydroxy-6-(3-methyl-2-butenyl)-3′-methoxyisoflavone (lupisoflavone) (1b). Compound **16b** (130 mg, 0.225 mmol) was dissolved in a mixture of methanol (3 ml) and dioxane (3 ml), followed by the addition of 10% NaOH (1 ml, 2.5 mmol). The similar work up of the reaction mixture (as in the case of compound **1a**) gave 6-prenylisoflavone **1b** (52 mg, 62%) as a pale yellow crystalline solid, mp 161–163 °C. ^{1}H NMR (see Table 1); IR (KBr) ν_{max} 3435, 3085, 2949, 1649, 1517, 1459, 1205, 1068 cm^{-1}; UV λ_{max} nm ($\log\varepsilon$) (MeOH): 267sh (4.39), 220 (4.36), (+$AlCl_3$) 341 (3.97), 274sh (4.39), (+NaOAc) 338 (4.02), 276sh (4.45); Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.39; H, 5.31.

4.1.25. 5,7,4′-Triacetoxy-6-(3-methyl-2-butenyl)-3′-methoxyisoflavone (17b). Acetylation of **1b** (50 mg, 0.13 mmol) was achieved in a similar manner (as in the case of compound **17a**) to give **17b** (54 mg, 80%) as a colourless crystalline solid, mp 154–156 °C. ^{1}H NMR ($CDCl_3$) δ: 1.67 and 1.75 (each 3H, s, CH_3), 2.33, 2.35 and 2.43 (each 3H, s, $COCH_3$), 3.30 (2H, br d, CH_2), 3.86 (3H, s, OCH_3), 5.01 (1H, br t, =CH), 6.97 (1H, dd, J=8.3 and 1.7 Hz, $C_{6'}$–H), 7.06 (1H, d, J=8.3 Hz, $C_{5'}$–H), 7.12 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.22 (1H, s, C_8–H), 7.87 (1H, s, C_2–H). Anal. Calcd for $C_{27}H_{26}O_9$: C, 65.68; H, 5.25. Found: C, 65.93; H, 4.95.

4.1.26. MW-synthesis of 2′,4′-bis(benzyloxy)-3′-iodo-3,4-methylenedioxy-6′-methoxymethoxychalcone (7c) and 2′,4′-bis(benzyloxy)-6′-hydroxy-3′-iodo-3,4-methylenedioxychalcone (8c). A mixture of **5** (4.0 g, 7.7 mmol) and **6c** (1.60 g, 10.6 mmol) was dissolved in alc. KOH (3.0 g, 53 mmol in 50 ml EtOH). The reaction mixture was irradiated under MW for 6 min (2 min×3 times irradiation, 1–2 min interval/irradiation), and monitored by TLC to establish completion. A similar treatment of the reaction mixture (as in the case of compound **8a**) gave **8c** (4.15 g, 89%, two steps yield from **5**) as a yellow solid, mp 161–163 °C. ^{1}H NMR ($CDCl_3$) δ: 4.86 and 5.21 (each 2H, s, $PhCH_2$), 5.99 (2H, s, O–CH_2–O), 6.42 (1H, s, $C_{5'}$–H), 6.69 (1H, d, J=1.7 Hz, C_2–H), 6.71 (1H, d, J=7.8 Hz, C_5–H), 6.89 (1H, dd, J=8.05 and 1.7 Hz, C_6–H), 7.24–7.52 (10H, m, Ar–H×10), 7.76 and 7.81 (each 1H, d, J=15.3 Hz, =CH), 13.69 (1H, s, $C_{6'}$–OH); Anal. Calcd for $C_{30}H_{23}IO_6$: C, 59.42; H, 3.82. Found: C, 59.29; H, 3.97.

4.1.27. MW-synthesis of 2′,4′-bis(benzyloxy)-6′-benzoyloxy-3′-iodo-3,4-methylenedioxychalcone (9c). Benzoyl chloride (1.21 g, 8.52 mmol) was slowly added to a mixture of **8c** (4.0 g, 6.6 mmol) in pyridine (40 ml). The reaction mixture was irradiated incessantly under MW at 125 °C for 6 min. The reaction mixture was worked up in a similar manner (as in the case of compound **9a**) to give **9c** (4.10 g, 89%) as a fluffy crystalline solid. ^{1}H NMR ($CDCl_3$) δ: 4.99 and 5.21 (each 2H, s, $PhCH_2$), 5.98 (2H, s, O–CH_2–O), 6.73 (1H, s, $C_{5'}$–H), 6.75–6.94 (3H, m, Ar–H×3), 7.24–7.52 (15H, m, Ar–H×15), 7.53 and 7.56 (each 1H, d, J=17.5 Hz, =CH); Anal. Calcd for $C_{37}H_{27}IO_7$: C, 62.55; H, 3.83. Found: C, 62.56; H, 3.97.

4.1.28. MW-synthesis of 1-[6-benzoyloxy-2,4-bis(benzyloxy)-3-iodophenyl]-2-(3,4-methylenedioxyphenyl)-3,3-dimethoxypropan-1-one (10c) and 5,7-bis(benzyloxy)-6-iodo-3′,4′-methylenedioxyisoflavone (11c). Compound **9c** (2.0 g, 2.8 mmol) was dissolved in a mixture of MeOH (25 ml) and $CHCl_3$ (6 ml), followed by the addition of HTIB (1.76 g, 4.48 mmol). The reaction mixture was irradiated under MW for 12 min (2 min×6 times irradiation, 1–2 min interval/irradiation) at 60 °C. The reaction mixture was worked up in a similar manner (as in the case of compound **10a**) to give crude acetal **10c** as a semisolid mass. This crude mass was hydrolyzed and cyclized under MWI for 5 min in a similar way (as in the case of compound **11a**) to give iodoisoflavone **11c** (0.78 g, 46%, two steps yield from **8c**), mp 205–206 °C. ^{1}H NMR ($CDCl_3$) δ: 5.07 and 5.26 (each 2H, s, $PhCH_2$), 5.99 (2H, s, O–CH_2–O), 6.75 (1H, s, C_8–H), 6.85 (1H, d, J=7.8 Hz, $C_{5'}$–H), 6.92 (1H,

dd, J=8.05 and 1.7 Hz, $C_{6'}$–H), 7.08 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.26–7.57 (10H, m, Ar–H×10), 7.80 (1H, s, C_2–H); Anal. Calcd for $C_{30}H_{21}IO_6$: C, 59.62; H, 3.49. Found: C, 59.36; H, 3.62.

Acetal **10c**: ^{1}H NMR ($CDCl_3$) δ: 3.03 and 3.22 (each 3H, s, OCH_3), 4.70 and 4.79 (each 1H, d, J=10.2 Hz, CH), 4.98 and 5.11 (each 2H, s, $PhCH_2$), 5.84 (2H, s, O–CH_2–O), 6.48 (1H, s, Ar–H), 6.50 (1H, d, J=7.8 Hz, Ar–H), 6.57 (1H, dd, J=7.8 and 1.7 Hz, Ar–H), 6.67 (1H, d, J=1.7 Hz, Ar–H), 7.25–7.65 (15H, m, Ar–H×15).

The similar treatment of compound **9c** (2.01 g, 2.82 mmol) with BTIB (1.89 g, 4.39 mmol) under MWI (2 min×6 times irradiation, 1–2 min interval/irradiation) at 60 °C gave crude acetal **10c**, which was cyclized under MWI for 6 min to give **11c** (547 g, 32%).

4.1.29. MW-synthesis of 5,7-bis(benzyloxy)-6-(3-hydroxy-3-methyl-1-butynyl)-3′,4′-methylenedioxyisoflavone (12c). Compound **11c** (2.0 g, 3.3 mmol) was dissolved in DMF (12 ml), followed by the successive addition of Et_3N (55 ml), $PdCl_2$ (30 mg, 0.16 mmol), PPh_3 (82 mg, 0.31 mmol) and CuI (32 mg, 0.16 mmol) and finally 2-methyl-3-butyn-2-ol (1.2 ml, 16 mmol). The similar treatment of the reaction mixture under MWI (2 min×4 times irradiation, 1–2 min interval/irradiation) (as in the case of compound **12a**) gave **12c** as a colourless crystalline solid (1.26 g, 68%), mp 188–190 °C. ^{1}H NMR ($CDCl_3$) δ: 1.50 (6H, s, CH_3×2), 5.20 and 5.21 (each 2H, s, $PhCH_2$), 5.98 (2H, s, O–CH_2–O), 6.71 (1H, s, C_8–H), 6.85 (1H, d, J=8.0 Hz, $C_{5'}$–H), 6.92 (1H, dd, J=8.0 and 1.7 Hz, $C_{6'}$–H), 7.08 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.25–7.52 (10H, m, Ar–H×10), 7.78 (1H, s, C_2–H); Anal. Calcd for $C_{35}H_{28}O_7$: C, 74.99; H, 5.03. Found: C, 74.75; H, 4.97.

4.1.30. 5,7-Dihydroxy-6-(3-hydroxy-3-methylbutyl)-3′,4′-methylenedioxyisoflavone (derrubone hydrate) (2c). Compound **12c** (500 mg, 0.895 mmol) was hydrogenolyzed over 5% Pd/C (80 mg) in a mixture of methanol (25 ml) and dioxane (25 ml) until the uptake of hydrogen ceased. The similar treatment of the reaction mixture (as in the case of compound **2a**) gave **2c** as a colourless crystalline solid (300 mg, 87%), mp 186–187 °C. ^{1}H NMR (see Table 1); IR (KBr) ν_{max} 3429, 3090, 2972, 2892, 1654, 1572, 1490, 1253, 1061 cm^{-1}; UV λ_{max} nm (log ε) (MeOH): 338 (3.87), 272sh (4.35), 219 (4.31), (+$AlCl_3$) 381 (3.0), 267sh (4.33), (+NaOAc) 292 (3.27), 233sh (4.45); Anal. Calcd for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.40; H, 5.29.

4.1.31. Synthesis of 7-benzoyloxy-5-hydroxy-6-(3-hydroxy-3-methylbutyl)-3′,4′-methylenedioxyisoflavone (13c). A mixture of **2c** (700 mg, 1.82 mmol), benzoyl chloride (0.25 ml, 2.2 mmol) and K_2CO_3 (2.51 g, 18.2 mmol) in acetone (25 ml) was heated at 45 °C under nitrogen for 25 min. The similar treatment of the reaction mixture (as in the case of compound **13a**) gave **13c** as a colourless crystalline solid (809 mg, 91%), mp 156–158 °C. ^{1}H NMR ($CDCl_3$) δ: 1.20 (6H, s, CH_3×2), 1.71 and 2.74 (each 2H, m, CH_2), 6.01 (2H, s, O–CH_2–O), 6.84 (1H, d, J=8.0 Hz, $C_{5'}$–H), 6.90 (1H, s, C_8–H), 6.94 (1H, dd, J=8.0 and 1.7 Hz, $C_{6'}$–H), 7.05 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.26–7.70 (5H, m, Ar–H×5), 7.94 (1H, s, C_2–H), 13.15 (1H, s, C_5–OH); Anal. Calcd for $C_{28}H_{24}O_8$: C, 68.85; H, 4.95. Found: C, 68.77; H, 4.85.

4.1.32. MW-synthesis of 7-benzoyloxy-6-(3-hydroxy-3-methylbutyl)-3′,4′-methylenedioxy-5-tosyloxyisoflavone (14c). A mixture of **13c** (800 mg, 1.63 mmol), tosyl chloride (468 mg, 2.45 mmol) and K_2CO_3 (2.50 g, 18.1 mmol) in acetone (25 ml) was irradiated incessantly under MW for 11 min. The reaction mixture was worked up in a similar manner (as in the case of compound **14a**) to give compound **14c** as a colourless crystalline solid (990 mg, 94%), mp 183–184 °C. ^{1}H NMR ($CDCl_3$) δ: 1.13 (6H, s, CH_3×2), 1.71 and 2.74 (each 2H, m, CH_2), 2.43 (3H, s, Ar–CH_3), 6.0 (2H, s, O–CH_2–O), 6.85 (1H, s, C_8–H), 6.84 (1H, d, J=8.0 Hz, $C_{5'}$–H), 6.87 (1H, dd, J=8.0 and 1.7 Hz, $C_{6'}$–H), 6.97 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.26–7.71 (9H, m, Ar–H×9), 7.83 (1H, s, C_2–H); Anal. Calcd for $C_{35}H_{30}O_{10}S$: C, 65.41; H, 4.71. Found: C, 65.29; H, 4.67.

4.1.33. MW-synthesis of 7-benzoyloxy-6-(3-methyl-2-butenyl)-3′,4′-methylenedioxy-5-tosyloxyisoflavone (15c). To a solution of **14c** (400 g, 0.622 mmol) in dry toluene (20 ml) was added $TsOH\cdot H_2O$ (1.16 ml of a 5.24×10^{-1} M solution in acetic acid). The reaction mixture was irradiated incessantly under MW at 117 °C (refluxing) for 20 min. The reaction mixture was worked up in a similar manner (as in the case of compound **15a**) to give the 6-alkenylisoflavone **15c** as a crystalline solid. The ^{1}H NMR spectrum showed that it was a mixture of 6-(3-methyl-2-butenyl)isoflavone **15c** and the regioisomer, 6-(3-methyl-3-butenyl)isoflavone **15c′** (**15c/15c′**=99:1). The isomeric mixture was recrystallized from a mixture of $CHCl_3$ and Me_2CO (5:1) to give **15c** (328 mg, 85% from **14c**) as a crystalline solid, mp 157–158 °C. ^{1}H NMR ($CDCl_3$) δ: 1.40 and 1.45 (each 3H, s, CH_3), 2.41 (3H, s, Ar–CH_3), 3.34 (2H, d, J=6.5 Hz, CH_2), 4.94 (1H, t, J=6.5 Hz, =CH), 6.0 (2H, s, O–CH_2–O), 6.83–7.96 (13H, m, Ar–H×13), 7.81 (1H, s, C_2–H); Anal. Calcd for $C_{35}H_{28}O_9S$: C, 67.63; H, 4.52. Found: C, 67.59; H, 4.41.

4.1.34. 7-Benzoyloxy-5-hydroxy-6-(3-methyl-2-butenyl)-3′,4′-methylenedioxyisoflavone (16c). Compound **15c** (400 mg, 0.640 mmol) was dissolved in dry CH_2Cl_2 (10 ml), followed by the addition of BCl_3 (0.37 ml, 1 M solution in CH_2Cl_2) in an ice bath. The similar treatment and work up of the reaction mixture (as in the case of compound **16a**) gave the 6-alkenylisoflavone **16c** (240 mg, 79%) as a colourless crystalline solid, mp 115–117 °C. ^{1}H NMR ($CDCl_3$) δ: 1.57 and 1.59 (each 3H, s, CH_3), 3.38 (2H, d, J=6.8 Hz, CH_2), 5.15 (1H, t, J=6.8 Hz, =CH), 6.01 (2H, s, O–CH_2–O), 6.84 (1H, s, C_8–H), 6.88 (1H, d, J=8.0 Hz, $C_{5'}$–H), 6.95 (1H, dd, J=8.0 and 1.7 Hz, $C_{6'}$–H), 7.05 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.25–7.69 (5H, m, Ar–H×5), 7.93 (1H, s, C_2–H), 13.13 (1H, s, C_5–OH); Anal. Calcd for $C_{28}H_{22}O_7$: C, 71.48; H, 4.71. Found: C, 71.62; H, 4.81.

4.1.35. Synthesis of 5,7-dihydroxy-6-(3-methyl-2-butenyl)-3′,4′-methylenedioxyisoflavone (derrubone) (1c). Compound **16c** (150 mg, 0.318 mmol) was dissolved in a mixture of methanol (3 ml) and dioxane (3 ml), followed by the addition of 10% NaOH (1.1 ml). The similar treatment and work up of the reaction mixture (as in the case of compound **1a**) gave 6-prenylisoflavone **1c** (92 mg, 79%) as a pale

yellow crystalline solid, mp 210–211 °C (lit.[24] 210–212 °C). ^{1}H NMR (see Table 1); IR (KBr) ν_{max} 3443, 3083, 2925, 2858, 1647, 1506, 1436, 1245, 1056 cm^{-1}; UV λ_{max} nm (log ε) (MeOH): 341 (4.03), 274sh (4.39), 223 (4.40), (+$AlCl_3$) 266sh (4.41), 222 (4.37), (+NaOAc) 341 (4.07), 276 (4.41), 234sh (4.45); Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.85; H, 4.95. Found: C, 68.63; H, 4.98.

4.1.36. 5,7-Diacetoxy-6-(3-methyl-2-butenyl)-3′,4′-methylenedioxyisoflavone (17c). Acetylation of **1c** (60 mg, 0.16 mmol) was achieved in a similar manner (as in the case of compound **17a**) to give **17c** (65 mg, 88%) as a colourless crystalline solid, mp 204–205 °C. ^{1}H NMR ($CDCl_3$) δ: 1.67 and 1.75 (each 3H, s, CH_3), 2.34 and 2.43 (each 3H, s, $COCH_3$), 3.25 (2H, br d, CH_2), 5.01 (1H, br t, =CH), 5.98 (2H, s, O–CH_2–O), 6.83 (1H, d, J=8.0 Hz, $C_{5'}$–H), 6.86 (1H, dd, J=8.0 and 1.7 Hz, $C_{6'}$–H), 6.99 (1H, d, J=1.7 Hz, $C_{2'}$–H), 7.20 (1H, s, C_8–H), 7.83 (1H, s, C_2–H). Anal. Calcd for $C_{25}H_{22}O_8$: C, 66.66; H, 4.92. Found: C, 66.49; H, 4.87.

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