Regioselective Synthesis of Prenylisoflavones. Syntheses of Allolicoisoflavone A, 2,3-Dehydrokievitone, and Related Compounds

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The palladium-catalyzed coupling reaction of 2′,4′,5,7-tetrakis(benzyloxy)-5′-iodoisoflavone (**12**), synthesized from the 5-iodochalcone **9**, with 2-methyl-3-butyn-2-ol gave the corresponding 5′-(3-hydroxy-3-methyl-1-butynyl)isoflavone **13**. The catalytic hydrogenation of **13** gave 2′,4′,5,7-tetrahydroxy-5′-(3-hydroxy-3-methylbutyl)isoflavone (**2**). Dehydration of the benzoate **14** of **2** afforded a mixture of 5′-(3-methyl-2-butenyl)isoflavone **15** and the isomer 5′-(3-methyl-3-butenyl)isoflavone **16**. The separation of **15** was accomplished by a treatment of the mixture (**15** and **16**) with mercury(II) nitrate. Hydrolysis of **15** afforded 2′,4′,5,7-tetrahydroxy-5′-prenylisoflavone (allolicoisoflavone A) (**1**). In a similar manner, 2′,4′,5,7-tetrahydroxy-8-prenylisoflavone (2,3-dehydrokievitone) (**3**) and 2′,4′,5,7-tetrahydroxy-8-(3-hydroxy-3-methylbutyl)isoflavone (2,3-dehydrokievitone hydrate) (**4**) were synthesized from the corresponding 8-iodoisoflavone **22**. The tetramethyl ether **5** of **3** was also prepared from the 8-iodotetramethoxyisoflavone **32**.

Prenyl (=3-methyl-2-butenyl) isoflavones and (3-hydroxy-3-methylbutyl)isoflavones are widely distributed in nature and have antifungal activity.[1] Some of them are known to be a phytoalexin, such as 2,3-dehydrokievitone and luteone.[1,2] Prenylisoflavones are also of importance as precursors of pyranoisoflavones and furanoisoflavones from a biogenetic aspect.[3] Usually, the prenyl and 3-hydroxy-3-methylbutyl groups in the isoflavones are contained as A- and/or B-ring substituents. Therefore, a straightforward synthesis of prenylisoflavones and (3-hydroxy-3-methylbutyl)isoflavones seems to be difficult. Although tetraoxygenated prenylisoflavones have been synthesized from suitable isoflavones by acid- and base-catalyzed alkylation, such procedures have resulted in relatively low yields, have not led to the syntheses of polyhydroxyisoflavones, and are not useful for the syntheses of polyhydroxyprenylisoflavones, because *O*- and di-alkylation, deprotection, and a lack of regioselectivity are common problems.[4] The reaction of aryl halides with terminal alkynes in the presence of a palladium(0) catalyst is efficient for the formation of C–C bonds and alkylation.[5] During the course of our synthetic studies of prenylphenol derivatives, we recently found that these compounds have been regioselectively synthesized by a palladium-catalyzed method.[6] Therefore, this methodology seems to be easily applicable to the regioselective synthesis of polyoxygenated prenylisoflavones and (3-hydroxy-3-methylbutyl)isoflavones via a coupling reaction of the corresponding iodoisoflavones with propargyl alcohol.

A new prenylisoflavone, allolicoisoflavone A [2′,4′,5,7-tetrahydroxy-5′-(3-methyl-2-butenyl)isoflavone] (**1**), having antifungal activity, was isolated from the root bark of the leguminous tree *Piscidia erythrina* L. (Jamaican dogwood),[7] and 2,3-dehydrokievitone [2′,4′,5,7-tetrahydroxy-8-(3-methyl-2-butenyl)isoflavone] (**3**), being known as a phytoalexin and 2,3-dehydrokievitone hydrate [2′,4′,5,7-tetrahydroxy-8-(3-hydroxy-3-methylbutyl)isoflavone] (**4**), were isolated from the roots of yellow lupin, *Lupinus luteus* L., cv Barpine (Leguminosae).[2] Each structure of these prenylisoflavones and hydroxyalkylisoflavones was identified by spectroscopic and chemical studies.

We wish to report here on the first syntheses of **1**, 2′,4′,5,7-tetrahydroxy-5′-(3-hydroxy-3-methylbutyl)isoflavone (**2**), **3**, **4**, 2′,4′,5,7-tetramethoxy-8-(3-methyl-2-butenyl)isoflavone (**5**), and 2′,4′,5,7-tetramethoxy-8-(3-hydroxy-3-methylbutyl)isoflavone (**6**) by using the palladium-catalyzed coupling reaction.[8]

Results and Discussion

The reaction of 4′,6′-bis(benzyloxy)-2′-hydroxyacetophenone[9] with chloromethyl methyl ether in the presence of *N*,*N*-diisopropylethylamine afforded the corresponding 2′-(methoxymethoxy)acetophenone **7**, and 2,4-bis(benzyloxy)-5-iodobenzaldehyde (**8**) was easily prepared by iodination of 2,4-bis(benzyloxy)benzaldehyde with iodine in the presence of silver trifluoroacetate[6,10] at room temperature (Chart 1). The condensation of **7**with the benzaldehyde **8** in the presence of potassium hydroxide gave the corresponding chalcone, and then the methoxymethyl group in the chalcone was cleaved by a treatment with hydrochloric acid in a mixture of methanol and chloroform to afford the 2′-hydroxychalcone **9**, which was converted into the acetate derivative **10**. An oxidative rearrangement of the acetate **10** with thallium(III)

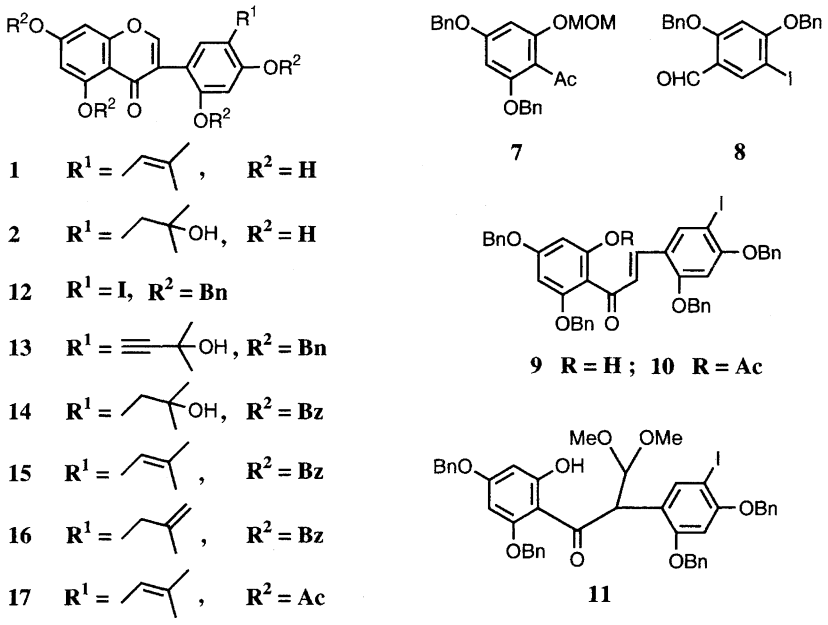
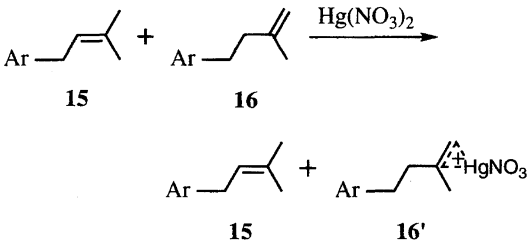


Chart 1.

nitrate trihydrate (TTN) gave the acetal derivative **11**, which was converted into the corresponding 5′-iodoisoflavone **12** by a treatment with 10% hydrochloric acid at 75 °C in high yield. The coupling reaction of **12** with 2-methyl-3-butyn-2-ol in the presence of Pd(0) gave the desired 5′-(3-hydroxy-3-methyl-1- butynyl)isoflavone **13** in good yield. The catalytic hydrogenation of **13** over Pd/C in a mixture of methanol and tetrahydrofuran at 18 °C gave 2′,4′,5,7-tetrahydroxy-5′-(3-hydroxy-3-methylbutyl)isoflavone (**2**), which has yet to be isolated from natural sources and whose ^{1}H NMR spectrum is given in Table 1.



(1)

The tetrabenzoate derivative **14** of **2** was dehydrated with *p*-toluenesulfonic acid monohydrate to give a mixture of the 5′-(3-methyl-2-butenyl)isoflavone **15** and the regioisomer 5′-(3-methyl-3-butenyl)isoflavone **16**. The ^{1}H NMR spectrum of the mixture of the benzoate derivatives (**15** and **16**) showed the ratio of **15** to **16** to be 82 : 18 [peaks due to $CH_2CH{=}C(CH_3)_2$ at δ = 3.32 (2H, d) and $CH_2CH_2C(CH_3){=}CH_2$ at δ = 4.70 (2H, s)]. The complete separation of **15** from the mixture (**15** and **16**) was significantly difficult either by chromatography or recrystallization. A solution to the problem was provided by treating of the mixture with aqueous mercury(II) nitrate (1.5 mol amt. to the isomer **16**) in tetrahydrofuran at room temperature to give the terminal alkylmercurinium ion **16′**, as shown by Eq. 1;[6,11] then, the unchanged benzoate **15** was quantitatively separated from the mixture (**15** and **16′**) by silica-gel column chromatography. The hydrolysis of **15** was carried out by a treatment with dilute aqueous sodium hydroxide to give the desired 2′,4′,5,7-tetrahydroxy-5′-(3-methyl-2-butenyl)-isoflavone (**1**), which was converted into 2′,4′,5,7-tetraacetoxy-5′-prenylisoflavone (**17**). The ^{1}H NMR spectral data for the synthetic 5′- prenylisoflavone **1** and the corresponding natural allolicoisoflavone A are given in Table 1. The ^{1}H NMR, IR, and UV spectral data for **1** were identical with those of natural 5′-prenylisoflavone (allolicoisoflavone A). On the basis of these results, the structure of natural allolicoisoflavone A was unequivocally established to be 2′,4′,5,7-tetrahydroxy-5′-(3-methyl-2-butenyl)isoflavone (**1**).

The reaction of 4′,6′-bis(benzyloxy)-2′-hydroxyacetophenone with iodine in the presence of silver trifluoroacetate gave 4′,6′-bis(benzyloxy)-2′-hydroxy-3′-iodoacetophenone,[12] which was converted into 4′,6′-bis(benzyloxy)-3′-iodo-2′-(methoxymethoxy)acetophenone[8] (**18**) (Chart 2). The condensation of **18** with 2,4-bis(benzyloxy)benzaldehyde gave the corresponding 2′-hydroxychalcone **19**. The oxidative rearrangement of the acetate **20**, derived from **19**, with TTN gave the acetal derivative **21**, which was converted into the corresponding 8-iodoisoflavone **22**. The coupling reaction of **22** with 2-methyl-3-butyn-2-ol in the presence of Pd(0) gave the 8-(3-hydroxy-3-methyl-1-butynyl)isoflavone **23**. Catalytic hydrogenation of **23** over Pd/C gave 2′,4′,5,7-tetrahydroxy-8-(3-hydroxy-3-methylbutyl)isoflavone (**4**). The ^{1}H NMR and UV spectral data for **4** were identical with those of a natural sample of 2,3-dehydrokievitone hydrate (Table 1). On the basis of these results, the structure of natural 2,3-dehydrokievitone hydrate was unequivocally established to be 2′,4′,5,7-tetrahydroxy-

Table 1. ^{1}H NMR (400 MHz, CD_3COCD_3) Data for the Prenylisoflavones **1**, **2**, **3**, and **4**[a)]

Compound	2-H	6-H	8-H	3′-H	5′-H	6′-H	Me	CH_2	CH=C	OH
1	8.16s	6.31d (J = 2.2 Hz)	6.46d (J = 2.2 Hz)	6.51s		7.00s	1.69s 1.71s	3.27d (J = 7.3 Hz)	5.34t (J = 7.3 Hz)	8.08br s, 8.36br s 9.74br s, 12.78s
Natural product[7)] (**1**)	8.15s	6.31d (J = 2.2 Hz)	6.46d (J = 2.2 Hz)	6.51s		7.00s	1.69s 1.71s	3.27d (J = 7.3 Hz)	5.34br t (J = 7.3 Hz)	12.82s
2	8.20s	6.32d (J = 2.0 Hz)	6.47d (J = 2.0 Hz)	6.31s		7.03s	1.23s (6H)	1.75m 2.67m		8.07s, 8.39s 9.76s, 12.79s
3	8.27s	6.40s		6.49d (J = 2.4 Hz)	6.44dd (J = 2.4, 8.3 Hz)	7.15d (J = 8.3)	1.66s 1.81s	3.46d (J = 7.3 Hz)	5.25t (J = 7.3 Hz)	8.39s, 8.52s 9.80br s, 12.72s
Natural product[2)] (**3**)	8.26s	6.39s		6.49d (Incomplete)	6.44dd (J = 1.7, 8.6 Hz)	7.18d (J = 8.6)	1.66s 1.81s	3.47br d (J = 7.1 Hz)	5.26br t (J = 7.1 Hz)	12.70s
4	8.26s	6.38s		6.49d (J = 2.4 Hz)	6.45dd (J = 2.4, 8.3 Hz)	7.15d (J = 8.3 Hz)	1.28s (6H)	1.73m 2.87m		8.31s, 8.46s 9.74br s, 12.69s
Natural product (**4**)	8.26s	6.37s		6.49d (Incomplete)	6.44dd (J = 2.2, 8.5 Hz)	7.15d (J = 8.5 Hz)	1.25s (6H)	1.73m 2.87m		12.68s

a) s: singlet; d: doublet; dd: double doublets; t: triplet; br: broad.

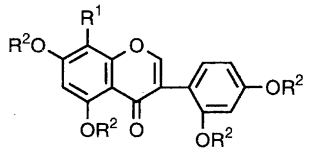
8-(3-hydroxy-3-methylbutyl)isoflavone (**4**). The tetrabenzoate derivative **24** of **4** was dehydrated to give a 85 : 15 mixture of the 8-(3-methyl-2-butenyl)isoflavone **25** and the isomer 8-(3-methyl-3-butenyl)isoflavone **26** by the ^{1}H NMR analysis. The 8-prenylisoflavone **25** was easily separated from the mixture (**25** and **26**) by a treatment with mercury(II) nitrate. Hydrolysis of **25** gave 2′,4′,5,7-tetrahydroxy-8-(3-methyl-2-butenyl)isoflavone (**3**). The ^{1}H NMR spectral data for the synthetic 8-prenylisoflavone **3** and natural 2,3-dehydrokievitone are given in Table 1. The ^{1}H NMR, IR, and UV spectral data for **3** were identical with those of natural 2,3-dehydrokievitone. The melting point of the synthetic 8-(3-methyl-2-butenyl)isoflavone **3** was not depressed by an admixture with natural 2,3-dehydrokievitone. On the basis of these results, the structure of natural 2,3-dehydrokievitone was unequivocally established to be 2′,4′,5,7-tetrahydroxy-8-(3-methyl-2-butenyl)isoflavone (**3**).

The condensation of 2′-benzyloxy-3′-iodo-4′,6′-dimethoxyacetophenone (**27**), synthesized by the iodination of 2′-hydroxy-4′,6′-dimethoxyacetophenone, followed by benzylation of the resultant compound, with 2,4-dimethoxybenzaldehyde gave the 2′-benzyloxychalcone **28**, which was converted into the 2′-hydroxychalcone **29** by a treatment with aluminum chloride. The oxidative rearrangement of the acetate **30** of **29** gave the 8-iodoisoflavone **32** via the corresponding acetal **31**. The coupling reaction of **32** with 2-methyl-3-butyn-2-ol, followed by hydrogenation of the resultant 8-(3-hydroxy-3-methyl-1-butynyl)isoflavone **33**, gave the 8-(3-hydroxy-3-methylbutyl)isoflavone **6**, which was dehydrated to give a mixture of 2′,4′,5,7-tetramethoxy-8-prenylisoflavone (**5**) and its isomer 2′,4′,5,7-tetramethoxy-8-(3-methyl-3-butenyl)isoflavone. The 8-prenylisoflavone **5** was also separated from the mixture by a treatment with mercury(II) nitrate. The ^{1}H NMR and UV spectral data for **5** were identical with those of 2,3-dehydrokievitone tetramethyl ether derived from natural 2,3-dehydrokievitone. Thus, syntheses of *O*-alkylprenylisoflavone derivatives turned out to be simple using the method described above.

The present palladium-catalyzed coupling reactions of iodoisoflavones with 2-methyl-3-butyn-2-ol have been shown to be an efficient and useful procedure for regioselective syntheses of polyhydroxyprenylisoflavones and *O*-alkylated prenylisoflavones. The excellent chemoselectivity of mercury(II) nitrate to internal and terminal alkenes has been shown to be remarkably useful for the recognition and separation of terminal alkenes.

Experimental

All of the melting points were measured on a Yanaco MP-J3 micro melting-point apparatus and are uncorrected. The ^{1}H NMR spectra were measured with a Hitachi R-24B spectrometer (60 MHz) and a JEOL EX400 spectrometer (400 MHz), using tetramethylsilane as internal standard (δ, ppm). The IR spectra were recorded on a JASCO FT/IR-230 spectrophotometer, and the UV spectra 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 with Kieselgel 60 F-254 (Merck).



3 R^1 =  , R^2 = H

4 R^1 =  , R^2 = H

5 R^1 =  , R^2 = Me

6 R^1 =  , R^2 = Me

22 R^1 = I, R^2 = Bn

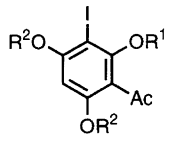
23 R^1 =  , R^2 = Bn

24 R^1 =  , R^2 = Bz

25 R^1 =  , R^2 = Bz

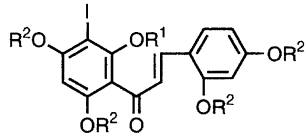
32 R^1 = I, R^2 = Me

33 R^1 =  , R^2 = Me



18 R^1 = MOM, R^2 = Bn

27 R^1 = Bn, R^2 = Me



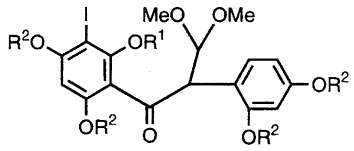
19 R^1 = H, R^2 = Bn

20 R^1 = Ac, R^2 = Bn

28 R^1 = Bn, R^2 = Me

29 R^1 = H, R^2 = Me

30 R^1 = Ac, R^2 = Me



21 R^1 = Ac, R^2 = Bn

31 R^1 = Ac, R^2 = Me

Chart 2.

4′,6′-Bis(benzyloxy)-2′-(methoxymethoxy)acetophenone (7). A mixture of 4′,6′-bis(benzyloxy)-2′-hydroxyacetophenone (5.04 g, 14.5 mmol), *N*,*N*-diisopropylethylamine (50 cm^3, 287 mmol), and chloromethyl methyl ether (16.5 cm^3, 217 mmol) in dichloromethane (130 cm^3) was stirred at room temperature for 3 h. The reaction mixture was poured into a mixture of ice and water, and neutralized with 2% hydrochloric acid. The mixture was extracted with dichloromethane, washed with water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was recrystallized from a mixture of benzene and hexane to yield **7** (4.71 g, 83%) as colorless prisms, mp 90—92 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=2.48 (3H, s, $COCH_3$), 3.46 (3H, s, OCH_3), 5.02 and 5.03 (each 2H, s, CH_2), 5.13 (2H, s, OCH_2O), 6.27 and 6.43 (each 1H, d, J=2 Hz, 3′-H and 5′-H), 7.3—7.4 (10H, m, $C_6H_5\times2$). Found: C, 73.17; H, 6.22. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16%.

2,4-Bis(benzyloxy)-5-iodobenzaldehyde (8). Silver trifluoroacetate (8.3 g, 37.7 mmol) was added to a solution of 2,4-bis(benzyloxy)benzaldehyde (10 g, 31.4 mmol) in chloroform (40 cm^3). To the suspension was added a solution of iodine (7.96 g, 31.4 mmol) in chloroform (250 cm^3) dropwise with stirring at room temperature until completion of the reaction, as judged by TLC. After stirring for an additional 30 min, the mixture was filtered and the separated silver iodide was washed with chloroform. The filtrate was washed with 5% aqueous sodium thiosulfate, 5% aqueous sodium hydrogencarbonate, and water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the resulting compound was recrystallized from a mixture of methanol and acetone to yield **8** (12.3 g, 88%) as colorless needles, mp 151.5—153 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=5.04 and 5.08 (each 2H, s, CH_2), 6.38 (1H, s, C_3-H), 7.28 (10H, s, $C_6H_5\times2$), 8.13 (1H, s, C_6-H). Found: C, 56.89; H, 3.81%. Calcd for $C_{21}H_{17}IO_3$: C, 56.77; H, 3.86%.

2,4,4′,6′-Tetrakis(benzyloxy)-2′-hydroxy-5-iodochalcone (9). A mixture of the acetophenone **7** (1.5 g, 3.8 mmol) and the 5-iodobenzaldehyde **8** (2.21 g, 5.0 mmol) was refluxed with stirring in the presence of potassium hydroxide (2.14 g, 38.1 mmol) in a mixture of ethanol (300 cm^3) and dioxane (100 cm^3) for 4 h. After the reaction mixture was concentrated to ca. 200 cm^3, ice-water and 10% hydrochloric acid were added to the residue to give yellow precipitates. The collected precipitates were dissolved in a mixture of chloroform (100 cm^3) and ethanol (50 cm^3). Conc. hydrochloric acid (4 cm^3) was added to the solution, and then the mixture was stirred at 40 °C for 3 h. The whole was extracted with chloroform, and the chloroform solution was washed with 5% aqueous sodium hydrogencarbonate and water, and dried (Na_2SO_4). After removal of the solvent, the resulting compound was recrystallized from a mixture of chloroform and methanol to give the 2′-hydroxychalcone **9** (2.25 g, 76%) as yellow needles, mp 135—137 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=4.93 and 4.96 (each 2H, s, CH_2), 5.00 (4H, s, $CH_2\times2$), 5.9—6.3 (3H, m, Ar-H×3), 7.1—7.9 (23H, m, $C_6H_5\times4$ and CH=×2 and Ar-H), 14.20 (1H, s, OH); Found: C, 66.41; H, 4.62%. Calcd for $C_{43}H_{35}IO_6$: C, 66.67; H, 4.55%.

2′-Acetoxy-2,4,4′,6′-tetrakis(benzyloxy)-5-iodochalcone (10). The chalcone **9** (4.70 g, 6.1 mmol) was converted into the acetate **10** by a treatment with acetic anhydride (100 cm^3)–pyridine (10 cm^3) at 110 °C for 2 h. To the reaction mixture were added water and ice to give precipitates. The collected precipitates were recrystallized

from a mixture of ethyl acetate and hexane to give the 2′-acetoxychalcone **10** (4.26 g, 86%) as pale yellow needles, mp 144—146 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=2.20 (3H, s, $COCH_3$), 4.95—5.20 (8H, m, $CH_2\times4$), 6.4—6.7 (3H, m, Ar-H×3), 7.00 and 7.73 (each 1H, d, J=16 Hz, CH=), 7.90 (1H, s, Ar-H). Found: C, 66.05; H, 4.66%. Calcd for $C_{45}H_{37}IO_7$: C, 66.19; H, 4.57%.

1-[4,6-Bis(benzyloxy)-2-hydroxyphenyl]-2-[2,4-bis(benzyloxy)-5-iodophenyl]-3,3-dimethoxypropan-1-one (11). After a mixture of the chalcone **10** (2.11 g, 2.6 mmol) and TTN (2.30 g, 5.2 mmol) was stirred in a mixture of methanol (600 cm^3) and chloroform (200 cm^3) at 40 °C for 5 h, 10% hydrochloric acid (17 cm^3) was added, and the mixture was stirred at room temperature for 1 h to give white precipitates. After removal of the precipitates by filtration, the filtrate was extracted with chloroform and the extract was washed with water and dried (Na_2SO_4). The organic solvent was removed under reduced pressure, and the resulting compound was chromatographed over a silica-gel flash column ($CHCl_3$ as a solvent) to give the acetal **11** (1.55 g, 72%) as a pale yellow oil; ^{1}H NMR (60 MHz; $CDCl_3$) δ=3.02 and 3.35 (each 3H, s, OCH_3), 4.8—5.3 (10H, m, $CH_2\times4$ and CHCH), 5.8—6.6 (3H, m, Ar-H×3), 7.1—7.6 (20H, m, $C_6H_5\times4$), 7.85 (1H, s, Ar-H), 13.70 (1H, s, OH).

2′,4′,5,7-Tetrakis(benzyloxy)-5′-iodoisoflavone (12). The acetal **11** (3.44 g, 4.1 mmol) in dioxane (75 cm^3) and methanol (300 cm^3) was stirred with 10% hydrochloric acid (60 cm^3) at 70 °C for 1.5 h. Water and ice were added to the reaction mixture to give precipitates. The collected precipitates were extracted with chloroform, washed with water, and dried (Na_2SO_4). After removal of the organic solvent, the resulting compound was chromatographed over a silica-gel column ($CHCl_3$: EtOAc=50 : 1 as a solvent) to give the 5′-iodoisoflavone **12**, which was recrystallized from a mixture of methanol and chloroform as pale yellow needles (2.82 g, 89%), mp 192—193 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=5.0 (2H, s, CH_2), 5.08 (4H, s, $CH_2\times2$), 5.20 (2H, s, CH_2), 6.5—6.6 (3H, m, Ar-H×3), 7.1—7.7 (21H, m, $C_6H_5\times4$ and Ar-H), 7.73 (1H, s, C_2-H). Found: C,66.60; H, 4.40%. Calcd for $C_{43}H_{33}IO_6$: C, 66.85; H, 4.30%.

2′,4′,5,7-Tetrakis(benzyloxy)-5′-(3-hydroxy-3-methyl-1-butynyl)isoflavone (13). To a solution of **12** (980 mg, 1.3 mmol) and 2-methyl-3-butyn-2-ol (0.35 cm^3, 3.8 mmol) in a mixture of triethylamine (25 cm^3) and DMF (6 cm^3) were added $PdCl_2$ (7.0 mg, 3 mol%), PPh_3 (20 mg, 6 mol%), and CuI (7.3 mg, 3 mol%); the mixture was then stirred under nitrogen at 60 °C for 2.5 h. After the reaction mixture was filtered through charcoal, the filtrate was concentrated under reduced pressure and extracted with ethyl acetate; the extract was then washed with 2% hydrochloric acid and water, and dried (Na_2SO_4). The resulting compound was purified by silica-gel column chromatography ($CHCl_3$: Me_2CO=20 : 1 as a solvent) and further recrystallized from a mixture of methanol and acetone to give the alkynylisoflavone **13** (694 mg, 75%) as colorless prisms, mp 220—222 °C; IR (KBr) ν 3420, 1649, 1612, 1499, 1286, 1159, 1025, 818, and 735 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.59 (6H, s, $CH_3\times2$), 2.20 (1H, br s, OH), 5.02, 5.08, 5.11, and 5.21 (each 2H, s, CH_2), 6.45—6.60 (2H, m, Ar-H×2), 7.1—7.6 (22H, m, $C_6H_5\times4$ and Ar-H×2), 7.67 (1H, s, C_2-H). Found: C, 78.95; H, 5.54%. Calcd for $C_{48}H_{40}O_7$: C, 79.10; H, 5.53%).

2′, 4′, 5, 7- Tetrahydroxy- 5′- (3- hydroxy- 3- methylbutyl)isoflavone (2). The isoflavone **13** (756 mg, 1.0 mmol) was hydrogenolyzed over Pd/C (5%) (400 mg) in methanol (90 cm^3) and THF (60 cm^3) at 18 °C until uptake of hydrogen ceased. After removal of the solvent under reduced presure, the resulting compound was purified by silica-gel column chromatography ($CHCl_3$: Me_2CO=1 : 1 as a solvent) and recrystallized from a mixture of dichloromethane and acetone to give the 5′-alkylisoflavone **2** (278 mg, 72%) as pale yellow prisms, mp 187—189 °C; IR (KBr) ν 3500, 3288, 1654, 1603, 1497, 1321, 1202, 1156, 1030, 897, and 812 cm^{-1}; UV λ_{max} nm (log ε) (MeOH) 260 (4.39), 290 (4.09), (+$AlCl_3$) 269 (4.36), 290_{sh} (4.00), 310_{sh} (3.91), 377 (3.63), (+NaOAc) 271 (4.42), 300_{sh} (4.08), 324 (4.03). Found: C, 64.31; H, 5.34%. Calcd for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41%.

2′,4′,5,7-Tetrakis(benzoyloxy)-5′-(3-hydroxy-3-methylbutyl)isoflavone (14). A mixture of **2** (930 mg, 2.5 mmol), benzoyl chloride (1.7 cm^3, 15 mmol), and potassium carbonate (6.9 g, 50 mmol) in acetone (100 cm^3) was refluxed with stirring under nitrogen for 3.5 h. After removal of potassium carbonate and the solvent, the residue was extracted with chloroform, washed with 2% hydrochloric acid and water, and dried (Na_2SO_4). The resulting compound was purified by silica-gel column chromatography ($CHCl_3$: Me_2CO=1 : 1 as a solvent) and further crystallized from methanol to give the benzoate **14** (1.83 g, 93%) as colorless needles, mp 129—131 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=1.12 (6H, s, $CH_3\times2$), 1.63 and 2.60 (each 2H, m, CH_2), 2.16 (1H, s, OH), 7.1—8.4 (24H, m, $C_6H_5CO\times4$ and Ar-H×4), 7.95 (1H, s, C_2-H). Found: C, 72.93; H, 4.74%. Calcd for $C_{48}H_{36}O_{11}$: C, 73.09; H, 4.60%.

2′, 4′, 5, 7- Tetrakis(benzoyloxy)- 5′- (3- methyl- 2- butenyl)isoflavone (15) and 2′,4′,5,7-Tetrakis(benzoyloxy)-5′-(3-methyl-3-butenyl)isoflavone (16). To a solution of **14** (466 mg, 0.59 mmol) in dry toluene (30 cm^3) was added *p*-toluenesulfonic acid monohydrate [0.52 cm^3 of a 5.25×10^{-1} mol dm^{-3} in acetic acid]; the mixture was stirred under nitrogen at 110 °C for 2 h. The reaction mixture was extracted with ethyl acetate, washed with 5% aqueous sodium hydrogencarbonate, 2% hydrochloric acid, and water, and dried (Na_2SO_4). After removal of the organic solvent, the resulting compound was chromatographed over a silica-gel flash column ($CHCl_3$: Me_2CO=90 : 1 as a solvent) to give a mixture of 5′-alkenylisoflavones (340 mg, 75%). The ^{1}H NMR spectrum of the mixture was shown to be a 82 : 18 mixture of 2′,4′,5,7-tetrakis(benzoyloxy)-5′-(3-methyl-2-butenyl)isoflavone (**15**) and the regioisomer 2′,4′,5,7-tetrakis(benzoyloxy)-5′-(3-methyl-3-butenyl)isoflavone (**16**). The mixture (**15** and **16**) (204 mg) in THF (30 cm^3) was reacted with 6.6×10^{-2} mol dm^{-3} $Hg(NO_3)_2\cdot H_2O$ (1.2 cm^3, 1.5 mol amt. to the isomer **16**) at room temperature for 50 min to give a mixture of the unchanged 5′-(3-methyl-2-butenyl)isoflavone **15** and the terminal alkylmercurinium ion **16′**. The reaction mixture was extracted with ether, washed with 5% aqueous sodium hydrogencarbonate and water, and dried (Na_2SO_4). After removal of the solvent, the residue was chromatographed over a silica-gel column ($CHCl_3$: Me_2CO=100 : 1 as a solvent) to give the 5′-(3-methyl-2-butenyl)isoflavone **15** (160 mg, 93%) as a colorless paste; ^{1}H NMR (60 MHz; $CDCl_3$) δ=1.55 and 1.67 (each 3H, s, CH_3), 3.32 (2H, d, J=7 Hz, CH_2), 5.23 (1H, t, J=7 Hz, CH=), 7.0—8.3 (24 H, m, $C_6H_5CO\times4$ and Ar-H×4), 7.90 (1H, s, C_2-H).

2′, 4′, 5, 7- Tetrahydroxy- 5′- (3- methyl- 2- butenyl)isoflavone (Allolicoisoflavone A) (1). The 5′-prenylisoflavone **15** (217 mg, 0.28 mmol) in THF (30 cm^3) and methanol (40 cm^3) was hydrolyzed with 10% aqueous sodium hydroxide (2 cm^3) under nitrogen at 45 °C for 40 min. To the reaction mixture were added water and dilute hydrochloric acid; the organic solvent was then evaporated under reduced pressure. The residue was extracted with ether, washed with water, and dried (Na_2SO_4). The resulting compound was chromatographed over a silica-gel column ($CHCl_3$: Me_2CO=5 : 1 as a solvent) to give the desired 5′- prenylisoflavone **1** (77 mg, 77%), which was crystallized from dichloromethane as pale-yellow prisms, mp 227—229 °C; IR (KBr) ν 3428, 1651, 1620, 1509, 1362, 1265, 1202, 1159, 1055, 1030, and 820 cm^{-1}; UV λ_{max} nm (log ε) (MeOH) 260 (4.43), 288 (4.13), (+$AlCl_3$) 269 (4.46), 292_{sh}

(4.10), 313$_{sh}$ (3.90), 375 (3.64), (+NaOAc) 270 (4.46), 295$_{sh}$ (4.15), 325 (4.05). Found: C, 67.51; H, 5.15%. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12%.

2′,4′,5,7-Tetraacetoxy-5′-(3-methyl-2-butenyl)isoflavone (17). Compound **1** (30 mg, 0.085 mmol) was converted into the tetraacetate **17** by a treatment with acetic anhydride (4 cm^3)–pyridine (0.8 cm^3) at 115 °C for 80 min. The resulting compound was recrystallized from a mixture of ethyl acetate and hexane as colorless needles (38 mg, 86%), mp 127—128.5 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=1.68 and 1.73 (each 3H, s, CH_3), 2.14, 2.31, 2.35 and 2.38 (each 3H, s, $COCH_3$), 3.23 (2H, d, J=7.3 Hz, CH_2), 5.20 (1H, t, J=7.3 Hz, CH=), 6.85 (1H, d, J=2.0 Hz, C_6-H), 7.00 (1H, s, $C_{3'}$-H), 7.09 (1H, s, $C_{6'}$-H), 7.24 (1H, d, J=2.0 Hz, C_8-H), 7.81 (1H, s, C_2-H); UV λ_{max} nm (log ε) (MeOH) 242 (4.41), 298 (3.88). Found: C, 64.20; H, 5.03%. Calcd for $C_{28}H_{26}O_{10}$: C, 64.36; H, 5.02%.

2,4,4′,6′-Tetrakis(benzyloxy)-2′-hydroxy-3′-iodochalcone (19). A mixture of 4′,6′-bis(benzyloxy)-3′-iodo-2′-(methoxymethoxy)acetophenone (**18**) (3 g, 5.8 mmol), which was prepared by methoxymethylation of 4′,6′-bis(benzyloxy)-2′-hydroxy-3′-iodoacetophenone, and 2,4-bis(benzyloxy)benzaldehyde (2.40 g, 7.5 mmol), was refluxed with stirring in the presence of potassium hydroxide (3.25 g, 57.9 mmol) in ethanol (350 cm^3) for 4 h. The reaction mixture was worked up in the same manner as in the case of the 2′-hydroxychalcone **9** to give the 3′-iodo-2′-hydroxychalcone **19**, which was recrystallized from a mixture of chloroform and methanol as yellow prisms (3.48 g, 78%), mp 148—150 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=4.95, 5.02, 5.03, and 5.23 (each 2H, s, CH_2), 6.12 (1H, s, $C_{5'}$-H), 6.31 (1H, dd, J=2.2 and 8.7 Hz, C_5-H), 6.48 (1H, d, J=2.2 Hz, C_3-H), 6.82 (1H, d, J=8.7 Hz, C_6-H), 7.3—7.5 (20H, m, $C_6H_5\times4$), 7.81 and 8.20 (each 1H, d, J=16 Hz, CH=). Found: C, 66.70; H, 4.53%. Calcd for $C_{43}H_{35}IO_6$: C, 66.67; H, 4.55%.

2′-Acetoxy-2,4,4′,6′-tetrakis(benzyloxy)-3′-iodochalcone (20). The chalcone **19** (4.98 g, 6.5 mmol) was converted into the acetate **20** by acetic anhydride-pyridine method. Pale-yellow prisms (4.34 g, 93%), mp 80—82 °C (from methanol–acetone); ^{1}H NMR (400 MHz; $CDCl_3$) δ=2.26 (3H, s, $COCH_3$), 4.91, 5.03, 5.07 and 5.08 (each 2H, s, CH_2), 6.35 (1H, s, $C_{5'}$-H), 6.5—6.6 (2H, m, C_3-H and C_5-H), 6.99 and 7.79 (each 1H, d, J=16.1 Hz, CH=). Found: C, 66.40; H, 4.62%. Calcd for $C_{45}H_{37}IO_7$: C, 66.19; H, 4.57%.

1-[2-Acetoxy-4,6-bis(benzyloxy)-3-iodophenyl]-2-[2,4-bis(benzyloxy)phenyl]-3,3-dimethoxypropan-1-one (21). After a mixture of the chalcone **20** (1.5 g, 1.8 mmol) and TTN (1.64 g, 3.7 mmol) was stirred in a mixture of methanol (360 cm^3) and chloroform (60 cm^3) at 40 °C for 2 h, 10% hydrochloric acid (18 cm^3) was added, and the mixture was stirred at room temperature for 2 h to give white precipitates. The reaction mixture was worked up in the same manner as in the case of the acetal **11** to give the acetal **21**, which was crystallized from methanol as colorless prisms (1.35 g, 84%), mp 177—178 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=2.20 (3H, s, $COCH_3$), 3.08 and 3.38 (each 3H, s, OCH_3), 4.6—5.0 (8H, m, $CH_2\times4$), 5.21 and 5.30 (each 1H, d, J=8.8 Hz, CH), 6.16 (1H, s, $C_{5'}$-H), 6.44 (2H, br s, C_3-H and C_5-H), 7.1—7.4 (21H, m, $C_6H_5\times4$ and Ar-H). Found: C, 63.97; H, 4.89%. Calcd for $C_{47}H_{43}IO_9$: C, 64.16; H, 4.93%.

2′,4′,5,7-Tetrakis(benzyloxy)-8-iodoisoflavone (22). The acetal **21** (2.19 g, 2.5 mmol) in THF (40 cm^3) and methanol (50 cm^3) was stirred in the presence of 10% aqueous sodium hydroxide (4 cm^3) at 35 °C for 45 min. The reaction mixture was neutralized with dilute hydrochloric acid, and then extracted with ethyl acetate, washed with water, and dried (Na_2SO_4). The organic solvent was removed under reduced pressure, and the resulting compound was chromatographed over a silica-gel column ($CHCl_3$ as a solvent) to give the 8-iodoisoflavone **22**, which was crystallized from methanol as colorless needles (1.51 g, 80%), mp 164—166 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=5.04, 5.05, 5.19, and 5.20 (each 2H, s, CH_2), 6.48 (1H, s, C_6-H), 6.6—6.7 (3H, m, Ar-H×3), 7.2—7.6 (20 H, m, $C_6H_5\times4$), 7.85 (1H, s, C_2-H). Found: C, 66.65; H, 4.45%. Calcd for $C_{43}H_{33}IO_6$: C, 66.85; H, 4.30%.

2′,4′,5,7-Tetrakis(benzyloxy)-8-(3-hydroxy-3-methyl-1-butynyl)isoflavone (23). To a solution of **22** (646 mg, 0.84 mmol) and 2-methyl-3-butyn-2-ol (0.3 cm^3, 3.1 mmol) in a mixture of triethylamine (12 cm^3) and DMF (5 cm^3) were added $PdCl_2$ (4.4 mg, 3 mol%), PPh_3 (13.2 mg, 6 mol%), and CuI (4.8 mg, 3 mol%); the mixture was then stirred under nitrogen at 80 °C for 2 h. The reaction mixture was worked up in the same manner as in the case of the 5′-alkynylisoflavone **13** to give the desired isoflavone **23**, which was recrystallized from a mixture of chloroform and methanol as colorless needles (450 mg, 75%), mp 222—224 °C; IR (KBr) ν 3421, 1648, 1592, 1565, 1411, 1304, 1174, 832, and 738 cm^{-1}; ^{1}H NMR (400 MHz; $CDCl_3$) δ=1.64 (6H, s, $CH_3\times2$), 2.11 (1H, s, OH), 5.04, 5.05, 5.18 and 5.20 (each 2H, s, CH_2), 6.45 (1H, s, C_6-H), 6.63 (1H, dd, J=2.2 and 7.8 Hz, $C_{5'}$-H), 6.66 (1H, d, J=2.2 Hz, $C_{3'}$-H), 7.2—7.6 (21H, m, $C_6H_5\times4$ and Ar-H), 7.82 (1H, s, C_2-H). Found: C, 78.90; H, 5.37%. Calcd for $C_{48}H_{40}O_7$: C, 79.10; H, 5.53%.

2′,4′,5,7-Tetrahydroxy-8-(3-hydroxy-3-methylbutyl)isoflavone (2,3-Dehydrokievitone Hydrate) (4). The isoflavone **23** (100 mg, 13.7 mmol) was hydrogenolyzed over Pd/C (5%) (500 mg) with stirring in methanol (105 cm^3) and ethyl acetate (50 cm^3) at 15—18 °C until the uptake of hydrogen ceased, as judged by TLC. The reaction mixture was worked up in the same manner as in the case of the isoflavone **2** to give the 8-alkylisoflavone **4**, which was crystallized from dichloromethane as pale yellow prisms (52 mg, 74%), mp 211—213 °C; IR (KBr) ν 3370, 3167, 1651, 1509, 1416, 1313, 1205, 979, and 843 cm^{-1}; UV λ_{max} nm (log ε) (MeOH) 265 (4.44), 290sh (4.03), 335sh (3.57), (+$AlCl_3$) 276 (4.40), 319 (3.87), 390 (3.60), (+NaOAc) 278 (4.39), 332 (3.92). Found: C, 64.40; H, 5.57%. Calcd for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41%.

2′,4′,5,7-Tetrakis(benzoyloxy)-8-(3-hydroxy-3-methylbutyl)isoflavone (24). A mixture of the isoflavone **4** (150 mg, 0.4 mmol), benzoyl chloride (1.0 g, 7.1 mmol), and potassium carbonate (1.4 g, 10.1 mmol) in acetone (20 cm^3) was refluxed with stirring under nitrogen for 7 h. The reaction mixture was worked up in the same manner as in the case of the isoflavone **14** to give the tetrakis(benzoyloxy)isoflavone **24**, which was crystallized from methanol as colorless needles (219 mg, 70%), mp 214—216 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=1.17 (6H, s, $CH_3\times2$), 1.74 and 2.92 (each 2H, m, CH_2), 7.09 (1H, s, C_6-H), 7.2—7.7 and 8.0—8.2 (23H, m, $C_6H_5CO\times4$ and Ar-H×3), 7.98 (1H, s, C_2-H). Found: C, 72.86; H, 4.62%. Calcd for $C_{48}H_{36}O_{11}$: C, 73.09; H, 4.60%.

2′,4′,5,7-Tetrakis(benzoyloxy)-8-(3-methyl-2-butenyl)isoflavone (25) and 2′,4′,5,7-Tetrakis(benzoyloxy)-8-(3-methyl-3-butenyl)isoflavone (26). To a solution of **24** (140 mg, 0.18 mmol) in dry toluene (10 cm^3) was added $TsOH\cdot H_2O$ (0.17 mmol); the mixture was stirred under nitrogen at 115 °C for 1 h. The reaction mixture was worked up in the same manner as in the case of the 5′-prenylisoflavone **15** to give a mixture of the 8-alkenylisoflavones (120 mg, 88%). The ^{1}H NMR (60 MHz; $CDCl_3$) spectrum of the mixture was shown to be a 85 : 15 mixture of 2′,4′,5,7-tetrakis(benzoyloxy)-8-(3-methyl-2-butenyl)isoflavone **25** and the regioisomer 2′,4′,5,7-tetrakis(benzoyloxy)-8-(3-methyl-3-butenyl)isoflavone **26**. The mixture (**25** and **26**) (120 mg) in THF (15 cm^3) was reacted with 6.6×10^{-2} mol dm^{-3} $Hg(NO_3)_2\cdot H_2O$ (0.7

cm^3, 1.5 mol amt. to the isomer **26**) at room temperature for 50 min to give a mixture of the unchanged 8-prenylisoflavone **25** and the terminal alkylmercurinium ion **26′**. The reaction mixture was worked up in the same manner as in the case of the isoflavone **15** to give the desired 8-prenylisoflavone **25**, which was crystallized from methanol as colorless needles (112 mg, 93%), mp 158—160 °C (mp 212—214 °C); ^{1}H NMR (400 MHz; $CDCl_3$) δ=1.55 and 1.60 (each 3H, s, CH_3), 3.52 (2H, d, J=6.8 Hz, CH_2), 5.14 (1H, t, J=6.8 Hz, CH=), 7.06 (1H, s, C_6-H), 7.20—8.20 (23H, m, $C_6H_5CO\times4$ and Ar-H×3), 7.97 (1H, s, C_2-H). Found C, 74.60; H, 4.49%. Calcd for $C_{48}H_{34}O_{10}$: C, 74.79; H, 4.45%.

2′,4′,5,7-Tetrahydroxy-8-(3-methyl-2-butenyl)isoflavone (2,3-Dehydrokievitone) (3). The isoflavone **25** (80 mg, 0.1 mmol) in a mixture of methanol (20 cm^3) and dioxane (20 cm^3) was hydrolyzed with 10% aqueous sodium hydroxide (9 cm^3) under nitrogen at 45 °C for 40 min. The resulting compound was purified by silica-gel column chromatography ($CHCl_3$: Me_2CO=50 : 1 as a solvent) to give the 8-prenylisoflavone **3**, which was crystallized from dichloromethane as colorless prisms (32 mg, 88%), mp 139—141 °C; IR (KBr) ν 3465, 3250, 1650, 1561, 1509, 1423, 1303, 1260, 1185, 1109, 979, and 813 cm^{-1}; UV λ_{max} nm (log ε) (MeOH) 266 (4.51), 335 (3.62), (+$AlCl_3$) 272 (4.46), 376 (3.39), (+NaOAc) 268 (4.42), 282 (4.35), 335 (3.74). Found C, 67.55; H, 5.40%. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12%.

2′-Hydroxy-3′-iodo-4′,6′-dimethoxyacetophenone. Silver trifluoroacetate (11.3 g, 51 mmol) was added to a solution of 2′-hydroxy-4′,6′-dimethoxyacetophenone (10 g, 51 mmol) in chloroform (100 cm^3). To the suspension was added a solution of iodine (13.0 g, 51 mmol) in chloroform (250 cm^3) dropwise with stirring at room temperature until completion of the reaction, as judged by TLC. The resulting compound was recrystallized from $CHCl_3$ to yield 2′- hydroxy-3′-iodo-4′,6′-dimethoxyacetophenone (13.45 g, 82%) as pale yellow needles, mp 205—206 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=2.60 (3H, s, $COCH_3$), 3.92 (6H, s, OCH_3), 5.98 (1H, s, $C_{5'}$-H), 14.85 (1H, s, OH). Found: C, 37.33; H, 3.40%. Calcd for $C_{22}H_{14}IO_6$: C, 37.26; H, 3.44%.

2′-Benzyloxy-3′-iodo-4′,6′-dimethoxyacetophenone (27). A mixture of 2′-hydroxy-3′-iodo-4′,6′-dimethoxyacetophenone (8.0 g, 24 mmol), benzyl chloride (3.4 cm^3, 29 mmol), and K_2CO_3 (15 g, 120 mmol) in DMF (80 cm^3) was stirred at 110 °C for 10 min to give the 2′-benzyloxy-3′-iodoacetophenone **27** (9.21 g, 88%) as colorless needles (from AcOEt–MeOH), mp 131—133 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=2.41 (3H, s, $COCH_3$), 3.80 and 3.85 (each 3H, s, OCH_3), 4.90 (2H, s, CH_2), 6.22 (1H, s, $C_{5'}$-H), 7.09—7.64 (5H, m, C_6H_5). Found: C, 49.35; H, 4.09%. Calcd for $C_{22}H_{15}IO_6$: C, 49.53; H, 4.16%.

2′-Benzyloxy-3′-iodo-2,4,4′,6′-tetramethoxychalcone (28). A mixture of the 3′-iodoacetophenone **27** (8.0 g, 19 mmol) and 2,4-dimethoxybenzaldehyde (3.86 g, 23 mmol) was refluxed with stirring in the presence of potassium hydroxide (5.44g, 95 mmol) in ethanol (350 cm^3) for 3 h. The resulting compound was recrystallized from $CHCl_3$–MeOH to yield **28** (9.80 g, 90%) as pale-yellow needles, mp 154—156 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=3.76 (9H, s, $OCH_3\times3$), 3.90 (3H, s, OCH_3), 4.91 (2H, s, CH_2), 6.28—6.57 (3H, m, C_3-H, C_5-H, and $C_{5'}$-H), 6.90 and 7.57 (each 1H, d, J=16 Hz, CH=), 7.05—7.43 (6H, m, C_6-H and C_6H_5). Found: C, 55.46; H, 4.38%. Calcd for $C_{26}H_{25}IO_6$: C, 55.72; H, 4.49%.

2′-Hydroxy-3′-iodo-2,4,4′,6′-tetramethoxychalcone (29). To a solution of 10% (w/v) anhydrous aluminum chloride in acetonitrile (50 cm^3, 16.1 mmol) was added **28** (3.0 g, 5.4 mmol) in acetonitrile (100 cm^3); the mixture was then stirred at 0 °C for 10 min. To the reaction mixture was added 2% hydrochloric acid (30 cm^3), and then the mixture was stirred at 50 °C for 30 min to give white precipitates. The separated precipitates were recrystallized from acetone to give **29** (1.77 g, 70%) as orange needles, mp 178—180 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=3.79 and 3.82 (each 3H, s, OCH_3), 3.93 (6H, s, $OCH_3\times2$), 5.93 (1H, s, $C_{5'}$-H), 6.37 (1H, d, J=2 Hz, C_3-H), 6.45 (1H, dd, J=2 and 8 Hz, C_5-H), 7.46 (1H, d, J=8 Hz, C_6-H), 7.71 and 8.10 (each 1H, d, J=16 Hz, CH=), 15.30 (1H, s, OH). Found: C, 48.72; H, 4.02%. Calcd for $C_{19}H_{19}IO_6$: C, 48.53; H, 4.07%.

2′-Acetoxy-3′-iodo-2,4,4′,6′-tetramethoxychalcone (30). The chalcone **29** (3.53 g, 7.5 mmol) was converted into the acetate **30** by the acetic anhydride-pyridine method. Pale-yellow needles (2.66 g, 70%), mp 152—153 °C (from MeOH–AcOEt); ^{1}H NMR (60 MHz; $CDCl_3$) δ=2.22 (3H, s, $COCH_3$), 3.80 (9H, s, $OCH_3\times3$), 3.91 (3H, s, OCH_3), 6.30—6.53 (2H, m, C_3-H and C_5-H), 6.48 (1H, s, $C_{5'}$-H), 7.40 (1H, d, J=8 Hz, C_6-H), 6.93 and 7.65 (each 1H, d, J=16 Hz, CH=). Found: C, 49.50; H, 4.22%. Calcd for $C_{21}H_{21}IO_7$: C, 49.24; H, 4.13%.

1-(2-Acetoxy-3-iodo-4,6-dimethoxyphenyl)-2-(2,4-dimethoxyphenyl)-3,3-dimethoxypropan-1-one (31) and 2′,4′,5,7-Tetramethoxy-8-iodoisoflavone (32). A mixture of the chalcone **30** (2.0 g, 3.9 mmol) and TTN (2.25 g, 5.1 mmol) was stirred in a mixture of methanol (400 cm^3) and chloroform (130 cm^3) at 40 °C for 4 h, and then 2% hydrochloric acid (10 cm^3) was added; the mixture was stirred at room temperature for 2 h to give white precipitates. The reaction mixture was worked up in the same manner as in the case of the acetal **11** to give the acetal **31** (1.65 g) as a paste; ^{1}H NMR (60 MHz; $CDCl_3$) δ=2.23 (3H, s, $COCH_3$), 3.12 and 3.40 (each 3H, s, OCH_3), 3.60 (6H, s, $OCH_3\times2$), 3.71 and 3.80 (each 3H, s, OCH_3), 4.98—5.10 (2H, m, CHCH), 6.15 (1H, s, Ar-H), 6.33 (1H, d, J=2 Hz, Ar-H), 6.36 (1H, dd, J=2 and 8 Hz, Ar-H), 7.12 (1H, d, J=8 Hz, Ar-H). The acetal **31** (1.65 g) in THF (60 cm^3) and methanol (80 cm^3) was stirred in the presence of 10% aqueous sodium hydroxide (7 cm^3) at 60 °C for 15 min. The resulting compound was crystallized from methanol to give the isoflavone **32** as colorless needles (1.13 g, 62%), mp 105—107 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=3.69 and 3.77 (each 3H, s, OCH_3), 3.91 (6H, s, $OCH_3\times2$), 6.31 (1H, s, C_6-H), 6.37—6.57 (2H, m, $C_{3'}$-H and $C_{5'}$-H), 7.17 (1H, d, J=8 Hz, $C_{6'}$-H), 7.78 (1H, s, C_2-H). Found: C, 48.73; H, 3.69%. Calcd for $C_{19}H_{17}IO_6$: C, 48.73; H, 3.66%.

8-(3-Hydroxy-3-methyl-1-butynyl)-2′,4′,5,7-tetramethoxyisoflavone (33). To a solution of **32** (950 mg, 2.0 mmol) and 2-methyl-3-butyn-2-ol (0.7 cm^3, 7.1 mmol) in a mixture of triethylamine (7 cm^3) and DMF (1.5 cm^3) were added $PdCl_2$ (11 mg, 3 mol%), PPh_3 (32 mg, 6 mol%), and CuI (12 mg, 3 mol%); the mixture was then stirred under nitrogen at 80 °C for 3 h. The resulting compound was recrystallized from a mixture of chloroform and methanol as colorless needles **33** (700 mg, 81%), mp 205—206 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=1.63 (6H, s, $CH_3\times2$), 3.70 and 3.79 (each 3H, s, OCH_3), 3.92 (6H, s, $OCH_3\times2$), 6.28 (1H, s, C_6-H), 6.37—6.60 (2H, m, $C_{3'}$-H and $C_{5'}$-H), 7.20 (1H, d, J=8 Hz, $C_{6'}$-H), 7.76 (1H, s, C_2-H). Found: C, 67.62; H, 5.96%. Calcd for $C_{24}H_{24}O_7$: C, 67.91; H, 5.70%.

8-(3-Hydroxy-3-methylbutyl)-2′,4′,5,7-tetramethoxyisoflavone (2,3-Dehydrokievitone Hydrate Tetramethyl Ether) (6). The isoflavone **33** (300 mg, 0.71 mmol) was hydrogenolyzed over Pd/C (5%) (70 mg) with stirring in methanol (105 cm^3) at 20 °C until the uptake of hydrogen ceased, as judged by TLC. The reaction mixture was worked up in the same manner as in the case of the isoflavone **2** to give the 8-alkylisoflavone **6**, which was purified by silica-gel column chromatography ($CHCl_3$: Me_2CO=5 : 1 as a

solvent) and crystallized from Me_2CO–Et_2O as colorless prisms (193 mg, 64%), mp 162—163 °C; ^{1}H NMR (60 MHz; $CDCl_3$) δ=1.30 (6H, s, $CH_3\times2$), 1.41—1.94 (2H, m, CH_2), 2.50—3.03 (2H, m, CH_2), 3.73 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.91 (6H, s, $OCH_3\times2$), 6.36 (1H, s, C_6-H), 6.38—6.60 (2H, m, $C_{3'}$-H and $C_{5'}$-H), 7.20 (1H, d, J=8 Hz, $C_{6'}$-H), 7.73 (1H, s, C_2-H); UV λ_{max} nm (log ε) (MeOH) 240_{sh} (4.35), 251_{sh} (4.50), 256 (4.52), 284 (4.10), 318 (3.81). Found: C, 67.16; H, 6.85%. Calcd for $C_{24}H_{28}O_7$: C, 67.27; H, 6.58%).

2′,4′,5,7-Tetramethoxy-8-(3-methyl-2-butenyl)isoflavone (5). To a solution of **6** (127 mg, 0.18 mmol) in dry toluene (10 cm^3) was added TsOH·H_2O (0.18 mmol); the mixture was stirred under nitrogen at 115 °C for 1 h. The reaction mixture was worked up in the same manner as in the case of the 5′-prenylisoflavone **15** to give a mixture of 8-alkenylisoflavones (120 mg, 88%). The ^{1}H NMR (60 MHz; $CDCl_3$) spectrum of the mixture was shown to be a 83 : 17 mixture of 2′,4′,5,7-tetramethoxy-8-(3-methyl-2-butenyl)isoflavone **5** and the regioisomer 2′,4′,5,7-tetramethoxy-8-(3-methyl-3-butenyl)isoflavone. The mixture was also reacted with aqueous Hg$(NO_3)_2$ in THF at room temperature. The resulting compound was purified by silica-gel column chromatography ($CHCl_3$: Me_2CO= 5 : 1 as a solvent) and crystallized from hexane-ether to give the desired 8-prenylisoflavone **5** as colorless prisms (79 mg, 65%), mp 85—87 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ=1.65 and 1.80 (each 3H, s, CH_3), 3.45 (2H, d, J=7.3 Hz, CH_2), 3.75, 3.83, 3.89 and 4.01 (each 3H, s, OCH_3), 5.20 (1H, t, J=7.3 Hz, CH=), 6.54 (1H, dd, J=2.4 and 8.3 Hz, $C_{5'}$-H), 6.60 (1H, d, J=2.4 Hz, $C_{3'}$-H), 6.68 (1H, s, C_6-H), 7.16 (1H, d, J=8.3 Hz, $C_{6'}$-H), 7.90 (1H, s, C_2-H); UV λ_{max} nm (log ε) (MeOH) 250_{sh} (4.48), 258 (4.50), 284_{sh} (4.06), 320 (3.75). Found C, 70.00; H, 6.10%. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38%.

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