# Synthesis of Licoisoflavone A and Related Compounds[1)]

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2′,4′,5,7-Tetrahydroxyisoflavone was partially benzoylated with benzoyl chloride to give 7-benzoyloxy-2′,4′,5-trihydroxyisoflavone. The condensation of the 7-(benzoyloxy)isoflavone with 2-methyl-3-buten-2-ol, followed by the hydrolysis of the resultant 3′-(3-methyl-2-butenyl)isoflavone gave licoisoflavone A. Its 5′-(3-methyl-2-butenyl) isomer was also synthesized from 5-benzoyloxy-2′,4′,7-trihydroxyisoflavone in a similar manner.

Licoisoflavone A was isolated from the roots of *Glycyrrhiza* spp. (Leguminosae) along with other flavonoids.[2)] The structure has been shown to be 2′,4′,5,7-tetrahydroxy-3′-(3-methyl-2-butenyl)isoflavone (**1**) on the basis of chemical and spectroscopic studies. In the continuation of our studies on the synthesis of isoflavones having 3-methyl-2-butenyl groups on the B ring,[3)] the present paper reports in detail the unambiguous synthesis of **1** to confirm the proposed structure of the natural isoflavone and its isomer [2′,4′,5,7-tetrahydroxy-5′-(3-methyl-2-butenyl)isoflavone] (**2**).

The condensation of 2,4-bis(benzyloxy)-6-hydroxyacetophenone (**3**) with 2,4-bis(benzyloxy)benzaldehyde gave 2,4,4′,6′-tetrakis(benzyloxy)-2′-hydroxychalcone (**4**) as a major product and 2′,4′,5,7-tetrakis(benzyloxy)-flavanone (**5**) as a minor product. A mixture of **4** and **5** was easily converted into the acetate (**6**) of **4**. The oxidative rearrangement of **6** with thallium(III) nitrate trihydrate[4)] in methanol, followed by the cyclization of the resultant compound with dilute hydrochloric acid gave the tetrakis(benzyloxy)isoflavone (**7**). The partial debenzylation of **7** with concd hydrochloric acid in acetic acid at 80 °C for 10 min gave the 5-hydroxyisoflavone (**8**). In the UV spectrum of **8**, the absorption maximum showed a bathochromic shift in the presence of aluminum chloride, and the $^1$H NMR spectrum of **8** also showed three benzyl methylene proton signals and the 5-hydroxyl proton signal. The 5-(benzoyloxy)isoflavone (**9**), which was obtained by the benzoylation of **8** with benzoyl chloride in pyridine, was converted into 5-benzoyloxy-2′,4′,7-trihydroxyisoflavone (**10**) by the hydrogenolysis over 10% palladium on charcoal in methanol–ethyl acetate. The condensation of **10** with 2-methyl-3-buten-2-ol in the presence of boron trifluoride etherate in anhydrous dioxane gave a 3-methyl-2-butenyl compound (**11**) and a bis(3-methyl-2-butenyl) compound (**12**).

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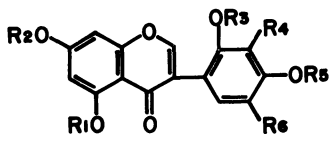
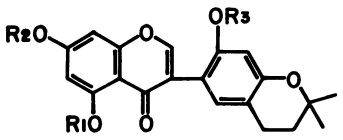
The $^1$H NMR spectrum of **11** showed the presence of two methyl groups as a singlet at $\delta$ 1.61, one methylene group as a doublet ($J$=7 Hz) centering at $\delta$ 3.06, one methine proton as a triplet ($J$=7 Hz) centering at $\delta$ 5.18, and two aromatic protons as each singlet at $\delta$ 6.33 (3′-H) and 6.66 (6′-H), respectively. The $^1$H NMR spectrum of **12** showed the presence of two 3-methyl-2-butenyl groups and one aromatic proton as a singlet at $\delta$ 6.57 (6′-H). Compound **12** was hydrolyzed with dilute alkali in a nitrogen atmosphere to give 2′,4′,5,7-tetrahydroxy-3′,



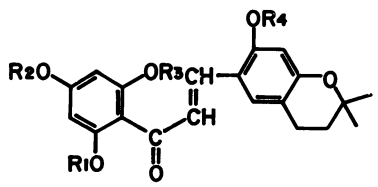

**1** $R_1=R_2=R_3=R_5=R_6=H$, $R_4=(CH_3)_2C=CHCH_2$
**2** $R_1=R_2=R_3=R_4=R_5=H$, $R_6=(CH_3)_2C=CHCH_2$
**7** $R_1=R_2=R_3=R_5=PhCH_2$, $R_4=R_6=H$
**8** $R_1=R_4=R_6=H$, $R_2=R_3=R_5=PhCH_2$
**9** $R_1=PhCO$, $R_2=R_3=R_5=PhCH_2$, $R_4=R_6=H$
**10** $R_1=PhCO$, $R_2=R_3=R_4=R_5=R_6=H$
**11** $R_1=PhCO$, $R_2=R_3=R_4=R_5=H$, $R_6=(CH_3)_2C=CHCH_2$
**12** $R_1=PhCO$, $R_2=R_3=R_5=H$, $R_4=R_6=(CH_3)_2C=CHCH_2$
**13** $R_1=R_2=R_3=R_5=H$, $R_4=R_6=(CH_3)_2C=CHCH_2$
**14** $R_1=R_2=R_3=R_5=CH_3CO$, $R_4=R_6=(CH_3)_2C=CHCH_2$
**15** $R_1=R_2=R_3=R_5=CH_3CO$, $R_4=H$, $R_6=(CH_3)_2C=CHCH_2$
**23** $R_1=R_2=R_3=R_4=R_5=R_6=H$
**24** $R_1=R_3=R_4=R_5=R_6=H$, $R_2=PhCO$
**25** $R_1=R_3=R_5=R_6=H$, $R_2=PhCO$, $R_4=(CH_3)_2C=CHCH_2$
**26** $R_1=R_3=R_4=R_5=H$, $R_2=PhCO$, $R_6=(CH_3)_2C=CHCH_2$
**27** $R_1=R_3=R_5=H$, $R_2=PhCO$, $R_4=R_6=(CH_3)_2C=CHCH_2$
**28** $R_1=R_2=R_3=R_5=CH_3CO$, $R_4=(CH_3)_2C=CHCH_2$, $R_6=H$

Structure 1.

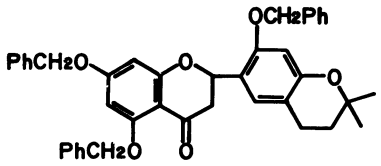
5′-bis(3-methyl-2-butenyl)isoflavone (**13**), which was converted into the tetraacetate (**14**). Compound **11** was hydrolyzed with dilute alkali in a nitrogen atmosphere to yield 2′,4′,5,7-tetrahydroxy-5′-(3-methyl-2-butenyl)isoflavone (**2**) (mp 232—234 °C). Compound **2** was converted into the tetraacetate (**15**) (mp 127—128 °C) and furthermore cyclized with concd hydrochloric acid in methanol to give the 3-(2,2-dimethyl-6-chromanyl)-4*H*-chromen-4-one (**16**) (mp 261—262 °C). The structure of **16** was further confirmed by the alternative unambiguous synthesis as described below.




**16** $R_1=R_2=R_3=H$
**21** $R_1=R_2=R_3=PhCH_2$
**22** $R_1=H$, $R_2=R_3=PhCH_2$




**18** $R_1=R_2=R_4=PhCH_2$, $R_3=H$
**20** $R_1=R_2=R_4=PhCH_2$, $R_3=CH_3CO$




**19**

Structure 2.

The condensation of **3** and 7-benzyloxy-6-formyl-2,2-dimethylchroman (**17**) gave the 3-(2,2-dimethyl-6-chromanyl)-1-phenyl-2-propen-1-one (**18**) as a major product and the 2-(2,2-dimethyl-6-chromanyl)-4-chromanone (**19**) as a minor product. A mixture of **18** and **19** was converted into the acetate (**20**) of **18**. The oxidative rearrangement of **20** with thallium(III) nitrate trihydrate, followed by the cyclization of the resultant compound gave two 3-(2,2-dimethyl-6-chromanyl)-4*H*-chromen-4-ones (**21**) and (**22**). A mixture of **21** and **22** was hydrogenolyzed over 10% palladium on charcoal to give compound **16**.

From these results, the isoflavone **2** has been found to be a structural isomer of licoisoflavone A (**1**).

The hydrogenolysis of **7** over 10% palladium on charcoal, followed by the partial benzoylation of the resultant tetrahydroxyisoflavone (**23**) with benzoyl chloride in pyridine gave the 7-(benzoyloxy)isoflavone (**24**). In the UV spectrum of **24**, the absorption maximum did not show a bathochromic shift in the presence of sodium acetate. The condensation of **24** with 2-methyl-3-buten-2-ol gave two 3-methyl-2-butenyl compounds (**25**) and (**26**), and one 3′,5′-bis(3-methyl-2-butenyl)isoflavone (**27**). The $^1H$ NMR spectrum of **26** showed the presence of one 3-methyl-2-butenyl group and two aromatic protons as each singlet at $\delta$ 6.46 (3′-H) and 6.84 (6′-H), respectively. Both compounds **26** and **27** were also hydrolyzed to give **2** and **13**, respectively. The $^1H$ NMR spectrum of **25** showed the presence of one 3-methyl-2-butenyl group and two aromatic protons as each doublet ($J$=8 Hz) centering at $\delta$ 6.42 (5′-H) and 6.81 (6′-H), respectively. Therefore, compound **25** was shown to be 7-benzoyloxy-2′,4′,5-trihydroxy-3′-(3-methyl-2-butenyl)isoflavone, which was hydrolyzed with dilute alkali to give the desired isoflavone (licoisoflavone A) (**1**). Compound **1** was subsequently converted into the tetraacetate (**28**). In Tables 1 and 2, the UV and $^1H$ NMR spectral data for the synthetic isoflavone **1** and its tetraacetate **28** are shown to be identical with those for natural licoisoflavone A and its tetraacetate, respectively.[2]

On the basis of these results, the structure of licoisoflavone A was confirmed to be 2′,4′,5,7-tetrahydroxy-3′-(3-methyl-2-butenyl)isoflavone (**1**).

Table 1. Mp and UV spectra of isoflavones[a]

| Compound | Mp $\theta_m$/°C | | $\lambda_{max}$/nm (log $\varepsilon$) |
|---|---|---|---|
| Licoisoflavone A (**1**) | 120—122[b] | (EtOH) | 266.5 (4.46), 339i (3.70) |
| (Natural)[1] | (111—113) | (EtOH+NaOAc) | 277 (4.53), 330 (4.00) |
| | | (EtOH+$AlCl_3$) | 269 (4.48), 307i (3.90), 365 (3.43) |
| Tetraacetate (**28**) | 149—150[b,c] | (EtOH) | 247 (4.42), 296 (3.87), 335i (3.42) |
| (Natural)[1] | (136—138) | | |

a) i: Inflection point. b) The melting points were measured with a Yanagimoto micro-melting-point apparatus. c) The melting point of the tetraacetate (**28**) was not depressed by admixture with natural licoisoflavone A tetraacetate.

TABLE 2. $^1$H NMR SPECTRA OF ISOFLAVONES[a)]

| Compound (Solvent) | 2-H | 6-H 8-H | 5'-H 6'-H | $(CH_3)_2C=CHCH_2$ | OH or OAc |
|---|---|---|---|---|---|
| Licoisoflavone A (**1**) (DMSO) | 8.11 (s) | 6.22 ($d_1$) 6.39 ($d_1$) | 6.36 ($d_2$) 6.76 ($d_2$) | 1.62 (3H, s, $CH_3$) 1.72 (3H, s, $CH_3$) 3.26 (2H, $d_3$, $CH_2$) 5.21 (1H, t, CH=) | 8.20, 9.24 10.75, 12.80 (each s or b) |
| Tetraacetate (**28**) ($CDCl_3$) | 7.76 (s) | 6.84 ($d_1$) 7.22 ($d_1$) | 6.97 ($d_2$) 7.14 ($d_2$) | 1.67 (6H, s, $CH_3\times2$) 3.22 (2H, $d_3$, $CH_2$) 5.03 (1H, t, CH=) | 2.11, 2.28 2.34, 2.40 (each 3H, s) |

a) s: Singlet. $d_1$, $d_2$, and $d_3$: Each doublet; $J$=2, 8, and 7 Hz, respectively. t: Triplet; $J$=7 Hz. b: Broad.

## Experimental

All the melting points are uncorrected. The IR spectra were taken on a Hitachi 215 spectrophotometer, and the UV spectra on a Hitachi 124 spectrophotometer. The $^1$H NMR spectra were measured with a Hitachi R-20 spectrometer (60 MHz), using tetramethylsilane as an internal standard ($\delta$, ppm). Column chromatography and thin-layer chromatography were carried out on Kieselgel 60 (70—230 mesh) and with Kieselgel 60 F-254 (Merck).

*2,4-Bis(benzyloxy)-6-hydroxyacetophenone (3).* Potassium carbonate (41.4 g) was added to a solution of 2,4,6-trihydroxyacetophenone (16.8 g) and benzyl chloride (25 g) in *N,N*-dimethylformamide (DMF) (100 ml) in a nitrogen atmosphere at 150—153 °C with stirring, and the mixture was vigorously stirred at 150—153 °C for 40 min. Potassium carbonate was filtered off, and the solvent was removed under reduced pressure. The residue was crystallized from a small amount of methanol to give a mixture of two compounds, which showed $R_f$ values of 0.39 and 0.49 on a silica-gel TLC plate [petroleum ether–1,2-dichloroethane (2:1)], respectively. The mixture was recrystallized from 1,2-dichloroethane to give the desired acetophenone **3** as colorless needles (9.1 g, 26%); mp 96—98 °C; $R_f$=0.39. Found: C, 75.59; H, 5.67%. Calcd for $C_{22}H_{20}O_4$: C, 75.86; H, 5.75%.

3-Benzyl-4,6-bis(benzyloxy)-2-hydroxyacetophenone was also obtained from the mother liquor by repeating recrystallization from ethyl acetate to give colorless needles (31.6 g, 31%); mp 111—112 °C; $R_f$=0.49. Found: C, 79.50; H, 5.88%. Calcd for $C_{29}H_{26}O_4$: C, 79.45; H, 5.94%.

*2,4,4',6'-Tetrakis(benzyloxy)-2'-hydroxychalcone (4) and 2',4',5,7-Tetrakis(benzyloxy)flavanone (5).* A mixture of **3** (10 g) and 2,4-bis(benzyloxy)benzaldehyde (10.2 g) was refluxed in the presence of piperidine (34 ml) in ethanol (200 ml) for 6 h to give yellow precipitates, which were collected by filtration. The precipitates were recrystallized from ethyl acetate to give **4** as yellow needles (11.5 g 68%); mp 146—147 °C. $^1$H NMR ($CDCl_3$) $\delta$=4.95 (2H, s, $C_6H_5C\underline{H}_2$), 5.01 (4H, s, $C_6H_5C\underline{H}_2\times2$), 5.03 (2H, s, $C_6H_5C\underline{H}_2$), 6.09 (1H, d, $J$=2 Hz, $C_{5'}$–H), 6.19 (2H, d, $J$=2 Hz, $C_3$–H and $C_{3'}$–H), 6.40 (1H, q, $J$=2 and 8 Hz, $C_5$–H), 6.81 (1H, d, $J$=8 Hz, $C_6$–H), 7.20—7.50 (20H, m, $C_6\underline{H}_5CH_2\times4$), 7.77 and 8.23 (each 1H, d, $J$=16 Hz, CH=), 12.78 (1H, s, OH). Found: C, 79.89; H, 5.63%. Calcd for $C_{43}H_{36}O_6$: C, 79.63; H, 5.56%.

The flavanone **5** was obtained from the mother liquor by repeating recrystallization from ethyl acetate as colorless needles (2.2 g, 11%); mp 159—161 °C. $^1$H NMR ($CDCl_3$) $\delta$=2.83—3.00 (2H, m, $C_3$–H), 5.04 (6H, bs, $C_6H_5C\underline{H}_2\times3$), 5.13 (2H, s, $C_6H_5C\underline{H}_2$), 5.68—5.94 (1H, m, $C_2$–H), 6.22 (2H, s, arom-H×2), 6.50—6.80 (2H, m, arom-H×2), 7.20—7.70 (21H, m, $C_6\underline{H}_5CH_2\times4$ and arom-H). Found: C, 79.90; H, 5.38%. Calcd for $C_{43}H_{36}O_6$: C, 79.63; H, 5.56%.

*2'-Acetoxy-2,4,4',6'-tetrakis(benzyloxy)chalcone (6).* Compounds **4** and **5** were converted into the acetate **6** by an acetic anhydride–sodium acetate method. Compound **6** was recrystallized from methanol–ethyl acetate to give pale yellow needles; mp 113—114 °C. $^1$H NMR ($CDCl_3$) $\delta$=2.17 (3H, s, $CH_3CO$), 4.91 (2H, s, $C_6H_5C\underline{H}_2$), 5.00 (4H, s, $C_6H_5C\underline{H}_2\times2$), 5.02 (2H, s, $C_6H_5C\underline{H}_2$), 6.47—6.65 (4H, s, arom-H×4), 7.12—7.61 (21H, m, $C_6\underline{H}_5CH_2\times4$ and arom-H), 6.99 and 7.81 (each 1H, d, $J$=16 Hz, CH=). Found: C, 78.51; H, 5.54%. Calcd for $C_{45}H_{38}O_7$: C, 78.26; H, 5.51%.

*2',4',5,7-Tetrakis(benzyloxy)isoflavone (7).* After a mixture of **6** (10 g) and thallium(III) nitrate trihydrate (7 g) was stirred in methanol (1.6 l) at 32—35 °C for 8 h, 10% hydrochloric acid (80 ml) was added and the solution then refluxed for 3 h. After cooling, the precipitates (thallium compound) were filtered off and the solvent removed under reduced pressure. The residue was crystallized from a small amount of methanol and recrystallized from methanol to give **7** as colorless needles (7.4 g, 79%); mp 178—179 °C. $^1$H NMR ($CDCl_3$) $\delta$=5.00, 5.02, 5.04, and 5.17 (each 2H, s, $C_6H_5C\underline{H}_2$), 6.44—6.72 (5H, m, arom-H×5), 7.00—7.50 (20H, m, $C_6\underline{H}_5CH_2\times4$), 7.68 (1H, s, $C_2$–H). Found: C, 79.80: H, 5.34%. Calcd for $C_{43}H_{34}O_6$: C, 79.88; H, 5.26%.

*2',4',7-Tris(benzyloxy)-5-hydroxyisoflavone (8).* A mixture of concd hydrochloric acid (2 ml) and acetic acid (10 ml) was added to a solution of **7** (1 g) in acetic acid (6 ml), and the mixture heated with stirring at 80 °C for 10 min. Water was added to the reaction mixture to give pale yellow precipitates, which were recrystallized from methanol–ethyl acetate to give **8** as pale yellow needles (0.73 g, 85%); mp 117—119 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 260 (4.57), 282.5 (4.20), 323i(3.65), (EtOH+NaOAc) 260.5 (4.58), 282.5 (4.22), 323i(3.68), (EtOH+$AlCl_3$) 273.5 (4.58), 309i(3.89), 375(3.65); $^1$H NMR ($CDCl_3$) $\delta$=5.04 (4H, s, $C_6H_5C\underline{H}_2\times2$), 5.09 (2H, s, $C_6H_5C\underline{H}_2$), 6.37—6.67 (5H, m, arom-H×5), 7.15—7.46 (15H, m, $C_6\underline{H}_5CH_2\times3$), 7.78 (1H, s, $C_2$–H), 12.00 (1H, s, OH). Found: C, 77.59; H, 4.94%. Calcd for $C_{36}H_{28}O_6$: C, 77.68; H, 5.07%.

*5-Benzoyloxy-2',4',7-tris(benzyloxy)isoflavone (9).* A mixture of **8** (2 g) and benzoyl chloride (1.67 ml) in pyridine (20 ml) was heated with stirring at 120 °C for 2 h. After cooling, the mixture was poured into ice-cold water and acidified with concd hydrochloric acid, extracted with ether, washed with aq sodium carbonate and water, and dried with sodium sulfate. The solvent was removed, and the residue recrystallized from 1,2-dichloroethane to give **9** as colorless needles (2.2 g, 90%); mp 155—157 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 235.5 (4.64), 248i (4.53), 281sh (4.22), 301.5i (3.98), (EtOH+$AlCl_3$) 233.5 (4.67), 247.5i (4.53), 280sh (4.23), 301.5i (3.98); $^1$H NMR (DMSO) $\delta$=4.99, 5.02, and 5.27 (each 2H, s, $C_6H_5C\underline{H}_2$), 6.45—6.80 (3H, m, arom-H×3), 7.03 and 7.17 (each 1H, d, $J$=2 Hz, arom-H), 7.20—8.10 (20H, m, $C_6\underline{H}_5CH_2$×3 and $C_6\underline{H}_5CO$), 8.14 (1H, s, $C_2$–H). Found: C, 77.99; H, 4.84%. Calcd for $C_{43}H_{32}O_7$: C, 78.18; H, 4.85%.

*5-Benzoylxoy-2',4',7-trihydroxyisoflavone (10).* Compound **9** (2 g) was hydrogenolyzed over 10% palladium on charcoal (0.4 g) in a mixture of ethyl acetate (200 ml) and methanol (80 ml) at 30 °C until the uptake of hydrogen ceased. The catalyst was filtered off, and the solvent removed under reduced pressure. The residue was recrystallized from methanol-ethyl acetate to give **10** as colorless needles (1.1 g, 90%); mp 211—213 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 237i (4.42), 250 (4.33), 260.5 (4.32), 301i (4.00), (EtOH+NaOAc) 260.5 (4.43), 297.5i (4.03), 327 (3.98), (EtOH+$AlCl_3$) 235 (4.50), 249.5i (4.33), 263 (4.22), 283 (4.14), 303i (3.88); $^1$H NMR (DMSO) $\delta$=6.05—6.45 (2H, m, arom-H×2), 6.60—7.40 (3H, m, arom-H×3), 7.45—8.20 (5H, m, $C_6H_5CO$), 8.05 (1H, s, $C_2$–H), 8.60—9.70 (2H, b, OH×2). Found: C, 67.69; H, 3.81%. Calcd for $C_{22}H_{14}O_7$: C, 67.69; H, 3.60%.

*5-Benzoyloxy-2',4',7-trihydroxy-5'-(3-methyl-2-butenyl)isoflavone (11) and 5-Benzoyloxy-2',4',7-trihydroxy-3',5'-bis(3-methyl-2-butenyl)isoflavone (12).* A solution of 2-methyl-3-buten-2-ol (0.32 ml) in anhydrous dioxane (10 ml) was gradually added to a solution of **10** (1 g) and boron trifluoride etherate (0.48 ml) in dioxane (42 ml) in a nitrogen atmosphere, and the mixture heated with stirring at 50 °C for 6 h. The reaction mixture was poured into ice-cold water and extracted with ether. The ethereal solution was washed with aq sodium hydrogencarbonate and dried with sodium sulfate. After the removal of the solvent, the residue was chromatographed over a silica-gel column with chloroform–ethyl acetate (3:1) to give two main products ($R_f$=0.75 and 0.24), respectively. The compound of $R_f$=0.24 was recrystallized from chloroform to give **11** as pale yellow prisms (261 mg, 22%); mp 180—182 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 250.5i (4.33), 263 (4.34), 291sh (4.14), (EtOH+NaOAc) 261.5 (4.46), 301sh (4.07), 328 (4.02), (EtOH+$AlCl_3$) 248.5i (4.35), 266 (4.22), 285 (4.17); $^1$H NMR (DMSO) $\delta$=1.61 (6H, s, $CH_3$×2), 3.06 (2H, d, $J$=7 Hz, $CH_2$), 5.18 (1H, t, $J$=7 Hz, CH=), 6.33 (1H, s, $C_{3'}$–H), 6.66 (1H, s, $C_{6'}$–H), 6.74 (1H, d, $J$=2 Hz, $C_6$–H), 6.81 (1H, d, $J$=2 Hz, $C_8$–H), 7.45—8.15 (5H, m, $C_6H_5CO$), 8.01 (1H, s, $C_2$–H), 8.50—9.60 (2H, b, OH×2). Found: C, 70.57; H, 4.78%. Calcd for $C_{27}H_{22}O_7$: C, 70.73; H, 4.84%.

The compound of $R_f$=0.75 was a viscous pale yellow oil, compound **12** (325 mg, 26%), which did not crystallize. $^1$H NMR (DMSO) $\delta$=1.66 and 1.69 (each 6H, s, $CH_3$×2), 3.08—3.42 (4H, m, $CH_2$×2), 4.92—5.37 (2H, m, CH=×2), 6.57 (1H, s, $C_{6'}$–H), 6.75 (1H, d, $J$=2 Hz, $C_6$–H), 6.88 (1H, d, $J$=2 Hz, $C_8$–H), 7.50—8.20 (5H, m, $C_6H_5CO$), 8.10 (1H, s, $C_2$–H).

*2',4',5,7-Tetrahydroxy-3',5'-bis(3-methyl-2-butenyl)isoflavone (13).* Compound **12** (325 mg) was hydrolyzed with a 4% aq solution of sodium hydroxide (3 ml) in methanol (50 ml) in a nitrogen atmosphere at 50 °C for 1 h. The reaction mixture was acidified with dilute hydrochloric acid and extracted with ethyl acetate. The ethyl acetate solution was washed with aq sodium hydrogencarbonate, water, and dried with sodium sulfate. After the removal of the solvent, the residue was chromatographed over a silica-gel column with chloroform-acetone (10:1) to give **13** as a viscous pale yellow oil (95 mg, 36%), which did not crystallize. $^1$H NMR ($CDCl_3$) $\delta$=1.71 and 1.82 (each 6H, s, $CH_3$×2), 3.27 and 3.49 (each 2H, d, $J$=7 Hz, $CH_2$), 5.24 (2H, t, $J$=7 Hz, CH=×2), 5.60 (1H, bs, OH), 6.20 (1H, d, $J$=2 Hz, $C_6$–H), 6.29 (1H, d, $J$=2 Hz, $C_8$–H), 6.70 (1H, s, $C_{6'}$–H), 7.86 (1H, s, $C_2$–H), 12.17 (1H, s, OH).

*2',4',5,7-Tetraacetoxy-3',5'-bis(3-methyl-2-butenyl)isoflavone (14).* Compound **13** was converted into the tetraacetate **14** by an acetic anhydride-sodium acetate method. Compound **14** was chromatographed over a silica-gel column with chloroform–acetone (50:1) and recrystallized from ethyl acetate as colorless prisms; mp 170—171 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 241 (4.46), 299 (3.89), 328 (3.37); $^1$H NMR ($CDCl_3$) $\delta$=1.68 (12H, s, $CH_3$×4), 2.09, 2.28, 2.33, and 2.40 (each 3H, s, $CH_3CO$), 3.18 (4H, d, $J$=7 Hz, $CH_2$×2), 4.85—5.42 (2H, m, CH=×2), 6.85 (1H, d, $J$=2 Hz, $C_6$–H), 7.00 (1H, s, $C_{6'}$–H), 7.24 (1H, d, $J$=2 Hz, $C_8$–H), 7.80 (1H, s, $C_2$–H). Found: C, 67.09; H, 5.74%. Calcd for $C_{33}H_{34}O_{10}$: C, 67.11; H, 5.80%.

*2',4',5,7-Tetrahydroxy-5'-(3-methyl-2-butenyl)isoflavone (2).* Compound **11** (83 mg) was hydrolyzed with a 4% aq solution of sodium hydroxide (3 ml) in methanol (40 ml) in a nitrogen atmosphere at 50 °C for 1 h. The reaction mixture was worked up in the same manner in the preparation of **13**. The resultant compound was chromatographed over a silica-gel column with chloroform–ethyl acetate (3:1), and recrystallized from dichloromethane–methanol to give **2** as pale yellow needles (32 mg, 50%); mp 232—234 °C. IR (KBr) 3430, 3200, 2960, 2915, 1650, 1615, 1505, 1440 $cm^{-1}$; UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 266 (4.41), 301i (4.15), 341i (3.77), (EtOH+NaOAc) 277.5 (4.48), 301i (4.22), 334.5i (4.05), (EtOH+$AlCl_3$) 273 (4.44), 313i (3.93), 374 (3.43); $^1$H NMR (DMSO) $\delta$=1.67 (6H, s, $CH_3$×2), 3.14 (2H, d, $J$=7 Hz, $CH_2$), 5.26 (1H, t, $J$=7 Hz, CH=), 6.23 (1H, d, $J$=2 Hz, $C_6$–H), 6.38 (1H, d, $J$=2 Hz, $C_8$–H), 6.45 (1H, s, $C_{3'}$–H), 6.83 (1H, s, $C_{6'}$–H), 8.10 (1H, s, $C_2$–H), 8.70—9.64 (2H, b, OH×2), 12.96 (1H, s, OH); one OH proton was not observed. Found: C, 67.53; H, 5.05%. 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 (15).* Compound **2** was converted into the tetraacetate **15** by an acetic anhydride-sodium acetate method. Compound **15** was recrystallized from ethyl acetate–petroleum ether to give colorless prisms; mp 127—128 °C. IR (KBr) 3070, 2970, 2940, 1785, 1650, 1630, 1500, 1435 $cm^{-1}$; UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 244 (4.47), 300 (3.82); $^1$H NMR ($CDCl_3$) $\delta$=1.70 and 1.72 (each 3H, s, $CH_3$), 2.12, 2.28, 2.82, and 2.86 (each 3H, s, $CH_3CO$), 3.22 (2H, d, $J$=7 Hz, $CH_2$), 5.22 (1H, t, $J$=7 Hz, CH=), 6.84 (1H, d, $J$=2 Hz, $C_6$–H), 6.99 (1H, s, $C_{3'}$–H), 7.08 (1H, s, $C_{6'}$–H), 7.22 (1H, d, $J$=2 Hz, $C_8$–H), 7.78 (1H, s, $C_2$–H). Found: C, 64.19; H, 5.00%. Calcd for $C_{28}H_{26}O_{10}$: C, 64.38: H, 4.99%.

*5,7-Dihydroxy-3-(7-hydroxy-2,2-dimethyl-6-chromanyl)-4H-chromen-4-one (16).* A mixture of **2** (42 mg) and concd hydrochloric acid (1.9 ml) was refluxed in methanol (9 ml) for 4 h. The reaction mixture was poured into water to give precipitates, which were recrystallized from aq methanol to give **16** as colorless needles (37 mg, 88%); mp 261—262 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 261 (4.44), 289sh (4.17), 337i (3.65), (EtOH+NaOAc) 271.5 (4.43), 302sh (4.15), 335sh (3.95), (EtOH+$AlCl_3$) 270.5 (4.47), 300i (4.10), 374 (3.64); $^1$H NMR (DMSO) $\delta$=1.28 (6H, s, $CH_3$×2), 1.72 and 2.62 (each 2H, t, $J$=7 Hz, $CH_2$), 6.18 (1H, d, $J$=2 Hz, $C_6$–H), 6.20 (1H, s, $C_{3'}$–H), 6.33 (1H, d, $J$=2 Hz, $C_8$–H), 6.82 (1H, s, $C_{6'}$–H), 8.08 (1H, s, $C_2$–H), 9.10 and 10.60 (each 1H, bs, OH), 12.88 (1H, s, OH). Found: C, 67.56; H, 4.98%. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H , 5.12%.

*7-Benzyloxy-6-formyl-2,2-dimethylchroman (17).* A mixture of 6-formyl-7-hydroxy-2,2-dimethylchroman[5] (1.9 g), benzyl chloride (1.6 ml), and anhydrous potassium carbonate (4 g) in DMF (50 ml) was heated with vigorous stirring at 150 °C for 1.5 h. Potassium carbonate was filtered off, and the solvent removed under reduced pressure. The residue was extracted with ether, and the ethereal solution dried with sodium sulfate. The ethereal extract was chromatographed over a silica-gel column with chloroform–petroleum ether (1:1) to give **17** as a colorless liquid (2.1 g, 72%). $^1$H NMR ($CDCl_3$) $\delta$=1.33 (6H, s, $CH_3$×2), 1.78 and 2.71 (each 2H, t, $J$=7 Hz, $CH_2$), 5.05 (2H, s, $C_6H_5C\underline{H}_2$), 6.40 (1H, s, $C_5$–H), 7.36 (5H, s, $C_6\underline{H}_5CH_2$), 7.61 (1H, s, $C_8$–H), 10.36 (1H, s, CHO).

*3-(7-Benzyloxy-2,2-dimethyl-6-chromanyl)-1-[2,4-bis(benzyloxy)-6-hydroxyphenyl]-2-propen-1-one (18) and 5,7-Bis(benzyloxy)-2-(7-benzyloxy-2,2-dimethyl-6-chromanyl)-4-chromanone (19).* A mixture of **3** (4.1 g) and **17** (3.2 g) was refluxed in the presence of piperidine (15 ml) in ethanol (200 ml) for 6 h to give yellow precipitates. The precipitates were recrystallized from ethyl acetate to give **18** as yellow needles (3.5 g, 52%); mp 158—160 °C. $^1$H NMR ($CDCl_3$) $\delta$=1.34 (6H, s, $CH_3$×2), 1.72 and 2.46 (each 2H, t, $J$=7 Hz, $CH_2$), 4.97 (4H, s, $C_6H_5C\underline{H}_2$×2), 5.03 (2H, s, $C_6H_5C\underline{H}_2$), 6.07 (1H, d, $J$=2 Hz, $C_{5'}$–H), 6.16 (1H, d, $J$=7 Hz, $C_{3'}$–H), 6.30 (1H, s, $C_3$–H), 6.89 (1H, s, $C_6$–H), 7.21—7.45 (15H, m, $C_6\underline{H}_5CH_2$×3), 7.77 and 8.20 (each 1H, d, $J$=16 Hz, CH=). Found: C, 78.74; H, 6.16%. Calcd for $C_{41}H_{38}O_6$: C, 78.57; H, 6.11%.

The flavanone **19** was obtained from the mother liquor by silica-gel column chromatography with chloroform–hexane (5:1), and recrystallized from ethyl acetate to give colorless needles (0.15 g, 2%); mp 155—157 °C. $^1$H NMR ($CDCl_3$) $\delta$=1.34 (6H, s, $CH_3$×2), 1.79 (2H, t, $J$=7 Hz, $CH_2$), 2.60—3.10 (4H, m, $C_3$–H and $CH_2$), 5.01 (4H, s, $C_6H_5C\underline{H}_2$×2), 5.13 (2H, s, $C_6H_5C\underline{H}_2$), 5.64—5.98 (1H, m, $C_2$–H), 6.22 (2H, s, arom-H×2), 6.44 and 7.23 (each 1H, s, arom-H), 7.27—7.71 (15H, m, $C_6\underline{H}_5CH_2$×3). Found: C, 78.42; H, 6.04%. Calcd for $C_{41}H_{38}O_6$: C, 78.57; H, 6.11%.

*3-(7-Benzyloxy-2,2-dimethyl-6-chromanyl)-1-[2-acetoxy-4,6-bis(benzyloxy)phenyl]-2-propen-1-one (20).* Compound **18** and **19** were converted into the acetate **20** by an acetic anhydride–sodium acetate method. The compound **20** was recrystallized from methanol–ethyl acetate to give pale yellow needles; mp 143—144 °C. $^1$H NMR ($CDCl_3$) $\delta$=1.35 (6H, s, $CH_3$×2), 1.80 and 2.70 (each 2H, t, $J$=7 Hz, $CH_2$), 2.19 (3H, s, $CH_3CO$), 4.95 (2H, s, $C_6H_5C\underline{H}_2$), 5.02 (4H, s, $C_6H_5C\underline{H}_2$×2), 6.38—6.53 (3H, m, arom-H×3), 6.99 and 7.81 (each 1H, d, $J$=16 Hz, CH=), 7.12—7.49 (16H, m, $C_6\underline{H}_5CH_2$×3 and arom-H). Found: C, 77.16; H, 5.77%. Calcd for $C_{43}H_{40}O_7$: C, 77.22; H, 6.03%.

*5,7-Bis(benzyloxy)-3-(7-benzyloxy-2,2-dimethyl-6-chromanyl)-4H-chromen-4-one (21) and 7-Benzyloxy-3-(7-benzyloxy-2,2-dimethyl-6-chromanyl)-5-hydroxy-4H-chromen-4-one (22).* After a mixture of **20** (3 g) and thallium(III) nitrate trihydrate (7 g) was stirred in methanol (800 ml) at 35—37 °C for 4 h, 10% hydrochloric acid (40 ml) was added to the mixture, and the solution refluxed for 3 h. The reaction mixture was worked up in the same manner as in the preparation of **7**. The resulting compounds were chromatographed over a silica-gel column with chloroform to give two main compounds **21** (0.96 g, 33%) and **22** (1.1 g, 39%), respectively. Compound **21** was crystallized from ether–petroleum ether to give colorless prisms; mp 133—134.5 °C. $^1$H NMR ($CDCl_3$) $\delta$=1.31 (6H, s, $CH_3$×2), 1.75 and 2.70 (each 2H, t, $J$=7 Hz, $CH_2$), 4.94, 5.01, and 5.14 (each 2H, s $C_6H_5C\underline{H}_2$), 6.43 (3H, s, arom-H×3), 7.08 (1H, s, arom-H), 7.13—7.65 (15H, m, $C_6\underline{H}_5CH_2$×3), 7.68 (1H, s, $C_2$–H). Found: C, 78.79; H, 5.72%. Calcd for $C_{41}H_{36}O_6$: C, 78.82; H, 5.81%.

Compound **22** was crystallized from methanol to give pale yellow needles; mp 145—147 °C. $^1$H NMR ($CDCl_3$) $\delta$=1.34 (6H, s, $CH_3$×2), 1.79 and 2.75 (each 2H, t, $J$=7 Hz, $CH_2$), 5.00 and 5.10 (each 2H, s, $C_6H_5C\underline{H}_2$), 6.43 (2H, s, arom-H×2), 6.50 and 7.03 (each 1H, s, arom-H), 7.29 and 7.38 (each 5H, s, $C_6\underline{H}_5CH_2$), 7.18 (1H, s, $C_2$–H), 12.95 (1H, s, OH). Found: C, 76.33; H, 5.83%. Calcd for $C_{34}H_{30}O_6$: C, 76.39; H, 5.66%.

*Another Synthesis of 5,7-Dihydroxy-3-(7-hydroxy-2,2-dimethyl-6-chromanyl)-4H-chromen-4-one (16).* A mixture (1.66 g) of **21** and **22** was hydrogenolyzed over 10% palladium on charcoal (300 mg) in a mixture of ethyl acetate (150 ml) and methanol (150 ml) until the uptake of hydrogen ceased. After the catalyst was filtered off, the solvent was removed under reduced pressure. The residue was recrystallized from aq methanol to give **16** as colorless needles (650 mg); mp 261—262 °C [no depression in a mixed-melting-point determination with the 3-(2,2-dimethyl-6-chromanyl)-4*H*-chromen-4-one **16** synthesized above]. The $^1$H NMR spectrum of the compound synthesized here was also identical with that of the 3-(2,2-dimethyl-6-chromanyl)-4*H*-chromen-4-one **16** synthesized above.

*2',4',5,7-Tetrahydroxyisoflavone (23).* Compound **7** (5 g) was hydrogenolyzed over 10% palladium on charcoal (1.7 g) in methanol (220 ml) until the uptake of hydrogen ceased. The catalyst was filtered off, and the solvent removed under reduced pressure. The residue was recrystallized from methanol to give **23** as pale yellow prisms (2.17 g, 97%); mp 255—256 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 261.5 (4.38), 288i (4.15), (EtOH+NaOAc) 271.5 (4.36), 297i (4.09), 327 (3.97), (EtOH+$AlCl_3$) 271.5 (4.42), 301i (3.98), 375 (3.53); $^1$H NMR (DMSO) $\delta$=6.21 (1H, d, $J$=2 Hz, $C_6$–H), 6.29 (1H, q, $J$=2 and 8 Hz, $C_{5'}$–H), 6.37 (2H, d, $J$=2 Hz, $C_{3'}$–H and $C_8$–H), 6.96 (1H, d, $J$=8 Hz, $C_{6'}$–H), 8.12 (1H, s, $C_2$–H), 8.38—10.44 (3H, b, OH×3), 12.86 (1H, s, OH). Found: C, 62.72; H, 3.66%. Calcd for $C_{15}H_{10}O_6$: C, 62.94; H, 3.50%.

*7-Benzoyloxy-2',4',5-trihydroxyisoflavone (24).* Benzoyl chloride (0.88 ml) in anhydrous ether (15 ml) was gradually added to a solution of **23** (1.8 g) in pyridine (30 ml) in an ice bath, and the mixture stirred at 2—5 °C for 5.5 h. The reaction mixture was poured into ice-cold

water, acidified with concd hydrochloric acid, and allowed to stand overnight in a refrigerator to give precipitates. The precipitates were collected by filtration and recrystallized from methanol to give **24** as pale yellow prisms (914 mg, 37%); mp 212—213 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 256 (4.50), 343i (3.54), (EtOH+NaOAc) 255 (4.50), 341i (3.60), (EtOH+$AlCl_3$) 264.5 (4.54), 383.5 (3.63); $^1$H NMR (DMSO) $\delta$=6.29 (1H, q, $J$=2 and 8 Hz, $C_{5'}$-H), 6.36 (1H, d, $J$=2 Hz, $C_{3'}$-H), 6.87 (1H, d, $J$=2 Hz, $C_6$-H), 7.04 (1H, d, $J$=8 Hz, $C_{6'}$-H), 7.19 (1H, d, $J$=2 Hz, $C_8$-H), 7.59—8.22 (5H, m, $C_6H_5CO$), 8.32 (1H, s, $C_2$-H), 8.87—10.17 (2H, b, OH×2), 12.88 (1H, bs, OH). Found: C, 67.68; H, 3.64%. Calcd for $C_{22}H_{14}O_7$: C, 67.69; H, 3.59%.

*7-Benzoyloxy-2',4',5-trihydroxy-3'-(3-methyl-2-butenyl)isoflavone (25), 7-Benzoyloxy-2',4',5-trihydroxy-5'-(3-methyl-2-butenyl)isoflavone (26), and 7-Benzoyloxy-2',4',5-trihydroxy-3',5'-bis(3-methyl-2-butenyl)isoflavone (27).* A solution of 2-methyl-3-buten-2-ol (0.39 ml) in anhydrous dioxane (10 ml) was gradually added to a mixture of **24** (1.2 g) and boron trifluoride etherate (0.57 ml) in dioxane (40 ml) in a nitrogen atmosphere, and the mixture heated with stirring at 51—53 °C for 6 h. The reaction mixture was worked up in the same manner as in the preparation of **11**. The resulting products were chromatographed over a silica-gel column with 1,2-dichloroethane–acetone (20:1) to give three main fractions, which showed $R_f$ values of 0.88, 0.63, and 0.24 on a silica-gel TLC plate with 1,2-dichloroethane–acetone (20:1), respectively. The second fraction ($R_f$=0.63) was recrystallized from methanol to give the desired isoflavone **25** as pale yellow needles (250 mg, 18%); mp 165—167 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 263.5 (4.54), (EtOH+NaOAc) 264.5 (4.51), 316sh (3.83), (EtOH+$AlCl_3$) 269 (4.55), 384 (3.41); $^1$H NMR (DMSO) $\delta$=1.64 and 1.73 (each 3H, s, $CH_3$), 3.33 (2H, d, $J$=7 Hz, $CH_2$), 5.24 (1H, t, $J$=7 Hz, CH=), 6.42 (1H, d, $J$=8 Hz, $C_{5'}$-H), 6.81 (1H, d, $J$=8 Hz, $C_{6'}$-H), 6.86 (1H, d, $J$=2 Hz, $C_6$-H, 7.13 (1H, d, $J$=2 Hz, $C_8$-H), 7.55—8.20 (5H, m, $C_6H_5CO$), 8.25 (1H, s, $C_2$-H), 8.28 and 9.38 (each 1H, s, OH), 12.86 (1H, s, OH). Found: C, 70.95; H, 4.73%. Calcd for $C_{27}H_{22}O_7$: C, 70.73; H, 4.84%.

The third fraction ($R_f$=0.24) was recrystallized from dichloromethane to give the 5'-(3-methyl-2-butenyl)isoflavone **26** as pale yellow needles (169 mg, 12%); mp 124—126 °C. UV $\lambda_{max}$ nm (log $\varepsilon$) (EtOH) 255 (4.48), 317.5i (3.77), (EtOH+NaOAc) 253 (4.49), 318i (3.81), (EtOH+$AlCl_3$) 264 (4.52), 287i (4.23), 381 (3.68); $^1$H NMR (DMSO) $\delta$=1.68 (6H, s, $CH_3$×2), 3.17 (2H, d, $J$=7 Hz, $CH_2$), 5.27 (1H, t, $J$=7 Hz, CH=), 6.46 (1H, s, $C_{3'}$-H), 6.82 (1H, d, $J$=2 Hz, $C_6$-H), 6.84 (1H, s, $C_{6'}$-H), 7.12 (1H, d, $J$=2 Hz, $C_8$-H), 7.57—8.24 (5H, m, $C_6H_5CO$), 8.29 (1H, s, $C_2$-H), 9.04, 9.30, and 12.84 (each 1H, s, OH). Found: C, 70.95; H, 4.68%. Calcd for $C_{27}H_{22}O_7$: C, 70.73; H, 4.84%.

Compound **26** was hydrolyzed with dilute alkali to give the isoflavone **2**.

The first fraction ($R_f$=0.88) gave the 3',5'-bis(3-methyl-2-butenyl)isoflavone **27** as a viscous pale yellow oil (375 mg, 23%), which did not crystallize. $^1$H NMR ($CDCl_3$) $\delta$=1.77 and 1.85 (each 6H, s, $CH_3$×2), 3.30 and 3.54 (each 2H, d, $J$=7 Hz, $CH_2$), 5.28 (2H, d, $J$=7 Hz, CH=×2), 5.63 (1H, s, OH), 6.78 (1H, d, $J$=2 Hz, $C_6$-H), 6.97 (1H, d, $J$=2 Hz, $C_8$-H), 7.45—8.25 (6H, m, $C_6H_5CO$ and $C_{6'}$-H), 8.00 (1H, s, $C_2$-H), 12.28 (1H, s, OH).

Compound **27** was hydrolyzed with dilute alkali to give the isoflavone **13**.

*2',4',5,7-Tetrahydroxy-3'-(3-methyl-2-butenyl)isoflavone (Licoisoflavone A) (1).* Compound **25** (180 mg) was hydrolyzed with a 4% aq solution of sodium hydroxide (3 ml) in methanol (55 ml) in a nitrogen atmosphere at 50 °C for 1.5 h. The reaction mixture was worked up in the same manner as in the preparation of **2**. The resulting compound was recrystallized from aq methanol to give the desired isoflavone **1** as pale yellow prisms (70 mg, 50%); mp 120—122 °C. IR (KBr) 3350, 2900, 1650, 1605, 1500, 1447 $cm^{-1}$. Found: C, 67.55; H, 5.03%. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12%.

*2',4',5,7-Tetraacetoxy-3'-(3-methyl-2-butenyl)isoflavone (28).* Compound **1** (licoisoflavone A) was converted into the tetraacetate **28** by an acetic anhydride–sodium acetate method. Compound **28** was recrystallized from ethanol to give colorless needles; mp 149—150 °C. IR (KBr) 2960, 2920, 1770, 1650, 1620, 1480, 1430 $cm^{-1}$. Found: C, 64.51; H, 4.73%. Calcd for $C_{28}H_{26}O_{10}$: C, 64.38; H, 4.99%.

The properties of this synthetic isoflavone (**1**) and its tetraacetate (**28**) were fully consistent with those of natural licoisoflavone A and its tetraacetate, respectively.

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## References

1) Part of this work was previously reported as a preliminary communication: M. Tsukayama, K. Fujimoto, T. Horie, Y. Yamashita, M. Masumura, and M. Nakayama, *Chem. Lett.*, **1982**, 675.

2) T. Kinoshita, T. Saitoh, and S. Shibata, *Chem. Pharm. Bull.*, **26**, 141 (1978).

3) M. Nakayama, S. Hayashi, M. Tsukayama, T. Horie, and M. Masumura, *Chem. Lett.*, **1978**, 879; M. Nakayama, S. Eguchi, S. Hayashi, M. Tsukayama, T. Horie, T. Yamada, and M. Masumura, *Bull. Chem. Soc. Jpn.*, **51**, 2398 (1978); M. Tsukayama, K. Fujimoto, T. Horie, M. Masumura, and M. Nakayama, *Heterocycles*, **22**, 261 (1984).

4) L. Farkas, A. Gottsegen, and M. Nógrádi, *J. Chem. Soc., Perkin Trans. 1*, **1974**, 305.

5) W. Stech, *Can. J. Chem.*, **49**, 1197 (1971).