

**The Synthesis of 6', 7'-Dimethoxychromano[3', 4' : 2, 3]-  
4'', 5''-dihydrofurano[3'', 2'' : 6, 7]chromanone**

by

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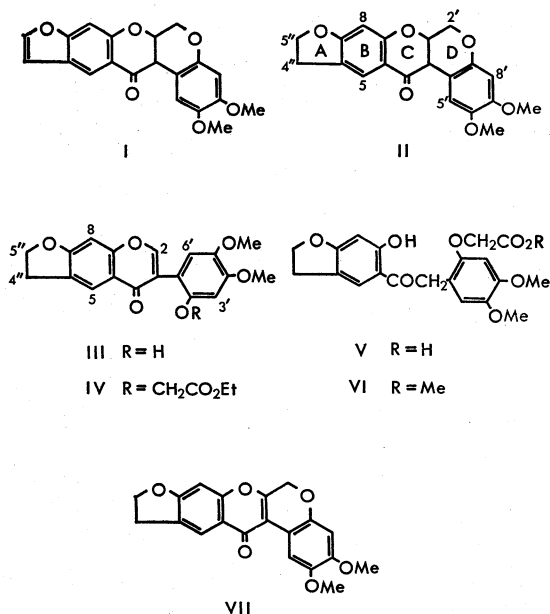
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The condensation of 2'-hydroxy-4', 5'-dimethoxy-4'', 5''-dihydrofurano[3'', 2'' : 6, 7]-isoflavone with ethyl bromoacetate in the presence of anhydrous potassium carbonate in acetone gave 2'-ethoxycarbonylmethoxyisoflavone derivative. The treatment of this compound with dilute alkali gave 5-*o*-(2-carboxymethoxy-4, 5-dimethoxyphenyl)acetyl-6-hydroxycoumaran, which is easily converted into methyl ester with diazomethane. By the ring closure of the methyl ester with sodium methoxide, 6', 7'-dimethoxychromeno[3', 4' : 2, 3]-4'', 5''-dihydrofurano[3'', 2'' : 6, 7]chromone was obtained. The reduction of this compound with sodium borohydride, followed by Oppenauer oxidation, yielded the title compound.

Isoelliptone (I) was isolated from yam beans (*Pachyrrhizus erosus*) by Norton and Hansberry<sup>1)</sup> and its chemical structure was assigned an 6', 7'-dimethoxychromano[3', 4' : 2, 3]furano[3'', 2'' : 6, 7]chromanone with a linear A/B/C/D arrangement on the mass fragmentation pattern and on biogenetic grounds by Reed and Wilson<sup>2)</sup>, and Ollis<sup>3)</sup>. The author has reported the syntheses of isoelliptone and its demethoxy-derivatives by a convenient method of preparing derrisic acid derivatives<sup>4-6)</sup>. In continuation of the syntheses of rotenoids, this paper will describe the synthesis of 6', 7'-dimethoxychromano[3', 4' : 2, 3]-4'', 5''-dihydrofurano[3'', 2'' : 6, 7]chromanone (dihydroisoelliptone) (II) from 2'-hydroxy-4', 5'-dimethoxy-4'', 5''-dihydrofurano[3'', 2'' : 6, 7]isoflavone (III) by the modification of a procedure reported earlier<sup>4-7)</sup>.

The reaction of III<sup>8)</sup> with ethyl bromoacetate in the presence of anhydrous potassium carbonate in acetone gave a 2'-ethoxycarbonylmethoxy-4', 5'-dimethoxy-4'', 5''-dihydrofurano [3'', 2'' : 6, 7] isoflavone (IV), mp 188-189°C, in good yield. The hydrolysis and ring cleavage of IV with an alcoholic potassium hydroxide solution gave acid (V), mp 224-225°, which yielded its methyl ester (VI), mp 191-192°C, when treated with diazomethane in dioxane. In the NMR spectrum\*<sup>1</sup> of

\*<sup>1</sup> The NMR spectra were measured with a Hitachi R-20 spectrometer, using tetramethylsilane as the internal standard ( $\delta$ -values in CDCl<sub>3</sub>); s, singlet; t, triplet.



VI (Fig. 1), a signal of a phenolic hydroxy group is observed at  $\delta$  12.97. This fact indicates the presence of an intramolecular hydrogen bonding to an adjacent

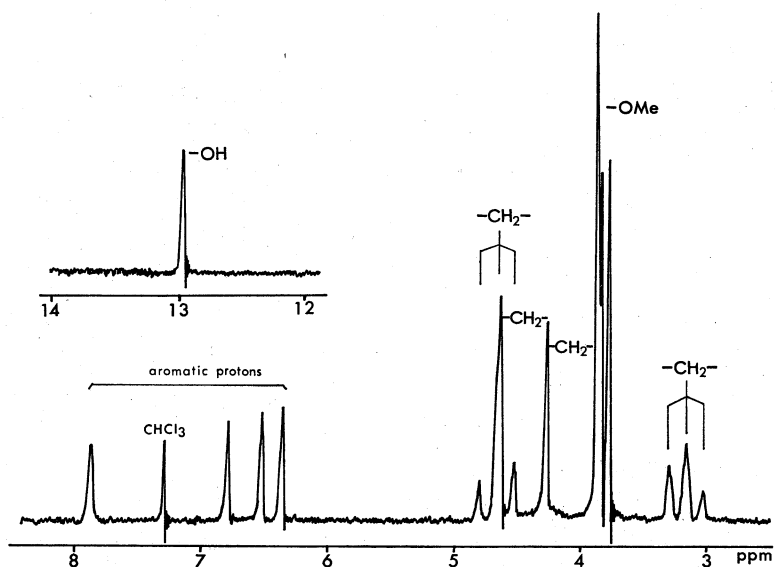


Fig. 1 NMR Spectrum of VI in CDCl<sub>3</sub>

carbonyl group of VI. Furthermore, the proton signals of two methylene groups have been observed at  $\delta$  4.63, and 4.26, and those of the other two methylene groups on ring A at  $\delta$  4.63, and 3.17, respectively. The ultraviolet spectra\*<sup>2</sup> (Fig.

\*<sup>2</sup> The ultraviolet spectra were measured with a Hitachi UV spectrophotometer Model 323.

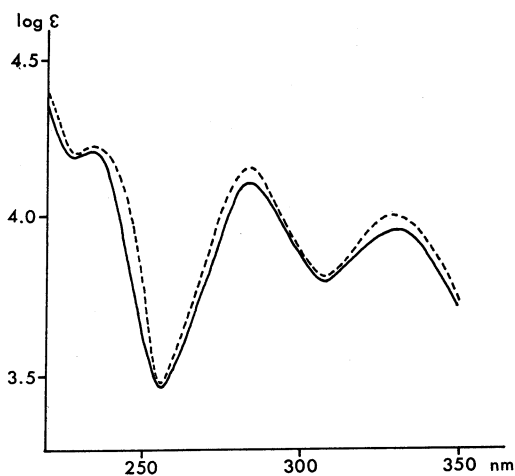


Fig. 2 UV Spectra of V (—) and VI (----) in EtOH

2) of V and VI are also similar to that of the already known derrisic acid described in earlier reports<sup>4-6</sup>). On the basis of these facts, the structures of V and VI are assigned to 5- $\omega$ -(2-carboxymethoxy-4,5-dimethoxyphenyl)acetyl-6-hydroxycoumaran and its methyl ester, respectively. The cyclization of ester (VI) with sodium methoxide<sup>9</sup>) gave 6',7'-dimethoxychromeno[3',4':2,3]-4'',5''-dihydrofuran-[3'',2'' : 6,7]chromone (VII) (dihydrodehydroisoelliptone), mp 243-244°C, in a fairly good yield. In the infrared spectrum<sup>\*3</sup> of VII, a strongly characteristic absorption of  $\alpha, \beta$ -unsaturated carbonyl group is observed at 1635  $\text{cm}^{-1}$ . The NMR spectrum of VII (Fig. 3) exhibits the proton signals of methylene group at 2'-position at  $\delta$  5.05 $\tau$ , and of those on ring A at  $\delta$  4.78 $\tau$  and 3.35 $\tau$ , respectively. In addition, the signals of methoxyl and aromatic protons are observed at  $\delta$  4.00 $\tau$ , 3.92 $\tau$  (each 3H,

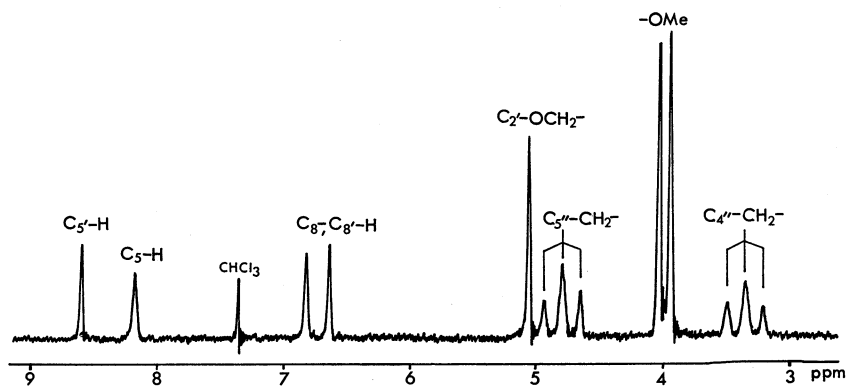


Fig. 3 NMR Spectrum of VII in  $\text{CDCl}_3$

\*3 The infrared spectra were measured in Nujol with a Hitachi IR spectrophotometer Model 285.

-OCH<sub>3</sub>), 8.55<sub>s</sub> (1H, C<sub>5'</sub>-H), 8.13<sub>s</sub> (1H, C<sub>5</sub>-H), 6.78<sub>s</sub> and 6.59<sub>s</sub> (each 1H, C<sub>4</sub>- and C<sub>8</sub>-H). The NMR spectrum of VII is similar to that of dehydroisoeleptone reported by the author<sup>5</sup>. According to the method of Matsui et al.<sup>10</sup>, VII was reduced with sodium borohydride in dioxane and subsequently, without any purification, was subjected to Oppenauer oxidation to give chromanone (II), mp 203-205°C. The infrared spectrum of II shows an absorption of the carbonyl group at 1670 cm<sup>-1</sup>. In the NMR spectrum of II (Fig. 4), signals due to the two protons

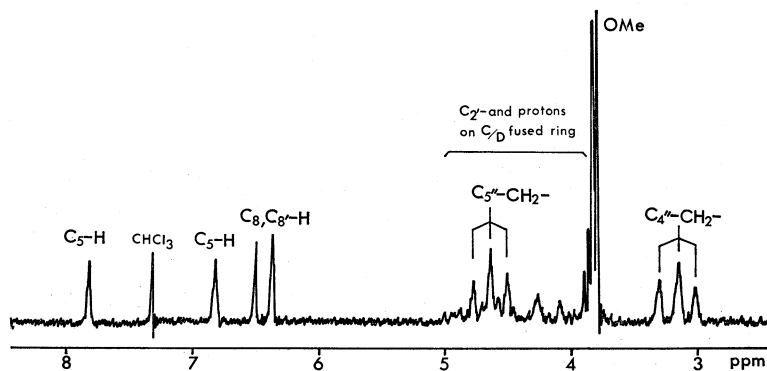


Fig. 4 NMR Spectrum of II in CDCl<sub>3</sub>

on the C/D ring fused position and the methylene protons at 2'-position are observed at  $\delta$  3.8-5.0 as an ABCD system. These results have the close similarity of that of isoeleptone previously reported<sup>6</sup>. The mass spectrum\*<sup>4</sup> of II is shown in Fig. 5. This spectrum exhibits the characteristic fragmentation pattern of the compounds containing the chromanochromanone ring system at mass number below  $m/e$  193<sup>3</sup>. The ion  $m/e$  354 is the molecular ion. The base ion is observed at

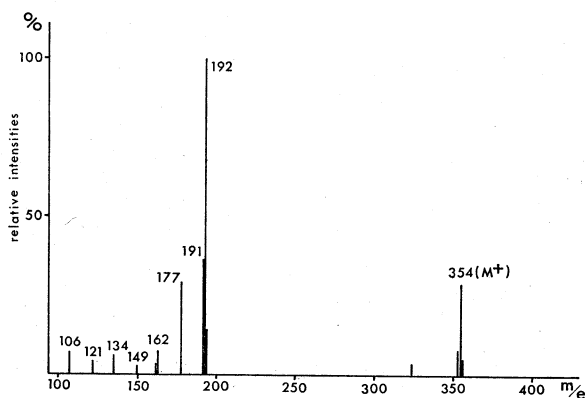
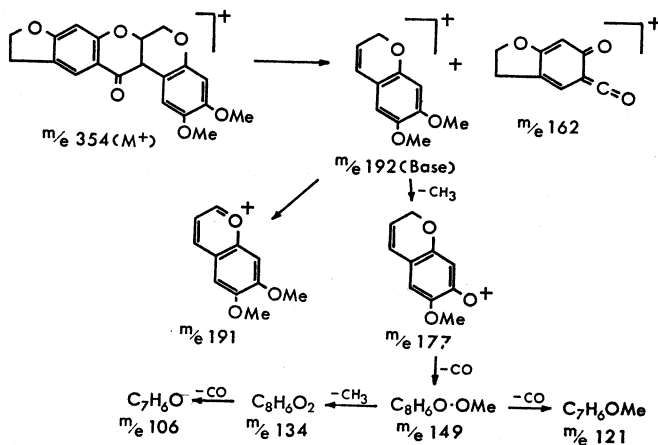


Fig. 5 MS Spectrum of II

\*<sup>4</sup> The mass spectrum was measured with a Hitachi mass spectrometer Model RMU-6MG using direct insertion probe; electron impact energy, 70 eV; temperature, 220°C.

$m/e$  192, which must cause the fragmentation of the dimethoxy chroman group and, furthermore, the residual ion in this fragmentation is observed at  $m/e$  162. The ion  $m/e$  177 is also derived from the ion  $m/e$  192. The formation of these ions and others is shown in Scheme. As a result of these facts, the structure of II is elucidated.



### EXPERIMENTAL\*5

2'-Ethoxycarbonylmethoxy-4', 5'-dimethoxy-4'', 5''-dihydrofurano[3'', 2'' : 6, 7]-isoflavone (IV). A mixture of 2'-hydroxy-4', 5'-dimethoxy-4'', 5''-dihydrofurano[3'', 2'' : 6, 7]isoflavone (III) (1.0g), ethyl bromoacetate (600mg) and anhydrous potassium carbonate (3.0 g) in acetone (100 ml) was refluxed for 24 hr. After inorganic salts had been filtered off, the solvent was condensed to 20 ml and the residual solution was diluted with water. The separated solid was collected, washed with water and then crystallized from ethanol to give IV as colorless needles, mp 188-189°C; yield, 1.0g. IR : 1730, 1645  $\text{cm}^{-1}$  (CO); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ) : 250;\*6 (4.35), 304(4.22).

Found : C, 64.55 ; H, 5.34%. Calcd for  $\text{C}_{23}\text{H}_{22}\text{O}_8$  : C, 64.78 ; H, 5.20%.

5- $\omega$ -(2-Carboxymethoxy-4, 5-dimethoxyphenyl)acetyl-6-hydroxycoumaran (V). A mixture of IV (150mg) and 10% potassium hydroxide solution (10ml) in ethanol (25ml) was refluxed on an oil bath for 2 hr. The solvent was then removed as much as possible and acidified with 10% hydrochloric acid. The separated solid was collected, washed with water and crystallized from ethanol to give V as colorless microneedles, mp 224-225°C; yield, 120mg. This substance showed brown color

\*5 All the melting points were not adjusted.

\*6 i=inflection.

with alcoholic ferric chloride. IR: 3260(OH), 1730, 1635  $\text{cm}^{-1}$  (CO); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 235.5(4.22), 283.5(4.13), 330(3.98).

Found: C, 61.64; H, 5.44%. Calcd for  $\text{C}_{20}\text{H}_{20}\text{O}_8$ : C, 61.86; H, 5.16%.

*Methyl ester* (VI) of V. To a solution of V (1.0g) in refreshed dioxane (80 ml), the ethereal diazomethane was added, the mixture was then allowed to stand overnight. The solvent was removed under reduced pressure to dryness, and the residue was crystallized from ethanol to give VI as colorless microneedles, mp 191–192°C; yield, 1.0g. This substance showed greenish brown with alcoholic ferric chloride. IR: 1760, 1640  $\text{cm}^{-1}$  (CO); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 235.5(4.23), 283.5(4.16), 330(4.02). NMR: 12.97<sub>s</sub>, 7.88<sub>s</sub>, 6.80<sub>s</sub>, 6.52<sub>s</sub>, 6.36<sub>s</sub> (each 2H), 4.63<sub>s</sub>, 4.26<sub>s</sub> (each 2H), 4.63<sub>t</sub>, 3.17<sub>t</sub> (each 2H, J=8.0 Hz), 3.86<sub>s</sub>, 3.83<sub>s</sub>, 3.77<sub>s</sub> (each 3H).

Found: C, 62.55; H, 5.56%. Calcd for  $\text{C}_{21}\text{H}_{22}\text{O}_8$ : C, 62.68; H, 5.51%.

6',7'-Dimethoxychromeno[3',4':2,3]-4''-5''-dihydrofurano[3'',2'':6,7]chromenone (*Dihydrodehydroisoelliptone*) (VII). To a refluxing solution of VI (1.1g) in anhydrous methanol (100ml), a sodium methoxide solution (prepared from 70mg of Na and 5ml of anhydrous methanol) was added drop by drop for 30 minutes. After that, the mixture was refluxed for 3 hr and then allowed to stand overnight at the temperature in the room. The crystals which were deposited were dissolved in dichloromethane, passed through a short column of alumina (ca. 5g), and crystallized from dichloromethane-ethanol (1:1 v/v) to give VII as light yellow microneedles, mp 243–244°C; yield, 0.85g. IR: 1635  $\text{cm}^{-1}$  (CO); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm (log  $\epsilon$ ): 231(4.45), 280(4.38), 310(4.36). NMR: 8.55<sub>s</sub>, 8.13<sub>s</sub>, 6.78<sub>s</sub>, 6.59<sub>s</sub> (each 1H), 5.05<sub>s</sub>(2H), 4.78<sub>t</sub>, 3.35<sub>t</sub> (each 2H, J=8.0 Hz), 4.00<sub>s</sub>, 3.92<sub>s</sub> (each 3H).

Found: C, 68.01; H, 4.76%. Calcd for  $\text{C}_{20}\text{H}_{16}\text{O}_6$ : C, 68.18; H, 4.54%.

6',7'-Dimethoxychromano[3',4':2,3]-4''-5''-dihydrofurano[3'',2'':6,7]chromanone (*Dihydroisoelliptone*) (II). A solution of sodium borohydride (100mg) in absolute ethanol (5ml) was added drop by drop to a solution of VII (200mg) in dioxane (20ml). The mixture was warmed at 50–60°C for 30 min and then allowed to stand overnight at shade temperature. Acetone (20ml) was added to the reaction mixture to decompose the excessive reducing agent, and the solvent was removed under reduced pressure to dryness. The residual solid was dissolved in chloroform, washed with water and dried on calcium chloride. The evaporation of chloroform under reduced pressure furnished crude chromanol, without any purification, this product was employed in the next reaction. Aluminum isopropoxide (4.0g) was added to a solution of the crude chromanol in absolute benzene (40ml) and refreshed acetone (30ml), after which the mixture was gently refluxed for 12 hr. The reaction mixture was cooled, diluted with benzene (200ml), washed

with diluted sulfuric acid and water, and then dried on calcium chloride. After the solvent had been removed under reduced pressure to dryness, the solid was chromatographed on silicagel (ca. 10g) in dichloromethane and then crystallized from dichloromethane-ethanol (1:1 v/v) to give II as colorless microneedles, mp 203-205°C; yield, 120mg. IR: 1670 cm<sup>-1</sup> (CO); UV  $\lambda_{max}^{OHCl_3}$  nm (log  $\epsilon$ ): 284.5 (4.17), 328(3.99). NMR: 7.81<sub>s</sub>, 6.83<sub>s</sub>, 6.50<sub>s</sub>, 6.38<sub>s</sub> (each 1H), 4.62<sub>t</sub>, 3.15<sub>t</sub> (each 2H, J=8.0 Hz), 3.82<sub>s</sub>, 3.79<sub>s</sub> (each 3H). MS(m/e): 354(M<sup>+</sup>), 192(base), 191, 177, 162, 149, 134, 121, 106.

Found: C, 67.51; H, 4.93%. Calcd for C<sub>20</sub>H<sub>18</sub>O<sub>6</sub>: C, 67.79; H, 5.12%.

Now that my task is finished, I should like to register here my sincere thanks to Professor Kenji Fukui and the members of his laboratory, Department of Chemistry of Hiroshima University, for the measurement of the NMR spectra and the microanalyses.

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