The Synthesis of Irisolone

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Irisolone, a colorless substance, was isolated from the rhizomes of *Iris nepalensis* D. Don by Gopinath et al.¹⁾ They also established its structure as 4'-hydroxy-5-methoxy-6, 7-methylenedioxyisoflavone (I) on the basis of analytical, spectroscopic and degradative studies. It is one of the few isoflavones which contain a methylenedioxy group in the condensed benzene ring, the only others so far known being tlatlancuayin²⁾ and maxima substance A.³⁾ Further, it is an unusual type of isoflavone in that the oxygenation pattern is at positions 5, 6 and 7. This class includes irigenin,⁴⁾ tectorigenin,⁵⁾ muningin,⁶⁾ podospicatin,⁷⁾ caviunin,⁸⁾ and tlatlancuayin as well as irisolone. The present paper will describe the total synthesis of irisolone, its methyl ether and some related compounds.

The methylation of irisolone has yielded the methyl ether (II), which can be converted by dilute alkali hydrolysis into 6hydroxy-2-methoxy-3, 4-methylenedioxyphenyl 4-methoxybenzyl ketone (III).¹⁾ The ether II has been reformed by the treatment of the deoxybenzoin III with sodium and ethyl

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⁴⁾ W. Baker, J. Chem. Soc., 1928, 1022.

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⁶⁾ F. E. King, T. J. King and A. J. Warwick, J. Chem. Soc., 1952, 96.

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⁸⁾ O. R. Gottlieb and M. T. Mahalhaes, J. Org. Chem., 26, 2449 (1961).

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formate.¹⁾ The synthesis of the deoxybenzoin III was achieved in two ways. The first method involved the condensation reaction of 3-methoxy - 4, 5 - methylenedioxyphenol (IV). The phenol IV underwent the Hoesch reaction with 4-methoxybenzyl cyanide to give a deoxybenzoin. In previous papers9) it was demonstrated that the phenol IV was substituted not at the 6-position but at the 2position in the Hoesch condensation. Therefore, the condensation product was thought to be the ketone III. In order to elucidate the structure of the product, a second, unambigous method of synthesis was explored. 5, 7-Dihydroxy-4'-methoxy - 2 - methylisoflavone (V),¹⁰ when subjected to para hydroxylation, afforded 5, 7, 8-trihydroxy-4'-methoxy-2-methylisoflavone (VI). Subsequent methylenation using the potassium hydroxide - acetone method gave 5-hydroxy-4'-methoxy-7, 8-methylenedioxy-2-methylisoflavone (VII). The benzylation of VII with benzyl chloride yielded 5-benzyloxy-4'-methoxy-7, 8 - methylenedioxy - 2 - methylisoflavone (VIII), which was then smoothly converted by boiling dilute alkali into 6benzyloxy-2-hydroxy-3, 4-methylenedioxyphenyl 4-methoxybenzyl ketone (IX). The ketone IX was first methylated in the 2-position, using the potassium carbonate - acetone method, to a methyl ether (X), and then debenzylated with hydrogen to give the deoxybenzoin III identical with the above ketone. The melting point of the deoxybenzoin was the same as that reported in the literature for the ketone obtained from natural irisolone methyl ether by Gopinath et al.¹⁾ Irisolone methyl ether could be obtained according to the method of Gopinath et al.¹⁾ (Table I).

Table I. The melting points of irisolone and its derivatives ($^{\circ}C$)

	Synthetic compound	Natural compound
Irisolone (I)	251-252	250-251*1 (269-270) ¹)
Acetate of I	162-163	156-1571)
Irisolone methyl ether (II)	182—183	179—181*1 (184—185) ¹⁾
5-Demethyl deriv. of II	211-212	214-2151)

The methylation of VII with dimethyl sulfate yielded 4',5-dimethoxy-7,8-methylenedioxy-2-methylisoflavone (XI), which was then converted into 2-hydroxy-6-methoxy-3,4-methylenedioxyphenyl 4-methoxybenzyl ketone (XII).



⁹⁾ K. Fukui and T. Matsumoto, This Bulletin, 36, 806 (1963); 37, 266 (1964).

¹⁰⁾ W. Baker and R. Robinson, J. Chem. Soc., 1926, 2713. *1 Natural irisolone and its methyl ether, kindly supplied by Dr. Gopinath, were measured in this laboratory.



 $\begin{array}{ccc} XIX & R = H \\ XX & R = Me \end{array}$

The resulting ketone gave the original isoflavone XI with acetic anhydride and was condensed with ethyl formate to give 4', 5-dimethoxy-7, 8-methylenedioxyisoflavone (XIII), an isomer of irisolone methyl ether (II).

The phenol IV underwent the Hoesch reaction with 4-hydroxybenzyl cyanide to give 6hydroxy-2-methoxy-3, 4-methylenedioxyphenyl 4-hydroxybenzyl ketone (XIV). The same ketone XIV was also obtained from the corresponding amine XV, which was synthesized by the catalytic reduction of a nitroketone XVI; the ketone XVI was derived in turn from 4-nitrobenzyl cyanide by the Hoesch condensation. The ketone XIV was indentical with that obtained from the degradation of natural irisolone by Gopinath et al.¹⁾ The resulting ketone XIV underwent ring closure with ethyl orthoformate or ethyl formate to give 4'hydroxy - 5 - methoxy - 6, 7 - methylenedioxyisoflavone (I), which agreed with natural irisolone (Table I). The identity of the product was established by methylation as well as by demethylation to known products.

The ring closure of the ketone XIV with acetic anhydride gave a monoacetate (XVII), which was then smoothly converted into the 2-methyl derivative (XVIII) of irisolone. By similar methods, 4'-nitroisoflavones (XIX and XX) were also obtained from the ketone XVI.

The ultraviolet absorption spectra of natural and synthetic methylenedioxyisoflavones are shown in Figs. 1 and 2 and Table II. In most



Fig. 1. Ultraviolet spectra of natural (.....) and synthetic irisolone (....) in ethanol.



Fig. 2. Ultraviolet spectra of XIII (---), natural (.....) and synthetic irisolone methyl ether (.....) in ethanol.



Fig. 3. Infrared spectra of synthetic (A) and natural irisolone (B) in Nujol.

^{*2} Inflexion point.

	Substituent					2					
	OH	OAc	OMe	Me	O-CH ₂ -O	$\lambda_{max} m \mu (\log \varepsilon)$					
Irisolone (I)											
(synthetic)	4'		5		6,7	266	(4.51)	325	(3.83)		
(natural)	4′		5		6,7	266	(4.49)	325	(3.82)		
Acetate of I		4'	5		6,7	262	(4.45)	323	(3.81)		
Irisolone methyl ether (II)											
(synthetic)			4',5		6,7	266	(4.53)	325	(3.83)		
(natural)			4',5		6,7	266	(4.52)	325	(3.83)		
XIII			4',5		7,8	260	(4.52)	338	(3.75)		
5-Demethyl deriv. of II	5		4'		6,7	274	(4.50)	336*	² (3.59)		
XVII		4'	5	2	6,7	246	(4.43)	320	(3.83)		
XVIII	4′		5	2	6,7	248	(4.42)	320	(3.85)		
XI			4',5	2	7,8	256	(4.51)	335	(3.83)		
VII	5		4'	2	7,8	264	(4.46)	353	(3.64)		

TABLE II. ULTRAVIOLET SPECTRA OF SOME METHYLENEDIOXYISOFLAVONE

(in ethanol)

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cases, there are two characteristic peaks, at ca. 260 (band I) and ca. $325 \text{ m}\mu$ (band II). The displacement effect of the substitution is similar to that reported in previous papers.¹¹⁾ The absorption curve of XIII (a methylenedioxy group in the 7, 8-positions) is different from that of II (the group in the 6,7-positions) (Fig. 2).

Experimental*3

5, 7, 8-Trihydroxy-4'-methoxy-2-methylisoflavone (VI).-To a cooled, stirred solution of 5, 7-dihydroxy-4'-methoxy-2-methylisoflavone $(V)^{10}$ (4.5 g.) in aqueous sodium hydroxide (4%, 120 ml.), an aqueous solution of potassium persulfate (7.5 g. in 150 ml.) was added drop by drop over a 2 hr. period at 15-20°C. The mixture was allowed to stand at room temperature for 24 hr. and then acidified to litmus with dilute hydrochloric acid. The unchanged compound which had separated out was filtered off, and the filtrate was then heated with concentrated hydrochloric acid (90 ml.) and sodium sulfite (9.0 g.) on a steam bath for 30 min. On cooling, the brown precipitates were collected, washed with water, and then recrystallized from acetone to give VI as yellow needles (or prisms), m. p. 288-289°C (decomp.); yield, 1.2 g. It gave a green ferric chloride reaction in ethanol.

Found : C, 64.87; H, 4.61. Calcd. for $C_{17}H_{14}O_6$: C, 64.96; H, 4.47%.

5-Hydroxy - 4' - methoxy - 7, 8 - methylenedioxy-2methylisoflavone (VII). - Into a mixture of VI

(1.6 g.), potassium hydroxide (0.9 g.) and ethanol (15 ml.) in water (15 ml.), air having been excluded by a stream of nitrogen gas, methylene sulfate (1.1 g.) in acetone (20 ml.) was stirred at 45-50°C. The mixture was kept at 45-50°C for another 80 min. and then diluted with aqueous potassium hydroxide. The yellow precipitates were collected, washed with dilute hydrochloric acid, and then water, and recrystallized from aqueous acetone to give VII as yellow needles, m. p. 190-191°C; yield 450 mg. It gave a green ferric chloride reaction in ethanol. IR : 1665 (C=O), 1034 (=C-O-C), 923 cm^{-1} (O-CH₂-O).

Found : C, 66.16; H, 4.43. Calcd. for $C_{18}H_{14}O_6$: C, 66.25; H, 4.32%.

5-Benzyloxy-4' - methoxy - 7, 8 - methylenedioxy-2methylisoflavone (VIII).-The isoflavone VII (1.1 g.) was refluxed with dry acetone (100 ml.), benzyl chloride (450 mg.), sodium iodide (0.1 g.) and anhydrous potassium carbonate (15 g.) for 30 hr. Inorganic salts were filtered off and washed with warm acetone, and the combined acetone solution was distilled off. The residue was washed with water and recrystallized from acetone to give VIII as colorless needles, m. p. 195-196°C; yield 0.7 g. IR: 1646 (C=O), 1028 (=C-O-C), 915 cm^{-1} (O- CH_2-O).

Found : C, 72.42; H, 4.99. Calcd. for $C_{25}H_{20}O_6$: C, 72.10; H, 4.84%.

6-Benzyloxy-2-hydroxy-3,4-methylenedioxyphenyl 4-Methoxybenzyl Ketone (IX).—A mixture of VIII (600 mg.), aqueous potassium hydroxide (10%, 10 ml.) and ethanol (100 ml.) was refluxed for 2 hr. under a stream of nitrogen gas. The solvent was removed in vacuo, and the residue was acidified with dilute hydrochloric acid. The yellow precipitates were collected, washed with water, and then crystallized from aqueous acetone to give IX as pale yellow needles, m. p. 148-149°C; yield 420 mg. It gave a green ferric chloride reaction in ethanol.

¹¹⁾ K. Fukui and T. Matsumoto, J. Sci. Hiroshima, Univ.,

Ser. A-II, 28, 47 (1964); J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi), 85, 793 (1964); This Bulletin, 38, 612 (1965).

All melting points are uncorrected; the ultraviolet spectra were measured in ethanol, while the infrared spectra were measured in Nujol.

IR: 1663 (C=O), 1031 (=C-O-C), 915 cm⁻¹ (O-CH₂-O). UV: $\lambda_{max}^{\text{EtOH}} m \mu$ (log ε); 247 (4.12), 296 (4.10), 351 (3.53).

Found : C, 70.70 ; H, 5.28. Calcd. for $C_{23}H_{20}O_6$: C, 70.40 ; H, 5.14%.

6-Hydroxy-2-methoxy-3, 4-methylenedioxyphenyl 4-Methoxybenzyl Ketone (III).-From IV.-3-Methoxy-4, 5-methylenedioxyphenol $(IV)^{12}$ (3.7 g.) and 4-methoxybenzyl cyanide (3.7 g.) were dissolved in dry ether (70 ml.), and then fused zinc chloride (1.0 g.) was added. The mixture was saturated with dry hydrogen chloride in an ice bath and allowed to stand overnight. After the ether layer had been decanted, the ketimine hydrochloride was washed with dry ether and then hydrolyzed by heating it with water (40 ml.) on a water bath for 30 min. The solid which had separated on cooling was extracted with ethyl acetate; the extract was washed with aqueous sodium bicarbonate and then with water. After the solvent had been evaporated, the residue was distilled. The distillate (bath temperature 180-240°C/0.01 mm. Hg.) was collected and recrystallized from methanol to give III as yellow needles, m. p. 114-115°C (reported m. p. $113-114^{\circ}C^{1}$); yield, 820 mg. It gave a green ferric chloride reaction in ethanol. IR: 1662 (shoulder), 1632 (C=O), 1035 (=C-O-C), 936 cm^{-1} (O-CH₂-O). UV: $\lambda_{max}^{\text{EtOH}} \ \mu \mu \ (\log \varepsilon)$; 245.5 (4.08), 286.5 (4.14), 355 (3.72).

Found : C, 64.39 ; H, 5.10. Calcd. for $C_{17}H_{16}O_6$: C, 64.55 ; H, 5.10%.

From IX.—The ketone IX (360 mg.) was refluxed with dry acetone (40 ml.), dimethyl sulfate (4 drops), and anhydrous potassium carbonate (4.0 g.) for 27 hr. The crude product X, was dissolved into ethyl acetate, and the solution was washed with aqueous potassium hydroxide (5%) and then with water. After the solvent had been evaporated, the residue was dissolved into ethanol (50 ml.) and in the presence of Pd-C (10%, 1.0 g.), the solution was shaken with hydrogen at room temperature for 5 hr. The reaction mixture was filtered, and the filtrate was evaporated. The residue was recrystallized from methanol to give III as yellow needles, m. p. 114—115°C; yield 90 mg. This compound was identical with the above sample.

4', 5 - Dimethoxy - 6, 7 - methylenedioxyisoflavone (Irisolone Methyl Ether) (II). — The ketone III (150 mg.) was condensed with ethyl formate (15 ml.) and sodium (0.2 g.) as described by Gopinath et al.¹⁾ Recrystallization from methanol gave II (40 mg.) as colorless plates, m. p. $182-183^{\circ}C^{*4}$ reported m. p. $184-185^{\circ}C^{13}$). It was found identical with the natural irisolone methyl ether (m. p. 179– $181^{\circ}C^{*1,*43}$) which had been supplied by Gopinath, by mixed melting point measurement and infrared and ultraviolet spectral comparisons. This substance dissolves into concentrated sulfuric acid to give a yellow solution. IR : 1647 (C=O), 1021(=C-O-C), 925 cm⁻¹ (O-CH₂-O).

Found : C, 66.04 ; H, 4.21. Calcd. for $C_{18}H_{14}O_6$: C, 66.25 ; H, 4.32%.

4', 5-Dimethoxy-7, 8-methylenedioxy-2-methylisoflavone (XI).—A mixture of VII (830 mg.), dimethyl sulfate (2.0 ml.), anhydrous potassium carbonate (10 g.) and dry acetone (80 ml.) was refluxed for 30 hr. The reaction mixture was then filtered, and the inorganic residue was washed with hot acetone. The evaporation of acetone left a solid which was triturated with water, filtered, and crystallized from aqueous acetic acid to give XI as colorless needles, m. p. 214—215°C; yield 750 mg. It dissolves into concentrated sulfuric acid to give a yellow solution. IR: 1668 (C=O), 1029 (=C-O-C), 923 cm⁻¹ (O-CH₀-O).

Found : C, 67.08 ; H, 4.94. Calcd. for $C_{19}H_{16}O_6$: C, 67.05 ; H, 4.75%.

2-Hydroxy-6-methoxy-3, 4-methylenedioxyphenyl 4-Methoxybenzyl Ketone (XII).—A mixture of the isoflavone XI (560 mg.), potassium hydroxide (1.0 g.), water (10 ml.) and ethanol (60 ml.) was refluxed for 2 hr. under a stream of nitrogen gas. The reaction mixture was then treated in the usual manner. The product was recrystallized from ethanol to give the ketone XII as yellow plates, m. p. 133–134°C; yield, 460 mg. It gave a green ferric chloride reaction in ethanol. IR: 1671 (C=O), 1033 (=C-O-C), 915 cm⁻¹ (O-CH₂-O). UV: $\lambda_{max}^{\text{EtOH}} m\mu$ (log ε); 246.5 (4.11), 295.5 (4.15), 349 (3.56).

Found: C, 64.49; H, 5.31. Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10%.

When the ketone XII (200 mg.) was heated with anhydrous sodium acetate (200 mg.) and acetic anhydride (10 ml.), the parent isoflavone, XI (80 mg., m. p. $214-215^{\circ}$ C), was obtained.

4', 5 - Dimethoxy - 7, 8 - methylenedioxyisoflavone (XIII).—The ketone XII (600 mg.) in ethyl formate (25 ml.) was added to sodium powder (0.6 g.) at -10° C and left in the refrigerator for 3 days; then the product was worked up. The ether residue gave the isoflavone XIII, which crystallized from aqueous acetone as colorless needles, m. p. 179—181°C; yield 250 mg. It was soluble in concentrated sulfuric acid to give a reddish yellow solution and depressed to 150—152°C on admixture with natural irisolone methyl ether (m. p. 179—181°C*1). IR : 1651 (C=O), 1030 (=C-O-C), 920cm⁻¹ (O-CH₂-O).

Found : C, 66.47 ; H, 4.47. Calcd. for $C_{18}H_{14}O_6$: C, 66.25 ; H, 4.32%.

6-Hydroxy-2-methoxy-3, 4-methylenedioxyphenyl 4-Nitrobenzyl Ketone (XVI). — To a solution of 3-methoxy-4, 5-methylenedioxyphenol (IV) (4.4 g.) in dry ether (100 ml.), a mixture of 4-nitrobenzyl cyanide (4.4 g.) and anhydrous zinc chloride (3.0 g.) in dry chloroform (100 ml.) was added. The resulting mixture was saturated with dry hydrogen chloride at 0°C. The reaction mixture was then treated in the usual manner. Recrystallization from aqueous acetone gave the ketone XVI as yellow needles, m. p. 165—167°C; yield, 3.2 g. It gave a green ferric chloride reaction in ethanol. IR: 1623 (C=O), 1515, 1331 (NO₂), 1039 (=C-O-C), 923 cm⁻¹ (O-CH₂-O).

Found: C, 58.04; H, 4.13; N, 4.21. Calcd. for $C_{16}H_{18}O_7N$: C, 58.01; H, 3.96; N, 4.23%.

¹²⁾ A. F. Wagner, E. Walton, A. N. Wilson, J. O. Rodin and F. W. Holly, J. Am. Chem. Soc., 81, 4983 (1959).

^{*4} The sample was dried in vacuo at 110°C for 2 hr.

6-Hydroxy-2-methoxy-3, 4-methylenedioxyphenyl 4-Aminobenzyl Ketone (XV).—A solution of the ketone XVI (2.0 g.) in ethyl acetate (120 ml.) was submitted to catalytic reduction at room temperature in the presence of Pd-C (10%, 1.5 g.). After the catalyst had been filtered, the filtrate was evaporated; the residue was then recrystallized from methanol to give XV as yellow plates, m. p. 170— 172°C; yield 1.5 g. It gave a green ferric chloride reaction in ethanol. IR : 3453, 3373, 1595, 1340 (NH₂), 1623 (C=O), 1044 (=C-O-C), 929 cm⁻¹ (O-CH₂-O).

Found: C, 63.58; H, 5.35; N, 4.68. Calcd. for $C_{16}H_{15}O_5N$: C, 63.78; H, 5.02; N, 4.65%.

6-Hydroxy-2-methoxy-3, 4-methylenedioxyphenyl 4-Hydroxybenzyl Ketone (XIV).-From IV.-From the ketone IV (600 mg.), 4-hydroxybenzyl cyanide (700 mg.) and anhydrous zinc chloride (0.3 g.) in dry ether (20 ml.), synthesis was carried out by a method similar to that used for XVI. The product was extracted with ethyl acetate, and the extract was washed with aqueous sodium bicarbonate and then water. After the solvent had been evaporated, the residue was distilled. The distillate (bath temperature 180-240°C/0.04 mmHg) was collected and recrystallized from ether-petroleum ether to give XIV as yellow needles, m.p. 152-153°C (reported m. p. 159-160°C¹); yield, 70 mg. It gave a ferric green chloride reaction in ethanol. IR : 1630 (C=O), 1051 (=C-O-C), 934 cm⁻¹ (O-CH₂-O). UV : $\lambda_{max}^{EtOH} m \mu (\log \varepsilon)$; 245 (4.07), 287 (4.14), 355 (3.72).

Found : C, 63.40 ; H, 4.89. Calcd. for $C_{16}H_{14}O_6$: C, 63.57 ; H, 4.67%.

From XV.—A solution of sodium nitrite (400 mg.) in water (12 ml.) was added to a suspension of the ketone XV (800 mg.) in dilute sulfuric acid (25%, 55 ml.) at 0°C. After the solution had been stirred at $0-5^{\circ}C$ for another hour, the excess nitrous acid was decomposed with urea (350 mg.). The solution was added drop by drop into a boiling solution of cupric sulfate (40 g.) in water (50 ml.). The reaction mixture was cooled and extracted with ether. The ether solution was washed with water, dried, and evaporated, and the residue was distilled. The distillate (bath temperature 180-220°C/0.01 mmHg) was collected and then recrystallized from ether - petroleum ether to give XIV as yellow microneedles, m. p. 152-153°C; yield, 80 mg. This substance was identical with the above sample.

An acetate (m. p. $89-90^{\circ}$ C) was obtained by the acetic anhydride-pyridine method. IR : 1762, 1723 (OAc), 1623 (C=O), 1021 (=C-O-C), 915 cm⁻¹ (O-CH₂-O).

Found : C, 62.14 ; H, 4.60. Calcd. for $C_{20}H_{18}O_8$: C, 62.17 ; H, 4.70%.

4'-Hydroxy-5-methoxy-6, 7-methylenedioxyisoflavone (Irisolone) (I).—a) The ketone XIV (2.0 g.) in ethyl formate (60 ml.) was added to sodium (2.0 g.) at -10° C, left in a refrigerator for 3 days, and the product worked up. Recrystallization from aqueous pyridine gave I as colorless prisms, m. p. 251—252°C (reported m. p. 269—270°C¹); yield, 1.1 g. This substance was soluble in aqueous sodium hydroxide (5%) and dissolves into concentrated sulfuric acid to give a yellow solution. It was found identical with the natural irisolone (m. p. $250-251^{\circ}C^{*1}$) which was supplied by Gopinath, by mixed melting point measurement and infrared and ultraviolet spectral comparisons. IR : 1645 (C=O), 1028 (=C-O-C), 920 cm⁻¹ (O-CH₂-O).

Found : C, 65.47 ; H, 3.85. Calcd. for $C_{17}H_{12}O_6$: C, 65.38 ; H, 3.87%.

b) A mixture of the ketone XIV (600 mg.), ethyl orthoformate (1.5 ml.), dry pyridine (4.0 ml.) and piperidine (0.3 ml.) was refluxed for 4 hr. under a stream of nitrogen gas. The product which had separated on cooling was recrystallized from aqueous pyridine to give I as colorless prisms, m. p. $251-252^{\circ}C$; yield, 40 mg. It was identical with the above sample.

The Reaction of Synthetic Irisolone (I). — An acetate (m. p. $162-163^{\circ}$ C) was prepared according to the Gopinath method¹) (reported m. p. $156-157^{\circ}$ C¹). IR : 1767 (OAc), 1649 (C=O), 1026 (=C-O-C), 926 cm⁻¹ (O-CH₂-O).

Found : C, 64.26 ; H, 3.92. Calcd. for $C_{19}H_{14}O_7$: C, 64.40 ; H, 3.98%.

The acetate (310 mg.) was refluxed with aqueous sodium hydroxide (10%, 3.0 ml.) and methanol (40 ml.) for 5 min. The parent isoflavone, I (m. p. $251-252^{\circ}C$, 240 mg.), was thus obtained.

According to the method of Gopinath et al.,¹⁾ the isoflavone I was easily converted into II (m. p. $182-183^{\circ}$ C) with dimethyl sulfate. II was demethylated with aluminum chloride in ether to give 5-hydroxy-4'-methoxy-6, 7-methylenedioxyisoflavone (m. p. $211-212^{\circ}$ C, pale yellow plates) (reported m. p. $214-215^{\circ}$ C¹) according to the method of Gopinath et al.¹)

Found : C, 65.43 ; H, 3.84. Calcd. for $C_{17}H_{12}O_6$: C, 65.38 ; H, 3.87%.

4'-Acetoxy-5-methoxy-6,7-methylenedioxy-2methylisoflavone (XVII). — A mixture of the ketone XIV (80 mg.), anhydrous sodium acetate (200 mg.) and acetic anhydride (4.0 ml.) was refuxed for 30 hr. The excess acetic anhydride was removed in vacuo. The residue was washed with water and then recrystallized from methanol to give XVII as colorless plates, m. p. $201-202^{\circ}C$; yield 60 mg.

Found : C, 65.27 ; H, 4.36. Calcd. for $C_{20}H_{16}O_7$: C, 65.21 ; H, 4.38%.

4'-Hydroxy - 5 - methoxy - 6, 7 - methylenedioxy-2methylisoflavone (XVIII). — A mixture of the acetate XVII (420 mg.), ethanol (60 ml.) and an aqueous sodium hydroxide solution (5%, 5.0 ml.) was refluxed for 5 min. After the solvent had been removed in vacuo, the residue was dissolved in water and then acidified. The precipitates were collected, washed with water, and recrystallized from methanol or acetone to give XVIII as colorless prisms, m. p. $284-285^{\circ}C$; yield, 230 mg. It dissolves into concentrated sulfuric acid to give a yellow solution.

Found : C, 66.12 ; H, 4.15. Calcd. for $C_{18}H_{14}O_6$: C, 66.25 ; H, 4.32%.

5-Methoxy-6, 7-methylenedioxy-4'-nitroisoflavone (XIX).—A mixture of the ketone XVI (1.0 g.), ethyl orthoformate (5.0 ml.), dry pyridine (8.0 ml.) and piperidine (0.5 ml.) was refluxed for 6 hr. The brown precipitates which separated on cooling were

collected, washed with ethanol, and then recrystallized from ethyl acetate to give XIX as pale yellow needles, m. p. 209–211°C; yield, 0.5 g. UV: $\lambda_{max}^{\rm EtOH} m\mu$ (log ε); 241*² (4.28), 289 (4.36), 315*² (4.23).

Found: C, 59.70; H, 3.44; N, 4.20. Calcd. for $C_{17}H_{11}O_7N$: C, 59.82; H, 3.26; N, 4.10%.

5-Methoxy-6, 7-methylenedioxy-2-methyl-4' -nitroisoflavone (XX).—A mixture of the ketone XVI (1.0 g.), acetic anhydride (25 ml.) and anhydrous sodium acetate (1.0 g.) was refluxed for 24 hr. The reaction mixture was treated in the usual manner. The product was recrystallized from acetone to give XX as yellow rhombic plates, m. p. 219—220°C; yield, 0.8 g. UV: $\lambda_{max}^{\rm EtOH}$ m μ (log ε); 241.5*² (4.35), 284.5 (4.33), 312*² (4.11). Found : C, 60.67; H, 3.80; N, 3.69. Calcd. for $C_{18}H_{13}O_7N$: C, 60.85; H, 3.68; N, 3.94%.

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