23. 6-*Methoxyfuroflavone, a New Component of the Seeds of* Pongamia glabra.

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From the seeds of *Pongamia glabra*, a new furoflavone has been isolated. Its structure has been established as 6-methoxy-4-oxo-2-phenylfuro[2,3-*h*]-1-benzopyran and confirmed by synthesis.

Pongamia glabra is one of the commonest trees of India, and its seed-oil is plentiful. A serious difficulty in its industrial utilisation is the development of colour on storage, not only of the oil but also of the soap obtained from it. A detailed study of the seeds and of the oil has been undertaken to get information about the chromogenic factors present in them. Earlier work led to the isolation of karanjin, pongamol, and glabrin.[1,2] In the present investigation the seed kernels were extracted with light petroleum in two stages, yielding oils A and B. Ethanol-extraction of the defatted seeds provided sucrose and a nitrogenous compound (glabrin [2]). Aqueous extraction of the residue gave a saponin resembling glabrosaponin.[3]

From oil A the non-fat components were separated by extraction with ethanol; this extract deposited karanjin. The remaining extract was subjected to countercurrent distribution between aqueous acetic acid and light petroleum, and pongamol was obtained. Oil B had little of glyceride portion and deposited karanjin. The residual oil was chromatographed on an alumina column. The first fraction, eluted with light petroleum, contained karanjin, and the second, eluted with light petroleum–benzene, was pongapin which was first isolated by Row [4] from the root bark of the Australian *Pongamia pinnata*. The third fraction, eluted by benzene, was a new compound (see below). Finally, ethanol eluted a brownish-yellow oil which resinified within 2 months. The deterioration of colour in the pongamia oil and soap during storage seemed to be due to this fraction.

The new compound, $C_{18}H_{12}O_4$, m. p. 191°, contains one methoxyl group and has prominent flavone-carbonyl absorption at 1640 cm.$^{-1}$. With aqueous alcoholic potassium hydroxide it yielded acetophenone and an *o*-hydroxy-acid, $C_{10}H_8O_5$. When absolute alcoholic potassium hydroxide was used, benzoic acid and an *o*-hydroxy-ketone, $C_{11}H_{10}O_4$, were obtained. These reactions agreed with the behaviour of a flavone derivative without a substituent in the 2-phenyl group. The ultraviolet absorption spectrum shows bands at 271 and 305 mμ; these two bands are very similar to those of karanjin [4] and pinnatin,[5] which indicates that the new compound has the furoflavone skeleton with the furan ring attached to the condensed benzene ring; from the results of alkali fission the methoxyl should be present in the benzo-ring. Among the possibilities, analogy with karanjin and pongamol, which accompany the new furoflavone, was considered. In an angular furoflavone structure the methoxyl could be at the 5- or the 6-position. The 5-methoxy-compound (V), described by Pavanaram and Row,[5] was not available for comparison, and it has now been prepared by a new method. This compound is different from the new furoflavone which should, therefore, be the 6-methoxy-compound; this structure has been confirmed by synthesis.

Pavanaram and Row [5] synthesised the 5-methoxy-compound (V) by employing 5-acetyl-4-hydroxy-6-methoxycoumarone as the intermediate and building up the flavone structure. In the present synthesis a more convenient alternative has been adopted; the appropriate flavone is first prepared and the furan ring finally built up. Chrysin was

[1] Seshadri, *Tetrahedron*, 1959, **6**, 177.
[2] Rao and Rao, *Proc. Indian Acad. Sci.*, 1941, **14**, *A*, 123.
[3] Murti and Seshadri, *Proc. Indian Acad. Sci.*, 1944, **20**, *A*, 279.
[4] Row, *Austral. J. Sci. Res.*, 1952, **5**, *A*, 754.
[5] Pavanaram and Row, *Austral. J. Chem.*, 1956, **9**, 132.

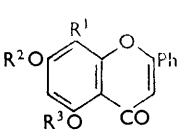
converted into the 7-*O*-allyl-5-*O*-methyl derivative (II) by partial allylation in the 7-position followed by methylation of the 5-position. It underwent smooth Claisen migration, giving 8-allyl-7-hydroxy-5-methoxyflavone (III). The furan ring was built up by the method of Aneja, Mukerjee, and Seshadri.[6] Ozonolysis of the 8-allyl-7-hydroxyflavone (III) proceeded satisfactorily in formic acid, and the aldehyde (IV) was cyclised with polyphosphoric acid in the next step, giving a good yield of 5-methoxy-4-oxo-2-phenylfuro[2,3-*h*]-1-benzopyran (V).

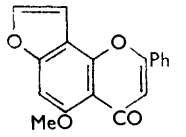
(I) $R^1 = R^3 = H$, $R^2 = C_3H_5$

(II) $R^1 = H$, $R^2 = C_3H_5$, $R^3 = Me$

(III) $R^1 = C_3H_5$, $R^2 = H$, $R^3 = Me$

(IV) $R^1 = CH_2 \cdot CHO$, $R^2 = H$, $R^3 = Me$





(V)

The synthesis of the methoxyfuroflavone (XVI) was carried out as follows. 4-Benzyloxy-2-hydroxyacetophenone was subjected to persulphate oxidation, and the dihydroxy-

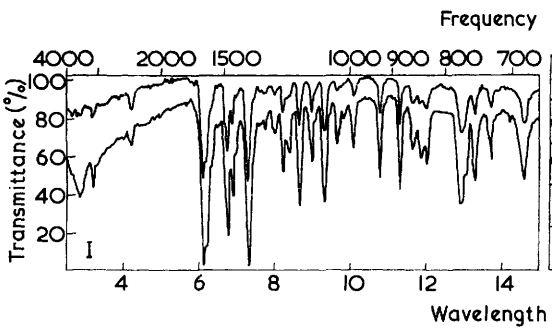


FIG. 1.

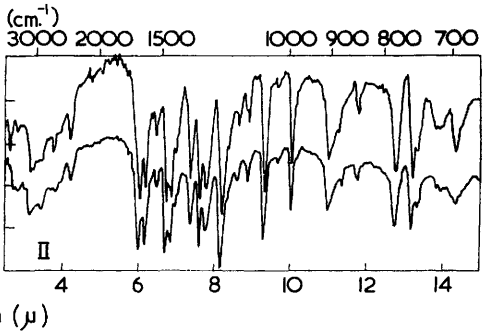


FIG. 2.

FIGS. 1 and 2. Infrared absorption spectra in potassium bromide.

FIG. 1. 6-Methoxy-4-oxo-2-phenylfuro[2,3-*h*]-1-benzopyran. Upper curve, synthetic; lower curve, natural.

FIG. 2. 7-Hydroxy-4-methoxybenzofuran-6-carboxylic acid. Upper curve, natural; lower curve, synthetic.

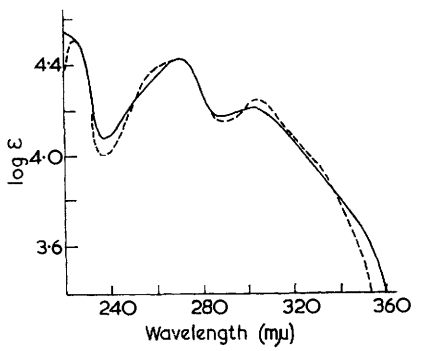


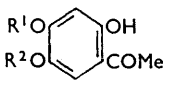
FIG. 3. Ultraviolet absorption spectra of synthetic (full curve) and natural (broken curve) 6-methoxy-4-oxo-2-phenylfuro[2,3-*h*]-1-benzopyran.

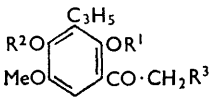
compound (VI) partially methylated and debenzylated to yield the acetophenone (VIII). Partial allylation in the 4-position and Claisen migration then yielded 3-allyl-2,4-dihydroxy-5-methoxyacetophenone (X).

[6] Aneja, Mukerjee, and Seshadri, *Tetrahedron*, 1958, **2**, 203.

The next step of flavone-ring closure was effected by using the dibenzoate (XI), and carrying out the Baker–Venkataraman transformation with pyridine–potassium hydroxide and final debenzoylation. Final furan-ring closure was carried out by the ozonolysis

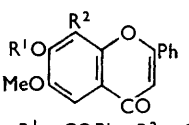
(VI) $R^1 = C_7H_7$, $R^2 = H$
(VII) $R^1 = C_7H_7$, $R^2 = Me$
(VIII) $R^1 = H$, $R^2 = Me$
(IX) $R^1 = C_3H_5$, $R^2 = Me$



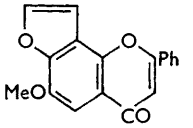


(X) $R^1 = R^2 = R^3 = H$
(XI) $R^1 = R^2 = COPh$, $R^3 = H$
(XII) $R^1 = H$, $R^2 = R^3 = COPh$

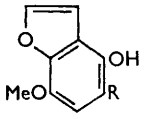
method already mentioned. The synthetic product was identical, in melting point and spectra, with the natural sample of furoflavone. As further confirmation, the synthetic compound was degraded by alcoholic and aqueous-alcoholic potassium hydroxide; the



(XIII) $R^1 = COPh$, $R^2 = C_3H_5$
(XIV) $R^1 = H$, $R^2 = C_3H_5$
(XV) $R^1 = H$, $R^2 = CH_2{\cdot}CHO$



(XVI)



(XVII) R = COMe
(XVIII) R = CO_2H

ketone and acid obtained were identical with those from the natural furoflavone. The hydroxy-ketone should, therefore, be 5-acetyl-4-hydroxy-7-methoxycoumarone (XVII) and the acid 4-hydroxy-7-methoxycoumarone-5-carboxylic acid (XVIII).

Experimental

Light petroleum, b. p. 40—60°, was used for crystallisation, and that with b. p. 60—80° for extraction.

Extraction.—The ripe seeds of *Pongamia glabra* were obtained from the President's Estate, New Delhi, in March 1959. The powdered seed-kernels (9 lb.) were extracted (Soxhlet) with light petroleum (4·5 l.) for 80 hr. The solvent was evaporated, giving oil A (1·5 l.). The residual seeds were extracted with light petroleum (4·5 l.) for 150 hr., giving oil B (75 c.c.).

The defatted seeds (1 lb.) were similarly extracted with ethanol (1·7 l.) in two stages. First extraction for 3 hr. removed a viscous brown oil. A second extraction was continued for a further 100 hr. and the extract was concentrated to 300 c.c., cooled, and left for a day, during which colourless crystals separated. They were washed with ethanol, and crystallisation from water–ethanol–ether gave cubes (300 mg.), m. p. 290° (decomp.), $\alpha_D^{14·5}$ −57·3° (in water) (Found: C, 47·8; H, 7·7%). They contained nitrogen. The m. p. and analysis corresponded to those of glabrin.[2] The alcoholic mother-liquor was evaporated and the residual brownish viscous liquid was kept in a refrigerator for 2 weeks; the crystals which separated were sucrose, m. p. and mixed m. p. 182° (decomp.) (from water–ethanol–ether), α_D^{32} 66·2°.

The seeds (400 g.) left after ethanol-extraction were extracted with boiling water (800 c.c.) for 4 hr. The extract was filtered and centrifuged. On addition of an excess of ethanol, it deposited a colourless semi-solid. The mixture was centrifuged and the supernatant liquid decanted. The semi-solid was washed with ethanol, centrifuged, and dried in a vacuum-desiccator, to give a powder (4·2 g.), m. p. 270—275° (decomp.), insoluble in organic solvents. It did not dissolve completely in water, but gave a turbid colloidal solution which foamed and did not produce a colour with alkali or ferric chloride. These and the other properties correspond to those of glabrosaponin.[3]

Oil A: Karanjin and Pongamol.—Oil A was extracted in a liquid–liquid extractor with ethanol (1 l.) for 40 hr. The extract was concentrated under reduced pressure, leaving a dark brown oil (175 c.c.) that in 10 days at 0° deposited karanjin (4 g.). The oil was decanted and the crystals were washed with light petroleum. The washings were evaporated and the residue was mixed with the decanted oil. The mixture was taken up in glacial acetic acid (600 c.c.)

and shaken with light petroleum (600 c.c.) and water (600 c.c.). The lower (aqueous acetic acid) layer was separated and shaken with light petroleum (200 c.c.) and water (100 c.c.), and left for a month, during which yellowish-brown crystals of pongamol (3 g.) were deposited. The combined light-petroleum layers were shaken with aqueous acetic acid (1 : 1; 600 c.c.) and set aside for 3 days, during which brownish-yellow crystals of pongamol (2 g.) separated at the interface. The upper (light petroleum) layer was again shaken with aqueous acetic acid (1 : 3; 10 × 50 c.c.), and when the lower aqueous acetic acid extract was worked up as described above it yielded more pongamol (1 g.). The light-petroleum layer was evaporated and left in a refrigerator for a few days; it deposited sticky brown crystals which were purified to yield pongamol (2 g.). The total yield of pongamol was 8 g.

Oil B: Karanjin, Pongapin, and the New Furoflavone.—Oil B, left in a refrigerator for 10 days, deposited yellow crystals of karanjin (1 g.), which were washed with light petroleum. The washings were evaporated and mixed with the decanted oil, dissolved in benzene, and passed down a column of alumina (3 × 44 cm.). Light petroleum (1·2 l.) eluted karanjin (1 g.). Light petroleum–benzene (1 : 1; 2 l.) eluted pongapin (15 mg.) which crystallised from methanol as colourless needles, m. p. 190—191° alone or mixed with an authentic sample. Benzene (2·5 l.) eluted a new *furoflavone* which crystallised from methanol as colourless cubes (100 mg.), m. p. 190—191°, mixed m. p. with pongapin 130° (Found: C, 73·6; H, 4·5. $C_{18}H_{12}O_4$ requires C, 74·0; H, 4·1%). It gave a bright yellow colour with concentrated sulphuric acid and also when reduced with magnesium and hydrochloric acid.

Alkaline Hydrolysis of the New Furoflavone.—(*a*) The furoflavone (300 mg.) was refluxed with alcoholic 8% potassium hydroxide (2 c.c.) for 8 hr. The solvent was removed under reduced pressure, water (15 c.c.) was added, and the reddish-brown solution was acidified with hydrochloric acid and extracted three times with ether; the ether extract was extracted successively with 5% aqueous sodium hydrogen carbonate (3 × 8 c.c.) and 5% aqueous sodium hydroxide (3 × 8 c.c.). The hydrogen carbonate extract was acidified, and the precipitate centrifuged and crystallised from methanol, yielding the fission acid as pale yellow needles (3 mg.), m. p. 207° (decomp.), giving a greenish-blue ferric reaction (see next paragraph). On addition of water, the mother-liquor deposited pale yellow crystals which, after vacuum-sublimation, had m. p. 118°, undepressed by benzoic acid. The sodium hydroxide extract was acidified and the precipitate centrifuged and crystallised from aqueous methanol, yielding pale yellow needles (7 mg.) of the fission ketone, m. p. 107°, giving greenish-blue ferric reaction. In m. p. (mixed m. p. undepressed) and in circular paper chromatography it agreed with the fission ketone obtained from the synthetic methoxyfuroflavone (XVI). By the pyridine–iodine oxidation, the fission ketone gave the fission acid, m. p. 207° (decomp.).

(*b*) The furoflavone (30 mg.) was refluxed with aqueous alcoholic potassium hydroxide (H_2O 1 c.c.; EtOH 1 c.c.; KOH 0·2 g.) for 4 hr. in an inert atmosphere. As much alcohol as possible was distilled off and the remaining solution was steam-distilled; the distillate gave acetophenone 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 238°. The remaining solution was acidified and extracted three times with ether, and the ethereal solution extracted with 5% aqueous sodium hydrogen carbonate (3 × 10 c.c.). The extract was acidified and the precipitate crystallised from methanol, yielding pale yellow needles (8 mg.) of the fission acid (XVIII), m. p. 207° (decomp.) and giving a greenish-blue ferric reaction (Found: C, 57·5; H, 4·5. $C_{10}H_8O_5$ requires C, 57·7; H, 3·9%).

5-*Methoxy*-4-*oxo*-2-*phenylfuro*[2,3-h]-1-*benzopyran.*—(*a*) 7-*Allyloxy*-5-*hydroxyflavone* (I). Allylation of chrysin (5·0 g.) with allyl bromide (1 mol.), acetone, and potassium carbonate gave the *product* which crystallised from ethanol as colourless needles (4·8 g.), m. p. 145—146°, giving a violet-red ferric reaction (Found: C, 73·5; H, 5·0. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8%).

(*b*) 7-*Allyloxy*-5-*methoxyflavone* (II). Methylation of the allyl ether (I) (3 g.) with an excess of dimethyl sulphate, acetone, and potassium carbonate for 30 hr. gave the *product.* Crystallisation from ethanol gave colourless needles (2·7 g.), m. p. 129—130° (Found: C, 73·5; H, 5·4. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

(*c*) 8-*Allyl*-7-*hydroxy*-5-*methoxyflavone* (III). The flavone (II) (2 g.) was heated for 2 hr. at 190°/0·5 mm. The *product* formed colourless needles (1·7 g.), m. p. 278—279° (from ethanol) (Found: C, 73·7; H, 5·2. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). It gave no ferric reaction.

(*d*) 5-*Methoxy*-4-*oxo*-2-*phenylfuro*[2,3-h]-1-*benzopyran* (V). Ozonised oxygen (3%; 150 c.c./min.) was passed for ½ hr. through a solution of the 8-allylflavone (III) (400 mg.) in formic acid (50 c.c.) at 3°. The solution was allowed to warm to room temperature and then shaken

with hydrogen in the presence of 5% palladised charcoal (400 mg.) until the rapid absorption of hydrogen ceased. The filtered solution was evaporated under reduced pressure, and the residual dark yellow oil heated at 100° with polyphosphoric acid (10 c.c.) for 20 min., cooled, and poured on ice. The solid that separated was extracted with chloroform, and the extract was washed with 5% aqueous sodium hydroxide and then with water, dried (Na_2SO_4), and passed down a column of alumina. Elution of the column with chloroform yielded the *furoflavone* (210 mg.); it formed pale yellow needles, m. p. 182—183° (from chloroform–light petroleum), depressed to 120° by admixture with the new furoflavone (Found: C, 73·4; H, 4·6. $C_{18}H_{12}O_4$ requires C, 73·9; H, 4·1%). $\lambda_{max.}$ (in EtOH) 271, 320 mμ. It gave a green colour on warming with concentrated sulphuric acid.

6-*Methoxy*-4-*oxo*-2-*phenylfuro*[2,3-h]-1-*benzopyran*.—(*a*) 4-*Benzyloxy*-2,5-*dihydroxyacetophenone* (VI). A stirred solution of 4-benzyloxy-2-hydroxyacetophenone (5 g.) in a mixture of pyridine (100 c.c.) and aqueous sodium hydroxide (6 g. in 100 c.c.) was treated with aqueous potassium persulphate (10·5 g. in 250 c.c.) for 3 hr., set aside for 24 hr., and acidified; the unchanged substituted acetophenone (2·8 g.) was filtered off. The filtrate was extracted with ether and then treated with sodium sulphite (10 g.) and concentrated hydrochloric acid (125 c.c.), and kept in a boiling-water bath for 30 min.; golden-yellow needles separated. The mixture was cooled and filtered and the residue washed with water and dried (1·3 g.). The filtrate, on ether-extraction, provided some more of the *compound* (100 mg.). Crystallisation from aqueous ethanol gave pale yellow long needles, m. p. 160°, giving a deep-green ferric colour (Found: C, 69·8; H, 5·7. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4%).

(*b*) 4-*Benzyloxy*-2-*hydroxy*-5-*methoxyacetophenone* (VII). Methylation of the dihydroxyacetophenone (VI) (2·2 g.) with dimethyl sulphate (1 mole), acetone, and potassium carbonate yielded a *product* which crystallised from ethanol (charcoal) as pale yellow needles (2 g.), m. p. 130°, giving a green ferric reaction (Found: C, 70·3; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

(*c*) 2,4-*Dihydroxy*-5-*methoxyacetophenone* (VIII). 5% Palladised charcoal (0·45 g.) and dry ethyl acetate (50 c.c.) were saturated with hydrogen gas. The benzyloxyacetophenone (VII) (0·45 g.) in ethyl acetate (50 c.c.) was then added, and absorption of hydrogen allowed until 43 c.c. had been rapidly absorbed (35°). The solution was filtered and evaporated. Crystallisation of the *product* from hot water gave colourless plates (300 mg.), m. p. 172—173°, giving a green ferric reaction (Found: C, 59·4; H, 6·0. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5%).

(*d*) 4-*Allyloxy*-2-*hydroxy*-5-*methoxyacetophenone* (IX). Allylation of compound (VIII) (4·8 g.) by boiling for 10 hr. with allyl bromide (1 mol), acetone, and potassium carbonate gave an oily *product* which crystallised from light petroleum as pale yellow needles (3·5 g.), m. p. 50°, giving a green ferric reaction (Found: C, 65·7; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%). With pyridine–benzoyl chloride it gave a *monobenzoate*, m. p. 106° (Found: C, 70·5; H, 6·0. $C_{19}H_{18}O_5$ requires C, 70·0; H, 5·6%).

(*e*) 3-*Allyl*-2,4-*dihydroxy*-5-*methoxyacetophenone* (X). The allyloxyacetophenone (IX) (2 g.) was heated for 1·5 hr. under reduced pressure (20 mm.) in an oil bath at 180°. The *product* was taken up in ether, extracted with 5% aqueous sodium carbonate, and reprecipitated with acid. Crystallisation from benzene–light petroleum (1 : 3) gave pale yellow needles (1·7 g.), m. p. 118°, giving a green ferric reaction (Found: C, 64·8; H, 6·8. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

(*f*) 3-*Allyl*-2,4-*dibenzoyloxy*-5-*methoxyacetophenone* (XI). Dihydroxyacetophenone (X) (0·65 g.) in dry pyridine (3·5 c.c.) was refluxed with benzoyl chloride (3·7 c.c.) for ½ hr., cooled, and poured into ice-cold dilute hydrochloric acid. The oily product was extracted with ether and washed with 5% aqueous sodium carbonate and water, and the ether evaporated. The *benzoate* crystallised from aqueous ethanol as plates (0·85 g.), m. p. 172—173° (Found: C, 72·5; H, 5·3. $C_{26}H_{22}O_6$ requires C, 72·5; H, 5·1%).

(*g*) 3-*Allyl*-α-*benzoyl*-4-*benzoyloxy*-2-*hydroxy*-5-*methoxyacetophenone* (XII). A mixture of the dibenzoate (XI) (0·6 g.), powdered potassium hydroxide (0·5 g.), and dry pyridine (2·5 c.c.) was heated at 40° for 2 hr., then acidified with 20% acetic acid, and the yellow precipitate was collected, washed with water, and dried. The *product* formed deep yellow needles (0·45 g.), m. p. 146° (from benzene–light petroleum), giving a greenish-yellow ferric reaction (Found: C, 72·0; H, 5·2. $C_{26}H_{22}O_6$ requires C, 72·5; H, 5·1%).

(*h*) 8-*Allyl*-7-*benzoyloxy*-6-*methoxyflavone* (XIII). The above diketone (XII) (600 mg.)

was heated with acetic acid (30 c.c.) and fused sodium acetate (2 g.) at 100° for 2 hr. The mixture was diluted with water, and the precipitate filtered off, washed with water, and dried. The *product* formed pale yellow needles (500 mg.), m. p. 201—202° (from benzene–light petroleum) (Found: C, 75·3; H, 5·3. $C_{26}H_{20}O_5$ requires C, 75·7; H, 4·9%).

(*i*) 8-*Allyl*-7-*hydroxy*-6-*methoxyflavone* (XIV). The above benzoyloxyflavone (XIII) (420 mg.) was refluxed with ethanolic 15% potassium hydroxide (21 c.c.) for ½ hr. As much alcohol as possible was distilled off, the solution was acidified with 10% hydrochloric acid, and the precipitate was filtered off, washed with aqueous sodium hydroden carbonate and water, and dried. The *product* formed colourless needles (300 mg.), m. p. 234—235° (from ethanol) (Found: C, 73·4; H, 5·2. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

(*j*) 6-*Methoxy*-4-*oxo*-2-*phenylfuro*[2,3-*h*]-1-*benzopyran* (XVI). Ozonised oxygen (3%; 150 c.c./min.) was passed through a solution of the allylflavone (XIV) (400 mg.) in formic acid (100 c.c.) at 5° for 30 min. The solution was worked up as described above; the oily aldehyde was heated with polyphosphoric acid (10 c.c.) at 100° for 15 min., the mixture poured on ice, and the *product* filtered off and washed with aqueous sodium hydroxide and water. Crystallisation from methanol gave pale yellow needles (230 mg.), m. p. 190° alone or mixed with the natural furoflavone and giving a yellow solution with concentrated sulphuric acid (Found: C, 73·7; H, 4·5. $C_{18}H_{12}O_4$ requires C, 73·9; H, 4·1%).

Alkaline hydrolysis of the synthetic 6-methoxyfuroflavone (XVI) with alcoholic and aqueous-alcoholic potassium hydroxide gave the same fission ketone, m. p. 107°, and fission acid, m. p. 206° (decomp.), as those obtained from the natural furoflavone.

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