458. *Furano-compounds. Part VIII. The Synthesis of* iso*Visnagin and a Partial Synthesis of Visnagin.*

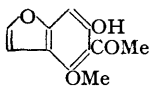
By J. R. Clarke, George Glaser, and Alexander Robertson.

The partial synthesis of visnagin from natural visnagone (I) and its condensation with piperonal to form a styryl derivative afford decisive evidence that visnagin is a furanochromone type (III). In the course of unsuccessful attempts to prepare visnagone the isomeric ketone, 6-hydroxy-4-methoxy-7-acetylcoumarone, has been obtained from which the furanochromone *iso*visnagin (VI; R = Me) has been synthesised. The transformation of visnagin into *iso*visnagin is described.

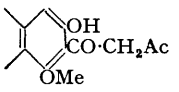
From a study of the hydrolytic fission of visnagin, occurring in the seeds of *Ammi visnaga*, and the subsequent degradation of the ketone visnagone thus formed, Späth and his collaborators (*Ber.*, 1941, **74**, 1492) concluded that the parent compound was the linear furanochromone (III) but the evidence presented, though it clearly shows that in visnagone (I) the acetyl residue

is in the 5-position, does not exclude the possibility of visnagin being the linear isomeric 4-methylfuranocoumarin. Accordingly, the experiments now described had as their objective a rational synthesis of visnagin.

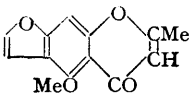
In considering a general synthetical approach to compounds of the type (III) it appeared to us more feasible in the first instance to attempt to build up the γ-pyrone system on a suitable coumarone residue rather than to form the furanochromone from an already existing hydroxychromone, more especially since this kind of procedure had already been successfully employed in the synthesis of furanocoumarins (Part IV, *J.*, 1939, 930, and unpublished work). Further, the final two stages of this process had already been used in the formation of furanochromones prepared to demonstrate the orientation of *O*-monomethylusnetol (Curd and Robertson, *J.*, 1933, 1173; the first synthesis of a furanochromone) and of euparin and tetrahydroeuparin (Kamthong and Robertson, *J.*, 1939, 933). As a preliminary step in the present investigation therefore, it has been shown that 5-methoxy-2-methylfurano(4′ : 5′ : 6 : 7)chromone (III), identical in every way with visnagin, can be conveniently synthesised by the cyclisation of the *diketone* (II) resulting from the interaction of visnagone (I) from natural sources with ethyl acetate in the presence of sodium. Further, the condensation of (III), natural or synthetical, with piperonal to give a 2-*styrylchromone* is in agreement with the 2-methylchromone structure assigned to visnagin.



(I.)

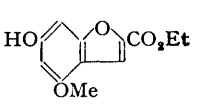


(II.)

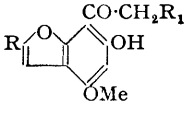


(III.)

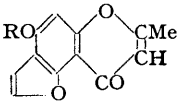
The stages required to complete the synthesis of visnagin, *viz.*, the preparation of visnagone (I), have not yet been achieved, and the remaining experiments described were occasioned primarily on this account but led ultimately to a successful synthesis of one of the two possible angular isomerides of visnagin which we have termed iso*visnagin* (VI; R = Me) and which we suspect may be a minor constituent of the seeds.



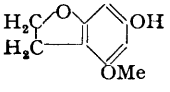
(IV.)



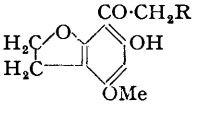
(V.)



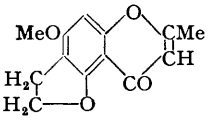
(VI.)



(VII.)



(VIII.)

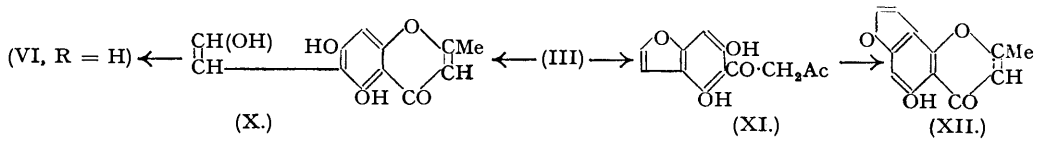


(IX.)

Application of the Hoesch reaction with acetonitrile, or of the Friedel–Crafts reaction with acetyl chloride, to the coumarone (IV), where the carbethoxy-group serves to protect the reactive 2-position (compare Part II, *J.*, 1939, 921; Part IV, *loc. cit.*), gave only one *C*-acetyl derivative of (IV). This compound must have the structure (V; R = CO_2Et, R_1 = H), because on hydrolysis and subsequent decarboxylation of the resulting *keto-acid* (V; R = CO_2H, R_1 = H) it gave rise to a *ketone* isomeric and not identical with visnagone. Since visnagone has been shown to have the *C*-acetyl group in the 5-position the synthetical ketone, which we have named *iso*visnagone and which gives a ferric reaction in alcohol indicating the presence of a hydroxyl group in the *o*-position to a carbonyl group, must be the 7-*acetyl* derivative (V; R = R_1 = H). It is noteworthy that the behaviour of (IV) with the Hoesch and the Friedel–Crafts reaction is analogous to that with the Gattermann reaction (Part IV, *loc. cit.*). From the ketone (V, R = R_1 = H), *iso*visnagin (VI; R = Me) was synthesised by way of the *diketone* (V; R = H, R_1 = Ac) according to the procedure employed for visnagin. Similarly, the application of the Friedel–Crafts reaction to 6-hydroxy-4-methoxycoumaran (VII) gave only the 7-*acetylcoumaran* (VIII; R = H), identical with a specimen prepared by the hydrogenation of *iso*visnagone (V, R = R_1 = H), and on condensation with ethyl acetate this ketone (VIII; R = H) gave rise to the *diketone* (VIII; R = Ac) the cyclisation of which furnished *dihydro*iso*visnagin* (IX).

In a projected synthesis of *O*-methylvisnagone, 2 : 6-*dimethoxy*-4-*allyloxyacetophenone* was transformed into 4-*hydroxy*-2 : 6-*dimethoxy*-3-*allylacetophenone* but so far we have been unable to determine the conditions whereby the *acetate* of the latter could be degraded to the required *o*-acetoxyphenylacetaldehyde which on deacetylation and subsequent cyclisation would be expected to give *O*-methylvisnagone, a specimen of which is readily formed by methylation of visnagone by the methyl iodide–potassium carbonate method.

The syntheses of *methyl* 2 : 6-*dihydroxy*-4-*methoxy*-3-*formyl*- and -3-*acetyl*-*benzoate* were effected in view of their possible conversion into visnagone.



In an attempt to prepare the parent hydroxyfuranochromone from visnagin (III) by demethylation it was found that the latter on being gently refluxed with concentrated hydriodic acid gave rise to a somewhat resinous product from which a well-crystallised phenolic compound was isolated. This substance, which was soluble in alkali and had only a very faint ferric reaction, gave *iso*visnagin on methylation and is therefore the *furanochromone* (VI; R = H). The identity of *iso*visnagin obtained by this route with authentic material was confirmed by the preparation of the characteristic *styryl* derivative from piperonal, and by the fact that on hydrolytic fission with boiling 20% aqueous potassium hydroxide it gave rise to *iso*visnagone identical with a synthetical specimen. The formation of nor*iso*visnagin (VI; R = H) in this manner was entirely unexpected because, although isomerides of norvisnagin could arise during the demethylation process by either of the following routes, *viz.* (*a*) opening of the furan ring with the formation of (X) followed by re-cyclisation involving the 5-hydroxyl group to give the angular compound nor*iso*visnagin (VI; R = H) or (*b*) opening of the γ-pyrone ring to yield the intermediate diketone (XI) and subsequent cyclisation to form the alternative angular product (XII), yet only the latter change (*b*) was envisaged by analogy with the behaviour of wogonin and its ethers on demethylation (Wesseley and co-workers, *Monatsh.*, 1930, **56**, 97; 1932, **60**, 26; Hattori, *Ber.*, 1939, **72**, 1914; Saski and Seshadri, *Proc. Indian Acad. Science*, 1946, **24**, No. 2, Section A, 243). Clearly, however, the process (*a*) prevails, and in spite of a careful search a second crystalline product of the hydriodic acid reaction could not be isolated from the residues left on the purification of (VI; R = H). Thus at present we have no evidence of the isomeric change by way of route (*b*) taking place to any appreciable extent, if at all.

Experimental.

Visnagin (III).—When the initial reaction between visnagone (Späth *et al.*, *loc. cit.*) (1 g.), ethyl acetate (10 ml.), and sodium (1 g.) had subsided, the mixture was heated on the steam-bath for 4 hours with the addition of more acetate (2 ml.) and sodium (1 g., in small portions) after 1 hour. Next day a small amount of unchanged sodium in the reaction mixture was destroyed by addition of a little methanol, and after having been diluted with water (200 ml.) the solution was acidified with acetic acid. Thus precipitated as a brown oil, the product gradually solidified and then on crystallisation from aqueous alcohol gave the 6-*hydroxy*-4-*methoxy*-5-*acetoacetylcoumarone* (II) in colourless platelets (0·35 g.), m. p. 80—81°, which on being dried in a vacuum over phosphoric oxide had m. p. 95—96° [Found, in dried material: C, 62·8; H, 4·7; OMe, 12·1. $C_{12}H_9O_4(OMe)$ requires C, 62·9; H, 4·8; OMe, 12·5%]. This substance, which gives a red ferric reaction in alcohol, is moderately soluble in methanol, warm benzene, or chloroform and readily soluble in acetone or acetic acid.

When a solution of the foregoing diketone (0·25 g.) in alcohol (5 ml.) containing 3 drops of concentrated hydrochloric acid was boiled for 1 minute and cooled, the mixture deposited visnagin, which formed pale yellow prisms (0·2 g.), m. p. 140° from methyl alcohol, undepressed on admixture with an authentic specimen [Found: C, 68·0; H, 4·5; OMe, 13·2. Calc. for $C_{12}H_7O_3(OMe)$: C, 67·9; H, 4·4; OMe, 13·5%]. On being warmed, the yellow solution of the substance in sulphuric acid became orange-red, and then dark red changing to violet on dilution with water. Sodium methoxide (from 0·3 g. of sodium) in methanol (15 ml.) was added to a solution of visnagin (1 g.) and piperonal (1 g.) in methanol (20 ml.), and the mixture heated on the steam-bath for 10 minutes; 48 hours later the solid was collected, washed with a little methanol, and crystallised from dilute acetic acid, giving the *styryl* derivative (1·1 g.) in pale yellow needles, m. p. 220°, sparingly soluble in alcohol, ethyl acetate, or benzene (Found: C, 69·4; H, 4·1. $C_{21}H_{14}O_6$ requires C, 69·6; H, 3·9%).

Ethyl 6-*Hydroxy*-4-*methoxy*-7-*acetylcoumarone*-2-*carboxylate* (V; R = CO_2Et, R_1 = H).—(A) A cooled solution of ethyl 6-hydroxy-4-methoxycoumarone-2-carboxylate (Part IV, *loc. cit.*) (2 g.) in ether (400 ml.), containing acetonitrile (7 ml.) and zinc chloride (3 g.), was slowly saturated with hydrogen chloride and a pale brown oil slowly separated. After the addition of an excess of ether 4 days later, the solvent was decanted and the residual dark red liquid was washed with fresh ether (3 × 50 ml.)

and then dissolved in water (150 ml.). When this solution was almost neutralised (faintly acid to Congo-red paper) with aqueous sodium carbonate, filtered from traces of dark solid, and then heated on the steam-bath for ½ hour, the *ethyl 6-hydroxy-4-methoxy-7-acetylcoumarone-2-carboxylate* gradually separated as a buff-coloured solid (0·5 g.) and on recrystallisation from methanol formed clusters of elongated colourless needles, m. p. 162°, readily soluble in acetone, benzene, or ethyl acetate, and having a violet ferric reaction in alcohol (Found : C, 60·6; H, 5·2. $C_{14}H_{14}O_6$ requires C, 60·4; H, 5·1%). On being warmed, the yellow solution of the ketone in sulphuric acid became violet and then red-brown. The 2 : 4-*dinitrophenylhydrazone* formed red needles, m. p. 295°, from much ethyl acetate (Found : N, 12·0. $C_{20}H_{18}O_9N_4$ requires N, 12·2%).

(B) Powdered aluminium chloride (3 g.) was gradually added during 15 minutes to a suspension of ethyl 6-hydroxy-4-methoxycoumarone-2-carboxylate (2 g.) in nitrobenzene (70 ml.) (agitate) kept at below 5°, and 2 days later the dark red mixture was poured on ice (50 g.). An ethereal solution of the product and nitrobenzene was washed with aqueous sodium hydrogen carbonate to remove hydrochloric acid and then with water, dried, and evaporated on the steam-bath. When the residual nitrobenzene liquor was mixed with an excess of light petroleum (b. p. 60—80°), filtered, and kept at 0° for 16 hours, the ketone (1·6 g.) gradually separated, and on recrystallisation from methanol had m. p. 162°, identical in every way with material prepared by method (A). The 2 : 4-dinitrophenylhydrazone had m. p. and mixed m. p. 295°.

When the light petroleum–nitrobenzene liquors were subjected to distillation in a current of steam a further quantity of ketone (0·15 g.) was isolated from the residual aqueous solution.

An examination of the residues left from the purification of the keto-ester (V; R = CO_2Et, R_1 = H), formed by either method (A) or (B), failed to reveal the presence of the desired isomeride, ethyl 6-hydroxy-4-methoxy-5-acetylcoumarone-2-carboxylate, required for the preparation of visnagone.

6-Hydroxy-4-methoxy-7-acetylcoumarone (iso*Visnagone*) (V, R = R_1 = H).—A solution of the foregoing ketonic ester (1 g.) in aqueous-alcoholic potassium hydroxide (from 1·5 g. of potassium hydroxide, 18 ml. of alcohol, and 12 ml. of water) was refluxed for ¾ hour, cooled, diluted with water (50 ml.), and acidified with dilute hydrochloric acid. Crystallisation of the resulting gelatinous precipitate from warm alcohol gave *6-hydroxy-4-methoxy-7-acetylcoumarone-2-carboxylic acid* (V; R = CO_2H, R_1 = H) in stellate clusters of colourless needles (0·8 g.), m. p. 307—309° (decomp.), moderately soluble in warm alcohol, acetone, or ethyl acetate, and having a purple-red ferric reaction in alcohol [Found : C, 57·8; H, 4·2; OMe, 12·8. $C_{11}H_7O_5(OMe)$ requires C, 57·6; H, 4·0; OMe, 12·4%]. The sulphuric acid reaction of this acid was identical with that of the ethyl ester.

Decarboxylation of the acid (2 g.) was effected with gently boiling quinoline (60 ml.) (oil-bath), containing copper bronze (1 g.), during ½ hour, and a filtered solution of the cooled reaction mixture in much ether was washed with hydrochloric acid and then with aqueous sodium hydrogen carbonate, and then extracted with 8% aqueous sodium hydroxide (40 ml. × 10). Acidification of the combined alkaline extracts gave *6-hydroxy-4-methoxy-7-acetylcoumarone* (V, R = R_1 = H) (1·4 g.), which formed pale yellow rectangular leaflets, m. p. 134—136°, from methanol (charcoal), readily soluble in benzene, acetone, or ethyl acetate and almost insoluble in light petroleum (Found : C, 64·3; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·9%). This substance gave an emerald-green ferric reaction in alcohol and a yellow solution in sulphuric acid which on being heated became cherry-red, then violet, and finally brown. The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in orange-red needles, m. p. 282° (Found : N, 14·5. $C_{17}H_{14}O_7N_4$ requires N, 14·5%).

Decarboxylation of the acid by means of hot glycerol gave a poor yield of the ketone.

7-Methoxy-2-methylfurano(2′ : 3′ : 5 : 6)chromone (iso*Visnagin*) (VI, R = Me).—To a solution of the foregoing ketone (0·5 g.) in ethyl acetate (15 ml.) sodium (0·7 g., in small pieces) was gradually added and after the initial reaction had subsided the mixture was heated on the steam-bath for 5 hours; after 3 hours more sodium (0·3 g.) and ester (3 ml.) were added. The cooled reaction mixture was treated with a little methanol to destroy traces of unchanged sodium, diluted with ice-water, and acidified with acetic acid. Next day the *6-hydroxy-4-methoxy-7-acetoacetylchromone* (V; R = H, R_1 = Ac) (0·4 g.) was collected and, after having been sublimed in high vacuum, was crystallised from light petroleum (b. p. 60—80°), forming yellow needles, m. p. 138—139°, soluble in alcohol or benzene and having a green ferric reaction in alcohol (Found : C, 62·9; H, 4·7. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·9%).

A solution of this diketone (0·2 g.) in acetic acid (8 ml.) containing 3 drops of concentrated hydrochloric acid was boiled for 1 minute, cooled, and the *furanochromone* (VI, R = Me) precipitated by the addition of water. Crystallised from alcohol, this compound formed colourless needles, m. p. 247°, and gave a colourless solution in sulphuric acid exhibiting a faint purple fluorescence, unchanged on being warmed (Found : C, 67·6; H, 4·6. $C_{13}H_{10}O_4$ requires C, 67·8; H, 4·4%).

6-Hydroxy-4-methoxycoumaran (VII).—The synthesis of this compound, obtained as a low-melting solid, and its characterisation by formation of a *p*-nitrobenzoate, was described in Part IV (*loc. cit.*), the final stage of which was the simultaneous hydrogenation and debenzylation of 6-benzyloxy-4-methoxycoumarone in acetic acid. It has now been found that when this reaction is carried out in methanol with a palladium–charcoal catalyst the product is free from resinous material and can be crystallised from carbon tetrachloride–light petroleum (b. p. 60—80°), forming colourless irregular prisms, m. p. 77° (Found : C, 65·5; H, 6·0. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·0%), which gave the *p*-nitrobenzoate, m. p. 159—160°.

6-Hydroxy-4-methoxy-7-acetylcoumaran (VIII, R = H).—(A) Hydrogenation of 6-hydroxy-4-methoxy-7-acetylcoumarone (0·5 g.) in acetic acid (40 ml.) with a palladium–charcoal catalyst (from 0·05 g. of palladium chloride and 0·5 g. of charcoal) was complete in about ½ hour and on isolation the resulting *coumaran* (VIII, R = H) formed pale yellow needles, m. p. 128°, from methanol, readily soluble in benzene or ethyl acetate and moderately soluble in light petroleum, and having an emerald-green ferric reaction in alcohol (Found : C, 63·2; H, 6·1. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 248°, from ethyl acetate (Found : N, 14·2. $C_{17}H_{16}O_7N_4$ requires N, 14·4%).

(B) Acetyl chloride (0·8 ml.) was added to a well-stirred solution of 6-hydroxy-4-methoxycoumaran (1 g.) in nitrobenzene (50 ml.), maintained at 0°, followed by aluminium chloride (2·4 g., in two portions), the resulting yellow solution (cooled) was agitated for 1 hour, and 2 days later the mixture was treated with ice and extracted with ether. The combined ethereal extracts were washed with aqueous sodium hydrogen carbonate, dried, and evaporated, and the residual liquor mixed with light petroleum (b. p. 60—80°) (250 ml.). Extraction of the latter mixture with 10% aqueous sodium hydroxide (50 ml. × 10) and acidification of the combined extracts with hydrochloric acid gave a ketonic product (0·95 g.), having a dark purple ferric reaction, which on crystallisation from alcohol furnished 6-hydroxy-4-methoxy-7-acetylcoumaran (0·6 g.) in pale yellow needles, m. p. 128°, identical in every way with a specimen prepared by method (A). The 2 : 4-dinitrophenylhydrazone had m. p. and mixed m. p. 248°.

Dihydroisovisnagin (IX).—Interaction of the foregoing ketone (0·45 g.) with ethyl acetate (10 ml.) and sodium (0·6 g.) on the steam-bath for 4½ hours with the addition of more acetate (2 ml.) and sodium (0·2 g.) after 3 hours gave rise to 6-*hydroxy*-4-*methoxy*-7-*acetoacetylcoumaran* (VIII, R = Ac) (0·3 g.), forming clusters of yellow needles, m. p. 135—136°, from light petroleum (b. p. 60—80°) (Found : C, 62·3; H, 5·8. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%). This substance is readily soluble in alcohol, acetone, or benzene and has a red-purple ferric reaction in alcohol. A solution of the compound (0·17 g.) in acetic acid (6 ml.) containing 4 drops of concentrated hydrochloric acid was boiled for 2 minutes, cooled, diluted with water, filtered from a trace of brown solid, saturated with ammonium sulphate, and extracted with ether. Evaporation of the washed and dried extracts left the *chromone* (IX) (0·09 g.), which separated from ligroin in tiny colourless prisms, m. p. 193—194° (decomp.) after sintering at 187° (Found : C, 67·0; H, 5·4. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). On being warmed the almost colourless solution of this compound in concentrated sulphuric acid became violet.

Dihydrovisnagone.—Hydrogenation of visnagone (isolated from chellol glucoside; unpublished work) dissolved in acetic acid with a palladium–charcoal catalyst gave the *dihydro*-derivative which separated from methyl alcohol in pale lemon-yellow needles, m. p. 101·5°, readily soluble in ethyl acetate, benzene, or acetone and having a blood-red ferric reaction in alcohol (Found : C, 63·5; H, 5·9%). The 2 : 4-*dinitrophenylhydrazone* formed scarlet needles, m. p. 225°, from ethyl acetate (Found : N, 14·6. $C_{17}H_{16}O_7N_4$ requires N, 14·4%).

4-*Hydroxy*-2 : 6-*dimethoxy*-3-*allylacetophenone.*—A mixture of 4-hydroxy-2 : 6-dimethoxyacetophenone (Curd and Robertson, *J.*, 1931, 1241) (2·5 g.), allyl bromide (2·5 g.), potassium carbonate (6 g.), and acetone (80 ml.) was refluxed for 3½ hours, filtered (wash salts with acetone), and evaporated, leaving the *allyl ether* (2·5 g.) as a crystalline mass. Recrystallised from light petroleum (b. p. 40—60°), the compound formed small prisms, m. p. 56—57°, readily soluble in alcohol, benzene, or ethyl acetate (Found : C, 65·8; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%). A mixture of this ether (3 g.) and dimethylaniline (20 ml.) was refluxed for 5 hours in an atmosphere of nitrogen, and a solution of the cooled liquor in ether (150 ml.) was washed with dilute hydrochloric acid to remove the base and then extracted with 15% aqueous sodium hydroxide (50 ml. × 6) to remove the resulting *allylphenol*. After acidification of the combined alkaline extracts and subsequent saturation with ammonium sulphate this phenol (2·2 g.) was isolated with ether and crystallised from light petroleum (b. p. 40—60°), forming slender colourless needles, m. p. 71—72°, readily soluble in alcohol or benzene (Found : C, 66·2; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%). In an attempt to effect the rearrangement in the absence of a solvent (compare Baker and Lothian, *J.*, 1935, 628) the product was an intractable tar.

Acetylation of the allylphenol by the acetic anhydride–pyridine method gave the *acetate*, forming tiny, colourless needles, m. p. 33—34°, from light petroleum (b. p. 40—60°) (Found : C, 64·7; H, 6·5. $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5%).

Methyl 2 : 6-*Dihydroxy*-4-*methoxy*-3-*formylbenzoate.*—When a mixture of methyl 2 : 6-dihydroxy-4-methoxybenzoate (Herzig and Wenzel, *Monatsh.*, 1901, **22**, 215) (2 g.), hydrogen cyanide (2 ml.), zinc cyanide (2 g.), and ether (150 ml.) was saturated with hydrogen chloride the aldimine began to separate in the course of 1 hour. After the addition of excess ether next day, the product was collected, washed with ether to remove excess of hydrogen chloride, and dissolved in water (150 ml.). Aqueous sodium hydrogen carbonate was added until the solution was only faintly acid to Congo-red, and the mixture heated on the steam-bath for 15 minutes. Next day the resulting *aldehyde* (2 g.) was collected, and crystallised from alcohol (charcoal), forming elongated silky, colourless needles, m. p. 177·5°, having a blood-red ferric reaction in alcohol (Found : C, 52·8; H, 4·4. $C_{10}H_{10}O_6$ requires C, 53·1; H, 4·4%). The *semicarbazone* separated from acetic acid in pale yellow needles, m. p. 230° (Found : N, 14·7. $C_{11}H_{13}O_6N_3$ requires N, 14·8%).

Condensation of the same ester (5 g.) with acetonitrile (12 ml.) in ether (150 ml.) by means of zinc chloride (5 g.) and excess of hydrogen chloride according to Hoesch's method gave rise to a semi-solid ketimine which on hydrolysis with water (200 ml.) on the steam-bath for 20 minutes furnished *methyl* 2 : 6-*dihydroxy*-4-*methoxy*-3-*acetylbenzoate* (1·9 g.), forming colourless needles, m. p. 144°, from alcohol (Found : C, 55·2; H, 5·1. $C_{11}H_{12}O_6$ requires C, 55·0; H, 5·0%). This ketone gave a reddish-brown ferric reaction in alcohol and formed a 2 : 4-*dinitrophenylhydrazone* which separated from ethyl acetate in orange needles, m. p. 212—213° (Found : N, 13·5. $C_{17}H_{16}O_9N_4$ requires N, 13·3%). Unchanged ester (3 g.) was recovered from the ethereal liquors decanted from the ketimine. The use of a smaller proportion of acetonitrile in the reaction mixture led to poorer yields of ketone.

Demethylation of Visnagin.—Acetic anhydride (20 ml.) was carefully added to concentrated hydriodic acid (14 ml.) containing visnagin (2 g.), and the mixture gently refluxed (oil-bath) for 30 minutes. The cooled dark red solution was diluted with water (200 ml.) containing a little sodium hydrogen sulphite to remove traces of free iodine, and the pale yellow flocculent precipitate was collected and washed with water and then with a little methanol. Crystallised from dilute acetic acid, this product (0·4 g.) gave 7-*hydroxy*-2-*methylfurano*(2′ : 3′ : 5 : 6)*chromone* (VI, R = H) as a *hydrate* in almost colourless prisms, m. p. 318° (decomp.), which have a very faint green ferric reaction in alcohol and are sparingly soluble in methanol, alcohol, or acetone (Found, in material dried in a vacuum at room temperature : C, 61·1; H, 4·3. $C_{12}H_8O_4,H_2O$ requires C, 61·5; H, 4·3%. Found, in material dried at 120° for 2 hours : C, 66·6; H, 3·8. $C_{12}H_8O_4$ requires C, 66·7; H, 3·7%).

A mixture of this compound (0·25 g.), potassium carbonate (1 g.), acetone (30 ml.), and methyl iodide (2 ml.) was refluxed for 16 hours, filtered, evaporated, and the pale brown residual solid crystallised from dilute methanol, giving *iso*visnagin in almost colourless slender prisms (0·2 g.), m. p. 247°, identical in every way with a specimen obtained by direct synthesis (Found : C, 68·1 ; H, 4·6%). Interaction of this material (0·1 g.) with piperonal (0·1 g.) in 6% methanolic sodium methoxide on the steam-bath during 1½ hours gave rise to the *styryl* derivative of *iso*visnagin, which formed slender yellow needles, m. p. 244°, from dilute acetic acid and was identical with a specimen, m. p. 244°, prepared in the same manner from synthetical *iso*visnagin (Found : C, 69·3 ; H, 3·7. $C_{21}H_{14}O_6$ requires C, 69·5 ; H, 3·9%). When *iso*visnagin (0·1 g.), prepared from visnagin by the hydriodic acid method, was refluxed with 20% aqueous potassium hydroxide (20 ml.) for 1 hour, and the cooled solution acidified with acetic acid, a bulky white precipitate separated. On crystallisation from methanol this product gave *iso*-visnagone (50 mg.) in pale yellow rectangular platelets, m. p. 134°, identical in every way with a synthetical specimen.

Addition of water to the methanol washings of the crude demethylation product and to the dilute acetic acid liquors left on purification of (VI, R = H) gave a small amount of an alkali-soluble powder which had a dark green ferric reaction in alcohol, changing to dull purple on dilution with water and which may contain norvisnagin or the isomeride (XII). So far all attempts to obtain a crystalline compound from this material have been unsuccessful. Methylation of the crude product by the methyl iodide–potassium carbonate method yielded an amorphous powder which was insoluble in aqueous alkali and had a negative ferric reaction but a definite compound could not be isolated.

The authors are indebted to Messrs. Imperial Chemical Industries Limited for a grant in aid of this work.

UNIVERSITY OF LIVERPOOL. [*Received, January 29th,* 1948.]