

## 72. *Furano-compounds. Part IX. The Synthesis of Kellin and Related Compounds.*

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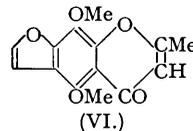
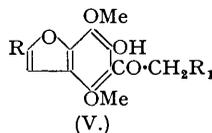
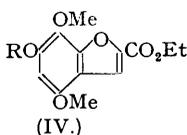
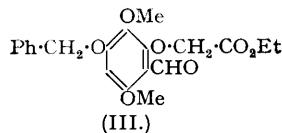
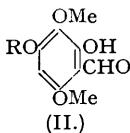
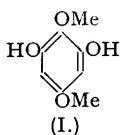
The synthesis of kellinone (V; R and R<sub>1</sub> = H), a degradation product of the furanochromone, kellin, has been achieved by way of the stages (I), (II; R = H), (II; R = Ph·CH<sub>2</sub>), (III), (IV; R = Ph·CH<sub>2</sub>), (IV; R = H), and (V; R = CO<sub>2</sub>H, R<sub>1</sub> = H). Obtained from (V; R and R<sub>1</sub> = H) by the standard method, the diketone (V; R = H, R<sub>1</sub> = Ac) is readily converted into kellin (VI), identical with natural material.

By means of the accessible intermediate kellinone a series of furano-flavanones and -flavones has been synthesised.

IN their analytical studies on the structure of kellin, a major constituent of the alcoholic extract of *Ammi visnaga* seeds, Späth and Gruber (*Ber.*, 1938, **71**, 106) obtained a ketone, kellinone, for which, since it could be degraded to furan-2 : 3-dicarboxylic acid and to 2 : 5-dimethoxy-4 : 6-diethoxy-3-acetylbenzoic acid, they proposed the structure (V; R and R<sub>1</sub> = H). In consequence these authors concluded that kellin was the linear furanochromone (VI) and is thus the analogue of the furanocoumarin, *isopimpinellin*. This assignation of structure (VI) to kellin has now been completely vindicated by the following synthesis according to the general procedure outlined in Part VIII (*J.*, 1948, 2260).

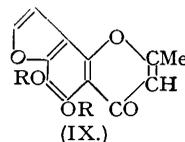
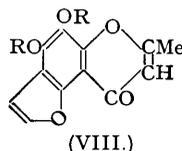
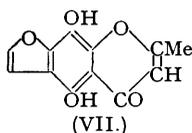
From the dimethoxyresorcinol (I) an excellent yield of the 2 : 4-dihydroxy-3 : 6-dimethoxybenzaldehyde (II; R = H) was obtained by Gattermann's procedure, and on benzylation this substance gave the *benzyl ether* (II; R = Ph·CH<sub>2</sub>), the orientation of which follows from its ferric reaction in alcohol and its ultimate conversion into (IV; R = Ph·CH<sub>2</sub>). Interaction of (II; R = Ph·CH<sub>2</sub>) with ethyl bromoacetate in the presence of potassium carbonate in boiling

acetone gave rise to the *phenoxyacetate* (III); this, on cyclisation with alcoholic sodium ethoxide, furnished the *coumarone-2-carboxylate* (IV; R = Ph·CH<sub>2</sub>) which was debenzylated by means of hydrogen and a palladium-charcoal catalyst, yielding *ethyl 6-hydroxy-4:7-dimethoxycoumarone-2-carboxylate* (IV; R = H). The presence of the carbethoxy-group in the 2-position of (IV; R = Ph·CH<sub>2</sub>) serves to inhibit the saturation of the reactive double bond in the furan residue during hydrogenolysis, whilst in (IV; R = H) this group serves to protect the reactive 2-position of the furan residue during the subsequent Friedel-Crafts reaction.



The condensation of (IV; R = H) with acetyl chloride by means of aluminium chloride in nitrobenzene and subsequent isolation of the product with the aid of aqueous sodium hydroxide furnished the *ketonic acid* (V; R = CO<sub>2</sub>H, R<sub>1</sub> = H), and not the expected ester (V; R = CO<sub>2</sub>Et, R<sub>1</sub> = H). On decarboxylation, the acid (V; R = CO<sub>2</sub>H, R<sub>1</sub> = H) gave rise to kellinone (V; R = H, R<sub>1</sub> = H), identical with a specimen prepared from natural kellin. A small amount of the *acetate* of (IV; R = H) invariably accompanied the compound (V; R = CO<sub>2</sub>H, R<sub>1</sub> = H) in the Friedel-Crafts reaction product. The interaction of kellinone with ethyl acetate and sodium resulted in the formation of the *diketone* (V; R = H, R<sub>1</sub> = Ac) which on cyclisation yielded kellin (VI), identical with natural material (cf. Späth and Gruber, *loc. cit.*). In agreement with this structure (VI), the methyl group in the 2-position of the chromone residue readily reacted with piperonal in alkaline media to form a *styrylchromone*.

In the course of attempts to prepare the parent dihydroxyfuranochromone (VII) from kellin, it was found that on being subjected to demethylation by means of boiling hydriodic acid kellin gave rise to a somewhat resinous product from which only one crystalline *substance* has been isolated so far; variation of the conditions employed in the demethylation process gave the same result. Methylation of this substance by the methyl iodide-potassium carbonate method yielded a dimethyl ether, isomeric and not identical with kellin, for which we propose the name *isokellin*. The retention of the 2-methylchromone nucleus in *isokellin* is demonstrated by its ability to form a *styryl* derivative with piperonal under the usual conditions.



Taking into account the behaviour of visnagin (Part VIII, *loc. cit.*) under similar conditions, it would seem that the demethylation and the ultimate formation of an isomeric kellin in this manner may involve either (a) the furan ring with the compound (VIII; R = H) as an intermediate, or (b) the pyrone ring with (IX; R = H) as an intermediate. Consequently *isokellin* may be represented by either formula (VIII; R = Me) or (IX; R = Me), of which, by analogy with *isovisnagin* (Part VIII, *loc. cit.*), the former is regarded as being the more probable, but a final decision on this point must await an independent synthesis of *isokellin*.

So far as we are aware the only example of a known naturally occurring furanoflavone is karanjin, but it seems likely that further examples of this group will be brought to light (*e.g.*, see Baker and Simmonds on ginkgetin, *J.*, 1940, 1370), and in view of the accessibility of kellinone we have synthesised typical furano-flavanones and -flavones having this nucleus. The condensation of (V; R = H, R<sub>1</sub> = H) with anisaldehyde by the standard method gave rise to the *styryl ketone* (X), and on being boiled with alcoholic phosphoric acid this was converted into an equilibrium mixture of (X) and the *flavanone* (XI) from which (XI) was isolated

by fractional crystallisation. In this cyclisation the almost complete absence of resinification (polymerisation) of the furano-derivatives in hot acidic reagents is remarkable.



Similarly the *styryl ketone* from (V; R = H, R<sub>1</sub> = H) and piperonal gave rise to a mixture from which 5 : 8-*dimethoxy-3''* : 4''-*methylenedioxyfuran*(4' : 5' : 6 : 7)*flavanone* was isolated.

For the synthesis of the flavones of type (XIII) from kellinone we preferred the diketone method to the well-known Robinson arylation process, thus avoiding the application of high temperatures as well as the formation of 3-acylflavone derivatives. By means of the migration process discovered by Baker (*J.*, 1933, 1381; 1940, 1370; cf. Mahal and Venkataraman, *J.*, 1934, 1767) the *benzoate*, *p-methoxybenzoate*, and *veratroate* of kellinone were converted into the corresponding diketones (XII; R = benzoyl), (XII; R = *p*-methoxybenzoyl), and (XII; R = veratroyl) and on cyclisation the latter furnished respectively the furanoflavones (XIII; R = H, R<sub>1</sub> = H), (XIII; R = H, R<sub>1</sub> = OMe), and (XIII; R and R<sub>1</sub> = OMe).

#### EXPERIMENTAL.

**2 : 5-Dimethoxyresorcinol.**—This phenol was prepared essentially according to the route devised by Robinson and his co-workers (*J.*, 1929, 74) with the following modifications. In the benzylation of pyrogallol a 60% increase in the amount of potassium carbonate employed doubled the yield of tribenzyl ether, and in the oxidation of the ether (40 g.) with nitric acid (*d* 1.185) instead of acid (*d* 1.19) the yield of quinone was increased from 15 g. to 18 g. 2 : 6-Dibenzoyloxyquinol (20 g.) was methylated with methyl sulphate (27 g., added in 4 portions) and potassium carbonate (100 g.) in boiling acetone (250 ml.) in the course of 4 hours. The mixture was treated with water (800 ml.), and 24 hours later the dimethyl ether (21 g.) was collected and crystallised from alcohol, forming colourless prisms (18.5 g.). This ether (6 g.), dissolved in methanol (400 ml.), was debenzylated by means of hydrogen and a 10% palladium-charcoal catalyst (2 g.) in the course of 35 minutes, and after the separation of the catalyst the solution was evaporated in a vacuum and the residual solid crystallised from hot water (90 ml.), giving the dihydrate of 2 : 5-dimethoxyresorcinol in plates (2.85 g.), m. p. 61—62°, which on being dried over phosphoric oxide in a vacuum yielded anhydrous material, m. p. 87°.

**2 : 4-Dihydroxy-3 : 6-dimethoxybenzaldehyde** (II; R = H).—A solution of the foregoing dimethoxyresorcinol (10 g.) in ether (200 ml.) containing hydrogen cyanide (10 ml.) was saturated with hydrogen chloride at 0°, and next day the crystalline aldimine was collected, washed with ether, and dissolved in water (300 ml.). When this solution was almost neutralised with solid sodium carbonate and then heated on the water-bath for ½ hour, the *aldehyde* quickly separated. Next day the solid (10.5 g.) was collected, washed, and crystallised from methanol (charcoal), forming elongated, faintly yellow needles, m. p. 197°, almost insoluble in water, sparingly soluble in cold alcohol, benzene, or chloroform, and readily soluble in acetone [Found : C, 54.1; H, 5.0; OMe, 29.8. C<sub>7</sub>H<sub>4</sub>O<sub>3</sub>(OMe)<sub>2</sub> requires C, 54.5; H, 5.1; OMe, 31.3%]. In alcohol the compound gives a dark red ferric reaction. The 2 : 4-*dinitrophenylhydrazone* separated from dilute acetic acid in tiny dark red prisms, m. p. 290° (Found : N, 14.4. C<sub>15</sub>H<sub>14</sub>O<sub>8</sub>N<sub>4</sub> requires N, 14.8%).

**Ethyl 3-Benzoyloxy-2 : 5-dimethoxy-6-formylphenoxyacetate** (III).—The foregoing aldehyde (4 g.) was monobenzylated with benzyl bromide (2.8 ml.) and potassium carbonate (12 g.) in boiling acetone (200 ml.) in the course of 1½ hours, and, after the removal of the potassium salts (wash with hot acetone), the solution was evaporated and the product triturated with water. Crystallised from methanol and then ethanol, the *monobenzyl ether* (II; R = Ph·CH<sub>2</sub>) (3.8 g.) formed colourless needles, m. p. 125°, having a dark red alcoholic ferric reaction (Found : C, 66.7; H, 5.5. C<sub>16</sub>H<sub>16</sub>O<sub>5</sub> requires C, 66.6; H, 5.6%). This compound is readily soluble in benzene, acetone, or chloroform. The 2 : 4-*dinitrophenylhydrazone* separated from dilute acetic acid in scarlet plates, m. p. 272° (Found : N, 12.0. C<sub>22</sub>H<sub>20</sub>O<sub>8</sub>N<sub>4</sub> requires N, 11.9%).

A solution of the benzyl ether (4 g.) in acetone (75 ml.), containing ethyl bromoacetate (2 ml.) and potassium carbonate (10 g.), was refluxed for 5 hours, *i.e.*, until a test portion of the product gave a negative ferric reaction, and the *phenoxyacetate* (III) isolated as an oil which gradually crystallised. This material was washed with a little ether (20 ml.) to remove traces of oily impurities and then purified from a large volume of light petroleum (b. p. 60—80°), forming long, slender prisms (5.0 g.), m. p. 85°, having a negative ferric reaction (Found : C, 64.5; H, 6.0. C<sub>20</sub>H<sub>22</sub>O<sub>7</sub> requires C, 64.2; H, 5.9%). The *semicarbazone* crystallised from acetic acid in needles, m. p. 154° (Found : N, 9.6. C<sub>21</sub>H<sub>25</sub>O<sub>7</sub>N<sub>3</sub> requires N, 9.7%).

**Ethyl 6-Hydroxy-4 : 7-dimethoxycoumarone-2-carboxylate** (IV; R = H).—Alcoholic sodium ethoxide (from 0.5 g. of sodium and 20 ml. of alcohol) was added to a suspension of ethyl 3-benzoyloxy-2 : 5-dimethoxy-6-formylphenoxyacetate (6 g.) in absolute alcohol (40 ml.), and the mixture agitated until

the solid had dissolved (10 minutes). On being kept at room temperature (40 minutes), the mixture gradually deposited *ethyl 6-benzyloxy-4 : 7-dimethoxycoumarone-2-carboxylate* (IV; R = Ph·CH<sub>2</sub>) as a mass of yellow prisms which were collected and washed with a little cold alcohol and then with water; a further small quantity of the product was obtained by addition of water to the filtrate. Recrystallised from 95% alcohol, the coumarone formed almost colourless prisms (2.8 g.), m. p. 87°, slightly soluble in methanol or warm light petroleum and readily soluble in acetone or ethyl acetate (Found: C, 67.6; H, 5.6. C<sub>20</sub>H<sub>20</sub>O<sub>6</sub> requires C, 67.5; H, 5.6%). On being warmed, the yellow solution of the coumarone in sulphuric acid becomes red.

Acidification of the aqueous filtrate from the crude ester gave *3-benzyloxy-2 : 5-dimethoxy-6-formylphenoxyacetic acid* which on repeated crystallisation from water, formed white needles, m. p. 142°, sparingly soluble in alcohol or benzene (Found: C, 62.8; H, 5.3. C<sub>18</sub>H<sub>18</sub>O<sub>7</sub> requires C, 62.4; H, 5.2%).

The absorption of hydrogen (150 ml.; theory 130 ml.) by a solution of the foregoing benzyl ether of the coumarone (2 g.) in acetic acid (100 ml.) containing a palladium-charcoal catalyst, was complete in 10–15 minutes, and after removal of the catalyst by filtration the filtrate was diluted with water (300 ml.). Next day the resulting *ethyl 6-hydroxy-4 : 7-dimethoxycoumarone-2-carboxylate* (IV; R = H) which had separated was collected and recrystallised from aqueous alcohol, forming colourless slender needles (1.3 g.), m. p. 131°, readily soluble in acetone or ethyl acetate and having a red sulphuric acid reaction (Found: C, 59.0; H, 5.3. C<sub>13</sub>H<sub>14</sub>O<sub>6</sub> requires C, 58.7; H, 5.3%). Prepared by the acetyl chloride-pyridine method, the *acetate* of this compound crystallised from methanol in short prisms, m. p. 104° (Found: C, 58.2; H, 5.4. C<sub>15</sub>H<sub>16</sub>O<sub>7</sub> requires C, 58.4; H, 5.2%).

*6-Hydroxy-4 : 7-dimethoxy-5-acetylcoumarone* (Kellinone) (V; R and R<sub>1</sub> = H).—Aluminium chloride (4 g.) was added in several portions in the course of 15 minutes to a solution of ethyl 6-hydroxy-4 : 7-dimethoxycoumarone-2-carboxylate (2 g.) and acetyl chloride (2 ml.) in pure nitrobenzene (70 ml.) kept below 4°. The mixture, which was vigorously stirred, was kept at about 4° for 2 hours and then at room temperature for 48 hours, then poured on ice (500 g.). 3 Hours after the addition of light petroleum (b. p. 60–80°) (150 ml.), the aqueous layer was removed and the light petroleum-nitrobenzene layer was extracted with aqueous sodium hydrogen carbonate (50 ml. × 2) and then with 6% aqueous sodium hydroxide (50 ml. × 5). Acidification of the combined aqueous sodium hydroxide extracts with hydrochloric acid gave a flocculent precipitate of *6-hydroxy-4 : 7-dimethoxy-5-acetylcoumarone-2-carboxylic acid* (V; R = CO<sub>2</sub>H, R<sub>1</sub> = H) which crystallised from methanol in tiny yellow needles (0.35 g.), m. p. 252°, moderately soluble in benzene or chloroform, and having a green ferric reaction in alcohol [Found: C, 55.6; H, 4.1; OMe, 19.9. C<sub>11</sub>H<sub>8</sub>O<sub>5</sub>(OMe)<sub>2</sub> requires C, 55.7; H, 4.3; OMe, 22.1%].

Acidification of the combined sodium hydrogen carbonate washings gave a small quantity of material having a reddish ferric reaction, whilst distillation of the light petroleum and nitrobenzene in a current of steam after the separation of the foregoing acid (V; R = CO<sub>2</sub>H, R<sub>1</sub> = H) left a product which was found by comparison with an authentic specimen to be the acetate of the initial coumarone (IV; R = Ac), and which, on deacetylation by treatment with concentrated sulphuric acid for 2 minutes followed by addition of excess of water, gave a precipitate of the parent coumarone (IV; R = H), m. p. 130–131°, after purification.

The coumaronecarboxylic acid (0.3 g.) was decarboxylated by being gently refluxed with absolute quinoline (10 ml.) containing copper bronze (0.3 g.) for 25 minutes. After addition of ether (50 ml.), the filtered solution was extracted with 2N-hydrochloric acid (20 ml. × 5) to remove quinoline, then with aqueous sodium hydrogen carbonate to remove traces of unchanged acid, and finally with 7% aqueous sodium hydroxide (15 ml. × 6). The combined alkaline extracts were acidified with hydrochloric acid, saturated with ammonium sulphate, and extracted several times with ether. Evaporation of the dried ethereal extracts left a brown oil which gradually solidified, and then on crystallisation from aqueous methanol gave *6-hydroxy-4 : 7-dimethoxy-5-acetylcoumarone* in light brown prisms (0.075 g.) which on repeated purification from the same solvent (charcoal) formed small yellow prisms (0.05 g.), m. p. 100°, having a green ferric reaction and being identical with a natural specimen of kellinone [Found: C, 60.7; H, 5.2; OMe, 25.7. Calc. for C<sub>10</sub>H<sub>8</sub>O<sub>5</sub>(OMe)<sub>2</sub>: C, 61.0; H, 5.1; OMe, 26.3%]. The 2 : 4-*dinitrophenylhydrazone* formed slender brick-red needles, m. p. 245°, from dilute acetic acid (Found: N, 13.5. C<sub>18</sub>H<sub>16</sub>O<sub>8</sub>N<sub>4</sub> requires N, 13.5%).

Attempts to decarboxylate the acid by sublimation in a vacuum in the presence of copper bronze gave very poor yields of impure kellinone.

*Kellin* (VI).—When the vigorous reaction between kellinone (2 g.), ethyl acetate (25 ml.), and sodium (2 g., added in small pieces) had subsided the mixture was heated on the steam-bath for 5 hours with addition of more sodium (1 g., in small pieces) after 2 hours. After addition of a little methanol to destroy traces of metallic sodium, and subsequent dilution with water (300 ml.), the mixture was acidified with acetic acid, giving a brown oil which gradually solidified, and was then dissolved in much light petroleum (b. p. 80–100°). Part of the solvent was distilled, leaving a saturated solution which on cooling deposited crystalline material; recrystallisation of this several times from benzene-light petroleum (b. p. 60–80°) gave the *diketone* (V; R = H, R<sub>1</sub> = Ac) in small yellow prisms (0.9 g.), m. p. 105°, having a red ferric reaction in alcohol (Found: C, 60.5; H, 5.1. C<sub>14</sub>H<sub>14</sub>O<sub>6</sub> requires C, 60.4; H, 5.0%).

When a solution of the diketone (0.5 g.) in alcohol (8 ml.) containing 4 drops of concentrated hydrochloric acid was boiled for 1 minute, the resulting yellowish solution, on cooling, deposited kellin in colourless elongated prisms (0.3 g.) which after recrystallisation from aqueous alcohol had m. p. 153°, undepressed on admixture with a natural specimen [Found: C, 64.2; H, 4.6; OMe, 22.4. Calc. for C<sub>12</sub>H<sub>6</sub>O<sub>3</sub>(OMe)<sub>2</sub>: C, 64.6; H, 4.6; OMe, 23.8%].

On being heated on the steam-bath for 10 minutes, the yellow mixture of kellin (1 g.), piperonal (1 g.), sodium methoxide (from 0.3 g. of sodium), and methanol (35 ml.) became deep orange, and on cooling deposited the *styril* derivative which formed yellow needles (1.2 g.), m. p. 239°, from dilute acetic acid (Found: C, 67.5; H, 4.2. C<sub>22</sub>H<sub>16</sub>O<sub>7</sub> requires C, 67.3; H, 4.1%). This compound, which is sparingly soluble in alcohol, benzene, or ethyl acetate, gives a dark red sulphuric acid reaction.

*Demethylation of Kellin*.—Hydriodic acid (28 ml.; *d* 1.7, freshly distilled over red phosphorus) was

carefully added to a cooled mixture of kellin (2 g.) and acetic anhydride (20 ml.), the resulting clear red solution was gently refluxed (oil-bath) for  $\frac{1}{2}$  hour, and the cooled mixture was poured on ice (70 g.), giving rise to a yellow flocculent precipitate mixed with a small amount of a brown oil. Sufficient saturated aqueous sodium hydrogen sulphite to remove liberated iodine was added, and the compound was collected 24 hours later and repeatedly crystallised from aqueous acetic acid and then from a little absolute acetic acid, forming deep yellow prisms (0.5 g.), m. p. 252°, sparingly soluble in the usual organic solvents except acetic acid, and giving a green ferric reaction in alcohol (Found: C, 61.7; H, 3.5.  $C_{12}H_8O_5$  requires C, 62.0; H, 3.5%). When gently warmed, the yellow solution of this compound in sulphuric acid became green, blue, and then dark crimson. On being shaken or kept in air, the green solution of the compound in 8% aqueous sodium hydroxide rapidly became dark brown. The mother liquors left on purification of the demethylation product gave only intractable tarry material.

When a mixture of the foregoing product (0.5 g.), acetone (50 ml.), potassium carbonate (3 g.), and methyl iodide (1 ml.) was refluxed for 28 hours, the chromone gradually dissolved and the solution became almost colourless. After separation of the potassium salts (wash 3 times with hot acetone), the solution was evaporated and the residue triturated with water. Crystallisation of the resulting solid from dilute methanol gave *isokellin* in cream-coloured needles (0.44 g.), m. p. 176°, insoluble in aqueous alkali or cold light petroleum, moderately soluble in alcohol, and readily soluble in the other common organic solvents [Found: C, 64.7; H, 4.4; OMe, 20.5.  $C_{12}H_8O_3(OMe)_2$  requires C, 64.6; H, 4.6; OMe, 23.8%]. On being warmed, the yellow solution of the substance in concentrated sulphuric acid becomes green, then blue, and finally scarlet red.

A mixture of *isokellin* (0.6 g.), piperonal (0.6 g.), sodium methoxide (from 0.2 g. of sodium), and methanol (30 ml.) was refluxed for 15 minutes and then kept at room temperature for 48 hours. Crystallisation of the resulting yellow product from dilute acetic acid gave the *styril* derivative in slender yellow needles (0.6 g.), m. p. 226°, having a dark red sulphuric acid reaction (Found: C, 67.6; H, 4.4.  $C_{22}H_{16}O_7$  requires C, 67.3; H, 4.1%).

5 : 8 : 4'-*Trimethoxyfuranone* (4' : 5' : 6 : 7) *flavanone* (XI).—50% Aqueous sodium hydroxide (4 g.) was added to a warm solution of kellinone (2 g.) and anisaldehyde (1.3 g.) in alcohol (25 ml.), the red mixture refluxed for 1 hour on the steam-bath, and the cooled dark red solution diluted with water (100 ml.) and acidified (litmus) with 2*N*-hydrochloric acid. Thus precipitated, the resulting red-brown oil slowly solidified, and on crystallisation from methanol gave 6-*hydroxy*-4 : 7 : 4'-*trimethoxy*-5-*cinnamoylcoumarone* (X) (2.2 g.) in yellow needles, m. p. 141°, having a dark red ferric reaction and a similar sulphuric acid reaction (Found: C, 67.6; H, 5.1.  $C_{20}H_{14}O_6$  requires C, 67.7; H, 5.1%).

When a mixture of phosphoric acid (from 5.5 g. of oxide and 10 ml. of water), alcohol (125 ml.), and the aforementioned styril ketone (1 g.) was refluxed for 48 hours and part of the solvent (50 ml.) evaporated under reduced pressure, the residual liquor gradually deposited crystalline material. By successive evaporation of the filtrate from this solid (A) two further crops (B) and (C) were obtained, and the residual liquor was then poured into water, giving a yellow precipitate (D). Products (B) and (C), which gave only a faint ferric reaction, were combined and crystallised 3 times from methanol, giving the *flavanone* (XI) in tiny, glistening, orange plates (0.23 g.), m. p. 141°, having a negative ferric reaction and a red sulphuric acid reaction (Found: C, 67.8; H, 5.2%). A mixture of the flavanone and unchanged styril ketone had m. p. 115–120°.

The fractions (A) and (D) consisted almost wholly of unchanged styril ketone, m. p. and mixed m. p. 141°, after purification.

5 : 8-*Dimethoxy*-3' : 4'-*methylene*dioxyfuranone (4' : 5' : 6 : 7) *flavanone*.—Kellinone (2 g.) was condensed with piperonal (1.3 g.) by the procedure employed for anisaldehyde; on crystallisation from aqueous acetone, the resulting 6-*hydroxy*-4 : 7-*dimethoxy*-3' : 4'-*methylene*dioxy-5-*cinnamoylcoumarone* formed tiny red plates with a bronze sheen (2 g.), m. p. 153°, having a dark red ferric reaction in alcohol and a red sulphuric acid reaction (Found: C, 65.4; H, 4.4.  $C_{20}H_{16}O_7$  requires C, 65.2; H, 4.3%).

The styril ketone (1 g.) was cyclised with phosphoric acid in boiling alcohol, and the solution concentrated as in the case of the foregoing analogue. From the concentrated reaction mixture fractions (A) and (B) were obtained, of which (A) consisted of a mixture of yellow and red crystals. Extraction of (A) with boiling methanol removed the red crystals which consisted of unchanged ketone; recrystallisation of the yellow residue from aqueous acetone gave the flavanone in pale yellow rectangular prisms (0.2 g.), m. p. 181°, having a negative ferric reaction and a red sulphuric acid reaction (Found: C, 65.4; H, 4.3%). Fraction (B) consisted of unchanged styril ketone, m. p. 153°, after purification.

5 : 8-*Dimethoxyfuranone* (4' : 5' : 6 : 7) *flavone* (XIII; R and R<sub>1</sub> = H).—Benzoyl chloride (3 ml.) was added in portions during the course of 5 minutes to an agitated solution of kellinone (4 g.) in pyridine (25 ml.), and the mixture gently warmed for 10 minutes. Next day the orange-red mixture was poured into water (200 ml.), and after having been well washed with dilute hydrochloric acid and then with water the resulting *benzoate* was crystallised from methanol, forming colourless rhombic plates (4.3 g.), m. p. 97°, insoluble in aqueous sodium hydroxide and having a negative ferric reaction (Found: C, 67.3; H, 5.0.  $C_{19}H_{16}O_6$  requires C, 67.1; H, 4.7%).

A mixture of this ester (3 g.) and powdered sodamide (6 g.) was heated in toluene (60 ml.) on the steam-bath with occasional shaking for 10 hours, and the brown solid collected, washed with benzene, dried, and dissolved in iced water. On being saturated with carbon dioxide, the solution deposited a red-brown oil which gradually solidified, and on crystallisation from methanol gave the *diketone* (XII; R = PhCO) in bright red needles (1.3 g.). Recrystallisation of this material gave a mixture of red and yellow needles, m. p. 103°, from which, by crystallisation from benzene-light petroleum (b. p. 60–80°), red needles, m. p. 103°, were isolated (Found: C, 67.4; H, 4.7.  $C_{19}H_{16}O_8$  requires C, 67.1; H, 4.7%). This compound gives a dark red ferric reaction.

When the orange-red solution of the foregoing diketone (0.5 g.) in acetic acid (25 ml.) containing 5 drops of concentrated hydrochloric acid was boiled for 1 minute, the colour first changed to a deeper red and then became yellow; on addition of water (150 ml.) the solution deposited the *flavone* which formed short yellow prisms (0.3 g.), m. p. 180°, after slight sintering at 177°, having a negative ferric

reaction and a red sulphuric acid reaction (Found: C, 70.8; H, 4.5.  $C_{18}H_{14}O_5$  requires C, 70.8; H, 4.4%).

5 : 8 : 4'-Trimethoxyfurano(4' : 5' : 6 : 7)flavone (XIII; R = H,  $R_1$  = OMe).—Prepared by the method used for the benzoate, the *p*-methoxybenzoate of kellinone formed colourless plates, m. p. 117°, from methanol, readily soluble in the usual organic solvents except alcohol and light petroleum (Found: C, 64.7; H, 5.3.  $C_{20}H_{18}O_7$  requires C, 64.9; H, 4.9%). By means of sodamide (5 g.) in toluene (50 ml.) on the steam-bath for 10 hours this ester (2.5 g.) was converted into the isomeric diketone (XII; R = *p*-methoxybenzoyl) which formed yellow prisms (1.4 g.), m. p. 169°, from benzene-light petroleum (b. p. 60—80°), sparingly soluble in alcohol and moderately soluble in benzene, acetone, or acetic acid (Found: C, 65.3; H, 5.0.  $C_{20}H_{18}O_7$  requires C, 64.9; H, 4.9%). In alcohol the ferric reaction of this substance is greenish yellow, rapidly changing to dark red.

Cyclisation of this diketone (0.5 g.) with boiling acetic acid (25 ml.) containing a little hydrochloric acid gave rise to the flavone (XIII; R = H,  $R_1$  = OMe) which separated from methanol and then ethanol in pale yellow needles (0.35 g.), m. p. 184°, moderately soluble in benzene or acetone and readily soluble in chloroform (Found: C, 68.4; H, 4.7.  $C_{20}H_{16}O_6$  requires C, 68.2; H, 4.6%).

5 : 8 : 3' : 4''-Tetramethoxyfurano(4' : 5' : 6 : 7)flavone (XIII; R and  $R_1$  = OMe).—The veratroate (4 g.) from kellinone (3 g.) separated from methanol in colourless plates, m. p. 130° (Found: C, 63.2; H, 5.1.  $C_{21}H_{20}O_8$  requires C, 63.0; H, 5.0%). A mixture of this ester (2.5 g.), sodamide (5 g.), and toluene (50 ml.) was heated on the steam-bath for 12 hours; after isolation from its sodio-derivative, the resulting diketone (XII; R = veratroyl) was purified from benzene-light petroleum (b. p. 60—80°), forming red prisms (1.0 g.), m. p. 125°, and giving an olive green ferric reaction in alcohol which changed to dark red in a few seconds (Found: C, 63.4; H, 5.1.  $C_{21}H_{20}O_8$  requires C, 63.0; H, 5.0%).

Cyclisation of the foregoing diketone (0.5 g.) in boiling acetic acid (25 ml.) containing 3 drops of concentrated hydrochloric acid during 30 seconds gave rise to the flavone (XIII; R and  $R_1$  = OMe) which was precipitated with water (100 ml.) and then recrystallised from methanol, forming flat yellow prisms (0.4 g.), m. p. 182°, moderately soluble in benzene or acetone and readily soluble in chloroform (Found: C, 65.7; H, 4.7.  $C_{21}H_{18}O_7$  requires C, 65.9; H, 4.7%).

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