234. *Reaction of Primary Amines with* o-*Hydroxydibenzoylmethanes, and the Preparation of Derivatives of Flavone Imine.*

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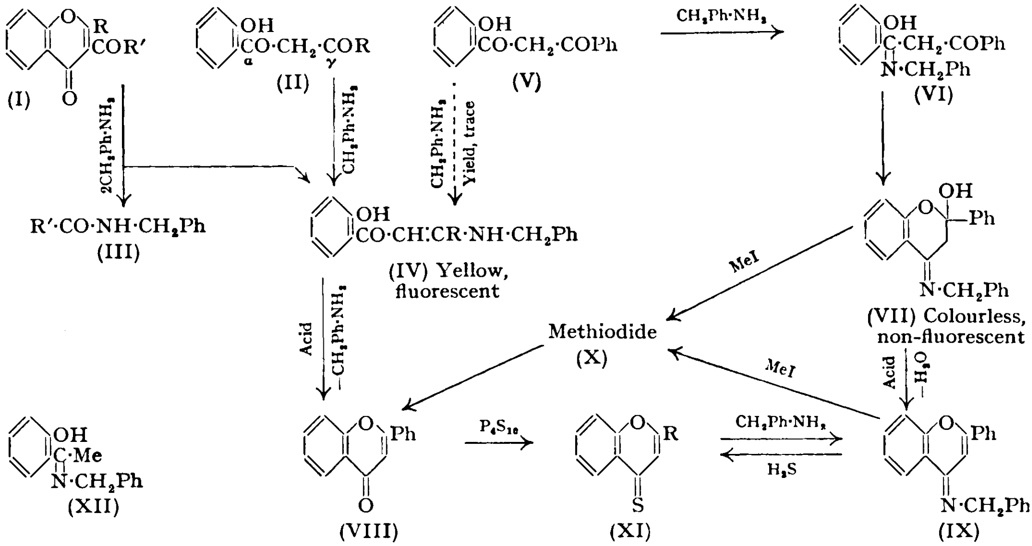
Reaction of benzylamine with 3-benzoylflavone gives *N*-benzylbenzamide and the yellow 2-β-benzylaminocinnamoylphenol (IV; R = Ph), but the latter is obtained only in traces from benzylamine and *o*-hydroxydibenzoylmethane, the main product being a colourless isomeride now shown to be 2-hydroxyflavanone benzylimine (VII). This hydroxyflavanone is readily dehydrated under acid conditions to give flavone benzylimine (IX), and this and other derivatives of flavone alkyl- or aryl-imines resist acid hydrolysis. The flavone imines may also be prepared by reaction of 4-thionflavone, or more readily 4-thionflavone methiodide, with primary bases. The flavone alkylimines react with excess of hydrogen sulphide to give 4-thionflavone, and are converted into flavones by reaction of their methiodides with alkali.

An attempt has been made to determine the factors governing the relative reactivity of the two carbonyl groups in substituted *o*-hydroxydibenzoylmethanes (XIII) by studying their reaction with benzylamine. Observations have been made on the anhydroacetyl derivatives of acyl-*o*-hydroxybenzoylmethanes which are all found to be derivatives of 2-methylchromone, and on some " diflavones."

Reaction of an *o*-hydroxyacetophenone with the anhydride and sodium salt of an aliphatic or aromatic acid gives a 3-acyl-2-alkyl- or -aryl-chromone (I; R = R′ = alkyl or aryl), and these compounds are similarly formed from the 1 : 3-diketones (II; R = alkyl or aryl) (see Baker, *J.*, 1933, 1381; Baker and Butt, *J.*, 1949, 2142, where references to earlier work are given). If, in the 1 : 3-diketone (II), R is a different radical from that in the acid $R'\cdot CO_2H$ whose anhydride and sodium salt are employed, then the 3-acylchromone produced may be either (I) or the isomer where R and R′ are interchanged, since a triacylmethane is involved as an intermediate. Although hydrolysis cannot be relied upon to distinguish between these isomerides owing to the possibility of ring opening, Baker and Butt (*loc. cit.*) and Baker and Glockling (*J.*, 1950, 2759) have shown that reaction with benzylamine serves to differentiate between them by cleavage of the 3-acyl group as an acylbenzylamide (III) and formation of a yellow, highly fluorescent, unsaturated ketone (IV; R = alkyl or aryl). The ketones (IV) where R is an alkyl group derived from a 3-acyl-2-alkylchromone may also be prepared by direct condensation of benzylamine with an alcoholic solution of the 1 : 3-diketone (II; R = alkyl) (Baker and Butt, *loc. cit.*).

The reactions are not quite the same in the 2-arylchromone (flavone) series. Thus, although 3-benzoylflavone (I; R = R′ = Ph) yielded *N*-benzylbenzamide (III; R′ = Ph) and the yellow, fluorescent 2-β-benzylaminocinnamoylphenol (IV; R = Ph) (Baker and Glockling, *loc. cit.*), it has now been found that only a trace of (IV; R = Ph) is obtained from *o*-hydroxydibenzoylmethane (V) and benzylamine, the main product being a colourless, non-fluorescent, non-phenolic compound isomeric with (IV; R = Ph). The present investigation is concerned mainly with the nature of the reactions between primary amines and *o*-hydroxyphenyl-1 : 3-diketones (II). Reference may be made to the article by Cromwell (*Chem. Reviews*, 1946, **38**, 90) which deals *inter alia* with the reaction of amines with 1 : 3-diketones. The work now described appears to afford the first instance of the condensation of a primary amine with a 1 : 3-diketone to give two isomeric products arising from reaction at each of the carbonyl groups.

2-β-Benzylaminocinnamoylphenol (IV; R = Ph) prepared from 3-benzoylflavone (I; R = R′ = Ph), and its colourless isomeride prepared from *o*-hydroxydibenzoylmethane (V) are not interconvertible, thus excluding the unlikely possibilities that they might be either polymorphs or enamine and ketimine isomerides. The representation of (IV) as an enamine rather than as its, probably tautomeric, ketimine form, is preferable on account of its intense yellow colour and fluorescence, which indicate a high degree of conjugation. The colourless compound is hence a structural isomeride of (IV; R = Ph), and it appeared probable that it had been formed by condensation of benzylamine with the carbonyl group attached to the phenolic nucleus in (V) to give first the Schiff's base (VI), which then undergoes cyclisation to the non-phenolic semi-acetal (VII). This view of the structures of the yellow and the colourless isomeride as (IV; R = Ph) and (VII) respectively has now been established by a study of both compounds.



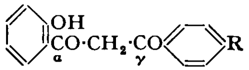
The yellow, fluorescent compound (IV; R = Ph) when heated with acetic acid and a little hydrochloric acid at 100° (conditions used for the cyclisation of *o*-hydroxydibenzoylmethanes to flavones) gave benzylamine hydrochloride and flavone (VIII) in high yield. Under the same conditions the colourless, isomeric compound (VII) underwent dehydration, giving the sparingly soluble hydrochloride of a base, $C_{22}H_{17}ON$. This base is flavone benzylimine (IX); it is also formed from (VII) by heating it with glacial acetic acid, and is obtained as its picrate by treating (VII) with ethanolic picric acid. A more direct synthesis of flavone benzylimine (IX) is by heating 4-thionflavone (XI; R = Ph; see the following paper) with benzylamine in alcoholic solution, and it is also produced under very mild conditions from 4-thionflavone methiodide (following paper) and benzylamine. The reaction between 4-thionflavone and benzylamine is reversible; when flavone benzylimine is treated with hydrogen sulphide in alcoholic solution, 4-thionflavone separates in 72% yield. Flavone benzylimine (IX) gives a yellow methiodide (X), also obtained from (VII) by heating it with methanolic methyl iodide; (X) is hydrolysed by warming it with aqueous methanol and a trace of sodium hydroxide, giving flavone (VIII) and, unexpectedly, benzylamine as the only isolable base. The structure of this methiodide has not been established; if it is a simple quaternary methiodide its hydrolysis must be accompanied by at least partial loss of the methyl group from the nitrogen atom. Flavone benzylimine is stable to hot hydrochloric acid, an abnormal behaviour for a Schiff's base. The stability may be connected with the electromeric change, $-\overset{\curvearrowright}{O}-CPh\overset{\curvearrowright}{=}CH-\overset{|\,\curvearrowright}{C=}N-$, which is possible in flavone benzylimine and would be expected to reduce the chemical reactivity of the $-\overset{|}{C}=N-$ group.

The dehydration of the non-fluorescent compound to give flavone benzylimine (IX), coupled with the facts that it is non-phenolic, being insoluble in aqueous sodium hydroxide, and that it gives neither a ferric chloride reaction nor a derivative with copper acetate, proves that it is 2-hydroxyflavanone benzylimine (VII). The formation of this cyclic semi-acetal from (VI) has a close parallel in the cyclisation of ketose sugars to pyranose forms, and it is likely that such compounds are involved in the ring closure of acyl-*o*-hydroxybenzoylmethanes (II) to chromones and flavones.

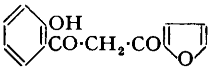
A similar colourless, non-fluorescent compound was obtained from *o*-hydroxydibenzoylmethane (V) by reaction with *n*-butylamine. This 2-hydroxyflavanone *n*-butylimine was dehydrated by warm acetic acid to flavone *n*-butylimine, which proved to be identical with a specimen prepared from 4-thionflavone and *n*-butylamine. A similar series of reactions employing *n*-octylamine gave the colourless 2-hydroxyflavanone *n*-octylimine and flavone *n*-octylimine. The latter reacted with hydrogen sulphide to give 4-thionflavone in 91% yield.

The yellow, fluorescent compounds (IV) readily form metallic complexes. Thus, although 2-β-benzylaminocinnamoylphenol (IV; R = Ph), 2-β-benzylaminocrotonoylphenol (IV; R = Me), and 2-β-*n*-hexylaminocrotonoylphenol are not soluble in aqueous sodium hydroxide, they give deep green colours with ferric chloride, and yield rather insoluble, dark green copper complexes with cupric acetate. Owing to their insolubility it has not been possible to determine the molecular weights of these copper derivatives, but analysis shows that they unexpectedly contain one molecule of (IV) to each copper atom which has replaced two hydrogen atoms. For example, 2-β-*n*-hexylaminocrotonoylphenol, $C_{16}H_{23}O_2N$, gives a cupric derivative, $(C_{16}H_{21}O_2NCu)_n$ (*n* is most probably 2 or 3). This differs from the usual ratio of two molecules of the hydroxy-carbonyl or related compound to each atom of copper, a ratio which is found in, for example, the copper derivative of *o*-hydroxyacetophenone benzylimine (XII).

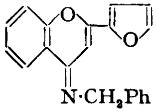
Some observations may be recorded in connection with the condensation of benzylamine and other primary amines with acyl-*o*-hydroxybenzoylmethanes (II). The nature of the reaction product, a yellow compound of the type (IV) or a colourless compound of the type (VII), is determined by the initial condensation of the benzylamine with either the α- or the γ-keto-group of the side chain attached to the phenolic nucleus, and this will be governed by the relative cationoid character of the two carbon atoms of the carbonyl groups, possibly by effects due to enolisation, and by steric factors.



(XIII)



(XIV)



(XV)

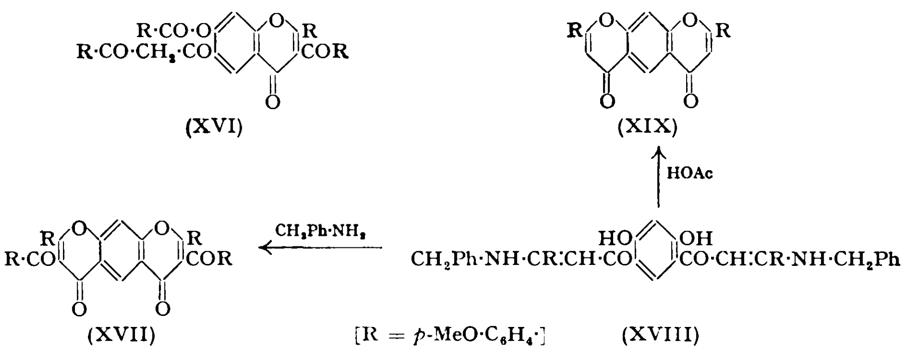
With acetyl-*o*-hydroxybenzoylmethane (II; R = Me) condensation occurs exclusively at the γ-carbonyl group, which is undoubtedly the more cationoid of the two and the less subject to steric effects, giving (IV; R = Me). With *o*-hydroxydibenzoylmethane (XIII; R = H) containing a less reactive γ-carbonyl group, the condensation takes place mainly at the α-carbonyl group, giving 2-hydroxyflavanone benzylimine (VII) in 79% yield and only a 1% yield of (IV; R = Ph). *o*-Hydroxy-*p*′-methoxydibenzoylmethane (XIII; R = OMe) with an even less cationoid γ-carbonyl group reacts exclusively at the α-carbonyl group to give 2-hydroxy-4′-methoxyflavanone benzylimine. *p*-Chloro-*o*′-hydroxydibenzoylmethane (XIII; R = Cl) reacts almost exclusively at the α-carbonyl group to give 4′-chloro-2-hydroxyflavanone benzylimine, but the yellow colour of the reaction mixture indicates the presence of a trace of (IV; R = p-Cl·C_6H_4), but this could not be isolated. Broadly speaking, these results are in accord with expectations, but it is clear from the work of Lapworth and Manske (*J.*, 1928, 2533), who studied the stability of aromatic aldehyde cyanohydrins, that no simple relation exists between the cationoid properties of the carbonyl group and the expected electronic effects of substituents in the aromatic nucleus. Again, Bradley and Robinson (*J.*, 1926, 2356) found that the interpretation of the hydrolysis of substituted dibenzoylmethanes was not simple, and this was also found to be the case for the reaction of hydroxylamine with dibenzoylmethanes (Shenoi, Shah, and Wheeler, *J.*, 1940, 247).

2-Hydroxy-4′-methoxyflavanone benzylimine and 4′-chloro-2-hydroxyflavanone benzylimine (cf. VII) were dehydrated by acetic acid at 100° to give 4′-methoxy- and 4′-chloro-flavone benzylimines, respectively (cf. IX); these flavone alkylimines readily gave picrates. o-Hydroxy-p'-nitrodibenzoylmethane (XIII; R = NO_2) reacted differently with benzylamine giving, in methanolic solution, a small yield of 4′-nitroflavone by direct cyclisation, but the main reaction was cleavage of the molecule with formation of methyl p-nitrobenzoate and o-hydroxyacetophenone benzylimine (XII). 2-Hydroxy-4 : 6-dimethoxydibenzoylmethane did not react with benzylamine under the conditions employed. 2-Furoyl-o-hydroxybenzoylmethane (XIV) reacted with benzylamine at the α-carbonyl group, giving the colourless 2-2′-furyl-2-hydroxychromanone benzylimine, which was dehydrated by acetic acid to 2-2′-furylchromone benzylimine (XV).

*Anhydroacetyl Derivatives of Acyl-*o-*hydroxybenzoylmethanes.*—It appears to be a general rule that if a diketone (II; R = alkyl or aryl) is heated with acetic anhydride and sodium acetate, the product is a 3-acyl derivative of 2-methylchromone. Thus, anhydroacetylation of o-hydroxydibenzoylmethane and of 4-methyl-2-propionoacetylphenol gives 3-benzoyl-2 methylchromone and 2 : 6-dimethyl-3-propionylchromone respectively, the nature of the products having been established by reaction with benzylamine (Baker and Butt, *loc. cit.*). Two further examples have now been found. 2-Furoyl-o-hydroxybenzoylmethane (XIV), acetic anhydride, and sodium acetate give 3-2′-furoyl-2-methylchromone; this reacts with benzylamine to give 2-β-benzylaminocrotonoylphenol (IV; R = Me). Anhydroacetylation of o-hydroxy-p'-nitrodibenzoylmethane (XIII; R = NO_2) gives 2-methyl-3-p-nitrobenzoylchromone (I; R = Me; R′ = p-NO_2·C_6H_4), giving with benzylamine 2-β-benzylaminocrotonoylphenol (IV; R = Me) and N-benzyl-p-nitrobenzamide, p-NO_2·C_6H_4·CO·NH·CH_2Ph.

The same tendency to give 2-methylchromones is shown by the facts that (*a*) 2 : 6-dimethyl-3-propionylchromone is the sole product of the propionylation of 2-acetoacetyl-4-methylphenol (Baker and Butt, *loc. cit.*), and (*b*) 2-acetoacetylphenol reacts with benzoic anhydride and triethylamine to give 3-benzoyl-2-methylchromone (this paper).

The Structure of Some Derivatives of "Diflavone."—Algar, McCarthy, and Dick (*Proc. Roy. Irish Acad.*, 1933, **41**, 155) proposed structure (XVI) for the product obtained by



(XVI) (XIX) (XVII) [R = p-MeO·C_6H_4·] (XVIII)

fusing 4 : 6-diacetylresorcinol with p-methoxybenzoic anhydride and sodium p-methoxybenzoate (Allan and Robinson's flavone synthesis). This reaction has now been repeated, and has also been carried out with p-methoxybenzoic anhydride in triethylamine (cf.

Kuhn and Low, *Ber.*, 1944, **77**, 202). In each case, the same product was isolated, but the yield was much better from the latter reaction.

The structure (XVII) assigned to the product was proved by reaction with benzylamine, which gave the strongly fluorescent 4 : 6-di-(β-benzylamino-4-methoxycinnamoyl)resorcinol (XVIII) and *N*-benzyl-*p*-methoxybenzamide $MeO·C_6H_4·CO·NH·CH_2Ph$. This behaviour is analogous to that of other 3-aroylflavones (see Baker and Glockling, *loc. cit.*). The 4 : 6-di-(β-benzylamino-4-methoxycinnamoyl)resorcinol was cyclised by acetic–hydrochloric acids, with loss of benzylamine, giving " 4 : 4′-dimethoxydiflavone " (XIX) previously described by Algar, McCarthy, and Dick (*loc. cit.*).

EXPERIMENTAL

M.p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

2-β-*Benzylaminocinnamoylphenol* (IV; R = Ph).—The following method is more satisfactory than that described by Baker and Glockling (*loc. cit.*). 3-Benzoylflavone (5·9 g.), benzylamine (4·4 c.c.), and dry pyridine (45 c.c.) were heated under reflux for 20 hours, cooled, and poured into dilute acetic acid. The precipitate was collected and crystallised from ethanol, giving 2-β-benzylaminocinnamoylphenol (4·7 g., 79%) as yellow needles, m. p. 96—98° (lit., m. p. 98°). Its alcoholic solution gave a deep green colour with ferric chloride.

2-*Hydroxyflavanone Benzylimine* (VII).—*o*-Hydroxydibenzoylmethane (2·5 g.), benzylamine (1·25 c.c.), and ethanol (25 c.c.) were heated for 2·5 hours and cooled, and the precipitate (2·7 g., 79%), m. p. 170° (decomp.), was collected and crystallised from ethanol (150 c.c.), giving 2-*hydroxyflavanone benzylimine* as colourless prisms, m. p. 175° (decomp.) (Found: C, 80·1; H, 5·5; N, 4·3. $C_{22}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·3%). It is not fluorescent in ultra-violet light, is insoluble in aqueous sodium hydroxide, and gives no colour with ferric chloride or derivative with ethanolic cupric acetate.

Concentration of the original, fluorescent alcoholic mother-liquors and crystallisation of the product from ethanol gave 2-β-benzylaminocinnamoylphenol (42 mg., 1%), m. p. and mixed m. p. 96—98°.

Reaction of 2-β-*Benzylaminocinnamoylphenol with Acetic–Hydrochloric Acid. Formation of Flavone and Benzylamine.*—A mixture of 2-β-benzylaminocinnamoylphenol (IV; R = Ph) (642 mg.), glacial acetic acid (10 c.c.), and concentrated hydrochloric acid (1 c.c.) was heated on a steam-bath for 10 minutes and poured into water. After cooling to 0°, the crystalline precipitate (390 mg., 90%) was collected, washed, dried, and crystallised from light petroleum (b. p. 60—80°), giving flavone, m. p. and mixed m. p. 96—97°.

The original aqueous mother-liquors were evaporated under diminished pressure and the residue was washed with ether and dried, giving benzylamine hydrochloride (81 mg., 29%), m. p. and mixed m. p. 256°.

Flavone Benzylimine (IX).—(a) *Dehydration of* 2-*hydroxyflavanone benzylimine by acetic–hydrochloric acid.* A mixture of 2-hydroxyflavanone benzylimine (1 g.), glacial acetic acid (10 c.c.), and concentrated hydrochloric acid (1 c.c.) was heated on a steam-bath for 10 minutes, then poured into water, and the precipitate (1·05 g., 100%) was collected. This hydrochloride (250 mg.), m. p. 270° (decomp.), was dissolved in boiling water, 2N-sodium hydroxide was added until the mixture was slightly alkaline, and after cooling in a refrigerator the precipitate (160 mg., 71%) was crystallised from aqueous ethanol, giving *flavone benzylimine* (IX) as colourless needles, m. p. 95—96° (Found: C, 84·5; H, 5·6; N, 4·6. $C_{22}H_{17}ON$ requires C, 84·9; H, 5·5; N, 4·5%).

(b) *Dehydration of 2-hydroxyflavanone benzylimine with acetic acid.* 2-Hydroxyflavanone benzylimine (1 g.) in glacial acetic acid (10 c.c.) was heated on a steam-bath for 10 minutes, cooled, poured into water, and neutralised with aqueous sodium carbonate. The precipitate (860 mg., 90%) was collected and crystallised from aqueous ethanol, giving flavone benzylimine, m. p. and mixed m. p. 95—96°.

(c) *From 4-thionflavone.* 4-Thionflavone (100 mg.; see following paper), ethanol (10 c.c.), and benzylamine (1 c.c.) were heated on a steam-bath for 2·5 hours. Hydrogen sulphide was evolved and the deep-red colour of the 4-thionflavone gradually faded. Water was then added, and the precipitate collected and crystallised from aqueous ethanol, giving flavone benzylimine (124 mg., 95%), m. p. and mixed m. p. 95—96° (Found: N, 4·7%).

(d) *From 4-thionflavone methiodide.* Benzylamine (5 drops) was added to a suspension of 4-thionflavone methiodide (100 mg.; see following paper) in ethanol (5 c.c.). Methanethiol was evolved and the red colour of the methiodide disappeared almost immediately. After the mixture had been kept for 15 minutes at room temperature, water was added and the crystalline flavone benzylimine was collected (58 mg., 71%); after crystallisation it had m. p. and mixed m. p. 95—96°.

Flavone benzylimine picrate, prepared by mixing ethanolic solutions of either flavone benzylimine or 2-hydroxyflavanone benzylimine (VII) and of picric acid, forms a yellow powder, m. p. 242° (decomp.), insoluble in most organic solvents (Found: C, 62·2; H, 3·5; N, 10·4. $C_{22}H_{17}ON,C_6H_3O_7N_3$ requires C, 62·2; H, 3·7; N, 10·4%). *Flavone benzylimine hydrochloride* (63 mg., 88%), m. p. 270° (decomp.), was formed when concentrated hydrochloric acid was added to a solution of flavone benzylimine (64 mg.) in 10% acetic acid (10 c.c.); it could not be recrystallised (Found: N, 3·3; Cl, 9·2. $C_{22}H_{17}ON,HCl$ requires N, 4·0; Cl, 10·2%).

Flavone benzylimine was recovered as its hydrochloride after being heated under reflux for 4 hours with concentrated hydrochloric acid and sufficient glacial acetic acid to dissolve it.

Reaction of Hydrogen Sulphide with Flavone Benzylimine (IX).—Hydrogen sulphide was passed at room temperature into a solution of flavone benzylimine (0·5 g.) in ethanol (15 c.c.) for ½ hour. 4-Thionflavone rapidly separated from the red solution and was collected after 2 hours, washed with water, and dried (yield 0·277 g., 72%; m. p. 87°). Crystallisation from light petroleum (b. p. 60—80°) gave the pure compound, m. p. and mixed m. p. 88°.

Flavone Benzylimine Methiodide (X) *and its Hydrolysis.*—Flavone benzylimine (760 mg.) and methyl iodide (10 c.c.) in methanol (10 c.c.) were heated for 6 hours, the methanol removed, and the solid which separated was collected, washed with ether, and dried, giving *flavone benzylimine methiodide* (576 mg., 52%) as minute, yellow crystals, m. p. 266° (decomp. after darkening at 258°). This methiodide was also obtained by boiling 2-hydroxyflavanone benzylimine (VII) with methanolic methyl iodide (Found: C, 60·3; H, 4·2; N, 3·3; I, 28·8. $C_{22}H_{17}ON,CH_3I$ requires C, 60·9; H, 4·5; N, 3·1; I, 28·0%). Flavone benzylimine methiodide (1·39 g.), ethanol (100 c.c.), and water (100 c.c.) containing 2N-sodium hydroxide (1·6 c.c., 1 equiv.) were heated under reflux for 48 hours. Concentrated hydrochloric acid (10 c.c.) was added, and the ethanol removed under reduced pressure. Flavone (590 mg., 87%), m. p. and mixed m. p. 96—97°, was collected, and the filtrate was evaporated under reduced pressure, the residue dissolved in a small volume of hot ethanol and filtered, and ether added. Colourless plates of benzylamine hydrochloride (271 mg., 61%) separated, m. p. and mixed m. p. 256—258°; on admixture with *N*-methylbenzylamine hydrochloride (m. p. 177—179°) it melted at *ca.* 140—150°. *N*-Methylbenzylamine hydrochloride was recovered unchanged when it replaced the flavone benzylimine methiodide in the above experiment.

2-Hydroxyflavanone n-*Butylimine.*—A mixture of *o*-hydroxydibenzoylmethane (5 g.), *n*-butylamine (1·53 g.), and methanol (100 c.c.) was heated for 3 hours and concentrated to 50 c.c., and water added. The precipitate (2·23 g., 36%) was crystallised from methanol, giving *2-hydroxyflavanone* n-*butylimine* as colourless prisms, m. p. 148° (decomp.) (Found: C, 76·9; H, 7·1; N, 4·8. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·2; N, 4·7%)

Flavone n-*Butylimine.*—(*a*) 2-Hydroxyflavanone *n*-butylimine (114 mg.) was heated on a steam-bath with glacial acetic acid (3·5 c.c.) for 10 minutes, cooled, poured into water, and neutralised with aqueous sodium carbonate. The precipitate of *flavone* n-*butylimine* (98 mg., 91%) separated from aqueous methanol as colourless platelets, m. p. 44—45° (Found: C, 82·4; H, 7·1; N, 5·0. $C_{19}H_{19}ON$ requires C, 82·3; H, 6·9; N, 5·0%).

(*b*) 4-Thionflavone (150 mg.), *n*-butylamine (0·5 c.c.), and methanol (10 c.c.) were heated for 1·5 hours and cooled; water was added until the solution was slightly cloudy, and the latter was placed in a refrigerator. The solid (117 mg., 67%) was collected and crystallised from aqueous methanol, giving flavone *n*-butylimine, m. p. and mixed m. p. 44—45°.

2-Hydroxyflavanone n-*Octylimine.*—As in the previous case, *o*-hydroxydibenzoylmethane (2·5 g.), *n*-octylamine (2 c.c.), and ethanol (25 c.c.) gave *2-hydroxyflavanone* n-*octylimine* (3 g., 82%) as colourless plates, m. p. 110°, from light petroleum (b. p. 60—80°) or from aqueous ethanol (Found: C, 78·1; H, 8·5; N, 3·9. $C_{23}H_{29}O_2N$ requires C, 78·6; H, 8·3; N, 4·0%).

Flavone n-*Octylimime.*—(*a*) 2-Hydroxyflavanone *n*-octylimine (400 mg.) in acetic acid (4 c.c.) gave *flavone* n-*octylimine* (300 mg., 80%) as colourless, silky needles, m. p. 51—53°, from aqueous methanol (Found: C, 82·5; H, 7·8; N, 4·2. $C_{23}H_{27}ON$ requires C, 82·9; H, 7·8; N, 4·2%).

(*b*) 4-Thionflavone (100 mg.) and *n*-octylamine (0·5 c.c.) in ethanol (10 c.c.) gave, as in the previous case, flavone *n*-octylimine (101 mg., 72%), m. p. and mixed m. p. 51—53°. When treated in alcoholic solution with hydrogen sulphide (as described in the case of flavone benzylimine) it gave 4-thionflavone in 91% yield.

o-*Hydroxyacetophenone Benzylimine* (XII).—Benzylamine (1·96 g.) was added to *o*-hydroxyacetophenone (2·3 g.) in ethanol (10 c.c.). Heat was evolved and the precipitate (3·34 g., 88%) which separated on cooling was collected and crystallised from ethanol, giving o-*hydroxyacetophenone benzylimine* as pale green needles, m. p. 117·5—118·5° (Found: C, 80·0; H, 6·8; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%). This compound shows an intense blue-green fluorescence in ultra-violet light, gives a wine-red ferric chloride reaction, and is insoluble in dilute alkali. It dissolves in dilute acid with loss of colour, and the odour of o-hydroxyacetophenone is apparent. With cupric acetate it gave a *copper* derivative, which separated from a large volume of ethanol as intensely dark-green prisms, m. p. 194—196° [Found: C, 70·0; H, 5·2; N, 5·4; Cu, 12·4. $(C_{15}H_{14}ON)_2Cu$ requires C, 70·4; H, 5·5; N, 5·5; Cu, 12·4%].

2-β-n-*Hexylaminocrotonoylphenol*.—*n*-Hexylamine (1·1 mol.) was added to a solution of 2-acetoacetylphenol (1 mol.) in ethanol at room temperature. The resulting yellow, fluorescent solution deposited bright yellow crystals which were collected after 2 days and recrystallised from ethanol (yield, 67%). This 2-β-n-*hexylaminocrotonoylphenol* has m. p. 95—96° (Found: C, 73·3; H, 8·8; N, 5·6. $C_{16}H_{23}O_2N$ requires C, 73·6; H, 8·8; N, 5·4%). The *copper* derivative separated in almost quantitative yield when ethanolic solutions of 2-β-*n*-hexylaminocrotonoylphenol and of cupric acetate were mixed. After recrystallisation from a large volume of benzene it formed a mass of thread-like, green needles, m. p. 270° [Found: C, 59·8; H, 6·6; N, 4·3; Cu, 19·8. $(C_{16}H_{21}O_2NCu)_n$ requires C, 59·5; H, 6·5; N, 4·3; Cu, 19·7%].

Copper Derivatives of 2-β-*Benzylamino-crotonoyl- and -cinnamoyl-phenol*.—The first *copper* derivative was prepared as in the previous case, and obtained in green, thread-like needles from dioxan, m. p. 278° [Found: C, 62·45; H, 4·5; N, 4·2; Cu, 18·2. $(C_{17}H_{15}O_2NCu)_n$ requires C, 62·1; H, 4·6; N, 4·25; Cu, 19·3%]; the second *copper* derivative separated from pyridine–ethanol as a dark green powder, m. p. 312° (decomp.) [Found: C, 68·3; H, 4·7; N, 3·5; Cu, 18·0. $(C_{22}H_{17}O_2NCu)_n$ requires C, 67·6; H, 4·4; N, 3·6; Cu, 16·3%].

Reaction of Benzylamine with o-*Hydroxy*-p′-*methoxydibenzoylmethane* (XIII; R = OMe). 2-*Hydroxy-4′-methoxyflavanone Benzylimine*.—The diketone (XIII; R = OMe) (1 g.), benzylamine (0·45 c.c.), and methanol (30 c.c.) were heated for 3 hours, and the solution was concentrated and cooled. The solid (0·87 g., 65%) was collected (the mother-liquors were not fluorescent), dried, and recrystallised from aqueous methanol (charcoal), giving 2-*hydroxy-4′-methoxyflavanone benzylimine* as colourless plates, m. p. 160° (decomp.) (Found: C, 76·5; H, 5·6; N, 4·2. $C_{23}H_{21}O_3N$ requires C, 76·9; H, 5·9; N, 3·9%).

4′-*Methoxyflavone Benzylimine*.—2-Hydroxy-4′-methoxyflavanone benzylimine (95 mg.) and glacial acetic acid (3 c.c.) were heated on a steam-bath for 10 minutes and poured into aqueous sodium carbonate. The solid (74 mg., 82%) was collected, washed, dried, and crystallised from ethanol, giving 4′-*methoxyflavone benzylimine* as long, colourless needles, m. p. 134—135° (Found: C, 80·9; H, 5·5; N, 4·0. $C_{23}H_{19}O_2N$ requires C, 80·9; H, 5·6; N, 4·1%). Its solution in ethanol shows a vivid blue fluorescence in ultra-violet light. With ethanolic picric acid it gave a *picrate* as a yellow powder, m. p. 252° (decomp.) (Found: C, 61·2; H, 3·9; N, 9·6. $C_{23}H_{19}O_2N,C_6H_3O_7N_3$ requires C, 61·1; H, 3·9; N, 9·8%).

o-(p-*Chlorobenzoyloxy*)*acetophenone*.—A mixture of *p*-chlorobenzoyl chloride (13·8 g.), o-hydroxyacetophenone (10·7 g.), and dry pyridine (30 c.c.) was kept overnight and poured into dilute hydrochloric acid and ice. The solid was collected, washed, dried, and crystallised from ethanol, giving o-(p-*chlorobenzoyloxy*)*acetophenone* (17·3 g., 81%) as colourless plates, m. p. 92—93° (Found: C, 65·4; H, 4·2; Cl, 12·5. $C_{15}H_{11}O_3Cl$ requires C, 65·6; H, 4·0; Cl, 12·9%).

p-*Chloro*-o′-*hydroxydibenzoylmethane* (XIII; R = Cl).—The preceding ester (20 g.) in dry pyridine (200 c.c.) was mechanically stirred and treated at room temperature with powdered potassium hydroxide (5 g.). After 3 hours, the mixture was poured into dilute acetic acid and ice, and the solid collected, washed, dried, and recrystallised from ethanol, giving p-*chloro*-o′-*hydroxydibenzoylmethane* (12·15 g., 61%) as fine, yellow needles, m. p. 122—124° (Found: C, 65·6; H, 4·1; Cl, 14·0. $C_{15}H_{11}O_3Cl$ requires C, 65·6; H, 4·0; Cl, 12·9%). It gave an intense wine-red colour with ferric chloride.

4′-*Chloroflavone*.—The preceding diketone (500 mg.), acetic acid (5 c.c.), and concentrated hydrochloric acid (5 drops) were heated on a steam-bath for 15 minutes and poured into water, and the solid (430 mg., 92%) was collected, dried, and crystallised from ethanol, giving 4′-*chloroflavone* as long, colourless needles, m. p. 188—189° (Found: C, 70·2; H, 3·5; Cl, 14·1. $C_{15}H_9O_2Cl$ requires C, 70·2; H, 3·5; Cl, 13·8%).

Reaction of Benzylamine with p-*Chloro*-o′-*hydroxydibenzoylmethane* (XIII; R = Cl). 4′-*Chloro-2-hydroxyflavanone Benzylimine*.—As in the previous case, the solid (4·45 g., 84%), obtained after heating the diketone (XIII; R = Cl) (4 g.) with benzylamine (4 c.c.) in ethanol

(100 c.c.) for 7 hours, was crystallised from aqueous methanol (charcoal) and then from benzene, giving *4′-chloro-2-hydroxyflavanone benzylimine* as microscopic, colourless plates, m. p. 158° (decomp.) (Found : C, 72·2; H, 4·8; N, 3·7; Cl, 11·7. $C_{22}H_{18}O_2NCl$ requires C, 72·6; H, 4·95; N, 3·95; Cl, 9·8%). The original mother-liquors were fluorescent but the substance responsible was present only in traces.

4′-Chloroflavone Benzylimine.—The above benzylamine derivative (500 mg.) was cyclised by warming it with glacial acetic acid (5 c.c.) in the usual way and gave *4′-chloroflavone benzylimine* (360 mg., 76%), which separated from aqueous ethanol as fine, colourless needles, m. p. 131° (Found : C, 75·7; H, 4·5; N, 4·3; Cl, 10·4. $C_{22}H_{16}ONCl$ requires C, 76·4; H, 4·6; N, 4·1; Cl, 10·3%). It was characterised as its *picrate*, a yellow powder, m. p. 250° (decomp.) (Found : C, 58·3; H, 3·4; N, 9·8; Cl, 6·2. $C_{22}H_{16}ONCl,C_6H_3O_7N_3$ requires C, 58·5; H, 3·3; N, 9·8; Cl, 6·2%).

o-*Hydroxy*-p′-*nitrodibenzoylmethane* (XIII; R = NO_2).—*o*-(*p*-Nitrobenzoyloxy)acetophenone (Doyle, Gógan, Gowan, Keane, and Wheeler, *Proc. Roy. Dublin Soc.*, 1948, **24**, 304) (6·7 g.) in dry pyridine (100 c.c.) was stirred at room temperature with powdered potassium hydroxide (1·7 g.). After 3 hours the mixture was poured on dilute hydrochloric acid and ice, and the crude diketone was collected, washed, dried (5·43 g., 81%), and crystallised from benzene, giving *o*-hydroxy-*p*′-nitrodibenzoylmethane (3·74 g., 56%) as deep yellow prisms, m. p. 200—201°. Doyle *et al.* (*loc. cit.*) rearranged the ester in presence of ethyl sodioacetoacetate and obtained a 47% yield of crude diketone; they recorded m. p. 198—201°.

Reaction of Benzylamine with o-*Hydroxy*-p′-*nitrodibenzoylmethane* (XIII; R = NO_2). *Formation of* o-*Hydroxyacetophenone Benzylimine* (XII), *Methyl* p-*Nitrobenzoate, and 4′-Nitroflavone.*—(*a*) The diketone (1·47 g.), benzylamine (0·6 c.c.), and methanol (200 c.c.) were heated for 2·5 hours, the solvent was removed under diminished pressure, and the residue triturated with benzene. The insoluble material (0·11 g., 8%) crystallised from acetic acid and then from acetone, giving 4′-nitroflavone, as colourless needles, m. p. 237—239°, undepressed when mixed with an authentic specimen (Doyle *et al.*, *loc. cit.*, give m. p. 236°). Light petroleum (b. p. 60—80°) was added to the benzene filtrate, and the solid (0·6 g.; 52%) which separated on cooling was crystallised from aqueous methanol, giving *o*-hydroxyacetophenone benzylimine, m. p. and mixed m. p. 117·5—118·5°.

(*b*) In another experiment, the diketone (1 g.) and benzylamine (0·85 c.c.) in methanol (100 c.c.) were heated for 1·75 hours, then cooled, and 2N-sulphuric acid (100 c.c.) added to hydrolyse the *o*-hydroxyacetophenone benzylimine. The precipitate (107 mg., 11%) was collected and identified as 4′-nitroflavone. The filtrate was diluted with water and neutralised with 2N-sodium hydroxide, and the precipitate (0·32 g., 36%) which separated was collected and crystallised from ethanol, giving methyl *p*-nitrobenzoate, m. p. and mixed m. p. with an authentic specimen, 95—96° (Wilbrand and Beilstein, *Annalen*, 1863, **128**, 263).

2-*Hydroxy*-4 : 6-*dimethoxydibenzoylmethane.*—Powdered potassium hydroxide (1·6 g.) was added to 2-benzoyloxy-4 : 6-dimethoxyacetophenone (7 g.; Gulati and Venkataraman, *J.*, 1936, 267) in dry pyridine (35 c.c.) and, after being shaken overnight at room temperature, the mixture was poured into dilute hydrochloric acid and ice. The product solidified on storage and was recrystallised from ethanol (charcoal), giving *2-hydroxy-4 : 6-dimethoxydibenzoylmethane* (1·78 g., 26%) as colourless prisms, m. p. 128—130° (Found: C, 68·3; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·3%). This compound was described by Gulati and Venkataraman (*loc. cit.*) as an oil. It gave an intense green ferric chloride colour. It was recovered unchanged after treatment with benzylamine in boiling alcoholic solution.

5 : 7-*Dimethoxyflavone.*—The above diketone (100 mg.) in glacial acetic acid (2·5 c.c.) with concentrated hydrochloric acid (1 drop) gave, in the usual way, 5 : 7-dimethoxyflavone (60 mg., 64%), m. p. 143—145° after drying under diminished pressure over phosphoric anhydride (Gulati and Venkataraman, *loc. cit.*, give m. p. 143°).

2-2′-Furyl-2-hydroxychromanone Benzylimine.—2-Furoyl-*o*-hydroxybenzoylmethane (XIV) (3·85 g.; Baker, Ollis, and Weight, forthcoming publication) and benzylamine in ethanol (100 c.c.) gave in the usual way *2-2′-furyl-2-hydroxychromanone benzylimine* (2·75 g., 51%) as colourless plates, m. p. 158—159° (decomp.), from ethanol (charcoal) (Found : C, 74·7; H, 5·3; N, 4·3. $C_{20}H_{17}O_3N$ requires C, 75·2; H, 5·3; N, 4·4%).

2-2′-Furylchromone Benzylimine (XV).—The preceding hydroxychromanone was warmed with glacial acetic acid and gave as in previous cases *2-2′-furylchromone benzylimine* (72% yield) as colourless, silky needles, m. p. 120—122°, from ethanol (Found : C, 79·7; H, 5·2; N, 4·6. $C_{20}H_{15}O_2N$ requires C, 79·7; H, 5·0; N, 4·65%).

3-2′-Furoyl-2-methylchromone.—2-Furoyl-*o*-hydroxybenzoylmethane (XIV) (1 g.), acetic anhydride (5 c.c.), and anhydrous sodium acetate (1 g.) were heated at 150—160° for 20 minutes, cooled, and poured into water. The solid was collected, washed, dried, and crystallised from aqueous methanol, giving 3-2′-*furoyl*-2-*methylchromone* (0·62 g., 56%) as colourless needles, m. p. 148—150° (Found : C, 70·4; H, 3·9. $C_{15}H_{10}O_4$ requires C, 70·9; H, 3·9%).

Reaction of Benzylamine with 3-2′-*Furoyl*-2-*methylchromone. Formation of* 2-β-*Benzylaminocrotonoylphenol.*—The chromone (0·4 g.), benzylamine (0·4 c.c.), and ethanol (10 c.c.) were heated for 2 hours, and the solution was concentrated. The solid (0·22 g.) was collected and crystallised from ethanol, giving 2-β-benzylaminocrotonoylphenol, m. p. and mixed m. p. 123—124°.

Action of Acetic Anhydride on o-*Hydroxy*-p′-*nitrodibenzoylmethane* (XIII; R = NO_2). *Formation of* 2-*Methyl*-3-p-*nitrobenzoylchromone.*—*o*-Hydroxy-*p*′-nitrodibenzoylmethane (1 g.), acetic anhydride (5 c.c.), and anhydrous sodium acetate (1 g.) were heated for 15 minutes, cooled, and poured into water. The solid (1·03 g., 96%) was washed, dried, and crystallised from ethanol, giving 2-*methyl*-3-p-*nitrobenzoylchromone* as colourless needles, m. p. 202—204° (Found : C, 66·1; H, 3·8; N, 4·7. $C_{17}H_{11}O_5N$ requires C, 66·0; H, 3·6; N, 4·5%).

This chromone (0·5 g.) and benzylamine (0·4 c.c.) in pyridine (5 c.c.) were heated on a steam-bath for 2·5 hours, boiled for ¾ hour, and poured into dilute hydrochloric acid. The precipitate was crystallised from ethanol, giving 2-β-benzylaminocrotonoylphenol (0·26 g., 61%), m. p. and mixed m. p. 123—124°. Water was added to the mother-liquors and the solid (0·41 g., 100%) was crystallised from aqueous ethanol and then from benzene–light petroleum (b. p. 60—80°), giving *N*-benzyl-*p*-nitrobenzamide, m. p. and mixed m. p. 141—143°.

Reaction of Benzoic Anhydride with 2-*Acetoacetylphenol. Formation of* 3-*Benzoyl*-2-*methylchromone.*—2-Acetoacetylphenol (1 g.), benzoic anhydride (5 g.), and triethylamine (5 c.c.) were heated at 160° for 4 hours, water (40 c.c.) was added, and the mixture was heated for 2 hours. The cooled product was triturated with 2N-sodium carbonate, and the solid washed with water, dried, and crystallised from ethanol, giving 3-benzoyl-2-methylchromone (644 mg., 44%), m. p. and mixed m. p. with an authentic specimen, 117° (cf. Müller, *J.*, 1915, **107**, 872, who gives m. p. 118°).

" 3 : 3′-*Dianisoyl*-4 : 4′-*dimethoxydiflavone* " (XVII).—This compound was prepared in 18% yield by the method of Algar, McCarthy, and Dick (*loc. cit.*), but the product was difficult to purify and was erroneously given structure (XVI). The following method gave a 36% yield.

Anisic anhydride (25 g.), 4 : 6-diacetylresorcinol (2·5 g.), and triethylamine (10 c.c.) were stirred for 7 hours at 160°, poured into 5% aqueous sodium carbonate (300 c.c.), and heated for 2 hours. The solid which separated on cooling was crystallised from chloroform–ethanol, giving a pale brown powder (6·23 g., 70%), m. p. 218—225°, which after recrystallisation from glacial acetic acid gave " 3 : 3′-dianisoyl-4 : 4′-dimethoxydiflavone " [5′ : 5″-*dianisoyl*-6′ : 6″-*di*-p-*methoxyphenyldipyrono*(2′ : 3′-1 : 2)(3″ : 2″-4 : 5)*benzene*] (XVII) (3·25 g.) as colourless needles, m. p. 233—235° [Found : C, 72·3; H, 4·4; OMe, 17·1. $C_{38}H_{18}O_6(OMe)_4$ requires C, 72·6; H, 4·3; OMe, 17·9%]. This m. p. was undepressed when the specimen was mixed with the material prepared according to Algar, McCarthy, and Dick, who obtained pale yellow needles, m. p. 233—235°.

4 : 6-*Di*-(β-*benzylamino*-4-*methoxycinnamoyl*)*resorcinol* (XVIII).—The preceding compound (1 g.) and benzylamine (0·66 c.c.) in dry pyridine (25 c.c.) were heated for 16 hours and poured into dilute hydrochloric acid, and the solid collected, dried, and crystallised from benzene (yield 0·5 g.; 55%) and then from chloroform–ethanol. The *compound* (XVIII) formed short, yellow prisms, m. p. 200° (Found : C, 75·2; H, 5·6; N, 4·3; OMe, 9·4. $C_{40}H_{36}O_6N_2$ requires C, 75·0; H, 5·6; N, 4·4; OMe, 9·7%). It showed a vivid yellow fluorescence in ultra-violet light.

Addition of light petroleum (b. p. 60—80°) to the mother-liquors from the first benzene crystallisation gave *N*-benzyl-*p*-methoxybenzamide as a solid which separated from aqueous ethanol as colourless needles (0·30 g., 43%), m. p. and mixed m. p. with an authentic specimen, 131° (Beckmann, *Ber.*, 1904, **37**, 4138, gives m. p. 131°).

" 4 : 4′-*Dimethoxydiflavone* " (XIX).—The preceding dibenzylamino-derivative (100 mg.), glacial acetic acid (5 c.c.), and concentrated hydrochloric acid (5 drops) were heated on a steam-bath for 1 hour, during which time colourless needles separated. After cooling, this precipitate was collected and crystallised from chloroform-ethanol, giving " 4 : 4′-dimethoxydiflavone " [6′ : 6″-*di*-p-*methoxyphenyldipyrono*(2′ : 3′-1 : 2)(3″ : 2″-4 : 5)*benzene*] (XIX) (40 mg., 60%) as colourless needles, m. p. 320—322° (Algar *et al.*, *loc. cit.*, give m. p. 321—322°).

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