

530. *An Unambiguous Synthesis of 3-Aroylflavones and Their Reaction with Benzylamine.*

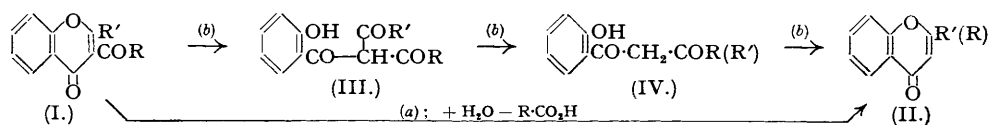
By WILSON BAKER and F. GLOCKLING.

Isomeric pairs of methoxylated 3-aroylflavones (I) and (X) have been prepared from the benzoyl-*o*-hydroxybenzoylmethanes (IV) and (VIII). The latter were condensed with aromatic aldehydes R'-CHO and R-CHO, respectively, to give the arylidene derivatives (VII) and (IX), and these were then oxidised with selenium dioxide to the 3-aroylflavones (I) and (X). Treatment of the 3-aroylflavones, *e.g.*, (X), with benzylamine resulted in all cases in the loss of the 3-aroyl group as an aroylbenzylamide (XII), and formation of an unsaturated benzylamino-compound (XI); this general reaction may be used to orient any compound (I) where R and R' are alkyl or aryl groups.

AN *o*-hydroxyacetophenone reacts with the anhydride and the sodium salt of an aliphatic acid to give a 3-acyl-2-alkylchromone (I; R = R' = alkyl), alkaline hydrolysis of which yields a 2-alkylchromone (II; R' or R = alkyl) by loss of the acyl group (von Kostanecki *et al.*, *Ber.*, 1901, **34**, 102, 2946). A similar process using the anhydride and the sodium salt of an aromatic acid has been much used for the preparation of flavones (Allan-Robinson synthesis) (II; R' or R = aryl), and here also the primary product is generally a 3-aroylflavone (I; R = R' = aryl) (Baker, *J.*, 1933, 1383). The loss of the 3-acyl group may be either direct (*a*) or indirect (*b*), the latter course involving hydrolytic opening of the pyrone ring to give a triacylmethane (III) which passes *via* a diacylmethane (IV) into (II) (for a discussion of the hydrolysis of 3-acylchromones and -flavones, see Baker, *loc. cit.*; Baker and Butt, *J.*, 1949, 2145). Only in the cases of compounds (I) where R and R' are identical would both methods of hydrolysis necessarily give the same product (II).

Intermediates involved in the formation of these 3-acyl compounds (I) have been shown to be the di- and tri-acylmethanes (IV) and (III) (Baker, *loc. cit.*; Doyle, Gógan, Gowan, Keane, and Wheeler, *Proc. Roy. Dublin Soc.*, 1948, **24**, 291). Hence in the reaction between a diacyl-

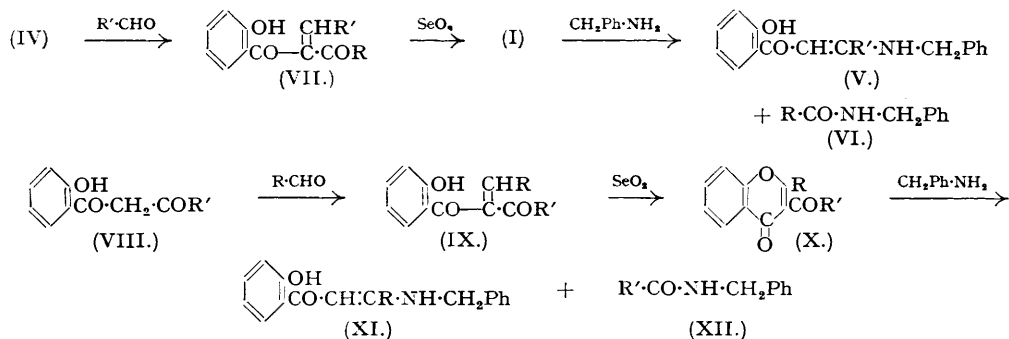
methane (IV) containing the group $\cdot\text{CO}\cdot\text{R}$ and the anhydride and the sodium salt of an acid $\text{R}'\cdot\text{CO}_2\text{H}$, it is not possible to say whether the product is the 3-acylchromone (I) or its isomeride



(X). Alkaline hydrolysis is unable to distinguish with certainty between two such isomeric structures, because if the pyrone rings open the same 2-alkylchromone might result in each case.

Baker and Butt (*loc. cit.*) showed that 3-acylchromones, *e.g.*, (I), react with benzylamine by removal of the 3-acyl group as an acylbenzylamide and opening of the pyrone ring with formation of yellow fluorescent compounds (V). Thus the acetylation of benzoyl-*o*-hydroxybenzoylmethane (IV; R = Ph) was shown to give 3-benzoyl-2-methylchromone (I; R = Ph, R' = Me), and not 3-acetylflavone (I; R = Me, R' = Ph), although alkaline hydrolysis yields flavone (II; R' = Ph). In order to prove conclusively that reaction with benzylamine proceeded in the way mentioned, it was decided to attempt the unambiguous synthesis of pairs of isomeric 3-acyl compounds, (I) and (X), and then to see if each compound would react with benzylamine in the expected manner. The acylation of a diacylmethane (IV) was clearly inadmissible as a synthetical method, and would in any case probably lead to only one (unoriented) of the desired isomerides, so a new synthetical process had to be devised.

It has now been found possible to make use of Mahal, Rai, and Venkataraman's flavone synthesis (*J.*, 1935, 866; for other references see Adams, "Organic Reactions," 1949, Vol. V, pp. 341, 360 *et seq.*), in which an *o*-hydroxychalcone, $\text{o}\text{-HO}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{CH}:\text{CHAr}$, is oxidised to a flavone by selenium dioxide, and this has led to the unambiguous preparation of pairs of isomeric 3-aryylflavones, (I) and (X), where R and R' are different aryl groups. Four such pairs of isomers have been prepared and submitted to reaction with benzylamine; each compound smoothly undergoes the expected cleavage, thus proving the generality of the method for determining the structure of 3-aryylflavones and related compounds. Attempts to apply the selenium dioxide reaction to the synthesis of acylflavones (I; R' = aryl, R = alkyl) have given anomalous results.



The following synthesis of 3-(3:4:5-trimethoxybenzoyl)flavone (X; R = Ph, R' = 3:4:5-trimethoxyphenyl) is typical of the method used for the preparation of the 3-aryylflavones. *o*-Hydroxyacetophenone was treated with 3:4:5-trimethoxybenzoyl chloride and pyridine, and the resulting *o*-(3:4:5-trimethoxybenzoyloxy)acetophenone was converted by molecular rearrangement with potassium hydroxide in anhydrous pyridine into *o*-hydroxybenzoyl-3':4':5'-trimethoxybenzoylmethane (VIII; R' = 3:4:5-trimethoxyphenyl) in over 70% yield (Baker-Venkataraman transformation; see Baker, *loc. cit.*; Doyle *et al.*, *loc. cit.*). Reaction of this dibenzoylmethane with benzaldehyde in boiling ethanol in presence of piperidine yielded the benzylidene derivative (IX; R = Ph, R' = 3:4:5-trimethoxyphenyl), and reaction of this in boiling *n*-amyl-alcoholic solution with selenium dioxide for 17 hours gave 3-(3:4:5-trimethoxybenzoyl)flavone (X; R = Ph, R' = 3:4:5-trimethoxyphenyl) in 58% yield. The isomeric flavone (I; R = Ph, R' = 3:4:5-trimethoxyphenyl) was similarly prepared from 2-benzoyloxyacetophenone *via* benzoyl-*o*-hydroxybenzoylmethane (IV; R = Ph),

ω -benzoyl- ω -hydroxybenzoyl-3 : 4 : 5-trimethoxystyrene (VII; R = Ph, R' = 3 : 4 : 5-trimethoxyphenyl), and final oxidation with selenium dioxide.

Reaction of these isomeric flavones with benzylamine was effected in boiling pyridine solution. 3-(3 : 4 : 5-Trimethoxybenzoyl)flavone gave 3 : 4 : 5-trimethoxybenzobenzylamide (XII; R' = 3 : 4 : 5-trimethoxyphenyl) and 2-(β -benzylaminocinnamoyl)phenol (XI; R = Ph), while 3-benzoyl-3' : 4' : 5'-trimethoxyflavone (I; R = Ph, R' = 3 : 4 : 5-trimethoxyphenyl) gave benzobenzylamide (VI; R = Ph) and 2-(β -benzylamino-3 : 4 : 5-trimethoxycinnamoyl)-phenol (V; R' = 3 : 4 : 5-trimethoxyphenyl).

The table names other 3-aroyleflavones which have been similarly prepared, and the products obtained by their reaction with benzylamine.

3-Aroylflavones.	Products obtained by reaction with benzylamine.
3-Benzoylflavone	2- β -Benzylaminocinnamoylphenol and benzobenzylamide
3- <i>o</i> -Anisoylflavone	2- β -Benzylaminocinnamoylphenol and <i>o</i> -anisobenzylamide
3-Benzoyl-2'-methoxyflavone	2-(β -Benzylamino-2-methoxycinnamoyl)phenol and benzobenzylamide
3- <i>p</i> -Anisoylflavone	2- β -Benzylaminocinnamoylphenol and <i>p</i> -anisobenzylamide
3-Benzoyl-4'-methoxyflavone	2-(β -Benzylamino-4-methoxycinnamoyl)phenol and benzobenzylamide
3-Veratroylflavone	2- β -Benzylaminocinnamoylphenol and veratrobenzylamide
3-Benzoyl-3' : 4'-dimethoxyflavone	2-(β -Benzylamino-3 : 4-dimethoxycinnamoyl)phenol and benzobenzylamide
4'-Methoxy-3-veratroylflavone	2-(β -Benzylamino-4-methoxycinnamoyl)phenol and veratrobenzylamide

3-*o*-Anisoylflavone undergoes demethylation when heated with aqueous hydrobromic acid in acetic acid, giving 3-*o*-hydroxybenzoylflavone without loss of the 3-aroyle group. This product is an *o*-hydroxy-ketone, and as such might undergo the Dakin oxidation with hydrogen peroxide in alkaline solution to give catechol and flavone-3-carboxylic acid (see Baker, Jukes, and Subrahmanyam, *J.*, 1934, 1682), but it was found to be unchanged under the usual reaction conditions.

EXPERIMENTAL.

(Light petroleum refers to the fraction, b. p. 60—80°. M. p.s are uncorr. Microanalyses are by Mr. W. M. Eno, Bristol, and Drs. Feiler and Strauss, Oxford.)

o-(3 : 4 : 5-Trimethoxybenzoyloxy)acetophenone.—3 : 4 : 5-Trimethoxybenzoyl chloride (25 g.), *o*-hydroxyacetophenone (12.5 g.), and anhydrous pyridine (60 c.c.) were heated on the steam-bath for $\frac{3}{4}$ hour, poured into dilute hydrochloric acid and ice, and the solid was collected, washed, and crystallised from ethanol, giving *o*-(3 : 4 : 5-trimethoxybenzoyloxy)acetophenone (23.1 g.) as long needles, m. p. 108° (Found, in material twice recrystallised from ethanol: C, 65.5; H, 5.5. C₁₈H₁₈O₆ requires C, 65.5; H, 5.5%).

o-*p*'-Anisoyloxyacetophenone.—This ketone was prepared from *p*-anisoyl chloride and *o*-hydroxyacetophenone as in the preceding case. It was obtained as plates (90%), m. p., after 4 crystallisations from ethanol, 113—114° (Found: C, 70.6; H, 5.1; OMe, 11.5. C₁₅H₁₁O₃·OMe requires C, 71.1; H, 5.2; OMe, 11.5%).

o-Veratroloxyacetophenone.—This compound was similarly obtained as plates from ethanol (yield 84%) which, after several crystallisations from ethanol and then from benzene-light petroleum, had m. p. 129° [Found: C, 68.2; H, 5.3; OMe, 20.4. C₁₅H₁₀O₂(OMe)₂ requires C, 68.0; H, 5.3; OMe, 20.7%].

Benzoyl-*o*-hydroxybenzoylmethanes (IV; R = aryl).—These compounds were prepared as in the following example. *o*-(3 : 4 : 5-Trimethoxybenzoyloxy)acetophenone (22 g.) in anhydrous pyridine (80 c.c.) was treated at 40° with powdered potassium hydroxide (4 g.), and the mixture shaken vigorously for $\frac{1}{4}$ hour. The thick yellow suspension of the potassium salt of the diketone was poured into excess of 20% acetic acid, and the yellow solid collected, washed, and dried. After crystallisation from ethanol-benzene, *o*-hydroxybenzoyl-3' : 4' : 5'-trimethoxybenzoylmethane (16 g.) was obtained as yellow needles, m. p. 135—136° (Found: C, 65.5; H, 5.5. C₁₈H₁₄O₆ requires C, 65.5; H, 5.5%). Benzoyl-*o*-hydroxybenzoylmethane, m. p. 120°, was obtained in 80% yield after one crystallisation from ethanol (Doyle *et al.*, *loc. cit.*, record an 83% yield of crude product). *o*-Anisoyl-*o*-hydroxybenzoylmethane was obtained in 62% yield, with m. p. 80°, after crystallisation from ethanol-benzene (cf. Baker and Besly, *J.*, 1940, 1106, who effected the migration with potassium carbonate in toluene). *p*-Anisoyl-*o*-hydroxybenzoylmethane formed yellow needles (68% yield), m. p. 111°, from ethanol (Found, in material twice crystallised from ethanol: C, 70.8; H, 5.2. C₁₆H₁₄O₄ requires C, 71.1; H, 5.2%). *o*-Hydroxybenzoylveratroylmethane formed yellow plates (72%), m. p. 130°, from benzene [Found, in material crystallised 4 times from benzene: C, 68.0; H, 5.2; OMe, 19.8. C₁₅H₁₀O₃(OMe)₂ requires C, 68.0; H, 5.3; OMe, 20.7%].

Arylidene Derivatives of Benzoyl-*o*-hydroxybenzoylmethanes (as VII and IX; R and R' = aryl).—The arylidene derivatives of the benzoyl-*o*-hydroxybenzoylmethanes were prepared as in the following example. *o*-Hydroxybenzoyl-3' : 4' : 5'-trimethoxybenzoylmethane (11.6 g.) in ethanol (150 c.c.) was boiled for $\frac{1}{2}$ hour with benzaldehyde (4.0 g.) and a few drops of piperidine. The pale yellow needles which separated after cooling to 0° were collected, washed, dried (12.7 g.), and recrystallised from benzene-light petroleum, giving ω -*o*-hydroxybenzoyl- ω -3 : 4 : 5-trimethoxybenzoylstyrene as colourless needles, m. p. 155° (Found: C, 71.9; H, 5.3. C₂₅H₂₂O₆ requires C, 71.7; H, 5.3%). Condensation of benzaldehyde with benzoyl-*o*-hydroxybenzoylmethane yielded ω -benzoyl- ω -*o*-hydroxybenzoylstyrene

(95%), as colourless prisms, m. p. 158—160°, from ethanol (Found: C, 80.0; H, 4.9. $C_{22}H_{16}O_3$ requires C, 80.5; H, 4.9%). Benzaldehyde and *o*-anisoyl-*o*-hydroxybenzoylmethane gave ω -*o*-anisoyl- ω -*o*-hydroxybenzoylstyrene as pale yellow needles, m. p. 125—126°, from ethanol (72% yield) (Found, in material crystallised several times from ethanol and then from benzene-light petroleum: C, 76.8; H, 5.2; OMe, 8.5. $C_{22}H_{15}O_3 \cdot OMe$ requires C, 77.1; H, 5.0; OMe, 8.7%). Reaction of benzoyl-*o*-hydroxybenzoylmethane with *o*-anisaldehyde gave ω -benzoyl- ω -*o*-hydroxybenzoyl-2-methoxystyrene (84%) as colourless, rectangular prisms, m. p. 135—136°, from ethanol (Found, in substance crystallised twice from ethanol and once from benzene-light petroleum: C, 76.9; H, 5.1; OMe, 8.7. $C_{22}H_{15}O_3 \cdot OMe$ requires C, 77.1; H, 5.0; OMe, 8.7%). From *p*-anisoyl-*o*-hydroxybenzoylmethane and benzaldehyde was obtained ω -*p*-anisoyl- ω -*o*-hydroxybenzoylstyrene (93%), which separated from ethanol as colourless prisms, m. p. 171—172° (Found: C, 76.9; H, 5.0; OMe, 8.7. $C_{22}H_{15}O_3 \cdot OMe$ requires C, 77.1; H, 5.0; OMe, 8.7%). Benzoyl-*o*-hydroxybenzoylmethane and *p*-anisaldehyde gave ω -benzoyl- ω -*o*-hydroxybenzoyl-4-methoxystyrene (87%), which formed colourless needles, m. p. 133—134°, from ethanol (Found: C, 76.2; H, 5.0; OMe, 8.8. $C_{22}H_{15}O_3 \cdot OMe$ requires C, 77.1; H, 5.0; OMe, 8.7%). Benzaldehyde and *o*-hydroxybenzoylveratroylmethane gave ω -*o*-hydroxybenzoyl- ω -veratroylstyrene (86%) which, after 5 crystallisations from ethanol (charcoal at first), was obtained as colourless prisms, m. p. 158—159° [Found: C, 74.0; H, 5.3; OMe, 15.7. $C_{22}H_{14}O_3(OMe)_2$ requires C, 74.2; H, 5.2; OMe, 16.0%]. Veratraldehyde and benzoyl-*o*-hydroxybenzoylmethane gave ω -benzoyl- ω -*o*-hydroxybenzoyl-3 : 4-dimethoxystyrene (83%), which separated from benzene-light petroleum as colourless needles, m. p. 153—154° [Found, in material recrystallised from ethanol and again from benzene-light petroleum: C, 74.3; H, 5.4; OMe, 15.2. $C_{22}H_{14}O_3(OMe)_2$ requires C, 74.2; H, 5.2; OMe, 16.0%]. Trimethoxybenzaldehyde and benzoyl-*o*-hydroxybenzoylmethane gave ω -benzoyl- ω -*o*-hydroxybenzoyl-3 : 4 : 5-trimethoxystyrene (94%), which was crystallised twice from ethanol and obtained as fine, colourless needles, m. p. 150.5° [Found: C, 71.9; H, 5.1; OMe, 21.8. $C_{22}H_{13}O_3(OMe)_3$ requires C, 71.7; H, 5.3; OMe, 22.2%]. *p*-Anisaldehyde and *o*-hydroxybenzoylveratroylmethane gave ω -*o*-hydroxybenzoyl-4-methoxy- ω -veratroylstyrene (83%); after several crystallisations from ethanol, this formed colourless needles which became yellow on melting at 131—132° [Found: C, 71.5; H, 5.2; OMe, 20.9. $C_{22}H_{13}O_3(OMe)_3$ requires C, 71.7; H, 5.3; OMe, 22.2%].

Preparation of 3-Aroylflavones (I and X; R and R' = aryl).—These compounds were prepared from the corresponding benzoyl-*o*-hydroxybenzoylstyrenes by oxidation with selenium dioxide in amyl-alcoholic solution. The 3-arylfavones were not always easily isolated from the reaction mixtures, and the procedure adopted for working up the product depended on whether the 3-aryl group in the flavone was methoxylated (method A) or unsubstituted (method B).

Method A. 3-(3 : 4 : 5-Trimethoxybenzoyl)flavone. ω -*o*-Hydroxybenzoyl- ω -3 : 4 : 5-trimethoxybenzoylstyrene (6.2 g.) in *n*-amyl alcohol (100 c.c.) was refluxed with selenium dioxide (6.0 g.) for 17 hours, and the solution was then filtered hot, and the solid elementary selenium washed with a little hot amyl alcohol. To the filtrate was now added light petroleum and, after cooling to 0°, the solid product was collected and crystallised from ethanol (yield, 3.6 g.), and then from benzene-light petroleum, giving 3-(3 : 4 : 5-trimethoxybenzoyl)flavone as colourless prisms, m. p. 163° [Found: C, 72.1; H, 4.9; OMe, 22.4. $C_{22}H_{11}O_3(OMe)_3$ requires C, 72.1; H, 4.8; OMe, 22.4%].

Method B. 3-Benzoyl-2'-methoxyflavone. ω -Benzoyl- ω -*o*-hydroxybenzoyl-2-methoxystyrene (10 g.) in *n*-amyl alcohol (50 c.c.) was boiled under reflux for 12 hours with selenium dioxide (10 g.), and the filtered solution was subjected to steam-distillation to remove the amyl alcohol. The non-volatile residue was extracted into benzene, and the benzene solution was washed with aqueous sodium carbonate and water, dried, and distilled to dryness under diminished pressure, and the residual material was crystallised from ethanol (yield 6.1 g.). Further crystallisation from ethanol, then from benzene-light petroleum, and finally from ethanol gave the pure 3-benzoyl-2'-methoxyflavone as colourless plates, m. p. 139° (Found: C, 77.5; H, 4.6; OMe, 9.0. $C_{22}H_{13}O_3 \cdot OMe$ requires C, 77.5; H, 4.5; OMe, 8.7%).

3-Benzoylflavone was prepared (method B) from ω -benzoyl- ω -*o*-hydroxybenzoylstyrene and crystallised from ethanol (yield 56%). Further crystallisation gave the pure compound as long, colourless needles, m. p. 130—131° (Found: C, 80.9; H, 4.3. Calc. for $C_{22}H_{14}O_3$: C, 80.8; H, 4.3%).

3-*o*-Anisoylflavone, prepared (method A) from ω -*o*-anisoyl- ω -benzoylstyrene, was crystallised from ethanol (yield 87%). For analysis it was crystallised several times from ethanol and then from benzene-light petroleum, giving colourless irregular prisms, m. p. 129° (Found: C, 78.1; H, 4.6; OMe, 8.7. $C_{22}H_{13}O_3 \cdot OMe$ requires C, 77.5; H, 4.5; OMe, 8.7%).

3-*p*-Anisoylflavone was prepared (method A) from ω -*p*-anisoyl- ω -*o*-hydroxybenzoylstyrene and crystallised from ethanol (yield 70%). Recrystallisation from the same solvent gave the pure substance as colourless, irregular plates, m. p. 168° (Found: C, 77.3; H, 4.7; OMe, 8.7%).

3-Benzoyl-4'-methoxyflavone was prepared by the oxidation of ω -benzoyl- ω -*o*-hydroxybenzoyl-4-methoxystyrene (method B) and crystallised from ethanol (yield 72%). Further crystallisation from the same solvent gave colourless prisms, m. p. 143° (Found: C, 77.7; H, 4.8. $C_{22}H_{14}O_4$ requires C, 77.5; H, 4.5%).

3-Veratroylflavone was prepared by oxidation of ω -*o*-hydroxybenzoyl- ω -veratroylstyrene (method A), and after one crystallisation from ethanol gave a crude product (85%), m. p. 115—135°. A persistent impurity was removed by boiling the product in ethanol with charcoal and recrystallising it several times from the same solvent, giving, finally, small, colourless prisms which softened at 120° and melted at 165—166° [Found: C, 75.1; H, 4.7; OMe, 14.5. $C_{22}H_{12}O_3(OMe)_2$ requires C, 74.6; H, 4.7; OMe, 16.1%].

3-Benzoyl-3' : 4'-dimethoxyflavone was prepared from ω -benzoyl- ω -*o*-hydroxybenzoyl-3 : 4-dimethoxystyrene (method B) and crystallised from ethanol (yield 71%). The pure substance was obtained by

crystallising twice from benzene–light petroleum, and then from ethanol, giving colourless prisms, m. p. 165° (Found: C, 74.4; H, 4.6; OMe, 15.6%).

3-Benzoyl-3': 4': 5'-trimethoxyflavone, prepared from ω -benzoyl- ω -o-hydroxybenzoyl-3: 4: 5-trimethoxystyrene by method B, was crystallised from ethanol (yield 57%). Further crystallisation from ethanol, then from benzene–light petroleum, and finally from ethanol, gave colourless prisms, m. p. 165° [Found: C, 72.7; H, 5.4; OMe, 20.9. $C_{22}H_{11}O_3(OMe)_3$ requires C, 72.1; H, 4.8; OMe, 22.4%].

4'-Methoxy-3-veratroylflavone was obtained by the oxidation of ω -o-hydroxybenzoyl-4-methoxy- ω -veratroylstyrene (method A) and crystallised from ethanol (89% yield). As in the case of 3-veratroylflavone this product contained a persistent impurity which was removed by boiling the ethanolic solution with charcoal and repeated crystallisation from the same solvent, giving finally colourless crystalline aggregates, m. p. 161° (Found: C, 72.2; H, 4.8%).

Reaction of Benzylamine with 3-Benzoylflavone.—3-Benzoylflavone (0.2 g.) in benzene (2 c.c.) was treated with benzylamine (0.14 g.), and the resulting yellow solution was heated on the water-bath for 8 hours. After removal of the benzene under diminished pressure the oily residue was treated with water and a little ethanol, and after solidification had occurred the product was crystallised twice from ethanol, giving yellow needles (0.09 g.), m. p. 98° (Found: C, 80.2; H, 5.6; N, 4.4. $C_{22}H_{19}O_2N$ requires C, 80.2; H, 5.8; N, 4.2%). This 2- β -benzylaminocinnamoylphenol (XI; R = Ph) exhibits a brilliant yellow fluorescence in ultra-violet light. The above ethanolic mother-liquors yielded by careful crystallisation a further amount (0.05 g.) of the same substance, and a smaller quantity of the more soluble and difficultly isolable benzobenzylamide (XII; R' = Ph), which, after crystallisation from light petroleum, formed colourless needles, m. p. 106–107°, undepressed when mixed with a specimen, m. p. 106–107°, prepared by the method of Dermer and King (*J. Org. Chem.*, 1943, 8, 169) from methyl benzoate and benzylamine.

Reaction of Benzylamine with 3-o-Anisoylflavone.—The flavone (1.0 g.) in anhydrous pyridine (10 c.c.) and benzylamine (0.65 g.) was boiled under reflux for 12 hours, cooled, poured into dilute hydrochloric acid, the yellow oil extracted into ether–benzene, the extracts were dried ($MgSO_4$) and the solvents removed finally under diminished pressure. The yellow product was crystallised twice from ethanol (yield after one crystallisation, 0.73 g.), giving yellow needles, m. p. 98°, undepressed on admixture with the specimen of 2- β -benzylaminocinnamoylphenol prepared as above. The material (0.62 g.) contained in the alcoholic mother-liquors was crystallised from ethanol and then 3 times from benzene–light petroleum, giving o-anisobenzylamide as colourless prisms, m. p. 87–88° (Found: C, 74.9; H, 6.5; N, 5.1; OMe, 12.7. $C_{14}H_{12}ON \cdot OMe$ requires C, 74.7; H, 6.2; N, 5.8; OMe, 12.9%).

Reaction of Benzylamine with 3-Benzoyl-2'-methoxyflavone.—The flavone (1.0 g.) was treated with benzylamine as in the previous case. The product was crystallised once from ethanol (15 c.c.), giving 2-(β -benzylamino-2-methoxycinnamoyl)phenol as greenish-yellow cubes (0.88 g.), which, after further crystallisation from ethanol and then from benzene–light petroleum, had m. p. 125° (Found: C, 76.9; H, 5.9; N, 3.9; OMe, 8.6. $C_{22}H_{18}O_2 \cdot OMe$ requires C, 76.9; H, 5.9; N, 3.9; OMe, 8.6%). Dilution of the mother-liquors with water gave crude benzobenzylamide (0.57 g.), which, after two recrystallisations from ethanol, had m. p. and mixed m. p. 105–106°.

Reaction of Benzylamine with 3-p-Anisoylflavone.—Treatment of this flavone (1 g.) in pyridine (25 c.c.) with benzylamine (0.65 g.) as in the previous cases gave a mixture from which was isolated, by crystallisation from ethanol, 2- β -benzylaminocinnamoylphenol (total yield 0.77 g.) as yellow needles, m. p. and mixed m. p. 98°. The mother-liquors were diluted, and after being boiled with charcoal, deposited fine, colourless needles of p-anisobenzylamide (0.1 g.), m. p. 125–128°, raised to 131° after 2 further crystallisations (Beckmann, *Ber.*, 1904, 37, 4138, records m. p. 131°).

Reaction of Benzylamine with 3-Benzoyl-4'-methoxyflavone.—The flavone (1.0 g.) in benzene (10 c.c.) was treated with benzylamine (0.65 g.) as in the previous cases, the reaction product was shaken with cold ethanol (15 c.c.), and the solid 2-(β -benzylamino-4-methoxycinnamoyl)phenol (0.45 g.) collected. Two recrystallisations from ethanol gave the pure compound as yellow needles, m. p. 127–127.5° (Found: C, 76.5; H, 6.1; N, 4.0. $C_{22}H_{21}O_3N$ requires C, 76.9; H, 5.9; N, 3.9%). The ethanolic mother-liquors gave by concentration a further quantity (0.32 g.) of this substance, and the final liquors, after dilution with water, treatment with charcoal, and filtration while hot, yielded a small quantity (ca. 0.1 g.) of benzobenzylamide, m. p. and mixed m. p. 107°.

Reaction of Benzylamine with 3-Veratroylflavone.—The flavone (1.0 g.) in pyridine (10 c.c.) was boiled under reflux with benzylamine (0.6 g.) for 16 hours. The reaction product isolated in the usual way was dissolved in boiling ethanol, and on cooling deposited yellow needles of 2-(β -benzylaminocinnamoyl)phenol (0.74 g.), m. p. and mixed m. p. 98°. The mother-liquors were concentrated, and when kept deposited crude veratrobenzylamide (0.5 g.), which after twice crystallising from aqueous methanol formed colourless needles, m. p. 137° [Found: C, 71.2; H, 6.3; N, 4.9; OMe, 23.6. $C_{14}H_{11}ON(OMe)_2$ requires C, 70.8; H, 6.3; N, 5.2; OMe, 22.9%].

Reaction of Benzylamine with 3-Benzoyl-3': 4'-dimethoxyflavone.—The flavone (1.0 g.) in pyridine (10 c.c.) was boiled with benzylamine for 15 hours. The product, isolated as in the previous cases, was crystallised from ethanol, giving yellow plates (0.92 g.) of 2-(β -benzylamino-3: 4-dimethoxycinnamoyl)phenol, which, after further crystallisation from benzene–light petroleum and again from ethanol, had m. p. 144° [Found: C, 74.1; H, 6.0; N, 3.6; OMe, 15.6. $C_{22}H_{17}O_2N(OMe)_2$ requires C, 74.0; H, 5.9; N, 3.6; OMe, 15.9%]. The mother-liquors yielded benzobenzylamide (0.37 g.), which, after two recrystallisations from aqueous ethanol, had m. p. and mixed m. p. 105–106°.

Reaction of Benzylamine with 3-(3: 4: 5-Trimethoxybenzoyl)flavone.—The flavone (1.0 g.), pyridine (10 c.c.), and benzylamine (0.55 g.) were boiled together for 9 hours, and the products isolated in the usual way and crystallised from ethanol (10 c.c.). 2-(β -Benzylaminocinnamoyl)phenol (0.63 g.) separated as

yellow needles, which after recrystallisation from ethanol had m. p. and mixed m. p. 98°. The diluted mother-liquors were extracted with ether, and the extract deposited colourless needles of 3 : 4 : 5-*trimethoxybenzobenzylamide* (0.15 g.), which, after crystallising 3 times from aqueous ethanol, formed colourless needles, m. p. 141° [Found: C, 67.7; H, 6.3; N, 4.8; OMe, 31.3. $C_{14}H_{13}ON(OMe)_3$ requires C, 67.3; H, 6.9; N, 4.6; OMe, 30.7%]. Further quantities of the phenol (0.13 g.) and of the amide (0.28 g.) were obtained by suitable crystallisation of the mother-liquors.

Reaction of Benzylamine with 3-Benzoyl-3' : 4' : 5'-trimethoxyflavone.—The flavone (1.0 g.) was treated with benzylamine as in the previous case, and the isolated reaction product was crystallised from ethanol, giving 2-(β -benzylamino-3 : 4 : 5-*trimethoxycinnamoyl*)phenol (0.80 g.), which, after twice crystallising from ethanol, formed bright yellow prisms, m. p. 115° [Found: C, 71.7; H, 5.9; N, 3.4; OMe, 21.6. $C_{22}H_{16}O_2N(OMe)_3$ requires C, 71.6; H, 6.0; N, 3.3; OMe, 22.2%]. Dilution of the mother-liquors gave crude benzobenzylamide (0.5 g.), which after crystallisation from aqueous ethanol had m. p. and mixed m. p. 106—107°.

Reaction of Benzylamine with 4'-Methoxy-3-veratroylflavone.—The flavone (1.0 g.), pyridine (10 c.c.), and benzylamine (0.55 g.) were boiled for 16 hours, and the product, isolated as usual, was crystallised from ethanol, giving 2-(β -benzylamino-4-methoxycinnamoyl)phenol (0.75 g.), m. p. and mixed m. p. 126—127°. Addition of water to the mother-liquor gave veratrobenzylamide, which after crystallisation from aqueous methanol was obtained as needles, m. p. and mixed m. p. 137°.

3-o-Hydroxybenzoylflavone.—3-*o*-Anisoylflavone (1.0 g.) was boiled under reflux with glacial acetic acid (30 c.c.) and aqueous hydrobromic acid (40 c.c.; 48%) for 8 hours. The solid which separated after the addition of water (200 c.c.) was collected, washed, dried (0.91 g.), and crystallised 3 times from ethanol, giving colourless plates, m. p. 199—200° (Found, in material dried at 100° for $\frac{3}{4}$ hour: C, 77.6; H, 4.5. $C_{22}H_{14}O_4$ requires C, 77.1; H, 4.1%). This 3-*o*-hydroxybenzoylflavone gives no colour with ferric chloride in alcohol, and shows only very weakly phenolic properties. It is insoluble in aqueous sodium hydroxide, but forms a sodium salt in aqueous-acetone solution of this alkali.

The authors are grateful to the Department of Scientific and Industrial Research for a maintenance allowance (awarded to F. G.), and to the Directors of Imperial Chemical Industries Limited for a grant.

THE UNIVERSITY, BRISTOL.

[Received, June 19th, 1950.]