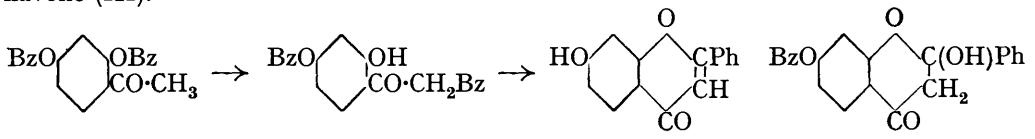
322. *Molecular Rearrangement of Some* o-*Acyloxyacetophenones and the Mechanism of the Production of* 3-*Acylchromones.*

By Wilson Baker.

In an attempt to prepare its benzyl ether, 4-O-*benzoylresacetophenone* (prepared from benzoyl chloride, resacetophenone, and aqueous sodium hydroxide) was heated in benzene with benzyl chloride (1 mol.) and anhydrous potassium carbonate; the product (20% yield), however, was ω : 4-*dibenzoylresacetophenone* (2-*hydroxy*-4-*benzoyloxydibenzoylmethane*) (II). Alkaline hydrolysis of the weakly phenolic compound yielded both acetophenone and benzoic acid, and cold concentrated sulphuric acid converted it smoothly into 7-hydroxyflavone (III).



(I.) (II.) (III.) (IV.)

It was evident that the benzyl chloride had taken no essential part in the formation of (II), and this was confirmed by its preparation from 4-*O*-benzoylresacetophenone and also from resacetophenone by the action of one and two molecules of benzoyl chloride respectively in benzene in presence of potassium carbonate (yields, about 20%). The interaction of three molecules of benzoyl chloride and resacetophenone under similar conditions was very slow, and the yield was only 8%.

The result of the last experiment made it very unlikely that the ω-benzoylation resulted from a direct attack on the methyl group by benzoyl chloride, and, further, no dibenzoylmethane was obtained by treating acetophenone with benzoyl chloride in benzene in presence of potassium carbonate. It was then found that resacetophenone dibenzoate (I), when heated with benzene or toluene and potassium carbonate, underwent intramolecular rearrangement, giving ω : 4-dibenzoylresacetophenone (II).

The migration concerns solely the *o*-benzoyloxy-group, since it occurs neither in 4-*O*-benzoylresacetophenone nor in *p*-benzoyloxyacetophenone, and, further, if two different

aroyl radicals esterify the hydroxyl groups of resacetophenone, only the one in the ortho-position migrates: *e.g.*, from 4-O-*benzoyl*-2-O-*anisoylresacetophenone* was obtained ω : 4-*dianisoylresacetophenone*, convertible into 7-hydroxy-4'-methoxyflavone. ω : 4-Dianisoylresacetophenone was also obtained both by the action of anisoyl chloride on resacetophenone (4-O-*anisoylresacetophenone* was obtained as a by-product) and by the rearrangement of *resacetophenone dianisate*.

The *o*-hydroxydibenzoylmethanes produced by molecular rearrangement separate as their bright yellow potassium salts. The potassium has displaced hydrogen in the 1 : 3-diketonic portion of the molecule and not that of the phenolic hydroxyl group, since, *e.g.*, (II) is rapidly removed from its benzene solution by boiling with potassium carbonate, whereas an *o*-hydroxyacetophenone forms no potassium salt under these conditions. The salts may, therefore, be completely freed from other products by washing with hot benzene and yield almost pure *o*-hydroxydibenzoylmethanes by decomposition with water. Their formation, however, necessarily involves the liberation of a molecule of water, which may cause partial hydrolysis of the benzoyl (or other aroyl) groups, this in turn leading to the production of benzoic acid, then potassium benzoate, and liberation of another water molecule. It is, therefore, not surprising that the yields obtained in these molecular rearrangements are only 20—40% of the theoretical.

In certain cases the rearrangement is accompanied by intermolecular reaction; *e.g.*, 4-*O*-benzoyl-2-*O*-anisoylresacetophenone gives ω : 4-dianisoylresacetophenone, and 2-O-*benzoyl*-4-O-*acetylresacetophenone* gives ω : 4-dibenzoylresacetophenone (II), both in poor yield. The formation of (II) during the attempted benzylation of 4-*O*-benzoylresacetophenone probably involves partial exchange of the benzoyl group for the benzyl group with liberation of benzoyl chloride; this will then attack 4-*O*-benzoylresacetophenone with formation of resacetophenone dibenzoate (I), which then undergoes the normal rearrangement.

The ring closure of the *o*-hydroxydibenzoylmethanes is effected with concentrated sulphuric acid or with boiling acetic acid and sodium acetate. Hydrolysis of any aroyloxy-groups occurs in both methods, although frequently it is incomplete in the latter; ring closure, however, occurs rapidly and hydrolysis may then be completed with methyl-alcoholic potash. Ring closure without hydrolysis of the aroyloxy-groups is rapidly effected by hot acetic acid containing a trace of hydrochloric acid (compare Wittig, *Annalen*, 1925, **446**, 155); *e.g.*, (II) is converted into 7-*benzoyloxyflavone*. Ring closure probably takes place through a 2-hydroxyflavanone derivative (IV), which then loses a molecule of water; it is also possible that (IV) may be an intermediate during the migration of the benzoyl group.

The generality of the new rearrangement is made evident by the following examples. *o*-Benzoyloxyacetophenone gave *o*-hydroxydibenzoylmethane in 32% yield, from which flavone was quantitatively prepared. *Resacetophenone diveratrate* gave ω : 4-*diveratroylresacetophenone*, from which 7-*hydroxy*-3' : 4'-*dimethoxyflavone* was prepared. *Gallacetophenone tribenzoate* furnished ω : 3 : 4-*tribenzoylgallacetophenone*, convertible into 7 : 8-dihydroxyflavone. Resacetophenone and cinnamoyl chloride in presence of toluene and potassium carbonate gave directly 7-*cinnamoyloxy*-2-*styrylchromone* and 4-O-*cinnamoylresacetophenone*; and 2 : 4-dihydroxyphenyl benzyl ketone, treated with benzoyl chloride and potassium carbonate in toluene, gave 7-hydroxy-2 : 3-diphenylchromone (Baker and Robinson, J., 1925, **127**, 1985). Slightly modified treatment after the reaction led to the isolation of 2-*hydroxy*-4-*benzoyloxyphenyl benzyl ketone* and 2-hydroxy-4-benzoyloxybenzoic acid, the latter evidently arising by hydrolysis of the intermediate dibenzoylmethane derivative. Neither resacetophenone diacetate nor 4-O-*benzoyl*-2-O-*acetylresacetophenone* underwent rearrangement.

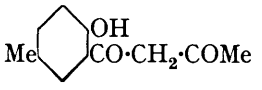
The synthesis of flavones and related compounds through the *o*-hydroxydibenzoylmethanes involves the use of only the theoretical amount of the appropriate acid chloride (compare the recent modification of the " fusion " method; Chavan and Robinson, this vol., p. 368) and very mild temperature conditions, and is thus of interest in connexion with the synthesis of flavone glucosides. Although the migrations here described were

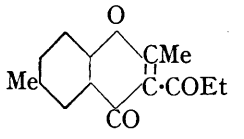
actually carried out at about 95°, resacetophenone dibenzoate (I) is slowly transformed into ω : 4-dibenzoylresacetophenone (II) by the usual reagents at 35°, a 24% yield being obtained after 14 days; a complete synthesis of a flavone has thus been effected below 35°.

The production of *o*-hydroxydibenzoylmethanes by migration furnishes an explanation of the formation of the 3-acylated chromones which are sometimes isolated when an *o*-hydroxyacetophenone is heated with the anhydride and the sodium salt of a carboxylic acid. Thus resacetophenone, acetic anhydride, and sodium acetate yield 7-acetoxy-3-acetyl-2-methylchromone (Tahara, *Ber.*, 1892, **25**, 1302; Nagai, *ibid.*, p. 1287; von Kostanecki and Rozycki, *Ber.*, 1901, **34**, 107). Acylation in position 3 does not always occur, but it must be remembered that in nearly all the cases in which the reaction has since been used for the synthesis of flavones, flavonols, etc., the whole product of the reaction has been hydrolysed with alcoholic sodium or potassium hydroxide, so that a 3-acylated derivative, if present, would lose its acetyl group. Several cases are, however, recorded of the production of 3-acylated chromones in the naphthalene series (Bhullar and Venkataraman, J., 1931, 1165; Menon and Venkataraman, *ibid.*, p. 2591).

3-Acylation is probably much more general than is usually supposed, for, when the product is worked up with prevention of hydrolysis, 3-acylchromones seem to be invariably isolated. Thus Algar, McCarthy, and Dick (*Proc. Royal Irish Acad.*, 1933, **41**, 155) report the isolation of 3 : 3′-dibenzoyldiflavone from the product of interaction of resdiacetophenone, benzoic anhydride, and sodium benzoate, and it has now been found that benzoic anhydride and sodium benzoate act upon resacetophenone to give *7-benzoyloxy-3-benzoylflavone* and a much smaller amount of 7-benzoyloxyflavone. 7-Benzoyloxy-3-benzoylflavone is readily hydrolysed to 7-hydroxyflavone.

Two explanations of the formation of these acylated chromones have been advanced. (1) Schneider and Kunau (*Ber.*, 1921, **54**, 2302) suggested that an acyl group might be directly introduced into the 3-position of a preformed chromone: this type of reaction, however, is unknown (see Wittig, *Annalen*, 1925, **446**, 159). (2) Wittig (*loc. cit.*) rejected the possibility of intermediate 1 : 3-diketone formation, since the methyl ether of 2-acetyl-3 : 5-dimethylphenol gave no 1 : 3-diketone when boiled with acetic anhydride and sodium acetate; and in order to account for the formation of the 3-acyl derivatives he proposed a series of reactions which require, for example, that the action of propionic anhydride and sodium propionate on 2-acetoacetyl-4-methylphenol (V) should give 3-propionyl-2 : 6-dimethylchromone (VI) and not the isomeric 3-acetyl-6-methyl-2-ethylchromone (VII).

(V.) 



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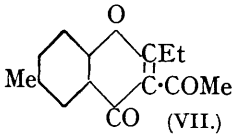

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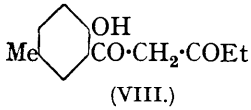

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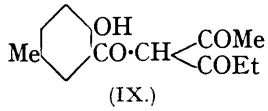


(IX.)

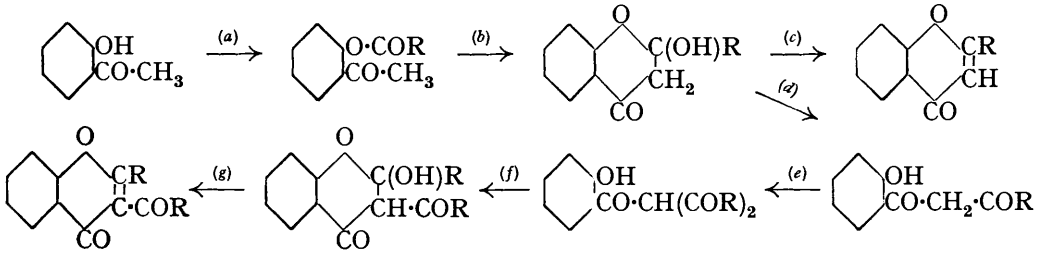
The actual product of this reaction was regarded as (VI) because on boiling with aqueous sodium carbonate it yielded 2 : 6-dimethylchromone (*loc. cit.*, p. 203). This observation has now been verified, but it must be pointed out that hydrolysis experiments are not to be relied upon in deciding the constitution of such compounds, since, if the chromone ring opens during the reaction, identical products might be expected from both (VI) and (VII).

It has now been found that the product formed by heating *2-propionoacetyl-4-methylphenol* (VIII) (prepared from 2-acetyl-4-methylphenol, ethyl propionate, and sodium), acetic anhydride, and sodium acetate is identical with that obtained by heating 2-acetoacetyl-4-methylphenol (V), propionic anhydride, and sodium propionate. This fact at once disproves Wittig's mechanism, which requires these reactions to give isomeric pro-

ducts (VII) and (VI) respectively, and also shows that (VIII) and (V) do not each first undergo esterification of the phenolic group, followed by dehydration,* since this would require the production of the isomeric compounds (VI) and (VII) respectively.

The only explanation in harmony with the new observation is that acylation occurs on the methylene carbon atom of the 1 : 3-diketone, so that both (V) and (VIII) yield the same intermediate (IX), which will then undergo ring closure presumably in one direction only, the product being *probably* correctly regarded by Wittig as 3-propionyl-2 : 6-dimethylchromone (VI).

The following mechanism for the production of chromones and 3-acylated chromones when an *o*-hydroxyacetophenone is heated with the anhydride and the sodium salt of a carboxylic acid may now be advanced :



(*a*) Esterification of the phenolic hydroxyl group. (*b*) Closure to a 2-hydroxyflavanone (or possibly a 2-acyloxyflavanone); a compound of this type has been isolated by Wittig (*Annalen*, 1925, **446**, 203) by boiling 4-chloro-2-*iso*butyrylphenol with acetic anhydride and sodium acetate, loss of water being impossible. (*c*) Loss of a molecule of water with production of the chromone. (*d*) Alternatively to (*c*), the ring of the 2-hydroxyflavanone may open to give the diketone under the influence of the sodium salt of the acid. (*e*) Acylation of the methylene carbon atom to give a triacylmethane derivative. This step is, perhaps, best regarded as a direct *C*-acylation rather than migration of an acyl group from the phenolic oxygen atom, since, if such migration occurred through the 2-hydroxyflavanone, isomeric and not identical products might be expected from compounds (V) and (VIII). (*f*) Closure to the 2-hydroxy-3-acylflavanone, followed by (*g*) dehydration to the 3-acylchromone.

The preparation of a 1 : 3-diketone by migration of an aliphatic acid radical in an *o*-acyloxyacetophenone has not yet been effected, and, owing to subsequent reactions, there can be no direct proof that an aromatic acid radical can migrate under the influence of its anhydride and sodium salt. No reasonable doubt, however, can now be entertained that such reactions may occur.

Experimental.

4-O-*Benzoylresacetophenone*.—To a stirred solution of resacetophenone (60·8 g.) in water (300 c.c.) containing sodium hydroxide (18 g.), benzoyl chloride (60 g.) was added during 2 hours. The solid product was crystallised from much alcohol (yield, 70 g.) and on recrystallisation formed small plates, m. p. 106—107° (Found : C, 69·8; H, 4·7. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%). It gave a cherry-red colour with alcoholic ferric chloride. The *acetyl* derivative (boiling acetic anhydride) separated from methyl alcohol in pale cream-coloured prisms, m. p. 82—83° (Found : C, 68·5; H, 4·9. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%).

Resacetophenone Dibenzoate (I).—A mixture of resacetophenone (30·4 g.), pyridine (60 c.c.), and benzoyl chloride (56·2 g.; 2 mols.) was heated on the steam-bath for 15 minutes, poured into water, and stirred with dilute hydrochloric acid and then with alcohol. After it had solidified, the product was washed with cold alcohol, dried at room temperature (yield, 53 g.), and crystallised from methyl alcohol, forming six-sided plates, m. p. 80—81° (Found : C, 73·0;

* This mechanism is implied in the statement of Algar, McCarthy, and Dick (*loc. cit.*) that the interaction of 4 : 6-dibenzoylacetoresorcinol with acetic anhydride and sodium acetate yields 3 : 3′-dibenzoyl-2 : 2′-dimethyldichromone. It is now evident, however, that the substance may equally well be the isomeric 3 : 3′-diacetyldiflavone. Again, Müller's " acetyl derivative " of *o*-hydroxydibenzoylmethane—really the anhydroacetyl derivative—may be either 3-acetylflavone or 3-benzoyl-2-methylchromone.

H, 4·6. Calc. for $C_{22}H_{16}O_5$: C, 73·3; H, 4·5%). This substance was prepared in an impure state by Torrey and Kipper (*J. Amer. Chem. Soc.*, 1907, **29**, 80) from resacetophenone and benzoyl chloride at 100—170°; when prepared in this manner, it is very difficult to purify, but is identical (mixed m. p.) with that described above.

4-O-*Acetylresacetophenone*.—Powdered resacetophenone (40 g.) and anhydrous sodium acetate (40 g.) were stirred with acetic anhydride (80 c.c.), finally at 50°. The product precipitated by water formed prisms (40 g.) from methyl alcohol; m. p. 75—76° (see Tahara, *Ber.*, 1892, **25**, 1300).

2-O-*Benzoyl*-4-O-*acetylresacetophenone*.—Benzoyl chloride (14·1 g.) was added to 4-*O*-acetylresacetophenone (19·4 g.) in pyridine (50 c.c.), and after 12 hours the product was poured into water and extracted with ether. The extracts were shaken successively with water, dilute hydrochloric acid, and dilute aqueous sodium carbonate, dried over calcium chloride, and distilled, leaving an oil (26 g.) which solidified when stirred under ligroin (b. p. 40—60°). This separated from a little methyl alcohol in thick rhombic plates, m. p. 67° (Found: C, 68·7; H, 4·8. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%).

ω : 4-*Dibenzoylresacetophenone* (II).—(A) *Benzoylation of* 4-O-*benzoylresacetophenone*. 4-*O*-Benzoylresacetophenone (12·8 g.), toluene (50 c.c.), freshly ignited potassium carbonate (20 g.), and benzoyl chloride (7 g.; 1 mol.) were stirred on the steam-bath for 15 hours [a yellow colour gradually developed after about 4 hours, and toluene (50 c.c.) was added after 7 hours owing to thickening of the mixture]. The liquid was filtered hot, and the solid washed with hot benzene, dried, stirred into cold water, collected, dried, and recrystallised from benzene, giving ω : 4-dibenzoylresacetophenone (II) (3·9 g.). When benzyl chloride (7·6 g.) was substituted for the benzoyl chloride, the reaction was complete in 6 hours, (II) (3·5 g.) being obtained as before.

(B) *Benzoylation of resacetophenone*. Resacetophenone (15·2 g.), toluene (100 c.c.), anhydrous potassium carbonate (40 g.), and benzoyl chloride (28·1 g.; 2 mols.) were stirred as above for 5 hours, toluene (100 c.c.) being added after 2 hours; (II) (yield, 5·7 g.) was isolated as before (the original benzene filtrate yielded 13·4 g. of crude 4-*O*-benzoylresacetophenone).

(C) *Rearrangement of resacetophenone dibenzoate* (I). Resacetophenone dibenzoate (20 g.), toluene (200 c.c.), and potassium carbonate (60 g.) were stirred on the steam-bath for 4 hours. (II) was isolated as usual, washed with cold methyl alcohol, dried at a moderate temperature (yield, 16·5 g.), and converted into 7-hydroxyflavone by method (a) (below) (yield, 5·3 g., 40% calculated on the dibenzoate).

(D) *Rearrangement of* 2-O-*benzoyl*-4-O-*acetylresacetophenone*. Rearrangement (of 10 g.) was effected as under (C), and, after crystallisation from acetone, pure ω : 4-dibenzoylresacetophenone (0·1 g.), m. p. and mixed m. p. 167°, was isolated.

ω : 4-*Dibenzoylresacetophenone* separates from benzene in yellow lustrous needles, m. p. 167° (Found: C, 73·3; H, 4·7. $C_{22}H_{16}O_5$ requires C, 73·3; H, 4·5%). It also crystallises from alcohol or acetone, but some loss of material occurs. Its alcoholic solution develops a reddish-brown coloration with ferric chloride. It is insoluble in cold aqueous sodium hydroxide, but gives a yellow solution on warming.

7-*Hydroxyflavone* (III).—(a) ω : 4-Dibenzoylresacetophenone (5 g.) was boiled for 6 hours with acetic acid (50 c.c.) and sodium acetate (10 g.), and the product poured into water. 7-Hydroxyflavone separated from methyl alcohol in needles, m. p. 240° (yield, 90%), and its acetyl derivative from alcohol in needles, m. p. 129—130° (compare Robinson and Venkataraman, J., 1926, 2345).

(b) ω : 4-Dibenzoylresacetophenone (5 g.) was dissolved in concentrated sulphuric acid (25 c.c.). The yellow colour of the solution rapidly faded and a bright blue fluorescence developed; after 4 hours the solution was poured into water, and the 7-hydroxyflavone was collected and crystallised as before (yield, 76%).

7-*Benzoyloxyflavone*.—ω : 4-Dibenzoylresacetophenone (2 g.) was heated on the steam-bath for 5 minutes with acetic acid (19 c.c.) and concentrated hydrochloric acid (1 c.c.) and poured into water. The solid separated from alcohol in long lustrous needles, m. p. 157—158° (Found: C, 76·9; H, 4·1. $C_{22}H_{14}O_4$ requires C, 77·2; H, 4·1%).

Resacetophenone Dianisate.—Prepared from resacetophenone (15·2 g.), pyridine (30 c.c.), and anisoyl chloride (34·1 g.) as in the case of resacetophenone dibenzoate, this *compound* (41 g.) separated from much alcohol in bunches of tiny crystals, m. p. 118° (Found: C, 68·6; H, 4·9. $C_{24}H_{20}O_7$ requires C, 68·6; H, 4·8%).

4-O-*Benzoyl*-2-O-*anisoylresacetophenone*.—A mixture of 4-*O*-benzoylresacetophenone (12·8 g.), pyridine (25 c.c.), and anisoyl chloride (8·6 g.; 1 mol.) was heated on the steam-bath for 15

minutes, and treated with dilute hydrochloric acid. The solid separated from alcohol (charcoal) in prismatic needles (11·5 g.), m. p. 109—110° (Found: C, 70·7; H, 4·6. $C_{23}H_{18}O_6$ requires C, 70·8; H, 4·6%).

ω : 4-*Dianisoylresacetophenone*.—(A) *Anisoylation of resacetophenone*. The compound was prepared in the same way as the corresponding dibenzoyl derivative (method B), anisoyl chloride (34·1 g.; 2 mols.) being used and the mixture heated for 20 hours. The solid residue after filtration and washing with benzene was worked up as before, pure ω : 4-*dianisoylresacetophenone* (7·9 g.; 19%) being obtained. It is very sparingly soluble in alcohol, but separates from benzene in irregular growths of microscopic yellow crystals, m. p. 170—171° (Found: C, 69·0; H, 5·0. $C_{24}H_{20}O_7$ requires C, 68·6; H, 4·7%). Its properties are similar to those of the benzoyl analogue (II), but the solution in concentrated sulphuric acid shows a greenish-blue fluorescence which slowly turns vivid blue, this behaviour being characteristic of 7-hydroxy-4′-methoxyflavone (Robinson and Venkataraman, J., 1926, 2346). The benzene filtrate and washings (above) yielded an oil which solidified in contact with alcohol. This product (20 g.) proved to be crude 4-O-*anisoylresacetophenone*: it is best prepared by shaking an aqueous alkaline solution of resacetophenone (1 mol.) with anisoyl chloride (1 mol.) (compare preparation of 4-*O*-benzoylresacetophenone) and after crystallisation from methyl alcohol and then ethyl acetate, in which it is rather readily soluble, it is obtained in compact flat prisms, m. p. 151° (Found: C, 66·9; H, 4·8. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%). Its solution in alcohol gives a dull purplish-red colour with ferric chloride.

(B) *Rearrangement of resacetophenone dianisate*. The reaction (15 hours) and subsequent isolation of the product were effected in the manner described for the rearrangement of resacetophenone dibenzoate. The ω : 4-dianisoylresacetophenone (6·5 g.) was converted directly into 7-hydroxy-4′-methoxyflavone (2·5 g.) (*vide infra*).

(C) *From* 4-O-*benzoyl*-2-O-*anisoylresacetophenone*. This was done as in the previous case, but the reaction was appreciably slower. After crystallising from benzene and then twice from acetone, the compound was identical (m. p. and mixed m. p.) with ω : 4-dianisoylresacetophenone.

7-*Hydroxy*-4′-*methoxyflavone* (*Pratol*).—ω : 4-Dianisoylresacetophenone (3 g.), acetic acid (30 c.c.), and sodium acetate (6 g.) were refluxed for 8 hours, the solution poured into water, and the resulting solid heated for a few minutes with weak methyl-alcoholic potassium hydroxide, diluted, precipitated by carbon dioxide, collected, and recrystallised from alcohol (charcoal). It separated in very pale yellow, prismatic needles (1·3 g.), m. p. (rapid heating) 263—264° (Found in material dried at 150° in a vacuum over phosphoric anhydride: C, 71·8; H, 4·8. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%). The acetyl derivative (boiling acetic anhydride, 3 hours) separated from alcohol in dimorphic forms, colourless, long, silky needles (*X*) and compact, less soluble hexagonal plates (*Y*) which always exhibited a pale violet colour; when the alcoholic suspension of (*X*) and (*Y*) was warmed, the former dissolved and all subsequently crystallised in the form (*Y*). Both forms appeared to melt at 176—177°, but since it was impossible to obtain (*X*) entirely free from (*Y*), (*X*) was probably converted into the more stable form (*Y*) before melting. 7-Acetoxy-4′-methoxyflavone (Robinson and Venkataraman, *loc. cit.*) and acetyl pratol (Power and Salway, J., 1910, **97**, 231) are described as colourless needles from alcohol, m. p. 166°, and this is doubtless the true m. p. of the unstable form (*X*). The more stable form has not previously been described.

Solution of ω : 4-dianisoylresacetophenone in concentrated sulphuric acid and precipitation by water gave a non-crystalline yellow product, which dissolved in concentrated sulphuric acid with a vivid blue fluorescence. The alteration in the fluorescence of pratol in concentrated sulphuric acid is hence accompanied by chemical change.

o-*Benzoyloxyacetophenone*.—*o*-Hydroxyacetophenone (13·6 g.) (Freudenberg and Orthner, *Ber.*, 1922, **55**, 1748), pyridine (20 c.c.), and benzoyl chloride (14·1 g.) were heated on the steam-bath for 15 minutes. The product solidified when poured into dilute hydrochloric acid; it was washed with dilute aqueous sodium hydroxide and then water and crystallised from alcohol (the solution being cooled to 0°); yield, 13 g.; m. p. 87—88°. Anschütz and Scholl (*Annalen*, 1911, **379**, 338) prepared it by the Schotten–Baumann method.

o-*Hydroxydibenzoylmethane*.—*o*-Benzoyloxyacetophenone (10 g.), potassium carbonate (30 g.), and toluene (100 c.c.) were stirred on the steam-bath for 8 hours and the yellow solid was collected, washed with benzene, and stirred into dilute acetic acid. The *o*-hydroxydibenzoylmethane crystallised from methyl alcohol in thin yellow prisms (3·2 g.), m. p. 121°. It gave a deep reddish-brown colour with ferric chloride in alcohol. Müller (J., 1915, **107**, 872) records m. p. 120°, and a violet colour with ferric chloride in alcohol.

Flavone.—*o*-Hydroxydibenzoylmethane (1 g.) was (a) dissolved in concentrated sulphuric acid (10 c.c.), the yellow colour fading in a few seconds, and after 5 minutes poured into water; or (b) boiled with acetic acid (10 c.c.) and sodium acetate (2 g.) for ½ hour and poured into water. The flavone from (a) had m. p. 96—97°; both specimens crystallised from ligroin (b. p. 60—80°) in colourless tufts of fine needles, m. p. 98°. The yields were almost quantitative.

p-*Benzoyloxyacetophenone.*—*p*-Hydroxyacetophenone was prepared by the method described for the *o*-derivative (Freudenberg and Orthner, *loc. cit.*) and recrystallised from benzene; yield, 40 g. from 100 g. of phenyl acetate. The benzoyl derivative was prepared in the same way as *o*-benzoyloxyacetophenone and crystallised from alcohol; yield, 18 g.; m. p. 134—135° (see Tanret, *Bull. Soc. chim.*, 1894, **11**, 949; Charon and Zamanos, *Compt. rend.*, 1901, **133**, 741).

Resacetophenone Diveratrate.—Prepared from resacetophenone (13·7 g.), pyridine (30 c.c.), and veratroyl chloride (36·1 g.) as in the case of the dibenzoate, this *compound* separated from ethyl acetate–alcohol in tufts of prismatic needles (30 g.), m. p. 151—152° (Found: C, 65·0; H, 5·1. $C_{26}H_{24}O_9$ requires C, 65·0; H, 5·0%).

ω : 4-*Diveratroylresacetophenone.*—Resacetophenone diveratrate (15 g.) was dissolved in boiling toluene (150 c.c.), and the solution stirred on the steam-bath with potassium carbonate (45 g.) for 6 hours. The *product* (8·5 g.) was isolated in the usual way (see corresponding dibenzoyl derivative); after twice crystallising from acetic acid containing a little alcohol, it was obtained in fine, yellow, prismatic needles, m. p. 159—160° (Found: C, 64·7; H, 4·9. $C_{26}H_{24}O_9$ requires C, 65·0; H, 5·0%). In alcohol it gives a greenish-brown colour with ferric chloride.

7-*Hydroxy*-3′ : 4′-*dimethoxyflavone.*—A mixture of ω : 4-diveratroylresacetophenone (5 g.), acetic acid (50 c.c.), and sodium acetate (10 g.) was boiled for 8 hours and poured into water. The product was collected, heated with dilute methyl-alcoholic potassium hydroxide for 5 minutes, diluted, and acidified. 7-*Hydroxy*-3′ : 4′-*dimethoxyflavone*, crystallised from acetic acid–alcohol and then from 50% acetic acid, formed small rhombic plates, m. p. 255° (Found in material dried at 150° in a vacuum: C, 68·1; H, 4·7. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%). The solution in alcohol shows a marked blue-violet fluorescence, and develops no colour with ferric chloride. The solutions in dilute aqueous sodium hydroxide and concentrated sulphuric acid are pale yellow and devoid of fluorescence.

Gallacetophenone Tribenzoate.—To gallacetophenone (16·8 g.; recrystallised from water) in *dry* pyridine (50 c.c.), benzoyl chloride (42·2 g.) was added in portions below 50°. After being kept for 24 hours at room temperature, the product was poured into water, and ethereal extracts were shaken twice with water, then with dilute hydrochloric acid and again with water, dried, and distilled. The thick oily product slowly solidified when rubbed with alcohol and ligroin (b. p. 80—100°) and was finally washed with cold alcohol (yield, 37 g.); m. p. 116—117°. It slowly separated from warm methyl alcohol in compact nodular growths, m. p. 118—119° (Found: C, 72·3; H, 4·3. $C_{29}H_{20}O_7$ requires C, 72·5; H, 4·2%).

ω : 3 : 4-*Tribenzoylgallacetophenone.*—Gallacetophenone tribenzoate (40 g.), toluene (400 c.c.), and potassium carbonate (120 g.) were stirred on the steam-bath for 6 hours. The yellow solid was collected, washed with benzene, dried, stirred into water, and again collected. After boiling with acetic acid–alcohol and cooling, a yellow crystalline powder (18 g.) was obtained. The *compound* separated from acetic acid in small yellow prisms, m. p. 193—194° (Found: C, 72·2; H, 4·3. $C_{29}H_{20}O_7$ requires C, 72·5; H, 4·2%). Its solution in alcohol gave a reddish-brown colour with ferric chloride, and it dissolved in warm aqueous sodium hydroxide with a yellow colour.

7 : 8-*Dihydroxyflavone.*—ω : 3 : 4-Tribenzoylgallacetophenone (5 g.), acetic acid (50 c.c.), and sodium acetate (10 g.) were boiled for 6 hours. The product obtained by dilution with water was heated for 5 minutes with dilute methyl-alcoholic potassium hydroxide, diluted, acidified with acetic acid, again collected, and crystallised twice from alcohol (charcoal) (yield, 60%). It formed pale yellow, rhombic prisms or plates, m. p. 243° (varies with rate of heating). Its solutions in dilute aqueous sodium hydroxide and concentrated sulphuric acid exhibited no fluorescence (compare Venkataraman, J., 1929, 2221). The diacetyl derivative formed needles from alcohol, m. p. 198°.

Cinnamoylation of Resacetophenone.—This was done in the same way as the benzoylation of resacetophenone (method B), toluene (100 c.c.) and cinnamoyl chloride (33·3 g.; 2 mols.) being used, and the mixture heated for 8 hours. The solids were treated in the usual way and recrystallised from acetic acid. The solution deposited flocculent matter, and after filtration was left undisturbed for 2½ hours; compact yellow crystals (*A*; 3·1 g.) then separated, the filtrate

subsequently depositing minute yellow crystals (*B*; 4·2 g.). (*A*), twice crystallised from acetic acid, had m. p. 216—217° (Found: C, 79·7; H, 4·7. $C_{26}H_{18}O_4$ requires C, 79·2; H, 4·6%). In concentrated sulphuric acid the solution is bright orange but quickly fades to yellow, and it possesses a faint green fluorescence (magnesium light). The substance is very sparingly soluble in alcohol and the solution gives no coloration with ferric chloride; it is insoluble in aqueous sodium hydroxide. There can be little doubt that it is 7-*cinnamoyloxy*-2-*styrylchromone*. Compound (*B*) was twice crystallised from acetic acid and formed small yellow prisms, m. p. 131° (Found: C, 72·0; H, 5·0. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%). In alcohol it gives a dull-red colour with ferric chloride, and it is soluble in alkaline solutions only on heating, and the substance is therefore 4-O-*cinnamoylresacetophenone*. The original toluene filtrate and washings deposited crystals (7 g.), from which pure (*A*) (2·7 g.) and (*B*) (0·5 g.) were isolated.

2 : 4-*Dihydroxyphenyl Benzyl Ketone*.—The following method is suitable for preparing the compound in quantity (compare Chapman and Stephen, J., 1923, **123**, 404). Resorcinol (100 g.) and phenylacetonitrile (100 g.) in dry ether (400 c.c.) were saturated with hydrogen chloride at room temperature in presence of powdered anhydrous zinc chloride (20 g.). After 2 days, ether (400 c.c.) was added, and then decanted from the ketimine hydrochloride, which was heated with water for 2 hours. The ketone, extracted with chloroform, was transferred to dilute sodium hydroxide solution, and precipitated by hydrochloric acid (yield, 120 g.). Recrystallisation from benzene gave the almost pure ketone (100 g.).

2-*Hydroxy*-4-*benzoyloxyphenyl benzyl ketone*, prepared from the preceding ketone, benzoyl chloride (1 mol.), and excess of dilute aqueous sodium hydroxide and recrystallised from acetic acid and then from alcohol, formed flat prisms, m. p. 121—122° (Found: C, 75·6; H, 5·0. $C_{21}H_{16}O_4$ requires C, 75·9; H, 4·9%). The position of the benzoyl group is inferred from the facts that the substance gives a cherry-red colour with ferric chloride in alcohol and dissolves in dilute aqueous sodium hydroxide only on heating.

7-*Hydroxy*-2 : 3-*diphenylchromone*.—2 : 4-Dihydroxyphenyl benzyl ketone (11·4 g.), toluene (200 c.c.), potassium carbonate (40 g.), and benzoyl chloride (14 g.; 2 mols.) were stirred for 8 hours on the steam-bath. The solids were collected, washed with benzene and water in the usual way, and crystallised from a small quantity of alcohol (charcoal); 7-hydroxy-2 : 3-diphenylchromone was identified as its acetyl derivative, m. p. and mixed m. p. 208—209°. If water is added after the benzoylation, the aqueous layer yields 2-hydroxy-4-benzoyloxybenzoic acid on acidification—minute needles from benzene, m. p. 190—191° (Found: C, 64·8; H, 3·8. Calc. for $C_{14}H_{10}O_5$: C, 65·1; H, 3·9%) (Bergmann and Dangschat, *Ber.*, 1919, **52**, 382, record m. p. 193—194°); the benzene layer yields 2-hydroxy-4-benzoyloxyphenyl benzyl ketone (4·5 g.).

7-*Benzoyloxy*-3-*benzoylflavone*.—(A) A finely powdered mixture of resacetophenone (10 g.), benzoic anhydride (60 g.), and sodium benzoate (12 g.) was heated for 8 hours at 200°. The sticky product was ground to a paste with sodium carbonate and ice, collected after the addition of a large volume of ice-cold water, and dissolved in hot alcohol (100 c.c.). After 12 hours, solid (12·2 g.) separated which, recrystallised from alcohol–benzene (3 : 1), formed faintly yellow, prismatic needles, m. p. 167° (Found: C, 78·2; H, 4·3. $C_{29}H_{18}O_5$ requires C, 78·0; H, 4·1%). The alcoholic mother-liquors were concentrated and yielded 7-benzoyloxyflavone (4·5 g.). (B) ω : 4-Dibenzoylresacetophenone (2 g.) was heated with benzoic anhydride (12 g.) and sodium benzoate (2·5 g.) for 8 hours at 200°, and the product isolated exactly as under (A), 7-benzoyloxy-3-benzoylflavone (1·2 g.) being isolated from the first crystallisation. 7-*Benzoyloxy*-3-*benzoylflavone* dissolves in concentrated sulphuric acid to a pale yellow solution devoid of fluorescence (compare 7-benzoyloxy- and 7-hydroxy-flavone, which dissolve to colourless solutions with a powerful blue fluorescence). Hydrolysis (of 2 g.) in alcohol (10 c.c.) with potassium hydroxide (2 g.) in water (4 c.c.) for ½ hour on the steam-bath, dilution (odour of acetophenone), and precipitation with carbon dioxide gave 7-hydroxyflavone (0·3 g.).

2-*Propionoacetyl*-4-*methylphenol* (VIII).—*p*-Tolyl acetate, b. p. 214°, was prepared in 84% yield from *p*-cresol (200 g.), 10% aqueous sodium hydroxide (900 c.c.), ice, and acetic anhydride (200 g.) (see Chattaway, J., 1931, 2495), and converted into 2-acetyl-4-methylphenol by the method of Auwers and Anschütz (*Ber.*, 1921, **54**, 1553). 2-Acetyl-4-methylphenol (20 g.) was added to powdered sodium (8 g.) and redistilled ethyl propionate (60 c.c.; b. p. 98·5—100°) and when the vigorous reaction had ceased the mixture was heated on the steam-bath for ½ hour. The product was shaken with crushed ice (100 g.) and the yellow sodium salt was collected, washed with ice-cold water, then ether, and decomposed by treatment with acetic acid (25 c.c.). Addition of water caused the separation of 2-*propionoacetyl*-4-*methylphenol* as an oil which rapidly solidified (15·6 g.). It separated from light petroleum (b. p. 80—100°) in colour-

less, thick, rectangular prisms, m. p. 75—76° (Found : C, 70·1; H, 6·7. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). Its alcoholic solution gives a deep brownish-red coloration with ferric chloride.

6-*Methyl*-2-*ethylchromone*.—2-Propionoacetyl-4-methylphenol (2 g.) was boiled for 2 minutes with acetic acid (10 c.c.) and a few drops of concentrated hydrochloric acid, and poured into ice-water. The solid crystallised from light petroleum (b. p. 40—60°) in long flat prisms, m. p. 51° (Found : C, 76·6; H, 6·3. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%). Its solution in concentrated sulphuric acid is colourless and exhibits a weak blue fluorescence.

2-*Acetoacetyl*-4-*methylphenol* (V).—Prepared from 2-acetyl-4-methylphenol (20 g.) and ethyl acetate (110 c.c.; alcohol-free) in the manner described above for 2-propionoacetyl-4-methylphenol (yield, 16·5 g.), this compound separated from light petroleum (b. p. 60—80°) in compact prisms, m. p. 99° (Wittig, *Ber.*, 1924, **57**, 88, records m. p. 94·5—96°) (Found : C, 68·8; H, 6·3. Calc. for $C_{11}H_{12}O_3$: C, 68·8; H, 6·3%). It gives a dark brownish-red colour with alcoholic ferric chloride, and in concentrated sulphuric acid it gives a colourless solution with a rather weak blue fluorescence.

2 : 6-Dimethylchromone, prepared from 2-acetoacetyl-4-methylphenol as described in the case of 6-methyl-2-ethylchromone, separated from light petroleum (b. p. 60—80°) in long colourless prisms, m. p. 103° (Wittig records m. p. 99·5—100°) (Found : C, 76·0; H, 5·9. Calc. for $C_{11}H_{10}O_2$: C, 75·8; H, 5·7%).

3-*Propionyl*-2 : 6-*dimethylchromone* (VI).—(A) 2-Propionoacetyl-4-methylphenol (5 g.) was boiled for 5 minutes with acetic anhydride (20 c.c.) and sodium acetate (5 g.), and then shaken with water. An ethereal extract was shaken with aqueous sodium hydroxide and dried; the residue after evaporation of the ether solidified and then crystallised from light petroleum (b. p. 40—60°) in long colourless needles (1·6 g.), m. p. 82° (Found : C, 72·9; H, 6·4. Calc. for $C_{14}H_{14}O_3$: C, 73·1; H, 6·1%). (B) 2-Acetoacetyl-4-methylphenol (8 g.) was boiled for 2 minutes with propionic anhydride (16 g.) and sodium propionate (8 g.), and the product worked up as described by Wittig (*Annalen*, 1925, **446**, 203). 2 : 6-Dimethylchromone (0·75 g.) was isolated as its hydrochloride and also pure 3-propionyl-2 : 6-dimethylchromone (2·1 g.), m. p. and mixed m. p. with specimen prepared as under (A), 81—82° (Found : C, 73·2; H, 6·3%).

Hydrolysis. (A) 3-Propionyl-2 : 6-dimethylchromone (0·5 g.) was boiled for an hour with 2*N*-sodium carbonate (15 c.c.) and alcohol (5 c.c.). After dilution, ether extracted an oil which partly crystallised; by crystallisation from light petroleum 2 : 6-dimethylchromone (0·1 g.), m. p. and mixed m. p. (with product prepared by direct closure of 2-acetoacetyl-4-methylphenol) 103°, was isolated. If the alcohol is omitted, *p*-cresitonic acid (below) may be isolated after the ether extraction, but scarcely any 2 : 6-dimethylchromone is produced. (B) Hydrolysis of both 3-propionyl-2 : 6-dimethylchromone and 2 : 6-dimethylchromone with 2*N*-sodium hydroxide for 1 hour yields *p*-cresitonic acid, m. p. 152° (Found : C, 62·9; H, 5·5. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·2%).

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