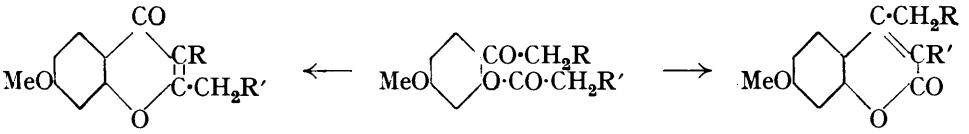
64. *Studies in the Pyrone Series. Part III. The Influence of the Phenyl Group in the Kostanecki Reaction.*

By I. M. Heilbron, D. H. Hey, and B. Lythgoe.

Previous work has revealed that the Kostanecki reaction cannot be used as a general method for the synthesis of chromones and naphtha-γ-pyrones (Heilbron, Heslop, and Howard, J., 1933, 1263), since it may produce a chromone, a coumarin, or a mixture of both. It may be presumed that, in the reaction between an *o*-hydroxyphenyl ketone and a mixture of the anhydride and the sodium salt of a fatty or substituted fatty acid, the initial stage involves the formation of an *O*-acyl ketone (I) (compare Baker, J., 1933, 1381), which can lose water in one of two ways, to give either the chromone (II) or the coumarin (III).



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

The course of the reaction has been shown to be dependent not only on the acid anhydride and the salt used, but also on the nature of the *o*-hydroxyphenyl ketone (Heilbron, Hey, and Lythgoe, J., 1934, 1581); replacement of sodium acetate and acetic anhydride by the corresponding derivatives of propionic or butyric acid favours coumarin formation, and an ethyl ketone (R = Me) shows a far greater disposition towards the formation of chromones than does the corresponding methyl ketone (R = H).

In further experiments on the mechanism of the Kostanecki reaction, the influence of a phenyl group (a) in the sodium salt and the anhydride of the fatty acid and (b) in the side chain of the ketone has been examined, by the methods previously described (compare Heilbron, Hey, and Lythgoe, *loc. cit.*), with regard to the production of both chromone and coumarin.

Derivatives of phenylacetic acid have already been employed by other workers, but in most cases under complicated conditions. For example, both Bargellini and Venkataraman frequently use a mixture of sodium phenylacetate and acetic anhydride; although in specific cases the use of such a mixture may afford the best means for the preparation of a particular pyrone, its employment in any attempt to elucidate the mechanism of the reaction is of doubtful value. Prolonged boiling of sodium phenylacetate with acetic anhydride must lead to the formation of some sodium acetate and phenylacetic anhydride as well as possibly the mixed anhydride. By the action of the above mixture on *o*-hydroxyacetophenone (Mahal and Venkataraman, J., 1933, 617), resacetophenone (Bargellini, *Gazzetta*, 1925, **55**, 945; *Atti R. Accad. Lincei*, 1925, **2**, 261), respropiophenone (Chadha, Mahal, and Venkataraman, J., 1933, 1462), and 2-acetyl-1-naphthol (Bargellini, *Atti R. Accad. Lincei*, 1925, **2**, 261; Cheema and Venkataraman, J., 1932, 918) 3-phenylcoumarins were obtained, but when the same mixture was used on 2-propionyl-1-naphthol, 2-phenylacetyl-1-naphthol, and 1-phenylacetyl-2-naphthol (Chadha, Mahal, and Venkataraman, *loc. cit.*) the products were the same chromones as are obtained when a mixture of sodium acetate and acetic anhydride is used. In the latter cases, therefore, the sodium phenylacetate plays no apparent part in the reaction. Baker and Eastwood (J., 1929, 2906) made a similar observation on the action of a mixture of sodium phenylacetate and acetic anhydride on 2 : 4-dihydroxyphenyl benzyl ketone, the product being a 3-phenyl-2-methylchromone, but when the acetic anhydride was replaced by phenylacetic anhydride the anticipated 3-phenyl-4-benzylcoumarin was formed. In the present investigation, therefore, the acid of the sodium salt used is always the same as that of the anhydride.

It has now been found that when either 2-hydroxy-4-methoxyacetophenone or 2-hydroxy-4-methoxypropiophenone is heated with sodium phenylacetate and phenylacetic anhydride the product has almost exclusively the coumarin structure, the compounds

formed being 7-methoxy-3-phenyl-4-methylcoumarin (III; R = H, R′ = Ph) and *7-methoxy-3-phenyl-4-ethylcoumarin* (III; R = Me, R′ = Ph) respectively, although with the latter ketone a small quantity of the isomeric chromone, *7-methoxy-2-benzyl-3-methylchromone* (II; R = Me, R′ = Ph), also was isolated.

The products of these reactions were identified, if coumarins, both by degradation and by synthesis; *e.g.*, 7-methoxy-3-phenyl-4-methylcoumarin on ring fission and methylation yielded 2 : 4-*dimethoxy-α-phenyl-β-methylcinnamic acid*, and similar treatment of 7-methoxy-3-phenyl-4-ethylcoumarin gave 2 : 4-*dimethoxy-α-phenyl-β-ethylcinnamic acid*. The synthesis of the two coumarins was effected by condensation of α-acetyl- and α-propionylphenylacetonitrile severally with resorcinol in the presence of sulphuric acid and subsequent methylation. 7-Hydroxy-3-phenyl-4-ethylcoumarin has been prepared by Chadha, Mahal, and Venkataraman (*loc. cit.*) by hydrolysis of the product obtained by heating respropiophenone with sodium phenylacetate and acetic anhydride. A repetition of this experiment gave a product identical with that obtained on demethylation of 7-methoxy-3-phenyl-4-ethylcoumarin, although the melting point of both specimens (268°) was somewhat higher than that given by the above authors (254°). The two isomeric chromones, which could arise from the above Kostanecki reactions, were also synthesised by an unambiguous method. Condensation of 2 : 4-dimethoxyacetophenone with ethyl phenylacetate in the presence of sodium gave 2 : 4-*dimethoxy-ω-phenylacetylacetophenone*, which on ring closure yielded *7-methoxy-2-benzylchromone* (II; R = H, R′ = Ph), and methylation of 2 : 4-dimethoxy-ω-phenylacetylacetophenone gave 2 : 4-dimethoxy-α-phenylacetylpropiophenone, which on ring closure gave 7-methoxy-2-benzyl-3-methylchromone (II; R = Me, R′ = Ph) identical with the chromone isolated from the action of sodium phenylacetate and phenylacetic anhydride on 2-hydroxy-4-methoxypropiophenone.

On the other hand, the action of the sodium salt and the anhydride of both acetic and propionic acid on 2-hydroxy-4-methoxyphenyl benzyl ketone gives rise to almost exclusive chromone formation, the products being 7-methoxy-3-phenyl-2-methylchromone (II; R = Ph, R′ = H) and *7-methoxy-3-phenyl-2-ethylchromone* (II; R = Ph, R′ = Me) respectively. These results are in agreement with previous applications of the Kostanecki reaction to benzyl ketones (Baker and Robinson, J., 1925, **127**, 1984; Cheema and Venkataraman, *loc. cit.*; Chadha, Mahal, and Venkataraman, *loc. cit.*). An unambiguous synthesis of these two chromones from 2-hydroxy-4-methoxyphenyl benzyl ketone and ethyl acetate or propionate in the presence of sodium was attempted but without success. It was possible, however, to obtain a *methylenedioxystyryl* derivative of 7-methoxy-3-phenyl-2-methylchromone. Further, the melting point of this chromone agrees with that of the product obtained by methylation of 7-hydroxy-3-phenyl-2-methylchromone (Baker and Robinson, *loc. cit.*). The latter compound, obtained from the action of sodium acetate and acetic anhydride on 2 : 4-dihydroxyphenyl benzyl ketone, must have the γ-pyrone structure, since it is not identical with 7-hydroxy-4-benzylcoumarin obtained from resorcinol and ethyl γ-phenylacetoacetate in the presence of sulphuric acid (Sonn and Litten, *Ber.*, **1933**, **66**, 1518), which is the isomeric coumarin that could arise from the above reaction.* With regard to the corresponding 2-ethylchromone, no styryl derivative could be prepared (compare Heilbron, Hey, and Lowe, J., **1934**, 1311), but a consideration of all the known facts leaves little doubt as to the validity of the structure suggested.

These results are entirely in agreement with theoretical prediction, since in each case it is the hydrogen at the reactive methylene group between phenyl and carbonyl which takes part in the ring closure. This influence is sufficiently powerful to outweigh the weaker

* The ethyl γ-phenylacetoacetate of Attwood, Stevenson, and Thorpe (J., 1923, **123**, 1762) is now stated to be ethyl α-phenylacetoacetate (Sonn and Litten, *loc. cit.*). Its use by Baker and Robinson (*loc. cit.*) in condensation with resorcinol in the presence of sulphuric acid therefore gives rise to 7-hydroxy-3-phenyl-4-methylcoumarin (m. p. 225—226°), a compound previously prepared by Jacobson and Ghosh (J., 1915, **107**, 1053), and not 7-hydroxy-4-benzylcoumarin. The preparation of the latter by Sonn and Litten gives rise to a product (m. p. 214—215°), which is apparently identical neither with Hannach and Kostanecki's 7-hydroxy-2-benzylchromone (m. p. 183°; *Ber.*, 1902, **35**, 867) nor with Baker and Robinson's 7-hydroxy-3-phenyl-2-methylchromone (m. p. 240°). The arguments used by Baker and Robinson therefore remain unaffected.

effects introduced either by replacing the methyl ketone by the ethyl ketone, or by using derivatives of propionic acid in place of those of acetic acid. The influence of the phenyl group on the course of the Kostanecki reaction, though more powerful, *is in the same direction* as that of the methyl group. When substituted in the sodium salt and the acid anhydride, both groups favour coumarin formation, but when substituted in the hydroxyacetophenone side chain both groups favour chromone formation.

Note on the Action of Sodium Propionate and Propionic Anhydride on 2-Hydroxy-4-methoxyacetophenone.—This action (Heilbron, Hey, and Lythgoe, *loc. cit.*) is stated to have given 7-methoxy-3 : 4-dimethylcoumarin, together with a small quantity of a second compound, m. p. 81—82°, which gave the correct analysis for the isomeric chromone but was erroneously stated to depress the melting point of 7-methoxy-2-ethylchromone (m. p. 81°; Heilbron, Hey, and Lowe, *loc. cit.*). Repetition of this reaction has shown that the compound of m. p. 81—82° is in fact the latter chromone. The condensation of 2-hydroxy-4-methoxyacetophenone with ethyl propionate in the presence of sodium has also been re-examined and found to yield 5-methoxy-2-propionoacetylphenol, m. p. 83·5° (and not 101° as erroneously reported previously), identical with the diketone obtained from 7-methoxy-2-ethylchromone on ring fission.

Experimental.

Phenylacetic Anhydride.—The following method gave good results: phenylacetic acid (50 g.) and acetic anhydride (150 g.) were boiled in a flask fitted with a Lapworth column, which was jacketed by vapour from boiling acetic acid. The temperature at the head of the column was maintained at 116—120° and after 4 hours 30 c.c. of distillate had been collected, the greater portion of which boiled below 120°. After removal of the excess of acetic anhydride under reduced pressure, the residual phenylacetic anhydride solidified. On crystallisation from light petroleum (b. p. 80—100°) colourless needles were obtained, m. p. 72° (yield, 35 g.).

Action of Sodium Phenylacetate and Phenylacetic Anhydride on 2-Hydroxy-4-methoxyacetophenone.—Sodium phenylacetate (20 g.), phenylacetic anhydride (30 g.), and 2-hydroxy-4-methoxyacetophenone (15 g.) were heated together under reflux at 180° for 8 hours. The product was poured into water and distilled with steam to remove unchanged reactants. An ethereal extract of the residue, after being washed with aqueous alkali to remove traces of 2-hydroxy-4-methoxyacetophenone and dried, deposited 7-methoxy-3-phenyl-4-methylcoumarin which on recrystallisation from alcohol separated in colourless needles (12 g.), m. p. 106·5° (Found: C, 76·4; H, 5·5. Calc. for $C_{17}H_{14}O_3$: C, 76·7; H, 5·3%).

The coumarin gave no depression in melting point on admixture with a specimen prepared by the action of α-acetylphenylacetonitrile on resorcinol in the presence of sulphuric acid (Ghosh, J., 1916, **109**, 109; compare also Baker and Robinson, *loc. cit.*), with subsequent methylation as follows: the hydroxy-coumarin (m. p. 225°, 1·6 g.) was dissolved in dry acetone (75 c.c.) and boiled under reflux for several hours with the addition of methyl iodide (0·5 c.c.) and potassium carbonate (1 g.) (compare Robertson, Robinson, and Struthers, J., 1928, 1457). After removal of solvent, water was added, and the separated solid collected, dissolved in alcohol, boiled with charcoal and filtered. The 7-methoxy-3-phenyl-4-methylcoumarin (1·3 g.) separated in long needles, m. p. 106·5°. Chakravarti (*J. Indian Chem. Soc.*, 1931, **8**, 136) gives m. p. 104°.

A portion of the coumarin was subjected to hydrolytic fission by the method of Canter and Robertson (J., 1931, 1875). The coumarin (4 g.) was boiled under reflux with 20% aqueous sodium hydroxide (50 c.c.) and methyl alcohol (50 c.c.) for about 2 hours, until no turbidity was observed on dilution of a test portion. After the addition of more alkali (30 c.c.) and methyl alcohol (30 c.c.) the cold solution was treated with methyl sulphate (35 c.c.), added in small quantities with frequent shaking. More alkali was then added, and the solution boiled under reflux to hydrolyse any methyl ester formed. The product precipitated on acidification was treated with sodium bicarbonate solution, which left a residue (2 g.) of unchanged coumarin re-formed from hydroxycinnamic acid which had escaped methylation. Acidification of the bicarbonate solution precipitated 2 : 4-*dimethoxy-α-phenyl-β-methylcinnamic acid* (2·2 g.), which separated from dilute acetic acid in colourless needles, m. p. 153·5° (Found: C, 72·3; H, 5·95. $C_{18}H_{18}O_4$ requires C, 72·4; H, 6·0%).

Evaporation of the ethereal mother-liquor from which the coumarin had separated left an oil (2 g.), which was kept over-night in presence of alcoholic sodium ethoxide (1 g. of sodium in

60 c.c. of alcohol). The resulting solution was diluted with water, washed with ether, and acidified with acetic acid. The oil precipitated was extracted with ether and washed with aqueous sodium hydroxide. Acidification of the aqueous alkaline solution produced only a slight cloudiness, indicating the almost complete absence of any hydroxydiketone and hence of chromone. Evaporation of the ethereal extract yielded a further quantity of 7-methoxy-3-phenyl-4-methylcoumarin (1·8 g.).

7-Methoxy-2-benzylchromone.—A solution of 2 : 4-dimethoxyacetophenone (13 g., m. p. 40°) (Perkin, Robinson, and Turner, J., 1908, **93**, 1108) in ethyl phenylacetate (35 g., b. p. 227°) (Volhard, *Annalen*, 1897, **296**, 2, footnote) was added to powdered sodium (1·75 g.). The reaction was at first controlled by cooling in ice and then completed by heating on the steam-bath for ½ hour. When cold, ether was added and the granular sodium salt which slowly separated was collected and washed with ether. A portion (4 g.) was dissolved in glacial acetic acid (15 c.c.), and on addition of water the free diketone separated as an oil, which solidified. On crystallisation from methyl alcohol 2 : 4-*dimethoxy-ω-phenylacetylacetophenone* (2·5 g.) separated in faintly yellow crystals, m. p. 91° (Found : C, 71·9; H, 5·8. $C_{18}H_{18}O_4$ requires C, 72·4; H, 6·0%). After the diketone (1·5 g.) had been boiled for 15 minutes with glacial acetic acid (20 c.c.) and hydrobromic acid (3 c.c., *d* 1·47), and the solution poured into dilute aqueous alkali, the precipitated *7-methoxy-2-benzylchromone* was extracted with ether; it crystallised from dilute acetic acid in colourless needles, m. p. 192° (Found : C, 76·1; H, 5·7. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%).

Action of Sodium Phenylacetate and Phenylacetic Anhydride on 2-Hydroxy-4-methoxypropiophenone.—The reaction between sodium phenylacetate (15 g.), phenylacetic anhydride (30 g.), and 2-hydroxy-4-methoxypropiophenone (10 g.) was carried out as described above for the corresponding reaction with 2-hydroxy-4-methoxyacetophenone. The product was treated in a similar manner, evaporation of the ethereal solution yielding large colourless crystals of *7-methoxy-3-phenyl-4-ethylcoumarin* (7 g.), which after recrystallisation from alcohol melted at 115° (Found : C, 77·4; H, 5·7. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%). A portion of the coumarin (1 g.) was demethylated by heating on the steam-bath for 2 hours with a mixture (20 c.c.) of equal parts of hydriodic acid (*d* 1·7) and glacial acetic acid. The solution was poured into dilute sodium carbonate solution and extracted with ether. The ethereal extract was washed with sodium thiosulphate solution, the solvent evaporated, and the residual 7-hydroxy-3-phenyl-4-ethylcoumarin crystallised from alcohol, forming colourless needles (0·3 g.), m. p. 268° (compare Chadha, Mahal, and Venkataraman, *loc. cit.*). A further portion of the coumarin (2 g.) was subjected to hydrolytic fission by the method previously described for 7-methoxy-3-phenyl-4-methylcoumarin, giving unchanged coumarin (0·6 g.) and 2 : 4-*dimethoxy-α-phenyl-β-ethylcinnamic acid* (0·9 g.), which crystallised from dilute acetic acid in colourless needles, m. p. 137° (Found : C, 73·0; H, 6·4. $C_{19}H_{20}O_4$ requires C, 73·0; H, 6·4%).

Evaporation of the ethereal mother-liquor from which the coumarin had separated yielded an oil (2·5 g.), to which was added an alcoholic solution of sodium ethoxide (1·5 g. of sodium in 70 c.c. of alcohol). After 12 hours, addition of water precipitated an oil, which was extracted with ether. The crude chromone obtained on removal of the solvent crystallised from alcohol in colourless needles (0·8 g.) of *7-methoxy-2-benzyl-3-methylchromone*, m. p. 102·5° (Found : C, 77·1; H, 5·8. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%). Acidification of the alkaline layer with acetic acid precipitated an oil, an ethereal extract of which was washed with aqueous sodium hydroxide. Only a minute quantity of oil was liberated on acidification of the alkaline washings, but evaporation of the ethereal extract yielded a further quantity (1·5 g.) of 7-methoxy-3-phenyl-4-ethylcoumarin.

α-Propionylphenylacetonitrile was prepared by the method of Dimroth and Feuchter (*Ber.*, 1903, **36**, 2242) and obtained in colourless needles (from aqueous alcohol), m. p. 61—62°. The above authors record m. p. 70°, and Walther and Schickler (*J. pr. Chem.*, 1897, **55**, 344), using a similar method, obtained a product, m. p. 58°.

7-Methoxy-3-phenyl-4-ethylcoumarin.—To an intimate mixture of α-propionylphenylacetonitrile (3 g.) and resorcinol (2·2 g.) was added, drop by drop, concentrated sulphuric acid (8·5 c.c.). After standing over-night, the yellowish crystalline mass was poured on ice, and the separated solid boiled under reflux with 10% sulphuric acid (100 c.c.). The separated 7-hydroxy-3-phenyl-4-ethylcoumarin (3·6 g.) was washed with water; it crystallised from alcohol in fine needles, m. p. 268°. The hydroxycoumarin (0·8 g.) was methylated by boiling under reflux for 16 hours with acetone (200 c.c.), methyl iodide (2 c.c.), and potassium carbonate (4 g.). After removal of solvent the addition of water precipitated 7-methoxy-3-phenyl-4-ethylcoumarin (0·6 g.), which crystallised from aqueous methyl alcohol in colourless needles, m. p. 115°, not

depressed by the coumarin obtained by the action of sodium phenylacetate and phenylacetic anhydride on 2-hydroxy-4-methoxypropiophenone.

7-Methoxy-2-benzyl-3-methylchromone.—The sodium salt of 2 : 4-dimethoxy-ω-phenylacetylacetophenone (10 g.), prepared as described above, was boiled under reflux for 6 hours with acetone (150 c.c.) and methyl iodide (5 c.c.). After removal of solvent and addition of water, the product was extracted with ether, evaporation of which gave a viscous non-crystallisable oil. A portion (1 g.) was boiled for 10 minutes with glacial acetic acid (50 c.c.) containing hydrobromic acid (2·5 c.c., *d* 1·47). The cold solution was poured into dilute aqueous alkali, from which ether extracted a dark tarry material. The solution obtained by trituration with light petroleum and decantation from insoluble resinous matter deposited 7-methoxy-2-benzyl-3-methylchromone, which on recrystallisation from the same solvent gave colourless needles (0·7 g.), m. p. 102·5°, not depressed by the chromone isolated from the action of sodium phenylacetate and phenylacetic anhydride on 2-hydroxy-4-methoxypropiophenone.

2-Hydroxy-4-methoxyphenyl Benzyl Ketone.—2 : 4-Dihydroxyphenyl benzyl ketone (22·8 g., m. p. 114°) (Chapman and Stephen, J., 1923, **123**, 406), methyl iodide (14·2 g.), and potassium carbonate (13 g.) were boiled under reflux for 12 hours with acetone (200 c.c.). After evaporation of the acetone and addition of water, the separated solid was collected, washed with water, and crystallised from 95% alcohol, giving 2-hydroxy-4-methoxyphenyl benzyl ketone (22 g.) in colourless needles, m. p. 90°. Tambor's method (*Ber.*, 1910, **43**, 1884) gave less satisfactory yields.

Action of Sodium Acetate and Acetic Anhydride on 2-Hydroxy-4-methoxyphenyl Benzyl Ketone.—The product of heating 2-hydroxy-4-methoxyphenyl benzyl ketone (9 g.), sodium acetate (25 g.), and acetic anhydride (35 g.) for 5 hours at 160° was treated as in the previous Kostanecki reactions. Partial evaporation of the ethereal solution caused deposition of 7-methoxy-3-phenyl-2-methylchromone (6·8 g.), which separated from 95% alcohol in long needles, m. p. 136° (compare Baker and Robinson, *loc. cit.*) (Found : C, 76·7; H, 5·7. Calc. for $C_{17}H_{14}O_3$: C, 76·7; H, 5·3%). Evaporation of the ethereal mother-liquor left a brown oil, which, after standing over-night with alcoholic sodium ethoxide (2 g. of sodium in 100 c.c. of alcohol), was poured into water. Extraction with ether yielded a further quantity of 7-methoxy-3-phenyl-2-methylchromone (1·6 g.). The aqueous alkaline layer was acidified with acetic acid and extracted with ether. The ethereal extract was washed with aqueous sodium hydroxide and after removal of solvent the residual small quantity of oil on trituration with methyl alcohol yielded some 2-hydroxy-4-methoxyphenyl benzyl ketone (m. p. and mixed m. p. 90°), but no coumarin was detected. Acidification of the alkaline washings yielded only a minute quantity of oily matter.

7-Methoxy-3′ : 4′-methylenedioxy-2-styryl-3-phenylchromone.—A solution of the above chromone (0·5 g.) and piperonal (0·3 g.) in alcohol (30 c.c.) containing sodium (0·05 g.) was kept for 3 days at room temperature. The *styryl* derivative which separated crystallised from alcohol in pale yellow needles (0·3 g.), m. p. 246° (Found : C, 75·8; H, 4·4. $C_{25}H_{18}O_5$ requires C, 75·8; H, 4·5%).

Action of Sodium Propionate and Propionic Anhydride on 2-Hydroxy-4-methoxyphenyl Benzyl Ketone.—The ketone (10 g.), sodium propionate (20 g.), and propionic anhydride (30 g.) were heated together under reflux for 8 hours at 190°. The product was poured into water and distilled with steam. The pale brown, crystalline residue was recrystallised from absolute alcohol, giving *7-methoxy-3-phenyl-2-ethylchromone* (8 g.) in long colourless needles, m. p. 119·5° (Found : C, 76·9; H, 5·6. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%). The alcoholic mother-liquor was kept over-night with a solution of sodium ethoxide (2 g. of sodium), the total volume being approximately 100 c.c. The solution was diluted with water and treated as described previously. No coumarin was detected, the only products isolated being a further quantity of the ethylchromone and some 2-hydroxy-4-methoxyphenyl benzyl ketone.

Action of Sodium Propionate and Propionic Anhydride on 2-Hydroxy-4-methoxyacetophenone.—A mixture of 2-hydroxy-4-methoxyacetophenone (40 g.), sodium propionate (100 g.), and propionic anhydride (150 g.) was heated in an oil-bath at 200° for 48 hours. The mixture was poured into water, and propionic acid removed with steam. From the solid residue, by treatment with ether, 7-methoxy-3 : 4-dimethylcoumarin (10 g.) was obtained, which crystallised from alcohol in long needles, m. p. 142° (Found : C, 70·6; H, 5·95. Calc. for $C_{12}H_{12}O_3$: C, 70·6; H, 5·9%). The ethereal solution was repeatedly washed with aqueous alkali to remove unchanged hydroxy-ketone (8 g.). Evaporation of the ether, followed by distillation of the residue at 3 mm., yielded a yellow oil (28 g.), which gradually solidified and after crystallisation from alcohol gave a further quantity of the coumarin (8 g.). The alcoholic mother-liquor,

after standing over-night in the presence of alcoholic sodium ethoxide (10 g. of sodium; total volume of solution, 250 c.c.), was diluted with water, and the separated oil extracted with ether. After removal of solvent from the dried extract, the residue was agitated with light petroleum, and the separated solid (2·5 g.) crystallised from alcohol, 7-methoxy-2-ethylchromone being obtained in colourless needles, m. p. 82° (Found: C, 70·5; H, 5·9. Calc. for $C_{12}H_{12}O_3$: C, 70·6; H, 5·9%), not depressed by the authentic chromone prepared by the method of Heilbron, Hey, and Lowe (*loc. cit.*).

Acidification of the aqueous alkaline solution with acetic acid liberated an oil, which was extracted with ether. The ethereal solution was washed first with aqueous sodium carbonate, which removed 2-hydroxy-4-methoxybenzoic acid (1·5 g., m. p. and mixed m. p. 157°), and then with aqueous sodium hydroxide, which extracted 5-methoxy-2-propionoacetylphenol (3·6 g., m. p. and mixed m. p. 83·5°) (Found: C, 64·9; H, 6·2. Calc. for $C_{12}H_{14}O_4$: C, 64·8; H, 6·3%). Evaporation of the ether gave a further quantity of 7-methoxy-3 : 4-dimethylcoumarin (9·9 g.).

An alternative method of treating the product after the initial separation of coumarin consisted in the repeated extraction of the distillate (47 g.) with a mixture of equal parts of concentrated hydrochloric acid and water. Neutralisation of the acid extract deposited 7-methoxy-2-ethylchromone (13·4 g.), which separated from ether–light petroleum in cubes, m. p. 82°. The residue from the extraction gave 7-methoxy-3 : 4-dimethylcoumarin (19·5 g.), which separated from aqueous alcohol in colourless needles, m. p. 142°.

5-Methoxy-2-propionoacetylphenol.—This was prepared by the method of Heilbron, Hey, and Lowe (*loc. cit.*). The precipitated diketone was boiled in alcoholic solution with charcoal, and after filtration 5-methoxy-2-propionoacetylphenol separated in colourless needles, m. p. 83·5°.

A portion of the diketone (0·5 g.) was boiled for 5 minutes with glacial acetic acid (5 c.c.) and a few drops of concentrated hydrochloric acid. The solution was poured into water and extracted with ether, and the extract washed with aqueous sodium carbonate. Evaporation of the ether gave 7-methoxy-2-ethylchromone, which was recrystallised from ether–light petroleum (m. p. and mixed m. p. 82°). A second portion of the diketone (1 g.) was boiled under reflux for ½ hour with 10% aqueous sodium hydroxide (60 c.c.). The cold solution was acidified and extracted with ether, and the extract washed first with aqueous sodium carbonate and then with aqueous sodium hydroxide. Acidification of the carbonate washings liberated 2-hydroxy-4-methoxybenzoic acid, which separated in needles from dilute acetic acid (0·5 g., m. p. and mixed m. p. 157°). The sodium hydroxide washings were acidified and extracted with ether, evaporation of which gave 2-hydroxy-4-methoxyacetophenone, which separated from aqueous alcohol in needles (m. p. and mixed m. p. 48°).

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