271. *Reactions of* o-*Hydroxybenzylidenediacetophenones. Part I. Reaction with Acids.*

By Douglas W. Hill.

The reactions of *o*-hydroxybenzylidenediacetophenones have received but little attention. The parent substance (I) was first obtained by Cornelson and Kostanecki (*Ber.*, 1896, **29**, 240) from the interaction of 2 mols. of acetophenone and 1 mol. of salicylaldehyde in the presence of strong alkali. Feuerstein and Kostanecki (*Ber.*, 1898, **31**, 710) found that it was converted on heating with dilute hydrochloric acid into acetophenone, dihydrochalkone,* and a yellow compound, m. p. 131°, which they formulated as 4-phenacylideneflavene (III). Since this was obtained in a yield of 50%, they postulated the occurrence of two simultaneous reactions from 2 mols. of (I): (i) hydrolysis to the acetophenone and chalkone, and (ii) ring closure to 4-*phenacylflavene* (II), which was then dehydrogenated by the

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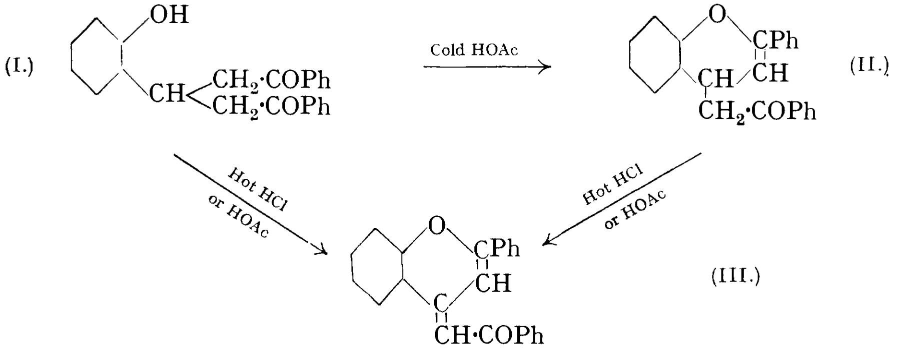
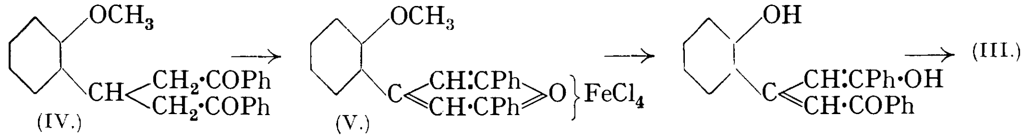
* The identity of this compound has been definitely established in this laboratory by Dr. A. S. Gomm, who compared a specimen obtained by the above method with an authentic specimen prepared by the reduction of chalkone.

chalkone to (III), the chalkone being reduced to dihydrochalkone. As benzylidenediacetophenones without an *o*-hydroxy-group have been prepared by condensation in the presence of hydrochloric acid, however (see, *e.g.*, Blumstein and Kostanecki, *Ber.*, 1900, **33**, 1481; Rupe and Veit, *Chem. Zentr.*, 1906, I, 1417), the rôle ascribed to the acid in this hypothesis appears improbable.



The same phenacylideneflavene was obtained by Dilthey and Floret (*Annalen*, 1924, **440**, 89) from *o*-methoxybenzylidenediacetophenone (IV) by oxidation to the triphenylpyrylium salt (V), demethylation of this, and treatment of the product with pyridine, the reaction being assumed to proceed according to the scheme

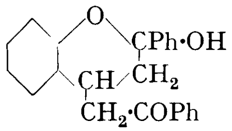


This is an unusual reaction, as was pointed out by Irvine and Robinson (J., 1927, 2086), who found that 2-hydroxy-5-methoxybenzylidenediacetophenone behaved like the parent substance when treated with dilute hydrochloric acid, yielding acetophenone, phenyl β-(2-hydroxy-5-methoxyphenyl)ethyl ketone, and 6-methoxy-4-phenacylideneflavene in the required quantities.

It is not necessary to use hydrochloric acid for the conversion. It occurs equally well, though more slowly, in glacial acetic acid, and this reagent has the advantage that under suitably mild conditions—standing in the cold or very short heating—the intermediate colourless 4-phenacylflavene can be isolated. From *o*-hydroxybenzylidenediacetophenone itself, this compound was isolated in nearly quantitative yield, but in other cases it could only be recovered in much smaller amount, the reaction product consisting mainly of the corresponding phenacylidene-derivative. 2-*Hydroxy*-4-*methoxybenzylidenediacetophenone* yielded only 14% of pure 7-*methoxy*-4-*phenacylflavene*, but 2-hydroxy-5-methoxybenzylidenediacetophenone gave 55% of pure 6-*methoxy*-4-*phenacylflavene*. All the phenacylflavenes on further treatment with either hydrochloric or glacial acetic acid were converted into the yellow phenacylideneflavenes, the corresponding substituted hydrochalkones, and acetophenone.

The fact that yields of over 50% of intermediate compound have been obtained indicates that the first stage of the reaction is the conversion of the whole of the starting material into phenacylflavene, as opposed to the 50% conversion postulated by Feuerstein and Kostanecki. The compounds usually isolated are therefore all derived from these 4-phenacylflavenes, although, as might be expected, it has not been found possible to isolate more than a 50% yield of phenacylideneflavene. The course of the reaction may therefore be represented by the scheme above.

The formation of the phenacylflavenes closely resembles the dehydrating action of glacial acetic acid in the conversion of certain chromanols into chromenes (Löwenbein, *Ber.*, 1924, **57**, 1517; Heilbron and Hill, J., 1927, 2005); this similarity suggests that ring closure may have occurred during the condensation, and that the *o*-hydroxy-derivatives of benzylidenediacetophenone may perhaps be better formulated as chromanols of type (VI). The fact that the corresponding chalkones are soluble in alkali, whilst these compounds are quite insoluble, lends support to this view, which would also account for the difference in hydrolytic action of acids on *o*-hydroxy- and on unsubstituted benzylidenediacetophenones. Further work is in progress in this connexion.



(VI.)

EXPERIMENTAL.

4-*Phenacylflavene*.—A solution of *o*-hydroxybenzylidenediacetophenone (5 g.) in glacial acetic acid (16 c.c.) was kept at room temperature for 24 hours. A small quantity of white solid (A) which separated was filtered off, whereupon the filtrate deposited a mass of almost colourless needles; these were recrystallised from light petroleum (b. p. 60—80°). The solid (A) was redissolved in glacial acetic acid (8 c.c.), and on standing deposited a pale yellow solid, which was also crystallised from light petroleum. The acetic acid mother-liquors were poured into water, and the solid product dried and extracted with light petroleum (the insoluble residue was crystallised from alcohol and proved to be unchanged starting material; 1·3 g.). All the samples from light petroleum were combined and recrystallised from the same solvent. Thus were obtained 2·5 g. of glistening colourless, silky needles, m. p. 96° [Found (micro): C, 84·37; H, 5·74. $C_{23}H_{18}O_2$ requires C, 84·66; H, 5·52%].

In another experiment, the above diacetophenone (5 g.) was heated for 10 minutes with glacial acetic acid (20 c.c.). The pale yellow solution on cooling deposited faintly yellow needles. Both these and the filtrate were worked up as before, and 4 g. of an identical substance, m. p. 96°, were obtained.

4-*Phenacylflavene* is insoluble in alkali and soluble in most organic solvents; it is unchanged by heating with water, but is converted into the phenacylidene-derivative by hot acids.

4-*Phenacylideneflavene*.—A solution of *o*-hydroxybenzylidenediacetophenone (5 g.) in glacial acetic acid (30 c.c.) was boiled for one hour. The solution, which had darkened considerably, was poured into water, and the oil solidified after several days. The solid crystallised from alcohol as yellow needles (2·3 g.), m. p. 128° (Feuerstein and Kostanecki give 128°) [Found (micro): C, 85·05; H, 5·30. Calc. for $C_{23}H_{16}O_2$: C, 85·20; H, 5·00%]. The same compound was obtained by boiling 1 g. of 4-phenacylflavene in glacial acetic acid (10 c.c.) for 45 mins.

From three experiments, using 5, 5, and 20 g. of *o*-hydroxybenzylidenediacetophenone and 10 mins.' refluxing with 10 times the weight of 10% hydrochloric acid, the yields of phenacylideneflavene were 2·15, 2·20, and 9·20 g. respectively. Acetophenone was removed from the reaction mixture by steam distillation, the residue in the flask was basified with sodium hydroxide to dissolve hydrochalkone, and the remaining yellow solid was crystallised from alcohol. In no instance was the yield of this compound more than 50% of that theoretically possible.

2-*Hydroxy*-4-*methoxybenzylidenediacetophenone*.—A solution of 2-hydroxy-4-methoxybenzaldehyde (15 g.) and acetophenone (24·5 g.) in alcohol (110 c.c.) was treated with a hot solution of sodium hydroxide (30 g. in 30 c.c. of water). The resulting deep red solution was kept over-night, poured into water (5000 c.c.), and the mixture occasionally stirred until the sparingly soluble sodium salt of the 4-methoxychalkone, formed as a by-product, had all dissolved. The insoluble solid was crystallised twice from alcohol, separating as silvery plates, m. p. 181° (13·5 g.) [Found (micro): C, 76·93; H, 5·85. $C_{24}H_{22}O_4$ requires C, 77·00; H, 5·88%].

7-*Methoxy*-4-*phenacylflavene*.—A suspension of the above diacetophenone (5 g.) in glacial acetic acid (20 c.c.) was gently heated until complete solution occurred (7 mins.). On cooling, the yellow solution deposited 1 g. of unchanged starting material. The residual acetic acid solution was poured into water and steam-distilled, the material remaining in the flask was basified with caustic potash, and the insoluble solid crystallised from alcohol. The yellow solid so obtained was dissolved in a large volume of light petroleum (b. p. 60—80°), from which yellow needles (1 g.), m. p. 153°, separated (phenacylidene-derivative, see below). On evaporation, the solution deposited a mixture of white and yellow crystals which were separated by fractional crystallisation from the same solvent. By this means pure 7-*methoxy*-4-*phenacylflavene* was obtained as hard clumps of colourless needles (0·5 g.), m. p. 85—86° [Found (micro): C, 80·72; H, 5·59. $C_{24}H_{20}O_3$ requires C, 80·67; H, 5·60%].

7-*Methoxy*-4-*phenacylideneflavene*.—2-Hydroxy-4-methoxybenzylidenediacetophenone (10 g.) was boiled under reflux for 45 mins. with glacial acetic acid (60 c.c.). The solution was poured into water and steam-distilled, and the residue in the flask basified with caustic soda. The insoluble solid was crystallised several times from alcohol, and obtained as yellow needles (4·3 g.), m. p. 153° [Found (micro) : C, 81·28; H, 5·10. $C_{24}H_{18}O_3$ requires C, 81·36; H, 5·09%]. The same compound (1·9 g.) was obtained from diacetophenone (5 g.) and 10% hydrochloric acid (100 c.c.) by a similar process.

The alkaline solution was acidified, and extracted with ether. The extract yielded phenyl β-(2-hydroxy-4-methoxyphenyl)ethyl ketone as a brown oil which could not be crystallised; but its *semicarbazone* was obtained as small colourless needles (from methyl alcohol), m. p. 177—178° [Found (micro) : N, 12·93. $C_{17}H_{19}O_3N_3$ requires N, 13·40%].

6-*Methoxy*-4-*phenacylflavene*.—2-Hydroxy-5-methoxybenzylidenediacetophenone was prepared according to Irvine and Robinson (*loc. cit.*), except that 1·75 mols. of acetophenone were used in order to improve the yield (further increase leads to an oily product). This compound (3 g.) was dissolved with slight warming in glacial acetic acid (20 c.c.) and kept at room temperature for 2 days. No solid separated, so the solution was poured into water, and the precipitated solid collected, and crystallised from light petroleum (b. p. 60—80°), 0·4 g. of unchanged starting material remaining undissolved. The *phenacylflavene* separated after two crystallisations from light petroleum as colourless needles (1·5 g.), m. p. 118—119° [Found (micro) : C, 80·85; H, 5·76. $C_{24}H_{20}O_3$ requires C, 80·67; H, 5·60%]. When treated with boiling glacial acetic acid, it was converted into the phenacylideneflavene, which was also obtained (1·8 g.) by refluxing the diacetophenone (4 g.) with glacial acetic acid; it had m. p. 146—147°, and agreed with the product described by Irvine and Robinson (*loc. cit.*).

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THE UNIVERSITY, BRISTOL.

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