XXXVI.—*The Condensation of Certain β-Ketonic Esters with o-Hydroxymonostyryl Ketones.*

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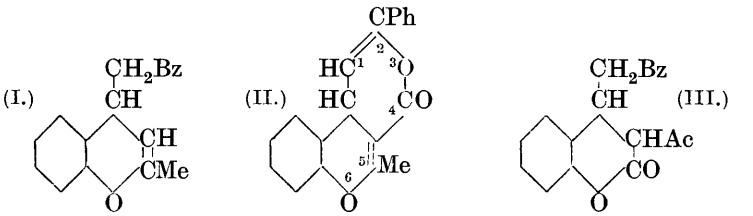
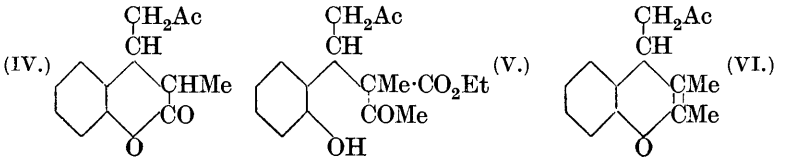
IT has been shown (Heilbron and Hill, J., 1927, 918) that, contrary to the findings of Forster and Heilbron (J., 1924, **125**, 340), the sole reaction products of the condensation of ethyl acetoacetate with phenyl 2-hydroxystyryl ketone under various conditions are 4-phenacyl-2-methyl-1 : 4-benzopyran (I) and 2-phenyl-5-methyl-3 : 4-coumalo-6-benzopyran (II). The failure to isolate 3-acetyl-4-



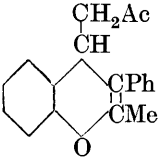
phenacyldihydrocoumarin (III) has led to the investigation now described, in which the interaction of certain α-substituted β-ketonic esters with *o*-hydroxymonostyryl ketones has been examined with a view to determine whether dihydrocoumarin ring formation is possible under such conditions.

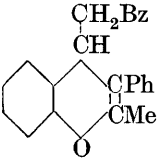
The interaction of ethyl methylacetoacetate with 2-hydroxystyryl methyl ketone was first studied, as it was considered that the introduction of a methyl group into the β-ketonic ester would tend to prevent γ-pyran ring formation and result in the formation of 4-acetonyl-3-methyldihydrocoumarin (IV). This, however, did not prove to be the case, for the substance actually isolated from the reaction mixture had an empirical formula $C_{14}H_{16}O_2$, which corresponds to the loss of the carbethoxyl group and one molecule of water from the primary additive product (V). A consideration of the structure of the latter clearly shows that water can only have been eliminated by a prior hydrolysis of the carbethoxyl group, followed by loss of carbon dioxide. γ-Pyran formation then ensues in the normal manner to yield 4-*acetonyl*-2 : 3-*dimethyl*-1 : 4-*benzopyran* (VI). In a similar manner, phenyl 2-hydroxystyryl ketone yielded 4-*phenacyl*-2 : 3-*dimethyl*-1 : 4-*benzopyran*.



The condensation of ethyl phenylacetoacetate with *o*-hydroxymonostyryl ketones was next investigated, since it was thought that the substitution of the phenyl group for the methyl radical of the β-ketonic ester might influence the reaction in favour of dihydrocoumarin ring formation. The reaction, however, followed the normal course, yielding *4-acetonyl-3-phenyl-2-methyl-1 : 4-benzopyran* (VII) and *4-phenacyl-3-phenyl-2-methyl-1 : 4-benzopyran* (VIII).

(VII.)





(VIII.)

The study of these condensations was also extended so as to include ethyl oxalacetate, ethyl cyanoacetate, and ethyl malonate, but, strangely enough, no evidence has as yet been adduced of the addition of these esters to an ethenoid linkage containing an *o*-hydroxyl group. Even under the most drastic conditions the ketone has been recovered unchanged. The failure to isolate an additive product is surprising when it is considered that ethyl cyanoacetate and ethyl malonate are in a general way more reactive than ethyl acetoacetate.

The reaction between ethyl malonate and phenyl 2-hydroxystyryl ketone was studied exhaustively. After the reactants had been kept in concentrated sodium ethoxide solution at room temperature for 10 weeks, coumarin-α-carboxylic acid was isolated. Normal addition at the ethenoid linkage had therefore been superseded by scission of the ketone in the presence of alkali, with formation of acetophenone and salicylaldehyde, and the latter had then condensed with ethyl malonate in the normal manner (Stuart, J., 1886, **49**, 366). This is reminiscent of a case observed by Vorländer (*Annalen*, 1896, **294**, 334), who found that the condensation of ethyl malonate with 4-methoxystyryl *iso*propyl ketone in presence of alcoholic sodium ethoxide resulted in considerable quantities of *p*-methoxycinnamic acid being formed.

EXPERIMENTAL.

4-Acetonyl-2 : 3-dimethyl-1 : 4-benzopyran (VI).—2-Hydroxystyryl methyl ketone (5 g.) dissolved in the minimum quantity of absolute alcohol (distilled over calcium), containing ethyl methylacetoacetate (7·5 g.), was treated with sodium ethoxide (from 1·7 g. of sodium) in alcohol (25 c.c.), and the homogeneous, red solution kept at room temperature for 8 days; it became lighter in colour and a small

quantity of sodium carbonate was deposited. After removal of the latter, the mixture was gradually diluted with water; long, colourless needles then separated. Recrystallised three times from aqueous alcohol, the pyran was obtained (yield, 3·5 g.) in large, colourless plates, m. p. 141°. It is almost insoluble in cold aqueous alkali, but dissolves readily on warming. With concentrated sulphuric acid it develops a yellow coloration (Found : C, 77·9; H, 7·7. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%).

4-*Phenacyl*-2 : 3-*dimethyl*-1 : 4-*benzopyran* was prepared in a similar manner from phenyl 2-hydroxystyryl ketone. The filtrate, after removal of sodium carbonate, was diluted with water, the viscous, brown oil which separated was taken up in ether, and the moist ethereal solution vigorously scratched. A dark yellow solid was slowly deposited which, when pressed on a porous tile to remove adherent oily matter and recrystallised repeatedly from benzene, in which it was but moderately soluble, formed minute, colourless needles, m. p. 179° (Found: C, 81·8; H, 6·5. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%).

4-*Acetonyl*-3-*phenyl*-2-*methyl*-1 : 4-*benzopyran* (VII).—A hot solution containing 2-hydroxystyryl methyl ketone (8·1 g.), absolute alcohol (40 c.c.), and ethyl phenylacetoacetate (12 g.) was treated with alcoholic sodium ethoxide (2·6 g. of sodium). The mixture, which immediately assumed a deep red colour, was kept at room temperature for 3 days. After decanting from deposited sodium carbonate, the clear solution was slowly diluted with water; rosettes of slender needles contaminated with a brown, viscous oil then slowly separated. These were recrystallised from glacial acetic acid and finally from acetone, from which the pure substance was deposited in long, colourless needles, m. p. 186—187°. It is sparingly soluble in hot or cold aqueous alkali, but dissolves in concentrated sulphuric acid to a pale yellow solution (Found : C, 81·7; H, 6·4. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%).

4-*Phenacyl*-3-*phenyl*-2-*methyl*-1 : 4-*benzopyran* (VIII).—A mixture of phenyl 2-hydroxystyryl ketone (7 g.), absolute alcohol (50 c.c.), and ethyl phenylacetoacetate (7·5 g.) was treated with alcoholic sodium ethoxide (1·6 g. of sodium), and the red solution kept at room temperature for 6 days. On dilution with water, a dark, viscous oil slowly separated, which was dissolved in acetone and the solution vigorously scratched. A red, amorphous solid was thus deposited, which was repeatedly crystallised from acetone in the presence of blood-charcoal. When pure, the compound separated in colourless prisms, m. p. 219—221° (with preliminary darkening). It is sparingly soluble in the usual organic solvents with the exception of chloroform and pyridine, insoluble in hot

aqueous alkali, and gives a pale yellow coloration with concentrated sulphuric acid (Found : C, 84·9; H, 6·0. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%).

Condensation of Ethyl Malonate with Phenyl 2-Hydroxystyryl Ketone.—Phenyl 2-hydroxystyryl ketone (10 g.) and ethyl malonate (11 g.) were dissolved in the minimum quantity of absolute alcohol and treated with alcoholic sodium ethoxide (from 3 g. of sodium). The homogeneous, red solution was kept at room temperature for 10 weeks, an amorphous, red solid slowly separating. This was collected and thoroughly washed with dilute hydrochloric acid and finally with water. The dried product crystallised from benzene (with blood-charcoal) in long, colourless needles, m. p. 190°. The melting point of coumarin-α-carboxylic acid ascribed by various authors varies between 187° and 191° (Found : C, 62·6; H, 5·3. Calc. for $C_{10}H_6O_4$: C, 62·6; H, 5·3%).

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