

CCV.—*The Isomerism of the Styryl Alkyl Ketones.*
Part III. Methoxy-2- and 4-hydroxystyryl Alkyl Ketones.

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IN order to confirm the results of the investigations on the isomerism and behaviour towards alkali of the hydroxystyryl alkyl ketones (J., 1924, **125**, 2099; 1925, **127**, 2539) various derivatives of 2-hydroxystyryl methyl ketone and analogous compounds have been prepared and examined.

5-Methoxy-2-hydroxystyryl methyl ketone (Heilbron and Whitworth, J., 1923, **123**, 238), like the 2-hydroxy-compound, exists in a yellow and a colourless form of identical m. p. and is partly converted into the red *sodium* salt of 5 : 5'-dimethoxy-2 : 2'-dihydroxydistyryl ketone in alkaline solution. This change occurs instantly with the yellow isomeride, but only very slowly with the colourless modification; the colourless form of 2-hydroxystyryl methyl ketone also develops the usual red colour in similar circumstances.

The colourless form of 4-methoxy-2-hydroxystyryl methyl ketone has been isolated; it is stable in air and resembles the colourless form of 2-hydroxystyryl methyl ketone in properties. The yellow form (Heilbron and Whitworth, *loc. cit.*) has not been obtained pure and is under investigation.

The yellow crystalline condensation product, m. p. 83°, of 3-methoxysalicylaldehyde and acetone obtained by Heilbron and Whitworth (*loc. cit.*), and regarded by them as β -hydroxy- β -3-methoxy-2-hydroxyphenylethyl methyl ketone, has also been described by Nomura and Nozawa (*Sci. Rep. Tōhoku Imp. Univ.*, 1918, **7**, 79), who consider it a hydrate of 3-methoxy-2-hydroxystyryl methyl ketone. Further examination indicates that it is a hydrate rather than an aldol. In addition to the benzoyl derivative of 3-methoxy-2-hydroxystyryl methyl ketone already obtained from it by Heilbron and Whitworth (*loc. cit.*) an *acetyl* derivative of the unsaturated ketone has been prepared. Both compounds, on hydrolysis, yield the hydrated substance. Moreover, condensation of this compound with 3-methoxysalicylaldehyde produces the symmetrical distyryl ketone. Again, crystallisation of the hydrated substance from dry benzene yields, as a second crop, colourless needles which, on removal of the solvent, immediately absorb water to form the original yellow compound of m. p. 83°. 3-Methoxy-2-hydroxystyryl methyl ketone, however, could not be isolated. From the compound of m. p. 83°, by crystallisation from an anhydrous solvent, Nomura and Nozawa (*loc. cit.*) obtained

an unsaturated ketone of m. p. 77—77·5°. This m. p. for 3-methoxy-2-hydroxystyryl methyl ketone is anomalous in three respects : (i) all ketones of this type melt at about 130°; (ii) removal of water from an aldol or a hydrate invariably causes a rise in m. p.; (iii) the symmetrical distyryl ketone has a normal m. p.

In Part I the compound of m. p. 83° was assumed to have the aldol structure, and the fact that it could not be isomerised was taken as evidence of the geometric nature of the isomerism of this class of ketones. In view of the present observations this evidence cannot be taken as conclusive.

The yellow form of 3-methoxy-4-hydroxystyryl methyl ketone (Francesconi, *Gazzetta*, 1908, **38**, ii, 70; McGookin and Heilbron, *J.*, 1924, **125**, 2104) is peculiar in being exceedingly stable, resisting isomerisation except by extreme methods. When, however, concentrated alkali is added to its alkaline solution, the salt precipitated is that of the colourless form. Hence it is assumed that the salts of both isomerides are in equilibrium in alkaline solution.

The yellow form of 3-methoxy-4-hydroxystyryl methyl ketone changes on fusion into the colourless modification of the same m. p.—a similar change doubtless accounts for the identity of the m. p.'s of each pair of isomerides throughout this series of ketones. Both forms of this substance resemble those of 2-hydroxystyryl methyl ketone by dissolving in alkali, the yellow form to yield a red solution and the colourless isomeride to give a yellow solution which assumes a red colour on standing. In both instances the red colour is due to the *sodium* salt of 3 : 3'-dimethoxy-4 : 4'-dihydroxydistyryl ketone. Hence styryl methyl ketones are capable of condensing to a slight extent with 4-hydroxyaldehydes in the presence of alkalis (compare Buck and Heilbron, *J.*, 1922, **121**, 1095).

EXPERIMENTAL.

5-Methoxy-2-hydroxystyryl Methyl Ketone.—The colourless modification was obtained, by boiling the yellow isomeride (Heilbron and Whitworth, *loc. cit.*) with water containing a trace of acid, in needles, m. p. 124°, soluble in alcohol or benzene. It dissolves in alkali to a yellow solution which develops a deep red colour after 12 hours (Found : C, 68·5; H, 6·3. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%).

5 : 5'-Dimethoxy-2 : 2'-dihydroxydistyryl Ketone.—When 40% sodium hydroxide (10 c.c.) was added to a solution of the yellow isomeride of 5-methoxy-2-hydroxystyryl methyl ketone (2 g.) in 20% sodium hydroxide (30 c.c.), lustrous, green needles separated. An aqueous solution of these, on acidification, gave the distyryl ketone (1·2 g.), which crystallised from alcohol in orange needles,

m. p. 158°, soluble in acetone but almost insoluble in benzene (Found : C, 69.6; H, 5.6. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5%).

4-Methoxy-2-hydroxystyryl Methyl Ketone.—The following is the best modification of Heilbron and Whitworth's method. To a solution of 4-methoxysalicylaldehyde (9 g.) and acetone (16 g.) in alcohol (100 c.c.), sodium hydroxide (200 c.c. of 20%) was added. After 3 days the red mixture was diluted with water (1000 c.c.), cooled to 0°, and almost neutralised with dilute sulphuric acid (rise of temperature or excess of acid caused the production of tar). The product (10 g.) was crystallised from benzene and from chloroform-hexane and obtained in colourless needles, m. p. 131°. It was readily soluble in alkali to a yellow solution which developed a deep red colour after 12 hours.

4 : 4'-Dimethoxy-2 : 2'-dihydroxydistyryl Ketone.—A mixture of 2 mols. of 4-methoxysalicylaldehyde (10 g.), 1 mol. of acetone (2 g.), and alcohol (40 c.c.) was treated with sodium hydroxide (250 c.c. of 20%) and warmed on the water-bath for 10 minutes. The deep red solution deposited, after 12 hours, lustrous green needles of the *sodium* salt of the distyryl ketone. From an aqueous solution of this, almost neutralised at 0°, the *ketone* was precipitated as a yellow solid. It crystallised from cold aqueous alcohol in brown plates, m. p. 170°, soluble in alcohol, but almost insoluble in benzene. It is unstable and produces a red solution with an intense green fluorescence when warmed in alcohol (Found : C, 69.6; H, 5.6. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5%).

3-Methoxy-2-hydroxystyryl Methyl Ketone Hydrate (?).—This compound (Heilbron and Whitworth, *loc. cit.*) formed yellow plates, m. p. 83°, from aqueous alcohol. It crystallised from dry benzene in similar yellow plates, but the second crop of crystals consisted of colourless, hygroscopic needles. These dissolved in alkali to form an orange-red solution which developed the usual deep red colour on standing.

3-Methoxy-2-acetoxystyryl Methyl Ketone.—The hydrated compound (10 g.) was boiled for an hour with acetic anhydride (150 c.c.), the hot solution poured into an excess of water, and almost neutralised with sodium carbonate. The precipitate produced (10 g.) crystallised from alcohol in colourless needles, m. p. 91°, soluble in benzene or hot water (Found : C, 66.4; H, 6.1. $C_{13}H_{14}O_4$ requires C, 66.6; H, 6.0%).

3 : 3'-Dimethoxy-2 : 2'-dihydroxydistyryl Ketone.—The sodium salt that separated after 24 hours from a solution of 3-methoxysalicylaldehyde (50 g.) in acetone (80 g.) and sodium hydroxide (600 c.c. of 2.5%) to which 10% sodium hydroxide (240 c.c.) had been added was dissolved in water and acidified. The ketone precipitated

crystallised from aqueous alcohol in orange needles, m. p. 182° (Found : C, 69.6; H, 5.5. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5%).

3-Methoxy-4-hydroxystyryl Methyl Ketone.—A solution of vanillin (50 g.) in acetone (120 c.c.) and alcohol (50 c.c.) was treated with sodium hydroxide (100 c.c. of 20%) and kept for 12 hours. Long, yellow needles of the *sodium* salt of the colourless isomeride were produced; the *ketone* obtained from these crystallised from aqueous alcohol in colourless needles, m. p. 129°, soluble in acetone or benzene. It dissolved in alkali to a yellow solution which turned red after 12 hours.

3 : 3'-Dimethoxy-4 : 4'-dihydroxydistyryl Ketone.*—(a) On boiling, a solution of the preceding colourless isomeride (25 g.) in sodium hydroxide (200 c.c. of 20%) became deep red and acetone was evolved. When the evolution of this had ceased, after 15 minutes, the solution was cooled, and sodium hydroxide (40%) added until a precipitate formed. Lustrous green needles of the *sodium* salt of the distyryl ketone slowly separated. The *ketone* obtained from these crystallised from chloroform in pale yellow needles, m. p. 142° (Found : C, 69.6; H, 5.6. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.5%).

This compound was very soluble in alcohol or acetone, moderately easily soluble in chloroform, but almost insoluble in benzene. It forms an orange-red *hydrate*, m. p. 121°, containing one molecule of water when crystallised from an aqueous solvent (Found : C, 65.8; H, 5.9. $C_{19}H_{18}O_5 \cdot H_2O$ requires C, 66.2; H, 5.8%). The hydrate loses water when heated in a steam-oven or crystallised from a non-aqueous solvent.

(b) A better yield (15 g.) of the distyryl ketone was obtained by gradually adding concentrated hydrochloric acid (50 c.c.) to a solution of vanillin (25 g.) in acetone (90 c.c.) cooled in a freezing mixture. A dark violet-red coloration was observed and from the mixture, kept at 0° for 4 days, green-black crystals separated. These were filtered off, washed well with ether, and decomposed by dissolution in excess of sodium hydroxide (10%). The free distyryl ketone was obtained from this solution as before.

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* This compound has recently been prepared by Nomura and Hotta (*Sci. Rep. Tôhoku Imp. Univ.*, 1925, **14**, 119).
