

CXXXII.—*The Reactivity of Doubly-conjugated Unsaturated Ketones. Part III. Unsymmetrical Hydroxy- and Methoxy-derivatives.*

By JOHANNES SYBRANDT BUCK and ISIDOR MORRIS HEILBRON.

It has previously been shown (Heilbron and Buck, T., 1921, **119**, 1500) that *p*-dimethylaminobenzaldehyde readily condenses with *o*-hydroxystyryl methyl ketone, in presence of alkali, to yield a complex composed of one molecule of 4'-dimethylamino-2-hydroxy-distyryl ketone and one molecule of *p*-dimethylaminobenzaldehyde, which latter component can be replaced by other compounds, such as benzene, alcohol, etc. The abnormal behaviour of this substance induced us to study in closer detail the methods of preparation, and the properties of other doubly-conjugated unsaturated ketones. On examining the literature it was found that, although various symmetrically substituted distyryl ketones had been prepared, the only unsymmetrical compound of this class, containing a 2-hydroxyl group, described, was 2-hydroxydistyryl ketone (Kostanecki and Maron, *Ber.*, 1898, **31**, 728). The authors have now condensed *o*-hydroxystyryl methyl ketone (Harries, *Ber.*, 1891, **24**, 3180) with various substituted benzaldehydes, in the presence of sodium hydroxide. In general, the reaction proceeds rapidly in the presence of strong alkali, so that by stopping the condensation after a determined period, a good yield of the unsymmetrically substituted ketone is obtained. If other conditions are applied, such as more dilute solutions or a longer reaction period, the yield is much diminished, and the product is contaminated with the corresponding symmetrically substituted ketones, which, as already shown (Heilbron and Buck, *loc. cit.*), tend to be produced by the fission of the first-formed unsymmetrical ketone.

In this work, very definite limitations soon became apparent. In no case could a substituted benzaldehyde, containing a *p*-hydroxyl group, be condensed by the above-described reaction, the unchanged reagents being recovered, or, on more vigorous treatment, oily or resinous substances being produced. Protocatechualdehyde, vanillin, β -resorcyraldehyde, and *p*-hydroxybenzaldehyde were investigated, but in no case could the desired condensation product be obtained, even under the most varied conditions. A similar difficulty was encountered by Perkin, Robinson, and Turner (T., 1908, **93**, 1085), who failed to condense β -resorcyraldehyde with 1-hydrindones, whereas *p*-methoxysalicylaldehyde readily entered into condensation (Perkin and Robinson, T., 1907, **91**, 1073). That,

however, the inhibiting factor is not due solely to the presence of a hydroxyl group in the para-position to the aldehydic group is shown by the fact that both *p*-hydroxybenzaldehyde and vanillin readily condense with acetone to yield the corresponding substituted styryl methyl ketones. On the other hand, we have failed to bring about condensation in alkaline solution between either protocatechualdehyde or β -resorcyraldehyde and acetone, and the conclusion may thus be drawn that an accumulation of hydroxyl groups in the aldehyde either inhibits the condensation altogether, or that condensation takes place, yielding the polyhydroxy-unsaturated ketone, which, when formed, immediately breaks down under the conditions of the experiment.

In order to test the validity of the latter deduction, a condensation was attempted between *o*-hydroxystyryl methyl ketone and gentisaldehyde, in which no *p*-hydroxyl group is present. The result was somewhat unexpected, for although no unsymmetrical distyryl ketone was isolated as such, *o*-hydroxystyryl methyl ketone was recovered in a form hitherto unobserved, being obtained in colourless prisms, which melt at the same temperature as the ordinary yellow form, but exhibit very marked differences in behaviour.

The difference between the two forms does not appear explicable simply on the assumption of *cis*- and *trans*-isomerism, such as has been observed by Haber with piperonylideneacetone (*Ber.*, 1891, 24, 618), but is probably dependent on the presence of an *o*-hydroxyl group forming, in one case, a ring system with the carbonyl oxygen atom, in the manner postulated in Part I of these communications. The whole question is at present being investigated in detail and will be dealt with in a separate paper.

The isolation of this new modification of *o*-hydroxystyryl methyl ketone appears to us only explicable on the assumption that condensation with formation of the unsymmetrical polyhydroxy-distyryl ketone must actually have taken place in the first instance, followed immediately by the fission of the labile condensation product. On this view, gentisaldehyde would function, until completely resinified by the alkali present, after the manner of an ordinary catalyst.

The failure to isolate polyhydroxy-unsymmetrical distyryl ketones cannot then be attributable to any peculiar property of the hydroxy-aldehydes themselves, but solely to the instability of such ketones in presence of alkali, this being most marked in those containing either a *p*-hydroxyl group in one of the benzene rings or an accumulation of such groups.

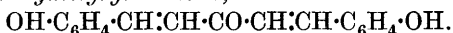
Control condensations were carried out where possible by the

converse method of condensing salicylaldehyde with a substituted styryl methyl ketone, but it was generally found that this reaction was unsatisfactory and the products obtained were oily in character and difficult to manipulate. 3-Methoxy-4-hydroxystyryl methyl ketone (vanillylideneacetone) and *p*-hydroxystyryl methyl ketone failed to condense with salicylaldehyde and were recovered unchanged from the reaction mixture.

The ketones described in the experimental part have not yet been fully examined as regards their activity, but this is less than in the case of 4'-dimethylamino-2-hydroxydistyryl ketone. None of the compounds combines with solvents, but the degree of additivity may be gauged by that of 4'-methoxy-2-hydroxydistyryl ketone, which forms additive compounds with *m*-dinitrobenzene and *p*-dimethylaminobenzaldehyde. The action of hydroxylamine, phenylhydrazine, and semicarbazide on these ketones also appears to be abnormal.

EXPERIMENTAL.

3' : 2-Dihydroxydistyryl Ketone,



—Twelve grams of *m*-hydroxybenzaldehyde were dissolved, together with 16 grams of *o*-hydroxystyryl methyl ketone, in 70 c.c. of absolute alcohol, and the solution was treated with 24 c.c. of 50 per cent. sodium hydroxide solution (3 mols. NaOH). After standing for three hours at room temperature, the solution was diluted with water, cooled with ice, and carefully neutralised with dilute acetic acid. A semi-solid mass was thus precipitated, which was allowed to harden and twice crystallised from aqueous alcohol. The ketone obtained in this way was finally purified by boiling with benzene, in which it is very sparingly soluble, but which removes traces of some readily soluble impurity. It crystallises out with one molecule of water in the form of a yellowish-green, crystalline powder, melting at 137° with the production of a deep green liquid (Found: C = 71.6; H = 5.8. $\text{C}_{17}\text{H}_{14}\text{O}_3\cdot\text{H}_2\text{O}$ requires C = 71.8; H = 5.6 per cent.).

In order to prove that the molecule of water is not constitutional, the *dibenzoyl* derivative was prepared. It forms pale yellow prisms melting at 112–113°, and corresponds with a simple dibenzoyl compound (Found: C = 78.24; H = 4.86. $\text{C}_{31}\text{H}_{22}\text{O}_5$ requires C = 78.48; H = 4.64 per cent.).

2'-Methoxy-2-hydroxydistyryl Ketone.—6.8 Grams of *o*-methoxybenzaldehyde and 8.1 grams of *o*-hydroxystyryl methyl ketone, dissolved in 25 c.c. of ethyl alcohol, were treated with 40 c.c. of 10 per cent. sodium hydroxide solution (2 mols. NaOH). After

leaving the mixture to stand, the sodium salt, which had separated out over-night in the form of dull red crystals, was filtered off, suspended in water, and decomposed with dilute acetic acid. The crude yellow precipitate thus obtained (13 grams) was purified by two recrystallisations from benzene, using animal charcoal as decolorising agent. When pure, the ketone forms a pale apple-green, crystalline mass, melting at 129° , moderately soluble in the usual solvents (Found: C = 76.9; H = 5.8. $C_{18}H_{16}O_3$ requires C = 77.0; H = 5.7 per cent.).

3'-Methoxy-2-hydroxydistyryl Ketone.—This ketone was only prepared with difficulty, very small yields being obtained. The following preparation was the best of several carried out. 6.8 Grams of *m*-methoxybenzaldehyde and 8.1 grams of *o*-hydroxystyryl methyl ketone were dissolved together in 25 c.c. of 92 per cent. alcohol, and the solution was then treated with 40 c.c. of 10 per cent. sodium hydroxide solution (2 mols.). After standing over-night, the mixture was diluted with water, cooled with ice, and neutralised with dilute acetic acid. The ketone was precipitated in yellow flocks which, on filtering, tended to yield a gum-like mass, which became superficially brown on standing in air. By working up the product from a benzene-ether mixture, with the addition of light petroleum, a yield of nodular yellow crystals (about 1.5 grams) was obtained. The remainder of the product formed a limpid yellow oil of unknown constitution. For analysis, the ketone was recrystallised from benzene, in which it is moderately soluble. It forms small, canary-yellow, crystalline nodules, and melts at 128° to a deep green liquid (Found: C = 77.1; H = 5.8. $C_{18}H_{16}O_3$ requires C = 77.0; H = 5.7 per cent.).

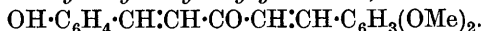
4'-Methoxy-2-hydroxydistyryl Ketone.—Twelve grams of *o*-hydroxystyryl methyl ketone and 13.6 grams of anisaldehyde were dissolved in 70 c.c. of absolute alcohol, and the solution was treated with 16 c.c. of 50 per cent. sodium hydroxide solution (2 mols. NaOH). On standing at room temperature, bright red needles of the sodium salt separated out. These were suspended in ice-water and decomposed with dilute acetic acid. A yellow, gummy product separated which, after hardening, was filtered off and recrystallised from aqueous acetone. For analysis, it was recrystallised twice from chloroform and finally from benzene. The ketone forms tiny, yellow needles, melting at 139° to a green liquid. It is moderately soluble in benzene or chloroform, and very soluble in alcohol or acetone (Found: C = 76.9; H = 5.7. $C_{18}H_{16}O_3$ requires C = 77.0; H = 5.7 per cent.).

The *p*-dimethylaminobenzaldehyde additive product is readily obtained by dissolving equimolecular portions of the aldehyde and

ketone in the minimum quantity of hot absolute alcohol, and allowing the mixture to cool. The compound separates out as lemon-yellow prisms, melting at 91—92° (Found: C = 75.3; H = 6.5. $C_{27}H_{27}O_4N$ requires C = 75.5; H = 6.3 per cent.).

The *m*-dinitrobenzene additive product, prepared in a similar manner, is obtained as an orange-coloured, crystalline powder, melting at 117° (Found: N = 6.2. $C_{24}H_{20}O_7N_2$ requires N = 6.2 per cent.).

3' : 4'-Dimethoxy-2-hydroxydistyryl Ketone,

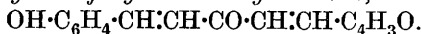


—16.4 Grams of veratraldehyde and 16.2 grams of *o*-hydroxystyryl methyl ketone were dissolved together in 40 c.c. of absolute alcohol and treated with 16 c.c. of 50 per cent. sodium hydroxide solution (2 mols. NaOH). After the mixture had stood for ten minutes, 150 c.c. of water were added. The whole soon set to a solid mass, which was now again diluted with a further 100 c.c. of water. After three hours, the brilliant red needles of the sodium salt were filtered off, suspended in water, and decomposed with acetic acid. A yellow, gummy mass, which hardened on standing, was thus obtained, from which, however, the ketone was extremely difficult to obtain pure. Better results were obtained by first recrystallising the sodium salt from an alcohol-ethyl acetate mixture, then suspending it in benzene, and decomposing it with the exact amount of glacial acetic acid. On heating the mixture, the ketone went into solution and, after filtration, was allowed to crystallise out. This product was then repeatedly recrystallised from benzene, in which it is only moderately soluble, animal charcoal being used as decolorising agent. The ketone consists of apple-green, rhombic crystals which melt at 140—141° with the production of a deep green liquid (Found: C = 73.5; H = 5.9. $C_{19}H_{18}O_4$ requires C = 73.6; H = 5.8 per cent.).

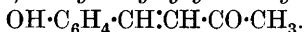
3' : 4'-Methylenedioxy-2-hydroxydistyryl Ketone.—6.5 Grams of *o*-hydroxystyryl methyl ketone and 5.9 grams of piperonal were dissolved together in 100 c.c. of absolute alcohol, and the solution was then treated with 32 c.c. of 10 per cent. sodium hydroxide solution (2 mols.). After standing thirty hours at room temperature, the mixture was diluted with ice-water and neutralised with dilute acetic acid. The bright yellow product was allowed to harden and crystallised from a mixture of alcohol and benzene. Yield (crude) 10.5 grams. For analysis, the ketone was recrystallised three times from alcohol-benzene mixture. It consists of golden-yellow needles, melting at 170—171° (slow heating) with frothing and decomposition. The compound is moderately soluble in alcohol with a yellow colour, but only slightly soluble in benzene,

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the solution in this case being more nearly orange in colour (Found: C = 73.2; H = 4.7. $C_{18}H_{14}O_4$ requires C = 73.5; H = 4.8 per cent.).

2-Hydroxystyryl Furfurylidenemethyl Ketone,

—Sixteen grams of *o*-hydroxystyryl methyl ketone and 10 grams of furfuraldehyde were dissolved in 70 c.c. of absolute alcohol, and 16 c.c. of 50 per cent. sodium hydroxide solution (2 mols. NaOH) then added to the mixture. As heat was developed in the reaction, the mixture was diluted with 50 c.c. of water and cooled with ice-water. After standing over-night, the reaction mixture was poured into 700 c.c. of ice-water and neutralised with dilute acetic acid. The product, which had an ochre colour and the appearance of a solidified oil, was recrystallised from ethyl acetate, using animal charcoal. Only a small portion was thus obtained crystalline, the remainder being oily. For analysis, the crystalline product was recrystallised three times from absolute alcohol, and, finally, once from benzene, in which it is rather sparingly soluble. The ketone forms bright yellow, glistening prisms, melting at 162–163°, with violent frothing and the production of the characteristic dark green liquid (Found: C = 75.0; H = 5.1. $C_{15}H_{12}O_3$ requires C = 75.0; H = 5.0 per cent.).

New Modification of o-Hydroxystyryl Methyl Ketone,

—5.4 Grams of *o*-hydroxystyryl methyl ketone and 5.1 grams of gentisaldehyde were dissolved together in 50 c.c. of absolute alcohol, and the solution was then treated with 4 mols. of sodium hydroxide (5.3 grams NaOH in 7.5 c.c. of water). After a few minutes, 10 c.c. of water were added and, shortly afterwards, a dark solid commenced to separate out. The whole was left over-night and the deep brown mixture then diluted with water and neutralised with dilute acetic acid. As very little solid separated, the solution was accordingly saturated with brine and extracted with ether. After drying over calcium chloride, the ether was distilled off and the residual oil immediately taken up in benzene. On standing, 2.5 grams of a faintly yellow solid separated out which, after twice recrystallising from boiling benzene, using animal charcoal, was obtained in long, colourless prisms, melting at 139° and showing no depression when mixed with a specimen of the original *o*-hydroxystyryl methyl ketone (Found: C = 73.9; H = 6.3. $C_{10}H_{10}O_2$ requires C = 74.1; H = 6.2 per cent.).

p-Hydroxystyryl Methyl Ketone.—The only method given in the literature for the preparation of *p*-hydroxystyryl methyl ketone is that of Zincke and Muhlhausen (*Ber.*, 1903, **36**, 134), who obtained

the compound in poor yield by means of acid condensation. We have now prepared this ketone very conveniently by the following method :

Four grams of *p*-hydroxybenzaldehyde were dissolved in 15 c.c. of acetone and the solution was then treated with 5.3 c.c. of 50 per cent. sodium hydroxide solution (2 mols. NaOH). Ten c.c. of water were then added and the mixture was gently warmed for a few moments. By the following day, the whole had solidified to an orange-red, crystalline mass, which was dissolved in water and decomposed with dilute hydrochloric acid, when a golden-yellow oil, which solidified on standing, separated out. The yield was practically theoretical. After recrystallisation, first from dilute acetone and then from boiling water, using animal charcoal, the ketone was obtained in long, almost colourless needles, melting at 114—115° (Zincke and Muhlhausen give the melting point as 102—103°) (Found: C = 74.0; H = 6.3. Calc., C = 74.1; H = 6.2 per cent.).

In conclusion, we desire to express our thanks to the Department of Scientific and Industrial Research for a grant to one of us (J. S. B.) which has enabled this investigation to be undertaken.

DEPARTMENT OF ORGANIC CHEMISTRY,
THE UNIVERSITY OF LIVERPOOL.

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