CXLIX.—*The Isomerism of the Styryl Alkyl Ketones. Part IV. 4-Hydroxy- and Some Derivatives of 2-Hydroxy-styryl Alkyl Ketones.*

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THE examination of a further series of styryl alkyl ketones has led to some interesting developments and to a confirmation of the earlier work (J., 1924, **125**, 2099; 1925, **127**, 2539; 1926, 1578).

5-Bromo-2-hydroxystyryl methyl ketone (Part I) reacts in alkaline solution like the 2-hydroxy-compound with the production of the sodium salt of the distyryl ketone. In addition to the yellow distyryl ketone described by Fabinyi and Széki (*Ber.*, 1907, **40**, 3455), a colourless *isomeride* of different m. p. has now been prepared. Instances of isomerism amongst the distyryl ketones are rare, although this type of ketone could exist in three isomeric forms.

Zincke and Muhlhausen (*Ber.*, 1903, **36**, 129) and Vorländer (*Ber.*, 1925, **58**, 118) obtained green and yellow forms of 4 : 4′-dihydroxydistyryl ketone. Straus (*Annalen*, 1910, **374**, 40) described yellow and colourless modifications of 4 : 4′-dimethoxydistyryl ketone of different m. p.'s. Heilbron and Whitworth (J., 1923, **123**, 238) prepared 4′-dimethylamino-2-hydroxy-3-methoxydistyryl ketone in two red forms having differing m. p.'s. Dickinson, Heilbron, and Irving (J., 1927, 1888) isolated 3 : 3′-dimethoxy-4 : 4′-dibenzyloxydistyryl ketone and an isomeride of different m. p. Glaser and Tramer (*J. pr. Chem.*, 1927, **116**, 331) described a green form of 2 : 2′-dihydroxydistyryl ketone obtained by heating the ordinary yellow isomeride. The present authors were able to isolate only a green, impure specimen of dipheno*spiro*pyran by this treatment (Part I). Glaser and Tramer (*loc. cit.*) also prepared a green form of 4 : 4′-dihydroxy-3 : 3′-dimethoxydistyryl ketone which must be an isomeride of the compound described in Part III and by Nomura and Hotta (*Sci. Rep. Tôhoku Imp. Univ.*, 1925, **14**, 119). Glaser and Tramer also discuss the fission occurring in the molecules of unsaturated ketones which has already been considered in the present series.

2-*Hydroxy*-4-*methoxystyryl ethyl ketone*, 2-*hydroxy*-4-*methoxystyryl* n-*propyl ketone*, 2-*hydroxy*-3-*methoxystyryl ethyl ketone*, 2-*hydroxy*-3-*methoxystyryl* n-*propyl ketone*, 4-*hydroxystyryl methyl ketone*, 4-*hydroxystyryl ethyl ketone*, and 2-*hydroxystyryl* iso*propyl ketone* were found to be similar to the ketones previously described.

Nomura and Nozawa (*Sci. Rep. Tôhoku Imp. Univ.*, 1918, **7**, 79) described the preparation of 3-hydroxystyryl methyl ketone by the direct method. Attempts to repeat the condensation both in acid and in alkaline media resulted in the production of a buff-coloured, amorphous solid, possibly a polymeride of the simple ketone, into which it could not be converted. The simple ketone was prepared by the method of Murai (*Sci. Rep. Tôhoku Imp. Univ.*, 1925, **14**, 149) from 3-nitrostyryl methyl ketone, which the present authors found to melt at a temperature higher than that recorded by Murai (*loc. cit.*) and by Vorländer (*Annalen*, 1897, **294**, 273). Attempts to isolate the 3-amino-compound previously prepared by Miller and Rhode (*Ber.*, 1890, **23**, 1881), as an oil, were unsuccessful.

No distyryl ketone is produced by the action of alkali on 4-hydroxystyryl methyl ketone, and this compound will not condense with 4-hydroxybenzaldehyde in alkaline media, previous observations on the failure of 4-hydroxybenzaldehydes to condense under these conditions (Part I) or to react only to a very slight extent (Part II) thus being confirmed. 4 : 4′-Dihydroxydistyryl ketone has been prepared only by acid condensation (compare Zincke and Muhlhausen, *loc. cit.*; Vorländer, *loc. cit.*).

Attempts to prepare 2-hydroxystyryl benzhydryl ketone by the direct condensation of salicylaldehyde and benzhydryl methyl ketone in presence of 40% potassium hydroxide solution, sodium ethoxide or piperidine were unsuccessful, although benzhydryl methyl ketone has been condensed with benzaldehyde and its 4-methoxy-derivative by Rack (*Ber.*, 1923, **56**, 1130).

In order to prove that aldehydes do not react with the methylene groups of ketones in the presence of alkalis, attempts were made to condense salicylaldehyde with diethyl ketone and with 2-hydroxystyryl ethyl ketone under these conditions without success. Even the reactive 4-dimethylaminobenzaldehyde would not condense with 2-hydroxystyryl ethyl ketone in alkaline media.

The hydroxystyryl alkyl ketones so far described are of two types. The ketones of both types undergo fission in alkaline media, furnish red solutions more or less readily when boiled with concentrated hydrochloric acid, and exist each in isomeric forms of identical m. p. The ketones of type I all contain the group $>CH{:}CH{\cdot}CO{\cdot}CH_3$ and their fission products recombine in alkaline solution to form the distyryl ketones. The ketones of type II contain the group $>CH{:}CH{\cdot}CO{\cdot}CH_2R$, where R is any alkyl group, and their fission products recombine in alkaline media with the formation of high-melting, unsaturated substances of undetermined nature.

Styryl ketones of a third type have now been prepared which differ from those of types I and II in that (i) alkali has no action, other than solvent action, upon them even on prolonged exposure, and (ii) they are not attacked by boiling concentrated hydrochloric acid.

2-*Hydroxystyryl* tert.-*butyl ketone*, 2-*hydroxystyryl phenyl ketone*, and 2-*hydroxystyryl* iso*butenyl ketone* belong to this class. The second of these compounds has not been isomerised, but the other two exist in the usual isomeric forms.

2-Hydroxystyryl *iso*butenyl ketone (I) is formed in small yield by the condensation of salicylaldehyde with mesityl oxide in alkaline solution, the main products being 2-hydroxystyryl methyl ketone and 2 : 2′-dihydroxydistyryl ketone, which are formed thus (X denotes $HO{\cdot}C_6H_4$) :

$$\text{(I.)}\quad X{\cdot}CH{:}CH{\cdot}CO{\cdot}CH{:}CMe_2 \xrightarrow{H_2O} X{\cdot}CH{:}CH{\cdot}COMe + COMe_2.$$

$$2X{\cdot}CHO + Me_2CO = (X{\cdot}CH{:}CH)_2CO + 2H_2O.$$

Other instances of isomerism amongst the styryl ketones (see table) appear in the literature, although they have not previously been recognised. In addition a number of styryl aryl ketones are known, the isomeric forms having different m. p.'s ; data regarding these compounds will be published elsewhere.

	M. p. of forms.		
Ketone.	Yellow.	Colourless.	Reference.
4-Methoxystyryl methyl	—	73°	Einhorn and Grabfeld, *Ann.*, 1888, **243**, 362.
	—	72—74	Baeyer and Villiger, *Ber.*, 1902, **35**, 1189.
	74—75°	—	Nomura and Nozawa, *loc. cit.*
3·Nitro-4-methoxystyryl methyl	159	159(?)	Einhorn and Grabfeld, *loc. cit.*
2·Methoxystyryl methyl	—	48—50	Auwers, *Ann.*, 1917, **413**, 279.
	50	—	Heilbron and Buck, J., 1921, **119**, 1500.
	50	—	Faillebin, *Ann. Chim.*, 1925, **4**, 410.
3·Methoxy·4·ethoxystyryl methyl	106	106	Dickinson, Heilbron, and Irving, J., 1927, 1888.
3-Nitrostyryl phenyl	145—146	—	Sorge, *Ber.*, 1902, **35**, 1065.
	145	—	Ruhemann, J., 1903, **83**, 1371.
	—	143—144	Bodforss, *Ber.*, 1916, **49**, 2795.
2-Methoxystyryl phenyl	58—59	—	Stobbe and Wilson, J., 1910, **97**, 1732.
	—	60	Forster and Heilbron, J., 1924, **125**, 340.
4·Methoxystyryl phenyl	107	—	Pfeiffer, *Ann.*, 1917, **412**, 253.
	—	106—107	Stockhausen and Gattermann, *Ber.*, 1892, **25**, 3535.
4·Aldehydostyryl phenyl	125	125(?)	Lendenfeld, *Monatsh.*, 1906, **27**, 169.
4·Methoxy·β·phenylstyryl phenyl	113	—	Klages and Tetzner, *Ber.*, 1902, **35**, 3965.
	—	113	Das and Ghosh, J., 1919, **115**, 817.

EXPERIMENTAL.

5 : 5′-*Dibromo*-2 : 2′-*dihydroxydistyryl Ketone*.—The sodium salt slowly separated in green crystals from the red solution produced by treatment of the monostyryl methyl ketone with alkali. Acidification of a solution of these crystals produced the free ketone, which separated from alcohol in bright yellow crystals, m. p. 188°. It can also be prepared by the usual condensation methods (i) from 5-bromo-2-hydroxystyryl methyl ketone and 5-bromosalicylaldehyde, and (ii) from 5-bromosalicylaldehyde and acetone. A solution of the aldehyde (50 g.) in 10% aqueous sodium hydroxide (150 c.c.) was diluted with 700 c.c. of water, and acetone (7·2 g.) introduced. After 4 days, the green crystals that had separated were collected, dissolved in water, and almost neutralised with dilute acetic acid, and the ketone was precipitated with carbon dioxide. Recrystallisation from benzene produced yellow, matted crystals, m. p. 188°. The mother-liquor furnished a greyish solid which, after recrystallisation, separated in colourless, rhombic crystals, m. p. 174·5° (Found : C, 48·3 ; H, 2·95 ; Br, 37·95. $C_{17}H_{12}O_3Br_2$ requires C, 48·1 ; H, 2·8 ; Br, 37·7%). This compound dissolved in alkali with a yellow colour, being thus distinguished readily from the yellow isomeride. A mixture of the two forms melted at 174·5°.

Many of the styryl ketones described below were obtained by the following alkali-condensation method. A solution of the aldehyde and the ketone in alcohol (80—150 c.c.) was treated with 20% sodium hydroxide solution and after a time (12 hours—3 days) an aqueous solution of the crystals that had separated, or the original liquid if no crystals separated, was acidified; the styryl ketone obtained was crystallised from alcohol or benzene.

2-*Hydroxy*-4-*methoxystyryl ethyl ketone*, obtained from 2-hydroxy-4-methoxybenzaldehyde (10 g.), methyl ethyl ketone (5 g.), and alkali (250 c.c.), formed yellow crystals, m. p. 123°, which rapidly became green when kept. Recrystallisation then yielded colourless needles, m. p. 123° (Found : C, 69·4; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). The colourless form dissolved in alkali, giving a yellow solution which turned orange in 5 days.

2-*Hydroxy*-4-*methoxystyryl propyl ketone*, obtained from 2-hydroxy-4-methoxybenzaldehyde (9 g.), methyl *n*-propyl ketone (20 g.), and alkali (150 c.c.), formed yellow needles, m. p. 111—112°. The colourless form, obtained in the usual way, melted at 111—112° and gave a yellow alkaline solution which developed an orange tint after 8 days (Found : C, 70·9; H, 7·35. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

2-*Hydroxy*-3-*methoxystyryl ethyl ketone*, prepared from 2-hydroxy-3-methoxybenzaldehyde (20 g.), methyl ethyl ketone (9·5 g.), and alkali (25 g. KOH in 155 c.c. water), was obtained as a hydrate in pale yellow needles, m. p. 77—79°, which could be dehydrated only by heating in a steam-oven. The product crystallised from benzene–hexane in colourless needles, m. p. 86·5°, the solution of which in alkali was orange-coloured (Found : C, 69·5; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%).

2-*Hydroxy*-3-*methoxystyryl propyl ketone*, obtained from 2-hydroxy-3-methoxybenzaldehyde (10 g.), methyl *n*-propyl ketone (5 g.), and alkali (400 c.c.), formed colourless, arrow-shaped crystals (from alcohol), m. p. 82·5°, giving an orange solution in alkali (Found : C, 70·9; H, 7·1. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

3-*Hydroxystyryl Methyl Ketone*.—(i) In an attempt to prepare this ketone from 3-hydroxybenzaldehyde (12 g.), acetone (5 c.c.), and alkali (100 c.c. of 20% KOH), a dark brown, amorphous substance was obtained which, on solution in methyl alcohol and fractional precipitation with water, gave a buff-coloured solid which resisted all attempts at further purification and decomposed at a high temperature without melting. Vacuum distillation of 20 g. of the solid only yielded a few c.c. of a dark, uncrystallisable oil with a phenolic odour.

(ii) 3-Hydroxybenzaldehyde (13 g.) in acetone (30 c.c.) was cooled in ice, and dry hydrogen chloride passed in; a dark violet solid then separated. The product contained chlorine but was easily freed from hydrochloric acid by water, with the formation of the amorphous solid already described.

(iii) The method of Murai (*loc. cit.*) was followed. The 3-nitrostyryl methyl ketone obtained as an intermediate was a pale yellow solid of m. p. 99—100° (Found: N, 7·45. Calc. for $C_{10}H_9O_3N$: N, 7·3%). The 3-hydroxystyryl methyl ketone consisted of faintly coloured crystals of m. p. 97—98°. Its yellow solution in alkali slowly turned orange.

4-*Hydroxystyryl methyl ketone*, obtained from 4-hydroxybenzaldehyde (25 g.), acetone (12 g.), and alkali (250 c.c.), formed yellow needles, m. p. 52—62°, containing water which was removed by crystallisation from absolute alcohol, pale lemon-yellow crystals, m. p. 111—112°, then separating. The colourless isomeride of identical m. p. could be prepared by the usual methods or by the addition of 40% alkali to the condensation mixture; in the latter case the sodium salt separated in deep yellow needles [Found: (yellow isomeride) C, 73·8; H, 6·2; (colourless isomeride) C, 73·6; H, 6·2. $C_{10}H_{10}O_2$ requires C, 74·0; H, 6·2%].

The mother-liquor from the preparation of 4-hydroxystyryl methyl ketone contained a small quantity of a yellow, crystalline compound, m. p. 220° (Found: C, 75·8, 76·0; H, 5·2, 5·2%), the constitution of which has not been determined.

4 : 4′-*Dihydroxydistyryl Ketone.*—Dry hydrogen chloride was passed into a solution of 4-hydroxybenzaldehyde (25 g.) and acetone (6 g.) in absolute alcohol (100 c.c.); a blackish solid soon separated which turned green on the addition of water. Crystallisation from alcohol then yielded yellow plates, m. p. 237—238°. Acid condensation of 4-hydroxybenzaldehyde and 4-hydroxystyryl methyl ketone gave the same compound.

4-*Hydroxystyryl ethyl ketone* was obtained from 4-hydroxybenzaldehyde (25 g.), methyl ethyl ketone (15 g.), and alkali (300 c.c. of 15%; warming on the water-bath) as a yellow oil which crystallised in the ice-chest; it then separated from cold aqueous alcohol in yellow needles and from hot alcohol in colourless needles (Found: C, 74·6; H, 6·9. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%), both having m. p. 115°.

4-*Hydroxystyryl propyl ketone*, obtained from 4-hydroxybenzaldehyde (25 g.), methyl *n*-propyl ketone (15 g.), and alkali (200 c.c.), separated from cold aqueous alcohol in yellow crystals, m. p. 80—83°, of a hydrate which, on recrystallisation from benzene–hexane, gave yellow needles, m. p. 90°. The colourless isomeride of the same m. p. was produced in the usual way [Found: (yellow form) C, 75·5; H, 7·45; (colourless form) C, 75·3; H, 7·4. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%].

2-*Hydroxystyryl* iso*propyl ketone*, obtained from methyl *iso*propyl ketone (50 g.), salicylaldehyde (72 g.) and alkali (700 c.c.), separated from ice-cold alcohol in yellow crystals, m. p. 107°. This form was very unstable and passed readily into the colourless modification, m. p. 107° (Found : C, 75·9; H, 7·4. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

2-*Hydroxystyryl* tert.-*Butyl Ketone*.—A solution of pinacolin (18 g.), salicylaldehyde (18 g.), and sodium hydroxide (10 g.) in alcohol (200 c.c.) was warmed on a water-bath for $\frac{1}{2}$ hour. After 7 days, the excess of pinacolin was removed by evaporation (otherwise an uncrystallisable oil separated on acidification), and the solution was diluted with water and poured into dilute acetic acid. Crystallisation of the product from cold aqueous alcohol gave yellow needles, m. p. 128°, which were easily converted into the colourless form of identical m. p. (Found : C, 76·0; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·8%). Both forms give yellow solutions in alkali.

2-*Hydroxystyryl* iso*Butenyl Ketone* (I).—Salicylaldehyde (38 g.) was dissolved in alcohol (100 c.c.), and 20% sodium hydroxide solution (200 c.c.) added. Pure mesityl oxide (30 g.) was gradually run in with mechanical stirring. After 12 hours, the dark red sodium salt produced was filtered off and treated with water; a small amount of material remaining undissolved was found to be the required *ketone*, which, on recrystallisation, yielded yellow crystals, m. p. 141°. On acidification, the sodium salt furnished 2 : 2′-dihydroxydistyryl ketone, and the original filtrate gave 2-hydroxystyryl methyl ketone. A colourless *isomeride*, m. p. 141°, of 2-hydroxystyryl *iso*butenyl ketone was prepared by the usual methods. The pure ketone dissolved in concentrated alkali solution with a yellow colour which was unchanged on standing, but after the addition of salicylaldehyde the solution turned red in 2 hours and longer treatment caused the separation of the sodium salt of 2 : 2′-dihydroxydistyryl ketone. No coloration was produced when 2-hydroxystyryl *iso*butenyl ketone was boiled with concentrated hydrochloric acid (Found : C, 76·9; H, 7·0. $C_{13}H_{16}O_4$ requires C, 77·2; H, 6·9%).

2-*Hydroxystyryl Phenyl Ketone*.—This ketone was prepared by a modification of Bablich and Kostanecki's method (*Ber.*, 1896, **29**, 233). It gives an orange-red sodium salt, and an orange solution in alkali. An alcoholic solution of the sodium salt was made by dissolving the ketone in the exact amount of standard sodium ethoxide solution, and six fractions were obtained by successive additions of dry ether. All the sodium salts thus precipitated and also the salt obtained on evaporation of the final filtrate gave 2-hydroxystyryl phenyl ketone on acidification. Boiling in high-boiling solvents in presence of acids, exposure to ultra-violet light, and heating in an autoclave failed to isomerise this ketone, the yellow form being recovered in every case.

During the preparation of this ketone red needles separated from the reaction mixture. Treatment of these crystals with water caused the precipitation of a small amount of a yellow solid which proved to be 2-hydroxybenzylidenediacetophenone. When pure and of constant melting point, it consisted of colourless plates of m. p. 129°, which is lower by 2° than that recorded. The compound is insoluble in alkali of less than 15% strength, but dissolves in more concentrated alkali, yielding yellow solutions.

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