378. *Chalkones: Reactivity of Some Aryl Alkoxystyryl Ketones and their Dihalides.*

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An investigation of the reaction of some aryl alkoxystyryl ketones and their dihalides has shown that the alkoxystyryl nucleus, if free from halogen, is readily halogenated. Potassium iodide in acetone removes the side-chain halogen from the chalkone dihalides, and this reaction can be used to determine the position of the halogen in the nucleus. The side-chain halogen atom adjacent to the nucleus containing the alkoxy-group is readily replaced by alkoxyl on treatment with alcohols. The dihalides with alcoholic potassium cyanide give β-aroyl-α-phenylpropionitriles. With bases the chalkone dihalides give α-halogenostyryl derivatives and β-alkoxystyryl ketones. The production of *iso*oxazoles from the dihalides by the action of hydroxylamine and the condensation of the chalkones with acetoacetic ester have also been examined. The production of benzylidenecoumaranones in place of flavones from *o*-hydroxy- or *o*-acetoxy-phenyl alkoxystyryl ketone dibromides probably depends on whether or no a β-alkoxy-compound is intermediately formed.

The dihalides of phenyl alkoxystyryl ketones (phenyl αβ-dihalogeno-β-alkoxyphenylethyl ketones) are of interest; the β-halogen atom is readily replaced by alkoxyl on treatment with alcohols (see, *e.g.*, Dodwadmath and Wheeler, *Proc. Indian Acad. Sci.*, 1935, **2**, 439) and the majority of the *o*-hydroxy- and *o*-acetoxy-phenyl αβ-dibromo-β-phenylethyl ketones yielding benzylidenecoumaranones in place of flavones on treatment with hot alcoholic alkali contain an alkoxyl group in the β-phenyl nucleus (Warriar, Khanolkar, Hutchins, and Wheeler, *Current Science*, 1937, **5**, 475).

Halogenation of Dihalides.—*p*-Tolyl *p*-methoxystyryl and 3 : 4-methylenedioxystyryl ketones and their corresponding *dihalides* ($R\cdot CO\cdot CHX\cdot CHX\cdot R'$; $R = p$-tolyl; $R' = p$-anisyl or 3 : 4-methylenedioxyphenyl; X = Cl or Br) are readily halogenated in the alkoxyphenyl nucleus to give the corresponding p-*tolyl* αβ-*dihalogeno*-β-*halogenophenylethyl ketones* ($R\cdot CO\cdot CHX\cdot CHX\cdot R''$; R'' = 3-X-*p*-anisyl or 6-X-3 : 4-methylenedioxyphenyl).

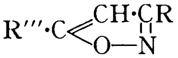
Action of Potassium Iodide on the Dihalides.—The position of the nuclear halogen atom in the R'' dihalides was fixed by treating these compounds with potassium iodide in acetone solution; the parent halogeno-chalkones ($R\cdot CO\cdot CH{:}CHR''$) were thus obtained with the separation of iodine, from presumably an intermediate unstable di-iodide ($R\cdot CO\cdot CHI\cdot CHIR''$). The four halogeno-chalkones thus obtained were unambiguously synthesised from *p*-methylacetophenone and, respectively, 3-chloro- and 3-bromo-anisaldehyde and 6-chloro- and 6-bromo-piperonal. Further *dihalides* ($R\cdot CO\cdot CHX\cdot CHXR''$), in which the nuclear and the side-chain halogen differed, were prepared from these halogeno-chalkones.

Action of Alcohols on the Dihalides.—When the dihalides ($R\cdot CO\cdot CHX\cdot CHX\cdot R'''$; $R''' = R'$ or R'') were heated with methyl or ethyl alcohol, the halogen atom α to the alkoxyphenyl nucleus was replaced by alkoxyl with elimination of hydrogen halide; a number of p-*tolyl* α-*halogeno*-β-*alkoxy*-β-*phenylethyl ketones* [$R\cdot CO\cdot CHX\cdot CH(OR'''')R'''$; R'''' = OMe or OEt] were thus prepared. The labile nature of one of the bromine atoms in phenyl αβ-dibromo-β-*p*-anisylethyl ketone was first observed by Pond and Shoffstall (*J. Amer. Chem. Soc.*, 1900, **22**, 658); various reasons can be adduced to show that it is the halogen atom nearer the alkoxyphenyl nucleus which is labile (Dodwadmath and Wheeler, *loc. cit.*), the simplest being that the nucleus containing the activating alkoxy-group may be expected to influence the nearer bromine atom. Bromine is more readily replaced than chlorine; the presence of a nuclear halogen atom in the alkoxyphenyl nucleus does not inhibit replacement by alkoxyl, as does the nitro-group (Dodwadmath and Wheeler, *loc. cit.*). The alkoxy-group in the α-halogeno-β-alkoxy-compounds is also labile, and can be replaced by bromine on treatment with concentrated hydrobromic acid (cf. Werner, *Ber.*, 1906, **39**, 27); the other hydrohalogenic acids do not give definite products. p-*Tolyl* α-*chloro*-β-*bromo*-β-*alkoxyphenylethyl ketones* ($R\cdot CO\cdot CHCl\cdot CHBrR'''$) were thus obtained for the first time.

Action of Potassium Cyanide on the Dihalides.—Dodwadmath and Wheeler (*loc. cit.*) observed that the action of warm alcoholic potassium cyanide on phenyl αβ-dibromo-β-phenylethyl ketone gave β-benzoyl-α-phenylpropionitrile, synthesised by Hann and Lapworth (J., 1904, **85**, 1359) by the action of hydrogen cyanide on phenyl styryl ketone. It has now been found that some chalkone dihalides with cold alcoholic potassium cyanide give the corresponding chalkones, which are apparently intermediates in the production of the *propionitriles* [$R\cdot CO\cdot CH_2\cdot CH(CN)R'''$] obtained in the warm from the dihalides and potassium cyanide. Possibly an unstable mononitrile [$R\cdot CO\cdot CHX\cdot CH(CN)R'''$] or a dinitrile [$R\cdot CO\cdot CH(CN)\cdot CH(CN)R'''$] is formed, and cyanogen halide or cyanogen is eliminated; hydrolysis may then produce hydrogen cyanide. The structure of the nitriles follows from Hann and Lapworth's result with phenyl styryl ketone (*loc. cit.*). An anomalous result was obtained when *p*-tolyl αβ-dichloro-β-3-chloro-*p*-anisylethyl ketone gave with potassium cyanide in the cold p-*tolyl* α : 3-*dichloro*-4-*methoxystyryl ketone*, the potassium cyanide acting as an alkali (see next section).

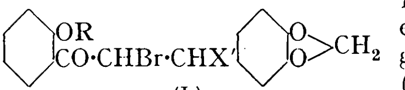
The nitriles yield the corresponding *propionic acids* [$R\cdot CO\cdot CH_2\cdot CH(CO_2H)R'''$] on hydrolysis, though in one instance *p*-toluic acid was obtained. The use of the chalkone dihalides provides sometimes a more satisfactory synthesis of these acids than Hann and Lapworth's method using the chalkone and hydrogen cyanide. The acids are important in the production of tetralone derivatives (cf. Richardson, Robinson, and Seijo, this vol., p. 835).

Action of Bases on the Chalkone Dihalides.—The dihalides under investigation, like other αβ-dihalogeno-ketones, gave with pyridine or one molecular proportion of sodium methoxide α-halogenostyryl derivatives ($R{\cdot}CO{\cdot}CX{:}CHR'''$). These compounds are also obtained by heating the α-halogeno-β-alkoxy-ketones [$R{\cdot}CO{\cdot}CHX{\cdot}CH(OR'''')R'''$; cf. Pond and Shoffstall, *loc. cit.*], and in one case from a dihalide by the action of potassium cyanide in the cold (see preceding section). The action of bases in excess on the chalkone dihalides may take various courses dependent on the groups present (Kohler and Addinall, *J. Amer. Chem. Soc.*, 1930, **52**, 3728). With the present dihalides, β-*alkoxystyryl ketones* [$R{\cdot}CO{\cdot}CH{:}C(OR'''')R'''$] were obtained usually in the form of oils (cf. for the mechanism, Dufraisse and Gerald, *Compt. rend.*, 1921, **173**, 985). These β-alkoxystyryl ketones are also formed by the action of one molecular proportion of sodium alkoxide on the α-halogeno-β-alkoxy-ketones [$R{\cdot}CO{\cdot}CHX{\cdot}CH(OR'''')R'''$]. They were readily hydrolysed to the tautomeric *diketones* ($R{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}R'''$). The enolic form in which the diketones chiefly exist is probably $R{\cdot}C(OH){:}CH{\cdot}CO{\cdot}R'''$; alkoxyl being a stronger electron source than methyl (anisole is more readily halogenated than toluene), the electron drift will be from R''' to R.

Action of Hydroxylamine on the Dihalides.—The dihalides $R{\cdot}CO{\cdot}CHX{\cdot}CHXR'''$ with hydroxylamine hydrochloride and alkali gave the iso*oxazoles*  $R'''{\cdot}C{<}\begin{matrix}CH{\cdot}CR\\ O{-}N\end{matrix}$; in the cases examined here, the same *iso*oxazoles were obtained by the action of hydroxylamine hydrochloride on the corresponding diketones. On the other hand the dibromide $Ph{\cdot}CO{\cdot}CHBr{\cdot}CHBr{\cdot}C_6H_4{\cdot}OMe$ gave 3-phenyl-5-anisyl*iso*oxazole, whereas the diketone $Ph{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}C_6H_4{\cdot}OMe$ gave 5-phenyl-3-anisyl*iso*oxazole (Weygand and Bauer, *Annalen*, 1927, **459**, 123). The results are probably determined by the enolic form which preponderates in the unsymmetrical diketone; it cannot be assumed, however, that hydroxylamine necessarily attacks the keto- in preference to the hydroxy-group of the enolic form of the diketones (cf. Weygand and Bauer, *loc. cit.*).

Condensation of the Chalkones with Acetoacetic Ester.—The chalkones condense readily with acetoacetic ester to give *ethyl* 6-*alkoxyphenyl*-4-p-*tolyl*-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylates*, which lose carbethoxyl on hydrolysis. The resulting cyclo*hexenones* could not be converted into the corresponding phenols by addition of bromine and elimination of hydrogen bromide (cf. Petrov, *Ber.*, 1930, **63**, 901).

Production of Flavones and Benzylidenecoumaranones.—Several attempts have been made to explain the dual production of flavones and the isomeric benzylidenecoumaranones from the dibromides of some *o*-acetoxy- and *o*-hydroxy-phenyl styryl ketones (cf. Cullinane and Philpott, J., 1929, 1761). Auwers and Anschütz (*Ber.*, 1921, **54**, 1543) showed that low temperatures favoured the production of flavones, but offered no explanation of this fact. The following experiments indicate that the production of benzylidenecoumaranones in place of flavones from *o*-hydroxy- or *o*-acetoxy-aryl alkoxystyryl ketone dibromides probably depends on whether or no a β-alkoxy-compound is formed. *o*-Acetoxyphenyl αβ-dibromo-β-3 : 4-methylenedioxyphenylethyl ketone (I; R = Ac, X' = Br) gave 3' : 4'-methylenedioxyflavone (a) on direct heating, (b) with hot pyridine, (c) with hot or cold aqueous sodium hydroxide containing acetone, and (d) with cold aqueous alcoholic sodium hydroxide (Auwers and Anschütz, *loc. cit.*) or sodium carbonate: with (e) hot aqueous alcoholic sodium hydroxide (Feuerstein and Kostanecki, *Ber.*, 1899, **32**, 316) or carbonate, the 3' : 4'-methylenedioxybenzylidenecoumaran-2-one was obtained; intermediate formation of the ethoxy-compound (I; R = Ac, X' = OEt) is to be expected with hot alcohol.



(I.)

o-*Hydroxyphenyl* αβ-*dibromo*-β-3 : 4-*methylenedioxyphenylethyl ketone* (I; R = H, X' = Br) gave similar results except that with hot pyridine no definite product was obtained. o-*Hydroxyphenyl* α-*bromo*-β-*ethoxy*-β-3 : 4-*methylenedioxyphenylethyl ketone* (I; R = H, X' = OEt), on being heated above the m. p. or with pyridine, gave the flavone; with sodium hydroxide or sodium carbonate in hot or cold acetone or alcohol, the benzylidenecoumaranone was obtained. Once the ethoxy-compound is formed, neither alcohol nor heat is necessary for the production of benzylidenecoumaranone; all that is required is that sodium hydroxide or sodium carbonate shall be present; a definite synthesis of these compounds is thus provided. Work in progress has shown that *o*-hydroxynaphthyl alkoxystyryl ketone dibromides, which, so far, have given only flavones with alcoholic alkali, give ethoxy-bromides and then coumaranone derivatives if the solubility of the dibromide in alcohol is increased by addition of chloroform. Chalkone dibromides derived from phloracetophenone also give benzylidenecoumaranones with alcoholic alkali (Cullinane and Philpott, *loc. cit.*) even though there is no alkoxy-group in the phenylethyl nucleus. This phenomenon is being separately investigated; it may be mentioned that heating these dibromides provides a certain synthesis of the flavones; chrysin (Warriar *et al.*, *loc. cit.*) and apigenin have thus been synthesised in this laboratory from dibromides from which previously only arylidenecoumaranones had been obtained (Kostanecki and Tambor, *Ber.*, 1899, **32**, 2260).

EXPERIMENTAL.

Compounds are numbered for brevity in cross reference. Recrystallisation was from alcohol unless another solvent is mentioned. The compounds are colourless unless otherwise stated.

Chalkones.—The following chalkones were prepared from *p*-methylacetophenone and the corresponding aldehyde in presence of alcoholic alkali (Sorge, *Ber.*, 1902, **35**, 1069): *p*-tolyl *p*-methoxystyryl ketone (1) (Petrov, *Ber.*, 1930, **63**, 901); *p*-tolyl 3 : 4-methylenedioxystyryl ketone (2) (Sorge, *loc. cit.*); p-*tolyl 3-chloro-4-methoxystyryl ketone* (3), m. p. 114° (Found : Cl, 12·6. $C_{17}H_{15}O_2Cl$ requires Cl, 12·4%); p-*tolyl 3-bromo-4-methoxystyryl ketone* (4), m. p. 122° (Found : Br, 24·3. $C_{17}H_{15}O_2Br$ requires Br, 24·2%); p-*tolyl 6-chloro-3 : 4-methylenedioxystyryl ketone* (5), m. p. 139° (Found : Cl, 12·0. $C_{17}H_{13}O_3Cl$ requires Cl, 11·7%); and p-*tolyl 6-bromo-3 : 4-methylenedioxystyryl ketone* (6), m. p. 150° (Found : Br, 23·2. $C_{17}H_{13}O_3Br$ requires Br, 23·2%). All these chalkones are yellow.

An improved method for the preparation of 3-chloro-*p*-anisaldehyde consists in passing chlorine (1 mol.) through an acetic acid solution of *p*-anisaldehyde, and precipitating the product by addition of water.

Side-chain Halogenation of the Chalkones.—The respective chalkones gave the following dihalides on treatment with halogen (1 mol.) in cold glacial acetic acid : p-*tolyl αβ-dichloro-β-*p-*anisylethyl ketone* (7), m. p. 142° (Found : Cl, 21·9. $C_{17}H_{16}O_2Cl_2$ requires Cl, 22·0%); p-*tolyl αβ-dibromo-β-*p-*anisylethyl ketone* (8), m. p. 172° (Found : Br, 38·9. $C_{17}H_{16}O_2Br_2$ requires Br, 38·7%); p-*tolyl αβ-dichloro-β-3 : 4-methylenedioxyphenylethyl ketone* (9), m. p. 140° (Found : Cl, 21·2. $C_{17}H_{14}O_3Cl_2$ requires Cl, 21·1%); p-*tolyl αβ-dibromo-β-3 : 4-methylenedioxyphenylethyl ketone* (10), m. p. 144° (Found : Br, 37·6. $C_{17}H_{14}O_3Br_2$ requires Br, 37·6%); p-*tolyl αβ-dibromo-β-3-chloro-*p-*anisylethyl ketone* (11), m. p. 176° (Found : halogen, 44·0. $C_{17}H_{15}O_2ClBr_2$ requires halogen, 43·8%); p-*tolyl αβ-dichloro-β-3-bromo-*p-*anisylethyl ketone* (12), m. p. 126° (Found : halogen, 37·2. $C_{17}H_{15}O_2Cl_2Br$ requires halogen, 37·6%); p-*tolyl αβ-dibromo-β-6-chloro-3 : 4-methylenedioxyphenylethyl ketone* (13), m. p. 169° (Found : halogen, 42·1. $C_{17}H_{13}O_3ClBr_2$ requires halogen, 42·4%); and p-*tolyl αβ-dichloro-β-6-bromo-3 : 4-methylenedioxyphenylethyl ketone* (14), m. p. 160° (Found : halogen, 36·2. $C_{17}H_{13}O_3Cl_2Br$ requires halogen, 36·3%).

Nuclear Halogenation of Chalkones (1) *and* (2).—The precipitate of (7) obtained when chlorine was passed through a solution of (1) (20 g.) in acetic acid (160 c.c.) dissolved with evolution of hydrogen chloride on continued passage of chlorine (2 mols.) and p-*tolyl αβ-dichloro-β-3-chloro-*p-*anisylethyl ketone* (15) (16 g.), m. p. 125°, separated after 12 hours (Found : Cl, 29·9. $C_{17}H_{15}O_2Cl_3$ requires Cl, 29·8%). p-*Tolyl αβ-dibromo-β-3-bromo-*p-*anisylethyl ketone* (16), m. p. 176°, was prepared by the action of bromine (2 mols.) on (1) in hot glacial acetic acid (Found : Br, 48·7. $C_{17}H_{15}O_2Br_3$ requires Br, 48·9%). The ketone (2) similarly yielded p-*tolyl αβ-dichloro-β-6-chloro-3 : 4-methylenedioxyphenylethyl ketone* (17), m. p. 157° (Found : Cl, 28·6. $C_{17}H_{13}O_3Cl_3$ requires Cl, 28·7%), and p-*tolyl αβ-dibromo-β-6-bromo-3 : 4-methylenedioxyphenylethyl ketone* (18), m. p. 175° (Found : Br, 47·7. $C_{17}H_{13}O_3Br_3$ requires Br, 47·6%). All the halogen compounds were crystallised from acetic acid or benzene.

Action of Potassium Iodide on the Dihalides.—The position of the nuclear halogen in (15), (16), (17) and (18) is fixed by the fact that, when these compounds are boiled with potassium iodide (2 mols.) in acetone for 3 hours, iodine separates, and the solutions yield respectively the corresponding chalkones (3), (4), (5) and (6) (mixed m. p. comparison).

Action of Alcohols on the Chalkone Dihalides.—The following β-alkoxy-compounds separated from cooled solutions of the corresponding dihalides in methyl or ethyl alcohol which had been boiled from 1—8 hours, the longer period being necessary with the chloro-compounds: p-*tolyl α-chloro-β-methoxy-β-*p-*anisylethyl ketone* (19), m. p. 107° (Found: Cl, 11·3. $C_{18}H_{19}O_3Cl$ requires Cl, 11·1%); p-*tolyl α-bromo-β-ethoxy-β-*p-*anisylethyl ketone* (20), m. p. 103° (Found: Cl, 11·1. $C_{19}H_{21}O_3Cl$ requires Cl, 10·7%), p-*tolyl α-bromo-β-methoxy-β-*p-*anisylethyl ketone* (21), m. p. 114° (Found: Br, 21·9. $C_{18}H_{19}O_3Br$ requires Br, 22·1%); p-*tolyl α-bromo-β-ethoxy-β-*p-*anisylethyl ketone* (22), m. p. 105° (Found: Br, 21·8. $C_{19}H_{21}O_3Br$ requires Br, 21·2%); p-*tolyl α-chloro-β-methoxy-β-3-chloro-*p-*anisylethyl ketone* (23), m. p. 108° (Found: Cl, 19·9. $C_{18}H_{18}O_3Cl_2$ requires Cl, 20·1%); p-*tolyl α-chloro-β-ethoxy-β-3-chloro-*p-*anisylethyl ketone* (24), m. p. 128° (Found: Cl, 19·0. $C_{19}H_{20}O_3Cl_2$ requires Cl, 19·4%); p-*tolyl α-bromo-β-methoxy-β-3-chloro-*p-*anisylethyl ketone* (25), m. p. 126° (Found: C, 54·4; H, 4·5; halogen, 29·0. $C_{18}H_{18}O_3ClBr$ requires C, 54·4; H, 4·6; halogen, 29·1%); p-*tolyl α-chloro-β-ethoxy-β-3-bromo-*p-*anisylethyl ketone* (26), m. p. 128° (Found: halogen, 27·7. $C_{19}H_{20}O_3ClBr$ requires halogen, 28·1%); p-*tolyl α-bromo-β-methoxy-β-3-bromo-*p-*anisylethyl ketone* (27), m. p. 101° (Found: Br, 35·9. $C_{18}H_{18}O_3Br_2$ requires Br, 36·3%); p-*tolyl α-bromo-β-ethoxy-β-3-bromo-*p-*anisylethyl ketone* (28), m. p. 103° (Found: Br, 34·9. $C_{19}H_{20}O_3Br_2$ requires Br, 35·1%); p-*tolyl α-chloro-β-methoxy-β-3:4-methylenedioxyphenylethyl ketone* (29), m. p. 94° (Found: Cl, 10·7. $C_{18}H_{17}O_4Cl$ requires Cl, 10·6%); p-*tolyl α-chloro-β-ethoxy-β-3:4-methylenedioxyphenylethyl ketone* (30), m. p. 95° (Found: C, 65·8; H, 5·1; Cl, 10·3. $C_{19}H_{19}O_4Cl$ requires C, 65·8; H, 5·5; Cl, 10·1%); p-*tolyl α-bromo-β-methoxy-β-3:4-methylenedioxyphenylethyl ketone* (31), m. p. 120° (Found: Br, 21·1. $C_{18}H_{17}O_4Br$ requires Br, 21·2%); p-*tolyl α-bromo-β-ethoxy-β-3:4-methylenedioxyphenylethyl ketone* (32), m. p. 115° (Found: Br, 20·7. $C_{19}H_{19}O_4Br$ requires Br, 20·5%); p-*tolyl α-chloro-β-methoxy-β-6-chloro-3:4-methylenedioxyphenylethyl ketone* (33), m. p. 114° (Found: Cl, 19·5 $C_{18}H_{16}O_4Cl_2$ requires Cl, 19·3%); p-*tolyl α-chloro-β-ethoxy-β-6-chloro-3:4-methylenedioxyphenylethyl ketone* (34), m. p. 95° (Found: Cl, 18·9. $C_{19}H_{18}O_4Cl_2$ requires Cl, 18·6%); p-*tolyl α-bromo-β-methoxy-β-6-bromo-3:4-methylenedioxyphenylethyl ketone* (35), m. p. 121° (Found: Br, 35·4. $C_{18}H_{16}O_4Br_2$ requires Br, 35·1%); and p-*tolyl α-bromo-β-ethoxy-β-6-bromo-3:4-methylenedioxyphenylethyl ketone* (36), m. p. 104° (Found: Br, 34·4. $C_{19}H_{18}O_4Br_2$ requires Br, 34·1%).

Action of Hydrobromic Acid on the α-Chloro-β-alkoxy-compounds.—The ketone (20), when kept in contact with concentrated hydrobromic acid for 12 hours, yielded p-*tolyl α-chloro-β-bromo-β-*p-*anisylethyl ketone* (37), m. p. 154° (benzene) (Found: C, 55·6; H, 4·4; halogen, 31·7. $C_{17}H_{16}O_2ClBr$ requires C, 55·5; H, 4·4; halogen, 31·4%). p-*Tolyl α-chloro-β-bromo-β-3-chloro-*p-*anisylethyl ketone* (38), m. p. 157° (benzene) (Found: C, 50·8; H, 3·8; halogen, 37·3. $C_{17}H_{15}O_2Cl_2Br$ requires C, 50·7; H, 3·7; halogen, 37·6%), p-*tolyl α-chloro-β-bromo-β-3-bromo-*p-*anisylethyl ketone* (39), m. p. 161° (carbon tetrachloride) (Found: halogen, 44·0. $C_{17}H_{15}O_2ClBr_2$ requires halogen, 43·8%), p-*tolyl α-chloro-β-bromo-β-3:4-methylenedioxyphenylethyl ketone* (40), m. p. 137° (light petroleum) (Found: halogen, 30·5. $C_{17}H_{14}O_3ClBr$ requires halogen, 30·3%), and p-*tolyl α-chloro-β-bromo-β-6-chloro-3:4-methylenedioxyphenylethyl ketone* (41), m. p. 165° (light petroleum) (Found: C, 49·0; H, 3·2; halogen, 36·7. $C_{17}H_{13}O_3Cl_2Br$ requires C, 49·0; H, 3·1; halogen, 36·3%), were similarly prepared from (23), (26), (30), and (34) respectively and hydrobromic acid.

Action of Potassium Cyanide on the Dihalides in the Cold.—The compound (10), when shaken for 6 hours with half its weight of potassium cyanide dissolved in cold alcohol, gave the chalkone (2) (mixed m. p. comparison). The corresponding chalkones (4) and (6) were likewise obtained from the halides (16) and (18). The compound (8), similarly treated, gave β-p-*toluoyl-α-*p-*anisylpropionitrile* (42), m. p. 106° (Found: C, 77·3; H, 6·1; N, 5·1. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1; N, 5·0%). On the other hand the filtrate obtained after removal of the solid residue from a mixture of (15) (10 g.), potassium cyanide (3·8 g.), and alcohol (100 c.c.) which had been shaken in the cold for 3 hours gave, on keeping, a precipitate (5·5 g.) of p-*tolyl α:3-dichloro-4-methoxystyryl ketone* (43), which formed yellow needles, m. p. 115° (Found: Cl, 22·0. $C_{17}H_{14}O_2Cl_2$ requires Cl, 22·1%). Here potassium cyanide acts as a weak alkali.

Action of Potassium Cyanide on the Dihalides in the Warm.—The filtrate obtained after removal in the warm of the solid residue from a mixture of (16) (10 g.), potassium cyanide (3·6 g.) in water (5 c.c.), and alcohol (100 c.c.) which had been heated under reflux for 5 hours gave, on keeping, β-p-*toluoyl-α-3-bromo-*p-*anisylpropionitrile* (44) (4·2 g.), m. p. 135° (Found:

Br, 22·3. $C_{18}H_{16}O_2NBr$ requires Br, 22·4%). The compounds (8), (10), and (18), respectively, gave under similar conditions (42), β-p-*toluoyl*-α-3 : 4-*methylenedioxyphenylpropionitrile* (45), m. p. 115° (Found : C, 73·7; H, 5·1; N, 5·2. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1; N, 4·8%), and β-p-*toluoyl*-α-6-*bromo*-3 : 4-*methylenedioxyphenylpropionitrile* (46), m. p. 149° (Found : Br, 21·4. $C_{18}H_{14}O_3NBr$ requires Br, 21·5%). The nitrile (42), β-p-*toluoyl*-α-3-*chloro*-p-*anisylpropionitrile* (47), m. p. 144° (Found : Cl, 11·0. $C_{18}H_{16}O_2NCl$ requires Cl, 11·3%), and the nitrile (45) were also obtained by direct addition of hydrogen cyanide to the chalkones (1), (3), and (2) by Hann and Lapworth's method (*loc. cit.*).

Hydrolysis of the Nitriles.—A mixture of (45) (2·5 g.), 2N-sodium hydroxide (25 c.c.), and alcohol (15 c.c.), which had been heated under reflux at 100° for 8 hours, was filtered, and acidified with hydrochloric acid (1 : 1) to precipitate β-p-*toluoyl*-α-3 : 4-*methylenedioxyphenylpropionic acid* (48), m. p. 160° (dilute alcohol) (Found : C, 69·2; H, 5·3; equiv., 311·2. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·1%; equiv., 312), as an oil which afterwards solidified. β-p-*Toluoyl*-α-6-*bromo*-3 : 4-*methylenedioxyphenylpropionic acid* (49), m. p. 188° (dilute alcohol) (Found : C, 55·3; H, 3·9; Br, 20·9; equiv., 392·2. $C_{18}H_{15}O_5Br$ requires C, 55·2; H, 3·8; Br, 20·5%; equiv., 391), was similarly obtained from (46). Direct hydrolysis of the crude product obtained by treating (17) with alcoholic potassium cyanide gave a paste, which on precipitation from sodium carbonate solution yielded *p*-toluic acid (mixed m. p. comparison) (Found : C, 70·4; H, 5·9. Calc. : C, 70·6; H, 5·9%).

Action of Bases on the Chalkone Dihalides. Preparation of α-Halogenostyryl Ketones.—A solution of sodium methoxide (0·7 g. of sodium) and the compound (7) (10 g.) in methyl alcohol (50 c.c.) was boiled under reflux for 1 hour, filtered while hot from sodium chloride, and cooled; p-*tolyl* α-*chloro*-4-*methoxystyryl ketone* (50) (5·5 g.), m. p. 98° (Found : C, 70·9; H, 5·2; Cl, 12·3. $C_{17}H_{15}O_2Cl$ requires C, 71·2; H, 5·2; Cl, 12·4%), separated. This was also obtained (mixed m. p. comparison) by heating (7) with pyridine at the b. p. for 10 seconds, diluting the cooled solution with alcohol, and washing the resulting precipitate with dilute hydrochloric acid; alternatively the cooled pyridine solution was diluted with ether, and the pyridine removed with dilute hydrochloric acid. The compound (19) evolved methyl alcohol at 155° and left (50) as an oil which solidified on keeping. p-*Tolyl* α-*bromo*-4-*methoxystyryl ketone* (51), m. p. 102° (Found : C, 61·6; H, 4·6; Br, 24·4. $C_{17}H_{15}O_2Br$ requires C, 61·6; H, 4·5; Br, 24·2%), the ketone (43), p-*tolyl* 3-*chloro*-α-*bromo*-4-*methoxystyryl ketone* (52), m. p. 117° (Found : halogen, 31·7. $C_{17}H_{14}O_2ClBr$ requires halogen, 31·6%), p-*tolyl* α-*chloro*-3-*bromo*-4-*methoxystyryl ketone* (53), m. p. 107° (Found : halogen, 31·5. $C_{17}H_{14}O_2ClBr$ requires halogen, 31·6%), p-*tolyl* α : 3-*dibromo*-4-*methoxystyryl ketone* (54), m. p. 114° (Found : Br, 38·9. $C_{17}H_{14}O_2Br_2$ requires Br, 39·0%), p-*tolyl* α-*chloro*-3 : 4-*methylenedioxystyryl ketone* (55), m. p. 85° (Found : Cl, 11·9. $C_{17}H_{13}O_3Cl$ requires Cl, 11·7%), p-*tolyl* α-*bromo*-3 : 4-*methylenedioxystyryl ketone* (56), m. p. 80° (Found : Br, 22·9. $C_{17}H_{13}O_3Br$ requires Br, 23·2%), p-*tolyl* α : 6-*dichloro*-3 : 4-*methylenedioxystyryl ketone* (57), m. p. 114° (Found : Cl, 21·1. $C_{17}H_{12}O_3Cl_2$ requires Cl, 21·2%), p-*tolyl* 6-*chloro*-α-*bromo*-3 : 4-*methylenedioxystyryl ketone* (58), m. p. 130° (Found : halogen, 30·9. $C_{17}H_{12}O_3ClBr$ requires halogen, 30·5%), p-*tolyl* α-*chloro*-6-*bromo*-3 : 4-*methylenedioxystyryl ketone* (59), m. p. 124° (Found : halogen, 30·8. $C_{17}H_{12}O_3ClBr$ requires halogen, 30·5%), and p-*tolyl* α : 6-*dibromo*-3 : 4-*methylenedioxystyryl ketone* (60), m. p. 130° (Found : Br, 37·8. $C_{17}H_{12}O_3Br_2$ requires Br, 37·7%), were obtained from the corresponding chalkone halides by the action of sodium methoxide (1 mol.) or of pyridine. The mixed dihalides (37), (38), and (39) with pyridine yielded respectively (50), (43), and (53). The compounds (51), (43), and (54) were also obtained by heating (22), (24), and (28) above the m. p. until evolution of alcohol ceased. All the α-halogenostyryl compounds are yellow.

Action of Bases on the Chalkone Dihalides. Preparation of 1 : 3-*Diketones.*—Addition of water to a mixture of (15) (20 g.), and sodium (3 g.) in methyl alcohol (60 c.c.), which had been heated under reflux for 1 hour, gave an oil; this solidified when the whole was boiled with concentrated hydrochloric acid (10 c.c.) for an hour, and yielded 3-*chloro*-p-*anisoyl*-p-*toluoylmethane* (61) (13 g.), m. p. 135° (Found : Cl, 12·1. $C_{17}H_{15}O_3Cl$ requires Cl, 11·7%). The *copper* salt (62), obtained by heating (61) in alcoholic solution with copper acetate, separated from bromobenzene in green needles, m. p. 258° (Found : Cl, 10·3. $C_{34}H_{28}O_6Cl_2Cu$ requires Cl, 10·7%). 3-*Bromo*-p-*anisoyl*-p-*toluoylmethane* (63), similarly prepared from (16), had m. p. 122° (Found : Br, 23·4. $C_{17}H_{15}O_3Br$ requires Br, 23·1%). 3 : 4-*Methylenedioxybenzoyl*-p-*toluoylmethane* (64), from (9) and (10), had m. p. 114° [Found : C, 72·2; H, 5·1. $C_{17}H_{14}O_4$ requires C, 72·4; H, 4·9%. Found : enol (Meyer, *Annalen*, 1911, **380**, 212) in freshly prepared 0·3% methyl- or ethyl-alcoholic solution, 92·9, 93·5%; in 0·3% ethyl-alcoholic solution which had been kept for 2 days, 100%], and gave a *copper* salt (65), m. p.

268° [Found: C, 65·0; H, 4·3. $(C_{17}H_{13}O_4)_2Cu$ requires C, 65·4; H, 4·2%]. Addition of water to a mixture of (18) (6·2 g.) and sodium (0·8 g.) in methyl alcohol (75 c.c.) which had been heated under reflux for 1 hour precipitated p-*tolyl 6-bromo-β-methoxy-3 : 4-methylenedioxystyryl ketone* (66) as a yellow amorphous solid (2·6 g.), m. p. 107° after crystallisation (Found: C, 57·7; H, 4·1; Br, 21·3. $C_{18}H_{15}O_4Br$ requires C, 57·6; H, 4·0; Br, 21·3%); it was also obtained (mixed m. p.) by the action of sodium methoxide (1 mol.) on (35). p-*Tolyl 6-bromo-β-ethoxy-3 : 4-methylenedioxystyryl ketone* (67), m. p. 127°, was prepared similarly to (66) by means of sodium ethoxide (Found: Br, 20·7. $C_{19}H_{17}O_4Br$ requires Br, 20·6%). The compounds (66) and (67) were readily hydrolysed with hot hydrochloric acid and yielded *6-bromo-3 : 4-methylenedioxybenzoyl-*p-*toluoylmethane* (68), m. p. 110° (Found: Br, 22·1. $C_{17}H_{13}O_4Br$ requires Br, 22·2%). The diketones and their enol ethers are yellow.

Action of Hydroxylamine on the Halides.—p-*Tolyl α-bromo-3 : 4-methylenedioxystyryl ketoxime* (69) (1·2 g.), m. p. 164° (Found: C, 56·8; H, 3·9; N, 3·8; Br, 21·7. $C_{17}H_{14}O_3NBr$ requires C, 56·7; H, 3·9; N, 3·9; Br, 22·2%), was obtained by heating a mixture of (56) (2 g.), hydroxylamine hydrochloride (1 g.), and alcohol (50 c.c.) with a trace of hydrochloric acid under reflux for 4 hours and evaporating the product.

A mixture of (10) (11 g.) in alcohol (100 c.c.) and of hydroxylamine hydrochloride (3·5 g.) in water (10 c.c.) was treated at the b. p. with aqueous potassium hydroxide (8·5 g. in 10 c.c. of water); after the reaction had ceased, the resulting red liquid was filtered from potassium bromide and cooled to precipitate *5-(3′ : 4′-methylenedioxyphenyl)-3-*p-*tolyl*iso*oxazole* (70) (4 g.), m. p. 135° (Found: C, 72·8; H, 4·5; N, 5·3. $C_{17}H_{13}O_3N$ requires C, 73·0; H, 4·7; N, 5·0%), also obtained (3 g.) by heating under reflux for 4 hours a mixture of (64) (5 g.), hydroxylamine hydrochloride (4 g.), and alcohol (50 c.c.).

*5-(6′-Bromo-3′ : 4′-methylenedioxyphenyl)-3-*p-*tolyl*iso*oxazole* (71), m. p. 127° (Found: C, 57·0; H, 3·4; N, 3·6; Br, 22·5. $C_{17}H_{12}O_3NBr$ requires C, 57·0; H, 3·4; N, 3·9; Br, 22·4%), was similarly prepared from (18) and from (68).

Condensation of Chalkones with Acetoacetic Ester.—A mixture of ethyl acetoacetate (6·5 g.), sodium ethoxide (0·65 g. of sodium), and (3) (10 g.) in absolute alcohol (100 c.c.) was heated under reflux for 4 hours and cooled to separate *ethyl 6-*m-*chloro-*p-*anisyl-4-*p-*tolyl-*Δ^3-cyclo*hexen-2-one-1-carboxylate* (72) (11·5 g.), m. p. 136° (Found: Cl, 9·3. $C_{23}H_{23}O_4Cl$ requires Cl, 8·9%). *Ethyl 6-*m-*bromo-*p-*anisyl-4-*p-*tolyl-*Δ^3-cyclo*hexen-2-one-1-carboxylate* (73), m. p. 123° (Found: Br, 17·8. $C_{23}H_{23}O_4Br$ requires Br, 18·1%), *ethyl 6-(3′ : 4′-methylenedioxyphenyl)-4-*p-*tolyl-*Δ^3-cyclo*hexen-2-one-1-carboxylate* (74), m. p. 145° (Found: C, 72·8; H, 6·0. $C_{23}H_{22}O_5$ requires C, 73·0; H, 5·8%), *ethyl 6-(6′-chloro-3′ : 4′-methylenedioxyphenyl)-4-*p-*tolyl-*Δ^3-cyclo*hexen-2-one-1-carboxylate* (75), m. p. 154° (Found: Cl, 8·1. $C_{23}H_{21}O_5Cl$ requires Cl, 8·6%), and *ethyl 6-(6′-bromo-3′ : 4′-methylenedioxyphenyl)-4-*p-*tolyl-*Δ^3-cyclo*hexen-2-one-1-carboxylate* (76), m. p. 167° (Found: Br, 17·5. $C_{23}H_{21}O_5Br$ requires Br, 17·5%), were similarly prepared from (4), (2), (5), and (6) respectively.

Production of cyclo*Hexenones.*—The paste obtained by heating (72) for 4 hours at 150° in a sealed tube with 10% hydrochloric acid (1 mol.) solidified on being washed with sodium carbonate solution and gave *5-*m-*chloro-*p-*anisyl-3-*p-*tolyl-*Δ^2-cyclo*hexenone* (77), m. p. 120° (Found: C, 73·0; H, 5·9; Cl, 11·0. $C_{20}H_{19}O_2Cl$ requires C, 73·4; H, 5·8; Cl, 10·9%). *5-*m-*Bromo-*p-*anisyl-3-*p-*tolyl-*Δ^2-cyclo*hexenone* (78), m. p. 122° (Found: Br, 21·5. $C_{20}H_{19}O_2Br$ requires Br, 21·6%), *5-(3′ : 4′-methylenedioxyphenyl)-3-*p-*tolyl-*Δ^2-cyclo*hexenone* (79), m. p. 130° (Found: C, 78·1; H, 5·8. $C_{20}H_{18}O_3$ requires C, 78·3; H, 5·9%), *5-(6′-chloro-3′ : 4′-methylenedioxyphenyl)-3-*p-*tolyl-*Δ^2-cyclo*hexenone* (80), m. p. 151° (Found: Cl, 10·1. $C_{20}H_{17}O_3Cl$ requires Cl, 10·4%), and *5-(6′-bromo-3′ : 4′-methylenedioxyphenyl)-3-*p-*tolyl-*Δ^2-cyclo*hexenone* (81), m. p. 153° (Found: C, 62·3; H, 4·4; Br, 20·8. $C_{20}H_{17}O_3Br$ requires C, 62·2; H, 4·4; Br, 20·7%), were similarly obtained from (73), (74), (75), and (76). The *cyclo*hexenones are yellow.

Production of Flavones and Benzylidenecoumaranones.—Treatment of *o*-hydroxyphenyl 3 : 4-methylenedioxystyryl ketone with the theoretical quantity of bromine in carbon disulphide gave o-*hydroxyphenyl αβ-dibromo-β-3 : 4-methylenedioxystyryl ketone* (82), m. p. 145° (carbon tetrachloride) (Found: Br, 37·1. $C_{16}H_{12}O_4Br_2$ requires Br, 37·3%). This compound or *o*-acetoxyphenyl αβ-dibromo-β-3 : 4-methylenedioxystyryl ketone (83), on being heated with alcohol, gave o-*hydroxyphenyl α-bromo-β-ethoxy-β-3 : 4-methylenedioxystyryl ketone* (84), m. p. 107° (Found: C, 54·9; H, 4·4. $C_{18}H_{17}O_5Br$ requires C, 54·9; H, 4·3%). The transformations of (82), (83), and (84) into the corresponding flavone and benzylidenecoumaranone are described in the introduction.

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