18. *Chalkones : Reactivity of Aryl o-Alkoxystyryl Ketone Dibromides and the Synthesis of Flavones therefrom.*

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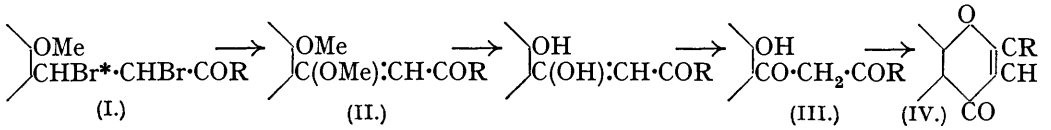
Aryl β : 2-dialkoxystyryl ketones (II), which are readily obtained from the corresponding chalkone dibromides, yield flavones on treatment with hydrogen bromide in acetic acid. These dibromides undergo many of the reactions already described for aryl *p*-alkoxystyryl ketone dibromides (J., 1937, 1798); in both the *o*- and the *p*-alkoxystyryl dibromides, the side-chain halogen atom adjacent to the nucleus containing the alkoxy-group is replaced by alkoxyl on treatment with alcohols.

Aryl β : 2-dialkoxystyryl ketones (II), which are readily obtained from the corresponding chalkone dibromides (I) (cf. Nadkarni, Warriar, and Wheeler, J., 1937, 1798) by treatment with alcoholic sodium alkoxide, pass directly into flavones (IV) under the action of hydrogen bromide in acetic acid. Isolation of the intermediate diketones (III) is unnecessary (cf. Algar and Hanway, *Proc. Roy. Irish Acad.*, 1934, **42**, *B*, 9). This method for the synthesis of flavones may sometimes be preferable to the usual Kostanecki method involving the dibromides of *o*-hydroxyaryl styryl ketones; there is no possibility of formation of benzylidenecoumaranones (cf. Nadkarni *et al.*, *loc. cit.*), and the *o*-alkoxyarylaldehydes required in the synthesis of (I) are, on the whole, more readily obtainable than *o*-hydroxyacetophenones.

The reactivity of (I) has also been examined on the lines followed by Nadkarni *et al.* (*loc. cit.*) with similar results. Of interest is the observation that the bromine atom in bromodiaroylmethanes, R'·CO·CHBr·COR, is strongly positive, and is replaced by



hydrogen on treatment with hydrogen bromide in acetic acid, with potassium iodide in aqueous acetone, or with alcoholic potassium cyanide (cf. Nicolet, *J. Amer. Chem. Soc.*, 1921, **43**, 2081).

Experimental.

Chalkones.—The following chalkones were prepared from the corresponding acetophenones and aldehydes in presence of alcoholic alkali (Sorge, *Ber.*, 1902, **35**, 1069) : phenyl *o*-methoxystyryl ketone (1) (Pfeiffer, *Annalen*, 1916, **412**, 308); *phenyl 5-bromo-2-methoxystyryl ketone* (2), which separated from alcohol with $2H_2O$ and had, after drying at 70°/12 mm., m. p. 110° [Found : H_2O, 10·4; Br (in dried material), 25·2. $C_{16}H_{13}O_2Br,2H_2O$ requires H_2O, 10·2%. $C_{16}H_{13}O_2Br$ requires Br, 25·3%]; *p*-tolyl *o*-methoxystyryl ketone (3) was obtained only as a paste, which, however, gave (8) (see below); and phenyl *m*-methoxystyryl ketone (4) (Bauer and Vogel, *J. pr. Chem.*, 1913, **88**, 334). All these chalkones are yellow.

Bromination of the Chalkones.—The respective chalkones gave the following dibromides on treatment with bromine (1 mol.) in cold carbon tetrachloride or glacial acetic acid : phenyl

αβ-dibromo-β-*o*-anisylethyl ketone (5) (Auwers and Brink, *Annalen*, 1932, **493**, 218); *phenyl αβ-dibromo-β-5-bromo-o-anisylethyl ketone* (6), m. p. (benzene) 158° (Found: Br, 50·4. $C_{16}H_{13}O_2Br_3$ requires Br, 50·2%); and *phenyl αβ-dibromo-β-m-anisylethyl ketone* (7), m. p. (aqueous acetone) 122° (Found: Br, 40·2. $C_{16}H_{14}O_2Br_2$ requires Br, 40·2%); (3) with bromine (1 mol.) gave a paste only.

The *o*-alkoxystyryl ketones and their dibromides are readily brominated in the 5-position in the alkoxystyryl nucleus; thus (6) was directly obtained from (1) by treatment with bromine (2 mols.) in warm glacial acetic acid; this result establishes the position in which the bromine atom enters the nucleus. p-*Tolyl αβ-dibromo-β-5-bromo-o-anisylethyl ketone* (8), m. p. (benzene) 159—160° (Found: Br, 49·0. $C_{17}H_{15}O_2Br_3$ requires Br, 48·9%), was similarly obtained from (3). Nuclear bromination of (4) occurs in the 6-position in the 3-alkoxyphenyl nucleus (see Bauer and Vogel, *loc. cit.*).

Action of Potassium Iodide on the Dibromides.—Iodine separated when (5) or (6) was boiled with potassium iodide in aqueous acetone for 3 hours, and the solution yielded (1) or (2) respectively on dilution.

Action of Alcohol on the Dihalides.—The *o*-alkoxy-group, like the *p*-alkoxy-group (cf. Nadkarni *et al.*, *loc. cit.*), renders labile the side-chain halogen atom adjacent to the alkoxyphenyl nucleus (I*). Phenyl α-bromo-β-ethoxy-β-*o*-anisylethyl ketone (9) separated as a paste from a solution of (5) in ethyl alcohol, which had been boiled for 5 hours and filtered hot. Its constitution followed from the fact that, when heated with hydrogen bromide in acetic acid for 3 hours, the side-chain alkoxy-group was replaced by bromine, (5) being re-formed (cf. Nadkarni *et al.*, *loc. cit.*). Further, (9) evolved alcohol when heated at 225°/10 mm. and gave *phenyl α-bromo-o-methoxystyryl ketone* (10), m. p. (alcohol) 106° (Found: Br, 25·8. $C_{16}H_{13}O_2Br$ requires Br, 25·3%).

Action of Pyridine on the Chalkone Dibromides.—As with other chalkone dibromides, treatment with hot pyridine yielded yellow α-bromostyryl derivatives. Thus (10) separated when (5) was heated with pyridine at the b. p. for 20 seconds and the solution diluted with alcohol; before crystallisation it was washed with dilute hydrochloric acid and with water. *Phenyl α : 5-dibromo-o-methoxystyryl ketone* (11), m. p. (alcohol) 103—104° (Found: Br, 40·2. $C_{16}H_{12}O_2Br_2$ requires Br, 40·4%), p-*tolyl α : 5-dibromo-o-methoxystyryl ketone* (12), m. p. (alcohol) 127° (Found: Br, 38·8. $C_{17}H_{14}O_2Br_2$ requires Br, 39·0%), and *phenyl α-bromo-m-methoxystyryl ketone*, m. p. (alcohol) 100—101° (Found: Br, 25·4. $C_{16}H_{13}O_2Br$ requires Br, 25·3%), were similarly prepared from (6), (8) and (7) respectively. Compounds (6) and (8) were regenerated when (11) and (12) were kept overnight in solution in glacial acetic acid containing hydrogen bromide.

Preparation of Aryl β-Methoxystyryl Ketones.—*Phenyl 5-bromo-β : 2-dimethoxystyryl ketone* (13), m. p. (methyl alcohol) 122° (Found: Br, 23·4. $C_{17}H_{15}O_3Br$ requires Br, 23·1%), separated from a solution of (6) (8 g.) and sodium methoxide (1 g. of sodium) in methyl alcohol (120 c.c.) which had been heated under reflux for 2 hours and diluted with water. *Phenyl 5-bromo-2-methoxy-β-ethoxystyryl ketone*, m. p. (alcohol) 127° (Found: Br, 21·8. $C_{18}H_{17}O_3Br$ requires Br, 22·2%), p-*tolyl 5-bromo-β : 2-dimethoxystyryl ketone* (14), m. p. (methyl alcohol) 96° (Found: Br, 22·6. $C_{18}H_{17}O_3Br$ requires Br, 22·2%), p-*tolyl 5-bromo-2-methoxy-β-ethoxystyryl ketone*, m. p. (alcohol) 113° (Found: Br, 21·2. $C_{19}H_{19}O_3Br$ requires Br, 21·3%), *phenyl 6-bromo-β : 3-dimethoxystyryl ketone*, m. p. (methyl alcohol) 93° (Found: Br, 23·1. $C_{17}H_{15}O_3Br$ requires Br, 23·1%), and *phenyl 6-bromo-3-methoxy-β-ethoxystyryl ketone*, m. p. (alcohol) 96° (Found: Br, 22·1. $C_{18}H_{17}O_3Br$ requires Br, 22·2%), were similarly prepared from the corresponding chalkone dibromides and alkali alkoxide.

Preparation of 1 : 3-Diketones.—The oily suspension obtained by adding water (100 c.c.) to a solution of (6) (20 g.) and sodium ethoxide (2·4 g. of sodium) in ethyl alcohol (80 c.c.), which had been boiled under reflux for 1½ hours, gave a yellow solid (9·4 g.) after it had been heated at 100° with concentrated hydrochloric acid (10 c.c.) for 2 hours. The product, *benzoyl-5-bromo-o-anisoylmethane* (15), m. p. (alcohol) 96° (Found: Br, 23·7. $C_{16}H_{13}O_3Br$ requires Br, 24·0%), separated from alcohol in yellow needles and gave a deep violet colour with alcoholic ferric chloride. *5-Bromo-o-anisoyl-p-toluoylmethane* (16), m. p. (alcohol) 122° (Found: Br, 23·4. $C_{17}H_{15}O_3Br$ requires Br, 23·1%), was similarly prepared from (8), sodium methoxide being used. *Bromobenzoyl-5-bromo-o-anisoylmethane* (17), m. p. (aqueous acetone) 166° (Found: Br, 38·8. $C_{16}H_{12}O_3Br_2$ requires Br, 38·9%), separated when a current of air, which had previously been passed through a solution of bromine (5 g.) in chloroform (10 c.c.), was led at 0° into a solution of (15) (10 g.) in chloroform (30 c.c.), which was then evaporated. *Bromo-5-bromo-o-anisoyl-p-toluoylmethane* (18), m. p. (alcohol) 178° (Found: Br, 37·2. $C_{17}H_{14}O_3Br_2$

requires Br, 37·5%), was similarly prepared from (16) (cf. Neufville and Pechmann, *Ber.*, 1890, **23**, 3375). The positive nature of the side-chain bromine atom in (17) and (18) has been mentioned in the introduction.

Preparation of Flavones.—6-Bromoflavone, m. p. and mixed m. p. with an authentic sample, 192—193° (Kostanecki and Ludwig, *Ber.*, 1898, **31**, 2951, give m. p. 189—190°), separated when water was added to a solution of (13) (4 g.) in glacial acetic acid (40 c.c.) containing hydrogen bromide, which had been kept overnight; (15) and (17) treated in the same way yielded the same product (Found : Br, 26·9. Calc. for $C_{15}H_9O_2Br$: Br, 26·6%). 6-*Bromo-4'-methylflavone*, similarly prepared from (14), had m. p. (alcohol) 197° (Found : Br, 25·5. $C_{16}H_{11}O_2Br$ requires Br, 25·4%). The bromine atom in these bromoflavones is not replaced by hydrogen on treatment with hydriodic acid, being in this respect different from the bromine atom in 6-bromo-5 : 7-dimethoxyflavones (cf. Hutchins and Wheeler, *Current Sci.*, 1938, **6**, 605).

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