19. *Chalkones : Reactivity of Naphthyl* p-*Alkoxystyryl Ketones and their Dihalides.*

By G. V. Deshmukh and T. S. Wheeler.

The reactivity of some naphthyl *p*-alkoxystyryl ketones and their halides has been examined on lines previously described for chalkones of the benzene series (J., 1937, 1798). The synthesis of some naphthalene analogues of chalkone derivatives is described.

Nadkarni, Warriar, and Wheeler (J., 1937, 1798) examined the reactivity of some phenyl *p*-alkoxystyryl ketones and their dihalides towards various reagents : the work has now been extended to chalkones of the naphthalene series, and the synthesis of some naphthalene analogues of chalkone derivatives effected.

Some reactions of phenyl 6-bromo-3 : 4-methylenedioxystyryl ketone (Dodwadmath and Wheeler, *Proc. Indian Acad. Sci.*, 1935, **2**, 438) and of its derivatives are also described. It has been found that phenyl α-bromo-β-ethoxy-β-(6-bromo-3 : 4-methylenedioxyphenyl)-ethyl ketone (I) (Dodwadmath and Wheeler, *loc. cit.*), treated with sodium methoxide in methyl alcohol, gives *phenyl* 6-*bromo*-β-*methoxy*-3 : 4-*methylenedioxystyryl ketone* (IV) and that the corresponding β-methoxyphenylethyl ketone with alcoholic sodium ethoxide yields the β-*ethoxystyryl* derivative. This interchange of alkoxyl with elimination of hydrogen bromide probably occurs with intermediate formation of an α-bromostyryl compound (II) and of an acetylenic compound (III) (cf. Dufraisse and his collaborators, *Compt. rend.*, 1922, **174**, 1631 ; 1924, **178**, 573 ; Nadkarni *et al.*, *loc. cit.*) :

$$\underset{\text{(I.)}}{\mathrm{R{\cdot}CO{\cdot}CHBr{\cdot}CH(OEt)R'}} \longrightarrow \underset{\text{(II.)}}{[\mathrm{R{\cdot}CO{\cdot}CBr{:}CHR'}]} \longrightarrow$$

$$\text{(III.)}\quad [\mathrm{R{\cdot}CO{\cdot}C{\vdots}CR'}] \longrightarrow \mathrm{R{\cdot}CO{\cdot}CH{:}C(OMe)R'} \quad \text{(IV.)}$$

$$[\mathrm{R} = \mathrm{Ph};\ \mathrm{R'} = \mathrm{C_6H_2Br(CH_2O_2)}]$$

Experimental.

Chalkones.—Phenyl 6-bromo-3 : 4-methylenedioxystyryl ketone (1) (Dodwadmath and Wheeler, *loc. cit.*) and 1-*hydroxy*-2-*naphthyl* 6-*bromo*-3 : 4-*methylenedioxystyryl ketone* (2), m. p. (carbon tetrachloride) 210° (Found : Br, 20·3. $C_{20}H_{13}O_4Br$ requires Br, 20·2%), were prepared from 6-bromopiperonal and the corresponding acetophenones in presence of alcoholic alkali (Sorge, *Ber.*, 1902, **35**, 1069). 1-*Acetoxy*-2-*naphthyl* 6-*bromo*-3 : 4-*methylenedioxystyryl ketone* (3), prepared from (2) by treatment with acetic anhydride and fused sodium acetate, had m. p. (carbon tetrachloride) 173—174° (Found : Br, 18·4. $C_{22}H_{15}O_5Br$ requires Br, 18·3%). 1-*Methoxy*-2-*naphthyl* 6-*bromo*-3 : 4-*methylenedioxystyryl ketone* (4), m. p. (alcohol–acetone) 144—145° (Found : Br, 19·2. $C_{21}H_{15}O_4Br$ requires Br, 19·5%), separated on dilution of a suspension of (2) (10 g.) in acetone (200 c.c.), which had been carefully treated with methyl sulphate (7 g.) and aqueous potassium hydroxide (40% ; 25 c.c.) and heated under reflux for 1 hour. Compound

(4) was also prepared from 6-bromopiperonal and 1-methoxy-2-acetylnaphthalene in the usual way. Compound (2) separated from a solution of (4) in glacial acetic acid containing hydrogen bromide which had been kept for 12 hours and poured into aqueous sodium hydrogen sulphite. All these chalkones are yellow.

Condensation of Chalkones with Ethyl Acetoacetate.—*Ethyl* 4-*phenyl*-6-(6′-*bromo*-3′ : 4′-*methylenedioxyphenyl*)-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate* (12 g.), m. p. (alcohol–acetone) 133—134° (Found : Br, 17·5. $C_{22}H_{19}O_5Br$ requires Br, 18·0%), separated on dilution of a solution of sodium ethoxide (1·4 g. of sodium), ethyl acetoacetate (8 g.), and (1) (10 g.) in alcohol, which had been heated under reflux for 3 hours. *Ethyl* 4-(1′-*hydroxy*-2′-*naphthyl*)-6-(6″-*bromo*-3″ : 4″-*methylenedioxyphenyl*)-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate*, m. p. (alcohol–acetone) 219—220° (Found : Br, 15·8. $C_{26}H_{21}O_6Br$ requires Br, 15·7%), was similarly prepared from (2).

Halogenation of the Chalkones.—4-*Bromo*-1-*hydroxy*-2-*naphthyl* 6-*bromo*-3 : 4-*methylenedioxystyryl ketone*, m. p. (carbon tetrachloride) 249° (Found : Br, 33·5. $C_{20}H_{12}O_4Br_2$ requires Br, 33·6%), separated from a suspension of (2) (10 g.) in chloroform (50 c.c.) and carbon disulphide (50 c.c.), which had been treated at 0° with a solution of bromine (1 mol.) in carbon disulphide (25 c.c.) and kept overnight at 0°, and the solvent evaporated. Substitution preceding addition is not found with chalkones containing phenyl groups only (cf. Dean and Nierenstein, *J. Amer. Chem. Soc.*, 1925, **47**, 1682). The position of the nuclear bromine atom is fixed by analogy with the results obtained by Torrey and Brewster (*J. Amer. Chem. Soc.*, 1909, **31**, 1323) on bromination of 2-acetyl-1-naphthol. Twice the quantity of bromine being used, (2) and (4), treated as described above, yielded, respectively, 4-*bromo*-1-*hydroxy*-2-*naphthyl* αβ-*dibromo*-β-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*ethyl ketone* (5), m. p. (carbon tetrachloride) 215—216° (Found : Br, 49·8. $C_{20}H_{12}O_4Br_4$ requires Br, 50·3%), and 4-*bromo*-1-*methoxy*-2-*naphthyl* αβ-*dibromo*-β-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*ethyl ketone* (6), m. p. (benzene–light petroleum) 187—188° (Found : Br, 49·0. $C_{21}H_{14}O_4Br_4$ requires Br, 49·2%). Compound (3) with 1 mol. of bromine gave 1-*acetoxy*-2-*naphthyl* αβ-*dibromo*-β-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*ethyl ketone* (7), m. p. (benzene–light petroleum) 184° (Found : Br, 40·1. $C_{22}H_{15}O_5Br_3$ requires Br, 40·1%), the acetoxy-group inhibiting nuclear substitution. *Phenyl* αβ-*dichloro*-β-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*ethyl ketone* (8), prepared from (1) by treatment with chlorine (1 mol.) in glacial acetic acid, had m. p. (benzene–light petroleum) 149—150° (Found : halogen, 37·9. $C_{16}H_{11}O_3Cl_2Br$ requires halogen, 37·6%).

These dihalides readily react with ammonia. *Phenyl* 6-*bromo*-β-*amino*-3 : 4-*methylenedioxystyryl ketone*, m. p. (alcohol) 153° (Found : Br, 23·4. $C_{16}H_{12}O_3NBr$ requires Br, 23·1%), separated from a suspension of phenyl αβ-dibromo-β-(6-bromo-3 : 4-methylenedioxyphenyl)-ethyl ketone (9) (Dodwadmath and Wheeler, *loc. cit.*) in concentrated alcoholic ammonia which had been kept for 5 days (cf. Ruhemann and Watson, J., 1904, **85**, 1173, 1181, 1323).

β-*Benzoyl*-α-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*propionitrile*, m. p. (alcohol) 120° (Found : N, 4·1; Br, 22·2. $C_{17}H_{12}O_3NBr$ requires N, 3·9; Br, 22·3%), separated on dilution of a cold alcoholic solution of (9) containing potassium cyanide, which had been heated under reflux for 3 hours.

Action of Alcohols on Naphthalene Chalkone Halides.—As with chalkones of the benzene series, so in the naphthalene series, the β-halogen atom adjacent to a *p*-alkoxyphenyl nucleus is reactive towards alcohols (cf. Nadkarni *et al.*, *loc. cit.*). 4-*Bromo*-1-*methoxy*-2-*naphthyl* α-*bromo*-β-*ethoxy*-β-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*ethyl ketone* (10), m. p. (alcohol) 126—127° (Found : Br, 38·9. $C_{23}H_{19}O_5Br_3$ requires Br, 39·0%), separated from a cold alcoholic solution of (6), which had been heated under reflux for 6 hours. 4-*Bromo*-1-*methoxy*-2-*naphthyl* α-*bromo*-β-*methoxy*-β-(6-*bromo*-3 : 4-*methylenedioxyphenyl*)*ethyl ketone*, m. p. (methyl alcohol) 150—151°, was similarly prepared by means of methyl alcohol (Found : Br, 40·1. $C_{22}H_{17}O_5Br_3$ requires Br, 39·9%).

Action of Pyridine on the Dihalides.—4-*Bromo*-1-*methoxy*-2-*naphthyl* α : 6-*dibromo*-3 : 4-*methylenedioxystyryl ketone*, m. p. (alcohol) 127—128° (Found : Br, 42·3. $C_{21}H_{13}O_4Br_3$ requires Br, 42·2%), separated from a solution of (6) in pyridine which had been heated for 10 minutes and diluted with alcohol and with water. *Phenyl* α : 6-*dibromo*-3 : 4-*methylenedioxystyryl ketone* (11), m. p. (alcohol) 123—124° (Found : Br, 39·2. $C_{16}H_{10}O_3Br_2$ requires Br, 39·0%), and *phenyl* α-*chloro*-6-*bromo*-3 : 4-*methylenedioxystyryl ketone* (12), m. p. (alcohol) 125° (Found : halogen, 31·9. $C_{16}H_{10}O_3ClBr$ requires halogen, 31·6%), were also prepared from (9) and (8) respectively. These α-halogenostyryl ketones are yellow.

1 : 3-*Diphenyl*-5-(6′-*bromo*-3′ : 4′-*methylenedioxyphenyl*)*pyrazole*, m. p. (alcohol) 163—164° (Found : Br, 19·3. $C_{22}H_{15}O_2N_2Br$ requires Br, 19·1%), separated as an oil from mixed solutions of phenylhydrazine (1 g.) in acetic acid (25 c.c.), and of (11) or (12) (2 g.) in alcohol (25 c.c.),

which had been heated together under reflux for 4 hours; it solidified after it had been kept at 0° for 12 hours (cf. Auwers and Hügel, *J. pr. Chem.*, 1935, **143**, 157).

Action of Sodium Alkoxide on Dihalides.—The chalkone dihalides not containing hydroxyl ortho to the keto-group give β-alkoxystyryl derivatives on treatment with excess of alcoholic sodium alkoxide. *Phenyl* 6-*bromo*-β-*ethoxy*-3 : 4-*methylenedioxystyryl ketone* (13) (5 g.), m. p. (alcohol) 134—135° (Found : Br, 21·1. $C_{18}H_{15}O_4Br$ requires Br, 21·3%), separated from a solution of (9) (10 g.) and sodium ethoxide (1 g. of sodium) in alcohol (50 c.c.), which had been heated under reflux for 3 hours and kept at 0° for 12 hours. *Phenyl* 6-*bromo*-β-*methoxy*-3 : 4-*methylenedioxystyryl ketone* (14), m. p. (methyl alcohol) 79—80° (Found : Br, 22·4. $C_{17}H_{13}O_4Br$ requires Br, 22·2%), was similarly prepared from (9), a solution of sodium methoxide in methyl alcohol being used. 6-*Bromo*-3 : 4-*methylenedioxydibenzoylmethane*, m. p. (alcohol) 125—126° (Found : Br, 23·4. $C_{16}H_{11}O_4Br$ requires Br, 23·1%), separated as an oil, which afterwards solidified, from a mixture of (13) and dilute hydrochloric acid (5%), which had been boiled for 3 hours and kept at 0° for 12 hours.

Compound (14) was also obtained by the action of sodium methoxide in methyl-alcoholic solution on phenyl α-bromo-β-ethoxy-β-(6-bromo-3 : 4-methylenedioxyphenyl)ethyl ketone (Dodwadmath and Wheeler, *loc. cit.*), and (13) was prepared from phenyl α-bromo-β-methoxy-β-(6-bromo-3 : 4-methylenedioxyphenyl)ethyl ketone (Dodwadmath and Wheeler, *loc. cit.*) and sodium ethoxide in alcoholic solution (see introduction).

Chalkones containing hydroxyl ortho to the keto-group give flavones with alcoholic alkali unless a β-alkoxy-compound is intermediately formed (Nadkarni *et al.*, *loc. cit.*). 6 : 6′-*Dibromo*-3′ : 4′-*methylenedioxy*-7 : 8-*benzoflavone* (15), m. p. (chloroform–alcohol) above 275° (Found : C, 50·3; H, 2·2; Br, 34·4. $C_{20}H_{10}O_4Br_2$ requires C, 50·6; H, 2·1; Br, 33·8%), separated from a solution of (5) (2 g.) in alcohol or acetone, which had been treated with 2N-sodium hydroxide (2 c.c.) and kept for 12 hours. It gave a yellow coloration with red fluorescence with concentrated sulphuric acid. Compound (15) was also obtained when (5) was heated under reduced pressure above the m. p. or under reflux with alcoholic potassium cyanide for 4 hours (cf. Hutchins and Wheeler, *Current Sci.*, 1938, **6**, 605), or with pyridine. Compound (7), similarly treated with aqueous-alcoholic sodium hydroxide or pyridine, gave 6′-*bromo*-3′ : 4′-*methylenedioxy*-7 : 8-*benzoflavone*, m. p. (chloroform–alcohol) 245—246° (Found : C, 60·3; H, 2·6. $C_{20}H_{11}O_4Br$ requires C, 60·7; H, 2·8%), which reacted similarly to (15) with concentrated sulphuric acid. Formation of the β-ethoxy-compound of the type of (10) by preliminary heating with alcohol with addition of chloroform to increase the solubility of the dibromide and promote reaction, leads to the production of benzylidenecoumaranones. Thus 6′-*bromo*-3′ : 4′-*methylenedioxy*-1-*benzylidene*-5 : 6-*benzocoumaran-2-one*, m. p. (alcohol) 264° (Found : Br, 20·5. $C_{20}H_{11}O_4Br$ requires Br, 20·3%), separated when the pasty mass obtained by heating (7) (2 g.) for 12 hours under reflux with absolute alcohol (50 c.c.) and chloroform (25 c.c.) was boiled with 2N-sodium hydroxide (2 c.c.) and alcohol (10 c.c.). It gave a red coloration with concentrated sulphuric acid.

ROYAL INSTITUTE OF SCIENCE, BOMBAY.

[*Received, November 23rd*, 1938.]