153. *Chalkones : Reactions of* o-*Hydroxyphenyl* 6-*Methoxy*-2 : 3-*benzostyryl Ketone and of Some Derivatives.*

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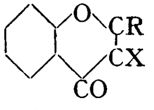
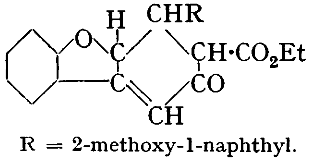
o-*Hydroxyphenyl* 6-*methoxy*-2 : 3-*benzostyryl ketone* and its *dibromide* react like analogous compounds of the phenyl series to yield, among other compounds, naphthalene analogues of flavones, flavonols and benzylidenecoumaranones. Further, the dibromide reacts with alcohol in the same manner as the corresponding *o*- and *p*-alkoxyphenyl analogues (cf. Nadkarni *et al.*, J., 1937, 1798). The characteristic reactions of the keto-ethylene group are shown by naphthylidenecoumaranones in spite of the presence of a cyclic linkage.

o-*Hydroxyphenyl* 6-*methoxy*-2 : 3-*benzostyryl ketone*, $C_6H_4(OH)\cdot CO\cdot CH{:}CH\cdot C_{10}H_6\cdot OMe$ (I) reacts like the simpler chalkones of the phenyl series with (a) alkaline hydrogen peroxide (flavonol synthesis of Algar and Flynn, *Proc. Roy. Irish Acad.*, 1934, **42**, *B*, 1), (b) ethyl acetoacetate (Knoevenagel, *Annalen*, 1894, **281**, 58), and (c) *cyclo*hexanone (Hill, J., 1935, 1115) to form, respectively, (a) 2-(2'-*methoxy*-1'-*naphthyl*)-3-*chromonol* (II), also prepared from the dibromide of (V) by the method of Auwers and Müller (*Ber.*, 1908, **41**, 4233: Auwers and Pohl, *Annalen*, 1914, **405**, 243), (b) *ethyl* 4-o-*hydroxyphenyl*-6-(2'-*methoxy*-1'-*naphthyl*)-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate*, and (c) the Michael addition compound, 2-β-o-*hydroxybenzoyl*-α-2'-*methoxy*-1'-*naphthylethyl*cyclo*hexanone*.

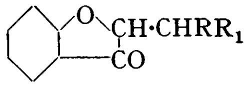
The *dibromide* of (I) reacts with alcohol in the same manner as the corresponding *o*- and *p*-alkoxyphenyl analogues (cf. Nadkarni *et al.*, J., 1937, 1798; Bhagwat and Wheeler, J., 1939, 94) to give o-*hydroxyphenyl* α-*bromo*-β-*ethoxy*-β-2-*methoxy*-1-*naphthylethyl ketone* (III). With alcoholic potassium cyanide, the dibromide yields 2-(2'-*methoxy*-1'-*naphthyl*)-*chromone* (IV), and (III) with alcoholic soda gives 1-(2'-*methoxy*-1'-*naphthylidene*)*coumaran*-2-*one* (V) (cf. Hutchins and Wheeler, J., 1939, 91).



R = 2-methoxy-1-naphthyl.
II (X = OH)
IV (X = H)



R = 2-methoxy-1-naphthyl.
(VI.)



R = 2-methoxy-1-naphthyl.
R₁ = 2-keto*cyclo*hexyl.
(VII.)

The characteristic reactions of the keto-ethylene group are not affected by the cyclic linkage in (V). The bromine atom in the *dibromide* of (V), adjacent to the methoxy-naphthyl nucleus, is, like the corresponding bromine atom in the dibromide of (I), labile towards alcohols; further (V) undergoes the normal addition reactions with ethyl acetoacetate and *cyclo*hexanone to give respectively *ethyl* 2-(2'-*methoxy*-1'-*naphthyl*)-3 : 4-1'' : 2''-*coumarano*-Δ^4-cyclo*hexen*-6-*one*-1-*carboxylate* (VI) and 1-(2'-*keto*-1'-cyclo*hexyl*-2''-*methoxy*-1''-*naphthylmethyl*)*coumaran*-2-*one* (VII). The composition assigned to (VI) is based on the chalkone analogy (see Rao and Wheeler, J., 1939, 1004) and is confirmed by the formation of an *oxime.*

EXPERIMENTAL.

Chalkones.—o-*Hydroxyphenyl* 6-*methoxy*-2 : 3-*benzostyryl ketone* (1), m. p. (alcohol) 142° (Found : C, 79·2; H, 5·4. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%), separated as a yellow powder from a mixture of 2-methoxy-1-naphthaldehyde (2) (10 g.) [prepared from β-naphthyl methyl ether by the method described by Adams and Levine (*J. Amer. Chem. Soc.*, 1923, **45**, 2373), modified by addition of aluminium chloride in dry ether (Shah and Laiwalla, J., 1938, 1828) and potassium chloride (Arnold and Sprung, *J. Amer. Chem. Soc.*, 1938, **60**, 1699)], *o*-hydroxyacetophenone (3) (8 g.) and alcohol (60 c.c.), which had been treated with aqueous sodium hydroxide (15 c.c. of 50%), heated at 60° for 30 minutes, kept for 24 hours, diluted with ice-cold water and acidified with dilute hydrochloric acid. The *acetyl* derivative (sodium acetate–acetic anhydride method) separated from alcohol in yellow needles, m. p. 107° (Found : C, 76·2; H, 5·3. $C_{22}H_{18}O_4$ requires C, 76·3; H, 5·2%). o-*Anisyl* 6-*hydroxy*-2 : 3-*benzostyryl ketone*, m. p. (alcohol–acetone) 153° (Found : C, 79·0; H, 5·4. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%), was similarly prepared from 2-hydroxy-1-naphthaldehyde (4) (Pandya and Vahidy, *Proc. Indian Acad. Sci.*, 1937, **6**, 181) and *o*-methoxyacetophenone (5).

o-*Hydroxyphenyl* 6-*hydroxy*-2 : 3-*benzostyryl ketone*, m. p. (alcohol) 140° (Found : C, 78·8; H, 5·3. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·8%), was obtained by heating (1) with powdered anhydrous aluminium chloride (2 mols.) for 2 hours at 125°, the product being treated with cold dilute hydrochloric acid; it was also prepared by condensing (3) and (4) as described for (1) above.

o-*Anisyl* 6-*methoxy*-2 : 3-*benzostyryl ketone*, m. p. (alcohol) 103° (Found : C, 79·3; H, 5·5. $C_{21}H_{18}O_3$ requires C, 79·2; H, 5·7%), was similarly prepared from (2) and (5). All the above chalkones were yellow.

2'-*Hydroxy*-5 : 6-*benzoflavylium chloride* separated after 4 days from a solution of (3) (1·7 g.) and (4) (2 g.) in anhydrous ethyl acetate, which had been saturated with dry hydrogen chloride. The product crystallised from glacial acetic acid containing a trace of hydrochloric acid in bluish-red leaflets, m. p. 215—220° (decomp.) (Found : Cl, 10·9. $C_{19}H_{13}O_2Cl$ requires Cl, 11·5%).

Compounds derived from the Chalkone (1).—2-(2'-*Methoxy*-1'-*naphthyl*)-3-*chromonol* (6), m. p. (alcohol) 239° (Found : C, 74·9; H, 4·5. $C_{20}H_{14}O_4$ requires C, 75·4; H, 4·4%), separated from a solution of (1) (1·2 g.) in alcohol (50 c.c.) containing N/2-alcoholic potash (18 c.c.) which had been gradually treated with hydrogen peroxide (30%; 10 c.c.), kept for 4 hours, diluted with water, and acidified with dilute sulphuric acid. Compound (6) was also prepared by treating a boiling solution of the dibromide (11; see below) (0·5 g.) in alcohol (30 c.c.) with alcoholic potassium hydroxide (0·25 g. in 40 c.c.). The resulting purple liquid was cooled and acidified, alcohol removed by evaporation, water added, and the yellow chromonol recovered by filtration. The *acetyl* derivative of (6) had m. p. (alcohol) 173° (Found : C, 72·8; H, 4·3. $C_{22}H_{16}O_5$ requires C, 73·3; H, 4·4%).

Ethyl 4-o-*hydroxyphenyl*-6-(2'-*methoxy*-1'-*naphthyl*)-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate* (7), m. p. (alcohol) 187° (Found : C, 75·3; H, 5·3. $C_{26}H_{24}O_5$ requires C, 75·0; H, 5·8%), separated from a cooled mixture of (1) (5 g.), ethyl acetoacetate (6 c.c.), sodium ethoxide (0·6 g. of sodium), and alcohol (100 c.c.) which had been heated under reflux for 4 hours. The *semicarbazone*, m. p. (alcohol) 172° (Found : N, 9·0. $C_{27}H_{27}O_5N_3$ requires N, 8·9%), and the *oxime*, m.p. (dilute acetic acid) 212° (Found : N, 3·2. $C_{26}H_{25}O_5N$ requires N, 3·2%), of (7) were prepared in the usual manner.

2-β-o-*Hydroxybenzoyl*-α-2'-*methoxy*-1'-*naphthylethyl*cyclo*hexanone*, m.p. (alcohol) 178° (Found : C, 77·3; H, 6·5. $C_{26}H_{26}O_4$ requires C, 77·6; H, 6·5%), was prepared by heating a mixture of (1) (1 g.), finely divided sodium (0·2 g.), *cyclo*hexanone (2 c.c.), and anhydrous ether (100 c.c.) under reflux for 4 hours, keeping the product overnight, and then carefully treating it with dilute hydrochloric acid. The required substance was recovered by evaporating the ethereal layer.

o-*Hydroxyphenyl* αβ-*dibromo*-β-2-*methoxy*-1-*naphthylethyl ketone* (8), m. p. (chloroform–light petroleum) 152° (decomp.) (Found : Br, 34·4. $C_{20}H_{16}O_3Br_2$ requires Br, 34·4%), was obtained by careful bromination of (1) in chloroform solution in the cold.

Compounds derived from the Dibromide of (1).—o-*Hydroxyphenyl* α-*bromo*-β-*ethoxy*-β-2-*methoxy*-1-*naphthylethyl ketone* (9), m. p. (alcohol) 179° (Found : Br, 19·0. $C_{22}H_{21}O_4Br$ requires Br, 18·6%), separated from a cold solution of (8) in ethyl alcohol, which had been heated under reflux for 10 hours and kept overnight.

2-(2′-*Methoxy*-1′-*naphthyl*)*chromone*, m. p. (acetic acid) 178° (Found : C, 79·0; H, 5·3. $C_{20}H_{14}O_3$ requires C, 79·4; H, 4·6%), separated from an alcoholic solution of (8), which had been mixed with a concentrated aqueous solution of potassium cyanide (3 mols.) and heated under reflux for 8 hours. It gave a yellow coloration with concentrated sulphuric acid.

1-(2′-*Methoxy*-1′-*naphthylidene*)*coumaran*-2-*one* (10), m. p. (alcohol) 178° and mixed m. p. with preceding chromone, 139—140° (Found : C, 79·8; H, 4·6. $C_{20}H_{14}O_3$ requires C, 79·4; H, 4·6%), which gave a purple coloration with concentrated sulphuric acid, was prepared by treating a solution of (9) (1 g.) in alcohol (20 c.c.) with aqueous sodium hydroxide (4 c.c. of 10%), heating the mixture at 60° for 15 minutes, and keeping the product overnight. The 2 : 4-*dinitrophenylhydrazone* of (10) (Found : N, 11·4. $C_{26}H_{18}O_6N_4$ requires N, 11·6%) formed orange needles, which, after being washed with alcohol containing hydrochloric acid, had m. p. (alcohol) 238°.

Compounds derived from the Naphthylidenecoumaranone (10).—1-(2′-*Methoxy*-1′-*naphthylidene*)*coumaran*-2-*one dibromide* (11), m. p. (chloroform–light petroleum) 158° (Found : Br, 35·1. $C_{20}H_{14}O_3Br_2$ requires Br, 34·6%), separated on careful bromination of (10) in chloroform solution in the cold.

1-*Bromo*-1-(*ethoxy*-2′-*methoxy*-1′-*naphthylmethyl*)*coumaran*-2-*one*, m. p. (alcohol) 165° (Found : Br, 18·0. $C_{22}H_{19}O_4Br$ requires Br, 18·7%), was prepared by heating (11) under reflux with ethyl alcohol for 8 hours.

Ethyl 2-(2′-*methoxy*-1′-*naphthyl*)-3 : 4-1″ : 2″-*coumarano*-Δ^4-cyclo*hexen*-6-*one*-1-*carboxylate* (12), m. p. (alcohol) 174° (Found : C, 74·8; H, 5·7. $C_{26}H_{22}O_5$ requires C, 75·4; H, 5·3%), separated when a solution of (10) (5 g.), ethyl acetoacetate (6 c.c.), and sodium ethoxide (0·6 g. of sodium) in alcohol (40 c.c.), which had been heated under reflux for 4 hours, was cooled. The *oxime*, m. p. (dilute acetic acid) 188° (Found : N, 3·3. $C_{26}H_{23}O_5N$ requires N, 3·3%), was prepared in the usual way.

A mixture of (10) (0·1 g.), finely divided sodium (0·025 g.), *cyclo*hexanone (0·3 c.c.), and dry ether (20 c.c.) was heated under reflux for 4 hours, cooled, kept overnight, and acidified with dilute hydrochloric acid. The ethereal layer on evaporation yielded 1-(2′-*keto*-1′-cyclo*hexyl*-2″-*methoxy*-1″-*naphthylmethyl*)*coumaran*-2-*one*, m. p. (alcohol) 184° (Found : C, 77·8; H, 6·5. $C_{26}H_{24}O_4$ requires C, 78·0; H, 6·0%).

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