

# CHALKONES: PREPARATION OF SOME HYDROXY-CHALKONES, THEIR BROMINATION AND STUDY OF THE REACTIVITY OF THE BROMO DERIVATIVES

BY H. P. VANDREWALLA AND G. V. JADHAV

(Department of Organic Chemistry, Royal Institute of Science, Bombay  
and The Karnatak College, Dharwar)

Received July 23, 1948

(Communicated by Dr. R. C. Shah, F.A.Sc.)

THE Chalkones were prepared according to the method of Sorge.<sup>1</sup> The bromination of these chalkones gave bromo derivatives, but in the case of dihydroxy compounds, it was observed that the nucleus containing -OH groups was more reactive than the double bond in the molecule.

The reactivity of these dibromide derivatives was examined with potassium iodide, potassium hydroxide, sodium alkoxide, pyridine and potassium cyanide.

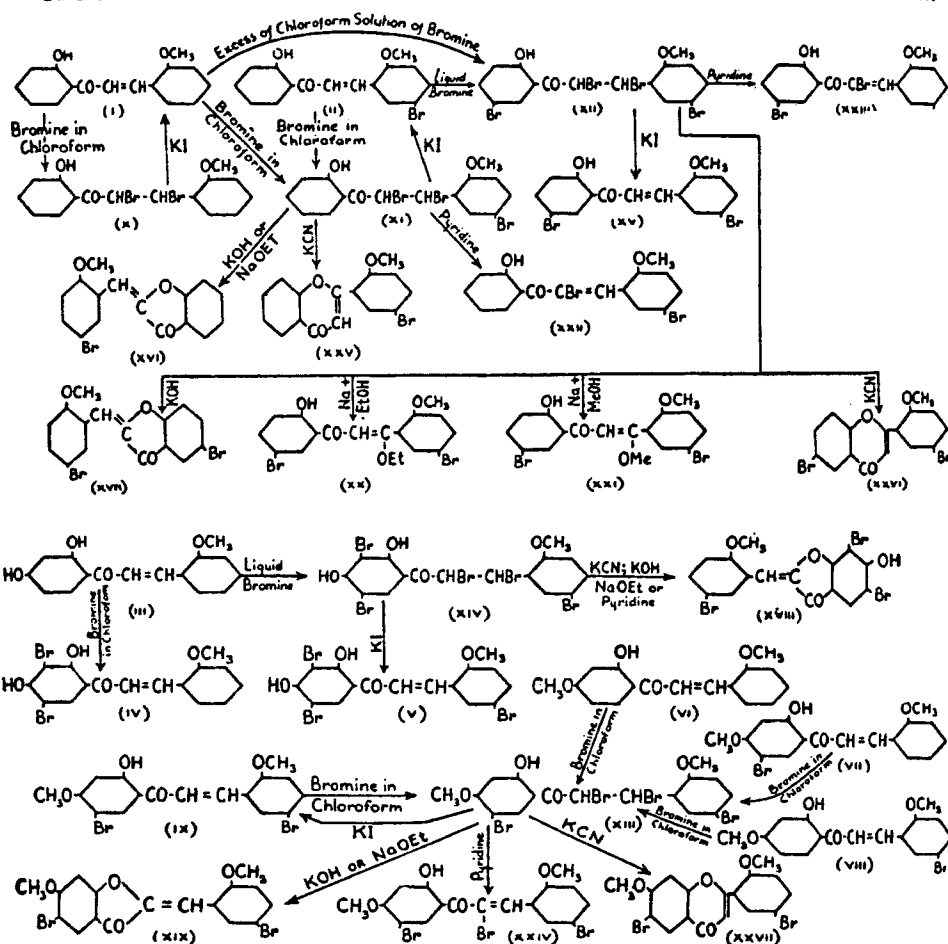
With potassium iodide both bromine atoms of the dibromide were found labile, when the corresponding styryl ketones were obtained, whose constitutions were proved by mixed melting points with authentic specimens. (cf. Dodwadmath and Wheeler<sup>2</sup>; Barne and Payton<sup>3</sup>; Nadkarni, Warrior and Wheeler<sup>4</sup>).

With potassium hydroxide these dibromides gave benzylidene coumaranones. Similar results were obtained with sodium alkoxide, except in the case of the ketone (XII) when  $\beta$ -alkoxy-styryl ketones were obtained, thus pointing to the more reactive nature of the  $\beta$  bromine atom (cf. Cullinane and Phillipott<sup>5</sup>; Kölher and Addinall<sup>6</sup>; Price and Bogert<sup>7</sup>; Nadkarni, Warrior and Wheeler<sup>4</sup>; Bhagwat and Wheeler<sup>8</sup>; Rao and Wheeler<sup>9</sup>).

With Pyridine ketones (XI), (XII) and (XIII) gave  $\alpha$ -bromostyryl ketones (XXII), (XXIII) and (XXIV) respectively whilst the ketone (XIV) gave the coumaranone (XVIII) (cf. Nadkarni, Warrior and Wheeler<sup>4</sup>; Bhagwat and Wheeler<sup>8</sup>; Rao and Wheeler<sup>9</sup>).

Potassium cyanide gave flavones (XXV), (XXVI) and XXVII) in the case of ketones (XI), (XII) and (XIII) respectively, whilst ketone (XIV) gave the coumaranone (XVIII) (cf. Hutchins and Wheeler<sup>10</sup>; Rao and Wheeler<sup>9</sup>).

## DIAGRAMMATIC PRESENTATION OF RESULTS OF CHALKONES BY H.P.VANDREWALLA AND G.V.JADHAV.



These results point out that the reactivity of the bromine atoms depend upon the nature of the reagent as well as on the substituents in the phenyl part of the ketone molecule. With more basic reagents  $\beta$ -bromine atom is more reactive than the  $\alpha$ -one.

## EXPERIMENTAL.

The chalcones were prepared by dissolving the requisite ketone and aldehyde in alcohol and a strong caustic potash solution at ordinary temperature. The mixture, after a suitable period, was diluted with water, alkali neutralised and crystallised from a suitable solvent. The compounds are described in Table I.

TABLE I

Name of Chalkone	Name in Quantity of Ketone	Name and Quantity of aldehyde	Quantity of KOH	Time	Solvent	Cryst. Shape	m.p.	Found %	Formula requires %
2-Hydroxyphenyl- $\beta$ -2'-methoxystyryl ketone (I)	O-Hydroxyacetophenone (20 g.)	O-Methoxybenzaldehyde (20 g.)	40 g. in 40 c.c.	Over night	Alcohol	Yellow needles	110-11°	C, 75.2; H, 5.8	C <sub>16</sub> H <sub>14</sub> O <sub>3</sub> requires C, 75.6; H, 5.6
2-Hydroxyphenyl- $\beta$ -2'-methoxy-5'-bromostyryl ketone (II)	O-Hydroxyacetophenone (2 g.)	2-Methoxy-5-bromobenzaldehyde (3.5 g.)	6 g. in 8 c.c.	do	Acetic acid	do	120-21°	Br, 24.4	C <sub>16</sub> H <sub>13</sub> O <sub>3</sub> Br requires Br, 24.3
2,4-Dihydroxyphenyl $\delta$ -2'-methoxystyryl ketone (III)	Resacetophenone (20 g.)	O-Methoxybenzaldehyde (18 g.)	60 g. in 80 c.c.	48 hrs.	Acetic acid	do	191-92°	C, 70.8; H, 5.4	C <sub>16</sub> H <sub>14</sub> O <sub>4</sub> requires C, 71.1; H 5.2
2,4-Dihydroxy-3,5-dibromophenyl- $\beta$ -2'-methoxystyryl ketone (IV)*	3:5-Dibromoresacetophenone (2 g.)	O-Methoxybenzaldehyde (1.5 g.)	6 g. in 8 c.c.	48 hrs.	Acetic acid	do	168-69°	Br, 37.8	C <sub>16</sub> H <sub>12</sub> O <sub>4</sub> Br <sub>2</sub> requires Br, 37.4
2,4-Dihydroxy-3:5-dibromophenyl- $\beta$ -2'-methoxy-5'-bromostyryl ketone (V)†	3:5-Dibromoresacetophenone (2 g.)	2-Methoxy-5-bromobenzaldehyde (1.5 g.)	6 g. in 8 c.c.	24 hrs.	do	do	194-95°	Br, 47.1	C <sub>16</sub> H <sub>11</sub> O <sub>4</sub> Br <sub>3</sub> requires Br, 47.3
2-Hydroxy-4-methoxyphenyl- $\beta$ -2'-methoxystyryl ketone (VI)	Peanol (10 g.)	O-Methoxybenzaldehyde (8 g.)	20 g. in 30 c.c.	24 hrs.	Alcohol	do	93-94°	C, 71.5; H, 5.8	C <sub>17</sub> H <sub>16</sub> O <sub>4</sub> requires C, 71.8; H, 5.6
2-Hydroxy-4-methoxy-5-bromophenyl- $\beta$ -2'-methoxystyryl ketone (VII)	5-Bromopeanol	do	do	do	Acetic acid	do	158-59°	Br, 22.1	C <sub>17</sub> H <sub>15</sub> O <sub>4</sub> Br, requires Br 22
2-Hydroxy-4-methoxyphenyl $\beta$ -2'-methoxy-5'-bromostyryl ketone (VIII)	Peanol	2-Methoxy-5-bromobenzaldehyde	do	do	do	do	127-28°	Br, 21.6	C <sub>17</sub> H <sub>15</sub> O <sub>4</sub> Br requires Br 22
2-Hydroxy-4-methoxy-5-bromophenyl $\beta$ -2'-methoxy-5'-bromostyryl ketone (IX)	5-Bromopeanol	2-Methoxy-5-bromobenzaldehyde	do	do	do	do	191-92°	Br, 36.6	C <sub>17</sub> H <sub>14</sub> O <sub>4</sub> Br <sub>2</sub> requires Br, 36.2

(\*) This was also obtained by boiling for 5 hours ketone (III) (3 g.) in chloroform (300 c.c.) and leaving the reaction mixture overnight at room temperature.

(†) This was also obtained by boiling under reflux ketone (XIV) with alcoholic potassium iodide solution.

The bromination of these chalkones was carried in chloroform medium with 10 per cent. solution of bromine in chloroform and the bromo derivatives were obtained after the removal of the solvent and crystallised from a suitable solvent. The compounds are described in Table II. When liquid bromine was used for bromination, the solid was washed with sodium bisulphite before crystallisation.

#### *Action of potassium iodide*

The ketone (X) was dissolved in acetone (40 c.c.) and potassium iodide (1 g.) was added to it. The mixture was then boiled under reflux for about 45 minutes. The solid obtained after the removal of the solvent was washed with sodium thiosulphate solution and finally crystallised from alcohol in yellow needles, m.p. 110–11°. It was found identical with (I) by mixed melting point.

The ketone (XI) under similar conditions gave ketone (II). The ketone (XII) when refluxed with potassium iodide in acetone solution for two hours gave *2-hydroxy-5-bromophenyl β-2'-methoxy-5'-bromostyryl ketone (XV)*. It crystallised from acetic acid in yellow needles, m.p. 156–57°. Found: Br, 38·6,  $C_{18}H_{12}O_3$  Br<sub>2</sub> requires Br, 38·8 per cent.

The ketone (XIV) under similar conditions gave ketone (V) and ketone (XIII) gave the ketone (IX).

#### *Action of potassium hydroxide*

The ketone (XI) (2 g.) was dissolved in acetone (500 c.c.), 10 per cent. solution of caustic potash (20 c.c.) was added to it and the mixture boiled under reflux for about five minutes. The solid obtained on cooling was washed with water and finally crystallised from alcohol in yellow needles, m.p. 161–62°. It gave red colour with sulphuric acid. Found: Br, 24·6,  $C_{16}H_{11}O_3$ Br requires Br, 24·2 per cent. It should be *2'-methoxy-5'-bromobenzylidene coumaranone (XVI)*.

Ketone (XII) under similar conditions gave *5-bromo-2'-methoxy-5'-bromobenzylidene coumaranone (XVII)*. It crystallised from acetic acid in yellow needles, m.p. 173–74°. It gave red colour with sulphuric acid. Found: Br, 39·2,  $C_{18}H_{16}O_3$  Br<sub>2</sub> requires Br, 39·02 per cent.

Ketone (XIV) under similar condition gave *5:7 dibromo-6-hydroxy-2'-methoxy-5'-bromobenzylidene coumaranone (XVIII)*. It crystallised from a mixture of acetic acid and nitrobenzene in yellow needles, m.p. 298–99°. Found: Br, 47·2;  $C_{18}H_9O_4$ Br<sub>3</sub> requires Br, 47·5 per cent. It gave red colour with sulphuric acid.

TABLE II

Name of the Ketone	Vol. of chloroform	Amount of bromine solution	No. from Table I and quantity of ketone used	Temp. of reaction and time	Colour and shape of crystal	Solvent	m.p.	Found %	Formula requires %
2-Hydroxyphenyl $\alpha$ - $\beta$ -dibromo- $\beta$ -2-methoxyphenyl ethyl ketone (X)	25 c.c.	35 c.c.	(I), 5 g.	10-15°; 1 hr.	Yellow plates	Chloroform and petroleum ether	162-63°	Br, 38.9	C <sub>16</sub> H <sub>14</sub> O <sub>3</sub> Br <sub>2</sub> requires Br, 38.7
2-Hydroxyphenyl $\alpha$ - $\beta$ -dibromo- $\beta$ -2-methoxy-5-bromophenyl ethyl ketone (XI)	(i) 25 c.c. (ii) 10 c.c.	70 c.c. 12 c.c.	(I), 5 g. (II), 2 g.	Room Temp. 4 hrs. 10°, 1 hr.	Yellow needles do	Acetic acid and nitrobenzene do	178-79°	Br, 48.8	C <sub>16</sub> H <sub>13</sub> O <sub>3</sub> Br <sub>3</sub> requires Br, 48.7
2-Hydroxy-5-bromophenyl- $\alpha$ - $\beta$ -dibromo- $\beta$ -2'-methoxy-5'-bromophenyl ethyl ketone (XII)*	10 c.c.	2 g. (liquid bromine)	(II), 1 g.	Boiled for ½ hr. and 1½ at room temp. for 24 hrs.	Yellow plates	do	225-26°	Br, 55.9	C <sub>16</sub> H <sub>12</sub> O <sub>3</sub> Br <sub>4</sub> requires Br, 55.9
2-Hydroxy-4-methoxy-5-bromophenyl $\alpha$ - $\beta$ -dibromo- $\beta$ -2'-methoxy-5'-bromophenyl ethyl ketone (XIII)†	10 c.c.	14 c.c.	(IX), 1 g.	Room temp. 24 hr. after boiling for 1 hr.	Small yellow plate	Acetic acid	208-09°	Br, 53.3	C <sub>17</sub> H <sub>14</sub> O <sub>4</sub> Br <sub>4</sub> requires Br, 53.2
2,4-Dihydroxy-3,5-di-bromophenyl $\alpha$ - $\beta$ -dibromo- $\beta$ -2'-methoxy-5'-bromophenyl ethyl ketone (XIV)	..	Liquid bromine 36 g.	(III), 10 g.	Room temp. short time	Yellow plates	Acetic acid and nitrobenzene	219-20°	Br, 59.6	C <sub>16</sub> H <sub>11</sub> O <sub>4</sub> Br <sub>5</sub> requires Br, 59.98

(\* This was also obtained from (I) by using a large excess of chloroform solution of bromine at room temperature.

(†) This was also obtained from (VD), (VII) & (VIII) by bromination in chloroform solutions.

Ketone (XIII) under similar conditions gave *5-bromo-6-methoxy-2'-methoxy-5'-bromo-benzylidene coumaranone (XIX)*. It crystallised in yellow needles from acetic acid, m.p. 258–59°. Found: Br, 36.7;  $C_{17}H_{12}O_4Br_2$  requires Br, 36.4 per cent. It gave red colour with sulphuric acid.

#### *Action of sodium alkoxide*

*2-Hydroxy-5-bromo-phenyl- $\beta$ -ethoxy- $\beta$ -2'-methoxy-5'-bromo-styryl ketone (XX)*.—The ketone (XII) was boiled with metallic sodium and ethyl alcohol for about three hours and the solid obtained on cooling crystallised from acetic acid in yellow needles, m.p. 160–61°. Found: Br, 35.1;  $C_{18}H_{16}O_4Br_2$  requires Br, 35.1 per cent.

*2-Hydroxy-5-bromo-phenyl- $\beta$ -methoxy- $\beta$ -2'-methoxy-5'-bromostyryl ketone (XXI)*, was obtained from ketone (XII) when methyl alcohol was used in place of ethyl alcohol with metallic sodium, m.p. 174–75°. Found: Br, 36.5;  $C_{17}H_{14}O_4Br_2$  requires Br, 36.2 per cent.

When, however, ketones (XI), (XIII) and (XIV) were treated with sodium ethoxide coumaranones (XVI), (XIX) and (XVIII) respectively.

#### *Action of pyridine*

*2-Hydroxyphenyl  $\alpha$ -bromo- $\beta$ -2'-methoxy-5'-bromo-styryl ketone (XXII)*; The ketone (XI) (1 g.) was boiled with pyridine (5 c.c.) for about five minutes and then diluted with excess of alcohol. The solid separated was washed with hydrochloric acid and finally crystallised from alcohol, in yellow needles, m.p. 134–35°. Found: Br, 39.2;  $C_{16}H_{12}O_3Br_2$  requires 38.8 per cent.

*2-Hydroxy-5-bromo-phenyl  $\alpha$ -bromo- $\beta$ -2'-methoxy-5'-bromostyryl-ketone (XXIII)* was obtained from ketone (XII) by treatment with pyridine and working up as above. It crystallised from acetic acid in yellow needles, m.p. 165–66°. Found: Br, 48.4;  $C_{16}H_{11}O_3Br_3$  requires Br, 48.9 per cent.

Ketone (XIII) under similar conditions gave *2-hydroxy-4-methoxy-5-bromo- $\alpha$ -bromo- $\beta$ -2'-methoxy-5'-bromostyryl ketone (XXIV)* of m.p. 253–54°. Found: Br, 45.9;  $C_{17}H_{13}O_4Br_3$  requires Br, 46.1 per cent.

Ketone (XIV), however, under similar conditions gave the coumaranone (XVIII) described before.

#### *Action of potassium cyanide*

*2'-Methoxy-5'-bromo-flavone (XXV)*.—Ketone (XI) (2 g.) *n*-propyl alcohol (60 c.c.) and potassium cyanide (2 g. in 100 c.c. water) were boiled under reflux for about forty-five minutes. The product obtained after the removal of the solvent crystallised from alcohol in white needles, m.p. 162–63°. It

gave yellow coloration with sulphuric acid. (Found: Br, 24.5;  $C_{16}H_{11}O_3Br$ , requires Br, 24.2 per cent.)

6-Bromo-2'-methoxy-5'-bromo-flavone (XXVI) was obtained from ketone (XII) by the interaction with potassium cyanide as above. It also gave yellow coloration with sulphuric acid. It crystallised from acetic acid in white needles, m.p. 173-74°. Found: Br, 39.2;  $C_{16}H_{10}O_3Br_2$ , requires Br, 39.02 per cent.

6-Bromo-7-methoxy-2'-methoxy-5'-bromo-flavone (XXVII) was similarly obtained from ketone (XIII), m.p. 260-61°. Found: Br, 36.7;  $C_{17}H_{12}O_4Br_2$ , requires Br, 36.4 per cent.

Ketone (XIV), however, when similarly treated gave the coumaranone (XVIII) already described.

One of the authors (H. P. V.) has to thank late Dr. N. R. Nadkarni for suggesting the problem.

## REFERENCES

1. Sorge .. *Ber.*, 1902, 35, 1069.
2. Dodwadmath and Wheeler .. *Proc. Ind. Acad. Sc.*, 1935, 2 A, 438.
3. Barne and Payton .. *J. Am. C. S.*, 1936, 1300.
4. Nadkarni, Warrior and Wheeler .. *Soc.*, 1937, 1798.
5. Cullinane and Phillipott .. *Ibid.*, 1929, 1761.
6. Köhler and Addinall .. *J. Am. C. S.*, 1930, 3728.
7. Price and Bogert .. *Ibid.*, 1934, 2442.
8. Bhagwat and Wheeler .. *Soc.*, 1939, 94.
9. Rao and Wheeler .. *Ibid.*, 1939, 1004.
10. Hutchins and Wheeler .. *Ibid.*, 1939, 91.