[CONTRIBUTION FROM RANADE INSTITUTE, DEPARTMENT OF CHEMISTRY, UNIVERSITY OF POONA]

SYNTHESIS OF DIHYDROFLAVONOLS AND FLAVONOLS

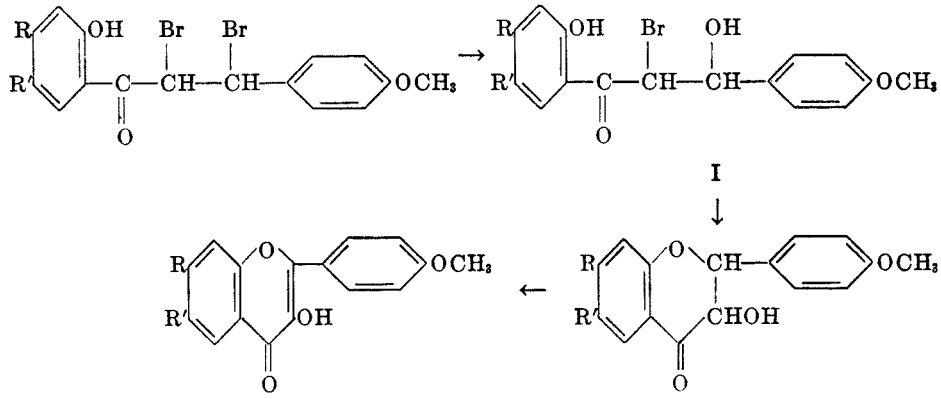
M. G. MARATHEY

Received October 8, 1954

Dihydroflavonols (flavonolones) are 3-hydroxy flavanones and are found to occur in nature, *e.g.* Fustin in the young fustic and the yellow cedar, Ampelopsin in the *Ampelopsio melioefolia*, etc. From the point of view of biogenesis dihydroflavonols seem to occupy an important place in the evolution of anthoxanthins.

A number of methods have been evolved for the synthesis of dihydroflavonols: (a) from an *o*-hydroxy chalkone or flavanone by the action of alkaline hydrogen peroxide [Murakami (1) 1935], (b) by converting a chalkone dibromide into its diacetate and further cyclization with hydrochloric acid [Oyamada (2) 1939], (c) by the action of lead tetraacetate on flavonones and subsequent deacetylation by HCl gas in a nitrogen atmosphere, [Oyamada (3) 1943], and (d) recently by reduction of flavonols to dihydroflavonols with sodium hydrosulphide as a reducing agent [Geissman (4) 1952].

Dihydroflavonols have now been synthesized from *o*-hydroxy- or *o*-acetoxychalkone dibromides of the type RCOCHBrCHBrR′, where R′ contains a methoxy or benzyloxy group in the *para* position, by the action of aqueous acetone and sodium carbonate. Formation of a dihydroflavonol was proposed to take place through a β-hydroxy derivative formed by the action of water on the β-bromine atom [Marathey (5) 1952; Marathey (6) 1953]. These β-hydroxy derivatives have been isolated in a few cases and the postulation made in the earlier work has been found to be correct [Marathey (7) 1954]. Thus the reaction could be represented as follows:



I R = −H, R′ = −CH_3
II R = −CH_3, R′ = −H.

In determining the scope and limitations of this reaction, it was suggested that the mechanism of the formation of a flavonol is parallel to the mechanism of the Alger and Flynn (8) (1934) oxidation of *o*-hydroxychalkones by alkaline hy-

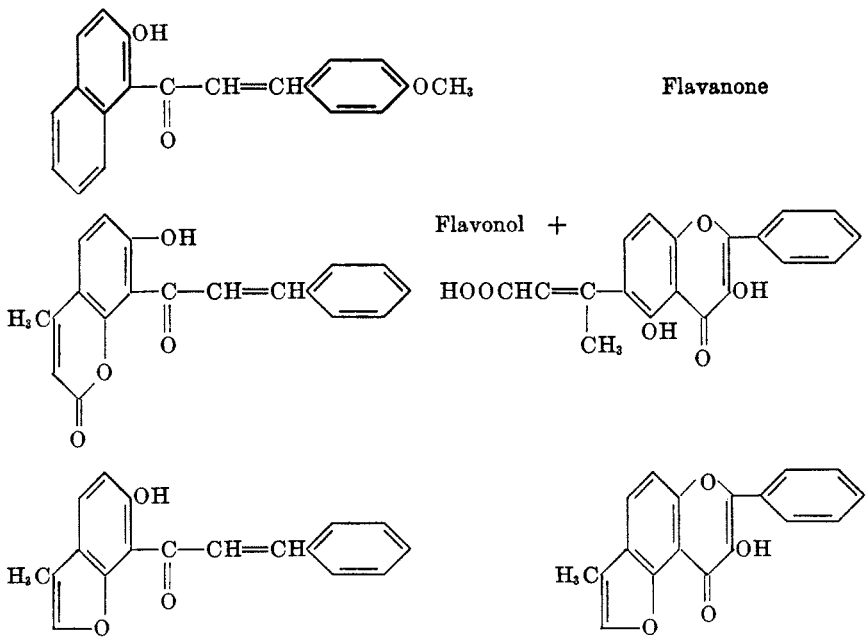
drogen peroxide [Marathey (9) 1953] and it has also been found out that a substitution of a methoxy group in 6′-position of a chalkone alters the course of the reaction resulting in the formation of benzalcoumaranones.

The present work deals with determining the effect of benzene ring substitution in the 5′:6′-position of an *o*-hydroxy- or *o*-acetoxy-chalkone.

When 1-acetyl-2-naphthol (III) was condensed with anisaldehyde, a mixture of 2′-hydroxy-5′:6′-benzo-4-methoxychalkone (IV), m.p. 120° and 4′-methoxy-5:6-benzoflavanone (V), m.p. 143° was obtained. The chalkone (IV) gave its acetate, m.p. 112° (VI) which when brominated with one mole of bromine gave 2′-acetoxy-5′:6′-benzo-4-methoxychalkone dibromide (VII), m.p. 154°. The flavanone (V) on bromination gave 4′-methoxy-3-bromo-5:6-benzoflavanone (VIII), m.p. 120°. Both VII and VIII on treatment with cold alcoholic alkali gave 4′-methoxy-5:6-benzoflavone (IX), m.p. 162°. On boiling with ethyl alcohol VII gave 2-acetoxy-1-naphthyl α-bromo-β-ethoxy-β-*p*-methoxyphenylethyl ketone (X), m.p. 140°, which when treated with alcoholic alkali gave 4′-methoxy-4:5-benzobenzylidene coumaranone (XI) m.p. 164°, which could also be obtained from VII by the treatment with hot alcoholic alkali.

Then the dibromide (VII), was treated with aqueous acetone and 2-acetoxy-1-naphthyl α-bromo-β-hydroxy-β-*p*-methoxyphenylethyl ketone (XII), m.p. 167°, was obtained. The β-hydroxy-derivative (XII), was found to be more stable than I and II and remained unchanged with 10% sodium carbonate or sodium acetate in acetone. With alkali also it did not give the corresponding flavonol and further work is in progress.

As a flavonol could not be obtained through the β-hydroxy-derivative (XII),



the chalkone (IV) was subjected to alkaline hydrogen peroxide oxidation. In this attempt also no flavonol could be obtained and the major part of the reaction was isomerization of the chalkone (IV) to the flavanone (V) which also remained unchanged when treated separately with alkaline hydrogen peroxide.

It appears that the effect of a 5′:6′-benzo substitution in an *o*-hydroxychalkone or a chalkone dibromide is to hinder the formation of a flavonol, similar to a —OCH_3 substitution in 6′-position where benzalcoumaranone is the product of the reaction. However, with an α-pyrono substitution in 5′:6′-position, some flavonol is obtained along with the corresponding *trans*-β-methyl-cinnamic acid derivative, while with a 5′:6′-furano substitution the hinderance is almost negligible and the reaction proceeds to the formation of a flavonol derivative in the usual way (Paper under publication). Thus, the hinderance produced by a 5′:6′-substitution in a chalkone decreases in the following order (a) 5′:6′-benzo-, (b) α-pyrono-, and (c) -furano.

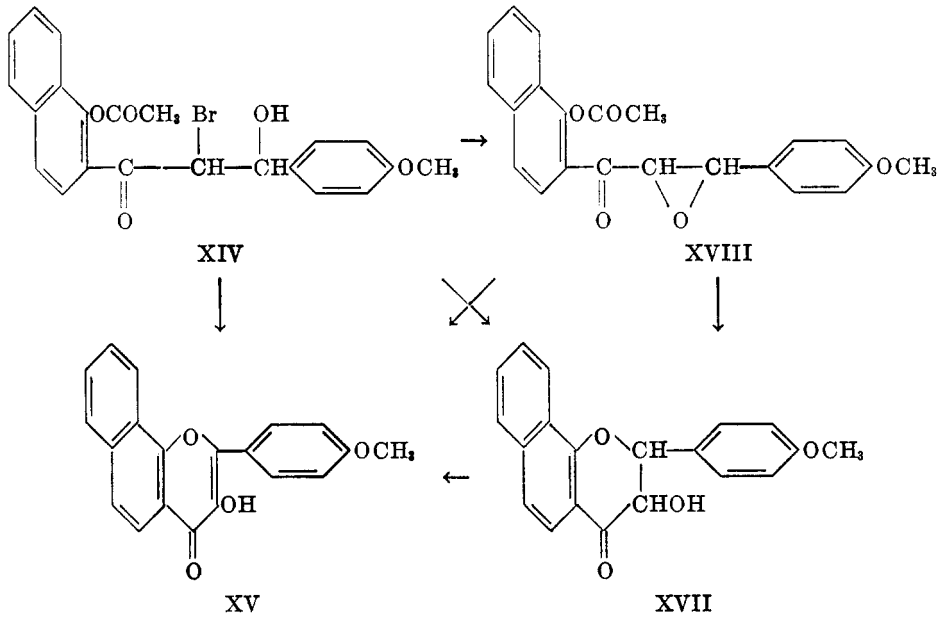
It may be mentioned here that in studying the effect of substitutions on the Alger and Flynn oxidation of chalkones Geissman (10) (1948) has shown that a 6′-methoxy substitution in an *o*-hydroxy chalkone alters the course of the reaction and benzal coumaranones are the main product. Geissman suggests that there is an inhibition of resonance between the anionic oxygen atom and the *ortho* carbonyl group with a result in the increase of the acidity at the α-carbon atom and further assumes that the chalkone oxide, which however could not be isolated, is a common intermediate in the formation of a flavonol and a benzal coumaranone. Anand (11) and others (1949) have shown that in spite of the presence of a methoxy group in the 6′-position of a chalkone if there is a free hydroxy group in the 4-position, the reaction runs smoothly to give a flavonol. They suggest that the assumption of the chalkone oxide structure as a common intermediate (*cf.* Geissman) is not essential and they have explained the formation of a flavonol and a benzal coumaranone with a glycol derivative as the first intermediate step.

However, the results that have been mentioned above, clearly show the change in the course of the reaction, in spite of a methoxy substitution or even without any substitution in the side phenyl ring. It appears that the formation of a flavonol or a benzal coumaranone from an *o*-hydroxy chalkone depends not only on the resonance between the anionic oxygen atom and the *ortho* carboxyl group or on the resonance between the anionic oxygen atom and the hydroxyl group in the side phenyl ring but also on the nature of the substitution in the 6′ or 5′:6′-positions in the *o*-hydroxy chalkones.

Now, when 2′-acetoxy-3′:4′-benzo-4-methoxychalkone dibromide (XIII), m.p. 137°, [Keller (12) 1899] was heated with aqueous acetone, 2-hydroxy-1-naphthyl α-bromo-β-hydroxy-β-*p*-methoxyphenylethyl ketone (XIV), m.p. 130°, was obtained, which when treated with alkali gave 4′-methoxy-7:8-benzoflavonol (XV), m.p. 249°, [Kostanecki (13) 1904] along with 2′-hydroxy-3′:4′-benzo-4-methoxychalkone (XVI), m.p. 158°. The flavonol (XV) was also obtained by subjecting the chalkone (XVI) to alkaline hydrogen peroxide oxidation. 4′-Methoxy-7:8-benzodihydroflavonol (XVII), m.p. 207°, was obtained when

the β-hydroxy derivative (XIV) was treated with alkaline hydrogen peroxide under mild conditions. The dihydroflavonol (XVII) in turn gave the flavonol (XV) on treatment with alcoholic alkali.

The β-hydroxy-derivative (XIV), when subjected to the action of sodium acetate in acetone, gave another intermediate compound (XVIII), m.p. 125°, which has been assigned the constitution 2′-acetoxy-3′:4′-benzo-4-methoxy-chalkone oxide [Marathey (14) 1954]. With the isolation of a chalkone oxide of the type mentioned above it can now be stated that the formation of a flavonol from a chalkone dibromide is a stepwise reaction and can be represented as follows:



After having seen the effect of various substitutions in the different positions in the benzene ring, attention was directed to the effect of a carboxylic group in the benzene ring on the formation of a dihydroflavonol.

2-Hydroxy-acetophenone-5-carboxylic acid (XIX) was condensed with anisaldehyde in the presence of sodium hydroxide. 2-Hydroxy-4-methoxychalkone-5′-carboxylic acid (XX), m.p. 234°, was obtained which when brominated with bromine in acetic acid gave 2′-hydroxy-4-methoxychalkone-5′-carboxylic acid dibromide (XXI), m.p. 163°. The dibromide (XXI), when heated with aqueous acetone gave 2-hydroxy-5-carboxylphenyl α-bromo-β-hydroxy-β-*p*-methoxyphenylethyl ketone (XXII), m.p. 167°, which when treated with 10% sodium carbonate gave 4′-methoxy-6-carboxyl dihydroflavonol (XXIII), m.p. 340°, which was also obtained when the chalkone (XX) was treated with alkaline hydrogen peroxide under mild conditions. The β-hydroxy derivative (XXII), when treated with alkali gave 4′-methoxy-6-carboxyl flavonol (XXIV), m.p. 335°, along with the chalkone (XX). The flavonol (XXIV) was also obtained

from the chalkone (XX) by alkaline hydrogen peroxide oxidation and from the dihydroflavonol (XXIII) by treatment with alkali.

The dibromide (XXI), when heated with alcohol gave 2-hydroxy-5-carboxylphenyl α-bromo-β-ethoxy-β-*p*-methoxyphenylethyl ketone (XXV), m.p. 165°, which when treated with alkali gave 4′-methoxy-5-carboxy-benzylidene coumaranone (XXVI), m.p. 332°. 4′-Methoxy-6-carboxylflavone (XXVII), m.p. 342°, was obtained when the chalkone dibromide (XXI) was treated with cold alcoholic alkali.

EXPERIMENTAL

Preparation of α-bromo-β-hydroxy derivatives by the action of aqueous acetone on the corresponding chalkone dibromides. The *o*-hydroxychalkones were refluxed with aqueous acetone (4:6, H_2O:Me_2CO) till a clear solution was obtained (5 to 10 minutes). The reaction mixture was diluted with water and the product obtained was filtered and washed with water.

2-Hydroxy-5-methylphenyl α-bromo-β-hydroxy-β-(p-methoxyphenyl)ethyl ketone (I). Yield, 0.42 g. from 1 g. On treatment with 10% Na_2CO_3, it gives 4′-methoxy-6-methyldihydroflavonol, m.p. 160°, and with sodium hydroxide gives 4′-methoxy-6-methylflavonol, m.p. 192°, along with some 4′-methoxy-6-methylflavanone.

2-Hydroxy-4-methylphenyl α-bromo-β-hydroxy-β-(p-methoxy-phenyl)ethyl ketone (II). Yield, 0.2 g. from 0.59 g. It gives the 4′-methoxy-7-methyldihydroflavonol and 4′-methoxy-7-methylflavonol on treatment with 10% Na_2CO_3 and sodium hydroxide, respectively.

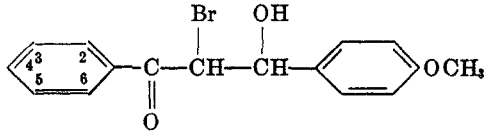
2-Acetoxy-5:6-benzophenyl α-bromo-β-hydroxy-β-p-methoxyphenylethyl ketone (XII). Yield, 0.3 g. from 0.5 g. A mixture melting point with the original chalkone bromide (VII), m.p. 154°, shows a depression (130–132°). It remains almost unchanged on treatment with (a) aqueous acetone and sodium acetate and (b) 10% Na_2CO_3 in acetone.

2-Acetoxy-3:4-benzo-phenyl-α-bromo-β-hydroxy-β-p-methoxyphenyl ketone (XIV). Yield, 0.6 g. from 1 g. Mixture melting point with the original chalkone dibromide (XIII), m.p. 137°, shows considerable depression. It is susceptible to the action of heat and alkali.

Preparation of chalkones. The following chalkones have been synthesized by condensing the corresponding *o*-hydroxyacetophenones with anisaldehyde in the presence of alcohol and 10 *N* NaOH. The reaction mixtures were brought to the boiling point, allowed to stand

TABLE I

BROMOHYDRINS



Text Ref.	Sbst.	m.p., °C.	Anal (Br)		FeCl₃	Recryst.
			Calc'd	Found		
I	2-Hydroxy-5-methyl-	145	21.9	22.2	Brown	HOAc and EtOH
II	2-Hydroxy-4-methyl-	120	21.9	21.7	Brown	EtOH
XII	2-Acetoxy-5,6-benzo-	164	18.1	17.9	—	EtOH
XIV	2-Acetoxy-3,4-benzo-	130	18.1	18.2	—	EtOH

at room temperature for 24 hours, and acidified with dilute HCl (1:1); the products obtained were filtered off.

2'-Hydroxy-5':6'-benzo-4-methoxychalkone (IV). 1-Acetyl-2-naphthol (12 g.) was dissolved in alcohol (30 ml.) and aldehyde (9 g.) and alkali (20 ml.) were added to it. The product obtained was crystallized from a mixture of alcohol and acetic acid (m.p. 135–140°, 15 g.) and was further fractionally crystallized from alcohol. The chalkone, m.p. 120°, 8.5 g.; the flavanone (V), m.p. 143°, 6 g., reddish-yellow needles.

IV gives a brown coloration with alcoholic ferric chloride and is amost insoluble in dilute alkali. On treatment with alkaline hydrogen peroxide, it gives the flavanone (V), m.p. 143°.

Anal. Calc'd for $C_{20}H_{16}O_3$: C, 79.1; H, 5.3.
Found: C, 78.9; H, 5.4.

The flavanone (V), m.p. 143°, is insoluble in dilute alkali and does not give a coloration with alcoholic ferric chloride. It forms glistening plates. When treated with alkaline H_2O_2, it remains unchanged.

Anal. Cald'd for $C_{20}H_{16}O_3$: C, 79.1; H, 5.3.
Found: C, 78.8; H, 5.3.

2'-Hydroxy-4-methoxychalkone-5'-carboxylic acid (XX). 3-Acetyl-4-hydroxybenzoic acid (9 g.) was dissolved in alcohol (30 ml.) and anisaldehyde (7 g.) and alkali (18 ml.) were added to it. The solid was crystallized from acetic acid, m.p. 234°, as yellow, soft, needles. Yield, 7.5 g.

It gives a red coloration with alcoholic ferric chloride and is soluble in dilute alkali.

Anal. Calc'd for $C_{17}H_{14}O_5$: C, 68.5; H, 4.7.
Found: C, 68.3; H, 4.9.

Acetate of 2'-hydroxy-5':6'-benzo-4-methoxychalkone (VI). The chalkone (IV), m.p. 120°, (3 g.) was refluxed with acetic anhydride (3.5 ml.) with traces of fused sodium acetate for half an hour. The reaction mixture was poured into water, filtered, and crystallized from alcohol, m.p. 112°, as white, soft crystals. Yield, 2.8 g.

It does not give a coloration with alcoholic ferric chloride and regenerates the original chalkone with alcoholic alkali.

Anal. Calc'd for $C_{22}H_{18}O_4$: C, 76.3; H, 5.2.
Found: C, 76.1; H, 5.4.

Preparation of o-acetoxychalkone dibromides. The *o*-acetoxychalkones were dissolved in glacial acetic acid and bromine in acetic acid (25% w/v., 1 mole) was added to the solution. The precipitate obtained was filtered off and weighed.

2'-Acetoxy-5':6'-benzo-4-methoxychalkone dibromide (VII). The chalkone acetate, (2.8 g.) in acetic acid (5 ml.) and bromine in acetic acid (5.12 ml.) were added together. The mixture was filtered after 15 minutes to give white, powdery crystals, m.p. 154°. Yield, 2.8 g.

The dibromide does not give a coloration with alcoholic ferric chloride and is insoluble in cold dilute sodium hydroxide. It is susceptible to the action of alcohol, water and heat.

Anal. Calc'd for $C_{22}H_{18}Br_2O_4$: Br, 31.6. Found: Br, 31.9.

2'-Acetoxy-3':4'-benzo-4-methoxychalkone dibromide (XIII). 2'-Acetoxy-3'-4'-benzo-4-methoxychalkone, (5.6 g.) in acetic acid (10 ml.) and bromine in acetic acid (10.24 ml.) were added together. The precipitate obtained was filtered after half an hour and washed with alcohol, m.p. 135°. Yield, 5 g.

2'-Hydroxy-4-methoxychalkone dibromide-5'-carboxylic acid (XXI). 2'-Hydroxy-4-methoxychalkone-5'-carboxylic acid (0.6 g.) in acetic acid (10 ml.) and bromine in acetic acid (1.28 ml.) were added together with constant stirring. The mixture was filtered after 3 hours and washed with alcohol, m.p. 163°; white, soft prismatic crystals, yield, 0.7 g.

The acid gives a red coloration with alcoholic ferric chloride and is susceptible to the action of heat, water, and alcohol.

Anal. Calc'd for $C_{17}H_{14}Br_2O_5$: Br, 34.9. Found: Br, 34.8.

4'-Methoxy-5:6-benzoflavone (IX). The dibromide (VII), m.p. 154° (0.5 g.), was suspended in alcohol (10 ml.) and 10 *N* sodium hydroxide (1 ml.) was added to it. The reaction mixture

turned red and a yellow solid precipitated. It was crystallized from a mixture of alcohol and acetic acid, m.p. 162°, 0.25 g. of yellow needles.

It does not give a color with alcoholic ferric chloride and is insoluble in cold dilute alkali. It gives a yellow coloration with conc'd H_2SO_4.

Anal. Calc'd for $C_{20}H_{14}O_3$: C, 79.5; H, 4.6.

Found: C, 79.3; H, 4.8.

4'-Methoxy-4:5-benzobenzylidene coumaranone (XI). The dibromide, m.p. 154° (0.5 g.), was dissolved in hot alcohol (10 ml.) and 10 *N* NaOH (2 ml.) was added to it. The reaction mixture turned red and a yellow solid separated as in the previous experiment. It was crystallized from a mixture of alcohol and acetic acid, m.p. 164°, as reddish-yellow needles. Yield, 0.2 g.

It does not give a color with alcoholic ferric chloride and is insoluble in cold dilute alkali. It gives a red coloration with conc'd H_2SO_4. The mixture melting point with the flavone, m.p. 162°, shows considerable depression (148–152°).

Anal. Calc'd for $C_{20}H_{14}O_3$: C, 79.5; H, 4.6.

Found: C, 79.2; H, 4.8.

The bromide, m.p. 154°, when heated with alcohol gave a gummy product (β-ethoxy) which could not be purified further but which gave the benzal coumaranone, m.p. 164°, on treatment with alkali.

2'-Acetoxy-3':4'-benzo-4-methoxychalkone oxide (XVIII). The β-hydroxy derivative, m.p. 130° (0.5 g.), was suspended in acetone and crystalline sodium acetate (0.5 g.) was added to it. The reaction mixture was brought to the boiling point and the substance dissolved. It was diluted with water after ten minutes, filtered, and crystallized from alcohol, m.p. 125°, 0.25 g. of white, soft crystals.

It does not give a coloration with alcoholic ferric chloride and it is susceptible to the action of heat and alkali. It is free from bromine.

Anal. Calc'd for $C_{22}H_{18}O_5$: C, 72.9; H, 5.0.

Found: C, 72.7; H, 5.1.

4'-Methoxy-7:8-benzodihydroflavonol (XVII). The chalkone oxide, m.p. 125° (0.1 g.) was heated with acetone (10 ml.) and 10% Na_2CO_3 (5 ml.) for five minutes. The reaction mixture was diluted with water, filtered and crystallized from acetic acid, m.p. 207°, as yellowish needles.

It does not give a coloration with alcoholic ferric chloride. It is susceptible to the action of alkali.

Anal. Calc'd for $C_{20}H_{16}O_4$: C, 75.0; H, 5.0.

Found: C, 74.8; H, 5.3.

The dihydroflavonol, m.p. 207°, was also obtained when (a) the chalkone dibromide, m.p. 130°, was heated with aqueous acetone and then treated with 10% Na_2CO_3 and when (b) the β-hydroxy-derivative, m.p. 130°, was heated for a short time with 10% Na_2CO_3.

4'-Methoxy-7:8-benzoflavonol (XV). The chalkone oxide, m.p. 125° (0.1 g.), was dissolved in alcohol (5 ml.) and 10 *N* NaOH (0.5 ml.) was added to it. The reaction mixture was diluted, acidified with dilute hydrochloric acid (1:1, 2 ml.), and filtered after one hour. The flavonol, m.p. 247°, was crystallized from acetic acid.

Anal. Calc'd for $C_{20}H_{14}O_4$: C, 75.5; H, 4.4.

Found: C, 75.4; H, 4.7.

Some 2'-hydroxy-3':4'-benzo-4-methoxychalkone, m.p. 158°, was also obtained from the mother liquor of crystallization of the flavonol.

4'-Methoxy-7:8-benzoflavonol. From 2'-hydroxy-3':4'-benzo-4-methoxychalkone. The chalkone, m.p. 158° (0.9 g.), was suspended in hot alcohol (25 ml.) and hydrogen peroxide (1.5 ml., 100 vol.) and 2 *N* NaOH (3 ml.) were added to it. The reaction mixture was again brought to the boiling point when a vigorous effervescence was observed and the color of the reaction mixture changed from red to yellow. It was acidified, filtered, and the solid was crystallized from acetic acid after one hour, m.p. 247°.

The flavonol, m.p. 247°, was also obtained when (a) the chalkone dibromide, m.p. 137°,

was heated with aqueous acetone and treated with alkali and when (b) the β-hydroxy derivative, m.p. 130°, was treated with alkali. In this case 2′-hydroxy-3′:4′-benzo-4-methoxychalkone was also obtained from the mother liquor of crystallization of the flavonol.

4′-Methoxydihydroflavonol-6-carboxylic acid (XXIII). The β-hydroxy derivative, m.p. 167° (0.5 g.), was warmed with 10% Na_2CO_3 (5 ml.) and the reaction mixture was allowed to stand for 1 hour when it was diluted, acidified with dilute hydrochloric acid, filtered, and crystallized from acetic acid, m.p. 338–340°, as yellow needles.

It does not give a coloration with alcoholic ferric chloride, and is free from bromine.

Anal. Calc'd for $C_{17}H_{14}O_6$: C, 65.0; H, 4.6.

Found: C, 64.8; H, 4.9.

4′-Methoxydihydroflavonol-6-carboxylic acid. From 2′-hydroxy-4-methoxychalkone-6-carboxylic acid. The chalkone, m.p. 234° (0.3 g.), was suspended in alcohol (20 ml.) and hydrogen peroxide (0.1 ml. 100 vol., 1 mole) and 2 *N* NaOH (0.5 ml., 1 mole) were added to it. The reaction mixture was allowed to stand for 24 hours at room temperature and then acidified with dilute hydrochloric acid (1:1), filtered, and the solid was crystallized from acetic acid. The dihydroflavonol, m.p. 340°, resulted.

4′-Methoxyflavonol-6-carboxylic acid (XXIV). The β-hydroxy derivative, m.p. 167° (0.5 g.), was dissolved in hot alcohol (10 ml.) and 10 *N* NaOH (1 ml.) was added to it. The reaction mixture was allowed to stand for 4 hours and then acidified with hydrochloric acid, filtered, and fractionally crystallized from acetic acid. The flavonol, m.p. 335°, was obtained in short yellow needles along with the corresponding chalkone, m.p. 234°.

It gives a reddish-brown coloration with alcoholic ferric chloride and is soluble in dilute alkali. It is free from bromine.

Anal. Calc'd for $C_{17}H_{21}O_6$: C, 65.4; H, 3.9.

Found: C, 65.1; H, 4.1.

4′-Methoxyflavonol-6-carboxylic acid. From 2′-hydroxy-4-methoxychalkone-6-carboxylic acid. The chalkone, m.p. 234° (0.6 g.), was suspended in alcohol (20 ml.) and hydrogen peroxide (1 ml., 100 vol., 5 moles) and 2 *N* NaOH (2 ml.) were added to it. The reaction mixture was brought to the boiling point when it turned yellow. It was allowed to stand for 1 hour and was acidified with hydrochloric acid, filtered, and the solid was crystallized from acetic acid.

The flavonol, m.p. 333°, was also obtained when (a) the dihydroflavonol, m.p. 340°, was treated with alkali and when (b) the chalkone dibromide, m.p. 163°, was treated with aqueous acetone and alkali.

4′-Methoxyflavone-6-carboxylic acid (XXVII). The chalkone dibromide, m.p. 163° (0.5 g.), was suspended in alcohol (10 ml.) and 5 *N* NaOH (5 ml.) was added to it. The reaction mixture was acidified after 4 hours, filtered and the solid was crystallized from acetic acid. Yellowish, wooly needles, m.p. 340–342°. Yield 0.2 g.

It is free from bromine and does not give coloration with ferric chloride in alcohol. It is soluble in dilute alkali.

Anal. Calc'd for $C_{17}H_{12}O_6$: C, 68.9; H, 4.1; Neut. Equiv., 296.

Found: C, 68.6; H, 4.2; Neut. Equiv., 291.

2-Hydroxy-5-carboxyphenyl α-bromo-β-ethoxy-β-p-methoxyphenylethyl ketone (XXV). The chalkone dibromide, m.p. 163° (0.5 g.), was refluxed with alcohol (10 ml.) for 15 minutes and the reaction mixture was cooled. A precipitate was obtained which was crystallized from alcohol; m.p. 165°, soft, white crystals.

It gives a red coloration with alcoholic ferric chloride and is susceptible to the action of alkali. A mixture melting point of this with the original chalkone dibromide, m.p. 163°, shows considerable depression.

Anal. Calc'd for $C_{19}H_{19}BrO_6$: Br, 18.9. Found: Br, 18.6.

4′-Methoxybenzylidenecoumaranone-5-carboxylic acid (XXVI).

The β-ethoxy derivative, m.p. 165° (0.5 g.), was dissolved in hot alcohol (10 ml.) and 5 *N* NaOH (5 ml.) was added to it. The reaction mixture was acidified after two hours; the solid was filtered and crystallized from acetic acid; m.p. 332–334°, small yellow needles.

This acid is four times as soluble as the corresponding flavone, m.p. 342°. It does not give a coloration with alcoholic ferric chloride, it is free from bromine, and it is soluble in dilute alkali.

Anal. Calc'd for $C_{17}H_{12}O_5$: C, 68.9; H, 4.1; Neut. Equiv., 296.
Found: C, 68.8; H, 4.4; Neut. Equiv., 291.

SUMMARY

The effect of a 5′:6′-benzo substitution in an *o*-hydroxychalkone dibromide or *o*-hydroxychalkone has been found to hinder the formation of a dihydroflavonol and a flavonol by the action of aqueous acetone and alkali and alkaline hydrogen peroxide respectively. If however, the substitution is in 3′:4′-position both the corresponding chalkone dibromide and the chalkone give dihydroflavonol and flavonol. In addition it has also been found that the β-hydroxy derivative gives the corresponding chalkone oxide and the formation of a flavonol from a chalkone dibromide appears to proceed through the β-hydroxy derivative—an essential intermediate step, the chalkone oxide and the dihydroflavonol.

The presence of 5′-carboxylic group in an *o*-hydroxychalkone dibromide or an *o*-hydroxychalkone does not alter the course of the reactions and flavonols can be obtained in the usual way.

Acknowledgment. My thanks are due to Dr. S. K. Kulkarni Jatkar, Head of the Dept. of Chemistry, University of Poona, Poona-4, for his keen interest during the course of this work.

POONA-4, INDIA.

REFERENCES

(1) MURAKAMI AND IRIE, *Proc. Imp. Acad. (Tokyo)*, **11,** 229 (1935).
(2) OYAMADA, *Ann.*, **538,** 44 (1939).
(3) OYAMADA, *J. Chem. Soc. Japan*, **64,** 331, 335, 471 (1943).
(4) GEISSMAN AND LISCHNER, *J. Am. Chem. Soc.*, **74,** 3001 (1952).
(5) MARATHEY, *Science and Culture (India)*, **16,** 527 (1952).
(6) MARATHEY, *J. Univ. Poona*, **4,** 73 (1953).
(7) MARATHEY, *Science and Culture (India)*, **19,** 516 (1954).
(8) ALGER AND FLYNN, *Proc. Roy. Irish. Acad.*, **B42,** 1 (1934).
(9) MARATHEY, *J. Univ. Poona*, **4,** 83 (1953).
(10) GEISSMAN AND FUKUSHIMA, *J. Am. Chem. Soc.*, **70,** 1686 (1948).
(11) NITYANAND, IYER, AND VENKATRAMAN, *Proc. India Acad. Sci.*, **29A,** 203 (1949).
(12) KELLER AND KOSTANECKI, *Ber.*, **32,** 1035 (1899).
(13) KOSTANECKI, *Ber.*, **41,** 784 (1904).
(14) MARATHEY, *Science and Culture (India)*, **20,** 135 (1954).