The chalcones or phenyl styryl ketones are unsaturated ketones, containing the reactive keto-ethylenic group:

\[- \text{C} - \text{CH} = \text{CH} - \]

These compounds are also known as benzylidene acetophenones or benzalacetophenones, which were named 'Chalcones' by Kostanecki and Tambor(1). In American Chemical Abstracts they are also termed as 3-phenyl acrylophenones, while 2'-hydroxy chalcones are known as o-cinnamoyl phenols.

The chalcones are intermediate compounds useful for the synthesis of various heterocyclic compounds such as flavanones, flavones, flavonols, anthocyanins, benzalcoumaranones, phlobatannins as well as certain compounds like deoxybenzoins and hydantoins, which are of some therapeutic value.

Several of them are found to exist in nature in free state or in the form of glycosides. Polyhydroxy derivatives are found to occur as partially or completely methylated derivatives.

The chalcones have been found to be useful in proving the structures of natural products like hemlock tannin(2), cyanomaclurin(3), ploretin (4), eriodictyol and homoeriodictyol (5), naringenin and sakuranetin (6) etc.
In view of their great reactivity and their close relationship to flavanones, flavones, flavonols, and dihydroflavonols, chalcones have been investigated since long. There has been a considerable interest in their study as intermediates for substances of therapeutic importance (7, 8, 9). The deoxybenzoins derived from chalcones are found to be good anaesthetics, antispasmodics and mydriatics. Some chalcones and flavanones are found to exhibit vitamin P-like activity (10). Schraufstätter and Deutsch (11) and Calcinari (12) have also reported antibacterial properties of some chalcones. Krbechek (13) reported some dihydrochalcones to be about 2000 times sweeter than sucrose. Some chalcones have been suggested as remedy for cancer (14, 15). Misra and Tiwari (16) have reported 4-hydroxy-3-nitro-1-naphthyl chalcone derivatives as potential germicides. Misra and Kushwaha (17) have also reported phenanthryl and naphthyl chalcones as potential germicides. Vibhute (18) has reported antimicrobial activity of some halochalcones and flavones. Bradsher, Brown and Blue (19) prepared chalcones having antifungal activity.

Some flavanones and flavonols (20) are reported to have stabilizing effect on vitamin A.

Da Re Verlicchi and Setniker (21) reported that 3-methyl-6-diethylaminomethyl flavone is a highly active antispasmodic (about 14 times more active than papaverine).
NOMENCLATURE

The chalcones have been given different nomenclatures from time to time. In the numbering system used by Chemical Abstracts, the prime numbers are given to the phenyl ring nearer the carbonyl group.

\[ \text{Diagram I} \]

The British Chemical Abstracts and Journal of Chemical Society have followed the following numbering system:

\[ \text{Diagram II} \]

In this thesis the chalcones prepared have been numbered according to the system of Chemical Abstracts(I).
SYNTHETIC METHODS OF PREPARING CHALCONES:

A general method of preparing chalcones consists in condensing an appropriate ketone with an aldehyde in the presence of a suitable condensing agent. The condensation takes place with the elimination of a water molecule:

\[
\text{R} - \text{C} - \text{CH}_3 + \text{O} = \text{C} - \text{R} \xrightarrow{-\text{H}_2\text{O}} \text{R} - \text{C} - \text{CH} = \text{CH} - \text{R}
\]

Claisen and Claparede(22) were the earlier workers who condensed the aliphatic ketones with aromatic aldehydes. They first prepared a simple benzylideneacetone by heating benzaldehyde (1 mol) and acetone (1 mol) in the presence of acetic anhydride (2 mols) and zinc chloride, which was found to be identical with Engler and Leist's acetocinnamone(23).

\[
\text{CH}_3 - \text{C} - \text{CH}_3 + \text{C}_6\text{H}_5\text{CHO} \xrightarrow{\text{HCl}} \text{CH}_3 - \text{C} - \text{CH} = \text{CH} - \text{C}_6\text{H}_5
\]

They extended the above reaction to aromatic ketones and prepared benzylideneacetophenone by the condensation of acetophenone with benzaldehyde.

In this reaction they have used dry hydrochloric acid gas in place of zinc chloride as a condensing agent.

Baeyer and Becker(24) isolated an intermediate in a pure state during the condensation of p-nitrobenzaldehyde with acetone; the product could be converted into
The isolation of an intermediate was possible in this particular instance because of the nitro group which adds to the stability of such a compound. The above results clearly indicate that the reaction is an aldol type condensation.

**CONDENSING AGENTS**

(1) **Dry Hydrochloric Acid Gas**

In the synthesis of chalcones from aromatic ketones by condensation with aldehydes, dry hydrochloric acid gas has been used as a condensing agent in a suitable solvent like dry ethyl acetate at 0°C(22). This condensing agent does not succeed in all the cases. However, it has been extensively used by Russell and Todd(25) to prepare chalcones required in connection with synthetic preparations of compounds.
related to natural phlobatanins.

In order to avoid complications arising due to the presence of free hydroxy groups, they employed benzoylated ketones and aldehydes as the starting materials and obtained benzoyloxychalcones, which yielded the corresponding hydroxychalcones on debenzoylation. They synthesized butein (2',4',3,4-tetrahydroxychalcone) from resacetophenone dibenzoate and protocatechuic aldehyde-dibenzoate, to get tetrabenzoyl butein from which free butein was obtained on debenzoylation.

Lyle and Paradis (26), and Marathey (27) used methanolic solution of dry hydrochloric acid gas at 0°C. Sipos, Dobo and Czukor (28) also successfully used ethanolic solution saturated with dry hydrogen chloride and concluded that electron donating groups in the aldehyde favour condensation by hydrogen chloride and electron withdrawing substituents favour condensation by sodium hydroxide.

Tsukerman (29) also used this condensing agent in the preparation of chalcones containing a selenophene nucleus.

Cussac and Boucherle (30) reported chalcones derived from 3-acetylpyridine with different aldehydes using dilute (1:1) hydrochloric acid, while Hermes (31) used concentrated hydrochloric acid and condensed p-methacetoephonone with Vanillin. Recently Onoda and Tetsuko (32) used hydrochloric acid as condensing agent for preparation of chalcone.
(2) **Alkali**

The condensation by alkali is generally more affected in presence of an aqueous solution of a suitable concentration. This condensing agent has been extensively used by several investigators for the synthesis of chalcones (33-38).

The condensation of resacetophenone and gallacetophenone with benzaldehyde in presence of alkali was carried out by Ellison (39) and later on by Mahal, Rai and Venkatraman (40). Instead of the expected chalcones the corresponding flavanones were obtained. The condensation of aldehydes other than benzaldehyde did not succeed; but resacetophenone 4-benzyl ether readily gave chalcones with benzaldehyde, anisaldehyde, etc (41). Alkali has been successfully used as a condensing agent with resacetophenone and its ethers (42-48), 2-6 dihydroxyacetophenone and its monomethyl ether (49-51), galloyacetophenone (39,52,53), phloracetophenone (54-57) and quinacetophenone, its mono and dimethyl ethers (58-60). The chalcones from hydroxy and methoxy aldehydes and 3-acetylguaiaicol have been prepared by Smith and Paulson (61).

Schraufstätter and Deutsch (62) have synthesised several hydroxy, bromo and nitrochalcones using sodium or potassium hydroxide as a condensing agent. Several workers (63-70) have also used alkali in the preparation of nitro and amino chalcones.
Chalcones containing halogens have been prepared by several workers (71-75) using alkali as a condensing agent. Several workers (76-80) have successfully used alkali as a condensing agent in the preparation of iodochalcones. Fluorochalcones have been prepared from fluoroacetophenone (87, 88). Chen, Chen and Ueng (89) prepared chalcones from fluorobenzaldehydes using alkali as a condensing agent.

Chalcones containing cyano group have been prepared by Merchant, Mehta, and Desai (90). Chalcones containing nitro and bromo groups were prepared using alkali as a condensing agent (91-93). Ambekar, Dandegaonkar, Jolad and Rajgopal (94) used alkali as a condensing agent in the synthesis of 2'-hydroxy-4'-methoxychalcone. Devitt, Timoney and Vickars (95) have prepared the 2-heterocyclic substituted chromones and related chalcones, by the base catalysed condensation of 2'-hydroxy-acetophenones with heterocyclic aldehydes. Kushwaha, Dinkar and Lal (96) have prepared chalcones having heterocyclic nucleus using alkali.

Lespagnol, Lesieur and Ponce (97) prepared chalcones from 5-acetylsalicylic acid and 5-acetylsalicylamide. Dzurilla and Kristian (98) prepared chalcones from 3- and 4-isothiocyanatoacetophenones using sodium hydroxide.

Shah (99) has recorded various chalcones derived from 5-hydroxy-6-acetyl-4-methylcoumarin using 40-50% alkali. Chalcones containing pyrrole (100), thiophenone (101-103),
pyridine (104-106) and quinoline nucleii (107-109) have also been reported.

Base catalysed synthesis of chalcones containing ferrocene (110) and selenophene nucleii (111) have also been reported.

Recently Kyogoku Kazuaki (112) prepared isoprenyl chalcones using potassium hydroxide as condensing agent.

(3) Phosphorus Oxychloride

Vyas and Shah (113), and Raval and Shah (114) have used phosphorus oxychloride as a condensing agent. They condensed acetophenone with various aldehydes and obtained the corresponding chalcones.

They also condensed the monomethyl ether of quinacetophenone with benzaldehyde and anisaldehyde but instead of the expected chalcones the corresponding flavanones were obtained.

Kuroda, Matsukuma and Nakasmura (115) condensed acetophenones obtained from anisole and other polymethoxybenzenes with various methoxyaldehydes in presence of anhydrous aluminium chloride to get the chalcones. Similarly chalcones from thymolmethyl ether have been also described. Szell and Sipos (116) successfully condensed 2-hydroxy-5-nitroacetophenone with benzaldehyde in presence of anhydrous aluminium chloride.

Cheng, Pournari and Tirouflet (117) have used piperidine and synthesised chalcones from 2-hydroxy-5-(chloor, nitro;
acetyl amino and cyano) acetophenones with pyrrole-2-aldehyde. Jerzmanowaka and Podwinski (118) successfully used piperidine in the preparation of \( C \)-methylchalcones.

Breslow and Hauser (119) have used boron trifluoride as a condensing agent and obtained the chalcone from acetophenone by condensation with benzaldehyde.

Besides the above mentioned condensing agents, an aqueous borax solution (120), amino acids (121) have also been used as condensing agents for chalcone synthesis. The use of perchloric acid is also reported (122).

**MECHANISM OF THE CHALCOME FORMATION**

From the above review of various condensing agents used in the chalcone synthesis, it is clear that the condensation of a ketone with an aldehyde is affected mainly by two types of condensing agents.

1. alkaline reagents usually sodium or potassium hydroxide.
2. acidic reagents like dry hydrochloric acid gas, anhydrous aluminium chloride, phosphorous oxychloride etc.

It is clear that the chalcone formation proceeds through an aldol type of condensation and is catalysed by acid or alkali. The following mechanism of reaction is suggested;

Base Catalysed

\[
\begin{align*}
\text{Base Catalysed} \\
\text{(a)} & \quad R - C - \text{CH}_3 + B \xleftrightarrow{\text{3. » 2}} R - C - \text{CH}_2 + BH
\end{align*}
\]
(b) \[ R' - C = 0 \xrightarrow{\text{H}} R' - \overset{\ddagger}{C} - \overset{\ddagger}{0} \]

(c) \[ R - C - CH_2 + \overset{\ddagger}{\text{CH}} - R' \xrightarrow{\text{BH}} R - C - CH_2 - CH - R' + BH \]

\[ \xrightarrow{\text{H}} R - C - CH_2 - CH - R' + B^- \] (I)

(d) \[ R - C - CH_2 - CH - R' \xrightarrow{\text{H}_2O} R - C - CH = CH - R' + H_2O \]

Acid Catalysed:

(a) \[ R - C = 0 \xrightarrow{\text{CH}_3} R - \overset{\ddagger}{C} - \overset{\ddagger}{0} + \overset{\ddagger}{\text{H}} \]

\[ \xrightarrow{\text{CH}_3} R - \overset{\ddagger}{C} - \overset{\ddagger}{0} - \overset{\ddagger}{\text{H}} \xrightarrow{\text{CH}_2} R - \overset{\ddagger}{C} - \overset{\ddagger}{\text{OH}} + \overset{\ddagger}{\text{H}} \]

(b) \[ R' - C = 0 \xrightarrow{\text{H}} R' - \overset{\ddagger}{C} - \overset{\ddagger}{0} + \overset{\ddagger}{\text{H}} \xrightarrow{\text{H}} R' - \overset{\ddagger}{C} - \text{OH} \]

(c) \[ R - C = CH_2 \xrightarrow{\text{OH}} R - \overset{\ddagger}{C} - CH_2 + \overset{\ddagger}{\text{CH}} - R' \]

\[ \xrightarrow{\text{OH}} R - \overset{\ddagger}{C} - CH_2 - CH - R' \xrightarrow{\text{OH}} R - C - CH_2 - CH - R' \]

\[ \xrightarrow{\text{OH}} R - C - CH = CH - R' + H_2O \]
The intermediate aldol type product(I) readily undergoes dehydration even under mild conditions, particularly when R and R' are aromatic.

PROPERTIES AND TESTS

The chalcones are generally coloured—usually yellow, orange, red or brown. They are comparatively more soluble than the corresponding flavanones in ethanol and ethyl acetate. 2'-Hydroxychalcones dissolve in dilute alkali with an orange to deep red colour.

COLOUR REACTIONS

The following colour reactions are used to distinguish them:

(1) They generally give a characteristic deep red colour with a violet tinge with concentrated sulphuric acid. However this test is not reliable as some flavanones also give this colour test.

(2) 2'-Hydroxychalcones give a reddish brown colour with ethanolic ferric chloride.

(3) According to Wilson chalcones give a brilliant yellow to orange colour with a boric acid-citric acid-acetone reagent. He used this test successfully to distinguish between a chalcone and flavanone. This test is claimed to be specific for o-hydroxy and
methoxychalcones. It is not given by flavanones and simple aromatic ketones.

(4) Compounds related to chalcones like flavanones, flavones and flavonols when reduced with magnesium and hydrochloric acid in ethanolic solution give a pinkish colour due to the formation of pyrylium salts. The chalcones do not give this test.

(5) King and White(124) showed that on treating C_{15} compounds with acetic anhydride and a drop of concentrated sulphuric acid, chalcones, flavanones and aurones gave an orange to purple colour. Krishnamurthy and Seshadri(125) have extended this test and reported that perchloric acid and zinc chloride are also capable for generating acetylium ion which accounted for the colour reaction.

(6) Benzyldiene compounds on pyrolytic oxidation with lead dioxide liberate benzaldehyde which can be detected by appearance of a yellow fleck on a filter paper moistened with a suspension of thiobarbituric acid in phosphoric acid(126).

**Reactivity of Chalcones**

As already stated the chalcones contain a ketoethylenic group; hence they are found to be reactive towards several
reagents and also can be cyclised to different heterocyclic derivatives by suitable reactions. The reactivity of the keto-ethylenic group in chalcones has been the subject of a large number of investigations. Some of the reactions are briefly described below:

**Action of Phenylhydrazine**

The presence of ketonic group in a compound is detected by preparing its phenylhydrazone or 2,4-dinitrophenylhydrazone usually obtained as a crystalline substance (127). Sometimes if it contains a labile hydrogen, ring closure takes place giving a pyrazoline instead of the expected hydrozone. Raiford and Peterson (128) found that phenylhydrazones when brought in contact with bromine vapour, changes its colour from yellow to orange and then to brick red. Under the same treatment, pyrazoline derivative turns green instantaneously (129, 130).

**Reaction with Hydroxylamine**

Reaction with hydroxylamine gives generally isoxazolines, probably through the formation of an oxime:

\[
R - CO - CH = CH - R' \xrightarrow{NH_2OH} R - C\equiv CH
\]

\[
\xrightarrow{NCH - R'}\]

\[
\xrightarrow{OH}
\]
However, the reaction is not simple and besides the oxime and isoxazoline other products like hydroxylamino ketone, hydroxylamino oxime, disubstituted hydroxylamine, etc. may be formed depending upon the nature of substituents and the proportion of the reactants (131-133).

**Action of Nitric Acid**

Van Der Lee (134) and Røddelien (135) while studying the effect of nitric acid on chalcones found that nitro group is added to the ethylenic linkage; 3-3' dinitrochalcone gave on treatment with absolute nitric acid, 3-3' trinitrochalcone.

![Diagram of nitrochalcone transformation](image)

**Action of Hydrocyanic Acid**

A chalcone on treatment with potassium cyanide in acetic acid solution gives a 3-cyano-1,3-diphenylpropan-1-one (a. X = CN) and a sparingly soluble product (b) formed by double addition (136-138).
Action of Benzene and its Homologues

It has been reported that the addition of benzene and its homologues to a chalcone in presence of anhydrous aluminium chloride affords an \( \alpha: \beta \) diarylpropiophenone (139-143).

Action of Reactive Methylene Ester

Acetoacetic ester and its derivatives add to the ethylenic double bonds of the chalcone in presence of sodium ethoxide or diethylamine (144-148). Davey and Gwilt (149) obtained such adducts from halo and nitrochalcones.

\[ X = \text{CH}_3\text{-CO}-\text{CH}-\text{COOEt}; \text{CH} (\text{COOEt})_2. \]

On the other hand, instances are known in which the adduct \( X = \text{COOEt} \) cyclises to a \[ \text{CHCOCH}_3 \]

2,4 diphenyl-cyclohexenone derivative (150-155).
Sammour, El-zimlity and Abdel-maksoud (156) reacted ethyl acetoacetate in presence of piperidine by refluxing in n-butanol. Use of anhydrous potassium carbonate as a condensing agent has also been reported (157).

These cyclohexenone carboxylate esters on heating with alkali hydrolyse to acids which undergoes decarboxylation to produce cyclohexenones in a single step:

![Chemical structure of cyclohexenone carboxylate esters](image)

Malonic ester itself and several malonic ester derivatives add to the ethylenic bond normally to give several types of side products including cyclic compounds (158-160).

**Action of Bromine on Chalcones**

The chalcone adds a molecule of bromine, and under the usual conditions, dibromide is obtained.

![Chemical structure of the reaction between chalcone and bromine](image)
A dibromide of a simple benzylideneacetophenone was first prepared by Claisen and Claparede (161) and Pond, York and Moore (162) also prepared dibromide of the chalcones. Vanderwala and Jadhav (163) have exhaustively investigated the action of bromine on the chalcones derived from many o-hydroxyacetophenones and have reported that one molecule of bromine adds to the double bond. Dibromides were prepared by brominating the chalcones in acetic acid medium (164-167).

Wheeler and Dodwadmath (168) found during their work on chalcones that bromine first enters at the double bond very easily and if the reaction is continued, bromine enters the nucleus also. They further found that the styryl nucleus is more reactive of the two.

It may be noted that if bromine is present in both the nuclei of the chalcone molecule, the addition to the double bond takes place rather easily.

Reactivity of Dibromides

The dibromides undergo several reactions depending upon which of the bromine atom is reactive. Some of the important reactions are briefly described below:

(a) Debromination

It has been shown by several workers that potassium iodide in acetone removes the side-chain bromine atoms from the dibromide of the chalcone giving the original chalcone
with the liberation of iodine (51, 163, 169-171).

This reaction is generally used to distinguish a chalcone from a flavanone

\[
\text{R-C-CH-CH-R'} + 2\text{KI} \rightarrow \text{R-C-CH=CH-R'} + 2\text{KBr} + \text{I}_2
\]

Pyridine (172), stannous chloride (173) and anhydrous aluminium chloride in carbon disulphide (174) have also been used for debromination.

(b) Caustic Potash

The dibromides of the o-hydroxy or acetoxychalcones on treatment with potassium hydroxide give either flavones or the isomeric coumaranones. This depends upon the comparative reactivity of the \( \alpha \) and \( \beta \) - bromine atoms which would be eliminated as hydrogen bromide before the acetoxy group is hydrolysed (175, 163).

\[
\text{Chalcone dibromide} \quad \text{Coumaranone} \quad \text{Flavone}
\]
Cullinane and Philpott (176) suggested that bromine in the phenyl nucleus favoured the production of benzylidene coumaranones. The extensive work carried out by Wheeler and Dodwadmath (168) explains satisfactorily the dual course of the reaction. The chalcone dibromides which give benzylidene coumaranones rather than flavones could be divided into two classes.

a. Those derived from o-hydroxy-phenyl p-alkoxystyryl ketones and

b. Those derived from 2-hydroxy-4,6-dimethoxyphenyl-styryl ketones.

In the first case the chalcone dibromides contain a labile bromine atom to the keto group which can be replaced by alkoxy group on boiling with ethanol. The labile atom is more activated by the presence of o- or p methoxy group in the styryl nucleus.

Donnelly and co-workers (177) reinvestigated the work of Emilewicz and Kostanecki (178) and showed that the product is a mixture of aurones and flavones, the latter being the major constituents. Aurone formation by phloracetophenone derived chalcone dibromides could be due to the combined effects of the various groups present.
(c) Pyridine

Nadkarni, Warriar, and Wheeler (150) found that in the reaction of a chalcone dibromide with pyridine the $\beta$-bromine atom was eliminated as hydrogen bromide leading to the formation of $\alpha$-bromostyryl ketone (see also other references of Wheeler and co-workers).

\[
\begin{align*}
R-C-CH-CH-R' & \quad R-C=CH-R' \\
\mid & \quad \mid \\
O \text{ Br} \text{ Br} & \quad O \text{ Br}
\end{align*}
\]

Ghiya and Marathey(179) investigated the reaction of chalcone dibromides with pyridine and found debromination and subsequent nuclear bromosubstitution in chalcone takes place via an intermolecular mechanism.

Jadhav and Vanderwala(161) found that different products like the $\alpha$-halogen styryl ketone or coumaranone were obtained depending upon the number and position of the hydroxy groups in the ketonic nucleus.

(d) Potassium Cyanide

Dodwadmath and Wheeler(169) showed that the dibromides of simple chalcones give with potassium cyanide the corresponding propionitrile derivatives. Similar nitriles have also been prepared by Nadkarni, Warriar and Wheeler(171), Jadhav and Vanderwala(163,164) found that 2'-hydroxychalcone dibromide gave the corresponding flavone or coumaranone.
(e) **Amines**

Cromwell and Mercer (180) obtained \( \alpha, \beta \) or \( \beta \)-aryl or alkyl-aminochalcones by treatment with secondary amines in ethanol at a low temperature in absence of light. Sammour and Elkasaby (174) have also obtained adduct with morpholine and piperidine.

(f) **Ethanol**

Chalcone dibromides when refluxed in ethanol give \( \alpha \)-bromo \( \beta \) ethoxycompound (181-84).

(g) **Acetic Acid**

Chalcone dibromide when heated in acetic acid cyclized to 3-bromoflavanone (184).

**SYNTHESIS OF FLAVANONES**

2'-Hydroxychalcones can be cyclised to the corresponding flavanones using either dilute acids like hydrochloric, sulphuric or phosphoric or by the action of dilute alkali.
(1) **Acid Isomerisation**

The ortho-hydroxy chalcones are converted into the corresponding flavanones by refluxing them with dilute hydrochloric or sulphuric acid (3 to 10\%). This method has been extensively used by several workers (185-187). Sometimes the conversion is not complete and a mixture of a chalcone and a flavanone is obtained. Nierenstein (188) converted the chalcones to the corresponding flavanones by the above method using phosphoric acid but he obtained the flavanones in poor yield.

Russell and Clark (59) found that in those cases where the hydroxychalcone had an o-hydroxy group in the styryl nucleus, acidification of the alkaline solution after debenzoylation caused cyclisation to an anthocyanidin.

(ii) **Base Isomerisation**

The chalcone is dissolved in slightly more than the required amount of dilute sodium hydroxide (1\%) equivalent to all the free hydroxy groups present. A little ethanol is added and the solution refluxed and left overnight at room-temperature. The crude chalcone-flavanone mixture is precipitated by the addition of dilute acetic acid, and separated by crystallisation from a suitable solvent (189, 190).

Sometimes a flavanone is directly obtained instead of a chalcone in presence of alkali, probably as a result of
the isomerisation of the chalcone formed to the corresponding flavanone under the action of alkali (191, 190). Shinoda and Sato (192) have stated that in case of ketone derived from phloroglucinol, a flavanone is obtained instead of a chalcone probably on account of the fact that the presence of hydroxy group at the 6th position makes 2-hydroxy group so reactive that the intermediate chalcone formed undergoes ring closure and changes to the flavanone.

Seshadri and Venkateswarlu (49) have improved the technique of working up the reaction mixture in the above method by using ethyl acetate as a solvent for flavanones. Sodium acetate has also been used in the conversion of 2'-hydroxychalcones to the corresponding flavanones (117, 193). This method is of special value in the preparation of glycoside derivative of hydroxyflavanones.

Kraemer, Halpaap and Friesberg (194) obtained flavanones by refluxing chalcones derived from different hydroquinone ketones and various aldehydes in presence of piperidine.

SYNTHESIS OF FLAVONES

The first synthesis of flavone, as already described, was accomplished by heating a dibromide of 2-hydroxychalcone with ethanolic alkali (195). This method of synthesis was however, unreliable as in certain cases benzylidene
coumaranone(I) was obtained instead of the expected flavone(II).

Kostanecki and Feuerstein(196) converted 2'-hydroxychalcones to the corresponding flavanones by treatment with dilute acid. The flavanone obtained in this manner was then treated with bromine and the resulting product on treatment with ethanolic potassium hydroxide gave the flavone. N-Bromosuccinimide has been also successfully used for this bromination.

2'-Hydroxychalcones were directly cyclised to flavones (40, 197, 199) by treatment with selenium dioxide. This method is much used. Flavanones can also be converted to flavones using this reagent.
Narsimhachari and Seshadri (200) used iodine in presence of ethanol and sodium acetate as a dehydrogenating agent for the conversion of hydroxy flavanones to the corresponding flavones.

Bose, Chakrabarti and Sanyal (201) prepared flavones by heating chalcone in presence of palladised charcoal in vaccuo. Litkei and Bognar (166) prepared flavones by treating chalcone dibromides with ammonia in methyl alcohol.

**SYNTHESIS OF FLAVONOLS**

The flavonols or 3-hydroxy flavones like galangin, kemferol, fisetin, herbacetin; morin etc. occur in nature as yellow pigments. A good deal of work has been carried out on the synthesis of flavonols from the corresponding chalcones containing resorcinol and phloroglucinol nuclei (201-203).

Some of the common methods used for the synthesis are:

1. From coumaranones (204)
(2) By heating flavanone with amyl nitrite in acidic ethanolic solution and acid isomerisation of the isonitro derivative (205, 49).

(3) o-Hydroxy chalcones are converted into flavonols by the action of hydrogen peroxide (206-214).

\[ \text{Flavonol} \]
\[ \text{Chalcone} \]

Murakami and Irie (208) have oxidised chalcones and obtained the flavonols as well as dihydroflavonols in major part. They have suggested the use of trimethylamine or ammonium hydroxide in place of sodium hydroxide.

Wheeler (215) has observed that chalcones of phloracetophenone on oxidation with cold hydrogen peroxide in presence of alkali gave the corresponding aurones, but when the oxidation was carried out in hot, mainly the flavonols were formed.

(4) 3-Hydroxyflavanone can be obtained by treating a chalcone dibromide with silver acetate in acetic anhydride and then cyclizing with hydrochloric acid (216).
The product thus obtained may also be dehydrogenated to the flavonols by means of palladium with cinnamic acid or maleic anhydride as a hydrogen acceptor (217).

(5) Marathey (218) has synthesised flavonols by direct condensation of an aldehyde and a ketone derivative using sodium peroxide as a condensing agent.

(6) Winicki and co-workers (219) reported that a flavone could directly be oxidised by Udenfriend reagent (a buffered solution of ascorbic acid and ferrous ion chelate) in position 3' and 4'. Under optimum conditions 3-hydroxyflavone or flavonol was formed by a non-radical complex process.

Spectroscopy:

The spectroscopic methods are important in elucidating the structure of naturally occurring organic compounds.

Ultra-Violet Spectra:

The ultraviolet spectra of chalcones have been studied by various workers (220-227). It is observed that all the chalcones show two main regions of absorption, one in the range of 320-380 nm (referred to as band-I) arising probably due to the contribution of the cinnamoyl grouping and probably due to \( \pi - \pi^* \) electronic transition of the whole molecule while the other absorption lies in the range of 225-270 nm.
(referred to as band-II) which has been regarded as a contribution of the benzoyl grouping. The intensity of the latter band is usually weaker than the intensity of the band-I. This conclusion is in agreement with the generalisation advanced by Jurd and Horowitz (222). Substitution in ring-A of chalcone molecule causes invariably a red-shift of band-II while the shift in Band-I seems to be dependent upon the nature and the position of the substituents.

**Infra-Red Spectra:**

Study of the infra-red spectra of chalcones leads to the following interesting conclusions with regard to (i) carbonyl absorption (ii) ethylenic absorption. A carbonyl group shows absorption at 6.02 μ and -C = C- gives absorption at 6.15 μ. Rasmussen and co-workers (228) studied the effect of conjugation of the double bond with a carbonyl group in ketones and assigned 6.07 - 6.17 μ range. Nayak and co-workers (229) studied the effect of substitution in the aromatic ring of chalcone on position of the -C = C- stretching vibrations. They assigned 6.23 μ (sharp) and 6.36 μ (medium) bands in chalcone and corresponding bands in substituted chalcones to this type of vibration. Silver and Boykin (230) studied in detail the relating effect of substituents on carbonyl stretching of chalcone. Randall and co-workers (231) and Bellamy (232) assigned the 6.30-6.35 μ and 6.39 μ band respectively in chalcone to the
phenyl alkene stretching vibrations. The assignment of infrared bands in the case of substituted chalcones have been also made by other workers (233-239).

NMR Spectra:

The application of nuclear magnetic resonance (NMR) spectroscopy to the structure analysis of flavonoids is now well established. Highly alkylated flavonoids are sufficiently soluble in the commonly used solvent, deuterio chloroform (CDCl₃) for direct NMR analysis.

Proton signals obtained in NMR spectra of flavonoids generally occur in the range 0-9 ppm most fall into a number of well separated groups.
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