2. Review of Literature

As per title we want to synthesis Pyrimidine Heterocyclic compound with the help of Chalcone synthesis we synthesis Pyrimidine Heterocyclic compound base on chalcone derivatives for that out line of synthesis reactions are as follows.

There are a number of methods for the synthesis of chalcones including the classical methods of Claisen-Schmidt, Witting reaction, and Friedel-Crafts acylation

1. The Claisen-Schmidt Reaction

The Claisen-Schmidt condensation between acetophenone and benzaldehyde derivatives is an important C-C bond forming reaction which allows unsaturated ketone such as chalcones tobe obtained (23). It is the most frequently used means of establishing the C6-C3-C6 flavonoid nucleus owing to the availability of starting materials such as 2-hydroxyacetophenone and a C6-C1 unit, of benzaldehyde derivatives toobtain a 2’-hydroxychalcone . Compound bearing Aringsubstituent provided by the acetophenone (indicated as R1) and B-ring substituent provided by the benzaldehyde (indicated as R2). The classical Claisen-Schmidt reaction is routinely carried out using aqueous sodium or potassium hydroxide or ethanolic sodium ethoxide at 50°C over a period of several hours. The benzaldehyde derivative is often used in slightly more than equivalent amounts. The extensive conjugation of the products causes them to absorb light in the visible region, lending them a yellow color . Aldol condensations (24) are important in organic synthesis, providing a good way to form carbon–carbon bonds. The Robinson annulations (25) reaction sequence features an aldol condensation; the Wieland-Miescher ketone product is an important starting material for many organic syntheses. Aldol condensations are also commonly discussed in university level organic chemistry classes as a good bond-forming reaction that demonstrates important reaction mechanisms. In its usual form, it involves the nucleophilic addition of a ketone enolate to an aldehyde to form a β-hydroxy ketone, or "aldol" (aldehyde + alcohol), a structural unit found in many naturally occurring molecules and pharmaceuticals.
2. Synthesis of Chalcones via Suzuki Coupling Reaction

An efficient synthesis of chalcones is carried out based on the Suzuki coupling reaction between benzoyl chlorides and phenylvinylboronic acid (26). Phenylvinylboronic acid is prepared by dehydrogenative borylation of para-methoxystyrene by pinacolborane oxidative addition-dehydrogenation catalyzed by the rhodium complex, RhCl(cod) to give para-methoxyphenylethenylboronic acid pinacol ester. Oxidative cleavage of using sodium periodate in THF/water to form the para-methoxyphenylethenylboronic acid required for the Suzuki coupling step. The coupling between and afforded 3',4',4-trimethoxy chalcone using anhydrous toluene as solvent and catalyzed by tetrakis(triphenylphosphine)palladium and base; cesium carbonate. Chalcones and coumarins are important naturally occurring plant constituents and display a wide range of pharmacological and biological activities. In an environmentally benign approach, synthesis of biphenyl chalcone and coumarin derivatives was successfully accomplished via Suzuki coupling by using PEG-400 as a solvent under microwave irradiation. Salient feature of this methodology includes: short reaction time, good to excellent yields, and prominent tolerance of different functional groups.

3. The Von-Konstanecki Method

This is a general method for synthesizing flavones which involves a reaction of 2-Methoxybenzoate (27) and acetophenone in the presence of sodium to form The diketone compound is formed via Claisen condensation. A treatment of with an acid afforded
compound and elimination of water formed flavones. Flavonoids are benzo-γ-pyrone derivatives consisting of phenolic and pyran rings and are classified according to substitutions. The polyphenolic structure allows a large number of further substitutions, including phenolic hydroxy groups, methoxy groups, O-sugars, C-sugars, and sulfates, thus producing an extremely diverse range of derivatives. Dietary flavonoids differ in the arrangements of hydroxyl, methoxy, and glycosidic side groups, and in the conjugation between the A- and B- rings. Structurally, they consist of two main groups, the 2-phenylchromans (the flavonoids, including flavanones, flavones, flavonols, flavan-3-ols, and anthocyanidins) and the 3-phenylchromans (the isoflavonoids, including isoflavones, isoflavans, and pterocarpans).

4. Friedel-Crafts Acylation

Besides the Claisen-Schmidt reaction, chalcones can also be synthesized by direct Friedel-Crafts acylation of a phenol (28). In this approach the phenol becomes the A-ring while the acylating agent provides both the B-ring carbons and the three carbon bridge to form C6-C3-C6 unit. Friedel-Crafts acylation of 2,4-dimethyl-1,3,5-triolbenzene with 3-phenylpropionyl chloride gave 2’,4’,6’-trihydroxy-3’,5’-dimethylchalcon. The Friedel–Crafts reactions are a set of reactions developed by Charles Friedel and James Crafts in 1877 to attach substituents to an aromatic ring. There are two main types of Friedel–Crafts reactions: alkylation reactions and acylation reactions. Both proceed by electrophilic aromatic substitution. The general reaction scheme is shown below.

5. Synthesis of Chalcone using Borontrifluoride-etherate

Narender and Reddy developed a new methodology by using borontrifluoride-etherate to synthesize several substituted chalcones (29). The advantages of this method over the existing methods are high yields, simple work-up, short reaction times, no side reactions,
and separation is needed to get the products. This method is solvent free reactions and applicable for reactions involving liquid reactants which are base sensitive functional groups such as esters and amides. Chalcones are secondary metabolites of terrestrial plants, precursors for the biosynthesis of flavonoids and exhibit various biological activities. Condensation of substituted acetophenones with various aromatic aldehydes in the presence of boron trifluoride-etherate at room temperature gave chalcones in 75–96% yield.

6. Naturally Occurring Chalcones

Naturally occurring chalcone have been reported to have multiple biological and pharmacological activities. The Antioxidant Properties is mainly depends on the substitution group of chalcones. Licochalcone A is a naturally occurring chalcone isolated from the roots of Glycyrrhiza inflata (licorice) which is proved to have in vitro and in vivo antimalarial and antileishmanial activities. Monoterpene-chalcone conjugates, including two novel compounds isorubraine and sumadain, and a known compound rubraine from the seeds of Alpinia katsumadai. The seeds of Alpinia katsumadai are used in traditional Chinese medicine (TCM) as an antiemetic agent and for the treatment of stomach disorders. The bioactivities of the compounds were evaluated for cytotoxic activities by MTT method in one human liver cancer cell line HepG2, and two human breast cancer cell lines MCF-7 and MDA-MB-435. The results implied that compound signified potent activity against the three cell lines.

7. Synthesis of Chalcones via Microwave Irradiation

The combination of supported reagents and microwave irradiation can be used to carry out a wide range of reactions in short times and with high conversions and selectivity, without the need of solvents (31). This approach proved beneficial since it offers several advantages over conventional heating techniques and accelerates the organic reactions. The air dried paste of 2’-hydroxyacetophenone, benzaldehyde and anhydrous K₂CO₃ is subjected to microwave irradiation for 3-5 minutes to 16 produce 2’-hydroxychalcones. This reaction gave a cleaner product with a high yield (80-90%). 1,3-Diphenylpropenones (chalcones) are well known for their diverse array of bioactivities. Hydroxyl group substituted chalcones are the main precursor in the synthesis of flavonoids. Till date various methods have been developed for the synthesis of these very
interesting molecules. Continuing our efforts for the development of simple, eco-friendly and cost-effective methodologies, we report here a solvent free condensation of aryl ketones and aldehydes using iodine impregnated alumina under microwave activation. This new protocol has been applied to a variety of substituted aryl carbonyls with excellent yield of substituted 1,3-diphenylpropenones.

![Chemical Reaction](image)

R, R' = -H, -OH, -OMe, -Cl etc.

8. Ganguly’s Synthesis of Flavone

Ganguly and co-workers modified the Baker-Venkataraman method of synthesizing flavones. In this modified procedure, 2’,4’,6’- trihydroxyacetophenone (33) and 2’,4’-dihydroxyacetophenone were heated with benzoyl chloride in the presence of base catalysts, (DBU) and pyridine afforded 3-acylflavones and , respectively. Further reaction of the acylflavones of and with 5% potassium carbonate gave flavones and, respectively as shown in Precursors of flavones are successfully synthesized using modified Baker-Venkataraman reactions. Flavones (flavus = yellow), are a class of flavonoids based on the backbone of 2-phenylchromen-4-one. Apart from flavones other flavonoids are isoflavonoids, derived from 3-phenylchromen-4-one structure, and neoflavonoids, derived from 4-phenylcoumarine structure. The three flavonoid classes are all ketone-containing compounds, and as such, are anthoxanthins (flavones and flavonols).

9. Biosynthesis of Chalcones

All chalcones derived their carbon skeleton from two basic compounds. Flavonoids and other compound associated with flavanoids are derived from this chalcone intermediate stereo specific action, oxidative rearrangement and others. Chalcone in which the next process after chalcone will lead to the production of flavonoids and its derivative. Cinnamate, 4-coumarate and 4-coumaroyl-CoA are involved during the synthesis natural of chalcone. Chalcone synthase or naringenin-chalcone synthase (CHS) is an enzyme ubiquitous to higher plants and belongs to a family of polyketide synthase.
enzymes (PKS) known as type III PKS. Type III PKSs are associated with the production of chalcones, a class of organic compounds found mainly in plants as natural defense mechanisms and as synthetic intermediates. CHS was the first type III PKS to be discovered. It is the first committed enzyme in flavonoid biosynthesis. The enzyme catalyzes the conversion of 4-coumaroyl-CoA and malonyl-CoA to naringenin chalcone.(34)