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A Comprehensive Review on Synthesis and Biological Activity of Chalcone

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ABSTRACT

In the present review, the synthesis and biological activities have been reviewed. Chalcones are α, β unsaturated ketones (trans,1-3 diaryl-2-propen-1-one) consisting of two aromatic rings (A & B) attached by α, β unsaturated carbonyl system with a variety of substituents.[1] chalcone plays an important role in diverse pharmacological activities like antioxidant, anti-inflammatory, antifungal, antimicrobial, anticancer, antibacterial, antiviral, antituberculosis, etc. Chalcone is a common simple scaffold found in many naturally occurring compounds.[2] Chalcone is derived from the Greek word 'Chalcose', which means bronze, the color of naturally occurring chalcones.[3] Chalcone is one of the important scaffolds exhibiting unique biological and medicinally beneficiary molecules. Many chalcones-based compounds have revealed antitumor activities through different mechanisms of action, including the disruption of the cell cycle, induction of apoptosis, inhibition of angiogenesis, inhibition of tubulin polymerization, and anti-estrogenic activity. [4] Chalcone derivatives are considered valuable species because they possess a keto ethylenic moiety, CO–CH═CH–.[5] Chalcones are the condensation products of aromatic aldehyde with acetophenones in attendance of the catalyst.[6] Chalcones are the main precursors for the biosynthesis of flavonoids and isoflavonoids.[7] Chalcones and their derivatives are very important in medicinal chemistry, displaying a wide range of important pharmacological activities.[8] chalcone derivatives heterocyclic chalcones were produced through the bio-isosteric replacement of chalcones. especially Pyrazole derivatives have a long history of application in agrochemicals and the pharmaceutical industry as herbicides and active pharmaceuticals. The recent success of pyrazole COX-2 inhibitor has further highlighted the importance of these heterocyclic rings in medicinal chemistry.[9]

1 INTRODUCTION:

Chalcone is one of the important scaffolds exhibiting unique biological and medicinally beneficiary molecules. Many chalcones-based compounds have revealed antitumor activities through different mechanisms of action, including the disruption of the cell cycle, induction of apoptosis, inhibition of angiogenesis, inhibition of tubulin polymerization, and anti-estrogenic activity.

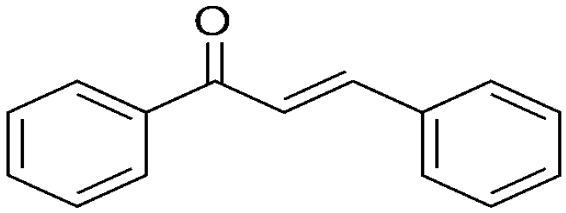

Fig:01 – Structure of chalcone

Various structural modifications were performed in the chalcone's primary structure either by altering the aryl moiety or the enone linker. Interestingly, a lot of effective anticancer agents have been developed as a result of these modifications. In addition, several heterocyclic chalcones were produced through the bioisosteric replacement of chalcones aryl groups by various heterocyclic rings such as thiazole, imidazole, indole, benzothiophene, and that displayed strong and selective antitumor effect.**[10]**

Antioxidants are agents, which can inhibit or delay the oxidation of an oxidizable substrate in a chain reaction. Chalcones belong to the largest class of plant secondary metabolites. Which, in many cases, serve in plant defense mechanisms to counteract reactive oxygen species (ROS) to survive and prevent molecular damage and damage by microorganisms, insects, and herbivores. They are known to possess antioxidant character at various extents.

Chalcone and the dimer showed significant antifungal properties against Aspergillus fumigates and Cryptococcus neoformans. Both compounds were particularly effective against Cryptococcus neoformans. However, none of those chalcones displayed any noticeable antifungal activity against Aspergillus flavus, A. nigeria, or Candida albicans. Glabrata.**[11]**

2. Methods of Chalcone Synthesis:

2.1 synthesis of chalcone derivatives of 2-acetyl naphthalene

Chalcones 1a–g was constructed by treating 2-acetyl naphthalene with benzaldehyde and substituted benzaldehyde in methanol and potassium hydroxide, and the constructed derivatives exhibited antibacterial and antifungal activities.[12]

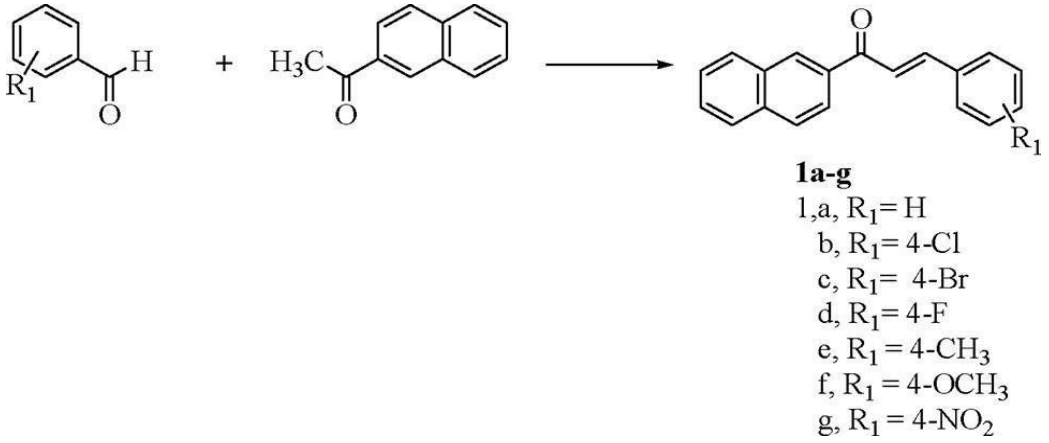

Fig: 02- synthesis of chalcone derivatives of 2-acetyl naphthalene

2.2 Synthesis of Chalcone from Phenyl Halide

Chalcone was prepared by reaction of phenyl halide and styrene in carbon monoxide and pd catalyst.[13]

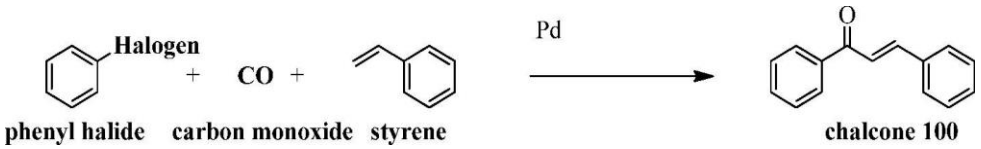

Fig: 03-Synthesis of Chalcone from Phenyl Halide

2.3 Synthesis of Chalcone Derivatives from Benzoyl Chlorides

Ynones were synthesized by reaction of benzoyl chlorides and phenylacetylenes using Sonogashira conditions described in a literature procedure. Ynones undergo deuterations using the H-Cube system using D2O instead of water. Continuous-Flow Deuteration Reaction. Chalcone was synthesized by reaction of benzoyl chloride with styryl boronic acid 103 in anhydrous toluene and in the presence of Pd(PPh3)4 and CsCO3. Also from the reaction of cinnamoyl chloride 104 and phenylboronic acid in anhydrous toluene and in the presence of Pd(PPh3)4 and CsCO3, the reaction proceeds via the Suzuki–Miyaura coupling reaction.[14]

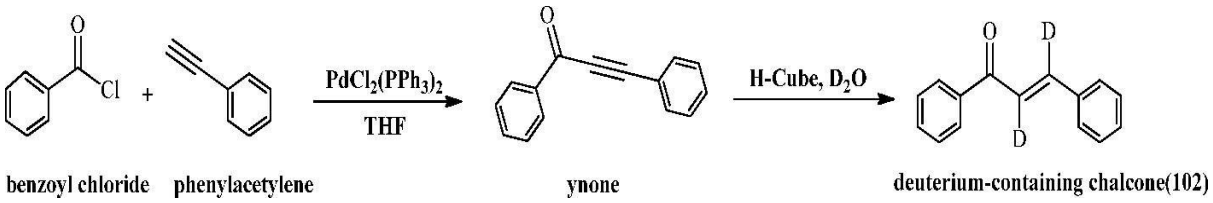

Fig:04- Synthesis of Chalcone Derivatives from Benzoyl Chlorides

2.4 Synthesis of Sappanchalcone

Reagents and conditions:

(a) CH3COOH, polyphosphoric acid, 60 °C, 30 min;

(b) 2′,4′-dihydroxyacetophenone, 12 M KOH, ultrasound-assisted, 80 °C, 8 h.

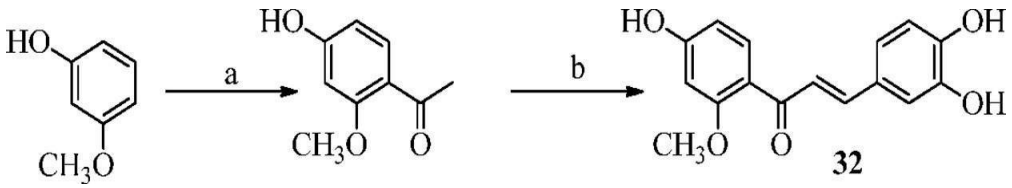

Fig:05- Synthesis of Sappanchalcone

2.5 Synthesis Various Methods Employed to Prepare Chalcones

Several synthetic pathways have been suggested for the synthesis of chalcones, as depicted in One method involves the preparation of chalcones from benzoyl chlorides and phenyl vinyl boronic acid through a Suzuki coupling reaction. However, in the classical approach, there is a higher likelihood of byproduct formation, which subsequently decreases the overall yield. [15,16.17]

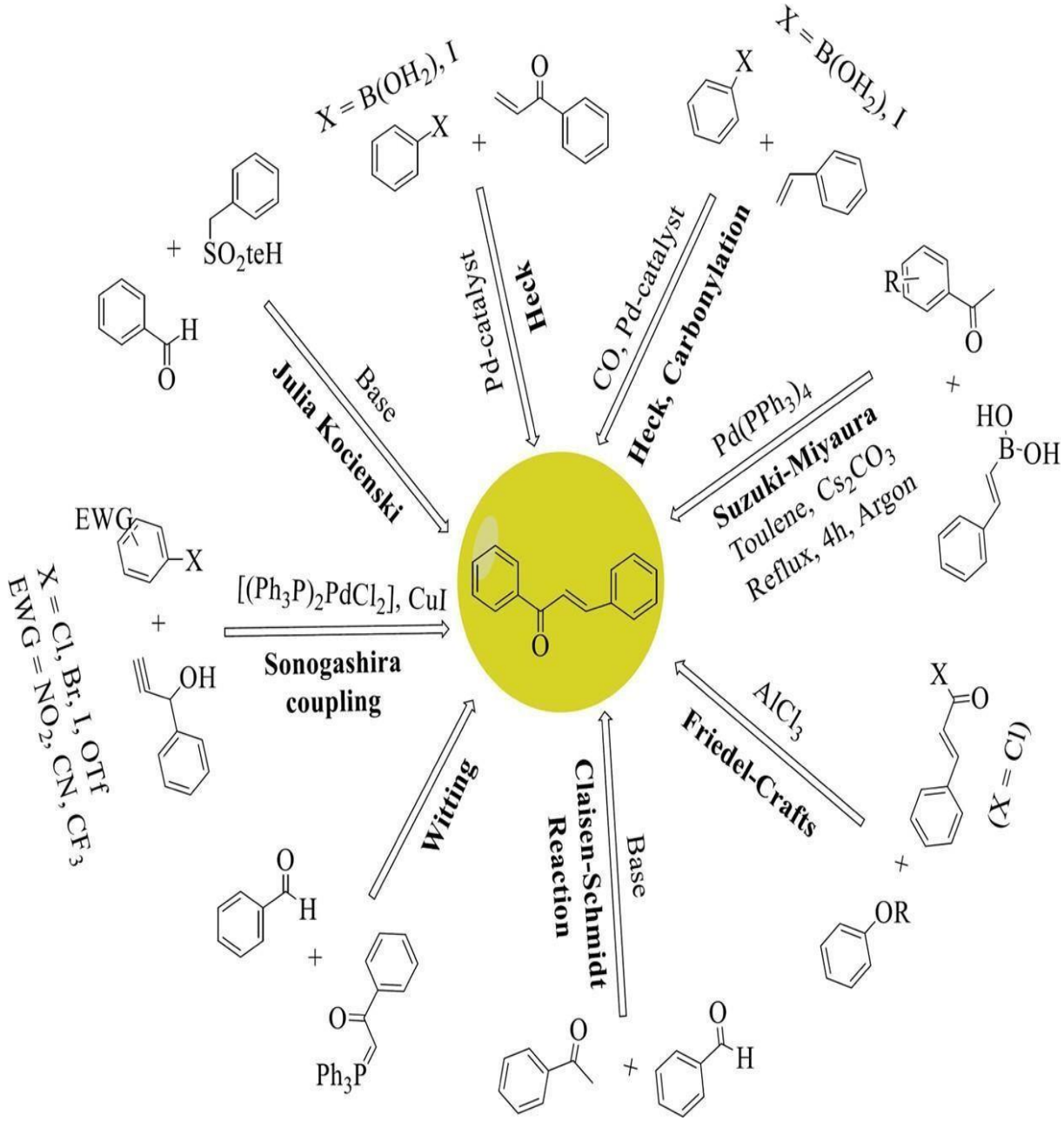

Fig :06- Synthesis Various Methods Employed to Prepare Chalcones

3. Biological activities of Chalcones:

Chalcones and their derivatives are the most active compounds that are known for their broad spectrum of activity. Antioxidant, Antimicrobial, Anti-inflammatory, Anticancer etc.

3.1 Antioxidant:

Antioxidants are the compounds that inhibit the oxidation process. This substance can prevent or slow damage to cells caused by free radicals. Oxidation is a chemical reaction that generates free radicals, thereby leading to chain reactions that may damage the cells of organisms and hence responsible for oxidative stress resulting in chronic diseases such as heart diseases, stroke, cancer, arthritis, respiratory diseases, Parkinson's disease, and other inflammatory conditions. [18]

3.2 Antimicrobial:

Antimicrobial agents are the drugs used to treat infectious diseases caused by different types of bacteria and fungi. The use of these drugs is now common, and continuous efforts are put in by the scientific community to search for newer antimicrobial agents due to antimicrobial resistance shown by the microbes.[19]

3.3Anticancer:

Cancer is a widely spreading disease all over the world, necessitating the need to develop new anticancer agents. Anticancer or antineoplastic drugs are those that are effective in the treatment of malignant or cancerous diseases. The design, synthesis, and antitumor potential of chalcones were studied against human breast adenocarcinoma MCF-7 cells in a concentration-dependent manner. Leo et al. reported the chalcone derivatives for cytotoxicity against human tumor cells.[20]

3.4 Anti-inflammatory:

Anti-inflammatory drugs are the drugs that are used to reduce pain and inflammation. In other words, these are pain-relieving drugs. These drugs work mainly by inhibiting the cyclooxygenase enzymes, COX-1 and COX-2, that produce prostaglandins.[21]

4. Conclusion

Chalcone are Which can be used in various therapeutically beneficial medicinal syntheses. One of these is "Chalcone" The word chalcone is derived from the Greek word 'Chalcose', which means bronze which is the color of naturally occurring chalcones.[2] The Chalcone family is important and has great interest because of its synthetic and biosynthetic approaches. Chalcone belongs to the flavonoid class of phenolic compounds, forming the largest bioactive natural product group.[3] Chalcone is a simple moiety found in many naturally occurring plants, fruits, and vegetables. The synthesized chalcone has been reported to exert multiple beneficial properties such as antioxidant, antiviral, antibacterial, antifungal, anti-tuberculosis, anticancer etc.

5. Acknowledgement:

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In addition to some biological properties referred before, in particular in paragraph 2 of this review, chalcones display a wide range of biological activities with interest in therapeutics.

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