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Science College / Chemistry Department

Synthesis, reactions, and bioactive compounds of chalcones and their derivatives

A Project Submitted to the Scientific Committee in The Chemistry Department in Partial Fulfillment of the Requirement for the Degree of Bachelor Science in Chemistry

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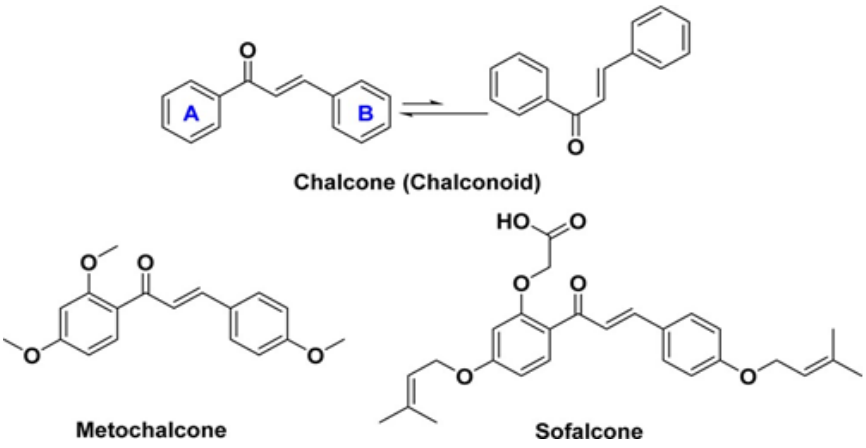
Abstract

Chalcone is an aromatic ketone that forms the central core of many important biological compounds, which are known as chalcones. Chalcones are the biogenetic precursors of favonoids and isofavonoids, which are abundant in plants. Chalcones are active lead molecules in medicinal chemistry for the discovery of new drugs. Here, we review properties, biosynthesis and structural diversity of natural chalcones. Then, we present the synthesis of chalcones and their biological activities with focus on structure–activity relationships. Pharmaceutically important are also discussed

1. Introduction

Heterocyclic compounds are the cyclic organic compounds which contain at least one hetero atom, the most common heteroatoms are the nitrogen, oxygen and sulphur but heterocyclic rings containing other hetero atoms are also widely known. Carbocyclic compound a cyclic organic compound containing all carbon atoms in ring formation. Heterocyclic compounds considered one of the vital classes of organic compounds, which are used in many biological fields, due to it is activity in multiple illnesses. Biological molecules such as DNA and RNA, chlorophyll, hemoglobin, vitamins and many more contains the heterocyclic ring in major skeleton. There are a lot of heterocyclic compounds which are have application in many common diseases such as chalcone . A chalcone is a simple chemical scaffold of many naturally occurring compounds and has a widespread distribution in vegetables, fruits, teas, and other plants.The word “chalcone” is derived from the Greek word “chalcos”, meaning “bronze”, which results from the colors of most natural chalcones.Chalcone compounds have a common chemical scaffold of 1,3-diaryl-2-propen-1-one, also known as chalconoid, that exists as trans and cis isomers, with the trans isomer being thermodynamically more stable The chalcone family has attracted much interest not only from the synthetic and biosynthetic perspectives but also due to its broad interesting biological activities. Therapeutic applications of chalcones trace back thousands of years through the use of plants and herbs for the treatment of different medical disorders, such as cancer, inflammation, and diabetes. Several chalcone-based compounds have been approved for clinical use. For example, metochalcone was once marketed as a choleretic drug, while sofalcone was previously used as an antiulcer and mucoprotective drug.



Scheme 1. Structures of chalcone and two clinically approved chalcone -based drugs.

1.1. Occurrence of Chalcones:

Chalcones are secondary plant metabolites, belonging to the flavonoid family that are abundantly present in edible plants, particularly fruits and vegetables. Therefore, chalcones belong to an important class of plant flavonoids (C_6-C_3-C_6 system) .Chalcones and their derivatives are important intermediates of the flavonoid biosynthetic pathway. Flavonoids are an important group of naturally occurring bioactive compounds. The majority of naturally occurring chalcones are polyhydroxylated aromatic compounds abundantly found in fruits, grains, legumes, vegetables, and beverages such as tea, coffee, red wine, beer, etc. The medicinal benefits of polyhydroxylated chalcones are mainly attributed due to their free radical scavenging activity (antioxidant property), which in turn mitigates oxidative stress-induced tissue damage associated with some chronic disorders such as cardiovascular diseases, inflammatory diseases and neurological disorders, and certain infectious diseases.

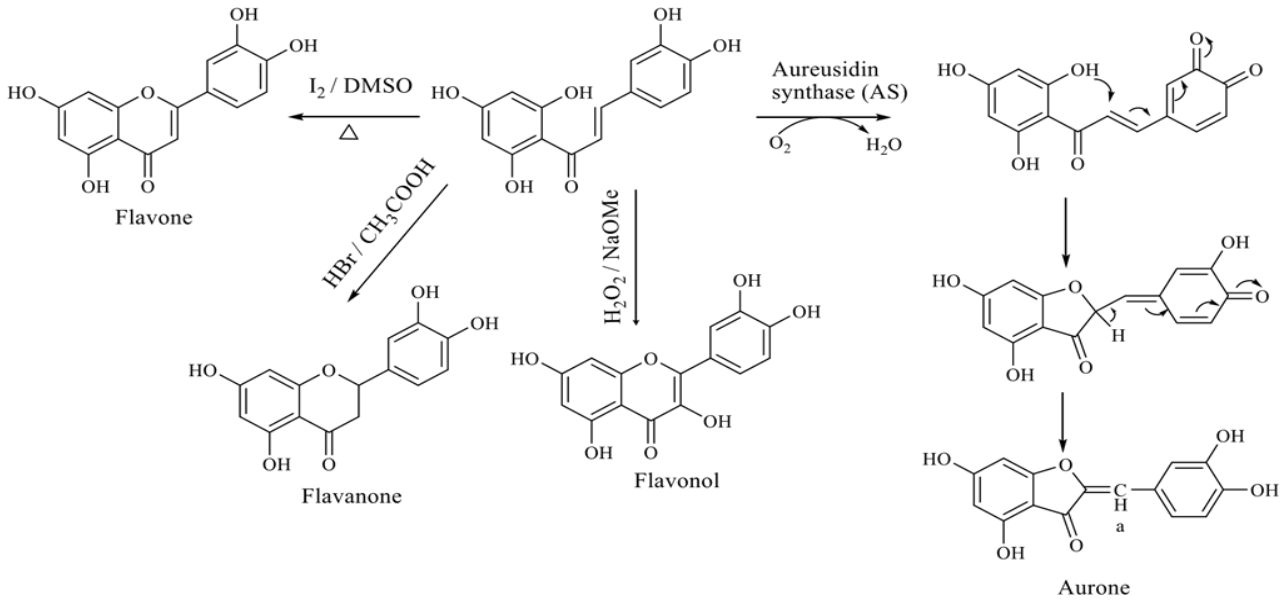
1.2 Physical and chemical properties

- Chalcones occur not only in flowers but also in leaves, fruits, roots, stems and all parts of the plant kingdom. The naturally occurring chalcones are generally crystalline solids, and they possess different colors including yellow, orange and brown. Chalcones are more stable than relative flavonoids and isoflavonoids. Chalcones are well soluble in alcohols, aqueous acidic and alkaline solutions, as well as in organic solvents, such as acetone, chloroform and dichloromethane. In alkaline solutions, they exhibit deep red or orange red colors. All chalcones are positive to Wilson test, i.e., pink colorization with conc. H_2SO_4. Also, chalcones treated with alcoholic ferric chloride solution resulted in violet colorization; this indicates the presence of free phenolic hydroxyl groups. Chalcones undergo isomerization reactions to give flavonoids . Chalcones on heating with traces of iodine in dimethylsulfoxide for 2 h give the corresponding flavones.

- Flavanones can be easily achieved through cyclization of chalcones treated with hydrobromic acid in glacial acetic acid. In this isomerization reaction, partial demethylation and debenzylation may occur.

- Chalcones were converted into flavonols by their oxidation using hydrogen peroxide in methanolic sodium hydroxide solution.

- Another important isomerization reaction is known to be the formation of aurones from the chalcone precursors in the presence of aureusidin synthase. The initial transformation of the *o*-dihydroxy groups of B- ring to an *o*-diquinone is a significant conversion because with one or without hydroxyl groups in ring B are anonymous at present.



Scheme 2: Isomerization reactions of chalcones such as flavanone, flavonol and aurone

2. Synthesis of chalcone and their derivatives

Chalcones are generally prepared by condensation reactions via base or acid catalysis. Although chalcones are one type of easily synthesizable α,β-unsaturated ketone, a growing number of new techniques and procedures have recently been reported because of their interesting biological activities and the development of various catalysts or reaction conditions.

6. Medicinal applications of chalcones

The chalcones and their derivatives have enormous importance in medicinal chemistry even in the twenty-first century because of their broad spectrum of the therapeutic potential and pharmacological properties. The chalcones derivatives show a variety of biological activities including anticancer, antibacterial, anticonvulsant, anti-HIV **14-16, Antidiabetic 17-20** antihyperglycemic, anti-inflammatory **30-34**, antileishmanial **35-38**, antimicrobial **9-13**, antioxidant **41-44**, antiprotozoal, antitubercular **45, 46**, and antiviral, anti-ulcerative. Some chalcones from synthetic as well as natural origin were acknowledged as active against tumor

cells along with antioxidant principles, by inhibiting superoxide production and lipid peroxidation, Millepachine (5) is isolated from *Millettia pachycarpa*. Licochalcone A (6) , isolated from *Glycyrrhiza inflate,* is another anticancer chalcone which exhibited toxicity toward L1210 leukemia and B16 melanoma cells. A new class of chalcone (7) proposed as an antimitotic agent by increasing the survival of mice inoculated with L1210 leukemia with doses range of 2.655.0 mg/kg. Butein (**8**) is another natural chalcone which can suppress the several human cancers including breast cancer, colon carcinoma, osteosarcoma and hepatic stellate cells in vitro

Scheme 35 :Diverse biological activities of chalcone

8. Characterization of Chalcones

The structure of the synthesized chalcones can be characterized by IR, NMR and mass spectroscopy.

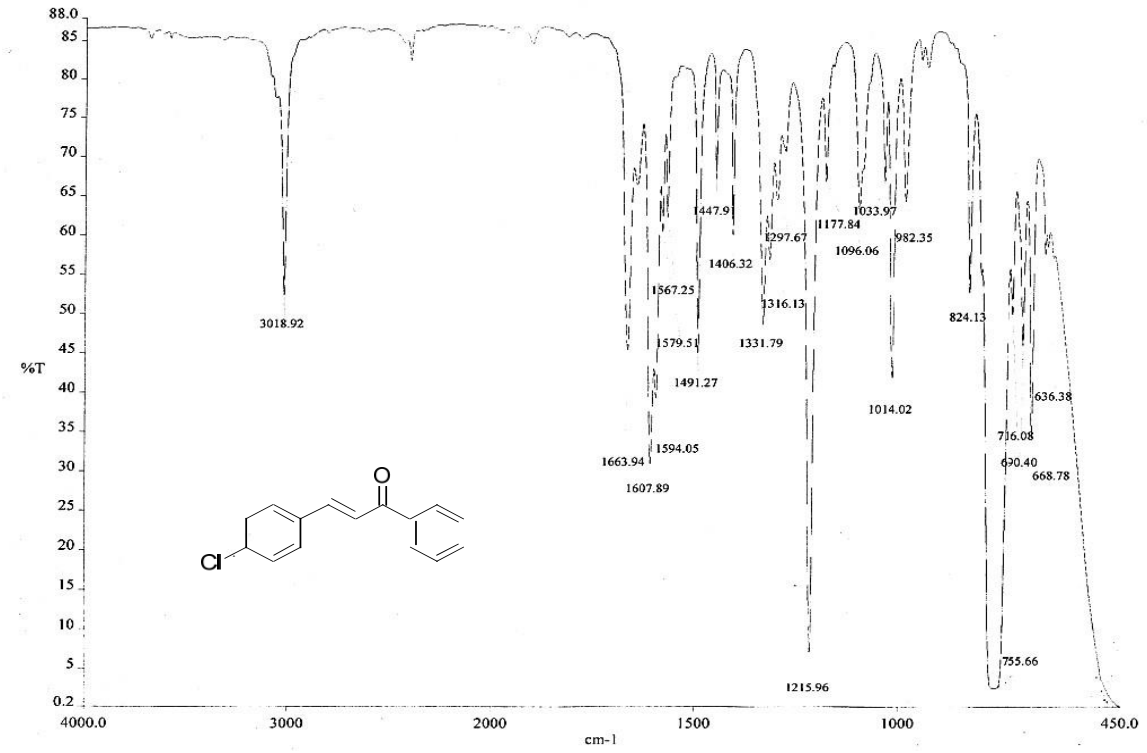
- UV Spectrum

The UV spectrum of chalcones consists of two essential absorption band: band I and relatively a minor band, band II. In chalcones, band I usually appears in 340–390 nm, although a minor inflection or peak often occurs at 300–320 nm. Band II appears in 220–270 nm.

- IR Spectrum

In the IR spectra of chalcones asymmetric and symmetric stretching vibrations of the aromatic C–H bonds are seen at 3120–3080 cm^{-1} and 3060–3040 cm^{-1} ranges with two low intensity bands. C–H stretching band of the =C–H group is observed at 3030–3010 cm^{-1}. The bands at 1610–1570 cm^{-1} are assigned to the vibrations of the aromatic ring. The inplane deformation of the =C–H bond is appeared as broad weak band at 1460–1430 cm^{-1}. The carbonyl stretching vibrations for the enones (=C–C=O) can be found between 1650 and 1685 cm^{-1}.

IR Spectra



Scheme 45;IR spectrum of *trans*-4-chlorochalcone ($CHCl_3$ solution)

1. NMR Spectrum

The $_1$H-NMR spectrum of double bonds of chalcones were seen at 5.4 and 6.1 ppm.

The aromatic regions were observed at 6.9–8.1 ppm.

In $_{13}$C-NMR spectrum of chalcones, the carbonyl carbon usually appears between δ 186.6 and 196.8. The α- and β- carbon atoms with respect to the carbonyl group give characteristic signals between δ 116.1–128.1 and δ 136.9–145.4 respectively.

^{1}H NMR Spectra

Conclusion

This review provides a brief overview of chalcone chemistry and discusses different methods for synthesizing and describing chalcone derivatives, which have a wide range of thier biological activities, potential medical uses and industrial applications. Also, chalcones are involved in different Michael addition reactions and act as precursors for other substances like flavonoids and coumarins through these processes; thus, they have attracted attention of scientists due to their distinct structures and pharmacological characteristics. Additionally, chalcones are adaptable and can be used for synthesis of several products for food, medicine, cosmetic, and skincare applications. Chalcone derivatives are fascinating compounds with numerous applications in the medicinal, pharmacological, and optical fields.

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زانکۆی سەڵاحەدین-هەولێر

کۆلێژی زانست

بەشی کیمیا

دروستکردن و کارلێککردن و پێکهاتە چالاکە زیندووەکانی چالکۆنەکان و وەرگیراوەکانیان

پرۆژەیەک پێشکەش بەلێژنەی زانستی کراوە لە بەشی کیمیا

لە بەشی جێبەجێکراو پێو یستی بۆ پلەی زانستی بەکالۆریۆ س لە کیمیا

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