Send Orders of Reprints at reprints@benthamscience.org

1394 *Mini-Reviews in Medicinal Chemistry*, **2012**, *12*, **1394-1403**

Synthesis and Biological Evaluation of Chalcone Derivatives (Mini Review)

Syed Nasir Abbas Bukhari*, Malina Jasamai and Ibrahim Jantan

Drug and Herbal Research Center, Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Kuala Lumpur, 50300, Malaysia

Abstract: Chalcones are the principal precursors for the biosynthesis of flavonoids and isoflavonoids. A three carbon α, β-unsaturated carbonyl system constitutes chalcones. Chalcones are the condensation products of aromatic aldehyde with acetophenones in attendance of catalyst. They go through an assortment of chemical reactions and are found advantageous in synthesis of pyrazoline, isoxazole and a variety of heterocyclic compounds. In synthesizing a range of therapeutic compounds, chalcones impart key role. They have showed worth mentioning therapeutic efficacy for the treatment of various diseases. Chalcone based derivatives have gained heed since they own simple structures, and diverse pharmacological actions. A lot of methods and schemes have been reported for the synthesis of these compounds. Amongst all, Aldol condensation and Claisen-Schmidt condensation still grasp high up position. Other distinguished techniques include Suzuki reaction, Witting reaction, Friedel-Crafts acylation with cinnamoyl chloride, Photo-Fries rearrangement of phenyl cinnamates etc. These inventive techniques utilize various catalysts and reagents including $SOCl_2$ natural phosphate, lithium nitrate, amino grafted zeolites, zinc oxide, water, Na_2CO_3, PEG400, silicasulfuric acid, $ZrCl_4$ and ionic liquid etc. The development of better techniques for the synthesis of α, β- unsaturated carbonyl compounds is still in high demand. In brief, we have explained the methods and catalysts used in the synthesis of chalcones along with their biological activities in a review form to provide information for the development of new-fangled processes targeting better yield, less reaction time and least side effects with utmost pharmacological properties.

Keywords: Chalcones, Claisen-Schmidt condensation, flavonoids, anticancer, Anti-inflammatory.

INTRODUCTION

Chalcones are precursors in the synthesis of several beneficial compounds such as flavonoids and isoflavonoids [1]. Flavonoids are the regular constituents of human diet. Chalcones are made up of a three carbon α, β-unsaturated carbonyl system. Condensation of aromatic aldehydes with acetophenones in presence of catalyst yield chalcones [2]. Chalcones initiate a miscellany of chemical reactions together with the synthesis of pyrimidine, isoxazoles and pyrazolines. Chalcones act as mediators in the synthesis of useful therapeutic compounds. Special consideration has been given to chalcones because of their simple structures and diverse pharmacological activities. Noteworthy activities of chalcones are listed in Table **2**. Owing to these stated reasons, the synthesis of chalcones and chalcone based functionalized derivatives are still under taken. Many researchers around the world have reported schemes for the synthesis of these compounds. Among all the stated methods, Aldol condensation and Claisen-Schmidt condensation still hold the prime position. The superlative method for the synthesis of chalcones is the conventional Claisen-Schmidt condensation in the presence of aqueous alkaline bases [3], $Ba(OH)_2$ [4], LiOH, microwave irradiation and ultrasound irradiation [5]. Other famous techniques include Suzuki reaction [6], Witting reaction, Friedel-Crafts acylation with cinnamoyl chloride and Photo-Fries rearrangement of phenyl cinnamates.

*Address correspondence to this author at the Faculty of pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300, Kuala Lumpur, Malaysia; Tel: 0060142765730;
E-mail: snab_hussaini@yahoo.com

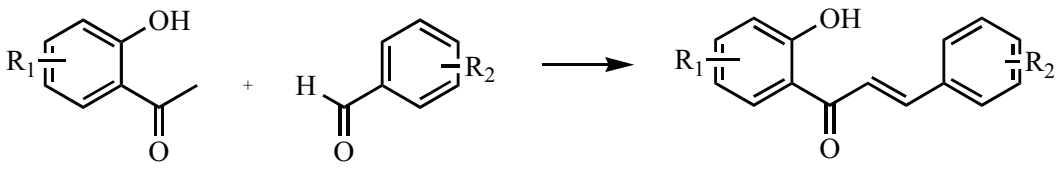
Chalcone synthesis via aldol condensation requires two-steps, aldol formation and dehydration. Given that aldol addition is reversible, Claisen-Schmidt condensation using enol ether has came out as an alternative pathway. Aldol reaction is also performed under acidic conditions [7] courtesy HCl, BF_3, B_2O_3, and *p*-toluenesulfonic acid. In the past few years, a range of adapted methods for the synthesis of chalcones have been reported. These innovative techniques use various catalysts and reagents including $SOCl_2$ [8] natural phosphate, lithium nitrate [9], amino grafted zeolites [10], zinc oxide, water [11], Na_2CO3 [12], PEG400 [13], silicasulfuric acid [14], $ZrCl_4$ and ionic liquid [15]. The accomplishment of these novel methods has been hindered by limitations e.g. harsh reaction condition, toxic reagents, strong acidic or basic conditions, prolonged reaction times, poor yields and low selectivity. The development of improved strategies for the synthesis of α, β- unsaturated carbonyl compounds is still required. In summary, this paper explained the methods and catalysts used in the synthesis of chalcones to provide information for the development of new processes which will give better yield, less reaction time and minimum by products. We have also abridged the biological activities of synthetic chalcones along with references to show the importance of chalcones and also to provide the information for discovery of new derivatives with better therapeutic activities.

DIFFERENT SYNTHETIC METHODS

The Claisen-Schmidt Reaction

The condensation (Scheme **1**) between acetophenone and benzaldehyde derivatives yielding α, β-unsaturated ketone

1875-5607/12 $58.00+.00



(1) **(2)** **(3)**

Scheme (**1**). The Claisen-Schmidt Reaction.

e.g. chalcone is referred to as Claisen-Schmidt reaction [16]. It is the best method of instituting the C6-C3-C6 flavonoid nucleus owing to the accessibility of preliminary materials such as 2- hydroxyacetophenone (**1**) and a C6-C1 unit of benzaldehyde derivatives (**2**) to acquire a 2′-hydroxychalcone (**3**). 2′-hydroxychalcone (**3**) includes A-ring substituent supplied by the acetophenone (indicated as R_1) and B-ring substituent contributed by the benzaldehyde (indicated as R_2). The conventional Claisen-Schmidt reaction is typically carried out by aqueous sodium or potassium hydroxide or ethanolic sodium ethoxide at 50°C for several hours. Normally, the benzaldehyde derivative is used in excess. Light is absorbed in the visible region courtesy extensive conjugation of products formed, lending them yellow colour [17].

THE ALLAN-ROBINSON CONDENSATION

The Allan-Robinson Condensation is used mainly to synthesize flavones with chalcones as their precursors. The condensation of 2,4,6-trihydroxyacetophenone (**4**) with aromatic anhydrides (**5**) catalysed by the salt of the same acid will make corymbosin (**6**) [18] (Scheme **2**).

SYNTHESIS OF CHALCONES *VIA* SUZUKI COUPLING REACTION

In Suzuki coupling reaction, benzoyl chlorides (**10**) and phenylvinylboronic acid (**9**), [6] were reacted to produce chalcones. Dehydrogenative borylation of *para*-methoxystyrene (**7**) by pinacolborane oxidative addition-dehydrogenation, catalyzed by the rhodium complex, $RhCI(cod)_2$ yielded *para*-methoxyphenylethenylboronic acid pinacol ester (**8**). Oxidative cleavage of (**8**) by sodium periodate in THF/water gave *para*methoxyphenylethenylboronic (**9**) mandatory for the Suzuki coupling reaction. The coupling between (**9**) and (**10**) formed 3′,4′,4-trimethoxychalcone (**11**) with anhydrous toluene as solvent, catalyzed by tetrakis(triphenylphosphine) palladium(0) and base; cesium carbonate as illustrated in (Scheme **3**) [6].

SYNTHESIS OF CHALCONES BY DIRECT CROSS-COUPLING REACTION

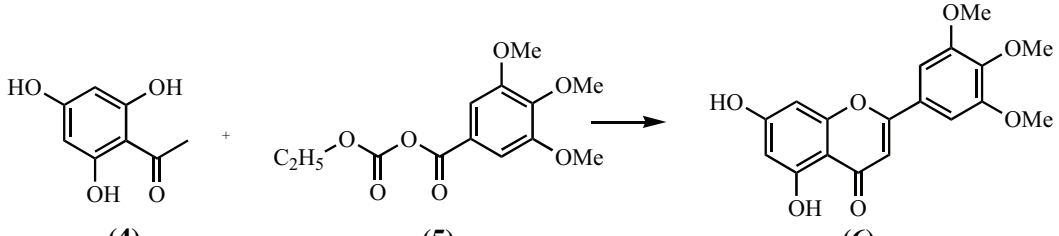
Benzoyl chlorides and potassium styryltrifluoroborates are cross-coupled directly to the corresponding α,β-unsaturated aromatic ketones catalysed by $PdCl_2$(dtbpf) under microwave heating. Microwave irradiated palladium-catalyzed direct cross-coupling reaction of benzoyl chlorides and potassium styryltrifluoroborates to form the corresponding α,β-unsaturated aromatic ketones has been reported for the first time [19].

SYNTHESIS OF CHALCONE USING BORONTRI-FLUORIDE-ETHERATE

A new technique was developed by Narender and Reddy (2007) using BF_3- Et_2O to create a variety of substituted chalcones. Priority has been given to this method because of high yields, simple work-up, short reaction times and no side reactions. This method has been employed for solvent free reactions and for reactions concerning liquid reactants which possess base sensitive functional groups e.g. esters and amides. *O*-acylated (**14**) or *N*-acylated chalcones (**17**) in high yields were produced by condensation reaction between *O*-acylated (**12**) or *N*-acylated acetophenone (**15**) and the individual aromatic aldehyde (**13**) or (**16**), catalyzed by BF_3-Et_2O [20] as illustrated in (Scheme **4**).

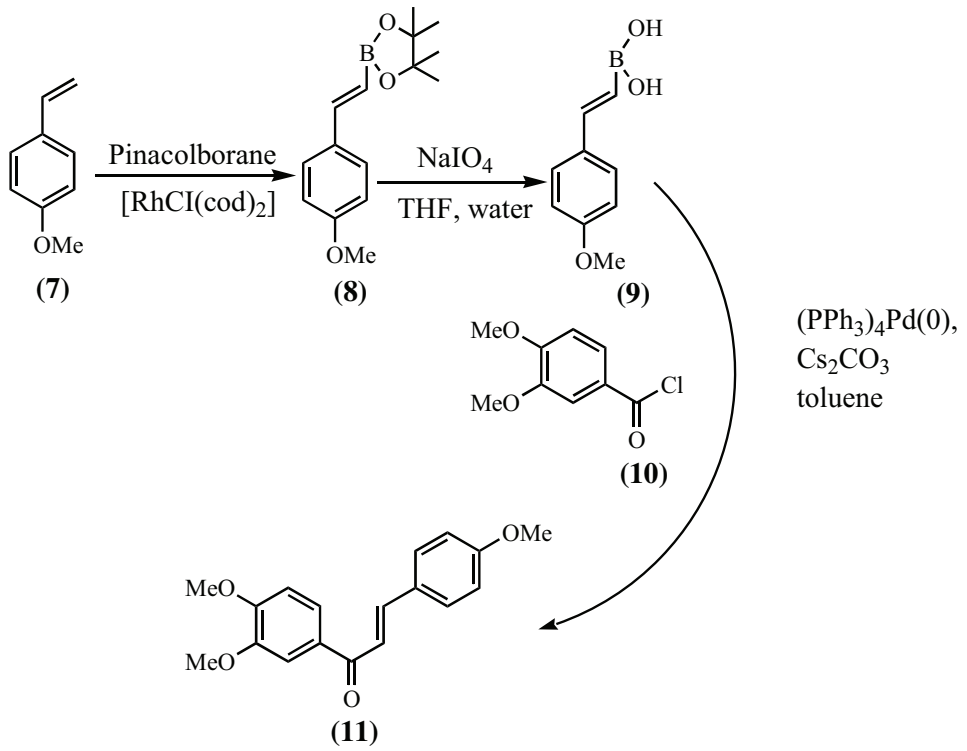
SYNTHESIS OF CHALCONES *VIA* MICROWAVE IRRADIATION

Without using solvents, the blend of supported reagents and microwave irradiation can be used to carry out a variety of reactions in short time intervals and with high conversions and selectivity. This approach appreciated by researchers because it presents copious advantages over conventional heating methods and fastens the organic reactions. Microwave irradiation was subjected to the air-dried paste of 2′-hydroxyacetophenone (**1**), benzaldehyde (**2**) and anhydrous K_2CO_3 for 3-5 minutes to fabricate

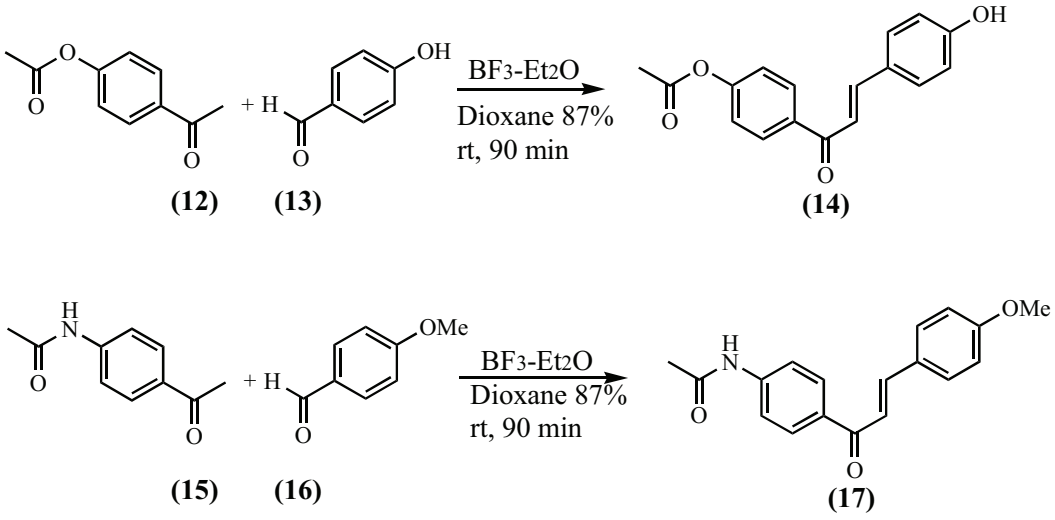


(4) **(5)** **(6)**

Scheme (**2**). The Allan-Robinson Condensation.



Scheme (**3**). Synthesis of Chalcones *via* Suzuki Coupling Reaction.



Scheme (**4**). Synthesis of *O*-acylated and *N*-acylated chalcones using BF_3-Et_2O.

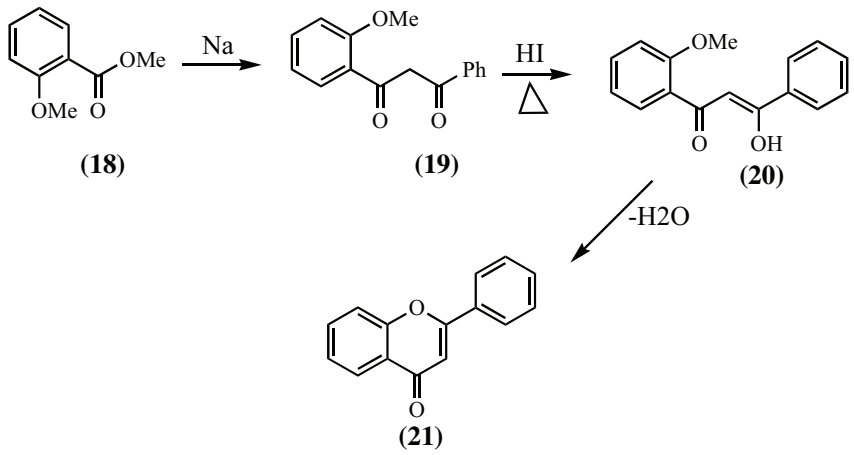
2′-hydroxychalcones (**3**). The product was clear solid with a high yield percentage (80-90%) [21].

THE VON-KONSTANECKI METHOD

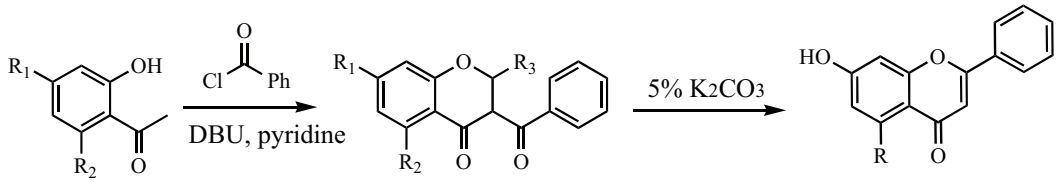
This is a widespread method for making flavones which involves a reaction of 2-methoxybenzoate (**18**) and acetophenone in attendance of sodium to form (**19**) as shown in (Scheme **5**). Diketone compound (**20**) was prepared by Claisen condensation . Flavones (**21**) were synthesized by the treatment of (**20**) with an acid afforded compound (**22**) and removal of water [22].

GANGULY'S SYNTHESIS OF FLAVONE

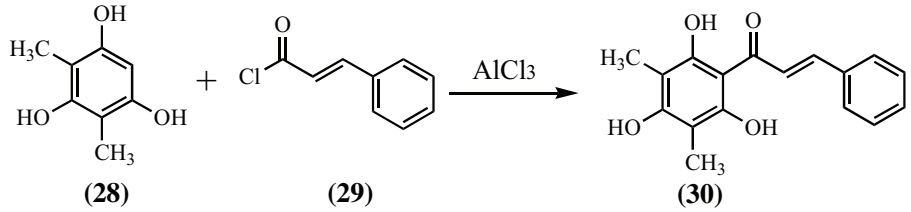
Baker-Venkataraman method of synthesizing flavones was modified by Ganguly and co-workers (2005). In this course of action, 2′,4′,6′- trihydroxyacetophenone (**22**) and 2′,4′-dihydroxyacetophenone (**23**) were heated with benzoyl chloride catalyzed by base Diazabicycloundecene (DBU), pyridine afforded 3-acylflavones (**24**) and (**25**). Flavones (**26**) and (**27**) were yielded by the additional reaction of acylflavones (**24**) and (**25**) with 5% potassium carbonate as shown in (Scheme **6**). Modified Baker-Venkataraman reactions were used in the synthesis of flavones precursors [23].



Scheme (**5**). The Von-Konstanecki Method.



Scheme (**6**). Ganguly's synthesis of flavones.



Scheme (**7**). Friedel-Crafts acylation producing chalcone.

FRIEDEL-CRAFTS ACYLATION

In addition to the Claisen-Schmidt reaction, chalcones can also be synthesized by direct Friedel-Crafts acylation of a phenol. In this course, the phenol develops into A-ring whilst the acylating agent presents both the B-ring carbons and the three carbon bridge to form C6-C3-C6 unit. 2′,4′,6′-trihydroxy-3′,5′-dimethylchalcone (**30**) was fabricated by Friedel-Crafts acylation of 2,4-dimethyl-1,3,5-triolbenzene (**28**) with 3-phenylpropionyl chloride (**29**) [24].

JULIA-KOCIENSKI OLEFINATION

An innovative role of Juliae_Kocienski olefination for the production of chalcones and flavanones has been illustrated [25]. New reagents such as 2-(benzo[d]thiazol-2-ylsulfonyl)-1-phenylethanones developed for Julia-Kocienski olefination, react with aldehydes in the presence of a base to give chalcones in good to excellent yields. Courtesy of one-pot intra-molecular cyclization, 2 (benzo[d]thiazol-2-ylsulfonyl)-1-(2-hydroxyphenyl) ethanone reacted with aromatic aldehydes and furnished flavanones in good yields.

GRINDING TECHNIQUE

A proficient and operationally simple reaction between substituted 2-acetyl-1-naphthol/2-acetyl-1-naphthol and diversely substituted benzaldehydes catalyzed by base gave chalcones in quantitative yield via grindstone technique [26]. Mild reaction conditions, no requirement of catalyst, non-hazardous, environmentally safer, excellent yield in short reaction time are notable advantages of this method.

VARIOUS CATALYSTS REPORTED FOR CHALCONE SYNTHESIS

Chalcones have been synthesized by a number of synthetic methods as described above. As catalyst is a necessary component of every technique, the researchers have used a variety of catalysts. Here the highlighted the catalysts that are reported for chalcone synthesis (Table **1**).

Table 1. Variety of Catalysts Used for Chalcone Synthesis

Sr. No	Catalysts	Description
1	Alkali	Alkali is used as an aqueous solution in suitable concentration viz. 30 %, 40 %, 50 % and 70 %. According to literature, about 75% of chalcones synthesis is accomplished by using alkali.
2	Activated hydrotalcites	In the presence of calcined-rehydrated hydrotalcites as solid-base catalysts, the Claisen–Schmidt condensation between benzaldehyde and acetophenone is executed [16].
3	Natural phosphate modified with sodium nitrate	A strongly basic catalyst prepared from economical precursors by impregnation of natural phosphate (NP) with a solution of sodium nitrate, followed by calcination at 900 °C [27].
4	Calcined sodium nitrate/natural phosphate	An extremely efficient basic catalyst produced by the alteration of natural phosphate (NP) with sodium nitrate by calcination for the Claisen–Schmidt condensation [28].
5	Carbon-Based Solid Acid	Aromatic aldehydes carry out cross-aldol condensation with ketones in the presence of carbon-based solid acid under solvent- free environment to obtain the consequent α,β-unsaturated aldol compounds in excellent yields [29].
6	Zn–Al hydrotalcite adhere ionic liquid	In Claisen–Schmidt condensation of 2-hydroxy acetophenone and benzaldehyde to chalcone and flavanone, the calcined Zn–Al (6) hydrotalcite is a dynamic catalyst [30].
7	$SOCl_2$/EtOH Catalytic system	Various substituted chalcones are synthesized by aldol condensation in the presence of $SOCl_2$/EtOH as a catalyst [8]. The reaction of $SOCl_2$ with absolute ethanol liberates HCl *in situ*.
8	Activity enhancement of natural phosphate catalyst by lithium nitrate	A new catalyst $LiNO_3$/NP is synthesized by the addition of small amounts of lithium nitrate to natural phosphate followed by calcination. Using low quantities of $LiNO_3$/NP under mild reaction conditions produces several chalcones [9].
9	Effect of Li on MgO catalyst	The effects of Li on the structure, surface basicity and catalytic activity of MgO for the synthesis of flavanone have been investigated by Jose A. *et al.* [31]. The rate of the Claisen–Schmidt condensation was increased by the introduction of low amounts of Li (i.e., ≤ 0.1 wt.%), which is the most important step in this process.
10	Re-usable hydroxyapatite	Using microwave irradiation, hydroxyapatite was discovered to be an efficient heterogeneous catalyst in Claisen–Schmidt condensation [32]. The catalyst activity was improved by water and was thought to act as a co-catalyst because of the high activation observed in its presence.
11	Acyclic acidic ionic liquids	The synthesis of chalcones by Claisen–Schmidt condensation has been catalysed by some recyclable acyclic SO_3H-functionalized ionic liquids [15]. Decantation technique separated chalcones from the catalyst.
12	Li–Al layered double hydroxides	The Claisen–Schmidt condensation between 2′-hydroxyacetophenone and benzaldehyde to form 2′-hydroxychalcone and the following isomerization of 2′-hydroxychalcone was catalysed by Li–Al layered double hydroxide solid [33].
13	Mesoporous zirconium phosphate	Synthesis of various industrially fundamental chemicals under microwave irradiation (MWI) without solvent over mesoporous zirconium phosphate (m-ZrP) has been reported [34]. By virtue of a precursor solution of zirconium carbonate complex as zirconium source and cetyltrimethylammonium bromide (CTAB) as a pore-directing agent, m-ZrP is synthesized by microwave irradiation in basic medium.
14	KF/natural phosphate	The strong basic activity of potassium fluoride supported on natural phosphate can be capably used to endorse the Claisen–Schmidt reaction of 2'-hydroxyacetophenones with benzaldehydes [35].
15	Amino grafted zeolites	The synthesis of chalcones via Claisen-Schmidt condensation between benzaldehyde and acetophenone by sonochemical and thermally activated reactions catalysed by a new-fangled zeolite has been reported [10]. The catalysts were primed by splicing amino groups on sodium and cesium swapped X zeolite.
16	Mesoporous AlSBA-15-SO_3H hybrid material	A mixture of aluminum isopropoxide, 3-mercaptopropyltriethoxysilane, tetraethoxysilane, and triblock copolymer surfactant was treated hydrothermally to make SBA-15 materials functionalized with both propylsulfonic acid groups and aluminum species (AlSBA-15-SO_3H) in single step [36].
17	Silicotungstic acid	The Claisen Schmidt condensation of aryl methyl ketones with a series of aromatic aldehydes at room temperature in the presence of the catalyst silicotungstic acid (STA) has synthesized 1,3-diaryl-2-propenones successfully [37]. This method provides a chemo-selective and well-organized synthesis of 1,3-diaryl-2-propenones in outstanding yields.
18	Sulfated Degussa titania	Sulfated TiO_2–P25 (Degussa titania) has been synthesized by sol–gel method via H_2SO_4. Lewis acidity of Degussa tiatania is increased by sulfate loading by H_2SO_4. This catalyst is reasonably priced, gives an excellent yield with less reaction time and effortlessly recyclable for the synthesis of quinaxalines, dipyridophenazines and chalcones under microwave irradiation [38].

(Table 1) contd….

Sr. No	Catalysts	Description
19	Alkaline-doped carbons	Two basic activated carbons (Na- and Cs-Norit) have been used as catalysts [5]. The order of activity is Na-Norit < Cs-Norit. Sonochemical irradiation has been utilized to synthesize chalcones.
20	Novel solid sulfonic acid from bamboo	Bamboo char sulfonic acid, a novel solid acid catalyst has been prepared and used in the synthesis of chalcones at high yields in a heterogenous acid system in solvent-free condition [39].
21	Aminopropylated silica sol–gel	Aminopropylated nanosilica was synthesized by an uncomplicated sol–gel process from tetraethyl orthosilicate (TEOS) and subsequently it was functionalized with dissimilar quantities of 3-aminopropyltriethoxysilane (APS) under toluene reflux [40].
22	TiO_2–SO_4^{2-}	The sol–gel method was used to prepare TiO_2–SO_4^{2-} by H_2SO_4. TiO_2–SO_4^{2-} is used for the production of chalcones under microwave irradiation [41]. The Lewis acidity of TiO_2 is increased by sulfate loading by H_2SO_4.
23	Bismuth(III)chloride	An environmental friendly method for the synthesis of chalcones by the Claisen_Schmidt condensation of aldehydes with ketones via ecological non-toxic bismuth(III)chloride catalyst under solvent-free condition has been reported [42].
24	$LiOH{\cdot}H_2O$	Commercially available $LiOH{\cdot}H_2O$ was reported to be an enormously resourceful twin commencement catalyst for Claisen–Schmidt condensation of various aryl methyl ketones with aryl/heteroaryl aldehydes, providing an easy synthesis of 1,3-diaryl-2-propenones under even-tempered conditions [43].
25	Acid-clays	A novel solvent free method of synthesis of trans-chalcones has been reported. The theme of the process is the ultrasound irradiation of the reagents (aryl methyl ketones and aryl aldehydes) catalyzed by industrial acid-montmorillonites [44].
26	Zirconium chloride	Zirconium chloride has been investigated to be a highly competent catalyst for the aldol condensation of aldehyde and ketone under solvent-free conditions, at room temperature [45].
27	Modified hydroxyapatite with sodium nitrate	The heterogeneous catalysis of the Claisen–Schmidt condensation with a small amount of sodium nitrate/hydroxyapatite produces chalcones expediently [46].
28	Iodine	The condensation of acetophenones with various aromatic aldehydes to prepare chalcones is reported to be catalyzed by molecular iodine [47].
29	Anhydrous K_2CO_3	Economical and non-toxic anhydrous K_2CO_3 has been used as the condensing agent in the latest study [48].
30	Silica-Sulphuric Acid Reagent	There are two series of α, β unsaturated ketones derived from biphenyl, 9H-fluorenyl, and ketones with a variety of substituted benzaldehydes, under solvent free conditions using silica-sulphuric acid as a reagent in an oven [49].
31	$NaOH$-Al_2O_3	$NaOH$-Al_2O_3 is used as a catalyst in a novel method for the synthesis of 1,3-diaryl-2-propene-1-ones via Claisen-Schmidt without using solvent [50].
32	Zinc oxide supported metal oxide catalysts	Liquid phase Claisen–Schmidt condensation was carried out between 20-hydroxyacetophenone and benzaldehyde to form 20-hydroxychalcone, followed by intramolecular cyclisation to make flavanone catalysed by zinc oxide supported metal oxide under solvent free condition [51].
33	Brønsted acidic ionic liquids as a dual catalyst	Conventional homogenous/heterogeneous catalysts and solvents for Claisen–Schmidt (CS) condensation between acetophenone and benzaldehyde to produce chalcones can be substituted by Brönsted acidic ionic liquids (ILs). The ILs exhibited superior catalytic and reusable abilities [52].
34	ZSM-5 catalysts	The reaction of 2'-hydroxyacetophenone with benzaldehyde was catalyzed by H-ZSM-5, Mg-ZSM-5 and Ba-ZSM-5 respectively at 140°C. The compounds were 2′-hydroxychalcone and flavanone [53].
35	Metal (II) complex catalysts	Complexes of Co(II), Ni(II), Cu(II), and Zn(II) acetates with 2,2′-bipyridine were effectual catalysts to afford α,β,-unsaturated ketones in high yields without producing any self condensation products [54].
36	Anhydrous $RuC1_3$	Cross aldol condensations of different ketones with various aromatic aldehydes in sealed tube under solvent free conditions is catalysed by anhydrous $RuC1_3$ devoid of any self condensations.
37	Hydrochloric acid	In a suitable solvent like ethylacetate, dry hydrochloric gas was used at 0°C as a condensing agent in a few syntheses of chalcones from aromatic ketones. Methanolic solution of dry hydrochloric acid gas was also employed by Lyle, Paradis [55] at 0°C.

Table 2. Biological Properties of Chalcone Derivatives

Sr. No.	Biological Activity	Functional Groups Promoting the Biological Activity	References (Number)	
			Specific	Others
1	Anti- Inflammatory	Methoxy groups at 3,4,5- and/or 3',4',5'-positions	Sawle *et al.* 2008 [56]	[57], [58], [59], [60], [61], [62]
		2′-Hydrophobic group (benzyloxy or cyclohexylmethoxy) in ring A; 6′ hydroxyl group in ring A	Yang *et al.* 2007 [63]	
		2′-Hydroxyl group in ring A	Jin *et al.* 2007 [64]	
		4′-Azide group in ring A; 4-methyl group in ring B	Chiaradia *et al.* 2008 [65]	
		EW groups in ring B, mainly at C-2	Zarghi *et al.* 2006 [66]	
2	Antifungal	Hydroxyl groups in ring B, mainly at C-2	Batovska *et al.* 2007 [67]	[62], [68]
3	Antibacterial	Hydrophilic groups (NO_2 or OH) in ring B	Sivakumar *et al.* 2007 [69]	[62], [68]
		2′- and 2-Hydroxyl groups	Ansari *et al.* 2005 [70]	
		Piperazinyl moiety at C-4′ in ring A; 3-nitro group in ring B	Tomar *et al.* 2007 [71]	
		Basic amino function (piperidine) removed from ring B by 4, 5 or 6 methylene groups	Nowakowska *et al.*2008 [72]	
		6′-Hydroxyl group in ring A; basic (N-methylpiperidin-4-yl) group at C- 5' in ring A	Liu *et al.* 2007 [73]	
4	Antimalarial	Basic group at C-4′ in ring A; 4- chloro group in ring B	Mishra *et al.* 2008 [74]	[75], [76], [77], [78], [79]
5	Antitumor	2- or 3-Hydroxyl group in ring B	Loa *et al.* 2008 [80]	[81]
6	Antimicrobial	nitro group at *m*-position in benzaldehyde ring is well tolerated in terms of activity against bacteria (S. aureus). presence of electron-attracting groups	V. Tomar *et al. 2007* [71]	[71], [72]
7	Antiviral		[82]	
8	Antitubercular		[83]	
9	Antioxidant	Catechol group in ring B; 2′-hydroxyl group in ring A	Cai *et al.* 2006 [84]	[60], [61], [85]
		3′-Prenyl group in ring A; 2′-hydroxyl group in ring A	Vogel *et al.* 2008 [60]	
		Pyrogallol group in ring A	Mohamad *et al.* 2004 [86]	
		2,3- or 3,4-Catechol groups in ring B; 2,5-hydroquinone motif in ring B	Kim *et al.* 2008 [87]	
		3,4-Catechol group in ring B; 3,4,5-pyrogallol group in ring B	Nishida & Kawabata 2006 [88]	
10	Anti-Mitotic	Methoxy groups in ring A	Boumendjel *et al.* 2008 [89]	[85]
11	Anti-Leishmanial	The sulphonamide 4-methoxychalcone derivatives exhibited a potential antileishmanial activity *in vitro*.	Carla R. *et al.* 2009 [90]	[91], [92]
12	Anti-Platelet	Pyridyl group substituent as ring-B and hydroxy group at position C-3 in ring-A	M. Vijaya *et al.* 2011 [93]	[94]
13	Anticancer	Lack of substituents in ring B	Li *et al.* 2008 [95]	[61], [62], [96]
		3′,4′,5′-Trimethoxy moiety in ring A; amino group in ring B	LeBlanc *et al.* 2005 [97], Pati *et al.* 2005 [98]	
		3-Prenyl group in ring B	Rao *et al.* 2008 [99]	
		4-Hydroxy group in ring B; dihydroxy motif in ring B; 3′-prenyl group in ring A of 2,5-dihydroxychalcones	Vogel *et al.* 2008 [60]	
		A substituent able to form hydrogen bonds at C-4 in ring B	Cabrera *et al.* 2007 [100]	

(Table 2) contd….

Sr. No.	Biological Activity	Functional Groups Promoting the Biological Activity	References (Number)	
			Specific	Others
14	Antihypertensive	-		[101]
15	Antiprotozoal	-		[102]
16	TNF-α and IL-6 inhibitors	-		[103]
17	Enzyme inhibitory activity	2′,4′,6′-Phloroglucinol motif in ring A	Jun *et al*. 2007 [104]	
		2,4-Resorcinol subunit in ring B	Khatib *et al*. 2005 [105]	

*other supporting references.

BIOLOGICAL ACTIVITIES OF CHALCONES

Chalcones and their derivatives are catching attention due to numerous pharmacological applications. So we have summarized the reported biological activities of chalcones along with references in Table **2** to show their importance and also to provide the information for discovery of new derivatives with better activities.

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

ACKNOWLEDGEMENTS

Author pays special thanks to Dr. Wahab bin Amjad, Dr. Waqas Ahmed and Dr. Adeel Butt for cooperation and useful suggestions in collection and compiling of literature data.

REFERENCES

[1] Avila, H.; Smania, E.; Monache, F.; Junior, A. Structure-activity relationship of antibacterial chalcones. *Bioorg. Med. Chem.,* **2008**, *16*, 9790–9794.

[2] Nowakowska, Z. *Eur.J.Med.Chem,* **2007**, *42*, 125.

[3] Rajendra Prasad Y; Lakshmana Rao A; Rambabu R; Ravi Kumar P Synthesis and biological evaluation of some novel chalcone derivatives. *Oriental J. Chem,* **2007**, *23*, 927-937.

[4] Srinivasa Rao M.; Kotesh J.; Narukulla R.; Duddeck H. Synthesis and spectroscopic characterization of some chromanochalcones and their dihydro derivatives. *Arkivoc,* **2004**, *xiv*, 96-102.

[5] Calvino V.; Picallo M.; López-Peinado A. J.; Martín-Aranda R. M.; Durán-Valle C. J. Ultrasound accelerated Claisen–Schmidt condensation: A green route to chalcones. *Appl. Surf. Sci.,* **2006**, *252*, 6071-6074.

[6] Eddarir, S.; Cotelle, N.; Bakkour, Y.; Rolando, C. An efficient synthesis of chalcones based on the Suzuki reaction. *Tetrahedron Lett.,* **2003**, *44* (28), 5359-5363.

[7] Konieczny, M. T.; Konieczny, W.; Sabisz, M.; Skladanowski, A.; Wakieć, R.; Augustynowicz-Kopeć, E.; Zwolska, Z. Acid-catalyzed synthesis of oxathiolone fused chalcones. Comparison of their activity toward various microorganisms and human cancer cells line. *Eur.J.Med.Chem,* **2007**, *42* (5), 729-733.

[8] Petrov, O.; Ivanova, Y.; Gerova, M. SOCl2/EtOH: Catalytic system for synthesis of chalcones. *Catal. Commun.,* **2008**, *9* (2), 315-316.

[9] Sebti, S. d.; Solhy, A.; Smahi, A.; Kossir, A.; Oumimoun, H. Dramatic activity enhancement of natural phosphate catalyst by lithium nitrate. An efficient synthesis of chalcones. *Catal. Commun.,* **2002**, *3* (8), 335-339.

[10] Perozo-Rondón, E.; Martín-Aranda, R. M.; Casal, B.; Durán-Valle, C. J.; Lau, W. N.; Zhang, X. F.; Yeung, K. L. Sonocatalysis in solvent free conditions: An efficient eco-friendly methodology to prepare chalcones using a new type of amino grafted zeolites. *Catal. Today,* **2006**, *114* (2–3), 183-187.

[11] Comisar, C. M.; Savage, P. E. Kinetics of crossed aldol condensations in high-temperature water. *Green Chem.,* **2004**, *6* (4), 227-231.

[12] Zhang, Z.; Wang, Y. W. D. G. W. Efficient and clean Aldol condensation catalyzed by sodium carbonate in water. *Chem. Lett.,* **2003**, *32* (10), 966-967.

[13] Tanemura, K.; Suzuki, T.; Nishida, Y.; Horaguchi, T. Aldol Condensation in Water Using Polyethylene Glycol 400. *ChemInform,* **2005**, *36* (38).

[14] Thirunarayanan G.; Vanangamudi G. Synthesis of some 4-bromo-1-naphthyl chalcones using silica-sulfuric acid reagent under solvent free conditions. *Arkivoc,* **2006**, *xii*, 58-64.

[15] Dong, F.; Jian, C.; Zhenghao, F.; Kai, G.; Zuliang, L. Synthesis of chalcones via Claisen–Schmidt condensation reaction catalyzed by acyclic acidic ionic liquids. *Catal. Commun.,* **2008**, *9* (9), 1924-1927.

[16] Climent, M. J.; Corma, A.; Iborra, S.; Velty, A. Activated hydrotalcites as catalysts for the synthesis of chalcones of pharmaceutical interest. *J. Catal.,* **2004**, *221* (2), 474-482.

[17] Shailendra Mandge; Hemendra P. Singh; S. Dutta Gupta; N.S. Hari Narayana Moorthy Synthesis and Characterization of Some Chalcone Derivatives. *Trends. Appl. Sci. Res.,* **2007**, *2*, 52-56.

[18] Fukui, K.; Matsumoto, T.; Nakamura, S.; Nakayama, M. Synthetic Studies of the Flavone Derivatives. VII. The Synthesis of Jaceidin. *Bull. Chem. Soc. Jpn.,* **1968**, *41*, 1413-1417.

[19] Al-Masum, M.; Ng, E.; Wai, M. C. Palladium-catalyzed direct cross-coupling of potassium styryltrifluoroborates and benzoyl chlorides—a one step method for chalcone synthesis. *Tetrahedron Lett.,* **2011**, *52* (9), 1008-1010.

[20] Narender, T.; Papi Reddy, K. A simple and highly efficient method for the synthesis of chalcones by using borontrifluoride-etherate. *Tetrahedron Lett.,* **2007**, *48* (18), 3177-3180.

[21] Srivastava, Y. K. Ecofriendly Microwave Assisted Synthesis of Some Chalcones. *Rasayan J. Chem.,* **2008**, *1*, 884-886.

[22] Nakanishi, K., *Natural Products Chemistry*. Kodansha Ltd: Tokyo, 1975; Vol. 2.

[23] Ganguly, A. K.; Kaur, S.; Mahata, P. K.; Biswas, D.; Pramanik, B. N.; Chan, T. M. Synthesis and properties of 3-acyl-γ-pyrones, a novel class of flavones and chromones. *Tetrahedron Lett.,* **2005**, *46* (23), 4119-4121.

[24] Bohm, A. B., *Introduction to Flavonoids*. Harwood Academic Pub: London, 1998.

[25] Kumar, A.; Sharma, S.; Tripathi, V. D.; Srivastava, S. Synthesis of chalcones and flavanones using Julia–Kocienski olefination. *Tetrahedron,* **2010**, *66* (48), 9445-9449.

[26] S Zangade; S Mokle; A Vibhute; Y Vibhute An Efficient and Operationally Simple Synthesis of Some New Chalcones by Using Grinding Technique. *Chem. Sci. J.,* **2011**, *Volume 2011*.

[27] Sebti, S. d.; Solhy, A.; Tahir, R.; Abdelatif, S.; Boulaajaj, S. d.; Mayoral, J. A.; García, J. I.; Fraile, J. M.; Kossir, A.; Oumimoun, H. Application of natural phosphate modified with sodium nitrate in the synthesis of chalcones: a soft and clean method. *J. Catal.,* **2003**, *213* (1), 1-6.

[28] Sebti, S. d.; Solhy, A.; Tahir, R.; Boulaajaj, S. d.; Mayoral, J. A.; Fraile, J. M.; Kossir, A.; Oumimoun, H. Calcined sodium nitrate/natural

phosphate: an extremely active catalyst for the easy synthesis of chalcones in heterogeneous media. *Tetrahedron Lett.,* **2001**, *42* (45), 7953-7955.

[29] Zali, A.; Ghani, K.; Shokrolahi, A.; Keshavarz, M. H. Carbon-Based Solid Acid as an Efficient and Reusable Catalyst for Cross-Aldol Condensation of Ketones with Aromatic Aldehydes under Solvent-Free Conditions. *Chin. J. Catal.,* **2008**, *29* (7), 602-606.

[30] Kunde, L. B.; Gade, S. M.; Kalyani, V. S.; Gupte, S. P. Catalytic synthesis of chalcone and flavanone using Zn–Al hydrotalcite adhere ionic liquid. *Catal. Commun.,* **2009**, *10* (14), 1881-1888.

[31] Cortes-Concepcion, J. A.; Patcas, F.; Amiridis, M. D. Effect of Li on the catalytic activity of MgO for the synthesis of flavanone. *Appl. Catal., A,* **2010**, *386* (1–2), 1-8.

[32] Solhy, A.; Tahir, R.; Sebti, S.; Skouta, R.; Bousmina, M.; Zahouily, M.; Larzek, M. Efficient synthesis of chalcone derivatives catalyzed by re-usable hydroxyapatite. *Appl. Catal., A,* **2010**, *374* (1–2), 189-193.

[33] French, D.; Schifano, P.; Cortés-Concepción, J.; Hargrove-Leak, S. Li–Al layered double hydroxides as catalysts for the synthesis of flavanone. *Catal. Commun.,* **2010**, *12* (2), 92-94.

[34] Sinhamahapatra, A.; Sutradhar, N.; Roy, B.; Pal, P.; Bajaj, H. C.; Panda, A. B. Microwave assisted synthesis of fine chemicals in solvent-free conditions over mesoporous zirconium phosphate. *Appl. Catal., B,* **2011**, *103* (3–4), 378-387.

[35] Macquarrie, D. J.; Nazih, R.; Sebti, S. KF/natural phosphate as an efficient catalyst for synthesis of 2[prime or minute]-hydroxychalcones and flavanones. *Green Chem.,* **2002**, *4* (1), 56-59.

[36] Wei Li; Kejin Xu; Leilei Xu; Jianglei Hu; Fengyan Ma; Yihang Guo Preparation of highly ordered mesoporous AlSBA-15–SO3H hybrid material for the catalytic synthesis of chalcone under solvent-free condition. *Appl. Surf. Sci.,* **2010**, *256*, 3183-3190.

[37] Rajput, J. K.; Kaur, G. Silicotungstic acid catalysed Claisen Schmidt condensation reaction: an efficient protocol for synthesis of 1,3-diaryl-2-propenones. *Tetrahedron Lett.,* **2012**, *53* (6), 646-649.

[38] Krishnakumar, B.; Swaminathan, M. Solvent free synthesis of quinoxalines, dipyridophenazines and chalcones under microwave irradiation with sulfated Degussa titania as a novel solid acid catalyst. *J. Mol. Catal. A: Chem.,* **2011**, *350* (1–2), 16-25.

[39] Xu, Q.; Yang, Z.; Yin, D.; Zhang, F. Synthesis of chalcones catalyzed by a novel solid sulfonic acid from bamboo. *Catal. Commun.,* **2008**, *9* (7), 1579-1582.

[40] Romanelli, G.; Pasquale, G.; Sathicq, Á.; Thomas, H.; Autino, J.; Vázquez, P. Synthesis of chalcones catalyzed by aminopropylated silica sol–gel under solvent-free conditions. *J. Mol. Catal. A: Chem.,* **2011**, *340* (1–2), 24-32.

[41] Krishnakumar, B.; Velmurugan, R.; Swaminathan, M. TiO2–SO42− as a novel solid acid catalyst for highly efficient, solvent free and easy synthesis of chalcones under microwave irradiation. *Catal. Commun.,* **2011**, *12* (5), 375-379.

[42] Kumar, D.; Suresh; Sandhu, J. S. An efficient green protocol for the synthesis of chalcones by a Claisen–Schmidt reaction using bismuth(III)chloride as a catalyst under solvent-free condition. *Green Chem. Lett. Rev.,* **2010**, *3* (4), 283-286.

[43] Bhagat, S.; Sharma, R.; Sawant, D. M.; Sharma, L.; Chakraborti, A. K. LiOH·H2O as a novel dual activation catalyst for highly efficient and easy synthesis of 1,3-diaryl-2-propenones by Claisen–Schmidt condensation under mild conditions. *J. Mol. Catal. A: Chem.,* **2006**, *244* (1–2), 20-24.

[44] Chtourou, M.; Abdelhédi, R.; Frikha, M. H.; Trabelsi, M. Solvent free synthesis of 1,3-diaryl-2-propenones catalyzed by commercial acid-clays under ultrasound irradiation. *Ultrason. Sonochem.,* **2010**, *17* (1), 246-249.

[45] Kumar, A.; Akanksha Zirconium chloride catalyzed efficient synthesis of 1,3-diaryl-2-propenones in solvent free conditions via aldol condensation. *J. Mol. Catal. A: Chem.,* **2007**, *274* (1–2), 212-216.

[46] Sebti, S.; Solhy, A.; Tahir, R.; Smahi, A. Modified hydroxyapatite with sodium nitrate: an efficient new solid catalyst for the Claisen-Schmidt condensation. *Appl. Catal., A,* **2002**, *235* (1-2), 273-281.

[47] Sashidhara, K. V.; Rosaiah, J. N.; Kumar, A. Iodine-Catalyzed Mild and Efficient Method for the Synthesis of Chalcones. *Synth. Commun.,* **2009**, *39* (13), 2288-2296.

[48] Jayapal.M.R.; Sreedhar.N.Y. Anhydrous K2CO3 as Catalyst for the synthesis of Chalcones under Microwave Irradiation. *J. Pharm. Sci. Res.,* **2010**, *2*, 644-647.

[49] Thirunarayanan, G.; Vanangamudi, G. Synthesis of Some Aryl Chalcones Using Silica-Sulphuric Acid Reagent under Solvent Free Conditions. *E-J. Chem.,* **2007**, *4* (1), 90-96.

[50] S.R.Sarda; W.N.Jadhav; S.R.Bhusare; S.K.Wasmatkar; S.A.Dake; R.P.Pawar Solvent-free NaOH-Al2O3 supported synthesis of 1,3-diaryl-2-propene-1-ones. *Int. J. Chem.Tech. Res.,* **2009**, *1*, 265-269.

[51] Saravanamurugan, S.; Palanichamy, M.; Arabindoo, B.; Murugesan, V. Solvent free synthesis of chalcone and flavanone over zinc oxide supported metal oxide catalysts. *Catal. Commun.,* **2005**, *6* (6), 399-403.

[52] Shen, J.; Wang, H.; Liu, H.; Sun, Y.; Liu, Z. Brønsted acidic ionic liquids as dual catalyst and solvent for environmentally friendly synthesis of chalcone. *J. Mol. Catal. A: Chem.,* **2008**, *280* (1–2), 24-28.

[53] Saravanamurugan, S.; Palanichamy, M.; Arabindoo, B.; Murugesan, V. Liquid phase reaction of 2′-hydroxyacetophenone and benzaldehyde over ZSM-5 catalysts. *J. Mol. Catal. A: Chem.,* **2004**, *218* (1), 101-106.

[54] Kazuo Irie; Ken-ichi Watanabe Aldol Condensations with Metal(II) Complex Catalysts. *Bull. Chem. Soc. Jpn.,* **1980**, *53*, 1366-1371.

[55] Lyle, R. E.; Paradis, L. P. Acid-catalyzed Condensations. II.1 The Condensation of Benzaldehyde with Substituted Acetophenones. *J. Am. Chem. Soc.,* **1955**, *77* (24), 6667-6668.

[56] Sawle, P.; Moulton, B. E.; Jarzykowska, M.; Green, C. J.; Foresti, R.; Fairlamb, I. J. S.; Motterlini, R. Structure−Activity Relationships of Methoxychalcones as Inducers of Heme Oxygenase-1. *Chem. Res. Toxicol.,* **2008**, *21* (7), 1484-1494.

[57] Yang, H.; Shin, H.; Cho, S.; Bang, S.; Song, G.; Ju, J. Structural require- ment of chalcones for the inhibitory activity of interleukin-5. *Bioorg. Med. Chem.,* **2007**, *15*, 104-111.

[58] Lee, S. H.; S., S. G.; Kim, J. Y.; Y., J. X.; Kim, H. D.; Sohn, D. H. *Eur.J.Pharmacol.,* **2006**, *532*, 178.

[59] Rajendra, P. Y.; Srinivasa, R. A.; Rambabu, R. *Asian J. Chem.,* **2009**, *21*, 907.

[60] Vogel, S.; Ohmayer, S.; Brunner, G.; Heilmann, J. *Bioorg. Med. Chem.,* **2008**, *16*, 4286.

[61] Bandgar, B. P.; Gawande, S. S.; Bodade, R. G.; Totre, J. V.; Khobragade, C. N. Synthesis and biological evaluation of simple methoxylated chalcones as anticancer, anti-inflammatory and antioxidant agents. *Bioorg. Med. Chem.,* **2010**, *18* (3), 1364-1370.

[62] Bandgar, B. P.; Gawande, S. S. Synthesis and biological screening of a combinatorial library of β-chlorovinyl chalcones as anticancer, anti-inflammatory and antimicrobial agents. *Bioorg. Med. Chem.,* **2010**, *18* (5), 2060-2065.

[63] Yang, H.-M.; Shin, H.-R.; Cho, S.-H.; Bang, S.-C.; Song, G.-Y.; Ju, J.-H.; Kim, M.-K.; Lee, S.-H.; Ryu, J.-C.; Kim, Y.; Jung, S.-H. Structural requirement of chalcones for the inhibitory activity of interleukin-5. *Bioorg. Med. Chem.,* **2007**, *15* (1), 104-111.

[64] Jin, F.; Jin, X.; Jin, Y.; Sohn, D.; Kim, S.-A.; Sohn, D.; Kim, Y.; Kim, H. Structural requirements of 2′,4′,6′-tris(methoxymethoxy) chalcone derivatives for anti-inflammatory activity: The importance of a 2′-hydroxy moiety. *Arch. Pharmacal Res.,* **2007**, *30* (11), 1359-1367.

[65] Chiaradia, L. D.; dos Santos, R.; Vitor, C. E.; Vieira, A. A.; Leal, P. C.; Nunes, R. J.; Calixto, J. B.; Yunes, R. A. Synthesis and pharmacological activity of chalcones derived from 2,4,6-trimethoxyacetophenone in RAW 264.7 cells stimulated by LPS: Quantitative structure–activity relationships. *Bioorg. Med. Chem.,* **2008**, *16* (2), 658-667.

[66] Zarghi, A.; Zebardast, T.; Hakimion, F.; Shirazi, F. H.; Praveen Rao, P. N.; Knaus, E. E. Synthesis and biological evaluation of 1,3-diphenylprop-2-en-1-ones possessing a methanesulfonamido or an azido pharmacophore as cyclooxygenase-1/-2 inhibitors. *Bioorg. Med. Chem.,* **2006**, *14* (20), 7044-7050.

[67] Batovska, D.; Parushev, S.; Slavova, A.; Bankova, V.; Tsvetkova, I.; Ninova, M.; Najdenski, H. Study on the substituents' effects of a series of synthetic chalcones against the yeast Candida albicans. *Eur.J.Med.Chem.,* **2007**, *42* (1), 87-92.

[68] Siddiqui, Z. N.; Praveen, S.; Musthafa, T. N. M.; Ahmad, A.; Khan, A. U. Thermal solvent-free synthesis of chromonyl chalcones, pyrazolines and their *in vitro* antibacterial, antifungal activities. *J. Enzyme Inhib. Med. Chem.,* **2012**, *27* (1), 84-91.

[69] Sivakumar, P. M.; Seenivasan, S. P.; Kumar, V.; Doble, M. Synthesis, antimycobacterial activity evaluation, and QSAR studies of chalcone derivatives. *Bioorg. Med. Chem. Lett.,* **2007**, *17* (6), 1695-1700.

[70] Ansari, F. L.; Nazir, S.; Noureen, H.; Mirza, B. Combinatorial Synthesis and Antibacterial Evaluation of an Indexed Chalcone Library. *Chem. Biodiversity,* **2005**, *2* (12), 1656-1664.

[71] Tomar, V.; Bhattacharjee, G.; Kamaluddina; Kumar, A. *Bioorg. Med. Chem.,* **2007**, *17*, 5321.
[72] Nowakowska, Z.; Kedzia, B.; Shroeder, G. *Eur.J.Med.Chem,* **2008**, *43*, 707.
[73] Liu, X. L.; Xu, Y. J.; Go, M. L. Functionalized chalcones with basic functionalities have antibacterial activity against drug sensitive Staphylococcus aureus. *Eur.J.Med.Chem.,* **2008**, *43* (8), 1681-1687.
[74] Mishra, N.; Arora, P.; Kumar, B.; Mishra, L. C.; Bhattacharya, A.; Awasthi, S. K.; Bhasin, V. K. Synthesis of novel substituted 1,3-diaryl propenone derivatives and their antimalarial activity *in vitro*. *Eur.J.Med.Chem.,* **2008**, *43* (7), 1530-1535.
[75] Valla, A.; Valla, B.; Cartier, D.; Guillou, R.; Labia, R.; Florent, L. Newsyntheses and potentialantimalarialactivitiesofnewretinoid-likechalcones. *Eur.J.Med.Chem,* **2006**, *41*, 142-146.
[76] Dominguez, J. N.; León, C.; Rodrigues, J.; Domínguez, N. G.; Gut, J.; Rosenthal, P. J. *IL Farmaco.,* **2005**, *60*, 307.
[77] Motta, L. F.; Gaudio, A. C.; Takahata, Y. *Inter. Elect. J. Mol. Design.,* **2006**, *5*, 555.
[78] Dominguez, J. N.; Charris, J. E.; Lobo, G.; Gamboan, N.; Dominguez, N. G.; Moreno, M. M.; Riggione, F.; Sanchez, E.; Olson, J.; Rosenthal, P. J. *Eur.J.Med.Chem,* **2001**, *36*, 555.
[79] Liu, M.; Wilairat, P.; Go, M. L. *J. Med. Chem.,* **2002**, *45*, 1735.
[80] Loa, J.; Chow, P.; Zhang, K. Studies of structure–activity relationship on plant polyphenol-induced suppression of human liver cancer cells. *Cancer Chemother. Pharmacol.,* **2009**, *63* (6), 1007-1016.
[81] Seo, W.; Ryu, Y.; Curtis-Long, M.; Lee, C.; Ryu, H.; Jang, K. Evaluationof anti-pigmentary effect of synthetic sulfonylamino chalcone. *Eur.J.Med.Chem,* **2010**, *45*, 2010-2017.
[82] Trivedi, J. C.; Bariwal, J. B.; Upadhyay, K. D.; Naliapara, E. D.; Joshi, S. K.; Pannecouque, C. C.; Clercq, E. D.; Shah, A. K. *Tetrahedron Lett.,* **2007**, *48*, 8472.
[83] Lin, Y. M.; Zhou, Y.; Flavin, M. T.; Zhow, L. M.; Nie, W.; Chen, F. C. *Bioorg. Med. Chem.,* **2002**, *10*, 2795.
[84] Cai, Y.-Z.; Mei, S.; Jie, X.; Luo, Q.; Corke, H. Structure–radical scavenging activity relationships of phenolic compounds from traditional Chinese medicinal plants. *Life Sci.,* **2006**, *78* (25), 2872-2888.
[85] Gacche, R. N.; Dhole, N. A.; Kamble, S. G.; Bandgar, B. P. *Enz. Inhib. Med. Chem.,* **2008**, *23*, 28.
[86] Habsah, M.; Faridah, A.; Dharma, P.; Nordin H, L.; Abdul Manaf, A.; Mohd Aspollah, S.; Taufiq Y. Y, H.; Hiroe, K.; Nobuji, N. DPPH Free Radical Scavenger Components from the Fruits of Alpinia rafflesiana Wall. ex. Bak. (Zingiberaceae). *Z. Naturforsch., C: J. Biosci.,* **2004**, *59*, 811-815.
[87] Kim, B.-T.; O, K.-J.; Chun, J.-C.; Hwang, K.-J. ChemInform Abstract: Synthesis of Dihydroxylated Chalcone Derivatives with Diverse Substitution Patterns and Their Radical Scavenging Ability Toward DPPH Free Radicals. *ChemInform,* **2008**, *39* (42), no-no.
[88] Nishida, J.; Kawabata, J. DPPH Radical Scavenging Reaction of Hydroxy- and Methoxychalcones. *Biosci., Biotechnol., Biochem.,* **2006**, *70* (1), 193-202.
[89] Boumendjel, A.; Boccard, J.; Carrupt, P.-A.; Nicolle, E.; Blanc, M.; Geze, A.; Choisnard, L.; Wouessidjewe, D.; Matera, E.-L.; Dumontet, C. Antimitotic and Antiproliferative Activities of Chalcones: Forward Structure–Activity Relationship. *J. Med. Chem.,* **2008**, *51* (7), 2307-2310.
[90] Andrighetti-Fröhner, C. R.; de Oliveira, K. N.; Gaspar-Silva, D.; Pacheco, L. K.; Joussef, A. C.; Steindel, M.; Simões, C. M. O.; de Souza, A. M. T.; Magalhaes, U. O.; Afonso, I. F.; Rodrigues, C. R.; Nunes, R. J.; Castro, H. C. Synthesis, biological evaluation and SAR of sulfonamide 4-methoxychalcone derivatives with potential antileishmanial activity. *Eur.J.Med.Chem.,* **2009**, *44* (2), 755-763.
[91] Ducki, S.; Forrest, R.; Hadfield; Kendall, A.; Lawrence, R. J.; McGown, A. T.; Rennison, D. *Bioorg. Med. Chem.,* **1998**, *8*, 1051.
[92] Aponte, J. C.; Castillo, D.; Estevez, Y.; Gonzalez, G.; Arevalo, J.; Hammond, G. B.; Sauvain, M. *In vitro* and *in vivo* anti-Leishmania activity of polysubstituted synthetic chalcones. *Bioorg. Med. Chem. Lett.,* **2010**, *20* (1), 100-103.
[93] Vijaya Bhaskar Reddy, M.; Tsai, W.-J.; Qian, K.; Lee, K.-H.; Wu, T.-S. Structure–activity relationships of chalcone analogs as potential inhibitors of ADP- and collagen-induced platelet aggregation. *Bioorg. Med. Chem.,* **2011**, *19* (24), 7711-7719.
[94] Boeck, P.; Falco, C. A. B.; Leal, P. C.; Yunes, R. A.; Filho, V. C.; Torres-Santos, E. C.; Rossi-Bergmann, B. *Bioorg. Med. Chem. ,* **2006**, *14*, 1538.
[95] Li, F.; Awale, S.; Tezuka, Y.; Kadota, S. Cytotoxic constituents from Brazilian red propolis and their structure–activity relationship. *Bioorg. Med. Chem.,* **2008**, *16* (10), 5434-5440.
[96] Zhao, L.; Jin, H.; Sun, L.; Piaoa, H.; Quana, Z. *Bioorg. Med. Chem.,* **2005**, *15*, 5027.
[97] LeBlanc, R.; Dickson, J.; Brown, T.; Stewart, M.; Pati, H. N.; VanDerveer, D.; Arman, H.; Harris, J.; Pennington, W.; Holt Jr, H. L.; Lee, M. Synthesis and cytotoxicity of epoxide and pyrazole analogs of the combretastatins. *Bioorg. Med. Chem.,* **2005**, *13* (21), 6025-6034.
[98] Pati, H. N.; Holt, H. L.; LeBlanc, R.; Dickson, J.; Stewart, M.; Brown, T.; Lee, M. Synthesis and cytotoxic properties of nitro and aminochalcones. *Medicinal Chemistry Research,* **2005**, *14* (1), 19-25.
[99] Rao, G. V.; Swamy, B. N.; Chandregowda, V.; Reddy, G. C. Synthesis of (±)Abyssinone I and related compounds: Their anti-oxidant and cytotoxic activities. *Eur.J.Med.Chem.,* **2009**, *44* (5), 2239-2245.
[100] Cabrera, M.; Simoens, M.; Falchi, G.; Lavaggi, M. L.; Piro, O. E.; Castellano, E. E.; Vidal, A.; Azqueta, A.; Monge, A.; de Ceráin, A. L.; Sagrera, G.; Seoane, G.; Cerecetto, H.; González, M. Synthetic chalcones, flavanones, and flavones as antitumoral agents: Biological evaluation and structure–activity relationships. *Bioorg. Med. Chem.,* **2007**, *15* (10), 3356-3367.
[101] Bonesi, M.; Loizzo, M. R.; Statti, G. A.; Michel, S.; Tillequin, F.; Menichini, F. The synthesis and Angiotensin Converting Enzyme (ACE) inhibitory activity of chalcones and their pyrazole derivatives. *Bioorg. Med. Chem. Lett.,* **2010**, *20* (6), 1990-1993.
[102] Hayat, F.; Moseley, E.; Salahuddin, A.; Van Zyl, R. L.; Azam, A. Antiprotozoal activity of chloroquinoline based chalcones. *Eur. J. Med. Chem.,* **2011**, *46* (5), 1897-1905.
[103] Bandgar, B. P.; Patil, S. A.; Korbad, B. L.; Nile, S. H.; Khobragade, C. N. Synthesis and biological evaluation of β-chloro vinyl chalcones as inhibitors of TNF-α and IL-6 with antimicrobial activity. *Eur.J.Med.Chem.,* **2010**, *45* (6), 2629-2633.
[104] Jun, N.; Hong, G.; Jun, K. Synthesis and evaluation of 2′,4′,6′-trihydroxychalcones as a new class of tyrosinase inhibitors. *Bioorg. Med. Chem.,* **2007**, *15* (6), 2396-2402.
[105] Khatib, S.; Nerya, O.; Musa, R.; Shmuel, M.; Tamir, S.; Vaya, J. Chalcones as potent tyrosinase inhibitors: the importance of a 2,4-substituted resorcinol moiety. *Bioorg. Med. Chem.,* **2005**, *13* (2), 433-441.

Received: April 22, 2012 Revised: July 02, 2012 Accepted: July 05, 2012