

**ULTRASOUND ASSISTED GREEN SYNTHESIS OF 2-FURAN-2-YL-4H-CHROMEN-4-ONES FROM CHALCONES**GOPAL K. KAKADE<sup>1</sup>, SURESH G. VEDPATHAK<sup>2\*</sup>

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**ABSTRACT**

**Objective:** To report the ultrasound-assisted synthesis of some bioactive 2-furan-2-yl-4H-chromen-4-one derivatives

**Methods:** Oxidative cyclization of chalcones using iodine in dimethyl sulfoxide for the synthesis.

**Results:** Some bioactive 2-furan-2-yl-4H-chromen-4-one derivatives were synthesized from corresponding chalcones in the presence of iodine in dimethyl sulfoxide under ultrasound irradiation at ambient reaction conditions.

**Conclusion:** The use of ultrasound irradiation gave the advantages of higher yields, lower reaction time and simplicity compared to conventional methods for the synthesis of 2-furan-2-yl-4H-chromen-4-one derivatives.

**Keywords:** Chromen-4-one, Chalcones, Iodine, Ultrasound irradiation

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## INTRODUCTION

Ultrasound-assisted organic synthesis is another "Green" method used in many organic synthetic pathways for high efficiency, low waste, and low energy requirements. With high-intensity sound or ultrasound, radiation produces acoustic cavities, which can create extreme physical and chemical conditions in the cold fluid. The driving force for such synthesis has many benefits to clean and safe technologies for the environment, which reduces the production of source waste with better yields and selection, thereby increasing the recovery and quality of the product for crystallization and product recovery and refining processes. Sonication allows the use of non-activated and crude reagents as well as an aqueous solvent system; therefore it is friendly and non-toxic. Ultrasound is widely used for improving the traditional reactions that use expensive reagents, strongly acidic conditions, long reaction times, high temperatures, unsatisfactory yields and incompatibility with other functional groups [1]. In this context, the use of ultrasound to accelerate reactions has proven to be a particularly important tool for meeting the Green Chemistry goals of minimization of waste and reduction of energy requirements [2].

Chromones and chromen-4-ones, benzoannulated  $\gamma$ -pyrone [3, 4], are considered as privileged structures [5] widely distributed in nature known for their potential pharmacological activities [6-9]. An efficient synthetic route has been reported for the synthesis of 2-alkyl-substituted chroman-4-ones [10]. The incorporation of various functional groups to present highly substituted structures have successfully carried via distinct Pd-mediated cross-coupling reactions [11, 12], Mannich reactions [13], and a  $\text{SmI}_2$ -KHMDS-mediated Reformatsky type reaction [14]. Recently, some substituted chromone and chroman-4-one derivatives have been reported as potent and highly selective SIRT2 inhibitors [15]. As part of our ongoing research in the field of green chemistry directed synthesis, we herein wish to report a straightforward and conveniently efficient alternative protocol for the synthesis of diversely functionalized furan substituted chromen-4-ones from chalcones under ultrasound irradiation.

## MATERIALS AND METHODS

Commercially available AR grade chemicals were used for synthesis.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on 400 MHz Varian Mercury plus 400 MHz FT NMR spectrometer in  $\text{CDCl}_3$  using signals for residual protons and carbon atoms of the solvent as the references. Melting points were determined on the melting point apparatus (Model MP-96) and were not corrected. The progress of the reaction and purity of the product was monitored by TLC on Merck Silica gel 60 F254 UV-254 plates.

### General procedure for the synthesis of chalcones

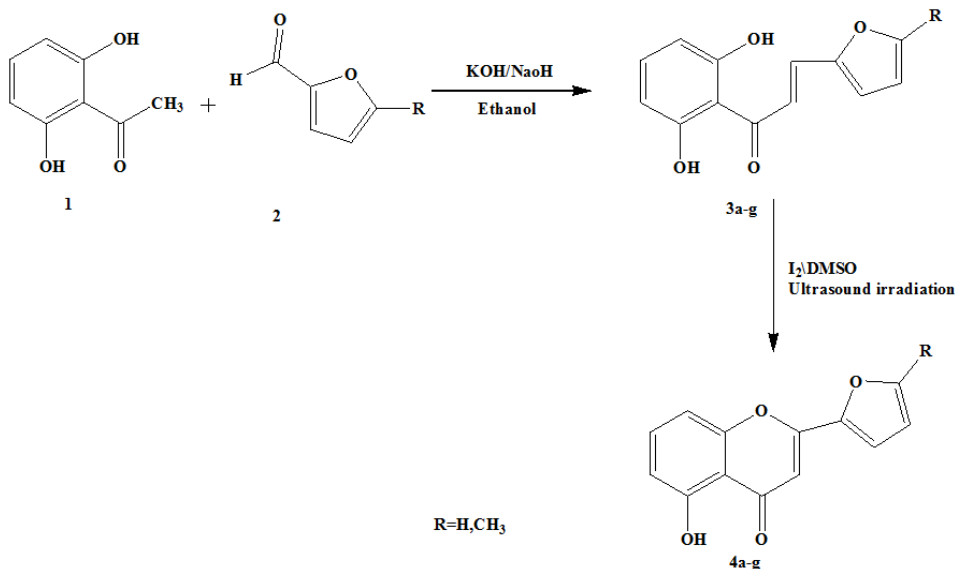
Chalcones were prepared by method reported in literature [16]. To a solution of substituted 2-hydroxyacetophenone (0.1 mol) in ethanol (15 ml), substituted heterocyclic aldehyde (0.1 mol) was added. To this mixture aqueous potassium hydroxide (60%) was poured gradually with constant stirring and continues the stirring for 1.5 h. After complete addition, the reaction mixture was kept for 14-16 h at room temperature. The potassium salt of chalcone was separated by ice-cold 10% hydrochloric acid (20 ml). The separated solid was filtered and washed with ice-cold water (2x30 ml) till the washing was neutral to litmus. Recrystallized the compound with ethanol and dried at room temperature.

#### **General procedure for the synthesis of 2-furan-2-yl-4H-chromen-4-ones**

To a solution of chalcone (0.01 mol) in 20 ml dimethyl sulfoxide, catalytic quantity of iodine was added. The mixture was then placed in an ultrasonic bath for the periods shown in table 1, at 20-25 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured on ice-cold water; the separated solid was filtered washed with cold water followed by a dilute sodium-thiosulphate solution. The product was crystallized from ethanol.

#### **RESULTS AND DISCUSSION**

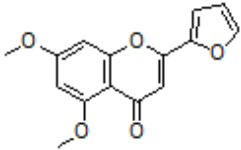
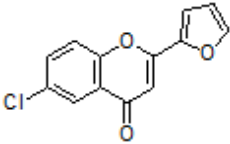
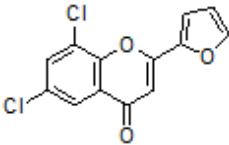
The intermediate, chalcones were synthesized by reacting equimolar amounts of furfuraldehyde with different 2-hydroxyacetophenones in the presence of 10% potassium hydroxide in ethanol by Claisen-Schmidt condensation. The cyclization of chalcones was then achieved by using catalytic amount of iodine in dimethyl sulfoxide under ultrasound irradiation (Scheme 1). The starting materials 3a-g on ultrasound irradiation afforded compounds 4a-g within a few minutes in better yields than the conventional method (table 1). The use of ultrasound irradiation gave the advantages of higher yields, lower reaction time and simplicity compared to conventional methods.



**Scheme 1: Synthesis of 2-(5-substituted-furan-2-yl)-4H-chromen-4-ones**

**Table 1: Properties of compounds 4a-g**

Entry	Structure	Reaction time (min)	Color	Molecular weight	M. P °C	Yield %
4a		30	Yellowish-brown	242	219-220	82
4b		45	Coffee brown	228	271-272	73
4c		50	Pale yellow	245	274-275	70
4d		35	White	272	179-180	82

4e		40	White	272	115-116	77
4f		55	Off white	247	143-144	78
4g		70	White	281	192-193	69

All the compounds were characterized by using IR, and  $^1\text{H}$  NMR data. Generally, the flavones and flavonols exhibit absorption in 320-380 nm regions and 240-270 nm regions [17]. Compound 4a showed two absorption bands in the range of 339 nm for carbonyl group and 258 nm for hydroxyl group. The IR spectra of 4a revealed broad band for  $\alpha$ ,  $\beta$ -carbonyl group absorption at  $\nu_{\text{max}}$   $1691\text{ cm}^{-1}$  and a broad band at  $1097\text{ cm}^{-1}$  due to the presence of ether linkage (C-O-C).  $^1\text{H}$  NMR spectra of 4a revealed chemo selectivity of the cyclo condensation. The presence of a singlet at 6.71 reveals the presence of pyrone ring. All the  $\delta$  values of protons are in accordance with the reported values.

$^{13}\text{C}$  NMR spectrum of compound 4a revealed fourteen distinctive carbon signals at  $\delta\text{C}$  14.1, 109.3, 110.1, 110.4, 110.9, 112.3, 113.2, 136.9, 145.2, 154.7, 158.3, 162.2, 168.6, 181.9. Finally, in the mass spectrum, molecular ion peak is observed at  $m/z$  242 [ $\text{M}^+$ ], 243 [ $\text{M}^+ + 1$ ] and 244 [ $\text{M}^+ + 2$ ] confirms the structure of the compound 4a. The compound 4b-g are the same as obtained by the reported conventional procedure. The spectral analysis of these compounds is in accordance with the reported values [17, 18].

## CONCLUSION

A general and green method has been developed for the synthesis of 2-(5-substituted-furan-2-yl)-4H-chromen-4-ones from furan substituted chalcones in dimethyl sulfoxide in the presence of iodine as catalyst under ultrasound irradiation at ambient conditions. The use of ultrasound irradiation gave the advantages of higher yields, lower reaction time and simplicity compared to conventional methods.

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## AUTHORS CONTRIBUTIONS

Both the authors have contributed equally.

## CONCLUSION OF INTERESTS

The authors confirm that this article content has no conflict of interest.

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