

# Synthesis of Bioactive Chromone Derivatives

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## Manuscript Details

Available online on <http://www.irjse.in>  
ISSN: 2322-0015

Editor: Dr. Arvind Chavhan

## Cite this article as:

Tagad Vinayak T. Synthesis of Bioactive Chromone Derivatives, *Int. Res. Journal of Science & Engineering*, January 2018 | Special Issue A3 | : 39-42.

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## ABSTRACT

Chromones (1-benzopyran-4-ones) and Chromone derivatives are naturally occurring compounds ubiquitously found in the plant kingdom, and therefore present in representative amounts in a normal human diet. These phytochemicals possess a wide spectrum of biological activities - such as anti-inflammatory, antifungal, antimicrobial, antiviral, antitumour and anticancer-mainly due to their well-recognized antioxidant properties, which stem from their ability to neutralize active forms of oxygen and to cut off free radical processes. Here we successfully synthesize some chromone derivatives by using substituted phenols in laboratory at room temperature. Crystalline products were characterized using sophisticated techniques such as FT-IR, NMR and mass spectrophotometric methods.

**Keywords:** chromones; derivatives; biological activity.

## INTRODUCTION

The chromone classes of compounds it was found that they are associated with various physiological and biological properties and find importance in medicine. Taking these facts in to consideration it was thought worthwhile to synthesize a series of such compounds. A number of scientists in the past have tried to find out some relationship between chemical structure and physiological or biological properties. It is now well established fact that the activity of the compounds depends upon three factors. The first and perhaps most important is the heterocyclic moiety present in particular compound. The second factor is the nature of the substituents and the third factor is the position of substituent's in these compounds.

Chromone derivative have received significant attention owing to their diverse range of biological properties viz. blood platelet disaggregation, antimicrobial, anthelmintic, antibacterial, anti-inflammatory, anti-hypertensive, antifungal.

There is growing interest in the pharmacological potential of natural products is chromones constitute an important group of natural products. Chemically, they consist of open chain flavanoids in which the two aromatic rings are joined by a three carbon  $\alpha$ ,  $\beta$  unsaturated carbonyl system. The presence of a reactive  $\alpha$ ,  $\beta$  unsaturated keto function in chromones is found to be responsible for their antimicrobial activity [1]. In recent years a variety of chromones have been reviewed for their cytotoxic, anticancer chemopreventive and mutagenic as well as antiviral, insecticidal and enzyme inhibitory properties [2,3]. A number of chromones having hydroxy, alkoxy groups in different position have been reported to possess anti-bacterial [4], antiulcer [5], antifungal [6], antioxidant [7], vasodilatory [8], antimitotic [9], antimalarial [10], antileishmanial [11] and inhibition of chemical mediators release, inhibition of leukotriene B4 [12], inhibition of tyrosinase [13,14] and inhibition of aldose reductase [15] activities. Appreciation of these findings motivated us to synthesize chromones as a potential template for antimicrobial agents. It must be noted that this scaffold provides substitution pattern on benzylidene acetophenones nucleus.

The main objectives of chromones synthesis are not only for the development of more diverse and complex bioactive compounds for biological activity and structure activity relationship studies but also for the applications in medicinal chemistry, such as preparation of fluorescence probes, due to photochemical properties of chromones. Chromone derivatives have high potential in drug discovery. Synthesis of large compound libraries is a general trend in a modern drug discovery process. In recent years a lot of synthetic method to construct the Chromone ring appeared. We want to study the synthesis of chromones by some methods they may include acid as catalyst, base as catalyst, microwave irradiation assisted synthesis, solid-supported synthesis, and other methods.

The present work describes the synthesis of series of some Chromones. With referring literature of the above classes of compounds it was found that they are associated with various physiological and biological properties and find importance in medicine. Taking these facts in to consideration it was thought worthwhile to synthesize a series of such compounds.

## METHODOLOGY

The synthesized compound for its own identification like different types of bonds, functional groups, carbon skeleton, polarity, molecular weight, refractive index etc. different chemical and physical methods are available. We know that chemical method becomes time consuming and wastage of much chemicals. Chemical method gives ideas about functional group, aromaticity. Saturation, unsaturation and which elements present in the compounds. However, analysis by chemical method can't reach up to structure of the compound. Overcome this time consuming and wastage of much chemicals, physical method become fast and gives more structural information about chemicals without wastage of chemicals.

The melting points of synthesized compounds were determined in open capillary tubes using melting point apparatus, expressed in  $^{\circ}\text{C}$  and are uncorrected. The IR spectra of compounds were recorded on Shimadzu Affinity-1 FTIR in KBr disc and absorption bands are expressed in  $\text{cm}^{-1}$ . The  $^1\text{H}$  NMR spectra in DMSO were recorded on Bruker WM 400FT MHz spectrometer and chemical shift were reported as parts per million (ppm) down field using TMS as internal standard. The HRMS spectra on dic-ms600mz were recorded on Bruker Compass Data Analysis. The purity of the compounds was checked by TLC on silica gel Glassplates using ethyl acetate: hexane (1:3) solvent system.

## RESULTS AND DISCUSSION

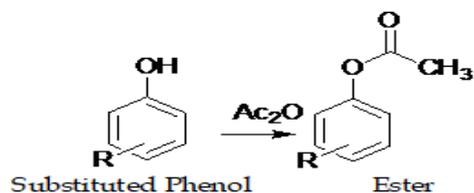
### Synthesis of Chromone

#### Experimental:

##### Step-I

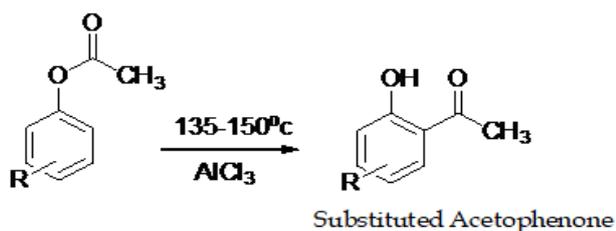
5gm of phenol, 6 ml acetic anhydride and 5 ml pyridine (dry) take in dry conical flask keep for

overnight, second day pour over crushed ice, Organic layer separated by separating funnel. Organic layer separate by anhydrous sodium sulphate or magnesium sulphate. Distilled organic layer above 200°C.



### Step-II

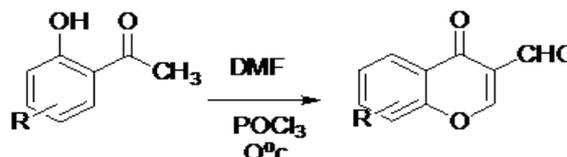
Take 6gm anhydrous  $\text{AlCl}_3$  in 50ml round bottom flask. Attach air condenser and then add above ester to the flask, reaction start within 2 min. After 10 minutes heat the reaction mixture in round bottom flask for two hours between 135-150°C, allow to stands for overnight then keep the flask in ice bath and add crushed ice to the flask. Product will separate within two days. Filter the product and recrystallize with alcohol.



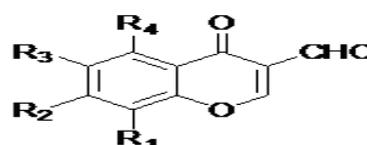
### Step-III

5gmacetophenone dissolve in minimum amount of DMF. Take 8-10 ml DMF in round bottom flask and cool to 0°C and 15ml  $\text{POCl}_3$  dropwise, this ice cold

solution. Add above solution in RBF dropwise exothermic reaction then stir the reaction mixture for 30 min at room temperature. Stir for 15 min. then keep reaction for overnight. Second day pour mixture over crushed ice(25gm). Keep for 2-3 hrs. Solid get separated. Recrystallize with alcohol and if insoluble in alcohol then recrystallize with acetic acid.



### Substituted Chromone



A series of Different Chromones prepared as follows.

Sr.No.	R1	R2	R3	R4
1	Cl	H	Cl	H
2	H	H	Cl	H
3	H	$\text{CH}_3$	H	$\text{CH}_3$
4	H	H	Br	H
5	H	$\text{CH}_3$	H	H
6	$\text{CH}_3$	H	$\text{CH}_3$	H
7	H	H	$\text{CH}_3$	H
8	H	Cl	H	Cl
9	H	$\text{CH}_3$	Cl	H

Sr.No.	Name of the compound	Melting point(°C)	%Yield
1	6,8dichloro-4-oxo-4H-Chromene-3-carbaldehyde	171	79
2	6, chloro-4-oxo-4H-Chromene-3-carbaldehyde	157	83
3	6-bromo -4-oxo-4H-Chromene-3-carbaldehyde	193	85
4	7 methyl -4-oxo-4H-Chromene-3-carbaldehyde	157-165	89
5	6,8 dimethyl -4-oxo-4H-Chromene-3-carbaldehyde	187-190	84
6	6,chloro-7methyl -4-oxo-4H-Chromene-3-carbaldehyde	183-185	90
7	5,7 dimethyl -4-oxo-4H-Chromene-3-carbaldehyde	165	92
8	6, methyl -4-oxo-4H-Chromene-3-carbaldehyde	173	84
9	5,7 dichloro-4-oxo-4H-Chromene-3-carbaldehyde	185	85

### Spectral Analysis of some Chromones:

- 6,8dichloro-4-oxo-4H-Chromene-3-carbaldehyde:**  $^1\text{H NMR}$ : (300 MHz, DMSO)  $\delta$ : 10.079 (s, 1H, -CHO), 9.038 (s, 1H, 7-H), 8.264 (s, 1H, 5H), 8.007 (s, 1H, 2-H). HRMS:  $m/z$  [ $\text{M}^+$ ] Calculated for  $\text{C}_{10}\text{H}_4\text{O}_3\text{Cl}_2$ : 243.4000; Found: 242.9613.
- 6, chloro-4-oxo-4H-Chromene-3-carbaldehyde:**  $^1\text{H NMR}$ : (300 MHz, DMSO)  $\delta$ : 10.093 (s, 1H, -CHO), 8.952 (s, 1H, 2-H), 8.042 (s, 1H, 5-H), 7.933 (s, 1H, 7-H); 7.835 (s, 1H, 8-H); HRMS:  $m/z$  [ $\text{M}^+$ ] Calculated for  $\text{C}_{10}\text{H}_5\text{O}_3\text{Cl}$ : 209.0000; Found: 209.0004.

3. **6-bromo-4-oxo-4H-Chromene-3-carbaldehyde**: <sup>1</sup>H NMR: (300 MHz, DMSO)  $\delta$ : 10.098 (s, 1H, -CHO), 8.964 (s, 1H, 2-H), 8.200 (s, 1H, 5H), 8.060 (s, 1H, 7-H); 7.700 (s, 1H, 8-H); HRMS: m/z [M<sup>+</sup>] Calculated for C<sub>10</sub>H<sub>5</sub>O<sub>3</sub>Br: 253.4000; Found: 254.9474.
4. **7 methyl-4-oxo-4H-Chromene-3-carbaldehyde**: <sup>1</sup>H NMR: (300 MHz, DMSO)  $\delta$ : 10.114 (s, 1H, -CHO), 8.881 (s, 1H, 2-H), 8.032 (d, 1H, 5H), 8.017 (d, 1H, 6-H); 7.574 (s, 1H, 8-H); 3.368 (s, 3H, CH<sub>3</sub>); HRMS: m/z [M<sup>+</sup>] Calculated for C<sub>11</sub>H<sub>8</sub>O<sub>3</sub>: 188.8000; Found: 189.0549.
5. **6,8 dimethyl-4-oxo-4H-Chromene-3-carbaldehyde**: <sup>1</sup>H NMR: (300 MHz, DMSO)  $\delta$ : 10.121 (s, 1H, -CHO), 8.921 (s, 1H, 2-H), 7.757 (s, 1H, 5-H), 7.753 (s, 1H, 7-H); 3.354 (s, 3H, 8-CH<sub>3</sub>); 2.435 (m, 3H, 6-CH<sub>3</sub>); HRMS: m/z [M<sup>+</sup>] Calculated for C<sub>12</sub>H<sub>10</sub>O<sub>3</sub>: 203.0000; Found: 203.0708.
6. **6, chloro-7methyl-4-oxo-4H-Chromene-3-carbaldehyde**: <sup>1</sup>H NMR: (300 MHz, DMSO)  $\delta$ : 10.088 (s, 1H, -CHO), 8.917 (s, 1H, 2-H), 8.008 (s, 1H, 5-H), 7.828 (s, 1H, 8-H); 3.353 (s, 3H, 7-CH<sub>3</sub>); 2.435 (m, 3H, 6-CH<sub>3</sub>); HRMS: m/z [M<sup>+</sup>] Calculated for C<sub>11</sub>H<sub>7</sub>O<sub>3</sub>Cl: 223.2000; Found: 223.0158.

#### Acknowledgement :

Author was thankful for Board of College and University Development (BCUD), Savitribai Phule Pune University for the giving financial support for this project. Also I am thankful to the Principal, Jijamata College of Science and Arts, Dnyaneshwarnagar for the providing laboratory facility for the completion of this work.

**Conflicts of interest:** The authors stated that no conflicts of interest.

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