



Synthesis, Characterization and Antimicrobial Screening of Some Fluorinated Chromones and Chlorochromones

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ABSTRACT

4-Bromo-2-fluorobenzaldehyde when treated with substituted hydroxyacetophenones yields chalcones 3. These chalcones were cyclized using DMSO/I₂ gave the compound 2-(4-Bromo-2-fluorophenyl)-4*H*-chromen-4-one 4. Chalcones on treatment with DMSO/CuCl₂ yields 2-(4-bromo-2-fluorophenyl)-3-chloro-4*H*-chromen-4-one 5. The structures of compounds have been established on the basis of spectral data. These compounds were screened for their antimicrobial activities.

Key words: Fluorinated Chromones, Chlorochromones, Antimicrobial activity.

INTRODUCTION

A Fluorinated compound plays a vital role in a chemical and biochemical sciences. As per literature over 10% of newly registered pharmaceutical drugs and some 40% of newly registered agrochemicals contain one or more fluorine atoms¹.

Halogeno substituted chromones with heterocyclic substituent at 2-position are reported to have broncho-dilatory² and coronary-spasmolytic³ properties.

Chalcones and their analogues having an α , β -unsaturated carbonyl system are very versatile

substrates for the evaluation of various organic reactions.⁴

The chalcones were found to have good antibacterial, analgesic and anti-inflammatory activities.⁵

Compounds containing chromone moiety are synthetically versatile molecules with a reactive carbonyl group having considerable significance for their biological activities⁶⁻⁷ and for their reactivity with nucleophiles, which allow the synthesis of a wide variety of heterocycles. Chromones are reported to exhibit anti-inflammatory,⁸ antimicrobial,⁹⁻¹⁰ anticancer,¹¹ antiallergic¹² and coronary vasodilator¹³ activity. Some chromones

has potential HIV-integrase inhibition activity¹⁴⁻¹⁸. Chromones can be used as fungicides and stimulants for the central nervous system¹⁸.

The various methods for the synthesis of 3-halochromones were reported by different co-workers. Gammill¹⁹ synthesized 3-halochromone from enaminoketone with halogen containing reagents.

RESULTS AND DISCUSSION

2-Hydroxyacetophenones **1** on treatment with fluorinated aldehydes **2** afforded compound **3** chalcones. Chalcone showed IR absorption bands at 3523 cm⁻¹ due to -OH functionality. ¹H NMR shows peak at 12.30 δ due to -OH protons. The structure of compounds were also confirmed by Mass spectrum.

Compound **3** on treatment with DMSO and catalytic amount of I₂ yields compound **4** chromones. Compound **4** showed IR absorption band at 1670 cm⁻¹ due to C=O functionality and gives characteristic ¹H NMR signals for protons. This structure is also confirmed by Mass spectrum.

Compound **4** on treatment with DMSO and CuCl₂ yields compound **5** chlorochromones. Chlorochromones are confirmed by IR frequencies like

1662 cm⁻¹ for C=O and 1108 cm⁻¹ for Ar-Cl. This structure is also confirmed by ¹H NMR and Mass spectrum.

Antimicrobial activity

Synthesized compounds were screened for their antibacterial activities against the bacteria *E. coli*, *B. subtilis* and *A. niger* using standard antibiotic drug Streptomycin. The biological activities of these compounds have been evaluated by turbidity method using DMSO as a solvent. MIC was determined after 48 hr or 72 hr incubation. Incubation zone were measured in mm and results obtained are shown in Table 2. Most of the compound showed moderate and few compound showed good antibacterial activity against *E. coli* & *B. subtilis*.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT spectrophotometer in a KBr disc. ¹H NMR spectra were recorded on a Bruker Avance II 400 MHz spectrophotometer DMSO-d₆ as a solvent and TMS as an internal standard (chemical shift in δ values). Mass spectra were obtained on a Finnigan mass spectrometer. Purity of the compounds was checked by TLC on silica gel G plates.

Table 1: Characterization data of synthesized compounds

Compd.	R	M.P.(°C)	Time(hrs)	Yield (%)
3a	4-Methyl	110	24	60
3b	3,5-Dimethyl	102	24	65
3c	4-Chloro,3-methyl	178	24	72
3d	4-Bromo	140	24	78
3e	3,5-Dichloro	162	24	80
4a	4-Methyl	165	3.5	72
4b	3,5-Dimethyl	182	3	75
4c	4-Chloro,3-methyl	228	3.5	70
4d	4-Bromo	175	4	78
4e	3,5-Dichloro	235	3.5	76
5a	4-Methyl	145	4	58
5b	3,5-Dimethyl	130	4	65
5c	4-Chloro,3-methyl	202	3.5	70
5d	4-Bromo	220	3.5	64
5e	3,5-Dichloro	170	3.5	74

Table 2: Antibacterial activity of compounds 3-5

Compd.	<i>E. coli</i>	<i>B. subtilis</i>	<i>A. niger</i>
3a	8	8	8
3b	7	9	8
3c	8	9	8
3d	8	8	9
3e	9	10	8
4a	8	7	6
4b	7	9	6
4c	8	9	8
4d	9	8	7
4e	8	9	6
5a	9	10	8
5b	10	9	8
5c	9	9	9
5d	8	8	8
5e	9	9	10
Streptomycin	8	9	11

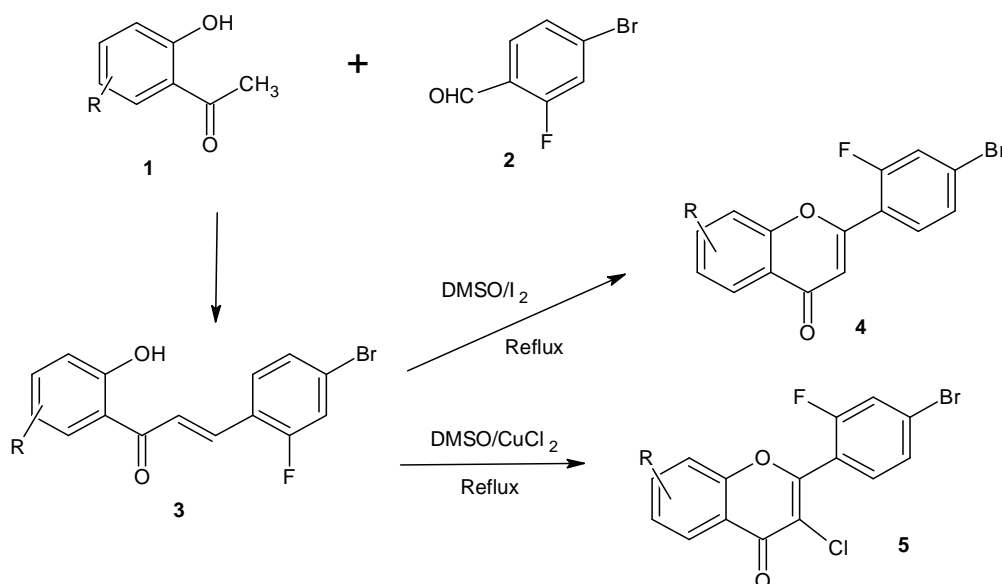
General Procedure**(2E)-3-(4-Bromo-2-fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one**

2-Hydroxyacetophenone (0.005 mol) **1** and aldehyde **2** (0.005 mol) were taken in 100 ml RBF with 25 ml ethanol. To this reaction 2 gm of NaOH/KOH was added and resulting reaction was stirred at room temperature for 24-36 hrs. Then contents were poured over crushed ice and acidify with Conc. HCl, solid thus obtained were separated by filtration and crystallized from proper solvent to get compound **3**. Their characterization data is given in the table

Spectral Data**3a**

IR(KBr) cm^{-1} : 3523 (-OH stretch), 1642 (C=O), 1612-1573 (Ar -C=C- Stretch).

$^1\text{H NMR}$ (DMSO- d_6): 2.34 (s, Ar- CH_3), 6.86-8.12 (m, 5 Ar-H and $^{\alpha}$ -olefinic H, 7.84 $^{\beta}$ -olefinic H. Mass: (M+); m/z 335

**Scheme 1:****2-(4-Bromo-2-fluorophenyl)-4H-chromen-4-one**

Chalcones **3** (0.001 mol) was dissolved in 15 ml of DMSO and to this catalytic amount of I₂ (about 0.5g) was added. The reaction mixture was then heated under reflux for 2 hr. Cold water was

added to the flask and the separated product was filtered and washed with water followed by dil. sodium thiosulphate solution to remove excess of iodine. The product was crystallized from alcohol.

Spectral Data**4a**

IR IR(KBr) cm^{-1} : 2925 (Aliphatic C-H stretch), 1635 (C=O stretch), 1132 (Ar-F). $^1\text{H NMR}$ (DMSO- d_6): 2.45 (s, Ar- CH_3), 6.75 (1H), 7.56-8.20 (m, 6 Ar-H), Mass: (M+); m/z 334

2-(4-bromo-2-fluorophenyl)-3-chloro-4H-chromen-4-one

Compound **3** (0.001 mol) was dissolved in 15 mL of DMSO and to this reaction mixture excess of CuCl_2 (2 g) was added. The reaction mixture was heated under mild reflux for 3h and left

overnight. Then 100 mL of ice cold water was added in it. The solid obtained was filtered and washed with dil. HCl followed by water. The product was crystallized from alcohol. The data of the synthesized compounds is given in Table 1.

Spectral Data

5c: IR (KBr) cm^{-1} : 3075 (Aromatic C-H Stretch), 1665 (C=O), 1135 (C-F stretch), 1078 (Ar-Cl stretch).

$^1\text{H NMR}$ (DMSO- d_6): 2.51 (s, Ar- CH_3), 7.63-8.13(m, 5 Ar-H) Mass: (M+); m/z 402

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