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# SYNTHESIS AND SPECTRAL ANALYSIS OF SOME PYRAZOLE DERIVATIVES

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## Abstract

*Synthetic pyrazole derivatives (5a-f) have been synthesized using conventional method producing good yield in ethanol with hydrazine in presence of acid. The oxidative cyclization reaction of chalcones (3a-f), with iodine crystals in presence of DMSO gives good yield of chromone (4a-f) derivatives these synthesized compounds were confirmed by IR, $^{1}H$ NMR and mass spectral data.*

***Keywords:*** *chalcones, chromones, pyrazoles, o-hydroxyacetophenones, fluorinated aromatic aldehyde.*



## Introduction

Fluorine atom plays an important role in the field of chemical and biochemical sciences. The literature survey revealed that after nitrogen, fluorine occupies the pposition of the second most hetro eliment in the field of life science oriented research. More than 10% of newly registered pharmaceutil drugs and near about 40% of newly registered agrochemical contain one or more atom. Fluorinated heterocycles have been associated with anti-inflammatory agents and psycho pharmaceuticals, anti-microbial, anti-lung cancer and act as selective inhibitors of biosynthesis of amineric neurotransmitters.

By the synthetic point of view chromones are important in the synthesis of the various heterocyclic compounds. Chromones are from flavonide family. In nature chromones are mostly in the form of 2-phenyl chromones called as iso-flavones which are found in fruits and vegetables.

Chromones and other related ring systems have several interesting biological activates. According to literature survey chromone compounds are associated with various physiological and biological properties and thus find important use in medicine.

In view of these chromones has been the subject of considerable interest in the past decadas. A series of sulfonamide derived chromones are inhibitors of carbonic anhydrase, show in vitro antibacterial and antifungal activity. 4-chromone and 2-chromone derivatives show antibacterial, antioxidant activity. During the last decades the 5-hydroxy-2-styrilchromone were obtained from the green algae [chrysophaeum] against leukemia cells. Chromones having heterocyclic substitunt at 2-position have been reported to possess anti-bacterial, anti-fungal, anti-inflammatory, anti-microbial, anti-hypertensive activities. Some chromones have potential antirthythmic activity as well as HIV- integrase inhibition activity. Some chromones showed anti-cancer, anti-inflammatory effects.

As like chromones, chalcones are also shows the medicinal properties. Chalcones constitute an important group of natural product and some of them possess wide range range of biological activities such as anti-bacterial, anti-tumor, anti-cancer, anti-malarial and anti-tubercular. Literature survey revealed that chalcones have broad spectrum of activites like anti-inflammatory, insecticidal, anti-viral, anti-microbial etc.

Chalcones are natural compounds found in many plants and they are also synthetically prepared. These substances are of a high interest due to their uses as precursor in the synthesis of a number of heterocyclic compounds. Chalcones are α-β-unsaturated carbonyl compounds that are major intermediates in the synthesis of natural product. They are known to possess many biological activites fungicidal properties.

Prazole an important class of compounds in medicinal chemistry, constitute the basic framework of drugs such as celecoxib and are well recognized for their multifaceted pharmacological and medicinal application. Pyrazole derivatives have been associated with various biological activities such as anti-inflammatory, fungicidal and antibacterial activity.

Keeping in view of these obserivations and in continuation of our work on chalcone, pyrazoline, chromone, and pyrazole derivatives herein we wish to report synthesis of these heterocycles (scheme-1) containing fluorinated benzene moiety.

**Result and Discussion:**

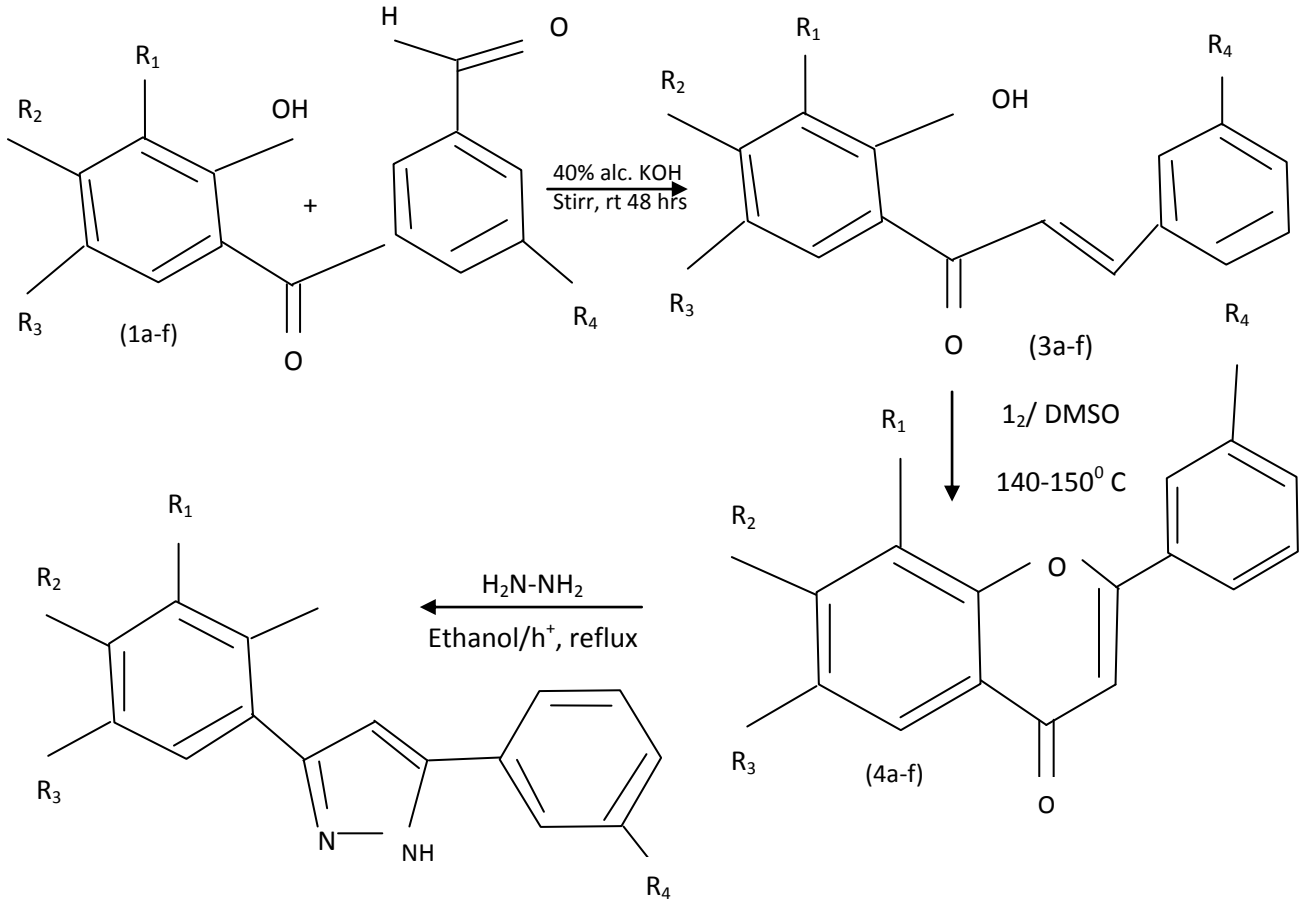
Outline of synthesis of 2-(3-flurophenyl)-8-methy-chromen-4-one and 2-(5-(3-fluorophenyl)-1H-pyrazol-3-yl)-4-methyphenal are summarized in schame-1. The precursor

compounds (E)-3-(3-fluorophenyl)-1-(2-hydroxy-5-methylphenyl) prop-2-en-1-one was prepaid by claisen-schmidt condehydes in presence of ethanol/KOH.

The clalcones (3a-f) were characterized by IR, $^1$H NMR, Mass spectrometry. The $^1$H NMR spectra of chalcone 3b showed characteristic feature singles due to olefinic proton α H dd at 5.98 б, J ≈15.98 Hz and βHz trans geometry.

The chromones and pyrazoles also showed the $^1$H NMR characteristic feature singnal of olefin α H at 5.88 б singlet and –OH and NH singlet at 9.10 бand 8.6 б respectively.

**Scheme I**




**Experimental section:**

All the recorded melting points were determined in open capillaries in liquid paraffin bath and are uncorrected. The progress of reaction was monitored with thin layer chromatography using silica gel-G (Merck). IR spectra have been recorded on a perkin Elmer spectrum version 10.4.2 FTIR spectrophotometer. $^1$H NMR spetra have been recorded on Bruker Avance-II 400 MHz NMR spectrophotometer using $CDCl_3$ as a solvent and tetra methyl silence

as internal standard. Signal values have been shown in б (ppm). The mass spectra have been recorded on a waters, Q-TOf Micromass (LC-MS) mass spectrometer.

**Synthesis of (E)-3-(3-fluorophenyl)-1-(2-hysroxy-5-methypl)prop-2-en-1-one (3a)**

In 25 ml round bottom flaks 3- flurocarbaldehyde 1 (0.02 mol) and substituted 2-hydroxy acetphenone 2 (0.02 mol) w2as dissolved in 40 ml of alcohol. To this reaction mixture 40% KOH (10 ml) was added. The reaction mixture was stirred at room temperature for 48 hours. Then the contact was poured into crushed ice and neutralized with concentrated hydrochloric acid yellow solid thus obtained was filtered, dried and neutralized with concentrated hydrochloric acid . Yellow solid thus obtained was filtered, dried and crystallized by above procedure are listed in table 1.

3a: IR ($cm^{-1}$): 3354 (O-H), 1692 (Conj. C=O), 1617, (C=C), 1224(C-F).

$^1$H NMR (б) 11.15 (s, O-H), 7.17 to 8.20 (7H Ar-H), 6.97 (dd, 1H, 16.12Hz), 5.4 (dd,1H,15.2Hz), 2.36 (s,Ar-$CH_3$).

MS: (m/z): 257 ($m^{+1}$).

3b: IR ($cm^{-1}$): 3073 (O-H), 1647 (Conj. C=O), 1580(C=C), 1219 (C-F), 785(C-CL).

$^1$H NMR (б) 13.25 (s, O-H), 7.17 to 7.96 (8H Ar-H and – CH+cH-).

MS : (m/z): 312 ($m^{+1}$).

**Synthesis Of 2-(3-Fluorophenyl-8-Methy-4h-Chromen-4-0One (4a-F):**

Chalcone (0.002 mole) was dissolved in 10-15 ml DMSO. To this reaction mixture catalytic amount of iodine (about 4 crystals) was added. Contents were heated at 140-150$^0$ C in oil bath for 3 hours and left overnight. The progress of reaction was monitored by TLC. After completion amount of reaction the reaction mixture was poured over crushed ice containing 3-4 gm of sodium thiosulphate. The products were separated by filtrated by filtration, washed with water, dried and purified by recrystalization from acetic acid to afford pure compound of chromones .

4a : IR ($cm^{-1}$):1692 conj. (C=O), 1617(C=C),1224 (-C-F), 1112 (C-O).

$^1$H NMR (400 MHz, $CDCL_3$, б): 7.17-8.20 (m, 7H aromatic), 5.40 (s, 1H, chromone), 2.36(s, Ar-$CH_3$).

MS: ($M^{+1}$) : 255.

**Synthesis of 2-(5-(3- fluorophenyl)-1H-pyrazol-3-yl)-4-methylphenol:**

Compounds (0.003 mole) were taken in 100 ml round bottom fleks with 15 ml ethanol. To this reaction mixture 1 ml hydrate was added and the contents were heated under refluxed for 4hr. then to the reaction mixture 1 ml glacial acetic acid and heating was continued for further 3hrs. after complete heating contents were cooled to room temperature and poured over crushed ice. The solid thus obtained was separated by filtration with the help of spectral data. Their characterization data is given in the table -1.

IR: ($\upsilon_{max}$, $cm^{-1}$) 5a: 3350 (-OH), 3650 (-N-H), 1597 (-C=N), 3.3 (s, one of the 1H methylene proton), 6.78 to 8.17 (m, 7H Ar-H), 9.1 (s1H,-OH).

Mass (m/z): (M+1): 269.

**Table-1: characterization data of synthesized compounds (3a-f), (4a-f) and (5a-f)**

| Compound | $R_1$ | $R_2$ | $R_3$ | $R_4$ | M.P.($^0$C) | Yield (%) |
|---|---|---|---|---|---|---|
| 3a | H | H | $CH_3$ | F | 141 | 78 |
| 3b | CI | H | CI | F | 182 | 79 |
| 3c | H | H | Br | F | 178 | 62 |
| 3d | H | H | CI | F | 184 | 71 |
| 3e | H | $CH_3$ | CI | F | 240 | 76 |
| 3f | H | H | H | F | 80 | 75 |
| 4a | H | H | $CH_3$ | F | 145 | 70 |
| 4b | CI | H | CI | F | 154 | 66 |
| 4c | H | H | Br | F | 165 | 77 |
| 4d | H | H | CI | F | 178 | 75 |
| 4e | H | $CH_3$ | CI | F | 158 | 69 |
| 4f | H | H | H | F | 143 | 70 |
| 5a | H | H | $CH_3$ | F | 159 | 73 |
| 5b | CI | H | CI | F | 211 | 68 |
| 5c | H | H | Br | F | 205 | 70 |
| 5d | H | H | CI | F | 180 | 65 |
| 5e | H | $CH_3$ | CI | F | 168 | 78 |
| 5f | H | H | H | F | 142 | 73 |

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