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Synthesis, Characterization and Antimicrobial Analysis of Some Chromones Containing Pyrazole Moiety

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ABSTRACT

We have developed a protocol for the synthesis of some Chromones by using I2 in DMSO from various chalcones. All the synthesized chromones were characterized by IR, NMR and Mass spectral data. Along with this synthesized compounds have been screened for their antimicrobial activity against gram +ve and Gram –ve microorganisms. A few of this compounds show moderate antimicrobial activity.

Keywords : chromones, chalcones, antimicrobial, Gram +ve and Gram –ve microorganisms.

I. INTRODUCTION

From the Greek word chroma, the word chromone is derived which indicates that many chromone derivatives shows a broad variation of color spectrum. A derivative of benzopyrane substituted keto group on the pyran ring is the chromone ring system or 1-4 benzopyrone. These derivatives are isomeric to coumarin. A major class of naturally occurring compounds constitute by chromone are biologically active [1]. Among the variety of heterocyclic systems, chromones are the majority widely investigated. In the past decades, chromones [2] have been the subject of the extensive chemical interest. Chromone shows various biological activity, some of the biological activities attributed to chromone derivatives include antibacterial [3-4], antifungal [5-10], anticancer [11-12], antioxidant [13-15], neuroprotective [16], HIV-inhibitory [17], antimicrobial [18, 19]. Chromone derivatives are present in large amounts in the diet of humans due to their abundance in plants and their low mammalian toxicity [20]. Flavonoids [21] which are most abundantly distributed in nature, that are also chromones. Some commonly occurring chromones are Eugenitol [22], Peucenin [23] and Isoeugenitol [24]. Also chromones are well known for their anti-inflammatory [25], antiulcer [26], antioxidant [27], biocidal [28], wound healing [29] and immune stimulatory [30] activities.

II. EXPERIMENTAL

In liquid paraffin bath, melting points of synthesized compounds were recorded in open capillaries and which are uncorrected. The purity was checked of the synthesized compounds by using TLC, in which silica

gel coated plates obtained from Merck as a stationary phase and solvent mixture of ethyl acetate and hexane as a mobile phase. Infrared spectra of synthesized compounds were recorded on Schimadzu-FT-IR Spectrophotometer using potassium bromide pellet technique and the absorption bands are expressed in cm-1. 1H NMR spectra of synthesized compounds were recorded on Varian 400 MHz and Mercury YH 300 MHz instrument in solvents DMSO-d6, CDCl3 and TMS as an internal standard, the chemical shift data were expressed as δ values relative to TMS and in hertz (Hz) coupling constants (J) were expressed. By using electro-spray method (ES), on Macromass mass spectrophotometer (Waters), mass spectra were recorded.

III. GENERAL EXPERIMENTAL PROCEDURE

General experimental Procedure for the synthesis of 2-(3-(5-bromothiophen-2-yl)-1-(4-fluorophenyl)-1H-pyrazol-4-yl)-6-chloro-4H-chromen-4-one (2c):

(0.25 gm, 0.0007 mmole) of chalcone **1c** was dissolved in 15 ml. of DMSO. To this reacting mixture catalytic amount of cuprous chloride ($CuCl_2$) was slowly added. In an oil bath, this reaction mixture was heated for 4 hr at 120°C. Completion of reaction (monitored by TLC), this reaction mass was left overnight. 10 ml. of cold water was slowly added to this flask and the separated product was filtered, then washed with water followed by dil. HCl for many times. It was washed with water again, dried under the vacuum and recrystallized from ethanol to get **2g**. The compounds **2(a-h)** were prepared, following by this general procedure. Physical data of these synthesized compounds are recorded in **Table 1**. Structures of these compounds have been confirmed by IR, ^{1}H NMR and Mass spectra.

IR (2b) (cm^{-1}): 1034(Ar-Br), 1264(C-O), 1524(C=N), 1578(Ar-C=C), 1618(C=C), 1724(C=O).

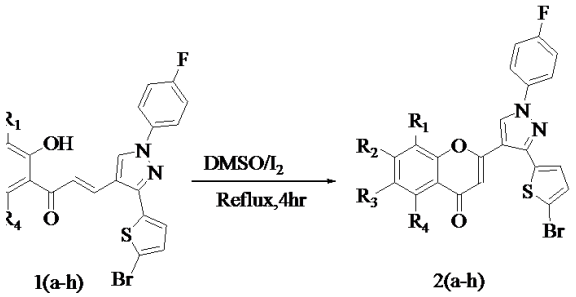
^{1}H NMR (2b) (DMSO-d_6) δ ppm: 2.452(s,3H), 6.695 (s,1H,Chromone-H), 6.943-6.961(d,2H,Ar-H,*J*=7.2Hz),7.163-7.204 (m,4H,Ar-H), 7.294-7.331 (m,3H,Ar-H), 8.051 (s,1H,Pyrazole-H).

ES-MS (2b) (m/z): 482(M+1), 483(M+2), 484(M+3)

IR (2c) (cm^{-1}): 732(C-Cl), 1055(Ar-Br), 1271(C-O), 1531(C=N), 1565(Ar-C=C), 1615(C=C), 1705(C=O).

^{1}H NMR (2c) (DMSO-d_6) δ ppm: 6.756 (s,1H,Chromone-H), 7.125-7.145 (d,2H,Ar-H, *J* =8 Hz),7.454-7.469 (d,2H,Ar-H,J=6Hz), 7.564-7.602 (m,3H,Ar-H), 7.861-7.921(m,2H,Ar-H),7.895(s,1H,Pyrazole-H).

ES-MS (2c) (m/z): 501(M+1), 502(M+2), 503(M+3)



Scheme 1: Synthesis of various (*E*) 2-(3-(5-bromothiophen-2-yl)-1-(4-fluorophenyl)-1H-pyrazol-4-yl)-4H-chromen-4-one

Table 1: Physical data of compounds 2(a-h)

Comp.	R_1	R_2	R_3	M.P. (°C)	Yield (%)
2a	H	H	H	168-170	81
2b	H	H	CH_3	192-194	69
2c	H	H	Cl	222-224	81
2d	Cl	H	Cl	216-218	78
2e	H	H	F	226-228	76
2f	H	CH_3	Cl	196-198	70
2g	H	H	Br	214-216	73
2h	CH_3	H	CH_3	200-202	79

IV. RESULT AND DISCUSSION

Eight new chromones derivatives have been synthesized successfully having good yields. The newly synthesized chromones derivatives have been confirmed using ^{1}H NMR, melting point range, Mass, IR spectral analysis. By using disc diffusion method,

all newly synthesized compounds were screened for antimicrobial activity.

Antimicrobial activity: Compounds **2(a-h)** were screened for their antimicrobial activity against Gram positive (*Enterobacter aerogenes, Salmonella abony, Salmonella typh, Pseudomonas aerogenosa, Escherichia coli, Shigella boydii)* and Gram negative pathogens(*Staphylococcus aureus, Megaterium Bacillus, Bacillus subtilis, Bacillus cereus*) by paper disc diffusion method using tetracyclin as a reference standard drug. By using Nystatin as standard drug, antifungal activity was screened against *Aspergillus niger, Saccharomyces cerevisiae, Candida albicans* at 100 µg/ml concentration. Culture media was Muller Hinton agar. In mm The zone of inhibition was measured, after the 24 hr of incubation at 37°C. Microbial data for 2(a-h) are summarized in **Table 2.**

Table 2: Antimicrobial Analysis Data

	Bacterial pathogens										Fungal pathogen		
	Gram negative pathogen						Gram positive pathogen						
Compounds	*Salmonella typhi*	*Enterobacter*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Salmonella abony*	*Shigella boydii*	*Bacillus subtilis*	*Bacillus*	*Staphylococcus aureus*	*Bacillus cereus*	*Candida albicans*	*Saccharomyces cerevisiae*	*Aspergillus niger*
2a	10	08	11	09	13	06	-	10	06	07	-	06	10
2b	07	09	12	14	13	-	09	11	09	-	10	-	07
2c	08	04	10	08	11	05	-	05	01	11	15	-	12
2d	-	09	07	-	05	-	04	10	12	-	14	04	04
2e	-	11	09	18	09	-	-	04	17	-	12	-	08
2f	09	-	11	16	13	-	05	10	14	-	13	-	12
2g	-	04	05	-	08	-	-	11	17	-	-	-	15
2h	12	-	10	09	11	04	12	07	08	-	07	08	06
DMSO	-	-	-	-	-	-	-	-	-	-	-	-	-
STND.	22	20	20	33	21	26	25	20	30	25	24	20	25

*Standard for bacterial pathogens-tetracyclin, for fungal pathogens-nystatin

V. CONCLUSION

In conclusion, we have successfully synthesized chromone derivatives starting from chalcones, these newly synthesized chromone derivatives were screened against Gram positive as well as Gram negative bacterial strains and some of these compounds show moderate activity as compared to standard drug. The obtained data through the present work shows a good agreement between the experimental and computed spectral data.

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