Synthesis and Antimicrobial Activity of Some Aldehyde Derivatives of 3-Acetylchromen-2-one

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Abstract: Some new 3-(substituted)-chromen-2-one have been synthesized by condensation of 3-acetylchromen-2-one with various aromatic aldehyde in presence of ethanol and alkali. The synthesized compounds were identified by spectral data and screened for their antibacterial activity against *B. pumilis*, *B. subtilis* and *E. coli* and antifungal activity against *A. niger* and *Candida albicans*. Among the synthesized compounds, some compounds of aryl chromen, which are having electron releasing substituent such as methoxy and hydroxyl at various positions, showed moderate to considerable antibacterial and antifungal activities.

Keywords: Chromen, Synthesis, Antibacterial activity, Antifungal activity.

Introduction

Chromen moiety display interesting biological activities including anti-inflammatory¹, analgesic², antifungal³, antibacterial⁴, antiviral⁵, antipsychotic⁶, antituberculosis⁷, anti-HIV⁸, and anticarcinogenic⁹ activities. In the present study, we synthesized different 3-(substituted)-chromen-2-one derivatives by condensing 3-acetylchromen-2-one¹⁰ with different aromatic aldehyde in presence of alcohol and alkali. The structures of the various synthesized compounds are assigned on the basis of elemental analysis and spectral studies^{11,12}. These compounds were also screened for antimicrobial activity.

Experimental

Melting points were determined by open ended capillary tube in the electrical melting point apparatus and are uncorrected and the purity of the compounds were checked by TLC using

silica gel as stationary phase and the spots were visually detected in an iodine chamber. The structures of the compounds were elucidated by IR (Perkin-Elmer) in KBr disc and ^1H NMR (Bruker Spectrospin AV 400 MHz Spectrometer using TMS as an internal standard).

General procedure for the preparation of chromens (a-f)

A mixture of 3-acetylchromen-2-one¹⁰ (0.0304 mol) and appropriate aldehyde (0.0304 mol) was stirred in water (40 mL) and ethanol (25 mL) in presence of sodium hydroxide (0.0302 mol) for 5 h. The reaction mixture was kept overnight in an ice bath. Then the above mixture was poured into a beaker containing water. The precipitated product was filtered and recrystallized from ethanol (Scheme 1). The characterization data of these compounds are described in Table 1 & 2.

Scheme 1. Synthesis of some new 3-(substituted)-chromen-2-one (**a-f**)

Table 1. Characterization data of the compounds (**a-f**)

Compd.	Molecular Formula	m.p., $^{\circ}\text{C}$	Yield, %	Elemental analysis, %					
				C		H		O	
				Found	Calcd.	Found	Calcd.	Found	Calcd.
a	$\text{C}_{20}\text{H}_{17}\text{O}_3\text{N}$	66	78	89.42	89.56	5.90	5.94	10.12	10.23
b	$\text{C}_{19}\text{H}_{14}\text{O}_4$	62	69	68.56	68.58	5.10	5.16	11.72	11.80
c	$\text{C}_{21}\text{H}_{18}\text{O}_6$	72	88	85.18	85.38	4.63	4.88	10.23	10.36
d	$\text{C}_{21}\text{H}_{18}\text{O}_6$	69	85	85.18	85.38	4.63	4.88	10.23	10.36
e	$\text{C}_{19}\text{H}_{14}\text{O}_5$	71	74	66.45	66.58	3.28	3.21	9.98	9.79
f	$\text{C}_{18}\text{H}_{10}\text{O}_3\text{Cl}_2$	82	91	82.69	82.74	4.81	5.01	11.24	11.37

Table 2. Spectral data of the compounds (**a-f**)

Compd.	IR (KBr, cm ⁻¹)	¹ H NMR (CDCl ₃ , ppm)
a	1725(-C=O), 1359.57(C-N, stretch, 3 ^o amine), 1439.6(CH ₃), 1595.81 (-C=C-), 1066.44, 1231.33(-C=C-O-C-)	2.206(s, 3H, CH ₃), 3.314(s, CH ₃), 6.645-7.12(m, Ar-H), 2.85-2.93 (s, 6H, -N(CH ₃) ₂)
b	1730(-C=O), 1447.31(-CH ₃) 1596.77 (-C=C-), 1600(-C=C-)2812.67(-O-CH ₃)	3.951(3H, -O-CH ₃), 6.712-8.085 (m, Ar-H), 6.2(d, 1H, C ₂ H),
c	1735(-C=O), 1638(-CH=CH-), 1180(-O-CH ₃), 1602(-C=C-)	3.98(9H, s, 3xO-CH ₃), 6.89(1H, d, -CO-CH=), 7.73(1H, d, -CH-Ar), 7.41-7.82(4H, m, Ar-H)
d	1728(-C=O), 1642(-CH=CH-), 1182 (-O-CH ₃), 1622(-C=C-), 1185(-O-CH ₃)	3.78(3H, d, O-CH ₃), 6.85(1H, d, -CO-CH=), 7.43(1H, d, -CH-Ar), 7.56-7.95(4H, m, Ar-H)
e	1741(-C=O), 1635(-CH=CH-), 1178(-O-CH ₃), 1612(-C=C-)	3.89(3H, s, 3xO-CH ₃), 6.98(1H, d, -CO-CH=), 7.78(1H, d, -CH-Ar), 9.81(1H, s, -OH), 6.78-7.02(7H, m, Ar-H)
f	1728(-C=O), 1650(-CH=CH-), 1610(-C-Cl), 1257.36(-C=C-O-C-)	6.91(1H, d, -CO-CH=), 7.61(1H, d, -CH-Ar), 7.32-7.96(7H, m, Ar-H)

Results and Discussion

Antimicrobial activity¹³

Cup plate method¹³⁻¹⁵ using Mueller-Hinton agar medium was employed to study the preliminary antibacterial activity of (**a-f**) against *B.pumilis*, *B.substilis* and *E.coli*. The agar medium was purchased from HiMedia Laboratories Ltd., Mumbai, India. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure¹⁴⁻¹⁶. Each test compounds (5 mg) was dissolved in 5 mL of dimethyl sulfoxide (1000 µg/mL). Volume of 0.05 mL and 0.1 mL of each compound were used for testing. gentamycin was used as a reference drug and dimethyl sulfoxide as a control, which did not revealed any inhibition.

Same cup plate method using Sabouraud Dextrose Agar (SDA) medium was employed to study the preliminary antifungal activity of (**a-f**) against *A. niger* and *candida albicans*. The SDA agar medium was purchased from HiMedia Laboratories Ltd., Mumbai, India. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure¹⁴⁻¹⁶. Each test compounds (5 mg) was dissolved in 5 mL of dimethyl sulfoxide (1000 µg/mL). Volume of 0.05 mL and 0.1 mL of each compound were used for testing. Griseofulvin was used as a reference drug and dimethyl sulfoxide as a control, which did not revealed any inhibition.

The cups each of 9 mm diameter were made by scooping out medium with a sterilized cork borer in a petri dish, which was streaked with the organisms. The solutions of each test compound (0.05 and 0.1 mL) were added separately in the cups and petri dishes and were subsequently incubated. Zone of inhibition produced by each compound was measured in mm and the results are presented in Table 3.

Table 3. Zone of inhibition of compound (a-f)

Compd.	<i>B.pumilis</i>		<i>B. subtilis</i>		<i>E.coli</i>		<i>A.niger</i>		<i>C.albicans</i>	
No	0.05 mL	0.1 mL	0.05 mL	0.1 mL	0.05 mL	0.1 mL	0.05 mL	0.1 mL	0.05 mL	0.1 mL
a	10	11	--	05	10	12	--	06	11	13
b	11	14	13	15	14	16	15	17	13	15
c	15	20	16	19	14	18	14	16	17	19
d	14	18	15	18	14	17	15	19	14	17
e	13	15	15	16	14	16	14	17	12	13
f	--	05	06	10	10	12	08	10	12	13
GM	21	25	20	21	18	20	*	*	*	*
GF	*	*	*	*	*	*	19	20	20	23

GM – Gentamycin, GF – Griseofulvin, (*) indicates activity not done, (--) indicates no zone of inhibition

Conclusion

All the newly synthesized compounds were structure elucidated by spectral data and screened for their antimicrobial activity. Among all the tested compounds (**b**), (**c**), (**d**) and (**e**) displayed considerable activity against all the pathogenic organisms.

From the above results, it is interesting to note that aryl chromen, which are having electron releasing substituent such as methoxy and hydroxyl at various positions, showed moderate to considerable antibacterial and antifungal activities. It also notes that increasing methoxy group, increases the activity.

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