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Synthesis and Antimicrobial Activity of Some New Chalcones of 3-Acetyl-Thiophene

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ABSTRACT

Chalcones are commonly found in fruit, vegetables, nuts, seeds, stems and flowers. For centuries, preparations containing these compounds as the principal bioactive constituents have been used to treat human diseases. Increasingly, this class of natural products is becoming the subject of antimicrobial research, and many groups have isolated and identified the structures of chalcones. However, several high-quality investigations have examined the relationship between chalcone structure and antibacterial activity and these are in close agreement. In addition, numerous research groups have sought to elucidate the antibacterial mechanisms of action of selected chalcones. Hence a series of some new chalcones have been synthesized by condensation of 3-acetyl-thiophene with various aromatic aldehydes in 40% alkali. The synthesized compounds were identified by spectral data and screened for antimicrobial activity. Some of these compounds showed moderate to considerable anti-microbial activity.

Key words: Chalcone, Synthesis, antimicrobial activity.

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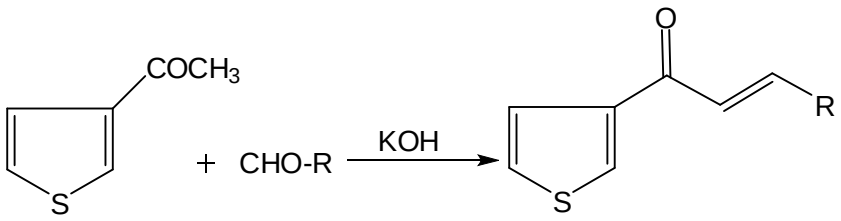
INTRODUCTION

Chalcones display interesting biological activities, including antimalarial,[1] anti-inflammatory,[2] cytotoxic,[3-4] anticancer[5,6] and antimicrobial activities[7,8]. In the present study we synthesized some new Chalcones (1-8) by the reaction of 3-acetyl-thiophene with different aromatic aldehydes. The structures of the various synthesized compounds are assigned on the basis of elemental analyses, IR and ^{1}H NMR spectral data. These compounds were also screened for their antimicrobial activity.

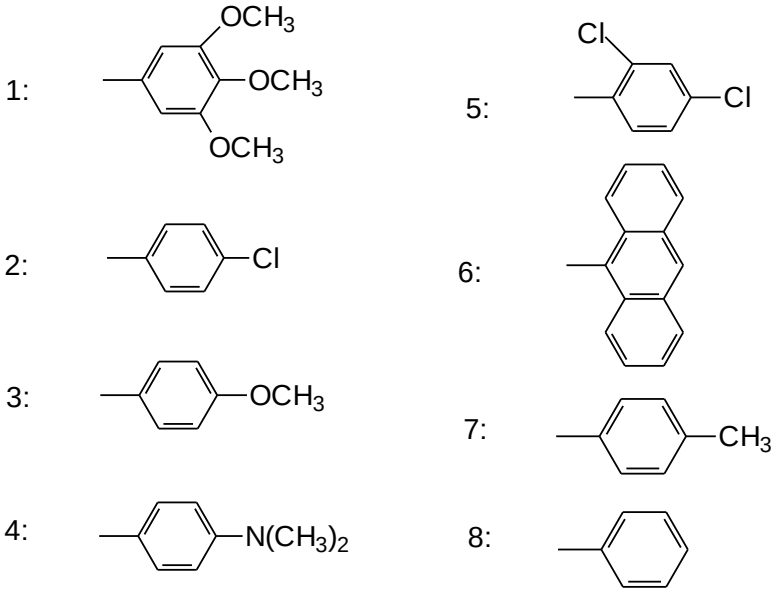
MATERIALS AND METHODS

Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra was recorded in the indicated solvent on Bruker WM 400 MHz spectrometer with TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer. Microanalyses were performed on Carlo Erba EA-1108 element analyzer and were within the ± 0.5% of the theoretical values. Column chromatography was performed on silica gel (Merck, 60-120 mesh).

General procedure for the preparation of chalcones:.



(1-8)



Scheme I: Synthesis of some new Chalcones of 3-acetyl-thiophene (1-8)

A mixture of 3-acetyl-thiophene (0.01mol) and appropriate aldehyde (0.01 mol) was stirred in ethanol (30 ml) and then an aqueous solution of KOH (40%, 15 ml) added to it. The mixture was kept overnight at room temperature and then it was poured in crushed ice and acidified with HCl. The solid separated was filtered and crystallized from ethanol (Scheme I). The characterization data of these compounds is described in Table-I & II

Antimicrobial activity:

Cup plate method[8,9] using Mueller-Hinton agar medium was employed to study the preliminary antibacterial activity of (1-8) against *B. pumilis, B. substilis, E.*coli. and *P. Vulgaris.* The agar medium was purchased from HI media Laboratories Ltd., Mumbai, India. Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure. Each test compound (5 mg) was dissolved in 5 mL of dimethyl sulfoxide (1000 µg/mL). Volumes of 0.05 mL and 0.1 mL of each compound were used for testing.

Same cup plate method using PDA medium was employed to study the preliminary antifungal activity of (1-8) against *A. niger* and *P. crysogenium*. The PDA medium was purchased from HI media Laboratories Ltd., Mumbai, India. Preparation of nutrient broth, subculture, base layer medium and PDA medium was done as per the standard procedure. Each test compound (5 mg) was dissolved in 5 mL of dimethyl sulfoxide (1000 µg/mL). Volumes of 0.05 mL, and 0.1 mL of each compound were used for testing.

The cups each of 9mm 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 were subsequently incubated. Benzyl Penicillin and Fluconazole were used as standard reference drugs (200 & 500 µg/ml respectively) and Dimethyl Sulphoxide as a control which did not reveal any inhibition. Zone of inhibition produced by each compound was measured in mm and the results are presented in table-III & IV.

RESULTS AND DISCUSSION

The screening results revealed that the compounds 1-8 showed significant antimicrobial activity. In particular compounds 2, 4, 5 & 6 showed moderate to considerable antibacterial and antifungal activities against all the organisms employed at a conc. of 1000 µg/mL (0.1 ml dose level) and are comparable to that of standard drugs Benzyl penicillin and Fluconazole respectively. From the above results it is interesting to note that mono chloro, dimethyl amino, dichloro substituted benzene ring, anthracene, at position 4 of the chalcones exhibited moderate

antibacterial activity and antifungal activity when compared to that of methoxy substituted, methyl substituted, unsubstituted benzene ring at position-4 of chalcones.

Table-I. Physical data of compounds (1-8)

Compd.	m.f.	m.p. (°C)	yield (%)	Elemental analyses (%)					
				C		H		O	
				Found	Calcd.	Found	Calcd.	Found	Calcd.
1	$C_{16}H_{16}O_4S$	135	95	43.00	43.20	43.10	43.20	10.50	10.80
2	$C_{13}H_9OSCl$	110	96	52.24	52.00	35.94	36.00	9.36	9.00
3	$C_{14}H_{12}O_2S$	70	86	48.55	48.20	41.57	41.30	7.12	6.83
4	$C_{15}H_{15}OSN$	100	83	45.44	45.45	45.68	45.45	3.42	3.03
5	$C_{13}H_8OSCl_2$	95	92	51.62	52.00	32.06	32.00	3.92	4.00
6	$C_{21}H_{16}OS$	140	80	54.90	53.84	41.11	41.02	2.59	2.56
7	$C_{14}H_{12}OS$	105	89	50.06	50.00	42.76	42.85	3.61	3.51
8	$C_{13}H_{10}OS$	90	87	52.09	52.00	40.11	40.00	4.06	4.00

Table II. Spectral data of the compounds (1-8)

Compd	IR (KBr, cm^{-1})	^1H NMR ($CDCl_3$, ppm)
1	3330 (-OH), 1720 (-C=O), 1650 (-CH=CH), 1175 (-OCH3), 650 (C-S)	7.69 (1H, d, J=16Hz , -CO-CH=), 7.89 (1H, d, J=16Hz ,=CH-Ar), 3.90-3.95 (9H, s, 3X-OCH_3), 7.20 (1H, m, C-4^1-H), 7.28 (2H, d, C-2^1-H, C-5^1-H), 7.78 (2H, s, C-2-H, C-6-H).
2	1725 (-C=O), 1640 (-CH=CH), 850 (C-Cl), 650 (C-S)	7.70 (1H, d, J=16Hz , -CO-CH=), 7.88 (1H, d, J=16Hz ,=CH-Ar) 7.80 (1H, d, J=9Hz, C-5^1-H), 7.58 (2H, d, C-3-H, C-5-H), 7.40 (2H, d, C-2-H, -C-6-H), 7.38(1H, d, J=16Hz , C-3-H,), 7.20 (1H, m, C-4^1-H).
3	1720 (-C=O), 1648 (-CH=CH), 1170 (-OCH_3), 666 (C-S)	6.94 (1H, d, J=16Hz ,-CO-CH=), 7.61 (1H, d, J=16Hz ,=CH-Ar), 7.86 (2H, d, C-3^1-H, -C-5^1-H), 7.68 (2H, d, C-3-H, -C-5-H), 7.18 (1H, m, C-4^1-H), 6.92 (2H, d, -C-2-H, -C-6-H).
4	1730 (-C=O), 1638 (-CH=CH), 1180 ($N(CH_3)_2$),676 (C-S)	6.70 (1H, d, J=16Hz ,-CO-CH=), 7.55 (1H, d, J=16Hz , =CH-Ar), 3.05 (1H, s, $N(CH_3)_2$), 7.86 (2H, d, C-5^1-H, C-3^1-H), 7.82 (2H, d, C-3-H, C-5-H), 7.63 (2H, d, C-2-H, C-6-H), 7.17 (1H, m, C-4^1-H).
5	1735 (-C=O), 1636 (-CH=CH), 855 (C-Cl), 686 (C-S)	7.31 (1H, d, J=16Hz , -CO-CH=), 7.87 (1H, d, J=16Hz , =CH-Ar) 7.71 (1H, d, J=8Hz, -C-5-H), 7.69 (1H, d, J=9Hz,-C-3^1-H), 7.67 (1H, d, -C-6-H), 7.48 (1H, s, -C-3-H) , 7.20 (1H, m, -C-4^1-H).
6	1710 (-C=O), 1655 (-CH=CH), 645 (C-S)	7.44 (1H, d, J=16Hz , -CO-CH=), 7.74 (1H, d, J=16Hz , =CH-Ar) 8.83 (1H, d, J=9Hz, C-5^1-H), 8.09 (1H, m, C-4^1-H), 8.06 (1H, d, J=9Hz, C-3^1-H), 7.18-7.79 (10H, m, Ar-H).
7	1732 (-C=O), 1645 (-CH=CH), 652 (C-S)	7.39(1H, d, J=16Hz , -CO-CH=), 7.56 (1H, d, J=16Hz , =CH-Ar), 7.88 (1H, d, J=9Hz, -C-5^1-H), 7.68 (2H, d, -C-2-H, -C-6-H), 7.58 (1H, d, J=8Hz, -C-3^1-H), 7.23 (2H, d, -C-3-H, -C-5-H), 7.19 (1H, m, -C-4^1-H).
8	1700 (-C=O), 1650 (-CH=CH), 650 (C-S)	7.69 (1H, d, J=16Hz , -CO-CH=), 7.84 (1H, d, J=16Hz ,=CH-Ar), 7.19 (1H, m, C-4-H), 7.87 (1H, d, J=9Hz, C-5^1-H), 7.44 (1H, m, C-4^1-H), 7.42 (1H, d, J=9Hz, C-3^1-H,),7.40(2H, d, C-3-H, C-5-H), 7.64 (2H, m, C-2-H, C-6-H).

Antimicrobial activity:

Table. III. Antibacterial activity of chalcones (1-8):

organisms	1		2		3		4		5		6		7		8		C	S 0.05 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	0.05 mL	0.1 mL	0.05 mL	0.1 mL	0.05 mL	0.1 mL	0.05 mL	0.1 mL		
B. pumilis	9	10	11	12	10	11	12	16	12	14	12	13	8	8	7	8	-	16
B. substilis	10	10	13	15	12	12	16	18	13	13	16	17	7	8	9	9	-	16
E. coli	8	9	12	12	11	13	18	18	14	16	13	15	8	7	8	8	-	14
P. Vulgaris	7	7	13	14	13	13	17	17	10	12	12	14	6	8	-	9	-	14

C: Control (DMSO); S: Standard (Benzyl Penicillin)

Table. IV. Antifungal activity of Chalcones (1-8):

organisms	1		2		3		4		5		6		7		8		C	S 0.05 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	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. niger	7	7	10	11	10	-	12	14	10	11	10	13	-	-	-	-	-	20
Penicillium chrysogenum	6	7	9	12	11	10	10	12	-	7	11	11	-	8	6	6	-	20

C: Control (DMSO); S: Standard (Fluconazole

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