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Synthesis And Antimicrobial Activity Of Some New Chalcones Of 3-Acetyl-2,5-Dimethylfuran

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Abstract: ***Eight new Chalcones were synthesized by condensing 3-acetyl-2,5-dimethylfuran with aldehyde derivatives in dilute ethanolic potassium hydroxide solution at room temperature according to Claisen-Schmidt condensation. All these compounds were characterized by means of their IR, Mass and ^{1}H NMR spectroscopic data and microanalyses. The antimicrobial activity of these compounds was evaluated by the cup plate method.***

Keywords: Chalcones, Synthesis, Antimicrobial activity.

I. INTRODUCTION

Chalcones either natural or synthetic are known to exhibit various biological activities. They have been reported to possess antioxidant, antimalarial, antileishmanial, antiinflammatory, antitumor and antibacterial activity. The presence of a reactive α,β-unsaturated keto function in Chalcones is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituent on the aromatic rings. In the present communication we report the reaction of 3-acetyl-2,5-dimethylfuran with different aromatic aldehydes to form Chalcones (1-8). The structures of the various synthesized compounds were assigned on the basis of elemental analyses, IR, H NMR and mass spectral data. These compounds were also screened for their antimicrobial activity.

II. EXPERIMENTAL

Melting points were determined on a capillary melting point apparatus and are uncorrected. H NMR spectra was recorded in the indicated solvent on Bruker AMX 400 MHz spectrometer with TMS as internal standard. The mass spectra of the compounds were recorded on Agilent 1100 ESI-Mass (Turbo Spray) using positive mode ionization method. Elemental analyses were carried out with a Perkin-Elmer model 2400 series II apparatus. The results of elemental analyses (C,H,N) were within ± 0.4 % of the calculated values. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer. Column chromatography was performed on silica gel (Merck, 100-200 mesh).

GENERAL PROCEDURE FOR THE PREPARATION OF CHALCONES (1-8)

Equimolar quantities (0.005 mol) of 3-acetyl-2,5-dimethylfuran and respective aldehydes were mixed and dissolved in minimum amount of alcohol. To this, aqueous potassium hydroxide solution (50%, 7.5 mL) was added slowly and mixed occasionally for 24 h, at room temperature. Completion of the reaction was identified by TLC using silica gel-G. After completion of the reaction, the mixture was poured onto crushed ice, acidified if necessary with dilute hydrochloric acid, and the solid that separated was isolated by filtration, dried and purified by column chromatography on silica gel (100- 200 mesh, Merck), with a mixture of ethyl acetate and hexane as the mobile phase(scheme1). The Characterization data of these compounds is described in Table-1 and 2.

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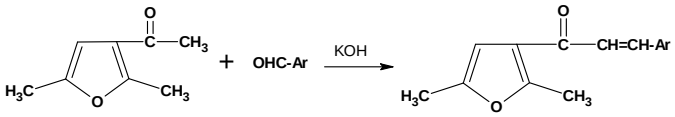
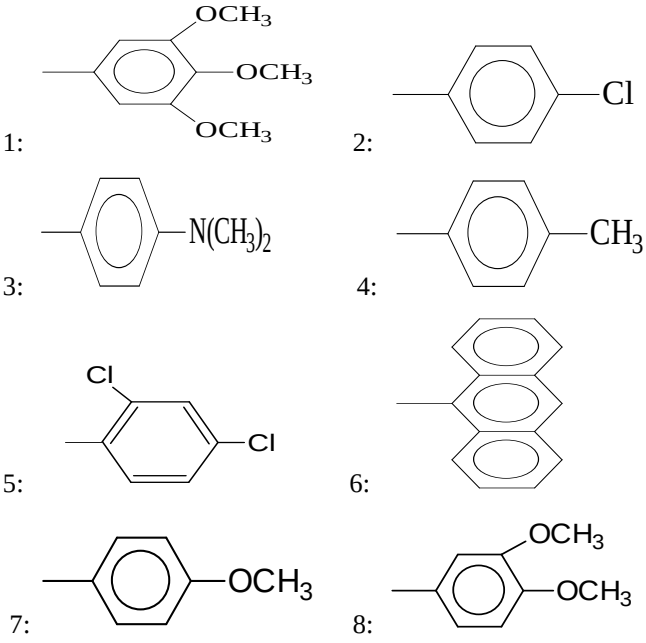
REACTION



(1-8)



Scheme1: Synthesis of Chalcones of 3-acetyl -2,5-dimethylfuran

Compound	Molecular formula	Melting point (°C)	Yield (%)	Elemental analysis (%)					
				C		H		N	
				Found	Calculated	Found	Calculated	Found	Calculated
1	$C_{18}H_{20}O_5$	154	71	68.23	68.34	6.28	6.37	-	-
2	$C_{15}H_{13}ClO_2$	139	68	69.25	69.23	5.03	5.01	-	-
3	$C_{17}H_{19}NO_2$	112	73	75.82	75.83	7.05	7.06	5.22	5.20
4	$C_{16}H_{16}O_2$	153	75	80.04	80.02	6.68	6.66	-	-
5	$C_{15}H_{12}Cl_2O_2$	132	71	61.24	61.22	4.06	4.08	-	-
6	$C_{23}H_{18}O_2$	138	78	84.65	84.64	5.58	5.56	-	-
7	$C_{16}H_{16}O_3$	87	73	75.02	75.01	6.28	6.25	-	-
8	$C_{17}H_{18}O_4$	121	69	71.34	71.32	6.30	6.29	-	-

Table 1: Physical data of compounds (1-8)

ANTIMICROBIAL ACTIVITY

Cup plate method 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 3 and 4.

Compound	IR (KBr, cm^{-1})	^{1}H NMR ($CDCl_3$, ppm)
1	1655 (C=O), 1602 (C=C quadrant of Ar), 1505(CH=CH), 1125 (O-CH_3), 1048 (C-O-C)	3.90-3.95 (9H, s, 3x-OCH_3), 6.71 (1H, s, C-4'-H), 7.20 (1H, d, J= 17Hz, -CO-CH=), 7.81 (1H, d, J= 17Hz, =CH-Ar), 6.90 (2H, s, C-2″-H and C-6″-H), 2.2(3H,s,Ar-CH_3), 2.7(3H,s, Ar-CH_3).
2	1664 (C=O), 1584 (C=C of Ar), 1520 (CH=CH), 1060 (C-O), 855 (C-Cl)	6.41 (1H, s, C-4'-H),7.10 (1H, d, J=17Hz,-CO-CH=), 7.70 (1H, d,J= 17Hz, =CH-Ar), 7.58 (2H, d,J= 8Hz, C-3″-H and C-5″-H), 7.40 (2H, d,J= 8Hz, C-2″-H and C-6″-H), 2.3(3H,s, Ar-CH_3), 2.6(3H,s, Ar-CH_3).
3	1658 (C=O), 1588 (C=C of Ar), 1502 (CH=CH), 1185 (-N(CH_3)$_2$) 1082 (C-O)	3.05 (6H, s, -N(CH_3)$_2$), 6.58 (1H, s, C-4'-H), 7.25 (1H, d, J=17Hz, -CO-CH=), 7.87(1H, d, J=17Hz, -CH=Ar), 6.75(2H,d, J=8.5 Hz, C-2″-H and C-6″-H), 7.55 (2H,d, J=8.5Hz, C-3″-H andC-5″-H), 2.05 (3H,s, Ar-CH_3), 2.5(3H,s, Ar-CH_3).
4	1641 (C=O), 1583 (C=C of Ar), 1505 (CH=CH), 1076 (C-O)	2.60 (3H, s, Ar-CH_3), 6.30 (1H, s, C-4'-H), 7.23 (1H, d, J=17Hz, -CO-CH=), 7.77 (1H, d, J= 17Hz, -CH=Ar), 7.56 (2H, d, J=9Hz,C-3″-H and C-5″H), 7.3 (2H, d, J=9Hz, C-2″-H and C-6″-H), 2.3(3H,s, Ar-CH_3), 2.4(3H,s, Ar-CH_3).
5	1648 (C=O), 1609 (C=C of Ar), 1510 (CH=CH), 1080 (C-O), 868 (C-Cl)	6.3 (1H,s,C-4'-H), 7.1 (1H, d, J=17Hz, -CO-CH=), 7.99 (1H, d, J=17Hz, =CH-Ar), 7.3 (1H, d, J=8Hz, C-6″-H), 7.4(1H,s,C-3″-H), 7.6(1H,d,J=9HZ,C-5″-H), 2.3(3H,s, Ar-CH_3), 2.6(3H,s, Ar-CH_3).
6	1633 (C=O), 1591 (C=C of Ar), 1506 (CH=CH), 1070 (C-O)	6.20 (1H, s, C-4'-H), 7.36 (1H, d, J=17Hz, -CO-CH=), 7.68 (1H, d, J=17Hz, =CH-Ar), 7.50-8.90 (9H, Ar-H), 2.3(3H,s, Ar-CH_3), 2.7(3H,s, Ar-CH_3).
7	1664 (C=O), 1585 (C=C of Ar), 1505 (CH=CH), 1133 (O-CH_3), 1055 (C-O-C)	3.85 (3H, s, OCH_3), 6.3 (1H, s, C-4'-H), 6.9 (1H, d, J=17Hz, -CO-CH=), 7.1-7.6 (4H, m, C-2″, 3″, 5″and 6″-H), 7.7 (1H, d, J=17Hz, =CH-Ar), 2.3(3H,s, Ar-CH_3), 2.5(3H,s, Ar-CH_3).
8	1656 (C=O0, 1590 (C=C of Ar), 1513 (CH=CH), 1166 (O-CH_3), 1062 (C-O-C)	3.92 (6H, s, -OCH_3), 6.35 (1H, s, C-4'-H), 6.89 (1H, d, J=16Hz, -CO-CH=), 7.02-7.3 (2H, m, C-5″and 6″-H), 7.18 (1H,s, C-2″-H), 7.7 (1H, d, J=16Hz, =CH-Ar), 2.3(3H,s, Ar-CH_3), 2.6(3H,s, Ar-CH_3).

Table 2: Spectral data of the compounds (1-8)

Organisms	1		2		3		4		5		6		7		8		S		C
	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL	
	Zone of inhibition(in mm)																		
A.niger	16	20	17	21	17	23	14	17	15	17	18	20	17	20	17	20	23	23	-
C.albicans	17	21	15	20	24	25	16	21	20	22	22	20	21	22	22	23	27	23	-
R.oryzae	17	19	15	18	16	18	13	18	13	16	14	19	15	18	15	18	27	21	-

Table 3: Antimicrobial activity of Chalcones(1-8)

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Organisms	1		2		3		4		5		6		7		8		S		C
	50	100	50	100	50	100	50	100	50	100	50	100	50	100	50	100	50	100	
	µg/mL		µg/mL		µg/mL		µg/mL		µg/mL		µg/mL		µg/mL		µg/mL		µg/mL		
	Zone of inhibition(in mm)																		
A.niger	16	20	17	21	17	23	14	17	15	17	18	20	17	20	17	20	23	23	-
C.albicans	17	21	15	20	24	25	16	21	20	22	22	20	21	22	22	23	27	23	-
R.oryzae	17	19	15	18	16	18	13	18	13	16	14	19	15	18	15	18	27	21	-

Table 4: Antifungal activity of Chalcones(1-8)

III. CONCLUSION

The screening results revealed that the compounds 1-8 showed significant antimicrobial activity. In particular compounds 3,4,7 and 8 showed moderate to considerable antibacterial activity against all the organisms employed at a conc. of 1000 µg/mL (0.1 mL dose level) and are comparable to that of standard drug Benzyl Penicillin. Similarly compounds 3,7 and 8 showed moderate to considerable antifungal activity against all the organisms employed at a conc. of 1000 µg/mL (0.1 mL dose level) and are comparable to that of standard drug Fluconazole.

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