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Synthesis and Antimicrobial Activity of Some Novel Chalcones Containing 3-Hydroxy Benzofuran

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Abstract

2-Acetyl-3-hydroxy benzofuran were allowed to react separately with different aromatic aldehydes in presence of 50% alkaline medium to yield the corresponding 3-hydroxy benzofuran substituted chalcones. The compounds obtained were identified by spectral data and screened for antimicrobial activity.

Key words: Benzofuran, chalcone, antimicrobial activity.

Introduction

Chalcones are products of condensation of simple or substituted aromatic with simple or substituted acetophenones in presence of alkali. Chalcone constitute an impartment group of natural products and some of them possess a wide range of biological activities such as antimicrobial (Prasad,Y. et al. 2008) anticancer (Jevwon et al. 2005) antitubercular (Shivakumar et al. 2005), antiviral (Churkin et al. 1982) etc.

Geiger and Conn (Walton et al. 1945) during their chemical studies on the structure of clavicin found that a structural feature which was responsible for antibacterial activity was α, β unsaturated keto functional group. The diverse properties of chalcones have prompted us to synthesize them in order to study their antimicrobial activity. The present work deals with the reaction of 2-acetyl-3-hydroxy-benzofuran (1) with different aromatic aldehydes (2) to form chalcones (3a-h) and the structure of all the various synthesized compounds were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. These compounds were screened for their antimicrobial activity.

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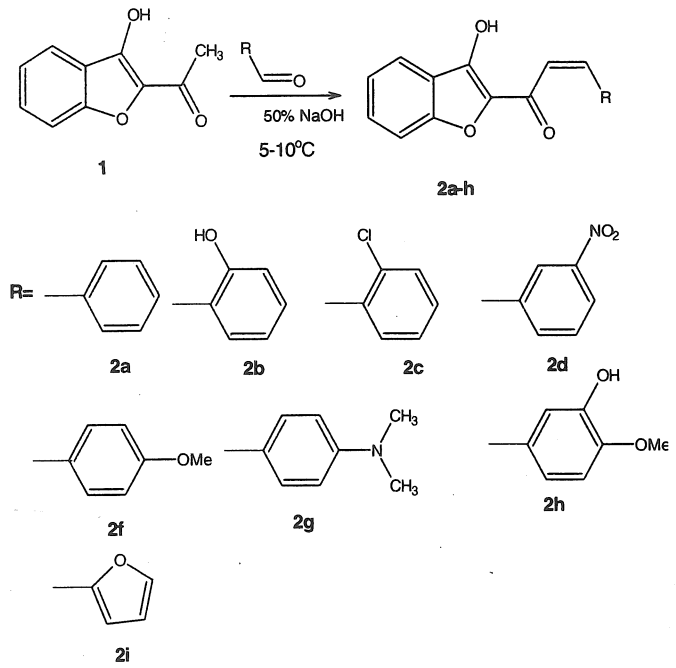
Experimental

Melting points were determined with open capillary. FTIR spectra were recorded on a Shimadzu FTIR model 8010 spectrophotometer, 1H NMR spectra were recorded in $CDCl_3$ on a Bruker supercon FT-NMR instrument using TMS as internal standard.

General procedure for the preparation of 1-(3' Hydroxy benzofuran -2-yl)-3-aryl-2-propene-1-ones (chalcones) A solution of 2-acetyl-3-hydroxy benzofuran (85g, 0.005 mole) and aromatic aldehydes (0.005 mole) in ethanol (12 ml) was cooled to 5 to 10°C in an ice bath. The cooled solution was treated with drop wise addition of aqueous sodium hydroxide (2.5 ml, 50%).

The reaction mixture was magnetically stirred for 30 min and then left over night. The resulting dark solution was diluted with ice water and carefully acidified using diluted hydrochloric acid. The benzofuran analogues of chalcone which crystallized were collected by filtration after washing with sodium bicarbonate and water. It was further purified by crystallization from ethanol.

Scheme-1



Characterization data of the synthesized compounds are reported in Table-1

Table 1. Characterization data of compounds

Compound	R	Mol. Formula	%Yield	M.P (°C)	Found (Calcd) %		
					C	H	N
2a	H	$C_{17}H_{12}O_3$	62	80	72.31 (72.27)	4.65 (4.54)	-
2b	OH	$C_{17}H_{12}O_4$	51	75	73.01 (72.85)	4.44 (4.28)	
2c	Cl	$C_{17}H_{11}O_3Cl$	56	134	68.57 (68.45)	3.81 (3.69)	
2d	NO_2	$C_{17}H_{11}NO_5$	72	75	66.20 (66.01)	3.71 (3.55)	4 44.76 (4.85)
2e	OCH_3-	$C_{18}H_{14}O_4$	45	62	73.51 (73.46)	4.71 (4.76)	
2f	-N<	$C_{19}H_{17}NO_3$	67	110	74.15 (74.26)	5.61 (5.53)	4.71 (4.73)
2h	C_4H_3O	$C_{15}H_{10}O_4$	89	78	71.01 (70.86)	4.08 (3.93)	

1-(3-hydroxy benzofuran-2-yl)-3-(4-Chlorophenyl)-2-propene-1-one (2c)
FTIR: 1650(C=0), 1630(C=C), 1080 (C-O-C) and 3400 cm-1(-OH);
1H NMR ($CDCl_3$): δ 6.70- 7.60 (m, 9H, Ar-H), 7.70(d, 1H, -COCH=), 8.10(d, 1H, =CH-Ar), 7.9(s,1H,-OH),

1-(3-hydroxy benzofuran-2-yl)-3-(4-Nitrophenyl)-2-propene-1-one (2d)
FTIR: 1655 (C=O), 1620(C=C), 1090(C-O-C) and 3410 cm-1 (-OH);
1H NMR ($CDCl_3$): δ 6.70- 7.50 (m, 9H, Ar-H), 7.60(d, 1H, -COCH=), 8.0(d, 1H,=CH-Ar), 7.7(s,1H,-OH)

1-(3-hydroxy benzofuran-2-yl)-3-(4-Methoxyphenyl)-2-propene-1-one (2e)
FTIR: 1660(C=O), 1618(C=C), 1092(C-O-C) and 3410 cm-1 (-OH);
1H NMR ($CDCl_3$): δ 7.30- 7.60 (m, 9H, Ar-H), 7.70(d, 1H, -COCH=), 8.10(d, 1H, =CH-Ar), 7.8(s,1H,-OH)

Antimicrobial Activity

All the newly synthesized compounds were screened for antimicrobial activity against both gram positive *S.aureus* and gram negative *E.coli* bacteria and antifungal activity against *C.albicans* and *A.flavus* according to cup plate method (Vagdevi,.et al., 2006) at a concentration of 0.005 mol/ml. Streptomycin and Gresofulvin were used as standard for comparison of antibacterial and antifungal activity (Kumar,1996). Indian Pharmacopoeia, 1996).Solvent dimethyl formamide (DMF) was used as control. The results of screening are given in Table 2 and 3.

Table 2. Antibacterial activity

No	Compounds	*Mean zone of inhibition (in mm)*			
		Staphylococcus aureus		*Escherichia coli*	
		50µg	100µg	50µg	100µg
1	Procaine penicillin	19	23	-	-
2	Streptomycin	-	-	20	24
3	2 a	12	15	9	12
4	2 b	13	15	8	10
5	2 c	14	16	11	12
6	2 d	12	15	7	11
7	2 e	11	14	8	10
8	2 f	15	17	9	12
9	2 g	13	14	8	9
10	2 h	13	15	10	9
11	3 a	13	16	8	12
12	3 b	12	18	7	11
13	3 c	13	16	10	11
14	3 d	14	18	8	10
15	3 e	13	17	9	12

Table 3. Antifungal activity

No	Compounds	Mean zone of inhibition (in mm)			
		Candida albicans		*Asperagillus flavus*	
		50mg	100mg	50mg	100mg
1	Griseofulvin	21	24	21	24
2	2 a	13	16	12	15
3	2 b	18	21	17	21
4	2 c	18	20	16	22
5	2 d	12	15	19	22
6	2 e	19	22	20	22
7	2 f	14	16	14	15
8	3 a	10	11	11	16
9	3 b	14	15	16	19
10	3 c	11	14	12	15
11	3 d	12	14	20	23
12	3 e	15	18	19	22

Results and Discussions

From the results, it is evident that most of the compounds are very weakly active and few are moderately active against *Staphylococcus aureus* and *Escherichia coli* but compounds 2c, 2d possess very good activity against fungi *Aspergillus flavus* and compound 2b showed moderate activity all bacteria and fungi tested.

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