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Synthetic and Antimicrobial Studies of Some New Chalcones of 3-Bromo-4-(*p*-tolyl sulphonamido) acetophenone

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Abstract Eleven new chalcones have been sysnthesised by condensing 3-bromo-4-(p-tolyl sulphonamido) acetophenone with different aromatic aldehydes using the method or Rohrman et al. The antimicrobial activity of these chalcones has been tested by adopting "paper disc diffusion plate method", against various pathogenic fungi(10) and bacteria (9). It has been found that the chalcones have considerable antifungal activity but less antibacterial activity. The results show that these chalcones may find use as antifungal agents.

Key words: Chalcones, Antomicrobial study.

Introduction

Sulphonamides are well known for their therapeutic activity[1], chalcone derivatives also possess anthelmintic[2], germicidal[3]. Antimicobial[4-5] and carcenogenic[6] activities. It was throught worthwhile to synthesise some bromo sulphonamido chalcones and study their antimicrobial activity against various fungi and bacteria.

Eleven bromo sulphonamideo chalcones have been prepared by condensing 3-bromo-4-(p-tolyl-sulphonamido) acetophenone with different aromatic aldehydes adopting the method.[7]

Experimental

In the preparation of 3-bromo-4-(p-tolyl sulphonamideo) acetophenones, two steps are involved.

Preparation of 3-bromo-4-(p-tolyl sulphonamido) acetophenone :

It is also accomplished into two steps:

(a) Synthesis of 3-bromo-4-amino acetophenone - It was prepared by acetylation of acetanilide by "Friedel-Craft's reaction" and the acetylated product then subjected to bromination to get bromo-aceto acetanilide. To separate the side chain acetanilide dissolved in pyridine and residue was taken and hydrolysed in presence of alcoholic KOH solution to get 3-bromo-4-amino acetophenone.

(b) Condensation of 3-bromo-4-amino acetophenone with p-tolyl sulphonyl chloride - Solution of 3-bromo-4-amino acetophenone and p-tolyl sulphonyl chloride in benzene were mixed together and concentrated on water bath. The product was crystallised from ethanol.

Preparation of 3'-bromo-4-(p-tolyl sulphonamido) chalcone

To a solution of 3-bromo-4-(p-tolyl sulphonamido) acetophenone (0.01 mole) and an aromatic Aldehyde (0.01 mole) in minimum quantity of hot aldehyde free alcohol, added 10% (10 ml) of aq. NaOH. The mixture was stirred for 3 hours at 25-30°C and kept at 0°C for 24 hrs. The product was filtered and recrysytallised from ethanol. Melting points were recorded on Toshniwal melting point apparatus and are tabulated in Table –I.

The chalcones thus prepared were characterised by halochromium test with conc. H_2SO_4 and their IR[7] and UV[8] spectra.

IR.(KBr) – 1312 cm^{-1} (-CH=CH-),1675 cm^{-1} (-C=O), 150-1145 cm^{-1}- (SO2-) 3500-3200 cm^{-1} (-NH-) 600-400 cm^{-1}(-C-Br).

ethanol 270-320 nm ($\alpha : \beta$ **unsaturated ketone)**

λ **max**

Investigations on the Antimicrobial Activity of the chalcones:

The antimicrobial activity of these chalcones was tested by "paper disc diffusion plate method[9]". For the determination of antifungal activity, about 20 ml of sterilized PDA –(potato-dextrose-agar) and in case of antibacterial screening, oxoid nutrient medium was poured in each sterilised petridish and before gelation of the media, about 2 ml of homogeneous mixture of fungi/bacteria in cool sterilise broth of potato and dextrose/beef extract and peptone respectively was mixed in each petridish. After half an hour, when the media was gelatinized, discs of 6 mm size prepared from Whatman filter paper (No.1) thoroughly moistened with the solution of chalcone (4%) in ethylene glycol were placed over the seeded media and incubated at 32 ±1°C and 28 ±1°C for 72 hours in case of fungi and 24 hours in case of bacteria respectively.

Activity of standard antifungal drug, gresiofulvin and antibacterial drug, streptomycin were also checked under the same conditions and concentration. Solvent ethylene glycol also tested for their antimicrobial activity and has shown no activity.

The experiments were performed in duplicate and average zones of inhibition in mm (including the size of the discs have been recorded and tabulated in Tables II and III).

Results and Discussion

On going through the results of antifungal activity (Table II), it has been observed that 3'-bromo-4'-(p-tolyl sulphonamido)chalcone and 2-hydorxy-3'-bromo-4'-(p-tolyl sulphonamido) chalcone having very good activity (108.7 and 78.26%) when compared with a standard antifungal drug "gresiofulvin" against fusarium moniliform. 2,4-dihydroxy-3'-bromo-4'(p-tolyl sulphonamido) chalcone shows good activity (78.26% and 65.21%) against Gleosporium sp. and Rhizopus stolonifer.

3,4-Dimethoxy,5,3'dibromo-4'(p-tolyl sulphonamido)chalcone shows very good activity (70.37%, 65.21% and 66%) against Acremonium furcatum, Rhizopus stolonifer and Chaetomium sp.

4-Nitro-3'-bromo-4'(p-tolyl sulphonamido) chalcone inhibits the growth of Gleosporium sp. as equivalent to the standard gresiofulvin and its activity is 70% against Chaetomium sp.

Remaining chalcones have shown considerable activity against most of the tested fungi; except against Aspergillus niger and Absidium sp. against which all these compounds are inactive.

The results of antibacterial activity has shown that 4-methoxy-3'-bromo-4'(p-tolyl sulphonamido) chalcone have 72.41% activity against Lactobacillus sp. and activity of 2,4-dihydroxy-3'-bromo-4'-(p-tolyl sulphonamido)chalcone against Pseudomonas putida is also good 75.86% to the standard 'streptomycin'. None of the chalcones have found to be active against Rhizopus lequminosarum, Serratia bachoria and Salmonella typhi (Table III).

On the basis of the results of these antimicrobial efficacies, it can be concluded that these chalcones may find use as antifungal agents.

Table - I

S.No.	Name of the compound	Molecular formula	M.pt.(°C)	Yeild (%)	% C Found	% C Calcu.	% H Found	% H Calcu.
1.	3'-Bromo-4'-(p-t.s.)C.	$C_{22}H_{18}O_3NSBr$	330 (not melted)	60%	56.92	57.64	3.19	3.93
2.	2-Hydroxy-3'-bromo-4'-(p-t.s.) C.	$C_{22}H_{18}O_4NSBr$	260(D)	78%	55.01	55.69	3.53	3.79
3.	2,4-ihydroxy-3'-bromo-4'-(p-t.s.) C.	$C_{22}H_{18}O_5$ NSBr	200(D)	65%	52.89	53.87	3.45	3.67
4.	2-Methoxy-3'-bromo-4'- (p-t.s.) C	$C_{23}H_{20}O_4NSBr$	300 (not melted)	45%	55.98	56.55	3.96	4.09
5.	4-Methoxy-3'-bromo-4'- (p-t.s.) C	$C_{23}H_{20}O_4NSBr$	97	60%	56.02	56.55	4.00	4.09
6.	3-Methoxy-4-hydroxy-3'-bromo-C(p-t.s.) C	$C_{23}H_{20}O_5NSBr$	220	75%	54.15	54.76	3.62	3.96
7.	3-Methoxy-4-hydroxy-3',5-dibromo-4'-(p-t.s.) C	$C_{23}H_{19}O_5NSBr_2$	270(D)	70%	47.03	47.50	3.05	3.27
8.	3,4-Dimethoxy-3',5-dibromo-4'-(p-t.s.)C	$C_{24}H_{21}O_5NSBr_2$	260(D)	65%	47.93	48.40	3.33	3.52
9.	3-Nitro-3'-bromo-4'- (p-t.s.) C	$C_{22}H_{17}O_5N_2SBr$	320(D)	80%	52.06	52.69	3.19	3.39
10.	4-Nitro-3'-bromo-4'- (p-t.s.) C	$C_{22}H_{17}O_5N_2SBr$	310(D)	78%	51.96	52.96	3.20	3.39
11.	4-Chloro-3'-bromo-4'- (p-t.s.) C	$C_{22}H_{17}O_3NSClBr$	300(D)	40%	53.52	53.82	3.16	3.46

Here, (p-t.s.)C. denotes (p-tolyl sulphonamido) chalcone.

Table II

S.No.	Names of the compound	Zones of inhibition in mm Name of the organism tested									
		Fusa rium monili form	Colleto-trichum dematium	Rhizopus stolonifer	Asper gillius niger	Alter-naria sp	Acre-monium furcatum	Gleos porium sp	Chaetomium sp.	Curvularia lunata	Absidum sp.
1	3'-Bromo-4'-(p-t.s.)C.	25.0	8.0	7.0	-	-	8.0	8.0	9.0	8.0	-
2.	2-Hydroxy-3'-bromo-4'-(p-t.s.)C.	18.0	-	12.0	-	11	8.0	9.5	9.0	7.0	-
3.	2,4-Dihydroxy-3'-bromo-4'-(p-t.s.)C.	10.0	7.0	15.0	-	-	13.0	18.0	10.5	-	-
4.	2-Methoxy-3'-bromo-4'(p-t.s.)C.	9.5	-	7.0	-	7	-	8.5	8.5	9.0	-
5.	4-Methoxy-3'-bromo-4'(p-t.s.)C.	8.0	8.0	12.0	-	12	9.0	8.0	14.0	-	-
6.	3-Methoxy-4-hydroxy-3' bromo-4'-(p-t.s.)C.	8.5	11.0	8.0	-	7	-	8.0	9.0	10.0	-
7.	3-Methoxy-4-hydroxy-3',5-dibromo-4'-(p-t.s.)C.	10.0	8.0	7.0	-	8	13.0	10.5	15.0	-	-
8.	3,4-Dimethoxy-3',5-dibromo-4'-(p-t.s.)C.	10.0	8.0	15.0	-	-	19.0	10.0	16.5	8.0	-
9.	3-Nitro-3'-bromo-4'-(p-t.s.)C.	8.0	-	-	-	-	9.0	8.0	7.0	-	-
10.	4-Nitro-3'-bromo-4'-(p-t.s.)C.	8.0	-	12.0	-	-	-	25.0	17.5	-	-
11.	4-Chloro-3'-bromo-4'-(p-t.s.)C.	10.0	8.0	9.0	8.0	8	10.0	8.0	10.0	9.0	10.0
	Control Gresiofulvin	23.0	24.5	23.0	23.0	23.0	27.0	25.0	25.0	23.0	25.0

Here, (p-t.s.)C. denotes (p-tolyl sulphonamido) chalcone. (-) denotes no activity.

Table III

S.No.	Names of the compound	Zones of inhibition in mm Name of the organism tested								
		Escheria-chia coli	Lactobacillius sp	Pseudomonas putina	Rhizobium japanicum	Rhizobium-lequminosa	Salmonella typhi	Serratia bachoria	Staphylococcus aureus	Vibrio-cholarae
1.	3'-Bromo-4'(p-t.s.)C.	-	9.0	9.0	8.0	-	-	-	-	8.0
2.	4-Chloro-3'-bromo-4' (p-t.s.)C.	11.5	10.5	10.5	8.0	-	-	-	-	10.5
3.	2-Hydroxy-3'-bromo-4' (p-t.s.)C.	-	8.0	8.0	8.0	-	-	-	-	-
4.	2,4-Dihydroxy-3'-bromo-(p-t.s.)C.	-	11.0	22.0	10.0	-	-	-	-	8.0
5.	2-Methoxy-3'-bromo-4'-(p-t.s.)C.	8.0	8.0	9.0	9.0	-	-	-	-	10.0
6.	4-Methoxy-4-hydroxy-3'-(p-t.s.)C.	8.0	21.0	16.0	10.0	-	-	-	8.0	10.0
7.	3-Methoxy-4-hydroxy-3'-(p-t.s.)C.	-	8.0	9.0	8.0	-	-	-	-	10.0
8.	3-Methoxy-4-hydroxy-3', 5-dibromo-4'-(p-t.s.)C.	-	9.5	9.0	10.0	-	-	-	-	9.0
9.	3,4-Dimethoxy-3',5-dibromo-4'-(p-t.s.)C.	-	10.0	-	-	-	-	-	-	10.0
10.	3-Nitro-3'-bromo-4'-(p-t.s.)C.	-	11.0	10.0	10.0	9.0	-	-	-	10.0
11.	4-Nitro-3'-bromo-4'-(p-t.s.)C.	-	9.0	16.0	9.5	-	-	-	-	10.0
	Control Streptomycin	28.0	29.0	29.0	28.0	34.0	43.5	28.0	35.0	35.0

(p.t.s.)C. denotes – (p-toly1 sulphonomido) chalcone (-) denotes no activity.

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