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NOTE

Synthesis of 2,4-Diaryl-2,3-Dihydro-1,5-Benzothiazepines as Antibacterial and Antifungal Agents

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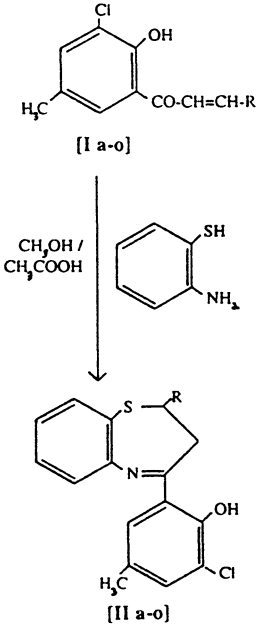
o-Aminophenol reacts with chalcones **(I)** in methanol and acetic acid to give 3-(2-aminophenylmercapto)-3-amyl-propiophenones **(II)** which immediately undergo cyclisation *in situ* to give 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines **(IIIa).**

Benzothiazepine derivatives are known to possess antiserotonic[1], neuroleptic[2], psychotropic[3], antianginal and antidepressant[4] activities. 2,3-Dihydro-1,5-benzothiazepin-4-(4H)-ones are found to be psychosedative[5, 6]. Although some benzothiazepines are reported as coronary vasodilatory[8].

Preparation of 4(3′-chloro-2′-hydroxy-5′-methylphen-1′-yl)-2-sub-phenyl-2,3-dihydro-1,5-benzothiazepine

A solution of 3′-chloro-2′-hydroxy-5′-methyl chalcone (0.01 mol) and *o*-aminothiophenol (**I**, 0.011 mol) in anhydrous methanol (100 mL) and glacial acetic acid (10 mL) was refluxed for 2 h, and cooled. The separated product was filtered and crystallized from ethanol to give (**II a–o**).



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IR Spectra: 1610 ν(C=N), 780 ν(C—Cl stret.), 870 (thiazepine ring) cm^{-1}.

NMR Spectra: (δ, ppm), 2.31 (CH_2 of thiazepine), 4.33 (CH of thiazepine), 6.76 (OH), 7.63–8.50 (Ar—H).

All the melting points were determined in open capillaries and are uncorrected. IR spectra of the compounds were recorded on a Perkin-Elmer 577 spectrophotometer and PMR spectra ($CDCl_3$: TMS as internal standard) on a Varian spectrophotometer Model No. XL-300).

Antibacterial activity: The antibacterial activity of title compounds is evaluated against *Staphylococcus aureus* and *Escherichia coli* by paper disc method and compared with standard drugs like amoxycillin and cloxacilin. Compounds Nos. **b, c, h, m** have shown maximum activity against *S. aureus* and *E. coli*.

Compounds **f, j** are inactive against *S. aureus* and *E. coli* while rest of the compounds have shown medium activity against both the bacteria.

Antifungal activity: The antifungal activity of the title compounds was evaluated against *C. albicans* by paper disc technique and compared with the standard drug nystatin.

Compounds Nos. **d, f, i** and **j** are inactive, while rest of the compounds have shown poor activity against fungi.

TABLE-1: PHYSICAL DATA OF COMPOUNDS **II (a–g)**

No.	R	m.f.	m.p. °C (Yield %)	Antibacterial activity (24 h)		Antifungicidal activity (48 h)
				S. aureus	*E. coli*	C. albicans
a	Phenyl	$C_{22}H_{18}ONClS$	130 (63)	11	15	16
b	2-furfuryl	$C_{20}H_{16}ONClS$	109 (60)	17	15	14
c	2-chlorophenyl	$C_{22}H_{17}ONCl_2S$	171 (65)	16	17	13
d	4-chlorophenyl	$C_{22}H_{17}ONCl_2S$	136 (62)	12	NA	NA
e	4-N,N-dimethyl aminophenyl	$C_{24}H_{23}ON_2ClS$	153 (67)	17	14	12
f	3,4-methylene dioxyphenyl	$C_{23}H_{18}O_3NClS$	139 (60)	NA	NA	NA
g	2-nitrophenyl	$C_{22}H_{17}O_3N_2ClS$	165 (71)	15	13	13
h	3-nitrophenyl	$C_{22}H_{17}O_3N_2ClS$	154 (68)	17	12	11
i	4-nitrophenyl	$C_{22}H_{17}O_3N_2ClS$	142 (70)	15	14	NA
j	4-hydroxyphenyl	$C_{22}H_{18}O_2NClS$	148 (62)	NA	NA	NA
k	3-aminophenyl	$C_{22}H_{19}ON_2ClS$	168 (65)	NA	13	11
l	4-methoxyphenyl	$C_{23}H_{20}O_2NClS$	116 (68)	15	15	14
m	4-methylphenyl	$C_{23}H_{20}ONClS$	171 (72)	11	16	13
n	2-hydroxyphenyl	$C_{22}H_{18}O_2NClS$	97 (69)	12	13	11
o	4-hydroxy-3-methoxyphenyl	$C_{23}H_{20}O_3NClS$	160 (67)	12	13	9
	Standard Drugs					
	Amoxycillin			25	–	–
	Cloxacillin			–	28.0	–
	Nystatin			–	–	27.0

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