Asian Journal of Chemistry Vol. 13, No.1 (2001), 341–343

NOTE

Synthesis of Some Biologically Active Isoxazolines

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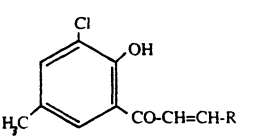
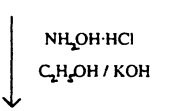
Various 2-hydroxychalcones have been condensed with hydroxylamine hydrochloride to yield isoxazolines. The compounds have been characterised by elemental analysis, IR and NMR spectra.

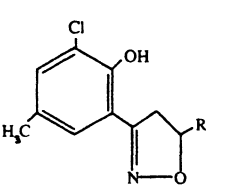
The unsaturation present in the chalcones is responsible for many novel reactions[1]. Among them the pyrazolines and isoxazolines are of prominence. Isoxazolines are reported to be active fungicides and insecticides. These compounds owe their activities to the heterocyclic ring present in the structure[2–4]. The reaction is not simple; besides the oxime and isoxzolines line, other products like hydroxylmine ketone, hydroxylamino oxime, disubstituted hydroxylamine, etc. may be formed depending upon the nature of substituents and the proportion of the reactants[5–7].

Melting points were determined in open capillary and are uncorrected. IR spectra were recorded in KBr on Perkin-Elmer-377 spectrophotometer and NMR were recorded on Varian model EM-360L spectrophotometer. Satisfactory elemental analyses were obtained.



[I a-o]





[II a-o]

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Preparation of 3{3′-chloro-2′-hydroxy-5′-methyl phen-1′-yl}-5-sub-2-isoxazoline

A mixture of 3′-chloro-2′-hydroxy-5′methyl-chalcone[2] (I, 0.01 mol) and hydroxylamine hydrochoride (0.02 mol) in ethanol (25 mL) was refluxed on water bath at 60–70°C for 4 h. The reaction mixture was then cooled and acidified with glacial acetic acid. The solid separated was filtered, washed with water, dried and crystallized from ethanol (Table-1 **a–o**).

TABLE-1
PHYSICAL DATA OF COMPOUNDS **1 (a–o)**

No.	R	m.f.	m.p. (°C) (Yield %)	Antibacterial activity (24 h)		Antifungi-cidal activity (48h)
				S. aureus	*E. coli*	
a	Phenyl	$C_{16}H_{12}O_2NCl$	150 (75)	17	NA	NA
b	2-furfuryl	$C_{14}H_{10}O_3NCl$	131 (70)	19	15.	12
c	2-chlorophenyl	$C_{16}H_{11}O_2NCl_2$	114 (80)	NA	11	9
d	4-chlorophenyl	$C_{16}H_{11}O_2NCl_2$	148 (82)	7	NA	8
e	4-N,N-dimethyl aminophenyl	$C_{18}H_{17}O_2N_2Cl$	166 (60)	NA	NA	NA
f	3,4-methylenedioxyphenyl	$C_{17}H_{12}O_2NCl$	108 (68)	NA	NA	NA
g	2-nitrophenyl	$C_{16}H_{11}O_4N_2Cl$	125 (72)	12	7	8
h	3-nitrophenyl	$C_{16}H_{11}O_4N_2Cl$	139 (72)	14	9	7
i	4-nitrophenyl	$C_{16}H_{11}O_4N_2Cl$	163 (78)	13	16	NA
j	4-hydroxyphenyl	$C_{16}H_{12}O_3N_2Cl$	121 (72)	11	13	12
k	3-aminophenyl	$C_{16}H_{13}O_2N_2Cl$	171 (67)	18	14	11
l	4-methoxyphenyl	$C_{17}H_{14}O_3NCl$	133-35 (72)	16	19.	10
m	4-methylphenyl	$C_{17}H_{14}O_3NCl$	159 (78)	12	17.	8
n	2-hydroxyphenyl	$C_{16}H_{12}O_3NCl$	172 (68)	11	13	7
o	4-hydroxy-3-methoxyphenyl	$C_{17}H_{14}O_4NCl$	181 (70)	11	15	9
	Standard Drugs					
	Amoxycillin			25	–	–
	Cloxacillin			–	28	–
	Nystatin			–	–	27

IR (KBr): The isoxazolines show sharp band around 830 and 880 cm^{-1} in addition to a medium intensity band around 1620 cm^{-1}. These bands are due to (N—O) and (C=N) stretching vibrations. Disappearence of (C=O) in the spectra of the compounds marks the condensation followed by ring closure.

NMR ($CDCl_3$): 2.25 (—CH_2 of methylenedioxy), 3.8 (—OCH_3), 6.99

(—OH), 7.17–8.43 (Ar—H). 2.47 (CH_2— of isoxazolines), 3.34 (CH isoxazolines) (δ_{PPM}).

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. Compound Nos. **b, k, l, m** have shown maximum activivity against *S.aureus* and *E. coli.*

c and **a, d** are inactive against *S. aureus* and *E. coli* respectively while rest of the comnpounds have shown poor 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 standard drug nystatin.

Compounds No. **a, e, i and f** are inactive while rest of the compounds have shown weak activity against fungi, *i.e., C. albicans.*

ACKNOWLEDGEMENTS

Authors are thankful to RSIC, IIT, Bombay, India for recording ^{1}H-NMR and to GSFC Baroda for recording IR spectra.

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(*Received*: 17 June 2000; *Accepted*: 16 November 2000) AJC- 2179