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NOTE

Synthesis and Antimicrobial Study of Some New Chlorosubstituted Isoxazolines

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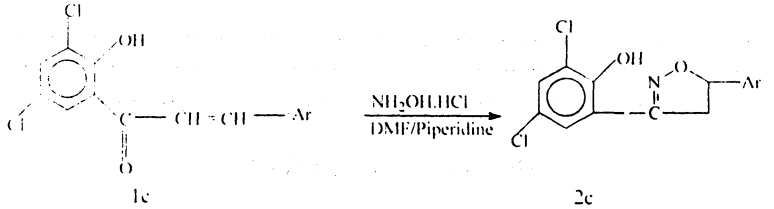
Chlorosubstituted chalcones (**1a–d**) were allowed to react with hydroxylamine hydrochloride in DMF containing a little piperidine to give isoxazoline in 1.5 h and yields were found to be 75–80%. These compounds show antibacterial activity when assayed against some common human pathogens.

Key Words: Synthesis, Antimicrobial activity, Chlorosubstituted isoxazolines.

It has been reported that the heterocyclic compounds containing isoxazoline ring present a broad spectrum of biological activity[1-3]. From literature survey it has also been revealed[4] that substituents in the phenyl ring enhance their antibacterial activity. We report here the synthesis of some hetrocyclic chlorosubstituted isoxazolines from chalcone on reaction with hydroxylamine hydrochloride in DMF containing a little piperidine. The antibactarial activity of these compounds has been tested against some gram positive (*S. aureus* and *B. subtilis*) and gram negative (*E. coli* and *P. aeruginosa*) bacteria.

A mixture of chalcone (**1c**) (0.01 mole and hydroxylamine hydrochloride (0.02 mole) was refluxed in DMF (25 mL) containing piperidine (0.5 mL) for 1.5 h. The reaction mixture was then poured in cold water and acidified with 1 : 1 HCl. The solid thus obtained was crystallised from ethanol-acetic acid mixture to get



1c 2c

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the compound **(2c)**. It gives colouration with ferric chloride solution and dissolves in NaOH indicating therehy the presence of free phenolic —OH group.

The spectral analysis of compound **2c** is as under:

IR (nujol) show absorption band at 3200–3080 ν(OH), 1630 ν(C=N), 1460 $\nu(CH_2)$, 1160 ν(C—O), 940 ν(N—O), 870 ν(2-furyl) and 740 cm^{-1} ν(C—Cl). UV showed λ_{max} 365 nm. Corresponding to $n \rightarrow \pi^*$ (transition) PMR ($CDCl_3$) showed 3.0 (dd, 1H, CH_A—CH), 3.5 (dd, 1H, CH—H_B), 5.5 (dd, 1H, CH—C), 6.7 to 7.85 (nm, 5H, Ar—H), 11.75 (S 1H, OH—).

Melting points recorded are uncorrected. The purity of the compounds was tested by TLC on microscopic slides with silica gel layers in benzene and carbon tetrachloride.

From elemental analysis, chemical properties and spectral data, the compound **(2c)** assigned the structure 3-(2′-hydroxy-3′,5′-dichlorophenyl)-5-(2′-furyl) isoxazoline. Similarly the compounds **(2a–b)** were prepared by the action of hydroxylamine hydrochloride on chalcones **(1a–b)**. The elemental analysis and physical data of compounds **(2a–c)** along with compound **(2c)** is listed in Table-1.

TABLE-1
ANALYTICAL AND PHYSICAL DATA OF ISOXAZOLINES **(2a–c)**

S. No.	m.f.	Yield (%)	N (%)	
			Found	Calculated
2a	$C_{15}H_{11}N_2O_4Cl_2$	78	7.82	7.90
2b	$C_{15}H_{11}NO_3Cl_2$	75	4.40	4.32
2c	$C_{13}H_9NO_3Cl_2$	81	4.66	4.69

The compounds **(2a–c)** were assayed against human pathogens gram positive *S. aureus, B. subtilis* and gram negative *E. coli, P. aeurginosa* by disc diffusion method[5] at concentration 100 μg/mL in solvent DMF using nutrient agar medium of 14 mm depth. The disc size was 6.25 mm in diameter. The zones of inhibition were measured in mm using the following standard:

Zone of inhibition in mm: up to 8 mm, less active ; 10 to 12 mm, moderate active; 12 to 14 mm, highly active.

TABLE-2
ANTIBACTERIAL ACTIVITY DATA OF COMPOUNDS **(2a–c)**

Compound	Substituents (Ar)	Zones of inhibition in mm			
		S. aureus	*P. aeruginosa*	*B. subtilis*	*E. coli*
2a	—C_6H_4—NO_2	15	14	11	14
2b	—C_6H_4—OH	14	15	10	16
2c	—C_4H_3—O	14	14	12	15

Most of the compounds prepared show significant antibacterial activity. The zone of inhibition was highest against *S. areus*, *E. coli* and *P. aeruginosa* and moderate against *B. subtilis.*

The bacterial species used for screening are common human pathogens. S. aureus causes supportive and invasive lesions leading to pus formation. *E. coli* causes secondary infection of wounds, eye and urinary tract infection, *B. subtilis* is responsible for urinary tract infection. The compounds **(2a–c)** may find application for therapeutic purposes in human diseases, provided they are non-toxic to human constitution.

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