

SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME NEW ISOXAZOLINES

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ABSTRACT

Substituted acetophenones on condensation with anthraldehyde yields chalcones (Ia-j) which on cyclization with hydroxylamine hydrochloride furnishes the corresponding 3-(substituted phenyl)-5-(9-anthryl) isoxazolines (IIa-j). All these compounds have been screened for their antibacterial activity and some of the compounds exhibited good activity.

Key words : Isoxazalines, Antibacterial activity

INTRODUCTION

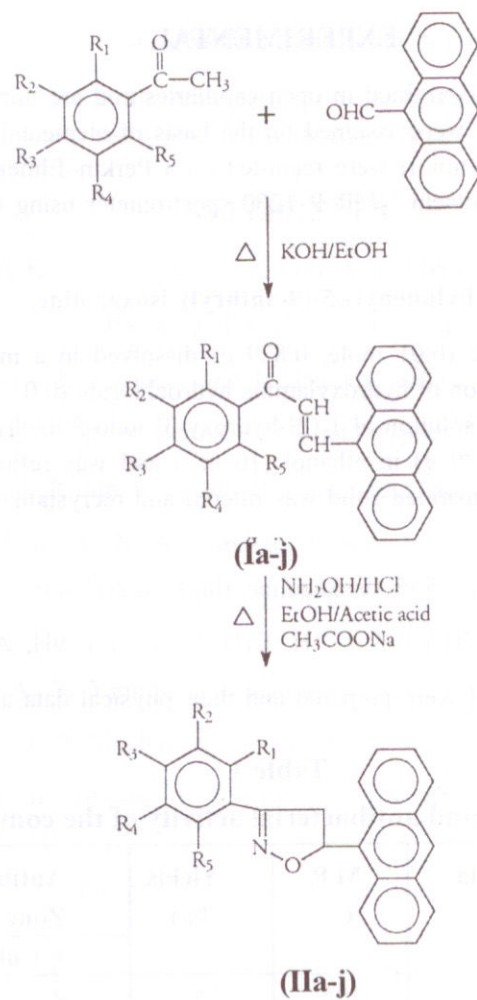
Among a wide variety of heterocycles that have been explored for developing pharmaceutically important molecules, isoxazolines is one of them. Large number of isoxazoline derivatives have been found to possess antibacterial,¹⁻³ antitubercular,⁴ antidiabetics⁵ and antifungal⁶⁻⁷ activity. Anilido isoxazoline synthesised by Zarif and Yammi⁸ were found to possess remarkable bactericidal activity against gram +ve and gram -ve bacteria. Mittal and Singhal⁹ have reported antibacterial and antifungal activity in 3-methyl-4-(4'-bromo-2'-methyl benzene azo)-5-isoxazoline. Considering the biological activity of isoxazolines and the fact that isoxazolines having 5-(9-anthryl) moiety, have not been reported so far, the present work was undertaken.

Substituted acetophenones on condensation with anthraldehyde yielded the corresponding 1-(substituted phenyl)-3-(9-anthryl)-2-propen-1-ones i.e. chalcones¹⁰ (Ia-j). Chalcones (Ia-j) on treatment with hydroxyl amine hydrochloride in ethanol and glacial acetic acid and sodium acetate afforded the corresponding 3-(substituted phenyl)-5-(9-anthryl)-isoxazolines (IIa-j) (Scheme-I)

Antibacterial activity

The activity was determined using disc diffusion method¹¹ by measuring the inhibition zones in mm. All the compounds were screened against *E. coli* and *S. aureus*.

Looking to the structure activity relationship, marked inhibition was observed in compounds bearing chloro and methyl substituents.



Scheme-I

Sr. No.	R ₁	R ₂	R ₃	R ₄	R ₅
a	OH	I	H	Br	H
b	OH	I	H	Cl	H
c	OH	I	H	CH ₃	H
d	OH	Cl	H	I	H
e	OH	I	CH ₃	Cl	H
f	OH	I	H	I	H
g	H	I	OH	I	H
h	H	I	OH	CH ₃	H
i	OH	H	H	Br	H
j	OH	H	H	Cl	H

EXPERIMENTAL

All melting points were determined in open capillaries and are uncorrected. The structures of the compounds synthesized were assigned on the basis of elemental analysis, IR and NMR spectral data. The IR spectra (nujol) were recorded on a Perkin-Elmer spectrophotometer and PMR spectra obtained on a Hitachi NMR R-1200 spectrometer using CDCl_3 as a solvent and TMS as an internal standard.

3-(2'-hydroxy-3'-iodo-5'-methylphenyl)-5-(9-anthryl) isoxazoline.

Anhydrous sodium acetate (0.01 mole, 0.829 g) dissolved in a minimum amount of hot acetic acid was added to solution of hydroxylamine hydrochloride (0.01 mole, 0.79 g) in ethanol (10 mL). This was added to a solution of 1-(2'-hydroxy-3'-iodo-5'-methyl phenyl)-3-(9-anthryl)-2-propen-1-one (0.01 mole 4.79 g) in ethanol (10 mL) and was refluxed for 6 hr. and then poured over ice cold water. Separated solid was filtered and recrystallized from ethanol to give **IIc**, m.p., 153°C, yield 75%.

IR : 3270 (OH), 1610 (C=N), 1465 (isoxazoline ring), 802 (N-O).

^1H NMR : 3.5-3.7 (dd, 2H, CH_2) 6.7 (t, 1H, CH) 7.0-8.2 (m, 9H, Ar-H).

Similarly other members **II a-j** were prepared and their physical data and antibacterial activity are recorded in Table - 1

Table 1
Physical data and antibacterial activity of the compounds.

Sr. No.	Mol. Formula*	M.P. °C	Yields (%)	Antibacterial activity Zone of inhibition in mm	
				E.Coli	S. Aureus
a	$\text{C}_{23}\text{H}_{15}\text{O}_2\text{IBrN}$	195	75	4	Nil
b	$\text{C}_{23}\text{H}_{25}\text{O}_2\text{ICIN}$	180	70	14	12
c	$\text{C}_{24}\text{H}_{18}\text{O}_2\text{IN}$	153	80	18	08
d	$\text{C}_{23}\text{H}_{15}\text{O}_2\text{ICIN}$	181	76	17	14
e	$\text{C}_{24}\text{H}_{17}\text{O}_2\text{IN}$	150	72	Nil	10
f	$\text{C}_{23}\text{H}_{15}\text{O}_2\text{I}_2\text{N}$	201	75	12	15
g	$\text{C}_{23}\text{H}_{15}\text{O}_2\text{I}_2\text{N}$	190	70	Nil	Nil
h	$\text{C}_{24}\text{H}_{18}\text{O}_2\text{IN}$	143	75	Nil	17
i	$\text{C}_{23}\text{H}_{16}\text{O}_2\text{BrN}$	168	80	16	12
j	$\text{C}_{23}\text{H}_{16}\text{O}_2\text{CIN}$	199	78	13	17

* All the compounds gave satisfactory C, H, N analysis

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