POTENTIAL ANTIBACTERIAL AGENTS: 5-IMIDAZOLONES DERIVATIVES

Anjani Solankee*, Sejal Solankee and Ghanshyam Patel
Department of Chemistry, B. K. M. Science College, Valsad-396001
(Affiliated to The Veer Narmad South Gujarat University, Surat-395007). India
E-mail: dranjani_solankee@yahoo.com

ABSTRACT

*A series of 1-(5'-bromofuran-2'-carboxamido)-2-phenyl-4-(benzylidene / substituted benzylidene)-5-imidazolones **(Ia-j)** have been synthesized and evaluated for antibacterial activity. The structures of the newly synthesized compounds were confirmed on the basis of spectral data and physical data.*

Keywords: *oxazolones, imidazolones, spectral data, antibacterial activity*

INTRODUCTION

The synthesis of heterocyclic compounds has always drawn the attention of chemists over the years mainly because of their important biological properties. Particularly, the role of 5-imidazolones, which are endowed with unique structure and potent antibacterial [1] activity. Diverse biological activities such as anti-inflammatory [2], antitubercular [3], antiviral [4] and antifungal [5] have been found to be associated with 5-imidazolone derivatives.

Recently, 1,2,4-trisubstituted-5-imidazolones have been reported to possess MonoAmino Oxidase [MAO] inhibitory and anticonvulsant [6] activities. Keeping in view of above observation and in a continuation of our work [7-9] on the synthesis of 5-imidazolones, it is though of interest to synthesis a new series of 5-imidazolones **(Ia-j)**. 5-Imidazlones have been prepared by the condensation of different 5-oxazolones (Azlactons) with 5-bromofuran-2-carbohydrazide. 5-Oxazolone derivatives have been prepared by Erlenmeyer condensation of hippuric acid with the different substituted aldehydes in the presence the of sodium acetate and acetic anhydride. All he synthesized compounds were evaluated for *in vitro* antibacterial activity against four different strain viz. *S. aureus* (MTCC 96), *B. subtilis* (MTCC 441) (Gram-positive bacteria), and *E. coli* (MTCC 443), *S. paratyphi-B* (MTCC 733) (Gram-negative bacteria) by agar diffusion method.

EXPERIMENTAL

All melting points were determined in open capillary and are uncorrected. The IR spectra were recorded on Perkin – Elmer 237 spectrophotometer. ^{1}H NMR spectra on a Bruker Avance DPX 300 MHz spectrometer with $CDCl_3$ used as a solvent and tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in part per million (ppm) downfield from the internal standard and signals are quoted as *s* (singlet) and *m* (multiplate). The reactions are followed up and the purity of products is carried out on pre-coated TLC plates (Silica gel 60 F254 , Merck) of 0.25mm thickness eluted with visualized with UV (254nm) or iodine.

Preparation of 1-(5'-bromofuran-2'-carboxamido)-2-phenyl-4-(4'-methoxy benzylidene)-imidazoline-5-one (Ij)

A mixture of 2-phenyl-4-(4'-methoxyenzylidene)-oxazole-5-one (0.01 mol), 5-bromofuran-2-carbohydrazide (0.01 mol) and pyridine (15 mL) were taken in a round bottom flask and refluxed for 13 h in the presence of a few drops of glacial acetic acid. After that the reaction

mixture was a poured into crushed ice and neutralized with conc. HCl. The solid separated out was filtered, washed with water, dried and recrystallized from ethyl alcohol to give (**Ij)**.
IR (KBr) cm^{-1}: =CH str. (3000), C=C (1639), -CH str [1,4-substitution] (838), C-O-C (1259), C=O (1662, -CONH), C=O(1734, Imidazolone ring), C-Br (634); ^{1}H NMR ($CDCl_3$) δ ppm : 3.9 (*s*, 3H, p-OC<u>H</u>$_3$), 6.6 (*s,* 1H, -C<u>H</u>-Ar), 7.0-8.3 (*m*, 12H, -Ar-<u>H</u> + Ar-C<u>H</u>= + C<u>H</u> of furan ring), 9.1 (*s*, 1H, -CON<u>H</u>)
Similarly the remaining compounds **(Ia-i)** were prepared by this method. Their physical data are given in **Table-I**

RESULT AND DISCUSSION

Antibacterial activity

All the synthesized compounds were screened for their antibacterial activity against S. *aureus* (MTCC-96), *B. subtilis* (MTCC-441) [Gram-positive bacteria] and *E. coli* (MTCC-443), *S. paratyphi-B* (MTCC-733) [Gram-negative bacteria] by using agar diffusion method of A. L. Barry [10]. Known antibiotic Ciprofloxacin was used as standard drug. The screening results indicate that compounds **Ia**, **Ib** and **Ih** were found to moderately active against *S. aureus* (MTCC-96). Compounds **Id**, **Ie**, **If**, **Ig** and **Ij** were found to be less active against *S. aureu*s (MTCC-96), whereas compounds **Ic** and **Ii** were found to be inactive be active against *S. aureu*s (MTCC-96). Compounds **Ia**, **Ib**, **Id**, **Ig** and **Ii** were found to be active against *B. subtilis* (MTCC-441).Compounds **Ic** and **Ie** were found to be moderately active against *B. subtilis* (MTCC-441), whereas compound **If**, **Ih** and **Ij** was found to be less active against *B. subtilis* (MTCC-441).
Compounds **Ib**, **Ic**, **Ie**, **Ii** and **Ij** were found to be moderately active against *E. coli* (MTCC-443), where as **Ia**, **Id**, **If**, **Ig** and **Ih** were found to be less active against *E. coli* (MTCC-443). Compounds **Ia**, **Id**, **Ie**, **Ig**, **Ih**, **Ii** and **Ij** were found to be moderately active against *S. paratyphi-B* (MTCC-733). Compounds **Ib**, **Ic** and **If** were found to be less active against *S. paratyphi-B* (MTCC-733).

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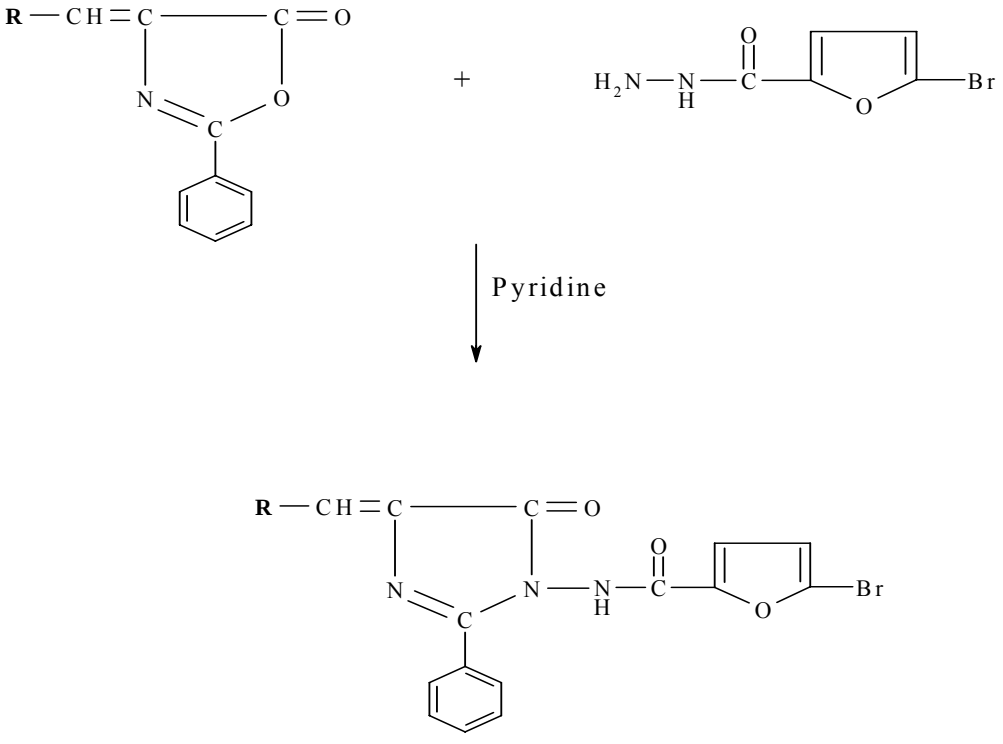
TABLE I: Molecular formula, melting point and yields of compounds **(Ia-j)**

Compd.	R	Molecular Formula	M.P ºC	*Yield (%)*
Ia	Phenyl	$C_{21}H_{14}BrN_3O_3$	218	*70*
Ib	2-Chlorophenyl	$C_{21}H_{13}BrClN_3O_3$	106	*71*
Ic	3-Chlorophenyl	$C_{21}H_{13}BrClN_3O_3$	123	*73*
Id	4-Chlorophenyl	$C_{21}H_{13}BrClN_3O_3$	108	*70*
Ie	3-Bromophenyl	$C_{21}H_{13}Br_2N_3O_3$	90	*70*
If	4-Bromophenyl	$C_{21}H_{13}Br_2N_3O_3$	125	*71*
Ig	2-Nitrophenyl	$C_{21}H_{13}BrN_4O_5$	120	*68*
Ih	3-Nitrophenyl	$C_{21}H_{13}BrN_4O_5$	103	*69*
Ii	4-Nitrophenyl	$C_{21}H_{13}BrN_4O_5$	115	*68*
Ij	*4-Methoxyphenyl*	$C_{22}H_{16}BrN_3O_4$	*207*	*69*

TABLE II: Antibacterial activity of the compounds (**Ia-j)**

Compd	*R*	Antibacterial Activity Diameter of zone of inhibition (in mm)			
		S. aureus **MTCC-96**	***B. subtilis*** **MTCC-441**	***E. coli*** **MTCC-443**	***S. paratyphi-B*** **MTCC-733**
Ia	Phenyl	17	18	13	18
Ib	2-Chlorophenyl	15	20	15	13
Ic	3-Chlorophenyl	-	14	16	14
Id	4-Chlorophenyl	13	19	14	18
Ie	3-Bromophenyl	11	15	15	19
If	4-Bromophenyl	13	12	12	14
Ig	2-Nitrophenyl	12	19	14	15
Ih	3-Nitrophenyl	14	13	14	16
Ii	4-Nitrophenyl	-	20	16	15
Ij	4-Methoxyphenyl	13	13	18	19
	Ciprofloxacin (Standard Drug)	20	22	24	25



SCHEME

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