Int. J. Chem. Sci.: 6(2), 2008, 1106-1110

SYNTHESIS AND ANTIBACTERIAL SCREENING OF SOME NOVEL IMIDAZOLIN-5-ONES

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ABSTRACT

Some novel 1-(6'-methylpyridine-3'-carboxamido)-2-phenyl-4-(benzylidine/substituted benzylidene)-imidazolin-5-ones **(1a-e)** have been prepared by refluxing the mixture of 5-oxazolones with 6-methylpyridine-3-carboxyhydrazide in pyridine. All the synthesized compounds were screened for their antibacterial activity. The structures of synthesized compounds have been characterized by elemental analysis and spectral data.

Key words : Imidazolin-5-ones, 5-Oxazolones, Antibacterial activity

INTRODUCTION

Literature survey reveals that imidazolin-5-ones have exhibited promising biological and pharmacological activities[1,2]. These are found to be effective as anticonvulsant[3], antibacterial[4], antitubercular[5], anti-HIV[6] and anticancer[7] agents. 1,2,4-Trisubstituted-imidazolin-5-ones have been reported to possess mono amino oxidase (MAO) inhibitory activity[8]. The methods for the synthesis of imidazolin-5-ones have been reported[9, 10].

In the present work, inidazolin-5-ones have been prepared by condensation of 6-methylpyridine-3-carboxyhydrazide with different azalactones. These azalactones have been prepared by Erlenmeyer condensation of hippuric acid with different aldehydes in presence of sodium acetate and acetic anhydride[11].

EXPERIMENTAL

All the melting points were determined in an open capillary and are uncorrected. The reactions were monitored on TLC. The IR spectra were recorded in KBr pellets on a

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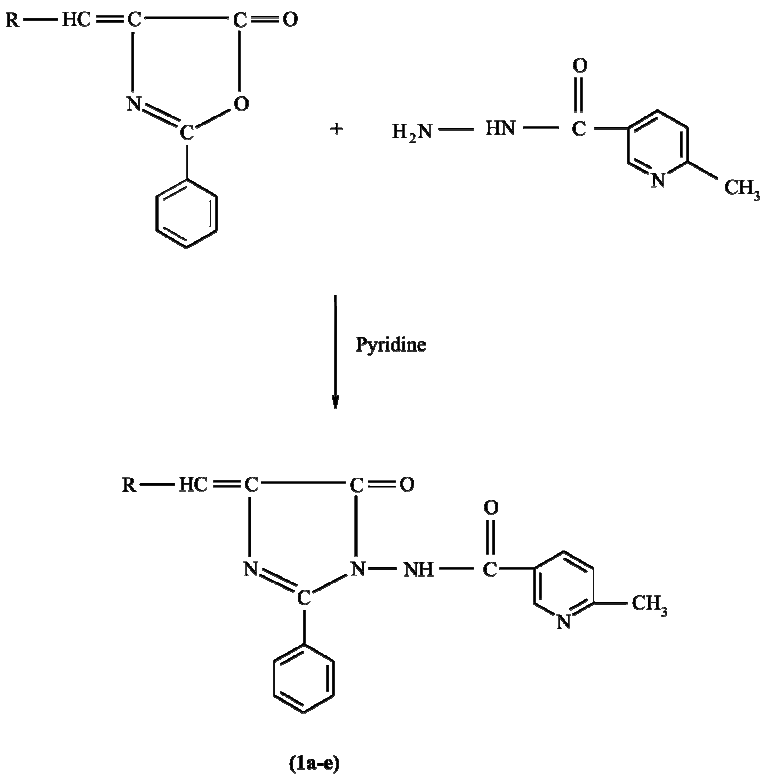
Perkin-Elmer 237 spectrophotometer and ^{1}H NMR spectra on a Bruker Avance DPX 400 MHz spectrometer with $CDCl_3$ as a solvent, using TMS as internal reference. Elemental analyses were carried out on a Carlo Erba 1108 model analyzer.

Preparation of 1-(6'-methylpyridine-3'-carboxamido)-2-phenyl-4-(4'-methoxy benzylidene) imidazolin-5-one (1e)

A mixture of 2-phenyl-4-(4'-methoxy benzylidene)-oxazole-5-one (0.01 mole), 6-methylpyridine-3-carboxyhydrazide (0.01 mole) and pyridine (10 mL) were taken in a round-bottom flask and refluxed for 12 hr in presence of few drops of glacial acetic acid. After that, the reaction mixture was poured into crushed ice and neutralized with HCl. The product thus obtained was filtered and washed with water, dried and recrystallised from alcohol.



(1a-e)

Scheme 1

Yield 71%; m.p. 218 ^oC; IR (KBr, cm^{-1}): 1692 (C=O), 1637 (C=N), 1713 (C=O, imidazolone ring) 805 (C-N, *s*-triazine); ^{1}H NMR ($CDCl_3$): δ 2.45 (s, 3H, $-CH_3$), 3.83 (s,

3H, -OCH_3), 7.00 to 9.00 (m, 12, Ar-H) and 10.4 (s, 1H, -CONH).

Similarly remaining compounds **(Ia-d)** were prepared by the same method. Their physical and analytical data are represented in Table 1.

Table 1. Physical and analytical data of compounds (1a-e)

Compound	R	Molecular formula	M.P. (°C)	Elemental analysis			
				C (%)		N (%)	
				Found	Calcd.	Found	Calcd.
(1a)	Phenyl	$C_{23}H_{18}N_4O_2$	173	72.23	72.25	14.67	14.66
(1b)	2-Chlorophenyl	$C_{23}H_{17}N_4O_2Cl$	120	66.28	66.27	13.46	13.45
(1c)	3-Chlorophenyl	$C_{23}H_{17}N_4O_2Cl$	119	66.24	6.27	13.43	13.45
(1d)	2-Nitrophenyl	$C_{23}H_{17}N_5O_4$	105	4.66	64.64	16.42	16.39
(1e)	4-Methoxyphenyl	$C_{24}H_{20}N_4O_3$	204	69.92	69.90	13.57	13.59

Table 2. Antibacterial activity of compounds (1a-e)

Compound	R	Antibacterial activity			
		Zone of inhibition (in mm)			
		S. aureus **(MTCC 96)**	***B. subtilis*** **(MTCC 441)**	***E. coli*** **(MTCC 443)**	***S. paratyphi-B*** **(MTCC 733)**
(1a)	Phenyl	14	16	12	10
(1b)	2-Chlorophenyl	13	17	14	-
(1c)	3-Chlorophenyl	13	18	13	-
(1d)	2-Nitrophenyl	15	21	13	13
(1e)	4-Methoxyphenyl	11	19	11	14
Std. drug	Ciprofloxacin	22	20	24	25

Antibacterial activity

All the synthesised compounds were screened for their antibacterial activity using Agar cup plate diffusion technique[11]. They were screened for their antibacterial activities

against *S. aureus* (MTCC 96)*, B. subtilis* (MTCC 441) (Gram-positive) and *E. coli* (MTCC 443)*, S. paratyphi-B* **(**MTCC 733) (Gram-negative) bacteria in nutrient agar medium. The sterilized agar media [2.4 % (w/v) agar-agar, 5 % (w/v) NaCl, 3 % (w/v) peptone, pH (6.8 to 7.0)] was poured into Petri dishes and allowed to solidify. On the surface of the media, microbial suspension was spread over the agar plates to solidify. A stainless steel cylinder (pre-sterilized) was used to bore the cavities. All the synthesised compounds dissolved in DMF (100 µg/mL) were placed serially in the cavities, with the help of micropipette. It was then allowed to diffuse for 10 minutes in a refrigerator. The plates were incubated at 37 °C for 24 hours. After incubation, the diameter of zone of inhibition was measured in mm. Under similar conditions, controlled experiment was carried out by using ciprofloxacin as standard drug for comparison.

RESULTS AND DISCUSSION

By visualizing activity data, it could be observed that compounds containing R = phenyl and 2-nitrophenyl are found to be moderately active against *S.aureus* (MTCC 96). The compounds containing R = phenyl, 2-chlorophenyl, 3-chlorophenyl, 2-nitrophenyl and 4-methoxyphenyl are found to be active against *B.subtilis* (MTCC 441).The compounds bearing R = 2-chlorophenyl is found to be moderately active against *E.coli* (MTCC 443). In case of *S.paratyphi-B* (MTCC 733), the compounds containing R = 4-methoxyphenyl is found to be moderately active. The remaining compounds were found to be less active or inactive against all the bacteria.

ACKNOWLEDGEMENT

The authors are thankful to B. K. M. Science College, Valsad for providing research facilities and to Head, Microbiology Department for carrying out antibacterial activity.

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Accepted : 10.11.2007