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Synthesis and Antimicrobial Activity of 2-{[(4'-Arylidine-5'-Oxo-2'-Phenyl) Imidazolyl]-1'-Yl}-3-(4-Hydroxyphenyl) Propanoic Acids

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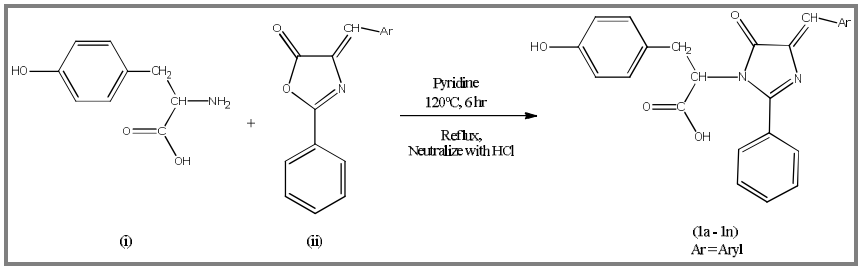
ABSTRACT

Derivatives of 5-oxo-imidazoline exhibited good therapeutic activity, with a view of getting to synthesis 2-{[(4'-arylidine-5'-oxo-2'-phenyl)imidazolyl]-1'-yl}-3-(4-hydroxyphenyl) propanoic acids (1a–1n) have been synthesized, all the derivatives were undergone characterized by IR, ^{1}H NMR and Mass spectral characterization methods. All the synthesized compounds (1a–1n) were evaluated for their antimicrobial activity at 40 µg concentration.

Graphical Abstract



Keywords: 5-Oxo-imidazolines, Antimicrobial activities, Characterization, Reflux.

INTRODUCTION

Derivatives of 5-Oxo-imidazoline exhibited good therapeutic activities like antibacterial [**1-4**], anticonvulsant [**5-7**], potent CNS depressant activity [**8, 9**] sedative and hyonotic [**10**], Hypotensive [**11,12**] Local anesthetic [**13**], antineoplastic [**14**], antihistamine [**15**], antipyretic and analgesic [**16, 17**],antiinflammatory [**18, 19**] etc. 2-{[(4'-arylidine-5'-oxo-2'-phenyl) imidazolyl]-1'-yl}-3-(4-hydroxy phenyl) propanoic acids (1a–1n) have been produced by the condensation under reflux of 2-amino-3-(4-hydroxyphenyl)propanoic acid with different azlactones or oxazolones in presence of pyridine.

The structures of the manufactured complexes were apportioned based on elemental analysis, TLC, Fourier transfer infrared spectroscopy, ^{1}H NMR and Fast ion Bombardment assisted Mass

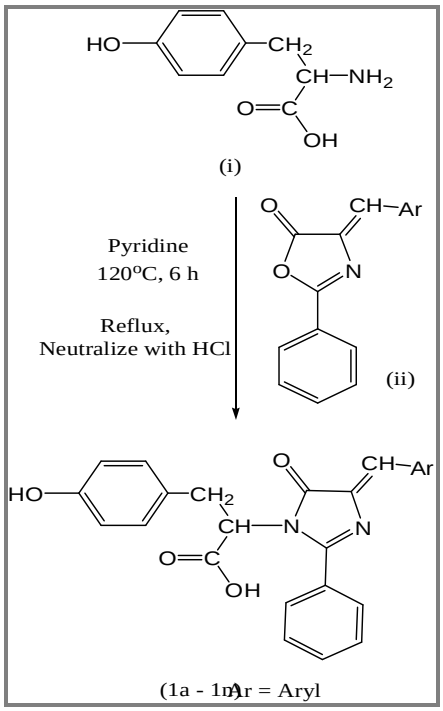
Spectroscopic analysis. The antibacterial and antifungal activity was assayed by cup-plate method [20]. All the synthesized compounds were evaluated with their potent antibacterial activity against Gram+ve bacteria *B. subtilis* and *S. aureus* whereas Gram–ve bacteria against E. *coli* and *P. aeruginosa*. Antifungal activity towards *A. niger,* Antimicrobial activity taken at 40 µg concentration by cup-plate method. Zone of inhibition have calculated in mm.

Antimicrobial activity of synthesized compounds (1a–1n) was compared with known standard drugs e.g. Ampicillin, Chloramphenicol, Norfloxacin and Griseofulvin at some concentration.

MATERIALS AND METHODS

Melting points were taken in open glass capillary tubes are uncorrected. IR spectra (cm^{-1}) were recorded on Shimadzu-435-IR Spectrophotometer and ^{1}H-NMR Spectra on Bruker Spectrometer (400MHz) using TMS as an internal standard, chemical shift in δ ppm.

Synthesis of 2-{[(4'-arylidine-5'-oxo-2'-phenyl) imidazolyl]-1'-yl}-3-(4-hydroxyphenyl)propanoic acids (1h): A blend of 2-amino-3-(4-hydroxyphenyl)propanoic acid; (1.81 g, 0.01 m); (E)-2-{[4-(3',4'-dimethoxybenzylidene)-5-oxo-2-phenyl}oxazole (3.09g, 0.01 m) and pyridine (10 mL). the reaction blend refluxed for 6 h at 120°C temperature. After completion of reaction mixture checked with Thin Layer Chromatography, the reaction mixture poured into crushed ice, filtered, dried and recrystallization with methanol. M.P. 96°C, % yield: 81.4%. Elemental analysis: C, 68.63; H, 5.12; N, 5.93; O, 20.32;$C_{27}H_{24}N_2O_6$; Found C, 67.92; H, 5.05; N, 5.80; O, 20.06. ^{1}H NMR (DMSO); 3.7-3.8 (5, 6H, 2 × OCH_3); 2.0 - (5, 2H, -CH_2); – 2.11 (5, 1H, CH); 6.5-7.7 (m, 12H, Ar-H); 9.2(5, 1H-COOH); 7.8 - (5, 1H, CH); 4.9 – (s, 1H, OH). IR (KBR) (cm^{-1}): 2920 Str. (C-H asym); 2851 C-H def (asym); 1422 (C-H 0.0.Pdef); 1368 (C-H Str; aromatic); 3028 (C=C Str.); 1593 (C-N Str.); 1265 (C-O-C Str.); 1705 (>C=O Str.); 3028 (Vinyl –CH=CH Str.); 2931 (O-H Str.); 1263 (C-O Str.). M/Z: 486, 472, 458, 442, 428, 414, 398, 383, 367, 355, 339, 322, 308, 293, 277, 264, 248, 234, 219, 205, 190, 177, 162, 151 (B.P); 133, 121, 105, 91, 77, 65, 44, 41, 40. Similarly other compounds (1a–1n) have been synthesized (Scheme 1).



Scheme 1. Flow of reaction

RESULTS AND DISCUSSION

Antimicrobial Activity: Antimicrobial activity of compounds (1a–1n) were taken by cup-plate method [20-25] whereas gram positive bacteria *B. subtilis, S. aureus* and Gram-negative bacteria *E. coli, P. Aeruginosa* and antifungal activity were taken by *A. niger*, all the antimicrobial activity of compounds (1a–1n) were compared with known standard drugs eg: Ampicillin, Chloramphenicol, Norfloxacin and Griseofulvin at same concentration 40 µg (Table 1-3).

Table 1. Physical Constants of compound (1a–1n)

S. No.	Ar	M.F.	M.W.	M.P. (°C)	% Yield	% Nitrogen	
						Th	Found
1a	C_6H_5-	$C_{25}H_{20}N_2O_4$	412.4	85	78.4	6.79	6.49
1b	2-OH-C_6H_4-	$C_{25}H_{20}N_2O_5$	428.4	123	74.4	6.54	6.29
1c	3-OH-C_6H_4-	$C_{25}H_{20}N_2O_5$	428.4	108	81.4	6.54	5.63
1d	2-Cl-C_6H_4-	$C_{25}H_{19}ClN_2O_4$	446.9	116	76.4	6.27	6.18
1e	4-Cl-C_6H_4-	$C_{25}H_{19}ClN_2O_4$	446.9	118	73.4	6.27	5.55
1f	4-OCH_3-C_6H_4-	$C_{26}H_{22}N_2O_5$	442.5	130	79.4	6.33	5.77
1g	4-OH-3-OCH_3-C_6H_3-	$C_{26}H_{22}N_2O_6$	458.5	102	72.4	6.11	5.38
1h	3,4-$(OCH_3)_2$-C_6H_3-	$C_{27}H_{24}N_2O_6$	472.5	96	81.4	5.93	5.68
1i	2-NO_2-C_6H_4-	$C_{25}H_{19}N_3O_6$	457.4	117	74.4	9.19	8.93
1j	3-NO_2-C_6H_4-	$C_{25}H_{19}N_3O_6$	457.4	90	78.5	9.19	9.11
1k	4-NO_2-C_6H_4-	$C_{25}H_{19}N_3O_6$	457.4	190	76.5	9.19	8.25
1l	C_4H_4O-	$C_{23}H_{18}N_2O_5$	402.4	105	77.5	6.96	6.28
1m	4-$N(CH_3)_2$-C_6H_4-	$C_{27}H_{25}N_3O_4$	455.5	105	78.5	9.22	8.94
1n	C_6H_5CH=CH-	$C_{27}H_{22}N_2O_4$	438.5	112	83.5	6.39	5.61

Table 2. Antimicrobial activity of compounds (1a – 1n)

Antimicrobial Activity: (Zone of inhibition in mm)					
Compound No.	Antibacterial activity				Antifungal activity
	Gram +ve bacteria		Gram –ve bacteria		
	B. subtilis	*S. aureus*	*E. coli*	*P. aeruginosa*	*A. niger*
1a	15	10	11	09	11
1b	**18**	**15**	**16**	08	08
1c	12	13	14	09	08
1d	**17**	**16**	**14**	09	**13**
1e	**16**	**18**	**15**	**11**	09
1f	11	13	10	08	08
1g	09	14	11	09	**15**
1h	**17**	**18**	13	**12**	**16**
1i	11	10	12	10	10
1j	12	11	**14**	11	09
1k	14	11	12	10	08
1l	09	11	10	09	08
1m	11	13	14	**12**	12
1n	13	**16**	08	08	11
Ampicillin	18	19	13	10	0
Chloramphenicol	13	15	15	12	0
Norfloxacin	15	14	12	13	0
Griseofulvin	0	0	0	0	14

Table 3. Comparable antimicrobial activity of compounds (1a–1n)

Antimicrobial Activity: (Zone of inhibition in mm)					
Compound No.	Antibacterial activity				Antifungal activity
	Gram +ve bacteria		Gram –ve bacteria		
	B. subtilis	*S. aureus*	*E. coli*	*P. aeruginosa*	*A.niger*
1a–1n	1b, 1d, 1e, 1h	1b, 1d, 1e, 1h, 1n	1b, 1d, 1e, 1j	1e, 1h	1d, 1g, 1h

APPLICATION

The method of synthesis can be applied for manufacturing of various active pharmaceutical ingredients for activities against noted microbes viruses and fungus.

CONCLUSION

The compounds 1b, 1d, 1e, 1h showed good antimicrobial activity compared with known standard drugs.

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