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Synthesis and Antimicrobial Activity of 2-{[(4'-Arylidine-5'oxo-2' phenyl) Imidazolyl]-1'-Yl}-3-Keto-1,5-Dimethyl-2-Phenyl Pyrazole

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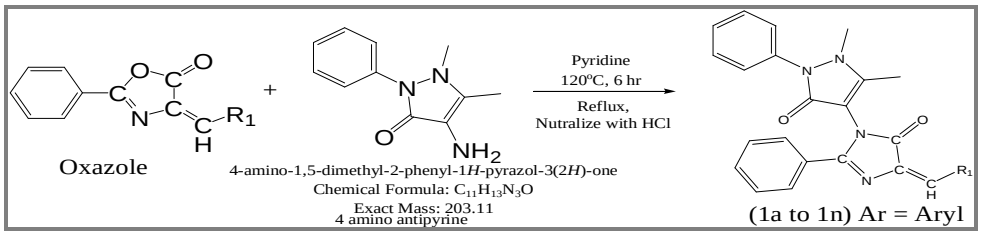
ABSTRACT

5-Oxo-imidazoline derivatives exhibited good therapeutic activity, with a view of getting to synthesis 2-{[(4'-arylidine-5'oxo-2'phenyl) imidazolyl]-1'-yl}-3-keto-1,5-dimethyl-2-phenyl pyrazole (1a–1n) have been synthesized, all the synthesized compounds were characterized by TLC, IR, ^{1}H NMR, Mass spectral data. All the synthesized compounds (1a–1n) were screened for their antimicrobial activity at 40 µg concentration.

Graphical Abstract



Keywords: 5-Oxo-imidazolines, Antimicrobial activities.

INTRODUCTION

5-Oxo-imidazoline derivatives shows good therapeutic activities like bacterial [**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**], anti-inflammatory [**18, 19**] etc. 2-{[(4'-arylidine-5'oxo-2'phenyl) imidazolyl]-1'-yl}-3-keto-1,5-dimethyl-2-phenyl pyrazole (1a–1n) have been synthesized by the condensation of 4-amino-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one with different azalctones or oxazolones in presence of pyridine.

The structures of the synthesized compounds were assigned based on elemental analysis, TLC, IR, ^{1}H NMR and mass spectral analysis. The antibacterial and antifungal activity was assayed by cup-plate method [**25**]. All the synthesized compounds evaluated their antibacterial activity against Gram +ve bacteria *B. subtilis*, *S.aureus* whereas Gram –ve bacteria against *E.coli*, *P. aeruginosa*. Antifungal

activity towards *A. niger* Antimicrobial activity taken at 40 µg concentration by cup-plate method. Zone of inhibition is 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

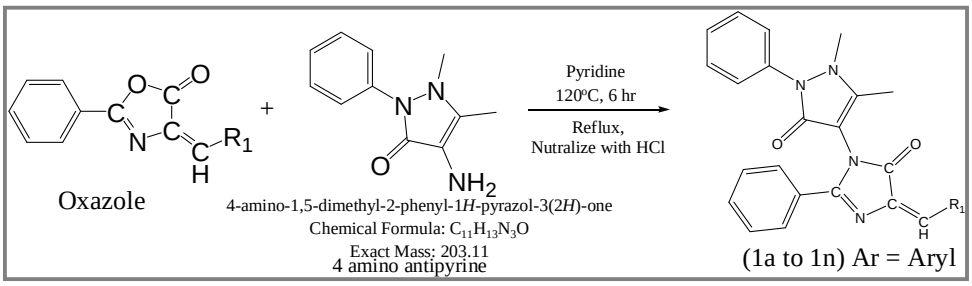
Melting points were taken in open glass capillary tubes are uncorrected. IR spectra (cm^{-1}) were recorded on Shimadzu-435-IR Spectrophotometer and ^{1}H-NMR Spectra on Bruker Spectrometer (400MHz) using TMS as an internal standard, chemical shift in δ ppm.

Synthesis of 2-{[4'-(3'4'-dimethoxyphenylidine)-5'-oxo-2'-phenyl) imidazolyl]-1'-yl}-3-keto-1,5-dimethyl-2-phenyl pyrazole (1h): A mixture of 4-amino-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one; (2.03 g, 0.01 m); (E)-2-{[4-(3',4'-dimethoxybenzylidene)-5-oxo-2-phenyl}oxazole (3.09 gm, 0.01 m) and pyridine (10 mL). the reaction mixture refluxed for 6 h at 120°C temperature. After completion of reaction mixture checked with TLC, the reaction mixture poured into crushed ice, filtered, dried and recrystallization with methanol. M.P. 155°C, % yield: 82.9%. Elemental analysis: C, 70.73; H, 5.30; N, 11.33; $C_{29}H_{26}N_4O_4$; Found C, 70.40; H, 5.29; N, 11.30. ^{1}H NMR (DMSO); 3.7-3.8 (5, 4H, 2 × OCH_3); 2.0 - (5, 2H, -CH_2) – 4.8 (5, 1H, -CH); 6.9-7.8 (m, 134, Ar-H); 8.0 (5-1H-COOH). IR (KBR) (cm^{-1}): 2920 Str. (C-H asym); 2851 C-H def (asym); 1422 (C-H 0.0.P def); 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.). M/Z: 494, 479, 463, 440, 417, 402, 389, 375, 360, 346, 332, 308, 294, 290, 254, 247, 230, 204, 188, 176, 165, 151, 131, 119, 105 (B.P); 91, 77, 56, 44, 40.

Similarly other compounds (1a–1n) have been synthesized (Table 1).

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

S. No.	Aryl	M.F.	M.W.	M.P. (°C)	% Yield	% Nitrogen	
						Theoretical	Found
1a	C_6H_5-	$C_{27}H_{22}N_4O_2$	434.5	145	74.80	12.89	12.82
1b	2-OH-C_6H_4-	$C_{27}H_{22}N_4O_3$	450.5	176	71.81	12.44	12.33
1c	3-OH-C_6H_4-	$C_{27}H_{22}N_4O_3$	450.5	165	81.83	12.44	12.39
1d	2-Cl-C_6H_4-	$C_{27}H_{21}ClN_4O_2$	468.9	159	79.84	11.95	11.89
1e	4-Cl-C_6H_4-	$C_{27}H_{21}ClN_4O_2$	468.9	205	82.82	11.95	11.92
1f	4-OCH_3-C_6H_4-	$C_{28}H_{24}N_4O_3$	464.5	161	75.83	12.06	12.03
1g	4-OH-3-OCH_3-C_6H_3-	$C_{28}H_{24}N_4O_4$	480.5	140	72.85	11.66	11.52
1h	3,4-$(OCH_3)_2$-C_6H_3-	$C_{29}H_{26}N_4O_4$	494.5	155	82.97	11.33	11.30
1i	2-NO_2-C_6H_4-	$C_{27}H_{21}N_5O_4$	479.5	148	78.90	14.61	14.56
1j	3-NO_2-C_6H_4-	$C_{27}H_{21}N_5O_4$	479.5	100	75.99	14.61	14.58
1k	4-NO_2-C_6H_4-	$C_{27}H_{21}N_5O_4$	479.5	98	78.95	14.61	14.53
1l	C_4H_4O-	$C_{25}H_{20}N_4O_3$	424.5	215	78.97	13.20	13.15
1m	4-$N(CH_3)_2$-C_6H_4-	$C_{29}H_{27}N_5O_2$	477.6	172	75.06	14.66	14.59
1n	C_6H_5CH=CH-	$C_{29}H_{24}N_4O_2$	460.5	144	72.07	12.17	12.14



Scheme 1. Synthesis of 2-{[4'-(3'4'-dimethoxyphenylidine)-5'-oxo-2'-phenyl) imidazolyl] -1'-yl}-3-keto-1,5-dimethyl-2-phenyl pyrazole (1h).

Antimicrobial activity: Antimicrobial activity [21-24] of compounds (1a–1n) were taken by cup-plate method [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, e.g. Ampicillin, Chloramphenical, Norfloxacin and Griseofulvin at same concentration 40 µg (Table 2).

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	13	9	10	11	10
1b	**18**	13	9	9	11
1c	14	13	**13**	**14**	10
1d	**17**	**16**	11	**13**	**14**
1e	15	13	**14**	9	**12**
1f	**18**	15	10	10	9
1g	11	**16**	12	8	10
1h	**17**	**16**	14	11	11
1i	**16**	**15**	13	9	8
1j	13	8	**16**	**14**	**13**
1k	9	13	**16**	9	9
1l	12	10	14	10	10
1m	**17**	10	**15**	8	10
1n	12	14	9	**13**	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

RESULTS AND DISCUSSION

The compounds 1c, 1d, 1h, 1i, 1j showed good antimicrobial activity compared with known standard drugs (Table 3). The modern work leads to a convenient synthetic method for the synthesis of new moieties which exhibits significant antimicrobial activities. Further exploration with appropriate structural modification of the above compounds may result in therapeutically useful products.

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, 1f, 1h, 1i, 1m	1d, 1g, 1h, 1i	1c, 1e, 1i, 1j,1m	1c, 1d, 1j, 1n	1d, 1e, 1j

APPLICATION

This work leads to a convenient synthetic method for the synthesis of new moieties which exhibits significant antimicrobial activities. Further exploration with appropriate structural modification of the prepared compounds may result in therapeutically useful products.

CONCLUSION

The compounds 1c, 1d, 1h, 1i, 1j showed good antimicrobial activity compared with known standard drugs. The modern work leads to a convenient synthetic method for the synthesis of new moieties

which exhibits significant antimicrobial activities. Further exploration with appropriate structural modification of the above compounds may result in therapeutically useful products.

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