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Synthesis, characterization and antimicrobial screening of novel substituted 5-oxo-imidazoline

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ABSTRACT

4-N,N-dimethyl amino benzaldehyde condensed with hydrazine hydrate in methanol medium furnished N-amino-4-N,N-dimethyl amino phenyl azomethine (1a). Different aromatic aldehyde on treatment with benzoyl glycine in acetic unhydride and sodium acetate medium results 4-substituted benzylidin-2-phenyl-5-oxazolinones (2a-g).

4-substituted benzylidin-2-phenyl-5-oxazolinones (2a-g) on refluxing with N-amino-4-N,N-dimethyl amino phenyl azomethine (1a) in pyridine medium yields 1-(4'-N,N-dimethyl amino benzylidine amino)-2-phenyl-4-(substituted benzylidin)-5-oxo-imidazoline (3a-g).

The newly synthesised compounds were characterized on the basis of elemental analysis and 1H NMR, IR spectral data. The synthesized compounds have been screened for their antimicrobial activity against gram +ve and gram -ve bacteria. Some of the products exhibited comparable activity with non standard drugs at same concentration.

Key words: Oxazoline, Oxo Imidazoline, azomethine, antimicrobial activity.

INTRODUCTION

The imidazolinones are reported to exhibit a wide variety of therapeutic activities such as anticonvulsant[1], sedative and hypnotics[2], potent CNS depressant[3], antihistamine[4], local anaesthetic[5], fungicidal[6], anti inflammatory[7], mono amino oxidase(MAO) inhibitory[8], anti allergic[9], potent antiparkinsonian activity[10], hypotensive[11], bactericidial[12], insecticidal[13], anthelmintic[14] antipyretic and analgesic[15].

Analysis of imidazoline derivative, its mode of action, their biodegradation and various application have been studided16. Synthesis and antimicrobial study of 5-imidazolinone having azo moiety is recently studied[17].

Recently pharmaceutical study and particularly leishmanicidal activity of 5-imidazolinone has been carried out18-20. Now a days an efficient method for the synthesis of long chain dialkyl diamino imidazolines by the reaction of diethylene triamine and several fatty acids under non solvent microwave irradiation using calcium oxide as support is used21.

In the present communication we are reporting the synthesis of 1-(4'-N,N-dimethyl amino benzylidene amino)-2-phenyl-4-substituted benzyliden-5-oxo-imidazoline and there antimicrobial activity by Cup Plate Method22.

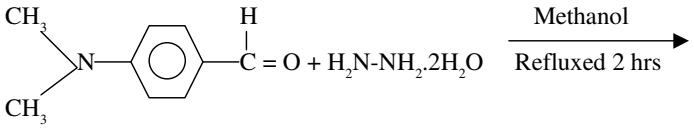
EXPERIMENTAL

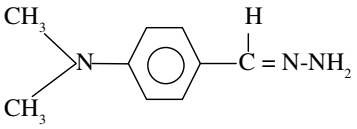
The preparation is divided in three steps.

Step 1 - Preparation of of N-amino-4-N,N-

dimethyl amino phenyl azomethine

A mixture of 4-N,N-dimethyl amino benzaldehyde (1.49 gm), (0.01 M) in methanol (25 ml) and hydrazine hydrate (0.3 ml, 0.01 ml) was refluxed for 2 hrs. The content were poured into crushed ice and excess of hydrazine hydrate was neutralized with HCl. The product was crystallized from dioxane.

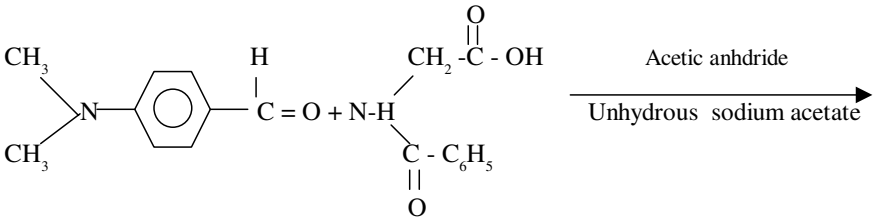


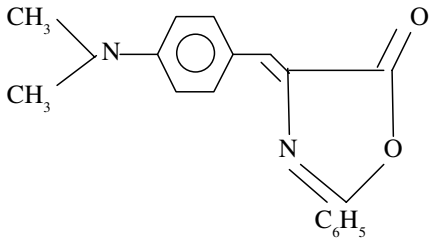


(1a)

Step 2 - Preparation of 4-(4'-N,N-dimethyl amino benzylidene)-2-phenyl-5-oxazolinone23

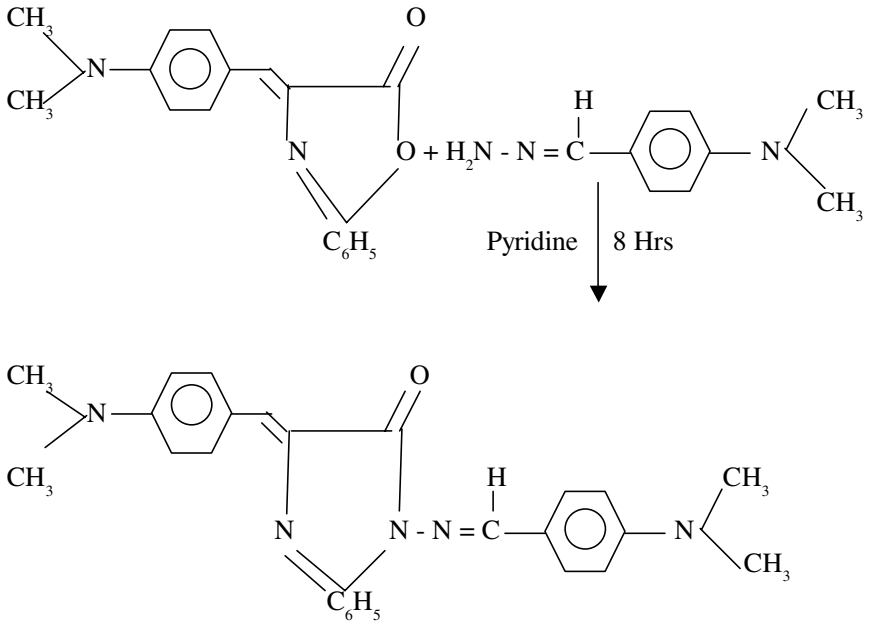
Mixture of (a) 4-N,N-dimethyl amino benzaldehyde (1.49 gm, 0.01 m) and benzoyl glycine (1.8 gm 0.01 M), acetic anhydride (2.86 ml) and anhydrous sodium acetate (0.82 gm, 0.01 m) in 50 ml conical flask. The mixture is heated with constant stirring. As soon as the mixture has liquidified completely, transfer the flask to a water bath and heat for two hours. Then add 10 ml of ethanol slowly and allow the mixture to stand for over night. Filtered and recrystallised the product from benzene.





Step 3 - Preparation of 1-(4'-N,N-dimethyl amino benzylidene amino)-2-phenyl 4-(4"-N,N-dimethyl amino benzyliden)-5-oxo-imidazoline

To a mixture of N-amino-4-N,N-dimethyl amino phenyl azomethine (1.63 gm, 0.01 m) and 4-(4'-N,N-dimethyl amino benzylidine)-2-phenyl-5-oxazolione (2.92 gm, 0.01 m), 10 ml of dry pyridine was added. This content was refluxed for 8 hrs. The excess of pyridine was removed under reduced pressure and resulting mass was poured into cursched ice and HCl (3 : 1). The solid product was filtered, washed with cold water and recrystalized with DMF.



(3a)

Properties

It is solid, signal red coloured crystalline compound having m.pt. 165°C.

From analytical data the molecular formula is C27H27N5O and its molecular weight is 437.

The IR spectrum was recorded in Nujol

IR

C - H str in CH3	2911 cm-1	
Aromatic	C - H str	3030 cm-1
	C = C str	1604 cm-1
Imidazoline	C = O str	1763 cm-1
Nucleus	C = N str	1647 cm-1
	C - N str	1162 cm-1

The PMR spectra was recorded in $CDCl_3$

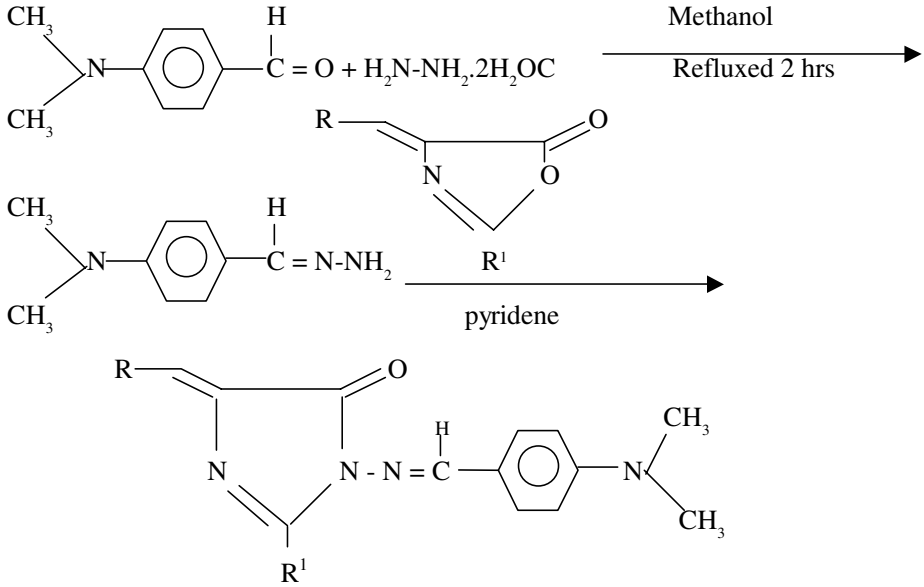
3.03 δ (S, 6 H, $N(CH_3)_2$, attached to 4-benzylidine)

3.9 δ (S, 6 H, $N(CH_3)_2$, attached to phenyl azomethine)

6.70 to 8.13 δ (m, 15 H, 13 Ar -H + 2 = CH)

Table 1: Formation of 1-(4'-N,N-dimethyl amino benzylidene amino)2-(substituted)-4-(substiututed benzyliden)-5-oxo imidazoline

Entry	Compound	R	R1	Molecular Formula	M.W.	% Yield	m.p. °C	Colour	Elemental Analysis (%) Found (Calculated)			
									C	H	N	S
1	3a	4-N,N-dimethy amino phenyl	C_6H_5	$C_{27}H_{22}N_5O$	437	79	165	Signal Red	72.22 (74.14)	6.10 (6.17)	15.08 (16.01)	- -
2	3b	4-methoxy phenyl	C_6H_5	$C_{26}H_{24}N_4O_2$	424	76	149	Yellow	72.15	5.52	13.00	-
						2		Orange	74.20 (76.14)	5.44 (5.58)	13.69 (14.21)	- -
5	3e	2-furfuryl	C_6H_5	$C_{23}H_{20}N_4O_2$	384	70	152	Faint Orange	69.92 (71.87)	5.04 (5.20)	14.12 (14.58)	- -
6	3f	2-nitrophenyl	C_6H_5	$C_{25}H_{21}N_5O_3$	439	74	105		(73.58)	(5.66)	(13.20)	-
3	3c	2-hydroxy phenyl	C_6H_5	$C_{25}H_{22}N_4O_2$	410	80	154	Sunrise	69.78 (73.17)	5.28 (5.36)	13.42 (13.65)	- -
4	3d	Phenyl	C_6H_5	$C_{25}H_{22}N_4O$	394	72	13	Golden Yellow	66.20 (68.33)	4.60 (4.78)	15.48 (15.94)	- -
7	3g	2-thenyl	C_6H_5	$C_{23}H_{20}N_4O_5$	400	76	122	Faint Green	67.78 (69.00)	4.80 (5.00)	12.48 (14.00)	7.56 (8.00)
8	3h	4-N,N-dimethyl amino phenyl	CH_3	$C_{22}H_{25}N_5O$	375	74	151	Brown	68.56 (70.40)	6.36 (6.66)	17.98 (18.66)	- -
9	3i	4-methoxy phenyl	CH_3	$C_{21}H_{19}N_4O_2$	359	74	153	Biscuit	67.98 (70.19)	5.15 (5.29)	15.48 (15.59)	- -
10	3j	2-hydroxy phenyl	CH_3	$C_{20}H_{20}N_4O_2$	348	70	164	Golden Yellow	5.38 (68.96)	5.38 (5.74)	15.64 (16.09)	- -
11	3k	Phenyl	CH_3	$C_{20}H_{20}N_4O$	332	76	146	Dark Red	70.56 (72.28)	5.64 (6.02)	16.58 (16.86)	- -
12	3l	2-furfuryl	CH_3	$C_{18}H_{18}N_4O_2$	322	76	172	Faint Yellow	65.00 (67.08)	5.48 (5.59)	15.88 (17.39)	- -
13	3m	2-nitrophenyl	CH_3	$C_{20}H_{19}N_5O_3$	377	80	114	Mikado	62.12 (63.66)	4.80 (5.03)	18.34 (18.56)	- -
14	3n	2-thenyl	CH_3	$C_{18}H_{18}N_4O_5$	338	70	92	Mustard	62.12 (63.90)	5.18 (5.32)	16.40 (16.56)	9.12 (9.46)



Where R & R^1 are listed in table No. 1

From this spectral data interpretation, the compound is 1-(4'-N,N- dimethyl amino benzylidine amino)-2-phenyl-4-(4"-N,N-dimethyl amino benzyliden)-5-oxo-imidazoline.

Similarly other 2-phenyl derivatives of 5-oxo-imidazoline were prepared from N-amino-4-N,N-dimethyl amino phenyl azomethine and 4-substituted benzylidine-2-phenyl 5-oxo oxazolines

Table 2 : Antimicrobial Activity of substituted 5-Oxo imidazolines (3a - n) by Cup-plate Method

Compound	Gram +ve		Gram -ve	
	Bacillus magatherium	***Bacillus subtilis***	***Proteus vulgaris***	***Escherichia coli***
3a	+++	-	++	++
3b	+	+	-	++
3c	-	-	-	++
3d	+++	++	++	+++
3e	+	-	++	++
3f	++	++	+++	+++
3g	-	++	++	+++
3h	++	-	-	+
3i	++	+++	+	++
3j	++	+	+	++
3k	+++	++	+	+++
3l	++	+++	+	++
3m	+++	+	+++	+++
3n	++	+	++	++

and 2-methyl derivatives of 5-oxo-imidazoline were prepared from N-amino-4-N,N-dimethyl amino phenyl azomethine and 4-substituted benzylidine-2-methyl 5-oxo oxazolines and are stated in tabel 1.

Antimicrobial Activity

The newly synthesized compounds were screened for their anti microbial activities, which were determined by using Cup Plate Method by measuring zone of inhibition in mm. All compound were screened for their antimicrobial activity against gram positive (*Bacillus magatherium, Bacillus subtilis*) and gram negative (*Escherichia Coli, Protills vulgaris*) bacteria at a concentration of 100 mg/ml. The activity was compared with known antibodies viz. chloramphenacol at same concentration. The zone of inhibition were recorded after incubation for 24 hours using vernier calliber. Inhibition zone record of the compounds cleraly indicates that 3a, 3d, 3k and 3m were highly active against *Bacillus magatherium*, 3d, 3f, 3g, 3k and 3m were highly active against *Escherichia coli*, where as moderately active against *Bacillus subtilis* and *Proteus vulgaris*. The result of sensitivity of various pathogenic bacteria to the various newly synthesised compounds are shown in table 2.

REFERENCES

1. Pandya K.C., Kurien P.N. and Surange V.R.. *J. Indian Chem. Soc.* **11**,823(1934).
2. Goldberg M.W. and Lehr. H.H., *Chem. Abstr.* **47,** 6987d (1953).
3. Wright W.B., Brabander H. J., Hardy R.A. and Ostenberg A.C. *J.Med. Chem.*, **9**: 852 (1966), *Chem. Abst.* **66**: 1463g (1967).
4. Grenshaw Ronnie R. and George Luke M. Can. C.A., **1**: 130, 306 *Chem. Abstr* **98**: 16649 (1983).
5. Neidballa U. and Boettcher I.. Ger. Offen 2856, 909 (Cl. Co7D 233184); *Chem Abstr* 94, 15732 e (1981).
6. Reddy C.V., Sastry K., Shrinivasa Rao, Rastogi K., Jain M.L. and Bedi G.S. *Indian J. Chem.* **28B**(12): 1096-98 (1989).
7. Trivedi B H. and Shah V.H., *J. Pharma. Sci.* **54**(3): 119 (1992).
8. Dwivedi C., Halbison R.D., Ali B. and Parmar S.S., *J. Pham. Sci.* **63**: 1124 (1974).
9. Kumar P., Nath C. and Shanker K.. *P. Pharmazie* **40**: 267 (1985).
10. Johnnes Karjalainen Arto, Kurker, Kauko, Oliva Anteropathi Seppo and Sulen Lennat. *Eur. Pat. Appl.* E. P. **58**, 047. *Chem. Abstr.* **98**: 16692 m (1983).
11. Dave A.M., Bhatt K N., Undavia N.K. and Trivedi P.B. *J. Indian Chem. Soc.* **64**: 348 (1967).
12. Agripat S. R., *Neth. Appl.* 6, 611, 087 (1987), *Chem. Abstr.* **68**, 29699z (1968).
13. Sharma C.R. and Shridhar D.R. *Indian Pat. IN* 154-314 (1984), *Chem. Abstr.* **105**: 133738 (1938).
14. Srivastava R.P. and Sharma Satyavan. *Indian J. Chem.* **30B**: 859 (1991).
15. Whitriety Joel G., U.S. U.S.4, 348, 404 (1982), *Chem. Abstr.* **98**: 16690 (1983).
16. Tyagi Rashmi, Tyagai V.K. and Pandey S.K.. *J. Oleo Sci.* **56**: 211-222 (2007).
17. Wadekar M.P., *Der. Pharma Chemica*, **2**(1): 76-81 (2010)
18. Khan K.M., Mughal U.R., Samreen N.A.. *J. Enzym. Inhi. Med. Chem.* **25**(1): 29, 37 (2007).
19. Mohd. Amir, Kumar Arun and Ali Israr. *Indian J. Chem.* **48B:** 1288-1293 (2009).
20. Desai N.C., Bhavsar A.M. and Baldaniya B.B. *Indian J. Pharma. Sci.* **71**(1): 90-94 (2009).
21. Bajpai Divya and Tyagi V.K., *Academic Press* Online 15 Jan. 2008.
22. Kavangh F., *Analytical Microbiology. Academic Press*, New York (1963).
23. Vogel Text book of Practical Organic Chemistry (Fifth Edition) 1155-1156 (1956).