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Synthesis and Characterization of Some Novel Derivatives of 4-Hydroxymethylene-2-aryl-2-oxazolin-5-one as Potential Antibacterial Agents

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Derivatives of 4-hydroxymethylene-2-aryl-2-oxazolin-5-one were synthesized by the reaction of 4-(N,N-dimethyl amino methylene)-2-aryl-2-oxazolin-5-ones with sodium ethoxide in ethanol at room temperature. The synthesized compounds were characterised by elemental and spectral analysis. The antibacterial activities of synthesised compounds were screened against *S. aureus* and *E. coli* at different concentrations.

Key Words: Synthesis, 4-Hydroxymethylene-2-aryl-2-oxazolin-5-one derivatives, Antibacterial.

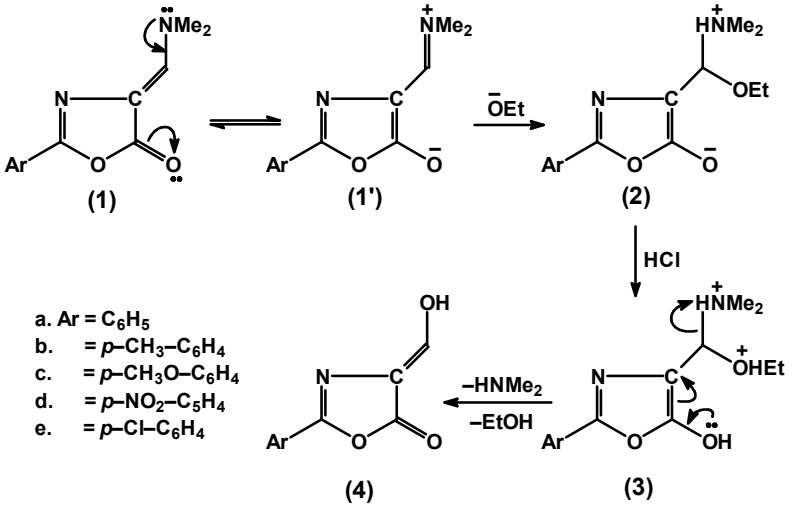
INTRODUCTION

The oxazolone derivatives play an important role in the field of heterocyclic chemistry due to its wide applicability in medicinal therapy. It is used as antimicrobial agents[1-3], antiparasite[4] and antifungal agents[5]. Some oxazolone derivatives have also been reported as antihypertensive agents[6], alcohol antagonists[7], antitumor[8,9] and for treatment of Parkinson's diseases[10].

The derivatives of 4-hydroxymethylene-2-aryl-2-oxazolin-5-one (**4**) were synthesised by the reaction of 4-(N,N-dimethyl amino methylene)-2-aryl-2-oxazolin-5-ones (**1**) with sodium ethoxide in ethanol at room temperature (**Scheme-I**). The compound **1** was synthesised by known method[11]. The derivatives of synthesised compound **4** have been characterized by the elemental analysis and spectroscopic methods. Here we wish to report the antibacterial activity of synthesised compound against *S. aureus* and *E. coli* at different concentrations.

EXPERIMENTAL

All melting points are uncorrected. Melting points were determined on a Buchii apparatus (Capillary Method). All the micro analyses were carried out on a Coleman carbon, hydrogen and nitrogen analyzers. The IR spectra were recorded on a Perkin-Elmer model 720 & 257 spectrophotometer.



Scheme-I

^{1}H NMR spectra were recorded on a Varian A- 60D AND Jeol FX-90Q spectrometer. The chemical shifts are reported in δ ppm downfield from TMS, which was used as an internal standard.

4-(N,N-Dimethylaminomethylene)-2-aryl-2-oxazolin-5-ones (1a-e): Phosphorous oxychloride (6.25 mL, 67.0 mmol) was added to a stirred solution of N-aroyl glycine (25.0 mmol) in dry DMF (15 mL). The reaction mixture was stirred at room temperature for 1 h and poured into the crushed ice and stirred for 0.5 h to get solid product. It was filtered and recrystallized from ethanol to give the yellow crystals of pure products.

4-Hydroxy methylene-2-aryl-2-oxazolin-5-ones (4a-e): Oxazolone (**1**) (1.0 mmol) was stirred with sodium ethoxide, prepared from sodium (50 mg) in absolute ethanol at room temperature for 1 h. The solvent was evaporated, addition of water to the reaction mixture gave a clear solution, which was acidified with dilute hydrochloric acid (up to pH = 4).The solid product obtained was filtered, washed with cold water (3 to 4 times) and dried to afford the compound (4), which was recrystallised from ethanol. The elemental and spectral analyses are given in Tables 1 and 2.

Antibacterial activity: The antibacterial activity of synthesized compound was tested by employing filter paper disk method[12]. The representative organism selected for antibacterial activities were *S. aureus* and *E. coli* at different concentrations.

The antibacterial activity in terms of zone of inhibition of growth shown by various compounds has been listed in Table-3.

TABLE-1
PHYSICAL AND ELEMENTAL ANALYSIS OF COMPOUND **4a-e**

Ar	m.p. (ºC)	Yield (%)	m.f.	Elemental analysis (%): Calcd. (Found)		
				C	H	N
C_6H_5	136-137	69	$C_{10}H_7NO_3$	63.49 (63.21)	3.73 (3.71)	7.40 (7.37)
p-CH_3-C_6H_4	101-102	55	$C_{11}H_9NO_3$	64.02 (64.60)	4.46 (4.65)	6.89 (6.85)
p-OCH_3-C_6H_4	162	62	$C_{11}H_9NO_4$	60.27 (60.05)	4.14 (4.23)	6.39 (6.37)
p-NO_2-C_6H_4	154	53	$C_{10}H_6N_2O_5$	51.29 (51.10)	2.58 (2.62)	11.97 (11.92)
p-Cl-C_6H_4	137-138	72	$C_{10}H_6NO_3Cl$	53.71 (53.49)	2.70 (2.72)	6.26 (6.24)

TABLE-2
SPECTRAL DATA OF COMPOUND **4a-e**

Ar	IR (KBr, ν_{max}, cm^{-1})	1H NMR (DMSO-d_6): 90 MHz δ (ppm)	Mass (m/z) (%)
C_6H_5	3454, 1757, 1695	4.78 (bs, 1H, OH, exchanges with D_2O), 7.20-7.62 (m, 3H, ArH), 7.82 (s, 1H, =CH), 7.89-8.10 (m, 2H, ArH)	189 (M^+, 67) 105 (100), 77 (88)
p-CH_3-C_6H_4	3456, 1755, 1630	2.44 (s, 3H, CH_3), 5.62 (bs, 1H, OH, exchanges with D_2O), 7.89 (s, 1H, =CH), 7.31, 8.04- (A_2B_2, 4H, *J* = 9Hz, ArH)	203 (M^+, 22), 148 (10), 118 (100), 91 (60), 76 (7)
p-OCH_3-C_6H_4	3454, 1790, 1776, 1693, 1628	3.87 (s, 3H, OCH_3), 6.60 (bs, 1H, OH, exchanges with D_2O), 7.84 (s, 1H, =CH), 7.20, 8.05 (A_2B_2, 4H, *J* = 9Hz, ArH)	219 (M^+, 29), 134 (100), 91 (19), 77 (21)
p-NO_2-C_6H_4	3456, 1756, 1691, 1610	4.87 (bs, 1H, OH, exchanges with D_2O), -8.24 (s, 1H, =CH), 8.11, 8.38 (A_2B_2, 4H, *J* = 9Hz, ArH)	234 (M^+, 4), 166 (34), 149 (100), 119 (32)
p-Cl-C_6H_4	3458, 1757, 1695, 1631	4.91 (bs, 1H, OH, exchanges with D_2O), -7.84 (bs, 1H, =CH), 7.58, 7.96 (A_2B_2, 4H, *J* = 9Hz, ArH)	223 (M^+, 47), 156 (41), 139 (100), 111 (57)

RESULTS AND DISCUSSION

The antibacterial actions may not be the numerical sum of all toxophoric functions in the compound. It may be possible in a congregation of such toxophoric functions, the role of only a few key factors are apparently important.

TABLE-3
ANTIBACTERIAL ACTIVITY OF OXAZOLIN-5-ONE DERIVATIVES **4(a-e)**

Substituents	Zone of inhibition (mm)			
	S. aureus		*E. coli*	
Ar	100 μg mL^{-1}	10 μg mL^{-1}	100 μg mL^{-1}	10 μg mL^{-1}
$-C_6H_5$	20	8	18	7
p-CH_3-C_6H_4	21	9	20	8
p-OCH_3-C_6H_4	20	9	19	9
p-NO_2-C_6H_4	24	14	22	10
p-Cl-C_6H_4	25	15	23	11

Number of replicates in each case = 3

The growth of both organism *S. aureus* and *E. coli* are inhibited to some extent by all screened compounds. Hence all are antibacterial agents.

The compound having chloro and nitro group at *para*-position in the oxazolone derivatives is more toxic.

Oxazolone derivatives have been nearly same order of antibacterial activity against both the test organism. All the compound shows more antibacterial activity as the concentration increases.

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REFERENCES

1. J.W. Cornforth, in eds.: H.T. Clarke, J.R. Johnson and R. Robinson, In the Chemistry of Pencillin, Princeton University Press, Princeton, p. 743 (1949).
2. V. Du. Vigneaud, J.L. Wood and M.E. Wright, in eds.: H.T. Clarke, J.R. Johnson and R. Robinson, In the Chemistry of Pencillin, Princeton University Press, Princeton, p. 892 (1949).
3. I. Lupsa, *Rev. Chim. (Bucharest)*, **25**, 525 (1974).
4. G. Jommi, F. Mauri and G. Riva, Britain Patent, 1,250,973 (1971).
5. E. Otazo, L. Cordova and V. Pustovarov, *Sobre-Deriv. Cana. Azucar*, **10**, 20 (1976).
6. K. Urano, Y. Tomioka, K. Okubo, K. Yamazaki and A. Nagamatsu, Japan Patent, 01,29,369 (1989).
7. L. Beregi, P. Hugon, J. Duhault and J.C. Poingnant, German Patent, 02,310,827 (1973).
8. E. Etschenberg, H. Jacobi and W. Opitz, German Patent, 02,904,512 (1980).
9. E. Etschenberg, W. Opitz and S. Raddatz, U.S. Patent, 4,310,517 (1982).
10. C.G. Wermuth and J. Cahn, France Patent, 02,170,870 (1973).
11. K.K. Singh and R.M. Singh, *Indian J. Chem.*, **33B**, 232 (1994).
12. A.W. Bauer, W.M.M. Kirby, J.C. Sherris and M. Turk, *Am. J. Clin. Pathol.*, **45**, 493 (1966).

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