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NOTE

Synthesis and Antimicrobial Activity of Some 1,2,4-trisubstituted Imidazolinones

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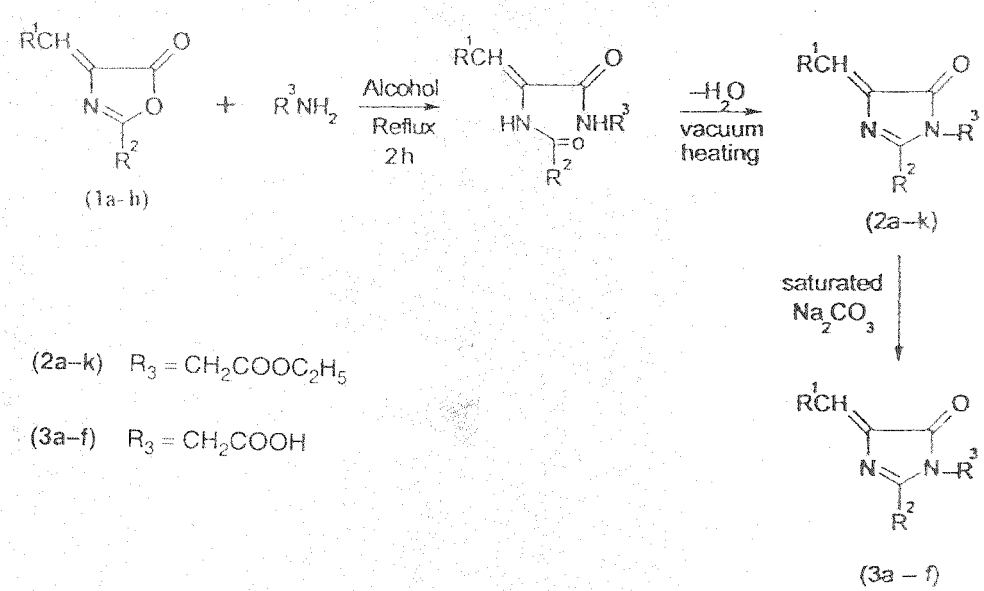
The titled derivatives have been synthesized by the reaction between azalactones and glycine ethyl ester and hydrolyzing the product thus obtained. The products have been characterized by IR, NMR and elemental analysis and screened for their antimicrobial activity.

Key Words: Synthesis, Antimicrobial activity, 1,2,4-Trisubstituted imidazolinones.

The nitrogen heterocycles have received considerable attention in recent years due to their biological and physiological activity. Their properties like central nervous system depressant[1], anticonvulsant[2] and monoamine inhibitor are of great significance. Amino acids are precursors of various macromolecules in biological systems[3]. With a view to extend the scope and validity of these observations, a new imidazolinones containing amino acid moiety is synthesized and screened for their antimicrobial activity.

Melting points were determined in open capillary and are uncorrected. IR spectra were recorded in nujol mull using Hitachi 270-50 double beam spectropho-



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tometer. Mass spectra were recorded on Finnigan MAT 8200 spectrometer. ^{1}H NMR spectra were recorded on a Unity Plus 300 Varian spectrometer using TMS as internal standard. The nitrogen analyses were found to be within the permissible limits.

CHARACTERISATION DATA OF COMPOUNDS

Compd.	Substituents			Yield	m.p.	m.f.	N Analysis Found (Calcd.)
	R^1	R^2	R^3	(%)	(°C)		(%)
2a	C_6H_5	C_6H_5	$CH_2COOC_2H_5$	71	108	$C_{20}H_{18}N_2O_3$	8.3 (8.4)
2b	4-Cl-C_6H_4	C_6H_5	$CH_2COOC_2H_5$	70	105	$C_{20}H_{17}N_2O_3Cl$	7.48 (7.6)
2c	2-Cl-C_6H_4	C_6H_5	$CH_2COOC_2H_5$	65	93	$C_{20}H_{17}N_2O_3Cl$	7.5 (7.6)
2d	4-OCH_3-C_6H_4	C_6H_5	$CH_2COOC_2H_5$	74	125	$C_{21}H_{20}N_2O_4$	7.8 (7.7)
2e	2-OH-C_6H_4	C_6H_5	$CH_2COOC_2H_5$	65	165	$C_{20}H_{18}N_2O_4$	7.8 (8)
2f	4-$N(CH_3)_2$-C_6H_4	C_6H_5	$CH_2COOC_2H_5$	62	130	$C_{22}H_{23}N_3O_3$	11 (11.1)
2g	Furfuryl	C_6H_5	$CH_2COOC_2H_5$	50	117	$C_{18}H_{16}N_2O_4$	8.4 (8.6)
2h	4-CH_3-C_6H_4	4-Cl-C_6H_4	$CH_2COOC_2H_5$	64	150	$C_{21}H_{19}O_3N_2Cl$	7.5 (7.3)
2i	4-OCH_3-C_6H_4	2-Cl-C_6H_4	$CH_2COOC_2H_5$	61	143	$C_{21}H_{19}N_2O_4Cl$	7.15 (7)
2j	4-CH_3-C_6H_4	2-Cl-C_6H_4	$CH_2COOC_2H_5$	64	115	$C_{21}H_{19}O_3N_2Cl$	7.42 (7.3)
2k	C_6H_5	CH_3	$CH_2COOC_2H_5$	69	228	$C_{15}H_{16}N_2O_3$	10.45 (10.3)
3a	C_6H_5	CH_3	CH_2COOH	48	250	$C_{13}H_{12}N_2O_3$	11.3 (11.5)
3b	C_6H_5	C_6H_5	CH_2COOH	46	198	$C_{18}H_{14}N_2O_3$	9.2 (9.1)
3c	4-Cl-C_6H_4	C_6H_5	CH_2COOH	51	216	$C_{18}H_{13}N_2O_3Cl$	8.3 (8.1)
3d	4-OCH_3-C_6H_4	C_6H_5	CH_2COOH	48	195	$C_{19}H_{16}N_2O_4$	8.4 (8.1)
3e	2-Cl-C_6H_4	C_6H_5	CH_2COOH	47	198	$C_{18}H_{13}N_2O_3Cl$	8.3 (8.15)
3f	4-CH_3-C_6H_4	4-Cl-C_6H_4	CH_2COOH	48	190	$C_{19}H_{15}N_2O_3Cl$	7.8 (7.9)

Preparation of 2-Aryl-4-arylidene-2-oxazolin-5-one (1a–h)

The starting compounds 2-aryl-4-arylidene-2-oxazolin-5-one **(1a–h)** and glycine ethyl ester were prepared according to reported method.

Preparation of 2-aryl-4-arylidene-1-carbethoxymethyl-2-imidazolin-5-one (2a–k)

A mixture of 4-arylidene-2-aryl-2-oxazolin-5-one (0.01 mol), glycine ethyl ester (0.01 mol) and ethanol (10 mL) was heated under reflux for 2 h over a water bath. It was then cooled and poured into cold water. The precipitated amide was filtered, washed with water and dried. The dried amide was heated in vacuum[4] at 180°C in an oil bath for 2 h. It was then cooled and dissolved in benzene and petroleum ether added. The yellow coloured imidazolinone was filtered, washed and dried. It was then recrystallized from ethanol.

^{1}H NMR for compound **(2a)**: 4.49 δ (s, 2H, —CH_2); 7.25–7.72 δ (10H, Ar-H), 4.15–4.17 δ (q, 2H, —CH_2), 1.17–1.22 δ (t, 3H, —CH_3). Mass for compound **(2a)**: m/z –334 (M^+), 305, 289, 261, 247, 190, 130, 117, 105, 89, 77.

Preparation of 2-aryl-4-arylidene-1-carboxymethyl-2-imidazolin-5-one (3a–f)

2-Aryl-4-arylidene-4-carbethoxy methyl-2-imidazolin-5-one **(2a–k)** (2 g) was dissolved in ethanol (15 mL) and heated with saturated sodium carbonate solution (10 mL) for 1 h. After refluxing it was cooled and acidified using dilute HCl. The product formed was filtered, washed with cold water, dried and recrystallized from alcohol.

^{1}H NMR for compound **(3d)**: 3.5 δ (s, 3H, —OCH_3) 4.49 δ (s, 2H, —CH_2), 9–8.2 δ (m, 9H, Ar-H); mass for compound **(3d)**: m/z –336 (M^+), 305, 291, 277, 162, 146, 134, 117, 105, 77.

Antimicrobial activity

The compounds **(2a–3f)** were tested for their antibacterial activity against *E. coli* and *S. typhimurium* by cup-plate method at a concentration of 100 μg in acetone. Chloramphenicol was used as standard drug. The zone of inhibition was compared with the standard drug after 24 h of incubation at 37°C for antimicrobial activity. Most of the compounds showed good activity against the two bacterial strains. The activity of some of the compounds is found to be very close to the standard drug.

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