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Antimicrobial Activity of Acylaminoacids and Acylaminoacid Amides Synthesised from Imidazolinone by the Simultaneous Reduction and Hydrolysis

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***Abstract*: Four Acylaminoacids and Acylaminoacid amides synthesised by the simultaneous reduction and hydrolysis of 2-aryl-4-arylidene-2-imidazolin-5-ones(I) compounds have been screened in vitro for microbial activity against bacterial species (Bacillus subtilis, Micrococcus Sp, pseudomonas aeruginosa and Serratid mascersans), fungal pathogens (Aspergillus niger, Aspergillus flavus, Alternaria sp and Fasuriun sp) have shown remarkable activity against these pathogens**

***Keywords*: Antimicrobial, Acylaminoacids**

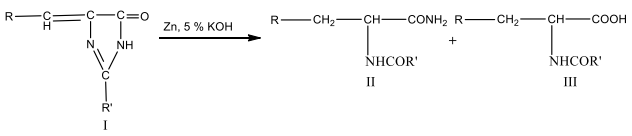
1. Introduction

Only a few of the several methods available for the synthesis of α-amino acids directly afford acylamino acid amides (II) and acyl amino acids (III). Compounds II are used as O-acylating reagents for serine, while III are largely used for resolution of amino acids and synthesis of peptide

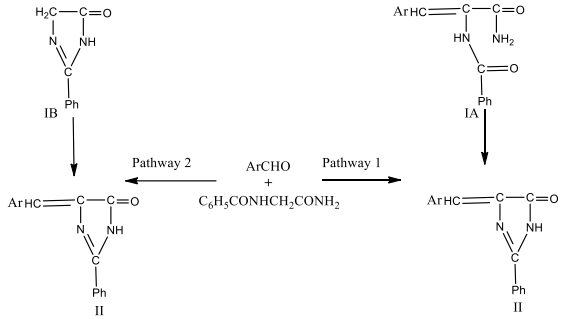
Metallic zinc in presence of KOH solution reduces the double bond exocyclic to the imidazoline ring. The reduced product is hydrolysed by KOH solution to acylamino acid amides and acyl amino acids (scheme I) Imidazolinones required for this work were prepared by condensing aromatic aldehydes with a mixture of glycine ethyl ester hydrochloride and m-toluimidic acid ethyl ester hydrochloride in presence of sodium bicarbonate (scheme II)

The imidazolinoes were converted in to acyl amino acid amides and acyl amino acids by heating imidazolinone (2g) with zinc dust (5g)and 5% KOH solution(5mL) under reflux for one hour .After cooling to room temperature the precipitated acyl amino acid amide along with zinc dust was filtered off washed with water .The acyl amino acid amide was recovered from zinc by dissolving in ethanol (200mL).The volume of ethanol solution was reduced to 50mL .after cooling the crystallized acyl amino acid amide was filtered and dried

The aqueous solutions after removal of zinc dust and acylaminoacid amide was acidified with Conc. hydrochloric acid, acyl amino acid was precipitated it was filtered and dissolved in sodium carbonate solution and filtered. The filtrate on acidification yielded pure acylamino acid.



Scheme I



Scheme I

Table 1
Synthesised Acylamino acid amides

Compound(II)	R	R'	m.p(^{0}C)
II(a)	Phenyl	m-Tolyl	236
II(b)	4-Chlorophenyl	m-Tolyl	262
II(c)	4-Methoxy phenyl	m-Tolyl	258
II(d)	3,4- Methylenedioxyphenyl	m-Tolyl	289

Table 2
Synthesised Acylamino acids

Compound(II)	R	R'	m.p(^{0}C)
III(a)	Phenyl	m-Tolyl	165
III(b)	4-Chlorophenyl	m-Tolyl	191
III(c)	4-Methoxy phenyl	m-Tolyl	196
III(d)	3,4- Methylenedioxyphenyl	m-Tolyl	198

2. Antimicrobial activity

A. Antibacterial activity

The stock solutions of all compound are prepared in acetone These were screened against bacterial species viz. Bacillus stubtilis, Micrococcus sp, Pseudomonas aeruginosa and

Table 3
Antibacterial activity

Comp	Test bacteria (zone of inhibition)															
	I*				II*				III*				IV*			
	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml
II(a)	4.3	4.6	5.1	5.6	3.2	3.5	3.9	4.2	5.6	5.9	7.2	7.2	8.5	8.7	8.9	9.5
II(b)	3.2	3.8	3.9	4.2	NZ	NZ	0.52	1.1	2.6	3.2	3.8	4.1	6.2	6.8	7.3	7.6
II(c)	NZ	2.1	3.2	4.5	5.9	6.4	6.8	7.2	4.2	5.6	5.9	6.2	5.2	5.7	5.9	6.3
II(d)	1.3	1.9	2.5	2.8	5.3	5.9	6.4	6.9	3.2	3.5	3.9	4.2	NZ	2.3	2.3	2.6
III(a)	8.2	8.5	8.9	9.1	7.2	7.6	7.5	7.9	0.2	NZ	0.6	0.9	1.9	2.3	2.5	2.9
III(b)	2.6	2.9	3.5	3.6	NZ	1.2	2.8	3.5	4.6	3.2	3.5	3.6	3.6	3.9	3.9	4.1
III(c)	NZ	2.3	2.4	2.9	6.2	6.2	6.3	6.5	2.2	2.5	2.4	2.9	4.2	4.6	4.5	4.6
III(d)	3.6	3.2	3.8	3.9	1.2	1.9	2.5	3.2	5.2	5.6	5.6	5.9	NZ	0.5	0.4	0.9

I* Bacillus stubtilis, II*. Micrococcus sp, III*. Pseudomonas aeruginosa, IV*. Serratid mascersans, NZ-No Zone

Table 4
Antifungal activity

Comp	Test fungi (zone of inhibition)															
	I*				II*				III*				IV*			
	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml	1 mg/ml	2 mg/ml	4 mg/ml	8 mg/ml
II(a)	5.2	5.8	6.8	6.9	6.2	6.9	7.2	7.5	4.2	5.6	6.2	8.2	5.6	6.3	6.8	7.1
II(b)	3.2	5.2	6.9	7.8	6.2	6.5	6.5	6.9	8.2	8.6	8.6	8.9	6.2	6.3	6.2	6.5
II(c)	6.2	6.5	6.4	6.5	5.9	5.9	6.2	6.3	7.3	7.6	7.9	7.9	9.2	9.8	10.3	10.6
II(d)	8.2	8.3	8.6	8.9	6.3	6.5	6.3	6.8	6.2	6.5	6.8	7.2	5.3	5.1	6.2	6.5
III(a)	7.3	7.6	7.9	8.1	5.2	5.3	5.3	5.6	8.2	8.5	8.9	9.3	7.2	7.1	7.3	7.3
III(b)	5.2	5.6	5.8	5.9	4.3	4.6	4.6	4.6	3.2	3.5	3.9	4.3	6.2	6.3	6.1	6.5
III(c)	5.1	5.7	5.3	5.9	4.2	4.6	4.8	4.9	5.1	5.6	5.8	5.9	6.2	6.4	6.3	6.9
III(d)	8.2	8.3	8.4	8.9	5.3	5.6	5.8	5.8	8.6	8.9	9.2	9.5	7.6	7.9	7.9	8.1

I* Aspergillus Niger, II* Aspergillus flavus, III* Alternaria sp, IV* Fusarium sp

Serratid mascersans by disc diffusion method. Sterile 6mm disc was obtained from Hi media, impregnated with 5mg/ml of compounds and air dried under laminar airflow at room temperature for 8 hours. The bacterial culture was adjusted to 0.5 Mc Farland standards and swab inoculated on Muller Hinton Agar (MHA)plate. The inoculated plates were kept at room temperature for 30 minutes. The impregnated discs were placed on MHA plates along with positive control, and incubated at 370C for 18 hours. The positive controls used in this experiment were ciprofloxin, tetracycline and polymixin(10µg/disc)

B. MIC Determination

The MIC determination was performed for the compound by disc diffusion method Discs of 1, 2, 4 & 8 were prepared The MIC for all the test organisms were read by naked eye and tabulated (Table 3).

C. Antifungal activity

The compounds were screened against six fungal species viz.Aspergillus niger, Aspergillus flavus, Alternaria sp and Fusarium sp For antifungal activity by agar block method the concentration used for screening was 5mg/ml .The concentration used for MIC determination were 1,2,4&8 mg/ml. The solutions for these compounds were added to freshly prepared SDA medium before solidification at the above concentration and mixed uniformly and transferred to sterilized Petri plates. The plates were allowed to solidifying, a small piece of agar cube was cut and removed from the centre of the agar plate and was replaced by same volume of agar cube out from a lawn culture plate of the test organism. The inoculated plates were incubated at room temperature for 48 hours. After 48 hours of incubation the plates were observed for growth (Table 4).

3. Conclusion

This paper presented an overview on antimicrobial activity of acylaminoacids and acylaminoacid amides synthesised from imidazolinone by the simultaneous reduction and hydrolysis

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