Derivatisation of 4 –Oxothiazolidines and their Biological Activity

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Abstract: The derivatives of 4-oxothiazolidines, 3(a-j), 5 methyl-4-oxothiazolidlines 4(a-j) and 5-ethanoic acid-4-oxothiazolidines 5(a-j) were prepared by reacting N[1-aza-2-(substituted phenyl)vinyl] (2-amino-5-nitro phenyl) carboxamides 2(a-j) with thioglycollic acid, thiolactic acid and thiomalic acid respectively, and these N[1-aza-2-(substituted phenyl) vinyl] (2-amino-5-nitro phenyl) carboxamides 2(a-j) were synthesized by hydrolysis of N-[1-aza-2(substituted phenyl) vinyl] [2 acetamido 5 nitro phenyl] carboxamides 1 (a-j). Reaction between N- amino- (2-amino)-5-nitro phenyl) carboxamide and different aldehydes gives N-(1-aza-2-(substituted phenyl) vinyl) (2-acetamido-5-nitrophenyl) carboxamides 1(a-j). On the basis of spectral analysis these compounds were characterized and tested for their biological activity.

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I. INTRODUCTION

4-thiazolidinone derivatives have been prepared and used as intermediates in organic synthesis [1,2]. The nucleus of 4-oxo-thiazolidine has a significant place in medicinal chemistry due to a large range of biological activities [3]. Some of the biological activities such as anti-HIV [4], bactericidal [5,6], anticonvulsant [7], tuberculostatic [8], anti-inflammatory [9], analgesic agent [10], antiproliferative [11], antihypertensive agent [12] and potentiation of pentobarbital induced sleeping time are associated with 4-thiazolidinone derivatives [13]. Looking at the medicinal importance of 4-thiazolidinone derivatives, the present work reports the synthesis of some new 4- thiazolidinone derivatives.

4-Oxothiazolidines 3 (a-j), 5- methyl-4-oxothiazolidines 4 (a-j) and 5-ethanoic acid 4-oxothiazolidines 5(a-j) were prepared by reacting N-[1-aza-2-(substituted phenyl) vinyl] (2amino-5 nitro phenyl) carboxamides 2 (a-j) with thioglycollic acid, thiolactic acid and thiomalic acid respectively 2(a-j) were synthesis by hydrolysis of N-[1-aza-2-(substituted phenyl) vinyl] (2-amino-5 nitro phenyl) carboxamides 1(a-j). Reaction between N-amino-(2-amino-5-nitro-phenyl) carboxamides and different aldehydes give N-[1-aza-2-(substituted phenyl) vinyl] (2-acetamido-5-phenyl) carboxamides 1 (a-j). The compounds have been identified on the basis of elemental and spectral studies.

Antimicrobial activities

4 thiazolidinone ring system respectively), 1570-1515 (-CO-NH) group), 750-700 (C-Cl group).

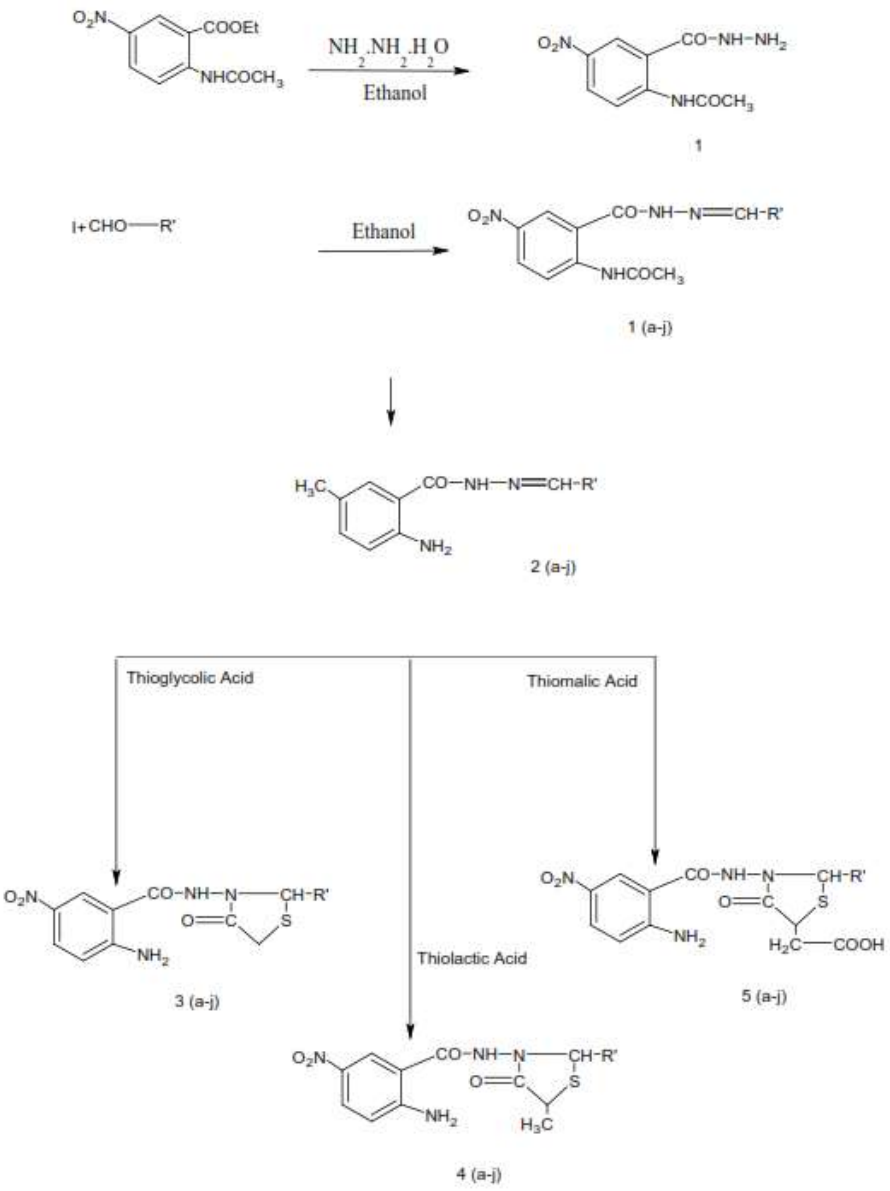
All compounds were screened for antibacterial activity against *escherichia coli* and *staphylococcus aureus* using agar cup-borer method. The concentration of sample taken for the test was 50µg. Penicillin (3-4mm zone of inhibition), Tetracycline (3-4mm zone of inhibition) were used as standards. Dimethyl formamide was used as solvent control. The compounds were also screened for antifungal activity against c*andida albicans.*

Experimental

Melting points are checked. The purity of the compounds was also checked by TLC. IR spectra were recorded in KBr on infra-red spectrophotometer M-500.

Preparation of (2-amino-5-nitric-phenyl)-N-[2-4-chlorophenyl)-4-oxo-(1,3-thiazolidine-3-yl)] carboxamide (3g)

N-[1-aza-2-(4-chloro phenyl) vinyl] (2-amino-5nitro phenyl) carboxamide (2g) (0.01 mol) and thioglycollic acid (0.01 mol) were heated at 120-125^{0}C in an oil bath for 12 hr. The reaction mixture was cooled and treated with 10% $NaHCO_3$ solution. The product was isolated, filtered and recrystallized from 95% ethanol (Table-1). IR: 1600 and 1600 (C=O and amide group respectively), 1640 (>C=O of thiazolidinone ring) 1430 (CH deformation of CH_2-CO- group), 1260, 1170-1075 (C-N linkage and



Similarly other compounds were prepared and their physical data are given in Table-1.

Preparation of (2-amino-5-nitric-phenyl)-N-[2-4-chlorophenyl)-5-methyl-4-oxo (1,3-thiazolidine-3-yl)],Carboxamide (4g)

N-[1-aza-2(substituted phenyl) vinyl] (2-amino-5-nitro phenyl) carboxamide 2g (0.01 mol) and thiolactic (0.01 mol) were heated at 120-125^{0}C in an oil bath for 12 hr. The reaction mixture was cooled and treated with 10% $NaHCO_3$ solution. The product was isolated, filtered and recrystallized from 95% ethanol (Table-1). IR: 1570-1515 (CO-NH group), 2950-2850 (CH group), 1640 (>C=O of thiazolidinone ring), 1390-1370 (CH_3 group), 1260 (C-N linkage), 1170-1075 (4-thiazolidinone ring system). Similarly other compounds were prepared and their physical data are given in Table-1

Table 1
Physical data for 4-thiazolidinones

Compound		Mp (^0C)	Yield (%)	Mol. Formula
3a	4-Hydroxy 3 Methoxy phenyl	97	76	$C_{17}H_{16}N_4O_6S$
3b	3,4,5 Trimethoxy phenyl	143	73	$C_{19}H_{20}N_4O_7S$
3c	Vinyl phenyl	120	70	$C_{18}H_{16}N_4O_4S$
3d	4-Methoxy phenyl	85	74	$C_{17}H_{16}N_4O_5S$
3e	2-Hydroxy phenyl	165	69	$C_{16}H_{14}N_4O_5S$
3f	6-Amino -4N,N-dimethyl,2-,Hydroxy phenyl	120	75	$C_{20}H_{24}N_4O_5S$
3g	4-Chloro phenyl	122	72	$C_{16}H_{13}CIN_4O_4S$
3h	4-Hydroxy phenyl	198	68	$C_{16}H_{14}N_4O_5S$
3i	3-Nitro phenyl	130	70	$C_{16}H_{13}N_5O_6S$
3j	3,4 Dimethoxy phenyl	110	71	$C_{18}H_{18}N_4O_6S$
4a	4-Hydroxy 3 Methoxy phenyl	115	75	$C_{18}H_{18}N_4O_6S$
4b	3,4,5 Trimethoxy phenyl	162	73	$C_{20}H_{22}N_4O_7S$
4c	Vinyl phenyl	126	71	$C_{19}H_{18}N_4O_4S$
4d	4-Methoxy phenyl	98	72	$C_{18}H_{18}N_4O_5S$
4e	2-Hydroxy phenyl	171	70	$C_{17}H_{16}N_4O_5S$
4f	6-Amino -4N,N-dimethyl,2-,Hydroxy phenyl	160	75	$C_{21}H_{26}N_6O_5S$
4g	4-Chloro phenyl	131	71	$C_{17}H_{15}CIN_4O_5S$
4h	4-Hydroxy phenyl	142	68	$C_{17}H_{16}N_4O_5S$
4i	3-Nitro phenyl	135	70	$C_{17}H_{15}N_5O_6S$
4j	3,4 Dimethoxy phenyl	125	72	$C_{19}H_{20}N_4O_6S$
5a	4-Hydroxy 3 Methoxy phenyl	130	77	$C_{19}H_{18}N_4O_8S$
5b	3,4,5 Trimethoxy phenyl	179	70	$C_{21}H_{22}N_4O_9S$
5c	Vinyl phenyl	170	68	$C_{20}H_{18}N_4O_7S$
5d	4-Methoxy phenyl	115	72	$C_{19}H_{18}N_4O_7S$
5e	2-Hydroxy phenyl	203	70	$C_{18}H_{18}N_4O_7S$
5f	6-Amino -4N,N-dimethyl,2-,Hydroxy phenyl	149	74	$C_{22}H_{26}N_6O_7S$
5g	4-Chloro phenyl	160	69	$C_{19}H_{16}N_4O_7S$
5h	4-Hydroxy phenyl	168	70	$C_{19}H_{16}N_4O_7S$
5i	3-Nitro phenyl	178	68	$C_{18}H_{15}N_5O_8S$
5j	3,4 Dimethoxy phenyl	159	70	$C_{20}H_{20}N_4O_8S$

Table -2
Antimicrobial Activity of Compounds
(Diameter of Zone of Inhibition in mm)

Compound	S.aureus	E.coli	C.albicans
3a	04	06	10
3b	04	06	12
3c	04	04	10
3d	06	04	10
3e	06	07	08
3f	07	10	08
3g	06	09	09
3h	06	09	06
3i	07	08	06
3j	07	08	08
4a	04	06	07
4b	04	06	06
4c	06	07	10
4d	05	08	07
4e	05	08	08
4f	08	08	12
4g	06	08	06
4h	06	07	04
4i	07	09	10
4j	06	07	10
5a	06	10	08
5b	05	12	06
5c	06	10	07
5d	06	11	09
5e	06	10	08
5f	10	06	10
5g	10	05	11
5h	08	04	10
5i	07	06	08
5j	03	06	08

Preparation of 2-{3-[(2-amino-5-nitro phenyl) carbonyl-amino]-2-(4-chloro phenyl)-4-oxo-1,3-thiazolidine-5-yl} ethanoic acid(5g)

N-[1-Aza-2-(4-chloro phenyl) vinyl] (2-amino-5-phenyl) carboxamide 3g (0.01mol) and thiomalic acid were heated in an oil bath for 12 hr at 120-125^{o}C. The reaction mixture was cooled and treated with 10% NaHCO3 solution, the product was isolated and crystallized from 95% Ethanol(Table-1) IR: 1570-1515(CO-NH group), 2950-2850(-CH group), 1640(C=O of thiazolidinone) 1390-1370(-CH_3 group), 1260(C-N linkage), 1170-1075(thiazolidinone ring system), 1470-1430(-CH2group), 3000-2750(COOH group), 750-700(C-Cl group). Similarly other compounds were prepared and their physical data are given in Table-1

CONCLUSION

Various 4-Oxothiazolidines derivatives have been prepared and used as intermediates in organic synthesis .These compounds are screened for bioactivity like antibacterial and antifungal activity. All these derivatives are found to be bioactive.

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