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Synthesis Charcterization and Antimicrobiological Activity of 4-Thiazolidinone Derivatives with Furan and Pyridine Moeities

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Abstract: Isoniazid (1) on reaction with 5-arylfuran-2-carboxaldehydes (2a-e) yield N'-((5-Arylfuran-2-yl) methylene) isonicotinohydrazide (3a-e). Post reaction of these hydrazones (3a-e) with mercapto acetic acid afforded N-(4-oxo-2-(5-Arylfuran-2-yl) thiazolidin-3-yl) isonicotinamide (4a-e). Such 4-thiazolidinone derivatives were then treated with phenyl sulphonamide diazonium chloride yielded the compounds (N-(2-(5-arylfuran-2-yl)-4-oxo-5-(2-(4-sulfamoylphenyl) hydrazono) thiazolidin-3-yl) isonicotinamide (5a-e). The structures of these series of heterocycles were assigned by analytical and spectral feature. All the were also evaluated for their antibacterial and antifungal activities.

Keywords: Isoniazid, Schiff base, thiazolidine, diazonium salt, spectroscopy antibacterial and antifungal activities**.**

I. INTRODUCTION

An azomethine group (-CH=N-) (known as Schiff base) is an intermediate for heterocycles compounds with good pharmacological activity etc[1-6.] One of the compound, furan-2-carbaldehydes in an agriculture renewal product possess a carbonyl group as a reactive centre. There are numbers of products can form via this intermediate[7-10] .The with known anti T. B. drug say Isoniazid can form Schiff base with furan aldehyde. The 4-thiazolidinones derivatives based on Schiff bases has not repeated so far. However, 4-Thiazolidinone and its derivatives exhibit various pharmacological properties[11-16]. Hence, it was thought to merge 4- thiazolidinone with isoniazid and furan moieties. This may which may enhance the drug activity up to some extent, some of the above mentioned biological activities. Thus the present communication comprises the study of new derivatives of Isoniazid - thiazolidinone - furan system.. The whole synthetic approach schematically drown as follow (Scheme-I)

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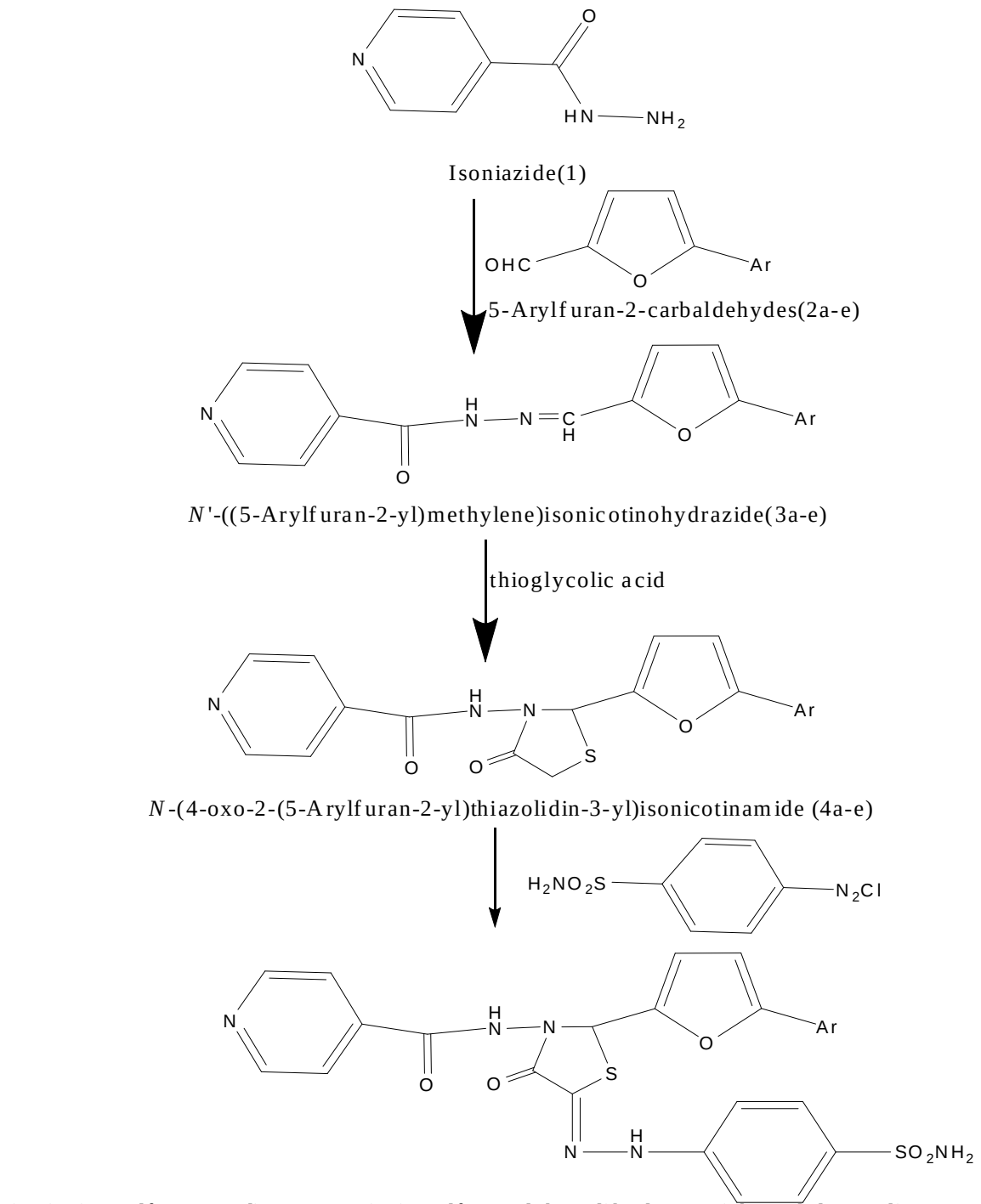

Where, Ar = (a) C_6H_5 (b) 4-CH_3-C_6H_4 (c) 4-Cl-C_6H_4 (d) 4-NO_2-C_6H_4 (e) 2,4-Cl_2-C_6H_3

SCHEME - 1

II. EXPERIMENTAL

Material and Methods

The C,H,N- content of sample were determine by carlo erba C H N analyser . The IR spectra of all compound were recorded in KBr pellets on a Nicolet 400D spectrometer and 1H NMR spectra were recorded in deuterated DMSO on a

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Bruker spectrometer at 400 MHz. LC-MS of all samples taken on LC-MSD-Trap-SL_01046. All the chemical used were of pure grade.

***Preparation* N'-((5-Arylfuran-2-yl)methylene) isonicotinohydrazide (3a-e)**

A suspension of Isoniazid (1), (10 mmol) and the 5-Arylfuran-2-carbaldehydes (2a-e) (10mmol) in ethanol (15ml) was refluxed on a water bath for 2 hrs. The pastry mass obtained. The liquid was decanted and then dry ether was added to get the solid powder it was air dried, and recrystallized R spirit .The characterization data of these compounds are given in Table -1.

Table:-1 Characterization Data of Compounds (3a-e)

Compd.	Molecular formula (Mol.wt.)	LC-MS Data	Yield %	M.P.* ^{0}C	Elemental Analysis					
					%C		% H		%N	
					Found	Calcd.	Found	Calcd.	Found	Calcd.
3a	$C_{17}H_{13}N_3O_2$ (291)	294	88	205-207	70.0	70.09	4.4	4.50	14.4	14.42
3b	$C_{18}H_{15}N_3O_2$ (305)	308	86	210-211	70.8	70.81	4.9	4.95	13.7	13.76
3c	$C_{18}H_{12}N_3O_2Cl$ (325.5)	337	79	208-209	62.6	62.68	3.6	3.71	12.8	12.90
3d	$C_{17}H_{12}N_4O_4$ (336)	343	78	214-216	60.7	60.71	3.5	3.60	16.6	16.66
3e	$C_{18}H_{12}N_2O_2Cl_2$ (321)	336	80	217-219	60.1	60.19	3.3	3.37	7.7	7.80

***** Uncorrected

***Preparation of* N-(4-oxo-2-(5-Arylfuran-2-yl)thiazolidin-3-yl) isonicotinamide(4a-e)**

A mixture derivatives (3a-e)(10mmol) and marcapto acetic acid (10 mmol) in Tetra hydro furan (THF) (30ml), Anhydrous $ZnCl_2$ was added as pinch . The mixture was refluxed for 15 hrs. The solvent was then decanted to get a bulk product, which was dissolved in isopropanol and passed through a column of silica gel using isopropanol: THF (8:2; v/v) mixture as eluent. The elute was concentrated and the product was isolated from as 4-thiazolidinones (4a-e). The characterization data of these compounds are given in Table -2.

Table:-2 Characterization Data of Compounds (4a-e)

Compd.	Molecular formula (Mol.wt.)	LC-MS Data	Yield %	M.P.* ^{0}C	Elemental Analysis							
					%C		%H		%N		%S	
					Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
4a	$C_{19}H_{15}N_3O_3S$ (365)	372	69	211-212	62.4	62.45	4.1	4.14	11.4	11.50	8.7	8.78
4b	$C_{20}H_{17}N_3O_3S$ (379)	388	60	205-207	63.3	63.31	4.5	4.52	11.0	11.07	8.4	8.45
4c	$C_{19}H_{14}N_3O_3SCl$ (399.5)	405	59	166-168	57.0	57.07	3.5	3.53	10.5	10.51	8.0	8.02
4d	$C_{19}H_{14}N_4O_5S$ (410)	417	67	149-150	55.6	55.60	3.4	3.44	13.6	13.65	7.8	7.81
4e	$C_{19}H_{13}N_3O_3S_2Cl$ (433)	447	64	168-169	52.5	52.55	3.0	3.02	9.6	9.68	7.3	7.38

***** Uncorrected

Preparation of (N-(2-(5-arylfuran-2-yl)-4-oxo-5-(2-(4-sulfamoylphenyl)hydrazono) thiazolidin-3-yl) isonicotinamide (5a-e)

The hydrazo derivatives were prepared by method reported for other 4-thiazolidine derivatives [18]

A solution of 4-thiazolidinone (4a-e) (10mmol) in isopropanol (30ml) and sodium acetate (50g) was stirred in cold bath of temperature 0-5°C. Cold diazotised solution (0-5°C) of 4-amino sulphonamide (10mmol) was added drop wise to this solution with good stirring (0-5°C). The solid products were filtered off and air dried. M. P. > 250°C, The characterization data projected in table 3.

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Table:-3 characterization Data of Compounds (5a-e)

Compd.	Molecular formula (Mol.wt.)	LC-MS Data	Yield %	M.P.* ^{0}C	Elemental Analysis							
					%C		%H		%N		%S	
					Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
5a	$C_{25}H_{20}N_6O_5S_2$ (548)	563	89	261-262	54.7	54.73	3.6	3.67	15.3	15.32	11.6	11.69
5b	$C_{26}H_{22}N_6O_5S_2$ (562)	588	80	255-257	55.4	55.50	3.9	3.94	14.9	14.94	11.3	11.40
5c	$C_{25}H_{19}N_6O_5S_2Cl$ (582.5)	596	89	266-268	51.4	51.50	3.2	3.28	14.3	14.41	10.9	11.00
5d	$C_{25}H_{19}N_7O_7S_2$ (593)	512	87	269-270	50.5	50.58	3.2	3.23	16.5	16.52	10.7	10.80
5e	$C_{25}H_{18}N_6O_5S_2Cl_2$ (616)	631	84	268-269	48.6	48.63	2.9	2.94	13.5	13.61	10.3	10.39

***** Uncorrected

III. BIOLOGICAL SCREENING

Antimicrobial activities

The antimicrobial activities of all series of compounds (3a-e,4a-e,5a-e) were evaluated in terms of antibacterial and antifungal activities.

Table:-4 Antibacterial Activity of Compounds (3a-e)

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiella promioe
3a	55	54	57	49
3b	56	53	52	57
3c	58	54	66	53
3d	62	59	58	52
3e	69	68	78	60

Table:-5 Antibacterial Activity of Compounds (4a-e)

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiella promioe
4a	56	55	59	52
4b	57	57	58	59
4c	59	58	68	56
4d	63	59	67	54
4e	70	70	79	67

Table:-6 Antibacterial Activity of Compounds (5a-e)

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiella promioe
5a	58	57	61	54
5b	59	59	59	61
5c	61	60	69	58
5d	64	62	69	55
5e	72	71	81	69

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Antifungal Activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *Nigrospora Sp, Aspergillus niger, Botrydepladia thiobromine, and Rhizopus nigricum***,** *Fusarium oxyporium*. Potato dextrose agar (PDA) medium. Such a PDA medium was used as a cultural food[20]
The fungicidal activity measured in % age growth of inhibition of all the compound (3a-e, 4a-e and 5a-e) is shown in Tables-7- 9.

Table:-7 Antifungal Activity of Compounds (3a-e)

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
3a	58	51	60	56	66
3b	67	68	61	61	67
3c	67	65	68	60	65
3d	66	66	69	71	63
3e	69	70	71	76	75

Table:-8 Antifungal Activity of Compounds (4a-e)

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
4a	60	53	62	58	67
4b	68	69	64	67	69
4c	71	68	72	63	68
4d	68	67	71	73	65
4e	72	73	74	78	77

Table:-9 Antifungal Activity of Compounds (5a-e)

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
5a	62	55	63	60	68
5b	69	71	65	68	71
5c	73	69	74	65	69
5d	69	69	72	74	67
5e	74	75	76	79	79

IV. RESULTS AND DISCUSSION

It was performed that Isoniazid (1), on condensation with 5-Arylfuran-2-carbaldehydes (2a-e), yields N'-((5-Arylfuran-2-yl) methylene) isonicotinohydrazide (3a-e). There structures of (3a-e) were assigned by elemental analysis and IR and NMR spectra further the IR band at 1620-1640 (C=N), 3030-3080 cm^{-1} (C-H, of Ar.), 1675-1685(C=O), 1185(C-O-C), 2950, 1370 cm^{-1} (-CH_3),1085(-Cl),1550, 1370(-NO_2). ^{1}H NMR signals: 6.6 – 8.9 (10H, m, Ar - H), 11.8-11.9 (1H, s,-CONH), 8.4-8.8 (1H, s,-N=CH), 3b; 2.41 (3H, s,-CH_3). The C, H, N analysis data of all compounds are presented in Table -1.

The structures assigned to N-(4-oxo-2-(5-Arylfuran-2-yl)thiazolidin-3-yl) isonicotinamide(4a-e) were supported by the elemental analysis and IR spectra showing an absorption bands at 1690cm^{-1} (C=O of thiazolidinone ring), 718cm^{-1} (C-S-C of thiazolidinone ring), 3075-3095cm^{-1} (CH_2 of thiazolidinone ring), 3030-3080cm^{-1} (C-H, of Ar.), 1675-1685 cm^{-1} (-CONH), 1185(C-O-C), 1085(-Cl),1550,1370(-NO_2), 2950, 1370 cm^{-1} (-CH_3). ^{1}H NMR: 3.85-3.95 (2H, s,-CH_2 of the ring), 5.95-5.96 (1H, s,-CH), 6.6 – 8.9 (10H, m, Ar - H), 8.1-8.2 (1H, s,-CONH), 4b; 2.41 (3H, s,-CH_3). The C, H, N, S analysis data of all compounds are presented in Table-2.

The structures assigned to N-(4-oxo-2-(5-Arylfuran-2-yl)thiazolidin-3-yl) isonicotinamide(5a-e) were supported by the elemental analysis and IR spectra showing an absorption bands at 1690cm^{-1} (C=O of thiazolidinone ring), 718cm^{-1} (C-S-C of thiazolidinone ring), 3075-3095cm^{-1} (CH_2 of thiazolidinone ring), 3030-3080cm^{-1} (C-H, of Ar.), 1675-1685

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cm^{-1} (-CONH), 1185(C-O-C), 1085(-Cl),1550,1370(-NO_2) 2850, 2950, 1370 cm^{-1} (-CH_3),3372 cm^{-1} (NH),1365,1185 cm^{-1} (SO_2). ^{1}H NMR: 3.85-3.95 (2H, s,-CH_2 of the ring), 5.95-5.96 (1H, s,-CH), 6.6 – 8.9 (14H, m, Ar - H), 8.1-8.2 (1H, s,-CONH), 4b; 2.41 (3H, s,-CH_3), The C, H, N, S analysis data of all compounds are presented in Table-2.

The examination of elemental analytical data reveals that the elemental contents are consistent with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure. The final structure of all compounds is confirmed by LC-MS. LC-MS data of all compounds are presented in Tables-1,2 and 3.

V. CONCLUSION

The reaction of Isoniazid (1) with 5-Arylfuran-2-carbaldehydes(2a-e), yields Schiff bases of N'-((5-Arylfuran-2-yl)methylene)isonicotinohydrazide (3a-e), which on reaction with mercapto acetic acid yielded N-(4-oxo-2-(5-Arylfuran-2-yl)thiazolidin-3-yl) isonicotinamide(4a-e) followed by hydrazo derivatives (5a-e) , their structured were predicated by the elemental and spectral analysis. Newly prepared compounds were shows moderate to good antibacterial and antifungal activities.

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