

SYNTHESIS AND EVALUATION OF N-[6-PHENYL-2-(5-ARYLFURAN-2-YL)-4-THIOXO-(2H)-1,3,5-OXADIAZIN-3(4H)-YL] ISONICOTINAMIDES AS ANTIMICROBIAL AGENTS

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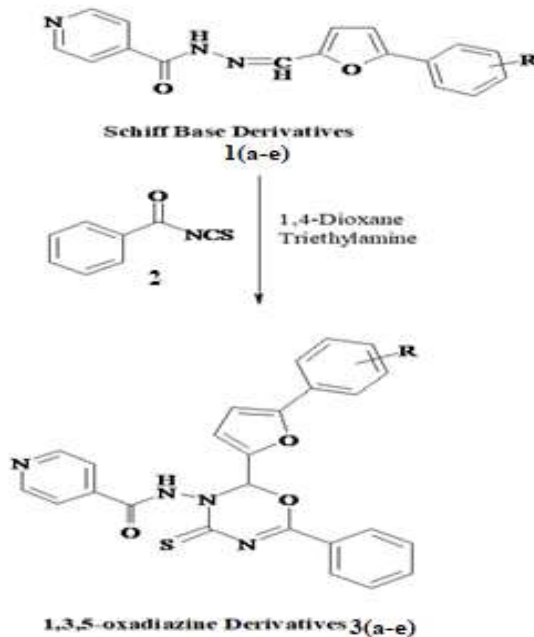
Abstract: The novel heterocyclic compounds, 1,3,5-oxadiazine derivatives [2a-e] were synthesized by mixing Schiff base derivatives based on 5-arylfurfural [1a-e] with benzoyl isothiocyanate in appropriate solvent and elevated temperature. The isolated 1,3,5-oxadiazine derivatives [2a-e] after proper drying were characterized by using advanced techniques like IR spectroscopy, NMR spectroscopy and by Mass spectroscopy. Their antibacterial activity has also been monitored against common microbes.

Keywords: 1,3,5-oxadiazine derivatives, Isoniazid, furfural, spectroscopic characterization and Antimicrobial activity.

I. INTRODUCTION

One of the significant heterocyclic compound with bioactive diversity have been confirmed by oxadiazine. Oxadiazine demonstrated number of biological and pharmacological activities like, antibacterial, plant-growth regulating, antifungal, anti-inflammatory, cardiovascular, antitumor, antiviral, insecticidal and monoamine oxidase inhibition [1-6]. Also Isoniazid also one of the important heterocyclic compounds due to its excellent medicinal properties [7]. In continuous of our earlier research [8], the present article covers the oxadiazine derivatives derived from Schiff's base of Isoniazid. The whole research work is seen as follows.

Fig.1: Synthesis of novel 1,3,5-oxadiazine derivatives



Where, R = 4-H, 4-Cl, 4-Br, 4-F, 3-NO₂

II. EXPERIMENTAL

MATERIALS AND METHODS

Isoniazid was obtained from local market. Benzoyl isothiocyanate were prepared in laboratory as reported process in literature [9]. N'-((5-(4-Alkylphenyl) furan-2-yl) methylene) isonicotinohydrazide (1a-e) were prepared by our earlier communication.[8] The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ¹H NMR and ¹³C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046

Synthesis of N-(6-substitutedphenyl-2-(5-phenylfuran-2-yl)-4-thioxo-2H-1,3,5-oxadiazin-3(4H)-yl)isonicotinamide (2a-e)

The 1,3,5-oxadiazine derivatives of Isoniazid (4a-e) were synthesized by reported methods in the literature [10-12].

A mixture of schiff bases of Isoniazid (1a-e) (0.01 mole), benzoyl isothiocyanate (0.01 mole), and triethyl amine (three drops) in 1,4-dioxane (20 ml) was refluxed for 2 hours. The separated solid that formed upon dilution with water (20 ml) was filtered, dried, and recrystallized from toluene to give yellow crystals of 1,3,5-oxadiazine product (2a-e) which were obtained in 60-70% yield and other characterization data of these compounds are given in Table -1.

Table:-1 Analytical Data and Elemental Analysis of Compounds (2a-e)

Compd.	Molecular formula (Mol.wt.)	Yield	M.P.* °C	Elemental Analysis							
				%C		%H		%N		%S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
2a	C ₂₅ H ₁₈ N ₄ O ₃ S (454.50)	65	126- 128	66.00	66.07	4.00	3.99	12.30	12.33	7.00	7.05
2b	C ₂₅ H ₁₇ N ₄ O ₃ SCl (488.95)	67	132- 135	61.40	61.41	3.50	3.50	11.50	11.46	6.70	6.56
2c	C ₂₅ H ₁₇ N ₄ O ₃ SBr (533.40)	68	142- 145	56.30	56.29	3.20	3.21	10.50	10.50	6.00	6.01
2d	C ₂₅ H ₁₇ N ₄ O ₃ SF (472.49)	66	155- 157	63.50	63.55	3.60	3.63	11.90	11.86	6.80	6.79
2e	C ₂₅ H ₁₇ N ₅ O ₅ S (499.50)	65	165- 167	60.10	60.11	3.40	3.43	14.00	14.02	6.40	6.42

* Uncorrected LC-MS Molecular ion peak of 2a: 455.60, 2c: 534.50

III. Antimicrobial activity

The antimicrobial activities of all the compounds were studied against gram-positive bacteria and gram-negative bacteria.[13] The Zone of Inhibition (in mm) measured. All compounds were found moderate to good actives for microbes.

Table:-2 Antibacterial Activity of Compounds (2a-e)

Compound (Designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	<i>B.megaterium</i>	<i>S.Aureus</i>	<i>E.Coli</i>	<i>Ps.Aeruginosa</i>
2a	16	10	08	15
2b	17	17	15	13
2c	12	17	11	08
2d	12	11	15	12
2e	17	09	13	15

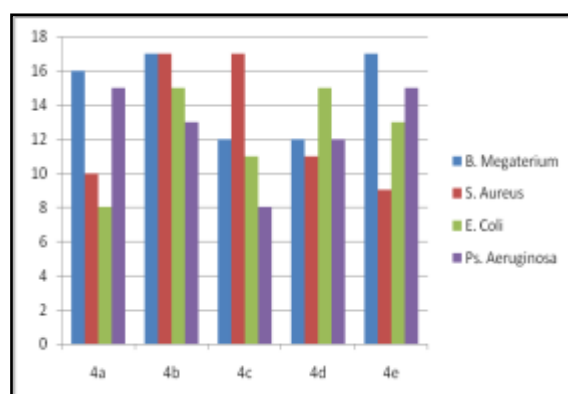


Figure 1. Antimicrobial activity of compounds 2a to 2e

IV. RESULTS AND DISCUSSION

The structures of N-(6-substitutedphenyl-2-(5-phenylfuran-2-yl)-4-thioxo-2H-1,3,5-oxadiazin-3(4H)-yl)isonicotinamide (2a-e) were confirmed by elemental analysis and IR spectra showing an absorption band at 1000-1400 (C-N of oxadiazine), 1350 (C=S of oxadiazine), 1298(C-O-C of oxadiazine),1620-1640 (C=N), 3030-3080 cm^{-1} (C-H, of Ar.),1675-1685 (C=O),2950, 1370 cm^{-1} (-CH),1085(-Cl),700(C-Br),1250(C-F),1550,1370(-NO₂). ¹H NMR : 7.4- 9.5 (m, Aromatic), 4.3(s, C₂H of oxadiazine),11.2-11.4 (s,-CONH) and 6-4.9(s,NH). ¹³CMR spectral Features (δ , ppm):102-133(Phenyl), 165(-C=O and C=S), 169(O-C= N) and 86(O-C-N). The C, H, N analysis data of all compounds are presented in Table -1.

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure. The final structure of selected compounds is confirmed by LC-MS which is consistent with predicted structure.

V. CONCLUSION

The reaction of schiff bases of Isoniazid (1a-e) with benzoyl isothiocyanate, synthesized N-(6-substitutedphenyl-2-(5-phenylfuran-2-yl)-4-thioxo-2H-1,3,5-oxadiazin-3(4H)-yl)isonicotin amide (2a-e).Their structured were predicated by the elemental and spectral analysis. Newly prepared compounds were shows moderate to good antimicrobial activities.

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