Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN 0976-9595

Research Article

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SPIRO DERIVATIVES OF 1,2,4-TRIAZOLE

Nunna G Rameshbabu*[1], Sheetal Gulati[2], H. S Patel[3]

[1]*Research Scholar, Rabindranath Tagore University, Bhopal, Madhya Pradesh, India*

[2]*Department of Chemistry, Rabindranath Tagore University, Bhopal, Madhya Pradesh, India*

[3]*Ex. Head, Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India*

**Corresponding author: rbnunna@yahoo.co.in*

ABSTRACT

Present research article reports synthesis, characterization and antimicrobial activity of Spiro derivatives of 1,2,4-triazole [2a-e]. Spiro derivatives [2a-e] were synthesized by reacting 5-Arylidine compounds [1a-e] with 2-aminophenol. The Spiro derivatives [2a-e] were characterized by using advanced analytical tools like NMR spectroscopy, IR spectroscopy and by Mass spectroscopy. All the newly synthesized Spiro derivatives of 1,2,4-triazole were evaluated for their Antimicrobial activity.

Keywords: Spiro derivatives, 1,2,4-triazole, Antimicrobial activity.

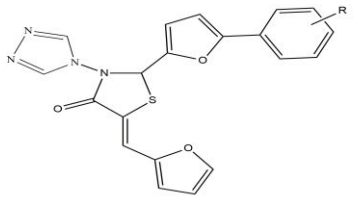
1. INTRODUCTION

The organic Spiro-compounds characterize a significant group of naturally occurring stuffs illustrated via extremely prominent biological and medicinal properties like, antimicrobial activity, antifungal activity, anti-viral and anti-cancer, etc. [1-7]. Many natural and biologically active compounds and drug molecules contains the organic Spiro-compounds as one of the most important constituent. 4-Amino-1,2,4-triazole is one of the important heterocyclic compounds due to their pharmaceutical and biological activity like, anti-tuberculer, antitumor, antileishmanial, anti-convulsant, anticancer, anti-inflammatory, antibacterial, antimicrobial activity, etc. [8-14]. As a result of these valuable activities, many researchers have paid particular consideration to discover diverse and proficient methodologies to produce this class of compounds. The present article covers the synthesis of Spiro-compounds which contains triazole and evaluation of them for their antimicrobial activity. The whole reaction path shown is as follows.

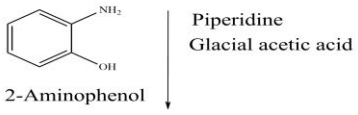
2. EXPERIMENTAL

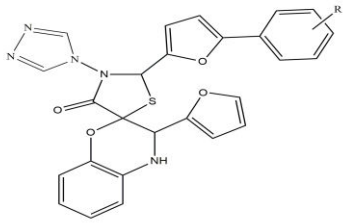
2-Amino phenol, piperidine, ethanol, glacial acetic acid was procured from local market. All the other chemicals used directly without any purification. 5-Arylidine derivatives (1a-e) were prepared in our earlier research work [15].

Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ^{1}H NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz.

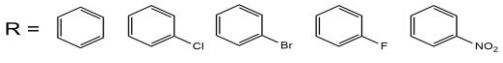


5-Arylidine derivatives [1a-e]





Spiro compound [2a-e]



Reaction Scheme

2.1. Preparation of 2'- (5- (subsitutedphenyl) furan-2-yl)-3-(furan-2-yl)-3'-(4H-1,2,4-triazol-4-yl)-3,4-dihydro spiro [benzo [b] [1,4] oxazine-2,5'-thiazolidin]-4'-one [2a-e]

The Spiro derivatives (2a-e) were prepared from respective 5-Arylidine derivatives (1a-e) by reported method given in literature [16, 17].

A mixture of 2-(5-(substitutedphenyl) furan-2-yl)-5-(furan-2-ylmethylene)-3-(4H-1,2,4-triazol -4-yl) thiazolidin-4-one(1a-e) (0.01 mol), 2-aminophenol (0.01 mol) and few drops of piperidine was refluxed in ethanol (50 mL) for 4 hours, then glacial acetic acid (10 mL) was added to the reaction mixture and heating was continued for further 2 hours. The reaction mixture was cooled to room temperature, left overnight and the resultant solid precipitated was filtered, dried and recrystallized from ethanol to obtain Spiro compounds, 2'-(5-(substitute-dphenyl)furan-2-yl)-3-(furan-2-yl)-3'-(4H-1,2,4-triazol-4-yl)-3,4-dihydro spiro[benzo[b][1,4] oxazine-2,5'-thiazo-lidin]-4'-one [2a-e]. The formation of Spiro derivatives (2a-e) is presented in scheme 1.The all 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	$C_{26}H_{19}N_5O_4S$ (497.53)	52	145-147	62.80 62.77	3.80 3.85	14.00 14.08	6.40 6.44
2b	$C_{26}H_{18}N_5O_4SCl$ (531.97)	53	138-140	58.70 58.70	3.40 3.41	13.20 13.16	6.00 6.03
2c	$C_{26}H_{18}N_5O_4SBr$ (576.42)	52	143-145	54.20 54.18	3.10 3.15	12.20 12.15	5.50 5.56
2d	$C_{26}H_{18}N_5O_4SF$ (515.52)	54	142-144	60.60 60.58	3.50 3.52	13.60 13.59	6.20 6.22
2e	$C_{26}H_{18}N_6O_6S$ (542.52)	52	147-148	57.60 57.56	3.30 3.34	15.50 15.49	5.90 5.91

***** *Uncorrected LC-MS data of 2c-577.45, 2e-543.63*

2.2. Antimicrobial activity

The Antimicrobial activity of all the compounds was studied against gram-positive bacteria (*B. megaterium* and *S. Aureus*) and gram-negative bacteria (*E.coli and Ps.Aeruginosa*) at a concentration of 50μg/ML by agar cup plate method [18, 19]. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds 2c was found more toxic for microbes. All compounds found to be less or moderate active shown in table 2.

3. RESULTS AND DISCUSSION

The IR spectra of 2'-(5-(subsitutedphenyl)furan-2-yl)-3-(furan-2-yl)-3'-(4H-1,2,4-triazol-4-yl)-3,4-dihydrospiro [benzo[b][1,4]oxazine-2,5'-thiazolidin] -4'-one [2a-e] shows an absorption bands at 1696-1698 cm^{-1} (C=O stretching), 3350-3380cm^{-1}(-NH-).3040-3080 cm^{-1} (Aromatic C-H stretching), 720cm^{-1} (C-S-C of thiazolidinone ring), 1185 (C-O-C), 1625-1650 cm^{-1} (C=N), 1080 cm^{-1} (-Cl), 1555,1375 cm^{-1} (-NO_2), 710 cm^{-1} (C-Br), 1255 cm^{-1} (C-F). ^{1}H NMR: 5.07-5.08(s, oxazine proton), 5.88-5.92(d, thiazolidinone proton), 7.70-7.74(m, furan proton), 8.03-9.12 (m, Aromatic proton), 8.30-8.32 (s, Triazole proton). ^{13}CMR spectral Features (δ, ppm): 51.6-51.8 (Thiazolidinone carbon), 69.4-69.8 (oxazine carbon), 113-118 (furan carbon), 128 -135 (Aromatic carbon), 145.8-146.2 (Triazole carbon), 166.8-169.6 (C=O). The C, H, N, S analysis data of all compounds are presented in table 1.

The C, H, N, S analysis data of all compounds are presented in table 1. LC-MS of selected samples B2 and B4 show the peak respectively at 577.45 and 543.63, which assign the molecular weight of compound.

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.

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

Compound (Designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B. megaterium	*S. Aureus*	*E. Coli*	*Ps. Aeruginosa*
2a	16	15	15	08
2b	12	12	08	11
2c	18	18	11	16
2d	12	12	13	18
2e	11	08	08	22

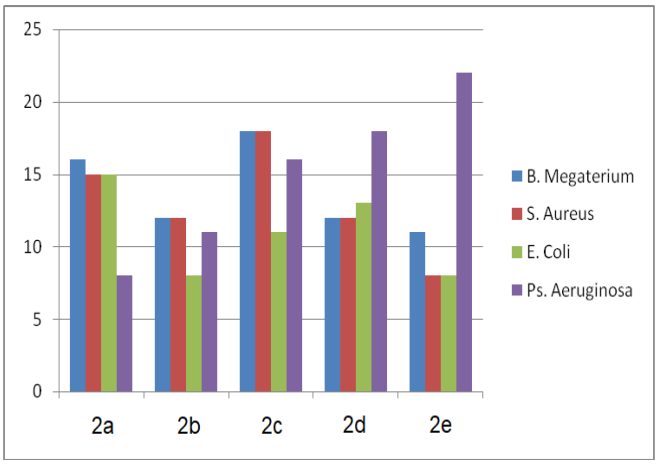


Fig. 1: Antimicrobial activity comparison of Compound (2a-e)

4. CONCLUSION

The present research work describes the synthesis and evaluation of the antimicrobial activity of Spiro derivatives of 4-Amino-1,2,4-triazole. The synthesized compounds, therefore, present a new scaffold that can be used to as lead in the development of novel antimicrobial agents.

5. ACKNOWLEDGEMENT

The authors are thankful to Head, Department of Chemistry for providing laboratory facilities.

6. REFERENCES

1. Majid MH, Alishiri T. *Advances in Heterocyclic Chemistry*, 2014; **113**:1-66.
2. Ruby S, Ganaie SA, Aakash S, Archana C. *Synthetic Communications*, 2019; **49(1)**:80-93.
3. Ghatpande NG, Jadhav SJ, Kaproormath RV, Soliman ME, Shaikh MS. *Bioorganic & Medicinal Chemistry*, 2020; **28(23)**:115813.
4. Dey P, Kundu A, Sang HH, Kyeong SK, et al. *Biomolecules*, 2020; **10(9)**:1260.
5. Das P, Boone S, Mitra D, Turner L, et al. *RSC Advances,* 2020; **10**:30223.
6. Nakul K, Chhagan L, Bijendra S, Patel AK. *Asian Journal of Chemistry*, 2020; **32(5)**:1255-1258.
7. Bogdanov AV, Ilyuza FZ, Alexandra DV, et al. *Chemistry Select,* 2019; **4(20)**:6162-6166.
8. Barbara K, Czarnomysy R, Wysokiński M, Rudolf A, et al. *J. Enzym. Inhib. Med. Chem.*, 2020; **35**:993-1002.
9. Liao L, Caibao J, Jianwen C, Jinguo S, et al. *J. Med. Chem.*,2020; **190**:112114.
10. Ahmed AM, Reedy EL, Soliman NK, *Scientific Reports*, 2020; **10**:6137.
11. Chu XM, Wang C, Wang WL , Liang LL, et al. *Eur. J. Med. Chem.*, 2019; **166**:206-223.
12. Fan YL, Xing K, Liu M. *J. Heterocycl. Chem.*, 2018; **55(4)**:791-802.
13. Zhiwen Z, Qiao W, Zhonghua S, Chengxia T, et al. *Chin. J. Org. Chem.,* 2017; **37**:232-236.
14. ElSaghier AM, Mounier AM, Omyma AAA, Asmaa MK, et al. *Med. Chem. Res.*, 2019; **28**:169-181.
15. Nunna GRB, Patel HS, Gulati S. *Int. Advanced Research Journal in Science, Eng. and Tech.*, 2019; **6(1)**:33-38
16. ElOssaily YA, Zaki RM, Metwally SA. *Journal of Scientific Research*, 2014; **6(2)**:293-307.
17. Ziarani GM, Razieh M, Lashgari N. *ARKIVOC*, 2016; **(i)**:1-81.
18. Shah PJ, Patel HS, Patel BP. *Journal of Saudi Chemical Society*, 2013; **17**:307-313.
19. Godkar PB. *Textbook of Medical Lab. Tech.*, *Bhalani Pub. House, Mumbai*, 1996; 326, 332,382.