Asian J. Adv. Basic Sci.: **2018, 6***(3),* 14-16
ISSN (Print): 2454 – 7492
ISSN (Online): 2347 – 4114
www.ajabs.org

Synthesis, Characterization and Biological Evaluation of 3,7-substituted-1[(5-sulfanyl-1,3,4-oxadiazol-2-yl)methyl]pyrido[2,3-b]pyrazin-2(1H)-onederivatives

S. S. Dhok[1] & S. E. Bhandarkar[1*]

[1] *Government Vidarbha Institute of Science and Humanities, Amravati- 444604, (M.S.), INDIA*

[*] *Correspondence: E-mail: sarikadhok07@gmail.com*

(Published 22 Feb, 2018)

ABSTRACT: Ethyl-(3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl)acetate were synthesized from 3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl on condensation with ethyl chloroacetate.Ethyl(3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl)-acetohydrazide were synthesised from the reaction ofethyl(3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl)-acetatewith hydrazine hydrate. The compounds of 3,7-substituted-1-[(5-sulfanyl-1,3,4-oxadiazol-2-yl)-methyl]-pyrido-[2,3-b]-pyrazin-2-(1H)-one were synthesised from ethyl(3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl)-acetohydrazideon cyclisation with carbon disulphide in methanolic potassium hydroxide .The isolated products were recrystallized from chloroform. The compounds thus synthesized have been characterized by chemical, physical, and spectral data. All of these titled synthesized compounds have been examined for antimicrobial study and are found to possesses very good antimicrobial activities

Keywords: Biological evaluation; Characterization; pyrazine and Synthesis.

INTRODUCTION: The interest in Heterocyclic compounds is mainly due to their biological activities such as antimicrobial activity[1-5].A review on pyrazine shows that the molecules having pyrazine nucleusthey possess varieties of activities like antibacterial anti-inflammatory[6]. Pyrazine derivatives play a significant role as anti-tuberculosis[7-8], antifilarial agents[9], anti-fungal[10-11], antidepressant[12], vitro anticancer activity[13], antihypertensive agent[14], antiprotiferative[15].

Hence, Considering the scope of pyrazine derivatives we have synthesized novel 3,7-substituted-1[(5-sulfanyl-1,3,4-oxadiazol-2-yl)-methyl]-pyrido-[2,3-b]-pyrazin-2-(1H)-one compounds and studied for their biological activities.

MATERIALS AND METHOD: The melting points (ºC) were measured by open capillary method. IR spectra (υ max in cm-1) were observed on a Shimadzu FTIR 8300 spectrophotometer using KBr pellets. The 1H NMR spectra were observed on DRX-300 (300 MHZ) instrument taking $CDCl_3$ as solvent (chemical shift in δppm) and internal standard as TMS . Thin Layer Chromatography on silica gel-G, was used to found the purity of the compounds.

RESULT AND DISCUSSION:

Synthesis of ethyl-(3,7-substituted-2-oxo-pyrido-[2,3-b]pyrazin-1-(2H)-yl)acetate: 3,7-Substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl & potassium carbonate were refluxed in acetone for 4 hr. Progress of the reaction was checked by TLC. After removal of acetone, the residue was added to chilled water, acidified with acetic acid.

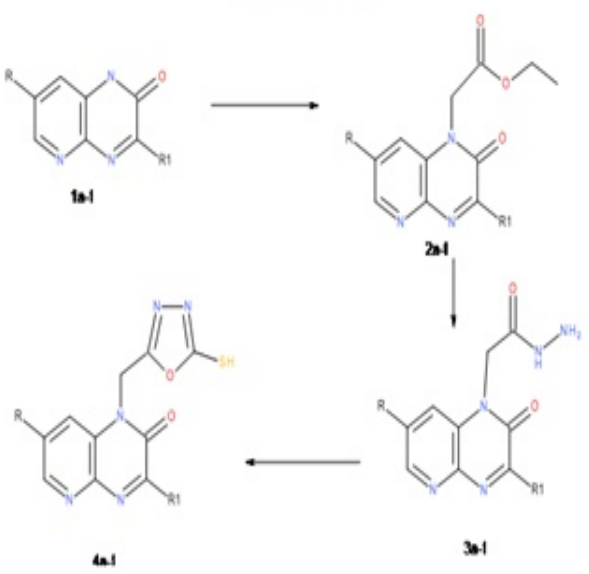
Synthesis of ethyl-(3,7-substituted-2-oxo-pyrido-[2,3-b]pyrazin-1(2H)-yl)acetohydrazide: Ethyl-(3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl)-acetate & hydrazine hydrate in methanol was refluxed for 6 hrs. The reaction mixture was then kept in deep –freezer over night.

Synthesis of 3,7-substituted-1-[(5-sulfanyl-1,3,4-oxadiazol-2-yl)-methyl]-pyrido-[2,3-b]-pyrazin-2-(1H)-one: Ethyl-(3,7-substituted-2-oxo-pyrido-[2,3-b]-pyrazin-1-(2H)-yl)-acetohydrazide were mixed with potassium hydroxide dissolved in methanol & the resulting mixture was cooled to 0^0C. To this mixture slowly added distilled carbon disulfide while stirring & it was slowly heated to reflux & reflux was continued till the completely evolution of hydrogen sulphide gas. Progress of the reaction was checked by TLC. The product was dissolved in water & acidified by using acetic acid at 0-5^0C.

Table 1: Physical Properties.

Sr .No.	Compound No.	R	R_1	Molecular formula	M. Pt. ^0C	% Yield	% Nitrogen		R.F. Value
							Found	Calculated	
1	2a	Cl	C_6H_5	$C_{18}H_{21}ClN_2O_3$	235	52	08.23	08.25	0.51
2	2b	Cl	CH_3	$C_{13}H_{13}ClN_2O_3$	247	55	09.95	09.98	0.53
3	2c	Cl	C_2H_5	$C_{14}H_{15}ClN_2O_3$	213	57	09.50	09.51	0.56
4	2d	Cl	Cl	$C_{12}H_{10}Cl_2N_2O_3$	223	53	09.28	09.30	0.61
5	2e	CH_3	CH_3	$C_{14}H_{16}N_2O_3$	198	49	10.75	10.77	0.57
6	2f	CH_3	Cl	$C_{13}H_{13}ClN_2O_3$	274	51	09.95	09.98	0.53
7	3a	Cl	C_6H_5	$C_{16}H_{19}ClN_4O_2$	278	49	16.73	16.74	0.53
8	3b	Cl	CH_3	$C_{11}H_{11}ClN_4O_2$	249	46	21.00	21.01	0.58
9	3c	Cl	C_2H_5	$C_{12}H_{13}ClN_4O_2$	215	43	19.94	19.96	0.54
10	3d	Cl	Cl	$C_{10}H_8Cl_2N_4O_2$	231	47	19.50	19.51	0.52
11	3e	CH_3	CH_3	$C_{12}H_{14}N_4O_2$	196	48	22.73	22.76	0.56
12	3f	CH_3	Cl	$C_{11}H_{11}ClN_4O_2$	248	50	21.00	21.01	0.58
13	4a	Cl	C_6H_5	$C_{16}H_{10}ClN_5O_2S$	238	45	18.81	18.84	0.53
14	4b	Cl	CH_3	$C_{11}H_8ClN_5O_2S$	253	44	22.60	22.62	0.54
15	4c	Cl	C_2H_5	$C_{12}H_{10}ClN_5O_2S$	259	41	21.62	21.64	0.56
16	4d	Cl	Cl	$C_{10}H_5Cl_2N_5O_2S$	284	42	21.19	21.21	0.52
17	4e	CH_3	CH_3	$C_{12}H_{11}N_5O_2S$	205	47	24.19	24.22	0.57
18	4f	CH_3	Cl	$C_{11}H_8ClN_5O_2S$	252	43	22.61	22.62	0.54

SCHEME



Spectral Analysis of 4d

IR (ν_{max}) (cm^{-1}) : 3200 (S-H, str) , 3090(Ar-H) ,2967(C-H, str) ,1705 (C=O, str), 1668(C=N,str), 1317(C-N-C,str),1157(C-O, str) , C-O-C (1145& 1036 str), 745(C-Cl ,str) ,740(C-Cl ,str).

NMR: 7.65(m,2H,Ar-H) 5.49(s,2H,CH_2), 4.1 (s,1H,SH).

Table 2: Antimicrobial Activities.

Comp. No	Antimicrobial activity			
	E-coli	*P. mira-bilis*	*S. aureas*	*P. aeruginosa*
2a	15	14	10	14
2b	13	16	14	14
2c	17	14	18	18
2d	18	17	18	17
2e	10	09	16	06
2f	14	13	14	17
3a	15	16	11	14
3b	14	16	14	18
3c	17	15	18	18
3d	18	17	16	17
3e	11	09	15	07
3f	14	13	15	12
4a	15	16	11	14
4b	14	16	14	18
4c	17	16	18	18
4d	18	18	16	17
4e	11	07	15	10
4f	15	15	14	07

Strongly active, range 14-18mm; weakly active, range 6-10 mm; moderately active, range 11-13mm

CONCLUSION: Thus from above results it was observed that these heterocyclic compoundswere found more active against *staphylococcus aureas*, *pseudomonas aeruginosa* , *escherichia coli*, *proteus mirabilis*, So those compounds can be easily be used for the treatment of diseases caused by test pathogens, only when they does not have toxic and other side effects..

REFERENCES:

1. Sherekar V. M., Bhandarkar S. E. Synthesis and biological evaluation of 3-(4-chloro-1-hydroxynaphthalen-2-yl)-5-aryl-1-substituted-pyrazoles Der Pharma Chemica International Journal of Current Pharmaceutical Research vol. 7 issue 2; 2015;10-1
2. Bhandarkar SE. Synthesis and characterization of 3-(1-hydroxy naphthalene -2-yl)-5-(furane 2-yl)-1-substituted pyrazoline. Orient J Chem 2014; 30(1): 361-363.
3. Bhandarkar S. E., Khobragade B. Synthesis and Biological study of 2-(5-aryl-4,5-dihydro-1-Substituted pyrazole-3-yl)-substituted naphthalene 1-ol. Advanced Materials Research,Trans Tech Publications Volume 1110; 2015; 306-310.
4. Sherekar V. M. and Bhandarkar S. E. 1-4Synthesis and characterization of pyrazoline derivatives obtained from 4-bromo-naphthalen-1-ol Der Pharma Chemica, 2015;7(3), 1-4.
5. Dhok S. S. and Bhandarkar S. E. Synthesis, Characterisation & biological evaluation of 9,10-bicyclo-3-substituted- pyrazine-2-(1H)-one.Am.J. Pharm Tech Res. 2017; 7(2) 176-180.
6. Dhok S. S. and Bhandarkar S. E. A Review on pyrazin-2(1H)-one derivatives possessing biological activity. International Journal of Research in Pharmacy &Chemistry 2015, 5(2); 312-316.
7. Janduorek. O., Dolezal. M., Klementova. M., Kralova K., Pesko. M., Microwave assisted synthesis of new pyrazinamide analogus & their biological evaluation, Universitas Comeniana Bratislavensis, MCMXIX, facultas Rerum Naturalium, 1-12.
8. Spaia S., Magoula I., Tsapas G., Vayonas G. (2000) "Effect of pyrazinamide and probenecid on peritoneal urate transport kinetics during continuous ambulatory peritoneal dialysis". PeritDial Int 20 (1): 47–52.
9. Singh B. K., Mishra M., Saxenaa N., Yadav G. P., Maulik P. R., Sahoo M. K., Gaur R. L., Murthy P. K., Tripathi R. P. Synthesis of 2-sulfanyl-6-methyl-1,4-dihydropyrimidines as a new class of antifilarial agents. Eur J Med Chem. 2008; 43: 2717–2723.
10. Abd El-Wahab. A. H. F, Bedair. A. H, Eid. F. A, El-Haddad. A. F, Adawy El-Deeb. A. M and El-Sherbiny. G. M, Pyrazine-2-substituted carboxamide derivatives: synthesis, antimicrobial and *Leuconostoc mesenteroides* growth inhibition activity, J. Serb. Chem. Soc. 2006; 71 (5): 471–481.
11. Chaluvaraju K C and Bhat. I K, Synthesis and Antimicrobial Activities of AminoBenzylated Mannich Bases of Pyrazinamide, International Journal of ChemTechResearch CODEN (USA): IJCRGG ISSN: 0974-4290, 2010; 2(3): 1368-1371.
12. P. A. Bonnet, A. Michel, F. L. aurentetal., "Synthesis and antibronchospastic activity of 8alkoxy-and 8(alkylamino)imidazo[1,2-a]pyrazines," Journal of Medicinal Chemistry, vol.35, no. 18, pp. 3353–3358, 1992.
13. Sosnicki J. G., Struk L., Kurzawski M., Peruzynska M., Maciejewska G., Dro zdzik M. Regioselective synthesis of novel 4,5-diaryl functionalized 3,4-dihydropyrimidine-2(1H)-thiones via a non-Biginelli-type approach and evaluation of their in vitroanticancer activity. Org Biomol Chem. 2014; 12: 3427–40.
14. Rovnyak G. C., Atwal K. S., Hedberg A., Kimball S. D., Moreland S., Gougoutas J. Z., O'Reilly B. C., Schwartz J., Malley M. F. Basic 3-substituted-4-aryl-1,4-dihydropyrimidine-5carboxylic acidesters. Potent antihypertensive agents. J Med Chem.
15. F. Azam, I. A. Ibn-Rajab, and A. A. Alruiad, "Adenosine A2A receptor antagonists asnovel anti-Parkinsonian agents: a review of structure-activity relationships," Pharmazie, vol. 64, no. 12, pp.771–795, 2009.