AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Synthesis, Characterization and Antimicrobial Study of Some Novel Chloro Substituted Isoxazoles

V. D. Mane[*1], D. T. Mahajan[2], P. R. Rajput[2]

1. Department of Chemistry, S. K. College, Akola, India.

2. Department of Chemistry, Vidyabharti Mahavidyalaya,Amaravti, India.

ABSTRACT

In the present study a series of 3-(2-Hydroxy-3, 5-dichlorophenyl)-5-(4-chloro phenyl) isoxazole (8a) and 3-(2-Hydroxy-3, 5-dichlorophenyl)-5-(2, 4-chloro phenyl) isoxazole (8b) have been synthesized by refluxing the chalconedibromide (6a) and (6b) with hydroxyl amine hydrochloride in ethanol containing catalytic amount of piperidine. The formation of the above synthesized compounds was confirmed on the basis of their chemical tests and spectral analysis. The synthesized heterocycles then screen for their antimicrobial activity against some kahrip plant pathogens viz. *AlternariaMacrospor, XanthomonasCampestris, Pseudomonas syringae and Fusarium Spp.* From the above study the result revealed that isoxazole derivatives shows good to moderate antimicrobial activity against plantpathoges.

Keywords: Chalcones, chalconedibromide, plant pathogens, antimicrobial activity, isoxazole.

*Corresponding Author Email: vivekvdm@rediffmail.com

Received 15 July 2015, Accepted 27 July 2015

Please cite this article as: Mane VD *et al.*, Synthesis, Characterization and Antimicrobial Study of Some Novel Chloro Substituted Isoxazoles. American Journal of PharmTech Research 2015.

INTRODUCTION

Isoxazole is a five membered heterocyclic compound containing oxygen and nitrogen atoms in the 1,3 positions placed in the heterocyclic ring. From the literature survey it is revealed that many workers have synthesized different isoxazole[1-5]. Heterocyclic compounds are veryuseful moiety in the fields of medicinal and pharmaceutical chemistry and have been reported to exhibit a variety of biological activities[6,7] such as antimicrobial[8], antiarthetic[9], anticoagulant[10]

MATERIALS AND METHOD

The all the heterocyclic compounds have been synthesized by using conventional method in laboratory

Preparation of 2-hydroxy 3, 5-dichloroacetophenone (2a)

2-hydroxy 3, 5-dichloroacetate (50 ml) was mixed with anhydrous $AlCl_3$ (120 gm) and heated at 120^oC for 45 minutes on the paraffin oil bath. The reaction mixture were decomposed by taking ice cold water containing a few amount of HCl acid and allowing the solution to fall drop by drop into cold water with constant stirring . A greenish white solid of compound (2a) was obtained.

Preparation of 2-hydroxy-3, 5-dichlorophenyl-4-p-chlorochalcone (3a, 3b)

2-Hydroxy-3, 5-dichloroacetophenone (2a) (0.01mol) and p-chlorobenzaldehyde and p, m-dichlorobenzaldehyde (0.01mol), was dissolved in ethanol (25ml). after that in this solution the 40% 30 ml NaOH solution is added drop wise with constant stirring getting the saffron color solid kept it overnight after that acidify this solid by 50% HCL solution, affords a yellow solid was filtered, washed with sodium bicarbonate (10%) followed by water. The crude product was crystallized from ethanol acetic acid.

Synthesis of 2-hydroxy 3, 5-dichlorophenylchalconedibromide (6a, 6b)

2-hydroxy 3, 5-dichlorophenyl chalcone (3a) and(3b) (0.01 mol 3.26, 3.65gm respectively) was dissolved in bromine -acetic acid reagent (25%, w/v) (6.4 ml). The reagent was added drop wise with constant stirring. After complete addition of reagent, the reaction mixture was kept at room temperature for about 30 minutes. The solid product thus separated was filtered and washed with a little petroleum ether to get the compound (6a) and (6b).

Synthesis of 2-hydroxy-3, 5-dichlorophenyl isoxazole (8a, 8b)

A mixture of chalconedibromides (6a) and (6b) (0.01 mol, 4.84 and 5.18 g, respectively) and hydroxyl amine hydrochloride (0.02 mol, 2.78gm) was refluxed in ethanol (20 ml) and piperidine (1ml) for about 3.5 hours. After cooling the reaction mixture was acidified with dil. HCl (1:1). The solid product separated was filtered, washed with sodium bicarbonate solution (5 %) and water.

The product was finally crystallized from ethanol-acetic acid mixture to get the compound (8a) and (8b).

Characterization of the compounds

Melting points of all synthesized compounds were determined in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer 1000 Spectrophotometer in KBr. NMR spectra were recorded on Bruker advance 400 NMR spectrometer using TMS as internal standard and chemical shift were expressed in δ ppm.

1. Compound: Chalcone (3a)

I.R. (KBr): cm – 3500 (-OH phenolic), 3074 (=CH str. in alkene), 1643 (>C=O str. in ketone), PMR: δ 7.44 -7.91 (m, 2H, -CH=CH); 7.44 -8.37 (m, 6H, Ar H); 13.26 (s, 1H, Ar-OH). U. V.:- λ max 344 nm. Corresponding to n →π*

2. Compound: Chalcone (3b)

I.R. (KBr): cm-3368-3500 (-OH phenolic), 3068 (aromatic –CH stretching). 1641 (>C=O str.in ketone), PMR: δ 8.27-8.31(m, 5H, Aromatic) 7.2-7.78 (2H, CH-CH); 13.19 (s, 1H, Ar-OH) U. V:- λ max 344 nm. Corresponding to n →π* shows conjugation in aromatic molecule

3. Compound: Dibromide (6a)

I.R. (KBr): cm – 3700 (-OH phenolic), 2981 (aromatic str.), 2882 (aliphatic CH str.), 1654(-C=O str.), 1319 (O-H bending).1093(C-Cl str.), PMR: δ 2.5 (d, 1H, -CO-CH-Br); 3.5 (d, 1H,-CHBr-CHBr); 7.4-8.4 (m, 6H, Ar-H).12.04(s, 1H, Ar-OH), U. V.:- λ max 314 nm. Corresponding to n →π*

4. Compound: Dibromide (6b)

I.R. (KBr): cm – 3700 (-OH phenolic), 3074 (aromatic str.), 3007 (aliphatic CH str.), 1654(-C=O str.), 1313 (O-H bending),1103(C-Cl str.) , PMR: δ 3.9 (d, 1H, -CO-CH-Br); 7.5-7.7 (d,1H,-CHBr-CHBr); 7.1-8.4 (m, 5H, Ar-H).11.90(s, 1H, Ar-OH), U. V.:- λ max 300 400 nm. Corresponding to n →π*

5. Compound: Isoxazole (8a)

I.R. (KBr): cm – 3600 (w, -OH phenolic), 3082 (s, aromatic str.), 1462 (-C-N str.), 1282 (s,- N=N-str.),1107 (Cl-C) PMR: δ 6.7 (isoxazole proton), 7.3-7.5 (d, 2H, C-H),7.5-8.5 (d, 2H, C-H), 7.87 (s, 1H, C-H), 7.6 (d, 2H, C-H), U. V.:- λ max 400 nm. Corresponding to n →π*

6. Compound: Isoxazole (8b)

I.R. (KBr): cm – 3600 (w, -OH phenolic), 3070 (s, aromatic str.), 1462(-C-N str.), 1282(s,- N=N-str.), 1091 (Cl-C)PMR: δ 8.0 (d HAr-H).10.53(s, 1H, Ar-OH), 7.75, 7.5, 7.9, 7.6 (d H Ar-H), 8.1 (s H isoxazole proton) U. V.:- λ max 400 nm. Corresponding to n →π*

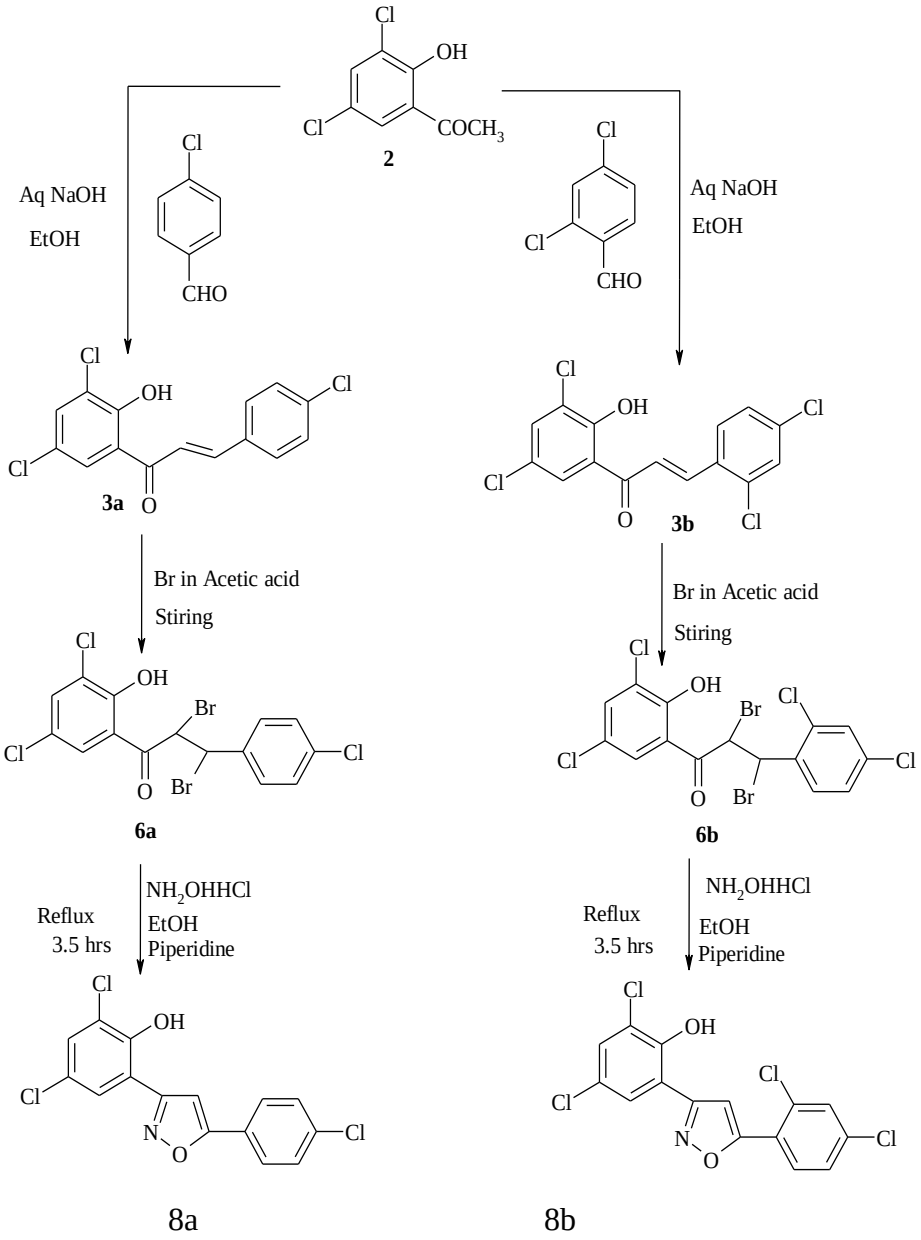

Figure 1: The flow diagram of the isoxazole synthesis.

RESULTS AND DISCUSSION

Table 1: Physical data of the synthesized compounds

Sr. No.	Name of the compounds	M.P. ^{o}C	R f value
1	2	93	0.84
2	3a	215	0.62
3	3b	176	0.66
4	6a	190	0.71
5	6b	170	0.78
6	8a	120	0.58
7	8b	95	0.62

Antimicrobial activity

Antimicrobial activities of all synthesized compounds were determined by cup plate method. All plant pathogens were purchased from NCIM Pune, Institute of Microbial Technology, Chandigarh and Plant pathology department ICAR New Delhi. The agar medium and PDA were purchased from Hi- media lab. Mumbai. The stock solution of test 1000µg/ml were prepared by dissolving appropriate quantities of test compounds in DMSO, The stock inoculums of the microbes was prepared by the inoculation the 5o ml nutrient broth with test organisms and incubating it at 37 ± 2^0C for 24 hrs the zone of inhibition was measured by Himedia scale[11,12].

Table 2: Antimicrobial screening of the synthesized compounds

Sr. No.	Name of the compounds	Zone of Inhibition (mm)			
		Xanthomonas Campestris	***Alternaria Macrospora***	***Fusarium Spp.***	***Pseudomonas syringae***
1	2	17	12	22	23
2	3a	---	12	15	15
3	3b	12	15	15	19
4	6a	33	26	25	13
5	6b	30	30	18	16
6	8a	---	25	17	14
7	8b	16	18	11	11
8	Control	18	16	14	14

CONCLUSION

The above result revealed that the synthesized compounds have showed good to moderate antimicrobial activity against all plant pathoges.

ACKNOWLEDGMENT

Authors are thankful to the principle Dr. F. C. Raghuwanshi Vidyabharti mahavidyalaya Amaravati for providing laboratory facility, also grateful to Dr. J. M. Saboo and Management of Shankarlal Khandelwal College, Akola, Dr. D. D. Bhokare and Dr. P. S. Pande Dept. of chemistry for their valuable help.

REFERENCES

1. Behara R K, Behra A K, Pradhan Rosy Patra M. Installation of biologically active heterocyclic nuclei into spiro compounds derived from cyclohexanone and diphenyl thiobarbituric acid. Indian J Chem. 2006; 45B: 933-42.
2. Singh B, Singh Varjeet. A facial synthesis of steroidal pyrazoles, isoxazoles and pyrimidines from testosterone .Indian J Chem. 2006; 45 B: 959-66.

3. Peesapathi V, Bathini Shrinivas. Synthesis and characterization of new isoxazole derived from benzosuberones, Indian J Chem.2006; 45 B: 1753-56.
4. Siddiqui Zeba N, Asad Mohammad. New heterocyclic derivatives of 3-formyl-4-hydroxycoumarin, Indian J Chem.2006;45 B: 2704-09.
5. Rajanarendar E, Mohan G. Kalyanrao E, Siva Rami Reddy A, Praveen B, Shrinivasa Rao M. Synthesis, antimicrobial and mosquito larvicidal activity of N-protected amino acids/ peptide isoxazoles. Indian J Chem., 2008;47 B: 781-6.
6. Bhaskar Chakraborty, Manjit Singh Chhetri, Saurav Kafley and Amalesh Samanta. Synthesis and antibacterial activities of some novel isoxazolidine derivatives derived from N-phenyl-α-chloronitrone in water Indian J Chem. 2010; 49B:209-215.
7. Ajay Kumar K, Lokeshwari DM and Vasanth Kumar G. Evaluation and studies on the structural impact of substituted 4, 5-dihydroisoxazoles on their biological activities. Int J Pharm Sci DrugRes.2012; 4 (4): 236- 9.
8. Sandeep G, Ranganath Y S, Bhasker S, Rajkumar N, Synthesis and biological screening of some novel coumarin derivatives. Asian J Research Chem. 2009, 2(1).
9. Patterson JW, Chenug PS, Ernest M J. 3-Carboxy-5-methyl-N-[4-(trifluoromethyl)phenyl]-4-isoxazolecarboxamide, a new prodrug for the antiarthritic agent 2-cyano-3-hydroxy-N-[4-(trifluoromethyl) phenyl]-2-butenamide. Indian Med Chem. 1992; 35: 507.
10. Zhang D, Raghvan N, Yuan-Chen S, Zhang H, Quan M, Lecureux L, Patron L, Lam P, Bonacorsi S, Knabb R, Skiles G, He K, Reductive Isoxazole ring opening of the anticoagulant razaxaban is the major metabolic clearance pathway in rats and dogs, Drug metabolism and dispersion,2008;36(2): 303-315.
11. Samy R P, Ignacimuthu S, Sen A. Screening of 34 Indian medicinal plants for antibacterial properties, J. Ethnopharmacol 1998; 62:173-81.
12. Barry A, L.The Antimicrobic susceptibility test: principles and practices, Illus Lea and Febiger*:* Philadelphia, Pa., USA. 180: (1976), Bio, Abstr, 64(5), 25183(1977).