WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 10, 770-776. Research Article ISSN 2277–7105

SYNTHESIS, SPECTRAL STUDY, ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF 3-(2'-n-BUTYLBENZOFURAN-3'-YL)-5-ARYL-ISOXAZOLES.

Rakesh P. N. Roshan[1], D. M. Purohit[2] and Sandip K. Matariya[3*]

[1]R.K.University, Rajkot, (Guj), India

[2]Shri M&N. Virani Science College, Department of Chemistry, Kalawad Road, Rajkot-390005, (Guj), India.

[3]*Smt. S. M. Panchal Science College, Department of Chemistry, Talod, (Guj), India.

Article Received on
26 March 2018,
Revised on 15 April 2018,
Accepted on 06 May 2018
DOI: 10.20959/wjpr201810-12305

***Corresponding Author**
K. Matariya
Smt. S. M. Panchal Science College, Department of Chemistry, Talod, (Guj), India.

ABSTRACT

3-(2'-n-butylbenzofuran-3'-yl)-5-aryl-isoxazoles (4a-4k) have been synthesized. The synthesized products have been assayed for their antimicrobial activity against Gram+ve, Gram-ve bacteria and fungi. All the synthesized products were assigned with IR, ^{1}HNMR, Mass Spectra, TLC, and elemental analysis. Some of the products showed moderate activity, compare with known standard drugs eg. Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole.

INTRODUCTION

Isoxazoline derivatives showed a vital role largely due to the wide ranging of therapeutic and agrochemical activities. Taking into consideration diverse biodynamic activities such as Antibacterial[1-2], Anticonvulsant[3-4], Anticholestermic[5], Anticancer[6], Anthelmintics[7], Antiinflammatory[8-9], Adenosine antagonist[10], Fungisides[11-12], Herbicides[13-14], Hypoglycemic[15], Muscle relaxant[16-17], Nematocidal[18], Insecticidal[19], Antiviral[20] etc. In this fact to interesting biological activities, it appeared to interest to synthesized some new Isoxazolines (4a-4k) have been synthesized by the condensation of (E)-1-(2'-n-butylbenzofuran-3'-yl)-3-aryl-prop-2-ene-1-ones with hydroxylamine hydrochloride. Chalcones of (3a-3k) have been synthesized by the condensation of 1-(2'-n-butylbenzofuran-3'-yl)ethanone with aromatic aldehyde in the presence of aqueous NaOH, 1-(2'-n-butylbenzofuran-3'-yl)ethanone have been synthesized by the acetylation of 2-n-butylbenzofuran with acetyl chloride in the presence of anhydrous

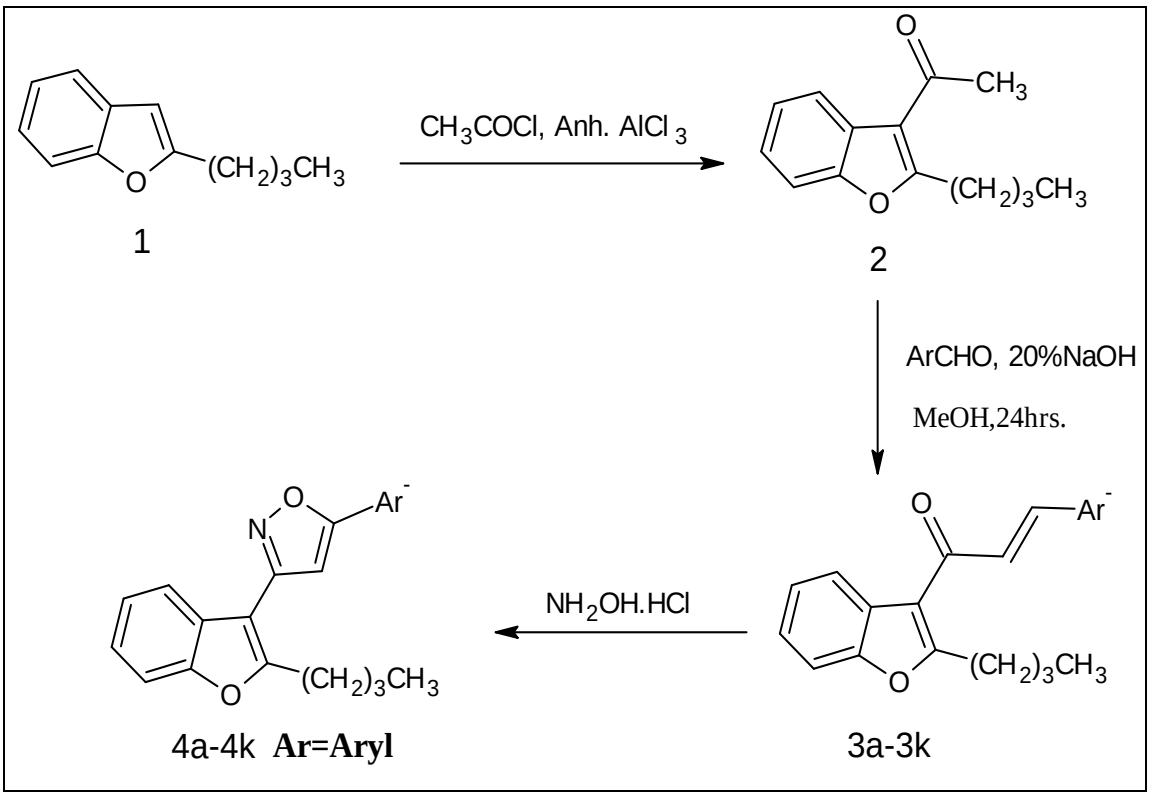
$AlCl_3$. All the products (4a-4k)were assigned with IR, ^{1}HNMR, Mass Spectra, TLC and Elemental analysis. The physical data recorded in Table no: I. Antimicrobial activity recorded in Table no: II and comparable antimicrobial compared with known standard drugs represented in Table no: III.

ANTIMICROBIAL ACTIVITY

All the products (4a-4k) were tested for their antimicrobial activity by Cup-plate method[21] against the Gram positive Bacteria *Bacillus megaterium*; *S.aureus,* Gram negative bacteria *Escherichia coli*, *S.Taphimarium* and for antifungal activity against *Aspergillus niger*, *Anrobacter awamori* at a concentration of 50µg/ml, using DMF as a solvent. After 24hrs of incubation at 37°C, the zone of inhibition were measured in mm. The activity was compared with known standard drugs viz. Ampicillin, Chloramphenicol, Norfloxacin, Fluconazole at the same concentration (50µg/ml) which is represented in Table no II.

All the synthesized compounds (4a-4k)showed moderate to good and remarkable activities compared with known standard drugs at same concentration which is represented in Table no III.

REACTION SCHEME



EXPERIMENTAL SECTION

All the melting points were measured in open glass capillary method and are uncorrected. IR absorption Spectra (in cm^{-1}) were recorded on a SHIMADZU IR-435 spectrophotometer using KBr pellet method, ^{1}HNMR spectra on BRUKER (300mHz) spectrometer using DMSO as internal standard (chemical shift in δppm) and Mass spectra on a Jeol-JMSD 300 Mass spectrometer at 70ev. The compounds were routinely checked by TLC method using silica gel G.

(1) Synthesis of 1-(2'-n-butylbenzofuran-3'-yl)ethanone

Methylene dichloride (20ml) was chilled to 0-5°C. Anhydrous Aluminium chloride (2.0gm, 0.015mol) and acetyl chloride (1.0ml, 0.15mol) were added slowly drops by drops at 0-5°C. Reaction mixture was stirred at 0-5°C for 30minutes. 2'-n-butylbenzofuran (1.74gm, 0.01mol) was added slowly to the reaction mass at 0-5°C. After completion of addition, temperature of reaction mass was raised up to 30-35°C. Reaction mixture was stirred at 30-35°C for 4hrs. After completion of the reaction, the reaction mixture was poured in to ice cold water. Layers were separated. Methylene dichloride layer was washed with water. To get required product from Methylene dichloride layer, Methylene dichloride distilled out under reduced pressure. 2-n-butylbenzofuran-3-yl ethanone oily product is formed. Yield: 85.00%, B.P.:87°C

(2) Synthesis of (E)-1-(2'-n-butylbenzofuran-3'-yl)-3-(4''-methoxyphenyl)-prop-2-ene-1-one (3e).

1-(2'-n-butylbenzofuran-3'-yl) ethanone (2.16gm, 0.01m),4-Methoxybenzaldehyde (1.36gm, 0.01m), methanol(20ml), 20% NaOH (20ml). The reaction mixture was stirred for 24 hrs. at room temperature. Completion of reaction checked with TLC. The reaction mixture was poured into crushed ice, filtered and dried. Yield:78.28% ; M.P.:161°C; (Required: C:79.04;H:6.58%; $C_{22}H_{22}O_3$; Found: C:79.04 ;H:6.58%;). IR(KBr)(cm^{-1}): 2968(C-H Str. Asym);2832(C-H Str. Sym);1457(C-H Str. Def); 3047(C-H Str., aromatic);1537(C=C-Ring skeletal);1189(C-H Str., i.p.def);728(C-H Str., o.o.P.def); 1680 (C=0 str.); 1138(C-O-C); 1620(-CH=CH Str.);^{1}HNMR (δ ppm): 0.85-0.89(3H,t,-C<u>H</u>$_3$); 1.22-1.30(2H,m, -C<u>H</u>$_2$-CH$_3$);1.32-1.66(2H,q,-C<u>H</u>$_2$-CH$_2$-CH$_3$);2.51-2.66(2H,t,C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$);3.84(3H,s,-OC<u>H</u>$_3$);6.97-7.86(10H,m,Ar-<u>H</u>). m/z:334,327,311,301,281,269,246,230,210,209,183,167, 144,139,121,108,91,77,64,44,41. Similarly other Chalcones (3a-3k)have been synthesized.

(3) Synthesis of 3-(2'-n-butylbenzofuran-3'-yl)-5-(4''-methoxyphenyl)-isoxazole (4e).

A solution of (E)-1-(2'-n-butylbenzofuran-3'-yl)-3-(4''-methoxyphenyl)-prop-2-en-1-one (3.34gm, 0.01 mol) and hydroxylamine hydrochloride (0.15gm, 0.02 mol) refluxed in water bath for 8 hrs. After completion of the reaction, the reaction mixture was poured into crushed ice water. Filter and dried. Yield :80.03% ; M.P.:209°C; (Required: C:75.99;H:6.04;N:4.03%, $C_{22}H_{21}O_3N$; Found: C:75.92 ;H6.01:N:4.00%;). IR(KBr)(cm^{-1}): 2968(C-H Str. Asym);2855(C-H Str. Sym);1426(C-H Str. Def); 3073(C-H Str., aromatic);1556(C=C-Ring skeletal);1194(C-H Str., i.p.def);762(C-H Str., o.o.P.def);1325 (C-N Str.);1252(C-O-C); 1536(C= N Str.);^{1}HNMR (δ ppm): 1.23-1.28(3H,t,-C<u>H</u>$_3$); 1.30-1.32(2H,m, -C<u>H</u>$_2$-CH$_3$);1.59-1.66(2H,q,-C<u>H</u>$_2$-CH$_2$-CH$_3$);2.51-2.66(2H,t,C<u>H</u>$_2$-CH$_2$-CH$_2$-CH$_3$);3.83(3H,s,-OC<u>H</u>$_3$);6.98-8.77(10H,m,Ar-<u>H</u>). m/z:348,327,313,301,298,268,251,224,210,209,183,177,157,144(BP), 133,121,108,90,77,64,54,41,40.

Similarly other Isoxazolines (4a-4k)have been synthesized. The physical data of compounds represented in Table-I and antimicrobial activity of compounds (4a-4k) have been represented in Table-II and comparable antimicrobial activity represented in Table-III.

Table-I: The physical data of compounds (4a-4k)

Compounds	Ar	Molecular formula	M.P. °C	% Yield	%Nitrogen	
					Calculated	Found
4a	C_6H_5-	$C_{21}H_{19}O_2N$	144	81.18	4.41	4.35
4b	2-Cl-C_6H_4-	$C_{21}H_{18}O_2NCl$	156	83.29	3.98	3.92
4c	4-Cl-C_6H_4-	$C_{21}H_{18}O_2NCl$	181	84.35	3.98	3.95
4d	4-F-C_6H_4-	$C_{21}H_{18}O_2NF$	193	79.47	4.17	4.12
4e	4-OCH_3- C_6H_4-	$C_{22}H_{21}O_3N$	209	80.03	4.03	4.00
4f	2,5-$(OCH_3)_2$- C_6H_3-	$C_{23}H_{23}O_4N$	178	78.92	3.71	3.69
4g	3,4-$(OCH_3)_2$- C_6H_3-	$C_{23}H_{23}O_4N$	184	75.88	3.71	3.70
4h	3,4,5-$(OCH_3)_3$- C_6H_2-	$C_{24}H_{25}O_5N$	195	83.76	3.44	3.42
4i	2-OH-C_6H_4-	$C_{21}H_{19}O_3N$	210	87.65	4.20	4.15
4j	3-NO_2-C_6H_4-	$C_{21}H_{18}O_4N_2$	205	78.43	7.73	7.71
4k	4-NO_2-C_6H_4-	$C_{21}H_{18}O_4N_2$	219	78.43	7.73	7.65

Table-II.

Compounds	Ar.	Antibacterial activity Zone of inhibition in mm				Antifungal activity Zone of inhibition in mm	
		Gram +ve bacteria		Gram –ve bacteria			
		B.mega	***S.aureus***	***E.coli***	***S.Taphimarium***	***A. niger***	***A. awamori***
4a	C_6H_5-	15	17	16	13	14	12
4b	2-Cl-C_6H_4-	16	18	19	16	17	15
4c	4-Cl-C_6H_4-	19	21	21	19	21	22
4d	4-F-C_6H_4-	18	20	18	17	20	21
4e	4-OCH_3- C_6H_4-	15	14	13	15	16	17
4f	2,5-$(OCH_3)_2$- C_6H_3-	16	17	16	18	18	20
4g	3,4-$(OCH_3)_2$- C_6H_3-	18	19	20	19	15	16
4h	3,4,5-$(OCH_3)_3$- C_6H_2-	19	21	22	17	21	19
4i	2-OH-C_6H_4-	17	18	20	18	18	17
4j	3-NO_2-C_6H_4-	16	21	18	20	19	18
4k	4-NO_2-C_6H_4-	18	20	21	22	17	21

Table-III: Comparable antimicrobial activity.

(Compared with known standard drugs)

Compound	Maximum antimicrobial activity Zone of inhibition in mm					
	B.mega	***S.aureus***	***E.coli***	***S.Taphimarium***	***A. niger***	***A. awamori***
(4a-4k) (50µg/ml)	4c,4h	4c,4d,4g, 4h,4j,4k	4b,4c,4g, 4h,4i,4k	4c,4g,4j,4k	4c,4d,4h, 4j	4c,4d,4f,4h,4k
Ampicillin 50µg/ml	22	21	20	21	-	-
Chloramphenicol 50µg/ml	21	22	23	20	-	-
Norfloxacin 50µg/ml	23	20	22	21	-	-
Fluconazole 50µg/ml	-	-	-	-	21	21

CONCLUSION

The compounds 3-(2'-n-butylbenzofuran-3'-yl)-5-aryl-isoxazole (4a-4k) have been synthesized. Some of the compounds 4c, 4d, 4g, 4h, 4j, 4k showed good remarkable antibacterial and antifungal activity compared with known standard drugs e.g: Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole.

ACKNOWLEDGEMENTS

The authors are thankful to principal Smt.S.M.Panchal Science College Talod, (Guj), India and Director, SPC Lifesciences Pvt. Ltd. Baroda (Guj), India for providing research facilities. Thankful to Head, Department of Chemistry, Saurastra University, Rajkot for ^{1}HNMR and

Mass Spectral analysis, thankful to Head, Department of Pharmaceutical Chemistry, Saurastra University, Rajkot for IR Spectral analysis and also thankful to, The Director Dr. J.G.Daboriya (Darshan Pharmachem Pvt. Ltd, Ankleshwar) for antimicrobial analysis facilities.

REFERENCES:

1. G. P. Reddy, E. Rajendra and A. K. Murthy, Indian J. Heterocycl, 1994; 3: 233, Chem. Abstr, 1995; 122: 105724e.
2. T. Tochiro, K. Shrji, I. Shinji, M. Hiroshi, S. Akira, V. Hiroshi,; Gen. Offen. DE, 1983; 3,237,149 (Cl. CO7A 261114).
3. T. U. Quazi,;Pak. J. Sci. Ind. Res, 1984; 27: 326, Chem. Abstr.,103, 12339m (1985).
4. R. Major, B. Eisele, P. Mutler and H. Grube,; Ger. Offen. DE, 3621372 (1988); Chem. Abstr, 1988; 108: 67456r.
5. D. R P.Li W. Hwang Chen Shen C. W., C. L Huang, T. W. Chen. J. Med. Chem, 2003; 46: 1706.
6. S. Rung and D. Dus,; Pharmazie, 1994; 49: 727, Chem. Abstr, 1995; 122: 55934h.
7. Vamanauchi Pharm. Co. Ltd.; Jpn Kokai Koho JP, 58,148,858 (Cl. CO7D 207/333) (1982).
8. P. T. Gallagher, T. A. Hicka and G. W. Mullier, Eur. Pat. Ep, 1988; 2, 57, 882; Chem. Abstr, 1988; 108: 6499K.
9. A. Ando and R. W. Stevens,; PCT Int. Appl. WO, 94,12,481.
10. W. Wells, A. Michele, H. Todd, H. Dennis,; US Pat. Appl. Publ. US, 2002; 49: 213.
11. I. A. Shehata and R. A. Glannoh,; J. Het. Chem, 1987; 24: 1291.
12. M. Mackie, H. S. Anthony, W. J. R. Howe, S. P. John and W. S. Marry,; Brit.; UK Pat. Appl. GB 2,265,371.
13. G. D. Diana and C. P. Michel,; S. African ZA, 81,03,105 (1981); Chem. Abstr, 1983; 98: 1667.
14. M. Moriyusu, H. Yusui,; Gen. Offen. DE, 3,237,149 (Cl. CO7A 261114) (1983);
15. A. K. Banerjee,; Arzneim Forsch., 44, 863 (1994); Chem. Abstr, 1995; 122: 160522n.
16. M. Tibor, P. S. Neil and S. P. Henry, Gount,; PCT Int. Appl. WO 9414782 (Cl. C 07D 261/08);
17. Inai Masatoshi, Tanaka Akie, Goto Kyoto,; Jpn Kokai Tokkyo Koho JP, 07,215,952 (95, 215, 952) (1995);
18. Nippon Chemiphar Co. Ltd.; Jpn. Kokai Koho JP, 58,46,077 (Cl. CO7A 261/14) (1983);

19. T. Taate, K. Natira and H. Fukhola,; Chem. Pharm. Buld, 1987; 35(9): 37769.
20. D. J. David, D. B. Allon and E. A. Frederick,; Ger. Offen, 1977; 2,723,688 (Cl. A01N 9/28).
21. A.L. Barry; ‘’The antimicrobial succeptibility Test Principal and Practices, Edicted by Illus lea and Fabiger 180, Bio. Abstr, 1976; 64: 25183.