Biospectra : Vol. 10(2), Sept., 2015, pp 111-114
An International Biannual Refereed Journal of Life Sciences

Interdisciplinary Science

ISSN : 0973-7057

Synthesis of some 5-(4-substituted aryl)-4, 5-dihydro-3-(naphtha [2,1-b] furan-2-yl) isoxazole as potential antimicrobial agents

Dhanaji V. Jadhav*
Y. C. Art and Science College, Mangrulpir. 444403 (INDIA)

Received : 11th July, 2015; Revised : 22nd August, 2015

Abstract : A series of new arylisoxazole derivative were prepared by cyclocondentation route of various substituted chalcones in presence of alcoholic solution of potassium hydroxide at reflux temperature. A synthesized isoxazolinewere characterized by means of their IR, 1H NMRdata and elemental analysis. The synthesized isoxazoline derivatives were evaluated for antimicrobial and antifungal activities, some of them were found to possess significant activity.

Keywords : Naphthofuran, Chalcone, arylisoxazolines.

INTRODUCTION

The few natural products are derivatives of naphthalene. Nitrogen, oxygen and sulphur containing heterocyclic compounds have received considerable attention due to their wide range of pharmacological activity. Isoxazole[1] based heterocyclic compounds have occupied unique place in the field of medicinal chemistry. Isoxazole derivative exhibit antibiotic[2-4], antibacterial[5], antitubercular[6], antifungal[7-9], antiinflammatory[10], analgesic[11] activity. Some of them have been used as photosensitizer, supersensitizer[12,13]. Fertility control and pregnancy maintenance[14]. It has been also reported that substituted isoxazolines were active as herbicides and plant growth regulators[15] and the control of phyto-pathogen[16]. The naphthofuran derivatives have been shown to exhibit cytotoxic activity[17], keeping these reports in view and in continuation of our search for more potent naphthofuran derivative[18,21]. The synthetic application, characterization and biological activities of naphthofuran derivatives have been investigated earlier[22-23]. It was though worthwhile to synthesize new derivatives of naphtho[2,1-*b*]furan-2-yl isoxazole by simple method and investigate them for biological activities.

*Corresponding author :
Phone : 08275273020
E-mail : jadhavd68@gmail.com

Experimental

Melting points were determined on an open capillary melting point apparatus and are uncorrected. IR spectra were recorded on Perkin- Elmer spectrophotometer in the range 4000 – 400 cm^{-1} in Nujol mull and KBr pellets, PMR spectra were recorded with TMS an internal standard using $CDCL_3$ and DMSO- d_6 as solvent. All the compounds have been recrystallized from ethanol.

Synthesis of 2-acetyl naphtho[2,1-*b*]furan (1)[21]

A 250ml 4-necked round bottom flask fitted with overhead mechanical stirrer, a dropping funnel, a thermometer and reflux condenser with child water circulation. Flask was charged with 2-hydroxy-1-naphthaldehyde (17.80gm, 0.10mole), chloroacetone 10.75gm, 0.11mole) and anhydrous potassium carbonate (15gm, 0.11mole) were refluxed in dry acetone (75ml). for 12 h. potassium salt were filtered off and the filtrate on removed of solvent and on trituration with ethanol gave the pale yellow crystals of 2-acetyl naphtho[2,1-*b*]furan(1). The sample was purified by absolute ethanol. m.p. 98°C yield 60%.

Typical experimental procedure for synthesis of 1-(naphtho[2,1-*b*]furan-2-yl)-3-*p*-tolylprop-2-en-1-one (2a-f)

Flask was charged with mixture of 2-acetyl naphtho[2,1-*b*]furan (4.20gm,0.02mole)(1) and 2-methyl

benzaldehyde (2.91gm, 0.022mole) it was stirred in ethanol (50ml) and then potassium hydroxide (50%) (10ml) was added portion wise, keeping the temperature below 10^0C throughout the addition. The mixture was kept for 36h. After completion of reaction, reaction mixture was poured in to crushed ice and the solid obtained was filtered under vacuum. It was washed firstly with sodium carbonate solution and then with water, dried and the product was crystallized from ethanol to afford the pure product in 60-70% yield (2b). Same procedure is extended for other compound of the series. The physical and characterization data of the chalcones are shown in TABLE I.

Synthesis of 5-(4-chlorophenyl)-4,5-dihydro-3-(naphtha[2,1-*b*]furan-2-yl) isoxazole (3a-f)

A mixture of 3-(4-chlorophenyl)-1-(naphtho[2,1-*b*]furan-2-yl)prop-2-en-1-one (3.32gm, 0.01mole) (2e)and hydroxylamine hydrochloride 1.39gm, 0.02mole) was dissolved in 15ml ethanol and potassium hydroxide (1.4gm, 0.025mole) was added. The reaction mixture was refluxed for 6 h. After cooling the reaction mixture it was poured in ice cold water with stirring and neutralized carefully with acetic acid. The obtained solid filtered, washed with sodium carbonate solution and then washed with water. The obtained product was recrystallized from absolute alcohol to obtain (3e). Compound (3a-f) were prepared similarly from (2a-f). The physical data of the isoxazole are shown in TABLE I.

TABLE I: Physical and characterization data of the synthesized compound.

Comp.	Mole. Formula	Mole. Weight	M. P.	Yield %	Elements %	
					N	
					Calc	Found
2a	$C_{21}H_{14}O_2$	298	130	62	-	-
2b	$C_{22}H_{16}O_2$	312	153	65	-	-
2c	$C_{21}H_{14}O_3$	314	170	68	-	-
2d	$C_{22}H_{16}O_3$	340	134	70	-	-
2e	$C_{21}H_{13}O_2Cl$	332.7	145	60	-	-
2f	$C_{19}H_{12}O_2S$	304.4	193	69	-	-
3a	$C_{21}H_{14}O_2N$	330.1	129	60	4.47	4.2
3b	$C_{22}H_{16}O_2N$	344.1	122	65	4.26	4.3
3c	$C_{21}H_{14}O_3N$	346	187	61	4.41	4.3
3d	$C_{22}H_{16}O_3N$	372	97	70	4.08	4.1
3e	$C_{21}H_{13}O_2NCl$	364.7	173	68	4.03	4.2
3f	$C_{19}H_{12}O_2SN$	336.4	113	68	4.32	4.4

Purification:

Crude product was dissolve in 10 ml absolute ethanol and heated up to 70^0C to get clear solution and cooled slowly up to 10^0C, filtered, sucked and dried in vacuum to offered pure compound. Under similar condition, a compound of this series has been carried out. Results are summarized in TABLE I. Good to excellent yields and perfect selectivity was obtained in cases.

Spectral discussion:

Compound 2b:

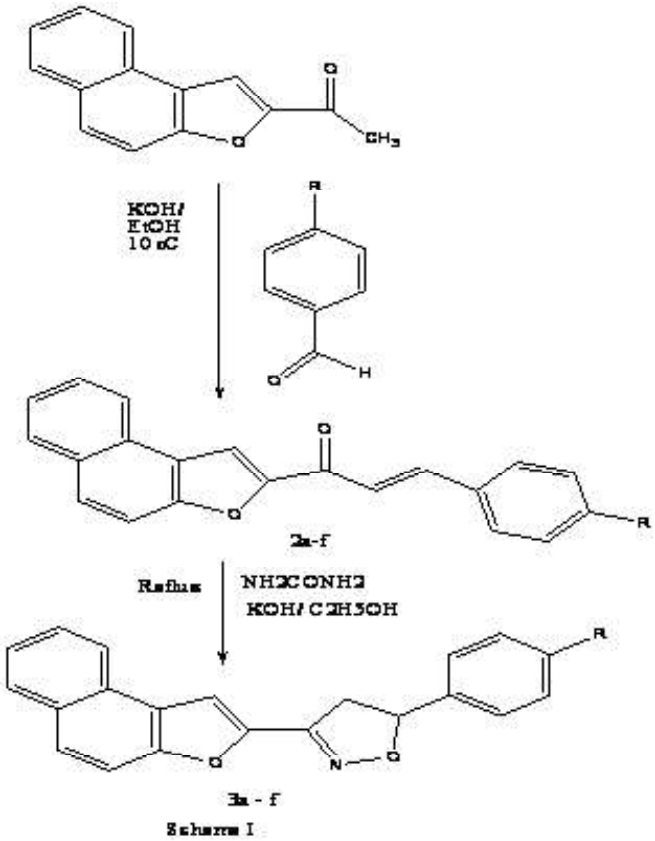
IR: (KBr, t•max, cm^{-1}) 3060 (Ar-CH str.), 2923 and 2854 (-CH_3 str.) 1650 (C=O str. in ketone), 1596 (C=C str.) 1542 (C=C str. in Ar.) 1450 and 1357 (-CH_3 def.) 1141 and 1041 (C-O-C str.) 748 (Ar-H opb).

^{1}H NMR: ($CDCl_3$ in ä ppm): 6.55(d, 1H,CO-CH), 6.85 (d, 1H, C=CH), 7.12- 7.98 (complex m, 11H, Ar-H), 3.11(s, Ar-CH_3).

Compound (3e):

IR: (KBr, t•max, cm^{-1}): 3457 (N-H str.), 3020 (Ar-H str.), 1676 (C=N str.), 1552 (Ar C=C str.) 1453- 1385 (N-O-C str.) 1215 (C-H def.) 757- 669 (Ar-H opd.)

^{1}H NMR: ($CDCl_3$ in ä ppm): 6.93-8.41 (m, 11H, Ar-proton), 6.85 (d, 1H C=CH), 6.37 (d, 1H N-H), 3.11 (d, 2H).



Scheme I

Antimicrobial Activity:

In the present study, filter paper disc diffusion plate method was employed to evaluate the antimicrobial activity[24-25]. The zone of inhibition was compared with standard drug. Results are summarized in Table II. Investigation of antibacterial activity revealed that the compounds (3a-f) showed significant antibacterial activity. The compound (3a), (3b) and (3e) were found to be more potent on the bacterial strains. Compound (3a-f) showed significant antifungal activity.

The results clearly revealed the contribution of electron releasing groups on the aromatic ring in enhancing the microbial activity.

Compound	Antibacterial activity(Zone of inhibition in mm)				Antifungal activity			
	E.coli	S.thypi	S.aureus	E.substillis	A.nigar	P.chrysogenum	F.moneliforme	C.albicuns
3a	10	10	23	14	-ve	+ve	+ve	-ve
3b	11	13	18	13	+ve	-ve	+ve	+ve
3c	9	11	18	12	+ve	+ve	+ve	-ve
3d	8	9	21	15	-ve	+ve	-ve	-ve
3e	12	18	25	21	+ve	+ve	-ve	-ve
3f	8	11	20	17	-ve	-ve	-ve	+ve

CONCLUSION

We believe that these synthesized and characterization compounds of 5-(4-substituted aryl)-4,5-dihydro-3-(naphtha[2,1-*b*]furan-2-yl) isoxazole will help in the modern development of heterocyclic chemistry as antimicrobial activity.

ACKNOWLEDGEMENT

The author thankful to Dr. M. S. Shingare, Dr. R. A. Mane Dr. B. A. M. University, Aurangbad, Dr. N. D. Shinde SCS College, Omerga and Dr. V.Y. Jadhav for providing necessary facility and helpful suggestion.

REFRENCES

1. **Blatt A.H. *J. Amer.*** *Chem. Soc.* **71**, 1861, (1949)
2. **Urbanski T.**, *Gruzlica,* **26,** 889, 1958.
3. **Carradonna C., Stein M.L., and Ikram M.** *Annali Chem.,* 49, 2083 (1959)
4. **Gorg H.G. and Shing P.P.,** *j. Med. Chem.* 13, 1250,(1970)
5. **Okuda T., Kitamura and Azik K.** *Ann. Proc. Gifu Coli. Pharm.* 5, 29 (1955)
6. **Carradona C. and Stain M.L.,** *FarmacoEdn. Sci.,* 15, 647 (1960)
7. **Shingare M.S. and Gavande N. G.** *Ind. J. Chem.* 26B, 351,(1987)
8. **Shingare, Thore and Shinde.** *Oriental J. Chem.* V-II No.2, 135 (1995)
9. **Mittal A,K. and Singhal O.P.** *j.Ind.Chem.Soc.* 59, 711 (1982)
10. Sankyo Co. Ltd. *Chem. Abstr.* 94(3), 103342_h, (1981)
11. **Howe et. al.** *Chem. Abstr.* 99(4) 41311_h (1981)
12. **Brosken Kayeset.** al. *J. Am. Chem. Soc.* 73, 5322 (1951)
13. **Zeno,** *J. Pharma. Soc.Japan.* 73, 595 (1953)
14. Sankyo Co. Ltd. *Chem. Abstr.* 94(3), 30741_g (1981)
15. **Devenport James,** *Chem. Abstr.,* 95(12), 203926 (1981)
16. **Von auwer K. and Muller H.,** *J. Pr. Chem.,* 137, 102 (1933)
17. **Aziz G., Nosseir M.H. et. al.** *Ind. J. Chem. Sect.B.,* 14, 286 (1976)
18. **R.V.Bornnet, P.A.Cage, S.F. Hunt, I.J.Walter, R.P.Austin,** PTC Int. Appl. WO2003024966, *Chem. Abstr.* 138, 271701v (2003)
19. **S.M.Sondhi, N. Shingh, M. Johar, A. Kumar;** Bioorg Med. Chem., 13, 6158 (2005)
20. **S.M.Sondhi, N.R.Goyal, A.M.Lahoti, N. Shingh, R.Shukla, R.Raghubir;** Bioorg Med. Chem., 13, 3185 (2005)
21. **P.Molina, E.aller, A.Lorengo, P.I.Cremadis, I.Rioja, A.Vbeda, M.Terencio, M.Alcaraz;** *J. Med. Chem.,* 44, 1011(2001)
22. **Sanjeevan S Gaikwadet. al.** *Organic Chemistry an Indian Journal.,* 8(7), 241- 244, (2012)
23. **V S Suryawanshi et. al.** *E- Journal of Chemistry.,* 9(1), 175- 180, (2012)
24. **Bunty A L,** Antimicrobial susceptibility test; Principal and practice; Edited by Illus, Lea and Febirg, Philadelphia, PA; USA, 180, (1976).
25. **Saundane A R, Rudresh K, Satyanarayan N D and Hiremath S P;** *Indian J Pharm. Sci.,* 60(6), 379- 383, (1998).

* * *