"GREEN SYNTHESIS AND ANTIFUNGAL ACTIVITY OF BENZAOXAZOLE DERIVATIVES"

P.R. Padole[1], H. G. Wankhade[1], B.N.Berad[1] and S.S. Ubarhande[2]
[1]Shri Shivaji Science College, Amravati
[2,]G.S.Tompe Arts, Commerce and Science College, Chandur Bazar.

ABSTRACT

Various 2-Substituted Benzaoxazoles derivatives in moderate to good yield have been prepared in a one-pot reaction by condensation of 2-aminophenol and different aromatic acids in the present of ammonium chloride as a catalyst and ethanol as solvent 80^0-90^0C. The reaction is green and economically viable. The characterization of newly synthesized compounds was made by chemical properties and FT-IR,^{1}H-NMR and Mass Spectra. The advantage of this method is extremely mild reaction conditions, short reaction time, high yield, simple experimental technique and compliance with green chemistry protocols. A comparative antifungal study has also been carried out on the fungus *Fusariumudum.*

Key words- 2 amonophenol, Aldehyde, benzimidazole, catalyst, Green chemistry and antimicrobial acivity.

1.INTRODUCTION-

Five- membered aromatic heterocyclic rings containing a C=N bond, such as benzoxazole, benzimidazole, and benzothiazole are important structural units in natural products, and in synthetic pharmaceutical and agrochemical compounds[1,2]. These compounds received a considerable amount of attention for their biological and therapeutic activities[3,4]. Recently, a survey showed that only 5% of all reactions achieved in the process research groups of three major pharmaceutical companies involve construction of a heteroaromatic rings.[5] Therefore, the development of new methods for the synthesis of nitrogen-containing heterocycles is still a focus of intense and containing interest in the organic chemistry, as well as in pharmaceutical and agrochemical chemistry.Molecules with benzoxazole, benzimidazole and benzothiazole moieties are attractive targets for synthesis since they often exhibit diverse and important biological properties. These heterocycles have shown different pharmacological activities such as antibiotic [6], antifungal [7], antiviral [8], anticancer [9], antimicrobial [10], and antiparkinson[11]properties.Number of methods for the synthesis of 2- substituted benzoxazoles. Majority of them were obtained by the classical methods by using the different catalyst.Mohammadpoor-Baltork et al., [14]described an efficient method for the preparation of benzoxazoles, from reactions of orthoesters with *o*-substituted aminoaromatics and in the presence of silica sulfuric acid under heterogeneous and solvent-free conditions.In this connection we are reporting the synthesis of some 2-substituted benzoxazole by using 2-aminophenol and different aromatic aldehydes by using the new green route.

2.EXPERIMENTAL

The melting points of all synthesized compound were recorded using hot paraffin bath and are uncorrected. ^{1}H NMR spectra ($CDCl_3$) were recorded on Bruker Advance II 400 NMR spectrophotometer using TMS as internal standard. IR spectra were recorded on Perkin-Elmer-1800 FTIR spectrophotometer in the frequency range 4000-450 cm^{-1} in Nujol mull and as KBr pellets. Mass spectra were recorded on a LC-MS Q-Tof Micro, Mass analyzer (Shimadzu). Chemicals used were of AR grade. The purity of the compound was checked on silica gel-G plates by TLC.

2.1. Preparation of 2-Phenyl -2,3- dihydrobenzo [d] oxazole – (la)

Preparation of 2-Phenyl -2,3- dihydrobenzo [d] oxazole was carried out by the reaction of 2-amino phenol (1.09gm) and benzaldehyde in 5 ml of ethanol. NH_4Cl (0.5gm) was added to the mixture as a catalyst. The resulting mixture was stirred for 6-8 hrs at 80^0c. The completion of the reaction was confirmed by reaction mixture poured in to ice cold water and product was precipitate out. It was crystallized from ethanol to yield 2- phenyl -2,3- dihydrobenza [d] oxazol, (1a) m.p. 180^0c. The molecular formula was established as $C_{13}H_{11}NO$ (Colour-Brown)

2.2. Preparation of 2-(4-methoxy phenyl)-2,3 dihydrobenzo [d] oxazol (1a)

Preparation of 2-Phenyl -2,3- dihydrobenzo [d] oxazole was carried out by the reaction of 2-amino phenol (1.09gm) and anisaldehyde in 5 ml of ethanol. NH_4Cl (0.5gm) was added to the mixture as a catalyst. The resulting mixture was stirred for 6-8 hrs at 80^0c. The completion of the reaction was confirmed by reaction mixture poured in to ice cold water and product was precipitate out. It was crystallized from ethanol to yield 2- phenyl -2,3- dihydrobenza [d] oxazol, (1a) m.p. 75^0c. The molecular formula was established as $C_{14}H_{13}NO_2$ (Colour-Brown).All other compounds (3c-e) were synthesized in similar manner by treatment of (1) with substituted aromatic aldehyde (2c- e) respectively Table No. 1

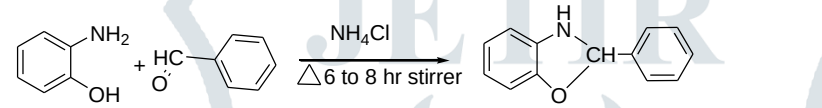
Table No.1.

Table No.1

Reaction of 2amoniphenol (1) (0.01 mole) with different aromatic aldehyde. (2) (0.01 mole) :

Sr. No	**Product (3)**	**-R (2a-e)**	**Yield (%)**	**Melting Point^{0}C**	**Molecular Formula**
1	3a	benzaldehyde	70.88	140	$C_{13}H_{11}No.$
2	3b	anisaldehyde	80.00	70	$C_{14}H_{13}NO$
3	3c	salicylaldehyde	65.33	164	$C_{13}H_{11}NO_2$
4	3d	5-chloro salicylaldehyde	76.12	160	$C_{13}H_{10}ClNO_2$
5	3e	vanillin	80.23	100	$C_{14}H_{13}NO_2.$

Reaction scheme:-



2-aminophenol benzaldehyde 2-phenyl 2,3 dihydrobenzoxazole

3.RESULT DISCUSSION

In order to synthesized substituted Benzaoxazoles derivatives (3), a relatively more versatile yet simplified procedure was perceived. Our argument have been that an instantaneous condensation of 2- aminophenol and aromatic aldehyde at 80- 90 ^oC to affords substituted Benzaoxazoles with the use of NH_4Cl as catalyst. The strategy worked well affording the desired product in respectable yields. The present reaction have been relatively faster, as anticipated, comp aired to those in conventional solution phase synthesis. It is necessary to mention that in all cases the conversion was never 100 %. Some amount of starting material recovered after each reaction. The compound 3a-3e were assayed for their antifungal activities adainst the test *Fusarium udumat 26* ± *2* ^OC by poisoned food technique. Potato dextrose agar (PDA) was used as a basal medium to evaluate the efficiency of these synthesized products. A chemical fungicide, Mancozed was used as a slandered for this process. Compound 3 showed comparable activity (72% inhibition) and compound (3) showed highest activity (80 .85 and 87 % respectively) than that (73%) of the standard.

4.AKNOLEGEMENT

Authors are thanks full to ***Dr.V.G. Thakare*** , Principal Shri Shivaji Science College, Amravati for providing all necessary facilities to research works and also thanks fully to Director, R.S.I.C.(SAIF), Punjab University, Chandigarh for providing IR, NMR & Mass spectra.

5.REFERENCE

1. McKee, M. L.; Kerwin, S. M. Bioorg. Med. Chem. 2008, 16, 1775.
2. Mortimer, C. G.; Wells, G.; Crochard, J. P.; Stone, E. L.; Bradshaw, T. D.; Stevens, F. G.; Westwell, A. D. J. Med. Chem. 2006, 49, 179.
3. Grobler, J. A.; Dornadula, G.; Rice, M. R.; Simcoe, A. L.; Hazuda, D. J.; Miller, M. J. Biol. Chem. 2007, 282, 8005.
4. Rasmussen, K.; Hsu, M. A.; Yang, Y. Neuropsychopharmacology. 2007, 32, 786.
5. Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. Org. Biomol. Chem. 2006, 4, 2337.
6. Evans, D.A.; Sacks, C.E.; Kleshick, W.A.; Taber, T.R. *J.Am.Chem.Soc*. **1979**, 101, 6789-6791.
7. Yamato, M. *J. Pharm. Soc. Jpn*. **1992**, 112, 81-99.
8. Song, X.; Vig, B.S.; Lorenzi, P.L.; Darch, J.C.; Townsend, L.B.; Amidon, G.L. *J.Med. Chem*.**2005**, 48, 1274-1277.
9. Kumar, D.; Jacob, M.R.; Reynolds, M.B.; Kerwin, S.M. *Bioorg. Med. Chem*. **2002**, 10, 3997-4004.
10. Yildiz-Oren, I.; Yalcin, I.; Aki-Sener, E.; Ucarturk, N. *Eur. J. Med. Chem*. **2004**, 39, 291-29.
11. Scott, L.J.; Dunn, C.J.; Mallarkey, G.; Sharpe, M. *Drugs***2002**, 62, 1503-1538.
12. Padalkar, V. S.; Gupta, V. D.; Phatangare, K. R.; Patil, V. S.; Umape, P. G.; Sekar, N. *Green Chemistry Letters and Reviews*. **2012**, 5 (2), 139-145