Research Paper www.ijcps.com

International Journal of
Chemical and Pharmaceutical Sciences
2012, Dec., Vol. 3 (4)

ISSN: 0976-9390
IJCPS

One step synthesis, characterization and anti-fungal activity of benzoxazole against candida albicans

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ABSTRACT

Benzoxazole is a well known compound synthesised from ortho amino phenol. A convenient one-step method for the preparation of benzoxazole is described. Ortho amino phenol reacts with formic acid in the presence of boric acid as a catalyst and ethanol as a solvent. As per the thin layer chromatography (TLC) report the compound was seperated by column chromatography and characterised by Infrared and Nuclear Magnetic Resonance Spectroscopy . The antifungal activity of the synthesized compound was screened by cup and plate method against candida albicans.

Key words: Benzoxazole, Column chromatography, Infrared spectroscopy, Antifungal activity.

1. INTRODUCTION

Benzoxazole is a heterocyclic organic compound that has benzene fused with oxazole ring containing one oxygen atom and one nitrogen atom. It is a clear to yellowish low melting solid, insoluble in water. Benzoxazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures. It is found with in the chemical structures of pharmaceutical drugs such as flunoxaprofen. Its aromaticity makes it relatively stable, although as a heterocycle, it has reactive sites which allow for functionalization. The main objective of the synthetic chemistry and medicinal chemistry is to synthesize the compounds that give more yield with purity and show promising activity as therapeutic agents with lower toxicity. Benzoxazole is a very useful compound to synthesise the various medicinal compound and its derivatives are very useful compound with well known biological activity such as antibacterial, antifungal, antifungal, analgesic, anti-inflammatory and antitubercular.

2. Experimental procedure

2.1. Chemicals and Solvents

Chemicals; Ortho amino phenol was used from SD Fine, formic acid, iodine and boric acid were used from Nice. Solvents; Ethanol was used from Brampton, methanol was used from SRL, ethyl acetate and petroleum ether were used from Spectrochem.

2.2. Instrumentation

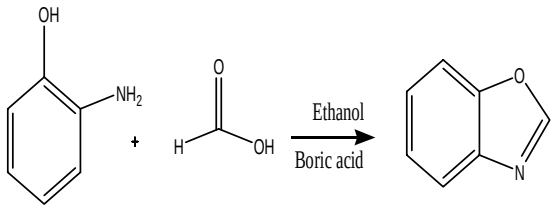
Magnetic stirrer was used from REMI. Melting points were recorded on BMQR 796 series digital melting point apparatus. Thin layer chromatography analyses were carried out on 5x20 cm aluminium foiled silicagel coated plates from MERCK using an ethyl acetate and petroleum ether mixture (1:3) as solvent. Infrared spectroscopy were recorded by using KBr pellets on Perkin Elmer and NMR spectroscopy were recorded by using ^{1}H(300MHZ), ^{13}C(75MHZ) on Bruker MSL Spectrometer.

2.3. Synthesis

2.3.1. Procedure

5 Mmole of ortho amino phenol and 5 Mmole of formic acid was added with 60 ml of ethanol and mixed well by using magnetic stirrer for half an hour. The reaction mixture was added with 1 Mmole of boric acid and reflux for 37 hours at 80^{o}c.

Figure – 1: Sheme-I



O-AMINO PHENOL FORMIC ACID BENZOXAZOLE

2.3.2. Recrystalization

The solvent (ethanol) was separated out from the reaction mixture by rota evaporator and dried well. The powdered reaction mixture was added with 30 ml of distilled water and poured into the separating funnel and shake well for 5 minutes and added 50 ml of ethyl acetate and

shake well for 5 minutes. The water layer was separated out and added saturated sodium chloride solution shaked well and the sodium chloride layer was separated out. The ethyl acetate reaction mixture was added with small amount of sodium sulphate and thin layer chromatography (TLC) was carried out in the mixture of petroleum ether and ethyl acetate in the 3:7 ratio.

2.3.3. Column Chromatography

Silicagel was used as a stationary phase (150-200 mesh) and ethyl acetate with petroleum ether mixture was a mobile phase. Size of the column was 50 cm. Size of the stationary phase n column was 25 cm. Size of the reaction mixture was 1.5 cm. Breadth of the column was 1.5 cm. Mobile phase ratio was 3:7 of ethyl acetate and petroleum ether mixture. Rf value of the compound was 0.69.

2.4. Characterization

2.4.1. IR

The m.p 30^0 c , light yellow solid, TLC rf - 0.65, yield 90%, IR (KBR pellet) in cm-1: 3098 (Ar C-H stretching), 1454,1537,1592 (C=C stretching), 1661(C=N stretching), 746(C-H out of plane pending).

2.4. 2. ^{1}H-NMR

(CDCl3) δ-7.25(4H, Ar), 7.92(1H, Ar).

2.4.3. ^{13}C-NMR

(CDCl3) δ-141(Ar,C1), 119(Ar,C2), 124.7(Ar,C3), 123.2(Ar,C4), 110.2(Ar,C5), 150.3(Ar,C6), 153.1(Ar,C7).

2.5. Antifungal activity

2.5.1. Cup and Plate method procedure

2.5.1.1. Preparation of muller-hinton agar

Beef extract-300gm, peptone-17.5gm, starch-1.5gm, agar-17gm, cold distilled water-1000ml. All the ingredients were weighed and suspended in 1000ml of cold distilled water and heated to boiling. The pH of the media was adjusted to 7.4 5M sodium hydroxide solution. Then 5-20ml of this agar medium was transferred into boiling tube and plugged with non-absorbent cotton. The tube containing agar medium was sterilized by pressur controlled heat sterilizations technique use an autoclave at 15lbs at 121^0 c for 20 minutes. After that the agar medium was melted, cooled and inoculated with fungus such as Candida albicans and poured into sterile petri dish to get uniform thickness 5-6mm. Cups were made out in the other plate using sterile cork borer(6dm). Then the cups were charged with appropriate concentration of the standard such as ketoconazole (100µg/ml) likewise the cups were also charged with the series of newly synthesized benzoxazole 50µg/ml, 100µg/ml and incubated at 37^0 c for 24 hours. The diameter of zone of inhibition around the cups were measured and tabulated in the following table 1.

Table-1: Diameter of zone of inhibition

Compound code	Zone of inhibition (mm) Organism- Candida albicans
BO 1(50µg/ml)	21
BO 1(100µg/ml)	23
Ketoconazole (standard)	25
Ethanol (control)	15

3. Result and Discussion

The benzoxazole was synthesized by one pot reaction involving of ortho amino phenol with formic acid in the presence of boric acid as a catalyst and ethanol as a solvent. Synthesized benzoxazole were recrystalized by water and ethyl acetate mixture. The pure compound was separated by column chromatography as per the thin layer chromatography (TLC) report. The purity of the newly synthesized benzoxazole were confirmed by melting point (uncorrected) and tlc.

The chemical structure was confirmed by Infrared and NMR Spectroscopy. The aromatic stretching (Ar-H) was confirmed by the peak at the range of 3080-3100 cm-1. The C=C ring stretching was confirmed by the peak at the range of 1450-1600 cm-1. The C=N ring stretching was confirmed by the peak at 1661 cm-1.

The aromatic peak was confirmed at 7.25 ppm and Oxazole ring proton was confirmed at 7.92 ppm. The sixth carbon peak of the fused ring was confirmed at 150.3 ppm, the seventh carbon peak was confirmed at 153.1ppm.

The newly synthesized benzoxazole were found to active against candida albicans. The zone of inhibition at the concentrations of 50µg/ml was found at 21mm and 100µg/ml was found at 23mm as compared with standard (ketoconazole) 100µg/ml was found at 25mm.

4. CONCLUSION

The simple and one pot method for the synthesis of benzoxazole. The compound were successfully synthesized and purified by recrystalization method and the compound was separated by column chromatography. The chemical structure of the compound was

confirmed by infrared spectroscopy. The *in vitro* antifungal activity of the newly synthesized benzoxazole shows good activity measured by cup and plate method against Candida albicans.

5. REFERENCES

1. Wang Y, Sarris K, Sauuer DR and Djuri SW. Tetrahedron Lett., 2006; 47: 4823-4826.
2. Sum PE, How D, Torres N, Newman H, Petersen PJ and Mansour TS. Bioorg. Med., Chem. Lett. 13, 2607-2610.
3. Misra RS, Barthwal JP, Parmar SS and Brumleve SJ, J. Pharm. Sci., 2006; 63: 401-404.
4. Koyama E, Yang G, Tsuzuki S and Hiratani K. Eur. J. Org. Chem., 2002; 1996-2006.
5. Giorgioni G and Accorroni B. Med. Chem. Res, 2005; 14, 57-73.
6. Oksuzoglu E and Arpaci OT. Med. Chem. Res, 2008; 16, 1-14.
7. Jauhari PK, Bhavani A and Varalwar S. Med. Chem. Res, 2008; 17: 412-424.
8. Arpaci OT and Yildiz I, Eur. J. Med. Chem., 2008; 7: 1423-1431.
9. Gao M and Wang M. Eur. J. Med. Chem., 2008; 53: 1570-1574.
10. Combrink KD and Gulgeze HB. Bioorg. Med. Chem. Lett., 2007; 17: 4784-4790.
11. Huang S and Hsei I. Bioorg. Med. Chem., 2006; 14: 6106-6119.
12. Sondhi SM, Singh N, Kumar A, Lazach O and Meijer L. Bioorg. Med. Chem., 2006; 14, 3758-3765.
13. Medebielle M, Mohand S, Burkhloder C, Dolbier WR, laumand G and Aubertin AM., J. Flu. Chem., 2005; 126, 533-540.
14. Sum P, How D, Torres N, Newman H, Petersen PJ and Mansour TS. Bioorg. Med. Chem. Lett. 13: 2607- 2610.
15. Tudanca PLL, Labeaga L, Innerarity A. Cires LA, Tapia I, Mosquera R and Orjales A. Bioorg. Med. Chem., 2003; 11: 2709-2714.
16. Paramashivappa R, phanikumar P, Subba rao PV and Srinivasa rao A. Bioorg. Med. Chem. Lett., 2003; 13: 657- 660.