RACPS-2022
Online National Conference on Recent Advances in Chemical and Physical Sciences
In Association with International Journal of Scientific Research in Science and Technology
Volume 9 | Issue 17 | Print ISSN: 2395-6011 | Online ISSN: 2395-602X (www.ijsrst.com)

Evaluation of Antimicrobial Activity of 4-(Benzo[D]Thiazol-2-Yl) Phenol and Its Derivatives

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ABSTRACT

The synthesis of 4-(benzo[d]thiazol-2-yl)phenol**(3) (Scheme-1)**by reaction of 2-aminobenzenethiol**(1)**and 4-hydroxybenzaldehyde**(2)**reflux in presence of toluene as a solvent. This reaction mixture is kept for overnight, the crystals of 4-(benzo[d]thiazol-2-yl)**(3)**obtained. Filtered and dried.As well as synthesis of 4-(benzo[d]thiazol-2-yl)-2-methoxyphenol**(5) (Scheme-2)** by reaction of 2-aminobenzenethiol**(1)**and4-hydroxy-3-methoxybenzaldehyde**(4)**reflux with toluene as a solvent. This reaction mixture is kept for overnight, the crystals of 4-(benzo[d]thiazol-2-yl)-2-methoxyphenol**(5)**obtained. Filtered and dried.

The structures for the synthesized compounds are assigned on the basis of IR, [1]HNMR and Mass spectral studies.

KEYWORDS: 2-amino benzenethiol, 4-hydroxybenzaldehyde, 4-(benzo[d]thiazol-2-yl), toluene, 4-hydroxy-3-methoxybenzaldehyde, 4-(benzo[d]thiazol-2-yl)-2-methoxyphenol

I. INTRODUCTION

The resistance of pathogenic bacteria and fungi to available antibiotic drugs has been posing a challenge to chemists and pharmacists. An interest in the design and development of new active antimicrobial agents can be ascribed to both the increasing emergency of bacterial resistance to antibiotic therapy and newly emerging pathogens[1,2]. Recently, the discovery of new compounds to deal with resistant bacteria and fungi has become one of the most important areas of antibacterial and antifungal research. The heterocyclic scaffold, benzothiazole is a privileged system with multiple applications. A number of 2-aminobenzothiazoles were intensively developed in the 1950s as central muscle relaxants. Riluzole(1) (6-trifluoromethoxy-2-benzothiazoleamine, PK-26124,RP-25279) acts as a glutamate neurotransmission agent in biochemical, electrophysiological and behavioral experiments[3]. Research has been carried out recently on benzothiazole derivatives which are found to possess diverse chemical reactivity and wide spectrum of biological activities. The benzothiazole pharmacophore unit is found in several drugs which exhibit antimicrobial[4], antitumor[5], antioxidant behaviors[6] and as an acetyl cholinesterase[7] enzyme inhibitor. It is well documented that the unique frame work of benzothiazole is found in many antagonists like Ca+2 channel, LTD4 and orexin receptors[8]. By bearing in mind the aforesaid pharmacological applications of benzothiazole derivatives, our

group has synthesized recently 3-(2-(benzo[d]thiazol-2-yl)phenoxy)-1-(substituted acyclic/cyclic amino)propan-1-one derivatives and found them to be potent antimicrobial agents[9]. The chemistry of organophosphorus compounds has been growing rapidly since these molecules are involved in various biological processes, such as important substrates in the drug and pro-drugs synthesis. The phosphorus molecules play a vital role in medicinal and agricultural chemistry[10]. They also offer attractive possibilities for structural, synthetic and mechanistic studies[11]. Particularly, phosphoramidates have attained a distinctive reputation in P-chemistry since they act as pro-drugs and drugs in the antiviral and antitumor therapy[12]. The cyclic phosphorus derivative, cyclophosphamide is a pro-drug and it has been used in anticancer therapy[13]. The phosphoramidates in which the phosphate group is bonded with acyclic/cyclic/aryl amines or amino acid residues could develop lipophileicity[14] and as a result enriches their bioavailability and biological potency. These groups can also modify the physicochemical properties of active benzothiazole motif. The phosphoramidate derivatives of 5-nitroquinolin-8-ol and 5-nitroindazole synthesized recently by our group showed potential antimicrobial and antioxidant activities[15] and these results encouraged us to study the synthesis of title compounds and evaluate their bioactivity.

II. EXPERIMENTAL SECTION

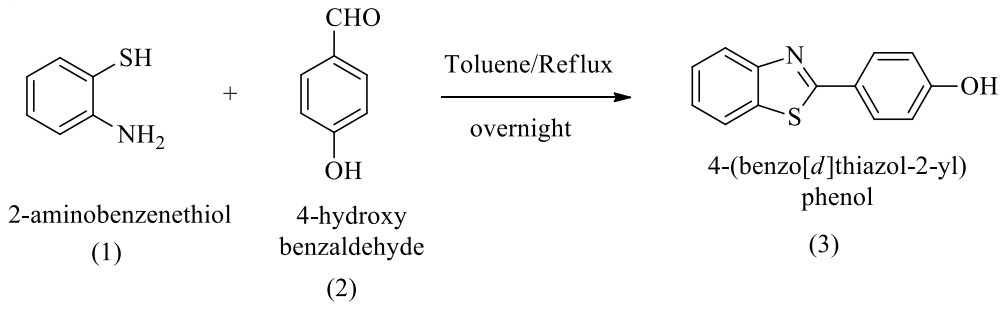
All melting points were determined in open capillary tube and were uncorrected. IR spectra were recorded with potassium bromide pellets technique, ^{1}H NMR spectra were recorded on AVANCE 300 MHz Spectrometer in DMSO using TMS as internal standard. Mass spectra were recorded on a FT VG-7070 H Mass Spectrometer using EI technique at 70 eV. All the reactions were monitored by thin layer chromatography.

III. MATERIAL AND METHODS

1. Synthesis of 4-(benzo[d]thiazol-2-yl)phenol :

In the present work, we report synthesis of 4-(benzo[d]thiazol-2-yl)phenol**(3) (Scheme-1)** by reaction of 2-amino benzenethiol**(1)** and 4-hydroxybenzaldehyde**(2)** reflux in presence of toluene as a solvent. This reaction mixture is kept for overnight, the crystals of 4-(benzo[d]thiazol-2-yl) phenol**(3)**obtained. Filtered and dried. The Purity of compound was checked by TLC. The compound observed on TLC as single spot in benzene. Structures to these compounds are assigned on the basis of elemental analysis and spectral data.

Scheme 1



2-aminobenzenethiol (1)

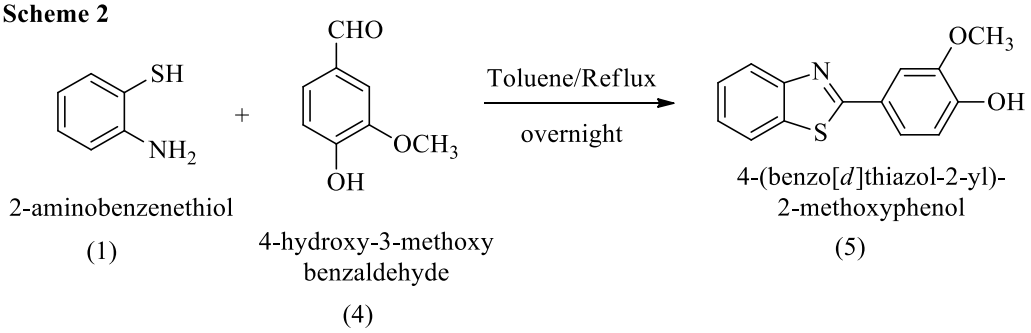
4-hydroxy benzaldehyde (2)

4-(benzo[*d*]thiazol-2-yl) phenol (3)

2. Synthesis of 4-(benzo[d]thiazol-2-yl)-2-methoxy phenol :

In the present work, we report synthesis of 4-(benzo[d]thiazol-2-yl)-2-methoxyphenol**(5) (Scheme-2)** by reaction of 2-aminobenzenethiol**(1)** and 4-hydroxy-3-methoxybenzaldehyde**(4)**reflux with toluene as a solvent. This reaction mixture is kept for overnight, the crystals of 4-(benzo[d]thiazol-2-yl)-2-methoxyphenol**(5)**obtained. Filtered and dried. The Purity of compound was checked by TLC. The compound observed on TLC as single spot in benzene. Structures to these compounds are assigned on the basis of elemental analysis and spectral data.

Scheme 2



2-aminobenzenethiol (1)

4-hydroxy-3-methoxy benzaldehyde (4)

4-(benzo[*d*]thiazol-2-yl)-2-methoxyphenol (5)

Chemical analysis :

1. 4-(benzo[d]thiazol-2-yl) phenol (3)

IR:(KBr/cm^{-1}) :3410 (-OH), 1621 (C=N), 1610-1590 (C=C), 780 (C-S),EI-MS: (m/z:RA%) :228 (M+1), **Elemental analysis:**$C_{13}H_9NOS$ Calculated: (%) C, 68.70; H, 3.99; N, 6.16; O, 7.04; S, 14.11 Found (%) : C, 68.68; H, 3.95; N, 6.10; O, 7.01; S, 14.08

2. 4-(benzo[d]thiazol-2-yl)-2-methoxy phenol (5)

IR:(KBr/cm^{-1}) :3405 (-OH), 1620 (C=N), 1615-1595 (C=C), 784 (C-S),EI-MS: (m/z:RA%) :258 (M+1), **Elemental analysis:**$C_{14}H_{11}NO_2S$ Calculated: (%) C, 65.35; H, 4.31; N, 5.44; O, 12.44; S, 12.46 Found (%) : C, 65.30; H, 4.30; N, 5.42; O, 12.42; S, 12.41

IV. RESULTS AND DISCUSSION

Substituted benzothiazoles exert adverse effects on viruses and also act on yeasts and fungi. The antiviral screening results of MBT showed significant activity against two out of three viruses tested. The antifungal effects of MBT were also tested against *Aspergillus niger*with a suspension of spore-free mycelium homogenate as inoculum, and a 33 mg L–1 MBT concentration was the lower limit for 100% growth inhibition after five days of cultivation. Similar results, although obtained under other conditions, are described for the fungus *Trichophyton rubrum*. It was observed that for complete growth inhibition of *Microsporumgypseum*and *Epidermophyton floccosum,* MBT concentration had to exceed 50 mg L–1. The results of a study suggested that the thiol group of MBT is essential for its toxicity, since benzothiazole (BT)

was not an active fungicide. However, in another experiment the presence of zinc destroyed the fungicidal activity of MBT, and this contradicts what was suggested above.

The antifungal activity of 4-(benzo[d]thiazol-2-yl) phenol, a significant inhibitory activity against *Aspergillus niger*, *Penicillium roquefortl,* and *Chaetomium globosum* was observed. On the other hand, 4-(benzo[d]thiazol-2-yl)-2-methoxy phenol exhibited potent inhibitory activity against *Aspergillus niger*and *Chaetomium globosum*.

V. CONCLUSION

Substituted benzothiazoles have been widely explored for industrial applications since their discovery. However, the biological activity of this class of compounds deserves further investigation. This becomes clear when microbial infections are considered. Although the research on this subject is incipient, the number of reports disclosing the effects of MBTs on pathogens of clinical interest has recently been increasing. Substituted 4-(benzo[d]thiazol-2-yl)phenolhave been shown to be promising, which calls for the design of more efficient antimicrobial, anthelmintic, anti-inflammatory, and anti-allergic agents. Future studies will undoubtedly uncover unexpected properties and applications. Advances in this field will require analyses of the structure-activity relationships of MBTs, as well as the mechanisms of action of these compounds.

ACKNOWLEDGEMENTS

The authors are thankful to the Principal, Degloor College, Degloor for providing laboratory facilities and the Director, Indian Institute of Chemical Technology, Hyderabad for providing spectra.

VI. REFERENCES

[1]. Cohen, M. L. Nature. 2000, 406, 762-767. doi:10.1038/35021206.

[2]. Barrett, C. T.; Barrett, J. F. Curr. Opin. Biotechnol. 2003, 14, 621-626. doi:10.1016/j.copbio.2003.10.003.

[3]. (a) Zarate, Jr, C. A.; Payne, J. L.; Quiroz, J.; Sporn, J.; Denicoff, K. K.; Luckenbaugh, D.; Charney, D. S.; Manji, H. K. Am. J. Psychiatry. 2004, 161, 171-174; (b) Coric, V.; Taskiran, S.; Pittenger, C.; Wasylink, S.; Mathalon, D. H.; Valentine, G.; Saksa, J.; Wu, Y. T.; Gueorguieva, R.; Sanacora, G.; Malison, R. T.; Krystal, J. H. Biol. Psychiatry. 2005, 58, 424-428; (c) Mathew, S. J.; Amiel, J. M.; Coplan, J. D.; Fitterling, H. A.; Sackeim, H. A.; Gorman, J. M. Am. J. Psychiatry. 2005, 162, 2379- 2381.

[4]. (a) Palmer, P. J.; Trigg, R. B.; Warrington, J. V. J. Med. Chem. 1971, 14248-251.

[5]. (a) Hall, I. H.; Peaty, N. J.; Henry, J. R.; Easmon, J.; Heinisch, G.; Purstinger, G. Arch. Pharm. (Weinheim). 1999, 332, 115-123; (b) Bénéteau, V.; Besson, T.; Guillard, J.; Léonce, S.; Pfeiffer, B. Eur. J. Med. Chem. 1999, 34, 1053-1060; (c) Hutchinson, I.; Bradshaw, T. D.; Stevens, M. F. G.; Westwell, A. D. Bioorg. Med. Chem. Lett. 2003, 13, 471-474.

[6]. (a) Ivanov, S. K.; Yuritsyn, V. S. Neftekhimiya. 1971, 11, 99-107; (b) Ivanov, S. K.; Yuritsyn, V. S. Chem. Abstr. 1971, 74, 124487m.

[7]. Nagel, A. A.; Liston, D. R.; Jung, S.; Maher, M.; Vincent, L. A.; Chapin, D.; Chen, Y. L.; Hubbard, S.; Ives, J. L.; Jones, S. B. J. Med. Chem. 1995, 38, 1084-1089.

[8]. (a) Kashiyama, E.; Hutchinson, I.; Chua, M. S.; Stinson, S. F.; Phillips, L. R.; Kaur, G.; Sausville, E. A.; Bradshaw, T. D.; Westwell, A. D.; Stevens, M. F. G. J. Med. Chem. 1999, 42, 4172-4184; (b) Lau, C. K.; Dufresne, C.; Gareau, Y.; Zamboni, R.; Labelle, M.; Young, R. N.; Metters, K. M.; Rochette, C.; Sawyer, N.; Slipetz, D. M.; Charette, L.; Jones, T.; McAuliffe, M.; McFarlane, C.; Ford-Hutchinson, A. W. Bioorg. Med. Chem. 1995, 5, 1615-1620.

[9]. Sreedhar, B.; Veera Reddy, T.; Naga Raju, C.; Padmavathi, V.; Vidya Sagar Reddy, G. Der Pharma Chemica. 2015, 7, 42-47.

[10].(a) Engel, R. Chem. Rev. 1977, 77, 349-367; (b) Hiratake, J.; Oda, J. Biosci. Biotechnol. Biochem. 1997, 61, 211-218; (c) Schug, K. A.; Lindner, W. Chem. Rev. 2005, 105, 67-114.

[11].(a) Hartly, R. The Chemistry of Organophosphorous Compounds; John Wiley and Sons: New York, USA, 1996; (b) Corbridge, D. E. C. (Ed.). Phosphorous; Elsevier: New York, USA, 1990. [12] (a) Congiatu, C.; McGuigan, C.; Jiang,W. G.; Davies, G.; Mason, M. D. Nucleosides Nucleotides Nucl.Acids. 2005, 24, 485-489; (b) McGuigan, C.; Cahard, D.; Sheeka, H. M.; De Clercq, E.; Balzarini, J. J. Med. Chem. 1996, 39, 1748-1753; (c) McGuigan, C.; Harris, S. A.; Daluge, S. M.; Gudmundsson, K. S.; McLean, E. W.; Burnette, T. C.; Marr, H.; Hazen, R.; Condreay, L. D.; Johnson, L.; De Clercq, E.; Balzarini, J. J. Med. Chem. 2005, 48, 3504-3515; (d) Perrone, P.; Luoni, G. M.; Kelleher, M. R.; Daverio, F.; Angell, A.; Mulready, S.; Congiatu, C.; Rajyaguru, S.; Martin, J. A.; Le Pogam, S.; Najera, I.; Klumpp, K.; Smith, D. B.; McGuigan, C. J. Med. Chem. 2007, 50, 1840-1849.

[12].(a) Dirven, H. A. A. M.; Van Ommen, B.; Van Bladeren, P. J. Chem. Res. Toxicol. 1996, 9, 351-360; (b) Niculescu-Duvaz, I.; Spooner, R.; Marais, R.; Springer, C. J. Bioconjugate Chem. 1998, 9, 4-22.

[13].Zemlicka, J. Biochim. Biophys. Acta. 2002, 1587, 276-286.

[14].Munichandra Reddy, S.; Subba Rao, D.; Sudhamani, H.; Gnana Kumari, P.; Naga Raju, C. Phosphorus, Sulfur Silicon Relat. Elem. 2015, 190, 2005-2012.