Synthesis and Pharmacological Assessment of Benzothiazole

Dr. Alka Pradhan[1], Harshita Goyal[2], Nazish Khan[3]
Department of Chemistry
[1, 2, 3] Govt. Motilal Vigyan Mahavidyalaya , Bhopal

Abstract- *Benzothiazole is a class of heterocyclic compound having two hetero atoms namely sulphur and nitrogen. It is a two membered ring heterocyclic moiety, weak base. The analogues of benzothiazole and its derivatives have a significant role in research area especially in synthetic, medicinal and pharmaceutical chemistry because of its biological and pharmacological properties. So in present, the researchers are interested to work in this field. The small and simple benzothiazole nucleus possesses numerous pharmacological activities like- antitumor, antimicrobial, anti-inflammatory, anticonvulsant, and antidiabetic activities since, a wide range of methods are available for synthesizing benzothiazole nucleus and its derivatives but a real need exists for new procedures that support many kinds of structural diversity and various substitution. The present review deals with the common methods adopted and reported to focus the synthesis as well as cyclisation of benzothiazole nucleus.*

Keywords- Benzothiazole, Cyclization

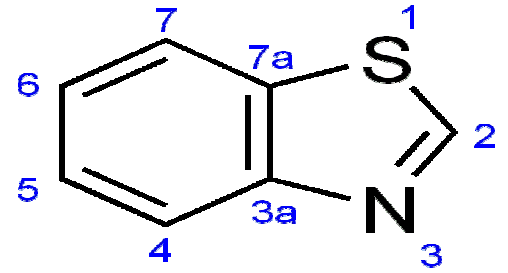
I. INTRODUCTION

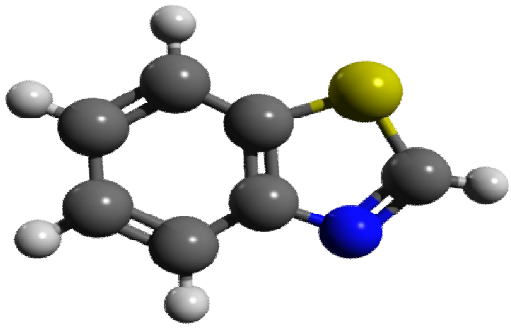
Benzothiazoles and several of their derivatives have been found to be greater interest in view of their varied biological and pharmacological properties [1]. Literature survey confirms different synthetic derivatives of benzothiazole have various biological activities like anti-tumar [2-3], antimicrobial, antibacterial, anthelmentic [4-7], antiinflammatory and antitubercular activities [8]. In view of biological significance of benzothiazole moiety, it is yet to be explored synthetically and biologically with several other important heterocyclic systems . This paper is based on synthesis and evaluation of benzothiazoles.

Benzothiazole is a privileged bicyclic ring system. Due to its potent and significant biological activities it has great pharmaceutical importance; hence, synthesis of this compound is of considerable interest. The small and simple benzothiazole nucleus if present in compounds involved in research aimed at evaluating new products that possess interesting biological activities.

A brief account of some commonly used methods to synthesize as well as cyclization of benzothiazole derivatives by using different type catalysts and various structural alterations conducted on benzothiazole ring Introducing aryl pharmacophore to benzothiazole at position 2 exhibited a wide range of biological properties specially cytotoxic activity.

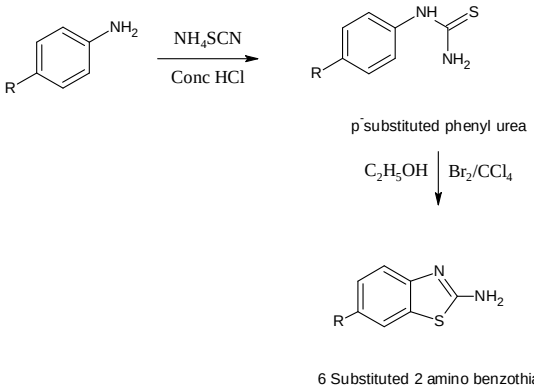
Structure of Benzothiazole





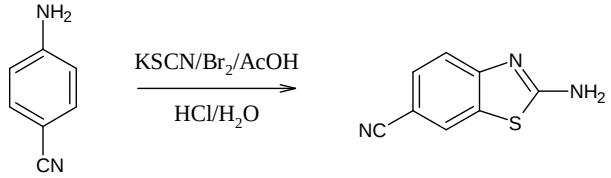
II. MAJOR SYNTHETIC PROCEDURES

1. Bele DS.et al have synthesized 6-substituted-2-amino benzothiazole using *p*-substituted aniline,NH4SCN and Conc HCl as a starting material. The synthetic scheme is given below

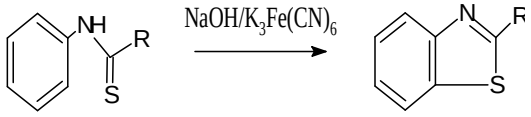


6 Substituted 2 amino benzothiazole

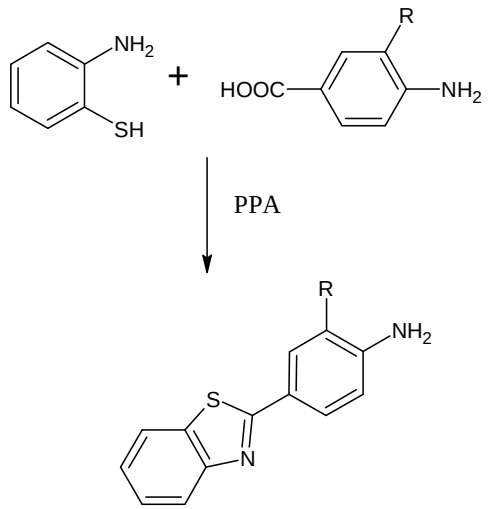
2. Synthesis of 2-aminobenzothiazole have been reported using substituted aniline, potassium thiocyanate and bromine in acidic condition at low temperature (0-5OC). For the acidic media acetic acid as solvent have been is used for the synthesis of 2-aminobenzothiazole.[9]



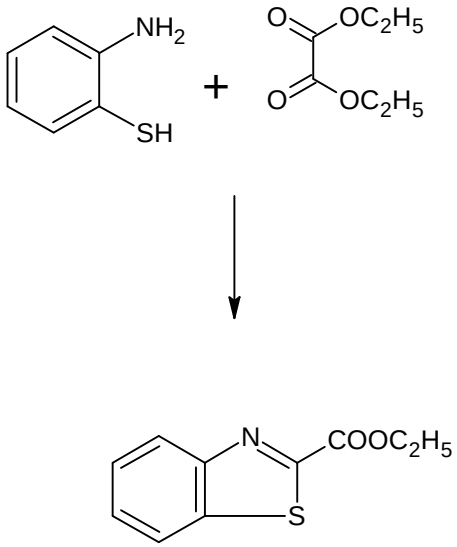
3. Kim, S. et. al. have been reported the synthetic method for 2- alkyl benzothiazole. In this method the thiobenzamides were cyclized to their corresponding phenylbenzothiazoles by a Jacobsen synthesis using the oxidizing agent potassium ferricyanide in aqueous sodium hydroxide (NaCN / K3Fe(CN)6) as cyclizing agents[10]. The synthetic scheme is given in **.**



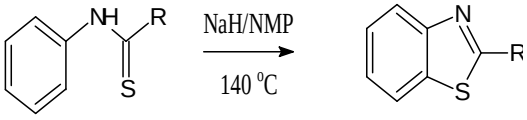
4. Ian, H. et al. have been reported the reaction of 2-thiolaniline with aromatic acid in the presence of polyphosphoric acid at 110OC for the synthesis of 2-aminobenzthiazole derivatives. The synthetic scheme is given in **.[**11]



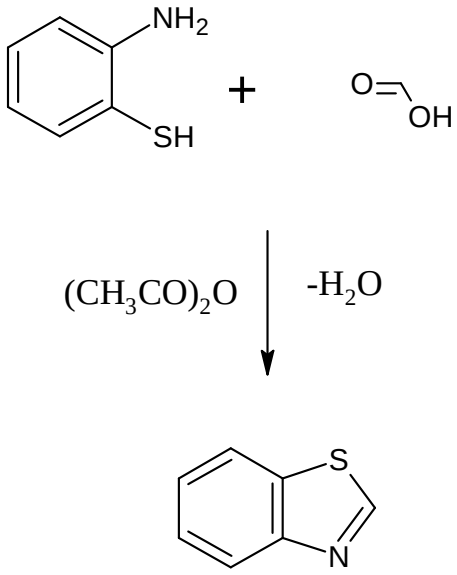
5. Rajeeva, B. et al. have been reported the synthesis of ethyl-2-benzothiazole carboxylate using *o*-aminothiophenol and diethyl oxalate as a starting material at mild reflux reaction condition for 4 hrs. The synthetic scheme is given in [12]



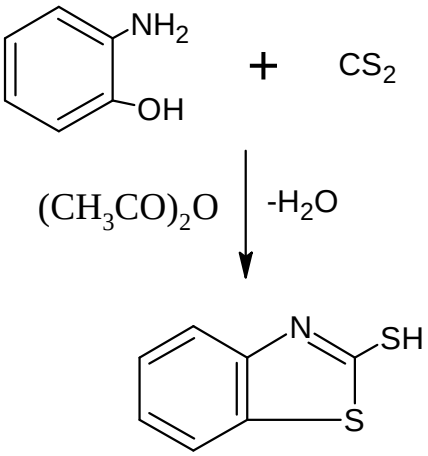
6. Bradshaw, T. D. et al. have been reported another method for cyclisation of thiobenzamides using sodium hydride in N-methylpyrrolidinone (NMP) as a cyclizing agent at 140OC of reaction mixture temperature. The synthetic scheme is given below:



7. Benzothiazole may be prepared by action of acid anhydrides (or) chlorides on o-aminophenols and formic acid in presence of acetic anhydride. [13 ,14]



8. 2-mercaptobenzothiazole is vulkanisation accelerator it may be prepared as follows. [13,14]



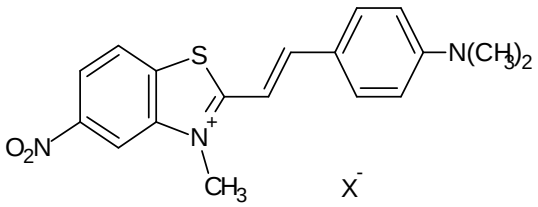
III. MEDICINAL IMPORTANCE

The high therapeutic properties of the Benzothiazole related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents. Benzothiazole drugs have broadened scope in remedying various dispositions in clinical medicines.

Antimicrobial activity:

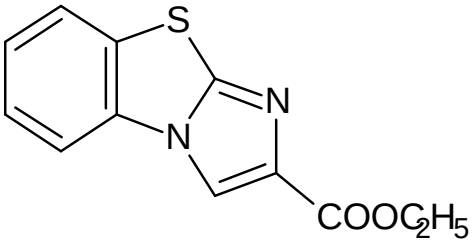
Microbes are the causative agents for various types of diseases like pneumonia, ameobiasis, typhoid, malaria, common cough, cold and various infections and cause some severe diseases like tuberculosis, influenza, syphilis, and AIDS etc.

Sigmundova I. et al synthesis some novel benzothiazole derivatives which have been tested in vitro for their antibacterial activity against four strains of Gram-positive bacteria: Staphylococcus aureus, Bacillus subtilis, Micrococcus luteus and Enterococcus faecalis.

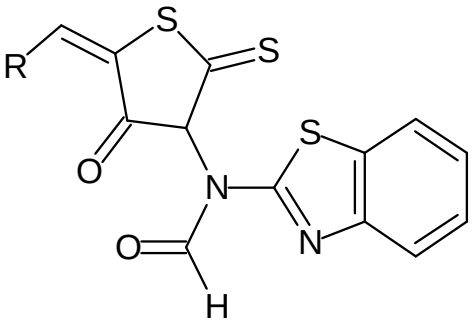


IV. ANTICANCER ACTIVITY

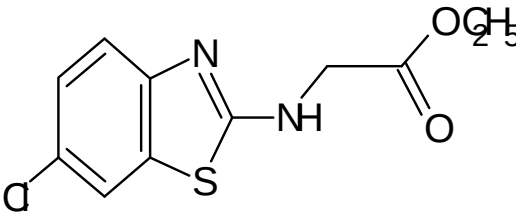
Kumbhare et al., in 2012¸ reported the synthesis of benzothiazolylthiocarbamides from catalytic amounts of 4-Dimethylaminopyridine followed by its chemo selective oxidative cyclization with 1,3-di-nbutylimidazoliumtribromide which afford the N-bis-benzothiazole derivatives. The synthesized compounds were tested against the two human monocytic cell lines and a mouse melanoma cell line and interestingly the all the compound shows more or less anticancer activity [15].



Malleshappa et al., 2012, has performed anticancer screening for 7-chloro-N-(2,6-dichlorophenyl)benzothiazol- 2-amine it reveals that compound shows good results against Non-Small Cell Lung Cancer causing cell lines [16].



Saarangi Ramesh et al synthesis some novel benzothiazole derivatives were screened against two selected fungal strains *Candida albicans* and *Aspergillus flavus* by using diffusion method using potato-dextrose agar media (20%) [17].



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