WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 8, 392-402. Review Article ISSN 2277– 7105

A SHORT REVIEW ON SYNTHESIS AND ITS MEDICINAL SIGNIFICANCE OF 1, 3 BENZOTHIAZOLE DERIVATIVES

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Article Received on
29 Feb. 2018,

Revised on 19 March 2018,
Accepted on 09 April 2018

DOI: 10.20959/wjpr20188-11925

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ABSTRACT

Benzothiazole nucleus plays an important role in heterocyclic chemistry due to its structural simplicity. A series of benzothiazole and its related products were synthesised by using different methods and evaluated for its biological activity. It remains one of the most typically studied heterocyclic compounds due to its wide range of pharmacological activities such as anticancer, antimicrobial, antifungal, antibacterial, anticonvulsant, anthelmintic, anti-tubercular, anti-inflammatory, antioxidant and anti-diabetic activities. Works of the literature shown that structural modification of benzothiazole derivatives have enhanced its biological activities and increased a great interest in the research field. The present review focuses on the synthesis of benzothiazoles derivatives with potential activities.

KEYWORDS: Heterocyclic compounds, Benzothiazole, Synthesis, Biological activities.

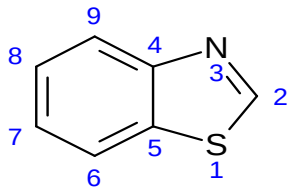
INTRODUCTION

Heterocyclic compounds are ubiquitous and plays a significant role in drug discovery. Nitrogen, sulfur and oxygen are the most typical heteroatoms. They are commonly distributed in nature and are crucial to our life.[1]

Heterocyclic compounds can be usually categorized into aliphatic or aromatic. The aromatic heterocyclic compounds are those which have a heteroatom in the ring and resemble more like benzene in some of their properties. Benzothiazole is heterocyclic aromatic compound. It contains benzene and a heterocyclic thiazole ring, occupies an important position in medicinal chemistry. Thiazole is a five membered ring system contains both nitrogen and

sulfur. These two rings together constitute the basic nucleus 1, 3- benzothiazole. The numbering in thiazole starts from sulfur.[2]

Benzothiazole moiety represents a principal component in heterocyclic compounds. These compounds show a broad spectrum of biological activities such as antimicrobial, anti-tubercular, antitumor, antimalarial, anticonvulsant, anthelmintic, analgesic and anti-inflammatory activity. Due to their biological and pharmacological properties, they are considered an important scaffold for the synthesis of the heterocyclic compound.[3]



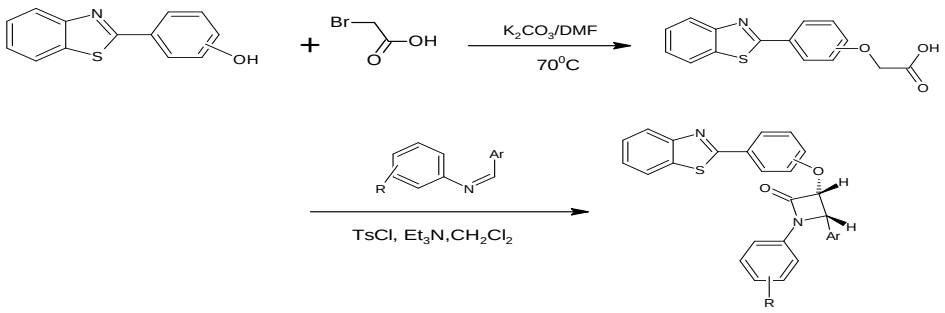
Chemical structure of 1, 3-benzothiazole

Fig. 1

Benzothiazole is a bicyclic ring system with a chemical formula C_7H_5NS. It is a weak base, having a variety of biological activities and still having greater attention in the scientific area. They are broadly found in the field of bioorganic and medicinal chemistry with application in new drug development.[4] The study of these privileged structures in drug discovery is a rapidly emerging in the field of medicinal chemistry.

Literature Review

Alborz M *et al*., (2018) synthesised some novel benzothiazole-substituted β- lactam hybrids and evaluated for their antimicrobial activities against Gram-positive and Gram-negative bacterial strains.[5]

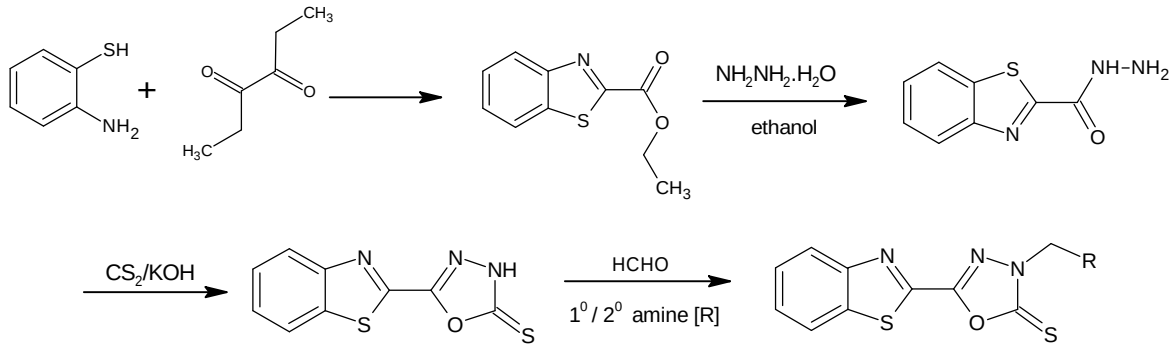


R = OMe, OEt, Me, Cl, H, N $(CH_3)_2$…

Ar = -$C_6H_5NO_2$, - C_6H_5Cl, -C_6H_5CH $(CH_3)_2$…

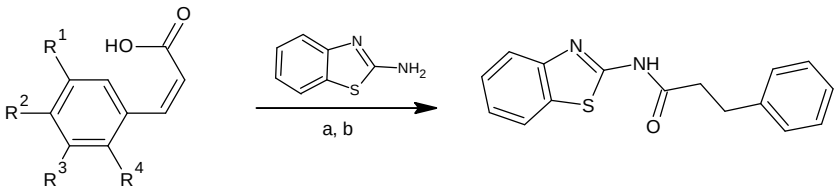
Scheme 1

Bhutani R *et al*., (2018) synthesised a small library of new benzothiazole clubbed oxadiazole-Mannich bases and evaluated for their in vivo anti-diabetic activity.[6]



Scheme 2

Nong W *et al*., (2018) synthesised a series of benzothiazole amide derivatives by nucleophilic substitution reaction between 2-aminobenzothiazole and different cinnamic acids. These compounds were evaluated for their *in vitro* hemostatic activities.[7]

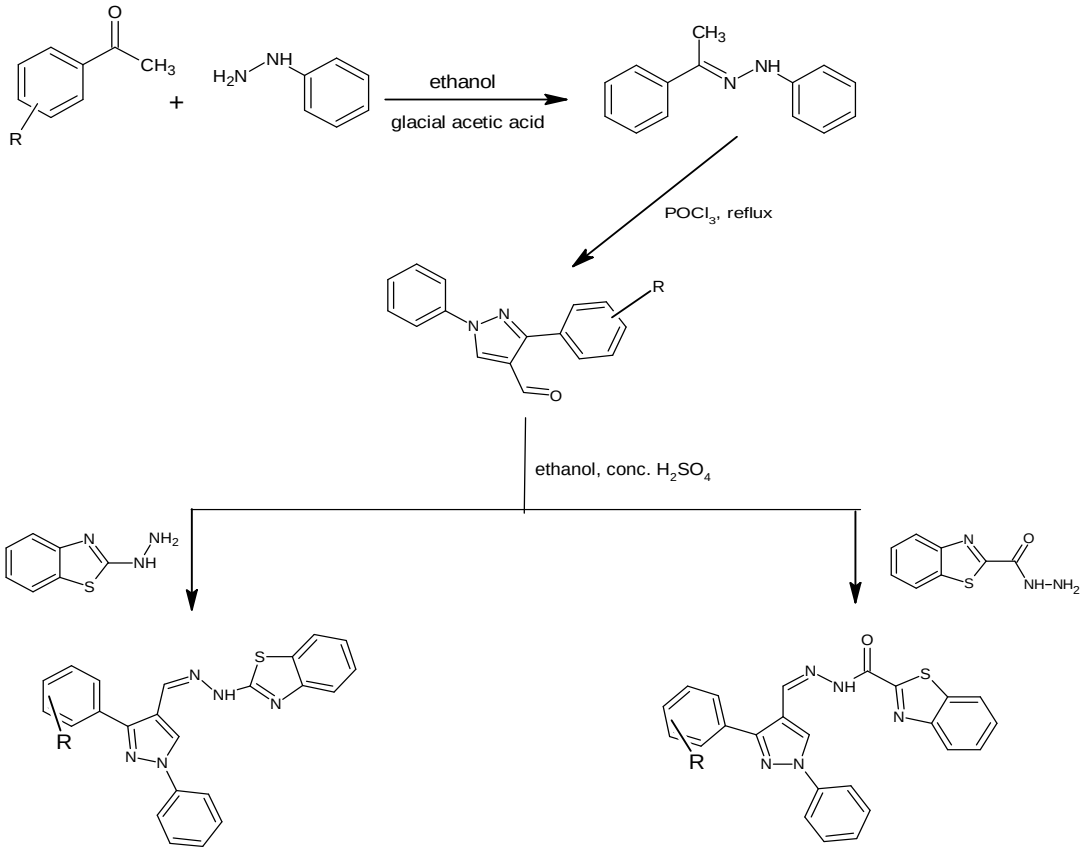


R^1 = H, OCH_3; R^2 = H, OCH_3, $OCOCH_3$; R^3 = H, OCH_3, $OCOCH_3$; R^4 = H, $OCOCH_3$

Reagents and conditions: (a) $SOCl_2$, DMF, 70^0 C, 5 min, 100%. (b) $NaHCO_3$, pH ¼ 6–7, 0–5^0 C to room temperature, 3 h, 88–93%.

Scheme 3

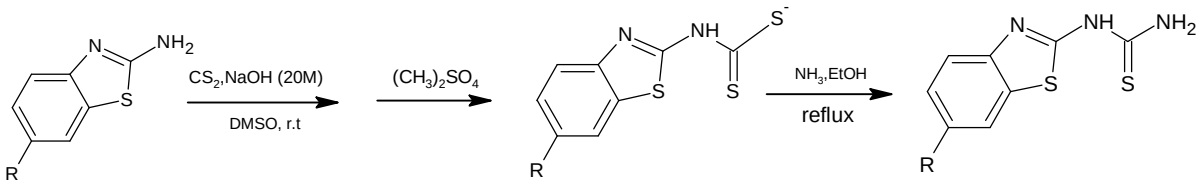
Bhat M *et al*., (2018) synthesised two novel series of the pyrazole-conjugated benzothiazole derivatives and evaluated for antioxidant, antimicrobial and anti-TB activities.[8]



R = H, p-OCH_3, p-OH, p-CH_3, p-Cl, p-Br, p-NO_2, m-NO_2, p-N $(CH_3)_2$

Scheme 4

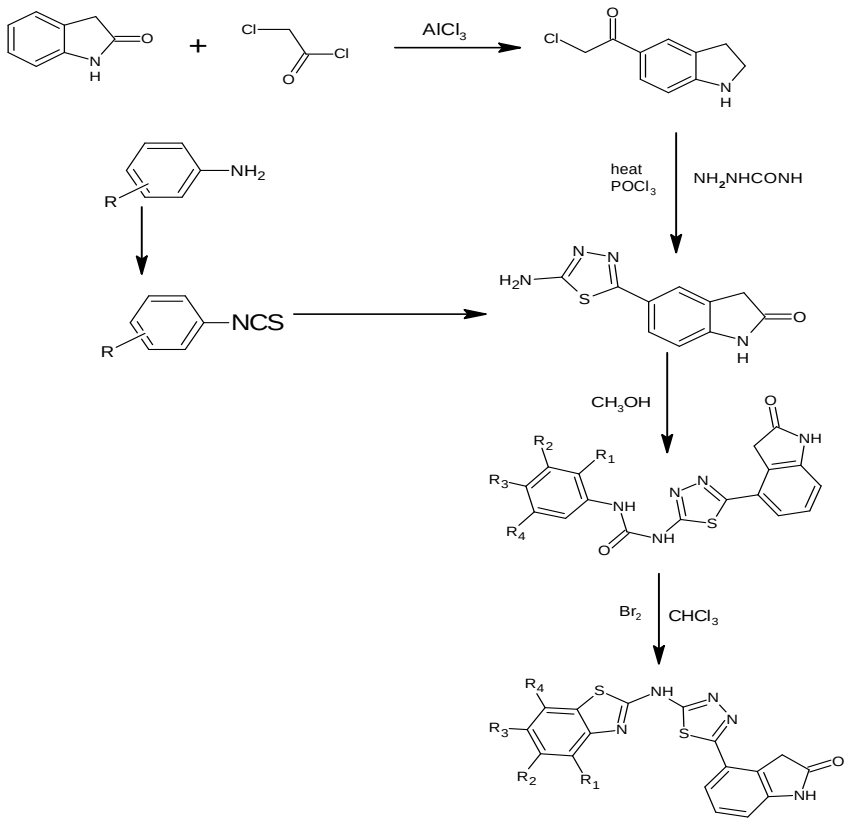
Eshkil F *et al*., (2017) synthesised some thiourea derivatives of benzothiazoles and screened for their anticancer activity.[9]



(a) R = H (b) R = CH_3 (c) R = OCH_3 (d) R = OEt

Scheme 5

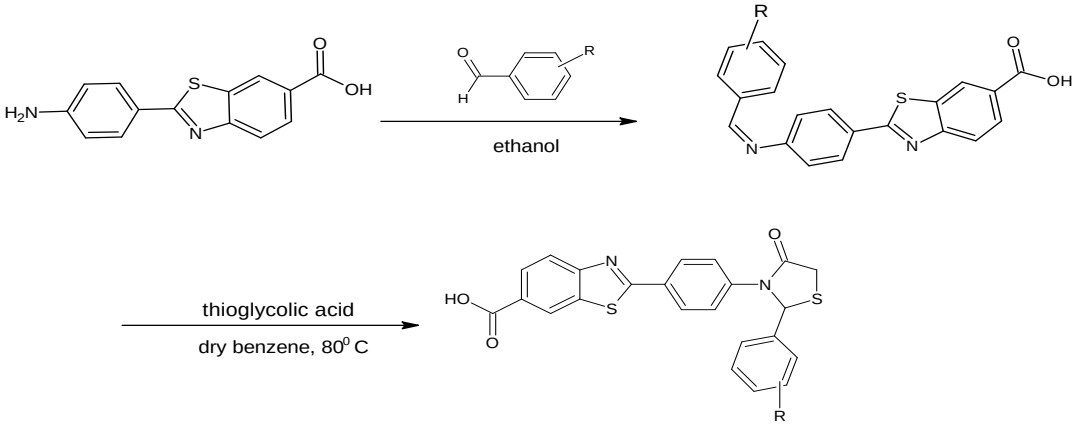
Dipesh K *et al*., (2016) reported the synthesis, characterisation of some benzothiazole derivatives bearing oxindole moiety and evaluated for their potential anticancer activity.[10]



R_1 = CH_3, Cl; R_2 = H, Cl; R_3 = H, Cl; R_4 = CH_3, H, Cl

Scheme 6

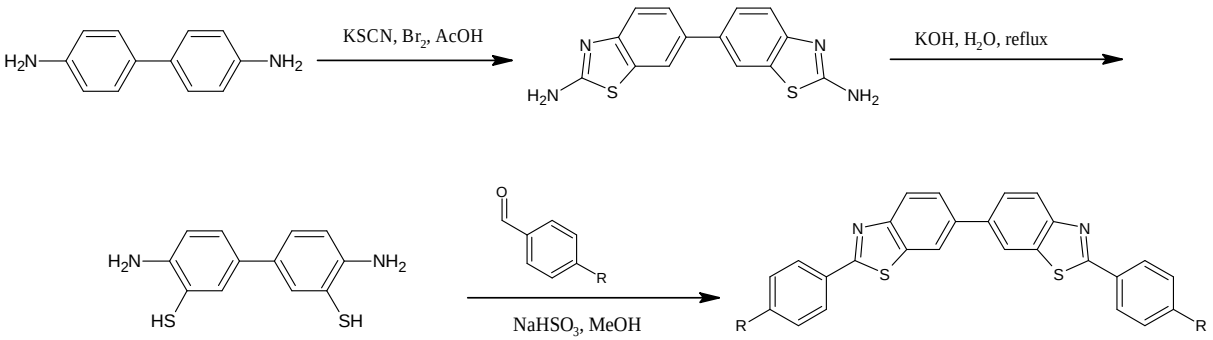
Prabhu P P *et al*., (2015) synthesised a novel series of 2-phenyl thiazolidinone substituted 2-phenyl benzothiazole-6-carboxylic acid derivatives by various benzothiazole schiff's bases on treatment with thioglycolic acid. All these compounds were screened for their in vitro anticancer activity.[11]



R = H, p-Cl, m-F, p-NO_2, p-OCH_3, p-CH_3, p-OH

Scheme 7

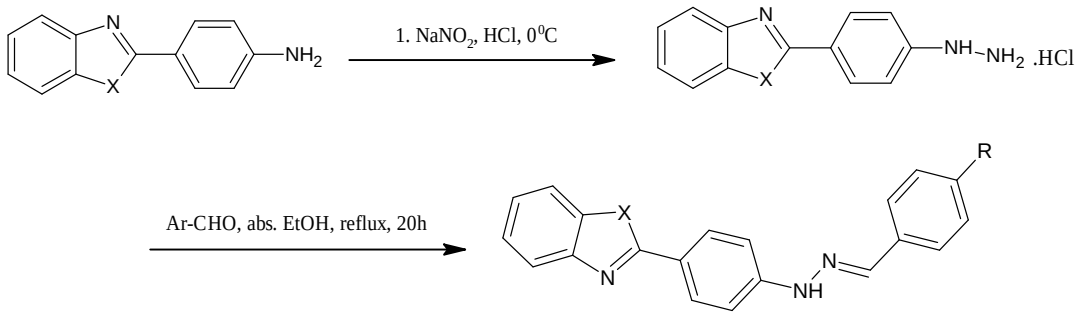
Yang M L *et al*., (2018) designed, synthesised a series of novel bis-benzothiazole derivatives and evaluated for their anti-proliferative activities on U937, HL60, and HeLa cells.[12]



R = H, Me, OMe, Et, OEt, NO_2, F, I, Cl, Br

Scheme 8

Labib M B *et al*., (2018) designed, synthesised series of azole-hydrazone derivatives of benzimidazole, benzoxazole, benzothiazole and carried out in vitro biological evaluation, dual EGFR /HER2 inhibitory activity, cell cycle analysis and molecular docking study as anticancer agents.[13]

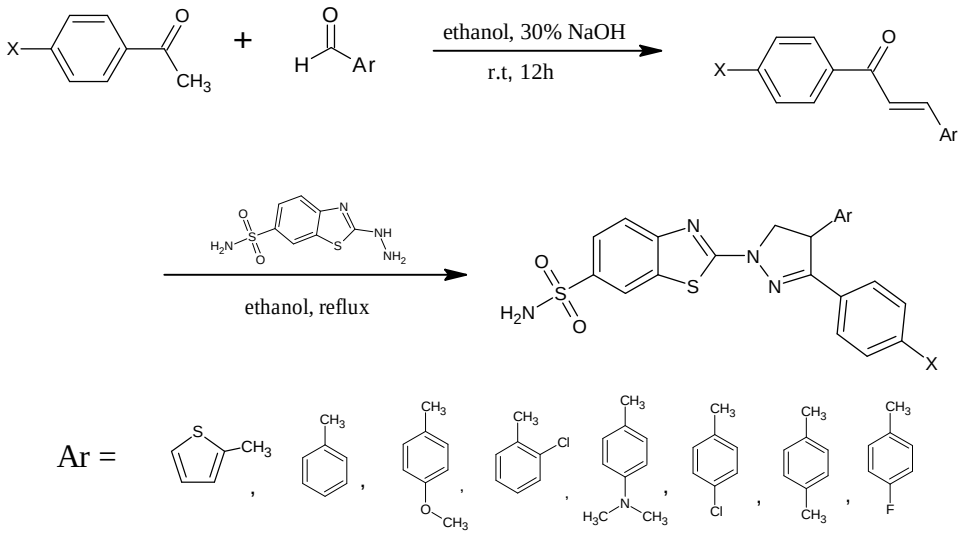


X = NH, O, S

R = OH, OCH_3, Cl, N $(CH_3)_2$, NO_2

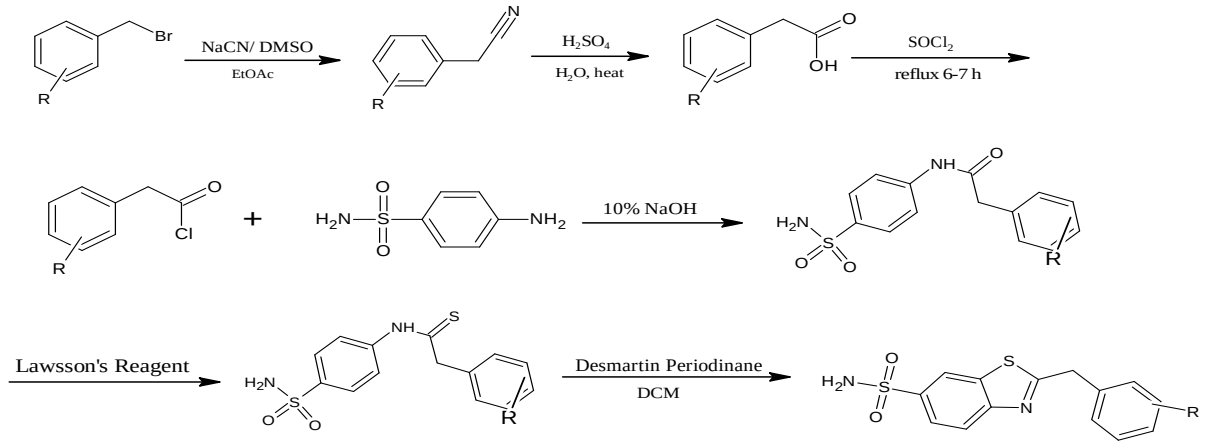
Scheme 9

Kharbanda C *et al*., (2014) synthesised some pyrazolines bearing benzothiazole and evaluated for their potential anti-inflammatory activity.[14]



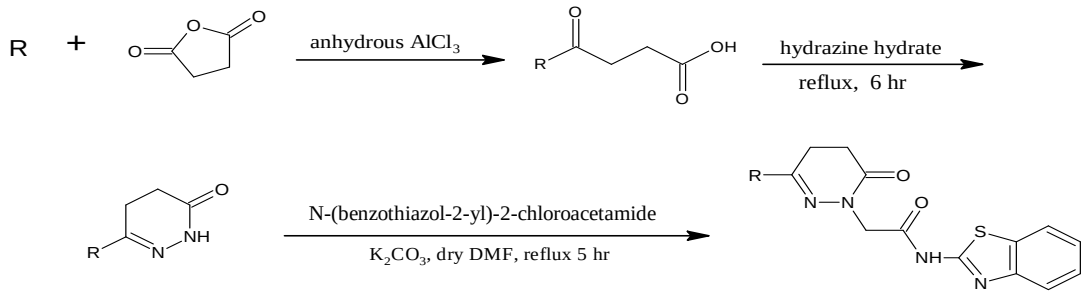
Scheme 10

Mahtab R *et al*., (2014) synthesised a series of novel 2-benzyl benzo[d] thiazole-6-sulfonamide derivatives from substituted benzyl bromide and evaluated for their potential anti-inflammatory activity.[15]



Scheme 11

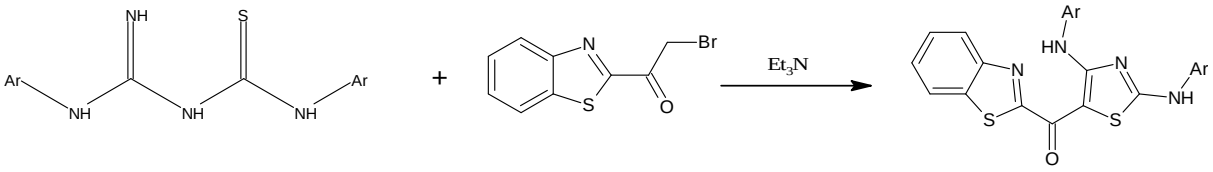
Partap S *et al*., (2018) designed, synthesised a series of new hybrid benzothiazole containing pyridazinones derivatives and evaluated for their anticonvulsant activity.[16]



R = Aromatic hydrocarbon

Scheme 12

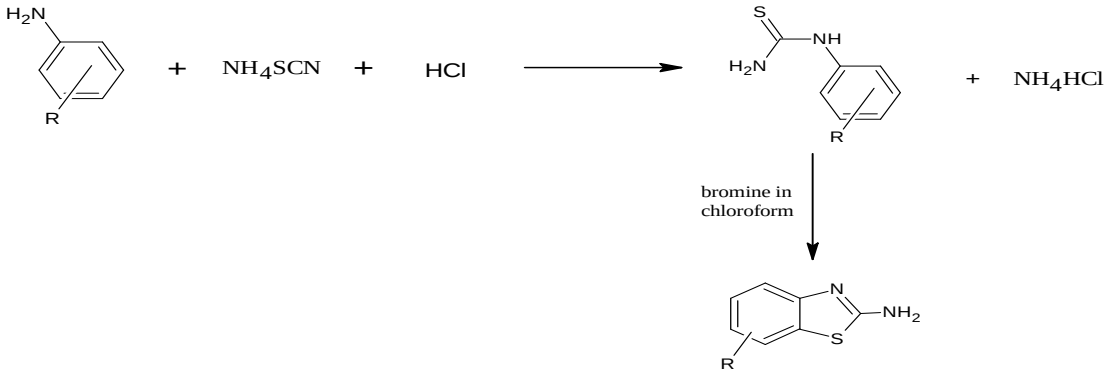
Kumari B *et al*., (2017) synthesised a series of novel bis-arylamino thiazoloyl benzothiazoles derivatives from 1-aryl-3-(N, N'-diarylamidino) thioureas and 2-(2-bromoacetyl) benzothiazole with triethylamine and evaluated antioxidant activities of synthesised compounds by DPPH free radical scavenging activity.[17]



Ar = Phenyl, 4-chlorophenyl, 4-methylphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, Ethyl n-propyl, N-butyl

Scheme 13

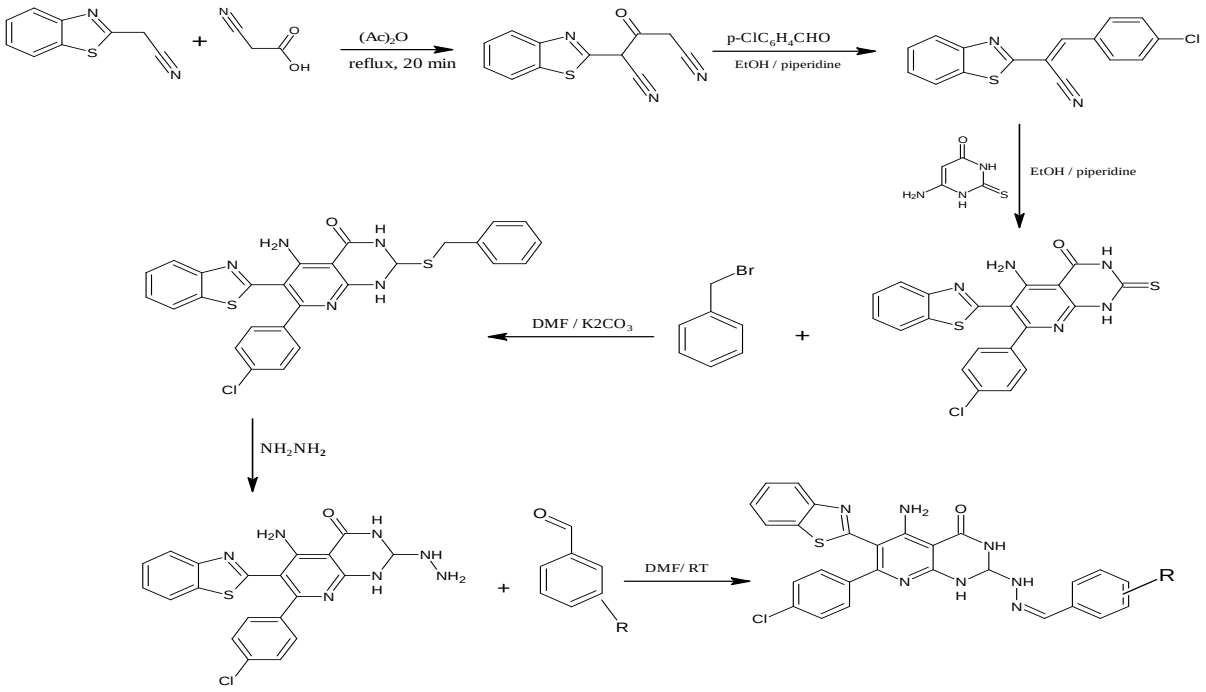
Raju D N *et al*., (2015) synthesised, characterised some novel substituted 2-amino benzothiazole derivatives and screened for analgesic activity.[18]



R = H, Cl, Br, NO_2, COOH

Scheme 14

Maddila S *et al*., (2016) synthesised a new series of 5-amino-6-(benzo[d]thiazol-2-yl)-2-(2-(substituted benzylidene) hydrazinyl)-7-(4-chlorophenyl) pyrido [2,3-d] pyrimidin-4(3H)-one derivatives and screened for their in vitro antibacterial activity, against Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli, Streptococcus pyogenes and Pseudomonas aeruginosa and for antifungal activity against Aspergillus flavus, Candida albicans, Aspergillus fumigatus, Penicillium marneffei and Mucor.[19]



R = H, 4-Cl, 2-Cl, 4-CH_3, 4-CH_3O, 4-F, 4-NO_2, 2, 4-$(CH_3)_2$, 4-NH_2, 4-C_2H_5, 4-CH $(CH_3)_2$

Scheme 15

CONCLUSION

From the above literature review, concluded that the benzothiazoles and its analogues possessing different biological activities have been synthesised by using different schemes. Researchers highlight the development of benzothiazole nucleus as a template for newer medicinal agents. Thus benzothiazole acts as a promising therapeutic agent in the area of drug discovery.

ACKNOWLEDGEMENT

I express my sincere respect and gratitude to my guide Dr. AKASH MARATHAKAM who has given valuable support cooperation and suggestions for completing this work. I would also like to thank my family and friends who helped me a lot in this review article.

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