Section A-Research paper

A REVIEW ON THE SYNTHESIS OF BENZOTHIAZOLE-BASED COMPOUNDS

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Abstract

Benzothiazoles have a significant impact on biochemistry and medicinal chemistry because of their great biologic and pharmacological activity. Undoubtedly, one of the biggest issues facing scientists today is the creation of chemical synthesis. With the reaction of 2-aminobenzenethiol by that of acids, ketones, aldehydes, cyclization and acyl chlorides of carbon dioxide and thioamide as raw materials, researchers presented significant advancements in the biosynthetic pathways of benzothiazole substances associated with green chemical reactions in this research article. In this review researchers predicted the biosynthetic pathways of benzothiazoles.

Keywords: 2-aminobenzenethiol; benzothiazoles; green chemistry; cyclization; condensation; Carbon dioxide; thioamide.

1. INTRODUCTION

The far more important biochemical activity has been found in heterocyclic compounds with nitrogen, sulphur, oxygen atoms [1]. A heterocyclic aromatic chemical is benzothiazole. These benzene and thiazole rings combine to form a bicyclic molecule. Thiazole (I) has a 5-membered ring at its centre that contains sulphur and nitrogen atoms in positions 1 as well as 3, respectively. In thiazoles, the sequence begins with the sulphur atom. Thiazole had first been described by Hantzsch and Waber in 1887, whereas Popp further validated its composition in 1889. The benzene is bonded to the 4th as well as 5th positions of the thiazole structures for the

formation of basicbenzothiazolestructure. The 1,3-benzothiazole (II) basic nucleus is made of these rings (Figure 1) [2].

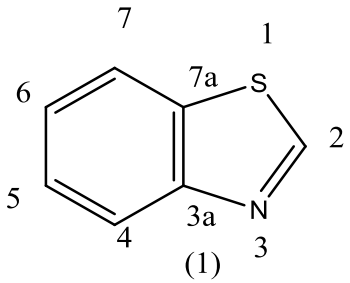
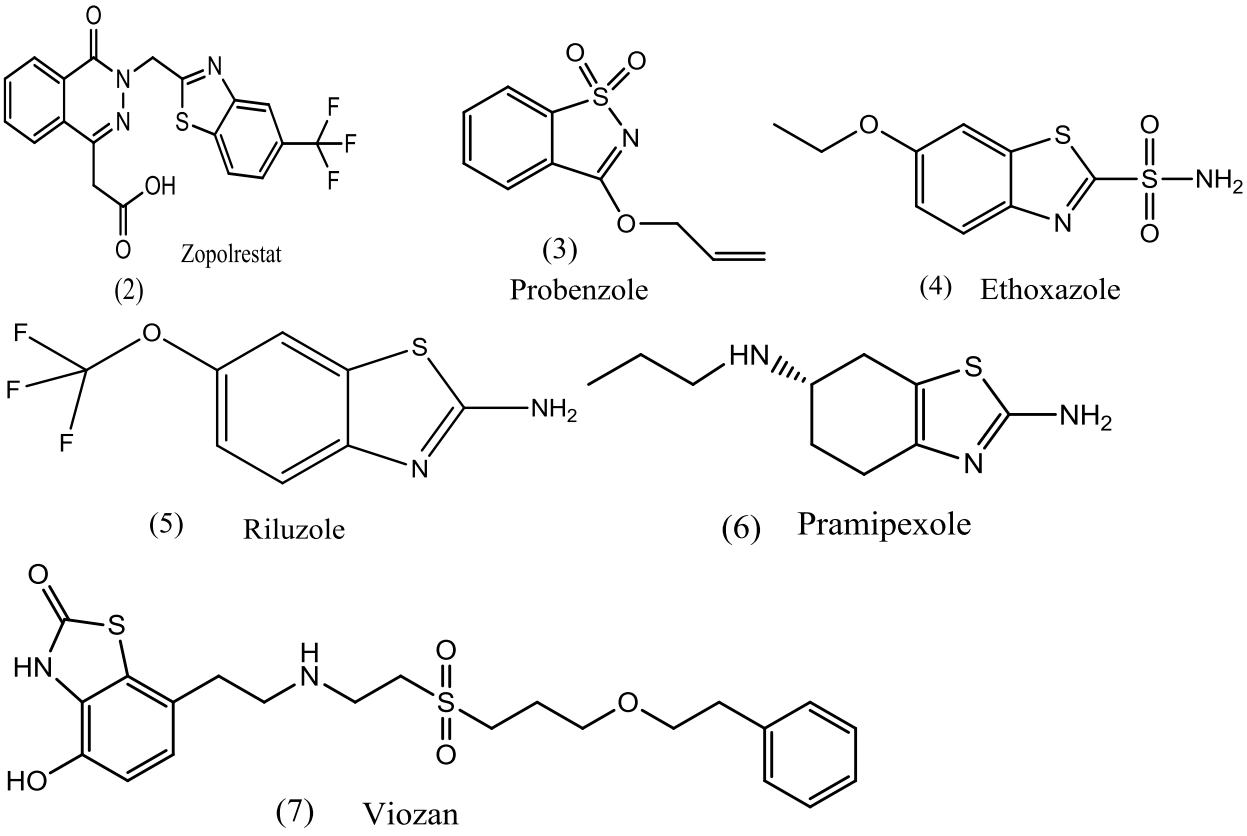


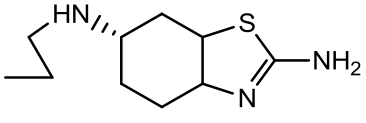
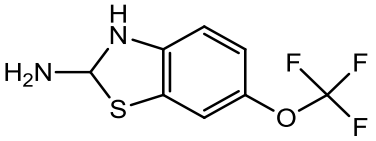
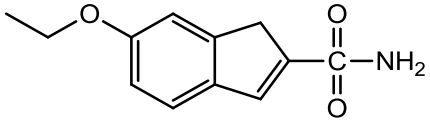
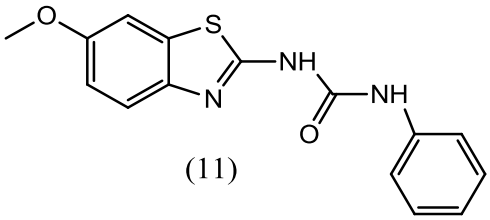
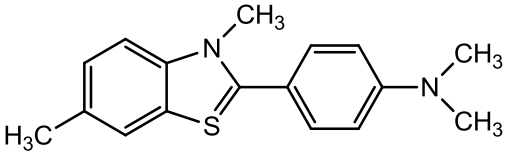
Figure 1. Numbering of Benzothiazole

The chemical name for this substance is benzothiazole, and its chemical formula is C_7H_5NS. With such a meltingboiling of 2°C as well as a boiling temperature of 227 to 228°C, it is mildly basic in nature. Benzothiazole has a molar weight of 135.19 g/mol as well as a density of 1.24 g/mol. Since of their pharmacological and biological activity, benzothiazole compounds have important role in the field of research, particularly in medicinal, pharmaceutical and synthetic chemistry. Additionally, the biologically active compounds of benzothiazoles serve as the core nucleus in a number of medications (Figure 2), such as zopolrestat (an aldose reductase blocker for such therapies of late-stage diabetes - related complications such as neuropathy as well as nephropathy),ethoxazolamide, probenazole and riluzole.



Moreover, there are other benzothiazole derivatives on the market now, as described in Table 1.

Table 1: Benzothiazole Derivatives in Marketed Preparations [4].

Sr no.	Compounds	Structure	Uses
1.	Pramipexole	 (8)	Parkinson's Therapy
2.	Riluzole	 (9)	Amyotrophic Sclerosis
3.	Ethoxzolamide	 (10)	Diuretics, ulcer and Glaucoma,
4.	Frentizole	 (11)	Immunosuppressant and anti-viral agent
5.	Thioflavin T	 (12)	Amyloid amazing agent

The relevance of this moiety has been emphasized in various published patents, a few of which are listed in Table 2.

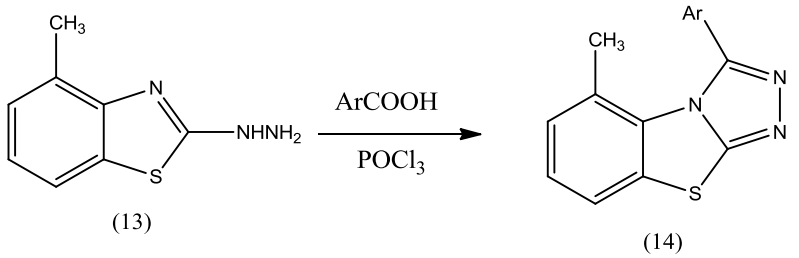
Table 2. Patents of benzothiazole

Sr No.	Patent No.	Dates	Applications	Applicants	References
1.	US20080227985 A1	Sep 18, 2008	US 12/049,235	Prasad Raje	5
2.	WO2008124393 A1	Oct 16, 2008	PCT/US2008/ 059024	Yun He et al.	6
3.	WO2009039553 A1	Apr 2, 2009	PCT/AU2007/ 001442	Keith Geoffrey Watson	7
4.	US20090118272	May 7,	US 12/333,425	Chunjian Liu	8

	A1	2009		et al.	
5.	US7553854 B2	Jun 30, 2009	US 11/737,069	James C. Sutton	9
6.	US8143258 B2[	Dec 1, 2009	US12628697	Masanori Okaniwa et al.	10
7.	WO2010066357 A1	Jun 17, 2010	PCT/EP2009/ 008499	JormaHassfeld	11
8.	WO2011075631 A1	Jun 23, 2011	PCT/US2010/ 060981	Alfonzo D. Jordan et al.	12
9.	US7928140 B2	Apr 19, 2011	US 12/221,416	Shon Booker	13
10.	EP2358689 A1	Aug 24, 2011	EP20090775337	Masanori Okaniwa et al.	14
11.	US20120095021 A1	Sep 14, 2011	US13232407	Ahmed Kamal et al.	15
12.	US20120101094 A1	Aug 28, 2012	US8252811B2	Wenge Xie et al.	16
13.	US8546393 B2	Oct 1, 2013	US 12/693,736	Eva Albert et al.	17
14.	US20130079340 A12	Mar 28, 2013	US 13/660,045	Florencio Zaragoza Dorwald et al.	18
15.	US20130004422 A1	Jan 03, 2013	US20130004422A1	W. E. Klunk et al.	19
16.	WO2014036242 A3	Aug 29, 2013	PCT/US2013/ 057264	Russell Dahl et al.	20
17.	US8691185 B2	Apr 8, 2014	US 13/548,014	Prasad Raje et al.	21
18.	WO2016079688 A1	Nov 11, 2015	PCT/IB2015/ 058919	Christine Schmitt et al.	22
19.	WO2017025980 A3	Apr 6, 2017	PCT/IN2016/ 000207	Kalpana Chauhan et al.	23
20.	WO2017063966 A1	Apr 20, 2017	PCT/EP2016/ 074122	Kai Thede	24
21.	WO2017120198 A1	Jul 13, 2017	PCT/US2017/ 012139	Jerry Yang	25

The heteroatoms sulphur and nitrogen are present in the ring that is responsible for wide range of therapeutic activities as it is already reported in the literature that the heterocyclic compounds with sulphur, nitrogen and oxygen have remarkable biological activities [26-27]. As a bicyclic compound, it has many potential uses in biomedical sciences, including: antitumor [29], antifungal [28], anti-convulsant [31], anti-bacterial [30], antiviral [38] effects, anti-inflammatory [33], analgesics [34], blood sugar [32] control, anthelmintics [35], anti-tubercular [37], an appetite suppressant [39], anti-malarial [36], and antihistamine agents [40]. It's the focal point of interest because it has so many potential pharmaceutical applications.

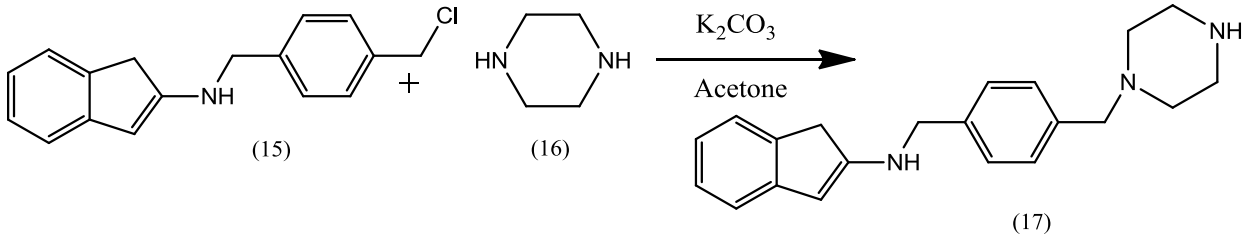
Various derivatives of benzothiazoles were produced by Dong and team. During 12 hours, 2-hydrazino-4-methylbenzothiazole was heated with carbonic acids as well as $POCl_3$ at a refluxing temperature. The resulting mixture, minus some $POCl_3$, was put into a bowl of ice water for cooling. After potassium hydroxide mixture was included in the solution, the precipitates was filtered as well as purified by recrystallization in alcohol to yield, numerous derivatives of triazolo-benzothiazoles (scheme 1) [41].



(13) (14)

Scheme 1. Synthesis of derivatives of triazolo-benzothiazoles compounds.

Multiple synthetic routes have been established for the production of benzothiazole analogues (Scheme 2). The new benzothiazole compounds with potential enzyme inhibitory actions towards Alzheimer's disease were produced and studied by Karaka et al. Compounds with the capacity to block the action of acetylcholinesterase (AChE), monoamine oxidase (MAO-A and MAO-B) and butyrylcholinesterase (BChE) were produced Research indicated that compound (1) significantly inhibited AChE as well as MAO-B enzyme activity. The results indicate that the shown compound dual inhibitory profile may make it useful in the treatment of Alzheimer's disease as well as Parkinson's disease [42].

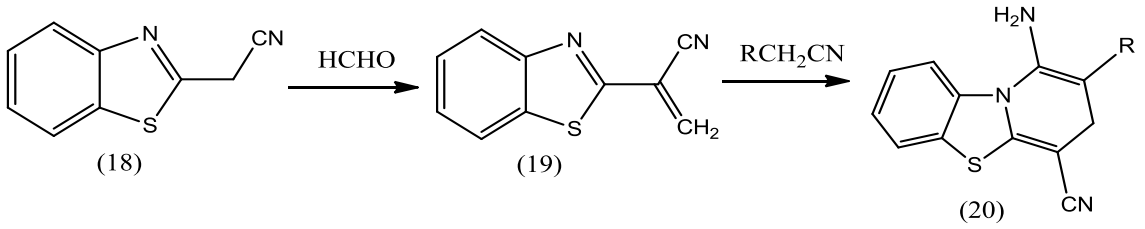


(15) (16) (17)

Scheme 2. Synthesis of N-(4-((piperazin-1-yl)methyl)benzyl)-1H-inden-2-amine and derivatives.

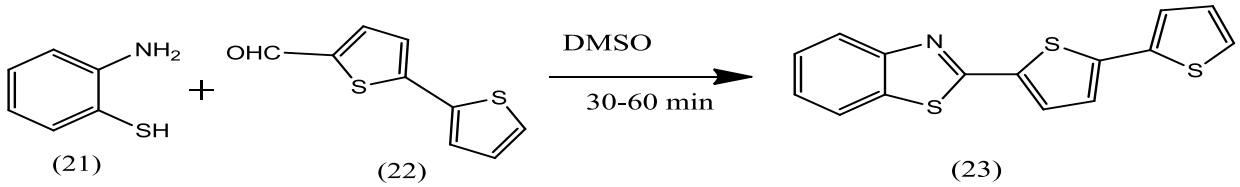
Recently, various carbonitrile derivatives of benzothiazole was synthesised by Zaki and his team by reacting derivatives of [1,3] benzothiazole-2-carbothioamide with formaldehyde,

cynomethylbenzothiazole and methylene reagent with in condition containing ethanol as well as triethylamine [43].



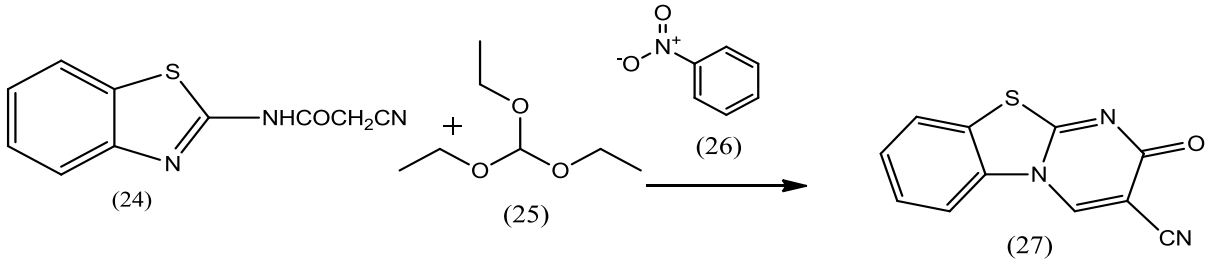
Synthesis 3. Synthesis of various derivativesof of [1,3] benzothiazole-2-carbothioamide.

Batista et al. noted that the 2-aminobenzenethiol can be condensed with 5-aldehyde bisthiophene substances under refluxing for 1 hour to produce 2-bisthiophene altered benzothiazole derivatives (Scheme 2). A thorough analysis of material fluorescence was performed. High efficiencies and sizable Stokes' shifts have been observed, together with bright fluorescence in the range of 450-600 nm. Because of their high levels of fluorescence, the chemicals discussed above may find use as fluorescence detection [44].



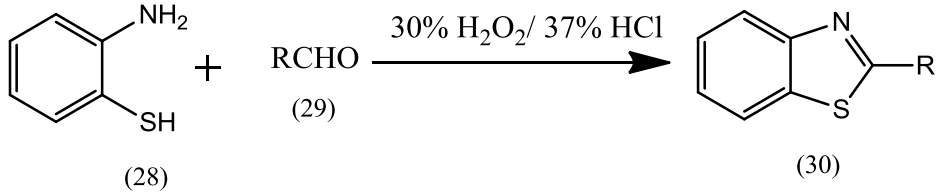
Scheme 4. Synthesis of 2-(5-(thiophen-2-yl)thiophen-2-yl)benzo[d]thiazole derivatives.

Stetinova J et al reported the synthesis of various derivatives of carbonitrile benzothiazole. They created it by synthesizing triethyl orthoformate with benzothiazolyl associated cynoacetamide throughout hot nitrobenzene [45].



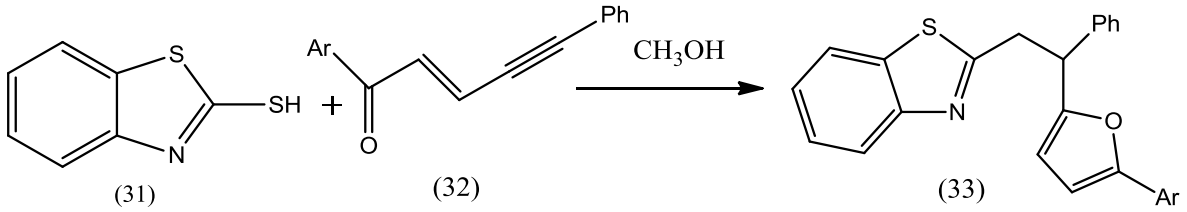
Scheme 5. Synthesis of carbonitrile benzothiazole derivatives.

To use a mixture of hydrogen peroxide and hydrochloric acid in ethanol where it will catalyze the reaction at room temperature for an hour, Guo and co-authors successfully synthesized benzothiazole substances with diverse substituents (Scheme 3). The compound, 2-Aminothiophenol, hydrogen peroxide, and hydrochloric acid were reacted. To add, this approach worked equally well for obtaining the necessary benzothiazoles by the use of aldehydes and substituents that areelectron-releasing orelectron withdrawing in nature. One got the advantages of employing this methoddue to their shorter time of reaction, simple and fast product separation, and high yield products [46].



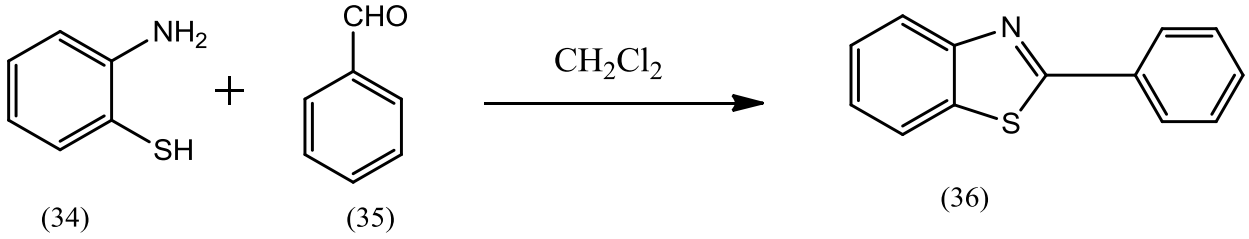
Scheme 6: Synthesis of Benzothiazole and derivatives from aldehydes.

At normal temperature, 2-Mercaptobenzothiazole undergoes cyclization when it interacts with ketones to produce benzothiazolyl furfuryl sulphides [112]. Evidently, functionalization to furans occurs through the intermediates (Scheme 60). Increased yields of the substances are generated by ketones having electron-acceptor heterocyclic in the substituent. Potential fungicides are compounds are obtained with good yield [47].



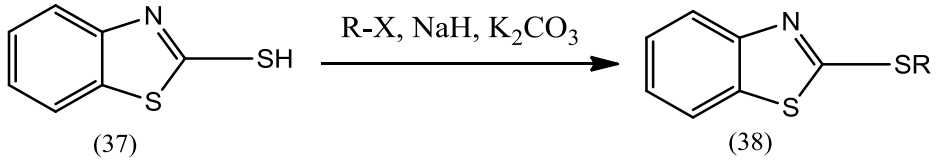
Scheme 7. Synthesis of benzothiazolyl furfuryl sulphides compounds.

This is a reaction between 2-aminobenzenethiol and benzaldehyde insolution of dichloromethane was shown to be efficiently catalyzed by the catalysts of polystyrene polymer grafted by iodine acetate, as reported by Kumar et al. [48]. This led to the synthesis of benzothiazole substances (Scheme 8). The catalysts were synthesized using an effective process, and it was then used in the combination production of benzimidazoles, that provided the advantages of solid substrate as well as the additional benefit of the diversification not even being destroyed in the libraries at any time. In addition, the catalyst was recycled just after process by first being transformed into polymer-supported iodobenzene, and then, by filtration, into poly[4-diacetoxyiodo] styrene (PDAIS). It's possible to recycle the catalyst multiple times without reducing its effectiveness.



Scheme 8. Synthesis of derivatives of 2-phenylbenzo[d]thiazole compounds.

According to the two-step process, compounds of thioethers with subsequent oxidation involving m-CPBA (Scheme 9) are used to create 2-benzothiazolyl sulfones. The sulfonates, which are common intermediates in chemical, polymer and biopharmaceutical chemistry, were produced in up to quantifiable yield by reducing the sulfones with that of sodium borohydride [49].

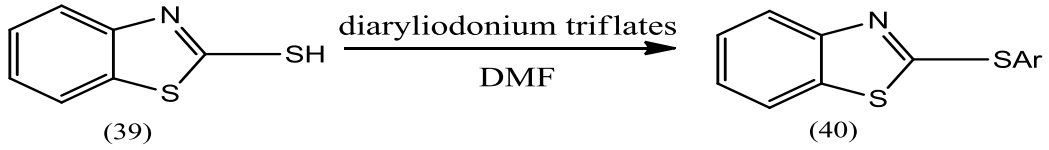


(37) (38)

R= $CH_3CH_2CH_2CH_2Cl$

Scheme 9. Synthesis of derivatives of 2-benzothiazolyl sulfones compounds.

The crucial step in the creation of 2-mercaptobenzothiazole compounds with strong biological processes is the potential application of the SH group. Consequently, aerobic 2-mercaptobenzothiazole S-arylation with diaryliodonium triflates in the presence of DMF at temperature 130°C without the use of a base or a metal catalyst was described (Scheme 10) This reaction produced the 2-(arylthio)benzothiazoles in excellent returns [50].

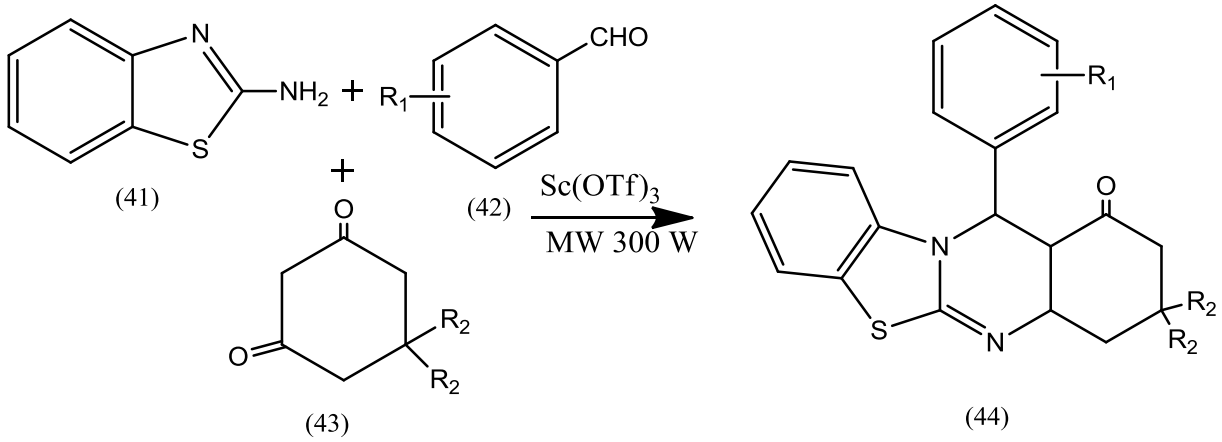


(39) (40)

Ar= C_6H_5

Scheme 10. Synthesis of derivatives of 2-(arylthio)benzothiazoles compounds.

For instance, reaction involving aromatic aldehydes, 2-aminobenzothiazole as well as the 1,3-diketones of theirradiation of microwave can be used to speed up the process without resorting to the use of solvent like $Sc(OTf)_3$ as the initiation (Scheme 11). A simultaneous response including carbonyl group stimulation, Knoevenagel condensing, azoles, the nucleophilic reaction, as well as intra - molecular cyclization is employed to obtain the desired products [51].



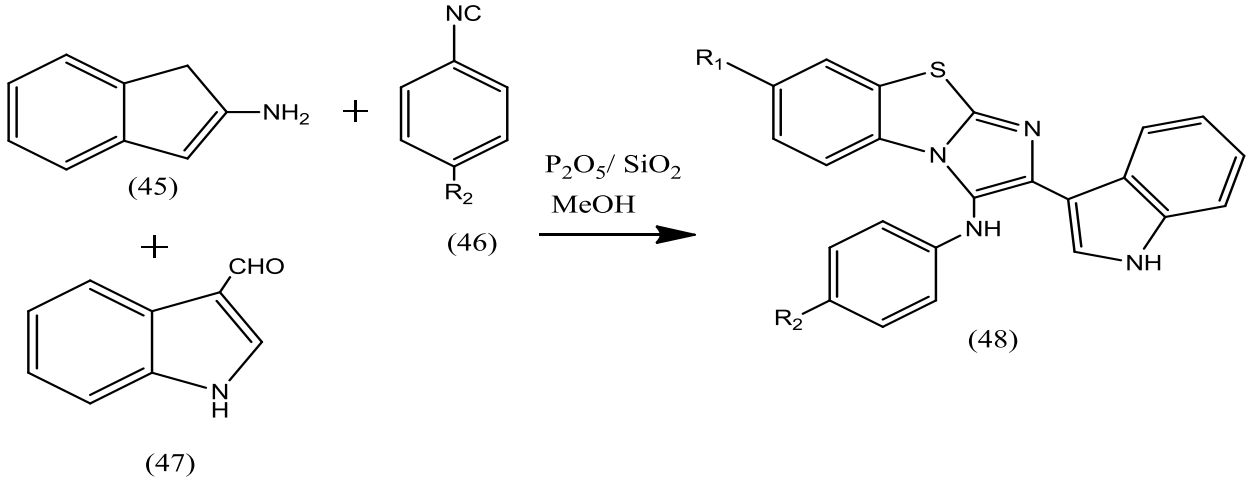
(41) (42) (43) (44)

R_1 = H, Me, NO_2, OMe

R_2 = H, Me

Scheme 11. Synthesis of derivatives of benzothiazole clubbed with quinazolinones.

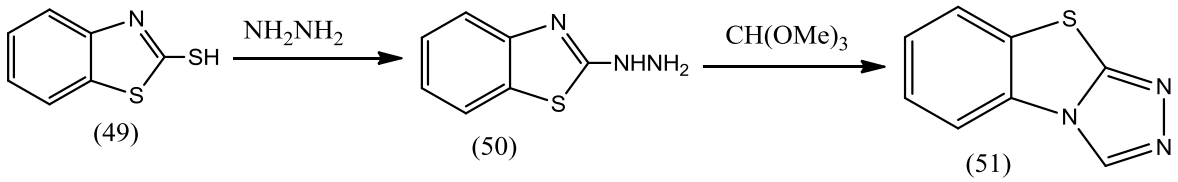
Another example 2 aminobenzothiazole aryl isocyanides derivatives and indole-3-carbaldehyde by using P_2O_5 on a support SiO_2, which results in the synthesis of 3-amino-2-(indol-3-yl)imidazo[2,1-b][1,3]benzothiazoles. In this particular instance, the sturdy P_2O_5/SiO_2 dehydrating properties allow the rapid release of water as the reaction result. The researchers used a protocol of green chemistry including ecofriendly solvents likely ethanol and methanol and simple regeneration of catalysts by washing it with hot ethanol as well as by drying it under the vacuum for at least 1 hour (Scheme 12) [52].



R_1 = H, NO_2, OMe, Me, Cl, Br
R_2 = H, Br

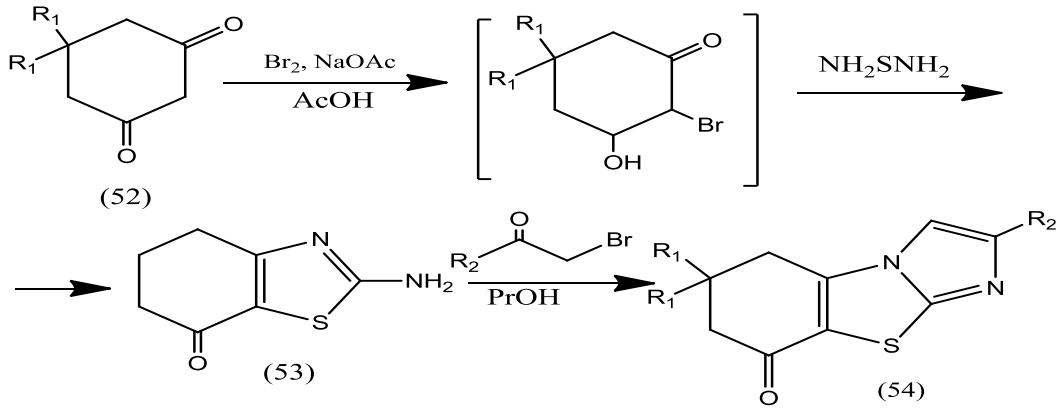
Scheme 12. Synthesis of derivatives of polycyclic 3-aminoimidazo[2,1-*b*](1,3)-benzothiazoles.

The method for producing 1,3,4-triazolo[2,1-b]benzothiazole out of a solution of trimethyl orthofonnate, 2 hydrazinobenzothiazole, with silica gel in the presence of xylene was described by Latrofal and his team [53].



Scheme 13. Synthesis of derivatives of 1,3,4-triazolo[2,1-b]benzothiazole compounds

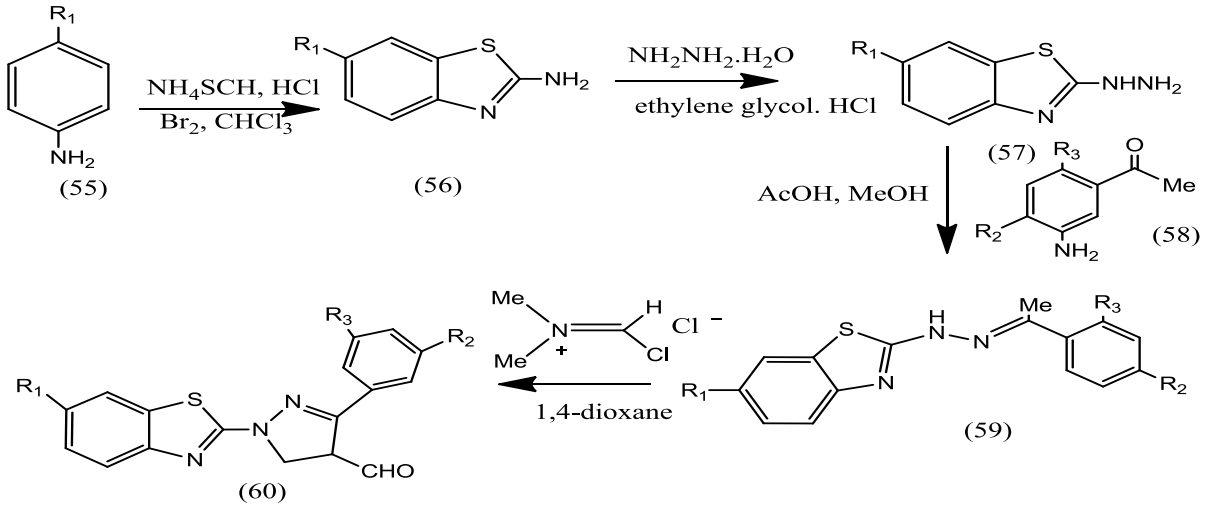
The necessary bioactive analogues of 2-aminobenzothiazole can also be obtained through a sequential synthesis of multistep using readily available reagents and chemicals. Compounds of tricyclic imidazo[2,1-b][1,3] benzothiazolones were synthesized by Galochkina et al. in two phases, as shown in (scheme 14). The by-products are chemicals with potential medical use [54].



R_2 = 4– BrC6H4, 4-NCC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$

Scheme 14. Synthesis of imidazo[2,1-*b*](1,3)benzothiazolones derivatives.

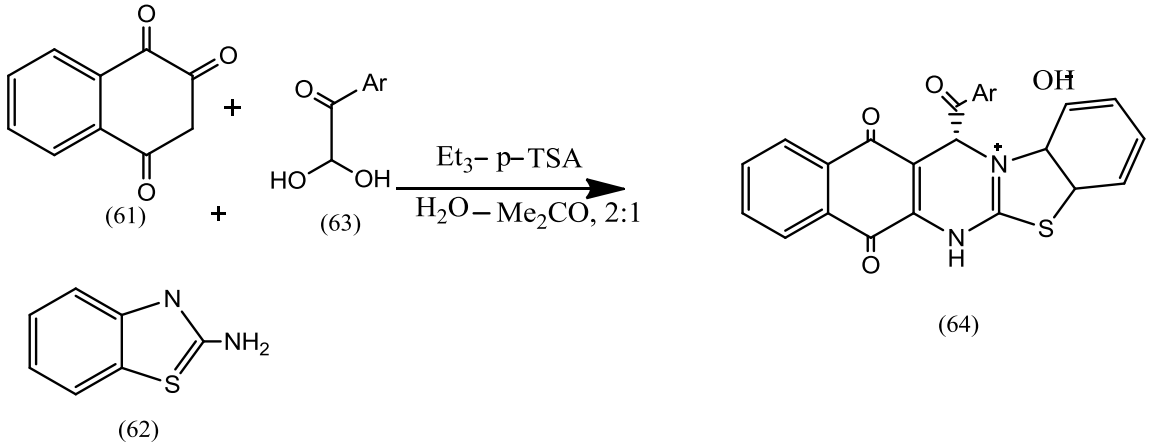
In the initial stage, the substance 2-aminodihydrobenzothiazol-7-ones were produced in situ by reacting 1,3-diketones using thiourea as well as bromine; subsequent steps included alkylation of the diketones using heteroaromatic-alpha halo ketones as well as intra-molecular cyclization. To synthesizeseries of benzothiazole-4-formylpyrazoles series, Bala et al. investigated that a multistep procedure for synthesis of benzothiazole derivatives (Scheme 15) [55].



R_1= H.OMe, F, Cl, Br
R_2= H,F, Br
R_3= H, Me, Cl, Br

Scheme 15. Synthesis of derivatives of benzothiazole-4-formylpyrazoles compounds.

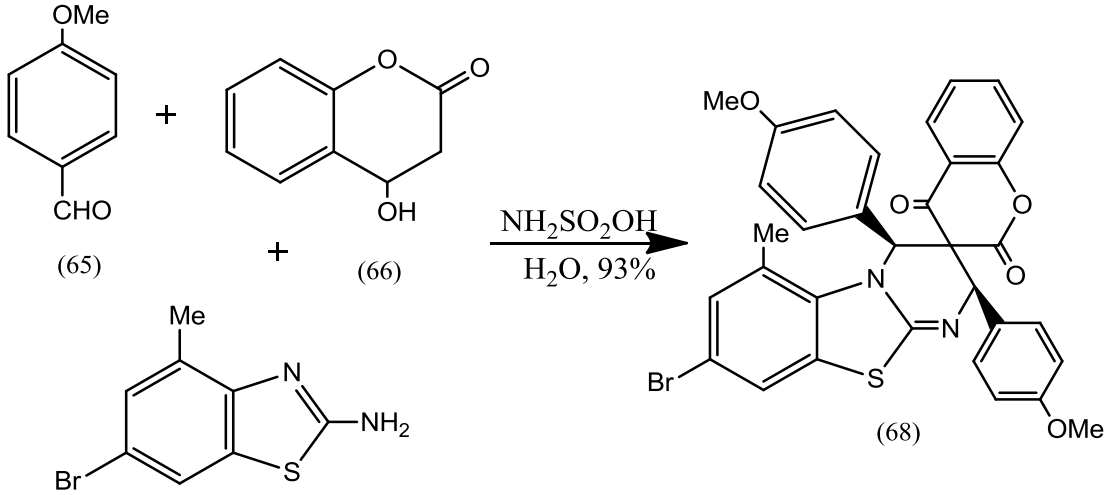
An approach was employed by the Nouri et al who catalyzed the synthesis of 2-aminobenzothiazole, the compound 2-hydroxy-1,4-naphthoquinone, as well as arylglyoxal monohydrates reacted at room temperature in the presence of Et_3N. (p-TSA– Et_3N). The mild reactions are readily present catalysts, straightforward isolation procedures as well as a high yield of compound (64) (78-84%) all attribute to the technique's ecological safety and efficacy [56].



(61) (62) (63) (64)

Scheme 16. Synthesis of derivatives of 2-hydroxy-1,4-naphthoquinone compounds.

Kumar et al. designed a multi-step process to make spiroheterocycle scaffolds with bioactive properties. Sulfamic acid was used to create a pseudo reaction between 4-hydroxycoumarin, 2-amino-6-bromo-4-methylbenzothiazole as well as 4-methoxybenzaldehyde in under 10 minutes, with a 93% output of the final products (Scheme 17). Synthesis of a second aldehyde compound with a unit of 2-aminobenzothiazole and Diels-Alder reactions of precursors are all components of the process. With a 92% yield and a 21-minute response time, ethanol had also been found tobe an effective solvent for this reaction [57].

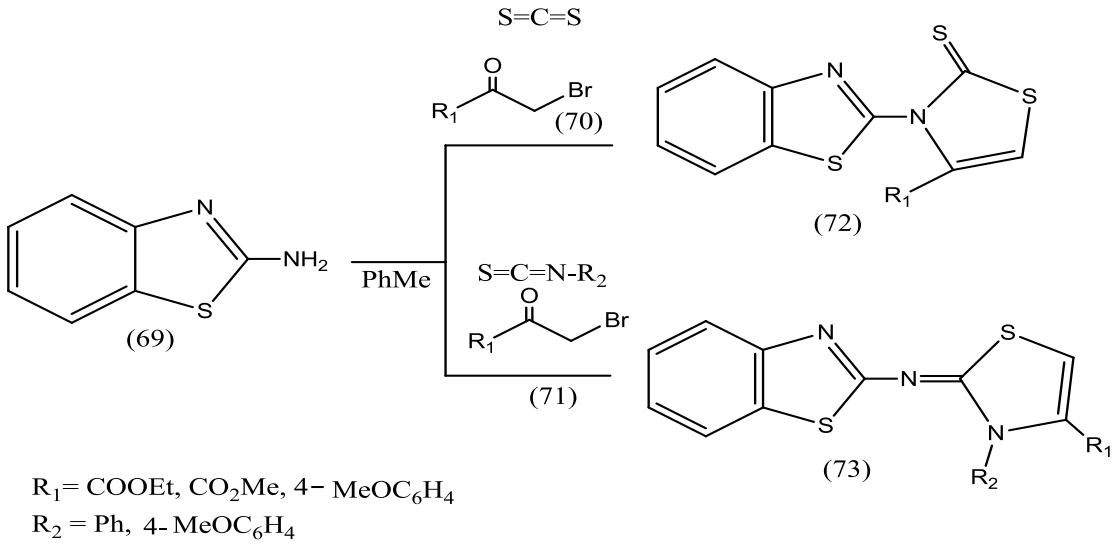


(65) (66) (67) (68)

Scheme 17. Synthesis of various derivatives of spiroheterocycle scaffolds.

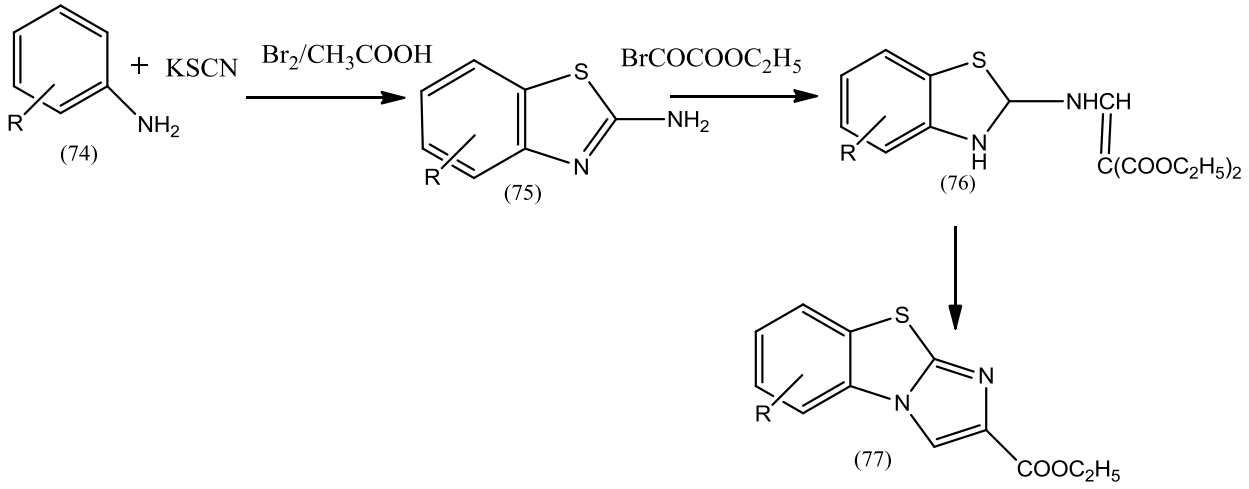
By adjusting 2-aminobenzothiazole as for various halo lactate probable alkyl-2-chloroacetylacetone as well as bromo ketone in the involvement of sulphide nucleophiles such as carbon disulfide as well as aryl isothiocyanate, Arab-Salmanabadi reported the production of twenty derivatives of bisthiazoles, a number of the active ingredients of which resulted in excellent returns near about 70-90%. The formation of Bisthiazoles entails the following steps: the introduction of carbon disulfide in to the 2-aminobenzothiazole, followed by the

condensation polymerization of the adduct initiation with alpha-halo carbonyl group, the enolization action of the precursor formed, as well as the cyclization reaction with abolishment of H_2O [58].



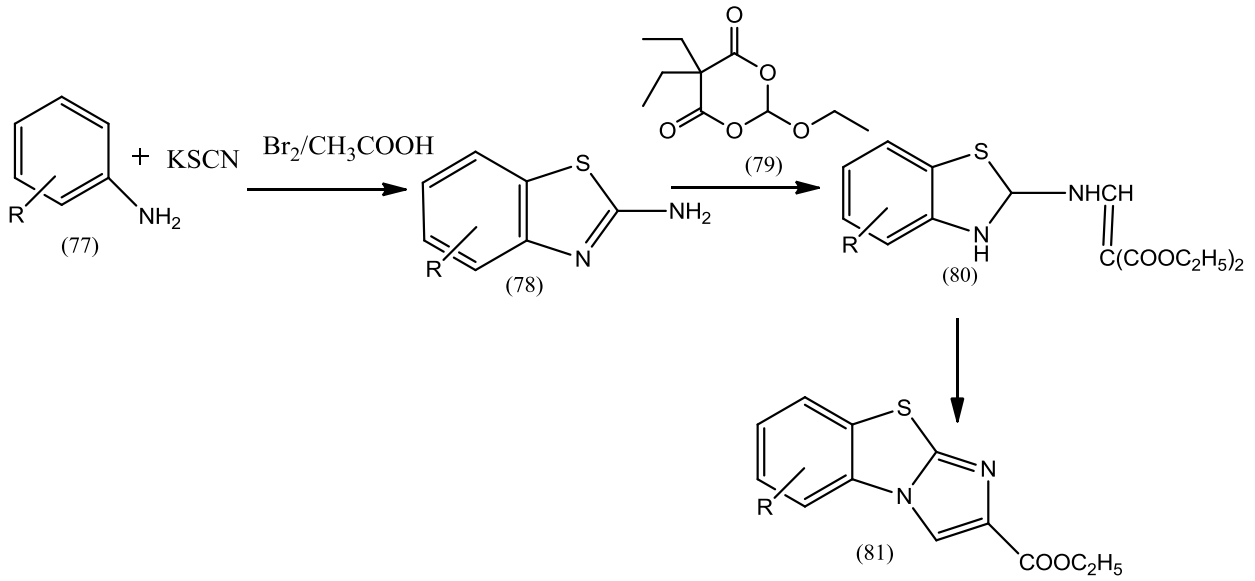
Scheme 18. Synthesis of various derivatives of Bisthiazoles compounds.

The synthesis of altered 2-ethoxycarbonylimidazo[2,1-b] benzothiazoles using aniline as well as potassium thio cyanate by employing acetic acid, bromine, as well as dimethyl formamide was reported by Trapani G et al. These compounds have anticancer action [59].



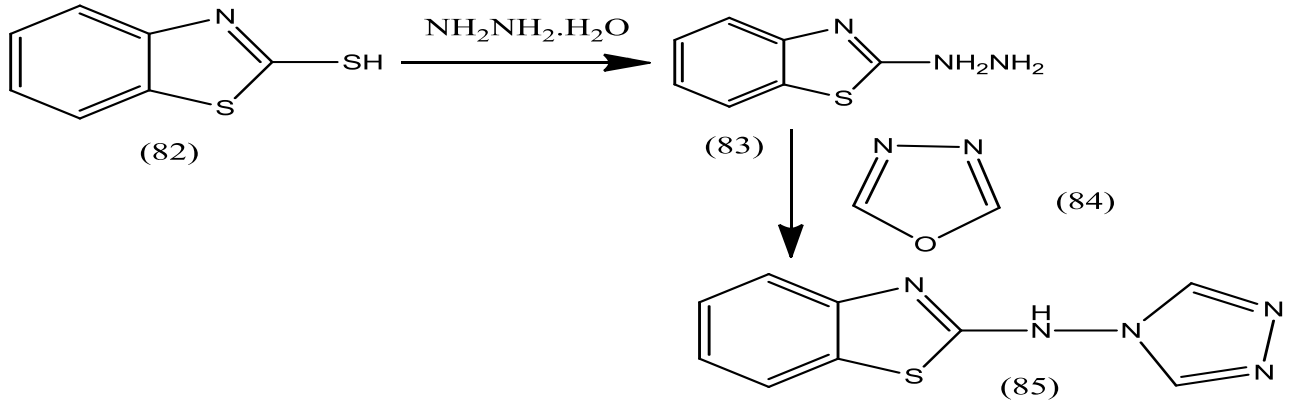
Scheme 19. Synthesis of various derivatives of Bisthiazoles compounds.

The synthesis of pyrimidine derivatives of benzothiazol-4-ones from different substituted anilines as well as potassium thiocynate there in involvement of acetic acid, bromine, and diethyl (ethoxymethylene) malonate was revealed by Trapanil G et al. (scheme 19) [60].



Scheme 20. Synthesis of various derivatives of 3-(ethoxycarbonyl)-4Hpyrimido[2,1-b]benzothiazol-4-ones compounds.

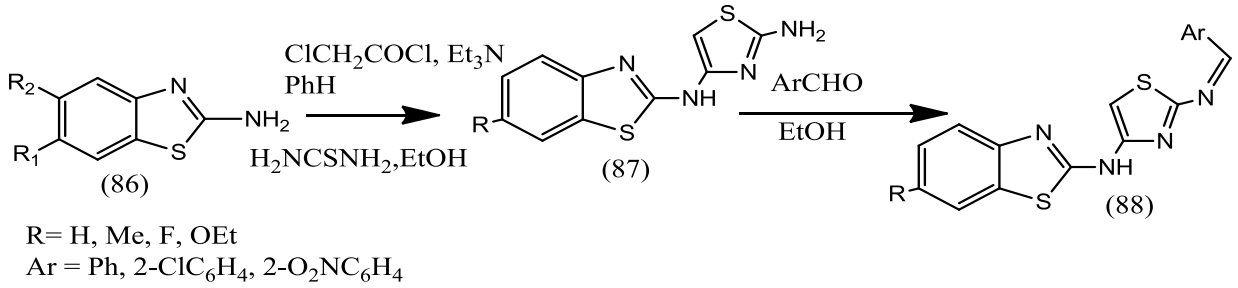
Both 5-chloro-2-mercaptobenzothiazole as well as 2-mercaptobenzothiazole (captax) were shown to be useful precursors for synthesizing 2-hydrazinobenzothiazole derivatives by Tarik and his team. With the help of reflux and reaction of the obtained derivative products of 2-hydrazinobenzothiazole well with oxadiazoles throughout water-free pyridine, as depicted in (Scheme 21), a sequence of unconventional 1,2,4-triazoles near about nine dependents on the benzothiazol-2-amine have been produced in better yields [61].



Scheme 21. Synthesis of derivatives of 2-hydrazinobenzothiazole compounds.

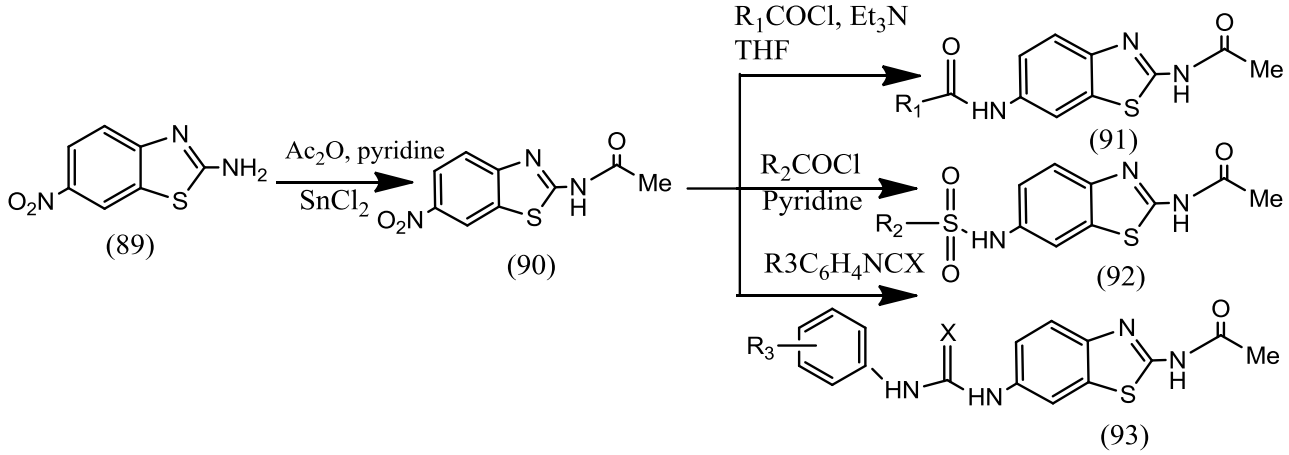
Amnerkar and colleagues tried a strategy in which entire steps in the biosynthetic pathways of amines as well as their Schiff bases included the acylation of 2-aminobenzothiazoles to compounds chloroacetyl chloride in the presence of dry PhH, acylation cyclization product to thiourea in the presence of absolute ethanol, and reactions of amines to numerous aromatic compounds (Scheme 22). While, near about twenty compounds were produced with yields

ranging from 58 to 79%. These compounds were discovered to have antihelmintic, antifungal and antibacterial action [62].



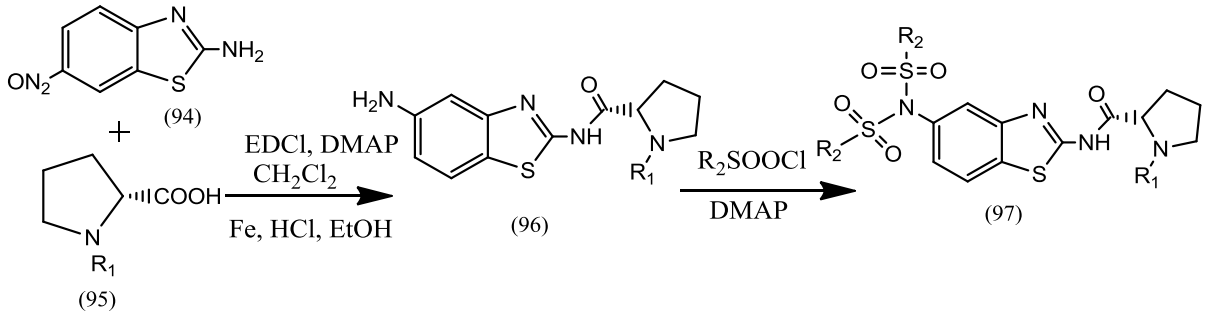
Scheme 22. Synthesis of Schiffs bases and compounds.

Scientists have created various 2-aminobenzothiazole derivatives substituted to 6-amido groups with higher anti-inflammatory activity, particularly from compositions of 2-amino-6-nitrobenzothiazole substances were generated by acylation of a substance 2-amino-6-nitrobenzothiazole using Ac_2O in pyridine presence including conversion of nitro group and within acylation byproduct by $SnCl_2$ in water as the solvent, and replacing of hydrogen present in amino group by acyl, sulfonyl or thiocarbamide structures. (Scheme 23) [63].



Scheme 23. Synthesis of derivatives of 6-*N*-functionalized associated 2-aminobenzothiazoles.

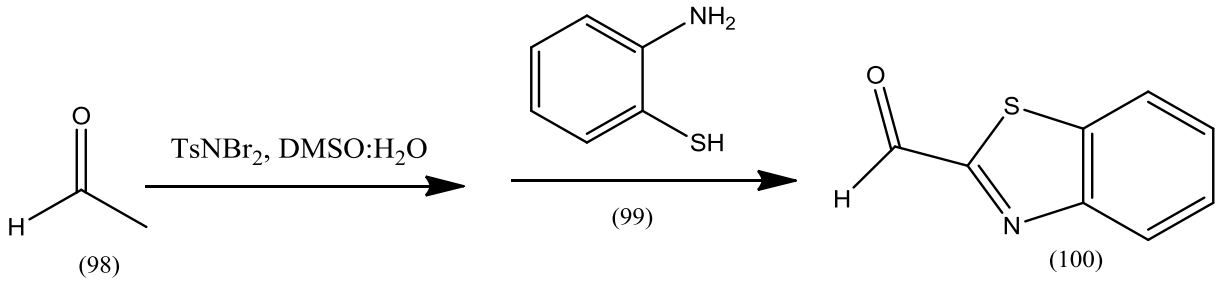
Liu et al. synthesizedvarious derivatives of disulfonamide. Near aboutsix derivatives relying on 2-amino-6-nitrobenzothiazole. To do this, proline triggered by DMAP has been present in the first stage of the reaction. Acetamide was produced after the nitro group being reduced (Fe/HCl), and it was further sulfonylated there at amino substituents (Scheme 24) [64].



R_2 = $Ph_2(3,4)$-FC_6H_4, 2-MeC_6H_4, 4-EtC_6H_4, 2-NOC_6H_4

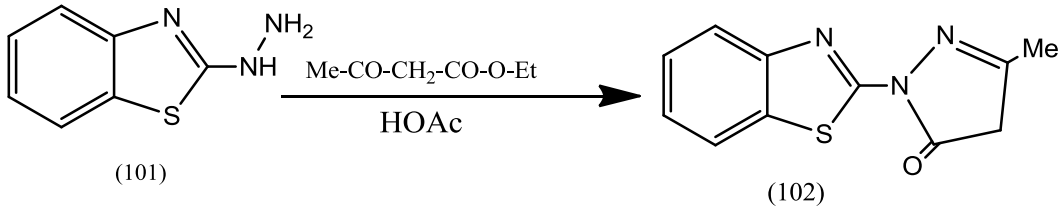
Scheme 24. Synthesis of derivatives of disulfonamide benzothiazole derivatives.

Loukrakpam as well as coworkers have created an effective one pot method for synthesising 2-acylbenzothiazoles from that of aryl methyl ketones as well as 2-aminobenzenethiol inside a metal-free environment. According to the framework, the aromatic ketones will be first regarded to $TsNBr_2$ in solvent DMSO at temperature 65°C for 3 hours to produce the intended products. The crude resulting mixture is then regarded with 2-aminobenzenethiol such as through condensation, oxidative dehydrogenation and Michael addition sequence (Scheme 25) [65].



Scheme 25. Synthesis of derivatives of benzo[d]thiazole-2-carbaldehyde

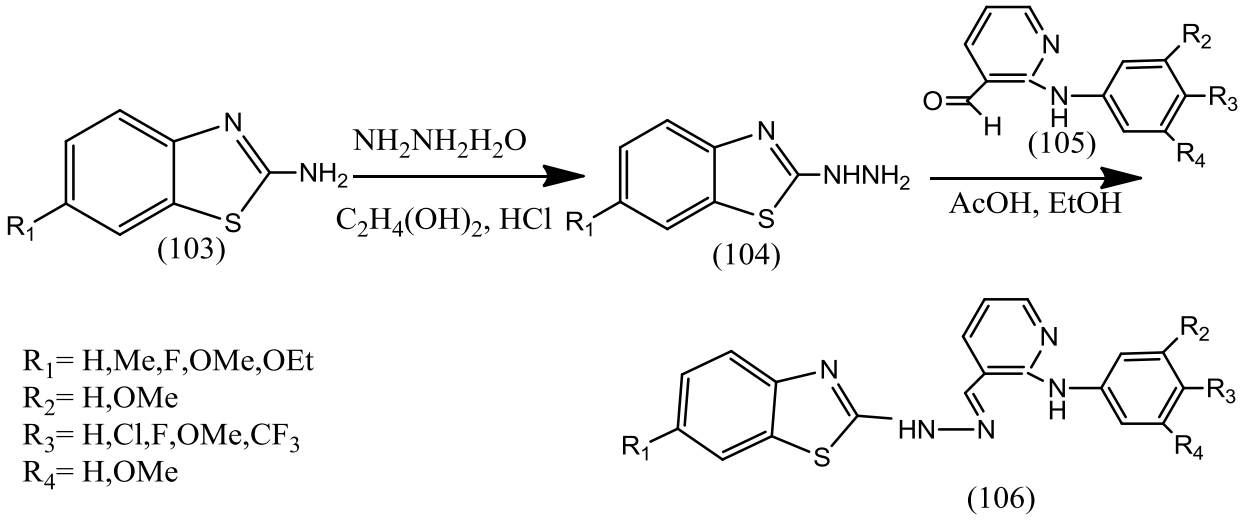
Deshmukh et al prepared 2-hydrazinobenzothiazole molecules in the devoid of a solvent using microwave. As compared to traditional heating, microwave irradiation allows the synthesis of compounds of 2-hydrazinobenzothiazole as well as other molecules to occur in a shorter time and produce a higher yield [66].



Scheme 26. Synthesis of derivatives of 1-(benzo[d]thiazol-2-yl)-3-methyl-1H-pyrazol-5(4H)-one.

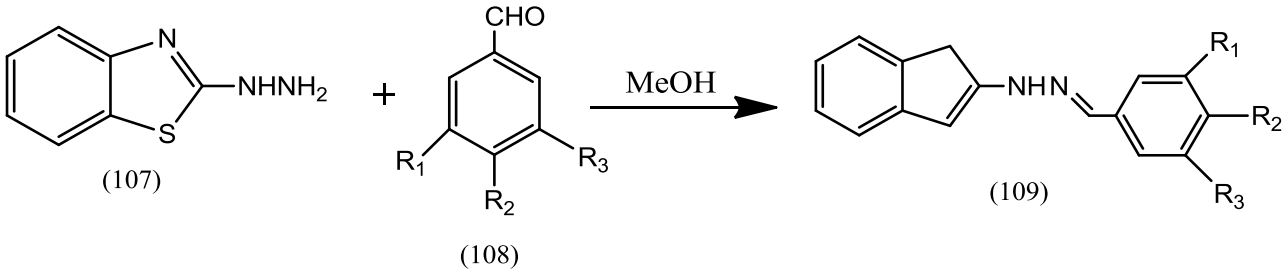
These hydrazine molecules replaced the amino group of 2-aminobenzothiazole, enabling for the production of a multitude of hydrazones with well-understood chemistry. The molecule of 6-substituted 2-hydrazinobenzothiazoles was produced by reacting corresponding 2-aminobenzothiazoles to the compounds hydrazine hydrate followed by treatment to multiple 2

(arylamino)nicotinealdehydes. (Scheme 27). Antiproliferative characteristics are included in the products. The compounds benzothiazole with aniline, all pharmacophores, can have electron-acceptor as well as electron-donor heteroatoms. Compounds with electron-donating groups in compound of benzothiazole remnants as well as the electron acceptor groups in the aniline aromatic rings had the best anticancer activity [67].



Scheme 27. Synthesis of derivatives of benzothiazole hydrazones by using 2-anilinopyridyl groups.

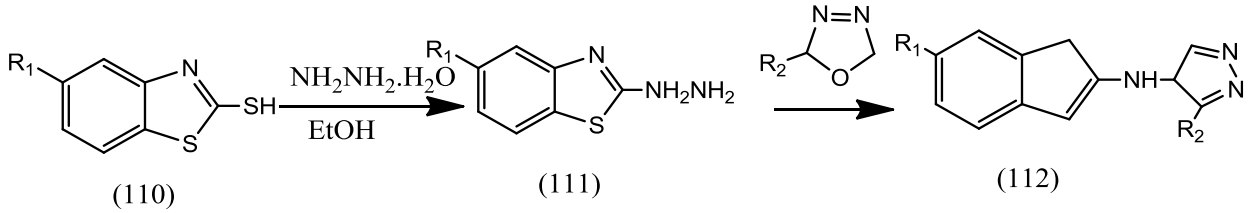
One further case in point is the creation of 2-hydrazinobenzothiazole, which is used in antimalarial drug production (Scheme 28). The framework link in benzothiazole substitution hydrazones was investigated, and it was discovered that the nitrogen, sulphur consisting of five-membered rings in the substituted benzothiazole hydrazones might be responsible for the antimicrobial activity [68].



Scheme 28. Synthesis of derivatives of benzothiazole hydrazones by using 2-anilinopyridyl groups.

Cyclic reaction of derivatives of aniline products to bromine as well as ammonium thiocyanate, followed by hydrazinolysis of the compounds of 2-aminobenzothiazoles, resulted in derivatives

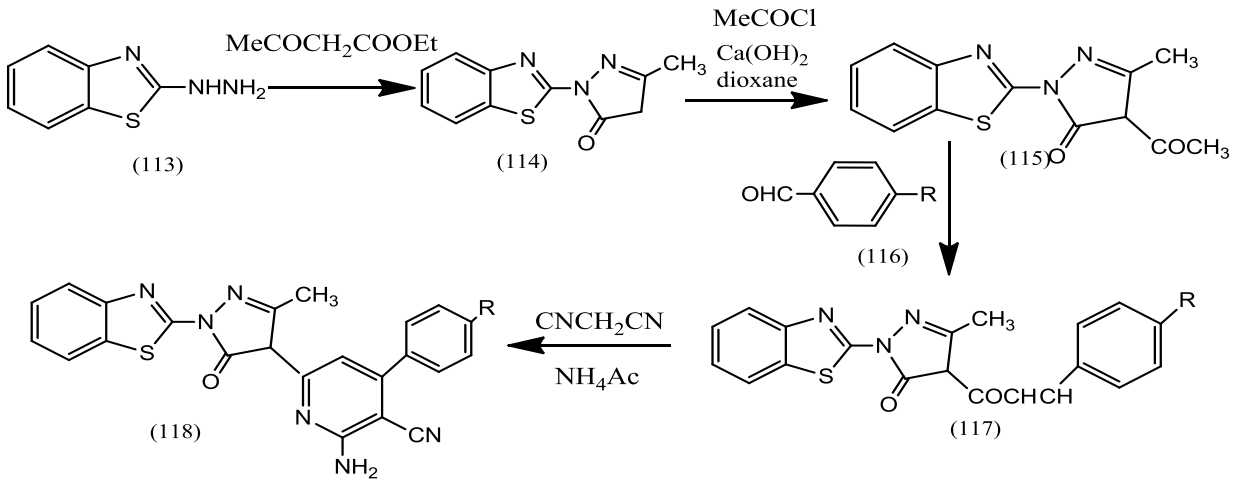
of 2-hydrazinylbenzothiazoles with alteration at position number 6, that were then crystallised with that of aromatic ketones and via alcohol to produce numerous derivatives of benzothiazole hydrazones. In 65% to 85% of the cases, the reactions of Vilsmeier-Haack transformed hydrazones into desirable products [69].



R_2= $PhOCH_2$, 4 $ClC_6H_4OCH_2$, 2,4-$Cl_2C_6H_3OCH_2$,PhOCH(Me)
R_1= H

Scheme 29. Synthesis of derivatives of benzothiazole-triazole compounds.

As more than just a result, 2-aminobenzothiazole and its derivatives have one promising synthetic future in the production of a diverse variety of heterocyclic structures, including spirocyclic as well as fused molecules. Recent study in this area have made great success in terms of discovering new benzothiazolium chemicals that are strong candidates for medications with varied biological functions. Both position and substituents nature in a benzothiazole substituent's aromatic rings, as well as the heterocycles which is formed by the presence of amino group derivatization of a primary amine, could have a major influence upon the action [70].

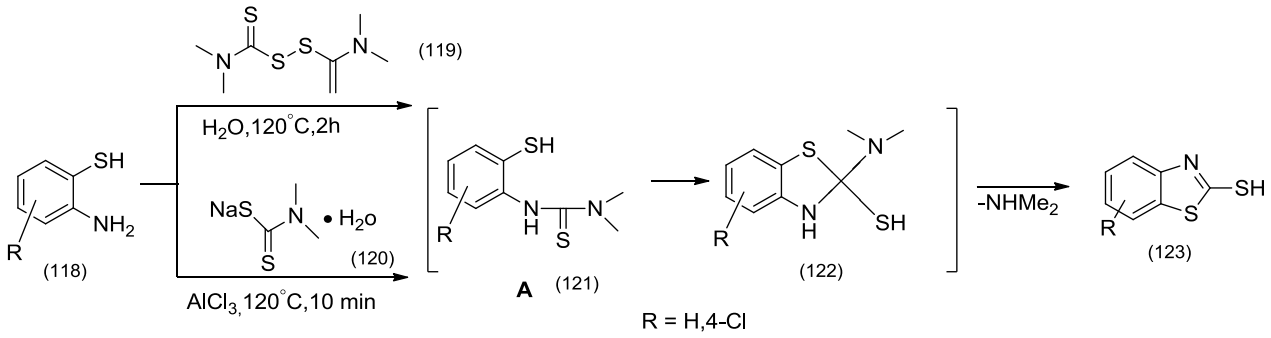


R= H, Cl, OCH_3, OH, NO_2

Scheme 30. Synthesis of derivatives of 2-aminonicotine nitriles from the benzothiazole derivatives.

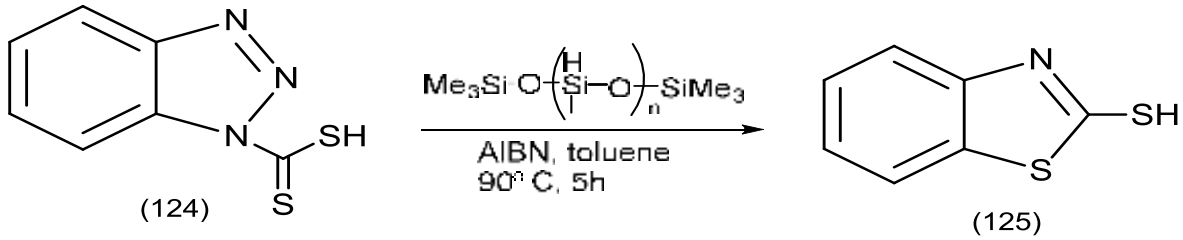
An efficient, simple, catalyst-free technique for producing precursors of possibly physiologically active compounds of 2-mercaptobenzothiazole derivatives in good yields was devised by

combining 2-aminothiophenols with water with tetramethylthiuram disulfide in such an oil bath (Scheme 31). Another alternative altered technique employed sodium dithiocarbamate in solution of DMF as a reactant as well as $AlCl_3$ as a catalyst. This reaction appears to proceed through the intermediary production of thiourea, that undergoes intramolecular cyclization, resulting in the removal of dimethylamine as well as the creation of the desired product [71].



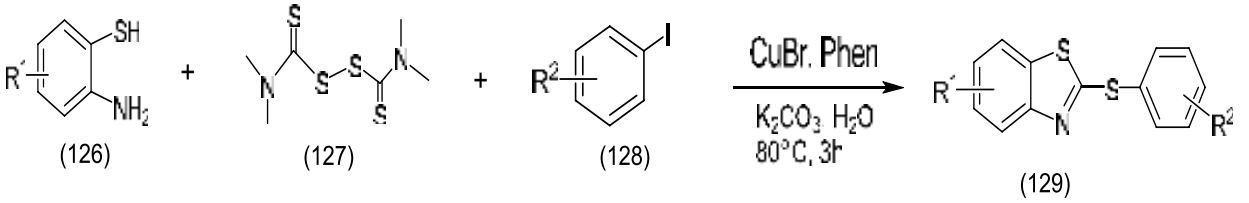
Scheme 31. Synthesis of 2-mercaptobenzothiazole derivatives from tetramethylthiuram disulfide.

The opening of ring of the 5 membered benzotriazole into the compound of aryl 1H-1,2,3-benzotriazole1-carbodithioates with consequent cyclization were done in the presence of an initiator using polymethylhydrosiloxane (PMHS) as well as the solvent as well as the reagent (Scheme 32). Formerly, the very hazardous tributyltin hydride n-Bu_3SnH was utilized in this process. The utilization of PMHS, a byproduct of synthesis of silicone, renders this method green as well as practicable, and it can be regarded an industrialized way to manufacture benzothiazoles [72].



Scheme 32. Synthesis of Mercaptobenzothiazoles from derivatives of N-thioacylbenzotriazoles

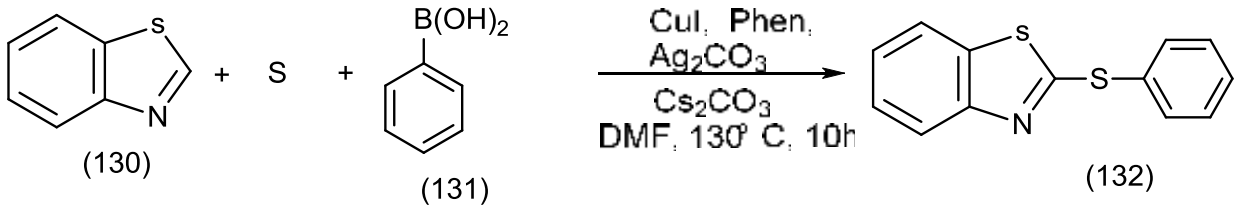
The in situ inter- as well as intramolecular reaction of o-aminothiophenols with that of tetramethylthiuram disulfidecauses the formation of the equivalent 2-mercaptobenzothiazoles, that were then intermolecularly coupled with Iodobenzenes. Amongst some of the catalysts of copper tested, CuBr at 80-degree Celcius was determined as the best temperature for the reaction. Several catalysts, including such Co, Fe and Ni, were ineffectual. The Synthetic 2-mercaptobenzothiazolederivatives with Cl, F, Br in the aryl ring groups were produced in great yield (76-84%). As a result, the procedure is economically valuable and beneficial in chemical chemistry due to the employment of low-cost catalysts, the simple ligands, water as that of solvent, as well as a mild reaction frequency [73].



R^1= H, R_2=Cl

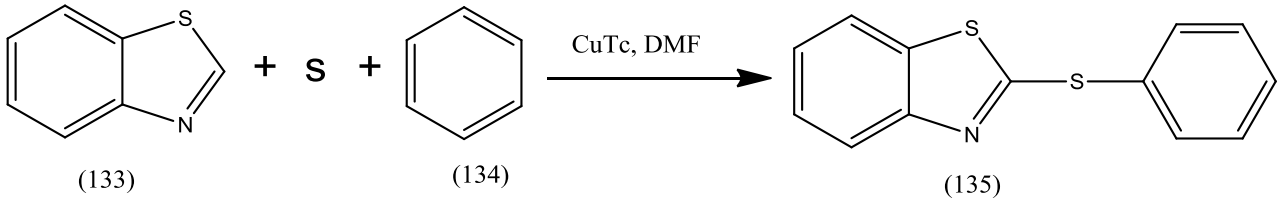
Scheme 33. Synthesis of 2-arylthiobenzothiazoles fromtetramethylthiuram disulfide, 2-mercaptobenzothiazole derivatives and Iodo benzene derivatives.

The outcome of a CuI-catalyzed the reaction of one-pot of benzothiazoles, sulphur, and aryl boronic acids was demonstrated to be highly dependent on the type of the oxidizing agent (Scheme 34) With a variety of oxidants tested, no response or even only small traces of the desired product were achieved. Of the several silver salts, Ag_2CO_3 had the maximum oxidative activity. Even though atom-economic as well as ecologically pure, above that the methodologies of assembling 2-mercaptobenzothiazoles such as through direct derivatization of the C2-H bond have drawbacks including such response temperatures reaching 120–140-degreeCelcius, the utilization of stoichiometric ratio of catalysts of copper, a powerful oxidant, as well as, in certain cases, particular ligands [74].



Scheme 34. Synthesis ofderivatives of 2-arylthiobenzothiazoles.

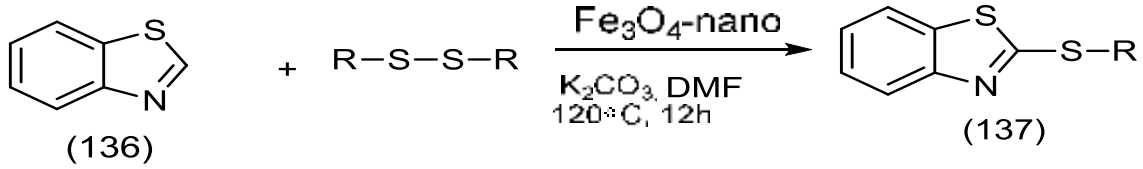
Photogenerated sulfanylation of something like the C and H connection in the derivatives of benzothiazoles by aryl(hetaryl) electrophiles with an elemental sulphur is an alternative method. The process depicted in (Scheme 35) takes place at ambient temperature under air in the copper(I) thiophene-2- carboxylate presence (CuTc) and can be utilized to synthesize a broad range of derivatives of alkyl(aryl) and hetaryl. As essential precursors in diaryl disulfides and photocatalysis are formed in situ [75].



Scheme 35. Synthesis of 2-(phenylthio)benzo[d]thiazole.

To create 2-(arylthio) benzothiazoles (Scheme 36), effective sulfanylation of something like the C2-H link in benzothiazole via disulfides employing nanosized Fe_3O_4 nanoparticles was

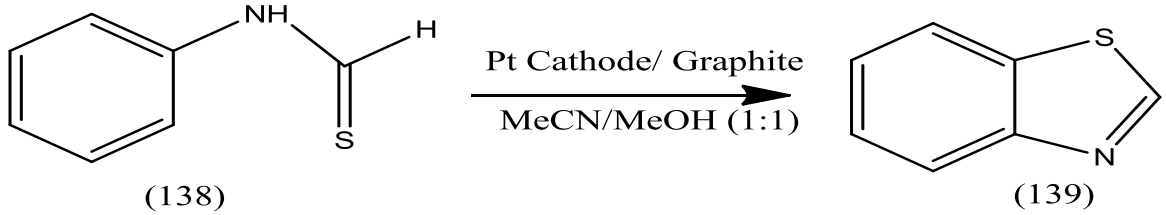
achieved. The nanoparticles powdered catalysts Fe_3O_4 appears to operate via energizing the group of disulfides through S-S bond breaking. The constituted anion is oxidized by the air's oxygen to retrieve the preliminary disulfide as well as the catalyst that are nanosized in nature. The technique's advantages include a non-inert environment, modest amounts of a highly effective catalyst, as well as recycling [76].



R = C_6H_5, 4-Me-C_6H_4, 4-NO_2-C_6H_4, 2-Cl-C_6H_4, C_4H_9

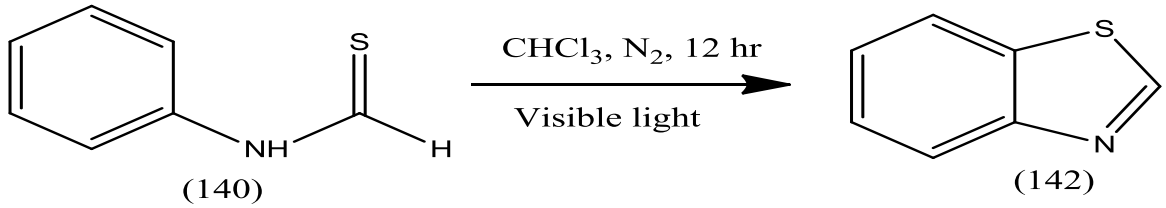
Scheme 36. Synthesis of benzothiazole derivatives by using disulfides.

Folgueiras et al. revealed that with a continuous flow electrochemical reactor, the catalyst-free as well as continuing to support biosynthetic pathway of benzothiazoles does have good to outstanding yields as well as higher efficiencies from that of arylthioamides (Scheme 37). The identified methodologies for the establishment of benzothiazoles were greatly improved by the following reaction with no requirement of a greater reactor in this technique [77].



Scheme 37. Synthesis of benzothiazole derivatives by using Pt Cathode/Graphite.

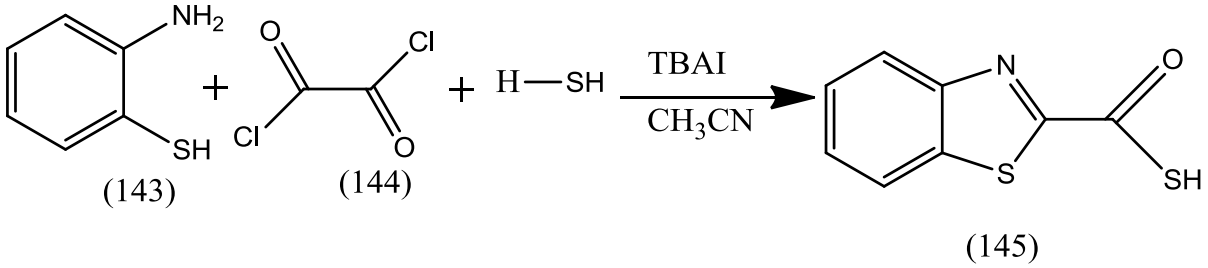
Xu and colleagues created an approach for forming intramolecular C-S bonds in substrates of aromatic in nature using visible light, as well as acquired excellent yields by cyclizing thioamide derivative products in an existence of 2,2,6,6-tetramethylpiperidine N-oxide (TEMPO) (Scheme 38). Noticeably, no additional transition-metal catalyst, photoredox catalyst as well as base is required for this photochemistry cyclization [78].



Scheme 38. Synthesis of benzothiazole derivatives from benzo[d]thiazole-2-carbothioic S-acid.

Dar and colleagues investigated reaction among oxalyl chloride, thiols and 2-aminothiophenol inside the existence of n-tetrabutylammonium iodide (TBAI) within 60°C to synthesize

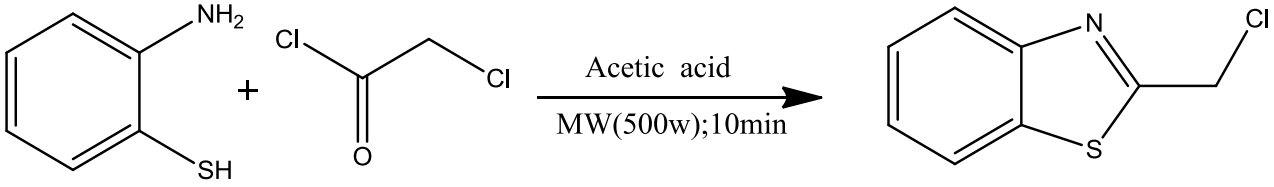
benzothiazoles compounds (Scheme 39). The current protocol favored the creation of the properties in high yields through the integrate the two of CN as well as CS bonds on a variety of substrates. The applications that are associated with this technique involves low reaction temperatures as well as excellent efficiency [79].



(143) (144) (145)

Scheme 39. Synthesis of benzo[d]thiazole-2-carbothioic S-acid.

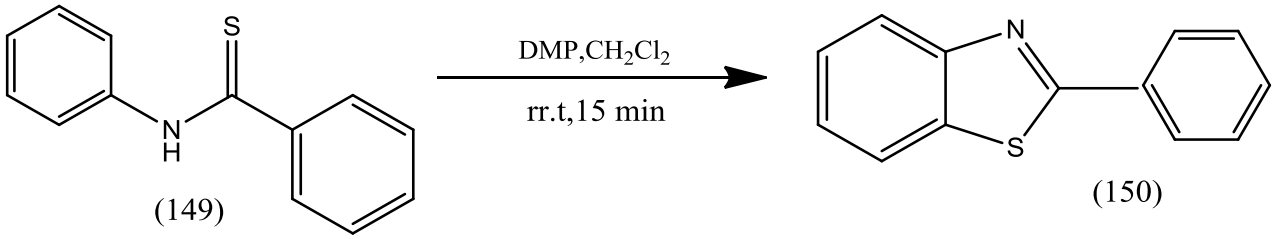
Luo and colleagues discovered that 2-chloromethyl-benzothiazole could've been synthesized by microwave-irradiating 2-aminothiophenols to chloroacetyl chloride throughout acetic acid for 10 minutes (Scheme 40). When compared to conventional techniques, microwave-related procedures were more effective and beneficial to the environment, taking less time as well as yielding a higher product [80].



(146) (147) (148)

Scheme 40. Synthesis of 2-(chloromethyl)benzo[d]thiazole.

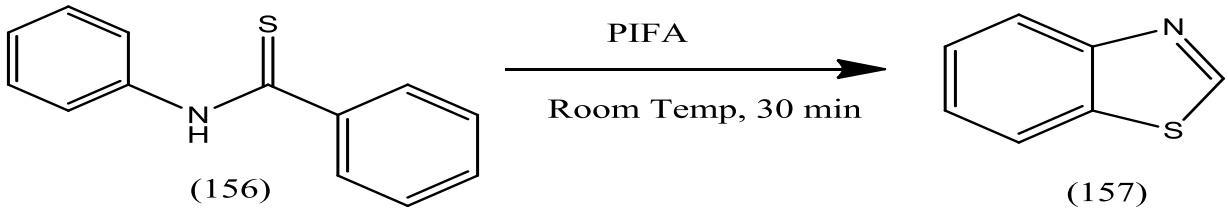
Bose and colleagues established an ecofriendly, effective, as well as rapid procedure again for biosynthetic pathways of benzothiazoles by cyclizing sulfamide substances in the presence of Dess-Martin periodinane as that of the motivator in the presence of dichloromethane as even the response solvent for about 15 minutes (Scheme 41). The method demonstrates that the similar sequences in good yield by a radical to offer the novel chemical oxybis benzothiazole which is additionally amenable to solid-phase synthesizing of combinatorial chemistry of heterocycles. The above technique offers benefits such as a shorter response cycle, high yield product [81].



(149) (150)

Scheme 41. Synthesis of 2-phenylbenzo[d]thiazole.

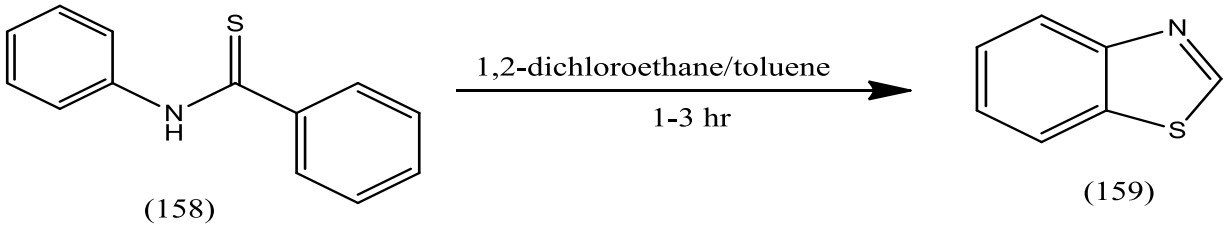
Under mild reaction conditions, Downer as well as colleagues examined a generalized method for such intramolecular condensation reaction of compounds of thiobenzamides to the compound benzothiazoles using cations of aryl radicals as the intermediates (Scheme 42). The use of phenyliodine(III) bis(trifluoroacetate) in presence of trifluoroethanol throughout acetonitrile throughout this method has been discovered to encourage cyclization in thirty minutes at room temperature to the moderate yield potential [82].



(156) (157)

Scheme 42. Synthesis of benzothiazole derivatives by using phenyliodine(III) bis(trifluoroacetate).

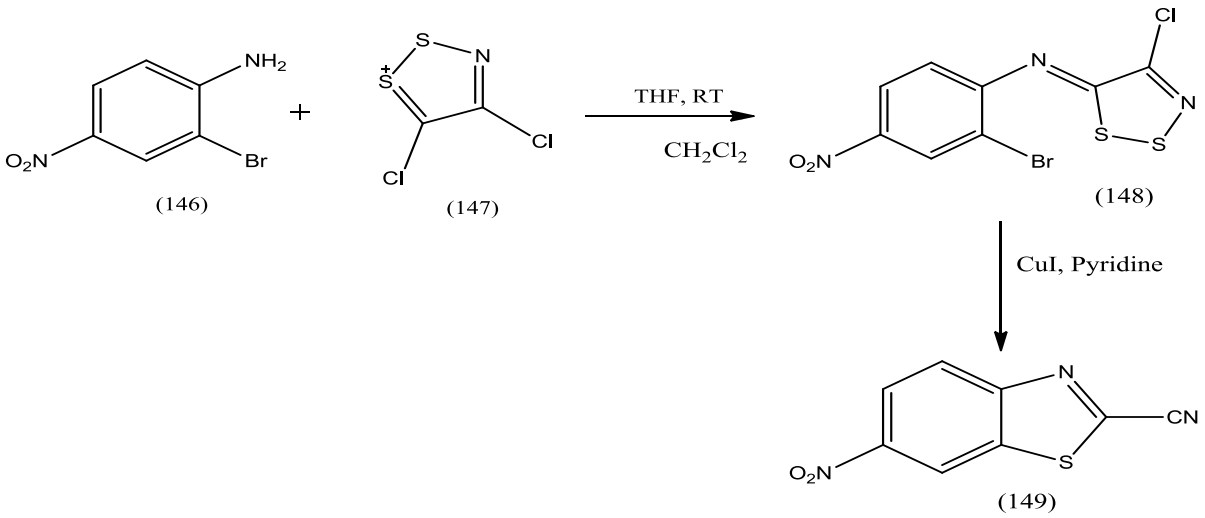
Rey and his teamreported that thioformanilides caused by chloranil under an irradiation in the presence of compound 1,2-dichloroethane as well as toluene at about 80 degree Celcius effectively synthesized 2-substituted derivatives of benzothiazoles (Scheme 43). The crucial step of the method was the abstract concept of atoms of hydrogen from the compounds of thiobenzamide by the triplet chloranil. The process was straightforward, and the heterocycles could be easily extracted from that of the reaction medium [83].



(158) (159)

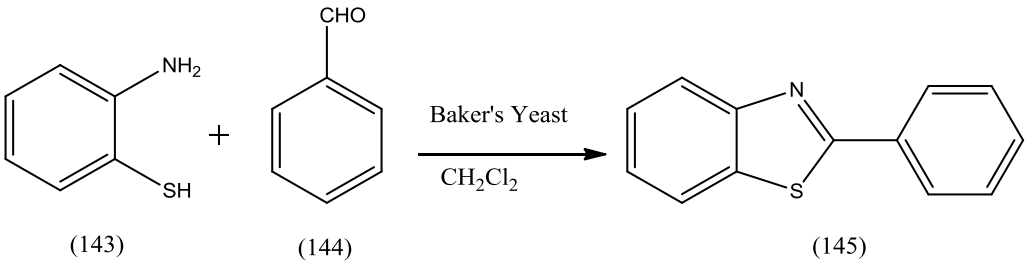
Scheme 43. Synthesis of benzothiazole derivatives by using 1,2-dichloroethane.

Appel's salt is used to react 2-Bromo-4-nitroaniline and produces the derivatives of nitroaniline compounds to make the benzothiazole core. The necessary benzothiazole could be produced by cyclizing this product (scheme 44) [84].



Scheme 44. Synthesis of derivatives of 6-nitrobenzo[d]thiazole-2-carbonitrile compounds.

Umesh R. Pratap has been capable of catalyzing the synthesis of 2-substituted analogues of benzothiazoles molecules in his laboratory by using baker's yeast that react 2-aminothiophenol using aldehydes in DCM. Mild reaction conditions can result in a yield of between good and excellent. Aldehyde , 2-aminothiophenol, with baker's yeast were combined with DCM and left to sit at room temperature for 24 hours. After that, the mixture was filtered through a layer of Celite, as well as the filtrate was vacuum-concentrated. The purified benzothiazole was obtained by recovering the solid material first from cooled liquid then crystallising it from the ethanol. Particularly well-studied are the external enzymes present in baker's yeast [85].



Scheme 45. Synthesis of derivatives of 2-phenylbenzo[d]thiazole compounds.

Conclusions

For just a long time, the mutual attraction and biology of heterocycles has been a fascinating topic for research in medicinal chemistry. A variety of heterocyclic derivatives with nitrogen as well as sulphur atoms end up serving as distinct and flexible scaffolds for investigational pharmaceutical research. Because of its diverse molecular design as well as remarkable liquid, optical, and electronic properties, means different things in different is among the most important heterocycles that has obtained overwhelmingly positive response. Despite significant progress in green methods of synthesis for benzothiazoles, the advancement of moderate reaction circumstances and inexpensive reaction systems remains a difficult problem. In the meantime, researchers must investigate the advancement of reaction structures that include various reaction conditions. Inside the future, researchers will focus on creating and perfecting efficient,

ecologically friendly, and cost-effective reaction processes to green up the existing reaction mechanism and simplify the reaction mechanism.

References

1. Doshi H, Thakkar S, Khirasariya P, Thakur MC, and Ray A: 6-tosyl-4,5,6,7-tetrahydro thieno [2,3c] pyridine-3-carboxamide analogs: synthesis, characterization, MO calculation and antibacterial activity. Appl Biochem Biotechnol 2015; 175: 1700-1709.
2. Hortan DA, Bourne GT and Symthe ML: The combinational synthesis of bicyclic privileged structures or privileged substructures. Chem Rev 2003; 103: 893-930.
3. Sana Tariq, Payal Kamboj, Mohammad Amir. Therapeutic advancement of benzothiazole derivatives in the last decennial period. Arch Pharm Chem Life Sci. 2019;352:e1800170. DOI: 10.1002/ardp.201800170
4. Ahmad K, Malik MS and Syed MAH: Therapeutic potential of benzothiazoles a patent review 2010-2014.
5. P. Raje, US20080227985 A1. 2008.
6. Y. He, Z. Liu, S. Huang, WO2008124393 A1. 2008.
7. K. G. Watson, Benzothiazole compounds, WO2009039553 A1, 2 Apr 2009.
8. C. Liu, K. Leftheris, J. Lin, US20090118272 A1. 2009.
9. J. C. Sutton, US7553854 B2. 2009.
10. M. Okaniwa, T. Takag, M. Hirose, US8143258B2. 2009.
11. J. Hassfeld, WO2010066357 A1. 2010.
12. A. D. Jordan, R. L. Desjarlais, D. J. Hlasta, M. H. Parker, C. Schubert,
13. K. B. White, WO2011075631 A1. 2011.
14. S. Booker, US7928140 B2. 2011.
15. M. Okaniwa, T. Takag, M. Hirose, EP2358689 A1. 24 Aug 2011.
16. A. Kamal, R. Shetti, P. Swapna, S. Azeeza, A. M. Reddy, I.A. Khan, S. T. Abdullah, S. Sharma, N. P. Kalia, US20120095021 A1. 2011.
17. W. Xie, B. Herbert, T. Nguyen, C. Gauss, A. Tehim, US20120101094 A1. 2012.
18. E. Alebrt, E. Bacque, C. Nemecek, A. Ugolini, S. Wentzler, US8546393 B2. 2013.
19. F. Z. Dorwald, US20130079340 A12. 2013.
20. W. E. Klunk, C. A. Mathis, J. Y. Wang, US20130004422 A1. 2013.
21. R. Dahl, A. Y. Lee, C. Kho, R. J. Hajjar, WO2014036242 A3. 2013.
22. P. Raje, W. E. Klunk, C. A. Mathis, Jr., Y. Wang, US8691185 B2. 2014.
23. C. Schmitt, J. P. Surivet, G. Chapoux, A. Mirre, J. Specklin,WO2016079688A1. 2015.
24. K. Chauhan, B. Kumari, WO2017025980 A3. 2017.
25. K. Thede, WO2017063966 A1. 2017.
26. Noel, S.; Cadet, S.; Gras, E.; Hureau, C. The benzazolesca_old: A SWAT to combat Alzheimer's disease. Chem. Soc. Rev. **2013**, 42, 7747–7762.
27. Prajapati, N.P.; Vekariya, R.H.; Borad, M.A.; Patel, H.D. Recent advances in the synthesis of 2-substituted benzothiazoles: A review. RSC Adv. **2014**, 4, 60176–60208.

28. Kok, S.H.L.; Gambari, R.; Chui, C.H.; Yuen, M.C.W.; Lin, E.;Wong, R.S.M.; Lau, F.Y.; Cheng, G.Y.M.; Lam,W.S.; Chan, S.H.; et al. Synthesis and anti-cancer activity of benzothiazole containing phthalimide on human carcinoma cell lines. Bioorg. Med. Chem. **2008**, 16, 3626–3631.
29. Luo, B.; Li, D.; Zhang, A.L.; Gao, J. Synthesis, antifungal activities and molecular docking studies of benzoxazole and benzothiazole derivatives. Molecules. **2018**, 23, 2457.
30. Bradshaw, T.D.; Westwell, A.D. The development of the antitumour benzothiazole prodrug, Phortress, as a clinical candidate. Curr. Med. Chem. **2004**, 11, 1009–1021.
31. Heo, Y.; Song, Y.S.; Kim, B.T.; Heo, J.N. A highly regioselective synthesis of 2-aryl-6-chlorobenzothiazoles employing microwave-promoted Suzuki–Miyaura coupling reaction. Tetrahedron. Lett. **2006**, 47, 3091–3094.
32. Vicini, P.; Geronikaki, A.; Incerti, M.; Busonera, B.; Poni, G.; Cabras, C.A.; Colla, P.L. Synthesis and biological evaluation of benzo [d] isothiazole, benzothiazole and thiazole Schi_ bases. Bioorg. Med. Chem,.**2003**, 11, 4785–4789.
33. Siddiqui, N.; Rana, A.; Khan, S.A.; Haque, S.E.; Alam, M.S.; Ahsan, W.; Ahmed, S. Anticonvulsant and Toxicity Evaluation of Newly Synthesized 1-[2-(3, 4-disubstituted phenyl)-3-chloro-4-oxoazetidin-1-yl]-3-(6-substituted-1, 3-benzothiazol-2-yl) ureas. Acta Chim. Slov. **2009**, 56, 462–469.
34. Danzeisen, R.; Schwalenstoecker, B.; Gillardon, F.; Buerger, E.; Krzykalla, V.; Klinder, K.; Schild, L.; Hengerer, B.; Ludolph, A.C.; Dorner-Ciossek, C.; et al. Targeted antioxidative and neuroprotective properties of the dopamine agonist pramipexole and its nondopaminergic enantiomer SND919CL2x [(+) 2-amino-4, 5, 6, 7-tetrahydro-6-Lpropylamino-benzathiazole dihydrochloride]. J. Pharmacol. Exp. Ther. **2006**, 316, 189–199.
35. Rajeeva, B.; Srinivasulu, N.; Shantakumar, S.M. Synthesis and Antimicrobial Activity ofSome New 2-Substituted Benzothiazole Derivatives. J. Chem. **2009**, 6, 775–779.
36. Su, X.; Vicker, N.; Ganeshapillai, D.; Smith, A.; Purohit, A.; Reed, M.J.; Potter, B.V.L. Benzothiazole derivatives as novel inhibitors of human 11_-hydroxysteroid dehydrogenase type 1. Mol. Cell. Endocrinol. **2006**, 248, 214–217.
37. Praveen, C.; Nandakumar, A.; Dheenkumar, P.; Muralidharan, D.; Perumal, P. Microwave-assisted one-pot synthesis of benzothiazole and benzoxazole libraries as analgesic agents. J. Chem. Sci. **2012**, 124, 609–624.
38. Nagarajan, S.R.; Crescenzo, G.A.; Getman, D.P.; Lu, H.F.; Sikorski, J.A.; Walker, J.L.; Mcdonald, J.J.; Houseman, K.A.; Kocan, G.P.; Kishore, N.; et al. Discovery of novel benzothiazole sulfonamides as potent inhibitors of HIV-1 protease. Bioorg. Med. Chem. **2003**, 11, 4769–4777.
39. Dogruer, D.S.; Ünlü, S.; ¸Sahin, M.F.; Yqilada, E. Anti-nociceptive and anti-inflammatory activity of some (2-benzoxazolone-3-yl and 2-benzothiazolone-3-yl) acetic acid derivatives. Il Farmaco. **1998**, 53, 80–84.

40. Jimonet, P.; Audiau, F.; Barreau, M.; Blanchard, J.C.; Boireau, A.; Bour, Y.; Coleno, M.A.; Doble, A.; Doerflinger, G.; Huu, C.D.; et al. Riluzole series. Synthesis and in vivo "antiglutamate" activity of 6-substituted-2-benzothiazolamines and 3-substituted-2-imino-benzothiazolines. J. Med. Chem. **1999**, 42, 2828–2843.
41. Dong Heng Shan., Quan Bin., Chai Er Feng. *Et al*.; The syntheses and crystal structure of novel 5-methhyl-3-substituted-1, 2, 4-triazolo [3,4- b]benzothiazoles; Journal of molecular structure, 2002; 41-47.
42. Karaca Ş, Osmaniye D, Sağlık BN, Levent S, Ilgın S, Özkay Y, Karaburun AÇ, Kaplancıklı ZA, Gundogdu-Karaburun N. Synthesis of novel benzothiazole derivatives and investigation of their enzyme inhibitory effects against Alzheimer's disease. RSC advances. 2022;12(36):23626-36.
43. Zaki M. E. A., Fadda A.A.,Samir K. *et al*.; Nitriles in organic syntheses : Synthesis of pyrido[2,1-b]benzothiazole and polyfunctionally substituted pyridines.Chemistry of heterocyclic compounds; 2003; 39; 1242-1248.
44. Batista, R.M.; Costa, S.P.; Raposo, M.M.M. Synthesis of new fluorescent 2-(20 , 2"-bithienyl)-1, 3-benzothiazoles. Tetrahedron Lett. 2004, 45, 2825–2828.
45. Stetinova J., Kada R., Lesko J. *et al.* Synthesis and reaction of some 2-aminobenzothiazoles; Molecules 1996; 1; 251-254.
46. Guo, H.Y.; Li, J.C.; Shang, Y.L. A simple and efficient synthesis of 2-substituted benzothiazoles catalyzed by H2O2 /HCl. Chin. Chem. Lett. 2009, 20, 1408–1410.
47. Golovanov, A.A.; Bekin, V.V.; Zlotskii, S.S.; Kunavin, Y.A.; Vologzhanina, A.V.; Gusev, D.M.; Bunev, A.S. A new example of cyclization of (*e*)-1,5-diarylpent-2-en-4-yn-1-ones to functionalized furan derivatives. *Chem. Heterocycl. Compd.* **2015**, *51*, 929–932.
48. Kumar, A.; Maurya, R.A.; Ahmad, P. Diversity oriented synthesis of benzimidazole and benzoxa/(thia) zole libraries through polymer-supported hypervalent iodine reagent. J. Combin. Chem. 2009, 11, 198–201.
49. Tran, C.; Flamme, B.; Chagnesa, A.; Haddad, M.; Phansavath, P.; Ratovelomanana-Vidal, V. A Practical Access to Functionalized Alkyl Sulfinates. *Synlett* **2018**, *29*, 1622–1626.
50. Zhang, B.; Kang, Y.; Yang, L.; Chen, X. A S-Arylation of 2-Mercaptoazoles with Diaryliodonium Triflates under Metal-Free and Base-Free Conditions. *Chem. Select.* **2016**, *1*, 1529–1532.
51. Mampuys, P., C. R. McElroy, J. H. Clark, R. V. A. Orru, and B. U. W. Maes. "Thiosulfonates as emerging reactants: synthesis and applications." *Advanced Synthesis & Catalysis* 362, no. 1 (2020): 3-64.
52. Khan, Takallum, and Ritu Yadav. "Month 2018 Silica-Supported P2O5 as an Efficient Heterogeneous Catalyst for the One Pot Synthesis of 3-Amino-imidazo [2, 1-b](1, 3) benzothiazole under Green Conditions." (2018).
53. Latrofal A., Carottil A. *et al*;. Synthesis and benzodiazepine receptor binding of some imidazo and pyrimido[2,14]benzothiazoles; European Journal of Medicinal Chemistry 1996; 31; 575-587.

54. Galochkina, A. V.; Bollikanda, R. K.; Zarubaev, V. V.; Tentler, D. G.; Lavrenteva, I. N.; Slita, A. V.; Chirra, N.; Kantevari, S. *Arch. Pharm. Chem. Life Sci*. **2019**, *352*, e1800225.
55. Nouri, A.; Marjani, A. P.; Khalafy, J. *J. Heterocycl. Chem.* **2019**, *56*, 2912.
56. Bala, R.; Kumari, P.; Sood, S.; Kumar, V.; Singh, N.; Singh, K. *J. Heterocycl. Chem*. **2018**, *55*, 2507.
57. Kumar, M.; Arya, A. K.; George, J.; Arya, K.; Pardasani, R. T. *J. Heterocycl. Chem*. **2017**, *54*, 3418.
58. Arab-Salmanabadi, S. *J. Heterocycl. Chem*. **2017**, *54*, 3600.
59. Trapani G., Franco M. *et al*.; Synthesis, in vitro and in vivo cytotoxicity, and prediction of the intestinal absorption of substituted 2-ethoxycarbonyl-imidazo [2, 1-b] benzothiazoles; European Journal of Pharmaceutical Sciences. 2001; 14; 209–216.
60. Trapani G., Franco M. *et al*; Synthesis and benzodiazepine receptor binding of some 4Hpyrimido [2,1-b] benzothiazol-4-ones; European Journal of Medicinal Chemistry 1992; 27; 39-44.
61. Tariq, S.; Alam, O.; Amir, M. *Arch. Pharm. Chem. Life Sci*. **2018**, *351*, e1700304.
62. Amnerkar, N.D.; Bhongade, B.A.; Bhusari, K.P. Synthesis and biological evaluation ofsome 4-(6-substituted-1,3-benzothiazol-2-yl)amino-1,3-thiazole-2-amines and their Schiff bases. *Arab. J. Chem.* **2015**, *8*, 545–552.
63. Sadhasivam, G.; Kulanthai, K. Synthesis, characterization, and evaluation of anti-inflammatory and anti-diabetic activity of new benzothiazole derivatives. *J. Chem. Pharm. Res.* **2015**, *7*, 425–431.
64. Liu, X.; Dong, Z.-B. A Review on Domino Condensation/Cyclization Reactions for the Synthesis of 2-Substituted 1,3-Benzothiazole Derivatives. *Eur. J. Org. Chem.* **2020**, *4*, 408–419.
65. Loukrakpam, D.C.; Phukan, P. $TsNBr_2$ Mediated Synthesis of 2-Acylbenzothiazoles and Quinoxalines from Aryl Methyl Ketones under Metal Free Condition. *Chemistry Select.* **2019**, *4*, 3180–3184.
66. Deshmukh MB, Jagtap SS and Deshmukh SA. Solvent free accelerated synthesis of 2-hydrazinobenzothiazole derivatives using microwave. Journal of Indian Chemical Society 2006; 83: 1055-1057.
67. Sultana, F.; Saifi, M.A.; Syed, R.; Mani, G.S.; Shaik, S.P.; Osas, E.G.; Godugu, C.; Shahjahanb, S.; Kamal, A. Synthesis of 2-anilinopyridyl linked benzothiazole hydrazones as apoptosis inducing cytotoxic agents. *New J. Chem.* **2019**, *43*, 7150–7161.
68. Tariq, S.; Alam, O.; Amir, M. Synthesis, p38α MAP kinase inhibition, anti-inflammatory activity, and molecular docking studies of 1,2,4-triazole-based benzothiazole-2-amines. *Arch. Pharm. Chem. Life Sci.* **2018**, *351*, e1700304.
69. Mahdi, M.F.; Al-Smaism, R.F.; Ibrachim, N.W. Synthesis, characterization and antibacterial evalution of novel 2-mercaptobenzothiazole derivatives bearing 2-aminonicotinonitrile moiety. *Eur. J. Chem.* **2016**, *7*, 8–13.

70. Liu, X.; Liu, M.; Xu, W.; Zeng, M.-T.; Zhu, H.; Chang, C.-Z.; Dong, Z.-B. An environmentally benign and efficient synthesis of substituted benzothiazole-2-thiols, benzoxazole-2-thiols, and benzimidazoline-2-thiones in water. *Green Chem.* **2017**, *19*, 5591–5598.
71. Yadav, M.S.; Singh, A.S.; Agrahari, A.K.; Mishra, N.; Tiwari, V.K. Silicon Industry Waste Polymethylhydrosiloxane-Mediated Benzotriazole Ring Cleavage: A Practical and Green Synthesis of Diverse Benzothiazoles. *ACS Omega* **2019**, *4*, 6681–6689.
72. Guo, T.; Wei, X.-N.; Zhu, Y.-L.; Chen, H.; Han, S.-L.; Ma, Y.-C. Copper-Catalyzed One-Pot Synthesis of Chalcogen-Benzothiazoles/Imidazo[1,2-*a*] pyridines with ulfur/Selenium Powder and Aryl Boronic Acids. *Synlett* **2018**, *29*, 1530–1536.
73. Gandeepan, P.; Mo, J.; Ackermann, L. Photo-induced copper-catalyzed C–H chalcogenation of azoles at room temperature. *Chem. Commun.* **2017**, *53*, 5906–5909.
74. Rafique, J.; Saba, S.; Frizon, T.E.A.; Braga, A.L. Fe_3O_4 Nanoparticles: A Robust and Magnetically Recoverable Catalyst for Direct C–H Bond Selenylation and Sulfenylation of Benzothiazoles. *Chem. Select.* **2018**, *3*, 328–334.
75. Azam, Mohammed Afzal, and Bhojraj Suresh. "Biological activities of 2-mercaptobenzothiazole derivatives: a review." *Scientia pharmaceutica* 80, no. 4 (2012): 789-824.
76. Wu, Feng-Ling, Waleed M. Hussein, Benjamin P. Ross, and Ross P. McGeary. "2-Mercaptobenzothiazole and its derivatives: syntheses, reactions and applications." *Current Organic Chemistry* 16, no. 13 (2012): 1555-1580.
77. Folgueiras-Amador, A.A.; Qian, X.Y.; Xu, H.C.; Wirth, T. Catalyst-and supporting-electrolyte-free electrosynthesis of benzothiazoles and thiazolopyridines in continuous flow. Chem. Eur. J. 2018, 24, 487–491.
78. Xu, Z.M.; Li, H.X.; Young, D.J.; Zhu, D.L.; Li, H.Y.; Lang, J.P. Exogenous photosensitizer-, metal-, and base-free visible-light-promoted C–H thiolation via reverse hydrogen atom transfer. Org. Lett. 2018, 21, 237–241.
79. Dar, A.A.; Shadab, M.; Khan, S.; Ali, N.; Khan, A.T. One-pot synthesis and evaluation of antileishmanial activities of functionalized S-alkyl/aryl benzothiazole-2-carbothioate scaffold. J. Org. Chem. 2016, 81, 3149–3160.
80. Luo, B.; Li, D.; Zhang, A.L.; Gao, J. Synthesis, antifungal activities and molecular docking studies of benzoxazole and benzothiazole derivatives. Molecules. 2018, 23, 2457.
81. Bose, D.S.; Idrees, M. Hypervalent Iodine Mediated Intramolecular Cyclization of Thioformanilides: Expeditious Approach to 2-Substituted Benzothiazoles. J. Org. Chem. 2006, 71, 8261–8263.
82. Downer-Riley, N.K.; Jackson, Y.A. Conversion of thiobenzamides to benzothiazoles via intramolecular cyclization of the aryl radical cation. Tetrahedron. 2008, 64, 7741–7744.
83. Rey, V.; Soria-Castro, S.M.; Argueello, J.E.; Peñéñory, A.B. Photochemical cyclization of thioformanilides by chloranil: An approach to 2-substituted benzothiazoles. Tetrahedron Lett. 2009, 50, 4720–4723.

84. Chi B. Vu, Jill C. Milne, David P. Carney, Jeffrey Song, Wendy Choy, Philip D. Lambert, David J. Gagne, Michael Hirsch, Angela Cote, Meghan Davis, Elden Lainez, Nekeya Meade, Karl Normington, Michael R. Jirousek, Robert B. Perni, Discovery of benzothiazole derivatives as efficacious and enterocyte-specific MTP inhibitors. J. Bioorg. & Med. Chem. 2009; 19: 1416-1420.
85. Umesh R. P., Jyotirling R. M., Dhanaji V. J., Ramrao A. M.. J. Bakers' yeast catalyzed synthesis of benzothiazoles in an organic medium Tetrahedron Letters, 2009; 50: 1352-1354.