Airo International Research Journal
Peer Reviewed Multidisciplinary Indexed Journal
ISSN: 2320-3714
Volume:23 Issue:3 December 2020

A STUDY ON THE DEVELOPMENT OF SOME NOVEL BENZOTHIAZOLES ON HETEROCYCLIC RING DERIVATIVES BY EVALUATING THE TARGETED COMPOUNDS THROUGH THE HETEROCYCLIC FUSED HYBRIDS MOLECULES

Dr. Usha Maroo
Professor, Department of Chemistry
SS College of Engineering, Udaipur (Raj.)

Abstract

Various heterocyclic derivatives containing nitrogen and sulfur atom fill in as an exceptional and adaptable framework for trial drug plan. Benzothiazole is an advantaged heterocyclic scaffold has a place with the family of bicyclic heterocyclic compounds sharing benzene core fused with five-membered ring thiazole. A portion of the benzothiazole derivatives with a push-pull structure are notable drug substances just as compounds reasonable as nonlinear optical materials, atomic dyads and chemo sensors. Benzothiazole, the bicyclic ring framework consists of thiazole ring fused with benzene ring. Benzothiazole moiety is little yet is fascinated by researchers in light of the distinctive biological activities by benzothiazole and their derivatives. As of late the synthesis of fused heterocyclic compounds looks for extraordinary attention of explores in the field of medicinal chemistry. Heterocycles have tremendous potential as the most promising lead molecules for the plan of new drugs. New 2-styryl benzothiazolium salts substituted on the heterocyclic ring have been integrated by the condensation of 3-alkyl-2-methylbenzothiazolium halides with 4-substituted benzaldehydes.

Keywords: Benzothiazoles, Heterocyclic ring, Derivatives, Fused, Hybrids, Molecules, etc.

1. INTRODUCTION

Various heterocyclic derivatives containing nitrogen and sulfur atom fill in as an exceptional and adaptable framework for trial drug plan. Isatin (1H-indolin-2, 3-Dione), is an endogenous Indole particle found in human (as a metabolite of adrenaline), which shows different pharmacological and biological exercises. In 1840, Erdmann and Laurent found Isatin as item coming about because of the oxidation of indigo color by nitric acid and chromic acid. Benzothiazole is one of the main heterocyclic compound, feeble base, having

shifted biological exercises and still of extraordinary logical interest now a days. They are broadly found in bioorganic and therapeutic chemistry with application in drug disclosure. Benzothiazole is a special bicyclic ring framework. Benzothiazoles are fused part rings, which contain the heterocyclic bearing thiazole. Sulfur and nitrogen atoms comprise the center structure of thiazole and numerous pharmacologically and biologically dynamic compounds. Thiazole is basically identified

With thiophene and pyridine, however in the greater part of its properties it looks like to the last mentioned.

Heterocyclic chemistry is one of the interesting parts of natural chemistry and heterocyclic compounds establish the biggest and most changed group of natural compounds. Heterocyclic compounds offer a serious level of primary variety and have colossal potential as the most encouraging molecules as lead structures for the plan of new drugs. They are natural compounds containing in any event one atom of carbon and at any rate one element other than carbon, for example, sulfur, oxygen or nitrogen and so forth inside a ring structure. Since in heterocycles, non-carbons supplant carbon atoms and are called heteroatom for example unique in relation to carbon and hydrogen. These structures (Fig.1) may involve either straightforward aromatic rings or non-aromatic rings. The heterocyclic compounds have generally a steady ring structure which doesn't promptly hydrolyze or depolymerize.

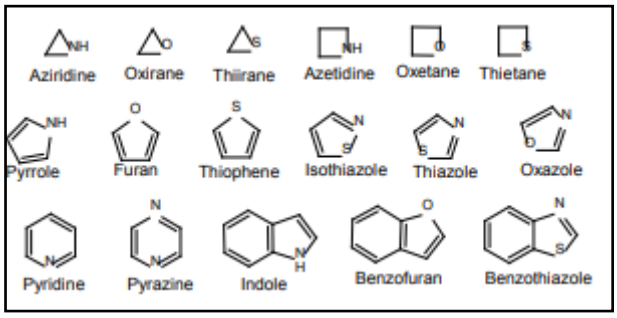


Figure 1: Structure and names of some common heterocycles

They are generally circulated in nature and are fundamental to life as they assume a critical job in the digestion of every single living cell. For instance proteins, hormones, photosensitizing shade chlorophyll, oxygen moving color hemoglobin, and hormones like kinetin, heteroauxin, serotonin and histamine along with a large portion of the sugars.

1.1 Benzothiazole

Benzothiazole (Fig. 2) is an advantaged heterocyclic scaffold has a place with the family of bicyclic heterocyclic compounds sharing benzene core fused with five-membered ring thiazole. Sulfur and nitrogen atoms include the center structure of thiazole

and various pharmacologically and biologically dynamic compounds. Benzothiazoles have promising biological profile and are anything but difficult to get to which makes this pharmacophore a fascinating moiety for exploratory drug planning.

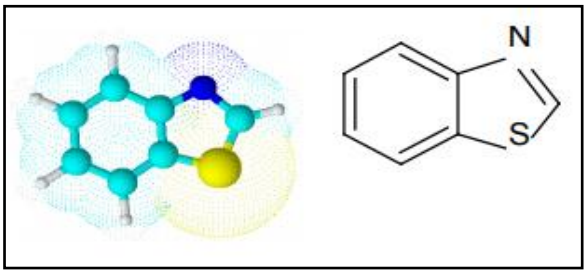


Figure 2: Benzothiazole

During the 1950s, various 2-aminobenzothiazoles were seriously concentrated as focal muscle relaxants. After at that point, therapeutic physicists have not looked into this family. Scholar's consideration was attracted to this arrangement when the pharmacological profile of Riluzole was found. Riluzole (6-trifluoromethoxy2-benzothiazolamine, Rilutek) was found to meddle with glutamate neurotransmission in biochemical, electrophysiological, and social trials.

2. N-RICH FUSED HETEROCYCLIC SYSTEMS

In every one of these fields, aromatic heterocyclic and poly-heterocyclic systems have gotten consideration in light of their improved presentation contrasted and aromatic hydrocarbons both in low molar mass and in polymer based materials. Some directly fused aromatic hydrocarbons, for example, pentacene, have demonstrated great charge transport qualities and, along with compounds containing contributor acceptor (D–A) gatherings, are among the most read classes of compounds for natural semiconductors. All things considered, higher acenes, for example, hexa-or heptacene and related compounds, experience the ill effects of significant downsides, for example, ecological precariousness, particularly under light conditions, which is dictated by their high energy HOMOs. The presentation of hetero atoms, for instance sulfur and nitrogen, demonstrated extremely viable for conquering that trouble. The conductive properties of fused aromatic hydrocarbons are identified with their redox properties as well as to strong state pressing. The overall guidelines on the methods of pressing of aromatic hydrocarbons were inferred a few years back: fused aromatic hydrocarbons are blessed with powerless H-bond donors (aromatic C–H) and feeble acceptors (π acceptor). Given the directionality of the π acceptor it isn't amazing that the essential pressing theme of fused aromatic hydrocarbons is the T contact (face-to-edge)

instead of the π stack (equal moved vis-à-vis, FF contact); accordingly, really planar graphite-like layers are not seen in the pressing of planar fused aromatic hydrocarbons, even of enormous size. Hence, the amalgamation of boundless π-stacked structures presents a difficult issue in material chemistry. The acknowledgment of boundless planar structures can be accomplished by in-plane covalent bonding (e.g., graphite, h-boron nitride) or by in-plane non-covalent bonding, yet for this situation molecules should be blessed with appropriate gatherings, appropriately situated to frame those planes by optional collaborations. Concerning these focuses, substitution of C_{Ar}–H bunches by nitrogen atoms in aromatic hydrocarbons can give a few enhancements. To begin with, pyridine-like N atoms in aromatic compounds are solid in-plane H-bond acceptors, favoring the arrangement of boundless planar layers of H-bonded molecules, through in-plane C_{Ar}-H•••N communications. Second, the more limited van der Waals range of nitrogen can bring about more limited stacking distances between the layers contrasted and those of all-carbon-containing compounds.

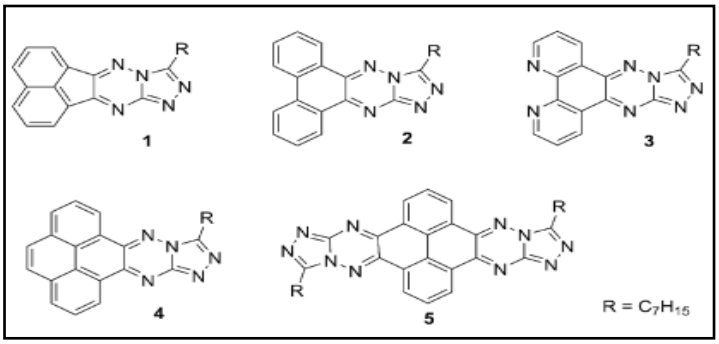


Figure 3: Chemical structures of the synthesized compounds

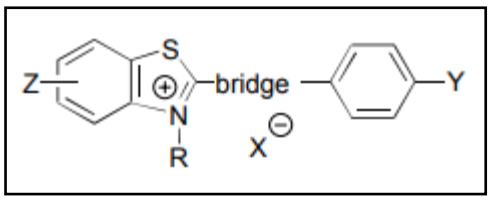
2.1 Fused heterocyclic as a potent biological agents

Heterocyclic compounds belong from therapeutically important family of natural compounds. Fused ring heterocyclic are likewise significant constituents of numerous accessible therapeutics agents. Normally heterocyclic aromatic compounds are generally circulated in creature and plant tissues. Over 90% of new drugs contains heterocyclic ring. Heterocyclic compounds have expanded biological exercises, since they are having capacity to tie reversibly to proteins. Restorative chemistry includes extraordinary utilization of heterocyclic compounds by converting them into powerful biological agents. As of late numerous specialists work to blend and screen fused heterocyclic compounds against a wide range of receptors, yielding a few dynamic compounds.

Numerous combinations of fused heterocyclic structures can be planned, to grow new substance element with adaptable physical, synthetic and biological properties. The rationale of fusion include mathematically unbending polycyclic structures which have three dimensional spatial orientation of substituent's which at last leads better biological profile because of the expanded restricting capacity . Writing audit uncovered huge biological exercises of these compounds, for example, antibacterial, anti-unfavorably susceptible, anti-inflammatory, antitumor, phsphodiesterase inhibition and insect Parkinsonism and so on Till now numerous significant revelations have been made based on rational drug development measure considering heterocyclic structure as a lead moiety.

3. SYNTHESIS OF NEW ANTIMICROBIAL BENZOTHIAZOLES SUBSTITUTED ON HETEROCYCLIC RING

A portion of the benzothiazole derivatives with a push-pull structure (conjugated framework with donor and acceptor end gatherings) are notable drug substances just as compounds reasonable as nonlinear optical materials, atomic dyads and chemo sensors. The bactericidal properties of 2-substituted benzothiazoles have been perceived for a long time, the best structures were perceived as 3-allyl and 3-propargyl benzothiazolium salts with pdialkylaminostyryl substituents. This work is a piece of the efficient investigation of biologically dynamic benzothiazole derivatives. Already, these compounds have been tried against model living being Euglena gracilis just as different microorganisms and QSAR study has been done. A new arrangement of benzothiazoles have been planned and incorporated. The underlying highlights connected with the higher action have been perceived as, Quaternary nitrogen atom in the benzothiazole; electron donor bunch Y in the p-position of the phenyl ring; allyl, propargyl or methyl bunch at the heterocyclic nitrogen.



The compounds with considerably higher action had been planned and arranged. Less attention has been paid to the impact of substituent Z in the benzene part of the heterocycle. The first arrangement of 91 compounds contained 4 compounds with Cl in position 4, seven compounds with 6-Cl, four compounds with 4-CH3 and eight with 6-CH3. The determined Free-Wilson movement contributions of these substituents are not

exceptionally high (6-Cl = 0.206; 6-CH3 = 0.235; 4-CH3 = 0.250; 4-Cl = 0.260). The biological action of compounds substituted on heterocyclic ring is increased in all cases.

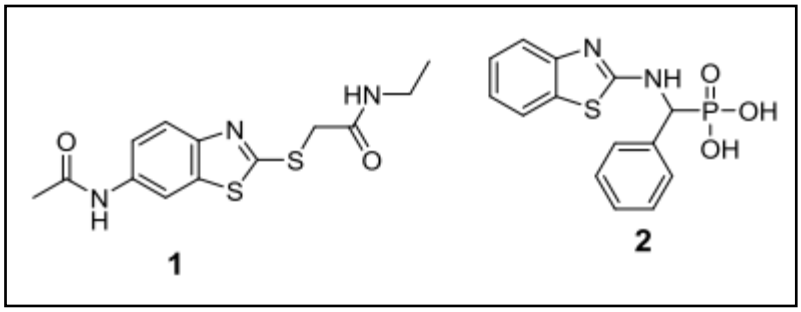
3.1 Evaluations of some novel benzothiazole derivatives as antimicrobial agents

Notwithstanding various endeavors to grow new underlying model in the quest for more powerful antimicrobials, benzothiazole still stay as one of the most adaptable class of compounds against microorganisms and hence, are valuable substructures for additional sub-atomic exploration. Benzothiazole derivatives have pulled in continuing interest in view of their changed biological exercises viz. anti-tumor, anti-tubercular, anti-malarial, anticonvulsant, antihelmintic, pain relieving, anti-inflammtory and anti-diabetic. Substituted 2-arylbenzothiazoles have arisen lately as a significant pharmacophore in non-invasive determination of Alzheimer's disease. As of late, benzothiazole derivatives have been assessed as potential amyloid-restricting analytic agents in neurodegenerative disease and as specific unsaturated fat amide hydrolase inhibitors. Azoles, specifically, 1, 2, 4-triazoles have indicated valuable antimicrobial movement. Azomethine linkage has likewise indicated a variety of biological exercises viz. antimicrobial and anti-inflammatory. These discoveries provoked us to integrate 5-[2-(1, 3-benzothiazol-2-yl-amino) ethyl]-4-(arylideneamino) - 3-mercapto-(4H)- 1, 2, 4-triazoles 6aeg having various substitutions on the aromatic ring having azomethine linkage and assessed for their antimicrobial movement.

4. BIOLOGICAL APPLICATIONS OF BENZOTHIAZOLE DERIVATIVE

In drug revelation and new chemo-therapeutics program heterocyclic systems give tremendous potential. They structure the core basis of characteristic bio-component and are likewise present in business drugs. Heterocyclic compounds have notable fundamental properties which are vital for drug revelation, for example, lipophilicity, extremity and solvency. Benzothiazole is one of the main classes of honored heterocycles found in different marine and earthly bioactive regular components. Benzothiozole are exploring to more powerful for the therapy/remedy for malignant growth. It is a genuine medical issue with a huge scope research continuing for creating novel potential antitumor moieties. Benzothiazole-2-thiol derivatives (2-((6-acetamidobenzo[d] thiazol-2-yl) thio) - N-ethyl acetamide) (1) were assessed compelling against disease causing cell and have additionally indicated antiproliferative exercises on HepG2 and MCF-7 cell line. Some newly orchestrated moieties γ-aminophosphonates consisting fluorine and benzothiazole units (((benzo[d]thiaole-2-yi amino) (phenyl-methyl) phosphonic acid) (2) were discovered to be dynamic against malignancy causing cells which have been

incorporated in ionic media with high return and short reaction time.



Benzothiazoles show a biological activity and a considerable measure of work has been done on the synthesis of new intense antibacterial and antifungal benzothiazoles. 2-(substitutedarylsulfonamido) -6-substituted (3) have detailed for their anti-bacterial activity against Bacillus subtilis, Salmonella typhi and S. looseness of the bowels.

4.1 Benzothiazole derivatives for their biological activities

Heterocyclic compounds containing oxygen, nitrogen and sulfur atoms have been distinguished to have the main biological activities. Benzothiazole is a heterocyclic aromatic compound. The compound is bicyclic which consists of a fusion of benzene with thiazole ring. It is a significant pharmacophore as benzothiazole and its novel analogs have been found to have a wide assortment of helpful activities in medicinal chemistry, for example, in anticancer, anti-HIV, antioxidant, anticonvulsant, trypanocidal agent, antitumor, antimicrobial, COX inhibitor, hypoglycemic, antidiabetic, antituberculosis, anti-urease and inhibitor of α-glucosidase.

Benzothiazole is a six-membered bicyclic heteroaromatic compound in which benzene ring is fused to the 4-and 5-positions of thiazole ring. Benzothiazoles are found in marine as well as earthbound normal compounds in an extremely less sum however have considerable pharmacological impacts, where they go about as fragrance constituents of tea leaves and cranberries which are delivered by growths named Aspergillus clavatus and Polyporus frondosus. The fission yeast Schizosaccharomyces pombe is a significant living being for the investigation of cellular biology. As eukaryotes, these yeasts can be utilized to consider measures that are conserved from yeast to people yet are missing from microorganisms, for example, organelle biogenesis or to examine the system, for example, transcription, translation and DNA replication, in which the eukaryotic components and cycles are essentially not quite the same as their bacterial partners. Different benzothiazole derivatives, for example, 2-aryl benzothiazole are according to most researchers because of its assorted structure and its uses as radioactive amyloid imaging agents. It is accounted for that the

isosters and derivatives of benzothiazole have antimicrobial activity against different kinds of gram positive and gram negative bacterias (e.g., E. coli, Pseudomonas aeruginosa, Enterobacter Staphylococcus epidermis, and so on).

5. BENZOTHIAZOLE ADAPTABLE HETEROCYCLIC NUCLEUS IN MEDICINAL CHEMISTRY

Benzothiazole, the bicyclic ring framework consists of thiazole ring fused with benzene ring. Benzothiazole moiety is little yet is fascinated by researchers in light of the distinctive biological activities by benzothiazole and their derivatives.

- **Anthelminthic activity:** the Synthesis and biological evaluation of some 4-(6-substituted-1, 3-benzothiazol-2-yl) amino-1, 3-thiazole-2-amines and their Schiff bases, and were assessed for their antibacterial, antifungal and anthelmintic activities. The outcomes demonstrated that few of the integrated aminobenzothiazole derivatives displayed critical antibacterial, antifungal and anthelmintic activities.

- **Antitumor activity:** the QSAR study and sub-atomic plan of benzothiazole derivatives and were discovered to be intense anticancer agents.

- **Antimicrobial activity:** the novel dipodal-benzimidazole, benzoxazole and benzothiazole from cyanuric chloride: Structural, photophysical and antimicrobial investigations, compounds displayed great antimicrobial activity, great warm soundness and photophysical properties with improved quantum yield.

- **Anti-inflammatory activities:** the novel 2-benzylbenzo[d] thiazole-6-sulfonamide derivatives. These compounds were screened for anti-inflammatory activity via carrageen an induced paw oedema technique in rodents at a portion of 100 mg/kg body weight. All the newly blended benzothiazole derivatives have indicated considerable anti-inflammatory activity.

6. CONCLUSION

As of late the synthesis of fused heterocyclic compounds looks for extraordinary attention of explores in the field of medicinal chemistry. Larger part of the drug compounds contains heterocyclic ring in their structures and these heterocyclic skeleton contributes fundamentally in the biological profile of drug. The heterocyclic compound assume huge job in engineered chemistry and numerous heterocyclic derivatives have been effectively combined as strong drug particle. The rational

plan of new substance elements by the fusion of two dynamic compounds is extremely viable technique towards the drug development draws near. This methodology turns out to be exceptionally helpful when both compound having synergistic or added substance activities. Lately heterocyclic compounds analogs and derivatives have pulled in wide attention because of their helpful biological and pharmacological properties. Heterocyclic chemistry is a critical part of chemistry dealing with synthesis, properties and applications of heterocycles. Heterocycles have tremendous potential as the most promising lead molecules for the plan of new drugs. New 2-styryl benzothiazolium salts substituted on the heterocyclic ring have been integrated by the condensation of 3-alkyl-2-methylbenzothiazolium halides with 4-substituted benzaldehydes. N-Rich fused-ring heterocyclic compounds containing the triazolo-triazine moiety show momentous properties both at the atomic level and in the strong state. A new class of N-rich fused heterocyclic compounds containing the triazolo-triazine moiety was combined and concentrated by cyclic voltammetry, UV/Vis spectroscopy, X-beam diffraction, and first principle computations. All the compounds show reversible or quasi-reversible reduction measures, with reduction potentials easily tunable within the class.

REFERENCES

1. Saini M, Kumar A, Dwivedi J and Singh R: A review: biological significances of heterocyclic compounds. International Journal of Pharma Sciences and Research, 2013; 4 (3): 66-70.

2. Brack W and Schirmer K: Effect-directed identification of oxygen and sulfur heterocycles as major polycyclic aromatic cytochrome P4501A-inducers in contaminated sediment. Environmental Science & Technology 2003; 37: 3062–70.

3. Parikh P, Marvaniya H and Sen J: Chemistry of bioactive tricyclic fused heterocyclic ring having one heteroatom. International Journal of Drug Development & Research 2011; 3 (2): 44-50.

4. Soni, Balram & Ranawat, Mahendra & Sharma, Rambabu & Anil, Bhandari & Sharma, Sanjay. (2010). Synthesis and evaluation of some new benzothiazole derivatives as potential antimicrobial agents. European journal of medicinal chemistry. 45. 2938-42. 10.1016/j.ejmech.2010.03.019.

5. Prajapat, Dr. (2018). Importance of Benzothiazole Motif in Modern Drug Discovery :Introduction. Modern

Approaches in Drug Designing. 1. 10.31031/MADD.2018.01.000517.

6. Fusco, Sandra & Maglione, Cira & Velardo, Amalia & Piccialli, Vincenzo & Liguori, Rosalba & Peluso, Andrea & Rubino, Alfredo & Centore, Roberto. (2016). N-Rich Fused Heterocyclic Systems: Synthesis, Structure, Optical and Electrochemical Characterization. European Journal of Organic Chemistry. n/a-n/a. 10.1002/ejoc.201501283.

7. Dolzhenko, Anton & Kalinin, Dmitrii & Kalinina, Svetlana. (2012). Fused Heterocyclic Systems with s-Triazine Ring. Part 21. Synthesis of Novel Trichloromethyl Substituted Azolo[1,3,5]triazines. HETEROCYCLES. 85. 2515. 10.3987/COM-12-12542.

8. Junaid, Ahmad & Lim, & Zhou, & Chui, & Dolzhenko, Anton. (2019). Fused Heterocyclic Systems with an s-Triazine Ring. 34. Development of a Practical Approach for the Synthesis of 5-Aza-isoguanines. Molecules. 24. 1453. 10.3390/molecules24081453.

9. El-Sayed, Hassan & Said, Said & Abd, & Amr, Abd El-Galil. (2014). Synthesis of some fused heterocyclic systems and their nucleoside candidates. Research on Chemical Intermediates. 40. 10.1007/s11164-012-1006-y.

10. Humphries, Mark & Ruprah, Parminder. (2010). ChemInform Abstract: Fused Heterocyclic Systems Having a Nitrogen Atom Common to Two or More Rings. Cheminform. 30. 10.1002/chin.199933313.

*****