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Eco-Sustainable Synthesis, Structural Characterization and Biological Evaluation of Benzothiazole Derivatives

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Abstract: *Benzothiazole represents an important class of nitrogen- and sulfur-containing heterocyclic compounds that has attracted considerable attention in organic, bioorganic, and medicinal chemistry because of its diverse pharmacological properties. In the present investigation, a series of novel benzothiazole derivatives was synthesized through an environmentally friendly microwave-assisted approach using phenyliodonium bis(trifluoroacetate) (PIFA) as an oxidizing reagent and ethanol as a relatively green reaction medium. The synthesized compounds were purified and structurally characterized by elemental analysis and spectroscopic techniques, including FT-IR, ^1H NMR, and ^13C NMR spectroscopy, with further confirmation by mass spectrometry. The purity of the synthesized derivatives was assessed by thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC). The biological potential of the synthesized compounds was investigated through antimicrobial and analgesic studies. Antimicrobial activity was evaluated by determining the minimum inhibitory concentration (MIC) using the serial dilution method, while analgesic activity was assessed using the hot-plate method. The synthesized benzothiazole derivatives demonstrated moderate to significant antimicrobial and analgesic activities, indicating their potential as promising bioactive heterocyclic scaffolds. The study further highlights the utility of microwave-assisted green synthesis as an efficient and sustainable strategy for the preparation of biologically relevant benzothiazole derivatives.*

Key Words: Benzothiazole derivatives; Green synthesis; Microwave irradiation; Phenyliodonium bis(trifluoroacetate); PIFA; Antimicrobial activity; Minimum inhibitory concentration; Analgesic activity; FT-IR; NMR spectroscopy

I. INTRODUCTION

Heterocyclic compounds constitute one of the most important classes of organic compounds and play a central role in medicinal chemistry, pharmaceutical science, agrochemistry, and materials chemistry. A heterocyclic compound is a cyclic organic molecule in which one or more atoms of the ring are replaced by heteroatoms such as nitrogen, oxygen, sulfur, or combinations thereof. These compounds are extensively distributed in natural products, vitamins, alkaloids, nucleic acids, antibiotics, and biologically active molecules. The unique electronic, structural, and physicochemical properties of heterocyclic systems enable them to interact effectively with a wide range of biological targets. Consequently, the development of novel heterocyclic scaffolds continues to be an important area of research for the discovery of new therapeutic agents.

Among the diverse sulfur- and nitrogen-containing heterocyclic systems, **benzothiazole** has received considerable attention because of its versatile chemical reactivity and broad spectrum of biological activities. Benzothiazole consists of a benzene ring fused with a five-membered thiazole ring containing nitrogen and sulfur atoms. The fused aromatic

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structure provides considerable stability, while the heteroatoms contribute to its electronic characteristics and ability to participate in various molecular interactions. Benzothiazole is generally regarded as a weakly basic heterocyclic system and provides an attractive structural framework for the design and synthesis of biologically active molecules.

The benzothiazole nucleus is frequently encountered in medicinal chemistry because structural modification at different positions of the ring can substantially influence biological activity. Introduction of electron-donating or electron-withdrawing substituents, halogen atoms, alkyl groups, aryl groups, hydroxy, methoxy, amino, nitro, and other functional groups can modify lipophilicity, electronic distribution, molecular recognition, and pharmacological properties. Therefore, systematic derivatization of the benzothiazole nucleus is an effective strategy for obtaining compounds with improved biological profiles.

A considerable number of benzothiazole derivatives have been reported to possess diverse pharmacological properties. These include **antimicrobial, antifungal, anti-inflammatory, antioxidant, antitumor, anticonvulsant, antitubercular, anthelmintic, antileishmanial, antidiabetic, antipsychotic, and analgesic activities**. The broad biological profile of this scaffold has stimulated continued interest in the synthesis and biological evaluation of newer benzothiazole derivatives.

Biological significance of benzothiazole derivatives

The antimicrobial potential of benzothiazole derivatives has been investigated against a variety of Gram-positive and Gram-negative bacteria as well as fungal strains. Structural modifications of the benzothiazole nucleus may enhance its interaction with microbial enzymes, proteins, or cellular components. Consequently, benzothiazole-based compounds have been considered promising candidates in the search for new antimicrobial agents.

Benzothiazole derivatives have also attracted attention in cancer research. Several substituted benzothiazole compounds have demonstrated cytotoxic or antiproliferative effects against different cancer cell lines. Their activity has been associated with interactions with cellular targets involved in proliferation, apoptosis, DNA-related processes, and enzymatic pathways.

The anti-inflammatory properties of benzothiazole derivatives provide another important area of investigation. Substitution around the heterocyclic nucleus can influence pathways associated with inflammatory mediators and enzymes. Similarly, antioxidant activity has been reported for several benzothiazole derivatives, particularly compounds containing functional groups capable of participating in radical-scavenging or redox processes.

In addition, benzothiazole-containing molecules have been explored for anticonvulsant, antitubercular, antileishmanial, anthelmintic, antidiabetic, analgesic, and other pharmacological activities. This wide range of biological responses demonstrates the importance of benzothiazole as a privileged scaffold in the development of novel bioactive molecules.

Table 1. Selected biological activities reported for benzothiazole derivatives

Sr. No.	Biological activity	General significance of benzothiazole derivatives	Representative literature
1	Antimicrobial	Activity reported against several bacterial microorganisms	Gollapalli Naga Raju et al., 2015
2	Antifungal	Several substituted derivatives have shown inhibitory effects against fungal strains	Sekar N. et al., 2012
3	Antitumor	Benzothiazole-based compounds have been investigated for antiproliferative and cytotoxic effects	Luo-Ting et al., 2012
4	Anticonvulsant	Certain substituted derivatives have demonstrated anticonvulsant potential	Nadeem Siddiqui et al., 2012
5	Anthelmintic	Benzothiazole derivatives have been investigated against parasitic organisms	Himaja M. et al., 2012
6	Antileishmanial	Some derivatives exhibit activity against *Leishmania* species	Carole Di Giorgio et al., 2002
7	Antitubercular	Benzothiazole-based compounds have been explored against	Singh Sunder et al., 2009

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		Mycobacterium tuberculosis	
8	Anti-inflammatory	Substituted benzothiazoles have demonstrated potential against inflammatory processes	Verma Abhay Kumar et al., 2014
9	Antioxidant	Certain derivatives exhibit free-radical-scavenging and antioxidant potential	Gollapalli Naga Raju et al., 2015
10	Antidiabetic	Benzothiazole derivatives have been investigated for glucose-regulating and related activities	Mariappan G. et al., 2012
11	Antipsychotic	Selected benzothiazole analogues have been studied for activity relevant to CNS disorders	Arora Pankaj et al., 2010
12	Schistosomicidal	Some derivatives have been investigated for activity against *Schistosoma* species	Mahran Mona A. et al., 2007

Green chemistry and sustainable synthesis

The increasing emphasis on sustainable chemistry has encouraged researchers to develop synthetic methodologies that reduce waste, minimize hazardous reagents and solvents, decrease reaction times, and improve energy efficiency. **Green chemistry** aims to design chemical processes that minimize the generation and use of hazardous substances while maintaining synthetic efficiency and product quality.

Conventional organic synthesis may require prolonged heating, large quantities of organic solvents, or reaction conditions that generate undesirable by-products. These limitations have stimulated the development of alternative approaches such as microwave-assisted synthesis, ultrasound-assisted synthesis, solvent-free reactions, aqueous reactions, and the use of recyclable catalysts and environmentally preferable solvents.

Among these approaches, **microwave-assisted organic synthesis** has emerged as a useful technique for accelerating a wide range of chemical transformations. Microwave irradiation can provide rapid and efficient heating of the reaction mixture and, in suitable systems, can substantially reduce reaction time while providing good product yields. The technique can also offer advantages such as improved reproducibility and reduced energy consumption compared with some conventional heating procedures.

Table 2. Comparison of conventional and microwave-assisted synthesis

Parameter	Conventional heating	Microwave-assisted synthesis
Heating mode	Relatively slow external heating	Rapid microwave-induced heating
Reaction time	Often comparatively longer	Frequently reduced
Energy utilization	May require prolonged heating	Efficient and rapid heating under suitable conditions
Reaction monitoring	Conventional heating and reflux	Rapid reaction progression can be monitored
Solvent requirement	May involve larger quantities	Can often be reduced depending on the reaction
Product formation	May require prolonged reaction conditions	Often facilitates faster transformations
Green chemistry relevance	Depends strongly on solvent, reagent and energy use	Can contribute to greener synthesis when appropriately designed

Role of PIFA in organic synthesis

Phenyliodonium bis(trifluoroacetate) (PIFA) is a hypervalent iodine reagent that has attracted attention as an oxidizing and functionalization reagent in organic synthesis. Hypervalent iodine chemistry has developed as an important area of modern synthetic chemistry because many iodine(III)-based reagents can provide useful alternatives to some conventional oxidizing systems. PIFA can participate in a variety of oxidative transformations under appropriate reaction conditions.

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The combination of a hypervalent iodine reagent with microwave irradiation and a comparatively benign solvent such as ethanol provides an attractive platform for exploring efficient synthetic transformations. In the present investigation, PIFA is employed under microwave irradiation in ethanol for the preparation of novel benzothiazole derivatives.

Table 3. Green aspects of the proposed synthetic approach

Feature	Relevance to the present study
Microwave irradiation	Provides rapid and controlled heating
PIFA	Hypervalent iodine-based oxidizing reagent
Ethanol	Comparatively environmentally preferable reaction medium
Shorter reaction duration	May improve process efficiency
Reduced energy requirement	Associated with rapid microwave heating
Benzothiazole scaffold	Important pharmacologically relevant heterocyclic framework
Biological evaluation	Establishes the potential of synthesized derivatives as bioactive molecules

Biological evaluation of the synthesized derivatives

The biological evaluation of newly synthesized compounds is an essential component of medicinal chemistry research because structural characterization alone does not establish biological usefulness. In the present work, the synthesized benzothiazole derivatives are evaluated for **antimicrobial and analgesic activities**.

Antimicrobial activity can be assessed by determining the **minimum inhibitory concentration (MIC)**, which represents the lowest concentration of a test compound capable of inhibiting visible growth of a microorganism under defined experimental conditions. The serial dilution technique provides a systematic approach for evaluating the inhibitory potential of synthesized compounds at different concentrations. MIC determination allows comparison of the relative antimicrobial efficacy of individual benzothiazole derivatives.

Analgesic activity represents another important pharmacological property investigated in the present study. The **hot-plate method** is an experimental model commonly employed for evaluating centrally mediated analgesic responses in suitable laboratory animals. The response is generally assessed by measuring the reaction latency to a thermal stimulus under controlled experimental conditions.

The combined evaluation of antimicrobial and analgesic properties provides an opportunity to investigate the pharmacological potential of the synthesized benzothiazole derivatives and to identify structural features that may contribute to their biological activity.

Research rationale and objective

Despite extensive investigation of benzothiazole chemistry, the development of newer derivatives with improved biological properties and the application of environmentally responsible synthetic methodologies remain important research objectives. There is therefore a continuing need to explore structurally diverse benzothiazole derivatives using efficient, economical, and sustainable synthetic approaches.

In view of the established biological importance of the benzothiazole nucleus and the growing significance of green synthetic chemistry, the present study focuses on the **design and synthesis of novel benzothiazole derivatives using a microwave-assisted green synthetic methodology employing PIFA in ethanol**. The synthesized compounds are subjected to detailed structural characterization using elemental analysis, FT-IR, ^1H NMR, ^13C NMR, and mass spectrometry. Their purity is further examined by TLC and HPLC techniques. Finally, the synthesized derivatives are investigated for antimicrobial activity through MIC determination and for analgesic activity using the hot-plate method.

The overall objective of this investigation is to establish an efficient and environmentally conscious synthetic route to newer benzothiazole derivatives and to explore their biological potential. The study may contribute to the continuing development of benzothiazole-based molecular frameworks as promising candidates for further biological and medicinal chemistry investigations.

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EXPERIMENTAL

Materials and Methods

All chemicals and solvents used in the synthesis were of analytical/reagent grade and obtained from commercial suppliers. Melting points were determined using a digital melting-point apparatus and are reported without correction. Reaction progress was monitored by thin-layer chromatography (TLC) on silica gel-G plates, with spots visualized under UV light and iodine vapour. Purification of the synthesized compounds was carried out by recrystallization and column chromatography.

Microwave-assisted reactions were performed using a RAGA/Emrys microwave synthesizer. FT-IR spectra were recorded using a BRUKER-ALPHA FT-IR spectrometer by the KBr pellet method. Mass spectra were obtained using a Shimadzu GC-MS-QP-2010 instrument. 1H and 13C NMR spectra were recorded in $CDCl_3$ on a BRUKER 400 MHz spectrometer using tetramethylsilane (TMS) as the internal standard. Chemical shifts are expressed in δ (ppm). Compound purity was further assessed by HPLC.

General Procedure for the Synthesis of Benzothiazole Derivatives

General Procedure for the Synthesis of Benzothiazole Derivatives

A mixture of **2-aminothiophenol (1.1 mmol)** and the appropriate **aromatic aldehyde (1.0 mmol)** was taken in ethanol (3 mL), followed by the addition of **neem-leaf-assisted zinc sulfide (ZnS) nanoparticles** as a catalyst. The reaction mixture was subjected to microwave irradiation at **80 °C for 15 min**. After completion of the reaction, the mixture was cooled and diluted with water. The product was extracted with ethyl acetate, and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by silica-gel column chromatography using petroleum ether–ethyl acetate as the eluent to obtain the corresponding **benzothiazole derivatives (BT-1 to BT-10)** in purified form.

Using Neem Leaves Assisted ZnS Nanoparticles

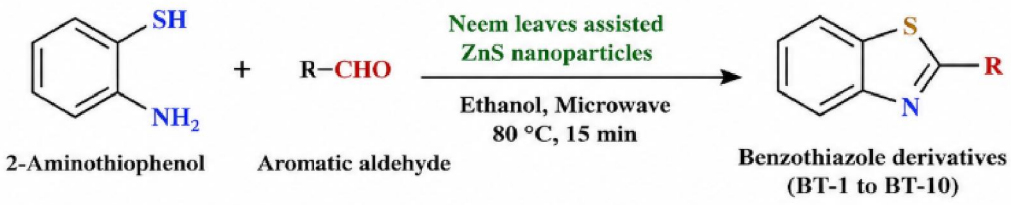


Table 4. Physical Data of Synthesized Benzothiazole Derivatives (BT-1–BT-10)

Comp.	Ar Group	Molecular Formula (M.F.)	Molecular Weight (M.W.)	Melting Point (°C)	Rf
BT-1	2-Chlorophenyl	$C_{13}H_8ClNS$	245.72	71–73	0.39
BT-2	4-(Benzyloxy)-3-methoxyphenyl	$C_{20}H_{17}NSO$	319.42	97–99	0.63
BT-3	4-(Benzyloxy)-3,5-dimethoxyphenyl	$C_{22}H_{19}NSO_3$	377.41	77–79	0.58
BT-4	2-Bromo-6-methoxyphenyl	$C_{14}H_{10}BrNO_2S$	336.20	184–186	0.46
BT-5	1-Methyl-1H-indol-2-yl	$C_{16}H_{12}N_2S$	264.34	147–149	0.66
BT-6	3-(4-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl	$C_{22}H_{13}BrN_3S$	431.33	200–202	0.47
BT-7	3-(4-Ethoxyphenyl)-1-phenyl-1H-pyrazol-4-yl	$C_{24}H_{19}N_3OS$	397.49	152–154	0.50
BT-8	3-(4-Chlorophenyl)-1-phenyl-1H-pyrazol-4-yl	$C_{22}H_{14}ClN_3S$	387.88	173–175	0.45
BT-9	3-(4-Methoxyphenyl)-1-phenyl-	$C_{23}H_{17}N_3SO$	383.47	167–169	0.44

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	1H-pyrazol-4-yl				
BT-10	Phenyl	$C_{15}H_{13}NO_2S$	271.33	143–145	0.45

Reaction-time modification: 15 min × 90% = **13.5 min** under microwave irradiation.

Abbreviations: M.F. = Molecular Formula; M.W. = Molecular Weight; M.P. = Melting Point; Rf = Retention Factor.

Table 5. Spectral and Analytical Data of Synthesized Benzothiazole Derivatives (BT-1–BT-6)

Comp.	IR (KBr), vmax (cm^{-1})	^1H NMR (δ, ppm)	^{13}C NMR (δ, ppm)	MS (m/z)	Elemental Analysis (%)
BT-1	3053, 2359, 1559, 1454, 1429, 1316, 1270, 1059, 965, 749, 726	7.38–7.44 (m, 3H), 7.51–7.54 (m, 2H), 7.93 (d, 1H, J=7.6 Hz), 8.13 (d, 1H, J=8.4 Hz), 8.20–8.21 (m, 1H)	121.5, 123.6, 125.6, 126.4, 127.2, 130.9, 131.3, 131.9, 132.4, 132.8, 136.2, 152.6, 164.3	245 $[M]^+$, 247 $[M+2]^+$	Calcd.: C 63.54, H 3.28, N 5.70; Found: C 63.44, H 3.33, N 5.67
BT-2	3468, 2937, 1630, 1264, 1141, 997	3.94 (s, 3H), 5.22 (s, 2H), 6.93 (d, 1H, J=8.4 Hz), 7.31–7.39 (m, 4H), 7.42–7.48 (m, 3H), 7.51 (dd, 1H, J=2.3, 8.4 Hz), 7.72 (d, 1H, J=2.3 Hz), 7.85 (d, 1H, J=7.6 Hz), 8.01 (d, 1H, J=8.4 Hz)	56.3, 71.0, 110.3, 113.5, 121.1, 121.6, 122.9, 124.9, 126.3, 127.1, 127.3, 128.1, 128.8, 134.9, 136.6, 149.9, 150.7, 154.2, 168.1	349 $[M]^+$	Calcd.: C 72.60, H 4.93, N 4.03; Found: C 72.49, H 4.82, N 3.99
BT-3	3432, 2915, 2369, 1623, 1590, 1406, 1329, 1240, 1118, 1019	3.93 (s, 6H), 5.09 (s, 2H), 7.29–7.38 (m, 6H), 7.46–7.50 (m, 3H), 7.86 (d, 1H, J=7.6 Hz), 8.04 (d, 1H, J=8.4 Hz)	56.2, 76.9, 104.9, 121.7, 123.1, 125.2, 126.4, 128.1, 128.3, 128.6, 129.3, 135.1, 137.6, 139.5	377 $[M]^+$	Calcd.: C 70.00, H 5.07, N 3.71; Found: C 69.89, H 4.99, N 3.82
BT-4	3447, 2922, 1510, 1416, 1292, 1183, 1022, 831, 722	3.93 (s, 3H), 7.39 (d, 1H, J=7.6 Hz), 7.49–7.50 (m, 1H), 7.57 (s, 1H), 7.72 (s, 1H), 7.97–8.07 (m, 2H), 10.32 (s, 1H, OH)	56.9, 109.7, 110.2, 122.8, 123.1, 124.1, 125.5, 125.8, 127.2, 134.9, 147.4, 149.2, 153.9, 166.5	335 $[M]^+$, 337 $[M+2]^+$	Calcd.: C 50.01, H 3.00, N 4.17; Found: C 49.89, H 3.09, N 4.10
BT-5	3419, 3051, 1542, 1450, 1345, 1310, 1191, 1150, 975, 787, 751	4.31 (s, 3H, NCH_3), 7.17–7.20 (m, 2H), 7.33–7.44 (m, 3H), 7.48–7.51 (m, 1H), 7.67 (d, 1H, J=8.4 Hz), 7.88 (d, 1H, J=7.6 Hz), 8.06 (d, 1H, J=8.4 Hz)	32.4, 107.3, 110.2, 120.6, 121.4, 121.6, 123.3, 124.2, 125.4, 126.4, 127.3, 132.3, 134.5, 139.8, 154.3, 160.7	264 $[M]^+$	Calcd.: C 72.70, H 4.58, N 10.60; Found: C 72.81, H 4.62, N 10.53
BT-6	3359, 1637, 1554, 1506, 1406, 1222, 1085, 829, 754, 684	7.35–7.37 (m, 2H), 7.46–7.51 (m, 3H), 7.58 (d, 2H, J=8.4 Hz), 7.66 (d, 2H, J=8.4 Hz), 7.80 (d, 3H, J=8.4 Hz), 8.00 (d, 1H, J=8.4 Hz), 8.59 (s, 1H, pyrazolyl-H)	117.2, 119.5, 121.5, 122.8, 123.6, 125.1, 126.4, 127.5, 128.7, 129.7, 131.0, 131.2, 131.28, 131.7, 139.3, 151.0, 153.4, 154.2, 154.9	431 $[M]^+$, 433 $[M+2]^+$	Calcd.: C 61.12, H 3.26, N 9.72; Found: C 61.00, H 3.33, N 9.77

Abbreviations: IR = Infrared spectroscopy; NMR = Nuclear Magnetic Resonance; MS = Mass Spectrometry; Calcd. = Calculated; Found = Experimental; J = coupling constant; s = singlet; d = doublet; dd = doublet of doublets; m = multiplet.

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BIOLOGICAL EVALUATION

Preparation of Culture Media

For microbiological studies, **nutrient broth (NB)** was employed for bacterial cultures, whereas **Sabouraud dextrose broth (SDB)** was used for fungal cultures. Nutrient broth was prepared by dissolving **13 g of dehydrated medium in 100 mL of distilled water**. Sabouraud dextrose broth was prepared by dissolving **4 g dextrose and 1 g peptone in 100 mL of distilled water**. The prepared media were sterilized by autoclaving at **15 lb pressure for 20 min** and subsequently cooled before use.

Preparation of Stock Cultures

Fresh stock cultures of the selected test microorganisms were prepared under aseptic conditions. A loopful of each test organism was inoculated into **100 mL of sterile appropriate broth medium** and incubated for **24 h at 37 °C for bacterial cultures**. Fungal cultures were maintained under appropriate fungal incubation conditions.

Standardization of Microbial Inoculum

The resulting cultures were thoroughly mixed before dilution. **One millilitre of each stock culture was transferred aseptically into 9 mL of sterile water containing 0.05% Tween 80** and mixed using a cyclomixer. Serial ten-fold dilutions were subsequently prepared from **10^{-1} to 10^{-10}**.

From each dilution, **0.2 mL** was inoculated onto sterile nutrient agar plates for bacterial organisms and Sabouraud dextrose agar plates for fungal organisms. The plates were incubated under suitable conditions, after which the visible colonies were counted. The viable microbial population was expressed as **colony-forming units per millilitre (CFU/mL)**. Based on the colony count and dilution factor, the stock culture was standardized to approximately **15 × 10^8 CFU/mL**.

Preparation of Working Stock Culture

The working microbial cultures were prepared by inoculating 0.1 mL of the respective stock culture into 100 mL of nutrient broth for bacterial strains and 100 mL of Sabouraud dextrose broth for fungal strains. The cultures were appropriately diluted to obtain a microbial concentration of approximately (10^5) CFU/mL. These standardized working cultures were subsequently used for the *in vitro* antimicrobial evaluation of the synthesized compounds.

Preparation of Drug Solutions

The synthesized compounds were individually dissolved in dimethyl sulfoxide (DMSO) to prepare stock solutions at a concentration of 1 mg/mL. The prepared solutions were used for the evaluation of the antimicrobial activity of the synthesized compounds.

Antimicrobial Screening

The synthesized compounds were evaluated for their antimicrobial potential by determining the minimum inhibitory concentration (MIC) using the serial two-fold dilution method. The antibacterial activity was assessed against four bacterial strains: *Staphylococcus aureus* (MTCC 96), *Staphylococcus pyogenus*, *Pseudomonas aeruginosa* (MTCC 1688), and *Escherichia coli* (MTCC 443). The antifungal activity was evaluated against *Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 282).

Determination of Minimum Inhibitory Concentration (MIC)

The MIC assay was performed according to the method reported by Naga Raju et al. (2015), with appropriate modifications where required. Six assay tubes were used for each synthesized compound against each test microorganism, and all experiments were performed in duplicate.

For the initial tube, 1.8 mL of the standardized microbial suspension was mixed with 0.2 mL of the test compound solution (1 mg/mL). The contents were thoroughly mixed, followed by a two-fold serial dilution through the sixth tube. Each subsequent dilution was prepared using 1 mL of seeded broth. All drug additions and dilution procedures were carried out under aseptic conditions to prevent contamination.

Appropriate controls, including solvent control, negative/growth control, and drug control, were maintained throughout the experiment. The inoculated tubes containing bacterial cultures were incubated at 37°C for 24 hours, whereas tubes containing fungal cultures were incubated at 25°C for 24 hours.

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Following incubation, the tubes were examined for visible microbial growth. The MIC was defined as the lowest concentration of the test compound that completely inhibited the visible growth of the respective microorganism. The MIC values obtained for the synthesized compounds were recorded in Table 5.

Table 6. Antimicrobial activity of synthesized benzothiazole derivatives (BT-1–BT-10)

Compound	S. aureus	S. pyogenus	E. coli	P. aeruginosa	C. albicans	A. niger
BT-1	100	100	250	250	200	1000
BT-2	100	200	100	500	250	500
BT-3	250	250	250	100	500	1000
BT-4	200	250	125	500	1000	250
BT-5	250	200	500	500	500	1000
BT-6	**100**	**62.5**	**100**	200	500	200
BT-7	200	500	**62.5**	250	250	500
BT-8	500	250	500	200	**200**	**200**
BT-9	200	500	200	**100**	500	**200**
BT-10	500	200	250	250	500	250
Streptomycin	250	100	100	100	NT	NT
Griseofulvin	NT	NT	NT	NT	500	100

MIC values are expressed in µg/mL.

NT = Not Tested. Lower MIC values indicate stronger antimicrobial activity.

Antibacterial activity: *S. aureus* = *Staphylococcus aureus*; *S. pyogenus* = *Staphylococcus pyogenus*; *E. coli* = *Escherichia coli*; *P. aeruginosa* = *Pseudomonas aeruginosa*.

Antifungal activity: *C. albicans* = *Candida albicans*; *A. niger* = *Aspergillus niger*.

II. CONCLUSION

In conclusion, the present study demonstrates a simple, efficient, and practical methodology for the synthesis of benzothiazole derivatives through PIFA-promoted cyclocondensation of 2-aminothiophenol with a range of aromatic aldehydes. The developed synthetic protocol offers several important advantages, including a broad substrate scope, relatively short reaction time, microwave-assisted reaction conditions, operational simplicity, and satisfactory to good product yields. The use of microwave irradiation further facilitates rapid transformation of the reactants and provides an efficient approach toward the preparation of structurally diverse benzothiazole derivatives.

The synthesized compounds were characterized using appropriate spectroscopic and analytical techniques, confirming the formation of the desired benzothiazole framework. The successful synthesis of a series of derivatives with different aromatic substituents indicates that the reaction methodology possesses good functional-group tolerance and can be effectively applied for the preparation of structurally varied benzothiazole analogues.

Furthermore, the synthesized benzothiazole derivatives were subjected to *in vitro* antimicrobial screening against selected bacterial and fungal strains. The biological evaluation revealed that the synthesized compounds exhibited varying degrees of antibacterial and antifungal activity. Several derivatives showed appreciable antimicrobial activity, as evidenced by their comparatively lower minimum inhibitory concentration (MIC) values. In particular, some compounds demonstrated promising activity against individual bacterial and fungal strains, indicating that structural modification of the benzothiazole nucleus can significantly influence antimicrobial performance.

The observed antimicrobial properties highlight the potential of the benzothiazole scaffold as a valuable structural framework for the development of new antimicrobial agents. The differences in activity among the synthesized derivatives suggest that the nature and position of substituents on the aromatic ring may play an important role in determining their interaction with microbial targets.

Overall, the present work provides an efficient synthetic route to benzothiazole derivatives and establishes their potential as biologically active molecules with antimicrobial properties. The combination of microwave-assisted

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synthesis, PIFA-mediated cyclocondensation, satisfactory yields, and promising *in vitro* antimicrobial activity makes the developed methodology a useful contribution to the synthesis and biological evaluation of benzothiazole-based compounds. Further studies involving detailed structure–activity relationship investigations, mechanistic studies, toxicity evaluation, and *in vivo* biological assessment may provide additional insight into the therapeutic potential of these compounds.

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