Indian Journal of Chemistry
Vol. 65, March 2026, pp. 270-274
DOI: 10.56042/ijc.v65i3.26166

Synthesis, characterization and antimicrobial study of substituted N-(1-(benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl) benzothiazol-2-amine derivatives

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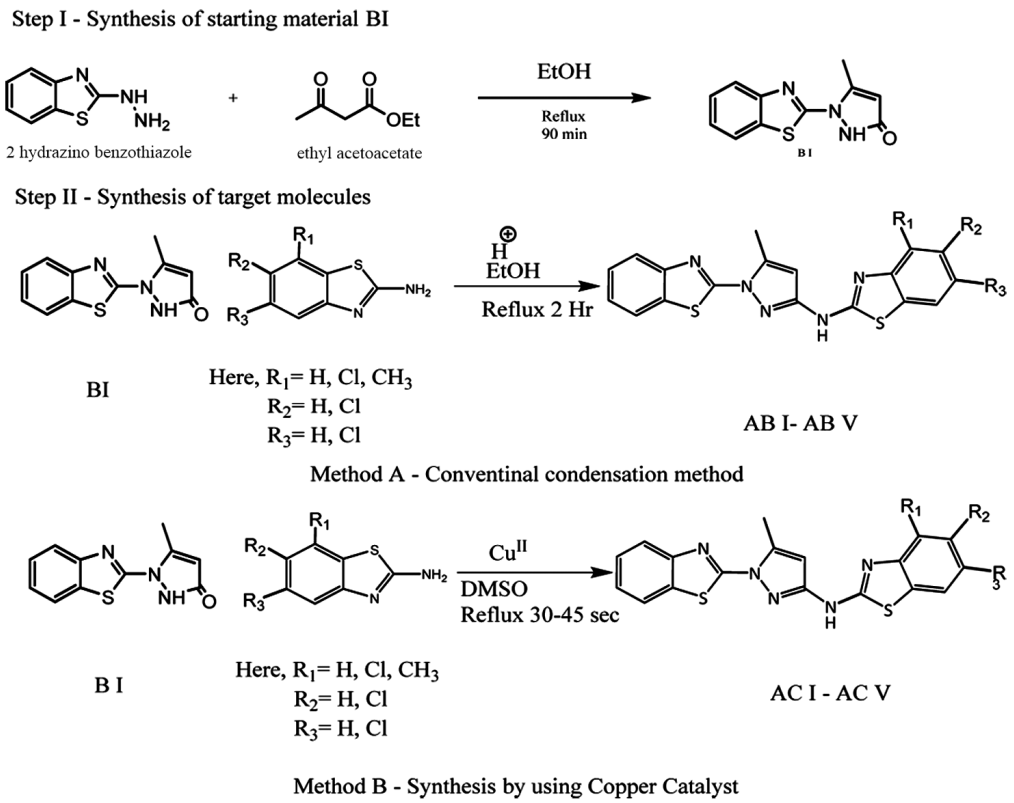
Received 3 December 2025; accepted (revised) 7 January 2026

Heterocyclylic derivatives of benzothiazole and pyrazole have been synthesized using both traditional and contemporary synthesis methods. The current study involves both conventional synthesis and catalyst-assisted techniques for the preparation of the desired organic compounds. Additionally, it includes the characterization of the synthesized compounds and a comparative analysis of traditional and modern methods in terms of reaction time, yield, and their applicability. A comprehensive overview of these compounds is presented, highlighting their chemical significance and potential applications in drug development. The central research question addresses the efficacy of synthesis methods and characterization techniques for these derivatives. This work not only contributes to the understanding of benzothiazole and pyrazole derivatives but also sheds light on their biological implications, aiming to pave the way for future research and application in pharmaceuticals.

Keywords: Heterocyclylic derivatives, Benzothiazole, Pyrazole, Synthesis methods, Catalyst, Dimethyl sulfoxide, NMR, FT-IR

Benzothiazolyl's chemical structure is the cornerstone of its significance in chemistry and industry. The fusion of benzene and thiazole rings creates a heterocyclic structure that is both stable and reactive. The aromatic benzene ring provides structural stability, while the thiazole ring, containing nitrogen and sulfur atoms, enhances the compound's reactivity and ability to participate in various chemical reactions[1]. These properties make benzothiazolyl an attractive scaffold for synthesizing a wide range of derivatives, each tailored for specific applications.

In the pharmaceutical industry, benzothiazolyl derivatives serve as essential building blocks for developing therapeutic agents. Their ability to interact with biological systems through hydrogen bonding, pi-stacking, and other interactions makes them ideal candidates for drug design and synthesis[2]. Benzothiazolyl compounds exhibit notable antimicrobial properties, which are invaluable in the development of antifungal and antibacterial drugs[3]. Furthermore, advancements in green chemistry have led to more sustainable synthetic pathways for benzothiazolyl derivatives, enhancing its appeal in environmentally conscious industries[4]. In agriculture, benzothiazolyl compounds play a critical role in agrochemicals, particularly as fungicides and pesticides. Their unique chemical structure allows them to effectively target and disrupt the growth of harmful organisms, thereby improving crop protection and yield[5]. Research continues to explore innovative and sustainable applications of benzothiazolyl derivatives in agriculture, aiming to reduce environmental impact while maintaining efficacy[6]. Materials science also benefits from benzothiazolyl's versatile properties. The compound is used in the development of advanced materials with enhanced stability, durability, and reactivity. Its incorporation into polymers and other materials has led to breakthroughs in various applications, including electronics, coatings, and textiles[7]. Benzothiazolyl-based fungicides and pesticides have been developed to protect crops and improve yield, contributing to food security and sustainable agriculture[8]. Benzothiazolyl's chemical properties are utilized in materials science to improve the stability and performance of polymers and advanced materials, leading to significant advancements in applications such as electronics, coatings, and textiles[9]. Benzothiazolyl derivatives are being explored in medicinal chemistry for their potential in personalized medicine and targeted therapies, as their interaction with specific biological targets may enhance treatment effectiveness while minimizing side effects[10].



Scheme 1 — Synthesis of substituted (E)-N,2-bis(benzo[d]thiazol-2-yl)-5-methyl-2,4-dihydro-3*H*-pyrazol-3-imine derivatives

Experimental Section

The melting points of all synthesized compounds were determined using the digital melting point apparatus from the Bio Techno Lab, and these values were recorded in °C while employing open capillary tubes. For the ^{1}H NMR spectra, a 500 MHz NMR spectrophotometer was utilized, with TMS serving as the internal standard and CDCl3 acting as the solvent. The FT-IR spectra were recorded using the IR Affinity 1 Spectrophotometer. Mass spectra were recorded on Alliance Micromass Mass spectrometer . Antimicrobial assessment was carried out by disc diffusion technique. E. coli, and S. aureus and Aspergilus niger (Fungi) were used for this assay. Positive control was used as standard commercial antibiotic disc *i.e.* tetracycline which was followed by four treated discs. Dimethyl sulfoxide was treated as negative control

Initially, we prepared the precursor 1-(benzothiazol-2-yl)-5-methyl-1,2-dihydro-3*H*-pyrazol-3-one for Scheme 1, designated as **BI**. Attack of amine on the ester function is thermodynamically favored when the reaction is conducted at higher temperature, whereas attack of amine on the ketone carbonyl is favored when reaction is conducted at room temperature[11]. This was achieved by heating 2 hydrazino benzothiazole (0.01 mol) and ethyl acetoacetate (0.01 mol) for one and half hour.

Two methods are performed to synthesisze substituted N-(1-(benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl)benzothiazol-2-amine derivatives. Method A followed conventional condensation in a ethanol solvent and in another method B the reaction here is facilitated by cupric bromide as a catalyst in the presence of DMSO.

1-(Benzothiazol-2-yl)-5-methyl-1,2-dihydro-3*H*-pyrazol-3-one (BI): According to Scheme 1, 2 hydrazino benzothiazole (0.01 mol) and ethyl acetoacetate (0.01 mol) were used and heated for 1.5 h, giving 79% yield. m.p.205°C. IR (KBr): 1715 cm^{-1} (C=O); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.2 (s, 3H, -CH_3), 3.5 (s, H, -CH), 5.5(s, H, NH) and 7.3-7.8 (m, 4H, Ar-H).

N-(1-(Benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl)benzothiazol-2-amine (AB I): According to Method A (Scheme 1), B I (0.01 mol) and 2-Aminobenzothiazole (0.01 mol) were dissolved in ethanol solvent and heated for 4-5 h, giving 75%

yield. m.p.195°C. IR (KBr): 1638 (C=N) and 2933 cm^{-1} (Ar-H); ^1H NMR (500 MHz, $CDCl_3$): δ 2.3 (s, 3H, $-CH_3$), 3.5 (s, H, -CH), 5.4 (s, H, -NH) and 7.3-8.0 (m, 9H, Ar-H); EI-MS (70 eV): *m/z* Calcd 364.06. Found: 363.03.

N-(1-(Benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl)-5-chlorobenzothiazol-2-amine (AB III): According to Method A (Scheme 1), B I (0.01 mol) and 2-Amino-5-chloro-benzothiazole (0.01 mol) were dissolved in ethanol and heated for 4-5 h, giving 73% yield. m.p.193°C. IR (KBr): 1635 (C=N) and 3125 cm^{-1} (Ar-H); ^1H NMR (500 MHz, $CDCl_3$): δ 2.5 (s, 3H, $-CH_3$), 3.6 (s, H, -CH), 5.4 (s, H, -NH) and 7.2-8.1 (m, 8H, Ar-H); EI-MS (70 eV): *m/z* Calcd 397.90. Found: 398.

N-(1-(Benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl)benzothiazol-2-amine (AC I): According to Method B (Scheme 1), B I (0.01 mol) and 2-Aminobenzothiazole (0.01 mol) were used in DMSO in presence of catalytic amount of Cupric Bromide and heated for 2-3 min, giving 85% yield. m.p.192°C. IR (KBr): 1618 (C=N) and 2941 cm^{-1} (Ar-H); ^1H NMR (500 MHz, $CDCl_3$): δ 2.3 (s, 3H, $-CH_3$), 3.6 (s, H, -CH), 5.45 (s, H, -NH) and 7.2-7.9 (m, 9H, Ar-H); EI-MS (70 eV): *m/z* Calcd 364.03. Found: 363.03.

N-(1-(Benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl)-5-chlorobenzothiazol-2-amine (AC III): According to Method B (Scheme 1), B I (0.01 mol) and 2-Amino-5-chloro-benzothiazole (0.01 mol) were used in DMSO in presence of catalytic amount of Cupric Bromide and heated for 2-3 min, giving 84% yield. m.p.194°C. IR (KBr): 1630 (C=N) and 3124 cm^{-1} (Ar-H); ^1H NMR (500 MHz, $CDCl_3$): δ 2.3 (s, 3H, -CH3), 3.7 (s, H, -CH), 5.45 (s, H, -NH) and 7.3-8.1 (m, 8H, Ar-H); EI-MS (70 eV): *m/z* Calcd 397.90. Found: 398.

N-(1-(Benzothiazol-2-yl)-5-methyl-1*H*-pyrazol-3-yl)-6-chlorobenzothiazol-2-amine (AC IV): According to Method B (Scheme 1), B I (0.01 mol) and 2-A mino-6-chloro-benzothiazole (0.01 mol) were used in DMSO in presence of catalytic amount of Cupric Bromide and heated for 2-3 min, giving 86% yield. m.p.174°C. IR (KBr): 1614 (C=N) and 2934 cm^{-1} (Ar-H); ^1H NMR (500 MHz, $CDCl_3$): δ 2.3 (s, 3H, $-CH_3$), 3.6 (s, H, -CH), 5.46 (s, H, NH) and 7.2-7.8 (m, 8H, Ar-H).

Results and Discussion

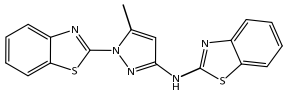
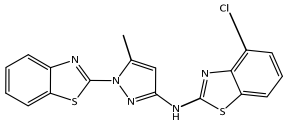
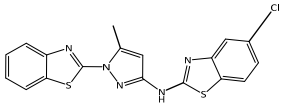
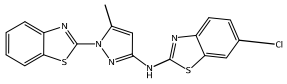
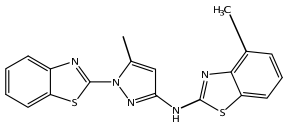
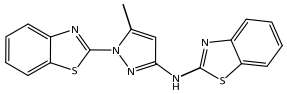
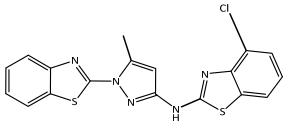
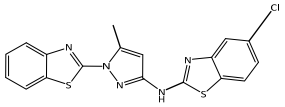
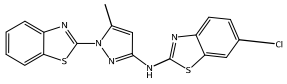
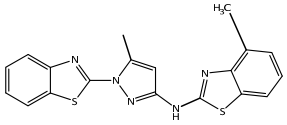
Method A - In this method, the reaction takes place in the presence of ethyl alcohol as the solvent. Both reactants B1 and substituted-2-amino benzothiazole are used in equal molar amounts and are dissolved in alcohol. This mixture is then refluxed for approximately 4-5 hours, after which the precipitate is filtered, washed with cold water, and dried to obtain the desired benzothiazole derivatives AB I – AB V (Table 1).

Method B - The reaction here is facilitated by cupric bromide as a catalyst in the presence of DMSO. Initially, B1 is dissolved in DMSO, and a small amount of cupric bromide catalyst is added to activate the substrate. Following this, an equimolar quantity of substituted-2-amino benzothiazoles is introduced, and the mixture is heated for 2-3 min. The precipitate formed is filtered, washed with cold water, and dried. The products AC I – AC V are then crystallized in dilute ethyl alcohol (Table 1).

Antimicrobial Activties

The evaluation of antimicrobial sensitivity of various test compounds against different bacteria and fungi was conducted after a 24-hour incubation period at 37°C. Streptomycin displayed significant effectiveness, achieving a zone of inhibition of 28 mm against both the Gram-positive bacteria Staphylococcus aureus and the Gram-negative bacteria *Escherichia coli*, while showing no activity against the fungus *Aspergillus niger*. Miconazole was effective against *Aspergillus niger*, displaying a zone of 28 mm, but was inactive against both *Staphylococcus aureus* and *Escherichia coli*. The negative control as DMSO indicated no inhibitory effects across any of the tested organisms. Among the other test compounds, AC-I presented sensitivity, with inhibition zones of 20 mm for *Staphylococcus aureus* and 21 mm for *Escherichia coli*. AC-II was resistant to both bacterial strains with zones of 13 mm and 12 mm, respectively, and no activity against *Aspergillus niger*. AC-III showed resistance with 14 mm for both bacteria, while AC-IV was effective against *Staphylococcus aureus* and *Escherichia coli* with sensitivity zones of 22 mm and 18 mm, respectively, but again without an effect on *Aspergillus niger*. AC-V demonstrated sensitivity with zones of 20 mm and 19 mm against *Staphylococcus aureus* and *Escherichia coli*, respectively, while showing no effect on *Aspergillus niger*.

Table 1 — Comparison of the performed methods in both schemes

S. No.	Scheme	Method	Solvent	Time of Reflux	Product	m.p. (°C)	Yield (%)
1	I	A	Ethanol	4-5 hrs	 AB I	192	75
2	I	A	Ethanol	4-5 hrs	 AB II	189	73
3	I	A	Ethanol	4-5 hrs	 AB III	191	78
4	I	A	Ethanol	4-5 hrs	 AB IV	170	71
5	I	A	Ethanol	4-5 hrs	 AB V	173	70
6	I	B	DMSO/Cu^{2+}	2-3 min	 AC I	190	86
7	I	B	DMSO/Cu^{2+}	2-3 min	 AC II	189	85
8	I	B	DMSO/Cu^{2+}	2-3 min	 AC III	194	84
9	I	B	DMSO/Cu^{2+}	2-3 min	 AC IV	174	86
10	I	B	DMSO/Cu^{2+}	2-3 min	 AC V	169	85

Conclusion

In the summary, the reactions of the schemes were conducted for an extended duration in an ethanol solvent. In contrast, the same reaction was performed using cupric bromide as a catalyst for only a few minutes in the presence of dimethyl sulfoxide, resulting in the formation of substituted benzothiazoles with yields and purities that were superior to those obtained

in the previous method. Various derivatives of benzothiazole, benzimidazole, and benzoxazole can be synthesized through an efficient and straightforward one-step procedure. This approach utilizes a copper-catalyzed condensation with dimethyl sulfoxide as the solvent, leading to moderate to excellent yields of the desired derivatives.

Acknowledgments

The authors expresses gratitude for the financial assistance obtained through a junior research fellowship from UGC-CSIR, India. The spectral analysis was conducted by CIC Laboratory at Shri Shivaji Science College, Amravati, for which the authors are appreciative.

Conflict of Interest

The authors declare no conflict of interest.

References

1 Bhat M & Belagali, S L, *Mini-Rev Org Chem*, 17 (2020) 323.
2 Keri R S, Patil M R, Patil S A & Budagumpi S, *Eur J Med Chem*, 89 (2015) 207.
3 Gill R K, Rawal R K & Bariwal J, *Archiv der Pharm*, 348 (2015) 155.
4 Gao X, Liu J, Zuo X, Feng X & Gao Y, *Molecules*, 25 (2020) 1675.
5 Zhilitskaya L V, Shainyan, B A & Yarosh N O, *Molecules*, 26 (2021) 2190
6 Nicholls A J & Baxendale I R, *Reactions*, 2 (2021) 175
7 Banerjee S, Payra S, & Saha A, *Curr Organocat,* 4 (2017) 164.
8 Badgujar N D, Dsouza M D, Nagargoje G R, Kadam P D, Momin K I, Bondge A S & More V S, *J Chem Rev*, 6 (2024) 202.
9 Law C S W & Yeong K Y, *Expert Opin Therap Pat*, 32 (2022) 299.
10 Keri R S, Patil M R, Patil S A & Budagumpi S, *Eur J Med Chem*, 89 (2015) 207.
11 Nadaraj V & Thamarai S S, *Indian J Chem*, 46B (2007) 1203.