Synthesis, Characterization & Biological Activity of 2-((5-Substitutedbenzo[d]thiazol-2-ylmethyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one Derivatives

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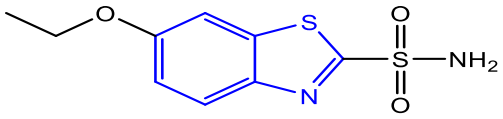
***Abstract*—Benzothiazole and indole derivatives are prominent pharmacophores in medicinal chemistry due to their diverse biological activities, including antimicrobial, anticancer, and anti-inflammatory properties. In this study, a series of fourteen novel compounds 2-(((5-substituted benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-ones[5(a-n)] were synthesized via a two-step route. The synthesis involved N-acylation of 2-phenylindole with chloroacetyl chloride, followed by nucleophilic substitution using 5-substituted benzo[d]thiazol-2-ylmethylamines in the presence of Cu_2O. The compounds were characterized by CHN elemental analysis, ^1H NMR, mass spectrometry, and melting point determination. Yields ranged from 16% to 55%. Antibacterial and antifungal activities were evaluated using the disc diffusion method at 250 µg/mL against Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida albicans. Compounds 5d and 5k exhibited the highest activity, with inhibition zones up to 25 mm. Structure-activity relationship (SAR) analysis revealed that halogenated and alkyl substitutions enhanced bioactivity, correlating with lipophilicity and membrane permeability. These findings highlight the potential of benzothiazole-indole hybrids as promising antimicrobial agents**

***Index Terms*—Benzothiazole derivatives, Indole derivatives, 2-phenylindole, 5-substituted benzo[d]thiazole, Antibacterial activity, Antifungal activity, N-acylation, Structure-activity relationship (SAR), Cu_2O-catalyzed synthesis, antimicrobial agents, Medicinal chemistry, Heterocyclic compounds, Spectroscopic characterization**

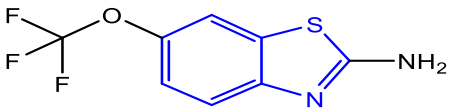
1. INTRODUCTION

Heterocyclic compounds represent some of the most important pharmacophores in medicinal chemistry, playing a crucial role in the synthesis of drugs with various pharmacological activities. Among them, five-membered heterocyclic compounds containing heteroatoms such as oxygen, nitrogen, and sulfur have demonstrated a broad spectrum of therapeutic properties. These structures hold vast significance in drug discovery and drug development processes due to their diverse biological activities and functional versatility (1,2). Benzothiazole is a bicyclic ring system, despite its relatively simple structure, plays a crucial role in research focused on the development of novel compounds with promising biological activities. These include antimicrobial (3), anticancer (4) anthelmintic, and anti-diabetic effects (5). In addition to its pharmacological relevance, benzothiazole has found industrial applications as an antioxidant and as a vulcanization accelerator.articularly, 2-substituted benzothiazoles have attracted considerable interest due to their unique structural features and versatile biological profiles. They have been explored as amyloid imaging agents (6) and anticancer agents [7]. Benzothiazole derivatives have demonstrated significant biological and pharmacological activity against a wide range of tumor and cancer cell lines, including HeLa, SW480, HepG2 (8), mammary and ovarian tumor cells (9), as well as colon, non-small-cell lung, breast subpanel cell lines (10), and hepatocellular carcinoma (HCC) (11).Furthermore,

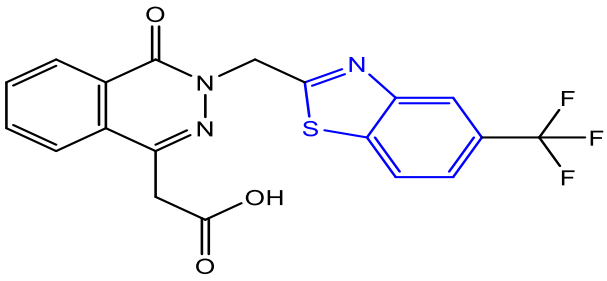
benzothiazole-based compounds have emerged as potent inhibitors of several key enzymes, such as EGFR, VEGFR, PI3K, topoisomerases, and thymidylate kinases. Numerous studies have focused on the design, synthesis, and biological evaluation of benzothiazole scaffold-based enzyme inhibitors, with several candidates progressing into various phases of clinical trials (12).Historically, as early as the 1950s, benzothiazole derivatives were investigated for their muscle-relaxant properties (13), highlighting their longstanding significance in medicinal chemistry.



Ethoxzolamide



Riluzole



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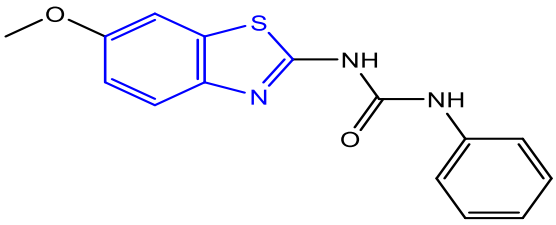
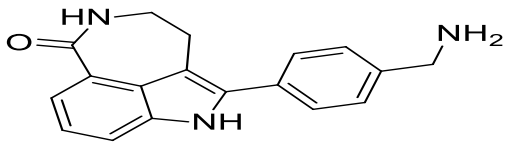
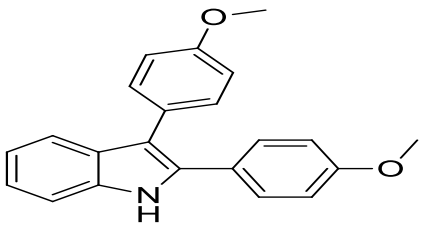


Frentizole

Indole derivatives have long fascinated researchers due to their diverse biological activities and therapeutic potential (14-17). As core structures in many natural products and pharmaceuticals, indoles are pivotal scaffolds in drug discovery and development.indole derivatives have been central to developing several important drugs. The indole alkaloid reserpine derived from the Rauwolfia plant has been used as an antihypertensive (18) and antipsychotic agent (19). The structural significance of indoles is further underscored by their presence in essential biomolecules such as serotonin and melatonin. Serotonin, a neurotransmitter with a critical role in regulating mood, appetite (20), and sleep (21), features an indole moiety, which is essential for its biological activity (22). Similarly, melatonin, another indole-based compound, regulates circadian rhythms (23) and has been investigated for its potential in treating sleep disorders (24) and as an antioxidant (23).It was reported that 2-phenylindole derivatives can bind with the estrogen receptor as well as microtubule receptors in case of estrogen-sensitive breast cancer and metastatic breast cancer, respectively.



Rucaparib



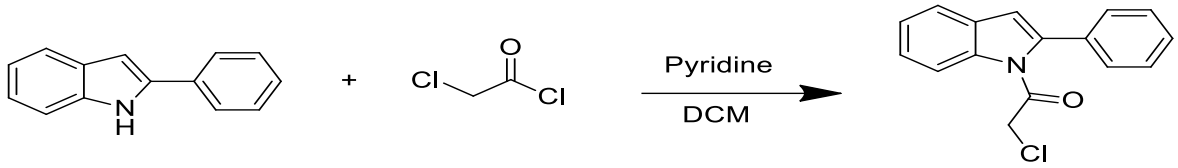
Indoxole

The importance of 2 phenylindole derivatives and benzothiazole derivatives motivated us to synthesize 2-(((5-substituted benzo[d]thiazol-2-yl) methyl)amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one derivatives[5(a-n)].

(((5-Substituted benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one derivatives were synthesized in two steps.

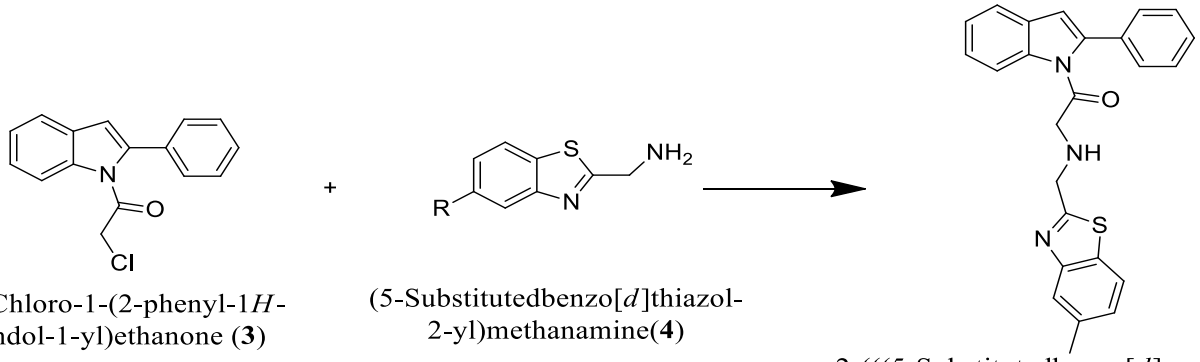
Step-1: Synthesis of N-acylation of 2-aryl indole from chloroacetyl chloride (1) with 2-phenyl

indole(2) produces the 2-chloro-1-(2-phenyl-1H- indol-1yl) ethenone (3).



2-Phenylindole (**1**) Chloroacetyl chloride (**2**) 2-Chloro-1-(2-phenyl-1*H*-indol-1-yl)ethanone (**3**)

Step-2: Synthesis of 2-(((5-substituted benzo[d]thiazol-2-yl)methyl)amino)-1-(2-phenyl-1H-indol-1-yl)ethan-1-one[5(a-n)] from the reaction of 2-chloro-1-(2-phenyl-1H- indol-1yl) ethenone (3) with 5-substitutedbenzothiazole-2-methylamines.



2-Chloro-1-(2-phenyl-1*H*-indol-1-yl)ethanone (**3**) (5-Substitutedbenzo[*d*]thiazol-2-yl)methanamine(**4**) 2-(((5-Substitutedbenzo[*d*]thiazol-2-yl)methyl)amino)-1-(2-phenyl-1*H*-indol-1-yl)ethanone[**5(a-n)**]

Combination	R
5a	-H
5b	-MeO
5c	-BnO
5d	i-Pro
5e	C_7H_5FO
5f	C_7H_5ClO
5g	C_2HFO_2
5h	$C_4H_8F_2O_2$
5i	CN
5j	Me
5k	C_2H_5
5l	F
5m	Cl
5n	Br

2. RESULTS AND DISCUSSION

A series of fourteen novel 2-(((5-substituted benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one derivatives [5(a-n)] were synthesized via a two-step synthetic route. The first step involved the N-acylation of 2-phenylindole with chloroacetyl chloride to yield the intermediate 2-chloro-1-(2-phenyl-1H-indol-1-yl)ethanone. In the second step, nucleophilic substitution was performed using various 5-substituted benzo[d]thiazol-2-ylmethylamines in the presence of Cu_2O as a catalyst in IPA at 92 °C.

The synthesized compounds were obtained in moderate yields ranging from 16% to 55%, with melting points ranging from 142 °C to 214 °C. The structural confirmation of the synthesized derivatives was achieved through detailed spectroscopic techniques including ^{1}H NMR, IR, mass spectrometry, and CHN elemental analysis. The NMR spectra of the compounds consistently revealed the presence of indole and benzothiazole protons, and the expected methylene and amine linkages. Elemental analyses were in close agreement with the calculated values, further supporting the proposed structures.

3. ANTIMICROBIAL ACTIVITY

All synthesized compounds were screened for their antibacterial activity against Bacillus subtilis and Staphylococcus aureus, and antifungal activity against Escherichia coli, Pseudomonas aeruginosa, and Candida albicans. The antimicrobial potential was evaluated using the disc diffusion method at a concentration of 250 µg/mL.

Among the derivatives, compound 5d (isopropoxy substitution) and compound 5k (ethyl substitution) exhibited the highest antimicrobial activity, with inhibition zones reaching up to 25 mm against S. aureus and 23 mm against B. subtilis. Compounds 5a, 5g, 5j, 5m, and 5n also displayed significant antimicrobial effects, notably outperforming the standard drug Riluzole in most cases. In contrast, compounds like 5f and 5e, despite having bulky or electron-withdrawing groups, showed moderate to low activity, possibly due to reduced membrane permeability or steric hindrance affecting target binding.

Interestingly, fluorinated and chlorinated derivatives (5l, 5m) demonstrated consistent inhibition against both Gram-positive and Gram-negative strains, aligning with prior studies highlighting halogen substitutions enhancing lipophilicity and bioavailability.

Structure-Activity Relationship (SAR)

The synthesized series of 2-(((5-substituted benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one derivatives [5(a-n)] were evaluated for their antibacterial and antifungal activities using the disc diffusion method. The SAR analysis focused on the influence of substituents at the 5-position of the benzothiazole moiety on antimicrobial potency.

Halogenated derivatives (5l: F, 5m: Cl, 5n: Br) displayed consistently strong antimicrobial activity against both Gram-positive and Gram-negative strains. This trend is attributed to enhanced lipophilicity and increased cell membrane permeability conferred by halogen atoms, in agreement with prior studies on halogen-substituted heterocycles.

Alkyl-substituted analogs (5d: i-Pr, 5j: Me, 5k: Et) exhibited notable potency, with compounds 5d and 5k demonstrating the highest zone of inhibition values (up to 25 mm). This enhancement is likely due to favorable hydrophobic interactions that facilitate bacterial cell penetration.

Compounds bearing methoxy (5b) and benzyloxy (5c) groups showed moderate activity. The presence of electron-donating groups increased lipophilicity modestly, yet did not substantially improve antimicrobial performance, possibly due to steric factors or suboptimal binding interactions.

Derivatives with bulky or strongly electron-withdrawing groups such as fluorobenzyl (5e) and dichlorobenzyl (5f) exhibited reduced antimicrobial activity, likely due to steric hindrance and diminished membrane permeability.

The nitrile-substituted compound 5i demonstrated moderate activity, suggesting that while the nitrile group may aid in target engagement through electron-withdrawing effects, it does not significantly enhance overall bioavailability.

Fluorinated alkoxy derivatives (5g: CF_2O, 5h: CF_2CH_2O) showed good to moderate activity, indicating that a fine balance of polarity and steric bulk may favor antimicrobial efficacy.

Overall, the SAR analysis highlights the critical role of electronic properties, lipophilicity, and steric considerations in modulating the antimicrobial potential of benzothiazole-indole hybrids. Halogen atoms and small alkyl chains at the 5-position proved to be the most effective substituents, offering promising leads for further structural refinement and development of potent antimicrobial agents.

	Antibacterial activity zone diameter in mm				Antifungal activity	logp
Compound	B.Subtills	S.Aureus	E.Coli	P.Aurg.	Candida Albicans	
5a	22	24	19	16	18.5	5.43
5b	21	23	18	15	17.3	5.31
5c	20	22	17	14	13.9	7.04
5d	23	25	19	17	19.1	5.96
5e	18	19	15	12	12.8	7.2
5f	17	18	14	11	11.7	8.16

5g	22	23	18	16	18.2	6.02
5h	21	22	17	15	17.1	5.63
5i	22	23	16	15	17.4	5.47
5j	21	22	19	16	18.7	5.92
5k	23	24	18	17	18.3	6.34
5l	21	21	17	15	17.2	5.59
5m	22	23	19	16	19.0	5.99
5n	22	23	18	16	18.0	6.26
Riluzole	15	13.5	9.1	7.2	15.0	3.95

Table 1 Antimicrobial activity by disc diffusion method of 2-((substituted - benzo[d]thiazol-2-ylmethyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one – 1(a-n) at 250 µg/ml.

4. EXPERIMENTAL PROCEDURE

All reagents and solvents used in the synthesis were purchased from Sigma-Aldrich and Merck and were used without further purification. Melting points of the synthesized compounds were determined using open-ended capillary tubes on a SELAC digital melting point apparatus and are reported in degrees Celsius (°C) without correction. Elemental analyses for carbon, hydrogen, and nitrogen (% C, H, N) were performed using a CE-400 CHN elemental analyzer.^{1}H and ^{13}C NMR spectra were recorded on a Bruker FT-NMR spectrometer operating at 500 MHz and 125 MHz, respectively, using DMSO-d_6 as the solvent. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as the internal standard. Splitting patterns are denoted as follows: s = singlet, d = doublet, t = triplet, and m = multiplet.The progress of reactions was monitored by thin-layer chromatography (TLC) on silica gel 60 F_{254} aluminum-backed plates (Merck KGaA, Darmstadt, Germany), with visualization under UV light (254 nm).

General Procedure for the Synthesis of of 2-((substituted - benzo[d]thiazol-2-ylmethyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one - 5(a-n):

To a stirred solution of 2-chloro-1-(2-phenyl-1H-indol-1-yl) ethanone (1.0 mmol) in 400 mL of isopropanol (IPA), the appropriate 5-substituted benzo[d]thiazol-2-ylmethanamine (1.55 mmol) was added dropwise at room temperature. Subsequently, Cu_2O (1.5 mmol) was added as a catalyst. The reaction mixture was heated at 75-82oC and stirred for 12-40 hours under ambient atmosphere. Reaction progress was monitored by thin-layer chromatography (TLC). Upon completion, the reaction mixture was cooled to room temperature and maintained for an additional 4 hours. It was then further cooled to -4 °C and stirred for 3 hours to facilitate precipitation. The resulting solid was filtered through a Celite pad and washed with 100 mL of 2-hydroxypropane. The crude product was purified by recrystallization using a mixture of isopropanol and ethyl acetate, affording the desired compounds 5(a-n) in yields ranging from 25% to 55%.

Characterization of Synthesized Compounds [5(a-n)]:

5a: 2-((benzo[d]thiazol-2-ylmethyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:

Yield: 32 %, M.P.: 172-177 °C. 1H-NMR(δ): 3.66(s, 2H, CH2), 3.80(s, 2H, CH2), 4.53(s, 1H, NH), 6.78-8.18(m,14H, Ar-H). Mass(m/z): 397.12(M+1). CHN analysis: Found: C (72.03%), H (4.76%), N (11.22%); Calc: C (72.52%), H (4.82%), N (10.57%);

5b: 2-(((5-methoxybenzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:

Yield: 35 %, M.P.: 155-157 °C. 1H-NMR(δ): 3.63(s, 2H, CH2), 3.74(s, 2H, CH2), 3.96(s, 3H, OCH3), 4.83(s, 1H, NH), 6.74- 8.18(m,13H, Ar-H). IR: 1682 cm-1, 3070 cm-1, 3385 cm-1, 3496 cm-1. Mass(m/z): 428.0 (M+1). CHN Analysis Found: C (69.89%), H (4.86%), N (10.12%); Calc: C (70.24%), H (4.95%), N (9.83%);

5c: 2-(((5-(benzyloxy) benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:

Yield: 30 %, M.P.: 168-172 °C. 1H-NMR(δ): 3.55(s, 2H, CH2), 3.82(s, 2H, CH2), 4.85(s,1H, NH), 5.35(s, 2H, CH2), 6.70 - 8.15(m,18H, Ar-H). IR: 1668 cm-1, 3085 cm-1, 3393 cm-1, 3503 cm-1. Mass(m/z): 504.0 (M+1). CHN Analysis Found: C (73.82), H (4.84%), N (9.02%): Calc: C (73.93), H (5.00%), N (8.34%).

5d: 2-(((5-isopropoxybenzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 43 %, M.P.: 202-208 °C. 1H-NMR(δ): 1.32 of (s, 6H, CH3), 3.62(s, 2H, CH2), 3.82(s, 2H, CH2), 4.16(s, 1H, NH), 4.70(m, 1H, CH), 6.72 - 8.26 (m,13H, Ar-H). IR: 1672 cm-1, 3045 cm-1, 3370 cm-1, 3495 cm-1. Mass(m/z): 456.0 of (M+1). CHN Analysis Found: C (70.84%), H (4.99%), N (10.13%); Calc: C (71.18), H (5.53%), N (9.22%).

5e: 2-(((5-((4-fluorobenzyl) oxy) benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 35 %, M.P.: 209-214 °C. 1H-NMR(δ): 3.70(s, 2H, CH2), 3.86(s, 2H, CH2), 4.22(s, 1H, NH), 5.30(s, 2H, CH2), 6.86- 8.32(17H, m, Ar-H). CHN Analysis: Found C (70.85%), H (4.00%), N (8.96%); Calc: C (71.38%), H (4.64%), N (8.06%).
5f: 2-(((5-((3,4-dichlorobenzyl) oxy) benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 50 %, M.P.: 187-1930C, 1H-NMR(δ): 3.60(s, 2H, CH2), 3.84(s, 2H, CH2), 4.32(s, 1H, NH), 5.26(s, 2H, CH2), 6.90-8.23(m, 16H, Ar-H). IR Frequencies: 1672 cm-1, 3087 cm-1, 3339 cm-1, 3521 cm-1. Mass(m/z): 572.0 (M+1), 573(M+2), 575(M+5). CHN Analysis: Found: C (64.83%), H (3.82%); N (8.03%); Calc: C (65.04%), H (4.05%), N (7.34%);
5g: 2-(((5-(difluoro methoxy) benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 55 %, M.P.: 178-1800C, 1H-NMR(δ): 3.63(s, 2H, CH2), 3.90(s, 2H, CH2), 4.33(s, 1H, NH), 7.35(s, 1H, CH), 6.70-8.30(m, 13H, Ar-H). IR Frequencies: 1650 cm-1, 3050 cm-1, 3320 cm-1, 3450 cm-1. Mass(m/z): 464.0 (M+1), CHN Analysis: Found: C (64.60%), H (3.95%), N (10.02%); Calc: C (64.78%), H (4.13%), N (9.07%);
5h: 2-(((5-(2,2-difluoroethoxy) benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 41 %, M.P.: 156-1590C. 1H-NMR(δ): 3.64(s, 2H, CH2), 3.89(s, 2H, CH2), 4.32(s, 1H, NH), 4.56(d, 2H, CH2), 5.73(t, 1H, CH), 6.68-8.28(m, 13H, Ar-H). IR Frequencies: 1661 cm-1, 3043 cm-1, 3371 cm-1, 3480 cm-1. Mass(m/z): 478.0(M+1). CHN Analysis: Found: C (65.02%), H (4.02%), N (9.11%); Calc: C (65.40%), H (4.43%), N (8.80%);

5i: 2-(((2-oxo-2-(2-phenyl-1H-indol-1-yl) ethyl) amino) methyl) benzo[d]thiazole-5-carbonitrile:
Yield: 34 %, M.P.: 145-1470 C, 1H-NMR(δ): 3.70(s, 2H, CH2), 3.84(s, 2H, CH2), 4.28(s, 1H, NH), 6.75-8.46(m, 13H, Ar-H). IR Frequencies: 1683 cm-1, 2242 cm-1, 3033 cm-1, 3375 cm-1, 3512 cm-1. Mass(m/z): 423.0 of (M+1). CHN Analysis: Found: C (70.89%), H (3.96%), N (14.22%); Calc: C (71.07%), H (4.29%), N (13.26%);
5j: 2-(((5-methylbenzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 26 %, M.P.: 166-168 °C, 1H-NMR(δ): 2.34(s, 3H, CH3), 3.56(s, 2H, CH2), 3.90(s, 2H, CH2), 4.20(s, 1H, NH), 6.73 - 8.28(m, 13H, Ar-H). Mass(m/z): 412.0 (M+1). CHN Analysis: Found: C (72.72%), H (4.96%), N (11.12%); Calc: C (72.97%), H (5.14%), N (10.21%);
5k: 2-(((5-ethylbenzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 23 %, M.P.: 170 - 1720C, 1H-NMR(δ): 1.20(t, 3H, CH3), 2.80(q, 2H, CH2), 3.70(s, 2H, CH2), 3.88(s, 2H, CH2), 4.30(s, 1H, NH), 6.80-8.30(m, 13H, Ar-H). Mass(m/z): 426.0(M+1). CHN Analysis: Found: C (73.04%), H (5.06%), N (10.11%); Calc: C (73.38%), H (5.45%), N (9.87%);

5l: 2-(((5-fluorobenzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 34 %, M.P.: 142-1460 c, 1H-NMR(δ): 3.62(s, 2H, CH2), 3.88(s, 2H, CH2), 4.18(s, 1H, NH), 6.86 - 8.32(m, 13H, Ar-H). Mass(m/z): 416.0 (M+1). CHN Analysis: Found: C (68.99%), H (3.96%), N (11.04%); Calc: C (69.38%), H (4.37%), N (10.11%);

5m: 2-(((5-chlorobenzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one
Yield: 35 %, M.P.: 155-157 °C, 1H-NMR(δ): 3.66(s, 2H, CH2), 3.88(s, 2H, CH2), 4.26(s, 1H, NH), 6.78 - 8.22(m, 13H, Ar-H). IR Frequencies Range: 860 cm-1 1678 cm-1, 3045 cm-1, 3400 cm-1, 3523 cm-1. Mass(m/z): 432.0 (M+1), 423(M+2). CHN Analysis: Found: C (66.19%), H (3.98%), N (10.18%); Calc: C (66.74%), H (4.20%), N (9.73%);
5n: 2-(((5-bromobenzo[d]thiazol-2-yl) methyl) amino) -1-(2-phenyl-1H-indol-1-yl) ethan-1-one:
Yield: 16 %, M.P.: 174-176 °C, 1H-NMR(δ): 3.55(s, 2H, CH2), 3.84(s, 2H, CH2), 4.20(s, 1H, NH), 6.75 - 8.41(m, 13H, Ar-H). Mass (m/z): 478.0(M+1), 480(M+2), CHN Analysis: Found: C (60.13%), H

(3.69%), N (9.08%); Calc: C (60.51%), H (3.81%), N (8.82%).

5. CONCLUSION

In summary, a novel series of fourteen 2-(((5-substituted benzo[d]thiazol-2-yl) methyl) amino)-1-(2-phenyl-1H-indol-1-yl) ethan-1-one derivatives [5(a-n)] were successfully synthesized via a concise two-step synthetic protocol involving N-acylation and Cu_2O-catalyzed nucleophilic substitution. Structural elucidation was confirmed through spectroscopic techniques and elemental analyses. Biological evaluation revealed that several derivatives, particularly compounds 5d and 5k, demonstrated potent antibacterial and antifungal activity, surpassing the reference drug Riluzole in many cases. Structure-activity relationship (SAR) analysis highlighted the influence of electronic and lipophilic properties of the substituents on antimicrobial efficacy. These findings underscore the potential of benzothiazole-indole hybrids as promising scaffolds for future development of antimicrobial agents, warranting further optimization and pharmacological exploration.

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