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Research Article

Expeditious Microwave-assisted Synthesis of 1,3-Benzoxazoles Incorporating Substituted Thiazolidinone Moieties

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ABSTRACT

The rapid synthesis of 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-aryl-1,3-thiazolidin-4-one 4(a-h) was achieved through microwave-assisted methods. This involved the reaction of Schiff bases derived from 2-(4-amino phenyl) benzoxazole 3(a-h) with ethanol, $SHCH_2COOH$ (thioglycolic acid) (1 mol, 0.92 mL), and $ZnCl_2$ (5 mol%) under microwave irradiation (400W, 146°C) for 3 to 4 minutes, resulting in excellent yields. Compound precursors 3(a-h) were prepared from aromatic aldehydes and 2-(4-amino phenyl) benzoxazole in ethanol, followed by microwave irradiation for 1 to 2 minutes, with reaction progress monitored via TLC. The expeditious reaction time is a notable advantage of this protocol. Comprehensive structural elucidation of the synthesized compounds involved elemental analysis, IR, NMR, ^{13}C-NMR, and mass spectroscopy. These newly synthesized compounds, 4(a-h), were subjected to *in-vitro* antimicrobial screening against *Staphylococcus aureus, Escherichia coli,* and antifungal screening against *Aspergillus niger*. The zone of inhibition in millimeters was measured using the cup plate method. Several compounds within the series exhibited substantial activity when compared to the standard drugs streptomycin and fluconazole.

Introduction

Heterocyclic compounds containing sulfur atoms have emerged as pivotal entities in the landscape of modern drug discovery, with thiazole standing out as a prominent exemplar. Sulfur heterocycles, such as thiazole, have been labeled "privileged structures" because of their presence in biologically active natural compounds, medicines, and a variety of synthetic intermediates.[1] with multifaceted utility.[2] These compounds serve as indispensable components in scaffold hopping strategies and as amide isosteres, facilitating the exploration of structure-activity relationships (SAR) during lead optimization. Consequently, thiazoles find extensive integration into drug design processes, forming core frameworks for the synthesis of chemical libraries. Recent years have borne witness to the synthesis and evaluation of a myriad of thiazole derivatives, exhibiting a wide spectrum of biological activities.

Within this panorama of derivatives, a saturated rendition of thiazoles, characterized by a solitary carbonyl group, emerges as "Thiazolidinone." These compounds, derived from thiazolidine, encompass a doubly unsaturated five-membered heterocyclic ring housing one sulfur, one nitrogen, and three carbon atoms, including a carbonyl moiety. Thiazolidinediones have manifested diverse pharmacological activities across various targets, engendering sustained research interest. This structural motif has garnered appellations such as the "wonder nucleus" and the "magic moiety." Its earliest appearance was noted in penicillin, marking a pivotal milestone in identifying this motif within natural products.[3] This discovery laid the groundwork for subsequent breakthroughs, exemplified by the emergence of ralitoline as an efficacious anti-convulsant, etozoline as an anti-hypertensive agent, pioglitazone as a hypoglycemic agent, and the revelation of thiazolidomycin's activity against *Streptomyces* species.

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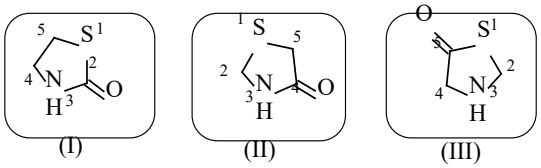


Fig. 1: Positional isomers in thiazolidinones

The classification of thiazolidinone derivatives pivots on the variable placement of the carbonyl group. While substituents at the 2-, 3-, and 5-positions confer variability, the most profound disparities in structure and properties are engendered by the positioning of the carbonyl group at 2 (I), 4 (II), or 5 (III) (Fig. 1).

This positional variance gives rise to distinct isomeric forms of thiazolidinones. Among these, thiazolidin-4-ones emanate as particularly captivating entities, incessantly capturing researchers' attention due to their efficacy spanning diverse pharmacological domains, encompassing antibacterial,[4-8] antifungal,[9] anti-inflammatory,[10] antiviral,[11,12] antitubercular,[13] and antitumor[14] properties. Their allure further escalates considering their roles as COX-1 inhibitors, bacterial enzyme inhibitors, non-nucleoside inhibitors of HIV type 1 reverse transcriptase (HIVRT), and anti-histaminic agents.[15] Recent years have witnessed a surge in research exploring the structure-activity relationships (SAR) intrinsic to thiazolidin-4-one derivatives. Notably, incorporating the thiazolidin-4-one ring into biologically active compounds, whether substituting or replacing another ring, profoundly influences electronic and binding properties, metabolic stability, lipophilicity, and pKa. This rich tapestry of biological responses has galvanized researchers to plumb this organic motif's depths, catalyzing further exploration into its potential.

The traditional synthetic methods for these compounds often involve time-consuming and resource-intensive processes. Consequently, there is a growing demand for innovative and expedited synthesis techniques that can streamline production while maintaining or enhancing product quality. In response to this need, this study aims to address these challenges by presenting a novel microwave-assisted synthesis approach for the efficient production of 1,3-benzoxazoles bearing substituted thiazolidinone moieties. By harnessing the power of microwave irradiation, this research endeavors to significantly reduce reaction times, improve yields, and offer a greener alternative to conventional methods. Additionally, the study seeks to explore the potential biological activities and industrial applications of the synthesized compounds. This research contributes to developing more sustainable synthetic methodologies and holds promise for discovering novel bioactive molecules and industrial advancements.

In light of the foregoing, this article embarks on a comprehensive expedition into the multifaceted realm of thiazolidin-4-one derivatives. The exploration encapsulates their structural flexibility, pharmacological promise, and contemporary relevance in the panorama of drug discovery endeavors.

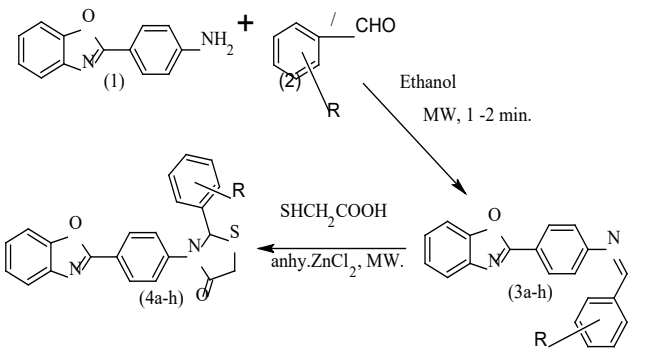
Materials And Methods

Synthesis

All chemicals and solvents used in this work were of synthetic grade purchased from Sigma-Aldrich, and local vendors and used without purification. The synthesized compounds' melting points were determined using the open capillary method. The progress of the reactions was monitored through thin-layer chromatography (TLC), employing commercially available silica gel plates (GF254). The visualization of compounds on the developed TLC plates was facilitated under UV light at a wavelength of 254 nm, thereby enhancing the sensitivity of compound detection. To purify the reaction products, column chromatography was employed. A stationary phase of 200 to 300 mesh silica gel (spectrochem) was utilized for this purpose. The nuclear magnetic resonance spectra (both ^{1}H and ^{13}C) were recorded using Bruker spectrometers operating at 400 and 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) with reference to the internal standard tetramethylsilane (TMS). The nature of peak splitting patterns was described using abbreviations such as br (broad), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants (J) were expressed in Hertz (Hz). Infrared spectra were recorded using a Perkin Elmer FTIR spectrometer by KBr pellet method. MASS recorded on BRUKER ESI-IT MS. The synthesis process made use of a domestic microwave system manufactured by ONIDA Company, operating under microwave-assisted conditions.

General Procedure for Synthesis of 2-(4-Aminophenyl) benzoxazole (1)

The scheme of synthesis for the benzoxazole derivatives was depicted in scheme I. A mixture of 2-amino phenol (0.01 mol), p-amino benzoic acid (0.01 mol), and 5 mL citric acid was combined in a beaker and subjected to microwave irradiation for one to three minutes. TLC monitored



Scheme I: Synthesis of benzoxazole derivatives(4a-h)

the progress of the reaction. The reaction mixture was then poured into ice-cold water, and the crude product obtained was filtered and subsequently recrystallized using ethanol.

General Procedure for Synthesis of Schiff Bases of 2-(4-Aminophenyl) benzoxazoles 3(a-h)

Equimolar quantities (0.01 mol) of substituted aromatic aldehyde (2) and 2-(4-aminophenyl) benzoxazole (1) were mixed in ethanol and exposed to microwave irradiation for 1 to 2 minutes. The resulting reaction mixture was poured into ice-cold water, and the crude product was filtered and recrystallized from ethanol.

General Procedure for Synthesis of 3-[4-(1,3-Benzoxazol-2-yl)phenyl]-2-aryl-1,3-thiazolidin-4-one 4(a-h)

In a 25 mL flask, a mixture of compound 3 (1 mol) in ethanol was combined with $SHCH_2COOH$ (thioglycollic acid) (1 mol, 0.92 mL) and $ZnCl_2$ (5 mol%) and placed in a microwave oven. The mixture was then irradiated (400W, 146°C) for 4 minutes. The completion of the reaction was verified using TLC. After irradiation, the mixture was diluted with ice-cold water. The resulting solid product was filtered, dried, and subsequently recrystallized from ethanol.

Biological Evaluation

The synthesized compounds (4a-h) were subjected to *in-vitro* antimicrobial screening against *Staphylococcus aureus* and *Escherichia* coli as well as antifungal screening against *Aspergillus niger*. The zone of inhibition was measured using the cup plate method. Several compounds within the series exhibited substantial activity against the tested microorganisms, with some showing better activity than standard drugs like streptomycin and fluconazole.

Antimicrobial and Antifungal activity

The synthesized compounds 4(a-h) were evaluated for their *in-vitro* antimicrobial activity against two bacterial strains, *S. aureus* and *E. coli* as well as one fungal strain, *A. niger*. The zone of inhibition was measured using the cup-plate method. Nutrient agar was employed as the culture medium for the bacteria, and Sabouraud dextrose agar was used for the fungus. Dimethyl sulfoxide (DMSO) 100 µL was used as the solvent control for antimicrobial activity testing. Standard antibiotics, streptomycin for antibacterial activity, and fluconazole for antifungal activity, were used as positive controls. *S. aureus* and *Escherichia coli* were streaked onto nutrient agar plates and incubated at 37°C for 24 hours. *A. niger* spores were harvested from Sabouraud dextrose agar plates and suspended in sterile distilled water to prepare a spore suspension. Sterile cotton swabs were used to uniformly spread the bacterial cultures on nutrient agar plates. A spore suspension (1 × 107 spores/mL) was evenly spread onto the Sabouraud dextrose agar plates for the fungal strain. After incubation, the diameter of the clear zones (zones of inhibition) around each well was measured in millimeters using a Vernier caliper. The results were recorded as the mean of triplicate experiments.

Overall, the results of these antibacterial and antifungal activity tests were used to assess the compounds' potential as antimicrobial agents and to compare their efficacy with standard antibiotic and antifungal drugs.

Results and Discussion

Out of several protocols for the synthesis of 4-thiazolidinone, the most common method is simple condensation of Schiff's bases with mercapto acid. The key functional group required for the reaction is an amine, carbonyl compound, and mercapto acid. This convergent route was envisaged to be highly significant due to easy accessibility of a large number of structurally diverse Schiff's bases, which can be easily prepared by reacting aromatic/heteroaromatic amine with large variety of commercially available aryl aldehydes under acidic conditions. So, to achieve our research goal for synthesis of 4-thiazolidinone (Fig. 2), we hypothesized utilization of 2-(4-amino phenyl) benzoxazole derived Schiffs bases and was prepared from 2-amino phenol and 4-amino benzoic acid using natural acid catalyst. This strategy will offer a valuable addendum in the biological profile.

After getting Schiff's bases, the optimization of the one-pot cyclization reaction of compound (3a) with thioglycolic acid was attempted by varying the solvents along with the quantity of $ZnCl_2$ (Table 1). A series of experiments were conducted using various solvents and solvent-free reaction conditions with both conventional and Microwave methods (Table 1, entries 1-9). The latter was more promising in that the reaction was very rapid affording the desired product 4a within 4 minutes (Table 1, entries 7-9) as compared to the former for about 5-12 hours (Table 1, entries 1–6) in solvents. The structure of the product was assigned on spectral analysis (Scheme-II).

Spectral Analysis

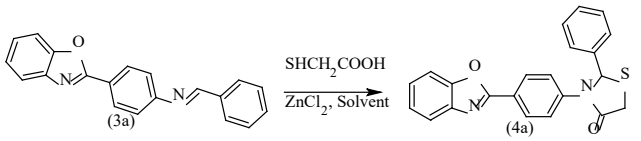
Compound 4a: 3-[4-(1,3-benzoxazol-2-yl) phenyl]-2-phenyl-1,3-thiazolidin-4-one

IR (KBr):υ =3072.92(-Ar-H),2900(-C-H),1690(>C=O), 751(C-S-C) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO): 7.00-8.10 (m, 13H, Ar-H), 6.5 (s, 1H, CH), 4.0(s,2H, CH_2)ppm.; ^{13}C-NMR (100MHz,DMSO):δ,172.3,163.2,151.0,141.9,142.5, 139 .1,128.7,127.7,127.8,126.1,125.9,124.7, ,122.8,122.1, 119.3,111.7,58.7,33.5ppm.

Compound 4b: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(4-chlorophenyl)-1,3-thiazolidin-4-one

IR (KBr):υ_{max}=3052(-Ar-H),2885(-C-H),1685(>C=O), 751(C-S-C) cm^{-1};^{1}H-NMR (400 MHz, DMSO):7.00-7.8 (m, 12H, Ar-H), 6.7 (s, 1H, CH), 4.1(s,2H, CH_2)ppm.; ^{13}C-NMR (100MHz, DMSO):δ 34.4, 63.6, 108.5, 120.3, 121.9, 122.4,

Table 1: Optimization of reaction conditions



S. No.	*Solvents (in mL)*	*Catalyst (in mol%)*	*Reaction temp (°C)*	*Reaction time (min.)*	*%Yield[b]*
1	Methanol	10	64	600	55
2	Ethanol	10	80	540	57
3	Toluene	10	105	800	50
4	1,4-Dioxae	10	100	600	60
5	DMF	10	115	500	64
6	Acetic acid	10	110	400	70
7	Ethanol	10	80	4	84[c]
8	Ethanol	5	80	4	83[c]
9	Solvent-free	10	100	4	72[c]

[a]Reaction conditions: 3a (1 mmol), thioglycolic acid (1 mmol), $ZnCl_2$, Solvent (10 mL); [b] Isolated yields after chromatography; [c]Microwave heating.

123.7, 124.8, 127.6, 129.5, 132.4, 134.7, 138.2, 140.1, 141.7,150.2, 163.8,172.6 ppm.

Compound 4c: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(4-fluorophenyl)-1,3-thiazolidin-4-one

IR (KBr):υ_{max}=3067(Ar-H),2838(-C-H), 1685 (>C=O), 1581 (Ar-C=C<), 751 (C-S-C) cm^{-1};^{1}H-NMR (400 MHz, DMSO): 6.8-7.9 (m, 12H, Ar-H), 6.5 (s, 1H, CH), 3.9(s,2H, CH_2)ppm. ^{13}C-NMR (100MHz,DMSO):δ 33.5, 62.7, 110.5, 114.9, 118.6, 120.9, 123.2, 124.3, 125.8, 128.1, 132.2, 135.8, 140.8, 141.5, 151.6, 162.4, 164.6, 170.6 ppm.

Compound 4d: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(4-nitrophenyl)-1,3-thiazolidin-4-one

IR (KBr): υ_{max}=3066(Ar-H),2933(CH),1650(>C=O),1519. 274(Ar-C=C<),1423(-C=N-),775(C-S-C) cm^{-1};^{1}H-NMR (400 MHz, DMSO):6.9-8.3 (m, 12H, Ar-H), 6.7 (s, 1H, CH), 3.5(s,2H, CH_2)ppm. ^{13}C-NMR(100MHz,DMSO):δ,189.2,171.2,167.7, 150.4 148.3, 134.3, 134.2,133.9,131.5,131.3 129.9, 129.6, 124.9, 121.1,119.8,112.5,56.4,33.4 ppm.; MS(EI): m/z=417(M+).

Compound 4e: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(2-hydroxy-3-methoxyphenyl)-1,3-thiazo- lidin -4-one

IR (KBr): υ= 3275(-OH),3099(Ar-H),2855(CH),1690 (>C=O),1569.27(Ar-C=C<),1494(-C=N-), 751(C-S-C) cm^{-1}.;^{1}H-NMR (400 MHz, DMSO): 8.1(s,1H, OH), 6.4-7.7 (m, 11H, Ar-H), 6.8 (s, 1H, CH),3.8(s,2H,CH_2) 3.9(s,3H, OCH_3) ppm.;^{13}C-NMR(100MHz,DMSO): δ,171.3, 164.2, 151.0, 147.8, 145.2, 142.1,139.6, 132.7,128.7,124.1,124.8,123.2,122.5,122.3, 120.2,119.5, 115.2,110.7, 54.7,56.5,32.6 ppm.

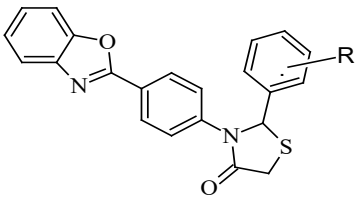


Figure 2: General Structure of Benzoxazole-Thiazolodinone derivatives

Compound 4f: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(3-bromophenyl)-1,3-thiazolidin-4-one

IR (KBr): υ= 3279(-OH),3065(Ar-H),2845(CH),1670 (>C=O), 1559(Ar-C=C<),1484(-C=N-), 761(C-S-C)cm^{-1}.;^{1}H-NMR (400 MHz, DMSO):7.0-7.6 (m, 12H, Ar-H), 6.5 (s, 1H, CH), 3.8 (s,2H,CH_2)ppm.;^{13}C-NMR (100MHz, DMSO): δ,171.4, 161.7, 151.0 146.8, 142.7 142.4, 142.1, 134.7,130.8,128.6,128.4 ,126.5,124.9,124.0,123.1,121.5,118.2,109.7,65.2,32 ppm.

Compound 4g: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(2-hydroxyphenyl)-1,3-thiazolidin-4- one

IR (KBr): υ= 3268(-OH),3093(Ar-H),2883(CH),1693 (>C=O), 1599.274(Ar-C=C<),1494(-C=N-),751(C-S-C)cm^{-1}.; ^{1}H-NMR (400 MHz, DMSO): 12.8 (s, 1H, -OH), 6.6-7.8 (m, 12H, Ar-H), 6.8 (s, 1H, CH), 3.5(s,2H, CH_2)ppm.; ^{13}C-NMR(100MHz,DMSO): δ,167.5,164.7,161.0, 152.1, 136.6,133.8,133.0,131.7, 131.5,131.1,129.4,121.3,119.8,119.4,119.2,117.0, 113.0, 52.1, 33.1 ppm.

Compound 4h: 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-(2-nitrophenyl)-1,3-thiazolidin-4-one

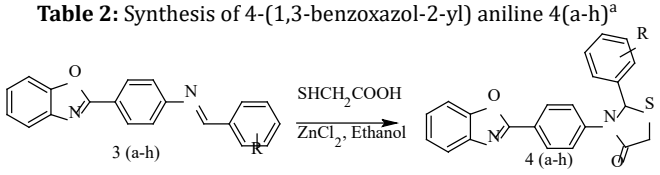
IR (KBr): υ= 3250(-OH),3063(Ar-H),2815(CH),1695 (>C=O),1596(Ar-C=C<),1476 (-C=N-),741(C-S-C)cm^{-1}.;^{1}H-NMR (400 MHz, DMSO):7.0-8.3 (m, 12H, Ar-H), 6.8 (s, 1H, CH), 3.9(s,2H, CH_2) ppm.;^{13}C-NMR (100MHz,DMS O):δ,173.2,161.7,150.6,148.5,142.5,142.4,135.1,133.2,134.3,129.6,128.4,127.5, 124.7,123.7, 122.3,121.3,118.2, 110.6, 57.5, 32.4 ppm.

After the optimization of reaction conditions, we evaluated the scope of the protocol by reacting structurally diverse Schiffs bases. The results are summarized in Table 2 In general, the corresponding 3-[4-(1,3-benzoxazol-2-yl) aryl]-2-aryl-1,3-thiazolidin-4-one[4(a-h)]were obtained in good to excellent yields in all the investigated cases. No significant electronic effects were observed for the electron-donating as well as electron-withdrawing substituents on Schiff bases. The use of microwave irradiation in the synthesis of 4-thiazolidinone shortens the reaction time with an increase in yields of product quantity.

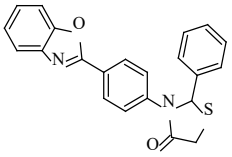
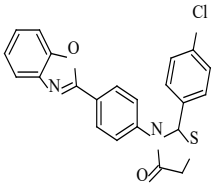
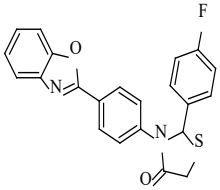
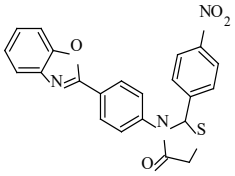
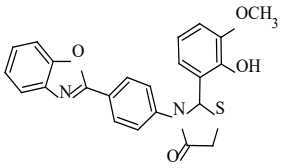
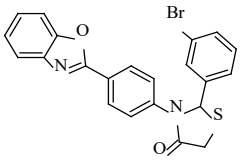
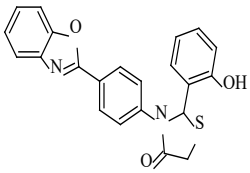
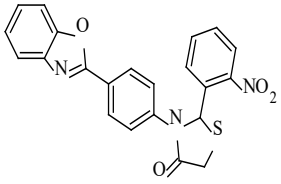
Characterization of Products

The identity of all synthesized compounds 4(a-h) were ascertained on the basis of IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy as well as physical constant. The physical and spectroscopic data were in full agreement with the proposed structures.

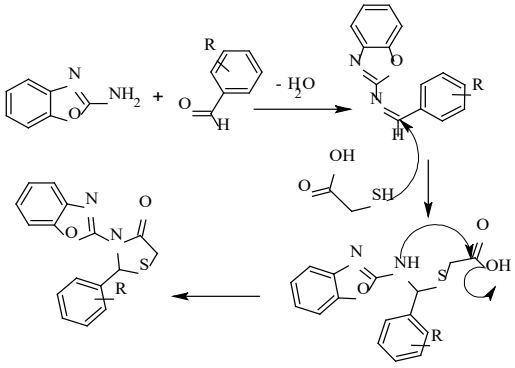
Table 2: Synthesis of 4-(1,3-benzoxazol-2-yl) aniline 4(a-h)[a]



Scheme II

Entry	Substrate (3) (R)	Product (4)	Yield[b] (%)	MP (^{0}C)[c]
1	H	 4a	83	153-155
2	4-Cl	 4b	82	121-122
3	4-F	 4c	78	111-115
4	4-NO_2	 4d	80	177-180
5	2-OH-3-OMe	 4e	79	211-212
6	3-Br	 4f	70	280-282
7	2-OH	 4g	76	249-251
8	2-NO_2	 4h	80	178-180

[a]Reaction conditions: 3 (1 mmol), thioglycolic acid (1mmol), $ZnCl_2$ (5 mmol), ethanol (10 ml); [b] Isolated yields after chromatography.



Scheme III: Plausible mechanism of formation of 1, 3-thiazolidin-4-one

The IR spectrum of compound **4a** shows an absorption band at 1720 cm^{-1} attributed to >C=O stretching of thiazolidine-4-one compounds, providing evidence for the closure of the ring. The ^{1}H-NMR spectra of the same compounds show singlet at 8.3 ppm due to –CH and signals at 4.0 to 4.12 ppm due to the presence of endocyclic -S-CH_2- protons. The ^{13}C-NMR and mass spectra of all same compounds is in agreement with the proposed structures.

Mechanism of formation of 1, 3-thiazolidin-4-one

The synthetic itinerary in the construction of 1,3-thiazolidin-4-ones involves three components (an aldehyde, an amine, and thioglycolic acid), either in a one or multi-step procedure. The possible mechanism for the formation of 1,3-thiazolidin-4-ones 4(a-h) proceed by initial formation of an imine from the reaction of aldehyde with amine, which undergoes electrocyclization by nucleophilic attack of sulfur, followed by intramolecular ring closer *via* water elimination (Scheme III).

Antimicrobial activity of Synthesized compounds

The synthesized compounds 4 (a-h) underwent *in-vitro* testing for their antimicrobial properties against *S. aureus*, *E. coli*, and *A. niger*. These tests involved measuring the zones of inhibition in millimeters. The antimicrobial screening was carried out using the cup-plate method at 100 mg/mL concentration, with nutrient agar as the culture medium and DMSO serving as the solvent control for antimicrobial activity. Streptomycin was used as the

Table 3: Biological evaluation of synthesized compounds 4(a-h)

Comp. (100 g/mL)	*Antibacterial activity (mm)*		*Antifungal activity (mm)*
	S. aureus	*E. coli*	*A. niger*
4a	18 ±1.5	15 ± 1.2	16 ± 1.0
4b	20 ± 1.7	20 ± 1.4	22 ± 1.0
4c	22 ± 1.3	17 ± 1.1	17 ± 1.0
4d	25 ± 2.0	18 ± 1.3	21 ± 1.0
4e	24 ± 1.8	18 ± 1.5	17 ± 1.0
4f	21± 1.6	17± 1.2	20± 1.0
4g	23 ± 1.5	17 ± 1.2	17 ± 1.0
4h	20 ± 1.6	19 ± 1.4	16 ± 1.0
Streptomycin	28 ± 1.7	17 ± 1.2	-
Fluconazole	-	-	22 ± 1.3

standard for antibacterial evaluation, while fluconazole was the standard for antifungal assessment.

The results in Table 3 revealed intriguing findings. Specifically, compounds 4b, 4c, 4d, 4f, 4g, and 4h demonstrated significant antibacterial activity against *E. coli*, showcasing their potential as effective antibacterial agents. In the case of *S. aureus*, compounds 4c, 4d, 4e, 4f, and 4g exhibited noteworthy antibacterial activity. For antifungal activity against *A. niger*, compounds 4b, 4d, and 4f displayed substantial activity comparable to the standard drug, fluconazole.

An interesting observation was made regarding the influence of electron-withdrawing groups such as -F, -NO_2, -Cl, -OH, and -OCH_3, which seemed to enhance both antibacterial and antifungal activities. The electron-withdrawing groups increase the lipophilicity of a molecule which can facilitate their entry into microbial cells. Once inside the cell, these compounds may disrupt cellular processes more effectively, leading to higher antibacterial and antifungal activities. In summary, introducing electron-withdrawing groups into compounds can enhance antibacterial and antifungal activities by altering the compounds' reactivity, lipophilicity, and target engagement. This observation provides valuable insights for the design of more effective antimicrobial agents and contributes to our understanding of structure-activity relationships in drug development.

The antimicrobial activity was moderate for the remaining compounds, suggesting the need for further research and optimization. These findings underscore the potential of these synthesized compounds as candidates for the development of novel antimicrobial agents.

Conclusion

This work represents a synthesis of a series of novel 3-[4-(1,3-benzoxazol-2-yl)phenyl]-2-aryl-1,3-thiazolidin-4-one derivatives by microwave assistance in excellent yields. The admirable antimicrobial screening demonstrates that the benzoxazole-derived thiazolidin-4-ones certainly hold immense promise to discover new antibacterial and antifungal agents. We believe that the synthetic protocol described herein would be useful for the synthesis of a variety of 4-thiazolidinones with high biological potential.

Current Protocol Offers Several Notable Merits

Operationally simple and short reaction time

The procedure is designed to be straightforward and easy to follow, allowing for efficient execution of the synthesis. The utilization of microwave irradiation facilitates rapid reaction times, significantly reducing the overall duration required for each step.

Use of Solid Catalyst like $ZnCl_2$

Incorporating a solid catalyst like $ZnCl_2$ simplifies the reaction setup and enhances the practicality of the protocol. Solid catalysts are known for their ease of handling, separation, and reuse, contributing to a more environmentally friendly process.

Excellent Yield

The protocol has demonstrated remarkable efficiency in yielding the desired products. The combination of microwave-assisted techniques and the use of appropriate reagents ensures high conversion rates, resulting in substantial product yields.

Potential Biological Activity

The synthesized compounds exhibit potential biological activity due to their unique structures, combining the 1,3-benzoxazole and thiazolidinone moieties. This opens up avenues for exploring their applications in pharmaceutical research, potentially leading to the discovery of novel therapeutic agents.

Overall, the described protocol stands out for its simplicity, efficiency, and the possibility of yielding compounds with valuable biological activities, making it a promising approach in the field of organic synthesis and medicinal chemistry.

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