Original Article

Synthesis and studying biological activity of new benzothiazole derivatives

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Abstract

A variety of novel tetrazole derivatives attached to the β-lactam ring was made utilizing heptanitrile in a reaction with generated azide-β-lactam derivatives, and these compounds were then studied using IR and NMR spectroscopy. Biological testing showed that most of the final compounds showed good antibacterial and antifungal activity, particularly derivative (b3), which shown antifungal and antibacterial efficacy that was on par with or even superior to that of the reference drugs Fluconazole and Amoxicillin.

Keywords: Tetrazole, Schiff base, β-Lactam, Anti-bacterial activity, Antifungal activity.

Introduction

In the 20th century, antibiotics prevented millions of deaths by removing the possibility of infection. More resistant bacterial strains have emerged in recent years as a result of the abuse of antimicrobial drugs [1], which has led to a rise in morbidity and mortality [2]. As a result, new antimicrobial agents with a safer, more affordable, and more effective mechanism of action are required [3]. The chemistry of heterocyclic compounds has long been a subject of interest in science. Recently, for pharmacological and biological purposes, it has become more important to synthesize new tetrazole compounds and study their biological and chemical activity. Tetrazoles 1, 2, 3, and 4 belong to a significant class of heterocyclic chemicals. In pharmaceutical and medical applications, these compounds exhibit a wide spectrum of biological activity, including antifungal and antibacterial [4-7], antiviral [8-9], antiviral [8-10], analgesic [11-15], anti-inflammatory [16-19], and antiulcer [20-22]. 2-Azetidinones, four-membered cyclic amides, are also referred to as β-lactams. The β-lactam ring is a structural component of well-known biologically active substances including penicillin and cephalosporin [23].

Tetrazole-β-lactams have drawn particular interest among β-lactams because some of their derivatives have demonstrated potential pharmaceutical applications, such as inhibition of cholesterol absorption [24], antimalarial [25–27], antibacterial [28], antiviral [29], anti-HIV [30], antioxidant [31], anticancer and anti-proliferative [32] activities. Tetrazole-β-lactams have additionally been employed as synthons for the production of heterocycles and other chemical compounds [33]. We are considering the importance of the two motif parts indicated above in light of the aforementioned conditions and as an extension of our continuing research, beta lactam and tetrazole. Here, we'd like to discuss the production of beta lactam tetrazole compounds. Each unique compound's in vitro antibacterial and antifungal properties were studied, as well as how the most effective tetrazole molecule interacted with pharmaceuticals.

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Experimental Techniques and Materials

The chemicals were provided by Fluka, Merck, and Acros Chemicals. Records of Bruker DMSO-d6 NMR spectra were made (1H-NMR at 300 MHz and for 13C-NMR at 75 MHz). Downfield chemical alterations from TMS were recorded in ppm. Each coupling constant is written in Hertz (J). FTIR spectra were run on a Shimadzu FT-IR 8300 spectrophotometer. Melting points have been researched using a computerized melting point device. Using different polarity solvent solutions, TLC was employed to track the reactions.

Synthesis of Schiff base (a-c) [34]

The entire synthesis was carried out in 100% ethanol by condensing an equimolar mixture of substituted amines (5-methoxybenzothiazol-2-amine) and benzaldehyde derivatives (4-Br-benzaldehyde, 4-Cl-benzaldehyde, 4-NO2-benzaldehyde). For 5-7 hours, the reaction mixture was stirred and refluxed, the ethanol-suspended benzothiazole (0.01 mol) was then progressively added to the ethanoic solution. In order to dissolve the benzaldehyde derivatives (0.01 mol) in ethanol, two drops of glacial acetic acid were added. The analysis of each response was conducted using thin layer chromatography. In a fume hood, the colored liquids evaporated at ambient temperature. The precipitates were then extensively cleaned in methanol before being dried in a desiccator.

1-(4-bromophenyl)-N-(benzothiazol-2-yl)methanimine (a): m.p. 178–180 ℃; yield, 81%; FTIR, ν (cm−1): 3133 (N=CH str.), 3090(Ar-H),2974, 2863(C-H, sym., asym.), 1617 (C=N str.), 1597 (C=C ring str.), 1356 (C–N str.), 1H NMR δ (ppm): 8.87 (s, N=CH, 1H), 7.63-7.25 (m, Ar-H, 8H), 13C NMR δ (ppm): 159.15(C2 thiazole ring), 153.78(N=CH), 155.98, 144.84, 133.25, 131.07, 130.11, 128.15, 123.84, 121.32, 114.55, 102.67(12Caromatic ring).

1-(4-chloro)-N-(benzothiazol-2-yl)methanimine (b): m.p. 147–149 ℃; yield, 84%; FTIR, ν (cm−1): 3154 (N=CH str.), 3085(Ar-H), 2957, 2865 (C-H, sym., asym.), 1618 (C=N str.), 1587(C=C ring str.), 1357 (C–N str.), 1H NMR δ (ppm): 8.81 (s, N=CH, 1H), 7.54-7.22 (m, Ar-H, 8H), 13C NMR δ (ppm): 157.47(C2 thiazole ring), 152.89(N=CH), 155.96, 143.57, 133.78, 131.04, 129.97, 128.87, 124.13, 121.74, 115.87, 104.68(12Caromatic ring).

1-(4-nitro)-N-(benzothiazol-2-yl)methanimine (c): m.p. 137–139 ℃; yield, 78%; FTIR, ν (cm−1): 3122 (N=CH str.), 3068(Ar-H),2964, 2847(C-H, sym., asym.), 1623 (C=N str.), 1591 (C=C ring str.), 1354 (C–N str.), 1H NMR) δ (ppm): 8.80 (s, N=CH, 1H), 7.55-7.23 (m, Ar-H, 8H), 13C NMRδ (ppm): 158.14(C2 thiazole ring), 153.15(N=CH), 156.04, 144.71, 133.70, 131.35, 130.19, 128.47, 123.58, 122.8, 114.47, 105.17 (12Caromatic ring).

preparation of β-Lactam derivatives (a1-c1) from Schiff bases [35]

A combination of produced Schiff base (0.01 mol) in dioxane as solvent (25 mL) and trimethylamine as the organic base was added dropwise, with chloroacetylchloride (0.012 mol). The solution of reactant was allowed to stand at room temperature for two days and stirred for eight to nine hours before being poured over crushed ice. The solvent was evaporated, and the yield was re-crystallized from ethanol. The analysis of each response was conducted using thin layer chromatography.

4-(4-bromophenyl)-3-chloro-1-(benzo[d]thiazol-2-yl)azetidin-2-one (a1): m.p. 133–135℃; yield, 75%; FTIR, ν (cm−1): 3081(Ar-H),2974, 2850(C-H, sym., asym.), 1729 (C=O str.), 1580(C=C ring str.), 1358(C–N str.), 1H NMR δ (ppm): 7.69-7.24 (m, Ar-H, 7H), 5. 43 (d, J = 4.7 Hz, CH-Cl lactam, 1H), 4.83 (d, J = 4.7 Hz, N-CH-C lactam, 1H), 13C NMR δ (ppm): 168.71 (C=O lactam)156.85(C2 thiazole ring), 154.65, 147.28, 132.78, 130.85, 129.18, 128.39, 122.62, 121.39, 115.75, 103.36 (12Caromatic ring), 71.48 (CH-Cl lactam), 62.18(N-CH- lactam).

4-(4-chlorophenyl)-3-chloro-1-(benzo[d]thiazol-2-yl)azetidin-2-one(b1): m.p. 144–146℃; yield, 76%; FTIR, ν (cm−1): 3092(Ar-H),2985, 2862(C-H, sym., asym.), 1731 (C=O str.), 1589(C=C ring str.), 1348(C–N str.), 1H NMR δ (ppm): 7.61-7.22 (m, Ar-H, 7H), 5. 44 (d, J = 4.7 Hz, CH-Cl lactam, 1H), 4.85 (d, J = 4.7 Hz, N-CH-C lactam, 1H), 13C NMR δ (ppm): 166.75(C=O lactam)155.94 (C2 thiazole ring), 153.58, 147.08, 133.35, 131.48, 128.29, 125.47, 121.28, 118.58, 114.52, 104.58(12Caromatic ring), 70.54 (CH-Cl lactam), 62.59(N-CH- lactam).

4-(4-nitrophenyl)-3-chloro-1-(benzo[d]thiazol-2-yl)azetidin-2-one (c1): m.p. 154–156 ℃; yield, 74%; FTIR, ν (cm−1): 3091(Ar-H), 2968, 2877(C-H, sym., asym.), 1735 (C=O str.), 1591(C=C ring str.), 1347(C–N str.), 1H NMR δ (ppm): 7.55-7.21 (m, Ar-H, 7H), 5. 45 (d, J = 4.7 Hz, CH-Cl lactam, 1H), 4.81 (d, J = 4.7 Hz, N-CH-C lactam, 1H), 13C NMR δ (ppm): 167.58 (C=O lactam)156.74(C2 thiazole ring), 153.71, 146.77, 133.54, 131.47, 128.54, 125.82, 122.85, 120.54, 118.08, 103.87, (12Caromatic ring), 72.45 (CH-Cl lactam), 62.45 (N-CH- lactam).

Synthesis of β-lactam azide derivatives (a2-c2)

The -lactam derivatives (a1-c1) were combined with the solvent at a concentration of 0.001 mol after being dissolved in 15 mL of DMF at a concentration of 0.00 mol. At a temperature of 60 to 65 ℃, the reaction is permitted to continue stirring. Once the reaction is complete, the organic layer is separated using petroleum ether, dried with (MgSO4), and the solvent is evaporated using a rotary evaporator (as determined by TLC).

3-azido-4-(4-bromophenyl)-1-(benzo[d]thiazol-2-yl)azetidin-2-one (a2): m.p. 157–159 ℃; yield, 76%; FTIR, ν (cm−1): 3087(Ar-H),2981, 2858(C-H, sym., asym.), 2130 (N3), 1731 (C=O str.), 1591(C=C ring str.), 1358(C–N str.), 1H NMR δ (ppm): 7.62-7.20 (m, Ar-H, 7H), 5.14 (d, J = 7.4 Hz, CH-N3 lactam, 1H), 4.73 (d, J = 7.4 Hz, N-CH-C lactam, 1H), 13C NMR δ (ppm): 168.66 (C=O lactam)158.71(C2 thiazole ring), 156.41, 147.47, 133.61, 132.74, 130.92, 129.23, 128.24, 122.18, 115.68, 102.78(12Caromatic ring),

63.47 (CH-N3 lactam), 60.15(N-CH- lactam).

3-azido-4-(4-chlorophenyl)-1-(benzo[d]thiazol-2-yl)azetidin-2-one (b2): m.p. 144–146 ℃; yield, 72%; FTIR, ν (cm−1): 3101(Ar-H),2967, 2871(C-H, sym., asym.), 2128(N3), 1722 (C=O str.), 1581(C=C ring str.), 1365(C–N str.), 1H NMR δ (ppm): 7.62-7.22 (m, Ar-H, 7H), 5.11(d, J = 7.4 Hz, CH-N3 lactam, 1H), 4.69 (d, J = 7.4 Hz, N-CH-C lactam, 1H), 13C NMR δ (ppm): 168.87 (C=O lactam)159.47 (C2 thiazole ring), 156.74, 150.91, 132.52, 132.24, 129.58, 128.17, 126.32, 120.45, 115.61, 103.58 (12Caromatic ring), 63.58(CH-N3 lactam), 60.18(N-CH-lactam).

3-azido-4-(4-nitrophenyl)-1-(benzo[d]thiazol-2-yl)azetidin-2-one (c2): m.p. 166–168 ℃; yield, 80%; FTIR, ν (cm−1): 3089(Ar-H),2960, 2865(C-H, sym., asym.),2132(N3), 1733 (C=O str.), 1585(C=C ring str.), 1365(C–N str.), 1H NMR δ (ppm): 7.61-7.21 (m, Ar-H, 7H), 5. 13 (d, J = 7.4 Hz, CH-N3 lactam, 1H), 4.74 (d, J = 7.4 Hz, N-CH-C lactam, 1H), 13C NMR δ (ppm): 169.55 (C=O lactam)157.74 (C2 thiazole ring), 155.17, 151.87, 146.08, 134.60, 129.87, 125.58, 122.54, 121.44, 114.58, 102.75 (12Caromatic ring), 65.14 (CH-N3 lactam), 60.24(N-CH- lactam).

Synthesis of tetrazole derivatives (a3-c3) [36]

A solution of nitrile derivative (heptanenitrile, 0.01 mol), -lactam azide derivatives (a2-c2) (0.02 mol), and ammonium chloride was added to 10 mL of N,N-dimethyformamide and heated at 120 °C for 8 hours (0.01 mol). Once the reaction was finished, the solvent was extracted at reduced pressure (as indicated by TLC), and the residue was carefully acidified with strong hydrochloric acid at pH=2 in an ice bath after being dissolved in water (100 mL). Using ethanol and glacial acetic acid, precipitated tetrazole was extracted, dried, and crystallized once again (1:5).

4-(4-bromophenyl)-3-(5-hexyl-1H-tetrazol-1-yl)-1-(benzo[d]thiazol-2-yl)azetidin-2-one (a3): m.p. 145–147 ℃; yield, 71%; FTIR, ν (cm−1): 3078 (Ar-H),2965, 2845(C-H, sym., asym.), 1732 (C=O ring str.), 1582(C=C ring str.), 1347 (C–N str.), 1H NMR δ (ppm): 7.51-7.22 (m, Ar-H, 3H), 5. 85 (d, J = 7.4 Hz, CH-tetrazole lactam, 1H), 5.72 (d, J = 7.4 Hz, N-CH-C lactam, 1H), 2.84 (t, J = 6.0 Hz, tetrazole ring-CH2, 2H), 1.96 –1.88 (m, tetrazole ring-CH2-CH2-, 2H), 1.47 –1.31 (m, (-CH2-)3, 6H), 0.85 (t, J = 6.0 Hz, -CH3, 3H); 13C NMR δ (ppm): 166.94 (C=O), 158.78 (C2 thiazole ring), 157.01, 151.57, 133.14, 130.74, 129.28, 128.17, 122.87, 115.28, 109.35 (12Caromatic ring), 154.87(1Ctetrazole ring), 64.18(1C, CH-tetrazole lactam), 60.68(1C, N-CH- lactam), 31.47, 29.58,26.75, 25.68, 22.48(4C, (-CH2-)5), 14.65(1C, -CH3).

4-(4-chlorophenyl)-3-(5-hexyl-1H-tetrazol-1-yl)-1-(benzo[d]thiazol-2-yl)azetidin-2-one (b3): m.p. 169–171 °C; yield, 73%; FTIR, ν (cm−1): 3104 (Ar-H),2970, 2885(C-H, sym., asym.), 1730 (C=O ring str.), 1586(C=C ring str.), 1358 (C–N str.), 1H NMR δ (ppm): 7.55-7.24(m, Ar-H, 3H), 5.76(d, J = 7.4 Hz, CH-tetrazole lactam, 1H), 4.86 (d, J = 7.4 Hz, N-CH-C lactam, 1H), 2.85 (t, J = 6.0 Hz, - tetrazole ring-CH2, 2H), 1.93–1.85 (m, tetrazole ring-CH2-CH2-, 2H), 1.47–1.29 (m, (-CH2-)3, 6H), 0.86 (t, J = 6.0 Hz, -CH3, 3H); 13C NMR δ (ppm): 166.81 (C=O), 158.74 (C2 thiazole ring), 158.47, 151.22, 132.28, 131.18, 129.08, 128.11, 124.25, 121.27,117.87, 106.47 (12Caromatic ring), 154.25 (1C tetrazole ring), 62.89 (1C, CH-triazole lactam), 61.12 (1C, N-CH- lactam), 31.25, 29.57,27.07, 25.47, 22.68(4C, (-CH2-)5), 14.18(1C, -CH3).

3-(5-hexyl-1H-tetrazol-1-yl)-1-(benzo[d]thiazol-2-yl)-4-(4-nitrophenyl)azetidin-2-one(c3) : m.p. 195–197 ℃; yield, 72%; FTIR, ν (cm−1): 3087 (Ar-H),2985, 2875(C-H, sym., asym.), 1738 (C=O ring str.), 1582(C=C ring str.), 1352 (C–N str.), 1H NMR δ (ppm): 7.54-7.22 (m, Ar-H, 3H), 5.76 (d, J = 7.4 Hz, CH-tetrazole lactam, 1H), 4.89 (d, J = 7.4 Hz, N-CH-C lactam, 1H), 2.93 (t, J = 6.0 Hz, tetrazole ring -CH2, 2H), 1.93–1.85 (m, tetrazole ring -CH2-CH2-, 2H), 1.49–1.30 (m, (-CH2-)3, 6H), 0.85 (t, J = 6.0 Hz, -CH3, 3H); 13C NMR δ (ppm): 166.78 (1C, C=O), 158.70 (C2 thiazole ring), 157.25, 149.92, 147.14, 137.38, 130.17, 129.52, 124.42, 121.48, 116.42, 109.28 (12Caromatic ring), 154.27(1Ctetrazole ring), 63.79 (1C, CH-tetrazole lactam), 60.92(1C, N-CH- lactam), 31.78, 29.58,27.65, 25.14, 22.30(4C, (-CH2-)5), 14.35(1C, -CH3).

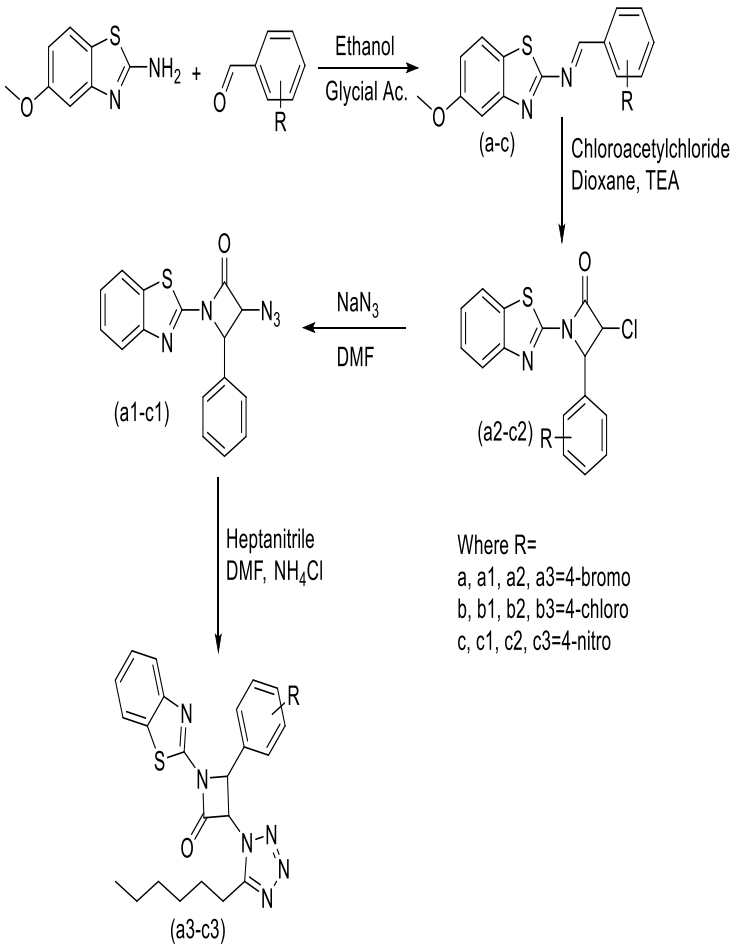
Anti-microbial screening

A range of Gram positive bacteria, such as (ATCC, 25922) Escherichia coli and (ATCC,29213) Staphylococcus aureus, were tested the target derivatives in vitro against. Their antifungal activity was tested against (Candida albicans) [37]. Mueller Hinton Agar was used to measure antibacterial activity (MHA). These bacteria were created as fresh inoculums and were then diluted with sterile normal saline. Once the reaction was finished, the solvent was extracted at reduced pressure (as indicated by TLC). With 0.5McFarland, the turbidity of these cultures was reduced. Utilizing sterilized cotton swabs, a reliable bacterial lawn was created. The wells were created by boring the afflicted plates with a 6 mm borer. Each sample was diluted by being dissolved in 1.0 mL of dimethylsulfoxide (DMSO), which was used as the bioassay's negative control, at a concentration of 100 g/mL. For 24 hours, these plates were incubated at 37°C. Ampicillin and fluconazole were employed as references drug, with concentrations ranging from 100 g/mL, while DMSO was used as a negative control. The diameter of the zone of inhibition (mm) utilized to measure the antibacterial activity of produced derivatives (a3-c3) was reported by subtracting the activity of the negative control.

Results and discussion

The produced -lactam azide derivatives (a2-c2) were refluxed with heptanenitrile at 120 °C using DMF as the solvent and NH4Cl as the catalyst to produce the synthetic tetrazole compounds (a3-c3) (Scheme 1). First, by stirring benzothiazol-2-amine and benzaldehyde derivatives and glacial acetic acid is present and 100% ethanol, Schiff base

derivatives (a1-c1) were created. The IR information showed that there were regions of absorption at 3154-3122 cm-1 (-N=CH-) and 1723-1717 cm-1 (-N=C-), while the 5-methoxybenzothiazol-2-amine (NH2) absorption band disappeared. The 1H NMR spectra revealed a multiple at 7.65-7.20 ppm corresponds to an aromatic proton, a doublet at 4.85-4.81 ppm for (-N-CH-), and a doublet at 5.45-5.43 ppm for (-CH-Cl) in the -lactam ring. While the 13C NMR spectra revealed additional signals attributable to carbonyl at a range of 168.71-166.75 ppm. The signal of the (N=CH) in the imine group was visible in the 1H NMR spectra between 8.87 and 8.82 ppm. The imine group carbon, on the other hand, caused a new signal to appear in the 13C NMR spectra in the range of 154.35-153.27 ppm. By reacting Schiff bases (a-c) and chloroacetyl chloride with triethyamine as an organic base and dioxane as the solvent, -lactam derivatives (a1-c1) were created. The IR spectra of the latter β-lactam derivatives displayed its presence of distinct absorption bands that matched the carbonyl groups in the range of 1735-1729 cm-1. carbon, as well as new signals in the region 72.45-70.54 ppm assigned to (CH-Cl lactam) and 62.18-62.59 ppm due to (N-CH- beta lactam) in -lactam ring. Refluxing -lactam derivatives (a1-c1) with sodium azide in DMF at a temperature of 60–65 ℃ degrees led to the creation of the -lactam azide derivatives (a2-c2). The IR data of the β-lactam azide derivatives showed the presence of distinct absorption bands at 2132-2128 cm-1 and 1733-1722 cm-1, which correspond to the N3 and carbonyl groups, respectively. The 1H NMR spectra revealed a multiplet at 7.63-7.20 ppm corresponds to an aromatic proton, a doublet at 4.74-4.69 ppm for (-N-CH-), and a doublet at 5.14-5.11 ppm for (-CH-N3) in the -lactam ring. The 13C NMR spectra revealed novel signals in the area of 169.55-168.66 ppm attributed to carbonyl carbon, 65.14-63.47 ppm assigned to (CH-N3 lactam), and 60.15-60.24 ppm attributed to (N-CH- lactam) in beta lactam ring.



Scheme 1. Synthesis heterocyclic derivatives

When heptanitrile and ammonium chloride were mixed into -lactam azide derivatives (a2-c2) in DMF to create novel tetrazole derivatives (a3-c3). The CN, N3 absorption band, which was present in the heptanitrile and beta lactam azide derivatives, was no longer detectable in the IR spectra. Additionally, they demonstrated the existence of bands of absorption for the carbonyl groups between 1738 and 1730 cm-1. Additional peaks at 3104 and 3078 cm-1, with (C-N) group-induced absorption bands at 1357 and 1348 cm-1, respectively, are seen as a result of substitution in the aromatic Ar-H. A multiple signal at 7.62-7.20 ppm, which corresponds to an aromatic proton, a doublet at 5.14-4.89 ppm, which corresponds to the (-N-CH- -lactam ring), and a doublet at 5.76-5.72 ppm, which corresponds to the –CH- beta lactam ring linked to the tetrazole ring are common signals in 1HNMR spectra. a triplet signal for the methylene protons that were linked to the tetrazole ring at 2.93-2.84 ppm. The 13C NMR spectra revealed brand-new signals in the region 154.87-154.25 ppm attributed to tetrazole ring carbon and in the range 166.94-166.78 ppm due to carbonyl carbon. However, additional signals in the range 64.18–62.89 ppm were attributed to (CH–) that was connected to the tetrazole ring, and 61.12–60.92 ppm were attributed to (N–CH–) in the -lactam ring. In contrast, the alkyl chain's carbon atom signal can be seen at a range of 32.78-14.18 ppm.

Antimicrobial activity

Gram-negative (ATTC-25922) Escherichia coli and Gram-positive(ATTC-25923) Staphylococcus aureuswere two pathogenic bacterial strains against which the synthesized compounds (a3-c3) were investigated for their antibacterial efficacy. These substances (a3-c3) were examined for their antifungal abilities against the pathogen Candida albicans (MTCC 227). Serial plate dilution was used to carry out the antibacterial activities, as reported in [37, 38]. Table 1 displays the minimum inhibitory concentrations (MICs) of the drugs under study. For antibacterial action, ampicillin was utilized as a reference medication, and fluconazole was used for antifungal activity.

Antibacterial activity

Table 1 displays the findings of the antibacterial screening of the produced compounds. Most of the compounds under investigation have rather weak antibacterial action. The synthesized compounds (a3-c3) displayed with MIC values, good to moderate activity between 65 and 90 g/mL. In particular, compounds (b3) and (c3) showed potent activity against E. coli (MIC values 75–85 g/mL), whilst (a3) demonstrated good activity (MIC 60 g/mL). Compounds (a3) and (c3) had good action (MIC values 85-80 g/mL) against the tested bacteria S. aureus when compared to the control drug, whereas (b3) showed moderate activity (MIC values 200 g/mL).

Antifungal activity

Table 1 displays the findings of the antifungal screening of the produced compounds. The synthesized compounds (a3-c3) showed better effectiveness against C. albicans than Fluconazole (MIC value: 150-250 g/mL).

Table 1. Compounds' biological profiles (a3-c3)

Compounds	Minimal inhibitory concentration (MIC) µg/Ml		
	Tested bacteria		Tested fungi
	Gram-negative	Gram-positive	
	E. coli	*S. aureus*	*C. albicans*
a3	85	60	80
b3	65	75	60
c3	80	85	70
Ampicillin	100	100	-
Fluconazole	-	-	250

Conclusions

For the first time, a novel form of tetrazole was successfully synthesized from commercially available benzothiazol-2-amine using a straightforward, useful, and efficient synthesis procedure. Compounds containing -Cl and -NO2 groups outperformed other compounds, according to a comprehensive the antimicrobial activity is examined of the target molecules. The prepared compounds (a3-c3) under investigation with Fluconazole as the placebo. When used exclusively against C. albicans, fluconazole was shown to be less effective than compound (b3) (MIC value: 150 g/mL). The synthesized compounds (a3-c3) shown good to moderate activity against E. coli and S. aureus, with MIC values in the range of 75-125 g/mL, when compared to the reference antibiotic ampicillin.

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