Our search for new antibiotics led to the syntheses and biological evaluation of new classes of dicarboxylic acid analogues. The syntheses involve nucleophilic addition of different substituted benzylamine, aniline, alkylamine, and 4-hydroxyl-L-proline with carbamoylbenzoic acid. The results of the antimicrobial activity as indicated by the zone of inhibition (ZOI) showed that Z10 is the most active against *Pseudomonas aeruginosa* (32 mm) and least active against *Candida stellatoidea* (27 mm) and Vancomycin Resistant *Enterococci* (VRE) (27 mm), while Z9 shows the least zone of inhibition (22 mm) against Methicillin Resistant *Staphylococcus aureus* (MRSA). The minimum inhibition concentration (MIC) determination reveals that Z10 inhibits the growth of tested microbes at a low concentration of 6.25 μg/mL, while Z9 and Z12 inhibit the growth of most microbes at a concentration of 12.5 μg/mL, recording the least MIC. The Minimum Bactericidal/Fungicidal Concentration (MBC/MFC) results revealed that Z10 has the highest bactericidal/fungicidal effect on the test microbes, at a concentration of 12.5 μg/mL, with the exception of *Candida stellatoidea* and Vancomycin Resistant *Enterococci* (VRE) with MBC/MFC of 25 μg/mL. The result of this investigation reveals the potential of the target compounds (Z1−3,5,7−12) in the search for new antimicrobial agents.

1. Introduction

Development of novel bioactive drugs in chemical warfare against bacteria, fungi, and other infectious diseases has become an important and challenging task for the synthetic and medicinal chemists. Many research programs are tailored towards the design and synthesis of new drugs, for their chemotherapeutic application. The emergence of antimicrobial resistance threatens the effective prevention and treatment of an ever increasing range of infections caused by bacteria, parasites, virus, and fungi. New resistance mechanisms are emerging and spreading globally; the appearance and widespread use of fake and substandard drugs have further compounded the problem [1]. The HIV epidemic around the world has led to an increase in the number of immunocompromised patients, which in turn has led to an increase in the number of systemic bacterial and fungal infections [2]. Compounds containing carboxylic acid functional groups are playing a major role in the field of medicine. Generally, they play an active and critical role in the biochemistry of human or animal physiology. They have been involved in studies as antibacterial [3], anti-inflammatory [4], antiplatelet [5], antimicrobial [6], anticancer [7], antifungal [8], and analgesic and antiseptic [9].

Currently, there are more than 450 clinically approved drugs containing a free carboxylic acid group [10]. To the best of our knowledge no biological studies and syntheses of these compounds have been reported. We present here the syntheses of different substituted carboxylic and dicarboxylic acid analogues, with electron withdrawing and donating groups (OH, OCH3, CH3, NO2, and F) and explored their potentials as antibacterial and antifungal drugs.
2. Materials and Methods

2.1. General Experimental Details. All chemicals and solvents were purchased from Sigma-Aldrich (Germany) and used as purchased without further purification. Thin-layer chromatography was performed using precoated silica gel 60 (F254) from MERCK (Germany). Spots on the TLC plates were visualized under UV light (254 nm and 366 nm) and by heating with 10% sulphuric acid in MeOH. The melting point was recorded using a Gallenkamp melting point apparatus. The UV-VIS analysis was carried out on a Perkin Elmer Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. The UV-VIS analysis was carried out on a Perkin Elmer Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell.

2.2. General Procedure for the Synthesis of \( Z_1\text{-3,5,7-12} \). A solution of 1,3-dioxo-2-benzofuran-5-carboxylic chloride (5 g, 23.8 mmol) was weighed into a round bottom flask containing 100 mL of KOHaq (5%) and then stirred for 30 min; the solid product (1,3-dioxo-2-benzofuran-5-carboxylic acid) was then filtered under suction. The products were pure enough for further reaction without further purification; this acid (0.3 g, 1.56 mmol) was further transferred to a 10 mL round bottom flask containing dichloromethane (7 mL) and a magnetic stirrer and 1.5 equiv. of different classes of amine were each added individually to the respective flasks and the mixture refluxed for at least two hours. The heat was then removed and the reaction stirred for a further 30 min. The reaction mixtures were allowed to stand at room temperature for a further 30 min; the solid precipitates were then filtered under suction and washed thoroughly with dichloromethane to remove any excess amines (Scheme I). After drying, they were recrystallized from dichloromethane to give the purified products (Table 1).

4-[(4-Fluorobenzyl)carbamoyl]benzene-1,5-dicarboxylic Acid (\( Z_2 \)). Bone white solid powder (55% yield) was prepared according to the general procedure from 1,3-dioxo-2-benzofuran-5-carboxylic acid 2 (0.3 g, 1.56 mmol), 4-fluorobenzylamine (0.26 g, 2.1 mmol), and DCM (7 mL) as solvent and purified by recrystallization with DCM. Melting point 173–175 °C, UV analysis \( \lambda_{\text{max}} \) (log e), 245 (4.39), 300 (3.92). IR (cm⁻¹): 2872 (COOH), 1603 and 1536 (CONH), 896 (=CH)

2.1. General Experimental Details. All chemicals and solvents were purchased from Sigma-Aldrich (Germany) and used as purchased without further purification. Thin-layer chromatography was performed using precoated silica gel 60 (F254) from MERCK (Germany). Spots on the TLC plates were visualized under UV light (254 nm and 366 nm) and by heating with 10% sulphuric acid in MeOH. The melting point was recorded using a Gallenkamp melting point apparatus. The UV-VIS analysis was carried out on a Perkin Elmer Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell. Lambda 35 UV/VIS Spectrometer, scanning from 200 to 400 nm. Absorbance was measured with a 1cm quartz cell.
| Sample | R | Product | Yield (%) |
|--------|---|---------|-----------|
| $Z_1$  | F | NH$^-$  | HO        | OH        | 99 |
| $Z_2$  | F | NH$^-$  | HO        | OH        | 55 |
| $Z_3$  | F | NH$^-$  | HO        | OH        | 35 |
| $Z_5$  | OH | COOH   | O         | O         | 78 |
| $Z_7$  | F | F       | OH        | OH        | 90 |
| $Z_8$  | NH | CH$_3$ | OH        | OH        | 54 |
| $Z_9$  | NH | CH$_3$ | OH        | OH        | 24 |
| $Z_{10}$ | NH | CH$_3$ | OH        | OH        | 65 |
| $Z_{11}$ | NH | CH$_3$ | OH        | OH        | 79 |
2-fluorobenzylamine (0.26 g, 2.1 mmol), and DCM (7 mL) as solvent and purified by recrystallization with DCM. Melting point 198–200°C, UV analysis \( \lambda_{\text{max}}(\log \epsilon) \), 245 (4.24), 300 (3.43). IR (cm\(^{-1}\)): 2839 (COOH), 1271 and 1248 (O-C), 1689, 1574 (CONH), 1385 and 1300 (C=C) and 907 (=CH).

Hydroxy-L-proline (0.28 g, 2.1 mmol), and toluene (7 mL) as solvent and purified by recrystallization with DCM. Melting point 135–136°C, UV analysis \( \lambda_{\text{max}}(\log \epsilon) \), 245 (3.86), 300 (2.95). IR (cm\(^{-1}\)): 2878, 2631 (COOH), 1273 and 1297 (O-C\(\text{Na}^+\)), 1687 and 1561 (CONH), 1603 and 1507 (C=C) and 847 (=CH). H-NMR (400 MHz, DMSO-d6) \( \delta \) 8.17 (d, H, J = 8.07 Hz, H-3), 7.94 (dd, H, J = 1.76, 8.07 Hz, H-4), 7.56–7.53 (m, H, Ar-H; H-4), 7.53–7.50 (m, H, Ar-H; H-5), 3.98 (s, H, H-10). C-NMR (100 MHz, DMSO-d6): 130.42 (C-4), 130.42 (d, H, J = 7.16 Hz, C-1), 129.76 (d, \( I_{CF} \) = 8.13 Hz, C-6), 124.78 (d, \( I_{CF} \) = 14.61 Hz, C-1), 124.44 (d, \( I_{CF} \) = 3.44 Hz, C-5), 115.15 (d, \( I_{CF} \) = 21.4 Hz, C-3), 36.77 (d, \( I_{CF} \) = 4.24 Hz, C-10). GC-MS (m/z, rel. int.) 317 [M\(^+\)]\(^{33} \) (91), 299.1 (100), 244.1 (32), 122.1 (24). LRMS 331.3 [M – Na\(^+\)]\(^{33} \) for C\(_{16}H\(_{12}F\)NO\(_{5}\), calculated mass 335.3 (Appendices 32–39).

2-[(2R,4R)-4-Carboxy-2-hydroxypyrrolidin-1-yl]carbonyl benzene-1,5-dicarboxylic Acid (Z\(_{38}\)). White solid powder (54% yield) was prepared according to the general procedure from 1,3-dioxo-2-benzofuran-5-carboxylic acid 2 (0.3 g, 1.56 mmol), butylamine (0.15 g, 2.1 mmol), and DCM (7 mL) as solvent and purified by recrystallization with DCM. Melting point 118–120°C, UV analysis \( \lambda_{\text{max}}(\log \epsilon) \), 245 (4.08), 300 (3.26). IR (cm\(^{-1}\)): 3061, 2959 (COOH), 1244, 1230 (C=C) and 907 (=CH). H-NMR (400 MHz, DMSO-d6) \( \delta \) 8.19 (d, H, J = 7.96 Hz, H-3), 7.97 (d, H, J = 7.96 Hz, H-4), 2.81 (t, H, J = 17.6 Hz, H-10), 1.34 (q, 2H, J = 7.16 Hz, H-3), 0.81 (t, H, J = 7.16 Hz, H-4). C-NMR (100 MHz, DMSO-d6): 168.19 (C-7), 168.16 (C-9), 167.92 (C-10), 167.34 (C-2), 136.23 (C-5), 132.47 (C-3), 130.47 (C-4), 129.62 (C-6), 129.45 (C-8), 128.74 (C-9), 115.84 (C-4), 113.26 (C-10), 39.96 (C-1), 28.20 (C-2).

2-[2-(4-Fluorobenzoyl)benzene-1,5-dicarboxylic Acid (Z\(_{12}\)]. Pale yellow solid powder (90% yield) was prepared according to the general procedure from 1,3-dioxo-2-benzofuran-5-carboxylic acid 2 (0.3 g, 1.56 mmol), 2,4-difluorobenzylamine (0.3 g, 2.1 mmol) and toluene (7 mL) as solvent and purified by recrystallization with DCM. Melting point 152–154°C, UV analysis \( \lambda_{\text{max}}(\log \epsilon) \), 245 (3.86), 300 (2.95). IR (cm\(^{-1}\)): 2878, 2631 (COOH), 1273 and 1297 (O-C\(\text{Na}^+\)), 1687 and 1561 (CONH), 1603 and 1507 (C=C) and 847 (=CH). H-NMR (400 MHz, DMSO-d6) \( \delta \) 8.71 (s, H, H-6), 8.12 (d, H, J = 8.00 Hz, H-4), 7.91 (dd, H, J = 1.20, 8.00 Hz, H-5), 7.61–7.54 (m, H, Ar-H; H-4), 7.49–7.46 (m, H, Ar-H; H-5), 3.98 (s, H, H-10). C-NMR (100 MHz, DMSO-d6): 130.42 (C-4), 130.42 (d, H, J = 7.16 Hz, C-1), 129.76 (d, \( I_{CF} \) = 8.13 Hz, C-6), 124.78 (d, \( I_{CF} \) = 14.61 Hz, C-1), 124.44 (d, \( I_{CF} \) = 3.44 Hz, C-5), 115.15 (d, \( I_{CF} \) = 21.4 Hz, C-3), 36.77 (d, \( I_{CF} \) = 4.24 Hz, C-10). GC-MS (m/z, rel. int.) 317 [M\(^+\)]\(^{33} \) (91), 299.1 (100), 244.1 (32), 122.1 (24), LRMS 331.3 [M – Na\(^+\)]\(^{33} \) for C\(_{16}H\(_{12}F\)NO\(_{5}\), calculated mass 335.3 (Appendices 32–39).
2-(Benzylcarbamoyl)benzene-1,5-dicarboxylic Acid (Z10). Creamy coarse powder (65% yield) was prepared according to the general procedure from 1,3-dioxo-2-benzofuran-5-carboxylic acid 2 (0.3 g, 1.56 mmol), benzylamine (0.23 g, 2.1 mmol), and DCM (7 mL) as solvent and purified by recrystallization with DCM. Melting point 189–190 °C. The compound was characterized by its melting point, UV/Vis analysis, and spectroscopic data. The compound was stable up to 48 h at 34 °C for fungi. About 5 discrete colonies were aseptically transferred using sterile wire loops into tubes containing sterile normal saline (0.85% NaCl) and were adjusted to a turbidity of 0.5 McFarland Standard. The suspensions were then inoculated on the surface of sterile Mueller-Hinton Agar plates using sterile cotton swabs. A sterile 6 mm diameter Cork borer was used to make holes (wells) into the set of inoculated Mueller-Hinton Agar. The wells were filled with different concentration of the test compounds. The plates were then incubated; all the tests were performed in triplicate and the antimicrobial activities were determined as mean diameter of inhibition zone (mm) produced by the test compounds.

3.3. Minimum Inhibition Concentration (MIC). The MIC was determined for the compounds using microbroth dilution method in accordance with National Committee for Clinical Laboratory Standard [12]. Serial dilution of the least concentration of the compounds that showed activity was prepared using test tubes containing 9 mL of double strength nutrient broth (OXOID). The test tubes were inoculated with the suspension of the standardized inoculum and incubated at 38 °C for 24 h. MICs were recorded as the lowest concentration of the compounds showing no visible growth (turbidity) in the broth.

3.4. Minimum Bactericidal and Minimum Fungicidal Concentration (MBC/MFC). The MBC/MFC was determined by aseptically inoculating aliquots of culture, from the minimum inhibition concentration (MIC) tubes that showed no growth, on sterile nutrient Agar (OXOID) plates incubated at 38 °C for bacteria and 34 °C for fungi for 48 h. The MBC/MFC was calculated as mean diameter of inhibition zone (mm) produced by the test compounds.
Table 2: Zone of inhibition (mm).

| Test organism | Z1 | Z2 | Z3 | Z4 | Z5 | Z6 | Z7 | Z8 | Z9 | Z10 | Z11 | Z12 | Sp | F1 |
|---------------|----|----|----|----|----|----|----|----|----|-----|-----|-----|----|----|
| MRSA          | 26 | 28 | —  | —  | —  | 22 | 28 | —  | 29 | 28  | —   | 35  | —  | —  |
| VRE           | —  | 24 | 29 | 24 | 24 | 27 | —  | 29 | 29 | 26  | 37  | 26  | —  | —  |
| S. aureus     | 27 | 29 | 24 | 24 | 24 | 27 | —  | 29 | 29 | 26  | 37  | 26  | 26 | 34 |
| S. pyogenes   | 25 | —  | 27 | 27 | —  | 24 | —  | 24 | —  | 24  | 34  | 34 | 34 | 34 |
| C. ulcerans   | —  | 24 | 23 | 26 | 24 | 28 | 30 | —  | —  | —   | 32  | —   | —  | —  |
| E. coli       | 29 | 27 | 26 | 26 | 26 | —  | —  | 27 | 25 | 37  | —   | —   | —  | —  |
| P. vulgaris   | —  | 24 | 24 | 24 | 30 | 31 | 28 | 32 | —  | —   | 24  | 35  | —  | —  |
| P. aeruginosa | —  | 22 | 42 | 42 | 27 | 29 | 30 | 27 | 39 | —   | 39  | —   | —  | —  |
| S. typhi      | 27 | 29 | 28 | 29 | 29 | 29 | 26 | 29 | 29 | 26  | 29  | 26  | —  | —  |
| S. dysenteriae| 29 | —  | 29 | 25 | —  | 27 | 24 | 29 | 29 | 27  | —   | 35  | —  | —  |
| C. albicans   | 24 | 27 | 24 | 24 | 30 | 31 | 28 | 32 | —  | 24  | 35  | —   | —  | —  |
| K. pneumonia  | 29 | 27 | 28 | 26 | 26 | 30 | —  | 24 | 42 | —   | 39  | —   | —  | —  |
| C. albicans   | 29 | —  | 29 | 25 | 27 | —  | 24 | —  | 40  | —   | —   | —   | —  | —  |
| C. krusei     | 27 | 28 | 24 | 26 | 25 | 24 | 22 | 28 | 24 | 27  | —   | 35  | —  | —  |
| C. tropicalis | 26 | 27 | 24 | 26 | 29 | 23 | 24 | —  | 30  | —   | —   | —   | —  | —  |
| C. stellatoidea| 26 | 27 | 28 | 29 | 27 | 27 | 28 | 27 | 23 | 24  | 34  | —   | —  | —  |

—: not determined.

Table 3: Minimum inhibitory concentration (MIC) (µg/mL).

| Test organism | Z1 | Z2 | Z3 | Z4 | Z5 | Z6 | Z7 | Z8 | Z9 | Z10 | Z11 | Z12 |
|---------------|----|----|----|----|----|----|----|----|----|-----|-----|-----|
| MRSA          | 12.50 | 6.2 | —  | —  | 6.2 | 6.2 | —  | 6.2 | 6.2 | —   | —   | —   |
| VRE           | —  | 6.2 | 6.2 | 6.2 | —  | 12.5 | 12.5 | 6.2 | —  | 12.5 | —   | —   |
| S. aureus     | 6.2 | 12.5 | 12.5 | —  | 6.2 | 6.2 | —  | 12.5 | 12.5 | 6.2 | 12.5 | 12.5 |
| S. pyogenes   | 12.5 | 6.2 | 6.2 | 6.2 | —  | 12.5 | —  | 12.5 | 6.2 | 6.2 | 12.5 | 6.2 |
| C. ulcerans   | —  | 12.5 | 12.5 | —  | 12.5 | 6.2 | 6.2 | 6.2 | 6.2 | —   | —   | —   |
| E. coli       | 6.2 | 6.2 | 6.2 | 6.2 | 12.5 | 12.5 | 6.2 | 6.2 | 6.2 | 6.2 | 12.5 | 12.5 |
| P. vulgaris   | —  | 12.5 | —  | 6.2 | 12.5 | —  | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 |
| P. aeruginosa | —  | 12.5 | 12.5 | 6.2 | 12.5 | —  | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 12.5 |
| K. pneumonia  | 6.2 | 6.2 | 6.2 | 6.2 | —  | 12.5 | 12.5 | 6.2 | 6.2 | 12.5 | 12.5 | 12.5 |
| S. typhi      | —  | 12.5 | 12.5 | 6.2 | 12.5 | —  | 12.5 | 6.2 | 12.5 | 12.5 | 12.5 | 12.5 |
| S. dysenteriae| 6.2 | 6.2 | 6.2 | 6.2 | —  | 12.5 | 12.5 | 6.2 | 12.5 | 12.5 | 12.5 | 12.5 |
| C. albicans   | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 12.5 |
| C. krusei     | 6.2 | 6.2 | 12.5 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 12.5 | 12.5 |
| C. tropicalis | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 12.5 |
| C. stellatoidea| 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 6.2 | 12.5 | 12.5 |

—: no MIC.

Table 2: Zone of inhibition (mm).

Table 3: Minimum inhibitory concentration (MIC) (µg/mL).

4. Results and Discussion

4.1. Chemistry. Our synthetic approach involved two steps (Scheme 1). In the first step, the acid chloride is hydrolysed by the aqueous KOH to form the corresponding carboxylic acid. The reaction takes place at room temperature under stirring condition for 30 min. The second step involves nucleophilic addition of the substituted amine, which attack the anhydride ring, breaking it open to form the second carboxylic acid group and an amide. This reaction was carried out in DCM under reflux condition for at least 2 h. The overall yields are given in the experimental section and they ranges between 35 and 99%.

The structures of the compounds were confirmed by the use of $^1$H and $^{13}$C NMR with application of 2D NMR where necessary.

4.2. Biological Results. The synthesised compounds were tested against eleven bacteria including two resistance bacteria, Methicillin Resistant *Staphylococcus aureus* (MRSA), Vancomycin Resistant *Enterococci* (VRE), and four fungi. The test compounds had significant zones of inhibitions against all tested organism as compared to the standard drug. Compound Z10 had the best activity among the compounds tested, with zone of inhibition ranging from 32 to 27 mm on the test microbes, but was not able to inhibit five bacteria (S. dysenteriae, P. aeruginosa, P. vulgaris, E. coli, and S. pyogenes) (Table 2). This was the compound without any substitution on the benzyl ring. Compounds Z7 and Z11 had zones ranging from 30 to 22 mm, while Z9 and Z8 were in the range between 29 and 24 mm. The zone of inhibition of Z7 and Z9, and Z12 was in the range between 28 and 20 mm, as compared to the zone of the standard drugs (32 to 40 mm).

Minimum inhibitory concentration (MIC) results (Table 3) reveal that a low concentration of 6.25 µg/mL of the test compounds (Z1−3, Z5,7−12) inhibited the growth of recorded as the lowest concentration of compounds showing no bacterial/fungal growth at all.
Table 4: Minimum bactericidal/fungicidal concentration (MBC/MFC) (μg/mL).

| Test organism | Z₁ | Z₂ | Z₃ | Z₅ | Z₇ | Z₉ | Z₁₀ | Z₁₁ | Z₁₂ |
|---------------|----|----|----|----|----|----|-----|-----|-----|
| MRS           | 25 | 12.5 | — | — | 50 | 12.5 | — | 12.5 | 12.5 |
| VRE           | — | 50 | — | 12.5 | — | 50 | 50 | 25 | — | 50 |
| S. aureus     | 25 | — | 25 | 25 | — | — | 25 | — | 25 | — |
| S. pyogenes   | 25 | — | 25 | 50 | — | 25 | — | 25 | — | — | 25 |
| C. ulcerans   | — | 25 | 50 | — | 25 | — | 25 | — | — | — | — |
| E. coli       | 12.5 | 25 | 25 | 12.5 | 25 | 25 | 50 | 12.5 | 12.5 | 25 |
| P. vulgaris   | — | — | 25 | 12.5 | 25 | — | — | — | 25 | 25 |
| P. aeruginosa | — | 25 | — | 25 | — | 25 | — | — | — | — |
| K. pneumonia  | 25 | 12.5 | 12.5 | — | 12.5 | 12.5 | 12.5 | 12.5 | 12.5 | 25 |
| S. typhi      | — | — | 25 | 12.5 | 12.5 | 25 | 25 | 12.5 | 25 | — |
| S. dysenteriae| 12.5 | 25 | — | 25 | 12.5 | 12.5 | 25 | 25 | 12.5 | 25 |
| C. albicans   | 50 | 25 | 25 | 50 | 25 | 12.5 | 50 | 12.5 | 12.5 | 25 |
| C. krusei     | 25 | 12.5 | 50 | — | 25 | 25 | 50 | 12.5 | 12.5 | 25 |
| C. tropicalis | — | 25 | — | 25 | 12.5 | 25 | 12.5 | 25 | 50 | 50 |
| C. stellatoidea| 25 | 25 | 12.5 | 12.5 | 25 | 25 | 12.5 | 50 | 25 | 25 | 50 |

—: no MBC/MFC.

the resistance bacteria (MRSA); the only exception was Z₄ which inhibited at 12.5 μg/mL. Three of the compounds (Z₂, Z₅, Z₁₀) inhibited the resistance VRE at a concentration of 6.25 μg/mL while Z₈, Z₉, and Z₁₂ inhibited VRE at a higher concentration of 12.5 μg/mL. Generally, other test microbes have shown MIC ranging between 6.25 and 50 μg/mL. These test compounds were also found to be both bactericidal and fungicidal at a concentration of 12.5 μg/mL, as recorded by the minimum bactericidal/fungicidal concentration (MBC/MFC) analysis (Table 4).

5. Conclusion

The different substituted test compounds were successfully synthesised and their structures were confirmed by NMR analysis. Generally, 2-(benzylcarbamoyl)benzene-1,5-dicarboxylic acid (Z₁₀) showed a better activity against resistance bacteria MRSA and VRE and other microbes. Although the test compounds were not as active as the standard drugs, sparfloxacin and fluconazole, the compounds may be employed in situations where there is resistance to antimicrobial drugs. Compound Z₁₀ is therefore a lead candidate in the search for an antimicrobial agent.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Acknowledgment

The authors wish to thank the School of Chemistry and Physics, University of KwaZulu-Natal, Durban, South Africa, for providing facilities to carry out this research.

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