Microwave Synthesis of 2,3-Disubstituted-5-methyl-1,3-imidazolidines-4-one Bearing Benzothiazole Moiety and Elementarily Assessment of Their Antibacterial Action

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Abstract. Diazotization of 2-aminobenzothiazole 1 through using sulfuric acid and sodium nitrite resulted in the formation of diazonium salt which reacted with alkaline solution of salicylaldehyde to produce azo-aldehyde derivative of benzothiazole 2. The resulting aldehyde 2 was condensed with the primary aromatic amines involving (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxyaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline) using microwave irradiation method in absolute ethanol to produce eight imines of benzothiazole 3a-h, respectively. The imine compounds 3a-h have been treated with L-alanine using microwave irradiation in tetrahydrofuran afforded eight new imidazolidines 4a-h containing benzothiazole moiety, respectively. Preliminary antibacterial activity of the target compounds was investigated in vitro using two kinds of bacteria, Escherichia coli (Gram-negative) and Staphylococcus aureus (Gram-positive). The results showed that the newly prepared imidazolidines (compounds 4c, 4d, 4f, 4g, and 4h) exhibited greater activities than gentamycin against Gram-positive bacteria. On the other hand, compounds 4e and 4f were also showed better activities against Gram-negative bacteria when compared with that of the control drug.

1. Introduction

Green chemistry includes the invention, design and application of products and processes to reduce the use and generation of hazardous substances\(^1\)\(^2\). The microwave irradiation technique afforded clean, simple, fast, efficient, and economic for the preparation of a wide number of organic compounds, have provided the momentum for many chemists to switch from conventional method to microwave assisted chemistry\(^3\). In the latter years microwave assisted organic reaction has emanated as new device in organic synthesis\(^4\).

Imidazolidines (saturated imidazoles), also known as tetrahydroimidazoles are biologically active nitrogen containing heterocyclic moiety which have been reported to shown wide array of significant bioactivities\(^5\). Imidazolidines-dione (hydantoins) and their derivatives are well known for their medicinal and many important non-medicinal applications\(^6\). The discovery of imidazolidine-dione and successfully developing novel hydantoins-based drugs for the treatment of epilepsy\(^7\). Imidazolidine-dione derivatives are reported to show the extensive range of biological activities such as anti-inflammatory\(^8\), analgesic agents\(^9\), antibacterial\(^10\), antifungal drugs\(^11\), antimicrobial\(^12\), antidepressant drugs are widely used\(^13\), commonly used in the treatment of epilepsy\(^14\) and antiarrhythmic\(^15\).

Benzothiazole comprises of thiazole ring fused with benzene and is also dubbed 1-thia-3-azaindene. It has been found to possess interesting biological activities\(^16\), antimalarial\(^17\), antihelmintic\(^18\), antibacterial and antifungal abilities\(^19\). Benzothiazole derivatives have been known for different biological properties including antimalarial, antitubercular, antihelmintic, anticonvulsant,
analgesic, anti-inflammatory, antidiabetic and antitumor activities\textsuperscript{20}, Further industrial applications as antioxidants\textsuperscript{21}.

Consequently, in this project, we reported here the microwave synthesis of imidazolidines bearing the biologically vigorous benzothiazole moiety that possibly have some biological activities.

2. Experimental

2.1. General.

All chemicals were utilized as provided from sigma Aldrich, Fluka and Merck. Microwave reactions have been performed on Domestic microwave oven in crucible. Analytical TLC has been done with silica gel 60 F\textsubscript{254} plates. Melting points have been measured on an Electro thermal Stuart SMP 30 capillary melting point apparatus and are uncorrected. IR spectra have been recorded on SHIMADZU FTIR–8400S Infrared Spectrophotometer as potassium bromide discs. \textsuperscript{1}H NMR spectra have been obtained using Avance III 500, NMR spectrometer, Bruker, Germany at 500 MHz in DMSO–\textit{d}_6 as solvent and TMS as an internal reference at a Faculty of Science, University of Tarbiat Modares, Iran. Elemental Analyses were performed with Perkin Elmer 300A Elemental Analyzer at a Faculty of Science, University of Tarbiat Modares, Iran.

2.2. Chemical methods.

2.2.1. (E)-5-(benzo[d]thiazol-2-yl diazenyl)-2-hydroxy benzaldehyde (2). has been prepared by method described in the literature\textsuperscript{22} as dark brown solid, mp 141-143 °C, yield 60 %; IR (cm\textsuperscript{-1}): 3429\textsubscript{br} (νO-H), 3068 (νC-H, benzene), 2856 and 2715 (νC-H, aldehyde), 1645 (νC=O, aldehyde), 1610 (νC=N, benzothiazole), 1502 and 1475 (νC=C, benzene), 1375 (νN=N), 759 (δo.o.p.C-H, benzene).

2.2.2. General procedure to prepare of imine compounds 3a-h\textsuperscript{23}. All reactions were carried out on Domestic microwave oven in crucible. Reactions contained the aldehyde derivative 2 (0.283 g, 1 mmol), equimolar amount (1 mmol) of aniline derivatives (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxyaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline respectively) and absolute ethanol (1 mL). The crucible was introduced to the center of a Domestic microwave oven and then heated (300-350W) for 25-30 minutes. TLC (n-hexane: EtOAc) indicated that the reactions have been completed. The products were washed with diethyl ether and recrystallized from absolute ethanol.

4-((E)-benzo[d]thiazol-2-yl diazenyl)-2-((E)-((4-(nitrophenyl)imino)methyl)phenol (3a):

IR (cm\textsuperscript{-1}): 3371 (νO-H), 3064 (νC-H, benzene), 1608 (νC=N, imine), 1589 (νC=N, benzothiazole), 1514 (νas.NO\textsubscript{2}), 1448 (νC=C, benzene), 1404 (νN=N), 1375 (νN=N), 759 (δo.o.p.C-H, benzene).

4-((E)-benzo[d]thiazol-2-yl diazenyl)-2-((E)-((3-(nitrophenyl)imino)methyl)phenol (3b):

IR (cm\textsuperscript{-1}): 3246 (νO-H), 3088 (νC-H, benzene), 1604 (νC=N, imine and νC=N, benzothiazole, vib. coupling), 1573 and 1502 and 1444 (νC=C, benzene), 1525 (νN=N), 1396 (νN=N), 1354 (νN=N), 758 (δo.o.p.C-H, benzene).

4-((E)-benzo[d]thiazol-2-yl diazenyl)-2-((E)-((4-(hydroxyphenyl)imino)methyl)phenol (3c):

IR (cm\textsuperscript{-1}): 3369 and 3298 (νO-H), 3032 (νC-H, benzene), 1610 (νC=N, imine and νC=N, benzothiazole, vib. coupling), 1514 and 1460 (νC=C, benzene), 1379 (νN=N), 827 (δo.o.p.C-H, benzene).
IR (cm⁻¹): 3371 and 3298 (vO-H), 3037 (vC-H, benzene), 2949 (vas.CH₃), 1622 (vC=N, imine), 1595 (vC=N, benzothiazole), 1512 and 1456 (vC=C, benzene), 1392 (vN=N), 821 (δo.o.p.C-H, benzene).

4-((E)-benzo[d]thiazol-2-yl diazeyl)-2-((E)-((2-methoxyphenyl)imino)methyl)phenol (3e):
IR (cm⁻¹): 3462 and 3265 (vO-H), 3064 (vC-H, benzene), 2968 (vas.CH₃), 2870 (vs.CH₂), 1633 (vC=N, imine), 1608 (vC=N, benzothiazole), 1533, 1500 and 1444 (vC=C, benzene), 1363 (vN=N), 831 (δo.o.p.C-H, benzene).

4-((E)-benzo[d]thiazol-2-yl diazeyl)-2-((E)-((4-bromomophenyl)imino)methyl)phenol (3f):
IR (cm⁻¹): 3369 and 3261 (vO-H), 3066 (vC-H, benzene), 1633 (vC=N, imine), 1606 (vC=N, benzothiazole), 1537, 1496 and 1442 (vC=C, benzene), 1367 (vN=N), 821 (δo.o.p.C-H, benzene).

4-((E)-benzo[d]thiazol-2-yl diazeyl)-2-((E)-((4-chloromphenyl)imino)methyl)phenol (3g):
IR (cm⁻¹): 3470 and 3265 (vO-H), 3061 (vC-H, benzene), 1633 (vC=N, imine), 1608 (vC=N, benzothiazole), 1570, 1533, 1500 and 1444 (vC=C, benzene), 1363 (vN=N), 831 (δo.o.p.C-H, benzene).

2.2.3. General procedure to prepare of imidazolidines 4a-h. A mixture of equimolar amounts of imine derivatives 3a-h (1 mmol) and L-alanine (0.089 g, 1 mmol) in tetrahydrofuran (1 mL) was heated (550-610W) in microwave oven for 20-25 min. TLC (n-hexane: EtOAc) indicated that the reactions have been completed. The products were washed with diethyl ether and recrystallized from absolute ethanol.

(E)-2-(5-benzo[d]thiazol-2-yl diazeyl)-2-hydroxyphenyl)-5-methyl-3-(4-nitrophenyl) imidazolidin-4-one (4a):
IR (cm⁻¹): 3234, vO-H and vN-H, imidazolidine, vib. coupling), 3057 (vC-H, benzene), 1664 (vC=O and δN-H, imidazolidine, vib. coupling), 1597 (vC=N, benzothiazole), 1510 (vas.NO₂), 1452 (vC=C, benzene), 1421 (vN=N), 1286 (vs.NO₂), 754 (δo.o.p.C-H, benzene); ¹H NMR: δ(ppm) = 1.24 (d, J = 6.7 Hz, 3H, CH₃), 3.84 (q, J = 6.7 Hz, 1H, CH-CH₃, imidazolidine), 6.52 (d, J = 7.8 Hz, 1H, N-CH-N, imidazolidine), 6.67-7.61 (m, 11H, Ar-H), 8.07 (s, 1H, N-H, imidazolidine), 9.51 (s, 1H, O-H). The signals at 2.49 ppm and 3.42 ppm assigned to DMSO and absorbed H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₈N₂O₄S: C, 58.22; H, 3.82; N, 17.71; S, 6.76; Found C, 57.86; H, 3.49; N, 17.42; S, 6.67.

(E)-2-(5-benzo[d]thiazol-2-yl diazeyl)-2-hydroxyphenyl)-5-methyl-3-(3-nitrophenyl) imidazolidin-4-one (4b):
IR (cm⁻¹): 3203, vO-H and vN-H, imidazolidine, vib. coupling), 3064 (vC-H, benzene), 2968 (vas.CH₃), 1668 (vC=O, imidazolidine), 1653 (δN-H, imidazolidine), 1604 (vC=N, benzothiazole), 1558 and 1454 (vC=C, benzene), 1510 (vas.NO₂), 1423 (vN=N), 1288 (vs.NO₂), 825 (δo.o.p.C-H, benzene); ¹H NMR: δ(ppm) = 1.24 (d, J = 6.7 Hz, 3H, CH₃), 3.78 (q, J = 7.0 Hz, 1H, CH-CH₃, imidazolidine), 6.52 (d, J = 8.1 Hz, 1H, N-CH-N, imidazolidine), 6.66-7.61 (m, 11H, Ar-H), 8.06 (s, 1H, N-H, imidazolidine). The signals at 2.49 ppm and 3.42 ppm assigned to DMSO and H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₈N₂O₄S: C, 58.22; H, 3.82; N, 17.71; S, 6.76; Found C, 58.57; H, 3.52; N, 17.35; S, 6.62.

(E)-2-(5-benzo[d]thiazol-2-yl diazeyl)-2-hydroxyphenyl)-3-(4-hydroxyphenyl)-5-methylimidazolidin-4-one (4c):
IR (cm⁻¹): 3209, vO-H and vN-H, imidazolidine, vib. coupling), 3093 (vC-H, benzene), 2987 (vas.C-H₂), 1668 (vC=O and δN-H, imidazolidine, vib. coupling), 1599 (vC=N,
benzothiazole), 1514 and 1456 (νC=O, benzene), 1413 (vN=N), 833 (δo.o.p.C-H, benzene); \(^1\)H NMR: δ(ppm) = 1.24 (d, J = 6.9 Hz, 3H, CH₃), 3.84 (q, J = 7.0 Hz, 1H, CH–CH₃, imidazolidine), 6.51 (d, J = 8.1 Hz, 1H, N–CH–N, imidazolidine), 6.66–7.66 (m, 11H, Ar–H), 8.07 (s, 1H, N–H, imidazolidine), 10.12 (s, 2H, 2×O–H). The signals at 2.49 ppm and 3.42 ppm due to DMSO and H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₉N₅O₃S: C, 62.01; H, 4.30; N, 15.72; S, 7.20; Found C, 61.61; H, 4.16; N, 15.59; S, 6.91.

(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-methoxyphenyl)-5-methylimidazolidin-4-one (4d): IR (cm⁻¹): 3203 (vO–H), 3171 (vN–H, imidazolidine), 3070 (vC–H, benzene), 2943 (vas.CH₃) 1674 (νC=O, imidazolidine), 1658 (δN–H, imidazolidine), 1606 (vC=N, benzothiazole), 1516 and 1454 (vC=C, benzene), 1427 (vN=N), 827 (δo.o.p.C-H, benzene); \(^1\)H NMR: δ(ppm) = 1.23 (d, J = 6.7 Hz, 3H, CH₃), 3.61 (s, 1H, O–CH₃), 3.85 (q, J = 6.6 Hz, 1H, CH–CH₃, imidazolidine), 6.52 (d, J = 8.0 Hz, 1H, N–CH–N, imidazolidine), 6.74–7.60 (m, 11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.51 (s, 1H, O–H). The signals at 2.49 ppm and 3.34 ppm attributed to DMSO and H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₉N₅O₃S: C, 62.73; H, 4.61; N, 15.24; S, 6.98; Found C, 62.44; H, 4.32; N, 15.21; S, 6.75.

(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2-methoxyphenyl)-5-methylimidazolidin-4-one (4e): IR (cm⁻¹): 3196s (vO–H and vN–H, imidazolidine, vib. coupling), 3059 (vC–H, benzene), 1674 (vC=O, imidazolidine), 1660 (δN–H, imidazolidine), 1612 (vC=N, benzothiazole), 1548, 1512 and 1452 (vC=C, benzene), 1425 (vN=N), 821 (δo.o.p.C-H, benzene); \(^1\)H NMR: δ(ppm) = 1.24 (d, J = 6.7 Hz, 3H, CH₃), 3.84 (q, J = 6.8 Hz, 1H, CH–CH₃, imidazolidine), 4.16 (s, 1H, O–CH₃), 6.53 (d, J = 8.1 Hz, 1H, N–CH–N, imidazolidine), 6.70–7.73 (m, 11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.64 (s, 1H, O–H). The signals at 2.49 ppm and 3.42 ppm assigned to DMSO and H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₈N₅O₃SBr: C, 62.73; H, 4.61; N, 15.24; S, 6.98; Found C, 62.36; H, 4.35; N, 15.15; S, 6.81.

(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-bromophenyl)-5-methylimidazolidin-4-one (4f): IR (cm⁻¹): 3189sh (vO–H and vN–H, imidazolidine, vib. coupling), 3061 (vC–H, benzene), 2943 (vCH₃), 1668 (vC=O and δN–H, imidazolidine, vib. coupling), 1604 (vC=N, benzothiazole), 1504 and 1452 (vC=C, benzene), 1425 (vN=N), 823 (δo.o.p.C-H, benzene); \(^1\)H NMR: δ(ppm) = 1.24 (d, J = 6.8 Hz, 3H, CH₃), 3.84 (q, J = 7.0 Hz, 1H, CH–CH₃, imidazolidine), 6.64 (d, J = 8.0 Hz, 1H, N–CH–N, imidazolidine), 7.00–7.61 (m, 11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.50 (s, 1H, O–H). The signals at 2.49 ppm and 3.42 ppm due to DMSO and H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₈N₅O₃SBr: C, 53.96; H, 3.33; N, 13.43; S, 6.09.

(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-chlorophenyl)-5-methylimidazolidin-4-one (4g): IR (cm⁻¹): 3419sh (vO–H and vN–H, imidazolidine, vib. coupling), 3063 (vC–H, benzene), 1680 (vC=O, imidazolidine), 1651 (δN–H, imidazolidine), 1618 (vC=N, benzothiazole), 1558, 1539, 1512 and 1454 (vC=C, benzene), 1421 (vN=N), 817 (δo.o.p.C-H, benzene); \(^1\)H NMR: δ(ppm) = 1.24 (d, J = 6.7 Hz, 3H, CH₃), 3.84 (q, J = 6.8 Hz, 1H, CH–CH₃, imidazolidine), 6.59 (d, J = 7.5 Hz, 1H, N–CH–N, imidazolidine), 7.02–7.61 (m, 11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.53 (s, 1H, O–H). The signals at 2.49 ppm and 3.37 ppm attributed to DMSO and H₂O in DMSO, successively; Anal. Calcd. for C₂₃H₁₈N₅O₃SCl: C, 59.54; H, 3.91; N, 15.10; S, 6.91; Found C, 58.19; H, 3.90; N, 15.01; S, 6.51.

(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2,4-dichlorophenyl)-5-methylimidazolidin-4-one (4h): IR (cm⁻¹): 3443sh (vO–H), 3213 (vN–H, imidazolidine), 3064 (vC–H, benzene), 2943, 1681 (vC=O, imidazolidine), 1651 (δN–H, imidazolidine, vib. coupling), 1610 (vC=N, benzothiazole), 1556, 1539, 1510 and 1456 (vC=C, benzene), 1423 (vN=N), 823 (δo.o.p.C-H, benzene); \(^1\)H NMR:
δ(ppm) = 1.23 (d, J = 6.8 Hz, 3H, CH$_3$), 3.84 (q, J = 7.0 Hz, 1H, CH–CH$_3$, imidazolidine), 6.59 (d, J = 7.1 Hz, 1H, N–CH–N, imidazolidine), 6.81–7.73 (m, 10H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.65 (s, 1H, O–H). The signals at 2.49 ppm and 3.33 ppm due to DMSO and H$_2$O in DMSO, successively. Anal. Calcd. for C$_{23}$H$_{17}$N$_5$O$_2$SCl$_2$:  C, 55.43;  H, 3.44;  N, 14.05;  S, 6.43; Found C, 54.06;  H, 3.29;  N, 13.94;  S, 6.41.

2.3. Elementarily antibacterial test.

The antibacterial activities of the latterly synthesized imidazolidines 4a–h have been scanted by the agar diffusion method using representative Gram (+) and Gram (–) bacteria on agar media. The test bacteria to assess the potential antibacterial action of the newly synthesized imidazolidines were Staphylococcus aurous (Gram-positive) and Escherichia coli (Gram-negative). The imidazolidines have been liquefied in dimethylsulfoxide to prepare the test solutions of 10 mg/mL concentration. Gentamycin have been used as a standard and the activities have been submitted as zones of inhibition for each compound (Table-2).

3. Results and Discussion

3.1. Chemistry.

The target compounds have been synthesized in order to Scheme-I. Eight intermediates were prepared as the platforms for the designated compounds through two steps. In the first step, initiator aldehyde 2 was prepared by reacting the diazonium salt of 2-aminobenzothiazole 1 with salicylaldehyde dissolved in sodium hydroxide solution using the method described previously. In the second step, the aldehyde derivative 2 was reacted with the primary aromatic amines including (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxynitroaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline) using microwave irradiation in absolute ethanol to produce eight Schiff bases of benzothiazole 3a–h respectively. In the following step, the compounds 3a–h have been allowed to react with L-alanine using microwave irradiation to yield imidazolidine derivatives of benzothiazole 4a–h in good yields (Table-1).

The chemical constructs of the target compounds synthesized have been deduced from IR, $^1$H NMR spectral means and elemental analysis which showed good congruity with the suggested structures.

![Scheme 1. Synthesis of 2,3-disubstituted-5-methyl-1,3-imidazolidines-4-one](image-url)
The IR and $^1$H NMR spectra of the demanded compounds 4a-h have been prescribed in minutiae in the Experimental part. The IR spectrum of azo-benzothiazole derivative 2 showed the loosing of a doublet band at 3375 and 3306 cm$^{-1}$ for (NH$_2$)str in 2-aminobenzothiazole 1 and arising of the following significant bands: the medium band at 1375 cm$^{-1}$ belong to azo group (N=N)str, the band at 3429 cm$^{-1}$ attributed to (O-H)str, the band at 1645 cm$^{-1}$ assigned to aldehydic (C=O)str., the benzothiazolic (C=N)str arose as strong band at 1610 cm$^{-1}$. IR spectra of benzothiazolic-imines 3a-h showed disappearing the band at 1645 cm$^{-1}$ attributed to aldehydic (C=O)str., also absence the doublet band for (NH$_2$)str in the starting amines at the commonly range 3400-3250 cm$^{-1}$ and appearing absorption band at the scope 1604-1633 cm$^{-1}$ due to the iminic (C=N)str. The benzothiazolic (C=N)str appeared at the range 1589-1610 cm$^{-1}$. The IR spectra of the benzothiazolic-imidazolidines 4a-h showed the appearance of strong band at the range 1664-1710 cm$^{-1}$ attributed to the (C=O)str of the imidazolidine ring. The spectra also showed the appearance of absorption band at the scope. 1651-1668 cm$^{-1}$ belong to the (N-H)bend of the imidazolidine ring. The benzothiazolic (C=N)str appeared at the range 1597-1618 cm$^{-1}$.

The structures of the imidazolidine compounds 4a-h have been confirmed by their $^1$H NMR spectra that appeared doublet at δ 1.24, 1.24, 1.24, 1.23, 1.24, 1.24 and 1.23 ppm, respectively belong to the methyl (CH$_3$) protons, the peak for the methine proton (CH$\text{-CH}_3$) of imidazolidine ring as a quartet at 3.84, 3.78, 3.84, 3.85, 3.84, 3.84 and 3.84 ppm, respectively. The (N-CH) proton of imidazolidine appeared as a doublet at 6.52, 6.52, 6.51, 6.52, 6.53, 6.64, 6.59 and 6.59 ppm, respectively. The (Ar-H) protons appeared at δ 6.66–7.73 ppm, the (N-H) proton of imidazolidine ring as a singlet at 8.07, 8.06, 8.07, 8.06, 8.06, 8.06 and 8.06 ppm, respectively. The (O-H) proton appeared as a singlet at 9.51, 9.49, 10.12, 9.51, 9.64, 9.50, 9.53 and 9.65 ppm, respectively. The methoxy protons (O-CH$_3$) in compounds 4d and 4e arose as a singlet at δ 3.61 and 4.16 ppm, consecutively.

Moreover, the (CHNS) elemental analysis findings were subsume ± 0.4% of the calculated values and in good congruity with the suggested chemical structures for compounds 4a-h given in the experimental part.

3.2. Antibacterial activities.
The antibacterial actions of the synthesized imidazolidines 4a-h have been evaluated via the agar diffusion method$^{24}$ using two strains of Gram (+) and Gram (−) bacteria on agar media, as indicated in Table-2. Dimethylsulfoxide has been used as solvent for the assayed compounds.
Table 1. SOME PHYSICAL PROPERTIES OF THE PREPARED COMPOUNDS

| Com. | Physical state       | Rf (developer)         | Mp (oC) | Yield (%) | Time (min.) | Mw (W) |
|------|----------------------|------------------------|---------|-----------|-------------|--------|
| 2    | Dark brown solid     | 0.69 (n-hexane/ EtOAc, 1:2) | 143-145 | 60        | -           | -      |
| 3a   | Brown solid          | 0.75 (n-hexane/ EtOAc, 1:2) | 223-225 | 78        | 30          | 350    |
| 3b   | Dark brown solid     | 0.77 (n-hexane/ EtOAc, 1:2) | 186-188 | 75        | 28          | 320    |
| 3c   | Dark brown solid     | 0.79 (n-hexane/ EtOAc, 1:2) | 178-180 | 79        | 27          | 300    |
| 3d   | Brown solid          | 0.89 (n-hexane/ EtOAc, 1:2) | 197-199 | 73        | 26          | 300    |
| 3e   | Dark brown solid     | 0.79 (n-hexane/ EtOAc, 1:2) | 201-203 | 77        | 30          | 310    |
| 3f   | Dark brown solid     | 0.86 (n-hexane/ EtOAc, 1:2) | 175-177 | 69        | 30          | 320    |
| 3g   | Brown solid          | 0.75 (n-hexane/ EtOAc, 1:2) | 208-210 | 76        | 28          | 320    |
| 3h   | Brown solid          | 0.79 (n-hexane/ EtOAc, 1:2) | 165-167 | 77        | 30          | 310    |
| 4a   | Yellow solid         | 0.89 (n-hexane/ EtOAc, 1:2) | 249-251 | 74        | 24          | 610    |
| 4b   | Dark orange solid    | 0.81 (n-hexane/ EtOAc, 1:2) | 243-245 | 73        | 23          | 600    |
| 4c   | Orange solid Dark    | 0.81 (n-hexane/ EtOAc, 1:2) | 299-301 | 70        | 22          | 600    |
| 4d   | Orange solid         | 0.79 (n-hexane/ EtOAc, 1:2) | 234-236 | 74        | 21          | 560    |
| 4e   | Orange solid         | 0.78 (n-hexane/ EtOAc, 1:2) | 204-206 | 77        | 20          | 550    |
| 4f   | Dark orange solid    | 0.83 (n-hexane/ EtOAc, 1:2) | 281-283 | 76        | 24          | 570    |
| 4g   | Yellow solid         | 0.79 (n-hexane/ EtOAc, 1:2) | 319(dec.) | 78     | 22          | 600    |
| 4h   | Dark brown solid     | 0.76 (n-hexane/ EtOAc, 1:2) | 288-290 | 79        | 22          | 600    |

Table 2. THE ANTIBACTERIAL ACTIVITY OF COMPOUNDS 4a-h AND GENTAMYCIN AS CONTROL DRUG

| Product       | Staphylococcus aureus (Gram-positive) | Escherichia coli (Gram-negative) |
|---------------|---------------------------------------|----------------------------------|
| 4a            | 0                                     | 0                                |
| 4b            | 11                                    | 0                                |
| 4c            | 20                                    | 17                               |
| 4d            | 19                                    | 0                                |
| 4e            | 12                                    | 0                                |
| 4f            | 20                                    | 16                               |
| 4g            | 18                                    | 0                                |
| 4h            | 22                                    | 0                                |
| DMSO          | 0                                     | 0                                |
| Gentamycin    | 15                                    | 15                               |
4. Conclusions
The microwave irradiation is considered efficient and economic technique including short reaction time and high yield in comparison with the conventional method. The rates of reactions of imines with alanine for formation of imidazolidines are approximately equal. All synthesized imidazolidines could be converted to the corresponding phenol salts which are completely soluble in water. The synthesized imidazolidines appeared higher biological action against Gram-positive bacteria than that of Gram-negative bacteria. Imidazolidine compounds 4c, 4d, 4f, 4g and 4h were found to be greater activity than gentamycin against Gram-positive bacteria, while compounds, 4c and 4f showed better activity to the control drug against Gram-negative bacteria.

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