Microwave Synthesis and Antibacterial Activities of New Imidazolidines Derived from 2-Aminobenzothiazole

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2-Aminobenzothiazole (**1**) was converted to the corresponding diazonium salt which was introduced in coupling reaction with alkaline solution of 2-hydroxybenzaldehyde as coupling reagent to give azo-benzothiazole derivative (**2**) bearing aldehyde group. The resulting aldehyde (**2**) was introduced in condensation reactions with the primary aromatic amines including (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxyaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline) using microwave irradiation technique in absolute ethanol to produce eight imine derivatives of benzothiazole (**3a-h**), respectively**.** Treatment of the resulting imines (**3a-h**) with glycine using microwave irradiation in tetrahydrofuran afforded eight new imidazolidines (**4a-h**) substituted with benzothiazole moiety, respectively. Preliminary *in vitro* antibacterial activity of the target compounds were investigated using two types of bacteria, *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative). The results indicated that the newly synthesized imidazolidines (compounds **4a**, **4b**, **4c**, **4d**, **4e**, **4g** and **4h**) exhibited greater activities than gentamycin against Gram-positive bacteria. On the other hand, compounds **4d** and **4h** were also showed better activities against Gram-negative bacteria when compared with that of the control drug (gentamycin).

Keywords: Imidazolidines, Imines, Benzothiazoles, Azo, Antibacterial activity.

INTRODUCTION

Imidazolidines (saturated imidazoles), also known as tetra-hydroimidazoles are biologically active nitrogen containing heterocyclic moiety which have been reported to shown wide array of significant bioactivities [1]. Moreover, the construction of optically active stereogenic center in a saturated heterocycle such as imidazolidine [2]. Imidazolidines have found therapeutic applications in drugs such as the well established phenytoin [3]. Among the wide range of biological activities of substituted hydantoins we can cite antidiabetic, anti-inflammatory, anti-viral, GHS and CB1 receptor antagonists[3] and more. Imidazo-lidine ring of such compounds yields molecules with variety of pharmacological properties, including anti-inflammatory, antifungal, antibacterial, hypoglycemic, schistosomicides anti-cancer activities [4], antihypertensive/anaesthetic [5], anti-arrhythmic [6], modulation of anxiety [7], antinociceptive activity [8], anti-Alzheimer's [9], antimicrobial [10], anti-nociceptive [11], antitumor [12], anti-trypanosoma cruzi [13], anti-depressant [14] and antifungal drugs [15]. Benzothiazole consists of thiazole ring fused with benzene and is also called 1-thia-3-azaindene. It is a weak base and thermally stable molecule [16]. In the 1990s, various pharmacological investi-

gations of newly synthesized benzothiazoles demonstrated interesting pharmacological activities and led to the develop-ment of new medications for treating diseases. They were studied extensively for their antiallergic, antiinflammatory [17], analgesic [18], antitumor [19], antiproliferative activities [20]. Benzothiazoles have been reported to be antioxidant agents [21], antitubercular [22], antipsychotic [23], anticonvulsant [24], anticancer agents [25], antiparasite activity [26], anti-malaria [27], *etc*.

EXPERIMENTAL

The chemicals were used as provided from Fluka, Sigma Aldrich and Merck. Microwave reactions were performed on domestic microwave oven in crucible. Analytical TLC was performed with silica gel 60 F_{254} plates. The reactions were monitored by TLC and visualized by development of the TLC plates with iodine vapour. Melting points were recorded on an Electro thermal Stuart SMP 30 capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on SHIMADZU FTIR-8400S infrared spectrophotometer as potassium bromide discs. ^{1}H NMR spectra was collected on Avance III 500, NMR spectrometer, Bruker, Germany at 500 MHz in DMSO-d_6 as

solvent and TMS as an internal standard at a Faculty of Science, University of Tarbiat Modares, Iran. (CHNS) Elemental analysis was carried out with Perkin Elmer 300A elemental analyzer at a Faculty of Science, University of Tarbiat Modares, Iran.

(*E*)-5-(Benzo[*d*]thiazol-2-yldiazenyl)-2-hydroxy benzaldehyde (**2**) was synthesized following the method described by Acton [28] as dark brown solid, m.p. 141-143 °C, yield 60 %; IR (cm⁻¹): 3429$_{br}$ ν(O-H), 3068 ν(C-H) benzene, 2856 and 2715 ν(C-H) aldehyde, 1645 ν(C=O) aldehyde, 1610 ν(C=N) benzothiazole, 1502 and 1475 ν(C=C) benzene,1375 ν(N=N), 759 δ(o.o.p.C-H) benzene.

General procedure for synthesis of imines (3a-h): All reactions were carried out on domestic microwave oven in crucible. Reactions contained the azoaldehyde 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 (300-350 W) for 25-30 min. TLC (*n*-hexane: EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-)((4-nitrophenyl)imino)methyl]phenol (3a): IR (cm⁻¹): 3371 ν(O-H), 3064 ν(C-H) benzene,1608 ν(C=N) imine, 1589 ν(C=N) benzothiazole, 1514 νas(NO₂), 1448 ν(C=C) benzene, 1404 ν(N=N), 1336 ν(s.NO₂), 758 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((3-nitrophenyl)imino)methyl]phenol (3b): IR (cm⁻¹): 3246 ν(O-H), 3088 ν(C-H) benzene, 1604 ν(C=N) imine and ν(C=N) benzothiazole, vib. coupling, 1573 and 1502 and 1444 ν(C=C) benzene, 1525 νas(NO₂), 1396 ν(N=N), 1354 ν(s.NO₂), 758 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((4-hydroxyphenyl)imino)methyl]phenol (3c): IR (cm⁻¹): 3369 and 3298 ν(O-H), 3032 ν(C-H) benzene, 1610 ν(C=N, imine and ν(C=N) benzothiazole, vib. coupling), 1514 and 1460 ν(C=C) benzene, 1379 ν(N=N), 827 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((4-methoxyphenyl)imino)methyl]phenol (3d): IR (cm⁻¹): 3371 and 3298 ν(O-H), 3037 ν(C-H) benzene, 2949 νas(CH₃), 1622 ν(C=N) imine, 1595 ν(C=N) benzothiazole, 1512 and 1456 ν(C=C) benzene, 1392 ν(N=N), 821 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((2-methoxyphenyl)imino)methyl]phenol (3e): IR (cm⁻¹): 3462 and 3265 ν(O-H), 3064 ν(C-H) benzene, 2968 νas(CH₃), 2870 ν(s.CH₃), 1633 ν(C=N) imine, 1608 ν(C=N) benzothiazole, 1533, 1500 and 1444 ν(C=C) benzene, 1363 ν(N=N), 831 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((4-bromophenyl)imino)methyl]phenol (3f): IR (cm⁻¹): 3369 and 3261 ν(O-H), 3066 ν(C-H) benzene,1633 ν(C=N) imine, 1608 ν(C=N) benzothiazole, 1506 and 1489 ν(C=C) benzene, 1363 ν(N=N), 821 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((4-chlorophenyl)imino)methyl]phenol (3g): IR (cm⁻¹): 3369 and 3263 ν(O-H), 3064 ν(C-H) benzene, 1633 ν(C=N) imine, 1606

ν(C=N) benzothiazole, 1537, 1496 and 1442 ν(C=C) benzene, 1367 ν(N=N), 821 δ(o.o.p.C-H) benzene.

4-[(E)-Benzo[*d*]thiazol-2-yldiazenyl]-2-[(E)-((2,4-dichlorophenyl)imino)methyl]phenol (3h): IR (cm⁻¹): 3470 and 3265 ν(O-H), 3061 ν(C-H) benzene,1633 ν(C=N) imine, 1608 ν(C=N) benzothiazole, 1570, 1533, 1500 and 1444 ν(C=C) benzene, 1363 ν(N=N), 831 δ(o.o.p.C-H) benzene.

General procedure for synthesis of imidazolidines (4a-h): A mixture of equimolar amounts of imine derivatives (**3a-h**) (1 mmol) and glycine (0.075 g, 1 mmol) in tetrahydrofuran (1 mL) was heated (550-610 W) in microwave oven for 20-25 min. TLC (*n*-hexane:EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol.

(E)-2-[5-(Benzo[*d*]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(4-nitrophenyl)imidazolidin-4-one (4a): IR (cm⁻¹): 3365$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling), 3074 ν(C-H) benzene, 1708 ν(C=O) imidazolidine, 1680 δ(N-H) imidazolidine, 1539 and 1456 ν(C=C) benzene, 1516 νas(NO₂), 1419 ν(N=N), 1321 νs(NO₂), 756 δ(o.o.p.C-H) benzene; ¹H NMR: δ (ppm) = 3.69 (d, *J* = 6.5 Hz, 2H, CH₂) imidazolidine, 6.63 (d, *J* = 8.1 Hz, 1H, CH) imidazolidine, 7.37–7.96 (11H, Ar–H), 8.14 (s, 1H, N–H) imidazolidine, 9.48 (s, 1H, O–H). The singlet signals around 2.49 ppm and 3.44 ppm attributed to DMSO and absorbed H₂O in DMSO, respectively; Anal. calcd. for C₂₂H₁₆N₆O₄S: C, 57.39; H, 3.50; N, 18.25; S, 6.96; Found C, 56.99; H, 3.45; N, 18.02; S, 6.96.

(E)-2-[5-(Benzo[*d*]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(3-nitrophenyl)imidazolidin-4-one (4b): IR (cm⁻¹): 3402$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling), 3074 ν(C-H) benzene, 1710 ν(C=O) imidazolidine, 1683 δ(N-H) imidazolidine, 1604 ν(C=N) benzothiazole, 1508 νas(NO₂), 1456 and 1421 ν(C=C) benzene, 1384 ν(N=N), 1323 νs(NO₂), 759 δ(o.o.p.C-H) benzene; ¹H NMR: δ (ppm) = 3.69 (d, *J* = 20.0 Hz, 2H, CH₂) imidazolidine, 6.62 (s, 1H, CH) imidazolidine, 6.92–7.97 (11H, Ar–H), 8.12 (s, 1H, N–H) imidazolidine, 9.56 (s, 1H, O–H). The singlet signals around 2.49 ppm and 3.42 ppm assigned to DMSO and absorbed H₂O in DMSO, respectively; Anal. calcd. for C₂₂H₁₆N₆O₄S:C, 57.39; H, 3.50; N, 18.25; S, 6.96; Found C, 57.01; H, 3.45; N, 18.12; S, 6.77.

(E)-2-[5-(Benzo[*d*]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(4-hydroxyphenyl)imidazolidin-4-one (4c): IR (cm⁻¹): 3200$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling, 3080 ν(C-H) benzene, 1670 ν(C=O) and δ(N-H) imidazolidine, vib. coupling, 1616 ν(C=N) benzothiazole, 1539, 1514 and 1454 ν(C=C) benzene, 1417 ν(N=N), 893 δ(o.o.p.C-H) benzene; ¹H NMR: δ (ppm) = 3.69 (d, *J* = 11.3 Hz, 2H, CH₂) imidazolidine, 6.63 (d, *J* = 7.3 Hz, 1H, CH) imidazolidine, 6.89–7.99 (11H, Ar–H), 8.12 (s, 1H, N–H) imidazolidine, 9.53 (s, 2H, 2×O–H). The singlet signals around 2.49 ppm and 3.43 ppm due to DMSO and absorbed H₂O in DMSO, respectively; Anal. calcd. for C₂₂H₁₇N₅O₃S: C, 61.24; H, 3.97; N, 16.23; S, 7.43; Found C, 60.88; H, 3.61; N, 16.30; S, 7.33.

(E)-2-[5-(Benzo[*d*]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(4-methoxyphenyl)imidazolidin-4-one (4d): IR (cm⁻¹): 3250$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling, 3074 ν(C-H) benzene, 2964 νas(CH₃) 1670 ν(C=O) and δ(N-H) imidazolidine, vib. coupling, 1602 ν(C=N) benzothiazole,

1514 and 1458 ν(C=C) benzene, 1421 ν(N=N), 829 δ(o.o.p.C-H) benzene; ^{1}H NMR: δ (ppm) = 3.69 (d, J = 12.8 Hz, 2H, CH$_2$) imidazolidine, 3.94 (s, 3H, O–CH$_3$), 6.63 (d, J = 8.3 Hz, 1H, CH) imidazolidine, 6.79–7.98 (11H, Ar–H), 8.15 (s, 1H, N–H) imidazolidine, 9.52 (s, 1H, O–H).The singlet signals around 2.49 and 3.42 ppm assigned to DMSO and absorbed H$_2$O in DMSO, respectively; Anal. calcd. for C$_{23}$H$_{19}$N$_5$O$_3$S:C, 62.01; H, 4.30; N, 15.72; S, 7.20; Found C, 61.88; H, 4.26; N, 15.51; S, 7.01.

(E)-2-[5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(2-methoxyphenyl)imidazolidin-4-one (4e): IR (cm^{-1}): 3192$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling, 3072 ν(C-H) benzene, 1681 ν(C=O) imidazolidine, 1653 δ(N-H) imidazolidine, 1610 ν(C=N) benzothiazole, 1558, 1541 and 1456 ν(C=C) benzene, 1423 ν(N=N), 823 δ(o.o.p.C-H) benzene; ^{1}H NMR: δ (ppm) = 3.69 (d, J = 12.8 Hz, 2H, CH$_2$) imidazolidine, 3.83 (s, 3H, O–CH$_3$), 6.77 (d, J = 8.3 Hz, 1H, CH) imidazolidine, 7.01–7.99 (11H, Ar–H), 8.15 (s, 1H, N–H) imidazolidine, 9.62 (s, 1H, O–H).The singlet signals around 2.49 and 3.39 ppm assigned to DMSO and absorbed H$_2$O in DMSO, respectively; Anal. calcd. for C$_{23}$H$_{19}$N$_5$O$_3$S:C, 62.01; H, 4.30; N, 15.72; S, 7.20; Found C, 62.37; H, 4.21; N, 15.36; S, 7.11.

(E)-2-[5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(4-bromophenyl)imidazolidin-4-one(4f): IR (cm^{-1}): 3176$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling, 3063 ν(C-H) benzene, 1666 ν(C=O) and δ(N-H) imidazolidine, vib. coupling, 1610 ν(C=N) benzothiazole, 1508 ν(C=C) benzene, 1415 ν(N=N), 823 δ(o.o.p.C-H) benzene; ^{1}H NMR: δ (ppm) = 3.69 (d, J = 23.8 Hz 2H, CH$_2$) imidazolidine, 6.54 (d, J = 8.0 Hz, 1H, CH) imidazolidine, 6.67–8.00 (11H, Ar–H), 8.15 (s, 1H, N–H) imidazolidine, 9.64 (s, 1H, O–H). The singlet signals around 2.49 and 3.51 ppm due to DMSO and absorbed H$_2$O in DMSO, respectively; Anal. calcd. for C$_{22}$H$_{16}$N$_5$O$_2$SBr: C, 53.45; H, 3.26; N, 14.17; S, 6.49; Found C, 52.08; H, 3.59; N, 13.93; S, 6.45.

(E)-2-[5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(4-chlorophenyl)imidazolidin-4-one (4g): IR (cm^{-1}): 3184$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling, 3066 ν(C-H) benzene, 1670 ν(C=O) and δ(N-H) imidazolidine, vib. coupling, 1610 ν(C=N) benzothiazole, 1523 and 1508 ν(C=C) benzene, 1417 ν(N=N), 893 δ(o.o.p.C-H) benzene; ^{1}H NMR: δ (ppm) = 3.69 (d, J = 23.8 Hz, 2H, CH$_2$) imidazolidine, 6.52 (d, J = 8.0 Hz, 1H, CH) imidazolidine, 6.67–7.99 (11H, Ar–H), 8.15 (s, 1H, N–H) imidazolidine, 9.17 (s, 1H, O–H).The singlet signals around 2.49 ppm and 3.39 ppm attributed to DMSO and absorbed H$_2$O in DMSO, respectively; Anal. calcd. for C$_{22}$H$_{16}$N$_5$O$_2$SCl:C, 58.73; H, 3.58; N, 15.57; S, 7.13; Found C, 58.64; H, 3.69; N, 15.23; S, 7.38.

(E)-2-[5-(Benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl]-3-(2,4-dichlorophenyl)imidazolidin-4-one (4h): IR (cm^{-1}): 3232$_{br}$ ν(O-H) and ν(N-H) imidazolidine, vib. coupling), 3082 ν(C-H) benzene, 1681 ν(C=O) imidazolidine, 1653 δ(N-H) imidazolidine, vib. coupling, 1608 ν(C=N) benzothiazole, 1554, 1541 and 1508 ν(C=C) benzene, 1423 ν(N=N), 819 δ(o.o.p.C-H) benzene; ^{1}H NMR: δ (ppm) = 3.68 (d, J = 7.4 Hz, 2H, CH$_2$) imidazolidine, 6.74 (d, J = 8.3 Hz, 1H, CH) imidazolidine, 7.01–8.14 (10H, Ar–H), 9.29 (s, 1H, N–H)

imidazolidine, 9.62 (s, 1H, O–H).The singlet signals around 2.49 and 3.35 ppm assigned to DMSO and absorbed H$_2$O in DMSO, respectively; Anal. calcd. for C$_{22}$H$_{15}$N$_5$O$_2$SCl$_2$: C, 54.55; H, 3.12; N, 14.46; S, 6.62; Found C, 54.21; H, 3.02; N, 14.22; S, 6.31.

Preliminary antibacterial assay: The antibacterial activities of the newly synthesized imidazolidines (**4a-h**) were determined by the agar diffusion method [29] using representative Gram (+) and Gram (–) bacteria on tryptic soya agar media. The test microorganisms to evaluate the potential antibacterial activity of the newly synthesized imidazolidines were *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative). The imidazolidines were dissolved in dimethyl sulfoxide to prepare the test solutions of10 mg/mL concentration. Gentamycin was used as a reference and the activities were presented as zones of inhibition for each compound.

RESULTS AND DISCUSSION

Amino group in 2-aminobenzothiazole (**1**) was diazotized using sodium nitrite and sulfuric acid to generate the corresponding diazonium salt which was directly introduced in coupling reaction with 2-hydroxy benzaldehyde dissolved in sodium hydroxide solution to give azo-benzothiazole derivative (**2**) containing aldehyde group. Aldehyde group of azo-benzothiazole derivative (**2**) was condensed 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 imine derivatives of benzothiazole (**3a-h**) respectively (**Scheme**s **I** and **II**). The resulting imines (**3a-h**) were allowed to react with the glycine a using microwave irradiation leading to the formation of imidazolidine derivatives of benzothiazole (**4a-h**) in good yields (Table-1).

The chemical structures of the target compounds synthesized were deduced from IR, ^{1}H NMR spectral measurements and (CHNS) elemental analysis and were in good agreement with the proposed structures.

The IR and ^{1}H NMR spectra of the desired compounds **4a-h** were described. The IR spectrum of azo-benzothiazole derivative (**2**) indicated the absence of a doublet band at 3375 and 3306 cm^{-1} for (NH$_2$) str. in 2-aminobenzothiazole (**1**) and appearance of the following characteristic bands: the medium band at 1375 cm^{-1} attributed to azo group (N=N) str, the broad band at 3429 cm^{-1} assigned to (O-H) str, the sharp and strong band at 1645 cm^{-1} belong to aldehydic (C=O) str., the benzothiazolic (C=N) str. appeared as strong band at 1610 cm^{-1}. IR spectra of the benzothiazolicimines (**3a-h**) showed disappearing the sharp and strong band at 1645 cm^{-1} for aldehydic (C=O) str., also disappearing the sharp doublet band for (NH$_2$) str. in the starting amines at the general range 3400-3250 cm^{-1} and appearing absorption band at the range 1633-1604 cm^{-1} assigned to the iminic (C=N) str. The benzothiazolic (C=N) str. appeared at the range 1610-1589 cm^{-1}. The IR spectra of the benzothiazolic-imidazolidines (**4a-h**) showed the appearance of strong band at the range 1710-1666 cm^{-1} attributed to the (C=O) str. of the imidazolidine ring. The spectra also showed the appearance of absorption band at the range 1683-1653 cm^{-1}
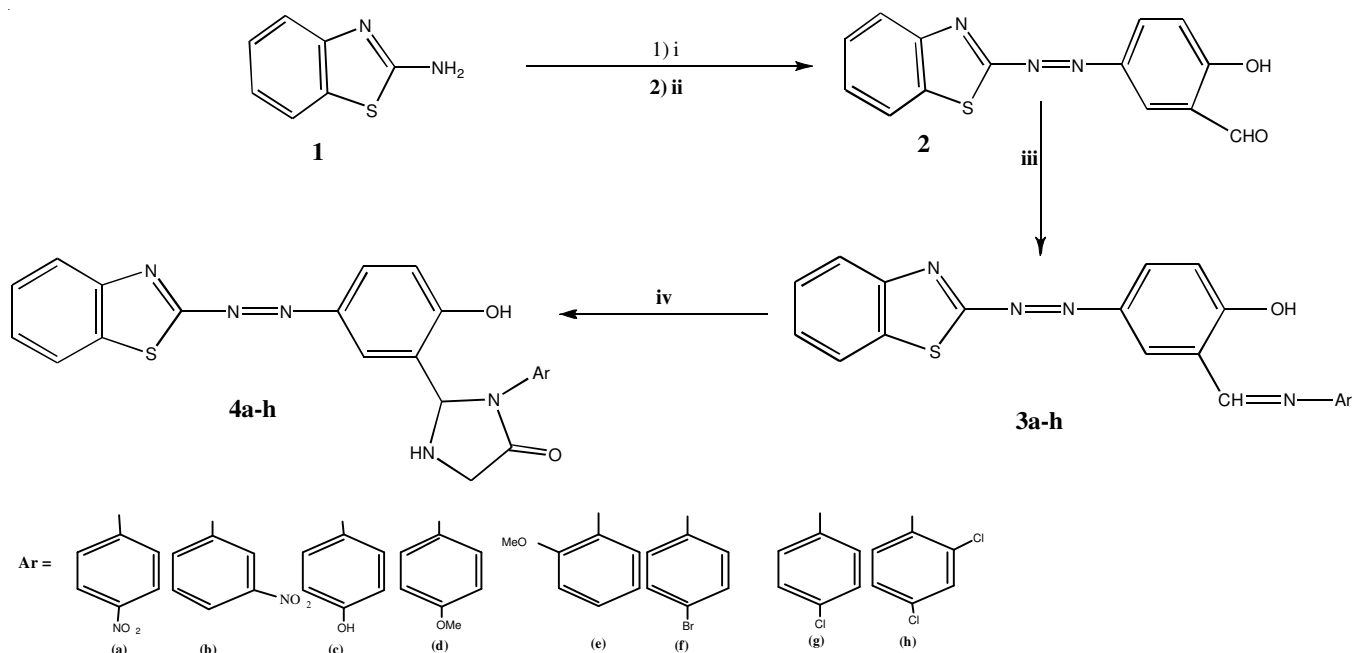
**Scheme-I:** Synthesis of imidazolidines, Reagents and conditions (i) NaNO₂, H₂SO₄, 0 °C; (ii) 2-hydroxybenzaldehyde, NaOH 10 %, 5 °C; (iii) Ar-NH₂,EtOH, MW (300-350 W), 25-30 min; (iv) glycine, THF, MW (550-610 W), 20-25 min

TABLE-1

PHYSICAL PROPERTIES OF THE SYNTHESIZED COMPOUNDS

Product	Colour	R_f (developer)	m.p. (°C)	Yield (%)	Time (min)	MW (W)
2	Dark brown solid	0.68 (*n*-hexane/EtOAc, 1:2)	141-143	60	–	–
3a	Brown solid	0.78 (*n*-hexane/EtOAc, 1:2)	221-223	78	30	350
3b	Dark brown solid	0.73 (*n*-hexane/EtOAc, 1:2)	184-186	75	28	320
3c	Dark brown solid	0.75 (*n*-hexane/EtOAc, 1:2)	176-178	79	27	300
3d	Brown solid	0.88 (*n*-hexane/EtOAc, 1:2)	195-197	73	26	300
3e	Dark brown solid	0.70 (*n*-hexane/EtOAc, 1:2)	199-201	77	30	310
3f	Dark brown solid	0.83 (*n*-hexane/EtOAc, 1:2)	173-175	69	30	320
3g	Brown solid	0.75 (*n*-hexane/EtOAc, 1:2)	206-208	76	28	320
3h	Brown solid	0.70 (*n*-hexane/EtOAc, 1:2)	163-165	77	26	310
4a	Orange solid	0.69 (*n*-hexane/EtOAc, 1:2)	281(dec.)	75	24	600
4b	Solid yellow	0.71 (*n*-hexane/EtOAc, 1:2)	322-324	78	23	600
4c	Dark orange solid	0.71 (*n*-hexane/EtOAc, 1:2)	219-221	75	23	550
4d	Dark orange solid	0.69 (*n*-hexane/EtOAc, 1:2)	134-136	78	22	550
4e	Yellow solid	0.68 (*n*-hexane/EtOAc, 1:2)	198-200	74	24	570
4f	Orange solid	0.73 (*n*-hexane/EtOAc, 1:2)	228-230	79	25	590
4g	Yellow solid	0.74 (*n*-hexane/EtOAc, 1:2)	180-182	78	25	600
4h	Dark brown solid	0.72 (*n*-hexane/EtOAc, 1:2)	233-235	76	23	610
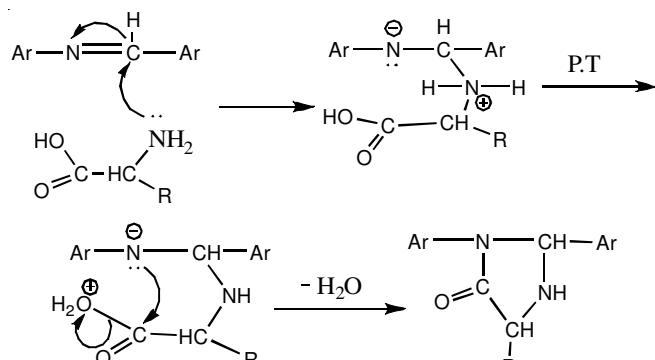
Scheme-II: Proposed mechanism for the formation of imidazolidine ring

assigned to the δ(N-H) bending of the imidazolidine ring. The benzothiazolic ν(C=N) str. appeared in the range 1616-1602 cm⁻¹.

The structures of imidazolidine compounds **4a-h** were proven by their ¹H NMR spectra (500 MHz, DMSO-d_6) which showed the peak for the methylene protons (CH₂) of imidazolidine ring as a doublet at δ 3.69, 3.69, 3.69, 3.69, 3.69, 3.69, 3.69 and 3.68 ppm, respectively. The (N-CH-N) proton of imidazolidine ring appeared as a doublet at 6.63, 6.62, 6.63, 6.63, 6.77, 6.54, 6.52 and 6.74 ppm, respectively. The (Ar-H) protons at δ 6.67-8.14 ppm, the (N-H) proton of imidazolidine ring as a singlet at 8.14, 8.12, 8.12, 8.15, 8.15, 8.15, 8.15 and 9.29 ppm, respectively. The (O-H) proton as a singlet at 9.48, 9.56, 9.53, 9.52, 9.62, 9.64, 9.17 and 9.62 ppm, respectively. The methoxy protons -OCH₃ in compounds **4d** and **4e** appeared as a singlet at δ 3.94 and 3.83 ppm, respectively.

Moreover, the (CHNS) elemental analysis results were within ± 0.4 % of the theoretical values and in good agreement with the proposed chemical structures for compounds **4a-h**.

Antibacterial activities: The antibacterial activities of the newly synthesized imidazolidines (**4a-h**) were evaluated by the agar diffusion method [29] using representative standard strains of Gram (+) and Gram (–) bacteria on tryptic soya agar media (Table-2). Dimethyl sulfoxide was used as solvent for the test compounds.

TABLE-2
ANTIBACTERIAL ACTIVITY OF COMPOUNDS (**4a-h**) AND GENTAMYCINAS CONTROL DRUG

Product	*Staphylococcus aureus* (Gram-positive)	*Escherichia coli* (Gram-negative)
4a	22	0
4b	18	15
4c	19	0
4d	16	16
4e	20	0
4f	0	10
4g	22	0
4h	21	17
DMSO	0	0
Gentamycin	15	15

Imidazolidine compounds **4a**, **4b**, **4c**, **4d**, **4e**, **4g** and **4h** were found to be greater activity than gentamycin against Gram-positive bacteria. Moreover, compounds **4d** and **4h** also showed better activity to the control drug against Gram-negative bacteria.

Conclusion

The microwave irradiation is efficient technique including short reaction time and high yield in comparison with the classical thermal method. The rates of reactions of imines with glycine 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 **4a**, **4b**, **4c**, **4d**, **4e**, **4g** and **4h** were found to be greater activity than gentamycin against Gram-positive bacteria, while compounds **4d** and **4h** showed better activity to the control drug against Gram-negative bacteria.

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