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Microwave Synthesis and Antibacterial Activities of Some Imidazolidine Derivatives Containing 1,3,4-Oxadiazole Moiety

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5-(4-Aminophenyl)-2-thiol-1,3,4-oxadiazole (**1**) was synthesized *via* the reaction of carbon disulfide with 4-aminobenzoyl hydrazide in presence of potassium hydroxide in absolute ethanol. Compound **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 azooxadiazole derivative **2** containing aldehyde group. The resulting aldehyde **2** was then introduced in condensation reactions with the primary aromatic amines including (4-bromoaniline, 4-chloroaniline, 4-nitroaniline, 3-nitroaniline, 4-methoxyaniline and 4-hydroxyaniline) using microwave irradiation technique in absolute ethanol to produce six imine derivatives of 1,3,4-oxadiazole (**3a-f**), respectively. Treatment of the resulting imines **3a-f** with glycine using microwave irradiation in tetrahydrofuran afforded six new imidazolidines **4a-f** substituted with 1,3,4-oxadiazole moiety, respectively. *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 **4d** and **4f**) showed enhanced activity against Gram-negative bacteria when compared with that of the control drug (gentamycin).

Keywords: Imidazolidines, 1,3,4-Oxadiazoles, Imines, Antibacterial activity.

INTRODUCTION

The imidazolidine is five-membered heterocycles containing two nitrogen atoms [1]. N-heterocyclic carbine (NHC)-derived complexes have been used as powerful catalysts for effecting many transformations [2]. Imidazolidine, a fully saturated imidazole heterocycle, is an important intermediate and building block in the construction of a variety of biologically active compounds [3]. Imidazolidine compounds showed a variety of biological activities such as antibacterial, antitubercular, antifungal, anti-HIV, antileishmanial, anti-nociceptive, anti-inflammatory and analgesic activities [4,5]. They are also used for the treatment of schistosomiasis infections [6], anticonvulsant activity and reduced toxicity [7], anti-diabetic [8]. Imidazolidines have antitumor, antiarrhytmic and antiandrogenic activity. The activity of imidazolidin-2,4-diones (hydantoin) depends on the nature of substitution of imidazolidine ring [9]. Among imidazolidine-2-ones phenytoin is known as antiepileptic drug and antihypertensive substance [10].

Oxadiazoles are cyclic compounds containing one oxygen and two nitrogen atoms in a five- membered ring. The sequence of these atoms may be different as 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,2,3-oxadiazole or 1,3,4-oxadiazole [11]. Oxadiazole moiety is derived from furan by replacing two -CH= group with two pyridine typed nitrogen (-N=) [12]. Five-membered N-containing heterocyclic aromatic compounds found in natural products [13]. Oxadiazoles have often been described as bioisosteres for amides and esters [14]. Furthermore the 1,3,4-oxadiazole derivatives have some industrial applications in the fields of dyes, photosensitivity electrical materials and liquid crystals [15]. 1,3,4-Oxadiazoles and their derivatives represent an important scaffold that has been found in many natural and synthesized molecules because of their remarkable biological activities [16] as anticancer [17], antifungal [18], antitumor [19], antibacterial [20], antiparasitic [22], anti-HIV [22], anti-infective [23], muscle relaxants [24], antiseptics [25] and cathepsin K inhibitors [26].

EXPERIMENTAL

The chemicals were used as provided from Fluka, sigma Aldrich, J.T. Baker 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 Tehran, Iran.

5-(4-Aminophenyl)-2-thiol-1,3,4-oxadiazole (**1**) was synthesized according to Yong and Wood method [27]. Pale yellow crystals, m.p. 234-236 °C, yield 82 %; IR (cm^{-1}): 3450 $\nu_{as.}(NH_2)$, 3354 $\nu_{s.}(NH_2)$, 3095 ν(N-H) thione form and ν(C-H) benzene, vib. coupling, 2951 and 2767 ν(N-H) intramolecularly hydrogen bonded, thione form, 2590 ν(S-H) thiol form, 1606s ν(C=N) oxadiazole and $\delta(NH_2)$ vib. coupling, 1514 and 1440 ν(C=C) benzene, 1066 ν(C=S) thione form, 839 δo.o.p.(C-H) benzene.

(*E*)-2-Hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)-phenyl)diazenyl)benzaldehyde (**2**) was synthesized following the method described by Acton [28] as red solid, m.p.: 204-206 °C, yield 79 %; IR (cm^{-1}): 3402br ν(O-H), 3190 ν(N-H) thione form, 3095 ν(C-H) benzene, 2937 and 2748 ν(N-H) intramolecularly hydrogen bonded, thione form, 2885 ν(C-H) aldehyde, 2580 ν(S-H) thiol form, 1662 ν(C=O) aldehyde, 1604 ν(C=N) oxadiazole, 1477 ν(C=C) benzene, 1411 ν(N=N), 1068 ν(C=S) thione form, 842 δo.o.p.(C-H) benzene.

General procedure for the synthesis of imines 3a-f: All reactions were carried out on domestic microwave oven in crucible. Reactions contained the aldehyde derivative **2** (0.326 g, 1 mmol), equimolar amount (1 mmol) of aniline derivatives (4-bromoaniline, 4-chloroaniline, 4-nitroaniline, 3-nitroaniline, 4-methoxyaniline and 4-hydroxyaniline, respectively) and absolute ethanol (1 mL). The crucible was introduced to the center of a domestic microwave oven and then heated at (300 W) for 25 min. TLC (*n*-hexane: EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol.

2-((*E*)-((4-Bromophenyl)imino)methyl)-4-((*E*)-(4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenol (3a): IR (cm^{-1}): 3352 ν(O-H), 3064 ν(N-H) thione form and ν(C-H) benzene, vib. coupling, 2943 and 2758 ν(N-H) intramolecularly hydrogen bonded, thione form, 2553 ν(S-H) thiol form, 1614s ν(C=N) imine and ν(C=N) oxadiazole, vib. coupling, 1508 and 1487 ν(C=C) benzene, 1413 ν(N=N), 1070 ν(C=S) thione form, 833 δo.o.p.(C-H) benzene.

2-((*E*)-((4-Chlorophenyl)imino)methyl)-4-((*E*)-(4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenol (3b): IR (cm^{-1}): 3327 ν(O-H) and ν(N-H) thione form, vib. coupling, 3074 ν(C-H) benzene, 2918 and 2756 ν(N-H) intramolecularly hydrogen bonded, thione form, 2580 ν(S-H) thiol form, 1612s ν(C=N) imine and ν(C=N) oxadiazole, vib. coupling, 1504 and 1491 ν(C=C) benzene, 1413 ν(N=N), 1068 ν(C=S) thione form, 831 δo.o.p.(C-H) benzene.

4-((*E*)-(4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)-diazenyl)-2-((*E*)-((4-nitrophenyl)imino)methyl)phenol (3c): IR (cm^{-1}): 3481 and 3363 ν(O-H), 3219 ν(N-H) thione form, 3080 ν(C-H) benzene, 2935 and 2760 ν(N-H) intramolecularly hydrogen bonded, thione form, 2594 ν(S-H) thiol form, 1597s ν(C=N) imine and ν(C=N) oxadiazole, vib. coupling, 1506s ν(C=C) benzene and $\nu_{as.}(NO_2)$ vib. coupling, 1411 ν(N=N), 1329 $\nu_{s.}(NO_2)$, 1066 ν(C=S) thione form, 840 δo.o.p.(C-H) benzene.

4-((*E*)-(4-(5-Mercapto-1,3,4-oxadiazol-2-yl)phenyl)-diazenyl)-2-((*E*)-((3-nitrophenyl)imino)methyl)phenol (3d): IR (cm^{-1}):3279 ν(O-H), 3072 ν(N-H) thione form and ν(C-H) benzene, vib. coupling, 2933 and 2748 ν(N-H) intramolecularly hydrogen bonded, thione form, 2573 ν(S-H) thiol form, 1604s ν(C=N) imine and ν(C=N) oxadiazole, vib. coupling, 1525s ν(C=C) benzene and $\nu_{as.}(NO_2)$ vib. coupling, 1415 ν(N=N), 1350 $\nu_{s.}(NO_2)$, 1066 ν(C=S) thione form, 840 δo.o.p.(C-H) benzene.

4-((*E*)-(4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)-diazenyl)-2-((*E*)-((4-methoxyphenyl)imino)methyl)phenol (3e): IR (cm^{-1}):3336 ν(O-H), 3055 ν(N-H) thione form and ν(C-H) benzene, vib. coupling, 2931 and 2750 ν(N-H) intramolecularly hydrogen bonded, thione form, 2835 $\nu(CH_3)$, 2555 ν(S-H) thiol form, 1610s ν(C=N) imine and ν(C=N) oxadiazole, vib. coupling, 1510 ν(C=C) benzene, 1415 ν(N=N), 1068 ν(C=S) thione form, 831 δo.o.p.(C-H) benzene.

2-((*E*)-((4-Hydroxyphenyl)imino)methyl)-4-((*E*)-(4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenol (3f): IR (cm^{-1}): 3340 and 3281 ν(O-H), 3032 ν(N-H) thione form and ν(C-H) benzene, vib. coupling, 2928 and 2812 ν(N-H) intramolecularly hydrogen bonded, thione form, 2596 ν(S-H) thiol form, 1610s ν(C=N) imine and ν(C=N) oxadiazole, vib. coupling, 1510 and 1479 ν(C=C) benzene, 1417 ν(N=N), 1072 ν(C=S) thione form, 829 δo.o.p.(C-H) benzene.

General procedure for the synthesis of imidazolidines (4a-f): A mixture of equimolar amounts of imine derivatives **3a-f** (1 mmol) and glycine (0.075 g, 1 mmol) in tetrhydrofuran (1 mL) was heated in microwave oven at (450-500 W) for 45 min. TLC (*n*-hexane:EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol.

3-(4-Bromophenyl)-2-(2-hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenyl)imidazolidin-4-one (4a): IR (cm^{-1}): 3421br ν(O-H), ν(N-H) thione form, ν(N-H) imidazolidine and ν(C-H) benzene, vib. coupling, 2955 and 2883 ν(N-H) intramolecularly hydrogen bonded, thione form, 2600 ν(S-H) thiol form, 1716 ν(C=O) imidazolidine, 1653 δ(N-H) imidazolidine, 1606 ν(C=N) oxadiazole, 1506 and 1489 ν(C=C) benzene, 1410 ν(N=N), 1035 ν(C=S) thione form, 846 δo.o.p.(C-H) benzene; ^{1}H NMR: δ (ppm) = 3.71 (s, 2H, CH_2 imidazolidine, 5.06 (s, 1H, CH imidazolidine, 7.10–8.11 (11H, Ar–H), 8.19 (s, 1H, N–H imidazolidine, 8.75 (s, 1H, O–H), 10.70 (s, 1H, S–H). The singlet signals around 2.48 ppm and 3.37 ppm attributed to DMSO and absorbed H_2O in DMSO, respectively; Anal. calcd. (%) for $C_{23}H_{17}N_6O_3SBr$: C, 51.40; H, 3.19; N, 15.64; S, 5.97; Found (%) C, 51.02; H, 3.46; N, 15.77; S, 5.95.

3-(4-Chlorophenyl)-2-(2-hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenyl)imidazolidin-4-one (4b): IR (cm^{-1}): 3389 ν(O-H), 3271 and 3194 ν(N-H) thione form and ν(N-H) imidazolidine, 3095 and 3053 ν(C-H) benzene, 2949 and 2883 ν(N-H) intramolecularly hydrogen bonded, thione form, 2600 ν(S-H) thiol form, 1716 ν(C=O)

imidazolidine, 1653s δ(N-H) imidazolidine, 1606 ν(C=N) oxadiazole, 1533 and 1494 ν(C=C) benzene, 1411 ν(N=N), 1035 ν(C=S) thione form, 846 δo.o.p.(C-H) benzene; ^{1}H NMR: δ (ppm) = 3.70 (d, *J* = 27.0 Hz, 2H, CH_2 imidazolidine, 5.02 (d, *J* = 14.1 Hz, 1H, CH imidazolidine, 7.11–7.95 (11H, Ar–H), 8.20 (s, 1H, N–H imidazolidine, 8.75 (s, 1H, O–H), 10.45 (s, 1H, S–H).The singlet signals around 2.49 ppm and 3.38 ppm assigned to DMSO and absorbed H_2O in DMSO, respectively; Anal. calcd. (%) for $C_{23}H_{17}N_6O_3SCl$:C, 56.04; H, 3.48; N, 17.05; S, 6.50; Found (%) C, 55.85; H, 3.66; N, 16.66; S, 6.17.

2-(2-Hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenyl)-3-(4-nitrophenyl)imidazolidin-4-one (4c): IR (cm^{-1}): 3365 br ν(O-H), 3230 ν(N-H) thione form and ν(N-H) imidazolidine, 3063 ν(C-H) benzene, 2935 and 2877 ν(N-H) intramolecularly hydrogen bonded, thione form, 2590 ν(S-H) thiol form, 1712 ν(C=O) imidazolidine, 1666 δ(N-H) imidazolidine, 1602 ν(C=N) oxadiazole, 1508 ν(C=C) benzene and $\nu_{as.}(NO_2)$ vib. coupling, 1413 ν(N=N), 1309 $\nu_{s.}(NO_2)$, 1051 ν(C=S) thione form, 844 δo.o.p.(C-H) benzene; ^{1}H NMR: δ (ppm) = 3.69 (d, *J* = 10.9 Hz, 2H, CH_2 imidazolidine, 6.57 (d, *J* = 8.4 Hz, 1H, CH imidazolidine, 7.27–8.04 (11H, Ar–H), 8.20 (s, 1H, N–H imidazolidine, 8.81 (s, 1H, O–H), 10.56 (s, 1H, S–H).The signals around 2.49 ppm and 3.41 ppm due to DMSO and absorbed H_2O in DMSO, respectively; Anal. calcd. (%) for $C_{23}H_{17}N_7O_5S$:C, 54.87; H, 3.40; N, 19.47; S, 6.37; Found (%) C, 54.50; H, 3.68; N, 19.11; S, 5.98.

2-(2-hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenyl)-3-(3-nitrophenyl)imidazolidin-4-one (4d): IR (cm^{-1}): 3354 br ν(O-H), 3248 ν(N-H) thione form and ν(N-H) imidazolidine, 3066 ν(C-H) benzene, 2937 and 2877 ν(N-H) intramolecularly hydrogen bonded, thione form, 2615 ν(S-H) thiol form, 1710 ν(C=O) imidazolidine, 1662 δ(N-H) imidazolidine, 1606 ν(C=N) oxadiazole, 1527 $\nu_{as.}(NO_2)$, 1508 and 1473 ν(C=C) benzene, 1413 ν(N=N), 1330 $\nu_{s.}(NO_2)$, 1049 ν(C=S) thione form, 840 δo.o.p.(C-H) benzene; ^{1}H NMR: δ (ppm) = 3.70 (d, *J* = 6.1 Hz, 2H, CH_2 imidazolidine, 6.64 (d, *J* = 11.0 Hz, 1H, CH imidazolidine, 7.24–8.09 (11H, Ar–H), 8.32 (s, 1H, N–H imidazolidine, 8.72 (s, 1H, O–H), 10.56 (s, 1H, S–H).The signals around 2.49 ppm and 3.40 ppm attributed to DMSO and absorbed H_2O in DMSO, respectively; Anal. calcd. (%) for $C_{23}H_{17}N_7O_5S$:C, 54.87; H, 3.40; N, 19.47; S, 6.37; Found (%) C, 54.47; H, 3.79; N, 19.11; S, 6.01.

(*E*)-2-(2-Hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenyl)-3-(4-methoxyphenyl)imidazolidin-4-one (4e): IR (cm^{-1}): 3325 br ν(O-H), ν(N-H), thione form and ν(N-H), imidazolidine, vib. coupling, 3070 ν(C-H) benzene, 2941 and 2727 ν(N-H) intramolecularly hydrogen bonded, thione form, 2887 ν(C-H)$_3$), 2594 ν(S-H) thiol form, 1720 ν(C=O) imidazolidine, 1680 and 1653 (dN-H, thione form and dN-H imidazolidine, 1606 ν(C=N) oxadiazole, 1512 and 1473 ν(C=C) benzene, 1413 ν(N=N), 1033 ν(C=S) thione form, 839 δo.o.p.(C-H) benzene; ^{1}H NMR: δ (ppm) = 3.71 (d, *J* = 27.2 Hz, 2H, CH_2 imidazolidine, 3.85 (s, 3H, O–CH_3), 5.02 (d, *J* = 22.2 Hz, 1H, CH imidazolidine, 6.65–8.18 (11H, Ar–H), 8.25 (s, 1H, N–H imidazolidine, 8.76 (s, 1H, O–H), 10.57 (s, 1H, S–H).The singlet signals around 2.48 ppm and 3.37 ppm assigned to DMSO and absorbed H_2O in DMSO, respectively; Anal. calcd. (%) for $C_{24}H_{20}N_6O_4S$:C, 59.01; H, 4.13; N, 17.20; S, 6.56; Found (%) C, 58.97; H, 4.02; N, 16.83; S, 6.21.

2-(2-Hydroxy-5-((4-(5-mercapto-1,3,4-oxadiazol-2-yl)phenyl)diazenyl)phenyl)-3-(4-hydroxyphenyl)imidazolidin-4-one (4f): IR (cm^{-1}): 3230 br ν(O-H), 3180 ν(N-H) thione form and ν(N-H) imidazolidine, 3066 ν(C-H) benzene, 2947 and 2885 ν(N-H) intramolecularly hydrogen bonded, thione form, 2605 ν(S-H) thiol form, 1720 ν(C=O) imidazolidine, 1651 δ(N-H) imidazolidine, 1606 ν(C=N) oxadiazole, 1514 ν(C=C) benzene, 1411 ν(N=N), 1035 ν(C=S) thione form, 840 δo.o.p.(C-H) benzene; ^{1}H NMR: δ (ppm) = 3.70 (s, 2H, CH_2 imidazolidine, 5.01 (d, *J* = 24.8 Hz, 1H, CH imidazolidine, 6.59–7.78 (11H, Ar–H), 8.21 (s, 1H, N–H imidazolidine, 10.35 (s, 2H, 2×O–H), 10.45 (s, 1H, S–H).The singlet signals around 2.49 ppm and 3.43 ppm due to DMSO and absorbed H_2O in DMSO, respectively; Anal. calcd. (%) for $C_{23}H_{18}N_6O_4S$: C, 58.22; H, 3.82; N, 17.71; S, 6.76; Found (%) C, 57.87; H, 4.18; N, 17.44; S, 6.40.

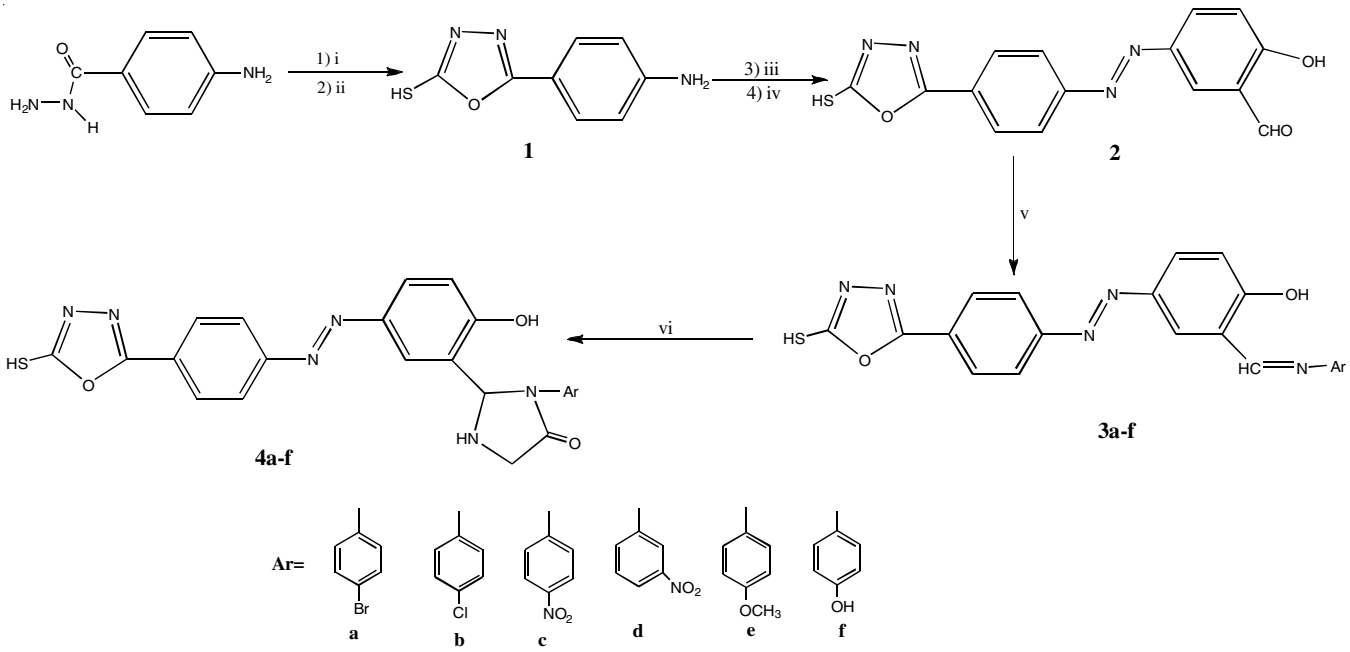
Preliminary antibacterial assay: The antibacterial activities of the newly synthesized imidazolidines **4a-f** were determined by the agar diffusion method [29] using representative Gram-positive and Gram-negative bacteria on tryptic soya agar media. The test microorganisms to evaluate the potential antibacterial activity of the newly synthesized imidazolidines were *Staphylococcus aurous* (Gram-positive) and *Escherichia coli* (Gram-negative). The imidazolidines were dissolved in dimethyl sulfoxide to prepare the test solutions of 10 mg/mL concentration. Gentamycin was used as a reference and the activities were presented as zones of inhibition for each compound (Table-2).

RESULTS AND DISCUSSION

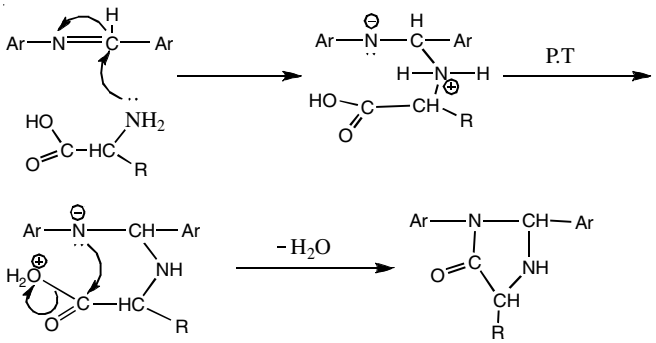
4-Aminobenzoic hydrazide was converted to 5-(4-aminophenyl)-2-thiol-1,3,4-oxadiazole (**1**) by treating it with carbon disulfide in presence of potassium hydroxide as catalyst in absolute ethanol [27]. Diazotization of amino group in compound **1** using sodium nitrite and hydrochloric acid generated the corresponding diazonium salt which was directly introduced in coupling reaction with 2-hydroxybenzaldehyde dissolved in sodium hydroxide solution to give azo-oxadiazole derivative **2** containing aldehyde group [28]. Aldehyde group of azo-oxadiazole derivative **2** was condensed with the primary aromatic amines including (4-bromoaniline, 4-chloroaniline, 4-nitroaniline, 3-nitroaniline, 4-methoxyaniline and 4-hydroxyaniline) using microwave irradiation in absolute ethanol to produce six imine derivatives of 1,3,4-oxadiazole **3a-f** respectively, as the platforms for this work (**Schemes I** and **II**). The resulting imines **3a-f** were allowed to react with glycine using microwave irradiation leading to the formation of imidazolidine derivatives of oxadiazole **4a-f** respectively in good yields (Table-1).

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

The IR spectrum of oxadiazole derivative **1** showed the disappearance of the sharp doublet band for hydrazide group



Scheme-I: Synthesis of imidazolidines, Reagents and conditions (i) CS_2, KOH, EtOH, 70 °C, 24 h; (ii) conc. HCl; (iii) $NaNO_2$, HCl, 0-5 °C; (iv) 2-hydroxybenzaldehyde, NaOH 10 %, 5 °C; (v) Ar-NH_2,EtOH, MW (300W), 25 min; (vi) glycine, tetrahydrofuran, MW (450-500 W), 45 min



Scheme-II: Proposed mechanism for the formation of imidazolidine ring

(-$NHNH_2$) at (3307, 3236) cm^{-1} and the strong band at 1627cm^{-1} due to (C=O) str, additionally the appearance of the following characteristic bands: the doublet band at 3450 and 3354 cm^{-1} assigned to (-NH_2) str that substituted in benzene ring, the strong band at 1606 cm^{-1} attributed to the oxadiazolic (C=N) str and (-NH_2) bend due to the vibration coupling interaction. The weak and strong bands at 2590 and 1066 cm^{-1} belong to (S-H) str and (C=S) str in thioenol and thioketone forms, respectively. The IR spectrum of azo-oxadiazole derivative **2** indicated the absence of a doublet band at 3450 and 3354 cm^{-1} for (-NH_2) str and appearance of the following characteristic bands: the weak band at 1411 cm^{-1} attributed to azo group (N=N) str, the broad band at 3402 cm^{-1} assigned to (O-H) str, the sharp and strong band at 1662 cm^{-1} belong to aldehydic (C=O) str, the oxadiazolic (C=N) str appeared as a weak band at 1604 cm^{-1} due to disappearance of the bending vibration of (-NH_2) group. IR spectra of the oxadiazolic-imines **3a-f** showed disappearing the sharp and strong band at 1662 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 a sharp and strong band at the range (1614-1597) cm^{-1} assigned to the iminic and oxadiazolic (C=N) str due to the vibration coupling interaction. The IR spectra of the imidazolidines **4a-f** showed the appearance of strong band

TABLE-1
PHYSICAL PROPERTIES OF THE SYNTHESIZED COMPOUNDS

Product	Colour	R_f (developer)	m.p. (°C)	Yield (%)	Time (min)	Microwave (W)
2	Red solid	0.68 (*n*-hexane/EtOAc, 1:3)	204-206	79	–	–
3a	Orange solid	0.81 (*n*-hexane/EtOAc, 1:3)	206-208	76	25	300-350
3b	Yellow solid	0.78 (*n*-hexane/EtOAc, 1:3)	181-183	81	25	300-320
3c	Dark orange solid	0.56 (*n*-hexane/EtOAc, 1:3)	175-177	91	25	300
3d	Yellow solid	0.75 (*n*-hexane/EtOAc, 1:3)	158-160	86	25	300
3e	Orange solid	0.68 (*n*-hexane/EtOAc, 1:3)	219-221	81	25	300-310
3f	Dark brown solid	0.72 (*n*-hexane/EtOAc, 1:3)	156-158	88	25	300-320
4a	Yellow solid	0.67 (*n*-hexane/EtOAc, 1:3)	224-226	85	45	450-600
4b	Yellow solid	0.68 (*n*-hexane/EtOAc, 1:3)	204-206	75	45	450-600
4c	Dark orange solid	0.56 (*n*-hexane/EtOAc, 1:3)	201-203	79	45	500-550
4d	Dark orange solid	0.62 (*n*-hexane/EtOAc, 1:3)	189-191	91	45	475-550
4e	Brown solid	0.62 (*n*-hexane/EtOAc, 1:3)	177-179	95	45	450-570
4f	Grey solid	0.51 (*n*-hexane/EtOAc, 1:3)	170-172	76	45	460-590

at the range 1712-1720 cm^{-1} attributed to the (C=O) str of the imidazolidine ring. The spectra also showed the appearance of absorption band at the range 1666-1651 cm^{-1} assigned to the (N-H)bend of the imidazolidine ring. The oxadiazolic (C=N) str appeared at the range 1606-1602 cm^{-1}.

The structures of imidazolidine compounds **4a-f** were proven by their ^{1}H NMR spectra (500 MHz, DMSO-d_6) which showed the peak for the methylene protons (CH_2) of imidazolidine ring as a doublet or singlet at δ 3.71, 3.70, 3.69, 3.70, 3.71 and 3.70 ppm, respectively. The (N-CH-N) proton of imidazolidine ring appeared as a doublet at 5.06, 5.02, 6.57, 6.64, 5.02 and 5.01 ppm, respectively. The (Ar-H) protons at δ 6.59-8.18 ppm, the (N-H) proton of imidazolidine ring as a singlet at 8.19, 8.20, 8.20, 8.32, 8.25 and 8.21 ppm, respectively. The (O-H) proton as a singlet at 8.75, 8.75, 8.81, 8.72, 8.76 and 10.35 ppm, respectively. The (S-H) proton as a singlet at 10.70, 10.45, 10.56, 10.56, 10.57 and 10.45 ppm, respectively. The methoxy protons (O-CH_3) in compound **4e** appeared as a singlet at δ 3.85ppm.

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-f**.

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

TABLE-2
ANTIBACTERIAL ACTIVITY OF COMPOUNDS **4a-f** AND GENTAMYCIN AS CONTROL DRUG

Product	*Staphylococcus aureus* (Gram-positive)	*Escherichia coli* (Gram-negative)
4a	0	0
4b	0	0
4c	8	0
4d	11	18
4e	13	0
4f	0	16
DMSO	0	0
Gentamycin	15	15

Imidazolidine compounds **4d** and **4f** were found to be better activity than gentamycin against Gram-negative bacteria.

Conclusion

The microwave irradiation is efficient technique including short reaction time and high yield in comparison with the classical heating method. The rates of reactions of imines **3a-f** with glycine for formation of imidazolidines **4a-f** are approximately equal. The prepared imidazolidines could be converted to the corresponding phenol salts to be totally soluble in water. The synthesized imidazolidines appeared higher effect against Gram-negative bacteria than that of Gram-positive bacteria. Imidazolidine compounds **4d** and **4f** were found to be better activity than gentamycin against Gram-negative bacteria.

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