WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 17, 736-748. Research Article ISSN 2277– 7105

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDY OF SOME NEW BENZIMIDAZOLE-2-THIONE DERIVATIVES

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Article Received on
26 October 2017,

Revised on 16 Nov. 2017,
Accepted on 06 Dec. 2017

DOI: 10.20959/wjpr201717-10357

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ABSTRACT

A series of Benzimidazole-2-thione derivatives synthesized by reaction of 2-[3′-chloro-1′methylthio-2′-propanol]-1-methyl-1*H*-benzimidazole **1(a-b)** with hydrazine hydrate afford 1′-(1-methyl-1*H*-benzimidazol-2-yl) sulfanyl-3′-hydrazinylpropan-2′-ol **2(a-b)** which on further heating with diethyl carbonate in presence of sodium methoxide gave 2-[3′-amino -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]-1-methyl-1*H*-benzimidazole **3(a-b)** which on further condensation with choloroacetyl chloride gave 2-[3′-(amino-2″- chloro acetamide)-5′-sulfanyl methyl -1′, 3′-oxazolidin-2′-one]- 1-methyl-1*H*-benzimidazole **4(a-b)** which on further treatment with KSCN gave 2-[3′-(amino-2″-thiocynato acetamide) -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]- 1-methyl-1*H*-benzimidazole **5(a-b)** which when refluxed in presence of solvent DMF formed 2″-imino-[1″-(5′-sulfanylmethyl-1′,3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-5″-one **6(a-b)** which when further refluxed with 2% HCl formed 1″-[(5′- sulfanyl methyl -1′, 3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-2″,5″dione **7(a-b)**. All synthesized novel Benzimidazole-2-thione derivatives were characterized by IR, NMR, Mass Spectroscopy and Elemental analysis. These compounds were screened against a series of Gram positive and Gram negative bacteria and showed significant to moderate activity.

KEYWORDS: Benzimidazole-2-thione, oxazolidine, thiazolidinone, antimicrobial activity.

INTRODUCTION

Substituted 2-mercapto benzimidazole derivatives have wide range of biological activities such as antimicrobial[1-2], antiprotozoal[3], cytological agent[4], anticonvulsant[5], antidiabetic[6-7], antitubercular[8], fungicidal[9], antagonists[10] and antiulcer.[11-12] These biological activities of substituted 2-mercaptobenzimidazole derivatives have drawn much attention of synthetic chemists towards synthesis of novel derivatives which are much more biologically potent. Thiazolidenone moiety is notable for biological and pharmacological activities such as antihelmintic[13], antibacterial[14], analgesic[15], anticonvulsant[16] and antifungal.[17] Oxazolidine moieties show diverse biological activities which includes hypoglycaemic activity[18], Anthelmintic activity[19], antidiabetic and antiobesity[20] and anticonvulsant[21] activity. Considering the above aspects, the present piece of research work was aimed to synthesize various benzimidazolethione derivatives and to study their biological activity.

MATERIALS AND METHODS

The reactions were monitored by TLC using 0.25 mm E-Merck silica gel plates, which were visualized in Iodine Chamber. Melting points were taken in open capillaries and are uncorrected. ^{1}H NMR spectra was performed in DMSO-d6 on 300 MHz using TMS as an internal standard.

SYNTHESIS OF COMPOUNDS

1′-(1-methyl-1*H*-benzimidazol-2-yl) sulfanyl-3′-hydrazinylpropan-2′-ol 2(a-b)

A mixture of 2-[3′-chloro-1′methylthio-2′-propanol**]-**1-methyl-1*H*-benzimidazole **1(a-b)** (22.76 g, 0.1 mol) and hydrazine hydrate (4.9 ml, 0.1mol) in absolute ethanol (50 ml) were stirred at room temperature for about 5-8 h. The solvent was removed under reduced pressure and the residue to offer the product **2(a-b)**. The solid precipitate was filtered off and recrystallized from methanol.

2-[3′-amino -5′- sulfanyl methyl -1′,3′-oxazolidin-2-one]-1-methyl -1*H*-benzimidazole 3(a-b)

1′-[(1-methyl-1*H*-benzimidazol-2-yl)sulfanyl]-3′-hydrazinylpropan-2′-ol **2(a-b)** and diethyl carbonate heated up to 110^o C in presence of sodium methoxide for about 8-10 h. The solvent was removed under reduced pressure and the residue to offer the product 2-[3′-amino-5′-sulfanyl methyl-1′,3′-oxazolidin-2-one]-1-methyl-1*H*-benzimidazole **3(a-b)** which was recrystallized from ethanol.

2-[3′-(amino-2″- chloro acetamide)-5′- sulfanyl methyl -1′, 3′-oxazolidin-2′-one]- 1-methyl-1*H*-benzimidazole 4(a-b)

In aspiration to synthesize compound **4(a-b),** choloroacetyl chloride (0.01 mol) was mixed in solution of 2[3′-amino-5′-sulfanylmethyl-1′,3′-oxazolidin-2-one]-1-methyl-1*H*-benzimidazole 3**(a-b)** (0.01 mol) in of dry benzene (50 ml) at 0-5^{o} C under stirring condition. Reaction mixture further refluxed for 7 h. After completion of reaction, solvent was removed under reduced pressure and reaction mass poured into water. Obtained solid was filtered, then dried and recrystallized from alcohol to obtain pure product 2-[3′-(amino-2″-chloro acetamide)-5′-sulfanyl methyl -1′, 3′-oxazolidin-2′-one]-1-methyl-1*H*-benzimidazole **4(a-b)**.

2-[3′-(amino-2″- thiocynato acetamide) -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]- 1-methyl-1*H*-benzimidazole 5(a-b)

Compounds 2-[3′-(amino-2″- chloro acetamide)-5′-sulfanyl methyl-1′,3′-oxazolidin-2′-one]-1-methyl-1*H*-benzimidazole **4(a-b)** (0.01 mol) was added in acetone (100ml) and stirred for 20 min. To the reaction mass KSCN (0.015 mol) was added at room temperature. Reaction was refluxed for 10 h. Completion of reaction was monitored by TLC using n-hexane: ethyl acetate (7:3) as a solvent system. After completion of reaction, reaction mass was cooled to room temperature and poured onto crushed ice pieces, precipitate was obtained. Solid product was filtered, washed with cold water, dried and recrystallized using ethanol gave 2-[3′-(amino-2″-thiocynato acetamide)-5′-sulfanyl methyl -1′, 3′-oxazolidin-2′-one]-1-methyl-1*H*-benzimidazole 5**(a-b)**.

2″-imino-[1″-(5′-sulfanylmethyl-1′,3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-5″-one 6(a-b).

Compounds 2-[3′-(amino-2″-thiocynato acetamide)-5′-sulfanyl methyl -1′,3′-oxazolidin-2′-one]-1-methyl-1*H*-benzimidazole 5**(a-b)** (0.01 mol) was refluxed in presence of solvent DMF (25 ml) at 150^{o} C over oil bath for 8 h. Reaction progress was monitored by TLC, after completion of reaction obtained mass was poured onto ice pieces to give crude product. The obtained product was then filtered, dried and recrystallized using ethanol to give 2″-imino-[1″-(5′-sulfanylmethyl-1′,3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-5″-one **6(a-b)**.

1″-[(5′- sulfanyl methyl -1′, 3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-2″,5″dione 7(a-b)

2″-imino-[1″-(5′-sulfanylmethyl-1′,3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-5″-one **6(a-b)** (0.01 mol) and 2% HCl (5 ml) in ethanol (25 ml) was refluxed for 6 h. The resulting mixture was cooled and neutralized with solid sodium bicarbonate the solid obtained. The solid was filtered off, washed with water, dried and recrystallized using ethanol to give 1″-[(5′- sulfanyl methyl -1′, 3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-2″,5″dione **7(a-b)**.

CHARACTERIZATION OF SYNTHESIZED COMPOUNDS

1′-(1-methyl-1*H*-benzimidazol-2-yl)sulfanyl-3′-hydrazinylpropan-2′-ol (2a)

Yellow solid, Yield: 67%, Melting Point: 220-224ºC. IR (KBr): 3521 (OH), 3401 (NH_2), 3301 (NH), 2985 (CH), 1560, 1310, 1188 cm^{-1}. ^1H NMR (300 MHz, DMSO-d6/TMS) δ 2.78-2.80 (d, 2H, CHHN, J= 4.02 Hz), δ 3.37-3.40 (d, 2H, SCH_2, J= 5.22 Hz), δ 3.72 (s, 3H, NCH_3),δ 3.80-3.86 (m, 1H, CH_2-CH-CH_2), δ 6.88-7.30 (m, 4H, Ar-H), δ 9.45 (s, 1H, NH, D_2O exchangeable), δ 10.45(s, 1H, NH, D_2O exchangeable) and δ 11.45 (s, 1H, OH, D_2O exchangeable). M^{+1}: 252.10. Elemental Analysis % Calculated for $C_{11}H_{16}N_4OS$: C, 52.36; H, 6.38; N, 22.20; S, 12.71. Found: C, 52.58; H, 6.49; N, 22.31; S, 12.88.

1′-(6-Fluoro-1-methyl-*1H*-benzimidazol-2-yl) sulfanyl -3′-hydrazinyl propan-2′-ol (2b)

Dark yellow solid, Yield: 59 %, Melting Point: 210-215ºC. IR (KBr): 3551 (OH), 3435 (NH_2), 3351(NH), 2995(CH), 1550, 1315, 1180 cm^{-1}. ^{1}HNMR. (300 MHz, DMSO-d6/TMS): δ 2.82-2.84 (d, 2H, CHHN, J = 4.02 Hz), δ 3.40-3.42 (d, 2H, SCH_2, J =5.2 Hz), δ 3.66 (s, 3H, NCH_3), δ 3.82-3.84 (m, 1H, CH_2-CH-CH_2), δ 6.98-7.30 (m, 3H, Ar-H), δ 9.50 (s, 1H, NH, D_2O exchangeable), δ 10.55 (s, 2H, NH, D_2O exchangeable) and δ 11.35 (s, 1H, OH, D_2O exchangeable). M^{+1}: 270.09. Elemental Analysis % Calculated for $C_{11}H_{15}N_4OS$: C, 48.87; H, 5.58; N, 20.75; S, 11.86. Found: C, 48.58; H, 5.49; N, 20.31; S, 11.38.

2[3′-amino -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]- 1-methyl-1*H*-benzimidazole (3a)

Brown solid, Yield: 61%, Melting Point: 201-204ºC. IR (KBr): 3435 (NH_2), 2291(CH), 1700 (C=O) of amide, 1566, 1318, 1238, 1181cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.72 (s, 3H, NCH_3), δ 3.82 (dd, 1H, C*H*HN, J = 16.5, J= 8.1 Hz), δ 3.96 (dd, 1H, CH*H*N, J = 16.5, J = 4.3 Hz), δ 4.30-4.32 (d, 2H, CH_2, J =3.3 Hz), δ 4.81 (m,1H, CH_2CHCH_2), δ 6.88-7.30 (m, 4H, Ar-H), δ10.45 (s, 2H, NH, D_2O exchangeable). M^{+1}: 278.08. Elemental

Analysis % Calculated for $C_{12}H_{14}N_4O_2S$: C, 51.78; H, 5.08; N, 20.13; S, 11.52. Found: C, 51.58; H, 5.18; N, 20.31; S, 11.38.

2-[3′-amino-5′-sulfanyl methyl-1′,3′-oxazolidin-2′-one]-6-fluoro-1-methyl-1*H*-benzimidazole (3b)

Brown solid, Yield: 72%, Melting Point: 215-119ºC. IR (KBr): 3435 (NH_2), 2281 (CH), 1705(C=O) of amide, 1556, 1325, 1218, 1181cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.68 (s, 3H, NCH_3), δ 3.74 (dd, 1H, C*H*HN, J = 16.5 J = 8.1 Hz), δ 3.86 (dd, 1H, CH*H*N, J= 16.5, J = 4.3 Hz), δ 4.30- 4.32 (d , 2H, CH_2, J = 3.3 Hz), δ 3.82 δ 4.81 (m, 1H, CH_2CHCH_2), δ 6.88-7.30 (m, 3H, Ar-H), δ 10.45 (s, 2H, NH, D_2O exchangeable M^{+1}:296.07. Elemental Analysis % Calculated for $C_{12}H_{13}N_4FO_2S$: C, 48.64; H, 4.41; F, 6.41; N, 18.9;.S, 10.82. Found: C, 48.71; H, 4.69; F, 6.71; N, 18.81; S, 10.89.

2-[3′-(amino-2″- chloro acetamide)-5′-sulfanyl methyl -1′, 3′-oxazolidin-2-one]- 1-methyl-1*H*-benzimidazole (4a)

Brown solid, Yield: 58%, Melting Point: 236-241ºC. IR (KBr): 3255 (NH), 2980 (CH), 2170 (CN), 1695(C=O) of amide, 1559, 1215, 1168cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.70 (s, 3H, NCH_3), δ 3.78 (dd, 1H, C*H*HN, J =16.5,J=8.1 Hz), δ 3.86 (dd, 1H, CH*H*N, J=16.5, J=4.31 Hz), δ 3.99 (s, 2H, CH_2), δ 4.29-4.31 (d, 2H, CH_2,J = 3.3 Hz), δ 4.80- 4.84 (m, 1H , CH_2CHCH_2), δ 6.88-7.30 (m, 4H, Ar-H), δ 10.65 (s, 1H, NH, D_2O exchangeable). M^{+2}: 377.43. Elemental Analysis % calculated for $C_{15}H_{15}N_5O_3S_2$: C, 47.73;H, 4.01; N, 18.55; S, 16.99. Found: C, 47.13;H, 4.31; N, 18.35; S,16.89.

2-[3′-(amino-2″- chloro acetamide) -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]-6-fluoro - 1-methyl-1*H*-benzimidazole (4b)

Yellow solid, Yield: 65%, Melting Point: 245-248ºC. IR (KBr): 3255 (NH), 2980 (CH), 1710 (C=O) of amide, 1569, 1315, 1178cm-1. 1H NMR (300 MHz, DMSO-d6/TMS): δ 3.75(s, 3H, NCH3), δ 3.80 (dd, 1H, CHHN, J=16.5, J=8.1Hz), δ 3.92 (dd, 1H, CH_2, J=16.5, J=4.3 Hz), δ 3.98 (s, 2H, CH_2), δ 4.35 (d, 2H, CH_2, J=3.3 Hz), δ 4.8- 4.81(m,1H, CH_2CHCH_2), δ 6.86-7.26 (m, 3H, Ar-H), δ 10.50 (s, 1H, NH, D_2O exchangeable). M^{+2}: 372.80. Elemental Analysis % Calculated for $C_{14}H_{14}ClF\ N_4O_3S$; C, 45.10; H, 3.79; Cl, 9.51; F, 5.10; N, 15.03; S, 8.60. Found: C, 45.20; H, 3.89; Cl, 9.61; F, 5.00; N, 15.13; S, 8.69.

2-[3′-(amino-2″- thiocynato acetamide) -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]- 1-methyl-1*H*-benzimidazole (5a)

Brown solid, Yield: 58%, Melting Point: 236-241ºC. IR (KBr): 3255 (NH), 2980 (CH), 2170 (CN), 1695(C=O) of amide, 1559, 1215, 1168cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.74 (s, 3H, NCH_3), δ 3.80 (s, 2H, CH_2), δ 3.88 (dd, 1H, CHHN, J=16.5,J=8.1 Hz), δ 4.08 (dd, 1H, CHHN, J=16.5,J=4.31 Hz), δ 4.29-4.31 (d, 2H, CH_2,J=3.3 Hz), δ 4.80- 4.84 (m, 1H , CH_2CHCH_2), δ 6.88-7.30 (m, 4H, Ar-H), δ 10.65 (s, 1H, NH, D_2O exchangeable). M^{+1}: 377.43. Elemental Analysis % calculated for $C_{15}H_{15}N_5O_3S_2$: C, 47.73;H, 4.01; N, 18.55; S, 16.99. Found: C, 47.13;H, 4.31; N, 18.35; S,16.89.

2[3′-(amino-2″- thiocynato acetamide) -5′- sulfanyl methyl -1′, 3′-oxazolidin-2-one]-6-fluoro- 1-methyl-1*H*-benzimidazole (5b)

Brown solid, Yield: 53%, Melting Point: 255-259ºC. IR (KBr): 3355 (NH), 2950 (CH), 2150 (CN), 1699 (C=O) of amide, 1550, 1275, 1168, 1062 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.70 (s, 3H, NCH_3), δ 3.80 (s, 2H, CH_2,), δ 3.86 (d, 1H, C*H*HN,J=16.5, J= 8.5 Hz), δ 8.06 (dd, 1H, CH*H*N, J=16.5, J= 4.31 Hz), δ 4.29-4.31 (d, 2H, CH_2, J= 3.3 Hz), δ 4.80-4.84 (m, 1H, CH_2CHCH_2), δ 6.78-7.30 (m, 3H, Ar-H), δ10.65 (s, 1H, NH, D_2O exchangeable). M^{+1}: 395.43. Elemental Analysis % calculated for $C_{15}H_{14}N_5FO_3S$**:** C, 45.56; H, 3.57; F, 4.80; N, 17.71; S, 16.22. Found: C, 45.36; H, 3.67; F, 4.70; N, 17.51; S, 16.52.

2″-imino-[1″-(5′- sulfanyl methyl -1′, 3′-oxazolidin-2′-one)-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-5″one (6a)

Brown solid, Yield: 78%, Melting Point: 220-225ºC.IR (KBr): 3255 (NH), 2910 (CH), 1709 (C=O) of amide, 1555, 1276, 1158cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.72 (s, 3H, NCH_3), δ 3.78 (dd, 1H, CHHN, J=17.9, J=8.1Hz), 3.84 (dd, 1H, CHHN, J=17.8, J= 4.2Hz), δ 4.10- 4.12 (d , 2H, CH_2, J=3.1 Hz), δ 4.30 (s, 2H, CH_2), δ 4.9(m, 1H, CH_2CHCH_2), δ 6.75-7.10 (m, 4H, Ar-H), δ 10.05 (s, 1H, NH, D_2O exchangeable). M^{+1}: 377.44. Elemental Analysis % calculated for $C_{15}H_{15}N_5O_3S_2$: C, 47.73; H, 4.01; N, 18.55; S, 16.99. Found: C, 47.79; H, 4.21; N, 18.55; S, 16.79.

2″-imino-[1″- (5′- sulfanyl methyl -1′, 3′-oxazolidin-2′-one)-6-fluoro-1-methyl-1*H*-benzimidazole]-1″,3″-thiazolidin-5″one (6b) .

Brown solid, Yield: 64%, Melting Point 220-225ºC. IR(KBr): 3250 (NH), 2910 (CH), 1698(C=O) of amide, 1568, 1256, 1148cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.68 (s, 3H, NCH_3), δ 3.80-4.02 (dd, 1H, CHHN, J=17.9, J=8.1Hz), 3.84 (dd, 1H, CHHN, J=17.8, J=

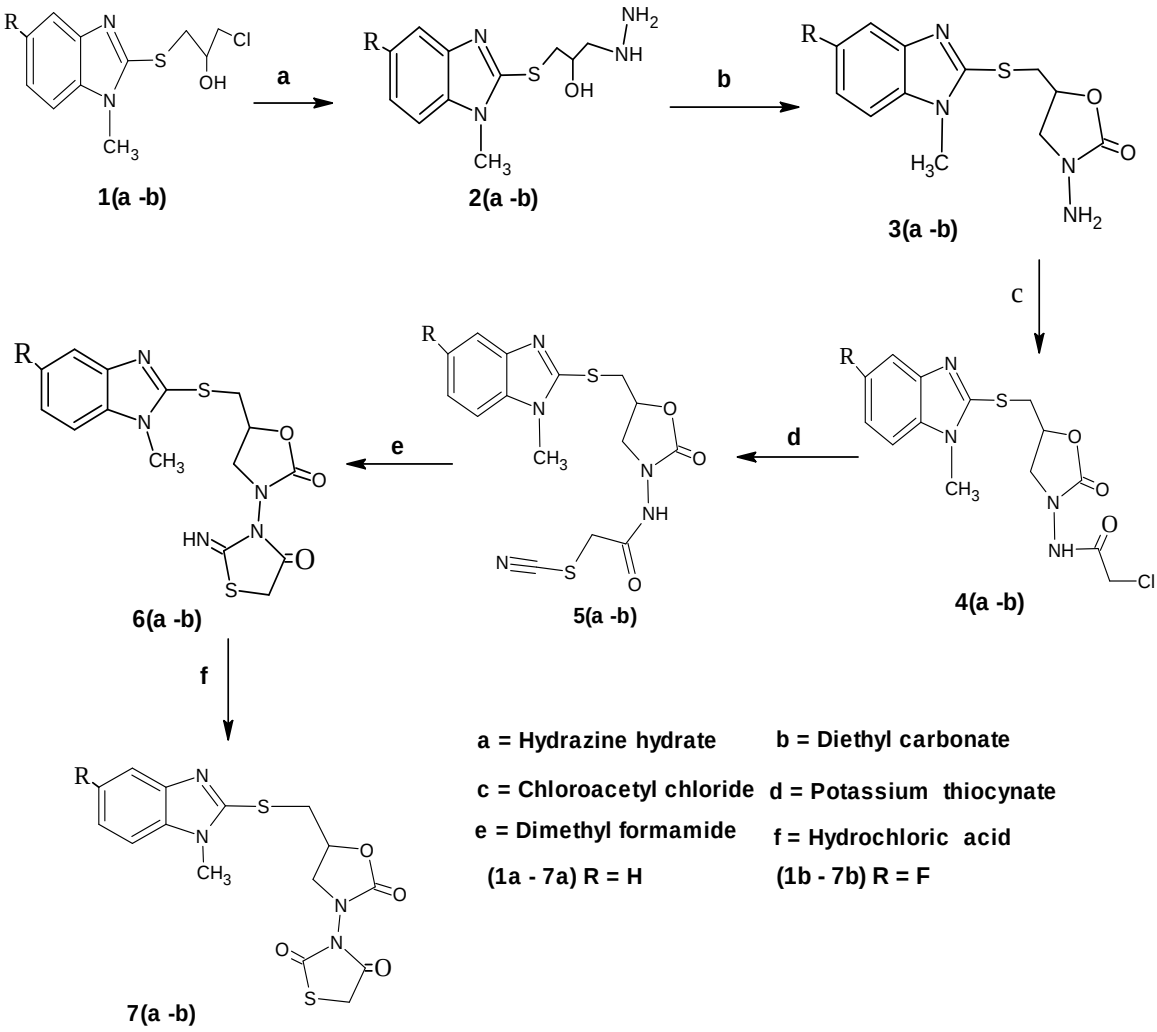
4.2Hz), δ 4.28-3.30 (d , 2H, CH_2, J=3.1 Hz), δ 4.42 (s, 2H, CH_2), δ 4.79 (m, 1H, CH_2CHCH_2), δ 6.75-7.10 (m, 3H, Ar-H), δ 9.90 (s, 1H, NH, D_2O exchangeable). M^{+1}: 395.44. Elemental Analysis % calculated for $C_{15}H_{14}N_5FO_3S_2$: C, 45.56; H, 3.57; F, 4.80; N, 17.71; S, 16.22. Found: C, 45.36; H, 3.77; F, 4.90;N, 17.61; S,16.02.

$1^{//}$-[($5^{/}$- sulfanyl methyl -$1^{/}$, $3^{/}$-oxazolidin-$2^{/}$-one)-1-methyl-1*H*-benzimidazole]-$1^{//}$,$3^{//}$-thiazolidin-$2^{//}$,$5^{//}$dione (7a)

Brown solid, Yield:68 %, MeltingPoint:210-214ºC, IR(KBr): 3260 (NH), 2980 (CH), 1708(C=O) of amide, 1548, 1276, 1248cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ 3.75 (s, 3H, NCH_3),δ 3.80 (dd, 1H, CHHN, J= 17.9, J= 8.1), δ 3.88 (dd, CHHN, J=17.9, J=4.3 Hz), δ 4.28-3.32 (d, 2H, CH_2, J=3.1 Hz), δ 4.35 (s, 2H, CH_2), δ 4.90(m, 1H, CH_2CHCH_2), δ 6.88-7.30 (m, 4H, Ar-H). M^{+1}: 378.42. Elemental Analysis % calculated for $C_{15}H_{14}N_4O_4S_2$: C, 47.61; H, 3.73; N, 14.83 S, 16.95. Found: C, 47.31; H, 3.63; N, 14.63; S, 16.75.

$1^{//}$-[($5^{/}$- sulfanyl methyl -$1^{/}$, $3^{/}$-oxazolidin-$2^{/}$-one)-6-fluoro-1-methyl-1*H*-benzimidazole]-$1^{//}$,$3^{//}$-thiazolidin-$2^{//}$,$5^{//}$dione (7b)

Brown solid, Yield: 69%, Melting Point: 193-197ºC, IR(KBr): 3260 (NH), 2980 (CH),1705 (C=O) of amide, 1548,1276,1248cm^{-1}.^{1}H NMR (300 MHz, DMSO-d6/TMS): δ δ 3.70 (s, 3H, NCH_3), δ 3.84 (dd,1H, CHHN, J= 17.9, J= 8.1), 3.95 (dd, CHHN, J=17.9, J=4.3 Hz), δ 4.28-3.32 (d, 2H, CH_2, J= 3.1 Hz), δ 4.35(s, 2H, CH_2), δ 4.90 (m,1H, CH_2CHCH_2), δ6.88-7.30(m,3H, Ar-H). M^{+1}: 396.41. Elemental Analysis % calculated for $C_{15}H_{13}FN_4O_4S_2$: C, 45.45; H, 3.33; F, 4.79; N, 14.13; S, 16.18. Found: C, 45.65; H, 3.23; F, 4.59; N, 14.23; S, 16.58.



ANTIMICROBIAL SCREENING

All the synthesized compounds: 2(a-b), 3(a-b), 4(a-b), 5(a-b) 6(a-b) and 7(a-b) were screened for their antibacterial activity by drug diffusion method by preparing the paper discs of the drug. The activity was tested against four bacterial strains *Bacillus subtilis, B. lactis, Pseudomonas aeruginosa* and *Escherichia coli* at concentrations 50 µg/ml and 100 µg/ml using DMSO as a solvent. The activities of compounds were compared with Nalidixic acid as reference drug. For drug diffusion, nutrient agar was prepared in sterile petri plate. Agar agar (1.2%) was used as solidifying agent. Paper discs (6.35 mm) were prepared using whatman filter paper no.1. They were soaked in sterile compound solutions under study and were placed onto the nutrient agar, on which the bacteria were inoculated by spread plate technique. The plates were incubated at 37^{o}C for 24 h. The extent of inhibition was observed by measuring zone of inhibition in mm. As DMSO also has antimicrobial activity, DMSO also was used as a blank and its zone of inhibition was measured.

Antibacterial activity Table: 1*

Compounds	Zone of inhibition (mm)							
	B. subtilis		*B. lactis*		*P. aeruginosa*		*E. coli*	
	50 ug	100 ug	50 ug	100 ug	50 ug	100 ug	50 ug	100 ug
2a	12	14	09	11	10	12	09	12
2b	14	16	10	14	14	16	10	14
3a	11	14	15	19	11	13	08	13
3b	12	15	10	12	09	11	15	19
4a	09	11	08	12	15	19	08	15
4b	14	17	14	18	10	13	14	17
5a	08	11	10	12	08	12	10	12
5b	11	13	15	18	15	18	14	18
6a	14	16	15	19	11	13	10	13
6b	14	17	14	18	15	19	08	09
7a	10	12	12	14	14	18	14	17
7b	15	19	15	18	08	12	15	19

*Disc size: 6 mm; standard: streptomycin; control: DMSO; duration: 24 h. resistant (< 11 mm), intermediate (12 to14 mm), sensitive (>15 mm).

RESULTS AND DISCUSSION

In the present work, previously synthesized 2-[3′-chloro-1′methylthio-2′-propanol**]**-1-methyl-1*H*-benzimidazole **1(a-b)** was used as the key intermediate for further synthesis of various derivatives. Thus, when compounds **1(a-b)** were treated with hydrazine hydrate provide hydrazine-compounds 2**(a-b).** IR spectra of compounds **2(a-b)** shows presence of strong band at 3521 (OH), 3401 (NH_2), 3301cm^{-1} (NH). ^{1}H NMR spectrum shows singlet at δ 9.45 (s, 1H, NH), δ 10.45 (s, 2H, NH), δ 11.45 (s, 1H, OH) which were D_2O exchangeable. MS shows m/z = 252.10 ($M^{+)}$. Elemental Analysis % Found: C 52.58; H, 6.49; N, 22.31; S, 12.88 require for $C_{11}H_{16}N_4OS$: C, 52.36; H, 6.38; N, 22.20; S, 12.71. From the spectral data confirmed that formation of hydrazine-compounds. **2(a-b)** which further heated with diethyl carbonate in presence of sodium methoxide gave 1, 3-oxazolidin-2-one compounds **3(a-b).** IR Spectrum of **3(a-b)** showed characteristics absorption band around 3435 (NH_2), 1700 (C=O) of amide and absence of band at 3561 (OH), 3301cm^{-1} (NH). ^{1}H NMR showed δ 10.45 (s, 2H, NH_2, D_2O exchangeable) and absence of δ11.45 (s, 1H, OH) and δ 9.45 (s, 1H, NH). MS shows m/z = 278.08 (M^+). Elemental Analysis % Found: C, 51.58; H, 5.18; N, 20.31; S, 11.38 requires for $C_{12}H_{14}N_4O_2S$: C, 51.78; H, 5.08; N, 20.13; S, 11.52. From the spectral data confirmed that formation of 1, 3-oxazolidin-2-one compounds. **3(a-b)** treated with choloroacetyl chloride gave amino acetyl chloride compounds **4(a-b).** IR spectrum shows 3255 (NH), 1715 (C=O) of amide and absence of strong band at 3435 cm^{-1} (NH_2). ^{1}H NMR spectrum showed δ 3.71 (s, 3H, CH_3), δ 3.78-3.86 (dd, 2H), δ 3.99(s, 2H, CH_2,), δ 4.29- 4.31

(d, 2H, CH_2), δ 4.80 - 4.84 (m, 1H, CH), δ 6.88 -7.30 (m, 4H, Ar-H), δ 10.25(s, 1H, NH, D_2O exchangeable). MS shows m/z 355.32 (M^{+2}). Elemental Analysis % Found: C, 47.48; H, 4.16; Cl, 9.90; N, 15.89; S, 9.14 require for $C_{14}H_{15}ClN_4O_3S$; C, 47.38; H, 4.26; Cl, 9.98; N, 15.79; S, 9.04. Spectral data confirmed the formation of N-acetyl chloride-1,3-oxazolidin-2-one compounds. **4(a-b)** further treated with KSCN gave N-acetyl thiocyanate-1,3-oxazolidin-2-one compounds **5(a-b)**. IR spectra showed band at 3255 (NH), 2170 (CN), 1695 cm^{-1} (HN-C=O). ^1H NMR showed δ δ 3.70 (s, 3H, CH_3), δ 3.80 (s, 2H, CH_2), δ 3.88 (dd, 1H, CHHN, J=16.5,J=8.1 Hz), δ 4.08 (dd, 1H, CHHN, J=16.5,J=4.31 Hz), δ 4.29-4.31 (d, 2H, CH_2,J=3.3), δ 4.80- 4.84 (m, 1H , CH_2CHCH_2), δ 6.88-7.30 (m, 4H, Ar-H), δ 10.65 (s, 1H, NH, D_2O exchangeable). MS m/z = 377.43 (M^+). Elemental Analysis % Found: C, 47.13; H, 4.31; N, 18.35; S, 16.89 require for $C_{15}H_{15}N_5O_3S_2$: C, 47.73;H, 4.01; N, 18.55; S, 16.99. From the spectral data confirmed the formation of N-acetyl thiocyanate -1, 3-oxazolidin-2-one. **5(a-b)** which was refluxed in presence of solvent DMF formed 1,3-oxazolidin-2-one **6 (a-b)**.

IR spectra showed presence of band at 3255 (N=H), 1709 cm^{-1} (NH-C=O) and absence of band at 2170 cm^{-1} (CN). ^1H NMR displayed singlet δ 3.72 (s, 3H, NCH_3), δ 3.78 (dd, 1H, C*H*HN, J=17.9, J=8.1Hz), 3.84 (dd, 1H, CH*H*N, J=17.8, J= 4.2Hz), δ 4.10- 4.12 (d , 2H, CH_2, J=3.1), δ 4.30 (s, 2H, CH_2), δ 4.90 (m, 1H, CH_2CHCH_2), δ 6.75-7.10 (m, 4H, Ar-H), δ 10.05 (s, 1H, NH, D_2O exchangeable). MS spectra m/z = 377.44 (M^{+1}). Elemental Analysis % Found: C, 47.79; H, 4.21; N, 18.55; S, 16.79 require for $C_{15}H_{15}N_5O_3S_2$: C, 47.73; H, 4.01; N, 18.55; S, 16.99. Spectral data confirmed the formation of N-(2-imino-1,3-thiazolidine-,5-dione)-1,3-oxazolidin-2-one. **6(a-b)** further refluxed with 2% HCl formed **7(a-b).** IR spectra shows presence of band at 3260 (NH), 1708(C=O) of amide[1] and absence of band at 3255 cm^{-1}(–N=H). ^1H NMR showed δ 3.75 (s, 3H, NCH_3), δ 3.80 (dd, 1H, CHHN, J= 17.9, J= 8.1), δ 3.88 (dd, CHHN, J=17.9, J=4.3 Hz), δ 4.28-3.32 (d, 2H, CH_2, J=3.1), δ 4.35 (s, 2H, CH_2), δ 4.90(m, 1H, CH_2CHCH_2), δ 6.88-7.30 (m, 4H, Ar) and absence of δ10.05 (s, 1H, N=H, D_2O exchangeable). MS m/z = 378.42 (M^{+1}). Elemental Analysis % Found: C, 47.31; H, 3.63; N, 14.63; S, 16.75 require for $C_{15}H_{14}N_4O_4S_2$: C, 47.61; H, 3.73; N, 14.83: S16.95. Spectral data confirmed the formation of N-1,3-thiazolidine-2,5-dione -1,3-oxazolidin-2-one **7(a-b)**. When the inhibition activity of all the synthesized compounds was compared with the standard it was observed that compounds 2b, 3b, 4b, 6a, 6b and 7b have considerable activity against *B. subtilis*. Compounds 3a, 4b, 5b, 6a, 5b and 7b have considerable activity against *B. lactis*. Compounds 2b, 4a, 5b, 6b, 7a and 7b have considerable activity against *E. coli*. While compounds 3b, 4b, 5b, 7a and 7b have shows considerable activity against *P. aeruginosa.*

CONLCUSIONS

Spectral techniques used in the scheme confirm the formation and synthetic route of novel Benzimidazole-2-thione derivatives. From the result of antibacterial activity it is seen that synthesized derivatives exhibited significant to moderate activity. This confirms that all the newly synthesized acetoxybenzohydrazide, 1,3-oxazolidin-2-one, amino - acetyl thiocyanate, 1,3-oxazolidin-2-one, 1,3-thiazolidine-2,5-dione derivatives of Benzimidazole-2-thione are biologically active towards the tested bacterial strains.

ACKNOWLEDGEMENT

The authors are grateful to Dr. S.T. Gadade, Principal, C.K. Thakur A.C.S. College, for providing laboratory and other facilities.

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