AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Synthesis and Anti-Microbial Activity of the Highly Substituted 2-(1H-Benzo[d] Imidazol-2-yl)-3-Oxobutanenitrile

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ABSTRACT

Imidazoles are nitrogen containing heterocyclic compounds, widely present in nature. The imidazole ring is a part of several important natural products, including purine, histamine, histidine and nucleic acid. Highly substituted imidazoles derivatives belong to a crucial structural motif that is seen in many pharmaceutically and biologically interesting molecules. They have been intensively used in medicinal chemistry as drugs such as antihistaminic[1], antiulcerative,[2] antihelmentic,[3] and antipsychotic.[4] Several benzimidazoles have been reported as antiviral,[7] anticoagulant,[8] antiinflammatory,[9] antibacterial[10] and anticancer agents.[11] The present work deals with the derivatization of 2-(1H-benzo[d]imidazol-2-yl)-3-oxobutanenitrile with thiazolidin-4-one, oxazolidin-4-one and azetidin-2-one and characterization. All the compounds were tested for biological activity against *E. coli*, *S. typhi*, *S. aureus* while streptomycin was used as standard.

Keywords: Imidazoles, Benzimidazole, Heterocyclic compound.

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Received 02 September 2014, Accepted 13 September 2014

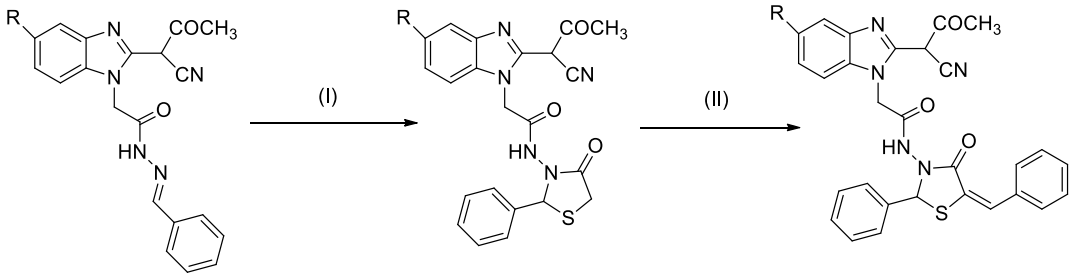
Please cite this article as: Chandan NS *et al*., Synthesis and Anti-Microbial Activity of the Highly Substituted 2-(1H-Benzo[d] Imidazol-2-yl)-3-Oxobutanenitrile. American Journal of PharmTech Research 2015.

INTRODUCTION

Benzimidazole as the heterocyclic compounds having influence on biological activity and in the practice of medicinal chemistry developed from an empirical one concerning organic synthesis of new compound based largely on the modification of the core structural substitution[1,2]. The high therapeutic properties of the Benzimidazole related drugs have encouraged the organic chemists to synthesize a large number of novel chemotherapeutic molecules. Benzimidazole derivatives have been intensively used in medicinal chemistry as drugs such as antihistaminic[3], antiulcerative[4], antihelmentic[5], and antipsychotic[6]. Some of their analogous show an array of biological activities, including non-nucleoside HIV-1 reverse transcriptase inhibitors[7], β-lactamase inhibitors, 20-HETE (20-Hydroxy-5,8,11,14-eicosatetraenoic acid) synthase inhibitors, carboxypeptidaseinhibitors, hemeoxygenase inhibitors[8] and they are selective inhibitors of cyclo-oxygenase-Cox-2[9], Several benzimidazoles have been reported as antiviral[10] anticoagulant[11] anti-inflammatory[12], anti-bacterial[13] and anti-cancer agents[14], Moreover benzimidazol-thione and alkyl-thiosubstituted benzimidazoles systems have been tested as potential anti-microbial[15], anti-bacterial[16], anti-tumor agents[17], anti-aging agents[18], anti-coagulants[19], anti-fungal[20], anti-tubercular[21], anti-diabetic[22] and anti-malarial[22]. Thiazolidenone[23-27], Oxazolidinone[28], Azetidinone[29] moieties are prominent for the biological and pharmacological activities. Kohli P. et.al[30] have reported some biologically active molecules of thiazolidinones and their arylidenes using marcaptobenzoxazole. Linezolid[31] is the first compound commercialized worldwide from the oxazolidinones class of anti-bacterial compound to treat multi-drug resistant gram positive infections. These findings stimulated our interest on incorporating, 1*H*-benzimidazole-2-acetonitriles, thiazolidenone, oxazolidenone and azitidene moieties in one framework with aim to obtain compounds of potent antimicrobial activities.

MATERIALS AND METHOD

All the Chemicals used in the synthesis of the compounds were obtained from Merck and were of analytical grade. Melting points of the compounds synthesized were determined using Thiele's melting point apparatus and were uncorrected. Purity of the compounds was checked by Thin Layer Chromatography using silica gel as stationary phase and combination of Ethyl acetate: Pet-ether as mobile phase. The IR, UV, NMR, Mass spectra of the synthesized compounds were recorded for the characterization from the University of Mumbai and Indian Institute of Technology (IIT) Mumbai. All the synthesized compounds were screened for their antimicrobial activities by drug diffusion method by preparing the discs of the drug.



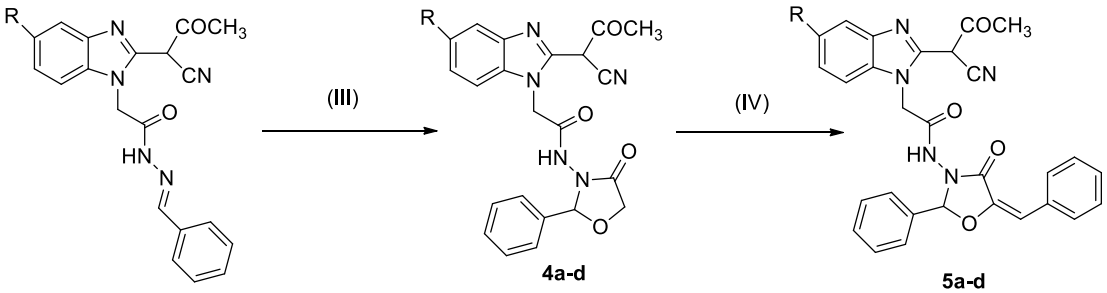
1a-d
R= H, CH_3, OCH_3, NO_2

2a-d

3a-d

Scheme 1: **Reagents and Conditions**: (I) $HSCH_2COOH$, $12MoO_3.H_3Po4$, 1,4-dioxane, reflux 3hrs.
(II) Benzaldehyde, Piperidine, benzene

Scheme 1: Preparation of Thiazolidenone



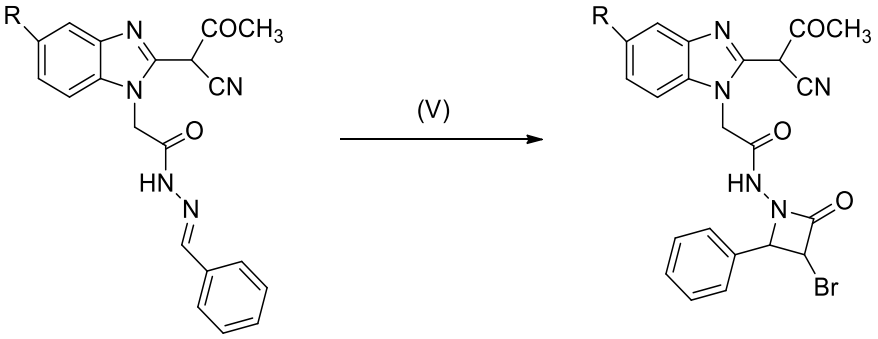
1a-d
R= H, CH_3, OCH_3, NO_2

4a-d

5a-d

Scheme 2: **Reagents and Conditions**: (**III**) $HOCH_2COOH$, $12MoO_3.H_3PO_4$, 1,4-dioxane, reflux 3hrs.
(**IV**) Benzaldehyde, Piperidine, benzene, reflux 3hrs.

Scheme 2: Preparation of Oxazolidenone



1a-d
R= H, CH_3, OCH_3, NO_2

6a-d

Scheme 3: **Reagents and Conditions**: (V) $BrCH_2COBr$, Isopropyl alcohol, Et_3N, reflux 5hrs.

Scheme 3: Preparation of Azitidene

RESULTS AND DISCUSSION

2-Acetocyano methyl-1*H*-benzimidazole was synthesized[32] and the same was on refluxed with bromoethyl acetate and result in the formation of ethyl-2-acetocyano methyl benzimidazole-1-acetate in quantitative yield. This was on further treatment with hydrazine hydrate gave 2-

acetocyano methyl-benzimidazole-1-acetic acid hydrazide and same was on reflux with benzaldehyde and gave the product as substituted N'-benzylidene-2-(2-(1-cyano-2-oxopropyl)-1H-benzo[d]imidazol-1-yl)acetohydrazide **1 a-d** (**scheme 1**) which we have exploited for the further modification of the substitution pattern of the Benzimidazole as the main core.

Synthesis of substituted 2-(2-(1-cyano-2-oxopropyl)-1H-benzo[d]imidazol-1-yl)-N-(4-oxo-2-phenylthiazolidin-3-yl) acetamide, 2(a-d) (scheme 1).

A mixture of **1(a-d)**[32] (10 mmol), thioglycolic acid (10 mmol) and phosphomolybdic acid (0.05 gm) was refluxed in dry 1,4-dioxane for 3 hrs. The reaction progress and completion of reaction was monitored by TLC. After completion of reaction, it was poured on to the ice water. The solid products **2(a-d)** were obtained, which were then washed with water, filtered, dried and recrystalized from ethanol.

2a compound M.P. 232-234 **^{o}C. Yield = 81%, IR (KBr):** 3360 cm^{-1} (>NH), 2976 cm^{-1} (CH), 2260 cm^{-1} (-C≡N), 1721 cm^{-1} and 1680 cm^{-1} >C=O stretching of -OCH_3 and -CONH resp., 1625 cm^{-1} (C=N) and other bands at 1599, 1512 and 1069 cm^{-1}. **^{1}H NMR (DMSO-*d_6*):** δ 2.42 (s, 3H,C_4- CH_3), δ 3.39 (s, 1H, C_2 -CH-) δ 3.81 (s, 2H, C_5 -CH_2), δ 4.54 (s,1H, C_2- CH-), δ 4.81 (s, 2H, -*N*-CH_2), δ 7.18-7.64 (m, 9H, Ar-H), δ 8.38 (s,1H, -NH, D_2O exchangeable). **Mass m/z (%) =** M^{+}433 (65). The other m/z peaks appeared at 240 (100), 212 (45), 198 (33), 193 (15), 183 (60), 165 (40), 155 (25), 129 (35), 102 (50), 87 (30), 76 (40) and 58 (30). Anal. calculated for: $C_{22}H_{19}O_3N_5S$, **C,** 60.96; **H,** 4.42**; N,** 16.16; **S,** 7.40 **Found : C,** 60.84; **H,** 4.37; **N,** 16.11, **S,** 7.43

2b compound M.P. 246-248 **^{o}C; Yield** 69 **%, IR(KBr):** 3379 cm^{-1} (>NH), 2959 cm^{-1} (CH), 2245 cm^{-1} (-C≡N), 1728 cm^{-1} and 1665 cm^{-1} >C=O stretching of -OCH_3 and –CONH resp., 1625 cm^{-1} (C=N), and other bands at 1589, 1528 1082 cm^{-1}. Anal. calculated for: $C_{23}H_{21}O_3N_5S$: **C,**61.73; **H** ,4.73; **N,**15.65; **S**,7.17. found: **C,** 61.51; **H**,4.77; **N**,16.01;**S,** 7.16.

2c compound M.P. 241-243 **^{o}C Yield** 69%, **IR (KBr):** 3377 cm^{-1} (>NH), 2971 cm^{-1} (CH), 2259 cm^{-1} (-C≡N), 1708 cm^{-1} and 1663 cm^{-1} (>C=O) stretching of $COCH_3$ and CONH resp., 1626 cm^{-1} (C=N), 1585, 1523, 1261 (ether) and 1073 cm^{-1}. Anal. calculated for: $C_{23}H_{21}O_4N_5S$: **C,** 59.60; **H** , 4.57; **N,** 15.11; **S**, 6.92. found: **C,** 58.49; **H**,4.51; **N**,15.08; **S,** 6.93.

2d compound M.P. 257-259 **^{o}C Yield** 74 **%, IR (KBr):** 3364 cm^{-1} (>NH), 2967 cm^{-1} (CH), 2241 cm^{-1} (-C≡N), 1711 cm^{-1} and 1655 cm^{-1} (>C=O) stretching of -$COCH_3$ and -CONH resp., 1636 cm^{-1} (C=N), 1596, 1539, 1531, 1345 (NO_2) and 1069 cm^{-1}. Anal. calculated for: $C_{22}H_{18}O_5N_6S$: **C,**55.22; **H** ,3.79; **N,**17.56; **S**,6.70. found: **C,** 54.95; **H**,3.70; **N**,17.41;**S,** 6.72.

Synthesis substituted N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-2-(2-(1-cyano-2-oxopropyl)-1H-benzo[d]imidazol-1-yl)acetamide, 3(a-d) (scheme 1).

Condensation of (10 mmol) **2(a-d**) with benzaldehyde (15 mmol) was carried out in the presence of piperidine. The reaction mixture was refluxed in benzene for 3 hrs and water removed azotropically. The reaction progress and completion were monitored by TLC. After completion of reaction, benzene was removed under reduced pressure. The crude products were purified by mixture of n-hexane and ethyl acetate to afford **3(a-d)**.

3a compound M.P. 267-269 **^{o}C Yield = 68%, IR (KBr):** 3320 cm^{-1} (>NH), 2980 cm^{-1} (–CH), 2259 cm^{-1} (-C≡N), 1706 cm^{-1} and 1660 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp., 1655 cm^{-1} (C=N), 1610, 1510 and 1074 cm^{-1}. **^{1}H NMR (DMSO-d_6):** δ 2.21 (s, 3H,C_4- CH_3), δ 3.22 (s, 1H, C_2 -CH), δ 4.60 (s,1H, C_2- CH), δ 4.73 (s, 2H, -*N*-CH_2), δ 5.39 (s, 1H, >CH-Ar), δ 7.09-7.40 (m, 14H, Ar-H), δ 8.57 (s, 1H, -NH, D_2O exchangeable). **Mass m/z (%) =** M^+ 521 (28), other peaks at 281 (55), 253 (25), 240 (40), 212 (30), 198 (44), 183 (100), 175 (60), 155 (50), 129 (14), 102 (40), 97 (30), 76 (45) and 68 (20). Anal. calculated for: $C_{29}H_{23}O_3N_5S$: **C,** 66.78; **H** , 4.44; **N,** 13.43; **S**, 6.15. found: **C,** 66.71; **H**, 4.39; **N**, 13.47;**S,** 6.14.

3b compound M.P. 276-277 **^{o}C Yield = 62%,** IR **(KBr):** 3325 cm^{-1} (NH), 2974 cm^{-1} (–CH), 2247 cm^{-1} (-C≡N), 1725 cm^{-1} and 1665 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH group resp., 1636 cm^{-1} (C=N), 1598, 1535 and 1036 cm^{-1}. Anal. calculated for: $C_{30}H_{25}O_3N_5S$: **C,** 67.27; **H** ,4.70; **N,** 13.08; **S**, 5.99. found: **C,** 67.17; **H**,4.77; **N**, 13.01;**S,** 5.98.

3c compound M.P. 281-283 **^{o}C Yield =65 %** IR **(KBr):** 3334 cm^{-1} (NH), 2961 cm^{-1} (CH), 2240 cm^{-1} (-C≡N), 1715 cm^{-1} and 1658 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH group resp., 1621 cm^{-1} (C=N) and other bands at 1595, 1527, 1252 (ether), 1054 cm^{-1}. Anal. calculated for: $C_{30}H_{25}O_4N_5S$: **C,** 65.32; **H** ,4.57; **N,** 12.707; **S**, 5.817. found: **C,** 65.377; **H**, 4.517; **N**, 12.68;**S,** 5.82.

3d compound M.P. 279-281 **^{o}C Yield = 69 %, IR (KBr):** 3371 cm^{-1} (NH), 2956 cm^{-1} (–CH), 2253 cm^{-1} (-C≡N), 1720 cm^{-1} and 1651 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH group resp., 1633 cm^{-1} (C=N), 1590, 1538, 1520, 1342 (NO_2) and 1089 cm^{-1}. Anal. calculated for: $C_{29}H_{22}O_5N_6S$: **C,** 61.48; **H** , 3.91; **N,** 14.86; **S**, 5.66. found: **C,** 61.41; **H**,3.94; **N**,14.81; **S,** 5.67.

Synthesis of substituted 2-(2-(1-cyano-2-oxopropyl)-1H-benzo[d]imidazol-1-yl)-N-(4-oxo-2-phenyloxazolidin-3-yl)acetamide, 4(a-d) (scheme 2).

A mixture of **1(a-d)** (10 mmol), glycolic acid (10 mmol) and phosphomolybdic acid (0.05 gm) was refluxed in dry 1,4 dioxane for 3 hrs. The reaction progress and completion of the reaction was monitored by TLC. After completion of reaction, reaction mass was poured onto the ice. The solid products **4(a-d)** obtained were then washed with water, filtered, dried and recrystalized from ethanol.

4a compound M.p. = 242-244 **^{o}C Yield =** 73%,. **IR (KBr):** 3324 cm^{-1} (>NH), 3040 cm^{-1} (CH), 2235 cm^{-1} (-C≡N), 1708 cm^{-1} and 1652 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp., 1620 cm^{-1} (C=N), along with other band 1590, 1360, 1262 (ether) cm^{-1}.

^{1}H NMR (DMSO-*d_6*): δ 2.41 (s, 3H, C_4-CH_3), δ 3.40 (s, 1H, C_2-CH-) δ 4.19 (s, 2H, C_5-CH_2), δ 4.55 (s, 1H, C_2-CH), δ 4.80 (s, 2H, -*N*-CH_2), δ 7.09-7.60 (m, 9H, Ar-H), δ 8.62 (s, 1H, -NH, D_2O exchangeable). **Mass m/z (%)** = M^+ 417 (55), other peaks at 240 (25), 212 (100), 198 (50), 183 (35), 177 (40), 155 (44), 149 (31), 129(35), 102 (30), 76(30) and 42(20). Anal. calculated for: $C_{22}H_{19}O_5N_5$: **C,** 63.30; **H** , 4.59; **N,** 16.78; found: **C,** 63.32; **H**, 4.61; **N**, 16.71.

4b compound M.p. = **265-267 ^{o}C; Yield = 67%, IR (KBr):** 3333 cm^{-1} (NH), 2940 (CH), 2243 cm^{-1} (-C≡N), 1701 cm^{-1} and 1661 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp., 1629 cm^{-1} (C=N), along with other band 1589, 1350, 1257 (ether), 1077 cm^{-1}. Anal. calculated for: $C_{23}H_{21}O_4N_5$: **C,** 64.03; **H** , 4.91; **N,** 16.23; found: **C,** 64.09; **H**, 4.97; **N**, 16.11.

4c compound M.p. = **251-253 ^{o}C; Yield = 61%, IR (KBr):** 3344 cm^{-1} (NH), 2956 cm^{-1} (CH), 2248 cm^{-1} (-C≡N), 1713 cm^{-1} and 1659 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp., 1638 cm^{-1} (C=N), 1597, 1356, 1274 (ether) and 1069 cm^{-1}. Anal. calculated for: $C_{23}H_{21}O_5N_5$: **C,** 61.74; **H** , 4.73; **N,** 15.65; found: **C,** 61.80; **H**, 4.75; **N**, 15.68.

4d compound M.p. = **260-262 ^{o}C; Yield = 70%, IR (KBr):** 3351 cm^{-1} (NH), 3015 cm^{-1} (-CH), 2257 cm^{-1} (-C≡N), 1716 cm^{-1} and 1649 cm^{-1} (>C=O) stretching of -$COCH_3$ and CONH resp., 1643 cm^{-1} (C=N), 1587, 1551, 1535, 1348 (NO_2), 1247 (ether) and 1079 cm^{-1}. Anal. calculated for: $C_{22}H_{18}O_6N_6$: **C,** 57.14; **H** , 3.92; **N,** 18.17; found: **C,** 57.19; **H**, 3.96; **N**, 18.07.

Synthesis of substituted (E)-N-(5-benzylidene-4-oxo-2-phenyloxazolidin-3-yl)-2-(2-(1-cyano-2-oxopropyl)-1H-benzo[d]imidazol-1-yl)acetamide, 5(a-d) (scheme 2).

Condensation of (10 mmol) **4(a-d)** with benzaldehyde (15 mmol) was carried out in the presence of piperidine and then reaction mass was refluxed in benzene for 3 hrs. Water was removed azotropically. The progress and completion of reaction was monitored by TLC. After completion of reaction benzene was distilled out at reduced pressure and futher the reaction mass was poured onto the ice to obtain **5(a-d)**. Product gained was then washed with water, filtered, dried and recrystalized from ethanol.

5a compound M.P. = 277- 279 **^{o}C; Yield =** 68%, **IR (KBr):** 3309 cm^{-1} (NH), 3045 cm^{-1} (-CH), 2208 cm^{-1} (-C≡N), 1720 cm^{-1} and 1665 cm^{-1} (>C=O) stretching of -$COCH_3$ and -CONH resp., 1627 cm^{-1} (C=N), 1595, 1525, 1240 (ether) and 1086 cm^{-1}, **1H NMR (DMSO-*d_6*):** δ 2.24 (s, 3H, C_4- CH_3), δ 3.43 (s, 1H, C_2-CH-), δ 4.58 (s,1H, C_2- CH), δ 4.79 (s, 2H, -*N*-CH_2), δ 5.31 (s, 1H, >CH-Ar), δ 7.17-7.52 (m, 14H, Ar-H), δ 8.48 (s, 1H, -NH,D_2O exchangeable).

Mass m/z (%) = M^+ 505 (40), other peaks at 265 (23), 240 (40), 237 (20), 212 (30), 198 (40), 183 (30), 159 (100), 155 (30), 129 (17), 102 (50), 80 (37), 76 (35) and 72 (30). Anal. calculated for: $C_{29}H_{23}O_4N_5$: **C,** 68.90; **H** , 4.59; **N,** 13.85. found: **C,** 68.93; **H**, 4.54; **N**, 13.87.

5b compound M.P.= 270-272 **^oC; Yield** = 65%, **IR (KBr):** 3331 cm^{-1} (NH), 2974 cm^{-1} (–CH), 2219 cm^{-1} (-C≡N), 1713 cm^{-1} and 1669 cm^{-1} (>C=O) stretching of -$COCH_3$ and CONH resp., 1623 cm^{-1} (C=N), 1599, 1528, 1233 (ether) and 1089 $cm.^{-1}$ Anal. calculated for: $C_{30}H_{25}O_4N_5$: **C,** 69.35; **H** , 4.85; **N,** 13.48. found: **C,** 61.51; **H**,4.77; **N**,16.01;**S,** 7.16.

5c compound M.P.= 274-276 **^oC; Yield** = 61%, **IR (KBr):** 3339 cm^{-1} (NH), 2962 cm^{-1} (–CH), 2241 cm^{-1} (-C≡N), 1721 cm^{-1} and 1659 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp., 1635 cm^{-1} (C=N), 1587, 1535, 1249 (ether) and 1079 $cm.^{-1}$ Anal. calculated for: $C_{30}H_{25}O_5N_5$:**C,**61.73; **H**, 4.73; **N,**15.65; **S**,7.17. found: **C,** 69.31; **H**,4.87; **N**, 13.43.

5d compound M.P.= 279-281**^oC; Yield** = 64%, **IR (KBr):** 3348 cm^{-1} (NH), 2945 cm^{-1} (-CH), 2247 cm^{-1} (-C≡N), 1727 cm^{-1} and 1641 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp., 1618 cm^{-1} (C=N), 1581, 1535, 1523, 1346, (NO_2), 1237 (ether) and 1091cm^{-1}. Anal. calculated for: $C_{29}H_{22}O_6N_6$: **C,** 63.2767.28; **H**, 4.03; **N,** 15.27. found: **C,** 67.19; **H**,4.74; **N**, 13.13.

Synthesis of substituted N-(3-bromo-2-oxo-4-phenylazetidin-1-yl)-2-(2-(1-cyano-2-oxopropyl)-1H-benzo[d]imidazol-1-yl)acetamide 6 (a-d) (scheme 3).

A mixture of **1(a-d)** (10 mmol) and bromoacetyl bromide (10 mmol) were refluxed in isopropyl alcohol in presence of catalytic amount of triethylamine for 5 hrs. The reaction progress was monitored by TLC, after completion of reaction solid products **6 (a-d)** obtained were filtered, then was washed with the water, dried and recrystalized from ethanol.

6a M.P.239-241 **^oC; Yield** = 61%, **IR (KBr):** 3305 cm^{-1}(NH), 2995 cm^{-1} (-CH), 2220 cm^{-1} (-C≡N), 1702 cm^{-1} and 1670 cm^{-1} (>C=O) stretching of -$COCH_3$ and -CONH resp., 1620 cm^{-1} (C=N), 1560, 1520, 1072 and 865 cm^{-1}. **^{1}H NMR (DMSO d_6):** δ 2.26 (s, 3H, $4^{/}$-CH_3), δ 3.37 (s, 1H, $4^{//}$-CH), δ 4.64 (s, 1H, $2^{/}$-CH), δ 4.87 (s, 2H, *N*-CH_2), δ 5.11 (s, 1H, $3^{//}$-CH), δ 7.19-7.62(m, 9H, Ar-H), δ 8.12 (s, 1H, -NH, D_2O exchangeable). **Mass m/z (%)** = M^+ 480 (33), M^{+2} 482 (32.24s) other peaks at 240 (30), 212 (43), 198 (30), 183 (58), 159 (50), 155 (36), 129 (100), 102 (35), 76 (52) and 52 (40). Anal. calculated for: $C_{22}H_{18}O_3N_5Br$: **C,** 55.01; **H** , 4.08; **N,** 14.17. found: **C,** 54.93; **H**, 3.73; **N**, 16.69.

6b M.P.247-249 **^oC; Yield** = 66%, **IR (KBr):** 3304 cm^{-1} (NH), 2971 cm^{-1} (-CH), 2268 cm^{-1} (-C≡N), 1712 cm^{-1} and 1668 cm^{-1} (>C=O) stretching of -$COCH_3$ and CONH resp., 1628 cm^{-1} (C=N), 1569, 1526, 1079 and 859 cm^{-1}. Anal. calculated for: $C_{23}H_{20}O_3N_5Br$: **C,** 55.88; **H**, 4.73; **N,**15.65; **S**,7.17. found: **C,** 55.79; **H**,4.17; **N**,14.23.

6c M.P. 262-264 **^{o}C; Yield** = 59%, **IR (KBr):** 3318 cm^{-1} (NH), 2985 cm^{-1} (-CH), 2236 cm^{-1} (-C≡N), 1709 cm^{-1} and 1687 cm^{-1} (>C=O) stretching of -$COCH_3$ and –CONH resp.,1638 cm^{-1} (C=N), 1563, 1525, 1238 ether 1077 and 868 cm^{-1}. Anal. calculated for: $C_{23}H_{20}O_4N_5Br$: **C,**54.13; **H** ,3.95; **N,**13.72. found: **C,** 54.17; **H**,3.94; **N**,13.78.

6d M.P.244-246 **^{o}C; Yield** = 62%, **IR (KBr):** 3347 cm^{-1} (NH), 2951 cm^{-1} (-CH), 2247 cm^{-1} (-C≡N), 1715 cm^{-1} and 1641 cm^{-1}(>C=O) stretching of -$COCH_3$ and -CONH resp., 1618 cm^{-1} (C=N), 1581, 1535, 1523, 1346 (NO_2), 1091 and 873 cm^{-1}. Anal. calculated for: $C_{22}H_{17}O_5N_6Br$: **C,**50.30; **H** , 3.26; **N,**16.00. found: **C,** 50.38; **H**,3.21; **N**,15.95.

Antimicrobial Activity

All the synthesized compounds **2(a-d), 3(a-d), 4(a-d), 5(a-d)** and **6(a-d)** were screened for their antimicrobial activities by drug diffusion method by preparing the discs of the drug. The activity was tested with *Staphylococcus aureus* (Gram positive), *Salmonella typhi* and *Escherichia coli* (Gram negative) bacterial strains taking Streptomycin, Ciprofloxacin and Cloxacillin as standard drugs. Further all antimicrobially active compounds were tested to find their minimal inhibitory concentration (MIC); using (50 µg/ml), (100µg/ml), (150µg/ml), (200µg/ml) concentrations.

Table 1: Antibacterial activity of compounds 2a-d, 3a-d, 4a-d 5a-d and 6a-d

Compd.No.	**Zone of inhibition in mm**											
	E. coli				***S. typhi***				***S. aureus***			
	50 µg	**100 µg**	**150 µg**	**200 µg**	**50 µg**	**100 µg**	**150 µg**	**200 µg**	**50 µg**	**100 µg**	**150 µg**	**200 µg**
2a	10	13	17	20	08	10	13	15	07	10	14	17
2b	11	13	15	18	12	12	15	17	09	12	16	18
2c	12	14	17	19	09	11	14	16	10	12	14	17
2d	11	13	16	18	10	11	13	15	11	10	12	15
3a	11	14	17	19	08	11	15	18	11	13	14	17
3b	12	15	17	19	10	12	15	19	09	11	13	16
3c	09	11	14	17	08	12	14	18	12	15	17	19
3d	10	12	14	16	09	11	13	16	10	13	16	18
4a	08	11	13	15	10	12	14	17	08	12	15	18
4b	11	13	15	17	11	12	14	16	10	12	15	19
4c	10	12	15	18	10	13	15	18	11	13	16	18
4d	09	12	15	17	08	10	13	16	07	09	11	14
5a	11	13	15	18	11	14	17	19	08	10	13	15
5b	08	11	14	17	10	12	15	17	11	13	15	18
5c	10	12	15	19	11	14	16	18	09	12	14	17
5d	11	13	15	18	10	12	15	18	11	13	16	19
6a	10	13	17	20	08	10	13	15	07	10	14	17
6b	11	13	15	18	12	12	15	17	09	12	16	18
6c	12	14	17	19	09	11	14	16	10	12	14	17

6d	11	13	16	18	10	11	13	15	11	10	12	15

Disc size: 6.35 mm; standard : streptomycin; control : DMSO; duration : 24 h. resistant (< 11 mm), intermediate (14 mm), sensitive(>15 mm).

CONCLUSION

From the antibacterial screening data it was concluded that the all compounds **2a-d to 6a-d** showed activity against gram negative microorganisms as well as gram positive organisms. The compounds having the thiazolidine as substituent showed little more activity as compared to the other substituents. The zones of inhibition were found to at 20 mm, 19 mm, 17 mm, and 16 mm as the highest inhibition zone against *E. coli, S.typhi and S. aureus* with concentration 200 g.

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