Available online at **www.joac.info**

ISSN: 2278-1862

Journal of Applicable Chemistry

2018, 7 (6): 1558-1564

(International Peer Reviewed Journal)

Synthesis and Antibacterial Activity of Benzothiazole Analogues

Gutta Lakshmi Prasanna[1], Y.Bharat[2], Reddymasu Sreenivasulu[3] and Mandava Venkata Basaveswara Rao[1]*

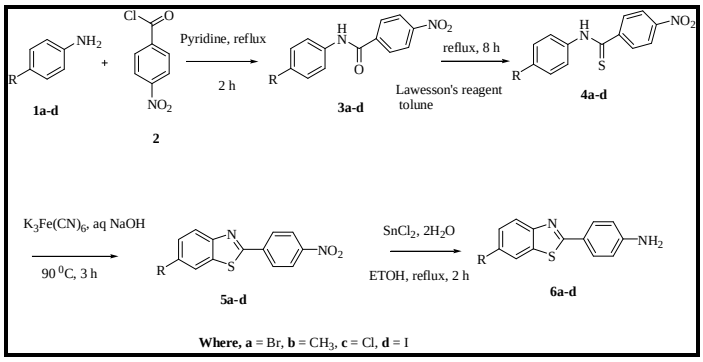
1. Department of Chemistry, Krishna University, Machilipatnam, Andhra Pradesh, **INDIA**
2. Department of Chemistry, Vignan University, Vadlamudi, Guntur Dist., **INDIA**
3. Department of Chemistry, University College of Engineering, JNTU, Kakinada-533 003, **INDIA**

Email: vbrmandava@yahoo.com, professormandava@gmail.com

ABSTRACT

A series of novel benzothiazole fused derivatives were designed, synthesized and screened for their antibacterial activity against Escherichia coli ***(MTCC 40)*** *(Gram-negative) and Staphylococcus aureus* ***(MTCC 96)****(Gram-positive) bacteria. Among them, derivative* ***8c*** *showed highest antibacterial activity against gram +ve and gram –ve bacteria.*

Graphical Abstract



Synthesis of 4-(6-substituted benzo[d]thiazol-2-yl) benzenamines (6a-d)

Keywords: Benzothiazole derivatives, Antibacterial activities and Chloramaphenicol.

INTRODUCTION

The bacterial infections which contribute most to the human diseases are also those in which emerging and microbial resistance is most evident. Some important examples include diarrhoeal diseases, respiratory tract infections, meningitis, penicillin-resistant Streptococcus Pneumoniae, vancomycin-resistant entercocci, and multi-resistant Mycobacterium Tuberculosis. When infections become resistant to first line antimicrobials, treatment has to be switched to second or third line drugs which are nearly always much more expensive and more toxic as well e.g. the drug needed to treat

multi drug-resistant form of tuberculosis are over 100 times more expensive than the first line drugs used to treat non-resistant forms.

Benzothiazoles are bicyclic ring system [**1**]. A number of 2-aminobenzothiazoles have been studied as central muscle relaxants and found to interfere with glutamate neurotransmission in biochemical, electrophysiological and behavioural experiments [**2**]. Benzothiazole ring made from thiazole ring fused with benzene ring. Thiazole ring is a five-member ring consists of one nitrogen and one sulphur atom in the ring. Benzothiazole derivatives have been studied and found to have various chemical reactivity and biological activity. It was found to be possessing pharmacological activities such as anti-viral, anti-bacterial, anti-microbial and fungicidal activities [**3**]. Benzothiazole nucleus containing molecules are also reported as anti-allergic [**4**], anti-diabetic [**5**], antitumor [**6**], anti-inflammatory [**7**], anti-helmintic [**8**] and anti-HIV agents [**9**]. 2-aryl substituted benzothiazoles show antitumor activity while condensed pyrimido-benzothiazoles and benzothiazolo-quinazolines showed anti-viral activity [**10, 11**]. Substituted 6-nitro and 6-aminobenzothiazoles have been reported for antimicrobial activity.

Most alarming of all are diseases where resistance is developing for all currently available drugs; current trends suggest that some diseases will have no effective therapies within the next ten years. So, there is a requirement to develop new replacement drug immediately which is effective against resistant bacteria having lesser toxicity as well as economical also. In view of the biological importance of the two compounds containing benzothiazole nucleus, we are successful in synthesizing 2-aminobenzothiazoles by developing novel methodology.

MATERIALS AND METHODS

General: All the chemicals and reagents were purchased from AVRA laboratories, Hyderabad, India and used without any further purification. Proton and carbon NMR was recorded on Brucker 300 MHz frequency instrument. Thecompletion of reaction was checked by TLC.

Synthesis of N-(4-substitutedphenyl)-4-nitrobenzamides (3a-d): 4-nitrobenzoyl chloride (0.027 mmol) was added slowly to a solution of the appropriately substituted aniline (0.027 mmol) in pyridine (10 mL). The resulting solution was stirred under reflux for 2 h and then poured into 400 mL water. The precipitate formed was collected and washed with dil HCl (60 mL), followed by water and methanol, to afford the final benzanilides **(3a-d)** as solid.

N-(4-bromophenyl)-4-nitrobenzamide (3a): Colour less solid. Yield: 90%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.03 (bs, NH), 8.11 (d, 2H, *J=8.49 Hz*), 7.09 (d, 2H, *J=8.78 Hz*), 7.40-7.32 (m, 3H), 7.29 (d, 1H, *J= 3.77 Hz*).

4-Nitro-N-p-tolybenzamide (3b): Colour less solid. Yield: 92%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.04 (bs, NH), 8.24 (d, 2H, *J=8.49 Hz*), 7.93(d, 2H, *J=8.78 Hz*), 7.68 (m, 2H), 7.11 (d, 2H, *J= 7.80 Hz*), 3.91 (s, 3H).

N-(4-chlorophenyl)-4-nitrobenzamide (3c): Pale yellow color solid. Yield: 85%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.9 (bs, NH), 8.23 (d, 2H, *J=8.49 Hz*), 8.00 (d, 2H, *J=8.49 Hz*), 7.68 (m, 2H), 7.33 (d, 2H, *J= 7.80 Hz*).

N-(4-idophenyl)-4-nitrobenzamide (3d): Pale yellow color solid. Yield: 90%.^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.03 (bs, NH), 8.11 (d, 2H, *J=8.49 Hz*), 7.09 (d, 2H, *J=8.78 Hz*), 7.40-7.32 (m, 2H), 7.29 (d, 2H, *J= 3.77 Hz*).

Synthesis of 4-(4-substituted phenyl)-4-nitrobenzothioamide (4a-d): To a solution of benzanilide (6g, 0.018 mol) in tolune, Lawes son's reagent (0.7 eq) was added and reflux it for 8h. After cooling,

solvent was removed with rotavapour and work-up with chloroform and water. Separation of the organic layer and evaporation followed by column chromatography gave solids.

4-(4-bromophenyl)-4-nitrobenzothioamide (4a): White solid, Yield: 90%, ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.98 (s, 1H), 8.26 (d, 2H, *J=8.3 Hz*), 7.67-7.71 (m, 3H), 7.15 (d, 2H, *J= 7.80 Hz*).

4-nitro-N-p-tolybenzothioamide (4b): White solid, Yield: 89%, ^{1}H NMR ($CDC1_3$, 300 MHz): δ 9.04 (bs, NH), 8.26 (d, 2H, *J=8.3 Hz*), 7.95 (d, 2H, *J=8.78 Hz*), 7.72 (d, 2H, *J=7.80 Hz*), 7.15 (d, 2H, *J=7.80Hz*).

N-(4-chlorophenyl)-4-itrobenzothioamide (4c): White solid, Yield: 90%, ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.95 (s, 1H), 8.15 (d, 2H, *J=8.3 Hz*), 7.65-7.71 (m, 3H), 7.25 (d, 2H, *J= 7.80 Hz*).

N-(4idoophenyl)-4-itrobenzothioamide (4d): White solid, Yield: 90%, ^{1}H NMR ($CDC1_3$, 300 MHz): δ 9.07 (bs, NH), 8.25 (d, 2H, *J=8.3 Hz*), 7.75 (d, 2H, *J=8.78 Hz*), 7.75 (d, 2H, *J= 7.80 Hz*), 7.17 (d, 2H, *J = 7.80 Hz*).

Synthesis of 6-substituted-2-(4-nitrophenyl)benzo[d]thiazole(5a-d): A solution of the substituted thiobenzanilide (0.017 mmol) in aqueous sodium hydroxide (8 equiv. in 50 mL of water) containing ethanol (3 mL) was added dropwise to a pre-heating solution of potassium ferricynade (4 eqv in 30 mL water) taken in a 250 mL RB flak at (0°C over a period of 60 min. The resulting solution was dried at 90°C for a further 2 h and then cooled to room temperature. The precipitate formed was filtered and washed with water. Product was purified by column chromatography (ethyl acetate/hexan) and by recrystallization to furnish the 4-(6-substitutedbenzo[d]thiazol-2-yl) benzenamines as yellow solids.

6-bromo-2-(4-nitrophenyl)benzo[d]thiazole (5a): Yellow solid, Yield: 75%. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.01(d, 2H, *J=8.4 Hz*), 7.87(d, 1H, *J= 8.7 Hz*), 7.80(d, 1H, *J=8.4 Hz*), 7.49(m, 1H), 7.33(t, 1H, *J=8.4 Hz*), 7.27(d, 1H, *J=8.4 Hz*).

6-methyl-2-(4-nitrophenyl)benzo[d]thiazole(5b): Yellow solid, Yield: 60%.^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.35(d, 2H, *J=8.87Hz*), 8.23 (d, 1H, *J= 8.87 Hz*), 8.07 (m, 1H), 7.63 (d, 1H, *J= 8.4 Hz*), 7.30 (d, 2H, *J=5.4 Hz*), 3.89 (s, 3H).

6-chloro-2-(4-nitrophenyl)benzo[d]thiazole(5c): Light yellow solid, Yield: 68%. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.03(d, 2H, *J=8.8 Hz*), 7.68 (d, 1H, *J= 8.37 Hz*), 7.26 (d, 1H, *J=8.37 Hz*), 7.01 (s, 1H), 6.9 (d, 2H, *J=8.4 Hz*).

6-ido-2-(4-nitrophenyl)benzo[d]thiazole(5d): Light yellow solid, Yield: 62%.^{1}H NMR ($CDC1_3$, 300MHz): δ8.35(d, 2H, *J=8.9 Hz*), 8.24 (s,1H, *J=8.9 Hz*), 7.42(d, 1H, *J=8.4 Hz*), 7.49(m, 1H), 7.33(t, 1H, *J=8.4 Hz*), 7.27(d, 1H, *J=8.4Hz*).

Synthesis of 4-(6-substituted benzo[d]thiazol-2-yl) benzenamines (6a-d): A solution of 6-substituted-2-(4-nitrophenyl)benzo[d]thiazole (8.65 mmol) in ethanol, tin (III) chloride dehydrate (25.98 mmol) was added and refluxed it for 2 h. The solvent was removed under vaccum and the resulting oil taken up in ethyl acetate (70 mL) was quenched with aq. $NaHCO_3$ solution. The resulting organic layer was separated and evaporated to leave a residue of the amine which was purified by column chromatography (eluent ethyl acetate/hexane) as yellow color solids.

4-(6-bromobenzo[d]thiazol-2-yl) benzenamines (6a): Light yellow solid, Yield: 85%. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.01(d, 2H, *J=8.4 Hz*), 7.84 (d, 1H, *J= 8.7 Hz*), 7.80 (d, 1H, *J=8.4 Hz*), 7.40 (dd, 1H, *J=8.4, 6.71 Hz*), 7.33 (t, 1H, *J=8.4 Hz*), 7.27 (d, 1H, *J=8.4 Hz*).

4-(6-methylbenzo[d]thiazol-2-yl) benzenamines (6b): Light yellow solid, Yield: 72%. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 7.90(m, 1H), 7.84 (d, 2H, *J= 8.28 Hz*), 7.51 (d, 1H, *J=6.2 Hz*), 7.16 (d, 1H, *J=6.02 Hz*), 6.17 (d, 2H, *J=8.4 Hz*), 4.02 (s, 2H), 3.91 (s, 3H).

4-(6-chlorobenzo[d]thiazol-2-yl) benzenamines (6c): Light yellow solid, Yield: 85%. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.01(d, 2H, *J=8.8 Hz*), 7.65 (d, 1H, *J= 8.37 Hz*), 7.23 (d, 1H, *J=8.37 Hz*), 6.9 (s, 1H), 6.87 (d, 2H, *J=8.8 Hz*), 4.06 (s, 2H).

4-(6-idobenzo[d]thiazol-2-yl) benzenamines (6d): Light yellow solid, Yield: 78%. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 7.84(d, 2H, *J=8.4 Hz*), 7.26(d, 1H, *J= 8.7 Hz*), 6.68 (d, 2H, *J=8.4 Hz*), 6.07 (dd, 1H, *J=8.4, 6.71 Hz*), 6.03 (d, 1H, *J=8.4 Hz*), 4.06 (s, 2H).

Synthesis of 6-substituted-2-(4-(2-methyl-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole(8a-h): The compounds were prepared by means of the paal-knorr reaction by condensing a 1,4-diketone with the appropriate aminobenzothiazole. The compound of diketone (2.28 mmol) and the suitable aniline (2.5 mmol) in the presence of p-toluenesulfonic acid (30 mg) in dry toluene (50 mL) was refluxed for 20 h using Dean-Stark apparatus. The reaction mixture was cooled, and concentrated. The crude material was purified by flash chromatography with hexane/ethyl acetate (7/3 v/v) mixture as the elutant to give 6-substituted-2-(4-(2-methyl-1H-pyrrol-1-yl) phenyl)benzo[d]thiazoleb **8a-h** as yellow color solids.

6-bromo-2-(4-(2-methyl-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole(8a): Pale yellow color solid, Yield: 92%. m.p: 180-182. ^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.03 (d, 1H, *J= 8.30 Hz*), 7.89 (d, 1H,*J= 8.67 Hz*), 7.67-7.5 (m, 2H), 7.25 (d, 1H, *J=8.3Hz*), 7.07(d, 2H, *J = 8.67 Hz*), 6.96 (d, 1H, *J= 8.60 Hz*), 6.26 (d, 1H, *J= 2.83 Hz*), 5.94 (d, 1H,*J= 2.89 Hz*), 2.13 (s, 3H);^{I3}C NMR ($CDC1_3$, 300 MHz): δ 13.55,117.10,96.65,96.98,99.28,105.84,115.79,125.26,132.92,137.68,138.01,153.72,155.25, 159.95,160.30, 166.73; MS (ESI): m/z 368.

6-methyl-2-(4-(2-methyl-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole (8b): Pale yellow color solid, Yield: 94%. m.p: 170-172.^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.09 (d, 2H, *J= 8.30 Hz*), 7.88 (d, 2H,*J= 8.67 Hz*), 7.85 (d, 1H, *J=8.30 Hz*), 7.47 (t, 1H,*J=8.3 Hz*), 7.38 (t, 1H, *J= 8.3Hz*), 7.27 (d, 1H, *J=8.30 Hz*), 6.29 (d, 1H, *J= 8.60 Hz*), 5.98 (d, 1H, *J= 2.83 Hz*), 2.11 (s, 3H), 1.95 (s, 3H);^{I3}C NMR ($CDC1_3$, 300 MHz): δ 14.13, 97.25,97.48, 105.49, 116.35, 132.28, 133.43,137.66,138.38, 153.12, 153.18, 154.28, 155.68, 160.38, 167.17; MS (ESI): m/z 304.

6-chloro-2-(4-(2-methyl-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole (8c): Pale yellow color solid, Yield: 89%. m.p: 181-182.^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.06 (d, 1H, *J= 8.30 Hz*), 7.8-7.41 (m, 4H), 7.3 (t, 1H, *J= 8.3Hz*),7.02 (d, 1H, *J = 8.67 Hz*), 6.9 (d, 1H, *J= 8.60 Hz*), 6.2 (d, 1H, *J= 2.83 Hz*), 5.9 (d, 1H,*J= 3.8 Hz*), 3.89 (s, 3H);^{I3}C NMR ($CDC1_3$, 300 MHz): δ 12.11, 55.65, 97.05, 97.43, 114.82, 116.22, 118.78, 133.00, 133.21, 137.60, 138.47, 146.12, 154.18, 155.58, 160.38; MS (ESI): m/z 324.

6-iodo-2-(4-(2-methyl-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole (8d): Pale yellow color solid, Yield: 90%. m.p: 151-152.^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.2 (d, 1H, *J= 8.30 Hz*), 7.91 (d, 1H,*J= 8.67 Hz*), 7.8-7.7 (m, 2H), 7.5-7.4 (m, 1H), 7.23(d, 2H, *J = 8.67 Hz*), 7.1 (d, 1H, *J= 8.60 Hz*), 6.4 (d, 1H, *J= 2.83 Hz*), 6.19 (d, 1H,*J= 2.89 Hz*), 2.3 (s, 3H);^{I3}C NMR ($CDC1_3$, 300 MHz): δ 14.37, 96.64, 96.98, 109.67, 110.54, 114.27, 132.54, 135.74, 137.39, 138.09, 146.47, 153.74, 155.20, 159.97, 167.04; MS (ESI):m/z 415.

6-bromo-2-(4-(2-methoxy-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole (8e): Pale yellow color solid, Yield: 89%. m.p: 183-185.^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.11 (d, 2H, *J= 8.30 Hz*), 7.9 (d, 1H,*J= 8.67 Hz*), 7.7 (d, 1H, *J=8.30 Hz*), 7.5(t, 1H,*J=8.3 Hz*), 7.46 (t, 1H, *J= 8.3Hz*), 7.3 (d, 2H, *J=8.30 Hz*),

6.06 (d, 2H, *J= 2.83 Hz*), 3.9 (s, 3H); ^{I3}C NMR ($CDC1_3$, 300 MHz):12.59, 56.00, 56.25, 100.70, 113.72, 116.14, 116.36, 132.17, 133.43, 138.06. 138.49, 147.56, 150.33, 153.59, 154.23, 165.84; MS (ESI): m/z 383.

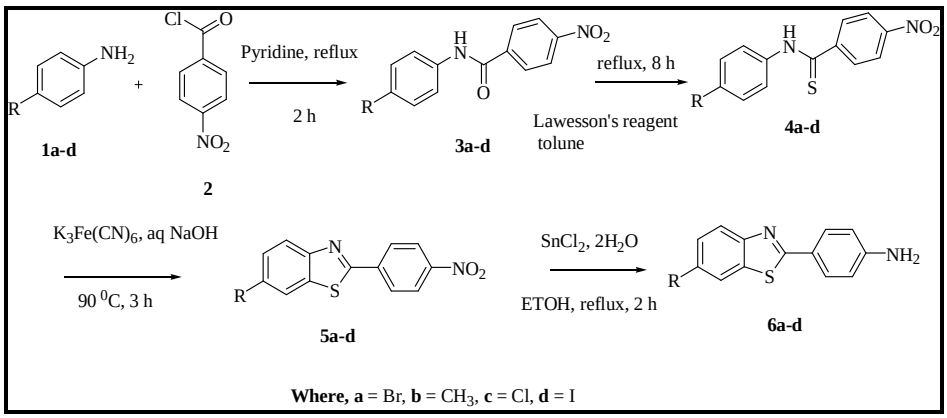
2-(4-(2-methoxy-1H-pyrrol-1-yl)phenyl)-6-methylbenzo[d]thiazole (8f): Pale yellow color solid, Yield: 82%. m.p: 176-177.^{1}H NMR ($CDC1_3$, 300 MHz): δ 7.8 (d, 2H, *J= 8.30 Hz*), 7.2 (d, 1H,*J= 8.67 Hz*), 7.14 (m, 3H),6.96 (d, 2H, *J= 8.60 Hz*), 6.26 (d, 1H, *J= 2.83 Hz*), 5.9 (d, 1H,*J= 2.89 Hz*), 2.41 (s, 3H), 2.2 (s, 3H,);^{I3}C NMR ($CDC1_3$, 300 MHz): δ 12.53, 19.28, 99.93, 106.38, 107.77, 108.04, 114.79, 115.40, 130.70, 132.80, 132.89, 138.53, 150.60, 160.44, 162.21, 165.88; MS (ESI): m/z 320.

6-chloro-2-(4-(2-methoxy-1H-pyrrol-1-yl)phenyl)benzo[d]thiazole (8g): Pale yellow color solid, Yield: 87%. m.p: 183-184.^{1}H NMR ($CDC1_3$, 300 MHz):δ 8.07 (d, 2H, *J= 8.30 Hz*), 7.97 (d, 1H,*J= 8.67 Hz*), 7.30 (d, 1H, *J=8.30 Hz*), 7.2 (m, 1H,*J=8.3 Hz*), 6.97 (t, 1H, *J= 8.3Hz*), 6.32 (d, 2H, *J=8.30 Hz*), 6.20(d, 2H, *J = 8.67 Hz*), 2.12 (s, 3H);^{I3}C NMR ($CDC1_3$, 300 MHz): 11.65, 99.75, 106.38, 107.69, 108.04, 115.05, 115.40, 130.70, 132.76, 132.92, 138.53, 150.60, 158.65, 160.78, 162.21, 165.88; MS (ESI): m/z 340.

6-iodo-2-(4-(2-methoxy-1H-pyrrol-1-yl) phenyl)benzo[d]thiazole (8h): Pale yellow color solid, Yield: 89%. m.p: 152-153.^{1}H NMR ($CDC1_3$, 300 MHz): δ 8.01 (d, 2H, *J= 8.30 Hz*), 7. 9 (d, 1H,*J= 8.67 Hz*), 7.5 (d, 1H, *J=8.30 Hz*), 7.18 (t, 1H,*J=8.3 Hz*), 6.9 (t, 1H, *J= 8.3Hz*), 6.38 (d, 2H, *J=8.30 Hz*), 6.027(d, 2H, *J = 8.67 Hz*), 3.82 (s, 3H); ^{13}C NMR ($CDC1_3$, 300 MHz):11.50, 98.75, 105.38, 107.69, 109.08, 115.05, 115.40, 130.70, 132.76, 132.95, 138.53, 150.60, 158.65, 160.78, 161.21, 165.88; MS (ESI): m/z 431.

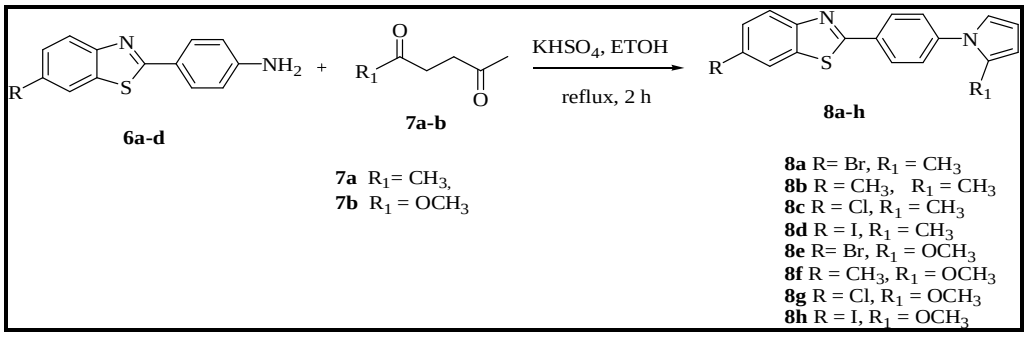
RESULTS AND DISCUSSION

The prepared of key intermediate 4-(6-bromobenzo[d]thiazol-2-yl) benzenamines (**6a-d**) has been carried out by a synthetic sequence as illustrated in scheme 1. The starting precursor-4-nitrobenzoyl chloride (**2**) is condensed with appropriately substituted aniline (**1a-d**) in pyridine under refluxing conditions for 2 h to afford such as 6-bromo, methyl, Chloro and iodo in addition to aniline. The benzanilides (**3a-d**) are then treated with Lawesson's reagent to convert the carbonyl functionality into a thiocarbonyl one by refluxing in tolune for overnight to provide thiobenzanilidies (**4a-d**) as light yellow solids. The thiobenzanilides on further treatment with aq. sodium hydroxide and potassium ferricynide at 90°C undergoes cyclization and affords substituted 4-(6-bromobenzo [d]thiazol-2-yl) benzenamines (**5a-d**) by tin (II) chloride dehydrated in refluxing ethanol to yield the final benzothiazole intermediates (**6a-d**).



Scheme 1. Synthesis of 4-(6-substituted benzo[d]thiazol-2-yl)benzenamines(6a-d)

A screening of various inorganic and organic reagents for promoting the Paal-Knor pyrrole synthesis has been carried out. Similarly different organic solvent also has been found for the reaction. Among them catalytic $KHSO_4$ the reaction respectively, Excellent yields of substituted pyrrols have been obtained in $KHSO_4$-catalyzed Paal-Knorr reactions of substituted alknes with substituted benzothiazole amines such as 6-chloro-2-(4-(2-methyl-1H-pyrrol-1-yl) phenyl)benzo[d]thiazole(**8a-h**) and shown in scheme 2. The mild reaction conditions were short easy isolation and high yield of the products. Finally the optimized reaction conditions for the Paal-knorr reaction potassium bisulphate as catalyst, ethanol as solvent under refluxing conditions have been employed for the synthesis of the substituted benzothiazoles (**8a-h**). The substituted benzothiazoles have been obtained in good to excellent yields.



Scheme 2. Synthesis of 6-substituted-2-(4-(2-methyl-1H-pyrrol-1-yl) phenyl)benzo[d]thiazoles (8a-h)

APPLICATION

Biological Evaluation

Antibacterial activity: In the present study, substituted benzothiazoles it is observed that good activity was shown by the prepared derivatives against the studied Gram positive bacteria and very poor activity against Gram negative bacteria and results were tabulated in table 1. The good and poor antibacterial activities of the prepared derivatives against Gram positive and Gram negative bacteria can be explained based on their cell outer layers. Gram positive bacteria have an ineffective and permeable outer barrier made of peptidoglycan layer, which is responsible for permeability of drug constituents. However, Gram negative bacteria have an impermeable outer membrane to drug constituents, as cell wall contains multilayered peptidoglycan and phospholipidic. Two compounds were screened, among them **8c** showed high activity.

Table 1. Antibacterial activity of the synthesized substituted benzothiazoles derivatives

Compound	Zone of inhibition (mm)*					
	Escherichia coli ***(MTCC 40)*** (Gram-negative)(Conc. Mg mL^{-1})			*Staphylococcus aureus****(MTCC 96)*** (Gram-positive)(Conc. µg/mL^{-1})		
	200	**100**	**50**	**200**	**100**	**50**
8a	15	11	5	17	12	5
8b	18	12	8	18	13	10
8c	27	20	19	29	21	19
8d	15	12	11	21	19	4
8e	22	11	6	22	18	7
8f	11	13	14	24	18	26
8g	28	24	20	31	29	24
8h	22	22	16	24	22	20
Chloramphenicol	31	30	21	33	30	23

** indicates average of triplicate*

CONCLUSION

A series of novel benzothiazole fused derivatives were designed, synthesized and screened for their antibacterial activity against *Escherichia coli* ***(MTCC 40)*** *(Gram-negative)* and *Staphylococcus aureus* ***(MTCC 96)****(Gram-positive) bacteria. Among them, derivative* **8c** showed highest antibacterial activity against gram +ve and gram –ve bacteria.

ACKNOWLEDGEMENT

Authors thank DST, Government of India for the financial support under the GPHDMS-NRDMS.

REFERENCES

[1]. P. Chaudhary, P. K. Sharma, A. Sharma, J. Varshney, Recent advances in pharmacological activity of benzothiazole derivatives, *Int J Curr Pharm Res.*, **2010**, 2, 5-11.
[2]. M. Bryson, B. Fulton, Benfield P. Riluzole, A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in amyotrophic lateral sclerosis, *Drugs*, **1996**, 52, 549-563.
[3]. S. P. Singh, S. Seghal, Synthesis and phototoxicity of some 2-(phenyl-or2-or3-thie-nyl)-4 substituted Thiazoles, Indian J Chem, **1988**, 27B, 941-943.
[4]. J. H. Musser, R. E. Brown, B. Love, K. Baily, H. Jones, R. Kahen, Synthesis of 2-(2,3-Dihydro-2-oxo-l,3,4-oxadiazol-5-yl) benzo heterocycles. A novel series of orally active antiallergic agents, *J Med Chem.*, **1984**, 27, 121-125.
[5]. S. R. Pattan, C. Suresh, V. D. Pujar, V. V. K. Reddy, V. P. Rasal, B. C. Kotti, Synthesis and antidiabetic activity of 2-amino[5"(4-sulphonylbenzylidine)-2, 4-thiazolidinenone]-7-chloro-6- flurobenzothiazole, *Indian J Chem*., **2005**, 4B, 2404-2408.
[6]. M. Yoshida, I. Hayakawa, N. Hyashi, T. Agatsuma, Y. Oda, F. Tanzawa. Synthesis and biological evaluation of benzothiazole derivatives as potent antitumor agents, *Bioorg Med Chem Lett*., **2005**, 15, 3328-3332.
[7]. P. Venkatesh, S. N. Pandeya. Synthesis, characterization and anti-inflammatory activity of some 2-amino benzothiazole derivatives, *Int J Chem Tech Res.*, **2009**, 1, 1354-1358.
[8]. D. Munirajasekhar, M. Himaja, V. S. Mali, A. Karigar, M. Sikarwar, Synthesis and Anthelmintic activity of 6-Substituted 2-Hydrazino-1, 3-Benzothiazoles, *J Pharm Res*., **2011**, 4, 2186-2187.
[9]. D. Bhavsar, J. Trivedi, S. Parekh, M. Savant, S. Thakrar, A. Bavishi, A. Radadiya, H. Vala, J. Lunagariya, M. Pamar, L. Paresh, R. Loddo, A. Shah, Synthesis and in vitro anti-HIV activity of N-1,3-benzo[d]thiazol-2-yl-2-(2-oxo-2H-chromen-4-yl)acetamide derivatives using MTT method, *Bioorg Med Chem Lett.*, **2011**, 21, 3443-3446.
[10]. T. D. Bradshaw, M. C. Bibby, J. A. Double, I. Fichtner, P. A. Cooper, M. C. Alley, S. Donohue, S. F. Stinson, J. E. Tomaszewjski, E. A. Sausville, Stevens MFG. Preclinical evaluation of amino acid prodrugs of novel antitumor 2-(4-amino-3-methylphenyl)benzothiazoles, *Mol Cancer Therapeutics*, **2002**, 1, 239-246.
[11]. I. Hutchinson, S. A. Jennings, B. R. Vishnuvajjala, A. D. Westwell, M. F. G. Stevens. Antitumor benzothiazoles. 16. Synthesis and pharmaceutical properties of antitumor 2-(4-amino phenyl)benzothiazole amino acid prodrugs, *J Med Chem.*, **2002**, 45, 744-747.