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Synthesis, Characterization and Biological Evaluation of Some Benzothiazole Derivatives as Potential Antimicrobial Agent.

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Abstract: *A new series of benzylidine-2-imino-6-nitro-1,3- benzothiazole , benzylidine-2-imino-6-methoxy-1,3-benzothiazole and benzylidine-2-imino-6-methyl-1,3- benzothiazole was synthesised by condensation with different aromatic aldehydes. The target molecules were synthesised by using different reaction conditions and greener approach. The products were readily obtained with 70-85 % yield. The structures of synthesized compounds were confirmed by physical, chemical and FT- IR, ^{1}H-NMR, LCMS, etc. spectroscopic techniques. The synthesized compounds were tested against representatives of gram-positive and gram- negative bacteria (staphylococcus aureus and Basillus subtilis.) by agar diffusion method using Amicacin and Gentamycin as control. The results indicate that the compounds possessed a broad spectrum of activity against the tested microorganisms.*

Keywords: *Benzothiazole moiety, aromatic aldehydes, antifungal agents, antimicrobial activity.*

I. Introduction

The benzothiazole ring is present in various marine or terrestrial natural compounds which have useful biological activities[1-5]. Benzothiazole derivatives have attracted a great deal of interest due to their anticancer[6], antitumor[7], anticonvulsant[8], antiviral[9], antibacteria[l0], antimicrobial[11] and fungicidal activities[12]. They are also useful as anti-allergic[13], anti-inflammatory[14]and anthelmintic[15] agents and as appetite depressants[16], intermediates for dyes[17], plant protectants[18], histamine H2antagonists[19] and photographic sensitizers[20]. On the other hand, careful literature survey revealed that thiazole, thiophene and pyrazole ring systems have occupied a unique position in the design and synthesis of novel biological active agents with remarkable analgesic and anti-inflammatory activities[21-23], in addition to their well documented potential antimicrobial activities [24-27]. Morever, thiazoles have found application in drug development for the treatment of hypertension [28], schizophrenia[29], HIV infections[30], and as new inhibitors of bacterial DNA gyrase B[31]. In addition, a large number of thiophene derivatives have found to exhibit pharmacological activity[32-34]. Furthermore, diverse chemotherapeutic activities have ascribed to pyrazoles as antimicrobial [35-36], antiparasitic[37], antivirial[38], and antineoplastic agents[39-42]. A detail literature survey indicates that benzothiazole ring system have a unique position in the designing and synthesis of novel biological active agents with remarkable analgesic and anti-inflammatory activities.The preliminary study of the structure- activity relationship reveals that electronic factors in benzothiazole ring has a great effect on a antimicrobial activity of these compounds.

In view of the above mentioned facts and in continuation of our interest in the synthesis of heterocycles containing benzothiazole moiety, we thought to design a new series using 2-amino derivative of benzothiazole. We report herein the synthesis and structural properties evaluation of some novel structure hybrids incorporating benzothiazole moiety and different aromatic aldehydes through imine linkages at 2-position of substituted benzothiazole. This was thought and suggested in an attempt to investigate the influence of structure variation on the anticipated biological activities, hoping to add some synthetic strategies and biological significance to the target molecules. The substitution pattern of benzothiazole ring was carefully selected so as to confer different electronic environment to the molecules.

II. Experimental

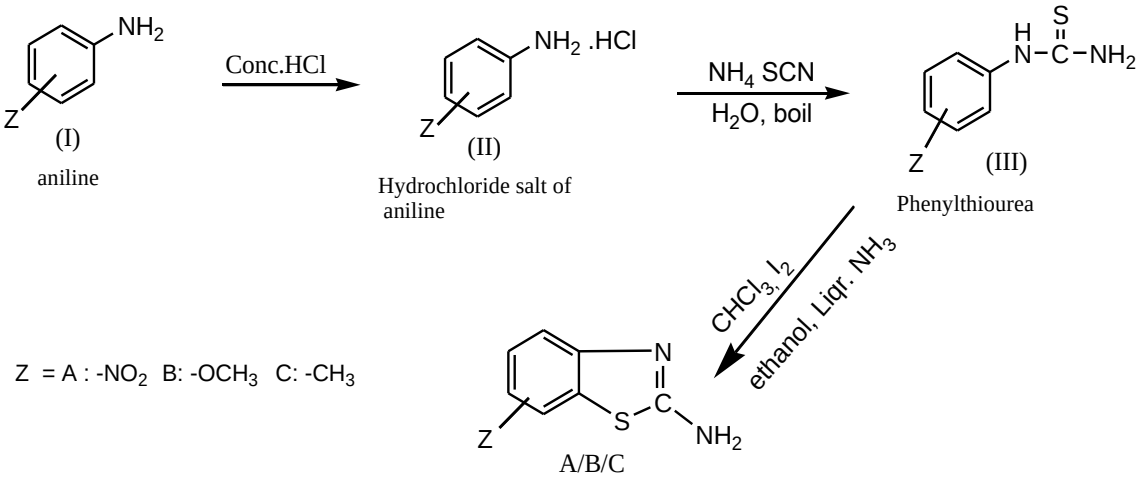
Reagents, Instrumentation, and Measurements:

Melting points were measured on a Veego VMP-PM melting point apparatus and IR spectra were recorded on Perkin Elmer Spectrum 100 FT-IR spectrometer. ^{1}H, and ^{13}C NMR spectra were recorded at 500.1 and 125.8 MHz respectively on a BRUKER Avance II 500 instrument with $CDCl_3$ / DMSO-d6 as solvent and TMS as internal standard. Mass spectra were recorded on a Waters Q-TOF spectrometer operating at an ionization potential of 30 eV. The course of the reactions was monitored and, the purity checked by TLC using silica gel 60 F_{254} Al-plates (Merck, Germany) in DCM: MeOH (9:1) solvent system. . Solvents unless otherwise specified, were of analytical reagent grade or of the highest quality commercially available. The structures of newly synthesized compounds were confirmed from the physico- chemical properties and different spectral data. The micro-organism *Staphylococcus aureus NCIM 2079 , Basillus subtilis NCIM 2010 Escherchia coli NCIM 2572*

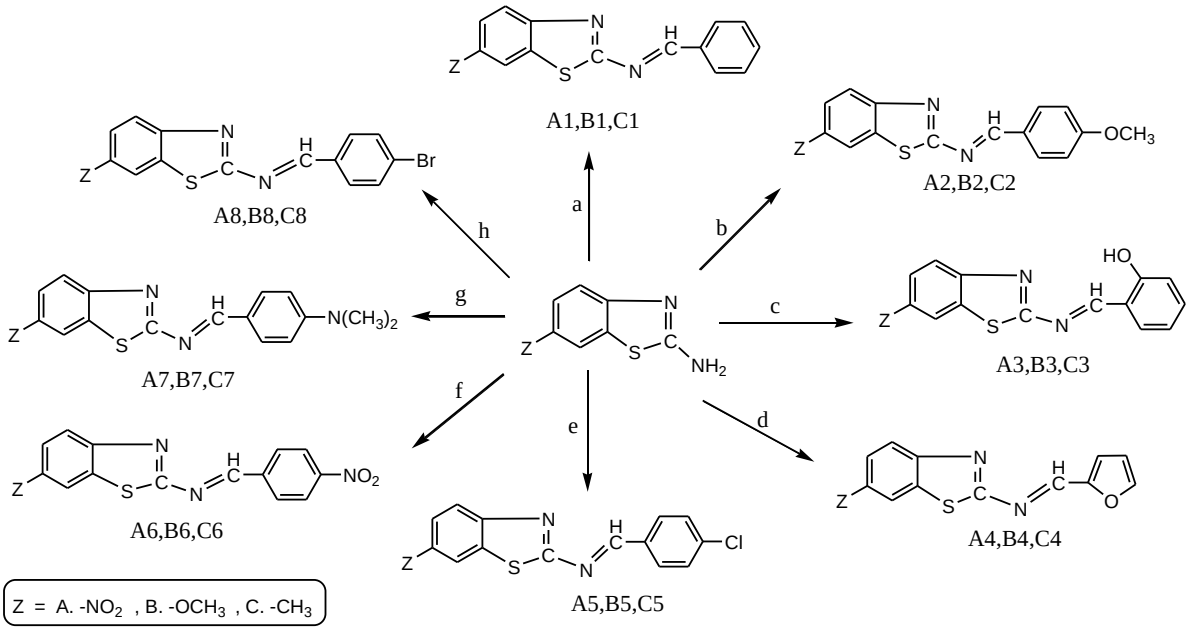
Pseudomonas aeruginosa NCIM 2053 Salmonella typhi NCIM 2501.Candida albicans NCIM 3471, Aspergillus fumigates NCIM 883,Penicillium chrysogenum NCIM 726 were purchased from the National Chemical Laboratory (NCL), Pune, India. 10 mm borer was used to prepare the cup in agar plate seeded with an appropriate microorganism. Four cups per plate at four corners and at equidistance were made. A 10 µL test sample was transferred with help of micropipette per well. Plates were immediately kept at 4^0C in refrigerator for 1 hr. and then shifted to BOD incubator. The plates were incubated at 35^0C± 0.5^0C for 24 hrs. Zone of inhibition was measured after 24 hrs of incubation and further evaluated for their (MIC) by using twofold serial dilution method. DMF alone was used as control at the same concentration and showed no zone of inhibition.

A loopful of culture was inoculated from the stock slant culture in 5 mL of Hi-sensitivity test broth (Muller-Hinton broth) and broth was incubated at 35^0C± 0.5^0C in BOD incubator for 18-20 hrs. After incubation, a loopful of actively growing culture was inoculated into 10 mL of Hi-sensitivity broth. The broth was incubated at 35^0C± 0.5^0C for 6-8 hrs. This culture was used for the inoculation of Hi-sensitivity test agar plates. Control experiments were also done.

2.1: Scheme 1: Synthesis of substituted 2- Amino-1, 3- Benzothiazole



Scheme 2: Synthesis of benzylidine-2-imino-6-nitro-1,3- benzothiazole , benzylidine-2-imino-6-methoxy-1,3-benzothiazole and benzylidine-2-imino-6-methyl-1,3-benzothiazole.



Reagents: (a) ethanol, $ZnCl_2$. phCHO, 5hrs (b) glacial acetic acid in ethanol, p-OCH_3 phCHO, 5hrs. (c) ethanol, $ZnCl_2$ acetic acid, p-OHphCHO, 3 hrs (d) ethanol, $ZnCl_2$, furfural, 5 hrs. (e) ethanol, $ZnCl_2$, p- ClphCHO, 6hrs. (f) acetic acid in ethanol, p-NO_2 phCHO, 6 hrs. (g) ethanol, p-N,N-$(CH_3)_2$phCHO, 4 hrs. (h) $ZnCl_2$ in ethanol, p- BrphCHO, 7.5hrs.

2.1.2: General procedure for the synthesis of 2- Amino-1, 3- Benzothiazole (A - C)

1.0 g (0.007 moles) of p-nitroaniline , 1.0 g (0.0081 moles) of anisidine, and 1.0 g (0.0093 moles) of p-toluidine respectively was treated with 8.0 ml conc. hydrochloric acid. The hydrochloride salt was dissolved in 25.0 ml of water and then added 0.9 g (0.011 moles) ammonium thiocyanate. The reaction mixture was refluxed for 1.5 hr and then cooled to room temperature and poured in 25.0 ml ice-cold water. Crystalline solid of p-nitro, p-methoxy and p-methylphenylthiourea obtained was filtered, washed with 25.0 ml cold water and vacuum dried. 1.0 g (0.0057 moles) phenylthiourea was treated with 2.2 g(0.0086 moles) iodine in 15.0 ml chloroform, the resulting reaction mixture was stirred for four hours at 20^0C. After the completion of reaction, 15.0 ml ethanol was added to reaction mixture and then basified with liquor ammonia, products obtained were filtered, washed with cold water, recrystallised from ethanol and vacuum dried to get A, B and C. **Scheme.1**

2.1.3:General procedure for the synthesis of Benzylidine-2-imino-6-nitro-1,3-benzothiazole (A1,B1,C1)

Compound **A/B/C** (0.5g, 26.5mmol was dissolved in 25 mL ethanol by heating and then added a pinch of anhydrous $ZnCl_2$. The reaction mixture was heated to reflux condition. A benzaldehyde solution (0.3mL, 28.1mmol in ethanol 5mL) was added drop wise at reflux temperature over a period of 20 min. The reaction mixture refluxed for 5hrs, after completion of reaction, ethanol was distilled out. The yellow colour precipitate obtained after cooling; the precipitate was filtered, washed, recrystallised from absolute alcohol and dried to give compound (**A1, B1, and C1**) **Scheme 2a.**

p-methoxybenzylidine-2-imino-6-nitro-1,3-benzothiazole(A2,B2,C2)

To a solution of compound **A/B/C** (0.5 g, 25.6mmol, 2-3 drops of glacial acetic acid in ethanol 20 mL) added drop wise p-anisaldehyde(0.4mL, 28.1mmol) in ethanol(5mL) at boiling temperature over a period of 25 min. The reaction mixture was refluxed for 5hrs. and then cooled to room temperature, yellow orange precipitate formed. The product obtained was filtered, washed, recrystallised from ethanol to give compound **(A2, B2, C2) Scheme 2b.**

o-hydroxybenzylidine-2- imino-6-nitro-1,3-benzothiazole (A3,B3,C3)

Compound **A/B/C** (0.5 g, 25.6mmol)was condensed with salicyldehyde(0.4mL, 28.1mmol) in ethanol(25mL) in presence of catalytic amount of $ZnCl_2$ and acetic acid at reflux temperature. The orange colour precipitate formed after cooling the reaction mixture to room temperature. The product was filtered, washed, recrystallised from ethanol to give compound **(A3, B3, C3) Scheme 2c.**

Furfurylidine-2- imino-6-nitro-1,3-benzothiazole (A4,B4,C4)

Compound A/B/C (0.5 g, 25.6mmol) was reacted with furfuraldehyde (0.3mL, 28.1mmol) in ethanol(25mL) in presence of catalytic amount of $ZnCl_2$. The reaction mixture was refluxed for 5 hrs and the cooled to room temperature. The gray colour precipitate was formed after cooling. The product was filtered, washed, recrystallised from absolute alcohol to give compound **(A4, B4, C4) Scheme 2d.**

p-chlorobenzylidine-2- imino-1,3-benzothiazole ***(A5,B5,C5)***

Compound was prepared by condensation of A/B/C (0.5 g, 25.6mmol) with p-chlorobenzaldehyde(0.395 g, 28.1mmol) in ethanol (25mL) in presence of catalytic amount of anhydrous $ZnCl_2$ .The pale yellow colour precipitate was formed after cooling the reaction mixture to room temperature. The product obtained was filtered, washed, recrystallised from alcohol to give compound **(A5, B5, C5) Scheme 2e.**

p-nitrobenzylidine-2-imino-6-nitro-1,3-benzothiazole (A6, B6, C6)

To a solution of compound A/B/C (0.5 g, 25.6mmol, 2-3 drops of glacial acetic acid in ethanol 20 mL) was added drop wise a solution of p-nitrobenzaldehyde (0.424g, 28.1mmol) in ethanol (5mL) at boiling temperature over a period of 20 min. The reaction mixture refluxed for 6 hrs and then cooled to room temperature. The product formed was filtered, washed, recrystallised from ethanol to give compound **(A6, B6, C6) Scheme 2f.**

p-N,N-dimethylaminobenzylidine-2-imino-6-nitro-1,3-benzothiazole (A7, B7, C7)

A compound **(A7, B7, C7)** was synthesised by condensation of p-N,N-dimethylaminobenzaldehyde (0.419 g, 28.1mmol) with compound A/B/C (0.5 g, 25.6 mmol) in ethanol(25mL). at reflux temperature. The reaction mixture refluxed for 4 hrs and then cooled to room temperature. The magenta colour product obtained was filtered, washed, recrystallised from absolute alcohol and dried to give compound **(A7, B7, C7) Scheme 2g.**

Synthesis of p-bromobenzylidine-2- imino-6-nitro-1,3-benzothiazole (A8, B8, C8)

To a solution of p-bromobenzaldehyde(0.519 g, 28.1mmol, pinch of anhydrous $ZnCl_2$ in ethanol 20 mL) was added drop wise a solution of compound A/B/C (0.5 g, 25.6 mmol in ethanol 5mL) at reflux temperature. The reaction mixture refluxed for 7.5hrs and then cooled to room temperature, the product obtained was filtered, washed, recrystallised from absolute alcohol and to give compound **(A8, B8, C8) Scheme 2h.**

Table 1. Physical data of the synthesised compounds.

Compd. No.	M.P. ^{0}C	Mol. Formula	Mol. Wt.	Elemental analysis % found			% yield
				C	H	N	
A1	224-226	$C_{14}H_9N_3SO_2$	283	60.02	03.11	15.12	70.99
A2	162-164	$C_{15}H_{11}N_3SO_3$	313	58.10	03.61	13.54	73.03
A3	240-242	$C_{14}H_9N_3SO_3$,	299	56.23	03.13	14.11	76.99
A4	280-282	$C_{12}H_7N_3SO_3$	273	52.58	02.71	15.51	67.95
A5	205-207	$C_{14}H_8N_3SO_2Cl$	317	53.07	02.63	13.33	65.80
A6	230-232	$C_{14}H_8N_4SO_4$	328	51.32	02.49	16.78	59.04
A7	245-247	$C_{16}H_{14}N_4SO_2$	326	59.21	04.11	17.23	76.40
A8	239-241	$C_{14}H_8N_3SO_2Br$	362	46.53	02.32	11.82	64.18
B1	110-112	$C_{15}H_{12}N_2SO$	268	67.35	04.66	10.32	81.15
B2	120-122	$C_{16}H_{14}N_2SO_2$	295	64.55	04.73	09.44	84.96
B3	140-142	$C_{15}H_{11}N_2SO_2$	283	63.86	04.02	10.10	87.38
B4	170-172	$C_{13}H_{10}N_2SO_2$	258	60.56	03.75	11.07	69.37
B5	125-127	$C_{15}H_{11}N_2SOCl$	305	59.21	03.55	09.32	69.65
B6	254-256	$C_{15}H_{11}N_3SO_3$	313	57.72	03.44	13.39	63.70
B7	190-192	$C_{17}H_{17}N_3SO$	311	65.73	05.62	13.61	73.78
B8	140-142	$C_{15}H_{11}N_2SOBr$	347	52.11	03.25	08.26	68.19
C1	112-114	$C_{15}H_{12}N_2S$	252	71.10	04.68	11.23	86.04
C2	165-167	$C_{16}H_{14}N_2SO$	282	68.23	04.63	10.21	82.75
C3	280-282	$C_{15}H_{12}N_2SO$	268	67.34	04.55	10.28	87.11
C4	225-227	$C_{13}H_{10}N_2SO$	242	64.88	04.34	11.72	78.80
C5	165-167	$C_{15}H_{11}N_2SCl$	286	62.65	03.87	10.11	68.80
C6	170-172	$C_{15}H_{11}N_3SO_2$	297	60.83	03.62	14.25	65.26
C7	140-142	$C_{17}H_{17}N_3S$	295	70.09	05.63	14.31	77.95
C8	210-212	$C_{15}H_{11}N_2SBr$	331	54.53	03.42	08.55	64.54

Benzylidine-2- imino-6-nitro-1,3-benzothiazole(A1)
Yellow colour crystals; **M^+283,** FTIR- 3091.34. ArC-H str. 2915azomethine C-H str. 1602-C=N thiazole str. 1676 -C=N str. 1297.23 -NO_2 str. ^{1}H NMR, 8.5 (s ,1H, azomethineCH=N-) 7.2-8.2 (m, 7H,Ar-H)

p-methoxybenzylidine-2-imino-6-nitro-1,3-benzothiazole(A2)
Yellow orange crystals; **M^+313,** FTIR- 3070 ArC-H Str , 2946 Azomethine ;C-H str, 1602 -C=N thiazole str. 1679 -C=N str. 1260 Ar-O-CH_3 str 1326 -NO_2 str. **,** ^{1}H NMR, 9.8 (s ,1H,azomethine –CH=N-), 3.8(s ,3H, OCH_3), 6.9-7.2 (m,3H, Ar-H), 7.8-7.9 (m, 4H, Ar'-H).

o-hydroxybenzylidine-2- imino-6-nitro-1,3-benzothiazole (A3)
Orange colour crystals; M^+299**,** FTIR- 3063.48 Ar -C-H str. 2929.50 azomethine C-H str, 1517.98 -C=N thiazole str. 1636.24 -C=N str. 3399.38 -OH str. 1328.64-NO_2 str. ^{1}H NMR, 8.5 (s ,1H,azomethine –CH=N-), 11.8 (s, 1H, OH), 7.2-7.5 (m, 3H, Ar-H),8.2-8.3(m,4H,Ar'-H).

Furfurylidine-2- imino-6-nitro-1,3-benzothiazole (A4)
Gray colour crystals; M^+273**. ,** FTIR- 3092 Ar-H str 2923 Azomethine C-H str 1518-C=N thiazole str 1571 -C=N str 1288 C-O-C str 1330 -NO_2 str. ^{1}H NMR- 8.5 (s ,1H,azomethine –CH=N-), 7.2-7.5 (m, 7H Ar-H

p-chlorobenzylidine-2- imino-1,3-benzothiazole (A5)
Pale yellow crystals; M^+317.5 FTIR- 3150 Ar-H str. 2960.00Azomethine C-Hstr 1592-C=N thiazole str. 1623 -C=N str. 758 Ar-Cl str. 1330 -NO_2 str. ^{1}H NMR, 9.1(s ,1H,azomethine– CH=N-) 7.2-8.5 (m,7H, Ar-H)

p-nitrobenzylidine-2-imino-6-nitro-1,3-benzothiazole (A6)
Yellow crystals; **M^+328,** FTIR- 3184 Ar-H str. 2985 Azomethine C-H str 1519 -C=N thiazole str. 1698 -C=N str. 1336 -NO_2 str. ^{1}H NMR, 9.2(s ,1H, CH=N), 7.2-7.5(m,3H,Ar-H),8.0-8.5 (m, 4H Ar'-H).

p-N,N-dimethylaminobenzylidine-2-imino-6-nitro-1,3-benzothiaz*ole *(A7)
Magenta colour crystals; M^+326; FTIR- 3092 Ar-H Str 2904 azomethine C-H str. 1571 -C=N thiazole str 1609 -C=N str, 2914 -N-C, 3^0 amine str. 1324 -NO_2 str. ^{1}H NMR- 8.9 (s ,1H,azomethine – CH=N-), 3.1 (s, 6H,-N(CH_3)$_2$), 6.7-7.2(m, 3H,Ar-H),7.9-8.1(m,4H,Ar'-H).

p-bromobenzylidine-2- imino-6-nitro-1,3-benzothiazole(A8)
Off white crystals; **M^+317,** FTIR- 3090 Ar -H str. 2950 azomethine C-H str. 1579 -C=N thiazole str. 1654 -C=N str. 875 Ar-Br, str. ^{1}H NMR- 9.1(s ,1H, -CH=N-), 7.5-7.7 (m, 3H, Ar-H), 7.9-8.3 (m,4H, Ar'-H).

Benzylidine-2- imino-6-methoxy-1,3-benzothiazole (B1)
Gray white color crystals; **M^+268;** FTIR- 3133 Ar-H Str, 2964 C-H str, 1548 -C=N thiazole str,1606 -C=N str, 1261Ar-O-CH_3 str. ^{1}H NMR- 9.0 (s ,1H, azomethine CH=N-), 6.6-7.1 (m,3H, Ar-H). 7.3-8.0(m, 5H, Ar'-H), 3.8(s, 3H,-OCH_3).

p- methoxybenzylidine-2- imino-6-methoxy-1,3-benzothiazole (B2)
Yellowish green crystals; **M^+295 .** FTIR- 2968, Ar-H Str. 2934 Azomethine C-H str, 1511-C=N thiazole str, 1598 -C=N str,1258 Ar-O-CH3 str. ^{1}H NMR, 8.9 (s ,1H,azomethine –CH=N-), 3.8-3.9 (s ,6H, -OCH_3), 6.9-7.0 (m, 3H, Ar-H), 7.2-7.9 (m,4H, Ar'-H).

o-hydroxybenzylidine-2-imino-6-methoxy-1,3-benzothiazole (B3)
Yellow crystals; **M^+283,** FTIR- 3066 Ar-H Str, 2901 azomethine C-H str, 1556 -C=N thiazole str 1598 -C=N str, 3443 -OH str 1227 O-CH_3 str. ^{1}H NMR-9.41(s ,1H,azomethine –CH=N-), 12.2 (s, 1H, O-H), 6.9-7.0 (m, 3H Ar-H), 3.8(s, 3H,-OCH_3), 7.3-7.8(m,4H,Ar'-H)

Furfurylidine-2- imino-6-methoxy-1,3-benzothiazole (B4)
Brown colour crystals; M^+258, FTIR-3111Ar-H Str, 2946azomethine str, 1604C=N thiazole str, 1641-C=N str, 1272C-O-C str, 1202 Ar-O-CH_3 str. ^{1}H NMR, 9.3(s ,1H,–CH=N-), 6.8-7.1 (m, 3H Ar-H), 3.8(s, 3H,-OCH_3), 7.1-7.4(m,3H,Ar'-H)

p-chlorobenzylidine-2- imino-6-methoxy-1,3-benzothiazole(B5)
Gray color crystals**; M^+305.5,** FTIR- 3113 Ar-H Str, 2971azomethine C-H str, 1550 -C=N thiazole str 1606 -C=N str, 810 Ar-Cl str, 1259 OCH_3 str. ^{1}H NMR, 9.4(s, 1H, azomethine –CH=N-), 6.8-6.9 (m, 3H Ar-H), 3.8(s, 3H,-OCH_3), 7.1-7.4(m,4H,Ar'-H)

p-nitrobenzylidine-2- imino-6-methoxy-1,3-benzothiazole (B6)
Dark orange crystals; **M^+313;** FTIR-3098 Ar-H str, 3033 azomethine C-H str, 1511-C=N thiazole str, 1597 -C=N str, 1387 -NO_2 sym str, 1213 O-CH_3 str.^{1}H NMR, 9.1(s, 1H, azomethine –CH=N-), 7.1-7.3 (m, 3H Ar-H), 3.8(s, 3H,-OCH_3), 7.9-8.3(m,4H,Ar'-H)

p-N,N-dimethylaminobenzylidine-2-imino-6-methoxy-1,3-benzothiazole (B7)
Orange colour crystals; **M^+ 311.** FTIR- 3000 Ar-H str, 2890 azomethine C-H str, 1529-C=N thiazole str, 1581 -C=N str, 2781 -N-C 3^0 amine str, 1222 OCH_3 str.). ^{1}H NMR- 8.7 (s ,1H, CH=N-),3.8(s, 3H,-OCH_3), 3.0(s, 6H,-$N(CH_3)_2$), 6.7-7.0 (m, 3H,Ar-H),7.2-7.8(m,4H,Ar'-H).

p-bromobenzylidine-2- imino-6-methoxy-1,3-benzothiazole(B8)
Green colour crystals**; M^+347.** FTIR- 3050 Ar-H Str, 2969 azomethine C-H str, 1490 -C=N thiazole str, 1606 -C=N str, 824 Ar-Br str, 1268 OCH_3 str. ^{1}H NMR-8.9(s, 1H, CH=N-), 7.0-7.2 (m, 3H Ar-H), 3.8(s, 3H,-OCH_3), 7.6-7.8(m, 4H, Ar'-H

Benzylidine-2-imino-6-methyl-1,3-benzothiazole (C1)
Off white colour crystals; **M^+252,** FTIR-3129 Ar -H str, 2965 azomethine C-H str, 1604 -C=N thiazole str, 1639 -C=N str, 2935 -CH_3 str. ^{1}H NMR, 8.1 (s ,1H, CH=N-), 7.2-7.2(m,3H,Ar-H), 2.5(s, 3H,Ar-CH_3), 7.4-7.6(m, 5H,Ar'-H)

p- methoxybenzylidine-2- imino-6-methyl-1,3-benzothiazole (C2)
Gray colour crystals; **M^+282,** FTIR- 3015 Ar-H str, 2900 azomethine C-H str, 1500 -C=N thiazole str, 1605-C=N str, 2829 -CH_3 str, 1255 OCH_3 str. ^{1}H NMR, 9.8 (s ,1H, CH=N-), 3.8 (s ,3H, OCH_3), 6.9-7.2 (m, 3H,Ar-H), 7.4-7.8 (m, 4H, Ar'-H), 2.5 (s, 3H, ArCH_3).

o-hydroxybenzylidine-2- imino-6-methyl-1,3-benzothiazole (C3)
Orange colour crystals; **M^+269.2,** FTIR- 3030 Ar-H str, 2940 azomethine C-H str, 1525 -C=N thiazole str 1591-C=N str, 3429 OH str, 2830 -CH_3 str. ^{1}H NMR, 8.8 (s ,1H,azomethine –CH=N-), 11.09 (s, 1H,OH), 6.6-7.1 (m, 3H Ar-H), 7.2-7.5(m,4H,Ar'-H), 2.1(s, 3H, Ar-CH_3)

Furfurylidine-2- imino-1,3-benzothiazole (C4)
Dark gray crystals; **M^+243.3** FTIR- 3021Ar-H str, 2902 azomethine C-H str, 1550 C=N thiazole str, 1604C=N str, 1387 C-O-C str, 2828 CH_3 str. ^{1}H NMR-8.7 (s, 1H, CH=N-), 6.8.-7.1 (m, 3H Ar-H); 7.6-8.2 (m, 3H, Ar'-H), 2.2(s, 3H, Ar-CH_3).

p-chlorobenzylidine-2- imino-6-methyl-1,3-benzothiazole (C5)
Buff colour crystals; **M^+286.5,** FTIR- 3039 Ar-H str, 2929 azomethine C-H str, 1521-C=N thiazole str, 1602 -C=N str. ^{1}H NMR, 8.0 (s ,1H, CH=N-), 7.0-7.5 (m, 3H Ar-H); 6.2-6.5 (m, 4H,Ar'-H), 2.5(s, 3H, Ar-CH_3).

p-nitrobenzylidine-2- imino-6-methyl-1,3-benzothiazole (C6)
Yellow crystals; **M^+297,** FTIR-2925 azomethine C-H str,1523 -C=N thiazole str,1592-C=N str, 1343-NO_2 str, 2853-CH_3 str. ^{1}H NMR, 9.1(s ,1H, =N-), 2.7(s,3H, Ar-CH_3), 7.2-7.7(m,3H,ArC-H), 8.2-8.3 (m, 4H Ar'-H)

Synthesis of p-N,N-dimethylaminobenzylidine-2-imino-6-methyl-1,3-benzothiazole (C7)
Red colour crystals; **M^+296.3,** FTIR- 3137Ar-H str, 2951 azomethine C-H str, 1583 -C=N thiazole str, 1610 -C=N str, 2828 N-C, 3^0 amine str, 2914 -CH_3 str. ^{1}H NMR, 8.7(s ,1H, CH=N-), 3.0 (s,6H,-N(CH_3)$_2$), 6.7-7.0 (m, 3H, Ar-H), 7.2-7.9(m, 4H, Ar'-H), 2.5(s,3H, Ar-CH_3).

p-bromobenzylidine-2- imino-6-methyl-1,3-benzothiazole(C8)
Light brown crystals; **M^+331;** FTIR- 3035 Ar -H str, 2927 azomethine C-H str, 1530 -C=N thiazole str, 1603 -C=N str, 0765 Ar-Br str, 2829 -CH_3 str. ^{1}H NMR,8.4(s ,1H, CH=N-), 7.0-7.6 (m, 3H, Ar-H), 8.0-8.4 (m, 4H, Ar'-H), 2.1 (s, 3H, ArCH_3).

III. Results And Discussion

Schiffs bases were prepared by condensing substituted 2-amino-1,3-benzothiazole with selected aromatic aldehydes. The nucleophilic addition of -NH_2 group of benzothiazole moiety to aromatic aldehydes is not so straight forward and easier due to the presence of azomethine nitrogen in heterocyclic ring. So different conditions were used to synthesis the target compounds, eg. azeotropic distillation method, use of dehydrating agents, catalysts, etc. All compounds were purified by recrystallization using absolute ethanol in order to avoid hydrolysis at varying rates of the compounds. The chemical structures were supported on the basis of LC-MS, elemental analysis, physic-chemical properties and spectrophotometric data. The experimental data obtained for each target molecule matches significantly with the reported data in literature and calculated. The method employed in preparation of benzothiazole derivative gives excellent practical yield and high purity with simple method and shorter reaction time without using harsh condition and solvents like benzene. The synthesis did not make use of a dehydrating agents like p-TSA, sulphuric acid, $CaCl_2$, etc to carry out the reaction. pH of reaction mixture was maintained mild acidic which gave maximum yield of the product. Compounds (B1, B5, B8, C1, C5, C8) were prepared by using a simple procedure with catalytic amount of $ZnCl_2$ which gave the yield between 65-80% and high purity as compared to the vigorous conditions reported in the literature. Compounds (A2, A3, A6, A7, B2, B3, B5, B8, C2, C3, C6, C8) were synthesized using catalytic amount of glacial acetic acid which avoided the use of sulphuric acid, phosphoric acid, etc and gave yield 70-83%. Therefore, it was a green approach used for the synthesis. Compounds (A4, B4, and C4) were prepared by using an azeotropic distillation method. All the compounds synthesised by the reported method were of high purity, excellent yield and experimental spectroscopic data resembles with the literature values.

Antimicrobial assays
Compounds: Test compounds were dissolved in DMSO at an initial concentration of 1 mg/ml and then were serially diluted in culture medium.
Bacterial strains: Gram-positive bacteria: *Staphylococcus aureus* NCIM 2079 , *Basillus subtilis* NCIM 2010, Gram-negative bacteria: *Escherchia coli* NCIM 2572 , *Pseudomonas aeruginosa* NCIM 2053, *Salmonella typhi* NCIM 2501 **Antibiotics:** Amicacin , Gentamycin
Fungal stains: *Candida albicans NCIM 3471, Aspergillus fumigates NCIM 883.* ***Antibiotics:*** *cycloheximide.*

All the synthesized compounds were evaluated *in vitro* for their antibacterial activities against the above microorganisms and results were compared with the standard antibacterial agent. While *in vitro* antifungal activities were evaluated against the fungal strains. The results were compared with antifungal agent *cycloheximide* and summarized in Table 2.

Table 2. In vitro antimicrobial activities of compounds.

Compounds	Zone of inhibition in mm		
	Bacteria		Fungi
	Gram	Gram –	

	B .subtilis	***S. aureus***	***S. typhi.***	***E. coli***	***P.aeruginosa***	***C.albicans***	***As. fumigates***
A1	08	14	08	14	10	13	18
A2	13	12	07	11	08	19	18
A3	10	11	06	11	08	16	10
A4	10	11	10	15	11	13	13
A5	10	15	07	11	11	12	11
A6	12	13	06	12	10	11	11
A7	11	12	06	11	14	10	21
A8	10	10	06	11	13	10	16
B1	10	11	12	06	09	11	13
B2	08	15	13	10	08	16	17
B3	08	14	07	08	08	13	15
B4	10	14	06	07	06	15	18
B5	10	14	06	05	10	10	10
B6	11	15	09	06	10	10	11
B7	10	15	07	06	11	18	12
B8	10	14	08	12	14	13	12
C1	13	10	13	11	08	14	12
C2	18	12	10	08	13	17	10
C3	19	11	10	08	06	12	10
C4	18	11	11	08	06	11	12
C5	16	11	14	10	08	10	11
C6	18	14	11	10	12	11	12
C7	18	12	12	10	10	15	12
C8	21	12	10	10	10	13	13
Amicacin	19	19	19	20	19	NT	NT
Gentamycin	28	25	29	27	25	NT	NT
cycloheximide.	NT	NT	NT	NT	NT	31	23

*Less active: 6–12 mm; moderately active: 13–19 mm; highly active: 20–30 mm; No inhibition or inhibition less than 5 mm; NT: not tested.

The results depicted in Table 2 revealed that all derivatives of 2-amino-1,3-benzothiazole demonstrated significant activity against the tested organisms.

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