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Green synthesis, characterization of substituted benzothiazole Schiff's Bases and their biological activities

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Abstract

Aromatic heterocyclic molecules are playing very vital role in chemical industries covers a large range application. Most of heterocyclic compounds are used as medicinal drug in different therapeutic targets. Substituted-benzothiazoles are one of the most important classes with bicyclic heterocyclic moiety. These moieties are playing key role for experimental drug design. Substituted Benzothiazole derivatives have power full pharmacological activities, few derivatives of substituted amino benzothiazoles Schiff's Bases have been synthesized from substituted aniline with ring closing from industrial generated waste salt. Structure elucidation and their biological activities of synthesized moieties performed.

Keywords: Green chemistry, Benzothiazole, Schiff's Bases, NMR, Mass and FTIR.

INTRODUCTION

The most important heterocyclic compounds such as thiazole is an important pharmacophore in drug discovery and development process in industries. Most of heterocyclic compound such as thiazole and their different derivatives covers vital range of therapeutics targets like anti-inflammatory, [1-5] antifungal, [6] antiviral, [7-8] analgesic, [9, 10] antioxidant, [11, 12] antipsychotic, [13] anticonvulsant, [14] and antidiabetic [15, 16] anti-tubercular, [17] anti-cancer, [18] etc. Thiazole is naturally abandoned in vitamin B (Thiamin). Vitamin B is water soluble, which helps the body to release energy from carbohydrates at the time of metabolism and its enzyme shows important role in decarboxylation of α-keto acid and as an electron sink. It is helpful for normal functioning of the nervous system due to its role in the synthesis of the acetylcholine a neurotransmitter. The most common dreadful disease like Cancer is affecting abnormal growth of cells. Genetic activity of cell is changes due to cancer. [19, 20] Globally, cancer is major leading causes of death. The WHO report (2018) shows more than 10 million people died by cancer disease, every year. About 0.3 million new patients for cancer are diagnosed in children aged between 1 and 19 years. [21, 22] It means there is no age factor for cancer disease. Cancer chemotherapy causes several adverse effects, which include multiple drug resistance, adverse events, unwanted side effects, and selectivity. Benzothiazole have Schiff's base [23-27] will increase the biological activities [28, 29] we also considered the acetophenone based moieties with functional group like NO_2, Br, OCH_3, [30, 31, 32] and Cl which enhanced the biological activities of synthesized drugs.

Reactions are performed with conventional approaches; effective and eco-friendly alternative routes are being developed with commercially available reagents and the principles of green chemistry. [33] Hazardous and toxic solvents avoid during synthesis of moieties. Industrial generated waste salts are used as regent in reactions and water is used as polar solvent, making the process relatively low-cost with generation of recyclable salt. Multistep reactions of the C-2-substituted benzothiazole played a special role in the designing of biologically active compounds. [34] The advantages of these reactions are effectiveness, simple experimental implementation and high yields.

EXPERIMENTAL

Materials and reagents:

All the chemicals, which have been used for synthesis of Schiff's base were supplied by Sigma Aldrich, Loba chemie and Merck. All the reactions were monitored and purity of the products was checked by thin-layer chromatography (TLC) and mixed melting point. TLC was performed on Merck 60 F-254 silica gel plates with visualization by short UV light and further with iodine chamber, as well as by gas chromatography (GC). The GC was performed on Shimadzu 2014 with capillary column (RTX5, 30 meter). Melting points were determined on Veego melting point apparatus in capillary tubes in silicon oil bath. 1H NMR and 13C NMR spectra were recorded on BRUKER AVANCE Neo 500 MHz NMR spectrometer. The sample was dissolved in $CHCl_3$. Chemical shifts are reported from internal tetramethylsilane standard and chemical shifts are given in δ units. Infrared spectra were taken on BRUKER AVANCE IVDR FTIR. The GC-MS spectra were recorded on a Shimadzu GC-MS.

Antimicrobial activity:

The antimicrobial activities of all the synthesized compounds were evaluated by the Kirby-Bauer disk diffusion method [35, 36]. The strains were procured from Institute of Microbial Technology, Chandigarh. All cultures were maintained at 4ºC. Cover nutrient agar slants throughout the experiment. The cultures were incubated overnight at 37ºC in nutrient broth before using for antimicrobial activity. Five hundred microliters of overnight old bacterial/fungal suspension were spread over the nutrient agar plates using a sterile cotton swab in order to get a uniform microbial growth. DMSO was used to dissolve synthesized compounds. Under aseptic conditions, empty sterilized discs (Whatman No. 5, 6 mm diameter) were impregnated with different concentrations (25, 50, 75, and 100 µg/disc) of respective synthesized compounds and placed on the agar surface. Paper disc moistened with aqueous DMSO was placed on seeded petri-plates as a vehicle control. The plates were left for 30 min. at room temperature to allow the diffusion of synthesized compounds and then incubated at 37 ºC for 24 h. The antimicrobial activity was evaluated by measuring the zone of inhibition against the test of microorganism. All experiments were carried out in triplicates.

General Procedure (4 a-c)

A mixture of substituted aniline **(1)** (1.0 mmol) and ammonium thiocyanate (1.1 mmol) in 30% hydrochloric acid (1.1 mmol) was stirred at 80°C for 6-8 hours, monitored by GC. The solid filtered gave **(2)**. Mixture of **(2)** (1.0 mmol) was mixed industrial waste salt (Sodium chloride/bromide) (2.0 mmol) followed by addition of sulphuric acid. It was stirred at 80°C for 1-2 hour, monitored by GC. The solid filtered gave **(3)**. Mixture of **(3)** (1.0 mmol) in water followed by addition of hydrazine hydrate (1.5 mmol) was stirred at 100-110°C for 1-2 hours. The progress was monitored by GC. The solid filtered gave **(4 a-c)**.

General method for the synthesis substituted-2-[(2*E*)-2-(1-phenylethylidene) hydrazinyl]-1, 3-benzothiazole derivatives (6 a-o):

A mixture of substituted 2-hydrazinyl-1, 3-benzothiazole **(4 a-c)** (1.0 mol.), and substituted aromatic ketones moiety (**5a-i)** (1.05 mol) was mixed in a 50 mL round bottom flask in aqueous media and refluxed for 4 h. The progress of the reaction was monitored by TLC and GC. The rate of reaction was controlled by applying occasional stirring. A crystalline solid was obtained. The product was filtered, washed with water and recrystallized from ethanol: water, which gave corresponding benzothiazole derivatives (6 a-o) as products. ^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm), ^{13}C NMR (500 MHz, $CDCl_3$) analysis and M+ ion peak in mass analysis of synthesised compounds (6 a-o) as follows:

4, 6-dimethyl-2-{(2*Z*)-2-[1-(3-nitrophenyl) ethylidene] hydrazinyl}-1, 3-benzothiazole (**6a**):

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.29 (s, 3H, CH$_3$), 2.34 (s, 3H, CH$_3$), 2.42 (s, 3H, CH$_3$), 6.9-9.4 (m, 6H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 13.3, 17.7, 21.0, 71.7, 124.2-147, 168.1, MS, m/z: 339 (M+H) +.

2-{(2*Z*)-2-[1-(2, 4-dichlorophenyl) ethylidene] hydrazinyl}-4, 6-dimethyl-1, 3-benzothiazole (6b):

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.28 (s, 3H, CH$_3$), 2.30 (s, 3H, CH$_3$), 2.45 (s, 3H, CH$_3$), 6.89-7.36 (m, 5H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 17.31, 18.0, 21.93, 118-146, 167.1; MS, m/z: 363.0 (M+H) +, m/z: 365.0 (M+H+2) +.

2-{(2*Z*)-2-[1-(4-bromophenyl) ethylidene] hydrazinyl}-4, 6-dimethyl-1, 3-benzothiazole (6c)

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.19 (s, 3H, CH$_3$), 2.41 (s, 3H, CH$_3$), 2.49 (s, 3H, CH$_3$), 6.97-7.68 (m, 6H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 13.24, 18.08, 21.28, 118.97 – 146.76, 168.0; MS, m/z: 373.0 (M+H) +, m/z: 375.0 (M+H+2) +.

2-{(2*Z*)-2-[1-(2-methoxyphenyl) ethylidene] hydrazinyl}-4, 6-dimethyl-1, 3-benzothiazole (6d)

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.20 (s, 3H, CH$_3$), 2.48 (s, 3H, CH$_3$), 2.52 (s, 3H, CH$_3$), 6.94-7.80 (m, 6H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 13.39, 18.71, 21.25, 113.82 – 160.91, 167.77; MS, m/z: 324.0 (M+H) +, m/z: 325.0 (M+H+2) +.

4, 6-dimethyl-2-[(2*Z*)-2-(1-phenylethylidene) hydrazinyl]-1, 3-benzothiazole (6e)

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.24 (s, 3H, CH$_3$), 2.44 (s, 3H, CH$_3$), 2.54 (s, 3H, CH$_3$), 7.01-7.88 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 13.53, 18.14, 21.29, 118.0 – 146.0, 167.98; MS, m/z: 293.0 (M+H) +, m/z: 294.0 (M+H+2) +.

4-methyl-2-{(2*Z*)-2-[1-(3 nitrophenyl) ethylidene] hydrazinyl}-1, 3-benzothiazole (6f)

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.37 (s, 3H, CH$_3$), 2.55 (s, 3H, CH$_3$), 7.09-8.26 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 13.28, 18.06, 76.76-77.27, 119.0 – 129.49, 1143.56, 147.89, 167.50; MS, m/z: 326.0 (M+H) +.

2-{(2*Z*)-2-[1-(2, 4-dichlorophenyl) ethylidene] hydrazinyl}-4-methyl-1, 3-benzothiazole (6g)

^{1}H NMR (500 MHz, CDCl$_3$-d6, ppm): δ 2.31 (s, 3H, CH$_3$), 2.51 (s, 3H, CH$_3$), 7.01-10.30 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, CDCl$_3$): δ 18.08, 18.26, 21.37, 23.88, 118.71 – 149.24, 176.51; MS, m/z: 349.0 (M+H) +, m/z: 351.0 (M+H+2) +.

2-{(2*Z*)-2-[1-(4-bromophenyl) ethylidene] hydrazinyl}-4-methyl-1, 3-benzothiazole (6h)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.07-2.177 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 6.97-7.59 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 13.23, 18.16, 118.87 – 136.57, 146.84-148.65, 167.93, 176.79; MS, m/z: 359.0 (M+H) +, m/z: 361.0 (M+H+2) +.

2-{(2*Z*)-2-[1-(2-methoxyphenyl) ethylidene] hydrazinyl}-4-methyl-1, 3-benzothiazole (6i)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.03 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 6.79-7.66 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 13.18, 18.44, 21.56, 55.34, 113.79 – 148.56, 160.98 – 176.72; MS, m/z: 311.0 (M+H) +.

4-methyl-2-[(2*Z*)-2-(1-phenylethylidene) hydrazinyl]-1, 3-benzothiazole (6j)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.31 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 7.03-8.88 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 13.63, 18.30, 21.57, 118.80-148.89, 176.77; MS, m/z: 281.0 (M+H) +.

2-{(2*Z*)-2-[1-(3-nitrophenyl) ethylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (6k)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.16 (s, 3H, CH_3), 7.10-8.80 (m, 7H, Ar-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 24.2, 115.20, 119.29, 121.50, 141.9 – 149.5, 169.80; MS, m/z: 327.0 (M+H) +.

2-{(2*Z*)-2-[1-(2, 4 dichlorophenyl)ethylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (6l)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.16 (s, 3H, CH_3), 7.08-8.70 (m, 6H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 24.2, 115.1, 121.5, 127.29, 128.9 – 149.5, 169.80; MS, m/z: 351.0 (M+H) +, m/z: 352.0 (M+H+2) +.

2-{(2*Z*)-2-[1-(4-bromophenyl) ethylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (6m)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.17 (s, 3H, CH_3), 7.10-8.69 (m, 7H, Ar-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 24.2, 115.1, 121.5, 127.29, 128.9 – 149.5, 169.80; MS, m/z: 361.0 (M+H) +, m/z: 362.0 (M+H+2) +.

2-{(2*Z*)-2-[1-(2-methoxyphenyl) ethylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (6n)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.14 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 6.94-7.48(m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 24.2, 56.0, 115.8, 121.3, 128.2 – 149.5, 166.8; MS, m/z: 312.0 (M+H) +, m/z: 313.0 (M+H+2) +.

2-[(2*Z*)-2-(1-phenylethylidene) hydrazinyl]-1, 3-benzothiazol-4-ol (6o)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.16 (s, 3H, CH_3), 7.10-8.80 (m, 7H, Ar-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 24.2, 115.20, 119.29, 121.50, 141.9 – 149.5, 169.80; MS, m/z: 282.0 (M+H) +, m/z: 284.0 (M+H+2) +.

2-{(2*Z*)-2-[2-methoxy-1-(morpholin-4-yl) ethylidene] hydrazinyl}-4, 6-dimethyl-1, 3-benzothiazole (7a)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 2.36 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 3.30 (s, 3H, CH_3), 3.70 (s, 2H, CH_2), 4.52 (t, 8H, CH_2), 6.94-7.28 (m, 3H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 18.27, 21.18, 118.63 – 148.6 3, 172.32; MS, m/z: 334.0 (M+H) +, m/z: 338.0 (M+H+3) +.

2-{(2*Z*)-2-[2-methoxy-1-(morpholin-4-yl) ethylidene]hydrazinyl}-4-methyl-1, 3-benzothiazole (7b)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 1.21 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 3.69 (s, 2H, CH_2), 4.26 (t, 8H, CH_2), 7.04-7.51 (m, 3H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 18.33, 21.10, 23.22, 118.63 – 150.863 172.94; MS, m/z: 320.0 (M+H) +.

2-{(2*Z*)-2-[2-methoxy-1-(morpholin-4-yl) ethylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (7c)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 3.27 (s, 3H, CH_3), 3.48 – 3.81 (t, 10H, CH_2), 7.10-7.43 (m, 3H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 48.61, 58.80, 66.5, 115.1 – 150.89, 169.8; MS, m/z: 321.0 (M+H) +, m/z: 322.0 (M+H+3) +.

2-{2-[1-(4-chlorophenyl)-4, 4-dimethylpentan-3-ylidene] hydrazinyl}-4, 6-dimethyl-1, 3-benzothiazole (8a)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 1.29 (s, 9H, CH_3), 2.20 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 1.33 (t, 2H, CH_2), 1.70 (t, 2H, CH_2), 6.89-7.45 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 17.70, 21.30, 27.0, 29.2, 30.2, 37.2, 71.7, 124.0 – 139.50, 158.9; MS, m/z: 397.0 (M+H) +.

2-{2-[1-(4-chlorophenyl)-4, 4-dimethyl pentan-3-ylidene] hydrazinyl}-4-methyl-1, 3-benzothiazole (8b)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 1.23 (s, 9H, CH_3), 2.53 (s, 3H, CH_3), 2.59 (t, 2H, CH_2), 2.84 (t, 2H, CH_2), 7.05-7.52 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 18.15, 27.89, 28.61, 30.71, 39.16, 118.59 – 151.07, 161.3, 172.66; MS, m/z: 397.0 (M+H) +.

2-{2-[1-(4-chlorophenyl)-4, 4-dimethyl pentan-3-ylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (8c)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 1.25 (s, 9H, CH_3), 2.55 (t, 2H, CH_2), 2.88 (t, 2H, CH_3), 7.09-7.43 (m, 7H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 27.0, 29.30, 30.20, 37.2, 115.1 – 151.70, 169.8; MS, m/z: 386.0 (M+H) +.

2-{2-[1-(2, 4-dichlorophenyl) pentylidene] hydrazinyl}-4, 6-dimethyl-1, 3-benzothiazol (9a)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 0.89 (s, 9H, CH_3), 2.30 (s, 3H, CH_3), 2.65 (t, 3H, CH_3), 1.38 (t, 2H, CH_2), 1.73 (t, 2H, CH_2), 2.90 (t, 2H, CH_2), 6.98-8.65 (m, 5H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 13.86, 18.13, 21.46, 22.68, 26.52, 30.89, 114.52 – 151.49, 158.98; MS, m/z: 406.0 (M+H) +, m/z: 408.0 (M+H+3) +.

2-{2-[1-(2, 4-dichlorophenyl) pentylidene] hydrazinyl}-1, 3-benzothiazol-4-ol (9b)

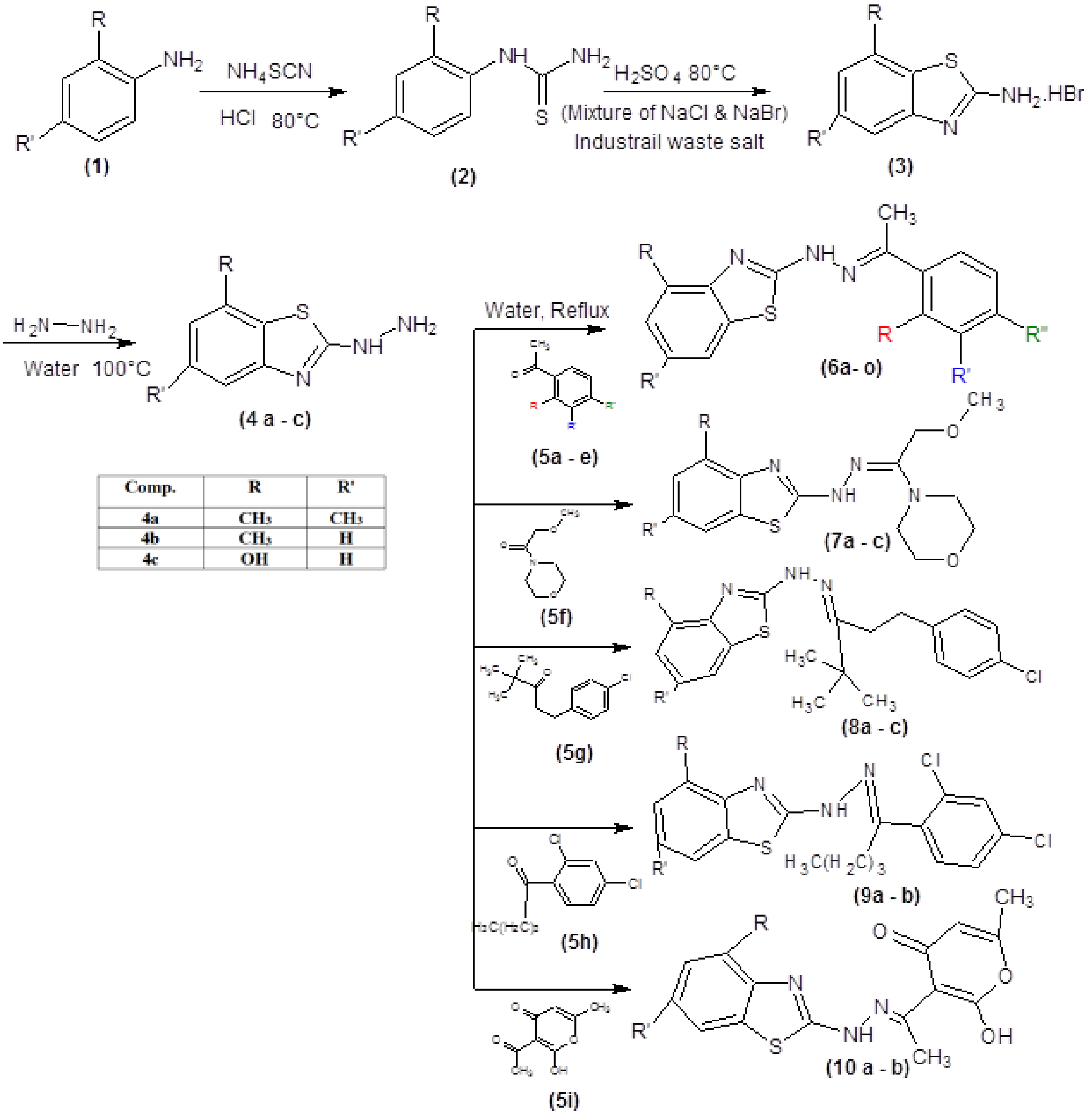
^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 0.88 1.32 (t, 2H, CH_2), 1.49 (t, 2H, CH_2), 2.39 (t, 2H, CH_2), 7.04,-7.43 (m, 6H, Ar-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 14.0, 22.6, 26.2, 27.0, 115.1 – 159.40, 169.8; MS, m/z: 393.0 (M+H) +.

3-{(1*E*)-1-[2-(4, 6-dimethyl-1, 3-benzothiazol-2-yl) hydrazinylidene] ethyl}-2-hydroxy-6-methyltetrahydro-4*H*-pyran-4-one (10a)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 1.35 (s, 3H, CH_3), 1.94 (s, 3H, CH_3), 2.14 (t, 3H, CH_3), 2.21 (t, 3H, CH_3), 3.25 (t, 1H, CH), 3.52 (t, 2H, CH_2), 4.32 (t, 1H, CH), 4.80 (t, 1H, CH), 7.14-7.87 (m, 2H, Ar-H; ^{13}C NMR (500 MHz, $CDCl_3$): δ 11.73, 16.83, 20.81, 28.61, 39.78, 98.35 – 170.05, 180.37, 204.58; MS, m/z: 347.4.0 (M+H) +.

3-{(1*E*)-1-[2-(4, 6-dimethyl-1, 3-benzothiazol-2-yl) hydrazinylidene] ethyl}-2-hydroxy-6-methy ltetrahydro-4*H*-pyran-4-one (10b)

^{1}H NMR (500 MHz, $CDCl_3$-d6, ppm): δ 1.35 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.98 (t, 3H, CH_3), 2.62 (d, 2H, CH_2), 3.83 (d, 1H, CH), 3.59 (d, 2H, CH_2), 4.32 (d, 1H, CH), 7.21-7.75 (m, 3H, Ar-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 14.9, 17.70, 20.80, 28.61, 40.70, 44.71, 121.5 – 151.7, 169.8, 211.6; MS, m/z: 333.4.0 (M+H) +.



Comp.	R	R'
4a	CH_3	CH_3
4b	CH_3	H
4c	OH	H

Scheme 1: Synthetic route of compounds

RESULTS AND DISCUSSION

A series of Substituted-2-[(2*E*)-2-(1-phenylethylidene) hydrazinyl]-1, 3-benzothiazole derivatives, (**6a-o)** was synthesized according to Scheme I. The physical data and yield of synthesized compounds (**6a-o)**, **(7a-c), (8a-c), (9a-b) and (10a-b)** are reported in Table 1**.**

The structure of the title compounds **(6a-o), (7a-c), (8a-c), (9a-b) and (10a-b)** was confirmed by FT-IR, NMR and MS. As a representative analysis of compound (**6a)** Figure-1, the direct IR spectrum showed C=C/C=N absorption bands at 1629-1475 cm^{-1}. The ^1H NMR spectrum of compound (**6a)** Figure-2 displayed three singlets at aliphatic region δ 2.29 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), and a multiplet at aromatic region at 6.9-9.4 (m, 6H, Ar-H; ^{13}C NMR spectrum of compound (**6a)** Figure-3 revealed the three signal of methyl carbon δ 13.3, 17.7, 21.0, and a signal at 71.7, connecting to Schiff's Bases. Aromatic carbons showed at 124.2-147, carbon between two hetro atoms (S and N) 168.1. Structure of compound (**6a)** Figure-4 was further confirmed by molecular ion peak at *m*/*z* 339 $(M+H)^+$. Structures of all the derivatives were ascertained similarly.

Table 1: Physical data and yield of synthesized compounds (6a-i)

Comp.	**R**	**R'**	**R"**	**Yield %**	**MP**
4a	-	-	-	95.40	178--180°C
4b	-	-	-	96.25	170--172°C
4c	-	-	-	90.82	119--123°C
6a	H	NO_2	H	89.7	246-249°C
6b	Cl	H	Cl	91.55	144-146°C
6c	H	H	Br	85.66	185-188°C
6d	OCH_3	H	H	86.8	153-155°C
6e	H	H	H	92.11	152-155°C
6f	H	NO_2	H	88.98	203-208°C
6g	Cl	H	Cl	81.85	138-145°C
6h	H	H	Br	94.22	112-117°C
6i	OCH_3	H	H	86.92	142-147°C
6j	H	H	H	87.82	101-105°C
6k	H	NO_2	H	78.55	119-123°C
6l	Cl	H	Cl	77.41	171-175°C
6m	H	H	Br	79.81	174-176°C
6n	OCH_3	H	H	90.11	154-158°C
6o	H	H	H	92.22	154-158°C
7a	-	-	-	79.62	179-183°C
7b	-	-	-	94.66	101-106°C
7c	-	-	-	88.55	154-158°C
8a	-	-	-	82.32	176-179°C
8b	-	-	-	84.26	133-138°C
8c	-	-	-	86.33	154-158°C
9a	-	-	-	87.23	168-171° C
9b	-	-	-	72.88	154-158°C
10a	-	-	-	75.68	205-208°C
10b	-	-	-	84.71	205-208°C

Antimicrobial Activity

The synthesized compounds **(6a-o), (7a-c), (8a-c), (9a-b) and (10a-b)** were screened for their antibacterial activity against the standard Gram-negative bacteria, *E. coli* (MTCC 443), *P. aeruginosa* (MTCC 1688) and Gram-positive *S. aureus* (MTCC 96), S. *pyogenus* (MTCC 442), Gentamycin, Ampicillin, and Chloramphenicol, Ciprofloxacin were used as reference. Antifungal activity against *C. albicans* (MTCC 227), *A. niger* (MTCC 282), *A. clavatus* (MTCC 1323). Nystatin and Greseofulvin were used as reference, which is a fast-growing non-pathogenic strain to assess the activity of the compounds in primary screening. The results of antimicrobial activity are reported in Tables 2 and 3.

Table 2: Antibacterial screening of compounds (6a-i) (zone of inhibition in mm)

ANTIBACTERIAL ACTIVITY TABLE				
Sample	***E. coli***	***P. aeruginosa***	***S. aureus***	***S. pyogenus***
6a	250	250	100	62.5
6b	250	50	200	125
6c	500	100	250	500
6d	500	250	500	100
6e	500	250	62.5	500
6f	250	62.5	100	250
6g	125	100	100	25
6h	500	250	500	250
6i	500	500	500	200
6j	125	250	50	100
6k	500	250	100	62.5
6l	100	62.5	250	500
6m	62.5	250	250	250
6n	100	250	125	125
6o	62.5	100	62.5	100
7a	250	500	250	250
7b	250	100	125	100
7c	100	250	125	250
8a	250	250	250	125
8b	125	100	125	100
8c	62.5	250	250	125
9a	125	125	100	125
9b	50	125	100	50

10a	500	250	500	500
10b	100	100	500	125
Gentamycin	0.05	1	0.25	0.5
Ampicillin	100	-	250	100
Chloramphenicol	50	50	50	50
Ciprofloxacin	25	25	50	50

Table 3: Antifungal screening of compounds (6a-i) (zone of inhibition in mm)

ANTIFUNGAL ACTIVITY TABLE			
Sample Code	***C. albicans***	***A. niger***	***A. clavatus***
6a	250	250	250
6b	250	500	500
6c	500	500	1000
6d	500	>1000	>1000
6e	500	>1000	>1000
6f	500	1000	1000
6g	250	500	1000
6h	>1000	500	>1000
6i	500	>1000	>1000
6j	500	500	250
6k	500	500	>1000
6l	500	500	>1000
6m	500	500	500
6n	200	250	250
6o	250	500	500
7a	500	500	>1000
7b	500	>1000	500
7c	250	100	100
8a	250	200	200
8b	1000	1000	500
8c	500	500	500
9a	500	250	>1000
9b	200	500	>1000
10a	>1000	>1000	>1000
10b	500	250	250

Nystatin	100	100	100
Greseofulvin	500	100	100

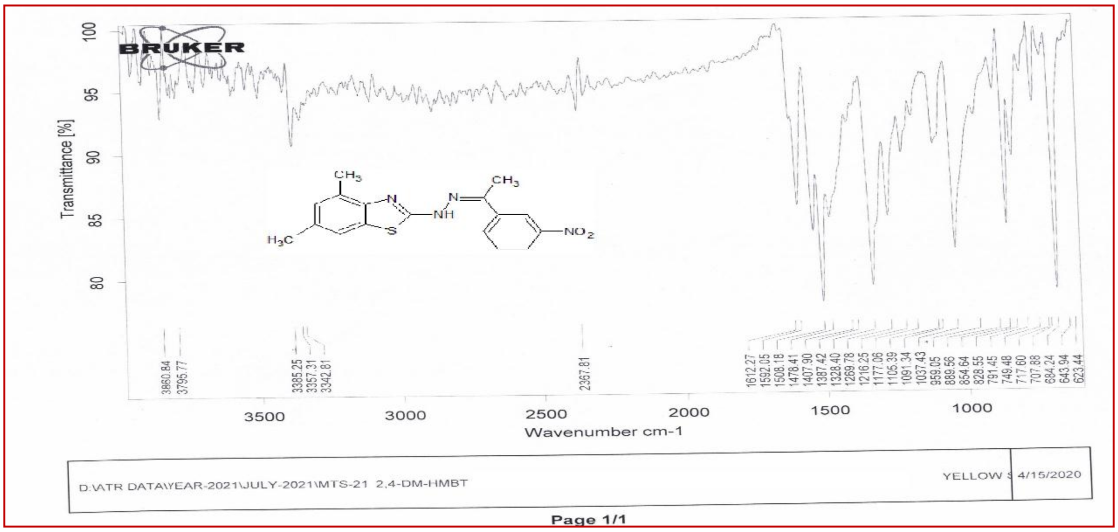


Figure 1: FT-IR Spectrum of compound (6a)

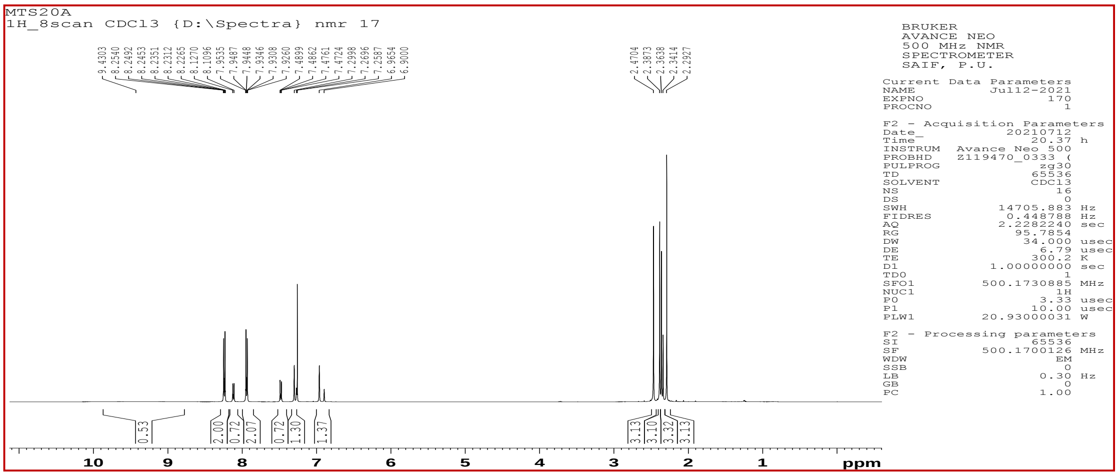
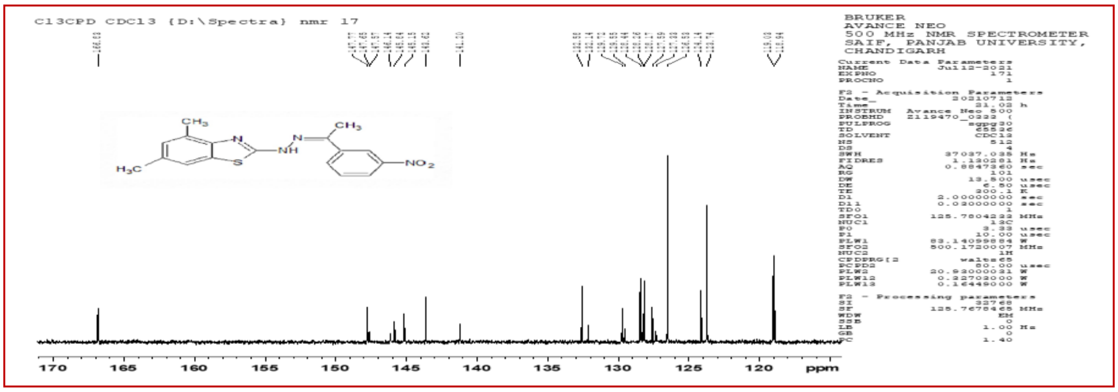


Figure 2: ^{1}H NMR Spectrum of compound (6a)



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BRUKER
AVANCE NEO
500 MHz NMR SPECTROMETER
SAIF, PANJAB UNIVERSITY,
CHANDIGARH

Current Data Parameters
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EXPNO                  171
PROCNO                   1

F2 - Acquisition Parameters
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TD                  65536
SOLVENT             CDCl3
NS                    512
DS                      4
SWH             37037.035 Hz
FIDRES           1.130281 Hz
AQ              0.8847360 sec
RG                    101
DW                 13.500 usec
DE                   6.50 usec
TE                  200.1 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          125.7804222 MHz
NUC1                  13C
P0                   3.33 usec
P1                  10.00 usec
PLW1          83.14099884 W
SFO2          500.1720007 MHz
NUC2                   1H
CPDPRG[2           waltz65
PCPD2               80.00 usec
PLW2          20.92000031 W
PLW12          0.22702000 W
PLW13          0.16449000 W

F2 - Processing parameters
SI                  32768
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SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
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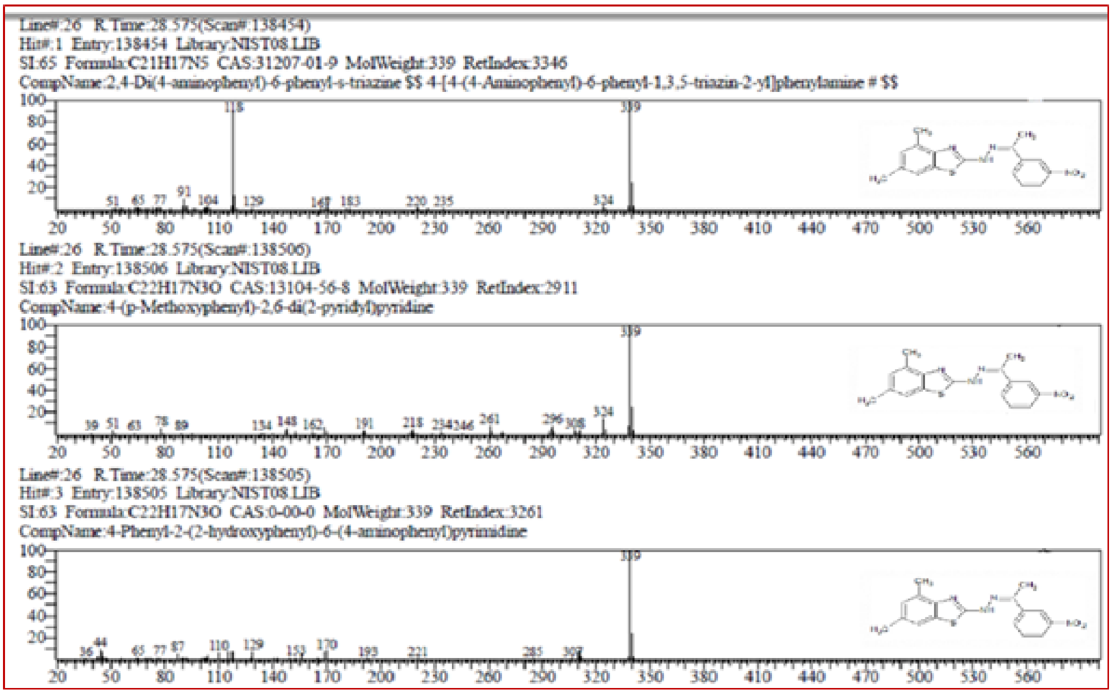
Figure 3: ^{13}C NMR Spectrum of compound (6a)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CompName:2,4-Di(4-aminophenyl)-6-phenyl-s-triazine $$ 4-[4-(4-Aminophenyl)-6-phenyl-1,3,5-triazin-2-yl]phenylamine # $$

Line#:26 R.Time:28.575(Scan#:138506)
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CompName:4-(p-Methoxyphenyl)-2,6-di(2-pyridyl)pyridine

Line#:26 R.Time:28.575(Scan#:138505)
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CompName:4-Phenyl-2-(2-hydroxyphenyl)-6-(4-aminophenyl)pyrimidine

Figure 4: Mass Spectrum of compound (6a)

CONCLUSION

In the present work, the synthesis and biological screening of benzothiazole derivatives has been reported. Out of all the synthesised (6a-o) compounds, 3-{(1*E*)-1-[2-(4, 6-dimethyl-1, 3-benzothiazol-2-yl) hydrazinylidene] ethyl}-2-hydroxy-6-methyltetrahydro-4*H*-pyran-4-one (10a) was found highly active against all the tested bacteria and fungus as compared to reference drugs. So, this process is commercially highly effective as it saves man power, time, utility, health and safety of man. It is environment friendly, because industrial waste has been used, which is critical to dispose.

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