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SYNTHESIS OF NOVEL 1,3,4-OXADIAZOLE DERIVATIVES AS POTENTIAL ANTIMICROBIAL AGENTS

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Abstract: Some new 3-acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles and 2-(3-chloro-1-benzo[*b*]thiophen-2-yl)-5-substituted phenyl-1,3,4-oxadiazoles have been synthesized and evaluated for antimicrobial activity. Initially, 3-chloro-1-benzo[*b*]thiophene-2-carbonyl chloride **(1)** was prepared from cinnamic acid in the presence of chlorobenzene and thionyl chloride. This compound **(1)** was treated with hydrazine hydrate to afford 3-chloro-1-benzo[*b*]thiophene-2-carbohydrazine **(2)** which was further reacted with various aromatic aldehydes to yield hydrazones **(3a-h)**. Further reaction of these hydrazones **(3a-h)** with acetic anhydride gave 3-acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles **(4a-h)**. Reaction of the same compounds **(3a-h)** in the presence of chloramine-T afforded 2-(3-chloro-1-benzo[*b*]thiophen-2-yl)-5-substituted phenyl-1,3,4-oxadiazoles **(5a-h)**. The structures of newly synthesized compounds **(4a-h)** and **(5a-h)** have been confirmed by spectroscopic techniques such as IR, ^{1}H NMR and elemental analysis. All the compounds were screened for their antibacterial activities against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* and for antifungal activity against *Candida albicans* and *Asperigillus niger.* The compounds exhibited significant antibacterial and moderate antifungal activities. Compounds **4c** and **4e** were found to be most potent with activities, even better than standard drug ciprofloxacin against *S. aureus* and *B. subtilis*.

Keywords: benzo[*b*]thiophene, 2,3-dihydro-1,3,4-oxadiazole, antifungal, antibacterial

Since their introduction, antimicrobials are one of most significant weapons in fighting bacterial infections. They have extremely benefited the health-related quality of human life. Over the past few decades, these health benefits are under threat as many commonly used antibiotics have become less effective against certain illnesses because of their toxic reactions and due to emergence of microbial resistance. Therefore, it is essential to investigate newer drugs with lower resistance (1, 2).

Beside this, the lack of new antifungal drugs ascends proportionally to the increasing occurrence of serious infections caused by yeast and fungi mainly in immunocompromised or in other way sensitive patients. Primary and opportunistic fungal infections continue to increase rapidly, and as a consequence of this situation, invasive fungal infections constitute a major cause of mortality for such patients. *Candida albicans* is one of the most common opportunistic fungi responsible for these kinds of infections. The current state of pharmacotherapy is briefly drawn out and most of attention is given to newly developed active entities. Established agents do not satisfy the medical needs completely as azoles are fungistatic and vulnerable to resistance, whereas polyenes cause serious host toxicity. Drugs in clinical development include modified azoles and a new class of echinocandins and pneumocandins. (3, 4)

Benzo[*b*]thiophenes are found to possess various biological activities such as antimicrobial (5, 6), antioxidant (7), anti-HIV (8), anticancer (9) and

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antiviral (10) activities. In addition, 1,3,4-oxadiazole is a versatile lead molecule for designing potent bioactive agents (11). This interesting group of compounds possesses diverse biological activity such as antimicrobial (12, 13), anti-inflammatory (14), antitubercular (15), anticonvulsant (16), anticancer (17), anti-HIV (18), hypoglycemic (19) and genotoxic (20) activities. In light of these interesting biological activities, it was our interest to synthesize some new 1,3,4-oxadiazole derivatives bearing benzo[*b*]thiophene and evaluate their antimicrobial potential.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents (ethanol, dioxane) used were of laboratory grade and solvents were purified by suitable methods (21). IR spectra (KBr, cm^{-1}) were recorded on JASCO FT/IR-410 spectrometer. ^1H NMR spectra were recorded on Brucker 300 MHz NMR spectrometer (chemical shifts in δ ppm) using tetramethylsilane (TMS) as an internal standard. The purity of the compounds was ascertained by thin layer chromatography on silica gel G in various solvent systems using iodine vapors as detecting agent. Reactions were carried out in a Daewoo KOG-370A domestic microwave oven at 2450 MHz. Elemental analysis was carried out using Carlo Erba 1106 CHN analyzer.

General method

The title compounds were prepared in the following steps:

Synthesis of 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride **(1)**

3-Chloro-benzo[*b*]thiophene-2-carbonyl chloride was prepared from cinnamic acid in the presence of chlorobenzene and thionyl chloride according to reported procedure (22).

Synthesis of 3-chloro-2-hydrazinocarbonylbenzo[*b*] thiophene **(2)**

The carbonyl chloride (2.31 g, 0.01 mol) **(1)** was dissolved in ethanol (50 mL) and to this hydrazine hydrate (85%, 3 mL) was added, and the mixture was heated under reflux for 4 h. The reaction mixture was evaporated under reduced pressure and the crude product was purified by crystallization from ethanol. The purity of the hydrazide was established by single spot on thin layer chromatography (TLC) plates using methanol : carbon tetrachloride (8 : 2, v/v) as solvent system. Yield 63%, m.p. 179-181°C (23).

Synthesis of 3-chloro-*N*'-(substituted phenylmethylidene)-1-benzo[*b*]thiophene-2-carbohydrazide (**3a-h)**

A mixture of compound **2** (2.13 g, 0.01 mol) and the appropriate aromatic aldehyde (0.01 mol) in dioxane (50 mL) was refluxed for 4-8 h. The reaction mixture was concentrated under reduced pressure, cooled and the obtained solid **(3a-h)** was filtered, washed with water and cold ethanol. The crude product was purified by crystallization from dioxane.

Synthesis of 3-acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles **(4a-h)**

A mixture of carbohydrazide (0.01 mol) **(3a-h)** and an excess of acetic anhydride (10 mL) was refluxed for 3-4 h. The acetic anhydride was distilled off and the residue was poured onto crushed ice. The solid thus obtained was collected by filtration, washed with water and recrystallized from ethanol. The purity of the product **(4a-h)** was confirmed by a single spot on TLC plate using methanol : carbon tetrachloride (8 : 2, v/v) as solvent system.

Synthesis of 2-(3-chloro-1-benzo[*b*]thiophen-2-yl)-5-substitutedphenyl-1,3,4-oxadiazoles **(5a-h)**

To a solution of hydrazones (0.01 mol) **(3a-h)** in ethanol (15 mL) chloramine-T (2.48 g, 0.01 mol) was added. The reaction mixture was irradiated with microwave at 300 W intermittently at 30 s intervals for specified time. After completion of reaction, as indicated by TLC, the reaction mixture was cooled and digested with cold water. The solid produced was filtered, washed with water and crystallized from methanol to give the title compounds **(5a-h)**.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-phenyl-2,3-dihydro-1,3,4-oxadiazole **(4a)**

IR (KBr, cm^{-1}): 3208 (CH, arom.), 1648 (C=O), 1590 (C=N), 1274, 1049 (C-O-C), 749 (C-Cl), 724 (C-S-C). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 6.78 (1H, s, O-CH-N-), 7.22-7.46 (5H, m, Ar-H), 7.59-7.86 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{18}H_{13}ClN_2O_2S$ found (calculated): C, 60.41 (60.59); H, 3.62 (3.67); N, 7.81 (7.85)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(4-fluorophenyl)-2,3-dihydro-1,3,4-oxadiazole **(4b)**

IR (KBr, cm^{-1}): 2976 (CH, arom.), 1656 (C=O), 1586 (C=N), 1273, 1038 (C-O-C), 768 (C-Cl), 724

(C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 6.78 (1H, s, O-CH-N-), 7.01-7.42 (4H, m, Ar-H), 7.59-7.87 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{18}H_{12}ClFN_2O_2S$ found (calculated: C, 57.62 (57.68); H, 3.19 (3.23); N, 7.38 (7.47)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(3-methoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole **(4c)**

IR (KBr, cm^{-1}): 2986 (CH, arom.), 1646 (C=O), 1588 (C=N), 1273, 1048 (C-O-C), 750 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 3.73 (3H, s, Ar-OCH_3), 6.78 (1H, s, O-CH-N-), 6.94-7.20 (4H, m, Ar-H), 7.59-7.87 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{19}H_{15}ClN_2O_3S$ found (calculated): C, 58.91 (58.99); H, 3.88 (3.91); N, 7.19 (7.24)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(2-chlorophenyl)-2,3-dihydro-1,3,4-oxadiazole **(4d)**

IR (KBr, cm^{-1}): 3035 (CH, arom.), 1648 (C=O), 1598 (C=N), 1268, 1039 (C-O-C), 748 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 6.95 (1H, s, O-CH-N-), 7.17-7.34 (4H, m, Ar-H), 7.59-7.87 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{18}H_{12}Cl_2N_2O_2S$ found (calculated): C, 55.21 (55.25); H, 3.01 (3.09); N, 7.04 (7.16)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(4-methoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole **(4e)**

IR (KBr, cm^{-1}): 2996 (CH, arom.), 1654 (C=O), 1578 (C=N), 1278, 1038 (C-O-C), 748 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 3.72 (3H, s, Ar-OCH_3), 6.78 (1H, s, O-CH-N-), 6.61 (2H, m, Ar-H), 7.39 (2H, m, Ar-H), 7.59-7.87 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{19}H_{15}ClN_2O_3S$ found (calculated): C, 58.91 (58.99); H, 3.84 (3.91); N, 7.19 (7.24)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(3-nitrophenyl)-2,3-dihydro-1,3,4-oxadiazole **(4f)**

IR (KBr, cm^{-1}): 3056 (CH, arom.), 1646 (C=O), 1588 (C=N), 1273, 1035 (C-O-C), 750 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 6.78 (1H, s, O-CH-N-), 7.59-7.87 (4H, m, Ar-H of benzothiophene), 7.88-8.11 (4H, m, Ar-H). Analysis: for $C_{18}H_{12}ClN_3O_4S$ found (calculated): C, 53.74 (53.80); H, 2.94 (3.01); N, 10.38 (10.46)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(4-chlorophenyl)-2,3-dihydro-1,3,4-oxadiazole **(4g)**

IR (KBr, cm^{-1}): 2988 (CH, arom.), 1647 (C=O), 1589 (C=N), 1273, 1039 (C-O-C), 750 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 6.78 (1H, s, O-CH-N-), 7.27-7.35 (4H, m, Ar-H), 7.59-7.87 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{18}H_{12}Cl_2N_2O_2S$ found (calculated): C, 55.21 (55.25); H, 3.02 (3.09); N, 7.14 (7.16)%.

3-Acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-(3-methoxy-4-hydroxyphenyl)-2,3-dihydro-1,3,4-oxadiazole **(4h)**

IR (KBr, cm^{-1}): 3250 (OH, arom.), 2988 (CH, arom.), 1646 (C=O), 1588 (C=N), 1273, 1039 (C-O-C), 750 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.15 (3H, s, -$COCH_3$), 3.67 (3H, s, Ar-OCH_3), 4.90 (1H, s, Ar-OH), 6.78 (1H, s, O-CH-N-), 6.90-7.12 (3H, m, Ar-H), 7.59-7.87 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{19}H_{15}ClN_2O_4S$ found (calculated): C, 56.61 (56.65); H, 3.68 (3.75); N, 6.91 (6.95)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-phenyl-1,3,4-oxadiazole **(5a)**

IR (KBr, cm^{-1}): 3053 (CH, arom.), 1605 (C=N), 1284, 1052 (C-O-C), 751 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.43-7.48 (5H, m, Ar-H), 7.78-8.21 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{16}H_9ClN_2OS$ found (calculated): C, 61.41 (61.44); H, 2.81 (2.90); N, 8.91 (8.96)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(4-fluorophenyl)-1,3,4-oxadiazole **(5b)**

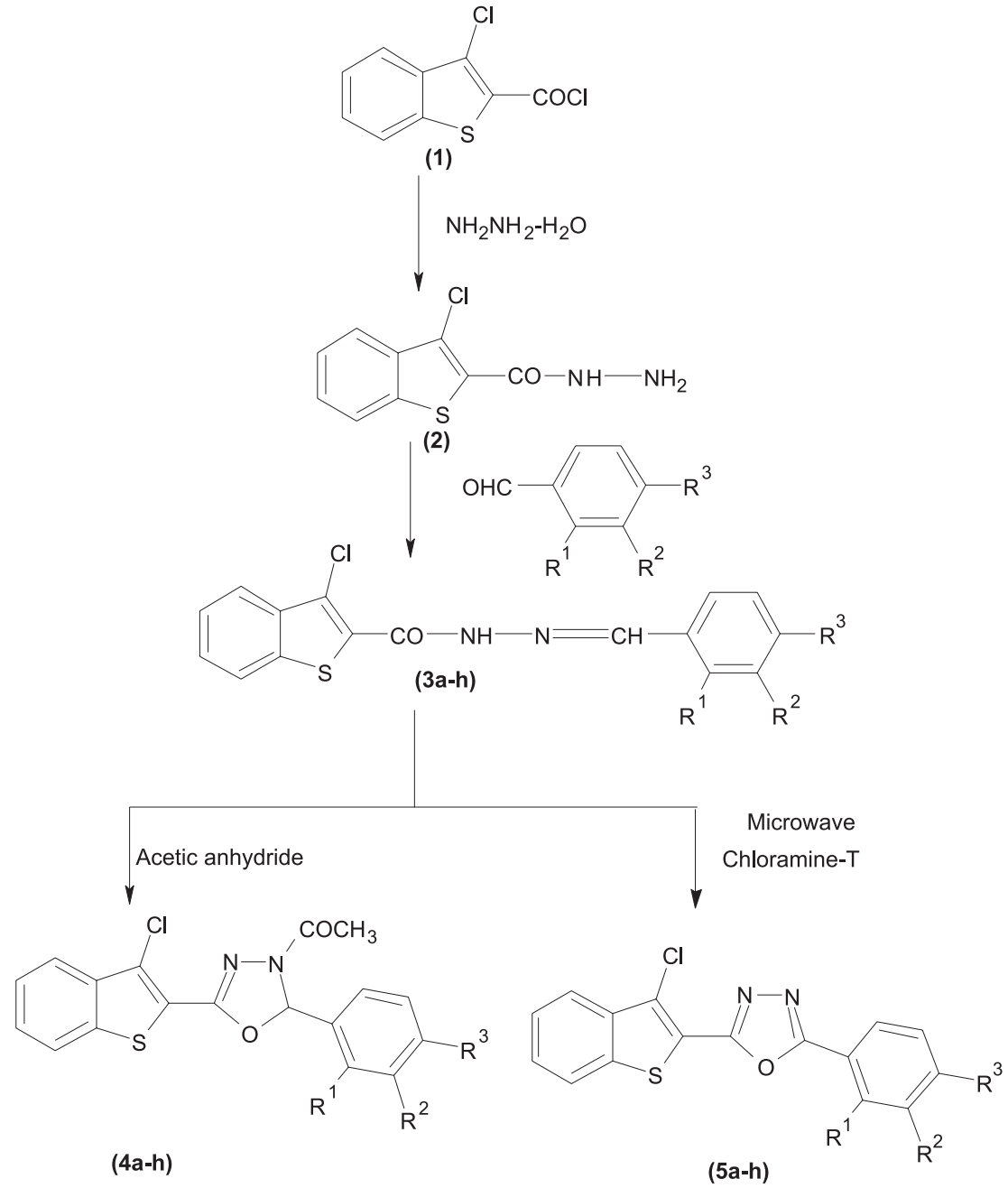
IR (KBr, cm^{-1}): 3023 (CH, arom.), 1615 (C=N), 1284, 1039 (C-O-C), 758 (C-Cl), 728 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.25 (2H, m, Ar-H), 7.46-7.96 (4H, m, Ar-H of benzothiophene), 8.20 (2H, m, Ar-H). Analysis: for $C_{16}H_8ClFN_2OS$ found (calculated): C, 58.06 (58.10); H, 2.39 (2.44); N, 8.39 (8.47)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(3-methoxyphenyl)-1,3,4-oxadiazole **(5c)**

IR (KBr, cm^{-1}, KBr): 3058 (CH, arom.), 1598 (C=N), 1288, 1038 (C-O-C), 751 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 3.73 (3H, s, Ar-OCH_3), 7.12-7.32 (3H, m, Ar-H), 7.46-7.96 (4H, m, Ar-H of benzothiophene), 8.15 (1H, m, Ar-H). Analysis: for $C_{17}H_{11}ClN_2O_2S$ found (calculated): C, 59.48 (59.56); H, 3.18 (3.23); N, 8.12 (8.17)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(2-chlorophenyl)-1,3,4-oxadiazole **(5d)**

IR (KBr, cm^{-1}): 3048 (CH, arom.), 1592 (C=N), 1288, 1035 (C-O-C), 748 (C-Cl), 724 (C-S-C).



Scheme 1. Synthesis of title compounds **(4a-h)** and **(5a-h)**

Compound	R^1	R^2	R^3	Compound	R^1	R^2	R^3
4a	H	H	H	**5a**	H	H	H
4b	H	H	F	**5b**	H	H	F
4c	H	OCH_3	H	**5c**	H	OCH_3	H
4d	Cl	H	H	**5d**	Cl	H	H
4e	H	H	OCH_3	**5e**	H	H	OCH_3
4f	H	NO_2	H	**5f**	H	NO_2	H
4g	H	H	Cl	**5g**	H	H	Cl
4h	H	OCH_3	OH	**5h**	H	OCH_3	OH

Table 1. Physical and analytical data of the synthesized compounds

Comp. no.	Mol. formula	Yield (%)	Mol. Wt.	M.p. (°C)	R_f value
4a	$C_{18}H_{13}ClN_2O_2S$	65	357	202-204	0.69
4b	$C_{18}H_{12}ClFN_2O_2S$	63	375	149-151	0.74
4c	$C_{19}H_{15}ClN_2O_3S$	56	387	182-184	0.62
4d	$C_{18}H_{12}Cl_2N_2O_2S$	47	391	153-155	0.59
4e	$C_{19}H_{15}ClN_2O_3S$	62	387	191-193	0.68
4f	$C_{18}H_{12}ClN_3O_4S$	60	402	187-189	0.76
4g	$C_{18}H_{12}Cl_2N_2O_2S$	57	391	141-143	0.77
4h	$C_{19}H_{15}ClN_2O_4S$	52	403	163-165	0.63
5a	$C_{16}H_9ClN_2OS$	85	313	174-176	0.72
5b	$C_{16}H_8ClFN_2OS$	88	331	201-203	0.78
5c	$C_{17}H_{11}ClN_2O_2S$	92	343	170-172	0.66
5d	$C_{16}H_8Cl_2N_2OS$	84	347	214-216	0.58
5e	$C_{17}H_{11}ClN_2O_2S$	77	343	191-193	0.71
5f	$C_{16}H_8ClN_3O_3S$	89	358	238-240	0.75
5g	$C_{16}H_8Cl_2N_2OS$	92	347	207-209	0.67
5h	$C_{17}H_{11}ClN_2O_3S$	78	359	193-195	0.74

^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.02-7.44 (4H, m, Ar-H), 7.46-7.96 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{16}H_8Cl_2N_2OS$ found (calculated): C, 55.31 (55.35); H, 2.28 (2.32); N, 8.01 (8.07)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(4-methoxyphenyl)-1,3,4-oxadiazole **(5e)**

IR (KBr, cm^{-1}): 3058 (CH, arom.), 1598 (C=N), 1288, 1038 (C-O-C), 751 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 3.77 (3H, s, Ar-OCH_3), 7.46-7.96 (4H, m, Ar-H of benzothiophene), 7.98-8.02 (4H, m, Ar-H). Analysis: for $C_{17}H_{11}ClN_2O_2S$ found (calculated): C, 59.51 (59.56); H, 3.19 (3.23); N, 8.14 (8.17)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(3-nitrophenyl)-1,3,4-oxadiazole **(5f)**

IR (KBr, cm^{-1}): 2998 (CH, arom.), 1588 (C=N), 1288, 1041 (C-O-C), 748 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.46-7.96 (4H, m, Ar-H of benzothiophene), 8.03-8.59 (4H, m, Ar-H). Analysis: for $C_{16}H_8ClN_3O_3S$ found (calculated): C, 53.68 (53.71); H, 2.21 (2.25); N, 11.71 (11.74)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(4-chlorophenyl)-1,3,4-oxadiazole **(5g)**

IR (KBr, cm^{-1}): 3048 (CH, arom.), 1592 (C=C), 1348 (C=N), 1288, 1039 (C-O-C), 748 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.02-7.44 (4H, m, Ar-H), 7.46-7.96 (4H, m, Ar-H of benzothiophene). Analysis: for $C_{16}H_8Cl_2N_2OS$ found (calculated): C, 55.31 (55.35); H, 2.28 (2.32); N, 8.01 (8.07)%.

2-(3-Chloro-1-benzo[*b*]thiophen-2-yl)-5-(3-methoxy-4-hydroxyphenyl)-1,3,4-oxadiazole **(5h)**

IR (KBr, cm^{-1}): 3250 (OH, arom.), 3048 (CH, arom.), 1592 (C=C), 1348 (C=N), 1288 (C-O-C), 748 (C-Cl), 724 (C-S-C). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 3.83 (3H, s, Ar-OCH_3), 4.90 (1H, s, Ar-OH), 7.46-7.96 (4H, m, Ar-H of benzothiophene), 7.98-8.05 (3H, m, Ar-H). Analysis: for $C_{17}H_{11}ClN_2O_3S$ found (calculated): C, 56.88 (56.91); H, 3.02 (3.09); N, 7.78 (7.81)%.

Biological activity

The activity was determined using disc diffusion method (24) by measuring zone of inhibition in mm. All the compounds, **(4a-h)** and **(5a-h)**, were

Table 2. Antimicrobial activity-sensitivity testing of compounds **(4a-h)** and **(5a-h)**

Compound no.	Zone of inhition in mm					
	Antibacterial activity				Antifungal activity	
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*	*C. albicans*	*A. niger*
4a	14	21	10	17	9	10
4b	18	19	12	15	10	11
4c	30	27	14	18	9	11
4d	19	22	11	18	10	11
4e	28	28	14	14	10	9
4f	14	19	10	15	10	10
4g	21	23	13	19	11	9
4h	14	20	10	16	9	10
5a	11	12	10	9	11	11
5b	10	12	9	11	12	12
5c	20	21	12	13	11	11
5d	20	22	16	18	10	11
5e	18	19	11	13	11	10
5f	11	13	10	11	10	11
5g	12	14	9	12	10	10
5h	10	13	9	11	10	11
Ciprofloxacin	26	26	28	25	-	-
Fluconazole	-	-	-	-	26	25

screened *in vitro* at concentration of 5 µg/disc for their antibacterial activity against two Gram-positive strains (*Staphylococcus aureus* and *Bacillus subtilis)* and two Gram-negative strains (*Escherichia coli* and *Pseudomonas aeruginosa)*. Antifungal evaluation was carried out against *Candida albicans* and *Aspergillus niger* at concentration of 5 µg/disc. Standard antibacterial drug ciprofloxacin (10 µg/disc) and antifungal drug fluconazole (10 µg/disc) were also tested under similar conditions against these organisms. All synthesized compounds exhibited significant antibacterial activities and moderate antifungal activities. Each experiment was done in triplicate and the average reading was taken.

RESULTS

Hydrazones **(3a-h)** were prepared by reaction of 3-chloro-2- hydrazinocarbonylbenzo[*b*]thiophene **(2)** with various aromatic aldehydes. These hydrazones **(3a-h)** were reacted to yield 3-acetyl-5-(3-chloro-1-benzo[*b*]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles **(4a-h)** by reacting with acetic anhydride. Another series of 2-(3-chloro-1-benzo[*b*]thiophen-2-yl)-5-substituted phenyl-1,3,4-oxadiazoles **(5a-h)** was synthesized by reacting hydrazones **(3a-h)** with chloramine-T under microwave irradiation. The synthetic procedure for preparation of title compounds is given in Scheme 1. Physical data of synthesized compounds are summarized in Table 1. The assigned structure and molecular formula of the newly synthesized compounds **(4a-h)** and **(5a-h)** were further confirmed and supported by ^{1}H NMR, IR data and elemental analysis which was in full agreement with proposed structures. The compounds were screened *in vitro* for their antibacterial and antifungal potential by disc diffusion assay against selected pathogenic bacteria and human pathogenic fungi. The results of antibacterial and antifungal activities are expressed in terms of zone of inhibition and presented in Table 2.

DISCUSSION AND CONCLUSION

Some novel 1,3,4-oxadiazole derivatives **(4a-h)** and **(5a-h)** have been synthesized and evaluated

for antimicrobial activities. The results of antimicrobial studies of newly synthesized compounds reveal that the compounds possess significant antibacterial and moderate antifungal activities. Compounds **4c** and **4e** with methoxy substitution were found to be most potent compounds of the series with antibacterial activity higher than that of standard drug i.e., ciprofloxacin against *S. aureus* and *B. subtilis*. Compounds **4b, 4g, 5c, 5d** and **5e** showed moderate activities against *S. aureus* and *B. subtilis*. All the other newly synthesized compounds showed either moderate activity or no activity against bacterial strains. In general, compounds **4a-h** have depicted more potent activities than compounds **5a-h**. Even though, the synthesized compounds did not exhibit appreciable antifungal activities, yet compounds **4b, 4c, 4e, 4g, 5c, 5d** and **5e** can be chosen for further studies aimed at producing antimicrobial agents with enhanced activity. The outstanding properties of this new class of antibacterial substances deserve further investigation in order to clarify the mode of action at molecular level, responsible for the activity observed. More extensive study is also warranted to determine additional physicochemical and biological parameters to have a deeper insight into structure-activity relationship and to optimize the effectiveness of this series of molecules.

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