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Research Article

SYNTHESIS OF 2-(8-BROMONAPHTHO[2,1-*B*]FURAN-2-YL)-5-ARYL-1,3,4-OXADIAZOLES AS POTENTIAL ANTIMICROBIAL AGENTS

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ABSTRACT

The reaction of ethyl 8-bromonaphtho[2,1-*b*]furan-2-carboxylate **2** obtained by the bromination of ethyl naphtho[2,1-*b*]furan-2-barboxylate **1** with hydrazine hydrate, afforded 8-bromonahtho[2,1-*b*]furan-2-carboxyhydrazide **3** which served as an excellent intermediate for the synthesis of title compounds. These were obtained by two different routes from hydrazide **3**. The first route involved the conversion of hydrazide **3** into N-aroyl 8-bromonaphtho[2,1-*b*]furan-2-carbohydrazides **4(a-f)**, which underwent smooth cyclization on treatment with phosphorus oxychloride to furnish 2-(8-bromonaphtho[2,1-*b*]furan-2-yl)-5-aryl-1,3,4-oxadiazoles **5(a-k)**. In the second methodology the oxadiazoles **5(a-k)** were obtained by converting hydrazide **3** into corresponding Schiff bases **6(a-k)** followed by ring closure using bromine in acetic acid in presence of anhydrous sodium acetate. The structures of newly synthesized compounds have been established by analytical and spectral studies. All the compounds in the series have been screened for their antibacterial and antifungal activities.

Keywords: Naphtho[2,1-*b*]furo-1,3,4-oxadiazoles, antibacterial activity, antifungal activity.

INTRODUCTION

Among the wide variety of heterocycles that have been explored for developing pharmaceutically important molecules, 1,3,4-oxadiazole derivatives have played a vital role in the medicinal chemistry. There are large number of synthetic compounds, encompassing oxadiazole nucleus, used as antibacterial[1-5], antifungal[6-7], anticonvulsant[8], anti-inflammatory[9-10] and anticancer[11] agents, when properly substituted in 2 and 5 positions.

The biheterocyclic compounds having 2-arylamino-1,3,4-oxadiazoles, obtained from oxidative cyclization of corresponding thiosemicarbazides have been shown to exhibit a broad spectrum of biological activities[12-14]. Some of naphtho[2,1-*b*]furo-1,3,4-oxadiazoles, synthesized in our laboratory, have been screened for antimicrobial activity and have been found to possess considerable antibacterial as well as antifungal activities[15-16]. The literature survey revealed that the replacement of one or more hydrogen atom by the corresponding number of halogen atom enhanced the biological profile of heterocyclic compounds by many folds[17]. Thus some of the biheterocyclic compounds having bromine atom at C-8 of naphthofuran moiety have been reported to exhibit considerable antibacterial activity[18]. Similarly bromosubstituted naphthofuran compounds exhibit muscarinic antagonist activity[19]. Further, introduction of a bromine atom provides more

routes for synthetic variation in the molecule under study and to synthesize pharmacologically interesting compounds compared to their non brominated analogues.

Encouraged by the wide spectrum of biological activities associated with biheterocyclic compounds containing naphtho[2,1-*b*]furan & 1,3,4-oxadiazole moieties and bromine bearing compounds and in continuation of our earlier work[20-26], we report in this paper the synthesis of title compounds by different routes and investigation of their biological activity.

MATERIALS AND METHOD

Melting points were determined by an open capillary method and are uncorrected. The IR spectra(in KBr pellets) were recorded on Shimadzu FTIR spectrum 8000 Spectrometer. The NMR spectra (^{1}H and ^{13}C) were recorded on Bruker-400 MHz Spectrometer, using $CDCl_3$ and DMSO-d_6 as solvent and TMS as internal standard reference. Chemical shifts are expressed as δ values [in ppm]. The mass spectra were recorded on Brucker Apex-II mass Spectrophotometer and Shimadzu LC-MS Instrument. Purity of compounds was checked by thin layer chromatography (TLC) on a silica gel plate and visualizing the spots under iodine vapour.

EXPERIMENTAL

Synthesis of ethyl 8-bromonaphtho[2,1-*b*]furan-2-carboxylate 2

To a solution of ethyl naphtho[2,1-*b*]furan-2-carboxylate **1** (2.4 g, 0.01 mol) in glacial acetic acid (50 ml), bromine(0.8 g, 0.01 mol) in glacial acetic acid (20 ml) was slowly added with stirring over a period of 1 h at a temperature of 0-5°C and the stirring was continued for 3 h. The reaction mixture was poured into ice-cold water and the solid obtained was filtered out. It was washed with water, dried and the product was recrystallised from ethanol.

Synthesis of 8-bromonaphtho[2,1-*b*]furan-2-carboxyhydrazide 3

An aqueous solution of hydrazine hydrate (15 ml, 99%) was added to a solution of ethyl 8-bromonaphtho[2,1-*b*]furan-2-carboxylate **2** (3.2g, 0.01 mol) in ethanol (30 ml). The reaction mixture was heated under reflux for 2 h and cooled to room temp. The hydrazide **3** that separated, as a solid, was collected and recrystallized from ethanol.

Synthesis of N- (aroyl-8-bromonaphtho[2,1-*b*]furan-2-carbohydrazides 4a-f

A mixture of compound **3** (3.05 g, 0.01 mol) and benzoyl chloride (1.4 g, 0.01 mol) was stirred at room temperature, followed by drop wise addition of aqueous sodium hydroxide (5 ml, 0.01 N), stirring was continued for further period of 1 h. The mixture was then poured into water, the product **4d**, thus obtained as solid was filtered, dried and recrystallized from ethanol.

Other compounds **4a-c, e-f** in the series were prepared similarly by using appropriately substituted benzoyl chlorides.

Synthesis of N-(arylmethylene)-8-bromonaphtho[2,1-*b*]furan-2-carbohydrazides (Schiff's base) 6a-k

To a solution of naphtho[2,1-*b*]furan-2-carbohydrazide **3** (3.05 g, 0.01 mol) in dioxane (15 ml), 4-methoxybenzaldehyde (1.36 g, 0.01 mol) was added. The reaction mixture was kept for reflux on water bath for 2 h. Then it was poured in to ice-cold water to get the product **6a** and the solid separated out was filtered and dried. The product was recrystallised from dioxane.

The compounds **6b-k** were synthesized similarly by using appropriate aldehydes.

Synthesis of 2-(8-bromonaphtho[2,1-*b*]furan–2-yl)-5-aryl-1,3,4-oxadizoles 5a-f

Method-A

The compound **4d** (3.3 g, 0.01 mol) was refluxed with phosphorous oxychloride (15 ml) for 3 h. cooled and poured into crushed ice with stirring. The solid thus separated was filtered and recrystallized from methanol.

The compounds **5a-c,** and **5e-f** were prepared by adopting same procedure from **4a-c, and 4e-f.**

Method-B

Compounds **6d** (3.93 g, 0.01 mol) and anhydrous sodium acetate (0.15 g) were mixed and suspended in glacial acetic acid (5 ml). Bromine (1 g) in glacial acetic acid (0.25 ml) was added to the above mixture with stirring. After a few minutes the mixture became warm and the colour of bromine faded. The mixture was stirred for a further period of 30 min. then decomposed in ice-cold water (100 ml). The product **5d** was collected and recrystallized from ethanol.

The compounds **5a-c,** and **5e-f** were prepared by adopting same procedure from **6a-c,** and **6e-f.**

The physical data of newly synthesized compounds are tabulated in Table – 1.

Evaluation of Biological activities

The compounds encompassing naphthofuran, and oxadiazoles are known to exhibit wide spectrum of biological activities. Hence, it was contemplated to evaluate newly synthesized compounds for antimicrobial activities by adopting literature procedure.

Antimicrobial activity

The newly synthesized compounds were screened for their antibacterial activity against *Bacillus substilis*, *Pseudomonas aerugenosa Staphyloccoccus pyogens*, *Staphylococcus aureus and* antifungal activity against *Aspergillus niger*, *Aspergillus flavus, Candida albicans* according to cup plate method[28] at a concentration of 0.005 mol/ml against all the organisms. Chloramphenicol and Fluconazole were used as standard drugs for antibacterial and antifungal activity respectively.The zone of inhibition was compared with the standard drug after 24 h of incubation at 25^0 C for antibacterial activity and after 48 h at 30^0 C for antifungal activity. The results of such studies are given in Table 2.

RESULT AND DISCUSSION

The starting material required for the present investigation, ethyl naphtho[2,1-*b*]furan-2 carboxylate **1**, was synthesized by a reported method from our laboratory[21]. Bromination of ester **1** afforded ethyl 8-bromonaphtho[2,1-*b*]furan-2-carboxylate **2** structure of which was established by spectral studies. The IR (KBr) spectrum exhibited absorption band at 1720 cm^{-1} due to ester carbonyl group. The 300 MHz ^1H NMR (DMSO-d_6) spectrum of **2** showed the signal at δ 1.46 triplet (3H) (J=7.12 Hz) and δ 4.48 quartet (2H) (J=7.11) indicating the presence of an ethyl group of ester and δ 7.2-8.5 multiplet (6H) for aromatic protons. The ^1H NMR was conspicuous by the absence of signal at δ 8.6, which was present in its precursor **1** due to the proton at C-8, confirming the bromination at C-8 of naphthofuran moiety. The mass spectrum showed the molecular ion peak at m/z 319 (M^+) and 321(M+2) corresponding to its molecular weight.

The key intermediate 8-bromonahtho[2,1-*b*]furan-2-carboxyhydrazide **3** was obtained by the condensation of **2** with hydrazine hydrate (99%) in presence of catalytic amount of concentrated hydrochloric acid in ethanol at reflux temperature. The IR spectrum of **3** exhibited characteristic bands at 3100 cm^{-1} and 3123 cm^{-1} due to –NH and $–NH_2$ absorption and 1656 cm^{-1} due to carbonyl group. In ^1H NMR spectrum D_2O exchangeable broad singlet (2H) at δ 4.15, multiplet (6H) at δ 7.6-8.4 and another singlet (1H) D_2O exchangeable at δ 7.85 appeared which were attributed to $–NH_2$, aromatic and –NH protons respectively.

The structure of **3** has been substantiated by its mass spectrum which exhibited peaks at m/z 305 (M^+) and 307 (M+2) and other peaks appearing at m/z 274, 272, 247, 210, 195, 168, 155, and 59 are in accordance with the fragmentation pattern of **3**.

Five different routes were employed to synthesize 2-(8-bromonaphtho[2,1-*b*]furan-2-yl)-1,3,4-oxadiazole derivatives, using hydrazide **3** as an intermediate.

In the first method, the hydrazide **3** was reacted with various aromatic acid chlorides in presence of base, to obtain N-aroyl-8-bromonaphtho[2,1-*b*]furan-2-carboxyhydrazides **4(a-f)** in moderate yield. The spectral data supported the formation of compounds **4(a-f)**. The IR spectrum of **4d** exhibited absorption bands at 3221 and 1694 cm^{-1} due to NH and C=O stretching frequencies respectively. ^1H NMR spectrum of **4d** substantiated the assigned structure, showing a multiplet at δ 7.45-8.4 due to 11 aromatic protons and two D_2O exchangeable singlets at δ 9.25 and δ 9.60 due to protons of two NH groups. The IR and ^1H NMR spectral data of these compounds is summarized in Table 3.

The compounds **4(a-f)** underwent ring closure on refluxing with phosphorus oxychloride and furnished 2-(8-bromonaphtho[2,1-*b*]furan-2-yl)-5-aryl-1,3,4-oxadiazoles **5(a-f)**. The structures assigned to **5(a-f)** were evident as their IR spectra showed absence of absorption bands due to two NH and carbonyl frequencies. Similarly ^1H NMR spectrum of **5d** was devoid of singlets at δ 9.25 and 9.60 due to protons due to two NH groups. The ^{13}C NMR spectrum of **5d** was recorded to confirm its structure, which showed absence of peak at δ 149.08 due to carbonyl carbon. The mass spectrum of **5d** exhibited peak at m/z 391corresponding to its molecular weight. The peaks appearing at m/z 374, 312, 214, 197, 181, 166, 146, 119, 103 were in accordance with the fragmentation pattern. The IR and ^1H NMR spectral data of these compounds is summarized in Table 4.

The oxadiazoles **5(a-k)** were also prepared by an alternative method, which involved the conversion of hydrazide **3** into corresponding Schiff bases i.e., N-(arylmethylene)-8-bromonaphtho[2,1-*b*]furan-2-carbohydrazides **6(a-k)** obtained by reacting **3** with appropriate aromatic aldehydes bearing electron withdrawing

and electron donating groups. The formation of compounds **6(a-k)** was confirmed by their IR spectra exhibiting absorption bands at 1654 cm^{-1} and 1606 cm^{-1} due to carbonyl and C=N stretching frequencies respectively. In ^1H NMR spectrum of **6a** a singlet at δ 3.87 due to $-OCH_3$ protons, a multiplet at 7.6-8.5 due to aromatic and –N=CH protons and a D_2O exchangeable singlet at δ 9.52 due to –CONH proton were observed. The structure assigned was substantiated by ^{13}C NMR (DMSO-d_6) spectrum of **6a**, which contained a peak at δ 149.08 due to carbonyl carbon and at δ 129.59 due to –CH=N carbon. The peak appearing at δ 55.43 was attributed to methoxy carbon atom. The bunch of peaks of 111.08, 114.37, 116.50, 123.94, 126.10, 126.77, 128.26, 128.47 were assignable to remaining carbon atoms. The same method was employed to yield compounds **6(b-f)** from **3** The IR and ^1H NMR spectral data of these compounds is summarized in Table 5.

The Schiff bases **6(a-k)** underwent oxidative cyclodehydrogenation to yield oxadiazoles **5(a-k)**. The products formed thus were identical with the oxadiazoles obtained from **4(a-f)** as indicated by superimposable spectra and study of mixed melting points.

The IR and ^1H NMR spectral data of these compounds is summarized in Table 4.

The compounds encompassing naphthofuran, oxadiazole ring systems are known to exhibit wide spectrum of biological activities. Hence, it was contemplated to evaluate newly synthesized compounds for antimicrobial activities by adopting literature procedure The compounds **2, 3, 4(a-b), 5a, 5d, 5f, 5(h-k), 6k,** exhibited very good activity against *Staphyloccoccus pyogens.* The compounds **4a, 5b 5c, 5e, 5h, 5j and 5k** showed moderate activity against *Staphylococcus aureus.* The compound **4b** possess excellent activity and **2**, **5(b-c) and 6j** exhibited very good antibacterial activity against *Pseudomonas aeruginosa*.. The compounds **3**, and **4f** exhibited very good activity against *Bacillus substilis.* The compounds **4b, 5b**, **5(e-f)**, **6a**, **6f**, **6(j-k)** were found to be significantly activity against *Bacillus substilis.* The comopound **6e** was the most potent compound, which exhibited excellent activity against *Aspergillum niger*. The compounds **3**, **4b**, **4e**, **5b**, **5e**, **6d** and **6k**, exhibited very good activity against *Aspergillum niger* .The compounds **4b**, and **5f** exhibited very good activity against *Aspergillus flavus*. The compounds **5c** and **6h** exhibited promising against *Aspergillus flavus.* The compounds **6g** and **6i** were found to be significantly active against *Candida albicans.* The remaining compounds were found to have moderate or slight active against tested organism and some of the compounds were found to be inactive.

Table 1: Physical and analytical data of newly synthesized compounds

Comp	R	M. P C	Yield (%)	Mol. Formula	Found (Calcd) %		
					C	H	N
2	-	145	94	$C_{15}H_{11}O_3Br$	56.43 (56.45)	3.45 (3.47)	-
3	-	185	97	$C_{13}H_9N_2O_2Br$	51.00 (51.17)	2.50 (2.97)	9.15 (9.18)
4a	4-OCH_3 C_6H_4	155	71	$C_{21}H_{15}N_2O_4Br$	57.31 (57.42)	3.40 (3.44)	6.31 (6.38)
4b	4-Cl C_6H_4	195	67	$C_{20}H_{12}N_2O_3BrCl$	54.11 (54.14)	2.71 (2.73)	6.29 (6.31)
4c	4-NO_2 C_6H_4	230	67	$C_{20}H_{12}N_3O_5$ Br	52.80 (52.88)	2.61 (2.66)	9.20 (9.25)
4d	C_6H_5	170	67	$C_{20}H_{13}N_2O_3Br$	58.65 (58.70)	3.158 (3.20)	6.72 (6.85)
4e	2-Cl C_6H_4	115	86	$C_{20}H_{12}N_2O_3BrCl$	54.10 (54.14)	2.70 (2.73)	6.25 (6.31)
4f	3-NO_2 C_6H_4	110	93	$C_{20}H_{12}N_3O_5Br$	52.78 (52.88)	2.65 (2.66)	9.15 (9.25)
5a	4-OCH_3 C_6H_4	170	81	$C_{21}H_{13}N_2O_3$ Br	59.53 (59.59	3.50 (3.57)	6.59 (6.62)
5b	4-Cl C_6H_4	245	71	$C_{20}H_{10}N_2O_2$ BrCl	56.00 (56.17)	2.65 (2.83)	6.45 (6.55
5c	4-NO_2 C_6H_4	260	92	$C_{20}H_{10}N_3O_4Br$	54.75 (54.81)	2.66 (2.76)	9.49 (9.59)
5d	C_6H_5	265	76	$C_{20}H_{11}N_2O_2Br$	61.00 (61.09)	3.28 (3.31)	7.10 (7.12)
5e	2-Cl C_6H_4	245	55	$C_{20}H_{12}N_2O_2$ BrCl	56.08	2.75	6.30

					(56.17)	(2.83)	(6.55)
5f	3-NO_2 C_6H_4	265	96	$C_{20}H_{12}N_2O_4Br$	54.76 (54.81)	2.65 (2.76)	9.46 (9.59)
5g	$C_{10}H_7O$	245	62	$C_{24}H_{15}N_2O_3Br$	62.56 (62.76)	3.25 (3.29)	6.05 (6.10)
5h	CH=CH C_6H_5	245	69	$C_{22}H_{15}N_2O_2Br$	63.00 (63.02)	3.59 (3.61)	8.62 (8.68)
5i	C_4H_3O	235	63	$C_{18}H_{11}N_2O_3Br$	56.32 (56.42)	2.15 (2.89)	7.22 (7.31)
5j	4-OH C_6H_4	285	69	$C_{20}H_{13}N_2O_3Br$	58.65 (58.70)	3.16 (3.20)	6.75 (6.85)
5k	4-OCH_3 3-OH C_6H_3	280	74	$C_{21}H_{15}N_2O_4Br$	57.39 (57.42)	3.39 (3.44)	6.30 (6.38)
6a	4-OCH_3 C_6H_4	170	81	$C_{21}H_{15}N_2O_3$ Br	59.63 (59.59)	3.50 (3.57)	6.759 (6.62)
6b	4-Cl C_6H_4	245	71	$C_{20}H_{12}N_2O_2BrCl$	56.00 (56.17)	2.65 (2.83)	6.45 (6.55)
6c	4-NO_2 C_6H_4	260	92	$C_{20}H_{12}N_3O_4Br$	54.75 (54.81)	2.66 (2.76)	9.49 (9.59)
6d	C_6H_5	265	76	$C_{20}H_{13}N_2O_2Br$	61.22 (61.09)	3.28 (3.31)	7.10 (7.12)
6e	2-Cl C_6H_4	245	55	$C_{20}H_{12}N_2O_2BrCl$	56.08 (56.17)	2.75 (2.83)	6.30 (6.55)
6f	3-NO_2 C_6H_4	265	96	$C_{20}H_{12}N_3O_4Br$	54.76 (54.81)	2.65 (2.76)	9.46 (9.59)
6g	$C_{10}H_7O$	245	62	$C_{24}H_{15}N_2O_3Br$	62.56 (62.76)	3.25 (3.29)	6.05 (6.10)
6h	CH=CH C_6H_5	245	69	$C_{22}H_{15}N_2O_2Br$	63.00 (63.02)	3.59 (3.61)	8.62 (6.68)
6i	C_4H_3O	235	63	$C_{18}H_{11}N_2O_3Br$	56.32 (56.42)	2.15 (2.89)	7.22 (7.31)
6j	4-OH C_6H_4	285	69	$C_{20}H_{13}N_2O_3Br$	58.65 (58.70)	3.16 (3.20)	6.75 (6.85)
6k	4-OCH_3 3-OH C_6H_3	280	74	$C_{21}H_{15}N_2O_4Br$	57.39 (57.42)	3.39 (3.44)	6.30 (6.38)

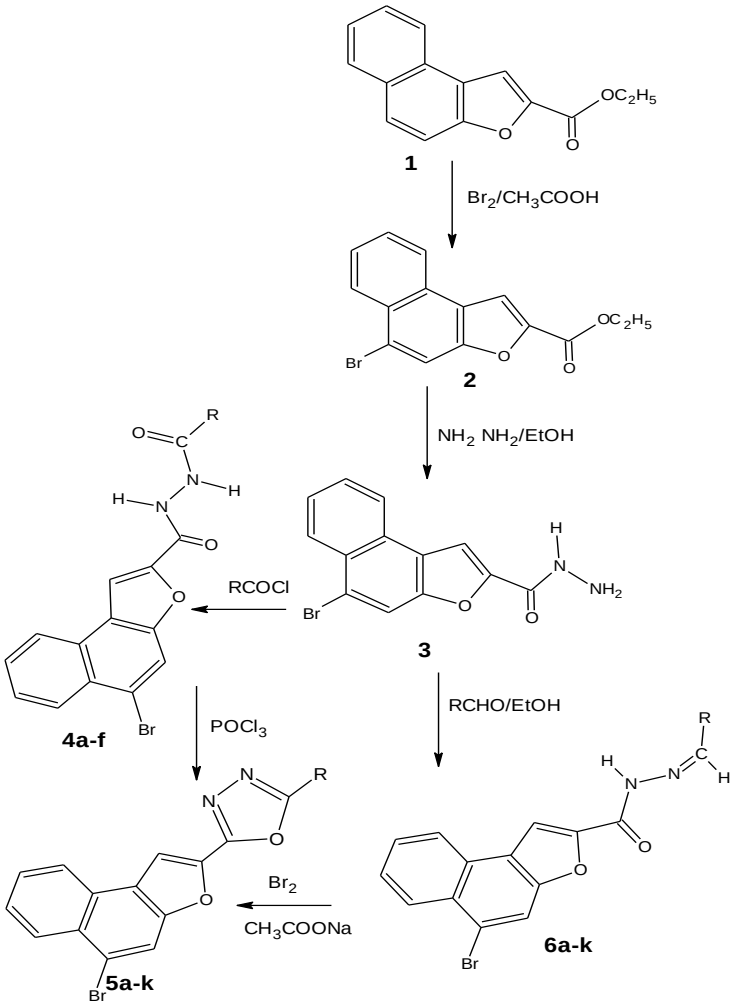
Table 2: Antimicrobial activity data of prepared compounds

Comp	R	Zone of inhibition in mm						
		Antibacterial activity				Antifungal activity		
		B. substilis	***P. aeruginosa***	***S. pyogenes***	***S. aureus***	***A. niger***	***C. albicans***	***A. flavus***
2	-	18	23	22	15	14	15	12
3	-	25	15	18	17	18	12	16
4a	4-OCH_3 C_6H_4	18	16	19	18	14	17	17
4b	4-Cl C_6H_4	23	25	22	17	19	15	22
4c	4- NO_2 C_6H_4	18	18	10	15	7	16	-
4d	C_6H_5	10	17	13	10	14	12	-
4e	2-Cl C_6H_4	13	15	13	12	20	11	-
4f	3-NO_2 C_6H_4	25	12	16	12	7	12	13
5a	4-OCH_3-C_6H_4	19	18	18	17	12	18	16
5b	4-Cl- C_6H_4	20	24	14	19	19	16	13
5c	4-NO_2- C_6H_4	17	20	12	18	14	11	16
5d	- C_6H_5	13	15	22	17	8	11	-
5e	2-Cl- C_6H_4	20	19	16	18	19	15	14
5f	3-NO_2- C_6H_4	20	13	21	17	14	11	22
5g	$C_{10}H_7O$	17	16	15	17	11	17	13
5h	-CH=CH-C_6H_5	18	17	18	18	12	16	13
5i	Furfural	16	16	19	17	13	18	13
5j	4-OH- C_6H_4	17	15	18	18	11	20	14
5k	3-OCH_3-4-OH C_6H_3	19	16	20	19	14	20	15
6a	4-OCH_3-C_6H_4	20	16	-	-	11	11	-
6b	4-Cl- C_6H_4	17	10	-	-	13	12	-
6c	4-NO_2- C_6H_4	16	16	-	-	8	12	11

6d	- C_6H_5	17	18	-	-	18	10	9
6e	2-Cl- C_6H_4	18	11	-	-	22	10	16
6f	3-NO_2- C_6H_4	20	-	-	-	-	11	-
6g	$C_{10}H_7O$	15	15	-	-	-	22	13
6h	-CH=CH-C_6H_5	10	15	-	-	14	10	19
6i	Furfural	15	18	-	-	11	21	13
6j	4-OH- C_6H_4	20	23	-	10	14	13	8
6k	3-OCH_3-4-OH C_6H_3	20	-	18	17	19	18	-
(Standard) Chloamphenicol		35	25	24	26	-	-	-
Flucanazole		-	-	-	-	22	24	26

Zone of inhibition in millimeters.

Scheme-1



R		R	
a	4OCH_3-C_6H_4	f	3NO_2 C_6H_4
b	4Cl C_6H_4	g	Naphthaldehyde
c	4NO_2 C_6H_4	h	CH=CH C_6H_5
d	C_6H_5	i	Furfural
e	2Cl C_6H_4	j	4OH C_6H_4
		k	3OCH_3 4OH C_6H_3

Table-3: IR and 1H NMR Spectral data of 8-Bromonaphtho [2,1-b]furan-2- carbohydrazide (4a-f)

Comp.	R	IR (KBr)cm^{-1}		^{1}H NMR in ppm
		NH	C=O	
4a	4-OCH_3-C_6H_4	3200	1657	δ 3.87 (s, 3H, OCH_3), δ 7.6-8.5 (m, 10H, ArH) δ 9.52, 9.48 (s, 2H, 2NH)
4b	4-Cl-C_6H_4	3210	1625	δ 7.5-8.1 (m, 10H, ArH), δ9.55, 9.30 (s, 2H, 2NH)
4c	4-NO_2-C_6H_4	3217	1684	δ 7.55-8.1 (m, 10H, ArH), δ11.02, 10.99 (s, 2H, 2NH)
4d	C_6H_5	3217	1687	δ 7.45-8.4 (m, 11H, ArH), δ9.6, 9.25(s, 2H, 2NH)
4e	2-Cl-C_6H_4	3208	1680	δ 7.6-8.2 (m, 10H, ArH), δ9.51, 9.28 (s, 2H, 2NH)
4f	3-NO_2-C_6H_4	3214	1685	δ 7.55-8.1 (m, 10H, ArH), δ11.00, 10.94 (s, 2H, NH)

Table – 4: IR and 1H NMR Spectral data of 2-(8-bromonaphtho [2,1-b]furan–2-yl)-5-aryl-1,3,4-oxadizoles (5a-f)

Comp.	R	IR (KBr) cm^{-1}	^{1}H NMR ($CDCl_3$)
		C=N	
5a	4-OCH_3-C_6H_4	1608	δ 3.9(s, 3H, OCH_3), δ 7.12-8.4 (m, 10H, ArH)
5b	4-Cl-C_6H_4	1606	δ 7.3-8.3 (m, 10H, ArH)
5c	4-NO_2-C_6H_4	1625	δ 7. 4-8.6 (m, 10H, ArH)
5d	-C_6H_5	1606	7.5-8.5 (m, 11H, ArH)
5e	2-Cl-C_6H_4	1610	7.2-8.7 (m, 11H, ArH)
5f	3-NO_2-C_6H_4	1624	δ 7.2-8.4 (m, 10H, ArH)

Table-5: IR and 1H NMR Spectral data of N-[(aryl)methylene]-8-bromonaphtho[2,1-b]furan-2-carbohydrazides [Schiff's base](6a-k)

Comp.	Ar	IR (KBr) cm^{-1}		^{1}H NMR in ppm
		C=N	C=O	
6a	4-OCH_3-C_6H_4	1606	1655	δ 3.87 (s, 3H, OCH_3), δ 6.9-8.5 (m, 10H, ArH & N=CH) δ 9.52 (s, 1H, CONH)
6b	4-Cl-C_6H_4	1594	1648	δ 7.2-8.6 (m, 11H, ArH & N=CH), δ 9.7 (s, 1H, CONH)
6c	4-NO_2-C_6H_4	1598	1675	δ 7.3-8.61 (m, 11H, ArH & N=CH), δ 9.23 (s, 1H, CONH)
6d	-C_6H_5	1603	1647	δ 7.4-8.5 (m, 11H, ArH & N=CH), δ 9.68 (s, 1H, CONH)
6e	2-Cl-C_6H_4	1610	1680	δ 7.4-8.5 (m, 11H, ArH & N=CH), δ 9.4 (s, 1H, CONH)
6f	3-NO_2-C_6H_4	1596	1670	δ 7.3-8.61 (m, 11H, ArH & N=CH), δ 9.22 (s, 1H, CONH)
6g	$C_{10}H_7O$	1609	1685	δ 4.18 (b, 1H, OH), δ 7.1-8.55(m, 13H, ArH & N=CH), δ 10.1 (s, 1H, CONH)
6h	-CH=CH-C_6H_5	1600	1668	δ 7.4-8.5 (m, 14H, ArH & N=CH, CH=CH), δ 9.2 (s, 1H, CONH)
6i	Furfural	1609	1685	δ 7.1-8.2 (m, 10H, ArH & N=CH), δ 8.6 (s, 1H, NCH), δ 9.8 (s, 1H, CONH)
6j	4-OH-C_6H_4	1620	1684	δ 4.25 (b, 1H, OH), δ 7.2-8.6 (m, 11H, ArH & N=CH), δ 9.6 (s, 1H, CONH)
6k	3-OCH_3-4-OH C_6H_3	1615	1660	δ 3.82 (s, 3H, OCH_3), δ 4.22 (b, 1H, OH),δ 7.6-8.5 (m, 10H, ArH & N=CH) δ 9.54 (s, 1H, CONH)

CONCLUSION

The synthesis of novel biheterocycles comprising naphtho[2,1-*b*]furan and 1,3,4-oxadiazoles ring systems, containing bromine atom at position 8 of naphthofuran nucleus and various substitutents at position 5 of 1,3,4-oxadiazole nucleus has been carried out successfully. Overall conclusion is that introduction of bromine atom in position 8 of naphthofuran ring enhanced antimicrobial to certain extent as compared with the compounds without bromine atom in that position[16, 27]. In general, electron donating groups at position 5 of oxadiazole nucleus were found to exhibit more antimicrobial activity in comparison with the compound containing electron withdrawing groups in the same position.

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