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Synthesis and antimicrobial activities of 2-aryl-3,4-dihydro-4-oxo-5-bromobenzofuro[3,2-d]pyrimidines

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ABSTRACT

5-Bromo-3-amino-2-benzofurancarboxamide (1) on cyclisation with different aromatic aldehydes in ethanol gave corresponding 2-aryl-3,4-dihydro-4-oxo-5-bromobenzofuro[3,2-d]pyrimidines **(2-11)**. The structures of all the synthesized compounds have been assigned by spectral data. These compounds were screened for their antimicrobial activities.

KEYWORDS

5-Bromobenzofuron;
Pyrimidines;
Antimicrobial activities.

INTRODUCTION

Synthetic benzofuran derivatives have received considerable attention owing to their antimicrobial activity[1,2]. Benzofuran nucleus is widely distributed in natural product, particularly among plant kingdom. Many such compounds have been reported to possess very interesting pharmacological and physiological activities, such as insecticidal, fungicidal, antimicrobial and antioxidant properties[3,4]. The benzofuran ring system itself is a common structural element that appears in a large number of medicinally important compounds[5]. Pyrimidine ring fused benzofuran derivatives play vital role in many biological activities and as synthetic activities[6,12].

EXPERIMENTAL

General procedure

All the reagents were obtained commercially and used with further purification. The melting points were determined on an open capillary method and are uncorrected; IR spectra were recorded on Perkin-Elmer Spectrum ONE FTIR spectrophotometer. ^{1}H NMR spectra were recorded on AMX-400 AV III Solids NMR. The chemical shifts were expressed in the ppm (δ scale) downfield from TMS. Mass spectra were recorded on LCMS-2010A Data Report-Shimadzu and elemental analysis.

General procedure for the synthesis of 2-aryl-3,4-dihydro-4-oxo-5-bromobenzofuro[3,2-d]pyrimidines (2-11)

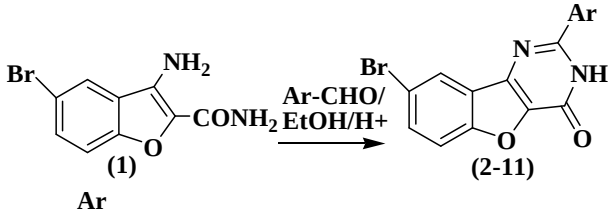
To a solution of 5-bromo-3-amino-2-benzofuran carboxamide(1) (0.001mol) in anhydrous ethanol (10ml) and aromatic aldehydes (0.001mol) and catalytic amount of conc. hydrochloric acid was added. The reaction mixture was heated at reflux temp for 4 hr. Upon cooling the solid separated was collected and crystallized from suitable solvents, physical and spectral data were described in the (TABLE 1).

RESULT AND DISCUSSION

5-Bromo-3-amino-2-benzofurancarboxamide **(1)**

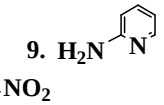
TABLE 1: Characterisation data of synthesized compounds (2-11)

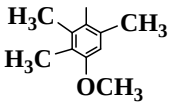
Comp no.	Yield (%)	M.P. (^{0}C)	Mol. formula	IR (cm^{-1})	^{1}H NMR (δ ppm)	CHN analysis (%); found/(Calculated)		
						C	H	N
2	69	260 (d)	$C_{16}H_9O_2N_2Br$	1700 cm^{-1}(CO),3220 cm^{-1} (NH)	s, 9.1 (-NH); m, 7-8 (Ar-H)	56.78 (56.30)	2.72 (2.64)	8.24 (8.21)
3	72	240 (d)	$C_{16}H_8O_2N_2ClBr$	3224 (NH),1747 (-CO)	S,9.4 (-NH), m,7-8(Ar-H)	51.22 (51.13)	2.09 (2.13)	7.51 (7.46)
4	60	190-191	$C_{18}H_{14}O_2N_3Br$	1747 (-CO), 3363 (NH)	S, 2 (6H, for –CH_3); m, 6.8-8 (Ar-H); s, 8.8 (NH)	56.66 (56.25)	3.71 (3.65)	10.81 (10.94)
5	64	276-278	$C_{16}H_8O_4N_3Br$	1667 (-CO), 3296 (NH)	-	49.86 (49.74)	2.11 (2.07)	1081 (10.88)
6	67	250-251	$C_{17}H_{11}O_3N_2Br$	1719 (-CO), 3276 (NH)	-	54.34 (54.99)	2.99 (2.96)	7.89 (7.99)
7	58	184-186	$C_{16}H_9O_3N_2Br$	1738 (CO), 3156 (NH)	-	-	-	-
8	76	194-195	$C_{17}H_{11}O_2N_2Br$	1718 (CO), 3122 (NH)	s, 7.3 (NH); s, 2.4 (-CH_3) m, 7.1-8.0 (Ar-H)	57.37 (57.46)	3.12 (3.10)	7.95 (7.89)
9	60	245-247	$C_{14}H_9O_2N_4Br$	-	-	48.81 (48.72)	2.67 (2.63)	16.18 (16.23)
10	54	226-228	$C_{20}H_{17}O_3N_2Br$	-	-	58.73 (58.13)	4.21 (4.13)	6.86 (6.78)
11	57	216-218	$C_{16}H_7O_4N_3Br_2$	1699 (CO), 3321 (NH)	s, 8.5 (NH); m, 7.1-8.2 (Ar-H)	48.78 (49.90)	1.96 (1.83)	10.80 (10.91)

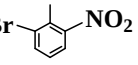


Ar

2. C_6H_5, 3. C_6H_4Cl(P), 4. $C_6H_4N(CH_3)_2$(P),
5. $C_6H_4NO_2$(P), 6. $C_6H_4OCH_3$(P), 7. C_6H_4OH
8. $C_6H_4CH_3$,







SCHEME

on reaction with substituted aromatic aldehydes in the presence of catalytic amount of acid gave corresponding 5-bromobenzofuran [3,2-d]pyrimidines **(2-11)** in acceptable yields. The structures of **(2-11)** were confirmed by analytical and spectral studies. The IR spectrum of compound **(2)** exhibited a broad absorption band at 3220 cm^{-1} due to NH stretching and another absorption band at 1700 cm^{-1}due to carbonyl group of pyrimidine ring. The ^{1}H NMR spectrum of compound **(2)** showed a multiplet at 7.5-8.0 δ due to aromatic protons and one singlet at 8.1 δ due to NH proton. Also, its mass spectra revealed a molecular ion peak at m/Z 343 (M^{+2}) corresponding to the molecular formula $C_{16}H_9O_2N_2Br$. The elemental analysis of the compound **(2)** shows C- 56.78% (found), (calculated 56.3%), H-2.72% (found), (calculated 2.64%) and N-8.24% (found), (calculated 8.21%) these values also corresponds to the molecular formula $C_{16}H_9O_2N_2Br$ and helps to elucidate the structure of compound **(2)**. The remaining all the synthesized compounds were confirmed by spectral and analytical data were discussed in TABLE 1. All the synthesized compounds were screened for antimicrobial activities.

Evaluation of antimicrobial activity

Antibacterial and antifungal activity

The *in vitro* antimicrobial activity was carried out against 24 hr old cultures of three bacteria and three fungi by cup-plate method. Compounds **(2-11)** has been tested for their antimicrobial activity against *S.aureus. B.subtils* and *E.coli* and antifungal activity against *A.niger, A.flamp* and *C.albicans* at a concentration of

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TABLE 2: Anti-microbial activity of the synthesized compounds

Compounds	Concc-^{n} (µg/ml) in DMF	* Zone of inhibition in mm					
		Antibacterial activity			Antifungal activity		
		S.aureus	*Bsubtilis*	*E.coli*	*A.niger*	*A.flamp*	*C.albicans*
2	1000	07	03	07	06	07	10
3	1000	06	08	08	07	06	09
4	1000	15	09	07	06	05	09
5	1000	05	09	03	09	06	16
6	1000	06	08	04	05	04	08
7	1000	12	14	07	11	13	12
8	1000	06	10	06	08	08	12
9	1000	07	04	05	15	07	15
10	1000	04	03	08	10	05	09
11	1000	05	07	08	14	08	10
Control	DMF	06	06	06	06	06	06
Standard	Ciprofloxin	9	12	10	-	-	-
Standard	Fluconazole	-	-	-	14	12	16

***Diameter of well (bore size) - 6 mm.**

1000 µg/ml in distilled DMF using cup plate diffusion method. Nutrient agar and potato dextrose agars were used to culture the bacteria and fungus respectively. The solution of Gentamycin 1000 µg/ml and Fluconazole 1000µg/ml were prepared in sterilized water and used as standards for comparison of antibacterial and anti-fungal activities respectively the results were discussed in TABLE 2.

The compounds **(4** and **7)** exhibiting good activity against *S.aureus* and compounds **(7)** showing good activity against *B.subtilis*. All remaining compounds exhibited moderate activity against all the organisms used for screening.

In anti-fungal activity the compounds **(4,5** and **12)** exhibited excellent activity against *A. niger* and compounds **(9)** and **(11)** exhibiting good activity against *A.niger* and compound **(7)** showed a good activity against *A.flamp* and compounds **(5** and **9)** showed a good activity against *C.albicans*, all remaining compounds exhibiting moderate activity against all the three organisms used for screening.

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