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Synthesis and Evaluation of Novel Oxopyrimidines Having Benzofuran Nucleus

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ABSTRACT:
The 6-(5-bromobenzofuran-2-yl)-3,4dihydro-4-substituted pyrimidin-2(1H)-onehave been synthesizedby the reaction of chalcones ofBenzofuran with urea in presence of potassium hydroxide in ethanol. All the compounds were synthesized by conventional method and characterized by IR and ^{1}H NMR analysis data. The synthesized compounds were screened for the antimicrobial activity.

Keywords: Benzofuran, oxopyrimidines, chalcone, antimicrobial activity

INTRODUCTION:

Heterocyclic synthesis has emerge powerful technique for generating new molecules useful for drug discovery [1]. Heterocyclic compounds provide scaffolds on whichpharmacophores can arrange to yield potent and selective drugs [2]. Benzofuran nucleus may be combinedwith nitrogen heterocycles in different ways. Several benzofuran compounds are reported to posses, antibacterial [3], antifungal [4], Anti-inflammatory [5], antidepressant [6], analgesic [7] and hypoglycemic activities [8]. It has already been pointedout that; benzofuran nucleus is very rarely associated with a nitrogen heterocycles.Dihydropyrimidines belong to an important class of heterocyclic compounds that have attracted interest due to their pharmacological and biological properties, such as antihypertensive, calcium channel blocking, alpha-1a-antagonism, neuropeptide Y(NPY) antagonism, antitumor, antibacterial, and anti-inflammatory activities[9-15]. The pyrimidine derivative MKC-442 is already in clinical trials and similar compounds are expected to inhibit the HIV virus [16]. Nucleosides containing the 5-substituted pyrimidine moiety have been demonstrated to inhibit growth of murine mammary carcinoma and HIV virus [17]. Pyrimidine based molecules with extended π-systems exhibited interesting fluorescent properties [18]. Synthetic strategies towards the dihydro pyrimidine nucleus involve one-pot to multistep approaches. In our present thesis work we are synthesizing new

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compound i.e. benzofuran fused with oxopyrimidine ring.

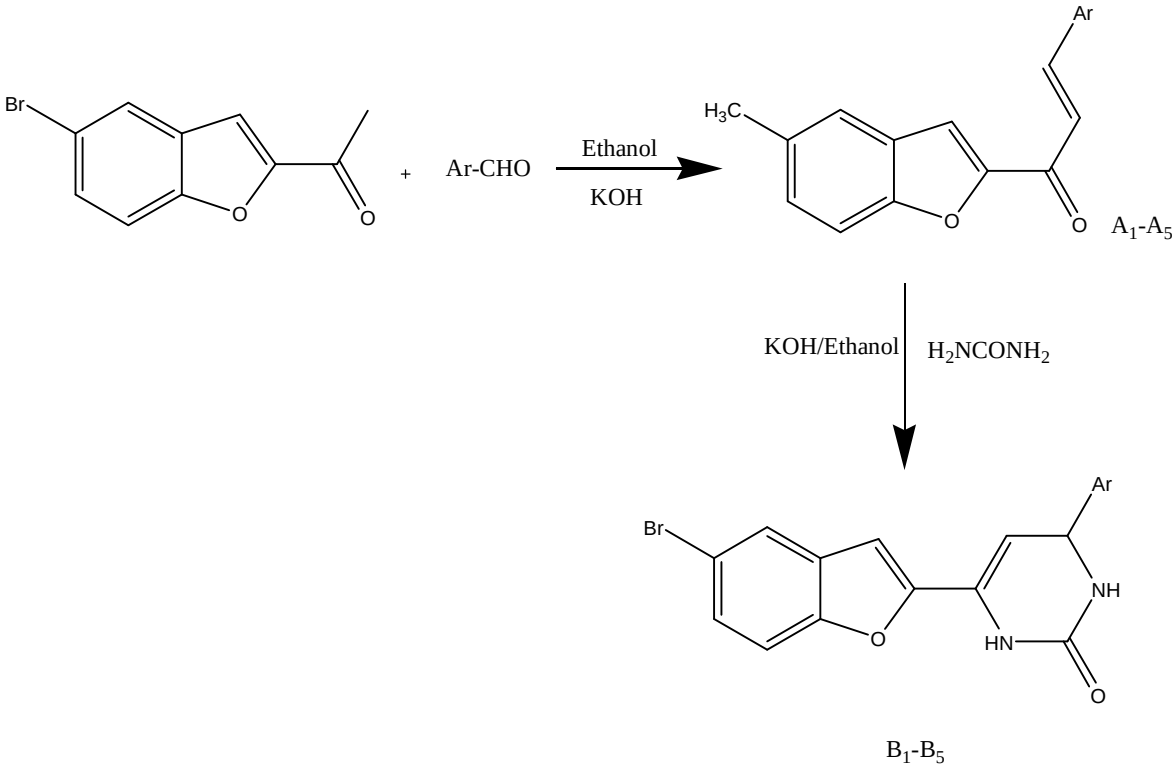
MATERIALS AND METHODS:

Melting points were determined on an open capillary melting point apparatus and are

Uncorrected. IR spectra were recorded on Brucker FT-IR (Alpha-P) spectrometer, ^{1}H NMR

Spectra were recorded in CDCl3 on Bruker "AVANCE 400" MHz spectrometer using TMS as an internal standardProgress of reaction was monitored by TLCusing ethylacetate: Pet.ether (2:8) solvent system and the spots were identifiedby iodinevapor chamber. Aromatic aldehydes, hydroxyl amine hydrochloride and KOH were purchased from Merk, India. The 2-acetyl benzofuran was prepared by Stoermer and Schaffer method [10, 11].All compounds have been recrystallized in ethanol.

REACTION SCHEME:



B_1-B_5

EXPERIMENTAL

Typical synthesis of 3-(4-chloro phenyl)-1-(5-bromobenzofuran-2-yl) prop-2-en-1-one (A_5).

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Equimolar quantities of 4-chlorobenzaldehyde (0.01mole), 1.40 gmand 2-acetyl-5-bromo benzofuran(0.01mole), 1.74gm were dissolved in minimum amount of ethanol.50 % 10 ml KOH solution was added slowly keeping the temperature of reaction mixture below 10^{o}C andthe reaction mixture was stirred for half an hrs. Then the mixture was kept for 24 hours at room temperature, the content of the flask was then made acidic carefully by drop wise addition of Conc.HCl and poured on crushed ice. The precipitate obtained was filtered, washed and crystallized from ethanol. Finally thecompound synthesized namely, 3-(4-chlorophenyl)-1-(5-bromobenzofuran-2-yl)prop-2-en-1-one(A_3),the completion of the reaction was monitored by TLC. Similarly various chalcones A_1-A_5were prepared.
Yield 70 %, MP: 131^{o}C.

Synthesis of 6-(5-bromobenzofuran-2-yl)-3,4dihydro-4-substituted pyrimidin-2(1H)-one from 3-(4-substituted)-1-(5-bromobenzofuran-2-yl) prop-2-en-1-one.

A suspension of chalcone (A_1) (0.01mole) and urea (0.02 mole) were dissolved in 40 ml of ethyl alcohol furtheralcoholic potassium hydroxide (50% solution.12 ml) was added.This mixture was refluxed for 7-8 hrs,the completion of the reaction was monitored by TLC, further on cooling the reaction mixture was poured on crushed ice with stirring and neutralized carefully with acetic acid. The obtained solid was filtered, washed with water and recrystallized from ethanol. Similarly various oxopyrimidines derivatives B_1-B_5 were prepared.Yield 59-66 %

Table-I Physical and analytical data of synthesized compounds (A_1-A_5)

Comp.	**Ar**	**Molecular formula**	**Yield %**	**M.P. ^{o}C**	**C %**	**H %**	**X %**
A_1	4-Methylphenyl	$C_{18}H_{13}BrO_2$	58	171	63.36	3.85	23.85
					(63.46)	**(3.29)**	**(24.01)**
A_2	4-Methoxy-phenyl	$C_{18}H_{13}BrO_3$	61	127	60.52	3.68	22.37
					(63.90)	**(4.08)**	**22.37**
A_3	4-hydroxy-phenyl	$C_{17}H_{11}BrO_3$	64	142	59.65	3.24	23.28
					(59.90)	**(3.30)**	**23.88**
A_4	4-Flurophenyl	$C_{17}H_{10}BrFO_2$	61	189	59.20	2.95	23.15(Br) 5.50 (F)
					(59.60)	**(2.89)**	**(23.08)Br 5.55(F)**
A_5	4-Chlorophenyl	$C_{17}H_{10}BrClO_2$	59	131	56.46	2.80	**(22.08)Br 9.80(Cl)**
					(56.30)	**(2.88)**	**(22.14)Br 9.72(Cl)**

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Table-II
Physical and analytical data of synthesized compounds (B_1-B_5)

Comp.	Ar	Molecular formula	Yield %	M.P. °C	Element analysis % cal. (found)			
					C %	H %	N %	X %
B_1	4-Methyl-phenyl	$C_{19}H_{15}BrN_2O_2$	59	168	59.55	3.95	7.31	20.85
					(59.66)	**(3.49)**	**(7.89)**	**20.75**
B_2	4-Methoxy-phenyl	$C_{19}H_{15}BrN_2O_3$	58	129	57.16	3.79	7.02	20.01
					(57.06)	**(3.20)**	**(7.34)**	**20.09**
B_3	4-hydroxy-phenyl	$C_{18}H_{13}BrN_2O_3$	57	176	56.12	3.40	7.27	20.74
					(56.36)	**(3.98)**	**(7.56)**	**20.94**
B_4	4-Fluro methyl	$C_{18}H_{12}BrFN_2O_2$	64	141	55.83	3.12	7.23	20.64(Br) 4.91(F)
					(55.45)	**(3.01)**	**(7.49)**	**20.94(Br) 4.71(F)**
B_5	4-Chloro-phenyl	$C_{18}H_{12}BrClN_2O_2$	61	162	53.56	3.00	6.94	**19.80(Br) 8.71(Cl)**
					(53.43)	**(3.56)**	**(6.87)**	**19.90(Br) 8.93(Cl)**

Spectral discussion:

3-(4-chloro phenyl)-1-(5-bromo benzofuran-2-yl) prop-2-en-1-one (A_5).

IR:(KBr, νmax, cm^{-1}): 2970 cm^{-1} (Ar--H),1679 cm^{-1}(C=O),1593 cm^{-1} (C=C), 1164 (C-O-C) 1455(CH=CH) . **^{1}H NMR:** ($CDCl_3$ in δ ppm) 6.40 (d, 1H,-CO-CH=), 7.01 (d, 1H, C=CH), 7.26-8.31(Complex m, 8H,Ar protons).

6-(5-bromobenzofuran-2-yl)-3,4-dihydro-4-p-tolylpyrimidin-2(1H)-one (B_1)

IR :(KBr, νmax, cm^{-1}): 3300-3500 cm^{-1} (N-H str.),2933 and 2837 (C-Harom.str.), 1664 cm^{-1}(C=O of N-CO-N),1251 cm^{-1} (C-O-C Str.),**^{1}H NMR:** ($CDCl_3$ in δ ppm): 2.39 (s,3H,Ar-CH_3), 5.58(s,1H,C_4 of oxopyrimidine),5.99(s,1H,C_5 of oxopyrimidine),6.96(s,2H,N-H of oxopyrimidine),6.70-7.70(Complex m, 8H,Ar protons).

Biological activity:

The antimicrobial activity was assayed by cup plate at the concentration of 500

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µg/ml.All the synthesized compounds were tested in vitro for their antibacterial activity against various microbes such as *S.typi* and *S.aureus*.The inhibition zone of the tested compounds was measured in mm.Antifungal activity against *A.niger*and *C.albicans*.Plate was incubated for 24hr for bacterial activity and 48 hr. for fungicidal activities.Pinicillin and Griseofulvin were used as standard. (Table-III)

Table-II Antimicrobial activity of the compounds

Compound	*Antibacterial activity Zone of inhibition (in mm)*		*Antifungal activity*	
	Salmonilatypi	*Staphylocus aureus*	*Aspergillusnigar*	*Candida albicans*
B_1	*16*	*28*	*+ ve*	*+ve*
B_2	*17*	*30*	*+ ve*	*+ve*
B_3	*19*	*32*	*+ve*	*+ve*
B_4	*18*	*34*	*+ ve*	*+ve*
B_5	*14*	*22*	*-ve*	*+ve*
Penicillin	*20*	*34*	-	–
Griseofulvin	–	–	*+ ve*	*+ ve*

Control (DMSO), (– ve) – No activity

Conclsion:

It has shows all prepared compounds have significant effect. It can be concluded from the Table III that compound **B_3**and **B_4** were active against both microbes such as *S.typi* and *S.aureus*.Compound**B_1,B_2,B_3&B_4** were found active against *A.nigar*, *C.albicans.*

REFERENCES:

1. Hermakens PH, Ottenheijm HC, Rees DC.*Solid-phase organic reactions II*: A *review of literature*. Nov95-nov96.Tetrahedron 1997;**53**:5643.
2. Gordon E, Barrett RW, Dower WJ, Foder SP. *J.MedChem*1994;**37**:1485.
3. Kirilmis C, Ahmedzade M, SüleymanS,Koca M, Kizirgil A. *Euro. J. Med.Chem.*, 2008, **43**, 300-308.

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4. Shazia N. Aslam, Philip C. Stevenson, SaraJ. Phythian, Nigel C. Veitch, David R. Hall..*Tetrahedron*, 2006, **62**, 4214-4226.
5. Balasaheb Y. Mane, Y.S.Agasimundin, B.Shivkumar, Devanand B. Shinde.*J. Chil. Chem. Soc*.,2009, **54(1)**, 77-79.
6. Malik WU, Mahesh VK, RaishighaniM.*Indian J.Chem*,1971, **9,** 655.
7. Fry DJ, Ficken EG, Burrows RW. *Brit.*,1969, **1**, 168495.
8. Brady BA, Kennedy JA, Süllivan WI..*Tetrahedron*,1973, **29,** 359-362.
9. Atwal K S, Rovnyak G C, O'Reilly B C, Schwartz J. J Org Chem1989; **54**: 5898-5907
10. Rovnyak G C, Kimball S D, Beyer B, Cucinotta G, Dimarco J D, Gougoutas J, Hedberg A, Malley M, McCarthy J P, Zhang R, Moreland S. J Med Chem 1995; **38**: 119 - 129.
11 Kappe C O, Fabian W. M. F., Semones M A. Tetrahedron 1997; **53:** 2803 -2816.
12 Hu E H, Sidler D R, Dolling U H. J Org Chem 1998; **63**: 3454-3457.
13 Atwal K S, Swanson B N, Unger S E, Floyd D M, Moreland S, Hedberg A, O'Reilly B C. J Med Chem 1991:806
14 Grover G J, Dzwonczyk S, McMullen D M, Normandin D E,Parham C S, Sleph P G, Moreland S. J CardiovascPharmacol 1995; **26**: 289 -294.
15 Rizzo R C, Tirado-Rives J, Jorgensen W L. J Med Chem 2001; **44**: 145 - 154.
16 Barral K, Courcambeck J, Pepe G, Balzarini J, Neyts J, Clercq E D, Camplo M. J Med Chem 2005**; 48:** 450-456 -
17 Itami K, Yamazaki D,Yoshida J. J Am ChemSoc 2004; 126: 15396 - 15397. [10] Biginelli P, GazzChimItal 1893; **23**: 360 -413.
18 Memarian H R, Mohammadpoor-Baltork I, Sadeghi M M, Samani Z S, Indian J Chem,2014,**32,**423-426.