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Synthesis, Characterization and Anti-microbial Activity of 3-{4-[3-chloro-2-(substitutedphenyl)-4-oxoazetidin-1yl] phenyl}-6-bromo-2-methylquinazoline-4-one

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ABSTRACT

Heterocyclic Compounds have so far been synthesized mainly due to the wide range of biological activities. Azetidine plays an important role in biological field. From these reviews we synthesized a new series of 3-{4-[3-chloro-2-(substituted phenyl)-4-oxoazetidin-1yl] phenyl}-6-bromo-2-methylquinazoline-4-one derived from the refluxes method of Schiff base in presence of tri-ethyl amine with chloro acetyl chloride is developed. The title compounds were characterized by element analysis, IR, NMR and spectral data. All the compounds were tested for their antibacterial and antifungal activities by Cup Borer method.

KEYWORDS

Azetidinones, IR, NMR, Cup Borer method.

INTRODUCTION

2-Azetidinones, commonly known as beta-lactams, are well-known heterocyclic compounds among the organic and medicinal chemists[1-3]. The activities of the famous antibiotics such as penicillin, cephalosporin, monobactams and carbapenems are attributed to the presence of 2-azetidinone ring in them. Azetidin-2-ones can be prepared from Schiff's bases, which are the condensation products of aldehydes and amino compounds. They are considered significant owing to their wide range of biological application. Recently, some other types of biological activity besides the antibacterial activity have been reported in compounds containing 2-azetidinone[4-6] ring.

From the literature, we found that several Azetidin-2-ones are known to display antimicrobial and therapeutic activities. Literature survey reveals scant mention of the above compounds with antimicrobial properties and hence more and more derivatives are worth tested for the possible medicinal applications

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EXPERIMENTAL

Melting points were taken in open capillary tube and were uncorrected. IR spectra were recorded on I.R. Spectrophotometer of Buck scientific Model No. 500 and instrument used for NMR Spectroscopy was Bruker Advance II 400 and DMSO used as internal standard. Solvent used were DMSO. Purity of the compounds was checked by TLC on silica- G plates. Anti microbial activities were tested by Cup-Borer method.

Procedure of 3-(4-{[(substitutedphenyl) methylene]amino}phenyl)-6-bromo-2-methyl quinazolin-4-one [1-(a-j)]

To a solution of 3-(4-aminophenyl)-6-bromo-2-methylquinazolin-4-one (0.01M) in absolute ethanol (60 ml), substituted aldehydes (0.01M) and a few drops of glacial acetic acid were added and the mixture refluxed for 10 h. It was then cooled, concentrated and poured into crushed ice and filtered. The product thus

obtained was purified by recrystallization from methanol to get compound 3-(4-{[(substitutedphenyl)methylene]amino}phenyl)-6-bromo-2-methylquinazolin-4-one.

IR ; [1-i] (Cm^{-1}) : 3350(-OH), 3064(=C-H, aromatic), 2926(-C-H, Stretch),1681(>C=O), 1614(>C=N-), 1539(>C=C<, aromatic ring), 1373(CH_3, bend), 1338(C-N), 1276(C-O-C), 540(C-Br).

^{1}H NMR (DMSO); [1-i]: 0.9066, singlate (3H) (-CH3), 3.9421, singlate (3H) (-OCH3), 8.3756, singlate (1H) (-N=CH-Ar), 6.5501-8.4065, multiplet at (11H) (Ar-H).

Procedure of 3-{4-[3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl]phenyl}-6-bromo-2-methylquinazolin-4-one.[2-(a-j)]

In a 100ml Round bottom flask 3-(4--[(substitutedphenyl)methylene]amino}phenyl)-6-bromo-2-methylquinazolin-4-one (0.01M) in 70ml benzene was taken.

Chloro acetyl chloride (0.01M) was added at room temperature with constant stirring and triethylamine 1ml was added and the reaction mixture was refluxed for 7 hours. After the completion of reaction, solvent was removed by vacuum distillation. The solid was filtered, dried and recrystallized from toluene.

IR(2i);(Cm^{-1}): 3091(=C-H,), 2884(-C-H stretch), 1705 (>C=O Stretch), 1653(>C=NStretch), 1558(>C=C<, aromatic),1394(-CH_3),1338(C-N),1252(-C-O),701(C-Cl),501(C-Br),3274(OH)

1H NMR (DMSO); (2g): 0.9224, Singlet (3H) (-CH_3), 3.1757, Doublet (1H) (>CH-Cl), 5.8278, Doublet (1H) (>CH-), 6.3621-8.5674, multiplate (11H) (Ar-H), 9.9660, Singlet (1H) (Ar-OH).

Reaction Scheme

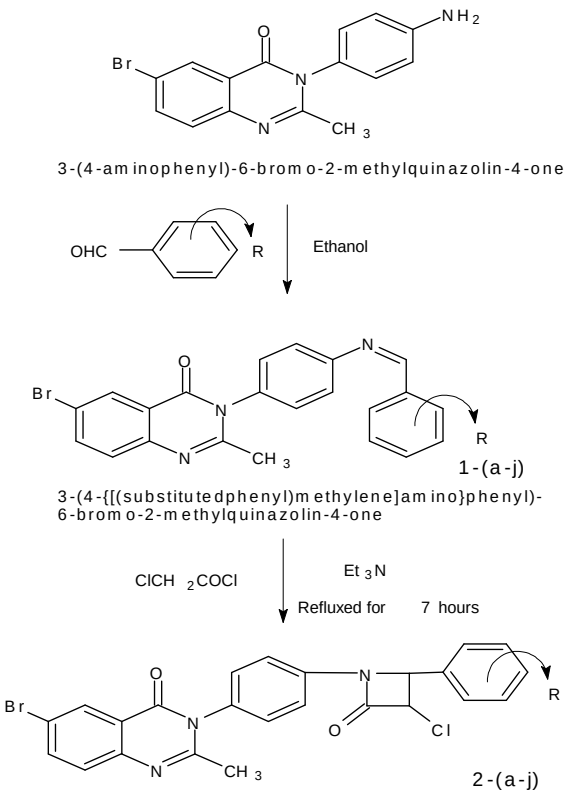

Table 1: Physical constant of 3-{4-[3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl]phenyl}-6-bromo-2-methylquinazolin-4-one

No.	Sub. No.	R	Molecular Formula	Mol. Wt. (g/m)	Yield (%)	M. P. ^{0}C	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
							Found	required	Found	required	Found	required
1	2a	-2-Cl	$C_{24}H_{16}BrCl_2N_3O_2$	529.21	79	110	54.43	54.47	3.01	3.05	7.90	7.94
2	2b	-4-Cl	$C_{24}H_{16}BrCl_2N_3O_2$	529.21	83	135	54.42	54.47	3.02	3.05	7.91	7.94
3	2c	-3-OCH_3,-4-OCH_3	$C_{26}H_{21}BrClN_3O_4$	554.81	84	128	56.24	56.28	3.80	3.82	7.53	7.57
4	2d	-H	$C_{24}H_{17}BrClN_3O_2$	494.76	75	163	58.22	58.26	3.43	3.46	8.44	8.49
5	2e	-2-OH	$C_{24}H_{17}BrClN_3O_3$	510.76	74	176	56.42	56.44	3.31	3.35	8.20	8.23
6	2f	-3-OCH_3,-4-OH	$C_{25}H_{19}BrClN_3O_4$	540.79	78	154	55.47	55.52	3.50	3.54	7.74	7.77
7	2g	-4-OH	$C_{24}H_{17}BrClN_3O_3$	510.76	81	120	56.40	56.44	3.32	3.35	8.20	8.23
8	2h	-4-$N(CH_3)_2$	$C_{26}H_{22}BrClN_4O_2$	537.83	83	180	58.02	58.06	4.10	4.12	10.39	10.42
9	2i	-4-OCH_3	$C_{25}H_{19}BrClN_3O_3$	524.79	84	202	57.18	57.22	3.61	3.65	7.98	8.01
10	2j	-3-NO_2	$C_{24}H_{16}BrClN_4O_4$	539.76	83	198	53.35	53.40	2.95	2.99	10.34	10.38

Table 2: Antimicrobial activities of 3-{4-[3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl] phenyl}-6-bromo-2-methylquinazolin-4-one

Sr. No.	Sample code	Microorganisms							*Yeast*
		E.coli NCIM 2066	*S.aureus* MTCC 737	*B.spizinzenii* MTCC 441	*P.aeruginosa* MTCC 1688	*S.paratyphi A* MTCC 735	*B.pumillus* MTCC 1607	*K.pneumoniae* MTCC 432	*C.albicans* MTCC 227
1	2a	21	20	22	15	22	21	20	NI
2	2b	20	23	21	14	19	22	20	20
3	2c	18	20	23	13	18	17	17	18
4	2d	17	18	18	12	16	19	15	18
5	2e	18	NI	19	17	19	19	18	19
6	2f	20	24	16	15	20	18	17	21
7	2g	20	16	19	16	NI	20	22	23
8	2h	17	17	21	13	15	20	19	22
9	2i	19	17	23	18	17	19	15	18
10	2j	21	20	22	15	19	20	16	22

Note: The digits in above cell are indicates diameter for the zone of inhibition in milimeter (mm)

CONCLUSION

The Main focus of this research work was to synthesize, characterize and evaluate antimicrobial activities of the newly synthesized Azetidinones derivatives, structures of synthesized compounds were confirmed and characterized with the help of analytical data's such as IR and ^{1}H-NMR. In summary, we have described the synthesis and antimicrobial activity of novel 3-{4-[3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl] phenyl}-6-bromo-2-methylquinazolin-4-one has shown good activity against the bacterial strains.

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