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Synthesis, Characterisation of some 2-azetidinone derivatives from 2-aminopyridine and evaluation of their antimicrobial activity

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ABSTRACT

In our present study 2-aminopyridine is condensed with different substituted aromatic aldehydes to form respective Schiff base. It was cyclised with chloro acetyl chloride to yield corresponding azetidinones. Structures of synthesised compounds were confirmed by physical and spectral analysis. The compounds are evaluated for their antimicrobial activities. The activities are due to cyclic CO-NH group in azetidinones. Some of the compounds have shown comparable antimicrobial activities .Out of these synthesized compounds, ***3c, 3e, and 3f*** *showed significant activity against all the microbial strains.*

Keywords: azetidinones, 2-amino pyridine, antimicrobial- screening

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INTRODUCTION

2-Azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds among the organic and medicinal chemists (1).The activity of the famous antibiotics such as penicillins, cephalosporins, monobactams and carbapenems are attributed to the presence of 2-azetidinone ring in them. Recently, some other types of biological activity besides the antibacterial activity have been reported in compounds containing 2-azetidinone ring. Such biological activities include antimicrobial, anti-tubercular, carbonic anhydrase inhibitors, local anesthetics, anti-inflammatory, anthelmintic, anticonvulsant, hypoglycemic activity(2,3,4).

2-amino pyridine is major moiety in the class of sulphonamide derivative. From these findings our research concentrates on the preparation of some Schiff base from 2- amino pyridine. These derivates on treatment with chloroacetyl chloride in presence of triethyl amine to form corresponding 3-chloro-4-phenyl-1-pyridin-2-ylazetidin-2-one derivatives

MATERIALS AND METHODS

Experimental

All the synthesized compounds were first purified by successive recrystallization using appropriate solvents . Melting points were determined in Melting point apparatus and the values were uncorrected . The purity of the compounds were determined by using TLC and iodine as the visualizing agent. IR spectra was determined by KBr pellets technique. ^{1}H.NMR was recorded by Burker AV.III-500 MHz using DMSO as solvent and TMS as internal standard. Chemical shifts were expressed in parts per million(ppm). Microanalyses for C,H,N were performed in Heraeus CHN Rapid Analyser and analyses indicated by the symbols of elements are wthin ±0.4% of theoretical values.The details of the synthesized compounds were shown in table no.1

(1) Synthesis of Schiff base

2- aminopyridine (0.01 mol) was dissolved in 30ml ethanol containing few drops of sulphuric acid . The appropriate aromatic aldehyde (0.01 mol) was added to the reaction mixture .It was refluxed for around 45 min , cooled and then poured into crushed ice.The solid obtained was filtered , washed with water and crystallized with ethanol(5,6,7).

(2) Synthesis of substituted azetidinones

To a stirred solution of substituted schiffs base (0.01 mol) , triethylamine in ethanol and chloroacetylchloride was added dropwise at room temperature . The reaction mixture was stirred for 5 hours and refluxed for 6 hours . A solid was obtained while cooling , which was recrystallised from ethanol and dried(8).

TLC for mobile phase: Benzene: ethyl acetate- 6:4

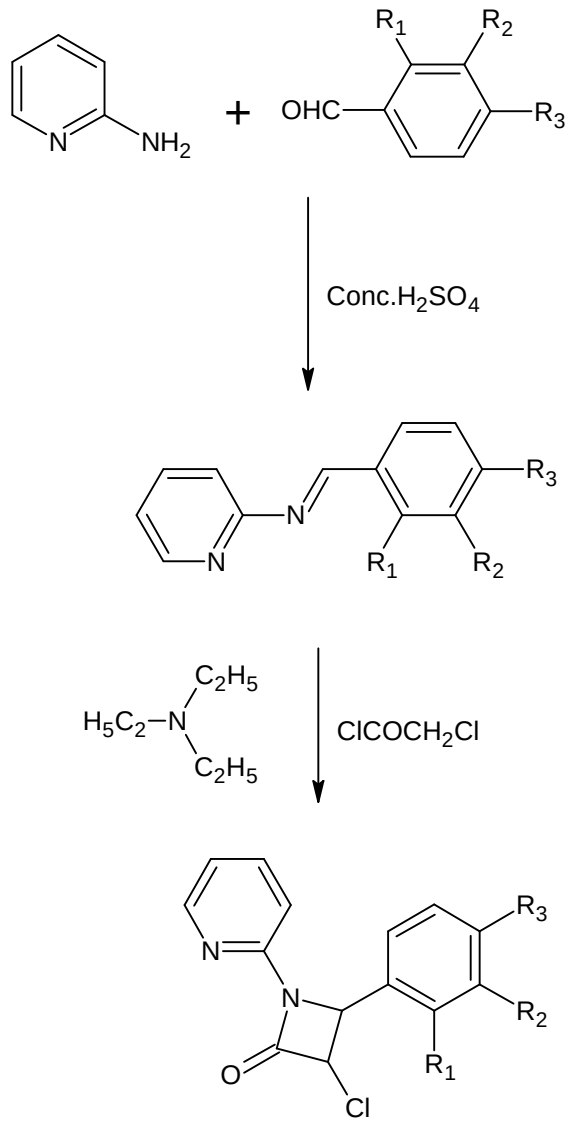
Table no:1 Details of the synthesized compounds

Compound code	R_1	R_2	R_3
3a	H	H	H
3b	H	H	$N(CH_3)$
3c	H	H	Cl
3d	H	H	OCH_3
3e	OH	H	H
3f	H	OCH_3	OH

Table no:2 Physical characterization of the synthesized compounds

compound	Molecular weight	Rf value	Melting point (^{0}C)	Elemental analysis Cal(found)		
				C	H	N
3a	258.70	0.67	144	65.00	4.29	10.83
3b	318.80	0.82	178	60.28	6.01	17.57
3c	310.17	0.47	222	54.21(54.10)	4.22(4.37)	13.55(13.61)
3d	305.75	0.61	165	58.92	5.27	13.74
3e	274.70	0.52	144	61.21(61.36)	4.04(4.12)	10.20(10.26)
3f	304.72	0.71	269	59.12(59.23)	4.30(4.39)	9.19(9.26)

Scheme of the present study



Compound 3a:
IR (KBr,cm^{-1}): 3021.52(Ar-CH),1632.21(N=C str), 1549.23(-CO-NH),806.61(CH-Cl)
^{1}H NMR(DMSO):7.8-8.1(4H of pyridine),6.7-6.9(5H of benzene),1.12(1H,CH-Cl),1.36(1H,N-CH-)

Compound 3c:
IR (KBr,cm^{-1}): 3011.52(Ar-CH),1632.41(N=C str), 1544.71(-CO-NH),808.54(CH-Cl), 1166.98(Ar-Cl),
^{1}H NMR(DMSO):7.65-8.41(4H of pyridine),6.67-6.94(4H of benzene),1.18(1H,CH-Cl),1.42(1H,N-CH-)

Compound 3d:
IR (KBr,cm^{-1}): 3041.56(Ar-CH),1636.56(N=C str), 1545.81(-CO-NH),810.54(CH-Cl), 2921.96(Methyl CH str),

Compound 3e:
IR (KBr,cm^{-1}): 1639.24(N=C str), 1548.81(-CO-NH),812.35(CH-Cl), 1375.30(OH-bend),

Compound 3f:
IR (KBr,cm^{-1}): 3031.52(Ar-CH),1629.48(N=C str), 1545.76(-CO-NH), 1373.37(OH-bend), 2926.43(Methyl CH str),
^{1}H NMR(DMSO):7.89-8.41(4H of pyridine),6.75-6.94(3H of benzene),1.14(1H,CH-Cl),1.35(1H,N-CH-)

***In vitro* Antimicrobial Screening**
The synthesized compounds were subjected to antimicrobial screening by cup plate method for zone of inhibition. The antibacterial activity was tested against various Gram positive and Gram negative bacteria and antifungal activity against various fungal strains compared with standard drug (Gentamycin and Griseofulvin) using solvent control (9). In order to account effects of DMSO a blank is also performed with that .The results were described in Table.3

Table no:3 Antimicrobial screening of the synthesized compounds

compounds	Zone of inhibition			
	Bacteria		Fungi	
	E.Coli	S.Aureus	C.Albicans	S.Cervisea
3a	0	8	11	3
3b	4	0	6	6
3c	14	13	18	13
3d	9	8	9	6
3e	12	13	20	14
3f	11	14	18	11
Standard(100µg/ml)	15	16	22	15
Solvent Control(DMSO)	-	-	-	-

(-) Indicates no activity

RESULT AND DISCUSSION

All the synthesized compounds were first purified by successive recrystallization using appropriate solvents. Then the synthesised compounds were subjected to spectral analysis such as FTIR ,^{1}H- NMR, and elemental analysis to confirm the structures .All the analytical structures show satisfactory result . The following peaks confirmed the formation of 2-azetidinones . The peaks at 1718-1687cm^{-1} , 806-800cm^{-1}, 1398.30cm^{-1} in FTIR have shown the groups of C=O, CH-Cl,C-N in 2-azetidinones respectively . In H-NMR Spectra the peaks at 1.4ppm and 2.18-2.52ppm for C-CH-Cl, N-CH-C groups have confirmed the formation of 2-azetidinones .

Some of the compounds have shown comparable antimicrobial activities .Out of these synthesized compounds, **3c, 3e, and 3f** showed significant activity against all the microbial organisms

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