SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF 2-AZETIDINONE DERIVATIVES OF 4-AMINO-1,2,4-TRIAZOLE

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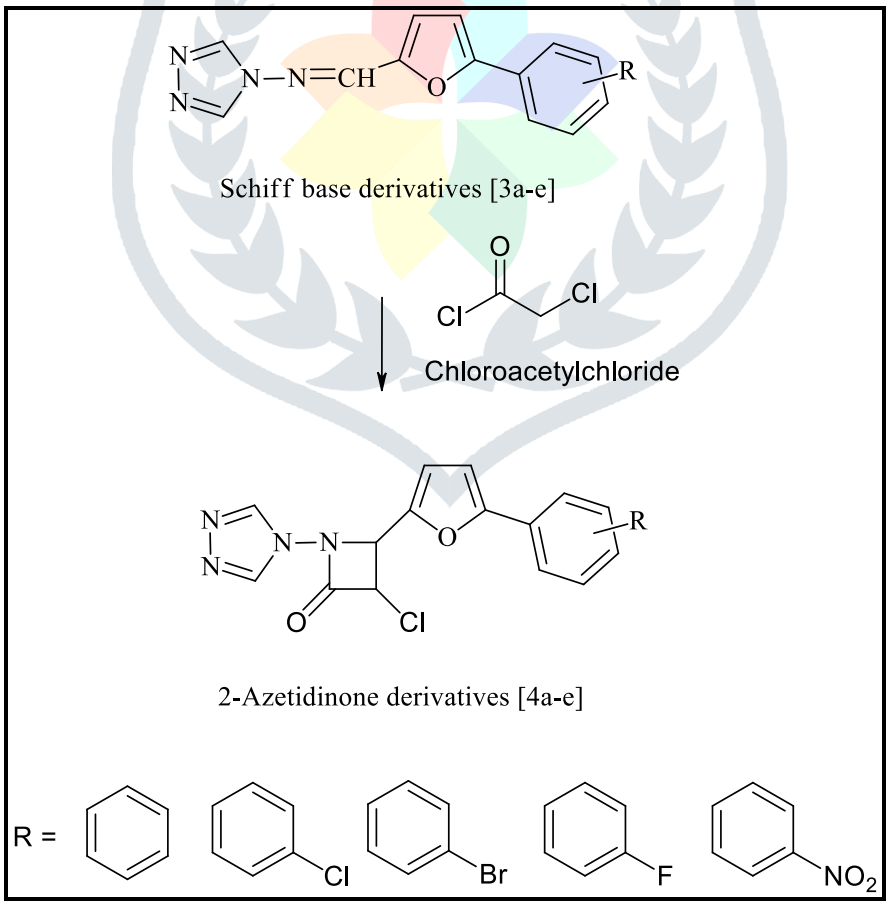
***Abstract*:** 2-Azetidinone derivatives, 3-chloro-4-(5-(subsitutedphenyl)furan-2-yl)-1-(4H-1,2,4-triazol-4-yl)azetidin-2-one [B1-5] were synthesized by reacting schiff base compounds, N-((5-(subsitutedphenyl)furan-2-yl)methylene)-4H-1,2,4-triazol-4-amine [A1-5] with chloro acetyl chloride. The newly synthesized 2-Azetidinone derivatives [B1-5] were characterized by using advanced analytical tools like NMR spectroscopy, IR spectroscopy and by Mass spectroscopy. All the newly synthesized compounds were evaluated for their Antimicrobial activity.

***Keywords*: 4-Amino-1,2,4-triazole,2-Azetidinone and antimicrobial activity.**

1. INTRODUCTION

4-Amino-1,2,4-triazole is one of the important heterocyclic compounds due to their pharmaceutical and biological activity like, antituberculer activity, antitumor activity, antileishmanial activity, anticonvulsant agents, anticancer activity, anti-inflammatory activities, antibacterial activities, antimicrobial activity, etc.[1-4] 2-Azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds.2-azetidinone derivatives demonstrates anti–Leukemic activity, tubercular activity, Anti-Inflammatory Activity, Anticonvulsant Agents, anticancer activity, anti- bacterial activity, antifungal activity, etc.[5-10] By reviewing the pharmaceutical and biological activity of 4-Amino-1,2,4-triazole and 2-Azetidinones,the present articles covers the synthesis of heterocyclic compounds which contains triazole and Azetidinones and evaluation of them for their Antimicrobial activity. The whole reaction path shown is as follow.



Reaction Scheme – 1

II. EXPERIMENTAL

2.1. Material and Methods

Chloroacetylchloride were procured from local market. All the other chemicals used directly without any purification.N-((5-(subsitutedphenyl)furan-2-yl)methylene)-4H-1,2,4-triazol-4-amine [A1-5] prepared by our earlier research work.[11]

Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively.

2.2. Preparation of 3-chloro-4-(5-(subsitutedphenyl)furan-2-yl)-1-(4H-1,2,4-triazol-4-yl) azetidin-2-one [B1-5]

The 2-Azetidinone derivatives (B1-5) were prepared from respective schiff base derivatives (A1-5) by reported method given in literature [12,13].

A schiff bases of (A1-5) (0.01 mole), Chloroacetyl chloride (0.02 mole), and triethyl amine (three drops) are charged into RBF using 1,4-dioxane (20 ml) solvent. The reaction mass were maintained 2 hour at reflux temperature. The solid were precipitated on cooling at o-10°C and stirred for 3- hours was filtered, dried in hot air oven at 40-45°C to give off white to light yellow crystals of 2-Azetidinone (B1-5). The overall yield obtained is about 60-70%.
The all characterization data of these compounds are given in Table -1.

Table:-1 Analytical Data and Elemental Analysis of Compounds (B1-5)

Compd.	Molecular formula (Mol.wt.)	Yield	M.P.* ^{0}C	Elemental Analysis					
				%C		%H		%N	
				Found	Calcd.	Found	Calcd.	Found	Calcd.
B1	$C_{15}H_{11}N_4O_2Cl$ (314.73)	65	132-133	57.20	57.24	3.50	3.52	17.80	17.80
B2	$C_{15}H_{10}N_4O_2Cl_2$ (349.17)	64	135-136	51.60	51.60	2.90	2.89	16.00	16.05
B3	$C_{15}H_{10}N_4O_2BrCl$ (393.62)	63	136-138	45.70	45.77	2.50	2.56	14.20	14.23
B4	$C_{15}H_{10}N_4O_2FCl$ (332.72)	65	148-150	54.10	54.15	3.00	3.03	16.80	16.84
B5	$C_{15}H_{10}N_5O_4Cl$ (359.72)	64	157-159	55.00	55.13	3.20	3.20	24.70	24.70

***** Uncorrected LC-MS data of B2-350.25,B4-333.80

III. ANTIMICROBIAL ACTIVITY

By agar cup plate method[14,15] the Antimicrobial activity of all the compounds was studied against gram-+ve bacteria (*B.megaterium* and *S.Aureus*) and gram- -ve bacteria (*E.coli and Ps.Aeruginosa*) at a concentration of 50µg/ML. A methanol system was used as control in this method. The area of inhibition of zone measured in mm. Compounds B4 was found more toxic for microbes. All compounds found to be less or moderate active shown in Tables -2.

Table:-2 Antibacterial Activity of Compounds (B1-5)

Compound (Designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B.megaterium	*S.Aureus*	*E.Coli*	*Ps.Aeruginosa*
B1	15	12	14	08
B2	17	15	08	12
B3	11	12	11	16
B4	15	16	11	14
B5	10	07	09	18

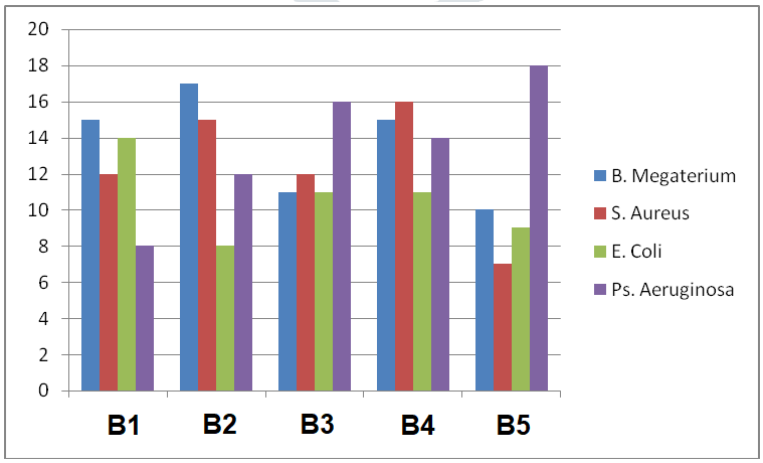


Figure 1 Antimicrobial activity comparison of Compound B1 to B5

IV. RESULTS AND DISCUSSION

The IR spectra of 3-chloro-4-(5-(subsitutedphenyl)furan-2-yl)-1-(4H-1,2,4-triazol-4-yl) azetidin-2-one [B1-5] showing an absorption bands at 3050-3053cm^{-1} (Aromatic C-H stretching),1298-1295 cm^{-1} (C-O-C of oxadiazine), 1667-1670 cm^{-1} (C=O stretching of Azetidinone),1625-1650 cm^{-1} (C=N),1080 cm^{-1} (-Cl),1555,1375 cm^{-1} (-NO_2), 710 cm^{-1} (C-Br), 1255 cm^{-1} (C-F). ^{1}H NMR: 5.25-5.27,5.62-5.65 (d, 2H of Azetidinone ring),7.43-9.25(m,7H of Aromatic) and 9.54-9.56(s,2H of triazole). ^{13}CMR spectral Features (δ, ppm):62-

65(Azetidinone ring),102-133(Aromatic,Furan,Triazole carbon), 165-166(C=O of Azetidinone ring). The C, H, N, S analysis data of all compounds are presented in Table-1.

The C, H, N, S analysis data of all compounds are presented in Table-1. LC-MS of selected samples B2 and B4 show the peak respectively at 350.25 and 333.80 which assign the molecular weight of compound,

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure.

V. CONCLUSION

The present study describes the synthesis and evaluation of the antimicrobial activity of 2-Azetidinone derivatives of 4-Amino-1,2,4-triazole. The synthesized compounds, therefore, present a new scaffold that can be used to as lead in the development of novel antimicrobial agents.

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