International Journal of
Medicinal Chemistry & Analysis

e ISSN 2249 – 7587
Print ISSN 2249 - 7595

www.ijmca.com

Research Article

SYNTHESIS AND CHARACTERISATION OF NOVEL SCHIFF'S BASE OF SULPHONAMIDE

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ABSTRACT

Currently used antimicrobial agents are not very useful due to the resistance developed by the microbes against them.The present study was aimed at synthesizing Schiff"s base of sulphonamide nucleus incorporated with para-substituted benzaldehyde showing good activity, with para- sulphonamido group playing a key role, and evaluating the potential of this agent as antimicrobial.The improvement achieved in potency of sulfonamide by introducing electron-withdrawing groups at the N1-position, which produced such highly potent drug as sulfadiazine, established the power of molecular modification in drug discovery. For the accomplishment of the proposed objective, the established method of synthesis with some modification was adopted, i.e. refluxing sulphonamide and para substituted derivative of benzaldehyde in absolute ethanol for 12-14 hours in water bath in Dean Stark Apparatus.The synthesized compound was subjected to physicochemical and spectral characterization.

Keywords: Antimicrobial Agent, Chemotherapy, Sulphonamides, Substituted benzaldehydes, Anti bacterial Agents, Anti fungal Agents, Heterocyclic.

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INTRODUCTION

Microbiologically produced drugs are known as antibiotics. The term antibiotic was introduced in 1942 by Waksman which mean substances produced by microorganism (microbial metabolic products) which suppress the growth of (static) or kill (cidal) the microorganism at very low concentrations. Several antibiotics have been identified and developed to the stage where they are of value in therapy of infectious diseases [1]. Sulpha drugs are a group of compounds used for eliminating a wide range of infections in human and other animal systems. Many therapeutically important sulphadrugs like sulphadiazine, sulphathiazole, sulphamerazine and so forth, posses SO_2NH_2moeity which is an important toxophoric function. The amide moiety is an important constituent of many biologically significant compounds.

The importance of sulphonamides nucleus is well established in pharmaceutical chemistry. The discovery of mode of action of sulfonamides led to development of many new and effective antimetabolites. Because of structural similarity of sulphonamides with PABA, it competes with this substrate for bacterial enzyme Dihydropteroate synthase (DHPs), thereafter inhibiting the formation of essential cofactor form. The improvement achieved in potency of sulfanilamide was done by introducing electron-withdrawing groups/heterocycles at the N1-position, which produced such highly potent drugs as sulfadiazine established the power of molecular modification in drug discoveryThe primary amino group (N-4) in sulfonamides is apparently vital for its activity against bacteria, since its substitution causes a loss of activity [2]. Schiff's Base was named

Access this article online

Home page: http://ijmca.com/

DOI: http://dx.doi.org/10.21276/ijmca.2017.7.2.3

Quick Response code

Received:29.05.17 **Revised**:06.06.17 **Accepted**:13.06.17

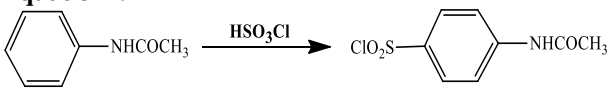
after Hugo Schiff, is a functional group that contains a carbon-nitrogendouble bond with the nitrogen atom connected to an aryl or alkyl group .Imine formation is acid catalysed, generally takes place fastest between pH 4 -5 and is slow at very low or very high pH [3,4].

MATERIAL AND METHODS

Procedure for step 1

A 500 ml two necked flask was equipped with a dropping funnel and a reflux condenser. Attached to the top of the condenser a device for the absorption of hydrogen chloride. 20g (0.148 mole) of dry acetanilide was placed in the round bottom flask and 50ml (90g; 0.77 mol) of a of chlorsulphonic acid in the dropping funnel and a calcium chloride guard tube was inserted into the later. Chlorsulphonic acid was added in small portions and flask was shaken from time to time to ensure thorough mixing. When the addition has been made, the reaction mixture was heated on a water bath for 1 hour in order to complete the reaction. Then it was allowed to cool and the oily mixture was poured in a thin stream with stirring into 300g of crushed ice (or ice water) contained in a 1- litre beaker. This operation was carried out carefully in the fume cupboard since excess of chlorsulphonic acid reacts vigorously with water. Flask was rinsed with a little and ice water and rinsing were added to the content of the beaker. Any lumps if formed were broken and mixture was stirred for several minutes in order to obtain a even suspension of granular white solid. *p*- acetamido benzene sulphonyl chloride was filtered off at the pump, washed with little cold water and drained well.

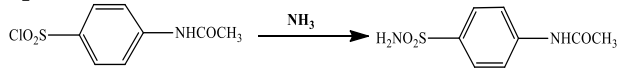
Equation1.



Procedure for Step 2

Mixture of 70ml of concentrated ammonia solution and 70ml of water was added to *p*-acetamido benzene sulphonyl chloride in a reaction flask. The contents of the flask were thoroughly mixed, and the mixture was heated with occasional swirling for 15 to 30 minutes. The sulphonyl chloride will be converted into pasty suspension of the corresponding sulphonamide. The suspension was cooled in ice, and then dilute sulphuric acid was added until the mixture is just acidic to litmus paper. Product was collected on Buchner funnel, washed with little cold water and drained as completely as possible. Product was dried at 100ºC, and is sufficiently pure [5].

Equation 2.

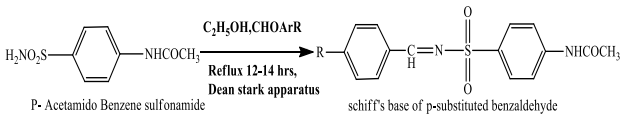


P- Acetamido Benzene sulhonyl chloride — P- Acetamido Benzene sulhonamide

Procedure for Step 3

A mixture of 2 (0.02 mole, 4.28g), p-substituted benzaldehyde (0.02 mole, 2.48 g) was taken in a Flat Bottom Flask fitted with $CaCl_2$ guard tube. Then 45 ml of absolute ethanol was added to it.1g of molecular sieves (4Å-5Å) and a pinch of $ZnCl_2$ (anhydrous) were added for absorption of water generated in reaction, refluxed for 12-14 hours in water bath in Dean Stark Apparatus. After the completion of reaction, the solvent was removed by vacuum distillation and reaction mixture poured in crushed ice. Schiff's base was filtered, dried and recrystallised from absolute ethanol [6-10].

Equation 3.



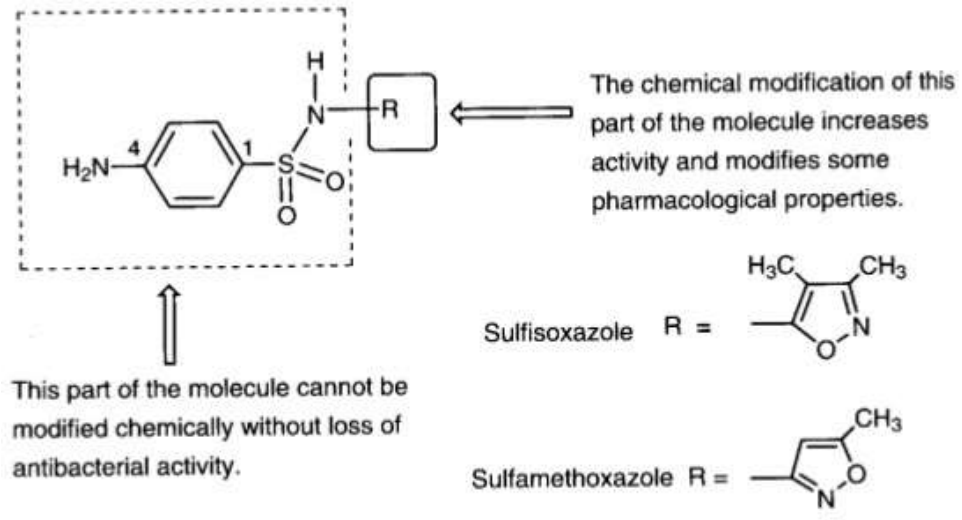
P- Acetamido Benzene sulfonamide — schiff's base of p-substituted benzaldehyde

Table 1. Characterization of synthesizes compounds

S.No	Compound	Mol. Formula	Mol. Wt.	Elemental Analysis	INTERPRETATIONS OF IR PEAKS	MOLECULAR ION PEAK
1.	Compound 1	$C_8H_8ClNO_3S$	232	C, 41.12; H, 3.45; Cl, 15.17; N, 5.99; O, 20.54; S, 13.72	C-H Aromatic peak at 3500-3050 NH peak at 3500-3100 C=O peak at 1780-1600 C=C Aromatic peak S=O peak of sulphonamides at 1375-1140 C-Cl peak at 800 – 600	Molecular ion peak at 232,234

2.	**Compound 2**	**$C_8H_{10}N_2O_3S$**	**214**	**C, 44.85; H, 4.70;N, 13.08; O, 22.40; S, 14.97**	**C-H Aromatic peak at 3500-3050 NH_2 peak at 3500-3400 NH peak at 3500-3100 C=C Aromatic peak C=O peak at 1780-1600 S=O peak of sulphonamides at 1375-1140**	**Molecular ion peak at 214,215 and 216**
3.	**Compound 3a**	**$C_{15}H_{14}N_2O_3S$**	**302**	**C, 59.59; H, 4.67; N, 9.27; O, 15.88; S, 10.61**	**C-H Aromatic peak at 3500-3050 NH_2 peak at 3500-3400 NH peak at 3500-3100 C=C Aromatic peak C=O peak at 1780-1600 S=O peak of sulphonamides at 1375-1140**	**Molecular ion peak at 302,303and 304**
4.	**Compound 3b**	**$C_{15}H_{13}N_3O_5S$**	**347**	**C, 51.87; H, 3.77;N, 12.10; O, 23.03; S, 9.23**	**C-H Aromatic peak at 3500-3050 NH_2 peak at 3500-3400 NH peak at 3500-3100 C=C Aromatic peak C=O peak at 1780-1600 S=O peak of sulphonamides at 1375-1140**	**Molecular ion peak at 347 and 348**
5.	**Compound 3c**	**$C_{15}H_{14}N_2O_4S$**	**318**	**C, 56.59; H, 4.43; N, 8.80; O, 20.10; S, 10.07**	**C-H Aromatic peak at 3500-3050 NH_2 peak at 3500-3400 NH peak at 3500-3100 C=C Aromatic peak C=O peak at 1780-1600 S=O peak of sulphonamides at 1375-1140**	**Molecular ion peak at 318 and 319**

Fig 1. SAR of Sulphonamides



RESULTS AND DISCUSSION

The synthesized compounds were subjected to physicochemical and spectral characterization. The compounds were purified by column chromatography by using different grades of silica gel of column packing. The Rf. values of synthesized compounds were determined. IR was done by applying 10 lbs sq. inch of pressure for about 2 minutes. The pellets were exposed to IR radiation using Shimadzu FTIR spectrophotometer to obtain the spectra. Mass spectra were recorded on Jeol/SX-102/DA-600 FAB mass spectrophotometer carried in SAIF department of CDRI, Lucknow. (Table 1) [11-13].

CONCLUSION

The importance of sulphonamides is well established in pharmaceutical chemistry. A considerable number of sulphonamides are well known as antibacterial, carbonic anhydrase inhibitor, anticancerous, anti-inflammatory agents [14]. Sulfonamides are widely used in clinical practice even six decades after their discovery because of their wide pharmacologic and pharmacokinetic profile. In the current trend, this choice has declined due to gradual increase in resistance to them. Even though they are safe drugs but many adverse reactions appeared which suggested scientists to synthesize new derivatives, which are devoid of any adverse effects [15]. Furthermore, accordingly in order to improve the previously observed activities it was decided to attach 4- amino sulphonyl phenyl group to some peculiar para substituted benzaldehydes [16]. The existing work shows that the sulphonamides nucleus acting as central and crucial scaffold with benzaldehydes derivatives having para substituents can lead to development of highly potent compounds having good to moderate level of various activities. After generating more and more new derivatives and assessing their biological activity data, one can go for exploration and study of the generated structures at molecular level and can easily correlate to their Structure Activity Relationshipwhich will give abetter model for the structure optimization. Thus, information obtained from this study can utilized as a tool for further development of novel drug molecules.

ACKNOWLEDGEMENT

I am thankful to SAIF department, CDRI Lucknow for their contribution to spectral studies

CONFLICT OF INTEREST

There is no conflict of interest in present study.

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Cite this article:
Smriti Sahu. Synthesis and Characterisation Of Novel Schiff's Base of Sulphonamide. *International Journal of Medicinal Chemistry & Analysis*, 2017; 7(2): 59-62. DOI: http://dx.doi.org/10.21276/ijmca.2017.7.2.3