

# Diazo Linkage Based Schiff Bases: Synthesis, Characterization and Their Biological Applications

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**Abstract-** The chemistry of compounds possessing Schiff base moiety and Diazo moiety have been an interesting field of research since long time. 4-aminoacetophenone was taken with thiourea which gives 4-(4-amino)phenyl-2-aminothiazole, which on reaction with sodium nitrite give its diazo salt. 4-(4-amino)phenyl-2-aminothiazole is then reacted with its diazo salt to obtain bis-thiazole. Diazo linkage containing bis-thiazole derivative 4-(4-amino-phenyl) -5-[4(4-amino)-thiazol-2-ylazo]-thiazole-2-ylamine, is further condensed with 'S aromatic aldehydes and ketones which gives a series of newly synthesized Schiff base. Synthesized derivatives of Schiff base are characterized by the physico-chemical, physiological and IR, NMR. All synthesized compounds are screened for their antibacterial and antifungal activity by using agar well diffusion method. The outcomes revealed that the compound 4A and 4B show excellent activity and compound 4D show moderate activity against *P. aeruginosa*. Similarly Compound 4A, 4B, and 4D are shown excellent against *E.coli* and compound 4C show mild anti-bacterial activity against *E.coli*. The compound 4C show excellent anti-fungal activity against *A. niger* and 4D show moderate against *A.niger*. Similarly compound 4B and 4D show moderate and compound 4A show excellent anti-fungal activity against *Candida albicans*.

**Keywords-** Diazo, Azomethine linkages and Biological applications.

## I. INTRODUCTION

Pathogens are micro-organisms that has the potential to cause disease. A few harmful microbes, for example less than 1% of bacteria, viruses and fungus invade our body causing illness and are accountable for the substantial morbidity and mortality. The chemistry of compounds possessing Schiff base moiety and diazo moiety have been a fascinating field of research since long time. Schiff Base Moiety (>C=N-) show various biological applications such as anti cancer<sup>[01]</sup>, anti tuberculostatic<sup>[02]</sup>, diuretic<sup>[03]</sup>, antibacterial<sup>[03]</sup>, anti fungal<sup>[03]</sup> and anti inflammatory<sup>[04]</sup>, apart from their role in dye and agrochemical industries.<sup>[05]</sup> Literature survey exposed that work on diazo moiety (-N=N-) have been broadly studied for its spacious range for their

therapeutic significance and furthermore important in pharmaceutical fields <sup>[06]</sup>

Diazo compounds have increased a lot of significance due to their diverse biological applications including antiseptics<sup>[07]</sup>, antineoplastics<sup>[08]</sup>, antibacterial<sup>[09-10]</sup> antidiabetics <sup>[11]</sup> and antitumor<sup>[12]</sup>. In addition to dye and pigment industry<sup>[13]</sup> the azo compounds are appropriate for biocidal treatment of textile materials because they exhibit biological activity.

## II. OBJECTIVE

Schiff base moieties are well known for their various physiological and pharmacological activities. On the other hand, Diazo moieties have been additionally found to have anti-inflammatory and other useful chemotherapeutic agents<sup>[14-15]</sup>.

Considering all the above facts, it was found that the Diazo moiety when introduced with the Schiff base moiety, the compound synthesized may have some remarkable pharmacological and microbiological activity.

## III. MATERIAL AND METHODS

All the chemical reagents and solvents were purchased commercially and used without any further purification. The melting points of compounds were recorded on a hot stage Gallen Kamp melting point apparatus in open capillary and was found uncorrected.

The characterization of synthesized compounds were determined by the <sup>1</sup>HNMR, infrared and physical properties.

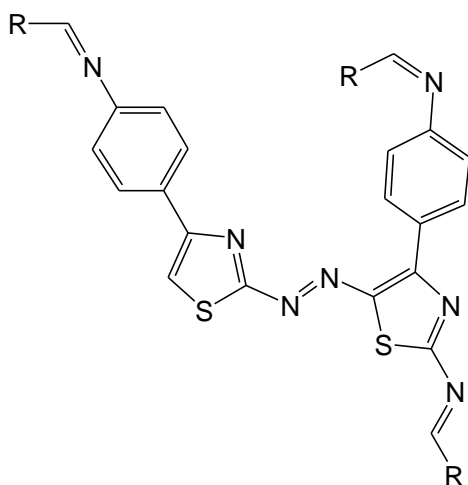
### Method of Synthesis of Schiff base series

4-aminoacetophenone was taken with thiourea which gives 4-(4-amino)phenyl-2-aminothiazole (**1**). This 4-(4-amino)phenyl-2-aminothiazole was then dissolved in HCl and diazotized by reacting with sodium nitrite (NaNO<sub>2</sub>) dissolved in water which gives its diazo salt (**2**). This diazotized thiazole (**2**) was substituted on the primary thiazole compound -(4-

amino)phenyl-2-aminothiazole (1) which gives a bis-thiazole compound 4-(4-amino-phenyl)-5-[4-(4-amino-phenyl)-thiazol-2-ylazo]-thiazol-2-ylamine (3).

A series of substituted aldehyde and ketone was then condensed with 4-(4-amino-phenyl)-5-[4-(4-amino-phenyl)-thiazol-2-ylazo]-thiazol-2-ylamine (3) dissolved in ethanol (3:1 molar ratio). The mixture was stirred for 2-3h for the completion of reaction, as monitored by TLC and was evaporated under reduced pressure. The product obtained was filtered off and recrystallized from ethanol/acetone to obtain Schiff bases (4A-4D).

#### General structure of Schiff Bases:



Where R = p-hydroxyacetophenone, benzophenone  
p-chlorobenzaldehyde, Vanillin

#### IV. RESULTS AND DISCUSSION

All novel synthesized Schiff bases were found to be stable in air at room temperature. They are soluble in Chloroform, DMSO and acetone, partially soluble in methanol and ethanol but insoluble in water. The physical properties of all synthesized compounds reported in table (1). The approximate yield recorded was 10-30% and their melting point ranged from 182- 218 °C.

All compounds are brown in colour and they gave satisfactory results for IR, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR.

**Table (1): Physical properties of newly synthesized Schiff bases with diazo moiety.**

Comp Code	Molecular Formula	Name of derivatives of Schiff's bases	Color	MP (°C)	Yield %
4A	C <sub>27</sub> H <sub>29</sub> N <sub>7</sub> S <sub>2</sub>	Benzhydrylidene-4-[4-(benzhydrylidene-amino)-phenyl]-5-[4-[4-(benzhydrylidene-amino)-phenyl]-thiazol-2-ylazo]-thiazol-2-yl-amine	Brown	198	36.11
4B	C <sub>39</sub> H <sub>24</sub> N <sub>10</sub> O <sub>6</sub> S <sub>2</sub>	(4-Nitro-benzylidene)-[4-{4-[(4-nitro-benzylidene)-amino]-phenyl}-5-{4-[(4-nitro-benzylidene)-amino]-phenyl}-thiazol-2-ylazo)-thiazol-2-yl]-amine	Red/Brown	216	36.78
4C	C <sub>39</sub> H <sub>24</sub> Cl <sub>2</sub> N <sub>7</sub> S <sub>2</sub>	(4-Chloro-benzylidene)-[4-{4-[(4-chloro-benzylidene)-amino]-phenyl}-5-{4-[(4-chloro-benzylidene)-amino]-phenyl}-thiazol-2-ylazo)-thiazol-2-yl]-amine	Brown	218	8.6
4D	C <sub>42</sub> H <sub>33</sub> N <sub>7</sub> O <sub>6</sub> S <sub>2</sub>	4-((E)-((4-(2-((E)-2-((Z)-(4-hydroxy-3-methoxybenzylidene)amino)phenyl)thiazol-1-5-yl)diazenyl)-4,5-dihydrothiazol-4-yl)phenyl)imino)methyl)-2-methoxyphenol	Brown	182	5.6

#### Infrared spectra of newly synthesized Schiff bases with Diazo moiety

They are characterized by a azomethine moiety (C=N) at 1668 cm<sup>-1</sup>, thiazole moiety (C=N) at 1591 cm<sup>-1</sup>, diazo moiety (N=N) at 1425 cm<sup>-1</sup>, (C-S) at 826 cm<sup>-1</sup>, (C-H) of the benzene ring at 2894 and (C-H) of -CH<sub>3</sub> at 3213 and few other stretching are mentioned in table (2).

**Table (2): Some infrared of newly synthesized Schiff bases with Diazo moiety.**

S.No	Group	cm <sup>-1</sup>
1	OH	3449
2	NO <sub>2</sub>	1341
3	C-Cl	687

#### <sup>1</sup>H-NMR spectrum of newly synthesized Schiff bases with diazo moiety

The <sup>1</sup>H-NMR spectrum of the Schiff base as shown in figure(2), was measured using DMSO as solvent. Spectral analysis of Schiff base show multiple peaks at δ =6.63-8.45 ppm attributed to the phenyl ring. The single peaks at δ =1.72 ppm due to the CH<sub>3</sub> group in the compound respectively. Schiff base H-C=N show single peak at δ=8.31 ppm which is assigned due to the presence of protons of azomethine group.[23,24]. The result are tabulated in table (3).

**Table 3: 1H -NMR data of the Schiff bases**

S.No	Group	$\delta$ (ppm)
1	CH <sub>3</sub> (methyl)	1.72
2	C-H (Phenyl ring)	6.63-8.45
3	C-H (azomethine)	8.31
4	O-H	9.85
5	C-S (Thiazole)	7.76

## V. BIOLOGICAL STUDIES

Antimicrobial screening was done using well-diffusion test given by Bauer *et al.*, (1966). The filter no. 1 disc of 6mm diameter was impregnated with different concentrations (20%, 50%, and 100%) of 4A, 4B, 4C and 4D. The disc was placed in the center of pre-inoculated culture plates and incubated for 24 hrs at 37 °C. After incubation, plates was observed for the sensitivity of the test extract against microorganisms in terms of zone of inhibition (ZOI). The zone of inhibition was measured by using transparent plastic ruler scale.

**Table 04: Antimicrobial activity of compound code 4(A-D) against pathogens.**

Code	Name of Bacteria	Bacterial Culture-Zone of Inhibition Concentration in % (mm)			Name of Fungal	Fungal Culture-Zone of Inhibition concentration in % (mm)		
		20	50	100		20	50	100
4A	<i>P.aeruginosa</i>	+	+	+	<i>Candida albicans</i>	+	+	+
	<i>Escherichia coli</i>	+	+	+	<i>Aspergillus niger</i>	-	-	-
4B	<i>P.aeruginosa</i>	-	+	+	<i>Candida albicans</i>	-	+	+
	<i>Escherichia coli</i>	-	+	+	<i>Aspergillus niger</i>	-	-	-
4C	<i>P.aeruginosa</i>	-	-	-	<i>Candida albicans</i>	-	-	-
	<i>Escherichia coli</i>	-	-	+	<i>Aspergillus niger</i>	+	+	+
4D	<i>P.aeruginosa</i>	-	-	+	<i>Candida albicans</i>	+	+	+
	<i>Escherichia coli</i>	-	+	+	<i>Aspergillus niger</i>	-	-	+

## VI. CONCLUSION

We have developed the easier and simple synthetic technique of Schiff base related diazo moiety containing derivatives and the reactions occurred much secured, under modest condition using reasonable solvents and reagents. The

anti-bacterial activity of newly synthesized novel Schiff bases with diazo moiety were effectively screened against Gram-negative *P. aeruginosa* and *E. coli* bacterial strains. Compound 4A and 4B show excellent activity against *P. aeruginosa* and compound 4D show moderate against *P. aeruginosa*. Compound 4C show moderate and 4A, 4B and 4D show excellent against *E.coli*.

The antifungal activity of synthesized compounds were checked against *Candida albicans* and *A.niger*. The compound 4C show excellent anti-fungal activity against *A. niger* and 4D show moderate against *A.niger*. Similarly compound 4B and 4D show moderate and compound 4A show excellent anti-fungal activity against *Candida albicans*.

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