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Research Article

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Studies on synthesis of aldimines: Part-III. synthesis, spectral characterization and bioactivity of salicylaldimines

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ABSTRACT

Compounds containing >C=N- (azomethine) were prepared from Salicylaldehyde with Aniline derivatives by conventional chemical synthesis method. The products are tested in process and the completion of reaction product formation was ascertained by TLC. The final products were characterized by physical viz. m.p., analytical viz. TLC, Instrumental viz. UV-Vis and FTIR spectral techniques. Results showed that all the marked activity coefficients(biopotential) for the studied compounds are less than the standard drug, Ketoconazole.

KEYWORDS: Imine, Aldimine or Azomethine, Salicylaldehyde, TLC and biological activity

INTRODUCTION

Schiff bases is a very big scaffold discovered by a German chemist, Hugo Schiff in 1864 [1]. They are condensation [2] products of primary amines and carbonyl compounds with the elimination of water molecule (Scheme 1). The class of compounds containing an imine or an azomethine (–HC=N–) group in their structure is known as imine compound. These compounds have been widely explored for industrial applications.

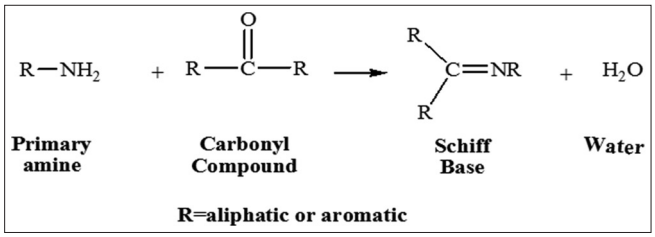
Schiff bases are of aromatic nature, more easily synthesized and more stable. Schiff's bases of aliphatic aldehydes are relatively unstable and readily polymerizable [3,4] while those of aromatic aldehydes having effective conjugation are more stable [5].

The catalyst used for >C=N- formation are acidic and basic in nature [6] and operates through protonation of carbonyl carbon. The reaction is reversible and the equilibrium must often be shifted towards forward direction by the removal of water, either by distillation or with a drying agent such as molecular sieve or $TiCl_4$ [7-8].

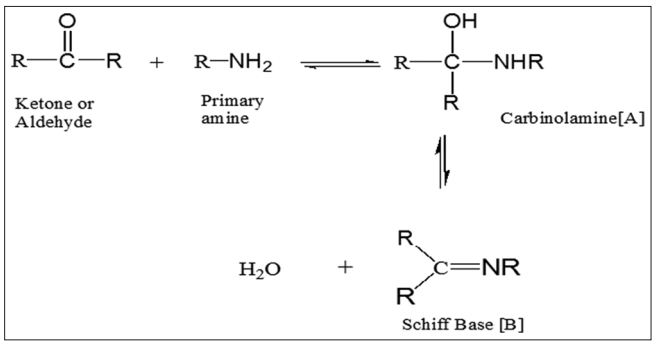
The mechanism of formation of Schiff base is as given in Scheme 2.

Survey of Literature showed following outcomes. The formation constants of some transition metal ions - binary complexes containing Schiff bases resulting from condensation of salicylaldehyde with aniline, 2-aminopyridine, 4-aminopyridine and 2-aminopyrimidine were determined pH-metrically in ethanolic medium (80%, v/v). The solid complexes have been synthesized and studied by thermogravimetric analysis [9]. The conductive polymers were prepared by using imine derivatives. Schiff bases as an electrical conductor possess a variety range of use as catalysts in photo-electrochemical processes, micro-electronic equipment and electrode materials, organic batteries or electrochromic display device [10].

The organic compounds were studied by spectral [11] method. In addition to spectral method literature shows reports on the electrochemical characterization of aldimines [12-14] and ketimines [15] and some complexes were studied by electrochemical kinetics [16-17]. The aldimines and ketimines are useful as antibacterial agent [18-19] antifungal agent [20-21] and also in the treatment of cancer [22]. Recently, we have reported [23] aldimines from Benzaldehyde with seven different aromatic amines viz. Aniline, 2-Choro-aniline, 3-Choro-aniline, 4-Choro-aniline, 2-Nitro-aniline, 3-Nitro-aniline and 4-Nitro-aniline. Similarly, aldimine



Scheme 1: General reaction of formation of Schiff base or Aldimine

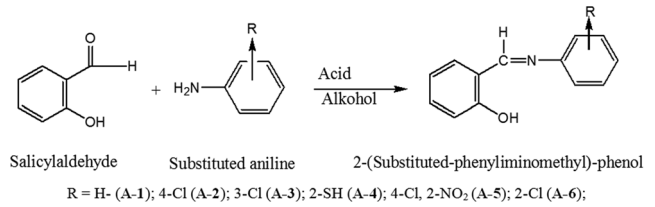


Scheme 2: General steps in formation of Schiff base or Aldimine via an Intermediate, Carbinolamine

from Benzaldehyde with Aniline and reported [24] their TLC and spectral behaviour. The synthesis of salicylideneaniline and derivatives [25] and their spectral characterization and biological activity is also reported.

From above glimpses, we have proposed to study the reaction of Salicylaldehyde with Aniline and its varied derivatives viz. 4-Chloroaniline, 3-Chloroaniline, 2-Aminothiophenol, 4-Chloro-2-nitro aniline and 2-Chloroaniline further, to analyze their purity and characterization by colour, physical constant, yield and their FTIR spectra.

Scheme of Present Work



R = H- (A-1); 4-Cl (A-2); 3-Cl (A-3); 2-SH (A-4); 4-Cl, 2-NO_2 (A-5); 2-Cl (A-6);

MATERIALS AND METHODS

All the chemicals such as Ethyl acetate, Methanol, Salicylaldehyde, Aniline, 4- Chloroaniline, 3-Chloroaniline, 2-Aminothiophenol, 4-Chloro-2-nitro aniline and 2-Chloroaniline are of synthesis grade. The colour by visual method and the physical constants i.e. melting points were also recorded in °C, in one end sealed capillary and are uncorrected. FTIR spectral frequencies were measured on a Shimadzu FTIR Affinity-1 spectrophotometer using KBr pellet and λ_{max} values(in nm).

EXPERIMENTAL DETAILS

General Method of Synthesis for Imine or Schiff Base

The methanol solution of Salicylaldehyde and add to it an aniline solution in methanol in equimolar (0.02 mole) proportion, add few ml of acetic acid and the requisite amount of solvent methanol, is added into 250 ml round bottom flask, some porcelain pieces were also added into round bottom flask, at the last attach the reflux condenser.

The mixture of reaction is heated on water bath for 2 or more hours. The completion of reaction is decided on the basis of TLC monitoring. The heat is provided till to complete the reaction, checked by TLC till to consume all the aniline. In the reaction mass solid products were obtained. The products were recrystallized using ethanol, record the weight of dry product and calculate it's yield, determine the physical constant (m.p.) and abbreviate the product as A-1.

Similarly, using above procedure and replacing aniline by different aniline derivative, the products A-2 - A-6, were synthesized.

After confirming the desired molecular structures are confirmed, these Aldimines were screened for their anti-fungal activity by using disc diffusion method [24, 26].

RESULTS AND DISCUSSIONS

In the synthesis Salicylaldehyde is reacted with simple or substituted aniline to give the respective schiff base or aldimine. These are coloured products and gave experimental yields in the range of 88.80 to 97.34 %, their physical constant are determined and given in the Table 1. The TLC of aromatic amine and the Aldimine(purified) product was recorded which indicated the homoginicity of spots as shown in the Fig. 1. in the mobile phase. Their R_f values were also calculated and shown in Fig. 1. The photographs of the products as they are observed after purification are as given in Table 2.

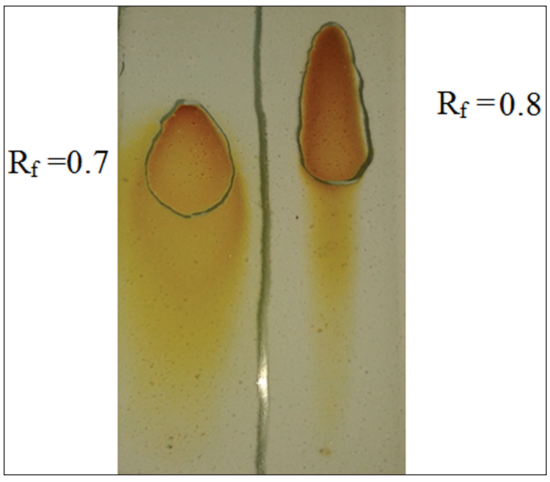


Figure 1: TLC monitoring for A-1

Table 1: The physical and analytical data for the synthesized aldimines, A-1 - A-6

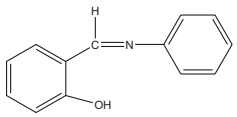
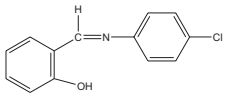
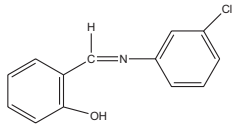
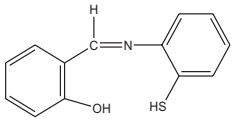
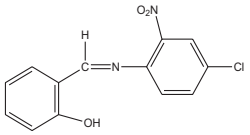
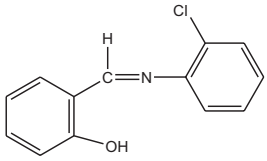
ID	Aniline used	M. Wt. of product	Colour of product	m.p./b.p. °C	Wt. in gm	Yield (%)
A-1	Aniline	197.23	Green	51	33.9	96.10
A-2	4- Chloroaniline	231.67	Yellow	72	9.22	91.28
A-3	3-Chloroaniline	231.67	Cadmium-Yellow	76	10.09	99.00
A-4	2-Aminothiophenol	229.29	Orange-Yellow	97	14.2	88.80
A-5	4-Chloro-2-nitro aniline	276.67	Orange	84	23.5	97.34
A-6	2-Chloroaniline	231.67	Olive Green	75	10.10	95.00

Table 2: Photographic Representation of Recrystallized Schiff base, A-1 – A-6

Sr. No.	Code	Amine used	Purified*Product
1	A-1	Aniline	
2	A-2	4-Chloroaniline	
3	A-3	3-Chloroaniline	
4	A-4	2-Aminothiophenol	
5	A-5	4-Chloro-2-nitroaniline	
6	A-6	2-Chloroaniline	

* *Ethanol*

Table 3: The FTIR Spectral Frequencies of the synthesized Aldimines, A-1 – A-6

Sr. No.	FTIR Frequencies, (cm^{-1})	Aldimine structure/Name with ID
1	ν-C-H (stretch) = 3066 ν-C=C = 1681 ν-C=N = 1660 ν-OH Ar =3650	 2-Phenyliminomethyl-phenol, **A-1**
2	ν-OH-Ar = 3650 ν-C=C = 1477 ν-C-Cl (stretch) =678 ν-C-H (stretch) =3066 ν-C=N = 1660	 2-[(4-Chloro-phenylimino)-methyl]-phenol, **A-2**
3	ν-OH-Ar =3650 ν-C=C = 1477 ν-C-Cl (stretch) =670 ν-C=N = 1660 ν-C-H (stretch) =3060	 2-[(3-Chloro-phenylimino)-methyl]-phenol. **A-3**
4	ν-OH-Ar =3327 ν-C-Cl=752 ν-C=C = 1481,1595 ν-C-H=3059 ν-C=N = 1645	 2-[(2-Mercapto-phenylimino)-methyl]-phenol. **A-4**
5	ν-OH-Ar =3493 ν-C-Cl=672 ν-C-H=3101 ν-C=C = 1475 ν-C=N = 1662 ν-NO_2 = 1360,1525	 2-[(4-Chloro-2-nitro-phenylimino)-methyl]-phenol, **A-5**
6	ν-OH Ar =3367 ν-C-CH_3=1386 ν- C-H=3057 ν- C=C = 1469 ν-mono sub=648	 2-[(2-Chloro-phenylimino)-methyl]-phenol, **A-6**

In general the exhibits the expected features of the standard FTIR spectra for this type of compound. The spectra of A-1 shows absorption at about 3650 cm^{-1} which indicate the presence of aromatic hydroxy(Ar-OH) group. In schiff bases there is band at 1681 cm^{-1} which may be attributed to >C=C< group. The band at 3066 cm^{-1} may be C-H stretching of aromatic ring. The spectra data for other Schiff bases A-1 to A-6 depicted in Table 3.

The FTIR spectra of the synthesized compounds were recorded and their assigned frequencies are shown in Table 3.

The FTIR spectra for A-1, depicted in Fig. 2 for the product of Salicylaldehyde and the Aniline.

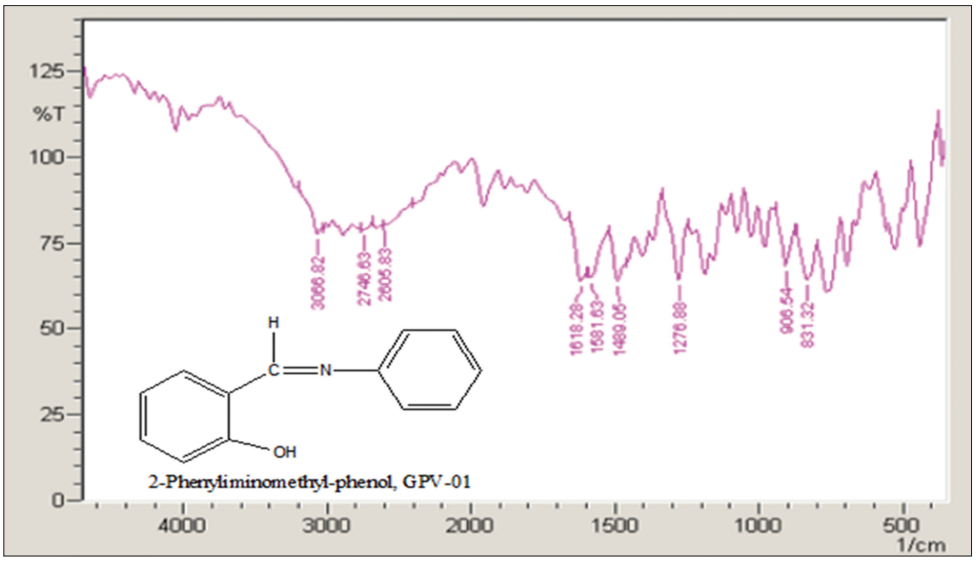


Figure 2: The representative FTIR spectra for >C=N- containing compound, A-1

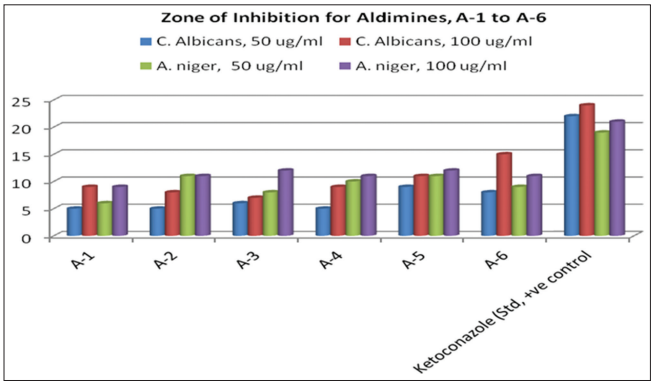


Figure 3: Graphical representation of the ZOI for the synthesized Aldimine, A-1 to A-6

Table 4: The antifungal activity data for>C=N- containing compound, A-1 to A-6

ID	*C. albicans*, (NCIM 3471)		*A. niger*, (NCIM 1196)	
	50 g/ml	100 g/ml	50 g/ml	100 g/ml
A-1	5	9	6	9
A-2	5	8	11	11
A-3	6	7	8	12
A-4	5	9	10	11
A-5	9	11	11	12
A-6	8	15	9	11
DMSO (-ve control)	-	-	-	-
Ketoconazole (Std, +ve control	22	24	19	21

On the basis of the spectral (FTIR) and chromatographic analysis by TLC spots, the structure of Aldimines are as depicted in Table 3.

Biological Activity

The Aldimine, A-1 to A-6 were screened for their fungal activity using disc diffusion method [23, 25], against strains like C. *albicans* (NCIM 3471) and A. *niger* (NCIM 1196). Results of the ZOI (zone of inhibition) are depicted in Table 3. It is seen that the synthesized compounds shows less activity as compare to the standard.

Antifungal activity of the compounds may be due to presence of >C=N- linkage. The ZOI is directly proportional to the degree of sensitivity of microbial strain and the concentration of the compound under test. The results of antibacterial activity against C. *albican* and A. *niger* are compare with that of the standard drug, Ketoconazole, are depicted in Table 4. Solvent DMSO is used as negative control. All the marked activity coefficients for the studied compounds are less than the standard drug, Ketoconazole. Graphical display of antifungal activity is shown in Fig. 3.

CONCLUSION

Aromatic aldehyde is reacted with aniline and substituted anilines to form Schiff bases which are useful to the society. The Schiff bases are well known intermediates for synthesizing of various compounds. Present work showed reaction (condensation) of an aromatic o-hydroxy-aldehyde (Salicylaldehyde) with aniline derivatives, gave formation of >C=N- containing compound. The two compounds characterized by TLC and the spectral studies. These Aldimines may be useful as building block by budding researchers. The synthesized compounds have antifungal activity as well. This outcome and their further reactions will be useful as building block for new Researchers.

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