



## Synthesis, characterization and anti-bacterial activity of novel schiff bases of pyridin-3 yl-carbohydrazide derivatives

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### Abstract

Heterocyclic compounds are cyclic compounds containing carbon and other heteroatoms. The most common heteroatoms are oxygen, nitrogen, and Sulphur. A heterocyclic compound is a cyclic compound that has atoms at least two different elements as members of its ring. A Schiff base (azomethine) is named after its inventor, Hugo Schiff and it is a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group but not hydrogen. Schiff bases of Pyridin-3 yl-carbohydrazide derivatives from ethyl nicotinate and different aromatic aldehydes. Schiff's bases are aromatic substituted imine compounds. These compounds are very important in the medicinal and pharmaceutical fields because of their wide spectrum of biological activity. Schiff's bases show antibacterial activity, antifungal activity, and also antitumor activity. Aromatic aldehydes were refluxed with ethyl nicotinate using ethanol as a solvent to form Schiff's bases. All chemicals are taken in equimolar concentrations. The synthesized compounds were characterized by melting point, solubility, percentage yield, TLC, and IR spectral analysis. All derivatives are evaluated for anti-bacterial activity by the cup plate method. The antibacterial activity of test compounds was compared against standard Streptomycin. The 5 synthesized compounds show moderate antimicrobial activity. The experimental work summarizes the synthesis and in-vitro antibacterial activity of Schiff base derivatives.

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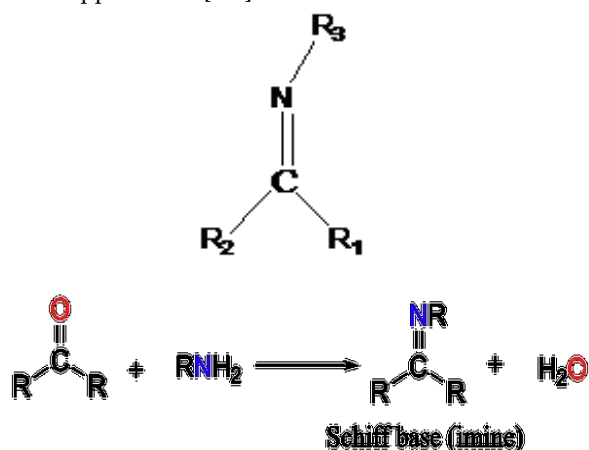
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### Introduction

Heterocyclic compounds are cyclic compounds containing carbon and other hetero atoms. The most common hetero atoms are oxygen, nitrogen and sulphur. A heterocyclic compound is a cyclic compound that has atoms at least two different elements as members of its ring. In Greek heteros

means different. More than half of the known organic compounds are heterocyclic compounds. Heterocyclic compounds are those where one or more atom(s) of the ring are hetero atoms, for example, N,O,S,P,As,Se,B, and so on (Greek word "heteros means different) [1-3]. More than half of the known organic compounds are heterocyclic compounds. A Schiff base (azomethine) is named after its inventor, Hugo Schiff and it is a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group but not hydrogen. Schiff bases have the general formula of  $R_1R_2C=NR_3$ , where  $R_3$  is an aryl or alkyl group that makes the Schiff base a stable imine. Schiff bases can be synthesized from a reaction of an aromatic amine and a carbonyl compound by a nucleophilic addition forming a hemiaminal, followed by dehydration to generate an imine. They can be considered a sub-class of imines, being either secondary ketimines or secondary aldimines depending on their structure. The term

is often synonymous with azomethine which refers specifically to secondary aldimines (i.e. R-CH=NR' where R' ≠ H). Schiff bases are derived from an amine and a carbonyl compound [2]. They are well known, versatile chelating agents with multiple donor atoms like O, N, S etc. A large number of metal complexes of multi-dentate Schiff base ligands with O, N, S donors have been reported with numerous applications [4-7].



Where R may be an aliphatic or an aromatic or hetero atom containing group.

Schiff bases of aliphatic aldehydes are relatively unstable and are readily polymerizable [8-11], while those aromatic aldehydes having an effective conjugation system are more stable. The formation of a Schiff base from aldehydes or ketones is a reversible reaction and generally takes place under acid or base catalysis [12-16], or upon heating. The formation is generally driven to the completion by separation of the product or removal of water, or both. Many Schiff bases can be hydrolyzed back to their aldehydes or ketones and amines by aqueous acid or base [17-20].

### Materials and Methods

Ethyl nicotinate, different aromatic aldehydes, ethanol, Porcelain chips, crushed ice.

#### Procedure for Synthesis

##### Materials required

Ethyl nicotinate, different aromatic aldehydes, ethanol, Porcelain chips, crushed ice.

##### Apparatus used

Round bottom flask, Reflux condenser, Beaker, Glass rod, Water bath, Tripod stand, Vacuum desiccator.

##### Instruments for characterization:

IR instrument used was Spercle Elmer DHF-1 FT-IR for IR spectra,

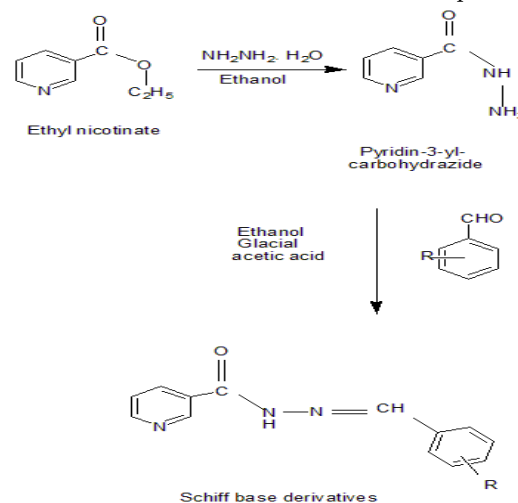
##### General Procedure

Procedure involves 2 Steps.

##### Step - 1: Synthesis of Compound: Nicotino Hydrazide

A mixture of 0.1 M (15.1gm) of ethyl nicotinate (compound 1) and 0.2 M (10gm) of hydrazine hydrate with 50% ethanol taken in round bottomed flask and then refluxed for 16 hours. Then the reaction mixture concentrated to half

volume and poured it into the crushed ice. The reaction was identified by TLC using silica gel (100-200 #, Merck) and ethyl acetate: ethanol (2:3) as mobile phase. The white precipitate was separated and recrystallized from ethanol. It was confirmed by spectral data; IR (cm<sup>-1</sup>): N-H, C=O and C=N observed at 3253.83, 1659.22 and 1588.90 respectively.



Scheme

Tab 01: List of various Aromatic Aldehydes used for scheme

S.No	CODE [SFB]	R
1.	4- Chloro Benzaldehyde [SFB 1]	
2.	4- Bromo Benzaldehyde [SFB 2]	
3.	4- Nitro Benzaldehyde [SFB 3]	
4.	4- Hydroxy Benzaldehyde [SFB 4]	
5.	4- Dimethyl amino Benzaldehyde [SFB 5]	

**Step - 2: Synthesis of Schiff Bases**

A mixture of compound 2 (1.47 gm, 0.001 M) and substituted benzaldehydes (0.001M) Were dissolved in absolute ethanol(40 ml) by the addition of a few drops of glacial acetic acid and refluxed for 6 hrs. The reaction was identified by TLC using silica gel (100-200 # , Merck) and ethyl acetate : ethanol (2:3) as Mobile phase. Then reaction mixture poured into ice cold water.

**Results and Discussion**

A total of 5 compounds were synthesized from one scheme and they were recrystallized by appropriate solvents. They were identified and characterized by various spectral methods. All the compounds were tabulated and characterization data was tabulated in Tab.1 &2.

**Tab 02: Synthesized Schiff base compounds**

\*Mobile phase = Ethyl acetate: ethanol (2:3).

Compound Code	Mole. Formula	Mole. Weight (g/mole)	Melting Point (°C)	R <sub>f</sub>	% Yield
SFB - 1	C <sub>13</sub> H <sub>10</sub> N <sub>3</sub> OCl	259.51	225-227	0.67	68.07
SFB - 2	C <sub>13</sub> H <sub>10</sub> N <sub>3</sub> OBr	304.31	179-181	0.72	62.38
SFB - 3	C <sub>13</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub>	270.74	230-232	0.82	63.38
SFB - 4	C <sub>13</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	241.34	132-131	0.77	53.02
SFB - 5	C <sub>15</sub> H <sub>16</sub> N <sub>4</sub> O	268.32	202-204	0.74	58.25

**Tab 03: Characterization data of synthesized compounds**

Code	Mole. Formula	Spectral Data
SFB - 1	C <sub>13</sub> H <sub>10</sub> N <sub>3</sub> OCl	IR (KBr): Cm <sup>-1</sup> : 3253.83 (Ar-NH; str.), 1482.22 (ArC=C; Str.), 1659.22 (C=O; str.), 1588.90(C=N; str.), 739.35(Ar-C-Cl, Bend).
SFB - 2	C <sub>13</sub> H <sub>10</sub> N <sub>3</sub> OBr	IR (KBr): Cm <sup>-1</sup> : 3250.20 (Ar-NH; str.), 1524.58 (ArC=C; Str.), 1647.96 (C=O; str.), 1585.80(C=N; str.), 822.21(Ar-C-Br, Bend).

SFB - 3	C <sub>13</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub>	IR (KBr): Cm <sup>-1</sup> : 3438.22 (Ar-NH; str.), 1474.20 (ArC=C; Str.), 1650.81 (C=O; str.), 1559.81(C=N; str.), 859.85(Ar-C-NO <sub>2</sub> , Bend).
SFB - 4	C <sub>13</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	IR (KBr): Cm <sup>-1</sup> : 3394.02 (Ar-NH; str.), 1513.65 (ArC=C; Str.), 1657.22 (C=O; str.), 1586.26(C=N; str.), 2178.23(Ar-O-H, Str.).
SFB - 5	C <sub>15</sub> H <sub>16</sub> N <sub>4</sub> O	IR (KBr): Cm <sup>-1</sup> : 3361.23 (Ar-NH; str.), 1455.57 (ArC=C; Str.), 1652.84 (C=O; str.), 1543.60(C=N; str.), 3007.57(Ar-C-CH <sub>3</sub> , Bend).

**Anti-bacterial activity of synthesized compounds**

Synthesized Schiff base derivatives were evaluated for Anti-bacterial activity with cup plate method at concentrations of 250µg/ml and 500µg/ml. Standard was taken as streptomycin Control was taken as ethanol. The results were tabulated in Tab.3.

**Tab 04: Anti-bacterial activity of synthesized compounds.**

S. No	Compound Code	Gm <sup>+ve</sup>				Gm <sup>-ve</sup>	
		<i>S.aureus</i>		<i>B. Pimilis</i>		<i>E.Coli</i>	
		250 µg/ml	500 µg/ml	250 µg/ml	500 µg/ml	250 µg/ml	500 µg/ml
1.	SFB - 1	10	11	-	13	11	12
2.	SFB - 2	14	16	13	15	13	16
3.	SFB - 3	13	14	12	13	14	17
4.	SFB - 4	-	11	10	11	-	-
5.	SFB - 5	10	10	-	11	10	12
Contr ol	Ethanol	-		-		-	
Stand ard	Strepto mycin (500 µg/ml)	18		20		20	

**Conclusion**

Schiff base is a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group but not hydrogen. In this work, ethyl nicotinate reacts with different aromatic aldehydes to give Schiff bases of Schiff bases of Pyridin-3 yl-carbohydrazide derivatives which are having biological importance.

Compounds show remarkable activity when compared with standard. Compounds show remarkable activity when compared with standard. SFB -3 is effective against Gram <sup>+</sup>ve and Gram <sup>-</sup>ve, SFB-1 and SFB-2 were found to have moderate activity against both Gram <sup>+</sup>ve and Gram <sup>-</sup>ve where as SFB-4 and SFB-5 are having insignificant activity when compared to standard Streptomycin. In the present study all synthesized compounds tested for anti bacterial activity and have shown significant activity when compared with standard drug Streptomycin.

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