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Synthesis and Biological Evolution of Some Heterocyclic Derivatives

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Abstract

Heterocyclic compounds, owing to their diverse applications including pharmaceuticals and industrial use, hold a prominent position within organic chemistry. This study focused on the synthesis and characterization of Schiff base compounds as a subset of heterocyclic molecules. Compound **[N1]** was synthesized by condensing 3,4 Diamino benzoic acid and 4-Dimethyl amino benzaldehyde, followed by subsequent reactions to yield compounds **[N2]**, **[N3]**, **[N4]**, and **[N5]**. Each compound was characterized through Fourier-transform infrared spectroscopy (FTIR). The FTIR spectra exhibited distinctive absorption bands signifying various functional groups within each compound. The spectra confirmed the presence of key bonds such as **OH**, **C=O**, **C=N**, **C-H**, and **S-H** within the compounds. This thorough characterization validated the successful synthesis of the Schiff base compounds and facilitated their structural analysis. The study underscores the importance of precise characterization in elucidating the structure and composition of novel compounds, contributing to the broader understanding of their potential applications.

Keywords:
Heterocyclic Derivatives, , Synthesis, Schiff Base Compounds, Fourier-Transform Infrared Spectroscopy (FTIR), Characterization

Introduction

The realm of heterocyclic compounds stands as a pivotal and expansive domain within the realm of organic chemistry. Its significance is underscored by its manifold applications, spanning industrial contexts to the discovery of pharmaceutical agents[1]. These compounds, distinct for incorporating diverse atom types, can manifest in saturated or unsaturated forms. Notably, when comprised solely of carbon atoms, they are termed "homocyclic compounds," while the inclusion of heteroatoms such as nitrogen, oxygen, and sulfur distinguishes heterocyclic compounds[2]. This class of compounds permeates the natural world, bearing multifaceted implications for life. Their involvement in essential biochemical materials, exemplified by nucleic acids with their heterocyclic units forming nucleic bases, underscores their biological importance. Additionally, the presence of heterocyclic rings, like furan and pyran structures housing oxygen atoms, characterizes key molecules such as sugars and vitamin C. Moreover, the family of vitamin B compounds, replete with nitrogen-bearing heterocyclic rings like pyridine-derived vitamin B6, play indispensable roles in amino acid metabolism[3]. Within the chemical landscape, Schiff bases emerge as a distinctive category of compounds. Named after Hugo Schiff, who first reported their synthesis, these compounds feature a carbon-nitrogen double bond [C=N], wherein the nitrogen atom forms a linkage with an aryl or alkyl group. Structurally, the presence of an R3 group stabilizes the iminic Schiff base, rendering it a nitrogen analog of aldehydes or ketones wherein the carbonyl group (C=O) gives way to an imine or azomethine group. Notably, the stability of Schiff bases hinges on the nature of the aldehyde precursor; aromatic aldehydes with effective conjugation systems are more stable than their aliphatic counterparts[5]. The foundational method for Schiff base synthesis, attributed to Schiff himself, entails the reaction between an aldehyde or ketone and a primary amine, often catalyzed by acids. Synthesizing Schiff bases involves the reaction of heterocyclic amines with

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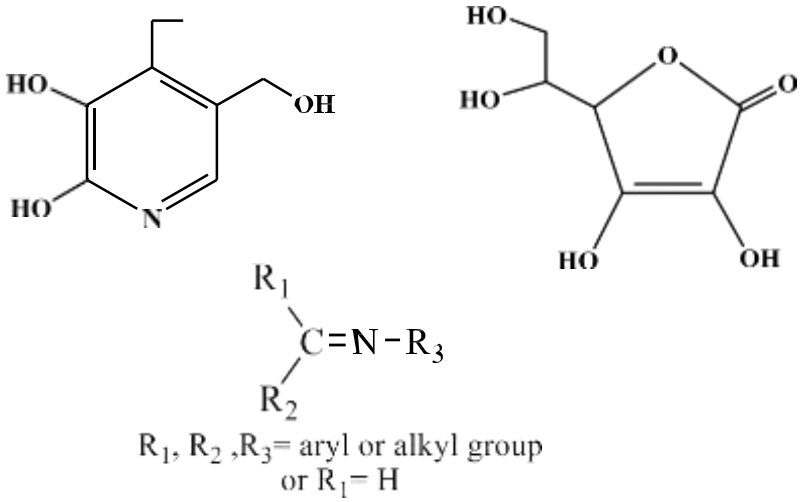
various aromatic aldehydes in an ethanol milieu, catalyzed by glacial acetic acid. The ensuing products are characterized using TLC and FTIR spectroscopy. The latter reveals absorption bands indicative of stretching vibrations, including the doublet for NH2 of the amine (symmetric and asymmetric stretching vibrations in the region of 3450-3220 cm-1, respectively), the vanishing C=O band of the aldehydes (1660-1740 cm-1), and the appearance of C=N bond stretching vibration (1580-1630 cm-1). Schiff bases assume significant roles across diverse applications, ranging from combating bacterial infections, tuberculosis, and cancer, to their proficiency in metal ion capture. Their utility extends to combating metal corrosion, wielding significance in analytical and industrial chemistry. Coined in honor of their originator, Schiff's bases have also forged a niche in coordination chemistry, readily forming stable complexes with transition metal ions. Notably, Schiff bases stemming from sulfa drugs are attracting substantial attention due to their advantageous applications. Beyond medicine, these compounds prove their mettle in ceramics, catalysis, glass production, and more, underpinning their relevance across a spectrum of scientific and technological realms.



Experimental Part

1. Devices Utilized

The experimental procedures encompassed a diverse array of devices aimed at compound preparation, spectral measurements, and physical property assessments. The following instruments were employed:

1. Electric Balance
2. Digital Melting Point Measurement Apparatus
3. Oven Apparatus
4. Hotplate Stirrer
5. Reflux Apparatus
6. Thermometer
7. Oil Bath
8. Infrared Measurement Device

Infrared measurements were executed utilizing the PERKIN ELMER SPECTRUM-65 within the spectral range of 400-5000 cm^-1 utilizing KBR discs within the Chemistry laboratory at Diyala University Department.

2. Chemicals

All chemicals and solvents utilized in the course of this study were procured from various sources as detailed in Table 2.1:

Table 2.1: Chemicals and Solvents

NO	Chemicals	Supplier	Chemical Formula
1	Ethanol absolute 99%	GCC	C2H5OH
2	3,4 Diamino benzoic acid	BDH	C7H8N2O2
3	4-Dimethyl amino benzoic acid	BDH	C9H11NO

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4	Glacial acetic acid 99%	BDH	C2H4O2
5	Maleic anhydride	BDH	C4H2O3
6	Phthalic anhydride	BDH	C8H4O3
7	Thiocarbonhydrazide	BDH	CH6N4S

3. Preparation of Compounds

Preparation of Compound N1 (C25H26N4O2)

A mixture composed of **0.001 mole** (*0.456 g*) of **3,4 Diamino benzoic acid**, **0.002 mole** (*0.894 g*) of **4-Dimethyl amino benzaldehyde**, **10 mL** of absolute ethanol, and **3 drops** of glacial acetic acid was subjected to reflux for **8 hours**. The reaction's completion was verified using TLC with the mobile phase of **ethyl acetate:hexane 1:3**. After cooling to room temperature, the resulting yellow crystalline solid was filtered, dried, and further purified through recrystallization from ethanol: water[9]. The physical properties of the compound are detailed in **Table 2.2**.

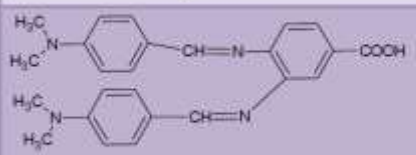
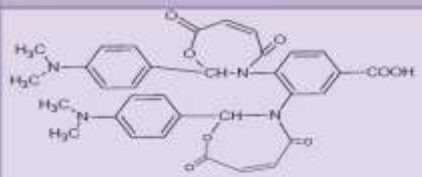
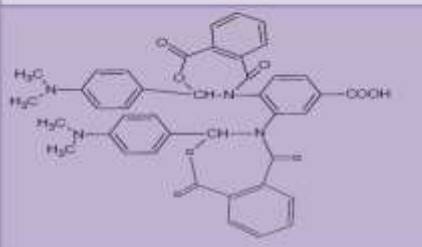
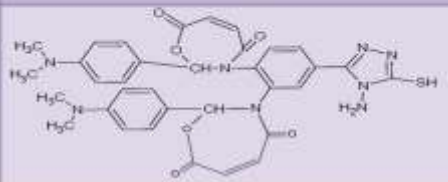
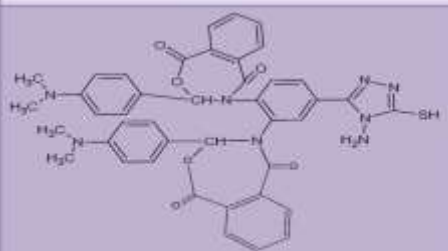
The subsequent sections (2.3.2, 2.3.4, and 2.3.5) follow a similar structure, outlining the preparation steps for compounds N2, N3, N4, and N5.

2.2 Physical Properties of Prepared Compounds

Table 2.2: Physical Properties of Prepared Compounds

NO	M.F	M.Wt (g/mol)	M.P (°C)	Yield (%)	Color
N1	(C25H26N4O2)	414	120-122	50	Greenish yellow
N2	(C33H30N4O8)	614	217-215	45	Green
N3	(C41H34N4O8)	710.7	214-212	54	Brown
N4	(C34H32N8O6S)	696	117-119	67	Brown
N5	(C42H36N8O6S)	780	>300	48	Dark Brown

Table shows the chemical structure for the prepared compounds

Comp .No	Comp. Structure
N_1	
N_2	
N_3	
N_4	
N_5	

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Results and Discussion

3.1 Characterization of Schiff Base Compounds

The synthesis of the compound [N1] involved the condensation of 3,4 Diamino benzoic acid and 4-Dimethyl amino benzaldehyde in absolute ethanol with a few drops of glacial acetic acid. The structural confirmation of the synthesized compounds was achieved through FTIR spectroscopy.

The FTIR spectrum (Fig. 1) of compound [N1] showcases distinctive absorption bands: An absorption peak at 3398 cm^-1 corresponding to the stretching vibration of OH groups. An absorption peak at 2913 cm^-1 attributed to the stretching vibration of aliphatic C-H bonds.

An absorption peak at 1661 cm^-1 attributed to the C=O stretching vibration.

An absorption peak at 1608 cm^-1 attributed to the stretching vibration of C=N bonds.

3.2 Characterization of Compound [N2]

Compound [N2] was synthesized by condensing compound [N1] with Malic anhydride in benzene as the solvent.

The FTIR spectrum (Fig. 2) of compound [N2] reveals significant absorption bands:

Peaks at 2500 cm^-1 and 3300 cm^-1 are attributed to the stretching vibrations of OH groups.

A peak at 1700 cm^-1 signifies the presence of the C=O lactone group.

A peak at 2925 cm^-1 corresponds to the stretching vibration of aliphatic C-H bonds.

3.3 Characterization of Compound [N3]

Compound [N3] was synthesized by condensing compound [N1] with phthalic anhydride in benzene as the solvent.

The FTIR spectrum (Fig. 3) of compound [N3] highlights notable absorption bands:

Peaks at 2500 cm^-1 and 3300 cm^-1 denote the stretching vibrations of OH groups.

A peak at 1706 cm^-1 is indicative of the C=O lactone group.

A peak at 2810 cm^-1 corresponds to the stretching vibration of aliphatic C-H bonds.

3.4 Characterization of Compound [N4]

Compound [N4] was synthesized through the fusion of substituted [N2] with thiocarbohydrazide. The FTIR spectrum (Fig. 4) displays:

Bands at 3214 cm^-1 and 3154 cm^-1, corresponding to the asymmetric and symmetric stretching vibrations of NH2.

A peak at 2921 cm^-1 representing the stretching vibration of aliphatic C-H bonds.

A peak at 1639 cm^-1 associated with the C=O stretching vibration.

A peak at 2679 cm^-1 attributed to the stretching vibration of S-H.

3.5 Characterization of Compound [N5]

Compound [N5] was synthesized by fusing substituted [N3] with thiocarbohydrazide. The FTIR spectrum (Fig. 5) reveals:

Bands at 3470 cm^-1, indicating the asymmetric and symmetric stretching vibrations of NH2.

A peak at 2921 cm^-1 signifying the stretching vibration of aliphatic C-H bonds.

A peak at 1698 cm^-1 corresponding to the C=O stretching vibration.

A peak at 2600 cm^-1 attributed to the stretching vibration of S-H.

The comprehensive FTIR analysis affirms the successful synthesis of the intended Schiff base compounds, confirming their structural composition and functional group assignments.

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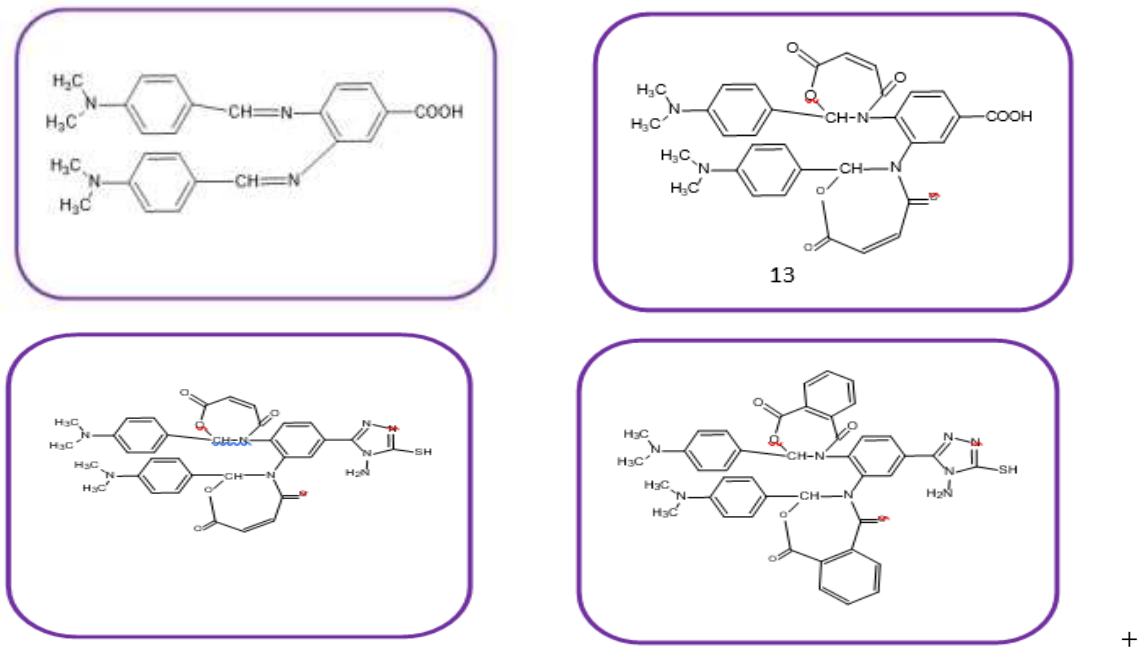

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