Formation, Characterization, Chromatographic and Microbial Behavior of (Inamine-Imine-Isatin) Reagents

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ABSTRACT

Inamine – Imine Isatin reagents were synthesized in present paper via more than reaction like imination reaction to formation imine compound – isatin, then imination reaction to synthesis mannich compound – isatin in same molecule, three reagents were prepared through two lines in different conditions (Schiff base and mannich base) linked with isatin compound. Spectral characterization of reagents with types of techniques (FT.IR, H.NMR, Mass) – spectrophotometric, then studying of compounds behavior toward (microbial and chromatography) effect.

Keywords: Inamine, Imine, Isatin, Reagent, Schiff base, Mannich base.

I. INTRODUCTION

Isatin which named in cyclic chemical structure (indole-2,3-dione) is one of indole derivatives. Isatin compound was first obtained in 1841 by Erdman with Laurent:

![Isatin Structure](image1)

Isatin derivatives have a broad applications (1-8) and uses of pharmacological actions as anxiogenic, sedative agents and a wide applications (9-20) of biological activities as antimicrobial, antifungal, anti-HIV.

![Anti-HIV Compounds](image2)

Fig. (1): Isatin Structure

Fig. (2): Isatin in Anti-HIV compounds
For the treatment or alleviation of diseases like respiratory diseases, heart diseases, hypertension, tumors, psychosis, industrial field, as dyes for wool.

And as a starting material in many reactions like in preparation of (imine compounds, inamine–mannich base, aldole reaction, or chalcone reaction, cyclization reaction, and in synthesis of various chemical derivatives).

**EXPERIMENTAL PART:**
Inamine-Imine–Isatin reagents were investigated through: FT-IR spectra (FT-IR 8300 Shimadzu) in the range (400-4000) cm⁻¹ as KBr discs, 1H.NMR– Spectra in DMSO–solvent, Mass spectra, chromatography applications with microbial studying:

**PROCEDURES:**
**Formation of Reagent {1}:**
Isatin (0.2 mole) refluxed with ortho-phenyl diamine (0.1 mole) for (3hrs) according to literatures with drops of glacial acetic acid, to produce precipitation, filtered, dried and re crystallized to produce imine-isatine compound, which (0.01 mole) reacted with (0.02 mole) of methylvaminebenzothiazol derivative and formaldehyde (CH₂O) in acid medium to give Inamine-imine-isatin reagent {1}.
Scheme.1: Formation of Inamine-Imine-Isatin Reagent {1}

Formation of Reagent {2}:
Imine-isatin compound from first step (0.01 mole) reacted with (0.02 mole) of ethylamineimidazole derivative and formaldehyde (CH₂O) in acid medium according to literatures(20, 21) to give Inamine-imine-isatin reagent {2}.

Scheme.2: Formation of Inamine-Imine-Isatin Reagent {2}
Formation of Reagent {3}:
Imine-isatin compound from first step (0.01 mole) reacted with (0.02 mole) of methylaminethiophene derivative and formaldehyde (CH₂O) in acid medium according to literatures (20, 21) to give Inamine-imine-isatin reagent {3}.

Scheme 3: Formation of Inamine-Imine-Isatin Reagent {3}

II. RESULTS AND DISCUSSION
Our reagents characterized with many spectral methods like (FT.IR, H.NMR, Mass) spectra and Chromatography with microbial studies:

Spectral Characterization:


Table (1): FT.IR data (cm⁻¹) of Reagents {1 - 3}

<table>
<thead>
<tr>
<th>Reagents</th>
<th>Other Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>{1}</td>
<td>(C=N-) Imine group: 1624 , (CO-N-) carbonyl of amide: 1681 , (C=N)</td>
</tr>
</tbody>
</table>
Endocycle: 1639 , (C=S) endocycle of benzothiazole : 712 .

\{ 2 \} (C=N-) Imine group: 1619 , (CO-N-) carbonyl of amide : 1687 , (C=N) 

\{ 3 \} (C=N-) Imine group: 1627 , (CO-N-) carbonyl of amide : 1684 , (C=S) of thiophene : 736 .

\(^1\)H.NMR- Spectra: showed peaks at \(\text{N-CH}_2\text{-N-}\) Protons : 2.34 , \(\text{CH}_3\text{-N-}\): 2.09 , Protons of Phenyl ring and Heterocycles : (6.95-7.78) in reagent \{ 1 \} , while it gave signals at \(\text{N-CH}_2\text{-N-}\) Protons : 2.72 , \(\text{C}_2\text{H}_5\text{-N-}\): 2.17 , \(\text{NH-}\) Proton of amine in imidazole : 5.62 , Protons of Phenyl ring and Heterocycles : (6.83-7.98) in reagent \{ 2 \} , (N-\text{CH}_2\text{-N-}) Protons : 2.56 , (CH_3-N-) : 2.15 , Protons of Phenyl ring and Heterocycles : (7.00-7.89) in reagent \{ 3 \} , and other signals in table (2).

\begin{table}[h]
\centering
\begin{tabular}{|c|c|}
\hline
Reagents & Other groups \\
\hline
\{ 1 \} & DMSO-d6(solvent): 2.50 , (N-CH\textsubscript{2}-N-) Protons: 2.34 , (CH\textsubscript{3}-N-): 2.09 , Protons of Phenyl ring and Heterocycles: (6.95-7.78). \\
\{ 2 \} & DMSO-d6(solvent): 2.50 , (N-CH\textsubscript{2}-N-) Protons: 2.72 , (C\textsubscript{2}H\textsubscript{5}-N-): 2.17 , (NH-) Proton of amine in imidazole: 5.62 , Protons of Phenyl ring and Heterocycles: (6.83-7.98). \\
\{ 3 \} & DMSO-d6(solvent): 2.50 , (N-CH\textsubscript{2}-N-) Protons: 2.56 , (CH\textsubscript{3}-N-): 2.15 , Protons of Phenyl ring and Heterocycles: (7.00-7.89). \\
\hline
\end{tabular}
\end{table}

The Mass Spectra: The spectra of the three reagents gave good results for formatted reagents and gave good evidence for their fragments in figures (4 - 6):
Chromatographic Behavior of Our Reagents:

Diluted solutions of reagents were prepared for injection through a syringe (Hamilton) in capacity (10ml) through gas carrier [Nitrogen (gas flow 25 ml/min)]. The reagents separated according to their polarity, their nature and their molecular weight, for this reason reagent [3] separated at the first time due to it has less molecular weight compared with other the reagents, figures (7 - 9).
Fig (7): Chromatogram of Reagent {1}

Fig (8): Chromatogram of Reagent {2}

Fig (9): Chromatogram of Reagent {3}
Microbial Behavior of Reagents:
Assay of activity for prepared derivatives have been screened for their antibacterial activities by agar through biological procedures\(^{(32-35)}\). The antimicrobial activities were done at three concentrations (3, 6, 9 micro gram) concentrations in (DMSO) solvent with bacteria: (bacteria K. Pneumona) and (E- Coli). These bacterial strains were incubated for 24 hr at 37°C.

Picture (1) : E- Coli

Picture (2) : K. Pneumona
RESULTS AND DISCUSSION

In this work, we tested our reagents for bio–Activity against two types of bacteria:

**Activity Assay**

The test of the sensitivity of the bacteria, which included work on two types of bacteria to measure the biological activity of certain reagents against: (bacteria K. Pneumona) and (E- Coli). Table (3) shows the diameter of inhibition zone for vehicles chemical measured in mm towards the bacteria.

<table>
<thead>
<tr>
<th>Reagents</th>
<th><em>K. Pneumona</em></th>
<th><em>E- Coli</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>{ 1 }</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>{ 2 }</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>{ 3 }</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

The results appeared that the Activity of formatted reagent { 1} the effectiveness of anti-resistant bacteria is much higher than other reagents in the inhibition of bacteria, sulfur and nitrogen atoms in benzothiazole gave higher activity than other reagents:

![Picture (3).The amount of inhibition of the compounds on E- Coli](image-url)
REFERENCES


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