Azotation and Coupling Reaction of Amino Oxadiazole Ligands with (Characterization, Chromatography, Solubility) Study

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Abstract

This paper involved reaction between two moles of semicarbazide with mole of diethyl malonate which refluxed for (17 hrs) in absolute ethanol then added (4 ml) of H\textsubscript{2}SO\textsubscript{4} to produce amino oxadiazole, the resulting compound used in azotation then coupling reaction with various coupling derivatives of phenol (p-hydroxy benzaldehyde, p-hydroxy benzoic acid, p-hydroxy nitrobenzene, p-hydroxy toluene, p-hydroxybenzophenol) to produce novel oxadiazole derivatives as a ligands. The above ligands were investigated through their spectral methods (UV-Vis, FTIR, \textsuperscript{1}HNMR, Mass), Chromatography technique and studying of solubility in series solvents.

Keywords: Soluble, Series, Hydroxyl.

Introduction

Oxadiazole ring is the core structure of various bio-molecules in nature, their chemical compounds have been used in pharmaceutical, industrial, drugs, coordination and in organic chemistry fields [1-9].

The presence of azo group (-N=N-) with Oxadiazole ring in same compound gave many uses and application [10-19] in biochemical field such antibacterial, anti-tumor and antifungal.

Experimental Part

The formatted azo ligands were prepared from chemical compounds (BDH and SIGMA COMPANIES) in high purity, I.R spectra were recorded on a Perkin Elmer-spectrum by KBr-disc.
NMR spectra were recorded 300 MHz spectrometer in using dimethyl sulphoxide., Mass spectra, Chromatography Studies, solubility in types of solvents. The preparations carried out according to papers\textsuperscript{(21-24)}

**Synthesis of Oxadiazole Derivative – Ligand [1]**

Diethyl malonate (0.01mole) cyclized with (0.2mole) of semicarbazide in acid medium for acceleration and refluxed for (16 hrs) to yield amino-oxadiazole, then the precipitation filtered and dried, which dissolved in (3 ml ) hydrochloric acid followed by addition of solution (sodium nitrite ) in ice path, then addition (0.02mole) of 4-hydroxy benzaldehyde according to literature\textsuperscript{(21)} to yield 82 % ligand [1].

**Synthesis of Oxadiazole Derivative – Ligand [2]**

Diethyl malonate (0.01mole) cyclized with (0.2mole) of semicarbazide in acid medium for acceleration and refluxed for (16 hrs) to yield amino-oxadiazole, then the precipitation filtered and dried, which dissolved in (3 ml ) hydrochloric acid followed by addition of solution (sodium nitrite ) in ice path, then addition (0.02mole) of 4-hydroxy benzoic acid according to literature\textsuperscript{(21)} to yield 74 % ligand [2].

**Synthesis of Oxadiazole derivative – Ligand [3]**

Diethyl malonate (0.01mole) cyclized with (0.2mole) of semicarbazide in acid medium for acceleration and refluxed for (16 hrs) to yield amino-oxadiazole, then the precipitation filtered and dried, which dissolved in (3 ml ) hydrochloric acid followed by addition of solution (sodium nitrite ) in ice path, then addition (0.02mole) of 4-hydroxy phenol according to literature\textsuperscript{(21)} to yield 76 % ligand [3].

**Synthesis of Oxadiazole Derivative – Ligand [4]**

Diethyl malonate (0.01mole) cyclized with (0.2mole) of semicarbazide in acid medium for acceleration and refluxed for (16 hrs) to yield amino-oxadiazole, then the precipitation filtered and dried, which dissolved in (3 ml ) hydrochloric acid followed by addition of solution (sodium nitrite ) in ice path, then addition (0.02mole) of 4-nitro phenol according to literature\textsuperscript{(21)} to yield 80 % ligand [4].

**Synthesis of Oxadiazole derivative – Ligand [5]**

Diethyl malonate (0.01mole) cyclized with (0.2mole) of semicarbazide in acid medium for acceleration and refluxed for (16 hrs) to yield amino-oxadiazole, then the precipitation filtered and dried, which dissolved in (3 ml ) hydrochloric acid followed by addition of solution (sodium nitrite ) in ice path, then addition (0.02mole) of 4-hydroxy toluene according to literature\textsuperscript{(21)} to yield 76 % ligand [5].

![Scheme 1: Formation of Oxadiazole derivatives Ligands 1 - 5](image)
Results and Discussion

The formatted oxadiazole derivatives ligands investigated through many techniques

Identification of Ligands by Spectra

Identification by UV-Vis

Through screening of wave length for all oxadiazole ligands with ethanol

![UV-Vis of Ligand 1](image1)
![UV-Vis of Ligand 2](image2)
![UV-Vis of Ligand 3](image3)
![UV-Vis of Ligand 4](image4)

Identification by FT-IR

It indicated to many bands at ((OH- )Phenol : 3300, (N=N) Azo: (1480, 1500), (CO-O )Carbonyl of aldehyde : 1700in compound(1), bands are appeared at (OH- )Phenol : 3337 ,(N=N) Azo: (1450, 1500) ,,(OH)Hydroxy of carboxyl : (2600-3000) ,(CO- O-) Carbonyl of carboxyl : 1730 in compounds (2) ,while other bands appeared at (OH-) Phenol : 3350,(N=N) Azo: (1450, 1500 ),(NO₂)Nitro group: (1380, 1530 )in compound (3) ,bands at (OH-)Phenol : 3384 ,(N=N) Azo: (1473 , 1505 ) in compound (4) ,bands at (OH-)Phenol : 3371 ,(N=N) Azo: (1460, 1515 ),(CH₃) Aliphatic:2987 in compound (5) ,Other bands summarized in Table (1).

![FT-IR of Ligand 1](image5)

<table>
<thead>
<tr>
<th>Ligands</th>
<th>Other Groups</th>
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</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(OH-) Phenol : 3300 , (N=N) Azo : (1480, 1500), (CO-O) Carbonyl of aldehyde: 1700</td>
</tr>
<tr>
<td>(2)</td>
<td>(OH-) Phenol : 3337 , (N=N) Azo : (1450, 1500), (OH) Hydroxy of carboxyl : (2600-3000), (CO-O) Carbonyl of carboxyl : 1730</td>
</tr>
<tr>
<td>(3)</td>
<td>(OH-) Phenol : 3350 , (N=N) Azo : (1450, 1500), (NO₂) Nitro group: (1380, 1530)</td>
</tr>
<tr>
<td>(4)</td>
<td>(OH-) Phenol : 3384 , (N=N) Azo : (1473, 1505)</td>
</tr>
<tr>
<td>(5)</td>
<td>(OH-) Phenol : 3371 , (N=N) Azo : (1460, 1515), (CH₃) Aliphatic: 2987</td>
</tr>
</tbody>
</table>

![FT-IR of Ligand 1](image6)
Identification by 1H.NMR

Which gave many signals at 6 DMSO-d₆(solvent ): 2.50 , (OH) Proton of Phenol: 11.62 , Protons of Aromatic ring : (7.19-7.691), (CH₂) proton of methyl: (3.69), (COH)Proton of Aldehyde : 12.51 in ligand (1), but ligand (2) gave peaks at (OH) Proton of Phenol: 11.51, Protons of Aromatic ring : (7.22-7.41), (CH₂) proton of methyl: (3.34), (COOH) Proton of carboxyl : 13.15, ligand(3) appeared peak at (OH) Proton of Phenol: 11.51, Protons of Aromatic ring : (6.84-7.88), (CH₂) proton of methyl: (3.32), while ligand (4) showed signals at Protons of (OH) Proton of Phenol: 11.36, Protons of Aromatic ring: (7.15-7.93), (CH₂) proton of methyl: (3.34). While ligand (5) showed signals (OH) Proton of Phenol: 11.76, Protons of Aromatic ring: (7.12-7.65), (CH₂) proton of methyl: (3.29), (CH₃)Protons of Methyl group: 1.02, and other signals in Table (2).

Table 2: H.NMR-data (δ - ppm) of Azo Ligands (1-5)

<table>
<thead>
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<th>Comp</th>
<th>Other groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>DMSO-d₆(solvent ): 2.50 , (OH) Proton of Phenol: 11.62 , Protons of Aromatic ring: (7.19-7.691), (CH₂) proton of methyl: (3.69), (COH)Proton of Aldehyde : 12.51</td>
</tr>
<tr>
<td>(2)</td>
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</tr>
<tr>
<td>(4)</td>
<td>DMSO-d₆(solvent ): 2.50 , (OH) Proton of Phenol: 11.36 , Protons of Aromatic ring: (7.15-7.93), (CH₂) proton of methyl: (3.34)</td>
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<td>(5)</td>
<td>DMSO-d₆(solvent ): 2.50 , (OH) Proton of Phenol: 11.76 , Protons of Aromatic ring: (7.12-7.65), (CH₂) proton of methyl: (3.29), (CH₃)Protons of Methyl group: 1.02</td>
</tr>
</tbody>
</table>
Identification by the Mass Spectroscopy

It gave compactable fragments for all parts of our ligands, all fragments in Figures (13, 14):

Study of Ligands by Chromatographic Technique

Series ligands solutions were diluted for injection in column of chromatography for studying of separation through their molecular weight and polarity according to containing of functional groups in their structures, Figures (15-18).
Effect of Solvents on Functional Groups in Ligands

The formatted Ligands in this work have high solubility in some of solvents but they are insoluble in other solvents, which depends on polarity of functional group which cause interaction (23) and mass of ligands., the results are summarized in Table (3).
Table 3: Effect of solvents on functional groups in ligands

<table>
<thead>
<tr>
<th>Ligands</th>
<th>Solvents</th>
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<tbody>
<tr>
<td></td>
<td>DMSO</td>
</tr>
<tr>
<td>(1)</td>
<td>+</td>
</tr>
<tr>
<td>(2)</td>
<td>+</td>
</tr>
<tr>
<td>(3)</td>
<td>+</td>
</tr>
<tr>
<td>(4)</td>
<td>+</td>
</tr>
<tr>
<td>(5)</td>
<td>+</td>
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References


