Synthesis and Characterization of Some oxadiazole, thiaadiazole Derivatives Using Benzilic Acid as Synthone

Mahmoud H. Mahmoud1, Salim J. Mohammed*2

Department of Chemistry, College of Science, University of Mosul, Iraq

Email*2:dr_salimiasim@yahoo.com

Abstract - This research includes synthesis of new oxadiazole and thiaadiazole derivatives from benzilic acid, which on reaction with semicarbazide or thiosemicarbazide gave 2-amino-1,3,4-oxa/thiaadiazole (2a and 2b) respectively, on treatment the later compounds with p-toluene sulfonyl chloride to give oxa/thiaadiazole compounds(3a,3b),while on reaction with p-chloro or o-chloro isocyanate afforded compounds (4a,4b) and (5a,5b)respectively. The synthesized compounds were identified by TLC and via spectral methods, their (FT-IR and1H-NMR) and measurements of some of its physical properties

Keywords-oxadaizole, thiaadiazole, biological activity

I. INTRODUCTION

In the recent years, there has been considerable interest in the chemistry of oxadiazole, thiaadiazoles and its derivatives because it has a broad range of biological and pharmacological properties. On the other hand amongst five membered heterocycles oxadiazoles and thiaadiazoles have attracted significant interest in medicinal, pesticide chemistry, polymer and material science. 1,3,4-oxadiazoles are biologically versatile compounds displaying a variety of biological effects which include antifungal, antiparasitic, anti-inflammatory and antimicrobial activities [1-3], antibacterial [4],also it has anticancer activity [5],while the thiaadiazoles compounds have a broad range of biological activity such as antimicrobial [6],anti-inflammatory [7] and antifungal [8]. Heterocyclic compounds, including oxadiazole and thiaadiazole, represent the vast majority of compounds used in the pharmaceutical industry, and their importance is a reflection of their important role in modern drug design [9].

II. EXPERIMENTAL SETUP

Melting points were measured on Electrothermal 9300 (uncorrected). FTIR spectra were recovered using KBr disk Fourier-Transform, Tensor Co. Brucker, 2003, Germany. 1HNMR spectra were obtained from Brucker (500 MHz) Swiss, using DMSO as solvent and TMS as internal standard.

A. Preparation of (2-amino-1,3,4-oxa/thiaadiazol-5-yl)diphenyl methanol (2a and 2b) [10]:

A mixture (0.01 mol) of benzilic acid, (0.01 mol) of thiosemicarbazide or semicarbazide hydrochloride and (5 ml) of phosphorous oxychloride in ice bath were refluxed for (1hrs.) with stirring, then mixture was cooled and poured in crushed ice with starring. The solid product was formed, then filtered and wash with excess of water, and recrystallized from ethanol to give the product (2a and 2b) as brown solid.

B. Preparation of N-(5-(hydroxydiphenylmethyl)-1,3,4--oxa/thiaadiazol-2-yl)-4-methylbenzenesulfonyamide(3a and 3b) [11]:

A mixture (0.01 mol) of compounds (2a or 2b) in (15 ml) of tetrahydrofuran, (0.01 mol) of p-toluene sulfonyl chloride and few drops from pyridine were refluxed for (3hrs.), the solvent was evaporated to give brown solid, filtered and recrystallized from ethanol to give the
product, physical and spectral data as shown in tables 1 and 2 respectively.

C. Preparation of 1-(3-chloro and 4-chlorophenyl)-3-(5-(hydroxydiphenylmethyl)-1,3,4-oxathiaadiazol2-y1)urea (4a, 4b) and (5a, 5b) [12]:

A mixture (0.01 mol) of compounds (2a or 2b), (0.01 mol) of 3-chloro or 4-chloro phenyl isocyanate were refluxed for (3 hrs.), the solvent was evaporated to give red solid, filtered and recrystallized from aqueous ethanol to give the product, physical as shown in table I.

Table I

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>m.p. (°C)</th>
<th>Yield (%)</th>
<th>Color</th>
<th>Crystallization solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>103-105</td>
<td>67</td>
<td>Light brown</td>
<td>Ethanol+ water</td>
</tr>
<tr>
<td>2b</td>
<td>143-145</td>
<td>66</td>
<td>Orange</td>
<td>Ethanol+ water</td>
</tr>
<tr>
<td>3a</td>
<td>173-175</td>
<td>86</td>
<td>red</td>
<td>Methanol</td>
</tr>
<tr>
<td>3b</td>
<td>150-153</td>
<td>90</td>
<td>Yellow</td>
<td>Methanol</td>
</tr>
<tr>
<td>4a</td>
<td>113-115</td>
<td>77</td>
<td>Pale red</td>
<td>Ethanol</td>
</tr>
<tr>
<td>4b</td>
<td>107-109</td>
<td>80</td>
<td>Red</td>
<td>Ethanol</td>
</tr>
<tr>
<td>5a</td>
<td>103-105</td>
<td>88</td>
<td>Orange</td>
<td>Ethanol+ water</td>
</tr>
<tr>
<td>5b</td>
<td>92-95</td>
<td>90</td>
<td>Orange</td>
<td>Ethanol+ water</td>
</tr>
</tbody>
</table>

III. RESULTS AND DISCUSSION

In view of the potential medical and biological activity of a number 1,3,4-oxadiazole and 1,3,4-thiaadiazole derivatives. Many of these compounds have interesting pharmacological properties. In the present work the synthesis of some substituted 1,3,4-oxadiazole and 1,3,4-thiaadiazole are achieved. We are using the benzylic acid as starting material to prepare some new oxadiazole, thiaadiazole derivatives, thus the benzylic acid on reaction with thiosemicarbazide or semi carbazole gave 2-amino-1,3,4-oxa/thiaadiazol (2a and 2b) respectively.

The FT-IR spectrum for compound (2a and 2b) manifests a strong absorption band at (1654 cm⁻¹ and 1690 cm⁻¹) due to stretching vibration of C=N group, at (3210 and 3273 cm⁻¹) for NH₂-group and at (744 and 753 cm⁻¹) for C-S-C group, while C-O-C groups were appear at (1070 and 1278 cm⁻¹) represented symmetrical and asymmetrical groups.

Then on reaction of (2a and 2b) with p-toluenesulfonyl chloride afforded oxathiaadiazole compounds (3a, 3b).

The FT-IR spectrum for compound (3a and 3b) showed a strong absorption band at (1655 and 1649 cm⁻¹) due to stretching C=N-group, also (3380 and 3290 cm⁻¹) due to NH₂-group in these compounds respectively, while SO₂-group it has appeared at (1120 and 1125 cm⁻¹) for symmetrical groups and at (1327 and 1321 cm⁻¹) for asymmetrical groups.

Finally, when the last two compounds reaction with p-chloro or o-chloro isocyanate, they give compounds (4a, 4b) and (5a, 5b) respectively.

The FT-IR spectrum for compound (4a, 4b) and (4a, 4b) showed multiple bands were shown in locations
representing the characteristic groups for these compounds and as shown in Table II.

**Table II**

<table>
<thead>
<tr>
<th>No.</th>
<th>NH</th>
<th>C=O</th>
<th>C=N</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>3194,3335 cm^{-1}</td>
<td>1690 cm^{-1}</td>
<td>1618 cm^{-1}</td>
</tr>
<tr>
<td>4b</td>
<td>3210,3342 cm^{-1}</td>
<td>1701 cm^{-1}</td>
<td>1604 cm^{-1}</td>
</tr>
<tr>
<td>5a</td>
<td>3198,3292 cm^{-1}</td>
<td>1710 cm^{-1}</td>
<td>1635 cm^{-1}</td>
</tr>
<tr>
<td>5b</td>
<td>3195,3287 cm^{-1}</td>
<td>1714 cm^{-1}</td>
<td>1612 cm^{-1}</td>
</tr>
</tbody>
</table>

The measured spectrum $^1$HNMR in (DMSO-d$_6$) in ppm as a model for the two compounds(4b and 5a) to make sure of the products of the prepared compounds so the $^1$HNMR spectra shows singlet band at $\delta$ (6.4 ppm)(1H) for OH group for each of the two compounds. Also the aromatic part for (H) showed multiplet in the range (7.32-7.53 ppm) and (7.09-7.93 ppm) respectively, while the protons of (NH) group were appeared at (8.9 and 10.0 ppm) as a singlet for NH which site in the middle for compounds (4b,5a) in addition the another NH which is attached with phenyl group were appeared at (9.8 and 11.4 ppm) respectively.

**IV. REFERENCES**


