INTRODUCTION

Amoxicillin (Fig. 1) is a well known antibiotic used to prevent bacterial infection and also used in the treatment for wide types of infections like (Staphylococcus, Streptococcus, H. influenza and H. pylori) and preventing the ulcers of returning. According to amoxicillin chemical structure, it can be used in medicine as well as in chemistry as a starting material in synthetic reactions [1]. One of the important reactions is cyclization [2-6] and already used in the synthesis of several industrial compounds [6-10], relaxant drugs like diazepam and oxazepam [11-17], different types of heterocyclic compounds [18-24] and other compounds in different applications [25-31].

The heterocyclic compounds containing imidazoles and thiazoles plays an important role in the field of medicinal chemistry [32,33]. Furthermore, due to the presence of (-NH2) group in the amoxicillin structure, this could be exploited to synthesize useful azo dyes and Schiff bases [1]. Thus, in this article, the authors reported the synthesis and characterization of few new amoxicillin ligands containing imidazole, thiazole, azo and imine groups.

EXPERIMENTAL

All the chemicals used were purchased from Sigma-Aldrich without any further purification. FT-IR spectra were recorded on Perkin Elmer-spectrum with KBr disc. 1H NMR were recorded at (400 MHz) by using (DMSO-d6) as a solvent and the thermal analyses were recorded on differential scanning calorimetry 601, (DSC)-Thermal analysis instrument. All the chemical shifts (δ) were reported in ppm relative to tetramethyl silane (TMS) as reference.

Synthesis of ligands containing imidazole unit: Amoxicillin (0.1 mol, 0.86 g) was refluxed with o-phenylenediamine (0.2 mol, 1.68 g) in the presence of HCl (4 N) for 3 h to yield imidazole amoxicillin ligand (1). Yield: 68 %; Rf: 0.52 TLC solvent (ethanol: dioxane). 1H NMR (400 MHz, DMSO-d6): δ (ppm) 11.29 (1H, OH), 5.34 (2H, NH2), 10.30 (1H, N-H-CO), 0.90 (6H, 2CH3); (7.54-7.83), (8H, 2Ph); 8.57 (1H, NH imidazole ring). IR (KBr, νmax, cm-1): 3350 (O-H), 3200 and 3280 (NH2), 3120 (N-H-CO), 1690 (C=O-N-), 1640 (C=N).

Now, imidazole amoxicillin ligand (1) (0.01 mol, 0.55 g) was refluxed for 2 h with benzaldehyde (0.01 mol, 0.38 g) in the
In this work, six new organic ligands linked with anil or azo group were synthesized as shown in Schemes I and II. In Scheme-I, carboxylic acid of amoxicillin was cyclized to thiazole and imidazole by the reaction of amoxicillin with aromatic amines in the presence of HCl to give the ligands 1 and 3. Then these ligands (1 and 3) were reacted with benzaldehyde to form Schiff base (2 and 4).

On the other hand, in Scheme-II the conversion of the ligands 1 and 3 to azo compounds was achieved by their reactions with 5-methyl-1-hydroxyphenol and resorcinol, respectively to give 5 and 6.

Solubility: The solubility of all the synthesized ligands were studied in various solvents. The solubility differs according to the functional groups present in the structure and polarity of the organic ligands. Table-1 shows the solubility results of these ligands.

**FT-IR analysis:** The absorption band at 3350 cm$^{-1}$ is assigned to OH of phenol, 3280-3200 cm$^{-1}$ due to amine group, 3120 cm$^{-1}$ for amide (CO-NH-) and 1640 cm$^{-1}$ for (C=N) endocycle of imidazole ring due to cyclization of diamine with carbonyl of carboxylic acid in ligand (1). The bands appeared at 3410 cm$^{-1}$ was due to OH of phenol, 3200 cm$^{-1}$ for amide (NH-CO), 3110 cm$^{-1}$ for amine of imidazole ring (NH), 1685 cm$^{-1}$ for carbonyl of amide (CO-NH-), 1632 cm$^{-1}$ for aliphatic of methyl group, 1454 cm$^{-1}$ for imidazole ring and (C-S) at 786 cm$^{-1}$ for thiazole ring in ligand (3).

Similarly, the bands appeared at 3418 cm$^{-1}$ for OH of phenol, 3228 cm$^{-1}$ for amide (NH-CO), 1692 cm$^{-1}$ for carbonyl of amide (CO-NH-) and 1640 cm$^{-1}$ for (C=N) endocycle of imidazole ring due to cyclization of diamine with carbonyl of carboxylic acid in ligand (2).

**RESULTS AND DISCUSSION**

In Scheme-I, the conversion of the ligands 1 and 3 to azo compounds was achieved by their reactions with 5-methyl-1-hydroxyphenol and resorcinol, respectively to give 5 and 6.

TABLE-I

<table>
<thead>
<tr>
<th>Organic ligands</th>
<th>Solubility Test of Organic Ligands in Different Solvents</th>
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<tbody>
<tr>
<td></td>
<td>C$_2$H$_5$OH</td>
</tr>
<tr>
<td>1</td>
<td>+</td>
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<td>2</td>
<td>+</td>
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<td>6</td>
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$^1$H NMR analysis: $^1$H NMR spectra was recorded in DMSO-d$_6$ as a solvent with its signal at 2.5 ppm. The proton of OH of phenol was showed at 11.29 ppm, signals at 5.34 ppm for NH$_3$, protons of amide group (NH-CO) at 10.30 ppm, methyl groups at 0.90 ppm, phenyl groups at 7.54-7.83 ppm, amine in imidazole ring at 8.57 ppm in ligand (1). Similar signals were also noted in ligand 2 for example, 11.20 ppm was for proton of OH phenol, 8.19 ppm for (CH=N) imine group, amide group (NH-CO) at 10.12 ppm, methyl groups at 0.98 ppm, phenyl groups at 7.42-7.99 ppm, amine in imidazole ring at 8.71 ppm.

For ligand 3, the protons of OH of phenol at 11.27 ppm, 5.14 ppm for NH$_3$, amide group (NH-CO) at 10.20 ppm, methyl groups at 1.10 ppm, phenyl groups at 7.54-7.88 ppm were observed. For ligand 4, the signals at 11.14 ppm for OH phenol, at 8.24 ppm for (CH=N) imine group, amide group (NH-CO) at 10.07 ppm, methyl groups at 1.09 ppm, phenyl groups at 7.11-7.78 ppm were observed.

The NMR spectra of ligands 5 and 6 are almost similar. The peaks appeared at 11.11-11.12 and 11.21-11.26 ppm were protons of OH phenol, amide group (NH-CO) at 9.08 and 9.17 ppm, methyl groups at 1.30 and 1.14-1.17 ppm, phenyl groups at 7.42-8.06 and 7.20-7.99 ppm were assigned to ligands 5 and 6, respectively.

Thermal analysis: All the ligands were characterized using thermal analysis which showed their stability against different temperatures. The thermograms of all the ligands are shown in Figs. 2-7.

Scheme-I: Preparation of the organic ligands (1-4)
Scheme-II: Preparation of organic ligands (5,6)
Fig. 6. Thermal curve of ligand 5

Fig. 7. Thermal curve of ligand 6

Conclusion

In this study, six new heterocyclic Schiff base and azo compounds containing thiazole and imidazole moiety were synthesized from amoxil. All the synthesized compounds were characterized using spectral and thermal techniques.

ACKNOWLEDGEMENTS

The authors thanks Science Center in Canada and Dr. Amani for the spectral analysis of the synthesized compounds.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES