
Synthesis, Characterization and Antibacterial Activity of Imidazole Derivatives of 1, 10-Phenanthroline and their Complexes under Solvent-Free Condition

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Abstract: Thirty Five new $MnL^1, CuL^1, CoL^1, NiL^1, CrL^1, FeL^1$ and ZnL^1 ($L^1 = 4\text{-methyl (1H-imidazo[5,6-f][1,10]phenanthroline)-2-ylphenol}$), $MnL^2, CuL^2, CoL^2, NiL^2, CrL^2, FeL^2$ and ZnL^2 ($L^2 = 2\text{-(1H-imidazo[4,5-f][1,10]phenanthroline-2-yl)-5-methoxyphenol}$), $MnL^3, CuL^3, CoL^3, NiL^3, CrL^3, FeL^3$ and ZnL^3 ($L^3 = (2,4,6\text{-Trimethoxy})\text{ Imidazo[5,6-f]1,10-phenanthroline}$, $MnL^4, CuL^4, CoL^4, NiL^4, CrL^4, FeL^4$ and ZnL^4 ($L^4 = 4\text{-Fluro Imidazo[5,6-f] 1,10-phenanthroline}$, $MnL^5, CuL^5, CoL^5, NiL^5, CrL^5, FeL^5$ and ZnL^5 ($L^5 = [4\text{-Hydroxy phenyl}]Imidazo [5,6-f]1,10-phenanthroline$ complexes were synthesized. L^1, L^2, L^3, L^4 and L^5 ligands were prepared by the condensation of 1,10-phenanthroline-5,6-dione with 2-hydroxy-4-methoxybenzaldehyde, paramethyl benzaldehyde, 2,4,6-Trimethoxy Benzaldehyde, 4-Fluro Benzaldehyde, 4-Hydroxy Benzaldehyde respectively. The structures of the compounds were determined by elemental analyses, IR, UV-Visible, $^1H\text{-NMR}$ and Mass Spectra. Antibacterial activity of the ligands and their metal complexes were tested against selected bacteria by disc diffusion method.

Keywords: 1, 10-Phenanthroline, Imidazole, complex, antibacterial activity.

1. INTRODUCTION

1, 10-Phenanthroline (phen) and its derivations play important roles for supramolecular assemblies because they can also provide bidentate N-donor sites for chelating with metal ions to form bridge ligands. Derivatives of phen are very important ligands in organ metallic chemistry, Systematic studies of substituted derivatives of phen have been successfully undertaken. 1, 10-phenanthroline, as well as some of its derived complexes, do exhibit antimicrobial properties. The photochemical and redox properties of complexes can be varied systematically through appropriate substitution on the phenanthroline rings. Firstly, we synthesized and characterized Cu(II), Co(II), Ni(II), Cr(II), Mn(II), Fe(II) and Zn(II) complexes with phen imidazole derivatives, which are 4-methyl (1H-imidazo[5,6-f][1,10]phenanthroline), 2-(1H-imidazo[5,6-f][1,10]phenanthroline-2-yl)-5-methoxyphenol, (2,4,6-Tirmethoxy) Imidazo[5,6-f]1,10-phenanthroline, 4-Fluro Imidazo[5,6-f] 1,10-phenanthroline, and [4-Hydroxy phenyl]Imidazo [5,6-f]1,10-phenanthroline. Secondly, these compounds were screened for antibacterial activity against such bacterial strains as *A. hydrophila*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *S. marcescens*, *E. aerogenes*, *B. subtilis*, *E. coli* and *E. faecalis*.

2. MATERIALS AND PHYSICAL MEASUREMENTS

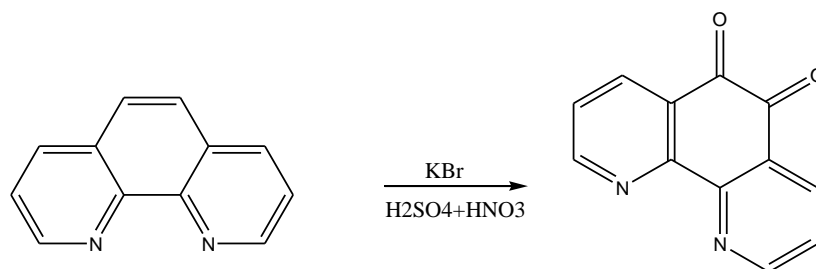
1, 10-phenanthroline-5, 6-dione was synthesized according to a published method. All the chemicals used for this work were obtained from Merck and Aldrich Chemical companies, were used as purchased. Melting point of synthesized compounds were determined in open-glass

capillaries on a stuart-SMP10 melting point apparatus and are uncorrected. Elemental analyses (C, H, N) were performed by using a Leco 932 elemental analyzer. ^1H NMR spectra were recorded on a Bruker 300 MHz spectrometer in DMSO- d_6 . The IR spectra were obtained using KBr discs on an Ati Unicam Mattson 1000 Series FT-IR spectrophotometer. The electronic absorption spectra in the 200–1100 nm range were obtained in DMF on a Shimadzu UV-1700 UV-Visible spectrophotometer mass spectral data were obtained using Positive ESI-MS m/z spectra. Magnetic susceptibility measurements were carried out by the Gouy method at room temperature using $\text{Hg}[\text{Co}(\text{SCN})_4]$ as a reference for calibrant. Conductivities of a 10–3M solution of the complexes were measured in DMF at 25 °C using a CMD 750 WPA model conductivity meter.

3. SCHEME

3.1. Step-I: Synthesis of 1, 10-Phenanthroline [5, 6-Dione]

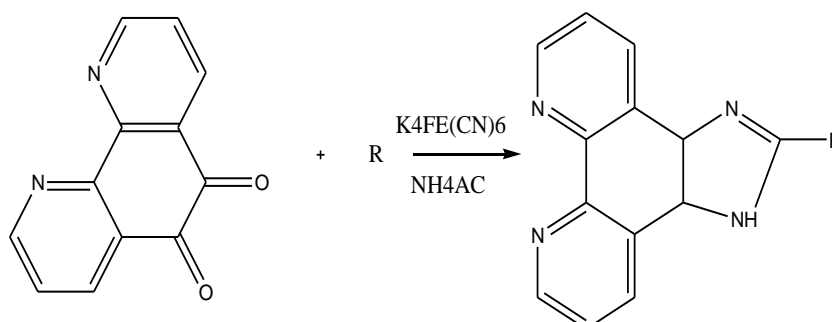
A mixture of 50.4mmol of 1,10 –Phenanthroline is mixed thoroughly with 50.4mmol of KBr, then added 150ml of Conc. H_2SO_4 drop wise later 50ml of HNO_3 is added similarly in a drop wise manner by maintaining the temperature at 0°C-10°C, then refluxed for 5hrs to eliminate Bromine, till the yellow colour mixture obtained. The obtained mixture is neutralized with dilute NaHCO_3 and the compound is extracted with dichloro methane, later the organic layer is separated to get the product.



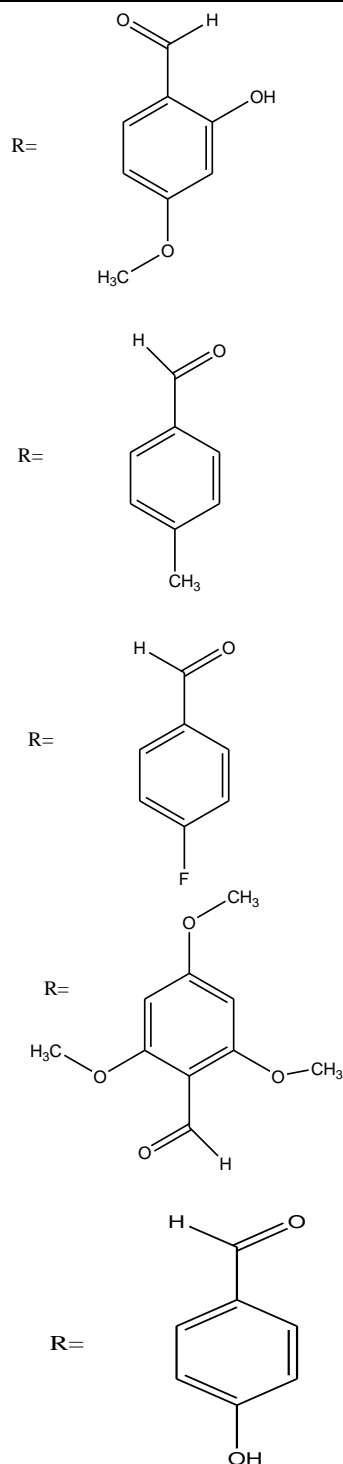
1,10-PHENANTHROLINE[5,6]DIONE IR:; ^1H NMR: (CDCl $_3$, 300MHz), 8.08(2H, CAr-H), 7.24(2H, CAr-H), 8.79(2H, CAr-H); IR: (KBr, cm $^{-1}$) 3375, 3025, 2927, 1591, 1147, 758, 701, 538 MS(ESI): m/z 205 $[\text{M}+\text{H}]^+$

3.2. Step-II: Synthesis of Ligands (L^1 , L^2 , L^3 , L^4 and L^5)

A Mixture of (1.0 g, 4.6mmol) of 1, 10-phenanthroline [5, 6] dione, (5.86 g, 13.3mmol) of ammonium acetate and substituted benzaldehyde derivates are grinded in a mortar pestle thoroughly using $\text{K}_4\text{Fe}(\text{CN})_6$ as catalyst then added few drops of glacial acetic acid to get the product, then the mixture is separated through column and tested with TLC (chloroform: methanol) in (1:1) ratio.



Where R=



2-HYDROXY4-METHOXY IMIDAZO[5,6-f]PHENANTHROLINE IR: (KBr,cm-1)v:3274–2456,1604,1591,1563,1544,1508,1256; ^1H NMR:(CDCl₃,300MHz), 15.81 (1H, s, OH),12.85 (1H, s, NH), 9.06–8.81 (4H, m, CAr – H), 7.86–7.71 (3H, m,CAr – H), 7.11–6.97 (2H, m,CAr –H) and 3.86 (3H, s,OCH₃); MS(ESI): m/z 325 [M+H]⁺

4-METHYL IMIDAZO[5,6-f]1,10-PHENANTHROLINE IR:(KBr,cm-1)v:3254–2436,1574,1561,1543,1514,1498,1156; ^1H NMR:(CDCl₃,300MHz), 12.05 (1H, s, NH), 9.01–8.71 (4H, m, CAr – H), 7.56–7.21 (3H, m,CAr – H), 6.97-6.70 (2H, m,CAr –H) and 3.46 (3H, s,OCH₃); MS(ESI): m/z 290 [M+H]⁺

2,4,6-TRIMETHOXY IMIDAZO[5,6-f]PHENANTHROLINE IR:(KBr,cm-1)v:3200–2256,1590,1481,1326,1373,1408,1120,780,765; ^1H NMR:(CDCl₃,300MHz), 12.85 (1H, s, NH),

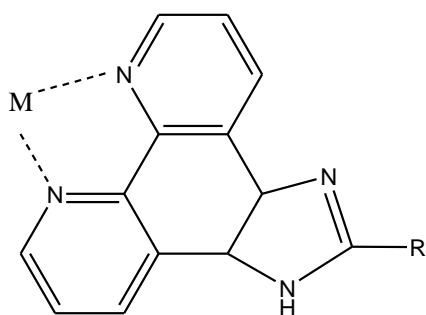
9.06–8.81 (4H, m, CAr – H), 7.86–7.71 (3H, m, CAr – H), 7.11–6.97 (2H, m, CAr – H) and 3.86 (9H, s, OCH₃); MS(ESI): m/z 369 [M+H]⁺

4-FLURO IMIDAZO[5,6-f]1,10-PHENANTHROLINE IR:(KBr,cm-1)v:3290,3140–2456,1599,1483,1539,1511,1479,1198; ¹H NMR:(CDCl₃,300MHz), 12.65 (1H, s, NH), 9.60–8.81 (4H, m, CAr – H), 7.56–7.31 (3H, m, CAr – H), and 7.20–6.97 (2H, m, CAr – H); MS(ESI): m/z 295 [M+H]⁺

4-HYDROXY PHENYL IMIDAZO[5,6-f]1,10-PHENANTHROLINE IR:(KBr,cm-1)v:3054–2356,1579,1399,1339,1411,1391,1298; ¹H NMR:(CDCl₃,300MHz), 13.81 (1H, s, OH), 12.09 (1H, s, NH), 9.16–8.81 (4H, m, CAr – H), 7.89–7.71 (3H, m, CAr – H), and 7.51–6.77 (2H, m, CAr – H); MS(ESI): m/z 298 [M+H]⁺

3.3. Step-III: Synthesis of Complexes

1mmol of liquid in 10ml of methanol is added to metal chelated methanolic solution, reflux for 3 to 4 hours the complex is precipitated filter it in hot condition. Wash with methanol and dry it in vacuum purity tested by TLC.



4. ANTIBACTERIAL ACTIVITY

The in vitro antibacterial screening effects of newly synthesized ligands (L¹, L², L³, L⁴ and L⁵) and their metal complexes were tested against various bacterial strains, (Gram Positive and Gram Negative) viz., *E.Coli*, *S.aureus*, *B.subtilis* and *K.Pneumoniae*. The antibacterial activities were evaluated by disc diffusion method using nutrient agar medium for antibacterial activity. All bacteria were inoculated into Nutrient Broth (Difco) and incubated for 24 h. In the agar well diffusion method (Mueller-Hinton Agar (Oxoid) for bacteria), the dilution plate method was used to enumerate microorganisms (10⁵ bacteria per mL) for 24 hr. Using a sterilized cork borer (6mm diameter), wells were dug in the culture plates. Metal complexes and ligands were performed at the fixed concentration of 2000 µg mL⁻¹ and compounds dissolved in DMF. Compounds dissolved in DMF were added (75 µL) to these wells. The petri dishes were left at 4 °C for 2 h and then the plates were incubated at 37 °C and 30 °C for bacteria (18–24 h). At the end of the period, inhibition zones formed on the medium were evaluated in millimeters. DMF was used as negative control under similar conditions for comparison. Ampicillin (AMP) was used as the reference drug in positive controls. The experiments were performed in triplicate.

5. STATISTICAL ANALYSIS

In this study, repeated measures analysis of variance was used to evaluate the data. Ligands and their metal complexes were analyzed for antibacterial activity at different temperatures. Statistical significance was determined using Duncan multiple comparison test and Bonferroni multiple comparison test was used for grouping within subject factors. SPSS 15.0, version 8, software was used in the statistical analyses.

6. RESULTS AND DISCUSSION

Elemental analyses indicate that the metal: ligand ratio is 1:1. The ligands L¹, L², L³, L⁴ and L⁵ were soluble in EtOH, DMF and DMSO, and the complexes in DMF and DMSO. The melting points of the all compounds were observed. In IR spectra of L¹, L², L³, L⁴ and L⁵, the bands are observed between 3300–3200 cm⁻¹ as broad bands are due to the OH stretching vibrations of H₂O molecules. The broadened band between 3100–2900 cm⁻¹ in IR spectra of the L¹, L², L³, L⁴

and L⁵ ligands is due to the stretching vibrations of the both NH of the imidazole ring and intramolecular hydrogen bonding (O–H...N) formed between phenolic OH and nitrogen atom of C=N group of imidazole ring. The same band was observed in IR spectra of metal complexes of these ligands. This observation confirmed that phenolic OH and nitrogen (C=N) of the imidazole ring do not participate in coordination. Moreover, the stretching vibration of the C=N group (imidazole ring) of the ligands L¹, L², L³, L⁴ and L⁵ were not significantly affected in their complexes, indicating that the nitrogen atom of this group is not involved in coordination for all the complexes. On the other hand, the bands of the C=N (phenanthroline ring) and C=C (Aromatic) groups were shifted to higher frequencies in all the complexes of L¹, L², L³, L⁴ and L⁵ the band at 1563 cm⁻¹ in the free ligand was shifted to higher frequencies (1577 cm⁻¹) in their complexes, that indicates the participation of the C=N (phenanthroline ring) groups in coordination of the metal ion. The bands of the N-H and O–H...N groups in all the complexes of L¹, L², L³, L⁴ and L⁵ shifted to negative frequencies after complexations. The N-H, O–H...N and Ar-O-CH₃ groups in all complexes of L¹, L², L³, L⁴ and L⁵. The negative frequency shifts of these groups may be attributed to flow of electrons from these groups to the phenanthroline ring due to electron flow from the nitrogen atom of the phenanthroline ring to the metal ion after complexations.

7. CONCLUSION

In this study, imidazole and phenanthroline containing L¹, L², L³, L⁴ and L⁵ complexes were synthesized and characterized. According to the IR data of the compounds, ligands (L¹, L², L³, L⁴ and L⁵) are coordinated to the metal ions through nitrogen atoms of the C=N (phenanthroline ring) groups. The results obtained from this research demonstrated that all synthesized compounds have antibacterial activity against the bacterial strains. In this sense, we think that the ligands and their metal complexes might be effective as antibacterial agents against bacteria.

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