Chapter-VII

7.1 Concluding Remarks

In the present dissertation, the catalytic activity of some transition metal borates have been explored in some important organic reactions used for the green synthesis of some Nitrogen containing Heterocyclic Compounds. Looking at the diverse applications of Heterocyclic compounds there are several works on the synthesis of these compounds but most of the works suffer from serious drawbacks like harsh reaction conditions, low yield of the products, use of expensive solvents and non-recyclability of the catalysts. So, in this research work focus has been made on the green synthesis of some Nitrogen containing Heterocyclic compounds using some Transition metal borates like Copper Borate, Iron Borate and Nickel Borate as catalysts thereby investigating their catalytic properties which has not been explored much.

In **Chapter-I** of the thesis, a general introduction to a few Nitrogen containing heterocyclic compounds like 2,4,5-triaryl imidazoles, 3,4-dihydropyrimidin-2[1H]-ones, 1-hydroxy-2-arylimidazole-3-oxides and 2-substituted benzimidazole and 1, 2-disubstituited benzimidazole has been given with emphasis on Green Chemistry, Multicomponent Reactions and Solvent free synthesis. This chapter also includes the recent literature review on the various green protocols followed for the synthesis of these Nitrogen containing Heterocyclic Compounds. The literature review has also been separated into various parts depending on the type of method followed for their synthesis like Classical methods, Solvent free synthesis, Microwave assisted and Ultrasound assisted synthesis. A brief introduction to transition metal borates and their applications in various fields have also been discussed in this chapter.

Chapter-II of the thesis includes the experimental section wherein a brief description of the chemicals and solvents used in this research has been described. This chapter also contains the information about various analytical and spectroscopic techniques like melting point determination, FT-IR, ^{1}HNMR, X-Ray Crystallography along with the information about various theoretical calculations and techniques that were performed in this work like DFT, Molecular Docking and Pharmacokinetic studies.

Chapter-III Section-A of the thesis contains the multi-component green synthesis of 2 4 5 Tri-aryl imidazole derivatives using Copper Borate (CuB_4O_7) as a catalyst under solvent free conditions. This environmentally green approach provided access to substituted imidazole derivatives in good to excellent yield using an unconventional and inexpensive CuB_4O_7 catalyst. The developed catalytic procedure was also found to be operative for a wide range of the aromatic aldehyde substrates.

In **Section-B** of **Chapter-III** the crystal structure of Bis[2-(4,5-diphenyl-1H-imizol-2-yl)-4-nitro-phenolato] copper (II) dihydrate complex is discussed along with its synthesis and Hirschfeld Surface analysis. This section also covers the evidence for the in-situ conversion of CuB_4O_7 into Cu $(OAc)_2.2H_2O$ in presence of NH_4OAc and this evidence led to the finding that whenever copper salts are used as a catalyst for the synthesis of 2,4,5-triarylimidazole derivatives in presence of ammonium acetate, these salts are readily converted into copper acetate dihydrate in the reaction mixture.

Chapter-III Section-C of the thesis includes the theoretical studies and calculations like DFT, Molecular Docking, Non-linear Optical Properties and Pharmacokinetic Studies of the selected 2,4,5 triaryl imidazole derivatives. From DFT studies, the optimized geometry of the compounds were determined along with some important properties like bond lengths, bond angles, dihedral angles. DFT studies also were used to find out some interesting parameters like the energies of HOMO, LUMO, the energy gap between the HOMO and LUMO and global chemical descriptors of the studied compounds. Molecular Docking studies of these compounds were carried out with insulin receptor protein (PDB ID: 1IR3) and the compounds showed a very good binding interaction with the protein. The pharmacokinetic properties like ADMET of these compounds were determined with the help of SwissADME database (http://www.swissadme.ch) and they showed no violation of Lipinski's rule thus qualifying the drug likeliness criteria.

In **Chapter-IV Section-A**, we were able to explore the catalytic efficiency of Iron Borate in the synthesis of 3,4-dihydropyrimidine-2-(1H)-ones (DHPMs) and the catalyst showed very good results with excellent yield of the products and the catalyst showed remarkable recyclability and could be used efficiently up to the 4^{th} run of the reaction

In **Section-B of Chapter-IV**, theoretical studies of the selected 3,4-dihydropyrimidine-2-(1H)-one derivatives (DP-1 to DP-3) have been done. The theoretical approach included DFT, Molecular Docking Studies, Non-Linear Optical Properties and Pharmacokinetic studies. Some theoretical Parameters like energies of Frontier Molecular orbitals (HOMO and LUMO), their energy gaps, global chemical descriptors, bond lengths, bond angles, dihedral angles,etc. which are very important for the study of structure of the complexes were calculated with the help of DFT. The compounds also showed promising NLO properties when compared with reference material Urea. Finally molecular docking study of these compounds was done with the protein 3DH4 and the compounds showed good interaction with the receptor protein.

Chapter-V Section A of the thesis includes synthesis of 1-hydroxy-2-arylimidazole-3-oxide derivatives under solvent free condition using inexpensive Copper borate (CuB_4O_7) catalyst. As we were unable to recover the catalyst Copper Borate in the reaction for the synthesis of 2,4,5-triaryl imidazoles as

discussed in Chapter-I, it was again attempted to use copper borate as catalyst in yet another famous organic reaction for the synthesis of 1-hydroxy-2-arylimidazole-3-oxides under solvent free conditions and in this case, we were able to recover the catalyst successfully and the catalyst did not lose its efficiency up to 5^{th} run of the reaction.

Chapter-V Section-B of the thesis includes the theoretical studies and calculations like DFT, Molecular Docking, Non-linear Optical Properties and Pharmacokinetic Studies of the selected and 1-hydroxy-2-arylimidazole-3-oxide derivatives. From the optimized geometry of these studied compounds various parameters like Bond length, Bond angles, energies of HOMO, LUMO and the energy gap between them, theoretical FT-IR vibrational frequencies, NLO properties, global chemical descriptors and MESP were calculated. The experimentally observed FT-spectra matched well with the theoretical FT-IR spectra for all the compounds under study. For Molecular Docking studies, the crystal structure of the protein 3ERT was downloaded from the Protein Data Bank (PDB). All the selected compounds under study showed good binding interactions with the chosen protein. For analyzing the drug likeliness of the selected compounds, their ADMET properties were also determined from online SwissADME database (http://www.swissadme.ch) and in no case any violation of Lipinski's Rule was observed.

Finally in **Chapter-VI** of the thesis, solvent free green synthesis of 2-substituted benzimidazole and 1, 2-disubstituted benzimidazole derivatives is reported using Nickel Borate as an efficient catalyst. The catalyst was found to be an efficient and versatile for the synthesis of the above-mentioned derivatives under green chemical condition. This process is advantageous due to its simple operational procedure and easy work-up of the product with minimal use of the hazardous solvent.

In Conclusion, we have been able to explore the catalytic activity of Copper Borate, Iron Borate and Nickel Borate in some solvent free multicomponent green reactions and thus we were able to prepare some very important Nitrogen Containing Heterocyclic Compounds like 2,4,5-triaryl imidazoles, 3,4-dihydropyrimidine-2-(1H)-ones, 1-hydroxy-2-arylimidazole-3-oxides, 2-substituted and 1, 2-disubstituted benzimidazoles in good yields. The borates that have been studied in this work have shown promising catalytic efficiency. Yet there are lot of other transition metal borates whose catalytic activity needs to be explored and in future more works in this field is highly expected.

APPENDIX-I

Supplementary spectra of Chapter III Section-A

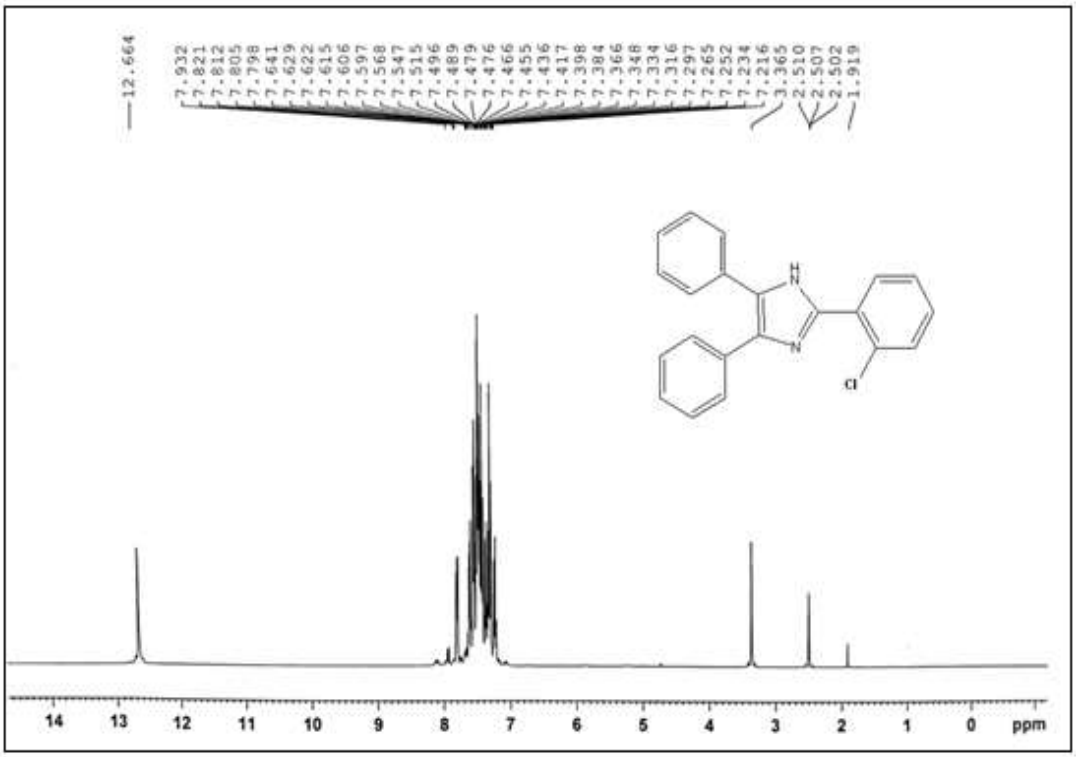

Fig. S. 3A.1. ^{1}H NMR spectra of 2-(2-chlorophenyl)-4,5-diphenyl-1H-imidazole (4e)

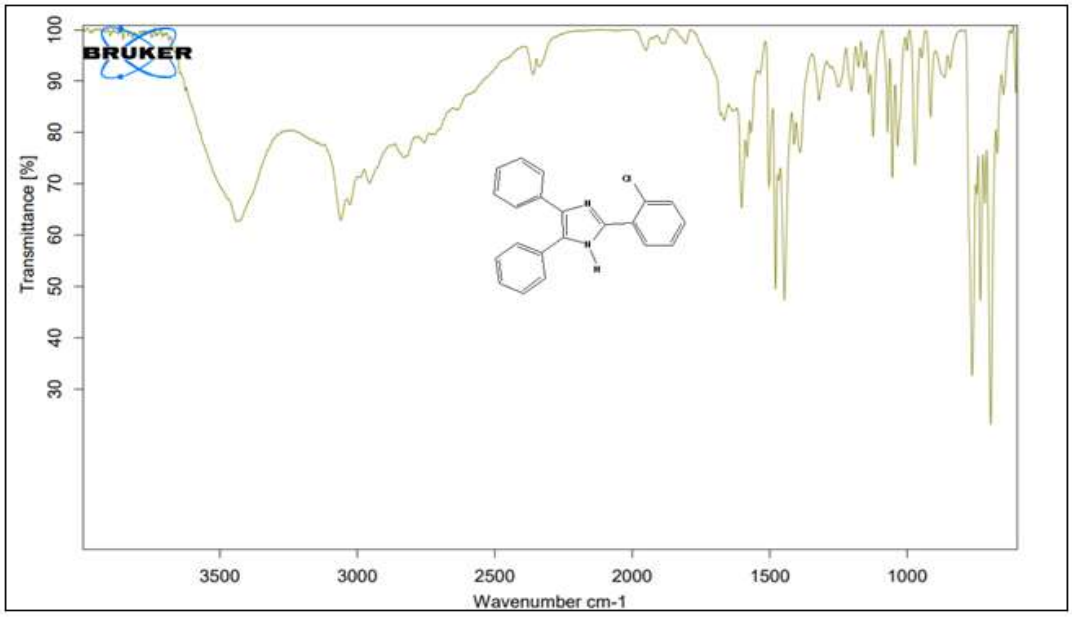

Fig. S. 3A.2. FT-IR spectra of 2-(2-chlorophenyl)-4,5-diphenyl-1H-imidazole (4e)

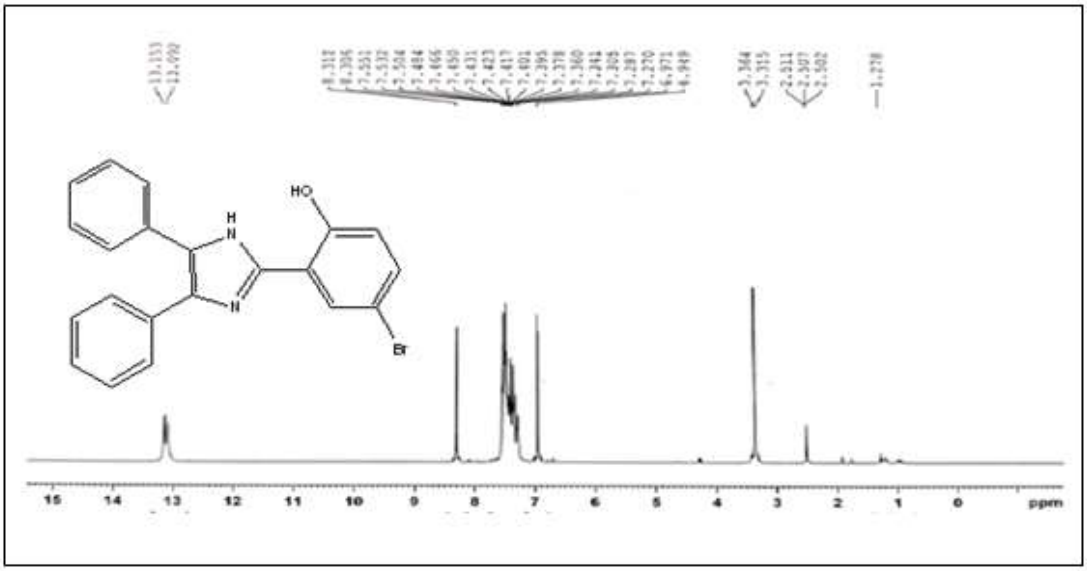

Fig. S. 3A.3. ^{1}H NMR spectra of 4-bromo-2-(4,5-diphenyl-1H-imidazol-2-yl)phenol (4m)

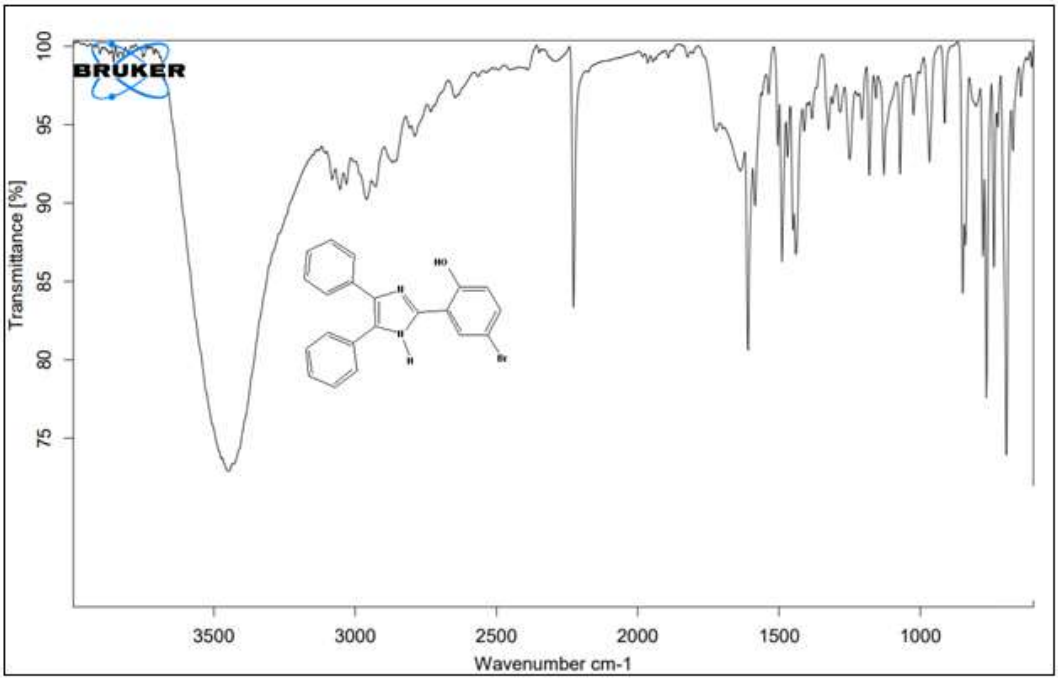

Fig. S. 3A.4. FT-IR spectra of 4-bromo-2-(4,5-diphenyl-1H-imidazol-2-yl)phenol (4m)

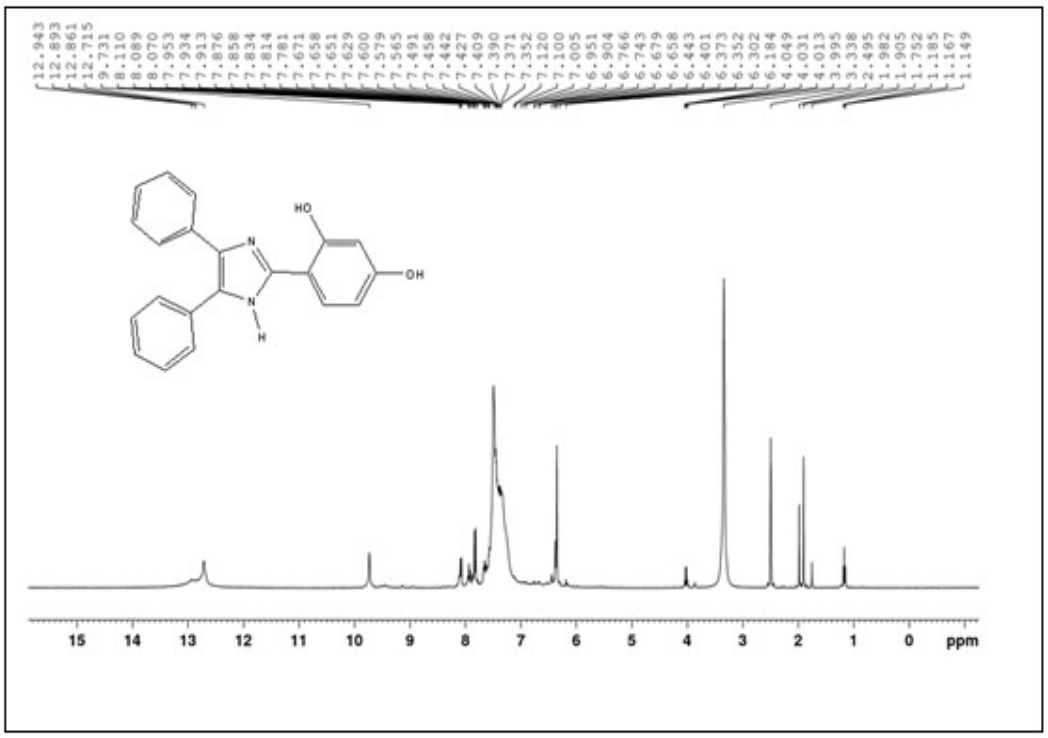

Fig. S. 3A.5. [1]H NMR spectra of 4-(4,5-diphenyl-1H-imidazol-2-yl)benzene-1,3-diol (4o)

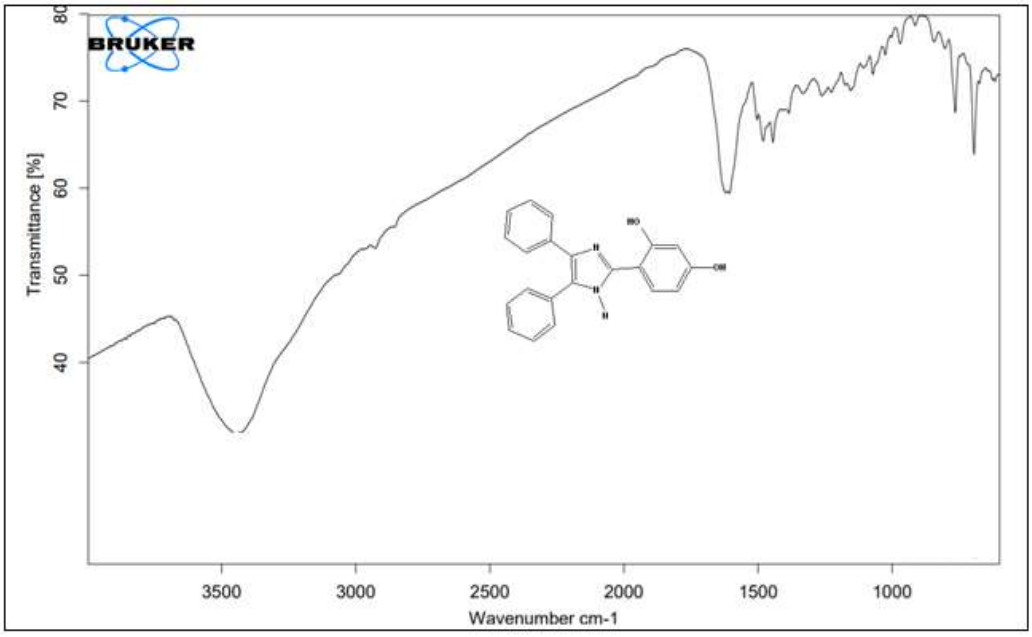

Fig. S. 3A.6. FT-IR spectra of 4-(4,5-diphenyl-1H-imidazol-2-yl)benzene-1,3-diol (4o)

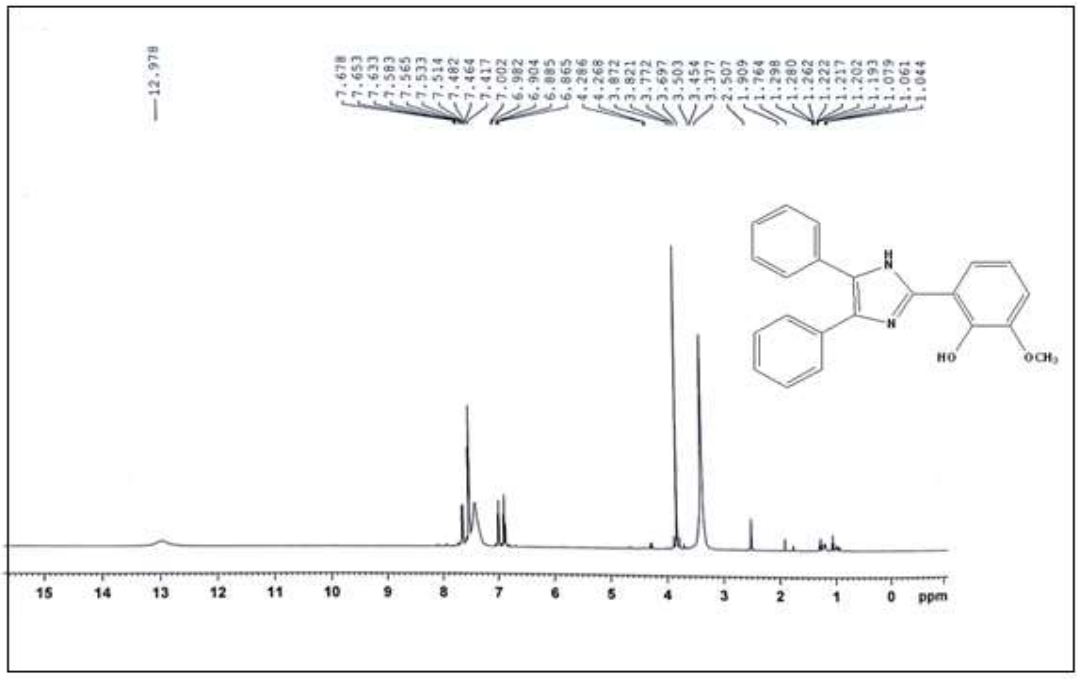

Fig. S. 3A.7. ^{1}H NMR spectra of 2-methoxy-6-(4,5-diphenyl-1H-imidazol-2-yl)phenol (4p)

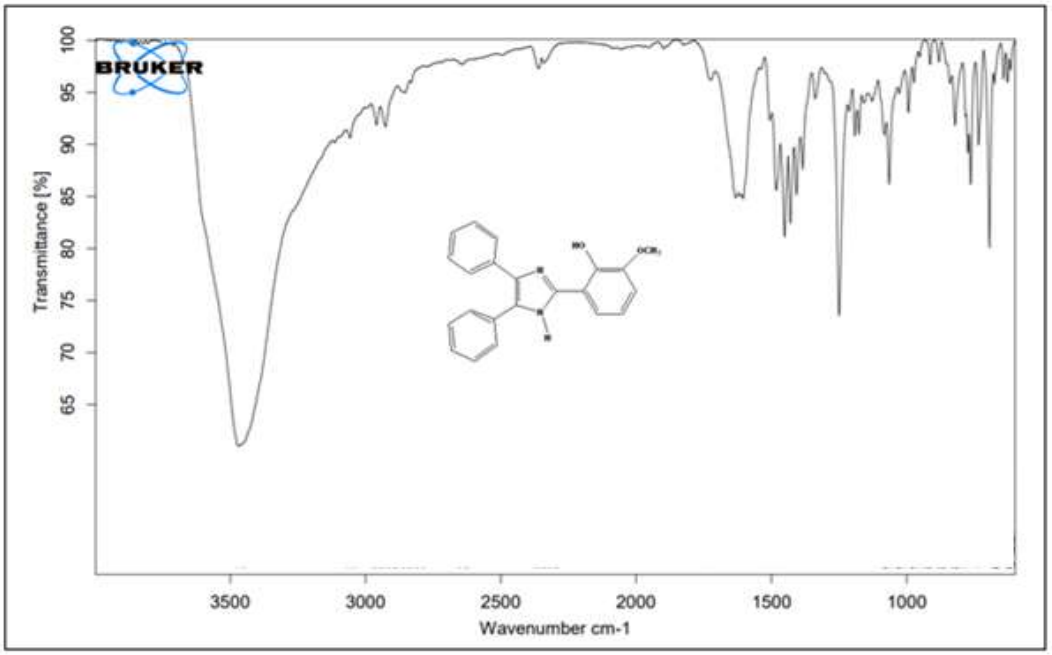

Fig. S. 3A.8. FT-IR spectra of 2-methoxy-6-(4,5-diphenyl-1H-imidazol-2-yl)phenol (4p)

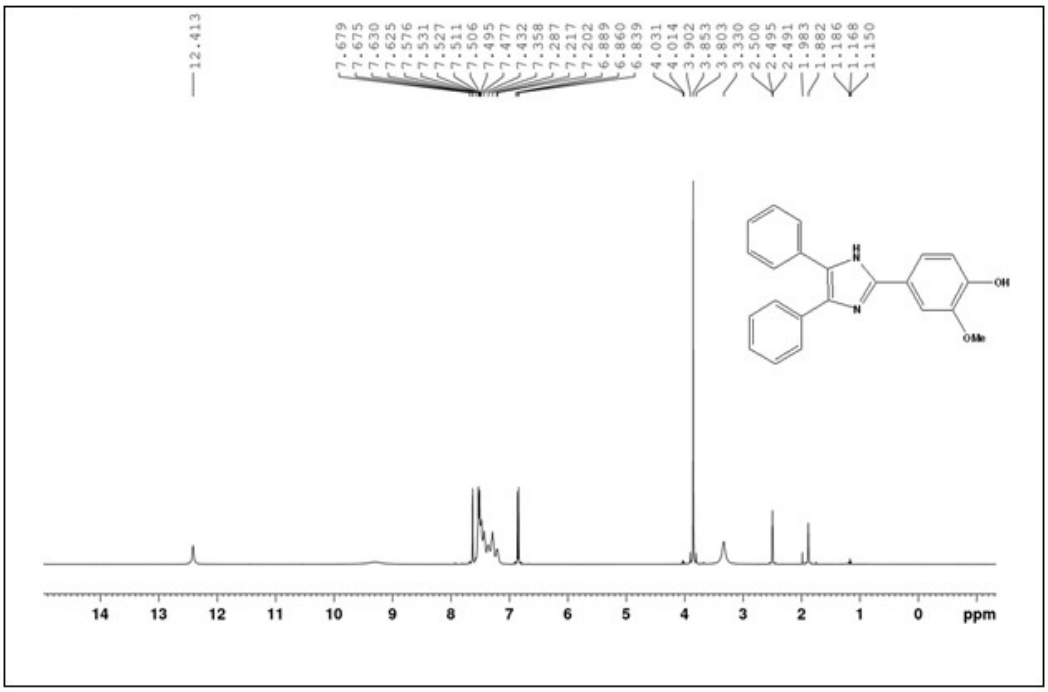

Fig. S. 3A.9. [1]H NMR spectra of 4-(4,5-diphenyl-1H-imidazol-2-yl)-2-methoxyphenol (4q)

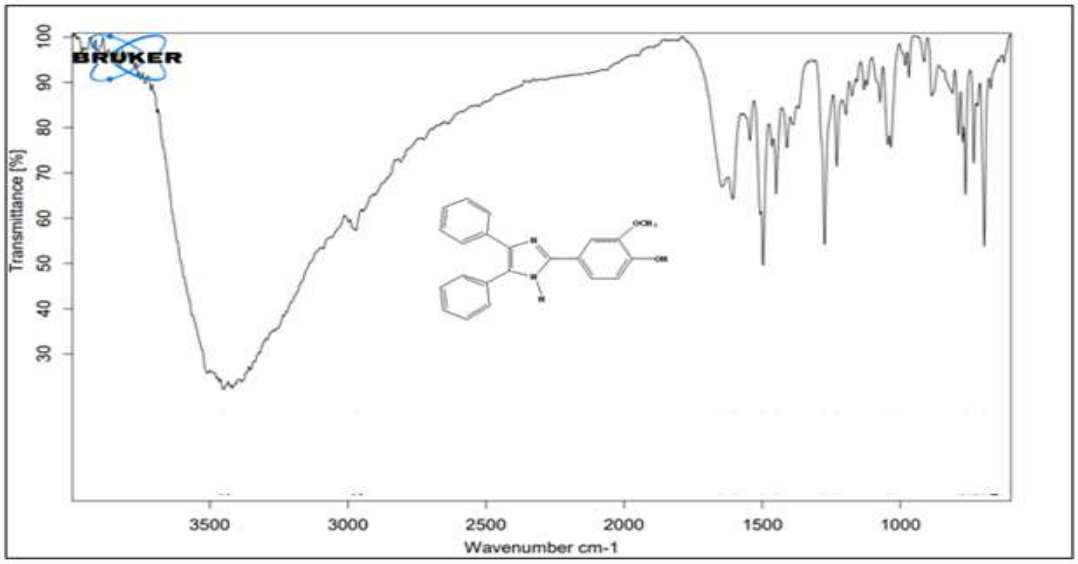

Fig. S. 3A.10. FT-IR spectra of 4-(4,5-diphenyl-1H-imidazol-2-yl)-2-methoxyphenol (4q)