International Journal of Chemical Science
www.chemicaljournals.com
Online ISSN: 2523-2843, Print ISSN: 2523-6075
Received: 04-04-2025, Accepted: 05-05-2025, Published: 20-05-2025
Volume 9, Issue 1, 2025, Page No. 10-12

Design and synthesis of metal complexes of azo compound containing thymol moiety

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Abstract
In the present work, synthesis of azo compounds containing hydroxyl group and amino group has been done by diazotization method and coupled with thymol. These newly synthesized azo compounds were characterized and confirmed by modern sophisticated techniques. After confirmation these newly synthesized azo compounds employed as ligand to form metal complexes of Ni and Cu. The metal complexes formed were may be acts as possible antibacterial or antifungal and it opens the new era for the future study on azo metal complexes.

Keywords: Thymol, azo compounds, cu metal azo complexes, ni metal azo complexes

Introduction

Thymol is a naturally occurring essential oil obtain from plant *Thymus vulgaris L.* It was observed that, thymol was used from ancient days as antioxidants to anti-tumor. It was also found that, it has been used in management of disease like many types of cancer, cardiovascular diseases, diabetes etc [1, 2]. Now a day's vast research is going on thymol to proves the pharmacological properties and wide spectrum of applications in different areas [3]. In connection with anti bacterial properties it shows Antibiofilm action against *E. Coli, L. monocytogenes, P. putida, S. aureus*, it also shows antifungal properties against *Fusarium spp., Aspergillus spp., Candida spp., as well as C. neoformans and C. laurentii* [4]. The oil obtained from plant *Thymus vulgaris L.* is known as thyme oil and it is used as anti-inflammatory and anti-microbial agents [5]. It is used as cleaning product and disinfectant due to its wide range of antibacterial, antifungal and antiviral activity, this is one of the natural alternatives to conventional chemical cleaners [6].

The molecular docking studies of some azo compound metal complexes of Fe (III), Co (II) and Cu (II) shows significant anti-inflammatory activity. In addition to this Gamma irradiation of variable concentrations of these complex also was investigated and shows increased colour bleaching property as increasing the absorbed dose in the range of 3, 5 and 10 kGy [7]. Metal complex of Cr (III), Fe (III), Mn (II), Co (II), Ni (II), Zn (II), Cu (II), and Cd (II) ions containing azo compound of 4-aminoantipyrine and 2-aminophenol shows good antimicrobial activity against *Staphylococcus aureus* and *Bacillus subtilis* as gram-positive bacteria, *Salmonella* sp. and *E. coli* as gram-negative bacteria, and fungal (*Aspergillus fumigatus* and *Candida albicans*) species [8]. Similar type study was reported by Walaa H. Mohamoud et.al that the metal complex of Cr(III), Mn(II), Fe(III), Co.(II), Ni(II), Cu(II), Zn(II) and Cd(II) ions with ligands containing azo compound of 2,6-diaminopyridine and *p*-methoxybenzaldehyde gives remarkable antimicrobial activity against some gram-negative, gram-positive bacteria as well as against some fungal species. Anti cancer evaluation studies against standard breast cancer cells also well performed in various concentrations also reported [9]. Azo ligands containing phloroglucinol and antipyrines exhibits good sorption activity towards heavy metal ions such as Co (II), Ni (II), Zn (II), Cu (II), and Cd (II) [10]. Azo of [4-((8-hydroxyquinolin-7 yl)-N (4-methylisoxazol-3-yl) benzenesulfonamide] allow to complex formation with Ni (II), Pt (IV), Pd (II), and Rh (III) in [1M:1L] molar ratio shows considerable antioxidant activity [11]. Azo Ligand synthesized from 4,4'-Methylenedianiline and 4-Bromoaniline and complex formation with Cu (II), Zn (II), Cd (II), and Ag(I) shows good antimicrobial activity against Gram-positive such as *Staphylococcus aureus*, *Enterococcus feacalis* and Gram-negative bacteria such as *E. coli*, *Pseudomonas aeruginosa* [12].

By considering the above all properties of thymol and different types of metal complexes of azo compounds, the author encourages to undertake the synthesis of azo compounds containing thymol moiety and formation of their metal complexes.

Materials and Methods

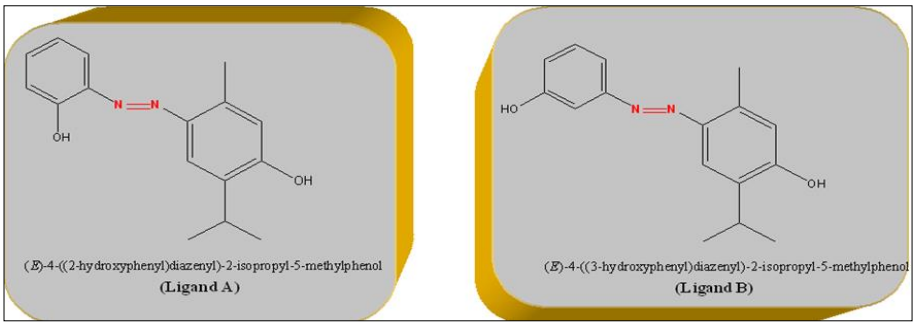
The chemicals were used in this work is of synthetic grade (S.D. Fine Chem. Ltd, Mumbai, India). The obtained products were characterized by ^{1}H NMR and IR. The melting points were determined and recorded by open capillary method and are subject to correction. The IR spectra were recorded on a Perkin-Elmer spectrum-one FTIR instrument in the form of KBr pallet. ^{1}H NMR spectra (Table I) were recorded in $CDCl_3$ on a Varian Mercury-YH-300 spectrometer using TMS as an internal standard. The purity of compounds was checked by TLC. The crude products were recrystallized from ethanol as solvent.

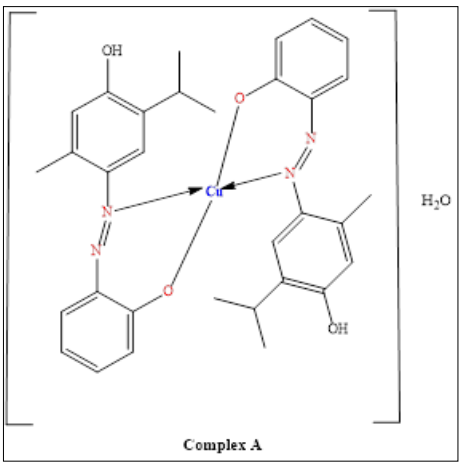
Preparation of Ligands: [(*E*)-4-((2-hydroxyphenyl) diazenyl)-2-isopropyl-5-methylphenol (Ligand -A)] 2-amino phenol (1.09 g, 0.01 mole) was mixed with Conc. HCl (2.5 mL) to the resultant suspension crushed ice (25 g) and $NaNO_2$ (2.5 mL, 4N) was added with stirring. Diazotization was carried out over 30 mins at 5° - 7°C and then diazonium salt solution was added drop wise at 5 to 10°C to the alkaline solution of thymol. The coupling reaction was stirred for 45 mins and the pH of the resultant mixture was adjusted to pH 7. The formed ligand product was filtered, washed with water and dried. Crude products were recrystallized with proper solvent.

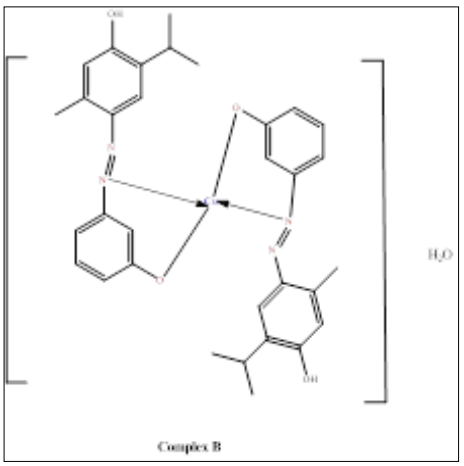
[(*E*)-4-((2-hydroxyphenyl)diazenyl)-2-isopropyl-5 methylphenol (Ligand -A)]: M. P. 186°C; IR (KBr) 1377.91 cm^{-1} of –C-N- aro stretching, 1572.29 cm^{-1} of –N=N- stretching, 1637.97 cm^{-1} of –C=C- aro stretching, 3178.98 cm^{-1} of aro –OH stretching, ^{1}HNMR (DMSO-d_6):δ 1.34 (d, 6H, two $–CH_3$), 2.38 (s, 3H, - CH_3 of thymol), 3.21 (m, 1H, isopropyl of thymol), 4.01 (bs, 1H, -OH of thymol), 4.44 (bs, 1H, -OH of amino phenol), 6.81 (s, 1H, aro. of thymol), 6.93 (dd. 1H aro. of amino phenol), 7.02 (dd, 1H aro. of amino phenol), 7.28 (dd, 1H aro. of amino phenol), 7.76 (dd, 1H aro. of amino phenol), 7.77 (s, 1H, aro. of thymol).

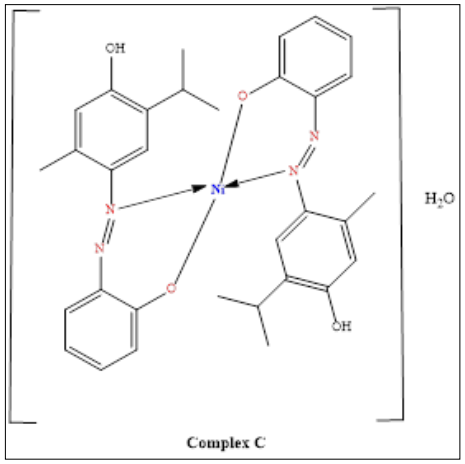
[(*E*)-4-((3-hydroxyphenyl)diazenyl)-2-isopropyl-5-methylphenol (Ligand -B)]: M. P. 162°C; IR (KBr) 1478.98 cm^{-1} of –C-N- aro stretching, 1586.59 cm^{-1} of –N=N- stretching, 1571.98 cm^{-1} of –C=C- aro stretching, 2971.42 cm^{-1} of aro –C-H stretching, ^{1}HNMR (DMSO-d_6):δ 1.34 (d, 6H, two $–CH_3$), 2.38 (s, 3H, - CH_3 of thymol), 3.22 (m, 1H, isopropyl of thymol), 3.73 (bs, 1H, -OH of amino phenol),3.86 (bs, 1H, -OH of thymol), 6.85 (s, 1H, aro. of thymol), 6.92 (dd. 1H aro. of amino phenol), 7.28 (dd, 1H aro. of amino phenol), 7.44 (dd, 1H aro. of amino phenol),7.49 (dd, 1H aro. of amino phenol), 7.78 (s, 1H, aro. of thymol).

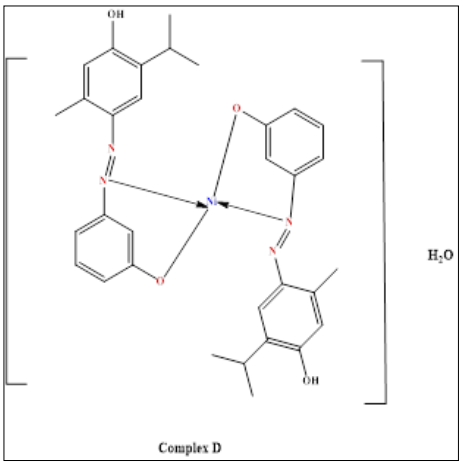
Preparation of Metal complexes [Complex A-D]:
Take 0.20 gm of ligand A or B azo compound in 100 ml beaker, add 15 ml alcohol and 15 ml of water in it. In another beaker 15 ml alcohol and 5 ml of water mixture was taken and dissolve the metal chloride salt in it ($NiCl_2$ $6H_2O$ or $CuCl_2$ $6H_2O$). After this add the metal chloride solution into the solution of ligand azo compound with constant stirring (Magnetic stirrer). After 30 to 35 mins metal complex crystals were precipitate out. For digestion purpose this reaction mixture was refluxed for 60 mins, on magnetic stirrer (precaution was taken that, the temperature of reaction mixture is not exceeds 80°C and stirring speed dose not exceeds 750 rpm). Finally, cool the reaction mixture and filter the obtained metal complex product and dry it.











Results and Discussion

The newly synthesized azo compounds i.e. ligands were primarily identified by their intense red colour and were characterized by IR and ^{1}HNMR. In IR spectra both ligands show the characteristic absorption peak of –N=N- at 1572.29 cm^{-1} and at 1586.59 cm^{-1} respectively (generally –N=N- absorbs between the range of 1465-1600 cm^{-1}). In ^{1}HNMR spectrum of both ligands, disappearance of peak at 6.69 (dd, 1H aro. para to -OH) clearly indicates the coupling of diazonium salt at para position to –OH of thymol.

The newly synthesized metal complexes show different solubility properties in different solvents. In water complex A, C and D are sparingly soluble, but complex B is slightly soluble, whereas in organic solvents such as methanol, acetone and chloroform all complexes are completely soluble.

Table 1: IR values comparison between expected values and observes values for all complexes

Functional groups	Observed value in Complex A	Observed value in Complex B	Observed value in Complex C	Observed value in Complex D	Expected value
-C-H	3000.56 cm^{-1}	3051.25 cm^{-1}	3065.21 cm^{-1}	3047.21 cm^{-1}	3300-2800 cm^{-1}
-N=N-	1390.62 cm^{-1}	1390.32 cm^{-1}	1370.52 cm^{-1}	1371.21 cm^{-1}	1600-1400 cm^{-1}
-C=C-	1352.24cm^{-1}	1365.25 cm^{-1}	1368.32 cm^{-1}	1362.54 cm^{-1}	1500-1400 cm^{-1}
Aro. –OH	3254.21 cm^{-1}	3254.54 cm^{-1}	3354.25 cm^{-1}	3362.54 cm^{-1}	4000-3500 cm^{-1}

In IR spectra of all metal complexes one thing is common that, the peak at 550–530 cm^{-1} appears due to presence of –O-M bond in amino phenol and metal ion i.e. formation of coordinate bond with metals, this gives the confirmation of formation of metal complexes.

Conclusion

Azo compounds containing thymol moiety was successfully synthesized by using amino phenols. They were characterized and confirmed by IR and ^{1}H NMR. Further, these newly synthesized azo compounds containing thymol moiety were used as ligand for the formation of metal complexes of Cu metal and Ni metal ions. No doubt further research needed for complete optimization and focus on various properties of such type of metal complexes. But this type research may open the new era or gateway to new researcher in the field of coordination chemistry.

Acknowledgement

The author thanks The Management and Principal, S. S. V. P. S's. L. K. Dr. P. R. Ghogrey Science College, Dhule (M. S.) INDIA for providing all the necessary facilities to complete the research work.

Conflict of Interest

The author declared no conflict of interest.

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