Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis, spectral characterization and catalytic activity of metal complexes with pyrazoline derivatives.

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ABSTRACT

Novel Cu(II), Co(II), Ni(II) and Zn(II) complexes of pyrazoline derivatives containing indole and naphthyl moieties were prepared. They were characterized using elemental analysis, FTIR, proton NMR, UV-Vis., molar conductance, magnetic susceptibility measurements and electrochemical studies. On the basis of molar conductance, magnetic moment and electronic absorption data, square planar geometry has been assigned for all the complexes. Further, it was subjected to catalytic reactions of phenol to catechol and to optimize reaction conditions for achieving better yield with higher turnover number.

Keywords: Pyrazoline, indole, catechol, phenol,

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INTRODUCTION

Heterocyclic molecules played a significant role in medicine and material research. Among the heterocycles, the indole moiety has been reported as active pharmacophore in the field of medicinal chemistry [1, 2]. Indole derivatives have positioned a unique place in the structural, materials and biochemistry because of its varied spectral and biological features [3-6]. In addition, the metal ions accelerate drug action and the efficiency of molecule may be enhanced upon coordination with metal [7].

The literature reports highlighted the importance of pyrazoline derivatives and their metal complexes possessed interesting biological actions. The incorporation of indole moiety makes versatile ligand systems. The chemical versatility of pyrazoline scaffold allows the introduction of different substituents on phenyl hydrazine core at different positions opened up new challenges for the fine tuning of the physico-chemical and structural properties of the resulting molecules. The position of different substituents have influenced the effect on the metal centre and may enhance the essential properties of therapeutic molecules such as solubility, stability etc and provide offer to behave as effective therapeutic molecules as alternative for existing molecules or drugs.

The distinct redox properties of copper complexes have been of great fascination to inorganic chemists since it naturally occurring as blue copper proteins [13]. Copper is one of the most abundant redox active metals which are responsible for redox center in catalysis [14-15]. There is a best correlation between redox potential and structure in which the most common structures for four-coordinate Cu^{2+} and Cu^+ complexes are square planar and tetrahedral, respectively[15] e.g. for blue copper electron transfer proteins use copper as a one electron relay, transferring between the cuprous and cupric oxidation states[16-17].

Catechol is produced by the hydroxylation of phenol using hydrogen peroxide.50%of synthetic catechol is consumed by the production of pesticides, perfumes and pharmaceuticals. [18]. Several industrially significant flavors and fragrances are prepared starting from catechol. Catechol is the conjugate acid of a chelating agent used widely in co-ordination chemistry. It is produced by a reversible two-electron, two-proton reduction of 1,2- benzoquinone [19,20].

In the present investigations we focused on the synthesis and characterization of ligands and their copper complexes. Further, the copper complexes were subjected to catalytic studies with respect to the conversion of phenol into catechol.

EXPERIMENTAL

Material

All chemicals and solvents were analar grade and were purchased from Merck. All supporting electrolyte solutions were prepared using analytical grade reagents.

Instrumentation

The amount of metal present in the metal complexes was estimated using ammonium oxalate method. Elemental analysis of ligands and their metal complexes were carried out using Elementar Vario EL III. Molar conductance of the complexes was measured using a coronation digital conductivity meter. The ^{1}H-NMR spectra of the ligands were recorded using TMS as internal standard. Chemical shifts are expressed in units of parts per million relative to TMS. The IR spectra of the ligands and their copper complexes were recorded on a Perkin-Elmer 783 spectrophotometer in 4000-200 cm^{-1} range using KBr disc. Electronic spectra were recorded in a Systronics 2201 Double beam UV-Vis., spectrophotometer within the range of 200-800 nm regions. Magnetic moments were measured by Guoy method and corrected for diamagnetism of the component using Pascal's constants. Cyclic voltammetry was performed on a CHI 604D electrochemical analyzer with three electrode system of glassy carbon as the working electrode, a platinum wire as auxiliary electrode and Ag/AgCl as the reference electrode. Tetrabutylammoniumperchlorate (TBAP) was used as the supporting electrolyte. Solutions were deoxygenated by eradication with N_2 previous to measurements.

Synthesis of ligand (L)

A solution of 1-acetyl-2-hydroxynapthalene (0.01 M) and indole-3-carboxaldehyde (0.01 M) in 40 ml methanolic NaOH (10% methanolic solution) was stirred for 6 hrs at room temperature. The solid precipitate (chalcone) obtained was washed with ice-cold water and then rectified spirit, dried. It was recrystallized from ethanol. A mixture of chalcone (0.01 M) and phenylhydrazine (L[16]) was refluxed in 40 mL of methanol for 8 hrs. The solution was poured into ice water which resulted into the precipitation of the ligand (L[16]). The precipitate was filtered and recrystallized from methanol. The recrystallized ligand was dried in a vacuum dessicator over fused calcium chloride.

Ligand (L[16]): Mol.formula $C_{27}H_{20}N_4O_3$, Mol wt. 448. Yield: 68%; CHN analysis: Calcd: C 72.31, H 4.49, N 12.49; Found: C 72.14, H 4.36, N 12.48. UV (nm): 346, 260 nm. FT-IR (cm^{-1}): 3286 (Ar O–H); 3080-3070 (Ar–H); 2968, 2899 (C–H); 1650 (C=N); 1228 (Ar C–OH). ^{1}H-NMR (ppm):3.16(J=4.0,17.2Hz, 4-Htrans, pyrazoline core, 1H, dd), 3.56 (J = 11.0, 17.4 Hz, 4-Hcis, pyrazoline core, 1H, dd), 5.24 (J = 4.0, 11.8 Hz, 5-H, 1H, dd), 6.48-7.56 (m, 15 Ar-H), 11.2 (1H,s, -OH), 9.6 (-NH, indole moiety), 3.6 (-CH=, indole core).^{13}C NMR (ppm): 125.2 (C1), 125.8 (C2), 122.6 (C3), 126.8 (C4), 132.4 (C5), 116.4 (C6), 152.6 (C7), 112.0 (C8), 134.8 (C9), 128.2 (C10), 156.4 (C11), 40.8 (C12), 53.4 (C13), 135.5 (C14), 100.6 (C15), 124.6 (C16), 119.6 (C17), 120.2 (C18), 119.6 (C19), 110.5 (C20), 134.9 (C21), 144.6 (C22), 11.6 (C23), 128.4 (C24), 116.2 (C25), 128.4 (C26), 11.6 (C27). MS(m/z): 449 [M+1]. LogP Found (calculated): 6.33 (6.20)

Synthesis of complexes

A solution of metal acetate (0.05 M) in 20 mL methanol was added to a stirred solution of ligand (s) (0.05 M) in 20 mL of methanol. The resulting mixture was stirred at room temperature till a precipitate of the complex formed. The precipitate was filtered and washed with cold methanol and hexane. The other metal complexes were prepared using similar procedure. The complexes were dried in a vacuum dessicator over fused calcium chloride**.**

Copper complex of L[16]: Mol.formula:$C_{29}H_{24}N_4O_6Cu$. Mol wt. 588. Yield: 58%; CHN analysis: Calcd: C 59.23, H 4.11, N 9.53, Cu 10.81; Found: C 59.10, H 3.94, N 9.46, Cu 10.69. UV (nm): 330, 252, 482 nm. FT-IR (cm^{-1}): 3170 (N–H), 1146 (C–N), 1580 (C=N), 536 (M–N), 476 (M–O).MS:m/z:589[M+1]. μ_{eff}(BM) = 1.94. Λ_m (S cm^{2}mol^{-1}) = 12.

Nickel complex of L[16]: Mol.formula $C_{29}H_{24}N_4O_6Ni$. Mol wt. 583. Yield: 64%; CHN analysis: Calcd: C 59.73, H 4.15, N 9.60, Ni 10.06; Found: C 59.56, H 3.98, N 9.46, Ni 9.92. UV (nm): 310, 248, 628 nm. FT-IR (cm^{-1}): 3170 (N–H), 1140 (C–N), 1572 (C=N), 544 (M–N), 478 (M–O). ^{1}H-NMR (ppm): 3.16 (1H, dd, J = 4.0, 17.2 Hz, 4-Htrans, pyrazoline core), 5.24 (1H, dd, J = 4.0, 11.8 Hz, 5-H, pyrazoline core), 3.56 (1H, dd, J = 11.0, 17.4 Hz, 4-Hcis, pyrazoline core), 6.48-7.56 (m, 15 Ar-H), 9.6 (-NH, indole moiety), 3.6 (-CH=, indole moiety). MS: m/z: 584 [M+1]. μ_{eff}(BM) =0. Λ_m (S cm^{2}mol^{-1}) = 10

Cobalt complex of L[16]: Mol.formula $C_{29}H_{24}N_4O_6Co$. Mol wt. 583. Yield: 62%; CHN analysis: Calcd: C 59.70, H 4.15, N 9.60, Co 10.10; Found: C 59.66, H 4.02, N 9.44, Co 9.90. UV (nm): 338, 264, 580 nm. FT-IR (cm^{-1}): 3170 (N–H), 1168 (C–N), 1588 (C=N), 547 (M–N), 480 (M–O). MS: m/z: 584 [M+1]. μ_{eff}(BM) = 4.84. Λ_m (S cm^{2}mol^{-1}) = 12.

Zinc complex of L[16]: Mol.formula $C_{29}H_{24}N_4O_6Zn$. Mol wt. 590. Yield: 60%; CHN analysis: Calcd: C 59.05, H 4.10, N 9.50, Zn 11.09; Found: C 58.90, H 3.96, N 9.34, Zn 10.86. UV (nm): 382, 260 nm. FT-IR (cm^{-1}): 3106 (N–H), 1140 (C–N), 1570 (C=N), 552 (M–N), 486 (M–O). ^{1}H-NMR (ppm): 3.16 (1H, dd, J = 4.0, 17.2 Hz, 4-Htrans, pyrazoline core), 5.24 (1H, dd, J = 4.0, 11.8 Hz, 5-H, pyrazoline core), 3.56 (1H, dd, J = 11.0, 17.4 Hz, 4-Hcis, pyrazoline core), 6.48-7.56 (m, 15 Ar-H), 9.6 (-NH, indole moiety), 3.6 (-CH=, indole moiety). MS: m/z: 591 [M+1]. μ_{eff}(BM) = 0. Λ_m (S cm^{2}mol^{-1}) = 7.

Catalytic protocol : Reaction of phenol into catechol

The oxidation of phenol (substrate) was performed as follows: 2–10 mM of H_2O_2 was added to the copper complex(es) (0.03 mM) in 10 mL of acetonitrile in the RB flask fitted with condenser. 1.0 mM of the substrate was added to the reaction mixture. The resulting solution was stirred for 32 hrs at RT. The extraction of substrate and product was performed from diethyl ether. The organic phase of the sample was performed

by gas chromatography. The identification of product was compared with commercial available substance. The blank experiment was performed for the oxidation of phenol without catalyst in the same experimental conditions.

RESULTS AND DISCUSSION

The preparation of pyrazoline derivatives (L) and their metal complexes are presented in scheme 1. The chalcones were prepared by the Claisen-Schmidt condensation of 1-acetyl-2-hydroxynaphathalene and indole-3-carboxaldehyde in the presence of basic medium. The obtained chalcones undergo cyclization with phenylhydrazine (L[1])/4-nitro (L[16]) under the basic condition leads to the formation of 2-pyrazoline derivatives bearing indole and naphthyl moieties. It was purified by column chromatographic technique. The pyrazoline derivatives were used as ligands to synthesise metal(II) complexes [ML(OAc)(H$_2$O)]   (Scheme 1).

All the prepared complexes were stable at room temperature (confirmed by TG measurements). The synthesized ligands and their metal complexes were checked by comparing the TLC with the starting materials, which resulted in a single spot different from the starting materials. They were non-hygroscopic solids and insoluble in ethanol and water but soluble in DMSO. The analytical data of the ligands and their metal(II) complexes were presented in the experimental section. They are well agreed with the theoretical values within the limit of experimental error. The structural features of ligands and their metal complexes were assigned on the basis of elemental analyses, IR, UV-Visible, NMR, electronic absorption spectra, FAB-MS and thermo gravimetric analysis [21].

Molar conductance measurements

The metal(II) complexes were dissolved in DMSO and the molar conductivities of 10^{-3} M of their solution at room temperature were measured. The lower molar conductivity values of metal complexes were found in the range of (6-16) ohm^{-1} cm^2 mol^{-1} suggested that the non-electrolyte nature of complexes [22]. The chemical test also confirmed that the there is no acetate ions in the outside coordination sphere.The pyrazoline derivatives (ligands) showed conductivity values due to the presence of hydroxyl group in the naphthyl moiety whereas in the case of metal complexes, the conductivity values are decreased due to the deprotonation of OH group (in the naphthyl moiety) in the pyrazoline core. It is concluded that the free ligand contain phenolic oxygen atom as coordinating site and essential for complexation or chelation.The analytical data are in a good agreement with the proposed stoichiometry [ML(OAc)$_2$] of all the complexes.

FT-IR

A strong vibrational band was observed in the region 1662–1654 cm^{-1} which is assignable to the ν(C=N) stretch frequency of pyrazoline derivatives. This band was shifted to lower vibrational frequencies due to the involvement of azomethine nitrogen in coordination with the metal complexes. In the ligands, the indole moiety contains –NH group was observed at 3312–3430 cm^{-1}. The phenolic C–O vibration was observed at 1356-1348 cm^{-1} in the ligands whereas there is a positive shift indicates that phenolic oxygen atom undergoes chelation with metal ions. Therefore, the azomethine nitrogen and phenolic oxygen atoms are donor sites present in the ligands to coordinate with metal ion through bidentate manner. The two absorption bands at 420-434 cm^{-1} and 496-520 cm^{-1} corresponds to ν(M-O) and ν(M-N) vibrations were observed in the complexes. Further, the ν(asym) and ν(sym) vibrational frequencies were appeared at 1534 cm^{-1} and 1420 cm^{-1} and the difference is ∼106 cm^{-1} which indicates that acetate ion coordinate to metal ion as monodentate. The new vibrational frequency was appeared in the region 3300-3500 cm^{-1} indicates that the water molecule bound or coordinated to metal ion. In addition, the frequency at 860 cm^{-1} was assigned to coordinated water molecule in the metal complexes [23, 24].

Electronic Spectral features

The electronic absorption band of the ligand, L[16] showed two bands at 260 nm and 332 nm indicates that π–π*and n-π* transition of the chromophore present in the pyrazoline derivative. These bands were shifted in the electronic absorption spectrum of the complexes to 254 nm and 324 nm due to coordination behavior [25].

The Cu(II) complex showed a broad absorption band around 496 nm may be assigned to $^2B_{1g} \to ^2A_{1g}$ transition. This indicates that the square planar geometry around the Cu(II) ion [26]. The zinc complex exhibited a band at 360 nm and may be assigned to intraligand transitions within the ligand molecules. This spectral behaviour is due to its d^{10} electron configuration with completely filled d orbital. The electronic spectrum of nickel complex of (L^{16}) showed a band appeared at 568 nm which is attributed to $^1A_{1g} \to ^1A_{2g}$ transition [27]. These transitions, as well as the measured value of the magnetic moment ($\mu_{eff} = 0$) suggested that a square planar geometry of the complexes. In the case of Co(II) complex of (L^{16}), square planar Co(II) complexes exhibited two bands around 632 nm and 546 nm which corresponds to the transitions $^2A_{2g} \to ^2B_{1g}$ and $^2A_{1g} \to ^2E_g$, respectively [20]. Similarly, all the other complexes showed spectral features.

Where

M = Cu(II), Ni(II), Co(II) & Zn(II)
X = -H (L^1)/ - 4-nitro(L^{16})
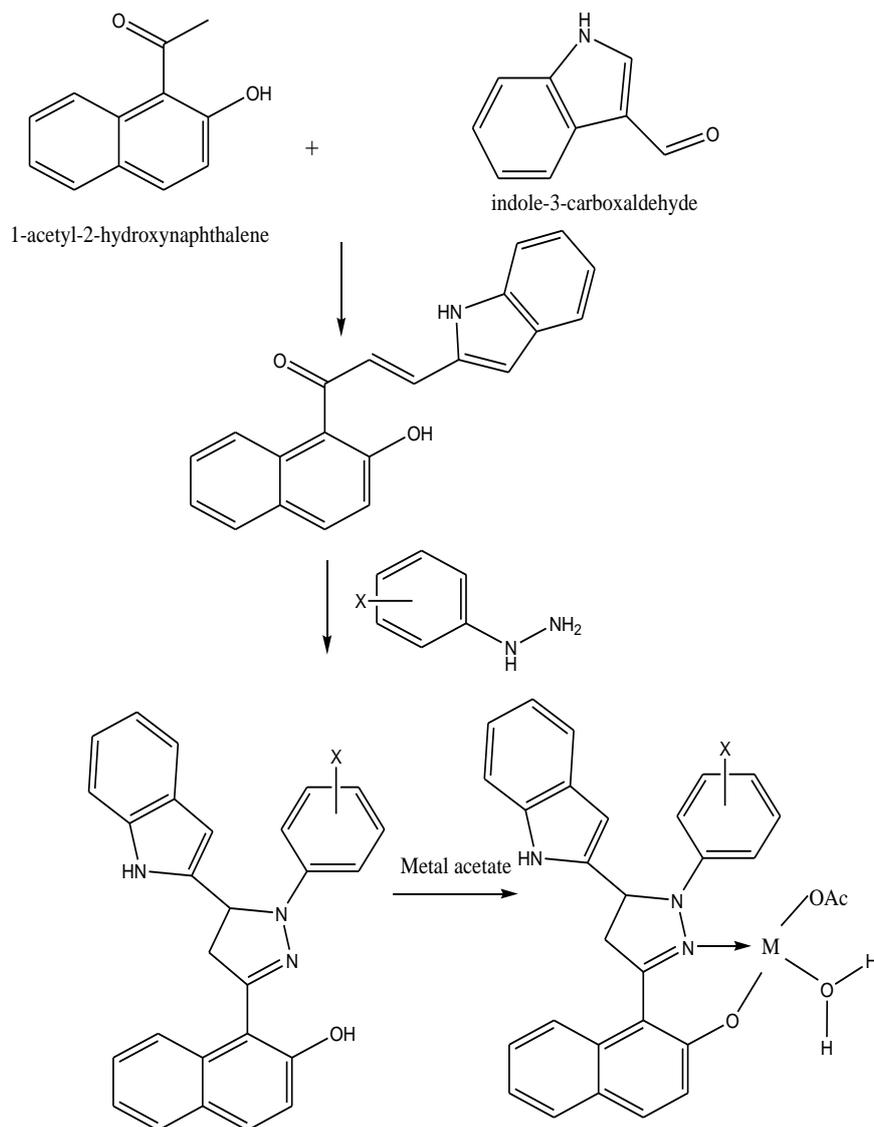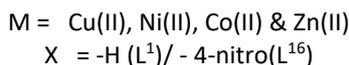
Scheme 1: Synthetic outline of metal complexes with pyrazoline derivatives

Catalytic study: Oxidation of Phenol

The catalytic oxidation of phenol into two products in the presence of H_2O_2 as oxidant and metal complex as catalyst, catechol (CAT) and hydroquinone (HQ) were formed and separated. In some instances, further oxidation of HQ leads to the formation of para-benzoquinone (*p*-BQ) (Scheme 2).
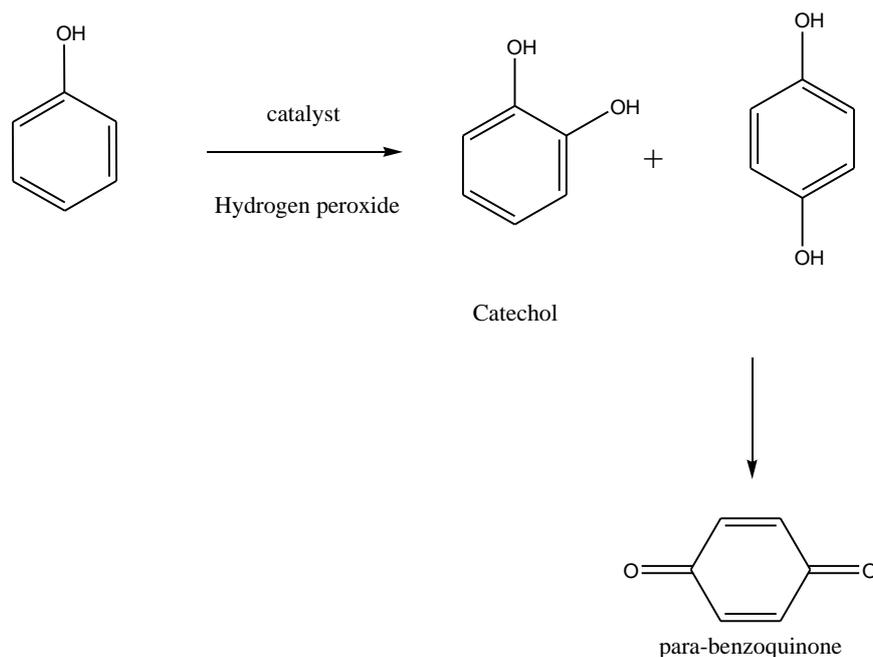
Scheme 2 Oxidation products for hydroxylation of phenol

Effect of oxidant/substrate mole ratio

To optimise the influence of oxidant, substrate, phenol mole ratio on the oxidation reaction at three different mole ratios (0.25:1, 0.5:1 and 0.75:1) were performed. The reaction mixture is taken as follows: Phenol (1M) and catalyst, copper complex (0.02 g) in 5 ml of DMF at 70°C for 7 hrs (Figure.3). It was observed that increasing the oxidant concentration and fixed concentration of substrate is increased the conversion five times. The low activity of the catalyst at low concentration of oxidant/substrate mole ratio may be resulted from decreased production of hydroxyl radicals and decreased concentration of intermediates. When the amount of oxidant was increased to double the amount, the percentage conversion was increased to greater extent. Therefore, the mole ratio of oxidant and substrate was chosen (0.75:1 mole ratio) for the conversion.
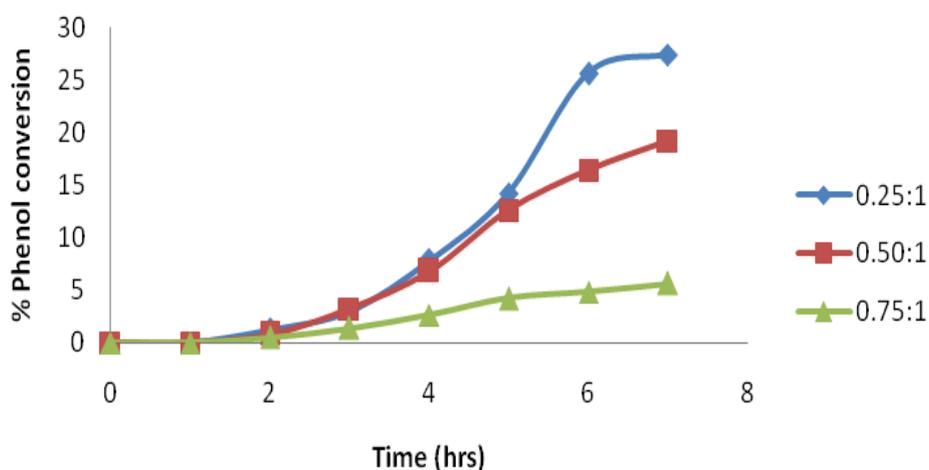
Figure 1: Effect of hydrogen peroxide: phenol molar ratio on % phenol conversion

Effect of reaction temperature

The reaction performance of catalyst was studied at different temperatures,viz. 40, 50, 60 and 70°C and no change in other parameters for 7 hrs.
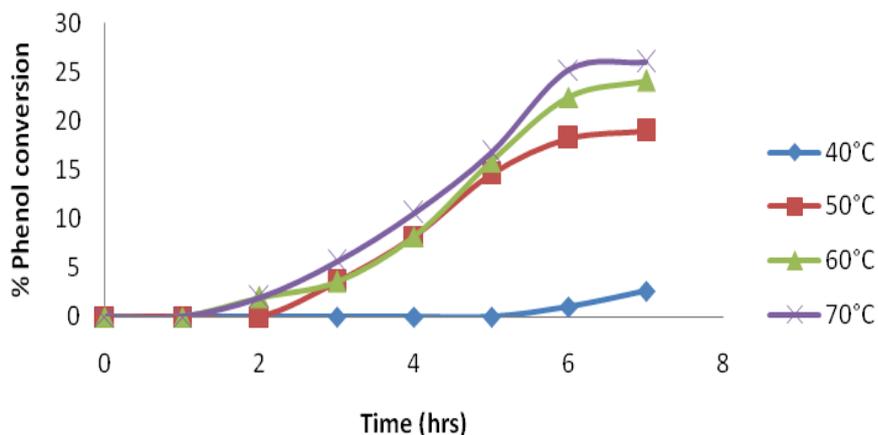
Figure 2: Effect of temperature on the oxidation of phenol

At a low temperature (40°C), the reaction progress showed that low reactivity activity and higher selectivity towards catechol formation. On increasing the temperature 40 to 70°C, the percentage conversion was increased to five times. Furthermore, with the increase of temperature to 80°C showed higher conversion for hydroxylation of phenol. It is concluded that at higher temperatures, the higher conversion of phenol into catechol was obtained (Figure.2). At higher reaction temperatures, there is a loss of hydrogen peroxide efficiency was noticed due to the thermal degradation of hydrogen peroxide.

Effect of solvents

The effect of solvent on catalytic reactivity was studied during the hydroxylation of phenol using five different solvents ranging from methanol, ethanol, dimethylformamide, ethyl acetate and DCM to non-polar solvent like hexane. There is no change in other reaction parameters. The influence of solvent affects the percentage yield, formation of product in the catalytic reaction.
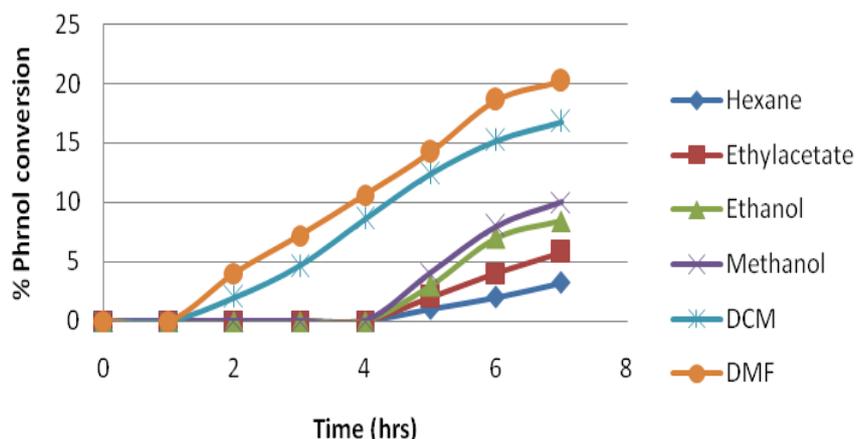
Figure 3: Effect of different solvents on the oxidation of phenol

The nature solvent polarity, solvation power etc play an important role in the reactivity of catalytic reaction. It may be affected the rate of the reaction as well as the selectivity of the product formation. The lower oxidation yields were observed in the non-polar solvent like ethyl acetate and hexane, respectively. Among the solvent molecules, the phenol oxidation was higher in DMF over 10 hrs reaction time. This may be due to DMF is coordinated to copper centre and facilitating a five-coordinated complex, where DMF occupied 5th coordination site (already four coordination sites are occupied by ligand(s), acetate and water molecules. The % phenol conversion in these solvents is arranged in the following decreasing order: DMF>> DCM

>methanol >ethanol > ethyl acetate > hexane. Therefore, DMF was selected to be the most suitable solvent in these catalytic reactions.

Effect of solvent volume

The solvent volume is also played a significant role in catalyst efficiency as shown in Figure. 3. Three different volumes, 4, 6 and 8 mL, were performed and monitored the catalytic conversion progress over period of time. On increasing the volume of solvent from 4 to 8 mL may lead to a noteworthy reduction in the overall catalytic performance over the 10 hrs time. Further, the increasing volume of solvent to 8 ml showed considerable decrease of catalytic activity. It is concluded that the increase of solvent volume leads to lower in conversion of phenol into catechol. On decreasing the volume of solvent below 4 ml may result in the formation of slurry mass without any conversion.
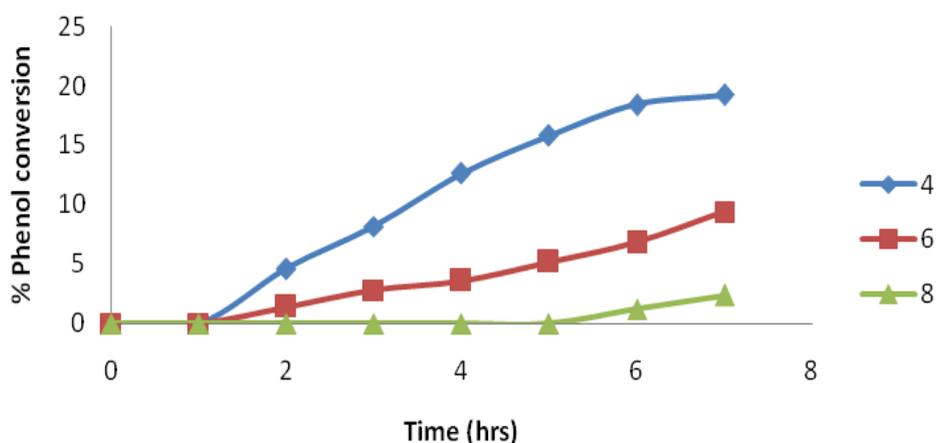

Figure 4 Effect of solvent volume on % phenol conversion

Effect of catalyst amount

The effect of amount of catalyst on the catalytic performance of phenol into catechol is shown in Figure.4. Three different amounts of catalyst were studied, viz. 0.01, 0.02 and 0.04 g and keeping the other parameters constant. The observed results indicated that the increasing the amount of catalyst from 0.01 g to 0.04 g leads to the conversion over the period of 6 hrs. Further, the catalyst amount increases from 0.01 to 0.04 g may be resulted in the increasing percentage conversion of phenol (Figure. 5). The higher amount of catalyst provide higher surface area for the adsorption of substrate molecule on the site. This may lead to the enhanced conversion of phenol due to the chemisorption of substrate and there by facilitating the conversion of phenol into catechol.
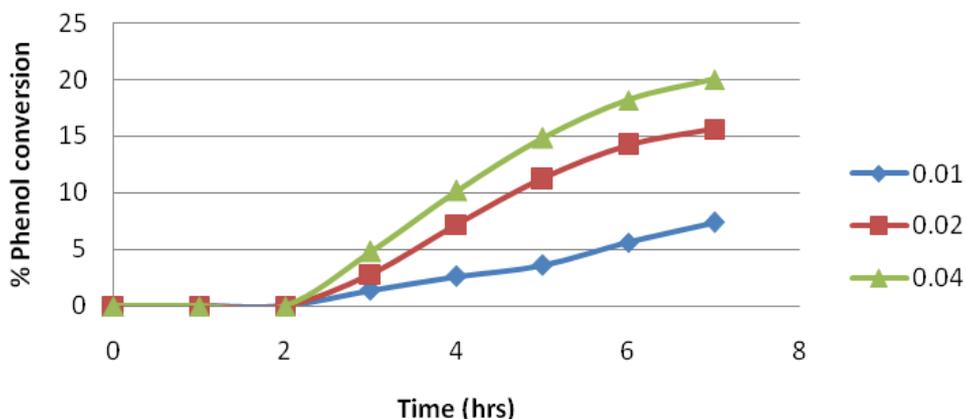

Figure 5: Effect of catalytic amount on % phenol conversion

Comparative studies of different copper catalysts

The optimized reaction conditions, i.e. phenol (0.04 mol), oxidant, H_2O_2/substrate, phenol molar ratio of 0.75: 1, catalyst (0.01 g), DMF (5 ml) and temperature (70°C) was selected and performed. It was observed that the catalytic conversion of phenol into catechol was achieved with higher reaction efficiency due to the presence of copper complex with pyrazoline derivative containing para-substituted nitro group in phenylhydrazine moiety as compared to other complexes (Table 1). In the case of halogen substitution, copper complex with pyrazoline derivative containing para-substituted chlorine in phenylhydrazine moiety may be enhanced catalytic activities as compared to other halogen in different position.
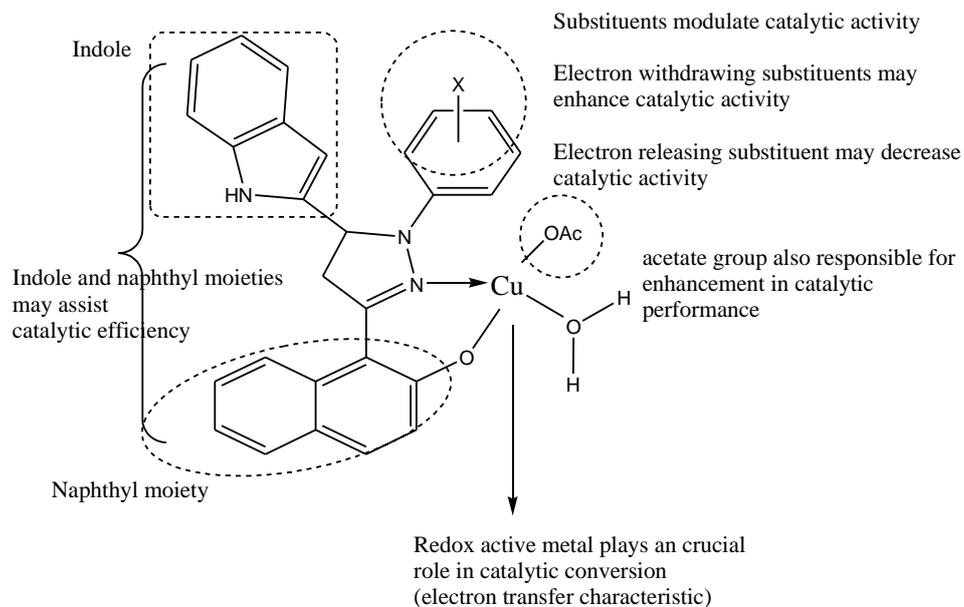

Figure 6: Pictorial sketch of substituent's and other groups may decides catalytic performance

Table 5: % Phenol conversion, product selectivity and TON value of copper complexes with different nitro substituted pyrazoline derivatives

Catalyst	% Phenol conversion	Product selectivity %			TON
		CAT	HQ	BQ	
L[16]	5.2	84.2	15.8	-	360
[CuL[16](OAc)(H₂O)]	30.8	86.4	13.6	-	3560
[CoL[16](OAc)(H₂O)]	26.2	70.2	29.8	-	1820
[NiL[16](OAc)(H₂O)]	28.4	74.6	25.4	-	1980
[ZnL[16](OAc)(H₂O)]	26.8	72.4	27.6	-	1880
Blank	0.4	80.8	19.2	-	86

Reaction conditions:

Substrate	:	Phenol,
Oxidant	:	H_2O_2,
Catalyst	:	Copper complex,
DMF	:	3 ml
Temperature	:	70 °C
Time	:	7 hrs.

Catalytic performance of catalyst

The catalytic efficiency is expressed in terms of turnover number (TON). The results indicated that the increasing order of the catalysts for catalytic performance is

CuL > NiL > CoL > ZnL
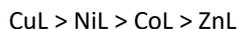
CONCLUSION

The design and synthetic approach was focused on the development of metal complexes of pyrazoline derivatives. Structural modification of copper complexes leads to increase in the surface area which makes it good catalyst. The catalytic efficiencies of prepared metal(II) complexes were performed for the oxidation of benzyl alcohol and phenol using H_2O_2 as an oxidant. The percentage of catalytic conversion was optimized by varying reaction conditions i.e. temperature, amount of catalyst (metal complex), solvent, oxidant concentration (H_2O_2). The observed results indicated that the catalytic conversion of copper complexes exhibited higher catalytic conversion rate than the other metal complexes at lower rate under optimum conditions. Particularly, the copper complex of pyrazoline derivative bearing *p*-NO_2 substituent as effective catalyst with the highest TONs attained as compared to other complexes. In the case of halogen substitution, copper complex with pyrazoline derivative containing para-substituted chlorine in phenylhydrazine moiety may be enhanced catalytic activities as compared to other halogen in different positions. The main advantages of the present catalyst are easy to synthesis, cheaper, higher product yield, higher thermal stability and electron transfer properties.

ACKNOWLEDGEMENT

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