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SYNTHESIS AND BIOLOGICAL ACTIVITY OF COPPER (II), NICKEL(II) AND COBALT(II) WITH TETRADENTATE SCHIFF BASES COMPLEXES DERIVED FROM 2-HYDROXY-1- NAPHTHALDEHYDE AND AROMATIC DIAMINES

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Abstract

2-hydroxy-1-napthaldehyde reacted with diaminophenol in absolute EtOH in a ratio 2:1 to give new Schiff bases (H_2L^1, H_2L^2 and H_2L^3). The obtained Schiff bases which were in tautomeric equilibrium (enol-imine O-H…N, keto-amine O…H-N forms) were used as ligands to coordinate Cu (II), Ni (II), and Co (II) leading complexes. The ligands and the complexes were characterized by physicochemical, elemental and spectroscopic analyses. The complexes exhibited 1:1 metal to ligand coordination ratio (ML^1) , (ML^2), (ML^3). Both Ligands and complexes were evaluated for antibacterial properties using disc diffusion method.. The complexes showed higher activity than the free ligands.

KEYWORDS: *Schiff Bases, Biological Activity, 2-Hydroxy-1-naphthaldehyde , Aromatic Diamines*

1. Introduction

Reaction between aldehydes with primary amines provides one of the most important and widely studied classes of chelating ligands called Schiff bases. These ligands are used as chelating ligands in the field of coordination chemistry and their metal complexes are of great interest for many years (*Aliyu et al 2011*). The use of Schiff bases as ligands in the formation of transition-metal complexes has been extensively studied owing to their intrinsic properties, such as versatile spectroscopic and electrochemical responsive receptors for charged and neutral gusts of these systems (*Feng et al 2007*). A large number of Schiff bases and their complexes have been studied for their interesting and important properties, e.g, their ability to reversibly bind oxygen, their catalytic activity in the hydrogenation of olefin(*Henrici and Olive 1984*), the transfer of amino group, (*Dugas and Penny 1981*) their Photo-chromic properties,(*Margerm and Miller 1971*) their Complexing ability towards some toxic metals. Schiff bases are used as substrates in the preparation of a number of industrial and biologically active compounds via ring closure, cyclo-addition, and replacement reaction (*Karia and Parsania 1999*). Moreover, Schiff bases are also known to have biological activities such as antimicrobial (*More et al 2001*), antifungal (*Baseer et al 2001*), antitumor (*Desai et al 2001*), as catalysts (*Sheldon and Kochi 1981*)and herbicides (*Samadiya and halve 2001*) . On the industrial scale, they have wide rang of applications such as dyes and pigments (*Sinddiqui et al 2006*) .

Tetradentate Schiff bases derived from 2 equivalent of salicylaldehyde and 1 equivalent of alkyl or aryl diamines have been known for decandes. Series of Copper (II) complexes with tetradentate Schiff base ligands derived from salicylaldehyde and polymethylenediamines of varying chain length have been synthesized by Lawrence (*Nathan et al 2003),* through the loss of the two hydroxyl protons, these ligands have been used to form neutral complexes with a number of divalent metal ions.

2-Hydroxy Schiff base ligands and their complexes, derived from the reaction of salicylaldehyde and 2-hydroxy-1-naphthaldehyde with amines have been extensively studied (*Fernandez et al 2001*).

This paper reports synthesis and biological activity of Copper (II), Nickel(II), and Cobalt (II) Schiff base complexes derived from 2-hxdroxy-1-naphthaldehyde and aromatic diamines.

2. Experimental

2.1 Materials and apparatus

The general chemicals employed in the study were of the best grade available and were obtained from Merck Ltd. And Sigma- Aldrich chemical co. and used without further purification. All solvents were of spectrometric grade. The infrared spectrum was performed on an Perkin Elmer Paragon 1000 IR spectrometer in the 4000 – 400 cm^{-1} region, using KBr pellets. Molar conductance measurements were carried out using (W E 30210 conductivity TVS meter). Magnetic Measurement were carried out using (Brüker B.M.6) instrument at the university of Mosel, Iraq. Melting points were recorded on a Stuart Scientific-SMP3 apparatus. Biological activity measurement were carried out on a Biological department, faculty of Science , University of Duhok.

2.2 Preparation of Schiff Bases (ligands)

All the Ligands were prepared by a standard method in which 2 equiv. (0.02mol) of 2-hydroxy-1-naphthaldehyde and 1 equiv. (0.01mol) of aromatic diamine are refluxed for 1-1.5 h in ethanol (about 50 ml). Upon cooling and /or reduction of the volume, the Ligands are formed. Products were then filtered, washed with ethanol and dried, as described in paper (*Panova et al 1983*).

2.3 Preparation of the complexes

All the Complexes were prepared by traditional reflux method,1 equiv. (0.01mol) metal-salt as acetate in methanol with 1 equiv. (0.01mol) of ligand also in methanol are mixed and refluxed for 15-30 min., Products were then cooled. The Complexes formed were then filtered, washed with ethanol and dried, as described in paper (*Panova et al 1983).*

2.4Antibacterial Activity test

The Ligands and Complexes were dissolved separately in dimethyl formamide (DMF) to produce two different concentrations (10^{-3}mg/ml and 10^{-4}mg/ml) per disc. They were placed on the surface of the culture and incubated at 37°C for 24h (*Ramon et al 2003*). The in vitro antibacterial activity was carried by disc diffusion method using (NCCLS 2003) with slight modification, the diameter of zone of inhibition produced by the complexes was measured.

3. Results and Discussion

3.1 Physicochemical properties

The Schiff bases ligands were prepared as orange and Brown crystalline solids. The color of Cu (II) complexes are chestnut, Brown and Dark Green. The color of Ni (II) complexes are Brown Reddish, Umber and Blackish Brown, while color of Co (II) complexes are Brown Teal, Umber and Blackish Green. Some physical properties of Schiff bases and its metal complexes are illustrated in Table (1). Solubility test carried out on the ligands in some common solvents showed that, they are soluble in methanol, ethanol and DMSO but insoluble in water, ether and CCl_4. The complexes are all readily soluble in DMSO only but insoluble in the other solvents Table 2. Molar conductivity values of the complexes in DMSO solution are in the rang 17-21 Ω^{-1}cm^{-1} confirmed the non-electrolytic nature of the complexes Table 1.

Table 1.physical properties of the Schiff bases and its metal-complexes

Ligands/ Complexes	**Colour**	**M.P./d.P.(°C)**	**Molar conductance (ohm^{-1}cm^{2}mol^{-1})**	**% Yield**
H_2L^1	Orange	224-226	17	79
H_2L^2	Light brown	244-246	18	89
H_2L^3	Dark Brown	>300	21	56
CuL^1	Chestnut	>300	25	60
CuL^2	Brown	245-247	19	57
CuL^3	Dark Green	>300	20	57
NiL^1	Brown Reddish	>300	22	55
NiL^2	Umber	225-227	20	55
NiL^3	Blackish brown	>300	18	56
CoL^1	Brown Teal	>300	19	58
CoL^2	Umber	250-252	21	54
CoL^3	Green Blackish	>300	18	58

M.p.= Melting point, d.p.= Decomposition point

H_2L^1= 1,2 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato

H_2L^2= 1,3 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato

H_2L^3= 1,4 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato
CuL^1 = 1,2 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato copper(II)
CuL^2 = 1,3 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato copper(II)
CuL^3 = 1,4N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato copper(II)
NiL^1 = 1,2 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato Nickel(II)
NiL^2 = 1,3 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato Nickel(II)
NiL^3 = 1,4 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato Nickel(II)
CoL^1 = 1.2 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato Cobalt(II)
CoL^2 = 1,3 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato Cobalt(II)
CuL^3 = 1,4 N,N- Bis (2-hydroxy -1-naphthyl) phenylenediaminato Cobalt(II)

Table 2: Solubility of the ligands and its metal- complexes

Solvents	**Ligands H_2L^1, H_2L^2,H_2L^3**	**Cu(II)Complexes CuL^1,CuL^2,CuL^3**	**Ni(II) Complexes NiL^1,NiL^2,NiL^3**	**Co(II) complexes CoL^1,CoL^2,CoL^3**
Water	**IS**	**IS**	**IS**	**IS**
Methanol	**S**	**SS**	**SS**	**SS**
Ethanol	**S**	**SS**	**SS**	**SS**
Acetone	**S**	**SS**	**SS**	**SS**
Ether	**S**	**SS**	**SS**	**IS**
CCl_4	**S**	**SS**	**SS**	**IS**
DMSO	**S**	**S**	**S**	**S**

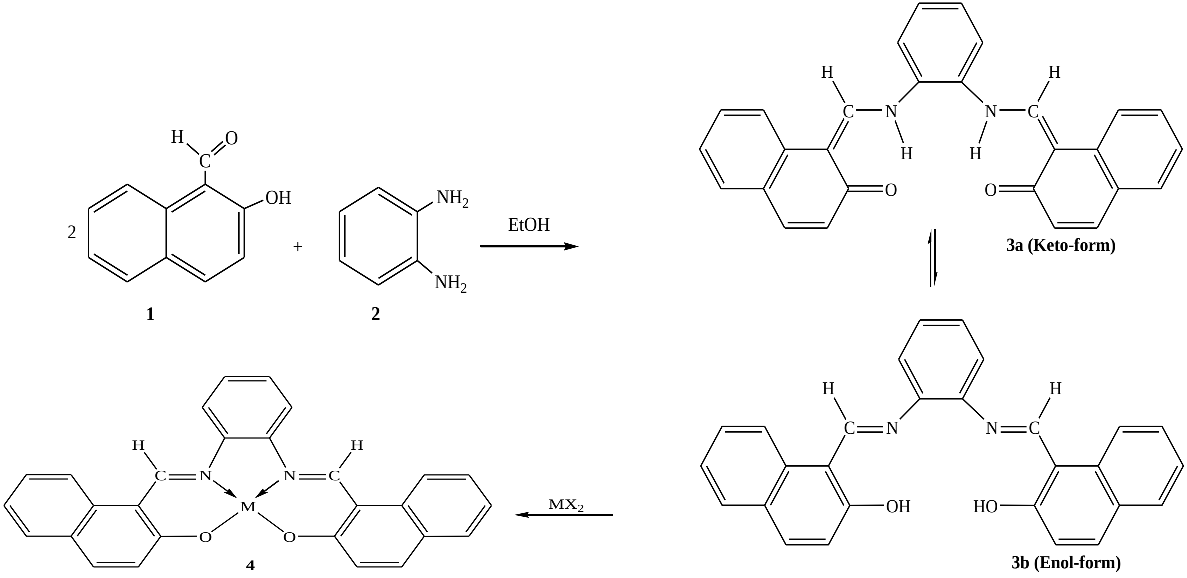
KEY: S-Soluble IS-Insoluble SS-Slightly Soluble

3.2 Spectroscopic /Infrared study and Magnetic Measurement

The synthetic procedure employed involved a condensation reaction between 2-hydro-1-naphthalaldehyde (1) with the primary aromatic amines (2) to produce Schiff bases ligands (3). Under this situation an imine group is observed. The three Schiff bases showed week and broad absorption band in the 3300-3800 cm^{-1} region, this is interpreted to be a sign of the presence of the enol forms. 2-hydroxy Schiff base ligands are of interest mainly due to the existence of (O-H…N and N-H…O) intra-molecular hydrogen bonding and tautomerism between the enol-imine and keto-enamine forms (*Unver et al 2000*) Scheme 1(3a,3b) . In the case of the complexes, this broad band appeared too due to existence of water in complexes lattice (*Quranni et al 2006*). The comparison of the spectra of the free ligands with those of their complexes within the range 1650-1178 cm^{-1} indicates that the ligands coordinate through N and O. The stretching vibration ν(C=N), ν(C=C) and ν(C-O) show very strong bands in the1632-1622, 1460-1440 and 1288-1210 cm^{-1} ranges, respectively. In this case, the band corresponding to the C=N stretching vibration for azomethine group –N=CH- (*Eder et al 2001*) is shifted to lower wavenumbers(2-12cm^{-1}), while its intensity decreases. In the meantime the ν(C-O) vibration shifts to higher wavenumbers. Two new absorption bands in the rang 593-508cm^{-1} and 512-444 cm^{-1} were observed are characteristic of Metal-O and Metal-N respectively (*FCGI 2008*) table 3 . These three facts are due to coordination of the metal ion through the oxygen atoms of ionized hydroxyl groups and nitrogen atoms from imino groups (*Asad et al 2011*) Scheme 1(4). The results of magnetic measurement for these complexes showed that all the prepared complexes are four- coordinated type square planer and the effective magnetic values moment agree with the suggested structure of the complexes (4).

Further extrapolation of the values by jobs method of continuous variation and formulae determination revealed 1:1 metal to ligand ratio. On this basis the structure given in scheme 1 (4) could be assign too the complexes.

Scheme 1: Preparation of Metal-Shiff Base Complexe



3.3 Antimicrobial studies

The antibacterial activity for the Schiff base and all the metal(II) Schiff base complexes were tested against five clinical isolates of Gram positive and Gram negative pathogenic Bacteria(Escherichia coli, streptococcus pyogenes, staphylococcus aureus and Klebsiella pneumonia(Tabl.4) . The diameter of inhibition zone (mm) was measured for each treatment. The results of antibacterial indicate that the complexes show more activity than the ligands and diameter of inhibition zone for Gram positive bacteria (S.aureus, S.pyogens) was greater than the inhibition zone for Gram negative(E.coli, K.pneumonia) under similar experimental conditions indicating that the gram positive strains were more sensitive than Gram negative. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane as explained by Tweedy's chelation theory (*Cotton and Wilkinson 1972*). Chelation considerably reduce the polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible electron delocalization over the whole chelate ring. Such chelation could also enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane (*Sudo et al 1997*, *Spino and Kirza 2000*).

Table 3: Values of stretching vibration of prepared ligands and complexes

Ligand / Complexe	**νC=N (cm^{-1})**	**ν C=C (cm^{-1})**	**ν C-O (cm^{-1})**	**ν M-O (cm^{-1})**	**ν M-N (cm^{-1})**
H_2L^1,H_2L^2,H_2L^3	1634	1460	1202		
CuL^1	1622	1448	1210	574	460
CuL^2	1628	1457	1228	508	444
CuL^3	1628	1440	1244	525	480
NiL^1	1624	1452	1253	593	512
NiL^2	1622	1460	1282	517	498
NiL^3	1626	1442	1222	540	496
CoL^1	1627	1442	1240	534	502
CoL^2	1630	1458	1288	522	487
CoL^3	1632	1452	1278	544	488

Table 4: Antimicrobial activity of Ligands and Complexes

Compound	**Diameter of inhibition zone (mm)**							
	Staphylococcus aureus G+		Streptococcus pyogenes G+		Escherichia coli G-		Klebsiella pneumonia G-	
	Conc mg/ml		Conc mg/ml		Conc mg/ml		Conc mg/ml	
	10^{-3}	10^{-4}	10^{-3}	10^{-4}	10^{-3}	10^{-4}	10^{-3}	10^{-4}
H_2L^1	S 6mm	S 4mm	S 5mm	S 5mm	R	R	R	R
H_2L^2	S 7mm	S 5mm	S 7mm	S 7mm	R	R	R	R
H_2L^3	S 7mm	S 6mm	S 5mm	S	R	R	R	R
CuL^1	R	R	R	R	R	R	R	R
CuL^2	R	S 12mm	S 12mm	R	S 10mm	S 10mm	S10mm	S 8mm
CuL^3	R	R	S10mm	R	S 12mm	R	R	R
NiL^1	S 14mm	S 10mm	R	S 10mm	R	R	R	R
NiL^2	S 15mm	S 10mm	S 8mm	S 10mm	R	R	R	R
NiL^3	S 13mm	S 13mm	R	S 11mm	R	R	R	R
CoL^1	R	S 13mm	R	S 12mm	R	S 12mm	R	R
CoL^2	S 14mm	S 15mm	S 14mm	S 13mm	R	S 10mm	R	S 8mm
CoL^3	S	R		R		R		R

S: Sensitive **R: Resistance** **G+: Gram positive** **G-: Gram negative** **mm: Millimeter**

Conclusion

Nine Complexes, Copper (CuL^1, CuL^2, CuL^3), Ni (NiL^1, NiL^2, Nil^3) and Co (CoL^1, CoL^2, CoL^3) with tetradentate O,N,N,O-donor Schiff Base derived from naphthaldehyde and aromatic diamino (L^1, L^2, L^3) have been synthesized and characterized. Characterization studies showed the complexes to be nonionic. The whole set of biological results should point out the use of this complexes as nutritional supplements with Biological activities relevant in prevention of bacterial and fungal diseases. They can be further evaluated for medicinal and/or environmental applications.

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تحضير والفعالية البيولوجية لمعقدات النحاس ،النيكل والكوبلت ثنائية التكافؤ مع قواعد شيف الرباعية مشتقة من 2-هيدروكسي-1-نفثالديهايد و امينات اروماتية

الخلاصة

2–هيدروكسي–1–نفثالديهايد يتفاعل مع امينات الفينول الثنائية بنسبة2 الى 1 في وسط الايثانول ليعطي قواعد شيف كليكاندات جديدة (H_2L^1, H_2L^2, H_2L^3) هذه قواعد شيف والتي هي في حالة توازن توتومري ($O\text{-}H\cdots N$, $O\cdots H\text{-}N$) استخدمت كليكاندات تتحد مع النحاس، النيكل والكوبلت ثنائية التكافؤ ليعطي معقدات. تم تشخيص كل من الليكاندات والمعقدات باستخدام الطرق الطيفية طيف الاشعة تحت الحمراءو كذلك قياسات المغناطيسية وقياسات التوصيلية المولارية وقد وجد ان الليكاندات المحضرة تتحد مع العناصر1 الى 1 ليعطي المعقدات (ML^1, ML^2, ML^3). تم اختبار الفعالية البايولوجية لكل من الليكاندات والمعقدات ووجد ان الفعالية البايولوجية للمعقدات اكبر من فعالية الليكاندات.

پوختە

چەند جورێن تفتێت شیف ژ پێکدانا (2-هیدروکیس-1- نفپالدیهاید) لگەل (دوانە ئەمین ڤینول) هاتینە ئامادەکرن وەك لیگاند (H_2L^1, H_2L^2, H_2L^3)، ئەڤ لیگاندێت هەنێ برێکا پێکئینانا ئێکسەر 1:1 لگەل رەگەزێن ڤەگوهاستنێ (Cu^{+2}, Ni^{+2}, Co^{+2}) ئەڤ ئالوزیێن هەنێ (ML^1, ML^2, ML^3) هاتینە ئامادەکرن. ئەڤ لیگاندێت هەنێ لگەل ئالوزیێن هاتینە ئامادەکرن هاتنە پشکنین ب کارئینانا رێکێن روناهییێ یان روناهیا تیشکی ل ژێر سوری دا و روناهیا وەرگرتنا ژێری و پیڤەرێن موگناتیسی. چالاکیا بایولوجی یا لیگاندا و ئالوزیێن ئامادەکری هاتە دیارکرن ، و د ئەنجامدا هاتە دیارکرن کو زوربەیا ڤان ئالوزییان چالاکیێن دژی وان بەکتریا ، و چالاکیا ئالوزان یا بهێزترە ژ لیگاندا.