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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SCHIFF BASE COBALT METAL COMPLEXES CONTAINNIG QUINAZOLINE

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ASTRACT-*Quinazoline nucleus is present in various compounds and it is responsible for diverse biological activities. This study focuses on the synthesis of new Schiff base ligands derived from* ***substituted benzaldehyde*** *and* ***2-chloroquinazoline-4-amine,*** *along with their cobalt metal complexes. The characterization of ligand and Cobalt metal complexes of IR and Elctronic spectra. New Schiff base ligands derived from substituted benzaldehyde and 2-chloroquinazoline-4-amine. Schiff base ligand and cobalt complex were screened for antibacterial activity against Pseudomonas, Aeurogenosa and Escherichia and fungicidal activity were tested against Aspergillus Niger and Trico derma.*

KEYWORDS: **Substituted benzaldehyde, 2-chloroquinazoline-4-amine, Schiff base, Cobalt metal complex, antibacterial activity and fungicidal activity**.

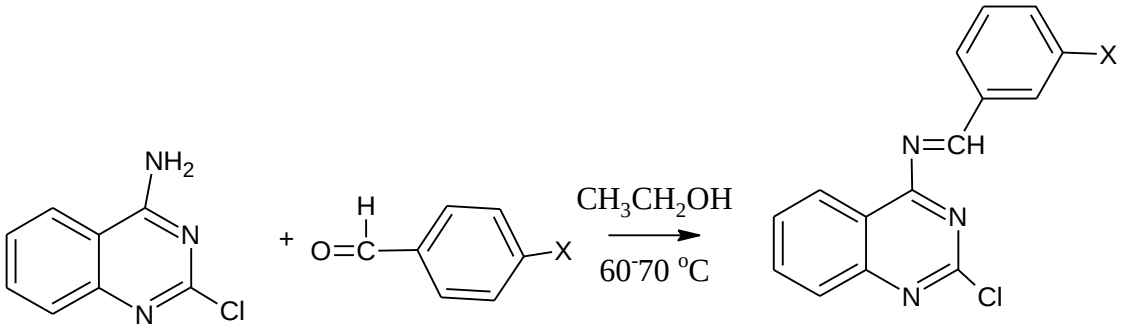
INTRODUCTION

In 1869 Griess prepared the first quinazoline derivative 2-cyano-3,4-dihydro-4-oxoquinazoline by the reaction of cyanogens with anthranilic acid. The bicyclic product was called bicyanoamido benzyl. The prepation of the quinazoline came many years later when Bischler and Lang obtained it by decarboxylation of the 2-carboxy derivative. In 1903 Gabriel prepared the quinazoline. The name was proposed by Widdege. The other names such as phenmiazine, benzyleneamidine,benzo-1,3-diazine,5,6-benzopyrimidine and 1,3-diazanapthaline. Quinazoline and its derivatives represent one of the most biologically class of heterocyclic compounds. Quinazoline is a compound made up of two fused six- membered aromatic ringssuch as benzene fused to pyrimidine[i-iv]. Quinazoline derivatives are excellent antimicrobial. Aromatic aldehydes have effective conjugated system and form more stable Schiff bases, where as aliphatic aldehydes are unstable and readily polymerize[v-vii]. Aldehydes are more reactive than the ketones. Schiff base ligand with aldehydes is formed more readily than Schiff base ligand with ketones.Quinazoline derivatives, which belong to the N-containing heterocyclic compounds, have caused universal concerns due to their widely and distinct biopharmaceutical activities. Researchers have already determined many therapeutic activities of quinazoline derivatives anti-cancer[viii], anti-inflammation[ix], anti-bacterial[x], analgesia[xi], anti-virus[xii], anti-malarial[xiii],anti-hypertension[xiv],anti-obesity[xv], anti-psychotic[xvi], anti-diabetes[xvii-xix] etc. Schiff base are potentially capable of forming stable complexes with metal ions.Many Schiff base complexes show

excellent catalytic activity in various reactions at high temperature and in the presence of moisture [xx-xxvi].

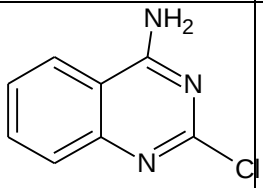
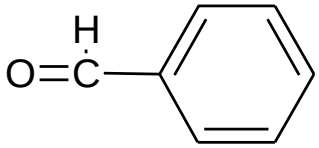
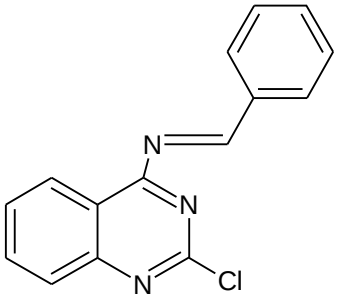
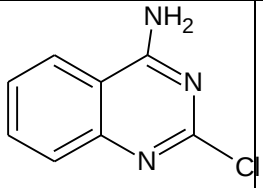
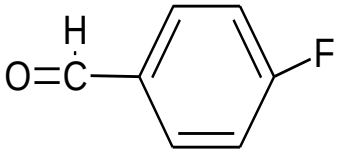
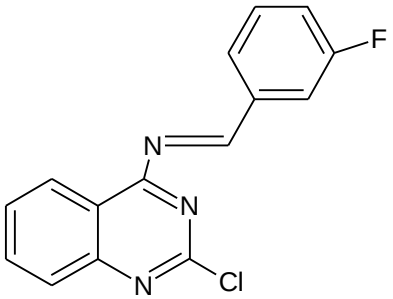
MATERIALS AND METHODS

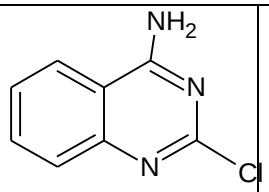
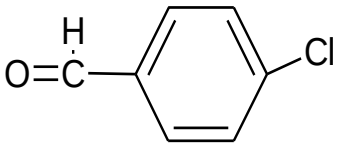
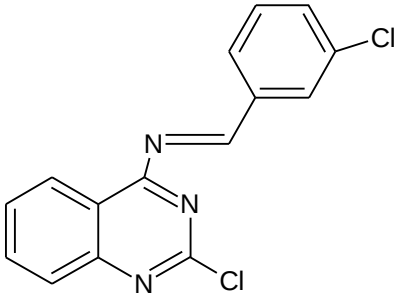
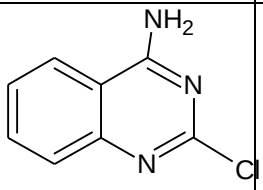
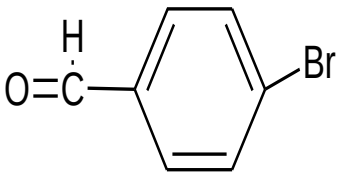
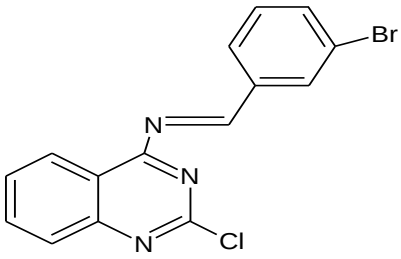
The equimolar quantities of substituted benzaldehyde and 2-chloroquinazoline-4-amine were taken in 500ml of round bottomed flask, 5ml of ethanol and 2-3 drops of glacial acetic acid was added and stirring the reaction mixture at 60-70^{0}C to form solid crude product was obtained poured on crushed ice and recrystallization in ethanol purity of the product tested by TLC



2-chloroquinazolin-4-amine Benzaldehyde derivative

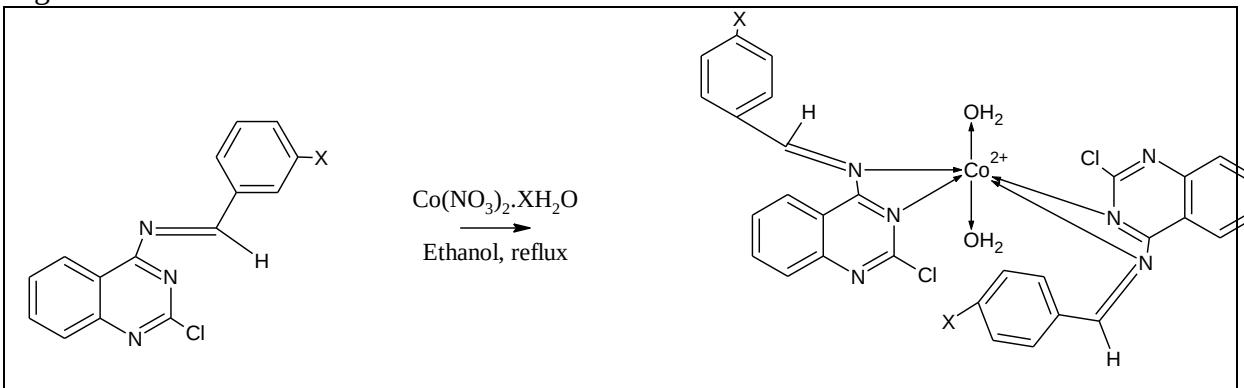
X = H, F,Cl,Br

S.NO	Reactant	Reactant	product
L1	 2-chloroquinazolin-4-amine	 Benzaldehyde	 N-(2-chloroquinazolin-4-yl)-1-phenylmethanimine
L2	 2-chloroquinazolin-4-amine	 4-Fluorobenzaldehyde	 N-(2-chloroquinazolin-4-yl)-1-(3-fluorophenyl)methanimine

L3	 2-chloroquinazolin-4-amine	 4-chlorobenzaldehyde	 1-(3-chlorophenyl)-N-(2-chlroquinazolin-4-yl)methanimine
L4	 2-chloroquinazolin-4-amine	 4-bromobenzaldehyde	 1-(3-bromophenyl)-N-(2-chloroquinazolin-4-yl)methanimine

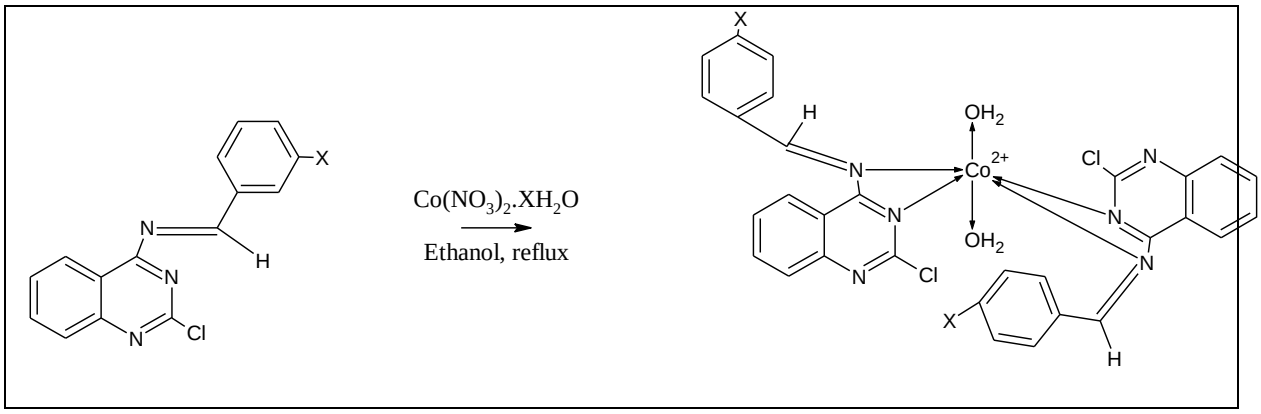
Synthesis of metal complex

The ethanol solution of 0.005moles of Schiff base and mixed with ethanol solution of 0.005moles of cobaltnitrate solution. The mixture was refluxed for 4-6 hours at 75-80^{0}C. The color complex formed have been filtered and dried in vacuum. The synthesis of metal complexes is given in scheme 2 and physical analytical data of ligand and its complexes are given in table 1



X=H,F,Cl,Br

CoL1 =H , CoL2 =F , CoL3 = Cl, CoL4 = Br



RESULTS AND DISCUSSION

IR spectram:

The IR spectra of the ligand show characteristic >C=N bands at 1617cm^{-1} region which are shifted to 1625-1636cm^{-1} which is confirmed (>C=N) coordinate to the metal ion. The lower to higher shift in this band is an noticeable indication of the involvement in the azomethine nitrogen atoms in complex formation. In the single aromatic at C-H band at 3035cm^{-1} which present in the complex for higher frequencies at 3250-3356cm^{-1} respectively, similarly aromatic C-C and aliphatic C-C frequencies complexes, all these facts supported by coordination of ligands.

Electronic spectra:

The electronic spectra of Schiff base shows the absorption bands in the region of 250to 370nm corresponding n-π^* and π-π^* transitions confirmed by the present of (>C=N) bond. The absorption band of Co(II) complex exhibits two transitions at 360nm to 680nm and is due to three transitions $^4A_1 \rightarrow {}^4B_1$, $^4A_1 \rightarrow {}^4B_2$ indicating octahedral geometry of cobalt complex which is further confirmed by magnetic moment at 4.94BM.

compound	Band position in nm	Assignment
L1	250 340	π-π^* n-π^*
L2	290 370	π-π^* n-π^*
L3	260 310	π-π^* n-π^*
L4	280 310	π-π^* n-π^*
CoL1	300 330 580 670	π-π^* n-π^* $^4A_1 \rightarrow {}^4B_1$ $^4A_1 \rightarrow {}^4B_2$
CoL2	260 390 580 650	π-π^* n-π^* $^4A_1 \rightarrow {}^4B_1$ $^4A_1 \rightarrow {}^4B_2$
CoL3	260 390	π-π^* n-π^*

	570 680	$^4A_1 \rightarrow {}^4B_1$ $^4A_1 \rightarrow {}^4B_2$
CoL4	270 340 600 680	π-π^* n-π^* $^4A_1 \rightarrow {}^4B_1$ $^4A_1 \rightarrow {}^4B_2$

RESULTS AND DISCUSSION

Antibacterial activity:

Antibacterial activity of all ligands and it'scomplex compounds againstStaphylococcusaureous, Streptococcus pyogenes,Pseudomonas aureginosa,EscherichaColi species were by disc diffusion method. The test compounds were dissolved in DMSO. For each compound 200ug/ml was taken for microbial screening against the Escherichia Coli. The bacteria were maintained in Nutrient agar Medium.Aseptic techniques were employed to prepare the culture medium of the test microorganisms were maintained on nutrient agar slant at 37^0c and 18-24hr.Zone of inhibition produced by each compound was measured in mm [xxvii-xxix].

Antibacterial activity of ligands at concentration 200ug/ml zone of inhibition in mm
Table-2

S.NO	S.aureus	S.pyogenes	P.aureginosa	E.Coli
L1	10.5	13.6	11.2	10.4
L2	12.7	12.4	12.8	12.7
L3	17.8	16.6	13.6	13.5
L4	12.5	14.2	13.7	10.3
CoL1	11.7	17.8	13.3	13.2
CoL2	12.4	18.9	14.6	13.6
CoL3	13.6	19.1	15.2	14.2
CoL3	14.3	20.2	16.1	15.4

Antifungal activity:

Aspergillus niger Conida are always present in air and cause contamination in laboratory culture of bacteria and fungi. It is also called as 'weed of the laboratory'. Over 30 species of Aspergillusniger have been recorded so far in India. Thom and Raper recognized more than 78 species of Aspergillus. These are of great importance because of their harmful as well as useful activities. When Aspergillus infects lungs in human being the symptoms resemble tuberculosis. Aspergillus now know to produce several deadly toxins on various food feed-stuffs which when eaten cause mycotoxicoses in animals and human beings. The fungi are always associated with fruits, vegetables. Food grains during storage and cause spoilage to these stored products. Strains of Aspergillusniger are used in the manufacture of citric acid, gluconic acid and itanoicacid[xxx-xxxi].

STUDY OF ANTIFUNGAL ACTIVITY OF SCHIFF BASE AGAINST A.NIGER
Table 3

Ligand	Conc 250ppm	Conc 500ppm	Conc 1000ppm
L1	35	26	20
L2	70	65	48
L3	89	100	50
L4	64	86	68

CoL1	70	90	78
CoL2	74	96	82
CoL3	82	98	86

Conclusion:

In the present research Schiff base and it's metal complexes were successfully synthesized and characterized. The characterization of Schiff base and metal complexes by FT-IR, Electric spectra which are suggested that metal complexes have octahedral geometry.The antibacterial activity against gram negative E.Coliand gram positive Bacillus substilis.

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References:

i Chandra goud V., Kush AK, "**Synthesis and n vitro Anti-tumour Activities of Novel 4-anilinoQuinazoline derivatives**" *Eur J Med Chem***2009**, vol*44*,Page no *3046*-305

ii Al-rashood ST, aboldahab IA, " **Synthesis and di hydrofolatereductase inhibition, antitumor testing and molecular modelling study of some new 4 quinazolinoneanalogs**" *Bio Org Med Chem* , **2006**, vol*14*, Page no 86088621

iii Vasdev N., Dorff PN, " **Synthesis of 6-acrylamido - 4-(2-[18F] fluoranilino) Quinazoline. A prospective irreversible EGFR binding probe** " *J labelled compd rad*, **2005**, vol*48*, Page no *109-115*

iv Wake ling AE, *Cancer res* , **2002**, vol*62*, Page no *5749*-575

v lagarsamy V, Solomon VR, "Synthesis **and pharmacological evaluation of some 3-phenyl- 2-substituted -3H-Quinazoline-4 one as analgesic, anti-inflammatory agents**"*BioOrgMedChem*,**2007**,vol*15*,Page no*235*-241

vi Baba M, Kawamura N, " **Synthesis of novel Quinoline and Quinazoline derivatives and their anti-inflammatory activities**" *J Med Chem* , **1996**, vol*39*, Page no *5176-5182*

vii K. Sudhakar Babu, V.Prabhakar, L.K. Ravindranath, M.SwarnaKumari, J.Latha, "**Synthesis, Characterization And Biological Evaluation Of NovelTrisubstitutedQuinazoline 1, 2, 4 Tri Azole Derivatives Bearing Cis-Substituted Pyrrolidine And Sulphone Moieties**". *European journal of pharmaceutical and medical research*, **2015**, *vol. 2, 873*-899

viii K. SudhakarBabu, V.Prabhakar, L.K. Ravindranath, M.SwarnaKumari, J.Latha,: "**Synthesis, Characterization and Biological Evaluation of NoveltrisubstitutedQuinazolineThiazole derivatives bearing trans substituted thiomorpholine and tetrazoles moieties**". *International Journal of Organicand Bioorganic Chemistry*, **2015**, *vol. 5:2, 15-24*

ix K.SudhakarBabu, V.Prabhakar, L.K. Ravindranath, J. Latha,: "**Synthesis,Characterization And Biological Evaluation of Novel Tri-substituted Quinazoline-1,3,4 oxadiazole Derivatives Bearing Cis-Substituted Thiomorpholine And Thiazolidin-4-One Moieties**". *Heterocyclic* letters

X K.SudhakarBabu, V.Prabhakar, L.K. Ravindranath, J. Latha,: "**Synthesis, Characterization And Biological Evaluation Of Novel Tri Substituted Quinazoline-IsatinMannich Bases Bearing Morpholine And BiphenylMoieties**".

Heterocyclic letters, **2015**, *Vol. 5::3 395*-411

Xi Li H, Huang R, "**Synthesis and Bio activity of 4-Quinazoline oxime Ethers**" *prog Nat Sci,* **1998**, *Vol. 8 page no 359-365.*

Xii Chandrika PM, Yakaiah T, "**Synthesis leading to novel 2,4,6 tri substitutedquinazoline derivatives and their antibacterial, cytotoxic activity against THP-1, HL-60 and A375 cell lines**", *Indian J chem,***2009**, *Vol. 48B, page no840-847*

Xiii Paneersalvam P, Raj T, "**Anti-convulsant activity of Schiff bases of 3-amino, 6, 8 - di bromo 2 phenyl Quinazoline -4-ones**" *Indian j Pharm sci,* **2010**, *Vol. 72, page no 375-378.*

Xiv Nandy P, Vishalakshi MT, "**Synthesis and anti-tuberculor activity ofmannich bases of 2-methl Quinazoline 4-ones**" *Indian J Heterocyclicchemistry,* **2006**, *Vol. 15, page no 293-294.*

Xv Saravanan G, Prakash CR, "**Synthesis and Evaluation of antioxidant activities of novel Quinazoline derivatives** ",*Int j Pharm sci,* **2010**, *Vol. 2,page no 83-86.*

Xvi Lakhan R, Singh OP, "**Studies on Quinazoline 4-one derivatives as Antimalarials**"*JIndian Chem Sci,***1987**,*vo l64, page no 316-318.*

Xvii Hess HJ,Cronin TH, "**Anti-Hypertensive2-amino Quinazoline-4 ones** "J*medChem***1968**, *Vol.11, page no 130-136.*

Xviii Sasmal S, Balaji G, " **Design and optimization of Quinazolinederivativesas melanin concentrating hormone receptor 1 antagonists "** *Bio org medchem let.,* **2012,** *Vol. 22, page no 3157-3162.*

Xix AlvaradoM,Barcelo M, **"Synthesis and Biological Evaluation of Quinazoline and cinnoline derivatives as potential a typical antipsychotics"** *ChemBiodivers*, **2006**, *Vol. 3, 106-117*

Xx Malamas MS, "**Quinazoline acetic acids and analogs as aldose reductase inhibitors** " *J Med Chem*, **1991,** *Vol. 34, page no 1492-1503*

Xxi Jensen F. R.; Goldman G. In Friedel-Crafts and Related Reactions; Olah, G., Ed.; Wiley-Interscience: New York, **1964**; *Vol. III,* pp *1319-1367.* (b) Simpkins, N. S. *Sulfones in Organic Synthesis;*Pergamon Press: Oxford,**1993**; and references therein.

Xxii Fumino H.; Mitsuru, K. JP Patent 61271271, 1986; *Chem. Abstr.1986, 106,61271271.* Keiichi, S.; Toru, O.; Aki, S. *JP Patent 04120050, 1992; Chem. Abstr. **1992**, 117, 150703.* Toshiaki, T.; Takeshi Y. *JP Patent 2001260544,2001; Chem. Abstr. 2001, 135, 264604.*

Xxiii Li, J. J.; Anderson, D.; Burton, E. G.; Cogburn, J. N.; Collins, J. T.; Garland,D. J.; Gregory, S. A.; Huang, H. C.; Isakson, P. C.; Koboldt, C. M.; Logusch,E. W.; Norton, M. B.; Perkins, W. E.; Reinhard, E. J.; Seibert, K.;Veenhuizem, A. W.; Zang, Y.; Reitz, D. B. *J. Med. Chem.* **1995**, *38, 4570.*

Xxiv Yoshino, H.; Ueda, N.; Niijma, J.; Sugumi, H.; Kotake, Y.; Koyanagi, N.;Yoshimatsu, K.; Asada, M.; Watanabe, T.; Nagasu, T.; Tsukahara, K.; Lijima,A.; Kitoh, K. *J. Med. Chem.* **1992**, *35, 2496.*

Xxv Zhu, Lina; Jin, Jing; Liu, Chang; Zhang, Chongjing; Sun, Yan; Guo, Yanshen;Fu, Decai; Chen, Xiaoguang; Xu,Bailing*Bioorganic and MedicinalChemistry*, **2011**, *vol. 19, #9p. 2797-2807.*

Xxvi GATEKEEPER PHARMACEUTICAL, INC.; GRAY, Nathanael, S.; ZHOU,Wenjun Patent: *WO2011/79231 A1*,**2011** ; *Location in patent: Page/Pagecolumn 86* ;

Xxvii GholamiDehbalaei, M.; Foroughifar, N.; Pasdar, H.; Khajeh-Amiri, A. N-Propyl benzoguanaminesulfonicacid supported on magnetic Fe_3O4nanoparticles: A novel

and efficient magnetically heterogeneous catalystfor the synthesis of 1,8-dioxo-decahydroacridine derivatives. New J. Chem. **2018**, 42, 327–335.

Xxviii Camus, A.; Marsich, N.; Lanfredi, A.M.M.; Ugozzoli, F.; Massera, C. Copper(II) nitrito complexes with2,20-dipyridylamine. Crystal structures of the [(acetato)(2,20-dipyridylamine)(nitrito-O,O0)copper(II)] and[(2,20-dipyridylamine) (nitrito-O,O0)(_-nitrito-O)copper(II)]2_2(acetonitrile). Inorg. Chim. Acta**2000**, 309, 1–9.

Xxix Mautner, F.A.; Vicente, R.; Massoud, S.S. Structure determination of nitrito- and thiocyanatocopper(II)complexes: X-ray structures of[Cu(Medpt)(ONO)(H2O)]ClO4(1),[Cu(dien)(ONO)]ClO(2)and[Cu2(Medpt)2(_N, SNCS)2](ClO4)(3) (Medpt= 3,30-diamino-N-methyldipropylamine and dien=diethylenetriamine). Polyhedron **2006**, 25, 1673–1680.

Xxx Eslami, A. Thermoanalytical study of linkage isomerism in coordination compounds: Part I. Reinvestigationof thermodynamic and thermokinetic of solid state interconversion of nitrito (ONO) and nitro (NO) isomers of pentaaminecobalt(III) chloride by means of DSC. Thermochim. Acta**2004**, 409, 189–193.

Xxxi Pasdar, H.; HedayatiSaghavaz, B.; Foroughifar, N.; Davallo, M. Synthesis, Characterization and AntibacterialActivityof Novel 1,3-Diethyl-1,3-bis(4-nitrophenyl)urea and Its Metal(II) Complexes. Molecules **2017**, 22, 2125.

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