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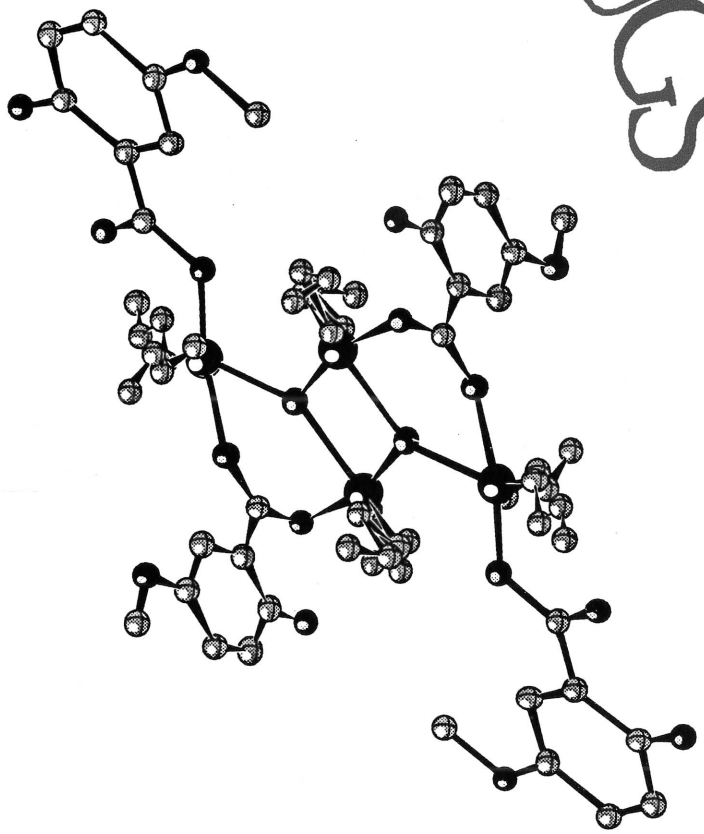
# METAL-BASED DRUGS





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# METAL-BASED DRUGS

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## ACTIVITY OF Pt(II) AND Ru(III) TRIAZOLOPYRIMIDINE COMPLEXES AGAINST PARASITES OF THE *GENUS LEISHMANIA*, *TRYPANOSOMAS* AND *PHYTOMONAS*

Juan M. Salas*,[1] Miguel Quirós,[1] Mohammad Abul Haj,[1] Rosa Magán,[2] Clotilde Marín,[2] Manuel Sánchez-Moreno[2] and René Faure[3]

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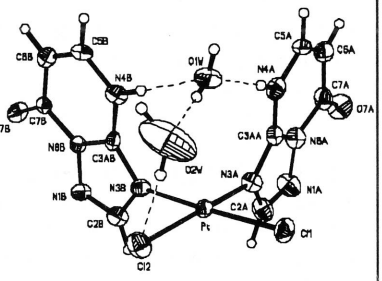
The synthesis and characterization of two Pt(II) complexes with the isomeric ligands 4,5-dihydro-5-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (5HtpO) and 4,7-dihydro-7-oxo-[1,2,4]-triazolo-[1,5-a]pyrimidine (7HtpO) are described, as well as a Ru(III) complex with 7HtpO. The crystal structure of cis-$[PtCl_2(7HtpO)_2].2H_2O$ has been solved by X-ray diffraction analysis. In vitro activity of the new isolated complexes against the epimastigote form of T. cruzi, procyclic form of T. b. brucei and promastigote form of L. donnovani and P. characias has also been studied. The three complexes markedly affect the growth of the parasites and none of them shows cytotoxicity against macrophage of the J774.2 line at the heaviest dosages used.

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## INTERACTION OF RUTHENIUM(II)-DIPYRIDOPHENAZINE COMPLEXES WITH CT-DNA: EFFECTS OF THE POLYTHIOETHER ANCILLARY LIGANDS

Teresa M. Santos*[1], João Madureira[1], Brian J. Goodfellow[1], Michael G. B. Drew[2], Júlio Pedrosa de Jesus[1], and Vitor Félix[1]

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The complexes $[Ru([9]aneS_3)(dppz)Cl]Cl$ **1** and $[Ru([12]aneS_4)(dppz)]Cl_2$ **2** ($[9]aneS_3$=1,4,7-trithiaciclononane and $[12]aneS_4$=1,4,7,10-tetrathiaciclododecane) were synthesised and fully characterised. These complexes belong to a small family of dipyridophenazine complexes with non-polypyridyl ancillary ligands. Interaction studies of these complexes with CT-DNA (UV/Vis titrations, steady-state emission and thermal denaturation) revealed their high affinity for DNA. Intercalation constants determined by UV/Vis titrations are of the same order of magnitude ($10^6$) as other dppz metallointercalators, namely $[Ru(II)(bpy)_2dppz]^{2+}$. Differences between **1** and **2** were identified by steady-state emission and thermal denaturation studies. Emission results are in accordance with structural data, which indicate how geometric distortions and different donor and/or acceptor ligand abilities affect luminescence. The possibility of non-covalent interactions between ancillary ligands and nucleobases by van der Waals contacts and H-bridges is discussed. Furthermore, complex **1** undergoes aquation under intra-cellular conditions and an equilibrium with the aquated form **1'** is attained. This behaviour may increase the diversity of available interaction modes.

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## TRANSITION METAL ION COMPLEXES OF SCHIFF-BASES. SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL PROPERTIES

Zahid H. Chohan*[1], Asifa Munawa[1] and Claudiu T. Supuran[2]

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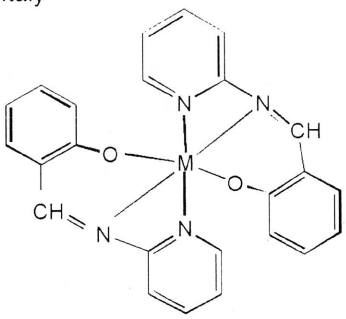
[2] Universita degli Studi, Dipartimento di Chimica, Laboratorio di Chimica Inorganica e Bioinorganica, Via Gino Capponi 7, I-50121 Florence, Italy

Some novel transition metal [Co(II), Cu(II), Ni(II) and Zn(II)] complexes of substituted pyridine Schiff-bases have been prepared and characterized by physical, spectral and analytical data. The synthesized Schiff-bases act as deprotonated tridentate for the complexation reaction with Co(II), Ni(II) and Zn(II) ions. The new compounds, possessing the general formula $[M(L)_2]$ where [M=Co(II), Cu(II), Ni(II) and Zn(II) and HL=$HL^1$, $HL^2$, $HL^3$ and $HL^4$] show an octahedral geometry. In order to evaluate the effect of metal ions upon chelation, the Schiff bases and their complexes have been screened for antibacterial activity against the strains such as *Escherichia coli, Staphylococcus aureus,* and Pseudomonas aeruginosa. The complexed Schiff bases have shown to be more antibacterial against one more bacterial species as compared to uncomplexed Schiff-bases.

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## NEW BORON ANALOGUES OF PYROPHOSPHATES AND DEOXYNUCLEOSIDE BORANOPHOSPHATES

Kamesh Vyakaranam[1], Geeta Rana[1], Narayan S. Hosmane*[1], and Bernard F. Spielvogel*[1,2]

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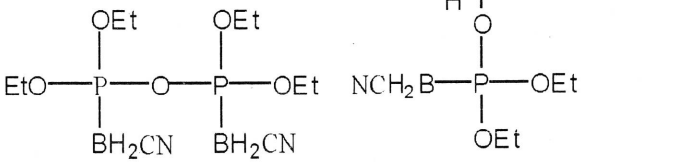
[2] Metallo-Biotech International, Inc., 663 Teal Court, DeKalb, IL 60115-6201, USA

Tetraethyldicyanoborane pyrophosphate (**2**) and 3'-(diethylphosphite-cyanoborano)-5'-dimethoxytrityl-$N^4$-benzoyl-deoxycytidine (**3**) have been synthesized in 70% and 76% yields, respectively. The compatibility of the substituted boranophosphates with common protecting groups is hereby demonstrated.







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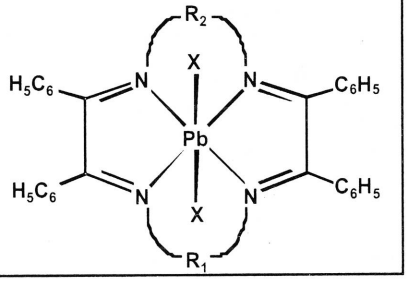
## ANTIANDROGEN AND ANTIMICROBIAL ASPECTS OF COORDINATION COMPOUNDS OF PALLADIUM(II), PLATINUM(II) AND LEAD(II)

R.V. Singh*[1], S.C. Joshi[2], Shalini Kulshrestha[1], Pooja Nagpal[1] and Anil Bansal[1]

[1]Department of Chemistry, [2]Department of Zoology, University of Rajasthan, Jaipur-302004, India

The complexes $M(MaL^n)(R_2)]Cl_2$ and $[Pb(MaL^n)(R_2)X_2]$ (M = $Pd^{II}$ or $Pt^{II}$ and X = Cl or $NO_3$) have been synthesized by the reactions of macrocyclic ligands ($MaL^n$) with metal salts and different diamines in 1:1:1 molar ratio in methanol. The complexes were characterized by elemental analyses, molecular weight determinations, conductivity measurements, IR, $^1$H NMR, $^{13}$C NMR, $^{195}$Pt NMR, $^{207}$Pb NMR, XRD and electronic spectral studies.
The macrocyclic ligand coordinates through the four azomethine nitrogen atoms which are bridged by benzil moieties. IR spectra suggest that the pyridine nitrogen is not coordinating. The palladium and platinum complexes exhibit tetracoordinated square-planar geometry, whereas a hexacoordinated octahedral geometry is suggested for lead complexes. The complexes have been evaluated for their antimicrobial effects on different species of pathogenic fungi and bacteria. The testicular sperm density, testicular sperm morphology, sperm motility, density of cauda epididymal spermatozoa and fertility in mating trails and biochemical parameters of reproductive organs have been examined and discussed.



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## CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF ERBIUM(III) COMPLEXES

S. B. Jagtap[1], N. N.Patil*[2] ,B. P.Kapadnis*[2] and B. A. Kulkarni[1]

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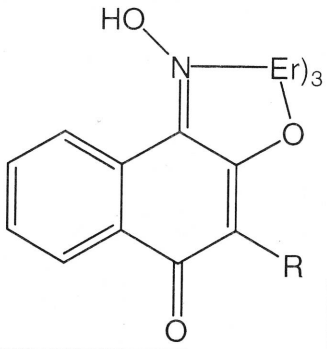
Erbium(III) metal complexes of 2-hydroxy-1,4-naphthoquinone-1-oxime and their C-3 substituted derivatives were synthesized. The complexes were characterized by melting point, elemental analysis, IR and $^1$HNMR spectroscopy and magnetic susceptibility. The antimicrobial activity of these complexes was determined by well diffusion method against the target microorganisms, *Staphylococcus aureus, Xanthomonas campestris, Pseudomonas aeruginosa, Candida albicans* and *Aspergillus niger.* The antimicrobial activity of ligands and their complexes was compared. It was seen that the ligands are more antifungal than antibacterial and the antimicrobial activity of the ligands reduced on complexation with erbium(III).

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## SSYNTHESIS, CHARACTERIZATION AND IN VITRO ANTIFUNGAL EFFECT OF SOME BUTYLTIN(IV) N-SUBSTITUTED 2-AMINOETHANETHIOLATES

A. Smicka[1], V. Buchta[2] and K. Handlir*[1]

[1] Department of General and Inorganic Chemistry, Faculty of Chemical Technology, University of Pardubice, nam. Cs. Legii 565, 532 10 Pardubice, Czech Republic
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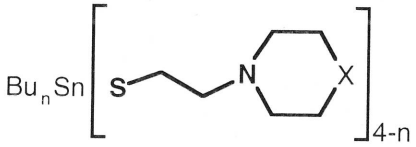
[2] Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Heyrovskeho 1203, 500 05 Hradec Kralove, Czech Republic <buchta@faf.cuni.cz>

Six new *N*-substituted di- and tributyltin cysteaminates (2-aminoethanthiolates) have been prepared and characterised by $^1$H, $^{13}$C and $^{119}$Sn NMR spectroscopy. All these compounds exhibit a considerable *in vitro* fungicidal activity against selected types of fungi (*Candida albicans*, *Candida krusei*, *Candida tropicalis*, *Candida glabrata*, *Trichosporon beigelii*, *Aspergillus fumigatus*, *Absidia corymbifera*, *Trichophyton mentagrophytes*). This activity is comparable to the commonly used drugs. The relationship between structure and fungicidal activity is discussed.




**1** n = 3; X = -$CH_2$-
**2** n = 3; X = -O-
**3** n = 3; X = -$NCH_3$
**4** n = 2; X = -$CH_2$-
**5** n = 2; X = -O-
**6** n = 2; X = -$NCH_3$

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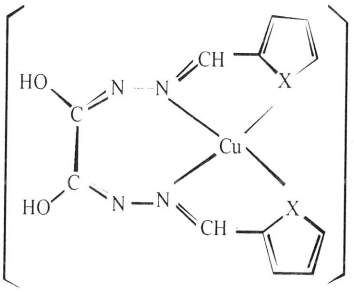
## COPPER(II) ACYLHYDRAZINATES. THEIR SYNTHESIS AND CHARACTERIZATION

Zahid H. Chohan*[1], M. A. Farooq[1] and Claudiu T. Supuran[2]

[1]Department of Chemistry, Islamia University, Bahawalpur, Pakistan
[2]Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Via Gino Capponi 7, I-50121, Firenze, Italy

Acylhydrazine derived furanyl and thienyl Schiff bases and their Cu(II) complexes have been prepared and characterized on the basis of their physical, spectral and analytical data. The preferred enolic form of the Schiff base function as a tetradentate ligand during coordination to the metal ion yielding a square planar complex. The Schiff bases and their complexes with different anions were tested for their antibacterial activity against bacterial species such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Klebsiella pneumonae*..



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