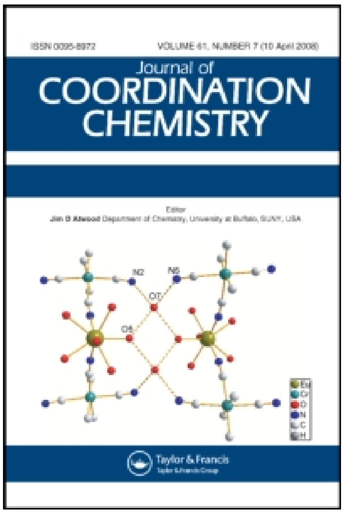


Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

ZINC(II), CADMIUM(II), MERCURY(II) AND LEAD(II) SEMIQUINONE-TYPE COMPLEXES OF A NEW SCHIFF-BASE LIGAND: ANTIBACTERIAL STUDIES

J. R. Anacona[a]; Erasto Bastardo[a]; J. Camus[b]
[a] Departamento de Química, Universidad de Oriente, Apartado, Cumand-Venezuela [b] Facultad de Ciencias, Universidad de Playa Ancha de Ciencias de la Education, Valparaiso, Chile

To cite this Article Anacona, J. R. , Bastardo, Erasto and Camus, J.(1999) 'ZINC(II), CADMIUM(II), MERCURY(II) AND LEAD(II) SEMIQUINONE-TYPE COMPLEXES OF A NEW SCHIFF-BASE LIGAND: ANTIBACTERIAL STUDIES', Journal of Coordination Chemistry, 48: 4, 513 — 520

To link to this Article: DOI: 10.1080/00958979908023591

URL: http://dx.doi.org/10.1080/00958979908023591

J. Coord. Chem., 1999, Vol. 48, pp. 513–520
Reprints available directly from the publisher
Photocopying permitted by license only

Published by license under
the Gordon and Breach Science
Publishers imprint.
Printed in Malaysia.

ZINC(II), CADMIUM(II), MERCURY(II) AND LEAD(II) SEMIQUINONE-TYPE COMPLEXES OF A NEW SCHIFF-BASE LIGAND: ANTIBACTERIAL STUDIES

J.R. ANACONA[a,*], ERASTO BASTARDO[a] and J. CAMUS[b]

[a]*Departamento de Química, Universidad de Oriente, Apartado Postal 208, Cumaná – Venezuela;* [b]*Facultad de Ciencias, Universidad de Playa Ancha de Ciencias de la Educatión, Valparaiso – Chile*

(Received 2 September 1998; Revised 16 November 1998; In final form 12 March 1999)

A new Schiff-base ligand LH_2, has been prepared by reaction of 2,9-diformyl-1,10-phenanthroline with 2,3-diamino-1,4-naphthoquinone. The formation and characterization of complexes of Zn(II), Cd(II), Hg(II) and Pb(II) with the semi-oxidized ligand LH is described. The $M(LH)X_2$ ($X = Cl$, Br and AcO) radical species are paramagnetic and the observed EPR signals in the solid state at room temperature, with *g* values close to the electron free *g* value are proof of the semiquinonic character of the ligand. The antibacterial activity of the ligand and the metal complexes prepared were tested against four bacteria strains and compared with the activity of penicillin.

Keywords: Antibacterial; Schiff-base; semiquinone; group 12 complexes

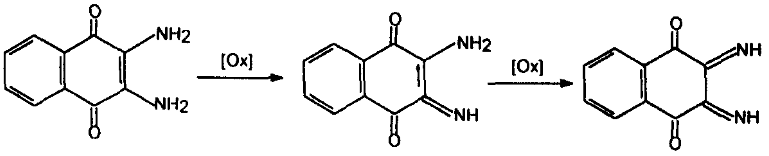
INTRODUCTION

Naphthoquinone derivatives are widely distributed in nature[1] and a number of compounds of this type have therapeutic properties.[2–4] The *in vitro* cytotoxicity of naphthoquinones has been extensively studied and toxic effects have been demonstrated in a variety of cell types. Interest in the chemistry of semiquinone-type complexes is greatly increased in recent years mainly because of the important role of quinone- and catechol-containing groups in

---

[*] Corresponding author. E-mail: janacona@sucre.udo.edu.ve.

biology.[5,6] 2,3-Diamino-1,4-naphthoquinone belongs to a special class of bidentate N,N-coordinators capable of undergoing both one- or two-electron oxidation, forming semiquinones and quinone-type compounds, respectively, as shown below,



where the semi-oxidized form is called the semiquinone radical. All three forms are known to bind metal ions forming five-membered chelate rings. Recently[7,8] we reported the preparation and properties of several transition metal charge transfer complexes based on 2,3-diamino-1,4-naphthoquinone and following these studies, we prepared a new diamagnetic Schiff-base ligand LH_2 formed through reaction between 2,3-diamino-1,4-naphthoquinone and 2,9-diformyl-1,10-phenanthroline in the presence of air. When the same reaction is carried out in the presence of the title metals, paramagnetic complexes of the semiquinone LH are formed, presumably because air oxidation occurs and the metal ion stabilizes the semiquinone form. A better understanding of the redox chemistry of these ligands in the presence of metal ions that may stabilize their catechol and semiquinone forms, will enhance our knowledge of the charge-transfer mechanisms involved in biological systems.

EXPERIMENTAL

Physical Methods

Fourier transform infrared (FTIR) spectra of the ligand and its metal complexes as KBr pellets were recorded in the spectral range 4000–400 cm^{-1} with a Perkin Elmer Series 2000 apparatus. FTIR spectra as polyethylene pellets were registered between 450–120 cm^{-1} by using a Brucker IFS 66V spectrophotometer. Spectra were scanned with a resolution of 2 cm^{-1}. Two hundred scans were accumulated for both the mid and far FTIR measurements. EPR spectra were recorded on a Brucker ECS 106 spectrometer by the X-band method (9.76 GHz). α-α'-Diphenyl-β-picrylhydrazyl free radical was used as the *g* marker. UV–Visible spectra were recorded by using a

Perkin Elmer recording spectrometer. The metals of the complexes were determined by atomic absorption spectroscopy after destruction by hot concentrated HNO_3 and $HClO_4$ 1 : 1 mixture. The contents of carbon, nitrogen and hydrogen were analyzed by the microlabs in the Venezuelean Institute of Scientific Research (IVIC). Magnetic susceptibilities were measured on a Johnson Matthey Susceptibility Balance at room temperature using $HgCo(NCS)_4$ as calibrant.

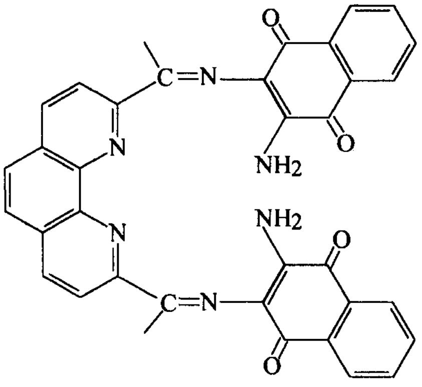
Antibacterial Activity Test

In vitro antibacterial activity of the ligand and the complexes were tested using the filter paper scrap diffusion method.[9] The chosen strains include G(+) *S. aureus* and *B. cereus* and G(−) *P. aeruginosa* and *E. coli*. The liquid medium containing the bacterial subcultures was autoclaved for 20 min at 15 lb pressure before inoculation. The bacteria were cultured for 24 h at 36°C in an incubator. Mueller Hinton broth was used for preparing basal media for the bioassay of the organisms. Nutrient agar was poured in a plate and allowed to solidify. The test compounds in DMSO solutions were added dropwise on a 10 mm diameter filter paper disk placed in the center of the agar plates. The plates were then kept at 5°C for 1 h and transferred to an incubator maintained at 36°C. The width of the growth inhibition zone around the disk was measured after 24 h of incubation. Four replicates were taken for each treatment.

Materials and Methods

All reactants and solvents were analytical grade where possible and purchased from Aldrich. All solvents were distilled by standard techniques before use.

The diamagnetic ligand LH_2 was prepared by mixing 2,3-diamino-1,4-naphthoquinone (2 mmol) and 2,9-diformyl-1,10-phenanthroline (1 mmol) in EtOH (40 mL) and the reaction mixture was heated under reflux for 10 h, then left to stand overnight. Solvent was removed by rotary evaporation until a precipitate appeared. After cooling, the solid was filtered, washed and dried *in vacuo* at room temperature. When 2,3-diamino-1,4-naphthoquinone (2 mmol) and 2,9-diformyl-1,10-phenanthroline (1 mmol) are refluxed in hot ethanolic solution while undergoing oxidation by atmospheric oxygen during 12 h in the presence of metal(II) salts (1 mmol), paramagnetic complexes of general type $M(LH)X_2$ (M = Zn(II), Cd(II), Hg(II) and Pb(II), X=Cl, Br, or AcO) were obtained. 2,3-Diamino-1,4-naphthoquinone and 2,9-diformyl-1,10-phenanthroline were synthesized from 2,3-dichloro-1,4-naphthoquinone and 2,9-dimethyl-1,10-phenanthroline, respectively, from published methods.[10,11]



LH_2

Results and Discussion

Elemental analyses, shown in Table I, agree well with the stoichiometry of the complexes. The complexes are maroon and appear to be air-stable solids, soluble in DMSO, slightly soluble in CH_3CN and insoluble in MeOH and water. The experimental conductivity values measured on 10^{-3} M solutions in DMSO at room temperature, fall in the range 2 : 1 electrolytes for the Zn(II) complex, in the range 1 : 1 electrolytes for the Cd(II) complex and in the range of nonelectrolytes for the Hg(II) and Pb(II) complexes attending the criteria of Geary.[12]

Infrared spectroscopy provides valuable information as to whether or not condensation to form hydrazone bonds has occurred. Disappearance of the absorption band from the vibration of the C=O bond of 2,9-diformyl-1,10-phenanthroline and appearance of the absorption band due to the vibration of the C=N bond proves that the Schiff-base LH_2 has been formed. The carbonyl groups from the 2,3-diamino-1,4-naphthoquinone occur at $1680\,cm^{-1}$ while terminal NH_2 groups give N–H vibrations at 3300 and $3200\,cm^{-1}$. The carbonyl groups from the 2,9-diformyl-1,10-phenanthroline occur at $1654\,cm^{-1}$ and disappeared completely upon condensation or in the prepared complexes. The spectra of the ligand LH_2 and the metal(II) complexes show a significant band at 1620 cm^{-1} which may be assigned to C=N stretching mode the Schiff base. The hydrazone signal does not overlap with the above bands and simple observation of the 1600–1700 cm^{-1} region indicates the success or failure of a reaction. A broad diffuse band of medium intensity in the 3500–3300 cm^{-1} region may be assigned to the O–H stretching vibration for lattice water. A strong band from C–H deformation is always seen from 820 to 850 cm^{-1}. For most of the metal complexes, the C=O stretching mode belonging to the naphthoquinonic derivative remains around 1680 cm^{-1} showing that the oxygen atom does not participate in coordination to the metal ions. The only exception was the lead(II) complex where this signal was observed at 1648 cm^{-1}. The presence of a M–N stretching vibration from 445 to 460 cm^{-1} for the metal complexes support coordination by the ligand as quadridentate N_4 chelating agent.[13]

The UV–Visible spectra of the free ligand and the metal complexes in DMSO solutions present three major absorption maxima in three distinct regions: 33350–34400, 26400–27750 and 24200–25400 cm^{-1}, presumably due to intraligand excitation. Because of the high degree of unsaturation of the ligand, the intense ultraviolet absorptions have tails in the visible region of the spectra.

Corrected magnetic moments have been calculated from the molar magnetic susceptibilities using Pascal's constants[14] and the values are limited within the interval 1.74–1.82 BM (Table I). These values clearly indicate that the complexes have one unpaired electron. The species $M(LH)X_2$ are paramagnetic and the EPR signals (Figure 1), with *g*-values close to the electron free *g*-values, are proof of the semiquinonic character of the ligand. No hyperfine splitting due to nuclear spin was observed, limiting structural analysis. The EPR signals support the interpretation that these complexes

TABLE I Analytical[a] and magnetic data of the ligand and its metal complexes

Compounds	C (%)	H (%)	N (%)	*Metal* (%)	μ_{eff} (BM)	*g*
$LH_2 \cdot HCl \cdot H_2O$	64.62 (64.71)	3.42 (3.65)	13.11 (13.32)		0.00	
$Zn(LH)Br_2 \cdot 2H_2O$	48.83 (48.79)	2.61 (2.75)	10.04 (10.05)	7.62 (7.82)	1.82	2.0020
$Cd(LH)Cl_2$	53.75 (53.80)	2.48 (2.51)	11.25 (11.08)	14.52 (14.82)	1.79	2.0042
$Hg(LH)Cl_2 \cdot 1/2\,H_2O$	47.45 (47.69)	2.31 (2.34)	9.57 (9.82)		1.80	2.0020
$Pb(LH)(CH_3COO)_2 \cdot H_2O$	49.33 (49.66)	2.98 (2.94)	9.11 (9.15)	22.10 (22.57)	1.74	2.0011

[a]*Calculated values are given in parenthesis.*

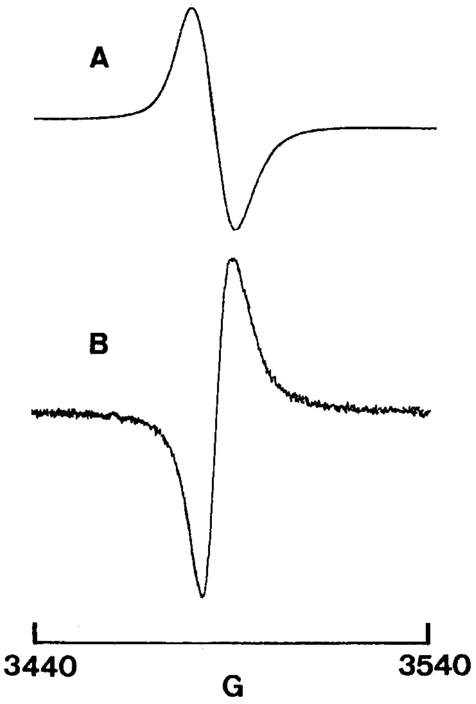


FIGURE 1 EPR spectrum (X band) at room temperature of $Cd(LH)Cl_2$ (A) and $Pb(LH)(CH_3COO)_2 \cdot H_2O$ (B) powders.

behave as radicals stabilized through the cation in which the unpaired electron is delocalized over the ligand. The oxidation has therefore been proposed to be a ligand rather than a metal-based process.

Structure of Complexes

The Schiff-base ligand has several potential donor atoms but, due to steric constraints, the ligand can provide a maximum of four donor atoms at any one time for coordination to a metal. On the assumption that four nitrogen atoms of the ligand are coordinated to the metal, as seems likely from inspection of molecular models and as found previously for similar complexes containing a N_4 donor set analyzed by X-ray diffraction methods,[15-18] it follows that the complexes contain four coordinate Zn(II), Cd(II) or Hg(II).

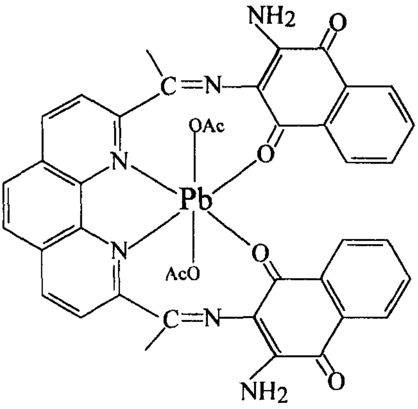


FIGURE 2 Proposed structure for $Pb(LH)(CH_3COO)_2 \cdot H_2O$ complex.

In the case of the Pb(II) complex, the strong IR band at $1680\,cm^{-1}$ assigned to ν (C=O) in the naphthoquinone spectrum shifts to lower frequencies at about $1648\,cm^{-1}$ upon complexation ($32\,cm^{-1}$), suggesting coordination by the ligand as a tetradentate N_2O_2 chelating agent, as can be seen in Figure 2. From models it appears that both a planar and approximately planar configuration of the ligand are possible, but without a full structural analysis one cannot make a distinction between these possibilities. Despite the crystalline nature of the products none proved suitable for X-ray structure determination. As the ligand is potentially tetradentate, it is quite feasible that the metal(II) ions are six coordinate with water molecule and/or halides at the vertices of a octahedron.

Biological Activity Test

The susceptibility of certain strains of bacterium towards the ligand and metal complexes can be judged by measuring the size of inhibition diameter. In general, when the compounds were tested against the *Staphylococcus aureus* strain they were found to possess lower activity than that of the sodium penicillinate itself. All compounds prepared showed inhibition diameters larger than sodium penicillinate against the *Bacillus cereus* strain, with the ligand more active than the complexes themselves as shown in Table II. Sodium penicillinate shows no activity against *Bacillus cereus* at concentrations lower that 20 μg/disk. The Hg(II) complex was the only one showing some activity against G(−) strains.

TABLE II Antimicrobial activity against *Bacillus cereus*

Compounds	*Concentration* (μg/disk)	*Zone of inhibition* (mm)
$LH_2 \cdot HCl \cdot H_2O$	20	15.1
	10	14.5
	2	14.0
$Zn(LH)Br_2 \cdot 2H_2O$	20	12.0
	10	9.6
	2	7.3
$Hg(LH)Cl_2 \cdot 1/2\,H_2O$	20	13.6
	10	11.0
	2	7.5
$Pb(LH)(CH_3COO)_2 \cdot H_2O$	20	9.4
	10	8.0
	2	7.0
Penicillin	20	11.4
	10	0.0
	2	0.0

Acknowledgments

We thank the CONICIT – Venezuela and CONICYT – Chile for financial support.

References

[1] R.H. Thomsom, *Naturally Occurring Quinones. III: Recent advances* (Chapman & Hall, London, 1987).
[2] A.T. Hudson, *Spec. Publ. R. Soc. Chem.*, **65**, 266 (1988).
[3] S. Eleff, N.C. Kennaway, N.R.M. Buist, V.M. Darley-Usmar, R.A. Capaldi, W.J. Bank and B. Chance, *Proc. Natl. Acad. Sci. USA*, **81**, 3529 (1984).
[4] G. Powis, *Pharmacol. Ther.*, **35**, 57 (1987).
[5] A. Brunmark and E. Cadenas, *Free Radic. Biol. Med.*, **7**, 435 (1989).
[6] E. Cadenas, *Biochem. Pharmacol.*, **49**, 127 (1995).
[7] J. Camus, A. Meghea and J.R. Anacona, *Polyhedron*, **15**, 2953 (1996).
[8] J. Camus, A. Meghea and J.R. Anacona, *Polyhedron*, **16**, 933 (1997).
[9] D. Liu and K. Kwasniewska, *Bull. Environm. Contam. Toxicol.*, **27**, 289 (1981).
[10] J.R. Hoover and A.E. Day, *J. Am. Chem. Soc.*, **76**, 4148 (1954)
[11] C.J. Chandler, L.W. Deady and J.A. Reiss, *J. Heterocyclic Chem.*, **18**, 599 (1981).
[12] W.J. Geary, *Coord. Chem. Rev.*, **7**, 81 (1971).
[13] D.X. West, R.M. Makeever, J.P. Scovill and D.L. Klayman, *Polyhedron*, **3**, 947 (1984).
[14] F.E. Mabbs and D.J. Machin, *Magnetism and Transition Metal Complexes* (Chapman & Hall, London, 1973).
[15] M.M. Bishop, J. Lewis, T.D. O'Donoghue and P.R. Raithby, *J. Chem. Soc., Chem. Comm.*, 476 (1978).
[16] Z.P. Haque, M. McParthlin and P.A. Tasker, *Inorg. Chem.*, **18**, 2920 (1979).
[17] J. Lewis and T.D. O'Donoghue, *J. Chem. Soc., Dalton Trans.*, 736 (1980).
[18] C.W.G. Ansell, J. Lewis, P.R. Raithby, A. Kabir, F.K. Khan, M.A. Malik, M.S. Khan and S.Z. Haider, *J. Bangladesh Acad. Sci.*, **10**, 215 (1986).