Transition Met. Chem., **24**, 478–480 (1999)

Manganese(II) and palladium(II) complexes containing a new macrocyclic Schiff base ligand: antibacterial properties

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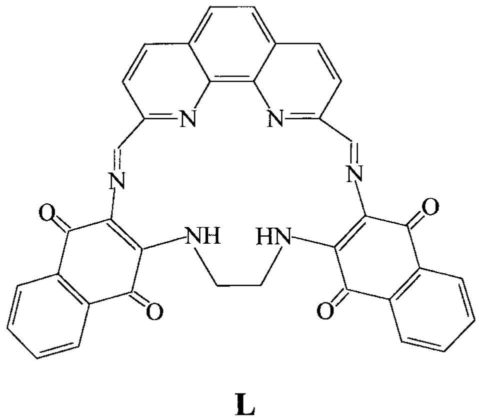
Summary

Complexes of tetradentate macrocyclic Schiff base ligand, L, with Mn^{II} and Pd^{II} ions have been synthesized by the template condensation of 1,10-phenanthroline-2,9-dicarboxaldehyde, 2,3-diamino-1,4-naphthoquinone and 1,2-dibromoethane in EtOH. The complexes were characterized by physicochemical and spectroscopic methods and an octahedral geometry is suggested for their structure. They have been screened for antibacterial activity against several bacteria, and the results are compared with the activity of penicillin.

Introduction

It is well known that transition metals(1) and group IIA metal ions(2) may act as templates for the preparation of Schiff base macrocyclic complexes. Typical experimental procedures yielding a wide range of macrocyclic complexes involve the reaction of a dicarbonyl compound with a diamine in the presence of an appropiate metal ion. It has been demonstrated by the Lewis group(3–6) that complexes of planar tetradentate or pentadentate macrocyclic ligands incorporating 1,10-phenanthroline may be prepared by template condensation of suitable dicarbonyl compounds with bis(hydrazine)-substituted heterocycles.

Recently, we reported(7–9) the synthesis and characterization of tetraaza and pentaaza macrocyclic complexes. Given that much complexes may reflect some of the well known biological features associated with naphthoquinones, we proposed to study the synthesis and characterization of complexes of a new macrocycle **L** (Scheme 1). These were obtained by the template condensation of 1,10-phenantroline-2,9-dicarboxaldehyde, 2,3-diamino-1,4-naphthoquinone and 1,2-dibromoethane in ethanol.



L

Scheme 1.

Experimental

Physical methods

I.r spectra were recorded on KBr pellets in the 4000–400 cm^{-1} range with a Perkin-Elmer Series 2000 FTIR spectrophotometer. Conductance measurements were made with a Wayne-Kerr Universal Conductance Bridge using 10^{-3} M solutions at room temperature in DMSO. ^1H n.m.r spectra were run at 80 MHz on a Varian spectrometer. U.v.-vis. spectra were recorded using a Perkin-Elmer spectrometer. Metal contents were determined by atomic absorption spectroscopy after destruction with hot concentrated HNO_3 and $HClO_4$ 1:1 mixture. C, H and N contents were analyzed by the microlabs in the Venezuelan 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 tests

In vitro bacterial activities of the Schiff base and its complexes were tested using the paper disc diffusion method. The chosen strains were 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 onto a petri plate and allowed to solidify. The test compounds were added dropwise to 10 mm diameter paper discs placed in the centre 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 disc 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 and the reactions were carried out under N_2.

The metal complexes were prepared by mixing 2,3-diamino-1,4-naphthoquinone (2 mmol) and 2,9-diformyl-1,10-phenanthroline (1 mmol) in dry EtOH (50 ml) and the reaction mixture was heated under

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reflux with stirring for 10 h. After this time an EtOH solution (10 cm^3) containing 1,2-dibromoethane (1 mmol) and the metal(II) chloride (1 mmol) was slowly added. Refluxing and stirring was continued for another 10 h and finally the solution was reduced in vol to about a half, giving a precipitate. This was collected by filtration, washed with MeOH and Et_2O and dried under vacuum over P_4O_{10}. $PdCl_2$ was first dissolved in EtOH–H_2O (10 cm^3) and concentrated NH_4OH (5 cm^3) before use. Upon stirring and warming all the solid dissolved. 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 using published methods(10–11).

Results and discussion

When 1,10-phenanthroline-2,9-dicarboxaldehyde, 2,3-diamino-1,4-naphthoquinone, Mn^{II} or Pd^{II} chlorides and 1,2-dibromoethane are boiled under reflux in a hot aqueous methanolic solution under a dinitrogen atmosphere, precipitates of $MLBr_2$ are obtained. Attempts to prepare metal complexes using Zn^{II}, Cu^{II} or Ni^{II} template ions were unsuccessful, probably due to kinetic causes and/or problems encountered in forming a transition state with the less accomodating metal ions. In the absence of a template ion, predominantly polymeric products are obtained.

Elemental analyses (Table 1) agree well with the proposed stoichiometry of the complexes. The complexes are coloured and appear to be air stable solids, soluble in DMSO and slightly soluble in acetonitrile. The conductivity values, measured on 10^{-3} mol dm^{-3} solutions in DMSO at room temperature, fall in the range for 2:1 electrolytes for the Mn^{II} complex and in the range for 1:1 electrolytes for the Pd^{II} complex, suggesting that, in the latter, one bromine atom is coordinated to the metal (Table 1).

The i.r. spectra of the complexes are similar, and reveal the absorptions expected for structure **L**. I.r. spectroscopy can provide valuable information as to whether or not condensation to form hydrazone bonds has occurred. Disappearance of the absorption band owing to $\nu(C{=}O)$ from 2,9-diformyl-1,10-phenanthroline and the appearance of an absorption band assigned to $\nu(C{=}N)$ indicates that the Schiff base has been formed. The carbonyl groups from 2,3-diamino-1,4-naphthoquinone appear at 1670 cm^{-1} while the 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 1700 cm^{-1}, and are completely absent in the spectra of the complexes. A significant band at 1625 cm^{-1}, in the spectra of the complexes may be assigned to $\nu(C{=}N)$ of the Schiff base. A broad diffuse band of medium intensity in the 3500–3300 cm^{-1} region may be assigned to lattice water. The $\nu(C{=}O)$ of the naphthoquinonic derivative is still present at *ca.* 1670 cm^{-1} in the metal complexes, showing that this oxygen atom does not participate in the coordination to the metal ions. The usual modes of the phenanthroline ring are observed. A medium intensity band appearing in the 2920–2950 cm^{-1} range corresponds to aliphatic $\nu(C{-}H)$ vibrations indicating that the 1,2-dibromoethane has reacted. No stretching C—Br mode in the region 550–600 cm^{-1} was detected, suggesting that the ring closure has occurred in both complexes.

Table 1. Analytical and conductivity data for the metal complexes

Compound	Found (Calcd.) (%) C	H	N	Metal	Λ (S cm^{-1} mol^{-1})[a]
$[Mn(L)Br_2]2H_2O$	50.8	2.8	10.0	6.5	68
	(50.7)	(3.1)	(9.9)	(6.7)	
$[Pd(L)Br_2]2H_2O$	47.7	2.6	9.3		28
	(47.8)	(2.9)	(9.3)		

[a] In DMSO; expected range are 20–40 and 50–80 for 1:1 and 1:2 electrolytes respectively.

The u.v-vis. spectra of the metal complexes in DMSO solution present three major absorptions maxima, at 298–305, 355–366 and 392–398 nm, presumably due to intraligand excitation. Because of the high degree of unsaturation of the macrocyclic ligand, the intense u.v. absorptions have tails in the visible region of the spectrum and this hampered assignment of the relatively weak d-d transitions. The manganese (II) complex shows very weak absorptions in the visible region probably due to spin-orbit forbidden transitions.

The ^1H n.m.r. spectra of the complexes show a multiplet in the region 7.1–9.0 ppm, which is assigned to aromatic ring protons. However, no band could be assigned to aldehyde or amine protons, suggesting that the proposed macrocyclic complexes are formed by the condensation reaction. Furthermore, in spite of the paramagnetic nature of the complexes, a singlet can be seen at 3.1–3.6 ppm and is assigned to the four equivalent methylene protons of the ethylene chain. These signals strongly suggest that ring closure has occurred. A singlet at 8.2–8.5 ppm could be assigned to the two equivalent carboximine protons (CH=N, 2H). The relative integrals are in good agreement with the required ratio of aromatic to aliphatic protons.

From the molar magnetic susceptibility values, corrected magnetic moments were calculated using Pascal's constants. The manganese(II) complex has a magnetic moment of 5.72 BM as predicted for a high spin d^5 system with five unpaired electrons, while the palladium(II) complex has a magnetic moment of 2.58 BM, typical of a high spin d^8 systems with two unpaired electrons. Both complexes therefore probably have distorted octahedral geometries.

Structure of complexes

Despite the crystalline nature of the products, neither proved suitable for X-ray structure determination. The Schiff base ligand has several potential donor atoms, but due to steric constraints, it can provide a maximum of four donor atoms to any one metal atom. An inspection of molecular models, along with consideration of the structures found previously by X-ray crystallography(12–15) for similar complexes containing a N_4 donor set, suggested that the macrocycle is approximately planar and tetradentate. Hence we conclude that metal(II) ions are octahedral with water molecules and/or bromines in the axial positions.

Biological activity tests

The susceptibility of certain strains of bacterium towards the macrocycle and its complexes was judged by measuring the size of bactericidal diameter. The results

Table 2. Antimicrobial activities of the metal complexes

Compound	(μg/disc)	Zone of Inhibition (mm) S. Aureus	B. Cereus	P. Aeruginosa	E. Coli
[Mn(L)Br_2]2H_2O	20	14.4	14.2	0.0	0.0
	10	12.7	13.1	0.0	0.0
	2	11.3	12.0	0.0	0.0
[Pd(L)Br_2]2H_2O	20	13.0	13.4	8.0	8.2
	10	9.5	11.7	7.7	8.0
	2	0.0	9.0	7.5	8.0
Penicillin	20	34.2	11.4	0.0	0.0
	10	13.4	0.0	0.0	0.0
	2	0.0	0.0	0.0	0.0

are given in Table 2. In general, the new compounds were found to be less effective against *Staphilococcus Aureus* than sodium penicillinate itself. However, the complexes showed inhibition diameters larger than sodium penicillinate against *Bacillus Cereus*. The palladium complex was the only one showing good activity against G(−) strains.

Acknowledgements

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

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(Received 29 October 1998;
Accepted 02 December 1998) TMC 4388