

Synthesis, characterization, crystal structure and DNA-binding study of four cadmium(II) pyridine-carboxamide complexes

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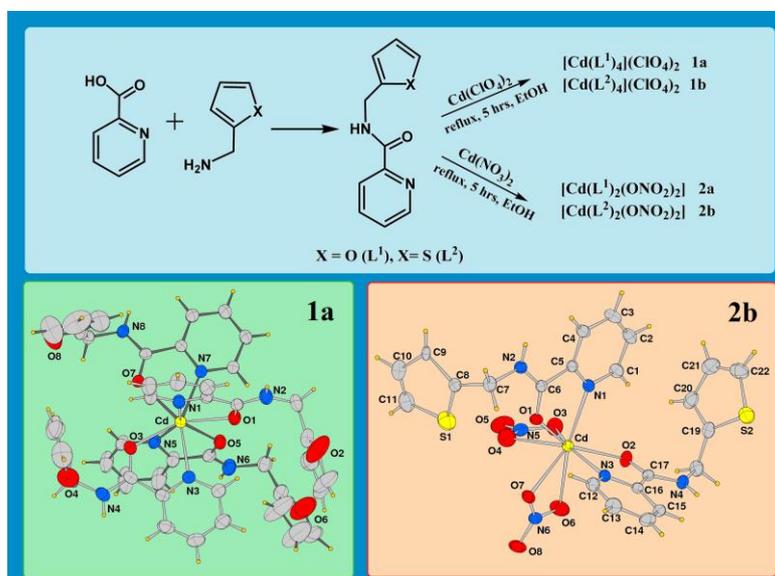
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Graphical Abstract:

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SYNOPSIS

Synthesis and characterization of four mononuclear eight coordinated cadmium(II) complexes with newly explored carboxamide derivatives and study of interaction with calf-thymus DNA are reported. The results suggest that neutral complexes **2a** and **2b** bind to DNA in an intercalative mode. On the other hand, cationic complexes **1a** and **1b** interact with DNA *via* weak intercalative or groove binding mode.



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Abstract. Treatment of perchlorate or nitrate salt of cadmium(II) with carboxamide derivatives (**L**) generated four novel mononuclear metal complexes, represented as $[\text{Cd}(\underline{\text{L}})_4](\text{ClO}_4)_2$ (**1a** and **1b**) and $[\text{Cd}(\underline{\text{L}})_2(\text{ONO}_2)_2]$ (**2a** and **2b**) in appreciable yields (**L** = **L**¹ = N-(furan-2-ylmethyl)-2-pyridine carboxamide and **L** = **L**² = N-(thiophen-2-ylmethyl)-2-pyridine carboxamide). The complexes have been characterized by FT-IR, UV-Visible spectra, elemental analysis and single crystal X-ray crystallographic analysis which revealed eight coordinated cadmium ions, but in different coordination environments depending on the counter anion used. In addition, electronic absorption, fluorescence spectroscopy and viscosity measurements revealed a significant interaction of the four complexes with CT-DNA *via* intercalative/groove binding mode. The intrinsic binding constant K_b obtained varies from 0.4×10^4 to $1.11 \times 10^5 \text{ M}^{-1}$. The results suggest that neutral complexes **2a** and **2b** bind to DNA in an intercalative mode. On the other hand, cationic complexes **1a** and **1b** bind with DNA *via* weak electrostatic/covalent interaction.

(Note: Compound numbers defined in the text of manuscript shall not appear in the Abstract)

Keywords. Cadmium(II) complex; carboxamide ligand; crystal structures; DNA binding study.

(Note: Keywords should be nouns! Choose them carefully. See the catalogue in the Journal website for guidance)

1. Introduction

The coordination chemistry of carboxamide derivatives, especially towards transition metal ions, has attracted a considerable interest and this attention arises from the fact that pyridine carboxamide complexes have been used in various fields such as in asymmetric catalysis,^{1,2} dendrimers,³ molecular receptor synthesis⁴ and also in the synthesis of compounds with possible antitumor properties.⁵⁻⁸ The carboxamide [-C(O)NH-] group of the primary structure of proteins represents an important ligand building unit in coordination chemistry, since its chelating nature imparts a unique...

Herein, we report an account of the synthesis, structural characterization and DNA binding study of cadmium(II) complexes of two carboxamide derivatives ($\underline{\mathbf{L}}$) formulated as $[\text{Cd}(\underline{\mathbf{L}})_4](\text{ClO}_4)_2$ ($\underline{\mathbf{1}}$), $[\text{Cd}(\underline{\mathbf{L}})_2(\text{ONO}_2)_2]$ ($\underline{\mathbf{2}}$), where $\underline{\mathbf{L}} = \mathbf{L}^1 = \text{N}-(\text{furan-2-ylmethyl})\text{-2-pyridinecarboxamide}$ or $\underline{\mathbf{L}} = \mathbf{L}^2 = \text{N}-(\text{thiophen-2-ylmethyl})\text{-2-pyridinecarboxamide}$. The binding constants K_b of these complexes with DNA have been obtained from UV-Vis spectra and the...

(Note: Introduction should be appropriate for the readership of this General Chemistry Journal)

2. Experimental

2.1 Materials and Physical measurements

The chemicals and reagents used for the synthesis were obtained from commercial sources. Solvents were distilled from an appropriate drying agent. Calf thymus-DNA (Bangalore Genie, India) and ethidium bromide (Sigma) were used as received. All other chemicals and solvents were of analytical grade. The elemental (C, H, N) analyses were performed on a Perkin Elmer model 2400 elemental analyzer. IR spectra and ^1H NMR spectra of complexes were recorded on a Perkin Elmer FTIR model RX1 spectrometer (KBr disc, $4000\text{--}400\text{ cm}^{-1}$) and on a Bruker Avance DPX 500 MHz spectrometer using DMSO-d_6 as solvent, respectively. The solution electrical conductivity was measured using Systronics 304 digital conductivity meter with a solution concentration of $ca. 10^{-3}$ M. The electronic absorption spectra were recorded on a JASCO UV-Vis/NIR spectrophotometer model V-570. The fluorescence spectra of the complexes bound to DNA were recorded with an excitation wavelength of 522 nm by using the Hitachi-4500 fluorimeter.

2.2 Synthesis of ligands \mathbf{L}^1 and \mathbf{L}^2

The organic ligands N-(furan-2-ylmethyl)-2-pyridinecarboxamide (\mathbf{L}^1) and N-(thiophen-2-ylmethyl)-2-pyridine-carboxamide (\mathbf{L}^2) have been prepared as previously reported and duly characterised by single crystal X-ray crystallography.¹⁷

2.3 Synthesis of cadmium(II) complexes

The complexes were synthesized following a procedure as described below. The organic compound (4.0 mmol, 816 mg of **L**¹ or 872 mg of **L**²) was dissolved in dry ethanol by stirring the mixture for 15 min. To this solution, an ethanolic solution of cadmium(II) perchlorate hexahydrate (Cd(ClO₄)₂·6H₂O, 419 mg, 1.0 mmol) (for **1**) or cadmium(II) nitrate tetrahydrate (Cd(NO₃)₂·4H₂O, 309 mg, 1.0 mmol) (for **2**) was added

2.3.1 *Complex 1a: [Cd(L¹)₄](ClO₄)₂*: Yield: 65–70% (0.772 g); C₄₄H₄₀CdCl₂N₈O₁₆: Anal. Found: C, 47.11; H, 3.55; N, 9.92; Cd, 9.97% Calc.: C, 47.18; H, 3.60; N, 10.00; Cd, 10.04% IR (cm⁻¹): ν_{C=N}, 1475, ν_{ClO₄⁻} 1087, 628, ν_{C=O} 1643, ν_{N-H} 3337; Conductivity (Λ_o, ohm⁻¹ cm² mol⁻¹) in MeOH: 214; ¹H NMR (δ, ppm in DmsO-d₆): 9.01 (t, 1H); 8.53 (d, 1H); 7.92 (m, 2H); 7.50 (m, 1H); 7.43 (s, 1H); 6.27 (t, 1H), 6.16 (-NH), 4.38 (s, 2H of CH₂).

2.3.2 *Complex 1b: [Cd(L²)₄](ClO₄)₂*: Yield: 65–70% (0.807 g); C₄₄H₄₀CdCl₂N₈O₁₂S₄: Anal. Found: C, 40.91; H, 3.25; N, 8.58; Cd, 11.53% Calc.: C, 41.02; H, 3.13; N, 8.70; Cd, 11.64%. IR (cm⁻¹): ν_{C=N}, 1469, ν_{ClO₄⁻} 1087, 628, ν_{C=O} 1634, ν_{N-H} 3314. Conductivity (Λ_o, ohm⁻¹ cm² mol⁻¹) in MeOH: 204. ¹H NMR (δ, ppm in dmsO-d₆): 9.24 (t, 1H); 8.47 (d, 1H); 7.95 (m, 2H); 7.60 (m, 1H); 7.31 (s, 1H); 7.01 (t, 1H), 6.20 (-NH), 4.40 (s, 2H of CH₂).

2.4 X-ray crystal structure analysis

X-ray single crystal data of **1a** and **2b** were collected at room temperature (296(2) K) using Mo-K_α radiation (λ = 0.71073 Å) on a SMART APEX II diffractometer equipped with CCD area detector. Data collection, data reduction, structure solution/refinement were carried out using the SMART APEX II package.¹⁸ The structures were solved by...

2.5 DNA binding experiments

Tris-HCl buffer solution (pH = 7.2) used in all the experiments involving CT-DNA was...

2.5.1 *EB competitive studies with fluorescence spectroscopy*: In the ethidium bromide (EB) fluorescence displacement experiment, 5.0 μL of EB tris-HCl solution (1.0 mM)...

2.5.2 *Viscosity measurements*: To adjudge the binding mode (groove/intercalative) of complex with DNA, viscosity measurements were performed by employing the...

3. Results and Discussion

3.1 Synthesis and characterization

The perchlorate and nitrate salt of cadmium(II) were reacted with two carboxamide derivatives **L**¹ and **L**² to form four new mononuclear cadmium complexes in ethanol medium at ambient temperature. The complexes, which revealed to be stable in air and soluble in methanol, DMF, DMSO, etc., were characterized by physico-chemical and spectroscopic tools.

3.2 Structure of complexes

3.2.1 *Crystal structure of 1a*: An Ortep view of complex **1a**, crystallizing in monoclinic system, space group *P*2₁/*c*, is depicted in Figure 1, and selected bond lengths and angles are listed in Table 2.

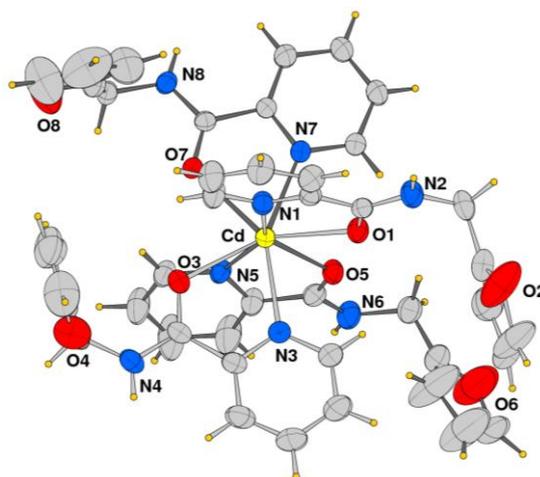


Figure 1. ORTEP view (ellipsoid probability at 30%) of the cationic complex **1a**, [Cd(L¹)₄]²⁺ (carbon atoms are not labelled for the sake of clarity).

The metal ion is coordinated by four chelating **L**¹ ligands through the pyridine nitrogen and carbonyl oxygen giving a distorted square antiprismatic geometry with a N₄O₄ chromophore. The asymmetric ligands **L**¹ chelate the metal with Cd-N and Cd-O bond distances in the range 2.397(5)-2.444(5) and 2.417(4)-2.459(4) Å, respectively...

3.2.2 *Crystal structure of 2b*: The X-ray diffraction study revealed that the complex crystallizes in monoclinic system, space group *P*2₁. The metal is coordinated by two N,O chelating **L**² and by two chelating nitrate anions leading to a neutral molecular...

4. Conclusions

Carboxamide ligands (**L**¹ and **L**²) obtained *in situ* from pyridine-2-carboxylic acid with furfuryl amine and 2-thiophenemethyl amine were reacted with perchlorate and nitrate salt of cadmium(II), separately, to afford four mononuclear cadmium complexes of formula $[\text{Cd}(\underline{\text{L}})_4](\text{ClO}_4)_2$ (**L**=**1a** and **1b**) and $[\text{Cd}(\underline{\text{L}})_2(\text{ONO}_2)_2]$ (**L**=**2a** and **2b**). The X-ray structural analysis indicated that the composition is anion dependent: in fact, perchlorate remained uncoordinated while the more coordinating nitrate anion is bound to cadmium(II) ion leading to cationic and neutral complexes, respectively. In this work, the detailed study is reported on the

(NOTE: Tables, Figures and Schemes shall be embedded in the Manuscript in appropriate locations)

Supplementary Information (SI)

Crystallographic data for the structural analyses of complexes **1a** and **2b** have been deposited with the Cambridge Crystallographic Data Centre bearing the CCDC Nos. 1438356 and 1438357, respectively. Copies of this information are available on request at free of charge from CCDC, Union Road, Cambridge, CB21EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.ac.uk or <http://www.ccdc.cam.ac.uk>). Plots of DNA binding experiments for complex **2b** from the absorbance and emission study and its comparison with the complex **1** and other reported cadmium(II) complexes (Figures S1–S4 and Tables S1 and S2) are available at www.ias.ac.in/chemsci.

(NOTE: Supplementary Information should be submitted as a separate file. The content of SI should be briefly stated here)

Acknowledgements

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