Synthesis and Characterization of Cd(II) Macrocyclic Schiff Base Complex with Two 2-Aminoethyl Pendant Arms

H. Keypour[a,*], A.A. Dehghani-Firouzabadi[a], M. Rezaeivala[b] and H. Goudarziafshar[c]
[a]Faculty of Chemistry, Bu-Ali Sina University, Hamedan 65174, Iran
[b]Department of Chemical Engineering, Hamedan University of Technology, Hamedan, 65155, Iran
[c]Department of Chemistry, Faculty of Science, Ilam University, P.O. Box 69315516, Ilam, Iran

A new pendant armed Schiff base macrocyclic complex of [CdL]$^{2+}$, was prepared *via* cyclocondensation of 2,6-bis(2-formylphenoxymethyl)pyridine with branched hexaamine in the presence of Cd(II) ion. The ligand was 23-membered oxaazamacrocycle having two 2-aminoethyl pendant arms [L: 3,28-dioxa-14,17-bis(aminoethyl)-11,14,17,20,34-pentaazatetracyclo[34.3.1] tetratriacontane-1(34), 4, 6, 8, 10, 20, 22, 24, 26, 30, 32-undecaene]. The complex was investigated by IR, ^{1}H NMR, microanalysis and MALDI mass spectroscopy. The structure of the complex was verified by *ab initio* HF-MO calculations using a standard 3-21G* basis set. This article introduces an unusual seven-membered chelate ring and shows that by its using, the Cd-N bonds lengths within the macrocycle would be longer and also Cd(II)-pendant amine bonds lengths would be shorter.

Keywords: Macrocyclic complex, Schiff base, Cadmium(II), Pendant arm, *Ab initio*

INTRODUCTION

The preparation of synthetic polyaza- or oxaaza-macrocyclic ligands bearing functional pendant donor groups and their subsequent ligation to various transition metals has been a popular area of research in recent years, mainly because the metal complexes of such ligands might be effective models for the protein-metal binding sites in metalloproteins in some biological systems, as potential therapeutic reagents or as multi-electron catalysts [1-7].

Cadmium(II) is an environmental pollutant which inhibits RNA polymerase activity *in vivo* [8,9], and reacts readily with proteins and other biological molecules. The macrocyclic chemistry of cadmium has been developed recently [10-13]. Previous works mainly focused on dinuclear or oxa-aza

*Corresponding author. E-mail: haskey1@yahoo.com

pendant arms macrocyclic complexes of cadmium [4,11-13]. Some mononuclear Cd(II) Schiff base [1+1] macrocyclic complexes have been reported [14-16]. In addition to providing a convenient entree to the formation of bis(pendant arm) pentaaza macrocyclic ligands, which are intrinsically difficult to synthesize [17], this approach produces potentially heptadentate ligands which allow the investigation of the chemistry of cadmium(II) complexes coordinated by a single ligand of high denticity.

We have been interested for some time in the design and synthesis of new macrocyclic Schiff base complexes, particularly, in the synthesis of CR-type [18,19]. These complexes are formed mainly from metal ion templated [1+1] cyclocondensation of 2,6-diacetylpyridine and a linear triamine or tripodal tetraamine [20-22]. The latter reactions produce tetraaza macrocycles carrying a single 2-aminoethyl pendant arm [19]. We have also produced Cd(II) pentaaza
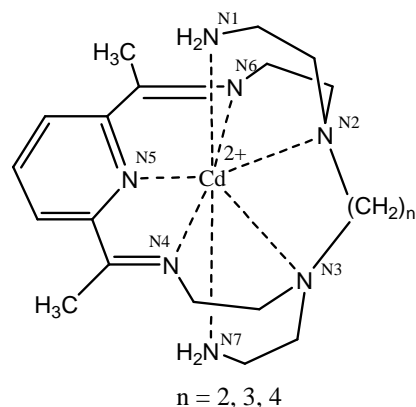
macrocyclic complexes with two 2-aminoethyl pendant arms, using branched hexaamines and 2,6-diacetylpyridine (Scheme 1) [23].

Herein, we report the result of a comparative investigation of the latter complexes with our recently synthesized Cd(II) complex which has been constructed from a bigger ring, more donor atoms and two 2-aminoethyl pendant arms. The Cd(II) template [1+1] cyclocondensation of 2,6-bis(2-formyl-phenoxymethyl)pyridine with appropriate branched hexaamine leads to the Cd(II) complex $[CdL]^{2+}$. This complex is based on the 23-membered oxaaza-macrocycle that has two 2-amino-ethyl pendant arms (Scheme 2). We also chose to access its structural parameters by undertaking *ab initio* molecular orbital calculations. To do this, we undertook a full geometry optimization at the HF/3-21G* level of theory, using LanL2DZ basis set for Cd.

EXPERIMENTAL

Physical Measurements

^{1}H NMR spectrum was obtained on a Varian 300 MHz

Scheme 1. Cd(II) complexes with two 2-aminoethyl pendant arms using branched hexaamines and 2,6-diacetyl-pyridine.

spectrometer. Infrared spectrum was recorded as KBr discs using a Perkin Elmer FT-IR spectrum GX spectrophotometer (4000-500 cm^{-1}). Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry was carried
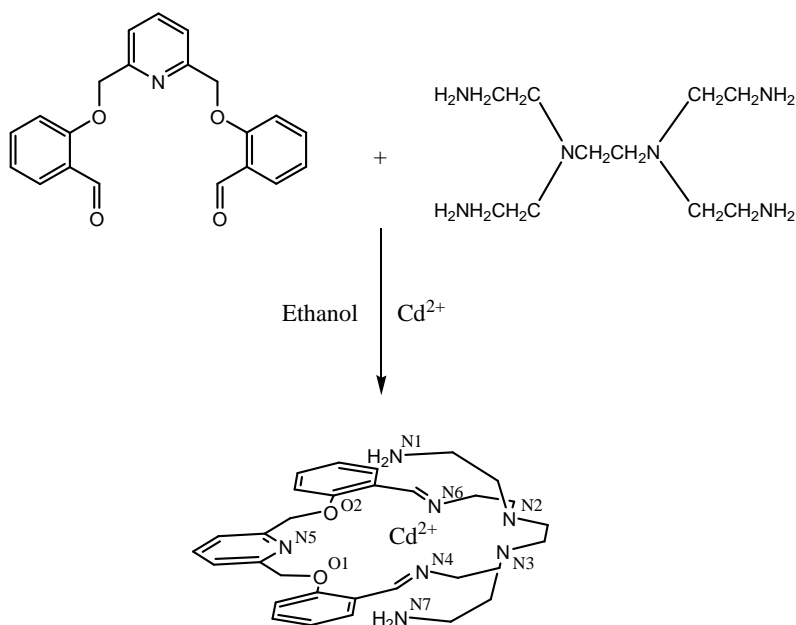
Scheme 2. The template condensation between 2,6-bis(2-formylphenoxymethyl)pyridine and hexamine in the presence of Cd(II).

821

out using a Micromass Tof Spec 2E spectrometer, with 2,5-dihydroxy benzoic acid as the matrix and dimethyl sulfoxide as the solvent.

Chemicals and Starting Materials

2,6-Bis(2-formylphenoxymethyl)pyridine and *N,N,N´,N´*-tetrakis(2-aminoethyl) ethane-1,2-diamine hexahydrobromide (ten. 6HBr) were prepared using the literature methods [24,25]. All reagents and solvents used were of analytical grade and purchased commercially.

Preparation of [CdL](NO$_3$)$_2$ Complex

The macrocyclic complex was prepared by a modification of the procedure of Alexander *et al*. [26]. A solution of NaOH (0.12 g, 3 mmol) in absolute EtOH (10 ml) was added to a suspension of the appropriate hexaamine (ten. 6HBr) (0.359 g, 0.5 mmol) in absolute EtOH (10 ml) and the mixture was stirred at room temperature. The mixture was filtered off to remove the precipitated NaBr and the filtrate was then added dropwise to a hot solution of Cd(NO$_3$)$_2$.4H$_2$O (0.165 g, 0.5 mmol) and 2,6-bis(2-formylphenoxymethyl)pyridine (0.178 g, 0.5 mmol) in absolute EtOH (50 ml) over a period of 2 h. After refluxing for 18 h, the solution was allowed to cool and then concentrated in a rotary evaporator. A yellow powder precipitated, which was filtered off, washed with cold diethyl ether and dried under vacuum. Yield: 0.39 g (68%). Anal. Calcd. for C$_{31}$H$_{41}$N$_9$O$_8$Cd: C, 47.73; N, 16.16; H, 5.30. Found: C, 47.39; N, 16.15; H, 5.52. IR (Nujol, cm^{-1}); 3296, 3241 ν(NH$_2$), 1635 ν(C=N)$_{imi}$, 1596 ν(C=C) and ν(C=N)$_{py}$, 1384 ν(NO$_3$). ^{1}H NMR (DMSO-d$_6$, ppm): δ 2.66-3.00 (20H), 3.87 (4H), 5.18 (4H), 7.01-7.82 (8H), 8.48-8.57 (3H), 8.86 (2H). MALDI-MS, m/z (%): [CdL]$^{2+}$-2H, 655 (30%).

Ab Initio Molecular-Orbital Calculation

A full minimization of the structure of the macrocyclic complex was performed at the *ab initio* HF level of theory using gradient techniques with the Gaussian 98 set of programs [27], on a Pentium-PC computer with a 1400 MHz processor. The effective core potential (ECP) standard basis set LanL2DZ [28], was utilized for cadmium. The full-electron standard basis set 3-21G* [29] was used for all other atoms. A starting semi-empirical structure for the *ab initio* calculation was arrived at by performing a minimization using the

HyperChem 5.02 program [30].

RESULTS AND DISCUSSION

Synthesis and Spectral Characterization

The synthesis of [CdL]$^{2+}$ complex was carried out via template [1+1] condensation of 2,6-bis(2-formylphenoxymethyl)pyridine and branched hexaamine in the presence of Cd^{2+} in ethanol (Scheme 2). The Schiff base macrocyclic complex was characterized by microanalysis, IR, ^{1}H NMR and MALDI mass spectroscopy. This compound is an air-stable solid with low solubility in DMSO. The microanalysis was consistent with the formulations given in the Experimental Section.

The IR spectrum of the complex was assigned and provided some information regarding the bonding in the complex. The data were consistent with the presence of imine bond for the coordinated Schiff base ligand, exhibiting the ν(C=N) mode at 1635 cm^{-1}, which was diagnostic for the Schiff base condensation, while no bands attributable to C=O group were detected. The spectrum exhibited a strong band at 1596 cm^{-1}, as expected, for the high energy ring vibrations of the pyridine. The presence of unreacted pendant primary amine groups in the complex was evident from their IR spectra, indicated by the appearance of two strong peaks at 3241 and 3296 cm^{-1} assigned to the symmetric and asymmetric NH$_2$ stretching modes [23]. The strong absorption bands at 1384, 1290, 836 and 748 cm^{-1} support the presence of nitrate groups as the counter-ions in the complex [31].

The ^{1}H NMR spectrum of [CdL]$^{2+}$ in DMSO shows a peak at 8.86 ppm, corresponding to the imine protons and a doublet of doublet (8.57 ppm) and a doublet (8.48 ppm) assigned to the *para*- and *meta*-pyridyl protons, respectively [23]. In the region characteristics of the benzene protons (7.82-7.01 ppm) multi-signals were found. The methylene hydrogen atoms adjacent to the pyridine show a peak at 5.18 ppm and the methylene hydrogen atoms adjacent to the imino bond give a broad signal at 3.87 ppm. The NH$_2$ protons and the protons on the adjacent methylene show signals at 3.00-2.66 ppm. Unfortunately, the poor solubility of the complex made it impossible to study the ^{13}C and 2D NMR spectral properties.

The MALDI mass spectrum of the complex also provided strong evidence for the formation of the macrocyclic complex

Keypour *et al.*

Table 1. Selected Calculated Bond Lengths (Å) and Bond Angles (deg) for $[CdL]^{2+}$. Calculated Cd-N Bond Lengths of $[CdL^5]^{2+}$ [25] are Indicated in Brackets

	$[CdL]^{2+}$
Cd-N(1)	2.293 (2.497)
Cd-N(2)	2.513 (2.333)
Cd-N(3)	2.482 (2.333)
Cd-N(4)	2.565 (2.325)
Cd-N(5)	4.080 (2.300)
Cd-N(6)	2.763 (2.325)
Cd-N(7)	2.257 (2.497)
Cd-O(1)	2.565 (----)
Cd-O(2)	4.580 (----)
N(1)-Cd-O(1)	105.8
N(1)-Cd-N(2)	74.1
N(1)-Cd-N(3)	107.4
N(1)-Cd-N(4)	84.7
N(1)-Cd-N(6)	81.8
N(1)-Cd-N(7)	161.6
N(7)-Cd-O(1)	85.8
N(7)-Cd-N(2)	91.3
N(7)-Cd-N(3)	78.1
N(7)-Cd-N(4)	113.4
N(7)-Cd-N(6)	82.8
N(6)-Cd-O(1)	96.6
N(6)-Cd-N(2)	70.2
N(2)-Cd-N(3)	73.6
N(3)-Cd-N(4)	68.7
N(4)-Cd-O(1)	64.5

with the L as a product of the template cyclocondensation of one molecule of dialdehyde with one molecule of *N,N,N´,N´-*tetrakis(2-aminoethyl)ethane-1,2-diamine. The peak in the spectrum of the complex was observed at m/z 655 corresponding to $[CdL]^{2+}$-2H. Additional peaks attributable to the fragments of the complex could be observed.

Ab Initio Studies

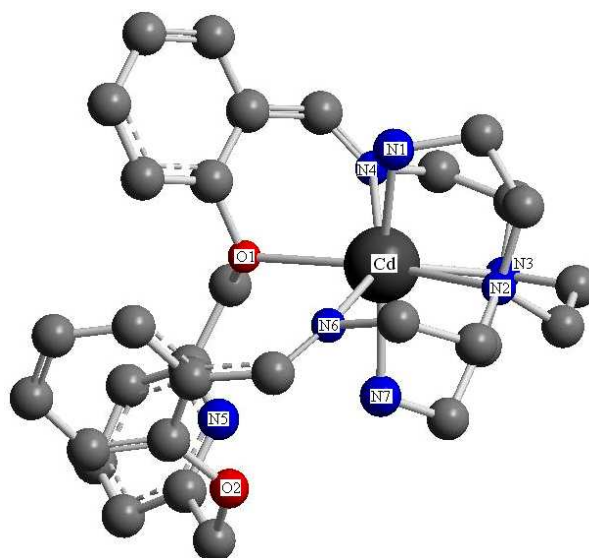As we were unable to prepare crystals suitable for X-ray

Fig. 1. The *ab initio* optimized structure of $[CdL]^{2+}$. Hydrogen atoms are omitted for clarity.

diffraction work containing the $[CdL]^{2+}$ cation, we chose to access its structural parameters by undertaking *ab initio* molecular orbital calculations. To do this, we assumed that the same mode of [1+1] cyclization as found for $[CdL^5]^{2+}$ [23] would hold, and thus undertook a full geometry optimization at the HF/3-21G* level of theory, using LanL2DZ basis set for Cd. We also made use of the same level of *ab initio* calculations for $[CdL]^{2+}$ to examine the comparability of the predicted gas phase structure with that determined in the solid state (Scheme 1). For $[CdL]^{2+}$, the pendant nitrogen to Cd(II) distances were predicted to be shorter than those observed for $[CdL^5]^{2+}$ (Table 1), because the large cavity of the macrocycle Cd(II) cation was shifted to one side of the macrocycle and Cd-N(py) was longer than other Cd-N bonds. To solve this problem, the Cd-N(py) was removed and Cd-O bond provided the seventh coordinate of the cadmium (Fig. 1). Selectively calculated bond distances and angles for the complex and $[CdL^5]^{2+}$ are shown in Table 1.

CONCLUSIONS

The Cd^{2+} ion is effective as a template for the Schiff base condensation of 2,6-bis(2-formylphenoxymethyl)pyridine with EDTA type hexamine ligand yielding oxaaaza-macrocyclic

823

complex. On the basis of *ab initio* calculations for $[CdL]^{2+}$, we believe that the metal ion is surrounded by a distorted pentagonal bipyramidal environment in this complex.

ACKNOWLEDGMENTS

REFERENCES

[1]   T.A. Kaden, Top. Curr. Chem. 121 (1984) 157.

[2]   S.R. Collinson, D.E. Fenton, Coord. Chem. Rev. 148 (1996) 19.

[3]   H. Adams, M.R.J. Elsegood, D.E. Fenton, S.L. Heath, S.J. Ryan, J. Chem. Soc., Dalton Trans. (1999) 2031.

[4]   M. Vicente, C. Lodeiro, H. Adams, R. Bastida, A. De Blas, D.E. Fenton, A. Macias, A. Rodriguez, T. Rodriguez-Blas, Eur. J. Inorg. Chem. (2000) 1015.

[5]   H. Okawa, H. Furutachi, D.E. Fenton, Coord. Chem. Rev. 174 (1998) 51.

[6]   P.V. Bernhardt, G.A. Lawrance, Coord. Chem. Rev. 104 (1990) 297.

[7]   D.G. Fortier, A. McAuley, J. Chem. Soc., Dalton Trans. (1991) 101.

[8]   K.B. Jacobson, J.E. Turner, Toxicology 60 (1980) 1.

[9]   H.A. Hidalgo, V. Koppa, E.S. Bryan, FEBS Lett. 64 (1976) 159.

[10] D. Dakternieks, Coord. Chem. Rev. 98 (1990) 279.

[11] K.R. Adam, C. Clarkson, A.J. Leong, L.F. Lindoy, M. McPartlin, H.R. Powell, S.V. Smith, J. Chem. Soc., Dalton Trans. (1994) 2791.

[12] X.Y. Xu, Z.L. Wang, Q.H. Luo, M.C. Shen, X.G. Zhou, Z.Y. Zhou, J. Coord. Chem. 43 (1998) 281.

[13] M. Qian, S. Gou, S. Chantrapromma, S.S. Sundara Raj, H.K. Fun, Q. Zeng, Z. Yu, X. You, Inorg. Chim. Acta 305 (2000) 83.

[14] D.A. Stotter, J. Inorg. Nucl. Chem. 38 (1976) 1866.

[15] S.M. Nelson, S.G. McFall, M.G.B. Drew, A.H. Bin Othman, N.B. Mason, J. Chem. Soc., Chem. Commun. (1977) 167.

[16] M.G.B. Drew, S.G. McFall, S.M. Nelson, J. Chem. Soc., Dalton Trans. (1979) 575.

[17] F. Denat, S. Brandes, R. Guilard, Synlett 5 (2000) 561.

[18] J.D. Curry, D.H. Busch, J. Am. Chem. Soc. 86 (1964) 592.

[19] H. Keypour, S. Salehzadeh, R.G. Pritchard, R.V. Parish, Inorg. Chem. 9 (2000) 5787.

[20] R.H. Prince, D.A. Stotter, P.R. Woolley, Inorg. Chim. Acta 9 (1974) 51.

[21] H. Keypour, D.A. Stotter, Inorg. Chim. Acta 19 (1976) L48.

[22] H. Keypour, D.A. Stotter, Inorg. Chim. Acta 33 (1979) L149.

[23] H. Keypour, H. Khanmohammadi, K.P. Wainwright, M.R. Taylor, J. Iranian, Chem. Soc. 1 (2004) 53.

[24] N.A. Bailey, D.E. Fenton, S.J. Kitchen, T.H. Lilley, M.G. Williams, P.A. Tasker, A.J. Tasker, L.F. Lindoy, J. Chem. Soc., Dalton Trans. (1991) 627.

[25] B.K. Wagnon, S.C. Jakels, Inorg. Chem. 28 (1989) 1923.

[26] M.D. Alexander, A. Van Heuvelen, H.G. Hamilton, Inorg. Nucl. Chem. Lett. 6 (1970) 445.

[27] M.J. Frich, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrazewski, J.A. Montgomery, Jr.R.E. Startmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malik, A.D. Rabuck, K. Raghavachar, J.B. Foresman, J. Cioslowski, J.V. Ortiz, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanyakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, M. Head-Gordon, E.S. Replogle, J.A. Pople, GAUSSIAN 98 (Revision A.3) Gaussian Inc. Pittsburgh, PA, USA, 1998.

[28] P.J. Hay, W.R. Wadt, J. Chem. Phys. 82 (1985) 299.

[29] K.D. Dobbs, W.J. Hehre, J. Comp. Chem. 8 (1987) 880.

[30] HyperChem, Release 5.02, Hypercube, Inc., Gainesville, 1997.

[31] C. Lodeiro, R. Bastida, A. de Blas, D.E. Fenton, A. Masias, A. Rodriguez, T. Rodriguez-Blas, Inorg. Chim. Acta 267 (1998) 55.