1. Introduction

Synthetic polyazamacrocycles and their metal complexes have fostered a considerable research field at the interface between chemistry and biology due to their diverse biomedical applications [1, 2, 3, 4, 5, 6, 7, 8], analytical [9], and industrial [10] applications. These physical, analytical, spectroscopic, electrochemical, structural, and biological investigations attract attention owing to the elevated thermodynamic stability, kinetic inertness, and significant biological activities of the resultant species. The latter includes antibacterial [1], antifungal [1], antioxidant [2], anti-inflammatory [3], antidiabetic [4], and antiproliferative [5] activities. The superiority of synthetic macrocyclic complexes as antitumor [6], anticancer [7], and anti-HIV [8] agents is well documented. The biological role of macrocyclic complexes is dependent on the nature of metal ions and their encapsulation/confinement patterns within the cavity defined by the specific macrocyclic ligand. In light of the above, it is reasonable to synthesize new tetraazamacrocyclic complexes and investigate their antibacterial activities.

Due to the multifarious applications [1, 2, 3, 4, 5, 6, 7, 8, 9, 10] of macrocyclic ligands, including differential behavior exhibited by their isomeric forms and their metal complexes in a wide variety of contexts, researchers continue to be fascinated by their chemistry and various applications, including in the development of metal-based drugs and imaging agents. Relevant to the present study are recent reports describing the antibacterial activities of cadmium compounds [11, 12, 13, 14]. These follow earlier studies, whereby cadmium(II) macrocyclic compounds were reported to exhibit potent antibacterial potential [13, 14]. In addition, we have also reported x-ray crystallographic studies of cadmium(II) macrocyclic compounds with other macrocycles [14, 15]. Though copper(II), nickel(II), and cobalt(III), and chromium(III) complexes of macrocyclic ligands described herein have been reported [16, 17], related studies on cadmium(II) have yet to be reported. So, it was thought of interest to prepare and characterize some new cadmium(II) macrocyclic complexes as well to study their antibacterial activities. In acknowledgment of the above, in this study the newly prepared cadmium macrocycles have been characterized and evaluated for their antibacterial activities.
antibacterial potential against selected bacteria. Such studies are moti-
vated by the life-threatening nature of such microbes especially in the
context of their ability to develop drug resistance to commonly employed
antibiotics. Thus, it is anticipated this study will contribute to the
universal challenge faced by researchers in this field: to develop specialized
drugs to combat the studied bacteria for the betterment of the human
population.

A significant number of metal complexes of different macrocycles
[18, 19, 20], including, those relevant to the present investigation,
14-membered octamethyl tetraazamacroyclic diene ligand (Me₈ [14]
diene), isomeric ligands (Lₐ, Lₐ, and Lₖ) and their N-pendent derivative
ligands, are available in the literature [21, 22, 23, 24, 25, 26]. In this
context, copper(II) and nickel(II) complexes with bis-hydroxyethyl (LBY
and LCY) and dimethyl (LBZ and LCZ) derivatives of the isomeric ligands Lₐ
and Lₖ have been studied [23, 24]. Moreover, some copper(II), nickel(II),
and cobalt(III) complexes of bis-cyanoethyl derivative (LCX) of isomeric
ligand Lₖ have been reported recently by our group [17]. In continuation
of these studies, 2,9-C-meso-Me₈ [14]diene dihydroperchlorate
(L/2HClO₄) [27], the isomeric ligand (Lₖ) [22] of its reduced analogue,
and the 1,8-N-pendent bis-cyanoethyl derivative (LCX) [17] of Lₖ have
been successfully prepared as per the literature; see Scheme 1 for
chemical diagrams. Thereafter, cadmium(II) compounds of the ligand LCX
have been prepared by direct interaction with cadmium(II) salts as well
as by axial ligand substitution reactions on the precursor compounds. The
synthesized compounds have been characterized by different analytical,
spectroscopic methods and antibacterial activities conducted. Herein, the
results of these investigations are described.

2. Experimental

2.1. Chemicals

Chemicals (Analytical grade, Sigma-Aldrich) were used without
further purification.

Precaution: At elevated temperature, perchlorates are explosive in nature.

2.2. Physical measurements

Microanalysis (CHNS) were determined on a CHNS-932 elemental
analyzer; melting point determinations were made on a electrothermal
2.3. Syntheses of ligands

2.3.1. L2HClO4, LC, and L CX

The parent octamethyl substituted ligand salt, L2HClO4, and three isomers LC, Lp, and LC of its reduced analogue were prepared as per literature methods [15, 21]. Moreover, the 1,8-N-pendant derivative ligand, L CX, from Lp has been synthesized (Scheme 1) as recently reported by our group [17].

2.4. Syntheses of cadmium(II) compounds of L CX

2.4.1. Syntheses of cadmium(II) compounds produced by the direct interactions of LCX with cadmium(II) salts (1–4)

L CX (0.418 g, 1.0 mmol) and 1.0 mmol of each of Cd(ClO4)2·6H2O, Cd(NO3)2·4H2O, Cd(CH3COO)2·3H2O, and CdCl2·H2O were separately dissolved in hot methanol (30 mL) and each of the salt solutions was added an acrylonitrile solution (5 mL) of L CX. The mixtures were heated on a water bath for 1 h and allowed to dry. The products were extracted with chloroform and the extracts were evaporated to dryness to give white solid products, i.e., [Cd(LCX)(ClO4)2]2H2O, [Cd(LCX)(NO3)2], [Cd(LCX)(CH3COO)2], and [Cd(LCX)]2, respectively. The products were then washed with ethanol followed by diethyl ether and stored in a desiccator over silica gel.

[Cd(LCX)(ClO4)2]2H2O (1): Color: white. Melting Point: 132 °C. M. W.: 765.98. Anal. Found: C, 38.33; H, 7.26; N, 10.1%. Calc. for Cd2H2O4CdCl2N2O4C: C, 37.60; H, 6.58; N, 10.97%. IR (cm−1) (Fig. S1(a), Supplementary Materials): ν(C=O) 1743cm−1, ν(C=O) 1638cm−1, ν(C=O) 1571cm−1; ν(C=O) 1416cm−1, ν(C=O) 1371cm−1, ν(C=O) 1310cm−1. Magnetic moment μ eff (BM): diamagnetic.

[Cd(LCX)(ClO4)2]2H2O (2): Color: white. Melting Point: 147 °C. M. W.: 655.083. Anal. Found: C, 43.92; H, 7.13; N, 17.9%. Calc. for Cd2H2O4CdCl2N2O4C: C, 45.32; H, 7.63; N, 17.95%. IR (cm−1) (Fig. S1(b), Supplementary Materials): ν(C=O) 1743 cm−1, ν(C=O) 1638 cm−1, ν(C=O) 1571 cm−1; ν(C=O) 1416 cm−1, ν(C=O) 1371 cm−1, ν(C=O) 1310 cm−1. Magnetic moment μ eff (BM): diamagnetic.

2.4.2. Syntheses of axial ligand substitution products of [Cd(L2)(ClO4)2]·2H2O (5–9)

[Cd(LCX)(ClO4)2]·2H2O (0.766 g, 1.0 mmol), KX (X = I, Br, Cl, and SCN), and NaNO2 (2.0 mmol) were dissolved/suspended separately in hot absolute methanol (30 mL) and mixed while hot. The mixtures were concentrated to 5 mL by heating on a water bath. On cooling, the mixtures were filtered off and the filtrates evaporated to dryness. The products were then extracted with CHCl3. On evaporation of the chloroform extracts, the solid white products [Cd(LCX)I2]·H2O, [Cd(LCX)Br2]·2H2O, [Cd(LCX)(ClO4)·2H2O, [Cd(LCX)(NO3)2]·2H2O, and [Cd(LCX)(NO3)(ClO4)]·2H2O were obtained, respectively, and dried in a desiccator over silica gel.

Analyzed: C, 35.88; H, 6.03; N, 10.47%. IR (cm−1) (Fig. S1(e), Supplementary Materials): ν(C=O) 1743 cm−1, ν(C=O) 1638 cm−1, ν(C=O) 1571 cm−1, ν(C=O) 1416 cm−1, ν(C=O) 1371 cm−1, ν(C=O) 1310 cm−1. Magnetic moment μ eff (BM): diamagnetic.

[Cd(LCX)Br2]·2H2O (6): Color: white. Melting Point: 143 °C. M. W.: 726.88. Anal. Found: C, 39.73; H, 6.09; N, 11.48%. Calc. for Cd2H2O4CdCl2N2O4C: C, 40.32; H, 7.15; N, 11.9%. IR (cm−1) (Fig. S1(f), Supplementary Materials): ν(C=O) 1743 cm−1, ν(C=O) 1638 cm−1, ν(C=O) 1571 cm−1, ν(C=O) 1416 cm−1, ν(C=O) 1371 cm−1, ν(C=O) 1310 cm−1. Magnetic moment μ eff (BM): diamagnetic.

[Cd(LCX)Cl2]·2H2O (7): Color: white. Melting Point: 129 °C. M. W.: 701.98. Anal. Found: C, 41.19; H, 7.15; N, 11.91%. Calc. for Cd2H2O4CdCl2N2O4C: C, 41.03; H, 7.18; N, 11.97%. IR (cm−1) (Fig. S1(g), Supplementary Materials): ν(C=O) 1743 cm−1, ν(C=O) 1638 cm−1, ν(C=O) 1571 cm−1, ν(C=O) 1416 cm−1, ν(C=O) 1371 cm−1, ν(C=O) 1310 cm−1. Magnetic moment μ eff (BM): diamagnetic.

[Cd(LCX)NO3]·2H2O (8): Color: white. Melting Point: 136 °C. M. W.: 665.26. Anal. Found: C, 46.81; H, 7.73; N, 16.79; S, 9.59%. Calc. for Cd2H2O4CdCl2N2O4C: C, 46.89; H, 7.37; N, 16.84; S, 9.64%. IR (cm−1) (Fig. S1(h), Supplementary Materials): ν(C=O) 1743 cm−1, ν(C=O) 1638 cm−1, ν(C=O) 1571 cm−1, ν(C=O) 1416 cm−1, ν(C=O) 1371 cm−1, ν(C=O) 1310 cm−1. Magnetic moment μ eff (BM): diamagnetic.

[Cd(LCX)(NO3)ClO4]·2H2O (9): Color: white. Melting Point: 117 °C. M. W.: 712.53. Anal. Found: C, 40.33; H, 7.15; N, 13.82%. Calc. for Cd2H2O4CdCl2N2O4C: C, 42.78; H, 7.37; N, 17.36%. IR (cm−1) (Fig. S1(i), Supplementary Materials): ν(C=O) 1743 cm−1, ν(C=O) 1638 cm−1, ν(C=O) 1571 cm−1, ν(C=O) 1416 cm−1, ν(C=O) 1371 cm−1, ν(C=O) 1310 cm−1. Magnetic moment μ eff (BM): diamagnetic.
two gram-positive i.e., *Bacillus wiedmannii* and *Bacillus aerus*, and three gram-negative bacteria, i.e., *Escherichia coli*, *Shigella flexneri* and *Salmonella typhi* by using the method described in our recent report [17]. For comparison, the activity of non-coordinated metal salt Cd(ClO4)2·6H2O was also tested against all bacteria. Tests were repeated thrice for statistical analysis and finally, the antibacterial activities of the tested compounds are reported by subtracting the values for solvent (negative control).

2.6. Crystal structure determination

The colorless crystals of LCX were isolated from the slow evaporation of its acetonitrile solution. Intensity data for a colorless crystal of LCX (0.12 × 0.15 × 0.17 mm) were measured at 298 K on a Rigaku/Oxford Diffraction XtaLAB Synergy diffractometer (Dualflex, Atlas32) fitted with CuKα radiation (λ = 1.54178 Å) so that θmax was 67.1° for 100% completeness. Data processing and gaussian absorption corrections were accomplished with CrysAlisPro [28]. The structure was solved by direct methods [29] and the refinement was by full-matrix least squares on F2 with anisotropic displacement parameters for all non-hydrogen atoms [30]. The C-bound hydrogen atoms were placed on stereochemical grounds and redefined with fixed distances and refined with fixed geometries. The unique N-bound hydrogen atom was located from a difference map and refined with N-H = 0.86 ± 0.01 Å. A weighting scheme of the form w = 1/(σ2(F²) + (0.061 P)² + 0.232P), where P = (F² + 2F0²)/3, was introduced in the refinement. Owing to poor agreement, one reflection, i.e., (2 1 1), was omitted from the final cycles of refinement. The programs WinGX [31], ORTEP-3 for Windows [31], PLATON [32], and DIAMOND [33] were also used in the study. Crystal data and refinement details are given in Table 1.

CCDC 2113786 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033).

3. Results and discussion

All of the newly prepared cadmium(II) compounds were isolated, as expected, as white powders. Analytical and spectroscopic data are given in the experimental section. While connectivity of the various ligands in the cadmium compounds have been established, regrettably, single crystals of the cadmium compounds could not be prepared for X-ray analysis for the determination of fine details of the molecular structures and supramolecular association. Since IR spectra were not recorded below 400 cm⁻¹, the bands for Cd–Cl, Cd–I, and Cd–Br, expected at around 260 cm⁻¹ in the spectra of [Cd(LCX)Cl₂], [Cd(LCX)Cl(ClO₄)₂]·2H₂O, [Cd(LCX)I₂]·2H₂O, and [Cd(LCX)Br₂]·2H₂O, were not detected. Magnetochemical studies indicate all compounds are diamagnetic species. The UV-visible spectra did not exhibit any d-d bands but displayed charge transfer bands as expected for d¹⁰ system. Consistent with previous work, the stereochemistry of the compounds does not change during axial substitution reactions [19], so the stereochemistry of axial ligand substitution products of [Cd(LCX)(ClO₄)₂]·2H₂O were assigned by comparison with the ¹H-NMR data of [Cd(LCX)(ClO₄)₂]·2H₂O.

3.1. L·2HClO₄, LC, and LCX

Ligands, L·2HClO₄ [22,27], LC [22, 27], and LCX [17] have been characterized as per the indicated literature.

3.1.1. Crystal and molecular structures of LCX

Crystals of LCX were obtained and subjected to an X-ray crystallographic study. The molecular structure of the centrosymmetric molecule is shown in Figure 1. The 14-membered ring has an extended chair conformation and is stabilized by intramolecular amine-N–H…N(tertiary amine) hydrogen bonds (N1–H1n…N2‘ = 2.257(11) Å, N1…N2‘ = 2.9550(13) Å with angle at H1n = 138.3(11)° for symmetry operation (i) 1-x, 1-y, 1-z). The chirality at each of the C1 and C5 atoms is S and, being a centrosymmetric molecule, the chirality at each of the C1 and C5 atoms is R. The amine-N2 atom carries a cyanoethyl substituent with the N2–C3–C4–C7 torsion angle of 175.66(12)° being indicative of an anti-periplanar (+ap) conformation.

In the absence of conventional hydrogen bonding, the supramolecular association in the crystal of LCX is largely devoid of directional interactions. Indeed, the only identifiable contacts within the standard distance criteria of PLATON [32] are methyl-C–H…N(cyano) contacts. From symmetry, each molecule forms four such contacts which extend laterally to form a square grid, these stack in an ...AAA... fashion in the crystal. Relevant diagrams and data are given in Fig. S6, Supplementary Materials.

![Figure 1](https://example.com/figure1.png)  
**Figure 1.** The molecular structure of LCX, showing the atom-labelling scheme and displacement ellipsoids at the 35% probability level. The molecule is disposed about an inversion center with unlabeled atoms related by the symmetry operation 1-x, 1-y, 1-z.
3.2. Cadmium(II) compounds of LCX

3.2.1. Cadmium(II) compounds (1–4) produced by the direct interaction of LCX with cadmium(II) salts

Six coordinated octahedral [Cd(LCX) (ClO4)2]•2H2O, [Cd(LCX) (NO3)2]•2H2O, [Cd(LCX) (CH3COO)2], and [Cd(LCX)Cl2] compounds prepared by the direct interaction of LCX with each of Cd(ClO4)2•6H2O, Cd(NO3)2•4H2O, Cd(CH3COO)2•3H2O, and CdCl2•2H2O, respectively. The infrared spectra exhibit bands in the ranges 3214-3255 cm⁻¹ for ν(C=O) and 1383-1395 cm⁻¹ for ν(C−H). Further, all compounds display bands due to ν(C−H) in the range 2246-2251 cm⁻¹ which contributes with 2245 cm⁻¹ in the spectrum of LCX [17]. This agreement thus provides strong evidence for the presence of N-pendant cyanooethyl branches in the ligand which are non-coordinating. The appearance of bands at 3433 cm⁻¹ and 1658 cm⁻¹ can be accounted for by the presence of water molecules of crystallization in the products [34, 35]. The infrared spectrum of [Cd(LCX) (ClO4)2]•2H2O displays perchlorate bands at around 1111, 1095, 1062 and 622 cm⁻¹, where the splitting of the band at 1095 cm⁻¹ into two medium bands at 1111 and 1062 cm⁻¹ is attributed to coordinated perchlorate [36]. The spectrum of [Cd(LCX) (NO3)2] shows a band at 1383 cm⁻¹ split into two medium bands at 1329 and 1445 cm⁻¹ which can be attributed to a coordinated NO3 group. The separation of the bands by 116 cm⁻¹ is consistent with a unidentate mode of coordination [37]. The spectrum of [Cd(LCX) (CH3COO)2] also exhibits strong bands at 1571 and 1416 cm⁻¹ with the separation of 155 cm⁻¹ giving evidence in favor of a unidentate mode of coordination by the CH3COO⁻ ion [38]. The molar conductance values for all four compounds in chloroform and for [Cd(LCX) (CH3COO)2] and [Cd(LCX)Cl2] in DMSO were found in the range of 0–28 Ω⁻¹ cm² molar⁻¹, which support their non-electrolyte nature [39] of these compounds, indicating the anions (ClO4, NO3, CH3COO, and Cl⁻) are coordinated to cadmium(II). By contrast, the molar conductance values (64-110 Ω⁻¹ cm² molar⁻¹) for [Cd(LCX) (ClO4)2]•2H2O and [Cd(LCX) (NO3)2] in DMSO, and [Cd(LCX)(CH3COO)2] and [Cd(LCX)Cl2] in CH3CN support 1:1 electrolytic character [40]. This is due to the conversion of the original octahedral geometry to square pyramidal as indicated by expression (1). Crystal structure determinations are available for an analog for the nitrate derivative in expression (1), namely [Cd(Lq) (NO3)(NO3)] [14] and [Cd(Lq) (NO3)(NO3)](NO)0.5H2O [15]. Here, one nitrate is weakly coordinated above the N4 plane and one nitrate is non-coordinating thereby providing indirect evidence for the formulation of the products in expression (1). Further, the values in the range 175-281 Ω⁻¹ cm² molar⁻¹ measured for [Cd(LCX) (ClO4)2]•2H2O and [Cd(LCX) (NO3)2] in CH3CN demonstrate the 1:2 electrolytic nature of these two compounds in this solvent due to the conversion of octahedral dianionic (ClO4 and NO3) species into octahedral diaqua species as revealed by expression (2).

\[\text{[Cd(LCX)(X)\text{H}_2\text{O}]_{n}\text{CH}_3\text{CN}} = \text{[Cd(LCX)(X)\text{H}_2\text{O}]}_{n}\text{CH}_3\text{CN} + n\text{H}_2\text{O} \]

(1)

\[\text{[Cd(LCX)(Y)\text{H}_2\text{O}]_{n}\text{NO}_3 = \text{[Cd(LCX)(H}_2\text{O}Y)]_{n}\text{NO}_3} \]

(2)

The 1H-NMR spectrum (Fig. S2, Supplementary Materials) of the diperclorotocadmioc(II) dihydrate compound [Cd(LCX) (ClO4)2]•2H2O exhibits overlapped signals corresponding to 24H. However, resolution of this multiplet shows that this signal is composed of two singlets and three doublets. The singlets at 1.255 and 1.312 ppm, each corresponding to 6H, can be assigned to equatorial and axial components of gem-dimethyl protons, respectively, whereas the doublets at 1.148, 1.215, and 1.303 ppm in the ratio of 1:1:2 corresponds to 3H, 3H, and 6H, respectively. The two doublets at 1.148 and 1.215 ppm can be assigned to two equatorial methyl protons on two chiral carbons and the doublet at 1.303 ppm to the axial methyl protons on the other two equivalent chiral carbons. Thus, a diaxial-diequatorial orientation, as revealed by the x-ray analysis (Chart 1) can be assigned to this compound. The spectrum further exhibits multiplets at 2.621, 3.428, and 3.665 ppm due to CH2, and at 4.026, 5.350, and 7.285 ppm due to CH, H2O and NH protons, respectively. The 13C NMR spectrum (Fig. S3, Supplementary Materials) exhibits only 12 resonances (half the number of total number of carbon atoms), which can be accounted for pairwisely equivalency of carbon atoms. This observation is in support of the symmetric diaxial-diequatorial orientation as has already been assigned on the basis of the 1H NMR spectrum. The four resonances in the region 18–35 ppm can be assigned to the eight carbon atoms of eight peripheral methyl carbons. The five resonances in the region 51–59 ppm can be accounted for by the 10 ring carbons and the three downfield resonances in the range of 66–68 ppm are attributed to pairwisely equivalent six carbons in the two cyanooethyl branches (−CH2−CH2-CN). Further, the 1H NMR spectrum (Fig. S4, Supplementary Materials) of [Cd(LCX) (NO3)2] revealed two singlets at 1.277 and 1.304 ppm with these being ascribed to the equatorial and axial methyl groups of two gem-dimethyl pairs. The spectrum further shows two doublets at 1.107 and 1.554 ppm, corresponding to 6H each, which arise due to two equatorial and two axial methyl groups, respectively, which are pairwise equivalent. So, [Cd(LCX) (NO3)2] should therefore, have two equatorially oriented and two axially oriented methyl groups on chiral carbons. However, the signals are not well resolved but are overlapped. The downfield signals (most are multiplets) at 2.070, 2.287, and 2.888 ppm due to CH2, and 3.426–3.786, and 7.825 ppm due to CH, and NH-protons. Hence, a similar diaxial-diequatorial structure (Str. 2, Chart 1) can also be assigned to [Cd(LCX) (NO3)2]. On the other hand, though the ligand of the complex [Cd(LCX) (ClO4)2]•2H2O contains 24 carbons, based on the above evidence and earlier discussion, structures Str. 1, 2, 3, and 4 (Chart 1) can be assigned to [Cd(LCX) (ClO4)2]•2H2O, [Cd(LCX) (NO3)2], [Cd(LCX) (CH3COO)2], and [Cd(LCX)Cl2], respectively.

3.2.2. Axial ligand substitution products derived from [Cd(LCX) (ClO4)2]•2H2O (5–9)

[Cd(LCX) (ClO4)2]•2H2O was subjected to axial substitution reactions with KX (X = I, Br, Cl, and SCN) and NaN3O2 in a 1:2 ratio to afford the six coordinated octahedral compounds [Cd(LCX)(X)2]•2H2O, [Cd(LCX)Br2]•2H2O, [Cd(LCX)(Cl)(ClO4)]2H2O, [Cd(LCX) (NCS)2]•2H2O, and [Cd(LCX) (NO3)2] (ClO4)2•2H2O, respectively. The infrared spectra exhibit bands at 3191-3241 cm⁻¹ for ν(C=O) and 1375-1377 cm⁻¹ for ν(C−N) [41]. The IR spectrum of [Cd(LCX)(NO2)(ClO4)]2H2O contains 24 carbons, based on the above evidence and earlier discussion, structures Str. 1, 2, 3, and 4 (Chart 1) can be assigned to [Cd(LCX) (ClO4)2]•2H2O, [Cd(LCX) (NO3)2], [Cd(LCX) (CH3COO)2], and [Cd(LCX)Cl2].
Ω−1 cm² mol⁻¹ are indicative of 1:1 electrolytes [40] owing to the conversion of octahedral species into square pyramidal species as indicated by expressions (3), (4a), and (4b). On the other hand, the value 201 Ω−1 cm² mol⁻¹ for [Cd(LCX)(NO₂)(ClO₄)]₂H₂O in CH₂CN gives evidence in favor of 1:2 electrolytic behavior [40] in this solvent due to conversion of the original octahedral mononitroperchlorato species into octahedral diaqua species as shown by expression (5).

\[
\text{[Cd(LCX)(ClO₄)]·2H₂O (1)} \quad \text{[Cd(LCX)(NO₂)]₂ (2)} \quad \text{[Cd(LCX)(CH₃COO)] (3)}
\]

\[
\text{[Cd(LCX)Cl] (4)} \quad \text{[Cd(LCX)I₂]·H₂O (5)} \quad \text{[Cd(LCX)Br₂]·2H₂O (6)}
\]

\[
\text{[Cd(LCX)Cl(ClO₄)]·2H₂O (7)} \quad \text{[Cd(LCX)(NCS)₂]·H₂O (8)} \quad \text{[Cd(LCX)(NO₂)(ClO₄)]·2H₂O (9)}
\]

Chart 1. Cadmium(II) compounds of LCX.

The ¹H NMR spectrum (Fig. S5, Supplementary Materials) of [Cd(LCX)I₂]·H₂O, an axial substitution product of [Cd(LCX) Cl(ClO₄)]·2H₂O, exhibits an overlapped pattern for the peripheral methyl groups which can be resolved into two parts. One part (region 1.2–1.4 ppm) contains a singlet at 1.339 ppm corresponding to 6H and two doublets at 1.210 and 1.312 ppm, each integrating to 3H. These resonances can be attributed to the equatorial components of gem-dimethyl groups and two equatorial methyl protons on two chiral carbons, respectively. Other resonances include two singlets at 1.541 and 1.563 ppm, and two doublets at 1.392 and 1.508 ppm, which are assigned to axial components of gem-dimethyl pairs and two axially oriented methyl protons on two equivalent chiral carbons, respectively. Thus, the diaxial-diequatorial orientation (Str. 5, Chart 1) assigned to this molecule, which requires methyl groups on C₇ and C₁₄ to be equatorial and those on C₂ and C₉ axially oriented or vice versa, is consistent with earlier observations in related studies [23, 45, 46]. Separate signals for equivalent methyl groups indicate the distortion in the substitution product. The spectrum further displays downfield multiplets at 2.875, 3.269 ppm, and 3.547 due to CH₂, and 4.706, 5.320, and 7.285 ppm, which are accounted for by CH, H₂O, and NH protons.
Table 2. Antibacterial activities of LCX and cadmium(II) compounds.

| Sample No. | Compounds | Gram-positive bacteria | Gram-negative bacteria |
|------------|-----------|------------------------|------------------------|
|            |           | Zone of inhibition in diameter (mm) | Zone of inhibition in diameter (mm) |
|            |           | B. wiedmannii 24 h | B. aerius 24 h | E. coli 24 h | S. fl exneri 24 h | S. typhi 24 h |
| 1          | [Cd(LCX) (ClO4)2]•2H2O | 0 | 0 | 0 | 0 | 0 |
| 2          | [Cd(LCX) (NO3)2] | 13 | 14 | 10 | 12 | 19 |
| 3          | [Cd(LCX) (CH3COO)2] | 9 | 12 | 9 | 11 | 17 |
| 4          | [Cd(LCX)Cl2] | 12 | 14 | 13 | 15 | 18 |
| 5          | [Cd(LCX)Br2] | 11 | 14 | 12 | 14 | 15 |
| 6          | [Cd(LCX)I2] | 20 | 13 | 11 | 10 | 9 |
| 7          | [Cd(LCX)Cl(ClO4)] | 19 | 15 | 14 | 11 | 12 |
| 8          | [Cd(LCX)Br2•2H2O] | 19 | 14 | 14 | 15 | 15 |
| 9          | [Cd(LCX)NO2 (ClO4)]•2H2O | 8 | 10 | 12 | 11 | 14 |
| 10 | Chloramphenicol | 12 | 12 | 11 | 10 | 13 |
| 11 | DMSO | 22 | 16 | 15 | 15 | 19 |

3.3. Antibacterial studies

Antibacterial activities of LCX and cadmium(II) complexes were investigated against two gram-positive (Bacillus wiedmannii, which causes foodborne illness, and Bacillus aerius, the causative agent of infectious diseases like burn infections, ear infections, etc.) and three gram-negative (Escherichia coli which causes cholangitis, urinary tract infections, etc.; Shigella flexneri, which causes diarrhea; and Salmonella typhi, responsible for high fever, diarrhea, and vomiting) bacteria. These bacteria are responsible a variety of diseases and there is an urgent need to develop effective drugs for treatment. Thus, in this context, we carried out antibacterial studies on the new cadmium(II) compounds to investigate their activities against these microbes. The evaluation of the MIC (minimum inhibitory concentration) of the test samples were determined and shown to be 5 mg/mL. Therefore, all of the test samples including controls and a non-coordinated cadmium(II) salt were studied at a concentration of 5 mg/mL. The macrocycle LCX was ineffective against all the tested bacteria as observed previously [23, 24, 47, 48]. The results are summarized in Table 2 and Supplementary Materials Fig. S7(a)–(e), and reveal that all of the cadmium(II) compounds of LCX exhibit remarkable antibacterial activity. Further, the data indicate distinctive activities against the studied bacteria. Thus, the dipechlorotatocadmium(II) (1), dinitratocadmium(II) (2), diacetatocadmium(II) (3), dichloridocadmium(II) (4), diisothiocyanatocadmium(II) (8), and mononitrophloracetatocadmium(II) (9) derivatives exhibit maximum activity against Salmonella typhi. By contrast, the didiodidocadmium(II) (5), dibromidocadmium(II) (6), and monochloroperoxidochlorthocadmium(II) (7) derivatives are most potent against Bacillus wiedmannii. Against Bacillus aerius, the most active compound was the dibromidocadmium(II) species (6), against E. coli, and the monochlorodiperoxidochlorthocadmium(II) (7) derivative was most potent, and against S. flexneri, (7) was most effective. The present cadmium(II) compounds revealed comparable activities to other reported cadmium(II) macroyclic compounds [13, 14]. By contrast to the negative control (DMSO), which was totally ineffective against all evaluated bacteria, the free salt [Cd(ClO4)2•6H2O] as well as the positive control (chloramphenicol) were highly potent. As the compounds are very stable, there is little possibility of dissociation of the compounds to release metal ion [47]. Elevated activities of the cadmium(II) complexes compared to LCX can be explained by the chelation theory [49]).

4. Conclusions

This study reveals the 1,8-N-pendent derivative ligand, LCX, underwent facile complexation with cadmium(II) perchlorate, nitrate, and cadmium(II) chloride salts to afford six coordinated octahedral compounds, [Cd(LCX) (ClO4)2•2H2O, [Cd(LCX) (NO3)2], [Cd(LCX) (CH3COO)2], and [Cd(LCX)Br2] respectively. The compound [Cd(LCX) (ClO4)2•2H2O underwent axial substitutions with KX (X = I, Br, Cl, and SCN) and NaN3 to furnish six coordinated octahedral substituted compounds [Cd(LCX)I2•2H2O, [Cd(LCX)Br2•2H2O, [Cd(LCX)I2•2H2O, [Cd(LCX)Br2•2H2O, [Cd(LCX)NO3•2H2O, and [Cd(LCX)Cl(ClO4)]•2H2O, respectively. All compounds were found to be non-electrolytes in CHCl3 as expected for octahedral geometries. The molar conductivity values of the compounds in DMSO and CH2CN is an indication of changes of geometry/ionization of these compounds in these solvents. Though the ligand LCX was found to be ineffective against all the bacteria tested, the cadmium(II) compounds of this ligand showed remarkably elevated activities against all the tested bacteria.

Declarations

Author contribution statement

Avijit Chakraborty: Performed the experiments; Wrote the Paper.
Saswata Rabi: Conceived and designed the experiments; Wrote the Paper.

Lucky Dey: Performed the experiments; Analyzed and interpreted the data.

Debashis Palit, Benu Kumar Dey: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Edward R.T. Tiekink: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Tapashi Ghosh Roy: Conceived and designed the experiments; Wrote the Paper.

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Data availability statement

Data included in article-supplementary material/referenced in article.
Declaration of interests statement

The authors declare no conflict of interest.

Additional information

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