Medbiotech Journal

MBTJ, 3(4): 139-143, 2019

Research Paper

Review of Phenanthroline Schiff-base Complexes of MN (II) and Study of their Biochemical Activities

Viktor H. Titovich[1]

Department of Chemistry, Tomsk State University, Russia

Received: 04 October 2019 Accepted: 24 November 2019 Published: 01 December 2019

Abstract

Three new Mn(II) macrocyclic Schiff-base complexes have been prepared via cyclocondensation of 2,9-dicarboxaldehyde-1,10-phenanthroline and three linear tetradentateamines via a metal-templated reaction and coordination features have been examined. The complexes are18- and 19-membered hexaazamacrocycles, and incorporate a 1,10-phenanthroline unit as an integral part of their cyclic structure. All complexes have been characterized by a variety of methods such as IR, elemental analysis, EI- Mass, and conductivity measurements Also the synthesized complexes were screened for their antibacterial activities against six bacterial strains and showed antibacterial effects.

Keywords*:* Macrocyclic Schiff base complexes; 2,9-dicarboxaldehyde-1,10-phenanthroline; Antibacterial effects; Hexa dentate

How to cite the article:
V. H. Titovich, Review of Phenanthroline Schiff-base Complexes of MN (II) and Study of their Biochemical Activities , Medbiotech J. 2019; 3(4): 139-143, DOI: 10.22034/mbt.2019.80874.

1. Introduction

Macrocyclic complexes are part of a number of fundamental biological systems. The importance of such complexes hasprovided a motivation for investigation of the metal ionchemistry of those biological systems as well as of cyclic ligand systems [1]. The development of the field of bioinorganicchemistry has been an important factor in spurringthe growth of interest in complexes of macrocyclic compounds [2]. The possibility of using synthetic macrocyle asmodels for biologically important systems has initiated abroad spectrum of research activities, ranging from synthesisof new ring systems. [3-10]. A review on macrocyle has revealed the importance of macrocycliccomplexes in biological processes such as photosynthesis anddioxygen transport [11], their catalytic properties [12], their potentialapplications as metal extractants and as radio-therapeutic [13]and medical imaging agents [14].

1,10-Phenanthroline is the parent of an important class of chelating agents. Compared to the more common 2,2'-dipyridyl system, 1,10-Phenanthroline has several distinct properties: the rigid structure imposed by the central ring means that the two nitrogen atoms are always held in juxtaposition. One other important property of the phenanthroline nucleus is its ability to act as a triplet-state photosensitizer, especially in complexes with lanthanides [15]. It has thus been extensively used in both analytical and preparativecoordination chemistry [16]. Schiff bases have been of great importance in many of the macrocyclic areas of chemistry. Many of the more

[1] Corresponding Author Email: v.titovich@gmail.ru

rational synthetic routes to macrocyclic ligands involve the use of a metal ion template to orient the reacting groups of linear substrates in the desired conformation prior to ring closure [17].

In previous works [18,19], we used some linear tetradentate amines to preparingsome Mn(II) macrocyclic Schiff base complexes. Also, in other works, we have used 2,9-dicarboxaldehyde-1,10phenanthroline as a precursor to achieve several kinds of cyclocondensation reactions with a series of multi-amine derivatives, and a number of macrocyclic Schiff base complexes and pendant armed macrocyclic Schiff base complexes have been prepared by the template reactions [20-22]. We have developed a general method for the synthesis of [1+1] macrocyclic complexes via cyclocondensation of 2,9-dicarboxaldehyde-1,10-phenanthroline with appropriate tetraamines in the presence of the manganese(II) ion (Scheme 1). The resulting complexes were characterized by IR spectra, elemental analysis,EI- Mass, molar conductance in all cases. We also explored the antibacterial activities of synthesized complexes against *S. aureus*, *B. cereus*, *C. xerosis*,*E. coli*, *K. pneuomoniae* and*P. vulgaris*.

2. Experimental Starting Materials

All solvents were of reagent grade quality and purchased commercially. Ethane-1,2diamine, propane-1,2-diamine, propane-1,3-diamine, 2,9-dicarboxaldehyde-1,10-phenanthroline and metalsalts were obtained from Merck and were used without further purification.

Caution: Perchlorate salts are potentially explosive. While we have not experienced any problems with the compounds described, they should be treated with caution and handled in small quantities.

2.1 Instrumentation

Elemental analyses were performed in a Carlo-Erba EA microanalyser. IR spectra were measured on a Perkin Elmer FT-IRGX spectrophotometer in the range of 4000-400 cm^{-1} by KBr pellet technique. Conductivimetry measurements were carried out in 10^{-3}mol dm^{-3}dimethylsolfoxide solutions at 25 ºC using a CARISON GLP32 conductivimeter. EI-mass spectra were recorded using 5973 Network Mass Selective Detector.

2.2 Antibacterial study Materials and methods

Six bacterial strains (three grams positive and three grams negative) were selected on the basis of their clinical importance in causing diseases in humans (Table 1). The strains selected for the study are *S. aureus* (ATCC 6538), *B. cereus* (ATCC 14579), *C. xerosis* (ATCC 373), (gram-positive bacterial strains), *E. coli* (ATCC 8739), *K. pneuomoniae* (MTCC 109), and *P.vulgaris* (lio), (gram-negative bacterial strains). These strains were screened for evaluation of antibacterial activities of the synthesized complexes.

2.3 Primary screening

The antibacterial activity of the macrocyclic complexes was evaluated by agar well diffusion method [23]. All the microbial cultures were adjusted to 0.5 McFarland standards, which is visually comparable to a microbial suspension of approximately 1.5 ×10^8c.f.u./ml [24]. 20 ml of agar media was poured into each petri plate these plates were then swabbed with a colony from inoculum of the test microorganisms and kept to adsorption for 15 min. Using sterile cork borer of 6 mm diameter, wells were bored into the seeded agar plates and these were loaded with 50 µl volume with concentration of 10 mg/ml of each compound reconstituted in dimethylsulphoxide (DMSO). All the plates were incubated at 37°C for 24h. Antibacterial activity of all the complexes was evaluated by measuring the diameter of zone of inhibition in mm. The medium with dimethylsulphoxide (DMSO) as solvent was used as a negative control whereas media with ciprofloxacin (standard antibiotic for gram positive) and gentamicin (standard antibiotic for gram negative) were used as positive control.

The experiments were performed in triplicates.

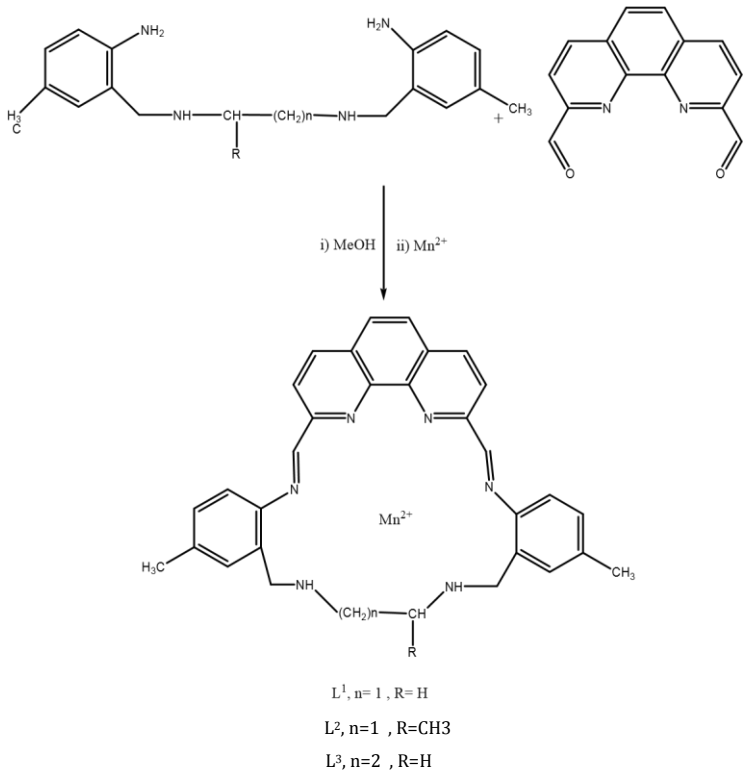
2.3 Determination of minimum inhibitory concentration (MIC)

Minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial compound that will inhibit the visible growth of microorganisms after overnight incubation. Minimum inhibitory concentrations are important in diagnostic laboratories to confirm resistance of microorganisms to antimicrobial agents and also to monitor the activity of new antimicrobial agents. The MIC of the macrocyclic complexes was tested against bacterial strains through a broth dilution method. In this method, the test concentrations of all the complexes were made from 2.5 to 0.01 mg/ml in the sterile wells of the micro-titer plates. In sterile microtitre plates (96-u-shaped wells) 50 µl of the sterile nutrient broth was poured in each well in three rows, then from fresh inoculums so formed (10^8c.f.u./ml diluted with 100 µl Nutrient broth to have 10^6c.f.u./ml) 50 µl of the suspension was poured in each well in the first and third row, second row was again filled with 50 µl of nutrient broth, finally the drug sample 50 µl was added in the first row diluting uniformly from 2.5 to 0.01 mg/ml till the 8th well. All the microtitre plates were incubated at 37 °C for 18–24 h. MIC was expressed as the lowest dilution, which inhibited

the growth of bacteria observed by lack of turbidity in the well.

2.4 General synthesis of complexes

The tetradentate amines and 2,9-dicarboxaldehyde-1,10-phenanthroline were prepared according to literature method [25,26]. Briefly, a solution of amines (0.5 mmol) in methanol was added dropwise to a refluxing solution of $Mn(ClO_4)_2.6H_2O$, (0.5 mmol) and 2,9-dicarboxaldehyde-1,10-phenanthroline (0.5 mmol) in the same solvent (20 mL). After refluxing for 24 h the solution was then concentrated in a rotary evaporator to ca. 5-10 mL. A small volume of diethyl ether was slowly added to the solution, producing a powdery precipitate. The product was filtered off, washed with cold diethyl ether and dried under vacuum (Scheme 1).



Scheme 1. The template condensation between 2,6-diacetylpyridine and tetradentate amines in the presence of the Mn(II) ion.

$[MnL1](ClO_4)_2$

Yield: 0.25g (66%).*Anal.* Calc. for $C_{30}H_{26}Cl_2MnN_6O_8$ (MW: 724.41): C, 49.74; H, 3.62; N, 11.60. Found: C,49.63; H, 3.70; N, 11.50 %.IR (KBr, cm^{-1}) 3270 ν(N-H)], 1634 $\nu(C=N)_{imi}$,1495,1592and 1609 [ν(C=C) and $\nu(C=N)_{Aro}$] and 1096, 623 $\nu(ClO_4^-)$. EI-Mass: (m/z, M^+) 624 $[MnL^1]ClO_4^+$, 525 $[MnL^1]^+$, 470 $[L^1]^+$. $\Lambda_m/\Omega^{-1}cm^2mol^{-1}$(in DMSO): 173(2:1).

$[MnL^2](ClO_4)_2$

Yield: 0.17g (44%).*Anal.* Calc. for $C_{31}H_{28}Cl_2MnN_6O_8$ (MW: 378.43) : C, 50.42; H, 3.82; N, 11.38. Found: C, 50.22; H, 3.90; N, 11.28 %.IR (KBr, cm^{-1}) 3266 ν(N-H)], 1650, 1638$\nu(C=N)_{imi}$, 1495,1590 and 1609 [ν(C=C) and $\nu(C=N)_{Aro}$] and 1095, 623 $\nu(ClO_4^-)$. EI-Mass: (m/z, M^+) 638 $[MnL^2]ClO_4^+$, 539$[MnL^2]^+$, 483 $[L^1]^+$. $\Lambda_m/\Omega^{-1}cm^2mol^{-1}$(in DMSO): 170 (2:1).

$[MnL3](ClO_4)_2$

Yield: 0.15g (38%).*Anal.* Calc. for $C_{31}H_{28}Cl_2MnN_6O_8$ (MW:738.43) : C, 50.42; H, 3.82; N, 11.38. Found: C,50.10; H, 3.91; N, 11.25 %. IR (KBr, cm^{-1}) 3226 ν(N-H)], 1643 $\nu(C=N)_{imi}$,1590, 1495 and 1604 [ν(C=C) and $\nu(C=N)_{Aro}$] and 1089, 623 $\nu(ClO_4^-)$.EI-MS: (m/z, M^+) 638 $[MnL^3]ClO_4^+$, 539 $[MnL^3]^+$, 483 $[L^1]^+$. $\Lambda_m/\Omega^{-1}cm^2mol^{-1}$(in DMSO): 168 (2:1).

3. Results and Discussion

3.1 Synthesis and Characterization

The diiminemacrocyclic complexes were synthesized by the metal template cyclocondensationof 2,9-dicarboxaldehyde-1,10-phenanthroline and three tetradenate amines in refluxing methanol in the presence of appropriate and manganese(II) salts. The complexes were

characterized by IR, element analysis, EI-MS. In all complexes exhibit a υ(C=N) vibration in the range 1634-1653 cm^{-1}, and also bands at ca. 1608-1609,1584-1592 and 1460 cm^{-1} associated with υ $(C=N)_{Aro}$ and υ (C=C) vibrations from the pyridine and phenylrings [27] are present in the spectra, but no bands for the free carbonyls or primary diamines are observed indicating that complete condensation has occurred. For the perchlorate complexes, absorptions attributable to ionic perchlorate were found at approximately 1090 and 623 cm^{-1} [28]. The lack of splitting of these bands suggests that the perchlorate anions are not coordinated [29].

3.2 Molar Conductivity

The molar conductance data of the Mn complexes were measured in DMSO solution for the 0.001M solutions at 25°C of the Schiff base metal complexes in DMSO. The molar conductivity was applied to help in the investigation of the geometrical structures of the complexes. Metal chelates have molar conductivity of 160–175 ohmcmmolindicating the 1:2 ionic nature in all cases [30]. These values are indicative of the presence two outer sphere perchlorate anions and are in agreement with the results obtained from the IR study.

Table 1. Minimum inhibitory concentration (MIC in mg/ml) of the macrocyclic complexes.

S.no	Bacterial Strains	Complexes		
		$[MnL^1](ClO_4)_2$	$[MnL^2](ClO_4)_2$	$[MnL^3](ClO_4)_2$
1.	S. aureus	0.318	0.223	0.197
2.	B. cereus	0.542	0.528	0.492
3.	C. xerosis	0.290	0.253	0.227
4.	E. coli	0.812	0.776	0.717
5.	K. pneuomoniae	0.797	0.713	0.679
6.	P. vulgaris	0.868	0.809	0.707

Table 2. Inhibition zones (mm) of complexes against bacterial strains.

Complex	Bacteria					
	S. aureus	B. cereus	C. xerosis	E. coli	K. pneuomoniae	P. vulgaris
$[MnL^1](ClO_4)_2$	22	20	22	18	17	16
$[MnL^2](ClO_4)_2$	24	21	25	21	21	20
$[MnL^3](ClO_4)_2$	25	23	26	22	24	23
ciprofloxacin	30	27	27	-	-	-
gentamicin	-	-	-	25	25	25

3.3 Antibacterial Activity

Antibacterial activity of the synthesized complexes was studied against some bacterial strains viz. *S. aureus*, *B. cereus*, *C. xerosis*, *E. coli*, *K. pneuomoniae*and *P.vulgaris*. Preliminary screening for all the complexes was performed at fixed concentration of 10 mg/ml. The results obtained were compared with standard antibiotics: ciprofloxacin (for gram-positive) and gentamicin (for gram-negative) bacterial strains. All the complexes were found to be active on both types of bacterial strains. On the basis of the data obtained for diameter of zone of inhibition all Mn(II) complexes were found to be very effective (Table 2).

The minimum inhibitory concentration of these complexes was determined by broth dilution method in which the effectiveness was observed at lower concentrations. According to table 1, the MIC values were showed that Mn(II) complexes were quite effective against on some bacterial strains.It is concluded that all the synthesized macrocyclic complexes showed the antibacterial activity, but they were found to be more potent inhibitors against gram positive bacterial strains.Results show that the Mn(II) macrocyclic Schiff base complexes are greater antibacterial effects against than the macroacyclic complexes one [31].

4. Conclusion

In summary, we report the successful synthesis of six new Mn(II) macrocyclic Schiff base complexes derived from template [1+1] cyclocondensation of

2,9-dicarboxaldehyde-1,10phenanthroline with linear aromatic amines in the presence of Mn(II) al ion. The complexes have been characterized by spectroscopic methods. Results of this research showed that all prepared chemicals have relatively antibacterial effects against the studied bacterial strains.

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