

Characterization and biological studies of some newly synthesized macrocyclic complexes of bivalent metal ions[†]

Devendra Kumar*, Shivangi Sharma and R. C. Sharma

Department of Chemistry, Institute of Basic Sciences, Dr. B. R. Ambedkar University, Khandari Campus, Agra-282 002, Uttar Pradesh, India

E-mail : dev_kumar26@indiatimes.com

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Abstract : Six new macrocyclic complexes, viz. $\{[BzO_3-18]\text{-pentaene } N_2O_2\}M(II)(H_2O)_2(Ac)_2$, where, $M^{2+} = Cu^{2+}, Co^{2+}$, $\{[BzO_3-18]\text{-pentaene } N_2O_2\}Ni(II)(Ac)_2$ and $\{[BzO_3-20]\text{-pentaene } N_2O_2\}M(II)(H_2O)_2(Ac)_2$, where, $M^{2+} = Cu^{2+}, Ni^{2+}, Co^{2+}$ have been synthesized by the reaction of 4,4'-butylenedioxydibenzaldehyde and *o*-phenylenediamine/*p*-phenylenediamine in presence of metal salts by adopting template method and characterized by elemental analyses, IR, ¹H NMR, electronic spectral studies and magnetic moment values. The all compounds were screened for their biological studies against two bacteria *Staphylococcus aureus* (Gram +ve) and *Escherichia coli* (Gram -ve) bacteria and fungi *Aspergillus niger* and *Aspergillus flavus*. Macrocyclic complexes were found more active as compared to their fragments.

Keywords : Characterization, biological studies, macrocyclic complexes.

Introduction

Macrocyclic complexes have generated continuous interest due to their applications in the field of industries, catalysis and biological systems¹⁻⁷. 1,4,7,10-tetraazacyclodecane-1,4,7,10-tetraacetic acid (DOTA), a potentially octadentate ligand has used to bind Ga^{3+} and produced one of the most stable complex for MRI application⁸ for radioactive diagnosis⁹ and treatment as anti-HIV agent¹⁰. They have also been used as sensitizers in dye sensitized solar cells¹¹. Recently, DNA cleavage studies¹² of few macrocyclic complexes have been reported. Keeping these facts in mind, it is proposed to design and synthesis few macrocyclic complexes by the reaction of dialdehyde and diamine with a view to study the biological applications of the complexes in antimicrobial studies. This is a part of our continuing investigations on the coordination chemistry of multidentate ligand containing NOS donors¹³⁻¹⁶.

Experimental

Synthesis of 4,4'-butylenedioxydibenzaldehyde (DL): 0.8 g (0.02 M) NaOH, dissolved in minimum volume of distilled water, was mixed with 2.5 g (0.02 M) *m*-hy-

droxy benzaldehyde, dissolved in 20 ml ethanol. The resulting mixture was refluxed under the atmosphere of N_2 for about an hour and cooled at room temperature. 1.98 ml (0.01 M) 1,4-dibromobutane was added to this solution drop by drop with constant stirring and the mixture was again refluxed under the atmosphere of N_2 for about 5 h with constant stirring. The obtained solution was concentrated to half of its original volume on water bath and cooled in refrigerator for over night. The obtained yellowish brown crystalline product was obtained. It was filtered, washed with little water, alcohol followed by ether. The product was recrystallized from warm ethanol and dried under reduced pressure in a vacuum desiccator over anhydrous $CaCl_2$.

Synthesis of macrocyclic complexes : 0.60 g (0.002 M) 4,4'-butylenedioxydibenzaldehyde (DL) dissolved in 15 ml methanol was mixed with 10-15 ml aqueous solutions of (0.002 M) metal salts (0.36 g copper acetate monohydrate/0.50 g nickel acetate tetrahydrate/0.50 g cobalt acetate tetrahydrate) and solutions were refluxed for 2-3 h. 0.22 g (0.002 M) *o*-phenylenediamine (OPDA)/*p*-phenylenediamine (PPDA) dissolved in 20 ml methanol was added to the above and the resulting contents were

[†]In honour of Professor Padmakar V. Khadikar.

again refluxed for about 4–6 h. On cooling, colored products were obtained which were filtered, washed with alcohol followed by ether and dried in vacuum desiccator over anhydrous CaCl_2 .

Physical and analytical measurements :

Purity of synthesized ligand and metal complexes was ascertained by determining the melting points of recrystallized samples on electrothermal melting point temperature instrument in open capillaries and thus uncorrected, running TLC plates for single spot. C, H and N analyses were made out on Elemental Vario EL-III Carlo Erba-1108 analyser, Infrared spectra were recorded on Perkin-Elmer spectrophotometer (Model RX-1). ^1H NMR spectra was recorded in DMSO solvent on NMR spectrophotometer Bruker DRX-300 (300 MHz FT-NMR with low and high temperature facility $-90\text{ }^\circ\text{C}$ to $+80\text{ }^\circ\text{C}$). The electronic spectra of the macrocyclic complexes were recorded in DMSO at room temperature on HE λ IOS α UV-Visible spectrophotometer.

Results and discussion

The physical and analytical data of the dialdehyde and its macrocyclic complexes are given in Table 1. All the complexes were colored and stable at room temperature and non hygroscopic in nature.

In the IR spectra of dialdehyde, two medium sharp intensity bands appeared at 1264 cm^{-1} and 1054 cm^{-1} which could be attributed due to asymmetric and symmetric $-\text{C}-\text{O}-\text{C}-$ stretching vibrations respectively. The

positions of these bands have shifted towards lower frequency by $20\text{--}30\text{ cm}^{-1}$ in its macrocyclic complexes suggesting the involvement of oxygen atom through $-\text{C}-\text{O}-\text{C}-$ linkage in coordination to metal atom. A strong band has been observed at 1698 cm^{-1} in IR spectra of dialdehyde which may be due to carbonyl stretching vibrations¹⁷ of aldehydic group. In the IR spectra of its macrocyclic complexes, this band has disappeared and a new intense band in the region $1602\text{--}1580\text{ cm}^{-1}$ has been observed which may be due to the azomethine group ($>\text{C}=\text{N}-$)^{18,19} linkage formed by the condensation of carbonyl group of dialdehyde with the diamine. The lowering of this linkage in metal complexes indicate the involvement of nitrogen of $>\text{C}=\text{N}-$ group in co-ordination with metal ion. Appearance of band in the region $1451\text{--}1444\text{ cm}^{-1}$ may be attributed due $-\text{CH}_2$ bending vibrations of polymethylene linkage. Medium sharp intensity band in the region $3030\text{--}3023$ and $1493\text{--}1481\text{ cm}^{-1}$ may be attributed due to the $-\text{C}-\text{H}$ stretching vibrations and $\text{C}=\text{C}$ of aromatic ring²⁰. A band in the region $1339\text{--}1324\text{ cm}^{-1}$ is probably due to $-\text{C}-\text{N}$ stretching vibrations. Appearance of two bands in the region $3427\text{--}3414$ and $879\text{--}870\text{ cm}^{-1}$ indicate the presence of co-ordinated water molecule(s) in the macrocyclic complexes. In the IR spectra of Ni complex with *o*-phenylenediamine, two bands are appeared at 1399 and 1724 cm^{-1} which may be attributed due to symmetric stretching vibrations and asymmetric stretching vibrations of co-ordinated acetate ions.

The appearance of some new bands, in the IR spectra of macrocyclic complexes, in the region $537\text{--}526$, 482--

Table 1. Physical and analytical data of 4,4'-butylenedioxydibenzaldehyde (DL) and its macrocyclic complexes

Sl. no.	Compd.	Chemical formula	Colour	M.p. ($\pm 1\text{ }^\circ\text{C}$)	Analysis (%) : Found (Calcd.)		
					Carbon	Hydrogen	Nitrogen
1.	DL	$\text{C}_{18}\text{H}_{18}\text{O}_4$	Yellowish brown	105	73.31 (72.48)	6.98 (6.04)	
2.	OPDA-DL Cu^{II}	$[\{\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\}\text{Cu}(\text{H}_2\text{O})_2(\text{CH}_3\text{COO}^-)_2]$	Dark brownish	260	59.69 (57.19)	6.22 (5.44)	5.65 (4.76)
3.	OPDA-DL Ni^{II}	$[\{\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\}\text{Ni}(\text{H}_2\text{O})_2(\text{CH}_3\text{COO}^-)_2]$	Dark green	200	62.98 (61.46)	5.88 (5.12)	6.06 (5.12)
4.	OPDA-DL Co^{II}	$[\{\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\}\text{Co}(\text{H}_2\text{O})_2(\text{CH}_3\text{COO}^-)_2]$	Brownish red	260	58.90 (58.03)	6.43 (5.52)	5.70 (4.83)
5.	PPDA-DL Cu^{II}	$[\{\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\}\text{Cu}(\text{H}_2\text{O})_2(\text{CH}_3\text{COO}^-)_2]$	Dark brownish	330	55.69 (57.19)	6.36 (5.44)	5.55 (4.76)
6.	PPDA-DL Ni^{II}	$[\{\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\}\text{Ni}(\text{H}_2\text{O})_2(\text{CH}_3\text{COO}^-)_2]$	Dark green	200	58.61 (57.64)	6.39 (5.48)	3.75 (4.80)
7.	PPDA-DL Co^{II}	$[\{\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\}\text{Co}(\text{H}_2\text{O})_2(\text{CH}_3\text{COO}^-)_2]$	Brownish red	260	59.00 (58.03)	6.33 (5.52)	5.68 (4.83)

471 cm^{-1} are probably due to the formation of M-O^{21} and M-N^{22} stretching vibrations respectively.

The ^1H NMR spectra of synthesized dialdehyde exhibits a triplet in the region of δ 1.14–1.19 ppm due to two protons of methylene linkage²³, a triplet in the region of δ 2.00–2.1 ppm due two protons of O-CH_2^{23} linkage. The multiplet in the region δ 7.0–7.50 ppm is due to aromatic protons and a singlet appeared in the region of δ 9.89 ppm is due to aldehydic proton.

The electronic spectra of both the Cu^{II} complexes display three bands, in the region 13333–12987, 17189–17094 and 24390–20619 cm^{-1} corresponding to the transitions $^2B_{1g} \rightarrow ^2A_{1g}$, $^2B_{1g} \rightarrow ^2B_{2g}$ and $^2B_{1g} \rightarrow ^2E_{1g}$ respectively. Appearance of these three bands suggests that Cu^{II} complexes have distorted octahedral geometry²⁴. The magnetic susceptibility values of Cu^{II} were found 1.88–1.92 B.M. which are in close agreement with the octahedral geometry.

Ni^{II} complexes exhibit three bands in the region 12739–12658, 18248–17544 and 26316–25575 cm^{-1} corresponding to the transitions $^3A_{2g} \rightarrow ^3T_{2g}$, $^3A_{2g} \rightarrow ^3T_{1g}$ and $^3A_{2g} \rightarrow ^3T_{1g}$ (*P*) respectively, which suggest that Ni^{II} complexes have octahedral geometry^{25,26}. The magnetic susceptibility values of Ni^{II} complexes were found 3.25–3.31 B.M. which are very close to the value for their octahedral environment.

The electronic spectra of Co^{II} complexes display three bands in the region 13106–13004, 15873–15038 and 21930–20833 cm^{-1} corresponding to the transitions $^4T_{1g} \rightarrow ^4T_{2g}$ (*F*), $^4T_{1g} \rightarrow ^4A_{2g}$ (*F*), $^4T_{1g} \rightarrow ^4A_{2g}$ respectively which suggests that Co^{II} complexes have an octa-

hedral geometry^{27,28}. The magnetic susceptibility values for these complexes were found 4.89–4.93 B.M., which are further in conformity for octahedral geometry.

On the basis of IR, electronic spectral, magnetic and analytical data, it assumed is that the 4,4'-butylenedioxydibenzaldehyde and its $\text{M}(\text{II})$ macrocyclic complexes with diamines have the following structures (Figs. 1, 2 and 3).

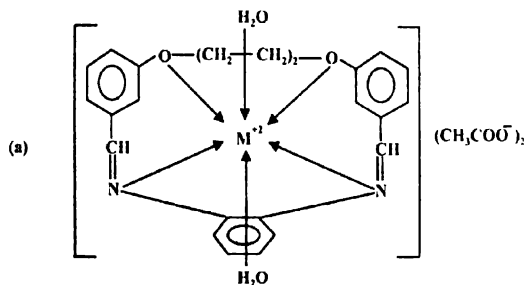


Fig. 1. $\{[\text{Bzo}_3\text{-[18]-pentaene N}_2\text{O}_2]\text{M}(\text{II})(\text{H}_2\text{O})_2\}(\text{Ac})_2$, where $\text{M}^{2+} = \text{Cu}^{2+}, \text{Co}^{2+}$.

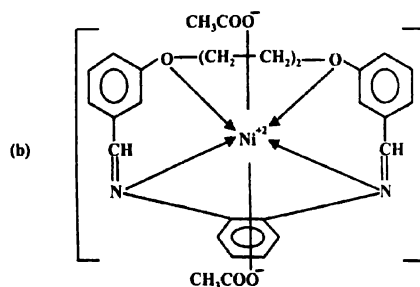


Fig. 2. $\{[\text{Bzo}_3\text{-[18]-pentaene N}_2\text{O}_2]\text{Ni}(\text{II})(\text{Ac})_2\}$.

Table 2. Minimum inhibitory concentration ($\times 10^{-3}$ mole) values of dialdehyde and macrocyclic complexes

Sl. no.	Compd.	Bacteria		Fungi	
		<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Aspergillus niger</i>	<i>Aspergillus flavus</i>
1.	$\text{C}_{18}\text{H}_{18}\text{O}_4$	83.8	83.8	83.8	83.8
2.	$\{[\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2]\text{Cu}(\text{H}_2\text{O})_2\}$ $(\text{CH}_3\text{COO}^-)_2$	21.2	21.2	42.5	42.5
3.	$\{[\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2]\text{Ni}\}$ $(\text{CH}_3\text{COO}^-)_2$	22.8	22.8	45.7	45.7
4.	$\{[\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2]\text{Co}(\text{H}_2\text{O})_2\}$ $(\text{CH}_3\text{COO}^-)_2$	21.5	43.1	43.1	43.1
5.	$\{[\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2]\text{Cu}(\text{H}_2\text{O})_2\}$ $(\text{CH}_3\text{COO}^-)_2$	21.2	21.2	42.5	42.5
6.	$\{[\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2]\text{Ni}(\text{H}_2\text{O})_2\}$ $(\text{CH}_3\text{COO}^-)_2$	21.4	21.4	42.8	42.8
7.	$\{[\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2]\text{Co}(\text{H}_2\text{O})_2\}$ $(\text{CH}_3\text{COO}^-)_2$	21.5	21.5	43.1	43.1

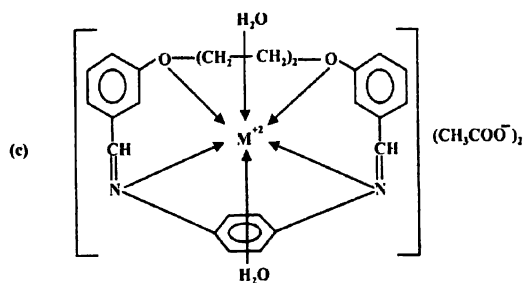


Fig. 3. $[\{Bzo_3-[20]\text{-pentaene } N_2O_2\}M(II)(H_2O)_2](Ac)_2$, where, $M^{2+} = Cu^{2+}, Ni^{2+}, Co^{2+}$.

Biological studies :

All synthesized compounds were screened for their biological activities *in vitro* against two bacteria *Staphylococcus aureus* (Gram +ve) and *Escherichia coli* (Gram -ve) and two fungi *Aspergillus niger* and *Aspergillus flavus* adopting serial dilution method²⁹. All compounds were found moderate active against both bacteria and fungi. It has been found that the biological activity of dialdehyde is increased in its macrocyclic complexes. Among the Cu^{II} , Ni^{II} and Co^{II} , Cu^{II} complexes were found most active against both the bacteria and fungi (Table 2).

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