Studies on room temperature synthesis and characterization of quasi-macrocyclic complexes of first row transition metals using malonyldihydrazide, phenyl hydrazine and o-chlorobenzaldehyde

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ABSTRACT

A novel series of seven quasi-macrocyclic complexes of transition metal ions such as Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) have been synthesized using malonyldihydrazide, phenyl hydrazine and o-chlorobenzaldehyde. The synthesized complexes were characterized using molar conductance, magnetic susceptibility measurements, IR, electronic and ^{1}H-NMR spectra. Based on the results obtained the complexes were proposed to have an octahedral geometry. The synthesized complexes were also screened for their antibacterial activities.

Keywords: Quasi-macrocyclic, malonyldihydrazide, phenyl hydrazine, chlorobenzaldehyde, octahedral, antibacterial.

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INTRODUCTION

The area of research including synthesis and applications of macrocyclic ligands is well known today. This area is vast and includes synthesis of both macrocyclic and quasi-macrocylic ligands and their metal complexes. Quasi-macrocyclic ligands are those involving three or more than three potential donor atoms, similar to macrocyclic, but are half cyclic in nature. The complexes formed utilizing these ligands are called as quasi-macrocyclic complexes.

Present paper is continuation of systematic research program going on in our laboratory in the area of macrocyclic, quasi-macrocyclic ligands and their metal complexes [1-4]. In present paper, we report synthesis and characterization of a series of seven quasi-macrocyclic complexes of transition metal ions such as Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) using malonyldihydrazide, phenyl hydrazine and o-chlorobenzaldehyde. The synthesized complexes were characterized using molar conductance, magnetic susceptibility measurements, IR, electronic and ^{1}H-NMR spectra. Based on results obtained the complexes were proposed to have an octahedral geometry. The synthesized complexes were also screened for their antibacterial activities.

EXPERIMENTAL SECTION

2.1 Materials and Methods

The entire chemicals used in present study were of AR grade. Diethyl malonate, hydrazine hydrate, phenyl hydrazine, o-chlorobenzaldehyde and metal salts used were procured from S. D. fine chemicals and Spectrochem Private Limited respectively. All the solvents used were distilled and dried using molecular sieves before use.

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The molar conductance values for all the synthesized complexes were measured by preparing their 10^{-3} M solutions in DMF solvent using Equiptronics conductivity meter with inbuilt magnetic stirrer (**Model Eq-664**) at room temperature. Magnetic susceptibility values were recorded using SES instrument's Guoy balance (**Model EMU-50**) at room temperature using copper (II) sulphate as a standard. These magnetic susceptibility values were utilized to calculate magnetic moments using spin only formula $\mu_{eff} = [n(n+2)]^{1/2}$ BM for all the synthesized complexes.

IR spectra were recorded as KBR pellets in the region of 4000-400 cm^{-1} on a Perkin Elmer Spectrophotometer. Electronic spectra were recorded in DMF by preparing 10^{-3} M solutions of complexes using Shimadzu UV-1600 spectrophotometer. ^{1}H-NMR spectrum (for Mn(II) complex as a sample study) was recorded on BRUKER AVANCE II 400 NMR Spectrometer using DMSO-d^6 (spectroscopic grade) solvent. Chemical Shifts are given in ppm relative to tetramethylsilane (TMS).

2.2 Synthesis of complexes
Synthesis of complexes is carried using template method. The synthesis scheme is completed in two steps. In the first step of synthesis of malonyldihydrazide was carried out. In second step synthesis of complexes was carried out by reacting malonyldihydrazide, phenyl hydrazine and o-chlorobenzaldehyde in presence of transition metal ions in methanolic medium at room temperature. The complex forming reaction was carried out in 1:1:2:2 molar ratios of transition metal, malonyldihydrazide, phenyl hydrazine and o-chlorobenzaldehyde respectively.

a) Synthesis of malonyldihydrazide:
The procedure used for synthesis of malonyldihydrazide was reported earlier [2, 5] and can be given as follows:

A methanolic solution of diethylmalonate (1 mol) was taken in a round bottom flask. To it was added hydrazine hydrate (2 mol) in methanol. The reaction mixture was refluxed for 5-7 hours. Progress of the reaction was checked by thin layer chromatographic technique using solvent system ethyl acetate (10 %) + Pet ether (90 %). After complete disappearance of starting material the reaction mixture was allowed to cool for one hour. After cooling for one hour white crystalline product was obtained. It was filtered, washed with methanol and recrystallized from ethanol. Melting point was checked. (M. P. = 149 °C).
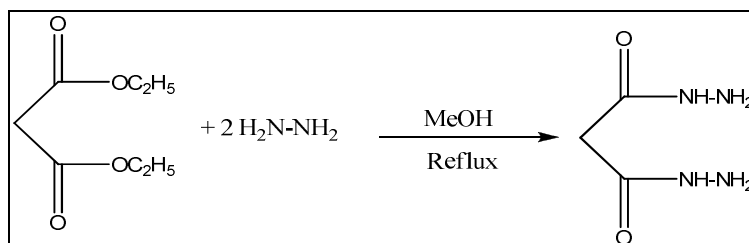

Figure 1. Synthesis of malonyldihydrazide

b) Synthesis of metal complexes:
General procedure used for the synthesis of metal complexes was as follows:

A methanolic solution of dissolved transition metal salts (2.5 mmol) was taken in a round bottom flask and was allowed to stir magnetically. Malonyldihydrazide (2.5 mmol) was dissolved in appropriate quantity of methanol by warming. The methanolic solution of malonyldihydrazide thus obtained, along with methanolic solution of phenyl hydrazine (5 mmol) were added to the solution of transition metal salts with constant stirring. The resulting mixture was allowed to stir magnetically for 1 hour. After 1 hour a methanolic solution of o-chlorobenzaldehyde (5 mmol) was added to the reaction mixture. The resultant mixture was then allowed to stir for additional 10 hours. The progress of reaction was checked by taking TLC in Chloroform-Methanol (10 %) solvent system after every 30 minutes. After 10 hours the stirring was stopped. The obtained solid product was filtered off, washed with methanol and dried in vacuo. Figure 2 represents the scheme used for synthesis of complexes.
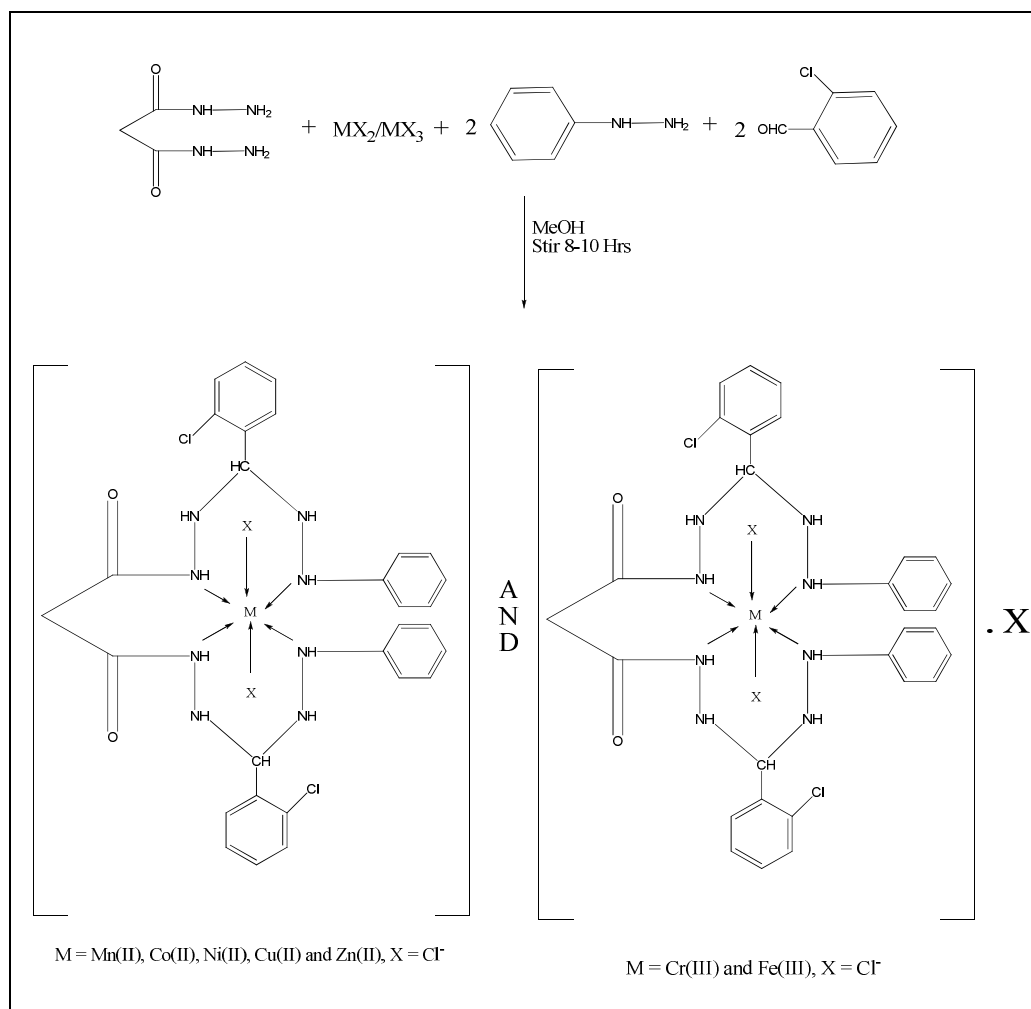
Figure 2. Synthesis of quasi-macrocyclic complexes of transition metals using malonyldihydrazide, phenyl hydrazine and o-chlorobenzaldehyde

2.3 In vitro Antibacterial activity
All the synthesized complexes were screened for their antibacterial activity using the disc diffusion method against selected pathogens such as *Escherichia coli* (MTCC- 443) and *S. aureus*. Complexes were dissolved in DMSO and sterilized by filtering through 0.45 μm Millipore filter. Nutrient agar NA was prepared and sterilized by an autoclave and transferred to previously sterilized petri plates. After solidification petri plates were inoculated with bacterial organisms in sterile nutrient agar medium at 45°C. Sterile Whatmann filter paper discs were impregnated with synthesized compounds at a concentration of 1 mg/disc was placed in the organism-impregnated petri plates under sterile condition. Standard antibiotic disc of streptomycin (100 μg/disc) was used as positive control while DMSO was used as negative control. Then the plates were incubated for 24 h at $37 \pm 1°C$ for antibacterial activity. The zone of inhibition was calculated by measuring the minimum dimension of the zone of no microbial growth around the disc [6].

RESULTS AND DISCUSSION

The general composition of synthesized quasi-macrocyclic complexes can be represented as $[M(C_{29}H_{30}N_8O_2)X_4]$ for divalent metal ions (where M = Mn(II), Co(II), Ni(II), Cu(II) and Zn(II)) and $\{[M(C_{29}H_{30}N_8O_2)X_4].X\}$ for trivalent metal ions (where M = Cr(III) and Fe(III)) and X = Cl⁻ in both these cases.

3.1 Physicochemical data

Observations such as color, melting point, percentage yield for all the synthesized complexes were recorded. The physicochemical data recorded along with the calculated molecular weight for all the synthesized quasi-macrocyclic complexes is represented in Table 1.

The melting points recorded for all the complexes were in the range 140-270 ^{0}C indicating towards thermal stability of all these synthesized complexes. The percentage yield was found to be in the range 60-75 % for all the synthesized complexes.

Table 1: Physicochemical data of the synthesized quasi-macrocyclic complexes

Proposed Molecular formula	Calculated Molecular Weight (gms)	Colour	Melting Point (^{0}C)	Percentage Yield (%)
$C_{29}H_{30}N_8O_2CrCl_5$	751.50	Gray	256	72
$C_{29}H_{30}N_8O_2MnCl_4$	718.94	Faint Orange	210	74
$C_{29}H_{30}N_8O_2FeCl_5$	755.35	Green	180	65
$C_{29}H_{30}N_8O_2CoCl_4$	722.93	Red	140	69
$C_{29}H_{30}N_8O_2NiCl_4$	722.69	Faint red	263	75
$C_{29}H_{30}N_8O_2CuCl_4$	727.55	Faint green	198	73
$C_{29}H_{30}N_8O_2ZnCl_4$	729.39	Faint orange	222	68

3.2 Solubility behaviour

Solubility behaviour of all the synthesized quasi-macrocyclic complexes was checked using different solvents such as water (WT), methanol (MT), ethanol (ET), chloroform (CL), dichloromethane (DCM), acetone (AC), ethyl acetate (EA), dimethyl sulphoxide (DMSO) and dimethyl formamide (DMF). The complexes were found to be partially soluble in methanol and water, completely soluble in DMSO and DMF, whereas in remaining solvents they were found to be insoluble.

3.3 IR spectra

IR spectra for all the synthesized complexes were recorded as KBr pellets in the region 4000-400 cm^{-1}. The close observation made at the structures of synthesized complexes indicated the presence of amide and amine groups (**in the form of -CO-NH-NH- group**) in the structure. Thus presence of absorption peaks in the range of 3000-3600 cm^{-1} in IR spectra recorded due to ν(N-H) stretching vibrations is expected [7]. In present investigation presence of absorption bands in the range 3190-3450 cm^{-1} in IR spectra recorded can be assigned due to ν(N-H) vibrations.

The carbonyl absorption of amide (i.e. amide I band) can be generally observed in the range 1650-1690 cm^{-1} in the IR spectra of solid substances [7]. In present investigation this band was observed around 1682 cm^{-1} in IR spectra of each of the complexes. The amide II band which is due to N-H bending in secondary amides is normally observed in the range 1570-1515 cm^{-1} [7]. In present investigation this band was observed around 1564 cm^{-1} in the spectra of each of the complexes.

Table 2. IR spectral data for all the synthesized quasi-macrocyclic complexes

Complexes	ν (N-H) (cm^{-1})	Amide I band ν (C=O) (cm^{-1})	Amide II band ν (N-H) bending (cm^{-1})	ν (M-N) (cm^{-1})
$C_{29}H_{30}N_8O_2CrCl_5$	3194.2 3407.4	1682.0	1564.2	457.1
$C_{29}H_{30}N_8O_2MnCl_4$	3194.1 3420.0	1682.2	1563.1	457.3
$C_{29}H_{30}N_8O_2FeCl_5$	3193.1 3399.0	1682.0	1563.3	457.1
$C_{29}H_{30}N_8O_2CoCl_4$	3194.2 3280.2	1682.1	1566.1	456.3
$C_{29}H_{30}N_8O_2NiCl_4$	3194.3 3402.9	1682.0	1563.5	458.3
$C_{29}H_{30}N_8O_2CuCl_4$	3193.2 3445.2	1680.7	1564.1	458.3
$C_{29}H_{30}N_8O_2ZnCl_4$	3194.4 3447.4	1683.8	1563.4	457.6

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The coordination of the ligand to the metal through nitrogen can be predicted based on the appearance of band at lower values in the spectra. Position of this band does not seem to be fixed and researchers have reported different values for this band ranging from 300-600 cm^{-1} [8-11]. In present investigation the band observed around 457 cm^{-1} in the IR spectra of each of the complexes can be assigned due to ν (M-N) vibrations. Presence of ν (M-Cl) band in the spectra of complexes is usually reported below 400 cm^{-1} region [12-13]. The said region was not scanned for present investigation. Table 2 represents results obtained from IR spectra recorded for all the synthesized quasi-macrocyclic complexes.

3.4 Electronic spectra
Electronic spectra of all the synthesized quasi-macrocyclic complexes were recorded by preparing their 10^{-3} M solutions in DMF solvent.

The electronic spectrum recorded for Cr(III) complex showed two bands at 440 and 580 nm which can be assigned to $^4A_{2g} \rightarrow {}^4T_{1g}$ (F) and $^4A_{2g} \rightarrow {}^4T_{2g}$ (F) transitions respectively. This observation supports to octahedral geometry of the complex. The presence of similar bands was confirmed by Thirunavukkarasu et al. in their research paper [14].

The electronic spectrum recorded for Mn(II) complex exhibited a band at 420 nm which can be assigned to $^6A_{1g} \rightarrow {}^4E_g$ transition. This observation supports to octahedral geometry of the complex. The presence of similar band was also confirmed by Chandra et al. in their research paper [15].

The electronic spectrum of Fe(III) complex exhibited bands at 500 and 650 nm which can be assigned to $^6A_{1g} \rightarrow {}^4E_g$ and $^6A_{1g} \rightarrow {}^4T_{1g}$ transitions respectively. This observation supports to octahedral geometry of the complex. Similar observation was reported by Sharma et al. in their research paper [16].

The electronic spectrum recorded for Co(II) complex exhibited bands at 460 and 700 nm which can be assigned to $^4T_{1g}$ (F) $\rightarrow {}^4A_{2g}$ and $^4T_{1g}$ (F) $\rightarrow {}^4T_{1g}$ (P) transitions respectively. Presence of similar bands was reported by Omar Nasman in the range 451-457 and 714-725 nm respectively in his research paper [16]. The electronic spectrum of Ni(II) complex exhibited a band at 500 nm which can be assigned to $^3A_{2g} \rightarrow {}^3T_{1g}$ (F) transition. This observation supports to octahedral geometry of the complex. The presence of similar band in the range 491-494 nm was confirmed by Omar Nasman in his paper [17].

The electronic spectrum of Cu(II) complex exhibited a band at 640 nm which can be assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition. The presence of similar band at 642 nm was reported by Rafat et al. in their research paper [18].

The electronic spectrum of Zn(II) complex did not exhibit any band due to d-d transition, as Zn(II) is d^{10} system with fully filled shell there is no scope for electronic transition [19-20].

Table 3. Electronic spectral data for all the synthesized quasi-macrocyclic complexes

Complexes	Absorbance (nm)	Assignment	Molar conductance ($ohm^{-1}cm^2 mol^{-1}$)	Magnetic moments μ_{eff}(BM)
$C_{29}H_{30}N_8O_2CrCl_5$	440 580	$^4A_{2g} \rightarrow {}^4T_{1g}$ $^4A_{2g} \rightarrow {}^4T_{2g}$(F)	65	3.95
$C_{29}H_{30}N_8O_2MnCl_4$	420	$^6A_{1g} \rightarrow {}^4E_g$	17	5.90
$C_{29}H_{30}N_8O_2FeCl_5$	500 650	$^6A_{1g} \rightarrow {}^4E_g$ $^6A_{1g} \rightarrow {}^4T_{1g}$	69	5.88
$C_{29}H_{30}N_8O_2CoCl_4$	460 700	$^4T_{1g}$(F) $\rightarrow {}^4A_{2g}$ $^4T_{1g}$(F) $\rightarrow {}^4T_{1g}$(P)	18	4.92
$C_{29}H_{30}N_8O_2NiCl_4$	500	$^3A_{2g} \rightarrow {}^3T_{1g}$(F)	20	2.86
$C_{29}H_{30}N_8O_2CuCl_4$	640	$^2E_g \rightarrow {}^2T_{2g}$	22	1.85
$C_{29}H_{30}N_8O_2ZnCl_4$	-------	---------	12	Diamagnetic

3.5 Magnetic properties
Magnetic moment values for all the synthesized complexes were recorded at room temperature using copper (II) sulphate as an internal standard.

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The synthesized complexes of Cr(III), Mn(II) and Fe(III) ions exhibited magnetic moment values of 3.95, 5.90 and 5.88 BM respectively. These values correspond to the presence of three and five (for both Mn(II) and Fe(III)) unpaired electrons in these complexes and thus indicate towards octahedral geometry of these complexes [19-20].

The magnetic moment values of 4.92, 2.86 and 1.85 BM recorded for Co(II), Ni(II) and Cu(II) complexes respectively correspond to the presence of 3, 2 and 1 unpaired electrons in these complexes and thus indicated towards octahedral geometry of the complexes [19-20]. The Zn(II) complex was found to be diamagnetic in nature consistent with (d^{10}) configuration of Zn (II) in the complex.

3.6 Molar conductance
Based on solubility behaviour observed for all the synthesized complexes molar conductance values were measured by preparing 10^{-3} M solutions in DMF as a solvent. The observed molar conductance values (12-25 ohm^{-1} cm^{-2} mol^{-1}) recorded for complexes with divalent metal ions Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) indicate towards their non-electrolytic behaviour [21]. The higher values (65 and 69 ohm^{-1} cm^{-2} mol^{-1}) recorded for complexes with trivalent metal ions Cr(III) and Fe(III) complexes indicate towards their 1:1 electrolytic behaviour [22].

3.7 ^{1}H-NMR Spectra
In present investigation ^{1}H-NMR spectrum for Mn(II) complex was recorded as a sample for study. The spectrum was recorded in DMSO-d^6 solvent against tetramethylsilane (TMS) as a standard. The major peaks obtained in the spectrum recorded are as follows:

A singlet peak for four protons observed at 2.2 ppm can be assigned to -NH- protons close to aromatic ring of aldehyde moiety. Another singlet peak for two protons observed at 3.10 ppm can be assigned to –CH$_2$- group coming from malonyldihydrazide moiety. The singlet peak for two protons observed at 3.96 ppm can be assigned to –NH- groups present on the phenyl hydrazine ring. The singlet peak observed for two protons at 5011 ppm can be assigned for –CH- protons of the aldehyde ring.

The peaks observed in the region of 6.6–7.8 ppm (i.e. 6.63-6.69 (1H-Ar),t, 6.99-7.02 (1H-Ar),t, 7.02-7.15 (5H-Ar),m, 7.43-7.45 (1H-Ar),d, 7.70-7.72 (1H-Ar)d,) can be assigned to aromatic protons present in the complex. Finally the singlet peak observed for two protons 9.58 ppm can be assigned for –NH- protons of amide groups which are coordinated to the metal and hence deshielded.

3.8 Antibacterial activity
All the synthesized complexes were screened for their antibacterial activities against *Escherichia coli and Styphyllococcus Aureus.* A zone of inhibition for all the synthesized complexes was measured and compared with standard antibiotic drug penicillin g.

The standard used have shown zone of inhibition of 13 and 15 mm against *E. coli* and *S. Aureus* respectively. Zone of inhibition values of 16, 15, 14 and 14 mm were recorded for complexes of Fe(III), Ni(II), Zn(II) and Mn(II) against *E. coli.* These complexes thus exhibited significant activity. Values of 12, 11 and 10 mm were recorded for Cu(II), Co(II) and Cr(III) complexes respectively. These complexes thus show moderate activity against *E. coli.* Zone of inhibition values of 16, 14 and 14 mm were recorded for complexes of Mn(II), Fe(III) and Cr(III) complexes respectively against *S. aureus.* These complexes thus exhibited significant activity. Zone of inhibition values recorded for Zn(II), Ni(II), Co(II) (13 mm each) and Cr(III) (12 mm each) indicated that these complexes show moderate activity against *S. aureus.* The results obtained are represented in Table 4.

Table 4. Antibacterial activity recorded for all the synthesized quasi-macrocyclic complexes

Complex	Zone of inhibition (in mm)	
	E. coli	*S. aureus*
$C_{29}H_{30}N_8O_2CrCl_5$	10mm	12mm
$C_{29}H_{30}N_8O_2MnCl_4$	14mm	16mm
$C_{29}H_{30}N_8O_2FeCl_5$	16mm	14mm
$C_{29}H_{30}N_8O_2CoCl_4$	11mm	13mm
$C_{29}H_{30}N_8O_2NiCl_4$	15mm	13mm
$C_{29}H_{30}N_8O_2CuCl_4$	12mm	14mm
$C_{29}H_{30}N_8O_2ZnCl_4$	14mm	13mm
Std (penicillin g)	**13mm**	**15mm**

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CONCLUSION

Room temperature synthesis of a series of seven quasi-macrocyclic complexes of transition metal ions such as Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) was carried out using malonyldihydrazide, phenylhydrazine and o-chlorobenzaldehyde. The synthesized complexes were characterized using various techniques of characterization. Based on the results obtained the complexes were proposed to have an octahedral geometry. All the synthesized complexes exhibited moderate to significant activity against the tested bacterial pathogens.

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