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One pot Synthesis of macro cyclic ligand complexes

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Abstract–

Novel tetraazamacrocyclic complexes of Cu(II), Co(II), Ni(II) and Zn(II) has been synthesized from the reaction of ethylenediamine with Meldrums acid and divalent metal ions using solid-supported perchloric acid ($HClO_4$-SiO_2) as a catalyst. The complexes were characterized by IR, ^{1}HNMR, EPR spectra, magnetic moments, conductance, thermal analysis (TGA and DTA), and powder X-ray analysis (XRD). The antimicrobial studies of these complexes against *Staphylococcus typhi*, *Staphylococcus aurieus*, *Escherichia coli*, *Bacillus subtilis* species by Minimum Inhibitory Concentration (MIC) method revealed that these complexes possess potent antibacterial activity.

Keyword: NMR, IR, Elemental Analysis, Antimicrobial Activity

INTRODUCTION

The diversified role played by the naturally occurring macrocycles in biological systems is well known. Several macrocyclic complexes have been reported to possess remarkable antibacterial, antifungal and anti-inflammatory activities[1-2] and are used as dyes and pigments, MRI contrast agents, and models for naturally occurring macrocycles.[3-6] In addition, macrocyclic nickel complexes find use in DNA recognition and oxidation[7] while copper complexes find use in DNA binding and cleavage.[8] Generally, macrocyclic complexes of type $[M(C_{16}H_{28}N_4)X_2]$, where M = Cu(II), Co(II), Ni(II), Zn(II) and X = Cl^-, NO_3^-, CH_3COO^- are prepared by refluxing ehylenediamine, acetonyl acetone and metal salt in methanol or ethanol (template method).[9]

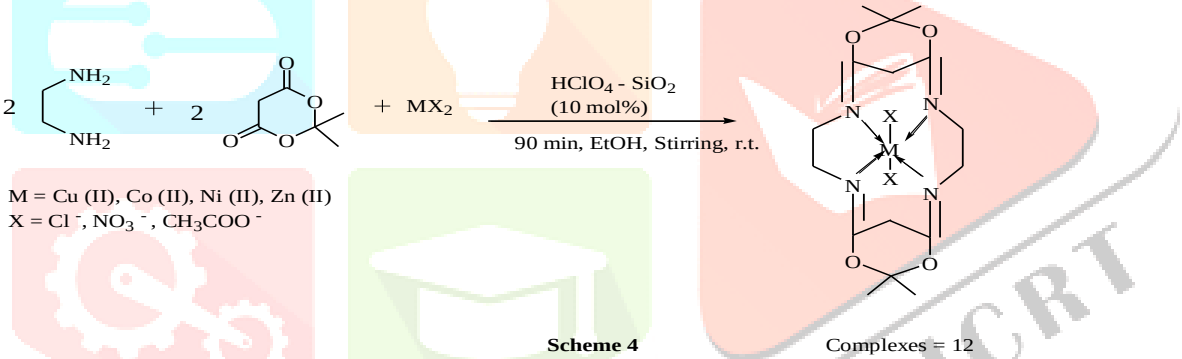
EXPERIMENTAL

Material and Methods of Analysis

IR spectra (400–4000 cm^{-1}) were recorded on Shimndzu FTIR spectrophotometer using KBR discs, and the absorption bands are expressed in cm^{-1}. ^1H NMR spectra were recorded in DMSO-d_6 with tetramethyl silane as an internal standard. Molar conductivity of 10^{-3} M solution in DMSO was obtained on C-100 Elico digital conductivity meter at room temperature. Magnetic susceptibilities were recorded on Guoy balance using AR grade $CuSO_4$ and $FeSO_4$ as standard. Analytical grade chemicals brought from Sigma-Aldrich, INC. were used throughout this work.

Present Work

Novel macrocyclic complexes of type $[M(C_{16}H_{24}N_4O_4)X_2]$ have been synthesized by non-template method utilizing solid-supported perchloric acid ($HClO_4$-SiO_2) as a catalyst at room temperature (Scheme 3 and 4). The investigated complexes were characterized and evaluated for their antimicrobial activity against four bacterial strains.



Scheme 4 Complexes = 12

Typical Procedure for the synthesis of $[Cu(C_{16}H_{24}N_4O_4)Cl_2]$

A mixture of ethylenediamine (10 mmol), copper chloride (5 mmol) and meldrums acid along with 10 mol% solid-supported perchloric acid in ethanol (50 mL) was stirred at room temperature for 90 min. The resulting colored complex along with insoluble catalyst was filtered, wash with ethanol, acetone and petroleum ether. To separate the catalyst, complex was dissolved in DMSO (2 x 15 mL) and then filtered. The filtrate was then concentrated under reduced pressure to afford shiny blue colored copper complex, which was dried over calcium chloride (65% yield).

RESULT AND DISCUSSION

Chemistry

The analytical data suggest the formula of macrocylic complexes as $[M(C_{16}H_{24}N_4O_4)X_2]$ where M = Co(II), Ni(II), Cu(II), Zn(II) and X = Cl^{-1}, NO_3^{-1} and CH_3COO^{-1}. The anion test is positive after decomposing the complexes with concentrated HNO_3, indicating their presence inside the coordination sphere.[9] Conductivity measurements in DMSO indicate them to be non electrolytic in nature (10-20 $ohm^{-1}cm^2mol^{-1}$).[10] The melting point of all complexes were above 200^0C and all complexes are intensively colored. Magnetic movement values suggest octahedral environment around metals (Table 1).[11]

Infrared spectra

The infrared spectra of complexes (Table 2) do not exhibit broad peak in the region 3230-3260 cm^{-1} for ν (NH_2) and strong peak in the region 1700-1720 cm^{-1} for ν (C=O) group. This confirms the condensation of acetyl dimedone/meldrums acid and amino groups of ethylene diamine.[12-13] The appearance of two new peaks in the region 1565-1606 cm^{-1} and 1000-1350 cm^{-1} for ν (C=N) and ν (C-N) respectively supports the formation of macrocyclic frame.[14] Further, the presence of peak in the region 420-460 cm^{-1} for ν (M-N) indicates coordination of azomethine nitrogen.[15-16]

NMR Spectra

. The ^{1}H NMR spectrum of $[M(C_{16}H_{24}N_4O_4)X_2]$ type complexes shows signal of -NCH_2CH_2N- protons (8H) at δ = 2.00 ppm, -CCH_2C- protons (4H) at δ = 2.60 ppm, while -CH_3 protons (12H) appeared at δ = 3.25 ppm

Antimicrobial activity

The *in vitro* antibacterial activities of synthesized complexes have been studied by disc diffusion method. The antibacterial activities were done at 100 µg /ml concentrations in DMF solvent using four bacterial strains (*S. typhi, S. aureus, E. coli and B. subtilis*) by the minimum inhibitory concentration (MIC) method.[41] These bacterial strains were incubated for 72 h at 27^0C. Standard antibacterial (Cefodox and Linazoid) were used for comparison under similar conditions. Activity was determined by measuring the diameter of the zone of inhibition (mm) (Table 8).

Table 8 indicated that Co(II) and Ni(II) complexes are more active against the bacterial strains *S. aureus* and *S.typhi* as compared to other bacterial strains. Cu (II) and Zn (II) complexes were found to be moderately active against all bacterial strains.

Conclusion

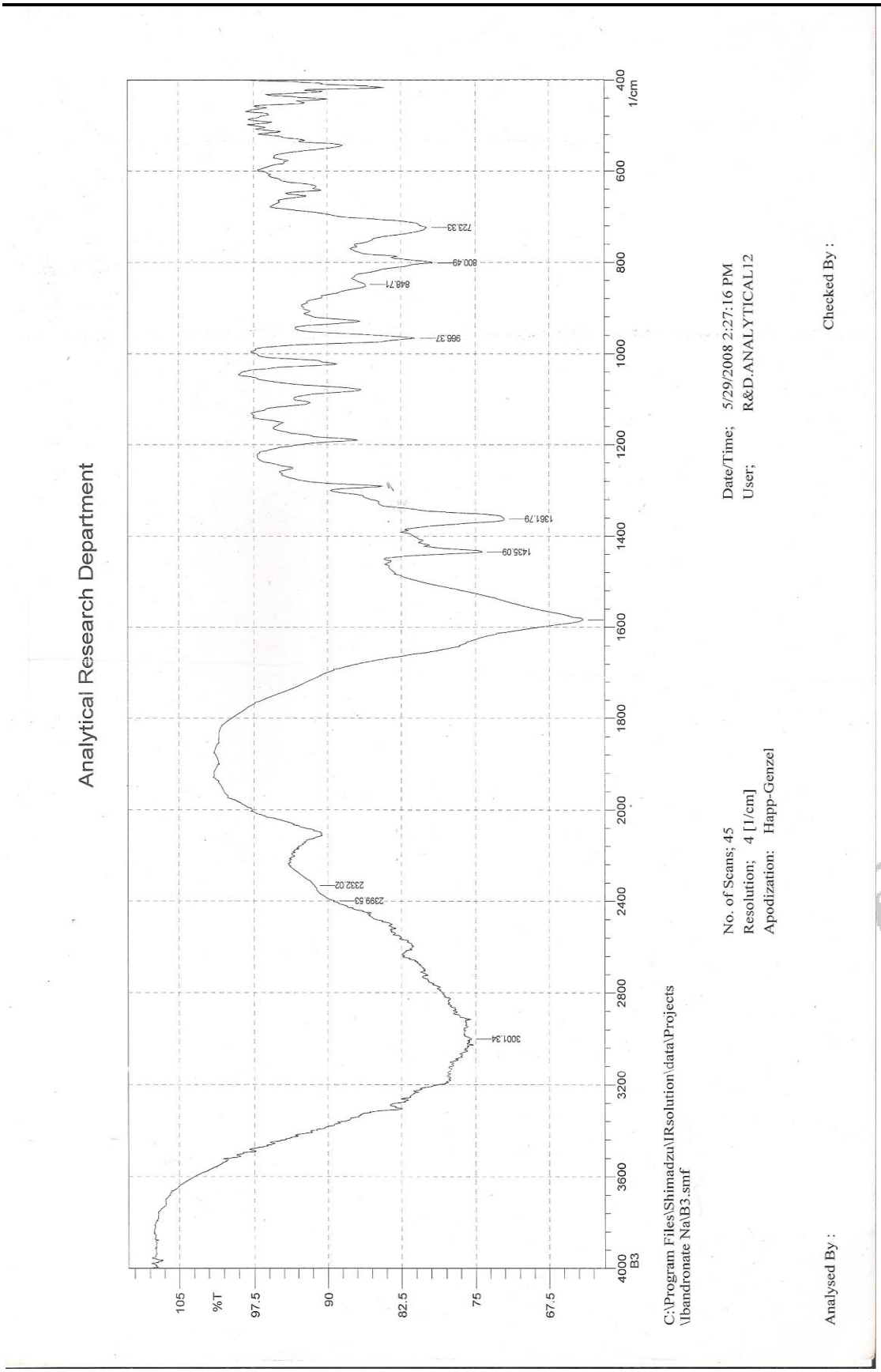
From analytical and spectral data of new series of macrocyclic ligand complexes, it is concluded that macrocyclic complexes acts as tetradentate with nitrogen donor transition metal complexes of the type [M ($C_{16}H_{24}N_4O_4$)X_2]. Where M= Co(II),Cu(II),Ni(II) and Zn(II).The infrared and magnetic moment data indicates octahedral environment at the metal centers. The complexes would be expected to exhibit the physiological properties with enhanced intensity. Antibacterial activity of some complexes are moderate.

Table No.1: Analytical data of [M($C_{16}H_{24}N_4O_4$)X_2]type complexes

Sr. No.	Mol. For. of Complex	Mol. Wt.	Colour	Melting Point	Elemental Analysis % Calcd. (Found) % C	% H	% N	λM ohm^{-1}cm^2 mol^{-1}	M.M B.M
1	[Cu($C_{16}H_{24}N_4O_4$)Cl_2]	470.83	Blue	225	40.838 (40.345)	5.138 (4.879)	11.899 (11.564)	11	1.77
2	[Cu($C_{14}H_{24}N_4O_4$)(NO_3)$_2$]	523.94	Dark Blue	230	36.679 (36.213)	4.617 (4.216)	16.04 (15.768)	09	1.76
3	[Cu($C_{14}H_{24}N_4O_4$)(CH_3COO)$_2$]	518.02	Blue	233	46.372 (46.005)	5.837 (5.398)	10.815 (10.432)	13	1.78
4	[Co($C_{14}H_{24}N_4O_4$)Cl_2]	466.23	Brown	236	42.219	5.188 (4.978)	12.017 (11.765)	08	4.80
5	[Co($C_{14}H_{24}N_4O_4$)(NO_3)$_2$]	519.33	Dark Brown	234	37 (36.879)	4.658 (4.269)	16.182 (15.876)	15	4.83
6	[Co($C_{14}H_{24}N_4O_4$)(CH_3COO)$_2$]	513	Black	239	46.788 (46.206)	5.889 (5.346)	10.912 (10.398)	14	4.82
7	[Ni($C_{14}H_{24}N_4O_4$)Cl_2]	466	Light Green	243	41.238 (40.877)	5.191 (4.904)	12.022 (11.788)	12	2.80
8	[Ni($C_{14}H_{24}N_4O_4$)(NO_3)$_2$]	519.11	Green	249	37.02 (36.658)	4.66 (4.289)	16.189 (15.877)	07	2.82
9	[Ni($C_{14}H_{24}N_4O_4$)(CH_3COO)$_2$]	513	Green	250	40.809 (40.306)	5.892 (5.576)	10.917 (10.345)	09	2.85
10	[Zn($C_{14}H_{24}N_4O_4$)Cl_2]	472.66	Buff	246	40.657 (40.231)	5.118 (5.079)	11.853 (11.346)	12	-
11	[Zn($C_{14}H_{24}N_4O_4$)(NO_3)$_2$]	525.77	Buff	255	36.551 (36.101)	4.601 (4.217)	15.984 (15.453)	12	-
12	[Zn($C_{14}H_{24}N_4O_4$)(CH_3COO)$_2$]	519	Buff	253	46.209 (45.890)	5.817 (5.532)	10.777 (10.621)	14	-

Table -2: IR spectra of complexes

Compound	$\nu(C=N)$	$\nu(C-N)$	$\nu(M-N)$
[Zn($C_{16}H_{24}N_4O_4$)Cl_2]	1575-1610	1000-1310	420-460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2399.53
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97.5
90
82.5
75
67.5
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3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
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Table -3: ^{1}H NMR spectra of complexes

Compound	$-CH_3$	$-NCH_2CH_2N-$	$-CCH_2C-$	$-CCH_2C-$
$[Zn(C_{16}H_{24}N_4O_4)(NO_3)_2]$	3.25	2.00	2.60	--

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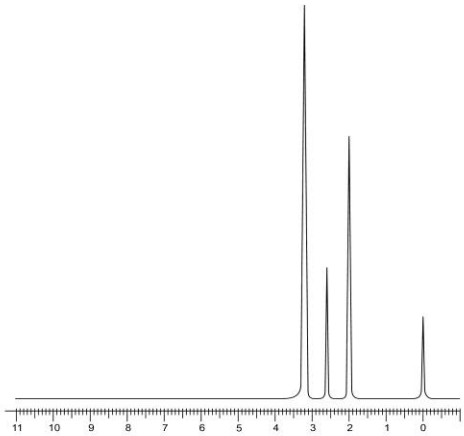

Current Data Parameters

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FIDRES.	125483 Hz
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RG	114
DW	60.800 use
DE	6.50 use
TE	295.0 K
D1	1.00000000 sec
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P1	14.30 use
PLW1	9.00000000 w
SFO1	400.1324710 MHz
F2 - Processing Parameters	
SI	65536
SF	400.1300000 MHZ
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Table 7: Antibacterial activity of comlexes of type $[M(C_{16}H_{24}N_4O_4)X_2]$

Sr. No.	Complex	Inhibition zone (mm)			
		S. typhi	*S. aureus*	*E. coli*	*B. subtilis*
1	$[Cu(C_{16}H_{24}N_4O_4)Cl_2]$	9	10	7	7
2	$[Cu(C_{16}H_{24}N_4O_4)(NO_3)_2]$	10	9	10	8
3	$[Cu(C_{16}H_{24}N_4O_4)(CH_3COO)_2]$	12	10	9	8
4	$[Co(C_{16}H_{24}N_4O_4)Cl_2]$	18	27	15	11
5	$[Co(C_{16}H_{24}N_4O_4)(NO_3)_2]$	17	16	15	12
6	$[Co(C_{16}H_{24}N_4O_4)(CH_3COO)_2]$	15	15	13	10
7	$[Ni(C_{16}H_{24}N_4O_4)Cl_2]$	17	14	15	14
8	$[Ni(C_{16}H_{24}N_4O_4)(NO_3)_2]$	16	14	12	12
9	$[Ni(C_{16}H_{24}N_4O_4)(CH_3COO)_2]$	22	19	16	17
10	$[Zn(C_{16}H_{24}N_4O_4)Cl_2]$	15	11	12	11
11	$[Zn(C_{16}H_{24}N_4O_4)(NO_3)_2]$	13	11	11	9
12	$[Zn(C_{16}H_{24}N_4O_4)(CH_3COO)_2]$	11	12	9	8
13	Cefodox	22	27	22	20
14	Linazoid	25	28	22	20

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