



SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION AND ANTIMICROBIAL PROPERTIES OF 18 TO 24 MEMBERED TETRAAZA MACROCYCLIC COMPLEXES OF Mn (II), Fe (II) AND Sn (II)

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ABSTRACT

Manganese (II), iron (II) and tin (II) macrocyclic complexes of polyamide groups have been synthesized by the template condensation of dicarboxylic acids (malonic acid, succinic acid, glutaric acid or adipic acid) with 1,4-diaminobutane in 1 : 2 : 2 molar ratios. All the complexes are soluble in polar solvents. The complexes have been characterized by IR, electronic spectral studies and magnetic measurements. An octahedral geometry has been assigned for the complexes. The electrical conductivity data in DMSO are as expected for 1 : 2 electrolytes. The formulation of the complexes of the type $[M(\text{Mac}^n)\text{Cl}_2]$ [where, $n = 1-4$, $M = \text{Mn (II), Fe (II) or Sn (II)}$] has been established on the basis of chemical composition.

Key words : Manganese (II), Iron (II) and Tin (II) complexes, Macrocyclic, Biological aspects.

INTRODUCTION

The chemistry of macrocyclic complexes has received much attention and such compounds have been extensively studied in recent years¹. Studies on macrocyclic complexes have shown that some of them are involved in important biological processes, such as photosynthesis and dioxygen transport in addition to their catalytic properties² which may lead to important industrial applications. Their enhanced kinetic and thermodynamic stabilities led to a widespread study of the features, which also influence their potential applications as metal extractants³, as radiotherapeutic⁴ and medical imaging agents⁵. The occurrence of the porphyrin rings in nature as ligands in such crucial and multiple roles as those spanned by the heme proteins, chlorophyll and vitamin B₁₂ suggest that some advantages might be associated with this macrocyclic structure⁶. There has been a spectacular growth in the interest in metal complexes with tetraazamacrocyclic ligands followed by the extensive work on the metal controlled template synthesis of macrocyclic species^{7,8}. However, in most of the polyamide macrocyclic complexes, the amide nitrogen is engaged in coordination and not the oxygen. Related properties have been observed in natural systems which are known to incorporate

interacting metal centres⁹. Macrocyclic complexes of transition metal (II) ions having oxo and aza groups show some interesting properties and biological functions such as being models for metalloproteins and oxygen carrier systems¹⁰. Transition metal complexes of nitrogen donor ligands have been studied in detail, on account of their stereochemistry and wide practical utility¹¹. These facts have led to a large amount of research involving such systems¹². Our ongoing work of tetraazamacrocyclic complexes involving such systems led us to describe the synthetic, spectroscopic and biocidal features of some manganese (II), iron (II) and tin (II) complexes.

EXPERIMENTAL

Dicarboxylic acids (Fluka) were used as received without further purification. 1,4-Diaminobutane was used as obtained from E. Merck and $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, FeCl_2 and SnCl_2 (BDH) were used without further purification. All the solvents used were of high purity and distilled in the laboratory before use. Moisture was excluded from the glass apparatus using CaCl_2 guard tubes.

Physical measurements and analytical methods

Molecular weights were determined by the Rast Camphor Method¹³. IR spectra were recorded as KBr discs, using a Nicolet Magna FTIR-550 Spectrophotometer and conductivity measurements were carried out in 10^{-3} M dimethylformamide solutions at 20°C using a Systronic Type-305 conductivity bridge. Nitrogen and chlorine were determined by Kjeldahl's and Volhard's methods, respectively¹⁴. Tin, iron and manganese were estimated gravimetrically.

Synthesis of the complexes

Weighed amount of SnCl_2 , $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ or FeCl_2 was added to the calculated amounts of dicarboxylic acid and 1,4-diaminobutane in 1 : 2 : 2 molar ratio using dry MeOH as the reaction medium. The resulting mixture was stirred for 7-9 hrs. The contents were kept at room temperature for 12 hrs. resulting in the formation of crystalline compounds. The products were repeatedly washed with methanol so as to assure their purity and dried. These compounds were recrystallized from benzene and dried again in vacuo. Their physical properties and analytical data are given in Table 1.

RESULTS AND DISCUSSION

The elemental analysis and spectral data suggest the formation of macrocyclic complexes $[\text{M}(\text{Mac}^n)\text{Cl}_2]$. The resulting complexes are coloured solids, having high melting points. These complexes are only slightly soluble in common organic solvents, but strongly soluble in DMF and DMSO. The monomeric nature of these complexes is confirmed by the molecular weight determinations. The conductivity values of 10^{-3} M solution in anhydrous DMF ($11-28 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$), showing them to be non-electrolytes. The IR spectral data of different complexes are given in Table 2. The formation of complexes has been revealed by the absence of $-\text{NH}_2$

Table 1. Physical properties and analytical data of manganese (II), iron (II) and tin (II) complexes

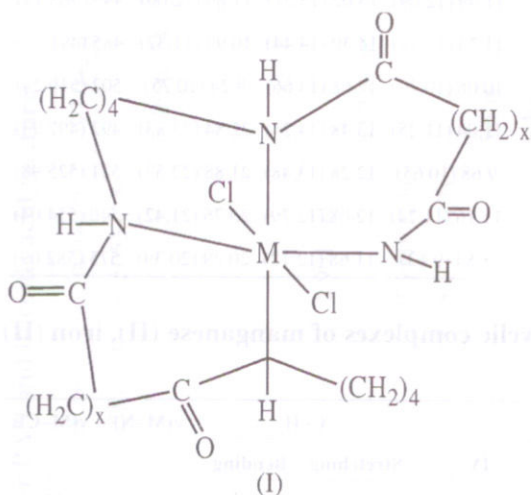
S. No.	Compound	Empirical formula	Physical Characteristics		Analysis % Found (Calcd.)			Mol. Weight Found (Calcd.)
			Colour	M.P. (°C)	N	Cl	M	
1.	[Mn(Mac ¹)Cl ₂]	C ₁₄ H ₂₀ N ₄ O ₄ Cl ₂ Mn	Orange	195	12.45 (12.90)	16.01 (16.33)	11.98 (12.65)	430 (434.18)
2.	[Mn(Mac ²)Cl ₂]	C ₁₆ H ₂₄ N ₄ O ₄ Cl ₂ Mn	Orange	198	11.94 (12.12)	14.12 (15.34)	11.24 (11.88)	445 (462.24)
3.	[Mn(Mac ³)Cl ₂]	C ₁₈ H ₂₈ N ₄ O ₄ Cl ₂ Mn	Orange	188	10.99 (11.43)	13.86 (14.46)	11.02 (11.21)	482 (490.29)
4.	[Mn(Mac ⁴)Cl ₂]	C ₂₀ H ₃₂ N ₄ O ₄ Cl ₂ Mn	Orange	205	9.75 (19.81)	12.58 (13.68)	9.95 (10.60)	505 (518.34)
5.	[Fe(Mac ¹)Cl ₂]	C ₁₄ H ₂₀ N ₄ O ₄ Cl ₂ Fe	Red	215	12.04 (12.87)	15.92 (16.29)	12.04 (12.83)	430 (435.08)
6.	[Fe(Mac ²)Cl ₂]	C ₁₆ H ₂₄ N ₄ O ₄ Cl ₂ Fe	Red	228	11.99 (12.09)	15.02 (15.31)	11.86 (12.06)	449 (463.14)
7.	[Fe(Mac ³)Cl ₂]	C ₁₈ H ₂₈ N ₄ O ₄ Cl ₂ Fe	Red	203	11.24 (11.41)	14.30 (14.44)	10.99 (11.37)	485 (491.19)
8.	[Fe(Mac ⁴)Cl ₂]	C ₂₀ H ₃₂ N ₄ O ₄ Cl ₂ Fe	Red	211	10.08 (10.79)	12.68 (13.66)	9.24 (10.75)	502 (519.24)
9.	[Sn(Mac ¹)Cl ₂]	C ₁₄ H ₂₀ N ₄ O ₄ Cl ₂ Sn	White	225	11.04 (11.25)	13.48 (14.24)	22.84 (23.83)	492 (497.93)
10.	[Sn(Mac ²)Cl ₂]	C ₁₆ H ₂₄ N ₄ O ₄ Cl ₂ Sn	White	201	9.68 (10.65)	12.28 (13.48)	21.88 (22.57)	521 (525.98)
11.	[Sn(Mac ³)Cl ₂]	C ₁₈ H ₂₈ N ₄ O ₄ Cl ₂ Sn	White	219	11.16 (11.74)	12.08 (12.79)	20.76 (21.42)	540 (554.04)
12.	[Sn(Mac ⁴)Cl ₂]	C ₂₀ H ₃₂ N ₄ O ₄ Cl ₂ Sn	White	198	8.84 (9.63)	11.68 (12.18)	20.29 (20.39)	575 (582.09)

Table 2. IR spectral data (in cm⁻¹) of macrocyclic complexes of manganese (II), iron (II) and tin (II)

Compounds	ν(N-H)	Amide bands				C-H		ν(M-N)	ν(M-Cl)
		I	II	III	IV	Stretching	Bending		
[Mn(Mac ¹)Cl ₂]	3220	1695	1476	1240	665	2930	1420	390	375
[Mn(Mac ²)Cl ₂]	3234	1690	1480	1253	672	2925	1406	410	405
[Mn(Mac ³)Cl ₂]	3262	1682	1486	1246	660	2918	1425	430	418
[Mn(Mac ⁴)Cl ₂]	3280	1675	1516	1262	674	2915	1418	445	432
[Fe(Mac ¹)Cl ₂]	3205	1678	1490	1268	625	2916	1435	395	384
[Fe(Mac ²)Cl ₂]	3230	1666	1482	1250	615	2905	1416	415	401
[Fe(Mac ³)Cl ₂]	3260	1655	1460	1242	587	2880	1428	410	395
[Fe(Mac ⁴)Cl ₂]	3275	1642	1465	1270	610	2875	1440	432	415
[Sn(Mac ¹)Cl ₂]	3170	1652	1430	1270	608	2860	1418	370	350
[Sn(Mac ²)Cl ₂]	3182	1645	1436	1263	602	2856	1410	395	342
[Sn(Mac ³)Cl ₂]	3190	1639	1446	1240	590	2835	1412	415	326
[Sn(Mac ⁴)Cl ₂]	3195	1635	1462	1248	582	2825	1405	405	332

stretching vibrations of the amino acid and -OH groups of the dicarboxylic acids. In the IR spectra of all the complexes, a single peak is observed in the region $3170\text{--}3280\text{ cm}^{-1}$ which may be assigned to $\nu(\text{NH})$ of amide group⁹. The amide (I), amide (II), amide (III) and amide (IV) groups are present at $1635\text{--}1695$, $1430\text{--}1490$, $1240\text{--}1270$ and $582\text{--}674\text{ cm}^{-1}$, respectively¹⁵. It provides a strong evidence for the presence of a closed cyclic product. Strong and sharp absorption bands appearing in the regions $2825\text{--}2930$ and $1405\text{--}1440\text{ cm}^{-1}$ in the complexes may be assigned to the C-H stretching and bending vibrational modes, respectively¹⁶. The presence of bands around $370\text{--}445\text{ cm}^{-1}$ is due to $\nu(\text{M-N})$ vibration, which unequivocally supports the coordination of the amide nitrogen to the metal ion. The bands at $326\text{--}432\text{ cm}^{-1}$ is due to $\nu(\text{M-Cl})$ vibrations¹⁷.

On the basis of the above discussion, the following structure may be assigned to the complexes-



where, M = Sn (II), Mn (II) and Fe (II)

$[\text{Mn}(\text{Mac}^1)\text{Cl}_2]$	$x = 1$
$[\text{Mn}(\text{Mac}^2)\text{Cl}_2]$	$x = 2$
$[\text{Mn}(\text{Mac}^3)\text{Cl}_2]$	$x = 3$
$[\text{Mn}(\text{Mac}^4)\text{Cl}_2]$	$x = 4$
$[\text{Fe}(\text{Mac}^1)\text{Cl}_2]$	$x = 1$
$[\text{Fe}(\text{Mac}^2)\text{Cl}_2]$	$x = 2$
$[\text{Fe}(\text{Mac}^3)\text{Cl}_2]$	$x = 3$
$[\text{Fe}(\text{Mac}^4)\text{Cl}_2]$	$x = 4$
$[\text{Sn}(\text{Mac}^1)\text{Cl}_2]$	$x = 1$
$[\text{Sn}(\text{Mac}^2)\text{Cl}_2]$	$x = 2$
$[\text{Sn}(\text{Mac}^3)\text{Cl}_2]$	$x = 3$
$[\text{Sn}(\text{Mac}^4)\text{Cl}_2]$	$x = 4$

Biological Screening

The antifungal activity was evaluated against *Fusarium oxysporum* and *Aspergillus niger* by the radial growth method¹⁸ using Czapek's agar medium having the composition, glucose 20 g, starch 20 g, agar-agar 20 g and distilled water 1000 mL. The compounds were mixed with the medium in different concentrations. The fungus was placed on the medium with the help of inoculum needle¹⁹. The linear growth of fungus was obtained by measuring the fungal colony diameter after 96 h.

The activity against bacteria was evaluated by the Inhibition Zone Technique²⁰. The organisms used in these investigations included *Pseudomonas cepacicola* (-) and *Staphylococcus aureus* (+). Further, the results of the bacterial activity have been compared with the

conventional fungicide, *Bavistin* and the conventional bactericide *Streptomycin* as standard. The results of the antifungal activity indicated that the metal chelates are more active than their parent diamine and dicarboxylic acids but less active than the respective metal salts. (Table 3).

Table 3. Antifungal activity of macrocyclic complexes of manganese (II), iron (II) and tin (II)

Compounds	Average percentage of inhibition after 96 h (Conc. in ppm)					
	<i>Fusarium oxysporum</i>			<i>Aspergillus niger</i>		
	50	100	200	50	100	200
Standard (Bavistin)	86	100	100	82	98	100
Malonic acid	68	76	84	45	48	57
Succinic acid	72	78	87	48	21	62
[Mn(Mac ¹)Cl ₂]	71	77	91	53	58	65
[Mn(Mac ²)Cl ₂]	78	84	93	59	68	77
[Fe(Mac ¹)Cl ₂]	67	74	85	48	52	61
[Fe(Mac ²)Cl ₂]	71	75	90	56	62	66
[Sn(Mac ¹)Cl ₂]	75	80	95	58	31	72
[Sn(Mac ²)Cl ₂]	82	90	99	67	71	80

In the case of antibacterial activity, the metal chelates, diamine, dicarboxylic acids and respective metal salts show similar type of behaviour as indicated in the case of antifungal activity (Table 4).

Table 4. Antibacterial activity of macrocyclic complexes of manganese (II), iron (II) and tin (II)

Compounds	Diameter (mm) of inhibition zone after 24 h (Con. in ppm)			
	<i>Pseudomonas cepacicola</i> (-)		<i>Staphylococcus Aureus</i> (+)	
	500	1000	500	1000
Standard (Streptomycin)	15	16	16	17
Malonic acid	4	5	5	6
Succinic acid	5	6	7	8
[Mn(Mac ¹)Cl ₂]	6	8	7	8
[Mn(Mac ²)Cl ₂]	9	10	9	11
[Fe(Mac ¹)Cl ₂]	7	8	8	10
[Fe(Mac ²)Cl ₂]	10	11	10	12
[Sn(Mac ¹)Cl ₂]	8	10	9	11
[Sn(Mac ²)Cl ₂]	9	12	10	13

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