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Synthesis and Characterization of New Macrocycles Containing Pendant Groups

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SYNTHESIS AND REACTIVITY IN INORGANIC AND METAL-ORGANIC CHEMISTRY
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Synthesis and Characterization of New Macrocycles Containing Pendant Groups

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ABSTRACT

The new ligands, 1,5,8,12-tetraaza-4-(1′,1′-dimethylethyl)-2-(1″,1″,2″,2″,3″,3″,3″-heptafluoropropyl)-9,11-(dimethyl)-cyclotetradeca-1,4,8,11-tetraene (L^1) and 1,5,9,13-tetraaza-4-(1′,1′-dimethylethyl)-2-(1″,1″,2″,2″,3″,3″,3″-heptafluoropropyl)-10,12-(dimethyl)-cyclohexadeca-1,4,9,12-tetraene (L^2), have been prepared by the reaction of 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione with ethylenediamine and acetyl acetone (L^1) and 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione with 1,3-diaminopropane and acetylacetone (L^2), respectively. Their complexes with Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), and Zn(II) ions have also been synthesized and characterized by elemental analyses, magnetic susceptibility measurements, molar conductance measurements, IR, EPR, ^{1}H NMR, and UV-Visible spectra. The molar conductance values show that the complexes of Fe(III) and Cr(III) are 1 : 1 electrolytes, the Ni(II) and Cu(II) complexes are 1 : 2 electrolytes

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while those of Mn(II), Co(II), and Zn(II) appear to be non-ionic. An octahedral structure has been proposed for all of these metal ions except for those of Cu(II) and Ni(II), which appear to be square-planar. The β values indicate a considerable orbital overlap in the metal–ligand bond. All of the compounds have been tested against gram-positive bacteria of *Staphylococcus aureus* and gram-negative bacteria of *Escherichia coli*. The results show that these compounds inhibit the growth of bacteria.

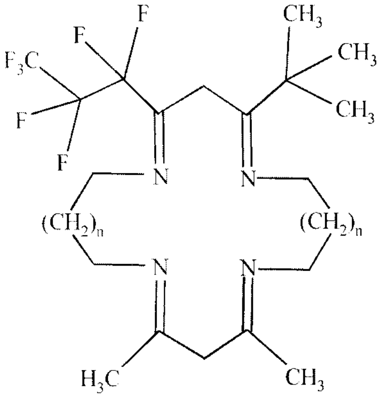
Key Words: L^1; L^2; Macrocycle; Pendant group.

INTRODUCTION

The coordination properties of macrocycles bearing pendant donor groups have evoked much interest, which has produced a rapid advance in the field of both biomimetic models and abiotic systems. A variety of metallated macrocycles containing different functional groups on the periphery have been reported. The syntheses and investigations of macrocyclic complexes are still of burgeoning research interest and this area is reviewed regularly.[1–5] The introduction of pendant groups in the macrocycle increases the stability of its complexes.[6,7] Macrocycles have wide applications in medicine, metal ion techniques, treatment of kidney stones, in cancer diagnosis, and in treatment of malignant tumors,[8] they have proved useful as magnetic resonance imaging (MRI) contrast agents.[9] 5-Fluorouracil has been found to be of immense use in cancer chemotherapy and has high antitumor activity.[10] Some new copper(II) complexes show antifungal activities[11] against phytopathogenic fungi.

Several compounds of transition metal ions act as effective antifungal agents[12] against *Aspergillus* and *Candida* species. Metal complexes of diketones have been used as metal extractants, substituted 1,4-dihydroquinozaline-2,3-dione exhibit physiological and pharmacological activities, while pyrazolopyrimidine-5,7-dione has been used as antibacterial agent. Because of the diverse application of diketones and macrocycles in biological systems, it seemed appropriate to synthesize macrocycles with pendant arms from diketones and to study their interaction with metal ion.

In this paper, we report the syntheses of 14- and 16-membered N_4 macrocycles, namely 1,5,8,12-tetraaza-4-(1′,1′-dimethylethyl)-2-(1″,1″,2″,2″,3″,3″,3″-heptafluoropropyl)-9,11-(dimethyl)-cyclotetradeca-1,4,8,11-tetraene (L^1), 1,5,9,13-tetraaza-4-(1′,1′-dimethyl-ethyl)-2-(1″,1″,2″,2″,3″,3″,3″-heptafluoropropyl)-10,12-(dimethyl)-cyclohexadeca-1,4,9,12-tetraene (L^2), and their transition metal complexes (Fig. 1). We are developing new pendant armed macrocyles in which methyl and fluoro groups act as pendant groups.



L^1: n = 0

L^2: n = 1

Figure 1. Structures of the macrocycles L^1 and L^2.

RESULTS AND DISCUSSION

The metal-free macrocycle L^1 was prepared by the interaction of 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione, ethylenediamine, and acetylacetone in 2 : 1 : 1 ratio in ethanol, while there is the formation of ligand L^2 when 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione reacts with 1,3-diaminopropane and acetylacetone in 2 : 1 : 1 ratio. The reactions for the formation of the ligands and their metal complexes are shown below

$$C_{10}H_{11}F_7O_2 + (CH_3CO)_2CH_2 + 2NH_2(CH_2)_2NH_2 \xrightarrow{\text{EtOH, Stir, Reflux}} \underset{L^1}{C_{19}H_{27}F_7N_4}$$

$$C_{10}H_{11}F_7O_2 + (CH_3CO)_2CH_2 + 2NH_2(CH_2)_3NH_2 \xrightarrow{\text{EtOH, Stir, Reflux}} \underset{L^2}{C_{21}H_{31}F_7N_4}$$

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$$L^1 + MCl_2 \xrightarrow{\text{HCl, Reflux}} [ML^1Cl_2]$$

$$L^1 + M'Cl_2 \xrightarrow{\text{HCl, Reflux}} [M'L^1]Cl_2$$

$$L^1 + M''Cl_3 \xrightarrow{\text{HCl, Reflux}} [M''L^1Cl_2]Cl$$

$$L^2 + MCl_2 \xrightarrow{\text{HCl, Reflux}} [ML^2Cl_2]$$

$$L^2 + M'Cl_2 \xrightarrow{\text{HCl, Reflux}} [M'L^2]Cl_2$$

$$L^2 + M''Cl_3 \xrightarrow{\text{HCl, Reflux}} [M''L^2Cl_2]Cl$$

where $M = $ Mn(II), Co(II), Zn(II), $M' = $ Ni(II), Cu(II), and $M'' = $ Cr(III), Fe(III).

The colors, melting points, and analytical data of the new macrocycles and their first row transition metal complexes are given in Table 1.

The elemental analyses suggest 1 : 1 (metal–ligand) stoichiometry and correspond to the composition of the type $[ML^1Cl_2]$, $[ML^2Cl_2]$, where $M = $ Mn(II), Co(II), Zn(II); $[M'L^1]Cl_2$, $[M'L^2]Cl_2$, where $M = $ Ni(II), Cu(II); and $[M''L^1Cl_2]Cl$, $[M''L^2Cl_2]Cl$, where $M'' = $ Cr(III), Fe(III). All the complexes are thermally stable. The molar conductance of the Mn(II), Co(II), and Zn(II) complexes of the ligands L^1 and L^2 in 10^{-3} M DMSO exhibited low molar conductivity values in the 10–34 $\text{ohm}^{-1}\,\text{cm}^2\,\text{mol}^{-1}$ range, suggesting that they are non-electrolytes. While the complexes of the trivalent metal ions Fe(III) and Cr(III) have molar conductivities (55–70 $\text{ohm}^{-1}\,\text{cm}^2\,\text{mol}^{-1}$) in the range reported for 1 : 1 electrolytes. For the $[NiL^1]Cl_2$, $[CuL^1]Cl_2$, and $[NiL^2]Cl_2$, $[CuL^2]Cl_2$ complexes the molar conductance falls in the 132–146 $\text{ohm}^{-1}\,\text{cm}^2\,\text{mol}^{-1}$ range showing 1 : 2 electrolytes.[13]

IR Spectra

The preliminary identification of the macrocyclic complexes was done from the IR spectra (Table 2). In 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione, the carbonyl stretching frequencies appear at 1660 cm^{-1}, however, the macrocyclic ligands gave no bands assignable to the $\nu(C{=}O)$ stretching mode, because $\nu(C{=}O)$ of keto group has been replaced by the $\nu(C{=}N)$ vibration. In the ligand L^1, the $\nu(C{=}N)$ vibration is observed at 1605 cm^{-1}, while in the ligand L^2 the $\nu(C{=}N)$ vibration is found to appear at 1610 cm^{-1}.

A comparison of the IR spectra of free macrocycles with those of their transition metal complexes indicated a substantial shift in the $\nu(C{=}N)$ (1565–1595 cm^{-1}) wave number region.[14] The decrease in the C=N

Table 1. Analytical data, melting points, colors, and percentage yield of ligands and their complexes.

Compounds (formula weight)	Color	M.p. (°C)	Yield (%)	Analysis % found (calcd.) C	H	N	Cl	M	Molar conductance (ohm^{-1} cm^2 mol^{-1})
(L^1) $C_{19}H_{27}F_7N_4$ (444.24)	Orange	110	60	51.03 (51.02)	6.01 (6.0)	12.4 (12.6)	—	—	—
[CrL^{1}Cl$_2$]Cl $C_{19}H_{27}Cl_3CrF_7N_4$ (602.60)	Light-green	280 d	58	37.08 (37.07)	4.4 (4.5)	9.2 (9.3)	17.50 (17.65)	8.52 (8.62)	65
[MnL^{1}Cl$_2$] $C_{19}H_{27}Cl_2F_7MnN_4$ (570.08)	Light-pink	275 d	50	40.01 (40.00)	4.5 (4.7)	9.7 (9.8)	15.80 (15.89)	9.65 (9.63)	10
[FeL^{1}Cl$_2$]Cl $C_{19}H_{27}Cl_3F_7FeN_4$ (606.45)	Brown	190 d	52	37.04 (37.06)	4.8 (4.5)	9.2 (9.3)	17.60 (17.53)	9.17 (9.20)	55
[CoL^{1}Cl$_2$] $C_{19}H_{27}Cl_2CoF_7N_4$ (574.07)	Dark-pink	245 d	58	39.06 (39.07)	4.8 (4.7)	9.6 (9.7)	12.28 (12.35)	10.25 (10.26)	34
[NiL^1]Cl$_2$ $C_{19}H_{27}Cl_2F_7N_4Ni$ (573.83)	Light-red	238 d	54	39.06 (39.07)	4.6 (4.7)	9.8 (9.7)	12.30 (12.35)	10.88 (10.90)	139
[CuL^1]Cl$_2$ $C_{19}H_{27}Cl_2CuF_7N_4$ (578.69)	Dark-green	265 d	62	39.02 (39.04)	4.6 (4.7)	9.5 (9.6)	12.17 (12.25)	10.92 (10.98)	132
[ZnL^{1}Cl$_2$] $C_{19}H_{27}Cl_2F_7N_4Zn$ (580.49)	White	290 d	64	39.03 (39.02)	4.6 (4.7)	9.4 (9.6)	12.18 (12.21)	11.22 (11.26)	28

(*continued*)

Table 1. Continued.

Compounds (formula weight)	Color	M.p. (°C)	Yield (%)	Analysis % found (calcd.)					Molar conductance (ohm^{-1} cm^2 mol^{-1})
				C	H	N	Cl	M	
(L^2) $C_{21}H_{31}F_7N_4$ (472.27)	Light-red	158	56	53.32 (53.36)	6.58 (6.61)	11.86 (11.85)	—	—	—
[CrL^2Cl_2]Cl $C_{21}H_{31}Cl_3CrF_7N_4$ (630.63)	Green	260 d	57	41.74 (41.75)	4.96 (4.95)	8.78 (8.80)	16.83 (16.86)	8.57 (8.61)	70
[MnL^2Cl_2] $C_{21}H_{31}Cl_2F_7MnN_4$ (598.11)	Dark-pink	205 d	47	42.14 (42.13)	5.25 (5.22)	9.39 (9.36)	11.87 (11.85)	9.20 (9.18)	13
[FeL^2Cl_2]Cl $C_{21}H_{31}Cl_3F_7FeN_4$ (634.48)	Dark-brown	220 d	50	39.70 (39.72)	4.90 (4.92)	8.80 (8.82)	19.78 (19.76)	8.83 (8.80)	58
[CoL^2Cl_2] $C_{21}H_{31}Cl_2CoF_7N_4$ (602.10)	Pink	275 d	52	41.82 (41.85)	5.16 (5.18)	8.26 (8.30)	11.79 (11.76)	9.82 (9.78)	32
[NiL^2]Cl_2 $C_{21}H_{31}Cl_2F_7N_4Ni$ (601.87)	Light-brown	241 d	48	41.90 (41.87)	5.25 (5.23)	9.34 (9.30)	11.80 (11.77)	9.76 (9.75)	146
[CuL^2]Cl_2 $C_{21}H_{31}Cl_2CuF_7N_4$ (606.72)	Blue	258 d	58	41.56 (41.53)	5.18 (5.15)	9.26 (9.23)	11.70 (11.68)	10.42 (10.47)	141
[ZnL^2Cl_2] $C_{21}H_{31}Cl_2F_7N_4Zn$ (608.5)	White	282 d	54	41.40 (41.41)	5.15 (5.13)	9.22 (9.20)	11.60 (11.65)	10.76 (10.74)	26

Table 2. IR spectra bands (cm^{-1}) of the ligands and their complexes.

Compounds	ν(C=N) (m)	ν(C–N) (s)	ν(C–C) (w)	ν(M–N) (s)	ν(M–Cl) (m)
Ligand [L^1]	1605	1410	1060	—	—
[CrL^1CL_2]Cl	1565	1390	1060	380	280
[MnL^1Cl_2]	1580	1385	1060	310	260
[FeL^1Cl_2]Cl	1585	1385	1060	395	275
CoL^1Cl_2]	1570	1390	1060	350	250
[NiL^1]Cl_2	1580	1390	1060	360	270
[CuL^1]Cl_2	1575	1387	1060	345	250
[ZnL^1Cl_2]	1570	1385	1060	340	275
Ligand [L^2]	1610	1410	1060	—	—
[CrL^2Cl_2]Cl	1580	1388	1055	385	295
[MnL^2Cl_2]	1595	1390	1060	320	300
[FeL^2Cl_2]Cl	1585	1385	1060	400	270
CoL^2Cl_2]	1570	1385	1055	325	275
[NiL^2]Cl_2	1575	1390	1055	350	260
[CuL^2]Cl_2	1580	1385	1060	345	280
[ZnL^2Cl_2]	1570	1387	1060	335	275

stretching frequencies has been attributed to the coordination of the metal ion via the nitrogen atom. The presence of a sharp band in the region 310–360 cm^{-1} for all the complexes can be assigned to ν(M–N), supporting the involvement of nitrogen in coordination. The metal to nitrogen bond is further confirmed by the decrease in the ν(C–N) stretching frequency by 20–25 cm^{-1} in all the complexes. The strong bands in trivalent metal ion Cr(III) and Fe(III) are observed in the 380–400 cm^{-1} region, due to greater coupling of chromium(III) and iron(III) with the ligand, which can be attributed to ν(M–N) vibration. The medium intensity bands of ν(M–Cl) have been observed at 250–300 cm^{-1} in all the complexes confirming the metal to chlorine coordination.

Electronic Spectra and Magnetic Moments

The magnetic moment values and electronic spectral bands are represented in Table 3. For the chromium(III) ion three spin-allowed transitions are expected from the $^4A_{2g}$ ground state to three excited quartet states. In the Cr(III) complexes of the ligands L^1 and L^2 the three bands observed (Table 3) are assigned to $^4T_{1g}(P) \longleftarrow A_{2g}(F)$, $^4T_{1g}(F) \longleftarrow {}^4A_{2g}(F)$,

Table 3. Electronic spectra bands, magnetic moments, and ligand field parameters of the macrocyclic complexes.

Compounds	Magnetic moment (B.M.)	Electronic bands (cm^{-1})	ε^a	Possible assignment	10 Dq (cm^{-1})	(B) (cm^{-1})	β
$[CrL^1Cl_2]Cl$	3.50	35,087	12	$^4T_{1g}(P) \longleftarrow {}^4A_{2g}(F)$	11,379	888	0.86
		22,220	10	$^4T_{1g}(F) \longleftarrow {}^4A_{2g}(F)$			
		17,240	13	$^4T_{2g}(F) \longleftarrow {}^4A_{2g}(F)$			
$[MnL^1Cl_2]$	5.60	24,390	18	$^4E_g(G) \longleftarrow A_{1g}$	9,022	694	0.72
		22,220	17	$^4T_{2g}(G) \longleftarrow {}^6A_{1g}$			
		16,666	19	$^4T_{1g}(G) \longleftarrow {}^6A_{1g}$			
$[FeL^1Cl_2]Cl$	5.90	23,250	16	$^4E_g(G) \longleftarrow {}^6A_{1g}$	8,155	663	0.61
		21,270	14	$^4T_{2g}(G) \longleftarrow {}^6A_{1g}$			
		17,240	13	$^4T_{1g}(G) \longleftarrow {}^6A_{1g}$			
$[CoL^1Cl_2]$	4.42	20,408	15	$^4T_{1g}(P) \longleftarrow {}^4T_{1g}(F)$	8,801	677	0.70
		15,873	13	$^4A_{2g}(F) \longleftarrow {}^4T_{1g}(F)$			
		12,195	11	$^4T_{2g}(F) \longleftarrow {}^4T_{1g}(F)$			
$[NiL^1]Cl_2$	Diamagnetic	22,222	11	Charge transfer	—	—	—
		20,000	10	$^1B_{1g} \longleftarrow {}^1A_{1g}$			
		18,607	12	$^1A_{2g} \longleftarrow {}^1A_{1g}$			
$[CuL^1]Cl_2$	1.80	27,027	20	Charge transfer	—	—	—
		18,518	21	$^2A_{1g} \longleftarrow {}^2B_{1g}$			
		15,115	18	$^2E_g \longleftarrow {}^2B_{1g}$			
$[ZnL^1Cl_2]$	Diamagnetic	—	—	—	—	—	—

[CrL^{2}Cl$_2$]Cl	3.72	36,360	14	$^4T_{1g}$(P) ⟵ $^4A_{2g}$(F)	11,624	966	0.94
		22,470	11	$^4T_{1g}$(F) ⟵ $^4A_{2g}$(F)			
		16,950	16	$^4T_{1g}$(F) ⟵ $^4A_{2g}$(F)			
[MnL^{2}Cl$_2$]	5.80	23,530	21	^4E_g(G) ⟵ $^6A_{1g}$	9,269	713	0.74
		21,740	13	^{4}T$_{2g}$(G) ⟵ $^6A_{1g}$			
		16,390	16	$^4T_{1g}$(G) ⟵ $^6A_{1g}$			
[FeL^{2}Cl$_2$]Cl	5.82	22,025	13	^4E_g(G) ⟵ $^6A_{1g}$	8,177	740	0.77
		20,830	10	^{4}T$_{2g}$(G) ⟵ $^6A_{1g}$			
		16,805	12	$^4T_{1g}$(G) ⟵ $^6A_{1g}$			
[CoL^{2}Cl$_2$]	4.57	19,608	17	$^4T_{1g}$(P) ⟵ $^4T_{1g}$(F)	9,073	709	0.73
		15,500	19	$^4A_{2g}$(F) ⟵ $^4T_{1g}$(F)			
		12,050	15	$^4T_{2g}$(F) ⟵ $^4T_{1g}$(F)			
[NiL^2]Cl$_2$	Diamagnetic	23,255	15	Charge transfer	—	—	—
		19,420	19	$^1B_{1g}$ ⟵ $^1A_{1g}$			
		18,690	14	$^1A_{2g}$ ⟵ $^1A_{1g}$			
[CuL^2]Cl$_2$	1.72	26,880	19	Charge transfer	—	—	—
		18,348	16	$^2A_{1g}$ ⟵ $^2B_{1g}$			
		15,037	12	^2E_g ⟵ $^2B_{1g}$			
[ZnL^{2}Cl$_2$]	Diamagnetic	—	—	—	—	—	—

[a] ε, dm^3 mol^{-1} cm^{-1}.

and $^4T_{2g}(F) \longleftarrow {}^4A_{2g}(F)$ transitions, respectively. The observed magnetic moment values are slightly lower (3.50–3.72 B.M.) than that calculated value for three unpaired electrons. However, these studies are indicative of an octahedral geometry[15] for Cr(III) ion.

The macrocyclic manganese(II) complexes showed effective magnetic moment values in the range 5.6–5.8 B.M., correspond to a high-spin state and are very close to the calculated values. The electronic spectra of the Mn(II) complexes of L^1 and L^2 in DMSO gave three bands at 24,390, 22,220, and 16,666 cm^{-1} for L^1 and at 23,530, 21,740, and 16,390 cm^{-1} for L^2, which can be assigned to $^4E_g(G) \longleftarrow {}^6A_1$, $^4T_{2g}(G) \longleftarrow {}^6A_{1g}$, and $^4T_{1g}$ (G) $\longleftarrow {}^6A_{1g}$ transitions, respectively, suggesting an octahedral environment[16] around the Mn(II) ion.

The iron(III) macrocyles displayed three main d–d bands (Table 3), these bands are attributed to the transitions $^4E_g(G) \longleftarrow {}^6A_1$, $^4T_{2g}(G) \longleftarrow {}^6A_{1g}$, and $^4T_{1g}(G) \longleftarrow {}^6A_{1g}$, respectively. The μ_{eff} values observed are 5.90 B.M. for L^1 and 5.82 B.M. for L^2. On the basis of the magnetic moment values and the electronic spectral bands, an octahedral geometry for the iron(III) is proposed.

The observed magnetic moment values of the cobalt(II) complexes are in the range expected for three unpaired electrons. The electronic spectra showed three bands at around 20,408, 15,873, and 12,195 cm^{-1} for the $[CoL^1Cl_2]$ complex and 19,608, 15,500, and 12,050 cm^{-1} for the $[CoL^2Cl_2]$ complex, which can be reasonably assigned to the $^4T_{1g}(P) \longleftarrow {}^4T_{1g}(F)$,^{4} $A_{2g}(F) \longleftarrow {}^4T_{1g}(F)$, and $^4T_{2g}(F) \longleftarrow {}^4T_{1g}(F)$ transitions, respectively. These transitions are characteristic of compounds with an octahedral stereochemistry of the Co(II) ion, a fact that is confirmed by the values of the effective magnetic moment. The three bands observed for each of the $[NiL^1]Cl_2$ and $[NiL^2]Cl_2$ complexes at 22,222, 20,000, 18,607 as well as 23,255, 19,420, 18,690 cm^{-1}. The former bands are at 22,222 and 23,255 cm^{-1} due to the charge transfer while the last two bands can be assigned to the transitions arising from the $^1A_{1g}$ ground state to the $^1B_{1g}$ and $^1A_{2g}$ excited states, respectively. This study showed square-planar geometry[17] around Ni(II) ion.

The electronic absorption spectra of the copper(II) complexes exhibit three bands. The bands at 27,027 cm^{-1} for $[CuL^1]Cl_2$ and at 26,880 cm^{-1} for $[CuL^2]Cl_2$ can be attributed to charge transfer. The other bands found at 18,518, 15,115 cm^{-1} for $[CuL^1]Cl_2$ and at 18,348, 15,037 cm^{-1} for $[CuL^2]Cl_2$ are assigned as ($^2A_{1g} \longleftarrow {}^2B_{1g}$, $^2E_g \longleftarrow {}^2B_{1g}$). These are characteristic of square-planar geometry around the copper(II) ion. The observed magnetic moment values of these compounds of the ligands L^1 and L^2 are 1.80 and 1.72 B.M., repectively, suggesting the square-planar[18] environment for Cu(II).

The 10 Dq values for the complexes follow the order Cr(III) > Mn(II) > Co(II) > Fe(III).

^{1}H NMR Spectra

The ^{1}H NMR spectra of the ligands L^1 and L^2 in DMSO-d_6 show a peak at 1.79–1.84 ppm due to the three terminal CH_3 groups. A triplet in the 1.82–1.86 ppm range may be assigned unambiguously to imine methyl ($CH_3C{=}N-$, 6H) protons and two singlets at δ 3.77 ppm and δ 3.80 ppm can be ascribed to the two methylene groups ($-C-CH_2-C-$, 2H). The peaks for $-CH_2-$ adjacent to the N-atom appear at 3.49 and at 3.47 ppm as triplets in the ligands L^1 and L^2, respectively. However, in the case of L^2 an additional $-CH_2-$ peak of the 1,3-propanediamine ring system appears at 3.82–3.91 ppm as a triplet.[19] The $[NiL^1]Cl_2$ and $[NiL^2]Cl_2$ complexes exhibit high δ values of CH_2 groups adjacent to nitrogen atom due the low electron density upon complex formation.

EPR Spectra

The EPR spectra of the polycrystalline Cu(II) complexes were recorded at room temperature. The $[CuL^1]$ and $[CuL^2]Cl_2$ complexes show $g_{II} = 2.16–2.19$ and $g_{\perp} = 2.01–2.07$, which support that the d_{x2-y2} orbitals may be the ground state. No hyperfine splitting is observed due to nuclear interaction of other nuclei. The values are in agreement with the square-planar geometry around the Cu(II) ion.

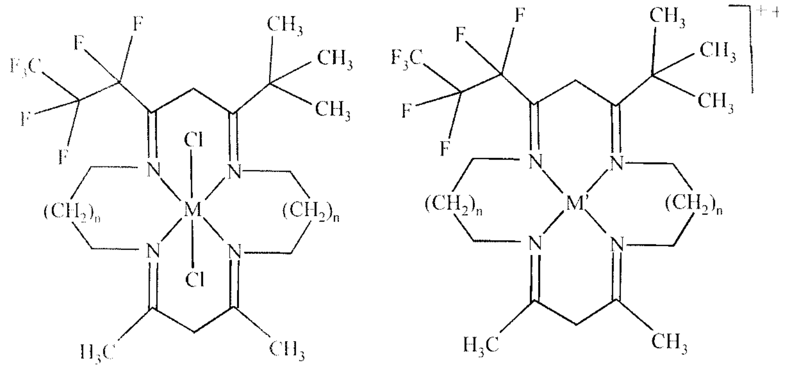
On the basis of above studies the structures in Fig. 2 has been proposed for the macrocyclic metal complexes [M = Mn(II), Co(II), and Zn(II); M′ = Ni(II) and Cu(II)].

Antibacterial Activity

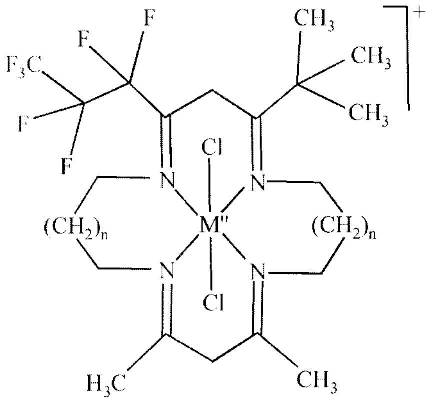
The screening results are recorded in Table 4. A comparative study of the ligands, their complexes, and metal salts indicate that the metal complexes show higher antibacterial activity than the free ligands, gentamicin the standard drug and metal(II) and (III) chlorides. In general, the metal complexes were found to have higher activities than those of the test compounds against the bacteria strains. It may be concluded that the compounds inhibit the growth of bacteria to a greater extent as the concentration is increased due to the effect of the metal ion on the normal cell process.

EXPERIMENTAL

1,1,2,2,3,3,3-Heptafluoro-7,7-dimethyl-4,6-octanedione (SCM), ethylenediamine (CDH), 1,3-diaminopropane, (E. Merck), acetylacetone (BDH),



L^1: n = 0
L^2: n = 1



L^1: n = 0
L^2: n = 1

Figure 2. Suggested structures of the metal complexes of L^1 and L^2. *Key:* M'' = Cr(III) and Fe(III).

transition metal(II) and metal(III) cholrides (S.D. Fine Chem.) were used as received.

Elemental analyses (C, H, N) were carried out with a Carlo Erba 1106 Thomas and Coleman analyzer. The IR spectra (4000–200 cm^{-1}) were recorded on a model 621 Perkin Elmer spectrophotometer. The UV-Visible spectra of the metal complexes in DMSO were recorded on a Lambda

Table 4. Antibacterial activity of ligands and complexes (zone formation in mm).

	S. aureus		*E. coli*	
Compounds	0.5 mg/mL	1.0 mg/mL	0.5 mg/mL	1.0 mg/mL
Gentamicin[a]	7	8	6	8
Ligand L^1	8	10	9	12
Ligand L^2	12	13	12	14
$[CrL^1Cl_2]Cl$	12	15	11	13
$[MnL^1Cl_2]$	12	16	10	17
$[FeL^1Cl_2]Cl$	15	17	14	16
$[CoL^1Cl_2]$	12	19	12	19
$[NiL^1]Cl_2$	13	16	10	14
$[CuL^1]Cl_2$	12	15	14	16
$[ZnL^1Cl_2]$	12	15	12	16
$[CrL^2Cl_2]Cl$	13	17	12	18
$[MnL^2Cl_2]$	14	17	13	17
$[FeL^2Cl_2]Cl$	14	19	13	20
$[CoL^2Cl_2]$	15	21	14	22
$[NiL^2]Cl_2$	11	15	11	15
$[CuL^2]Cl_2$	14	16	13	17
$[ZnL^2Cl_2]$	14	20	11	18
$CrCl_3$	9	11	7	10
$MnCl_2$	8	10	7	11
$FeCl_3$	9	11	8	9
$CoCl_2$	8	9	7	10
$NiCl_2$	7	8	6	8
$CuCl_2$	7	9	8	9
$ZnCl_2$	6	8	8	10

[a]Used as standard.

EZ201 Perkin–Elmer spectrophotometer and magnetic susceptibility measurements were done with a model 155 Allied Research vibration sample magnetometer at room temperature. The conductivity measurements were carried out on a CM-82T Elico conductivity bridge in DMSO. The EPR spectra were recorded on a Bruker Scientific X-band spectrometer (ESP-300). The ^{1}H NMR spectra of the macrocyclic ligands were run in DMSO-d_6 on a JOEL-FX-100 spectrometer. Chlorine was determined gravimetrically[20] and the metals were determined by EDTA titration.[21] The solvents were distilled and dried by conventional methods before use.

Synthesis of the Ligand 1,5,8,12-Tetraaza-4-(1′,1′-dimethylethyl)-2-(1″,1″,2″,2″,3″,3″,3″-heptafluoropropyl)-9,11-(dimethyl)-cyclotetradeca-1,4,8,11-tetraene (L^1)

To a solution of 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione (20 mmol, 4.6 mL) in ethanol (75 mL) were added acetylacetone (20 mmol, 2.0 mL) and ethylenediamine (40 mmol, 2.6 mL) continuously and drop-wise within 2 hr, in a 250 mL round bottom flask. The resulting mixture was refluxed for 7 hr, then cooled at 0°C and kept in a refrigerator for 4 days. An orange product was removed by filtration, washed with diethyl ether and hexane (1 : 1), and dried *in vacuo*. It was recrystallized in methanol. Yield, 5.5 g (60%).

Synthesis of the Ligand 1,5,9,13-Tetraaza-4-(1′,1′-dimethylethyl)-2-(1″,1″,2″,2″,3″,3″,3″-heptafluoro propyl)-10,12-(dimethyl)-cyclohexadeca-1,4,9,12-tetraene (L^2)

The ligand L^2 was synthesized by adding an ethanol (50 mL) solution of 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione (20 mmol, 4.6 mL), acetylacetone (20 mmol, 2.0 mL), and 1,3-diaminopropane (40 mmol, 3.2 mL) simultaneously very, very slowly drop-wise within 1 hr to a 250 mL round bottom flask. The mixture then was refluxed with stirring for 8 hr and then cooled at 0 °C. It was kept in a refrigerator for 5 days. The formed light-red product was filtered, washed with dry diethyl ether, and dried *in vacuo*. It was recrystallized in methanol. Yield, 5.5 g (56%).

Synthesis of Complexes of the Ligands L^1 and L^2

L^1 (10 mmol, 4.4 g) was dissolved in a mixture of methanol (40 mL) and conc. HCl mixture (1 mL) and nickel(II) chloride (10 mmol, 2.4 g) in methanol (25 mL) was added. The solution was refluxed for 3–4 hr. The light-red precipitate that formed was filtered, washed with hexane and dry diethyl ether (1 : 1) and dried *in vacuo*. Yield, 3.6 g (54%).

The nickel(II) complex of the ligand L^2 was synthesized by a similar method. The light-brown product that formed was filtered, washed with hexane, and dried *in vacuo*. Yield, 3.4 g (48%).

Similar procedures were employed for the synthesis of the Mn(II), Co(II), Cu(II), Zn(II) complexes of L^1. Yields, 50–64%.

To L^1 (10 mmol, 4.4 g) in methanol (40 mL) and conc. HCl (1 mL), a ferric(III) chloride (10 mmol, 1.6 g) solution in methanol (25 mL) was added.

The mixture was refluxed with stirring for 12 hr, yielding a brown solid product. The precipitate was filtered, washed with dry diethyl ether, and dried *in vacuo*. Yield, 3.7 g (52%).

The chromium(III) complex was synthesized by the similar above procedure. The light green precipitate was filtered, washed with dry diethyl ether, and dried *in vacuo*. Yield, 3.5 g (58%).

The complexes of the ligand L^2 were synthesized by the similar procedure as applied for the ligand L^1 complexes. Yields, 47–58%.

Bacterial Screening

The antibacterial activity of the ligands and their complexes were evaluated by the filter paper disc method.[22] In this method the sterile discs (5 mm diameter) of filter paper (Whatman No. 4) were dipped into the solution of the test compounds of 0.5–1.0 mg/ml concentrations in DMSO, placed over the seeded plates, left for diffusion and incubated at 37 °C for 24 hr. The compound diffusing into the nutrient agar plate prevents the growth of bacterium in a zone around the disc. Control plates for the solvent, gentamicin as the standard drug, and metal(II) and (III) chlorides were compared with the test compound.

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REFERENCES

1. Nicholas, J.H.; William, L.; Gllian, R. Arsenic(III) halide complexes with acyclic and macrocyclic thio and selenoether coligands. Synthesis and structural properties. Inorg. Chem. **2002**, *41*, 2070–2076.
2. Cronin, L.; Mount, A.R.; Parsons, S.; Robertson, N. A new class of macrocycle capable of binding exogenous metals. Synthesis, structure, magnetic and electrochemical properties of a Cu(II) trinuclear complex based upon 1,4,8,11-tetraazacyclotetradecane-2,3-dione [exo O_2] cyclam. J. Chem. Soc. Dalton Trans. **1999**, 1925–1927.

3. Lindoy, L.F. Transition metal complexes of synthetic macrocyclic ligands. Chem. Soc. Rev. **1975**, 421–441.
4. Atkinson, I.M.; Chartres, J.D.; Groth, A.M.; Lindoy, L.E.; Lowe, M.P.; Mechan, G.V.; Skelton, B.W.; White, A.H. New linked macrocyclic system. Interaction of paladium(II) and platinum(II) with tri-linked N_2S_2-donor macrocycles and their single-ring analogues. J. Chem. Soc. Dalton Trans. **2002**, 2801–2806.
5. Koike, T.; Kimura, E.; Nakimura, I.K.; Hashimato, Y.; Shiro, M. The first anionic Zn(II) complexes with a macrocyclic triamine. Chemical verification of the sulfonamide inhibition of carbonic anhydrase. J. Am. Chem. Soc. **1992**, *114*, 7338–7345.
6. Bianchi, A.; Calabi, L.; Giorgi, C.; Losi, P.; Marcani, P.; Palano, D.; Pauli, P.; Rossi, P.; Valtoncoli, B. Thermodynamic and structural aspects of manganese(II) complexes with polyamino polycarboxylic ligands based upon 1,4,7,10-tetraazacyclodecane (cyclen), crystal structure of dimeric $[MnL]_2$-$2CH_3OH$ containing the new ligand 1,4,7,10-tetraazacyclododecane. J. Chem. Soc. Dalton Trans. **2001**, 917–922.
7. Yeh, G.C.; Beatty, A.M.; Bashkar, J.K. Synthesis and characterization of cobalt-cage complexes with pendant phenol groups. Inorg. Chem. **1996**, *35*, 3828–3835.
8. Parker, D. Tumour targetting with radiolabelled macrocycle antibody conjugates. Chem. Soc. Rev. **1990**, *19*, 271–291.
9. Comblin, V.; Gilsoul, D.; Hermann, M.; Humblet, V.; Jacques, V.; Masbhi, M.; Sauvage, C.; Desteux, J.F. Designing new MRI contrast agents: a coordination chemistry challenge. Coord. Chem. Rev. **1999**, *185*, 451–470.
10. Shi, G.; Cal, W. δ,ε-unsaturated β,β-difluoro-α-keto esters, novel synthesis and utility as precursors of $\beta\beta$-difluoro-α-amino acids. J. Org. Chem. **1995**, *60*, 6289–6295.
11. Roy, T.G.; Hazari, S.K.S.; Dey, B.K.; Chakrabort, S.; Tiekink, E.R.T. Synthesis, characterization and antifungal activities of some new copper(II) complexes of octamethyltetraazacyclotetradecadiene. J. Metal-Based Drugs **1999**, *6*, 345–354.
12. Barboiu, M.; Supran, C.T.; Scozafova, A.; Gauran, C.; Diaconescu, P.; Bojin, M.; Iluc, V.; Cot, L. Antifungal macrocyclic supramolecular complexes of transition metal ion acting as lanosterol-1-4-β-demethylase inhibitors. J. Metal-Based Drugs **1999**, *6*, 101–110.
13. Geary, W.J. Molar conductances of coordination compounds. Coord. Chem. Rev. **1971**, *7*, 81–107.
14. Goutam, K.; Samajdar, S.; Datta, D. First Schiff base of vinylamine and an α-diketone: a novel *N*,*N* donor ligand with extensive conjugation. Synthesis, properties and its copper(I) complexes. J. Chem. Soc., Dalton Trans. **2000**, 1555–1558.

15. Singh, N.K.; Singh, S.B. Complexes of 1-isonicotinoyl-4-benzoyl-3-thiosemicarbazide with manganese(II), iron(III), chromium(III), cobalt(II) nickel(II), copper(II) and Zn(II). Transition Met. Chem. **2001**, *26*, 487–495.
16. Sankaran, S.; Athappan, P.; Rajgopal, G. Synthesis, spectral and redox properties of metal complexes of macrocyclic tetraaza chiral Schiff bases. Transition Met. Chem. **2001**, *26*, 588–593.
17. Suh, P.M.; Kim, S.K. Synthesis of dinickel(I) and dinickel(II) complexes of bismacrocyclic ligands. Inorg. Chem. **1993**, *32*, 3562–3564.
18. Goeta, A.E.; Howard, J.A.K.; Maffeo, D.; Paschmann, H.; William, J.A.G.; Yufit, D.S. Copper(II) complexes of the isomeric tetraaza macrocyclic ligands 1,11- and 1,8-*bis*-(2-pyridylmethyl)-1,8,11-tetraazacyclotetradecane and of the 1,4,11-tetraazacyclotetradecane-5,12-dione analogue at neutral and basic pH. J. Chem. Soc., Dalton Trans. **2000**, 1873–1880.
19. Song, B.; Storr, T.; Orving, C. Synthesis and solution studies of the complexes of trivalent lanthanides with the tetraazamacrocycle TETA-$(PO)_2$. Inorg. Chem. **2002**, *41*, 685–692.
20. Vogel, A.I. Gravimetric Analysis. In *A Text book of Quantitative Inorganic Analysis*; 3rd Ed.; Longman: London, 1968; 460–468.
21. Reilley, C.N.; Schmid, R.W.; Sadek, F.S. Chelon approach to analysis (I) survey of theory and application. J. Chem. Educ. **1959**, *36*, 555–564.
22. Collins, C.H. Microbiological Methods. Butler Worths: London, 1974; 364.

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