

Synthesis and spectroscopic characterization of cobalt(III) based supramolecular complexes bearing thymine and adenine[†]

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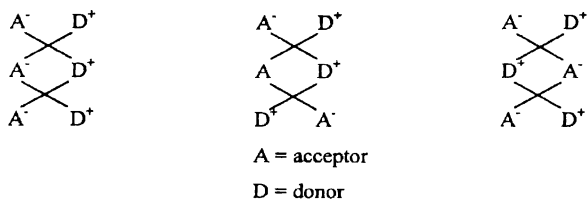
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Multifunctional ligand 5-cyano-6-(4-pyridyl)-2-thiouracil (L) possessing hydrogen bonding groups complementary to those found in nucleotide bases has been synthesized and complexed with *trans*-[Co(en)₂Cl₂]⁺Cl⁻ (en = ethylene diamine) resulting into two types of complexes [Co(en)₂LCl]²⁺.2Cl⁻ and [Co(en)₂L₂]³⁺.3Cl⁻. These complexes were allowed to react with thymine (T) and adenine (A) bases separately. Solid complexes thus synthesized have been characterized using elemental analysis, FAB mass, spectral (IR, UV-visible, ¹H NMR) and scanning electron microscopic (SEM) studies. Association of ligand (L) and its one representative complex [Co(en)₂LCl]²⁺.2Cl⁻ with thymine base has been studied by UV-visible spectrophotometry.

Control of molecular assembly using supramolecular interaction is a major area of contemporary research in chemistry and biochemistry¹. Varieties of supramolecular species have been synthesized by adopting the procedure of non-covalent assisted synthetic technique. This synthetic process primarily relies on the principle of stabilization provided by non-covalent interaction between recognition site incorporated within precursors².

Metal-based supramolecular complexes bearing hydrogen-bonding functionalities complementary to the nucleotide base pair have been used for inducing the formation of supramolecular mesophase and self-assembled nanostructures³ apart from their applications in the development of drugs. Therefore, there is vast domain of investigations into the design and development of molecular and supramolecular devices as the basis for chemical information processing and signaling as well as for the exploration of their relationship with biological phenomenon.

Different hydrogen bonding motifs exhibited by model systems have been illustrated in the following ways⁴ :



Complexes of AAA.DDD type have shown highest association followed by those of ADA.DAD type. There are four attractive secondary interactions in the system

AAA.DDD, two attractive and two repulsive in the system AAD.DDA, while in ADA.DAD all the four are repulsive in nature.

Further, it is increasingly clear that transition metal based self-assembly processes having bridging ligands for propagating the coordination geometries of metals⁵ can lead to functional supramolecular framework that exhibits interesting inclusion phenomena, molecular recognition properties, and unique forms of isomerism⁶. In this context, discrete and infinite square assemblies have attracted much interest owing to their ability to form cavities capable of entrapping electron-rich guests with high shape selectivity⁷. Additionally, the role of metal ions and their complexes in the treatment of biological disorders is also well established⁸. In this context, it would be of worth to mention that development of new metellopharmaceuticals based on platinum metals have been of significant importance. Thus, cobalt as a congener of rhodium was found most acceptable choice as rhodium complexes have shown good antitumor activity⁹.

Results and Discussion

Molecular compositions of the complexes determined on the basis of their elemental analysis and FAB mass data are shown in Table 1. The complexes were found thermally stable and soluble in DMSO only, whereas ligand (L) and [Co(en)₂Cl₂]⁺.Cl⁻ were soluble in methanol too. Electrical conductance values of the complexes [Co(en)₂LCl]²⁺.2Cl⁻ and [Co(en)₂L₂]³⁺.3Cl⁻ (10⁻³ M in DMSO) were observed as 42.84 and 54.06 Ω⁻¹ cm² mol⁻¹, respectively. The complexes were found to be diamagnetic.

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Table 1. Analytical, physical and VU-visible spectral data for the complexes

Compd. no.	Compd./ FAB mass data Found (calcd.)	Yield % Colour	Analysis % : Found/(calcd.)			λ_{\max} nm	$10^3 \epsilon_{\max}$ dm ³ mol ⁻¹ cm ⁻¹
			C	H	N		
1	C ₃₀ H ₃₄ N ₁₂ S ₂ O ₁₁ ; L ₂ T ₂ ·5H ₂ O 714 (712)	84.3 Yellow	44.89 (44.88)	4.10 4.23	20.82 20.94	270 360	2.30 1.10
2	C ₂₀ H ₂₄ N ₁₄ O ₅ S; LA ₂ ·4H ₂ O 498 (500)	80.2 Cream	41.93 (41.95)	4.15 4.19	34.70 34.26	260 340	7.00 0.60
3	C ₁₈ H ₃₄ N ₈ O ₃ SCl ₃ Co; [Co(en) ₂ LCl] ²⁺ ·2Cl ⁻ ·2C ₂ H ₅ OH [M·2Cl] ²⁺ 443 (445.5)	63.5 Green	35.70 (35.55)	5.46 5.50	18.16 18.45	275 340 480 504	2.40 2.00 0.22 0.20
4	C ₂₄ H ₃₈ N ₁₂ O ₇ S ₂ Cl ₃ Co; [Co(en) ₂ L ₂] ³⁺ ·3Cl ⁻ ·5H ₂ O [M·Cl] ³⁺ 713 (710)	61.2 Green	34.19 (34.17)	4.40 4.54	19.90 20.10	272 350 484 520	11.30 6.40 0.38 0.32
5	C ₁₉ H ₄₂ N ₁₀ O ₁₀ SCl ₃ Co; [Co(en) ₂ LTCl] ²⁺ ·2Cl ⁻ ·7H ₂ O [M·2Cl] ²⁺ 571 (570.5)	65.5 Green	29.55 (29.70)	5.38 5.40	18.09 18.24	250 340 480 504	3.20 1.10 0.47 0.45
6	C ₃₄ H ₄₀ N ₁₆ O ₆ S ₂ Cl ₃ Co; [Co(en) ₂ L ₂ T ₂] ³⁺ ·3Cl ⁻ [M·3Cl] ³⁺ 890 (891)	68.5 Green	41.68 (40.90)	3.98 4.0	22.23 22.45	250 350 484 512	11.00 3.60 0.15 0.076
7	C ₂₉ H ₃₇ N ₂₃ SOCl ₃ Co; [Co(en) ₂ LA ₃] ³⁺ ·3Cl ⁻ [M·3Cl] ³⁺ 812 (814)	40.2 Green	37.69 (37.80)	4.38 4.01	34.91 34.98	260 340 480 512	8.40 2.20 0.125 0.12

Infrared spectra : The free ligand peak observed at 2210 cm⁻¹ (C≡N) remained constant in the spectra of its metal complexes, indicating that C≡N group is not involved in the coordination with the metal ion. However, $\nu_{C=O}$ and ν_{NH} of both free ligand and thymine observed at 1680, 1740 and 3150, 3170 cm⁻¹, respectively, along with $\nu_{C=S}$ of the ligand observed at ~1125 cm⁻¹ shifted to lower energy by 5–10 cm⁻¹ in the spectra of their complexes. This indicated that the C=O, N–H and C=S groups of ligand are involved in bonding with the thymine. Similarly, bonding of adenine to ligand and its metal complexes was also identified by the change in peak positions of adenine observed at 3249 and 3115 cm⁻¹ (NH₂ + NH). Pyridyl skeletal vibration observed at ~1600 cm⁻¹ in the spectrum of the free ligand shifted to higher energy region (~1610 cm⁻¹) in the spectra of the complexes showing coordination of pyridine to the metal.

¹H NMR spectra : In order to gain further support for bonding of ligand and its metal complexes with thymine and adenine, their ¹H NMR spectra were compared. In the

spectrum of thymine complexed ligand (L₂T₂) (Fig. 1), N–H protons of the free thymine and of the free ligand observed at δ 10.8–11.3 and 12.0, respectively, shifted to upfield at δ 5.5 indicating that the thymine had interacted with the ligand. Similarly, the interaction of adenine with the ligand was also supported by the upfield shift of the adenine N–H and NH₂ protons (δ 7.6) at δ 13.6 and 8.8, respectively. Upfield shift of pyridyl protons from δ 8.9–7.9 to 6.9 and 7.8 in the spectra of [Co(en)₂LCl]²⁺·2Cl⁻ and [Co(en)₂L₂]³⁺·3Cl⁻, respectively, supported the coordination of pyridine with the metal ion. However, pyridyl protons were observed at δ 7.3, 8.9 and 7.9 in the spectrum of [Co(en)₂LTCl]²⁺·2Cl⁻, [Co(en)₂L₂T₂]³⁺·3Cl⁻ and [Co(en)₂LA₃]³⁺·3Cl⁻, respectively. The NH protons of [Co(en)₂LTCl]²⁺·2Cl⁻ and [Co(en)₂L₂T₂]³⁺·3Cl⁻ were observed at δ 10.6 and 12.8, respectively.

The NH and NH₂ protons of adenine shifted to δ 6.4 and 7.3, respectively. However, NH proton of ligand also shifted to high field at δ 9.6 whereas the NH and NH₂ pro-

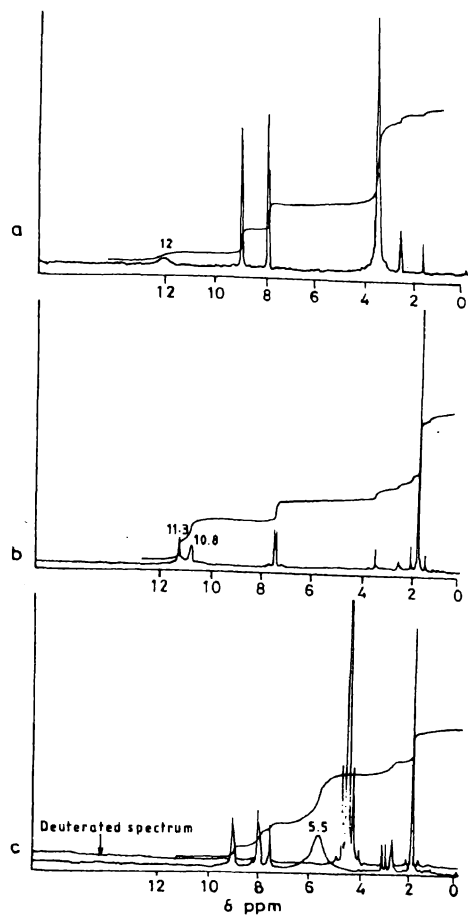


Fig. 1. ^1H NMR spectra of (a) ligand (L), (b) thymine (T) and (c) L_2T_2 .

tons of free adenine were observed at δ 13.6 and 8.8, respectively. Additionally, NH_2 and CH_2 protons of ethylenediamine group observed at δ 5.2 and 2.8, respectively, in the spectrum of $[\text{Co}(\text{en})_2\text{Cl}_2]^+.\text{Cl}^-$ remained constant in the spectrum of thymine and adenine attached metal complexes.

UV-visible spectra : The visible spectrum of complex $[\text{Co}(\text{en})_2\text{LCl}]^{2+}.\text{Cl}^-$ showed peaks at 480 and 504 nm which were assigned to $^1\text{A}_{1g} \rightarrow ^1\text{T}_{2g}$ and $^1\text{A}_{1g} \rightarrow ^1\text{T}_{1g}$ transitions, respectively¹⁰. The transition at lower energy (504 nm) was found to be splitted showing its *trans*-configuration. However, red-shift by 8–16 nm was observed in the spectra of the complexes. From the Table 1 it could also be observed that the metal complexes attached with thymine and adenine show changed peak at shorter wavelength (λ_{max} 250 nm) which may be possible since nucleotide bases also absorb in the similar region.

Furthermore, in order to check the interaction of thymine

with the ligand and complexes, variation in the spectral pattern of the free ligand upon addition of different amount of thymine was initially monitored spectrophotometrically as shown Fig. 2. To a solution of ligand (5 ml; $2.5 \times 10^{-5} \text{ M}$), different volume of thymine (1–7 ml; $2.5 \times 10^{-5} \text{ M}$) was added. From the spectrum it could be seen that thymine

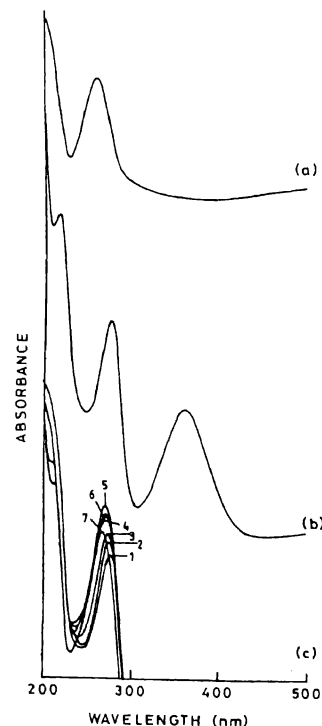


Fig. 2. UV-visible spectra of (a) free thymine, (b) free ligand and (c) spectral changes at λ_{max} 260 nm of the solution containing ligand (5 ml) upon addition of different volumes (1–7 ml) of thymine; concentrations of both the ligand and thymine were kept as $2.5 \times 10^{-5} \text{ M}$, in methanol.

peak (260 nm) gets enhanced maximum after the addition of its 5 ml solution is over along with the red-shift by 12 nm, indicating that 1 : 1 interaction of thymine with the free ligand had occurred.

In order to check the effect if any on the *d-d* transition of the metal complex, spectral variation at 352 nm (transition of the $[\text{Co}(\text{en})_2\text{LCl}]^{2+}.\text{Cl}^-$) upon addition of different amount of thymine was spectrophotometrically monitored and from the Fig. 3 it could be seen that a maximum change in the absorbance was observed again when 5 ml solution of thymine ($2.5 \times 10^{-5} \text{ M}$) was added to 5 ml solution of the complex $[\text{Co}(\text{en})_2\text{LCl}]^{2+}.\text{Cl}^-$.

Thus, on the basis of spectral studies, elemental analyses and FAB mass data, the proposed structures for the complexes are depicted in Fig. 4.

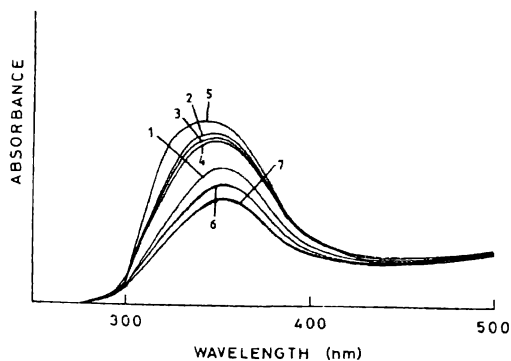


Fig. 3. Spectral variation in the transition of $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot \text{Cl}^-$ (5 ml) observed at 352 nm upon addition of different volumes (1–7 ml) of thymine; concentrations of both were kept as $2.5 \times 10^{-5} \text{ M}$.

The solid state microstructural characterization (XRD and optical microscopic studies) of the complexes have al-

ready been reported elsewhere¹⁴ which showed that the complexes except $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot 2\text{Cl}^-$ displayed orthorhombic crystal system whereas $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot 2\text{Cl}^-$ has tetragonal system. Scanning electron micrographs (SEM) of the various complexes taken at different magnification are shown (Fig. 5(a-d)). Marked change in the size and morphology of the particles could be seen. There is clear evidence of sharp boundaries in $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot 2\text{Cl}^-$ and $[\text{Co}(\text{en})_2\text{LClT}]^{2+} \cdot 2\text{Cl}^-$ which are not present in the micrographs of $[\text{Co}(\text{en})_2\text{L}_2]^{3+} \cdot 3\text{Cl}^-$ and $[\text{Co}(\text{en})_2\text{L}_2\text{T}_2]^{3+} \cdot 3\text{Cl}^-$. The distinct change of aspect ratio displays a characteristics features of the various growth conditions during solidification.

Conclusion :

Multifunctional ligand and its complexes with *trans*- $[\text{Co}(\text{en})_2\text{Cl}_2]^+ \cdot \text{Cl}^-$ have been found to be good template on which nucleotide bases were assembled through hydrogen-bonding.

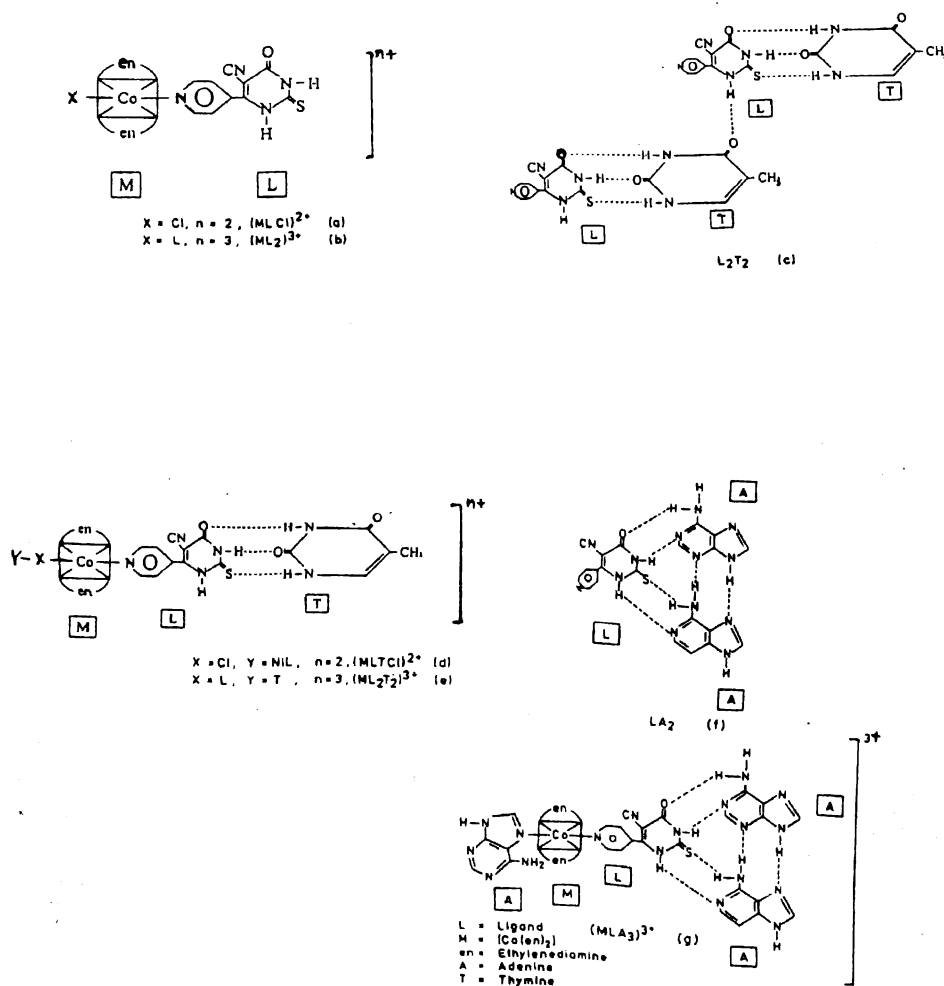


Fig. 4. Proposed structure of the complexes.

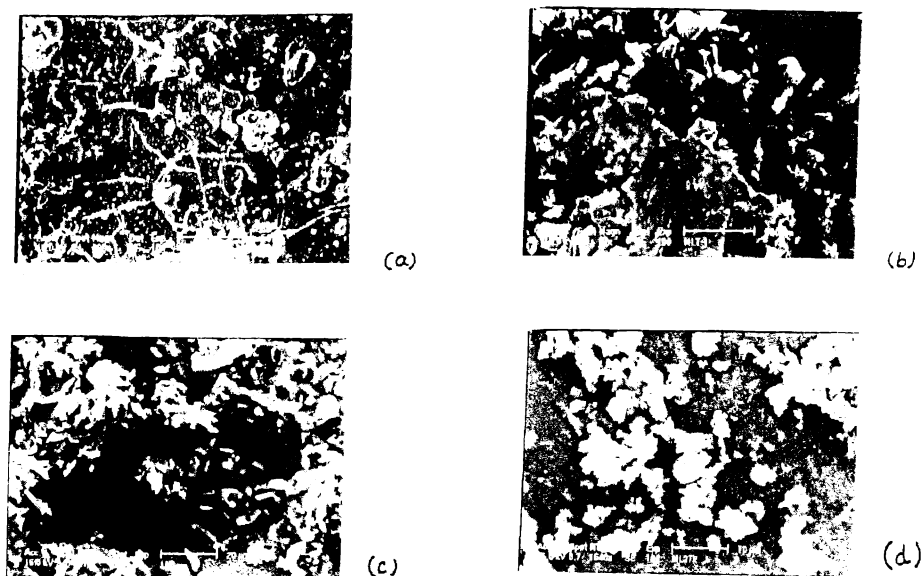


Fig. 5. Scanning electron micrographs of the complexes : (a) $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot 2\text{Cl}^-$, (b) $[\text{Co}(\text{en})_2\text{LCIT}]^{2+} \cdot 2\text{Cl}^-$, (c) $[\text{Co}(\text{en})_2\text{L}_2]^{3+} \cdot 3\text{Cl}^-$, (d) $[\text{Co}(\text{en})_2\text{L}_2\text{T}_2]^{3+} \cdot 3\text{Cl}^-$.

Experimental

Chemical supplied by Aldrich were used as such without further purification. Ligand 5-cyano-6-(4-pyridyl)-2-thiouracil (L) and $[\text{Co}(\text{en})_2\text{Cl}_2]^+ \cdot \text{Cl}^-$ were prepared using reported methods^{11,12}.

Synthesis of L_2T_2 and LA_2 : Free ligand 5-cyano-6-(4-pyridyl)-2-thiouracil (L) (0.230 g, 1 mmol) was added separately to a solution of thymine (0.126 g, 1 mmol) and adenine (0.270 g, 2 mmol) in methanol (~10 ml), which were stirred for 7–8 h. Corresponding solids were filtered and washed several times with methanol, followed by diethyl ether, then dried *in vacuo*.

Synthesis of $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot 2\text{Cl}^-$ (1) and $[\text{Co}(\text{en})_2\text{L}_2]^{3+} \cdot 3\text{Cl}^-$ (2) : A solution containing *trans*- $[\text{Co}(\text{en})_2\text{Cl}_2]^+ \cdot \text{Cl}^-$ (0.285 g, 1 mmol) and 5-cyano-6-(4-pyridyl)-2-thiouracil (L) (0.230 g, 1 mmol) in methanol (~15 ml) was refluxed for 8 h and then cooled in a refrigerator for 2 h. Microcrystalline solid thus obtained was washed several times with water, methanol followed by diethyl ether and finally dried *in vacuo* and analysed (Table 1) as $[\text{Co}(\text{en})_2\text{LCl}]^{2+} \cdot 2\text{Cl}^-$. To a solution of this solid (0.444 g, 1 mmol) in methanol (10 ml + few drops of DMSO), a solution of free ligand (L) (0.230 g, 1 mmol) in methanol (~5 ml) was added. The mixture was refluxed for 6 h, then cooled in a refrigerator for 2–3 h. The resulting microcrystalline solid was washed several times with methanol followed by diethyl ether, dried *in vacuo* and analysed as $[\text{Co}(\text{en})_2\text{L}_2]^{3+} \cdot 3\text{Cl}^-$ (Table 1).

To the solutions of complex 1 (0.445 g, 1 mmol) and complex 3 (0.713 g, 1 mmol) in methanol (20 ml + few drops of DMSO), 1 : 1 (1.26 g, 1 mmol) and 1 : 2 (0.252 g, 2 mmol) molar ratio of thymine in methanol (20 ml) was added separately while stirring. The corresponding solutions after stirring for 7 h yielded the solids which were washed with water, methanol and diethyl ether, then dried *in vacuo*.

Similarly, a hot solution of adenine (0.135 g, 1 mmol) in methanol (20 ml) was added to a solution of complex 1 (0.445 g, 1 mmol) in methanol (20 ml + few drops of DMSO) and stirred for 7–8 h. Upon cooling, the microcrystalline solid thus obtained was washed several times with water, methanol followed by diethyl ether and then dried *in vacuo*.

The complexes were analyzed gravimetrically for their metal content utilizing standard procedure¹³ after decomposing them in aqua regia. The microanalysis was done on a Carlo-Erba analyzer, whereas FAB mass data were obtained from a JEOL SX 102/DA-6000 spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix, at C.D.R.I., Lucknow, India. Molar conductance in DMSO solution (10^{-3} M) was measured at room temperature using a Systronics 303 conductivity meter. ^1H NMR spectra (DMSO- d_6) were recorded on a JEOL FX-90Q FT NMR spectrometer using $\text{Si}(\text{CH}_3)_4$ as an internal reference, UV-visible spectra on a Cary 2390 spectrophotometer, IR spectra (KBr) on a Jasco 5300 and scanning electron micrographs (SEM) on a Philips XL20 instrument.

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