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Molecular modeling of Bi(V)-MCs derived from streptomycin derivatives: synthesis and spectroscopic studies

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ABSTRACT

Streptomycin (SM) derivatives (L^1 and L^2) were used for complexation with Bi(V). Originated coordination patterns in molecular coordinates MCs-1 and MCs-2 along with their molecular models were characterized by various physiochemical, spectroscopic measurements i.e. IR, ^{1}H NMR, UV-V*is*, and mathematical calculations i.e. molecular modeling. Electronic absorption spectra of SM derivatives (L^1 and L^2) proved formation of MCs. Observed transitions showed important shifting in relative intensities. These evidences were detected and discussed. The infrared behavior of MCs was indicative of band transfer. Binding abilities of donor atom(s) of ligands were highly dependable on different constraints of ligands and Bi(V) binding capabilities. Molecular modeling of MCs produced a clear picture about three dimensional structure of SM derivatives (L^1 and L^2) with respect their concerned bond lengths and angles.

Keywords: Binding Abilities, IR Band Transfer, Intensities, Coordination patterns

INTRODUCTION

Bismuth compounds have been used in medicine for 200 years in a variety of intestinal disorders, because of their demulcent properties. Despite a long history of medicinal applications of many bismuth compounds, the mechanisms of bioactivity are not fully understood.[1] The isolation and characterization of bismuth complexes involving ester functionalities on bifunctional ligands demonstrates the use of ether as anchors for weaker donors and in the context of the medicinal relevance of bismuth compounds, offers the opportunity to study the interaction of all bio relevant functional groups with bismuth. The developing coordination chemistry of bismuth is hindered by the facile hydrolysis of most bismuth–element bonds to give the bismuthyl unit (BiO^+), which involves essentially quantitative precipitation.[2] The high thermal and hydrolytic stability of oxygen-bismuth bond[3] has enabled synthetic control using bifunctional ligands involving a ether anchor,[4,5] which offer the additional advantage of satisfying the high coordinative capacity of bismuth center and thereby inhibited intermolecular interactions and coordination patterns. Bi-MCs exhibited relatively high solubility allowing for crystallization, structural and spectroscopic characterization. In view of such difficulties, other approaches to treat and cure have been sought, such as biotherapy.[6,7] There clearly is a need to develop new treatments for this potentially life-threatening disease. Bismuth compounds have proven utility as fungicides and antitumor agents and treatment of a variety of other medical disorders.[8,9]

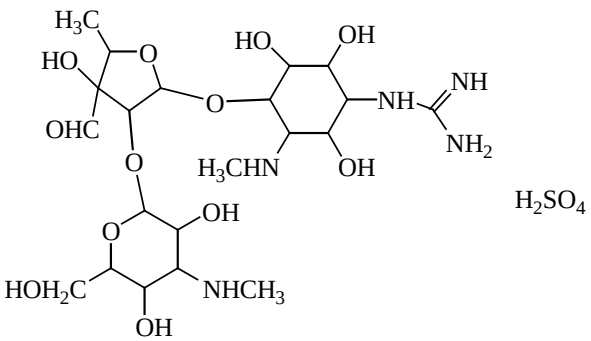

Figure1. Molecular structure of SM-L^1

Most obvious examples has been the widespread use of bismuth compounds, mainly colloidal bismuth sub citrate (CBS) and bismuth sub salicylate (BSS), in chronic diarrhea, acute diarrhea in children[10] and traveler's diarrhea.[11] In this

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letter we demonstrate a deeper look on the synthesis and spectroscopic techniques to understand the coordination aspects of Bi(V) complexes derived from streptomycin derivatives (figure 1).[12-14,19]

Table 1. Elemental analyses (Cal/found) and electronic spectra (nm) of SM (L^1 and L^2) and their respective MCs i.e. [Bi(V)SM-$L^1$and Bi(V)SM-L^2]

Compound	Colour/formula weight	C	H	N	S	Bi	(nm) λ_{max} (aqueous)
$C_{21}H_{40}N_5O_{16}S$	White/ 650.63	38.77 (38.41)	6.20 (6.01)	10.76 (10.12)	4.93 (4.23)	–	210 272
$C_{21}H_{37}BiN_5O_{16}S$	White/ 856.59	29.45 (29.02)	4.35 (4.25)	8.18 (8.01)	3.74 (3.12)	24.40 (24.20)	212 275
$C_{22}H_{42}N_5O_{16}S$	White/ 664.66	39.76 (39.32)	6.37 (6.25)	10.54 (10.10)	4.82 (4.01)	–	211 270
$C_{21}H_{39}BiN_5O_{16}S$	White/ 858.6	29.38 (29.12)	4.58 (4.22)	8.16 (8.10)	3.73 (3.06)	24.34 (24.05)	212 274

RESULTS AND DISCUSSION

It has subsequently been postulated that structural variations imposed on the parent streptomycin derivatives molecule should diversely influence the bioavailability of resulting derivatives through preferential formation of either type of MCs at will, see table 1.

Infrared Spectroscopy

I.R. spectra of free ligands were compared with MCs to detect coordination patterns. The important IR bands and their chelating abilities are given in table 2. In the IR spectra of streptomycin, important bands observed are at 3372-3176 cm^{-1} anti-symmetry merge at 3200–3220 cm^{-1} broad peaks merged with NH_2 peaks and SO_4^{-2} appeared in free ligand at 615-616 cm^{-1} shifted at 1112-1114 cm^{-1} (s) bind with metal ions at 464-462 cm^{-1} stretching vibration due to Bi–O bonding of assigned.

These bands appears for the new complex at the 1670-1665 cm^{-1} with shift of 15-16 cm^{-1}, ruling out the participation of carbonyl oxygen in the coordination.[3]

Table 2. Assignments of I.R. Spectra of SM (L^1 and L^2) and MCs i.e. [Bi(V)SM-$L^1$and Bi(V)SM-L^2]

Compound	ν_{OH} and NH_2 (cm^{-1})	$\nu_{C=O}$ (cm^{-1})	ν_{OH} (cm^{-1})	ν_{C-N} (cm^{-1})	ν_{SO_4} (cm^{-1})	Bi-O (cm^{-1})
$C_{21}H_{43}N_7O_{16}S$ [L^1]	3372, 3176	1670	3420	405	615	464
$C_{21}H_{42}BiN_7O_{16}S$	3220	1664	3405	403	1112	464
$C_{22}H_{42}N_5O_{16}S$ [L^2]	3373, 3175	1665	3412	406	616	462
$C_{21}H_{39}BiN_5O_{16}S$	3219	1650	3406	401	1113	463

^{1}H-NMR Spectra

The interaction of streptomycin was also studied in $CDCl_3$ by ^{1}H NMR spectroscopy. The assignment of ^{1}H NMR signals of streptomycin derivatives and MCs given in table 3. In both MCs spectro-chemical shifts appeared at 5.40, 3.50, 3.0, 2.51 and rest of protons merged with metal ions to confirm complex formation.

Table 3. ^{1}H NMR chemical shifts SM (L^1 and L^2) and MCs [Bi(V)SM-$L^1$and Bi(V)SM-L^2]

H–1 (3.38-3.31)	H–1′ 5.12^{sb}	H–1″ 5.40^{D}
H–2 a	H–2′ 4.22^{sb}	H–2″ 3.62^{dd}
H–3 (3.51-=3.37)		H–3″ 3.33-3.31
H–4 (3.50-3.35)	H–4′ 4.25^{q}	H–4″ 3.76^{dd}
H–5 (3.50-3.35)	H–5′ 1.12^{d}	H–6″ 3.15^{dd}
H–6 (3.35-3.32)	H–6′ 4.6^{s}	H–6″ 3.11^{dd}
		H–7″ 2.70^{s}

[a]correlation was not observed, b = broad, s = single, d = doublet q = quartet

Electronic Spectroscopy

The electronic spectroscopy of SM (L^1 and L^2) and MCs [Bi(V)SM-L^1 and Bi(V)SM-L^2] were studied in aqueous solution. In Bi-SM complex, it was observed that two peaks were detected in the range of 275-270 and 212-210 nm assigned to ($\pi \rightarrow \pi^*$) and ($n \rightarrow \pi^*$) due to charge transfer, figure 2.

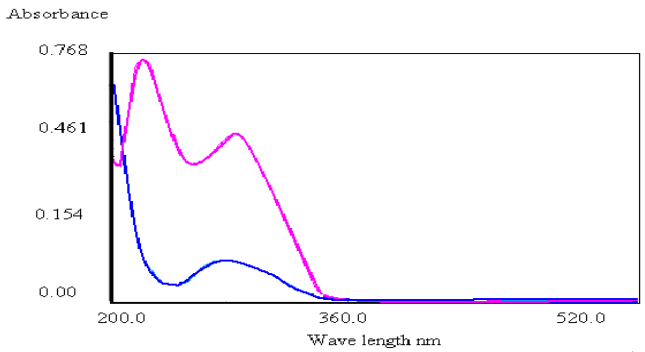

Figure 2. Electronic spectra of ligand (Blue) and Bi-(L^1) (Red)

In solution, the energy of this band did not undergo any dependence with respect to the nature of solvent. Transitions assigned to $\pi-\pi^*$ are due to the presence of M-O and >C=N chromospheres.[15]

MOLECULAR MODELING AN BOND LENGTHS OF SM (L^1 AND L^2) AND MCS [BI(V)SM-L^1AND BI(V)SM-L^2]

Molecular coordinates depend on hybridization of an atom and mode of bonding as a standard to judge specific interactions in molecular structure of SM (L^1 and L^2) and MCs [Bi(V)SM-$L^1$and Bi(V)SM-L^2].[16] If deviations in distances, angles or torsion were evidenced, specific electronic interactions should perhaps be pursued. In order to ascertain structural and geometrical features of Bi(V)SM-L^1 and Bi(V)SM-L^1 derivatives through spectral evidences, coordination capabilities of metal centre confirmed molecular geometries, figure 3-7.

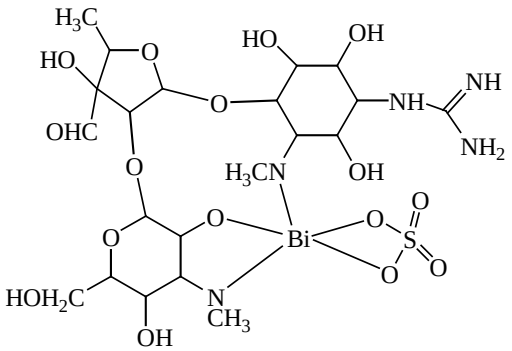

Figure 3. Molecular structure of Bi(V)SM-L^1

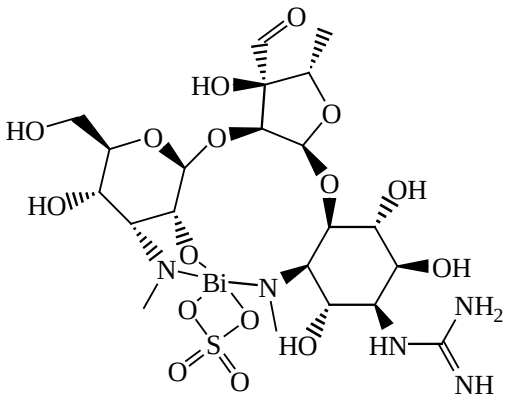

Figure 4. Stereo-structure of Bi(V)SM-L^1

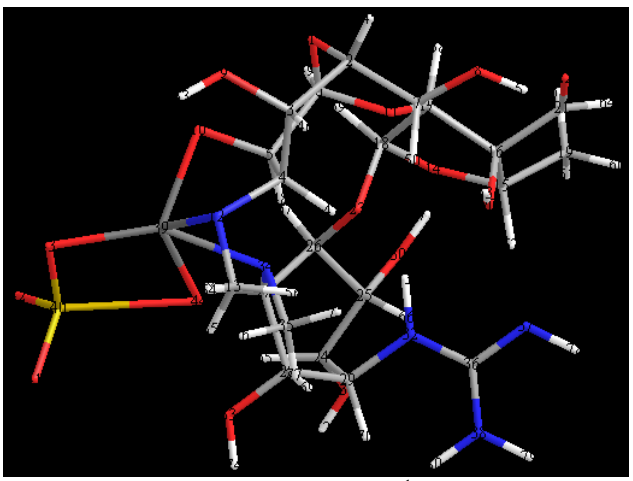

Figure 5. Stick-model of Bi(V)SM-L^1

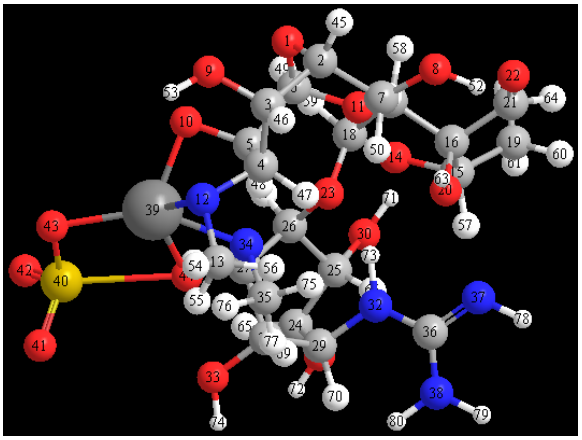

Figure 6. Ball-model of Bi(V)SM-L^1

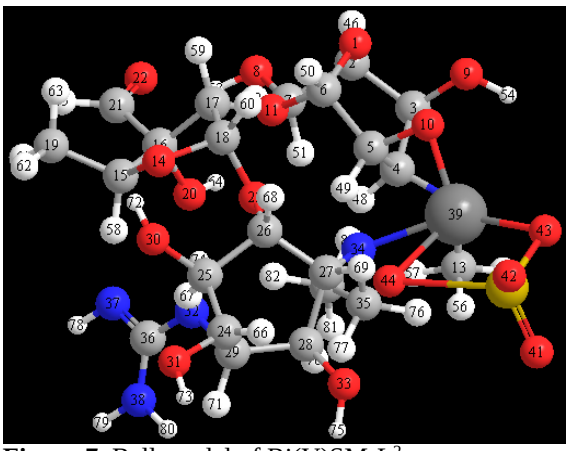

Figure 7. Ball-model of Bi(V)SM-L^2

EXPERIMENTAL

All the chemicals used were of analytical grade. Streptomycin derivatives were obtained from CDH, India. Sodium bismuthate (85%) purity obtained from BDH as source of Bi(V). The filtrate resulted a transparent solution of Bi(V).

Synthesis of MCs [Bi(V)SM-L^1 and Bi(V)SM-L^2]

Bi(V) is dissolved in the dilute solution of streptomycin sulphate derivatives prepared separately in CH_3OH and then the resultant solution was digested on magnetic stirrer 50 hr (1:1) (0.14) $HClO_4$ and (0.1 M) HCl, then a clear solution was obtained. The pH of the solution maintained by drop wise addition of NaOH (pH 3-4) and filtered for undissolved salt.

Instrumentation

All the chemicals and solvent used were of Analytical reagent grade and procured from Aldrich. Solvents were dried over 4 Å molecular sieves and then used. Solvents were purified by standard procedures.[17] Elemental analysis (C, H and N) of MCs were performed using a Carlo-Ebra 1106 elemental analyzer. Metal content was estimated on AA-640-13 Shimadzu flame atomic absorption spectrometer in solution prepared by decomposing the respective frameworks in hot concentrated HNO_3. IR spectra were recorded on a Perkin-Elmer FTIR spectrometer in KBr. Electronic spectra were recorded in water on a Beckman

DU-64 spectrometer with quartz cells. ^{1}H NMR spectra were recorded at ambient temperatures on Bruker AMX400 and DRX500 spectrometers with TMS as internal reference and $CDCl_3$ as solvent. Chemical shifts (δ) were expressed in parts per million (ppm) relative to (TMS) tetramethylsilane.

3D Molecular Modeling

Correct sequence of atoms was obtained to get reasonable low energy molecular models to determine their molecular representation in three dimensions. Complications of molecular transformations could be explored using output obtained.[18] An attempt to gain a better insight on molecular structure of MCs, geometric optimization and conformational analysis were performed using MM+2 force field.[16] Potential energy of molecule was the sum of following terms: $E = E_{str} + E_{ang} + E_{tor} + E_{vdw} + E_{oop} + E_{ele}$. where all E's represent energy values and found corresponds to given types of interaction. The subscripts str, ang, tor, vdw, oop and ele denote bond stretching, angular bonding, torsion deformation, van der waals interactions, out of plane bending and electronic interaction, respectively.

CONCLUSION

Commonly used antibiotics i.e. streptomycin derivatives were used as ligands. Binding abilities of Bi(V) demonstrated how it bind and how drugs were more effective after complexation. The binding abilities of Bi(V) change the stereochemistry of ligands as further characterized by physical measurements techniques. Molecular modeling produced bond angles and lengths gave a clear picture about their geometries and stereochemistry of the whole molecule.[19] Understanding of fundamental structural properties would help in making better biologically effective compounds[20] based on antibiotics.[21]

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SUPPLEMENTARY INFORMATION

The molecular modeling data and calculations for complexes are provided as supplementary information and can be downloaded from journal site.

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