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Interaction of metal ions with D-glucobenzothiazoline: isolation and characterization of the resultant products

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Abstract

Six different metal-ion complexes of D-glucobenzothiazoline were synthesized and characterized by analytical and spectral techniques. Formation of different types of species (ML and ML_2) were observed with Cu^{2+}, Ag^{+}, Cd^{2+}, Hg^{2+}, and Zn^{2+} ions. Existence of an anomeric mixture in the case of the Cu^{2+} complex is identified from the EPR spectra, and the results were further supported by the simulated spectra. The structures were proposed based on different studies. © 2002 Published by Elsevier Science Ltd.

Keywords: Benzothiazoline derivatives; Anomeric mixture; β Anomer; Levorotatory; Bonding and structural group parameters; Inversion of conformation; Simulated spectrum

1. Introduction

Studies pertaining to the interaction of metal ions with saccharides (and their derivatives) are of paramount importance in both chemistry and biology,[1] owing to the coexistence of these in chemical and biological systems.[2] Therefore, in this context, studies of the complexes formed between sugars and metal ions are relevant.[3] Saccharide derivatives containing O, S and O, N donor sites are used to synthesize different metal-ion complexes.[4] Some of these derivatives are capable of inducing reverse transformation in tumor cells.[5] Metal-ion complexes of D-glucocysteinethiazoline are reported.[6] Therefore, it is important to study the interaction of metal ions with saccharide derivatives possessing O-, N-, and S-type donor atoms using different spectral and analytical techniques. In continuation with our on going efforts in the synthesis and characterization of different metal-ion complexes with saccharides[7] and their derivatives, including *N*-glycosyl amines,[8] herein we report the results of the complexation studies of D-glucobenzothiazoline, H_6L (Fig. 1) towards Cu^{2+}, Ag^{+}, Cd^{2+}, Hg^{2+} and Zn^{2+}.

2. Experimental

All solvents were purified and dried prior to use by routine procedures. D-Glucose (Lancaster, UK), *o*-aminothiophenol (Lancaster, UK) and metal acetates (SRL, India) were purchased and used without further purification.

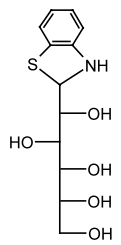

Fig. 1. Schematic representation of the structure of the ligand H_6L.

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UV–Vis spectra were recorded on a Shimadzu UV-2101 spectrophotometer in Me_2SO solution using a compound concentration of 0.01 M in the visible region and 0.0001 M in the UV region. Metal-to-ligand ratios were established based on the Job's plots executed at wavelengths 645, 345, 380 and 380 nm, respectively, for Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}. CD experiments were performed on a JASCO J-600 spectropolarimeter. EPR spectra were recorded in the solid phase as well as in Me_2SO solution on a Bruker ESP-300 spectrophotometer operating in the X-band mode at 300 and 77 K using 1,1-diphenyl-2′-picrylhydrazyl (DPPH) (g_e 2.0023) as a field marker. The ^1H and ^{13}C NMR spectra were measured on a Bruker Avance DRX500 spectrometer operating at 500 MHz for ^1H and 126 MHz for ^{13}C nuclei. FTIR spectra were recorded on an Impact 400 Nicolet FTIR spectrometer in KBr matrix in the region of 400–4000 cm^{-1}. The elemental analyses were performed on a Carlo–Erba elemental analyzer. Metal-ion content was determined using inductively coupled plasma-atomic emission spectra on a Labtam Plasmalab 8440 analyzer. While assigning the spectral data, several short forms were used and these include, 'Ar' for aromatic, 'Gly' for glycosidic, 'Sac' for saccharide and 'Ano' for anomeric.

H_6L.—The ligand was synthesized as per the literature procedure[9] and crystallized as the EtOH adduct, $H_6L{\cdot}0.25C_2H_5OH$: yield 10.19 g (71%); mp 118–120 °C; $[\alpha]_D^{25}$ −42° (*c* 1, Me_2SO); FTIR (KBr): 3345 *ν*(*O–H*) and *ν*(*N–H*), 2926, 2873 *ν*(*C–H*), 1650, 1579 *δ*(*N–H*) and *ν*(*C=C*), 1465 *ν*(*C–O*), 1395 *ν*(*C–N*), 1091 *δ*(*C–O*), 620 *ν*(*C–S*); UV (Me_2SO) *λ*/nm (*ε*/M^{-1} cm^{-1}): 264 (56,000), 320 (75,400); NMR (Me_2SO-d_6): ^1H *δ* 6.96 (dd, 1 H, Ar-*H*), 6.79 (q, 1 H, Ar-*H*), 6.48–6.59 (m, 2 H, Ar-*H*), 6.28 (q, 1 H, $^3J_{N-H,H-1}$ 3.89, $^3J_{N-H,H-1}$ 6.96, $^3J_{N-H,H'-1}$ 1.83 Hz, Gly-N*H*), 5.38 (dd, 0.5 H, $^3J_{H-1,H-2}$ 7.69 Hz, β form, 53%, Ano-*H*), 5.21 (dd, 0.5 H, $^3J_{H-1,H-2}$ 8.06 Hz, β form, 47%, Ano-*H*), 4.13–5.18 (5 H, Sac-O*H*), 3.37–3.88 (6 H, Sac-*H*); ^{13}C: *δ* 108.0–148.1 (12 C, Ar-*C*), 63.1–76.7 (12 C, Sac-*C*); FABMS: *m*/*z* 288 $[M+H]^+$; Anal. Calcd for $C_{12}H_{17}NO_5S{\cdot}0.25\ C_2H_5OH$: C, 50.24; H, 6.24; N, 4.69; S, 10.73. Found: C, 50.45; H, 6.90; N, 4.39; S, 10.11.

$Hg(H_5L)_2$ (**1**).—Mercuric acetate (0.319 g, 1 mmol) was dissolved by stirring in 15 mL of THF for 0.5 h. To this, H_6L (0.333 g, 1 mmol) dissolved in 15 mL of THF was added. The color of the solution changed to yellowish–green with the formation of a precipitate. The precipitate was separated and purified by dissolving in DMF and was reprecipitated by the addition of $CHCl_3$. The purification process was repeated twice successively. The product, thus obtained, was washed with $CHCl_3$ and then dried under vacuum. Yield 0.494 g (64%); mp 164–166 °C; $[\alpha]_D^{25}$ 80° (*c* 1, Me_2SO); FTIR (KBr): 3346 *ν*(*O–H*), 2923, 2889 *ν*(*C–H*), 1584(s), 1513(s) *δ*(*N–H*) and *ν*(*C=C*), 1437 *ν*(*C–O*), 1077 *δ*(*C–O*), 633 *ν*(*C–S*); UV (Me_2SO) *λ*/nm (*ε*/M^{-1} cm^{-1}): 265 (45,300), 328 (24,440); NMR (Me_2SO-d_6): ^1H *δ* 7.31 (dd, 1 H, Ar-*H*), 6.96 (q, 1 H, Ar-*H*), 6.74 (d, 1 H, Ar-*H*), 6.53 (t, 1 H, Ar-*H*), 5.75 (d, 1 H, $^3J_{N-H,H-1}$ 6.23 Hz, Gly-N*H*), 5.22 (d, 1 H, $^3J_{OH,H}$ 5.49 Hz, Sac-O*H*), 5.03 (d, 1 H, $^3J_{OH,H}$ 4.39 Hz, Sac-O*H*), 4.95 (d, 1 H, $^3J_{OH,H}$ 5.13 Hz, Sac-O*H*), 4.46 (t, 1 H, $^3J_{OH,H}$ 5.86, $^3J_{OH,H}$ 5.86 Hz, Sac-O*H*), 4.36 (t, 1 H, $^3J_{H-1,H-2}$ 8.42 Hz, Ano-*H*), 3.69 (d, 1 H, Sac-*H*), 3.63 (t, 1 H, Sac-*H*), 3.42–3.48 (m, 4 H, Sac-*H*), 3.32 (qu, 1 H, Sac-*H*), 3.18 (q, 1 H, Sac-*H*); ^{13}C: *δ* 112.8–146.7 (6 C, Ar-*C*), 67.0–85.3 (1 C, Sac-*C*), 61.0 (1 C, CH_2), 25.1 (1 C, CH_3); FABMS: *m*/*z* 775 $[M+H]^+$; CD (Me_2SO): 362 (positive Cotton effect) nm; Anal. Calcd for $C_{24}H_{32}HgN_2O_{10}S_2$: C, 37.28; H, 4.17; Hg, 25.94; N, 3.62; S, 8.29. Found: C, 37.83; H, 4.09; Hg, 25.36; N, 4.09, S; 7.85.

$Hg(HL^*)_2$ (**2**).—Hg(II) complex (**1**, 2.0 g, 2.59 mmol) was acetylated with Ac_2O (30 mL) in pyridine (40 mL) at rt for 16 h. Upon pouring the reaction mixture into ice-water, a yellow crystalline solid was produced, which was washed with water and recrystallized from aq acetone to give bis[*o*-(2,3,5,6-tetra-*O*-acetyl-D-glucofuranosylamino)benzenethiol]mercury(II) (**2**), where the ligand H_6L was per-*O*-acetylated to give H_2L^*. Yield 2.54 g (89%); mp 142–144 °C; $[\alpha]_D^{25}$ 200° (*c* 1, Me_2SO); NMR (Me_2SO-d_6): 7.35–7.36 (q, 1 H, Ar-*H*), 7.02–7.05 (t, 1 H, Ar-*H*), 6.77 (d, 1 H, Ar-*H*), 6.39–6.62 (t, 1 H, Ar-*H*), 5.82 (d, 1 H, $^3J_{N-H,H-1}$ 9.06 Hz, Gly-N*H*), 5.42–5.45 (t, 1 H, Sac-*H*), 5.19–5.24 (t, 1 H, $^3J_{H-1,H-2}$ 9.16 Hz, Ano-*H*), 5.02–5.06 (t, 1 H, Sac-*H*), 4.93–4.97 (t, 1 H, Sac-*H*), 4.12–4.16 (q, 2 H, Sac-*H*), 3.97–4.00 (q, 1 H, Sac-*H*), 1.96–2.01 (q, 12 H, –4CH_3); ^{13}C: 170.1 (1 C, CH_3COO), 169.8 (1 C, CH_3COO), 169.5 (1 C, CH_3COO), 169.3 (1 C, CH_3COO), 145.4 (1 C, Ar-*C*), 135.4 (1 C, Ar-*C*), 127.2 (1 C, Ar-*C*), 119.8 (1 C, Ar-*C*), 118.3 (1 C, Ar-*C*), 111.9 (1 C, Ar-*C*), 81.7 (1 C, Sac-*C*), 72.4 (1 C, Sac-*C*), 71.1 (1 C, Sac-*C*), 70.8 (1 C, Sac-*C*), 68.6 (1 C, Sac-*C*), 61.9 (1 C, Sac-*C*), 20.5 (1 C, CH_3COO), 20.4 (1 C, CH_3COO), 20.3 (1 C, CH_3COO), 20.3 (1 C, CH_3COO); Anal. Calcd for $C_{40}H_{48}HgN_2O_{18}S_2$: C, 43.29; H, 4.33; Hg, 18.09; N, 2.53; S, 5.77. Found: C, 43.51; H, 4.04; Hg, 18.57; N, 2.68; S, 6.25.

H_2L^*.—The mercury complex of the per-*O*-acetylated *N*-glycosyl amine (**2**, 1.5 g, 1.35 mmol) was dissolved in $CHCl_3$ (20 mL), and hydrogen sulfide was passed through the solution for 25 min. Removal of the precipitated HgS by filtration, followed by evaporation of the solvent, gave a syrup. The syrup upon trituration with EtOH gave *o*-(2,3,5,6-tetra-*O*-acetyl-D-glucopyranosylamino)benzenethiol (H_2L^*). Yield 1.01 g (82%); mp 124–126 °C; $[\alpha]_D^{25}$ −54° (*c* 1, Me_2SO); NMR (Me_2SO-d_6): ^1H *δ* 7.35–7.36 (q, 1 H, Ar-*H*), 7.02–7.05 (t, 1 H, Ar-*H*), 6.77 (d, 1 H, Ar-*H*), 6.39–6.62 (t, 1 H, Ar-*H*), 5.82 (d, 1 H, $^3J_{N-H,H-1}$ 9.06 Hz, Gly-N*H*),

5.42–5.45 (t, 1 H, Sac-*H*), 5.19–5.24 (t, 1 H, $^3J_{H\text{-}1,H\text{-}2}$ 9.16 Hz, Ano-*H*), 5.02–5.06 (t, 1 H, Sac-*H*), 4.93–4.97 (t, 1 H, Sac-*H*), 4.12–4.16 (q, 2 H, Sac-*H*), 3.97–4.00 (q, 1 H, Sac-*H*), 1.96–2.01 (q, 12 H, –4C*H*$_3$); ^{13}C: 169.3–170.1 (4 C, CH_3COO), 111.9–145.4 (6 C, Ar-*C*), 61.9–81.7 (6 C, Sac-*C*), 20.3–20.5 (4 C, CH_3COO); Anal. Calcd for $C_{20}H_{25}NO_9S$: C, 52.75; H, 5.49; N, 3.08; S, 7.03. Found: C, 52.42; H, 5.32; N, 3.22; S, 7.25.

Cu(H$_5$L)·H$_2$O (**3**).—This complex was synthesized by following the procedure described for the Hg(II) complex **1**. Yield 0.165 g (45%); mp 152–154 °C; $[\alpha]_D^{25}$ −250° (*c* 1, Me_2SO); FTIR (KBr): 3373, *ν*(*O–H*) and *ν*(*N–H*), 2931, 2874 *ν*(*C–H*), 1588, 1517 *δ*(*N–H*) and *ν*(*C=C*), 1453 *ν*(*C–O*), 1082 *δ*(*C–O*), 632 *ν*(*C–S*); UV (Me_2SO) *λ*/nm (*ε*/M^{-1} cm^{-1}): 277 (11,310), 345 (12,240); CD (DMSO): ~750, 360 (positive Cotton effect) nm; Anal. Calcd for $C_{12}H_{18}CuNO_6S$: C, 39.18; H, 4.93; Cu, 17.27; N, 3.81; S, 8.72. Found: C, 38.87; H, 4.32; Cu, 17.34; N, 4.29; S, 9.23.

Ag(H$_5$L)·3 H$_2$O (**4**).—This complex was synthesized by following the procedure described for the Hg(II) complex **1**, but using a 1:1 ratio of silver(I) acetate to H_6L in MeOH. Yield 0.220 g (56%); mp 142–144 °C; $[\alpha]_D^{25}$ −30° (*c* 0.5, Me_2SO); FTIR (KBr): 3367 *ν*(*O–H*) and *ν*(*N–H*), 2926 *ν*(*C–H*), 1624, 1582 *δ*(*N–H*) and *ν*(*C=C*), 1495 *ν*(*C–O*), 1077 *δ*(*C–O*), 634 *ν*(*C–S*); UV (Me_2SO) *λ*/nm (*ε*/M^{-1} cm^{-1}): 261 (16,870), 319 (9450); NMR (Me_2SO-d_6): ^{1}H *δ* 7.43 (br, 1 H, Ar-*H*), 6.83 (t, 1 H, Ar-*H*), 6.65 (d, 1 H, Ar-*H*), 6.33 (br, 1 H, Ar-*H*), 5.73 (s, 1 H, Gly-N*H*), 5.15 (s, 1 H, Sac-O*H*), 5.01 (br, 1 H, Sac-O*H*), 4.93 (br, 1 H, Sac-O*H*), 4.48 (t, 1 H, $^3J_{OH,H}$ 5.49, $^3J_{OH,H}$ 5.49 Hz, Sac-O*H*), 4.34 (br, 1 H, Ano-*H*), 3.64 (d, 1 H, Sac-*H*), 3.04–3.26 (m, 5 H, Sac-*H*); ^{13}C: *δ* 112.0–146.1 (1 C, Ar-*C*), 61.0–85.5 (1 C, Sac-*C*); FABMS: *m*/*z* 391 $[M+H]^+$; Anal. Calcd for $C_{12}H_{16}AgNO_5S$: C, 36.56; H, 4.09; Ag, 27.37; N, 3.55; S, 8.13. Found: C, 36.81; H, 3.98; Ag, 26.78; N, 3.23; S, 8.03.

Cd(H$_5$L)(CH$_3$COO)·H$_2$O (**5**).—This complex was synthesized and purified by adopting the procedure given for **1**. Yield 0.228 g (48%); mp 154–156 °C; $[\alpha]_D^{25}$ −10° (*c* 1, Me_2SO); FTIR (KBr): 3405 *ν*(*O–H*) and *ν*(*N–H*), 2925 *ν*(*C–H*), 1634, 1562 *δ*(*N–H*) and *ν*(*C=C*), 1421 *ν*(*C–O*), 1091 *δ*(*C–O*),675 *ν*(*C–S*); UV (Me_2SO) *λ*/nm (*ε*/M^{-1} cm^{-1}): 264 (24,790), 310 (11,200); NMR (Me_2SO-d_6): ^{1}H *δ* 7.29 (d, 1 H, Ar-*H*), 6.76 (qu, 1 H, Ar-*H*), 6.66 (d, 1 H, Ar-*H*), 6.42 (q, 1 H, Ar-*H*), 5.83 (d, 1 H, $^3J_{N-H,H\text{-}1}$ 8.06 Hz, Gly-N*H*), 5.57 (br, 1 H, Sac-O*H*), 5.00 (br, 1 H, Sac-O*H*), 4.87 (d, 1 H, $^3J_{OH,H}$ 18.6 Hz, Sac-O*H*), 4.46 (t, 1 H, $^3J_{OH,H}$ 5.86, $^3J_{OH,H}$ 5.86 Hz, Sac-O*H*), 4.36 (t, 1 H, $^3J_{H\text{-}1,H\text{-}2}$ 8.42 Hz, Ano-*H*), 3.43–3.68 (m, 3 H, Sac-*H*), 3.18–3.36 (m, 3 H, Sac-*H*), 1.82 (s, 3 H, –C*H*$_3$); ^{13}C: *δ* 178.5 (1 C, CH_3COO), 118.3–145.6 (1 C, Ar-*C*), 61.3–77.5 (1 C, Sac-*C*), 60.9 (1 C, CH_2), 22.5 (1 C, CH_3COO), 22.0 (1 C, CH_3); Anal. Calcd for $C_{14}H_{21}CdNO_8S$: C, 35.34; H, 4.45; Cd, 23.63; N, 2.94; S, 6.74. Found: C, 35.64; H, 4.16; Cd, 23.05; N, 2.91; S, 6.09.

Zn(H$_5$L)$_2$ (**6**).—This complex was synthesized and purified by adopting the procedure given for **1**. Yield 0.213 g (44%); mp 148–150 °C; $[\alpha]_D^{25}$ 10° (*c* 1, Me_2SO); FTIR (KBr): 3368 *ν*(*O–H*) and *ν*(*N–H*), 2934, 2875 *ν*(*C–H*), 1578, 1532 *δ*(*N–H*), and *ν*(*C=C*), 1433 *ν*(*C–O*), 1038 *δ*(*C–O*); 676 *ν*(*C–S*) UV (Me_2SO) *λ*/nm (*ε*/M^{-1} cm^{-1}): 293 (32,220), 376 (12,220); CD (Me_2SO): 375 nm (negative Cotton effect); Anal. Calcd for $C_{24}H_{32}N_2O_{10}S_2Zn$: C, 45.30; H, 5.03; N, 4.41; S, 10.09; Zn, 10.00. Found: C, 44.82; H, 5.36; N, 4.61; S, 9.83; Zn, 10.58.

3. Results and discussion

D-Glucobenzothiazoline, H_6L was synthesized and purified by repeated crystallizations from ethanol. ^{1}H and ^{13}C NMR spectra of H_6L indicated the formation of the benzothiazoline derivative of D-glucose in its open-chain form. As a result, a new asymmetric center is produced at C-1, and hence two isomeric products are expected to form. The CD maximum of H_6L near 290 nm is indicative of the presence of a mixture of diastereomers, as was also observed in the literature.[9] H_6L upon reaction with mercuric acetate yields $Hg(H_5L)_2$ (**1**), where the saccharide moiety is in the β-anomeric form. The ligand H_6L present in **1** was per-*O*-acetylated to give the corresponding mercury complex **2** possessing the tetra-*O*-acetylated form of H_6L, with a formula $Hg(HL^*)_2$. The per-*O*-acetylated ligand, H_2L^* was separated from the complex by demetallation using H_2S in order to remove the mercury as HgS. Both the ^{1}H and ^{13}C NMR spectra authenticated the formation of H_2L^*. Reaction of H_6L with different metal ions yielded isolable complexes of $Hg(H_5L)_2$ (**1**), $Hg(HL^*)_2$ (**2**), $Cu(H_5L)\cdot H_2O$ (**3**), $Ag(H_5L)\cdot 3\ H_2O$ (**4**), $Cd(H_5L)(CH_3COO)\cdot H_2O$ (**5**), and $Zn(H_5L)_2$ (**6**). The compounds **1**–**6** were characterized by analytical and spectral methods.

FAB mass spectral studies.—Mass spectra of the ligand H_6L and its complexes, Hg^{2+} **1** and Ag^+ **4** exhibited molecular-ion peaks and thereby the corresponding molecular weights were confirmed.

NMR studies.—The peaks observed in the ^{1}H and the ^{13}C NMR spectra of the metal-ion complexes, **1**, **2**, and **4**–**6**, were assigned by comparing these with the spectrum of H_6L. The comparisons revealed the formation of the metal-ion complexes. The proton signals of –NH and –OH were identified in the D_2O exchange studies.

^{1}H NMR studies. The $-NH_2$ peak observed around 4.92 ppm in the spectrum of the precursor, *o*-aminothiophenol was disappeared upon the formation of H_6L, and a new peak corresponding to the –NH of the

glycosylated product appeared around 6.28 ppm. The –SH peak of *o*-aminothiophenol (5.44 ppm) also disappeared upon glycosylation indicating the formation of the –C–S– bond between the saccharide and the thiol moiety. As the C-1 center is involved in the condensation reaction, the peak corresponding to the C-1–OH is lost. All this indicates the formation of the D-glucobenzothiazoline derivative H_6L.

The saccharide moiety present in H_6L and its metal-ion complexes, Hg^{2+} **1** (4.36 ppm, 8.42 Hz), $Hg(HL^*)_2$ **2** (5.81 ppm, 9.06 Hz), Ag^+ **4** (4.34 ppm, br), and Cd^{2+} **5** (4.36 ppm, 8.42 Hz) was found to exist in the β-anomeric form based on the observed chemical shifts and coupling constants of H-1, and the data is comparable with that reported in the literature.[10] On the other hand, the Zn^{2+} complex **6** exhibited a mixture of α and β anomers. The chemical shifts of the glycosyl –NH group in the metal-ion complexes, Hg^{2+} **1** (5.75 ppm), Ag^+ **4** 5.73 (broad), and Cd^{2+} **5** (5.83 ppm) exhibited upfield shifts when compared to that in the ligand H_6L (6.28 ppm). Representative ^1H NMR spectra of the complexes are shown in Fig. 2.

Skeletal protons of the saccharide moiety in the metal-ion complexes exhibited an overall downfield shift by about 0.1–0.2 ppm. On the other hand, both the upfield and the downfield shifts are observed with different aromatic protons in all these complexes, indicating the binding of –NH or –S or both with the metal ion. In the case of soft metal ions, such as Hg^{2+}, Cd^{2+}, and Zn^{2+}, binding with the sulfur is more favorable,

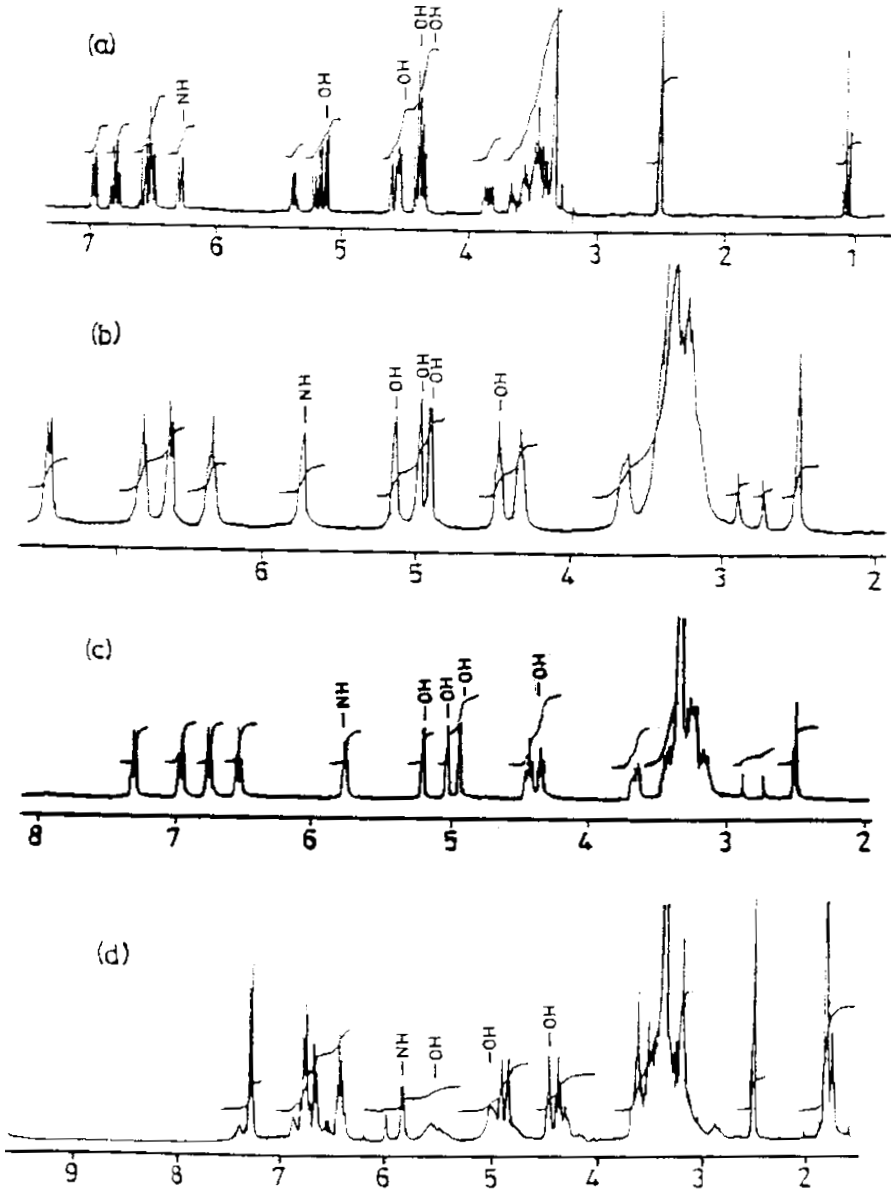

Fig. 2. ^1H NMR spectrum of the compounds in Me_2SO-d_6; (a) H_6L and its complexes; (b) Ag^+, **4**; (c) Hg^{2+}, **1**; and (d) Cd^{2+}, **5**.

and this makes the C-1 center of the saccharide susceptible to undergo intramolecular nucleophilic rearrangement at O-4, resulting in the formation of a furanose ring structure.

^{13}C NMR studies. Considerable downfield shifts were observed with the chemical shift of the carbon attached to the glycosyl –NH group in the metal-ion complexes, Hg^{2+} **1**, 134.8 ppm, $Hg(HL^*)_2$ **2**, 135.4 ppm, Ag^{+} **4**, 135.7 ppm, and Cd^{2+} **5**, 134.1 ppm when compared to that in the ligand (H_6L, 125.0 ppm), indicating the binding of sulfur and/or nitrogen donors with the metal centers. Interaction of hydroxyl groups with the metal ions is noticed based on the shifts observed in the δ values of the corresponding carbon centers of the saccharide moiety. Binding abilities of the –S-center with the central metal ion varies from one complex to another as shown by the downfield shift ($\Delta\delta C$S, ppm) observed with the metal-ion complexes, **1** (3.8), **2** (2.9), **4** (3.0), and **5** (9.3) when compared to the ligand H_6L. Binding of the glycosyl –NH group is further supported by the downfield shift ($\Delta\delta C$-1, ppm) observed in the anomeric carbon of the metal-ion complexes, **1** (8.7), **2** (5.1), **4** (8.9), and **5** (1.0), as compared to that in the ligand H_6L. The variation observed in the downfield shift seems to reflect on the binding ability as well as on the hard–soft character of the corresponding metal ions.

EPR studies.—Parameters, g and A were derived from EPR spectra of the copper complex **3**. As the geometry becomes more tetrahedral in nature, A becomes more isotropic, resulting in a smaller value of $A_{//}$ and at the same time higher value for $g_{//}$ and g_{iso}. The $g_{//}$ and $A_{//}$ parameters are only approximate because this complex exists as an anomeric mixture in solution. However, when this copper complex was synthesized using a mixture of $Cu(OAc)_2$ and $Zn(OAc)_2$ in a 1:9 ratio, the Cu^{2+} was found to adopt a tetrahedral structure of the host zinc complex based on the EPR studies. Since the g value of **3** is not significantly low ($g_{iso} = 2.0699$), it is unlikely that the d_{z^2} acts as the ground state, and furthermore, the presence of a compressed-tetragonal or rhombic octahedral or trigonal bipyramidal or cis-distorted octahedral environment for the Cu^{2+} ion is ruled out. No EPR evidence was obtained for the formation of the dimer even at 77 K. The parallel hyperfine components show two distinct copper centers, which may have come from the two different anomers (α, β isomers and it is denoted as site 'A' and 'B' in Fig. 2) of different concentrations. It is well known that in solution, the tumbling of copper complexes give average g and A. This results in an isotropic quartet, the intrinsic anisotropies (in the molecular frame) reflecting m_I dependent line widths of the type $a + bm_I + cm_I^2$. The hyperfine coupling constants for the two anomers were found to be $A_{//} = 120 - 125G$ and $A_{//} = 90–100G$. As the temperature was lowered, the species with $A_{//} = 100G$ seem to reduce in intensity. Thus, the EPR studies suggested a monomeric structure for **3**. The experimental EPR spectrum obtained for copper complex Cu^{2+} **3** in a Zn^{2+} matrix agrees well with the simulated spectra of a mixture of α and β anomers as shown in Fig. 3.

FTIR studies.—Formation of D-glucobenzothiazoline, H_6L was identified by comparing the FTIR spectra of the corresponding precursors. A preliminary comparison of the FTIR spectra of the metal-ion complexes **1**–**6** with the corresponding ligand spectrum, H_6L or H_2L^* indicated the complex formation. In the *vOH*

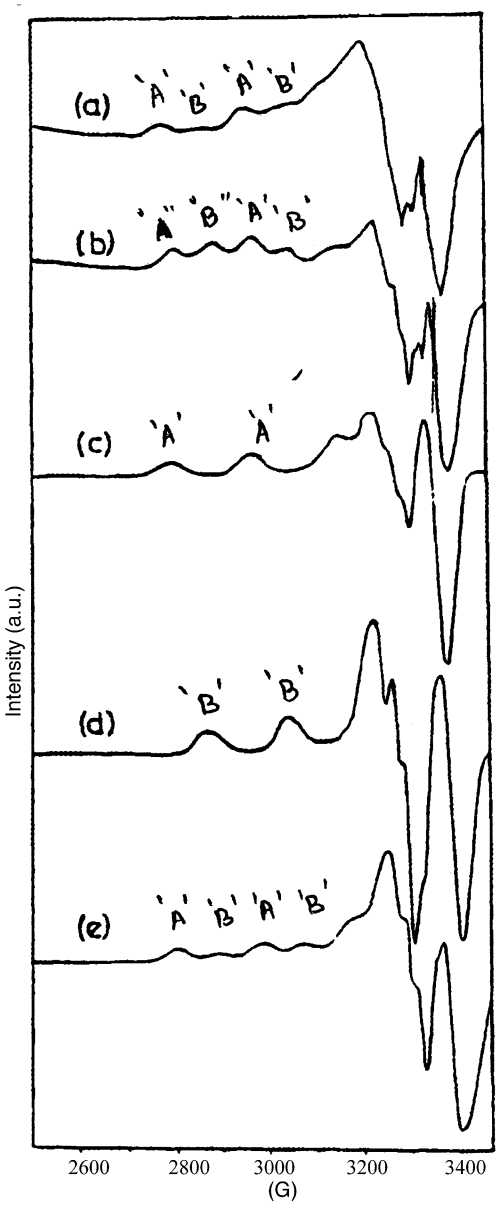

Fig. 3. EPR spectra of **3**: (a) synthesized from a mixture of $Cu(OAc)_2$ and $Zn(OAc)_2$ in 1:9 ratio (at rt, Me_2SO); (b) same as in (a) but measured at 77 K; (c) simulated spectrum of site 'A'; (d) simulated spectrum of site 'B'; and (e) simulated addition spectra of 'A' and 'B'.

region of the spectra, the complexes exhibited broad bands as compared to that of the ligand, indicating that the interactions associated with the saccharide –OH groups in the corresponding ligand are modified upon complex formation. Furthermore, the spectral changes observed in the case of metal-ion complexes in the region 1000–1500 cm^{-1} with *vCO*, *δCO* and *vCOC* vibrations are also indicative of the binding of the ligand.

Band shifts were observed with the saccharide skeletal (*vCO*) and the glycosyl amine (*δNH*) groups in the metal-ion complexes when compared to the ligand ones (H_6L, *vCO* 1465, and *δNH* 1650 cm^{-1}). The shifts observed in *vCO* and *δNH* indicate complex formation. Thus the binding of the glycosyl amine group is predominant over that of the saccharide –OH group, whereas in the case of the metal-ion complexes of Ag^+ **4** and Cd^{2+} **5**, the binding of the saccharide –OH group predominates.

The presence of the β-anomeric form in the metal-ion complexes, (H_6L, 743 and 905 cm^{-1}; **1**, 749 and 894 cm^{-1}; 753 and 899 cm^{-1}; **4** < 750 and 898 cm^{-1}; **5**, 751 and 900 cm^{-1}; **6**, 751 and 900 cm^{-1}) is indicated in the anomeric region of the spectra (950–500 cm^{-1}).[11] These results are further supported in the ^1H NMR studies.

Absorption studies.—Absorption spectra of the complexes **1**–**6** differ from their precursor spectra indicating that ligand H_6L or H_2L* is involved in complex formation with the corresponding metal ions. Complexes of Hg^{2+} **1**, Ag^+ **4**, and Cd^{2+} **5** exhibited similar absorption features where one of the bands is centered at 265 nm and the other at 320 nm. Comparison of these spectra with the corresponding ligand spectra indicated that the intensity of the former is increased dramatically upon complexation in the case of **1**, **4** and **5**. These spectral changes are attributable to the binding of the sulfur group to the metal-ion center in all these cases. In the case of the Zn^{2+} complex **6**, a broad band is observed around 375 nm that is assignable to the metal-to-ligand charge-transfer transition.

CD studies.—CD spectra of the complexes **1**, **3**, **4**, and **6** were compared with that of the ligand H_6L. The figure clearly indicates that large Cotton effects are observed with the complexes, Hg^{2+} **1**, Cu^{2+} **3**, and Zn^{2+} **6**, and almost no or only a weak Cotton effect is observed with the complex Ag^+ **4**. Complexes **1** and **3** exhibit Cotton effects that are opposite in sign to that of **6**, which is perhaps due to a change in the conformation that results in the inversion of the saccharide moiety. In the literature,[12] it has been reported that the Cu^{2+}-saccharide complexes showed opposite sign of rotation when compared to the corresponding saccharide complexes of VO^{2+}, Co^{2+} and Ni^{2+}. This is attributed to the inversion of the saccharide resulting in a conformational change from $^4C_1$ to $^1C_4$ as shown in Fig. 4.

Optical rotation studies.—The characteristics of the ligand in the metal-ion complexes are identified by the sign of the optical rotation, as well as by their specific rotation values. Direct evidence for the presence of α-D configuration is the high-positive specific rotation value (+80°) observed for **1**, which is due to the change in the conformation of the ligand bound to the metal center.

Thermal analysis.—Thermal degradation studies were carried out in a nitrogen atmosphere in the temperature range of 25–850°C, and the data are given in Table 1. Presence of water molecules was observed from the weight loss, and these were found to be 1, 2, 3, 1, and 2, respectively, in **1**, **3**, **4**, **5** and **6**. At high temperatures, the thermograms were found to be exothermic in nature. Complex Hg^{2+} **1** shows 100% degradation as expected, due to the low boiling of mercury and the easy decomposition of its oxides. In

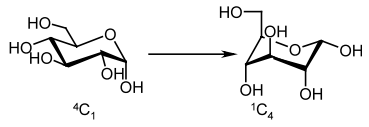

Fig. 4. Inversion of saccharide from $^4C_1$ to $^1C_4$.

Table 1
Thermal analysis data of the ligand H_6L and its metal-ion complexes **1**–**6**

Compound no.	Fragment (%)	Probable species	Temperature (°C)
H_6L	13.8	H_2O+CO	180
	59.9	$H_2O+2CO_2+SO_2$	300
	25.6	NO	530
Hg^{2+} **1**	15	H_2O+3CO	120
	66	$4CO_2+3NO+3SO_2$	360
	19	HgO	480
Cu^{2+} **3**	9.8	$2H_2O$	100
	30.3	$2CO+CO_2$	170
	12.20	CO	320
	27.2	$0.5NO_2+0.5SO_2$	360
	15.6	$0.5NO_2$	680
Ag^+ **4**	12.5	$3H_2O$	140
	40.3	$2.5CO+2CO_2$	240
	12.8	NO	440
	15.7	$0.5SO_2$	540
Cd^{2+} **5**	4	H_2O	120
	38	$2CO+CO_2+NO$	480
	16	1.5NO	500
	7	$0.25SO_2$	590
Zn^{2+} **6**	7.9	$2H_2O$	100
	49	$2CO+2CO_2+2NO$	350
	15	$0.5SO_2$	455
	22	NO_2	470

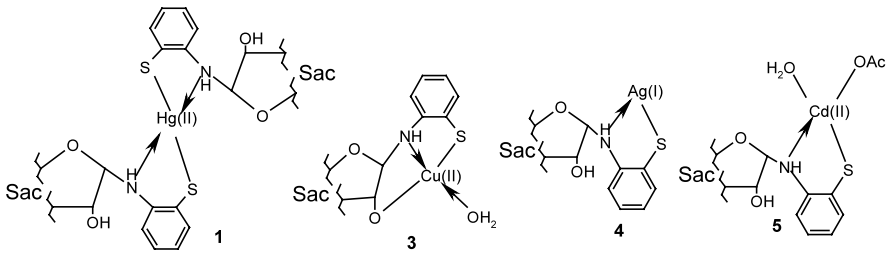

Fig. 5. Proposed structures of the metal-ion complexes **1** and **3**–**5**.

the case of the other complexes, the degradation is found to be in the range of 75-80%.

Solution interaction studies between the metal precursors and H_6L.—Solution interaction studies were carried out by absorption and CD titrations between the corresponding metal precursor and the ligand (H_6L) in methanol. The results obtained from a Job's plot showed the species formed to have metal-to-ligand ratios of 3:2, 2:1, 1:2 and 4:5, respectively, for Hg^{2+}, Cu^{2+}, Cd^{2+} and Zn^{2+}. However, the synthetic reactions carried out, as reported in this paper, resulted in the formation of the complexes with metal-to-ligand ratios of 1:2, 1:1, 1:1 and 2:1, respectively, for Hg^{2+}, Cu^{2+}, Cd^{2+} and Zn^{2+}. Thus the metal-to-ligand ratios observed with the isolated products of the synthetic reactions differ from the species observed in the solution interaction studies due to their solubility characteristics.

Nature of the products and conclusions.—Benzothiazoline derivatives[13] are versatile ligands having potential N-, S-, O-donor atoms and can coordinate in mono and/or in bidentate fashion. While the ligand H_6L exhibited resonances corresponding to five –OH groups, which is consistent with the open-chain form, the metal-ion complexes, **1**, **2**, and **4**–**6** exhibited only four –OH groups due to the formation of a furanose ring. In order to understand the different possible coordination modes between the ligand and the transition-metal ions, the existence of open and closed forms seem to be important. The aminothiophenol group attached to the C-1 position of the saccharide moiety plays a role in the stereochemistry of the resultant coordination compounds. Coordination chemistry of Hg^{2+} is important in view of its toxicity to living systems (by binding to the thiolate groups of cysteine residues), and thus there is need for detoxification of mercury as is generally carried out by some biological systems using metallothionines. While the Hg(II) and Zn(II) exhibited a 1:2 (metal-to-ligand) complex, Ag(I), Cu(II), and Cd(II) exhibited a 1:1 complex, where an acetate moiety was present in the coordination sphere of Cd(II) complex, only. Thus, the Ag(I) complex exhibits linear geometry, whereas all the other complexes exhibit either square-planar or tetrahedral geometry. In the absence of X-ray structures of these complexes, the conformational and structural characteristics cannot be explained in depth. Thus, the D-glucobenzothiazoline derivative may serve as a model compound. Based on the spectral data, the structures of the complexes, **1**, and **3**–**5** are proposed as shown in Fig. 5.

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