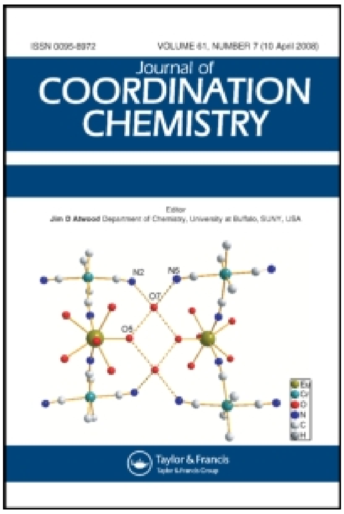

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Interaction of Co(II), Ni(II), Cu(II), and Zn(II) with *N*,*N*′-(aldose)$_2$-thiocarbohydrazide: synthesis, electrochemistry, and spectral characterization[†]

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Complexes of Co(II), Ni(II), Cu(II), and Zn(II) with *N*,*N*′-(aldose)$_2$–thiocarbohydrazide (LH_2) were synthesized, isolated as solid products and characterized by analytical means as well as by spectral techniques, FTIR, ^{1}H NMR, EPR, UV spectroscopy, and CD. All the metal ions formed M[LH]X complexes. Molar conductance values in DMF indicate non-electrolytic complexes. In DMSO with tetramethylammonium chloride supporting electrolyte, the copper complex displays irreversible cyclic voltammetric responses with E_p near −0.621 and 0.461 V *versus* Ag/AgCl at scan rate of 0.1 V s^{-1}. Probable structures for the complexes are proposed.

Keywords: D-Glucose; Thiocarbohydrazide; Metal(II) saccharide complexes; Metal ion interaction

1. Introduction

Carbohydrates have been used to prepare bioactive materials [1], better-targeted drugs [2], and functionalized hydrophobic materials [3]. Metal–carbohydrate interactions are significant in bioinorganic chemistry [4–6]. However, direct metal ion-carbohydrate interactions are difficult to study due to the multifunctionality, complicated stereochemistry, and weak coordinating ability typical of carbohydrates. Carbohydrate ligands with well-tailored binding groups for metal ions such as iminodiacetic acid [7], *tris*(2-aminoethyl)amine [8], 1,4,7-triazacyclononane [6], imino- [9], and amino- [10] phenols, ethylenediamine [11], 1,3-propanediamine [11, 12], and ethylenedicysteine [13] have been attached to carbohydrates to generate a well-defined binding environment and increase the stability of the resultant metal complexes. In our present investigation, thiocarbohydrazide is used as a coordinating fragment attached to carbohydrate through N-glycosylic linkage, providing N and S donor groups. The thiocarbohydrazide in the present investigation was used hoping that the toxophoric functional group –C=S will be away from the coordination site so that it can provide "point of attachment", a system which mimics certain classes of biological systems and such groups could be toxic to microbes when used as drugs. A potential benefit of

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[†] Dedicated to our mentor Professor Vinayak B. Mahale on the occasion of his 65th birthday.

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utilizing this approach is that the carbohydrate remains pendant, being available to interact with carbohydrate transport and metabolic pathways in the body.

2. Results and discussion

The ligand, *N*,*N'*-(aldose)$_2$–thiocarbohydrazide, was prepared by the well-known procedure for the formation of glycosides [11]. The hemiacetal group of carbohydrates (which contains the anomeric carbon) is reactive, and N-glycosidic bond forms readily with condensation of nitrogen-containing compounds. This condensation proceeds *via* release of one water. Glycosidic bonds are fairly stable. Co(II), Ni(II), Cu(II), and Zn(II) complexes of the ligand were prepared in basic medium at pH 8.5 ± 0.5. The isolated and purified metal(II)-saccharide complexes were soluble in methanol, ethanol, etc. Analytical data showed that there is one thiocarbohydrazide and two carbohydrate moieties for every metal (table 1). All complexes were non-electrolytic in nature.

2.1. *IR studies*

In the IR spectrum of the ligand, besides a broad band for the hydroxyl groups, a moderately sharp peak corresponding to $\delta_{\mathrm{N–H}}$ was at $1610\,\mathrm{cm}^{-1}$, which was shifted to higher energy compared with free thiocarbohydrazide, suggesting the glycosidic bond formation.

IR spectra of the complexes are quite different from their parent ligand, suggestive of complex formation. The spectra indicate cleavage of extensive intermolecular hydrogen bonds existing in the parent ligand [14, 15], resulting in a broad band at $3390 \pm 10\,\mathrm{cm}^{-1}$ with a shoulder at $3290 \pm 10\,\mathrm{cm}^{-1}$ upon complex formation. The νNH as compared to ligand is shifted to slightly higher energy. The band observed between 2920 and $2940\,\mathrm{cm}^{-1}$ is assigned to νCH indicating saccharide in the product.

Vibrations corresponding to the anomeric properties of the N-glycosyl amines were observed in the spectra; strong bands observed for all the complexes viz., 760–750, $640–530\,\mathrm{cm}^{-1}$, indicate the presence of both α and β anomers [15], consistent with observations made by NMR studies.

2.2. *^{1}H NMR studies*

The ^{1}H NMR spectra of the ligand and its Zn(II) complex were recorded in DMSO-d_6 and the assignments made by comparison. The comparison clearly demonstrates formation of metal–saccharide complex.

As glycosylation occurs at C-1 by condensation of the saccharide with the thiocarbohydrazide, the spectrum of the corresponding N-glycosyl amine product is devoid of the C–1–OH resonance which is present in the corresponding saccharide spectrum around 6.49–6.78 ppm.

The downfield shift in the glycosylic –NH proton was observed in the complex (9.20 ppm) compared with the ligand, which is at 8.97–8.95 ppm. The downfield shift of the glycosylic N–H in the metal–ion complex indicates coordination of glycosylic nitrogen to the metal.

Table 1. Elemental analysis, molar conductance, and magnetic moment data.

Compound (MW)	Percentage yield (%)	Found (Calcd)%					Molar conductance λ_m (cm^2 ohm l mol^{-1})	Magnetic moment (BM)
		C	H	N	M	Cl		
LH_2 430	65	35.7 (36.3)	6.8 (7.2)	12.7 (13.2)	–	–	–	–
[CoLCl] 524	60	29.2 (29.7)	4.3 (4.9)	10.1 (10.6)	10.8 (11.2)	6.8 (6.7)	1.4	4.4
[NiLCl] 523	70	29.3 (29.8)	3.9 (4.9)	10.2 (10.6)	11.0 (11.2)	7.3 (6.7)	3.8	3.1
[CuLCl] 528	60	28.9 (29.5)	4.2 (4.9)	11.1 (10.6)	11.8 (12.0)	7.1 (6.6)	2.2	1.91
[ZnLCl] 530	65	28.9 (29.4)	4.7 (4.9)	10.1 (10.5)	11.9 (12.3)	6.2 (6.8)	0.9	–

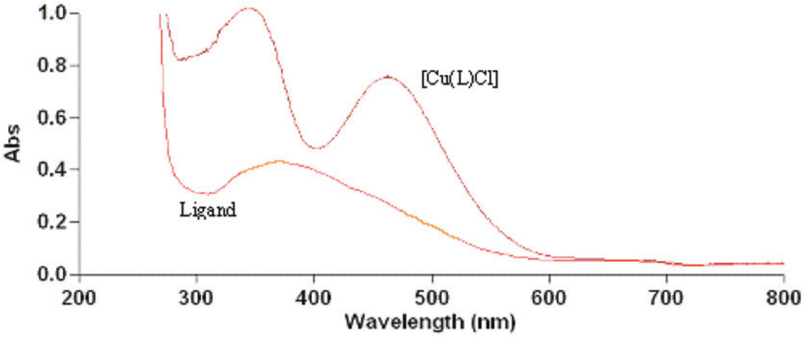


Figure 1. Electronic spectrum of ligand and copper complex.

It is expected that 2-OH groups could shift downfield comparing the chemical shift of the saccharide-OH of the ligand with the zinc complex, as this can be involved in formation of a five-membered chelate with the metal. However, the complex does not exhibit a downfield shift with either –OH group [16, 17]. In the ligand and zinc complex the C–1–H resonance is a doublet at 4.89 nm corresponding to the α and β anomers; two signals were observed for the C–1–NH (glycosyl) around 8.9–9.2 nm also indicating mixtures of anomers [13–17].

2.3. *Electronic spectra*

Comparison of the absorption spectrum of the ligand with that of the metal complexes show the band at 390 nm in the ligand shifted by 40–60 nm to lower wavelength in the metal complexes (figure 1). Except for the zinc complex, the complexes exhibit another band around 470 nm. The ratio of the intensities of both the bands varies slightly in the complexes [16].

2.4. *EPR studies*

The EPR spectrum of Cu(II) complex is recorded at room temperature (300 K), exhibiting a well-resolved signals giving $g_{\mathrm{iso}} = 2.09$ and the complex is isotropic [18].

2.5. *Electrochemistry*

The redox activities of ligand and its complexes were studied in the range +0.2 to −0.8 *versus* the ferrocene–ferrocenium redox system in DMSO (0.1 M tetraethylammonium chloride supporting electrolyte). No peak corresponding to the reduction has been observed down to −0.8 V, as the ligand is electrochemically inactive in the potential range studied; the nickel, cobalt, and zinc complexes were also electrochemically inactive. Cyclic voltammetric responses of copper complex with the scan rate varying from 0.1 to 0.5 $\mathrm{V\,s^{-1}}$ gives evidence for a quasi-reversible one-electron redox process (figure 2). The copper complex exhibits a pair of cathodic and anodic peak potentials at +0.210 V and +0.461 V, respectively, representing the Cu(II)/Cu(I) couple.

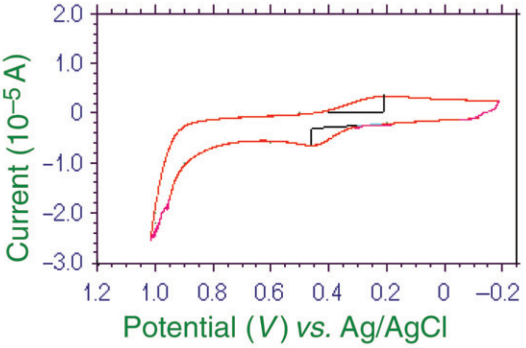


Figure 2. Cyclic voltammogram of copper complex at scan rate of $0.1\,\mathrm{V\,s^{-1}}$.

The observed parameters such as $\Delta E_p > 59\,\mathrm{mV}$ (ΔE_p is the difference in the anodic and cathodic peak potentials) and E_{pc} (cathodic peak potential) shifting negatively with increasing scan rate suggest the quasi-reversible nature of the system [19].

2.6. *CD studies*

CD measurements of ligand and complexes were carried out using 0.1 cm cell in the range 250–500 nm. In free sugars and glycosides, the asymmetric chromophores of significance in determining rotatory characteristics are ring and anomeric oxygens, which absorb in the range 200–250 nm [21].

The ligand with characteristic (+) curve centered at 280 nm indicates dextrorotatory, "*R*" configuration about the C-2 carbon [20] (Supplementary material). The CD spectra of the metal complexes are all exhibited a negative Cotton effect in the region 280–310 nm [16].

2.7. *Magnetic studies*

The magnetic moment values for the cobalt(II) complexes lie within the 4.4–4.6 B.M. range, consistent with a tetrahedral arrangement. For nickel(II) complex the value is in the range 3.1–3.3 B.M., consistent with a tetrahedral environment. For the copper(II) complex the magnetic moment is 1.91 B.M., appreciably above the spin-only value of 1.73 B.M. for Cu(II), suggesting square-planar structure for the complex [21]. The zinc(II) complex is diamagnetic.

2.8. *FAB mass studies*

The FAB mass spectra of the ligand and its complex are used to compare their composition. The ligand shows a molecular ion peak M^+ at $m/z = 431$. The molecular ion peaks for the cobalt, nickel, copper, and zinc complexes were observed at $m/z = 524$, 523, 529, and 531, respectively, with isotopic patterns for copper and chloride. The mass spectra indicate monomeric complexes.

2.9. *Thermal studies*

Thermogravimetric analyses from 25 to 800°C suggest that the complexes are stable at room temperature. The complexes exhibit similar decomposition patterns at higher temperature with two major steps. In copper complex (Supplementary material), the initial weight loss, 11%, in the temperature range 150–200°C is attributed to loss of chloride as HCl. A steady weight loss (62.02%) was observed up to 650°C due to the ligand. No weight loss is observed beyond 650°C, due to formation of the stable metal oxide. Similar decomposition patterns for the complexes suggest similar structures.

3. Experimental

3.1. *Materials, analytical methods, and physical measurements*

All solvents were distilled and dried before use by established procedures. Thiocarbohydrazide was prepared according to literature procedure [22]. D-Glucose (Qualigen Chemicals, India) is used as supplied. The hydrated metal salts were supplied by S-D fine chemicals and used without purification. The metal contents of the complexes were estimated after decomposition with a mixture of HCl and $HClO_4$ by gravimetric method (copper and nickel) and EDTA titration method (cobalt and zinc). Magnetic susceptibilities were measured at room temperature on a Faraday balance using $Hg[Co(SCN)_4]$ as calibrant. Electronic spectra were recorded using a UV-160A UV-Visible spectrophotometer (Shimadzu) in DMSO. The IR spectra were recorded as KBr pellets from 4000 to 400 cm^{-1} on a Nicolet 170 SX FT-IR spectrometer. The ^{1}H-NMR spectra of the ligand and its zinc(II) complex were recorded in DMSO-d_6 on a Bruker 300 MHz spectrometer using TMS as an internal standard. EPR spectrum of copper(II) complex was recorded at room temperature on a Varian E-4 X-band spectrometer using TCNE as *g*-marker. Thermogravimetric measurements were carried out in nitrogen on a Rigaku thermoflex instrument at a heating rate of 10°C min^{-1}. The FAB mass spectra were recorded on a JEOL EX 102/DA-6000 mass spectrometer/Data system using Argon/Xenon (6 kV, 10 mA) as the FAB gas. Conductivities were measured on 10^{-3} M solutions in DMSO using an ELICO-CM82 Conductivity bridge provided with a cell having cell constant 0.51. The cyclic voltammetry experiments were carried out with a three electrode apparatus using a CHI1110A electrochemical analyzer (USA). The CD measurements were made on a JASCO-J-715 spectropolarimeter using 0.1 cm cell. Electroanalytical measurements were performed using a CHI1110A electrochemical analyzer (USA). Cyclic voltammetric data were recorded using a glassy carbon working electrode (0.082 cm^2), a platinum counter electrode, and a Ag/Ag^+ reference electrode. Glassy carbon electrode surfaces were polished with 0.05 mm alumina, rinsed in water, and air-dried immediately before use. The positions of the electrochemical waves were compared to the potential of the ferrocene/ferrocenium couple. The DMSO solution (containing 0.1 M tetraethylammonium chloride, as supporting electrolyte, 10^{-3} molar of the ligand and each of the complexes) was placed in a single-compartment electrochemical cell and degassed by bubbling with N_2(g) saturated with DMSO. A N_2 atmosphere was continuously maintained above the solution while the experiments were in progress.

3.2. *Preparation of ligand*

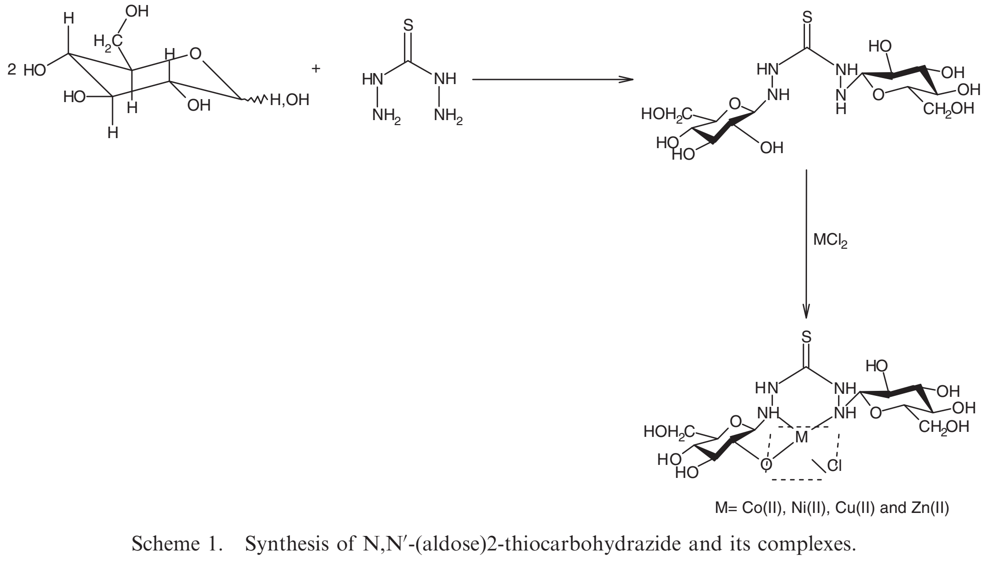
D-Glucose (2 g, 0.1802 mmol) is treated with thiocarbohydrazide (0.5884 g, 0.1602 mmol) in the presence of a small catalytic amount of NH_4Cl in refluxing methanol (50 mL) for 2 h. The separated product is washed with methanol and diethyl ether and dried under vacuum.

3.3. *Preparation of complexes*

The complex was prepared by addition of methanolic solution of metal(II) chloride (0.003 mol) with constant stirring to the ligand (0.003 mol) in the same solvent at room temperature. After a sufficient time of stirring, the reaction mixture was concentrated. The copper complex separates as dark greenish precipitate and cobalt, nickel and, zinc complexes precipitated after addition of isopropanol. All complexes were filtered and washed with methanol and dried in vacuum over P_2O_5.

4. Conclusion

The present study demonstrates the binding of N-Glycosyl saccharide and Co(II), Ni(II), Cu(II), and Zn(II) chlorides. Elemental analysis and molar conductance studies reveal mononuclear, non-electrolyte complexes. The "*N*,*N*′-(aldose)$_2$–thiocarbohydrazide" is a mixture of the α and β anomers. The specific rotation of the ligand is positive (dextrorotatory), consistent with the corresponding anomeric assignments. Complexation with different metal ions shows binding of the glycosylic-NH, C–2–OH group from one saccharide residue and –NH of the thiocarbohydrazide, as a monobasic, tridentate "ONN" donor. The structures are proposed as shown in scheme 1.



Scheme 1. Synthesis of N,N′-(aldose)2-thiocarbohydrazide and its complexes.

The M(II)–saccharide complexes exist at physiological pH, but complexation is favored under alkaline conditions. It is hoped metal-binding properties of D-Glucose would aid in understanding metal ions interacting with saccharides, as an actual biological system. Further work is in progress in our lab by selective blocking of the saccharide unit.

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References

[1] P. Sears, C.H. Wong. *Angew. Chem.*, **111**, 2446 (1999).

[2] M. Rouquayrol, W. Gaucher, J. Greiner, A.M. Aubertin, P. Vierling, R. Guedj. *Carbohydr. Res.*, **336**, 161 (2001).

[3] V. Sol, J.C. Blais, V. Carre, R. Granet, M. Guilloton, M. Spiro, P. Krausz. *J. Org. Chem.*, **64**, 4431 (1999).

[4] K.E. Bullok, M. Dyszlewski, J.L. Prior, C.M. Pica, V. Sharma, D. Piwnica-Worms. *Bioconjugate Chem.*, **13**, 1226 (2002).

[5] P. Klüfers, T. Kunte. *Chem. Eur. J.*, **9**, 2013 (2003).

[6] T. Tanase, H. Inukai, T. Onaka, M. Kato, S. Yano, S.J. Lippard. *Inorg. Chem.*, **40**, 3943 (2001).

[7] C. Dumas, R. Schibli, P.A. Schubiger. *J. Org. Chem.*, **68**, 512 (2003).

[8] T. Tanase, T. Onaka, M. Nakagoshi, I. Kinoshita, K. Shibata, M. Doe, J. Fujii, S. Yano. *Inorg. Chem.*, **38**, 3150 (1999).

[9] M.J. Adam, L.D. Hall. *Can. J. Chem.*, **60**, 2229 (1982).

[10] S.R. Bayly, C.L. Fisher, C.L.T. Storr, M.J. Adam, C. Orvig. *Bioconjugate Chem.*, **15**, 923 (2004).

[11] Y. Mikata, Y. Shinohara, K. Yoneda, Y. Nakamura, K. Esaki, M. Tanahashi, I. Brudzinska, S. Hirohara, M. Yokoyama, K. Mogami, T. Tanase, T. Kitayama, K. Takashiba, K. Nabeshima, R. Takagi, M. Takatani, T. Okamoto, I. Kinoshita, M. Doe, A. Hamazawa, M. Morita, F. Nishida, T. Sakakibara, C. Orvig, S. Yano. *J. Org. Chem.*, **66**, 3783 (2001).

[12] M.J. Chen, P.G. Heeg, W. Brauschweiger, H. Xie, P.G. Wang. *Angew. Chem.*, **111**, 1882 (1999).

[13] D.J. Yang, C.G. Kim, N.R. Schechter, A. Azhdarinia, D.F. Yu, C.S. Oh, J.L. Bryant, J.J. Won, E.E. Kim, D.A. Podoloff. *Radiology*, **226**, 465 (2003).

[14] V.N. Gristan, V.P. Panov, V.G. Kachur. *Carbohydr. Res.*, **112**, 11 (1983).

[15] H.A. Tajmir-Riahi. *Carbohydr. Res.*, **183**, 35 (1988).

[16] T. Mohan Das, C.P. Rao, E. Kolehmainen. *Carbohydr. Res.*, **335**, 151 (2001).

[17] T. Mohan Das, C.P. Rao, E. Kolehmainen. *Carbohydr. Res.*, **334**, 261 (2001).

[18] V.K. Revankar, V.H. Arali, V.B. Mahale. *Indian J. Chem.*, **29A**, 889 (1990).

[19] C. Ramachandraiah. *J. Am. Chem. Soc.*, **116**, 6733 (1994).

[20] T. Tanase, K. Mano, Y. Yamamoto. *Inorg. Chem.*, **32**, 3995 (1993).

[21] M. El-Tabl, F.A. El-Saied, M.I. Ayad. *Synth. React. Inorg. Met-Org. Chem.*, **32**, 1189 (2002).

[22] L.F. Audrieth, E.S. Scott, P.S. Kippur. *J. Org. Chem.*, **19**, 733 (1954).