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SPECTRAL, BIOLOGICAL, MAGNETIC AND CONDUCTANCE STUDIES ON THE COORDINATION COMPOUNDS OF A NEWLY SYNTHESIZED THIAZOLIDIN-4-ONE

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Abstract. A dry benzene solution of the Schiff base, N-(2-hydroxyphenyl)-3‘-carboxy-2‘-hydroxybenzylideneimine upon reacting with mercaptoacetic acid undergoes cyclization and forms N-(2-hydroxyphenyl)-C-(3‘-carboxy-2‘-hydroxyphenyl) thiazolidin-4-one, LH_3 (**I**). A MeOH solution of **I** reacts with Co^{II} and Cd^{II} ions and forms the monomeric coordination compounds, $[Co(LH)(MeOH)_3]$(**II**) and [Cd(LH)(MeOH)](**III**). The coordination compounds have been characterized on the basis of elemental analyses, molar conductance, molecular weight, spectral (IR, reflectance, NMR) studies and magnetic susceptibility measurements. **I** behaves as a dibasic tridentate OOS donor ligand in these compounds. The compounds are non-electrolytes (L_M = 5.1-7.8 mho cm^2 mol^{-1}) in DMF. A tetrahedral structure for **III** and an octahedral structure for **II** are suggested. The ligand (**I**) and its coordination compounds shows antibacterial and antifungal activities towards bacteria, *E. Coli*. (Gram Negative) and *S. Aureus* (Gram Positive) as well as towards fungus, *Candida Albicans*. *Keywords:* thiazolidin-4-one, coordination compounds, magnetic susceptibility, magnetically dilute, strong field and covalent character

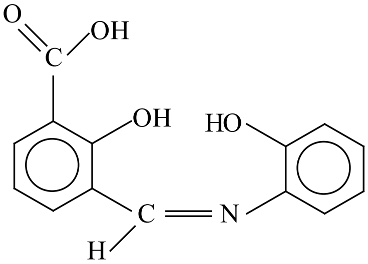
Keywords: spectral; biological; magnetic and conductance studies; newly synthesized thiazolidin-4-one

Introduction

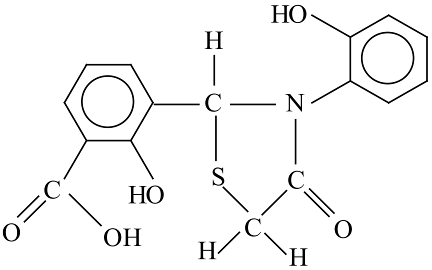
Thiazolidin-4-ones belong to an important group of heterocyclic compounds with carbonyl group at fourth position. These containing S and N in five member ring obtained by cyclocondensation of imines with mercaptoacetic acid. These are important class of heterocyclic compounds owing to their versatile pharmacological and industrial importance (Gashaw et al., 2013).

They have been studied extensively because of their ready accessibility, diversed chemical reactivity and broad spectrum of biological activities (Patel et al., 2011). The presence of a thiazolidinone ring in penicillin and related derivatives was the first recognition of its occurrence in nature (Pulici & Quartieri, 2005).

Thiazolidin-4-ones are also known to exhibit antibacterial (Sawale et al., 2012), antimicrobial (Ahirwar & Shrivastava, 2011), antifungal (Bhatt et al., 1994), antitubercular (Myangar et al., 2012) and antioxidant (Kato et al., 1999) activities. A perusal of the literature reveals that much has been reported on the syntheses and characterization (Belbehani & Ibrahim, 2012) of a variety of thiazolidin-4-ones, but little is known about their coordination compounds (Kumar et al., 2013a). Many drugs possess modified pharmacological properties in the form of the metal complexes (Anacona & Estacio, 2006). These facts prompted us to explore the ligational behavior of a newly synthesized thiazolidin-4-one, LH_3 (**I**) towards Co^{II} and Cd^{II} ions.



[**Schiff base**]



[**I**]

Experimental

Materials

2-Aminophenol [Loba-Chemie (Mumbai)], mercaptoacetic acid, dry benzene, sodium bicarbonate [Ranbaxy], cadmium(II) acetate dihydrate [Sarabhai], cobalt(II) acetate tetrahydrate [BDH] were used as received for the syntheses. 3-Aldehydo-2-hydroxybenzoic acid was synthesized by following the reported procedure (Kumar et al., 2010).

Analyses and physical measurements

The organic skeleton of the respective coordination compounds was decomposed by the slow heating of ~ 0.1 g of the latter, with conc. HNO_3. The residue was dissolved in minimum amount of conc. HCl and the corresponding metal ions were estimated as follows: The Co(II) and Cd (II) contents in the respective coordination compounds were estimated by the complexometric titration method against standardized EDTA solution using xylenol orange as an indicator. The C, H and N contents of LH_3 and its coordination compounds were determined by CHN Eager analyzer model-300. The S contents were estimated gravimetrically as $BaSO_4$. The molecular weight measurements were carried out by the Rast method using diphenyl as the solvent (Mann & Saunders, 1961).

The molar conductances (L_M) of the coordination compounds were measured in DMF with the help of a Toshniwal conductivity bridge (CL01-02A) and a dip type cell calibrated with KCl solutions. The IR spectra were recorded in KBr pellets (4000 – 400 cm^{-1}) on a Beckman-20 spectrophotometer. The reflectance spectra were recorded on a Beckmann DU spectrophotometer attached with a reflectance arrangement. The magnetic susceptibility measurements were carried out at room temperature, using $Hg[Co(NCS)_4]$ as the standard (Dutta & Syamal, 1993). The diamagnetic corrections were computed using Pascal's constants. The magnetic susceptibilities were corrected for temperature independent paramagnetism term (TIP) (Dutta & Syamal, 1993) using value of 200 ´ 10^{-6} cgs units for Co (II) ions.

Synthesis of the Schiff base

A MeOH solution (30 mL) of 2-aminophenol (1.09 g, 10 mmol) was added to a MeOH solution (30 mL) of 3-aldehydo-2-hydroxybenzoic acid (1.66 g, 10 mmol) and the mixture was refluxed for 2 *h*. The precipitates formed were suction filtered, washed with MeOH and dried *in vacuo* at room temperature over silica gel for 24 *h*. Yield = 87%. The elemental analyses of the compound gave the satisfactory results.

Synthesis of LH_3(**I**)

A dry benzene solution of the Schiff base (2.57 g, 10 mmol) and mercaptoacetic acid (0.92 g, 10 mmol) were refluxed for 12 *h* on a water bath. The mixture was cooled to room temperature and then was washed with 10% sodium bicarbonate solution. The benzene layer was separated using a separating funnel. The partial evaporation of the benzene layer gave a solid product, which was filtered, washed with and recrystallized from petroleum ether. Yield = 25%. *Anal*: (**I**, $C_{16}H_{13}NO_5S$) (obsd: C, 57.80%; H, 3.75%; N, 4.10%; S, 9.50%. calc.: C, 58.01%; H, 3.93%; N, 4.23%; S, 9.67%); IR bands (KBr): 2860cm^{-1} [ν(O—H) (intramolecular H-bonding)], 1700 cm^{-1} [ν(C==O)(thiazolidinone ring)], 1670 cm^{-1} [ν(C==O) (carboxylic)], 1575 cm^{-1} [ν(C—N)(thiazolidinone ring)],1525 cm^{-1} [ν(C—O) (phenolic)] and 835 cm^{-1} [ν(C—S)(thiazolidinone ring)].

Syntheses of coordination compounds of **I**

A MeOH solution (30-50 mL) of the appropriate metal salt (10 mmol) was added to a MeOH solution (50 mL) of **I** (3.31 g, 10 mmol) and the mixture was then refluxed for 3-4 *h*. The solid products formed were suction filtered, washed with and recrystallized from MeOH and were then dried as mentioned above. Yield = 50 – 80%.

Results and discussion

The nucleophilic addition reaction between 3-aldehydo-2-hydroxybenzoic acid and 2-aminopohenol followed by the elimination of one water molecule results in the formation of the Schiff base, N-(2-hydroxyphenyl)-3‘-carboxy-2‘-hydroxybenzylideneimine. A dry benzene solution of the above Schiff base reacts with mercaptoacetic acid and forms N-(2-hydroxyphenyl)-C-(3‘-carboxy-2‘-hydroxyphenyl)thiazolidin-4-one, LH_3 (**I**). The reaction of **I** with appropriate metal ions in 1:1 molar ratio in MeOH produces the coordination compounds, $[Co(LH)(MeOH)_3]$ and $[Cd(LH)(MeOH)]$. The formations of **I** from the Schiff base and the coordination compounds of the latter take place according to the Schemes **I** and **II**.

$$\text{Schiff base} \xrightarrow[\text{dry benzene}]{\text{HS-CH}_2\text{ COOH}} \mathbf{I}$$

Scheme 1. Preparative scheme of LH_3 (I)

$$LH_3 + Co(OAc)_2{\cdot}4H_2O \xrightarrow[\text{Reflux}]{\text{MeOH}} [Co(LH)(MeOH)_3] + 2CH_3COOH + 4H_2O$$

$$LH_3 + Cd\,(OAc)_2{\cdot}2H_2O \xrightarrow[\text{Reflux}]{\text{MeOH}} [Cd\,(LH)(MeOH)] + 2CH_3COOH + 2H_2O$$

Scheme 2. Preparative scheme of coordination compounds of LH_3 **(I)**

The coordination compounds are stable at room temperature. They are insoluble in H_2O, partially soluble in MeOH, EtOH and completely soluble in DMSO and DMF. Their molar conductance measurements (L_M = 5.1 – 7.8 mho $cm^2\ mol^{-1}$) in DMF indicate their non-electrolytic nature. The analytical data of **I** and its coordination compounds are presented in Table 1.

Table 1. Analytical, molar conductance (Λ_M) and molecular weight data of LH_3 [I] and its coordination compounds

Compound	Mol. Formula	ΛM (mho cm^2 mol^{-1})	Mol. wt obsd (calcd)	obsd(calcd)%				
				M	C	H	N	S
LH_3	$C_{16}H_{13}NO_5S$	–	331[a] (331.0)	–	57.80 (58.01)	3.75 (3.93)	4.10 (4.23)	9.50 (9.67)
$[Co(LH)(MeOH)_3]$	$CoC_{19}H_{23}NO_8S$	5.1	497.8[b] (483.9)	12.34 (12.17)	46.90 (47.12)	4.82 (4.75)	2.83 (2.89)	6.50 (6.61)
[Cd(LH)(MeOH)]	$CdC_{17}H_{15}NO_6S$	7.8	497.3[b] (473.4)	23.50 (23.74)	43.26 (43.09)	3.00 (3.17)	2.70 (2.96)	6.50 (6.76)

Abbreviations: [a]Mass spectral data, [b]Rast method data

Infrared spectral studies

The infrared spectra of the Schiff base, **I** and the coordination compounds of the latter were recorded in KBr and the prominent peaks (in cm^{-1}) are shown in **Table 2**. The Schiff base exhibits the ν(C==N)(azomethine) stretch at 1630 cm^{-1}. This band disappears in **I** and a new band due to the ν(C—N) (thiazolidinone ring) stretch (Shrivastava et al., 2012) appears at 1575 cm^{-1} indicating the conversion of the Schiff base into **I**. The formation of **I** is further supported by the appearance of a new band at 835 cm^{-1} due to the ν(C—S) (thiazolidinone ring) stretch (Kumar & Kumar, 2012). This band shows a negative shift by 20-40 cm^{-1} in the coordination compounds indicating the involvement of the S atom of the thiazolidinone moiety towards coordination (Kumar et al., 2013b). The ν(C==O)(thiazolidinone ring) stretch (Parekh et al., 2004) of **I** occurs at 1700 cm^{-1}. This band remains unchanged in the coordination compounds indicating the non-involvement of O atom towards the coordination. The strong band due to the intramolecular H-bonded OH group of phenolic and/or carboxylic acid moieties (Bahad et al., 2000) occurring at 2860 cm^{-1} disappears in the coordination compounds indicating the breakdown of H-bonding and subsequent deprotonation of the OH group followed by the involvement of phenolic and carboxylic acid O atoms towards coordination. The presence of a broad band at ~3400 cm^{-1} due to νν(O—H) (MeOH) and the decrease of νν(C—O)(MeOH) stretch from 1034 cm^{-1} to lower energy by 44 – 58 cm^{-1} in the coordination compounds indicate the involvement of the O atom of MeOH towards coordination (Kumar et al., 2013b). The appearance of two new bands between 1558 – 1570 cm^{-1}, ν_{as}(COO) and 1345-1356 cm^{-1}, ν_s(COO) stretches indicate the presence of the coordinated carboxylato group in the coordination compounds. The energy difference (Δν = 213 – 214 cm^{-1}) between these stretches is > 210 cm^{-1} and it indicates the monodentate nature of the carboxylato moiety (Anacona & Toledo, 2001). The ν(C—O) ф stretch (Kumar et al., 2013b) of **I** occurs at 1525 cm^{-1}. This band shifts to higher energy by 7 – 10 cm^{-1} in the coordination compounds indicating the involvement of phenolic O atom of either 3-aldehydo-2-hydroxybenzoic acid or 2-aminopohenol moieties towards coordination. On the basis of steric grounds, we suggest the non-involvement of phenolic (2-aminophenol moiety) O atom towards coordination.

Table 2.IR, reflectance spectral data (cm^{-1}) and magnetic moments of coordination compounds of LH_3 [I]

Compound	v_{as}(COO)	v_s(COO)	v(C–O) (phenolic)	N(C–S)	v(C–O) (MeOH)	n_{max}	Mag. moment (B. M.)
LH_3	–		1525	835	–	–	Diamagnetic

[Co(LH)(MeOH)$_3$]	1570	1356	1535	795	976	9150, 12950, 19100	4.71
[Cd(LH)(MeOH)]	1558	1345	1532	815	990	–	Diamagnetic

NMR spectral studies

The NMR spectra of **I** and [Cd(LH)(MeOH)] were recorded in DMSO-d_6. The chemical shifts (δ) are expressed in ppm downfield from TMS. The prominent resonance signals of these compounds were compared with the reported peaks (Nag et al., 2005). **I** exhibits a singlet at δ 17.5 ppm due to the carboxylic proton, a sharp singlet at δ 13.61 ppm due to phenolic proton, multiplets between δ 7.36 – 7.71 ppm due to the aromatic protons. The absence of the signal at δ 17.5 ppm due to the COOH proton in [Cd(LH)(MeOH)] indicates the deprotonation of the COOH group, followed by the involvement of its O atom in coordination. The absence of the resonance signal at δ 13.61 ppm due to the phenolic proton in [Cd(LH)(MeOH)] indicates the deprotonation of the phenolic OH group followed by its involvement in coordination (Kumar et al., 2015).

Reflectance spectral studies

The presence of three bands at 9150 12950 and 19100 cm^{-1} due to the $^4T_{1g}(F) \rightarrow {}^4T_{2g}(\nu_1)$,$^4T_{1g}(F) \rightarrow {}^4A_{2g}(\nu_2)$ and$^4T_{1g}(F) \rightarrow {}^4T_{1g}(\nu_3)$transitions, respectively suggests an octahedral arrangement of **I** around Co^{II} ions in [Co(LH)(MeOH)$_3$] (Lever, 1984). The ν_3/ν_1 value in the present Co^{II} compound is 2.09 which lies in the usual range (2.00-2.80), reported for the majority of octahedral Co^{II} compounds (Lever, 1984). The spectral parameters (Huheey, 1983) are: $10Dq$ = 10280 cm^{-1}, B' = 738 cm^{-1}, $\beta = B'/B$ = 0.76, β^0 = 24% and CFSE = −98.21 kJ mol^{-1}. The reduction of Racah parameter from the free ion value of 971 cm^{-1} to 738 cm^{-1} and the β^0 value of 24% indicate the covalent nature of the compound and the strong field nature of the tridentate ligand (Dutta et al., 1993).

Table 3. Antimicrobial activity of LH$_3$ [I] and its Coordination compounds (Zone of Inhibition in mm)

Compound	**E.Coli (Gram negative)**	**S. Aureus (Gram positive)**	***Candida Albicans***
LH$_3$	7	6	7
[Co(LH)(MeOH)$_3$]	8	7	9
[Cd(LH)(MeOH)]	10	10	10

Magnetic measurements

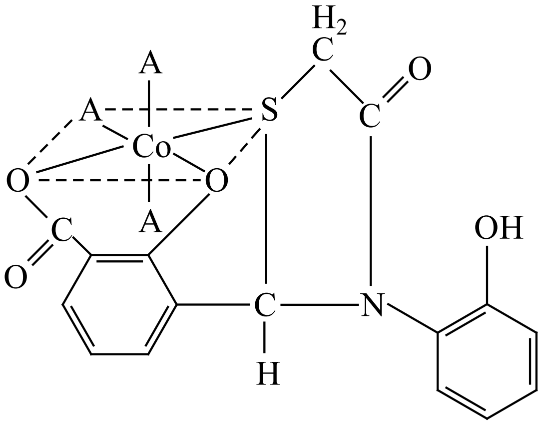
The room temperature magnetic moment of [Co(LH)$(MeOH)_3$] is 4.71 B.M. [Table 2). The value indicates its magnetically dilute high-spin nature (Cotton et al., 1999). The [Cd (LH)(MeOH)] is diamagnetic as expected.

Antimicrobial studies

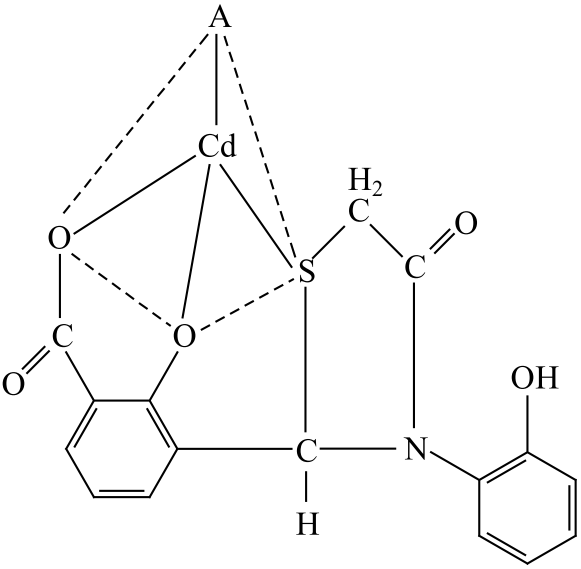
The antimicrobial activity of ligand (**I**) and its complexes were tested against fungus, *Candida Albicans* and bacteria, *E.Coli* (Gram negative) and *S. aureus* (Gram positive) by using disc diffusion method. Stock solution were prepared by dissolving compounds in DMSO. Under aseptic conditions, plain sterilised discs were soaked in solution of compounds for overnight. Test culture was spread over the plates containing Sabourads Dextrose Agar (SDA) for *Candida Albicans* and Mueller Hinton Agar (MHA) for *E.Coli* and *S. aureus* by using sterile swab. Inoculated plates were dried for 30 minutes and discs were placed on inoculated plates. The plates were left for 30 minutes at room temperature to allow diffusion. The plates were then incubated at 25^0C for 48 – 72 hours for *Candida Albicans* and at 37^0C for 24 hours for *E.Coli* and *S. aureus*. After incubation, diameter of zone of inhibition were noted for each disc (Table 3).

Conclusions

Thus, on the basis of analytical, molecular weight, spectral and magnetic studies, we suggest a tetrahedral structure, **III** for [Cd(LH)(MeOH)] and an octahedral structure **II** for [Co(LH)$(MeOH)_3$].



[**II**, A = MeOH]



[**III**, A = MeOH]

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