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Syntheses, Spectral Characterization of Ni Ions with Schiff Base Containing Aliphatic and Aromatic Hydrazide Moieties

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Abstract

C_2H_5OH solution of 3-ketobutanehydrazide and salicylhdrazide in equimolar ratio forms the corresponding Schiff base LH_3 and reacts with Ni(II) ions to forms [Ni(LH)(MeOH)$_3$]

1 Introduction

Aroyl hydrazones and their coordination compounds are known to possess the biological activities and inhibit many enzymatic reactions in the cell. Owing to their biological activities such as antifungal, antibacterial, antimycobacterial, antitumor, anti inflammatory, anti-HIV, leishmanicidal, trypanocidal, inhibitor of anthrax lethal factor, antidiabetic, antimalarial, and antipyretic, there has been an increasing interest towards the studies of the coordination compounds of the Schiff bases containing the hydrazone moiety during the past few decades [1–12]. The coordination compounds containing hydrazone moiety have been reported to act as analytical reagents, such as polymer coatings, fluorescent materials [13, 14], enzymes inhibitors, antifungal/antibacterial agents [15, 16], and corrosion inhibitors [17]. A perusal of the literature reveals thatmuch work has been carried out towards the coordination compounds of Schiff bases containing salicylhydrazide moiety [18–27]; however, no work seems to be reported on the coordination compounds of Schiff base derived from 3-ketobutanehydrazide and salicylhydrazide.Novel noncytotoxic salicylhydrazide-containing 1N inhibitors have been developed through substructure database search methods [28]. The developmental progress of the salicylhydrazide class of 1N inhibitors was halted due to cytotoxicity issues. The salicyloylhydrazide moiety has been reported to be the minimally required substructure for 1N inhibitory potency of the compounds [29]. The salicylhydrazides have also been proposed to inhibit 1N catalytic activity through chelation of the active site Mg^{2+}, and they exhibit cytotoxicity in the nano molar range. The replacement of one of the two phenols in N,N-bis-salicylhydrazide with an optimally substituted heterocyclic group (heavily substituted triazole groups) renders a novel class of noncytotoxic salicylhydrazides, greatly enhancing the therapeutic potential of this class of 1N inhibitors. Keeping in view the above importance of the compounds possessing hydrazone moiety,we thought it worthwhile to synthesize and characterize the Schiff base, LH3 (1) with Ni(II), ions.

2. Experimental

Materials. Nickel(II) acetate tetrahydrate, ethyl acetoacetate, methyl salicylate[Loba Chemie],hydrazine hydrate[Fisher Scientific],ammonium molybdate tetrahydrate,hexadecaaquaoctahydroxotetrazirconium(IV) chloride [BDH],DMSO, DMF, MeOH, EtOH, 1,4-dioxane, and THF [Ranbaxy] were used as received for the syntheses.Bis(acetylacetonato) dioxomolybdenum(VI) and hexadecaaquaoctahydroxotetrazirconium (IV) acetate were synthesized according to the literature procedures [30, 31]. **Analytical and PhysicalMeasurements**. The estimation ofmetal contents, spectral studies (IR, reflectance, 1H NMR, ESR), and the magnetic susceptibility measurements were carried out by the methods reported earlier [32]. The melting points of the compounds were determined on digital melting point apparatus (Stuart SMP-40). For the purification of KBHz, SHz and chromatographic separations were carried out using silica gel columns (160–200 mesh) of varying length. Thin-layer chromatography (TLC) was performed on commercial Merck plates coated with a 0.20mmlayer of silica gel. The molar conductances of the coordination compounds in DMSO were carried out using Toshniwal conductivity bridge (Model CL01-02A) and a dip type cell calibrated with KCl solution.Carbon, hydrogen, and nitrogen contents of the compounds were determined on a FLASHEA1112 CHNS (O) analyzer. The IR spectra of complexe was recorded in KBr (4000–250 cm−1) on a Fourier Transform Infrared spectrometer (Model RZX, Perkin Elmer). The reflectance spectra were recorded on a Hitachi-330UV-vis-NIR spectrophotometer.1H NMR spectra of 3-ketobutanehydrazide and complexe compound were recorded on an Avance-II (Bruker) FT NMR spectrometer at 400MHz using DMSO as a solvent and TMS as an internal standard. **Synthesis and Characterization**

Synthesis of 3-Ketobutanehydrazide (KBHz) Hydrazine hydrate (4.50 g, 100mmol) was added slowly with continuous stirring to an ice-cooled EtOH solution (30mL) of ethyl acetoacetate (15.0 g, 100mmol) during a period of 0.5 h. The reaction mixture was refluxed on a water bath for 2 h. The white compound separated out was suction filtered, washed with EtOH and recrystallised from EtOH, and dried in vacuo over silica gel at room temperature. The progress of the reaction was monitored on TLC using hexane and Et2O (1 : 1 v/v) as eluent. Color: white. M. p. = 186◦C. Yield: 10.5 g (90%).Anal. Calcd. for $C_4H_8N_2O_2$: C, 41.30; H, 6.91; N, 24.05; Found: C, 41.25; H, 6.95; N, 24.15. IR bands (cm−1): 3299 ν(OH) (intramolecular H-bond), 2898 ν(N–H) (intramolecular H-bond), 1678 ν(C=O) (keto), 1619 δ(NH2), and 1042 ν(N–N) (hydrazide). 1H NMR (400MHz; DMSO-d6; δ ,ppm): 1.28 (s, 3H, –CH_3), 2.59 (s, 2H, –CH_2), 5.25 (br, 2H, –NH_2) and 7.80 (br, 1H, –CONH).

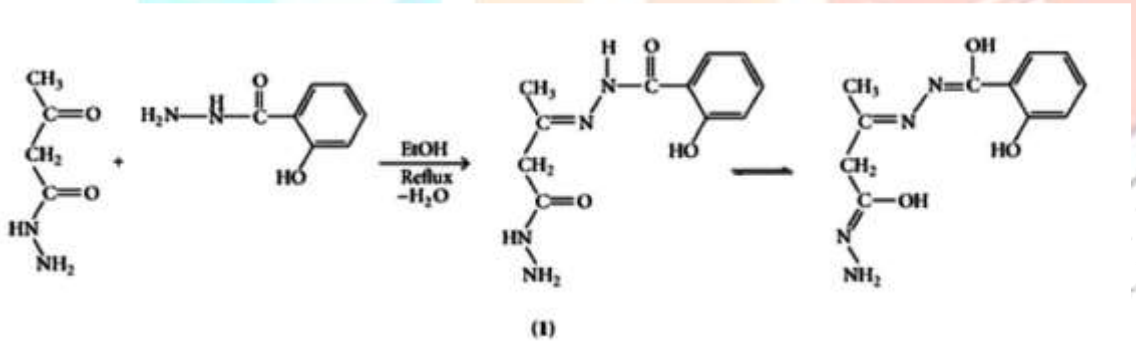
Synthesis of 1. 3-Ketobutanehydrazide (11.8 g, 100 mmol) and salicylhydrazide (15.0 g, 100mmol) were refluxed in EtOH(50 mL) on a water bath for 2 h. The excess of solvent was distilled off, and the yellow compound separated out was allowed to stand at room temperature. The compound was suction filtered, washed with EtOH and recrystallized from EtOH, and dried as mentioned above. The progress of the reaction was monitored on TLC using hexane and Et_2O (1 :1v/v) as eluent. Color: yellow. M. p. = 108◦C. Yield: 22.8 g (90%). Anal. Calcd. for $C11H_{14}N_4O_3$: C, 52.0; H, 5.65; N, 22.30; Found: C, 52.70; H, 5.70; N, 22.45. IR bands (cm−1):3267 ν(OH) (intramolecular H-bond), 2720 ν(N–H) (intramolecular H-bond), 1618 ν(C=N) (azomethine), 1533 ν(C–O), 1238 ν(C–O) (enol) and 1013 ν(N–N).1H NMR(400MHz; DMSO-d6; δ, ppm): 2.14 (s, 3H, $–CH_3$), 2.56 (s,2H, $–CH_2$), 5.24 (d, 2H, $–NH_2$), 6.84–7.80 (m, 4H, –ArH), 8.0 (s, 1H, –N=COH) (adjacent to aliphatic moiety), 9.9 (br,1H, –OH) (phenolic), 12.25 (s, 1H, –N=COH) (adjacent to aromatic moiety).

3. Results and Discussion

The nucleophilic addition reaction between 3-ketobutanehydrazide and salicylhydrazide in equimolar ratio in EtOH followed by the elimination of one water molecule results in the formation of the Schiff base, LH3 (1) (Scheme 1). A MeOH solution of 1 reacts with a MeOH solution of Ni(II), ions and forms the corresponding coordination compounds, 2–7 (Scheme 2).The coordination compounds are insoluble in H_2O,EtOH, dioxane, and THF, but they were soluble in DMF and DMSO. Their molar conductance data (3.5–11.8Ω^{-1} cm^2 mol^{-1} in DMSO) reveal their non electrolytic nature. They are stable up to 250◦C and get decomposed above this temperature. Attempts to obtain single crystal suitable for X-ray determination were unsuccessful. The structures of the synthesized ligand and metal complexe (Schemes 1 and 2) were established with the help of elemental analyses data, IR and NMR spectra.

Infrared Spectral Studies The IRspectra of KBHz and compound was recorded in KBr. The ν(C=N) (azomethine) stretch of 1 shifts to lower energy by 7–24 cm^{-1} indicating coordination through its azomethine N atom [38]. The ν(C–O) stretch of 1 occurring at 1532 cm^{-1} remains unaltered indicating the noninvolvement of phenolic O atom towards coordination [39]. The ν(C–O) (enolic) stretch of the Schiff base shifts from 1238 cm^{-1} to higher energy by 8–18 cm^{-1} in Ni coordination through its enolic O atom[39].Thus, 1 behaves as a dibasic tridentate ONO donor ligand in Ni coordinating through its azomethine N and both enolic O atoms. The involvement of enolic O and azomethine N atoms towards coordination is further supported by the appearance of new nonligand bands between 570–590 and 478–480 cm^{-1} due to the ν(M–O) and ν(M–N) vibrations in Ni complexe . These bands are in the expected order of increasing energy: ν(M–N)< ν(M–O) [40] as expected due to the greater dipole moment change in the M–O vibration, greater electronegativity of the O atom than N atom, and shorter M–O bond length than the M–N bond length [41].

Reflectance Spectral Studies Ni shows three bands at 9250, 15360, and 24095 cm^{-1} due to the $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$(ν 1),$^3A2g(F) \rightarrow {}^3T_{1g}(F)$(ν2) and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$(ν3) transitions, respectively, suggesting an octahedral geometry around the metal ion [46]. Using the free ion value of B = 1030cm^{-1}, the values of spectral parameters in Ni are as follows:10Dq = 9252cm^{-1}, B = 743.64 cm^{-1}β=0.72,β^0 =29% and CFSE = –132.79 kJmol^{-1}

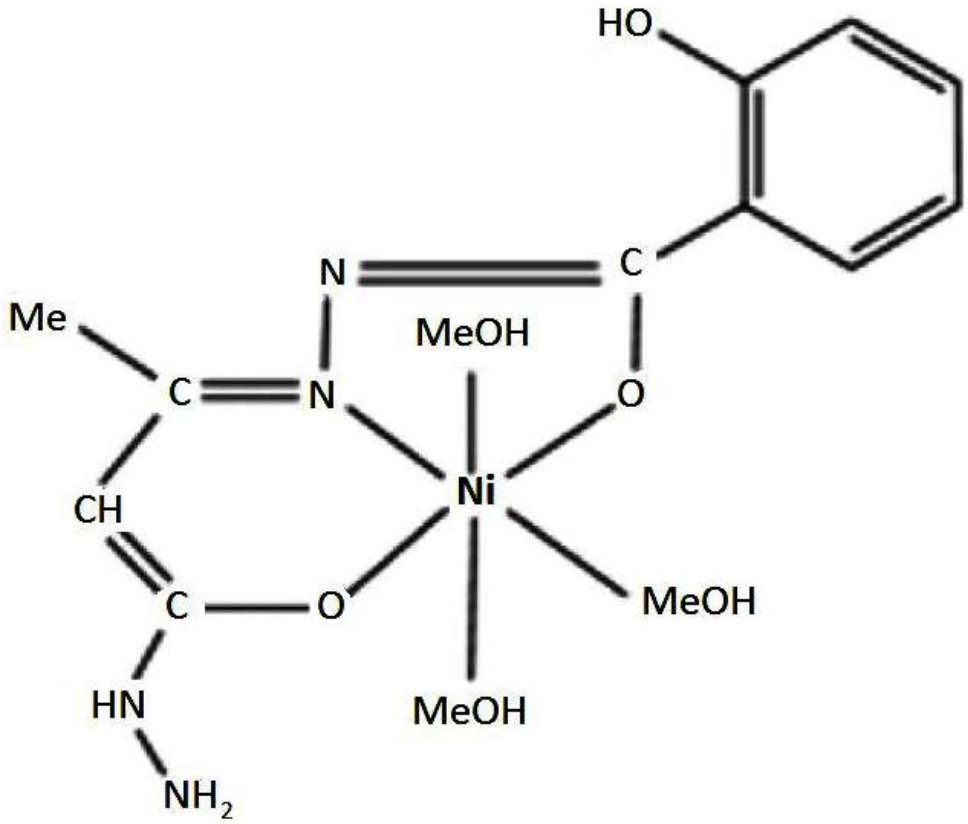


Scheme 1

$$Ni_3\ (1) + M(OAc)_2{\cdot}4H_2O \xrightarrow[\text{Reflux}]{\text{MeOH}} [Ni(LH)(MeOH)_3]\ (2) + 2AcOH + 4H_2O$$

1H NMR Studies The 1H NMR spectra of KBHz, 1 and 4–7 were recorded in DMSO-d6. The chemical shifts (δ) are expressed in ppm downfield from TMS [47]. The Schiff base (1) exhibits a singlet at δ 2.14 ppm due to the methyl protons, a singlet at 2.56 ppm due to the methylene proton, a doublet at δ 5.24 ppm due to the $–NH_2$ protons, a broad signal at δ 9.87 ppmdue to the phenolic proton, a multiplet at δ 6.84–7.80 ppm due to the aromatic protons, a singlet at δ 8.01 ppm due to –N=COH (adjacent to aliphatic moiety) proton, and a singlet at δ 12.24 ppm due to –N=COH (adjacent to aromatic moiety) proton. The absence of the resonance signals at δ 8.01 ppm and δ 12.24ppm due to the enolic protons (adjacent to aliphatic and aromatic moieties resp.) in 4–7 indicates the deprotonation of the enolic protons followed by the involvement of both enolic O atoms towards coordination.

Magnetic Measurements The magnetic moments of Ni is 3.17 B.M..This value lie in the normal range reported for themajority of magnetically dilute octahedral compound of Ni(II) ions [46].



Scheme 2

4. Conclusions

On the basis of the analytical data, valence requirements,conductance, spectral studies, and magnetic susceptibility measurements, it is proposed that 1 acts as a monobasic
tridentate ONO donor ligand in Ni coordinating through its azomethine N and both enolic O atoms which is paramagnetic .

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