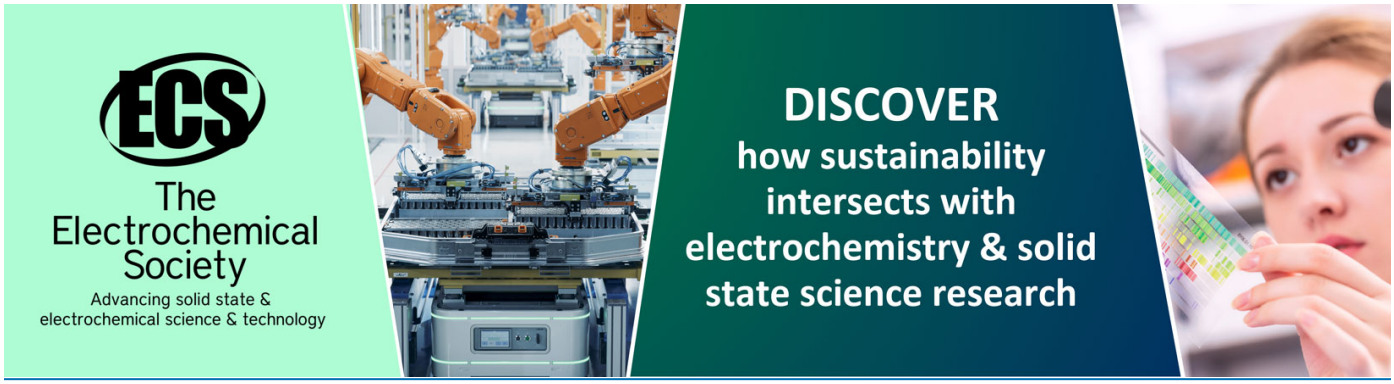
Synthesis and DNA binding study of Co (II) and V(IV) complexes with O, N, O tridentate 3-methoxysalicylaldehyde-semicarbazide based ligand



Synthesis and DNA binding study of Co (II) and V(IV) complexes with O,N,O tridentate 3-methoxysalicylaldehyde -semicarbazide based ligand

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Absract. Cobalt and vanadium complexes with (E)-2-(2-hydroxy-3-methoxybenzylidene)hydrazine-1-carboxamide were synthesized. The ligand was structurally characterized by FTIR, ^{1}HNMR and ^{13}CNMR spectroscopy. The interaction activity of ligand and complexes was investigated with DNA by spectroscopical and physical methods. The results showed an intercalative binding between the synthesized compounds and DNA.

Keywords: Methoxysalicylaldehyde, Semicarbazide, EDX, DNA, Viscosity

1.Introduction

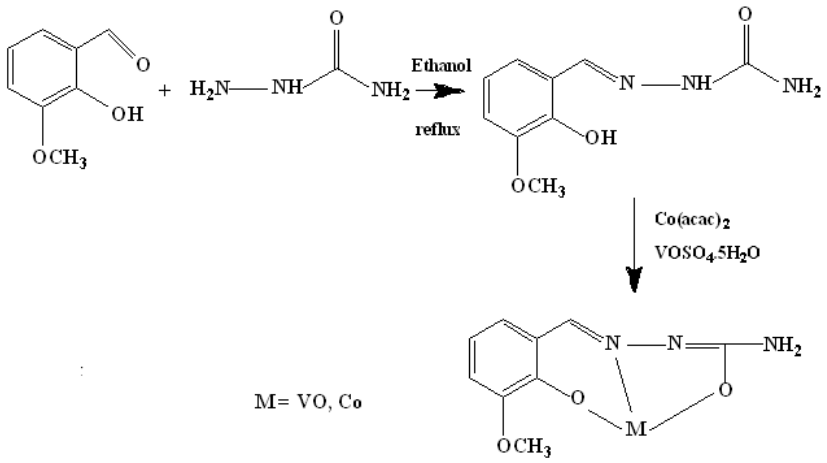
Sulfur and nitrogen donor ligands have received particular attention as one of the essential fields in coordination chemistry. Semicarbazones are among the main nitrogen/oxygen compounds which are provide variable binding modes, structural variety and biological applications [1-3]. The atoms coordination modes allow flexibility to semicarbazone ligands to coordinate with the metal ion that giving one or multi-nuclear complexes [4-7]. Semicarbazone metal complexes show perfect stability that can support the biological activity, reduces the toxicity and become a dependable source for creating novel biologically active compounds [8, 9].

Cobalt and vanadium are essential elements in biological systems [10]. The presence of cobalt in vitamin B12 makes it a regulator for the DNA synthesis. Cobalt uses as a supplement of the B12 vitamin due to it participates in the coenzyme of this vitamin [11]. In the other hand, vanadium complexes are described as therapeutic agents and promising drugs against diabetes, cancer and parasitic diseases [12, 13].

DNA has an important role in the biological processes because of its responsibility about intelligence and directed synthesis of biomolecules of enzymes and proteins during duplication and reproduction for genetic intelligence in living cells. Metal complexes are reported an attractive binding sites with DNA [14, 15]. Three noncovalent binding modes are well known; electrostatic, groove and intercalation [16–18]. Transition metal complexes have been received the large part of attention to create new nonradioactive tests of DNA construction [19, 20], new curative agents capable to cleave DNA, and DNA-mediated electron transfer reactions [21-23].

The biological properties of semicarbazones depend on the way that the metal ion is coordinated which determines the lipophilic properties that are responsible on the rate of entry into the cell [24]. The reported studies revealed that the complexes are higher bioactivities, lower side effects and lower drug-resistance than that of free ligand [25]. This work has

described the synthesis, characterization and DNA binding of vanadium and cobalt complexes based on semicarbazone which are explaining in scheme 1.



Scheme 1. Ligand and complexes general synthetic procedure

2.Experimental

2.1.Material and Instruments

All chemicals were obtained from Sigma Aldrich and used without more purification. DNA was obtained from human blood. FTIR spectra were conducted on a Shimadzu (FTIR -8400S, Japan) spectrometer using KBr pellets. Energy dispersive X-ray spectrometry (EDX) were recorded at room temperature. Electronic spectra were recorded by UV-Vis double-beam spectrophotometer (Spectroscan-80D, England). ^{1}HNMR and ^{13}CNMR recorded spectra by using DMSO-d_6 as solvent on a BRUKER 500 MHz spectrometer.

2.2. Synthesis of (E)-2-(2-hydroxy-3-methoxybenzylidene) hydrazine-1-carboxamide

A solution of 3-methoxysalicylaldehyde in (15 ml) ethanol dissolving (0.3735 g , 2.25 mmol) adding to semicarbazide solution in (15 ml) ethanol dissolving (0.25 g, 2.25 mmol). The resulting yellow solution was stirring for 2h with refluxing, filtered the solution with washing the precipitate by ethanol, then left to dried. Yield: 85%, mp:189-190 ˚C

2.3.Synthesis of vanadium complex

A solution of $VOSO_4$ $5H_2O$ (0.985 mmol, 0.25 g) dissolving in (20 ml) ethanol added to a solution of 3-methoxy-2 hydroxybenzaldehyde hydrazinecarboamide in (20 ml) ethanol dissolving (0.985 mmol, 0.2195 g). The red solution for 2h was refluxed, with filtration, by ethanol washing the precipitate, then left to dried. Yield: 80%, mp: 234-236 ˚C

2.4.Synthesis of cobalt complex

A solution of $Co(acac)_2$ in (20 ml) ethanol dissolving (0.25 g, 1.00 mmol) has been added to a solution of 3-methoxy-2- hydroxybenzaldehyde hydrazinecarboamide in (20 ml) ethanol dissolving (0.2195 g, 0.985 mmol) . The brown solution for 2 h was refluxed with filtration, and washed the precipitate with ethanol , then left to dried. Yield: 77%, mp: 243-245 ˚C

2.5.DNA binding assay

The DNA binding was performed in NaCl buffer (pH= 7.2), 6.3 mM Tris-HCl/50 mM. We prepared DNA stock solution in 6.3 mM Tris-HCl/50 mM of (pH= 7.2) buffer NaCl by dissolving a suitable amount of DNA at room temperature. For 48 h the product was stored in the refrigerator. A DNA buffered solution showed two UV absorbance at (260 and 280) nm a

ca.1.9: 1, ratio indicating the DNA was free of protein. The concentration of DNA was determined by the UV absorbance at 260 nm by using known molar absorption coefficient (6600 $M^{-1}cm^{-1}$) value [26], the reference (Tris/HCl buffer solution) was scanned from 230 nm to 600 nm.

measurements viscosity were achieved using a Cannon Manning Semi-Micro viscometer which is immersed in a water bath a thermostatic at 37 ^{0} C. By using digital stopwatch flow times were conducted manually. Calculating values viscosity from the observing the flow time DNA-containing solutions (t) using (t_0) for correcting the solvent mixture , $\eta = t - t_0$. The data viscosity were presented as $(\eta / \eta_0)^{1/3}$ versus [complex]/[DNA] where η and η_0 are the complex viscosity in presence of DNA and the viscosity of DNA alone respectively [27].

3.Results and Discussion

V(IV) and Co(II) complexes were synthesized with salicylaldehyde derivative based on semicarbazones. The complexes and ligand are strongly soluble in DMSO, air-stable, and strongly stable in aqueous solutions. UV and ^{1}H NMR spectra recording after preparation, (3, 30) days and 3 months, showing a high stability at room temperature.

The ligand showed^{1}H NMR , FTIR , and ^{13}C NMR spectra. In FTIR, the band of 3351 cm^{-1} to 3451 cm^{-1} due to υ (N–H) stretching, bands at about 3146 cm^{-1} corresponding to υ (O – H) group, ligand band at about 1585 cm^{-1} is due to υ (C=N) group, the bands at about 1600 cm^{-1} to 1612 cm^{-1} attributed to υ (C=N-N-C). band at about 1550 cm^{-1} to 1559 cm^{-1} is assigned to the stretching frequency of the phenolic bond (C – O). The chelation of semicarbazone ligand can easily be detected by monitoring the ligand position bands which are shifted to low or high energy upon complexation. The stretching phenolic(C–O) band has upward shifted to appeared in the region 1560-1568 cm^{-1}. In both complexes, υ (C=N) underwent a change in intensity and frequency, caused by complexation and downshifted to higher frequency to appeared in the region (1580 cm^{-1}). In ^{1}H NMR spectrum 'Figure 1 '.The signal appeared at (3.80) ppm attributed to the CH_3 protons of CH_3O group. doublet signals at (6.91) ppm and (7.34) ppm are due to the aromatic protons 4 and 6, respectively. The triplet signal at (6.74) ppm is due to the aromatic proton 5. a singlet signal emerged at 8.16 ppm is attributed to the proton of CH=N group. The broad signal emerged at (6.37) ppm is due to the NH_2 protons, whereas, the singlet signal emerged at (10.18) ppm is due to OH proton. In ^{13}C NMR spectrum, the carbon of the CH_3 group is appeared at 56.30 ppm, Figure 2. The signals in the range 112.65 ppm to 145.76 ppm are due to the aromatic carbons and the signals at 148.32 and 157.04 ppm are due to the carbons of (C=N) and (C=O), respectively.

The complexes were identified by the energy dispersive X-ray spectrometry (EDX) which confirmed that the ligands were successfully chelated with Co and V, Figure 3.

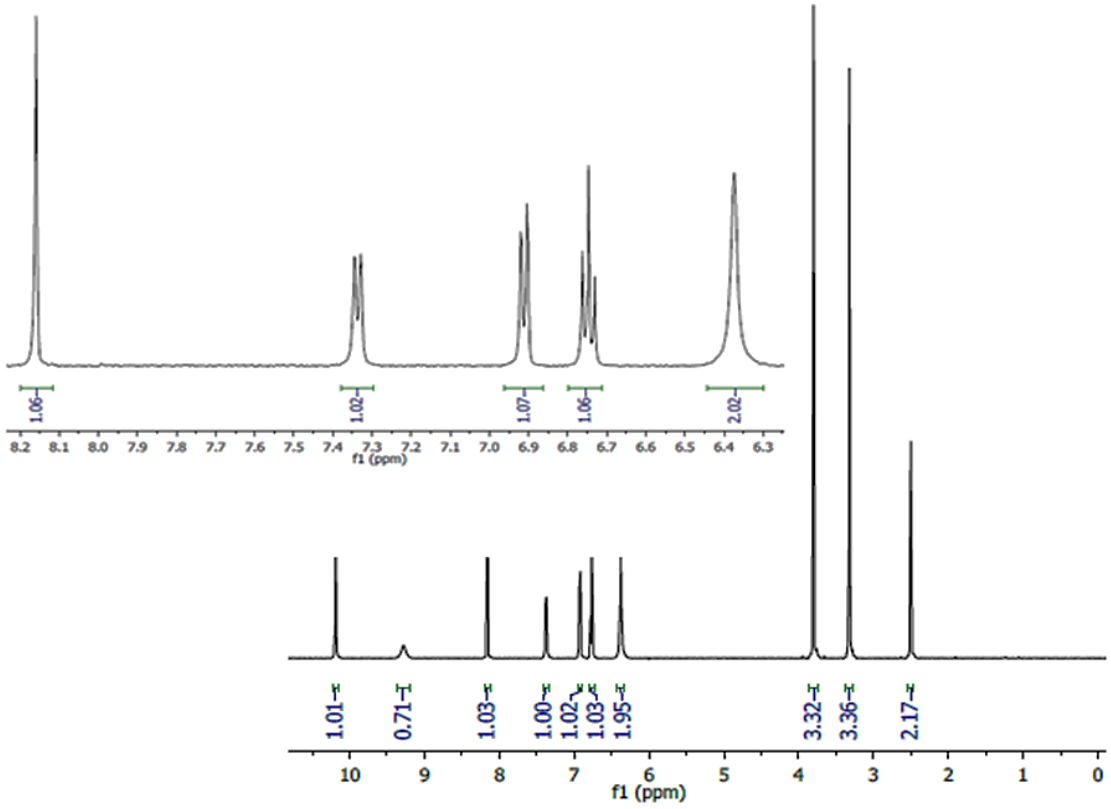


Figure 1. [1]HNMR spectrum of ligand.

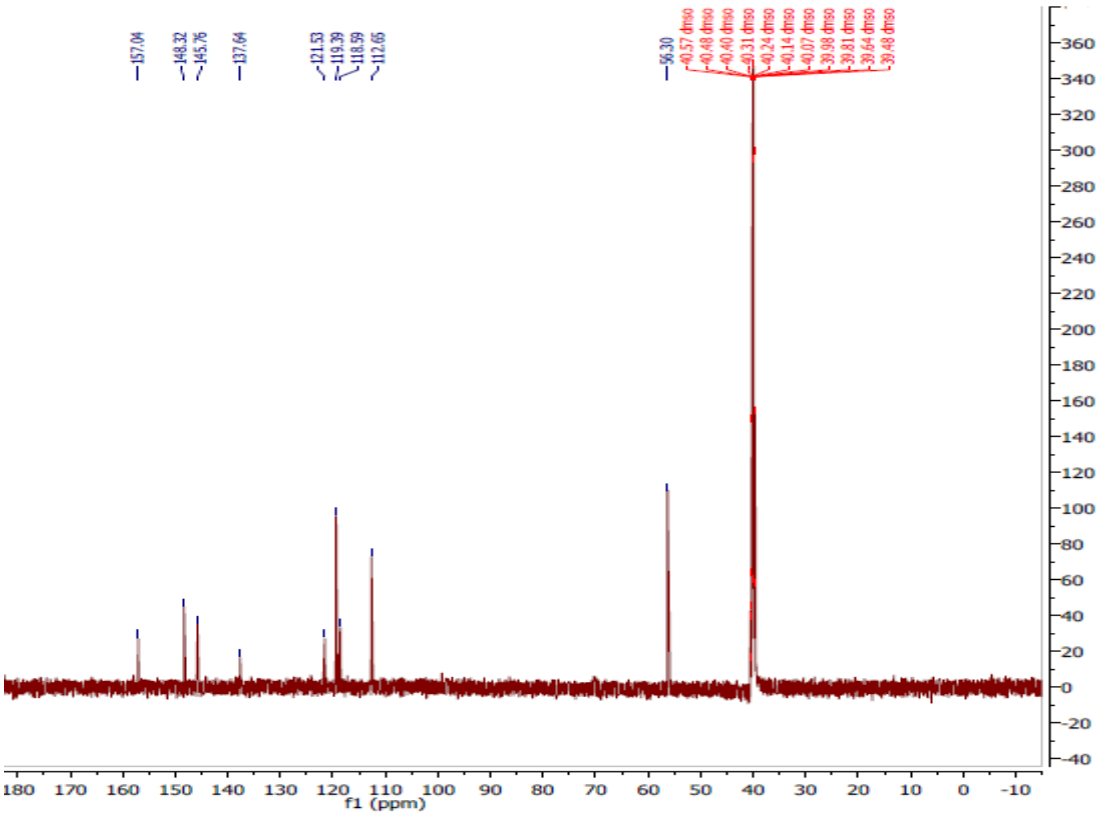


Figure 2. [13]CNMR spectrum of ligand.

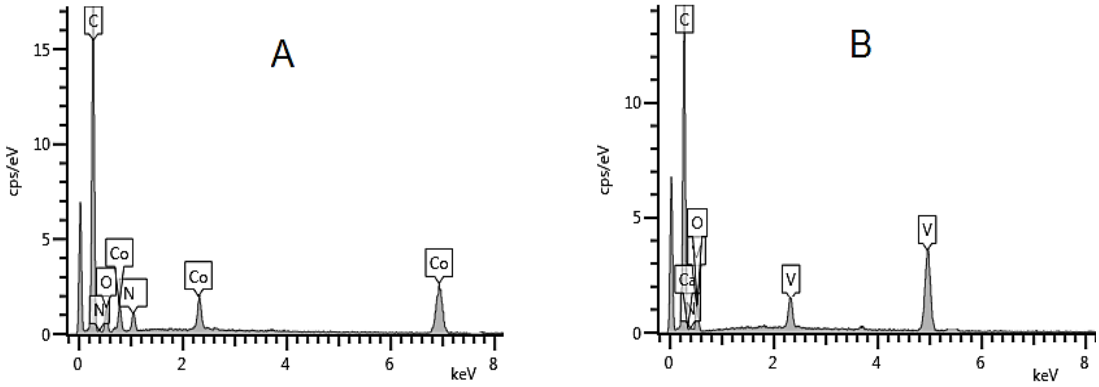


Figure 3. EDX analysis of cobalt complex (A) and vanadium complex (B).

3.1.Interaction with the DNA

3.1.1. studies of Electronic absorption

The electronic absorptions result studies are shown in (Figure 4). Ligand is exhibits two band absorptions at (245 nm and 352 nm) are attributed to transitions π-π* and n- π*, respectively. In addition, the complexes exhibited new bands at 403 nm and 670 nm are attributed to d-d transitions for the vanadium and cobalt complexes, sequentively. The π-π* absorption bands is chosen to track the DNA interaction with complexes and ligands . spectroscopic titrations revealed that the increased amounts of (DNA) are lead to decreasing in absorptions intensity (hypochromism) of the complexes and their ligands, Figure 4. This spectral behavior are suggests DNA intercalative binding, since lead to the hypochromism in spectral bands [28, 29].

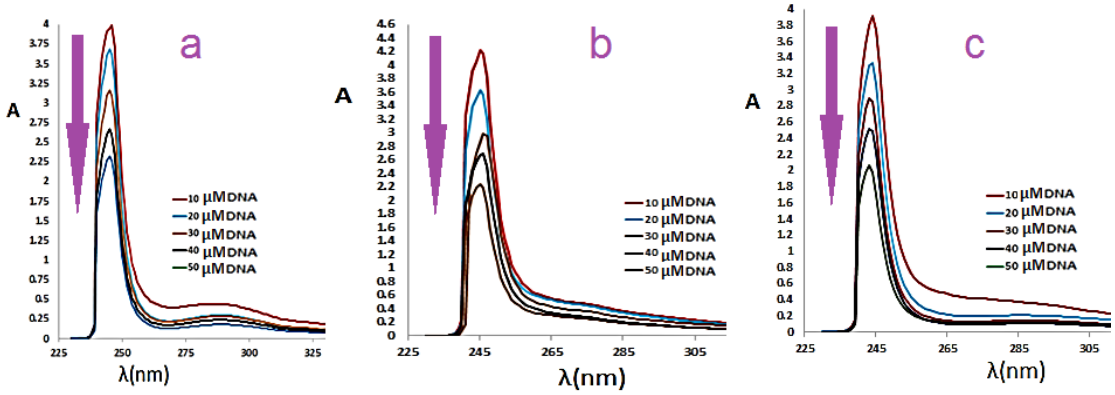


Figure 4. UV spectra of ligand (a) and its complex with cobalt (b) and vanadium (c). The arrows show the absorbance changes with DNA amounts .

3.1.2.Viscosity studies

Viscosity is one of the most important experiment that can be utilized to explain binding of compounds modes to DNA . . The results showed increases viscosity with increases amounts of ligand or complexes, Figure 5. These results have confirmed the intercalation of the compounds into DNA because the intercalation leads an stiffing and extension helix of DNA which consequently guide to increases viscosity of DNA solutions [30].

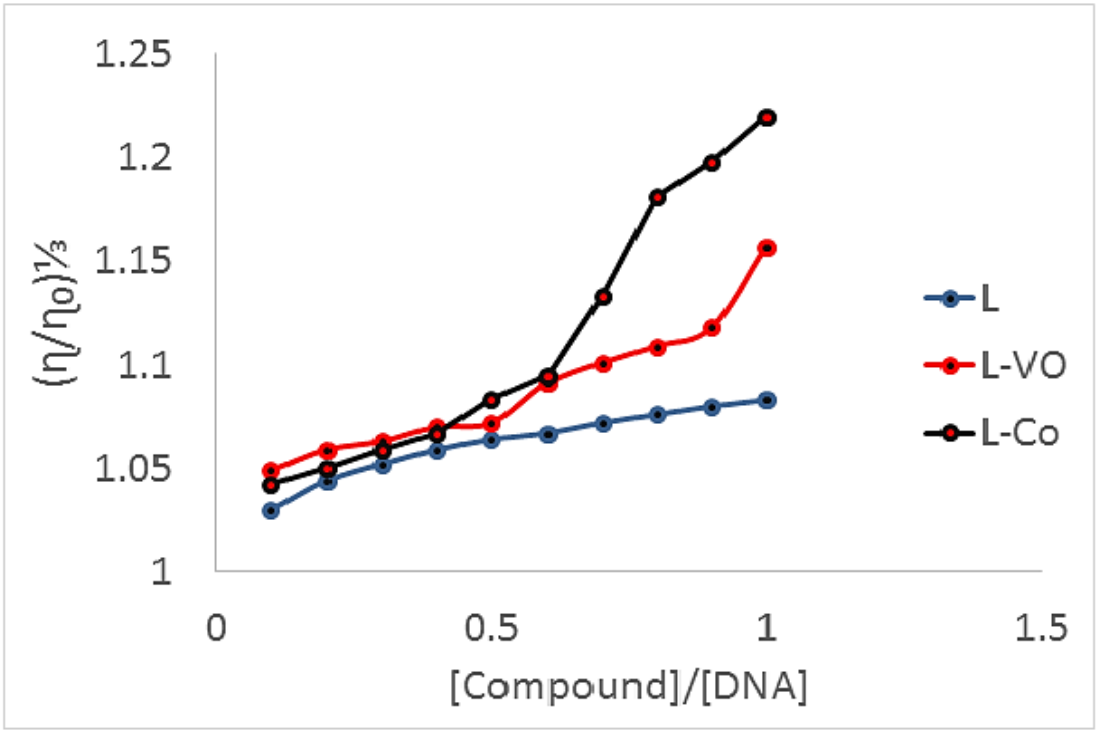


Fig. 5. Ligands and complexes viscometric results at 37 °C.

4.CONCLUSION

Two complexes of cobalt and vanadium with (E)-2-(2-hydroxy-3-methoxybenzylidene)hydrazine-1-carboxamid ligand were synthesized. The compounds were characterized by FTIR, ^{1}HNMR, ^{13}CNMR and EDX techniques. The interaction between the compounds and DNA was investigated. The results of UV–Vis spectroscopy and viscosity measurement showed a hypochromic shift and an intercalative mode. The obtained results have offering a promising therapeutic reagent for cancerous diseases.

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