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A New Cyclic Ligand and Complexes of Its Open-Chain Tautomer with Co(III) and Ni(II) Ions: Synthesis, Characterization and Thermal Properties

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A New Cyclic Ligand and Complexes of Its Open-Chain Tautomer with Co(III) and Ni(II)

Ions: Synthesis, Characterization and Thermal Properties

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ABSTRACT

In this study, a new ligand, $2-(p-tolyl)-1,2,3,4-tetrahydroquinazoline-2-carbaldehyde oxime, was synthesised from a condensation reaction of <math>\infty o_{-p}-tolyl$ -acetaldehyde oxime with 2-aminobenzylamine and then amine-imine-oxime complexes of this compound that formed with Co(III) and Ni(II) ions were obtained. All structures were characterised by spectral methods, elemental analysis, magnetic susseptibility, molar conductivity and thermal analyses. The results that were obtained show that the cyclic ligand, HL, undergoes a ring-opening reaction upon complexation with metal ions. The Co(III) and Ni(II) complexes have a metal-

¹ ACCEPTED MANUSCRIPT

ligand ratio of 1:2 and the imine ligand coordinates through the amine, imine and oxime groups nitrogen atoms with metal ions.

Keywords: 2–(*p*–Tolyl)–1,2,3,4–tetrahydroquinazoline–2–carbaldehyde oxime; Ring–chain tautomerism, Amine–imine–oxime; Co(III) complex; Ni(II) complex

INTRODUCTION

Quinazoline is composed of two fused six–membered simple aromatic rings, a benzene ring and a pyrimidine ring. Studies of the quinazoline compounds began only with discovery of febrifugine, a quinazolinone alkaloid, possessing anti–malarial potential^[1]. At present, quinazoline derivatives are used in the pharmaceutical industry because of wide variety of activities such as, anti–tumor^[2], anti–inflammatory^[3], anticonvulsant^[4] and antimicrobial^[5,6]. For example, 3–phenyl–2,4–dithioxo–1,2,3,4–tetrahydroquinazoline is a PDE7 inhibitor and new therapeutic agent for neuroprotection^[7]. Doxazosin mesylate is an α 1–selective alpha blocker that is used to treat high blood pressure and urinary retention^[8].

1,2,3,4–tetrahydroquinazolines include the benzene ring and the hexahydropyrimidine ring. The formation of tetrahydroquinazoline is a synthesis of a Schiff base from aldehydes^[9] and 2–aminobenzylamines; there is a ring–chain tautomeric equilibrium between the tetrahydroquinazoline and the Schiff bases^[9–12]. According to Sinkkonen and co–workers, in

² ACCEPTED MANUSCRIPT

1,3-unsubstituted tetrahydroquinazolines can exist ring-chain tautomeric equilibria containing cyclic form, aniline type and benzylamine type chain forms^[111]. According to García–Deibe and co-workers, the tetrahydroquinazoline compound is the most stable form of the two tautomers, and the ring-chain tautomerism of a 2-aryl–1,2,3,4-tetrahydroquinazoline can be exploit to induce reversible changes in the aminal–imine equilibrium, as desired, by coordination of a suitable metal ion^[13]. Recently, a few 2–substituted–1,2,3,4-tetrahydroquinazoline derivatives, containing substituted oxime, have been synthesised from a condensation reaction of α -carbonyl oxime with 2–aminobenzylamine (2–ABA), characterised in detail by us and used for complexation with some transition metal ions, i.e., Ni(II)^[14,15] and Co(III)^[15-18] complexes. The 2–substituted–1,2,3,4-tetrahydroquinazoline agents owing to the presence of three nitrogen atoms. Despite the fact that there are different substituents at 2–position in these ligands, the aniline type chain form is maintained in the complexes^[15-18].

In this work, the new cyclic ligand, 2–(*p*–tolyl)–1,2,3,4–tetrahydroquinazoline–2– carbaldehyde oxime, HL, and the complexes of its open–chain tautomer with Co(III) and Ni(II) metal ions were synthesised and characterised. These compounds have been characterised by spectral (¹H–NMR, ¹³C–NMR, FT–IR, mass, AAS) methods, elemental analyses, molar conductivity, magnetic susseptibility and thermal analysis (TG, DTG and DTA) techniques.

The studies described here allow us to conclude that Co(III) and Ni(II) coordination can be used to induce opening reactions of a tetrahydroquinazoline ring.

³ ACCEPTED MANUSCRIPT

EXPERIMENTAL

Materials and measurements

All chemicals and solvents were purchased from Merck, Aldrich or Lachema and were used without further purification.

Melting points were determined on a BÜCHI B–540 digital melting point apparatus and remained uncorrected. The molar conductivities of the complexes were measured by using a WTW model inoLab 730 conductivity meter. Magnetic susceptibility measurements were performed at room temperature with a Sherwood Scientific MK1 model Magnetic Susceptibility Balance. C, H and N microanalyses, metal analyses and mass spectra were carried out at the Technical and Scientific Research Council of Turkey, TUBITAK Bursa Test and Analysis Laboratory. FT–IR spectra were recorded in the 4000–400 cm⁻¹ region with a Thermo–Nicolet 6700 Fourier–Transform Infrared Spectrometer by using KBr pellets. The ¹H–NMR and ¹³C–NMR solution spectra were recorded at 25 °C on a Varian Mercury Plus 400 MHz spectrometer, utilising deuterated dimethylsulphoxide (DMSO–d₆) as a solvent. Thermal analysis curves (TG, DTG and DTA) were obtained using a Seiko Exstar 6200 thermal analyser in a dinamic dry air atmosphere (flow rate of 200 mL min⁻¹) at a heating rate of 10 °C min⁻¹ in the temperature range of 25–1000 °C using platinum crucibles.

Oxo-p-tolyl-acetaldehyde oxime, p-MeINAP

⁴ ACCEPTED MANUSCRIPT

Oxo-*p*-tolyl-acetaldehyde oxime (*p*-methyl isonitrosoacetophenone), *p*-MeINAP, was prepared according to a literature method^[19] with little modification. Nitrosation of 1–*p*-tolyl-ethanone with butyl nitrite afforded the corresponding *a*-carbonyl oxime, *p*-MeINAP. Structure of *p*-MeINAP was inferred from its FT-IR and NMR spectral data. The bands observed at 3422, 2905, 1676, 1598 and 979 cm⁻¹ were attributed to the *a*-carbonyl oxime *v*(O-H), *v*(H-C=N), *v*(C=O), *v*(C=N) and *v*(N-O) groups stretching vibrations, respectively. The ¹H-NMR spectrum of *p*-MeINAP displayed signals at δ 12.63 (s, 1H, OH, disappeared upon addition of D₂O), 8.01 (s, 1H, CH=N), 7.88 (d, *J*=8 Hz, 2H, CH_{aromatic}), 7.31 (d, J=8.4 Hz, 2H, CH_{aromatic}) and 2,36 (s, 3H, -CH₃) ppm. In the ¹³C-NMR spectrum of *p*-MeINAP, the signals appeared at δ 188.70, 148.13 and 21.64 ppm were attributed to the carbon atoms of carbonyl, azomethine and methyl groups. The *p*-MeINAP displayed a range of aromatic carbon resonances between δ 144.72–129.42 ppm.

Synthesis of 2-(p-tolyl)-1,2,3,4-tetrahydroquinazoline-2-carbaldehyde oxime, HL

A solution of 2-aminobenzylamine (2–ABA), (10.0 mmol, 1.22 g) in 5 mL of absolute ethanol was added dropwise to a solution of *p*–MeINAP (10.0 mmol, 1.63 g) in 15 mL of absolute ethanol. The reaction mixture was stirred for 2 h at room temperature and left for one day at room temperature. The reaction product was filtered, washed with cold ethanol and finally dried under vacuum (Scheme 1). Yield: 1.68 g, 63 % (white crystals). m.p.: 152 °C (decomposition). Anal. Calc. for $C_{16}H_{17}N_3O$ (267.3 g mol⁻¹) (%): C, 71.88; H, 6.41; N, 15.72.

⁵ ACCEPTED MANUSCRIPT

Found: C, 71.60; H, 6.48; N, 16.03. FT–IR (KBr pellet) v_{max} cm⁻¹: 3393, 3213 s, sh (N–H); 2748 (O–H---N); 2915 (H–C=N); 1607 (C=N_{oxime}); 940 m, sh (N–O). ¹H–NMR (DMSO–d₆) δ ppm, *J* Hz: 10.80 s, 1H (OH, disappeared upon addition of D₂O); 7.38 s, 1H (H–C=N); 7.43 d (*J*=8.0), 2H (CH_{aromatic}); 7.11 d (*J*=7.6), 2H (CH_{aromatic}); 6.89 dt (*J*=8.0, 1.6), 1H (CH_{aromatic}); 6.72–6.69 m, 2H (CH_{aromatic}); 6.43 dt (*J*=7.2, 1.2), 1H (CH_{aromatic}); 6.58 s, 1H (N⁽¹⁾H); 3.68 dd (*J*=18.6, 4.8), 1H (CH₂); 3.46 dd (*J*=16.0, 8.4), 1H (CH₂); 3.03 b, 1H (N⁽³⁾H); 2.24 s, 3H (CH₃). ¹³C–NMR (DMSO–d₆) δ ppm: 152.69 (H–C=N); 143.50 (C–C<^N_N); 140.71–114.75 (C_{aromatic}); 70.82 (>C<^N_N); 42.80 (CH₂); 21.05 (CH₃). *m/z*: 267.8 [HL]⁺.



Scheme 1. Synthesis of HL.

Synthesis of [Co(L)₂]Cl

⁶ ACCEPTED MANUSCRIPT

A solution of CoCl₂·6H₂O (1.50 mmol, 0.37 g) in ethanol (10 mL) was added dropwise

while stirring at room temperature to a solution of HL (3.00 mmol, 0.80 g) in ethanol (20 mL). Air–oxidation was achieved by stirring vigorously on air for 5 h. After 5 h, the precipitated orange–coloured compound was filtered, washed with cold ethanol several times, and dried under vacuum. The complex was named bis{(2–amino–benzylimino)–p–tolyl–acetaldehyde oximato}cobalt(III) chloride (Figure 1). Yield: 0.21 g, 22 %. m.p.: 212 °C (decomposition). Anal. Calc. for C₃₂H₃₂N₆O₂CoCl (627.0 g mol⁻¹) (%): C, 61.30; H, 5.14; N, 13.40; Co, 9.40. Found: C, 61.00; H, 5.09; N, 12.87; Co, 9.06. FT–IR (KBr pellet) v_{max} cm⁻¹: 3422 (NH₂); 2917 (H–C=N); 1612 w (C=N_{imine}); 1583 w (C=N_{oxime}); 1029 w (N–O); 454 w (M–N). ¹H–NMR (DMSO–d₆) δ ppm, *J* Hz: 6.87 s, 2H (H–C=N); 7.52–7.42 m, 8H (CH_{aromatic}); 7.24–7.04 m, 10H (CH_{aromatic}); 6.54 2H (NH₂); 4.86 d (*J*=14.4), 2H (CH₂); 4.77 d (*J*=14.4), 2H (CH₂); 2.43 s, 6H (CH₃). ¹³C–NMR (DMSO–d₆) δ ppm: 174.54 (Ph–C=N); 140.82 (H–C=N); 139.69–123.25 (C_{aromatic}); 53.55 (CH₂); 21.57 (CH₃). *m/z*: 626.7 [Co(L)₂Cl]⁺. μ_{eff} : diamagnetic. Molar conductance (methanol, Λ_M ohm⁻¹cm²mol⁻¹): 83.

Synthesis of [Ni(HL)₂]Cl₂

7 ACCEPTED MANUSCRIPT

A solution of NiCl₂·6H₂O (3.00 mmol, 0.71 g) in ethanol (10 mL) was added dropwise while stirring at room temperature to a solution of HL (3.00 mmol, 0.80 g) in ethanol (20 mL). The mixture was then stirred for 3 h at room temperature. After 3 h, the precipitated pink–coloured compound was filtered and washed with cold ethanol several times, and dried. The complex was named bis{(2–amino–benzylimino)–*p*–tolyl–acetaldehyde oxime}nickel(II) chloride (Figure 1). Yield: 0.63 g, 62 %; m.p.: 208 °C (decomposition). Anal. Calc. for $C_{32}H_{34}N_6O_2NiCl_2$ (664.2 g mol⁻¹) (%): C, 57.86; H, 5.16; N, 12.66; Ni, 8.84. Found: C, 57.60; H, 5.11; N, 12.30; Ni, 8.92. FT–IR (KBr pellet) v_{max} cm⁻¹: 3412 (NH₂); 3190 (OH); 2949 (H– C=N); 1611 w (C=N_{imine}); 1580 w (C=N_{oxime}); 958 w (N–O); 478 w (M–N). *m/z*: 591.7 [Ni(L)₂]⁺; 396.8 [Ni(HL)Cl₂]⁺. μ_{eff} : 2.90. Molar conductance (methanol, Λ_M ohm⁻¹cm²mol⁻¹): 148.

Figure 1

RESULTS AND DISCUSSION

The principal ligand HL was synthesised by the direct condensation of p-MeINAP with 2–ABA and reacted with Co(II) and Ni(II) chlorides, one compound was obtained in each reaction, $[Co(L)_2]Cl$ and $[Ni(HL)_2]Cl_2$, respectively. The FT-IR spectrum of the solid form of HL and the NMR spectra of the HL in DMSO-d₆ solution indicate that the ligand remains in ring form. The heterocyclic ring of the ligand was opened during the complexation and an aniline-type chain form occurred within the complexes. The overall results conclude that the complexes

8 ACCEPTED MANUSCRIPT

consist of two open-chain ligand and the open-chain amine-imine-oxime acts as a tridentate ligand through amine, imine and oxime nitrogen atoms. It was determined that cobalt(II) is becoming oxidised to cobalt(III) in the $[Co(L)_2]Cl$ compound.

The molecular structure of new ligand and its amine–imine–oxime complexes have been characterized by ¹H–NMR, ¹³C–NMR, FT–IR, mass spectra, AAS, elemental analyses, thermal analyses, molar conductivity and magnetic susseptibility measurements and the results are given in the Experimental Section.

Elemental Analysis, AAS, Magnetic Susceptibility and Conductance

The elemental analyses and AAS results are in reasonably good agreement with the proposed structures. The magnetic susceptibility measurement of the cobalt(III) complex reveals that the compound is diamagnetic, confirming the oxidation of cobalt(II) to cobalt(III) and structure's octahedral geometry^[15,17,18]. The effective magnetic moment of $[Ni(HL)_2]Cl_2$ is 2.90 B.M. for per nickel(II) ion, which corresponds to two unpaired electrons of a mononuclear octahedral Ni(II) complex. The molar conductance values of $[Co(L)_2]Cl$ and $[Ni(HL)_2]Cl_2$, measured in methanol solutions (~1 x 10⁻³ M), show that the Co(III) and Ni(II) complexes are 1:1 and 1:2 electrolytes, respectively^[20].

Mass Spectra

9 ACCEPTED MANUSCRIPT

The mass spectra of the ligand and open-chain tautomer Co(III) complex of this ligand confirmed the suggested formula by their molecular ion peaks. The mass spectrum of the free ligand that shows a molecular ion peak at m/z = 267.8 [HL]⁺ indicates the formation of the desired structure. The peak at m/z = 626.7 at the mass spectrum of the cobalt(III) complex can be attributed to the [Co(L)₂Cl]⁺ ions. The mass spectrum of the nickel(II) complex shows peaks at m/z = 591.7 and 396.8 corresponding to [Ni(L)₂]⁺ and [Ni(HL)Cl₂]⁺ ions, respectively.

FT-IR Spectra

The FT–IR spectrum of HL exhibited fairly strong bands at 3393, 3213 cm⁻¹ attributable to the v(N-H) vibration. The bands observed at 2915, 1607 and 940 cm⁻¹ were attributed to the oxime v(H-C=N), v(C=N) and v(N-O) groups stretching vibrations, respectively. The oxime (– OH) stretching vibration of HL appeared as a broad peak maximum at 2748 cm⁻¹, which was assigned to the intramolecular hydrogen bonding vibration (N····H–O–). In addition, in the FT– IR spectrum of the α -carbonyl oxime derivative p–MeINAP, the (C=O) stretching frequency of the carbonyl group appeared at 1676 cm⁻¹ but disappeared in the presence of the 1,2,3,4– tetrahydroquinazoline oxime, HL, demonstrating the formation of the new ligand.

In the FT–IR spectrum of the complexes, the bands at 3422 and 3412 cm⁻¹ are attributed to $v(-NH_2)$ of the amine–imine–oxime ligand for $[Co(L)_2]Cl$ and $[Ni(HL)_2]Cl_2$, respectively. In the FT–IR spectrum of the Co(III) complex, there is no v(O-H) band belonging to the oxime group, providing evidence for its deprotonation. On the other hand, in the FT–IR spectrum of the Ni(II) complex, the band at 3190 cm⁻¹ was associated with the (O–H) stretching vibrations. A

¹⁰ ACCEPTED MANUSCRIPT

band around 1612–1611 cm⁻¹ is attributable to the (C=N_{imine}) stretching vibration in the spectra of the Co(III) and Ni(II) complexes, which is absent in the spectra of the free ligand, indicating the coordination in the chain form. When the FT–IR spectra of the complexes are compared with those of the free ligand, the new v(C=N_{imine}) band is appeared and the v(C=N_{oxime}) band is shifted to a lower frequency. These situations indicate that the imine and oxime nitrogen atoms must be coordinated to the metal ion. The (N–O) of the oxime group vibration in the Co(III) complex is situated at a frequency significantly higher (~89 cm⁻¹) than that of the free ligand, owing to the coordination of the N atom and the increase in bond order of the N–O bond upon deprotonation.

NMR Spectra

¹H– and ¹³C–NMR spectra of the HL and open–chain tautomer Co(III) complex of this ligand are summarised in Experimental Section. The ¹H–NMR spectrum of the ligand showed three peaks as singlets at δ 10.80, 3.03 ppm and δ 6.58 ppm, which disappeared upon addition of D₂O and were assigned to the proton of the oxime group, the NH proton adjacent to the –CH₂ group and the other NH proton, respectively. The signals of the phenyl groups of the ligand are determined at ca. δ 7.43–6.43 ppm, the aldehyde proton adjacent to the oxime group resonated at δ 7.38 ppm and the signal corresponding to the resonance of methyl group protons showed at 2.24 ppm as a singlet. The resonances observed at 3.68 ppm and 3.46 ppm as an AB system was assigned to the –CH₂ group in the heterocyclic ring.

In the ¹³C–NMR spectrum of p–MeINAP, the signal of the carbon atom of carbonyl group appeared at 188.70 ppm but disappeared in the ¹³C–NMR spectrum of the

¹¹ ACCEPTED MANUSCRIPT

1,2,3,4-tetrahydroquinazoline oxime, which was evidence for the formation of new ligand. In addition, the ligand showed a signal corresponding to the quaternary carbon atom of the heterocyclic ring at δ 70.82 ppm, suggesting that the 1,2,3,4-tetrahydroquinazoline ring is formed^[14, 15, 17,18]. In the ¹³C-NMR spectrum of the HL, the signal at δ 152.69 ppm is attributed to the carbon atoms of HC=NOH group. The HL displayed a range of aromatic carbon resonances between δ 143.50–114.75 ppm. As for the carbon atoms of methylene and methyl groups in the ligand, they were observed at δ 42.80 ppm and δ 21.05 ppm, respectively.

A comparison of the ¹H–NMR and ¹³C–NMR spectra of the ligand with the Co(III) complex confirms the coordination of the aniline-type chain form of the ligand. In the ¹H–NMR spectrum of the Co(III) complex, the signal due to the –NOH group is absent and evidence for deprotonation of oxime group.

The chemical shift belonging to the –NH adjacent to the –CH₂ group in the HL disappeared from the ¹H–NMR spectrum of the Co(III) complex. After the complexation, the integrated ¹H–NMR spectrum of the Co(III) complex indicated proton resonances at ca. δ 6.54 ppm due to the presence of the –NH₂ group of imine oxime. The D₂O exchangeable peak was assigned by the formation of the aniline-type chain form in the Co(III) complex (Figure 1). In the Co(III) complex, the peaks due to the H–C=N group and methylene group of the HL showed an upfield shift and a downfield shift upon complexation with Co(III)^[15,17,18], respectively. This finding confirmed that the nitrogen atoms of the oxime group and imine group were coordinated to the metal ion. Additionaly, the phenyl and methyl protons are seen as multiplets at δ 7.52–7.04 ppm and as a singlet at δ 2.43 ppm, respectively.

The chemical shift due to the quaternary carbon atom in HL disappeared from the 13 C–NMR spectrum of Co(III) complex. However, after complexation a new resonance at δ 174.54 ppm was observed. The new resonance shows us that the heterocyclic ring of the ligand was opened during the complexation and the aniline type chain form occured in the Co(III) complex¹⁵. The chemical shifts belonging to the carbon atoms of oxime group and methylene group in the HL showed an upfield shift and a downfield shift on complexation with Co(III). These results substantiate the conclusion obtained by the ¹H–NMR study and demonstrate the involvement of the oxime nitrogen and the nitrogen adjacent to the –CH₂ group in coordination.

Thermal Analyses

Thermal stability data of the ligand and the complexes of its open-chain tautomer are listed in Table 1. The HL is stable up to 105 °C and then exhibits three exothermic decomposition stages. Decomposition is completed at 636 °C (Figure 2).

The Co(III) and Ni(II) complexes don't contain hydrated or lattice water molecules, which are consistent with the analytical and spectroscopic data. The Co(III) complex is thermally stable up to approximately 131 °C (Figure 3). After exceeding this temperature, the organic ligands start to decompose. Decomposition occurs in the temperature range of 131–604 °C in three steps, as shown by exothermic DTA peaks at 209, 431 and 530 °C. The mixture of Co_3O_4/CoO is caused by the removal of the organic ligands and halogen. The decomposition product Co_3O_4 is converted to CoO between 604 and 961 °C (DTA_{max}: 898 °C)^[21]. The weight loss of 90.0 % suggests that the final product may be CoO.

¹³ ACCEPTED MANUSCRIPT

TG–DTA curves for the Ni(II) complex are given in Figure 4. The complex shows three exothermic stages in the decomposition process. The total mass loss of the decomposition steps amounts to 87.8 % (calcd.: 88.7 %) for the Ni(II) complex. It corresponds to the removal of the HL ligands and chlorides leaving NiO as a residue.

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Compound	Temperatur	DTA _{max} , °C	Total weight loss		Assignment
	e		Found, %	Calculated,	
	range, °C			%	
HL	105 - 180	154(-)	13.3	*	**
	180 - 401	343(-)	52.6	*	**
		495(-)			
	401 - 636	545(-)	100	100	
		578(-)			

Table 1. TG–DTA data of HL and the complexes of its open-chain tautomer.

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[Co(L) ₂]Cl	131 – 221	209(-)	23.5	*	**
[Ni(HL)2]Cl2	221 - 464	431(-)	34.8	*	**
	464 - 604	530(-)	88.9	*	Co ₃ O ₄ /CoO
	604 - 961	898 <mark>(+)</mark>	90.0	88.1	CoO
	148 - 216	201(-)	16.1	*	**
	216 - 461	309(-)	34.0	*	**
		448(-)			
	461 – 555	525(-)	87.8	88.7	NiO

(+): endothermic, (-): exothermic, * :not computed, **: unknown

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FIGURE CAPTIONS



Figure 1. Suggested structures for the Co(III) and Ni(II) complexes.

Figure 2. TG, DTG and DTA curves of HL.



Figure 3. TG, DTG and DTA curves of [Co(L)₂]Cl.

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Figure 4. TG, DTG and DTA curves of [Ni(HL)₂]Cl₂.

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