Acta Materialia Turcica

Volume 1, December 2017, Pages 11-19

Synthesis, Characterization and Biological Activities of Novel a 1,2,3,4-tetrahydroquinazoline and Its Nickel(II) Complexes

A. T. COLAK[a,*], M. TAS[b], G. IREZ[c], H. GUNAY ACAR[d], O. BUYUKGUNGOR[e], F. COLAK[f]

[a] Dumlupınar University, Faculty of Arts and Sciences, Department of Chemistry, Kütahya, Turkey
[b] Ondokuz Mayıs University, Education Faculty, Department of Science Education, Samsun, Turkey
[c] Uludağ University, Arts and Sciences, Department of Chemistry, Bursa, Turkey
[d] Avrasya University, Vocational High School, Department of Chemistry Technology, Trabzon, Turkey
[e] Ondokuzmayıs University, Faculty of Arts and Sciences, Department of Physics, Samsun, Turkey
[f] Dumlupınar University, Faculty of Arts and Sciences, Department of Biology, Kütahya, Turkey

Abstract:
The 2-methyl-2-(1-hydroxyiminoethyl)-1,2,3,4-tetrahydroquinazoline (HL or **1**) and its novel Ni(II) complexes, square-planar $[Ni(L)(LH)]\cdot(NO_3)$ (**2**) and octahedral $[NiCl_2(LH)(H_2O)_2]\cdot(H_2O)$ (**3**), have been synthesized. The ligand and complexes have been characterized by means of elemental, IR, UV-Vis. spectroscopic studies, ^{1}H-NMR, ^{13}C-NMR, magnetic susceptibility, thermal analysis, mass spectroscopy and X-ray diffraction technique. The HL ligand crystallizes in the $P2_1/c$. Antimicrobial activity of ligand (**1**) and complexes (**2** and **3**) was evaluated by the agar diffusion method. Complex **2** showed weak antimicrobial activity against tested microorganism strains. Complex **3** exhibited moderate antimicrobial activity against tested microorganisms strains (*Staphylococcus epidermidis* and *Candida albicans*).
Keywords: 1,2,3,4-tetrahydroquinazoline - Oxime - Nickel Complex - Antimicrobial Activity - Ligand Synthesis.
DOI:

1. Introduction

1,2,3,4-tetrahydroquinazolines, which are heterocyclic compounds, are of interest as dihydrofolate reductase inhibitors, antitubercular and antibacterial agents [1]. 1,2,3,4-tetrahydroquinazolines can be prepared by the condensation of 1,3-diamines and substituted aldehydes or ketones in refluxing benzene or xylene with azeotropic mixing water removal (Figure 1) [1-3]. The 1,2,3,4-tetrahydroquinazolines may also be prepared by the simple method of slurring the reagents together in water at ambient temperature in a similar manner as in the synthesis of aromatic Schiff bases by the Tanaka's method [1,4].

The formation of 1,2,3,4-tetrahydroquinazolines is formally a synthesis of a Schiff bases from aldehydes [1] or ketones and there is a tautomeric equilibrium between the tetrahydroquinazolines and Schiff bases [1-3]. The equilibrium depends on the substituents at 2 positions in 1,2,3,4-tetrahydroquinazoline and the tautomeric equilibrium is described by the authors (Figure 1.a, Figure 1.b, Figure 1.c) [2,3]. A new tautomeric equilibrium classified as amine-imine type form was reported in a Nickel(II) complex prepared by a 1,2,3,4-tetrahydroquinazoline which contains oxime part, showing heterocyclic ring of tetrahydroquinazoline opened by metal complexation (Figure 1.d) [5].

In this work, a 2-subsitituted 1,2,3,4-tetrahydroquinazoline (**1**) was synthesized from 2-aminomethylaniline (2-aminobenzylamine) and

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

2,3-butanedione-2-oxime (as ketone) and its two new Nickel(II) complexes that were the heterocyclic ring of tetrahydroquinazoline protected during the complexation, were prepared and characterized.

The first aim of this study is to synthesize the 1,2,3,4-tetrahydroquinazoline derivative organic molecule. Then second aim is to investigate of metal salt effect. In this work two Nickel(II) ion complexes were synthesized with different metal salts in the same reaction conditions. We want to study on ligand and complexes spectroscopic thermic and magnetic behaviours. Finally researchers were analysed the antimicrobial activities of synthesized ligand and complexes.

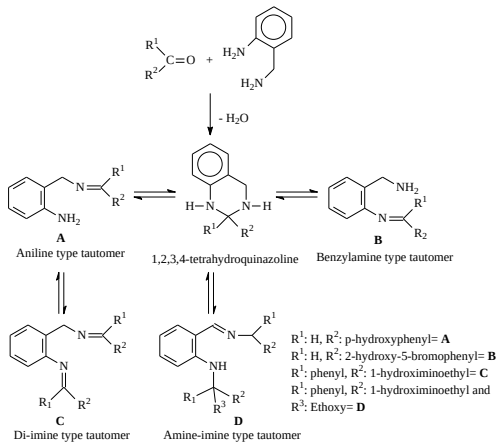

Figure 1. Synthesis and Tautomeric forms of the 1,2,3,4-tetrahydroquinazolines..

2. Experimental Studies

2.1. Materials and Measurements:

All chemicals and solvents used for the synthesis were of reagent grade. $NiCl_2{\cdot}6H_2O$, $Ni(NO_3)_2{\cdot}6H_2O$, 2,3-butanedione monoxime, 2-aminobenzylamine, C_2H_5OH (Aldrich) were used as received without any purification operation. Elemental analysis for C, H and N were carried out using a Vario EL II CHNS Elemental Analyzer. Magnetic susceptibility measurements were performed at room temperature using a Sherwood Scientific MK1 model Gouy magnetic balance. The mass spectra are recorded on Agilent 1100 Series LC/MSD Trap SLl by using methanol solutions. UV-vis spectra were obtained in the DMF solutions (10^{-3} mol/L) of the complex with a Shimadzu Pharmaspec UV-1700 spectrometer in the range of 1000-190 nm. FT-IR spectra were recorded in the 4000-400 cm^{-1} region with a Bruker Optics, Vertex 70 FT-IR spectrometer using KBr pellets. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian Mercury Plus 400 MHz FT-NMR spectrometer, utilizing deuterated dimethylsulphoxide as a solvent and TMS was used as an internal standard. Diamond TG/DTA thermal analyzer was used to record simultaneous TG and DTG curves in nitrogen and DTA curve in static air atmosphere at a heating rate of 10°Cmin^{-1} in the temperature range of 20-1000 °C using platinum crucibles.

2.2. Syntheses:

Synthesis of 2-methyl-2-(1-hydroxyiminoethyl)-1,2,3,4-tetrahydroquinazoline (1 or HL):

The synthesis of the Ligand (**1**) was shown in Figure 2.

The compound can be alternatively named as 1-(2-methyl-1,2,3,4-tetrahydroquinazolin-2-yl) ethanone oxime. A solution of 2-aminobenzylamine (10 mmol, 1.25 g) in ethanol (30mL) was added dropwise to a solution of 2,3-butanedione monoxime (10 mmol, 1.01 g) in ethanol at -5°C. After 2 hours, glacial acetic acid (1.5 mL) was added dropwise to the mixture.

The solutions were cooled to -15°C by a temperature-controlled bath and stirred for 6 h, then kept for 12 h and the crystalline products were collected by filtration and dried on air (Figure 1). The precipitated white crystal product was filtered, washed with water and then recrystallized from ethanol. Ligand (**1**) was collected with 77% yield. Melting point of the **1** was determinated as 147.5°C. Calculated mass values of **1** for $C_{11}H_{15}N_3O$ formula are C: 64.3, H:7.4 and N:20.5. Elementel analysis results are found as C: 64.5, H:7.5 and N:20.5.

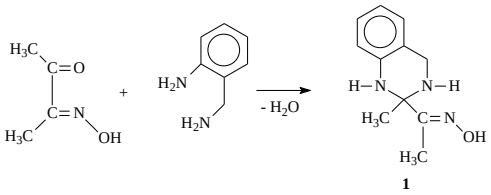

Figure 2. Synthesis of the 2-methyl-2-(1-hydroxyiminoethyl)-1,2,3,4-tetrahydroquinazoline.

Syntheses of 2 and 3:

A solution of HL (1 mmol, 0.205 g) in ethanol (20 mL) was added dropwise with stirring at 50ºC to a solution of $Ni(NO_3)_2{\cdot}6H_2O$ in ethanol (1 mmol, 0.291 g) or $NiCl_2{\cdot}6H_2O$ (1 mmol, 0.237 g) (25 mL).

Nickel salts and HL were solved in the ethanol and the solutions were stirred 5 h at 50°C. Then solutions were cooled to room temperature and filtered. The yellow (compound **2**) and red (compound **3**) solids (Figure 2) formed were filtered and washed with 20 mL of water-ethanol and washed

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

with 20 mL of water-ethanol and dried in air.

Compound (**2**) was collected with 45% yield. Calculated mass values of **2** for $C_{22}H_{29}N_7NiO_5$ formula (530.20 g/mol) are C: 49.84, H: 5.51 and N: 18.49. Elementel analysis results are found as C: 49.43, H: 5.36 and N: 18.33. Effective magnetic moment value is 0, so diamagnetic. LC-MS (m/z): 470.2 $[M+2]^+$.

Compound (**3**) was collected with 68% yield. Calculated mass values of **3** for $C_{11}H_{21}Cl_2N_3NiO_4$ formula (388.97 g/mol) are C: 42.01, H: 4.47 and N: 16.33. Elementel analysis results are found as C: 41.96, H: 4.43 and N: 16.28. Effective magnetic moment value is 2.99, so Ni(II) ion has two unpaired electrons. LC-MS (m/z): 434.9 $[M+CH_3OH]^+$.

Ligand (**1**) was collected with 77% yield. Melting point of the **1** was determinated as 147.5°C. Calculated mass values of **1** for $C_{11}H_{15}N_3O$ formula are C: 64.3, H:7.4 and N:20.5. Elementel analysis results are found as C: 64.5, H:7.5 and N:20.5.

2.3. X-ray Crystallography:

Intensity data were collected on an Image Plate Diffraction System (IPDS 2) from STOE using graphite-monochromated Mo-Kα radiation. Data collection and cell refinement was performed using X-Area [6] while X-Red32 [6] was used for data reduction. The structure was solved using Sir2004 [7] and refinement was done against F^2 using SHELXL-97 [8]. OrtepIII [9] was used for molecular graphics while the publication material was prepared using Wingx [10]. All non-hydrogen atoms were refined anisotropically. The C-H hydrogen atoms were positioned with idealized geometry and refined using a riding model. The N-H and O-H hydrogen atoms located in the difference map were refined isotropically using a riding model.

2.4. Antimicrobial Activity Test:

Assay of Agar Diffusion In-vitro:

The synthesized ligand and complexes were tested for their antimicrobial (antibacterial and antifungal) activities by disc-diffusion method [11,12]. A total of 10 microbial species including 7 bacteria, 2 yeasts and 1 mold were used as test organisms in this study. The antimicrobial activities were evaluated against gram positive (*Bacillus cereus* NRRL 3711, *Staphylococcus aureus* ATCC 25923, *S. epidermidis* NRRLB-4268, *Nocardia canis*) and gram negative (*Escherichia coli* ATCC 25922, *Proteus vulgaris* NRRL B-123, *Pseudomonas aeroginosa* ATCC 10145) bacteria, yeast cultures (*Candida albicans* ATCC 10231, *Rhodotorula rubra*) and fungi culture (*Aspergillus niger* ATCC 10949). Bacterial and fungal cultures were maintained on Nutrient slants at 4°C and were subcultured in petri dishes prior to use.

In the disc-diffusion method, steril paper disc (Ø 6mm) impregnated with 10 µL of the test compounds (dissolved dimethylsulfoxide compound at concentrations of 100 µg) were used. Test bacteria was transferred to tubes containing 4 to 5 mL Nutrient Broth. The test cultures were incubated at 37°C until they were visibly turbid. The density of these cultures was adjusted to 0.5 Mc Farland (at 625 nm, 0.08-0.1 absorbance) with sterile saline. A suspension containing approximately 10^8 CFU/ml for bacteria, 10^7 CFU/mL for yeasts and 10^5 CFU/mL for mould was spread on the plates of NA. The entire surface of the NA plates was inoculated by streaking with a sterile swab dipped into adjusted suspension. Then, the paper discs impregnated with the solutions of the ligand and compounds tested were placed on the surface of the media inoculated with the microorganisms. After pre-incubation for one hour at 4°C, the plates were incubated at 37°C for 24 h for bacterial strains, 48 h for yeast and for 72 h for fungi at room temperature. After incubation, the growth inhibition zones around the disc were observed indicating that the examined compound inhibits the growth of microorganisms. DMSO was used as a control under the same condition for tested microorganisms. Each assay in this experiment was repeated three times. Tetracycline (10 µg/disc) for bacteria and Nystatin (100U/disc) for yeast and fungi were used as positive controls.

3. Results and Discussion

In this work, a 2-subsitituted 1,2,3,4-tetrahydroquinazoline **1** was synthesized from 2-aminomethylaniline (2-aminobenzylamine) and 2,3-butanedione-2-oxime (as ketone) (Figure 2). Structure of **1** was determined by the NMR, IR spectroscopic techniques and X-ray single crystal analyses. Tautomeric forms of **1** were searched for by the NMR spectroscopy mainly in DMSO-d_6 and no sign for tautomeric forms in solution was found. The Nickel(II) complexes of **1** were prepared by using $Ni(NO_3)_2{\cdot}6H_2O$ for **2** and $NiCl_2{\cdot}6H_2O$ for **3** as precursors and characterized by using NMR, IR, mass spectroscopy, elemental and thermal analysis techniques.

3.1. Crystal Structure of 1:

The crystallographic data of **1** are summarized in Table 1 and selected bond lengths and angles and hydrogen bond geometries are listed in Table 2. The

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

molecular structures with intramolecular hydrogen bonds and inter molecular hydrogen bonds and C-H···π and N-H···π interactions of HL are shown in Figure 3 and Figure 4, respectively.

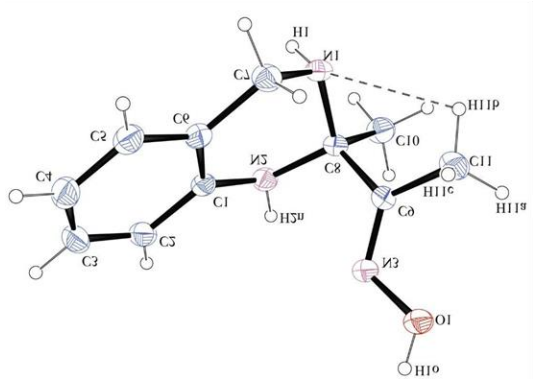

Figure 3. An ORTEP representation of **1** in 30% ellipsoid probability level.

1,2,3,4-tetrahydroquinazoline part of the ligand is not planar like similar quinazolines. The C7 atom has distorted tetrahedral environment. These results coincide with the phenyl analog of **1** [5]. The intramolecular hydrogen bond was found between the C11-H11b and N1 atoms (Table 2, Figure 3).

Table 1. Crystal data and structure refinement for compound **1**.

Crystal Data	
Formula	$C_{11}H_{15}N_3O$
Formula Weight [g/mol]	205.26
Crystal System	Monoclinic
Space group	P21/c (No. 14)
a, b, c [Å]	11.4063(8) 8.5365(8) 12.3751(9)
α, β, γ [°]	90 115.926(5) 90
V [Å^3]	1083.69(16)
Z	4
D(calc) [g/cm^3]	1.258
μ (MoKα) [mm]	0.084
F(000)	440
Crystal Size [mm]	0.11x0.35x0.54
Data Collection	
Temperature (K)	296
Radiation [Å]	MoKa 0.71073
Theta Min-Max [°]	2.0, 26.5
Dataset	-14: 14; -10: 10; -15: 15
Tot., Uniq. Data, R(int)	10360, 2244, 0.126
Observed data [I > 2.0 sigma(I)]	1613
Refinement	
Nref, Npar	2244, 145
R, wR2, S	0.0492, 0.1267, 1.03
w = 1/[s^2(Fo^2)+(0.0538P)^2+0.1250P]	where P=(Fo^2+2Fc^2)/3
Max. and Av. Shift/Error	0.00, 0.00
Min. and Max. Resd. Dens. [e/Å^3]	-0.21, 0.17

There were two types of intermolecular hydrogen bonds. One of them was D-H···A type and the other was D-H···π type (Figure 4 and Table 2). The O1 atom of **1** acted as hydrogen bond donor via its H1o atom to N1 atom of **1** at x, -y+1/2, z+1/2 and the C11 atom formed hydrogen bond via its H11C and H11B atom with the O1 atom of **1** at –x, -y+1, -z+1 and x, -y+1/2, z-1/2 to form D-H···A type intermolecular hydrogen bonds, respectively (Table 2, Fig. 2). N1 atom of the **1** formed hydrogen bond via its hydrogen atom with the phenyl ring at –x+1, -y, -z+1 and C2 atom composed hydrogen bond via its hydrogen atom with the phenyl ring at –x+1, y-1/2, -z+3/2 to form D-H···π type intermolecular hydrogen bonds, respectively (Table 2, Fig. 4).

Table 2. Selected bond lengths and angles and hydrogen bond geometries of **1**.

Bond	**Length**	**Bond**	**Length**
N1-C7	1.465(3)	C1-C6	**1.395(3)**
N1-C8	1.469(2)	C6-C7	1.510(3)
N1-H1	0.90(2)	C8-C9	1.529(3)
N2-C1	1.388(3)	C8-C10	1.523(3)
N2-C8	1.456(2)	C9-C11	1.496(3)
N2-H2n	0.85(2)	O1-H1o	0.8200
N3-C9	1.276(2)	O1-N3	1.403(2)
Bond	**Angle**	**Bond**	**Angle**
N1-C8-C10	108.75(14)	C1-N2-C8	118.44(15)
N1-C8-C9	109.92(14)	C1-N2-H2n	116.4(16)
N1-C8-N2	108.50(16)	C5-C6-C7	121.45(18)
N2-C1-C2	120.43(17)	C1-C6-C7	119.33(18)
N2-C1-C6	120.17(16)	C7-N1-C8	112.13(14)
N2-C8-C9	112.72(13)	C7-N1-H1	108.5(15)
N2-C8-C10	108.37(15)	C9-C8-C10	108.49(17)
N3-C9-C8	114.75(15)	C8-C9-C11	120.63(15)
N3-C9-C11	124.35(18)	C8-N1-H1	103.2(14)
N3-O1-H1o	109.00	C8-N2-H2n	114.3(17)
O1-N3-C9	112.22(14)	N1-C7-C6	113.67(17)

D-H···A	**D-H**	**H···A**	**D···A**	**D-H···A**
C11-H11B···N1	0.96	2.59	2.966(3)	103.8
C11-H11C···O1^{i}	0.96	2.96	3.437(3)	112.3
C11-H11B···O1^{ii}	0.96	3.00	3.922(3)	161.6
O1-H1o···N1^{iii}	0.82	2.05	2.8090(19)	153.1
N1-H1···Cg^{iv}	0.898	2.534	3.424	171.29
C2-H2···Cg^{v}	0.93	3.194	4.031	150.7

i: –x, -y+1, -z+1 iv: –x+1, -y, -z+1
ii: x, -y+1/2, z-1/2 v: –x+1, y-1/2, -z+3/2
iii: x, -y+1/2, z+1/2 Cg refer to center of phenyl ring

So, these intermolecular hydrogen bonds formed the three-dimensional network in solid state (Figure 4).

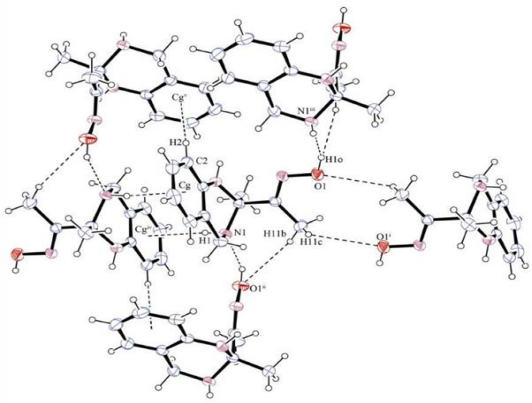

Figure 4. Intermolecular hydrogen bonds of **1** in solid state (intramolecular bonds omitted).

3.2. ^{1}H NMR Spectra of the 1 and 2:

NMR spectrum data for **1** and **2** were shown in Table 3.

In the ^{1}H NMR spectrum of the Ligand (**1**), a singlet peak for the OH proton of oxime group was observed at 8.24 ppm. The N-H proton adjacent to

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

the CH_2 groups in the heterocyclic ring resonated at 4.48 ppm (1H as a broad band) and the other one resonated at 4.62 ppm (1H). The CH_2 group in the hetero cyclic ring of the ligand resonated at 3.85, 3.81, 3.75 and 3.71 ppm (as quartet, 2H). The CH_3 protons adjacent to the oxime group resonated at 1.96 (3H) and the other one at 1.25 ppm (3H). The aromatic C-H protons resonated at 6.52-7.10 ppm (4H). In the ^{13}C NMR spectrum, **1** had the peaks at 9.60, 27.65, 43.24, 70.01, 115.26, 118.03, 120.66, 126.05, 127.58, 142.78 and 160.19 ppm as expected. The NMR and IR spectrum of **1** was in good agreement with the known oximes [5,13-16] and 1,2,3,4-tetrahydroquinazolines [2,3,5] and 2-Phenyl-2-(1-hydroxyiminoethyl)-1,2,3,4-tetrahydroquinazoline [5] which was the phenyl analog of the synthesized compound, and suitable for the synthesized **1.**

Table 3. NMR spectrum datas for **1** and **2**.

	CH_3	$CH_{3\text{-oxime}}$	CH_2	$NH_{\text{-}CH2}$	NH	$H_{aromatic}$
1	1.25	1.96	3.85, 3.81, 3.75 3.71	4.48 broad	4.62	6.52-7.10
2	1.75	2.14	4.81, 4.79, 4.77, 4.75	5.28 broad	4.14 and 4.10	6.73-7.20

	C11	C10	C7	C8	C2	C4	C6	C3	C5	C1
1	9.60	27.65	43.24	70.01	115.26	118.03	120.66	126.05	127.58	142.78
2	11.84	29.36	45.09	75.51	115.14	118.33	118.99	126.80	128.86	141.49

In the ^1H NMR spectrum, Complex **2** had a peak at 18.07 ppm (1H) indicating that the complex has an OH which was in oxime part [14]. The peaks at 5.28 for NH adjacent to the CH_2 (2H, as broad band), 4.81, 4.79, 4.77, 4.75 for CH_2 (4H, as quartet) and 4.14 and 4.10 for NH (2H) indicated that the heterocyclic ring in the ligand was not open during the complexation and coordination via NH which was adjacent to the CH_2, contrary to phenyl analog of the ligand. The CH_3 protons resonated at 1.75 (6H) and 2.14 (6H) ppm [5].

3.3. IR Spectra:

In the IR spectrum of the ligand, bands at 3390, 3340, 3279, 3174-3011, 2984-2850, 1610, 1500-1484, and 946 cm^{-1} belong to O-H, N2-H, N1-H, C-$H_{arom.}$, C-$H_{aliph.}$, C=N, -C-N- and N-O vibrations, respectively [5]. Elemental analyses, thermal analyses and mass spectral analyses results of **2** ($[Ni(L)(LH)]\cdot(NO_3)$) and **3** ($[NiCl_2(LH)(H_2O)_2]\cdot(H_2O)$) support each other. The IR spectra of **2** and **3** resemble each other indicating that the heterocyclic ring in **1** was not open during complexation in both complexes.

Complex **2** had bands at 3390 cm^{-1} (as shoulder) in their IR spectra, indicating O–H proton of the oxime group was not released upon complex formation [13,17-19]. But, the ^1H-NMR spectrum of the complex showed that the complex had one OH oxime proton. Therefore, these results indicate that hydrogen deprotonated from one oxime group while it did not from the other one in Complex **2**. This is inferred by the two peaks for C=N at 1614 and 1602 cm^{-1}. The peak at 3336 cm^{-1} was attributed to N2H, indicating that the N2H was not coordinated to metal. This is inferred by the peaks for N2H at 1500 cm^{-1} (1500 cm^{-1} for free **1**). The peak for N1-H which was at 3279 cm^{-1} in free ligand, was detected at 3200 cm^{-1}. The peak at 1484 cm^{-1} for N1-H in the free ligand shifted to 1446 cm^{-1} in Complex **2**, showing bonding to the metal through the nitrogen of N1H. The N-O absorption for free ligand at 946 shifted to a higher frequency (970 cm^{-1}) indicating that the oxime oxygen was not coordinated to the metal [5,13,18-20]. Thus, we may conclude from the overall IR results that the complex has both anionic and non-ionic ligands coordinating through their oxime nitrogen and nitrogen of heterocyclic ring of the ligand.

The thermal analyses results showed that Complex **3** has three moles of water and so it has broad band which overlapped O–H and N2H of the ligand at the 3450-3300 cm^{-1} in their IR spectra[11]. Complex **3** had one peak for C=N indicating that the oxime nitrogen coordinated to the metal at 1614 cm^{-1}. The peak at 1500 cm^{-1} for N2H remained as a non-shifting bond indicating that the N2H was not coordinated to metal. The peak for N1H, which was at 3279 cm^{-1} in free ligand, was detected at 3223 cm^{-1} and the peak at 1438 cm^{-1} for N1H in the free ligand shifted to 1460 cm^{-1} in Complex **3**, showing bonding to the metal through the nitrogen of N1H. The N-O vibration for free ligand shifted to 950 cm^{-1} indicating that the oxime oxygen was not coordinated to the metal [5,13,18-20]. The IR spectrum of **3** has also a peak at 1653 cm^{-1} showing that the aqua ligand is coordinated to this complex. Thus, we may conclude from the overall IR results that the complex has a neutral ligand coordinating through their oxime nitrogen and nitrogen of heterocyclic ring of **1** and aqua ligand.

3.4. Thermal Property:

$[Ni(L)(LH)]\cdot(NO_3)$ (2):

Complex **2** shows a three-stage mass loss (Figure 5). Compound **2** is thermally stable up to about 147ºC. The first stage in the temperature range of 147-242ºC corresponds to the exothermic elimination of nitrate anion and 2-aminobenzylamine molecule (DTG_{max} = 240ºC, found = 35.10, calcd. 34.73%). The exothermic second and third stages are related to the decomposition of the L molecule and

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

remaining of diacetylmonoxime in the range of 242–509ºC (DTG_{max} = 394 and 450ºC, found = 52.90, calcd. = 54.95%). The final decomposition product is NiO (found = 12.00%, calcd. = 14.08%).

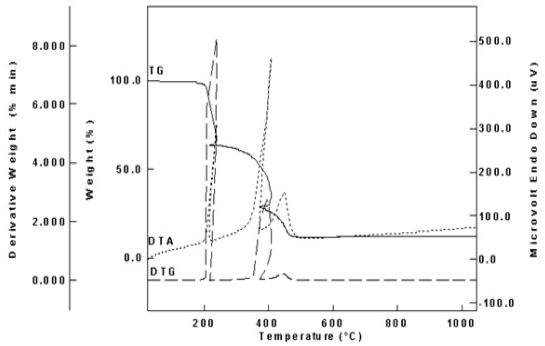

Figure 5. TG, DTG and DTA curves of **(2).**

$[NiCl_2(LH)(H_2O)_2]\cdot(H_2O)$ (3):

The TG-DTG and DTA curves of **3** are shown in Figure 6. The first and second stages are related to endothermic removal of two crystal and one coordinated water molecules in the temperature range of 35-218ºC (DTG_{max} = 67ºC for crystal water and 158ºC for coordinated water, mass loss found = 13.30, calcd. = 13.88%) [21]. The third and fourth exothermic stages between 218 and 392ºC are related to the release of two chloro ligands (DTG_{max} = 228 and 280ºC, found = 17.20, calcd. = 18.25%). The following three exothermic stages (DTG_{max} = 410, 498 and 569ºC) between 392 and 641ºC correspond to the loss of L molecule (found = 50.50, calcd. = 52.77%). The final decomposition product is NiO (found = 18.60%, calcd. = 19.20%).

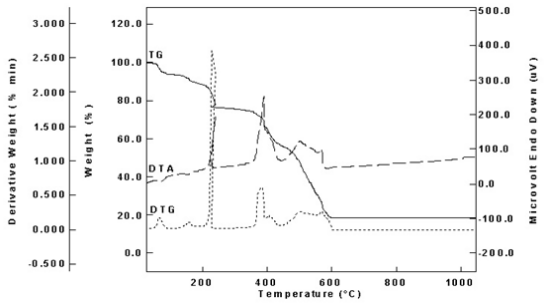

Figure 6. TG, DTG and DTA curves of **(3).**

3.5. UV-vis Spectra and Magnetic Susceptibilities:

The electronic spectrum of **2** in DMF solution (10^{-4} M) show absorptions in the UV region at 233, 263 and 280 nm (ε = 302, 759 and 735 L mol^{-1} cm^{-1}, respectively). This transition may be assigned to intra-ligand charge transfer (n→π* and π→π*) transitions. In electronic absorption spectrum of **2**, two d–d transitions are observed at 735 nm and 660 nm corresponding to the $^1A_{2g}\leftarrow{}^1A_{1g}$ (ε = 8 L mol^{-1} cm^{-1}) and $^1B_{1g}\leftarrow{}^1A_{1g}$ (ε = 14 L mol^{-1} cm^{-1}) transitions, respectively, supporting a square-planar structure [22].

UV–Vis spectrum of **3** in DMF solution (10^{-3} M) showed the expected π→π* bands at 224–242 nm. The bands in the range of 268-283 nm may be assigned to n→π* transitions of the aromatic ring and C=N chromophores of the 2-aminobenzylamine and diacetylmonoxime moieties. Electronic absorp-tion spectrum of **3** exhibits d–d transition bands at 728 nm (ε = 8 L mol^{-1} cm^{-1}) and 505 nm (ε = 25 L mol^{-1} cm^{-1}) attributable to $^3T_{2g}\leftarrow{}^3A_{2g}$ and $^3T_{1g}(F)\leftarrow{}^3A_{2g}$ which may be observed as doublet due to the spin–orbital coupling in a distorted octahedral environment [23]. The room temperature magnetic moment studies were carried out on powdered samples of the complexes. Complex **2** did not show any magnetic moment which indicates to the dia-magnetic nature in a square-planar geometry. Complex **3** exhibited magnetic moments in the range of 2.99 B.M at room temperature the corresponding to two unpaired electrons which suggest an octahedral geometry [24].

The suggested structures were illustrated in Figure 7 in the light of these data.

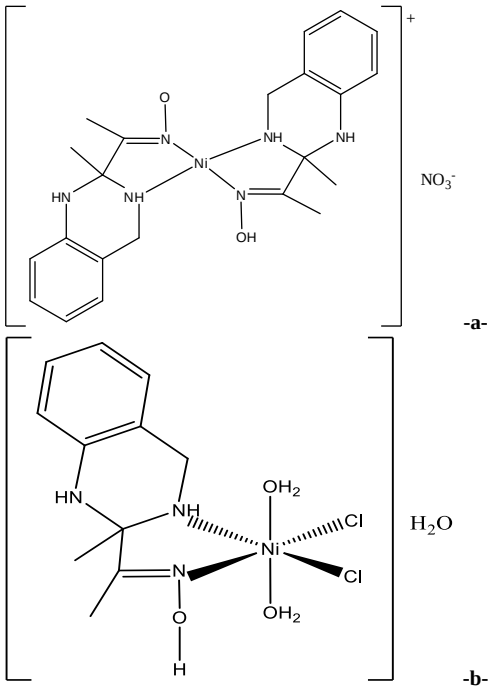

Figure 7. Suggested structures for a) Complex 2; b) Complex 3.

3.6. Antimicrobial Activity:

Ligand (**1**) and complexes (**2** and **3**) were screened with disc diffusion method for their antimicrobial activity against tested microorganisms.

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

The results of the antibacterial and antifungal activities were shown in Table 4. Ligand **1** exhibited very weak inhibition effects against tested micro-organisms. Complex **2** showed antibacterial and antifungal activity against the tested gram positive, gram negative bacterial strains, yeast and fungi, with the diameters of zone inhibition ranging between 7-8 mm. Complex **3** showed a moderate degree of antibacterial and anticandidal activity against the tested *S. epidermidis* and *C. albicans*, with an inhibition zone of 10 mm at 100µg/disc test concentration. It is suggested that the increased lipophilic character of metal complexes may be responsible for their more potent antimicrobial activity than the free amides. The permeation of complexes through the lipid layer of the cell membranes deactivates diverse cellular enzymes, which play a vital role in various metabolic systems of these microorganisms [25]. Complex **2** showed less antimicrobial activity against tested microorganisms when compared with Complex **3**. Complexes showed less antimicrobial activity against tested microorganisms when compared with standard antibiotics.

Table 4. Antimicrobial activities of **1**, **2** and **3** (discs Ø 6mm).

	Inhibition zone in diameter (mm/sensitive strains)				
	Ligand and Compounds			References antibiotics	
Test Microorganisms	**1** 100µg	**2** 100µg	**3** 100µg	Nystatin 100U/disc	Tetracycline 10µg/disc
Gram positive bacteria					
B. cereus	-	7	8		32
S. aureus	-	8	9		33
N. cants	7	7	8		22
S. epidermidis	7	7	10		15
Gram negative bacteria					
E. coli	7	7	8		25
P. aeroginosa	-	7	7		17
P. vulgaris	7	7	8		16
Yeast and Fungi					
C. albicans	-	8	10	20	
R. rubra	-	7	8	22	
A. niger	-	7	7	22	

-; no zone of inhibition

4. Conclusions

The 2-methyl-2-(1-hydroxyiminoethyl)-1,2,3,4-tetrahydroquinazoline (**1=LH**) and its novel Ni(II) complexes, square-planar $[Ni(L)(LH)]\cdot(NO_3)$ (**2**) and octahedral $[NiCl_2(LH)(H_2O)_2]\cdot(H_2O)$ (**3**), (L = anionic form of the ligand) have been synthesized. The ligand and complexes have been characterized by means of elemental, IR, UV-Vis., ^{1}H-NMR, ^{13}C-NMR spectroscopic studies, magnetic susceptibility, thermal analysis, mass spectroscopy and X-ray diffraction technique. The heterocyclic ring of the ligand was not open during the complexation. The newly synthesized complexes showed weak or moderate activity against all tested microorganisms.

Acknowledgments

The authors are indebted to the Dumlupinar University Research Found for support (Grant No: 2007/14). Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as the supplementary publication No. CCDC 735999. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44-1223-336033
E-mail: deposit@ccdc.cam.ac.uk

References

[1] W.H.Correa, S. Papadopoulos, P. Radnidge, B.A. Roberts, J.L. Scott, "Direct, efficient, solvent-free synthesis of 2-aryl-1,2,3,4-tetrahydroquinazolines", Green Chem. 4, 2002, 245-251.
Doi: 10.1039/B202729C

[2] A. Göblöys, L. Lázár, F. Fülöp, "Ring-chain tautomerism of 2-aryl-substituted-hexahydropyrimidines and tetrahydroquinazolines", Tetrahedron 58, 2002, 1011-1016.
https://doi.org/10.1016/S0040-4020(01)01196-6

[3] J. Sinkkonen, K.N. Zelenin, A.K.A. Potapov, I.V. Lagoda, V.V. Alekseyev, K. Pihlaja, "Ring-chain tautomerism in 2-substituted 1,2,3,4-tetrahydroquinazolines A 1H, 13C and 15N NMR study", Tetrahedron 59, 2003, 1939-1950.
https://doi.org/10.1016/S0040-4020(03)00148-0

[4] K. Tanaka, R. Shiraishi, "Clean and efficient condensation reactions of aldehydes and amines in a water suspension medium", Green Chem. 2, 2000, 272-273.
Doi: 10.1039/B006424F

[5] A.T. Çolak, M. Taş, G. İrez, O.Z. Yeşilel, O. Büyükgüngör, "Syntheses, Spectral, Thermal and Structural Characterization of 2-Phenyl-2-(1-hydroxyiminoethyl)-1,2,3,4-tetrahydroquinazoline and Its Novel Nickel(II) Complex", Z. Anorg. Allg. Chem. 633, 2007, 504-508.
Doi: 10.1002/zaac.200600343

[6] Stoe&Cie, X-Area (Version 1.18) and X-Red32 (Version 1.04), Stoe&Cie. Darmstadt, Germany, 2002.

[7] M.C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G. L. Cascarano, L. D. Caro, C. Giacovazzo, G. Polidori, R. Spagna, "SIR2004: an improved tool for crystal structure determination and refinement", J. Appl.

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

Crystallogr. 38, 2005, 381-388.
Doi: 10.1107/S002188980403225X

[8] Sheldrick G.M. "SHELXL-97: Program for the Refinement of Crystal Structures". Germany University of Göttingen, 1997.

[9] C.K. Johnson, M.N. Burnett, "ORTEP-III (version 1.0.2), Rep. ORNL-6895", Oak Ridge National Laboratory, Oak Ridge, TN (USA) (1996). Windows version: Farrugia L.J., University of Glasgow, Glasgow, Scotland (U.K.), 1997.

[10] L.J. Farrugia, "WinGX suite for small molecule single-crystal crystallography", J. Appl. Crystallogr. 32, 1999, 837-838.
Doi: 10.1107/S0021889899006020

[11] "National committee for clinical laboratory standards (NCCLS) Performance standards for antimicrobial disk susceptibility tests." Approved standard (M2-A4). National committee for clinical laboratory standards Villanova, PA. 1990a.

[12] "National committee for clinical laboratory standards. Methods for dilution antimicrobial susceptibility test for bacteria that grow aerobically. "Approved standard (M7-A2). National committee for clinical laboratory standards, Villanova, PA. 1990b.

[13] M. Taş, H. Batı, "Ligands consisting of a C=O and an –NH−R adjacent to the oxime group and their cobalt(II), nickel(II) and copper(II) complexes", J. Chem. Res, 2006, 87-92.

[14] A. Zülfikaroğlu, M. Taş, H. Batı, B. Batı, "The synthesis and Characterization of Substituted Aminomethylglyoximes and Amino phenylglyoximes and their Complexes with Some Transition Metals, Synth. React". Inorg.Met. Org. Chem. 33, 2003, 625-638.

[15] H. Batı, M. Taş, B. Batı, "The Synthesis and Characterization of New Unsymmetrical Vic-Dioximes and Their Complexes with Some Transition Metals", Synth. React. Inorg. Met. Org. Chem. 31, 2001, 541-548.
Doi: 10.1081/sim-100104785

[16] H. Batı, M. Taş, M. Macit, "The Synthesis and Characterization of Some New vic-Dioxime Ligands and Their Ni(II), Cu(II) and Co(II) Complexes, Synth. React. Inorg". Met.-Org. Chem. 28(8), 1998, 1371-1380.
https://doi.org/10.1080/00945719809349411

[17] M.V. Barybin, P.L. Diaconescu, C.C. Cummins, "Coordination Chemistry of a Chelating Amidoximato Ligand, Inorg". Chem. 40, 2001, 2892-2897.
Doi: 10.1021/ic0100370

[18] S. Sevagapandian, G. Rajagopal, K. Nehru, P. Athappan, "Copper(II), nickel(II), cobalt(II) and oxovanadium(IV) complexes of substituted β-hydroxyiminoanilides", Trans. Metal Chem. 25, 2000, 388-393.

[19] R.M. Srivastava, I.M. Brinn, J. O. Machura-Herrera, H.B. Faria, G.B. Carpenter, D. Andrade, C.G. Venkatesh, L. P. F. Morais, "Benzamidoximes: structural, conformational and spectroscopic studies", J. Mol. Struct. 406, 1997, 159-167.
https://doi.org/10.1016/S0022-2860(96)09452-5

[20] F. Karipçin, H.I. Uçan, I. Karataş, "Binuclear and mononuclear cobalt(II), nickel(II) and copper(II) complexes of 4,4′-bis(alkylaminoisonitrosoacetyl)diphenyl-methane derivatives", Trans. Metal Chem. 27, 2002, 813-817.

[21] M. Taş, H. Batı, "Co(II), Ni(II) and Cu(II) Complexes of 1,4-Di-(1-Hydroxyimino-2-Phenyl-2-Oxo-Ethylamino)Benzene Synthesis, Charac-terization and Thermal Studies", J. Therm. Anal. Cal. 85, 2006, 295-299.

[22] B. K. Singh, U. K., Jetley, R. K., Sharma, B. S. Garg, "Synthesis, characterization and biological activity of complexes of 2-hydroxy-3,5-dimethylacetophenoneoxime (HDMAOX) with copper(II), cobalt(II), nickel(II) and palladium(II)", Spectrochimica Acta Part A 68, 2007, 63-73.
https://doi.org/10.1016/j.saa.2006.11.001

[23] N. Tounsi, L. Dupont, A. Mohamadou, E. Guillon, M. Aplincourt, G. Rogez, "Synthesis of new Cu(II), Ni(II) and Co(II) complexes with a bis-amide ligand functionalized with pyridine moieties: Spectral, magnetic and electrochemical studies", Polyhedron 27, 2008, 3674-3682.
https://doi.org/10.1016/j.poly.2008.09.020

[24] M.C. Fernández-Fernández, R.B. Calle, A.

Corresponding Author E-mail: tolga.colak@dpu.edu.tr

Macías, L.V. Matarranz, P.P. Lourido, "Co(II), Ni(II) and Cu(II) complexes of new [1+1] and [2+2] macrocyclic ligands derived from 1,4-bis(2′-formylphenyl)-1,4-dioxabutane and cis-1,2-dia-minocyclohexane", Polyhedron 27, 2008, 2301-2308.
Doi: 10.1016/j.poly.2008.04.043

[25] F. Hamurcu, A. B. Gündüzalp, S. Çete S., B. Erk, "The synthesis, characterization and antimicrobial activity of N,N′-bis(2-thio-phenecarboxamido)-1,3-diaminopropane and N,N′-bis (2-furancarboxamido)-1,3-diamino-propane and their Cu(II), Zn(II), Co(III) complexes", Tran. Met. Chem. 33, 2008, 137-141.
Doi 10.1007/s11243-007-9028-9

Corresponding Author E-mail: tolga.colak@dpu.edu.tr