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A Study on N-Hydroxyamide Ethoxycarbonylhydrazones

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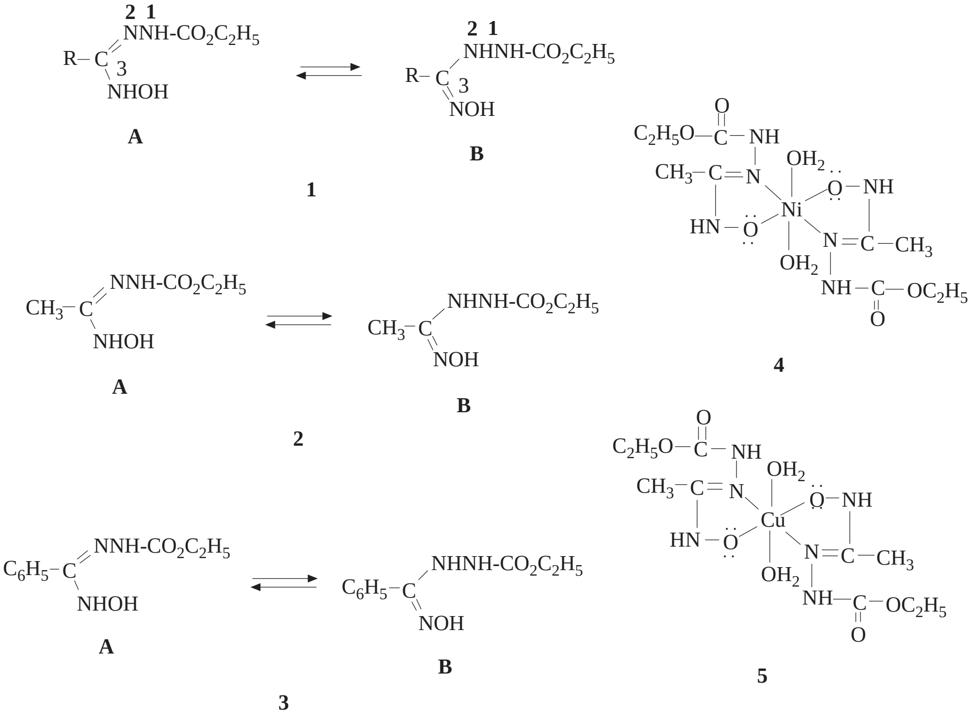
The structures and electronic properties of N-hydroxyamide ethoxycarbonylhydrazones were investigated by a quantum-chemical method AMl. The total energies, heats of formation, dipol moments, ionization potentials, proton affinities and energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) were calculated and discussed. The stabilities of the tautomeric forms and of E and Z isomers for these compounds were determined. The complex forming ability of these compounds with metal cations was also studied. The geometry and electronic properties of the complexes formed by N-hydroxyacetamide ethoxycarbonylhydrazone with Ni^{2+} and Cu^{2+} were investigated using ZINDO/1 semiempirical method. Moreover, these complexes were synthesized and identified.

Introduction

It has been reported that amidrazones are able to exhibit tautomerism between N^2 and N^3 atoms[1−5]. Some of amidrazones exist exclusively in amide hydrazone form whilst some others exist in hydrazide imide structure[6]. It has been shown that N^3-unsubstituted amidrazones exist exclusively in the amide hydrazone form[6−9]. On the other hand, compounds **1** (N-hydroxyamide ethoxycarbonylhydrazones **1A** or hydroxamic acid ethoxycarbonylhydrazides **1B**) have recently been reported as amidrazone derivatives[10]. These compounds are also subjected to tautomerism as shown in **Scheme 1.** For these compounds, the amide hydrazone structure has partly been supported by nmr data[10]. In fact the stability and related properties of the tautomers of compounds **1** are important in terms of alkylation, substitution, cyclocondensation and complex formation. For this reason, the present study was devoted to the investigation of the structures and electronic properties of the selected compounds of type **1** (compounds **2** and **3**). Moreover, the study also involves the investigation of the complexing ability of compounds **2** and **3** **(Scheme 1).**

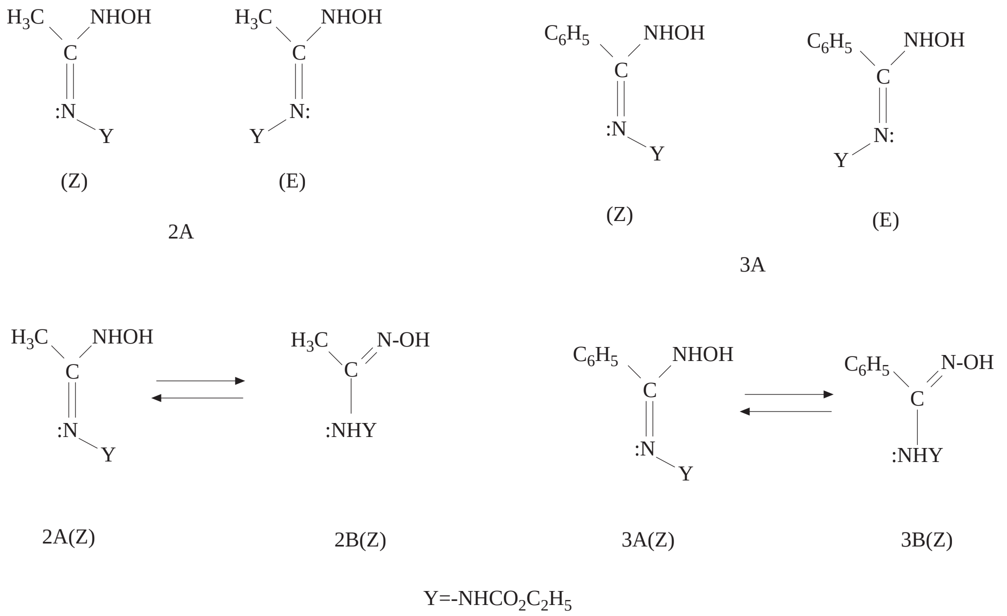


Scheme 1.

It is obvious that syn **(Z)** and anti **(E)** stereoisomers are possible for the amide hydrazone structures of compounds **2** and **3** investigated in this study (**2A** and **3A**, respectively) **(Scheme 2).** On the other hand, a tautomerism originating from the migration of NH proton of the NHOH group to the azomethine nitrogen must be considered for each stereoisomer of the two compounds. Thus, this tautomerism is shown in **Scheme 2** for the **Z** isomers of compounds **2** and **3**. Hence, a quantum-chemical investigation of the tautomers of these flexible molecules **2** and **3**, and the determination of their stable isomers would be important. On the other hand, molecules **2** and **3** having several basic centers may form various metal complexes. In general, the complexing ability of ligands is essentially related to their ionization potentials and proton affinities[11]. At the same time, a change of configuration affects the complexing ability of the ligands. For this reason, the conformational analysis and the theoretical calculations of protonation parameters of molecules **2** and **3** also appear important. A theoretical investigation of this type reveals that conformational, configurational or tautomeric change of the molecule may affect its proton affinity and the other electronic properties. In addition, the theoretical investigation of the metal complexes of **2** and **3** also appears important from the point of their stabilities and geometries.

Materials and Methods

In the present study, the conformational analyses of the molecules **2A** and **3A** and their tautomers **2B** and **3B** were performed using the semiempirical method AM1[12] and the stable isomers were determined. The proton affinity (PA) values for the azomethine nitrogens of the molecules **2A** and **3A** were calculated using AM1 treatment. Furthermore, the geometries and electronic properties of the predicted Ni^{2+} and Cu^{2+} metal complexes of **2A** were investigated using the semiempirical method ZINDO/1[13]. All calculations related to the study were made with the HyperChem 4.5 program on an IBM PC/AT-486 DX4-100 computer.



Scheme 2.

Experimental

In the experimental section of the study, the Ni^{2+} and Cu^{2+} complexes of compound **2** were synthesized and identified.

Melting points were determined with a Büchi oil heated melting point apparatus and are uncorrected. IR spectra were recorded as potassium bromide pellets using Perkin-Elmer 377 spectrophotometer. Combustion analyses were performed on a Carlo Erba 1106 Elemental Analyzer.

N-Hydroxyacetamide ethoxycarbonylhydrazone (acethydroxamic acid ethoxycarbonylhydrazide) ((**2**) was synthesized by a method previously reported[10]. The necessary compound ethyl acetate ethoxycarbonylhydrazone for the preparation of compound **2** was synthesized according to a published method[14]. The required chemicals were obtained from Fluka.

Synthesis of Complex **4**: Compound **2** (0.8058 g, 0.005 mol) was dissolved in 25 ml of absolute ethanol and a solution of $NiCl_2.6H_2O$ (0.5942 g, 0.0025 mol) in 10 ml of absolute ethanol was added dropwise with constant shaking. The pH of the mixture (pH=3.65) was raised to 5.00 by dropping triethylamine. After stirring on a water-bath for two hours, the mixture was cooled. The precipitate formed was washed with a small amount of water and subsequently with ethanol and ethyl ether. After drying in vacuo, the compound was identified as complex **4**. Yield: 0.882 g (85 %) of black crystals. M.p.>310°C; ir (KBr): 3420 (OH_2), 3230, 2980 (NH), 1660 (C=O), 1585 (C=N) cm^{-1}. The nmr and uv spectra of the compound could not be obtained due to the insolubility in an appropriate solvent.

Anal. Calcd. for $C_{10}H_{20}N_6O_6Ni.2H_2O$: C, 28.94; H, 4.86; N, 20.25

Found: C, 28.65; H, 4.62; N, 20.49

Synthesis of Complex **5**: Compound **2** (0.8058 g, 0.005 mol) was dissolved in 25 ml of absolute ethanol and a solution of $CuCl_2.2H_2O$ (0.4262 g, 0.0025 mol) in 10 ml of absolute ethanol was added dropwise with constant shaking. The pH of mixture (pH=3.20) was raised to 5.00 by dropping triethylamine. After stirring on a water-bath for 2 hours, the mixture was cooled. The precipitate formed was washed with a small amount of water and subsequently with ethanol and ethyl ether. After drying in vacuo, the compound was identified as complex **5**. Yield: 0.934 g (89 %) of gray crystals. M.p. 240-241°C (dec); ir (KBr): 3420 (OH_2), 3220, 2970 (NH), 1660 (C=O), 1585 (C=N) cm^{-1}. The nmr and uv spectra could not be obtained because of the insolubility of the compound in an appropriate solvent.

Anal. Calcd. for $C_{10}H_{20}N_6O_6Cu.2H_2O$: C, 28.61; H, 4.80; N, 20.01

Found: C, 28.36; H, 4.53; N, 19.64

Results and Discussion

The electronic properties of molecules **2A** and **3A** were investigated and their stabilities were determined with full geometry optimization by AM1 method. The calculated total energies (E_{tot}), the heats of formation (ΔH°_f), ionization potentials (IP), dipol moments (μ) and the energies of frontier molecular orbitals (E_{HOMO} and E_{LOMO}) are given in **Table 1.**

The results obtained indicate that Z isomers are more stable than E isomers for both these molecules. In other words, tautomers **2A** and **3A** exist exclusively in **Z** forms in ordinary conditions. The ionization potentials of **Z** isomers of both molecules are lower than those of the **E** isomers. An **Z** isomer possesses a higher electrodonor character than the corresponding **E** isomer.

Table 1. Total energies (in kcal/mol), heats of formation (in kcal/mol), ionization potentials (in eV), dipol moments (in Debye) and energies of frontier molecular orbitals (in eV) for **Z** and **E** isomers of molecules **2A** and **3A** (AM1).

Structure	$E_{tot.}$	ΔH°_f	IP	μ	E_{HOMO}	E_{LOMO}
2A (Z)	-54703.689	-64.977	9.259	2.663	-9.259	0.499
2A (E)	-54702.332	-63.620	9.432	1.196	-9.432	0.374
3A (Z)	-70084.517	-30.856	9.180	2.974	-9.180	-0.137
3A (E)	-70081.456	-27.796	9.278	4.750	-9.278	-0.314

Furthermore, the stabilities and electronic properties of the **Z** and **E** isomers of tautomers **2B** and **3B** were also investigated with full geometry optimization by AM1 treatment. The results obtained reveal that tautomers **2A** and **3A** are respectively more stable than tautomers **2B** and **3B** for both **Z** and **E** structures. Thus, it was calculated that **2A(Z)** is 3.870 kcal/mol more stable than **2B(Z)** and **3A(Z)** is 5.174 kcal/mol more stable than **3B(Z)** (The total energy values of **2B(Z)** and **3B(Z)** are -54699.819 kcal/mol and -70079.343 kcal/mol, respectively). This means that amide hydrazone forms (**2A** and **3A**) are more stable than hydrazide imide structures (**2B** and **3B**) for compounds **2** and **3**. In other words, compounds **2** and **3** exist exclusively in **A** tautomeric form under normal conditions.

In addition, the cations formed by the protonation of **Z** and **E** isomers of **2A** and **3A** at azomethine nitrogen were investigated with full geometry optimization using AM1 method. The calculated total energies (E_{tot}) and the heats of formation (ΔH°_f) are given in **Table 2.** The proton affinity (PA) values also given in **Table 2** were calculated using the equation below.

$$PA = \Delta H^\circ_f(H^+) + \Delta H^\circ_f(B) - \Delta H^\circ_f(BH^+)$$

Here, PA is the proton affinity, ΔH°_f (B) is the heat of formation for the molecule, $\Delta H^\circ_f(BH^+)$ is the heat of formation for the cation and $\Delta H^\circ_f(BH^+)$ is the heat of formation for proton (367.2 kcal/mol)[15].

Table 2. Total energies (in kcal/mol), heats of formation (in kcal/mol), and proton affinities (in kcal/mol) for protonated forms of **Z** and **E** isomers of molecules **2A** and **3A** (AM1).

Structure	$E_{tot.}$	ΔH_f°	PA
2A (Z).H$^+$	-54858.102	95.515	206.708
2A (E).H$^+$	-54857.278	96.339	207.241
3A (Z).H$^+$	-70244.446	124.120	212.224
3A (E).H$^+$	-70242.117	126.449	212.955

As seen in **Table 2, E** isomers of both molecules possess more proton affinity than **Z** isomers, respectively. Hence, despite the fact that the stability of **Z** isomers is higher than that of E forms, the complex formulation ability of **E** isomers with metal cations is higher than that of **Z** forms. On the other hand, it was observed in this study that the acidity of the medium containing compound **2** and Ni^{2+} or Cu^{2+} cation increases during the complex formation. For this reason, the substitution of the hydroxyl proton of **2** with a metal cation must be taken into consideration during the complexing process. Indeed, it is plausible that a metal cation may be linked to the oxygen and azomethine nitrogen as coordination centers, and it is apparent that the hydroxyl and azomethine groups of compound **2** must be found in a geometrically suitable position for the complex formation. In fact, the hydroxyl and azomethine groups have a more suitable position in the **E** isomer of compound **2** for a complexing process, as seen in **Figure 1.**

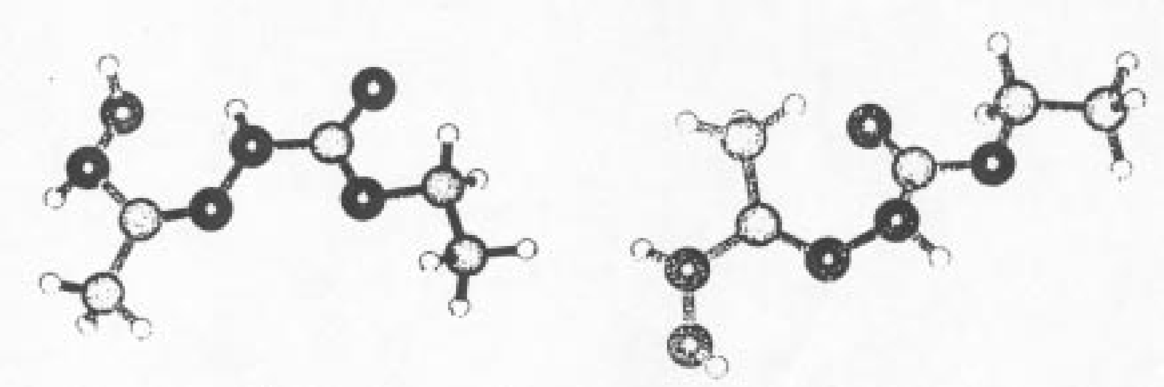


Figure 1. The optimized geometries of **Z** and **E** isomers of **2A** by AM1

Hence, if the complexing ability and optimized geometry of the isomers of **2** are taken into consideration, it is evident that the complex formation will occur via the **E** isomer of **2** in spite of the lower stability than **Z** form. Thus, the electronic properties and geometries of the predicted $\mathbf{M(2A)_2}$ type Ni^{2+} and Cu^{2+} complexes of compound **2** were investigated with full geometry optimization using ZINDO/1 method. This investigation reveals that complexes $\mathbf{Ni(2A)_2}$ and $\mathbf{Cu\ (2A)_2}$ have pseudotetrahedral and nearly square-flat structures, respectively. The calculated total energies (E_{tot}), the heats of formation (ΔH_f°), the charge densities of metal (Q_M), the energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) and bond lengths (v_{M-N} and v_{M-O}) are given in **Table 3.**

Table 3. Total energies (in kcal/mol), heats of formation (in kcal/mol), the charge densities of metal, energies of frontier molecular orbitals (in eV) and bond lengths (in Å) of complexes $\mathbf{Ni(2A)_2}$ **(I)** and $\mathbf{Cu(2A)_2}$ **(II)** (ZINDO/1).

Complex	E_{tot}	ΔH_f°	Q_M	E_{HOMO}	E_{LUMO}	v_{M-N}	v_{M-O}
I	-154631.686	-7536.145	+0.112	-5.734	6.628	1.970	2.020
II	-186937.282	-7373.364	-0.042	-5.632	5.286	1.843	1.888

It was found that the energy of the square-flat structure is higher than that of the pseudotetrahedral structure for complex **I** in a small degree. But, the square-flat structure is 5.801 kcal/mol more stable than the pseudotetrahedral structure for complex **II**. In the latter complex, the v_{M-N} and v_{M-O} bonds of the pseudotetrahedral structure are relatively longer than those of the square-flat structure. According to these results, a structural equilibrium "pseudotetrahedral $\rightleftharpoons$ square-flat" may be considered for the complexes $\mathbf{Ni(2A)_2(I)}$ and $\mathbf{Cu(2A)_2(II)}$.

The charge density values of the metal atoms in **Table 3** reveal that the negative charge of the ligand is partly transferred to the metal atom in both the complexes.

On the other hand, a $\mathbf{M(2A)_2(H_2O)_2}$ type structure is possible for the Ni^{2+} and Cu^{2+} complexes of compound **2** formed in a water-containing media. For this reason, the electronic properties and geometries of the predicted $\mathbf{Ni(2A)_2(H_2O)_2}$ **(4)**and $\mathbf{Cu(2A)_2(H_2O)_2}$ **(5)** complexes were also studied with full geometry optimization in this study using ZINDO/1 semiempirical method. This investigation indicates that both complexes have octahedral structure **(Figure 2** and **Figure 3.)**. The calculated total energies (E_{tot}), the heats of formation (ΔH_f°), the charge densities of metal (Q_M), the energies of frontier molecular orbitals (E_{HOMO} and E_{LUMO}) and bond lengths (v_{M-N}, v_{M-O} and v_{M-OH2}) for complexes **4** and **5** are given in **Table 4.**

Table 4. Total energies (in kcal/mol), heats of formation (in kcal/mol), the charge densities of metal, energies of frontier molecular orbitals (in eV) and bond lengths (in Å) of complexes $\mathbf{Ni(2A)_2(H_2O)_2}$ **(4)** and $\mathbf{Cu(2A)_2(H_2O)_2}$ **(5)** (ZINDO/1).

Complex	E_{tot}	ΔH_f°	Q_M	E_{HOMO}	E_{LUMO}	v_{M-N}	v_{M-O}	v_{M-OH2}
4	-202379.063	-7901.931	+0.085	-4.651	6.941	1.901	1.870	2.132
5	-209902.431	-7865.969	+0.021	-4.723	5.853	1.908	1.880	2.133

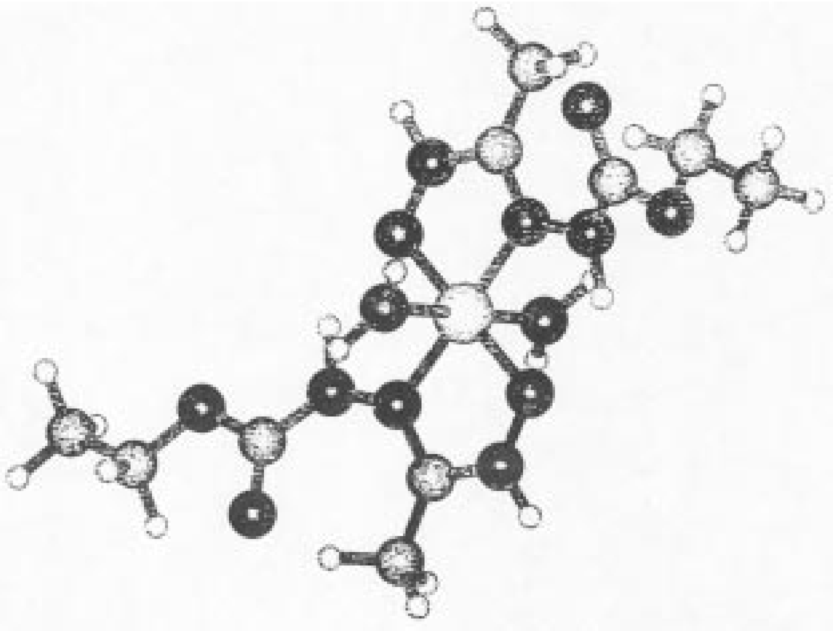


Figure 2. The optimized geometry of $\mathbf{Ni(2A)_2(H_2O)_2(4)}$ by ZINDO/1

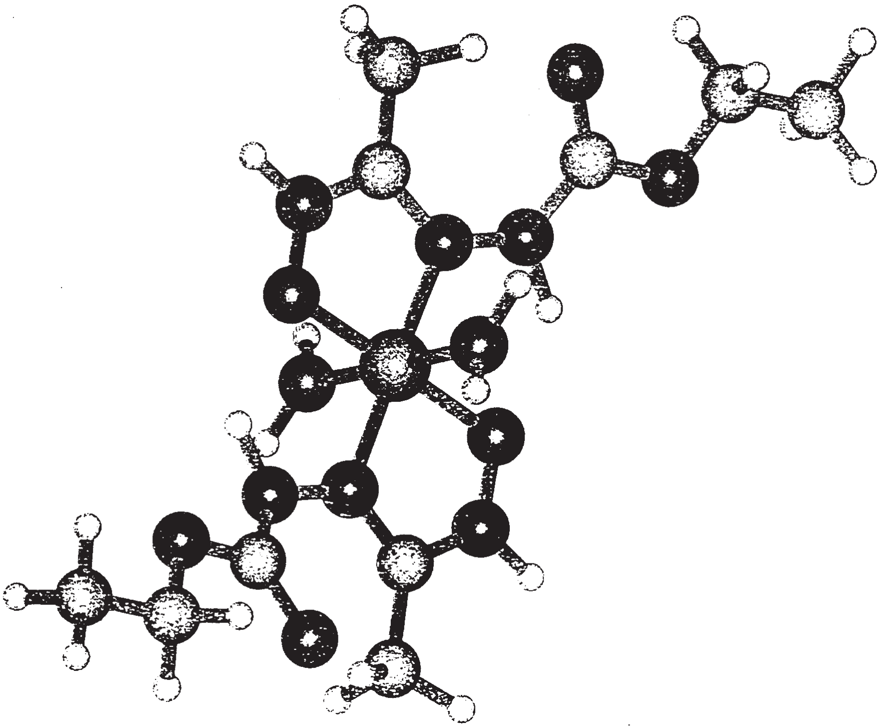


Figure 3. The optimized geometry of **Cu(2A)$_2$(H$_2$O)$_2$(5)** by ZINDO/1

The results obtained in **Table 3** and **Table 4** indicate that the Cu^{2+} complexes of compound **2** are more stable than the corresponding Ni^{2+} complexes. Moreover, the dihydrate complexes **4** and **5** are more stable than **I** and **II**, respectively.

The theoretical results related to Ni^{2+} and Cu^{2+} complexes of compound **2** are in agreement with the data given in the experimental section. The deep color and insolubility of complexes **4** and **5** are similar to those of the metal complexes of some amidrazones[5]. The preference of tautomers **A** by compound **2** and **3** is in accord with the nmr data reported previously[10]. The ring closure of compounds **2** and **3** leading to the formation of the corresponding 4-hydroxy-4,5-dihydro-1H-1,2,4-triazol-5-ones[10] is in agreement with the stability of their **Z** isomers.

Acknowledgement

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