Complexes of (*Z*)-2-Amino-α-(methoxyimino)-4-thiazoleacetic Acid with Some Transition Metals and their Scavenger Effects on $O_2^{-\cdot}$ Radicals

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Cobalt(II), nickel(II), copper(II), and zinc(II) complexes of (*Z*)-2-amino-α-(methoxyimino)-4-thiazoleacetic acid (HL) have been prepared and characterized by means of elemental analyses, IR, molar conductivity, ^{1}H NMR, and TGA measurements. The general formula for the complexes is ML_2. The IR and ^{1}H NMR spectra show that the ligand acts as bidentate ligand coordinating to the metal ions through the thiazole ring nitrogen and the carboxyl oxygen. The antioxidative activity of the complexes was tested. The result obtained showed that the suppression ratios of the complexes for $O_2^{-\cdot}$ are mostly higher than that of the ligand.

The chemistry of thiazoles, thiazole derivatives, and their metal complexes is well developed and continues to be studied because of their broad spectrum of biological activity, such as antibacterial, antitumour, antitrypanosomal, and antioxidative [1—3]. Moreover, in many cases it has been suggested that the biological activity of thiazoles and thiazole derivatives can be increased by their coordination with suitable metal ions [4, 5]. This idea led us to prepare (*Z*)-2-amino-α-(methoxyimino)-4-thiazoleacetic acid (HL) metal complexes with a view to evaluate their biological properties.

In the present paper, we report the preparation and characterization of Co(II), Ni(II), Cu(II), and Zn(II) complexes with HL and discuss their antioxidative activity for the first time.

EXPERIMENTAL

The chemicals used included cobalt(II) perchlorate ($Co(ClO_4)_2$), nickel(II) perchlorate ($Ni(ClO_4)_2$), copper(II) perchlorate ($Cu(ClO_4)_2$), and zinc(II) perchlorate ($Zn(ClO_4)_2$), reduced nicotinamide adenine dinucleotide (NADH), phenazine methosulfate (PMS), nitro blue tetrazolium (NBT). The ligand (*Z*)-2-amino-α-(methoxyimino)-4-thiazoleacetic acid (*I*) used herein was prepared according to the literature method [6]. All the solvents and reagents used were of anal. grade.

The C, H, and N data of the complexes were determined using an Erba 1106 elemental analyzer. The metal content was determined by titration with EDTA. IR spectra were recorded on a Nicolet-170SX FT-IR spectrophotometer using KBr discs in the range $\tilde{\nu}$ = 200—4000 cm^{-1}. ^{1}H NMR spectra were measured with a Bruker AC-E 200 spectrometer using DMSO-d_6 as solvent and TMS as internal reference. Electrolytic conductance measurements were made with a DDS-IIA molar conductometer with DMF as solvent (≈ 10^{-3} mol dm^{-3} solution) at 25 °C. TGA measurements were made in a nitrogen atmosphere between room temperature and 800 °C using a DuPont 1090 thermal analyzer. Absorbances were determined on a 751-spectrophotometer from Shanghai Analytical Equipment Factory at 560 nm.

Synthesis of the Complexes

HL (2 mmol) and NaOH (2 mmol) were dissolved in 10 cm^3 of methanol. The solution was added dropwise to a solution of $M(ClO_4)_2 \cdot 6H_2O$ (1 mmol) in 5 cm^3 of methanol. After stirring for 3 h at room temperature the precipitate was collected by filtration, washed with methanol several times and dried in a vacuum desiccator to constant mass.

Test for Scavenger Effects on $O_2^{-\cdot}$

The superoxide radicals ($O_2^{-\cdot}$) were produced by a system of NADH/PMS/NBT [7] and measured by the amount of NBT reduced by $O_2^{-\cdot}$. The final concentrations (in 5 cm^3) of the reagents used were c(NADH) = 79 μmol dm^{-3}, c(PMS) = 30 μmol dm^{-3}, c(NBT) = 75 μmol dm^{-3}, c(Tris-HCl buffer, pH = 8.0) = 0.01 mol dm^{-3}, and c(tested compound) = 3—4 μmol

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Table 1. Characterization of the Complexes

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%				M.p.	Molar conductivity
			Metal	C	H	N	°C	Ω^{-1} cm^2 mol^{-1}
II	$(C_6H_6N_3O_3S)_2Co$	459.34	11.67	31.72	2.81	18.04	245	8.74
			12.83	31.38	2.63	18.29		
III	$(C_6H_6N_3O_3S)_2Ni$	459.10	12.49	31.06	2.14	18.63	251	6.03
			12.78	31.39	2.63	18.30		
IV	$(C_6H_6N_3O_3S)_2Cu$	463.94	12.95	30.69	2.54	17.94	263	12.36
			13.70	31.07	2.61	18.10		
V	$(C_6H_6N_3O_3S)_2Zn$	465.78	13.84	30.47	2.32	18.45	261	8.12
			14.04	30.94	2.60	18.03		

Table 2. IR Spectra of HL and its Complexes

Compound	$\tilde{\nu}$/cm^{-1}						
	ν(C=O)	ν_{as}(COO$^-$)	ν_s(COO$^-$)	ν(C=N)	ν(C=N (thiazole ring))	ν(Ln—N)	ν(Ln—O)
I	1698			1614	1576		
II		1527	1325	1616	1541	494	436
III		1527	1321	1620	1549	496	437
IV		1529	1324	1619	1546	494	436
V		1526	1324	1619	1548	494	436

dm^{-3}. The reaction was carried out for 5 min at room temperature. The amount of reduced NBT was detected by the absorbance at 560 nm, since the reduced product, blue formazan, absorbs at this wavelength. The suppression ratio for $O_2^{-\bullet}$ was calculated from the following expression

$$\text{Suppression ratio} = 100 \times \frac{A_0 - A}{A_0}$$

where A is the absorbance in the presence of the ligand or its complexes and A_0 the absorbance in the absence of the ligand or its complexes.

RESULTS AND DISCUSSION

The results of analyses and molar conductivity of the newly prepared complexes are presented in Table 1. The elemental analyses data show that the complexes have the general formula ML_2. The complexes are air-stable and soluble in DMF, DMSO, and water, insoluble in methanol, ethanol, acetone, benzene, and ether. The molar conductivity values of the complexes in DMF at 25 °C show that all complexes are nonelectrolytes [8].

The important IR frequencies of the ligand and its complexes along with their relative assignments are given in Table 2. The strong band at 3440 cm^{-1} in the free ligand assigned to $\nu(NH_2)$ vibration of the terminal NH_2 group is unchanged or slightly shifted in all the complexes, suggesting that the NH_2 group is not involved in bonding. The bands at 1614 cm^{-1} and 1576 cm^{-1} in the free ligand were assigned to ν(C=N) (methoxyimino group) and ν(C=N) (thiazole ring) vibrations, respectively. The first band is unchanged or slightly shifted whilst the second band is shifted towards the vicinity of 1541—1549 cm^{-1} in all the complexes. Thus the results indicate that the nitrogen atom of methoxyimino group is not bonded and the nitrogen atom of thiazole ring is involved in the complex formation [9]. The band at 1698 cm^{-1} assignable to the ν(C=O) of the carboxyl group disappears upon the complexation. However, two new bands corresponding to ν_{as}(COO$^-$) and ν_s(COO$^-$) vibrations are observed at 1529 cm^{-1} and 1324 cm^{-1}, respectively. This shows that the carboxylate group coordinates to the metal ion. Since the separation between ν_{as}(COO$^-$) and ν_s(COO$^-$) is $\approx$ 200 cm^{-1}, the carboxylate group is coordinated unidentately to the metal ion in the present complexes [10].

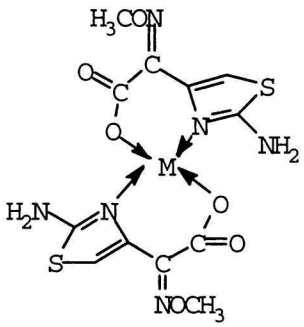
The IR spectra of all the complexes exhibit two more additional bands, which are not present in the spectrum of the ligand. These two bands appear at 494 cm^{-1} and 435 cm^{-1} and are attributed to ν(Ln—N) and ν(Ln—O), respectively. The presence of these bands confirms the coordination of metal ions through N and O atoms.

The ^{1}H NMR spectrum of HL exhibits three singlets at δ = 7.27, 6.89, and 3.88 assigned to —NH_2, C-5—H, and —OCH_3 groups, respectively. When coordinated to the metal ion in the complexes, the δ values of —NH_2 and C-5—H were shifted by 0.31, 0.42 to higher field. These results indicate the coordination of metal ion with the nitrogen atom of thiazole ring. The δ value of —OCH_3 was shifted only slightly,

which shows that the nitrogen atom of methoxyimino group is not involved in bonding. This is in agreement with the IR analytical conclusion.

The thermal decomposition of complexes has been studied as well. The thermograms of all the complexes are quite similar. The DTA curve of complexes has one sharp endothermic peak around 245—263 °C while the corresponding TG curves do not exhibit mass loss. The temperatures are in agreement with the determined melting points. The decomposition of these complexes starts around 303—312 °C and occurs through more than one stage. Heating to about 800 °C, the residue masses correspond to values calculated for MO (M = Co, Ni, Cu, Zn).

According to the aforementioned data, for the complexes prepared we propose the structure shown in Scheme 1.



Scheme 1. Suggested structure of the complexes.

The Scavenger Effects on $O_2^{-\cdot}$

The suppression percentage of the ligand and its complexes *IV* and *V* for $O_2^{-\cdot}$ radicals is summarized in Table 3. The results show that the ligand and its complexes have inhibiting activity for superoxide radicals $O_2^{-\cdot}$. Their inhibiting activity is greatly enhanced at higher concentrations. The reason for scavenging effects on superoxide radicals $O_2^{-\cdot}$ of the compounds may be the thiazole group in the ligand as well as in its complexes. Also, it has been observed that the suppression ratios of the complexes for $O_2^{-\cdot}$ are mostly higher than that of the ligand.

Table 3. Data of Scavenger Effects on $O_2^{-\cdot}$ of Ligand and its Complexes

Compound	Concentration / μmol dm^{-3}	Average suppression ratio for $O_2^{-\cdot}$/%
I	3.00	19.67
	4.00	36.12
IV	3.00	47.31
	4.00	63.30
V	3.00	32.25
	4.00	50.82

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