

# Synthesis, Characterization, and Antioxidative Action of Lanthanide Complexes of *N*-Benzoylacetoneglycine

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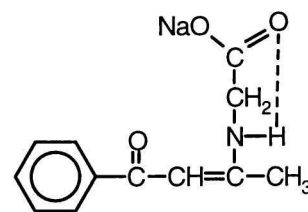
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*N*-Benzoylacetoneglycine behaving as an unstable monobasic tridentate ligand has been isolated in the stabler sodium salt which has been used to prepare the corresponding lanthanide(III) complexes. The complexes have been characterized by elemental analysis, molar conductance, thermal analysis, and spectral data.  $\beta$ -Ketoenamine structure of the ligand and the bonding in the lanthanide chelates have been discussed on the basis of IR and <sup>1</sup>H NMR spectral data. The nephelauxetic ratio ( $\beta$ ), bonding parameter ( $b^{1/2}$ ), and Sinha's covalence parameter ( $\delta$ ) reflect obvious covalent nature for the complexes. Both the lanthanide complexes and sodium salt of *N*-benzoylacetoneglycine are good antioxidants.

Although metal complexes of *N*-salicylideneamino acids and *N*-pyridoxylideneamino acids have been the subject of intensive investigation because of the important application in medicine and bioinorganic chemistry [1–5], much less attention has been paid to systems in which the Schiff bases of amino acids are derived from  $\beta$ -diketones [6–8]. Neglect of this type ligands of  $\beta$ -ketoimine-*N*-alkanoic acids seems to arise from their known hydrolytic instability [9]. Furthermore, those metal complexes primarily have been confined to transition elements whereas the coordination chemistry of amino acid Schiff bases towards lanthanide has received scant attention. In the present research, *N*-benzoylacetoneglycine has been stabilized in the form of its sodium salt and the complexes of this ligand with a series of lanthanide(III) ions have been prepared. Their antioxidative actions also have been determined.

The lanthanide complexes have been synthesized *via* sodium *N*-benzoylacetoneglycinate. All the newly synthesized complexes are coloured powder solids (Table 1), which are stable in air at least for several hours and soluble in water. After being put in the air for several days, they are not only insoluble in water, but also in common organic solvents except coordination solvents like THF, pyridine, dioxane, DMF, and DMSO. This phenomenon may result from the polymerization in the complexes after dehydration. The elemental analyses are in good agreement with the composition of Ln(HL)<sub>3</sub>·2H<sub>2</sub>O (Ln = trivalent lan-



Formula 1

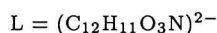
thanide cations, L = (C<sub>12</sub>H<sub>11</sub>O<sub>3</sub>N)<sup>2-</sup>). The low molar conductance values of the complexes are ascribed to their nonelectrolytic nature in DMF and are in accord with the expectation of the neutral complexes.

Infrared spectrum of sodium *N*-benzoylacetoneglycinate exhibits two strong bands at  $\tilde{\nu} = 1577 \text{ cm}^{-1}$  and  $1530 \text{ cm}^{-1}$  due to  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}\cdots\text{N} + \text{C}=\text{C})$  which suffer a shift to higher wavenumber by 5–8  $\text{cm}^{-1}$  and 8–10  $\text{cm}^{-1}$  after coordinating to Ln(III). The upward shift of  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}\cdots\text{N} + \text{C}=\text{C})$  bands is an evidence of enhanced chelate ring resonance on metal chelation [7]. This evidently indicates the participation of the carbonyl oxygen and enamine nitrogen atoms in coordination. It is further confirmed by the appearance of additional  $\nu(\text{Ln}-\text{O})$  and  $\nu(\text{Ln}-\text{N})$  bands at  $\tilde{\nu} = 415\text{--}430 \text{ cm}^{-1}$  and  $315\text{--}340$

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Table 1. Analytical Data and Molar Conductivities of the Complexes

Compound	Formula	$M_r$	$w_i(\text{calc.})/\%$ $w_i(\text{found})/\%$				Yield %	$\theta_{\text{decomp.}}$ °C	$\Lambda$ $\text{cm}^2 \Omega^{-1} \text{mol}^{-1}$	Colour
			Ln	C	H	N				
La(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> La	829.6	16.77	52.11	4.83	5.07	93	230	2.4	White
			16.83	52.20	4.78	5.09				
Pr(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Pr	831.6	16.97	51.98	4.81	5.05	90	228	2.2	Light green
			16.99	52.01	4.76	5.06				
Nd(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Nd	835.0	17.29	51.78	4.79	5.03	91	227	2.7	Yellow green
			17.41	51.92	4.71	5.05				
Sm(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Sm	841.1	17.90	51.41	4.76	5.00	87	225	2.5	Light yellow
			17.96	51.29	4.73	5.02				
Eu(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Eu	842.7	18.05	51.30	4.75	4.99	87	226	2.2	Light yellow
			18.21	51.36	4.78	4.96				
Dy(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Dy	853.2	19.06	50.67	4.69	4.96	85	222	1.9	Yellow
			19.26	50.71	4.71	4.93				
Er(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Er	858.0	19.51	50.39	4.67	4.90	84	228	2.9	Yellow
			19.68	50.28	4.63	4.90				
Y(HL) <sub>3</sub> · 2H <sub>2</sub> O	C <sub>36</sub> H <sub>40</sub> O <sub>11</sub> N <sub>3</sub> Y	779.6	11.42	55.46	5.13	5.39	86	225	2.8	Yellow
			11.51	55.32	5.16	5.36				

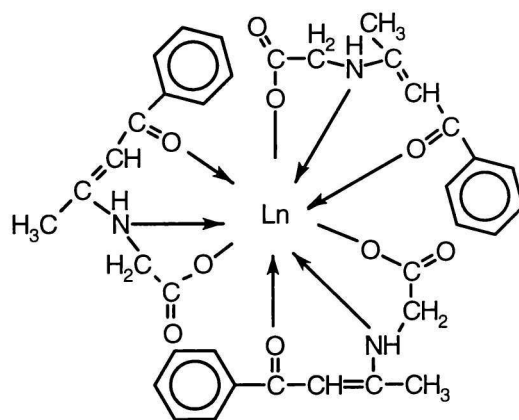


$\text{cm}^{-1}$ , respectively, in far IR region. Sodium salt of the ligand shows two other very strong bands at  $\tilde{\nu} = 1604 \text{ cm}^{-1}$  and  $1404 \text{ cm}^{-1}$  assigned to antisymmetric and symmetric stretching vibrations, respectively, of the carboxylate group [10]. The larger  $\Delta\tilde{\nu}(\text{COO})$  observed seems to be a consequence of intense internal hydrogen bond between the carboxylate and the enamine [10, 11].

A considerably broad band ranging from  $\tilde{\nu} = 3100 \text{ cm}^{-1}$  to  $3380 \text{ cm}^{-1}$  is observed in the spectrum of sodium *N*-benzoylacetoneglycinate due to the strongly hydrogen-bonded NH, which remains unaffected chiefly in the complexes but the band at  $\tilde{\nu} = 3095 \text{ cm}^{-1}$  shifts to  $3260\text{--}3270 \text{ cm}^{-1}$  because of the hydrogen bond damaged or broken after complexation with Ln(III) ions. This evidently indicates the existence of NH proton in the complexes without being replaced by Ln(III) ions. In view of the presence of hydration water, the complexes show broad bands of varying intensity in the region  $\tilde{\nu} = 3340\text{--}3410 \text{ cm}^{-1}$  which partly submerge the broad  $\nu(\text{N-H})$  band.

$^1\text{H}$  NMR spectrum of sodium *N*-benzoylacetoneglycinate exhibits a doublet centred at  $\delta = 3.72$  due to methylene protons ( $-\text{CH}_2-$ ), two sharp singlets at  $\delta = 3.44$  and  $\delta = 5.67$  ascribed to methyl ( $-\text{CH}_3$ ) and methenyl ( $=\text{CH}-$ ) protons, respectively, while NH proton signal occurs as a broad triplet peak around  $\delta = 11.29$ . Low-field value of NH signal is presumably due to intense internal hydrogen bond and its breadth due to quadrupole of the nitrogen nucleus [12]. In  $^1\text{H}$  NMR spectra of the complexes, the presence of unaffected NH proton signal further substantiates the result from IR spectra.

Thus, all evidences above suggest that the ligand acts in monobasic tridentate manner and bonds to Ln(III) ions through the carbonyl oxygen, enamine



Formula 2

nitrogen, and carboxy group. This obviously differs from the coordinating behaviour of transition metal ions [6–8].

Ultraviolet spectrum of sodium *N*-benzoylacetoneglycinate shows a strong band at  $\lambda = 340 \text{ nm}$ , characteristic of  $\beta$ -ketoenamine form [13], which shifts to  $\lambda = 360\text{--}375 \text{ nm}$  because of enhanced ring resonance on metal chelation.

In the visible region the sharp lines due to  $f-f$  transition originating within  $4f^n$  configuration of the lanthanide(III) ions are affected by the ligand on complexation. The shift of the absorption band to a lower wavenumber has been ascribed to a nephelauxetic effect. The extent of the red shift is related to covalence in the metal–ligand bond. The  $\beta$  values below one

**Table 2.** Electronic Spectral Data of the Lanthanide Complexes

Complexes	$\tilde{\nu}/\text{cm}^{-1}$	Assignment	Covalent parameters
Pr(HL) <sub>3</sub> · 2H <sub>2</sub> O	22730	<sup>3</sup> H <sub>4</sub> → <sup>3</sup> P <sub>2</sub>	$\beta = 0.9975$
	22220	→ <sup>3</sup> P <sub>1</sub>	$\delta = 0.2506$
	20835	→ <sup>3</sup> P <sub>0</sub>	$b^{1/2} = 0.02500$
	16590	→ <sup>1</sup> D <sub>2</sub>	
Nd(HL) <sub>3</sub> · 2H <sub>2</sub> O	19230	<sup>4</sup> I <sub>9/2</sub> → <sup>4</sup> P <sub>1/2</sub>	$\beta = 0.9932$
	18967	→ <sup>4</sup> G <sub>4/2</sub>	$\delta = 0.6753$
	17360	→ <sup>4</sup> G <sub>5/2</sub> , <sup>2</sup> G <sub>5/2</sub>	$b^{1/2} = 0.04123$
	16950	→ <sup>2</sup> H <sub>9/2</sub>	
Sm(HL) <sub>3</sub> · 2H <sub>2</sub> O	25000	<sup>6</sup> H <sub>5/2</sub> → <sup>4</sup> F <sub>9/2</sub>	$\beta = 0.9930$
	24700	→ <sup>6</sup> P <sub>3/2</sub>	$\delta = 0.7049$
	23800	→ <sup>4</sup> I <sub>13/2</sub>	$b^{1/2} = 0.04183$
	21430	→ <sup>4</sup> I <sub>11/2</sub> , <sup>4</sup> M <sub>15/2</sub>	
	20460	→ <sup>4</sup> I <sub>9/2</sub>	
	19950	→ <sup>4</sup> G <sub>7/2</sub>	
Dy(HL) <sub>3</sub> · 2H <sub>2</sub> O	23410	<sup>6</sup> H <sub>15/2</sub> → <sup>4</sup> G <sub>11/2</sub>	$\beta = 0.9925$
	22150	→ <sup>4</sup> I <sub>15/2</sub>	$\delta = 0.7498$
	21340	→ <sup>4</sup> F <sub>9/2</sub>	$b^{1/2} = 0.04330$
Er(HL) <sub>3</sub> · 2H <sub>2</sub> O	15314	<sup>4</sup> I <sub>15/2</sub> → <sup>4</sup> F <sub>9/2</sub>	$\beta = 0.9912$
	18467	→ <sup>4</sup> S <sub>3/2</sub>	$\delta = 0.8878$
	19120	→ <sup>2</sup> H <sub>11/2</sub>	$b^{1/2} = 0.04690$
	20513	→ <sup>4</sup> F <sub>7/2</sub>	
	22222	→ <sup>4</sup> F <sub>3/2</sub>	

**Table 3.** Data on Antioxidative Actions of Na(HL) and Lanthanide Complexes

Compound	Elimination of O <sub>2</sub> <sup>-</sup> radical			Elimination of OH <sup>·</sup> radical		
	Absorption	Dose	Inhibition	{Peak area}	Yield for ethene	Inhibition
		mg	%		$\mu\text{mol dm}^{-3}$	%
Control	0.827 ± 0.002	0	0	75397 ± 1983	0.928 ± 0.024	0
Na(HL)	0.467 ± 0.067	0.333	43.57	28625 ± 765	0.352 ± 0.009	62.0
	0.667 ± 0.017	0.167	19.38			
	0.750 ± 0.095	0.083	19.31			
La(HL) <sub>3</sub> · 2H <sub>2</sub> O	0.566 ± 0.029	0.333	37.62	19773 ± 481	0.243 ± 0.006	73.8
	0.650 ± 0.030	0.167	21.40			
	0.753 ± 0.007	0.083	8.95			
Pr(HL) <sub>3</sub> · 2H <sub>2</sub> O	0.457 ± 0.027	0.333	44.74	10871 ± 63	0.134 ± 0.001	85.6
	0.586 ± 0.016	0.167	29.14			
	0.752 ± 0.005	0.083	9.07			
Nd(HL) <sub>3</sub> · 2H <sub>2</sub> O	0.408 ± 0.018	0.333	50.67	15141 ± 1281	0.186 ± 0.016	79.7
	0.665 ± 0.005	0.167	19.59			
	0.734 ± 0.007	0.083	11.21			
Y(HL) <sub>3</sub> · 2H <sub>2</sub> O	0.550 ± 0.050	0.333	33.49	12362 ± 462	0.152 ± 0.006	83.6
	0.682 ± 0.068	0.167	17.54			
	0.770 ± 0.077	0.083	6.84			

$P < 0.05$  in the above experiments.

reflect the covalent nature of the bond between metal and ligand. The positive values of bonding parameter ( $b^{1/2}$ ) and Sinha's covalence parameter ( $\delta$ ) also support the occurrence of some covalent character in the metal—ligand bond [14, 15]. The comparative low magnitude of bonding parameter  $b^{1/2}$  reveals the involvement of 4f orbital metal—ligand bond in a very

low degree [16]. The bands of the electronic spectra along with their assignments and the values of  $\beta$ ,  $b^{1/2}$ , and  $\delta$  are presented in Table 2.

Thermal behaviours of the complexes are closely similar to each other. The DTA curve exhibits a wide endothermic peak at 110—125 °C, and the relevant TG curve shows mass loss of 4.1—4.6 % ascribable

to dehydration which corresponds to the liberation of two water molecules. At 222–230 °C, the complexes are decomposed (Table 1) and benzoylacetone is eliminated. The observed mass losses (49.3–56.6 %) coincide primarily with the theoretically calculated values (51.4–56.2 %). The thermal curves tend to steady at 680–720 °C. The fraction residues are 20.4–26.3 % corresponding to the percentages of  $\text{Ln}_2\text{O}(\text{CO}_3)_2$  in the complexes.

Superoxide radicals, produced by the reaction of NADH with PMS, can reduce NBT quantitatively to a blue substance. The amount of  $\text{O}_2^-$  radical and fraction of inhibition to superoxide radical can be calculated *via* spectroscopic measurement of the absorption of the reduced NBT [17].

$\text{OH}^\bullet$  radicals produced when  $\text{H}_2\text{O}_2$  reacts with ascorbate in the presence of  $\text{Fe}^{2+}$ —EDTA as a suitable metal catalyst, were detected as a result of ethene formation from methional. The percentage inhibition was calculated by gas chromatographic measuring of the amount of ethene [18, 19].

Data on antioxidative behaviour are listed in Table 3. It can be concluded that both the Na(HL) and lanthanide complexes are good antioxidants, and in most cases the complexes display more efficient antioxidative activities. Moreover, the concentration of test samples exerts a very large influence on the inhibition and the higher the concentration, the more efficient is the sample.

## EXPERIMENTAL

Lanthanide(III) chlorides were obtained by dissolving the corresponding oxide (99.95 %) purchased from Shanghai Yuelong Nonferrous Metal Co., Ltd., Shanghai, China in a stoichiometric amount of hydrochloric acid ( $\varphi_r = 1$ ). The solutions obtained were put on a water bath to evaporate until a crystal film appeared, cooled, and then the crystals were separated out. Reduced coenzyme I (NADH) was obtained from Lot in Germany. Nitroblue tetrazolium (NBT), phenazine methasulfate (PMS), methional [3-(methylthio)propionaldehyde], and trihydroxymethylaminomethane (Tris) were purchased from Sigma in USA. Ascorbate and other chemicals were biological or analytical grades.  $\text{K}_2\text{HPO}_4$ — $\text{KH}_2\text{PO}_4$  (PBS) and Tris-HCl buffers were prepared with deionized distilled water.

The lanthanide contents in all complexes were determined by heating the samples at 800 °C. The resulting residues were dissolved with hydrochloric acid ( $\varphi_r = 1$ ) and the solution was titrated with EDTA and xylenol orange as indicator. The contents of carbon, hydrogen, and nitrogen were measured on an Erba 1106 elemental analyzer. IR spectra were obtained in KBr pellets on a Nicolet 170SX infrared spectrometer.  $^1\text{H}$  NMR spectra were recorded on a FT-80A NMR spectrometer in  $\text{DMSO}-d_6$  solution, using TMS

as internal reference. Electronic spectra were recorded on a Shimadzu UV-240 spectrophotometer. Thermal analyses were carried out with a PCT-2 differential thermal analyzer in air.

## Sodium *N*-Benzoylacetoneglycinate

Glycine (1.5 g; 0.02 mol) was added to a solution of sodium hydroxide (0.8 g; 0.02 mol) in 95 % hot ethanol (40  $\text{cm}^3$ ) and the mixture was stirred until the solution became clear. Benzoylacetone (3.2 g; 0.02 mol) was then added and the mixture was refluxed on a water bath for 4 h when the solution turned pale yellow. On cooling the mixture in ice, needle-shaped crystal separated out. The product was recrystallized from 95 % ethanol and the colourless fine crystal was dried in vacuum. Yield 78 %, m.p. = 188–191 °C. For  $\text{C}_{12}\text{H}_{12}\text{O}_3\text{NNa}$  [Na(HL)]  $w_i$ (calc.) 59.75 % C, 4.98 % H, 5.81 % N;  $w_i$ (found): 59.68 % C, 4.94 % H, 5.76 % N. Sodium *N*-benzoylacetoneglycinate is stable in air and soluble in water, methanol, ethanol, acetone, pyridine, dioxane, THF, DMF, and DMSO. It decomposed at 280 °C.

## Complexes

The solution of lanthanide chloride (0.5 mmol) in methanol (5  $\text{cm}^3$ ) was added to the solution of sodium *N*-benzoylacetoneglycinate (1.5 mmol) in methanol (20  $\text{cm}^3$ ), whereupon the solid precipitated immediately. After 0.5 h of stirring, the precipitate obtained was filtered off, washed with methanol and dried over molecular sieves in vacuum. Yields 84–93 %.

## Elimination of Superoxide Radical

The solutions of NADH, NBT, and PMS were prepared with Tris-HCl buffer ( $c = 0.01$  mol  $\text{dm}^{-3}$ , pH = 8). The test samples, dissolved in a mixture of  $\text{Me}_2\text{CO}$ —DMF ( $\varphi_r = 1$  2), were added into the mixture of 1  $\text{cm}^3$  of NADH ( $c = 3.0 \times 10^{-5}$  mol  $\text{dm}^{-3}$ ) and 1  $\text{cm}^3$  of NBT ( $c = 2.25 \times 10^{-5}$  mol  $\text{dm}^{-3}$ ), followed by addition of 1  $\text{cm}^3$  of PMS ( $c = 3.0 \times 10^{-5}$  mol  $\text{dm}^{-3}$ ). The reaction systems were maintained at 37 °C, the normal human temperature for 5 min, then the absorption of the mixture at 560 nm was measured on a 721 spectrophotometer. The mixture of  $\text{Me}_2\text{CO}$ —DMF ( $\varphi_r = 1$  2), without dissolving the test samples, was used as the control group and its absorption  $A_0$  was recorded. The mean absorption was calculated, where  $(A_0 - A)/A_0$  stands for fraction of elimination. When  $A < A_0$ , the test sample exhibits antioxidative activity, whereas when  $A > A_0$ , it acts as an oxidative accelerant.

## Elimination of Hydroxyl Radical

The solutions of  $\text{Fe}^{2+}$ —EDTA, ascorbate, and me-

thional were prepared with PBS buffer ( $c = 0.01 \text{ mol dm}^{-3}$ ,  $\text{pH} = 7.4$ ). The test sample solutions of  $\text{Me}_2\text{CO}-\text{DMF}$  ( $\varphi_r = 1/2$ ) were added to the mixture of  $1 \text{ cm}^3$  of  $\text{Fe}^{2+}-\text{EDTA}$  ( $c = 3.0 \times 10^{-5} \text{ mol dm}^{-3}$ ) and  $1 \text{ cm}^3$  of methional ( $c = 3.0 \times 10^{-5} \text{ mol dm}^{-3}$ ), hence by addition of  $1 \text{ cm}^3$  of ascorbate ( $c = 6.0 \times 10^{-5} \text{ mol dm}^{-3}$ ). The reactions were carried out at  $37^\circ\text{C}$  for 30 min, then the ethene formed was measured by a gas chromatograph, and  $\text{Me}_2\text{CO}-\text{DMF}$  ( $\varphi_r = 1/2$ ) without the dissolved test samples acts as the control group. By the peak areas of the gas chromatograph, the ethene content of both the test samples ( $B$ ) and the control group ( $B_0$ ) was calculated. The  $(B_0 - B)/B_0$  stands for fraction of elimination. The higher the  $(B_0 - B)/B_0$ , the larger the antioxidative activity.

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