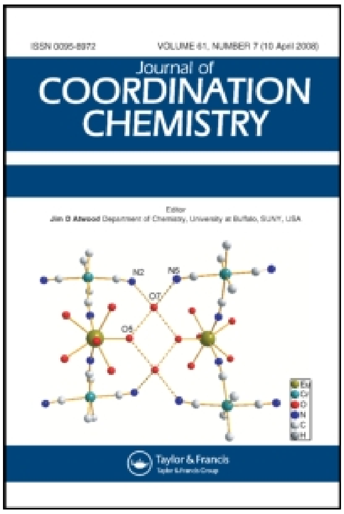

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SYNTHESIS AND ANTIOXIDATIVE ACTIVITY OF N-[(BENZOYLAMINO) THIOXOMETHYL]-GLYCINE COMPLEXES WITH RARE EARTH METALS

Ren Yan-ping[ab]; Bai Jun-feng[a]; Wang Liu-fang[a]; Wu Ji-gui[a]; Zhang Ying-nian[c]
[a] National Laboratory of Applied Organic Chemistry, Department of Chemistry, University, Lanzhou, P. R. C [b] Department of Applied Chemistry, Taiyuan University of Technology, Taiyuan [c] Lanzhou Teacher's College, Lanzhou, P. R. C

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NOTE

SYNTHESIS AND ANTIOXIDATIVE ACTIVITY OF N-[(BENZOYLAMINO) THIOXOMETHYL]-GLYCINE COMPLEXES WITH RARE EARTH METALS

REN YAN-PING[a,*,†], BAI JUN-FENG[a], WANG LIU-FANG[a,*], WU JI-GUI[a]
and ZHANG YING-NIAN[b]

[a]*National Laboratory of Applied Organic Chemistry, Department of Chemistry, Lanzhou University, Lanzhou, 730000, P.R.C;* [b]*Lanzhou Teacher's College, Lanzhou, 730050, P.R.C*

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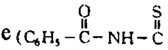
Nine new solid complexes of N-[(benzoylamino) thioxomethyl]-glycine  $(C_6H_5-\overset{O}{\overset{\|}{C}}-NH-\overset{S}{\overset{\|}{C}}$ -NH-CH$_2$COOH, HL) with rare earth metals (M) have been synthesized. Elemental analysis, IR, molar conductance, TG-DTA and ^{1}H NMR spectra have been used to characterize the complexes. The general formula of the complexes is $ML_3 \cdot 1.5CH_3OH$ (M = La, Ce, Nd, Sm, Gd, Dy, Er, Yb and Y). The antioxidative activity of La, Gd and Yb complexes was tested. The results obtained showed that the complexes possess scavenging effects on $O_2^{-\cdot}$ radicals. It was also found that some complexes inhibit lipid peroxidation of homogenate of mouse liver.

Keywords: Antioxidative activity; rare earth metals; N-[(benzoylamino)thioxomethyl]-glycine; complexes

INTRODUCTION

Complexes of thiourea and thiourea derivaties with transition and rare earth metals are receiving more and more attention. It is well known that these complexes have antitumor, antiviral, bacteriostatic and antioxidation activity.[1,2]

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[*] Authors for correspondence.

[†] Present address: Department of Applied Chemistry, Taiyuan University of Technology, Taiyuan, 030024

It was also reported that rare earth elements and their complexes with glycine have antitumor activity.[3,4] There appear to be no reports of the complexes of N-[(benzoylamino)thioxomethyl]-glycine (HL). Therefore, we now report the synthesis and characterization of rare earth complexes with HL and discuss their antioxidative activity.

This paper is one of a series of our investigation of metal complexes with HL. Further studies on the complexes of first row transition elements with HL are in progress.

EXPERIMENTAL

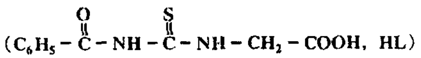
Measurements

Carbon, hydrogen and nitrogen were determined using a Carlo-Erba 1106 elemental analyser. The metal content of the complexes were estimated by titration with EDTA. The IR spectra were recorded on a Nicolet-170SX FT-IR spectrophotometer using KBr discs in the range 4000−200 cm^{-1}. ^1H NMR spectra were obtained using a Varian FT-80A spectrometer with d_6-acetone as the solvent and TMS as the internal reference. Thermal analyses were performed using a DuPont 1090 thermal analyser. Absorbances were determined on a 751-spectrophotometer at 532 and 560 nm.

Reagents

The chemicals used included rare earth (III) chlorides (MCl_3) which were obtained from the Reagent Factory of Shanghai; glycine (NH_2CH_2COOH); benzoyl chloride (C_6H_5COCl); ammonium sulfocyanate (NH_4SCN); nitroblue tetrazolium (NBT); trimethylaminomethane (IRIS); 2-thiobarbituric acid(TBA); L-methionine (MET); trichloroactetic acid (TCA) and riboflavine (VB_2) and all the reagents used are AR grade. All biochemical reagents were obtained from Sigma Chemical Company.

Synthesis of the Ligand



$(C_6H_5-\overset{\overset{O}{\|}}{C}-NH-\overset{\overset{S}{\|}}{C}-NH-CH_2-COOH,\ HL)$

An improved literature method[5] was used. It has some advantages, such as more rapid reaction, nearly 75% yield, and being a one step reaction.

C_6H_5COCl(0.010 mol) was poured into a freshly prepared 0.011 mol NH_4SCN solution in acetone (20 cm^3), and refluxed for 30 min. Then NH_2CH_2-COOH(0.010 mol) powder and acetone (20 cm^3), were added as rapidly as possible to maintain vigorous reflux. After refluxing for 6 h, excess cracked ice

TABLE I Melting point, analyses and molar conductances for the complexes

Compound	*m. p. (°C)*	*C%*	*H%*	*N%*	*RE%*	*Molar conductancein DMF (S cm^2 mol^{-1})*
HL	200	50.61 (50.42)	4.12 (4.20)	11.84 (11.96)		
NaL		46.27 (46.15)	3.34 (3.46)	10.88 (10.76)		70.30
LaL$_3$·1.5CH$_3$OH	193	41.95 (42.10)	3.75 (3.68)	9.28 (9.35)	15.32 (15.47)	8.70
CeL$_3$·1.5CH$_3$OH	195	41.90 (42.04)	3.80 (3.67)	9.25 (9.34)	15.46 (15.58)	6.50
NdL$_3$·1.5CH$_3$OH	196	41.86 (41.85)	3.70 (3.65)	9.26 (9.30)	15.85 (15.96)	6.76
SmL$_3$·1.5CH$_3$OH	192	41.35 (41.56)	3.56 (3.63)	8.79 (9.24)	16.67 (16.54)	5.20
GdL$_3$·1.5CH$_3$OH	208	41.09 (41.25)	3.64 (3.60)	9.20 (9.17)	17.20 (17.16)	5.55
DyL$_3$·1.5CH$_3$OH	190	40.89 (41.02)	3.62 (3.58)	9.24 (9.12)	17.56 (17.63)	4.85
ErL$_3$·1.5CH$_3$OH	205	40.76 (40.81)	3.42 (3.56)	9.15 (9.07)	17.80 (18.06)	5.45
YbL$_3$·1.5CH$_3$OH	210	40.30 (40.54)	3.62 (3.53)	8.80 (9.01)	18.74 (18.56)	4.98
YL$_3$·1.5CH$_3$OH	198	44.10 (44.58)	3.92 (3.89)	9.60 (9.90)	10.62 (10.48)	4.70

Calculated values in parentheses

was poured into the mixture with vigorous stirring. The resulting solid was collected, liberally washed with water, and then acetone and recrystallized from ethanol (95%) to give pure product, yield, 7.5g (75%); m. p. 200-201°C (lit, m. p. 199-200°C).[5]

The purity of the ligand obtained was confirmed by elemental analysis (see Table I), IR spectra, ^{1}H NMR and mass spectra.

Synthesis of the Sodium Salt of the Ligand (NaL)

HL was dissolved with equimolar sodium hydroxide (NaOH) methanol solution. The mixture was stirred until clear, then the solution was put on a water bath to evaporate until a crystal film appears. The product obtained was collected by filtration and dried over molecular sieves under vacuum. The purity of the product was also confirmed by elemental analysis and IR spectra.

Synthesis of the Complexes

3 mmol HL and 3 mmol NaOH were dissolved in 20 cm^3 methanol. Under stirring, a solution of MCl_3 (1 mmol) in methanol (20 cm^3) was added to the mixture and the precipitate appeared immediately. After stirring the mixture at room temperature for 2 h, the precipitate was collected by filtration, washed with methanol three times, and dried in a vacuum dessicator to constant weight. Nine rare earth (III) complexes with HL were prepared by the same method.

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

The superoxide radicals ($O_2^{-\cdot}$) produced in the system VB_2/MET/NBT[6] were measured by the amount of NBT reduced by $O_2^{-\cdot}$. The reaction mixture (3 cm^3) contained VB_2 (18 μmol/l), MET (3 mmol/l), NBT (225 μmol/l), tri-HCl buffer (0.05 mol/l) (pH = 7.5) and the tested compound (30-500 μmol/l). The reaction was left for 30 min under a fluorescent lamp (40 W). 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 $O_2^{-\cdot}$ was calculated from the following expression:

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

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

The inhibiting activity for lipid peroxidation of homogenate of mouse liver by HL and its complexes were determined by the literature procedure.[7] The little white mouse liver was quickly taken from the mouse body, washed to free it from residual blood in the physiological saline, then dried with filter paper: 5% homogenate of little white mouse liver was prepared with it. Then 1 cm^3 5% homogenate and 0.1 cm^3 DMF solution (4.0 mg/cm^3) of the ligand or its complexes were mixed together, the mixture was kept at 37°C for 1.5 h. 3.0 cm^3 of 20% TCA and 0.67% TBA was added, and the mixture was kept at 95°C for 10 min. The absorbance of the final mixture was measured at 532nm. The inhibiting activity was calculated from the following expression:

TABLE II Some characteristic IR data (cm^{-1}) and their assignments for the ligand and its typical complexes

Compound	*ν(OH) (CH_3OH)*	*$\nu_{as}(COO^-)$*	*$\nu_s(COO^-)$*	*$\Delta\nu$*	*ν(RE-O)*
NaL		1605	1404	201	
$LaL_3 \cdot 1.5CH_3OH$	3414	1588	1418	170	532
$CeL_3 \cdot 1.5CH_3OH$	3417	1585	1416	179	533
$GdL_3 \cdot 1.5CH_3OH$	3431	1579	1415	164	537
$DyL_3 \cdot 1.5CH_3OH$	3430	1581	1414	167	536
$YbL_3 \cdot 1.5CH_3OH$	3432	1576	1409	167	536

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

where the definitions of symbols (A_0, A) are the same as above.

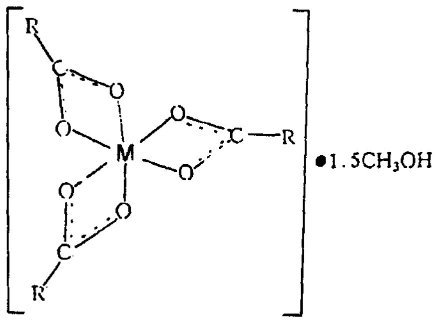
RESULTS AND DISCUSSION

Composition and Properties of the Complexes

Elemental composition, molar conductance and molecular formula of the complexes are listed in Table I. The complexes are stable in air and soluble in DMF and DMSO, insoluble in water, methanol and ethanol. As seen in Table I, the molar conductances of the complexes in DMF vary from 4.7-8.6 S cm^2 mol^{-1}, indicating that they are nonelectrolytes.[8]

IR Spectra

The important IR data of the ligand and its typical complexes are listed in Table II. The infrared spectra of the complexes are fundamentally similar which reveals that they have the same general structure, but differ from the free ligand HL. The characteristic ν(C=O) mode of the ligand carboxyl group (1708 cm^{-1}) disappeared upon complexation. However, the complexes displayed both symmetric and asymmetric stretching vibrations of COO^- (1409-1418, 1567-1588 cm^{-1}), compared with 1605 [$\nu_{as}(COO^-)$], 1404 [$\nu_s(COO^-)$] cm^{-1} of NaL, $\nu_s(COO^-)$ of the complexes increased slightly while $\nu_{as}(COO^-)$ decreased, that is $\Delta\nu$ [$\Delta\nu = \nu_{as}(COO^-) - \nu_s(COO^-)$] of the complexes is smaller than that of NaL which strongly suggests the coordination of the ligand carboxyl group with the M (III) ions as a bidentate chelate fashion.[9] Further support for the existence of the M-O bond is the presence of a new band at about 535 cm^{-1} due to ν(M-O). Other characteristic bands of ν(N-C-N), ν(C=S) and ν(C=O)



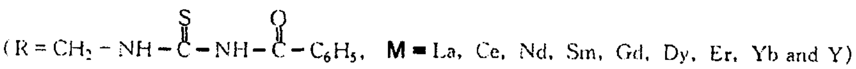

$$(R = CH_2-NH-\overset{\overset{S}{\|}}{C}-NH-\overset{\overset{O}{\|}}{C}-C_6H_5,\quad M = \text{La, Ce, Nd, Sm, Gd, Dy, Er, Yb and Y})$$

FIGURE 1 The proposed structure of $ML_3 \cdot 1.5CH_3OH$

(carbonyl group) vary less, showing that the N, S and O (carbonyl group) don't coordinate to the M (III) ions. The strong band of ν(OH) appears at 3414-3430 cm^{-1} in the IR spectra of all the complexes, proving the existence of methanol in these complexes consistent with the results of the thermal analyses.

Based on the above discussion, the probable structures of the complexes are shown in Figure 1.

Thermal Analyses

The thermographs of all the complexes are quite similar, but all differ obviously from HL. All the complexes have one sharp endothermic peak around 60°C in the DTA curve, and the percent weight losses of the relevant thermograms correspond to the percent contents of methanol in these complexes. These results agree with the composition of the complexes determined by elemental analyses. The temperature corresponding to methanol loss indicates that the methanol molecules are crystal methanol which has been confirmed by IR studies. The results of thermal analyses also suggest that these complexes have characteristic melting points (see Table I), in agreement with the determined melting point. The decomposition of these complexes starts around 462-468°C and occurs through more than one stage. Heating to about 800°C, the residue weights correspond to values calculated for M_2O_3(M = La, Ce, Nd, Sm, Gd, Dy, Er, Yb and Y). The above results are in agreement with the structure in Figure 1 for these complexes. Thermal analytical data are listed in Table III.

TABLE III The results of thermal analytical for the ligand and its typical complexes

Compound	*Methanol loss temp.* (°C)	*Methanol loss %*	*Decomposition temp.* (°C)	*% Weight loss*	*Residue* (800°C)
HL			483		
$LaL_3 \cdot 1.5CH_3OH$	40-64	5.25 (5.34)	478	17.25 (18.14)	La_2O_3
$SmL_3 \cdot 1.5CH_3OH$	38-70	5.36 (5.27)	468	18.50 (19.18)	Sm_2O_3
$GdL_3 \cdot 1.5CH_3OH$	36-62	5.14 (5.23)	462	19.10 (19.78)	Gd_2O_3
$DyL_3 \cdot 1.5CH_3OH$	39-65	5.45 (5.20)	473	21.13 (20.24)	Dy_2O_3

Calculated values in parentheses

^{1}H NMR of $LaL_3 \cdot 1.5\ CH_3OH$

The ^{1}H NMR spectra of HL and its La (III) complex were studied using d_6-acetone as the solvent and TMS as the internal reference. The ^{1}H NMR spectrum of HL exhibits: singlet at 11.43 ppm, triplet at 11.15-11.23 ppm, doublet at 4.31-4.35 ppm and multilet at 7.45-7.95 ppm assigned to -C(O)NH-, -NH-CH_2-, -CH_2- and , respectively. The carboxyl proton(-COOH) (HL) was unobserved. When coordinated to the lanthanum ion the δ value of -CH_2- shifted to 4.04 ppm, giving further evidence for coordination of La(III) ion with the carboxyl group of the ligand. The electron withdrawing capacity of La(III) in the complex is less than that of the carboxyl proton in HL. The δ values of other protons shift slightly. There is a new peak at 3.33 ppm ascribed to the CH_3- of the methanols in the complex, in agreement with the IR spectra and thermal analytical studies.

Antioxidative Activity

The antioxidative activity of typical complexes of a lighter rare earth (Sm) and a heavier rare earth (Gd, Yb) were determined. The suppression ratios of the ligand and its typical complexes for $O_2^{-\cdot}$ radicals and lipid peroxidation are summarized in Table IV. The results show that the ligand and its typical complexes possess scavenging effects on superoxide radicals $O_2^{-\cdot}$. Their inhibiting activity is slightly enhanced at higher concentrations. The reason for scavenging effects on superoxide radicals $O_2^{-\cdot}$ of the compounds may be the

TABLE IV Data of scavenging effect on $O_2^{-\cdot}$ and inhibiting results for lipid peroxidation of the ligand and its typical complexes

Ligand and complex	*Concentration* (μmol l^{-1})	*Average suppression ratio for* $O_2^{-\cdot}$ (%)	*Concentration* (μmol l^{-1})	*Average suppression ratio for the lipid peroxidation* (%)
HL	0.30 0.60 1.20	47.6 64.6 74.8	0.40	−87.2
$LaL_3 \cdot 1.5CH_3OH$	0.30 0.60 1.20	70.8 71.9 75.4	0.10	17.0
$GdL_3 \cdot 1.5CH_3OH$	0.30 0.60 1.20	69.0 69.3 72.8	0.10	15.2
$YbL_3 \cdot 1.5CH_3OH$	0.30 0.60 1.20	73.4 75.4 77.5	0.10	−23.4

presence of the C=S group in the ligand as well as its complexes.[10] The complexes of Sm and Gd have a strong inhibiting action to lipid peroxidation of homogenate of mouse liver, but the ligand and Yb complex accelerate lipid peroxidation of homogenate of mouse liver. Interpretation of the anomalous behavior of the Yb complex is uncertain.

Further studies on the detailed mechanism for the reaction of the complexes with superoxide are in progress.

References

1. K. Sakurai, T. Miura and T. Ogiso, *Yakugaku Zasshi* **106**, 1034 (1986); *Chem. Abstr.* **106**, 95942c (1987).
2. W.E. Curtis, N.B. Parker, S.L. Linas and J.E. Repine, *Superoxide Dismutase Chem. Biol. Med., Proc. Int. Conf.* 4th, 111 (1985); *Chem. Abstr.*, **106**, 46597k (1987).
3. S.K. Shukla, *Inorg. Chim.* **144**, 94 (1983).
4. L.J. Anghileri, *Arzneimittlel-Forsh* **793**, 25 (1975).
5. D.T. Elmore and P.A. Toseland, *J. Chem. Soc.* 4533 (1954).
6. J.D. Bewleg, *Physiological aspects of desiccation tolerance, Ann. Rev. Plant Physiol.* **30**, 195 (1979)
7. C.A. Riely and G. Cohen, *Science* **183**, 208 (1974).
8. W.J. Geary, *Coord Chem. Rev.* **7**, 81 (1971).
9. L.M. Li, G.F. Zeng, W.D. Zhuang and S.Q. Xi, Acta Chimica Sinica (China) **46**, 9 (1988); *Chem. Abstr.* **108**, 176135k (1988).
10. J.G. Horsfall and S. Nich, *Contrib. Boyle Thompson Inst.* **16**, 361 (1951).