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Chemistry of Dithiocarbamate Derivatives of Amino Acids. I. Study of some Dithiocarbamate Derivatives of Linear α-Amino Acids and their Nickel(II) Complexes

MANUEL CASTILLO

Departamento de Química Inorgánica, Facultad de Química, Universidad de Sevilla, Sevilla, Spain

JULIO J. CRIADO, BENIGNO MACIAS* and MARIA V. VAQUERO

Departamento de Química Inorgánica, Facultad de Farmacia, Universidad de Salamanca, Salamanca, Spain

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Abstract

The barium dithiocarbamate derivates of the α-amino acids glycine, DL-alanine, DL-2-aminobutyric acid, DL-norvaline and DL-norleucine have been synthesized. The crystal structure of the glycine derivative was determined. The anions were used to obtain the corresponding nickel(II) complexes in acid form. The complexes are diamagnetic, and coordination takes place in a near-square planar geometry around the Ni(II) ion through the sulphur atoms of the dithiocarbamate moiety, the structure having been confirmed by IR, ^{1}H NMR, UV–Vis spectroscopies and chemical analysis.

Introduction

The dithiocarbamate moiety has received much attention in recent years, due to its ability to act as a bidentate ligand.

Dithiocarbamates may easily undergo many different reactions thus being useful when studying substitution reactions in cation-bonded ligands or between the ligands themselves; these substances have been recently joined to insoluble polymers such as aminocellulose, and the resulting materials can be used to remove all traces of heavy metal ions from aqueous solutions; metal dithiocarbamates have been successfully used in agriculture for controlling insects and fungi, in treatment of alcoholism, estimation of copper, and so on [1].

The introduction of the dithiocarbamate group in α-amino acids gives rise to molecules with up to three ligating residues: amino(N), dithiocarbamate ($-CS_2^-$) and carboxylate ($-COO^-$). Many proteins have cystein and methionine residues and so dithiocarbamate derivatives of α-amino acids may be valid as models to study the coordination of proteins to metallic cations. Complexes of Ni(II) with alkanethiols, where coordination takes place through the sulphur atoms, have been used to study the active centers existing in urease from jack bean (*Canavalia ensiformis*) [2].

However, the complexes formed between metallic cations and dithiocarbamate derivatives of α-amino acids have rarely been reported in the literature [3]. In the present paper, the synthesis and characterization of complexes of Ni(II) and dithiocarbamate derivatives of linear α-amino acids, where coordination takes place through the sulphur atoms, the carboxylic residue being in acidic form, are described.

Experimental

Synthesis of the Ligands

The dithiocarbamate-derivates of the α-amino acids glycine, DL-alanine, DL-2-aminobutyric acid, DL-norvaline and DL-norleucine (Fluka A.G., p.a.) have been synthesized following a method similar to that described by Musil and Irgolic [4]. The amino acid (50 mmol) is reacted with an aqueous solution of $Ba(OH)_2 \cdot 8H_2O$ (Fluka A.G., p.a.) (55 mmol) and the suspension is magnetically stirred until total solution is achieved. In order to overcome the precipitation of barium carbonate, the presence of air should be avoided. Acetone (Carlo Erba, rpe) is then added, until its content is *ca.* 40% of the total volume, and CS_2 (60 mmol) is added dropwise. Formation of the barium salt takes place according to the reaction:

$$H_2N{-}CH(R){-}COOH \xrightarrow[(2)\ CS_2]{(1)\ Ba(OH)_2} Ba(S_2C{-}NH{-}CH(R){-}COO)$$

(R = H, Me, Et, Pr, Bu)

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*Author to whom correspondence should be addressed.

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Once the CS_2 is dissolved, the solution is kept at 0 °C for 12 h. Addition of ethanol (Carlo Erba, rpe) yields a white precipitate that is filtered and washed with diethylether. Purification is carried out by dissolution in water and precipitation with ethanol (final yield: 85–90%). All compounds were white and contain three molecules of crystallization according to the weight loss measured at 120–150 °C in a thermogramme of these compounds, and all were optically inactive.

The glycine-derivate was obtained in a crystalline form by slow evaporation of the solvent at room temperature.

Synthesis of the Complexes

An aqueous solution of $NiCl_2 \cdot 6H_2O$ (Fluka A.G., p.a.) is added dropwise to an aqueous solution of the barium dithiocarbamate (molar ratio $Ni^{2+}:Ba^{2+} = 1:2$). The light green colour of the original nickel(II) solution immediately darkens, indicating the fast formation of a new compound. In the case of the glycine derivate, a precipitate is soon formed that was characterized as $Ba[Ni(gly\ dtc)_2] \cdot 3H_2O$.

In order to withdraw the barium cation from the complex, the aqueous solution was transferred to a separation funnel, diethylether was added and then a 0.1 N HCl solution was added dropwise. In this way, the reaction taking place can be written as:

$$2Ba(S_2C{-}NH{-}CH(R){-}COO) + Ni^{2+} \xrightarrow[(2)\ HCl]{(1)\ Et_2O} Ni[S_2C{-}NH{-}CH(R){-}COOH]_2$$

(R = H, Me, Et, Pr, Bu)

The amount of HCl to be added is that stoichiometrically needed to react with barium to yield $BaCl_2$.

It should be noted that addition of the acid solution should be carried out after the addition of Et_2O, so the neutral complex is removed to the organic phase before it is destroyed by the acidic medium.

The solvent is removed in a rotary vacuum evaporator at 40 °C, thus obtaining an olive–green powder that is repurified in Et_2O (yield 70–75%). All compounds were diamagnetic and optically inactive.

Table I gives the chemical analysis data, both for the ligands and the complexes.

Methods

Chemical analysis (C, H and N) of the ligands and of the complexes was carried out by conventional methods. Nickel and barium contents were determined by atomic absorption, with a Perkin-Elmer, Model 2380 instrument.

Thermal analysis of the ligands was performed in a Perkin-Elmer TGS-2 instrument, in air, at a heating schedule of 10 °C min^{-1}. Optical activity measurements were carried out in standard conditions in a Perkin-Elmer-241 polarimeter. Magnetic susceptibilities were determined at room temperature in a Stanton MC-5 Gouy-type balance. The IR spectra (KBr pellets) were recorded in a double-beam Beckman Acculab-10 spectrophotometer (4000–250 cm^{-1}). The electronic spectra were recorded in a Shimadzu UV-240 instrument. Finally, a Varian model XL-200 spectrophotometer was used to record the ^1H NMR spectra, using D_2O and acetone-d_6 to dissolve the ligands and the complexes, respectively.

Results and Discussion

Figures 1 and 2 show the bond distances and bond angles in the glycine–dithiocarbamate derivate, and the unit cell, as determined by X-ray diffraction; more comprehensive data will be published elsewhere [5].

TABLE I. Chemical Analysis of the Ligands and the Complexes

Compounds	% Found					% Calculated				
	C	H	N	Ba	Ni	C	H	N	Ba	Ni
Ba(gly dtc)·$3H_2O$	10.21	2.85	4.26	40.27		10.57	2.64	4.11	40.35	
Ba(DL-ala dtc)·$3H_2O$	14.02	3.26	3.82	38.55		13.54	3.10	3.95	38.75	
Ba(DL-2-am·but dtc)·$3H_2O$	15.63	3.58	3.71	37.03		16.28	3.53	3.80	37.28	
Ba(DL-norval dtc)·$3H_2O$	18.86	4.08	3.29	35.56		18.83	3.92	3.66	35.91	
Ba(DL-norleu dtc)·$3H_2O$	20.75	4.33	3.31	34.47		21.19	4.29	3.53	34.65	
Ni(gly dtc)$_2$	21.19	2.39	7.98		16.40	20.05	2.22	7.80		16.36
Ni(DL-ala dtc)$_2$	25.17	3.21	7.34		15.09	24.81	3.10	7.23		15.33
Ni(DL-2-am·but dtc)$_2$	29.35	3.92	6.86		14.31	28.92	3.85	6.74		14 43
Ni(DL-norval dtc)$_2$	33.60	4.87	6.24		13.48	32.51	4.51	6.32		13.62
Ni(DL-norleu dtc)$_2$	36.93	6.12	6.08		12.76	35.67	5.09	5.94		12.90
Ba[Ni(gly dtc)$_2$]·$3H_2O$	12.96	2.46	5.12	24.66	10.58	13.13	2.20	5.10	24.96	10.67

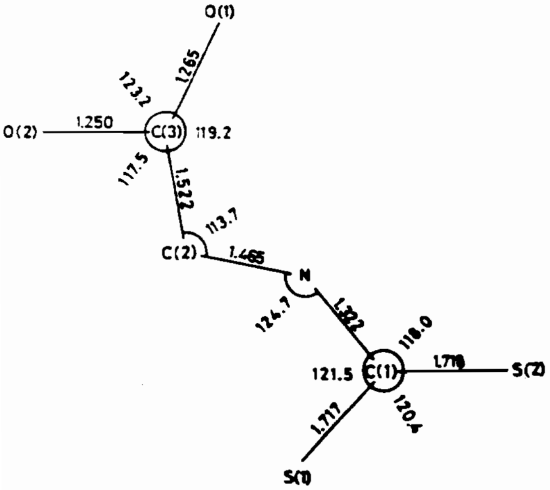


Fig. 1. Molecular structure of Ba(gly dtc)•3H$_2$O.

The C–O distances in the carboxylate group are shorter than that corresponding to a simple C–O bond (1.43 Å), but longer than that corresponding to a double C–O bond (1.20 Å). The C–N distance in the dithiocarbamate group (1.322 Å) is shorter than that found in the C–N moiety of the amino acid fragment (1.465 Å), which coincides with that corresponding to a single C–N bond (1.47 Å). Finally, the same features are observed in the CS$_2$ group (experimental C–S 1.717 Å; simple C–S 1.82 Å, double C–S 1.60 Å). These data suggest that the bonding in the S$_2$CN moiety is partially multiple, thus also leading to a charge delocalization. Simple bond theories would then predict a sp^2 character for both C atoms and for the N atom, which would be in agreement with the bond angles (close to 120°) found here.

The main features found in the IR spectra of the ligands and of the complexes, have been summarized in Table II.

A band between 1140–1100 cm^{-1} has been assigned to the $\nu_{C(2)-N}$ mode; on the contrary, the band at 1515–1470 cm^{-1} has been ascribed to the $\nu_{C(1)-N}$ vibration; this band is recorded at larger wavenumbers, as corresponds to a larger bond order.

The carboxylate group, $-COO^-$, is identified by the ν_{as} and ν_s modes of the C=O group at 1605–1560 and 1425–1395 cm^{-1} in the case of the ligands. On the contrary, the complexes show a strong band at 1700 ± 5 cm^{-1} due to the C=O stretching vibration of the carboxylic group.

The assignation of the bands due to the $-CS_2$ moiety has caused great controversy in the literature. Usually, two bands, close to 1000 and 660 cm^{-1} respectively, have been assigned to the stretching

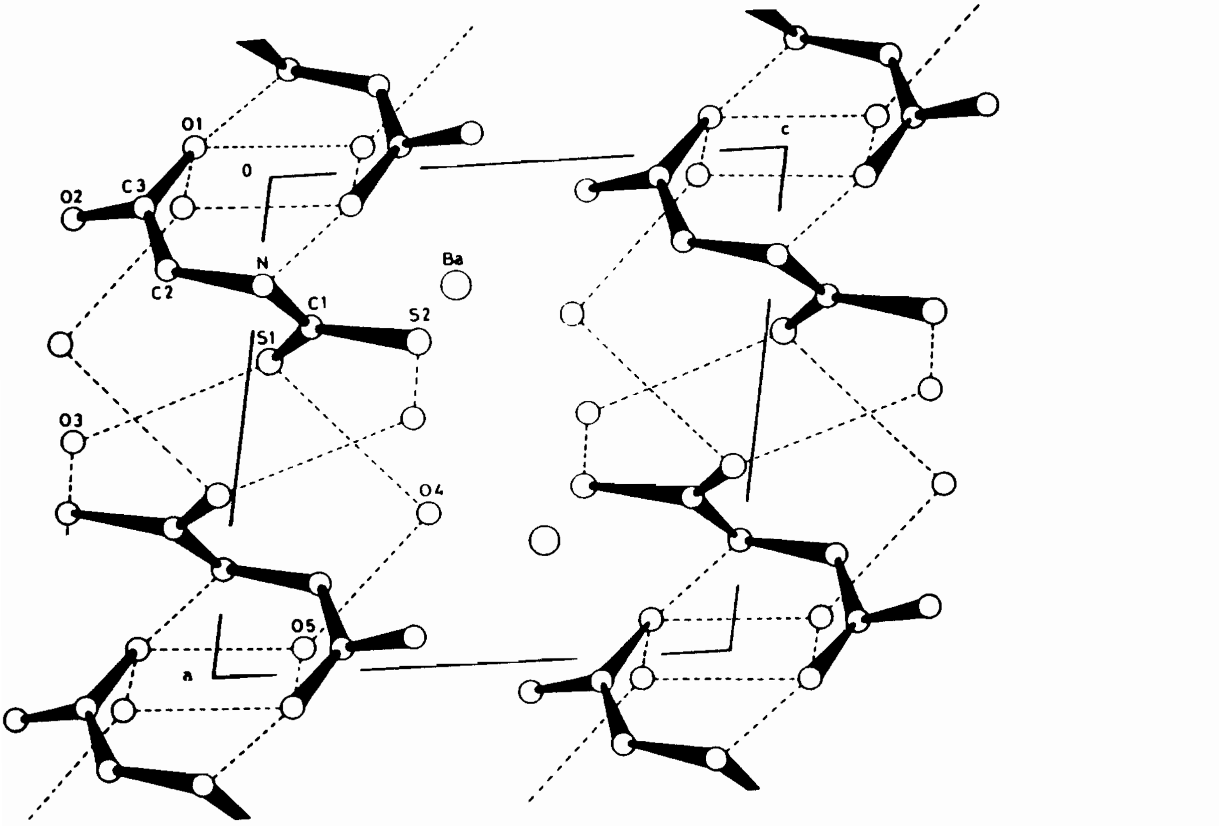


Fig. 2. Unit cell of Ba(gly dtc)•3H$_2$O.

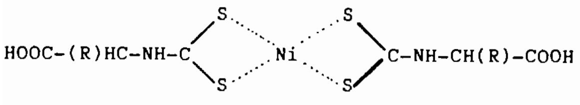
TABLE II. IR spectra data of the ligands and the complexes

	ν(C(2)–N)	ν(C(1)–N)	νCOOH	$\nu(COO^-)$		ν(C=S)		ν(Ni–S)
				ν_{as}	ν_s	ν_{as}	ν_s	
Ba(gly dtc)·$3H_2O$	1155	1505		1565	1410	1000	595	
Ba(DL-ala dtc)·$3H_2O$	1150	1515		1535	1405	950	620	
Ba(DL-2-am·but dtc)·$3H_2O$	1150	1475		1545	1400	995	630	
Ba(DL-norval dtc)·$3H_2O$	1160	1475		1555	1405	965	660	
Ba(DL-norleu dtc)·$3H_2O$	1150	1470		1585	1420	950	660	
Ni(gly dtc)$_2$	1125	1495	1700			1005	640	380
Ni(DL-ala dtc)$_2$	1170	1500	1700			980	660	370
Ni(DL-2-am·but dtc)$_2$	1150	1510	1695			985	660	360
Ni(DL-norval dtc)$_2$	1145	1510	1700			965	660	365
Ni(DL-norleu dtc)$_2$	1140	1505	1700			980	655	370
Ba[Ni(gly dtc)$_2$]·$3H_2O$	1100	1450		1580	1400	950	645	380

vibrations of this group. However, some authors [6, 7] have assigned these bands to carbon–sulphur vibrations in the C=S and C–S groups, respectively; more recently [8, 9], the bands have been assigned to the ν_{as} and ν_s modes of the $-CS_2$ group, this assignation being more consistent with our own findings showing that both C–S distances are identical.

Finally, it should be mentioned that the band at 370 ± 10 cm^{-1}, not recorded in the spectra of the ligands, has been previously ascribed [10, 11] to the ν_{Ni-S} mode in compounds analogous to those studied here.

Although none of the complexes synthesized here has been obtained in the crystalline state, and thus the structure cannot be undoubtedly proposed, the other results suggest that coordination of the dithiocarbamate derivatives takes place in a near square-planar geometry through the sulphur donating atoms, Fig. 3. In such a case, the complexes would be diamagnetic, as experimentally observed. This same structure has been previously reported for compounds similar to those synthesized here [12, 13]. However, the local symmetry around the nickel(II) cation is not strictly D_{4h}, as usually the S–S distances between two sulphur atoms belonging to the same dithiocarbamate ligand is shorter than between two sulphur atoms in *cis* positions belonging to two ligands, *i.e.*, a D_{2h} symmetry. In such a case, while for a D_{4h} symmetry three d–d, Laporte forbidden, spin-allowed bands will be observed, four bands are expected in the case of a D_{2h} symmetry. The electronic spectra, Table III, were essentially identical in all five cases, and six bands were recorded.



(R = H, Me, Et, Pr, Bu)

Fig. 3. Proposed coordination of the dithiocarbamate derivative of α-amino acids around the nickel(II) ion.

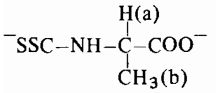
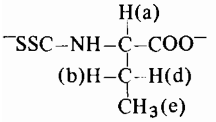
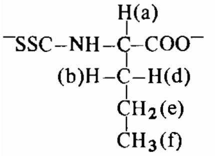
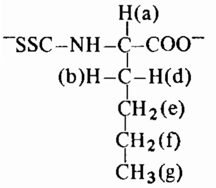
TABLE III. Electronic Spectra Data for the Nickel(II) Complexes

Transitions	λ_{max} (log ϵ)
$d_{xy} \rightarrow d_{x^2-y^2}$	650 (1.47)
$d_{z^2} \rightarrow d_{x^2-y^2}$	490 (1.30)
L → M	430 (2.77)
L → M	390 (3.25)
$\pi \rightarrow \pi^*$	320 (3.90)
$\pi \rightarrow \pi^*$	230 (3.90)

The two very intense bands at low wavelengths are due to transitions in the ligands. The ascription of the medium-intensity bands at 430 and 390 nm has been widely discussed in the literature, and several authors [14] ascribe them to metal → ligand charge transfer processes.

The intensities of the bands at 490 and 650 nm indicate that such bands are due to d–d, Laporte forbidden, spin-allowed transitions. Jϕrgensen [15] has reported two d–d bands at 487 and 634 nm in the visible spectra of dialkyl-dithiocarbamates of nickel(II). Similar positions have been reported by Dingle [12] in the spectrum of the diethyldithiocarbamate of nickel(II) and he ascribes them to transitions from the lower and higher full d orbitals to the unoccupied $d_{x^2-y^2}$ orbital ($d_{xy} \rightarrow d_{x^2-y^2}$ at 650 nm, and $d_{z^2} \rightarrow d_{x^2-y^2}$ at 490 nm; it should be noted that the unoccupied d orbital may be d_{xy} or $d_{x^2-y^2}$ according to the axis system chosen). The posi-

TABLE IV. Summary of ^{1}H NMR Data[a]

LL	Ba(LL)•3H$_2$O		Ni(HLL)$_2$	
	δ (ppm)	*J* (Hz)	δ (ppm)	*J* (Hz)
$^{-}SSC{-}NH{-}CH_2{-}COO^{-}$	CH$_2$ 4.03(s)		CH$_2$ 4.23(s)	
 $^{-}SSC{-}NH{-}\underset{CH_3(b)}{\overset{H(a)}{C}}{-}COO^{-}$	H(a) 4.38(q)	H(a)–H(b) 6.80	H(a) 4.66(q)	H(a)–H(b) 7.10
	H(b) 1.17(d)		H(b) 1.50(d)	
 $\begin{array}{rcl} & H(a) & \\ ^{-}SSC{-}NH{-} & C & {-}COO^{-} \\ (b)H{-} & C & {-}H(d) \\ & CH_3(e) & \end{array}$	H(a) 4.40(dd)	H(a)–H(b) 7.50	H(a) 4.56(dd)	H(a)–H(b) 8.25
	H(b) 1.67(m)	H(a)–H(d) 5.10	H(b) 1.92(m)	H(a)–H(d) 5.05
	H(d) 1.67(m)	H(b)–H(e) 7.50	H(d) 1.92(m)	H(b)–H(e) 7.40
	H(e) 0.73(t)	H(d)–H(e) 7.50	H(e) 1.01(t)	H(d)–H(e) 7.40
 $\begin{array}{rcl} & H(a) & \\ ^{-}SSC{-}NH{-} & C & {-}COO^{-} \\ (b)H{-} & C & {-}H(d) \\ & CH_2(e) & \\ & CH_3(f) & \end{array}$	H(a) 4.44(dd)	H(a)–H(b) 8.20	H(a) 4.62(dd)	H(a)–H(b) 8.80
	H(b) 1.58(m)	H(a)–H(d) 5.10	H(b) 1.92(m)	H(a)–H(d) 4.94
	H(d) 1.61(m)	H(b)–H(e) 7.30	H(d) 1.92(m)	H(a)–H(d) 4.94
	H(e) 1.18(x)	H(d)–H(e) 7.30	H(e) 1.46(x)	H(e)–H(f) 7.40
	H(f) 0.76(t)	H(e)–H(f) 7.30	H(f) 0.95(t)	
 $\begin{array}{rcl} & H(a) & \\ ^{-}SSC{-}NH{-} & C & {-}COO^{-} \\ (b)H{-} & C & {-}H(d) \\ & CH_2(e) & \\ & CH_2(f) & \\ & CH_3(g) & \end{array}$	H(a) 3.52(t)	H(a)–H(b) 6.05	not recorded	
	H(e) 1.63(m)	H(a)–H(d) 6.05		
	H(f) 1.14(m)			
	H(g) 0.69(m)			

[a] Symbols for multiplicity of the signals: s = singlet, d = doublet, t = triplet, q = quartet, x = sextet, m = complex multiplet, LL = amino acid dithiocarbamate derivative.

tions corresponding to the $d_{xz} \to d_{x^2-y^2}$ and $d_{yz} \to d_{x^2-y^2}$ transitions would be between those corresponding to the $d_{xy} \to d_{x^2-y^2}$ (650 nm) and $d_{z^2} \to d_{x^2-y^2}$ (490 nm) transitions, and as these two last bands are very broad, the former pair is usually missed in the spectrum. However Dingle [12], by using single crystals and polarized light, suggests the existence of two bands at 588 and 526 nm, due to the $d_{xz} \to d_{x^2-y^2}$ and $d_{yz} \to d_{x^2-y^2}$ transitions.

The spectra of the complexes recorded in the solid state (diffuse reflectance) are essentially identical to those recorded in diethylether solution, confirming that the local environment of the nickel(II) is maintained in the solid state.

The main features of the ^{1}H NMR spectra of the ligands and of the complexes have been summarized in Table IV. The positions of the signals in the spectra of the complexes are slightly shifted to larger δ values than in those of the corresponding ligands, as expected from the lower electron density in the complexes (neutral) than in the ligands (anionic). Protons on the Cβ with respect to the carboxylic group are diastereotopic, and then are magnetically different, giving rise to split, close signals, with different coupling constants. The δ and *J* values have been checked by selective decoupling.

For the alanine-derivate complex, a signal at 9.58 ppm has been recorded, due to the proton of the –NH– group, with a coupling constant of 8.4 Hz and a half-width of 7 Hz. This signal is generally missed in the other spectra, probably due to exchange with D_2O used as the solvent to record the spectra of the ligands.

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