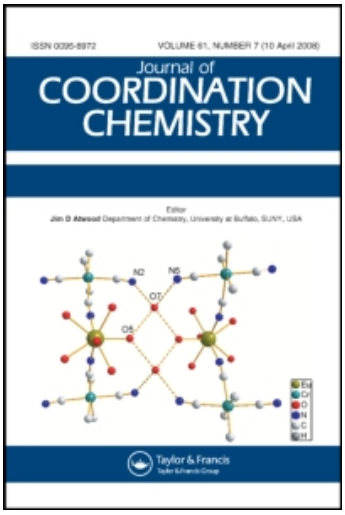

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

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To cite this Article Gutiérrez, RenÉ , Vázquez, Jaime , Vázquez, Rosa A. , Reyes, Yasmi , Toscano, R. Alfredo , Martinez, Marcos and Álvarez, Cecilio(2001) 'CHIRAL COMPLEXES BY DIRECT SYNTHESIS OF A BIOMOLECULE AND METAL POWDERS. CRYSTAL STRUCTURES OF THE DICHLORO[(-)-SPARTEINE-N,N']M(II) COMPLEXES (M = Cu, Zn)', Journal of Coordination Chemistry, 54: 3, 313 — 321
To link to this Article: DOI: 10.1080/00958970108022644
URL: http://dx.doi.org/10.1080/00958970108022644

J. Coord. Chem., 2001, Vol. 54, pp. 313–321
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CHIRAL COMPLEXES BY DIRECT SYNTHESIS OF A BIOMOLECULE AND METAL POWDERS. CRYSTAL STRUCTURES OF THE DICHLORO[(-)-SPARTEINE-N,N′]M(II) COMPLEXES (M = Cu, Zn)

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(Received 19 June 2000; In final form 28 February 2001)

Direct synthesis of chiral complexes dichloro[(-)-sparteine-N,N′]copper(II) **2** and dichloro[(-)-sparteine-N,N′]zinc(II) **3** derived from a biomolecule-namely the natural base (-)-sparteine- and elemental metals (Cu and Zn) in a CCl_4/DMSO solvent system (DMSO = dimethylsulfoxide) is reported. The complexes were partly characterized by spectroscopic methods and their structures were fully confirmed by single-crystal x-ray analysis. A comparison between the new crystal structures of **2** and **3** and that of the free ligand (-)-sparteine displayed only slight differences on the ligand framework.

Keywords: Direct synthesis; Chiral complexes; (-)-Sparteine

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INTRODUCTION

The widespread demand for new chiral metal complexes for their potential use in, *inter alia*, asymmetric synthesis and/or possible biological applications is increasingly growing, considering that ligands could show increased activity to a chelated metal rather than as free organic compounds [1]. Direct synthesis employing metal powders and organic ligands is also currently attracting intense study owing to the fascinating complexes of unusual stoichiometry and structures in comparison with those obtained in conventional synthesis, which usually involves a metal salt as a starting material. This "one-step" synthesis of metal complexes starting from *zero-valent* (more exactly, *elemental*) metals is an active research field which has undergone especially rapid progress over the last years [2].

On the other hand, several studies have established that (-)-sparteine, a naturally occurring tetracyclic tertiary diamine of the lupine alkaloid family, chelates divalent metal ions to form *pseudo*tetrahedral complexes and, for example, complexes of divalent calcium ion with (-)-sparteine are thought to be responsible for its pharmacological effectiveness as a muscle stimulant [3]. The steric inequivalence of the nitrogen donor atoms of (-)-sparteine leads to a number of interesting spectroscopic and structural phenomena besides its use as enantioselective catalysts [4].

These facts prompted us to explore the direct synthesis of chiral complexes derived from a biomolecule, particularly the natural base (-)-sparteine, and zero-valent metals as powders in a CCl_4/DMSO system, having in mind the profitable advantages that direct synthesis allows *i.e.*, easier and extremely simple reaction conditions, some peculiar properties of the compounds obtained, avoidance of impurities, *etc.* [2a,b]. Such advantages are particularly important with respect to this class of compounds, as reported in literature, involving long and/or tedious preparation of the reagents, careful conditions, *etc.* [5]. We report herein the preparation of the first chiral complexes dichloro[(-)-sparteine-N,N′]copper(II) **2** and dichloro[(-)-sparteine-N,N′]zinc(II) **3** obtained, to our knowledge, by this straightforward and expeditious method and the corresponding new crystal structures, as well as that of the free ligand.

RESULTS AND DISCUSSION

(-)-Sparteine reacts with elemental metals (Cu and Zn) as powders in a CCl_4/DMSO system yielding complexes **2** and **3** as green and yellow crystals after 1 to 12 h, respectively; the compounds were partly characterized by

spectroscopic methods. Thus, the IR spectrum (KBr) displayed strong absorption bands at 2952–2839 in both cases, owing to the C–H stretching frequencies of all the carbocyclic framework of the ligand, and the low frequency IR region showed bands at 469 and 437 as well as at 288 and 275 owing to v(Cu–N) and v(Cu–Cl) frequency absorptions, respectively, for the former compound. In the same manner, peaks at 462 and 437 along with other bands at 332 and 307 corresponding to v(Zn–N) and v(Zn–Cl) stretching absorptions for the latter compound were observed. These signals in the low frequency IR region are in agreement with those reported for similar complexes [5], excluding the deformation mode bands or lattice modes in the zone of the free ligand spectrum. NMR spectroscopies exhibited the expected signals for the hydrocarbon skeleton of the ligand, *i.e.*, in the ^{1}H NMR spectrum (400 MHz, $CDCl_3$), complex patterns at δ 3.9–1.4 ppm were observed for both complexes and, in the ^{13}C NMR spectrum (75 MHz, $CDCl_3$), signals at δ 70–17 ppm were also registered in both cases. The mass spectra exhibited peaks at *m/z* 368 and 370, which matches the expected molecular weight for complexes **2** and **3**, respectively, and the peak at *m/z* 234 belonging to the free ligand.

Single-crystal X-ray diffraction studies of the ligand (-)-sparteine (Fig. 1) and metal complexes **2,3** were performed to confirm metal coordination and to ascertain the crystal structure differences in the carbocyclic framework of the ligand (-)-sparteine with those for **2-3**, and comparing likewise with those previously reported for **2** and other sparteine derivatives [6, 7]. To our knowledge, the free ligand crystal structure is reported in this paper for the first time.

Figure 1 illustrates the tetracyclic skeleton of the (-)-sparteine ligand which may be considered built up of one *trans*-(*A*/*B*) and one *cis*-(*C*/*D*)-quinolizidine ring fused together in their 1,3 positions. The bond lengths and bond angles given in Table I are similar to those found in other sparteine derivatives [6]. The four individual six-membered ring conformations are found to be in chair conformation (see Tab. II) which is stabilized by a strong intramolecular $N1^+$–H1···N16 [N1···N16: 2.760(6) Å] 2.760(6) 128(6) partially weakened by being bifurcated for the nitrogen atom of the thiocyanate anion [N2···N19: 3.163(8) Å].

In comparison with the known monoclinic polymorph of dichloro [(-)-sparteine-N,N′]copper(II)) [7], the new crystallographic modification is orthorhombic (see Fig. 2) and the corresponding solid density is slightly higher. The sparteine moiety acting as a bidentate ligand induces a *pseudo*-tetrahedral environment around the copper(II) atom with only minor differences with respect to the monoclinic polymorph.

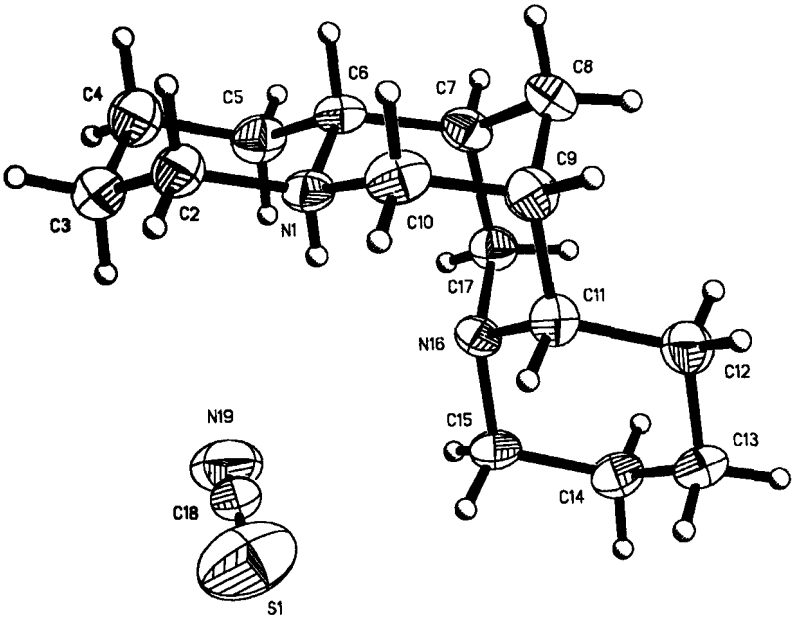

FIGURE 1 ORTEP drawing of compound **1**. Thermal ellipsoids at 30% probability level.

TABLE I Selected geometric parameters data for compounds **1–3**

Bond	*Sparteine ligand*	*Cu-complex*	*Zn-complex*
M—Cl1	–	2.2604(12)	2.2378(18)
M—Cl2	–	2.2241(13)	2.2308(17)
M—N1	–	2.008(4)	2.089(5)
M—N16	–	2.022(4)	2.086(4)
N1—C2	1.486(8)	1.507(6)	1.496(8)
N1—C6	1.516(7)	1.507(5)	1.512(7)
N1—C10	1.498(8)	1.486(6)	1.509(8)
N16—C11	1.481(7)	1.507(5)	1.511(7)
N16—C15	1.469(6)	1.507(6)	1.508(7)
N16—C17	1.458(6)	1.490(5)	1.491(7)
Angle	Ligand		
Cl1—M—C12	–	105.86(5)	116.17(8)
N1—M—N16	–	90.11(15)	88.96(19)
Cl1—M—N1	–	101.23(10)	106.18(13)
Cl2—M—N1	–	134.82(12)	122.73(14)
Cl1—M—N16	–	122.00(11)	111.81(15)
Cl2—M—N16	–	104.72(11)	107.70(15)
C2—N1—C6	111.7(5)	109.7(4)	110.3(5)
C2—N1—C10	110.7(4)	108.4(3)	107.6(5)
C6—N1—C10	112.8(4)	110.7(3)	109.1(5)
C11—N16—C15	110.5(5)	111.9(4)	110.5(5)
C11—N16—C17	112.8(4)	113.3(3)	112.7(4)
C15—N16—C17	112.7(4)	110.6(4)	111.4(5)

TABLE II Cremer and pople parameters data for compounds **1–3**

	Ligand	*Cu-complex*	*Zn-complex*	*Conformation*
Ring A	$q_2 = 0.013$ Å $q_3 = -0.582$ Å $Q_T = 0.582$ $\theta = 179°$ $\varphi_2 = 49°$	$q_2 = 0.017$ Å $q_3 = -0.586$ Å $Q_T = 0.586$ Å $\theta = 179°$ $\varphi_2 = 195°$	$q_2 = 0.053$ Å $q_3 = -0.559$ Å $Q_T = 0.561$ Å $\theta = 175°$ $\varphi_2 = 183°$	Chair
Ring B	$q_2 = 0.122$ Å $q_3 = -0.605$ Å $Q_T = 0.617$ Å $\theta = 169°$ $\varphi_2 = 4°$	$q_2 = 0.081$ Å $q_3 = -0.606$ Å $Q_T = 0.611$ Å $\theta = 173°$ $\varphi_2 = 358°$	$q_2 = 0.098$ Å $q_3 = -0.619$ Å $Q_T = 0.627$ Å $\theta = 171°$ $\varphi_2 = 344°$	Chair
Ring C	$q_2 = 0.062$ Å $q_3 = -0.598$ Å $Q_T = 0.601$ Å $\theta = 174°$ $\varphi_2 = 30°$	$q_2 = 0.119$ Å $q_3 = -0.584$ Å $Q_T = 0.596$ Å $\theta = 169°$ $\varphi_2 = 12°$	$q_2 = 0.110$ Å $q_3 = -0.582$ Å $Q_T = 0.593$ Å $\theta = 169°$ $\varphi_2 = 350°$	Chair
Ring D	$q_2 = 0.016$ Å $q_3 = -0.5551$ Å $Q_T = 0.551$ Å $\theta = 178°$ $\varphi_2 = 11°$	$q_2 = 0.066$ Å $q_3 = -0.530$ Å $Q_T = 0.534$ Å $\theta = 173°$ $\varphi_2 = 32°$	$q_2 = 0.060$ Å $q_3 = -0.548$ Å $Q_T = 0.551$ Å $\theta = 174°$ $\varphi_2 = 21°$	Chair

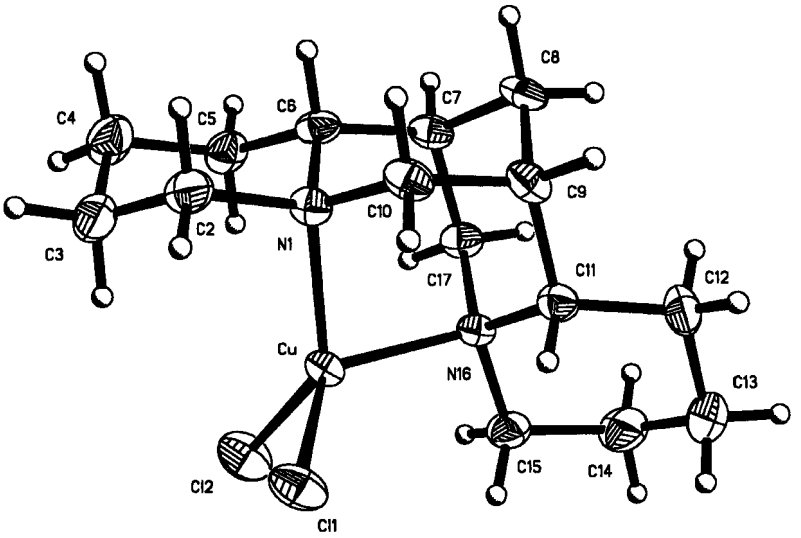

FIGURE 2 ORTEP drawing of complex **2**. Thermal ellipsoids at 30% probability level.

Contrary to the pattern observed in the copper-sparteine complexes where each of the Cu–N and the Cu–Cl coordination bonds are significantly different (Tab. I), in the zinc complex (see Fig. 3) the Zn–Cl and Zn–N

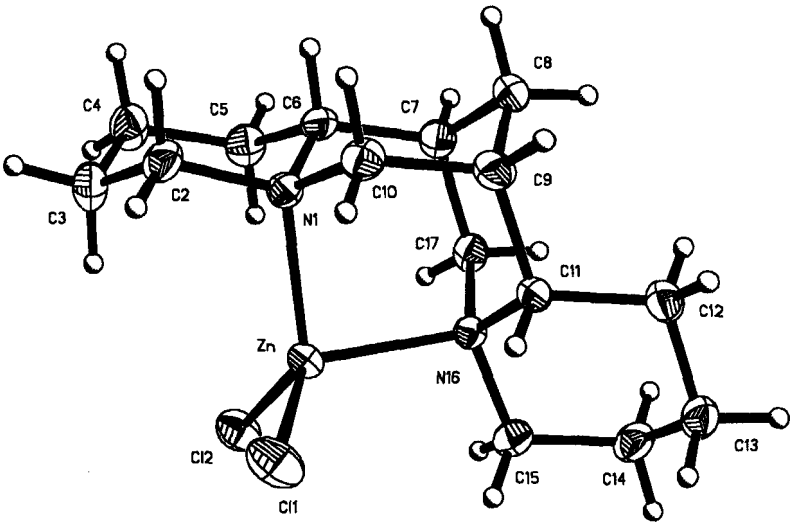

FIGURE 3 ORTEP drawing of complex **3**. Thermal ellipsoids at 30% probability level.

equivalent coordination bonds are practically the same. Although the N1–Zn–N16 bond angle is more acute than that of the copper complex, the rest of the bond angles tend to be closer to the ideal tetrahedral values and correlate well with those observed for the adduct of dimethylzinc and (-)-sparteine [5e].

Especially noteworthy is that **2** crystallizes differently than when obtained by conventional methods, *i.e.*, using metal salts, and the high purity of the complex as shown by some preliminary EPR studies, are directly connected to some peculiar properties of compounds prepared by direct synthesis.

CONCLUSION

In summary, the approach to chiral complexes by direct synthesis of a biomolecule such as (-)-sparteine and metal powders reaction conditions using mild is reported for the first time. Work is in progress with other biomolecules and chiral entities to broaden the scope.

EXPERIMENTAL SECTION

General Methods

^{1}H NMR and ^{13}C NMR spectra were recorded on a Jeol Eclipse 400 spectrometer, using $CDCl_3$ as solvent and TMS as internal reference.

IR spectra were recorded on a Perkin-Elmer 283 B or 1420 spectrophotometer using KBr compressed tablets. The electronic impact (El) ionization mass spectra were acquired on a JEOL JMS-AX505 HA Mass spectrometer operated in the positive ion mode. The acquisition conditions were ion source temperature 230°C, ionization energy 70 eV, emission current 0.14 μA and ionization current 100 μA. Melting points were measured using a Mel-Temp II apparatus and are uncorrected. All reagents were obtained from commercial suppliers and used without further purification.

Synthesis of Complexes 2 and 3

Metal powder (0.1 g, 1.5 mmol), (-)-sparteine (0.36 mL, 1.5 mmol), DMSO (3 mL) and CCl_4 (3 mL) were placed in a flask and the mixture was heated at 65°C with magnetic stirring until total dissolution of the metal was observed (0.5–2 h). The solution was filtered and allowed to stand at room temperature for 1–12 hours, respectively, after which crystals were formed. Sparteine complexes were filtered off and dried at room temperature, obtaining **2** and **3** in 94 and 91% yield, based on the pure products isolated. Suitable single-crystals of the free ligand were obtained from allowing equimolar amounts of (-)-sparteine and ammonium thiocyanate to stand in a dimethylsulfoxide/water mixture.

Complex dichloro[(-)-sparteine-N,N′]copper(II) **2**, m.p.: 165–166°C; $[\alpha]_D^{20} = -111°$ (EtOH); IR ν_{max} (KBr) cm^{-1}: 469(vs), 437(s) (Cu–N); 288(vs), 275(vs) (Cu–Cl). ^1H NMR (400 MHz, $CDCl_3$): δ 3.8–1.4 ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 77–18 ppm. MS-El (*m/z*): 368 (M^+).

Complex dichloro[(-)-sparteine-N,N′]zinc(II) **3**, m.p.: 266–267°C; $[\alpha]_D^{20} = -157°$ (EtOH); IR ν_{max} (KBr) cm^{-1}: 462(vs), 437(s) (Zn–N); 332(vs), 308(vs) (Zn–Cl). ^1H NMR (400 MHz, $CDCl_3$): δ 3.9–1.3 ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 77–17 ppm. MS-El (*m/z*): 370 (M^+).

X-Ray Structural Analysis

Crystals of compounds **1–3** were mounted on a Siemens P4/PC diffractometer using highly oriented graphite monochromated Mo-kα ($\lambda = 0.71073$ Å) radiation. The unit cell parameters, summarized in Table III, were obtained by least-square fit of 25 accurately centered reflections in the range $9° \leq 2\theta \leq 25°$, and the intensity data were collected at 293(2)° K in the range $3° \leq 2\theta \leq 50°$, using the $\varpi : 2\theta$ scan technique. Three standard reflections measured after every 97 reflections show no significant variation in the intensities. The data set was corrected for Lp and absorption

TABLE III Crystallographic data for compounds **1**–**3**

Compound	*Sparteine ligand*	*Cu-complex*	*Zn-complex*
Molecular formula	$C_{16}H_{27}N_3S$	$C_{15}H_{26}Cl_2N_2Cu$	$C_{15}H_{26}Cl_2N_2Zn$
F_w	293.47	368.82	370.65
Crystal dimensions(mm)	0.48 × 0.40 × 0.22	0.40 × 0.26 × 0.20	0.48 × 0.44 × 0.38
Crystal system	monoclinic	orthorhombic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimensions			
a(Å)	7.769(1)	11.041(1)	11.269(3)
b(Å)	13.391(1)	11.318(1)	11.955(3)
c(Å)	7.773(1)	13.136(1)(2)	12.465(3)
β(°)	100.05(1)	–	–
V(Å^3)	796.25(16)	1641.5(2)	1679.3(7)
Z	2	4	4
D_{calc}	1.224	1.492	1.466
F(000)	320	772	776
Absorption coef. (mm^{-1})	0.199	1.648	1.773
Index ranges	$-9 \le h \le 9$	$-1 \le h \le 13$	$0 \le h \le 13$
	$-15 \le k \le 0$	$-1 \le k \le 13$	$0 \le k \le 14$
	$-9 \le l \le 0$	$-1 \le l \le 15$	$0 \le l \le 14$
Min/max transmission	0.9106/0.9576	0.5585/0.7340	0.4832/0.5522
Unique data collected	1460	2052	1709
No. of parameters refined	185	182	182
$R(F \ge 2\sigma(I))$[a]	0.0544	0.0322	0.0390
$wR^2(F \ge 2\sigma(I))$[b]	0.1374	0.0702	0.0898
S[c]	1.073	0.968	1.068
Flack parameter	−0.4(3)	0.02(2)	0.01(3)
Min/max residuals (eÅ^{-3})	−0.202/0.217	−0.234/0.389	0.340/0.472

[a] $R = ||Fo| - |Fo||/|Fo|$.
[b] $wR^2 = \{[w(Fo^2 - Fc^2)^2]/w(Fo)^2\}^{1/2}$.
[c] $S = \{[w(Fo^2 - Fc^2)^2]/(n-p)\}^{1/2}$; where n = no. of reflns. and p = no. of parameters refined.

effects (psi-scans). The structures were solved by direct methods [8] and refined by full matrix least squares using anisotropic thermal parameters for all non-hydrogen atoms. All the hydrogen atoms were included as fixed contributions and not refined, except for that bonded to the N1 atom of the sparteine ligand **1** whose positional parameters were refined. The idealized positions for hydrogen atoms were generated from the geometries about the attached carbon atoms, and forced to ride on it with a fixed isotropic temperature factor, $U = 1.2$ times the U_{eq} of the parent C-atom and C–H distance of 0.96 Å. The structure was refined by using SHELXL-97 [9]. The quantity minimized during the least squares analysis was $\sum(w\_F_o^2 - F_{c\_}^2)^2$, with $w = 1/[\sigma^2(F_o^2) + (AP)^2 + (BP)]$, where $P = (F_0^2 + 2F_c^2)/3$, (Compound 1: A = 0.0730, B = 0.336; Complex 2: A = 0.0305, B = 0; Complex 3: A = 0.0514, B = 0). The absolute structures were confirmed by refinement of the Flack parameter and the final models converged as shown in Table III.

Acknowledgements

We thank DGAPA for their financial support (Project IN-228799).

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