Synthesis and Characterization of Gold(III) Complexes of 1,4-Benzodiazepin-2-ones. Crystal Structure of Trichloro-[7-chloro-1-(cyclopropylmethyl)-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one]gold(III)

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The reaction of gold(III) chloride with several 1,4-benzodiazepin-2-ones, L, gives 1:1 adducts, (L)$AuCl_3$, which were characterized by IR, Raman and ^1H NMR spectroscopy. In the title compound the coordination of the ligand, ascertained through a X-ray structure determination, was shown to occur through the 4-nitrogen atom.*

Introduction

1,4-benzodiazepines are versatile tranquilizing and sedative hypnotic compounds which are now widely and successfully employed [1]. Gold derivatives have been used in chemotherapy since many years, the chief use nowadays being in the treatment of rheumatoid arthritis [2]. In addition, recent reports indicate that gold(III) derivatives are likely to have other biological effects [3]: thus the observation that $[AuCl_4]^-$ interacts with DNA suggests that gold(III) complexes may be found to have anticancer properties.

On these bases, following our interest in the chemistry of gold, we thought it worthwhile to investigate the interaction of a variety of typical benzodiazepin drugs with gold(III) chloride. Here we present the synthesis of some adducts, their spectroscopic properties and the X-ray structure of one of them. A preliminary account of this work has already been published [4], while other results concerning the interaction with divalent palladium and platinum will be reported elsewhere [26].

*Throughout this work, L indicates one of the following 1,4-benzodiazepin-2-ones: DIAZEPAM: 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one; PRAZEPAM: 7-chloro-1-(cyclopropylmethyl)-1-3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one; NIMETAZEPAM: 1,3-dihydro-1-methyl-7-nitro-5-phenyl-2H-1,4-benzodiazepin-2-one; LORAZEPAM: 7-chloro-5(o-chlorophenyl)-1,3-dihydro-3-hydroxy-2H-1,4-benzodiazepin-2-one; NITRAZEPAM: 1,3-dihydro-7-nitro-5-phenyl-2H-1,4-benzodiazepin-2-one.

Experimental

Elemental analyses (Table I) were performed on a Perkin-Elmer 240B Elemental Analyzer at the University of Sassari. Infrared spectra were recorded on a Perkin-Elmer 683B in nujol mull and chloroform solution. Raman spectra were obtained with a Coderg PHO spectrophotometer on solid samples; the source of exciting radiation at 568 nm was a Coherent Radiation Krypton ion laser. ^1H NMR were recorded at 80 MHz using a Varian CFT-20 spectrometer, at room temperature (298 K).

Preparation of the Adducts

The ligands, (L), were supplied by Roche and were used without further purification; the gold(III) chloride was obtained by reaction of $HAuCl_4 \cdot 3H_2O$ (Johnson Matthey Chemicals Ltd.) with thionyl chloride, according to a known procedure [5]. The adducts (L)$AuCl_3$ (*Ia–Va*) were prepared by mixing at room temperature a chloroform solution of ($AuCl_3$) (*ca.* 400 mg) with a solution of the ligand in the same solvent (molar ratio 1:1). After 24 hours, the solutions were concentrated to small volume to give a first crop; addition of diethyl ether to the solution gave a second crop. The combined precipitates were crystallized to give the analytical samples, orange-yellow, yields 70–80%. Crystals of complex *IIa*, suitable for X-ray diffraction, were obtained as small thin red plates, by slow evaporation of *ca.* 1/1 $CHCl_3/Et_2O$ solution. *Crystal data.* $C_{19}H_{17}AuCl_4N_2O$, $M = 628.1$, monoclinic, space group $P2_1/n$, $a = 12.542(2)$, $b = 9.269(2)$, $c = 19.574(3)$ Å, $\beta =$

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TABLE I. Analytical* and IR Data.

Compound	C	H	N	ν(C=O)	ν(C=N)
Diazepam, *I*				1680–85	1600
(Diazepam)$AuCl_3$, *Ia*	31.03 (32.65)	2.23 (2.21)	4.52 (4.76)	1695	1595
Prazepam, *II*				1670	1605
(Prazepam)$AuCl_3$, *IIa*	36.22 (36.31)	2.93 (2.71)	4.36 (4.46)	1695	1585
Nimetazepam, *III*				1675	1610
(Nimetazepam)$AuCl_3$, *IIIa*	32.00 (32.08)	2.15 (2.17)	6.36 (7.02)	1705	1590
Lorazepam, *IV*				1695	1615
(Lorazepam)$AuCl_3$, *IVa*	27.88 (28.82)	1.66 (1.60)	4.45 (4.48)	1715	1585
Nitrazepam, *V*				1690	1610
(Nitrazepam)$AuCl_3$, *Va*	31.77 (30.80)	2.26 (1.88)	7.16 (7.19)	1710	1590

*Calculated values in parenthesis.

102.67(1)°, $U = 2220(1)$ Å^3, $D_c = 1.879$ g cm^{-3}, $Z = 4$, μ(Mo-K$_\alpha$) = 71.1 cm^{-1}, $F(000) = 1200$ electrons.

Data Collection

A small flat crystal of approximate dimensions 0.2 × 0.15 × 0.05 mm was mounted on a Enraf-Nonius CAD-4 automatic diffractometer. Intensity data were collected by the ω-scan technique using Mo-K$_\alpha$ radiation ($\lambda = 0.71073$ Å) with a graphite single crystal monochromator in the incident beam. The standard CAD-4 centering, indexing and data collection programs were used. The unit cell parameters and the orientation matrix were obtained from least-squares fitting of 25 reflections having $8° < \theta < 13°$. 3876 reflections were collected with scan width taken as $\Delta\omega = 1.7 + 0.35 \tan\theta$, exploring the $\pm h, +k, +l$ region of the reciprocal space within a 2θ sphere of 48°. The scan speed was 3 deg min^{-1} and backgrounds were counted at the extreme points of the scan range for a total time equal to one half of the scan time.

A periodical re-measurement of three standard reflections during the data collection revealed a small crystal decay which was on the average about 7%. Moreover three orientation standards were checked after 200 reflections. If the standard deviation of the h, k, l values for any orientation reflection exceeded 0.07, a new orientation matrix was calculated by re-centering 22 reference reflections. Lorentz-polarization, decay and absorption corrections were applied. Absorption effects were corrected by an empirical method based on a set of ψ scans of reflections having χ values near 90° [6].

Structure Solution and Refinement

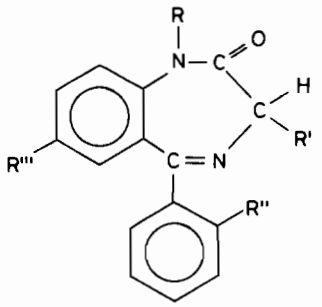
The positions of all non-hydrogen atoms were obtained by the usual Patterson and Fourier methods. The contributions of the scattering amplitudes of all the hydrogen atoms, kept fixed in their expected positions (C–H = 0.95 Å) and not refined, were included in the last cycles of the refinement. The final full-matrix least-squares refinement, carried out with 1380 reflections having $I \geq 3\sigma(I)$, with Au and Cl atoms treated anisotropically led to conventional R and R_w values of 0.056 and 0.054, respectively. Individual weights were taken as $w_{hkl} = \sigma^{-2}(F_o)$ where $\sigma(F_o) = \sigma(F_o^2)/2F_o$, $\sigma(F_o^2) = [\sigma^2(I) + (AI^2)]^{1/2}/Lp$ and A is an ignorance factor set equal to 0.04.

Scattering factors and anomalous dispersion factors were taken from ref. 7.

All the computations were performed on a PDP 11/34 computer using the Nonius Structure Determination Package (SDP) [8]. Johnson's ORTEP was used in preparing the drawing (Fig. 2). Final atomic coordinates are given in Table IV, bond distances and angles in Table V.

Results and Discussion

The interaction of gold(III) chloride was investigated with the following 1,4-benzodiazepin-2-ones:



I, DIAZEPAM: R = CH_3; R′ = R″ = H; R‴ = Cl
II, PRAZEPAM: R = $CH_2(\overline{CH-CH_2-CH_2})$; R′ = R″ = H; R‴ = Cl
III, NIMETAZEPAM: R = CH_3; R′ = R″ = H; R‴ = NO_2
IV, LORAZEPAM: R = H; R′ = OH; R″ = R‴ = Cl
V, NITRAZEPAM: R = R′ = R″ = H; R‴ = NO_2

The reaction was carried out in mild conditions, *i.e.* at room temperature in chloroform solution; in any case only the 1:1 adducts were isolated, *Ia–Va*, even when excess ligand was employed. In solution the adducts display a certain degree of ionization both in acetone and dichloromethane, the amount of ionization being a function of the nature of the substituents R–R‴. The range of observed Λ_M is rather wide, going from almost negligible values for complex *Ia* and *IIIa* (*Ia*, acetone, 12.2 ohm^{-1} cm^2 mol^{-1}, 2.6×10^{-4} *M*; *IIIa*, acetone, 19.4 ohm^{-1} cm^2 mol^{-1}, 2.6×10^{-4} *M*) to values of 94 (acetone) and 17.2 (dichloromethane) ohm^{-1} cm^2 mol^{-1} resp., in complex *IIa* (2.5×10^{-4} *M*).

For the latter derivative, whatever the species in solution, the evidence in the solid state of a monomeric neutral adduct of the type (L)$AuCl_3$ has been ascertained by the X-ray investigation (*vide infra*). The other complexes are likely to be of the same type: indeed, in the solid state, the existence of ionic isomers of the type $[L_2AuCl_2][AuCl_4]$ is ruled out by the IR spectra, where no bands assignable to the $[AuCl_4]^-$ anion are observed. On the other hand, a comparison of the IR spectra in the range 1750–1650 cm^{-1} suggests that in any case the coordination mode of the ligand is the same in the solid state and in solution ($CHCl_3$). In all the complexes *Ia–Va*, the two strong absorptions, attributed in the ligands to the prevailing contribution of ν(C=N) and ν(C=O) resp., are shifted to higher ($\nu_{C=O}$) and lower ($\nu_{C=N}$) wavenumber (see Table I), suggesting coordination to the metal through the 4-nitrogen atom.

The Raman and IR spectra of the adducts were studied in detail in the metal–halogen stretching region, where intense and easily recognizable bands occur (Table II). Vibrational spectra of square planar (L)$AuCl_3$ complexes in C_{2v} symmetry (the highest possible) should exhibit three ν(AuCl) stretching modes ($2a_1 + b_1$), *i.e.* the ν(Cl–Au–Cl) symmetric stretch (a_1), the ν(Cl–Au–Cl) asymmetric stretch (b_1) and the *trans* ν(Au–Cl) stretch (a_1), all of them being IR and Raman active. The IR spectra of several (L)$AuCl_3$ have been reported [9–15]: in any case the spectra show a strong absorption, ascribed to a b_1 vibration and a band, having variable intensity according to the nature of the ligand L at frequency lower than b_1, assigned to the stretch a_1 of the chlorine *trans* to the L ligand. In a few cases a weak or medium band is observed in the region between b_1 and a_1, assigned to the symmetric stretch ν(Cl–Au–Cl) of type a_1 [11, 12, 14]. The Raman spectra are reported to show, in agreement with the expected pattern, two strong absorptions of type a_1 and a weak band of type b_1 [12, 14, 15].

TABLE II. (AuCl) Stretching Frequencies (cm^{-1}).

Compound		(a_1)	(b_1)	(a_1)
(Diazepam)$AuCl_3$, *Ia*	IR	–	367s	–
	R	371s	364sh	337s
(Prazepam)$AuCl_3$, *IIa*	IR	–	362s	–
	R	364sh	–	345s
(Nimetazepam)$AuCl_3$, *IIIa**	IR	–	360s	–
	R	–	–	–
(Lorazepam)$AuCl_3$, *IVa*	IR	–	357s	–
	R	360s	–	335s
(Nitrazepam)$AuCl_3$, *Va*	IR	–	362s	–
	R	365s	–	344s

**IIIa* decomposes on laser light.

In the IR spectra of our derivatives, *Ia–Va*, only one strong band is observed, ascribed to the vibration of type b_1, *i.e.* to the stretching vibration which is accompanied by the greatest change of dipole moment. In no case was it possible to detect any absorption assignable to the stretches ν(Au–Cl) of type a_1. The Raman spectra show two bands, strong in any case but one (L = Prezepam, *IIa*): of the two absorptions, one is observed at frequency values lower than b_1, the other one at values very near to the band of type b_1. In the spectrum of complex *Ia* (L = Diazepam), a third absorption is found as a shoulder of the band occurring at a frequency near to b_1. The strong absorptions are assigned to the ν(Au–Cl) stretches of type a_1: of these, we assign the absorption at higher frequency to the symmetric stretch ν(Cl–Au–Cl) and the other one, at a lower wavenumber, to the ν(Au–Cl) of the chlorine *trans* to L. The assignment, although in agreement with that previously reported for the complexes (L)$AuCl_3$ where L is pyridine or a substituted pyridine [10], is to be considered tentative: indeed, even the Au–Cl distances found by X-ray in the case of complex *IIa* suggest that no remarkable difference is to be expected between the symmetric stretches of type a_1. It

TABLE III. ^{1}H NMR Data.[a]

Compound	Aromatic	$CH_2(3)$	$CH_3(1)$	$-CH_2-\overline{CH-CH_2-CH_2}$	$-CH_2-\overline{CH-CH_2-CH_2}$	$-CH_2-\overline{CH-CH_2CH_2}$	NH
Diazepam, *I*	7.79 7.37	4.75, 3.93(10.6)	3.5				
(Diazepam)$AuCl_3$, *Ia*	8.28 7.69	5.03, 4.66(12.75)	3.68				
Prazepam, *II*	7.86 7.08	4.64, 3.95(10.25)		4.15, 3.40(14.22)	0.96	0.24[b]	
(Prazepam)$AuCl_3$, *IIa*	8.1 7.08	5.04, 4.86(12.75)		4.37, 3.8(14.30)	1.22	0.47[b]	
Nimetazepam, *III*	8.59 7.42	4.86, 4.04(10.40)	3.46				
(Nimetazepam)$AuCl_3$, *IIIa*	8.21 7.94	5.16, 4.96(13.46)	3.77				
Lorazepam, *IV*	7.88 7.2						c
(Lorazepam)$AuCl_3$, *IVa*	8.59 7.4						8.57
Nitrazepam, *V*	8.61 7.63	4.48					9.76
(Nitrazepam)$AuCl_3$, *Va*	8.83 7.84	5.11					

[a]The chemical shifts are reported in p.p.m. (δ values), relative to TMS as internal standard; the J values, Hz, are in parenthesis. [b]Multiplet. [c]Not observed.

is noteworthy that in our complexes one of the bands of type a_1 is observed in the Raman spectra at a frequency somewhat higher than the frequency of the IR band of type b_1: such a behaviour, ($\nu_{a_1} > \nu_{b_1}$), which is not usual, has been previously observed in the complexes (py)$AuCl_3$ and (dipy)Au_2Cl_6 [15].

The ^{1}H NMR spectra of the ligands and of the complexes were recorded at room temperature in deuteroacetone, where most of the complexes are more soluble than in chlorinated solvents. For complex *Ia*, the spectrum was recorded also in $CDCl_3$; in both the solvents the general features of the spectrum were found to be the same, showing that the coordination mode of the ligand is not remarkably affected by the solvent. The chemical shifts and the other parameters are reported in Table III, while the spectrum of Prazepam (*II*), and of the corresponding gold complex, *IIa*, is shown in Fig. 1.

In the spectrum of benzodiazepin-2-ones, three well-separate sets of signals are observed. The first set at low fields (*ca.* 7–8 ppm) is given by the protons of the two aromatic rings, a and b (see Fig. 1), which form an ABC and AA'BB'C spin system with the exception of Lorazepam which forms an ABCD system. The second set, in the region (*ca.* 4–5 ppm) is related to the CH_2 group inside the heteroaromatic cycle and appears in the ligands *I*–*III* as a typical AB quartet. Thus, in the ligands having a substituent on the 1-nitrogen atom, the molecule has a fixed conformation at room temperature. In the spectrum of the ligand *V*, Nitrazepam, where an unsubstituted NH group is present in the cycle, one averaged signal is observed at room temperature for the CH_2 group; an AB spectrum is obtained, in acetone solution, only at -50 °C. In this case, for a single intramolecular exchange between two coupled sites ($AB \rightarrow A_2$) ($\Delta\nu_{AB} = \nu_A - \nu_B = 53.6$, $J_{AB} = 10.5$ Hz), at the coalescence temperature, we calculate a value of $\Delta G_c^* = 11$ Kcal/mol, in agreement with the values reported by Linscheid in a kinetic study relative to other benzodiazepins [16]. The third set, at higher field, contains the signals of the 1-nitrogen substituents, *i.e.* a CH_3 in *I* and *III* and $CH_2(\overline{CH-CH_2-CH_2})$ group in the ligand *II*. In the latter (Fig. 1) the $CH_2(\overline{CH-CH_2-CH_2})$ protons give a well resolved AB spectrum (4.15 ppm, 3.40 ppm) while the CH proton resonates around 1 ppm and the CH_2 of the cyclopropyl appear as an unresolved multiplet around 0.25 ppm. In the spectra of the gold complexes (*Ia*–*IVa*), all the signals are shifted to lower fields, the more affected being the protons of the CH_2 group inside the heterocycle. One of the B protons is more shifted than the other, so that the separation between the two sets of signals becomes narrower than in the ligands. In any case the AB pattern is retained, the H–H geminal coupling constants being larger than in the ligands. The large shift observed for the protons bonded to the 3-carbon atom suggests a coordi-

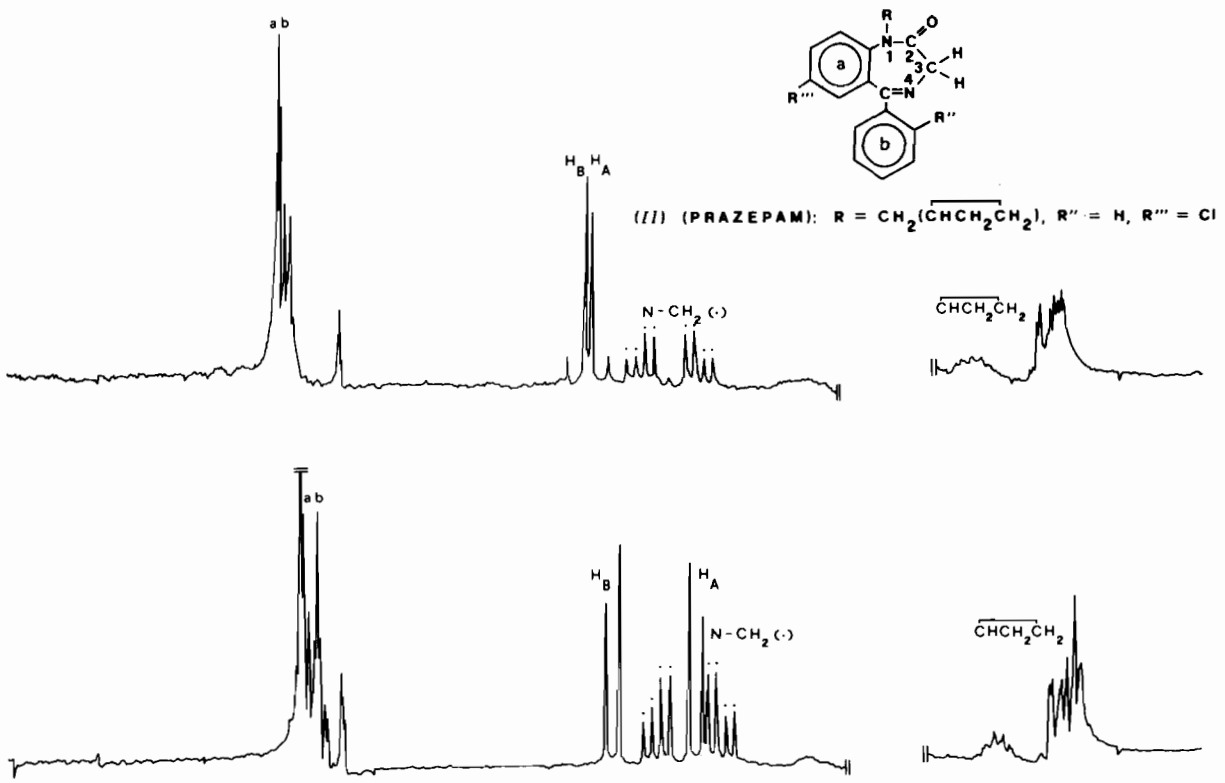


Fig. 1. ^{1}H NMR in deuteroacetone at room temperature. Top: compound *IIa*, (Prazepam)$AuCl_3$; bottom: ligand *II*, Prazepam.

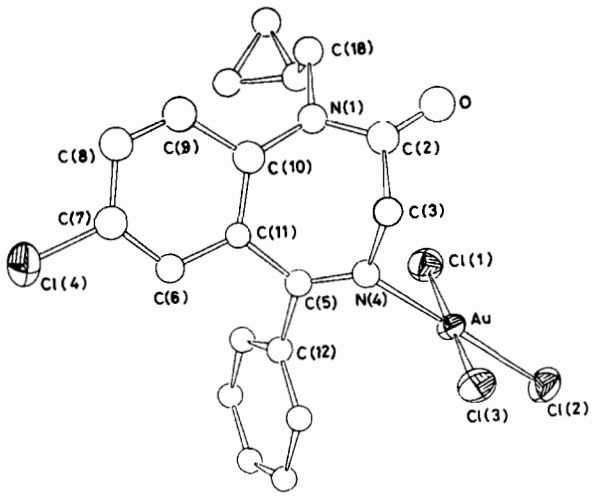


Fig. 2. ORTEP view of compound *IIa*, (Prazepam)$AuCl_3$. The hydrogen atoms have been omitted for clarity.

nation of the ligand to the metal through the 4-nitrogen atom even in acetone solution. The differences in the chemical shifts and in the J values are likely to be due to a modified electron distribution, in the presence of the coordinated metal, rather than to a change in the conformation of the ligand. The NMR spectrum of complex *Va* is more complicated. Indeed, all the three sets of signals are doubled: *e.g.* two sets of signals assignable to the CH_2 protons are observed, one in the same region involved in the complexes *Ia–IIIa* (see Table III), the other shifted to lower field. Thus, it seems that two species exist in solution, the presence of the free ligand being ruled out since it resonates at higher field. An NMR spectrum comparable with that of compounds *Ia–IVa* is observed only if the reaction is carried out at 0 °C and a first precipitate, obtained by addition of diethyl ether, is filtered off immediately from the mixture of reaction. The nature of the second species is uncertain: it might be either a linkage isomer or an adduct where the ligand has a different conformation.

Description of the Structure. Complex IIa

Crystals of the complex (Prazepam)$AuCl_3$ consist of a packing of monomeric molecules separated by normal van der Waals contacts. The gold(III) ion, bonded to three chlorine atoms and to the Prazepam ligand via the 4-nitrogen atom has, as usual, a square planar environment and lies 0.026 Å above the least-squares plane between atoms Au, Cl(1), Cl(2), Cl(3), and N(4) (see Table VI). No significant deviation from linearity can be observed for the atomic system N(4)–Au–Cl(2) (angle 179.01(45)°), while a small bending of the *trans* chlorine atoms Cl(1) and Cl(3)

TABLE IV. Positional and Thermal Parameters[‡] with Estimated Standard Deviations in Parentheses.

Atom	x	y	z	B(Å²)
Au	0.24808(8)	0.0648(1)	0.10652(4)	4.37(2)
Cl(1)	0.3849(5)	−0.084(1)	0.1606(3)	6.0(2)
Cl(2)	0.1756(5)	−0.1106(9)	0.0300(3)	6.8(2)
Cl(3)	0.1104(5)	0.220(1)	0.0593(3)	7.1(2)
Cl(4)	0.6392(6)	0.730(1)	0.2492(4)	8.3(2)
N(4)	0.311(1)	0.221(2)	0.1763(8)	3.1(4)*
C(5)	0.400(2)	0.280(3)	0.178(1)	3.5(5)*
C(3)	0.252(2)	0.247(2)	0.2335(9)	3.3(5)*
C(2)	0.310(2)	0.163(3)	0.298(1)	4.5(5)*
N(1)	0.413(1)	0.213(2)	0.3268(8)	3.7(4)*
O	0.265(1)	0.065(2)	0.3183(7)	5.5(3)*
C(11)	0.457(2)	0.373(2)	0.2347(9)	3.0(5)*
C(6)	0.513(2)	0.495(3)	0.219(1)	4.5(6)*
C(7)	0.571(2)	0.584(3)	0.270(1)	5.0(5)*
C(8)	0.570(2)	0.551(3)	0.338(1)	5.1(5)*
C(9)	0.518(2)	0.435(4)	0.355(1)	5.1(5)*
C(10)	0.456(2)	0.340(3)	0.307(1)	4.2(5)*
C(12)	0.454(2)	0.267(3)	0.115(1)	3.7(5)*
C(13)	0.558(2)	0.217(3)	0.125(1)	6.0(7)*
C(14)	0.606(2)	0.191(4)	0.065(1)	8.5(8)*
C(15)	0.541(2)	0.229(4)	0.004(2)	8.8(9)*
C(16)	0.443(2)	0.283(4)	−0.007(1)	8.3(8)*
C(17)	0.392(2)	0.307(3)	0.050(1)	4.9(6)*
C(18)	0.474(2)	0.128(3)	0.387(1)	5.3(6)*
C(19)	0.553(2)	0.033(4)	0.364(1)	8.0(8)*
C(20)	0.647(2)	−0.017(3)	0.420(2)	8.7(9)*
C(21)	0.655(3)	0.086(5)	0.370(2)	12(1)*

[‡]Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $4/3[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)]$.

TABLE V. Bond Distances (Å) and Angles (°).

Au–Cl(1)	2.272(7)	Cl(1)–Au–Cl(2)	91.4(3)
Au–Cl(2)	2.260(6)	Cl(1)–Au–Cl(3)	176.3(2)
Au–Cl(3)	2.278(7)	Cl(1)–Au–N(4)	88.7(5)
Au–N(4)	2.030(15)	Cl(2)–Au–Cl(3)	91.4(3)
Cl(4)–C(7)	1.70(3)	Cl(2)–Au–N(4)	179.0(5)
N(4)–C(5)	1.23(2)	Cl(3)–Au–N(4)	88.4(5)
N(4)–C(3)	1.49(2)	C(5)–N(4)–C(3)	120.(2)
C(5)–C(11)	1.46(2)	N(4)–C(5)–C(11)	125.(2)
C(5)–C(12)	1.54(3)	N(4)–C(5)–C(12)	120.(2)
C(3)–C(2)	1.52(3)	C(11)–C(5)–C(12)	115.(2)
C(2)–N(1)	1.37(2)	N(4)–C(3)–C(2)	108.(2)
C(2)–O	1.19(3)	C(3)–C(2)–N(1)	114.(2)
N(1)–C(10)	1.38(3)	C(3)–C(2)–O	120.(2)
N(1)–C(18)	1.48(2)	N(1)–C(2)–O	126.(2)
C(11)–C(6)	1.40(2)	C(2) N(1)–C(10)	124.(2)
C(11)–C(10)	1.45(2)	C(2)–N(1)–C(18)	115.(2)
C(6)–C(7)	1.38(3)	C(10)–N(1)–C(18)	121.(2)
C(7)–C(8)	1.36(3)	C(5)–C(11)–C(6)	120.(2)
C(8)–C(9)	1.34(3)	C(5)–C(11)–C(10)	121.(2)
C(9)–C(10)	1.39(3)	C(6)–C(11)–C(10)	119.(2)
C(12)–C(13)	1.35(3)	C(11)–C(6)–C(7)	123.(2)
C(12)–C(17)	1.40(3)	Cl(4)–C(7)–C(6)	121.(2)
C(13)–C(14)	1.45(3)	Cl(4)–C(7)–C(8)	122.(2)
C(14)–C(15)	1.32(3)	C(6)–C(7)–C(8)	117.(3)
C(15)–C(16)	1.30(3)	C(7)–C(8)–C(9)	122.(2)
C(16)–C(17)	1.41(3)	C(8)–C(9)–C(10)	125.(2)
C(18)–C(19)	1.47(3)	N(1)–C(10)–C(11)	123.(2)
C(19)–C(20)	1.51(4)	N(1)–C(10)–C(9)	123.(2)
C(19)–C(21)	1.36(4)	C(11)–C(10)–C(9)	114.(2)
C(20)–C(21)	1.39(4)	C(5)–C(12)–C(13)	120.(2)
		C(5)–C(12)–C(17)	117.(2)
		C(13)–C(12)–C(17)	123.(2)
		C(12)–C(13)–C(14)	120.(2)
		C(13)–C(14)–C(15)	114.(3)
		C(14)–C(15)–C(16)	128.(3)
		C(15)–C(16)–C(17)	121.(3)
		C(12)–C(17)–C(16)	114.(2)
		N(1)–C(18)–C(19)	109.(2)
		C(18)–C(19)–C(20)	116.(2)
		C(18)–C(19)–C(21)	116.(2)
		C(20)–C(19)–C(21)	58.(2)
		C(19)–C(20)–C(21)	56.(2)
		C(19)–C(21)–C(20)	67.(3)

towards N(4) [Cl(1)–Au–Cl(3) = 176.29(24)°] may be due to a repulsion among the bulkier chlorine ligands. The three Au–Cl bond lengths range from 2.260(6) to 2.278(7) Å and are equivalent within three e.s.d'.s., thus indicating a weak structural *trans*-influence of the nitrogen atom, comparable with that of the chloride ion [4]. The average value of 2.270 Å is in good agreement with that found in a number of other $(L)AuCl_3$ complexes [17–20]. The Au–N(4) distance of 2.030(15) Å is indicative of an essentially single bond, as can be shown by a comparison with the few values of similar Au(III)–N interactions reported so far in the literature (see for instance 2.022(13) Å in the B molecule of $(CH_3C_6H_4N_2C_6H_4CH_3)AuCl_3$ [18], 2.012(15) Å in $(NH_3)AuCl_3$ [21], and 1.978 Å (average) in $AuN_4C_{14}H_{26}O_2Cl$ [22] where the Au–N bonds belong to a planar six-membered heterocyclic ring displaying substantial π delocalization). The molecular parameters of the coordinated Prazepam ligand can be compared with those found for Diazepam in the free ligand [23] and in the complex $(Diazepam)_2CuCl_2$ [24]. The bonding parameters and the conformational features of the benzodiazepine molecules are essentially the same in all three cases, thus confirming that the coordination of a benzodiazepine molecule to a metal atom (via the 4-nitrogen atom) does not affect its geometry markedly. For instance, in all cases the seven-membered ring displays a boat-type conformation with similar dihedral angles between planes 1–2 and 2–3 (see Table VI), and the geometry around N(1) is trigonal planar. In $(Prazepam)AuCl_3$ the deviation from planarity of the C(10)–N(1)–C(18)–C(2)–O–C(3) fragment range from −0.07(2) to +0.06(2) Å, while the dihedral angle between the least-squares plane of this fragment and that of the

TABLE VI. Least-squares Planes through Selected Groups of Atoms in the Form $Ax + By + Cz + D = 0$.

		A	B	C	D
i) Equations of planes					
Plane	Atoms				
1	C(5), C(11), C(10), N(1)	−0.8729	0.4855	−0.0480	−2.6280
2	C(5), N(1), C(2), N(4)	0.4269	−0.8963	−0.1201	−0.9091
3	N(4), C(3), C(2)	−0.5250	−0.7941	−0.3061	−4.3097
4	Au, Cl(1), Cl(2), Cl(3), N(4)	0.7076	0.3238	−0.6281	0.7673
5	C(10), N(1), C(18), C(2), O, C(3)	0.5441	−0.5742	−0.6118	−2.9230
6	C(6), C(7), C(8), C(9), C(10), C(11)	−0.8271	0.5596	−0.0523	−2.1977

ii) Distances ($Å \times 10^3$) of selected atoms from planes

Plane	
4	Au 26(1), Cl(1) −20(6), Cl(2) 6(6), Cl(3) −20(7), N(4) 8(15)
5	C(10) −71(23), N(1) 31(17), C(18) 49(24), C(2) 3(23), O −70(16), C(3) 58(20)

iii) Angles (°) between selected pairs of planes

Planes	
1, 2	36.7
2, 3	58.4
5, 6	137.7

iv) Dihedral angles (°) between least-squares planes of the seven-membered rings in some benzodiazepine molecules

Planes	I[a]	II[b]	III[c]	IV[d]
1, 2	36.7	33.0	37.9	37.0
2, 3	58.4	62.0, 58.0*	58.4	59.9

[a]Present work. [b]Ref. 30. [c]Ref. 23. [d]Ref. 24. *Two independent molecules.

aromatic ring C(6)–C(10) is 137.7°. It seems likely that the similar shortening of both the N(1)–C(10) [1.382(25) Å] and N(1)–C(2) [1.371(23) Å] bond lengths, with respect to the expected value for a single $N(sp^2)$–$C(sp^2)$ distance (1.47 Å), may be due to a partial electron delocalization along the O–C(2)–N(1)–C(10) fragment, deriving from an extension of the aromatic character of the chlorophenyl ring and from the C=O π system. The C(5)–N(4) distance of 1.230(22) Å is typical of a localized double bond, thus supporting the view of a single Au–N(4) bond, as previously mentioned.

Concluding Remarks

On the basis of the preceding results a few conclusions can be drawn:

1) The reaction of gold(III) chloride with several 1,4-benzodiazepin-2-ones follows a simple pattern and in any case only 1:1 adducts are obtained. Such a behaviour is quite different from that observed with other metal salts, *e.g.* palladium(II) and platinum(II) halides [25, 26].

2) Although the interaction of these drugs has been investigated with several metal ions and different modes of coordination have been suggested [24, 25, 27–29], it is noteworthy that in the two complexes which were studied by X-ray, *i.e.* the gold(III) complex reported here and the copper(II) complex, $(Diazepam)_2CuCl_2$ [24], the ligand coordinates through the 4-nitrogen atom. The spectroscopic data on the whole suggest that the coordination is of the same type in the other gold derivatives *Ia–IVa* in the solid state and even in solution, while for complex *Va* species having different coordination or different conformation may be present.

3) The geometry of the organic molecule in the complexes is not considerably affected by the complexation to the gold (or the copper) atom. This might be significant pharmacologically even if the interrelation between the stereochemistry and the biological activity of these molecules is still not completely elucidated [23, 30, 31]: indeed, molecules with structures practically superimposable on the strucure of Diazepam have been found to have only minimal biological activity [32].

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