

The gold(III) tetrachloride salt of L-cocaine

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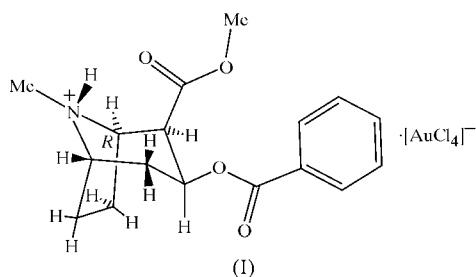
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The title salt, methyl (1*R*,2*R*,3*S*,5*S*,8*S*)-3-benzoyloxy-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate tetrachloroaurate(III), (C₁₇H₂₂NO₄)[AuCl₄], has its protonated N atom intramolecularly hydrogen bonded to the O atom of the methoxycarbonyl group [N⁺⋯O = 2.755 (6) Å and N—H⋯O = 136°]. Two close intermolecular C—H⋯O contacts exist, as well as five C—H⋯Cl close contacts. The [AuCl₄][−] anion was found to be distorted square planar.

Comment

Cocaine is a complex tropane alkaloid which occurs naturally in the leaves of the coca plant, *Erythroxylum coca*. In the United States, cocaine is one of the most widely abused illicit drugs, second only to marijuana (Drug Enforcement Administration, 2006). Pharmacologically, cocaine acts as a central nervous system stimulant, and has been used medically as a local anaesthetic. The structure of cocaine was originally determined by Willstätter & Müller (1898) by chemical means and was verified by a crystal structure analysis of L-cocaine hydrochloride by Gabe & Barnes (1963); this structure was redetermined by Zhu *et al.* (1999).



The gold chloride microcrystal test has been widely utilized for over 100 years (Lyons, 1885) by forensic scientists in the general scheme of analysis for cocaine. Microcrystal tests are one of the fastest and simplest techniques for differentiating L-cocaine from its seven stereoisomers (Allen *et al.*, 1981). Unlike some of the more sophisticated techniques, such as

mass spectrometry, microcrystal tests are inexpensive, and the only instrument required is an optical microscope. This test involves the addition of a 5% *w/v* solution of chloroauric acid in water (HAuCl₄·3H₂O) to a dilute aqueous acidified (HCl) solution of suspected cocaine, followed by observation of the resulting crystals microscopically (American Society for Testing and Materials, 2003). However, the interpretation of the resulting microcrystalline precipitate has been empirical and subject to the training and experience of the analyst (McCrone, 1992). In our study, single-crystal X-ray diffraction was used to determine the absolute configuration of the gold(III) tetrachloride salt of L-cocaine, (I), which has the same powder diffraction profile as the microcrystalline material.

Fig. 1 shows the asymmetric unit of (I). Compared with the structure reported by Zhu *et al.* (1999), the main difference in the L-cocaine cation is the rotation of the methoxycarbonyl group about the C2—C16 bond in (I). The L-cocaine—HCl structure reported by Zhu *et al.* (1999) has the methoxycarbonyl group rotated [torsion angle −138.4 (8)°] to allow hydrogen bonding between the protonated N atom and the methoxy O atom (designated O4 in this structure). In the present structure, (I), this torsion angle [C3—C2—C16—O4 = 89.9 (6)°] allows the protonated N atom to be hydrogen bonded to the carbonyl O atom [N1⋯O3 = 2.755 (6) Å and N1—H1A⋯O3 = 136°]. According to potential energy calculations performed by Zhu *et al.* (1999), the energy minimum for the methoxycarbonyl group occurs at a torsion angle of approximately 95–110°. The orientation of the methoxycarbonyl group found in (I) corresponds closely to the conformation found in the structure of (−)-norcocaine (Zhu *et al.*, 1994), which exhibits similar hydrogen bonding between protonated atom N1 and carbonyl atom O3.

The [AuCl₄][−] anion of (I) was found to be a distorted square plane, with the Au atom 0.0056 (8) Å above the best least-squares plane of the five-atom moiety. Two opposing Cl atoms are above the best plane by 0.0784 (14) Å and the other two are below the plane by −0.0812 (14) Å. In a search of the Cambridge Structural Database (CSD, Version 5.27, update of May 2006; Allen, 2002), 89 structures containing the gold tetrachloride anion are found. However, only 24 show the ‘bowing’ of the square-planar arrangement of the Au atom

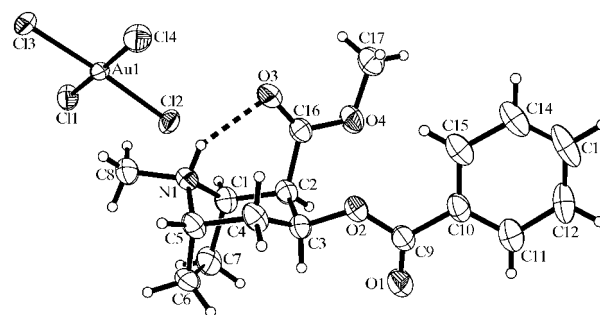


Figure 1

The asymmetric unit of (I). Displacement ellipsoids are drawn at the 30% probability level. The [AuCl₄][−] counter-ion was chosen on the basis of its proximity to the site of the positive charge on N1. The dashed line denotes the intramolecular hydrogen bond.

and the four Cl⁻ anions. Of these, only one shows flexing of the Cl⁻ anions slightly larger than that found here. Two opposing Cl⁻ anions in the structure of tetra(methylthio)tetrathiafulvalene bis(tetrachlorogold) (CSD refcode GEHSO01; Jones, 1989) are above the best plane by 0.087 Å and the opposite two are below the plane by -0.078 Å. All the other gold tetrachloride anions are more planar than that in (I), mostly forming a nearly perfect square-planar arrangement about the Au atom.

In (I), the hydrogen bonding between atom N1 and the carbonyl O atom of the methoxycarbonyl group (O3) is characterized by N1...O3 = 2.755 (6) Å and N1—H1A...O3 = 136°. In the structure of (-)-cocaine hydrochloride (Zhu *et al.*, 1999), there is a hydrogen bond between atom N1 and the Cl⁻ anion [3.058 (9) Å] and another weaker hydrogen bond between atom N1 and the methoxy O atom [2.894 (9) Å]. This latter hydrogen bond is made possible because of the rotation of the methoxycarbonyl group in this structure to present the methoxy O atom to the H atom on N1. In (I), since the methoxycarbonyl group is rotated by 131.5 (10)°, this hydrogen bond from N1 is to carbonyl atom O3.

Fig. 2 illustrates the hydrogen bonding and close contacts of (I). Two intermolecular close contacts are present (Table 2) within the 2.7 Å range that we employ as standard for non-bonded C—H...O packing interactions (Steiner, 1997). Also, five close contacts exist to three of the four Cl atoms of the anion; atom Cl1 has no close contacts (see Table 1). However, a symmetry-related [AuCl₄]⁻ anion is located such that the Cl1...Au1(1 - x, -½ + y, ½ - z) distance is 4.3742 (16) Å and the Au1—Cl1...Au1(1 - x, -½ + y, ½ - z) angle is 172.38 (6)°. The interplanar angle between the best least-squares planes of two [AuCl₄]⁻ anions is 82.81 (4)°, which results in a herring-

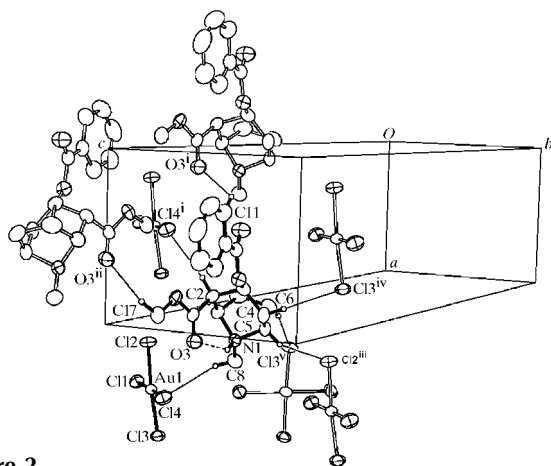


Figure 2
A diagram with unit-cell axes, showing the internal hydrogen bonding (dashed line) and close contacts (thin solid lines) for (I). Displacement ellipsoids are drawn at the 30% probability level. For clarity, all C-bound H atoms have been omitted unless they are involved in the bonding. Symmetry-related molecules involved in the close contacts are shown with open bonds to simplify the drawing. The close contacts shown involve parts of five other separate asymmetric units, of which one contains both O3ⁱ and Cl4ⁱ. The [AuCl₄]⁻ anion of the main molecule and the non-H atoms participating in the hydrogen-bonding interactions are also labelled. [Symmetry codes: (i) x - 1, y, z; (ii) x - ½, ½ - y, 2 - z; (iii) x, 1 + y, z; (iv) x - 1, 1 + y, z; (v) 3 - x, ½ + y, ½ - z.]

bone pattern of the [AuCl₄]⁻ anions, with atom Cl1 pointing directly at the Au atom of an adjacent anion.

Experimental

For the preparation of (I), L-cocaine hydrochloride (Sigma, lot No. 48 F0208) was dissolved in water to yield a 50 µg ml⁻¹ solution. This solution (200 µl) was combined with 0.5% acidified (HCl) gold(III) chloride (HAuCl₄·3H₂O) (200 µl) and allowed to crystallize. Extremely long gold parallelepiped crystals formed (m.p. 452 K). A crystal suitable for X-ray analysis was cut from one of these long rods.

Crystal data

(C ₁₇ H ₂₂ NO ₄)[AuCl ₄]	Z = 4
M _r = 643.12	D _x = 1.953 Mg m ⁻³
Orthorhombic, P2 ₁ 2 ₁ 2 ₁	Cu Kα radiation
a = 7.7358 (3) Å	µ = 17.33 mm ⁻¹
b = 9.4543 (5) Å	T = 295 (2) K
c = 29.9093 (13) Å	Parallelepiped, yellow
V = 2187.46 (17) Å ³	0.45 × 0.21 × 0.08 mm

Data collection

Bruker SMART CCD APEXII area-detector diffractometer	and SADABS (Bruker, 2005)
φ and ω scans	T _{min} = 0.042, T _{max} = 0.338
Absorption correction: numerical and multi-scan	14526 measured reflections
[SHELXTL (Sheldrick, 2004)]	3906 independent reflections
	3804 reflections with I > 2σ(I)
	R _{int} = 0.052
	θ _{max} = 68.5°

Refinement

Refinement on F ²	w = 1/[σ ² (F _o ²) + (0.0263P) ² + 0.9351P]
R[F ² > 2σ(F ²)] = 0.028	where P = (F _o ² + 2F _c ²)/3
wR(F ²) = 0.070	(Δ/σ) _{max} < 0.001
S = 1.05	Δρ _{max} = 0.59 e Å ⁻³
3906 reflections	Δρ _{min} = -0.96 e Å ⁻³
246 parameters	Absolute structure: Flack (1983), with 1468 Friedel pairs
H-atom parameters constrained	Flack parameter: 0.025 (14)

Table 1
Selected geometric parameters (Å, °).

Au1—Cl2	2.2669 (15)	Au1—Cl4	2.2766 (17)
Au1—Cl3	2.2732 (15)	Au1—Cl1	2.2843 (16)
Cl2—Au1—Cl3	175.52 (8)	Cl2—Au1—Cl1	90.66 (7)
Cl2—Au1—Cl4	89.17 (7)	Cl3—Au1—Cl1	90.37 (7)
Cl3—Au1—Cl4	90.08 (7)	Cl4—Au1—Cl1	176.33 (7)

Table 2
Hydrogen-bond and short-contact geometry (Å, °).

D—H...A	D—H	H...A	D...A	D—H...A
N1—H1A...O3	0.91	2.02	2.756 (6)	136
C11—H11...O3 ⁱ	0.93	2.62	3.24 (1)	125
C17—H17B...O3 ⁱⁱ	0.96	2.60	3.542 (9)	168
C5—H5...Cl2 ⁱⁱⁱ	0.98	2.90	3.633 (6)	132
C4—H4B...Cl3 ^{iv}	0.97	2.80	3.750 (6)	171
C6—H6A...Cl3 ^v	0.97	2.90	3.842 (7)	165
C8—H8B...Cl4	0.96	2.85	3.703 (8)	149
C2—H2...Cl4 ⁱ	0.98	2.78	3.759 (6)	173

Symmetry codes: (i) x - 1, y, z; (ii) x - ½, -y + ½, -z + 2; (iii) x, y + 1, z; (iv) x - 1, y + 1, z; (v) -x + 3, y + ½, -z + ¾.

All H atoms were found in electron-density difference maps. The methyl H atoms were placed in ideally staggered positions, with C—

H = 0.98 Å and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$. The methylene and methine H atoms were placed in geometrically idealized positions and constrained to ride on their parent C atoms, with C–H = 0.99 and 1.00 Å, respectively, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. The ammonium H atom was similarly placed in an idealized position, with N–H = 0.91 Å, and refined with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$.

Data collection: *SMART* (Bruker, 2006); cell refinement: *SMART*; data reduction: *SAINt-Plus* (Bruker, 2005); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2004); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3036). Services for accessing these data are described at the back of the journal.

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