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New potentially cytotoxic thiolatogold(I) complexes of 1,1′-bis(diphenylphosphino)ferrocene

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Abstract

1,1′-Bis[chlorogold(I) diphenylphosphino]ferrocene (**1**) was chosen as the starting material to synthesize new thiolato gold(I) complexes. This has been achieved by substituting the chlorine atoms by monofunctional and bifunctional thiolates affording 'open' thiolatogold complexes and trimetallic ferrocenophane-type structures, respectively. The new 1,1′-bis(2,6-dithia-1-phosphanyl)ferrocene (**7**) containing directly linked P and S atoms was also prepared but no gold complex was obtained. Compound **2** crystallizes in the monoclinic space group $P2_1/n$ with $a=10.263(2)$, $b=21.064(4)$, $c=16.259(3)$ Å, $\beta=97.06(2)°$ and $V=3.488(1)$ Å^3. The distance between the two gold atoms (3.06 Å) indicates a significant contact interaction. Compounds **2–5** have allowed antitumoral efficiency on human bladder and colon carcinoma.

Keywords: Crystal structures; Gold complexes; Thiolato complexes; Dithiaphosphanylferrocene complexes; Trinuclear complexes

1. Introduction

Among various drugs, the gold(I) thiomalate derivative 'Myocrisin', the gold(I) thioglucose derivative 'Solganol' and (*S*)-2,3,4,5-tetraacetyl-1-*β*-*O*-thioglucose(triethylphosphine)gold(I) 'Auranofin' are known to be effective in treatment of rheumatoid arthritis [1,2]. More recently, it has been discovered that Auranofin [3] and some other gold(I) compounds [4] also show interesting chemotherapeutic potential in cancer treatment. A large variety of gold(I) thiolate-containing compounds are described in the literature [5–10] but to our best knowledge, none of them was derived from a metallocene species. As bis(diphenylphosphino)ferrocene itself displays anticancer activity [11], it was chosen as candidate to coordinate various thiolato gold(I) groups.

2. Experimental

All reactions were conducted under an atmosphere of pure dry argon. Solvents were dried and deoxygenated over sodium/benzophenone ketyl and distilled immediately before use. Transfers were carried out via syringes or cannulas. $[Na(AuCl_4)]\cdot 2H_2O$ was a generous gift from the Johnson Matthey Technology Centre. 1,3-Dimercaptopropane, thiophenol, *p*-thiocresol and 3,4-dimercaptotoluene were purchased from Aldrich Chemie and were used directly as received. [(tht)AuCl] [12], 1,1′-bis[chlorogold(I) diphenylphosphino]ferrocene (**1**) [13] and 1,1′-bis(dichlorophosphino)ferrocene (**6**) [14,15] were prepared by the literature methods.

Microanalyses were performed by the Microanalysis Centre at UMIST (Manchester, UK). Melting points were determined with a Kofler apparatus without correction. ^{1}H, $^{13}C\{^1H\}$ and ^{31}P NMR spectra were recorded in $CDCl_3$ with a Bruker AC 200 spectrometer operating at 200.0, 50.3 and 81.0 MHz, respectively. Some of the $^{13}C\{^1H\}$ NMR spectra were recorded using the microprogramme Bruker J-MODX.Au. Chemical shifts are reported in δ units, parts per million downfield from internal tetramethylsilane for ^{1}H, $^{13}C\{^1H\}$, and from external H_3PO_4 for ^{31}P. Antitumor activity was assessed on an in vitro panel of two human tumor cell lines: bladder carcinoma (HT1376) and colon carcinoma (SW620). Cell cultures were grown in suitable media as monolayers at 37 °C in a 5% CO_2 atmosphere and seeded with a suspension of the tumor cells. After 72 h culture, the total cell protein was determined using sulforhodamine B [16]. The IC_{50}, the concentration of test compound giving

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50% survival with respect to controls, was calculated from the dose/response curves.

2.1. *Syntheses*

2.1.1. *[9] (1,1')Ferrocenophane (2)*

A solution (10 ml) of 1,3-dimercaptopropane (0.36 ml, 3.60 mmol) and sodium hydroxide (0.289 g, 7.20 mmol) in methanol (200 ml) was added dropwise to a suspension of **1** (0.184 g, 0.180 mmol) in acetone (10 ml) at room temperature. The resultant suspension was stirred for 1 h. The yellow solid formed was isolated by centrifugation, washed with methanol and diethyl ether, dried and recrystallized from dichloromethane/methanol (50/50) mixture. Yield 0.103 g, 54%. Decomposition at 210 °C. *Anal.* Calc. for $C_{37}H_{34}Au_2FeP_2S_2$: C, 42.1; H, 3.2; S, 6.1. Found: C, 42.4; H, 3.2; S, 6.5%. ^{31}P NMR: 30.5 (s).

2.1.2. *1,1'-Bis[(thiophenylgold(I)diphenyl)phosphino]ferrocene (3)*

This yellow compound was prepared from thiophenol (0.80 ml, 7.82 mmol), sodium hydroxide (0.313 g, 7.82 mmol) and **1** (0.199 g, 0.196 mmol) by a procedure similar to that given for **2**. Yield 0.177 g, 77%. Decomposition at 267 °C. *Anal.* Calc. for $C_{46}H_{38}Au_2FeP_2S_2$: C, 47.4; H, 3.3; S, 5.5. Found: C, 47.4; H, 3.2; S, 5.9. ^{31}P NMR: 31.0 (s).

2.1.3. *1,1'-Bis[(p-methylthiophenylgold(I)diphenyl)phosphino]ferrocene (4)*

A solution of sodium hydroxide in methanol 0.052 M (6 ml, 0.312 mmol) was added to a solution of *p*-thiocresol (0.039 g, 0.310 mmol) in methanol (20 ml). The mixture obtained was added dropwise to a suspension of **1** (0.158 g, 0.155 mmol) in acetone (10 ml). The resultant suspension was stirred for 1 h. The yellow solid was isolated by centrifugation, washed with methanol and diethyl ether, dried and recrystallized from dichloromethane/methanol (50/50) mixture. Yield 0.109 g, 59%. Decomposition at 238 °C. *Anal.* Calc. for $C_{48}H_{42}Au_2FeP_2S_2$: C, 48.3; H, 3.5; S, 5.4. Found: C, 48.2; H, 3.3; S, 5.8%. ^{31}P NMR: 31.1 (s).

2.1.4. *[8] (1,1')Ferrocenophane (5)*

This compound was prepared from sodium hydroxide 0.051 M (7 ml, 0.355 mmol), 3,4-dimercaptotoluene (0.027 g, 0.170 mmol) and **1** (0.174 g, 0.170 mmol) by a procedure similar to that reported for **4**. A yellow solid was obtained. Yield 0.102 g, 54%. Decomposition at 130 °C. *Anal.* Calc. for $C_{41}H_{34}Au_2FeP_2S_2$: C, 44.7; H, 3.1; S, 5.8. Found: C, 43.7; H, 3.3; S, 6.2%. ^{31}P NMR: 27.6 (s).

2.1.5. *1,1'-Bis(2,6-dithia-1-phosphanyl)ferrocene (7)*

A solution of **6** (0.770 g, 1.986 mmol) in diethyl ether (100 ml) was added very slowly at 0 °C to a solution of 1,3-dimercaptopropane (0.40 ml, 3.972 mmol) and triethylamine in excess (1.2 ml, 8.621 mmol), in the same solvent (150 ml). The suspension was filtered after warming to room temperature and the residues (polymer and triethylamine) were washed with 30 ml of diethyl ether. The filtrate was evaporated to dryness and afforded 0.429 g (47%) of a yellow amorphous powder. Decomposition at 90 °C. *Anal.* Calc. for $C_{16}H_{20}FeP_2S_4$: C, 41.9; H, 4.4; S, 28.0. Found: C, 41.6; H, 4.4; S, 26.3%. ^{31}P NMR: 31.5 (s).

Table 1
Crystallographic data for [9] (1,1')ferrocenophane (**2**)

Chemical formula	$C_{37}H_{34}Au_2FeP_2S_2$
Molecular weight	1054.5
Crystal size (mm)	0.22 × 0.23 × 0.33
Crystal system	monoclinic
Space group	$P2_1/n$ (No. 14)
a (Å)	10.263(2)
b (Å)	21.064(4)
c (Å)	16.259(3)
β (°)	97.06(2)
V (Å^3)	3.488(1)
Diffractometer	Enraf-Nonius CAD4
Z	4
D_{calc} (g cm^{-3})	2.048
λ (Å)	0.71069
μ(Mo Kα)	92.0
R [a]	0.0261
R_w [b]	0.0273

[a] $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|$.

[b] $R_w = (\Sigma w(|F_o| - |F_c|)^2/\Sigma F_o^2)^{1/2}$.

2.2. *Crystal structure analysis of [9](1,1')ferrocenophane (2)*

Brown–red prismatic crystals were grown from dichloromethane/methanol solution. Crystal data, data collection and processing parameters are reported in Table 1. Observed reflections were corrected for Lorentz and polarization. Absorption corrections were introduced by applying the DIFABS program [17]. Scattering factors for neutral atoms including *f* and *f'* were obtained from Ref. [18]. Calculations were performed with SHELX 76 and 86 packages [19,20]. The structure was solved by the heavy-atom method and refined by the full-matrix least-squares method in the isotropic approximation. Absorption correction was made at this stage of the refinement (min., max. transmissions = 1.23 and 0.78, respectively). The further refinement of the structure was carried out in the full-matrix anisotropic approximation. All hydrogen atoms were located in the difference Fourier synthesis. However, for further refinement, calculated idealized positions of these atoms were used. The positions of hydrogen atoms were refined using the 'rider' scheme and their isotropic thermal parameters were fixed at $U = 0.08$ Å^2. The final full-matrix least-squares converged to $R = 0.0261$, $R_w = 0.0273$; the weighting scheme in the form $[s^2(F) + 0.000037(F^2)]^{-1}$ was used. The final electron-density difference synthesis showed no peaks higher than 1.6 or lower than −0.5 e A^{-3}, the largest lying close to the metal atom. Table 2 lists atomic coordinates and equivalent isotropic thermal parameters for non-hydrogen atoms.

Table 2
Atomic coordinates and equivalent isotropic thermal parameters (Å^2 × 10^3) for non-hydrogen atoms for [9](1,1′)ferrocenophane (**2**)

Atom	x	y	z	U_{eq} ^{a}
Au1	−0.10443(4)	0.15811(3)	0.39170(0)	37(1)
Au2	0.01091(4)	0.19872(2)	0.23502(3)	31(1)
Fe1	−0.2950(2)	0.0403(1)	0.1748(1)	35(1)
P1	−0.3177(3)	0.1394(2)	0.3436(2)	33(2)
P2	0.0118(3)	0.1089(2)	0.1583(2)	31(2)
S1	0.0989(3)	0.1588(2)	0.4675(2)	62(2)
S2	0.0179(3)	0.3017(2)	0.2814(2)	47(2)
C11	−0.336(1)	0.0649(6)	0.2894(8)	40(7)
C12	−0.448(1)	0.0380(7)	0.2416(8)	47(7)
C13	−0.418(2)	−0.0243(7)	0.2185(9)	60(9)
C14	−0.286(2)	−0.0365(7)	0.2522(9)	6(1)
C15	−0.234(1)	0.0183(7)	0.2940(8)	48(7)
C21	−0.149(1)	0.0805(6)	0.1196(7)	33(6)
C22	−0.181(1)	0.0198(6)	0.0837(7)	41(7)
C23	−0.319(1)	0.0220(8)	0.0501(8)	50(8)
C24	−0.365(1)	0.0816(8)	0.0653(9)	56(9)
C25	−0.264(1)	0.1184(6)	0.1054(7)	38(6)
C1	0.212(1)	0.2048(7)	0.4139(8)	49(8)
C2	0.199(1)	0.2722(8)	0.4231(9)	59(9)
C3	0.067(1)	0.3035(8)	0.3921(9)	62(9)
C111	−0.409(1)	0.1999(6)	0.2799(7)	34(6)
C112	−0.343(1)	0.2425(6)	0.2385(8)	39(7)
C113	−0.407(1)	0.2870(7)	0.189(1)	59(9)
C114	−0.540(2)	0.2894(8)	0.1804(9)	6(1)
C115	−0.609(1)	0.2483(8)	0.2246(9)	62(9)
C116	−0.544(1)	0.2025(7)	0.2719(8)	48(7)
C121	−0.411(1)	0.1304(6)	0.4317(7)	37(6)
C122	−0.389(1)	0.1747(7)	0.4940(8)	55(8)
C123	−0.454(1)	0.1722(8)	0.5630(9)	63(9)
C124	−0.541(1)	0.1240(8)	0.5704(9)	59(9)
C125	−0.565(1)	0.0799(8)	0.5096(9)	6(1)
C126	−0.499(1)	0.0832(7)	0.4404(8)	52(8)
C211	0.105(1)	0.0422(6)	0.2013(8)	38(6)
C212	0.148(1)	−0.0040(6)	0.1518(8)	44(7)
C213	0.219(1)	−0.0555(7)	0.185(1)	59(9)
C214	0.250(1)	−0.0599(8)	0.268(1)	6(1)
C215	0.212(1)	−0.0149(8)	0.3199(9)	6(1)
C216	0.138(1)	0.0361(7)	0.2860(8)	48(8)
C221	0.087(1)	0.1272(5)	0.0657(7)	32(6)
C222	0.018(1)	0.1333(6)	−0.0121(7)	43(7)
C223	0.080(1)	0.1505(7)	−0.0786(8)	50(8)
C224	0.210(1)	0.1651(7)	−0.0704(9)	57(9)
C225	0.280(1)	0.1600(8)	0.007(1)	63(9)
C226	0.220(1)	0.1423(7)	0.0745(8)	48(8)

[a] Equivalent isotropic U_{eq} defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensors.

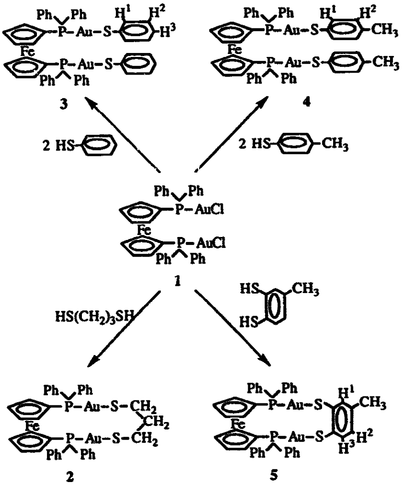
3. Results and discussion

The gold(I) thiolates **2**–**5** (Scheme 1) were prepared by substitution of the chlorine atoms of **1** by different aliphatic or aromatic thiolates prepared in situ by deprotonation of the corresponding thiols with sodium hydroxide, but other bases like potassium hydroxide [10,21–23], triethylamine [24] or ethanolamine [5] could also be used. The bridged metallocene **2** was obtained from propane dithiolate which shows a great tendency to react through both functional groups [5,21]. The twelve-membered ring obtained is quite new, since most of the dinuclear gold(I) rings described in the literature involve pure organic bridging ligands with eight or nine members [7,24–28], and it is only recently that Dávila et al. [21] and Narayanaswamy et al. [5] have prepared some compounds containing ten- to fourteen-membered rings.

As compound **3** is sparingly soluble in classical solvents like most of the thiolates [28], the polymeric nature or the existence of intermolecular associations cannot be assessed without further characterization. In contrast the phenyl substituted compound **4** is well soluble in dichloromethane as already reported in the literature for other substituted aromatic thiolates [5].

The ^{1}H NMR spectra of the compounds show signals of 1,1′-bis[gold(I) diphenylphosphino]ferrocene units and signals of the thiolate ligands (Table 3). For example for **5**, H^1 exhibits one doublet at 7.84 ppm (J_{meta} = 1.9 Hz), one double doublet at 6.69 ppm for H^2 (J_{ortho} = 7.8 Hz, J_{meta} = 1.4 Hz) and one doublet at 7.87 ppm for H^3 (J_{ortho} = 8.1 Hz). The ^{13}C{^{1}H} NMR signals (Table 4) for the compounds **2**, **3**, **4** and **5** are assignable to the different carbon atoms by examination of the coupling constants with phosphorus. This is not true for the β, *para* and thiolate carbon atoms which are too far away from the phosphorus atom. The thiolate part of **3** and **4** is not totally assignable. The ^{31}P NMR singlets for **2**, **3**, **4** and **5** (δ 30.5, 31.0, 31.1, 27.6, respectively) fall in the range observed for other P–Au–S compounds [29].

The ^{1}H NMR spectrum of **2** at r.t. shows that the structure in solution is not rigid. There are only two multiplets corresponding to ring protons as well as two signals of the protons of the trimethylene bridge. Such behavior probably is caused by the dissociation of the weak Au···Au bond found in the



Scheme 1.

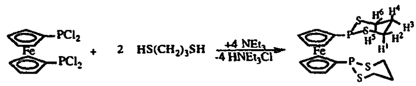
Table 3
^{1}H NMR data for the complexes

	CH_2, CH_3	Cp	Ph
2	2.08 (qt, 2H, H^2, ^3J(H–H) = 6.0 Hz) 3.49 (t, 4H, H^1, ^3J(H–H) = 6.0 Hz)	4.28 (m, 4H) 4.61 (m, 4H)	7.41–7.46 (m, 12H, *m*-H, *p*-H) 7.63–7.73 (m, 8H, *o*-H)
3		4.16 (m, 4H) 4.63 (m, 4H)	6.99 (d, 2H, H^3, S–Ph, J_{ortho} = 7.3 Hz) 7.10 (t, 4H, H^2, S–Ph, J_{ortho} = 7.1 Hz) 7.39–7.64 (m, 20H, P–Ph) 7.61 (d, 4H, H^1, S–Ph, J_{ortho} = 8.1 Hz)
4	2.24 (s, 6H)	4.16 (m, 4H) 4.64 (m, 4H)	6.93 (d, 4H, H^2, J_{ortho} = 7.8 Hz) 7.39–7.54 (m, 24H, P–Ph, H^1)
5	2.25 (s, 3H)	4.06 (m, 4H) 4.54 (m, 4H)	6.69 (dd, 1H, H^2, J_{ortho} = 7.8 Hz, J_{meta} = 1.4 Hz) 7.36–7.40 (m, 12H, P–Ph, *m*-H, *p*-H) 7.54–7.60 (m, 8H, P–Ph, *o*-H) 7.84 (d, 1H, H^1, J_{meta} = 1.9 Hz) 7.87 (d, 1H, H^3, J_{ortho} = 8.1 Hz)
7	1.25 (m, 2H, H^3) 1.77 (m, 2H, H^4, $^2J(H^4–H^3)$ = 14.3 Hz $^4J(H^4–P)$ = 2.5 Hz) 2.07 (m, 4H, H^2, H^6, $^3J(H^2–H^3) = {}^3J(H^6–H^3)$ = 6.5 Hz $^3J(H^2–H^4) = {}^3J(H^6–H^4)$ = 2.4 Hz) 2.59 (m, 4H, H^1, H^5, $^2J(H^1–H^2) = {}^2J(H^5–H^6)$ = 13.9 Hz $^3J(H^1–H^3) = {}^3J(H^5–H^3)$ = 5.2 Hz $^3J(H^1–H^4) = {}^3J(H^5–H^4)$ = 10.9 Hz $^3J(H^1–P) = {}^3J(H^5–P)$ = 2.3 Hz)	4.26 (m, 4H) 4.54 (m, 4H)	

solid state (see Section 3.1), followed by the rapid inversion of the cycle.

We also tried to prepare derivatives of diphosphorylated ferrocene containing sulfur atoms directly connected to phosphorus. For this purpose the bis-phosphorylated ferrocene **7** (Scheme 2) was prepared from tetrachloride **6** and 1,3-dimercaptopropane in the presence of triethylamine. In principle this reaction can lead to different products: complex **7**, which has a structure with a large ring comprising both phosphorus atoms, and various polymers. It was found that the desired product **7** can be isolated only if the reaction is carried out in very diluted solutions. Finally a satisfactory yield of 47% was obtained. The ^{1}H NMR spectrum of **7** contains the usual pattern for the 1,3-disulfa-2-phosphorinanes in chair conformation [30]. In the region of the aliphatic protons there are four groups of signals assigned to the corresponding axial and equatorial protons of the six-membered ring (the two carbon atoms linked directly to sulfur are chemically equivalent). The coupling constants of the geminal protons (i.e. 14 Hz) are the highest. J_{ax-ax} between two vicinal protons H^1 and H^4 or H^5 and H^4 is 10.9 Hz. However, the constants $^3J_{eq-eq}$ and J_{ax-eq} are lower (in the range 6–2 Hz), in accordance with the Karplus theory.

Unfortunately, all our attempts to prepare gold(I) complexes from the diphosphine **7** have so far systematically failed and a complete decomposition of the starting molecule has been observed.



6 **7**

Scheme 2.

3.1. Molecular structure of [9](1,1')ferrocenophane (2)

The molecular structure is shown in Fig. 1; bond lengths and bond angles are listed in Table 5. The molecule represents a macrocyclic trinuclear system but can also be thought of as a bicyclic one due to the Au(1)···Au(2) interaction. Although up to now an exhaustive explanation of the nature of the unusual interaction between the Au(I) d-cations is lacking, it is obvious that this interaction is of great importance in gold(I) chemistry [31–33]. It should be noted that the most reliable explanation of the nature of the interaction is the effects of electronic correlation strongly enhanced by relativistic effects [31]. The work of Schmidbaur [34] gave a value for the corresponding energy that falls in the range 25–37.5 kJ mol^{-1}. Such a value is close to that for a hydrogen bond and is dramatically higher than that usually found for normal van der Waals contacts. The Au(1)···Au(2) distance (3.061 Å) falls within the range 2.8–3.5 Å typical for gold–gold interactions in other Au(I) compounds [34–37].

The P(1)Au(1)Au(2)P(2) and S(1)Au(1)Au(2)S(2) torsion angles (−70.1 and −80.1°, respectively) correspond to a predicted C_2 arrangement of the linear –Au– fragments for molecular systems including an Au···Au interaction [31]. The auriophilic interaction leads to a restricted flexibility of the macrocycle and is mainly responsible for the conformation realized. Some geometrical distortions appear in the structure. The sum of the PAuAu and SAuAu angles (near

Table 4
$^{13}C\{^1H\}$ NMR data for the complexes

	CH_2, CH_3	Cp	Ph
2	29.0 (s) 39.4 (s)	73.0 (d, α-C, ^2J(C–P) = 7.5 Hz) 73.3 (d, C_{ipso}, ^1J(C–P) = 61.4 Hz) 76.2 (s, β-C)	128.8 (d, *m*-C, ^3J(C–P) = 11.4 Hz) 131.3 (s, *p*-C) 132.1 (d, C_{ipso}, ^1J(C–P) = 53.3 Hz) 133.9 (d, *o*-C, ^2J(C–P) = 13.7 Hz)
3		72.0 (d, C_{ipso}, ^1J(C–P) = 69.4 Hz) 74.7 (d, α-C, ^2J(C–P) = 14.1 Hz) 75.2 (d, β-C, ^3J(C–P) = 8.4 Hz)	123.6 (s, S–Ph) 128.1 (s, S–Ph) 129.0 (d, *m*-C, P–Ph, ^3J(C–P) = 11.4 Hz) 131.1 (d, C_{ipso}, P–Ph, ^1JC–P) = 55.6 Hz) 131.6 (s, *p*-C, P–Ph?) 132.9 (s, S–Ph?) 133.6 (d, *o*-C, P–Ph, ^2J(C–P) = 13.7 Hz) 141.5 (s, S–Ph)
4	20.9 (s)	71.9 (d, C_{ipso}, ^1J(C–P) = 63.4 Hz) 74.6 (d, α-C, ^2J(C–P) = 13.6 Hz) 75.3 (d, β-C, ^3J(C–P) = 8.6 Hz)	128.9 (s, S–Ph) 129.0 (d, *m*-C, P–Ph, ^3J(C–P) = 11.1 Hz) 131.2 (d, C_{ipso}, P–Ph, ^1J(C–P) = 55.8 Hz) 131.5 (s, *p*-C, P–Ph?) 132.8 (s, S–Ph?) 133.2 (s, S–Ph) 133.6 (d, *o*-C, P–Ph, ^2J(C–P) = 14.1 Hz) 137.2 (s, S–Ph)
5	20.8 (s)	72.8 (d, α-C, ^2J(C–P) = 5.0 Hz) 74.7 (d, C_{ipso}, ^1J(C–P) = 65.4 Hz) 76.0 (s, β-C)	123.9 (s, S–Ph) 128.7 (d, *m*-C, P–Ph, ^3J(C–P) = 10.7 Hz) 131.0 (s, *p*-C, P–Ph) 132.7 (d, C_{ipso}, P–Ph, ^1J(C–P) = 54.9 Hz) 133.0 (s, S–Ph) 133.6 (d, *o*-C, P–Ph, ^2J(C–P) = 14.5 Hz) 133.8 (s, S–Ph) 134.1 (s, S–Ph) 138.2 (s, S–Ph) 145.1 (s, S–Ph)
7	26.0 (d, ^2J(C–P) = 12.7 Hz) 26.8 (s)	73.1 (s, β-C) 73.6 (d, C_{ipso}, ^1J(C–P) = 53.5 Hz) 74.1 (d, α-C, ^2J(C–P) = 10.2 Hz)	

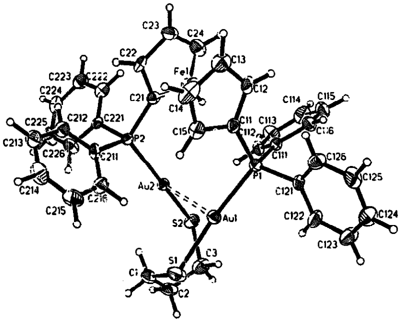


Fig. 1. ORTEP drawing for [9](1,1′)ferrocenophane (**2**) (30% ellipsoids).

Table 5
Selected bond lengths (Å) and angles (°) for [9](1,1′)ferrocenophane (**2**)

Au1···Au2	3.06	S1–C1	1.81(1)
Au1–S1	2.289(4)	C1–C2	1.44(2)
Au2–S2	2.295(4)	C2–C3	1.54(2)
Au1–P1	2.266(3)	S2–C3	1.81(2)
Au2–P2	2.267(3)	P1–C111	1.83(1)
P1–C11	1.80(1)	P2–C211	1.79(1)
P2–C21	1.79(1)	P1–C121	1.83(1)
Fe–Cp1	1.633	P2–C221	1.82(1)
Fe–Cp2	1.645		
P1Au1S1	164.7(1)	C1C2C3	118.(1)
P2Au2S2	165.4(1)	S2C3C2	116.(1)
Au2Au1P1	102.55(8)	Au1P1C11	111.1(4)
Au1Au2P2	104.65(8)	Au1P1C111	118.8(4)
Au2Au1S1	91.5(1)	Au1P1C121	108.8(4)
Au1Au2S2	84.46(9)	Au2P2C21	114.0(4)
Au1S1C1	109.7(5)	Au2P2C211	118.5(4)
Au2S2C3	109.9(5)	Au2P2C221	108.1(4)
S1C1C2	114.(1)		

194° for both Au atoms) clearly indicates that the two gold atoms tend to approach each other.

The Au–P (2.266(3) and 2.267(3) Å) and Au–S (2.289(4) and 2.295(4) Å) bond lengths lie within the range characteristic of these bonds in Au(I) compounds including the S–P–S fragment [38]. The ferrocene part of the molecule has a usual geometry: the orientation of the cyclopentadienyl ligands is eclipsed, the lengths Fe–c^1 and Fe–c^2 (c^1 and c^2 are the centroids of the corresponding Cp rings) are 1.633

and 1.645 Å, respectively, and the dihedral angle between the Cp planes is only 4.3°. The phosphine substituents in the Cp rings are in the adjacent eclipsed positions of the ferrocene system. The aliphatic chain between the sulfur atoms has an energetically favorable staggered conformation. However, the orientation of this chain with respect to the Au fragment (around Au–S single bonds) is asymmetrical; the Au(2)···H(1) distance (2.57 Å) is shorter than the sum of the van der Waals radii of the atoms (2.86 Å) indicating some possible influence between these two elements. No other short contacts with participation of gold atoms occur in the molecule

In the crystal, the molecules are combined by van der Waals interactions. There are no short intermolecular contacts in the crystal.

3.2. Antitumoral tests

Compounds **2**–**5** were practically inactive on bladder carcinoma HT 1376 and only a low efficiency was observed for **2** and **3** on colon carcinoma SW 620 ($IC_{50} = 100$ and 66.2, respectively, as compared to Cisplatin $IC_{50} = 19.2$ or Auranofin $IC_{50} = 7.0$).

4. Supplementary material

Tables of observed and calculated structure factors, atomic coordinates for hydrogen atoms and anisotropic thermal parameters are available from the authors upon request.

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