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Chiral phosphine ligands derived from sugars 10. Syntheses, structure, characterization, and antitumor activity of the gold(I) complexes with sugar-substructure phosphine ligands

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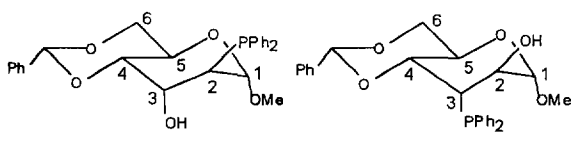
Abstract

Gold(I) complexes with sugar-substructure phosphine ligands [Au(*n*-MBPA)L] [*n*-MBPA = methyl 4,6-*O*-benzylidene-*n*-deoxy-*n*-(diphenylphosphino)-α-D-altropyranoside, HL = 1*H*-pyrimidine-2-thione (2-pymSH), 3,5-dimethyl-1*H*-pyrimidine-2-thione (2-pymmSH). **1**, $n = 2$, L = 2-pymS; **2**, $n = 3$, L = 2-pymS; **3**, $n = 2$, L = 2-pymmS; **4**, $n = 3$, L = 2-pymmS] have been prepared and characterized by ^{1}H, ^{13}C and ^{31}P NMR and molecular vibration spectra. Compound **2** crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 9.917(4)$, $b = 14.418(6)$, $c = 20.048(7)$ Å, and $Z = 4$, $R = 0.031$ for 2493 reflections with $I \geq 3\sigma(I)$. The mononuclear compound features a linear geometry for the gold atom defined by important parameters: Au–P 2.256(3) Å, Au–S 2.306(3) Å and P–Au–S 178.5(1)°. The altropyranose ring in **2** exhibits a distorted chair conformation. The preliminary experiment reveals that the gold(I) complexes with sugar-substructure phosphine ligands possess antitumor activity against P388 leukemia. © 1997 Elsevier Science S.A.

Keywords: Gold compound; Carbohydrate; Nuclear magnetic resonance; X-ray diffraction; Chiral phosphine; Antitumor activity

1. Introduction

Interest in complexes containing chromophore P–Au–S arises from the medicinal applications [1–7], and the photochemistry [8–12]. Auranofin [(2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranosato-*S*) (triethylphosphine)]gold(I) is efficacious and well tolerated, and exhibits therapeutic properties superior to the traditional chryso-therapeutic agents for the treatment of rheumatoid arthritis [13–15] and has also been found to be highly cytotoxic to tumor cell [16] and active against interperitoneal P388 leukemia [17]. Problems concerning the toxicity of these types of gold(I) compound have precluded some of them from further development as practical drugs [18]. The phosphine ligands in most of the complexes reported with the P–Au–S chromophore are commonly found to be organophosphines such as triphenylphosphine and triethylphosphine [1–7]. It is interesting to use the phosphines containing sugar substructure to prepare new gold(I) derivatives [19]. This contribution reports the synthesis and characterization of gold(I) complexes [Au(*n*-MBPA)L] [HL = 1*H*-pyrimidine-2-thione (2-pymSH), 3,5-dimethyl-1*H*-pyrimidine-2-thione (2-pymmSH). **1**, $n = 2$, L = 2-pymS; **2**, $n = 3$, L = 2-pymS; **3**, $n = 2$, L = 2-pymmS; **4**, $n = 3$, L = 2-pymmS] with chiral phosphines (*n*-MBPA = methyl 4,6-*O*-benzylidene-*n*-deoxy-*n*-(diphenylphosphino)-α-D-altropyranoside) derived from glucose [20,21], and the preliminary results of antitumor activity against P388 leukemia of 12 gold(I) complexes including **1–4**.



2-MBPA 3-MBPA

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2. Experimental

The ligands 1*H*-pyrimidine-2-thione (2-pymSH) and 3,5-dimethyl-1*H*-pyrimidine-2-thione (2-pymmSH) were used as-supplied. Sodium methoxide was prepared by dissolving sodium metal in dry methanol and then evaporating the solvent and drying under reduced pressure. Analytical-grade solvents were used without further purification. The chiral phosphines *n*-MBPA (*n* = 2, 3) [20,21] and the complexes [Au(*n*-MBPA)Cl] (*n* = 2, 3) [19] were prepared by the published methods.

Elemental analyses were performed by the Chemical Analysis Division of this Institute. Infrared (IR) spectra were measured on a Nicolet Magna-750 FT spectrometer (4000–100 cm^{-1}). Resonance Raman (RR) spectra were recorded on a Nicolet 910 FT-Raman spectrometer using Raman 1064 nm laser source at a resolution of 2 cm^{-1} with 300 scans. NMR spectra were measured in DMSO-d_6 on a Varian Unity-500 spectrometer operating at 499.98 MHz for ^1H, 125.71 MHz for ^{13}C, and 202.36 MHz for ^{31}P. Chemical shifts are expressed in parts per million (ppm) downfield from internal TMS (^1H and ^{13}C) or external 85% H_3PO_4 (^{31}P) standards as positive values. The general method has been used to detect the antitumor activity against P388 leukemia [17].

2.1. Preparations

2.1.1. General procedure

A CH_2Cl_2 solution (5 cm^3) of [Au(*n*-MBPA)Cl] (0.023 g, 0.033 mmol) was mixed with an MeOH solution (5 cm^3) of 2-pymSH or 2-pymmSH (0.035 mmol) containing MeONa (0.0019 g, 0.035 mmol). The mixture was stirred for 2 h at room temperature and left to stand overnight. The solution was filtered and the filtrate was left to evaporate slowly to obtain the desired products.

2.1.2. [Au(2-MBPA)(2-pymS)] (1)

Pale yellow, yield 81%. Found: C, 47.73; H, 4.06; N, 3.47%. Calc. for $C_{30}H_{30}AuN_2O_5PS$: C, 47.50; H, 3.98; N, 3.69%. ^1H NMR (δ): 8.44–7.04 [m, 18H, aryl-H], 5.44 [s, 1H, H(7)], 5.40 [d, 1H O*H*, $^4J_{HH}$ = 4.5 Hz], 4.81 [m, 1H, H(5)], 4.46 [d, 1H, H(1), $^3J_{PH}$ = 10.0 Hz], 4.26 [m, 1H, H(3)], 4.28 [m, 1H, H(6*a*), $^2J_{HH}$ = 10.5, $^3J_{HH}$ 5.0 Hz], 3.96 [d, 1H, H(2), $^2J_{PH}$ = 18.0 Hz], 3.88 [m, 1H, H(4)], 3.70 [t, 1H, H(6*e*), $^2J_{HH}$ = $^3J_{HH}$ = 10.5 Hz], 3.17 [s, 3H, OC*H*$_3$] ppm. ^{13}C NMR (δ): 180.3–116.3 [aryl-C], 101.5 [C(7)], 97.2 [C(1), $^2J_{PC}$ = 13.7 Hz], 77.3 [C(5)], 68.8 [C(6)], 64.0 [C(4)], 57.8 [C(3)], 55.4 [C(8)], 44.5 [C(2), $^1J_{PC}$ = 32.0 Hz] ppm. ^{31}P NMR (δ): 36.8 ppm. IR (CsI, disc): ν(aryl-H), 2933 (w), 2811(w); ν(C=C), 1496 (s); ν(Au–P), 393 (w); ν(Au–S), 317 (w) cm^{-1}. RR (KBr): ν (Au–P), 395 (w); ν(Au–S), 318 (w) cm^{-1}.

2.1.3. [Au(3-MBPA)(2-pymS)] (2)

Colorless, yield 90%. Found: C, 47.41; H, 4.03; N, 3.75%. Calc. for $C_{30}H_{30}AuN_2O_5PS$: C, 47.50; H, 3.98; N, 3.69%. ^1H NMR (δ): 8.40–6.72 [m, 18H, aryl-H], 5.72 [d, 1H O*H* $^4J_{HH}$ = 3.5 Hz], 5.58 [s, 1H, H(7)], 5.19 [m, 1H, H(5)], 4.67 [m, 1H, H(4)], 4.48 [s, 1H, H(1)], 4.21 [dd, 1H, H(6*e*), $^2J_{HH}$ = 10.0, $^3J_{HH}$ = 5.0 Hz], 4.12 [dd, 1H, H(3), $^2J_{PH}$ = 15.0 Hz, $^3J_{HH}$ = 6.0 Hz], 3.79 [t, 1H, H(6*a*), $^3J_{HH}$ = $^2J_{HH}$ = 10.0 Hz], 3.49 [d, 1H, H(2), $^3J_{PH}$ = 5.5 Hz], 3.24 [s, 3H, OCH_3] ppm. ^{13}C NMR (δ): 180.3–115.9 [aryl-C], 101.1 [C(7)], 99.8 [C(1)], 75.1 [C(4)], 69.1 [C(6)], 68.0 [C(2)], 61.1 [C(5)], 53.8 [C(8)], 40 [C(3)] ppm. ^{31}P NMR (δ): 34.1 ppm. IR (CsI, disc): ν(aryl-H), 2931 (w), 2885 (w); ν(C=C), 1539 (s); ν(Au–P), 395 (w); ν(Au–S), 320 (w) cm^{-1}. RR (KBr): ν(Au–P), 404 (w); ν(Au–S), 321 (w) cm^{-1}.

2.1.4. [Au(2-MBPA)(2-pymmS)] (3)

Pale yellow, yield 84%. Found: C, 48.75; H, 4.25; N, 3.34%. Calc. for $C_{32}H_{34}AuN_2O_5PS$: C, 48.86; H, 4.36; N, 3.56%. ^1H NMR (δ): 8.14–6.75 [m, 16H, aryl-H], 5.40 [s(br), 1H, O*H*], 5.22 [s, 1H, H(7)], 4.92 [m, 1H, H(5)], 4.47 [d, 1H, H(1), $^3J_{PH}$ = 10.0 Hz], 4.27 [m, 1H, H(6*a*)], 4.26 [m, 1H, H(3)], 3.95 [d, 1H, H(2)], $^2J_{PH}$ =

Table 1
Crystallographic data and data collection parameters for [Au(3-MBPA)(2-pymS)] (2)

Molecular formula	$C_{30}H_{30}AuN_2O_5PS$
M	758.58
Crystal dimensions (mm^3)	0.38×0.38×0.20
Space group	$P2_12_12_1$ (No. 19)
a (Å)	9.917(4)
b (Å)	14.418(6)
c (Å)	20.048(7)
V (Å^3)	2866(2)
Z	4
D_{calcd} ($g\,cm^{-1}$)	1.76
F(000)	1496
μ (mm^{-1})	5.281
T (K)	296
Scan mode	ω–2θ
$2\theta_{max}$ (deg)	49.9
T min–max	0.9655–1.0225
Index range	$-11 \le h \le 0, 0 \le k \le 17, 0 \le l \le 23$
No. reflections collected	2879
No. independent reflections	2879
No. observed reflections	2493 ($I \ge 3\sigma(I)$)
No. variables	361
S	0.92
$(\Delta/\sigma)_{max}$	0.02
$\Delta\rho_{max}$ (e^- Å^{-3})	0.66
$\Delta\rho_{min}$ (e^- Å^{-3})	−0.65
R [a]	0.031
R_w [b]	0.037

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

17.0 Hz], 3.86 [m, 1H, H(4)], 3.67 [t, 1H, H(6*a*)], 3.18 [s, 3H, OCH_3], 2.22 [s, 6H, aryl-CH_3] ppm. ^{13}C NMR (δ): 179.5–114.9 [aryl-C], 101.6 [C(7)], 97.3 [C(1)], 77.3 [C(5)], 68.9 [C(6)], 64.1 [C(4)], 58.0 [C(3)], 55.4 [C(8)], 44.6 [C(2)], 23.7 [aryl-CH_3] ppm. ^{31}P NMR (δ): 37.4 ppm. IR(CsI, disc): ν(aryl-H), 2920 (w), 2852 (w); ν(C=C), 1574 (s); ν(Au–P), 400 (w); ν(Au–S), 326 (w) cm^{-1}.

2.1.5. [Au(3-MBPA)(2-pymmS)] (4)

Pale yellow, yield 86%. Found: C, 48.68; H, 4.29; N, 3.44%. Calc. for $C_{32}H_{34}AuN_2O_5PS$: C, 48.86; H, 4.36; N, 3.56%. ^{1}H NMR (δ): 8.19–6.69 [m, 16H, aryl-H], 5.82 [s(Br), 1H, O*H*], 5.58 [s, 1H, H(7)], 5.09 [m, 1H, H(5)], 4.68 [m, 1H, H(4)], 4.49 [s, 1H, H(1)], 4.22 [dd, 1H, H(3), $^3J_{PH}$ = 10.5, $^2J_{HH}$ = 5.0 Hz], 4.19 [m, 1H, H(6*e*)], 3.78 [t, 1H, H(6*a*), $^3J_{HH}$ = $^2J_{HH}$ = 10.5 Hz], 3.52 [d, 1H, H(2), $^3J_{PH}$ = 6.5 Hz], 3.24 [s, 3H, OCH_3], 2.26 [s, 6H, aryl-CH_3] ppm. ^{13}C NMR (δ): 179.3–114.6 [aryl-C], 101.0 [C(7)], 99.8 [C(1)], 75.1 [C(4)], 69.0 [C(6)], 68.0 [C(2)], 61.1 [C(5)], 53.6 [C(8)], 40 [C(3)], 23.7 [aryl-CH_3] ppm. ^{31}P NMR (δ): 34.5 ppm. IR (CsI, disc): ν(aryl-H), 2929 (w), 2884 (w); ν(C=C), 1575 (s); ν(Au–P), 396 (w); ν(Au–S), 316 (w) cm^{-1}. RR (KBr): ν(Au–P), 398 (w); ν(Au–S), 315 (w) cm^{-1}.

Table 2
Fractional atomic coordinates and isotropic thermal parameters (with e.s.d.s in parentheses) for [Au(2-MBPA)(2-pymS)] (2)

Atom [a]	*x*	*y*	*z*	B_{eq} [b]
Au	0.23364(3)	0.41835(3)	0.11265(2)	2.71(1)
S	0.4599(3)	0.4129(2)	0.1390(2)	3.9(1)
P	0.0111(2)	0.4219(2)	0.0894(1)	2.2(1)
O(1)	0.0924(7)	0.4034(5)	0.2498(3)	3.1(3)
O(2)	−0.2559(7)	0.4598(4)	0.2406(3)	3.2(3)
O(4)	−0.0278(6)	0.6356(4)	0.1105(3)	2.2(2)
O(5)	−0.0066(8)	0.5436(4)	0.2797(3)	2.8(3)
O(6)	0.0906(8)	0.7391(5)	0.1776(3)	3.4(3)
N(1)	0.570(1)	0.3046(6)	0.2278(5)	3.6(4)
N(2)	0.364(1)	0.2496(7)	0.1806(4)	4.1(4)
C(1)	−0.028(1)	0.4470(6)	0.2691(5)	2.5(4)
C(2)	−0.132(1)	0.4309(6)	0.2152(5)	2.4(4)
C(3)	−0.104(1)	0.4812(6)	0.1486(4)	2.2(4)
C(4)	−0.0707(8)	0.5801(7)	0.1666(4)	2.3(4)
C(5)	0.035(1)	0.5900(7)	0.2209(5)	2.9(4)
C(6)	0.057(1)	0.6908(7)	0.2376(5)	2.8(5)
C(7)	−0.012(1)	0.7302(6)	0.1299(4)	2.6(4)
C(8)	0.203(1)	0.4191(8)	0.2951(5)	4.4(5)
C(11)	0.025(1)	0.7860(7)	0.0693(5)	2.7(4)
C(12)	0.157(1)	0.7944(8)	0.0487(6)	4.0(5)
C(13)	0.190(1)	0.8468(9)	−0.0085(7)	5.2(7)
C(14)	0.087(1)	0.8873(9)	−0.0437(6)	4.9(6)
C(15)	−0.042(1)	0.879(1)	−0.0232(6)	5.2(7)
C(16)	−0.075(1)	0.8304(9)	0.0336(6)	4.7(6)
C(21)	−0.059(1)	0.3059(6)	0.0841(5)	2.7(4)
C(22)	0.027(1)	0.2320(8)	0.0745(6)	4.0(6)
C(23)	−0.024(1)	0.1410(7)	0.0671(7)	4.6(6)
C(24)	−0.158(1)	0.1276(8)	0.0676(7)	5.0(7)
C(25)	−0.248(1)	0.1995(9)	0.0786(6)	4.9(6)
C(26)	−0.198(1)	0.2909(7)	0.0867(5)	3.2(5)
C(31)	−0.024(1)	0.4736(6)	0.0081(5)	2.4(4)
C(32)	0.061(1)	0.5439(8)	−0.0133(5)	3.5(5)
C(33)	0.039(1)	0.586(1)	−0.0755(5)	4.6(6)
C(34)	−0.068(1)	0.558(1)	−0.1140(5)	5.0(6)
C(35)	−0.149(1)	0.489(1)	−0.0942(5)	5.3(7)
C(36)	−0.128(1)	0.4448(8)	−0.0327(6)	4.2(6)
C(41)	0.463(1)	0.3118(7)	0.1880(5)	2.9(4)
C(43)	0.577(1)	0.228(1)	0.2648(7)	4.9(7)
C(44)	0.481(2)	0.1593(9)	0.2629(7)	5.3(8)
C(45)	0.376(1)	0.1746(8)	0.2199(7)	4.5(6)

[a] Atoms are labeled in agreement with Fig. 3.
[b] $B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* b_j^* a_i a_j$.

Table 3
Selected atomic distances (Å) and bond angles (deg) (with e.s.d.s in parentheses) for [Au(3-MBPA)(2-pymS)] (2)

Au–P	2.256(3)	Au–S	2.306(3)
S–C(41)	1.76(1)	P–C(21)	1.82(1)
P–C(31)	1.83(1)	P–C(3)	1.86(1)
O(5)–C(5)	1.42(1)	O(5)–C(1)	1.42(1)
O(6)–C(7)	1.40(1)	O(6)–C(6)	1.43(1)
O(4)–C(7)	1.43(1)	O(4)–C(4)	1.44(1)
O(1)–C(1)	1.40(1)	O(1)–C(8)	1.44(1)
O(2)–C(2)	1.39(1)	N(1)–C(41)	1.33(1)
N(1)–C(43)	1.33(1)	N(2)–C(41)	1.34(1)
N(2)–C(45)	1.34(1)	C(1)–C(2)	1.51(1)
C(2)–C(3)	1.54(1)	C(3)–C(4)	1.51(1)
C(4)–C(5)	1.51(1)	C(5)–C(6)	1.51(1)
C(7)–C(11)	1.50(1)	Au–N(1)	4.373(9)
Au–N(2)	3.074(9)	Au–Au	8.2797(5) [a]
P–Au–S	178.5(1)	C(41)–S–Au	100.1(4)
C(21)–P–C(31)	104.5(4)	C(21)–P–C(3)	103.0(4)
C(21)–P–Au	111.5(3)	C(31)–P–C(3)	105.4(4)
C(31)–P–Au	112.3(3)	C(3)–P–Au	118.8(3)
C(5)–O(5)–C(1)	112.4(7)	C(7)–O(6)–C(6)	111.0(8)
C(7)–O(4)–C(4)	110.5(7)	C(1)–O(1)–C(8)	113.7(8)
C(41)–N(1)–C(43)	116(1)	C(41)–N(2)–C(45)	114(1)
O(1)–C(1)–O(5)	110.8(8)	O(1)–C(1)–C(2)	108.3(7)
O(5)–C(1)–C(2)	110.9(8)	O(2)–C(2)–C(1)	107.2(8)
O(2)–C(2)–C(3)	109.4(7)	C(1)–C(2)–C(3)	115.1(8)
C(4)–C(3)–C(2)	106.1(7)	C(4)–C(3)–P	116.8(7)
C(2)–C(3)–P	116.5(6)	O(4)–C(4)–C(3)	113.7(7)
O(4)–C(4)–C(5)	107.7(7)	C(3)–C(4)–C(5)	114.4(8)
O(5)–C(5)–C(6)	108.2(8)	O(5)–C(5)–C(4)	110.7(8)
C(6)–C(5)–C(4)	110.5(9)	O(6)–C(6)–C(5)	108.5(8)
O(6)–C(7)–O(4)	110.6(8)	O(6)–C(7)–C(11)	109.1(8)
O(4)–C(7)–C(11)	108.5(7)	C(22)–C(21)–P	118.8(8)
C(26)–C(21)–P	121.3(8)	C(36)–C(31)–P	123.3(8)
C(32)–C(31)–P	117.2(8)	N(1)–C(41)–N(2)	127.0(10)
N(1)–C(41)–S	114.6(8)	N(2)–C(41)–S	118.6(8)
N(1)–C(43)–C(44)	123.0(10)	C(45)–C(44)–C(43)	115.0(10)
N(2)–C(45)–C(44)	125.0(10)		

[a] Symmetry operation: $-x, 3/2+y, 5/2-z$.

2.2. Crystallography

X-ray diffraction studies were performed at room temperature on an Enraf–Nonius CAD-4 diffractometer for [Au(3-MBPA)(2-pymS)] **2**, using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The data

sets were corrected for Lorentz and polarization effects and for absorption employing an analytical procedure; crystal data and experimental conditions are compiled in Table 1.

The structure was solved by the Patterson method. Fourier-difference maps enabled all the non-hydrogen atoms to be located, which were refined with anisotropic thermal parameters by a full-matrix least squares procedure based on F. The positions of all the hydrogen atoms except for that of hydroxy groups were generated geometrically (C–H bond fixed at 0.96 Å), being accompanied by respective isotropic thermal parameters assigned and allowed to ride on their respective parent C atoms, while the hydrogen atoms of the hydroxy groups were located by the method of electron-difference, but all of them were not refined. Final refinement details are also given in Table 1. Fractional atomic coordinates are listed in Table 2 and selected interatomic parameters in Table 3. All calculations were performed on a MICRO-VAX 3100 computer using the Rigaku/MSC TEXSAN V2.1 program package [22].

Tables of hydrogen atom coordinates, anisotropic thermal parameters, torsion angles and complete lists of bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.

3. Results and discussion

3.1. Molecular vibration spectra

The compounds [Au(n-MBPA)Cl] ($n = 2,3$) react readily with 2-pymSH or 2-pymmSH in basic solution at room temperature to form the complexes [Au(n-MBPA)L] [**1**, $n = 2$, L = 2-pymS; **2**, $n = 3$, L = 2-pymS; **3**, $n = 2$, L = 2-pymmS; **4**, $n = 3$, L = 2-pymmS] in high yields. Although the IR stretching frequencies attributed to ν(P–C) cannot be assigned owing to overlapping of the ring vibration of the thiolate anion, the absorption for ν(Au–P) stretching mode in the range of 404–393 cm^{-1} for **1–4** are assignable and comparable to those reported for the compounds [Au(n-MBPA)X] (395–368 cm^{-1}, $n = 2$, 3) [19], [{Au(3-MBPA)}$_3$S]Cl [384 cm^{-1} (IR), 390 cm^{-1} (RR)] [23], and [Au(PR_3)X] (361–381 cm^{-1}, X = Cl, Br, SCN) [24]. The band at ca. 3260 cm^{-1} [ν(N–H)] for 2-pymSH and 2-pymmSH

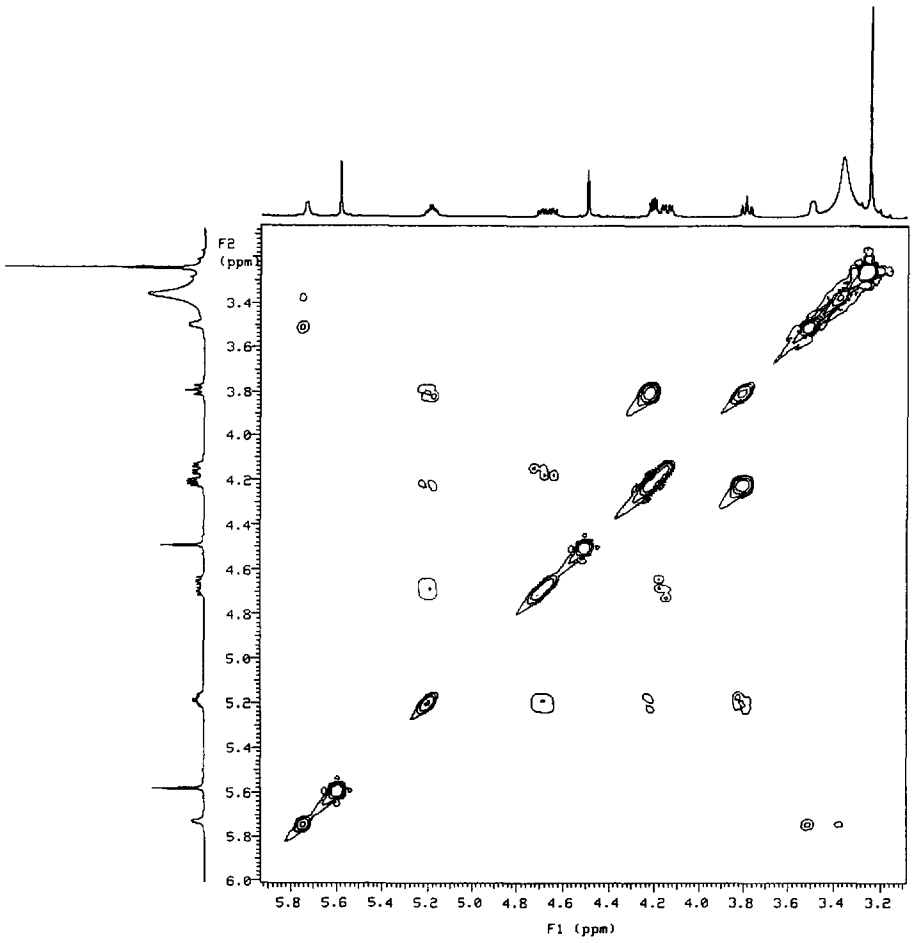

Fig. 1. Partial ^{1}H–^{1}H COSY spectrum of [Au(3-MBPA)(2-pymS)] (**2**).

disappeared in the complexes **1–4**, suggesting deprotonation of the thione. Since gold(I) has greater affinity for S than for N donor, the formation of Au–S bond in the complexes is expected, although the deprotonated ligand can coordinate to Au(I) either through the N or the S atom [25]. This is supported by the presence of new bands in the range of 326–315 cm^{-1} assigned to ν(Au–S) for **1–4**. The assignments are reasonable in view of the reported ν(Au–S) in 303–291 cm^{-1} for [Au(PR_3)(SCN)] [24], 314 cm^{-1} for [{Au(3-MBPA)}$_3$S]Cl [23], and 365 cm^{-1} for [Au(PPh_3)($C7H_7N_4O_2S$)] [26], even though the last one shows somewhat high frequency. The intensities of the ν(Au–P) and ν(Au–S) for **1–4** are weak in both IR and RR spectra, reflecting the low symmetry of the molecule.

3.2. NMR spectra

The integrations for ^{1}H NMR spectra are consistent with the formulations of the complexes as [Au(*n*-MBPA)L] (n = 2, 3, L = 2-pymS, 2-pymmS). Even at 500 MHz, the ^{1}H NMR spectra cannot be analyzed easily, mainly owing to long-range virtual coupling [27]. Therefore the ^{1}H–^{1}H COSY (Fig. 1 for **2**) and ^{1}H–^{13}C HMQC (Fig. 2 for **2**) techniques were applied to solve this difficulty. For **2**, the signals at 4.21 and 3.79 ppm correlating to 69.1 ppm in the ^{1}H–^{13}C HMQC spectrum (Fig. 2), indicating a CH_2 group, are assigned to H(6*e*) and H(6*a*) respectively. In the ^{1}H–^{1}H COSY spectrum (Fig. 1), the signal at 5.19 ppm is assigned to H(5) [C(5) at 61.1 ppm], which is correlated to both H(6*e*) and H(6*a*) and H(4) at 4.67 ppm (C(4) at 75.1 ppm). The signal at 4.15 ppm correlated to H(4) is then assigned to H(3) [the signal of C(3) is immersed in that of DMSO]. The correlations of H(3)–H(2) and H(2)–H(1) are not observed, implying that the torsion angles of H(3)–C(3)–C(2)–H(2) and H(2)–C(2)–C(1)–H(1) are close to 90° in the DMSO solution. In comparison with the spectra of the free ligand 3-MBPA and the complex [Au(3-MBPA)Cl] [19], the signals at 4.49 ppm and 3.49 ppm are assigned to H(1) and H(2) respectively, and C(1) and C(2) at 99.8 ppm and 68.0 ppm respectively. The ^{1}H and ^{13}C NMR spectra of **1**, **3**, and **4** can be assigned similarly.

On replacing Cl^- by 2-pymS or 2-pymmS anion, the signals of the protons on the carbon atoms of the altropyranose rings linked directly to the phosphorus atom shift downfield: the resonance of H(2) shifts from

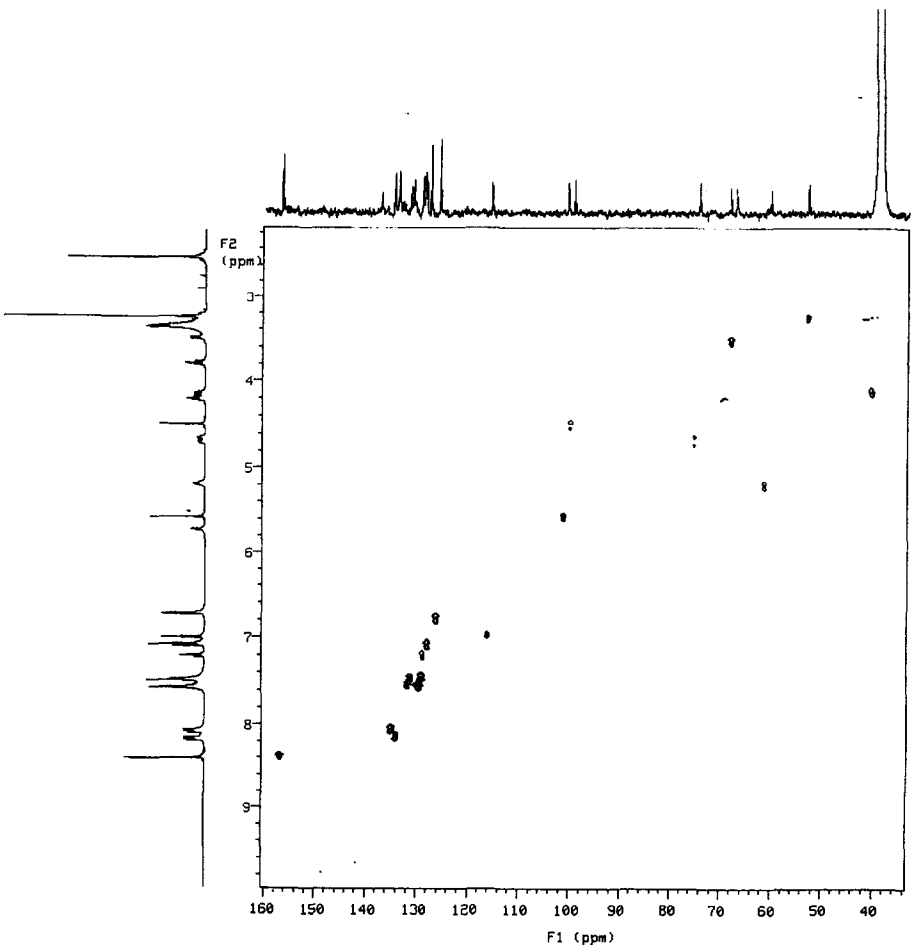

Fig. 2. Partial ^{1}H–^{13}C HMQC spectrum of [Au(3-MBPA)(2-pymS)] (**2**).

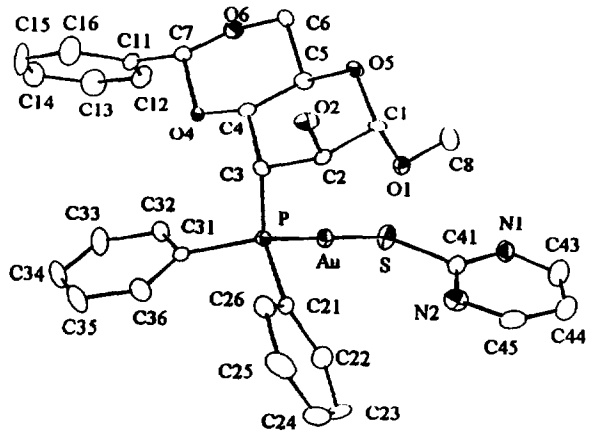

Fig. 3. Crystal structure of [Au(3-MBPA)(2-pymS)] showing the atom-labeling scheme with 20% probability.

3.60 ppm in [Au(2-MBPA)Cl] [19] to 3.96 ppm in [Au(2-MBPA)(2-pymS)] **1** and 3.95 ppm in [Au(2-MBPA)(2-pymmS)] **3**, and that of H(3) from 3.77 ppm in [Au(3-MBPA)Cl] [19] to 4.12 ppm in [Au(3-MBPA)(2-pymS)] **2** and 4.22 ppm in [Au(3-MBPA)(2-pymmS)] **4**. The position of the other protons of altropyranose rings change little. Similar shifting was also observed in the $^{31}P\{^{1}H\}$ NMR spectra, in which the single peaks at 36.8 ppm for **1** and 37.4 ppm for **3** shift downfield by 6.5 ppm and 7.1 ppm respectively, in comparison with that of the starting material [Au(2-MBPA)Cl] (30.3 ppm) [19]. Similar comparison to [Au(3-MBPA)Cl] (28.3 ppm) [19] gives that the signals at 34.1 ppm for **2** and 34.5 ppm for **4** shift downfield by 5.8 ppm and 6.2 ppm respectively. These results are consistent with the fact that the gold atom perturbs locally the electron distribution of the alkyl protons [27]. Noteworthy is the equivalence of the H(43) and H(45) of 2-pymS ligand and the equivalence of protons of two CH_3 groups of 2-pymmS in the spectra of the respective complexes, suggesting the probability of free rotation about the C–S bond in solution in contrast to that found in the solid-state structure of **2** (see below).

3.3. Crystal and molecular structure

The molecular structure of [Au(3-MBPA)(2-pymS)] **2** is illustrated in Fig. 3. The Au atom in [Au(3-MBPA)(2-pymS)] **2** possesses a linear geometry with the P–Au–S angle of 178.5(2)°, which is in the range previously observed for similar compounds [170.1(2)–179.6(1)°] [4,26]. The angle in **2** is just smaller than those in $[\{Au(3\text{-}MBPA)\}_3S]Cl$ [179.6(1)°] [24] and in $[Au(PPh_3)(C_7H_7N_4O_2S)]$ (178.6(2)°) [26], while larger than those in the closely related complexes $[Au(PPh_3)(2\text{-}pymS)]$ [(**5**), 174.7(1)°] [4] and [Au(3-MBPA)(2-pyS)] [177.6(1)°, 2-pySH = pyridine-2-thione] [19]. As can be seen from Fig. 3, the 2-pymS anion is orientated in such a way so as to place the N(2) atom in the close proximity of the Au atom. The Au · · · N(2) separation of 3.074(9) Å being less than the 3.25 Å of the sum of the van der Waals radii for the two atoms [28], indicates that there is interaction between them. However, this separation is larger than that in $[Au(PPh_3)(2\text{-}pymS)]$ [Au · · · N, 2.951(8) Å] [4], which may be responsible for the lesser deviation in the P–Au–S angle from that in the ideal linear geometry about the Au atom. There are no significant intermolecular contacts in the lattice of **2** and the closest Au · · · Au′ separation is 8.2797(5) Å.

The Au–P [2.306(3) Å] and Au–S [2.256(3) Å] distances for **2** lie in the range of 2.248(2)–2.292(2) Å and 2.291(6)–2.339(3) Å respectively, in the compounds containing the P–Au–S linkage [4,26]. The trans-influence is observed by the Au–P distance in **2** being slightly longer than that in the closely related complex $[Au(PPh_3)(2\text{-}pymS)]$ [(**5**), 2.253(2) Å] [4], and the Au–S distance is shorter than that in **5** [2.310(3) Å]. This fact indicates that the donor ability of 3-MBPA toward gold(I) is slightly less than that of PPh_3 [19].

The C–S distance of 1.76(1) Å in **2** is comparable to that of 1.748(9) Å for **5** and consistent with the presence of a monodentate thiolate ligand, although there is the Au · · · N(2) interaction in **2**. The 2-pymS anion in **2** is planar with the deviation of ±0.02(1) Å from the least-squares plane and the Au atom lies out of this plane by −0.848(6) Å leading to a torsion angle Au–S–C(41)–N(2) of 22.0(9)°, being larger than that in **5** (3.5°) [4].

As can be seen from Fig. 3, the pyranose and 4,6-*O*-benzylidene rings adopt a distorted chair conformation: the torsion angles of the pyranose ring range from 60(1)° of C(1)–O(5)–C(5)–C(4) to −48(1)° of C(1)–

Table 4
Antitumor activity against P388 leukemia of the gold(I) complexes with sugar-substructure phosphine ligands

Complex	10^{-5} g dm^{-3}	10^{-6} g dm^{-3}	10^{-7} g dm^{-3}
1	97.0	97.0	17.9
2	98.5	97.8	14.2
3	97.0	97.8	9.0
4	97.0	97.0	17.9
5 [a]	98.5	97.0	17.2
6 [a]	98.5	98.5	8.9
7 [a]	97.0	97.0	9.7
8 [a]	98.5	55.2	10.0
9 [a]	98.5	98.5	86.0
10 [a]	97.0	97.0	5.2
11 [a]	94.9	96.0	27.9
12 [a]	91.0	98.5	24.3

[a] These complexes were synthesized according to Ref. [19]: **5**, [Au(2-MBPA)Cl]; **6**, [Au(3-MBPA)Cl]; **7**, [Au(2-MBPA)(2-pyS)] (2-pySH = 2-mercaptopyridine); **8**, [Au(3-MBPA)(2-pyS)] (2-pySH = 2-mercaptopyridine); **9**, [Au(2-MBPA)(2-bimS)] (2-bimSH = 2-mercaptobenzimidazole); **10**, [Au(3-MBPA)(2-bimS)] (2-bimSH = 2-mercaptobenzimidazole); **11**, [Au(2-MBPA)(2-mpoS)] (2-mpoSH = 2-mercaptopyridine-1-oxy); **12**, [Au(3-MBPA)(2-mpoS)] (2-mpoSH = 2-mercaptopyridine-1-oxy).

C(2)–C(3)–C(4) [average ±54(1)°], and those of the 4,6-*O*-benzylidene ring from 64(1)° of O(6)–C(7)–O(4)–C(4) to 55(1)° of O(4)–C(4)–C(5)–C(6) [average ±59(1)°]. The substituents PPh_2, OH, and OMe in **2** are in pseudo-axial positions, as suggested by the torsion angles P–C(3)–C(2)–O(2) [−155.2(6)°] and O(2)–C(2)–C(1)–O(1) [169.5(7)°], confirming the observation of the aforementioned ^1H–^1H COSY spectra, of which the torsion angles of H(3)–C(3)–C(2)–H(2) and H(2)–C(2)–C(1)–H(1) for **1** and **2** are close to 90° in DMSO solutions.

3.4. Antitumor activity

Twelve gold(I) complexes containing the chiral phosphines with sugar substructure are effective in inhibiting the increase in P388 leukemia, in which the activity of complex **9** is very high even at 10^{-7} mol dm^{-3} (Table 4). Further studies on the antitumor properties of these gold(I) complexes are in press.

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References

[1] D.M.P. Mingos, J. Yau, S. Menzer and D.J. Williams, *J. Chem. Soc. Dalton Trans.*, (1995) 319.
[2] J. Yau, D.M.P. Mingos, S. Menzer and D.J. Williams, *J. Chem. Soc. Dalton Trans.*, (1995) 2575.
[3] S.J.B. Price, M.J. Dimartino, D.T. Hill, R. Kuroda, M.A. Mazid and P.J. Sadler, *Inorg. Chem., 24* (1985) 3425.
[4] P.D. Cookson and E.R.T. Tiekink, *J. Chem. Soc. Dalton Trans.*, (1993) 259.
[5] (a) J. Vicente, M.-T. Chicote, P. Gonzalez-Herrero and P.G. Jones, *J. Chem. Soc. Dalton Trans.*, (1994) 3183. (b) F. Bonati, A. Burini, B.R. Pietroni, E. Giorgini and B. Bovio, *J. Organomet. Chem., 344* (1988) 119.
[6] S.J. Berners-Prince, P.S. Jarrett and P.J. Sadler, *Inorg. Chem., 26* (1987) 3074.
[7] J.M. Forward, D. Bohmann, J.P. Fackler, Jr. and R.J. Staples, *Inorg. Chem., 34* (1995) 6330.
[8] W.B. Jones, J. Yuan, R. Narayanaswamy, M.A. Young, R.C. Elder, A.E. Bruce and M.R.M. Bruce, *Inorg. Chem., 34* (1995) 1996.
[9] Z. Assefa, B.G. McBurnett, R.J. Staples and J.P. Fackler, Jr., *Inorg. Chem., 34* (1995) 4965.
[10] Z. Assefa, B.G. McBurnett, R.J. Staples, J.P. Fackler, Jr., B. Assmann, K. Angermaier and H. Schmidbaur, *Inorg. Chem., 34* (1995) 75.
[11] D.M. Roundhill, *Photochemistry and Photophysics of Metal Complexes*, Plenum, New York, 1994.
[12] P. Pyykko, J. Li and N. Runeberg, *Chem. Phys. Lett., 218* (1994) 133.
[13] A.E. Finkelstein, D.T. Walz and V. Batista, *Ann. Rheum. Dis., 35* (1976) 251.
[14] F.E. Berglof, K. Berglof and D.T. Walz, *J. Rheumatol., 5* (1978) 68.
[15] A.E. Finkelstein, F.R. Roisman, V. Batista, F.G. de Nudelman, E.H. Titto, M. Misraji and D.T. Walz, *J. Rheumatol., 7* (1980) 160.
[16] T.M. Simon, D.H. Kunishima, D.H. Vibert and A. Lorber, *Cancer Res., 41* (1981) 94.
[17] C.K. Mirabelli, R.K. Johnson, C.M. Sung, L. Faucette, K. Muirhead and S.T. Crooke, *Cancer Res., 45* (1985) 32.
[18] G.F. Rush, D.W. Alberts, D. Meunier, K. Leffler and P.F. Smith, *Toxicologist, 7* (1987) 59.
[19] (a) J.C. Shi, X.Y. Huang, D.X. Wu, Q.T. Liu and B.S. Kang, *Inorg. Chem., 35* (1996) 2742. (b) J.C. Shi, T.B. Wen, G.T. Lu, D.X. Wu, Q.T. Liu and B.S. Kang, *J. Coord. Chem.*, in press.
[20] J.C. Shi, M.C. Hong, D.X. Wu, Q.T. Liu and B.S. Kang, *Chem. Lett.*, (1995) 685.
[21] J.C. Shi, D.X. Wu, G.T. Lu, M.C. Hong, D.X. Wu, Q.T. Liu, B.S. Kang and H.Q. Wang, *Chin. J. Chem., 14* (1996) 454.
[22] Molecular Structure Corporation, *TEXSAN, TEXRAY Structure Analysis Package, Revised*, 1987 (MSC, 3200A Research Forest Drive, The Woodlands, TX 77381, USA).
[23] J.C. Shi, B.S. Kang and T.C.W. Mak, *J. Chem. Soc. Dalton Trans.*, in press.
[24] C.A. McAuliffe, R.V. Parish and P.D. Randall, *J. Chem. Soc. Dalton Trans.*, (1979) 1730.
[25] T.S. Lobana, P.K. Bhatia and E.R.T. Tiekink, *J. Chem. Soc. Dalton Trans.*, (1989) 749 and references cited therein.
[26] E. Colacio, A. Romerosa, J. Ruiz, P. Román, J.M. Gitiérrez-Zorrilla, A. Vegas and M. Martinez-Ripoll, *Inorg. Chem., 30* (1991) 3743 and references cited therein.
[27] M.T. Razi, P.J. Sadler, D.T. Hill and B.M. Sutton, *J. Chem. Soc. Dalton Trans.*, (1983) 1331.
[28] J.E. Huheey, *Inorganic Chemistry. Principles of Structure and Reactivity*, Harper and Row, New York, 3rd edn., 1983.