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Chemistry in Environmentally Benign Media. 7.[1] Chelating Hydroxymethyl-Functionalized Bisphosphines as Building Blocks to Water-Soluble and *in-Vitro*-Stable Gold(I) Complexes. Synthesis, Characterization, and X-ray Crystal Structures of $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$ and $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl_2$

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The reactions of water-soluble bisphosphines $(HOH_2C)_2PC_6H_4P(CH_2OH)_2$ (**1**) and $(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2$ (**2**) with $NaAuCl_4$, in aqueous media, or $AuClPPh_3$, in biphasic media (aqueous/organic), produced the water/alcoholic-soluble Au(I) complexes $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$ (**3**), $[Au\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl$ (**4**), and $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl_2$ (**5**) in near quantitative yields. Stability and cysteine-challenge studies of **3** indicate the kinetic inertness of these new complexes. Complex **5** is luminescent in the solid state at room temperature. When excited at 280 nm in non-degassed water at room temperature, the emission spectrum shows a high-energy band at 310 nm and a low-energy band at 560 nm. The large Stokes shift for the low-energy band implies that the emission is phosphorescence. The X-ray structures of **3** and **5**, reported in this paper, confirm the gold(I) structures of this new generation of water-soluble transition metal complexes. All compounds were characterized by ^{31}P and ^{1}H NMR spectroscopy and mass spectroscopy. X-ray data for **3**: monoclinic, $P2_1/m$, $a = 9.8715(5)$ Å, $b = 9.9465(5)$ Å, $c = 14.5621(8)$ Å, $\beta = 106.5930(10)°$, $Z = 2$, $R = 0.032$ ($R_w = 0.050$). X-ray data for **5**: monoclinic, $C2/c$, $a = 29.7128(14)$ Å, $b = 16.7062(8)$ Å, $c = 22.3762\ (11)$ Å, $\beta = 117.6970(10)°$, $Z = 16$, $R = 0.051$ ($R_w = 0.072$).

Introduction

Considerable research has been focused on the development of water-soluble gold-containing compounds because of their potential in chemotherapeutic applications. For example, Auranofin [(2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranosato-*S*)-(triethylphosphine)gold(I)] has been shown to be effective for the treatment of rheumatoid arthritis.[2,3] Studies demonstrate that this agent is superior to the traditional chrysotherapeutic drugs. Auranofin and related gold(I) compounds have been found to be active against interperitoneal P388 leukemia and are also cytotoxic to specific tumor cells.[4,5]

Compounds of gold that contain the gold-198/199 isotope are important in the development of radiopharmaceuticals for use in nuclear medicine. Gold-199 has a half-life of 3.2 days and decays with a *β* emission of 0.46 MeV and a *γ* emission of 0.158 MeV. Labeling of specific biomolecular vectors (e.g. peptides or proteins) with gold-199 has been implicated as an important basis in the design of tumor-specific radiopharmaceuticals for use in the diagnosis and therapy of human cancer.[6,7]

Despite significant medical applications of gold-containing compounds, the development of specific ligand systems to produce water-soluble, kinetically inert, and *in-vivo*-stable complexes of gold with optimum toxicities is still in its infancy.[8,9] In this context, we decided to explore the utility of 1,2-bis(bis(hydroxymethyl)phosphino)benzene (HMPB, **1**) and 1,2-bis(bis(hydroxymethyl)phosphino)ethane (HMPE, **2**) as complexing agents toward gold precursors. Our reasoning is based on recent studies from our laboratory which demonstrated that hydroxymethyl phosphines **1** and **2** produce water-soluble and kinetically inert complexes with several transition metal precursors that include rhenium, palladium, and platinum.[10,11] Our studies have also demonstrated that this new generation of phosphines **1** and **2** produce complexes with technetium-99m that are highly stable *in vivo* and clear, primarily, via the kidneys as undecomposed complexes.[12,13] As part of our ongoing efforts aimed at the design and development of pharmaceuticals and radiophamaceuticals, we, herein, report the formation of novel water-soluble mono- and dinuclear gold(I) complexes derived from the (hydroxymethyl)phosphine frameworks **1** and **2**. X-ray

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crystallographic investigations to confirm the molecular constitutions of the mononuclear complex $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$ (**3**) and the dinuclear complex $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl_2$ (**5**) are also described.

Experimental Section

All reactions were carried out under purified nitrogen by standard Schlenk techniques. Solvents were purified and dried by standard methods and distilled under nitrogen prior to use. $NaAuCl_4$ and $AuClPPh_3$ were purchased from Alfa and Strem Chemical Co., respectively, and used without further purification. Cysteine was purchased from Sigma Chemical Co. and used without further purification. The syntheses of $(HOH_2C)_2PC_6H_4P(CH_2OH)_2$ (**1**) and $(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2$ (**2**) have been previously reported.[11] Nuclear magnetic resonance spectra were recorded on a Bruker ARX-300 spectrometer using D_2O or CD_3OD as the solvent. The ^1H NMR chemical shifts are reported in parts per million, downfield from an external standard of $SiMe_4$. The ^{31}P NMR (121.5 MHz) spectra were recorded with 85% H_3PO_4 as an external standard, and positive chemical shifts lie downfield of the standard. UV−vis spectra were measured at 298 K with a Perkin-Elmer Lambda 3 spectrophotometer. Excitation and Emission spectra were measured at 298 K with a 650-40 Perkin-Elmer Spectrofluorimeter. Mass spectra were performed by Washington University, St. Louis, MO.

Synthesis of $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$ (3). An aqueous solution (5 mL) of $NaAuCl_4$ (0.5 mmol) was added dropwise to $(HOH_2C)_2PC_6H_4P(CH_2OH)_2$ (2.5 mmol) also in water (5 mL) at 25 °C with constant stirring. The reaction mixture continued to stir for 2 h, and the product was filtered off as a white solid in 90% yield. HRFAB/MS calcd for $C_{20}H_{32}O_8P_4Au$: 721.0713. Found $[M^+]$: *m/z* 721.0699. Mp: 163−165 °C (dec). ^1H NMR (CD_3OD): δ 4.40, 4.23 (AB quartet, 16 H, $^2J_{HH} = 12.92$ Hz, $P(CH_2OH)_2$), 7.64 (m, 4 H, C_6H_4), 8.12 (m, 4 H, C_6H_4). ^{13}C NMR (CD_3OD): δ 62.4 (m, $P(CH_2OH)_2$), 132.4 (s, C_6H_4), 134.1 (s, C_6H_4), 141.4 (m, C_6H_4). ^{31}P NMR (CD_3OD): δ 12.2 (s).

Synthesis of $[Au\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl$ (4). An aqueous solution (5 mL) of $NaAuCl_4$ (0.5 mmol) was added dropwise to $(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2$ (2.5 mmol) also in water (5 mL) at 25 °C with constant stirring. The reaction mixture continued to stir for 2 h, and the sample was concentrated to 1 mL under reduced atmosphere and loaded onto a preconditioned Waters Sep-Pak Vac column (C18, 10 g, 35 mL). The column was eluted with water, followed by methanol. Collection of the methanol fractions and removal of the solvent afforded the desired product in 85% yield. HRFAB/MS calcd for $C_{12}H_{32}O_8P_4Au$: 625.0713. Found $[M^+]$: *m/z* 625.0720. ^1H NMR (D_2O): δ 1.84 (s, 4 H, CH_2CH_2), 4.00, 3.56 (AB quartet, 8 H, $^2J_{HH} = 13.53$ Hz, $P(CH_2OH)_2$). ^{13}C NMR (D_2O): δ 19.0 (m, CH_2CH_2), 58.8 (m, $P(CH_2OH)_2$). ^{31}P NMR (D_2O): δ 18.6 (s).

Synthesis of $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl_2$ (5). $AuClPPh_3$ (4.0 mmol) in dichloromethane (5 mL) was added to $(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2$ (2.0 mmol) in water (5 mL) at 25 °C under constant stirring. The reaction mixture continued to stir for 3 h, upon which the aqueous layer was separated and concentrated under reduced pressure. The solid exhibits a bright greenish-yellow luminescence in the solid state at room temperature under a hand-held UV lamp. HRFAB/MS calcd for $C_{12}H_{32}O_8P_4Au_2Cl$: 857.0066. Found $[M^+]$: *m/z* 857.0062. Mp: 153−156 °C. ^1H (D_2O): δ 2.48 (br s, 8H, PCH_2CH_2P), 4.40 (s, 16 H, PCH_2OH). ^{13}C NMR (D_2O): δ 14.3 (br s, PCH_2CH_2P), 56.4 (br s, PCH_2OH). ^{31}P NMR (D_2O): δ 36.9 (s).

Cysteine-Challenge Study for $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$. Cysteine (2.2 mmol) in a water/methanol mixture (75/25, 5 mL) was added to $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$ (0.2 mmol) also in a water/methanol mixture (75/25, 5 mL) at 25 °C under constant stirring. The ^{31}P NMR spectrum of the mixture was recorded at various time intervals.

X-ray Data Collection and Processing. The crystal data and details of data collection for complexes **3** and **5** are given in Table 1. Clear colorless crystals of **3** suitable for X-ray diffraction were obtained from slow evaporation of a methanol solution at room temperature. Clear colorless crystals of **5** suitable for X-ray diffraction were obtained from methanol/diethyl ether at solution −20 °C. Intensity data were collected on a Siemens SMART CCD system using the ω scan mode. Data were corrected for absorption using the program SADABS, which is based on the method of Blessing.[14] Crystal decay was less than 1% and a correction was deemed unnecessary. The programs used for the crystallographic computations are reported in ref 15. Atomic coordinates and their equivalent isotropic displacement coefficients for both **3** and **5** are listed in Tables 2 and 3, respectively.

Table 1. Crystal Data for Complexes **3** and **5**

formula	$C_{20}H_{32}ClO_8P_4Au{\cdot}H_2O$	$C_{12}H_{32}Cl_2O_8P_4Au_2$
space group	$P2_1/m$	$C2/c$
fw	774.80	893.12
a, Å	9.8715(5)	29.7128(14)
b, Å	9.9465(5)	16.7062(8)
c, Å	14.5621(8)	22.3762(11)
α, deg	90.0	90.0
β, deg	106.5930(10)	117.6970(10)
γ, deg	90.0	90.0
T, K	295(2)	295(2)
λ, Å	0.709 30	0.709 30
Z	2	16
$F(000)$	764	6720
V, Å^3	1370.27(12)	9834.6(8)
ρ_{calc}, g/cm^3	1.878	2.413
ρ_{obsd}, g/cm^3	not measured	not measured
μ, mm^{-1}	5.72	12.39
R_1, R_w[a]	0.032, 0.050	0.051,0.072

[a] $R_1 = \sum(||F_o| - |F_c||)/\sum(|F_o|)$; $R_w = [[\sum w(|F_o| - |F_c|)^2)/\sum w(|F_o|)^2]]^{1/2}$.

Table 2. Atomic Parameters (x, y, z, and B_{eq}) for Complex **3**

	x	y	z	B_{eq}[a]
Au	0.79431(2)	$^1/_4$	0.216145(15)	1.948(12)
P1	0.96181(12)	0.41306(11)	0.29552(8)	1.92(4)
P3	0.6876(2)	$^1/_4$	0.04946(12)	1.91(6)
P4	0.5614(2)	$^1/_4$	0.23235(12)	2.14(6)
O1	0.7980(4)	0.6148(4)	0.3193(3)	3.72(17)
O2	1.0777(5)	0.4527(5)	0.1528(3)	4.68(22)
O5	0.8560(5)	0.4120(5)	−0.0111(3)	4.93(22)
O7	0.5298(5)	0.5179(5)	0.2570(4)	4.25(21)
C1	1.1108(5)	0.3209(4)	0.3734(3)	1.98(16)
C6	1.3426(5)	0.3206(6)	0.4879(4)	2.98(21)
C5	1.288(5)	0.3894(5)	0.4317(4)	2.51(18)
C7	0.9114(6)	0.5360(5)	0.3758(4)	2.84(19)
C8	1.0456(6)	0.5242(6)	0.2267(4)	3.18(21)
C11	0.4971(7)	$^1/_4$	0.0307(5)	2.3(3)
C12	0.4417(7)	$^1/_4$	0.1104(5)	2.2(3)
C13	0.2955(8)	$^1/_4$	0.0940(6)	3.0(3)
C14	0.2045(8)	$^1/_4$	0.0002(7)	3.6(3)
C15	0.2607(9)	$^1/_4$	−0.0773(6)	3.5(3)
C16	0.4045(8)	$^1/_4$	−0.0631(5)	3.0(3)
C17	0.7120(6)	0.3945(6)	−0.0216(4)	3.71(24)
C19	0.4980(6)	0.3919(6)	0.2918(4)	3.16(22)
Cl	0.2514(3)	$^3/_4$	0.46163(23)	4.97(12)
OW	0.3780(9)	$^3/_4$	0.2856(7)	6.7(5)

[a] B_{eq} is the mean of the principal axes of the thermal ellipsoid.

Results and Discussion

Reactions of 1,2-Bis(bis(hydroxymethyl)phosphino)benzene (HMPB, 1) and 1,2-Bis(bis(hydroxymethyl)phosphino)ethane (HMPE, 2) with $NaAuCl_4$. Interaction of an aqueous solution of sodium tetrachloroaurate with 5 equiv of the bisphosphines **1** and **2** afforded the new gold(I) complexes $[Au\{(HOH_2C)_2PC_6H_4P(CH_2OH)_2\}_2]Cl$ (**3**) and $[Au\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl$ (**4**) (Scheme 1), respectively, in near quantitative yields. The use of excess ligand for these reactions becomes

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Table 3. Atomic Parameters (x, y, z, and B_{eq} for Complex **5**

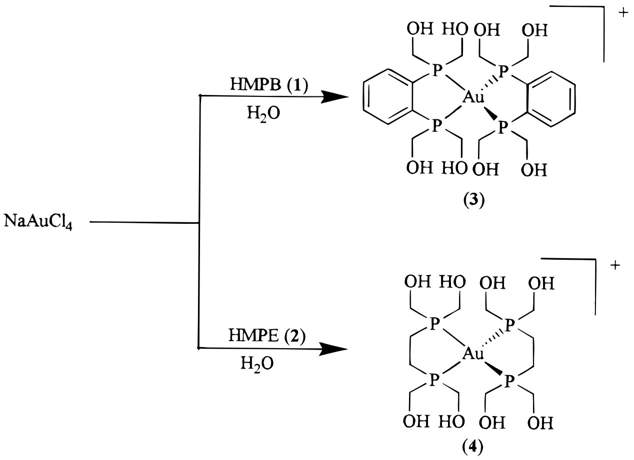
	x	y	z	B_{eq}[a]
Au1A	0.274541(21)	0.07932(4)	0.013204(25)	3.03(3)
Au2A	0.218081(20)	−0.07075(4)	−0.007032(25)	2.96(3)
P1A	0.33321(13)	0.03063(22)	0.11687(18)	3.27(17)
P2A	0.21544(14)	−0.05704(24)	0.09373(18)	3.51(19)
P3A	0.21208(14)	0.12732(22)	−0.08805(18)	3.35(18)
P4A	0.21649(14)	−0.08486(22)	−0.11098(17)	3.06(18)
O1A	0.3854(4)	−0.1028(6)	0.1782(5)	5.1(6)
O2A	0.4148(6)	0.0971(11)	0.1190(8)	10.9(12)
O3A	0.1340(6)	0.0290(12)	0.0408(9)	14.8(15)
O4A	0.1804(5)	−0.1285(8)	0.1739(6)	7.2(8)
O5A	0.1846(4)	0.2616(6)	−0.1660(6)	6.0(7)
O6A	0.1525(10)	0.1486(15)	−0.0318(12)	9.3(7)
O6′A	0.1319(14)	0.0560(22)	−0.0836(17)	8.7(10)
O7A	0.2745(4)	−0.0702(7)	−0.1747(6)	6.1(8)
O8A	0.2212(8)	−0.2475(13)	−0.1140(11)	5.1(5)
O8′A	0.1879(8)	−0.2404(13)	−0.1045(10)	4.6(4)
C1A	0.3112(5)	0.0227(9)	0.1803(7)	3.5(7)
C2A	0.2762(6)	−0.0516(10)	0.1704(7)	4.4(9)
C3A	0.3573(5)	−0.0685(8)	0.1124(7)	3.6(7)
C4A	0.3905(6)	0.0911(9)	0.1596(8)	4.3(8)
C5A	0.1814(6)	0.0330(12)	0.0969(8)	6.1(11)
C6A	0.1821(6)	−0.1397(11)	0.1093(9)	5.8(11)
C7A	0.2027(6)	0.0731(9)	−0.1652(6)	4.0(8)
C8A	0.1797(5)	−0.0097(9)	−0.1753(7)	3.9(8)
C9A	0.2243(7)	0.2293(10)	−0.1021(8)	5.3(11)
C10A	0.1475(7)	0.1296(11)	−0.0962(9)	6.1(12)
C11A	0.2792(6)	−0.0802(9)	−0.1086(8)	4.5(9)
C12A	0.1877(6)	−0.1833(9)	−0.1501(7)	4.7(9)
Au1B	0.034210(21)	−0.17910(4)	0.01176(3)	3.35(3)
Au2B	−0.024190(22)	−0.32903(4)	−0.01373(3)	3.27(3)
P1B	0.03661(15)	−0.16583(24)	0.11550(18)	3.53(19)
P2B	0.03329(15)	−0.38211(24)	0.08918(19)	3.85(21)
P3B	0.03626(14)	−0.19259(23)	−0.08964(18)	3.49(19)
P4B	−0.08272(13)	−0.28378(21)	−0.11917(17)	3.03(17)
O1B	−0.0234(6)	−0.1683(10)	0.1759(7)	9.8(12)
O2B	0.0486(12)	−0.0081(19)	0.1239(16)	9.5(9)
O2′B	0.0817(13)	−0.0873(20)	0.2346(16)	11.0(10)
O3B	0.0508(5)	−0.5130(8)	0.1671(6)	7.5(9)
O4B	0.0934(7)	−0.4538(11)	0.0454(8)	6.4(11)
O4′B	0.625(3)	0.088(4)	0.159(3)	14.4(22)
O5B	0.1218(9)	−0.2764(13)	−0.0460(11)	9.7(6)
O5′B	0.0493(16)	−0.349(3)	−0.0911(21)	6.9(11)
O6B	0.0758(5)	−0.1227(8)	−0.1630(6)	6.4(8)
O7B	−0.1456(4)	−0.1590(6)	−0.1816(5)	5.2(6)
O8B	−0.1449(6)	−0.4010(10)	−0.1243(9)	11.7(13)
C1B	0.0693(8)	−0.2456(10)	0.1781(7)	6.3(12)
C2B	0.0441(7)	−0.3242(10)	0.1644(7)	5.2(11)
C3B	−0.0275(7)	−0.1573(14)	0.1110(10)	7.2(13)
C4B	0.0714(7)	−0.0739(12)	0.1629(8)	5.7(11)
C5B	0.0142(6)	−0.4819(10)	0.1040(9)	5.6(10)
C6B	0.0981(6)	−0.3981(12)	0.0926(10)	6.4(11)
C7B	−0.0225(6)	−0.1897(8)	−0.1637(7)	3.9(8)
C8B	−0.0579(5)	−0.2639(9)	−0.1784(6)	3.8(8)
C9B	0.0681(7)	−0.2831(10)	−0.0989(8)	5.4(10)
C10B	0.0721(7)	−0.1146(11)	−0.1043(8)	5.7(10)
C11B	−0.1129(6)	−0.1914(9)	−0.1169(7)	4.3(8)
C12B	−0.1338(6)	−0.3558(9)	−0.1662(7)	4.6(9)
C11	0	0.9965(4)	$^1/_4$	7.9(6)
C12	0	0.4315(5)	$^1/_4$	6.4(4)
C13	0.25719(19)	0.2266(4)	0.24472(23)	7.0(3)
C14	0.1436(3)	−0.6914(4)	0.0051(3)	7.5(4)
C15	0.2006(4)	−0.2586(6)	0.0040(5)	8.3(6)
C16	0.0372(5)	0.0077(10)	0.0044(7)	8.7(4)
C17	0.3876(10)	0.0487(15)	−0.0008(12)	6.9(6)

[a] B_{eq} is the mean of the principal axes of the thermal ellipsoid.

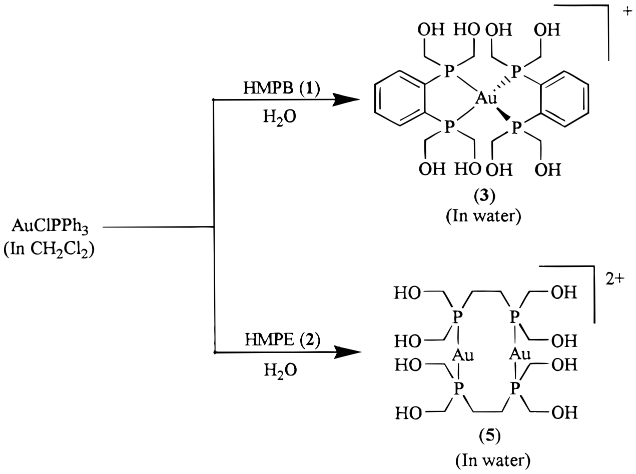
apparent as the phosphines reduce Au(III) in $NaAuCl_4$ to Au(I) in the corresponding complexes **3** and **4**.

The molecular constitutions of **3** and **4** were confirmed by fast atom bombardment mass spectroscopy ([M^+], m/z = 721.0699 for **3**; m/z = 625.0720 for **4**). The ^{31}P NMR spectra of **3** and **4** consisted of singlets at 12.2 and 18.6 ppm, respectively, indicating a pronounced downfield shift compared to the parent ligands **1** and **2** ($\Delta\delta$ = 43.4 for **3** and 43.7 for **4**).

Scheme 1



Scheme 2



It is interesting to note that in the ^1H NMR spectra of both **3** and **4**, the coupling of the phosphorus and the methylene protons (of $-CH_2OH$), across two bonds, is absent and that that the methylene protons resonate as AB quartets ($^2J_{HH}$ = 12.92 Hz for **3** and 13.53 Hz for **4**), suggesting the diastereotopic nature of these hydrogens. The final confirmation of the structure of **3** has come from X-ray crystallographic investigations of the single crystals, as outlined in the following sections.

Reactions of 1,2-Bis(bis(hydroxymethyl)phosphino)benzene (HMPB, 1) and 1,2-Bis(bis(hydroxymethyl)phosphino)ethane (HMPE, 2) with $AuClPPh_3$ under Aqueous−Organic Biphasic Media. 1,2-Bis(bis(hydroxymethyl)phosphino)benzene (**1**), in water, upon interaction with 1 equiv of $AuClPPh_3$, in dichloromethane, produced the cationic complex **3** in near quantitative yields (Scheme 2). The ^{31}P and ^1H NMR and mass spectrometric data were identical to the product obtained from the reaction of **1** with sodium tetrachloroaurate as described in Scheme 1. In sharp contrast, the reaction of **2** with $AuClPPh_3$, under biphasic conditions, produced a different product (Scheme 2) as compared to its reaction with sodium tetrachloroaurate (Scheme 1). The isolation of various products depending on whether one starts with a gold(III) or gold(I) precursor has been reported.[16] The mass spectrometric data of this new product ([M^+], m/z = 857.0066) indicated it to be a dinuclear gold(I) complex $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]^{2+}$ (**5**), as formulated in Scheme 2. The ^{31}P NMR spectrum of **5**, which consisted of a singlet at 36.9 ppm, indicates a pronounced downfield shift ($\Delta\delta$ = 62 ppm) compared to the mononuclear

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(16) Eggleston, D. S.; McArdle, J. V.; Zuber, G. E. *J. Chem. Soc., Dalton Trans.* **1987**, 677.

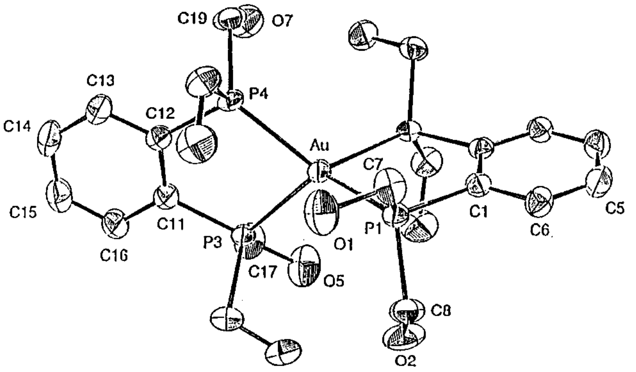

Figure 1. ORTEP diagram, of **3** with 50% probability ellipsoids.

Table 4. Selected Bond Distances (C) and Angles (deg) for **3**[a]

Au−P1	2.3683(11)	Au−P3	2.354(2)
Au−P1a	2.3683(11)	Au−P4	2.378(2)
P1−Au−P1a	86.44(4)	P1a−Au−P3	123.21(4)
P1−Au−P3	123.21(4)	P1a−Au−P4	102.78(4)
P1−Au−P4	120.78(4)	P3−Au−P4	86.66(6)

[a] a atom at *x*, 0.5 − *y*, *z*.

complexes **3** and **4**. The final confirmation of the molecular constitution of **5** was obtained from its X-ray crystal structure, as discussed in the following sections.

It is important to recognize that in the reaction of **1** (or **2**) with AuClPPh$_3$ under biphasic conditions (Scheme 2), typically 95−98% of the metal precursor from the dichloromethane phase was transferred into the phosphine-containing aqueous phase in approximately 30 min upon simply stirring the respective solutions. Separation and evaporation of the aqueous phases from the reactions produced the mononuclear gold(I) complex **3** and the dinuclear complex **5**, respectively.

X-ray Crystallographic Investigations of [Au{(HOH$_2$C)$_2$PC$_6$H$_4$P(CH$_2$OH)$_2$}$_2$]Cl (3) and [Au$_2${(HOH$_2$C)$_2$PCH$_2$CH$_2$P(CH$_2$OH)$_2$}$_2$]Cl$_2$ (5). The molecular structure of **3** was further confirmed by X-ray crystallography. An ORTEP diagram of the cationic molecule is shown in Figure 1, and selected bond distances and bond angles are listed in Table 4. The asymmetric unit consists of the complex cation [Au{(HOH$_2$C)$_2$PC$_6$H$_4$P(CH$_2$OH)$_2$}$_2$]$^+$, one noncoordinating chloride counterion, and a single water molecule. The gold atom is coordinated by four phosphorus atoms in a distorted tetrahedral arrangement, where the chelate ring angles are 86.4° and 86.7° for P1−Au−P1a and P3−Au−P4, respectively. These angles are smaller than ideal angles and are compensated by larger nonchelate angles P1−Au−P3, P1−Au−P4, P1a−Au−P3, and P1a−Au−P4 with an average of 122.0°. The Au−P distances range from 2.354 to 2.368 Å with an average of 2.367 Å, consistent with the previously reported values for Au−P bonds.[17,18]

Tetrahedral coordination with gold(I), although less prevalent, has been achieved with monodentate phosphines (e.g., [Au(PMePh$_2$)$_4$][BF$_4$] and [(TPA)$_4$Au][PF$_6$], where TPA is 1,3,5-triaza-7-phosphaadamantane).[19,20] Compounds **3** and **4** provide rare examples of gold(I) complexes consisting of coordination of bisphosphine in a tetrahedral geometry similar to that found for the bisphosphine complex [Au(DPPE)$_2$]$^+$.[17,18]

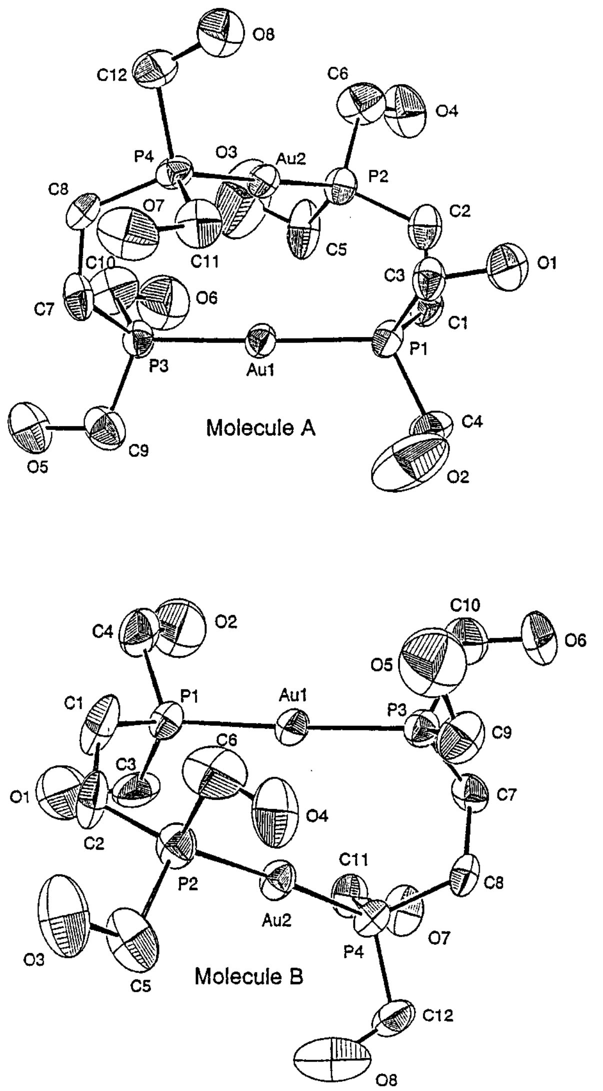

Figure 2. ORTEP diagram of **5**, with 50% probability ellipsoids for the two crystallographically independent molecules A and B in the asymmetric unit.

Table 5. Selected Bond Distances (C) and Angles (deg) for **5**[a]

Au1a−P1a	2.307(3)	Au1b−P1b	2.300(4)
Au1a−P3a	2.305(4)	Au1b−P3b	2.309(4)
Au2a−P2a	2.304(4)	Au2b−P2b	2.313(4)
Au2a−P4a	2.316(3)	Au2b−P4b	2.313(3)
P1a−Au1a−P3a	176.36(14)	P1b−Au1b−P3b	177.09(13)
P2a−Au2a−P4a	177.24(13)	P2b−Au2b−P4b	176.53(14)

[a] a atom at symmetry position $^1/_2 - x$, $^1/_2 - y$, $-z$. b atom at symmetry position $^1/_2 + x$, $^1/_2 + y$, z.

Crystals of **5** suitable for X-ray diffraction analysis were produced from a methanol/ether solution (at −20 °C). The asymmetric unit is comprised of the dicationic complex [Au$_2${(HOH$_2$C)$_2$PCH$_2$CH$_2$P(CH$_2$OH)$_2$}$_2$]$^{2+}$ with two crystallographically independent molecules and two chloride counterions per molecule. The ORTEP diagrams of the two molecules are shown in Figure 2, and selected bond distances and bond angles are listed in Table 5. Both of the gold atoms are coordinated by two phosphorus atoms in a near linear environment, with bond angles of 176.4, 177.2, 177.1, and 176.5° for P1a−Au1a−P3a, P2a−Au2a−P4a, P1b−Au1b−P3b, and P2b−Au2b−P4b, respectively. The average Au−P distance in **5** is 2.308 Å, consistent with the values previously reported for Au−P bonds.[21]

Aurophilicity in [Au$_2${(HOH$_2$C)$_2$PCH$_2$CH$_2$P(CH$_2$OH)$_2$}$_2$]Cl$_2$ (5). The fact that gold(I) centers in **5** are bound to the

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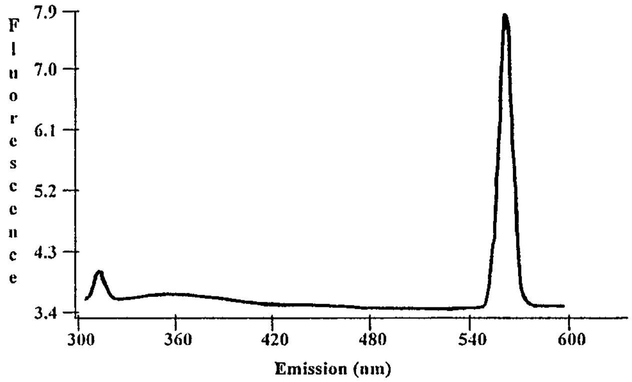

Figure 3. Room temperature emission spectra of **5** in water.

phosphines only and that they are not bridged (by halogens or pseudohalogens) becomes important in the context of determining the extent the Au(I)−Au(I) interactions which, sometimes, is referred to as the degree of aurophilicity.[22] The X-ray crystallographic data of **5** indicated a distance of 2.9324(9) Å (2.9478(9) Å for the second molecule in the asymmetric unit) for the Au−Au interaction. This magnitude for the Au−Au distance is short and suggests the operation of an "aurophilic" Au−Au attraction. A Au−Au distance of 2.9265(5) Å reported for $[Au_2(DMPE)_2](Cl)_2$ is among the shortest distances noted and suggests significant aurophilic characteristics.[21] The classical theory of chemical bonding does not offer an explanation for such strong gold−gold interactions. Recent studies involving relativistic and correlation effects have offered more satisfactory rationale for the aurophilicity properties in gold(I) compounds.[23,24]

Luminescence Studies of $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl_2$ (5). The absorption spectrum of $[Au_2\{(HOH_2C)_2PCH_2CH_2P(CH_2OH)_2\}_2]Cl_2$ in water (1.25×10^{-4} M) is dominated by a broad absorption band tailing from 250 to 310 nm. The solid compound exhibits a greenish-yellow luminescence under a hand-held UV lamp. Preliminary excitation studies of a non-degassed sample of **5** in water (5×10^{-4} M) at 280 nm resulted in emission spectra with a high-energy band at 310 nm and a low-energy band at 560 nm (Figure 3). The high-energy emission band may be assigned to a singlet to singlet transition originating from a ligand to metal charge transfer excitation. The low-energy band may be attributed to Au−Au interactions and is consistent with similar compounds.[25−28] The large Stokes shift between the absorption and the low-energy emission band suggests that the band is due to a triplet to singlet transition resulting in phosphorescence.[25−30] Additional studies to determine the quantum yields and lifetimes of the excited states are underway.

The quenching of singlet $^1\Delta_g$ O_2 has been proposed to be relevant in the mechanism of action of gold pharmaceuticals for the treatment of rheumatoid arthritis.[31] However, examples of gold(I) complexes which luminescence in aqueous solution have only recently been discovered.[32] Therefore, the ability of complex **5** to luminesce in aqueous media may provide additional insight toward the electronic nature of gold(I) species *in vivo.*

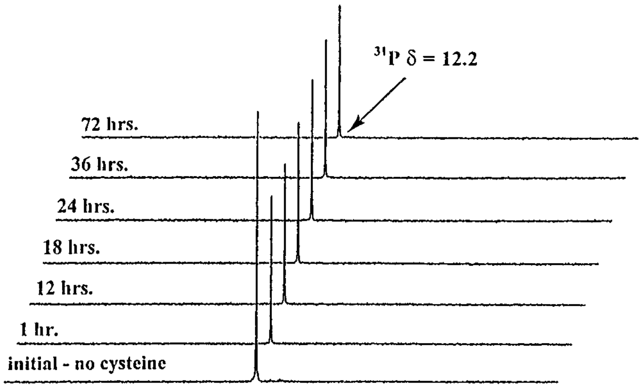

Figure 4. ^{31}P NMR spectra (121.5 MHz) of **3** in the presence of a 10-fold excess cysteine at various time points.

Kinetic Inertness Studies. The extent of the kinetic inertness of **3**, in water/methanol, was determined by recording ^{31}P NMR spectra of a solution (10 mg/mL) at different time intervals. The results indicate no change in the spectra over 7 days and demonstrate the high stability of **3**. Additional experiments to understand the *in vitro* stability of **3** were performed by challenging their aqueous solutions for trans chelation with cysteine. Typically, aqueous solutions of **3** were allowed to interact with approximately a 10-fold excess of cysteine (in water). The aliquots of this mixture were monitored by ^{31}P NMR spectroscopy. It is remarkable to note that no detectable decomposition occurred over 72 h (Figure 4).

Conclusions

The coordination chemistry of (hydroxymethyl)phosphines **1** and **2** with $NaAuCl_4$ or $AuClPPh_3$ offers opportunities for the development of water-soluble gold complexes with mono- (e.g., **3** and **4**) and bimetallic (e.g., **5**) structural characteristics. The high kinetic inertness of this new class of gold complexes in water and also in the presence of excess cysteine may be attributed to the presence of hydroxymethyl substitutents around the metal center. Presumably, electronic repulsions between the hydroxymethyl substituents (present in **3**−**5**) and nucleophiles (−OH or −SH) will keep the metal center well-shielded from nucleophilic attack.

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Supporting Information Available: Tables giving complete crystallographic experimental details, bond distances and angles, positional parameters for all atoms, anisotropic thermal parameters, and hydrogen atom coordinates of **3** and **5** and a figure showing their thermal ellipsoid plot (20 pages). Ordering information is given on any current masthead page.

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