



**SYNTHESIS AND CHARACTERIZATION OF
TRIORGANOPHOSPHINEGOLD(I)
THIOLATES**

by

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Amended version of Table 4.4.2.

Complex	H ²	H ⁹	H ⁸	Phenyl Protons	H _a	H _b
6-MPH	8.45(s)	13.62(br,s)	8.26(s)	-	-	-
[dppm(Au(6-MP)) ₂]	8.36(s)	13.12(br,s)	8.17(s)	7.95 - 7.37(br,m)	4.64(m)	-
[dppe(AuCl)(Au(6-MP))]	8.36(s)	13.25(br,s)	8.09(s)	7.87 - 7.47(br,m)	3.02(m)	-
[dppe(Au(6-MP)) ₂]	8.37(s)	13.13(br,s)	8.24(s)	7.89 - 7.49(br,m)	3.04(m)	-
[dppp(AuCl)(Au(6-MP))]	8.40(s)	13.22(br,s)	8.20(s)	7.74 - 7.50(br,m)	3.07(m)	1.73(m)
[dppp(Au(6-MP)) ₂]	8.38(s)	13.18(br,s)	8.19(s)	7.83 - 7.42(br,m)	3.16(m)	1.89(m)

Note: Coupling constants, in parentheses, are in units of Hertz: a: ³J_{H-H}, b: ³J_{P-H} and c: ²J_{P-H}.

DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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ABSTRACT

The aim of this work was to synthesize a range of novel triorganophosphinegold(I) 6-mercaptapurinate complexes and to evaluate their potential anti-arthritic activity. The resultant complexes are based on the P–Au–S moiety, structurally related to the widely available pharmaceutical Auranofin, where the phosphorus atom is part of a triethylphosphine ligand and the sulphur atom derived from a tetraacetylated thioglucose anion.

Via alteration of the identity of the triorganophosphine group, a variety of complexes were synthesized from triorganophosphinegold(I) chloride precursors, falling into three main types: 1) triorganophosphinegold(I) 6-mercaptapurinate complexes with the general formula $[R_3PAu(6-MP)]$, where $R_3P = Et_3P, Cycl_3P, PhMe_2P, Ph_3P, (o-Tol)_3P, (m-Tol)_3P$ or $(p-Tol)_3P$; 2) $[\mu-1,n-bis(diphenylphosphino)alkane]gold(I) chloride gold(I) 6-mercaptapurinate$ complexes with the general formula $[(Ph_2P(CH_2)_nPPh_2)(AuCl)(Au(6-MP))]$ where $n = 2$ or 3 ; and 3) $[\mu-1,n-bis(diphenylphosphino)alkane]bis(gold(I) 6-mercaptapurinate)$ complexes with the general formula $[(Ph_2P(CH_2)_nPPh_2)(Au(6-MP))_2]$ where $n = 1, 2$ or 3 . These complexes and the triorganophosphinegold(I) chloride precursors were characterized using multinuclear magnetic resonance, infrared and Fast Atom Bombardment mass spectroscopic techniques. Unambiguous structure determinations of a selection of the complexes were achieved by single crystal X-ray crystallographic methods. Unit cell dimensions were: $[PhMe_2PAuCl]$, orthorhombic space group $P2_12_12_1$, $a = 12.639(4)$, $b = 16.931(6)$, $c = 9.458(3)$ Å, $V = 2024(1)$ Å³ and $Z = 4$; $[Ph_3PAu(6-MP)].C_2H_5OH$, triclinic space group $P\bar{1}$, $a = 11.066(3)$, $b = 13.552(3)$, $c = 8.705(2)$ Å, $\alpha = 91.51(2)$, $\beta = 113.06(2)$, $\gamma = 89.69(2)^\circ$, $V = 1200.8(5)$ Å³ and $Z = 2$; and $[(o-Tol)_3PAu(6-MP)].C_2H_5OH$, monoclinic space group $P2_1/n$, $a = 10.067(2)$, $b = 10.518(2)$, $c = 25.416(4)$ Å, $\beta = 98.42(2)^\circ$, $V = 2662.1(9)$ Å³ and $Z = 4$. The structures were refined to final R values of 0.035, 0.034 and 0.040, respectively, for reflections satisfying the $I \geq 3.0\sigma(I)$ criterion: 1608, 3978 and 4183, respectively. The results for $[PhMe_2PAuCl]$ were utilized, in part, for a cone-angle to bond length correlation

study on triorganophosphinegold(I) chloride complexes. The structures of $[\text{Ph}_3\text{PAu}(6\text{-MP})]$ and $[(o\text{-Tol})_3\text{PAu}(6\text{-MP})]$ revealed a near linear P–Au–S chromophore, with angles of $173.71(6)$ and $177.03(8)^\circ$, respectively. A crystal structure analysis of a closely related triorganophosphinegold(I) thiolate complex, $[\text{Cycl}_3\text{PAu}(6\text{p}2\text{-TU})]$, revealed a similar P–Au–S chromophore with an angle of $177.6(1)^\circ$. Unit cell dimensions were: monoclinic space group $P2_1/c$, $a = 9.539(2)$, $b = 16.452(4)$, $c = 16.880(2)$ Å, $\beta = 95.37(2)^\circ$, $V = 2637.4(8)$ Å³ and $Z = 4$. The final refinement value was $R = 0.043$, for 3695 reflections with $I \geq 3.0\sigma(I)$. The results for the three thiolate complexes were utilized in a correlation study of cone-angles to intramolecular parameters for triorganophosphinegold(I) thiolate complexes in general.

The combined microanalytical, spectroscopic and crystallographic studies verified the formation of all the thionucleobase complexes mentioned above and demonstrated that the gold centre is linearly bound to both the phosphorus and sulphur atoms.

A number of the triorganophosphinegold(I) 6-mercaptopurinate complexes were tested for their anti-arthritis activity in Dark Agouti rats with promising results.

ABBREVIATIONS

Å	Angström
br	broad
°C	degree Celsius
¹³ C NMR	carbon-13 nuclear magnetic resonance
Cycl	cyclohexyl
d	doublet
dd, dm, dt	doublet of doublets, multiplets, triplets
dec.	decomposition point
dppe	μ-1,2-bis(diphenylphosphino)ethane
dppm	μ-bis(diphenylphosphino)methane
dppp	μ-1,3-bis(diphenylphosphino)propane
Et	ethyl
FAB-MS	Fast Atom Bombardment - mass spectroscopy
g	gram
¹ H NMR	proton nuclear magnetic resonance
Hz	hertz
IR, ir	infrared spectroscopy
^x J _{AB}	coupling constant between nuclei A and B over x bonds
m	multiplet (nmr)
m	medium (ir)
M	molar (mol dm ⁻³)
[M] ⁺	molecular ion
2mbaH	2-mercaptobenzoic acid
6m2-TUH	6-methyl-2-thiouracil
Me	methyl
MHz	mega-hertz

ml	millilitre
mmol	millimole
m.p.	melting point
6-MPH	6-mercaptapurine
MW	molecular weight
m/z	mass to charge ratio
6p2-TUH	6-n-propyl-2-thiouracil
NMR, nmr	nuclear magnetic resonance (Fourier Transform)
N.O.	not observed
Obs.	obscured
^{31}P NMR	phosphorus-31 nuclear magnetic resonance
Ph	phenyl
PhO	phenoxy
ppm	parts per million
q	quartet
s	singlet (nmr)
s	strong (ir)
sh	shoulder
t	triplet
TMS	tetramethylsilane
<i>m</i> -Tol	<i>meta</i> -tolyl
<i>o</i> -Tol	<i>ortho</i> -tolyl
<i>p</i> -Tol	<i>para</i> -tolyl
2-TUH	2-thiouracil
vs	very strong
w	weak
%Y	percentage yield
$\delta(\text{A-B})$	bending frequency of A-B bond
λ	wavelength
$\nu(\text{A-B})$	stretching frequency of A-B bond

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