

GOLD(I) PHOSPHINE COMPLEXES AND THEIR POTENTIAL APPLICATION AS ANTI-TUMOUR AGENTS

A dissertation submitted in fulfillment of the requirements of the degree

of

Master of Science

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February 2005

Abstract

The monodentate phosphine complexes bu^i_3PMX (**2a**: M = Cu, X = Cl, **2b**: M = Cu, X = I, **2c**: M = Ag, X = Cl, **2d**: M = Au, X = Cl) were synthesised in high yields from bu^i_3P and MX. Their reaction with $[\text{Li}\{\mu\text{-N(R)C}(\text{bu}^t)\text{C(H)R}\}]_2$ (R = SiMe₃) gave the monomeric complexes $\text{bu}^i_3\text{PCuN(R)C}(\text{bu}^t)=\text{C(H)R}$ (**3a**) and $\text{bu}^i_3\text{PMC(H)RC}(\text{bu}^t)=\text{NR}$ (**3b**: M = Ag, **3c**: M = Au) in moderate to high yields. The bonding mode in the 1-aza-allyl complexes **3a-c** was found to depend strongly on the metal ion, with **3a** being an enamide complex and **3b** and **3c** iminoalkyl complexes.

The reaction of bidentate ligand dpmaaH₂ (2,3-bis(diphenylphosphino)maleic acid) with R₂Sn-precursors led to novel dialkyl tin dpmaa complexes (R₂Sn)(O,O dpmaa) (**6**) (where **6a**, R = Me; **6b**, R = Bu) were synthesized.

Complexation of the tin/phosphine complexes led to the heterobimetallic complexes {Au[(dpmaaO,O)(SnR₂)]₂}Cl (**7a** and **8a**) {Au[(dpmaaO,O)(SnR₂)](dpmaaH₂)}Cl (**7b** and **8b**) (where **7a** and **8a**, R = Me; **7b** and **8b**, R = Bu) and the mixed metal complexes {Au[(dpmaaO,O)(RuCl)]₂}Cl (**9a**) {Au[(dpmaaO,O)(SnBu₂)(dpmaaO,O)RuCl]}Cl (**9b**) and {Au[(dpmaaO,O)(RuCl)](dpmaa)}Cl (**9c**).

All compounds were fully characterised by multinuclear NMR spectroscopy and microanalysis (not **3a**, **3b**, **4** and **5**) solid state IR spectroscopy (KBr-pellets) (**4-9**) and mass spectrometry (**6-8**). The solid state structures of complexes **2c**, **2d**, **3c**, **6a** and **6b** (two polymorphs) have been determined by X-ray crystallography revealing the presence of rare trimeric macrocycles in the case of **6a** and **6b**.

The anti-tumour activity of the metal complexes (**6b** and **7-9**) was tested on a single cell-line (except **7a** and **8a** which were on eight cell-lines) and their activity was compared to cisplatin.

Declaration

I declare that this dissertation is my own, unaided work submitted for the degree of Master of Science in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other university.

...Messai A. Mamo.....

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18 day of February, 2005

Acknowledgements

First and foremost I would like to give special thanks to my supervisors Dr. Marcus Layh and Dr. Richard J. Bowen for their help and guidance during the course of this research.

It is also have the pleasure to acknowledge the assistance of the following people who have been kind enough to me in one way or other throughout this project; Manuel Frenandes for solving all the crystal structures in this project, Richard Mampa, the entire Inorganic Lab. occupants (B. Omondi, P. W. Gitari, Dr. J. Caddy, Dr. E. M. Coyanis, E. Kriel, S. D. Khanye), for the warm atmosphere they provided which made working in the laboratory enjoyable.

Finally I would also like to thank the School of Chemistry for allowing me undertaking studies for a M.Sc. degree and Mintek for a scholarship.

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Abbreviations

- ^1H NMR Proton Nuclear Magnetic Resonance
- ^{13}C NMR 13 carbon isotope Nuclear Magnetic Resonance
- ^{31}P NMR 31 Phosphorous Nuclear Magnetic Resonance
- ^{119}Sn NMR 119 tin isotope Nuclear Magnetic Resonance
- Bu^i iso butyl
- Bu^n normal butyl
- Bu^t tertiary butyl
- C_6D_6 deuterated benzene
- CDCl_3 deuterated chloroform
- Cell lines
 1. HCF-7 Breast carcinoma cells
 2. A2780 Human ovarian carcinoma cells
 3. A2780cis Human ovarian carcinoma cisplatin-sensitive sub line
 4. COLO colon cancer cells
 5. Hela cervical carcinoma cells
 6. MCF-12A breast non-tumorigenic cells
 7. B16 mouse melanoma
 8. Fibroblasts primary human fibroblasts cells

- d2pyp 2- pyridylphosphine
- d3pyp 3- pyridylphosphine
- d4pyp 4- pyridylphosphine
- $\text{d}_6\text{-DMSO}$ deuterated dimethyl sulphoxide
- depe $\text{Et}_2\text{P}(\text{CH}_2)_2\text{PEt}_2$
- dme dimethoxyethane
- dpmaa 2,3-bis(diphenylphosphino)maleic acid
- dpma 2,3-bis(diphenylphosphino)maleic anhydride
- dppe 1,2-bis(diphenylphosphino)ethane
- dppey *cis*-1,2-bis(diphenylphosphino)ethylene
- DMSO dimethyl sulphoxide
- Et ethyl
- IR
 1. b, broad
 2. s, strong
 3. m, medium
 4. w, weak
- K Kelvin scale for Temperature ($0\text{K} = -273.15^\circ\text{C}$)
- LL' $\text{CH}(\text{SiMe}_3)(\text{bu}^t)\text{NSiMe}_3$
- mV millivolt
- Me methyl
- MHz Mega Hertz

- NMR
 1. d, doublet
 2. dd, doublet of doublet
 3. m, multiplet
 4. s, singlet
 5. bs, broad line
- ppm part per million
- P-XRD Powder X-ray Diffraction
- RT room temperature
- thf tetrahydrofuran
- TPA 1,3,5-triaza-7-phosphaadamantane
- XRD X-ray Diffraction
- °C Degree Celsius