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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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Abstract

The monodentate phosphine complexes $bu^{i}_{3}PMX$ (**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 $bu^{i}_{3}P$ and MX. Their reaction with $[Li\{\mu\text{-}N(R)C(bu^{t})C(H)R\}]_2$ (R = $SiMe_3$) gave the monomeric complexes $bu^{i}_{3}PCuN(R)C(bu^{t})=C(H)R$ (**3a**) and $bu^{i}_{3}PMC(H)RC(bu^{t})=NR$ (**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 $dpmaaH_2$ (2,3-bis(diphenylphosphino)maleic acid) with R_2Sn-precursors led to novel dialkyl tin dpmaa complexes (R_2Sn)(O,O dpmaa) (**6**) (where **6a**, R = Me; **6b**, R = Bu) were synthesized.

Complexation of the tin/phosphine complexes led to the heterobimetallic complexes $\{Au[(dpmaaO,O)(SnR_2)]_2\}Cl$ (**7a** and **8a**) $\{Au[(dpmaaO,O)(SnR_2)][dpmaaH_2]\}Cl$ (**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**) $\{Au[(dpmaaO,O)(SnBu_2)(dpmaaO,O)RuCl)]\}Cl$ (**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.

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18 day of February, 2005

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Abbreviations

- ^{1}H 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 carcinomia cels
    3. A2780cis — Human ovarian carcinomia cisplatin-sensitive sub line
    4. COLO — colon cancer cells
    5. Hela — cervical carcinoma cells
    6. MCF-12A — breast non-tumourogenic cells
    7. B16 — mouse melanoma
    8. Fibroblasts — primary human fibroblasts cells

- d2pype — 2- pyridylphosphine
- d3pype — 3- pyridylphosphine
- d4pype — 4- pyridylphosphine
- d_6-DMSO — deuterated dimethyl sulphoxide
- depe — $Et_2P(CH_2)_2PEt_2$
- 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 — Infrared
    1. b, — broad
    2. s, — strong
    3. m, — medium
    4. w, — weak
- K — Kelvin scale for Temperature (0K = -273.15^{0}C)
- LL’ — $CH(SiMe_3)(bu^{t})NSiMe_3$
- mV — millivolt
- Me — methyl
- MHz — Mega Hertz

- NMR
    1. d, dublet
    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
- ^{0}C Degree Celsius