

# Exchange Reactions between Albumin-Au(I)-PEt<sub>3</sub> Complex and Me<sub>3</sub>PAuCl or *i*Pr<sub>3</sub>PAuCl: <sup>31</sup>P NMR Spectroscopic Studies

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The AlbSAuPEt<sub>3</sub> complex was prepared *in vitro* by reacting AlbSH with auranofin.<sup>§</sup> It is shown that the Et<sub>3</sub>PAu<sup>+</sup> entity is liable to exchange in the presence of Me<sub>3</sub>PAuX and *i*Pr<sub>3</sub>PAuX (X = Cl<sup>-</sup> or AtgS<sup>-</sup>; AtgS<sup>-</sup> = tetraacetyl thioglucose). <sup>31</sup>P NMR spectroscopy was used to follow these exchange reactions. Either Me<sub>3</sub>PAu<sup>+</sup> or *i*Pr<sub>3</sub>PAu<sup>+</sup> replaces Et<sub>3</sub>PAu<sup>+</sup> from the AlbSAuPEt<sub>3</sub> complex. Since the *i*Pr<sub>3</sub>P ligand is bulkier (reflected by its bigger Tollman cone angle), it is surprising that it replaces Et<sub>3</sub>PAu<sup>+</sup> almost equally as well as Me<sub>3</sub>PAu<sup>+</sup>. It is also demonstrated that Et<sub>3</sub>PAu<sup>+</sup> bound to the weak binding sites of albumin (primarily histidines) can be transferred to the stronger binding site which is AlbSAuPEt<sub>3</sub> to form the bis complex AlbS(AuPEt<sub>3</sub>)<sub>2</sub>. The transfer of Et<sub>3</sub>PAu<sup>+</sup> between protein species is relevant to mechanism by which gold may be transferred between proteins *in vivo*.

**Keywords:** : exchange reactions, gold(I), phosphine, albumin, <sup>31</sup>P NMR spectroscopy

## INTRODUCTION

Gold(I) drugs are extensively used in chrysotherapy, the treatment of rheumatoid arthritis, although the metabolism of gold and the mechanism(s) of chrysotherapy are not well understood [1,2]. Since various gold(I) species bind predominately to albumin in the blood stream *in vivo*

[3], the binding site and ligation of gold(I) have been topics of interest [4-8]. *In vitro* studies have demonstrated that the strong binding site is the free thiol residue cys-34 [4,6-8], of albumin. Auranofin, the second-generation gold drug AtgSAuPEt<sub>3</sub> = [(triethylphosphine)(2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosato-S)gold(I)] binds to albumin exclusively through the displacement of its tetra acetyl thioglucose ligand by cys-34 [6-10].

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