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SYNTHESIS OF CHLORO (DIETHYLALKOXYPHOSPHINE) GOLD (I) SALTS AND THEIR SUBSEQUENT CONVERSION TO S-DIETHYLALKOXYPHOSPHINE GOLD 2,3,4,6-TETRA-O-ACETYL-1-THIO-β-D-GLUCOPYRANOSIDES

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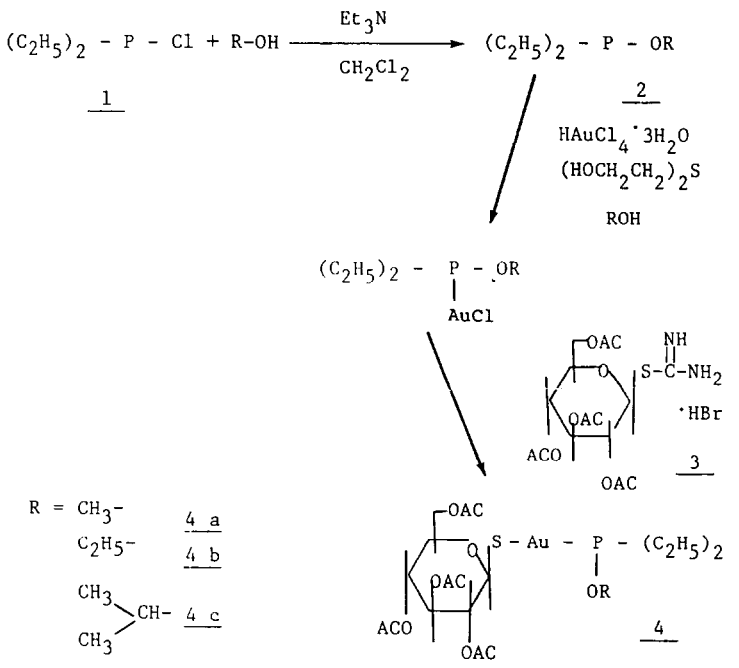
Summary: A novel alkoxy-interchange leading to a variety of alkoxy phosphine-gold-chlorides from one common starting material is reported.

In continuation of our studies of general methods for synthesizing phosphine-gold complexes as possible anti-arthritic agents[1], a homologous series of diethylalkoxyphosphine-gold (I) complexes has been prepared as intermediates for subsequent conversion to the appropriate glucopyranoside (Scheme I).

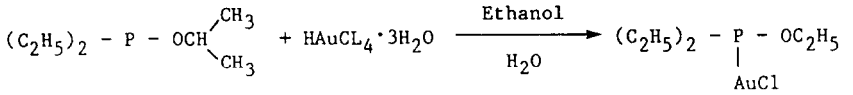


Scheme I

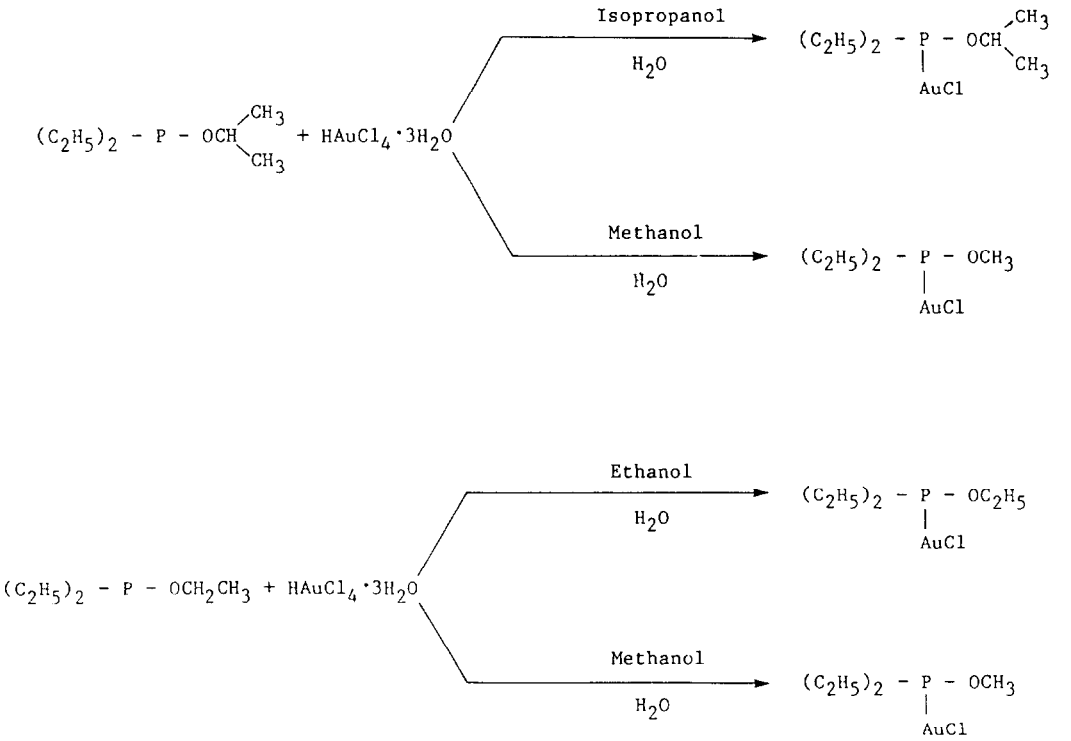
Each of the respective phosphines was synthesized[2], isolated by distillation, and characterized by Mass Spectroscopy and ^{1}H-NMR spectrum. Any additional handling of the phosphine was hampered

by their ease of oxidation to the corresponding phosphine oxide - detectable in the ^{1}H-NMR spectrum by a down field shift of 0.1 to 0.15 ppm. of the multiplet of the methine or methylene proton region of the respective alkoxy group.

Preparation of the alkoxyphosphine-gold-chloride intermediates in aqueous ethanol resulted in a new reaction product novel to this class of compounds. The use of an alcohol not common to the alkoxy group associated with the phosphine resulted in an "Alkoxy-Interchange". This interchange was first observed when the reaction of diethylisopropoxyphosphine (5) with auric acid was carried out in aqueous ethanol. The product was found to be diethylethoxyphosphine-gold-chloride (6) rather than the expected diethylisopropoxyphosphine-gold-chloride. The identity of this product was confirmed by G. C. Mass Spectroscopy.



This phenomenon presented an interesting route leading to a variety of alkoxyphosphine-gold-chloride intermediates from a common intermediate. The viability of this hypothesis was confirmed by carrying out the following reactions outlined in Scheme II.



Scheme II

Each of the indicated phosphine-gold-chlorides was fully characterized. The two methoxyphosphine-gold-chlorides resulting from Scheme II were shown to be identical. Thus the possibility of synthesizing a variety of alkoxyphosphine-gold intermediates from a single source of alkoxyphosphine proved to be realistic.

The alkoxyphosphine-gold-chlorides were successfully converted to their respective glucopyranosides (4) as indicated by Scheme I in yields of 70-75% and were thoroughly characterized by ^{1}H-NMR, IR, HPLC, and elemental analysies.

A general experimental procedure for synthesizing one of the designated analogues is provided in the following sections.

Preparation of Diethylalkoxyphosphine[2]

Diethylphosphinous chloride in methylene chloride was added slowly to a cold mixture of the appropriate alcohol and triethylamine in methylene chloride. After stirring for several hours in the cold, triethylamine hydrochloride was removed by filtration and the filtrate was concentrated and distilled at reduced pressure to give the appropriate pure diethylalkoxyphosphine.

Preparation of Chloro (diethylisopropoxyphosphine) gold

A solution of 2,2-thiodiethanol in a mixture of isopropyl alcohol and water was treated in the cold with an aqueous solution of auric acid. Stirring was continued in the cold until the solution became colorless indicating the reduction of gold to the gold (I) state. A chilled solution of the diethylalkoxyphosphine in isopropyl alcohol was then added and strirring was continued for an additional 1/2 hour. The aqueous mixture was thoroughly extracted with chloroform and the combined extracts concentrated to a residual oil under reduced pressure. The oily residue was used without further purification. Mass Spectrum showed the expected m+ at m/e 380 with one chlorine atom indicated.

Preparation of S-Diethylisopropoxyphosphine-gold 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside

2-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-2-thiopseudourea hydrobromide was dissolved in a mixture of water, isopropyl alcohol, and potassium carbonate and cooled. After a few minutes, chloro(diethylisopropoxyphosphine)gold was added and the solution was stirred for about one hour during which time the product precipitated. The product was filtered, washed with water, and recrystallized from isopropyl alcohol-water.[3]

ACKNOWLEDGEMENTS

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REFERENCES

1. B. M. Sutton, E. McGusty, D. T. Walz and M. J. DiMartino, J. Med. Chem., 15 1095-8, 1972; I. Lantos, U. S. 4,096,247; Smith Kline and French Labs., U. S. 3,676,554 and U. S. 3,708,579; E. McGusty and B. M. Sutton, U. S. 3,784, 687; P. E. Nemeth and B. M. Sutton, U. S. 3,635,945.

2. S. D. Harper and A. J. Arduengo, Tetrahedron Lett., 21, 4331-4, 1980; B. A. Arbuzo and N. I. Rezpolozhenskii, C. A. 48, 7540g, 1953.

3. Each of the isolated glucopyranosides were thoroughly characterized by G. C. Mass Spec., NMR, and elemental analysis:
(4a) - Mass Spec. (^{m}/e)680(m^{+}); $C_{19}H_{32}AuO_{10}PS$; C,33.54; H,4.74; S,4.71; Au,28.94. Found: C,33.31; H,4.71; S,5.01; Au,29.10.

(4b) - Mass Spec. (^{m}/e)694(m^{+}); $C_{20}H_{34}AuO_{10}PS$; C,34.59; H,4.93; S,4.62; Au,28.36. Found: C,34.48; H,4.62; S,4.81; Au,29.20. NMR ($CDCl_3$, TMS, 90MH_z): Methylene multiplet of ethoxy group at 3.85-4.35 ppm. integrates for two protons.

(4c) - Mass Spec. (^{m}/e)708(m^{+}); $C_{21}H_{36}AuO_{10}PS$; C,35.60; H,5.12; S,4.53; Au,27.8. Found: C,35.54; H,5.14; S,4.89; Au,28.00. NMR ($CDCl_3$, TMS, 90 MH_3): Methine multiplet of isopropylgroup at 4.35-4.80 ppm. integrates for one proton.

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