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# Cyclometalated gold(III) iminophosphoranes which incorporate carbohydrate groups

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ABSTRACT

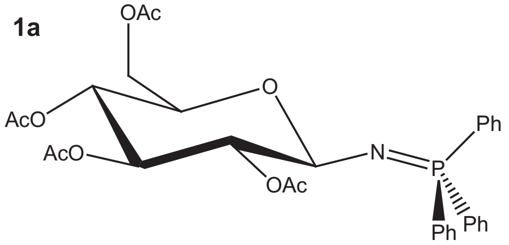
Iminophosphoranes with organic groups derived from D-glucose, D-galactose and L-arabinose have been used to prepare gold(III) dichloride complexes via mercurated intermediates, since direct cyclometallation was unsuccessful. Structures and full spectroscopic data are reported. Replacement of one or more of the chloride ligands by $PPh_3$, or by thiosalicylate gave new derivatives. Biological screening showed no enhanced activity relative to other alkyl or aryl analogues.

## 1. Introduction

Iminophosphoranes, $R_3P{=}N{-}R'$, are readily available with a wide variety of R and R′ groups [1,2]. Alper first showed that it was possible to produce cyclopalladated species by reacting $Ph_3P{=}NC_6H_4CH_3$ with $Na_2[PdCl_4]$ [3]. Direct cyclometallation has also been carried out with $Pd(OAc)_2$ or $Hg(OAc)_2$ [4] and with $PhCH_2M(CO)_5$ ($M$ = Mn or Re) [5]. An indirect route where the iminophosphorane is initially lithiated and then transmetalated has been used to prepare gold [6,7], rhodium, iridium [8], aluminium and gallium [9] cyclometalated iminophosphoranes. We have been particularly interested in cycloaurated iminophosphoranes, since the ligand is effective at stabilising the gold(III) oxidation state.

Sugar iminophosphoranes have long been known. Acetylated glycosyl azides react with $PPh_3$ in $Et_2O$, to give species such as **1a** [10]. These sugar iminophosphoranes are useful in organic synthesis; for example they can be used to reduce azides, to produce amides or to synthesis imines via the Aza–Wittig reaction [11]. However their use as ligands has not been investigated. Since other gold(III) iminophosphoranes have been shown to be catalytically and biologically active [12], the introduction of a carbohydrate moiety is interesting, since carbohydrates not only introduce chirality but can enhance biological activity as well. This paper reports the synthesis and characterisation of some novel cycloaurated iminophosphoranes.

**1a**



## 2. Results and discussion

### 2.1. Complexes of glycosyl iminophosphoranes

The Staudinger reaction [13] between an azide and a phosphine seemed the best route to iminophosphoranes so sugar azides were needed. Starting from D-glucose, D-galactose and L-arabinose, literature methods [14–16] readily produced acetylated glycosyl azides **2a**–**c**, by acetylation of the sugars with acetic anhydride and catalytic amounts of iodine, bromination with HBr in acetic acid, and nucleophilic substitution with $NaN_3$, Scheme 1.

The reaction can be extended to many other sugars such as disaccharides but is only applicable to 1,2-*trans* sugars, so mannose with the O2 oxygen in the axial position would not produce the azide product. Azides are notorious for their explosive nature, but as the percentage of nitrogen in the azide decreases they become less explosive. The Smith rule [11] is an indication of whether an

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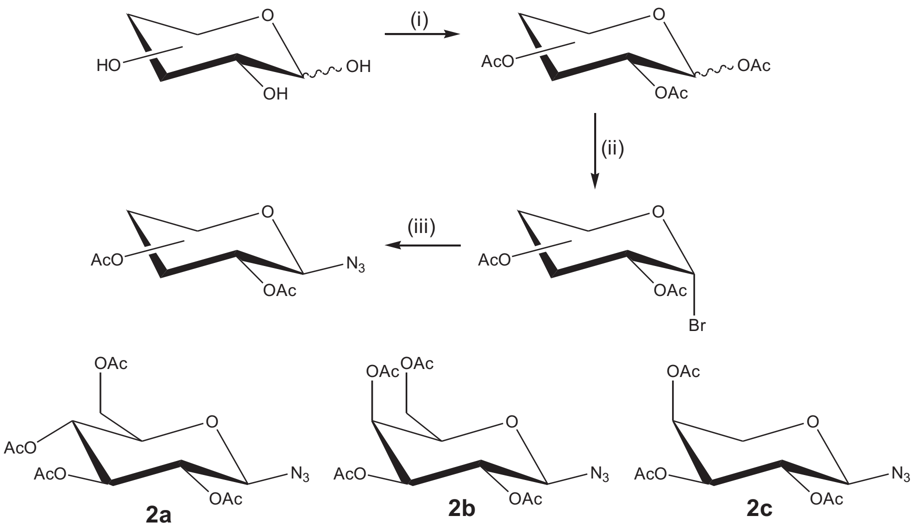


**Scheme 1.** General reaction scheme for the production of glycosyl azides. (i) Acetic anhydride, cat. $I_2$; (ii) HBr, acetic acid; (iii) $NaN_3$, acetone, $H_2O$.

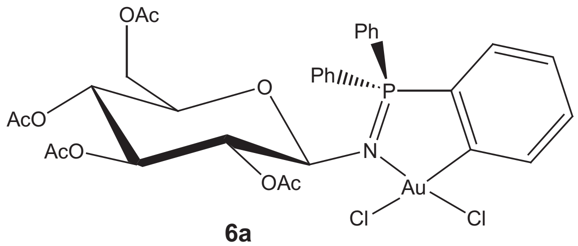
organic azide will be explosive. Since the nitrogen content of all the sugar azides was low no special precautions were taken with the manipulation of them.

Acetyl glucosyl azide was reacted with $PPh_3$ with a slight modification of the previous method [10] to produce **1a**, which was used without purification. The iminophosphorane $Ph_3P{=}N{-}Ph$, **3**, has been directly cyclometalated [5–7,17], so **1a** was tested to see if direct metallation was possible. $Pd(OAc)_2$, $Hg(OAc)_2$ and $PhCH_2Mn(CO)_5$ were all tried but no cyclometalated product could be isolated or detected by high resolution electrospray ionisation mass-spectrometry (ESI-MS) of an aliquot of the reaction mixture. To understand why, a structure determination of **1a** was carried out, shown in Fig. 1.

Compared with other iminophosphoranes with alkyl groups on the nitrogen the C–N (1.409(1) Å) and N=P (1.5744(10) Å) bond lengths are similar as is the C–N=P bond angle of 121.16(7)° [18,19]. The C–N=P bond angle for the aryl-substituted **3** is however larger at 130.4(3)° [20]. While the phosphorus is approximately tetrahedral there is a slight distortion in the N=P–C angles, with the carbon atoms *cis* to the nitrogen substituent having slightly larger angles. This is also seen in the structure of **3** [20] and for some other alkyl iminophosphoranes [18,19]. The torsion angle for C2–C1–N1–P1 is 176.8(1)°. The sugar portion of the molecule is as expected. A space filling model indicated that the nitrogen was sterically crowded in the solid state. Scheme 2 shows the proposed mechanism for the direct metallation by $Pd(OAc)_2$ [21–23] which starts with the coordination to the metal by the nitrogen. Presumably for **1a** the lack of availability of the nitrogen hinders the direct metallation. In support of this when **1a** was stirred with $PdCl_2$ in acetonitrile, under conditions where $Ph_3P{=}N{-}Ph$ forms the N-donor complex, $Pd[N(Ph){=}PPh_3]_2Cl_2$ [24], no product could be isolated or detected by ESI-MS. While the steric explanation for the lack of reactivity seems plausible, it should perhaps be noted that the solution NMR spectrum of **1a** does not show inequivalence of the Ph groups which would arise from hindered rotation about the C–N bond on the NMR time scale, so in solution conformations with the N exposed could be generated by twisting (c.f. Fig. 6 discussed below).

Since another route was needed, pre-metallation of the phosphine was investigated. Transmetallation from mercury to gold(I) and gold(III) has been used in a number of cases where direct auration is not feasible [25–29], and the mercurated diphosphine, **4**, was used by Kilpin et al. to produce a gold(III) iminophosphorane [30]. The phosphine was reacted with an azide to produce an intermediate mercurated iminophosphorane, which could be transmetalated with Au(III). The overall reaction is shown in Scheme 3.

The azide sugar **2a** was reacted with **4**. Monitoring of the reaction by $^{31}P$ NMR and ESI-MS showed that the intermediate mercurated iminophosphorane, **5a**, had fully formed after 1.5 h. Removal of the solvent gave **5a** which was used directly, after characterisation by $^{31}P$ NMR and ESI-MS. The ion $[AuCl_4]^-$ has been used to produce gold(III) iminophosphoranes [6,17,30]. To **5a** was added $[NMe_4][AuCl_4]$ and dry acetonitrile and the mixture stirred for several days in the dark. Monitoring by ESI-MS showed the slow disappearance of the mercurated sugar iminophosphorane and the appearance of the cyclometalated gold(III) compound. After separation of $HgCl_2$ by filtration, the solvent was removed under vacuum and recrystallisation of the residue gave air- and moisture-stable yellow crystals of **6a**.



**6a**

At room temperature after one month some decomposition was seen, with the development of the purple colour from colloidal elemental gold. However at −15 °C, crystals were stable for over a year. The other glycosyl azides **2b** and **2c** reacted similarly to give the analogues **6b** and **6c**.

### 2.1.1. ESI-MS

ESI-MS of the compounds **6a–c** showed several characteristic ions. The main ion was from the loss of a chloride to give $[M - Cl]^+$ with a less intense ion from $[M + Na]^+$. This is a different mode of ionisation from that seen for the mercurated intermediate **5**, which forms the ion $[M + H]^+$. This difference is because of the availability of the nitrogen to be protonated on **5**, since mercury only weakly interacts with the nitrogen while gold forms a strong bond.