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An Efficient Method for the Deprotection of Allyl Glycosides with Adjacent Azides: The Circumvention of Unwanted Dipolar Cycloaddition Products

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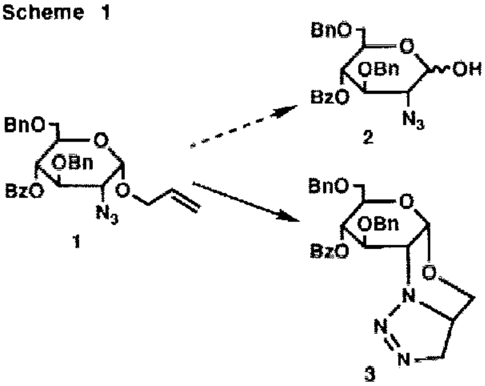
Key Words: Allyl glycoside, Deprotection, Dipolar cycloaddition.

Abstract: A two step deallylation scheme using (bis(methyldiphenylphosphine)) (1,5-cyclooctadiene) iridium (I) hexafluorophosphate and catalytic amounts of osmium tetroxide with trimethylamine *N*-oxide is used to deprotect allyl glycosides in the presence of an azide group at C-2. This method avoids the formation of intramolecular 1,3-dipolar cycloaddition products which are isolated during the deprotection using other procedures.

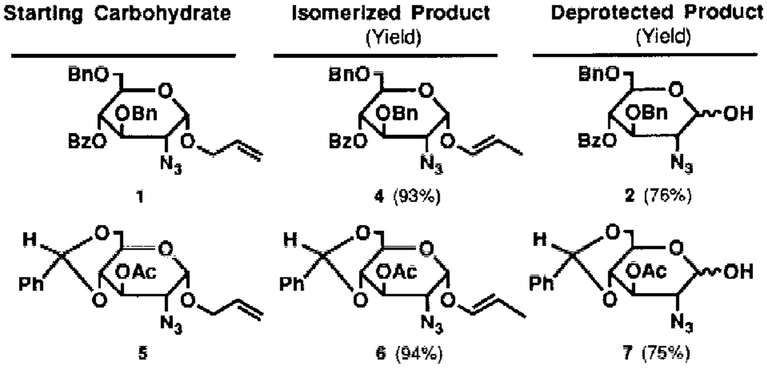
During our investigations into the synthesis of derivatives of N-acetyl glucosamine oligosaccharides, we required an efficient method to cleave an allyl group at the anomeric carbon in the presence of an adjacent azide.[1,2] Usually in such systems, deallylation was only possible after the reduction of the 2-azide group to an amino function.[3] Our attempts to remove the allyl group in the presence of a C-2-azide in compound **1** under conditions reported in the literature led mainly to the 1,3-dipolar cycloaddition product **3** (Scheme 1). In this letter we report that the reaction of **1** at ambient temperature with hydrogen-activated (bis(methyldiphenylphosphine)) (1,5-cyclooctadiene) iridium (I) hexafluorophosphate, followed by catalytic osmium tetroxide and trimethylamine *N*-oxide dihydrate affords a high yield of the deprotected product **2**, with no dipolar cycloaddition products.

Scheme 1

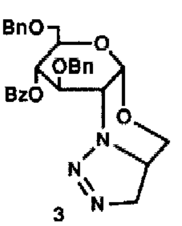


Common allyl deprotection procedures, in which the allyl group is isomerized to the more labile 1-propenyl group using potassium *tert*-butoxide,[4] Wilkinson's catalyst,[5] palladium on carbon,[6] palladium (II) chloride,[7] dihydridotetrakis (triphenylphosphine) ruthenium (II)[8] or (bis(methyldiphenylphosphine)) (1,5-cyclooctadiene) iridium (I) hexa-fluorophosphate[9] usually require heating the solution to reflux. We found that under these conditions compound **1** gave mainly the intramolecular 1,3-dipolar cycloadduct **3**. Although no reaction occurs with most of these catalysts at room temperature, the cationic iridium complex is able to perform the isomerization without any heating. We reasoned that the resulting *trans*-1-propenyl group could then be easily cleaved by catalytic osmylation.[10] In our hands the conversion of compound **1** to **2** proceeded in 76% yield using this two step procedure. Our method is fast, mild, simple to perform and can be applied to systems with a variety of protecting groups since it is specific for only the 1-propenyl group. It tolerates any acid- or base-labile substituents and uses only 1 mol-% of osmium tetroxide which has obvious advantages over standard mercuric salt hydrolysis methods.[11] We tested sugars with a variety of protecting groups (esters, acetals and ethers) to show the generality of this method (Scheme 2). The enol ethers **4** and **6** are stable and can be isolated from the isomerization step in high yields.

Scheme 2



Although the removal of the allyl protecting group in the presence of a neighboring azide is known to be problematic and low-yielding,[12,14] to our knowledge the unusual fused morpholine-Δ^2-1,2,3-triazoline ring structure **3** has never been reported to be the side product of these reactions. Compounds **3** and **8** can easily be obtained from **1** or **5** by heating in benzene.[15] Stored at room temperature these cycloaddition products are unstable; presumably they decompose by the extrusion of nitrogen to form the corresponding aziridine and imine derivatives.[16] Similar tricyclic morpholino-triazolines have been described as intermediates of a thermally induced intramolecular 1,3-dipolar cycloaddition of 2-allyloxy-phenyl azides.[17]



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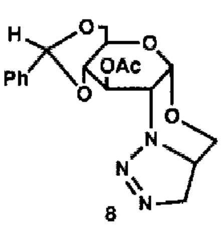

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A typical experimental procedure for the deallylation of compound **1** is given below. Hydrogen is bubbled for 15 minutes into a suspension of (bis(methyldiphenylphosphine)) (1,5-cyclooctadiene)iridium (I) hexafluorophosphate (100 mg, 0.12 mmol) in 20 mL of tetrahydrofuran. Immediately the iridium catalyst loses its pink color and starts to dissolve. This mixture is added to a stirred solution of allyl-2-azido-2-deoxy-4-O-benzoyl-3,6-di-O-benzyl-O-α-D-glucopyranoside (**1**)[18,21] (2.0 g, 3.8 mmol) in 40 mL of THF and the reaction is stirred for 12 h at room temperature under nitrogen. The solvent is removed under reduced pressure and compound **4** is taken up in 50 mL of dichloromethane. Trimethylamine *N*-oxide dihydrate (650 mg, 5.8 mmol) and osmium tetroxide (10 mg, 0.04 mmol) are added and the solution is stirred for 12 h at room temperature. The solvent is evaporated and the remainder purified by silica gel chromatography (ether / pentane 1.5 : 1) to yield **2**[21] (1.4 g, 76 % from **1**) as an oil.

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11) Paulsen[12] has described the isomerization of allyl groups using this iridium catalyst, but he used greater than stoichiometric amounts of mercuric salts to cleave the 1-propenyl group. Also Ogawa[13] applied his palladium(II) chloride/acetic acid method[7] to the deallylation in the presence of an adjacent azide.
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18) Compound **1** was obtained from 3,4,6-tri-O-acetyl-2-azido-2-deoxy-D-glucopyranosyl nitrate,[19] in which deacetylation and allyl glycosylation were performed with sodium and allyl alcohol similar to Paulsen's one-pot method,[20] then converted to 1 using standard procedures.

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21) All new compounds have elemental analysis and spectra that are consistent with the assigned structures. The ^{1}H-NMR data (500 MHz, $CDCl_3$, coupling constants in Hz) are given for compounds **1** - **4**.

1: 3.51 - 3.63 (m, 3 H), 4.06 - 4.19 (m, 3 H), 4.30 (dt, 1 H, J = 8.9, 14.8), 4.51 (s, 2 H), 4.62 (d, 1 H, J = 12.5), 4.77 (d, 1 H, J = 12.8), 5.06 (d, 1 H, J = 6.3), 5.29 (dd, 1 H, J = 3.9), 5.38 - 5.44 (m, 2 H), 6.01 (ddd, 1 H, J = 7.6, 11.4), 7.19 - 8.21 (m, 15 H).

2: 3.50 - 3.62 (m, 7 H), 3.76 (ddd, 1 H, J = 2.5, 7.6), 4.21 (t, 1 H, J = 9.9), 4.37 (dt, 1 H, J = 3.0, 5.7), 4.47 - 4.53 (m, 5 H), 4.60 - 4.65 (m, 2 H), 4.68 (dd, 1 H, J = 8.9), 4.76 - 4.81 (m, 3 H), 5.26 - 5.35 (m, 2 H), 5.39 (d, 1 H, J = 4.1), 7.14 - 8.15 (m, 30 H).

3: 2.79 (m, 1 H), 2.93 (dd, 1 H, J = 10.1), 3.06 (dd, 1 H, J = 2.4), 3.15 (dd, 1 H, J = 3.8), 3.37 (t, 1 H, J = 9.6), 3.50 - 3.59 (m, 2 H), 4.01 (dd, 1 H, J = 3.6), 4.18 - 4.23 (m, 2 H), 4.43 - 4.52 (m, 3 H), 4.72 (d, 1 H, J = 10.5), 4.98 (d, 1 H, J = 4.0), 5.42 (t, 1 H, J = 9.7), 7.13 - 8.11 (m, 15 H).

4: 1.60 (dd, 3 H, J = 2.1), 3.52 - 3.63 (m, 3 H), 4.08 (m, 1 H), 4.17 (t, 1 H, J = 9.8), 4.47 - 4.50 (m, 2 H), 4.62 (d, 1 H, J = 12.5), 4.79 (d, 1 H, J = 12.2), 5.20 (d, 1 H, J = 3.1), 5.32 (m, 1 H), 5.49 (t, 1 H, J = 10.0), 6.24 (dd, 1 H, J = 12.6), 7.13 - 8.18 (m, 15 H).

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