

# An Improved Direct Conversion of Hexoses to Hexo-2-uloses

Matteo Adinolfi, Gaspare Barone, Alfonso Iadonisi\*<sup>1</sup>

Dipartimento di Chimica Organica e Biologica, Università di Napoli "Federico II"  
Via Mezzocannone 16, I-80134 Napoli, Italy

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## Abstract

Hexo-2-uloses can be obtained from 2,3,4,6-tetra-*O*-benzyl-hexopyranoses by an improved procedure employing a Meerwein-Ponndorf-Verley/Oppenauer reaction induced by SmI<sub>2</sub>/O<sub>2</sub>/THP as the key step. © 1998 Elsevier Science Ltd. All rights reserved.

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Air-oxidised samarium diiodide [1] has been recently [2] shown to convert 2,3,4,6-tetra-*O*-benzyl aldohexopyranoses into 1,3,4,5-tetra-*O*-benzyl ketohexopyranoses through an intramolecular hydride shift [2, 3] from position 5 to position 1 of the starting compound. In the previous paper we found that, while the reaction of the tetrabenzyl D-galacto derivative **1** (Table, entry 1) in refluxing THF furnished the L-tagato derivative **2** with good yield (81%), tetrabenzyl L-sorbose **4** was obtained in lower yield (61%) from D-gluco derivative **3** (entry 3), substantial amounts of unreacted starting product being recovered. Starting from commercially available L-mannose and L-glucose, the reaction could afford in a very expeditious manner other rare ketoses such as L-fructose and D-sorbose, respectively, in addition to L-tagatose. Because of their biological interest these hexo-2-uloses are current targets of several chemical and enzymatic preparative procedures [4–8]. This synthetic potential prompted us to a further investigation to improve the yields and extend the scope of the reaction.

When 2,3,4,6-tetra-*O*-benzyl-D-mannose<sup>2</sup> **5** was treated with SmI<sub>2</sub>/O<sub>2</sub> in THF, 1,3,4,5-tetra-*O*-benzyl-D-fructose **6** was obtained with both modest yield (44%) and recovery (32%) (entry 5). Unsatisfactory results were also obtained when the reactivity of differently protected aldohexoses in hemiacetalic form was tested. In particular, the behaviour of the easily obtainable 2,3,4,6-tetra-*O*-acetyl aldohexoses from D-glucose, D-galactose and D-mannose was studied, but in all cases no intramolecular MPV/O reactions occurred, while

<sup>1</sup> Fax: +39 0815521217; e-mail: iadonisi@unina.it

<sup>2</sup> Cheaper D-forms of mannose and glucose were used for this study.

modest amounts (20-50% isolated yield) of 3,4,6-tri-*O*-acetyl aldohexoses, resulting from regioselective deacetylation at position 2 [9], were recovered.

Assuming that the level of conversion could be influenced by the reaction solvent we turned back our interest toward benzylated precursors and found that air oxidised samarium diiodide prepared in THP [10] is a much more efficient promoter for these intramolecular MPV/O reactions. As a matter of fact, in refluxing THP complete and high yielding conversion occurred (Table). Moreover, use of THP also resulted in a decrease of the reaction time.

In a typical procedure the tetrabenzyl aldohexose was dissolved in a freshly air-oxidised 0.1 M solution of  $\text{SmI}_2$  (2.2 eq.) in THP. The mixture was refluxed for the time shown in the Table, then treated with few drops of acetic acid and filtered through a short silica gel column. Usually the filtrate contained the hexo-2-ulose derivative in a satisfying purity ( $^1\text{H}$ -NMR). The product was then easily converted into the unprotected sugar by catalytic transfer hydrogenolysis [2, 11]. The protected hemiketal pyranoses **2**, **4**, and **6** may be used as convenient synthons, e.g. for the preparation of biologically important 6-deoxy 6-substituted hex-2-uloses [12].

**Table**

Reaction of 2,3,4,6-tetra-*O*-benzyl aldohexopyranoses with  $\text{SmI}_2/\text{O}_2$  in THP.

Starting compound	Entry	Solvent, Time	Product <sup>a</sup>	Yield
	1	THF, 4h		61% (32%) <sup>b</sup>
	2	THP, 1h		92% <sup>c</sup>
	3	THF, 4h		81% (5%) <sup>b</sup>
	4	THP, 45min		88% <sup>c</sup>
	5	THF, 4h		44% (33%) <sup>b</sup>
	6	THP, 3h		75% <sup>c</sup>

<sup>a</sup> Products exhibited  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra consistent with their structure. <sup>b</sup> Isolated yields and, in parenthesis, amount of starting compound recovered after chromatography (9:1 hexane-EtOAc or 98:2  $\text{CHCl}_3$ - $\text{Et}_2\text{O}$ ). <sup>c</sup> Isolated yields. Only traces of starting compound could be detected by  $^1\text{H}$  NMR analysis of the crude products.

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