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A Direct Conversion of Aldohexopyranose to Ketohexopyranose Benzyl Derivatives by Meerwein-Ponndorf/Oppenauer Reaction Induced by Air-oxidised Samarium Diiodide

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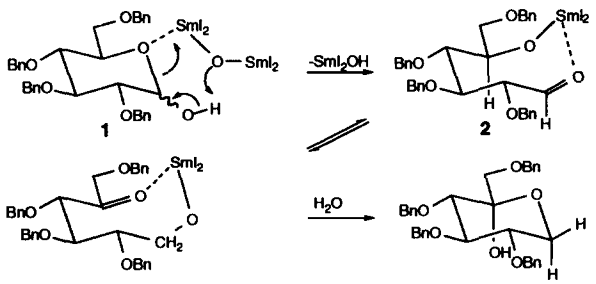
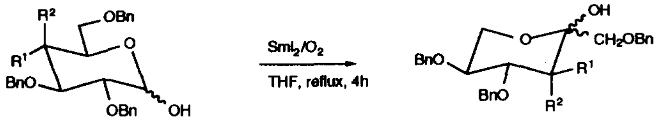
Abstract: 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose can be reduced at C-1 and oxidised at C-5 to give 1,3,4,5-tetra-*O*-benzyl-L-tagatopyranose and 1,3,4,5-tetra-*O*-benzyl-L-sorbopyranose, respectively, in good yields, through an intramolecular M-P/O reaction induced by preoxidised samarium diiodide. Copyright © 1996 Elsevier Science Ltd

Samarium reagents have been broadly applied to organic synthesis.[1,2] *Inter alia*, diiodosamarium alkoxides are well known as catalysts of Meerwein-Ponndorf and Oppenauer reactions.[3] On the other hand, in a study[4] of the rearrangement of terminal epoxides to methyl ketones, it has been shown that "$I_2SmOSmI_2$" or "SmIO" species, obtained by oxidation of SmI_2 in THF, display simultaneous basic (oxygen of a Sm-O bond) and Lewis acid character. In view of our interest in carbohydrate chemistry, we devised that these properties could cooperate in the generation, from a suitably protected hemiacetal form **1** of an aldohexose, of an alkoxy diiodosamarium intermediate **2** by proton abstraction from the anomeric hydroxyl group, ring opening and (C5)O-Sm(III) bonding (see Scheme), followed by intramolecular M-P/O reaction.

Scheme



As a matter of fact, we have found that samarium diiodide pre-oxidised by dry air induces the conversion of 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose **3** and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **4** into 1,3,4,5-tetra-*O*-benzyl-L-tagatopyranose **5** and 1,3,4,5-tetra-*O*-benzyl-L-sorbopyranose **6**, respectively, in good yields.



3 R¹ = H R² = OBn
4 R¹ = OBn R² = H

5 R¹ = H R² = OBn
6 R¹ = OBn R² = H

The reaction promoter was prepared by gently bubbling dry air through a 0.1 M THF solution of SmI_2 (7 mL, 0.7 mmol), whose initial blu color immediately turned to yellow. **3** (162 mg, 0.3 mmol) was added and the solution was refluxed for 4 h. After cooling, water was added and the mixture was extracted with ether. The organic layer was washed with aq sodium thiosulfate and evaporated. Column chromatography (silica gel, 9:1 hexane-AcOEt) of the residue gave **5** (131 mg, 81%). Starting compound **3** (8 mg, 5%) was also recovered. The analogous experiment performed with **4** gave **6** (61% yield) and starting **4** (32%). Compounds **5** and **6** were identified by NMR spectroscopy and chemical conversion to the corresponding methyl α-pyranosides and free hexuloses.[5]

Because of lack of knowledge about the actual structure of the Sm(III) species involved, a more reliable mechanistic path for the above conversion cannot be easily envisaged. However, when, after 1 h, 4-*t*-butylcyclohexanone (0.6 mmol) in dry *iso*-PrOH (1.5 mL) was added to the above reaction mixture (from 0.03 mmol of **3**), GC analysis (after 18 h) revealed that *ca.* 60% of the ketone had been reduced to alcohol. No reduction was observed in an experiment performed in absence of the sugar. This provided some support to the formation of Sm(III) alkoxides from the sugar.[3] This unprecedented use of the above samarium species to perform an intramolecular M-P/O reaction can constitute a new useful tool in carbohydrate synthetic chemistry, expecially in view of the simplicity of the experimental procedure. In contrast to previous reactions mediated by alkoxy samarium catalysts, promoter preparation and the reaction itself do not require deoxygenation of solvents or an inert atmosphere. It should be also noted that, although non-catalytic amounts of promoter are needed, good yields are observed (85% and 89% for **3** and **4**, respectively, if recovered starting materials are taken into account). We are currently exploring the extension of this procedure to other and differently protected monosaccharides.

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5. Compound **5** was obtained as anomeric mixture (^{13}C NMR ($CDCl_3$, 100 MHz): anomeric carbons at δ 97.2 and 98.7). It was converted to methyl α-L-tagatopyranoside (^{13}C NMR spectrum as reported[6]; m.p. 126-8 °C (from acetone); $[\alpha]_D$ = -55 (MeOH, c = 0,4); lit.[6]: m.p. 126-8 °C (from acetone) and $[\alpha]_D$ = -43.1 (MeOH, c = 0,88)) by glycosidation with CH_3OH/HCl (60 °C, 4 h) and debenzylation (1:9 CH_3OH-HCOOH/Pd-C, r. t., 2 h). Hydrolysis with 0.1 N TFA (30 min, 50 °C) gave L-tagatose (^{13}C NMR spectrum as reported[7]).

   Compound **6** was the α-anomer. ^1H NMR (C_6D_6, 400 MHz): δ 3.08 (1H, 2-OH), 3.56 (2H, ABq, J_{AB}=9.8 Hz, 1-H_2), 3.67 (1H, ddd, $J_{4,5}$=9.8, $J_{5,6ax}$=10.2, $J_{5,6eq}$=5.3, 5-H), 3.75 (1H, d, $J_{3,4}$=9.8, 3-H), 3.82 (1H, dd, $J_{6eq,6ax}$=10.2, 6-H_{eq}), 4.04 (1H, t, 6-H_{ax}), 4.14 (1H, t, 4-H), 4.37-5.08 (8H, four ABq, benzyl protons), 7.15-7.65 (phenyl protons). By irradiation of the 2-OH signal, NOE enhancement of the 4-H and 6-H_{ax} signals was observed. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 97.4 (C2), 82.8, 78.8 and 78.5 (C3, C4, C5), 75.7, 75.4, 73.8, 73.2, 72.0 and 61.0 (C1, C6 and four benzyl carbons), 127.7-128.5 and 137.8-138.8 (phenyl carbons). By glycosidation and debenzylation it was converted to methyl α-L-sorbopyranoside (^{13}C NMR spectrum as reported[7]; m.p. 120-2 °C (from acetone); $[\alpha]_D$ = -87 (H_2O, c = 0,4; lit.[8]: m.p. 120-2 °C and $[\alpha]_D$ = -88 (H_2O)). Hydrolysis gave L-sorbose (^{13}C NMR spectrum as reported[7]).
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