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Samarium diiodide-mediated synthesis of D-3,4,5,6-tetra-*O*-benzyl-*myo*-inositol

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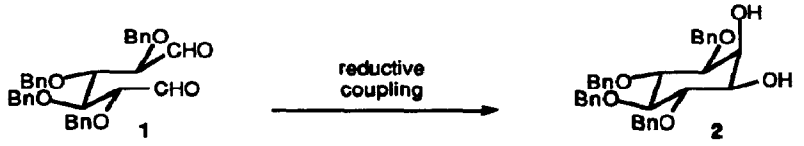
Abstract: The preparation of D-3,4,5,6-tetra-*O*-benzyl-*myo*-inositol in 5 steps from L-iditol is described, the cyclization step being a dialdehyde reductive coupling mediated by SmI_2.

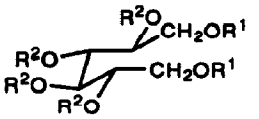
As part of a program aimed at obtaining substances that could alter the phosphoinositide pathway, a recently discovered signal transduction system[1], we have synthesized sulfur-containing analogs of *myo*-inositol[2], starting from D,L-1,4,5,6-tetra-*O*-benzyl-*myo*-inositol. In order to specifically prepare optically pure C-1-modified analogs, we needed to start from a single enantiomer, D-3,4,5,6-tetra-*O*-benzyl-*myo*-inositol **2**.



An attractive method to synthesize this precursor is to use the intramolecular coupling reaction of 1,6-dialdehyde **1**; since this compound has a C_2 symmetry axis, a *cis*-selective reaction would lead to a single *cis*-1,2-diol, bearing the desired *myo*-configuration. A similar approach to get the same diol **2** has been described by Ozaki et al.[3], but the pinacol coupling reaction of **1** using low-valent titanium species resulted in the formation of large amounts of the two corresponding *trans*-diols as well as of the desired *myo*-isomer. Hanessian et al.[4] recently reported that cyclic vicinal *cis*-diols were obtained as the preponderant or unique products of the reductive coupling reaction of various 1,5- and 1,6-dialdehydes using samarium diiodide[5]. These results prompted us to use this method for the preparation of D-3,4,5,6-tetra-*O*-benzyl-*myo*-inositol[6].

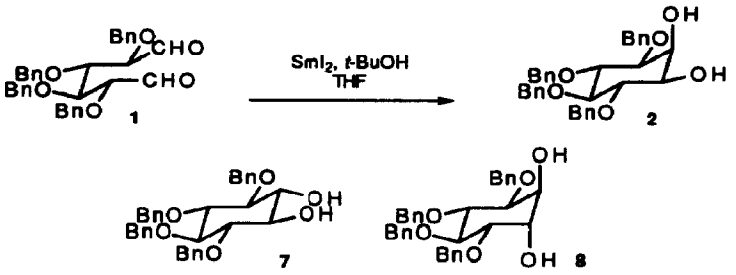
The synthesis of dialdehyde **1** was accomplished in 4 steps from L-iditol **3**, readily available from L-sorbose[7]. The two primary hydroxyl groups of **3** were selectively protected using triphenylmethyl chloride in pyridine, affording 1,6-di-*O*-triphenylmethyl-L-iditol **4**[8] in 68% yield. Benzylation of the other hydroxyl groups (NaH, benzyl bromide, THF, 75 %) was followed by

acid hydrolysis of the triphenylmethyl ethers of **5**[8], yielding diol **6**[8] (1 N HCl- dioxane, 58 %). Dialdehyde **1**[8] was then obtained by Swern oxidation of **6** in 89% yield.



3 $R^1 = R^2 = H$
4 $R^1 = CPh_3$, $R^2 = H$
5 $R^1 = CPh_3$, $R^2 = Bn$
6 $R^1 = H$, $R^2 = Bn$

The intramolecular reductive coupling conditions were then applied : dialdehyde **1** was treated with 2 equivalents of samarium diiodide in THF for 3 h at -78°C and 16 h at room temperature, in the presence of *tert*-butyl alcohol acting as *in situ* protonating agent for the reaction intermediate. We obtained the desired compound, 1,2-*cis*-diol **2**[8], as the major product, in 56% yield. The two *trans*-isomers **7** and **8** were isolated both in 4% yield; 18% of dialdehyde **1** was recovered. Thus, the stereoselectivity observed is very good and makes this method very useful for the preparation of D-3,4,5,6-tetra-*O*-benzyl-*myo*-inositol **2**, which is a valuable intermediate for the synthesis of various optically active inositol derivatives.



1 **2** **7** **8**

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4. Chiara, J. L.; Cabri, W.; Hanessian, S. *Tetrahedron Lett.* **1991**, *32*, 1125-1128.
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8. Selected physical data:
   4: $[\alpha]_D^{20}$ +12 (c 1.0, $CHCl_3$); **5**: $[\alpha]_D^{20}$ +4 (c 0.72, $CHCl_3$); **6**: $[\alpha]_D^{20}$ +10 (c 1.0, $CHCl_3$) ; **1**: $[\alpha]_D^{20}$ +9 (c 0.5, $CHCl_3$) ; **2**: $[\alpha]_D^{20}$ -22 (c 0.12, $CHCl_3$), mp 142°C; lit.[6c] $[\alpha]_D^{20}$ -24.3 (c 1.3, $CHCl_3$), mp 141-143°C; lit.[6a] $[\alpha]_D^{20}$ -25 (c 2.7, $CHCl_3$), mp 140-142°C.

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