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Preparation of 5-telluropentopyranose sugars from common pentose starting materials

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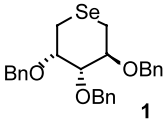
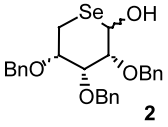
Abstract—2,3,4-Tri-*O*-benzyl-1,5-dideoxy-5-telluro-D-arabinose (**5**) and 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-telluro-L-arabinose (**7**) are readily prepared by treatment of D- and L-2,3,4-tri-*O*-benzyl-1,5-di-*O*-methanesulfonylarabitol with sodium telluride (Na_2Te) in ethanol.

It is well accepted that carbohydrates play an important role in a vast array of biological processes. Modified carbohydrates such as nitrogen, phosphorus and sulfur containing monosaccharides are of interest due to their wide variety of pharmacological activity and physiochemical properties. Examples include 5-deoxy-5-thio-D-glucose, which has been shown to be a potent inhibitor of cellular D-glucose transport and also selectively toxic to hypoxic tumor cells.[1] Other examples include *nojirimycin* and analogues, which are antibacterial agents and have been proposed as chemotherapeutic agents to treat HIV infection.[2]



1



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We reported recently that 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-pentopyranose and 2,3,4-tri-*O*-benzyl-5-deoxy-5-seleno-D-pentopyranose sugars (e.g. **1** and **2**) are readily prepared by thermolysis of the corresponding 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-pent-1-yl formate, or by treatment of 2,3,4-tri-*O*-benzyl - 5 - benzylseleno - 5 - deoxypentopyranose with samarium(II) iodide in THF;[3,4] these procedures represent the most efficient methods to date for preparing these rare selenium-substituted carbohydrate systems.

While selenium-containing compounds are well established as having important roles as new generation pharmaceuticals, exhibiting antioxidant, anti-inflammatory, hepatoprotectant, antiviral and antitumor properties,[5] and have provided effective treatments for several diseases including Kwashiokor[6] (a protein malnutrition disorder) and Keshan Disease[7] (a form of cardiomyopathy), there is yet no known physiological function associated with tellurium.[8] Indeed, only a handful of organic tellurides have been examined with the aim of developing compounds with medical use.[9–13] In addition, many organotellurides exhibit glutathione peroxidase (GSHpx) like activity superior to selenium containing mimics of GSHpx, such as *Ebselen*,[14,15] and are powerful antioxidants in vitro.[16]

As part of ongoing work, and given the inherent potential of tellurium-containing carbohydrates, we thought it would be interesting to prepare the hitherto unknown 1,5-dideoxy-5-telluro-D-pentopyranose series of sugars, analogues of the previously prepared selenosugars (**1**).

Accordingly, D-arabinose was converted into 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-D-arabitol (**3**) as described previously.[4] Subsequent conversion into the dimesylate (**4**) was achieved in 89% yield by the action of methanesulfonyl chloride and DMAP under standard conditions. To our delight, further reaction of 2,3,4-tri-*O*-benzyl-1,5-di-*O*-methanesulfonyl-D-arabitol (**4**) with sodium telluride (Na_2Te), prepared by the reduction of tellurium metal with sodium borohydride in ethanol,[17] afforded the required 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-telluro-D-arabinose (**5**) in 82% yield after purification by flash chromatography (Scheme 1). The ^{125}Te NMR spectrum of tellurosugar (**5**) revealed a single resonance at δ 77.3 consistent with the formation of the telluropane ring system,[18] while the ^{13}C NMR spectrum displayed the expected number of signals, including resonances at δ –6.1 and –2.4, consistent with

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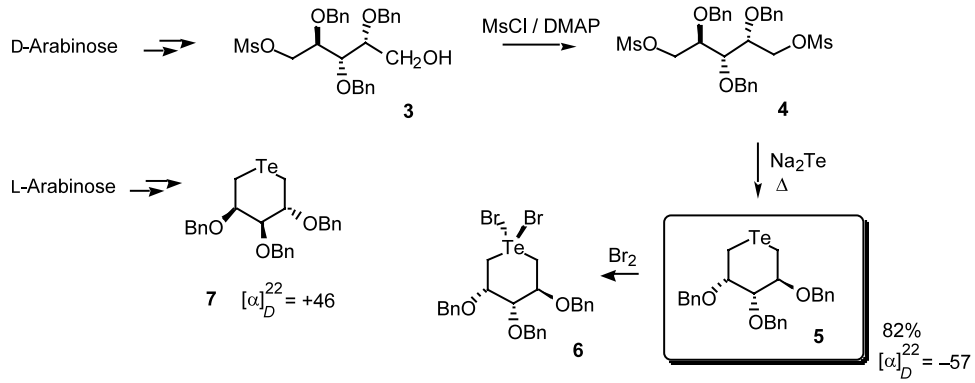

Scheme 1.

aliphatic carbon atoms attached to tellurium.[19] In addition, **5** proved to be optically active, with an $[\alpha]_D^{22}$ value of –57.

Unfortunately, **5** proved to be sufficiently labile to prevent the acquisition of quality microanalytical data; indeed, **5** appears to decompose by extrusion of elemental tellurium even on standing in the freezer. In addition, we were unable to observe a molecular ion by various mass spectrometric techniques, including electrospray ionization. Therefore, in order to provide conclusive evidence for its formation, tellurosugar (**5**) was further reacted with bromine in carbon tetrachloride to provide the significantly more stable 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-(dibromotelluro)-D-arabinose (**6**) as an orange sticky oil, unsuitable for X-ray analysis. Satisfyingly, dibromide (**6**) displayed a single signal at δ 748.8 in its ^{125}Te NMR spectrum as well as a a signal at m/z 597.0265 in its high resolution ESI spectrum, consistent with the loss of bromine from the molecular ion and providing strong evidence that we have indeed prepared the hitherto unknown telluroarabinose ring system (**5**).

In a similar manner, L-arabinose was converted into 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-telluro-L-arabinose (**7**). As expected, **7** exhibited identical spectroscopic properties to its enantiomer (**5**), the exception being the sign of its optical rotation; **7** proved to have an $[\alpha]_D^{22}$ value of +46.

We are currently examining the antioxidant properties of tellurosugars (**5**, **7**) and are exploring the preparation of analogous tellurosugars derived from ribose and xylose.

Acknowledgements

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