Glycosyloxyselenation–Deselenation of Glycals: a New Approach to 2′-Deoxy-disaccharides

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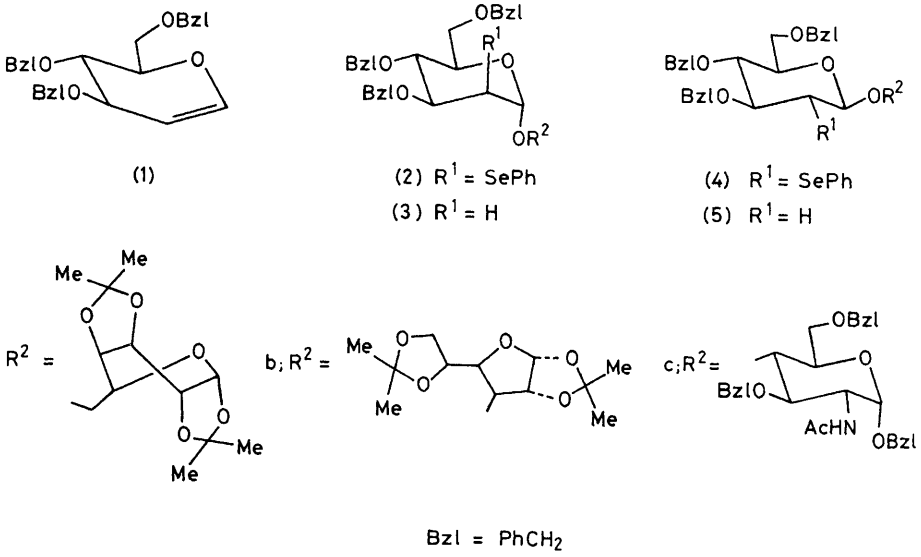
Summary Glycosyloxyselenation of 3,4,6-tri-*O*-benzyl-D-glucal followed by reductive removal of the phenylseleno-group demonstrates the potential of a novel synthetic approach to 2′-deoxy-disaccharides.

2′-DEOXY-α-(OR β)-DISACCHARIDES are sugar components of numerous natural products of biological significance, such as the macrolide[1] and the orthosomycin[2] groups of antibiotics and the anthracycline[3] group of antitumour drugs. For this reason, various procedures for synthesis of 2-deoxy-α-glycosides have been reported.[4] On the basis of the successful alkoxyselenation of both acyclic and cyclic vinyl ethers,[5] glycosyloxyselenation of pyranoid glycals could conceivably result in a new entry to oligosaccharides. We demonstrate in this communication the feasibility of this methodology using tri-*O*-benzyl-D-glucal[6] (**1**) as a representative example.



In a typical procedure, a solution of 3,4,6-tri-*O*-benzyl-D-glucal (**1**) (1 equiv.) in dry acetonitrile was treated at 0 °C for 5 min with an excess of phenylselenenyl chloride (1·5 equiv.), then with 2,4,6-trimethylpyridine (1·5 equiv.) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[7] (0·7 equiv.). After 1 day at room temperature followed by standard work-up, the crude product was chromatographed on silica gel to provide the α-linked disaccharide† (**2a**) (80%), $[\alpha]_D$ + 1·5°. A small amount (5%) of the β-disaccharide (**4a**) was also isolated, $[\alpha]_D$ −33·5°.

An example of effective α-glycosylation of a secondary sugar alcohol was provided by the reaction of (**1**) with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose,[7] where the disaccharide (**2b**) was obtained as a colourless foam (69%), $[\alpha]_D$ + 16°, together with a small amount of the β-disaccharide (**4b**)(5·7%), $[\alpha]_D$ −25·2°. Finally, benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside[8] was converted into the disaccharide (**2c**) (61%), $[\alpha]_D$ + 74°, compound (**4c**) being isolated as a by-product (8%), m.p. 116 °C (ethyl acetate–hexane), $[\alpha]_D$ + 24°. Because of the difficulties associated for a long time with the glycosylation of the 4-hydroxy-group of glucopyranoside derivatives, this last example is particularly significant.

In the three examples reported here, the overall reaction is a stereospecific *anti*-addition, tentatively explained as being the result of the regiospecific opening of an episelenonium ion. Furthermore, in the case of the selected glucal (**1**) and with the experimental conditions used, generation of that episelenonium ion which allows diaxial ring opening is largely favoured. The incoming phenylselenyl group may be directed in its addition through complexation with benzyloxy-groups.

The 2′-deoxy-2′-phenylseleno-disaccharides (**2a**—**c**) and

† All new compounds had satisfactory microanalytical and spectral properties. Optical rotations were measured for solution in chloroform at 20 °C.

(**4a**—**c**) were smoothly reduced by triphenyltin hydride[9] (toluene; reflux; 2 h) to give the corresponding 2′-deoxy-disaccharides (**3a**—**c**) and (**5a**—**c**) in excellent yield (90—95%). This 'glycosyloxyselenation–deselenation' sequence thus provides a new, stereoselective, and high-yielding route to 2′-deoxy-disaccharides.

We thank the Centre National de la Recherche Scientifique for financial support.

(*Received*, 30*th March* 1981; *Com.* 350.)

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