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The Regioselective Opening of 5-*O*-Benzyl-1,2:3,4-*O*-isopropylidene-D-psicofuranose With Organostannanes[1]

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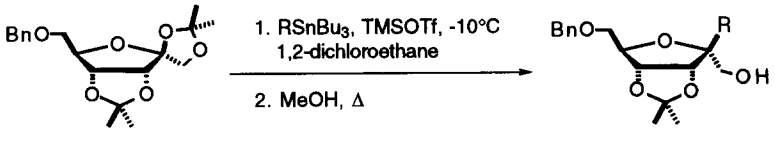
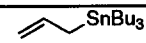
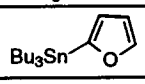
Abstract: The trimethylsilyl triflate mediated regioselective opening of 5-*O*-benzyl-1,2:3,4-*O*-isopropylidene-D-psicofuranose with organostannanes is presented. Hydrolysis of the initially formed 1-*O*-trimethylsilyl ether yields the products of *S*- and *C*-glycosidation with predominantly β-stereochemistry in good yields. The unusual addition of acetonitrile to the intermediate oxonium ion when the reaction is performed in this medium is also outlined.

A number of methods have been described for the introduction of different functional groups at a riboside anomeric center and their subsequent elaboration into natural and unnatural nucleosides.[2] Many of these methods are applicable solely to aldose sugars, the corresponding ketose nucleosides accessible only by multiple transformations.[3] In this letter, we wish to report the successful *C*- and *S*-glycosidation of 5-*O*-benzyl-1,2:3,4-*O*-isopropylidene-D-psicofuranose[4] (**1**) in a single step yielding predominantly the β-anomers.



(**1**) (**2-5**)

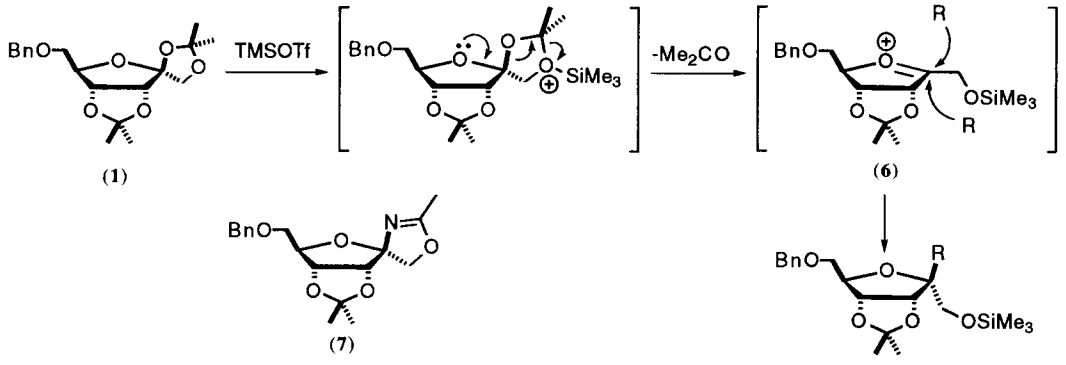
Thus; treatment of (**1**) with an excess of trimethylsilyl triflate (1.5 eq.) in the presence of an organostannane (2 eq.) in 1,2-dichloroethane at -10°C, followed by methanolic hydrolysis of the intermediate 1-*O*-trimethylsilyl ether, gives the corresponding products in good yields (see table). Separation of the anomers[5] is readily accomplished by flash chromatography either directly, or after protection of the resultant primary alcohol.

Reagent	Yield[a]	α:β	R	No.
	87	1:55	Allyl	2
Bu_3SnCN	95	1:6[b]	CN	3
Bu_3SnSPh	84	1:4	SPh	4
	20[c]	0:1		5

[a] All compounds gave spectral data (^1H ^{13}C NMR, IR, MS, HRMS) consistent with their assigned structures.
[b] Separable by chromatography after protection of the primary alcohol as its acetate. [c] Not optimized.

It was gratifying to note that formation of the β-anomers, in our case the desired products, was consistently preferred. This can be rationalized by consideration of the mechanism. If the reaction is envisaged

as proceeding initially with the TMSOTf mediated acetonide opening, liberation of a molecule of acetone results in a planar oxonium ion (**6**).[6] At this point attack of the incoming nucleophile is possible from both faces leading to either anomer of the product; here, it is apparent the steric bulk imparted by the remaining acetonide biases the direction of approach in favor of reaction at the β-face.



It is of interest to note performing the reaction in acetonitrile under the same conditions resulted in incorporation of the solvent, giving varying amounts of adduct (**7**) along with the desired product.[7] This arises from competing attack between the acetonitrile nitrogen and the relatively weakly nucleophilic organostannane. Addition to the β-face of oxonium ion (**6**) in a similar fashion as above followed by rearrangement leads to the spirooxazoline (**7**).

The successful incorporation of the allyl, cyano and furan[8] fragments provide synthetic entry to a range of natural and unnatural nucleosides and their derivatives. The elaboration of **2** and **4** into unnatural and *C*-nucleoside analogs of two naturally occurring ketose nucleosides will be reported in due course.[9]

Acknowledgments

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References and Notes

1. Contribution No. 925 from Chemical Research and Development.
2. For a review see: Hanessian, S.; Pernet, A.G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111-188.
3. a) Prisbe, E.J.; Smejikal, J.; Verheyden, J.P.H.; Moffatt, J.G. *J. Org. Chem.* **1976**, *41*, 1836-1846. b) Shroeder, W.; Hoeksema, H. *J. Am. Chem. Soc.* **1959**, *81*, 1767-1768. c) Farkas, J.; Sorm, F. *Coll. Czech. Chem. Commun.* **1963**, *28*, 882-886. d) Hrebabecky, H.; Farkas, J. *Coll. Czech. Chem. Commun.* **1974**, *39*, 1098-1106, 2115-2123. e) Elliot, R.D.; Niwas, S.; Riordan, J.M., Montgomery, J.A.; Secrist, J.A. III *Nucleosides & Nucleotides* **1992**, *11*, 97-119.
4. Mio, S.; Kumagawa, Y.; and Sugai, S. *Tetrahedron* **1991**, *47*, 2133-2144.
5. Assignment of the stereochemistry was achieved by analysis of n.O.e. difference spectra obtained from each anomer. In general, the β-anomer shows a strong positive interaction between the methylene of the pendant hydroxymethyl group and its cis proton (H-5); whereas, irradiation of the α-anomer at the same position exhibits a strong positive interaction with the protons above the ring (H-3, H-4).
6. In contrast to the mechanistic interpretation of a related reaction by Mio and coworkers[4] we believe isolation of the 1-*O*-trimethylsilyl ether as the initial product implies the liberation of a molecule of acetone prior to addition of the incoming nucleophile.
7. During the preparation of this manuscript Sano and coworkers noted a similar result in their synthesis of Hydantocidin, see: Sano, H.; Mio, S.; Tsukaguchi, N.; Sugai, S. *Tetrahedron* **1995**, *51*, 1387-1394.
8. For the elaboration of a 2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)furan into a number of *C*-nucleosides see: Hayashi, M.; Araki, A.; Maeba, I. *Heterocycles* **1994**, *34*, 569-574, and references cited therein.
9. Dillon, M.P.; Maag, H; Muszynski, D.M., manuscripts in preparation.

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