

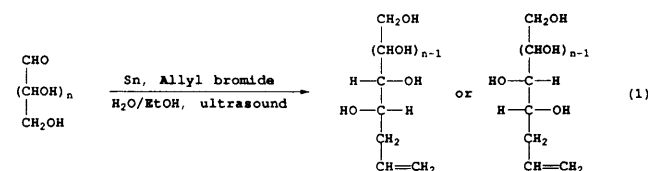
Carbon–Carbon Bond Formation in Aqueous Ethanol: Diastereoselective Transformation of Unprotected Carbohydrates to Higher Carbon Sugars Using Allyl Bromide and Tin Metal¹

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This report describes the “nucleophilic” addition of allyl groups to the carbonyl moieties of unprotected carbohydrates in aqueous/organic solvents (eq 1). These reactions are based on pro-



cedures developed and applied to non-sugar aldehydes and ketones by Luche,^{3–6} Nokami,⁷ Benezra,⁸ and others^{9,10} using reaction of allylic halides with zinc or tin metal in the presence of the carbonyl acceptor. When applied to carbohydrates, the reactions proceed with useful diastereoselectivity and permit the synthetic utilization of these water-soluble substrates directly in aqueous solutions without protection. The adducts were converted to higher carbon aldoses by ozonolysis of the deprotected polyols followed by suitable derivatization.

The yields reported in Table I were obtained in ethanol/water mixtures. Using tetrahydrofuran instead of ethanol did not improve the yield but did slow the rate. Commercially available tin powder (Alfa company; 100 mesh) was used, and the suspension of the reactants was sonicated for 12–18 h in an ultrasonic cleaning bath (Cole-Parmer 8852).¹¹ Although the pH drops sharply during the course of the reaction (typically to a value of “pH” = 1), we did not run the reaction under positive pH control. The polyols generated were acetylated to simplify the purification procedure.

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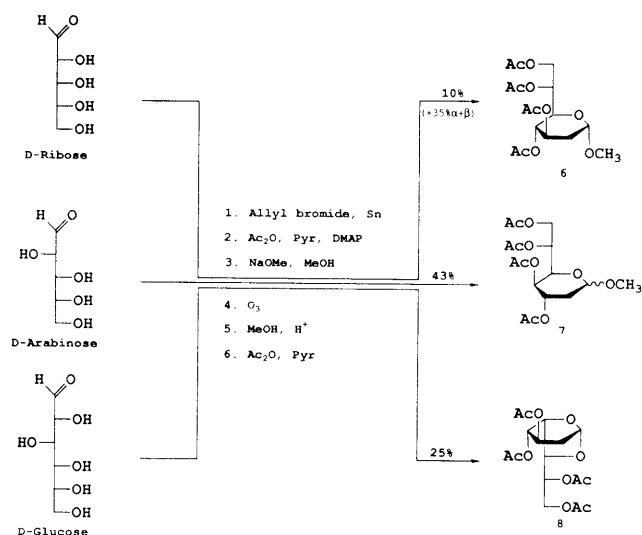
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Table I. Nucleophilic Addition of Allyl Groups to Aldoses

starting carbohydrate	product ^a	yield, ^b %	diastereomeric ratio ^c (threo:erythro)
D-erythrose	1	52	4.0:1
D-ribose	2	65	3.5:1
D-arabinose	3	85	5.5:1
D-glucose	4	70	6.5:1
D-mannose	5	90	6.0:1
2-deoxy-D-glucose ^d		26	1.5:1
2-NAc-D-glucose		0	—
2-NAc-D-mannose		0	—

^aReactions were carried out in 9:1 ethanol/water with 2 equiv each of tin powder (100 mesh) and allyl bromide and promoted by ultrasonication until completion (12–16 h). ^bBased on isolated peracetylated diastereomers. ^cDetermined from NMR. ^dDiastereomers not separated.

Scheme I. Conversions of D-Ribose, D-Arabinose, and D-Glucose to Heptose and Octose Derivatives **6**, **7**, and **8**

The yields reported in Table I were of isolated materials, following column chromatography over silica gel. Experimental details are given in supplementary material.

To assign the stereochemistry of the chiral center formed by addition of the allyl groups, we transformed three of the adducts (**2**, **3**, and **4**) to the corresponding heptose and octose derivatives **6**, **7**, and **8** by ozonolysis and appropriate derivatization (Scheme I). In the pyranose forms of these higher carbon sugars, the stereochemistry of the newly generated center could be assigned easily by analysis of coupling constants in the ¹H NMR spectra. For the major diastereomer formed in each reaction, the hydroxy function formed and that originally present at C-2 of the starting aldose have a threo relationship. This result is in agreement with observations made by Coxon et al.¹² for this type of reaction on aldehydes containing an asymmetric center adjacent to the carbonyl function. The diastereoselectivity is lower in the one case in which there is no hydroxy group present at C-2. For aldoses having *N*-acetyl groups in position 2, no reaction was observed under the reaction conditions used.¹³

This tin-promoted C–C bond forming reaction extends the range of synthetic methods applicable to unprotected sugars in protic solvents and should be especially useful in preparing higher carbon sugars. We are applying these methods to more highly functionalized systems and to other halide sources.

Supplementary Material Available: Experimental details for the preparation of **1–8** (7 pages). Ordering information is given on any current masthead page.

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